Enantioselective Total Syntheses of the Agelastatin and Trigonoliimine Alkaloids

by

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To my parents, Han, Jinsub and Ko, Chonghee

To my brother, Han, Changkyu

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Preface

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> Han, S.; Movassaghi, M. "Concise Total Synthesis and Stereochemical Revision of All (–)-Trigonoliimines." *J. Am. Chem. Soc.* **2011**, *133*, 10768–10771. Copyright 2011 American Chemical Society.

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ABSTRACT

I. Total Synthesis of the (–)-Agelastatin Alkaloids

The pyrrole-imidazole family of marine alkaloids, derived from linear clathrodin-like precursors, constitutes a diverse array of structurally complex natural products. The bioactive agelastatins are members of this family that possess a tetracyclic molecular framework incorporating C4–C8 and C7–N12 bond connectivities. We provide a hypothesis for the formation of the unique agelastatin architecture that maximally exploits the intrinsic chemistry of plausible biosynthetic precursors. We report the concise enantioselective total syntheses of all known agelastatin alkaloids including the first total syntheses of agelastatins C, D, E, and F. Our gram-scale chemical synthesis of agelastatin A was inspired by our hypothesis for the biogenesis of the cyclopentane C-ring and required the development of new transformations including an imidazolone-forming annulation reaction and a carbohydroxylative trapping of imidazolones.

II. Total Synthesis of the (–)-Trigonoliimine Alkaloids

The concise and enantioselective total syntheses of (–)-trigonoliimines A, B, and C are described. Our unified strategy to all three natural products is based on asymmetric oxidation and reorganization of a single bistryptamine, a sequence of transformations with possible biogenetic relevance. We revise the absolute stereochemistry of (–)-trigonoliimines A, B, and C.

Thesis Supervisor: Professor Mohammad Movassaghi
Title: Associate Professor of Chemistry

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Abbreviations

Å	angstrom
[α]	specific rotation
Ac	Acyl
Anis	para-anisaldehyde
app	apparent
aq	aqueous
atm	atmosphere
Boc	*tert*-butyloxycarbonyl
Br	broad
Bu	butyl
°C	degree Celsius
c	cyclo
c	concentration
c	centi
CAM	ceric ammonium molybdate
cat.	catalytic
cm	centimeter
cm^{-1}	wavenumber
CNS	central nervous system
cod	cyclooctadiene
COSY	correlation spectroscopy
D	days
D	doublet
D	deuterium
δ	parts per million
DART	direct analysis in real time
DDQ	2,3-dichloro-5,6-dicyano-1,4-benzoquinone
diam	diameter
DIC	diisopropylcarbodiimide
DMA	dimethylacetamide
DMAP	4-dimethylamino pyridine
DMF	*N*,*N*-dimethylformamide
DMSO	dimethylsulfoxide
DTBMP	2,6-di-*tert*-butyl-4-methylpyridine
dr	diastereomeric ratio
EC_{50}	half maximal effective concentration
Ee	enantiomeric excess
EI	electron ionization
equiv	equivalent
ESI	electronspray ionization
Et	ethyl

FT	Fourier transform
g	gram
GC	gas chromatography
h	hour
ht	height
HMBC	heteronuclear multiple bond correlation
HMPT	hexamethylphosphoramide
HPLC	high performance liquid chromatography
HRMS	high resolution mass spectroscopy
HSQC	heteronuclear single quantum correlation
Hx	hexyl
Hz	Hertz
i	iso
IBX	2-iodoxybenzoic acid
IR	infrared
J	coupling constant
L	liter
m	medium
m	meta
m	multiplet
m	milli
m	meter
M	molar
M	molecular mass
μ	micro
*m*CPBA	meta-chloroperbenzoic acid
Me	methyl
Mhz	megahertz
min	minute
mol	mole
M.p.	melting point
MS	mass spectrometry
m/z	mass to charge ratio
N	normal
NBS	*N*-bromosucinnimide
NMR	nuclear magnetic resonance
nOe	nuclear Overhauser effect
Nuc	nucleophile
o	ortho
p	para
Ph	phenyl
PMA	phophomolybdic acid
ppm	parts per million

PPTS	*para*-toluenesulfonic acid
Pr	propyl
pyr	pyridine
PYR	pyrimidine
q	quartet
ref	reference
R*f*	retention factor
RT	room temperature
s	sec
s	singlet
s	strong
SFO	system fluidics organizer
Str	stretch
t	tert
t	triplet
TC	thiophene-2-carboxylate
Tf	trifluoromethylsulfonate
TFA	trifluoroacetic acid
TFE	trifluoroethanol
THF	tetrahydrofuran
TLC	thin layer chromatography
TMS	trimethyl silyl
TMP	2,2,6,6-tetramethylpiperidine
Ts	para-toluenesulfonyl
TsOH	para-toluenesulfonic acid
UV	ultraviolet
Vis	visible
W	weak
Xphos	2-dicyclohexylphosphino-2',4',6'-triisopropylbiphenyl

Chapter I.

Total Synthesis of the (–)-Agelastatin Alkaloids

Introduction and Background

The agelastatins are a family of highly cytotoxic pyrrole-imidazole alkaloids, comprising a tetracyclic backbone structure with four contiguous stereogenic centers around the central C-ring. In 1993, Pietra and coworkers isolated (–)-agelastatins A (**1**) and B (**2**) from the Coral Sea sponge *Agelas dendromorpha* and chemically studied their unique tetracyclic structures.[1,2] (–)-Agelastatins C (**3**) and D (**4**) were isolated from *Cymbastela* sp. native to the Indian Ocean by Molinski and coworkers in 1998.[3] In 2010, Al-Mourabit and coworkers isolated (–)-agelastatins E (**5**) and F (**6**) from the New Caledonian sponge *A. dendromorpha*.[4] (–)-Agelastatin A (**1**) exhibits anti-neoplastic activities against multiple cancers such as breast, lung, colon, head, neck, and bladder cancers.[1] It inhibits osteopontin mediated neoplastic transformation and metastasis in addition to slowing cancer cell proliferation by causing cells to accumulate in the G_2 phase of the cell cycle.[5,6] A recent *in vivo* central nervous system (CNS) pharmacokinetic study showed that (–)-agelastatin A (**1**) can penetrate the CNS with permeation into CNS compartments including the brain, parenchyma, cerebrospinal fluid, and eyes.[7] (–)-Agelastatin A (**1**) also exhibits toxicity towards anrthropods,[3] and selectively inhibits the glycogen synthase kinase-3β.[8,9] In addition, agelastatin A (**1**) has been reported to possess potent insecticidal activity against brine shrimp, larvae of beet armyworm, and corn rootworm.[3]

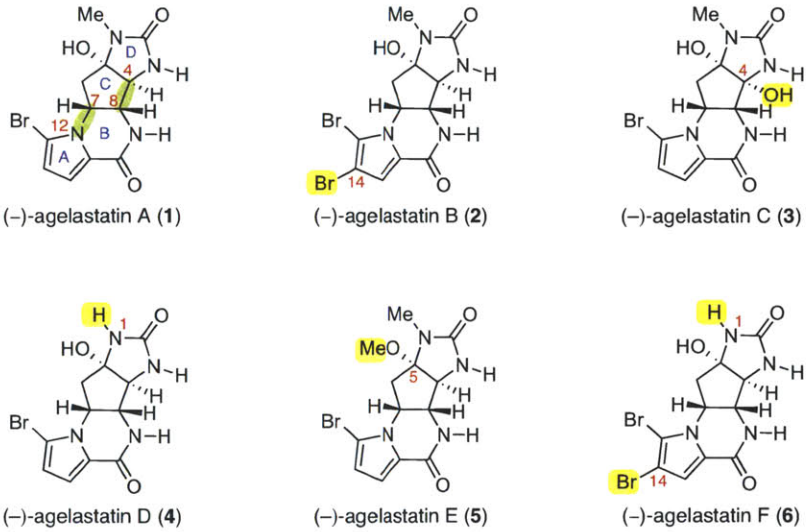
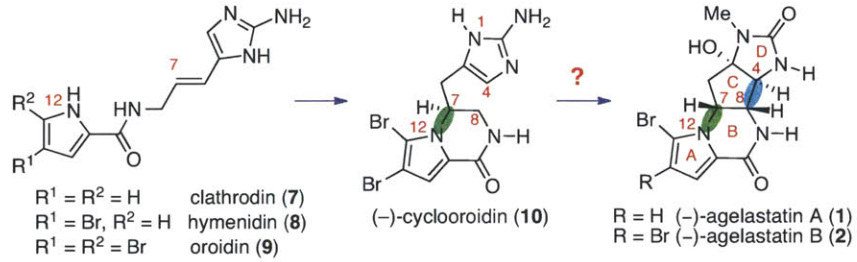
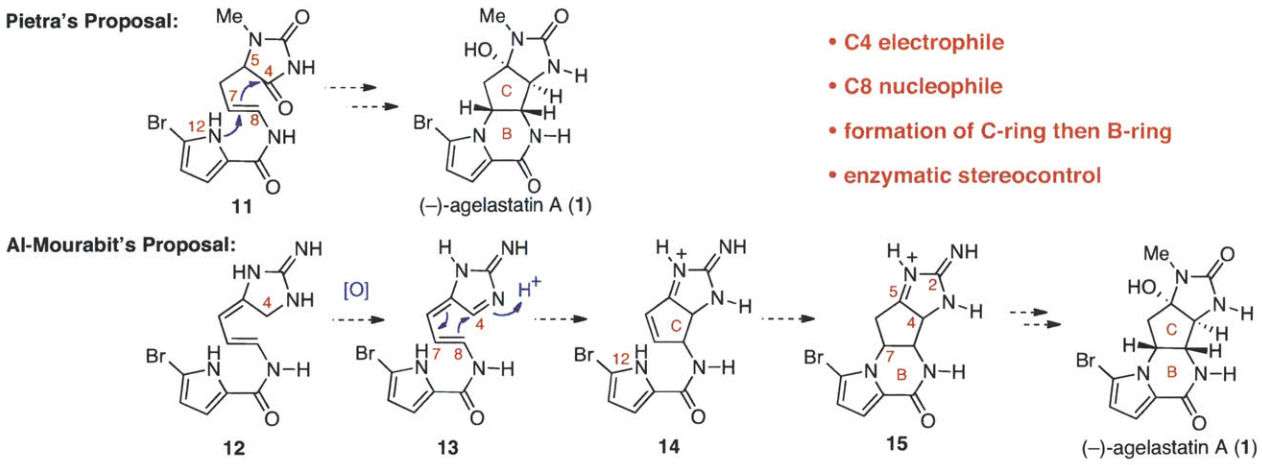


Figure 1. Structure of agelastatin alkaloids (**1**–**6**).

The agelastatins are the only isolated pyrrole-imidazole alkaloids with C4–C8 and C7–N12 connectivity, likely derived from a linear biogenetic precursor such as clathrodin (**7**),[10] hymenidin (**8**),[11] and oroidin (**9**)[12,13] (Scheme 1). Kerr and coworkers showed that histidine and ornithine (or proline) are the amino acid precursors for related pyrrole-imidazole alkaloids.[14] Prior to our synthetic report of all (–)-agelastatin alkaloids,[15] there were two reported biosynthetic hypotheses for agelastatin A (**1**) from its linear precursor (Scheme 2).[1a,16] Both biosynthetic hypotheses proposed that the formation of central the C-ring results from C8-nucleophilic trapping of a C4-electrophile in a clathrodin (**7**) derivative. Furthermore, these initial biosynthetic hypotheses suggest the formation of C-ring prior to B-ring, and attribute the stereochemical information present in (–)-agelastatin A (**1**) to the action of putative enzymes. In 2006, Lindel showed a conversion of oroidin (**9**) to cyclooroidin (**10**) under acidic condition.[17] However, biosynthetic or chemical explanation that links cyclooroidin (**10**) or its derivative to (–)-agelastatin A (**1**) was not present at the time that we set out this synthetic program (Scheme 1).

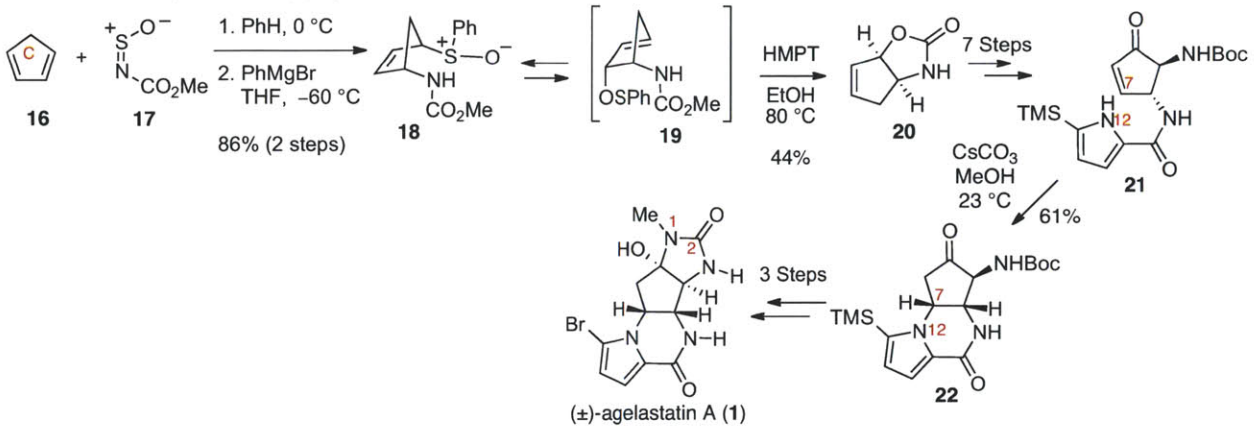


Scheme 1. Structurally related pyrrole–imidazole alkaloids.

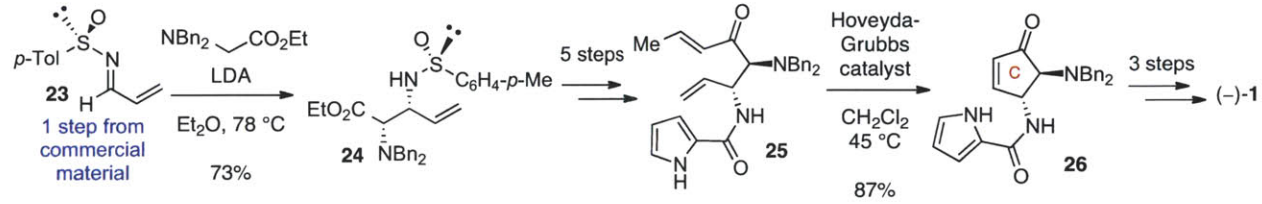


Scheme 2. Previously reported biosynthetic hypotheses for the formation of (–)-agelastatin A (**1**).

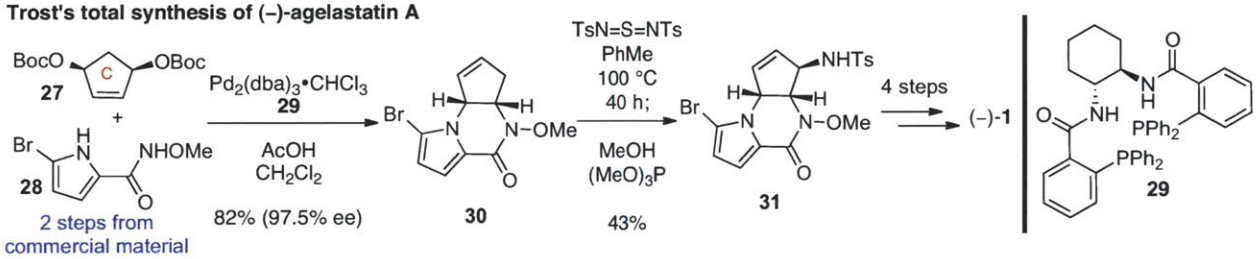
Weinreb's total synthesis of (±)-agelastatin A



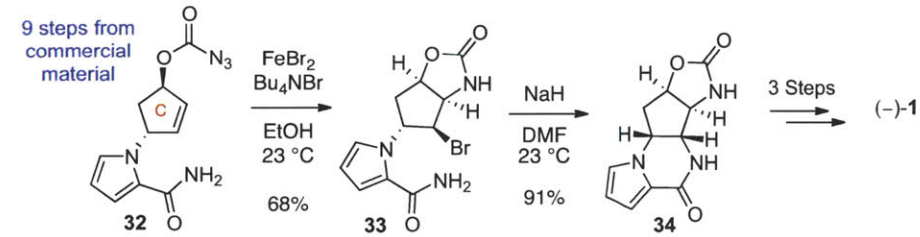
Davis' total synthesis of (–)-agelastatin A



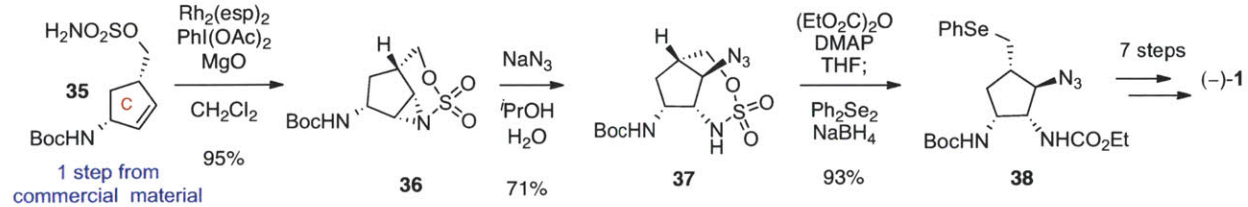
Trost's total synthesis of (–)-agelastatin A



Yoshimitsu and Tanaka's 2nd generation total synthesis of (–)-agelastatin A



Du Bois' total synthesis of (–)-agelastatin A



Scheme 3. Representative total syntheses of agelastatin A (**1**)

Table 1. Total syntheses of agelastatin A (**1**)

entry	research group	publication year	natural product	number of steps[a]	overall yield (%)	note
1	Weinreb	**1999**	(±)-agelastatin A	15	~7	1st total synthesis of agelastatin A
2	Feldman	**2002**	(–)-agelastatin A	15	3.6	1st enantioselective total synthesis of agelastatin A and B
3	Hale	**2003,2004**	(–)-agelastatin A	26	0.06	
4	Davis	**2005, 2009**	(–)-agelastatin A	11	15.7	
5	Trost	**2006, 2009**	(+)-agelastatin A	9	6.1	
6	Trost	**2006, 2009**	(–)-agelastatin A	8	9.6	formal synthesis
7	Ichikawa	**2007**	(–)-agelastatin A	27	5.1	
8	Chida	**2009**	(–)-agelastatin A	23	1.2	
9	Yoshimitsu	**2008**	(–)-agelastatin A	17	1.4	
10	Yoshimitsu	**2009**	(–)-agelastatin A	14	1.8	Yoshimitsu 2nd generation formal synthesis
11	Wardrop	**2009**	(±)-agelastatin A	14	8	
12	DuBois	**2009**	(–)-agelastatin A	11	15	
13	Movassaghi	**2010**	(–)-agelastatin A	8	22	total synthesis of (–)-agelastatins A–F completed
14	Movassaghi	**2010**	(–)-agelastatin A	7	15	
15	Hamada	**2011**	(–)-agelastatin A	10	17.3	formal synthesis
16	Maruoka	**2012**	(–)-agelastatin A	10	11.4	formal synthesis

a. Number of steps from commercially available material.

The potent biological activities, in conjunction with its intriguing molecular structure have prompted considerable efforts toward the total synthesis of agelastatin A (**1**), and **1** has served as an active arena for the development of new chemistry.[18] To date, 13 different research groups, including our own research group, reported inventive solutions toward the total synthesis of agelastatin alkaloids. In 1999, Weinreb completed the first total synthesis of (±)-agelastatin A (**1**) using a key *N*-sulfinyl dienophile hetero-Diels–Alder reaction (Scheme 3).[19] Notably, they formed the B-ring of **1** employing N12 addition to C7, a disconnection with potential biosynthetic relevance. Feldman reported the first enantioselective syntheses of (–)-agelastatins A (**1**) and B (**2**) applying an alkylidenecarbene C–H insertion reaction.[20] Hale applied an aziridine opening strategy to access synthetic sample of (–)-agelastatin A (**1**).[21] Davis's synthesis utilized a *N*-sulfinyl imine based methodology and ring-closing metathesis to efficiently secure (–)-agelastatin A (**1**) in 15.7% overall yield (Scheme 3).[22] Trost's elegant total synthesis of (+)-**1** and (–)-**1** utilized palladium-catalyzed asymmetric allylic alkylation reactions to construct the B-

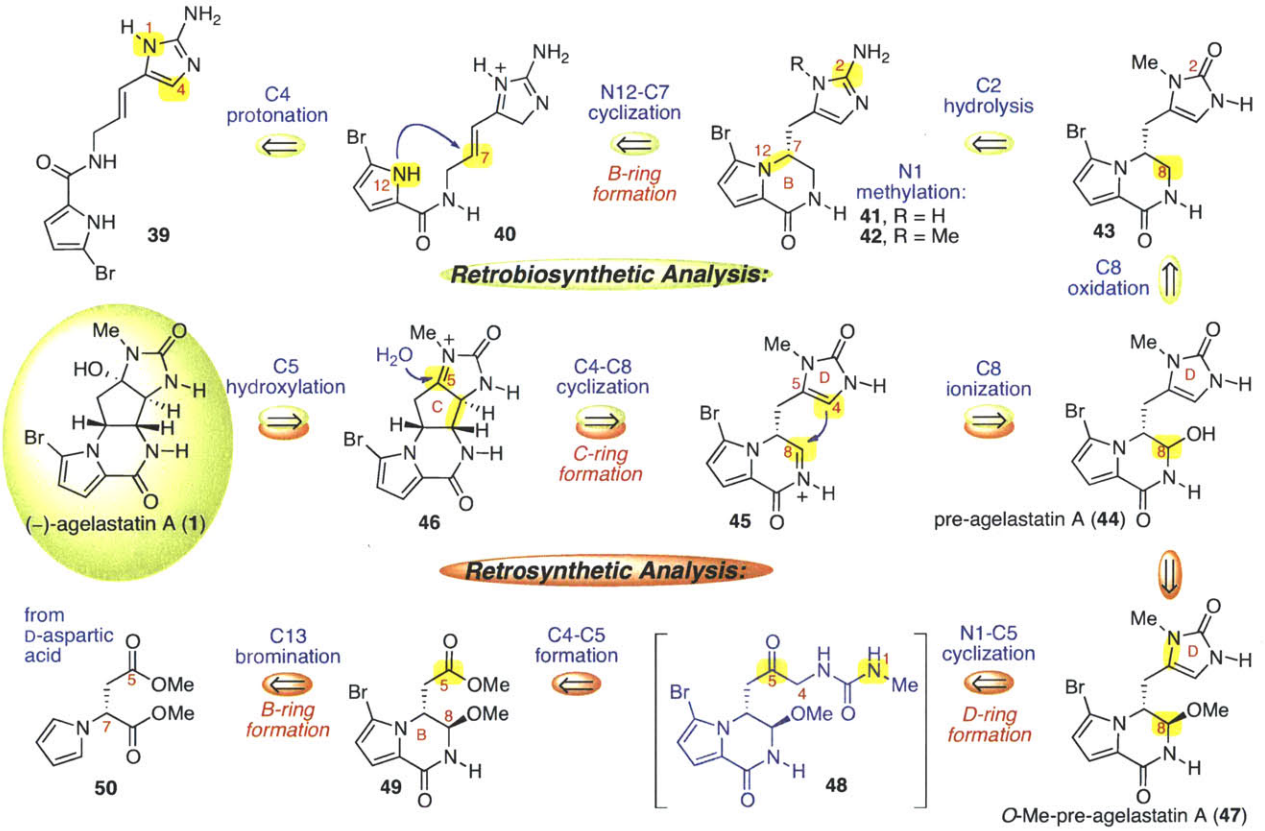
ring of the target natural product with excellent enantioselectivity (Scheme 3).[23] Ichikawa's[24] sigmatropic rearrangement of an allyl cyanate followed by Wardrop[25] and Chida's[26] respective use of the Overman rearrangement constituted additional successful total synthesis of **1**. Agelastatin A (**1**) has continued to serve as source of inspiration and furnished inventive applications of an aziridination strategy for its enantioselective total syntheses by Yoshimitsu and Tanaka,[27] Du Bois,[28] and Hamada.[29] In a subsequent report, Yoshimitsu could further optimize the synthetic sequence to (–)-**1**, utilizing a radical aminobromination strategy (Scheme 3).[30] Importantly, the robustness of Du Bois' synthetic approach was evidenced by their 270 mg preparation of (–)-**1** in a single pass (Scheme 3). Most recently, Maruoka completed the formal total synthesis of (–)-**1** using asymmetric Mannich reaction as a key step.[31] Interestingly, all of these syntheses focused on an early introduction of the central C-ring followed by further derivatization to the natural product **1**. Additionally, these reported syntheses of agelastatin A (**1**) do not focus on examining existing biosynthetic hypotheses for biogenesis of the intriguing tetracyclic framework using a C4–C8 bond forming strategy.[32] Distinct from these synthetic approaches, our biosynthetically inspired unified synthetic approach involving C4–C8 bond formation enabled the total synthesis of all (–)-agelastatins (**1**–**6**).[15]

Results and Discussion

Biosynthetic Hypothesis and Design Plan for Total Synthesis

The fascinating molecular architecture of the agelastatins and interest in evaluating our new hypothesis for the biogenetic origins of the C-ring involving cyclization with concomitant introduction of three stereocenters motivated the studies described here. We envisioned an advanced-stage biosynthetic sequence (Scheme 4) distinct from existing hypotheses (Scheme 2) that relies on: 1) reverse polarity in C-ring formation involving C4-nucleophilic trapping of a C8-electrophile for the C-ring formation, 2) introduction of the C-ring after the B-ring formation, and 3) substrate directed stereochemical control and use of intrinsic chemistry that is perhaps enhanced by the action of biosynthetic enzymes. Our retrosynthetic factoring of (–)-agelastatin A (**1**) inspired by our *retrobiosynthetic* analysis[15] of **1** is illustrated in Scheme 4. Ionization of the C5-hydroxyl of **1** followed by the strategic disconnection of C4–C8 reveals *N*-acyliminium ion **45** and clears the carbocyclic C-ring along with three stereocenters. The mechanistic development of a transform[33] linking **1** to **45** prompted consideration of a versatile precursor,

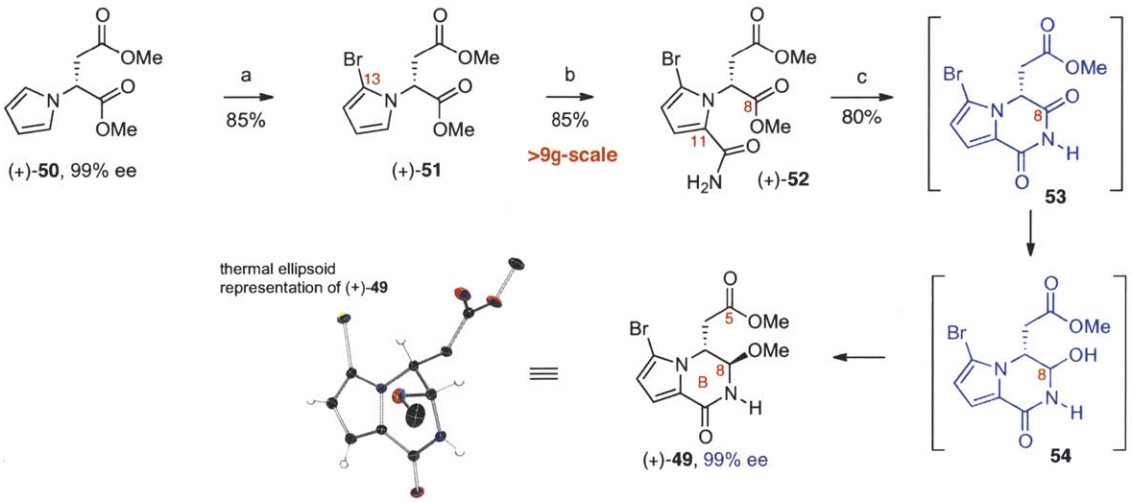
pre-agelastatin A (**44**, Scheme 4). In the forward direction, our hypothesis asserts that pre-agelastatin A (**44**) may be ionized to the C8-acyliminium ion **45**, allowing a 5-*exo*-trig cyclization via the kinetic trapping of the top face of the D-ring, followed by C5-hydroxylation to secure the C4-, C5-, and C8-stereocenters in the final stage of the biosynthesis (**44**→**1**, Scheme 4). We envisioned that pre-agelastatin A (**44**) would result from C2-hydrolysis and C8-oxidation of the cyclooroidin analogue **42**. Tricycle **42** would be formed by C4-protonation of linear precursor **39** followed by C7-trapping by the pyrrolyl-nitrogen (N12) via a 6-*exo*-trig cyclization.[34] Notably, this pathway suggests a link between the agelastatins and the natural product cyclooroidin (**10**, Figure 1),[35] and is consistent with Lindel's reported acid promoted conversion of oroidin (**9**) to tricycle **10**.[17] Motivated by the potential direct conversion of pre-agelastatin A (**44**) to (–)-agelastatin A (**1**), we targeted the related structure, *O*-methyl-pre-agelastatin A (**47**) and envisioned its concise synthesis from readily available D-aspartic acid derivative **50** (**50**→**47**, Scheme 1).



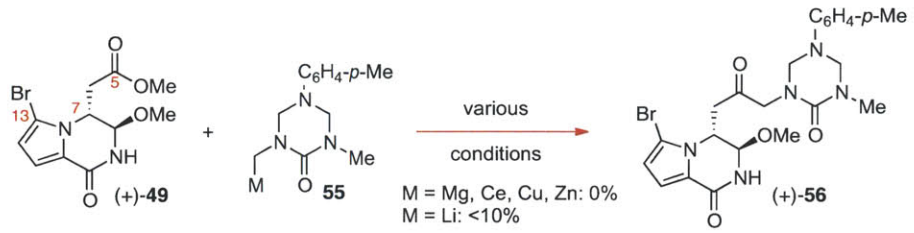
Scheme 4. Our retro(bio)synthetic analysis of (–)-agelastatin A (**1**) inspired by our biosynthetic hypothesis that involves intermediacy of pre-agelastatin A (**44**) in the final stage formation of the C-ring.

Total Synthesis of the Agelastatin Alkaloids

Our convergent synthesis for the desired *O*-methyl-pre-agelastatin A (**47**) commenced with pyrrole (+)-**50** (Scheme 5), accessible in one step from commercially available D-aspartic acid dimethyl ester.[36] Exposure of pyrrole (+)-**50** to *N*-bromosuccinimide (NBS) in the presence of 2,6-di-*tert*-butyl-4-methylpyridine (DTBMP) afforded the bromopyrrole (+)-**51** in 85% yield and 99% ee. Treatment of bromopyrrole (+)-**51** with chlorosulfonyl isocyanate afforded amide (+)-**52** in 85% yield on greater than 9-gram scale. Subsequently, addition of sodium borohydride followed by *p*-toluenesulfonic acid (TsOH) to a methanolic solution of (+)-**52** generated bicycle (+)-**49** as a single diastereomer in 80% yield and 99% ee. The X-ray crystal structure analysis of bicycle (+)-**49** confirmed its absolute and relative stereochemistry (Scheme 5).[37] The conversion of (+)-**52** to bicycle (+)-**49** occurs via formation and immediate C8-reduction of the imide **53**, preventing an undesired C7-epimerization.[38] Identical B-ring formation with the desbromopyrrole derivative of **52** resulted in significant erosion of enantiopurity. This observation was consistent with our postulate that the C7–H bond would be forced to adopt a pseudo-equatorial conformation to minimize allylic strain between the C13-bromine and C6-methylene, which suppressed undesired C7-deprotonation. Interestingly, the use of pyrrole (+)-**52**, possessing the C13-bromine present in all known agelastatins, provided chemical reactivity beneficial to our synthetic strategy (*vide infra*).

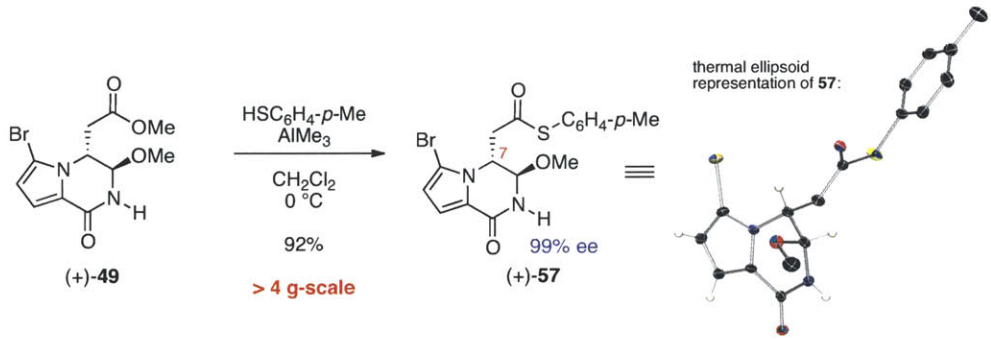


Scheme 5. Synthesis of bicycle (+)-**49**. Conditions: a) NBS, DTBMP, THF, 85%. b) $ClSO_2NCO$, MeCN, 0 °C; Na(Hg), NaH_2PO_4, 85%. c) $NaBH_4$, MeOH, 0 °C; $TsOH{\bullet}H_2O$, 23 °C, 80%.



Scheme 6. Attempted addition of metallated triazone to C13-bromo methylester (+)-**49**.

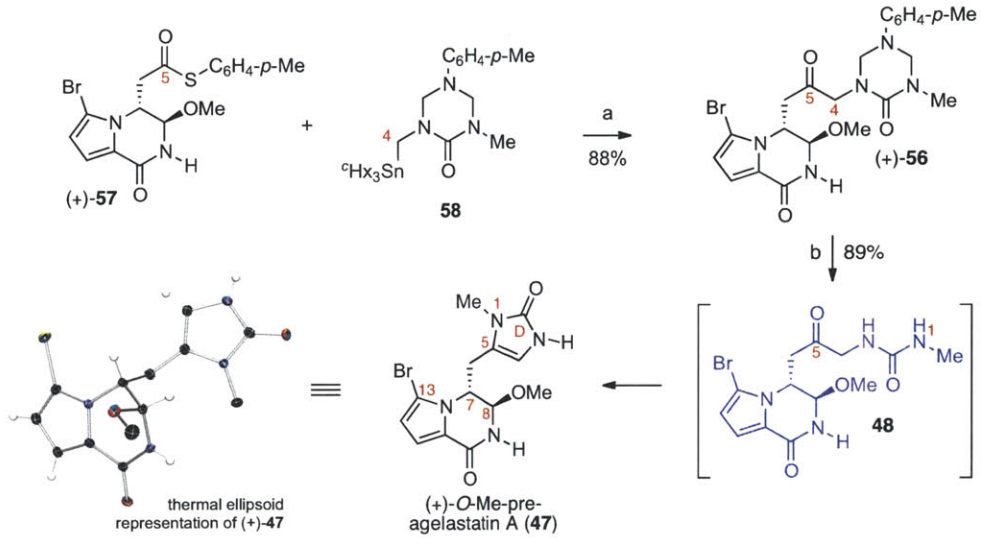
We next aimed to develop a general strategy for the introduction of the imidazolone[39] substructure present in the targeted pre-agelastatin **44**. Initially, we focused on the direct addition of transmetallated derivatives of triazone **55**[40,41] (Metal = Li, Mg, Cu, Ce, Zn, Scheme 6) to the bicyclic C5-ester (+)-**49**. When the lithiated triazone was allowed to react with methyl ester (+)-**49**, the reaction was plagued by undesired reactivity between the C13-bromide and the organolithium species, and ketone (+)-**56** could not be obtained in a synthetically useful yield (Scheme 6). In an attempt to solve this problem, we synthesized the corresponding Grignard reagent, organocerium, organocuprate, and organozinc derivatives, but these chemical species failed to add to methyl ester (+)-**49**. Furthermore, these metallated[42] triazone derivatives were generally unstable at temperatures above 0 °C. Thus, the development of a new strategy for the union of a stable metallated triazone and ester (+)-**49** as the prelude to introduction of the imidazolone was necessary.



Scheme 7. Synthesis of thioester (+)-**57**.

Inspired by studies of Liebeskind group, which reported the cross-coupling reaction between the thioester and organostannane,[43,44] we set our goal to develop an efficient metal mediated cross-coupling reaction between thioester derivative of methyl ester (+)-**49** and stannyl triazone derivative **55**. Thioester (+)-**57** was readily prepared in 92% yield through treatment of

ester (+)-**49** with trimethylaluminum and 4-methylbenzenethiol in dichloromethane (Scheme 7). The structure of (+)-**57** was secured via X-ray crystallographic analysis,[37] revealing the pseudo-equatorial C7–H bond.

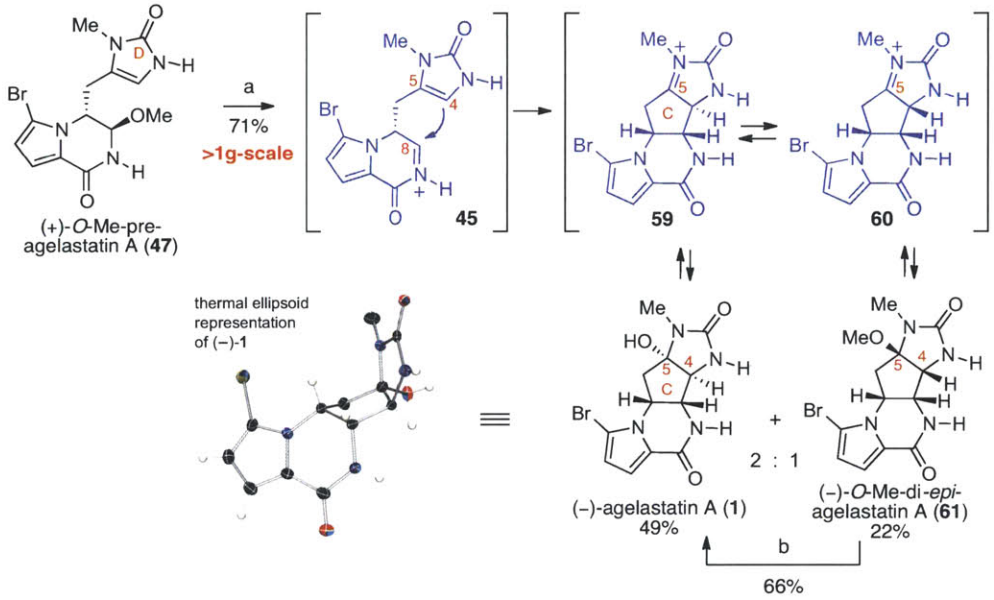


Scheme 8. Synthesis of the key intermediate (+)-*O*-methyl-pre-agelastatin A (**47**). Conditions: a) CuTC, THF, 50 °C, 88%. b) HCl (0.5 N), MeOH, 23 °C, 89%.[48]

After extensive experimentation, we found that the union of thioester (+)-**57** with the readily available triazone **58**[45] could be achieved efficiently in the presence of stoichiometric copper(I)-thiophene-2-carboxylate (CuTC) to give the ketone (+)-**56** in 88% yield (Scheme 8).[46] Exposure of triazone (+)-**56** to methanolic hydrogen chloride unraveled the keto-urea **48**, which upon spontaneous condensative cyclization[47] provided the desired (+)-*O*-methyl-pre-agelastatin A (**47**) in 89%[48] yield with 99% ee (Scheme 8). The structure of (+)-**47** was secured via X-ray crystallographic analysis, and its thermal ellipsoid representation illustrates that the C7-methylimidazolone and C8-methoxy group reside in a pseudo-diaxial conformation (C6-C7-C8-O8′ dihedral angle of 173°).[37]

With (+)-*O*-methyl-pre-agelastatin A (**47**) in hand, we proceeded to evaluate our hypothesis for C-ring biogenesis and rapid introduction of the C4-, C5-, and C8-stereocenters. Gratifyingly, heating an aqueous solution of (+)-**47** with methanesulfonic acid provided (–)-agelastatin A (**1**, Scheme 9) as the major product along with (–)-4,5-di-*epi*-agelastatin A (structure not illustrated) as the minor stereoisomer (2:1). Monitoring of this reaction by ^{1}H

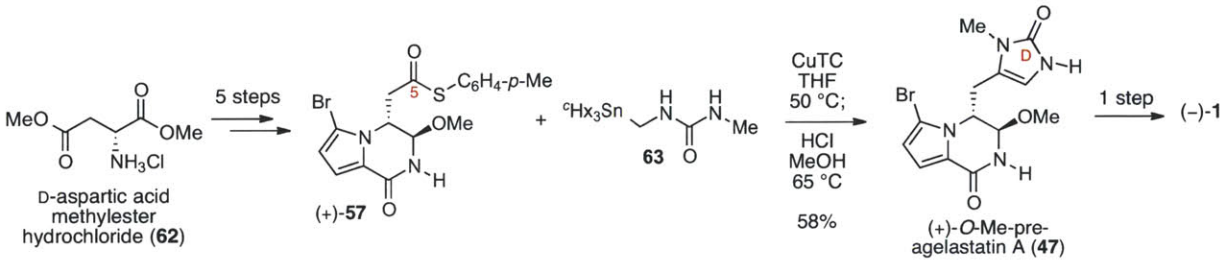
NMR revealed that (–)-4,5-di-*epi*-agelastatin A is the kinetic product, which equilibrates to the thermodynamically favored desired product (–)-agelastatin A (**1**). Careful analysis of the rate of solvolysis of each isomer illustrated that the C5-hydroxyl of (–)-4,5-di-*epi*-agelastatin A ionizes significantly faster than the corresponding C5-hydroxyl of (–)-agelastatin A (**1**). In the event, upon complete consumption of pre-agelastatin A (**44**), simple exposure of the reaction mixture to methanol efficiently converted (–)-4,5-di-*epi*-agelastatin A to (–)-*O*-methyl-di-*epi*-agelastatin A (**61**), enabling facile separation of (–)-**1** and (–)-**61** (Scheme 9).



Scheme 9. Gram-scale synthesis of (–)-agelastatin A (**1**). Conditions: a) $MeSO_3H$, H_2O, 100 °C; MeOH, 49% (–)-**1**, 22% (–)-**61**.[48] b) $MeSO_3H$, H_2O, 100 °C; MeOH, 66% (30% recovered (–)-**61**).[48]

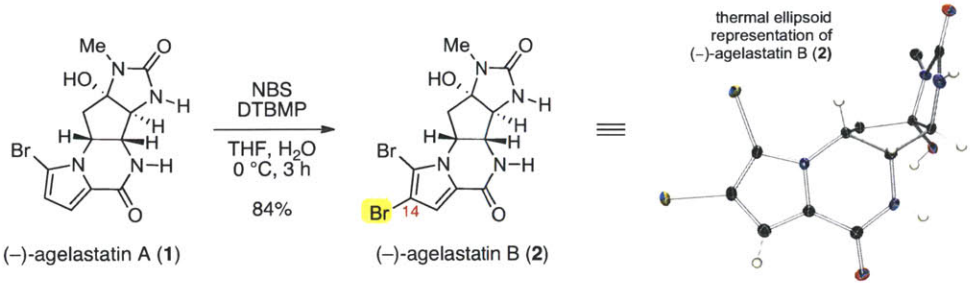
Under preparative conditions, our putative biomimetic cyclization of (+)-**47** afforded (–)-agelastatin A (**1**) in 49% yield (1.4 g, 99% ee) along with (–)-*O*-methyl-di-*epi*-agelastatin A (**61**) in 22% yield.[48] This constitutes a total chemical synthesis of (–)-agelastatin A (**1**) in eight steps for the longest linear sequence from commercially available starting material with 22% overall yield. Furthermore, resubmission of (–)-**61** to the above protocol afforded (–)-agelastatin A (**1**) in 66% yield along with recovered (–)-**61** (30%) post equilibration.[48] The structure of (–)-**1** was secured through X-ray crystallographic analysis (Scheme 9).[37] It should be noted that this 5-(enol*endo*)-*exo*-trig[49] type of cyclization with an acyliminium ion is a rare and challenging reaction as evidenced by the paucity of relevant examples in the literature.[50] Importantly, the

versatility of our new imidazolone annulation allows for the union of thioester (+)-**57** and the simple stannylurea derivative **63** ($^{c}Hx_3SnCH_2NH(CO)NHMe$) to afford (+)-*O*-methyl-pre-agelastatin A (**47**) without isolation of any intermediates, providing the shortest total synthesis of (–)-agelastatin A (**1**, 7-steps, Scheme 10) to date.[51]



Scheme 10. 7-Steps total synthesis of (–)-agelastatin A (**1**).[51]

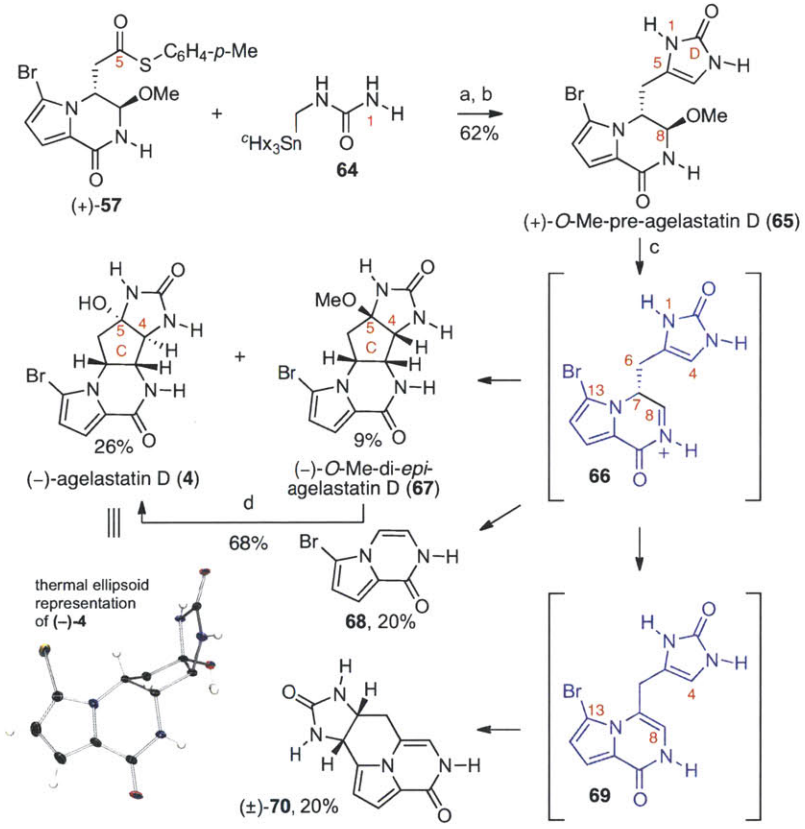
Under optimal conditions, treatment of (–)-agelastatin A (**1**) with NBS and DTBMP in a water–tetrahydrofuran solvent mixture afforded (–)-agelastatin B (**2**) in 84% yield (Scheme 11). Interestingly, X-ray crystallographic analysis of (–)-agelastatin B (**2**) revealed that its C-ring conformation is distinct from that of (–)-agelastatin A (**1**) as highlighted by the 25° and 31° difference in the C5-C4-C8-N9 and N1-C5-C4-C8 dihedral angles, respectively.[37]



Scheme 11. Total synthesis of (–)-agelastatin B (**2**).

Our new imidazolone annulation methodology proved most effective for accessing the desired pre-agelastatin D intermediate for the first synthesis of (–)-agelastatin D (**4**, Scheme 12). Under our optimized conditions, treatment of thioester (+)-**57** with stannylurea **64** and CuTC followed by exposure to methanolic hydrogen chloride afforded (+)-*O*-methyl-pre-agelastatin D (**65**) in 62% yield. With a successful synthetic access to (+)-*O*-methyl-pre-agelastatins D (**65**), we next investigated its conversion to (–)-agelastatin D (**4**). Application of our key cyclization

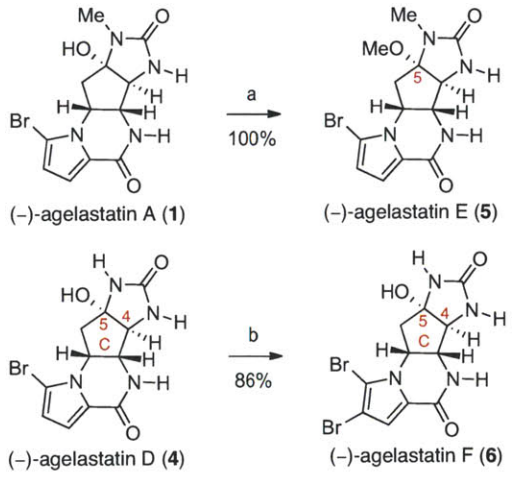
protocol described above (Scheme 9) indeed provided the first synthetic sample of (–)-agelastatin D (**4**) in 26% yield along with (–)-di-*epi*-agelastatin D (**67**, 9%, Scheme 12). The X-ray crystal structure analysis of (–)-agelastatin D (**4**) showed a C-ring conformation similar to (–)-**1**.[37] Resubmission of (–)-*O*-methyl-di-*epi*-agelastatin D (**67**) to $MeSO_3H$ in H_2O at reflux afforded (–)-agelastatin D (**4**) in 68% yield. While we were pleased to access (–)-**4** via our putative biomimetic cyclization, this key cyclization was plagued by competing reaction pathways involving the C6–C7 bond-cleavage, resulting in byproduct **68** (20%) and C4–C13 cyclization, giving byproduct **70** (20%). Formation of tetracycle **70** is consistent with a competing loss of methanol to afford pyrrolopyrazinone **69**, an observed intermediate, which prevents the desired C-ring formation and permits C13 to engage the imidazolone.[52]



Scheme 12. Total synthesis of (–)-agelastatin D (**4**). Conditions: (a) CuTC, THF, 50 °C; (b) HCl (0.5N), MeOH, 23 °C (62% (2-steps)); (c) $MeSO_3H$, H_2O, 100 °C; HCl, MeOH (26% (–)-**4**, 9% (–)-**67**, 20% **68**, 20% (±)-**70**). (d) $MeSO_3H$, H_2O, 100 °C; HCl, MeOH, 68%.

The formation of byproducts **68** and **70** indicates the attenuated C4-nucleophilicity of (+)-*O*-methyl-pre-agelastatin D (**65**) compared to (+)-*O*-methyl-pre-agelastatin A (**47**) in polar-protic solvent. Monitoring of the rates of deuterium incorporation at C4 position of (+)-*O*-methyl-pre-agelastatins A (**47**) and D (**65**) revealed that deuterium incorporation at C4 of (+)-**47** was ten time faster than (+)-**65**, consistent with its more efficient C4–C8 bond formation. Furthermore, C6–C7 bond fragmentation, requiring C5–C6 π-bond formation, is likely facilitated by diminished allylic strain imposed by the N1–H intermediate **66** compared to N1–Me derivative **45**. Interestingly, the observed lower efficiency of the desired cyclization with **65** compared to **47** echoes the scarcity of natural (–)-agelastatin D (**4**) compared to other *N*-methyl agelastatin alkaloids.[3,4,53]

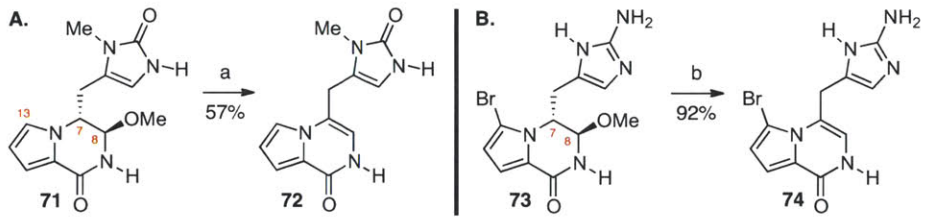
Furthermore, we have accessed the structures of the two newly isolated (–)-agelastatins E (**5**) and F (**6**) by their direct synthesis from (–)-agelastatin A (**1**) and D (**4**), respectively (Scheme 13). Heating a methanolic solution of (–)-agelastatin A (**1**) with Brønsted acid at 65 °C for 2 h afforded (–)-agelastatin E (**5**) in 100% yield (Scheme 13).[1c] A synthetic sample of (–)-agelastatin F (**6**) was generated in 86% yield by bromination of (–)-agelastatin D (**4**) under the optimal conditions described above for the synthesis of (–)-agelastatin B (**2**), thereby confirming its molecular structure.



Scheme 13. Total synthesis of (–)-agelastatin E (**5**) and (–)-agelastatin F (**6**). Conditions: (a) Amberlyst 15, MeOH, 65 °C, 100%. (b) NBS, DTBMP, THF, H_2O, 0 °C, 86%.

Our biosynthetically inspired strategy for the advanced stage C-ring formation drew on the intrinsic chemistry of our proposed pre-agelastatin intermediates for rapid generation of

molecular complexity, enabling a unified approach to all known agelastatin alkaloids. Collectively, our observations hint at a plausible sequence of events for the biogenesis of the alkaloids **1**–**6** (Scheme 4). For example, the C13-bromopyrrole and the imidazolinone substructures (present in all agelastatins) were critical in the successful C-ring cyclization. Treatment of the des-bromo derivative **71** under the optimized cyclization conditions did not afford the desired C-ring due to a more facile conversion to pyrrolopyrazinone **72** (57%,[48] Scheme 14),[54] suggesting a beneficial role for the allylic strain between the C13-bromine and C6-methylene to restrict the C7-methine in a pseudo-equatorial conformation during the key cyclization event. Additionally, the aminoimidazole **73** failed to undergo the desired cyclization reaction due to a more competitive pyrrolopyrazinone **74** formation (92%, Scheme 14), an observation we attribute to the greater propensity of the aminoimidazolone substructure to remain protonated and thus less nucleophilic under the reaction conditions.



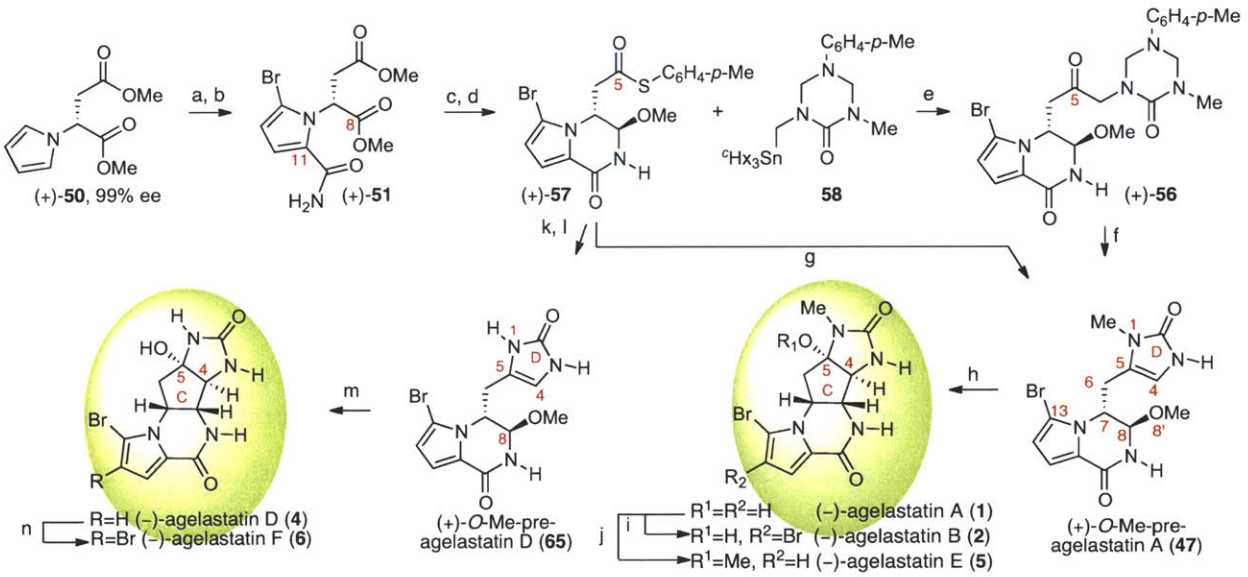
Scheme 14. Key observations concerning our bioinspired C-ring synthesis strategy. Attempted cyclization of **A**) desbromo-pre-agelastatin A (**71**) and **B**) imidazole derivative **73**. Reagents and conditions: (a) $MeSO_3H$, H_2O, 100 °C, 20 min, 57%.[48] (b) Dowex, H_2O, 100 °C, 92%.

Consequently, we suggest a higher probability for biosynthetic introduction of the C13-bromopyrrole and imidazolone substructures prior to C-ring formation. Moreover, our observations regarding the higher predisposition for the pre-agelastatin A derivative (+)-**47**, to undergo C-ring formation as compared to the desmethyl derivative (+)-**65** may suggest predominant N1-methylation prior to C-ring cyclization in the biogenesis of the agelastatins. The stereochemical outcome for the key C-ring cyclization is controlled by the C7-methine to secure the desired thermodynamically favored C4-, C5-, and C8-stereocenters. Specifically, the C5-center is controlled by the C4-stereochemistry to give a *cis*-fused CD-ring system upon hydroxylation. It is conceivable that putative agelastatin biosynthetic enzymes have evolved to enhance the innate stereoselectivity of compounds related to those utilized in our synthesis.[55]

While our total syntheses of alkaloids **1**–**6** do not confirm our hypothesis for their biogenesis, it is gratifying to have chemical validation for our proposed mode and timing of bond and ring formations in the biosynthesis of these alkaloids.

Conclusion

We have completed the total syntheses of the agelastatin alkaloids through a unified strategy inspired by our hypothesis for their biogenesis (Scheme 15). Key features of our syntheses include: 1) the concise multi-gram scale enantioselective synthesis of our proposed "pre-agelastatin" derivatives, 2) the use of the bromopyrrole substructure to suppress C7-deprotonation, 3) a versatile synthesis of imidazolone derivatives via a new [4+1] annulation strategy, 4) the validation of our bioinspired 5-*exo*-trig advanced stage C-ring formation, and 5) utilization of the intrinsic chemistry of plausible biosynthetic intermediates for rapid generation of molecular complexity. The overall efficiency of our strategy is highlighted by our 1.4 gram



Scheme 15. Summary of the enantioselective synthesis of the agelastatin alkaloids. Conditions: (a) NBS, DTBMP, THF, 85%. (b) $ClSO_2NCO$, MeCN, 0 °C; Na(Hg), NaH_2PO_4, 85%. (c) $NaBH_4$ MeOH, 0 °C; $TsOH{\bullet}H_2O$, 23 °C, 80%. (d) HSC_6H_4-*p*-Me, $AlMe_3$, CH_2Cl_2, 0 °C, 92%. (e) CuTC, THF, 50 °C, 88%.[46] (f) HCl (0.5N), MeOH, 65 °C, 89%.[48] (g) *c*-$Hx_3SnCH_2NH(CO)NHMe$ (**63**), CuTC, THF, 50 °C, HCl (0.5 N), MeOH, 65 °C, 58%.[51] (h) $MeSO_3H$, H_2O, 100 °C; MeOH, 49% (–)-**1**.[48] (i) NBS, DTBMP, THF, H_2O, 0 °C, 84%. (j) Amberlyst 15, MeOH, 65 °C, 100%; (k) $^cHx_3SnCH_2NH(CO)NH_2$ (**64**), CuTC, THF, 50 °C; (l) HCl (0.5N), MeOH, 23 °C, 62% (2 steps). (m) $MeSO_3H$, H_2O, 100 °C; HCl, MeOH, 26%. (n) NBS, DTBMP, THF, H_2O, 0 °C, 86%.

batch enantioselective synthesis of (–)-agelastatin A (**1**). With this most concise total chemical synthetic access to all natural agelastatin alkaloids and related derivatives, studies aimed at probing their chemical and biological mode of action are ongoing.

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45. Stannyltriazone **58** was prepared in two steps from commercial material on >10-gram scale via lithiation of the corresponding triazone followed by trapping with tricyclohexylstannyl chloride. See the experimental section for details.
46. With further optimization of the work-up procedure, Dr. Dustin Siegel showed that the CuTC mediated cross-coupling between (+)-**57** and **58** can be achieved in 96% yield on greater than 5-gram scale. For detailed experimental procedure, see: Ref. 15.
47. (a) Marckwald, W. *Chem. Ber.* **1892**, *25*, 2354–2373. (b) Duschinsky, R., Dolan, L. A. *J. Am. Chem. Soc.* **1946**, *68*, 2350–2355.
48. The reaction was developed and optimized in collaboration with Dr. Dustin Siegel. Final yield was adopted from Dr. Dustin Siegel's experimental result.
49. Baldwin, J. E.; Lusch, M. J. *Tetrahedron* **1982**, *38*, 2939–2947.
50. (a) Gramain, J. C.; Remuson, R. *Heterocycles* **1989**, *29*, 1263–1273. (b) Heaney, H.; Taha, M. O. *Tetrahedron Lett.* **1998**, *39*, 3341–3344.
51. The reaction was developed and optimized by Dr. Dustin Siegel. Final yield was adopted from Dr. Dustin Siegel's experimental result.
52. ^{1}H NMR monitoring of this reaction revealed the formation and slow consumption of **69**. At lower temperature (60 °C), **69** was recovered from the reaction mixture; its resubmission to the cyclization conditions afforded **70** in 24% yield.
53. Neither the optical rotation nor the ^{13}C NMR spectrum of agelastatin D (**3**) was obtained in the original isolation report as it was a minor component.
54. The C8-hydroxy derivative of **71** accounted for approximately 20% of the mass balance after 20 min. Prolonged exposure of **71**, the C8-hydroxy derivative of **71**, or **72** to the reaction conditions did not afford the desired cyclization.
55. The opposite C7-stereochemistry of (–)-cyclooroidin (**10**) compared to that of the agelastatins entreats the possibility that downstream biosynthetic enzymes may preferentially bind and consume derivatives of *ent*-cyclooroidin for the synthesis of the agelastatins.

Experimental Section

General Procedures. All reactions were performed in oven-dried or flame-dried round bottomed flasks or modified Schlenk (Kjeldahl shape) flasks. The flasks were fitted with rubber septa and reactions were conducted under a positive pressure of argon. Stainless steel syringes or cannulae were used to transfer air- and moisture-sensitive liquids. Where necessary (so noted), solutions were deoxygenated by argon purging for a minimum of 10 min. Flash column chromatography was performed as described by Still et al. using silica gel (60-Å pore size, 40–63 μm, 4-6% H_2O content, Zeochem).[1] Analytical thin–layer chromatography was performed using glass plates pre-coated with 0.25 mm 230–400 mesh silica gel impregnated with a fluorescent indicator (254 nm). Thin layer chromatography plates were visualized by exposure to ultraviolet light and/or by exposure to an ethanolic phosphomolybdic acid (PMA), an acidic solution of *p*-anisaldehyde (Anis), an aqueous solution of ceric ammonium molybdate (CAM), an aqueous solution of potassium permanganate ($KMnO_4$) or an ethanolic solution of ninhydrin followed by heating (<1 min) on a hot plate (~250 °C). Organic solutions were concentrated on Büchi R-200 rotary evaporators at ~10 torr (house vacuum) at 25–35 °C, then at ~0.5 torr (vacuum pump) unless otherwise indicated.

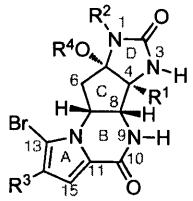
Materials. Commercial reagents and solvents were used as received with the following exceptions: dichloromethane, diethyl ether, tetrahydrofuran, acetonitrile, toluene, methanol, triethylamine, and pyridine were purchased from J.T. Baker (Cycletainer™) and were purified by the method of Grubbs et al. under positive argon pressure.[2] Copper thiophene 2-carboxylate (CuTC), a tan colored solid, was purchased from Matrix Inc. and was used as received. Chlorosulfonyl isocyanate was purchased from TCI and was used as received. Sodium Amalgam was freshly prepared before use.[3] The molarity of *sec*-butyllithium solutions were determined by titration using diphenylacetic acid as an indicator (average of three determinations).[4]

Instrumentation. Proton (^1H) and carbon (^{13}C) nuclear magnetic resonance spectra were recorded with Varian inverse probe 500 INOVA and Varian 500 INOVA spectrometers. Proton nuclear magnetic resonance (^1H NMR) spectra are reported in parts per million on the δ scale and are referenced from the residual protium in the NMR solvent ($CDCl_3$: δ 7.24 ($CHCl_3$), Toluene-d_8: δ 2.09 (Toluene-d_7); CD_3OD: δ 3.31 (CHD_2OD), Pyridine-d_5: δ 8.74 (Pyridine-d_4), DMSO-d_6: δ 2.50 (DMSO-d_5)). Data is reported as follows: chemical shift [multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, st = sextet, sp = septet, m = multiplet, app = apparent, br = broad), coupling constant(s) in Hertz, integration, assignment. Carbon-13 nuclear magnetic resonance (^{13}C NMR) spectra are reported in parts per million on the δ scale and are referenced from the carbon resonances of the solvent ($CDCl_3$: δ 77.23, Toluene-d_8: δ 20.40, CD_3OD: δ 49.15, Pyridine-d_5: δ 150.35, DMSO-d_6: δ 39.51). Data is reported as follows: chemical shift. Infrared data (IR) were obtained with a Perkin-Elmer 2000 FTIR and are reported as follows: [frequency of absorption (cm^{-1}), intensity of

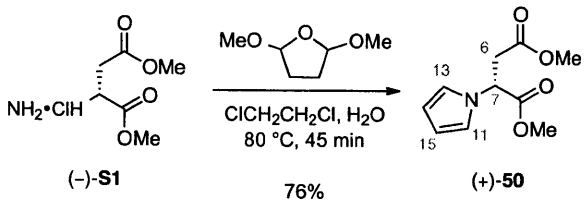
[1] Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923–2925.
[2] Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996**, *15*, 1518–1520.
[3] Sodium amalgam (5% wt) was prepared according to: Brasen, W. R.; Hauser, C. R. *Org. Synth.* **1954**, *34*, 56–57.
[4] Kofron, W. G.; Baclawski, L. M. *J. Org. Chem.* **1976**, *41*, 1879–1880.

absorption (s = strong, m = medium, w = weak, br = broad)]. Optical Rotation was recorded on a Jasco P-1010 Polarimeter (chloroform, Aldrich, Chromosolv Plus 99.9%; methanol, Aldrich, Chromosolv Plus 99.9%; pyridine, purified by the method of Grubbs et al.[2]). Chiral HPLC analysis was performed on an Agilent Technologies 1100 Series system. Semi-preparative HPLC was performed on a Waters system with the 1525 Binary HPLC Pump, 2489 UV/Vis Detector, SFO System Fluidics Organizer, and 2767 Sample Manager components. The structures of (–)-**1**, (–)-**2**, (–)-**4**, (+)-**47**, (+)-**49**, and (+)-**57** were obtained at the X-ray crystallography laboratory of the Department of Chemistry, Massachusetts Institute of Technology, with the assistance of Mr. Justin Kim. We are grateful to Dr. Li Li for obtaining the mass spectrometric data at the Department of Chemistry's Instrumentation Facility, Massachusetts Institute of Technology. High-resolution mass spectrometric data (HRMS) were recorded on a Bruker APEXIV 4.7 t FT-ICR-MS spectrometer using electrospray ionization (ESI) source or direct analysis in real time (DART) ionization source.

Positional Numbering System. In assigning the ^{1}H and ^{13}C NMR data of all intermediates en route to our total synthesis of (–)-**1** through (–)-**6** we have employed a uniform numbering system consistent with that of the final targets.



R^1 = H, R^2 = Me, R^3 = H, R^4 = H	(–)-agelastatin A (**1**)
R^1 = H, R^2 = Me, R^3 = Br, R^4 = H	(–)-agelastatin B (**2**)
R^1 = OH, R^2 = Me, R^3 = H, R^4 = H	(–)-agelastatin C (**3**)
R^1 = H, R^2 = H, R^3 = H, R^4 = H	(–)-agelastatin D (**4**)
R^1 = H, R^2 = Me, R^3 = H, R^4 = Me	(–)-agelastatin E (**5**)
R^1 = H, R^2 = H, R^3 = Br, R^4 = H	(–)-agelastatin F (**6**)



(+)-(*R*)-Dimethyl-2-(1*H*-pyrrol-1-yl)succinate (50):[5]

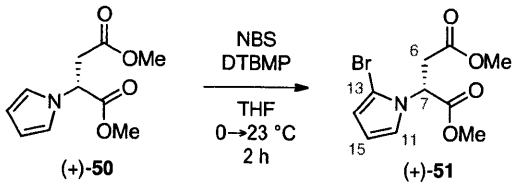
To a solution of (–)-dimethyl D-aspartate hydrogenchloride[6] (**S1**, 3.95 g, 20.0 mmol, 1 equiv) in water (30 ml) at 23 °C was added 1,2-dichloroethane (30 mL) via syringe followed by 2,5-dimethoxytetrahydrofuran (2.65 mL, 20 mmol, 1.00 equiv), and the resulting mixture was heated to 80 °C. After 45 min, the brown reaction mixture was cooled to 23 °C, and the aqueous layer was separated and was extracted with dichloromethane (3 × 30 mL). The combined organic layers were dried over anhydrous sodium sulfate and were concentrated under reduced pressure. The brown residue was purified by flash column chromatography (silica gel: diam. 4 cm, ht. 11 cm; eluent: 40% diethyl ether in hexanes) to afford pyrrole (+)-**50** (3.22 g, 76%) as colorless oil.

Pyrrole (+)-**50** was found to be 99% ee by chiral HPLC analysis [Welk-O (*S*,*S*); 3 mL/min; 2% isopropanol in hexanes; t_R(major) = 4.5 min, t_R(minor) = 5.2 min]. (+)-**50** could be stored for greater than a month as a solution frozen in benzene at –8 °C without any erosion of enantiomeric excess.

^{1}H NMR (500 MHz, $CDCl_3$, 21 °C):	δ 6.69 (t, J = 2.2 Hz, 2H, C_{11}**H**, C_{13}**H**), 6.15 (t, J = 2.1 Hz, 2H, C_{14}**H**, C_{15}**H**), 5.11 (dd, J = 7.9, 6.8 Hz, 1H, C_7**H**), 3.71 (s, 3H, O**CH$_3$**), 3.66 (s, 3H, O**CH$_3$**), 3.26 (dd, J = 16.8, 8.0 Hz, 1H, C_6**H$_a$**), 2.92 (dd, J = 16.7, 6.8 Hz, 1H, C_6**H$_b$**).
^{13}C NMR (125.8 MHz, $CDCl_3$, 21 °C):	δ 170.4, 170.0, 120.1, 109.2, 57.8, 53.0, 52.2, 37.5.
FTIR (neat) cm^{-1}:	3643 (m), 3466 (m), 3103 (m), 2956 (s), 1739 (br-s), 1557 (w), 1490 (s), 729 (s).
HRMS (DART) (*m/z*):	calc'd for $C_{10}H_{14}NNaO_4$, $[M+Na]^+$: 212.0917 found: 212.0911.
$[\alpha]_D^{22}$:	+71.3 (*c* 0.37, $CHCl_3$).
TLC (25% ethyl acetate in hexanes), R*f*:	0.50 (CAM, UV).

[5] For a previous report of the synthesis of (–)-**50** in 99% ee, see: Jefford, C. W.; de Villedone de Naide, F.; Sienkiewicz, K. *Tetrahedron: Asymmetry* **1996**, *7*, 1069–1076.

[6] (–)-Dimethyl D-aspartate hydrochloride (**S1**) can be purchased from commercial sources. Additionally, we prepared **S1** from (–)-D-aspartic acid in 99% yield on greater than 35 gram scale according to the following procedure: Gmeiner, P.; Feldman, P. L.; Chu-Moyer, M. Y.; Rapoport, H. *J. Org. Chem.* **1990**, *55*, 3068–3074.

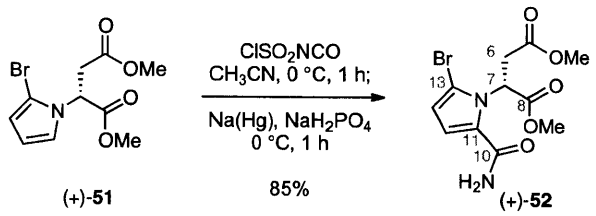


(+)-(*R*)-Dimethyl 2-(2-bromo-1*H*-pyrrol-1-yl)succinate (51):

N-Bromosuccinimide (NBS, 1.88 g, 10.6 mmol, 1.00 equiv) was added as solid in one portion to a solution of pyrrole (+)-**50** (2.25 g, 10.6 mmol, 1 equiv) and 2,6-di-*tert*-butyl-4-methylpyridine (DTBMP, 2.66 g, 12.7 mmol, 1.20 equiv) in tetrahydrofuran (53 mL) at 0 °C. After 1.5 h, the clear colorless reaction mixture was allowed to warm to 23 °C. After 30 min, the reaction mixture was quenched with a mixture of saturated aqueous sodium thiosulfate solution and saturated aqueous sodium bicarbonate solution (1:1, 100 mL). The solution was diluted with ethyl acetate (100 mL) and water (100 mL), and the layers were separated. The aqueous layer was extracted with ethyl acetate (2 × 100 mL), and the combined organic layers were dried over anhydrous sodium sulfate and were concentrated under reduced pressure. The sample of the crude colorless residue was purified by flash column chromatography (silica gel: diam. 5 cm, ht. 15 cm; eluent: 10% ethyl acetate in hexanes) to afford bromopyrrole (+)-**51** (2.60 g, 85%) as a colorless oil.

Bromopyrrole (+)-**51** was found to be 99% ee by chiral HPLC analysis [Welk-O (*R*,*R*); 3 mL/min; 2% isopropanol in hexanes; t_R(major) = 3.5 min, t_R(minor) = 4.1 min]. While neat (+)-**51** is sensitive toward long term storage, it could be stored for greater than a month as a solution frozen in benzene at –8 °C without any C_{13}→C_{14} bromine migration.

^{1}H NMR (500 MHz, $CDCl_3$, 21 °C):	δ 6.74 (ddd, J = 3.1, 1.9, 0.2 Hz, 1H, C_{11}**H**), 6.18-6.16 (m, 2H, C_{14}**H**, C_{15}**H**), 5.38 (t, J = 7.2 Hz, 1H, C_7**H**), 3.73 (s, 3H, O**CH$_3$**), 3.67 (s, 3H, O**CH$_3$**), 3.27 (dd, J = 16.8, 7.5 Hz, 1H, C_6**H$_a$**), 2.92 (dd, J = 16.8, 7.0 Hz, 1H, C_6**H$_b$**).
^{13}C NMR (125.8 MHz, $CDCl_3$, 21 °C):	δ 170.3, 169.8, 120.6, 111.7, 110.6, 102.1, 56.2, 53.3, 52.4, 37.2.
FTIR (neat) cm^{-1}:	3654 (w), 3468 (w), 3130 (m), 2954 (s), 1739 (br-s), 1437 (s), 1010 (s), 709 (s).
HRMS (ESI) (*m/z*):	calc'd for $C_{10}H_{12}BrNNaO_4$, $[M+Na]^+$: 311.9842 found: 313.9847.
$[\alpha]_D^{22}$:	+65.9 (*c* 1.06, $CHCl_3$).
TLC (25% ethyl acetate in hexanes) R*f*:	0.42 (CAM, UV).



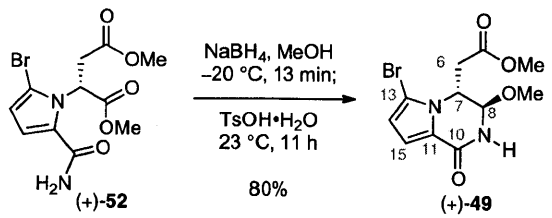
(+)-(*R*)-Dimethyl 2-(2-bromo-5-carbamoyl-1*H*-pyrrol-1-yl)succinate (52):

Chlorosulfonyl isocyanate (2.99 mL, 33.7 mmol, 1.05 equiv) was added slowly via syringe to a solution of bromopyrrole (+)-**51** (9.30 g, 32.1 mmol, 1 equiv) in acetonitrile (160 mL) at 0 °C. After 1 h, anhydrous powdered sodium phosphate monobasic (19.2 g, 160 mmol, 5.00 equiv) followed by freshly prepared sodium amalgam (5%-Na, 73.7 g, 160 mmol, 5.00 equiv) were added as solids to the reaction mixture. After 1h, the reaction mixture was diluted with ethyl acetate (530 mL), and silica gel (290 mL) was added to the reaction mixture. The resulting slurry was filtered through a plug of silica gel (diam. 9 cm, ht. 10 cm; eluent: ethyl acetate). The filtrate was concentrated under reduced pressure, and the residue was purified by flash column chromatography (silica gel: diam. 11 cm, ht. 10 cm; eluent: from 50% ethyl acetate in hexanes to ethyl acetate) to afford (+)-**52** (9.10 g, 85%) as white solid. Pyrrole (+)-**52** could be stored for greater than a month as a solution frozen in benzene at –8 °C. Exposure of (+)-**52** to alcoholic solvents, namely methanol, or base results in rapid lactamization and erosion of enantiomeric excess.

^{1}H NMR (500 MHz, $CDCl_3$, 21 °C)[7]:	δ 6.69 (br-d, J = 3.9 Hz, 1H, $C_{15}\mathbf{H}$), 6.23 (d, J = 4.1 Hz, 1H, $C_{14}\mathbf{H}$), 5.78 (br-s, 2H, $N_9\mathbf{H}_2$), 5.78 (br-s, 1H, $C_7\mathbf{H}$)[8], 3.69 (s, 3H, $OC\mathbf{H}_3$), 3.65 (s, 3H, $OC\mathbf{H}_3$), 3.59 (br-d, J = 14.4 Hz, 1H, $C_6\mathbf{H}_a$), 2.89 (br-dd, J = 16.4, 6.3 Hz, 1H, $C_6\mathbf{H}_b$).
^{13}C NMR (125.8 MHz, $CDCl_3$, 21 °C)[7]:	δ 171.2, 169.5, 162.5, 125.2, 115.1, 111.7, 111.7[8], 56.8, 53.0, 52.3, 37.3.
FTIR (neat) cm^{-1}:	3359 (m), 3191 (m), 2953 (m), 1740 (s), 1660 (m), 1602 (m), 1534 (w), 1438 (s), 1413 (m), 1272 (m), 1011 (m) 751 (m).
HRMS (DART) (*m/z*):	calc'd for $C_{11}H_{14}BrN_2O_5$, $[M+H]^+$: 333.0081 found: 333.0074.
$[\alpha]_D^{22}$:	+74.0 (*c* 1.25, $CHCl_3$).
M.p.:	45–49 °C.
TLC (33% in hexanes in ethyl acetate) R*f*:	0.44 (CAM, UV).

[7] Resonances at 21 °C are broadened due to atropisomerism.

[8] Resonance is obscured due to line broadening. At higher temperature in toluene-d_8 the signals are resolved; however, atropisomerism persist for ^{13}C NMR. ^{1}H NMR (500 MHz, Toluene-d_8, 80 °C) δ 6.30 (br-s, 1H, $C_7\mathbf{H}$), 6.27 (dd, J = 4.1, 1.1 Hz, 1H, $C_{15}\mathbf{H}$), 6.01 (dd, J = 4.1 0.6 Hz, 1H, $C_{14}\mathbf{H}$), 5.40 (br-s, 2H, $N_9\mathbf{H}_2$), 3.66 (dd, J = 16.5, 6.7 Hz, 1H, $C_6\mathbf{H}_a$), 3.37 (s, 3H, $OC\mathbf{H}_3$), 3.36 (s, 3H, $OC\mathbf{H}_3$), 2.86 (dd, J = 16.6, 6.5 Hz, 1H, $C_6\mathbf{H}_b$). ^{13}C NMR (125.8 MHz, Toluene-d_8, 80 °C; Minor rotamer resonances denoted by *) δ 170.7, 169.2, 162.9, 126.8, 115.1*, 114.9*, 114.8, 114.6*, 112.2*, 112.0*, 111.6, 111.4*, 110.9 (br), 57.1 (br), 52.3, 52.1*, 51.7*, 51.5, 51.3*, 37.9*, 37.7, 37.5*.

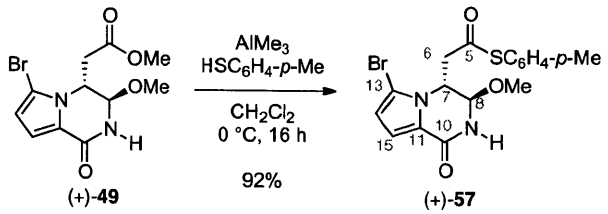


(+)-Methyl-2-((3*R*,4*R*)-6-bromo-3-methoxy-1-oxo-1,2,3,4-tetrahydropyrrolo[1,2-a]pyrazin-4-yl)-acetate (49):

Anhydrous methanol (17 mL, cooled to –20 °C) was added to (+)-**52** (573 mg, 1.72 mmol, 1 equiv) at –20 °C followed immediately by sodium borohydride (257 mg, 6.88 mmol, 4.00 equiv) as a solid in one portion (Note: Significant gas evolution was observed. The internal temperature remained below –10 °C). After 13 minutes, acetone (2.53 mL, 34.4 mmol, 20.0 equiv) was added slowly via syringe to the reaction mixture. After 6 min, the reaction mixture was diluted with methanol (34 mL, –20 °C), and *p*-toluenesulfonic acid hydrate ($TsOH•H_2O$, 2.17 g, 11.2 mmol, 6.50 equiv) in methanol (100 mL) was added slowly over a 10 min period, while maintaining an internal temperature of –20 °C. The resulting mixture (pH = 3) was allowed to slowly warm to 23 °C. After 11 h, the reaction mixture was basified with saturated aqueous sodium bicarbonate solution (pH = 7) and was concentrated under reduced pressure to a volume of approximately 15 mL. The resulting mixture was partitioned between dichloromethane (150 mL) and saturated aqueous sodium bicarbonate solution (150 mL). The layers were separated, and the aqueous layer was extracted with dichloromethane (3 × 150 mL). The combined organic layers were dried over anhydrous sodium sulfate, and were concentrated under reduced pressure to provide a white solid residue. This solid was purified by flash column chromatography (silica gel: diam. 3 cm, ht. 5.5 cm; eluent: 25% hexanes in ethyl acetate) to afford the bicycle (+)-**49** (435 mg, 90%) as white crystalline solid.

Bicycle (+)-**49** was found to be 99% ee by chiral HPLC analysis [Chiralpak AD-H; 0.54 mL/min; 21% isopropanol in hexanes; t_R(major) = 16.2 min, t_R(minor) = 11.6 min]. Crystals of the bicycle (+)-**49** suitable for X-ray diffraction were obtained from methanol.

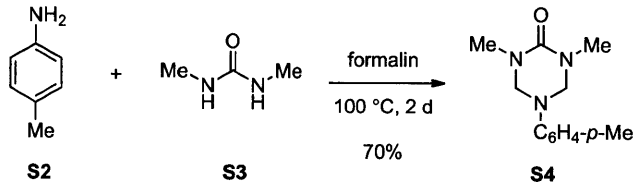
^{1}H NMR (500 MHz, $CDCl_3$, 21 °C):	δ 7.73 (br-d, J = 4.4 Hz, 1H, N_9**H**), 6.94 (d, J = 4.1 Hz, 1H, C_{15}**H**), 6.29 (d, J = 4.1 Hz, 1H, C_{14}**H**), 4.84 (dd, J = 9.8, 3.5 Hz, 1H, C_7**H**), 4.80 (dd, J = 4.8, 1.5 Hz, 1H, C_8**H**), 3.73 (s, 3H, OC**H**$_3$), 3.37 (s, 3H, OC**H**$_3$), 2.75 (dd, J = 17.0, 10.8 Hz, 1H, C_6**H**$_a$), 2.65 (dd, J = 17.0, 3.6 Hz, 1H, C_6**H**$_b$).
^{13}C NMR (125.8 MHz, $CDCl_3$, 21 °C):	δ 170.2, 159.7, 123.5, 115.3, 113.2, 106.3, 84.7, 55.2, 53.6, 52.5, 36.6.
FTIR (neat) cm^{-1}:	3226 (br-m), 2952 (m), 1736 (s), 1669 (s), 1553 (m), 1423 (s), 1384 (w), 1319 (m), 1088 (m).
HRMS (ESI) (*m/z*):	calc'd for $C_{11}H_{13}BrN_2NaO_4$, $[M+Na]^+$: 317.0131, found: 317.0135.
$[\alpha]_D^{22}$:	+128.1 (*c* 0.61, $CHCl_3$).
M.p.:	156–157 °C.
TLC (25% hexanes in ethyl acetate), R*f*:	0.31 (CAM, UV).



(+)-*S*-*p*-Tolyl-2-((3*R*,4*R*)-6-bromo-3-methoxy-1-oxo-1,2,3,4-tetrahydropyrrolo[1,2-a]pyrazin-4-yl)ethanethioate (57):

Trimethyl aluminum (2 M in toluene, 30.7 mL, 61.5 mmol, 5.00 equiv) was added slowly via syringe to a solution of 4-methylbenzenethiol (7.80 g, 61.5 mmol, 5.00 equiv) in dichloromethane (123 mL) at 0 °C. After 40 min, a pre-cooled solution (0 °C) of bicycle (+)-**49** (3.90 g, 12.3 mmol, 1 equiv) in dichloromethane (90 mL) was added via cannula. After 16 h, the light yellow reaction mixture was diluted with saturated aqueous potassium sodium tartrate solution (360 mL) and saturated aqueous sodium bicarbonate solution (250 mL). After 1h, the layers were separated and the aqueous layer was extracted with dichloromethane (3 × 250 mL). The combined organic layers were dried over anhydrous sodium sulfate and were concentrated under reduced pressure to afford an opaque white oil. The residue was purified by flash column chromatography (silica gel: diam. 5 cm, ht. 14 cm; eluent: 50% ethyl acetate in hexanes) to afford thioester (+)-**57** (4.8 g, 92%) as white crystalline solid. Crystals of the thioester (+)-**57** suitable for X-ray diffraction were obtained from isopropanol.

^{1}H NMR (500 MHz, $CDCl_3$, 21 °C):	δ 8.01 (br-d, J = 4.6 Hz, 1H, N_9**H**), 7.30 (app-d, J = 8.1 Hz, 2H, SAr-*o*-**H**), 7.24 (d, J = 7.9 Hz, 2H, SAr-*m*-**H**), 6.95 (d, J = 4.1 Hz, 1H, C_{15}**H**), 6.30 (d, J = 4.1 Hz, 1H, C_{14}**H**), 4.89 (app-dd, J = 10.4, 3.5 Hz, 1H, C_7**H**), 4.79 (dd, J = 4.8, 1.5 Hz, 1H, C_8**H**), 3.33 (s, 3H, OC**H**$_3$), 3.09 (dd, J = 16.6, 10.5 Hz, 1H, C_6**H**$_a$), 2.98 (dd, J = 16.6, 3.5 Hz, 1H, C_6**H**$_b$), 2.37 (s, 3H, SArC**H**$_3$).
^{13}C NMR (125.8 MHz, $CDCl_3$, 21 °C):	δ 194.9, 159.9, 140.6, 134.6, 130.5, 123.5, 123.0, 115.4, 113.2, 106.4, 83.6, 55.3, 53.7, 45.1, 21.6.
FTIR (neat) cm^{-1}:	3216 (s), 3094 (m), 2931 (s), 2248 (w), 1670 (br-s), 1553 (s), 1423 (s), 1318 (s), 1087 (s), 733 (s).
HRMS (DART) (*m/z*):	calc'd for $C_{17}H_{18}BrN_2O_3S$, $[M+H]^+$: 409.0216, found: 409.0212.
$[\alpha]_D^{22}$:	+97.8 (*c* 0.3, $CHCl_3$).
M.p.:	133–135 °C (dec.).
TLC (25% hexanes in ethyl acetate), R*f*:	0.42 (CAM, UV).

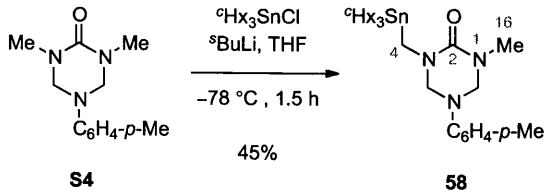


1,3-Dimethyl-5-(*p*-tolyl)-1,3,5-triazinan-2-one (S4):

p-Toluidine (**S2**, 12.2 g, 113 mmol, 1.00 equiv) was added as a solid to a solution of *N,N'*-dimethylurea (**S3**, 10.0 g, 113 mmol, 1 equiv) in formalin (37% wt in water, 18.4 ml, 227 mmol, 2.00 equiv) at 23 °C, and the resulting suspension was heated to 100 °C. After 2 d, the reaction mixture was allowed to cool to 23 °C, and was partitioned between dichloromethane (500 mL) and water (500 mL). The layers were separated, and the aqueous layer was extracted with dichloromethane (3 × 100 mL). The combined organic layers were dried over anhydrous sodium sulfate, and were concentrated under reduced pressure. The solid residue was purified by crystallization from hot hexanes to afford triazone **S4** (17.4 g, 70%) as a tan crystalline solid.[9]

^{1}H NMR (500 MHz, $CDCl_3$, 21 °C):	δ 7.06 (d, J = 8.5 Hz, 2H, NAr-*o*-**H**), 6.89 (d, J = 8.5 Hz, 2H, NAr-*m*-**H**), 4.60 (s, 4H, NC**H$_2$**N, NC**H$_2$**N), 2.85 (s, 6H, NC**H$_3$**, NC**H$_3$**), 2.27 (s, 3H, NArC**H$_3$**).
^{13}C NMR (125.8 MHz, $CDCl_3$, 21 °C):	155.9, 145.6, 132.0, 129.7, 119.2, 67.1, 32.1, 20.4.
FTIR (neat) cm^{-1}:	3029 (s), 2872 (s), 1638 (s), 1513 (s), 1451 (m), 1403 (m), 1294 (m), 1197 (m), 1093 (w).
HRMS (ESI) (*m/z*):	calc'd for $C_{12}H_{17}N_3NaO$, $[M+Na]^+$: 242.1264, found: 242.1275.
M.p.:	79–82 °C.
TLC (10% ethyl acetate in hexanes), R*f*:	0.80 (CAM, UV).

[9] The reaction procedure was developed and optimized in collaboration with Dr. Dustin Siegel. Final experimental procedure and yield were adopted from Dr. Dustin Siegel's experimental result.

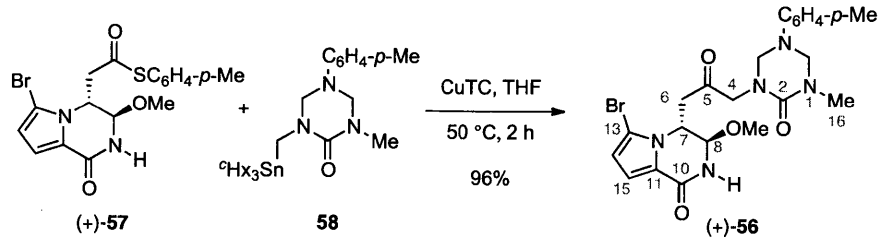


S4 **58**

1-Methyl-5-(*p*-tolyl)-3-((tricyclohexylstannyl)methyl)-1,3,5-triazinan-2-one (58):

To a solution of triazone **S4** (10.0 g, 46.0 mmol, 1 equiv) in tetrahydrofuran (400 mL) at −78 °C was added *sec*-butyllithium (1.4 M in cyclohexane, 34.5 mL, 48.0 mmol, 1.05 equiv) rapidly via cannula. After 10 min, the resulting bright orange mixture was added via cannula over a 15 min period to a solution of tricyclohexyltin chloride (20.3 g, 50.0 mmol, 1.10 equiv) in tetrahydrofuran (400 mL) at −78 °C. After 1.5 h, saturated aqueous ammonium chloride solution (100 mL) was added via syringe, and the resulting mixture was concentrated under reduced pressure. The residue was partitioned between dichloromethane (800 mL) and water (800 mL). The layers were separated, and the organic layer was washed with brine (800 mL), was dried over anhydrous sodium sulfate, and was concentrated under reduced pressure. The crude residue absorbed onto silica gel was purified by flash column chromatography (silica gel: diam. 6 cm, ht. 15 cm; eluent: hexanes then 10% ethyl acetate in hexanes) to afford stannyltriazone **58** (12.1 g, 45%) as a white solid.[9]

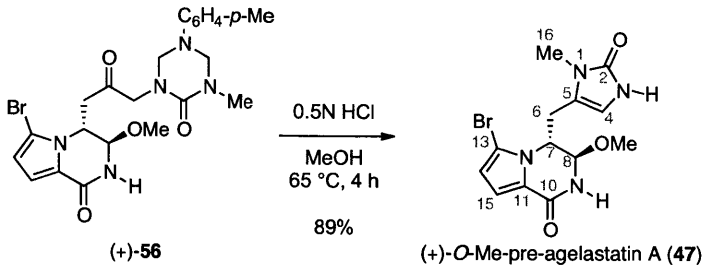
^{1}H NMR (500 MHz, $CDCl_3$, 21 °C):	δ 7.07 (dd, J = 8.7, 0.7 Hz, 2H, NAr-*o*-**H**), 6.89 (d, J = 8.5 Hz, 2H, NAr-*m*-**H**), 4.60 (s, 2H, NC**H$_2$**N), 4.58 (s, 2H, NC**H$_2$**N), 2.85 (s, 3H, NC**H$_3$**), 2.78 (t, J = 12.2 Hz, 2H, NC**H$_2$**Sn), 2.27 (s, 3H, NArC**H$_3$**), 1.82-1.74 (m, 6H, ^{c}Hx), 1.65-1.56 (m, 9H, ^{c}Hx), 1.52-1.13 (m, 18H, ^{c}Hx).
^{13}C NMR (125.8 MHz, $CDCl_3$, 21 °C):	δ 156.3, 146.1, 132.2, 130.0, 119.5, 69.2, 67.3, 32.7, 32.3, 29.5, 28.7, 27.9, 27.4, 20.8.
FTIR (neat) cm^{-1}:	2915 (s), 2844 (s), 1636 (s), 1515 (s), 1444 (s), 1407 (m), 1299 (s), 1201 (m), 991 (m).
HRMS (DART) (*m/z*):	calc'd for $C_{30}H_{50}N_3OSn$, $[M+H]^+$: 588.2987, found: 588.2982.
M.p.:	59–62 °C.
TLC (15% ethyl acetate in hexanes), R*f*:	0.20 (CAM, UV).



(+)-(3*R*,4*R*)-6-Bromo-3-methoxy-4-(3-(3-methyl-2-oxo-5-(*p*-tolyl)-1,3,5-triazinan-1-yl)-2-oxopropyl)-3,4-dihydropyrrolo[1,2-a]pyrazin-1(2*H*)-one (56):

A flask was charged with thioester (+)-**57** (173 mg, 0.423 mmol, 1 equiv), stannyltriazone **58** (298 mg, 0.508 mmol, 1.20 equiv), and copper(I)-thiophene-2-carboxylate (CuTC, 202 mg, 1.06 mmol 2.50 equiv) at 23 °C and placed under an argon atmosphere. Anhydrous tetrahydrofuran (8.4 mL) was added via syringe, and the entire reaction mixture was degassed thoroughly by passage of a stream of argon. After the reaction mixture was heated to 60 °C for 1 h, the resulting brown reaction mixture was allowed to cool to 23 °C, was diluted with ethyl acetate (10 mL) and saturated aqueous ammonium chloride solution (15 mL), and was stirred at 23 °C. After 15 min, the reaction mixture was diluted with water (10 mL) and ethyl acetate (10 mL). The layers were separated and the aqueous layer was extracted with ethyl acetate (2 × 10 mL). The combined organic layers were dried over anhydrous sodium sulfate and was concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel: diam. 3 cm, ht. 11 cm; eluent: 3% methanol in ethyl acetate then 7% methanol in ethyl acetate) and was lyophilized from benzene to afford ketone (+)-**56** (188 mg, 88%) as a light tan solid.

^{1}H NMR (500 MHz, $CDCl_3$, 21 °C):	δ 7.04 (dd, *J* = 8.6, 0.6 Hz, 2H, NAr-*o*-**H**), 6.93 (d, *J* = 4.0 Hz, 1H, C_{15}**H**), 6.89 (d, *J* = 8.5 Hz, 2H, NAr-*m*-**H**), 6.55 (d, *J* = 4.6 Hz, 1H, N_9**H**), 6.26 (d, *J* = 4.1 Hz, 1H, C_{14}**H**), 4.85 (ddd, *J* = 11.2, 2.8, 1.4 Hz, 1H, C_7**H**), 4.81 (d, *J* = 11.6 Hz, 1H, NC**H$_2$**N), 4.71 (d, *J* = 12.0, Hz, 1H, NC**H$_2$**N), 4.66 (dd, *J* = 11.7, 1.3 Hz, 1H, NC**H$_2$**N), 4.63-4.60 (m, 2H, C_8**H**, NC**H$_2$**N), 3.92 (d, *J* = 17.7 Hz, 1H, C_4**H$_a$**), 3.85 (d, *J* = 17.7 Hz, 1H, C_4**H$_b$**) 3.33 (s, 3H, O**CH$_3$**), 2.92 (s, 3H, C_{16}**H$_3$**), 2.79 (dd, *J* = 17.9, 11.2, Hz, 1H, C_6**H$_a$**), 2.39 (dd, *J* = 17.9, 2.9 Hz, 1H, C_6**H$_b$**), 2.23 (s, 3H, NArC**H$_3$**).
^{13}C NMR (125.8 MHz, $CDCl_3$, 21 °C):	δ 204.4, 159.5, 155.8, 145.4, 132.7, 130.1, 123.6, 119.4, 114.7, 112.7, 105.7, 83.4, 67.8, 66.8, 55.6, 55.0, 52.7, 41.1, 32.2, 20.7.
FTIR (neat) cm^{-1}:	3248 (m), 2921 (m), 1724, (m), 1667 (s), 1640 (s), 1514 (s), 1422 (s), 1316 (s), 1087 (m).
HRMS (ESI) (*m/z*):	calc'd for $C_{22}H_{26}BrN_5NaO_4$, $[M+Na]^+$: 526.1060, found: 526.1063.
$[\alpha]_D^{22}$:	+81.1 (c 0.62, $CHCl_3$).
M.p.:	101–105 °C.
TLC (5% methanol in ethyl acetate), R*f*:	0.20 (CAM, UV).



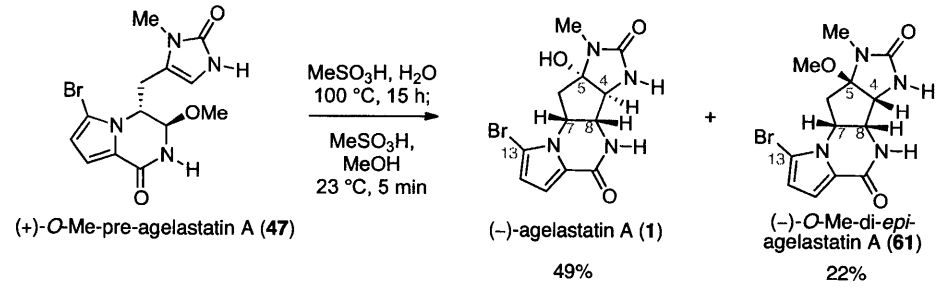
(+)-*O*-Methyl-pre-agelastatin A (47):

Aqueous hydrochloric acid solution (0.5 N, 23.8 mL, 11.9 mmol, 2.00 equiv) was added via syringe to a solution of ketone (+)-**56** (3.00 g, 5.90 mmol, 1 equiv) in methanol (1.18 L) at 23 °C, and the entire reaction mixture was degassed thoroughly by passage of a stream of argon. After the reaction mixture was heated to 65 °C for 4 h, the light pink reaction mixture was allowed to cool to 23 °C, and was concentrated to approximately 250 mL volume under reduced pressure. The resulting solution was basified to pH = 8 by the addition of a 5% aqueous ammonium hydroxide in methanol solution and the reaction mixture became a clear light orange color. A silica gel (50 mL) slurry in a 1% aqueous ammonium hydroxide in methanol solution (75 mL) was added and the resulting mixture was concentrated to dryness under reduced pressure. The crude residue adsorbed onto silica gel was purified by flash column chromatography (silica gel: diam. 5 cm, ht. 15 cm; eluent: 9% methanol, 1% ammonium hydroxide in chloroform to 13.5% methanol, 1.5% ammonium hydroxide in chloroform) to afford (+)-*O*-methyl-pre-agelastatin A (**47**, 1.87 g, 89%) as a light tan solid.[9]

(+)-*O*-Methyl-pre-agelastatin A (**47**) was found to be 99% ee by chiral HPLC analysis [Chiralcel OD-H; 0.8 mL/min; 35% isopropanol in hexanes; t_R(major) = 14.9 min, t_R(minor) = 12.1 min]. Crystals of (+)-*O*-methyl-pre-agelastatin A (**47**) suitable for X-ray diffraction were obtained from methanol. (+)-*O*-Methyl-pre-agelastatin A (**47**) is best used immediately in the following step; however, it could be stored as a dry solid at –8 °C under an argon atmosphere, or as a suspension frozen in benzene at –8 °C under an argon atmosphere for greater than a month. (+)-*O*-Methyl-pre-agelastatin A (**47**) is sparingly soluble in organic solvents, methanol, and water.

^{1}H NMR (500 MHz, CD_3OD, 21 °C):	δ 6.90 (dd, J = 4.1, 0.4 Hz, 1H, C_{15}**H**), 6.27 (d, J = 4.1 Hz, 1H, C_{14}**H**), 5.97 (t, J = 0.7 Hz, 1H, C_4**H**), 4.76 (d, J = 1.6 Hz, 1H, C_8**H**), 4.54 (ddd, J = 8.4, 6.1, 1.5 Hz, 1H, C_7**H**), 3.35 (s, 3H, OC**H$_3$**), 3.14 (s, 3H, C_{16}**H$_3$**), 2.95 (ddd, J = 15.4, 6.0, 0.8 Hz, 1H, C_6**H$_a$**), 2.78 (ddd, J = 15.4, 8.5, 0.8 Hz, 1H, C_6**H$_b$**).
^{13}C NMR (125.8 MHz, CD_3OD, 21 °C):	δ 161.2, 156.1, 124.5, 120.2, 116.1, 113.5, 108.8, 108.5, 84.9, 58.0, 55.2, 29.5, 27.7.
FTIR (neat) cm^{-1}:	3227 (br-m), 2936 (w), 1666 (s), 1552 (m), 1460 (w), 1421 (m), 1386 (w), 1319 (m), 1085 (m).
HRMS (ESI) (*m/z*):	calc'd for $C_{13}H_{15}BrN_4NaO_3$, $[M+Na]^+$: 377.0220, found: 377.0221.
$[\alpha]_D^{22}$:	+248.7 (c 0.032, methanol).
M.p.:	157-161 °C (dec.).

TLC (18% methanol, 2% ammonium hydroxide in chloroform), R*f*: 0.40 (CAM, UV).



(–)-Agelastatin A (1) and (–)-*O*-methyl-di-*epi*-agelastatin A (61):

A solution of methanesulfonic acid (10.9 mL, 168 mmol, 20.0 equiv) in water (100 mL) was added slowly via syringe to a solution of (+)-*O*-methyl-pre-agelastatin A (**47**, 2.97 g, 8.39 mmol, 1 equiv) in water (1.68 L) at 23 °C. The entire reaction mixture was degassed thoroughly by passage of a stream of argon, and the mixture was heated to 100 °C. After 15 h, the reaction mixture was allowed to cool to 23 °C and was basified to pH = 8 by addition of 5% aqueous ammonium hydroxide solution. The resulting mixture was concentrated under reduced pressure. The crude residue was dissolved in methanol (839 mL) and the resulting mixture was acidified to pH = 2 by the addition of a solution of 5% methanesulfonic acid in methanol (20 mL). After 5 min, the reaction mixture was basified to pH = 8 by addition of by addition of 5% aqueous ammonium hydroxide solution. The resulting mixture was concentrated under reduced pressure, and the crude residue adsorbed onto silica gel was purified by flash column chromatography (silica gel: diam. 7 cm, ht. 14 cm; eluent: 9% methanol, 1.0% ammonium hydroxide in chloroform to 13.5% methanol, 1.5% ammonium hydroxide in chloroform) to afford (–)-agelastatin A (**1**, 1.40 g, 49%) as a tan solid.[9] (–)-Agelastatin A (**1**) was found to be 99% ee by chiral HPLC analysis [Chiralpak AD-H; 0.53 mL/min; 10% isopropanol in hexanes; t_R(major) = 40.0 min, t_R(minor) = 24.5 min]. (–)-*O*-Methyl-di-*epi*-agelastatin A (**61**, 668 mg, 22%) was also isolated as light tan solid. (–)-Agelastatin A (**1**) is sparingly soluble in organic solvents, methanol, and water. Crystals of (–)-agelastatin A (**1**) suitable for X-ray diffraction were obtained from methanol.

(–)-agelastatin A (1):

^{1}H NMR (500 MHz, CD_3OD, 21 °C): δ 6.92 (d, J = 4.0 Hz, 1H, C_{15}**H**), 6.33 (d, J = 4.1 Hz, 1H, C_{14}**H**), 4.60 (app-dt, J = 11.9, 6.0 Hz, 1H, C_7**H**), 4.09 (d, J = 5.4 Hz, 1H, C_8H), 3.88 (s, 1H, C_4**H**), 2.81 (s, 3H, C_{16}**H**$_3$), 2.65 (dd, J = 13.1, 6.3 Hz, 1H, C_6**H**), 2.10 (app-t, J = 12.7 Hz, 1H, C_6**H**).

^{13}C NMR (125.8 MHz, CD_3OD, 21 °C): δ 161.6, 161.2, 124.3, 116.2, 113.9, 107.4, 95.8, 67.5, 62.3, 54.5, 40.1, 24.4.

FTIR (neat) cm^{-1}: 3269 (m), 2921 (w), 1651 (s), 1552 (w), 1423 (m), 1378 (w), 1090 (w), 746 (w).

HRMS (ESI) (*m/z*): calc'd for $C_{12}H_{13}BrN_4NaO_3$, $[M+Na]^+$: 363.0063, found: 363.0073.

$[\alpha]_D^{22}$: –87.6 (c 0.10, methanol).[10]

M.p.: 213–215 °C (dec.).

TLC (18% methanol, 2% ammonium hydroxide in chloroform), R*f*: 0.34 (CAM, UV).

(–)-*O*-methyl-di-*epi*-agelastatin A (61):

^{1}H NMR (500 MHz, CD_3OD, 21 °C): δ 6.90 (d, J = 4.1 Hz, 1H, C_{15}**H**), 6.33 (d, J = 4.1 Hz, 1H, C_{14}**H**), 4.95 (ddd, J = 10.4, 7.2, 5.1 Hz, 1H, C_7**H**), 4.42 (app-t, J = 5.4 Hz, 1H, C_8H), 4.22 (d, J = 5.9 Hz, 1H, C_4**H**), 3.13 (s, 3H, OC**H**$_3$), 2.69 (s, 3H, NC**H**$_3$), 2.53 (dd, J = 13.4, 7.1 Hz, 1H, C_6**H**), 2.32 (dd, J = 13.5 10.5 Hz, 1H, C_6**H**).

^{13}C NMR (125.8 MHz, CD_3OD, 21 °C): δ 162.4, 161.6, 124.9, 116.3, 114.3, 107.2, 100.1, 59.3, 58.6, 55.1, 49.9, 42.2, 24.9.

FTIR (neat) cm^{-1}: 3374 (m), 2951 (w), 1703 (s), 1659 (s), 1552 (m), 1424 (m), 1346 (w).

HRMS (ESI) (*m/z*): calc'd for $C_{13}H_{15}BrN_4NaO_3$, $[M+Na]^+$: 377.0220, found: 377.0220.

$[\alpha]_D^{22}$: –70.0 (c 0.042, methanol).

M.p.: 205–208 °C.

TLC (18% methanol, 2% ammonium hydroxide in chloroform), R*f*: 0.60 (CAM, UV).

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[10] Optical rotations from natural samples of (–)-agelastatin A (**1**):

$[\alpha]_D$ = –59.3 (c 0.13, methanol), Hong, T. W.; Jímenez, D. R.; Molinski, T. F. *J. Nat. Prod.*, **1998**, *61*, 158–161.

$[\alpha]_D^{26}$ = –88.9 (c 0.09, chloroform), Pettit, G. R.; Ducki, S.; Herald, D. L.; Doubek, D. L.; Schmidt, J. M.; Chapuis, J. *Oncol. Res.* **2005**, *15*, 11–20.

$[\alpha]_D^{25}$ = –58.5 (c 0.21, methanol), Tilvi, S.; Moriou, C.; Martin, M.; Gallard, J.; Sorres, J.; Patel, K.; Petek, S.; Debitus, C.; Ermolenko, L.; Al-Mourabit, A. *J. Nat. Prod.* **2010**, *73*, 720–723.

Optical rotations from synthetic samples of (–)-agelastatin A (**1**):

$[\alpha]_D^{20}$ = –65.5 (c 0.5, methanol), Feldman, K. S.; Saunders, J. C. *J. Am. Chem. Soc.* **2002**, *124*, 9060–9061.

$[\alpha]_D$ = –84.2 (c 1, methanol), Domostoj, M. M.; Irving, E.; Scheinmann, F.; Hale, K. J. *Org. Lett.* **2004**, *6*, 2615–2618.

$[\alpha]_D^{20}$ = –62.2 (c 0.18, methanol), Davis, F. A.; Deng, J. *Org. Lett.* **2005**, *7*, 621–623.

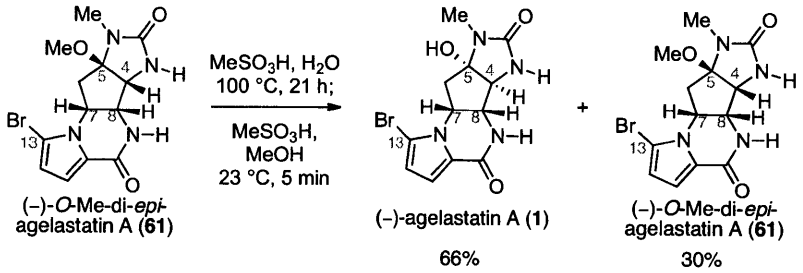
(+)-Agelastatin A, $[\alpha]_D$ = +53.2 (c 0.13, methanol), Trost, B. M.; Dong, G. *J. Am. Chem. Soc.* **2006**, *128*, 6054–6055.

$[\alpha]_D^{14}$ = –83.8 (c 0.21, methanol), Ichikawa, Y.; Yamaoka, T.; Nakano, K.; Kotsuki, H. *Org. Lett.* **2007**, *9*, 2989–2992.

$[\alpha]_D^{26}$ = –64.4 (c 0.15, methanol), Yoshimitsu, T.; Ino, T.; Tanaka, T. *Org. Lett.* **2008**, *10*, 5457–5460.

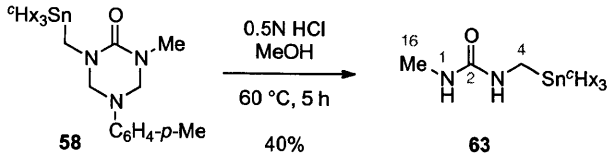
$[\alpha]_D^{23}$ = –83.4 (c 0.93, methanol), Hama, N.; Matsuda, T.; Sato, T.; Chida, N. *Org. Lett.* **2009**, *11*, 2687–2690.

$[\alpha]_D^{23}$ = –87.0 (c 1.1, methanol), When, P. M.; Du Bois, J. *Angew. Chem., Int. Ed. Engl.* **2009**, *48*, 3802–3805.



Equilibration of (–)-*O*-methyl-di-*epi*-agelastatin A (29) to (–)-agelastatin A (1):

A solution of methanesulfonic acid (613 μL, 9.44 mmol, 5.00 equiv) in water (10 mL) was added slowly via syringe to a solution of (–)-*O*-methyl-di-*epi*-agelastatin A (**61**, 668 mg, 1.89 mmol, 1 equiv) in water (378 mL) at 23 °C. The entire reaction mixture was degassed thoroughly by passage of a stream of argon and was heated to 100 °C. After 21 h, the reaction mixture was allowed to cool to 23 °C and was basified to pH = 8 by addition of 5% aqueous ammonium hydroxide solution. The resulting mixture was concentrated under reduced pressure. The crude residue was dissolved in methanol (378 mL) and the resulting mixture was acidified to pH = 2 by the addition of a solution of 5% methanesulfonic acid in methanol (20 mL). After 5 min, the reaction mixture was basified to pH = 8 by addition of by addition of 5% aqueous ammonium hydroxide solution. The resulting mixture was concentrated under reduced pressure, and the crude residue adsorbed onto silica gel was purified by flash column chromatography (silica gel: diam. 4 cm, ht. 14 cm; eluent: 9% methanol, 1.0% ammonium hydroxide in chloroform to 13.5% methanol, 1.5% ammonium hydroxide in chloroform) to afford (–)-agelastatin A (**1**, 421 mg, 66%) as a tan solid. (–)-*O*-Methyl-di-*epi*-agelastatin A (**61**, 200 mg, 30%) was also isolated as a light tan solid.[9]

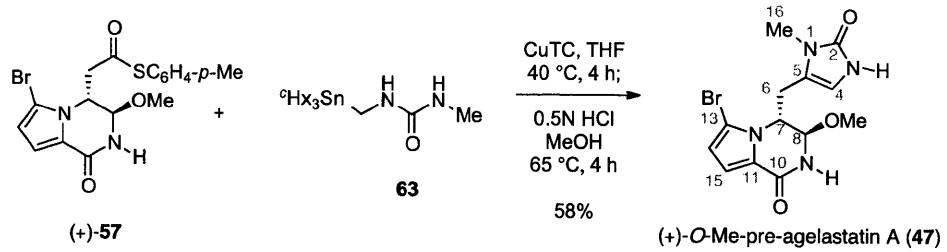


1-Methyl-3-((tricyclohexylstannyl)methyl)urea (63):

Aqueous hydrochloric acid solution (0.5 N, 2.30 mL, 1.15 mmol, 2.00 equiv) was added via syringe to a solution of stannyltriazone **58** (338 mg, 0.576 mmol, 1 equiv) in methanol (11.5 mL) at 23 °C, and the resulting mixture was heated to 60 °C. After 5 h, the reaction mixture was allowed to cool to 23 °C, and was neutralized with saturated aqueous sodium bicarbonate solution (4 mL). The resulting mixture was concentrated under reduced pressure, and the residue was partitioned between dichloromethane (50 mL) and water (50 mL). The layers were separated, and the aqueous layer was extracted with dichloromethane (2 × 50 mL). The combined organic layers were dried over anhydrous sodium sulfate and were concentrated under reduced pressure. The crude residue was purified by flash column chromatography (silica gel: diam. 2.5 cm, ht. 15 cm; eluent: 15% ethyl acetate in dichloromethane) to afford stannylurea **63** (104 mg, 40%) as a white crystalline solid.[9]

^{1}H NMR (500 MHz, $CDCl_3$, 21 °C):	δ 4.63 (br-s, 1H, N**H**), 4.33 (br-s, 1H, N**H**), 2.77 (br-d, *J* = 4.6 Hz, $C_{16}\mathbf{H}_3$), 2.75-2.65 (m, 2H, $C_4\mathbf{H}_2$), 1.85-1.74 (m, 6H, ^{c}Hx), 1.70-1.44 (m, 18H, ^{c}Hx), 1.36-1.16 (m, 9H, ^{c}Hx).
^{13}C NMR (125.8 MHz, $CDCl_3$, 21 °C):	δ 160.7, 32.5, 29.3, 27.5, 27.2, 26.9. 22.3.
FTIR (neat) cm^{-1}:	3357 (br-m), 2912 (s), 2842 (s), 1628 (s), 1580 (s), 1442 (m), 1279 (m), 1167 (w).
HRMS (ESI) (*m/z*):	calc'd for $C_{21}H_{40}N_2NaOSn$, $[M+Na]^+$: 479.2068, found: 479.2056.
M.p.:	144–148 °C.

TLC (15% ethyl acetate in dichloromethane), R*f*: 0.25 (CAM, UV).

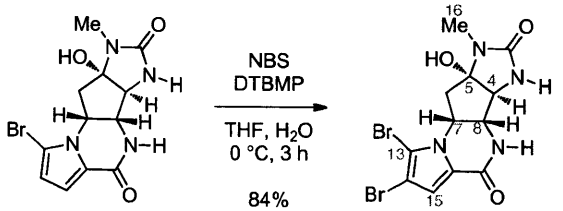


Direct synthesis of (+)-*O*-methyl-pre-agelastatin A (47):

Anhydrous tetrahydrofuran (1 mL) was added via syringe to a flask charged with (+)-**57** (20.0 mg, 49.0 μmol, 1 equiv), urea **63** (67.0 mg, 147 μmol, 3.00 equiv), and copper(I)-thiophene-2-carboxylate (CuTC, 23.3 mg, 123 μmol, 2.50 equiv) at 23 °C and under an argon atmosphere. The entire reaction mixture was degassed thoroughly by passage of a stream of argon, and the mixture was heated to 40 °C. After 4 h, the reaction mixture was allowed to cool to 23 °C, was diluted with methanol (7 mL), and was filtered through a plug of celite with methanol washings (3 × 1 mL). Aqueous hydrochloric acid solution (0.5 N, 196 μL, 98.0 μmol, 2.00 equiv) was added to the filtrate, and the resulting mixture was heated to 65 °C. After 4 h, the reaction mixture was allowed to cool to 23 °C and was basified to pH = 8 by the addition of a 5% aqueous ammonium hydroxide in methanol solution. The resulting mixture was concentrated under reduced pressure, and the crude residue adsorbed onto silica gel was purified by flash column chromatography (silica gel: diam. 1.5 cm, ht. 10 cm; eluent: 10% methanol in dichloromethane to 15% methanol in dichloromethane) to afford (+)-*O*-methyl-pre-agelastatin A (**47**, 10.0 mg, 58%) as a tan solid.[11]

(+)-*O*-Methyl-pre-agelastatin A (**47**) was found to be 99% ee by chiral HPLC analysis [Chiralcel OD-H; 0.8 mL/min; 35% isopropanol in hexanes; t_R(major) = 14.9 min, t_R(minor) = 12.1 min.

[11] The reaction procedure was developed and optimized by Dr. Dustin Siegel. Final experimental procedure and yield were adopted from Dr. Dustin Siegel's experimental result.



(–)-agelastatin A (**1**) (–)-agelastatin B (**2**)

(–)-Agelastatin B (2):

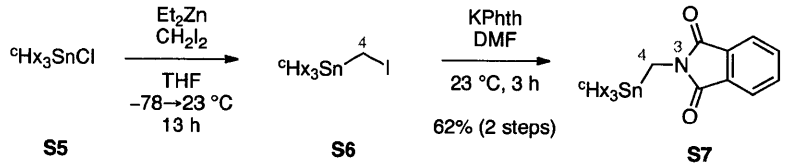
N-Bromosuccinimide (NBS, 5.0 mg, 28 μmol, 1.1 equiv) was added as a solid in one portion to a solution of (–)-agelastatin A (**1**, 9.1 mg, 27 μmol, 1 equiv) and 2,6-di-*tert*-butyl-4-methylpyridine (DTBMP, 8.3 mg, 41 μmol, 1.5 equiv) in water (500 μL) and tetrahydrofuran (1.00 mL) at 0 °C. After 2 h, a mixture of saturated aqueous sodium thiosulfate solution and saturated aqueous sodium bicarbonate solution (1:1, 100 μL,) was added, and the resulting mixture was purified directly by flash column chromatography (silica gel: diam. 1.5 cm, ht. 9 cm; eluent: 9% methanol, 1.0% ammonium hydroxide in chloroform to 13.5% methanol, 1.3% ammonium hydroxide in chloroform) to afford (–)-agelastatin B (**2**, 9.4 mg, 84%) as a white crystalline solid.

(–)-Agelastatin B (**2**) was found to be 99% ee by chiral HPLC analysis [Chiralpak AD-H; 0.53 mL/min; 10% isopropanol in hexanes; t_R(major) = 27.7 min, t_R(minor) = 21.1 min]. (–)-Agelastatin B (**2**) is sparingly soluble in organic solvents, methanol, and water. Crystals of (–)-agelastatin B (**2**) suitable for X-ray diffraction were obtained from methanol. For a thermal ellipsoid representation of (–)-agelastatin B (**2**), see page S58.

^{1}H NMR (500 MHz, CD_3OD, 21 °C):	δ 6.97 (s, 1H, C_{15}**H**), 4.60 (app-dt, J = 12.0, 6.0 Hz, 1H, C_7**H**), 4.11 (d, J = 5.4 Hz, 1H, C_8**H**), 3.88 (s, 1H, C_4**H**), 2.81 (s, 3H, C_{16}**H**$_3$), 2.68 (dd, J = 13.1, 6.5 Hz, 1H, C_6**H**$_a$), 2.12 (app-t, J = 12.6 Hz, 1H, C_6**H**$_b$).
^{13}C NMR (125.8 MHz, CD_3OD, 21 °C):	δ 161.5, 160.2, 124.9, 117.1, 108.9, 101.8, 95.7, 67.5, 62.2, 55.5, 40.0, 24.4.
FTIR (neat) cm^{-1}:	3219 (m), 2919 (m), 1639 (s), 1548 (m), 1497 (m), 1403 (m), 1360 (m).
HRMS (ESI) (*m/z*):	calc'd for $C_{12}H_{13}Br_2N_4O_3$, $[M+H]^+$: 418.9349, found: 418.9343.
$[\alpha]_D^{22}$:	–60.6 (c 0.018, methanol).[12]
M.p.:	211–214 °C (dec.).

TLC (18% methanol, 2% ammonium hydroxide in chloroform), R*f*: 0.25 (CAM, UV).

[12] Literature value: $[\alpha]_D^{20}$ = –60.3 (c 0.50, methanol), Feldman, K. S.; Saunders, J. C. *J. Am. Chem. Soc.* **2002**, *124*, 9060–9061.



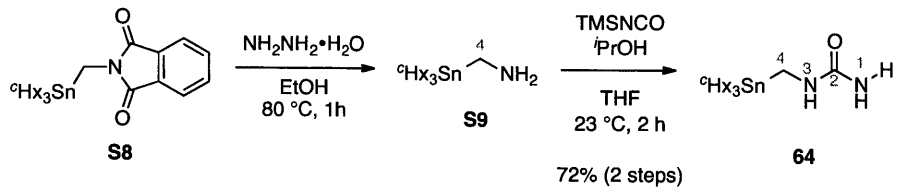
2-((Tricyclohexylstannyl)methyl)isoindoline-1,3-dione (S7): [13]

Diiodomethane (3.3 mL, 40 mmol, 5.0 equiv) was added dropwise via syringe to a solution of diethylzinc (1 M in hexanes, 20 mL, 20 mmol, 2.5 equiv) in tetrahydrofuran (27 mL) at –78 °C, and the reaction mixture was warmed to –40 °C. After 1 h, a solution of tricyclohexyltin chloride (**S5**, 3.3 g, 8.0 mmol, 1 equiv) in tetrahydrofuran (6 mL) was added via cannula, and the reaction mixture was warmed to 0 °C. After 3 h, the reaction mixture was allowed to warm to 23 °C. After an additional 12 h, the reaction mixture was partitioned between heptanes (80 mL) and water (26 mL). Aqueous hydrochloric acid solution (1 N, 30 mL) was added, and the layers were separated. The organic phase was washed with water (2 × 25 mL) and brine (25 mL), was dried over anhydrous sodium sulfate, and was concentrated under reduced pressure to afford crude **S6** as a white solid.

Crude **S6** was dissolved in dimethylformamide (40 mL), and potassium phthalimide (2.4 g, 13 mmol, 1.6 equiv) was added as a solid at 23 °C. After 3 h, the reaction mixture was partitioned between water (400 mL) and ethyl acetate (400 mL). The layers were separated, and the organic layer was washed with water (200 mL), was dried over anhydrous sodium sulfate, and was concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel: diam. 4 cm, ht. 11 cm; eluent: 2.5% ethyl acetate in hexane) to afford stannylphthalimide **S7** (2.6 g, 62% over 2 steps) as a light green solid.

^{1}H NMR (500 MHz, $CDCl_3$, 21 °C):	δ 7.75 (dd, J = 5.3, 3.1 Hz, 2H, Ar**H**), 7.62 (dd, J = 5.5, 3.1 Hz, 2H, Ar**H**), 3.19 (s, 2H, $C_4\mathbf{H}_2$) 1.86-1.74 (m, 6H, ^{c}Hx), 1.64-1.46 (m, 18H, ^{c}Hx), 1.30-1.10 (m, 9H, ^{c}Hx).
^{13}C NMR (125.8 MHz, $CDCl_3$, 21 °C):	δ 168.9, 133.7, 132.5, 122.8, 32.2, 29.3, 28.0, 27.2, 19.4.
FTIR (neat) cm^{-1}:	3451 (w), 2920 (s), 2843 (s), 1773 (s), 1705 (s), 1389 (s), 1056 (s), 879 (s), 717 (s).
HRMS (ESI) (*m/z*):	calc'd for $C_{27}H_{39}NNaO_3Sn$, $[M+Na]^+$: 552.1911, found: 552.1913.
M.p.:	68–71 °C.
TLC (9% ethyl acetate in hexane), R*f*:	0.5 (CAM, UV).

[13] For a previous report of the synthesis of compounds related to **S7**, see: Jensen, M. S.; Yang, C.; Hsiao, Y.; Rivera, N.; Wells, K. M.; Chung, J. Y. L.; Yasuda, N.; Hughes, D. L.; Reider, P. J. *Org. Lett.* **2000**, 2, 1081–1084.



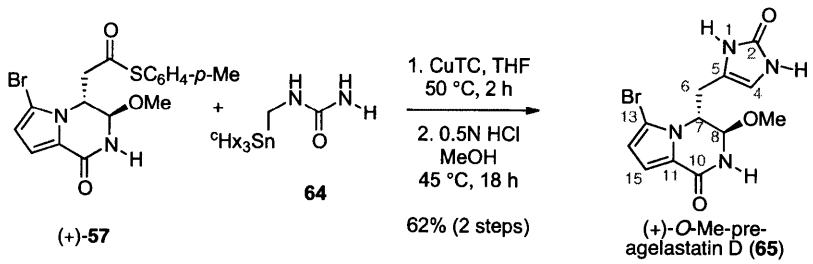
1-((Tricyclohexylstannyl)methyl)urea (34):

Hydrazine monohydrate (10.6 mL) was added dropwise via syringe to a solution of stannylphthalimide **S7** (2.61 g, 4.95 mmol, 1 equiv) in ethanol (80 mL) at 80 °C. After 1 h, the reaction mixture was allowed to cool to 23 °C, and was partitioned between water (480 mL) and diethyl ether (480 mL). The layers were separated, and the organic layer was washed with water (3 × 400 mL) and brine (200 mL), was dried over anhydrous sodium sulfate, and was concentrated under reduced pressure to afford stannylamine **S9**. Stannylamine **S9** was observed to be highly sensitive, and was used immediately in the following step.[14]

Stannylamine **S9** was dissolved in tetrahydrofuran (96 mL), and trimethylsilyl isocyanate (2.07 mL 14.4 mmol, 2.97 equiv) and isopropanol (590 μL, 7.66 mmol, 1.55 equiv) were added sequentially at 23 °C. After 2 h, water (10 mL) was added and the resulting mixture was concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel: diam. 4.0 cm, ht. 9 cm; eluent: 50% ethyl acetate in hexane) to afford stannylurea **64** (1.58 g, 72% over two steps) as a white crystalline solid.

^{1}H NMR (500 MHz, $CDCl_3$, 21 °C):	δ 4.46 (br-s, 2H, $N_1\mathbf{H}_2$), 4.39 (br-s, 1H, $N_3\mathbf{H}$), 2.75 (br-s, 2H, $C_4\mathbf{H}_2$), 1.88-1.78 (m, 6H, ^{c}Hx), 1.68-1.46 (m, 18H, ^{c}Hx), 1.36-1.16 (m, 9H, ^{c}Hx).
^{13}C NMR (125.8 MHz, $CDCl_3$, 21 °C):	δ 160.4, 32.5, 29.4, 27.3, 27.1, 23.0.
FTIR (neat) cm^{-1}:	3353 (m), 3207 (w), 2917 (s), 2845 (s), 1646 (s), 1589 (s), 1554 (s), 1444 (s), 1350 (m), 1169 (m).
HRMS (ESI) (*m/z*):	calc'd for $C_{12}H_{15}BrN_4NaO_4$, $[M+Na]^+$: 381.0169, found: 381.0182.
M.p.:	128–131 °C.
TLC (50% ethyl acetate in hexane), R*f*:	0.21 (CAM).

[14] For a previous report of the synthesis of derivatives related to **S9**, see: Pearson, W. H.; Stoy, P.; Mi, Y *J. Org. Chem.* **2004**, *69*, 1919–1939.

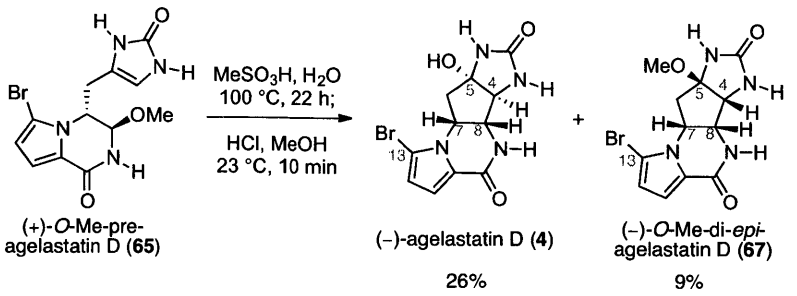


(+)-*O*-Methyl-pre-agelastatin D (65):

Anhydrous tetrahydrofuran (77 mL, degassed thoroughly by passage of a stream of argon) was added via cannula to a flask charged with thioester (+)-**57** (314 mg, 769 μmol, 1 equiv), urea **64** (1.02 g, 2.31 mmol, 3.00 equiv), and copper(I)-thiophene-2-carboxylate (CuTC, 306 mg, 1.54 mmol, 2.00 equiv) at 23 °C under an argon atmosphere, and the reaction mixture was heated to 50 °C. After 2 h, the reaction mixture was allowed to cool to 23 °C and was filtered through a plug of celite with methanol washings (3 × 10 mL). The resulting mixture was concentrated under reduced pressure, and the crude residue adsorbed onto silica gel was purified by flash column chromatography (silica gel: diam. 4.0 cm, ht. 10 cm; eluent: 14.0% methanol, 1.5% ammonium hydroxide in chloroform) to afford a mixture of the C4–C5 coupled open urea and N1–C5 hemiaminal cyclized diastereomers (194.1 mg) as a clear colorless oil. Aqueous hydrochloric acid solution (0.5 N, 2.20 mL, 1.08 mmol, 1.40 equiv) was added via syringe to a solution of this colorless oil in methanol (54 mL) at 23 °C, and the resulting mixture was heated to 45 °C under an argon atmosphere. After 18 h, the reaction mixture was allowed to cool to 23 °C and was neutralized with an 18.0% methanol, 2.0% ammonium hydroxide in chloroform solution. The resulting mixture was concentrated under reduced pressure, and the crude residue adsorbed onto silica gel was purified by flash column chromatography (silica gel: diam. 2.5 cm, ht. 10 cm; eluent: 14.0% methanol, 1.5% ammonium hydroxide in chloroform) to afford (+)-*O*-methyl-pre-agelastatin D (**65**, 162.2 mg, 62% over two steps) as a tan solid.

^{1}H NMR (500 MHz, CD_3OD, 21 °C):	δ 6.89 (dd, J = 4.0, 0.4 Hz, 1H, C_{15}**H**), 6.26 (d, J = 4.1 Hz, 1H, C_{14}**H**), 5.94 (t, J = 0.7 Hz, 1H, C_4**H**), 4.68 (d, J = 1.6 Hz, 1H, C_8**H**), 4.62 (ddd, J = 7.9, 6.9, 1.4 Hz, 1H, C_7**H**), 3.34 (s, 3H, OC**H**$_3$), 2.76 (ddd, J = 15.0, 6.8, 0.9 Hz, 1H, C_6**H**$_a$), 2.70 (ddd, J = 15.0, 7.7, 0.9 Hz, 1H, C_6**H**$_b$).
^{13}C NMR (125.8 MHz, CD_3OD, 21 °C):	δ 161.2, 157.2, 124.4, 118.7, 116.1, 113.4, 109.1, 108.7, 84.9, 57.8, 55.2, 30.7.
FTIR (neat) cm^{-1}:	3219 (br-s), 2936 (w), 2408 (w), 1680 (s), 1553 (m), 1459 (w), 1422 (m), 1387 (w), 1323 (m), 1088 (m).
HRMS (ESI) (*m/z*):	calc'd for $C_{12}H_{12}BrN_4NaO_3$, $[M+Na]^+$: 363.0063, found: 363.0053.
$[\alpha]_D^{22}$:	+234.5 (c 0.362, methanol).

TLC (14.0% methanol, 1.5% ammonium hydroxide in chloroform), R*f*: 0.29 (CAM, UV).



(–)-Agelastatin D (4), (–)-*O*-methyl-di-*epi*-agelastatin D (67), 68, and 70:

To a solution of (+)-*O*-methyl-pre-agelastatin D (**65**, 32.9 mg, 96.4 μmol, 1 equiv) in water (32 mL, degassed thoroughly by passage of a stream of argon) at 23 °C was added methanesulfonic acid (313 μL, 4.82 mmol, 50.0 equiv), and the reaction mixture was heated to 100 °C. After 22 h, the reaction mixture was allowed to cool to 23 °C, was basified to pH = 8 by addition of ammonium hydroxide, and was concentrated under reduced pressure. The residue was dissolved in methanol (32 mL) and the resulting mixture was acidified to pH = 3 by the addition of aqueous hydrochloric acid solution (1 N, 386 μL, 0.386 mmol, 4.00 equiv). After 10 min, the reaction mixture was basified to pH = 8 by the addition of ammonium hydroxide. The resulting mixture was concentrated under reduced pressure, and the crude residue adsorbed onto silica gel was purified by flash column chromatography (silica gel: diam. 2 cm, ht. 3 cm; eluent: 14.0% methanol, 1.5% ammonium hydroxide in chloroform) to afford (–)-agelastatin D (**4**, 8.2 mg, 26%) as a tan solid.

(–)-Agelastatin D (**4**) was found to be 99% ee by chiral HPLC analysis [Chiralpak AD-H; 0.53 mL/min; 10% isopropanol in hexanes; t_R(major) = 47.7 min, t_R(minor) = 29.3 min]. Crystals suitable for X-ray diffraction were obtained from methanol. For a thermal ellipsoid representation of (–)-agelastatin D (**4**), see page S62. (–)-Agelastatin D (**4**) was sparingly soluble in organic solvents, methanol, and water. (–)-Di-*epi*-methoxy-agelastatin D (**67**, 2.9 mg, 9%) was also isolated from the reaction mixture as a light yellow solid. An equal amount of pyrrolopyrazinone **68** and tetracycle **70** constituted approximately 40% of the mass balance.

(–)-agelastatin D (4):

^{1}H NMR (500 MHz, CD_3OD, 21 °C): δ 6.91 (d, J = 4.1 Hz, 1H, C_{15}**H**), 6.33 (d, J = 4.1 Hz, 1H, C_{14}**H**), 4.74 (app-dt, J = 11.9, 6.0 Hz, 1H, C_7**H**), 4.10 (d, J = 5.7 Hz, 1H, C_8**H**), 3.91 (s, 1H, C_4**H**), 2.54 (dd, J = 12.6, 6.6 Hz, 1H, C_6**H**$_a$), 2.21 (app-t, J = 12.4 Hz, 1H, C_6**H**$_b$).

^{1}H NMR (500 MHz, Pyridine-d_5, 21 °C): δ 9.20 (s, 1H, N**H**), 8.92 (s, 1H, N**H**), 8.82 (s, 1H, N**H**), 8.30 (s, 1H, N**H**), 7.28 (d, J = 3.9 Hz, 1H, C_{15}**H**), 6.42 (d, J = 3.9 Hz, 1H, C_{14}**H**), 5.13 (app-dt, J = 11.9, 6.0 Hz, 1H, C_7**H**), 4.66 (d, J = 2.2 Hz, 1H, C_4**H**), 4.44 (d, J = 5.5 Hz, 1H, C_8**H**) 2.95 (dd, J = 12.4, 6.5 Hz, 1H, C_6**H**$_a$), 2.84 (app-t, J = 12.2 Hz, 1H, C_6**H**$_b$).

^{13}C NMR (125.8 MHz, Pyridine-d_5, 21 °C): δ 162.1, 159.7, 125.5, 114.7, 113.0, 105.5, 93.1, 69.9, 62.7, 54.8, 44.5.

FTIR (neat) cm^{-1}: 3461 (br-s), 2360 (w), 1674 (s), 1640 (s), 1424 (w), 1218 (w), 1114 (w), 1073 (w), 734 (m).

HRMS (ESI) (*m/z*): calc'd for $C_{11}H_{11}BrN_4NaO_3$, $[M+Na]^+$: 348.9907, found: 348.9910.

$[\alpha]_D^{22}$: –43.2 (c 0.04, methanol),[15] –79.4 (c 0.02, pyridine).

TLC (18% methanol, 2% ammonium hydroxide in chloroform), R*f*: 0.18 (CAM, UV).

(–)-*O*-methyl-di-*epi*-agelastatin D (67):

^{1}H NMR (500 MHz, CD_3OD, 21 °C): δ 6.91 (d, *J* = 4.1 Hz, 1H, C_{15}**H**), 6.33 (d, *J* = 4.1 Hz, 1H, C_{14}**H**), 4.94-4.86[16] (m, 1H, C_7**H**), 4.41 (app-t, *J* = 5.3 Hz, 1H, C_8H), 4.22 (d, *J* = 5.6 Hz, 1H, C_4**H**), 3.25 (s, 3H, OC**H**$_3$), 2.64 (dd, *J* = 13.3, 7.2 Hz, 1H, C_6**H**$_a$), 2.20 (dd, *J* = 13.4, 10.8 Hz, 1H, C_6**H**$_b$).

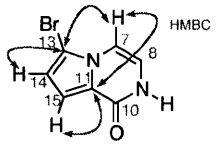
^{13}C NMR (125.8 MHz, CD_3OD, 21 °C): δ 162.8, 159.8, 125.8, 114.9, 113.2, 105.3, 97.0, 62.6, 58.3, 55.0, 49.5, 44.0.

FTIR (neat) cm^{-1}: 3428 (m), 1688 (s), 1647 (s), 1550 (s), 1422 (m), 1344 (w), 1068 (m).

HRMS (ESI) (*m/z*): calc'd for $C_{12}H_{13}BrN_4NaO_3$, $[M+Na]^+$: 363.0063, found: 363.0062.

$[\alpha]_D^{22}$: –78.1 (c 0.06, pyridine).

TLC (18% methanol, 2% ammonium hydroxide in chloroform), R*f*: 0.5 (CAM, UV).



68

pyrrolopyrazinone 68:

^{1}H NMR (500 MHz, CD_3OD, 21 °C): 7.29 (dd, *J* = 5.9, 0.8 Hz, 1H), 7.12 (dd, *J* = 4.3, 0.8 Hz, 1H), 6.72 (d, *J* = 5.9 Hz, 1H), 6.69 (d, *J* = 4.2 Hz, 1H).

^{1}H NMR (500 MHz, $CDCl_3$, 21 °C): δ 8.96 (s, 1H, N**H**), 7.16 (dd, *J* = 4.2, 0.8 Hz, 1H, C_{15}**H**), 7.09 (d, *J* = 5.96, 1H, C_7**H**), 6.61 (d, *J* = 4.2 Hz, 1H, C_{14}**H**), 6.55 (app-t, *J* = 5.8 Hz, 1H, C_8**H**).

^{13}C NMR (125.8 MHz, $CDCl_3$, 21 °C): δ 156.8[17], 125.0[17], 115.2, 114.3, 111.6, 106.6, 101.1.

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[15] Literature value: $[\alpha]_D^{25}$ = –12 (c 0.07, methanol), Tilvi, S.; Moriou, C.; Martin, M.; Gallard, J.; Sorres, J.; Patel, K.; Petek, S.; Debitus, C.; Ermolenko, L.; Al-Mourabit, A. *J. Nat. Prod.* **2010**, *73*, 720–723.

[16] Resonance is partially obscured by the H_2O resonance in CD_3OD.

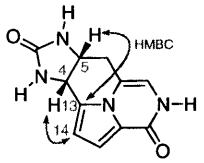
[17] Resonance is partially obscured due to low solubility/concentration, however, this signal is clearly observed via gHMBC analysis.

FTIR (neat) cm^{-1}: 3030 (w), 1656 (s), 1412 (m), 1360 (m), 1207 (w), 941 (m).

HRMS (ESI) (*m/z*): calc'd for $C_7H_6BrN_2O$, $[M+H]^+$: 212.9658, found: 212.9664.

TLC (18% methanol, 2% ammonium hydroxide in chloroform), R*f*: 0.69 (CAM, UV).

HMBC correlations (500 MHz, $CDCl_3$, 21 °C): C10-H8, C11-H14, **C11-H7**, **C11-H15**, C14-H15, C8-H7, C15-H14, C7-H8, **C13-H14**, **C13-H7**, C13-H15. Key correlations are shown in bold.



(±)-**70**

tetracycle 70:

^1H NMR (500 MHz, DMSO-d_6, 21 °C): δ 10.32 (d, *J* = 4.4 Hz, 1H, N**H**), 6.98 (s, 1H, N**H**), 6.87 (d, 1H, *J* = 3.9 Hz, 1H, C_{15}**H**), 6.61 (s, 1H, N**H**), 6.55 (d, *J* = 3.9 Hz, 1H, C_{14}**H**), 6.49 (d, *J* = 3.9, 1H, C_8**H**), 4.80 (d, *J* = 6.9 Hz, 1H, C_4**H**), 4.06 (app-dd, *J* = 10.5, 5.0 Hz, 1H, C_5**H**), 2.92 (dd, *J* = 16.2, 2.8 Hz, 1H, C_6**H**$_a$), 2.81 (dd, *J* = 16.2, 5.5 Hz, 1H, C_6**H**$_b$).

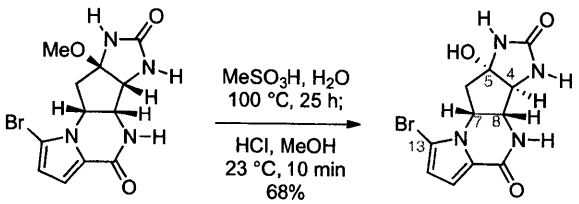
^{13}C NMR (125.8 MHz, DMSO-d_6, 21 °C): δ 162.7, 155.5, 127.0, 121.5, 111.9, 111.0, 110.8, 109.0, 48.5, 47.6, 25.5.

FTIR (neat) cm^{-1}: 3446 (bs), 2361 (w), 1644 (s), 1447 (w), 1194 (m), 1049 (w).

HRMS (ESI) (*m/z*): calc'd for $C_{11}H_{11}N_4O_2$, $[M+H]^+$: 231.0887, found: 231.0886.

TLC (18% methanol, 2% ammonium hydroxide in chloroform), R*f*: 0.24 (CAM, UV).

HMBC correlations (500 MHz, DMSO-d_6, 21 °C): C2-H4, C2-H1, C2-H3, C10-H8, **C13-H5**, C13-H14, C13-H15, C11-H14, C11-H15, C11-H9, C7-H6, C7-H5, C7-H8, C8-H6, **C14-H4**, C14-H15, C15-H14, C5-H6, C5-H4, C5-H1, C5-H3, C4-H6, C4-H1, C4-H3, C6-H4. Key correlations are shown in bold.



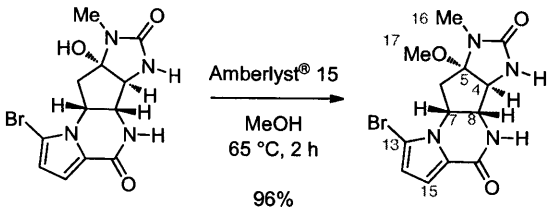
(–)-*O*-Me-di-*epi*-agelastatin D (**67**)

(–)-agelastatin D (**4**)

Equilibration of (–)-*O*-methyl-di-*epi*-agelastatin D (67) to (–)-agelastatin D (4):

Methanesulfonic acid (34 μL, 523 μmol, 57.3 equiv) was added to a solution of (–)-*O*-methyl-di-*epi*-agelastatin D (**67**, 3.11 mg, 9.12 μmol, 1 equiv) in water (4 mL, degassed thoroughly by passage of a stream of argon) at 23 °C, and the reaction mixture was heated to 100 °C. After 25 h, the reaction mixture was allowed to cool to 23 °C, was basified to pH = 8 by addition of ammonium hydroxide, and was concentrated under reduced pressure. The residue was dissolved in methanol (4 mL) and the resulting mixture was acidified to pH = 3 by the addition of aqueous hydrochloric acid solution (1 N, 42 μL, 0.042 mmol, 4.6 equiv). After 10 min, the reaction mixture was basified to pH = 8 by addition of ammonium hydroxide. The resulting mixture was concentrated under reduced pressure, and the crude residue adsorbed onto silica gel was purified by flash column chromatography (silica gel: diam. 1.5 cm, ht. 2.5 cm; eluent: 14.0% methanol, 1.5% ammonium hydroxide in chloroform) to afford (–)-agelastatin D (**4**, 2.02 mg, 68%) as a tan solid.

(–)-Agelastatin D (**4**) was found to be 99% ee by chiral HPLC analysis [Chiralpak AD-H; 0.53 mL/min; 10% isopropanol in hexanes; t_R(major) = 47.7 min, t_R(minor) = 29.3 min].



(–)-agelastatin A (**1**) (–)-agelastatin E (**5**)

(–)-Agelastatin E (5):[18]

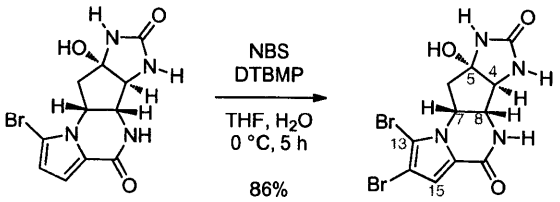
Amberlyst® 15 (50.0 mg) was added to a solution of (–)-agelastatin A (**1**, 20.0 mg, 58.6 μmol, 1 equiv) in methanol (11.6 mL) at 23 °C, and the resulting mixture was heated to 65 °C. After 2.5 h, the reaction mixture was filtered through a plug of cotton, and the filtrate was concentrated to afford (–)-agelastatin E (**5**, 21.0 mg, 100%) as a light tan solid. (–)-Agelastatin E (**5**) was sparingly soluble in organic solvents, methanol, and water.

^{1}H NMR (500 MHz, CD_3OD, 21 °C):	δ 6.91 (d, J = 4.0 Hz, 1H, C_{15}**H**), 6.33 (d, J = 4.1 Hz, 1H, C_{14}**H**), 4.62 (app-dt, J = 11.9, 6.1 Hz, 1H, C_7**H**), 4.12 (d, J = 5.6 Hz, 1H, C_8**H**), 4.09 (s, 1H, C_4**H**), 3.18 (s, 1H, C_{17}**H**$_3$), 2.79 (s, 3H, C_{16}**H**$_3$), 2.66 (dd, J = 13.2, 6.5 Hz, 1H, C_6**H**$_a$), 2.14 (app-t, J = 12.7 Hz, 1H, C_6**H**$_b$).
^{13}C NMR (125.8 MHz, CD_3OD, 21 °C):	δ 161.9, 161.1, 124.2, 116.2, 114.0, 107.5, 100.2, 62.1, 61.2, 53.9, 50.8, 39.3, 24.7.
FTIR (neat) cm^{-1}:	3239 (br-m), 2927 (m), 1703 (s), 1659 (s), 1552 (m), 1425 (s), 1377 (w), 1302 (w), 1198 (w), 1103 (m).
HRMS (DART) (*m/z*):	calc'd for $C_{13}H_{14}BrN_4O_3$, $[M–H]^-$: 353.0255, found: 353.0254.
$[\alpha]_D^{22}$:	–63.4 (c 0.054, methanol).[19]
M.p.:	186–190 °C (dec.).

TLC (18% methanol, 2% ammonium hydroxide in chloroform), R*f*: 0.60 (CAM, UV).

[18] For a previous report of the semi-synthesis of (–)-agelastatin E (**5**), see: D'Ambrosio, M.; Guerriero, A.; Chiasera, G.; Pietra, F. *Helv. Chim. Acta* **1994**, *7*, 1895–1902.

[19] Literature value: $[\alpha]_D^{25}$ = –28 (c 0.09, methanol), Tilvi, S.; Moriou, C.; Martin, M.; Gallard, J.; Sorres, J.; Patel, K.; Petek, S.; Debitus, C.; Ermolenko, L.; Al-Mourabit, A. *J. Nat. Prod.* **2010**, *73*, 720–723.



(–)-Agelastatin F (6):

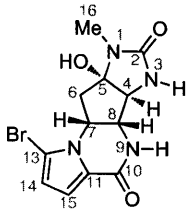
N-Bromosuccinimide (NBS, 5.9 mg, 33 μmol, 1.5 equiv) was added as a solid in one portion to a solution of (–)-agelastatin D (**4**, 7.17 mg, 21.9 μmol, 1 equiv) and 2,6-di-*tert*-butyl-4-methylpyridine (DTBMP, 6.7 mg, 33 μmol, 1.5 equiv) in water (1.5 mL) and tetrahydrofuran (3.0 mL) at 0 °C. After 5 h, the reaction mixture was quenched with a mixture of saturated aqueous sodium thiosulfate solution and saturated aqueous sodium bicarbonate solution (1:1, 125 μL). The resulting mixture was concentrated under reduced pressure, and the crude residue adsorbed onto silica gel was purified by flash column chromatography (silica gel: diam. 2 cm, ht. 2.5 cm; eluent: 14.0% methanol, 1.5% ammonium hydroxide in chloroform) to afford (–)-agelastatin F (**6**, 7.69 mg, 86%) as a white solid. (–)-Agelastatin F (**6**) is sparingly soluble in organic solvents, methanol, and water.

^{1}H NMR (500 MHz, CD_3OD, 21 °C):	δ 6.96 (s, 1H, C_{15}**H**), 4.73 (app-dt, J = 11.9, 6.0 Hz, 1H, C_7**H**), 4.12 (d, J = 5.6 Hz, 1H, C_8**H**), 3.91 (s, 1H, C_4**H**), 2.56 (dd, J = 12.8, 6.4 Hz, 1H, C_6**H**$_a$), 2.23 (app-t, J = 12.4 Hz, 1H, C_6**H**$_b$).
^{13}C NMR (125.8 MHz, CD_3OD, 21 °C):	δ 162.8, 160.2, 124.9, 117.0, 108.8, 101.8, 93.1, 69.5, 62.2, 55.8, 43.7.
FTIR (neat) cm^{-1}:	3200 (m), 2923 (m), 1677 (s), 1640 (s), 1557 (w), 1420 (m), 1117 (w).
HRMS (ESI) (*m/z*):	calc'd for $C_{11}H_{10}Br_2N_4NaO_3$, $[M+H]^+$: 426.9012, found: 426.9021.
$[\alpha]_D^{22}$:	–47.4 (c 0.10, methanol).[20]

TLC (18% methanol, 2% ammonium hydroxide in chloroform), R*f*: 0.25 (CAM, UV).

[20] Literature value: $[\alpha]_D^{25}$ = –34.3 (c 0.11, methanol), Tilvi, S.; Moriou, C.; Martin, M.; Gallard, J.; Sorres, J.; Patel, K.; Petek, S.; Debitus, C.; Ermolenko, L.; Al-Mourabit, A. *J. Nat. Prod.* **2010**, *73*, 720–723.

Table S1. Comparison of our data for (–)-agelastatin A (1) with literature:



(–)-agelastatin A (1)

Assignment	Pietra's Report[21] ^{1}H NMR, 300 MHz, CD_3OD	Du Bois' Report[22] ^{1}H NMR, 400 MHz, CD_3OD	This Work[23] ^{1}H NMR, 500 MHz, CD_3OD
C4	3.89 (br-s, 1H)	3.87 (br-s, 1H)	3.88 (s, 1H)
C6′	2.65 (br-dd, J = 12.9, 6.6 Hz, 1H)	2.64 (dd, J = 12.8, 6.4 Hz, 1H)	2.65 (dd, J = 13.1, 6.3 Hz, 1H)
C6″	2.10 (br-t, J = 12.3, 12.9, Hz, 1H)	2.09 (dd, J = 12.8, 12.4 Hz, 1H)	2.10 (app-t, J = 12.7 Hz, 1H)
C7	4.60 (m, J = 12.3, 6.6, 5.4 Hz, 1H)	4.59 (dt, J = 12.0, 6.0 Hz, 1H)	4.60 (app-dt, J = 11.9, 6.0 Hz, 1H)
C8	4.09 (br-d, J = 5.4 Hz, 1H)	4.08 (d, J = 5.6 Hz, 1H)	4.09 (d, J = 5.4 Hz, 1H)
C14	6.33 (d, J = 4.2 Hz, 1H)	6.32 (d, J = 4.0 Hz, 1H)	6.33 (d, J = 4.1 Hz, 1H)
C15	6.92 (br-d, J = 4.2 Hz, 1H)	6.90 (d, J = 4.0 Hz, 1H)	6.92 (d, J = 4.0 Hz, 1H)
C16	2.81 (s, 3H)	2.80 (s, 3H)	2.81 (s, 3H)

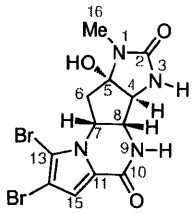
Assignment	Pietra's Report[21] ^{13}C NMR, 75 MHz, CD_3OD	Du Bois' Report[22] ^{13}C NMR, 125 MHz, CD_3OD	This Work[23] ^{13}C NMR, 125.8 MHz, CD_3OD
C2	163.00	161.4	161.6
C4	68.98	67.4	67.5
C5	97.24	95.6	95.8
C6	41.58	40.0	40.1
C7	55.96	54.4	54.5
C8	63.76	62.2	62.3
C10	162.65	161.1	161.2
C11	125.71	124.1	124.3
C13	108.80	107.3	107.4
C14	115.37	113.8	113.9
C15	117.59	116.0	116.2
C16	25.79	24.2	24.4

[21] The reference points for the residual protium and carbon resonances of the NMR solvent were not listed. D'Ambrosio, M.; Guerriero, A.; Debitus, C.; Ribes, O.; Pusset, J.; Leroy, S.; Pietra, F. *J. Chem. Soc., Chem. Commun.* **1993**, 1305–1306.

[22] The reference points for the residual protium and carbon resonances of the NMR solvent were not listed. When, P. M.; Du Bois, J. *Angew. Chem., Int. Ed. Engl.* **2009**, *48*, 3802–3805.

[23] In this report, the NMR spectra are referenced from the residual protium resonance, CD_3OD: δ 3.31 (CHD_2OD), and carbon resonance, CD_3OD: δ 49.15.

Table S2. Comparison of our data for (–)-Agelastatin B (2) with literature:



(–)-agelastatin B (**2**)

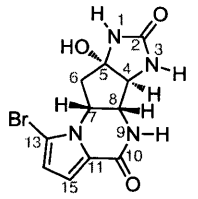
Assignment	**Feldman's Report**[24] ^{1}H NMR, 300 MHz, CD_3OD	**This Work**[23] ^{1}H NMR, 500 MHz, CD_3OD
C4	3.88 (s, 1H)	3.88 (s, 1H)
C6′	2.68 (dd, J = 13.1, 6.5 Hz, 1H)	2.68 (dd, J = 13.1, 6.5 Hz, 1H)
C6″	2.12 (t, J = 12.6 Hz, 1H)	2.12 (app-t, J = 12.6 Hz, 1H)
C7	4.60 (dt, J = 11.8, 6.0 Hz, 1H)	4.60 (app-dt, J = 12.0, 6.0 Hz, 1H)
C8	4.11 (d, J = 5.5 Hz, 1H)	4.11 (d, J = 5.4 Hz, 1H)
C15	6.96 (s, 1H)	6.97 (s, 1H)
C16	2.81 (s, 3H)	2.81 (s, 3H)

Assignment	**Feldman's Report**[24] ^{13}C NMR, 75 MHz, CD_3OD	**This Work**[23] ^{13}C NMR, 125.8 MHz, CD_3OD
C2	161.4	161.5
C4	67.6	67.5
C5	95.6	95.7
C6	40.0	40.0
C7	55.5	55.5
C8	62.1	62.2
C10	159.6	160.2
C11	111.0	124.9[25]
C13	108.6	108.9
C14	101.8	101.8
C15	117.0	117.1
C16	24.2	24.4

[24] The reference point for the residual protium of the NMR solvent was not listed. The ^{13}C NMR spectrum is referenced from the carbon resonance, CD_3OD: δ 49.00. Feldman, K. S.; Saunders, J. C. *J. Am. Chem. Soc.* **2002**, *124*, 9060–9061.

[25] We assign the C11 ^{13}C NMR resonance to the signal at δ 124.9.

Table S3. Comparison of our data for (–)-agelastatin D (4) with literature:



(–)-agelastatin D (**4**)

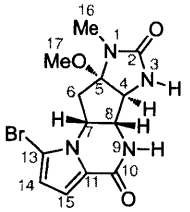
Assignment	Molinski's Report[26] ^{1}H NMR, CD_3OD	This Work[23] ^{1}H NMR, 500 MHz, CD_3OD
C4	3.91 (s, 1H)	3.91 (s, 1H)
C6′	2.54 (dd, J = 12.9, 6.5 Hz, 1H)	2.54 (dd, J = 12.6, 6.6 Hz, 1H)
C6′′	2.21(br-t, J = 12.9, 12.4, Hz, 1H)	2.21 (app-t, J = 12.4 Hz, 1H)
C7	4.73 (m, J = 12.4, 6.5, 5.4 Hz, 1H)	4.74 (app-dt, J = 11.9, 6.0 Hz, 1H)
C8	4.09 (d, J = 5.4 Hz, 1H)	4.10 (d, J = 5.7 Hz, 1H)
C14	6.33 (d, J = 4.1 Hz, 1H)	6.33 (d, J = 4.1 Hz, 1H)
C15	6.91 (br-d, J = 4.1 Hz, 1H)	6.91 (d, J = 4.1 Hz, 1H)

Assignment	This Work[27] ^{13}C NMR, 125.8 MHz, Pyridine-d_5
C2	162.1
C4	69.9
C5	93.1
C6	44.5
C7	54.8
C8	62.7
C10	159.7
C11	125.5
C13	105.5
C14	113.0
C15	114.7

[26] The reference points for the residual protium and carbon resonances of the NMR solvent and the magnetic field strength were not listed. Hong, T. W.; Jímenez, D. R.; Molinski, T. F. *J. Nat. Prod.*, **1998**, *61*, 158–161.

[27] The ^{13}C NMR for (–)-agelastatin D (**4**) has not been previously reported. In this report, the ^{13}C NMR spectrum is referenced from the carbon resonances, Pyridine-d_5: δ 150.35.

Table S4. Comparison of our data for (–)-agelastatin E (5) with literature:



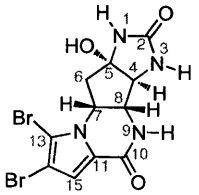
(–)-agelastatin E (**5**)

Assignment	Al-Mourabit's Report[28] ^{1}H NMR, 600 MHz, CD_3OD	This Work[23] ^{1}H NMR, 500 MHz, CD_3OD
C4	4.08 (br-s, 1H)	4.09 (s, 1H)
C6′	2.66 (dd, J = 12.9, 6.6 Hz, 1H)	2.66 (dd, J = 13.2, 6.5 Hz, 1H)
C6″	2.14 (br-t, J = 12.9, Hz, 1H)	2.14 (app-t, J = 12.7 Hz, 1H)
C7	4.62 (m, J = 12.6, 6.6 Hz, 1H)	4.62 (app-dt, J = 11.9, 6.1 Hz, 1H)
C8	4.11 (d, J = 5.4 Hz, 1H)	4.12 (d, J = 5.6 Hz, 1H)
C14	6.32 (d, J = 4.1 Hz, 1H)	6.33 (d, J = 4.1 Hz, 1H)
C15	6.91 (d, J = 4.1 Hz, 1H)	6.91 (d, J = 4.0 Hz, 1H)
C16	2.78 (s, 3H)	2.79 (s, 3H)
C17	3.18 (s, 3H)	3.18 (s, 3H)

Assignment	Al-Mourabit's Report[28] ^{13}C NMR, 150.8 MHz, CD_3OD	This Work[23] ^{13}C NMR, 125.8 MHz, CD_3OD
C2	162.2	161.9
C4	61.2	61.2
C5	101.0	100.2
C6	39.3	39.3
C7	53.9	53.9
C8	62.2	62.1
C10	161.2	161.1
C11	124.2	124.2
C13	107.4	107.5
C14	114.0	114.0
C15	116.2	116.2
C16	24.7	24.7
C17	50.8	50.8

[28] The NMR spectra are referenced from the residual protium resonance, CHD_2OD: δ 3.32, and carbon resonance, CD_3OD: δ 49.0. S. Tilvi, S.; Moriou, C.; Martin, M.; Gallard, J.; Sorres, J.; Patel, K.; Petek, S.; Debitus, C.; Ermolenko, L.; Al-Mourabit, A. *J. Nat. Prod.* **2010**, *73*, 720–723.

Table S5. Comparison of our data for (–)-agelastatin F (6) with literature:



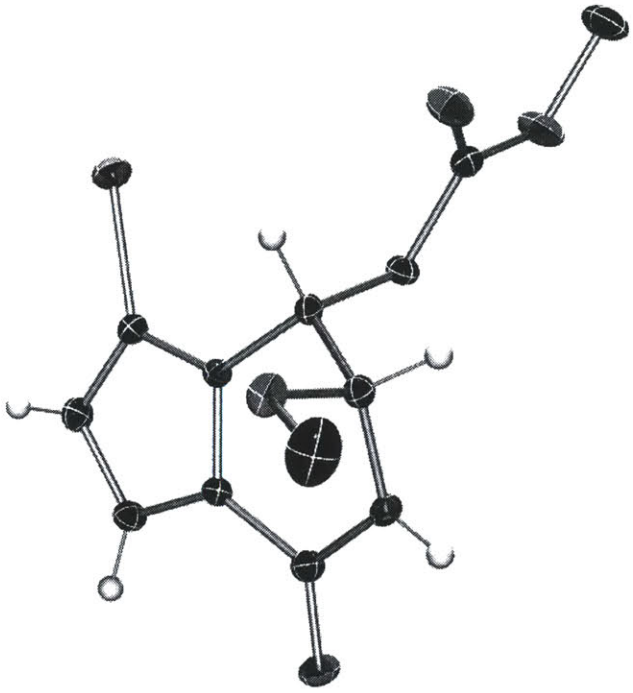
(–)-agelastatin F (**6**)

Assignment	**Al-Mourabit's Report**[28] ^{1}H NMR, 600 MHz, CD_3OD	**This Work**[23] ^{1}H NMR, 500 MHz, CD_3OD
C4	3.92 (br-s, 1H)	3.91 (s, 1H)
C6′	2.58 (dd, J = 12.9, 6.6 Hz, 1H)	2.56 (dd, J = 12.8, 6.4 Hz, 1H)
C6″	2.24 (br-t, J = 12.9 Hz, 1H)	2.23 (app-t, J = 12.4 Hz, 1H)
C7	4.74 (m, J = 12.6, 6.6 Hz, 1H)	4.73 (app-dt, J = 11.9, 6.0 Hz, 1H)
C8	4.14 (d, J = 5.5 Hz, 1H)	4.12 (d, J = 5.6 Hz, 1H)
C15	6.98 (s, 1H)	6.96 (s, 1H)

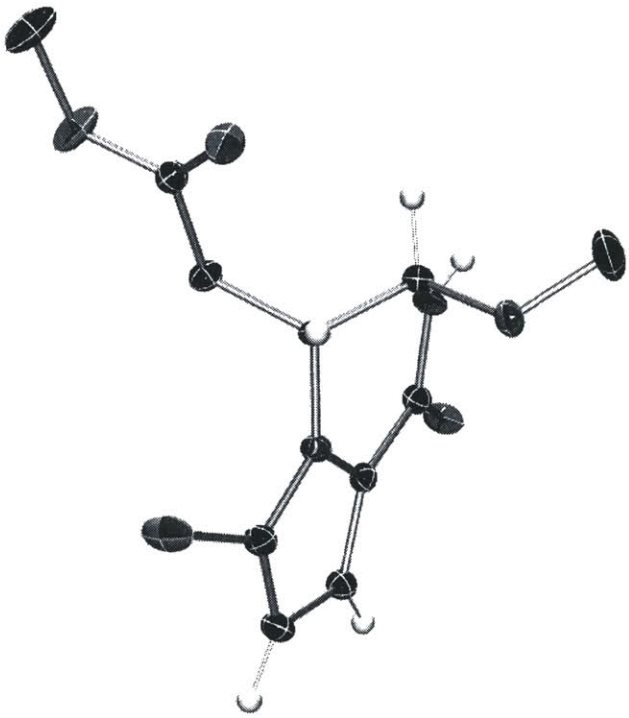
Assignment	**Al-Mourabit's Report**[28] ^{13}C NMR, 150.8 MHz, CD_3OD	**This Work**[23] ^{13}C NMR, 125.8 MHz, CD_3OD
C2	162.8	162.8
C4	69.5	69.5
C5	93.3	93.1
C6	43.7	43.7
C7	55.8	55.8
C8	62.2	62.2
C10	160.2	160.2
C11	125.0	124.9
C13	108.7	108.8
C14	101.1	101.8
C15	117.1	117.0

Crystal Structure of Bicycle (+)-49

View 1:



View 2:



View 3:

Table S6. Crystal data and structure refinement for bicycle (+)-**49**.

Identification code	10011	
Empirical formula	C11 H13 Br N2 O4	
Formula weight	317.14	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2(1)	
Unit cell dimensions	a = 8.4061(9) Å	a= 90°.
	b = 9.2037(10) Å	b= 90°.
	c = 17.3522(18) Å	g = 90°.
Volume	1342.5(2) $Å^3$	
Z	4	
Density (calculated)	1.569 Mg/m^3	
Absorption coefficient	3.070 mm^{-1}	
F(000)	640	
Crystal size	0.35 x 0.20 x 0.15 mm^3	
Theta range for data collection	2.35 to 29.56°.	
Index ranges	-11<=h<=11, -12<=k<=12, -24<=l<=24	
Reflections collected	35594	
Independent reflections	3764 [R(int) = 0.0403]	
Completeness to theta = 29.56°	100.0 %	
Absorption correction	None	
Max. and min. transmission	0.6559 and 0.4129	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3764 / 155 / 168	
Goodness-of-fit on F^2	1.030	
Final R indices [I>2sigma(I)]	R1 = 0.0224, wR2 = 0.0556	
R indices (all data)	R1 = 0.0241, wR2 = 0.0561	
Absolute structure parameter	0.009(6)	
Largest diff. peak and hole	0.646 and -0.476 $e.Å^{-3}$	

Table S7. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for bicycle (+)-**49**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Br(1)	4530(1)	12344(1)	7612(1)	25(1)
O(3)	-588(2)	11005(1)	7596(1)	22(1)
O(1)	3784(1)	7512(2)	5030(1)	21(1)
C(11)	4314(2)	9440(2)	5895(1)	13(1)
C(8)	1060(2)	10016(2)	5919(1)	13(1)
C(13)	4913(2)	11063(2)	6798(1)	15(1)
O(2)	1136(2)	11236(1)	5425(1)	18(1)
C(6)	1639(2)	9434(2)	7331(1)	15(1)
N(9)	1681(2)	8707(2)	5561(1)	15(1)
C(7)	1994(2)	10421(2)	6642(1)	12(1)
C(10)	3270(2)	8482(2)	5451(1)	14(1)
N(12)	3685(2)	10368(2)	6443(1)	13(1)

C(5)	194(2)	9954(2)	7768(1)	15(1)
O(4)	-98(2)	9125(1)	8382(1)	26(1)
C(14)	6335(2)	10625(2)	6477(1)	16(1)
C(16)	-1439(3)	9579(2)	8850(1)	30(1)
C(15)	5961(2)	9584(2)	5907(1)	15(1)
C(17)	16(3)	11172(3)	4806(1)	35(1)

Table S8. Bond lengths [Å] and angles [°] for bicycle (+)-**49**.

Br(1)-C(13)	1.8667(16)	O(2)-C(8)-C(7)	106.33(13)
O(3)-C(5)	1.2064(19)	N(9)-C(8)-C(7)	111.66(13)
O(1)-C(10)	1.232(2)	N(12)-C(13)-C(14)	109.66(14)
C(11)-N(12)	1.384(2)	N(12)-C(13)-Br(1)	120.57(12)
C(11)-C(15)	1.390(2)	C(14)-C(13)-Br(1)	129.74(12)
C(11)-C(10)	1.463(2)	C(8)-O(2)-C(17)	113.14(14)
C(8)-O(2)	1.4135(19)	C(5)-C(6)-C(7)	111.19(13)
C(8)-N(9)	1.452(2)	C(10)-N(9)-C(8)	122.51(14)
C(8)-C(7)	1.525(2)	N(12)-C(7)-C(8)	107.35(13)
C(13)-N(12)	1.362(2)	N(12)-C(7)-C(6)	110.72(13)
C(13)-C(14)	1.379(2)	C(8)-C(7)-C(6)	113.40(13)
O(2)-C(17)	1.430(2)	O(1)-C(10)-N(9)	122.42(15)
C(6)-C(5)	1.510(2)	O(1)-C(10)-C(11)	122.61(15)
C(6)-C(7)	1.532(2)	N(9)-C(10)-C(11)	114.93(14)
N(9)-C(10)	1.366(2)	C(13)-N(12)-C(11)	108.15(13)
C(7)-N(12)	1.463(2)	C(13)-N(12)-C(7)	127.87(14)
C(5)-O(4)	1.3321(19)	C(11)-N(12)-C(7)	123.63(13)
O(4)-C(16)	1.452(2)	O(3)-C(5)-O(4)	123.83(16)
C(14)-C(15)	1.413(2)	O(3)-C(5)-C(6)	124.62(15)
		O(4)-C(5)-C(6)	111.54(14)
N(12)-C(11)-C(15)	108.14(14)	C(5)-O(4)-C(16)	115.14(14)
N(12)-C(11)-C(10)	120.30(14)	C(13)-C(14)-C(15)	106.74(15)
C(15)-C(11)-C(10)	131.49(15)	C(11)-C(15)-C(14)	107.28(14)
O(2)-C(8)-N(9)	112.54(14)		

Symmetry transformations used to generate equivalent atoms:

Table S9. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for bicycle (+)-**49**. The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Br(1)	21(1)	28(1)	27(1)	-16(1)	3(1)	-7(1)
O(3)	21(1)	25(1)	21(1)	4(1)	4(1)	8(1)
O(1)	16(1)	22(1)	25(1)	-11(1)	1(1)	1(1)
C(11)	13(1)	14(1)	12(1)	-1(1)	1(1)	1(1)
C(8)	12(1)	13(1)	15(1)	-1(1)	0(1)	0(1)
C(13)	15(1)	15(1)	15(1)	-3(1)	0(1)	-2(1)
O(2)	20(1)	17(1)	17(1)	4(1)	-5(1)	0(1)
C(6)	15(1)	14(1)	16(1)	0(1)	3(1)	2(1)

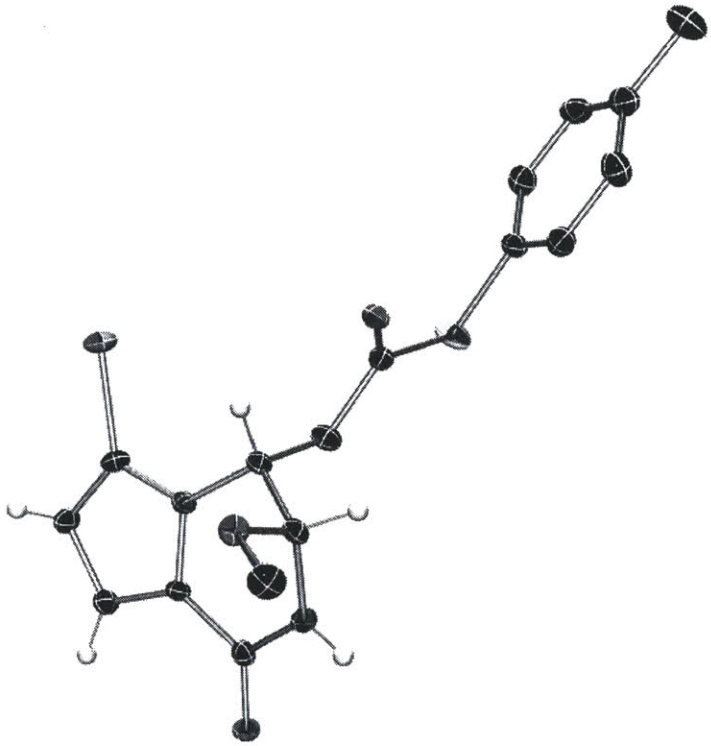
N(9)	11(1)	15(1)	19(1)	-5(1)	-1(1)	-1(1)
C(7)	10(1)	12(1)	14(1)	-1(1)	1(1)	-1(1)
C(10)	14(1)	15(1)	14(1)	-1(1)	0(1)	0(1)
N(12)	11(1)	14(1)	14(1)	-2(1)	1(1)	0(1)
C(5)	16(1)	14(1)	14(1)	-2(1)	0(1)	-2(1)
O(4)	33(1)	20(1)	24(1)	6(1)	16(1)	8(1)
C(14)	13(1)	18(1)	17(1)	-1(1)	-2(1)	-2(1)
C(16)	36(1)	23(1)	29(1)	2(1)	20(1)	3(1)
C(15)	13(1)	17(1)	16(1)	-1(1)	1(1)	1(1)
C(17)	38(1)	37(1)	28(1)	12(1)	-18(1)	-7(1)

Table S10. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for bicycle (+)-**49**.

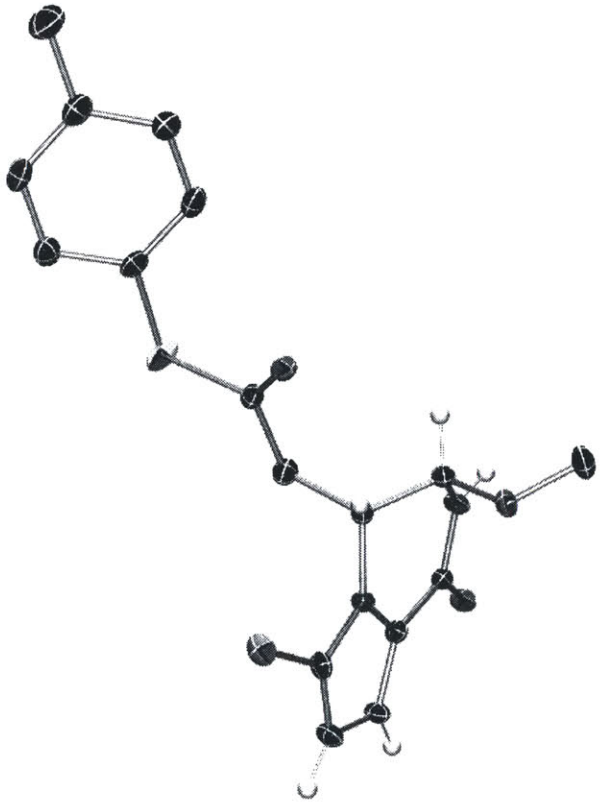
	x	y	z	U(eq)
H(8)	-75	9846	6065	16
H(6A)	1454	8430	7148	18
H(6B)	2569	9420	7681	18
H(9)	1070(20)	8200(20)	5292(12)	18
H(7)	1718	11442	6786	14
H(14)	7367	10959	6613	20
H(16A)	-1233	10550	9060	44
H(16B)	-1588	8890	9275	44
H(16C)	-2402	9605	8532	44
H(15)	6697	9077	5590	18
H(17A)	261	10338	4475	52
H(17B)	79	12068	4503	52
H(17C)	-1060	11065	5016	52

Crystal Structure of Thioester (+)-57

View 1:



View 2:



View 3:

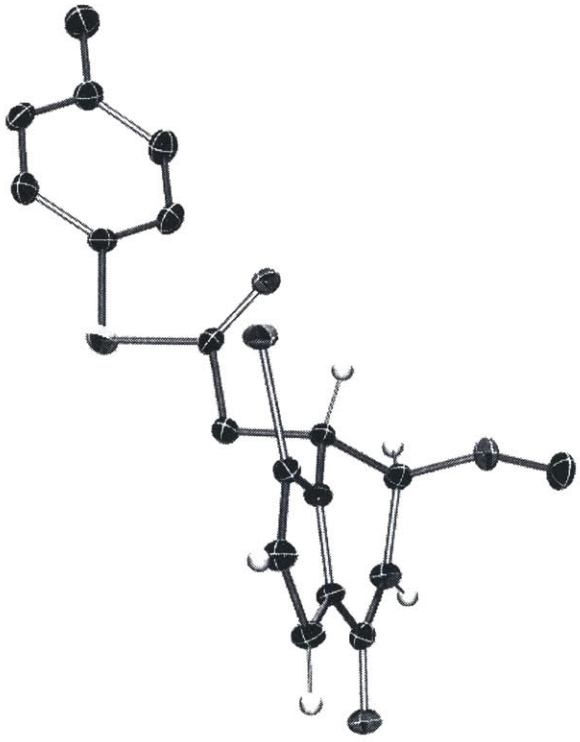


Table S11. Crystal data and structure refinement for thioester (+)-**57**.

Identification code	10013	
Empirical formula	C17 H17 Br N2 O3 S	
Formula weight	409.30	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)	
Unit cell dimensions	a = 9.2556(9) Å	a= 90°.
	b = 8.0917(8) Å	b= 91.799(2)°.
	c = 11.7613(12) Å	g = 90°.
Volume	880.41(15) Å^3	
Z	2	
Density (calculated)	1.544 Mg/m^3	
Absorption coefficient	2.470 mm^{-1}	
F(000)	416	
Crystal size	0.35 x 0.35 x 0.15 mm^3	
Theta range for data collection	1.73 to 29.13°.	
Index ranges	-12<=h<=12, -10<=k<=11, -16<=l<=16	
Reflections collected	19103	
Independent reflections	4583 [R(int) = 0.0383]	
Completeness to theta = 29.13°	99.9 %	
Absorption correction	None	
Max. and min. transmission	0.7082 and 0.4785	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4583 / 203 / 222	
Goodness-of-fit on F^2	1.008	
Final R indices [I>2sigma(I)]	R1 = 0.0251, wR2 = 0.0560	
R indices (all data)	R1 = 0.0282, wR2 = 0.0570	
Absolute structure parameter	0.014(5)	
Largest diff. peak and hole	0.519 and -0.232 e.Å^{-3}	

Table S12. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for thioester (+)-**57**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Br(1)	135(1)	9493(1)	3768(1)	20(1)
S(1)	3998(1)	4712(1)	5370(1)	26(1)
O(3)	1618(1)	4293(2)	4073(1)	17(1)
C(5)	2720(2)	5054(2)	4221(2)	15(1)
C(7)	2125(2)	6816(2)	2470(2)	14(1)
C(19)	2830(2)	1758(3)	7926(2)	22(1)
C(17)	3282(2)	3004(3)	6116(2)	18(1)
C(22)	2870(2)	1547(3)	5576(2)	21(1)
C(18)	3263(2)	3118(3)	7301(2)	21(1)
C(6)	3212(2)	6452(3)	3461(2)	18(1)
C(20)	2403(2)	297(3)	7410(2)	22(1)
C(23)	1951(3)	-1187(3)	8091(2)	33(1)

C(21)	2420(2)	214(3)	6216(2)	25(1)
O(1)	4980(2)	8576(2)	117(1)	18(1)
O(2)	1148(2)	5943(2)	706(1)	19(1)
C(11)	3137(2)	9187(2)	1394(2)	14(1)
N(12)	2177(2)	8549(2)	2165(1)	14(1)
C(13)	1509(2)	9849(2)	2670(2)	16(1)
C(16)	1114(2)	4835(3)	-239(2)	26(1)
N(9)	3697(2)	6443(2)	833(2)	16(1)
C(10)	4007(2)	8076(2)	723(2)	15(1)
C(8)	2425(2)	5821(2)	1393(2)	15(1)
C(15)	3040(2)	10894(3)	1419(2)	17(1)
C(14)	2000(2)	11308(3)	2229(2)	18(1)

Table S13. Bond lengths [Å] and angles [°] for thioester (+)-**57**.

Br(1)-C(13)	1.8635(17)	N(12)-C(7)-C(6)	110.21(16)
S(1)-C(17)	1.776(2)	C(8)-C(7)-C(6)	113.14(17)
S(1)-C(5)	1.789(2)	C(20)-C(19)-C(18)	121.9(2)
O(3)-C(5)	1.199(2)	C(22)-C(17)-C(18)	120.05(19)
C(5)-C(6)	1.521(3)	C(22)-C(17)-S(1)	122.48(16)
C(7)-N(12)	1.448(3)	C(18)-C(17)-S(1)	117.23(17)
C(7)-C(8)	1.533(3)	C(17)-C(22)-C(21)	119.72(19)
C(7)-C(6)	1.544(3)	C(19)-C(18)-C(17)	119.3(2)
C(19)-C(20)	1.381(3)	C(5)-C(6)-C(7)	112.71(16)
C(19)-C(18)	1.390(3)	C(19)-C(20)-C(21)	117.9(2)
C(17)-C(22)	1.387(3)	C(19)-C(20)-C(23)	121.89(19)
C(17)-C(18)	1.397(3)	C(21)-C(20)-C(23)	120.2(2)
C(22)-C(21)	1.387(3)	C(22)-C(21)-C(20)	121.2(2)
C(20)-C(21)	1.406(3)	C(8)-O(2)-C(16)	113.47(15)
C(20)-C(23)	1.510(3)	C(15)-C(11)-N(12)	108.31(16)
O(1)-C(10)	1.235(2)	C(15)-C(11)-C(10)	131.64(17)
O(2)-C(8)	1.414(2)	N(12)-C(11)-C(10)	120.04(17)
O(2)-C(16)	1.427(2)	C(13)-N(12)-C(11)	107.77(15)
C(11)-C(15)	1.385(3)	C(13)-N(12)-C(7)	128.29(16)
C(11)-N(12)	1.389(2)	C(11)-N(12)-C(7)	123.21(16)
C(11)-C(10)	1.456(2)	N(12)-C(13)-C(14)	109.77(16)
N(12)-C(13)	1.365(2)	N(12)-C(13)-Br(1)	120.69(14)
C(13)-C(14)	1.373(3)	C(14)-C(13)-Br(1)	129.53(15)
N(9)-C(10)	1.358(3)	C(10)-N(9)-C(8)	123.69(17)
N(9)-C(8)	1.457(2)	O(1)-C(10)-N(9)	122.22(18)
C(15)-C(14)	1.416(3)	O(1)-C(10)-C(11)	122.47(18)
		N(9)-C(10)-C(11)	115.29(17)
C(17)-S(1)-C(5)	104.18(9)		
O(3)-C(5)-C(6)	124.42(18)		
O(3)-C(5)-S(1)	124.72(15)	O(2)-C(8)-N(9)	112.99(15)
C(6)-C(5)-S(1)	110.86(14)	O(2)-C(8)-C(7)	105.37(15)
N(12)-C(7)-C(8)	107.21(15)	N(9)-C(8)-C(7)	111.24(16)

C(11)-C(15)-C(14)	107.20(18)	C(13)-C(14)-C(15)	106.95(19)

Symmetry transformations used to generate equivalent atoms:

Table S14. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for thioester (+)-**57**. The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2\ a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Br(1)	18(1)	24(1)	19(1)	-3(1)	8(1)	-4(1)
S(1)	20(1)	35(1)	24(1)	13(1)	-7(1)	-8(1)
O(3)	19(1)	16(1)	15(1)	2(1)	2(1)	0(1)
C(5)	17(1)	18(1)	12(1)	1(1)	1(1)	2(1)
C(7)	16(1)	12(1)	13(1)	1(1)	1(1)	-3(1)
C(19)	21(1)	30(1)	13(1)	3(1)	2(1)	2(1)
C(17)	12(1)	23(1)	17(1)	8(1)	-1(1)	1(1)
C(22)	22(1)	27(1)	14(1)	2(1)	-1(1)	6(1)
C(18)	20(1)	23(1)	18(1)	0(1)	-4(1)	2(1)
C(6)	19(1)	18(1)	17(1)	2(1)	-1(1)	-6(1)
C(20)	19(1)	28(1)	19(1)	6(1)	-1(1)	3(1)
C(23)	38(1)	32(1)	27(1)	10(1)	-2(1)	-8(1)
C(21)	31(1)	21(1)	21(1)	1(1)	-4(1)	2(1)
O(1)	20(1)	15(1)	19(1)	1(1)	7(1)	-1(1)
O(2)	21(1)	19(1)	16(1)	-4(1)	-3(1)	0(1)
C(11)	16(1)	14(1)	12(1)	2(1)	3(1)	-1(1)
N(12)	15(1)	12(1)	15(1)	1(1)	2(1)	-2(1)
C(13)	14(1)	20(1)	13(1)	-3(1)	3(1)	-2(1)
C(16)	33(1)	26(2)	18(1)	-7(1)	-2(1)	-3(1)
N(9)	19(1)	12(1)	18(1)	-1(1)	5(1)	0(1)
C(10)	17(1)	14(1)	13(1)	0(1)	-1(1)	2(1)
C(8)	19(1)	12(1)	15(1)	2(1)	1(1)	-2(1)
C(15)	22(1)	11(1)	18(1)	0(1)	4(1)	0(1)
C(14)	20(1)	14(1)	20(1)	-3(1)	5(1)	1(1)

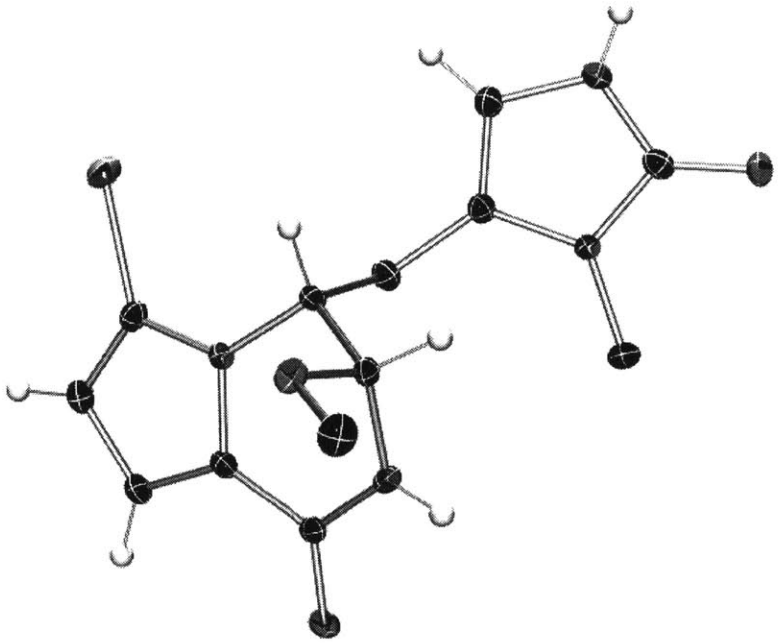
Table S15. Hydrogen coordinates ($x\ 10^4$) and isotropic displacement parameters ($Å^2 x\ 10^3$) for thioester (+)-**57**.

	x	y	z	U(eq)
H(7)	1129	6547	2719	17
H(19)	2827	1836	8732	26
H(22)	2896	1463	4772	25
H(18)	3544	4114	7674	25
H(6A)	4158	6159	3146	22
H(6B)	3347	7464	3925	22
H(23A)	2805	-1851	8298	49

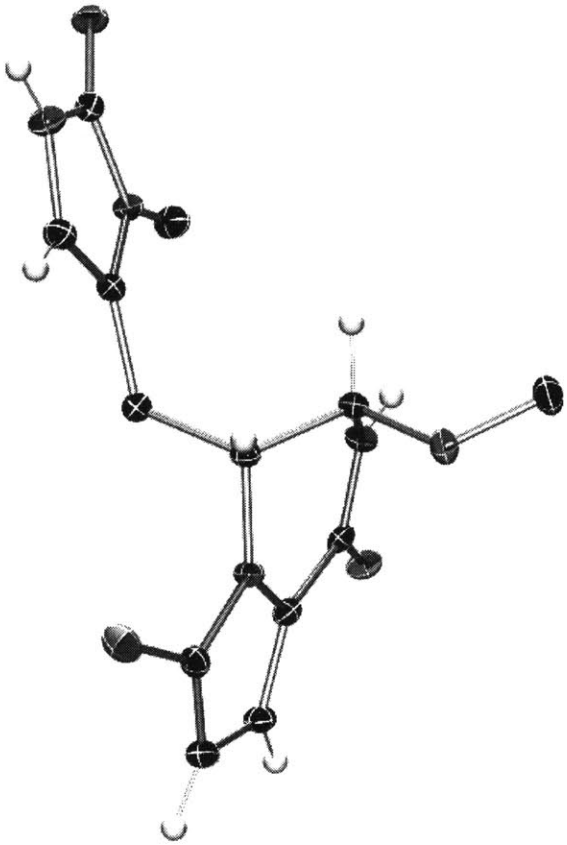
H(23B)	1270	-1858	7633	49
H(23C)	1485	-817	8783	49
H(21)	2118	-773	5842	30
H(16A)	1943	5053	-715	38
H(16B)	216	4999	-688	38
H(16C)	1159	3694	38	38
H(9)	4120(20)	5750(30)	416(17)	19
H(8)	2588	4638	1605	18
H(15)	3573	11647	975	20
H(14)	1699	12389	2428	21

Crystal Structure of (+)-*O*-Methyl-pre-agelastatin A (47)

View 1:



View 2:



View 3:

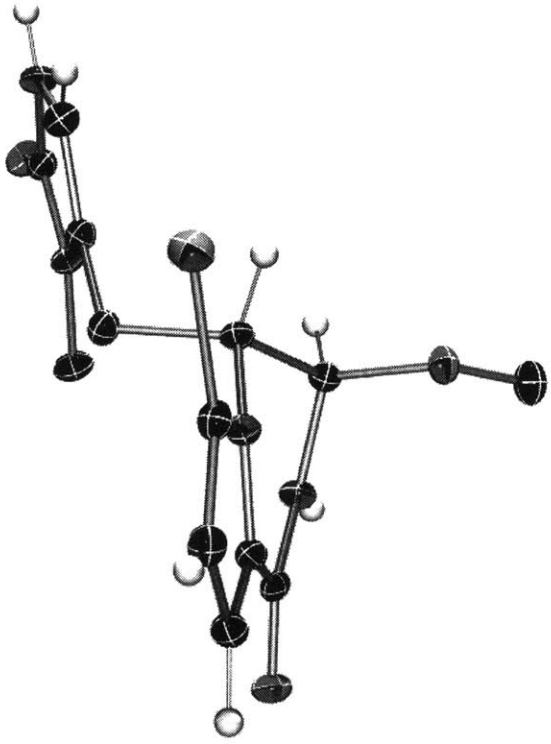


Table S16. Crystal data and structure refinement for (+)-*O*-methyl-pre-agelastatin A (**47**).

Identification code	10012	
Empirical formula	C14 H19 Br N4 O4	
Formula weight	387.24	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2(1)	
Unit cell dimensions	a = 10.3843(11) Å	a= 90°.
	b = 10.7461(11) Å	b= 90°.
	c = 14.0947(15) Å	g = 90°.
Volume	1572.8(3) $Å^3$	
Z	4	
Density (calculated)	1.635 Mg/m^3	
Absorption coefficient	2.640 mm^{-1}	
F(000)	792	
Crystal size	0.49 x 0.20 x 0.18 mm^3	
Theta range for data collection	2.38 to 29.56°.	
Index ranges	-14<=h<=14, -14<=k<=14, -19<=l<=19	
Reflections collected	31959	
Independent reflections	4413 [R(int) = 0.0524]	
Completeness to theta = 29.56°	100.0 %	
Absorption correction	None	
Max. and min. transmission	0.6479 and 0.3578	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4413 / 199 / 220	
Goodness-of-fit on F^2	1.016	
Final R indices [I>2sigma(I)]	R1 = 0.0276, wR2 = 0.0618	
R indices (all data)	R1 = 0.0327, wR2 = 0.0635	
Absolute structure parameter	-0.007(6)	
Largest diff. peak and hole	0.598 and -0.372 $e.Å^{-3}$	

Table S17. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for (+)-*O*-methyl-pre-agelastatin A (**47**). U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Br(1)	159(1)	5727(1)	8694(1)	19(1)
C(7)	299(2)	8579(2)	9501(1)	12(1)
O(1)	3736(1)	10457(1)	9284(1)	17(1)
N(9)	1768(2)	10252(2)	9958(1)	14(1)
C(13)	1556(2)	6821(2)	8716(2)	14(1)
C(4)	-2779(2)	9358(2)	8879(1)	16(1)
N(1)	-1764(2)	11168(2)	8930(1)	13(1)
O(2)	-3553(2)	12482(1)	9115(1)	18(1)
O(3)	1132(1)	8682(1)	11052(1)	16(1)

C(17)	1400(2)	9361(2)	11909(1)	20(1)
N(3)	-3662(2)	10316(2)	8998(1)	16(1)
C(15)	3436(2)	7809(2)	8539(1)	15(1)
C(8)	740(2)	9455(2)	10295(1)	12(1)
N(12)	1452(2)	7949(2)	9159(1)	12(1)
C(6)	-325(2)	9256(2)	8651(1)	15(1)
C(10)	2770(2)	9819(2)	9433(1)	12(1)
C(2)	-3051(2)	11429(2)	9029(1)	15(1)
C(16)	-794(2)	12148(2)	8888(2)	18(1)
C(11)	2611(2)	8564(2)	9047(1)	13(1)
C(5)	-1592(2)	9867(2)	8832(1)	14(1)
C(14)	2771(2)	6692(2)	8339(1)	16(1)
O(1S)	9175(2)	1656(2)	1844(1)	27(1)
C(1S)	7951(2)	1693(2)	1404(2)	24(1)

Table S18. Bond lengths [Å] and angles [°] for (+)-*O*-methyl-pre-agelastatin A (**47**).

Br(1)-C(13)	1.8678(19)	N(12)-C(13)-Br(1)	120.24(15)
C(7)-N(12)	1.457(2)	C(14)-C(13)-Br(1)	129.98(16)
C(7)-C(8)	1.532(3)	C(5)-C(4)-N(3)	107.96(19)
C(7)-C(6)	1.545(3)	C(2)-N(1)-C(5)	109.55(17)
O(1)-C(10)	1.234(2)	C(2)-N(1)-C(16)	121.94(17)
N(9)-C(10)	1.359(3)	C(5)-N(1)-C(16)	128.43(17)
N(9)-C(8)	1.448(3)	C(8)-O(3)-C(17)	113.06(15)
C(13)-N(12)	1.368(2)	C(2)-N(3)-C(4)	110.46(17)
C(13)-C(14)	1.375(3)	C(11)-C(15)-C(14)	107.40(18)
C(4)-C(5)	1.350(3)	O(3)-C(8)-N(9)	112.48(16)
C(4)-N(3)	1.388(3)	O(3)-C(8)-C(7)	106.02(15)
N(1)-C(2)	1.372(3)	N(9)-C(8)-C(7)	110.20(15)
N(1)-C(5)	1.416(3)	C(13)-N(12)-C(11)	107.54(17)
N(1)-C(16)	1.459(3)	C(13)-N(12)-C(7)	128.87(17)
O(2)-C(2)	1.252(3)	C(11)-N(12)-C(7)	122.15(16)
O(3)-C(8)	1.413(2)	C(5)-C(6)-C(7)	116.37(16)
O(3)-C(17)	1.439(2)	O(1)-C(10)-N(9)	121.63(19)
N(3)-C(2)	1.355(3)	O(1)-C(10)-C(11)	122.74(19)
C(15)-C(11)	1.380(3)	N(9)-C(10)-C(11)	115.62(18)
C(15)-C(14)	1.413(3)	O(2)-C(2)-N(3)	127.34(19)
N(12)-C(11)	1.382(3)	O(2)-C(2)-N(1)	126.9(2)
C(6)-C(5)	1.492(3)	N(3)-C(2)-N(1)	105.78(17)
C(10)-C(11)	1.464(3)	C(15)-C(11)-N(12)	108.65(18)
O(1S)-C(1S)	1.415(3)	C(15)-C(11)-C(10)	131.65(19)
		N(12)-C(11)-C(10)	119.69(18)
N(12)-C(7)-C(8)	106.31(16)		
N(12)-C(7)-C(6)	107.86(14)		
C(8)-C(7)-C(6)	113.71(16)	C(4)-C(5)-N(1)	106.24(18)
C(10)-N(9)-C(8)	122.66(17)	C(4)-C(5)-C(6)	129.41(19)
N(12)-C(13)-C(14)	109.78(18)	N(1)-C(5)-C(6)	124.23(18)

C(13)-C(14)-C(15) 106.60(18)

Symmetry transformations used to generate equivalent atoms:

Table S19. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for (+)-*O*-methyl-pre-agelastatin A (**47**). The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2\ a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Br(1)	22(1)	15(1)	20(1)	-4(1)	1(1)	-4(1)
C(7)	10(1)	12(1)	14(1)	-2(1)	1(1)	0(1)
O(1)	11(1)	18(1)	23(1)	2(1)	2(1)	0(1)
N(9)	14(1)	10(1)	17(1)	-2(1)	2(1)	-2(1)
C(13)	18(1)	12(1)	14(1)	-2(1)	-2(1)	0(1)
C(4)	16(1)	14(1)	17(1)	-2(1)	0(1)	1(1)
N(1)	11(1)	11(1)	17(1)	-2(1)	-1(1)	0(1)
O(2)	17(1)	14(1)	24(1)	-4(1)	-1(1)	4(1)
O(3)	20(1)	15(1)	12(1)	0(1)	-2(1)	-1(1)
C(17)	27(1)	21(1)	14(1)	-2(1)	-3(1)	1(1)
N(3)	11(1)	16(1)	21(1)	1(1)	2(1)	0(1)
C(15)	13(1)	16(1)	15(1)	0(1)	2(1)	3(1)
C(8)	12(1)	11(1)	13(1)	-1(1)	1(1)	1(1)
N(12)	11(1)	12(1)	14(1)	-1(1)	1(1)	1(1)
C(6)	14(1)	16(1)	14(1)	-1(1)	-1(1)	2(1)
C(10)	11(1)	12(1)	15(1)	4(1)	-3(1)	0(1)
C(2)	12(1)	19(1)	13(1)	-2(1)	-1(1)	1(1)
C(16)	14(1)	16(1)	25(1)	-3(1)	-1(1)	-3(1)
C(11)	11(1)	15(1)	13(1)	2(1)	0(1)	1(1)
C(5)	14(1)	14(1)	13(1)	-2(1)	-1(1)	1(1)
C(14)	17(1)	16(1)	16(1)	-1(1)	0(1)	4(1)
O(1S)	19(1)	29(1)	32(1)	6(1)	5(1)	-2(1)
C(1S)	27(1)	19(1)	25(1)	4(1)	-2(1)	-2(1)

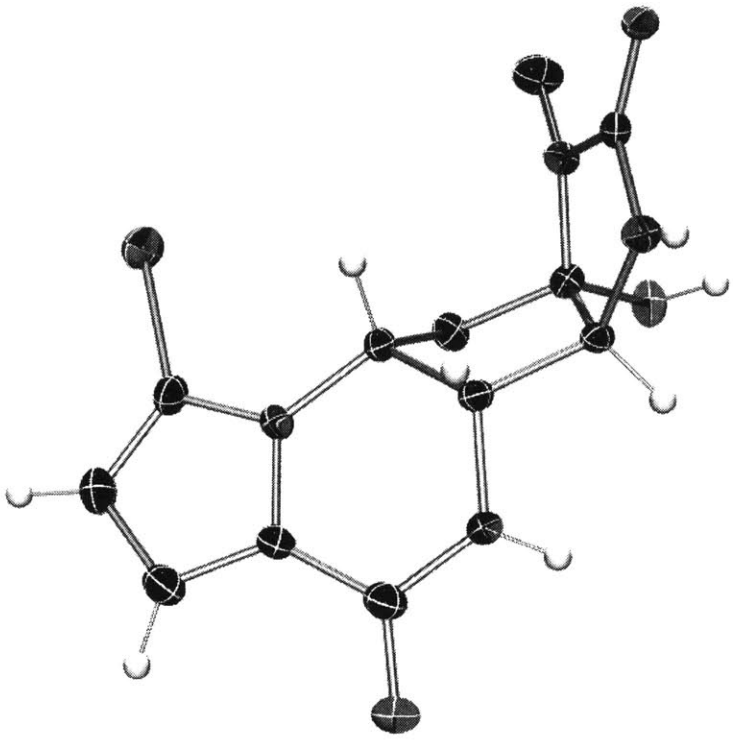
Table S20. Hydrogen coordinates ($x\ 10^4$) and isotropic displacement parameters ($Å^2 x\ 10^3$) for (+)-*O*-methyl-pre-agelastatin A (**47**).

	x	y	z	U(eq)
H(7)	-318	7952	9764	14
H(9)	1820(20)	10950(16)	10199(16)	16
H(4)	-2976	8497	8837	19
H(17A)	2117	9936	11799	31
H(17B)	1631	8777	12415	31
H(17C)	634	9834	12097	31
H(3)	-4461(16)	10210(20)	9060(17)	19
H(15)	4294	8004	8358	18

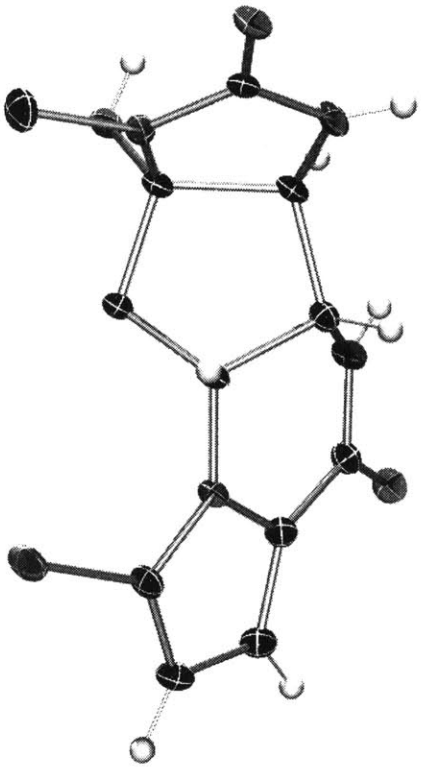
H(8)	-3	9980	10504	15
H(6A)	284	9898	8423	17
H(6B)	-440	8646	8131	17
H(16A)	-1189	12947	9057	27
H(16B)	-443	12197	8244	27
H(16C)	-99	11960	9336	27
H(14)	3098	5989	8009	20
H(1O1)	9730(20)	1980(20)	1516(16)	32
H(1S1)	7284	1498	1873	36
H(1S2)	7921	1080	890	36
H(1S3)	7799	2526	1145	36

Crystal Structure of (–)-Agelastatin A (1)

View 1:



View 2:



View 3:

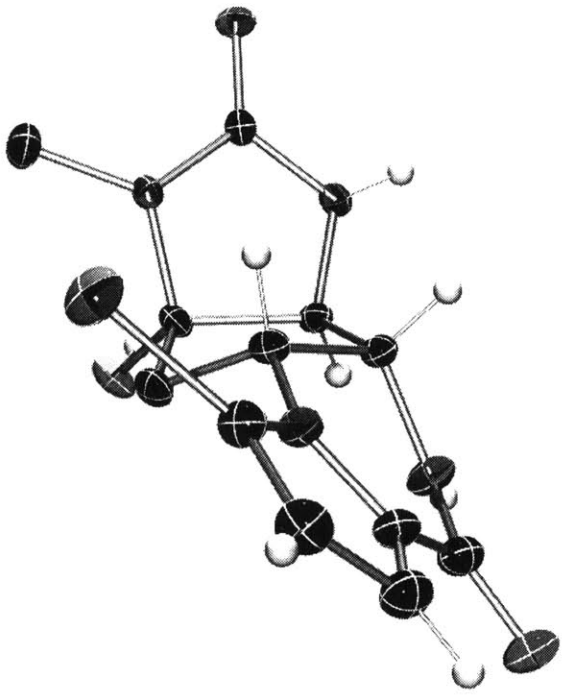


Table S21. Crystal data and structure refinement for (–)-agelastatin A (**1**).

Identification code	10026	
Empirical formula	C12 H16 Br N4 O4.50	
Formula weight	368.20	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)	
Unit cell dimensions	a = 13.5873(14) Å	a= 90°.
	b = 6.9161(7) Å	b= 98.786(2)°.
	c = 15.7114(17) Å	g = 90°.
Volume	1459.1(3) Å^3	
Z	4	
Density (calculated)	1.676 Mg/m^3	
Absorption coefficient	2.844 mm^{-1}	
F(000)	748	
Crystal size	0.48 x 0.25 x 0.04 mm^3	
Theta range for data collection	1.31 to 30.03°.	
Index ranges	-19<=h<=19, -9<=k<=9, -22<=l<=21	
Reflections collected	39133	
Independent reflections	8508 [R(int) = 0.0524]	
Completeness to theta = 30.03°	99.9 %	
Absorption correction	None	
Max. and min. transmission	0.8947 and 0.3422	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	8508 / 402 / 426	
Goodness-of-fit on F^2	1.017	
Final R indices [I>2sigma(I)]	R1 = 0.0346, wR2 = 0.0795	
R indices (all data)	R1 = 0.0437, wR2 = 0.0829	
Absolute structure parameter	0.015(5)	
Largest diff. peak and hole	0.875 and -0.490 e.Å^{-3}	

Table S22. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for (–)-agelastatin A (**1**). U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Br(1A)	10024(1)	9800(1)	4181(1)	20(1)
O(1A)	7655(1)	2032(3)	3166(1)	19(1)
O(2A)	5380(1)	12339(3)	4193(1)	15(1)
O(3A)	6575(1)	7489(3)	5834(1)	16(1)
N(1A)	6544(2)	10312(3)	4960(1)	13(1)
N(3A)	5476(2)	9051(3)	3910(2)	16(1)
N(9A)	6925(1)	4729(4)	3601(1)	16(1)
N(12A)	8666(1)	6765(3)	3693(1)	13(1)
C(2A)	5761(2)	10700(4)	4338(2)	13(1)
C(4A)	6100(2)	7438(4)	4214(2)	13(1)

C(5A)	6771(2)	8256(4)	5039(2)	13(1)
C(6A)	7840(2)	7741(4)	4947(2)	14(1)
C(7A)	7830(2)	7787(4)	3976(2)	12(1)
C(8A)	6834(2)	6839(3)	3592(2)	13(1)
C(10A)	7700(2)	3773(4)	3354(2)	15(1)
C(11A)	8604(2)	4898(4)	3361(2)	14(1)
C(13A)	9618(2)	7390(4)	3713(2)	15(1)
C(14A)	10170(2)	5986(4)	3382(2)	16(1)
C(15A)	9532(2)	4414(3)	3163(2)	16(1)
C(16A)	7030(2)	11771(4)	5551(2)	20(1)
Br(1B)	677(1)	1059(1)	-861(1)	30(1)
O(1B)	3160(2)	8724(3)	175(1)	28(1)
O(2B)	3843(1)	-1576(3)	2515(1)	17(1)
O(3B)	1898(1)	3202(3)	2824(1)	22(1)
N(1B)	2475(2)	446(3)	2140(1)	15(1)
N(3B)	3984(2)	1698(3)	2274(2)	16(1)
N(9B)	3293(2)	6008(4)	988(2)	21(1)
N(12B)	1965(2)	4066(3)	-199(2)	18(1)
C(2B)	3473(2)	41(4)	2325(2)	14(1)
C(4B)	3345(2)	3314(4)	2009(2)	14(1)
C(5B)	2286(2)	2529(4)	2096(2)	15(1)
C(6B)	1615(2)	3162(4)	1279(2)	18(1)
C(7B)	2307(2)	3044(4)	598(2)	16(1)
C(8B)	3300(2)	3896(4)	1057(2)	15(1)
C(10B)	2944(2)	6983(4)	254(2)	22(1)
C(11B)	2275(2)	5912(4)	-382(2)	20(1)
C(13B)	1303(2)	3459(4)	-886(2)	20(1)
C(14B)	1190(2)	4839(5)	-1516(2)	25(1)
C(15B)	1809(2)	6408(4)	-1198(2)	25(1)
C(16B)	1704(2)	-950(4)	2232(2)	26(1)
O(1W)	5937(1)	1920(3)	1936(2)	27(1)
O(2W)	3590(2)	477(4)	8668(2)	47(1)
O(3W)	4605(2)	3913(5)	9290(2)	59(1)

Table S23. Bond lengths [Å] and angles [°] for (–)-agelastatin A (**1**).

Br(1A)-C(13A)	1.870(3)	N(12A)-C(7A)	1.464(3)
O(1A)-C(10A)	1.239(3)	C(4A)-C(8A)	1.556(3)
O(2A)-C(2A)	1.252(3)	C(4A)-C(5A)	1.571(3)
O(3A)-C(5A)	1.419(3)	C(5A)-C(6A)	1.524(3)
N(1A)-C(2A)	1.357(3)	C(6A)-C(7A)	1.523(3)
N(1A)-C(5A)	1.456(3)	C(7A)-C(8A)	1.541(3)
N(1A)-C(16A)	1.459(3)	C(10A)-C(11A)	1.453(3)
N(3A)-C(2A)	1.350(3)	C(11A)-C(15A)	1.385(3)
N(3A)-C(4A)	1.438(3)		
N(9A)-C(10A)	1.350(3)		
N(9A)-C(8A)	1.465(3)	C(13A)-C(14A)	1.376(4)
N(12A)-C(13A)	1.360(3)	C(14A)-C(15A)	1.401(4)
N(12A)-C(11A)	1.391(3)	Br(1B)-C(13B)	1.868(3)

O(1B)-C(10B)	1.251(3)
O(2B)-C(2B)	1.244(3)
O(3B)-C(5B)	1.410(3)
N(1B)-C(2B)	1.372(3)
N(1B)-C(16B)	1.447(3)
N(1B)-C(5B)	1.463(3)
N(3B)-C(2B)	1.349(3)
N(3B)-C(4B)	1.437(3)
N(9B)-C(10B)	1.357(4)
N(9B)-C(8B)	1.465(3)
N(12B)-C(13B)	1.361(3)
N(12B)-C(11B)	1.388(4)
N(12B)-C(7B)	1.452(3)
C(4B)-C(8B)	1.541(4)
C(4B)-C(5B)	1.563(3)
C(5B)-C(6B)	1.521(4)
C(6B)-C(7B)	1.530(3)
C(7B)-C(8B)	1.546(3)
C(10B)-C(11B)	1.448(4)
C(11B)-C(15B)	1.384(4)
C(13B)-C(14B)	1.367(4)
C(14B)-C(15B)	1.416(4)

C(2A)-N(1A)-C(5A)	112.7(2)
C(2A)-N(1A)-C(16A)	123.4(2)
C(5A)-N(1A)-C(16A)	123.5(2)
C(2A)-N(3A)-C(4A)	112.4(2)
C(10A)-N(9A)-C(8A)	123.6(2)
C(13A)-N(12A)-C(11A)	107.9(2)
C(13A)-N(12A)-C(7A)	128.3(2)
C(11A)-N(12A)-C(7A)	123.82(19)
O(2A)-C(2A)-N(3A)	126.5(2)
O(2A)-C(2A)-N(1A)	124.5(2)
N(3A)-C(2A)-N(1A)	109.0(2)
N(3A)-C(4A)-C(8A)	113.5(2)
N(3A)-C(4A)-C(5A)	103.5(2)
C(8A)-C(4A)-C(5A)	105.46(18)
O(3A)-C(5A)-N(1A)	111.9(2)
O(3A)-C(5A)-C(6A)	107.80(19)
N(1A)-C(5A)-C(6A)	114.4(2)
O(3A)-C(5A)-C(4A)	115.33(19)
N(1A)-C(5A)-C(4A)	101.15(19)
C(6A)-C(5A)-C(4A)	106.22(19)
C(7A)-C(6A)-C(5A)	103.11(19)
N(12A)-C(7A)-C(6A)	113.87(19)
N(12A)-C(7A)-C(8A)	110.6(2)
C(6A)-C(7A)-C(8A)	104.85(19)
N(9A)-C(8A)-C(7A)	110.6(2)
N(9A)-C(8A)-C(4A)	108.67(19)
C(7A)-C(8A)-C(4A)	104.47(19)
O(1A)-C(10A)-N(9A)	122.2(2)
O(1A)-C(10A)-C(11A)	122.2(2)
N(9A)-C(10A)-C(11A)	115.5(2)
C(15A)-C(11A)-N(12A)	107.7(2)
C(15A)-C(11A)-C(10A)	131.8(3)
N(12A)-C(11A)-C(10A)	120.2(2)
N(12A)-C(13A)-C(14A)	109.8(2)
N(12A)-C(13A)-Br(1A)	120.95(18)
C(14A)-C(13A)-Br(1A)	129.24(18)
C(13A)-C(14A)-C(15A)	106.8(2)
C(11A)-C(15A)-C(14A)	107.9(2)
C(2B)-N(1B)-C(16B)	123.3(2)
C(2B)-N(1B)-C(5B)	111.8(2)
C(16B)-N(1B)-C(5B)	122.5(2)
C(2B)-N(3B)-C(4B)	112.60(19)
C(10B)-N(9B)-C(8B)	123.8(2)
C(13B)-N(12B)-C(11B)	107.7(2)
C(13B)-N(12B)-C(7B)	128.2(2)
C(11B)-N(12B)-C(7B)	124.0(2)
O(2B)-C(2B)-N(3B)	125.8(2)
O(2B)-C(2B)-N(1B)	125.8(2)
N(3B)-C(2B)-N(1B)	108.4(2)
N(3B)-C(4B)-C(8B)	114.7(2)
N(3B)-C(4B)-C(5B)	103.2(2)
C(8B)-C(4B)-C(5B)	106.0(2)
O(3B)-C(5B)-N(1B)	111.8(2)
O(3B)-C(5B)-C(6B)	109.9(2)
N(1B)-C(5B)-C(6B)	113.7(2)
O(3B)-C(5B)-C(4B)	114.8(2)
N(1B)-C(5B)-C(4B)	100.89(19)
C(6B)-C(5B)-C(4B)	105.5(2)
C(5B)-C(6B)-C(7B)	102.81(19)
N(12B)-C(7B)-C(6B)	115.4(2)
N(12B)-C(7B)-C(8B)	111.0(2)
C(6B)-C(7B)-C(8B)	103.9(2)
N(9B)-C(8B)-C(4B)	109.3(2)
N(9B)-C(8B)-C(7B)	110.5(2)
C(4B)-C(8B)-C(7B)	104.8(2)
O(1B)-C(10B)-N(9B)	120.4(3)
O(1B)-C(10B)-C(11B)	123.8(3)
N(9B)-C(10B)-C(11B)	115.7(3)
C(15B)-C(11B)-N(12B)	108.0(2)
C(15B)-C(11B)-C(10B)	131.6(3)

N(12B)-C(11B)-C(10B)	120.4(2)
N(12B)-C(13B)-C(14B)	110.2(3)
N(12B)-C(13B)-Br(1B)	120.4(2)
C(14B)-C(13B)-Br(1B)	129.4(2)
C(13B)-C(14B)-C(15B)	106.6(2)

C(11B)-C(15B)-C(14B) 107.4(3)

Symmetry transformations used to generate equivalent atoms:

Table S24. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for (–)-agelastatin A (**1**). The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2\ a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Br(1A)	13(1)	17(1)	30(1)	-5(1)	4(1)	-5(1)
O(1A)	20(1)	12(1)	25(1)	-2(1)	2(1)	0(1)
O(2A)	10(1)	13(1)	21(1)	2(1)	2(1)	1(1)
O(3A)	12(1)	22(1)	14(1)	4(1)	2(1)	0(1)
N(1A)	12(1)	13(1)	14(1)	-2(1)	1(1)	0(1)
N(3A)	11(1)	13(1)	22(1)	-1(1)	-4(1)	2(1)
N(9A)	12(1)	10(1)	25(1)	-1(1)	4(1)	-4(1)
N(12A)	10(1)	12(1)	16(1)	0(1)	2(1)	0(1)
C(2A)	8(1)	17(1)	14(1)	-1(1)	4(1)	0(1)
C(4A)	8(1)	14(1)	17(1)	2(1)	1(1)	1(1)
C(5A)	9(1)	13(1)	17(1)	0(1)	2(1)	1(1)
C(6A)	9(1)	16(1)	15(1)	-1(1)	2(1)	1(1)
C(7A)	9(1)	10(1)	18(1)	0(1)	2(1)	0(1)
C(8A)	11(1)	11(1)	16(1)	0(1)	1(1)	0(1)
C(10A)	14(1)	15(1)	16(1)	2(1)	0(1)	1(1)
C(11A)	15(1)	12(1)	16(1)	0(1)	3(1)	2(1)
C(13A)	12(1)	14(1)	20(1)	0(1)	2(1)	-4(1)
C(14A)	13(1)	17(1)	20(1)	3(1)	5(1)	3(1)
C(15A)	16(1)	13(1)	19(1)	1(1)	5(1)	2(1)
C(16A)	19(1)	16(1)	24(1)	-5(1)	-3(1)	-2(1)
Br(1B)	29(1)	26(1)	29(1)	-1(1)	-9(1)	-9(1)
O(1B)	38(1)	17(1)	29(1)	3(1)	1(1)	-3(1)
O(2B)	17(1)	14(1)	20(1)	0(1)	-2(1)	2(1)
O(3B)	16(1)	32(1)	18(1)	-3(1)	2(1)	8(1)
N(1B)	10(1)	16(1)	18(1)	2(1)	1(1)	1(1)
N(3B)	10(1)	17(1)	22(1)	0(1)	0(1)	1(1)
N(9B)	28(1)	14(1)	18(1)	0(1)	-2(1)	-4(1)
N(12B)	19(1)	17(1)	17(1)	2(1)	-2(1)	0(1)
C(2B)	13(1)	18(1)	11(1)	-1(1)	2(1)	-1(1)
C(4B)	13(1)	12(1)	17(1)	0(1)	0(1)	0(1)
C(5B)	11(1)	16(1)	17(1)	-3(1)	2(1)	2(1)
C(6B)	12(1)	21(1)	20(1)	2(1)	-1(1)	3(1)
C(7B)	16(1)	14(1)	15(1)	0(1)	-2(1)	1(1)
C(8B)	15(1)	12(1)	17(1)	0(1)	0(1)	0(1)
C(10B)	25(1)	18(1)	22(1)	2(1)	4(1)	2(1)
C(11B)	23(1)	16(1)	20(1)	2(1)	2(1)	2(1)
C(13B)	20(1)	21(1)	19(1)	-3(1)	-2(1)	-1(1)
C(14B)	26(1)	30(1)	18(1)	0(1)	-2(1)	0(1)
C(15B)	29(1)	23(2)	22(1)	4(1)	4(1)	2(1)

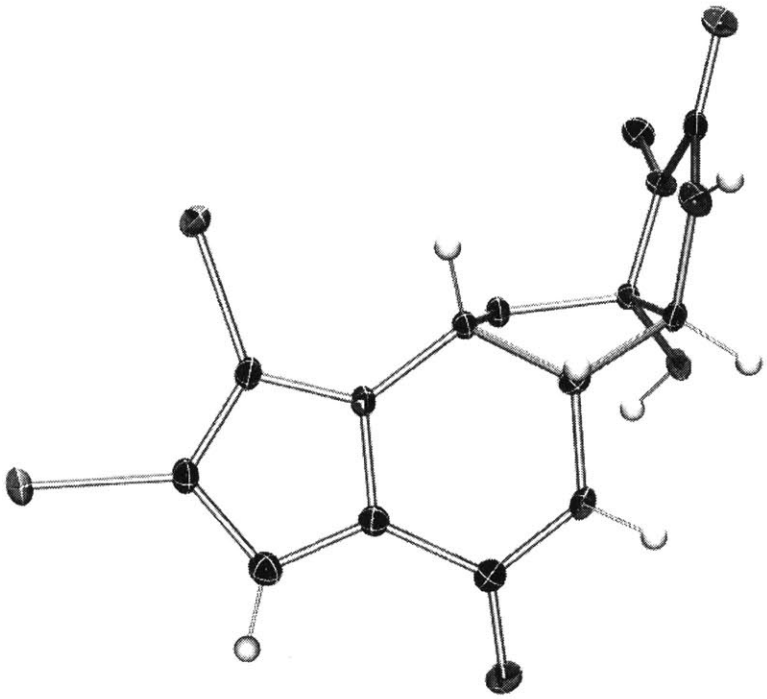
C(16B)	17(1)	23(1)	38(2)	5(1)	4(1)	-5(1)
O(1W)	16(1)	29(1)	36(1)	-3(1)	4(1)	-4(1)
O(2W)	68(2)	37(1)	39(2)	1(1)	17(1)	-4(1)
O(3W)	58(2)	52(2)	70(2)	14(2)	17(2)	4(2)

Table S25. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^{2}x 10^3) for (–)-agelastatin A (**1**).

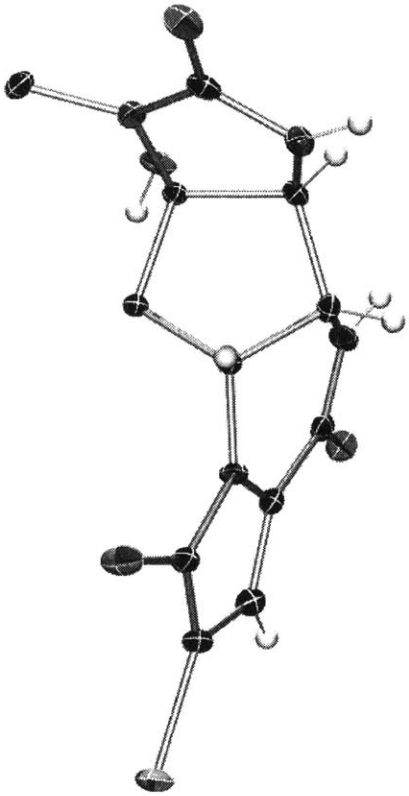
	x	y	z	U(eq)
H(3A)	5979(14)	7400(50)	5910(20)	24
H(3C)	5030(18)	8970(50)	3485(14)	19
H(9A)	6394(16)	4140(40)	3660(20)	19
H(4A)	5695	6311	4359	16
H(6A1)	8314	8702	5242	16
H(6A2)	8020	6441	5184	16
H(7A)	7831	9163	3780	15
H(8A)	6601	7324	2996	15
H(14A)	10852	6068	3316	20
H(15A)	9704	3226	2921	19
H(16A)	6673	13002	5450	31
H(16B)	7720	11939	5453	31
H(16C)	7023	11354	6146	31
H(3B)	2340(20)	2970(50)	3263(17)	33
H(3D)	4624(13)	1690(40)	2343(19)	20
H(9B)	3540(20)	6620(40)	1443(15)	25
H(4B)	3520	4449	2396	17
H(6B1)	1369	4497	1334	22
H(6B2)	1039	2280	1140	22
H(7B)	2412	1653	463	19
H(8B)	3876	3338	813	18
H(14B)	776	4761	-2060	30
H(15B)	1889	7585	-1492	30
H(16D)	2007	-2223	2361	39
H(16E)	1234	-1018	1694	39
H(16F)	1351	-553	2702	39
H(1WB)	5980(30)	3100(30)	1780(20)	40
H(1WA)	6400(20)	1660(50)	2325(18)	40
H(2WA)	3980(30)	1650(50)	8790(30)	70
H(2WB)	3620(30)	90(60)	9199(16)	70
H(3WA)	4290(30)	4630(70)	8840(30)	89
H(3WB)	5240(15)	4070(80)	9230(30)	89

Crystal Structure of (–)-Agelastatin B (2)

View 1:



View 2:



View 3:

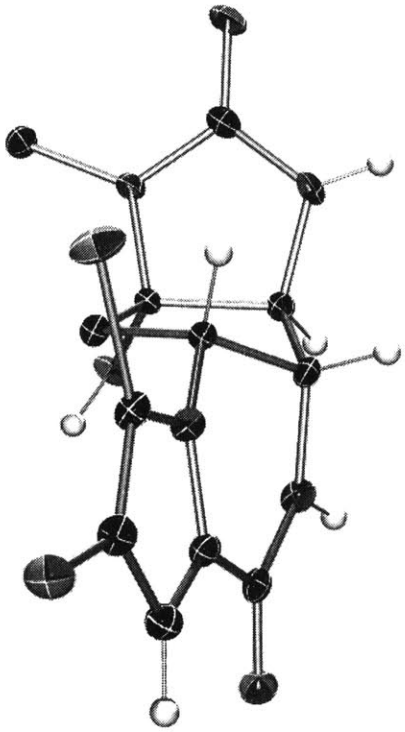


Table S26. Crystal data and structure refinement for (–)-agelastatin B (**2**).

Identification code	agb	
Empirical formula	C12 H12 Br2 N4 O3	
Formula weight	420.08	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)	
Unit cell dimensions	a = 6.7838(7) Å	a= 90°.
	b = 8.1180(9) Å	b= 100.117(2)°.
	c = 12.9579(14) Å	g = 90°.
Volume	702.51(13) Å^3	
Z	2	
Density (calculated)	1.986 Mg/m^3	
Absorption coefficient	5.785 mm^{-1}	
F(000)	412	
Crystal size	0.35 x 0.20 x 0.10 mm^3	
Theta range for data collection	1.60 to 29.13°.	
Index ranges	-9<=h<=9, -11<=k<=11, -17<=l<=17	
Reflections collected	12240	
Independent reflections	3735 [R(int) = 0.0338]	
Completeness to theta = 29.13°	99.9 %	
Absorption correction	None	
Max. and min. transmission	0.5954 and 0.2366	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3735 / 200 / 200	
Goodness-of-fit on F^2	1.009	
Final R indices [I>2sigma(I)]	R1 = 0.0227, wR2 = 0.0488	
R indices (all data)	R1 = 0.0243, wR2 = 0.0491	
Absolute structure parameter	0.012(6)	
Largest diff. peak and hole	0.492 and -0.270 e.Å^{-3}	

Table S27. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for (–)-agelastatin B (**2**). U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Br(1)	219(1)	10031(1)	-1432(1)	18(1)
N(12)	3774(3)	9351(2)	1377(2)	12(1)
O(1)	936(2)	11219(2)	3162(1)	17(1)
C(13)	3279(3)	9108(3)	324(2)	13(1)
Br(2)	4999(1)	8072(1)	-439(1)	20(1)
O(2)	4807(2)	6491(2)	4466(1)	15(1)
N(9)	4149(3)	10321(2)	3438(2)	14(1)
C(14)	1454(3)	9862(3)	-28(2)	15(1)
O(3)	11057(2)	5858(2)	3802(1)	18(1)
N(3)	9069(3)	8190(3)	3777(2)	15(1)
C(15)	788(3)	10545(3)	849(2)	15(1)

N(1)	7672(3)	5736(2)	3815(2)	12(1)
C(11)	2239(3)	10217(3)	1706(2)	13(1)
C(10)	2364(3)	10642(3)	2814(2)	13(1)
C(8)	5955(3)	9731(3)	3077(2)	12(1)
C(7)	5382(3)	8591(3)	2125(2)	10(1)
C(6)	4762(3)	6961(3)	2580(2)	12(1)
C(5)	5979(3)	6866(3)	3712(2)	10(1)
C(4)	7047(3)	8570(3)	3916(2)	11(1)
C(2)	9426(3)	6543(3)	3810(2)	14(1)
C(16)	7436(3)	3975(3)	3701(2)	15(1)

Table S28. Bond lengths [Å] and angles [°] for (–)-agelastatin B (**2**).

Br(1)-C(14)	1.870(2)	C(13)-C(14)-Br(1)	125.06(17)
N(12)-C(13)	1.362(3)	C(15)-C(14)-Br(1)	127.15(17)
N(12)-C(11)	1.384(3)	C(2)-N(3)-C(4)	111.91(19)
N(12)-C(7)	1.462(3)	C(11)-C(15)-C(14)	106.9(2)
O(1)-C(10)	1.231(3)	C(2)-N(1)-C(16)	124.0(2)
C(13)-C(14)	1.384(3)	C(2)-N(1)-C(5)	111.90(18)
C(13)-Br(2)	1.857(2)	C(16)-N(1)-C(5)	122.83(19)
O(2)-C(5)	1.397(3)	C(15)-C(11)-N(12)	108.6(2)
N(9)-C(10)	1.358(3)	C(15)-C(11)-C(10)	131.0(2)
N(9)-C(8)	1.466(3)	N(12)-C(11)-C(10)	120.32(19)
C(14)-C(15)	1.408(3)	O(1)-C(10)-N(9)	122.1(2)
O(3)-C(2)	1.240(3)	O(1)-C(10)-C(11)	122.4(2)
N(3)-C(2)	1.358(3)	N(9)-C(10)-C(11)	115.46(19)
N(3)-C(4)	1.448(3)	N(9)-C(8)-C(4)	107.60(18)
C(15)-C(11)	1.375(3)	N(9)-C(8)-C(7)	110.16(17)
N(1)-C(2)	1.359(3)	C(4)-C(8)-C(7)	102.86(17)
N(1)-C(16)	1.443(3)	N(12)-C(7)-C(8)	109.41(17)
N(1)-C(5)	1.458(3)	N(12)-C(7)-C(6)	113.27(17)
C(11)-C(10)	1.464(3)	C(8)-C(7)-C(6)	104.97(18)
C(8)-C(4)	1.528(3)	C(7)-C(6)-C(5)	105.61(17)
C(8)-C(7)	1.536(3)	O(2)-C(5)-N(1)	109.58(18)
C(7)-C(6)	1.537(3)	O(2)-C(5)-C(6)	113.45(16)
C(6)-C(5)	1.553(3)	N(1)-C(5)-C(6)	113.41(18)
C(5)-C(4)	1.562(3)	O(2)-C(5)-C(4)	112.21(18)
C(13)-N(12)-C(11)	108.44(18)	N(1)-C(5)-C(4)	101.94(16)
C(13)-N(12)-C(7)	128.84(19)	C(6)-C(5)-C(4)	105.65(18)
C(11)-N(12)-C(7)	121.58(19)	N(3)-C(4)-C(8)	113.20(18)
N(12)-C(13)-C(14)	108.33(19)	N(3)-C(4)-C(5)	102.22(17)
N(12)-C(13)-Br(2)	122.12(16)	C(8)-C(4)-C(5)	105.84(17)
C(14)-C(13)-Br(2)	129.36(18)	O(3)-C(2)-N(3)	126.5(2)
C(10)-N(9)-C(8)	125.5(2)	O(3)-C(2)-N(1)	124.6(2)
C(13)-C(14)-C(15)	107.7(2)	N(3)-C(2)-N(1)	108.85(19)

Symmetry transformations used to generate equivalent atoms:

Table S29. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for (–)-agelastatin B (**2**). The anisotropic

displacement factor exponent takes the form: $-2p^2[h^2 a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$

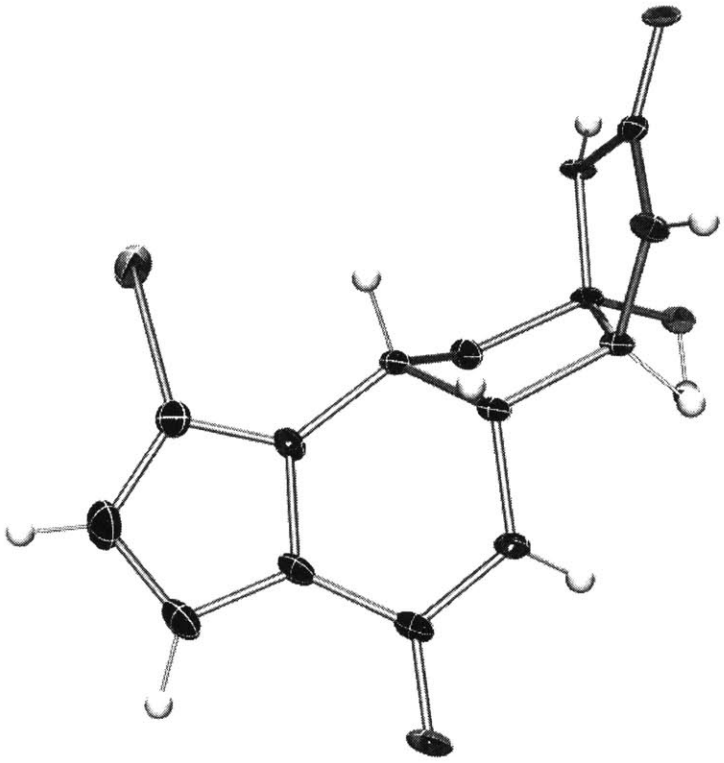
	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Br(1)	19(1)	23(1)	11(1)	3(1)	-2(1)	4(1)
N(12)	15(1)	12(1)	8(1)	1(1)	1(1)	2(1)
O(1)	18(1)	18(1)	17(1)	0(1)	7(1)	1(1)
C(13)	18(1)	12(1)	9(1)	0(1)	1(1)	2(1)
Br(2)	26(1)	24(1)	12(1)	0(1)	4(1)	11(1)
O(2)	9(1)	26(1)	10(1)	3(1)	1(1)	-1(1)
N(9)	18(1)	16(1)	9(1)	-3(1)	1(1)	2(1)
C(14)	18(1)	15(1)	10(1)	2(1)	0(1)	0(1)
O(3)	9(1)	26(1)	20(1)	-2(1)	2(1)	0(1)
N(3)	10(1)	16(1)	17(1)	1(1)	0(1)	-4(1)
C(15)	15(1)	15(1)	15(1)	2(1)	2(1)	1(1)
N(1)	10(1)	13(1)	14(1)	1(1)	2(1)	0(1)
C(11)	14(1)	10(1)	13(1)	0(1)	2(1)	1(1)
C(10)	17(1)	10(1)	13(1)	1(1)	4(1)	-2(1)
C(8)	14(1)	9(1)	13(1)	-1(1)	3(1)	0(1)
C(7)	11(1)	10(1)	9(1)	0(1)	0(1)	1(1)
C(6)	14(1)	11(1)	9(1)	0(1)	0(1)	0(1)
C(5)	9(1)	11(1)	8(1)	0(1)	2(1)	0(1)
C(4)	12(1)	13(1)	8(1)	-2(1)	1(1)	-1(1)
C(2)	11(1)	22(1)	8(1)	0(1)	1(1)	-1(1)
C(16)	16(1)	11(1)	17(1)	3(1)	2(1)	2(1)

Table S30. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for (–)-agelastatin B (**2**).

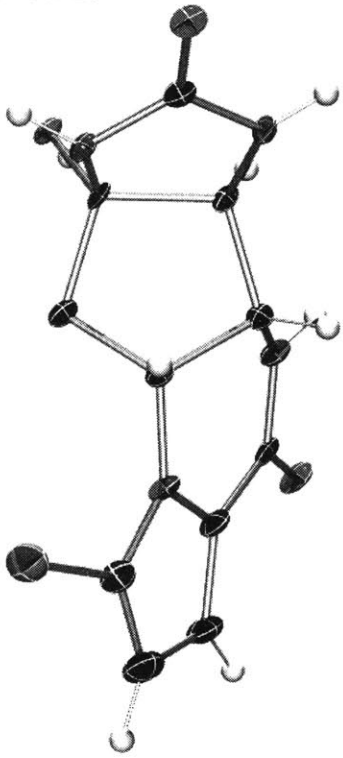
	x	y	z	U(eq)
H(2O2)	3570(30)	6500(30)	4190(20)	18
H(1N9)	4300(40)	10680(30)	4091(15)	17
H(1N3)	10050(30)	8880(30)	3900(20)	18
H(3A)	-430	11122	848	18
H(6)	6830	10660	2927	14
H(7)	6574	8405	1783	12
H(8A)	5086	6017	2156	14
H(8B)	3306	6953	2591	14
H(10)	7008	8984	4639	14
H(12A)	6600	3725	3022	22
H(12B)	6795	3544	4266	22
H(12C)	8753	3461	3736	22

Crystal Structure of (–)-Agelastatin D (4)

View 1:



View 2:



View 3:

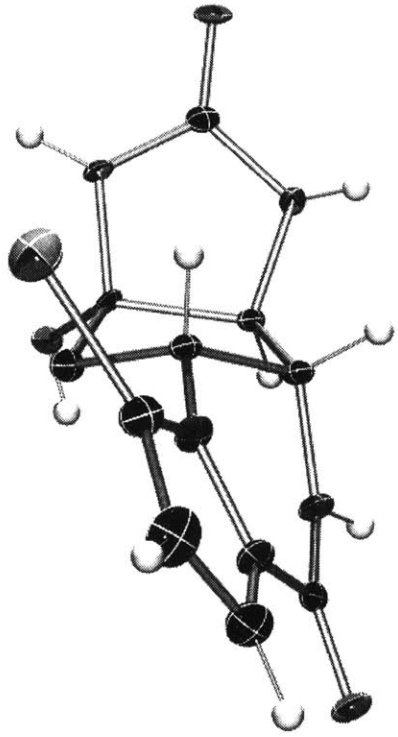


Table S31. Crystal data and structure refinement for (–)-agelastatin D (**4**).

Identification code	10087	
Empirical formula	C11 H11 Br N4 O3	
Formula weight	327.15	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2(1)	
Unit cell dimensions	a = 6.1269(7) Å	a= 90°.
	b = 6.8919(9) Å	b= 90°.
	c = 29.087(4) Å	g = 90°.
Volume	1228.2(3) Å^3	
Z	4	
Density (calculated)	1.769 Mg/m^3	
Absorption coefficient	3.357 mm^{-1}	
F(000)	656	
Crystal size	0.50 x 0.25 x 0.05 mm^3	
Theta range for data collection	1.40 to 30.48°.	
Index ranges	-8<=h<=8, -9<=k<=9, -41<=l<=41	
Reflections collected	33337	
Independent reflections	3716 [R(int) = 0.0679]	
Completeness to theta = 30.48°	99.9 %	
Absorption correction	None	
Max. and min. transmission	0.8501 and 0.2846	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3716 / 188 / 184	
Goodness-of-fit on F^2	1.161	
Final R indices [I>2sigma(I)]	R1 = 0.0464, wR2 = 0.1115	
R indices (all data)	R1 = 0.0515, wR2 = 0.1133	
Absolute structure parameter	0.046(11)	
Largest diff. peak and hole	1.323 and -1.028 e.Å^{-3}	

Table S32. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for (–)-agelastatin D (**4**). U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Br(1)	4297(1)	1321(1)	220(1)	24(1)
O(1)	11956(4)	-1060(4)	1580(1)	18(1)
O(2)	7309(4)	6416(4)	1862(1)	12(1)
O(3)	922(4)	4877(4)	2194(1)	14(1)
N(1)	3860(4)	5223(4)	1696(1)	11(1)
C(2)	2793(5)	4438(5)	2064(1)	11(1)
N(3)	4067(5)	3057(4)	2256(1)	12(1)
C(4)	6225(5)	2994(5)	2056(1)	10(1)
C(5)	6171(5)	4758(4)	1710(1)	10(1)
C(6)	7005(5)	3941(5)	1249(1)	13(1)

C(7)	6208(5)	1825(4)	1266(1)	10(1)
C(8)	6677(5)	1162(5)	1763(1)	11(1)
N(9)	8996(5)	658(4)	1814(1)	13(1)
C(10)	10128(5)	-366(5)	1494(1)	13(1)
C(11)	9127(6)	-516(5)	1045(1)	16(1)
N(12)	7237(5)	518(4)	943(1)	14(1)
C(13)	6672(6)	98(5)	497(1)	17(1)
C(14)	8155(7)	-1229(6)	316(1)	26(1)
C(15)	9677(6)	-1621(5)	667(1)	20(1)

Table S33. Bond lengths [Å] and angles [°] for (–)-agelastatin D (**4**).

Br(1)-C(13)	1.864(4)	C(8)-C(4)-C(5)	106.4(3)
O(1)-C(10)	1.244(4)	O(2)-C(5)-N(1)	108.2(3)
O(2)-C(5)	1.409(4)	O(2)-C(5)-C(6)	113.9(3)
O(3)-C(2)	1.244(4)	N(1)-C(5)-C(6)	112.3(3)
N(1)-C(2)	1.365(4)	O(2)-C(5)-C(4)	114.5(3)
N(1)-C(5)	1.452(4)	N(1)-C(5)-C(4)	102.0(2)
C(2)-N(3)	1.352(4)	C(6)-C(5)-C(4)	105.4(2)
N(3)-C(4)	1.446(4)	C(7)-C(6)-C(5)	102.3(3)
C(4)-C(8)	1.547(5)	N(12)-C(7)-C(6)	115.5(3)
C(4)-C(5)	1.578(5)	N(12)-C(7)-C(8)	110.1(3)
C(5)-C(6)	1.543(5)	C(6)-C(7)-C(8)	104.6(3)
C(6)-C(7)	1.538(5)	N(9)-C(8)-C(7)	110.1(3)
C(7)-N(12)	1.447(4)	N(9)-C(8)-C(4)	108.1(3)
C(7)-C(8)	1.544(5)	C(7)-C(8)-C(4)	103.9(3)
C(8)-N(9)	1.470(4)	C(10)-N(9)-C(8)	123.1(3)
N(9)-C(10)	1.360(5)	O(1)-C(10)-N(9)	121.3(4)
C(10)-C(11)	1.445(5)	O(1)-C(10)-C(11)	122.5(3)
C(11)-C(15)	1.381(5)	N(9)-C(10)-C(11)	116.1(3)
C(11)-N(12)	1.391(4)	C(15)-C(11)-N(12)	108.3(3)
N(12)-C(13)	1.373(5)	C(15)-C(11)-C(10)	131.0(3)
C(13)-C(14)	1.393(5)	N(12)-C(11)-C(10)	120.7(3)
C(14)-C(15)	1.408(6)	C(13)-N(12)-C(11)	107.7(3)
		C(13)-N(12)-C(7)	129.4(3)
C(2)-N(1)-C(5)	111.0(3)	C(11)-N(12)-C(7)	122.8(3)
O(3)-C(2)-N(3)	125.3(3)	N(12)-C(13)-C(14)	109.3(3)
O(3)-C(2)-N(1)	125.6(3)	N(12)-C(13)-Br(1)	120.6(3)
N(3)-C(2)-N(1)	109.0(3)	C(14)-C(13)-Br(1)	130.0(3)
C(2)-N(3)-C(4)	112.5(3)	C(13)-C(14)-C(15)	106.5(3)
N(3)-C(4)-C(8)	114.2(3)	C(11)-C(15)-C(14)	108.1(3)
N(3)-C(4)-C(5)	102.4(2)		

Symmetry transformations used to generate equivalent atoms:

Table S34. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for (–)-agelastatin D (**4**). The anisotropic

displacement factor exponent takes the form: $-2p^2[h^2 a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Br(1)	26(1)	25(1)	21(1)	-3(1)	-7(1)	1(1)
O(1)	13(1)	10(1)	31(1)	-1(1)	1(1)	5(1)
O(2)	10(1)	6(1)	20(1)	-2(1)	1(1)	-2(1)
O(3)	5(1)	15(1)	21(1)	-2(1)	0(1)	1(1)
N(1)	8(1)	9(1)	18(1)	1(1)	0(1)	4(1)
C(2)	9(1)	10(1)	15(2)	-3(1)	-2(1)	-1(1)
N(3)	12(1)	9(1)	15(1)	3(1)	3(1)	3(1)
C(4)	7(1)	7(1)	17(2)	0(1)	1(1)	0(1)
C(5)	8(1)	4(1)	17(2)	1(1)	-2(1)	2(1)
C(6)	12(1)	8(2)	18(2)	-2(1)	0(1)	-1(1)
C(7)	8(1)	9(1)	14(1)	-1(1)	0(1)	1(1)
C(8)	8(1)	11(1)	14(1)	0(1)	1(1)	2(1)
N(9)	10(1)	9(1)	20(1)	-2(1)	-2(1)	2(1)
C(10)	11(1)	5(1)	22(2)	1(1)	4(1)	-1(1)
C(11)	17(2)	8(1)	22(2)	-1(1)	3(1)	4(1)
N(12)	16(1)	8(1)	19(2)	-3(1)	0(1)	2(1)
C(13)	16(2)	14(2)	21(2)	-2(1)	-2(1)	-1(1)
C(14)	34(2)	17(2)	26(2)	-7(2)	-5(2)	-1(2)
C(15)	22(2)	12(2)	25(2)	-5(1)	4(1)	2(1)

Table S35. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for (–)-agelastatin D (**4**).

	x	y	z	U(eq)
H(1O2)	8600(40)	5990(60)	1906(15)	14
H(1N1)	3410(70)	6390(40)	1609(14)	13
H(1N3)	3770(70)	2630(70)	2528(9)	15
H(4)	7377	3178	2295	12
H(6A)	6362	4645	985	16
H(6B)	8617	4009	1229	16
H(7)	4595	1804	1214	12
H(8)	5710	60	1856	13
H(1N9)	9450(80)	550(70)	2091(8)	15
H(14)	8143	-1764	15	31
H(15)	10873	-2493	646	24

Chapter II.

Total Synthesis of the (–)-Trigonoliimine Alkaloids

Introduction and Background

In 2010, Hao and co-workers reported the isolation of structurally fascinating (+)-trigonoliimines A (**1**), and B (**2**) along with (–)-trigonoliimine C (**3**) from the leaves of *Trigonostemon lii* Y. T. Chang collected in Yunnan province of China (Figure 1).[1] They also examined trigonoliimines A (**1**) and C (**3**) in an anti-HIV assay where **1** was found to exhibit modest activity (EC_{50} = 0.95 μg/mL, TI = 7.9).[1] Fascinated by their unique molecular architecture and inspired by our hypothesis for their biogenesis, we have completed the first total synthesis of (–)-trigonoliimines A (**1**), B (**2**) and C (**3**) using a synthetic strategy based on asymmetric oxidation and reorganization of a single heterodimeric bistryptamine. This work allowed us to revise the absolute stereochemistry of all (–)-trigonoliimines.[2,3]

Oxidation and rearrangement of 2,3-disubstituted indole has served as an efficient strategy to access indoxyl moiety and has been applied in total synthesis of various alkaloids.[4] Representative examples are shown in Schemes 1 and 2. In 1979, Kishi and coworkers reported an oxidation of 2,3-disubstituted indole **5**, followed by base mediated alkyl shift to give indoxyl

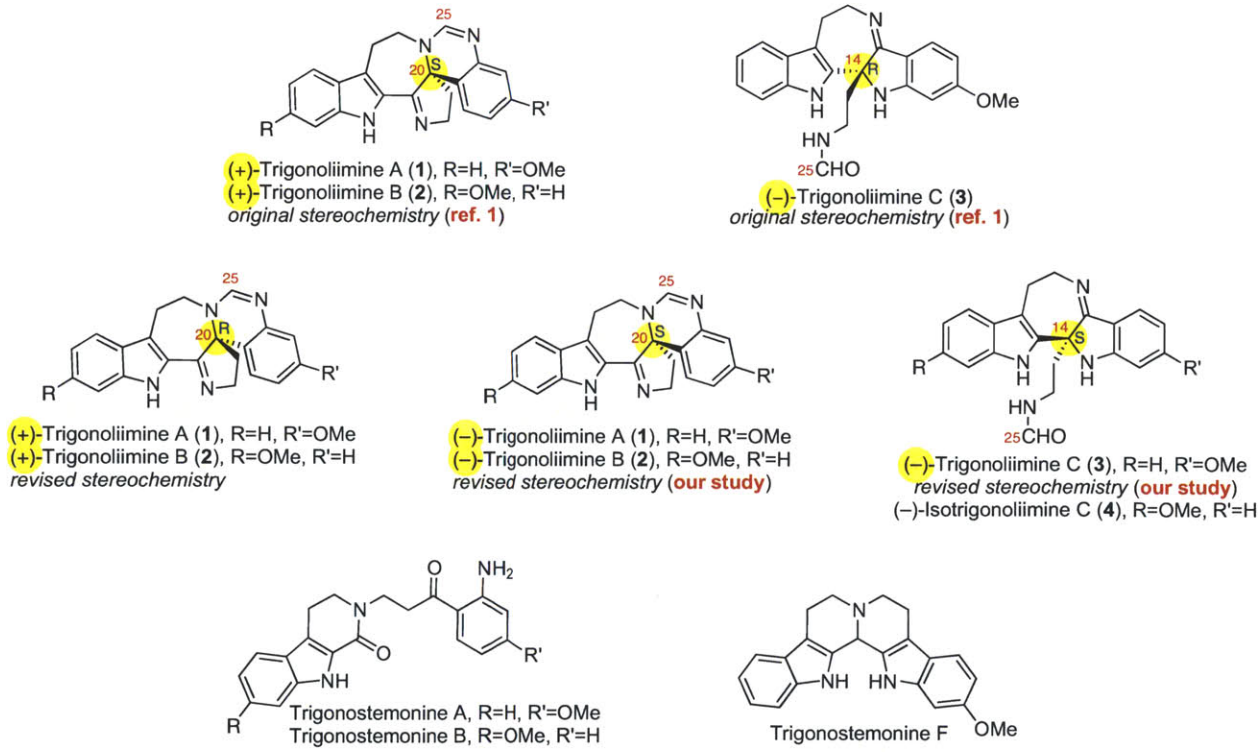
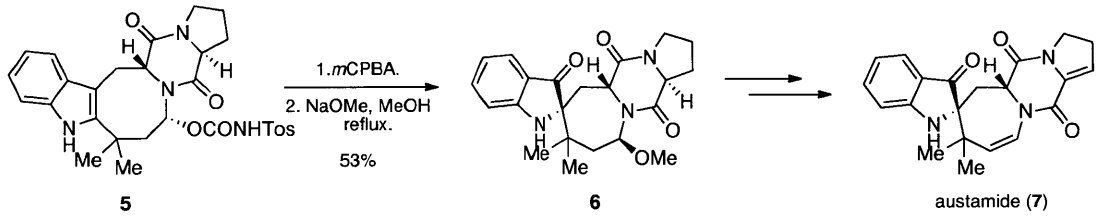
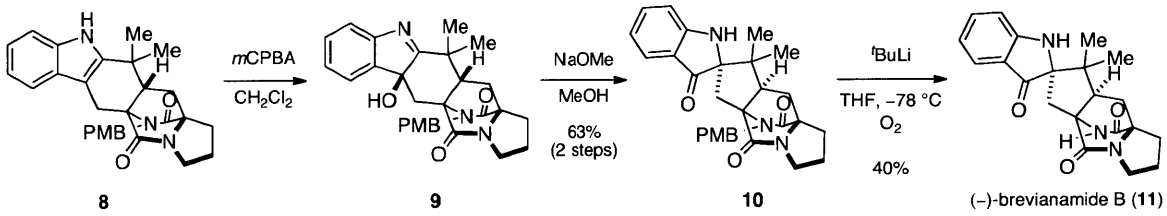


Figure 1. Representative trigonostemon alkaloids including the revised absolute stereochemistry of trigonoliimines A–C (**1**–**3**).

6 (53% yield), which was further derivatized to complete the total synthesis of (±)-austamide (**7**, Scheme 1).[4b] In 1990, Williams and coworkers reported the total synthesis of (–)-brevianamide B (**11**) by applying similar oxidation and rearrangement sequence to 2,3-disubstituted indole **8** (Scheme 2).[4c]



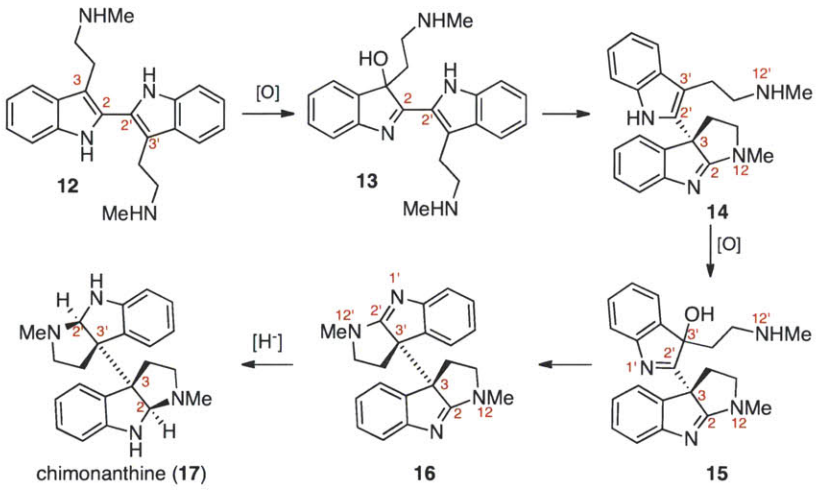
Scheme 1. Kishi's total synthesis of austamide (**7**).



Scheme 2. Williams' total synthesis of (–)-brevianamide (**11**).

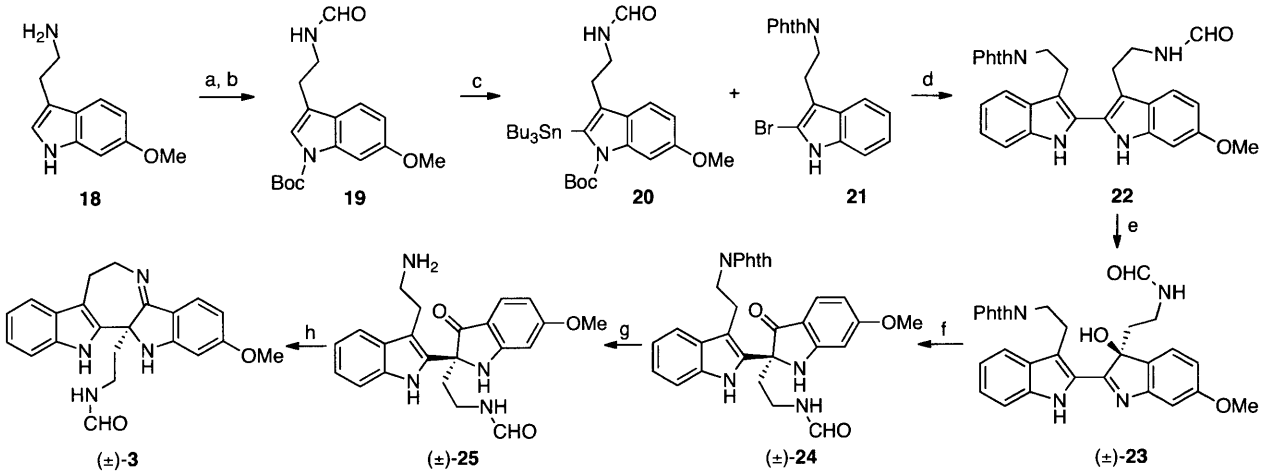
In 2008, our laboratory reported a hypothesis for the formation of calycanthaceous alkaloids from oxidation and rearrangement of a 2,2'-bistryptamine derivative (Scheme 3).[5] We hypothesized that the oxidation of 2,2'-bistryptamine **12** would give mono-oxidized hydroxyindolenine **13**, which after 1,2-aryl shift followed by cyclization of the amine moiety to the carbonyl group of the resulting oxindole intermediate would afford imine **14**. After another round of oxidation and rearrangement followed by reduction of **16**, we speculated the formation of chimonanthine (**17**). Our continued interest in this area yielded an efficient synthetic strategy involving oxidation and rearrangement of 2,3-disubstituted indoles, especially those with an aryl substituent at the 2-position, for an efficient access to oxindole products.[6] Despite the significant advancement in the area of asymmetric oxidation,[7] enantioselective oxidation of 2,3-disubstituted indole has remained a challenging problem.[8] Recently, Miller group, in collaboration with our laboratory, reported an asymmetric oxidation of 2,3-disubstituted indole using aspartyl based peptide catalyst.[9] The molecular structure of trigonoliimine alkaloids (Figure 1) drew our immediate attention upon their isolation due to their possible structural

relevance to hyroxyindolenine **13**, the intermediate in our hypothesis for the formation of chimonanthine (**17**) (Scheme 3). This observation, in conjunction with our interest in asymmetric oxidation of 2,3-disubstituted indole led us to set out the synthetic program aimed for the total synthesis of trigonoliimine alkaloids. Our first total synthesis of (–)-trigonoliimine A–C (**1**–**3**) and the related derivate (–)-isotrigonoliimine C (**4**), using asymmetric oxidation and reorganization of 2,3-disubstituted indole derivative and our revision of their absolute stereochemistry are described in detail in the following pages of this chapter.



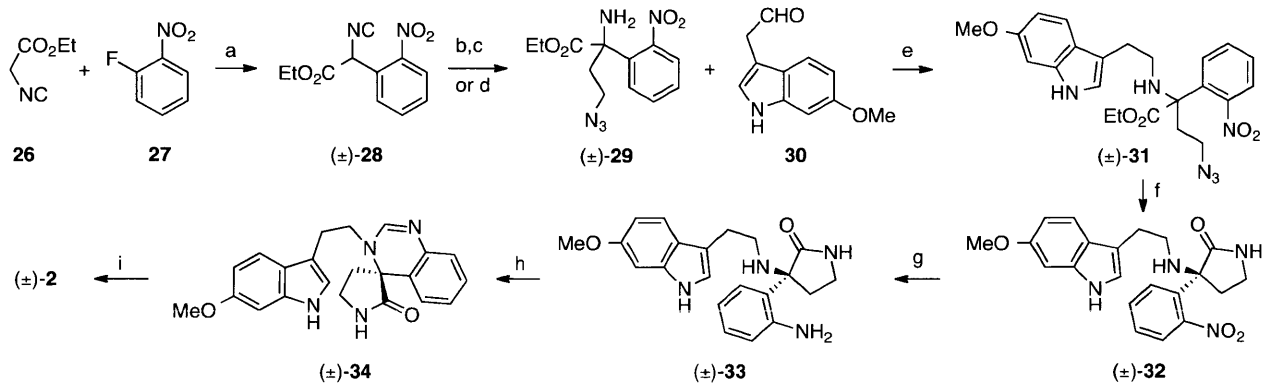
Scheme 3. Our group's hypothesis for the formation of chimonanthine (**17**) from bistryptamine derivative **12**.

Tambar and coworkers reported the total synthesis of (±)-trigonoliimine C using the same oxidation and rearrangement strategy (Scheme 4).[10,11] Their synthetic approach involved the union of 2-stannyltryptamine **20** derived from a Boc-directed lithiation and stannylation sequence and 2-bromotryptamine derivative **21** by Stille cross-coupling reaction (78% yield). The resulting bistryptamine **22** was treated with [bis(trifluoroacetoxy)iodo]benzene to afford hydroxyindolenine (±)-**23** in 67% yield along with its regioisomeric hydroxyindolenine (4% yield). Heating a solution of hydroxyindolenine (±)-**23** with hydrochloric acid in wet DMA at 150 °C yielded indoxyl (±)-**24** in 56% yield. Hydrazynolysis of phthalamide protecting group of indoxyl (±)-**24** followed by titanium isopropoxide mediated intramolecular condensation resulted in the formation of (±)-trigonoliimine C (**3**) in 81% yield over two steps.



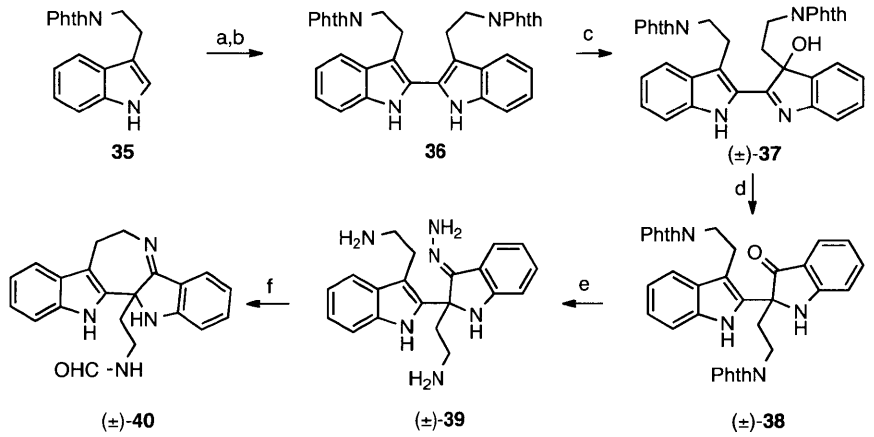
Scheme 4. Tambar's total synthesis of (±)-trigonoliimine C (**3**). Conditions: (a) HCO_2Et, reflux. (b) Boc_2O, DMAP, DMF, 23 °C, 72% (2 steps). (c) TMP, *n*-BuLi, Bu_3SnCl, THF, –78 °C, 86%. (d) $Pd(PPh_3)_4$, DMF, 110 °C, 78%. (e) $PhI(TFA)_2$, CH_3CN, H_2O, 0 °C, 67%. (f) HCl, DMA, H_2O, 150 °C, 56%. (g) NH_2NH_2, MeOH, CH_2Cl_2, 23 °C. (h) $Ti(O\textit{i}\text{-}Pr)_4$, THF, 70 °C, 81% (2 steps).

Recently, Zhu and coworkers reported the total synthesis of (±)-trigonoliimine B (**2**) using a late stage Bischler–Napieralski reaction (Scheme 5).[12] Their synthesis commenced with a nucleophilic aromatic substitution reaction between α-isocyanoacetate (**26**) and 2-fluoronitrobenzene (**27**) to afford α-aryl-α-isocyanoacetate (±)-**28** in 77% yield. Alkylation of (±)-**28** with 2-azidoiodoethane in the presence of sodium hydride in DMF (74% yield), followed by treatment with ethanolic hydrogen chloride gave amino ester (±)-**29** in 87% yield. This reaction sequence could be telescoped in one step procedure to give amino ester (±)-**29** in 70% yield (Scheme 5). Reductive amination between amine (±)-**29** and aldehyde **30** gave secondary amine (±)-**31** (quantitative yield), which after Staudinger reduction followed by calcium chloride treatment afforded lactam (±)-**32** in 72% yield. Reduction of the nitro group in lactam (±)-**32** in the presence of Raney nickel catalyst (81% yield), followed by treatment with trimethyl orthoformate in the presence of PPTS yielded the spirocycle (±)-**34** in 75% yield. For the key Bischler–Napieralski reaction, spirocycle (±)-**34** was treated with phosphoryl chloride in sulfolane at 80 °C to yield (±)-trigonoliimine B (**2**) in 51% yield.

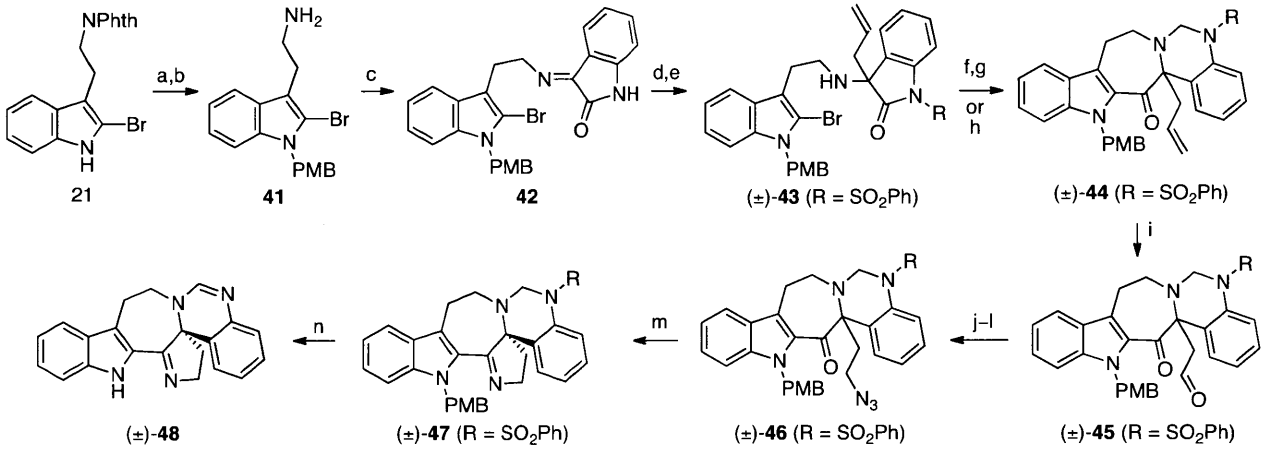


Scheme 5. Zhu's total synthesis of (±)-trigonoliimine B (**2**). Conditions: (a) Cs_2CO_3, DMSO, 23 °C, 77%. (b) $ICH_2CH_2N_3$, NaH, DMF, 23 °C, 74%. (c) Ethanolic HCl (1.25 M), 23 °C, 87%. (d) $ICH_2CH_2N_3$, NaH, DMF, 23 °C then ethanolic HCl (1.25 M), 23 °C, 70%. (e) $NaBH(OAc)_3$, CH_2Cl_2 23 °C, quantitative. (f) PPh_3, THF, H_2O, 60 °C then $CaCl_2$, MeOH, 80 °C, 72%. (g) H_2, Raney Ni, MeOH, 23 °C, 81%. (h) $HC(OMe)_3$, PPTS, 60 °C, 75%. (i) $POCl_3$, sulfolane, 80 °C, 51%.

In addition to these total syntheses reports, after our report of the total synthesis of all (–)-trigonoliimines,[2] Hao and Liu reported the synthesis of the skeleton of (±)-trigonoliimine C, using oxidation and 1,2-alkyl rearrangement (Scheme 6),[13] the same strategy used in our total synthesis of (–)-trigonoliimine C (**3**).[2] Shortly after, Shi and coworkers reported a synthetic approach to the hexacyclic skeleton of (±)-trigonoliimines A (**1**) and B (**2**) (Scheme 7).[14] In their studies, 2-bromotryptamine derivative **41**, derived from a known bromide **21** in 2 steps, was condensed with isatin in 92% yield, and the resulting imine **42** was allowed to react with allyl magnesium bromide followed by benzenesulfonylation to give tetracycle (±)-**43**. Upon treatment with *t*-BuLi, oxindole (±)-**43** underwent structural reorganization to give seven-membered intermediate (32% yield), which upon treatment with paraformaldehyde in the presence of cesium carbonate resulted in the formation of pentacycle (±)-**44** in 99% yield. Azide (±)-**46**, obtained in four steps from (±)-**44**, underwent aza-Wittig reaction upon treatment with triphenylphosphine to give imine (±)-**47** in 88% yield. Deprotection of the benezenesulfonyl and *p*-methoxybenzyl groups of imine (±)-**47** was achieved under dissolving metal reduction condition. The resulting aminal intermediate underwent facile air oxidation to give the hexacyclic skeleton of trigonoliimine (±)-**48** (90% yield over two steps).



Scheme 6. Hao's synthesis of the skeleton of (±)-trigonoliimine C (**3**). Conditions: (a) TFA. (b) DDQ, 1,4-dioxane, 80% (2 steps) (c) Oxone, acetone, $NaHCO_3$, 70%. (d) HCO_2H, $PhCH_3$, 110 °C, 50%. (e) 80% $NH_2NH_2{\bullet}H_2O$, CH_2Cl_2, MeOH, 23 °C, 86%. (f) HCOOEt, DMF, 65 °C, 40%.

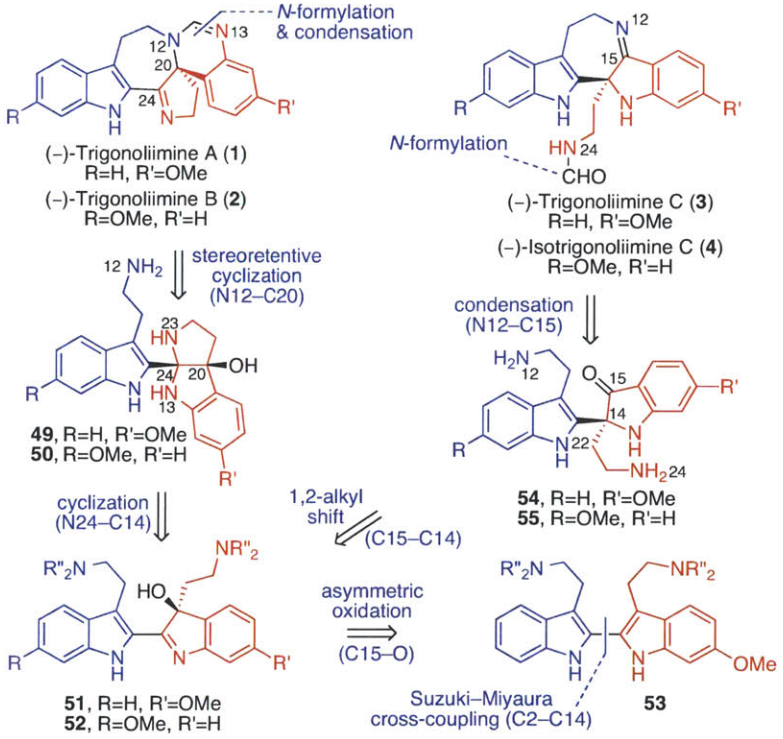


Scheme 7. Shi's synthesis of the hexacyclic skeleton of (±)-trigonoliimines A (**1**) and B (**2**). Conditions: (a) NaH, PMBCl, 0→23 °C, 65%. (b) $N_2H_4{\bullet}H_2O$, EtOH, reflux (c) Isatin, MeOH, 23 °C, 92%. (d) Allyl magnesium chloride, $BF_3{\bullet}Et_2O$, CH_2Cl_2, –40→23 °C, 81%. (e) NaH, $PhSO_2Cl$, THF, 0 °C, 96%. (f) *t*-BuLi, Et_2O, –40→23 °C, 32%. (g) $CsCO_3$, $(CH_2O)_n$, Na_2SO_4, THF, 23 °C,99%. (h) *t*-BuLi, Et_2O, –40→23 °C; H_2O, $(CH_2O)_n$, 23 °C, 30%. (i) OsO_4, $NMO{\bullet}H_2O$, THF, BuOH, H_2O, 23 °C; $NaIO_4$, 23 °C, 85%. (j) $NaBH_3CN$, THF, AcOH, 0 °C, 78%. (k) MsCl, Et_3N, CH_2Cl_2, 0→23 °C. (l) NaN_3, DMF, 23 °C, 71% (2 steps). (m) PPh_3, $PhCH_3$, reflux, 88%. (n) Na, NH_3 (l), –76→45 °C; air, 90%.

Results and Discussion

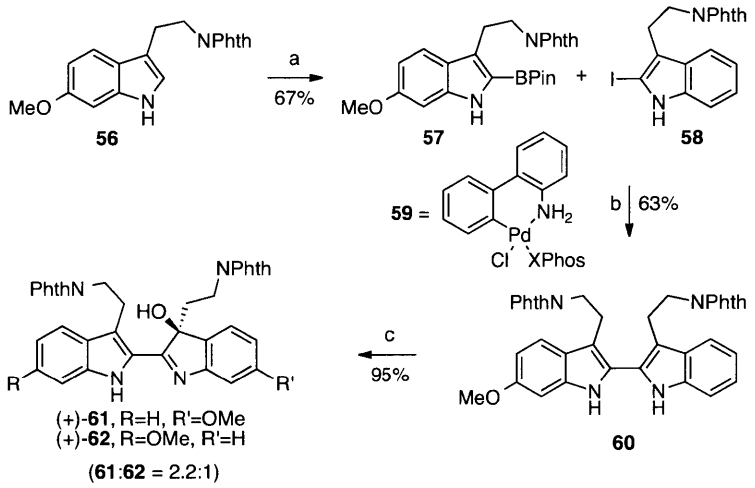
Our unified strategy for the enantioselective total synthesis of all known trigonoliimines was based on the hypothesis that bistryptamine heterodimer **53** (Scheme 8) could serve as a common biosynthetic precursor to these alkaloids. While the chemoselectivity of the oxidation of

bisindole **53** was envisioned to determine the ratio of regioisomeric hydroxyindolenines **51** and **52**, the stereoselectivity of the transformation was thought to provide a platform for the asymmetric synthesis of the trigonoliimines. We postulated that hydroxyindolenines **51** and **52** would serve as the branching point for divergent synthesis of the two distinct structural motifs found in trigonoliimine alkaloids (Scheme 8). Trigonoliimines A (**1**) and B (**2**) were expected to be accessed via a *stereoretentive* cyclization of N12 onto the C20 carbinol function of precursors **49** and **50**, respectively, followed by *N*-formylation and condensation (Scheme 8). The requisite *cis*-fused aminals **49** and **50** could result from intramolecular cyclization of hydroxyindolenines **51** and **52**, respectively. Alternatively, a stereospecific Wagner–Meerwein type rearrangement[15,16] of intermediates **51** and **52** was envisioned to provide the indoxyls **54** and **55**, respectively.[4,6] Intramolecular condensation of the N12 amine and the C15 ketone of indoxyls **54** and **55** in addition to N24 formylation was expected to provide trigonoliimine C (**3**) and isotrigonoliimine C (**4**). Thus, the enantioselective synthesis[7,9] of both regioisomeric hydroxyindolenines **51** and **52** was sought to address the asymmetric synthesis of alkaloids **1**–**4**.



Scheme 8. Retrosynthetic analysis of (–)-trigonoliimines A–C (**1**–**3**) and isotrigonoliimine C (**4**).

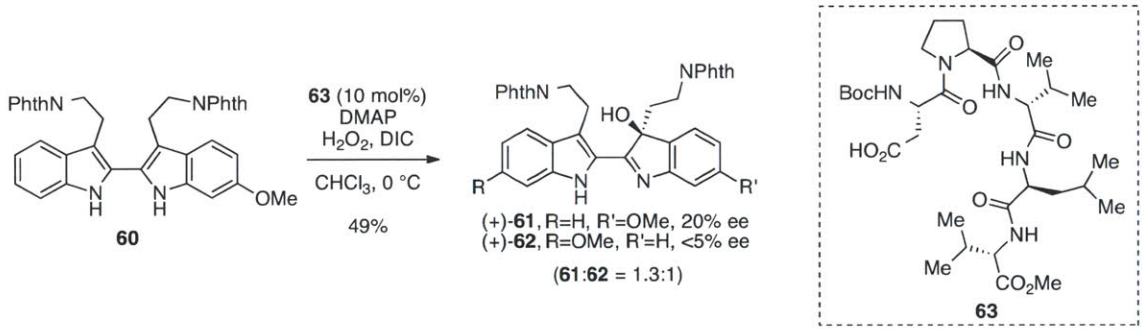
Our synthesis of the (–)-trigonoliimine alkaloids commenced with an iridium catalyzed[17] C2-borylation of the 6-methoxy-tryptamine derivative **56**.[18] We observed that using dichloromethane as solvent at 23 °C minimized the undesired borylation of the phthalimide substructure (Scheme 9). Access to bisindole **60** was possible via a Suzuki–Miyaura cross-coupling[19] of boronate **57** and 2-iodo-tryptamine **58**[9,20] using a variety of palladium sources in the presence of XPhos[21] and potassium phosphate at elevated temperatures, albeit in low and variable yields (7–44%). Alternatively, the use of Buchwald's aminobiphenyl precatalyst **59**[22] enabled a robust cross-coupling of pinacol boronate **57** and iodide **58** at 23 °C to give **60** in 31% yield. After an extensive screening of bases and additives, we noticed that the presence of both a halophile[23] and proper base was critical for the overall efficiency of this transformation. We discovered that the use of *silver phosphate* (2.0 equiv) and the precatalyst **59** optimally promoted this cross-coupling reaction, affording the desired bistryptamine **60** in 63% yield (Scheme 9).



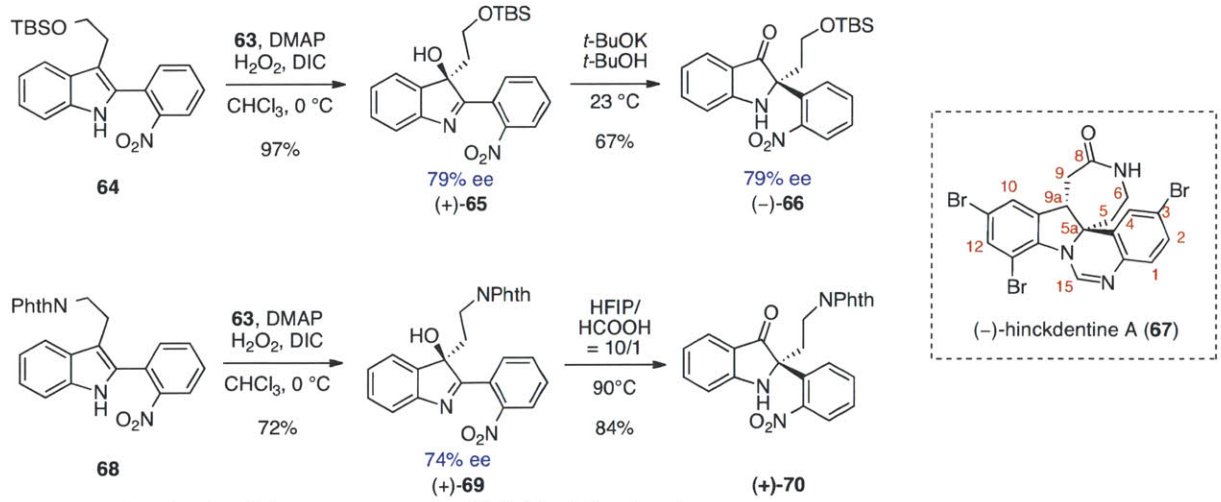
Scheme 9. Synthesis of hydroxyindolenines (+)-**61** and (+)-**62**. Conditions: (a) HBPin, $[Ir(OMe)(cod)]_2$ (10 mol%), 4,4'-di-^{t}Bu-2,2'-bipyridine, CH_2Cl_2, 23 °C. (b) Ag_3PO_4, **59** (20 mol%), $PhCH_3$, H_2O, 23 °C. (c) (+)-((8,8-dichlorocamphoryl)sulfonyl)oxaziridine, CH_2Cl_2, –35→23 °C.

The bistryptamine **60** was found to be sensitive to oxidation under a variety of conditions. In fact, simple exposure of bistryptamine **60** to air over 12 days resulted in autoxidation to (±)-hydroxyindolenines **61** and **62** (**61**:**62** = 1.5:1) in 27% yield along with recovered **60** (65%). Interestingly, the presence of regioisomeric pairs is commonly observed in the trigonostemon alkaloids family[24] (Figure 1) and the major autoxidation product (oxidation of 6-methoxy-indole substructure) is consistent with the major isolated trigonoliimines A (**1**) and C (**3**).[1] Given the

rapid oxidation of bistryptamine **60**, and based on observations on stereoselective oxidation of related derivatives,[4,6,8,9] we focused our attention on the use of oxaziridines. Under optimal conditions, treatment of bistryptamine **60** with readily available (+)-((8,8-dichlorocamphoryl)sulfonyl)oxaziridine (Davis' oxaziridine)[25] provided hydroxyindolenines (+)-**61** and (+)-**62** (**61**:**62** = 2.2:1, Scheme 9) in 95% yield and with an outstanding level of enantioselection for both isomers (96% ee, vide infra).[8,9] This solution provided efficient access to precursors for the enantioselective synthesis of alkaloids **1**–**4**. While the isomeric hydroxyindolenines (+)-**61** and (+)-**62** were separated for complete characterization and independent derivatization, separation of more advanced intermediates en route to alkaloids **1**–**4** proved most practical.



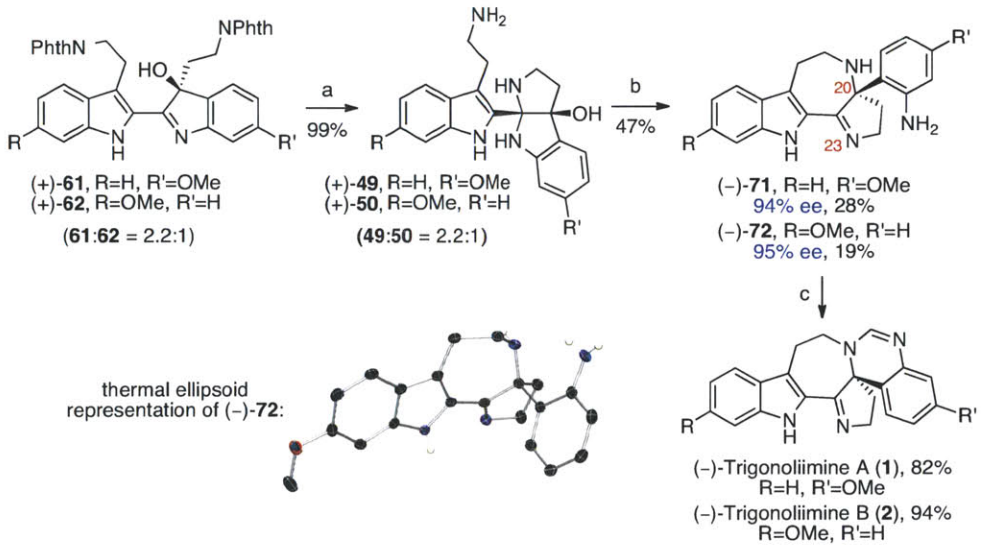
Scheme 10. Oxidation of bistryptamine **60** with Miller's catalytic system.



Scheme 11. Synthesis of the core structure of (−)-hinckdentine A

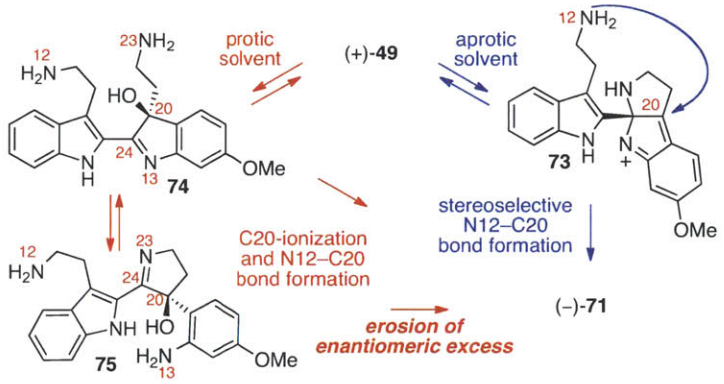
While (+)-((8,8-dichlorocamphoryl)sulfonyl)oxaziridine provided us with an excellent solution for the asymmetric oxidation of bistryptamine **60**, exposure of **60** to Miller's aspartyl

based catalytic asymmetric oxidation[9] condition afforded hydroxyindolenines (+)-**61** and (+)-**62** (**61**:**62** = 1.3:1, Scheme 10) in 20% ee and <5% ee, respectively. We speculate that the heterogeneity of the reaction mixture contributed to the low conversion and enantioselectivity of this reaction. However, Miller's catalytic system proved efficient for the asymmetric oxidation of 2,3-disubstituted indoles with 2-nitro-phenyl group in the 2-position (Scheme 11). Treatment of tryptophol derivative **64** with 10 mol% of Miller's catalyst **63**, 5 mol% of 4-dimethylaminopyridine (DMAP), 1.2 equivalent of hydrogen peroxide (H_2O_2) and 1.2 equivalent of *N,N'*-diisopropylcarbodiimide (DIC) in chloroform at 0 °C yielded the desired hydroxyindolenine (+)-**65** in 97% yield and 79% ee (Scheme 11). In the presence of potassium *t*-butoxide in *t*-butanol, hydroxyindolenine (+)-**65** could be converted to indoxyl (–)-**66** {79% ee, $[\alpha]_D^{24}$: –79.5 (c 0.15, chloroform)} via Wagner-Meerwein type 1,2-alkyl shift reaction.[4,15,16] Importantly, indoxyl derivative (±)-**66** served as an intermediate in Kawasaki's total synthesis of (±)-hinckdentine (**67**).[26,27] Furthermore, tryptamine derivative **68** could be converted to hydroxyindolenine (+)-**69** in 72% yield and 74% ee (Scheme 11), consistent with our previous report.[9] Notably, 2,3-disubstituted indole **68** was reluctant to oxidation with Davis' oxaziridines. Heating a solution of hydroxyindolenine (+)-**69** in hexafluoroisopropanol (HFIP) and formic acid mixture at 90 °C afforded indoxyl (+)-**70** in 84% yield. Indoxyl (+)-**70** would have potential significance for a more streamlined synthetic access to (–)-hinckdentine A (**67**).



Scheme 12. Total synthesis of (–)-trigonoliimines A (**1**) and B (**2**). Conditions: (a) $NH_2NH_2{\bullet}H_2O$, MeOH, 80 °C. (b) Martin's sulfurane, CH_2Cl_2, –78°C. (c) $CH(O^iPr)_3$, PPTS, CH_2Cl_2, 23 °C.

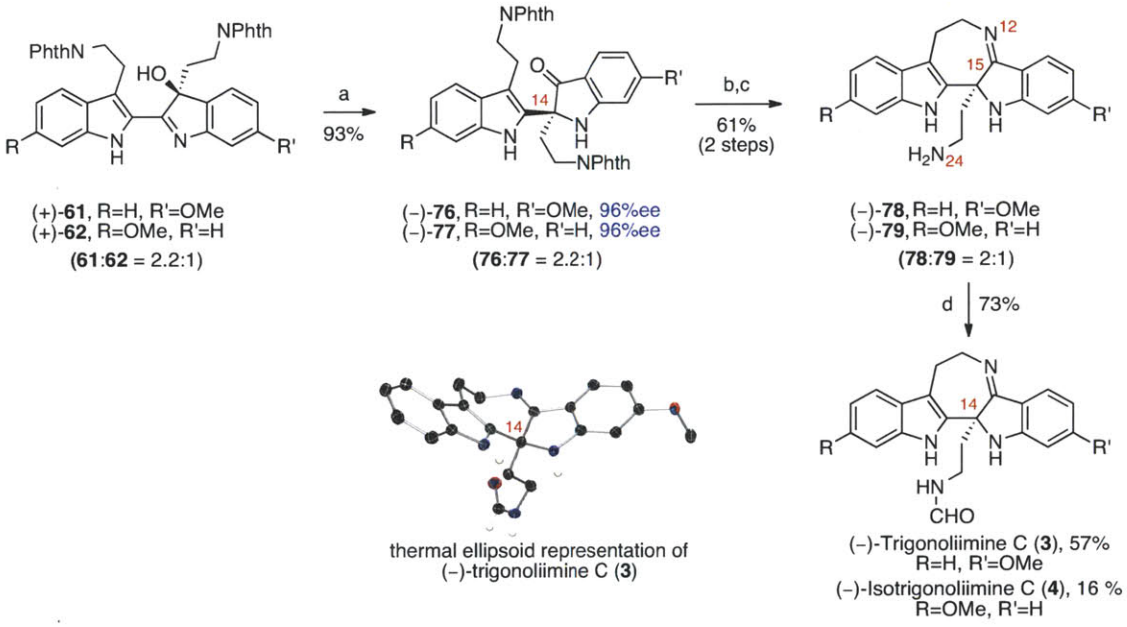
Unveiling the two amino groups of hydroxyindolenines (+)-**61** and (+)-**62** spontaneously provided the desired *cis*-fused aminals (+)-**49** and (+)-**50** (**49**:**50** = 2.2:1, Scheme 12), our proposed precursors for trigonoliimines A (**1**) and B (**2**), in 99% yield, respectively. Aminals (+)-**49** and (+)-**50** were separable at this stage, allowing their independent chemical examination and characterization. Interestingly, heating a solution of aminal (+)-**49** in trifluoroethanol (TFE) at 105 °C provided the desired azepane (–)-**71** in 34% yield with significant drop in enantiomeric excess (15% ee). On the other hand, aminal (+)-**50** led to almost complete decomposition under identical reaction conditions, highlighting the different chemical reactivity of the regioisomeric series of intermediates in our studies.



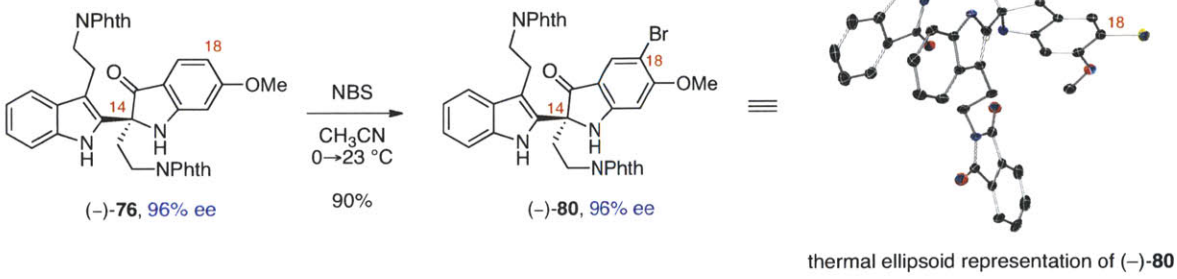
Scheme 13. Possible competing pathways in conversion of amino alcohol (+)-**43** to pentacycle (–)-**65**.

While ^{1}H NMR analysis of aminals (+)-**49** and (+)-**50** in deuterated chloroform were consistent with *cis*-fused pentacycles depicted in Scheme 12, the analysis of the same compounds in deuterated methanol revealed the presence of multiple species consistent with reversible formation of aminal and imine isomers (Scheme 13). We reasoned that the transmutation of (+)-**49** to (–)-**71**, as described above, likely affords the product with greatly diminished optical activity due to a low level of stereoselection in N12–C20 bond construction upon ionization of carbinol **75** at C20 (Scheme 13) or upon formation of a solvent/amine adduct of imine **74**. Gratifyingly, treatment of a solution of aminals (+)-**49** and (+)-**50** (**49**:**50** = 2.2:1) in dichloromethane with the Martin sulfurane reagent[28] at –78 °C provided the desired azepanes (–)-**71** and (–)-**72** in 47% combined yield (28% and 19% yield, respectively, after chromatographic separation). Importantly, azepanes (–)-**71** and (–)-**72** were obtained with minimal erosion of enantiomeric excess (94% ee and 95% ee, respectively). The X-ray crystal

structure analysis of pentacycle (–)-**72** (Scheme 12), the direct precursor for (–)-trigonoliimine B (**2**), unambiguously confirmed the molecular structure and coherently (*vide infra*) assigned the *S*-configuration at C20. Using optimal conditions, sequential treatment of pentacycle (–)-**71** with pyridinium *p*-toluenesulfonate (PPTS) and triisopropyl orthoformate in dichloromethane afforded (–)-trigonoliimine A (**1**) in 82% yield {$[\alpha]_D^{24}$= –294 (*c* 0.24, $CHCl_3$)} (Scheme 12). Under identical reaction conditions, the pentacycle (–)-**72** was converted to (–)-trigonoliimine B (**2**) in 94% yield {$[\alpha]_D^{24}$= –352 (*c* 0.32, $CHCl_3$)}. All ^1H and ^{13}C NMR data for our synthetic (–)-trigonoliimines A (**1**) and B (**2**) matched those provided in the isolation report,[1] confirming the molecular structure of these alkaloids.



Scheme 14. Total synthesis of (–)-trigonoliimine C (**3**) and (–)-isotrigonoliimine C (**4**). Conditions: (a) TFE, 102 °C. (b) $NH_2NH_2{\bullet}H_2O$, MeOH, 80 °C. (c) $Ti(OEt)_4$, THF, 42 °C. (d) *N*-formyl imidazole, THF, 23 °C.



Scheme 15. Synthesis and thermal ellipsoid representation of C18-bromoindoxyl (–)-**80**.

We next aimed to access (–)-trigonoliimine C (**3**) and (–)-isotrigonoliimine C (**4**) from the same versatile hydroxyindolenines described above via a divergent synthetic path employing a Wagner–Meerwein type 1,2-alkyl rearrangement.[15,16] We observed that exposure of hydroxyindolenines (+)-**61** and (+)-**62** to various Lewis acids gave the desired indoxyls (–)-**76** and (–)-**77** along with undesired oxindole byproducts. For example, in the presence of lanthanum trifluoromethanesulfonate in toluene at 80 °C, hydroxyindolenines (+)-**61** and (+)-**62** (**61**:**62** = 2.2:1) afforded the undesired oxindoles in 34% yield along with the desired indoxyls (56%). Upon treatment with europium trifluoromethanesulfonate in acetonitrile at 72 °C, hydroxyindolenines (+)-**61** and (+)-**62** (**61**:**62** = 2.2:1) afforded the undesired oxindoles in 50% yield along with the desired indoxyls in 48% yield. The choice of solvent with this rearrangement strongly influenced the ratio of indoxyl to oxindole.[6] After significant experimentation, we discovered that heating a solution of hydroxyindolenines (+)-**61** and (+)-**62** (**61**:**62** = 2.2:1) in TFE at 102 °C for 24.5 h resulted in selective formation of the corresponding indoxyls (–)-**76** and (–)-**77** (**76**:**77** = 2.2:1) in 93% combined yield (Scheme 14). The masking of the two amino groups in the form of phthalimides during this rearrangement was critical in the overall efficiency and selectivity for the formation of the desired products. Separation and independent analysis of indoxyls (–)-**76** and (–)-**77** revealed a high level of enantioselection (96% ee) in the synthesis of the corresponding hydroxylindolenines (+)-**61** and (+)-**62**. For the confirmation of the absolute stereochemistry, indoxyl (–)-**76** was treated with NBS to give C18-bromide (–)-**80** in 90% yield (Scheme 15). The high enantiomeric excess of bromide (–)-**80** (96% ee) in conjunction with its X-ray crystal data allowed for unequivocal assignment of the *S*-configuration at C14. While intermediates en route to (–)-trigonoliimine C (**3**) and (–)-isotrigonoliimine C (**4**) were separated for characterization and independent derivatization, delayed separation of isomers proved most practical similar to the case of (–)-trigonoliimines A (**1**) and B (**2**). Unraveling the two amino groups of indoxyls (–)-**76** and (–)-**77,** followed by condensative cyclization promoted by titanium ethoxide[29] as a one pot two–step procedure provided the cyclic imine (–)-**78** and (–)-**79** (**78**:**79** = 2:1) in 61% yield. Notably, we did not observe any of the undesired five-membered ring imines corresponding to condensation of the N24 with C15 carbonyl. Treatment of pentacyclic amines (–)-**78** and (–)-**79** with *N*-formyl imidazole followed by silica gel chromatographic separation provided (–)-trigonoliimine C (**3**)

{$[\alpha]_D^{24}$= –147 (*c* 0.12, $CHCl_3$)} and (–)-isotrigonoliimine C (**4**) ($[\alpha]_D^{24}$= –220 (*c* 0.10, $CHCl_3$)} in 57% and 16% yield, respectively. All ^1H and ^{13}C NMR data for our synthetic (–)-trigonoliimines C (**3**) matched those provided in the isolation report,[1] and analysis of the X-ray crystal structure of our synthetic (–)-**3** further confirmed the *S*-configuration at C14. Interestingly, while isotrigonoliimine C (**4**) has not been isolated from nature at this time, we have recognized the pentacyclic amine (–)-**79** as the *most* solvolytically sensitive compound amongst those discussed in this study.

Table 1. Specific rotation values of natural[1] and synthetic trigonoliimine A–C (**1**–**3**).

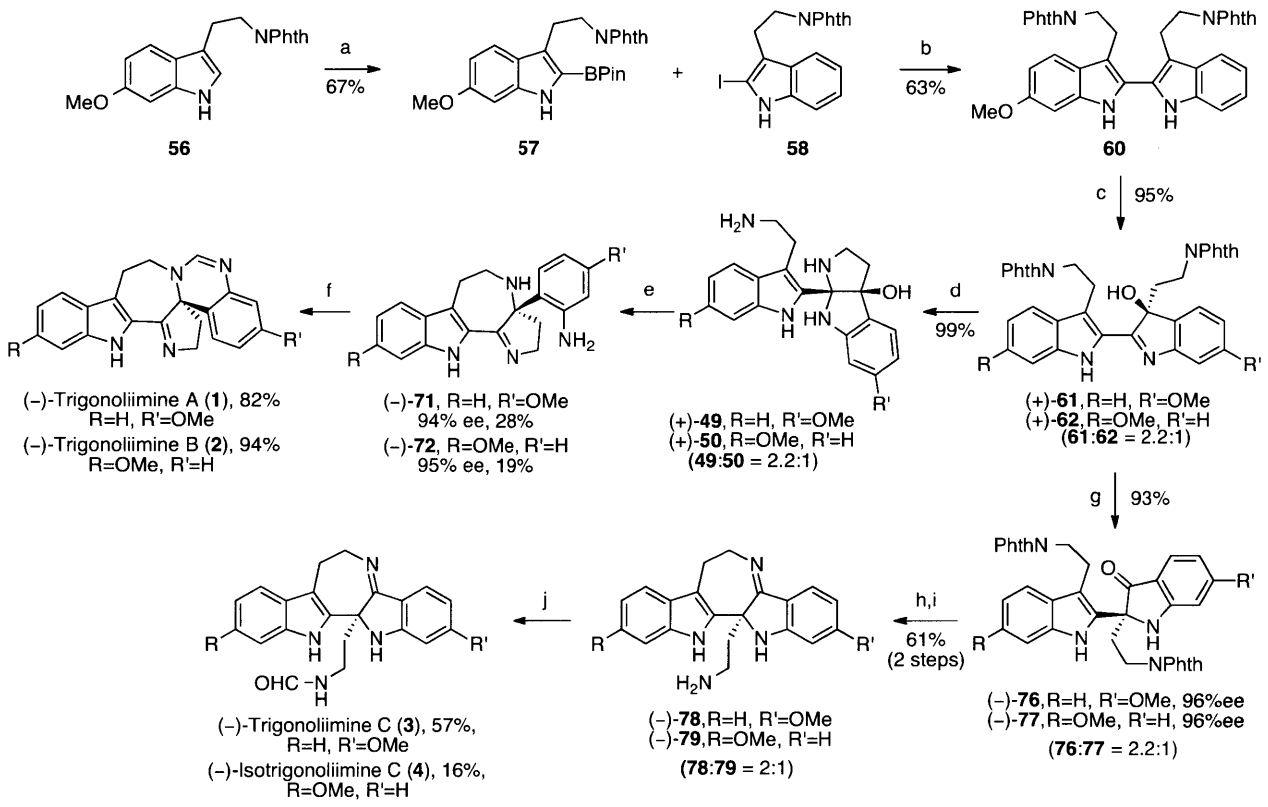
Entry	Alkaloids	Natural ($[\alpha]^{10}_D$)	Synthetic ($[\alpha]^{24}_D$)[a]
1	Trigonoliimine A	+13.3 (*c* 0.3, $CHCl_3$)	–294 (*c* 0.24, $CHCl_3$, 94% ee)
2	Trigonoliimine B	+5.0 (*c* 0.5, $CHCl_3$)	–352 (*c* 0.32, $CHCl_3$, 95% ee)
3	Trigonoliimine C	–4.8 (*c* 0.45, $CHCl_3$)	–147 (*c* 0.12, $CHCl_3$, 96% ee)

[a] % ee of the key precursor for the corresponding synthetic trigonoliimine.

The magnitude and sign of specific rotation of our synthetic trigonoliimines in conjunction with our X-ray crystal structure data provide valuable information regarding the stereochemistry of these alkaloids. Interestingly, all of our synthetic (–)-trigonoliimines A–C (**1**–**3**) showed a significantly larger magnitude of specific rotations compared to those reported for the naturally isolated samples (Table 1). Importantly, the enantiomeric excess[30] of our samples has been quantified by HPLC analysis of enantiomerically enriched samples of several intermediates against readily available racemic samples from our exploratory studies in this area. Additionally, our synthetic trigonoliimines A–C (**1**–**3**) derived from hydroxyindolenines (+)-**61** and (+)-**62** exhibit a negative sign in their specific rotation. However, naturally occurring trigonoliimines A (**1**) and B (**2**) were reported to have a positive sign in their specific rotations whereas trigonoliimine C (**3**) was reported to have a negative sign in its specific rotation. Furthermore, our three X-ray structures of highly enantiomerically enriched compounds (Schemes 12, 14, and 15) provide support for the need to revise the absolute stereochemical assignment of all trigonoliimines (Figure 1). While the absolute stereochemistry of our synthetic (–)-trigonoliimines A–C (**1**–**3**) are unequivocally assigned through our studies, given the reported

optical rotation values for the natural samples of **1–3**, we raise the possibility that either natural trigonoliimines A–C (**1–3**) were not isolated enantiomerically pure or the optical rotation values for the natural samples need to be revised.

Conclusion



Scheme 16. Total synthesis of (–)-trigonoliimines A–C (**1–3**) and isotrigonoliimine C (**4**). Conditions: (a) HBPin, $[Ir(OMe)(cod)]_2$ (10 mol%), 4,4'-di-^{t}Bu-2,2'-bipyridine, CH_2Cl_2, 23 °C. (b) Ag_3PO_4, **59** (20 mol%), $PhCH_3$, H_2O, 23 °C, 63%. (c) (+)-((8,8-Dichlorocamphoryl)sulfonyl)oxaziridine, CH_2Cl_2, −35→23 °C, 95%. (d) $NH_2NH_2{\bullet}H_2O$, MeOH, 80 °C, 99%. (e) Martin's sulfurane, CH_2Cl_2, −78 °C. (f) $CH(O^iPr)_3$, PPTS, CH_2Cl_2, 23 °C. (g) TFE, 102 °C, 93%. (h) $NH_2NH_2{\bullet}H_2O$, MeOH, 80 °C. (i) $Ti(OEt)_4$, THF, 42 °C, 61% (2 steps). (j) *N*-formyl imidazole, THF, 23 °C.

We have developed the first total syntheses of all trigonoliimine alkaloids inspired by a unified biosynthetic hypothesis[31] for oxidation and reorganization of a single bistryptamine precursor (Scheme 16). Our concise enantioselective syntheses of (–)-trigonoliimines A (**1**) and B (**2**) are seven steps from commercially available material and employ a critical stereoretentive condensative cyclization of hydroxyindolenines (+)-**61** and (+)-**62**, respectively. Our succinct

enantioselective syntheses of (–)-trigonoliimines C (**3**) and (–)-isotrigonoliimine C (**4**) are eight steps from commercially available material and draw on the application of the venerable Wagner–Meerwein rearrangement of the hydroxyindolenines (+)-**61** and (+)-**62**, respectively. Rapid access to the key intermediates is enabled by a Suzuki–Miyaura cross-coupling reaction using Buchwald's precatalyst (**59**) in conjunction with silver phosphate followed by a highly enantioselective oxidation at the enantiodetermining and branching point of our syntheses. Additionally, our studies allow us to revise the absolute stereochemistry of alkaloids (–)-**1**–**3**. The concise total synthesis of (–)-trigonoliimines A–C (**1**–**3**) highlights the power of *retrobiosynthetic analysis*[32] as a source of inspiration in the rational chemical factoring of natural product targets.

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Experimental Section

General Procedures. All reactions were performed in oven-dried or flame-dried round-bottomed flasks. The flasks were fitted with rubber septa and reactions were conducted under a positive pressure of argon. Stainless steel syringes or cannulae were used to transfer air- and moisture-sensitive liquids. Where necessary (so noted), solutions were deoxygenated by argon purging for a minimum of 10 min. Flash column chromatography was performed as described by Still et al. using silica gel (60-Å pore size, 40–63 μm, 4-6% H_2O content, Zeochem).[1] Analytical thin–layer chromatography (TLC) was performed using glass plates pre-coated with 0.25 mm 230–400 mesh silica gel impregnated with a fluorescent indicator (254 nm). Thin layer chromatography plates were visualized by exposure to ultraviolet light and/or by exposure to an ethanolic phosphomolybdic acid (PMA), an acidic solution of *p*-anisaldehyde (Anis), an aqueous solution of ceric ammonium molybdate (CAM), an aqueous solution of potassium permanganate ($KMnO_4$) or an ethanolic solution of ninhydrin followed by heating (<1 min) on a hot plate (~250 °C). Organic solutions were concentrated at 29–33 °C on rotary evaporators capable of achieving a minimum pressure of ~2 torr.

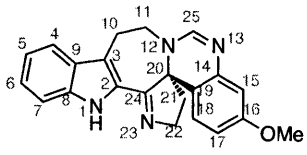
Materials. Commercial reagents and solvents were used as received with the following exceptions: dichloromethane, tetrahydrofuran, acetonitrile, toluene, methanol, and dimethylformamide were purchased from J.T. Baker (Cycletainer™) and were purified by the method of Grubbs et al. under positive argon pressure.[2] 6-Methoxyindole was purchased from Chem-Impex International, Inc.. All other solvents and chemicals were purchased from Sigma–Aldrich.

Instrumentation. Proton (^{1}H) and carbon (^{13}C) nuclear magnetic resonance spectra were recorded with Varian inverse probe 500 INOVA, Varian 500 INOVA and Bruker 400 AVANCE spectrometers. Proton nuclear magnetic resonance (^{1}H NMR) spectra are reported in parts per million on the δ scale and are referenced from the residual protium in the NMR solvent ($CDCl_3$: δ 7.24 ($CHCl_3$), CD_3OD: δ 3.31 (CHD_2OD), $CD_3OD/CDCl_3$ = 1/3: δ 3.31 (CHD_2OD), DMSO-d_6: δ 2.50 (DMSO-d_5)). Data is reported as follows: chemical shift [multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, app = apparent, br = broad), coupling constant(s) in Hertz, integration, assignment]. Carbon-13 nuclear magnetic resonance (^{13}C NMR) spectra are reported in parts per million on the δ scale and are referenced from the carbon resonances of the solvent ($CDCl_3$: δ 77.23, CD_3OD: δ 49.15, $CD_3OD/CDCl_3$ = 1/3: δ 49.15, DMSO-d_6: δ 39.51). Data is reported as follows: chemical shift or chemical shift (assignment). Infrared data (IR) were obtained with a Perkin-Elmer 2000 FTIR and are reported as follows: [frequency of absorption (cm^{-1}), intensity of absorption (s = strong, m = medium, w = weak, br = broad)]. Optical Rotations were recorded on a Jasco P-1010 Polarimeter (chloroform, Aldrich, Chromasolv Plus 99.9%; methanol, Aldrich, Chromasolv Plus 99.9%) and specific rotations are reported as follows: [wavelength of light, temperature (°C), specific rotation, concentration in grams/100 mL of solution, solvent]. Chiral HPLC analysis was performed on an Agilent Technologies 1100 Series system. Preparative HPLC was performed on a Waters system with the 1525 Binary HPLC Pump, 2489 UV/Vis Detector, 3100 Mass Detector, System Fluidics Organizer, and 2767 Sample Manager components. The structures of (–)-**3**, (–)-**72**, and (–)-**80** were obtained at the X-ray crystallography laboratory of the Department of

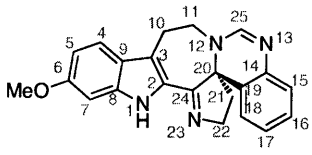
[1] Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923–2925.
[2] Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996**, *15*, 1518–1520.

Chemistry, Massachusetts Institute of Technology, with the assistance of Mr. Justin Kim. We are grateful to Dr. Li Li for obtaining the mass spectrometric data at the Department of Chemistry's Instrumentation Facility, Massachusetts Institute of Technology. High-resolution mass spectrometric data (HRMS) were recorded on a Bruker APEXIV 4.7 t FT-ICR-MS spectrometer using electronspray ionization (ESI) source or direct analysis in real time (DART) ionization source.

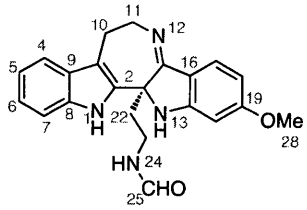
Positional Numbering System. In assigning the ^{1}H and ^{13}C NMR data of all intermediates en route to our total synthesis of (–)-**1**, (–)-**2**, (–)-**3**, and (–)-**4**, we have employed a uniform numbering system consistent with that of the final targets.



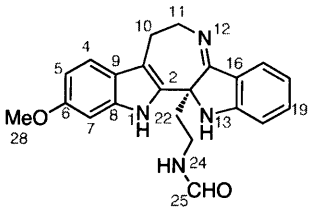
(–)-trigonoliimine A (**1**)



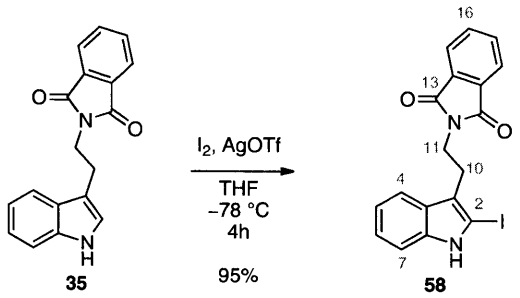
(–)-trigonoliimine B (**2**)



(–)-trigonoliimine C (**3**)



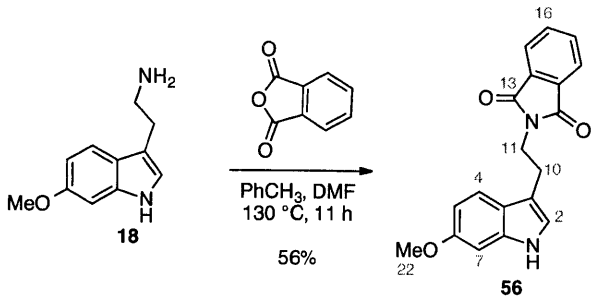
(–)-isotrigonoliimine C (**4**)



2-(2-(2-Iodo-1*H*-indol-3-yl)ethyl)isoindoline-1,3-dione (58):

Iodine (1.9 g, 7.6 mmol, 1.1 equiv) was added as a solid in one portion to a solution of tryptamine **35** (2.0 g, 6.9 mmol, 1 equiv) in anhydrous tetrahydrofuran (34 mL) at –78 °C. After 4 min, silver trifluoromethanesulfonate (AgOTf, 1.9 g, 7.6 mmol, 1.1 equiv) was added as a solid in one portion to the reaction mixture to form a yellow precipitate. After 4 h, sodium bicarbonate (1.3 g, 15 mmol, 2.2 equiv) was added as a solid in one portion, and the reaction mixture was allowed to warm to 23 °C. After 30 min, the resulting slurry was filtered through a plug of celite, and washed with ethyl acetate (200 mL). The resulting filtrate was quenched with a mixture of saturated aqueous sodium thiosulfate solution and saturated aqueous sodium bicarbonate solution (1:1, 200 mL), and the layers were separated. The aqueous layer was extracted with ethyl acetate (200 mL), and the combined organic layers were dried over anhydrous sodium sulfate, and were concentrated under reduced pressure. The sample of the crude residue was purified by flash column chromatography (silica gel: diam. 7 cm, ht. 10 cm; eluent: 33% ethyl acetate in hexanes) to afford iodide **58** (2.7 g, 95%) as a pale yellow solid.

^{1}H NMR (500.4 MHz, $CDCl_3$, 21 °C):	δ 7.99 (br-s, 1H, N_1**H**), 7.79 (dd, J = 5.5, 3.0 Hz, 2H, C_{15}**H**, C_{18}**H**), 7.67 (dd, J = 5.3, 3.0 Hz, 2H, C_{16}**H**, C_{17}**H**), 7.62 (d, J = 7.9 Hz, 1H, C_4**H**), 7.26 (d, J = 8.0 Hz, 1H, C_7**H**), 7.09 (ddd, J = 8.1, 7.0, 1.2 Hz, 1H, C_6**H**), 7.04 (app-td, J = 7.5, 0.9 Hz, 1H, C_5**H**), 3.91 (app-t, J = 7.5 Hz, 2H, C_{11}**H**$_2$), 3.06 (app-t, J = 7.5 Hz, 2H, C_{10}**H**$_2$).
^{13}C NMR (125.8 MHz, $CDCl_3$, 21 °C):	δ 168.5, 139.0, 134.1, 132.4, 127.7, 123.4 122.6, 120.3, 118.8, 118.1, 110.6, 78.5, 37.9, 26.3.
FTIR (neat) cm^{-1}:	3351 (s), 3058 (w), 2944 (w), 1770 (m), 1705 (s), 1397 (s), 1103 (m), 717 (s).
HRMS (DART) (*m/z*):	calc'd for $C_{18}H_{12}IN_2O_2$, $[M-H]^-$: 414.9949 found: 414.9945.
TLC (33% ethyl acetate in hexanes) R*f*:	0.50 (CAM, UV).

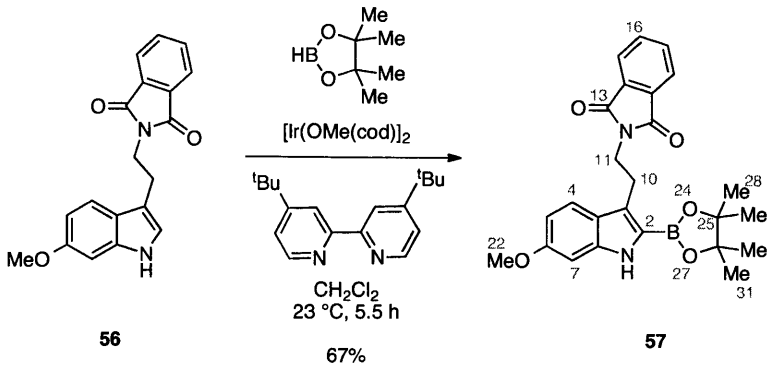


2-(2-(6-Methoxy-1*H*-indol-3-yl)ethyl)isoindoline-1,3-dione (56):

A suspension of 6-methoxytryptamine[3] (**18**, 2.00 g, 10.5 mmol, 1 equiv) in anhydrous dimethylformamide (DMF, 8.0 mL) at 23 °C was stirred vigorously under an argon atmosphere to result in a homogeneous solution. A portion of anhydrous toluene (105 mL) and additional anhydrous dimethylformamide (1.0 mL) was added to the homogenous solution of tryptamine derivative **18** in DMF. Phthalic anhydride (1.70 g, 11.6 mmol, 1.10 equiv) was added as a solid in one portion, the reaction flask was equipped with a Dean-Stark trap, and the reaction set-up was sealed under an atmosphere of argon and heated to 130 °C. After 11 h, the reaction mixture was allowed to cool to 23 °C and concentrated under reduced pressure to afford a black solid residue. This solid was purified by flash column chromatography (silica gel: diam. 5 cm, ht. 12 cm; eluent: 2.5% acetone in dichloromethane) to afford the indole **56** (1.9 g, 56%) as a yellow solid.

^{1}H NMR (500.4 MHz, $CDCl_3$, 21 °C):	δ 7.86 (br-s, 1H, N_1**H**), 7.81 (dd, J = 5.5, 3.0 Hz, 2H, C_{15}**H**, C_{18}**H**), 7.68 (dd, J = 5.5, 3.0 Hz, 2H, C_{16}**H**, C_{17}**H**), 7.57 (d, J = 8.6 Hz, 1H, C_4**H**), 6.96 (d, J = 2.3 Hz, 1H, C_2**H**), 6.81 (d, J = 1.9 Hz, 1H, C_7**H**), 6.77 (dd, J = 8.6, 2.2 Hz, 1H, C_5**H**), 3.97 (app-t, J = 7.8 Hz, 2H, C_{11}**H**$_2$), 3.81 (s, 3H, O**Me**), 3.09 (app-t, J = 7.7 Hz, 2H, C_{10}**H**$_2$).
^{13}C NMR (125.8 MHz, $CDCl_3$, 21 °C):	δ 168.6 (**C**$_{13}$, **C**$_{20}$), 156.8 (**C**$_6$), 137.1 (**C**$_8$), 134.1 (**C**$_{16}$, **C**$_{17}$), 132.4 (**C**$_{14}$, **C**$_{19}$), 123.4 (**C**$_{15}$, **C**$_{18}$), 122.0 (**C**$_9$), 120.9 (**C**$_2$), 119.7 (**C**$_4$), 112.6 (**C**$_3$), 109.7 (**C**$_5$), 94.8 (**C**$_7$), 55.9 (**C**$_{22}$), 38.7 (**C**$_{11}$), 24.7 (**C**$_{10}$).
FTIR (neat) cm^{-1}:	3391 (br-m), 1766 (w), 1706 (s), 1629 (w), 1397 (s), 1161 (w), 990 (w), 713 (m).
HRMS (DART) (*m/z*):	calc'd for $C_{19}H_{17}N_2O_3$, $[M+H]^+$: 321.1234 found: 321.1231.
TLC (5% acetone in dichloromethane) R*f*:	0.63 (CAM, UV).

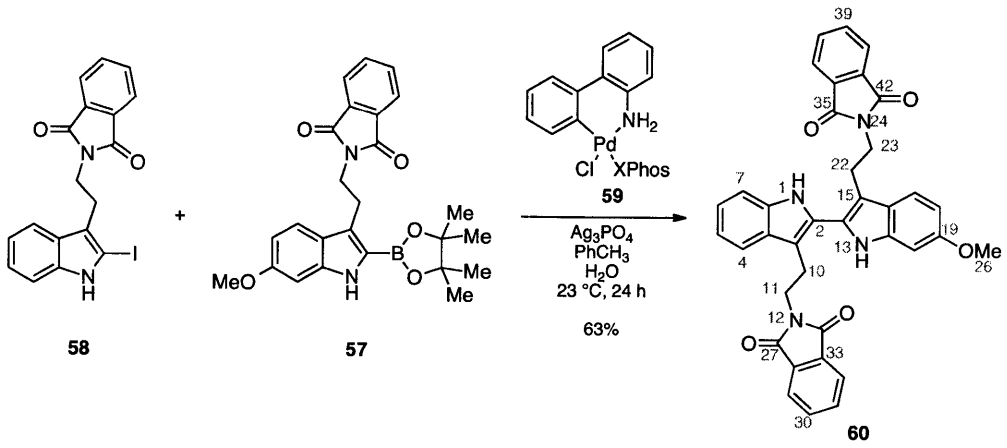
[3] 6-Methoxytryptamine (**18**) can be purchased from commercial sources. Additionally, it can be prepared from 6-methoxyindole: Woodward, R. B.; Bader, F. E.; Bickel, H.; Frey, A. J.; Kierstead, R. W. *Tetrahedron* **1958**, *2*, 1–57.



2-(2-(6-Methoxy-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-indol-3-yl)ethyl)isoindoline-1,3-dione (57):

Pinacol borane (873 μL, 5.84 mmol, 2.20 equiv) was added to a solution of indole **56** (850 mg, 2.65 mmol, 1 equiv), (1,5-cyclooctadiene)(methoxy)iridium(I) dimer (87.9 mg, 133 μmol, 5.00 mol%) and 4,4′-di-*tert*-butyl-2,2′-dipyridyl (71.2 mg, 265 μmol, 10.0 mol%) in degassed (purged with an argon stream) and anhydrous tetrahydrofuran (27.0 mL) sealed under an argon atmosphere at 23 °C. After 2.5 h, (1,5-cyclooctadiene)(methoxy)iridium(I) dimer (87.9 mg, 133 μmol, 5.00 mol%) was added at once to the reaction mixture and the contents resealed under an argon atmosphere. After 3 h, the resulting red homogeneous reaction mixture was purged with an air stream. After 10 min, silica gel (14 g) was added to the reaction mixture, and it was concentrated under reduced pressure. The resulting crude residue adsorbed onto silica gel was purified by flash column chromatography (silica gel: diam. 5 cm, ht. 10 cm; eluent: 20% ethyl acetate in hexane) to afford pinacol ester **57** (799 mg, 67.4%) as a yellow solid.

^{1}H NMR (500.4 MHz, $CDCl_3$, 21 °C):	δ 8.25 (br-s, 1H, N_1**H**), 7.76 (dd, J = 5.5, 3.0 Hz, 2H, C_{15}**H**, C_{18}**H**), 7.63 (dd, J = 5.5, 3.1 Hz, 2H, C_{16}**H**, C_{17}**H**), 7.58 (d, J = 8.6 Hz, 1H, C_4**H**), 6.73 (d, J = 1.8 Hz, 1H, C_7**H**), 6.71 (dd, J = 8.7, 2.2 Hz, 1H, C_5**H**), 3.96 (app-t, J = 7.2 Hz, 2H, C_{11}**H$_2$**), 3.79 (s, 3H, O**Me**), 3.33 (app-t, J = 7.2 Hz, 2H, C_{10}**H$_2$**), 1.27 (s, 12H, C_{28}**H$_3$** –C_{31}**H$_3$**).
^{13}C NMR (125.8 MHz, $CDCl_3$, 21 °C):	δ 168.4 (**C**$_{13}$, **C**$_{20}$), 158.0 (**C**$_6$), 139.1 (**C**$_8$), 133.8 (**C**$_{16}$, **C**$_{17}$), 132.5 (**C**$_{14}$, **C**$_{19}$), 125.5 (**C**$_2$), 123.2 (**C**$_{15}$, **C**$_{18}$), 123.0 (**C**$_9$), 120.5 (**C**$_4$), 110.4 (**C**$_3$), 110.4 (**C**$_5$), 94.0 (**C**$_7$), 83.9 (**C**$_{25}$, **C**$_{26}$), 55.7 (**C**$_{22}$), 39.4 (**C**$_{11}$), 24.9 (**C**$_{28}$–**C**$_{31}$), 24.7 (**C**$_{10}$).
FTIR (neat) cm^{-1}:	3391 (br-s), 2978 (s), 2937 (s), 2252(w), 1771 (s), 1712 (s), 1549 (s), 1268 (s), 1142 (s), 911 (s), 732 (s).
HRMS (DART) (*m/z*):	calc'd for $C_{25}H_{28}BN_2O_5$, $[M+H]^+$: 447.2186, found: 447.2118.
TLC (50% hexanes in ethyl acetate), R*f*:	0.73 (CAM, UV).



2,2'-((6-Methoxy-1*H*,1'*H*-[2,2'-biindole]-3,3'-diyl)bis(ethane-2,1-diyl))bis(isoindoline-1,3-dione) (60):

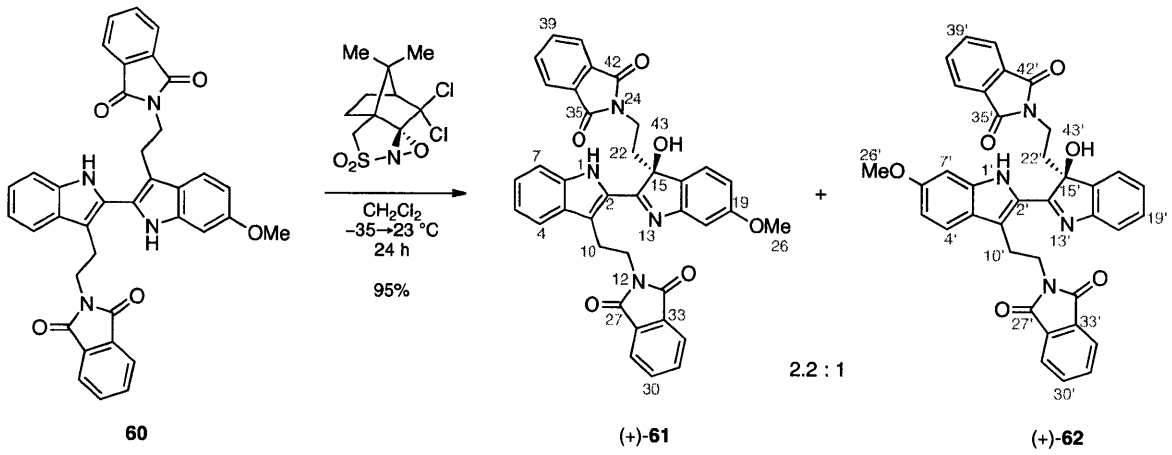
Degassed (purged with an argon stream) water (1.9 mL) was slowly added via syringe to a solution of pinacol ester **57** (0.300 g, 0.672 mmol, 1 equiv), iodide **58** (336 mg, 0.807 mmol, 1.20 equiv), palladium precatalyst[4] (**59**, 106 mg, 0.134 mmol, 20.0 mol%), and silver phosphate (574 mg, 1.34 mmol, 2.00 equiv) in degassed (purged with an argon stream) toluene (9.6 mL) at 23 °C, and the resulting solution was sealed under an argon atmosphere in the dark. After 24 h, brine (80 mL) was added to the reaction mixture and the heterogeneous mixture was extracted with dichloromethane (5 × 80 mL). The combined organic layers were dried over anhydrous sodium sulfate, were filtered and were concentrated under reduced pressure. The resulting crude residue was adsorbed onto silica gel (15 g) for loading, and was purified by flash column chromatography (silica gel: diam. 5 cm, ht. 8 cm; eluent: 1% acetone in dichloromethane) to afford dimeric indole **60** (256 mg, 63.0%) as a bright yellow solid. Structural assignment of **60** utilized additional information from gCOSY, HSQC and HMBC. Dimeric indole **60** was prone to air oxidation and therefore was immediately moved to the next step.

^{1}H NMR (500.4 MHz, DMSO-d_6, 21 °C): δ 10.98 (br-s, 1H, N_1**H**), 10.83 (br-s, 1H, N_{13}**H**), 7.70–7.64 (m, 8H, C_{37}**H**–C_{40}**H**, C_{29}**H**–C_{32}**H**), 7.60 (d, J = 7.9 Hz, 1H, C_7**H**), 7.48 (d, J = 8.6 Hz, 1H, C_{17}**H**), 7.30 (dt, J = 8.1, 0.8 Hz, 1H, C_4**H**), 7.10 (ddd, J = 8.1, 7.0, 1.1 Hz, 1H, C_6**H**), 7.01 (ddd, J = 7.9, 7.0, 1.0 Hz, 1H, C_5**H**), 6.77 (d, J = 2.2 Hz, 1H, C_{20}**H**), 6.69 (dd, J = 8.6, 2.3 Hz, 1H, C_{18}**H**), 3.79 (s, 3H, O**Me**), 3.77–3.73 (m, 4H, C_{11}**H**$_2$, C_{23}**H**$_2$), 3.01 (t, J = 7.5 Hz, 2H, C_{10}**H**$_2$), 2.97 (t, J = 7.7 Hz, 2H, C_{22}**H**$_2$).

^{13}C NMR (125.8 MHz, DMSO-d_6, 21 °C): δ 167.6 (**C**$_{27}$, **C**$_{34}$), 167.6 (**C**$_{35}$, **C**$_{42}$), 155.9 (**C**$_{19}$), 137.1 (**C**$_{21}$), 136.2 (**C**$_8$), 134.0 (**C**$_{30}$, **C**$_{31}$), 134.0 (**C**$_{38}$, **C**$_{39}$), 131.4 (**C**$_{28}$, **C**$_{33}$), 131.4 (**C**$_{36}$, **C**$_{41}$), 127.7 (**C**$_3$), 127.7 (**C**$_9$), 126.1 (**C**$_{15}$), 122.7 (**C**$_{29}$, **C**$_{32}$), 122.7 (**C**$_{37}$, **C**$_{40}$), 122.0 (**C**$_{16}$), 121.5 (**C**$_6$), 118.9 (**C**$_{17}$), 118.7 (**C**$_5$), 118.2 (**C**$_7$), 111.3 (**C**$_4$), 110.2 (**C**$_{14}$), 109.9 (**C**$_2$), 109.1 (**C**$_{18}$),

[4] Palladium precatalyst **59** was prepared according to the following procedure: Kinzel, T.; Zhang, Y.; Buchwald, S. L. *J. Am. Chem. Soc.* **2010**, *132*, 14073–14075.

	94.3 (**C**$_{20}$), 55.2 (**C**$_{26}$), 37.8 (**C**$_{11}$), 37.8 (**C**$_{23}$), 23.6 (**C**$_{22}$), 23.5 (**C**$_{10}$).
FTIR (neat) cm^{-1}:	3365 (br-w), 1766 (m), 1703 (s), 1398 (s), 1352 (m), 714 (s).
HRMS (ESI) (*m/z*):	calc'd for $C_{37}H_{28}N_4NaO_5$, $[M+Na]^+$: 631.1952, found: 631.1949.
TLC (1% acetone in dichloromethane), R*f*:	0.18 (CAM, UV).



(*S*)-2,2'-((3'-Hydroxy-6'-methoxy-1*H*,3'*H*-[2,2'-biindole]-3,3'-diyl)bis(ethane-2,1-diyl))bis(isoindoline-1,3-dione) (61) and (*S*)-2,2'-((3'-hydroxy-6-methoxy-1*H*,3'*H*-[2,2'-biindole]-3,3'-diyl)bis(ethane-2,1-diyl))bis(isoindoline-1,3-dione) (62):

A solution of (+)-(8,8-dichlorocamphorylsulfonyl)oxaziridine (198 mg, 0.645 mmol, 2.00 equiv) in degassed (purged with an argon stream) and anhydrous dichloromethane (16 mL) at –35 °C was cannula transferred to a solution of dimeric indole **60** (196 mg, 0.323 mmol, 1 equiv) in degassed (purged with an argon stream) and anhydrous dichloromethane (32 mL) at –35 °C under an atmosphere of argon. The reaction mixture was allowed to gently warm to 23 °C. After 24 h, the reaction mixture was concentrated under reduced pressure and the residue was purified by flash column chromatography (silica gel: diam. 2.5 cm, ht. 13 cm; eluent: 6% acetone in dichloromethane) to afford hydroxyindolenines (+)-**61** and (+)-**62** (2.2:1, **61**:**62**, 191 mg, 94.6%) as a yellow foam. Structural assignment of (+)-**61** utilized additional information from gCOSY, HSQC and HMBC.

(*S*)-2,2'-((3'-Hydroxy-6'-methoxy-1*H*,3'*H*-[2,2'-biindole]-3,3'-diyl)bis(ethane-2,1-diyl))bis(isoindoline-1,3-dione) (61)

^{1}H NMR (500.4 MHz, $CDCl_3$, 21 °C): δ 9.35 (s, 1H, N_1**H**), 7.75 (dd, *J* = 5.4, 3.1 Hz, 2H, C_{29}**H**, C_{32}**H**), 7.67 (dd, *J* = 5.4, 3.0 Hz, 2H, C_{30}**H**, C_{31}**H**), 7.53 (dd, *J* = 5.4, 3.1 Hz, 2H, C_{37}**H**, C_{40}**H**), 7.45 (dd, *J* = 5.5, 3.0 Hz, 2H, C_{38}**H**, C_{39}**H**), 7.35 (d, *J* = 8.1 Hz, 1H, C_{17}**H**), 7.25 (d, *J* = 6.3 Hz, 1H, C_7**H**), 6.82 (app-t, *J* = 7.6 Hz, 1H, C_6**H**), 6.68–6.64 (m, 2H, C_4**H**, C_5**H**), 6.50 (d, *J* = 2.2 Hz, 1H, C_{20}**H**), 6.44 (dd, *J* = 8.1, 2.3 Hz, 1H, C_{18}**H**), 4.29 (s, 1H, O_{43}**H**), 4.14 (ddd, *J* = 13.8, 8.7, 5.3 Hz, 1H, C_{11}**H**), 4.05 (dt, *J* = 13.5, 0.9 Hz, 1H, C_{11}**H**), 3.66 (s, 3H, O**Me**), 3.59–3.50 (m, 2H, C_{10}**H**, C_{23}**H**), 3.44–3.37 (m, 1H, C_{10}**H**), 3.30 (dt, *J* = 14.2, 5.9 Hz, 1H, C_{23}**H**), 2.70 (ddd, *J* = 14.5, 8.7, 6.0 Hz, 1H, C_{22}**H**), 2.09 (dt, *J* = 14.2, 5.6 Hz, 1H, C_{22}**H**).

^{13}C NMR (125.8 MHz, $CDCl_3$, 21 °C): 175.0 (**C**$_{14}$), 168.7 (**C**$_{27}$, **C**$_{34}$), 167.9 (**C**$_{35}$, **C**$_{42}$), 161.5 (**C**$_{19}$), 154.9 (**C**$_{21}$), 137.4 (**C**$_8$), 133.9 (**C**$_{30}$, **C**$_{31}$), 133.6 (**C**$_{38}$, **C**$_{39}$), 132.5 (**C**$_{28}$, **C**$_{33}$), 132.1 (**C**$_{36}$, **C**$_{41}$), 130.2 (**C**$_{16}$), 127.9 (**C**$_9$), 127.5 (**C**$_2$), 124.8 (**C**$_6$), 123.2 (**C**$_{29}$, **C**$_{32}$), 123.0 (**C**$_{17}$), 122.9 (**C**$_{37}$, **C**$_{40}$), 119.8 (**C**$_4$), 119.6 (**C**$_3$), 119.4 (**C**$_7$), 112.2 (**C**$_5$), 111.3 (**C**$_{18}$), 106.9 (**C**$_{20}$),

85.5 (**C**$_{15}$), 55.4 (**C**$_{26}$), 39.1 (**C**$_{11}$), 34.6 (**C**$_{22}$), 33.5 (**C**$_{23}$), 24.5 (**C**$_{10}$).

FTIR (neat) cm^{-1}: 3363 (br-s), 2939 (w), 2361 (w), 1771 (m), 1710 (s), 1617 (s), 1547 (m), 1397 (s), 1147 (m), 1021 (w), 718 (s).

HRMS (DART) (*m/z*): calc'd for $C_{37}H_{29}N_4O_6$, $[M+H]^+$: 625.2082, found: 625.2059.

$[\alpha]_D^{24}$: +252 (*c* 0.08, $CHCl_3$).

TLC (5% acetone in dichloromethane), R*f*: 0.18 (CAM, UV)

(*S*)-2,2'-((3'-Hydroxy-6-methoxy-1*H*,3'*H*-[2,2'-biindole]-3,3'-diyl)bis(ethane-2,1-diyl))bis(isoindoline-1,3-dione) (62)

^{1}H NMR (500.4 MHz, $CDCl_3$, 21 °C): δ 9.23 (s, 1H, $N_{1'}$**H**), 7.77 (dd, *J* = 5.4, 3.0 Hz, 2H, $C_{29'}$**H**, $C_{32'}$**H**), 7.66 (dd, *J* = 5.4, 3.0 Hz, 2H, $C_{30'}$**H**, $C_{31'}$**H**), 7.52 (dd, *J* = 5.5, 3.1 Hz, 2H, $C_{37'}$**H**, $C_{40'}$**H**), 7.47 (d, *J* = 6.8 Hz, 1H, $C_{17'}$**H**), 7.44 (dd, *J* = 5.5, 3.0 Hz, 2H, $C_{38'}$**H**, $C_{39'}$**H**), 7.08 (d, *J* = 8.7 Hz, 1H, $C_{4'}$**H**), 6.92–6.83 (m, 3H, $C_{18'}$**H**, $C_{19'}$**H**, $C_{20'}$**H**), 6.32 (dd, *J* = 8.8, 2.2 Hz, 1H, $C_{5'}$**H**), 6.08 (d, *J* = 1.5 Hz, 1H, $C_{7'}$**H**), 4.49 (s, 1H, $O_{43'}$**H**), 4.17 (ddd, *J* = 13.8, 9.1, 5.0 Hz, 1H, $C_{11'}$**H**), 4.02 (dt, *J* = 13.5, 5.4 Hz, 1H, $C_{11'}$**H**), 3.58–3.45 (m, 2H, $C_{10'}$**H**, $C_{23'}$**H**), 3.53 (s, 3H, O**Me**), 3.34–3.27 (m, 2H, $C_{10'}$**H**, $C_{23'}$**H**), 2.68 (ddd, *J* = 14.4, 8.3, 6.2 Hz, 1H, $C_{22'}$**H**), 2.10 (dt, *J* = 14.0, 5.8 Hz, 1H, $C_{22'}$**H**).

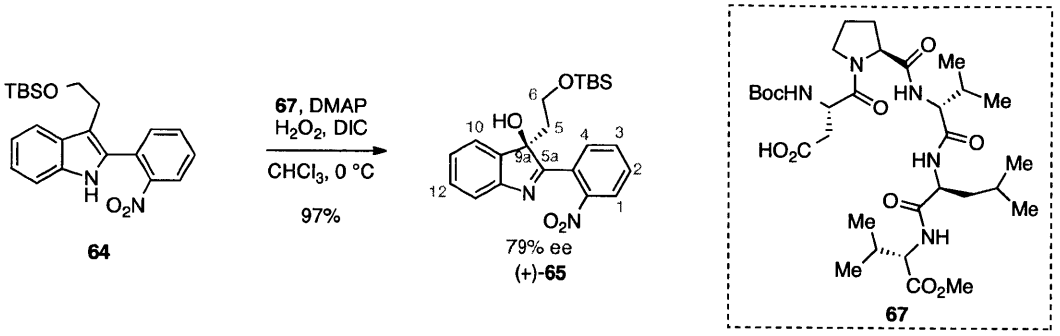
^{13}C NMR (125.8 MHz, $CDCl_3$, 21 °C): 173.6, 168.7, 167.9, 158.3, 153.3, 138.7, 138.1, 134.0, 133.5, 132.5, 132.1, 130.4, 126.6, 125.4, 123.2, 122.9, 122.6, 122.5, 120.5, 120.2, 120.2, 112.0, 93.5, 85.7, 55.1, 39.2, 34.5, 33.4, 24.6.

FTIR (neat) cm^{-1}: 3365 (br-w), 2932 (w), 2361 (w), 1771 (m), 1710 (s), 1626 (w), 1545 (m), 1396 (s), 1347 (m), 1240 (w), 717 (s).

HRMS (DART) (*m/z*): calc'd for $C_{37}H_{29}N_4O_6$, $[M+H]^+$: 625.2082, found: 625.2070.

$[\alpha]_D^{24}$: +121 (*c* 0.10, $CHCl_3$).

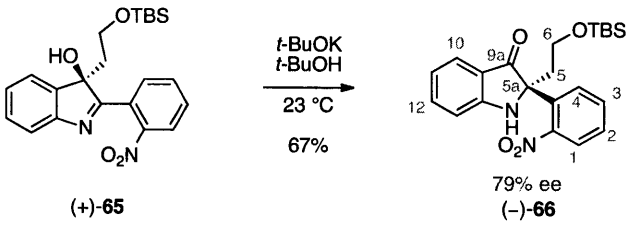
TLC (5% acetone in dichloromethane), R*f*: 0.18 (CAM, UV)



(*R*)-3-(2-((*tert*-butyldimethylsilyl)oxy)ethyl)-2-(2-nitrophenyl)-3*H*-indol-3-ol (65):

To a glass vial charged with tryptophol derivative **64** (22.6 mg, 57.0 μmol, 1 equiv) and catalyst **67** (3.7 mg, 5.7 μmol, 0.1 equiv) was added DMAP (0.35 mg, 2.9 μmol, 0.05 equiv) in chloroform (200 μL) and the reaction mixture was cooled to 0 °C. After 3 min, hydrogen peroxide (30 % w/w in water, 7.0 μL, 68 μmol, 1.2 equiv) was added to the reaction mixture. After 9 min, additional chloroform (80 μL) was added to the reaction mixture. After 4 min, DIC (10.7 μL, 68.4 μmol, 1.20 equiv) was added to the reaction mixture and the resulting dark orange solution was placed in a cryogenic cooler adjusted at 0 °C. After 22 h, the reaction mixture was diluted with chloroform (0.5 mL) and directly purified by flash column chromatography (silica gel: diam. 2.0 cm, ht. 11 cm; eluent: 13% ethylacetate in hexanes) to afford hydroxyindolenine (+)-**65** (22.9 mg, 97%) as a colorless oil. Hydroxyindolenine (+)-**65** was found to be 79% ee by chiral HPLC analysis [Chiralpak IC 0.5 mL/min; 80% hexanes, 20% isopropanol; t_R(major) = 12.4 min, t_R(minor) = 10.1 min].

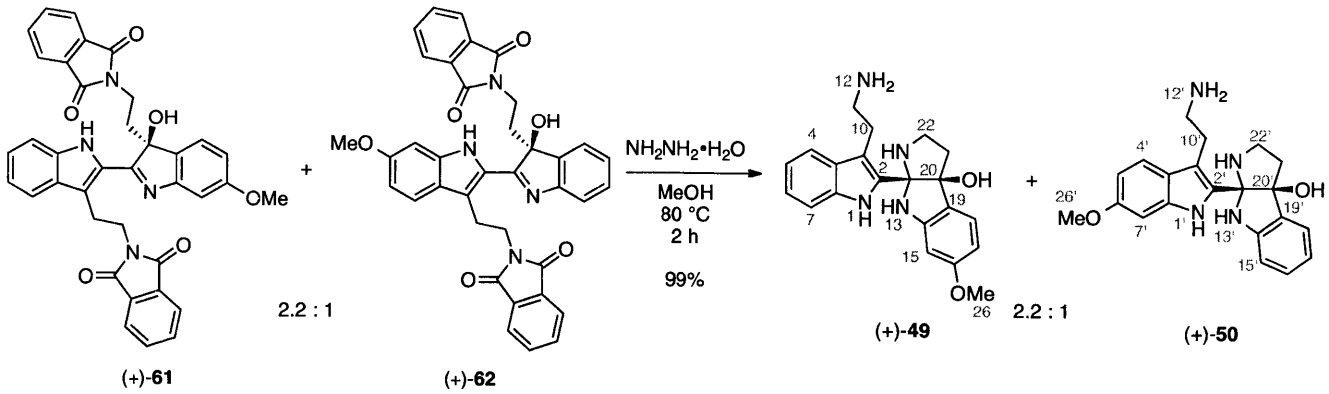
^{1}H NMR (500.4 MHz, $CDCl_3$, 21 °C):	δ 8.15 (dd, J = 7.7, 1.4 Hz, 1H), 7.93 (dd, J = 8.1, 1.1 Hz, 1H), 7.66 (dt, J = 7.6, 1.3 Hz, 1H), 7.58 (appt-dt, J = 7.7, 1.5 Hz, 1H), 7.51–7.49 (m, 1H), 7.46–7.45 (m, 1H), 7.35 (dt, J = 7.6, 1.4 Hz, 1H), 7.27 (dt, J = 7.4, 1.1 Hz, 1H), 5.11 (s, 1H), 3.98 (ddd, J = 10.6, 7.9, 4.1 Hz, 1H), 3.77 (ddd, J = 10.7, 6.1, 4.6 Hz, 1H), 2.21 (ddd, J = 12.6, 8.0, 4.6 Hz, 1H), 2.03 (ddd, J = 10.26, 6.1, 4.2 Hz, 1H), 0.88 (s, 9H), 0.04 (s, 3H), 0.04 (s, 3H).
^{13}C NMR (125.8 MHz, $CDCl_3$, 21 °C):	δ 177.6, 152.9, 149.4, 140.5, 132.5, 130.9, 130.4, 129.8, 129.6, 127.1, 124.6, 123.0, 122.1, 89.1, 61.1, 37.4, 26.0, 18.2, -5.5, -5.6.
FTIR (neat) cm^{-1}:	3406 (s), 2955 (s), 2857 (m), 1649 (w), 1538 (s), 1471 (m), 1361 (m), 1258 (m), 1984 (m), 838 (s).
HRMS (DART) (*m/z*):	calc'd for $C_{22}H_{29}N_2O_4Si$, $[M+H]^+$: 413.1891, found: 413.1890.
$[\alpha]_D^{24}$:	+136.1 (c 0.49, $CHCl_3$).
TLC (25% ethyl acetate in hexanes), R*f*:	0.43 (CAM, UV)



(*R*)-2-(2-((*tert*-butyldimethylsilyl)oxy)ethyl)-2-(2-nitrophenyl)indolin-3-one (66):

To a solution of hydroxyindolenine (+)-**65** (26.2 mg, 63.5 μmol, 1 equiv) in a freshly distilled *tert*-butanol (1.6 mL) under argon was added a solution of potassium *tert*-butoxide (3.8 mg, 32μmol, 0.50 equiv) in *tert*-butanol (1.6 mL) via syringe at 23 °C. After 16.5 h, saturated aqueous ammonium chloride solution (3 mL) was added to the reaction mixture and the resulting mixture was diluted with water (4.5 mL) and ethyl acetate (6 mL) and the layers were separated. The aqueous layer was extracted with ethylacetate (2 × 6 mL), and the combined organic layers were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The sample of the crude residue was purified by flash column chromatography (silica gel: diam. 2.0 cm, ht. 1 cm; eluent: 13% ethylacetate in hexanes) to afford indoxyl (–)-**66** (17.6 mg, 67%) as a yellow oil. Indoxyl (–)-**66** was found to be 79% ee by chiral HPLC analysis [Chiralpak IC 0.5 mL/min; 80% hexanes, 20% isopropanol; t_R(major) = 14.9 min, t_R(minor) = 24.8 min].

^{1}H NMR (500.4 MHz, $CDCl_3$, 21 °C):	δ 7.79 (appt-d, J = 7.4 Hz, 1H), 7.61 (td, J = 7.7, 0.6 Hz, 1H), 7.53–7.50 (m, 1H), 7.48 (ddd, J = 8.3, 7.1, 1.3 Hz, 1H), 7.36–7.35 (m, 2H), 6.90 (appt-t, J = 7.8 Hz, 1H), 6.86 (td, J = 8.2, 0.7 Hz, 1H), 6.13 (s, 1H), 3.79–3.72 (m, 2H), 2.53 (ddd, J = 14.9, 6.8, 2.9 Hz, 1H), 2.08 (ddd, J = 14.8, 9.7, 4.9 Hz, 1H), 0.84 (s, 9H), –0.09 (s, 3H), –0.10 (s, 3H).
^{13}C NMR (125.8 MHz, $CDCl_3$, 21 °C):	δ 201.5, 160.8, 150.9, 137.7, 131.0, 130.9, 129.7, 128.5, 125.3, 123.9, 120.6, 119.8, 113.7, 70.6, 60.1, 40.2, 26.0, 18.2, –5.7.
FTIR (neat) cm^{-1}:	3350 (m), 2954 (m), 2929 (m), 1705 (s), 1617 (s), 1533 (s), 1484 (m), 1369 (m), 1324 (m), 1258 (m), 1096 (s), 836 (s), 778 (s).
HRMS (DART) (*m/z*):	calc'd for $C_{22}H_{29}N_2O_4Si$, $[M+H]^+$: 413.1891, found: 413.1903.
$[\alpha]_D^{24}$:	–79.5 (c 0.15, $CHCl_3$).
TLC (17% ethyl acetate in hexanes), R*f*:	0.32 (CAM, UV)



(3a*S*,8a*S*)-8a-(3-(2-Aminoethyl)-1*H*-indol-2-yl)-6-methoxy-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indol-3a-ol (49) and (3a*S*,8a*S*)-8a-(3-(2-aminoethyl)-6-methoxy-1*H*-indol-2-yl)-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indol-3a-ol (50):

Hydrazine monohydrate (252 μL, 5.09 mmol, 20.0 equiv) was added to a solution of hydroxyindolenines (+)-**61** and (+)-**62** (2.2:1, **61**:**62**, 163.0 mg, 0.2601 mmol, 1 equiv) in methanol (25 mL) at 23 °C and the reaction flask was equipped with a reflux condenser, was sealed under an atmosphere of argon and heated to 80 °C. After 2 h, the resulting yellow homogeneous solution was allowed to cool to 23 °C and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel: diam. 5 cm, ht. 12 cm; eluent: 9% methanol, 1% ammonium hydroxide in chloroform) to afford hydroxyaminals (+)-**49** and (+)-**50** (2.2:1, **49**:**50**, 94.2 mg, 99.4%) as a yellow solid mixture. Structural assignment of (+)-**49** utilized additional information from gCOSY, HSQC and HMBC.

(3a*S*,8a*S*)-8a-(3-(2-Aminoethyl)-1*H*-indol-2-yl)-6-methoxy-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indol-3a-ol (49)

^{1}H NMR (500.4 MHz, $CDCl_3$, 21 °C): δ 9.10 (s, 1H, N_1**H**), 7.43 (d, J = 7.2 Hz, 1H, C_4**H**), 7.33 (dt, J = 8.1, 0.8 Hz, 1H, C_7**H**), 7.16 (d, J = 8.2 Hz, 1H, C_{18}**H**), 7.13 (ddd, J = 8.1, 7.0, 1.1 Hz, 1H, C_6**H**), 7.04 (ddd, J = 7.9, 7.0, 1.0 Hz, 1H, C_5**H**), 6.34 (dd, J = 8.2, 2.2 Hz, 1H, C_{17}**H**), 6.16 (d, J = 2.2 Hz, 1H, C_{15}**H**), 3.79 (s, 3H, O**Me**), 3.12 (app-dd, J = 9.1, 5.8 Hz, 1H, C_{22}**H**), 2.97–2.91 (m, 3H, C_{10}**H**, C_{11}**H**, C_{22}**H**), 2.72 (app-t, J = 10.5 Hz, 1H, C_{11}**H**), 2.54 (t, J = 11.5 Hz, 1H, C_{10}**H**), 2.32–2.21 (m, 2H, C_{21}**H**$_2$).

^{13}C NMR (125.8 MHz, $CDCl_3$, 21 °C): δ 161.4 (**C**$_{16}$), 151.4 (**C**$_{14}$), 136.1 (**C**$_2$), 134.4 (**C**$_8$), 129.5 (**C**$_9$), 125.6 (**C**$_{18}$), 125.0 (**C**$_{19}$), 121.7 (**C**$_6$), 119.0 (**C**$_5$), 118.3 (**C**$_4$), 111.5 (**C**$_7$), 110.2 (**C**$_3$), 104.6 (**C**$_{17}$), 94.3 (**C**$_{15}$), 89.5 (**C**$_{20}$), 89.2 (**C**$_{24}$), 55.5 (**C**$_{26}$), 42.5 (**C**$_{22}$), 41.5 (**C**$_{21}$), 41.1 (**C**$_{11}$), 26.4 (**C**$_{10}$).

FTIR (neat) cm^{-1}: 3394 (br-m), 2961 (m), 2931 (m), 2853 (m), 1618 (s), 1500 (s), 1459 (s), 1334 (s), 1198 (s), 1159 (s), 1132 (m), 748 (s).

HRMS (DART) (*m/z*): calc'd for $C_{21}H_{25}N_4O_2$, $[M+H]^+$: 365.1972, found: 365.1987.

$[\alpha]_D^{24}$: +61.1 (*c* 0.17, $CHCl_3$).

TLC (18% methanol, 2% ammonium hydroxide in chloroform), R*f*: 0.19 (CAM, UV).

(3a*S*,8a*S*)-8a-(3-(2-Aminoethyl)-6-methoxy-1*H*-indol-2-yl)-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indol-3a-ol (50)

^{1}H NMR (500.4 MHz, $CDCl_3$, 21 °C): δ 9.00 (s, 1H, $N_{1'}$**H**), 7.28 (d, *J* = 8.8 Hz, 1H, $C_{4'}$**H**), 7.28 (dd, *J* = 6.9, 0.9 Hz, 1H, $C_{18'}$**H**), 7.13 (td, *J* = 7.7, 1.3 Hz, 1H, $C_{16'}$**H**), 6.84 (d, *J* = 2.2 Hz, 1H, $C_{7'}$**H**), 6.78 (td, *J* = 7.4, 0.8 Hz, 1H, $C_{17'}$**H**), 6.71 (dd, *J* = 8.6, 2.2 Hz, 1H, $C_{5'}$**H**), 6.61 (d, *J* = 7.9 Hz, 1H, $C_{15'}$**H**), 3.81 (s, 3H, O**Me**), 3.12 (app-t, *J* = 7.2 Hz, 1H, $C_{22'}$**H**), 2.98–2.86 (m, 3H, $C_{10'}$**H**, $C_{11'}$**H**, $C_{22'}$**H**), 2.68 (app-t, *J* = 10.5 Hz, 1H, $C_{11'}$**H**), 2.53–2.47 (m, 1H, $C_{10'}$**H**), 2.34–2.25 (m, 2H, $C_{21'}$**H**$_2$).

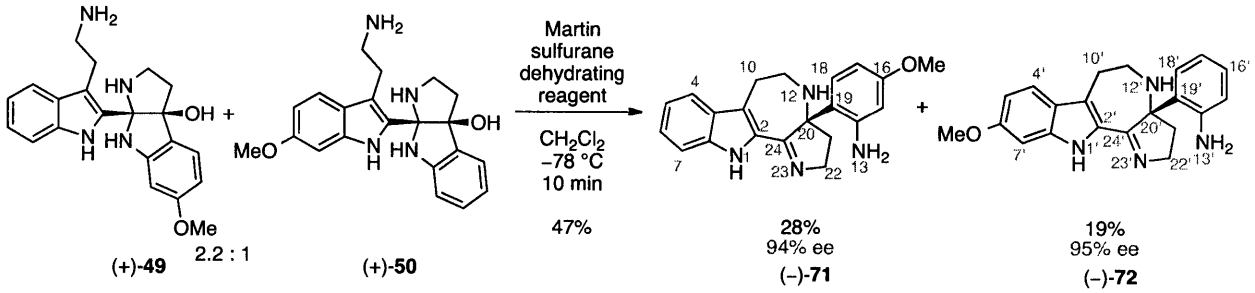
^{13}C NMR (125.8 MHz, $CDCl_3$, 21 °C): δ 156.5, 150.1, 135.1, 134.8, 132.7, 129.5, 125.3, 124.0, 119.5, 119.0, 110.1, 109.2, 108.4, 94.9, 89.8, 89.1, 55.9, 42.5, 41.6, 41.2, 26.5.

FTIR (neat) cm^{-1}: 3359 (br-m), 2927 (s), 1691 (w), 1610 (s), 1464 (s), 1205 (s), 751 (s).

HRMS (DART) (*m/z*): calc'd for $C_{21}H_{25}N_4O_2$, $[M+H]^+$: 365.1972, found: 365.1978.

$[\alpha]_D^{22}$: +34.6 (*c* 0.17, $CHCl_3$).

TLC (18% methanol, 2% ammonium hydroxide in chloroform), R*f*: 0.09 (CAM, UV).



(S)-2-(3,3a,4,5,6,11-Hexahydro-2H-pyrrolo[3',2':2,3]azepino[4,5-b]indol-3a-yl)-5-methoxyaniline (71) and (*S*)-2-(9-methoxy-3,3a,4,5,6,11-hexahydro-2*H*-pyrrolo[3',2':2,3]azepino[4,5-*b*]indol-3a-yl)aniline (72):

A solution of aminals (+)-**49** and (+)-**50** (2.2:1, **49**:**50**, 91.2 mg, 0.250 mmol, 1 equiv) in anhydrous dichloromethane (8 mL) at −78 °C under an atmosphere of argon was cannula transferred to a solution of bis[α,α-bis(trifluoromethyl)benzenemethanolato]diphenylsulfur (Martin's sulfurane dehydrating reagent, 202 mg, 0.300 mmol, 1.20 equiv) in anhydrous dichloromethane (5 mL) at −78 °C under an atmosphere of argon. After 10 min, saturated aqueous sodium bicarbonate solution (20 mL) was added to the reaction mixture and the resulting mixture was diluted with dichloromethane (5 mL), and the layers were separated. The aqueous layer was extracted with dichloromethane (2 × 20 mL), and the combined organic layers were dried over anhydrous sodium sulfate, and were concentrated under reduced pressure. The sample of the crude residue was purified by flash column chromatography (silica gel: diam. 2.5 cm, ht. 18 cm; eluent: 0.9% methanol, 0.1 % ammonium hydroxide in chloroform to 2.3% methanol, 0.3 % ammonium hydroxide in chloroform) to afford pentacycle (−)-**71** (24.2 mg, 27.9%) and pentacycle (−)-**72** (16.4 mg, 18.9%) as pale yellow solids. Structural assignment of (−)-**71** and (−)-**72** utilized additional information from gCOSY, HSQC and HMBC.

Pentacycle (−)-**71** was found to be 94% ee by chiral HPLC analysis [Chiralcel OD-H 0.5 mL/min; 100% hexanes to 20% hexanes in isopropanol over 80 min; t_R(major) = 65.1 min, t_R(minor) = 41.8 min]. Pentacycle (−)-**72** was found to be 95% ee by chiral HPLC analysis [Chiralcel OD-H 0.5 mL/min; 100% hexanes to 20% hexanes in isopropanol over 80 min; t_R(major) = 54.5 min min, t_R(minor) = 43.8 min]. Crystal of (−)-**72** was obtained by slow evaporation of saturated solution of (−)-**72** in chloroform.

(S)-2-(3,3a,4,5,6,11-Hexahydro-2H-pyrrolo[3',2':2,3]azepino[4,5-b]indol-3a-yl)-5-methoxyaniline (71)

^{1}H NMR (500.4 MHz, $CDCl_3$, 21 °C): δ 9.54 (s, 1H, N_1**H**), 7.48 (d, J = 8.0 Hz, 1H, C_4**H**), 7.35 (dt, J = 8.2, 0.8 Hz, 1H, C_7**H**), 7.24 (app-td, J = 7.6, 1.1 Hz, 1H, C_6**H**), 7.06 (ddd, J = 8.0, 7.0, 1.0 Hz, 1H, C_5**H**), 6.57 (d, J = 8.6 Hz, 1H, C_{18}**H**), 6.21 (d, J = 2.6 Hz, 1H, C_{15}**H**), 5.99 (dd, J = 8.5, 2.6 Hz, 1H, C_{17}**H**), 5.25 (s, 2H, N_{13}**H**$_2$), 4.01 (dd, J = 15.4, 7.7 Hz, 1H, C_{22}**H**), 3.67 (s, 3H, O**Me**), 3.45 (ddd, J = 15.5, 10.2, 5.5 Hz, 1H, C_{22}**H**), 3.22–3.10 (m, 2H, C_{11}**H**$_2$), 3.03–2.91 (m, 2H, C_{10}**H**$_2$), 2.75 (dd, J = 12.1, 5.7 Hz, 1H, C_{21}**H**), 1.93 (ddd, J = 12.1, 10.5, 7.8 Hz, 1H, C_{21}**H**).

^{13}C NMR (125.8 MHz, $CDCl_3$, 21 °C): δ 174.4 (**C**$_{24}$), 160.2 (**C**$_{16}$), 147.7 (**C**$_{14}$), 137.3 (**C**$_8$), 129.6 (**C**$_2$), 129.1 (**C**$_{18}$), 128.4 (**C**$_9$), 124.9 (**C**$_6$), 120.0

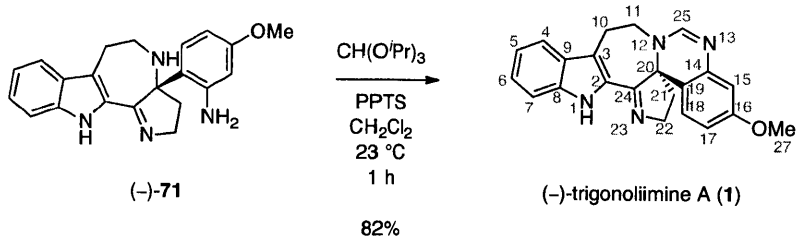
	($\mathbf{C}_5$), 119.8 ($\mathbf{C}_4$), 118.7 ($\mathbf{C}_3$), 114.9 ($\mathbf{C}_{19}$), 111.6 ($\mathbf{C}_7$), 102.5 ($\mathbf{C}_{17}$), 102.4 ($\mathbf{C}_{15}$), 75.6 ($\mathbf{C}_{20}$), 56.0 ($\mathbf{C}_{22}$), 55.2 ($\mathbf{C}_{26}$), 42.1 ($\mathbf{C}_{11}$), 40.9 ($\mathbf{C}_{21}$), 28.4 ($\mathbf{C}_{10}$).
FTIR (neat) cm^{-1}:	3286 (br-s), 2924 (s), 1599 (s), 1509 (m), 1450 (m), 1331 (m), 1211 (s), 748 (s).
HRMS (ESI) (*m/z*):	calc'd for $C_{21}H_{23}N_4O$, $[M+H]^+$: 347.1866, found: 347.1852.
$[\alpha]_D^{24}$:	–96.2 (*c* 0.15, $CHCl_3$).

TLC (9% methanol, 1% ammonium hydroxide in chloroform), R*f*: 0.41 (CAM, UV).

(*S*)-2-(9-Methoxy-3,3a,4,5,6,11-hexahydro-2*H*-pyrrolo[3',2':2,3]azepino[4,5-*b*]indol-3a-yl)aniline (72)

^{1}H NMR (500.4 MHz, $CDCl_3$, 21 °C):	δ 9.46 (s, 1H, $N_{1'}$**H**), 7.33 (d, *J* = 8.7 Hz, 1H, $C_{4'}$**H**), 7.02 (app-td, *J* = 7.6, 1.5 Hz, 1H, $C_{16'}$**H**), 6.78 (d, *J* = 2.1 Hz, 1H, $C_{7'}$**H**), 6.72 (dd, *J* = 8.7, 2.2 Hz, 1H, $C_{5'}$**H**), 6.69 (dd, *J* = 7.7, 1.3 Hz, 1H, $C_{18'}$**H**), 6.64 (dd, *J* = 7.9, 1.1 Hz, 1H, $C_{15'}$**H**), 6.44 (td, *J* = 7.5, 1.2 Hz, 1H, $C_{17'}$**H**), 3.99 (dd, *J* = 15.2, 7.7 Hz, 1H, $C_{22'}$**H**), 3.82 (s, 3H, O**Me**), 3.44 (ddd, *J* = 15.5, 10.3, 5.5 Hz, 1H, $C_{22'}$**H**), 3.18 (dt, 1H, *J* = 14.4, 5.0 Hz, 1H, $C_{11'}$**H**), 3.09 (ddd, *J* = 14.3, 9.6, 4.7 Hz, 1H, $C_{11'}$**H**), 2.99–2.92 (m, 1H, $C_{10'}$**H**), 2.86 (dt, *J* = 16.8, 4.7 Hz, 1H, $C_{10'}$**H**), 2.77 (dd, *J* = 12.2, 5.6, Hz, 1H, $C_{21'}$**H**), 1.94 (ddd, *J* = 12.1, 10.5, 7.8 Hz, 1H, $C_{21'}$**H**),
^{13}C NMR (125.8 MHz, $CDCl_3$, 21 °C):	δ 173.9 ($\mathbf{C}_{24'}$), 158.6 ($\mathbf{C}_{6'}$), 146.4 ($\mathbf{C}_{14'}$), 138.2 ($\mathbf{C}_{8'}$), 128.9 ($\mathbf{C}_{2'}$), 128.7 ($\mathbf{C}_{16'}$), 128.2 ($\mathbf{C}_{18'}$), 122.8 ($\mathbf{C}_{9'}$), 122.3 ($\mathbf{C}_{19'}$), 120.8 ($\mathbf{C}_{4'}$), 118.7 ($\mathbf{C}_{3'}$), 117.5 ($\mathbf{C}_{17'}$), 116.7 ($\mathbf{C}_{15'}$), 110.5 ($\mathbf{C}_{5'}$), 94.0 ($\mathbf{C}_{7'}$), 76.0 ($\mathbf{C}_{20'}$), 56.1 ($\mathbf{C}_{22'}$), 55.8 ($\mathbf{C}_{26'}$), 42.2 ($\mathbf{C}_{11'}$), 40.7 ($\mathbf{C}_{21'}$), 28.4 ($\mathbf{C}_{10'}$).
FTIR (neat) cm^{-1}:	3284 (br-m), 2924 (br-m), 1596 (s), 1495 (w), 1454 (w), 1273 (m), 752 (s).
HRMS (DART) (*m/z*):	calc'd for $C_{21}H_{23}N_4O$, $[M+H]^+$: 347.1866, found: 347.1876.
$[\alpha]_D^{25}$:	–176 (*c* 0.15, $CHCl_3$).

TLC (9% methanol, 1% ammonium hydroxide in chloroform), R*f*: 0.34 (CAM, UV).



(–)-**71**

(–)-trigonoliimine A (**1**)

(–)-Trigonoliimine A (1):

Anhydrous dichloromethane (4 mL) was added via syringe to a flask charged with pentacycle (–)-**71** (14.0 mg, 40.4 μmol, 1 equiv) and pyridinium *p*-toluenesulfonate (PPTS, 31.0 mg, 0.121 mmol, 3.00 equiv) at 23 °C under an atmosphere of argon to form a bright yellow solution. After 2 min, triisopropyl orthoformate (93.0 μL, 0.404 mmol, 10.0 equiv) was added to the reaction mixture. After 1h, saturated aqueous sodium bicarbonate solution (6 mL) was added to the reaction mixture and the resulting mixture was diluted with dichloromethane (2 mL), and the layers were separated. The aqueous layer was extracted with dichloromethane (2 × 6 mL), and the combined organic layers were dried over anhydrous sodium sulfate, and were concentrated under reduced pressure. The sample of the crude residue was purified by flash column chromatography (silica gel: diam. 2 cm, ht. 12 cm; eluent: 1.8% methanol, 0.2 % ammonium hydroxide in chloroform to 4.5% methanol, 0.5 % ammonium hydroxide in chloroform) to afford (–)-trigonoliimine A (**1**, 11.8 mg, 81.9%) as a pale yellow solid.

^{1}H NMR (500.4 MHz, DMSO-d_6, 21 °C): δ 11.50 (s, 1H, N_1**H**), 7.47 (s, 1H, C_{25}**H**), 7.45 (d, J = 7.9 Hz, 1H, C_4**H**), 7.34 (d, J = 8.2 Hz, 1H, C_7**H**), 7.16 (ddd, J = 8.1, 7.0, 1.1 Hz, 1H, C_6**H**), 7.00 (app-t, J = 7.9 Hz, 1H, C_5**H**), 6.56–6.55 (m, 3H, C_{15}**H**, C_{17}**H**, C_{18}**H**), 4.11 (dd, J = 16.1, 8.1 Hz, 1H, C_{22}**H**), 4.01 (dt, J = 14.3, 3.3 Hz, 1H, C_{11}**H**), 3.74 (app-t, J = 12.1 Hz, 1H, C_{11}**H**), 3.66 (s, 3H, O**Me**), 3.55 (ddd, J = 16.1, 9.9, 6.1 Hz, 1H, C_{22}**H**), 3.07 (app-d, J = 17.1 Hz, 1H, C_{10}**H**), 2.96 (ddd, J = 16.9, 12.1, 4.3 Hz, 1H, C_{10}**H**), 2.19–2.13 (m, 1H, C_{21}**H**), 2.06 (dd, J = 12.0, 5.8 Hz, 1H, C_{21}**H**).

^{1}H NMR (500.4 MHz, $CDCl_3/CD_3OD$ (3:1), 21 °C): δ 7.43 (d, J = 8.0 Hz, 1H, C_4**H**), 7.34 (d, J = 8.3 Hz, 1H, C_7**H**), 7.32 (s, 1H, C_{25}**H**), 7.20 (ddd, J = 8.2, 7.1, 1.1 Hz, 1H, C_6**H**), 7.03 (ddd, J = 8.0, 7.1, 0.9 Hz, 1H, C_5**H**), 6.65 (d, J = 2.0 Hz, 1H, C_{15}**H**), 6.57–6.53 (m, 2H, C_{17}**H**, C_{18}**H**), 4.13 (dd, J = 16.1, 8.1 Hz, 1H, C_{22}**H**), 3.92 (dt, J = 14.5, 3.5 Hz, 1H, C_{11}**H**), 3.84 (ddd, J = 14.3, 11.0, 3.1 Hz, 1H, C_{11}**H**), 3.70 (s, 3H, O**Me**), 3.65 (ddd, J = 16.1, 10.2, 5.9 Hz, 1H, C_{22}**H**), 3.19–3.08 (m, 2H, C_{10}**H**$_2$), 2.27 (dd, J = 12.3, 5.8 Hz, 1H, C_{21}**H**), 2.16 (ddd, J = 12.1, 10.3, 8.3 Hz, 1H, C_{21}**H**).

^{13}C NMR (125.8 MHz, DMSO-d_6, 21 °C): δ 166.5 (**C**$_{24}$), 159.6 (**C**$_{16}$), 150.2 (**C**$_{25}$), 143.1 (**C**$_{14}$), 136.5 (**C**$_8$), 128.0 (**C**$_2$), 127.1 (**C**$_9$), 123.4 (**C**$_6$), 123.2 (**C**$_{18}$), 119.2 (**C**$_5$), 119.1 (**C**$_4$), 115.6 (**C**$_3$), 115.0 (**C**$_{19}$),

111.6 ($\mathbf{C}_7$), 110.2 ($\mathbf{C}_{17}$), 109.3 ($\mathbf{C}_{15}$), 76.5 ($\mathbf{C}_{20}$), 56.2 ($\mathbf{C}_{22}$), 55.0 ($\mathbf{C}_{27}$), 46.6 ($\mathbf{C}_{11}$), 40.6 ($\mathbf{C}_{21}$), 29.2 ($\mathbf{C}_{10}$).

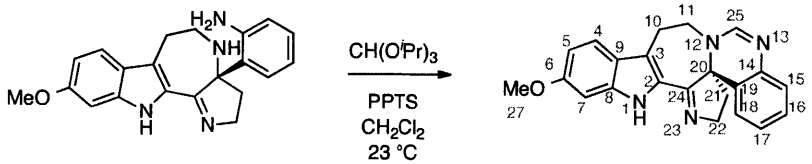
^{13}C NMR (125.8 MHz, $CDCl_3/CD_3OD$ (3:1), 21 °C): δ 168.2 ($\mathbf{C}_{24}$), 160.7 ($\mathbf{C}_{16}$), 150.5 ($\mathbf{C}_{25}$), 142.0 ($\mathbf{C}_{14}$), 137.4 ($\mathbf{C}_8$), 127.9 ($\mathbf{C}_9$), 127.2 ($\mathbf{C}_2$), 125.0 ($\mathbf{C}_6$), 123.9 ($\mathbf{C}_{18}$), 120.2 ($\mathbf{C}_5$), 119.6 ($\mathbf{C}_4$), 118.1 ($\mathbf{C}_3$), 114.5 ($\mathbf{C}_{19}$), 112.1 ($\mathbf{C}_7$), 112.0 ($\mathbf{C}_{17}$), 109.4 ($\mathbf{C}_{15}$), 77.5 ($\mathbf{C}_{20}$), 56.6 ($\mathbf{C}_{22}$), 55.6 ($\mathbf{C}_{27}$), 48.5 ($\mathbf{C}_{11}$), 41.1 ($\mathbf{C}_{21}$), 30.1 ($\mathbf{C}_{10}$).

FTIR (neat) cm^{-1}: 3406 (br-s), 1594 (s), 1488 (m), 1394 (w), 1251 (w), 1126 (w), 730 (s).

HRMS (ESI) (*m/z*): calc'd for $C_{22}H_{21}N_4O$, $[M+H]^+$: 357.1710, found: 357.1702.

$[\alpha]_D^{24}$: –294 (*c* 0.24, $CHCl_3$).

TLC (9% methanol, 1% ammonium hydroxide in chloroform), R*f*: 0.38 (CAM, UV).



(–)-**72** (–)-trigonoliimine B (**2**)

(–)-Trigonoliimine B (2):

Anhydrous dichloromethane (4.3 mL) was added via syringe to a flask charged with pentacycle (–)-**72** (16.4 mg, 47.3 μmol, 1 equiv) and pyridinium *p*-toluenesulfonate (PPTS, 33.3 mg, 0.130 mmol, 3.00 equiv) at 23 °C under an atmosphere of argon to form a bright yellow solution. After 2 min, triisopropyl orthoformate (99.5 μL, 0.433 mmol, 10.0 equiv) was added to the reaction mixture. After 1h, saturated aqueous sodium bicarbonate solution (6 mL) was added to the reaction mixture and the resulting mixture was diluted with dichloromethane (2 mL), and the layers were separated. The aqueous layer was extracted with dichloromethane (2 × 6 mL), and the combined organic layers were dried over anhydrous sodium sulfate, and were concentrated under reduced pressure. The sample of the crude residue was purified by flash column chromatography (silica gel: diam. 2 cm, ht. 11.5 cm; eluent: 2.6% methanol, 0.3 % ammonium hydroxide in chloroform) to afford (–)-trigonoliimine B (**2**, 15.9 mg, 94.3%) as a pale yellow solid. Structural assignment of (–)-**2** utilized additional information from gCOSY, HSQC and HMBC.

^{1}H NMR (500.4 MHz, $CDCl_3/CD_3OD$ (3:1), 21 °C): δ 7.33 (s, 1H, C_{25}**H**), 7.28 (dd, J = 8.7, 0.4 Hz, 1H, C_4**H**), 7.18 (td, J = 7.6, 1.4 Hz, 1H, C_{16}**H**), 7.10 (dd, J = 7.9, 1.2 Hz, 1H, C_{15}**H**), 6.99 (td, J = 7.6, 1.3 Hz, 1H, C_{17}**H**), 6.80 (d, J = 2.1 Hz, 1H, C_7**H**), 6.68 (dd, J = 8.7, 2.2 Hz, 1H, C_5**H**), 6.66 (dd, J = 7.8, 1.4 Hz, 1H, C_{18}**H**), 4.11 (dd, J = 16.0, 8.1 Hz, 1H, C_{22}**H**), 3.92–3.81 (m, 2H, C_{11}**H**$_2$), 3.78 (s, 3H, O**Me**), 3.63 (ddd, J = 16.0, 10.2, 5.9 Hz, 1H, C_{22}**H**), 3.12 (td, J = 17.3, 2.7 Hz, 1H, C_{10}**H**), 3.09–3.02 (m, 1H, C_{10}**H**), 2.28 (dd, J = 12.2, 5.7 Hz, 1H, C_{21}**H**), 2.15 (ddd, J = 12.2, 10.3, 8.3 Hz, 1H, C_{21}**H**).

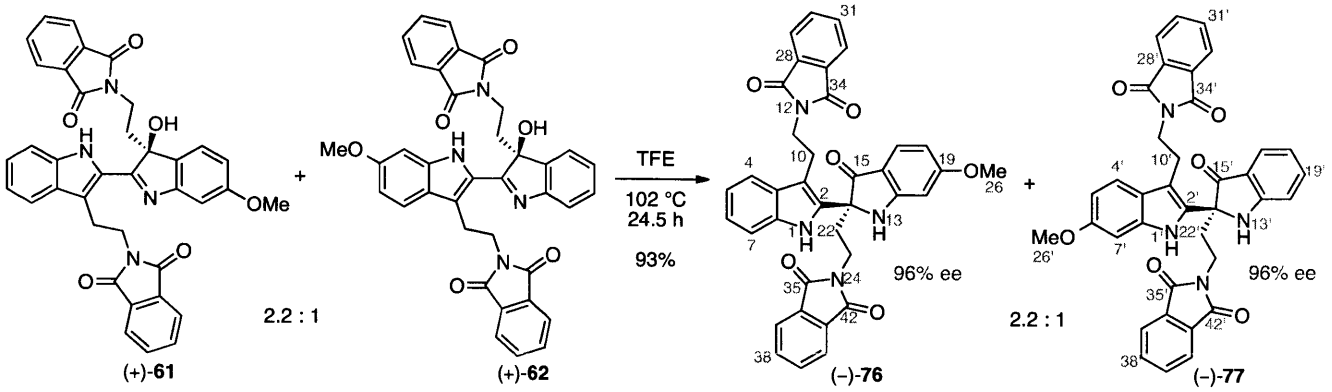
^{13}C NMR (125.8 MHz, $CDCl_3/CD_3OD$ (3:1), 21 °C): δ 167.7 (**C**$_{24}$), 158.8 (**C**$_6$), 150.2 (**C**$_{25}$), 140.7 (**C**$_{14}$), 138.6 (**C**$_8$), 129.5 (**C**$_{16}$), 126.3 (**C**$_2$), 126.0 (**C**$_{17}$), 124.7 (**C**$_{15}$), 122.9 (**C**$_{18}$), 122.5 (**C**$_9$), 122.1 (**C**$_{19}$), 120.5 (**C**$_4$), 118.9 (**C**$_3$), 111.2 (**C**$_5$), 94.5 (**C**$_7$), 77.6 (**C**$_{20}$), 56.4 (**C**$_{22}$), 55.8 (**C**$_{27}$), 48.7 (**C**$_{11}$), 41.0 (**C**$_{21}$), 30.2 (**C**$_{10}$).

FTIR (neat) cm^{-1}: 3406 (br-s), 1609 (s), 1590 (s), 1560 (m), 1478 (w), 1275 (w), 1164 (w), 754 (s).

HRMS (DART) (*m/z*): calc'd for $C_{22}H_{21}N_4O$, $[M+H]^+$: 357.1710, found: 357.1715.

$[\alpha]_D^{24}$: –352 (*c* 0.32, $CHCl_3$).

TLC (9% methanol, 1% ammonium hydroxide in chloroform), R*f*: 0.15 (CAM, UV).



(*S*)-2-(2-(2-(3-(2-(1,3-Dioxoisoindolin-2-yl)ethyl)-1*H*-indol-2-yl)-6-methoxy-3-oxoindolin-2-yl)ethyl)isoindoline-1,3-dione (76) and (*S*)-2-(2-(2-(2-(2-(1,3-dioxoisoindolin-2-yl)ethyl)-3-oxoindolin-2-yl)-6-methoxy-1*H*-indol-3-yl)ethyl)isoindoline-1,3-dione (77):

Trifluoroethanol (TFE, 15 mL) was added via syringe to a pressure vessel charged with hydroxyindolenines (+)-**61** and (+)-**62** (2.2:1, **61**:**62**, 150 mg, 0.239 mmol, 1 equiv). Tightly sealed reaction vessel was heated to 102 °C. After 24.5 h, the homogeneous orange reaction mixture was allowed to cool to 23 °C and was concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel: diam. 2.5 cm, ht. 12 cm; eluent: 3.3% acetone in dichloromethane) to afford indoxyls (–)-**76** and (–)-**77** as a yellow solid mixture (2.2:1, **76**:**77**, 140 mg, 93.3%). Structural assignment of (–)-**76** and (–)-**77** utilized additional information from gCOSY, HSQC and HMBC.

The indoxyls (–)-**76** and (–)-**77** could be separated at this stage by preparative HPLC [Waters X-Bridge preparative HPLC column, C18, 5 μm, 19 × 250 mm; 20.0 mL/min; 40% water in acetonitrile; t_R(**77**) = 8.5 min, t_R(**76**) = 9.5 min], but a more practical separation was possible after the next step. Indoxyl (–)-**76** was found to be 96% ee by chiral HPLC analysis [Chiralpak IC 0.7 mL/min; 45% hexanes in isopropanol; t_R(major) = 24 min min, t_R(minor) = 55 min]. Indoxyl (–)-**77** was found to be 96% ee by chiral HPLC analysis [Chiralpak IC 0.7 mL/min; 45% hexanes in isopropanol; t_R(major) = 29.5 min min, t_R(minor) = 35.5 min].

(*S*)-2-(2-(2-(3-(2-(1,3-Dioxoisoindolin-2-yl)ethyl)-1*H*-indol-2-yl)-6-methoxy-3-oxoindolin-2-yl)ethyl)isoindoline-1,3-dione (76)

^{1}H NMR (500.4 MHz, $CDCl_3$, 21 °C): δ 9.10 (s, 1H, N_1**H**), 7.87 (dd, *J* = 5.4, 3.0 Hz, 2H, C_{37}**H**, C_{40}**H**), 7.73 (dd, *J* = 5.4, 3.0 Hz, 2H, C_{38}**H**, C_{39}**H**), 7.61 (dd, *J* = 5.5, 3.0 Hz, 2H, C_{29}**H**, C_{32}**H**), 7.52 (dd, *J* = 5.5, 3.0 Hz, 2H, C_{30}**H**, C_{31}**H**), 7.49 (d, *J* = 7.9 Hz, 1H, C_4**H**), 7.42 (d, *J* = 8.7 Hz, 1H, C_{17}**H**), 7.22 (d, *J* = 8.1 Hz, 1H, C_7**H**), 7.05 (app-t, *J* = 8.1 Hz, 1H, C_6**H**), 6.97 (app-t, *J* = 7.9 Hz, 1H, C_5**H**), 6.78 (s, 1H, N_{13}**H**), 6.64 (d, *J* = 2.1 Hz, 1H, C_{20}**H**), 6.34 (dd, *J* = 8.7, 2.1 Hz, 1H, C_{18}**H**), 3.91–3.73 (m, 4H, C_{11}**H**$_2$, C_{23}**H**$_2$), 3.87 (s, 3H, O**Me**), 3.11 (t, *J* = 8.7 Hz, 2H, C_{10}**H**$_2$), 2.70–2.64 (m, 1H, C_{22}**H**), 2.41–2.36 (m, 1H, C_{22}**H**).

^{13}C NMR (125.8 MHz, $CDCl_3$, 21 °C): δ 198.2 (**C**$_{15}$), 168.8 (**C**$_{35}$, **C**$_{42}$), 168.7 (**C**$_{19}$), 168.3 (**C**$_{27}$, **C**$_{34}$), 163.4 (**C**$_{21}$), 135.5 (**C**$_8$), 134.3 (**C**$_{38}$, **C**$_{39}$), 134.0 (**C**$_{30}$, **C**$_{31}$), 132.4 (**C**$_{36}$, **C**$_{41}$), 131.7 (**C**$_{28}$, **C**$_{33}$), 131.1 (**C**$_2$), 128.6 (**C**$_9$), 126.8 (**C**$_{17}$), 123.5 (**C**$_{37}$, **C**$_{40}$), 123.2 (**C**$_{29}$, **C**$_{32}$), 122.5 (**C**$_6$), 119.8 (**C**$_5$), 118.1 (**C**$_4$), 111.9

($\mathbf{C}_{16}$), 111.2 ($\mathbf{C}_{7}$), 109.9 ($\mathbf{C}_{18}$), 108.7 ($\mathbf{C}_{3}$), 94.8 ($\mathbf{C}_{20}$), 68.2 ($\mathbf{C}_{14}$), 55.9 ($\mathbf{C}_{26}$), 39.0 ($\mathbf{C}_{11}$), 37.0 ($\mathbf{C}_{22}$), 33.7 ($\mathbf{C}_{23}$), 24.4 ($\mathbf{C}_{10}$).

FTIR (neat) cm^{-1}: 1768 (w), 1701 (s), 1609 (s), 1457 (w), 1394 (m), 1286 (w), 716 (s).

HRMS (DART) (*m/z*): calc'd for $C_{37}H_{27}N_4O_6$, $[M–H]^-$: 623.1936, found: 623.1936.

$[\alpha]_D^{24}$: –27.7 (*c* 0.26, $CHCl_3$).

TLC (5% acetone in dichloromethane), R*f*: 0.34 (CAM, UV).

(*S*)-2-(2-(2-(2-(2-(1,3-Dioxoisoindolin-2-yl)ethyl)-3-oxoindolin-2-yl)-6-methoxy-1*H*-indol-3-yl)ethyl)isoindoline-1,3-dione (77)

^1H NMR (500.4 MHz, $CDCl_3$, 21 °C): δ 8.89 (s, 1H, $N_{1'}\mathbf{H}$), 7.87 (dd, *J* = 5.4, 3.0 Hz, 2H, $C_{37'}\mathbf{H}$, $C_{40'}\mathbf{H}$), 7.72 (dd, *J* = 5.4, 3.0 Hz, 2H, $C_{38'}\mathbf{H}$, $C_{39'}\mathbf{H}$), 7.60 (dd, *J* = 5.5, 2.9 Hz, 2H, $C_{29'}\mathbf{H}$, $C_{32'}\mathbf{H}$), 7.52 (dd, *J* = 5.5, 3.2 Hz, 2H, $C_{30'}\mathbf{H}$, $C_{31'}\mathbf{H}$), 7.52 (d, *J* = 9.1 Hz, 1H, $C_{17'}\mathbf{H}$), 7.48 (ddd, *J* = 8.3, 7.1, 1.3 Hz, 1H, $C_{19'}\mathbf{H}$), 7.32 (d, *J* = 8.6 Hz, 1H, $C_{4'}\mathbf{H}$), 7.20 (d, *J* = 8.3 Hz, 1H, $C_{20'}\mathbf{H}$), 6.76 (app-t, *J* = 7.8 Hz, 1H, $C_{18'}\mathbf{H}$), 6.70 (d, *J* = 2.0 Hz, 1H, $C_{7'}\mathbf{H}$), 6.70 (s, 1H, $N_{13'}\mathbf{H}$), 6.61 (dd, *J* = 8.6, 2.3 Hz, 1H, $C_{5'}\mathbf{H}$), 3.89–3.71 (m, 4H, $C_{11'}\mathbf{H_2}$, $C_{23'}\mathbf{H_2}$), 3.78 (s, 3H, O**Me**), 3.11–3.03 (m, 2H, $C_{10'}\mathbf{H_2}$), 2.71–2.66 (m, 1H, $C_{22'}\mathbf{H}$), 2.37–2.32 (m, 1H, $C_{22'}\mathbf{H}$).

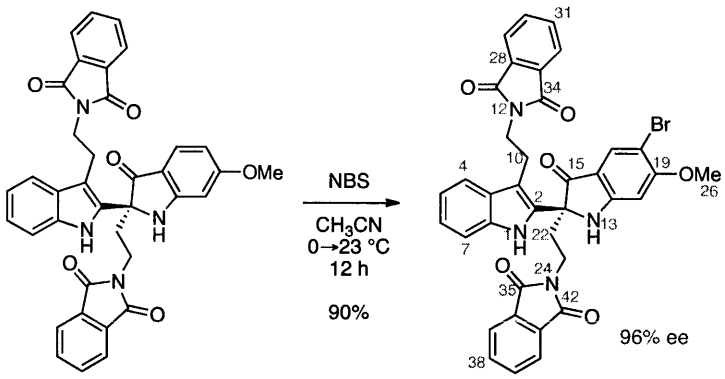
^{13}C NMR (125.8 MHz, $CDCl_3$, 21 °C): δ 200.9 ($\mathbf{C}_{15'}$), 168.7 ($\mathbf{C}_{35'}$, $\mathbf{C}_{42'}$), 168.3 ($\mathbf{C}_{27'}$, $\mathbf{C}_{34'}$), 161.0 ($\mathbf{C}_{21'}$), 156.9 ($\mathbf{C}_{6'}$), 138.4 ($\mathbf{C}_{19'}$), 136.3 ($\mathbf{C}_{8'}$), 134.2 ($\mathbf{C}_{38'}$, $\mathbf{C}_{39'}$), 133.9 ($\mathbf{C}_{30'}$, $\mathbf{C}_{31'}$), 132.4 ($\mathbf{C}_{36'}$, $\mathbf{C}_{41'}$), 131.7 ($\mathbf{C}_{28'}$, $\mathbf{C}_{33'}$), 128.8 ($\mathbf{C}_{2'}$), 125.4 ($\mathbf{C}_{17'}$), 123.5 ($\mathbf{C}_{37'}$, $\mathbf{C}_{40'}$), 123.1 ($\mathbf{C}_{29'}$, $\mathbf{C}_{32'}$), 123.0 ($\mathbf{C}_{9'}$), 119.2 ($\mathbf{C}_{18'}$), 118.9 ($\mathbf{C}_{4'}$), 118.5 ($\mathbf{C}_{16'}$), 113.1 ($\mathbf{C}_{20'}$), 110.0 ($\mathbf{C}_{5'}$), 109.2 ($\mathbf{C}_{3'}$), 94.5 ($\mathbf{C}_{7'}$), 67.8 ($\mathbf{C}_{14'}$), 55.8 ($\mathbf{C}_{26'}$), 39.0 ($\mathbf{C}_{11'}$), 36.7 ($\mathbf{C}_{22'}$), 33.8 ($\mathbf{C}_{23'}$), 24.3 ($\mathbf{C}_{10'}$).

FTIR (neat) cm^{-1}: 1769 (m), 1705 (s) 1615 (m), 1467 (w), 1396 (m), 716 (m).

HRMS (DART) (*m/z*): calc'd for $C_{37}H_{27}N_4O_6$, $[M–H]^-$: 623.1936, found: 623.1938.

$[\alpha]_D^{24}$: –23.2 (*c* 0.20, $CHCl_3$).

TLC (5% acetone in dichloromethane), R*f*: 0.34 (CAM, UV).



(–)-**76** (–)-**80**

(*S*)-2-(2-(2-(5-Bromo-2-(2-(1,3-dioxoisoindolin-2-yl)ethyl)-6-methoxy-3-oxoindolin-2-yl)-1*H*-indol-3-yl)ethyl)isoindoline-1,3-dione (80):

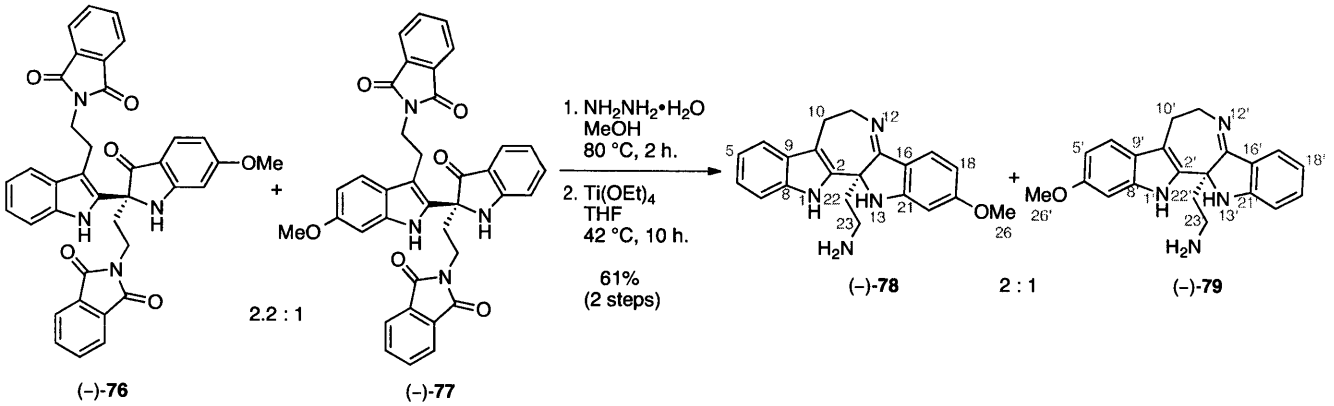
N-Bromosuccinimide (NBS, 2.4 mg, 0.013 mmol, 1.2 equiv) was added as a solid in one portion to a solution of indoxyl (–)-**76** (7.2 mg, 0.011 mmol, 1 equiv) in anhydrous acetonitrile (1.1 mL) at 0 °C and the reaction mixture was allowed to warm to 23°C. After 12 h, saturated aqueous sodium thiosulfate solution and saturated aqueous sodium bicarbonate solution (1:1, 3 mL) was added to the reaction mixture, the solution was diluted with dichloromethane (3 mL), and the layers were separated. The aqueous layer was extracted with dichloromethane (2 × 3 mL), and the combined organic layers were dried over anhydrous sodium sulfate and were concentrated under reduced pressure. The sample of the crude residue was purified by flash column chromatography (silica gel: diam. 1.5 cm, ht. 8 cm; eluent: 2.5% acetone in dichloromethane) to afford brominated indoxyl (–)-**80** (7.3 mg, 90%) as a yellow solid.

Brominated indoxyl (–)-**80** was found to be 96% ee by chiral HPLC analysis [Chiralpak IC 0.7 mL/min; 45% hexanes in isopropanol; t_R(major) = 20.7 min, t_R(minor) = 30 min]. Crystal of brominated indoxyl (–)-**80** was obtained by slow evaporation of a hexanes–dichloromethane (1:1, 0.5 mL) solution of (–)-**80** (7.2 mg).

^{1}H NMR (500.4 MHz, $CDCl_3$, 21 °C): δ 8.95 (s, 1H, N_1**H**), 7.87 (dd, *J* = 5.5, 3.0 Hz, 2H, C_{37}**H**, C_{40}**H**), 7.75 (dd, *J* = 5.4, 3.0 Hz, 2H, C_{38}**H**, C_{39}**H**), 7.61 (s, 1H, C_{17}**H**), 7.60 (dd, *J* = 5.6, 2.9 Hz, 2H, C_{29}**H**, C_{32}**H**), 7.52 (dd, *J* = 5.4, 3.1 Hz, 2H, C_{30}**H**, C_{31}**H**), 7.47 (d, *J* = 8.0 Hz, 1H, C_4**H**), 7.21 (app-dt, *J* = 8.1, 0.8 Hz, 1H, C_7**H**), 7.05 (ddd, *J* = 8.1, 7.0, 1.1 Hz, 1H, C_6**H**), 6.97 (ddd, *J* = 7.9, 7.0, 1.0 Hz, 1H, C_5**H**), 6.83 (s, 1H, N_{13}**H**), 6.75 (s, 1H, C_{20}**H**), 4.00 (s, 3H, O**Me**), 3.90–3.83 (m, 3H, C_{11}**H**, C_{23}**H**$_2$), 3.77–3.70 (ddd, *J* = 13.8, 10.4, 7.2 Hz, 1H, C_{11}**H**), 3.07 (ddd, *J* = 10.8, 6.4, 4.1 Hz, 2H, C_{10}**H**$_2$), 2.67 (dt, *J* = 14.6, 7.3 Hz, C_{22}**H**), 2.38 (dt, *J* = 14.5, 6.4 Hz, C_{22}**H**).

^{13}C NMR (125.8 MHz, $CDCl_3$, 21 °C): δ 197.1 (**C**$_{15}$), 168.8 (**C**$_{35}$, **C**$_{42}$), 168.3 (**C**$_{27}$, **C**$_{34}$), 163.9 (**C**$_{19}$), 162.1 (**C**$_{21}$), 135.6 (**C**$_8$), 134.4 (**C**$_{38}$, **C**$_{39}$), 134.0 (**C**$_{30}$, **C**$_{31}$), 132.4 (**C**$_{36}$, **C**$_{41}$), 131.6 (**C**$_{28}$, **C**$_{33}$), 130.4 (**C**$_2$), 129.5 (**C**$_{17}$), 128.5 (**C**$_9$), 123.5 (**C**$_{37}$, **C**$_{40}$), 123.2 (**C**$_{29}$, **C**$_{32}$), 122.7 (**C**$_6$), 119.9 (**C**$_5$), 118.2 (**C**$_4$), 112.4 (**C**$_{16}$), 111.3 (**C**$_7$), 108.9 (**C**$_3$), 103.8 (**C**$_{18}$), 94.9 (**C**$_{20}$),

	68.5 (**C**$_{14}$), 56.9 (**C**$_{26}$), 38.9 (**C**$_{11}$), 36.9 (**C**$_{22}$), 33.6 (**C**$_{23}$), 24.4 (**C**$_{10}$).
FTIR (neat) cm^{-1}:	3378 (br-m), 1770 (m), 1708 (s), 1609 (s), 1457 (m), 1397 (s), 1211 (m), 1034 (w), 717 (s).
HRMS (ESI) (*m/z*):	calc'd for $C_{37}H_{28}BrN_4O_6$, $[M+H]^+$: 703.1187, found: 703.1187.
$[\alpha]_D^{24}$:	–56.2 (*c* 0.15, $CHCl_3$).
TLC (5% acetone in dichloromethane), R*f*:	0.5 (CAM, UV).



(*S*)-2-(2-Methoxy-7,12,12b,13-tetrahydro-6*H*-azepino[3,2-*b*:4,5-*b*']diindol-12b-yl)ethanamine (78) and (*S*)-2-(10-methoxy-7,12,12b,13-tetrahydro-6*H*-azepino[3,2-*b*:4,5-*b*']diindol-12b-yl)ethanamine (79):

Hydrazine monohydrate (81.0 μL, 1.64 mmol, 10.0 equiv) was added via syringe to a solution of indoxyls (–)-**76** and (–)-**77** (2.2:1, **76**:**77**, 103 mg, 0.164 mmol, 1 equiv) in methanol (16 mL) under an atmosphere of argon at 23 °C, and the reaction flask was equipped with a reflux condenser, and the reaction set-up was sealed under an atmosphere of argon and heated to 80 °C. After 2 h, the pale yellow homogeneous reaction mixture was allowed to cool to 23 °C and the volatiles were removed under reduced pressure to result in a pale yellow solid. A solution of titanium ethoxide (153 μL, 0.656 mmol, 4.00 equiv) in anhydrous tetrahydrofuran (16 mL) was added via syringe to the yellow solid under an atmosphere of argon, and the resulting mixture was warmed to 42 °C. After 10 h, the reaction mixture was concentrated under reduced pressure, the crude residue adsorbed onto silica gel (6 g) was dry loaded and purified by flash column chromatography (silica gel: diam. 3 cm, ht. 9 cm; eluent: 6% methanol, 0.6% ammonium hydroxide in chloroform) to afford imines (–)-**78** and (–)-**79** (2:1, **78**:**79**, 34.6 mg, 60.9%, 2 steps) as a yellow solid mixture. Structural assignment of (–)-**78** utilized additional information from gCOSY, HSQC and HMBC.

(*S*)-2-(2-Methoxy-7,12,12b,13-tetrahydro-6*H*-azepino[3,2-*b*:4,5-*b*']diindol-12b-yl)ethanamine (78)

^{1}H NMR (500.4 MHz, CD_3OD, 21 °C): δ 7.46 (d, J = 8.6 Hz, 1H, C_{17}**H**), 7.43 (dt, J = 7.8, 1.0 Hz, 1H, C_4**H**), 7.32 (dt, J = 8.1, 0.9 Hz, 1H, C_7**H**), 7.09 (ddd, J = 8.2, 7.0, 1. Hz, 1H, C_6**H**), 6.99 (ddd, J = 7.9, 7.0, 1.0 Hz, 1H, C_5**H**), 6.34 (dd, J = 8.5, 2.3 Hz, 1H, C_{18}**H**), 6.32 (d, J = 2.1 Hz, 1H, C_{20}**H**), 4.31 (br-s, 1H, C_{11}**H**), 3.93 (br-s, 1H, C_{11}**H**), 3.80 (s, 3H, O**Me**), 3.12 (app-d, J = 16.4 Hz, 1H, C_{10}**H**), 2.95 (app-dt, J = 14.9, 3.4 Hz, 1H, C_{10}**H**), 2.81–2.69 (m, 2H, C_{23}**H**$_2$), 2.65–2.59 (m, 1H, C_{22}**H**), 2.40–2.34 (m, 1H, C_{22}**H**).

^{1}H NMR (500.4 MHz, CD_3OD, 21 °C)[5]: δ 7.59 (app-d, J = 9.4 Hz, 1H, C_{17}**H**), 7.47 (dt, J = 7.9, 0.9 Hz, 1H, C_4**H**), 7.41 (dt, J = 8.2, 0.8 Hz, 1H, C_7**H**), 7.16 (ddd, J = 8.2, 7.1, 1.1 Hz, 1H, C_6**H**), 7.04 (ddd, J = 8.0, 7.1, 0.9 Hz, 1H, C_5**H**), 6.46 (app-s, 1H, C_{20}**H**), 6.45 (dd, J = 8.7, 2.2 Hz, 1H, C_{18}**H**), 4.46 (td, J = 13.5, 2.9 Hz 1H, C_{11}**H**), 4.02 (dt, J = 13.7, 3.6 Hz 1H, C_{11}**H**), 3.88 (s, 3H, O**Me**), 3.24 (dt, J = 16.8, 3.0 Hz, 1H, C_{10}**H**),

[5] 2 equivalent of acetic acid-d_4 was added, which resulted in sharpening of peaks: See attached copies of spectra.

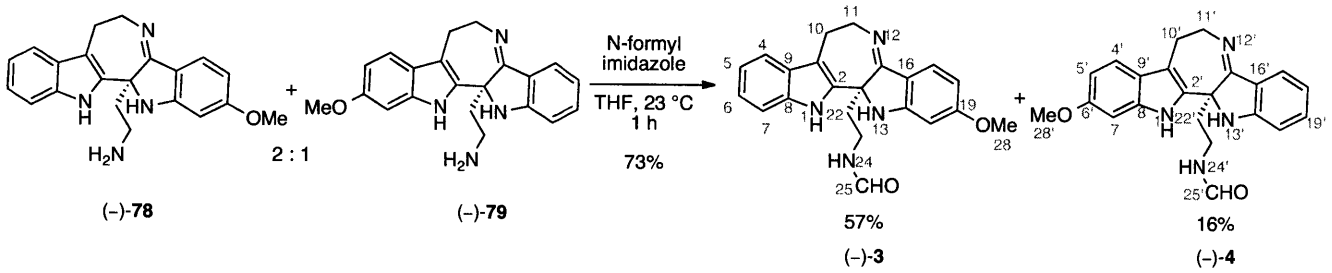
	3.15–3.11 (m, 1H, C_{10}**H**), 3.09–3.03 (m, 1H, C_{23}**H**), 2.93–2.88 (m, 1H, C_{23}**H**), 2.79–2.75 (m, 2H, C_{22}**H**).
^{13}C NMR (125.8 MHz, CD_3OD, 21 °C)[5]:	δ 176.9 (**C**$_{15}$), 170.8 (**C**$_{19}$), 162.7 (**C**$_{21}$), 137.4 (**C**$_8$), 129.5 (**C**$_9$), 128.1 (**C**$_2$), 126.8 (**C**$_{17}$), 123.9 (**C**$_6$), 120.6 (**C**$_5$), 119.1 (**C**$_4$), 112.5 (**C**$_{16}$), 112.3 (**C**$_{18}$), 112.3 (**C**$_7$), 111.3 (**C**$_3$), 94.7 (**C**$_{20}$), 69.8 (**C**$_{14}$), 56.7 (**C**$_{26}$), 46.0 (**C**$_{11}$), 39.1 (**C**$_{22}$), 36.9 (**C**$_{23}$), 25.1 (**C**$_{10}$).
FTIR (neat) cm^{-1}:	3180 (br-m), 2927 (m), 1612 (s), 1460 (m), 1303 (m), 1206 (m), 1165 (m), 741 (m).
HRMS (DART) (*m/z*):	calc'd for $C_{21}H_{23}N_4O$, $[M+H]^+$: 347.1866, found: 347.1856.
$[\alpha]_D^{24}$:	−179 (*c* 0.21, CD_3OD).

TLC (18% methanol, 2% ammonium hydroxide in chloroform), R*f*: 0.36 (CAM, UV).

(*S*)-2-(10-Methoxy-7,12,12b,13-tetrahydro-6*H*-azepino[3,2-*b*:4,5-*b*']diindol-12b-yl)ethanamine (79)

^{1}H NMR (500.4 MHz, CD_3OD, 21 °C):	δ 7.61 (dd, *J* = 7.3, 0.6 Hz, 1H, $C_{17'}$**H**), 7.36 (ddd, *J* = 8.3, 7.1, 1.2 Hz, 1H, $C_{19'}$**H**), 7.32 (d, *J* = 8.6 Hz, 1H, $C_{4'}$**H**), 6.90 (d, *J* = 2.1 Hz, 1H, $C_{7'}$**H**), 6.87 (d, *J* = 8.2 Hz, 1H, $C_{20'}$**H**), 6.79 (app-td, *J* = 8.0, 0.8 Hz, 1H, $C_{18'}$**H**), 6.69 (dd, *J* = 8.7, 2.2 Hz, 1H, $C_{5'}$**H**), 4.38 (app-td, *J* = 13.1, 2.6 Hz, 1H, $C_{11'}$**H**), 4.07 (app-dt, *J* = 12.4, 3.5 Hz, 1H, $C_{11'}$**H**), 3.81 (s, 3H, O**Me**), 3.14 (app-dt, *J* = 16.8, 3.3 Hz, 1H, $C_{10'}$**H**), 3.07–2.93 (m, 3H, $C_{10'}$**H**, $C_{23'}$**H**$_2$), 2.76 (ddd, *J* = 13.7, 12.1, 5.2 Hz, 1H, $C_{22'}$**H**), 2.63 (ddd, *J* = 13.5, 12.3, 4.5 Hz, 1H, $C_{22'}$**H**).
^{13}C NMR (100.6 MHz, CD_3OD, 21 °C)[5]:	δ 177.4, 158.4, 157.6, 138.1, 136.4, 129.1, 124.5, 124.1, 123.5, 120.4, 119.7, 112.7, 111.2, 110.4, 95.4, 67.9, 56.1, 48.0, 39.1, 37.3, 24.4.
FTIR (neat) cm^{-1}:	3271 (br-m), 2924 (m), 1647 (w), 1612 (s), 1465 (s), 1318 (m), 1252 (w), 1159 (m), 1030 (w), 750 (m).
HRMS (DART) (*m/z*):	calc'd for $C_{21}H_{23}N_4O$, $[M+H]^+$: 347.1866, found: 347.1876.
$[\alpha]_D^{24}$:	−194 (*c* 0.07, $CHCl_3$).

TLC (18% methanol, 2% ammonium hydroxide in chloroform), R*f*: 0.42 (CAM, UV).



(–)-Trigonoliimine C (3) and (–)-Isotrigonoliimine C (4):

Freshly prepared *N*-formyl imidazole[6] solution (0.0574 M solution in tetrahydrofuran, 1.80 mL, 0.105 mmol, 1.05 equiv) was added dropwise via syringe to a flask containing a mixture of amines (–)-**78** and (–)-**79** (2:1, **78**:**79**, 34.6 mg, 99.9 μmol, 1 equiv) at 23 °C and placed under an argon atmosphere. After 40 min, additional *N*-formyl imidazole[6] solution (0.0574 M solution in tetrahydrofuran, 200 μL, 11.7 μmol, 0.117 equiv) was slowly added to the reaction mixture. After 20 min, saturated aqueous sodium bicarbonate solution (14 mL) was added to the reaction mixture and the resulting mixture was diluted with dichloromethane (14 mL), and the layers were separated. The aqueous layer was extracted with dichloromethane (2 × 14 mL), and the combined organic layers were dried over anhydrous sodium sulfate, and were concentrated under reduced pressure. The sample of the crude residue was purified by flash column chromatography (silica gel: diam. 2.5 cm, ht. 9.5 cm; eluent: 2.2% methanol, 0.2 % ammonium hydroxide in chloroform) to afford (–)-trigonoliimine C (**3**, 21.3 mg, 57.0%) and (–)-isotrigonoliimine C (**4**, 5.8 mg, 15.5%) as yellow solids. Crystal of (–)-trigonoliimine C (**3**) was obtained by slow evaporation of a methanol (0.5 mL) solution of (–)-**3** (5.0 mg). Structural assignment of (–)-**4** utilized additional information from gCOSY, HSQC and HMBC.

(–)-Trigonoliimine C (3)

^{1}H NMR (500.4 MHz, DMSO-d_6, 21 °C): δ 10.79 (s, 1H, N_1**H**), 8.00 (app-s, 1H, N_{24}**H**), 7.93 (d, J = 1.7 Hz, 1H, C_{25}**H**), 7.40 (d, J = 7.8 Hz, 1H, C_4**H**), 7.34 (d, J = 7.8 Hz, 1H, C_7**H**), 7.31 (d, J = 8.2 Hz, 1H, C_{17}**H**), 7.07 (ddd, J = 8.1, 7.1, 1.1 Hz, 1H, C_6**H**), 6.97 (br-s, 1H, N_{13}**H**), 6.96 (app-t, J = 7.9 Hz, 1H, C_5**H**), 6.24 (d, J = 2.2 Hz, 1H, C_{20}**H**), 6.23 (dd, J = 10.4, 2.2 Hz, 1H, C_{18}**H**), 4.22 (app-dt, J = 13.8, 2.3 Hz, 1H, C_{11}**H**), 3.99 (app-dt, J = 11.8, 3.4 Hz, 1H, C_{11}**H**), 3.75 (s, 3H, O**Me**), 3.17–3.08 (m, 2H, C_{23}**H**$_2$), 3.05 (app-dt, J = 17.1, 3.2 Hz, 1H, C_{10}**H**), 2.80 (ddd, J = 16.7, 13.7, 3.2 Hz, 1H, C_{10}**H**), 2.54–2.48 (m, 1H, C_{22}**H**), 2.33–2.27 (m, 1H, C_{22}**H**).

^{1}H NMR (500.4 MHz, CD_3OD, 21 °C): δ 7.96 (s, 1H, C_{25}**H**), 7.50 (app-d, J = 9.3 Hz, 1H, C_{17}**H**), 7.43 (dt, J = 7.9, 0.9 Hz, 1H, C_4**H**), 7.33 (dt, J = 8.1, 0.8 Hz, 1H, C_7**H**), 7.10 (ddd, J = 8.1, 7.0, 1.1 Hz, 1H, C_6**H**), 7.00 (ddd, J = 7.9, 7.0, 0.9 Hz, 1H, C_5**H**), 6.36 (d, J = 2.4 Hz, 1H, C_{17}**H**), 6.36 (dd, J = 6.8, 2.2 Hz, 1H, C_{18}**H**), 4.42 (app-td, J = 14.3, 2.7 Hz, 1H, C_{11}**H**),

[6] *N*-Formyl imidazole was prepared according to the following procedure: Staab, H. A.; Polenski, B. *Liebigs Ann. Chem.* **1962**, *655*, 95–102.

4.01 (dt, J = 12.4, 3.5 Hz, 1H, C_{11}**H**), 3.82 (s, 3H, O**Me**), 3.30–3.28 (m, 2H, C_{23}**H$_2$**), 3.15 (dt, J = 16.7, 3.1 Hz, 1H, C_{10}**H**), 2.99 (ddd, J = 16.8, 13.5, 3.4 Hz, 1H, C_{10}**H**), 2.75 (ddd, J = 14.1, 10.2, 6.5 Hz, 1H, C_{22}**H**), 2.40 (ddd, J = 14.0, 8.9, 6.9 Hz, 1H, C_{22}**H**).

^{13}C NMR (125.8 MHz, DMSO-d_6, 21 °C): δ 170.0 (**C**$_{15}$), 164.2 (**C**$_{19}$), 161.0 (**C**$_{25}$), 156.6 (**C**$_{21}$), 134.8 (**C**$_8$), 131.9 (**C**$_2$), 127.9 (**C**$_9$), 123.4 (**C**$_{17}$), 121.3 (**C**$_6$), 118.4 (**C**$_5$), 117.7 (**C**$_4$), 116.5 (**C**$_{16}$), 110.8 (**C**$_7$), 108.7 (**C**$_3$), 105.3 (**C**$_{18}$), 93.8 (**C**$_{20}$), 66.3 (**C**$_{14}$), 55.2 (**C**$_{28}$), 46.6 (**C**$_{11}$), 39.5 (**C**$_{22}$), 33.6 (**C**$_{23}$), 23.3 (**C**$_{10}$).

^{13}C NMR (125.8 MHz, $CDCl_3/CD_3OD$ (3:1), 21 °C): δ174.1 (**C**$_{15}$), 166.1 (**C**$_{19}$), 162.9 (**C**$_{25}$), 158.3 (**C**$_{21}$), 135.7 (**C**$_8$), 130.8 (**C**$_2$), 128.7 (**C**$_9$), 124.9 (**C**$_{17}$), 122.5 (**C**$_6$), 119.5 (**C**$_5$), 118.3 (**C**$_4$), 116.2 (**C**$_{16}$), 111.2 (**C**$_7$), 110.2 (**C**$_3$), 108.1 (**C**$_{18}$), 95.1 (**C**$_{20}$), 67.6 (**C**$_{14}$), 55.8 (**C**$_{28}$), 47.2 (**C**$_{11}$), 39.8 (**C**$_{22}$), 34.6 (**C**$_{23}$), 24.0 (**C**$_{10}$).

^{13}C NMR (125.8 MHz, CD_3OD, 21 °C): δ 175.6 (**C**$_{15}$), 167.3 (**C**$_{19}$), 164.0 (**C**$_{25}$), 159.6 (**C**$_{21}$), 137.1 (**C**$_8$), 132.3 (**C**$_2$), 130.0 (**C**$_9$), 125.6 (**C**$_{17}$), 123.1 (**C**$_6$), 120.1 (**C**$_5$), 119.0 (**C**$_4$), 117.4 (**C**$_{16}$), 111.9 (**C**$_7$), 110.6 (**C**$_3$), 108.7 (**C**$_{18}$), 95.9 (**C**$_{20}$), 68.7 (**C**$_{14}$), 56.1 (**C**$_{28}$), 48.1 (**C**$_{11}$), 40.8 (**C**$_{22}$), 35.3 (**C**$_{23}$), 24.7 (**C**$_{10}$).

FTIR (neat) cm^{-1}: 3305 (br-w), 1732 (w), 1640 (s), 1610 (s), 1458 (m), 1376 (m), 1329 (m), 1300 (m), 1223 (w), 1029 (w), 735 (s).

HRMS (ESI) (*m/z*): calc'd for $C_{22}H_{23}N_4O_2$, $[M+H]^+$: 375.1816, found: 375.1818.

$[\alpha]_D^{24}$: −147 (*c* 0.12, $CHCl_3$).

TLC (18% methanol, 2% ammonium hydroxide in chloroform), R*f*: 0.52 (CAM, UV).

(–)-Isotrigonoliimine C (4):

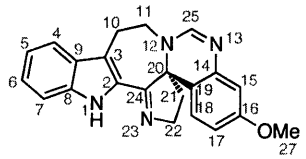
^{1}H NMR (500.4 MHz, CD_3OD, 21 °C): δ 7.95 (s, 1H, $C_{25'}$**H**), 7.59 (d, J = 7.8 Hz, 1H, $C_{17'}$**H**), 7.31 (app-dt, J = 9.5, 1.2 Hz, 1H, $C_{19'}$**H**), 7.30 (d, J = 8.7 Hz, 1H, $C_{4'}$**H**), 6.87 (d, J = 2.1 Hz, 1H, $C_{7'}$**H**), 6.84 (d, J = 8.1 Hz, 1H, $C_{20'}$**H**), 6.77 (app-t, J = 7.1 Hz, 1H, $C_{18'}$**H**), 6.67 (dd, J = 8.6, 2. 2 Hz, 1H, $C_{5'}$**H**), 4.43 (app-td, J = 14.7, 2.8 Hz, 1H, $C_{11'}$**H**), 4.06 (app-dt, J = 12.1, 3.5 Hz, 1H, $C_{11'}$**H**), 3.81 (s, 3H, O**Me**), 3.29–3.22 (m, 2H, $C_{23'}$**H$_2$**), 3.11 (app-dt, J = 16.5, 3.1 Hz, 1H, $C_{10'}$**H**), 2.96 (ddd, J = 16.8, 13.7, 3.4 Hz, 1H, $C_{10'}$**H**), 2.71 (ddd, J = 14.0, 10.5, 5.7 Hz, 1H, $C_{22'}$**H**), 2.39 (ddd, J = 14.0, 10.1, 5.8 Hz, 1H, $C_{22'}$**H**).

^{13}C NMR (125.8 MHz, CD_3OD, 21 °C): δ 176.6 (**C**$_{15'}$), 164.0 (**C**$_{25'}$), 158.1 (**C**$_{6'}$), 157.6 (**C**$_{21'}$), 137.8 (**C**$_{8'}$), 135.5 (**C**$_{19'}$), 130.8 (**C**$_{2'}$), 124.8 (**C**$_{16'}$), 124.3 (**C**$_{9'}$), 124.2 (**C**$_{17'}$), 120.2 (**C**$_{18'}$), 119.5 (**C**$_{4'}$), 112.6 (**C**$_{20'}$),

	110.6 ($\mathbf{C}_{3'}$), 110.1 ($\mathbf{C}_{5'}$), 95.4 ($\mathbf{C}_{7'}$), 68.0 ($\mathbf{C}_{14'}$), 56.1 ($\mathbf{C}_{28'}$), 48.6 ($\mathbf{C}_{11'}$), 40.7 ($\mathbf{C}_{22'}$), 35.4 ($\mathbf{C}_{23'}$), 24.4 ($\mathbf{C}_{10'}$).
FTIR (neat) cm^{-1}:	3278 (br-m), 2923 (br-m), 2361 (w), 1647 (s), 1613 (s), 1467 (m), 1316 (m), 1156 (m), 1027 (w), 745 (m).
HRMS (DART) (*m/z*):	calc'd for $C_{22}H_{21}N_4O_2$, $[M-H]^-$: 373.1670, found: 373.1684.
$[\alpha]_D^{24}$:	–220 (*c* 0.10, CH_3OH).

TLC (18% methanol, 2% ammonium hydroxide in chloroform), R*f*: 0.50 (CAM, UV).

Table S1. Comparison of our ^{1}H NMR data for (–)-trigonoliimine A (1) with literature data:



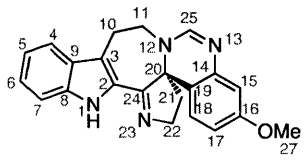
(–)-trigonoliimine A (**1**)

Assignment	Hao's Report[7] ^{1}H NMR, 500 MHz, DMSO-d_6	This Work[8] ^{1}H NMR, 500.4 MHz, DMSO-d_6, 21 °C
N1	11.50 (s, 1H)	11.5 (s, 1H)
C4	7.44 (d, J = 7.5 Hz, 1H)	7.45 (d, J = 7.9 Hz, 1H)
C5	6.99 (t, J = 7.5 Hz, 1H)	7.00 (app-t, J = 7.9 Hz, 1H)
C6	7.15 (t, J = 7.5 Hz, 1H)	7.16 (ddd, J = 8.1, 7.0, 1.1 Hz, 1H)
C7	7.32 (d, J = 7.5 Hz, 1H)	7.34 (d, J = 8.2 Hz, 1H)
C10α	3.06 (m, 1H)	3.07 (d, J = 17.1 Hz, 1H)
C10β	2.95 (m, 1H)	2.96 (ddd, J = 16.9, 12.1, 4.3 Hz, 1H)
C11α	4.00 (br-d, J = 14.5 Hz, 1H)	4.01 (dt, J = 14.3, 3.3 Hz, 1H)
C11β	3.74 (t, J = 12.5 Hz, 1H)	3.74 (app-t, J = 12.1 Hz, 1H)
C15	6.55 (overlapped, 1H)	6.56 (overlapped, 1H)
C17	6.54 (overlapped, 1H)	6.56 (overlapped, 1H)
C18	6.53 (overlapped, 1H)	6.55 (overlapped, 1H)
C21α	2.05 (m, 1H)	2.06 (dd, J = 12.0, 5.8 Hz, 1H)
C21β	2.14 (m, 1H)	2.19–2.13 (m, 1H)
C22α	3.55 (m, 1H)	3.55 (ddd, J = 16.1, 9.9, 6.1 Hz, 1H)
C22β	4.10 (m, 1H)	4.11 (dd, J = 16.1, 8.1 Hz, 1H)
C25	7.48 (s, 1H)	7.47 (s, 1H)
C27	3.65 (s, 3H)	3.66 (s, 3H)

[7] The reference points for the residual protium and carbon resonances of the NMR solvent were not listed. Tan, C. J.; Di, Y. T.; Wang, Y. H.; Zhang, Y.; Si, Y. K.; Zhang, Q.; Gao, S.; Hu, X. J.; Fang, X.; Li, S. F.; Hao, X. J. *Org. Lett.* **2010**, *12*, 2370–2373.

[8] In this report, the NMR spectra are referenced from the residual protium resonance, DMSO-d_6: δ 2.50 (DMSO-d_5), and carbon resonance, DMSO-d_6: δ 39.51.

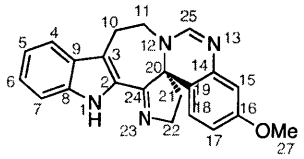
Table S2. Comparison of our ^{13}C NMR data for (–)-trigonoliimine A (1) with literature data:



(–)-trigonoliimine A (**1**)

Assignment	Hao's Report[7] ^{13}C NMR, 100 MHz, DMSO-d_6	This Work[8] ^{13}C NMR, 125.8 MHz, DMSO-d_6, 21 °C
C2	127.9	128.0
C3	115.6	115.6
C4	119.1	119.1
C5	119.1	119.2
C6	123.4	123.4
C7	111.7	111.6
C8	136.5	136.5
C9	127.1	127.1
C10	29.1	29.2
C11	46.6	46.6
C14	143.0	143.1
C15	109.2	109.3
C16	159.6	159.6
C17	110.3	110.2
C18	123.2	123.2
C19	115.0	115.0
C20	76.5	76.5
C21	40.6	40.6
C22	56.2	56.2
C24	166.4	166.5
C25	150.2	150.2
C27	55.1	55.0

Table S3. Comparison of our ^{13}C NMR data for (–)-trigonoliimine A (1) with literature data:

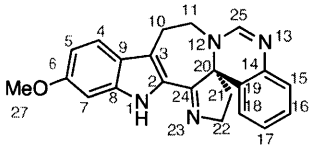


(–)-trigonoliimine A (**1**)

Assignment	Hao's Report[7] ^{13}C NMR, 100 MHz, $CDCl_3/CD_3OD$ (3:1)	This Work[9] ^{13}C NMR, 125.8 MHz, $CDCl_3/CD_3OD$ (3:1), 21 °C	Chemical Shift Difference Δδ δ (Hao's Report) - δ (This Report)
C2	126.5	127.2	–0.7
C3	117.4	118.1	–0.7
C4	119.0	119.6	–0.6
C5	119.6	120.2	-0.6
C6	124.3	125.0	–0.7
C7	111.4	112.1	–0.7
C8	136.8	137.4	–0.6
C9	127.2	127.9	–0.7
C10	29.4	30.1	–0.7
C11	47.9	48.5	–0.6
C14	141.0	142.0	–1.0
C15	108.6	109.4	–0.8
C16	160.1	160.7	–0.6
C17	111.4	112.0	–0.6
C18	123.2	123.9	–0.7
C19	113.7	114.5	–0.8
C20	77.2	77.5	–0.3
C21	40.4	41.1	–0.7
C22	56.0	56.6	–0.6
C24	167.4	168.2	–0.8
C25	149.9	150.5	–0.6
C27	55.0	55.6	–0.6

[9] In this report, the NMR spectra are referenced from the residual protium resonance, CD_3OD: δ 3.31 (CHD_2OD), and carbon resonance, CD_3OD: δ 49.15.

Table S4. Comparison of our ^{13}C NMR data for (–)-trigonoliimine B (2) with literature data:



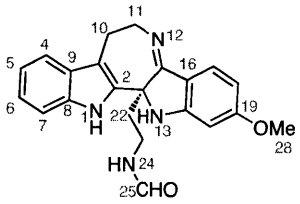
(–)-trigonoliimine B (**2**)

Assignment	Hao's Report[10] ^{13}C NMR, 100 MHz, $CDCl_3/CD_3OD$ (3:1)	This Work[9] ^{13}C NMR, 125.8 MHz, $CDCl_3/CD_3OD$ (3:1), 21 °C	Chemical Shift Difference Δδ δ (Hao's Report) - δ (This Report)
C2	125.1	126.3	–1.2
C3	117.7	118.9	–1.2
C4	119.3	120.5	–1.2
C5	110.0	111.2	–1.2
C6	157.6	158.8	–1.2
C7	93.4	94.5	–1.1
C8	137.4	138.6	–1.2
C9[11]	121.0	122.5	–1.5
C10	29.0	30.2	–1.2
C11	47.5	48.7	–1.2
C14	139.6	140.7	–1.1
C15	123.4	124.7	–1.3
C16	128.2	129.5	–1.3
C17	124.8	126.0	–1.2
C18	121.8	122.9	–1.1
C19[11]	121.3	122.1	–0.8
C20	76.5	77.6	–1.1
C21	39.8	41.0	–1.2
C22	55.2	56.4	–1.2
C24	166.6	167.7	–1.1
C25	149.0	150.2	–1.2
C27	54.6	55.8	–1.2

[10] The provided copy of the NMR spectra in the Supporting Information of the report indicates referencing of the residual carbon resonance of $CDCl_3$ at δ 76.51. Tan, C. J.; Di, Y. T.; Wang, Y. H.; Zhang, Y.; Si, Y. K.; Zhang, Q.; Gao, S.; Hu, X. J.; Fang, X.; Li, S. F.; Hao, X. J. *Org. Lett.* **2010**, *12*, 2370–2373.

[11] Our assignment of these resonances is supported by key HMBC signals (^1H, ^{13}C) in ppm: (2.28 ($C_{21}\mathbf{H}$), 122.1 ($\mathbf{C}_{19}$)), (6.68 ($C_5\mathbf{H}$), 122.5 ($\mathbf{C}_9$)), (6.80 ($C_7\mathbf{H}$),122.5 ($\mathbf{C}_9$)).

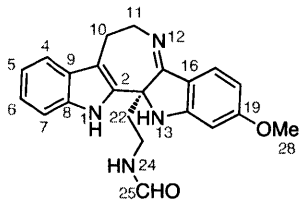
Table S5. Comparison of our ^{1}H NMR data for (–)-trigonoliimine C (3) with literature data:



(–)-trigonoliimine C (**3**)

Assignment	Hao's Report[7] ^{1}H NMR, 500 MHz, DMSO-d_6	This Work[8] ^{1}H NMR, 500.4 MHz, DMSO-d_6, 21 °C
N1	10.64 (s, 1H)	10.79 (s, 1H)
C4	7.41 (d, J = 7.5 Hz, 1H)	7.40 (d, J = 7.8 Hz, 1H)
C5	6.98 (t, J = 7.5 Hz, 1H)	6.96 (app-t, J = 7.9 Hz, 1H)
C6	7.08 (t, J = 7.5 Hz, 1H)	7.07 (ddd, J = 8.1, 7.1, 1.1 Hz, 1H)
C7	7.36 (d, J = 7.5 Hz, 1H)	7.34 (d, J = 7.8 Hz, 1H)
C10α	3.05 (br-d, J = 11.0 Hz, 1H)	3.05 (app-dt, J = 17.1, 3.2 Hz, 1H)
C10β	2.80 (t, J = 11.0 Hz, 1H)	2.80 (ddd, J = 16.7, 13.7, 3.2 Hz, 1H)
C11α	4.24 (t, J = 12.0 Hz, 1H)	4.22 (app-dt, J = 13.8, 2.3 Hz, 1H)
C11β	3.99 (br-d, J = 12.0 Hz, 1H)	3.99 (app-dt, J = 11.8, 3.4 Hz, 1H)
N13	6.83 (br-s, 1H)	6.97 (br-s, 1H)
C17	7.34 (d, J = 8.0 Hz, 1H)	7.31 (d, J = 8.2 Hz, 1H)
C18	6.26 (dd, J = 8.0, 2.5 Hz, 1H)	6.23 (dd, J = 10.4, 2.2 Hz, 1H)
C20	6.27 (d, J = 2.5 Hz, 1H)	6.24 (d, J = 2.2 Hz, 1H)
C22α	2.29 (m, 1H)	2.54–2.48 (m, 1H)
C22β	2.51 (m, 1H)	2.33–2.27 (m, 1H)
C23	3.14 (m, 2H)	3.17–3.08 (m, 2H)
N24	7.99 (br-s, 1H)	8.00 (app-s, 1H)
C25	7.93 (s, 1H)	7.93 (d, J = 1.7 Hz, 1H)
C28	3.77 (s, 3H)	3.75 (s, 3H)

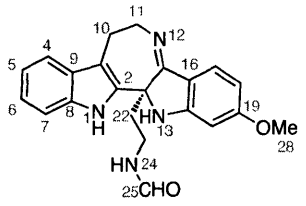
Table S6. Comparison of our ^{13}C NMR data for (–)-trigonoliimine C (3) with literature data:



(–)-trigonoliimine C (**3**)

Assignment	Hao's Report[7] ^{13}C NMR, 100 MHz, DMSO-d_6	This Work[8] ^{13}C NMR, 125.8 MHz, DMSO-d_6, 21 °C
C2	131.8	131.9
C3	108.8	108.7
C4	117.8	117.7
C5	118.6	118.4
C6	121.6	121.3
C7	110.9	110.8
C8	134.8	134.8
C9	127.9	127.9
C10	23.3	23.3
C11	46.5	46.6
C14	66.4	66.3
C15	170.3	170.0
C16	116.4	116.5
C17	123.6	123.4
C18	105.7	105.3
C19	164.3	164.2
C20	94.0	93.8
C21	156.8	156.6
C22	39.5	39.5
C23	33.6	33.6
C25	161.1	161.0
C28	55.3	55.2

Table S7. Comparison of our ^{13}C NMR data for (–)-trigonoliimine C (3) with literature data:

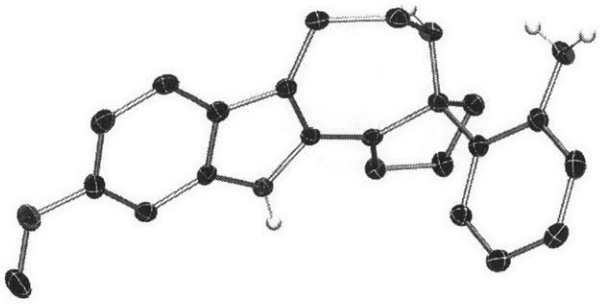


(–)-trigonoliimine C (**3**)

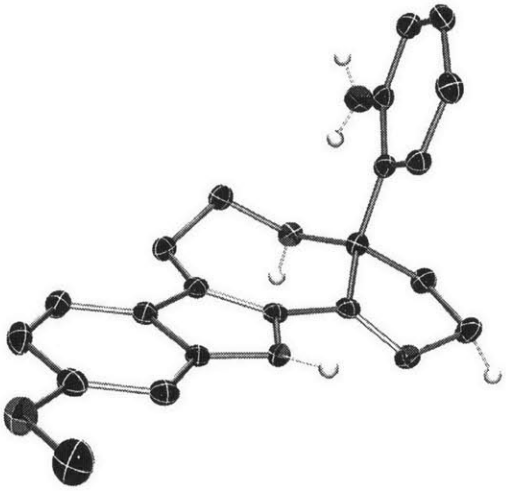
Assignment	Hao's Report[7] ^{13}C NMR, 100 MHz, $CDCl_3/CD_3OD$ (3:1)	This Work[9] ^{13}C NMR, 125.8 MHz, $CDCl_3/CD_3OD$ (3:1), 21 °C	Chemical Shift Difference Δδ δ (Hao's Report) - δ (This Report)
C2	131.4	130.8	0.6
C3	110.3	110.2	0.1
C4	118.5	118.3	0.2
C5	119.7	119.5	0.2
C6	122.7	122.5	0.2
C7	111.5	111.2	0.3
C8	136.3	135.7	0.6
C9	129.2	128.7	0.5
C10	24.3	24.0	0.3
C11	47.5	47.2	0.3
C14	68.1	67.6	0.5
C15	174.9	174.1	0.2
C16	116.5	116.2	0.3
C17	125.2	124.9	0.3
C18	108.4	108.1	0.3
C19	166.8	166.1	0.7
C20	95.3	95.1	0.2
C21	159.0	158.3	0.7
C22	40.2	39.8	0.2
C23	34.9	34.6	0.3
C25	163.4	162.9	0.5
C28	55.8	55.8	0.0

Crystal Structure of Pentacycle (–)-72

View 1:



View 2:



View 3:

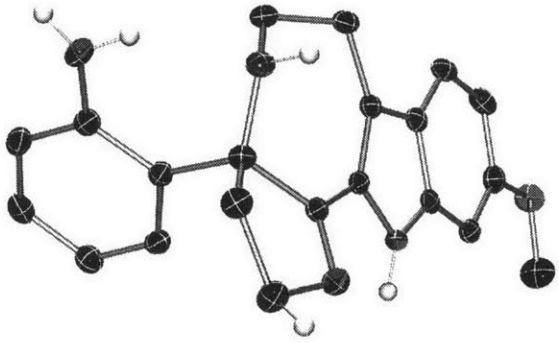


Table S8. Crystal data and structure refinement for **(–)-72**.

Identification code	x8_11097	
Empirical formula	C43 H45 Cl3 N8 O2	
Formula weight	812.22	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2(1)	
Unit cell dimensions	a = 15.1283(4) Å	a= 90°.
	b = 15.9902(4) Å	b= 90°.
	c = 16.2625(4) Å	g= 90°.
Volume	3933.97(17) $Å^3$	
Z	4	
Density (calculated)	1.371 Mg/m^3	
Absorption coefficient	2.502 mm^{-1}	
F(000)	1704	
Crystal size	0.20 x 0.20 x 0.15 mm^3	
Theta range for data collection	3.88 to 66.58°.	
Index ranges	-18<=h<=17, -18<=k<=19, -19<=l<=19	
Reflections collected	51159	
Independent reflections	6942 [R(int) = 0.0314]	
Completeness to theta = 66.58°	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7053 and 0.6345	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	6942 / 8 / 531	
Goodness-of-fit on F^2	1.058	
Final R indices [I>2sigma(I)]	R1 = 0.0305, wR2 = 0.0823	
R indices (all data)	R1 = 0.0306, wR2 = 0.0824	
Absolute structure parameter	0.008(8)	
Largest diff. peak and hole	0.595 and -0.385 $e.Å^{-3}$	

Table S9. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for **(–)-72**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
N(1A)	-3689(1)	3882(1)	9534(1)	15(1)
C(2A)	-3677(1)	3141(1)	9086(1)	16(1)
C(3A)	-4491(1)	3011(1)	8731(1)	16(1)
C(4A)	-5892(1)	3958(1)	8758(1)	20(1)
C(5A)	-6195(1)	4713(1)	9030(1)	24(1)
C(6A)	-5666(1)	5235(1)	9530(1)	22(1)
C(7A)	-4813(1)	5011(1)	9748(1)	19(1)
C(8A)	-4502(1)	4241(1)	9448(1)	16(1)
C(9A)	-5025(1)	3710(1)	8961(1)	17(1)
C(10A)	-4831(1)	2273(1)	8250(1)	21(1)
C(11A)	-4165(1)	1832(1)	7700(1)	22(1)
N(12A)	-3378(1)	1486(1)	8103(1)	22(1)
N(13A)	-2246(2)	1315(1)	6737(1)	40(1)
C(14A)	-2196(1)	2176(1)	6809(1)	27(1)
C(15A)	-1931(2)	2652(2)	6135(1)	35(1)
C(16A)	-1823(1)	3500(1)	6190(1)	33(1)
C(17A)	-1960(1)	3906(1)	6936(1)	29(1)
C(18A)	-2237(1)	3438(1)	7609(1)	20(1)
C(19A)	-2374(1)	2580(1)	7561(1)	19(1)
C(20A)	-2662(1)	2074(1)	8318(1)	17(1)
C(21A)	-1867(1)	1592(1)	8681(1)	20(1)
C(22A)	-1491(1)	2206(1)	9308(1)	21(1)
N(23A)	-2252(1)	2720(1)	9583(1)	18(1)
C(24A)	-2866(1)	2655(1)	9043(1)	16(1)
O(25A)	-6074(1)	5960(1)	9776(1)	31(1)
C(26A)	-5562(2)	6543(1)	10226(1)	35(1)
N(1B)	2900(1)	1460(1)	8783(1)	15(1)
C(2B)	3380(1)	723(1)	8724(1)	14(1)
C(3B)	3655(1)	604(1)	7926(1)	16(1)
C(4B)	3387(1)	1536(1)	6643(1)	18(1)
C(5B)	2993(1)	2266(1)	6391(1)	21(1)
C(6B)	2548(1)	2787(1)	6954(1)	20(1)

C(7B)	2468(1)	2579(1)	7774(1)	17(1)
C(8B)	2863(1)	1826(1)	8026(1)	15(1)
C(9B)	3322(1)	1300(1)	7472(1)	16(1)
C(10B)	4149(1)	-111(1)	7544(1)	18(1)
C(11B)	4794(1)	-565(1)	8101(1)	19(1)
N(12B)	4421(1)	-956(1)	8840(1)	19(1)
N(13B)	6073(1)	-1137(1)	9567(1)	23(1)
C(14B)	5939(1)	-311(1)	9799(1)	18(1)
C(15B)	6670(1)	161(1)	10049(1)	22(1)
C(16B)	6581(1)	966(1)	10346(1)	22(1)
C(17B)	5751(1)	1329(1)	10395(1)	22(1)
C(18B)	5022(1)	877(1)	10123(1)	18(1)
C(19B)	5092(1)	63(1)	9816(1)	16(1)
C(20B)	4256(1)	-415(1)	9553(1)	17(1)
C(21B)	3892(1)	-937(1)	10276(1)	20(1)
C(22B)	3285(1)	-317(1)	10712(1)	21(1)
N(23B)	2949(1)	239(1)	10058(1)	18(1)
C(24B)	3482(1)	199(1)	9450(1)	15(1)
O(25B)	2214(1)	3504(1)	6606(1)	25(1)
C(26B)	1812(2)	4099(1)	7141(1)	32(1)
C(1S)	565(1)	1315(1)	7530(1)	29(1)
Cl(1S)	-47(1)	437(1)	7202(1)	44(1)
Cl(2S)	69(1)	2242(1)	7185(1)	40(1)
Cl(3S)	649(1)	1313(1)	8611(1)	32(1)

Table S10. Bond lengths [Å] and angles [°] for **(–)-72**.

N(1A)-C(8A)	1.365(2)	C(19B)-C(20B)	1.539(2)
N(1A)-C(2A)	1.392(2)	C(20B)-C(24B)	1.537(2)
C(2A)-C(3A)	1.375(2)	C(20B)-C(21B)	1.544(2)
C(2A)-C(24A)	1.454(2)	C(21B)-C(22B)	1.527(2)
C(3A)-C(9A)	1.429(2)	C(22B)-N(23B)	1.476(2)
C(3A)-C(10A)	1.507(2)	N(23B)-C(24B)	1.278(2)
C(4A)-C(5A)	1.365(3)	O(25B)-C(26B)	1.425(2)
C(4A)-C(9A)	1.409(2)	C(1S)-Cl(2S)	1.754(2)
C(5A)-C(6A)	1.413(3)	C(1S)-Cl(3S)	1.7622(19)
C(6A)-O(25A)	1.373(2)	C(1S)-Cl(1S)	1.765(2)
C(6A)-C(7A)	1.385(3)		
C(7A)-C(8A)	1.405(3)	C(8A)-N(1A)-C(2A)	108.40(14)
C(8A)-C(9A)	1.406(2)	C(3A)-C(2A)-N(1A)	109.68(15)
C(10A)-C(11A)	1.521(3)	C(3A)-C(2A)-C(24A)	130.91(16)
C(11A)-N(12A)	1.466(2)	N(1A)-C(2A)-C(24A)	119.39(15)
N(12A)-C(20A)	1.476(2)	C(2A)-C(3A)-C(9A)	106.19(15)
N(13A)-C(14A)	1.383(3)	C(2A)-C(3A)-C(10A)	129.87(16)
C(14A)-C(15A)	1.394(3)	C(9A)-C(3A)-C(10A)	123.77(15)
C(14A)-C(19A)	1.409(3)	C(5A)-C(4A)-C(9A)	119.03(17)
C(15A)-C(16A)	1.369(3)	C(4A)-C(5A)-C(6A)	121.27(16)
C(16A)-C(17A)	1.391(3)	O(25A)-C(6A)-C(7A)	124.20(17)
C(17A)-C(18A)	1.390(3)	O(25A)-C(6A)-C(5A)	114.34(16)
C(18A)-C(19A)	1.391(3)	C(7A)-C(6A)-C(5A)	121.45(17)
C(19A)-C(20A)	1.537(2)	C(6A)-C(7A)-C(8A)	116.73(17)
C(20A)-C(24A)	1.533(2)	N(1A)-C(8A)-C(7A)	129.40(16)
C(20A)-C(21A)	1.545(2)	N(1A)-C(8A)-C(9A)	108.15(15)
C(21A)-C(22A)	1.525(2)	C(7A)-C(8A)-C(9A)	122.42(16)
C(22A)-N(23A)	1.483(2)	C(8A)-C(9A)-C(4A)	119.08(16)
N(23A)-C(24A)	1.283(2)	C(8A)-C(9A)-C(3A)	107.54(14)
O(25A)-C(26A)	1.415(3)	C(4A)-C(9A)-C(3A)	133.26(17)
N(1B)-C(8B)	1.365(2)	C(3A)-C(10A)-C(11A)	116.29(15)
N(1B)-C(2B)	1.388(2)	N(12A)-C(11A)-C(10A)	116.73(15)
C(2B)-C(3B)	1.377(2)	C(11A)-N(12A)-C(20A)	117.49(14)
C(2B)-C(24B)	1.455(2)	N(13A)-C(14A)-C(15A)	119.54(19)
C(3B)-C(9B)	1.427(2)	N(13A)-C(14A)-C(19A)	121.24(18)
C(3B)-C(10B)	1.501(2)	C(15A)-C(14A)-C(19A)	119.16(18)
C(4B)-C(5B)	1.374(3)	C(16A)-C(15A)-C(14A)	121.6(2)
C(4B)-C(9B)	1.404(2)	C(15A)-C(16A)-C(17A)	120.11(19)
C(5B)-C(6B)	1.409(3)	C(18A)-C(17A)-C(16A)	118.73(18)
C(6B)-O(25B)	1.375(2)	C(17A)-C(18A)-C(19A)	122.10(18)
C(6B)-C(7B)	1.379(3)	C(18A)-C(19A)-C(14A)	118.24(17)
C(7B)-C(8B)	1.407(2)	C(18A)-C(19A)-C(20A)	121.13(16)
C(8B)-C(9B)	1.413(2)	C(14A)-C(19A)-C(20A)	120.55(16)
C(10B)-C(11B)	1.516(2)	N(12A)-C(20A)-C(24A)	114.87(15)
C(11B)-N(12B)	1.467(2)	N(12A)-C(20A)-C(19A)	110.68(14)
N(12B)-C(20B)	1.467(2)	C(24A)-C(20A)-C(19A)	110.76(13)
N(13B)-C(14B)	1.389(2)	N(12A)-C(20A)-C(21A)	110.18(13)
C(14B)-C(15B)	1.399(3)	C(24A)-C(20A)-C(21A)	99.48(13)
C(14B)-C(19B)	1.413(2)	C(19A)-C(20A)-C(21A)	110.34(15)
C(15B)-C(16B)	1.382(3)	C(22A)-C(21A)-C(20A)	103.05(13)
C(16B)-C(17B)	1.385(3)	N(23A)-C(22A)-C(21A)	105.56(14)
C(17B)-C(18B)	1.391(3)	C(24A)-N(23A)-C(22A)	108.14(14)
C(18B)-C(19B)	1.397(2)	N(23A)-C(24A)-C(2A)	122.37(15)

N(23A)-C(24A)-C(20A)	115.45(15)
C(2A)-C(24A)-C(20A)	122.06(15)
C(6A)-O(25A)-C(26A)	117.49(15)
C(8B)-N(1B)-C(2B)	108.80(14)
C(3B)-C(2B)-N(1B)	109.94(15)
C(3B)-C(2B)-C(24B)	130.73(15)
N(1B)-C(2B)-C(24B)	119.27(15)
C(2B)-C(3B)-C(9B)	105.82(14)
C(2B)-C(3B)-C(10B)	130.28(15)
C(9B)-C(3B)-C(10B)	123.80(15)
C(5B)-C(4B)-C(9B)	118.96(16)
C(4B)-C(5B)-C(6B)	121.06(16)
O(25B)-C(6B)-C(7B)	124.46(17)
O(25B)-C(6B)-C(5B)	113.64(16)
C(7B)-C(6B)-C(5B)	121.90(16)
C(6B)-C(7B)-C(8B)	116.72(16)
N(1B)-C(8B)-C(7B)	130.28(16)
N(1B)-C(8B)-C(9B)	107.50(14)
C(7B)-C(8B)-C(9B)	122.22(15)
C(4B)-C(9B)-C(8B)	119.11(16)
C(4B)-C(9B)-C(3B)	132.93(16)
C(8B)-C(9B)-C(3B)	107.94(14)
C(3B)-C(10B)-C(11B)	116.00(14)
N(12B)-C(11B)-C(10B)	116.47(14)
C(20B)-N(12B)-C(11B)	117.55(13)
N(13B)-C(14B)-C(15B)	118.42(16)
N(13B)-C(14B)-C(19B)	122.73(16)
C(15B)-C(14B)-C(19B)	118.83(16)
C(16B)-C(15B)-C(14B)	121.81(17)
C(15B)-C(16B)-C(17B)	119.88(17)
C(16B)-C(17B)-C(18B)	118.87(16)
C(17B)-C(18B)-C(19B)	122.50(16)
C(18B)-C(19B)-C(14B)	118.02(16)
C(18B)-C(19B)-C(20B)	119.95(15)
C(14B)-C(19B)-C(20B)	121.95(15)
N(12B)-C(20B)-C(24B)	114.79(14)
N(12B)-C(20B)-C(19B)	111.88(14)
C(24B)-C(20B)-C(19B)	109.85(13)
N(12B)-C(20B)-C(21B)	110.10(13)
C(24B)-C(20B)-C(21B)	99.03(13)
C(19B)-C(20B)-C(21B)	110.49(14)
C(22B)-C(21B)-C(20B)	102.53(13)
N(23B)-C(22B)-C(21B)	105.28(14)
C(24B)-N(23B)-C(22B)	108.11(14)
N(23B)-C(24B)-C(2B)	122.13(15)
N(23B)-C(24B)-C(20B)	115.34(15)
C(2B)-C(24B)-C(20B)	122.49(14)
C(6B)-O(25B)-C(26B)	117.54(15)
Cl(2S)-C(1S)-Cl(3S)	110.59(12)
Cl(2S)-C(1S)-Cl(1S)	110.58(11)
Cl(3S)-C(1S)-Cl(1S)	109.71(11

Symmetry transformations used to generate equivalent atoms:

Table S11. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for **(–)-72**. The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2\ a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
N(1A)	12(1)	18(1)	16(1)	-1(1)	-3(1)	-2(1)
C(2A)	18(1)	15(1)	13(1)	2(1)	0(1)	-3(1)
C(3A)	18(1)	16(1)	14(1)	3(1)	-1(1)	-5(1)
C(4A)	14(1)	30(1)	17(1)	3(1)	0(1)	-4(1)
C(5A)	14(1)	37(1)	21(1)	4(1)	0(1)	3(1)
C(6A)	20(1)	28(1)	19(1)	1(1)	4(1)	5(1)
C(7A)	18(1)	24(1)	16(1)	0(1)	2(1)	-1(1)
C(8A)	15(1)	18(1)	13(1)	3(1)	2(1)	-2(1)
C(9A)	14(1)	23(1)	14(1)	4(1)	1(1)	-5(1)
C(10A)	20(1)	20(1)	24(1)	1(1)	-5(1)	-8(1)
C(11A)	26(1)	20(1)	21(1)	-3(1)	-6(1)	-8(1)
N(12A)	28(1)	16(1)	22(1)	0(1)	-4(1)	-5(1)
N(13A)	66(1)	32(1)	21(1)	-12(1)	6(1)	-1(1)
C(14A)	31(1)	29(1)	20(1)	1(1)	-4(1)	-1(1)
C(15A)	38(1)	47(1)	19(1)	1(1)	2(1)	2(1)
C(16A)	25(1)	46(1)	27(1)	17(1)	4(1)	4(1)
C(17A)	23(1)	26(1)	39(1)	11(1)	2(1)	0(1)
C(18A)	15(1)	21(1)	26(1)	1(1)	-1(1)	2(1)
C(19A)	18(1)	22(1)	18(1)	2(1)	-3(1)	0(1)
C(20A)	22(1)	14(1)	16(1)	-2(1)	-2(1)	-1(1)
C(21A)	25(1)	17(1)	19(1)	2(1)	1(1)	3(1)
C(22A)	20(1)	22(1)	20(1)	0(1)	-3(1)	6(1)
N(23A)	18(1)	18(1)	18(1)	-1(1)	-3(1)	2(1)
C(24A)	19(1)	14(1)	15(1)	3(1)	-1(1)	-3(1)
O(25A)	25(1)	35(1)	33(1)	-7(1)	0(1)	12(1)
C(26A)	33(1)	30(1)	42(1)	-8(1)	5(1)	9(1)
N(1B)	14(1)	18(1)	13(1)	-2(1)	1(1)	0(1)
C(2B)	12(1)	15(1)	17(1)	-3(1)	-1(1)	-2(1)
C(3B)	13(1)	16(1)	18(1)	-2(1)	-1(1)	-4(1)
C(4B)	21(1)	18(1)	17(1)	-3(1)	2(1)	-6(1)
C(5B)	27(1)	21(1)	15(1)	3(1)	-1(1)	-7(1)
C(6B)	18(1)	19(1)	23(1)	4(1)	-4(1)	-3(1)
C(7B)	15(1)	16(1)	21(1)	-2(1)	-1(1)	-2(1)

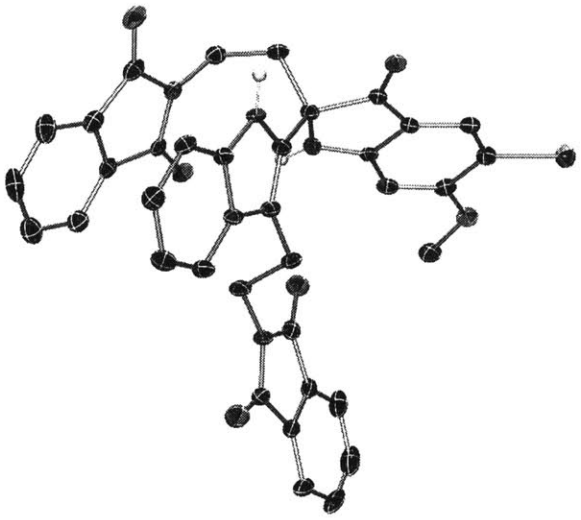
C(8B)	12(1)	18(1)	15(1)	0(1)	-1(1)	-5(1)
C(9B)	14(1)	17(1)	18(1)	-1(1)	-1(1)	-5(1)
C(10B)	19(1)	18(1)	17(1)	-4(1)	2(1)	-2(1)
C(11B)	20(1)	20(1)	18(1)	-4(1)	3(1)	2(1)
N(12B)	20(1)	15(1)	21(1)	-3(1)	1(1)	-1(1)
N(13B)	21(1)	21(1)	28(1)	-2(1)	-1(1)	8(1)
C(14B)	20(1)	20(1)	15(1)	4(1)	1(1)	2(1)
C(15B)	17(1)	30(1)	18(1)	4(1)	0(1)	4(1)
C(16B)	22(1)	26(1)	18(1)	2(1)	-3(1)	-6(1)
C(17B)	26(1)	19(1)	21(1)	-1(1)	-2(1)	-1(1)
C(18B)	18(1)	19(1)	18(1)	-1(1)	1(1)	2(1)
C(19B)	16(1)	18(1)	14(1)	2(1)	1(1)	1(1)
C(20B)	19(1)	14(1)	17(1)	1(1)	1(1)	0(1)
C(21B)	22(1)	17(1)	21(1)	4(1)	2(1)	-1(1)
C(22B)	21(1)	23(1)	20(1)	6(1)	4(1)	0(1)
N(23B)	17(1)	18(1)	19(1)	2(1)	2(1)	-1(1)
C(24B)	13(1)	15(1)	18(1)	-4(1)	-1(1)	-3(1)
O(25B)	31(1)	20(1)	25(1)	6(1)	0(1)	2(1)
C(26B)	42(1)	21(1)	35(1)	7(1)	1(1)	8(1)
C(1S)	26(1)	38(1)	23(1)	1(1)	3(1)	-5(1)
Cl(1S)	41(1)	48(1)	42(1)	-12(1)	13(1)	-18(1)
Cl(2S)	34(1)	46(1)	39(1)	19(1)	-5(1)	-3(1)
Cl(3S)	29(1)	44(1)	22(1)	6(1)	0(1)	4(1)

Table S12. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for **(–)-72**.

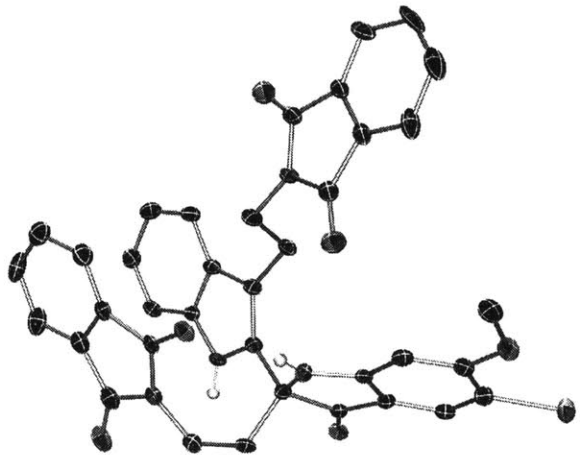
	x	y	z	U(eq)
H(1NA)	-3244(12)	4108(13)	9752(13)	18
H(4A)	-6260	3605	8436	24
H(5A)	-6772	4891	8881	29
H(7A)	-4456	5361	10083	23
H(10A)	-5328	2465	7902	26
H(10B)	-5070	1859	8644	26
H(11A)	-4473	1370	7413	27
H(11B)	-3966	2233	7274	27
H(4NA)	-3526(15)	1211(13)	8575(11)	26
H(2NA)	-2638(16)	1080(16)	7054(16)	47
H(3NA)	-2164(19)	1116(16)	6267(12)	47
H(15A)	-1821	2381	5625	42
H(16A)	-1655	3812	5718	39
H(17A)	-1865	4491	6985	35
H(18A)	-2336	3714	8118	25
H(21A)	-2061	1067	8949	24
H(21B)	-1427	1459	8250	24
H(22A)	-1227	1902	9779	25
H(22B)	-1031	2561	9054	25
H(26A)	-5340	6278	10728	52
H(26B)	-5930	7025	10372	52
H(26C)	-5063	6730	9889	52
H(1NB)	2759(14)	1665(12)	9255(10)	18
H(4B)	3698	1195	6262	22
H(5B)	3021	2423	5828	25
H(7B)	2160	2928	8150	21
H(10C)	4480	104	7063	22
H(10D)	3713	-522	7337	22
H(11C)	5091	-1006	7774	23
H(11D)	5254	-163	8275	23
H(4NB)	3943(12)	-1225(13)	8696(13)	22
H(2NB)	5619(13)	-1355(14)	9316(14)	28
H(3NB)	6590(12)	-1240(15)	9383(14)	28
H(15B)	7243	-79	10014	26
H(16B)	7088	1271	10517	26
H(17B)	5681	1877	10611	26
H(18B)	4455	1130	10147	22
H(21C)	3559	-1430	10076	24
H(21D)	4374	-1128	10643	24
H(22C)	2791	-612	10987	25
H(22D)	3616	7	11130	25
H(26D)	1295	3846	7406	49
H(26E)	1627	4589	6823	49
H(26F)	2237	4271	7563	49
H(1S)	1174	1279	7292	35

Crystal Structure of Bromoindoxyl (–)-80

View 1:



View 2:



View 3:

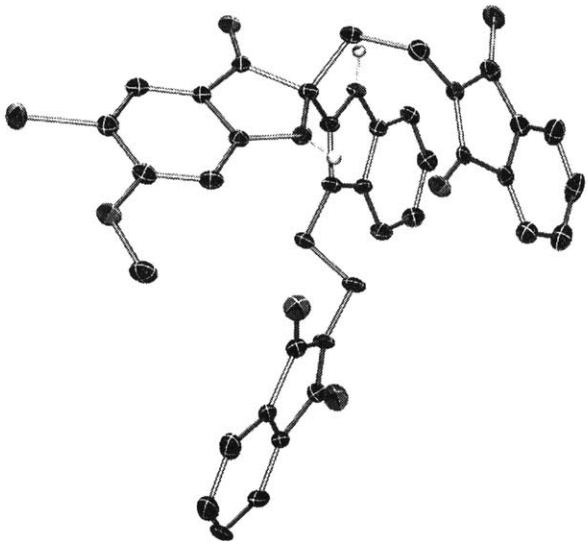


Table S13. Crystal data and structure refinement for (–)-**80**.

Identification code	x8_11013	
Empirical formula	C37.50 H28 Br Cl N4 O6	
Formula weight	746.00	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2	
Unit cell dimensions	a = 41.6761(19) Å	a= 90°.
	b = 7.7113(3) Å	b= 90°.
	c = 10.0688(5) Å	g = 90°.
Volume	3235.9(3) $Å^3$	
Z	4	
Density (calculated)	1.531 Mg/m^3	
Absorption coefficient	1.409 mm^{-1}	
F(000)	1524	
Crystal size	0.15 x 0.15 x 0.05 mm^3	
Theta range for data collection	1.95 to 30.32°.	
Index ranges	-57<=h<=59, -10<=k<=10, -14<=l<=14	
Reflections collected	61869	
Independent reflections	9654 [R(int) = 0.0571]	
Completeness to theta = 30.32°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9329 and 0.8164	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	9654 / 0 / 448	
Goodness-of-fit on F^2	1.181	
Final R indices [I>2sigma(I)]	R1 = 0.0476, wR2 = 0.0877	
R indices (all data)	R1 = 0.0564, wR2 = 0.0899	
Absolute structure parameter	0.021(7)	
Largest diff. peak and hole	0.338 and -0.686 $e.Å^{-3}$	

Table S14. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for (–)-**80**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Br(1)	8246(1)	-6823(1)	4487(1)	27(1)
O(1)	9328(1)	-4385(3)	7788(2)	19(1)
O(2)	7977(1)	738(3)	8040(2)	28(1)
O(3)	7878(1)	468(3)	12547(2)	31(1)
O(4)	8848(1)	2822(3)	8671(2)	21(1)
O(5)	9913(1)	1992(3)	9474(3)	30(1)
O(6)	7936(1)	-3445(3)	4962(2)	24(1)
N(1)	9392(1)	-1424(3)	10231(2)	15(1)
N(2)	8810(1)	-810(3)	7483(2)	17(1)
N(3)	9384(1)	2103(3)	8817(2)	17(1)
N(4)	8007(1)	624(3)	10322(3)	18(1)
C(1)	7801(1)	467(4)	11395(3)	21(1)
C(2)	7472(1)	321(4)	10793(3)	22(1)
C(3)	7177(1)	77(4)	11397(4)	33(1)
C(4)	6912(1)	-91(4)	10537(6)	44(1)
C(5)	6945(1)	-11(5)	9195(5)	42(1)
C(6)	7241(1)	237(4)	8590(4)	32(1)
C(7)	7505(1)	390(3)	9436(4)	22(1)
C(8)	7849(1)	600(4)	9106(3)	21(1)
C(9)	8354(1)	719(4)	10443(4)	22(1)
C(10)	8501(1)	-1089(4)	10288(3)	18(1)
C(11)	8859(1)	-1113(3)	10473(3)	17(1)
C(12)	9007(1)	-894(4)	11739(3)	16(1)
C(13)	8891(1)	-474(4)	13012(3)	22(1)
C(14)	9108(1)	-217(4)	14029(3)	23(1)
C(15)	9440(1)	-386(4)	13801(3)	22(1)
C(16)	9561(1)	-847(4)	12581(3)	18(1)
C(17)	9341(1)	-1069(4)	11549(3)	16(1)
C(18)	9102(1)	-1386(3)	9564(3)	16(1)
C(19)	9104(1)	-1492(4)	8064(3)	16(1)
C(20)	9107(1)	-3400(4)	7569(3)	15(1)
C(21)	8818(1)	-3620(4)	6793(3)	16(1)
C(22)	8701(1)	-5052(4)	6092(3)	19(1)
C(23)	8411(1)	-4923(4)	5465(3)	20(1)
C(24)	8228(1)	-3386(4)	5549(3)	19(1)
C(25)	8345(1)	-1924(4)	6197(3)	19(1)
C(26)	8646(1)	-2066(4)	6813(3)	15(1)
C(27)	7725(1)	-1982(5)	5155(3)	27(1)
C(28)	9403(1)	-634(4)	7459(3)	17(1)
C(29)	9416(1)	1348(4)	7502(3)	21(1)
C(30)	9100(1)	2835(3)	9275(3)	16(1)
C(31)	9174(1)	3577(3)	10596(3)	18(1)
C(32)	8978(1)	4401(4)	11490(3)	25(1)
C(33)	9109(1)	4899(4)	12687(3)	29(1)
C(34)	9431(1)	4592(4)	12970(4)	32(1)
C(35)	9628(1)	3787(4)	12057(4)	30(1)
C(36)	9495(1)	3281(4)	10862(3)	22(1)
C(37)	9637(1)	2402(4)	9695(3)	22(1)
Cl(1S)	10048(1)	3137(1)	5419(1)	29(1)
C(1S)	10000	5000	6421(4)	22(1)

Table S15. Bond lengths [Å] and angles [°] for (–)-**80**.

Br(1)-C(23)	1.895(3)	C(36)-C(37)	1.480(4)
O(1)-C(20)	1.213(3)	Cl(1S)-C(1S)	1.767(3)
O(2)-C(8)	1.202(4)	C(1S)-Cl(1S)#1	1.767(3)
O(3)-C(1)	1.204(4)		
O(4)-C(30)	1.215(3)	C(24)-O(6)-C(27)	117.6(2)
O(5)-C(37)	1.214(3)	C(17)-N(1)-C(18)	109.2(2)
O(6)-C(24)	1.355(3)	C(26)-N(2)-C(19)	111.3(2)
O(6)-C(27)	1.443(4)	C(30)-N(3)-C(37)	111.4(2)
N(1)-C(17)	1.371(4)	C(30)-N(3)-C(29)	122.8(2)
N(1)-C(18)	1.383(3)	C(37)-N(3)-C(29)	125.3(2)
N(2)-C(26)	1.363(4)	C(1)-N(4)-C(8)	113.1(2)
N(2)-C(19)	1.453(3)	C(1)-N(4)-C(9)	123.8(3)
N(3)-C(30)	1.390(3)	C(8)-N(4)-C(9)	123.1(3)
N(3)-C(37)	1.393(4)	O(3)-C(1)-N(4)	125.8(3)
N(3)-C(29)	1.453(4)	O(3)-C(1)-C(2)	129.3(3)
N(4)-C(1)	1.386(4)	N(4)-C(1)-C(2)	104.9(3)
N(4)-C(8)	1.390(4)	C(7)-C(2)-C(3)	122.0(3)
N(4)-C(9)	1.454(3)	C(7)-C(2)-C(1)	108.0(2)
C(1)-C(2)	1.503(4)	C(3)-C(2)-C(1)	130.0(3)
C(2)-C(7)	1.374(5)	C(2)-C(3)-C(4)	116.0(4)
C(2)-C(3)	1.384(4)	C(5)-C(4)-C(3)	121.8(3)
C(3)-C(4)	1.410(6)	C(4)-C(5)-C(6)	122.1(4)
C(4)-C(5)	1.360(7)	C(5)-C(6)-C(7)	116.3(4)
C(5)-C(6)	1.390(5)	C(2)-C(7)-C(6)	121.8(3)
C(6)-C(7)	1.394(4)	C(2)-C(7)-C(8)	108.8(3)
C(7)-C(8)	1.483(4)	C(6)-C(7)-C(8)	129.4(3)
C(9)-C(10)	1.531(4)	O(2)-C(8)-N(4)	125.2(3)
C(10)-C(11)	1.501(3)	O(2)-C(8)-C(7)	129.6(3)
C(11)-C(18)	1.383(4)	N(4)-C(8)-C(7)	105.2(3)
C(11)-C(12)	1.426(4)	N(4)-C(9)-C(10)	110.1(2)
C(12)-C(13)	1.407(4)	C(11)-C(10)-C(9)	113.3(2)
C(12)-C(17)	1.410(4)	C(18)-C(11)-C(12)	106.9(2)
C(13)-C(14)	1.380(4)	C(18)-C(11)-C(10)	130.4(3)
C(14)-C(15)	1.411(4)	C(12)-C(11)-C(10)	122.6(3)
C(15)-C(16)	1.373(4)	C(13)-C(12)-C(17)	118.9(3)
C(16)-C(17)	1.397(4)	C(13)-C(12)-C(11)	133.9(3)
C(18)-C(19)	1.513(4)	C(17)-C(12)-C(11)	107.1(2)
C(19)-C(28)	1.539(4)	C(14)-C(13)-C(12)	119.0(3)
C(19)-C(20)	1.553(4)	C(13)-C(14)-C(15)	120.6(3)
C(20)-C(21)	1.448(4)	C(16)-C(15)-C(14)	121.9(3)
C(21)-C(26)	1.395(4)	C(15)-C(16)-C(17)	117.2(3)
C(21)-C(22)	1.398(4)	N(1)-C(17)-C(16)	129.9(3)
C(22)-C(23)	1.368(4)	N(1)-C(17)-C(12)	107.7(2)
C(23)-C(24)	1.412(4)	C(16)-C(17)-C(12)	122.4(3)
C(24)-C(25)	1.392(4)	N(1)-C(18)-C(11)	108.9(3)
C(25)-C(26)	1.404(4)	N(1)-C(18)-C(19)	118.8(2)
C(28)-C(29)	1.530(4)	C(11)-C(18)-C(19)	132.2(2)
C(30)-C(31)	1.480(4)	N(2)-C(19)-C(18)	112.3(2)
C(31)-C(32)	1.371(4)	N(2)-C(19)-C(28)	111.6(2)
C(31)-C(36)	1.384(4)	C(18)-C(19)-C(28)	112.0(2)
C(32)-C(33)	1.377(5)	N(2)-C(19)-C(20)	102.8(2)
C(33)-C(34)	1.391(5)	C(18)-C(19)-C(20)	111.8(2)
C(34)-C(35)	1.381(5)	C(28)-C(19)-C(20)	105.8(2)
C(35)-C(36)	1.381(4)	O(1)-C(20)-C(21)	131.1(3)

O(1)-C(20)-C(19)	122.8(2)
C(21)-C(20)-C(19)	106.0(2)
C(26)-C(21)-C(22)	120.6(3)
C(26)-C(21)-C(20)	108.6(2)
C(22)-C(21)-C(20)	130.9(3)
C(23)-C(22)-C(21)	118.9(3)
C(22)-C(23)-C(24)	120.7(3)
C(22)-C(23)-Br(1)	120.3(2)
C(24)-C(23)-Br(1)	118.9(2)
O(6)-C(24)-C(25)	123.2(2)
O(6)-C(24)-C(23)	115.6(3)
C(25)-C(24)-C(23)	121.2(2)
C(24)-C(25)-C(26)	117.3(3)
N(2)-C(26)-C(21)	111.1(2)
N(2)-C(26)-C(25)	127.7(3)
C(21)-C(26)-C(25)	121.2(3)
C(29)-C(28)-C(19)	116.5(2)
N(3)-C(29)-C(28)	115.0(2)
O(4)-C(30)-N(3)	124.6(3)
O(4)-C(30)-C(31)	129.3(2)
N(3)-C(30)-C(31)	106.1(2)
C(32)-C(31)-C(36)	121.6(3)
C(32)-C(31)-C(30)	130.2(3)
C(36)-C(31)-C(30)	108.1(2)
C(31)-C(32)-C(33)	118.0(3)
C(32)-C(33)-C(34)	120.8(3)
C(35)-C(34)-C(33)	121.0(3)
C(34)-C(35)-C(36)	117.9(3)
C(35)-C(36)-C(31)	120.7(3)
C(35)-C(36)-C(37)	131.4(3)
C(31)-C(36)-C(37)	107.9(3)
O(5)-C(37)-N(3)	123.8(3)
O(5)-C(37)-C(36)	130.0(3)
N(3)-C(37)-C(36)	106.2(2)
Cl(1S)-C(1S)-Cl(1S)#1	110.3(2)

Symmetry transformations used to generate equivalent atoms: #1 -x+2,-y+1,z

Table S16. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for (–)-**80**. The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2\ a^{*2}U^{11} + \ldots + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

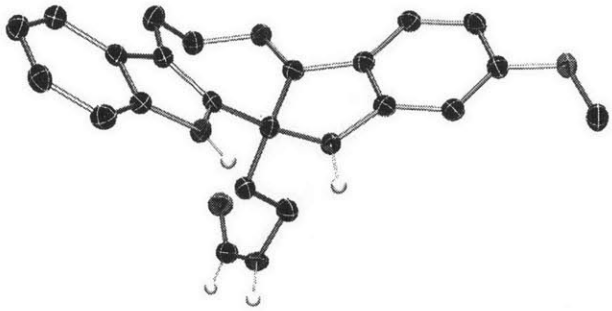
	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Br(1)	24(1)	26(1)	31(1)	-6(1)	-7(1)	-1(1)
O(1)	15(1)	21(1)	20(1)	4(1)	1(1)	2(1)
O(2)	31(1)	30(1)	22(1)	2(1)	2(1)	0(1)
O(3)	36(1)	36(1)	22(1)	0(1)	3(1)	-8(1)
O(4)	13(1)	26(1)	24(1)	4(1)	-4(1)	-1(1)
O(5)	14(1)	24(1)	51(1)	2(1)	-5(1)	1(1)
O(6)	15(1)	29(1)	29(1)	-1(1)	-6(1)	2(1)
N(1)	10(1)	21(1)	14(1)	1(1)	2(1)	0(1)
N(2)	14(1)	18(1)	20(1)	-3(1)	-3(1)	3(1)
N(3)	14(1)	14(1)	22(1)	2(1)	-2(1)	0(1)
N(4)	10(1)	24(1)	22(1)	-2(1)	2(1)	1(1)
C(1)	20(1)	17(1)	27(2)	-1(1)	6(1)	-2(1)
C(2)	14(1)	16(1)	36(2)	-6(1)	4(1)	0(1)
C(3)	20(2)	20(2)	60(2)	-6(2)	18(2)	-1(1)
C(4)	9(1)	23(2)	101(4)	-9(2)	11(2)	-2(1)
C(5)	17(2)	28(2)	82(3)	-15(2)	-10(2)	3(1)
C(6)	22(2)	22(2)	51(2)	-7(2)	-13(2)	2(1)
C(7)	12(1)	15(1)	38(2)	-6(1)	-1(1)	2(1)
C(8)	17(1)	18(1)	27(2)	-2(1)	-1(1)	3(1)
C(9)	9(1)	29(1)	26(1)	-2(1)	1(1)	2(1)
C(10)	11(1)	23(1)	21(2)	0(1)	1(1)	-1(1)
C(11)	12(1)	19(1)	20(1)	2(1)	1(1)	1(1)
C(12)	13(1)	15(1)	20(1)	2(1)	3(1)	3(1)
C(13)	18(1)	28(2)	18(1)	1(1)	4(1)	0(1)
C(14)	26(2)	28(2)	13(1)	2(1)	2(1)	3(1)
C(15)	24(2)	27(2)	16(1)	2(1)	-4(1)	-2(1)
C(16)	13(1)	20(1)	21(1)	6(1)	-1(1)	-1(1)
C(17)	15(1)	18(1)	15(1)	1(1)	1(1)	0(1)
C(18)	11(1)	19(1)	18(1)	0(1)	-1(1)	3(1)
C(19)	13(1)	20(1)	15(1)	-2(1)	0(1)	1(1)
C(20)	14(1)	17(1)	13(1)	0(1)	2(1)	1(1)
C(21)	14(1)	18(1)	14(1)	0(1)	1(1)	2(1)
C(22)	17(1)	21(1)	19(1)	3(1)	3(1)	3(1)
C(23)	18(1)	22(1)	20(1)	0(1)	-2(1)	0(1)
C(24)	15(1)	26(1)	17(1)	4(1)	-2(1)	0(1)
C(25)	15(1)	25(1)	16(1)	2(1)	0(1)	4(1)
C(26)	13(1)	20(1)	13(1)	0(1)	3(1)	-1(1)
C(27)	16(1)	31(2)	34(2)	2(2)	-2(1)	4(1)
C(28)	14(1)	24(2)	14(1)	6(1)	3(1)	2(1)
C(29)	19(1)	20(1)	23(2)	3(1)	2(1)	0(1)
C(30)	13(1)	9(1)	25(2)	3(1)	0(1)	-1(1)
C(31)	18(1)	11(1)	24(1)	4(1)	-3(1)	-1(1)
C(32)	21(1)	23(2)	30(2)	-1(1)	0(1)	0(1)
C(33)	41(2)	21(2)	25(2)	0(1)	0(1)	0(1)
C(34)	45(2)	19(2)	32(2)	-7(1)	-17(2)	3(2)
C(35)	28(2)	23(2)	38(2)	-4(1)	-14(1)	2(1)
C(36)	17(1)	18(1)	30(2)	4(1)	-5(1)	0(1)
C(37)	15(1)	20(1)	33(2)	5(1)	-5(1)	0(1)
Cl(1S)	32(1)	28(1)	28(1)	2(1)	7(1)	3(1)
C(1S)	17(2)	29(2)	21(2)	0	0	4(2)

Table S17. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for (–)-**80**.

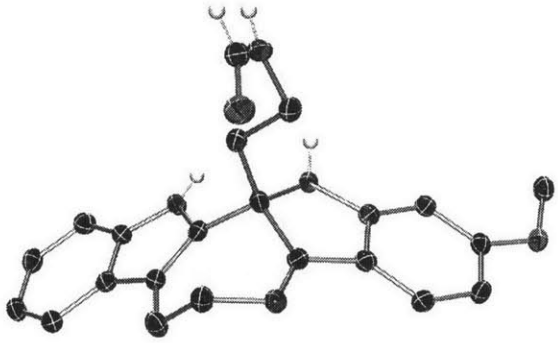
	x	y	z	U(eq)
H(1)	9580	-1642	9868	18
H(2)	8747	274	7555	21
H(3)	7155	27	12335	40
H(4)	6705	-264	10906	53
H(5)	6760	-129	8654	51
H(6)	7263	298	7652	38
H(9A)	8412	1202	11322	26
H(9B)	8441	1500	9750	26
H(10A)	8402	-1878	10947	22
H(10B)	8450	-1538	9392	22
H(13)	8667	-369	13169	26
H(14)	9033	76	14891	27
H(15)	9585	-175	14511	27
H(16)	9785	-1009	12445	22
H(22)	8821	-6098	6052	23
H(25)	8226	-873	6223	22
H(27A)	7687	-1812	6106	40
H(27B)	7520	-2203	4707	40
H(27C)	7824	-938	4781	40
H(28A)	9594	-1087	7929	21
H(28B)	9420	-1004	6520	21
H(29A)	9622	1731	7114	25
H(29B)	9242	1809	6933	25
H(32)	8760	4622	11290	30
H(33)	8978	5459	13328	35
H(34)	9516	4941	13803	38
H(35)	9849	3589	12245	36
H(1S)	10190	5144	6998	26
H(2S)	9810	4856	6998	26

Crystal Structure of (–)-Trigonoliimine C (3)

View 1:



View 2:



View 3:

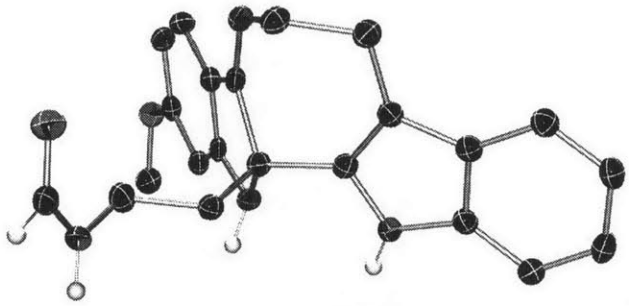


Table S18. Crystal data and structure refinement for (–)-Trigonoliimine C (**3**).

Identification code	d8_10127	
Empirical formula	C22 H22 N4 O2	
Formula weight	374.44	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2(1)	
Unit cell dimensions	a = 7.3013(2) Å	a = 90°.
	b = 7.5801(2) Å	b = 90°.
	c = 32.8941(8) Å	c = 90°.
Volume	1820.51(8) $Å^3$	
Z	4	
Density (calculated)	1.366 Mg/m^3	
Absorption coefficient	0.723 mm^{-1}	
F(000)	792	
Crystal size	0.20 x 0.20 x 0.10 mm^3	
Theta range for data collection	2.69 to 66.57°.	
Index ranges	-8<=h<=8, -9<=k<=9, -38<=l<=32	
Reflections collected	39871	
Independent reflections	3212 [R(int) = 0.0276]	
Completeness to theta = 66.57°	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9312 and 0.8688	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3212 / 3 / 263	
Goodness-of-fit on F^2	1.056	
Final R indices [I>2sigma(I)]	R1 = 0.0306, wR2 = 0.0798	
R indices (all data)	R1 = 0.0309, wR2 = 0.0802	
Absolute structure parameter	-0.1(2)	
Largest diff. peak and hole	0.220 and -0.160 $e.Å^{-3}$	

Table S19. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for (–)-trigonoliimine C (**3**). U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	-2704(2)	-52(2)	807(1)	33(1)
O(2)	7869(2)	5273(2)	53(1)	24(1)
N(12)	527(2)	5010(2)	1153(1)	21(1)
N(24)	95(2)	-1317(2)	890(1)	23(1)
N(1)	4158(2)	2386(2)	2060(1)	21(1)
N(13)	4710(2)	2433(2)	1197(1)	19(1)
C(21)	4949(2)	3584(2)	870(1)	19(1)
C(18)	4935(2)	6092(2)	256(1)	22(1)
C(16)	3426(2)	4649(2)	813(1)	20(1)
C(4)	1632(2)	4764(2)	2807(1)	23(1)
C(15)	2034(2)	4175(2)	1110(1)	19(1)
C(5)	2563(2)	4394(2)	3163(1)	23(1)
C(6)	4080(2)	3251(2)	3168(1)	24(1)
C(19)	6457(2)	4993(2)	318(1)	20(1)
C(9)	2249(2)	3997(2)	2444(1)	20(1)
C(22)	1756(2)	840(2)	1315(1)	21(1)
C(7)	4743(2)	2507(2)	2813(1)	24(1)
C(3)	1637(2)	4083(2)	2030(1)	20(1)
C(25)	-1709(2)	-1336(2)	853(1)	25(1)
C(26)	9348(2)	4038(2)	56(1)	26(1)
C(23)	1213(2)	293(2)	886(1)	26(1)
C(11)	-762(2)	4527(2)	1478(1)	23(1)
C(8)	3827(2)	2911(2)	2452(1)	20(1)
C(10)	-48(2)	5067(2)	1894(1)	25(1)
C(2)	2848(2)	3099(2)	1806(1)	19(1)
C(14)	2822(2)	2596(2)	1357(1)	19(1)
C(17)	3427(2)	5922(2)	503(1)	22(1)
C(20)	6502(2)	3733(2)	624(1)	20(1)

Table S20. Bond lengths [Å] and angles [°] for (–)-trigonoliimine C (**3**).

O(1)-C(25)	1.224(2)	C(16)-C(15)	1.454(2)
O(2)-C(19)	1.3661(18)	C(4)-C(5)	1.382(2)
O(2)-C(26)	1.430(2)	C(4)-C(9)	1.405(2)
N(12)-C(15)	1.277(2)	C(15)-C(14)	1.558(2)
N(12)-C(11)	1.471(2)	C(5)-C(6)	1.406(2)
N(24)-C(25)	1.323(2)	C(6)-C(7)	1.383(2)
N(24)-C(23)	1.468(2)	C(19)-C(20)	1.390(2)
N(1)-C(8)	1.373(2)	C(9)-C(8)	1.416(2)
N(1)-C(2)	1.379(2)	C(9)-C(3)	1.433(2)
N(13)-C(21)	1.3961(19)	C(22)-C(23)	1.523(2)
N(13)-C(14)	1.4817(19)	C(22)-C(14)	1.549(2)
C(21)-C(16)	1.387(2)	C(7)-C(8)	1.397(2)
C(21)-C(20)	1.396(2)	C(3)-C(2)	1.372(2)
C(18)-C(17)	1.374(2)	C(3)-C(10)	1.507(2)
C(18)-C(19)	1.403(2)	C(11)-C(10)	1.520(2)
C(16)-C(17)	1.404(2)	C(2)-C(14)	1.525(2)
C(19)-O(2)-C(26)	117.64(12)	C(23)-C(22)-C(14)	116.69(13)
C(15)-N(12)-C(11)	120.59(13)	C(6)-C(7)-C(8)	117.38(15)
C(25)-N(24)-C(23)	124.21(15)	C(2)-C(3)-C(9)	106.49(13)
C(8)-N(1)-C(2)	109.50(13)	C(2)-C(3)-C(10)	129.47(14)
C(21)-N(13)-C(14)	109.80(12)	C(9)-C(3)-C(10)	124.03(13)
C(16)-C(21)-C(20)	121.74(14)	O(1)-C(25)-N(24)	126.39(17)
C(16)-C(21)-N(13)	111.55(14)	N(24)-C(23)-C(22)	111.30(13)
C(20)-C(21)-N(13)	126.70(14)	N(12)-C(11)-C(10)	111.57(13)
C(17)-C(18)-C(19)	119.63(14)	N(1)-C(8)-C(7)	130.72(15)
C(21)-C(16)-C(17)	119.84(14)	N(1)-C(8)-C(9)	106.98(13)
C(21)-C(16)-C(15)	109.04(13)	C(7)-C(8)-C(9)	122.29(14)
C(17)-C(16)-C(15)	131.12(15)	C(3)-C(10)-C(11)	114.48(13)
C(5)-C(4)-C(9)	118.63(15)	C(3)-C(2)-N(1)	109.58(13)
N(12)-C(15)-C(16)	123.68(14)	C(3)-C(2)-C(14)	130.38(14)
N(12)-C(15)-C(14)	129.83(14)	N(1)-C(2)-C(14)	119.77(14)
C(16)-C(15)-C(14)	106.42(13)	N(13)-C(14)-C(2)	110.76(12)
C(4)-C(5)-C(6)	121.50(14)	N(13)-C(14)-C(22)	111.29(12)
C(7)-C(6)-C(5)	121.14(14)	C(2)-C(14)-C(22)	107.98(12)
O(2)-C(19)-C(20)	123.48(14)	N(13)-C(14)-C(15)	102.81(12)
O(2)-C(19)-C(18)	114.45(13)	C(2)-C(14)-C(15)	108.62(12)
C(20)-C(19)-C(18)	122.07(14)	C(22)-C(14)-C(15)	115.31(12)
C(4)-C(9)-C(8)	118.96(14)	C(18)-C(17)-C(16)	119.58(14)
C(4)-C(9)-C(3)	133.59(15)	C(19)-C(20)-C(21)	117.14(15)
C(8)-C(9)-C(3)	107.43(13)		

Symmetry transformations used to generate equivalent atoms:

Table S21. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for (–)-trigonoliimine C (**3**). The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + \ldots + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	39(1)	29(1)	30(1)	2(1)	-2(1)	6(1)
O(2)	25(1)	26(1)	20(1)	3(1)	5(1)	0(1)
N(12)	22(1)	22(1)	18(1)	1(1)	0(1)	2(1)
N(24)	33(1)	18(1)	20(1)	0(1)	-2(1)	4(1)
N(1)	23(1)	22(1)	17(1)	-1(1)	1(1)	4(1)
N(13)	22(1)	20(1)	16(1)	2(1)	2(1)	3(1)
C(21)	24(1)	19(1)	14(1)	-3(1)	-4(1)	-3(1)
C(18)	29(1)	21(1)	18(1)	4(1)	-1(1)	-1(1)
C(16)	22(1)	20(1)	18(1)	-2(1)	-2(1)	0(1)
C(4)	24(1)	23(1)	22(1)	0(1)	2(1)	0(1)
C(15)	24(1)	19(1)	15(1)	-1(1)	-3(1)	-1(1)
C(5)	26(1)	25(1)	19(1)	-3(1)	3(1)	-3(1)
C(6)	27(1)	28(1)	17(1)	1(1)	-2(1)	-5(1)
C(19)	24(1)	21(1)	16(1)	-3(1)	0(1)	-5(1)
C(9)	21(1)	18(1)	21(1)	0(1)	1(1)	-3(1)
C(22)	23(1)	21(1)	19(1)	2(1)	2(1)	1(1)
C(7)	25(1)	23(1)	23(1)	0(1)	-2(1)	1(1)
C(3)	22(1)	19(1)	18(1)	1(1)	2(1)	-1(1)
C(25)	34(1)	22(1)	17(1)	0(1)	-3(1)	1(1)
C(26)	25(1)	30(1)	22(1)	2(1)	5(1)	0(1)
C(23)	34(1)	24(1)	19(1)	1(1)	2(1)	-3(1)
C(11)	20(1)	27(1)	22(1)	3(1)	1(1)	3(1)
C(8)	23(1)	18(1)	19(1)	0(1)	2(1)	0(1)
C(10)	23(1)	31(1)	21(1)	0(1)	2(1)	7(1)
C(2)	20(1)	18(1)	18(1)	2(1)	0(1)	-3(1)
C(14)	21(1)	21(1)	16(1)	0(1)	2(1)	1(1)
C(17)	25(1)	20(1)	21(1)	2(1)	-1(1)	3(1)
C(20)	22(1)	20(1)	17(1)	-3(1)	-2(1)	-1(1)

Table S22. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for (–)-trigonoliimine C (**3**).

	x	y	z	U(eq)
H(24N)	550(30)	-2340(20)	952(6)	28
H(1N)	5110(20)	1760(20)	1977(5)	25
H(13N)	5170(20)	1380(20)	1173(6)	23
H(18)	4947	6947	45	27
H(4)	595	5521	2809	27
H(5)	2171	4925	3410	28
H(6)	4659	2985	3419	29
H(22A)	2515	-114	1433	25
H(22B)	628	926	1480	25
H(7)	5781	1751	2815	28
H(25)	-2290	-2457	863	29
H(26A)	9973	4086	319	39
H(26B)	10217	4334	-161	39
H(26C)	8869	2846	11	39
H(23A)	512	1259	756	31
H(23B)	2330	86	722	31
H(11A)	-964	3235	1474	27
H(11B)	-1954	5110	1428	27
H(10A)	234	6344	1889	30
H(10B)	-1030	4880	2097	30
H(17)	2391	6662	464	26
H(20)	7544	3003	665	24

Appendix A.

Spectra for Chapter I

solvent	$CDCl_3$

ACQUISITION	
sfrq	500.435
tn	H1
at	4.999
np	120102
sw	12012.0
fb	not used
bs	2
tpwr	56
pw	8.0
d1	0.100
tof	3003.2
nt	32
ct	10
alock	n
gain	not used

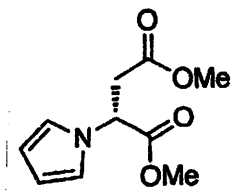
FLAGS	
il	n
in	n
dp	y
hs	nn

DISPLAY	
sp	-250.2
wp	6255.3
vs	8
sc	0
wc	250
hzmm	25.02
is	33.57
rfl	4138.4
rfp	3623.1
th	7
ins	100.000

ai cdc ph

DEC. & VT	
dfrq	125.845
dn	C13
dpwr	30
dof	0
dm	nnn
dmm	c
dmf	200
dseq	
dres	1.0
homo	n

PROCESSING	
wtfile	
proc	ft
fn	262144
math	f
werr	
wexp	
wbs	
wnt	wft



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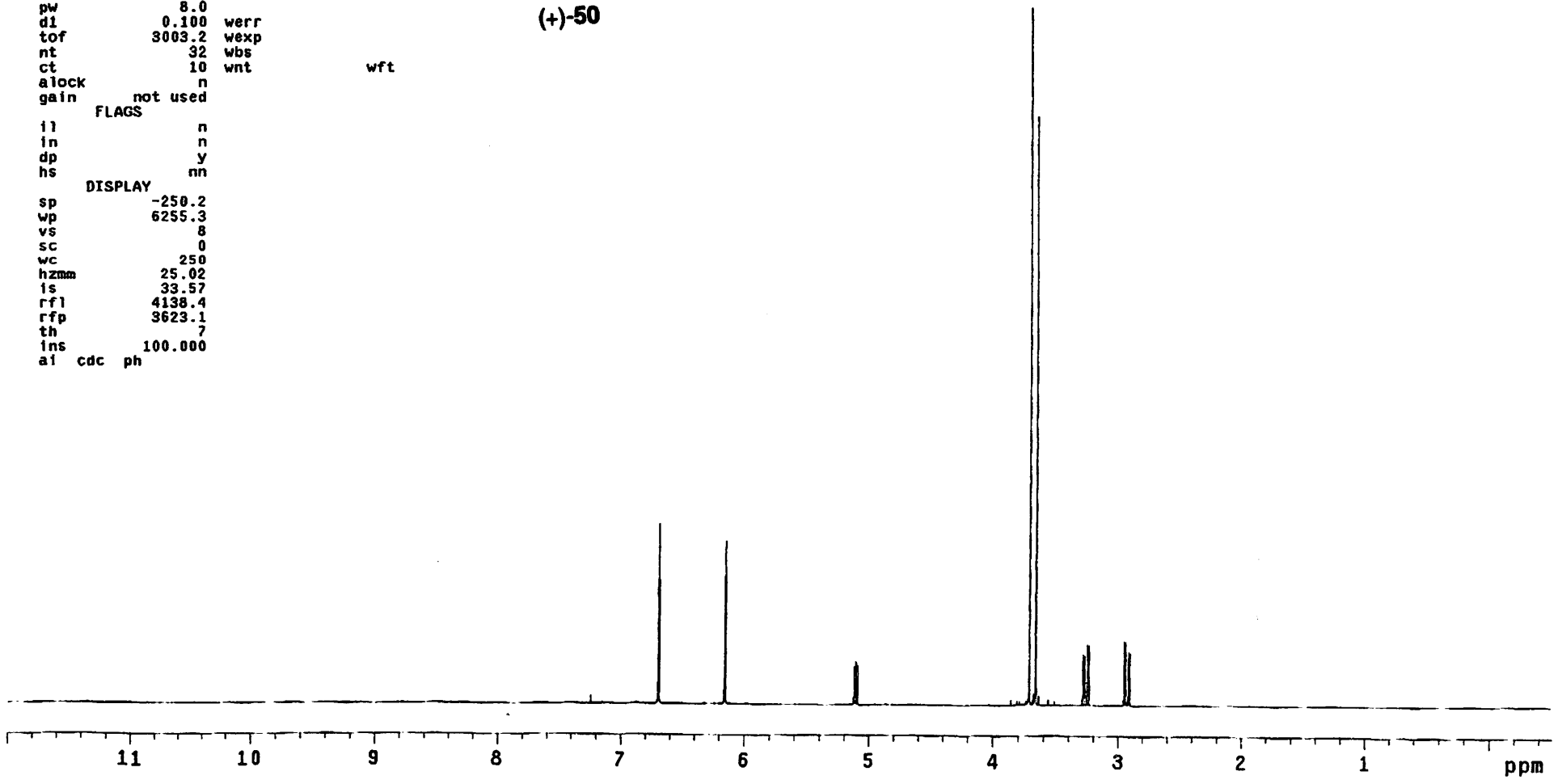


solvent	$CDCl_3$

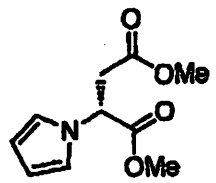
ACQUISITION	
sfrq	125.795
tn	C13
at	1.736
np	131010
sw	37735.8
fb	not used
bs	2
ss	1
tpwr	53
pw	6.9
d1	0.763
tof	531.4
nt	1000
ct	32
alock	n
gain	not used

FLAGS	
il	n
in	n
dp	y
hs	nn

DISPLAY	
sp	-6386.1
wp	37735.8
vs	21
sc	0
wc	250
hzmm	5.75
is	500.00
rfl	16024.3
rfp	9718.2
th	7
ins	1.000
ai	ph

DEC. & VT	
dfrq	500.229
dn	H1
dpwr	38
dof	-598.0
dm	y
dmm	w
dmf	10000
dseq	
dres	1.0
homo	n

PROCESSING	
lb	0.30
wtfile	
proc	ft
fn	131072
math	f
werr	
wexp	
wbs	
wnt	



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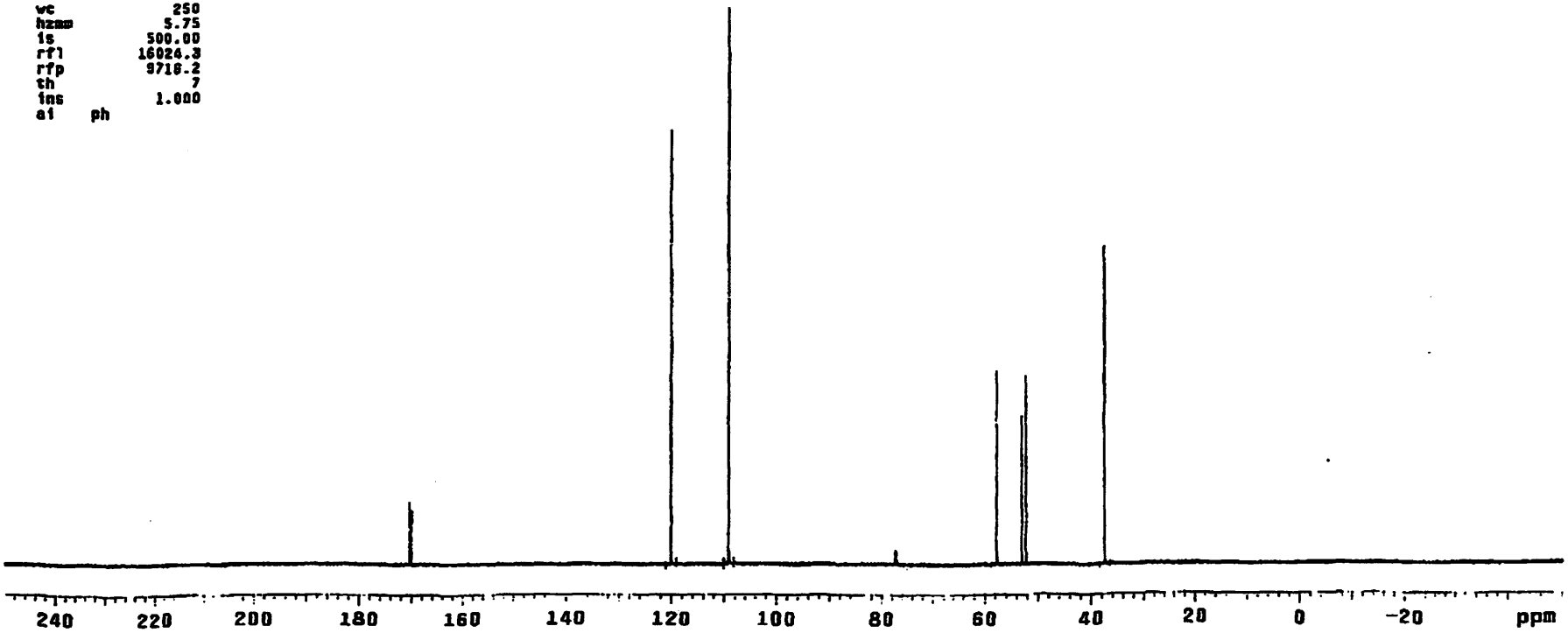
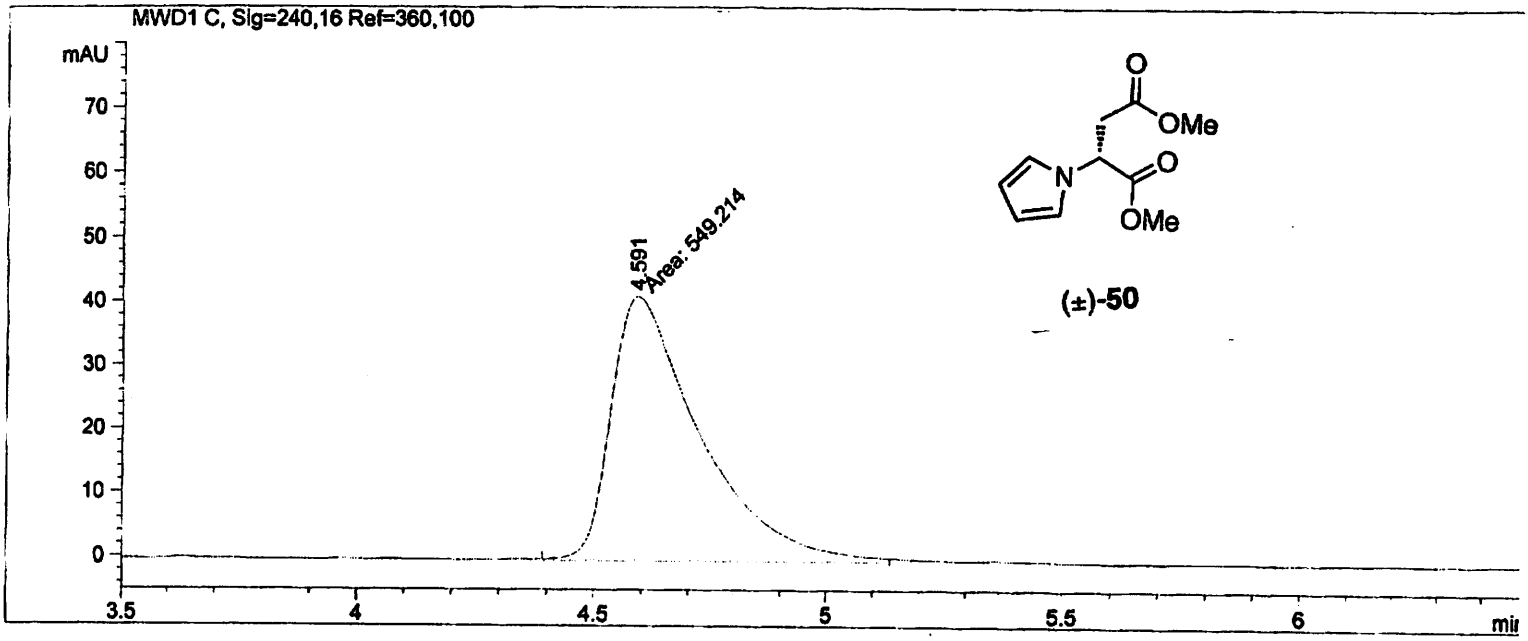


Injection Date	:	Seq. Line	: 1
Sample Name	:	Location	: Vial 91
Acq. Operator	:	Inj	: 1
		Inj Volume	: 1 µl
Acq. Method	:		
Last changed	:		
Analysis Method	:		
Last changed	:		



Area Percent Report

Sorted By	:	Signal
Multiplier	:	1.0000
Dilution	:	1.0000

Use Multiplier & Dilution Factor with ISTDs

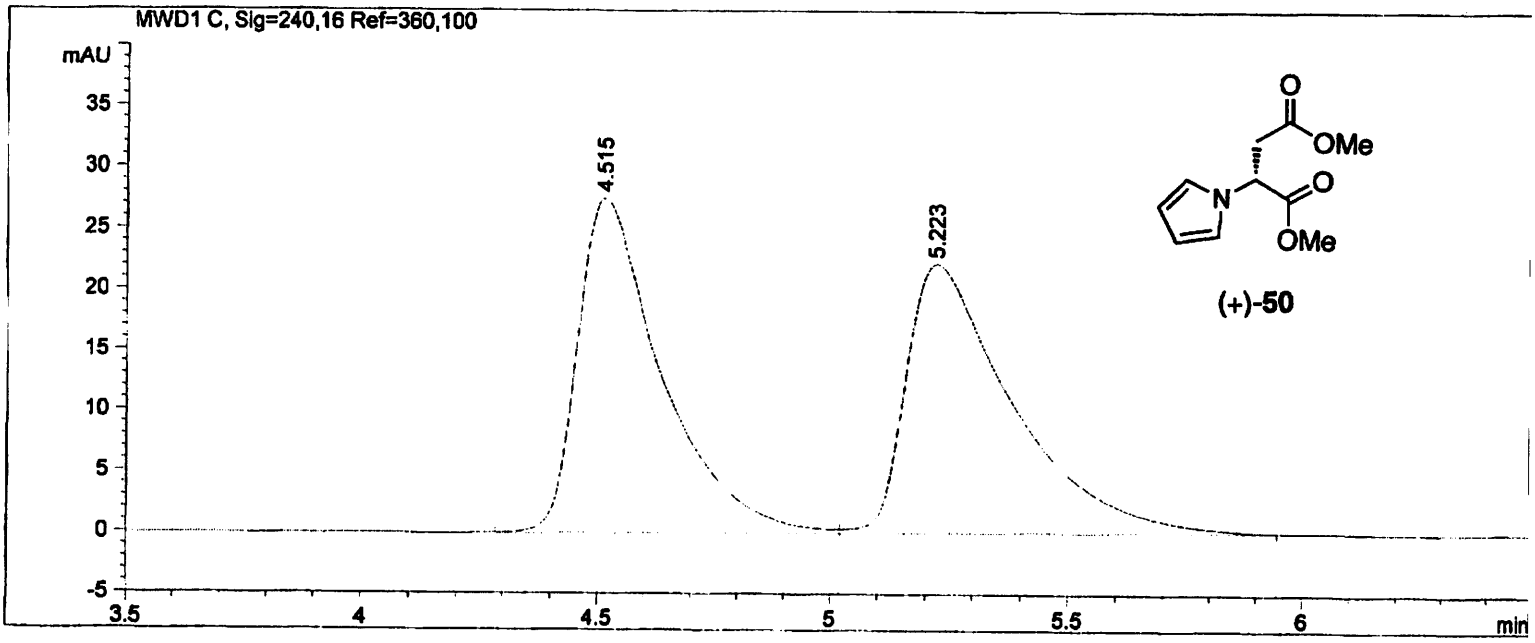
Signal 1: MWD1 C, Sig=240,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.591	MM	0.2209	549.21417	41.44402	100.0000
Totals :				549.21417	41.44402	

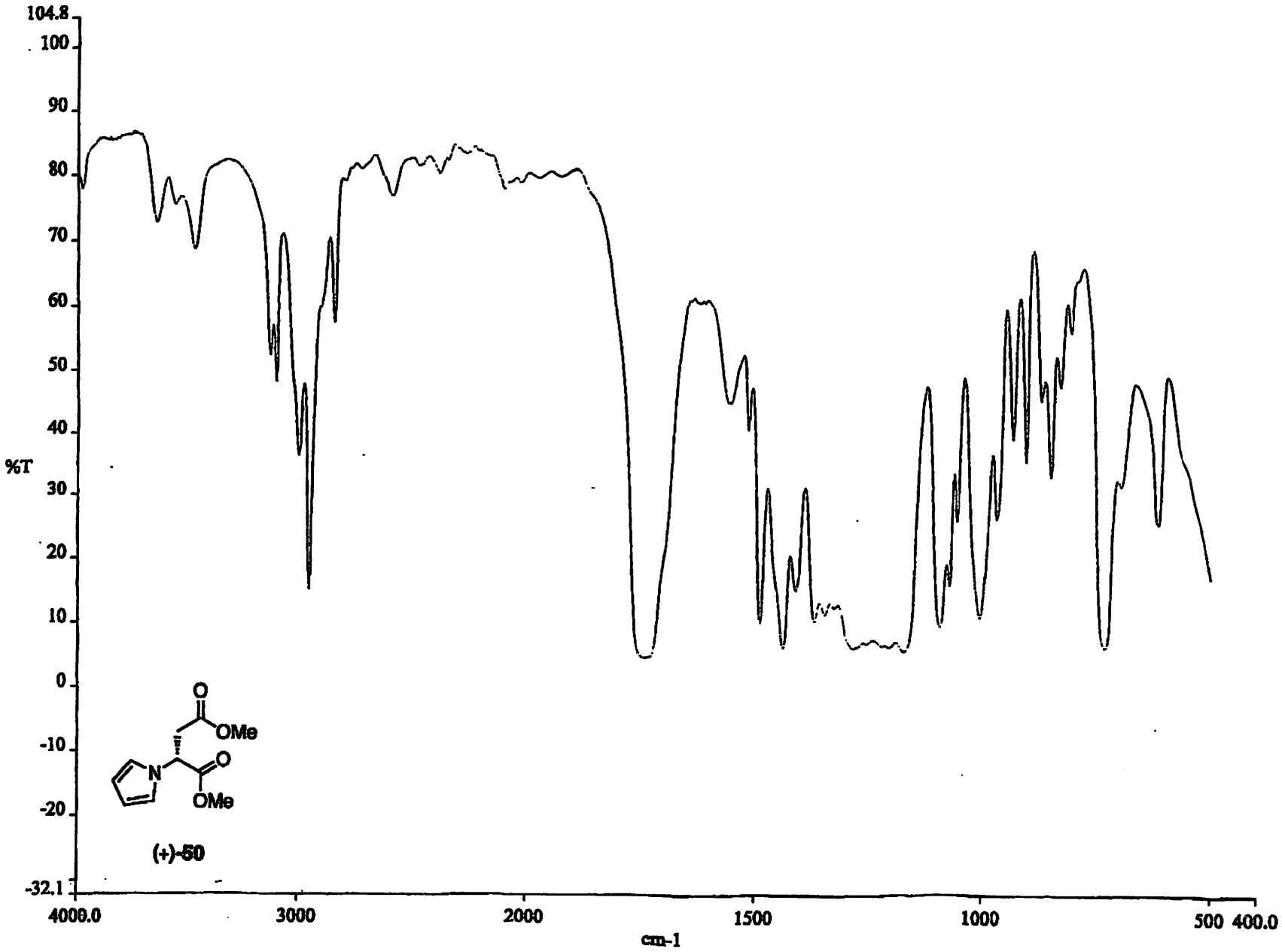
Results obtained with enhanced integrator!

*** End of Report ***

```
==========================================================================
Injection Date  :                                   Seq. Line :   1
Sample Name     :                                    Location : Vial 73
Acq. Operator   :                                        Inj :   1
                                                  Inj Volume : 1 µl
Acq. Method     :
Last changed    :
Analysis Method :
Last changed    :

==========================================================================
```




```
==========================================================================
                          Area Percent Report
==========================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: MWD1 C, Sig=240,16 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   4.515 BV    0.1810  342.47797   27.56392  50.0382
   2   5.223 VB    0.2221  341.95474   22.15433  49.9618

Totals :                   684.43271   49.71825

 Results obtained with enhanced integrator!
==========================================================================
                        *** End of Report ***
```


104.8
100
90
80
70
60
50
40
%T
30
20
10
0
-10
-20
-32.1
4000.0
3000
2000
1500
1000
500 400.0
cm-1
O
OMe
O
N
OMe
(+)-50

solvent	$CDCl_3$

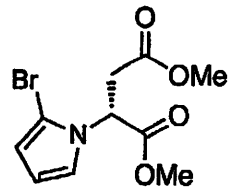
ACQUISITION	
sfrq	500.435
tn	H1
at	4.999
np	120102
sw	12012.0
fb	not used
bs	2
tpwr	56
pw	8.0
d1	0.100
tof	3003.2
nt	32
ct	22
alock	n
gain	not used

FLAGS	
il	n
in	n
dp	y
hs	nn

DISPLAY	
sp	-250.2
wp	6255.3
vs	7
sc	0
wc	250
hzmm	25.02
is	33.57
rfl	4137.5
rfp	3623.1
th	7
ins	1.000
ai cdc ph	

DEC. & VT	
dfrq	125.845
dn	C13
dpwr	30
dof	0
dm	nnn
dmm	c
dmf	200
dseq	
dres	1.0
homo	n

PROCESSING	
wtfile	
proc	ft
fn	262144
math	f
werr	
wexp	
wbs	
wnt	wft



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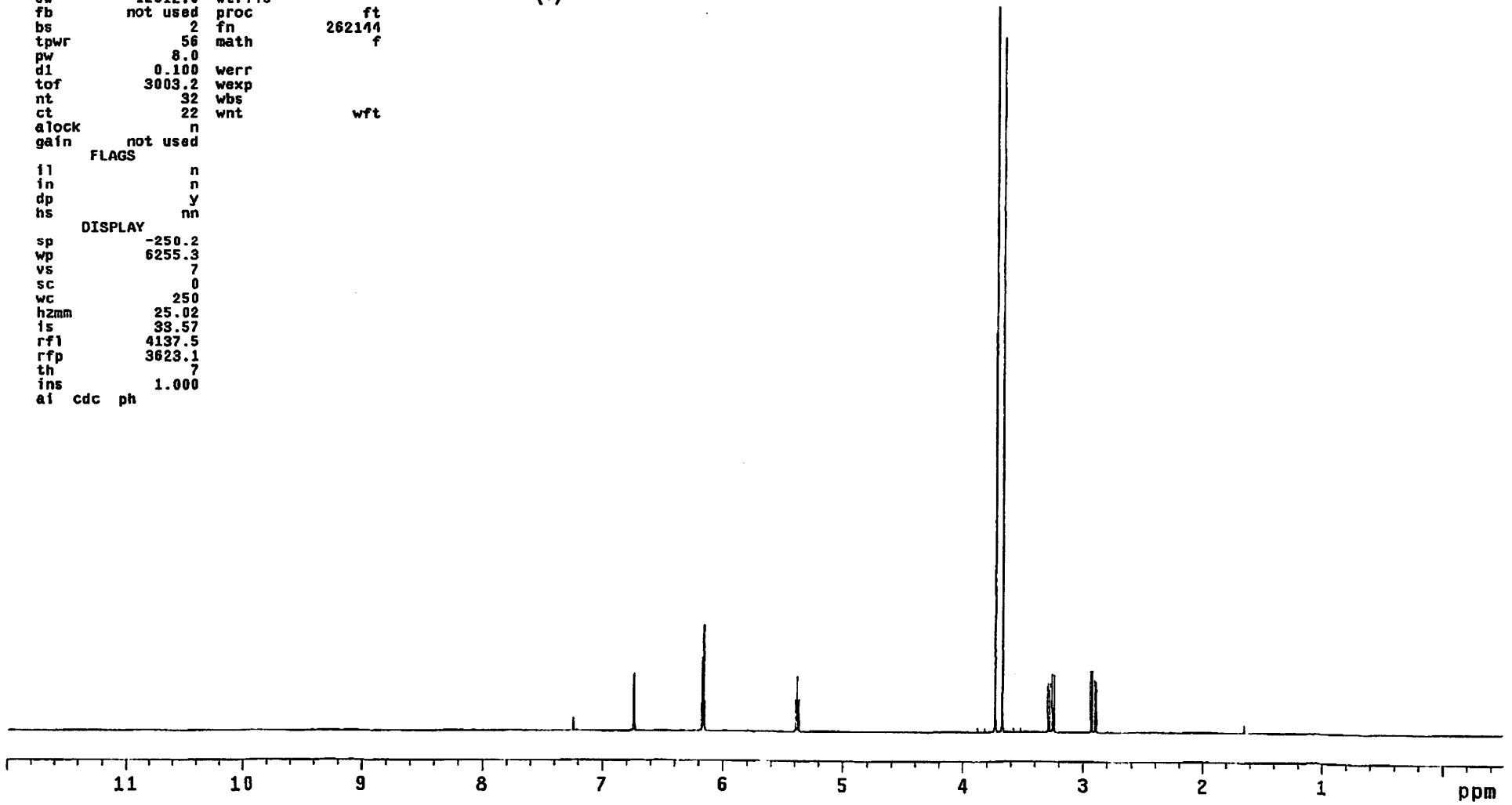


solvent	$CDCl_3$

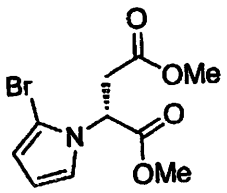
ACQUISITION	
sfrq	125.795
tn	C13
at	1.736
np	131010
sw	37735.8
fb	not used
bs	4
ss	1
tpwr	53
pw	6.9
d1	0.763
tof	631.4
nt	1e+06
ct	100
alock	n
gain	not used

FLAGS	
il	n
in	n
dp	y
hs	nn

DISPLAY	
sp	-6320.4
wp	37735.3
vs	193
sc	0
wc	250
hzmm	150.94
is	500.00
rfl	16006.2
rfp	9685.2
th	9
ins	1.000
ai	ph

DEC. & VT	
dfrq	500.229
dn	H1
dpwr	38
dof	-500.0
dm	y
dmm	w
dmf	10000
dseq	
dres	1.0
homo	n

PROCESSING	
lb	0.30
wtfile	
proc	ft
fn	131072
math	f
werr	
wexp	
wbs	
wnt	



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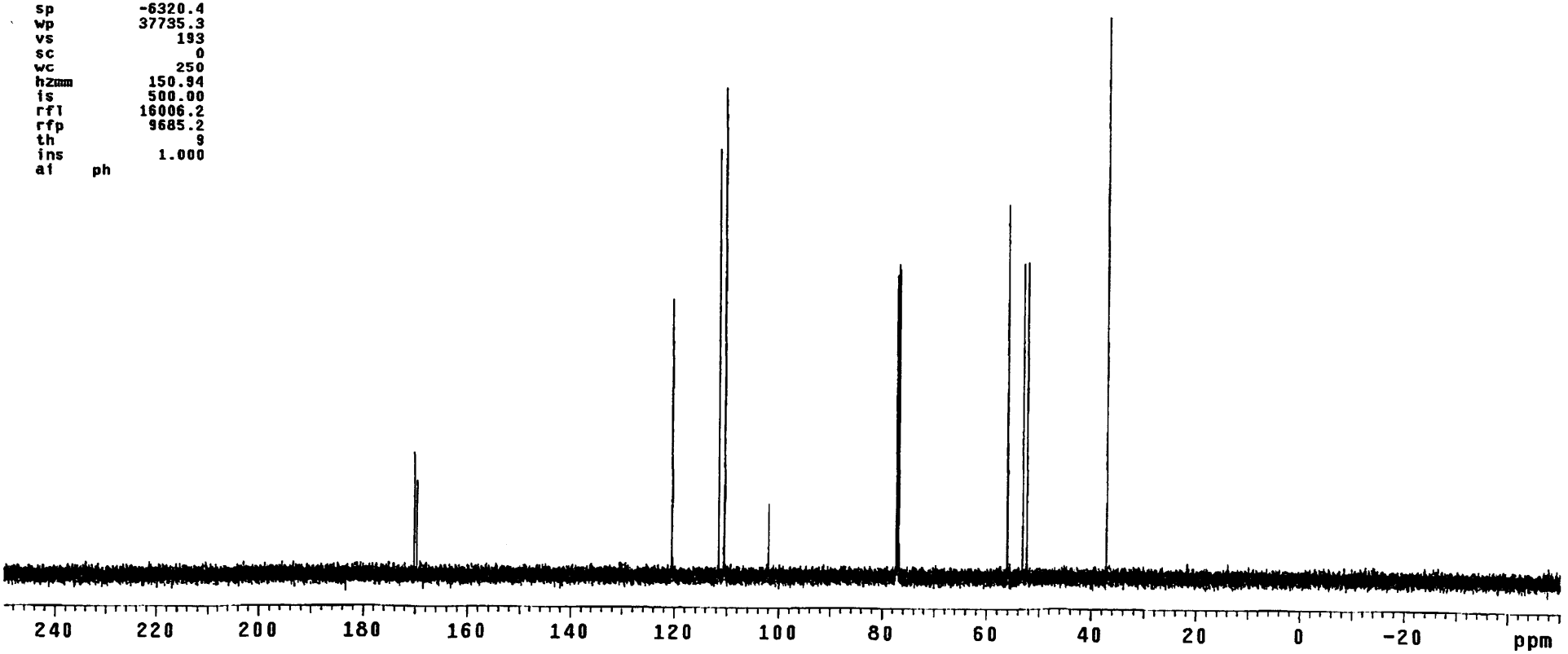
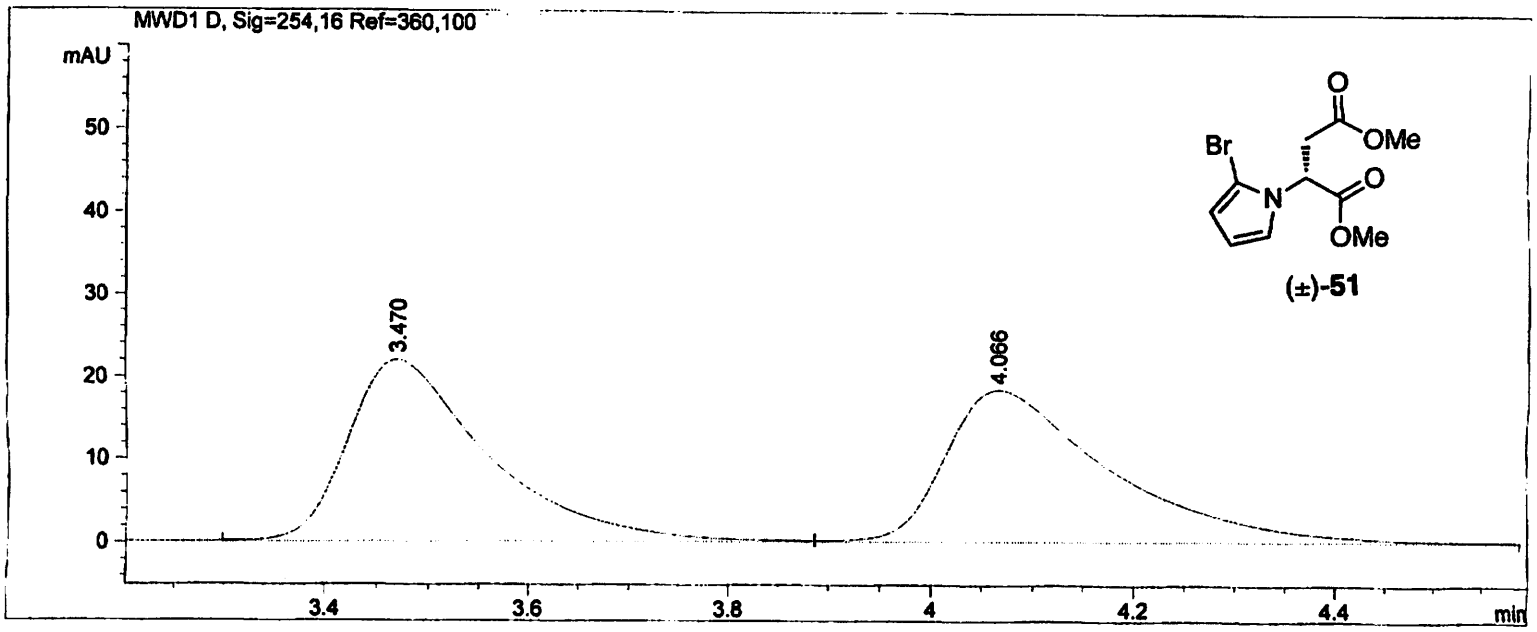
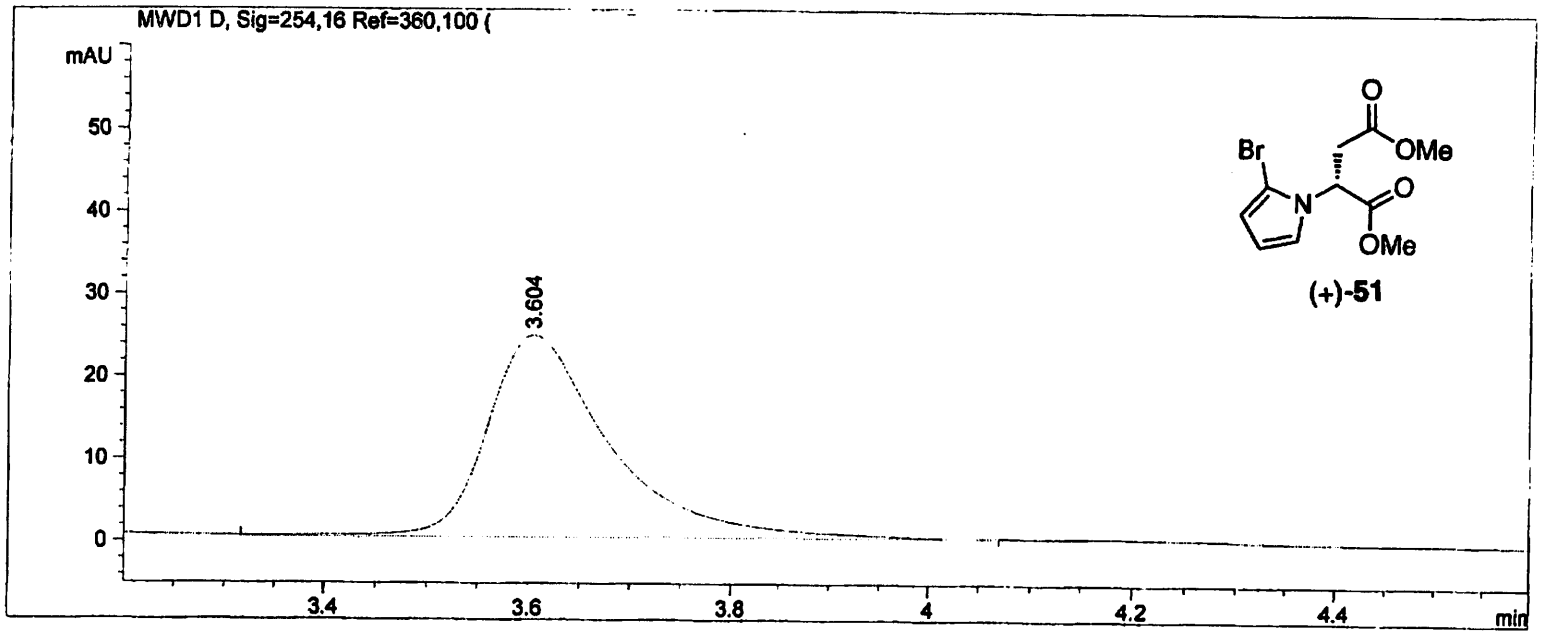


```
Injection Date  :                                   Seq. Line :   1
Sample Name     :                                    Location : Vial 74
Acq. Operator   :                                         Inj :   1
                                                  Inj Volume : 1 µl
Acq. Method     :
Last changed    :

Analysis Method :
Last changed    :
```

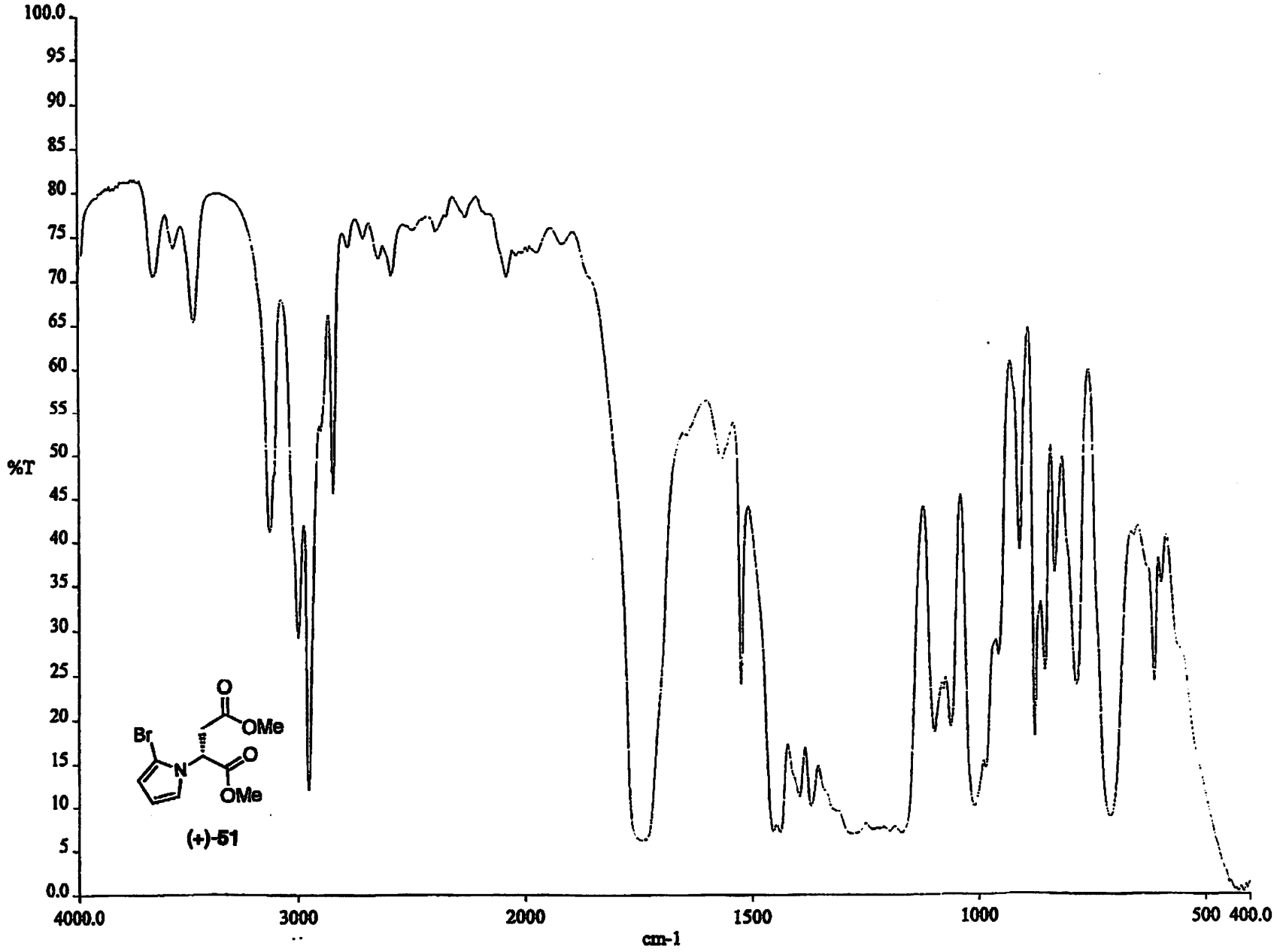



```
                        Area Percent Report

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: MWD1 D, Sig=254,16 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   3.470 BV    0.1392  209.35068   21.96089  49.9378
   2   4.066 VB    0.1622  209.87196   18.52020  50.0622

Totals :                    419.22264   40.48109

 Results obtained with enhanced integrator!

                        *** End of Report ***
```

```
Injection Date  :                                   Seq. Line :   1
Sample Name     :                                    Location : Vial 91
Acq. Operator   :                                        Inj :   1
                                                  Inj Volume : 1 µl
Acq. Method     :
Last changed    :
Analysis Method :
Last changed    :
```




```
                        Area Percent Report

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: MWD1 D, Sig=254,16 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   3.604 VP    0.1247  207.81982   24.56680 100.0000

Totals :                   207.81982   24.56680

 Results obtained with enhanced integrator!

                        *** End of Report ***
```


100.0
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0.0
%T
4000.0
3000
2000
1500
1000
500
400.0
cm-1
Br
N
O
OMe
O
OMe
(+)-51

solvent	$CDCl_3$

ACQUISITION	
sfrq	500.435
tn	H1
at	4.999
np	120102
sw	12012.0
fb	not used
bs	2
tpwr	56
pw	8.0
d1	0.100
tof	3003.2
nt	32
ct	18
alock	n
gain	not used

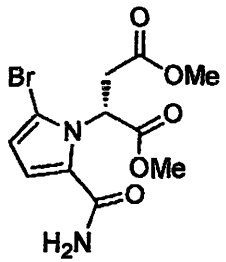
FLAGS	
il	n
in	n
dp	y
hs	nn

DISPLAY	
sp	-250.2
wp	6255.3
vs	19
sc	0
wc	250
hzmm	25.02
is	33.57
rfl	4139.7
rfp	3623.1
th	7
ins	100.000

af cdc ph

DEC. & VT	
dfrq	125.845
dn	C13
dpwr	30
dof	0
dm	nnn
dmm	c
dmf	200
dseq	
dres	1.0
homo	n

PROCESSING	
wtfile	
proc	ft
fn	262144
math	f
werr	
wexp	
wbs	
wnt	wft



(+)-52

solvent $CDCl_3$

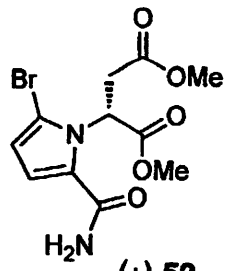
ACQUISITION	
sfrq	125.795
tn	C13
at	1.736
np	131010
sw	37735.8
fb	not used
bs	2
ss	1
tpwr	53
pw	6.9
d1	0.763
tof	631.4
nt	60000
ct	13308
alock	n
gain	not used

FLAGS	
il	n
in	n
dp	y
hs	nn

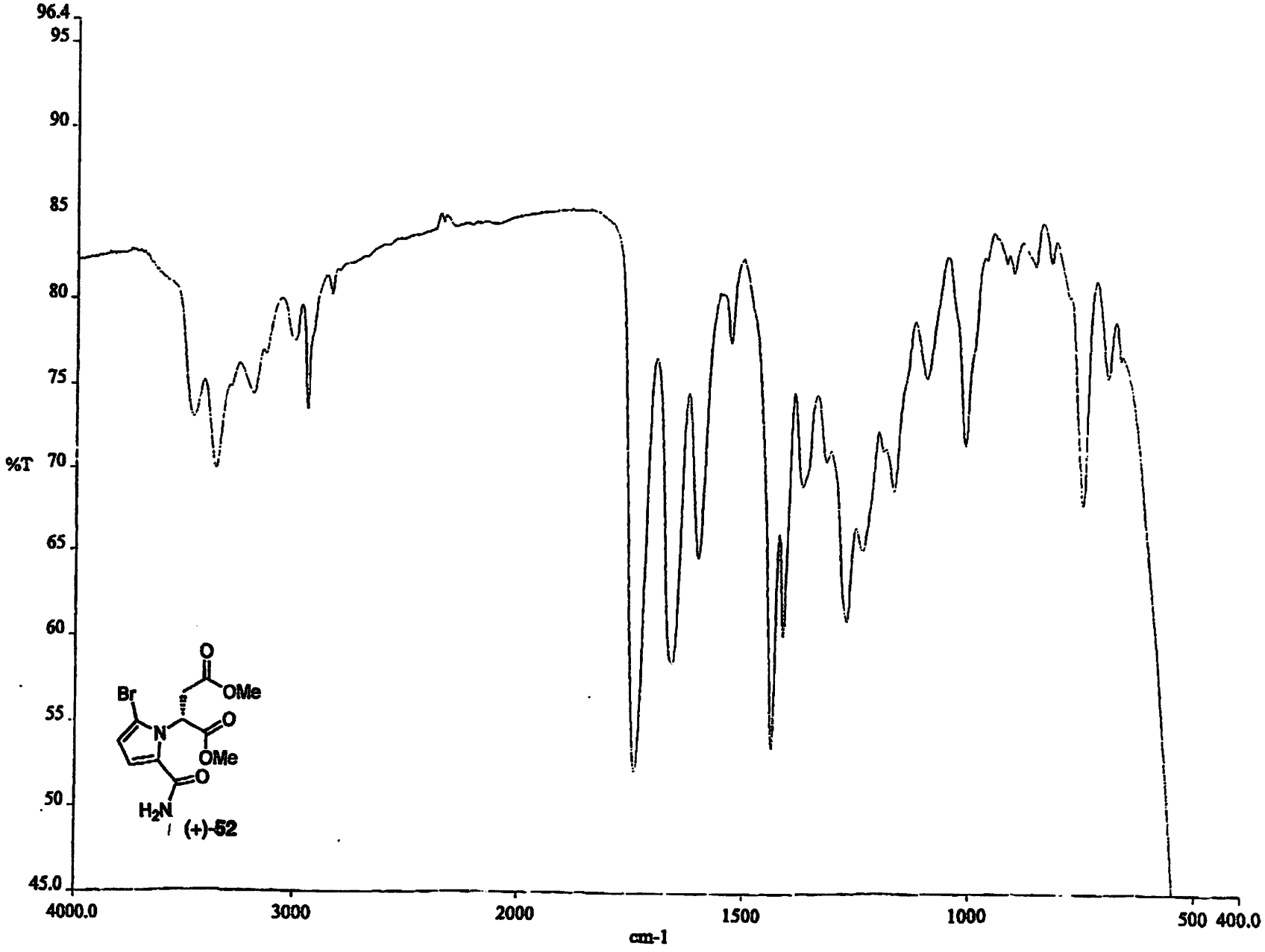
DISPLAY	
sp	-6292.0
wp	37735.3
vs	770
sc	0
wc	250
hzmm	150.94
is	500.00
rfl	16006.8
rfp	9714.2
th	20
ins	1.000
ai	ph

DEC. & VT	
dfrq	500.229
dn	H1
dpwr	38
dof	-500.0
dm	y
dmm	w
dmf	10000
dseq	
dres	1.0
homo	n

PROCESSING	
lb	0.30
wtfile	
proc	ft
fn	131072
math	f
werr	
wexp	
wbs	
wnt	



(+)-52


96.4
95
90
85
80
75
%T 70
65
60
55
50
45.0
4000.0
3000
2000
1500
1000
500 400.0
cm-1
Br
N
O
OMe
O
OMe
O
H2N
(+)-52

solvent	$CDCl_3$

ACQUISITION	
sfrq	500.435
tn	H1
at	4.999
np	120102
sw	12012.0
fb	not used
bs	2
tpwr	56
pw	8.0
d1	0.100
tof	3003.2
nt	32
ct	10
alock	n
gain	not used

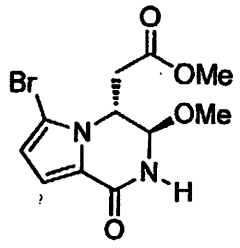
FLAGS	
il	n
in	n
dp	y
hs	nn

DISPLAY	
sp	-250.2
wp	6255.3
vs	11
sc	0
wc	250
hzmm	25.02
is	33.57
rfl	4138.9
rfp	3623.1
th	7
ins	100.000

ai cdc ph

DEC. & VT	
dfrq	125.845
dn	C13
dpwr	30
dof	0
dm	nnn
dmm	c
dmf	200
dseq	
dres	1.0
homo	n

PROCESSING	
wtfile	
proc	ft
fn	262144
math	f
werr	
wexp	
wbs	
wnt	wft



(+)-49

solvent	$CDCl_3$

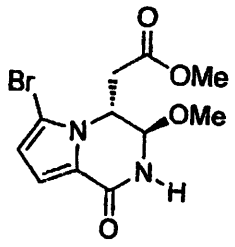
ACQUISITION	
sfrq	125.795
tn	C13
at	1.736
np	131010
sw	37735.8
fb	not used
bs	4
ss	1
tpwr	53
pw	6.9
d1	0.763
tof	631.4
nt	1e+07
ct	176
alock	n
gain	not used

FLAGS	
il	n
in	n
dp	y
hs	nn

DISPLAY	
sp	-6288.0
wp	37735.3
vs	665
sc	0
wc	250
hzmm	150.94
is	500.00
rfl	16002.7
rfp	9714.2
th	20
ins	1.000
ai	ph

DEC. & VT	
dfrq	500.229
dn	H1
dpwr	37
dof	-500.0
dm	y
dmm	w
dmf	10000
dseq	
dres	1.0
homo	n

PROCESSING	
lb	0.30
wtfile	
proc	ft
fn	131072
math	f
werr	
wexp	
wbs	
wnt	

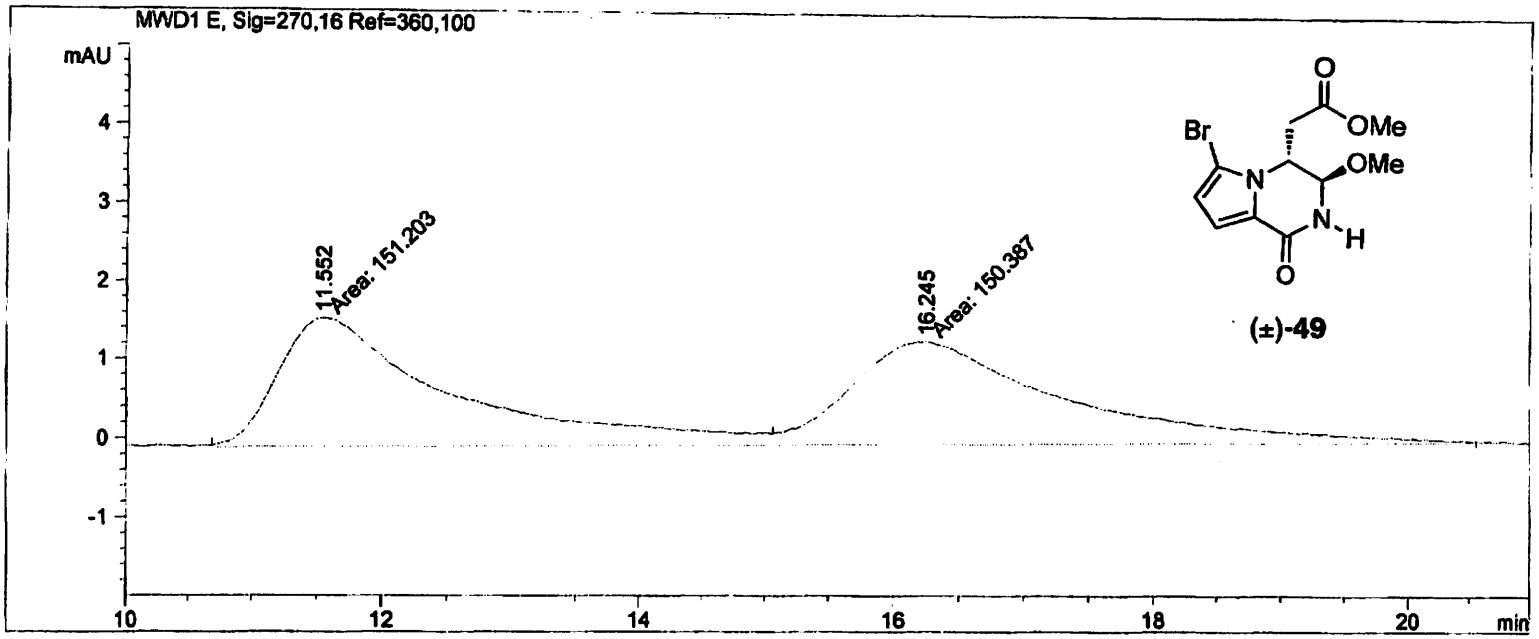


(+)-49

Inj : 1
Inj Volume : 1 µl

Acq. Method :
Last changed :
Analysis Method :
Last changed :

==========



==========

Area Percent Report

==========

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: MWD1 E, Sig=270,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.552	MF	1.5397	151.20343	1.63667	50.1354
2	16.245	FM	1.9061	150.38686	1.31497	49.8646
Totals :				301.59029	2.95164	

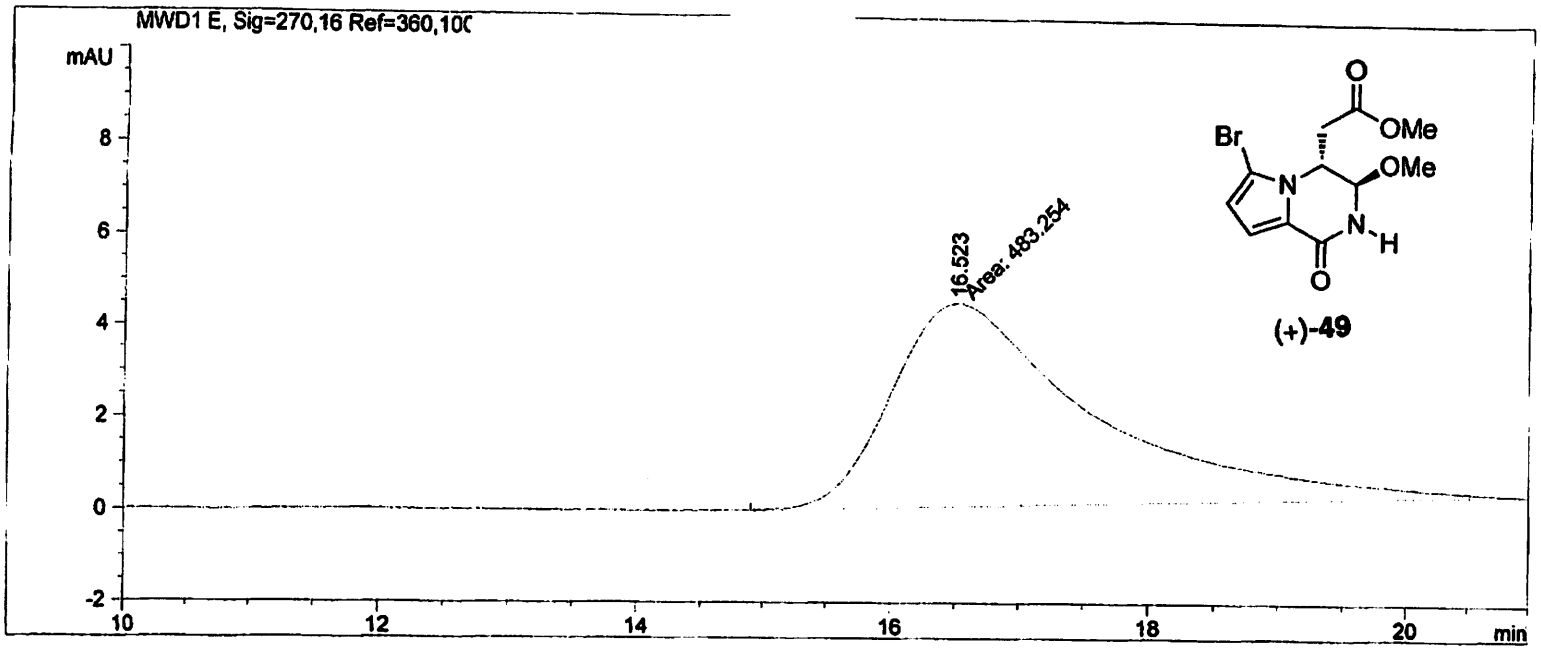
Results obtained with enhanced integrator!

==========

*** End of Report ***

Inj Volume : 1 µl

Acq. Method :
Last changed :
Analysis Method :
Last changed :



Area Percent Report

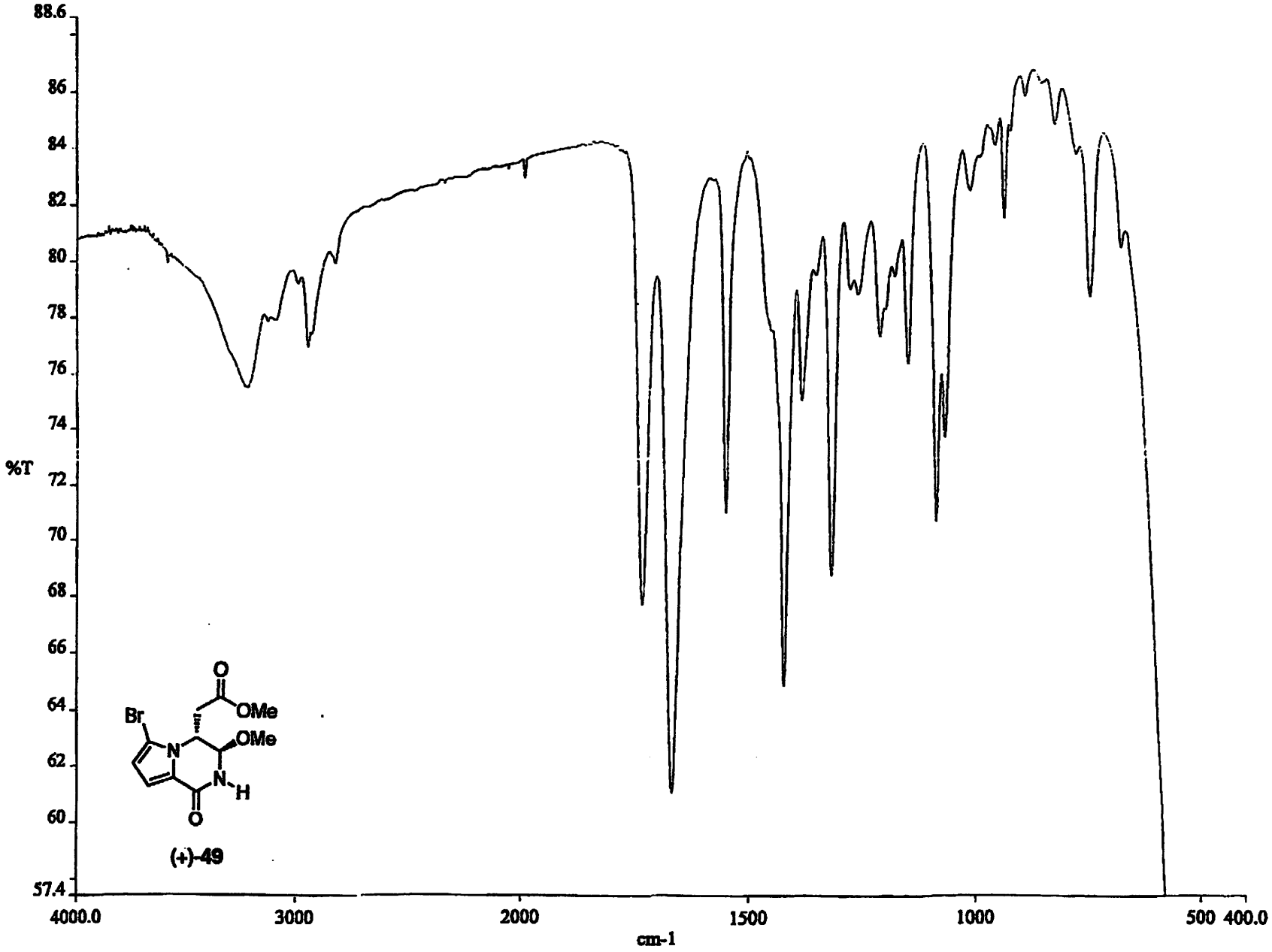
Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: MWD1 E, Sig=270,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.523	MM	1.8067	483.25354	4.45788	100.0000
Totals :				483.25354	4.45788	

Results obtained with enhanced integrator!

*** End of Report ***


88.6
86
84
82
80
78
76
74
72
70
68
66
64
62
60
57.4
%T
4000.0
3000
2000
1500
1000
500
400.0
cm-1
Br
O
OMe
OMe
N
N
H
O
(+)-49

solvent	$CDCl_3$

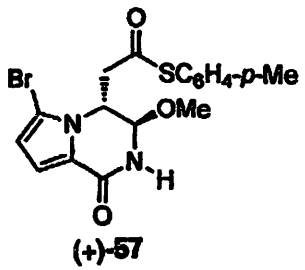
ACQUISITION	
sfrq	500.435
tn	H1
at	4.999
np	120102
sw	12012.0
fb	not used
bs	2
tpwr	56
pw	8.0
d1	0.100
tof	3003.2
nt	32
ct	20
alock	n
gain	not used

FLAGS	
il	n
in	n
dp	y
hs	nn

DISPLAY	
sp	-250.2
wp	6255.3
vs	14
sc	0
wc	250
hzmm	25.02
is	33.57
rfl	4139.0
rfp	3629.1
th	7
ins	100.000
ai cdc ph	

DEC. & VT	
dfrq	125.845
dn	C13
dpwr	30
dof	0
dm	nnn
dmm	c
dmf	200
dseq	
dres	1.0
homo	n

PROCESSING	
wtfile	
proc	ft
fn	262144
math	f
werr	
wexp	
wbs	
wnt	wft



(+)-57

solvent	$CDCl_3$

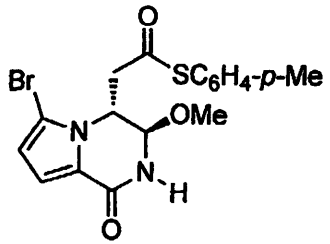
ACQUISITION	
sfrq	125.672
tn	C13
at	2.000
np	125588
sw	31397.2
fb	not used
bs	2
tpwr	59
pw	6.7
d1	3.000
tof	0
nt	5000
ct	710
alock	n
gain	not used

FLAGS	
il	n
in	n
dp	y
hs	nn

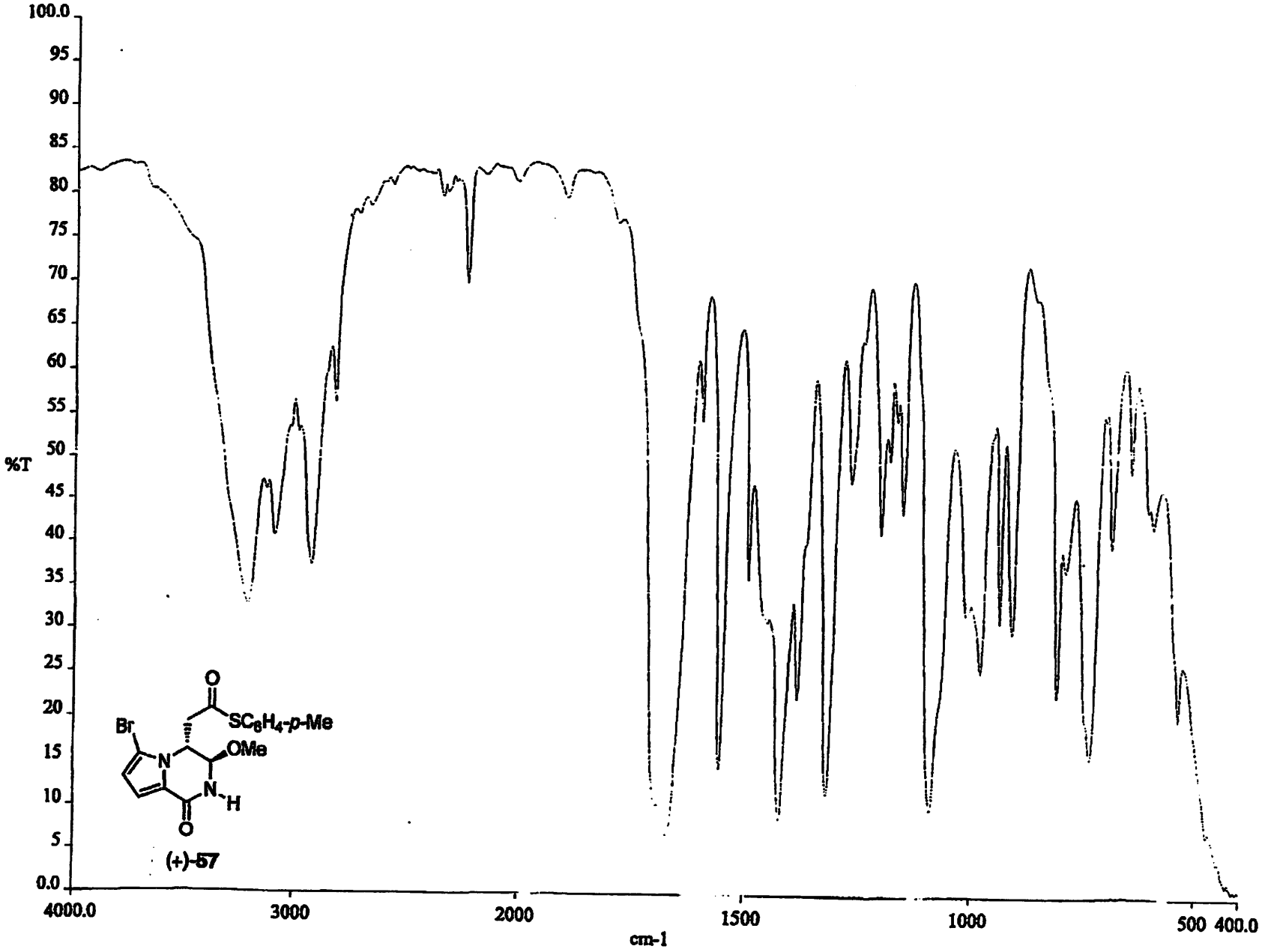
DISPLAY	
sp	-3766.1
wp	31396.7
vs	1340
sc	0
wc	250
hzmm	125.59
is	500.00
rfl	13471.3
rfp	9704.7
th	10
ins	100.000
ai cdc ph	

DEC. & VT	
dfrq	499.744
dn	H1
dpwr	34
dof	0
dm	yyy
dmm	w
dmf	10400
dseq	
dres	1.0
homo	n

PROCESSING	
lb	1.00
wtfile	
proc	ft
fn	131072
math	f
werr	
wexp	
wbs	
wnt	



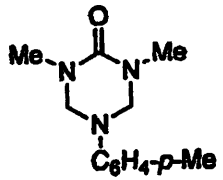
(+)-57


100.0
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0.0
%T
4000.0
3000
2000
1500
1000
500 400.0
cm-1
Br
N
OMe
N
H
O
O
SC6H4-p-Me
(+)-57

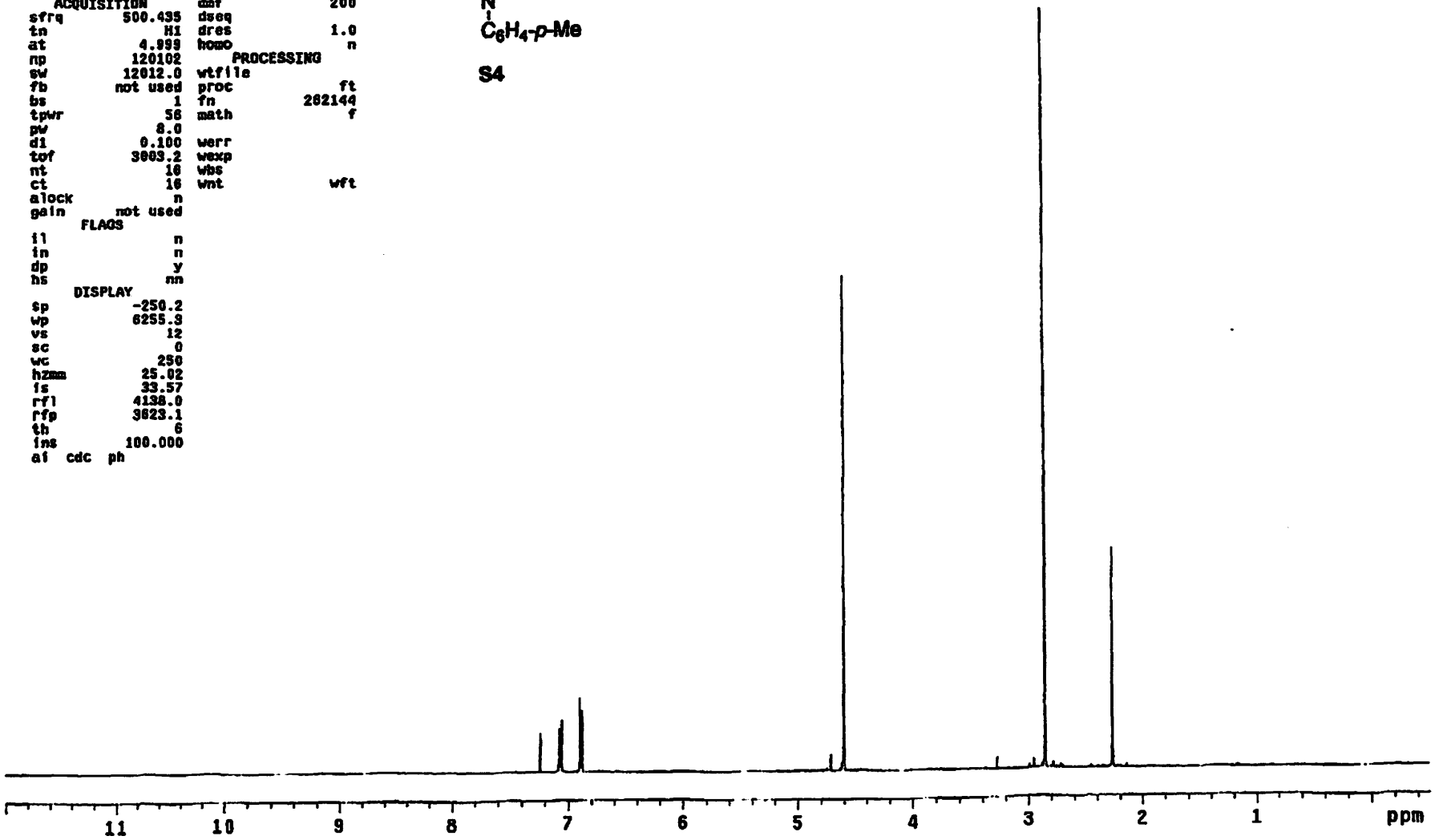
solvent	$CDCl_3$
ACQUISITION	
sfrq	500.435
tn	H1
at	4.999
np	120102
sw	12012.0
fb	not used
bs	1
tpwr	56
pw	8.0
d1	0.100
tof	3003.2
nt	16
ct	16
alock	n
gain	not used
FLAGS	
il	n
in	n
dp	y
hs	nn
DISPLAY	
sp	-250.2
wp	6255.9
vs	12
sc	0
wc	250
hzmm	25.02
is	33.57
rfl	4138.0
rfp	3823.1
th	6
ins	100.000

af cdc ph

DEC. & VT	
dfrq	125.845
dn	C13
dpwr	30
dof	0
dm	nnn
dmm	c
dmf	200
dseq	
dres	1.0
homo	n
PROCESSING	
wtfile	
proc	ft
fn	262144
math	f
werr	
wexp	
wbs	
wnt	wft



S4



solvent	CDCl3

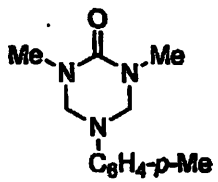
ACQUISITION	
sfrq	125.785
tn	C13
at	1.736
np	131010
sw	37735.8
fb	not used
bs	4
ss	1
tpwr	53
pw	6.8
d1	0.763
tof	631.4
nt	1e+09
ct	12
alock	n
gain	not used

FLAGS	
il	n
in	n
dp	y
hs	nn

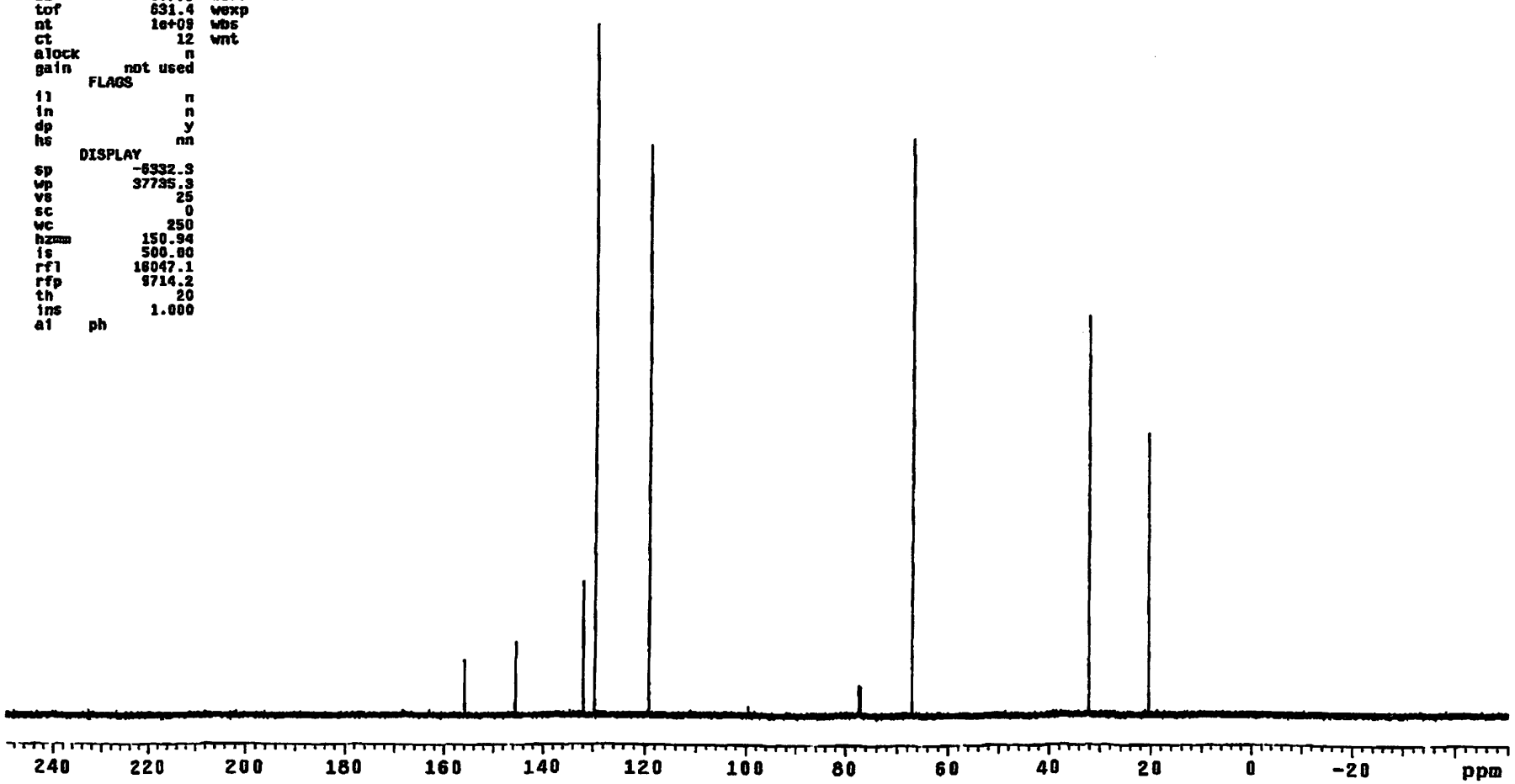
DISPLAY	
sp	-6332.3
wp	37735.3
vs	25
sc	0
wc	250
hzmm	150.94
is	500.80
rfl	16047.1
rfp	9714.2
th	20
ins	1.000
ai	ph

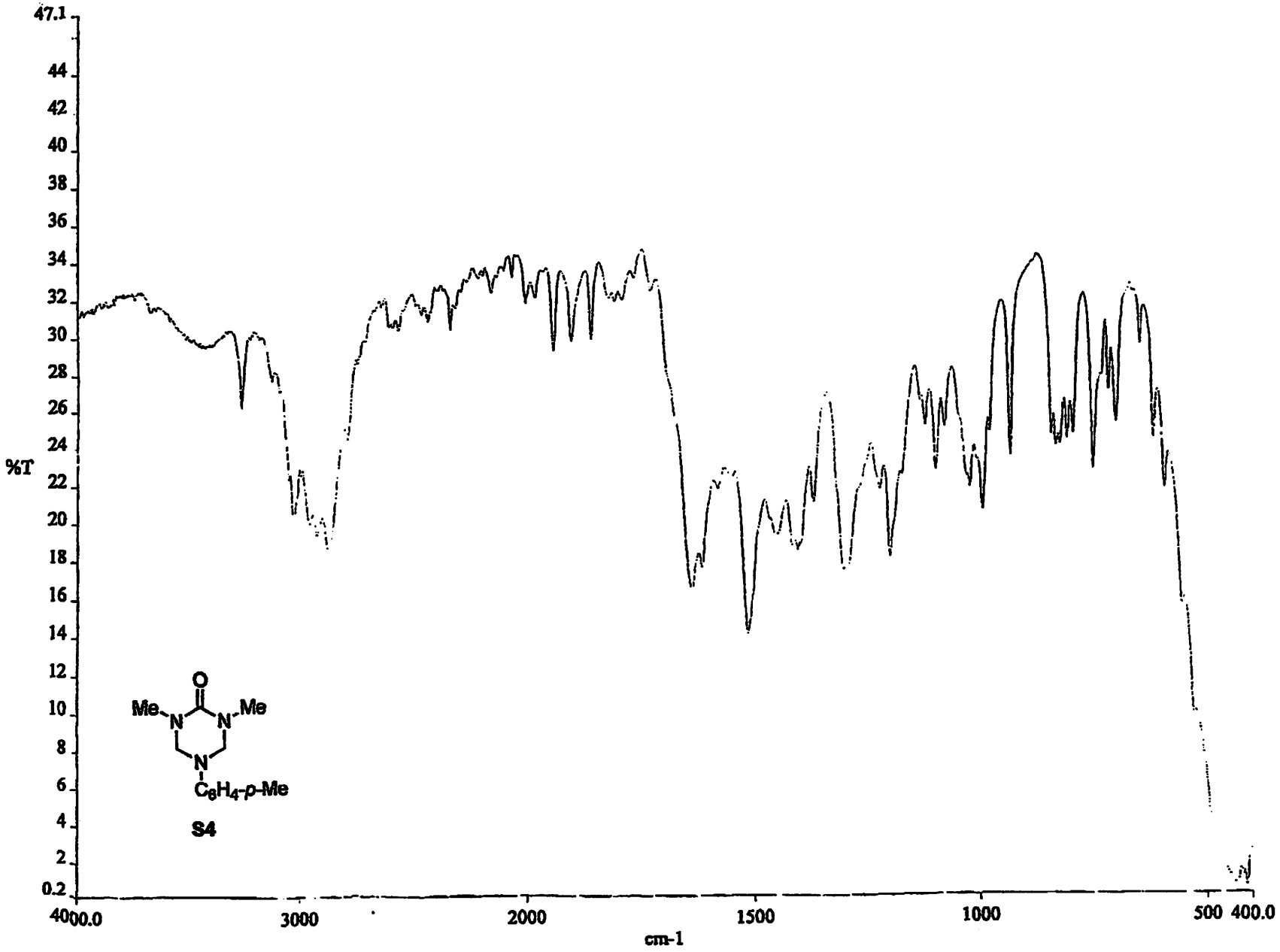
DEC. & VT	
dfrq	500.229
dn	H1
dpwr	38
dof	-500.0
dm	y
dmm	w
dmf	10000
dseq	
dres	1.0
homo	n

PROCESSING	
lb	0.30
wtfile	
proc	ft
fn	131072
math	f
werr	
wexp	
wbs	
wnt	



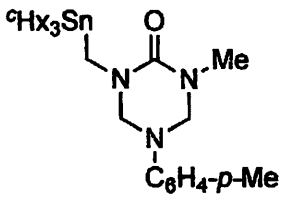
S4



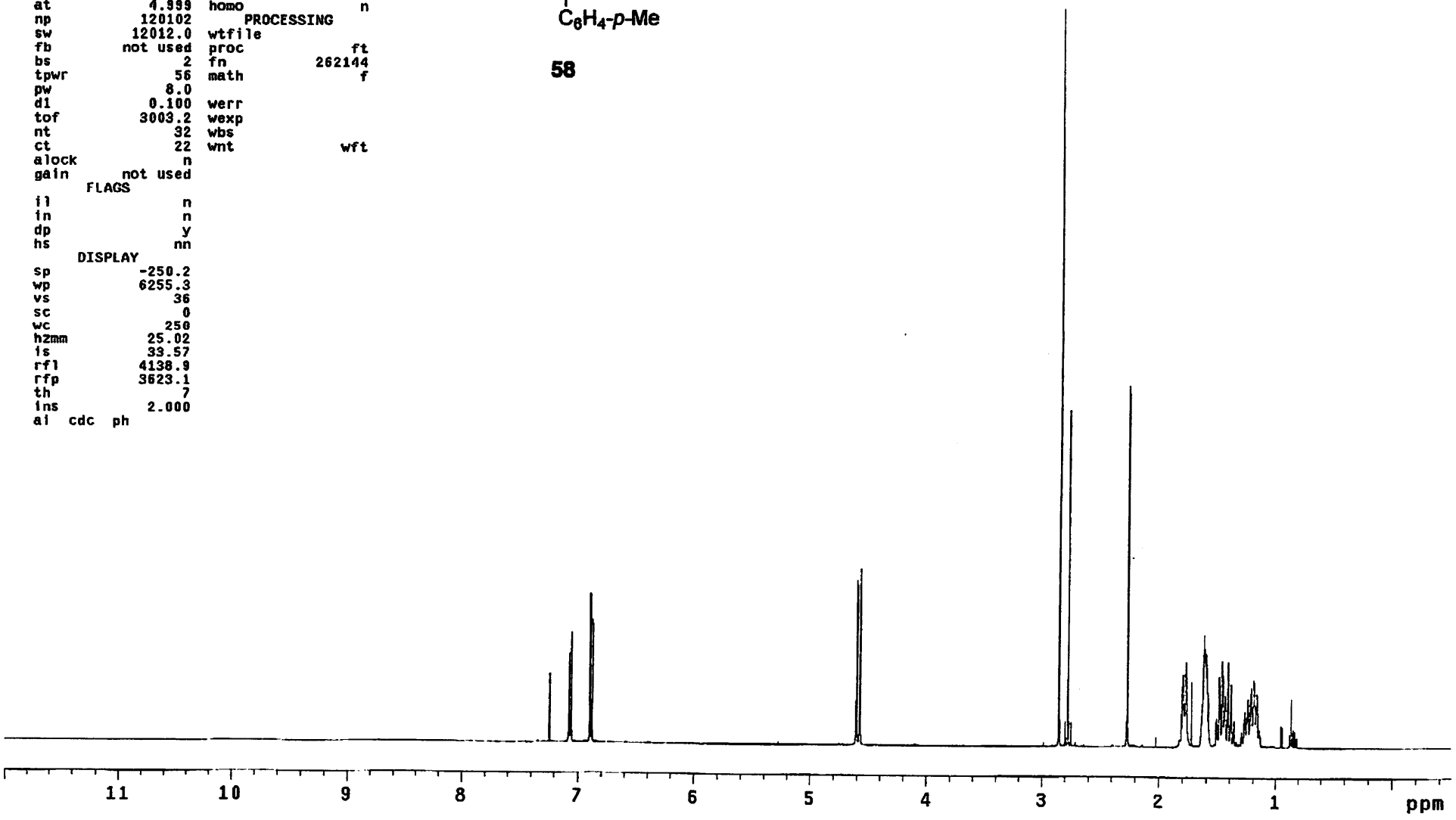

47.1
44
42
40
38
36
34
32
30
28
26
24
%T
22
20
18
16
14
12
10
8
6
4
2
0.2
4000.0
3000
2000
1500
1000
500
400.0
cm-1
Me
N
O
N
Me
N
C6H4-p-Me

S4

solvent	$CDCl_3$		
		DEC. & VT	
		dfrq	125.845
		dn	C13
		dpwr	30
		dof	0
		dm	nnn
		dmm	c
ACQUISITION		dmf	200
sfrq	500.435	dseq	
tn	H1	dres	1.0
at	4.999	homo	n
np	120102	PROCESSING	
sw	12012.0	wtfile	
fb	not used	proc	ft
bs	2	fn	262144
tpwr	56	math	f
pw	8.0		
d1	0.100	werr	
tof	3003.2	wexp	
nt	32	wbs	
ct	22	wnt	wft
alock	n		
gain	not used		
FLAGS			
il	n		
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-250.2		
wp	6255.3		
vs	36		
sc	0		
wc	250		
hzmm	25.02		
is	33.57		
rfl	4138.9		
rfp	3623.1		
th	7		
ins	2.000		
ai cdc ph			



58



solvent	CDCl3

ACQUISITION

sfrq	125.795
tn	C13
at	1.736
np	131010
sw	37735.8
fb	not used
bs	4
ss	1
tpwr	53
pw	6.9
d1	0.763
tof	631.4
nt	1e+06
ct	148
alock	n
gain	not used

FLAGS

il	n
in	n
dp	y
hs	nn

DISPLAY

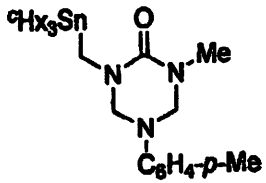
sp	-6296.7
wp	37735.3
vs	49
sc	0
wc	250
hzmm	150.94
is	500.00
rfl	16012.2
rfp	9714.9
th	6
ins	1.000
ai	ph

DEC. & VT

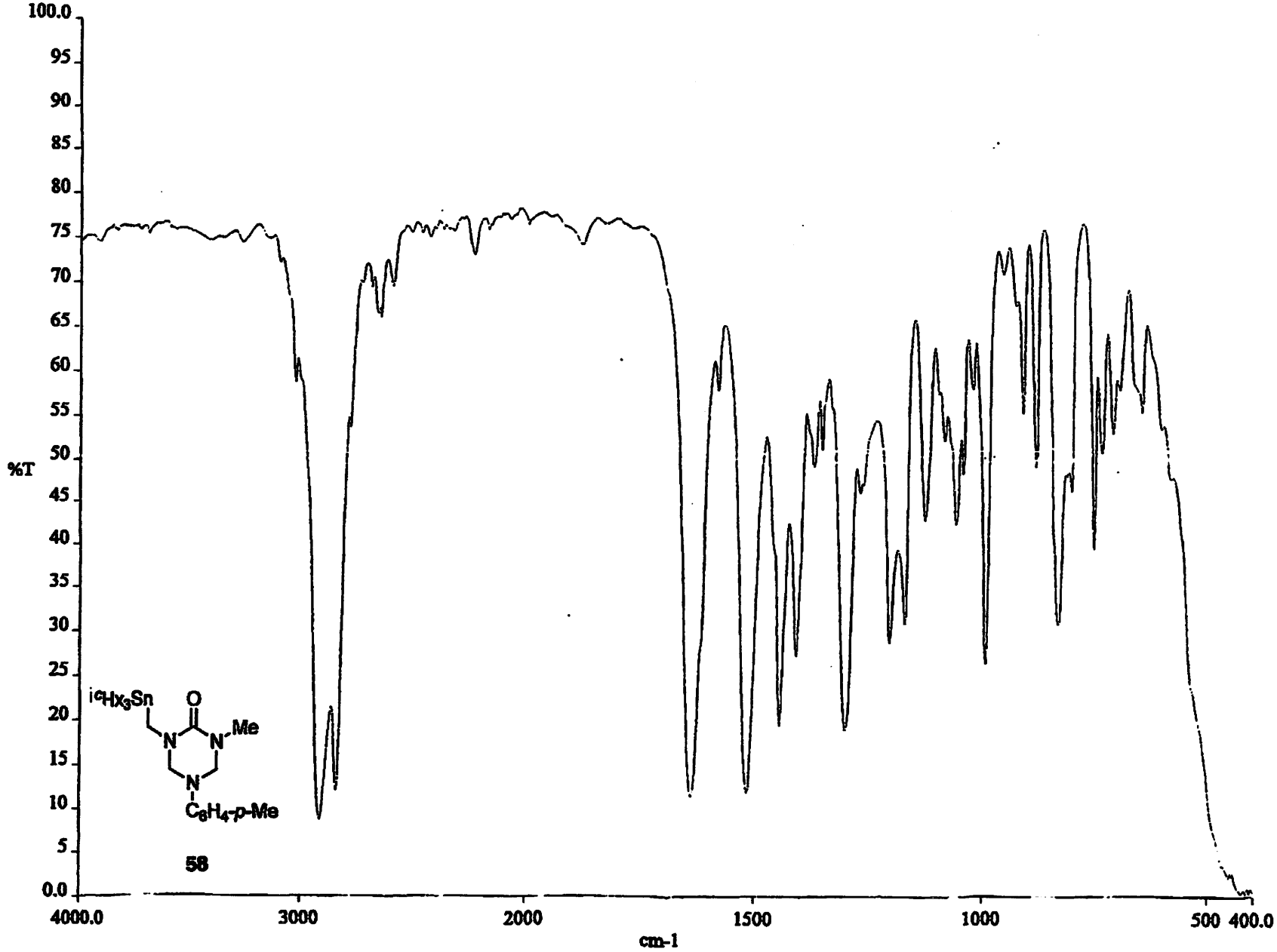
sfrq	500.229
dn	H1
dpwr	38
dof	-500.0
dm	y
dmm	w
dmf	10000
dseq	
dres	1.0
homo	n

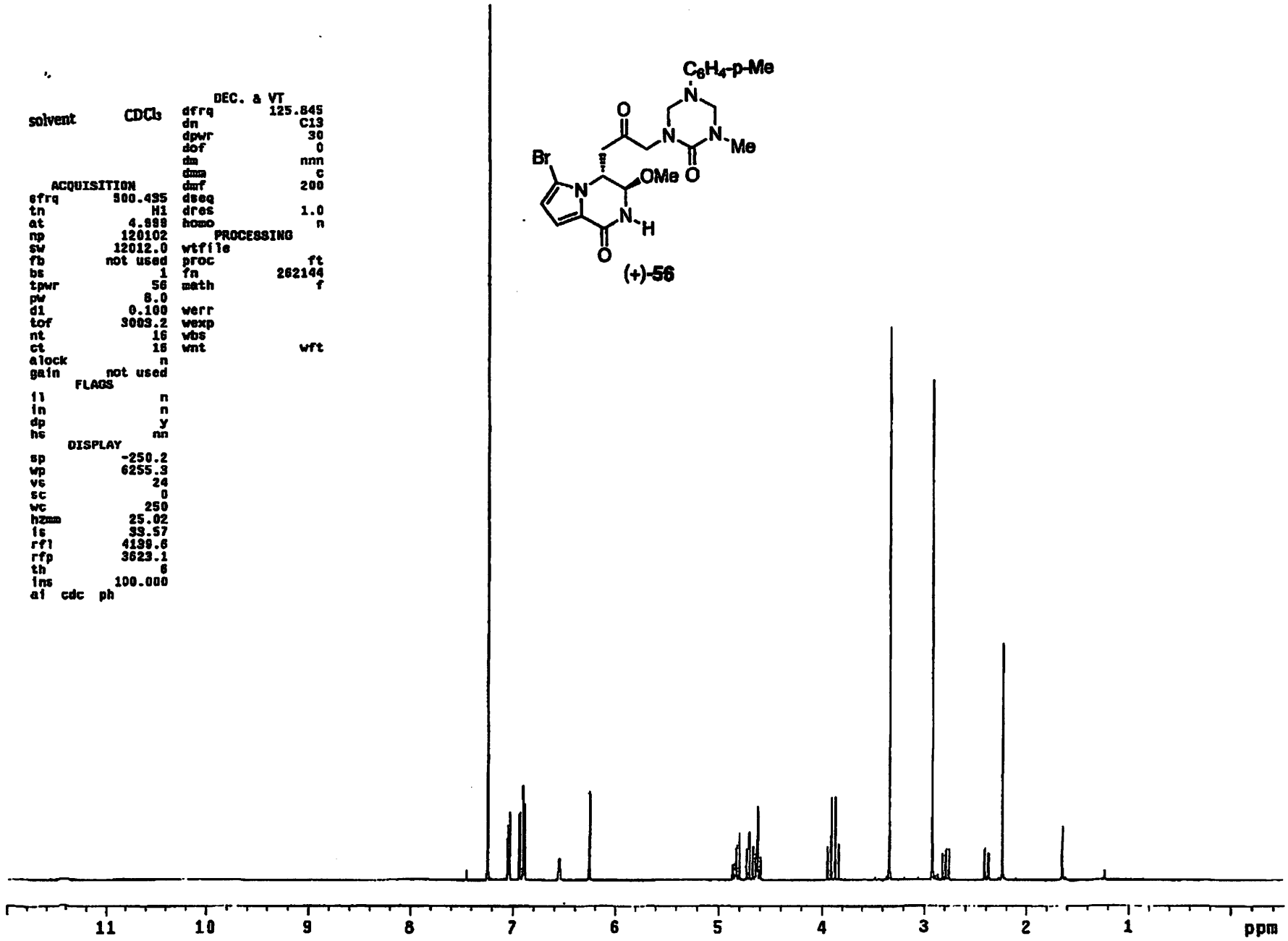
PROCESSING

lb	0.30
wtfile	
proc	ft
fn	131072
math	f
werr	
wexp	
wbs	
wnt	



58

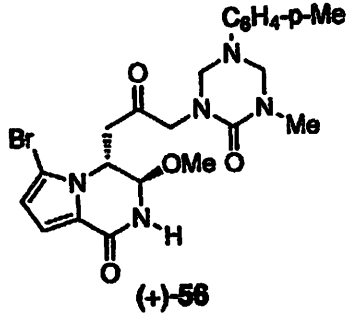

100.0
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0.0
%T
4000.0
3000
2000
1500
1000
500
400.0
cm-1
ⁱᶜHx3Sn
O
N
N
Me
N
C6H4-p-Me
58


solvent CDCl3
ACQUISITION
sfrq 500.495
tn H1
at 4.888
np 120102
sw 12012.0
fb not used
bs 1
tpwr 56
pw 8.0
d1 0.100
tof 3003.2
nt 16
ct 16
alock n
gain not used
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -250.2
wp 6255.3
vs 24
sc 0
wc 250
hzmm 25.02
is 39.57
rfl 4139.6
rfp 3623.1
th 6
ins 100.000
ai cdc ph
DEC. & VT
dfrq 125.845
dn C13
dpwr 30
dof 0
dm nnn
dmm c
dmf 200
dseq
dres 1.0
homo n
PROCESSING
wtfile
proc ft
fn 262144
math f
werr
wexp
wbs
wnt wft
C6H4-p-Me
N
O
N
N
Me
Br
OMe
O
N
N
H
O
(+)-56
11
10
9
8
7
6
5
4
3
2
1
ppm

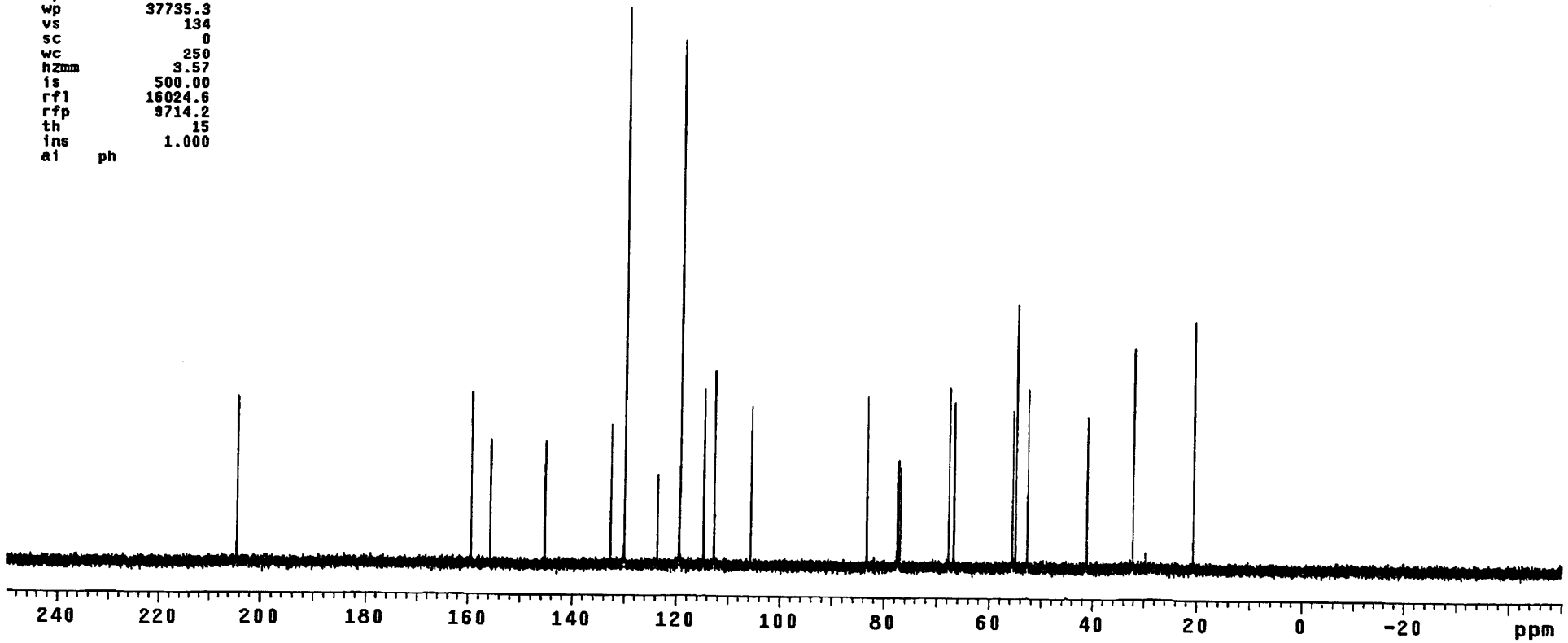
DS8-178-FR11-17-13C

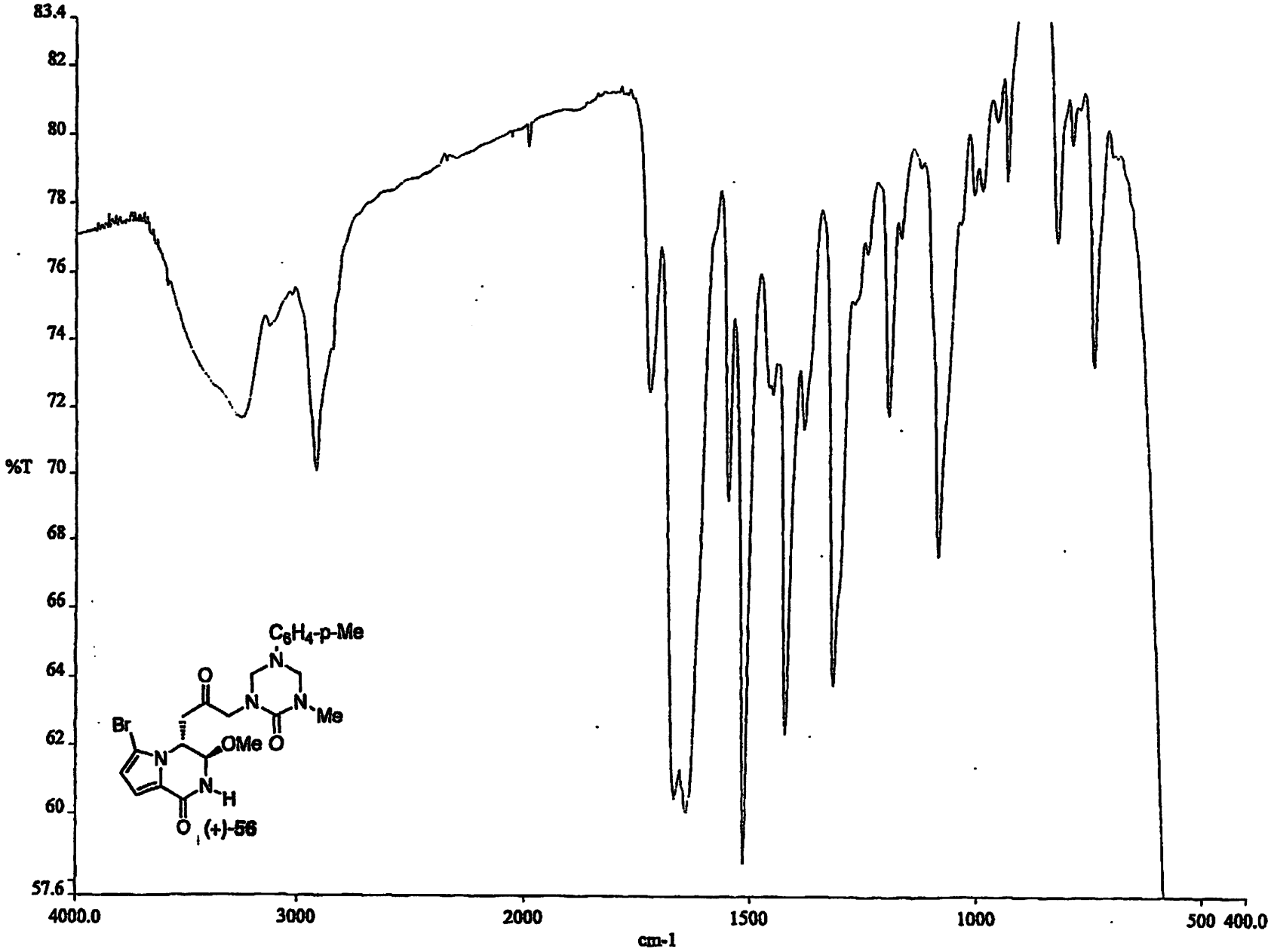
exp2 s2pul

SAMPLE		DEC. & VT	
date	Mar 19 2010	dfrq	500.229
solvent	CDCl3	dn	H1
file	/data/export/~	dpwr	38
home/movassag/Mds/~		dof	-500.0
Mds501/DS8-178-FR1~		dm	y
1-17-13C.fid		dmm	w
ACQUISITION		dmf	10000
sfrq	125.795	dseq	
tn	C13	dres	1.0
at	1.736	homo	n
np	131010	PROCESSING	
sw	37735.8	lb	0.30
fb	not used	wtfile	
bs	4	proc	ft
ss	1	fn	131072
tpwr	53	math	f
pw	6.9		
d1	0.763	werr	
tof	631.4	wexp	
nt	1e+09	wbs	
ct	60	wnt	
alock	n		
gain	60		
FLAGS			
il	n		
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-6309.9		
wp	37735.3		
vs	134		
sc	0		
wc	250		
hzmm	3.57		
is	500.00		
rfl	16024.6		
rfp	9714.2		
th	15		
ins	1.000		
ai	ph		



(+)-56




83.4
82
80
78
76
74
72
%T 70
68
66
64
62
60
57.6
4000.0
3000
2000
1500
1000
500 400.0
cm-1
C6H4-p-Me
N
O
N
N
Me
Br
OMe
O
N
N
H
O
(+)-56

solvent	CD_3OD

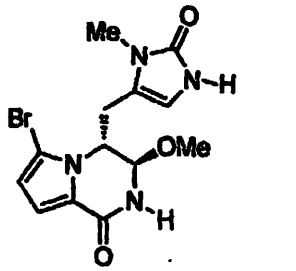
ACQUISITION	
sfrq	500.437
tn	H1
at	4.988
np	120102
sw	12012.0
fb	not used
bs	1
tpwr	56
pw	8.0
d1	0.100
tof	3009.2
nt	32
ct	32
alock	n
gain	not used

FLAGS	
il	n
in	n
dp	y
hs	nn

DISPLAY	
sp	-250.2
wp	6255.4
vs	45
sc	0
wc	250
hzmm	25.02
is	38.57
rfl	2159.2
rfp	1656.4
th	7
ins	100.000
ai cdc ph	

DEC. & VT	
dfrq	125.846
dn	C13
dpwr	30
dof	0
dm	nnn
dmm	c
dmf	200
dseq	
dres	1.0
homo	n

PROCESSING	
wtfile	
proc	ft
fn	262144
math	f
werr	
wexp	
wbs	
wnt	wft



(+)-*O*-Me-pre-agelastatin A (47)

solvent	CD_3OD

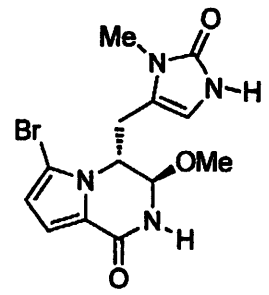
ACQUISITION	
sfrq	125.795
tn	C13
at	1.736
np	131010
sw	37735.8
fb	not used
bs	4
ss	1
tpwr	53
pw	6.9
d1	0.763
tof	631.4
nt	1e+09
ct	8268
alock	n
gain	60

FLAGS	
il	n
in	n
dp	y
hs	nn

DISPLAY	
sp	-6115.7
wp	37735.3
vs	4867
sc	0
wc	250
hzmm	150.94
is	500.00
rfl	12298.8
rfp	6182.5
th	5
ins	1.000
ai	ph

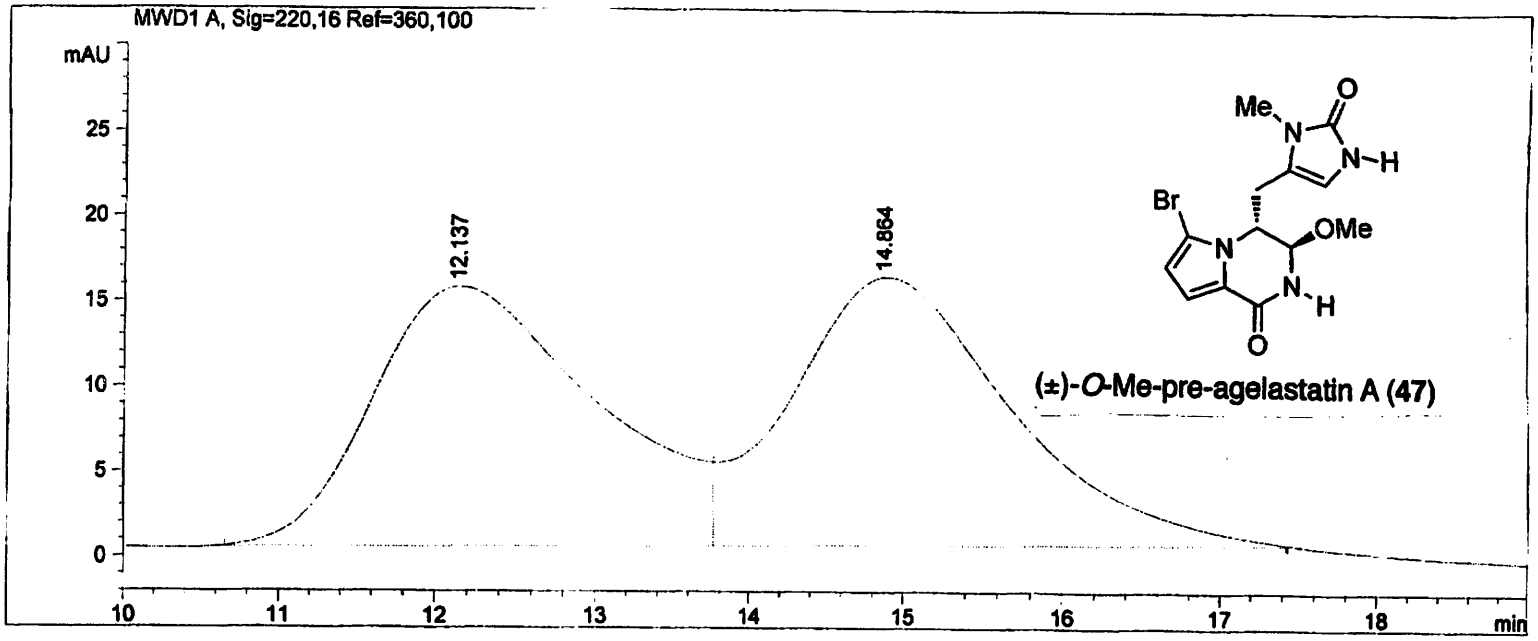
DEC. & VT	
dfrq	500.231
dn	H1
dpwr	38
dof	-500.0
dm	y
dmm	w
dmf	10000
dseq	
dres	1.0
homo	n

PROCESSING	
lb	0.30
wtfile	
proc	ft
fn	131072
math	f
werr	
wexp	
wbs	
wnt	



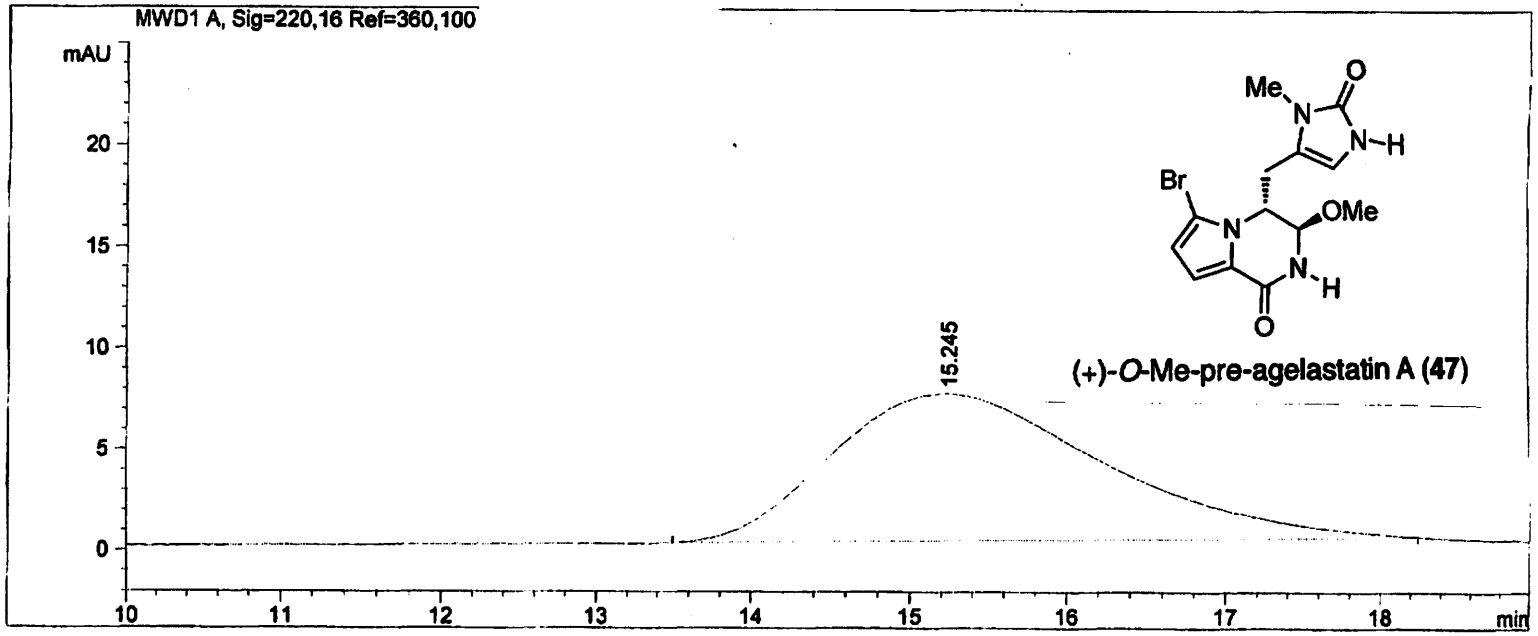
(+)-*O*-Me-pre-agelastatin A (47)

```
Injection Date  :                                   Seq. Line :   1
Sample Name     :                                    Location : Vial 61
Acq. Operator   :                                        Inj :   1
                                                   Inj Volume : 1 µl
Acq. Method     :
Last changed    :
Analysis Method :
Last changed    :
```

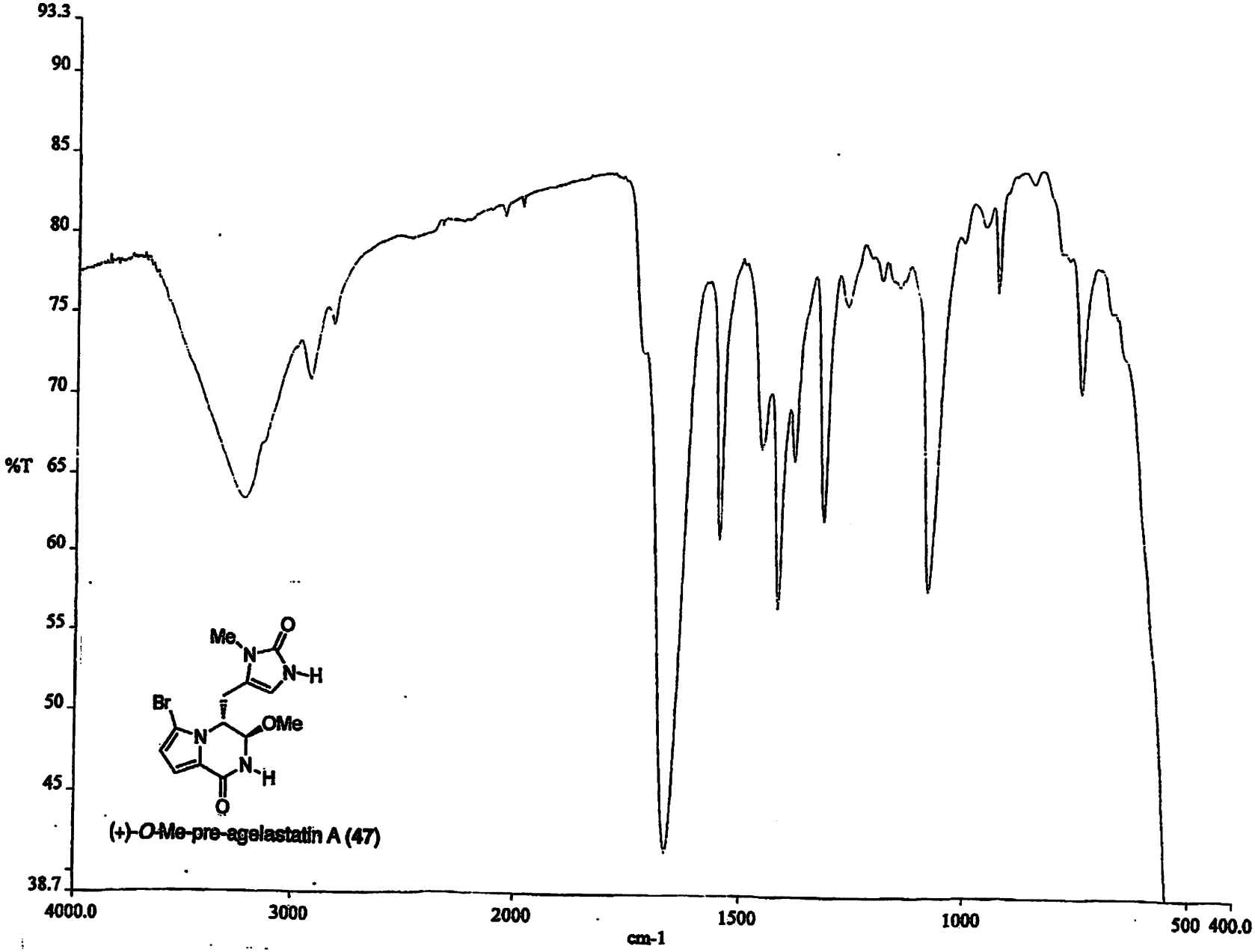


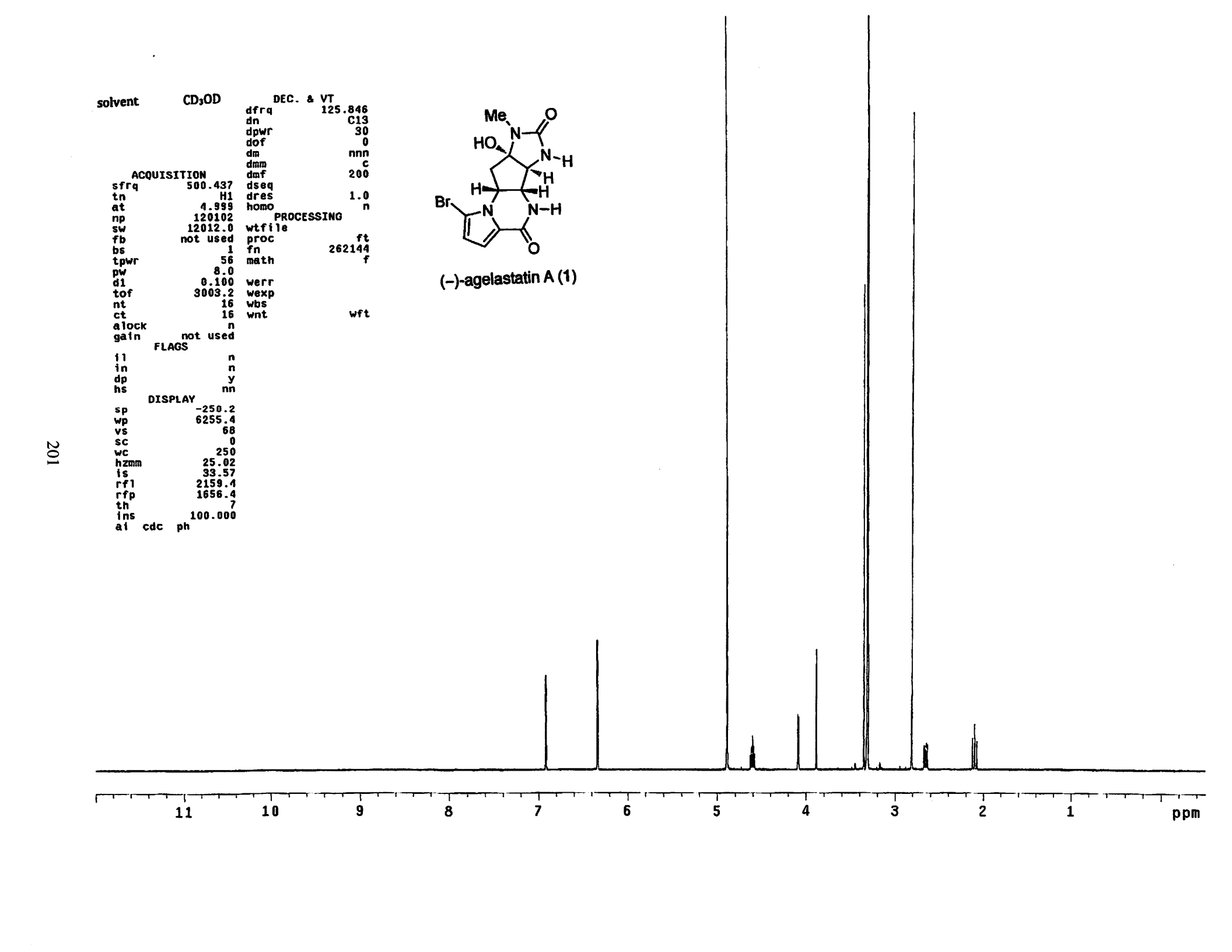

```
                        Area Percent Report

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: MWD1 A, Sig=220,16 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  12.137 BV    1.1608 1499.41431   15.28030  49.0828
   2  14.864 VB    1.1626 1555.45105   15.82612  50.9172

Totals :                  3054.86536   31.10642

 Results obtained with enhanced integrator!

                        *** End of Report ***
```

```
Injection Date  :                                   Seq. Line :   1
Sample Name     :                                    Location : Vial 91
Acq. Operator   :                                         Inj :   1
                                                  Inj Volume : 1 µl
Acq. Method     :
Last changed    :
Analysis Method :
Last changed    :
```




```
                        Area Percent Report

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: MWD1 A, Sig=220,16 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  15.245 PB    1.4033  875.68500    7.33223 100.0000

Totals :                   875.68500    7.33223

 Results obtained with enhanced integrator!

                        *** End of Report ***
```

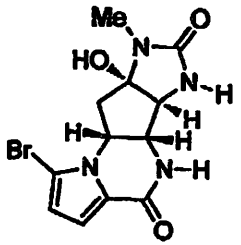

93.3
90
85
80
75
70
%T 65
60
55
50
45
38.7
4000.0
3000
2000
1500
1000
500 400.0
cm-1
Me
N
O
N-H
Br
N
OMe
N-H
O
(+)-O-Me-pre-agelastatin A (47)


solvent CD3OD
ACQUISITION
sfrq 500.437
tn H1
at 4.999
np 120102
sw 12012.0
fb not used
bs 1
tpwr 56
pw 8.0
d1 0.100
tof 3003.2
nt 16
ct 16
alock n
gain not used
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -250.2
wp 6255.4
vs 68
sc 0
wc 250
hzmm 25.02
is 33.57
rfl 2159.4
rfp 1656.4
th 7
ins 100.000
ai cdc ph
DEC. & VT
dfrq 125.846
dn C13
dpwr 30
dof 0
dm nnn
dmm c
dmf 200
dseq
dres 1.0
homo n
PROCESSING
wtfile
proc ft
fn 262144
math f
werr
wexp
wbs
wnt wft
Me
O
N
HO
N-H
H
H
H
Br
N
N-H
O
(–)-agelastatin A (1)
11
10
9
8
7
6
5
4
3
2
1
ppm

DS8-027-C12-FR30-13C

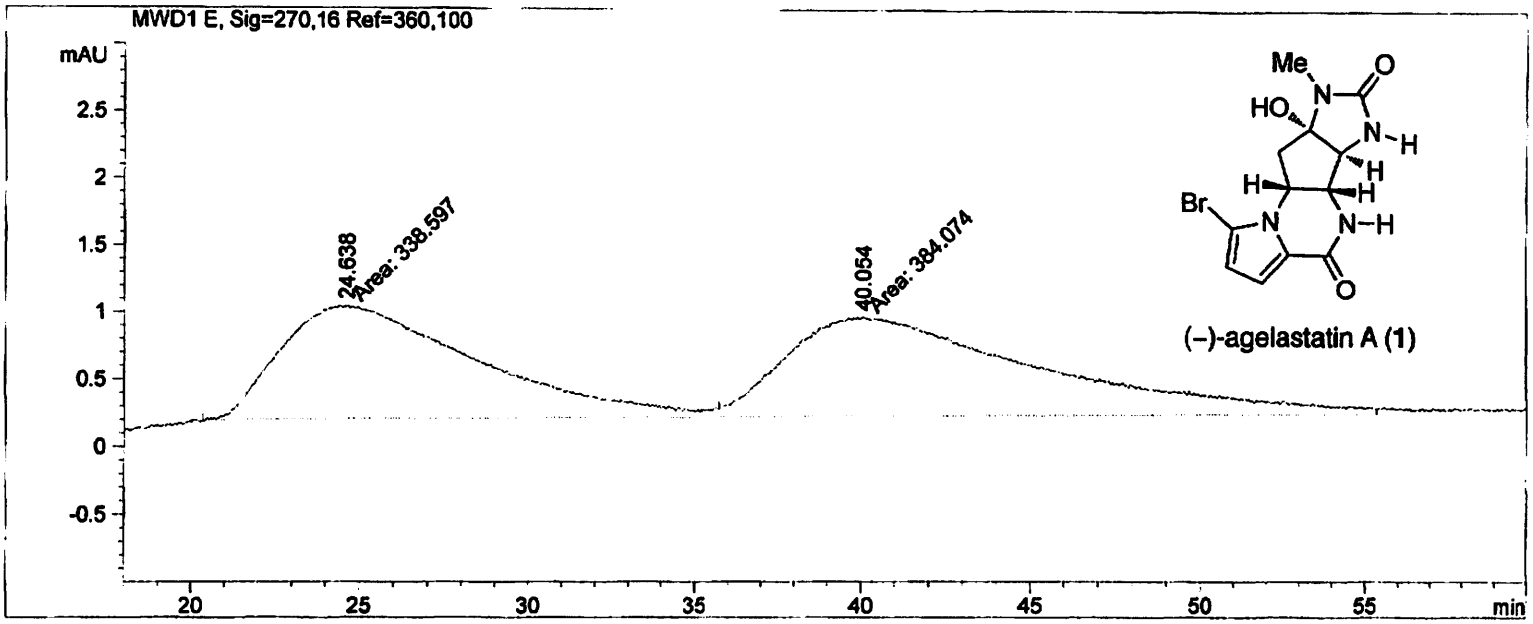
exp2 s2pul

SAMPLE		DEC. & VT	
date	Sep 8 2009	dfrq	500.231
solvent	CD3OD	dn	H1
file	/data/export/~	dpwr	38
home/movassag/Mds/~		dof	-500.0
Mds501/DS8-027-C12~		dm	y
-FR30-13C.fid		dmm	w
ACQUISITION		dmf	10000
sfrq	125.795	dseq	
tn	C13	dres	1.0
at	1.736	homo	n
np	131010	PROCESSING	
sw	37735.8	lb	0.30
fb	not used	wtfile	
bs	4	proc	ft
ss	1	fn	131072
tpwr	53	math	f
pw	6.9		
d1	0.763	werr	
tof	631.4	wexp	
nt	1e+09	wbs	
ct	21180	wnt	
alock	n		
gain	60		
FLAGS			
il	n		
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-6115.7		
wp	37735.3		
vs	4760		
sc	0		
wc	250		
hzmm	9.37		
is	500.00		
rfl	12298.8		
rfp	6182.5		
th	10		
ins	1.000		
ai	ph		



(–)-agelastatin A (1)

Injection Date	:	Seq. Line	: 1
Sample Name	:	Location	: Vial 91
Acq. Operator	:	Inj	: 1
		Inj Volume	: 5 µl
Acq. Method	:		
Last changed	:		
Analysis Method	:		
Last changed	:		



Area Percent Report

Sorted By	:	Signal
Multiplier	:	1.0000
Dilution	:	1.0000

Use Multiplier & Dilution Factor with ISTDs

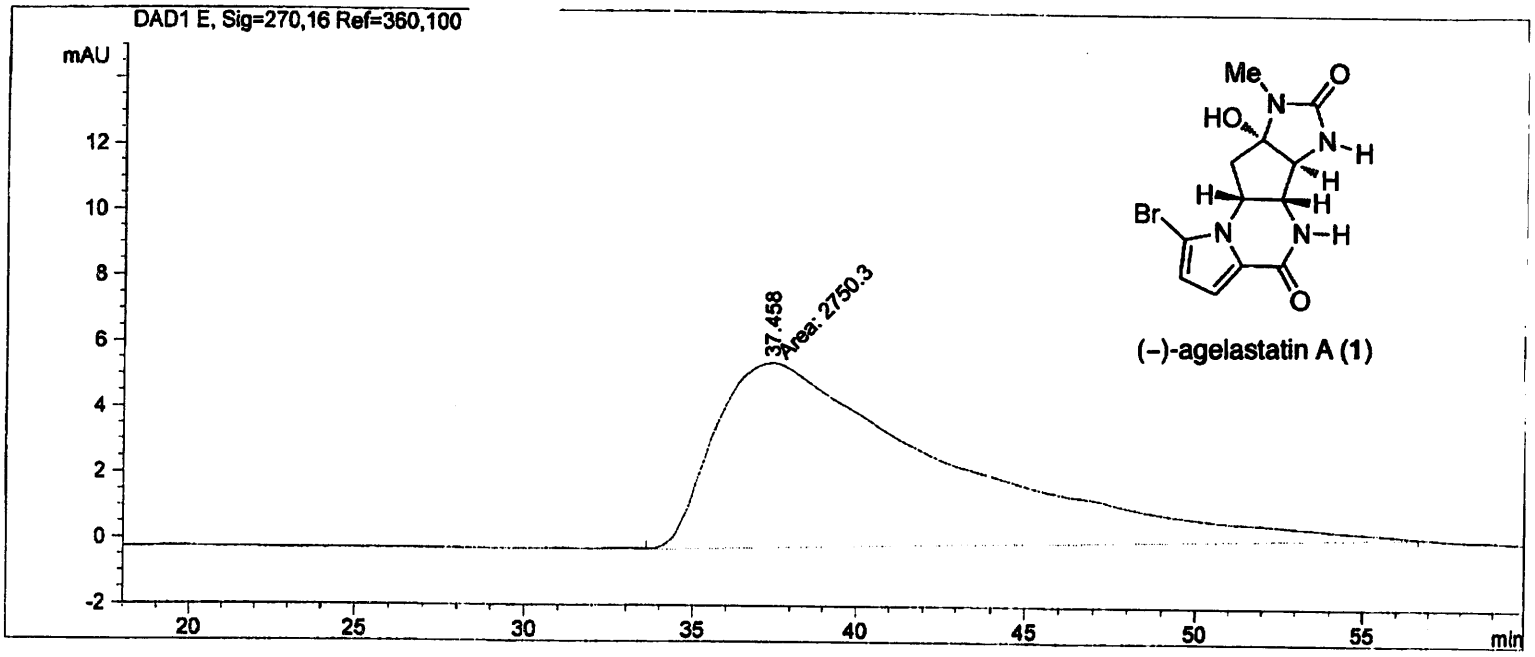
Signal 1: MWD1 E, Sig=270,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	24.638	MF	6.6959	338.59686	8.42801e-1	46.8535
2	40.054	FM	8.6223	384.07428	7.42408e-1	53.1465
Totals :				722.67114	1.58521	

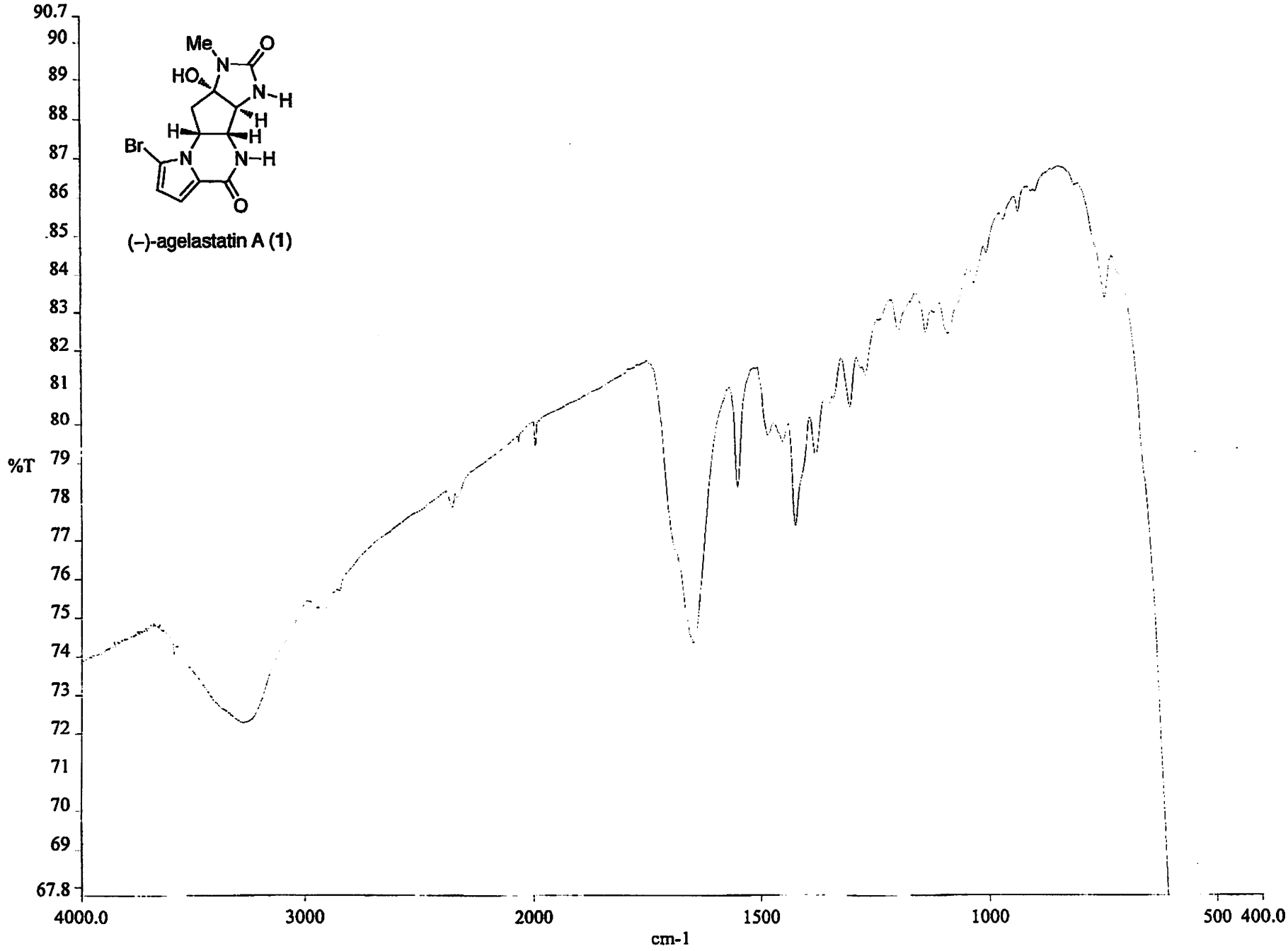
Results obtained with enhanced integrator!

*** End of Report ***

```
Injection Date  :                                   Seq. Line :   1
Sample Name     :                                    Location : Vial 91
Acq. Operator   :                                        Inj :   1
                                                 Inj Volume : 1 µl
Acq. Method     :
Last changed    :
Analysis Method :
Last changed    :
```




```
                        Area Percent Report

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 E, Sig=270,16 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|-------|
   1  37.458 MM    8.1336 2750.29980    5.63566 100.0000

Totals :                  2750.29980    5.63566

 Results obtained with enhanced integrator!

                        *** End of Report ***
```


90.7
90
89
88
87
86
85
84
83
82
81
80
79
78
77
76
75
74
73
72
71
70
69
67.8
%T
4000.0
3000
2000
1500
1000
500
400.0
cm-1
Me
HO
Br
(–)-agelastatin A (1)

solvent	CD_3OD

ACQUISITION	
sfrq	500.437
tn	H1
at	4.999
np	120102
sw	12012.0
fb	not used
bs	1
tpwr	56
pw	8.0
d1	0.100
tof	3003.2
nt	32
ct	32
alock	n
gain	not used

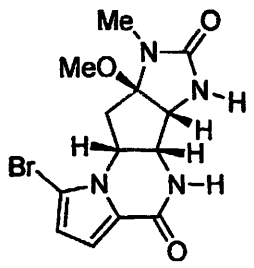
FLAGS	
il	n
in	n
dp	y
hs	nn

DISPLAY	
sp	-250.2
wp	6255.4
vs	136
sc	0
wc	250
hzmm	25.02
is	33.57
rfl	2159.0
rfp	1656.4
th	7
ins	100.000

al cdc ph

DEC. & VT	
dfrq	125.846
dn	C13
dpwr	30
dof	0
dm	nnn
dmm	c
dmf	200
dseq	
dres	1.0
homo	n

PROCESSING	
wtfile	
proc	ft
fn	262144
math	f
werr	
wexp	
wbs	
wnt	wft



(–)-*O*-Me-di-*epi*-agelastatin A (61)

solvent	CD_3OD

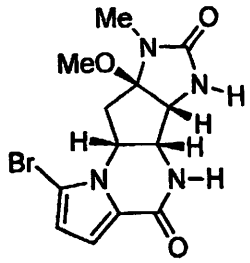
ACQUISITION	
sfrq	125.795
tn	C13
at	1.736
np	131010
sw	37735.8
fb	not used
bs	4
ss	1
tpwr	53
pw	6.9
d1	0.763
tof	631.4
nt	1e+09
ct	356
alock	n
gain	not used

FLAGS	
il	n
in	n
dp	y
hs	nn

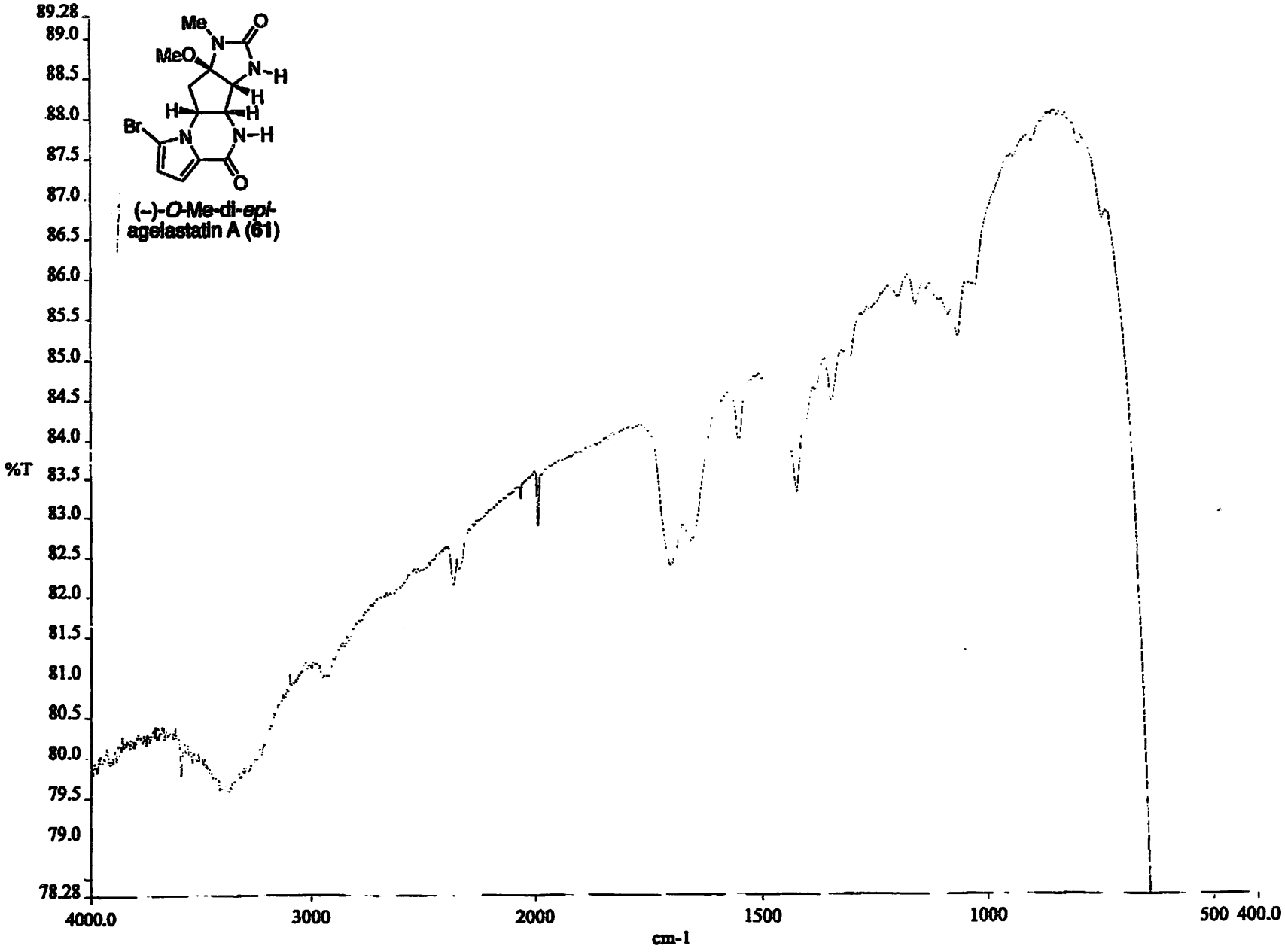
DISPLAY	
sp	-6117.5
wp	37735.3
vs	920
sc	0
wc	250
hzmm	150.94
is	500.00
rfl	12300.3
rfp	6182.2
th	7
ins	1.000
ai	ph

DEC. & VT	
dfrq	500.231
dn	H1
dpwr	38
dof	-500.0
dm	y
dmm	w
dmf	10000
dseq	
dres	1.0
homo	n

PROCESSING	
lb	0.30
wtfile	
proc	ft
fn	131072
math	f
werr	
wexp	
wbs	
wnt	



(–)-*O*-Me-di-*epi*-agelastatin A (61)


(–)-O-Me-di-epi-agelastatin A (61)
%T
89.28
89.0
88.5
88.0
87.5
87.0
86.5
86.0
85.5
85.0
84.5
84.0
83.5
83.0
82.5
82.0
81.5
81.0
80.5
80.0
79.5
79.0
78.28
4000.0
3000
2000
1500
1000
500 400.0
cm-1

solvent	$CDCl_3$

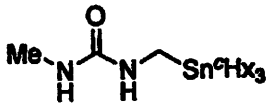
ACQUISITION	
sfrq	500.435
tn	H1
at	4.999
np	120102
sw	12012.0
fb	not used
bs	1
tpwr	56
pw	8.0
d1	0.100
tof	3003.2
nt	16
ct	16
alock	n
gain	not used

FLAGS	
il	n
in	n
dp	y
hs	nn

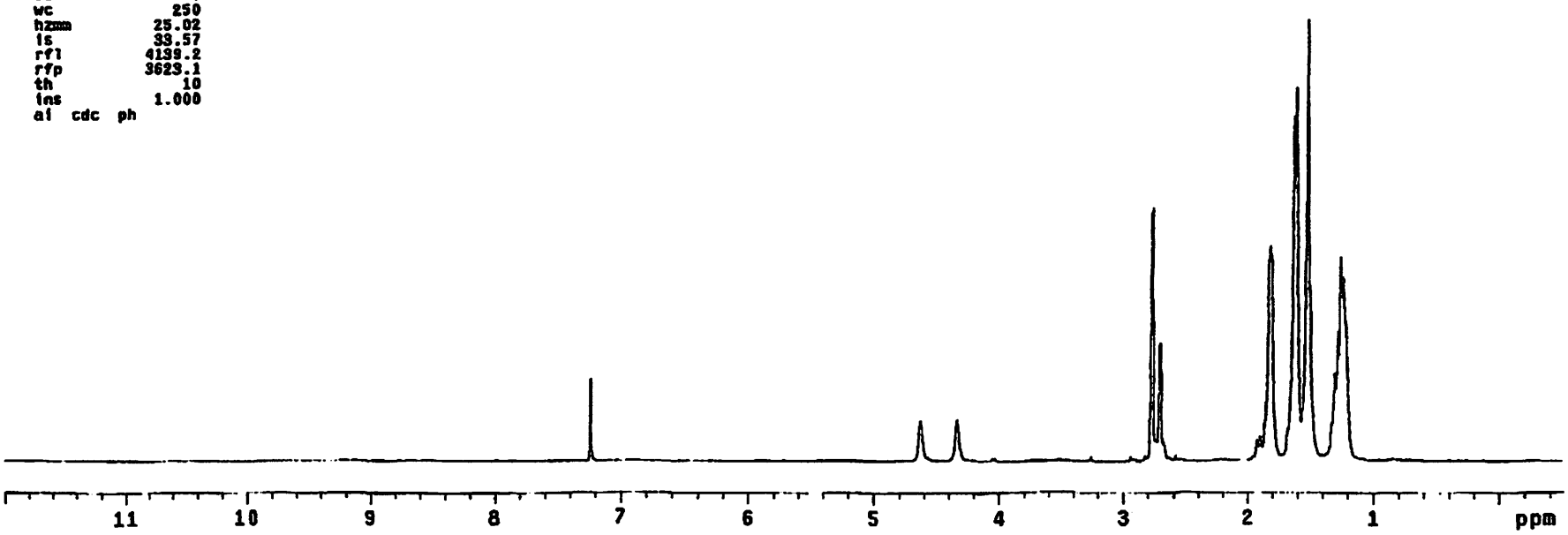
DISPLAY	
sp	-250.2
wp	6255.3
vs	111
sc	0
wc	250
hzmm	25.02
is	33.57
rfl	4139.2
rfp	3623.1
th	10
ins	1.000
ai cdc ph	

DEC. & VT	
dfrq	125.845
dn	C13
dpwr	30
dof	0
dm	nnn
dmm	c
dmf	200
dseq	
dres	1.0
homo	n

PROCESSING	
wtfile	
proc	ft
fn	262144
math	f
werr	
wexp	
wbs	
wnt	wft



63



solvent	$CDCl_3$

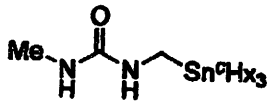
ACQUISITION	
sfrq	125.795
tn	C13
at	1.796
np	131010
sw	37735.8
fb	not used
bs	4
ss	1
tpwr	53
pw	8.9
d1	0.783
tof	631.4
nt	1e+09
ct	536
alock	n
gain	not used

FLAGS	
il	n
in	n
dp	y
hs	nn

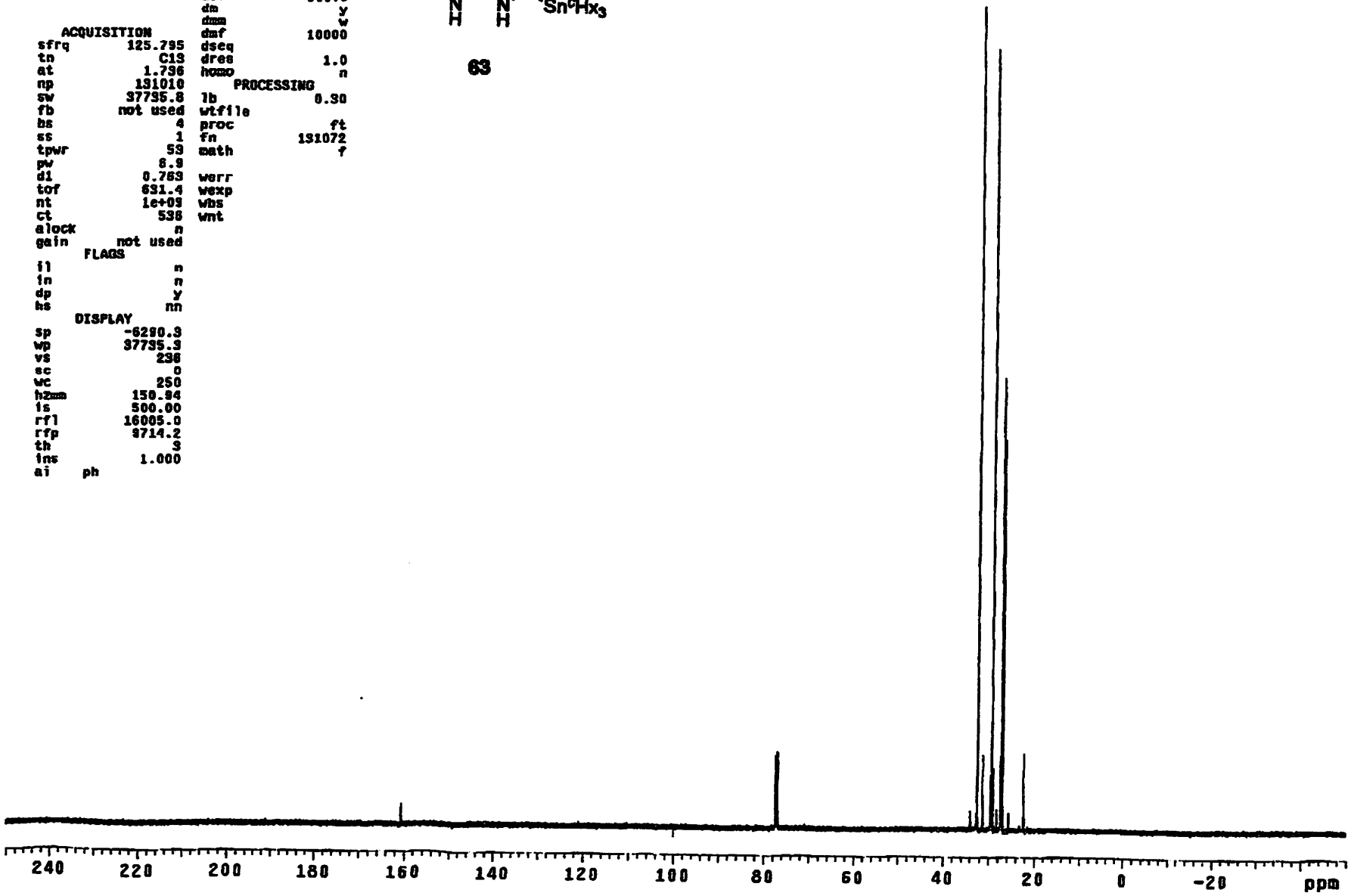
DISPLAY	
sp	-6280.3
wp	37735.3
vs	238
sc	0
wc	250
hzmm	150.84
is	500.00
rfl	16005.0
rfp	9714.2
th	3
ins	1.000
ai	ph

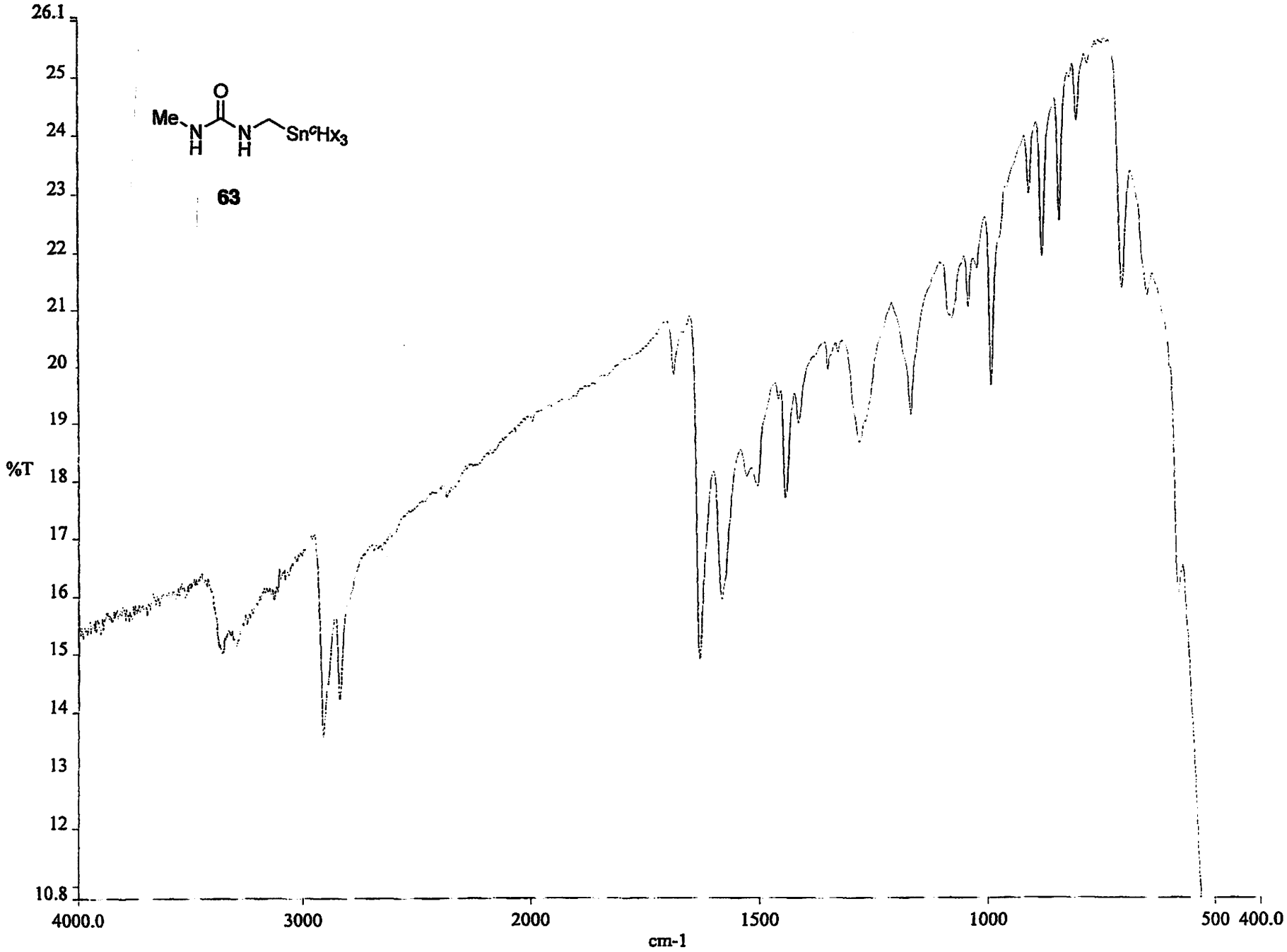
DEC. & VT	
dfrq	500.229
dn	H1
dpwr	36
dof	-500.0
dm	y
dmm	w
dmf	10000
dseq	
dres	1.0
homo	n

PROCESSING	
lb	0.30
wtfile	
proc	ft
fn	131072
math	f
werr	
wexp	
wbs	
wnt	



63




26.1
25
24
23
22
21
20
19
18
17
16
15
14
13
12
10.8
%T
Me
N
H
O
N
H
SnCHx3
63
4000.0
3000
2000
1500
1000
500
400.0
cm-1

solvent	CD_3OD

ACQUISITION	
sfrq	500.437
tn	H1
at	4.999
np	120102
sw	12012.0
fb	not used
bs	1
tpwr	56
pw	8.0
d1	0.100
tof	3003.2
nt	16
ct	16
alock	n
gain	not used

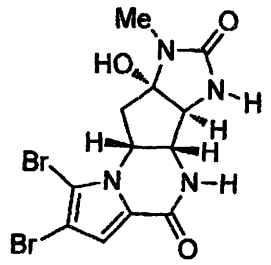
FLAGS	
il	n
in	n
dp	y
hs	nn

DISPLAY	
sp	-250.2
wp	6255.4
vs	63
sc	0
wc	250
hzmm	25.02
is	33.57
rfl	2159.4
rfp	1656.4
th	4
ins	100.000

ai cdc ph

DEC. & VT	
dfrq	125.846
dn	C13
dpwr	30
dof	0
dm	nnn
dmm	c
dmf	200
dseq	
dres	1.0
homo	n

PROCESSING	
wtfile	
proc	ft
fn	262144
math	f
werr	
wexp	
wbs	
wnt	wft



(-)-agelastatin B (2)

solvent	CD3OD

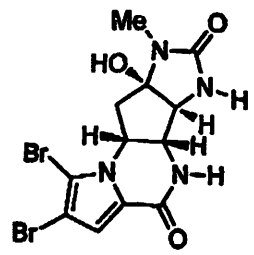
ACQUISITION	
sfrq	125.795
tn	C13
at	1.736
np	131010
sw	37735.8
fb	not used
bs	4
ss	1
tpwr	53
pw	6.9
d1	0.763
tof	631.4
nt	1e+09
ct	16156
alock	n
gain	60

FLAGS	
il	n
in	n
dp	y
hs	nn

DISPLAY	
sp	-6116.3
wp	37735.3
vs	3668
sc	0
wc	250
hzmm	150.94
is	0.01
rfl	12299.3
rfp	6182.5
th	12
ins	1.000
ai	ph

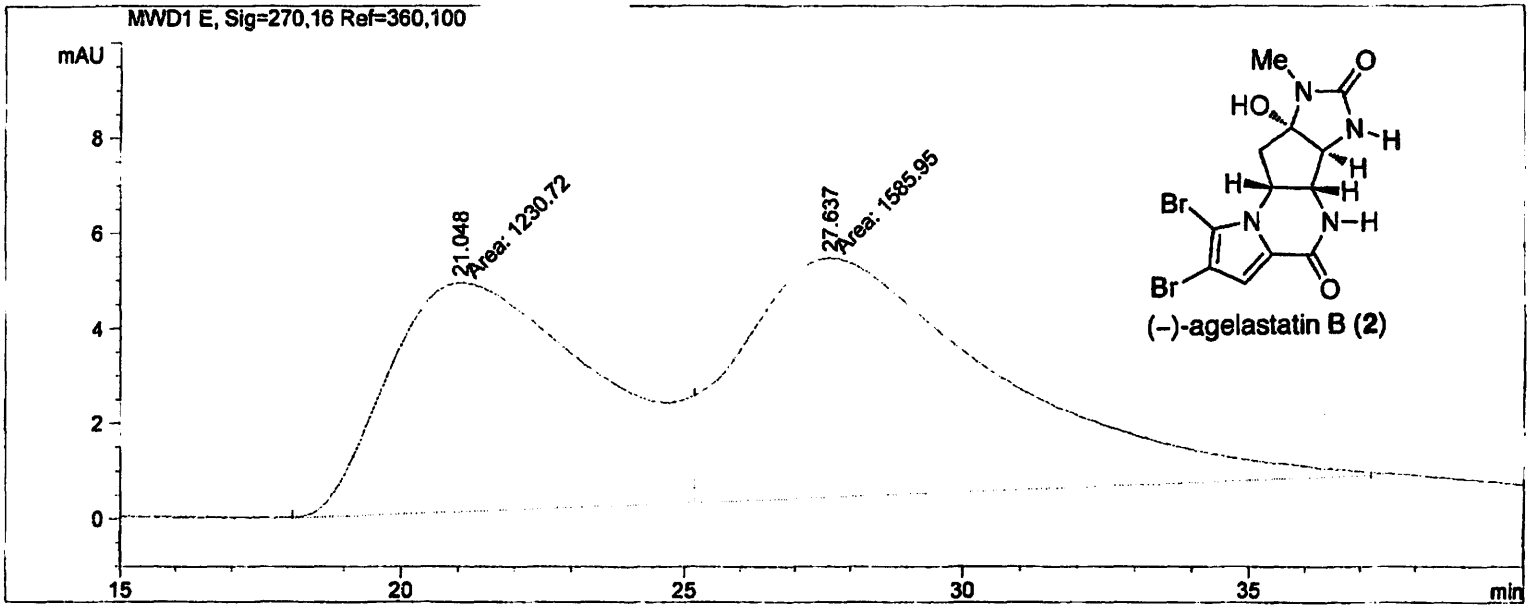
DEC. & VT	
dfrq	500.231
dn	H1
dpwr	38
dof	-500.0
dm	y
dmm	w
dmf	10000
dseq	
dres	1.0
homo	n

PROCESSING	
lb	0.30
wtfile	
proc	ft
fn	131072
math	f
werr	
wexp	
wbs	
wnt	



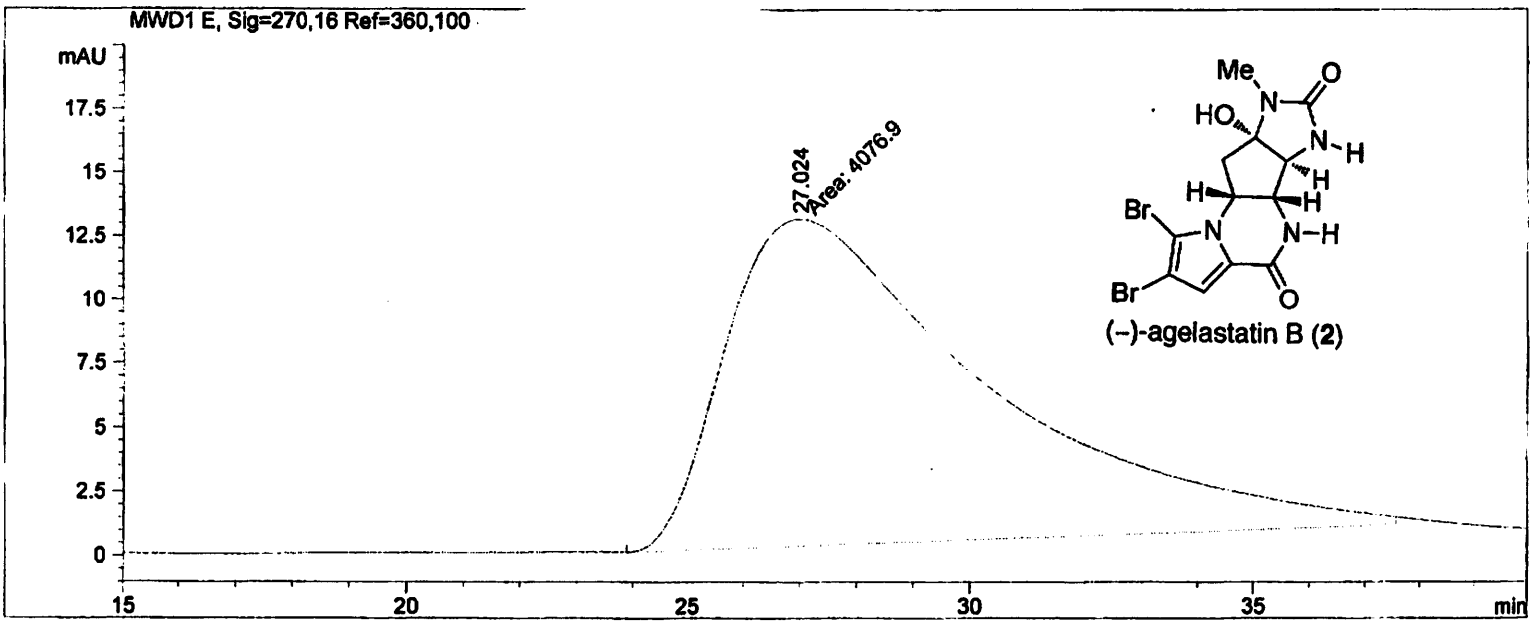
(-)-agelastatin B (2)

```
==========================================================================
Injection Date  :                                  Seq. Line :   1
Sample Name     :                                   Location : Vial 79
Acq. Operator   :                                        Inj :   1
                                                  Inj Volume : 3 µl
Acq. Method     :
Last changed    :

Analysis Method :
Last changed    :

==========================================================================
```

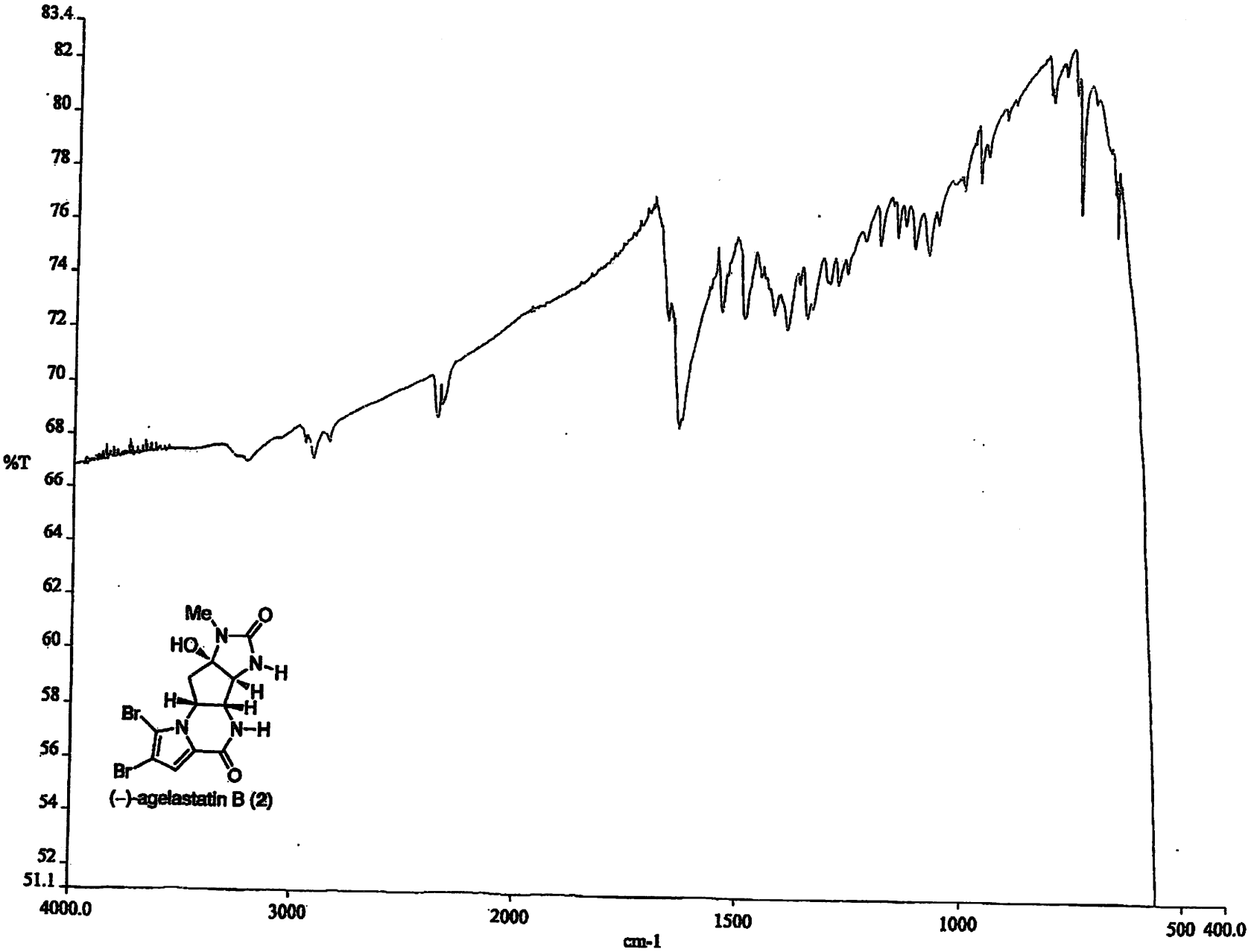



```
==========================================================================
                          Area Percent Report
==========================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: MWD1 E, Sig=270,16 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]       [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  21.048 MF    4.2737 1230.71851    4.79959  43.6941
   2  27.637 FM    5.2827 1585.95435    5.00365  56.3059

Totals :                  2816.67285    9.80324

 Results obtained with enhanced integrator!
==========================================================================
                          *** End of Report ***
```

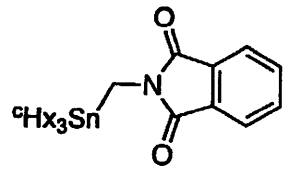
```
Injection Date  :                                   Seq. Line :   1
Sample Name     :                                    Location : Vial 80
Acq. Operator   :                                        Inj :   1
                                                  Inj Volume : 5 µl
Acq. Method     :
Last changed    :
Analysis Method :
Last changed    :
```



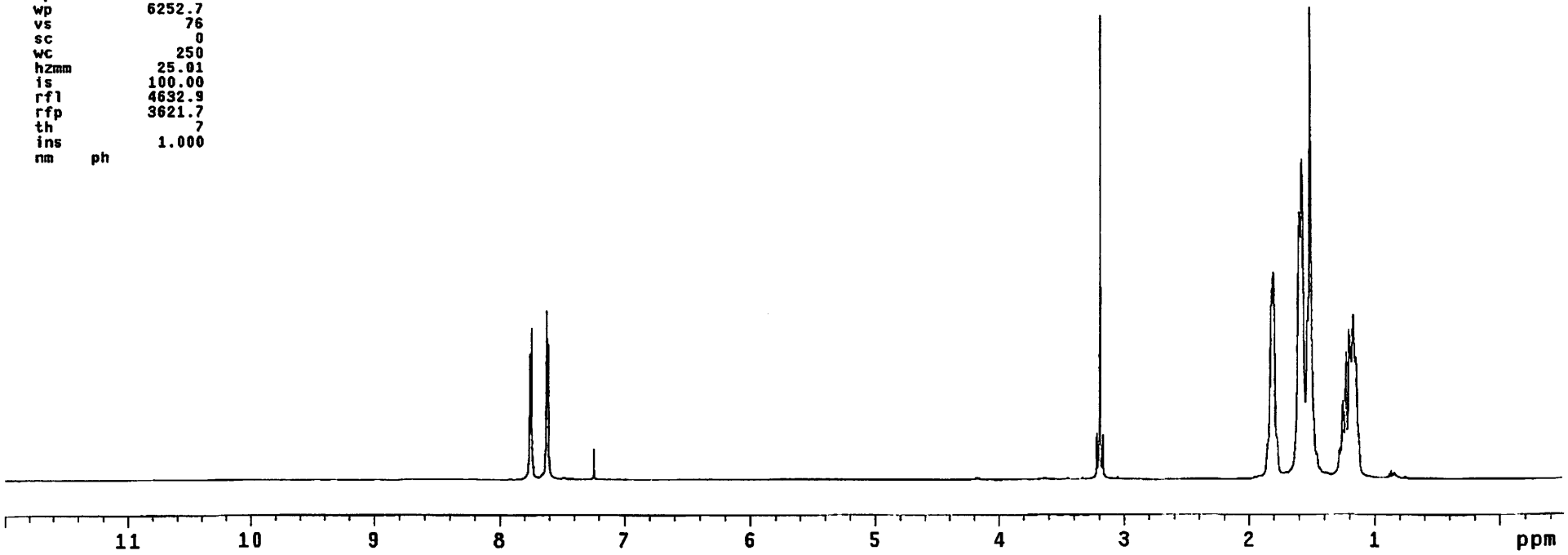

```
                        Area Percent Report

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: MWD1 E, Sig=270,16 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  27.024 MM    5.3130 4076.89722   12.78911 100.0000

Totals :                  4076.89722   12.78911

 Results obtained with enhanced integrator!

                        *** End of Report ***
```


83.4
82
80
78
76
74
72
70
68
%T
66
64
62
60
58
56
54
52
51.1
4000.0
3000
2000
1500
1000
500 400.0
cm-1
Me
HO
N
O
N-H
H
H
H
Br
N
N-H
Br
O
(–)-agelastatin B (2)

solvent	$CDCl_3$	DEC. & VT	
		dfrq	125.794
		dn	C13
		dpwr	38
		dof	0
		dm	nnn
		dmm	c
ACQUISITION		dmf	10000
sfrq	500.231	dseq	
tn	H1	dres	1.0
at	3.200	homo	n
np	64000	PROCESSING	
sw	10000.0	wtfile	
fb	not used	proc	ft
bs	2	fn	131072
ss	1	math	f
tpwr	58		
pw	9.0	werr	
d1	0	wexp	
tof	1498.2	wbs	
nt	16	wnt	
ct	16		
alock	n		
gain	not used		
FLAGS			
il	n		
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-250.2		
wp	6252.7		
vs	76		
sc	0		
wc	250		
hzmm	25.01		
is	100.00		
rfl	4632.9		
rfp	3621.7		
th	7		
ins	1.000		
nm	ph		



S7



solvent	$CDCl_3$

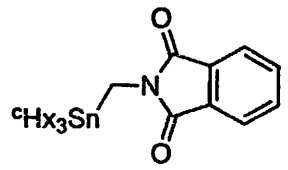
ACQUISITION	
sfrq	125.795
tn	C13
at	1.736
np	131010
sw	37735.8
fb	not used
bs	2
ss	1
tpwr	53
pw	6.9
d1	0.763
tof	631.4
nt	1000
ct	158
alock	n
gain	not used

FLAGS	
il	n
in	n
dp	y
hs	nn

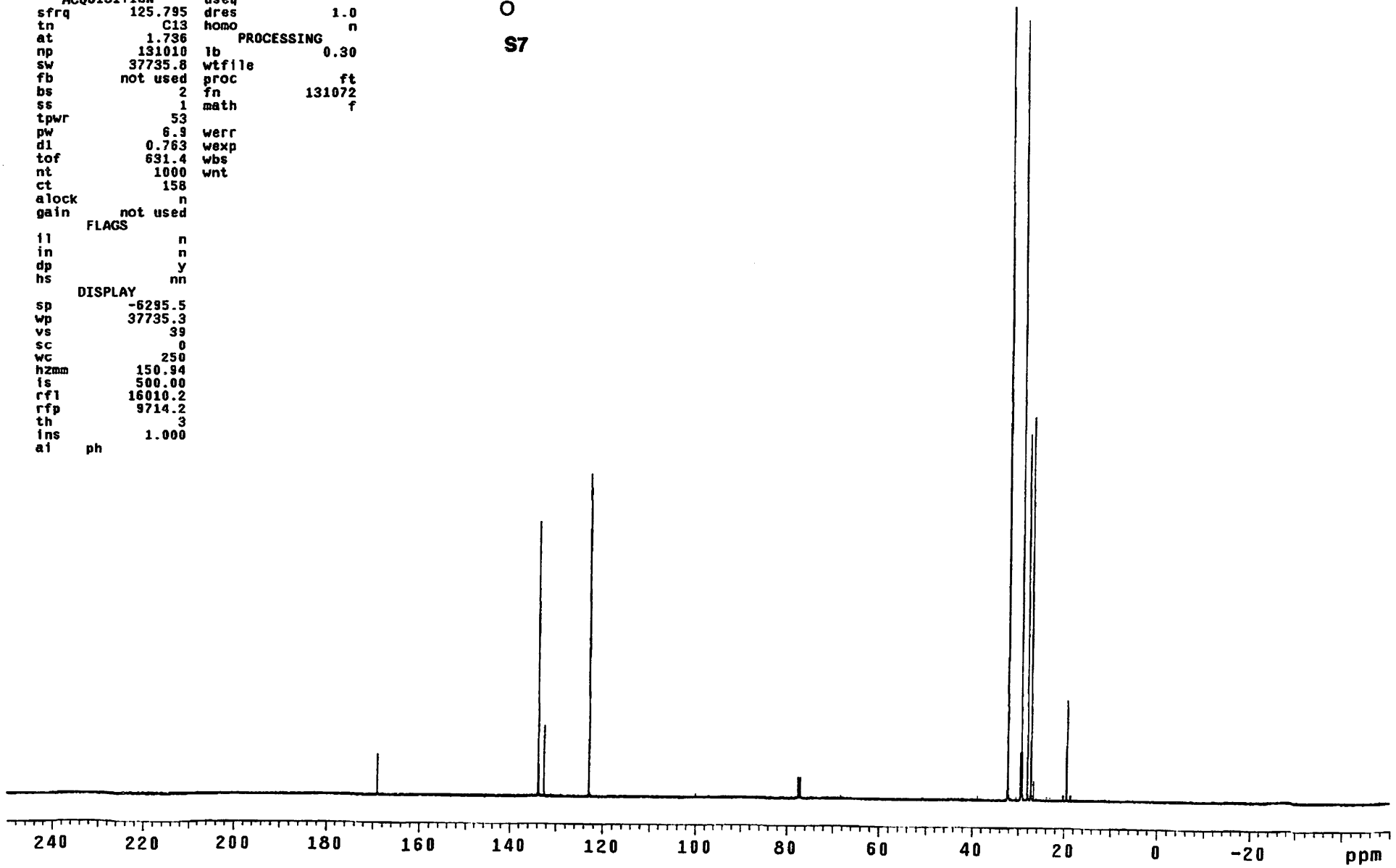
DISPLAY	
sp	-6295.5
wp	37735.3
vs	39
sc	0
wc	250
hzmm	150.94
is	500.00
rfl	16010.2
rfp	9714.2
th	3
ins	1.000
ai	ph

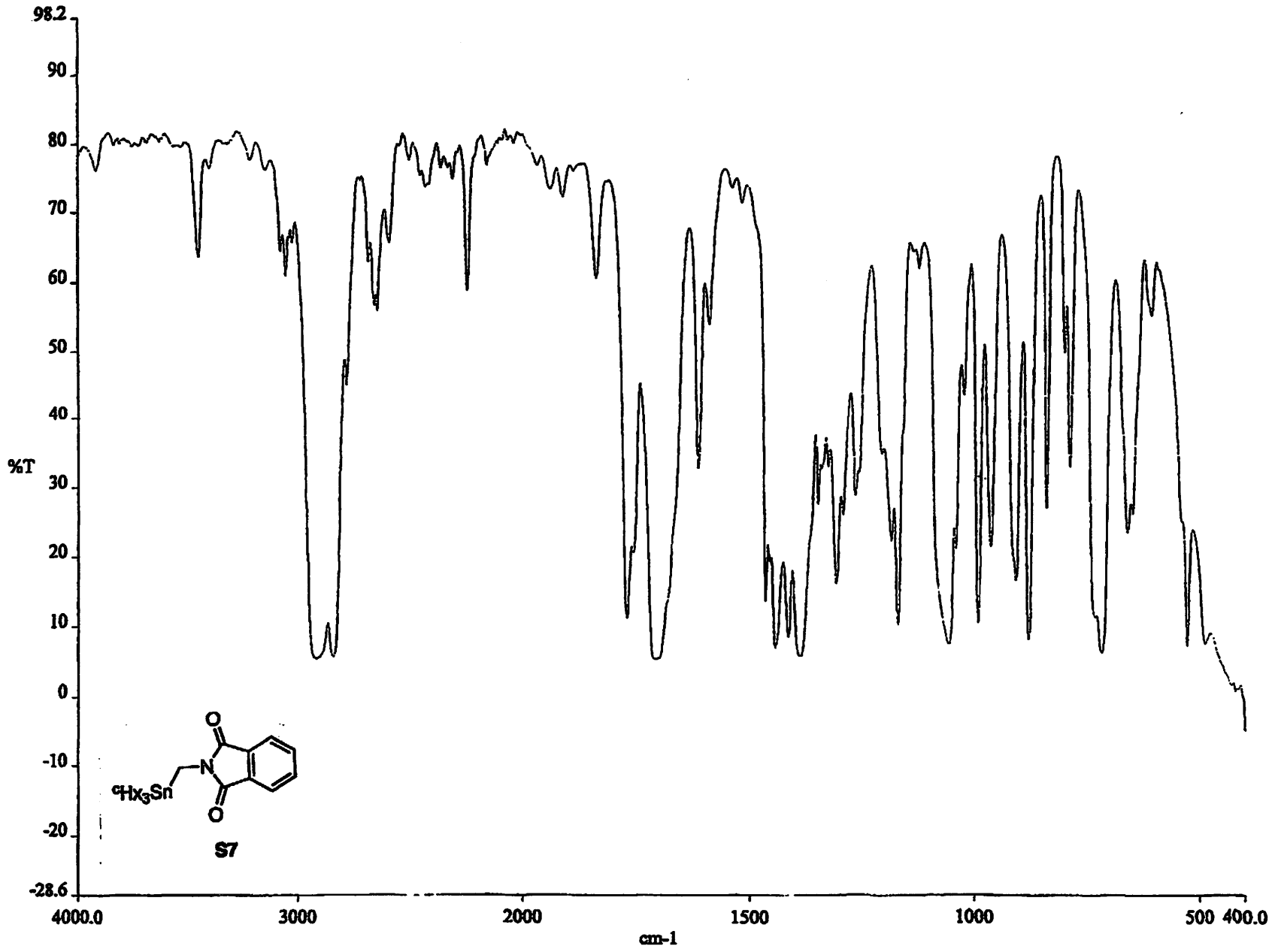
DEC. & VT	
dfrq	500.229
dn	H1
dpwr	38
dof	-500.0
dm	y
dmm	w
dmf	10000
dseq	
dres	1.0
homo	n

PROCESSING	
lb	0.30
wtfile	
proc	ft
fn	131072
math	f
werr	
wexp	
wbs	
wnt	



S7




98.2
90
80
70
60
50
40
%T
30
20
10
0
-10
-20
-28.6
4000.0
3000
2000
1500
1000
500 400.0
cm-1
cHx3Sn
O
N
O
S7

solvent	$CDCl_3$

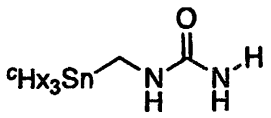
ACQUISITION	
sfrq	500.435
tn	H1
at	4.999
np	120102
sw	12012.0
fb	not used
bs	2
tpwr	56
pw	8.0
d1	0.100
tof	3003.2
nt	32
ct	24
alock	n
gain	not used

FLAGS	
il	n
in	n
dp	y
hs	nn

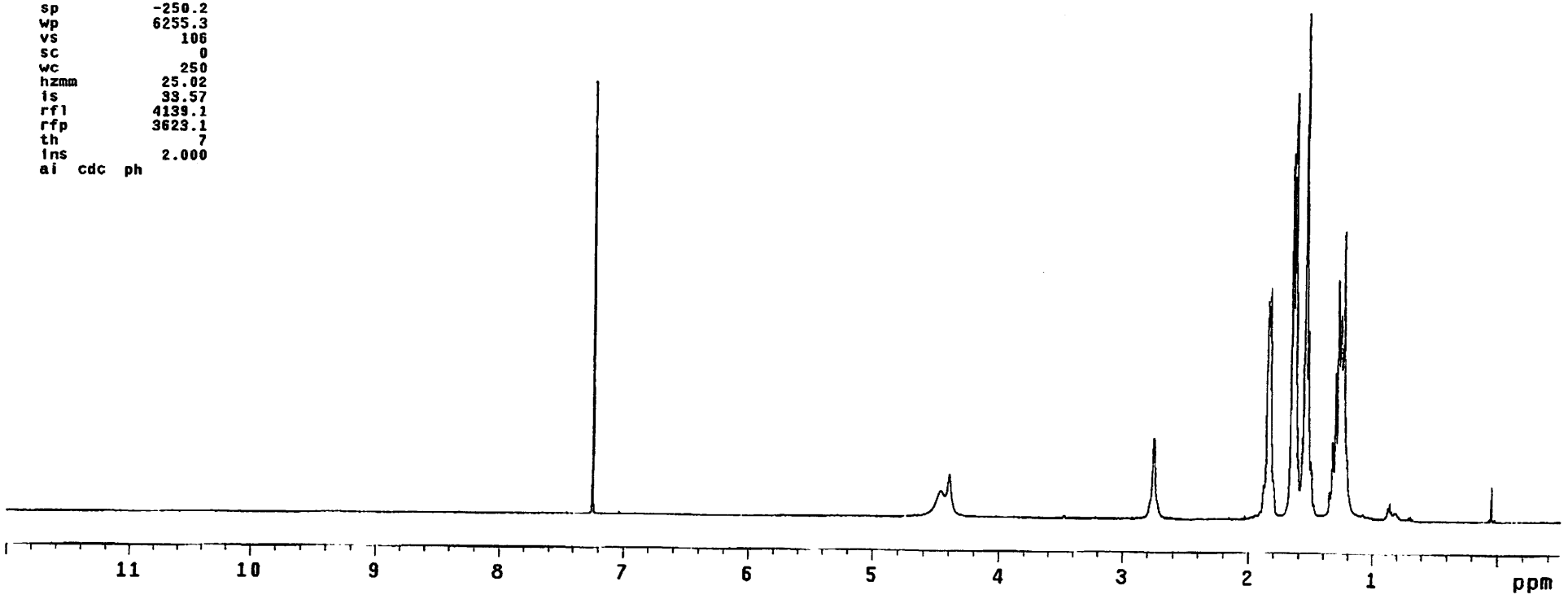
DISPLAY	
sp	-250.2
wp	6255.3
vs	106
sc	0
wc	250
hzmm	25.02
is	33.57
rfl	4139.1
rfp	3623.1
th	7
ins	2.000
ai cdc ph	

DEC. & VT	
dfrq	125.845
dn	C13
dpwr	30
dof	0
dm	nnn
dmm	c
dmf	200
dseq	
dres	1.0
homo	n

PROCESSING	
wtfile	
proc	ft
fn	262144
math	f
werr	
wexp	
wbs	
wnt	wft



64



solvent CDCl3

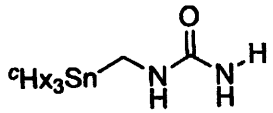
ACQUISITION	
sfrq	125.795
tn	C13
at	1.736
np	131010
sw	37735.8
fb	not used
bs	2
ss	1
tpwr	53
pw	6.9
d1	0.763
tof	631.4
nt	40000
ct	13630
alock	n
gain	60

FLAGS	
il	n
in	n
dp	y
hs	nn

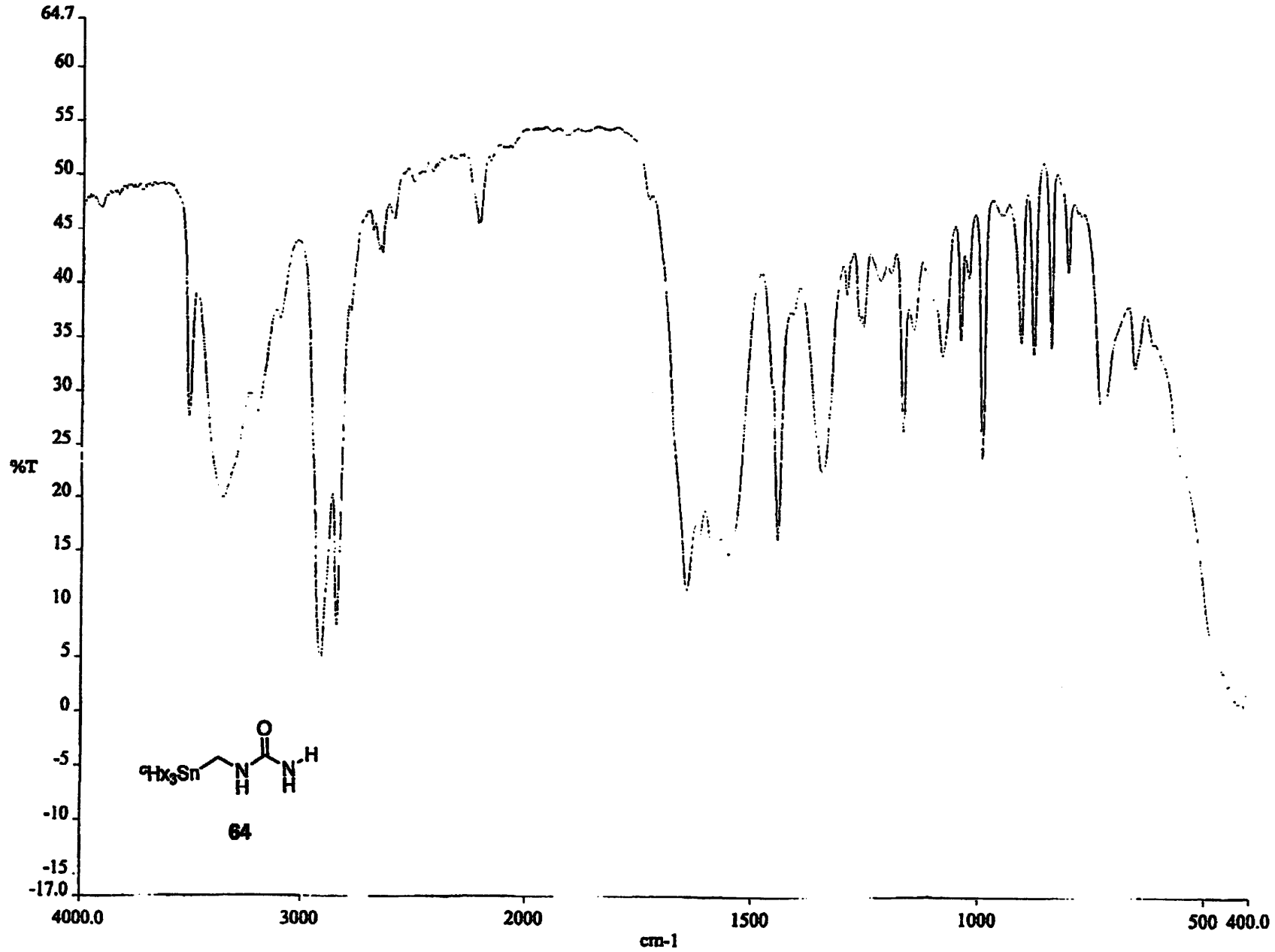
DISPLAY	
sp	-6287.5
wp	37735.8
vs	5116
sc	0
wc	250
hzmm	12.50
is	500.00
rfl	16002.4
rfp	9714.9
th	31
ins	1.000
ai	ph

DEC. & VT	
dfrq	500.229
dn	H1
dpwr	38
dof	-500.0
dm	y
dmm	w
dmf	10000
dseq	
dres	1.0
homo	n
temp	20.0

PROCESSING	
lb	0.30
wtfile	
proc	ft
fn	131072
math	f
werr	
wexp	
wbs	
wnt	



64


64.7
60
55
50
45
40
35
30
25
%T
20
15
10
5
0
-5
-10
-15
-17.0
4000.0
3000
2000
1500
1000
500 400.0
cm-1
O
H
N
N
H
H
64

solvent CD_3OD

ACQUISITION	
sfrq	500.437
tn	H1
at	4.999
np	120102
sw	12012.0
fb	not used
bs	2
tpwr	56
pw	8.0
d1	0.100
tof	3003.2
nt	32
ct	24
alock	n
gain	not used

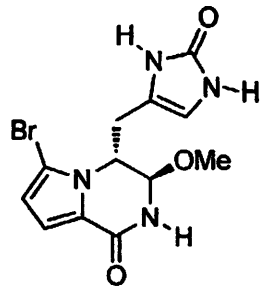
FLAGS	
il	n
in	n
dp	y
hs	nn

DISPLAY	
sp	-250.2
wp	6255.4
vs	13
sc	0
wc	250
hzmm	25.02
is	0.01
rfl	2159.4
rfp	1656.4
th	7
ins	1.000

al cdc ph

DEC. & VT	
dfrq	125.846
dn	C13
dpwr	30
dof	0
dm	nnn
dmm	c
dmf	200
dseq	
dres	1.0
homo	n

PROCESSING	
wtfile	
proc	ft
fn	262144
math	f
werr	
wexp	
wbs	
wnt	wft



(+)-*O*-Me-pre-agelastatin D (65)

solvent	CD_3OD

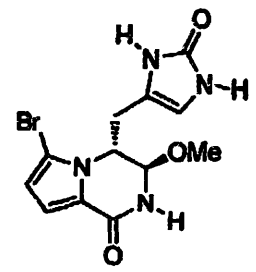
ACQUISITION	
sfrq	125.795
tn	C13
at	1.736
np	131010
sw	37735.8
fb	not used
bs	2
ss	1
tpwr	53
pw	6.8
d1	0.763
tof	631.4
nt	10000
ct	888
alock	n
gain	not used

FLAGS	
il	n
in	n
dp	y
hs	nn

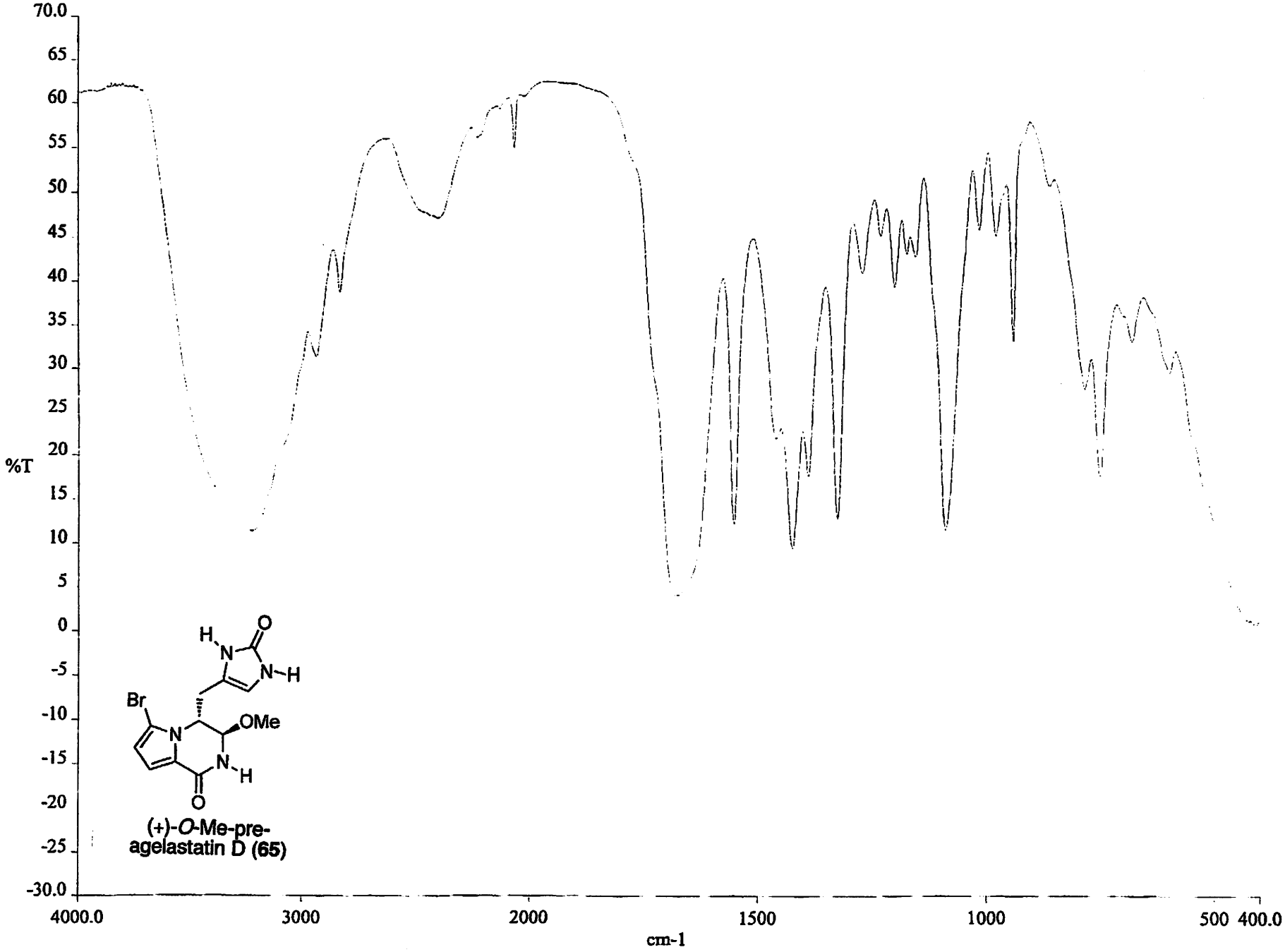
DISPLAY	
sp	-6118.7
wp	37735.3
vs	268
sc	0
wc	250
hzmm	2.78
is	500.00
rfl	12301.5
rfp	6182.2
th	20
ins	1.000
ai	ph

DEC. & VT	
dfrq	500.231
dn	H1
dpwr	38
dof	-500.0
dm	y
dmm	w
dmf	10000
dseq	
dres	1.0
homo	n

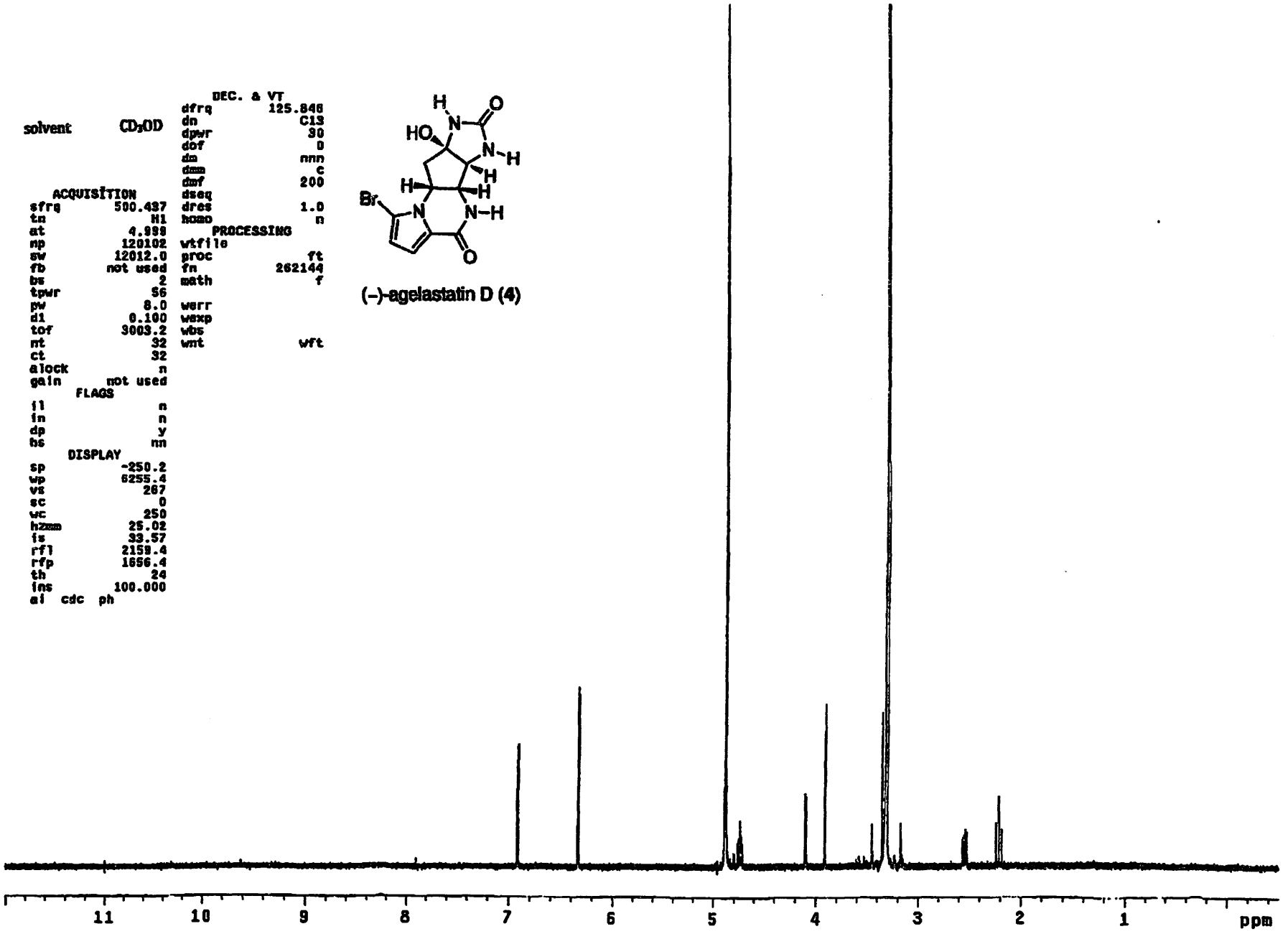
PROCESSING	
lb	0.30
wtfile	
proc	ft
fn	131072
math	f
werr	
wexp	
wbs	
wnt	

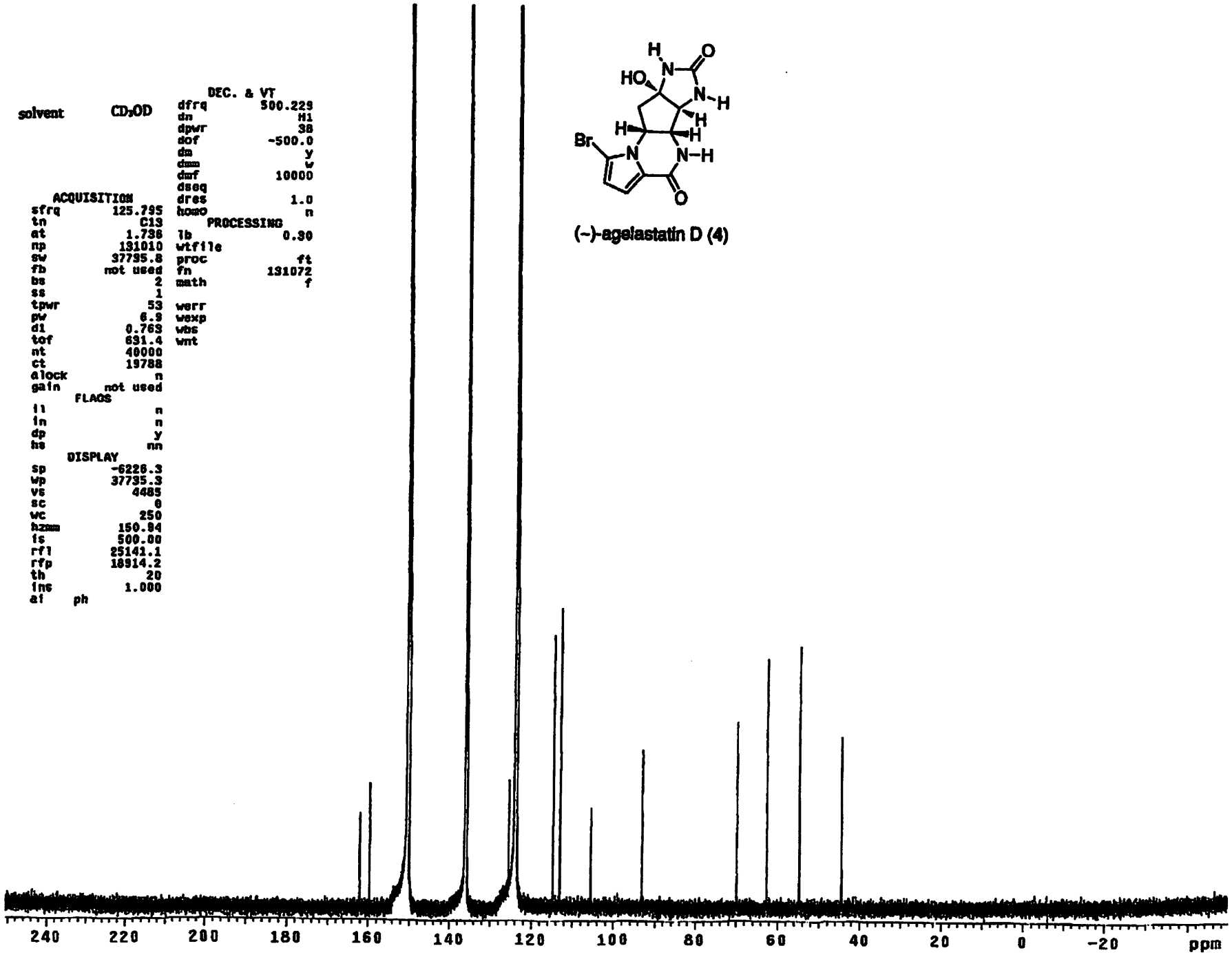


(+)-*O*-Me-pre-agelastatin D (65)



(+)-*O*-Me-pre-agelastatin D (65)


solvent CD3OD
ACQUISITION
sfrq 500.437
tn H1
at 4.998
np 120102
sw 12012.0
fb not used
bs 2
tpwr 56
pw 8.0
d1 0.100
tof 3003.2
nt 32
ct 32
alock n
gain not used
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -250.2
wp 6255.4
vs 287
sc 0
wc 250
hzmm 25.02
is 33.57
rfl 2159.4
rfp 1656.4
th 24
ins 100.000
ai cdc ph
DEC. & VT
dfrq 125.846
dn C13
dpwr 30
dof 0
dm nnn
dmm c
dmf 200
dseq
dres 1.0
homo n
PROCESSING
wtfile
proc ft
fn 262144
math f
werr
wexp
wbs
wnt wft
(–)-agelastatin D (4)
11
10
9
8
7
6
5
4
3
2
1
ppm

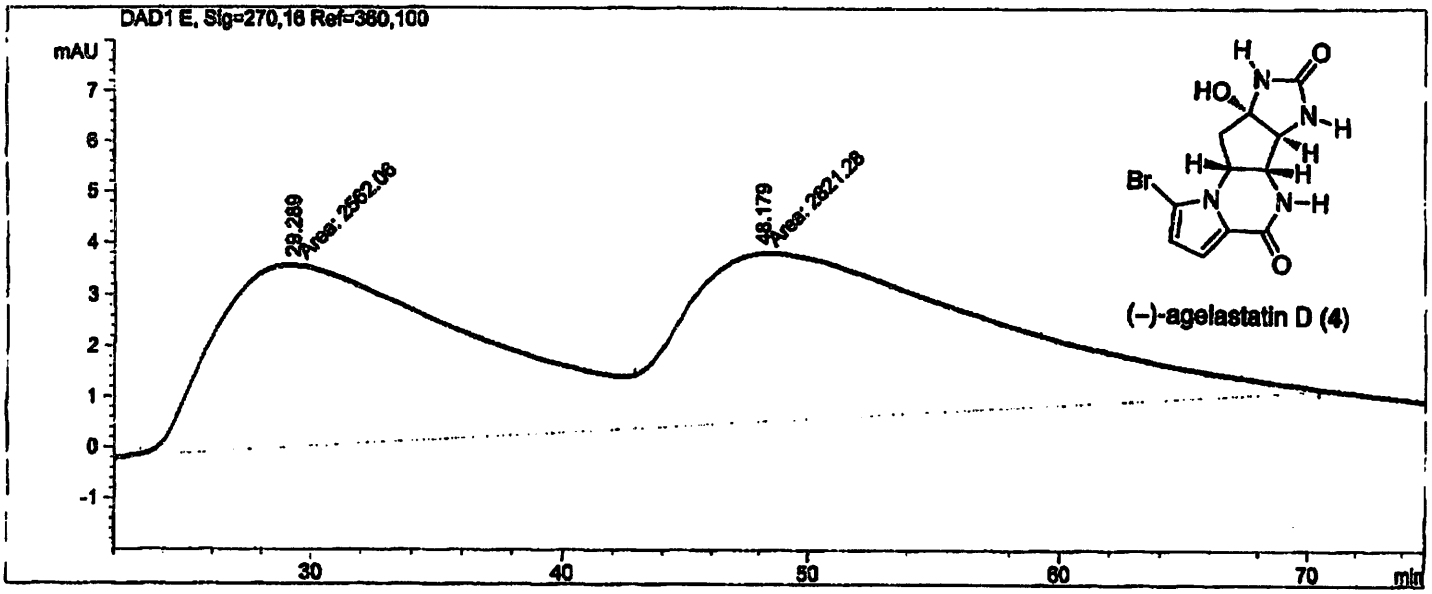

solvent CD3OD
ACQUISITION
sfrq 125.795
tn C13
at 1.736
np 131010
sw 37735.8
fb not used
bs 2
ss 1
tpwr 53
pw 6.9
d1 0.768
tof 631.4
nt 40000
ct 19788
alock n
gain not used
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -6228.3
wp 37735.3
vs 4485
sc 0
wc 250
hzmm 150.84
is 500.00
rfl 25141.1
rfp 18914.2
th 20
ins 1.000
ai ph
DEC. & VT
dfrq 500.229
dn H1
dpwr 38
dof -500.0
dm y
dmm w
dmf 10000
dseq
dres 1.0
homo n
PROCESSING
lb 0.30
wtfile
proc ft
fn 131072
math f
werr
wexp
wbs
wnt
(-)-agelastatin D (4)
240
220
200
180
160
140
120
100
80
60
40
20
0
-20
ppm

Injection Date :
Sample Name :
Acq. Operator :

Seq. Line : 1
Location : Vial 61
Inj : 1
Inj Volume : 1 µl

Different Inj Volume from Sequence ! Actual Inj Volume : 3 µl

Acq. Method :
Last changed :
Analysis Method :
Last changed :



Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 E, Sig=270,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	29.289	MF	11.8707	2562.06494	3.59718	47.5924
2	48.179	FM	14.0578	2821.28418	3.34485	52.4076

Totals : 5383.34912 6.94203

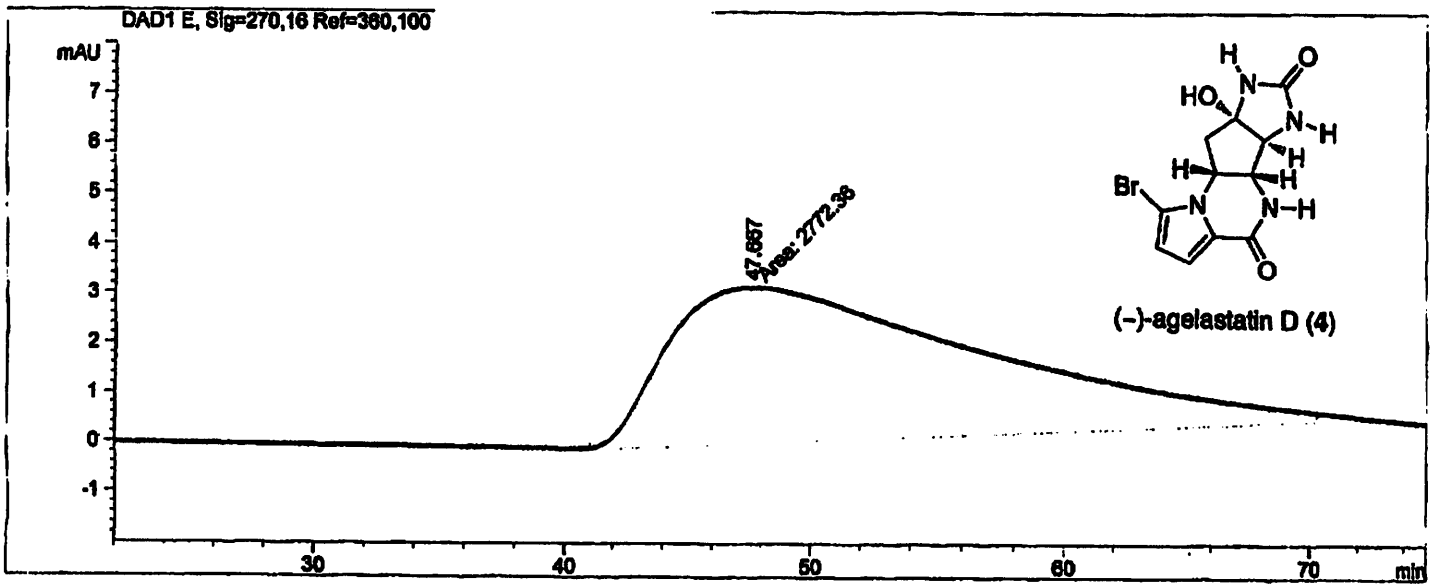
Results obtained with enhanced integrator!

*** End of Report ***

Injection Date :
Sample Name :
Acq. Operator :

Seq. Line : 1
Location : Vial 62
Inj : 1
Inj Volume : 1 µl
Inj Volume : 3 µl

Acq. Method :
Last changed :
Analysis Method :
Last changed :



Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

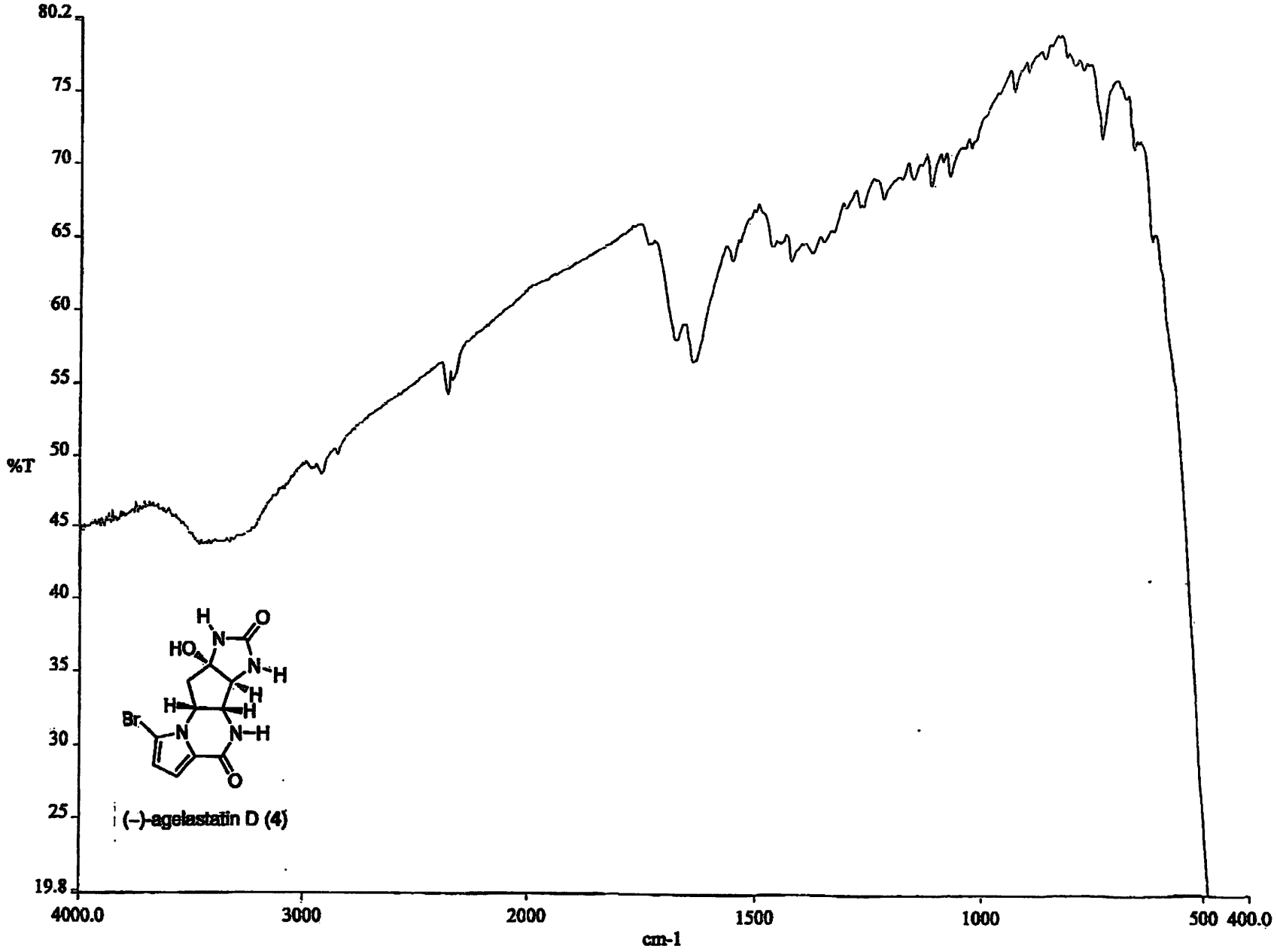
Signal 1: DAD1 E, Sig=270,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	47.667	MM	14.4059	2772.36328	3.20744	100.0000

Totals : 2772.36328 3.20744

Results obtained with enhanced integrator!

*** End of Report ***


80.2
75
70
65
60
55
50
45
40
35
30
25
19.8
%T
4000.0
3000
2000
1500
1000
500
400.0
cm-1
(–)-agelastatin D (4)

solvent	CD_3OD

ACQUISITION	
sfrq	500.437
tn	H1
at	4.999
np	120102
sw	12012.0
fb	not used
bs	2
tpwr	56
pw	8.0
d1	0.100
tof	3003.2
nt	32
ct	24
alock	n
gain	not used

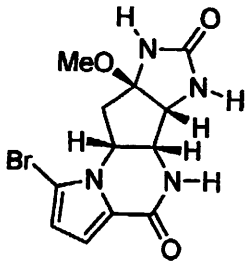
FLAGS	
il	n
in	n
dp	y
hs	nn

DISPLAY	
sp	-250.2
wp	6255.4
vs	99
sc	0
wc	250
hzmm	25.02
is	33.57
rfl	2159.5
rfp	1656.4
th	7
ins	100.000

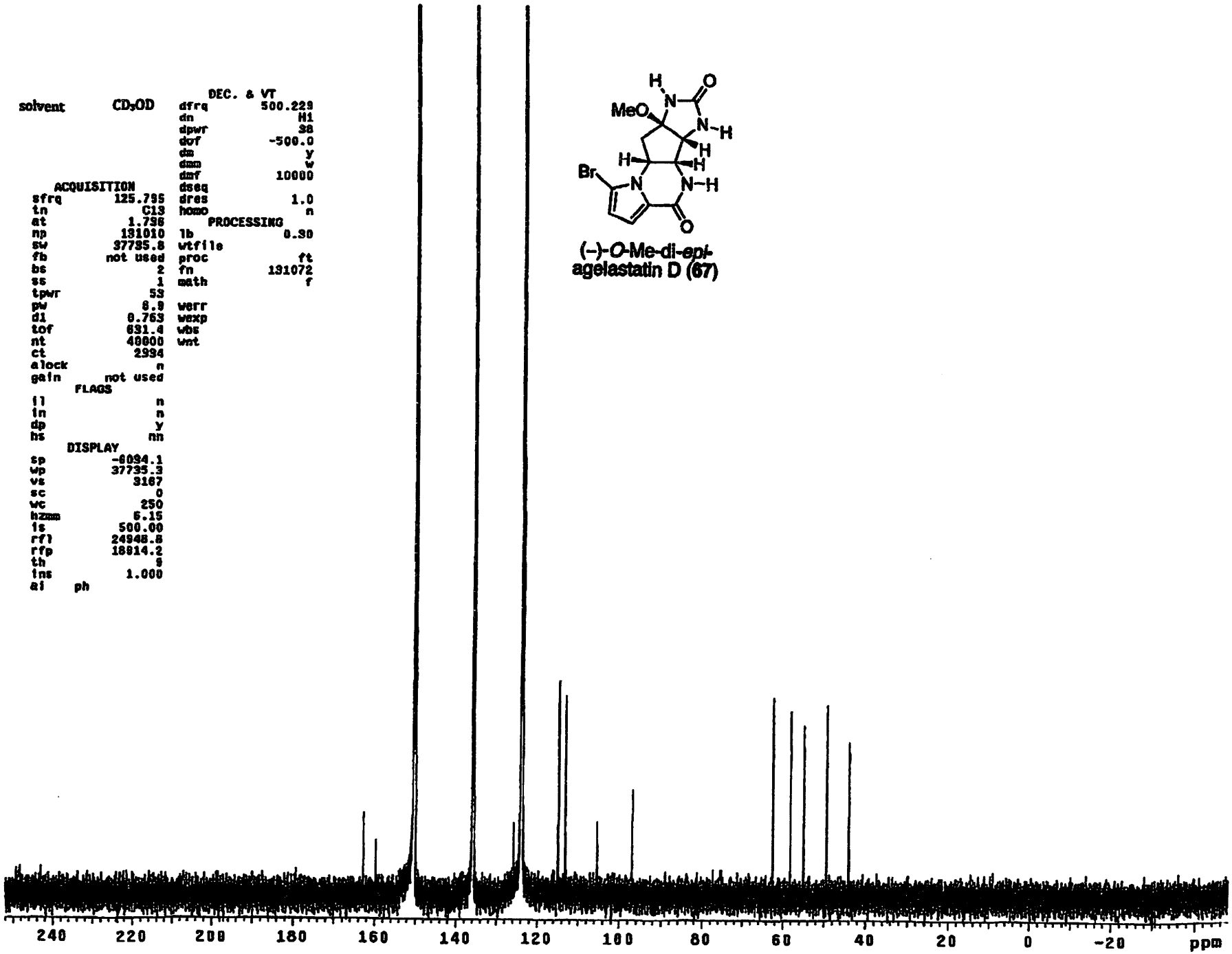
ai cdc ph

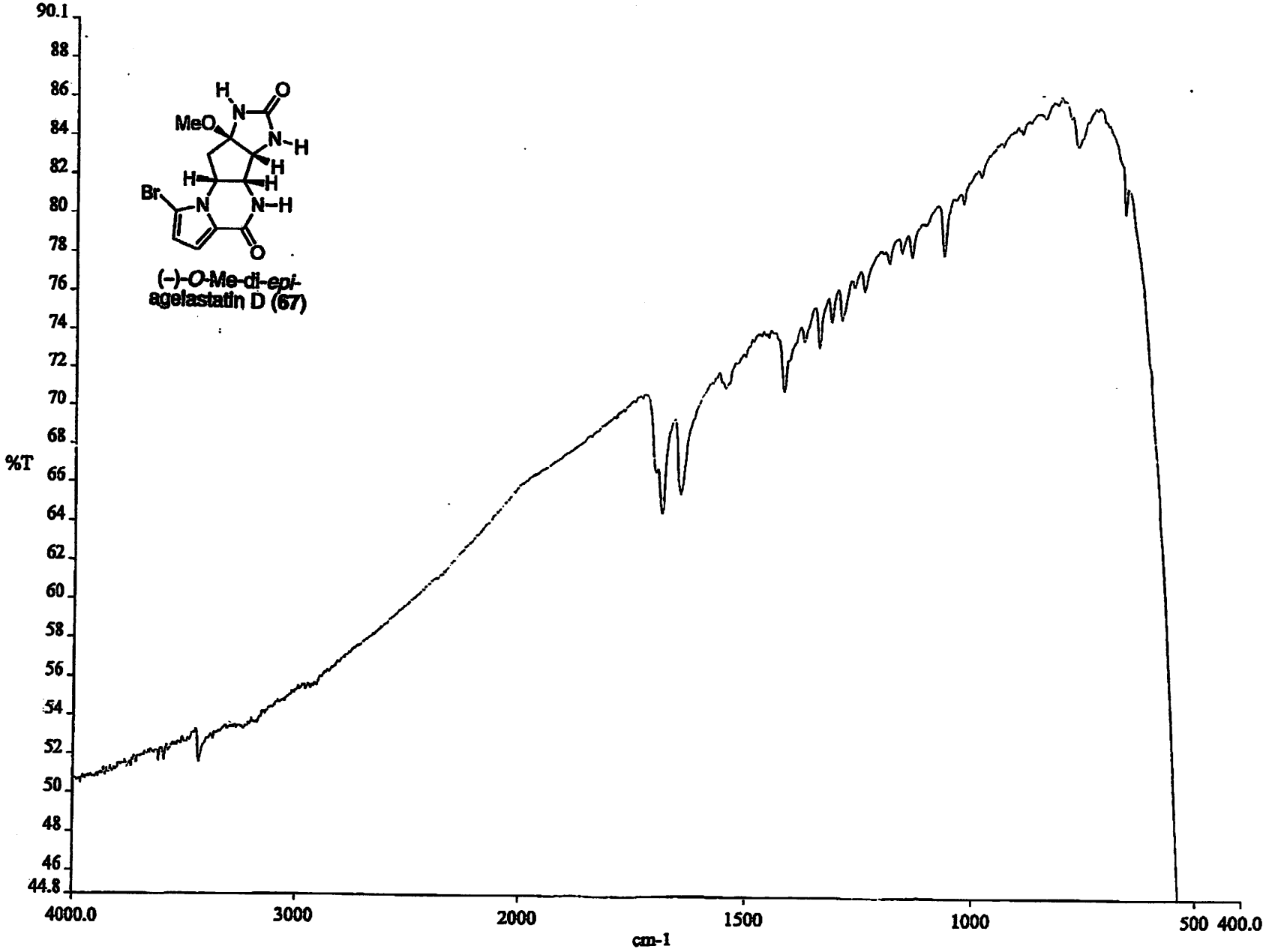
DEC. & VT	
dfrq	125.846
dn	C13
dpwr	30
dof	0
dm	nnn
dmm	c
dmf	200
dseq	
dres	1.0
homo	n

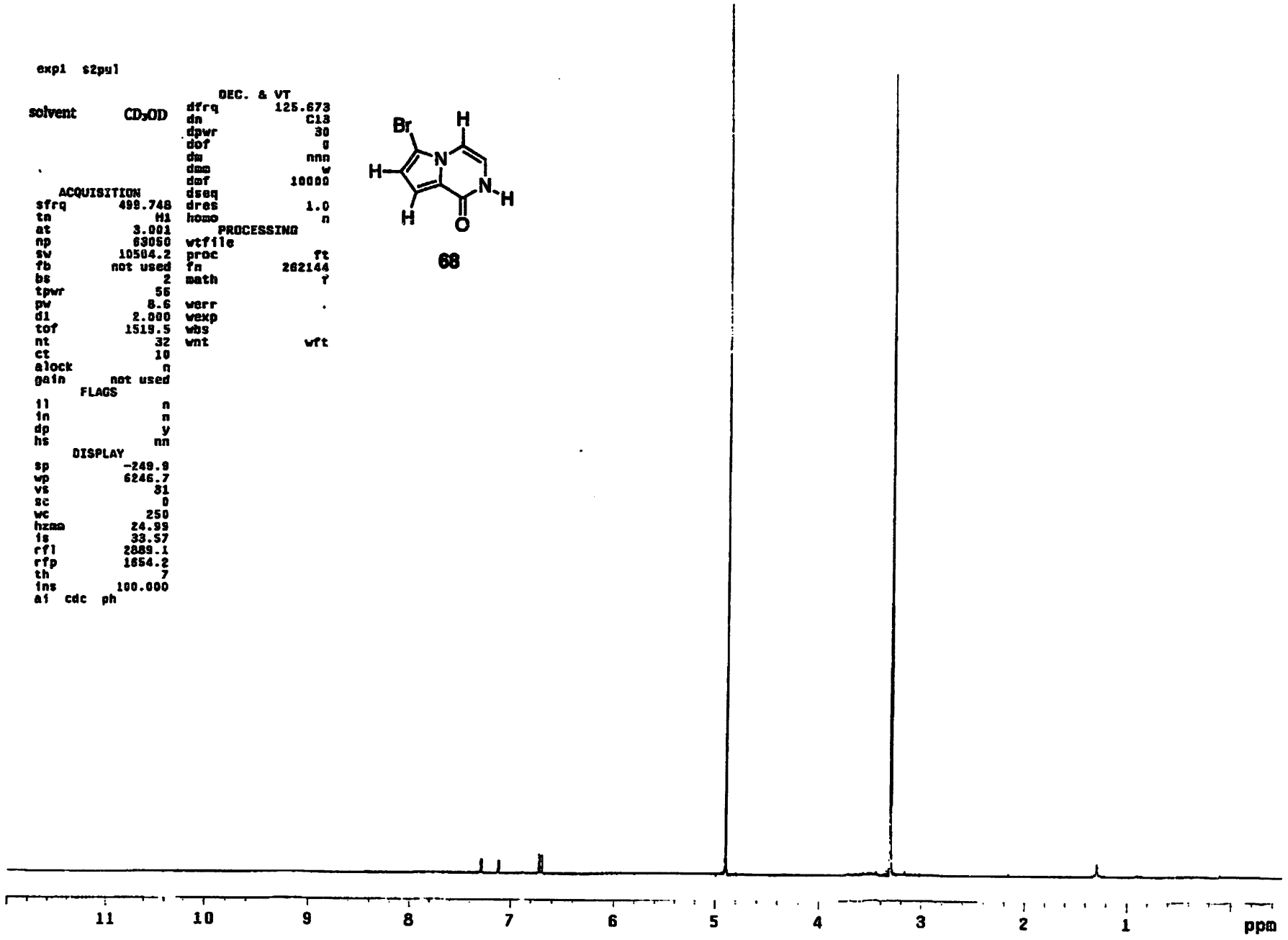
PROCESSING	
wtfile	
proc	ft
fn	262144
math	f
werr	
wexp	
wbs	
wnt	wft

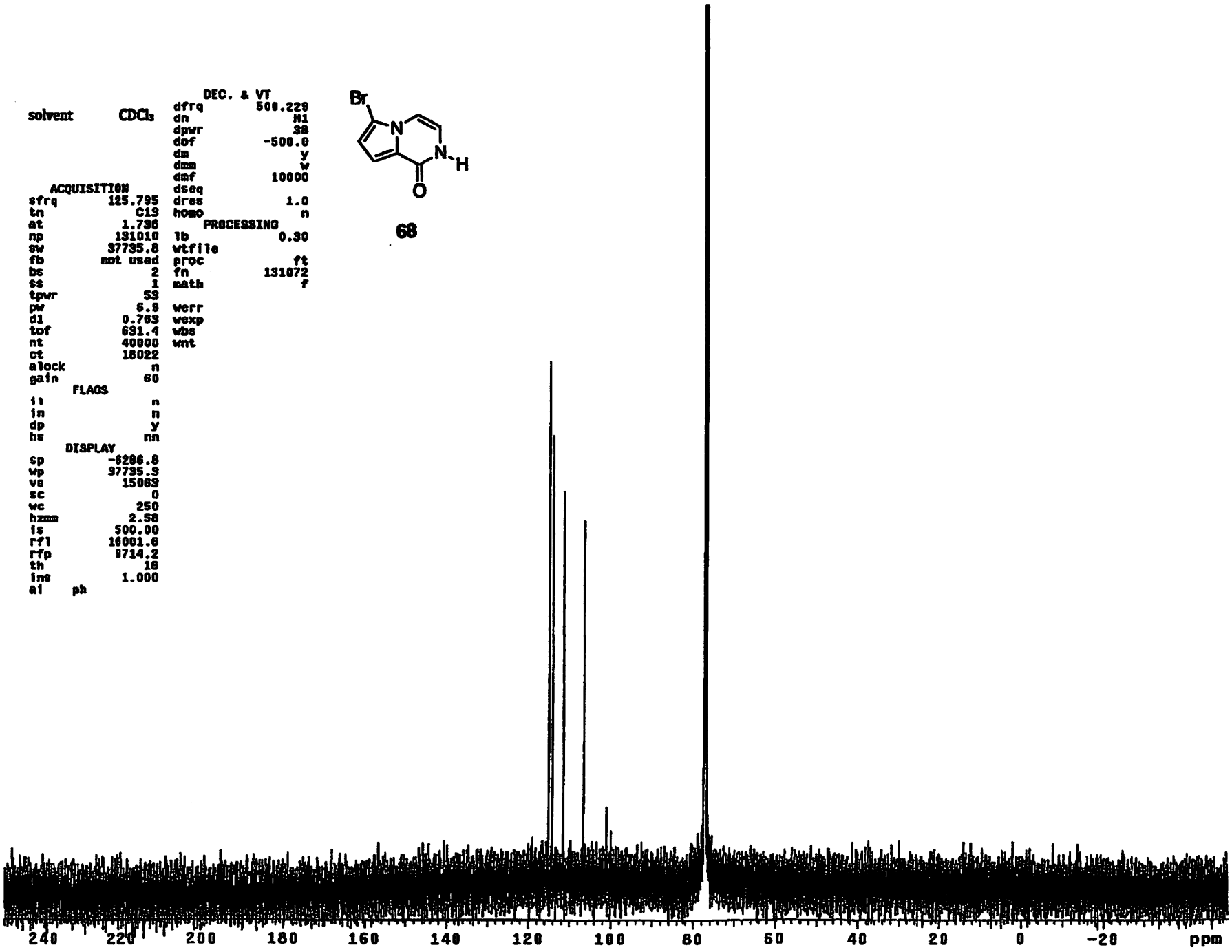


(–)-*O*-Me-di-*epi*-agelastatin D (67)


solvent CD3OD
ACQUISITION
sfrq 125.795
tn C13
at 1.798
np 131010
sw 37735.8
fb not used
bs 2
ss 1
tpwr 53
pw 8.9
dl 0.763
tof 631.4
nt 40000
ct 2994
alock n
gain not used
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -6094.1
wp 37735.3
vs 3167
sc 0
wc 250
hzmm 6.15
is 500.00
rfl 24948.8
rfp 18814.2
th 9
ins 1.000
ai ph
DEC. & VT
dfrq 500.229
dn H1
dpwr 38
dof -500.0
dm y
dmm w
dmf 10000
dseq
dres 1.0
homo n
PROCESSING
lb 0.30
wtfile
proc ft
fn 131072
math f
werr
wexp
wbs
wnt
(–)-O-Me-di-epi-agelastatin D (67)
240
220
200
180
160
140
120
100
80
60
40
20
0
-20
ppm


(–)-O-Me-di-epi-agelastatin D (67)
%T
cm-1
4000.0
3000
2000
1500
1000
500
400.0

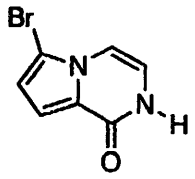

expl s2pul
solvent CD3OD
ACQUISITION
sfrq 499.748
tn H1
at 3.001
np 63050
sw 10504.2
fb not used
bs 2
tpwr 55
pw 8.6
d1 2.000
tof 1519.5
nt 32
ct 10
alock n
gain not used
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -249.9
wp 6246.7
vs 31
sc 0
wc 250
hzmm 24.99
is 33.57
rfl 2889.1
rfp 1654.2
th 7
ins 100.000
ai cdc ph
DEC. & VT
dfrq 125.673
dn C13
dpwr 30
dof 0
dm nnn
dmm w
dmf 10000
dseq
dres 1.0
homo n
PROCESSING
wtfile
proc ft
fn 262144
math f
werr .
wexp
wbs
wnt wft
Br
H
N
H
N
H
H
O
68
11
10
9
8
7
6
5
4
3
2
1
ppm


solvent CDCl3
ACQUISITION
sfrq 125.795
tn C13
at 1.736
np 131010
sw 37735.8
fb not used
bs 2
ss 1
tpwr 53
pw 6.9
d1 0.763
tof 691.4
nt 40000
ct 18022
alock n
gain 60
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -6286.8
wp 37735.9
vs 15063
sc 0
wc 250
hzmm 2.58
is 500.00
rfl 16001.6
rfp 9714.2
th 16
ins 1.000
ai ph
DEC. & VT
dfrq 500.229
dn H1
dpwr 38
dof -500.0
dm y
dmm w
dmf 10000
dseq
dres 1.0
homo n
PROCESSING
lb 0.30
wtfile
proc ft
fn 131072
math f
werr
wexp
wbs
wnt
Br
N
N
H
O
68
240
220
200
180
160
140
120
100
80
60
40
20
0
-20
ppm

gCOSY

solvent	$CDCl_3$
ACQUISITION	
sw	5497.5
at	0.186
np	2048
fb	not used
ss	16
d1	1.000
nt	40
2D ACQUISITION	
sw1	5497.5
ni	128
TRANSMITTER	
tn	H1
sfrq	500.432
tof	264.6
tpwr	56
pw	9.850
GRADIENTS	
gzlvl1	2000
gt1	0.001000
gstab	0.000500
DECOUPLER	
dn	C13
dm	nnn

FLAGS	
hs	nn
sspul	n
hsglvl	2000
SPECIAL	
temp	not used
gain	46
spin	0
F2 PROCESSING	
sb	-0.093
sbs	not used
fn	2048
F1 PROCESSING	
sb1	-0.047
sbs1	not used
proc1	lp
fn1	2048
DISPLAY	
sp	8.3
wp	5492.2
sp1	10.2
wp1	5492.2
rf1	-2.9
rfp	0
rf11	-4.8
rfp1	0
PLOT	
wc	147.0
sc	0
wc2	147.0
sc2	0
vs	81
th	6
ai cdc av	



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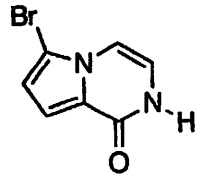
HSQC

solvent CDCl3

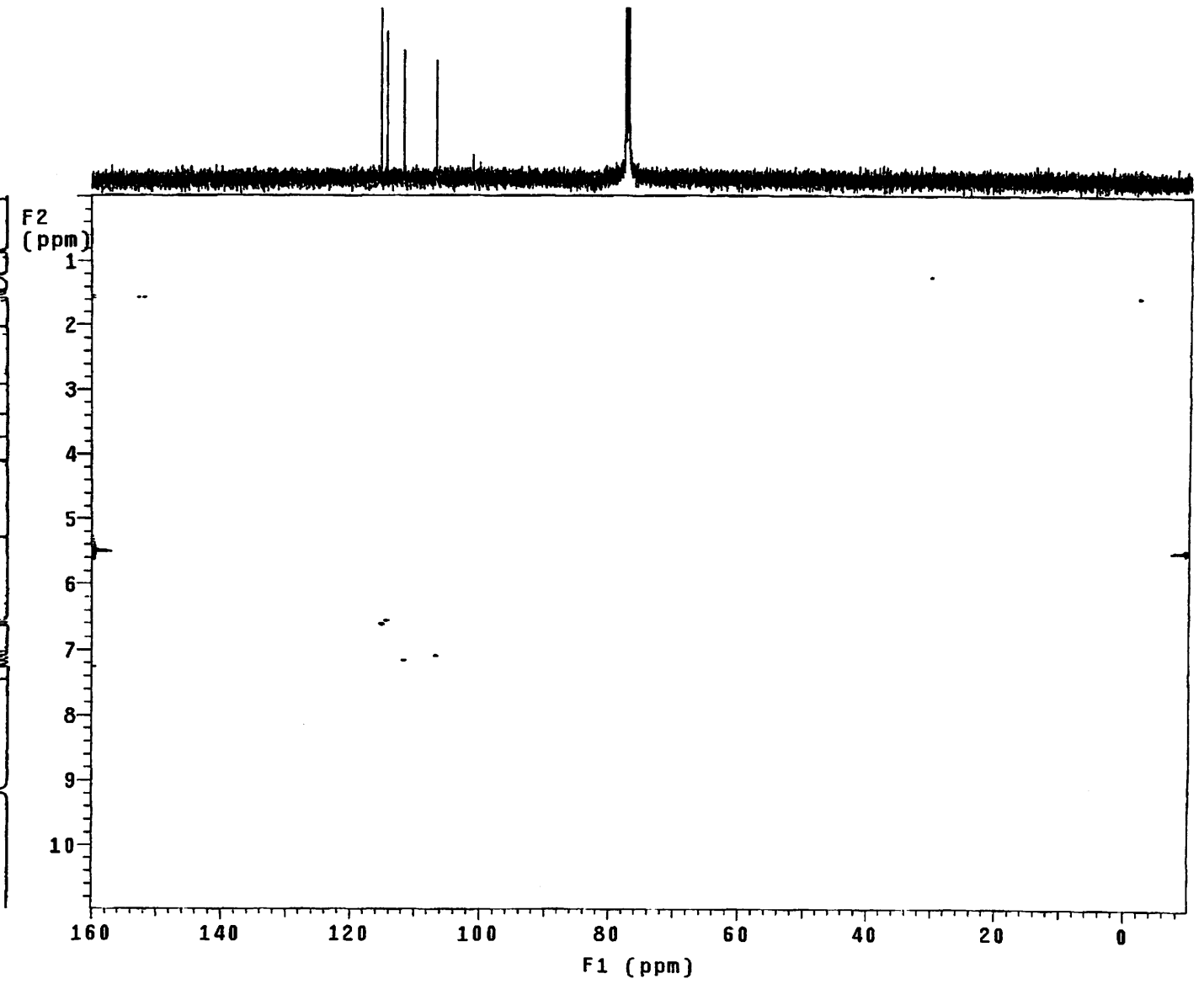
ACQUISITION	
sw	5497.5
at	0.100
np	1098
fb	not used
ss	256
d1	1.000
nt	31
2D ACQUISITION	
sw1	21361.8
ni	256
phase	arrayed
TRANSMITTER	
tn	H1
sfrq	499.744
tof	256.4
tpwr	56
pw	8.950
DECOUPLER	
dn	C13
dof	-2514.7
dm	nny
dmm	ccg
dmf	32200
dpwr	53
pwxlvl	59
pwx	18.000
HSQC	
j1xh	140.0
null	0.350
nullflg	n
mult	2

FLAGS	
hs	n
sspul	n
PFGflg	y
hsglvl	2000
SPECIAL	
temp	not used
gain	58
spin	0
PRESATURATION	
satmode	n
satpwr	0
satdly	0
satfrq	0
F2 PROCESSING	
gf	0.086
gfs	not used
fn	2048
F1 PROCESSING	
sb1	-0.024
sbs1	-0.024
proc1	lp
fn1	2048
DISPLAY	
sp	-5.1
wp	5492.2
sp1	-1231.6
wp1	21341.0
rfl	3314.7
rfp	9304.3
rfl1	15725.1
rfp1	14472.7
PLOT	
wc	250.0
sc	0
wc2	155.0
sc2	0
vs	256
th	2
ai cdc ph	

ACQUISITION ARRAYS	
array	phase
arraydim	512
1	phase
1	1
2	2



68



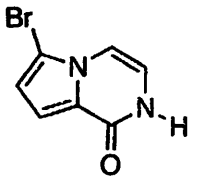
HMBC

solvent	$CDCl_3$

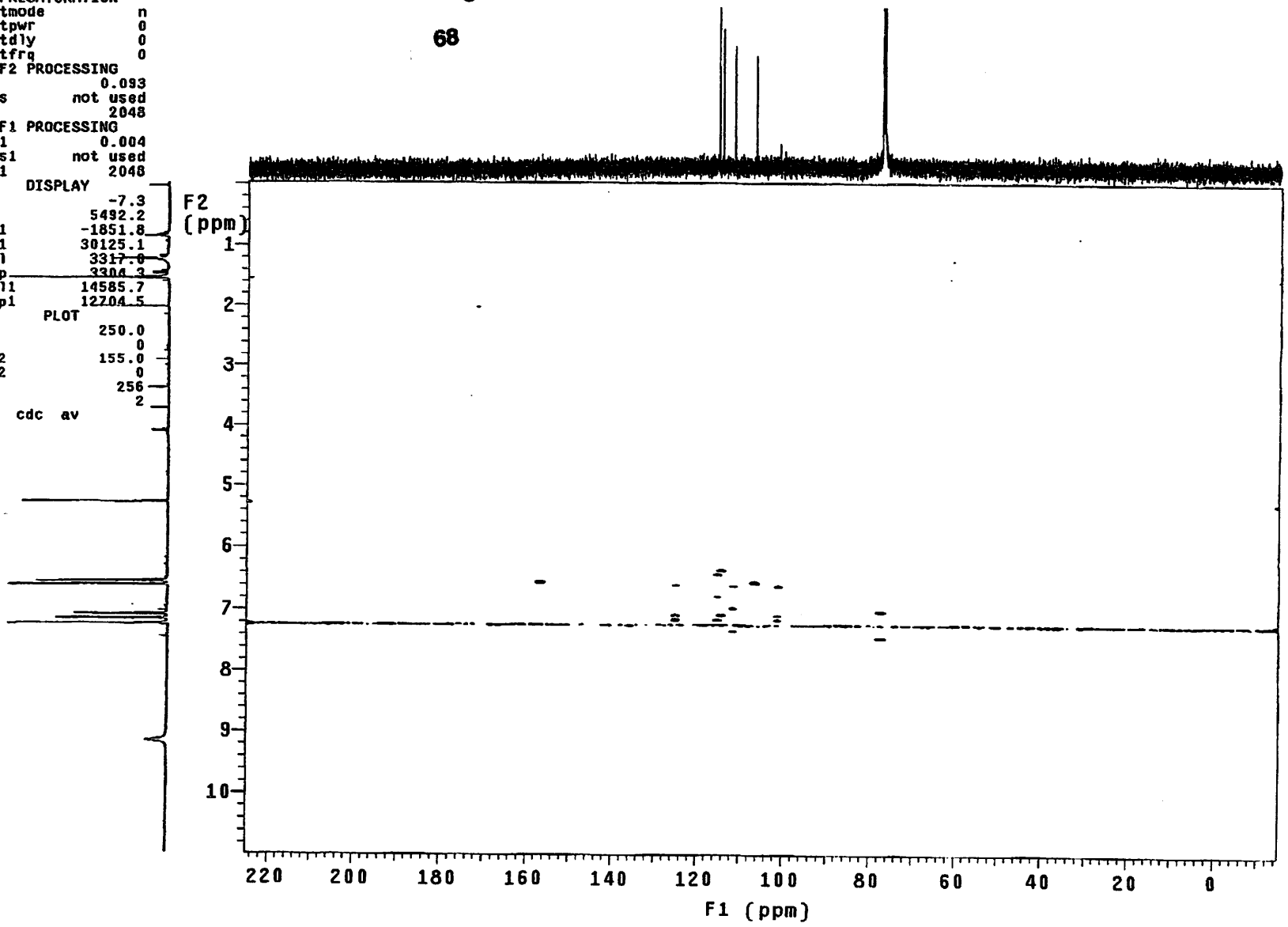
ACQUISITION	
sw	5497.5
at	0.186
np	2048
fb	not used
ss	32
d1	1.000
nt	40
2D ACQUISITION	
sw1	30154.5
ni	256
phase	arrayed
TRANSMITTER	
tn	H1
sfrq	499.744
tof	256.4
tpwr	56
pw	8.950
DECOUPLER	
dn	C13
dof	1255.1
dm	nnn
dmm	ccc
dmf	32200
dpwr	53
pwxlvl	59
pwx	18.000
HMBC	
j1xh	140.0
jnxh	8.0

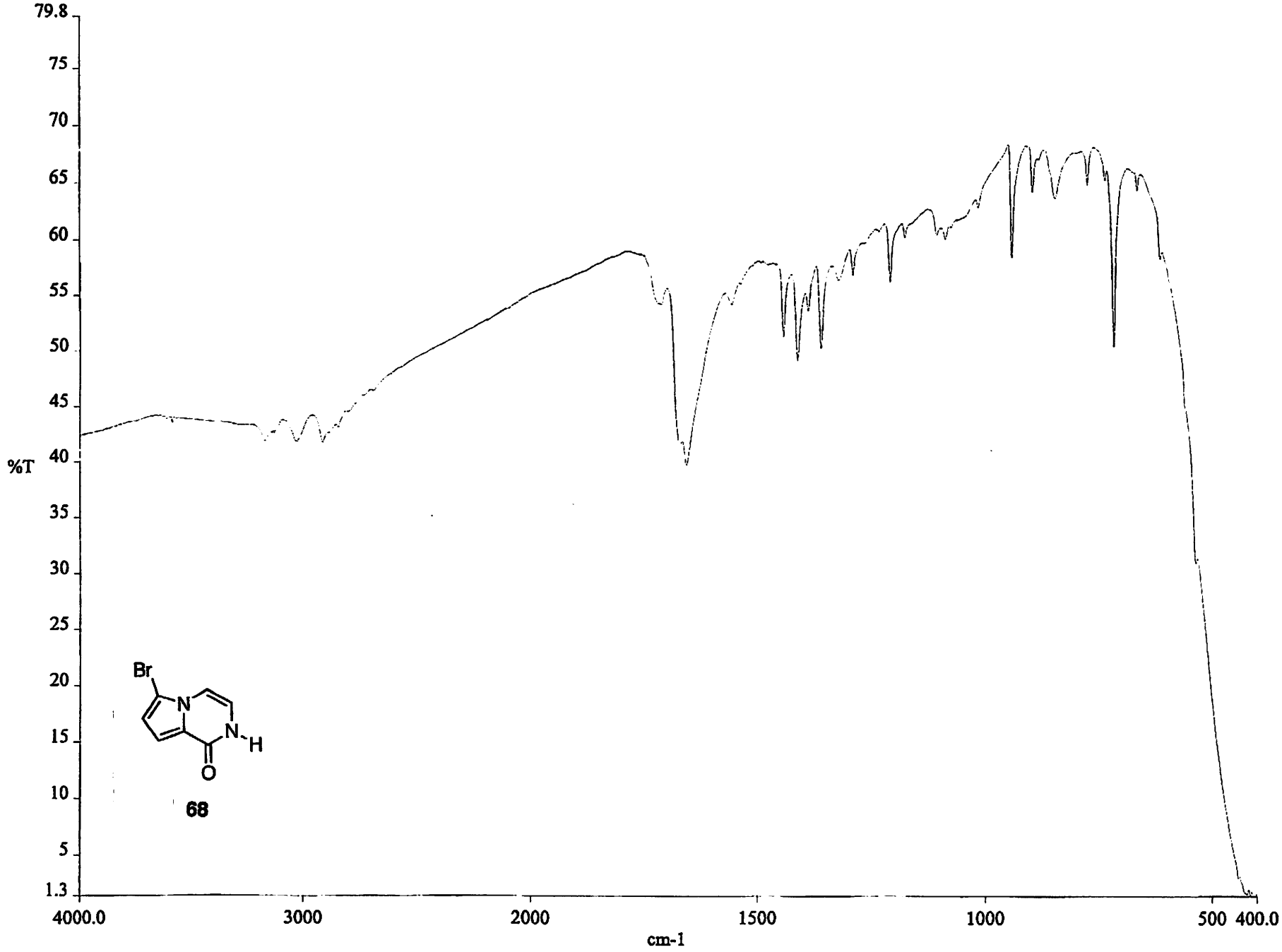
FLAGS	
hs	n
sspul	n
PFGflg	n
hsglvl	2000
SPECIAL	
temp	not used
gain	58
spin	0
PRESATURATION	
satmode	n
satpwr	0
satdly	0
satfrq	0
F2 PROCESSING	
sb	0.093
sbs	not used
fn	2048
F1 PROCESSING	
sb1	0.004
sbs1	not used
fn1	2048
DISPLAY	
sp	-7.3
wp	5492.2
sp1	-1851.8
wp1	30125.1
rf1	3317.0
rfp	3304.3
rf11	14585.7
rfp1	12704.5
PLOT	
wc	250.0
sc	0
wc2	155.0
sc2	0
vs	256
th	2
a1 cdc av	

ACQUISITION ARRAYS	
array	phase
arraydim	512
1	phase
1	1
2	2

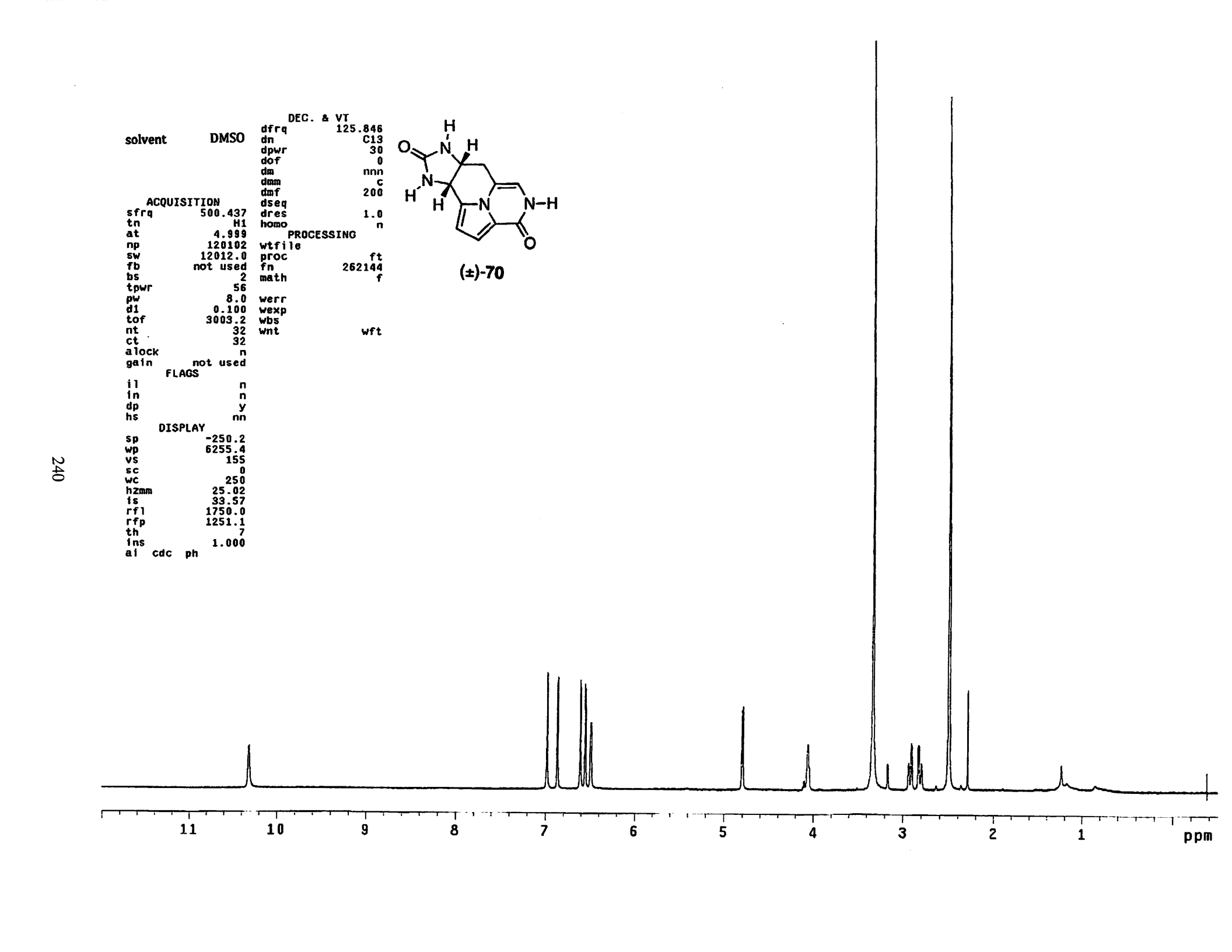


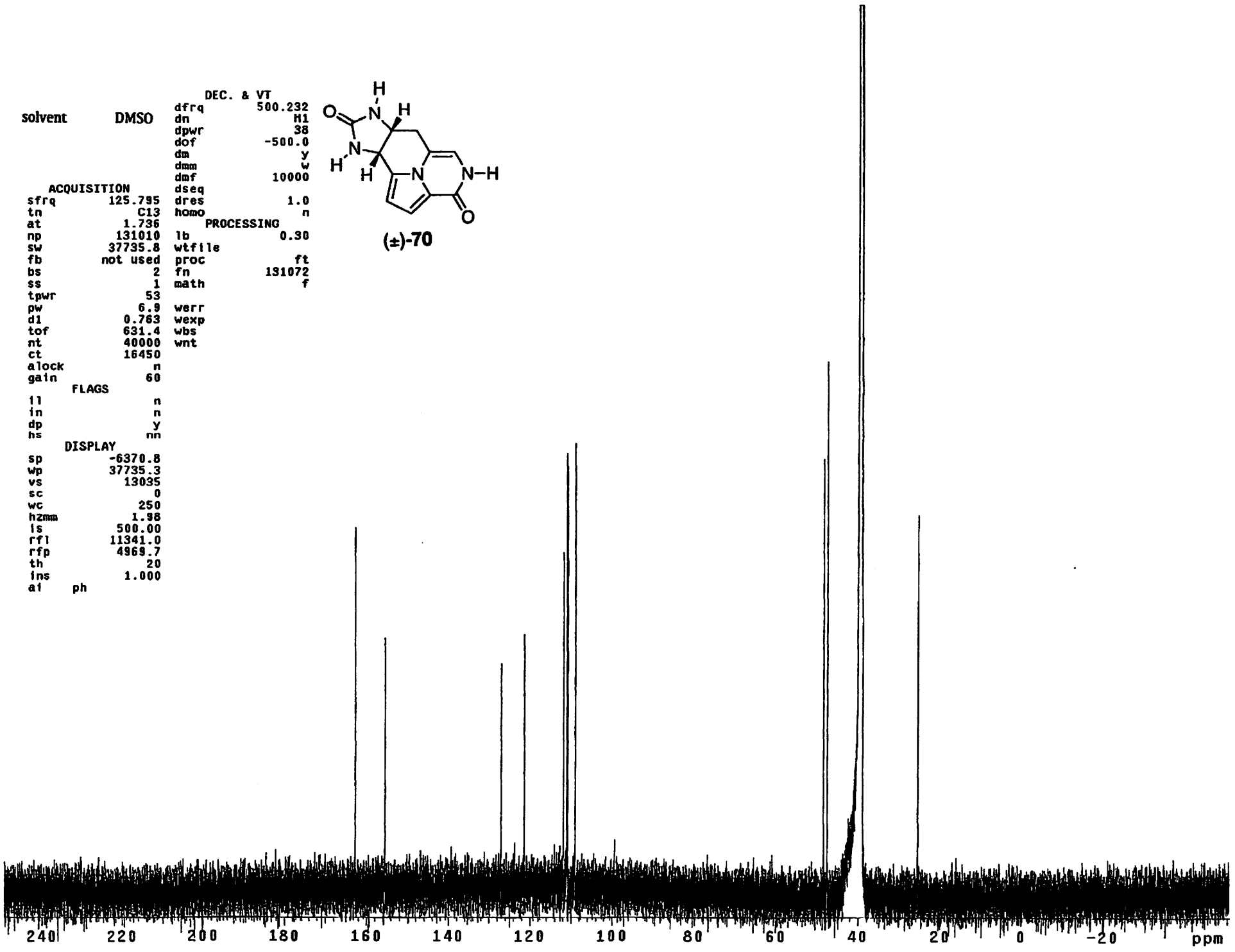
68




79.8
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
1.3
%T
4000.0
3000
2000
1500
1000
500
400.0
cm-1
Br
N
N
H
O

68


solvent DMSO
ACQUISITION
sfrq 500.437
tn H1
at 4.999
np 120102
sw 12012.0
fb not used
bs 2
tpwr 56
pw 8.0
d1 0.100
tof 3003.2
nt 32
ct 32
alock n
gain not used
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -250.2
wp 6255.4
vs 155
sc 0
wc 250
hzmm 25.02
is 33.57
rfl 1750.0
rfp 1251.1
th 7
ins 1.000
ai cdc ph
DEC. & VT
dfrq 125.846
dn C13
dpwr 30
dof 0
dm nnn
dmm c
dmf 200
dseq
dres 1.0
homo n
PROCESSING
wtfile
proc ft
fn 262144
math f
werr
wexp
wbs
wnt wft
(±)-70
11
10
9
8
7
6
5
4
3
2
1
ppm

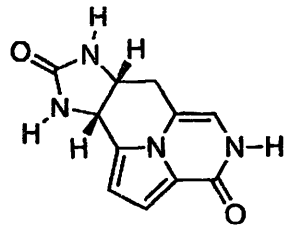

solvent DMSO
ACQUISITION
sfrq 125.795
tn C13
at 1.736
np 131010
sw 37735.8
fb not used
bs 2
ss 1
tpwr 53
pw 6.9
d1 0.763
tof 631.4
nt 40000
ct 16450
alock n
gain 60
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -6370.8
wp 37735.3
vs 13035
sc 0
wc 250
hzmm 1.98
is 500.00
rfl 11341.0
rfp 4969.7
th 20
ins 1.000
ai ph
DEC. & VT
dfrq 500.232
dn H1
dpwr 38
dof -500.0
dm y
dmm w
dmf 10000
dseq
dres 1.0
homo n
PROCESSING
lb 0.30
wtfile
proc ft
fn 131072
math f
werr
wexp
wbs
wnt
(±)-70
240
220
200
180
160
140
120
100
80
60
40
20
0
-20
ppm

gCOSY

solvent	DMSO

ACQUISITION	
sw	6000.6
at	0.171
np	2048
fb	not used
ss	16
d1	1.000
nt	50
2D ACQUISITION	
sw1	6000.6
ni	128
TRANSMITTER	
tn	H1
sfrq	499.747
tof	490.3
tpwr	56
pw	8.925
GRADIENTS	
gzlvl1	2000
gt1	0.001000
gstab	0.000500
DECOUPLER	
dn	C13
dm	nnn

FLAGS	
hs	nn
sspul	n
hsglvl	2000
SPECIAL	
temp	not used
gain	58
spin	0
F2 PROCESSING	
sb	-0.085
sbs	not used
fn	2048
F1 PROCESSING	
sb1	-0.043
sbs1	not used
proc1	lp
fn1	2048
DISPLAY	
sp	2.0
wp	5994.7
sp1	1.1
wp1	5994.7
rfl	3.8
rfp	0
rfl1	4.7
rfp1	0
PLOT	
wc	250.0
sc	0
wc2	160.0
sc2	0
vs	174
th	2
ai cdc av	



(±)-70

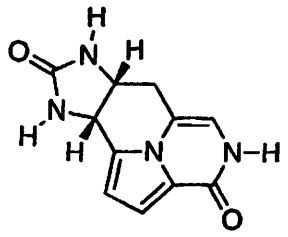
HSQC

solvent DMSO

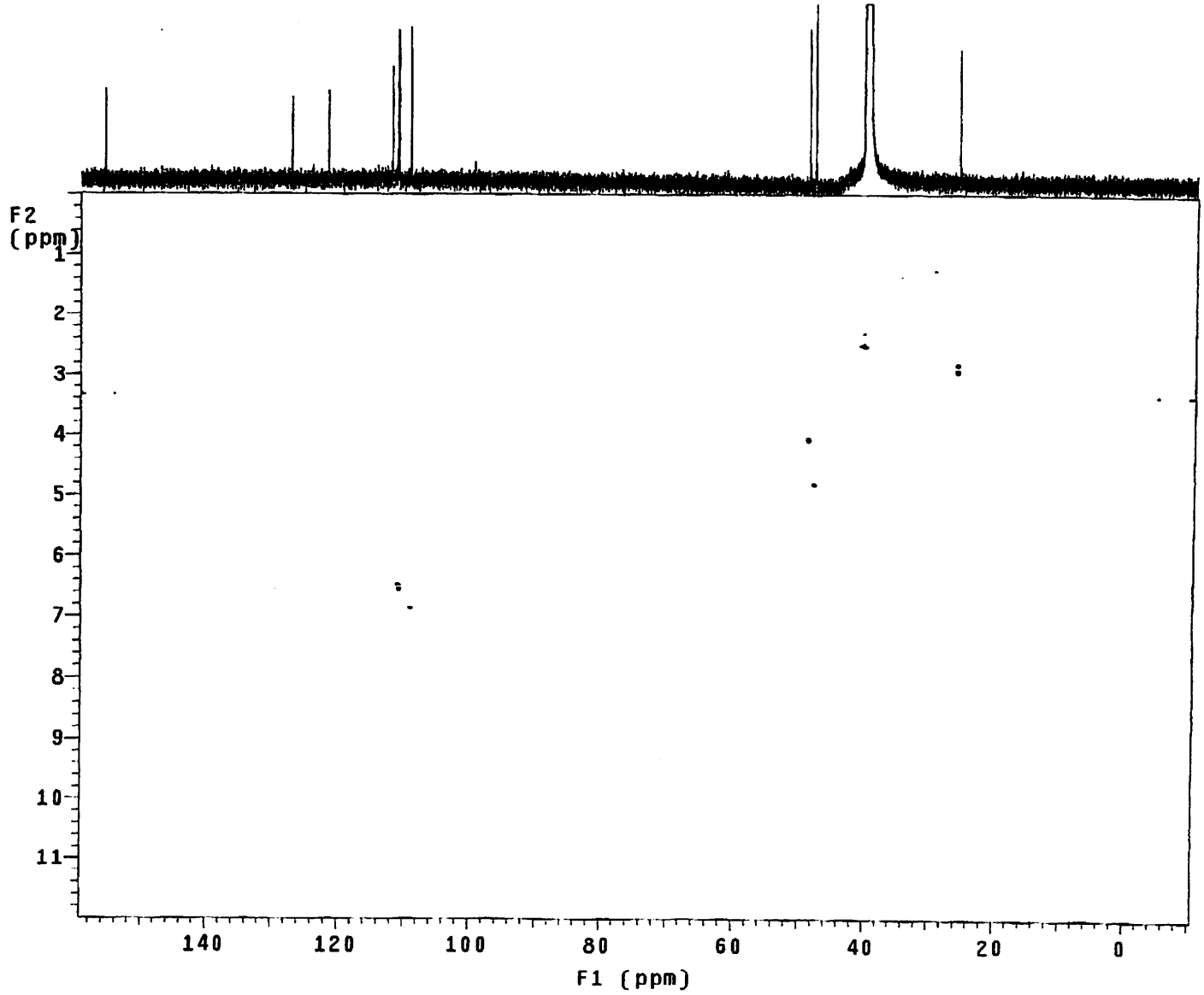
ACQUISITION	
sw	6000.6
at	0.100
np	1198
fb	not used
ss	256
d1	1.000
nt	42
2D ACQUISITION	
sw1	21361.8
ni	256
phase	arrayed
TRANSMITTER	
tn	H1
sfrq	499.747
tof	490.3
tpwr	56
pw	8.925
DECOUPLER	
dn	C13
dof	-2514.8
dm	nny
dmm	ccg
dmf	32200
dpwr	53
pwxlvl	59
pwx	18.000
HSQC	
j1xh	140.0
null	0.350
nullflg	n
mult	2

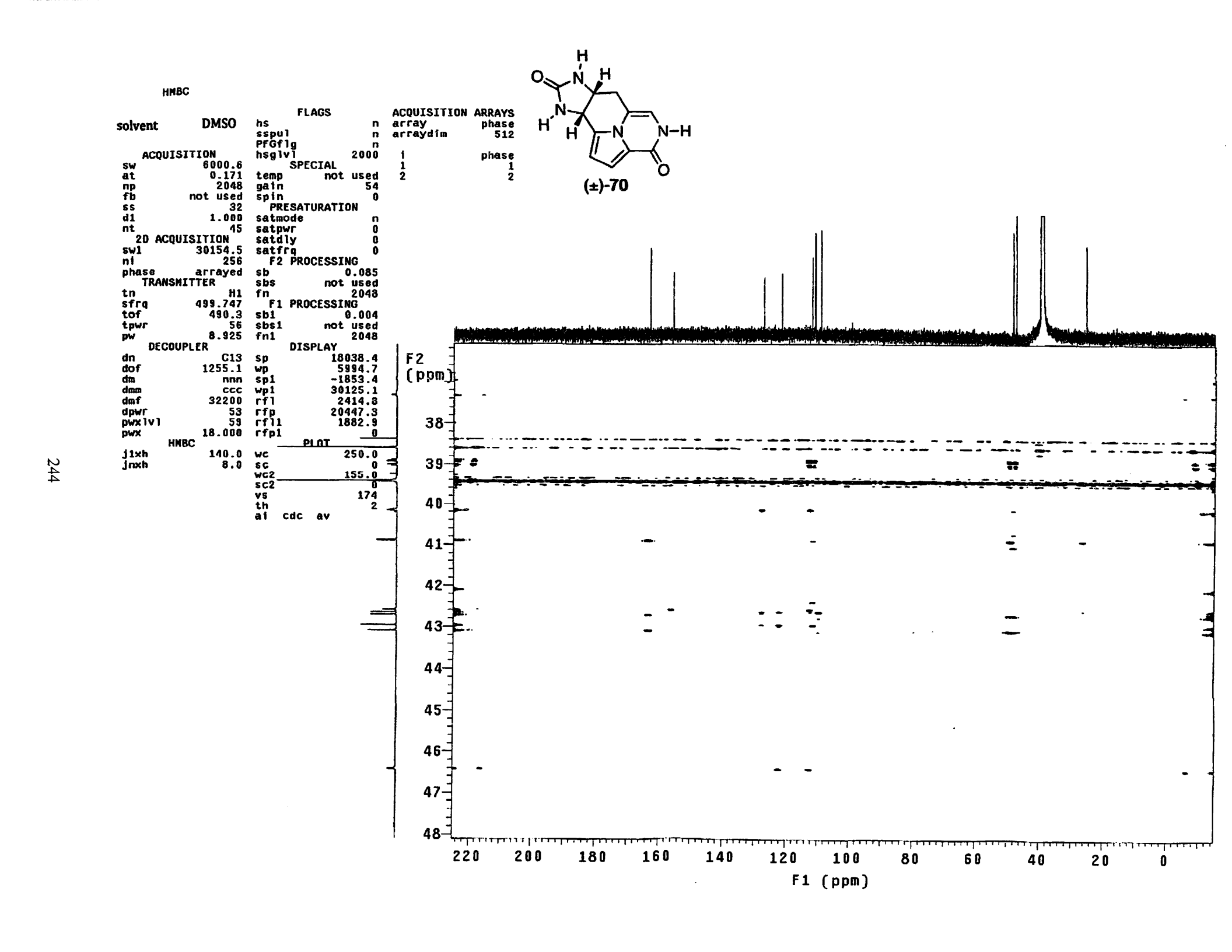
FLAGS	
hs	n
sspul	n
PFGflg	y
hsglvl	2000
SPECIAL	
temp	not used
gain	54
spin	0
PRESATURATION	
satmode	n
satpwr	0
satdly	0
satfrq	0
F2 PROCESSING	
gf	0.079
gfs	not used
fn	2048
F1 PROCESSING	
sb1	-0.024
sbs1	-0.024
proc1	lp
fn1	2048
DISPLAY	
sp	-1.6
wp	5994.7
sp1	-1321.9
wp1	21341.0
rf1	2036.7
rfp	2029.2
rfl1	7431.7
rfp1	6088.9
PLOT	
wc	170.0
sc	0
wc2	110.0
sc2	0
vs	124
th	2
ai cdc ph	

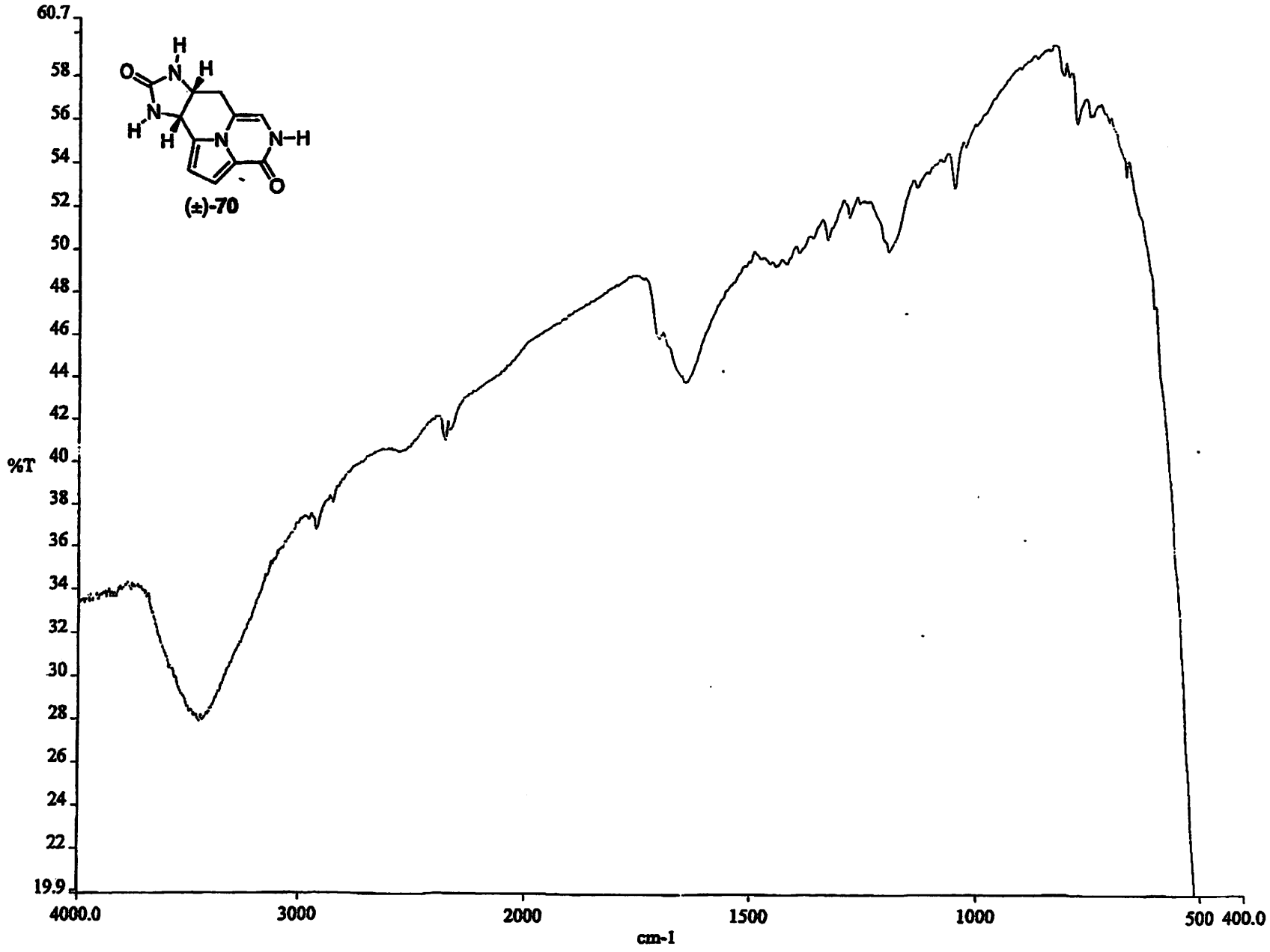
ACQUISITION ARRAYS	
array	phase
arraydim	512
i	phase
1	1
2	2



(±)-70




HMBC
solvent DMSO
ACQUISITION
sw 6000.6
at 0.171
np 2048
fb not used
ss 32
d1 1.000
nt 45
2D ACQUISITION
sw1 30154.5
ni 256
phase arrayed
TRANSMITTER
tn H1
sfrq 499.747
tof 490.3
tpwr 56
pw 8.925
DECOUPLER
dn C13
dof 1255.1
dm nnn
dmm ccc
dmf 32200
dpwr 53
pwx1v1 59
pwx 18.000
HMBC
j1xh 140.0
jnxh 8.0
FLAGS
hs n
sspul n
PFGflg n
hsglvl 2000
SPECIAL
temp not used
gain 54
spin 0
PRESATURATION
satmode n
satpwr 0
satdly 0
satfrq 0
F2 PROCESSING
sb 0.085
sbs not used
fn 2048
F1 PROCESSING
sb1 0.004
sbs1 not used
fn1 2048
DISPLAY
sp 18038.4
wp 5994.7
sp1 -1853.4
wp1 30125.1
rf1 2414.8
rfp 20447.3
rf11 1882.9
rfp1 0
PLOT
wc 250.0
sc 0
wc2 155.0
sc2 0
vs 174
th 2
ai cdc av
ACQUISITION ARRAYS
array phase
arraydim 512
i phase
1 1
2 2
(±)-70
F2 (ppm)
F1 (ppm)


60.7
58
56
54
52
50
48
46
44
42
40
38
36
34
32
30
28
26
24
22
19.9
%T
4000.0
3000
2000
1500
1000
500
400.0
cm-1
(±)-70

solvent	CD_3OD

ACQUISITION	
sfrq	500.437
tn	H1
at	4.999
np	120102
sw	12012.0
fb	not used
bs	1
tpwr	58
pw	8.0
d1	0.100
tof	3003.2
nt	16
ct	16
alock	n
gain	not used

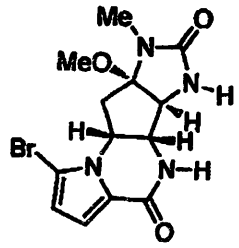
FLAGS	
il	n
in	n
dp	y
hs	nn

DISPLAY	
sp	-250.2
wp	6255.4
vs	16
sc	0
wc	250
hzmm	25.02
is	99.57
rf1	2159.7
rfp	1656.4
th	4
ins	100.000

ai cdc ph

DEC. & VT	
dfrq	125.848
dn	C13
dpwr	30
dof	0
dm	nnn
dmm	c
dmf	200
dseq	
dres	1.0
homo	n

PROCESSING	
wtfile	
proc	ft
fn	262144
math	f
werr	
wexp	
wbs	
wnt	wft



(-)-agelastatin E (5)

solvent CD_3OD

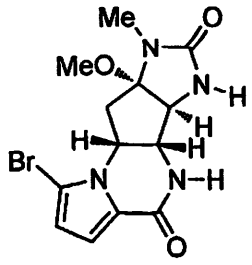
ACQUISITION	
sfrq	125.795
tn	C13
at	1.736
np	131010
sw	37735.8
fb	not used
bs	4
ss	1
tpwr	53
pw	6.9
d1	0.763
tof	631.4
nt	1e+09
ct	448
alock	n
gain	not used

FLAGS	
il	n
in	n
dp	y
hs	nn

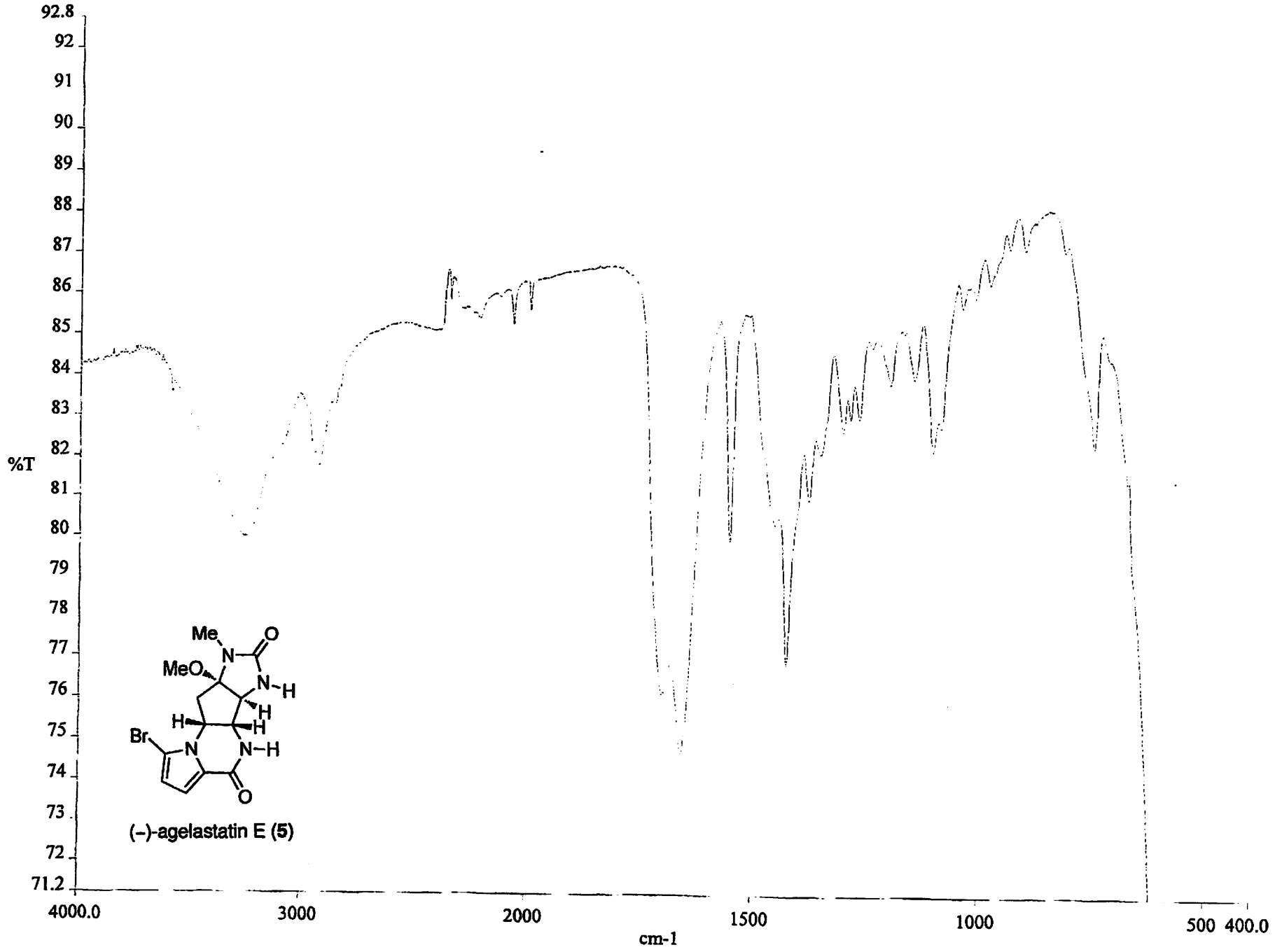
DISPLAY	
sp	-6118.1
wp	37735.3
vs	1265
sc	0
wc	250
hzmm	150.94
is	23000.00
rfl	12300.9
rfp	6182.2
th	11
ins	1.000
ai	ph

DEC. & VT	
dfrq	500.231
dn	H1
dpwr	38
dof	-500.0
dm	y
dmm	w
dmf	10000
dseq	
dres	1.0
homo	n

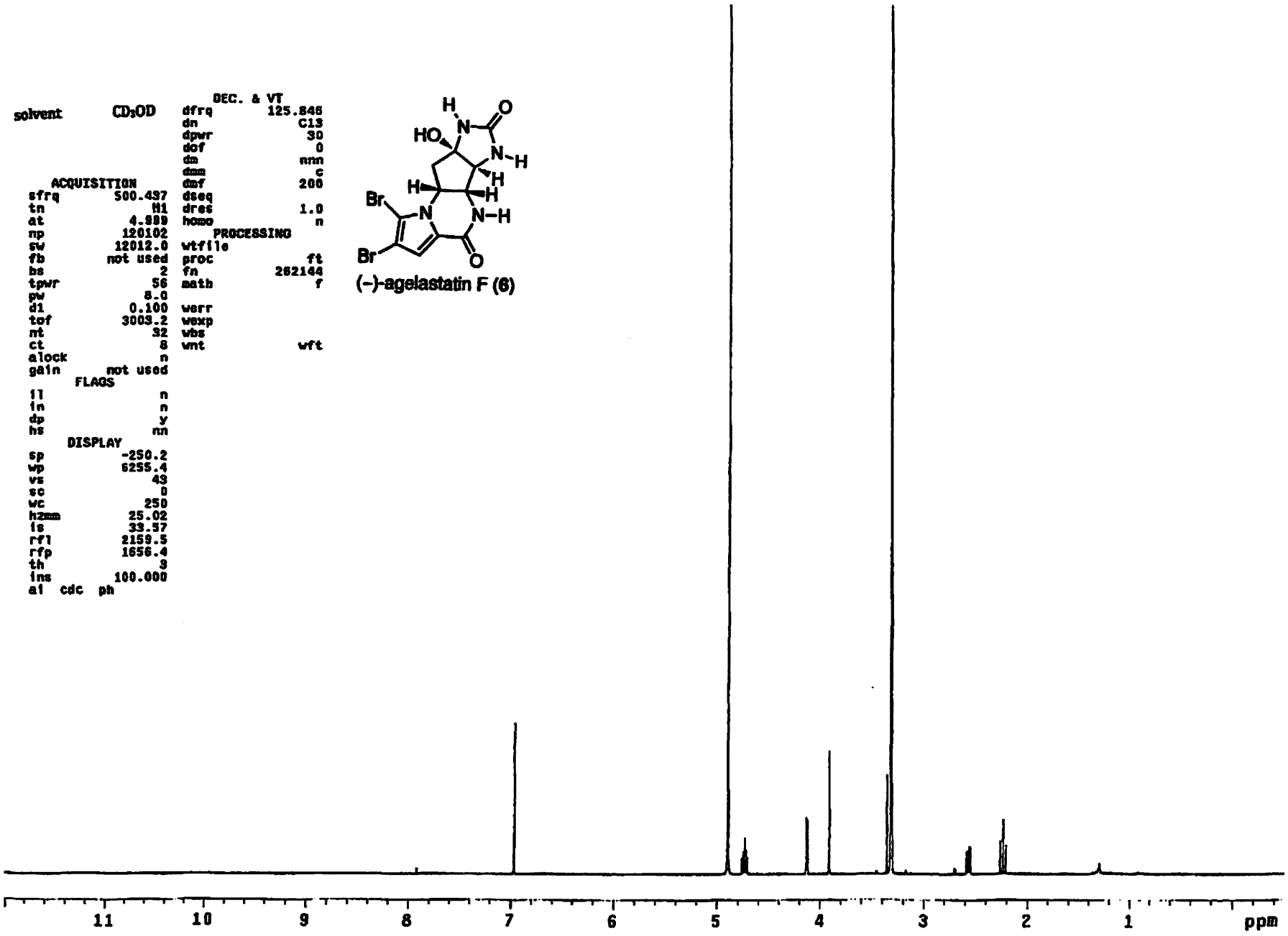
PROCESSING	
lb	0.30
wtfile	
proc	ft
fn	131072
math	f
werr	
wexp	
wbs	
wnt	



(–)-agelastatin E (5)



(–)-agelastatin E (**5**)


solvent CD3OD
ACQUISITION
sfrq 500.437
tn H1
at 4.989
np 120102
sw 12012.0
fb not used
bs 2
tpwr 56
pw 8.0
d1 0.100
tof 3003.2
nt 32
ct 8
alock n
gain not used
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -250.2
wp 6255.4
vs 49
sc 0
wc 250
hzmm 25.02
is 33.57
rfl 2159.5
rfp 1656.4
th 9
ins 100.000
ai cdc ph
DEC. & VT
dfrq 125.845
dn C13
dpwr 30
dof 0
dm nnn
dmm c
dmf 200
dseq
dres 1.0
homo n
PROCESSING
wtfile
proc ft
fn 262144
math f
werr
wexp
wbs
wnt wft
(-)-agelastatin F (6)
11
10
9
8
7
6
5
4
3
2
1
ppm

solvent	CD_3OD

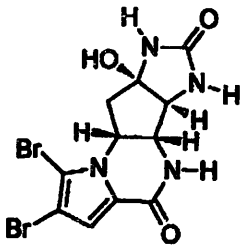
ACQUISITION	
sfrq	125.795
tn	C13
at	1.736
np	131010
sw	37735.8
fb	not used
bs	2
ss	1
tpwr	53
pw	6.9
d1	0.768
tof	631.4
nt	40000
ct	15698
alock	n
gain	not used

FLAGS	
fl	n
in	n
dp	y
hs	nn

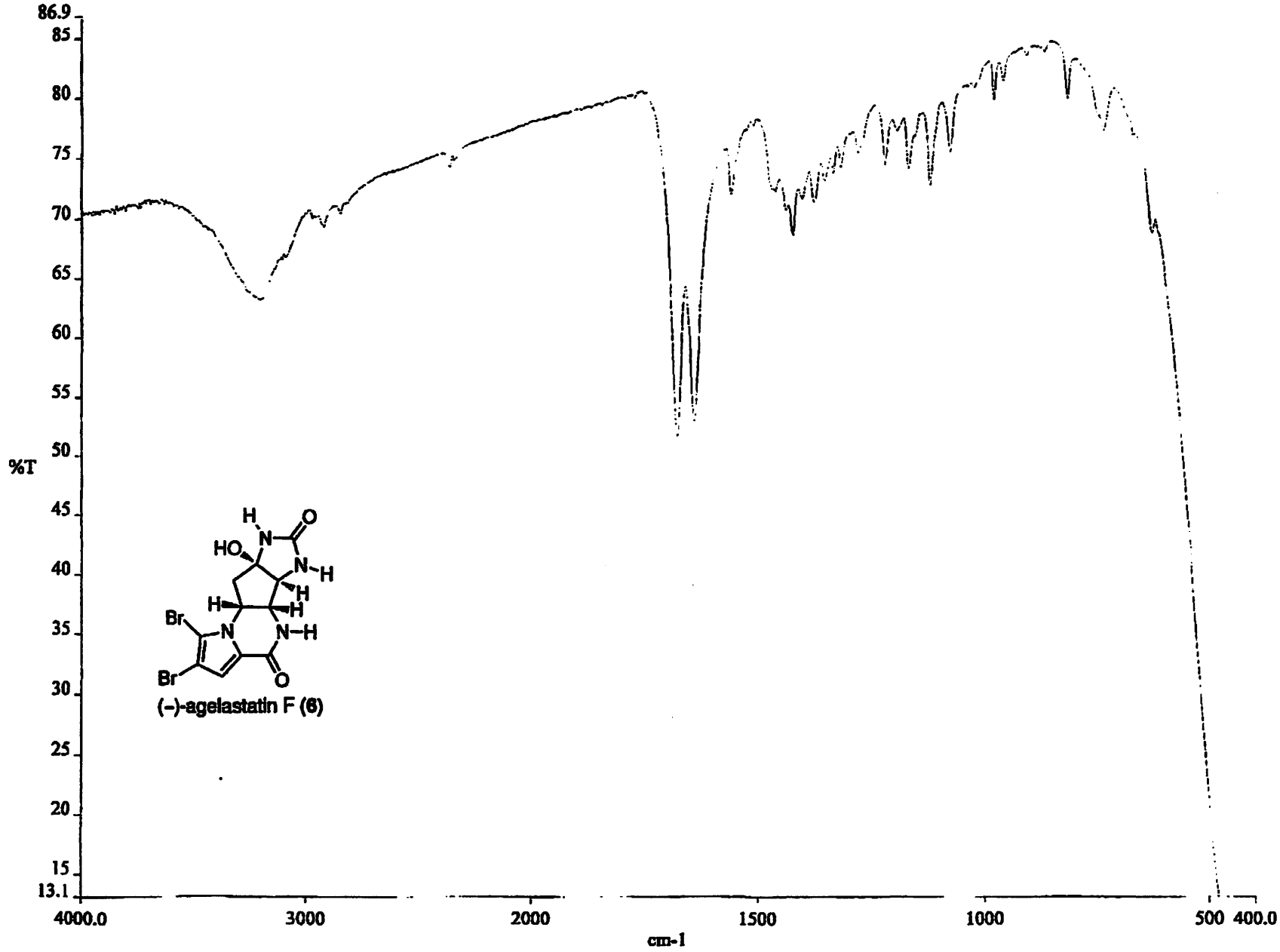
DISPLAY	
sp	-6116.4
wp	37795.3
vs	8340
sc	0
wc	250
hzmm	150.84
is	500.00
rfl	12299.2
rfp	6182.2
th	56
ins	1.000
ai	ph

DEC. & VT	
dfrq	500.231
dn	H1
dpwr	38
dof	-500.0
dm	y
dmm	w
dmf	10000
dseq	
dres	1.0
homo	n

PROCESSING	
lb	0.30
wtfile	
proc	ft
fn	131072
math	f
werr	
wexp	
wbs	
wnt	

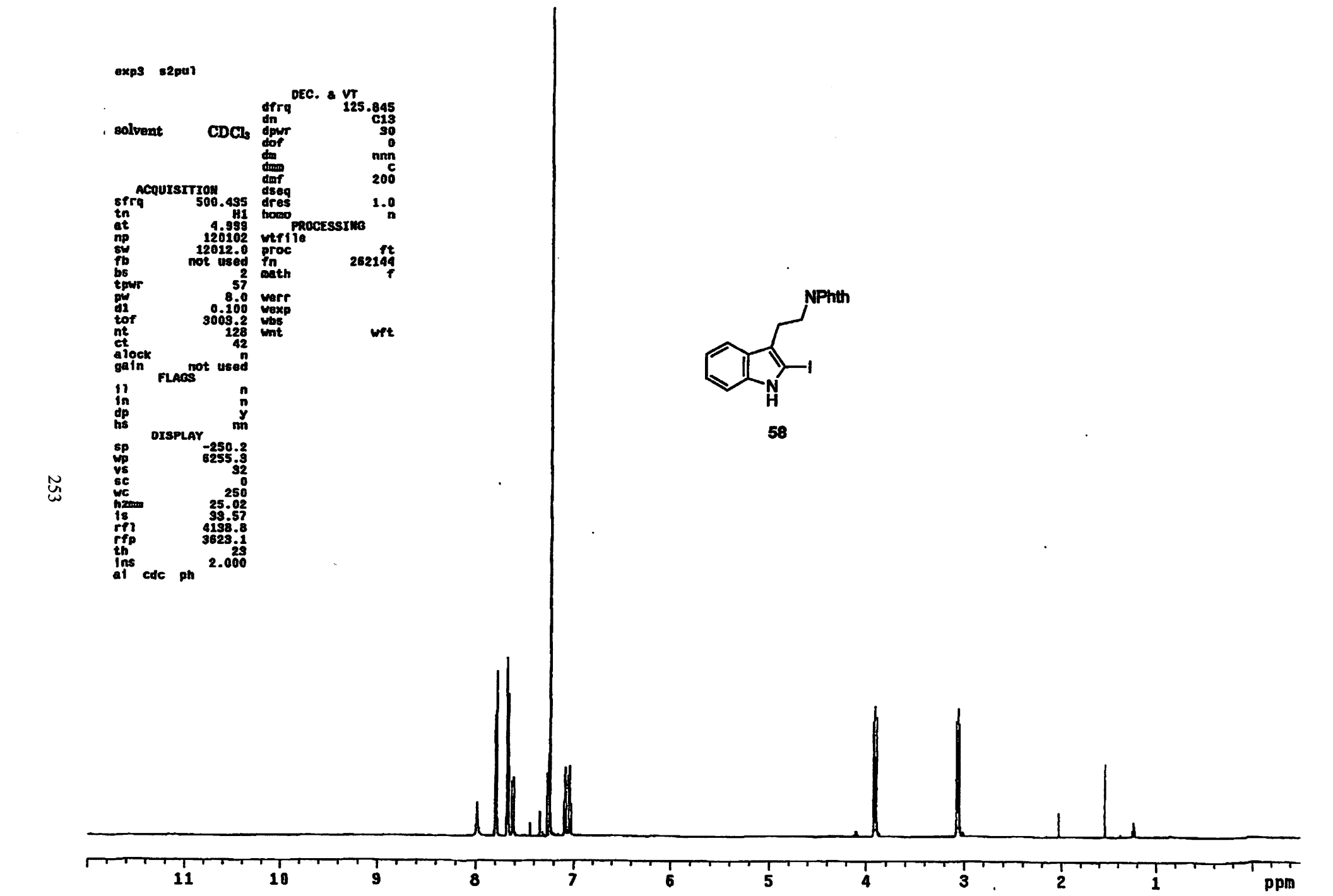


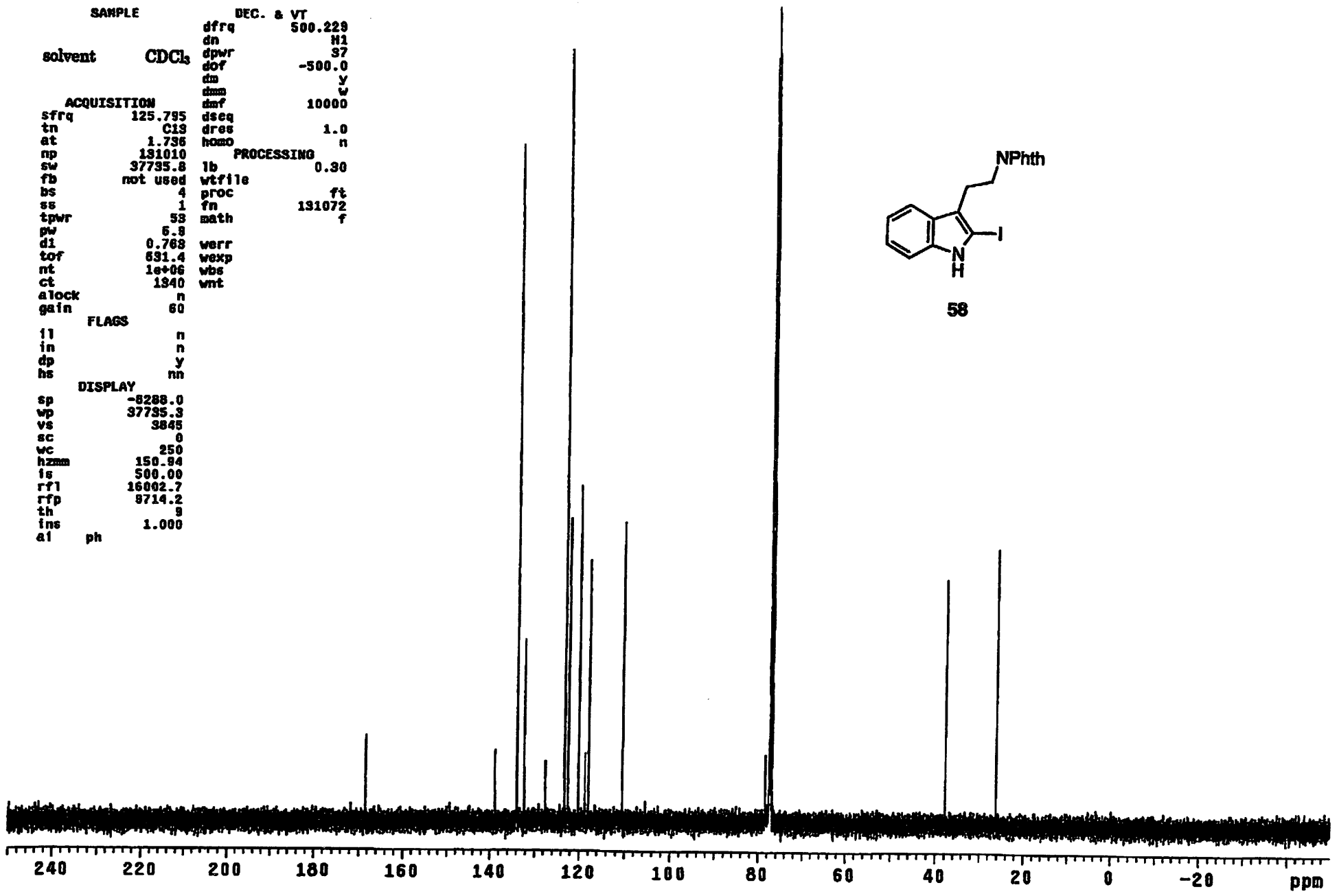
(-)-agelastatin F (6)

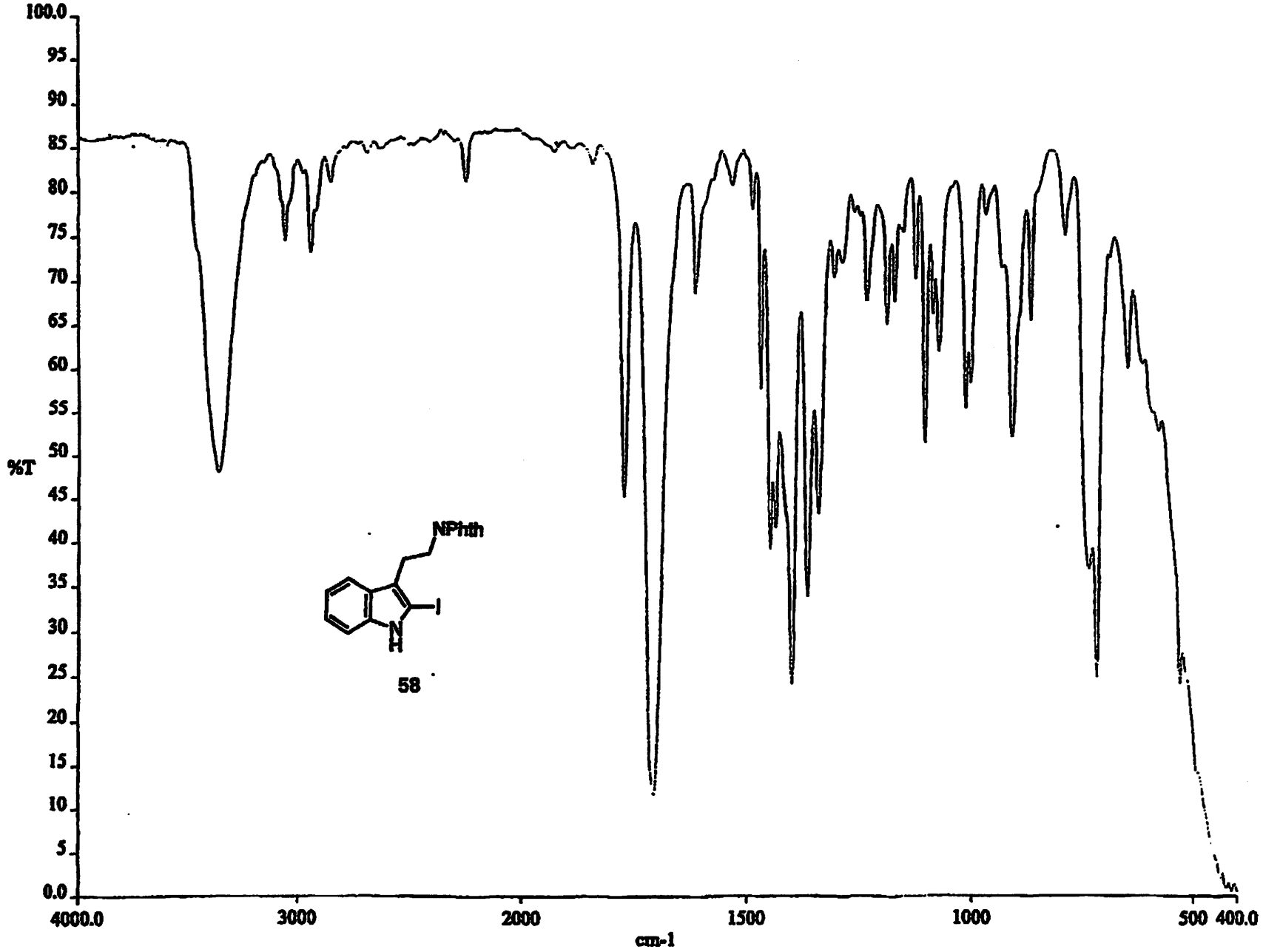

86.9
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
13.1
%T
4000.0
3000
2000
1500
1000
500
400.0
cm-1
(-)-agelastatin F (6)

Appendix B.

Spectra for Chapter II


exp3 s2pul
solvent CDCl3
ACQUISITION
sfrq 500.435
tn H1
at 4.999
np 120102
sw 12012.0
fb not used
bs 2
tpwr 57
pw 8.0
d1 0.100
tof 3009.2
nt 128
ct 42
alock n
gain not used
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -250.2
wp 6255.9
vs 32
sc 0
wc 250
hzmm 25.02
is 33.57
rfl 4138.8
rfp 3623.1
th 29
ins 2.000
al cdc ph
DEC. & VT
dfrq 125.845
dn C13
dpwr 30
dof 0
dm nnn
dmm c
dmf 200
dseq
dres 1.0
homo n
PROCESSING
wtfile
proc ft
fn 262144
math f
werr
wexp
wbs
wnt wft
NPhth
I
N
H
58
11
10
9
8
7
6
5
4
3
2
1
ppm


exp1 s2pul
SAMPLE
solvent CDCl3
ACQUISITION
sfrq 125.795
tn C13
at 1.736
np 131010
sw 37735.8
fb not used
bs 4
ss 1
tpwr 53
pw 6.8
d1 0.768
tof 631.4
nt 1e+06
ct 1840
alock n
gain 60
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -8288.0
wp 37735.3
vs 3845
sc 0
wc 250
hzmm 150.94
is 500.00
rfl 16002.7
rfp 8714.2
th 9
ins 1.000
ai ph
DEC. & VT
dfrq 500.229
dn H1
dpwr 37
dof -500.0
dm y
dmm w
dmf 10000
dseq
dres 1.0
homo n
PROCESSING
lb 0.30
wtfile
proc ft
fn 131072
math f
werr
wexp
wbs
wnt
NPhth
I
N
H
58
240
220
200
180
160
140
120
100
80
60
40
20
0
-20
ppm

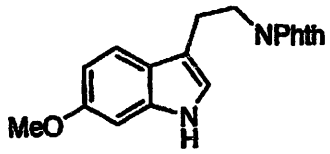

100.0
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0.0
%T
4000.0
3000
2000
1500
1000
500
400.0
cm-1
NPhth
I
N
H
58

```
exp1  s2pul

solvent        CDCl3

   ACQUISITION
sfrq         500.435
tn                H1
at             4.899
np            120102
sw           12012.0
fb         not used
bs                2
tpwr             57
pw              8.0
d1            0.100
tof          3003.2
nt                32
ct                28
alock              n
gain       not used
      FLAGS
il                 n
in                 n
dp                 y
hs                nn
     DISPLAY
sp            -250.2
wp            6255.3
vs                18
sc                 0
wc               250
hzmm           25.02
is             33.57
rfl          4139.0
rfp          3623.1
th                 6
ins            1.000
ai  cdc  ph

                DEC. & VT
dfrq          125.845
dn                C13
dpwr               30
dof                 0
dm                nnn
dmm                 c
dmf               200
dseq
dres              1.0
homo                n
     PROCESSING
wtfile
proc               ft
fn            262144
math                f
werr
wexp
wbs
wnt               wft
```



56

exp2 s2pul

solvent	$CDCl_3$

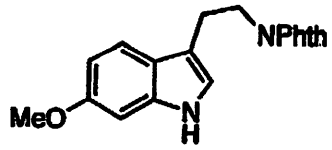
ACQUISITION	
sfrq	125.795
tn	C13
at	1.736
np	131010
sw	37735.8
fb	not used
bs	2
ss	1
tpwr	53
pw	6.9
d1	0.763
tof	631.4
nt	10000
ct	296
alock	n
gain	60

FLAGS	
il	n
in	n
dp	y
hs	nn

DISPLAY	
sp	-6289.2
wp	37735.8
vs	2201
sc	0
wc	250
hzmm	4.36
is	500.00
rfl	16004.7
rfp	9714.8
th	15
ins	1.000
ai	ph

DEC. & VT	
dfrq	500.228
dn	H1
dpwr	37
dof	-500.0
dm	y
dmm	w
dmf	10000
dseq	
dres	1.0
homo	n
temp	20.0

PROCESSING	
lb	0.30
wtfile	
proc	ft
fn	131072
math	f
werr	
wexp	
wbs	
wnt	



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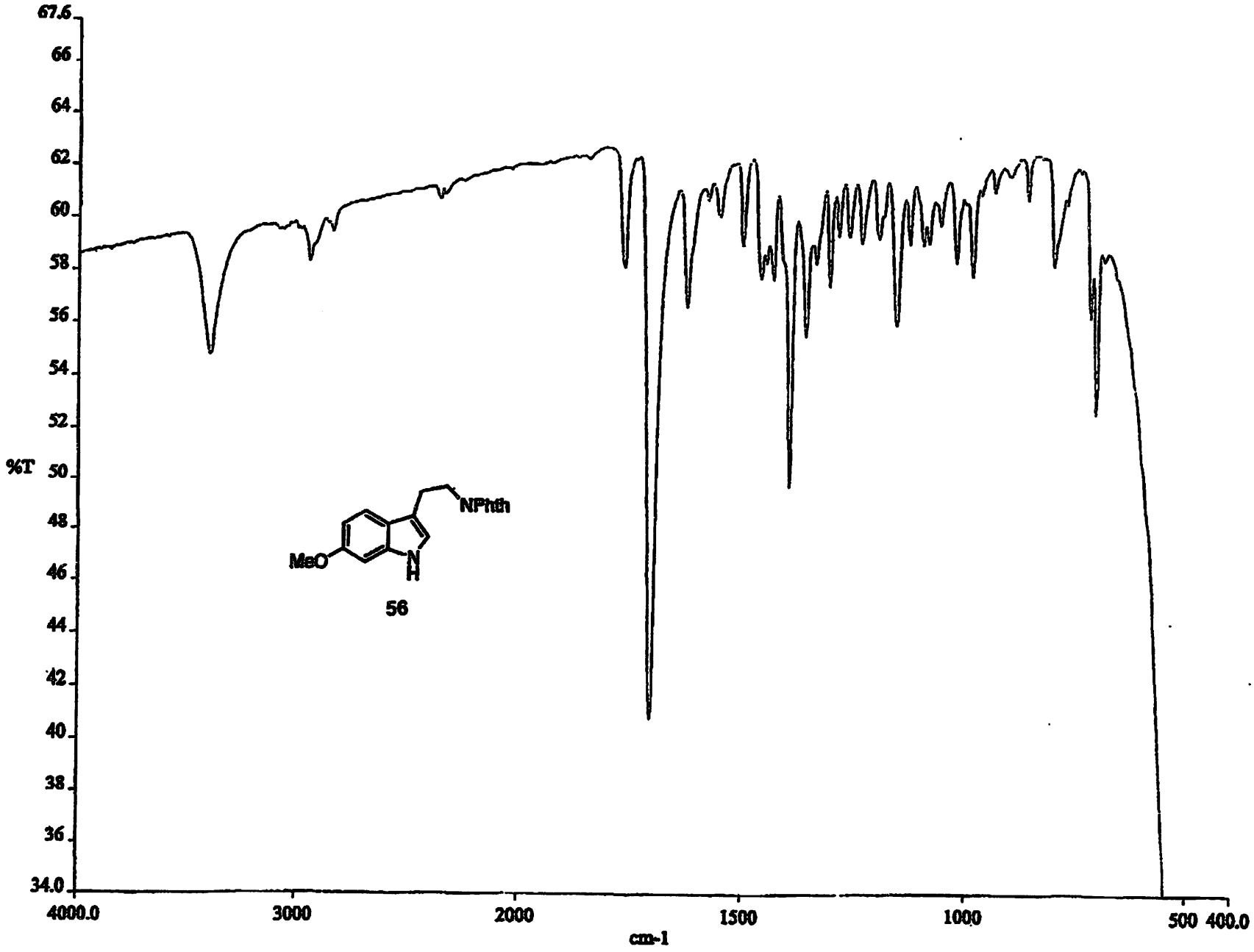
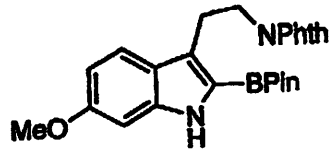

67.6
66
64
62
60
58
56
54
52
%T 50
48
46
44
42
40
38
36
34.0
4000.0
3000
2000
1500
1000
500 400.0
cm-1
NPhth
MeO
N
H
56

```
exp1  s2pul

solvent        CDCl3

   ACQUISITION
sfrq        500.495
tn              H1
at           4.999
np           120102
sw          12012.0
fb        not used
bs                2
tpwr             57
pw              8.0
d1            0.100
tof          3003.2
nt               32
ct               12
alock             n
gain      not used
      FLAGS
il                n
in                n
dp                y
hs               nn
    DISPLAY
sp           -250.2
wp           6255.3
vs               25
sc                0
wc              250
hzmm            1.12
is             33.57
rfl          4138.7
rfp          3823.1
th                7
ins          100.000
ai  cdc  ph

      DEC. & VT
dfrq        125.845
dn              C13
dpwr             30
dof               0
dm              nnn
dmm               c
dmf             200
dseq
dres            1.0
homo              n
    PROCESSING
wtfile
proc             ft
fn           262144
math              f
werr
wexp
wbs
wnt             wft
```



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exp2 s2pul

solvent	CDCl3

ACQUISITION

sfrq	125.795
tn	C13
at	1.736
np	131010
sw	37735.8
fb	not used
bs	2
ss	1
tpwr	53
pw	6.9
d1	0.783
tof	631.4
nt	10000
ct	76
alock	n
gain	60

FLAGS

il	n
in	n
dp	y
hs	nn

DISPLAY

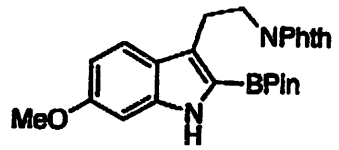
sp	-6289.8
wp	37735.3
vs	151
sc	0
wc	250
hzmm	46.61
is	500.00
rfl	16005.3
rfp	8714.9
th	10
ins	1.000
nm	ph

DEC. & VT

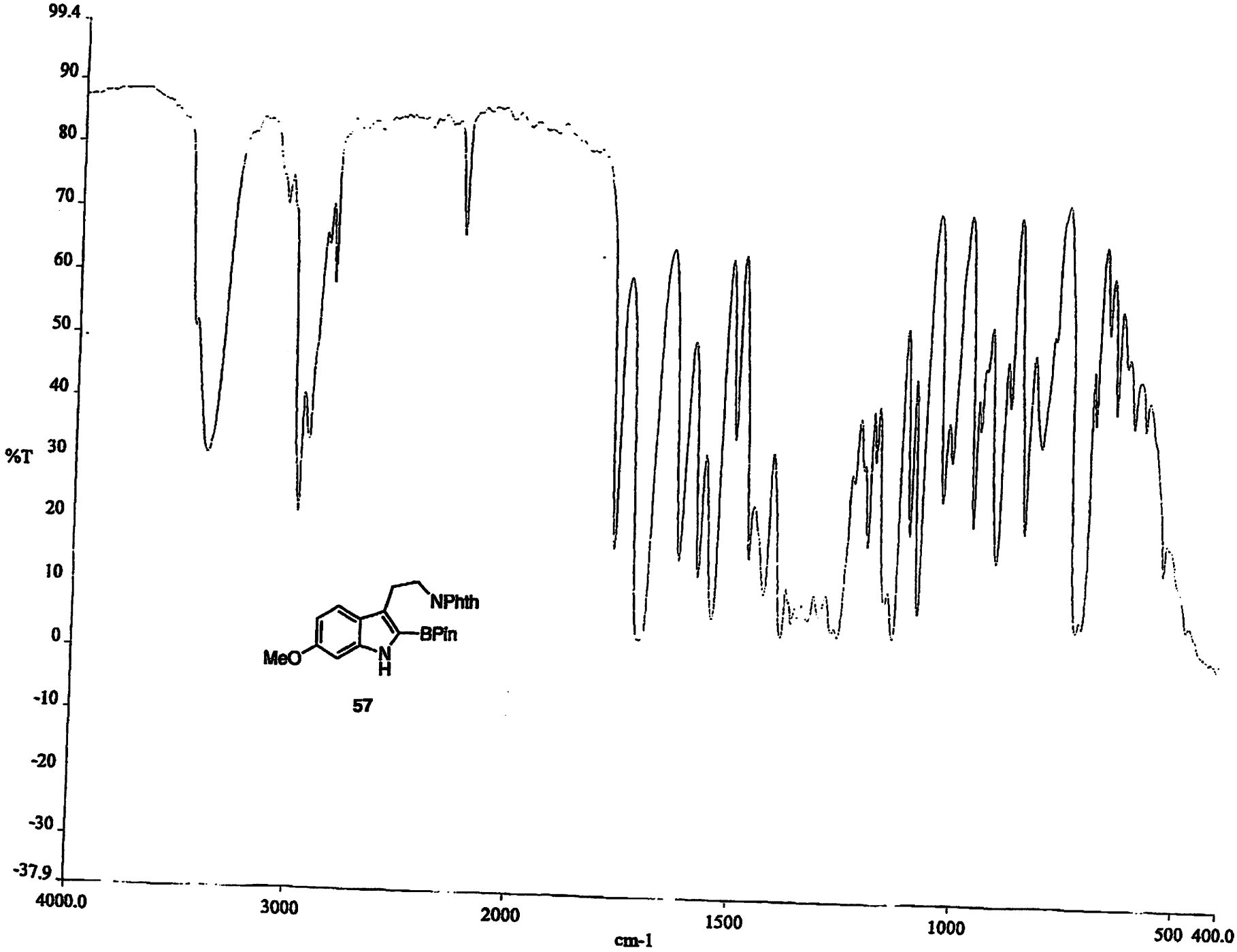
dfrq	500.229
dn	H1
dpwr	37
dof	-500.0
dm	y
dmm	w
dmf	10000
dseq	
dres	1.0
homo	n

PROCESSING

lb	0.30
wtfile	
proc	ft
fn	131072
math	f
werr	
wexp	
wbs	
wnt	

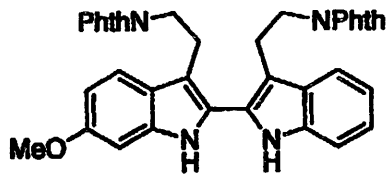


57

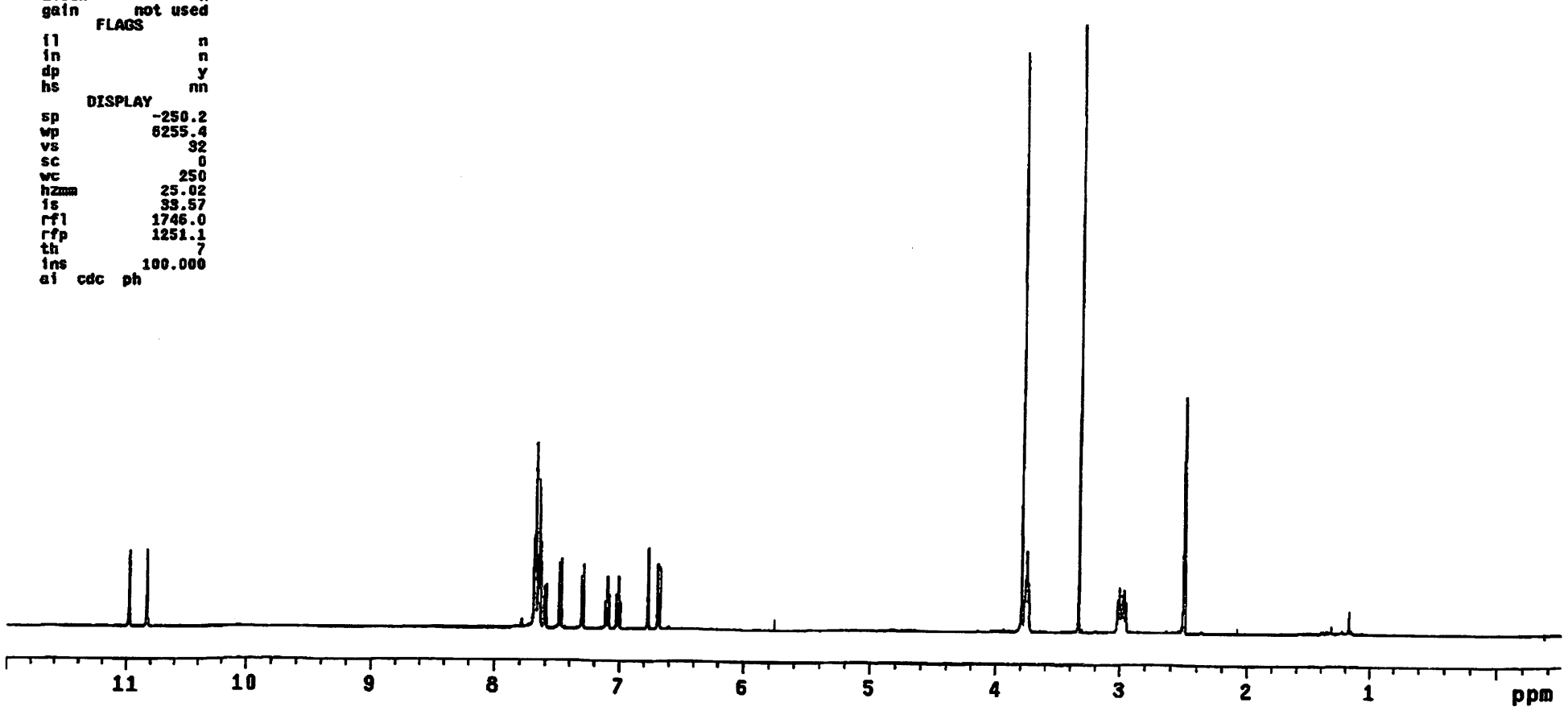

99.4
90
80
70
60
50
40
30
20
10
0
-10
-20
-30
-37.9
%T
4000.0
3000
2000
1500
1000
500 400.0
cm-1
NPhth
BPin
MeO
N
H

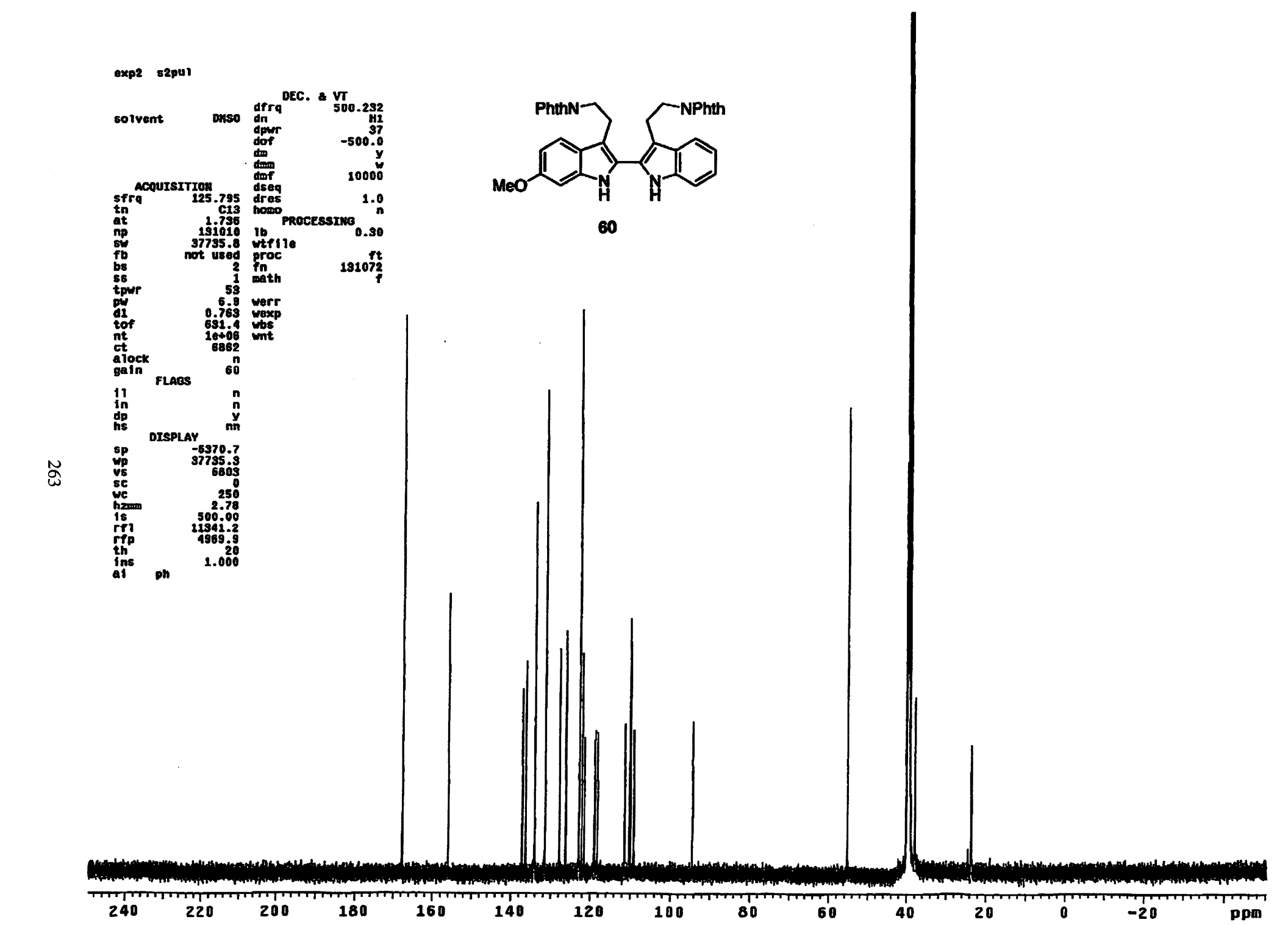
57

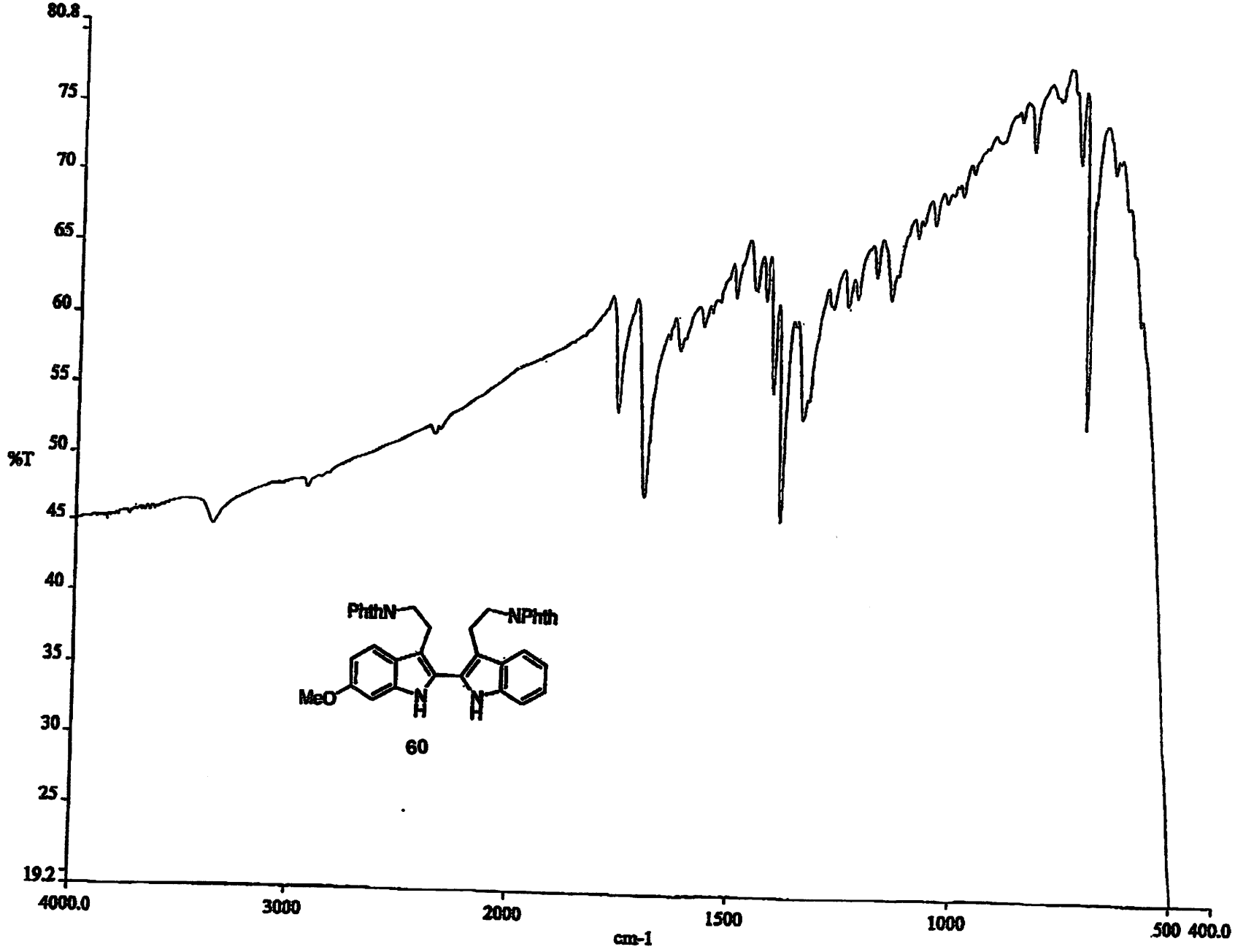
```
exp1  s2pul

                                DEC. & VT
                              dfrq          125.846
solvent          DMSO         dn                C13
                              dpwr               30
                              dof                 0
                              dm                nnn
                              dmm                 c
   ACQUISITION                dmf               200
sfrq          500.437         dseq
tn                H1          dres              1.0
at              4.999         homo                n
np             120102                PROCESSING
sw           12012.0          wtfile
fb          not used          proc                ft
bs                2           fn             262144
tpwr             57           math                f
pw              8.0           werr
d1            0.100           wexp
tof          3009.2           wbs
nt                32          wnt               wft
ct                12
alock              n
gain       not used
      FLAGS
il                 n
in                 n
dp                 y
hs                nn
     DISPLAY
sp            -250.2
wp            8255.4
vs                32
sc                 0
wc               250
hzmm           25.02
is             33.57
rfl            1746.0
rfp            1251.1
th                 7
ins          100.000
ai  cdc  ph
```



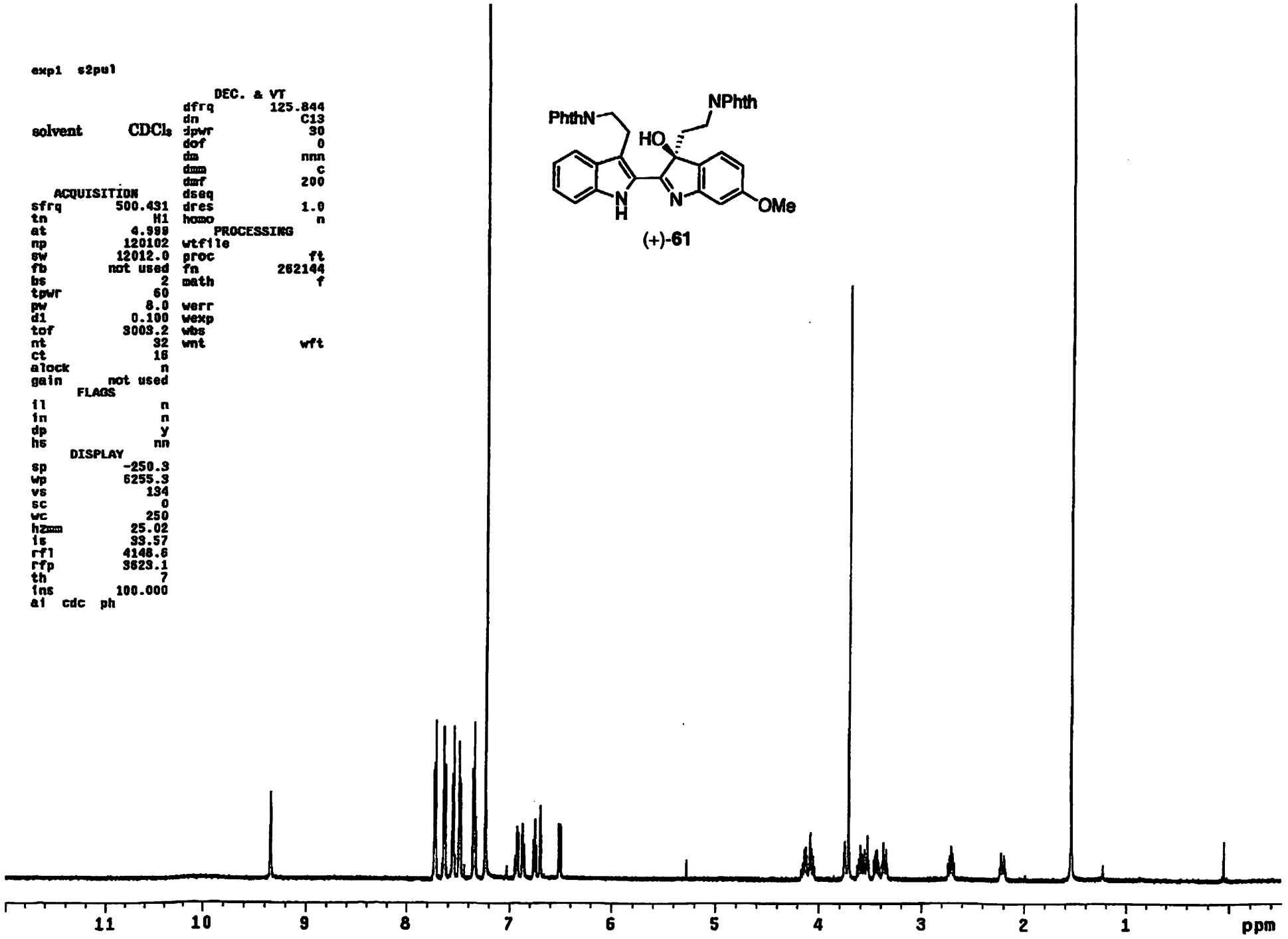
60




exp2 s2pul
solvent DMSO
ACQUISITION
sfrq 125.795
tn C13
at 1.736
np 131010
sw 37735.8
fb not used
bs 2
ss 1
tpwr 53
pw 6.9
d1 0.763
tof 631.4
nt 1e+06
ct 6862
alock n
gain 60
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -6370.7
wp 37735.3
vs 6803
sc 0
wc 250
hzmm 2.78
is 500.00
rfl 11341.2
rfp 4969.9
th 20
ins 1.000
ai ph
DEC. & VT
dfrq 500.232
dn H1
dpwr 37
dof -500.0
dm y
dmm w
dmf 10000
dseq
dres 1.0
homo n
PROCESSING
lb 0.30
wtfile
proc ft
fn 131072
math f
werr
wexp
wbs
wnt
PhthN
NPhth
MeO
N
H
N
H
60
240
220
200
180
160
140
120
100
80
60
40
20
0
-20
ppm


80.8
75
70
65
60
55
50
45
40
35
30
25
19.2
%T
4000.0
3000
2000
1500
1000
500
400.0
cm-1
PhthN
NPhth
MeO
N
H
N
H

60


exp1 s2pul
solvent CDCl3
ACQUISITION
sfrq 500.431
tn H1
at 4.999
np 120102
sw 12012.0
fb not used
bs 2
tpwr 60
pw 8.0
d1 0.100
tof 3003.2
nt 32
ct 16
alock n
gain not used
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -250.3
wp 6255.3
vs 134
sc 0
wc 250
hzmm 25.02
is 33.57
rf1 4148.6
rfp 3623.1
th 7
ins 100.000
ai cdc ph
DEC. & VT
dfrq 125.844
dn C13
dpwr 30
dof 0
dm nnn
dmm c
dmf 200
dseq
dres 1.0
homo n
PROCESSING
wtfile
proc ft
fn 262144
math f
werr
wexp
wbs
wnt wft
PhthN
NPhth
HO
N
H
N
OMe
(+)-61
11
10
9
8
7
6
5
4
3
2
1
ppm

exp2 s2pul

solvent CDCl3

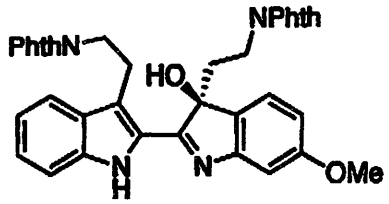
ACQUISITION	
sfrq	125.795
tn	C13
at	1.795
np	131010
sw	37735.8
fb	not used
bs	2
ss	1
tpwr	53
pw	5.9
d1	0.763
tof	631.4
nt	1e+06
ct	1162
alock	n
gain	80

FLAGS	
il	n
in	n
dp	y
hs	nn

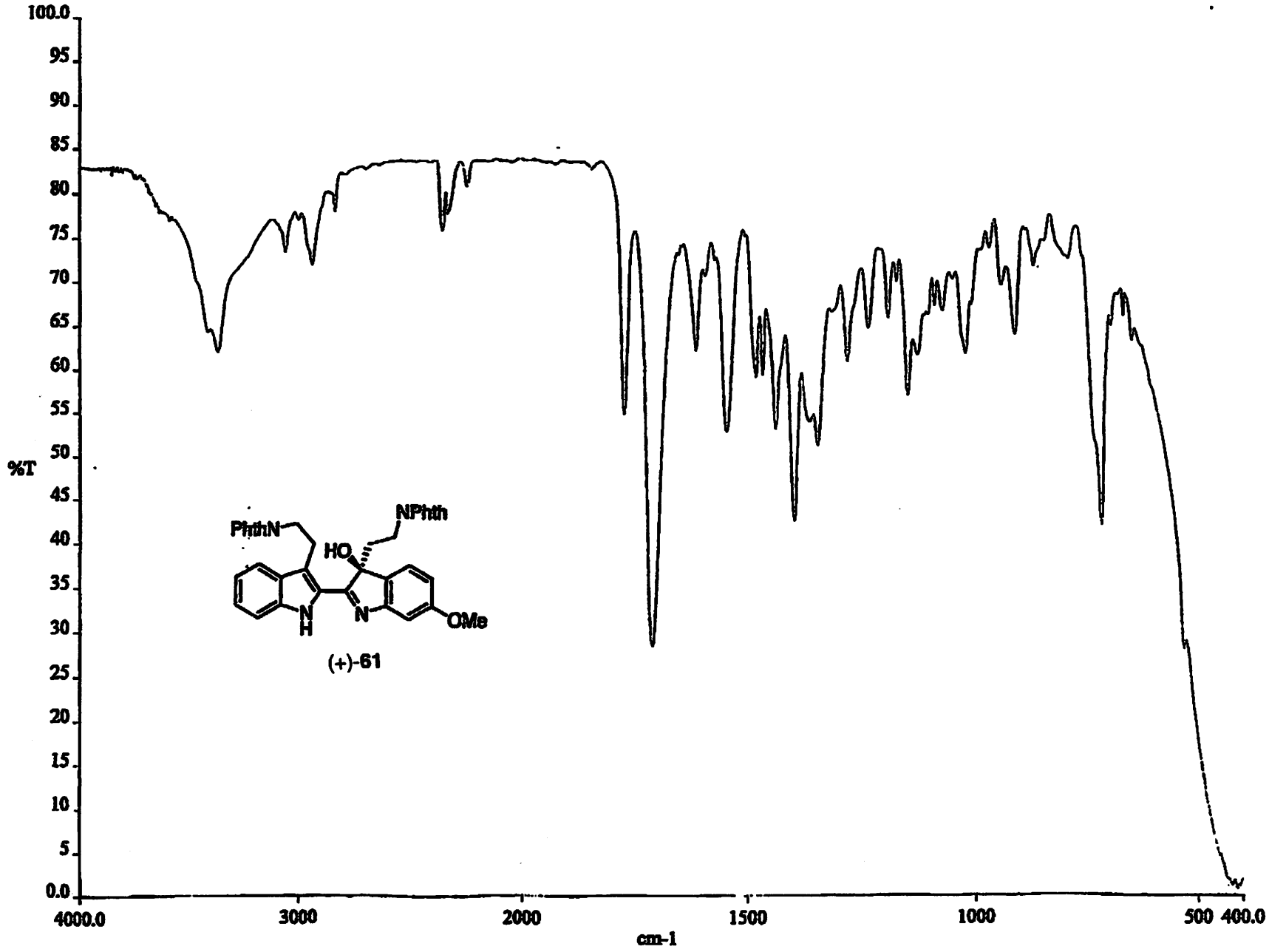
DISPLAY	
sp	-6285.8
wp	37735.3
vs	237
sc	0
wc	250
hzmm	2.18
is	500.00
rfl	16001.2
rfp	8714.9
th	18
ins	1.000
ns	ph

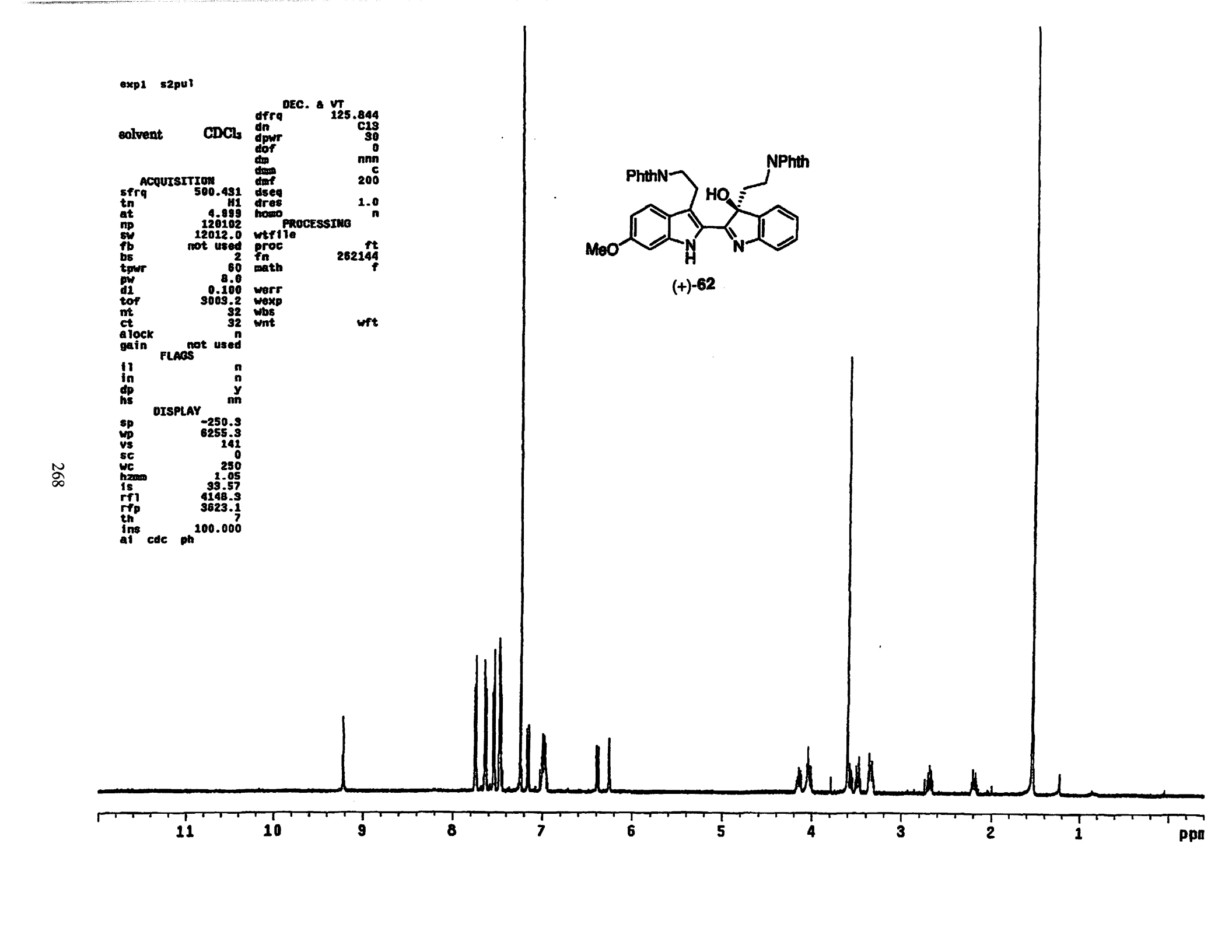
DEC. & VT	
dfrq	500.229
dn	H1
dpwr	37
dof	-500.0
dm	y
dmm	w
dmf	10000
dseq	
dres	1.0
homo	n

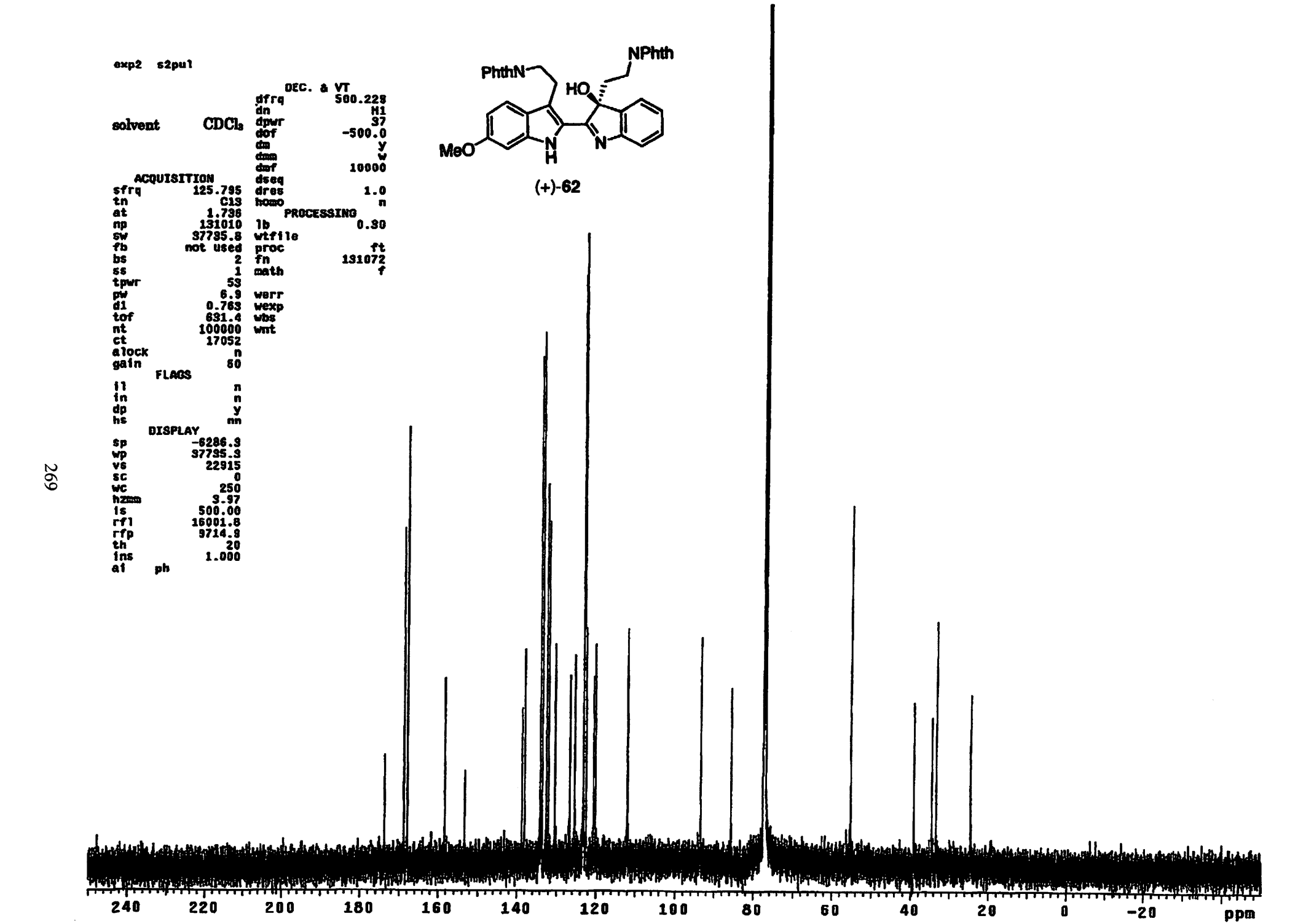
PROCESSING	
lb	0.30
wtfile	
proc	ft
fn	131072
math	f
werr	
wexp	
wbs	
wnt	

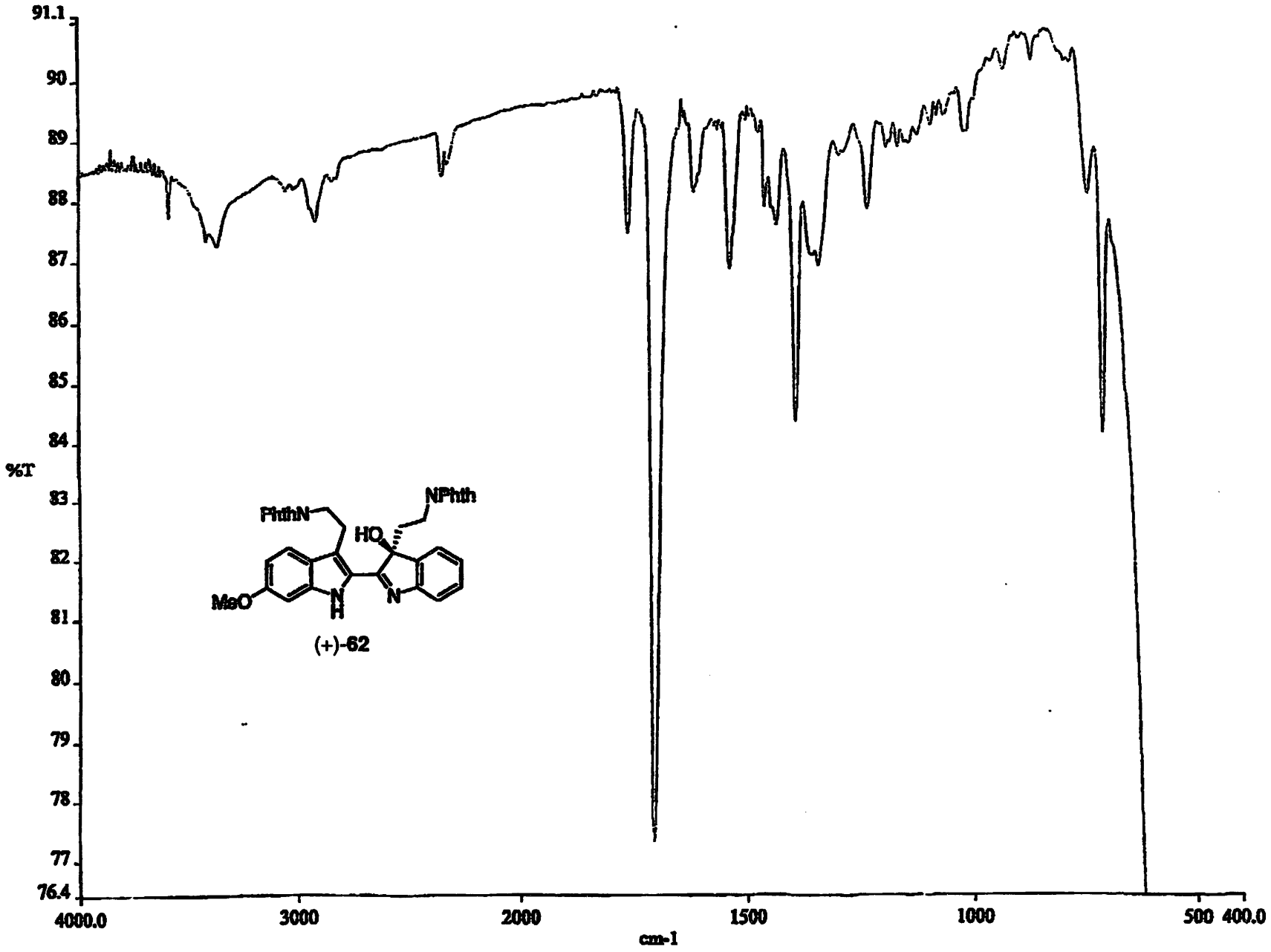


(+)-61


100.0
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0.0
%T
4000.0
3000
2000
1500
1000
500
400.0
cm-1
PhthN
NPhth
HO
N
H
N
OMe
(+)-61


expl s2pul
solvent CDCl3
ACQUISITION
sfrq 500.431
tn H1
at 4.899
np 120102
sw 12012.0
fb not used
bs 2
tpwr 60
pw 8.0
dl 0.100
tof 3003.2
nt 32
ct 32
alock n
gain not used
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -250.3
wp 6255.3
vs 141
sc 0
wc 250
hzmm 1.05
is 33.57
rfl 4148.3
rfp 3823.1
th 7
ins 100.000
ai cdc ph
DEC. & VT
dfrq 125.844
dn C13
dpwr 30
dof 0
dm nnn
dmm c
dmf 200
dseq
dres 1.0
homo n
PROCESSING
wtfile
proc ft
fn 262144
math f
werr
wexp
wbs
wnt wft
PhthN
NPhth
HO
MeO
N
H
N
(+)-62
11
10
9
8
7
6
5
4
3
2
1
ppm

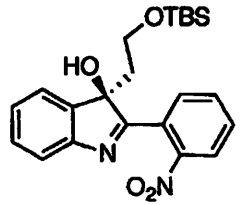

exp2 s2pul
solvent CDCl3
ACQUISITION
sfrq 125.795
tn C13
at 1.736
np 131010
sw 37735.8
fb not used
bs 2
ss 1
tpwr 53
pw 6.9
d1 0.763
tof 631.4
nt 100000
ct 17052
alock n
gain 60
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -6286.3
wp 37735.3
vs 22915
sc 0
wc 250
hzmm 3.97
is 500.00
rfl 16001.8
rfp 9714.9
th 20
ins 1.000
ai ph
DEC. & VT
dfrq 500.228
dn H1
dpwr 37
dof -500.0
dm y
dmm w
dmf 10000
dseq
dres 1.0
homo n
PROCESSING
lb 0.30
wtfile
proc ft
fn 131072
math f
werr
wexp
wbs
wnt
PhthN
NPhth
HO
MeO
N
H
N
(+)-62
240
220
200
180
160
140
120
100
80
60
40
20
0
-20
ppm


91.1
90
89
88
87
86
85
84
%T
83
82
81
80
79
78
77
76.4
4000.0
3000
2000
1500
1000
500 400.0
cm-1
PhthN
NPhth
HO
MeO
N
H
N

(+)-62

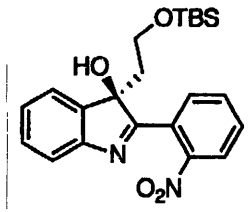
exp1 s2pul

		DEC. & VT	
solvent	CDCl3	dfrq	125.844
		dn	C13
		dpwr	30
		dof	0
		dm	nnn
		dmm	c
ACQUISITION		dmf	200
sfrq	500.431	dseq	
tn	H1	dres	1.0
at	4.999	homo	n
np	120102	PROCESSING	
sw	12012.0	wtfile	
fb	not used	proc	ft
bs	2	fn	262144
tpwr	60	math	f
pw	8.0		
d1	0.100	werr	
tof	3003.2	wexp	
nt	32	wbs	
ct	14	wnt	
alock	n		
gain	not used		
FLAGS			
il	n		
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-250.3		
wp	6255.3		
vs	15		
sc	0		
wc	250		
hzmm	25.02		
is	33.57		
rfl	4149.0		
rfp	3623.1		
th	7		
ins	100.000		
ai cdc ph			



(+)-**65**

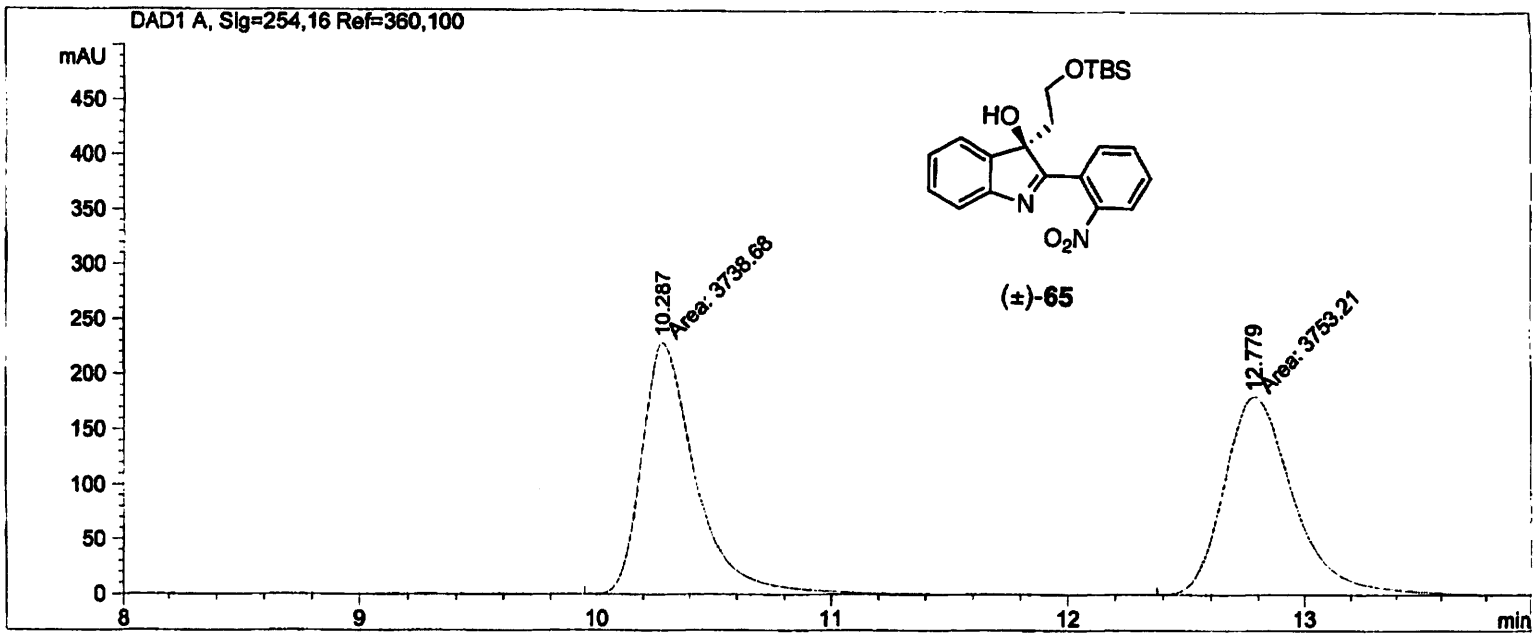
```
exp1  s2pul

                                    DEC. & VT
                                dfrq        500.229
solvent          CDCl3          dn               H1
                                dpwr             45
                                dof          -500.0
                                dm               y
                                dmm              w
                                dmf          10000
   ACQUISITION                  dseq
sfrq          125.795           dres            1.0
tn                C13           homo             n
at              1.736               PROCESSING
np             131010           lb             0.30
sw           37735.8            wtfile
fb         not used             proc             ft
bs                2             fn          131072
ss                1             math             f
tpwr             58
pw              6.9             werr
d1            0.763             wexp
tof           631.4             wbs
nt           100000             wnt
ct              112
alock             n
gain             60
      FLAGS
il                n
in                n
dp                y
hs               nn
     DISPLAY
sp          -6288.6
wp          37735.3
vs             1229
sc                0
wc              250
hzmm           6.29
is           500.00
rfl         16004.1
rfp          9714.9
th               12
ins           1.000
ai    ph
```



(+)-65

chiralpak IC-H 0.5 mL/min 80:20=Hx:IPA

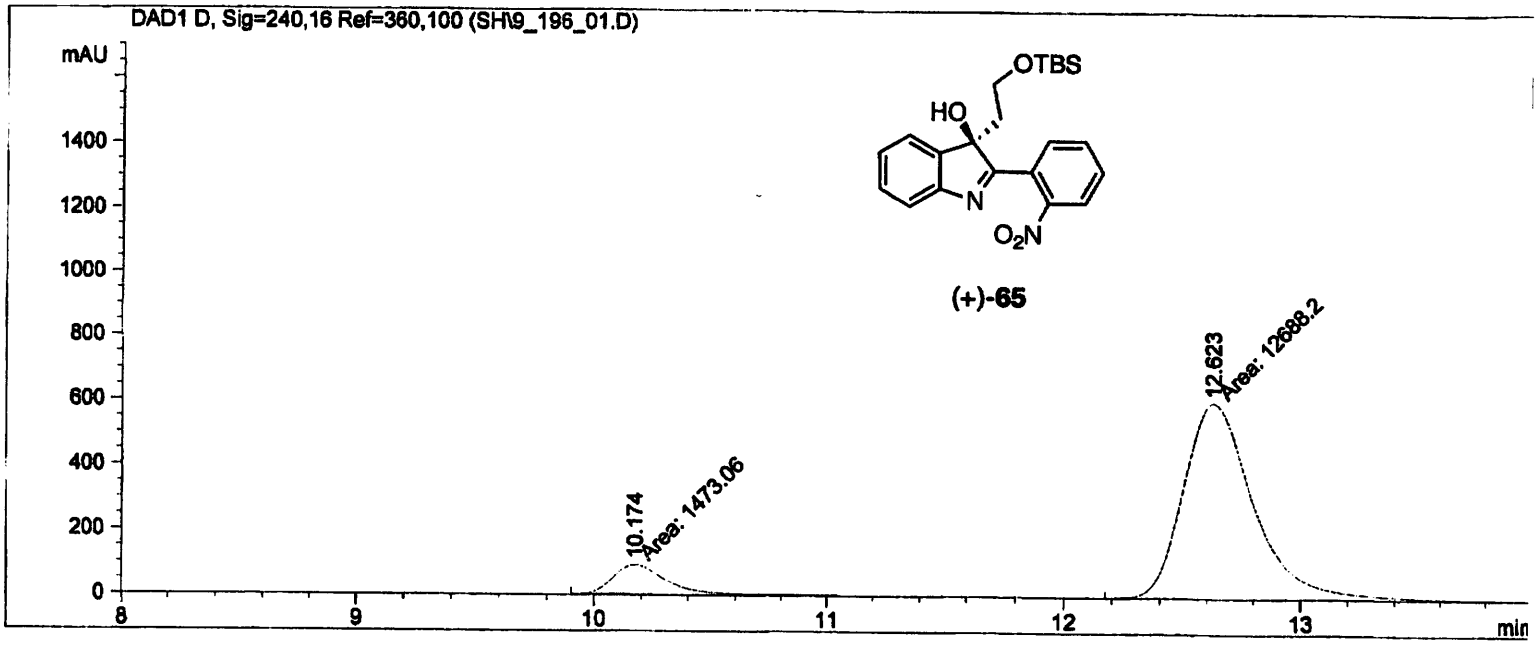
```
==========================================================================
Injection Date  :                                  Seq. Line :   3
Sample Name     :                                   Location : Vial 91
Acq. Operator   : SH                                    Inj :   1
                                                  Inj Volume : 0 µl
Different Inj Volume from Sequence !     Actual Inj Volume : 5 µl
Acq. Method     :
Last changed    :
Analysis Method :
Last changed    :

==========================================================================
```




```
==========================================================================
                        Area Percent Report
==========================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,16 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  10.287 MM    0.2718 3738.68066  229.28889  49.9031
   2  12.779 MM    0.3450 3753.20703  181.29138  50.0969

Totals :                  7491.88770  410.58028

 Results obtained with enhanced integrator!
==========================================================================
                        Summed Peaks Report
==========================================================================

Signal 1: DAD1 A, Sig=254,16 Ref=360,100
==========================================================================
                     Final Summed Peaks Report
==========================================================================

Signal 1: DAD1 A, Sig=254,16 Ref=360,100
```

chiralpak IC 80:20=Hx:IPA 0.5 mL/min

```
Injection Date  :                                    Seq. Line :   1
Sample Name     :                                     Location : Vial 91
Acq. Operator   : SH                                     Inj :   1
                                                   Inj Volume : 0 µl
Different Inj Volume from Sequence !      Actual Inj Volume : 5 µl
Acq. Method     :
Last changed    :
Analysis Method :
Last changed    :
```



Area Percent Report

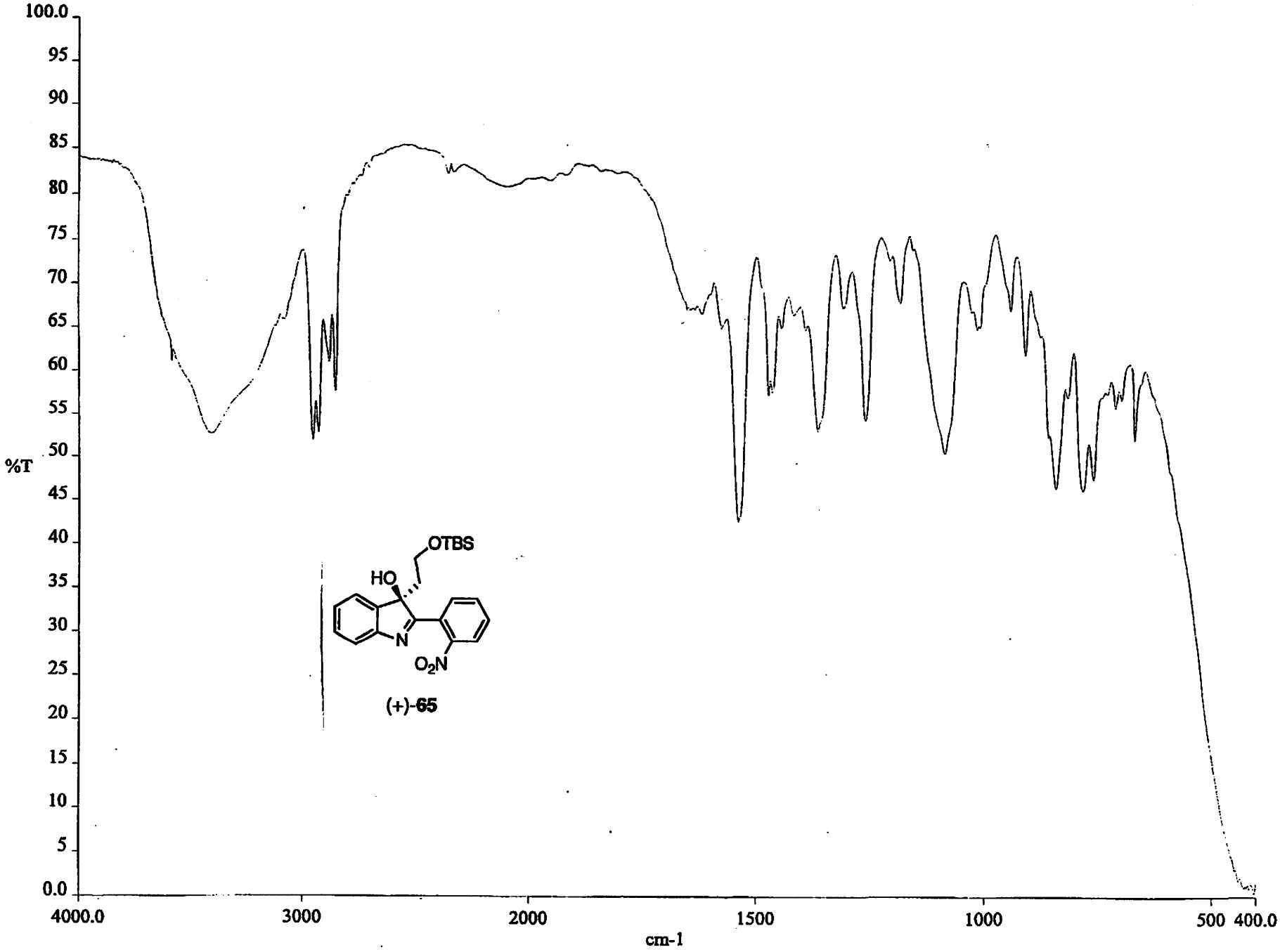
```
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 D, Sig=240,16 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|-------|
   1  10.174 MM    0.2661 1473.06104   92.25103  10.4020
   2  12.623 MM    0.3503 1.26882e4   603.61407  89.5980

Totals :                  1.41613e4   695.86510

 Results obtained with enhanced integrator!
```

Summed Peaks Report

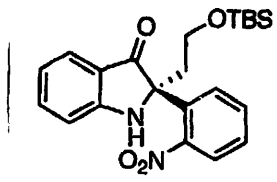
```
Signal 1: DAD1 D, Sig=240,16 Ref=360,100
```

Final Summed Peaks Report

```
Signal 1: DAD1 D, Sig=240,16 Ref=360,100
```


100.0
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0.0
%T
4000.0
3000
2000
1500
1000
500
400.0
cm-1
OTBS
HO
N
O2N
(+)-65

```
exp1  s2pul

                                    DEC. & VT
                                dfrq          125.844
solvent          CDCl3          dn                C13
                                dpwr               30
                                dof                 0
                                dm                nnn
                                dmm                 c
   ACQUISITION                  dmf               200
sfrq          500.431           dseq
tn                H1            dres              1.0
at              4.999           homo                n
np             120102               PROCESSING
sw           12012.0            wtfile
fb         not used             proc                ft
bs                2             fn             262144
tpwr             60             math                f
pw              8.0
d1              0.100           werr
tof           3003.2            wexp
nt                32            wbs
ct                32            wnt
alock              n
gain       not used
      FLAGS
il                 n
in                 n
dp                 y
hs                nn
     DISPLAY
sp             -250.3
wp             6255.3
vs                 10
sc                  0
wc                250
hzmm             4.18
is              33.57
rfl           4148.9
rfp           3623.1
th                 26
ins             1.000
ai  cdc  ph
```



(–)-66

exp1 s2pul

solvent	CDCl3

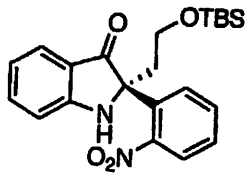
ACQUISITION	
sfrq	125.795
tn	C13
at	1.736
np	131010
sw	37735.8
fb	not used
bs	2
ss	1
tpwr	58
pw	6.9
d1	0.763
tof	631.4
nt	100000
ct	986
alock	n
gain	60

FLAGS	
il	n
in	n
dp	y
hs	nn

DISPLAY	
sp	-6287.5
wp	37735.3
vs	3064
sc	0
wc	250
hzmm	61.49
is	500.00
rfl	16003.0
rfp	9714.9
th	8
ins	1.000
ai	ph

DEC. & VT	
dfrq	500.229
dn	H1
dpwr	45
dof	-500.0
dm	y
dmm	w
dmf	10000
dseq	
dres	1.0
homo	n

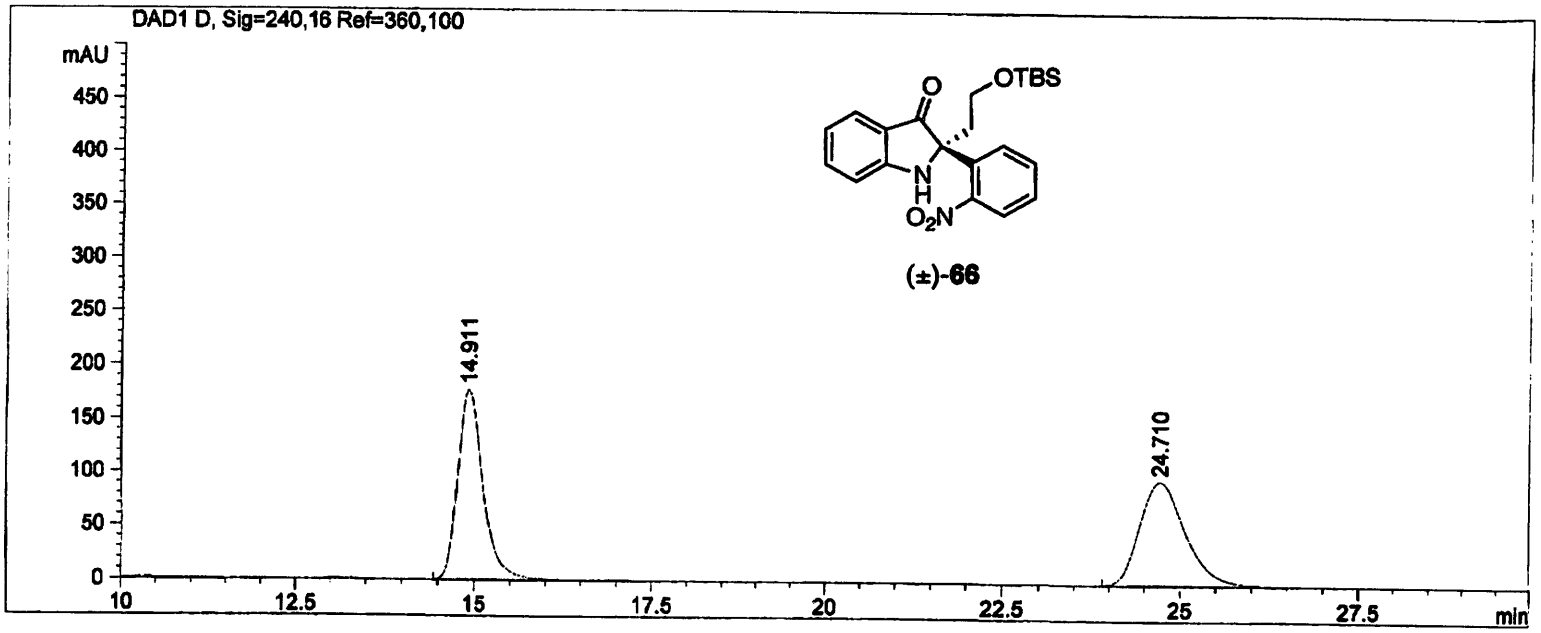
PROCESSING	
lb	0.30
wtfile	
proc	ft
fn	131072
math	f
werr	
wexp	
wbs	
wnt	



(–)-66

chiralpak IC 80:20=Hx:IPA 0.5 mL/min

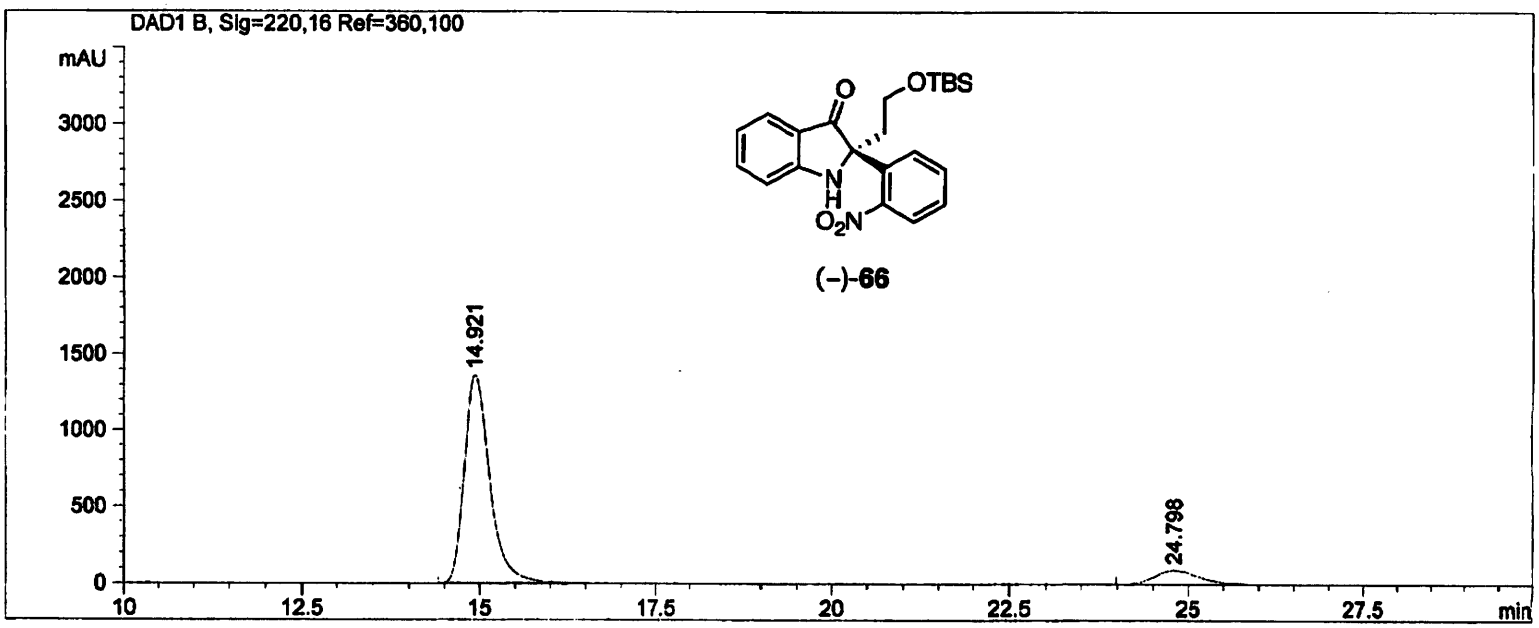
```
==========================================================================
Injection Date  :                                    Seq. Line :   1
Sample Name     :                                     Location : Vial 91
Acq. Operator   : SH                                      Inj :   1
                                                  Inj Volume : 0 µl
Different Inj Volume from Sequence !      Actual Inj Volume : 5 µl
Acq. Method     :
Last changed    :

Analysis Method :
Last changed    :

==========================================================================
```



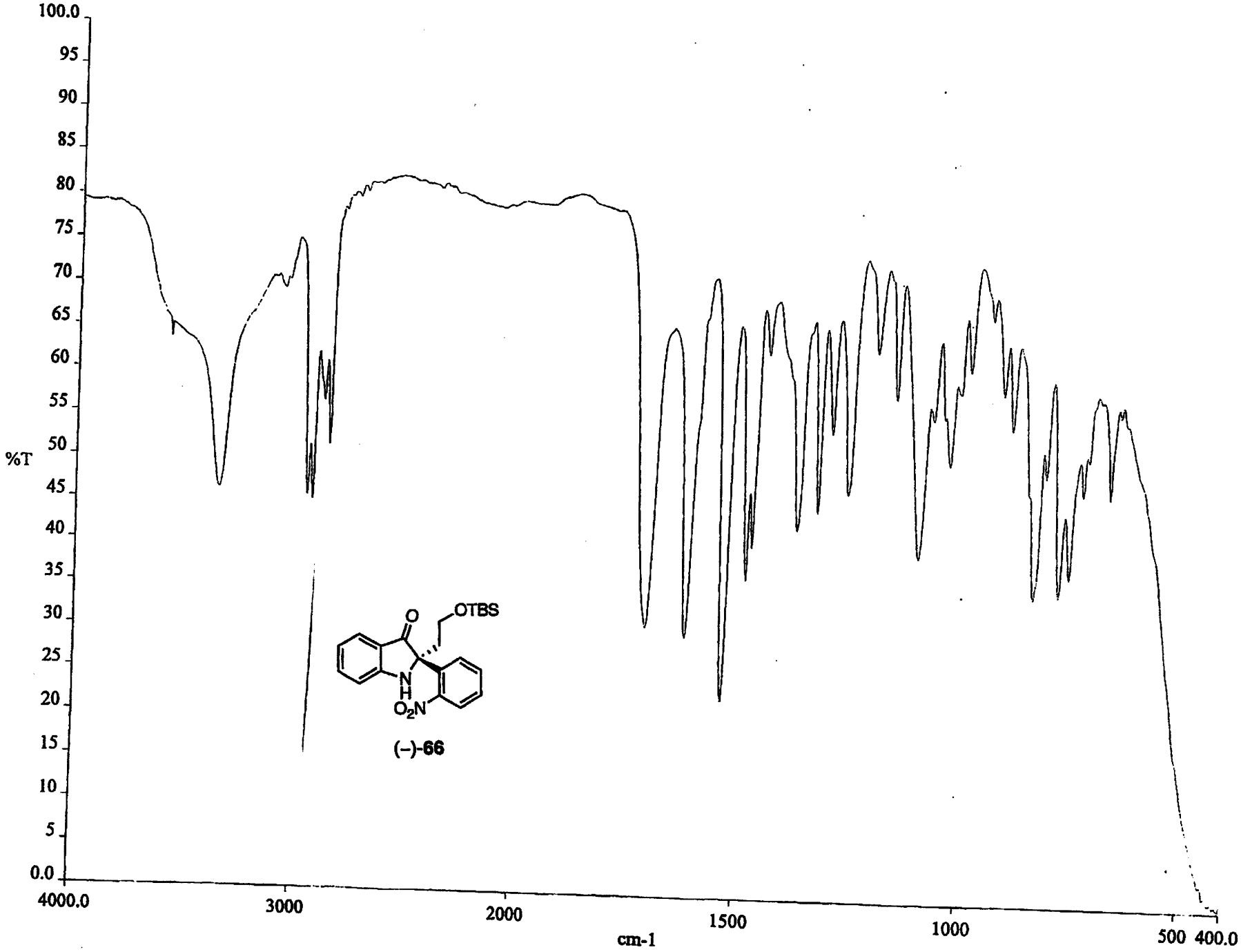

```
==========================================================================
                          Area Percent Report
==========================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 D, Sig=240,16 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|-------|
   1  14.911 BB    0.3701 4303.46680  177.35651  50.1508
   2  24.710 BB    0.6603 4277.58594   96.65764  49.8492

Totals :                  8581.05273  274.01414

 Results obtained with enhanced integrator!
==========================================================================
                          Summed Peaks Report
==========================================================================

Signal 1: DAD1 D, Sig=240,16 Ref=360,100
```

chiralpak IC 83:17=Hx:IPA 0.5 mL/min

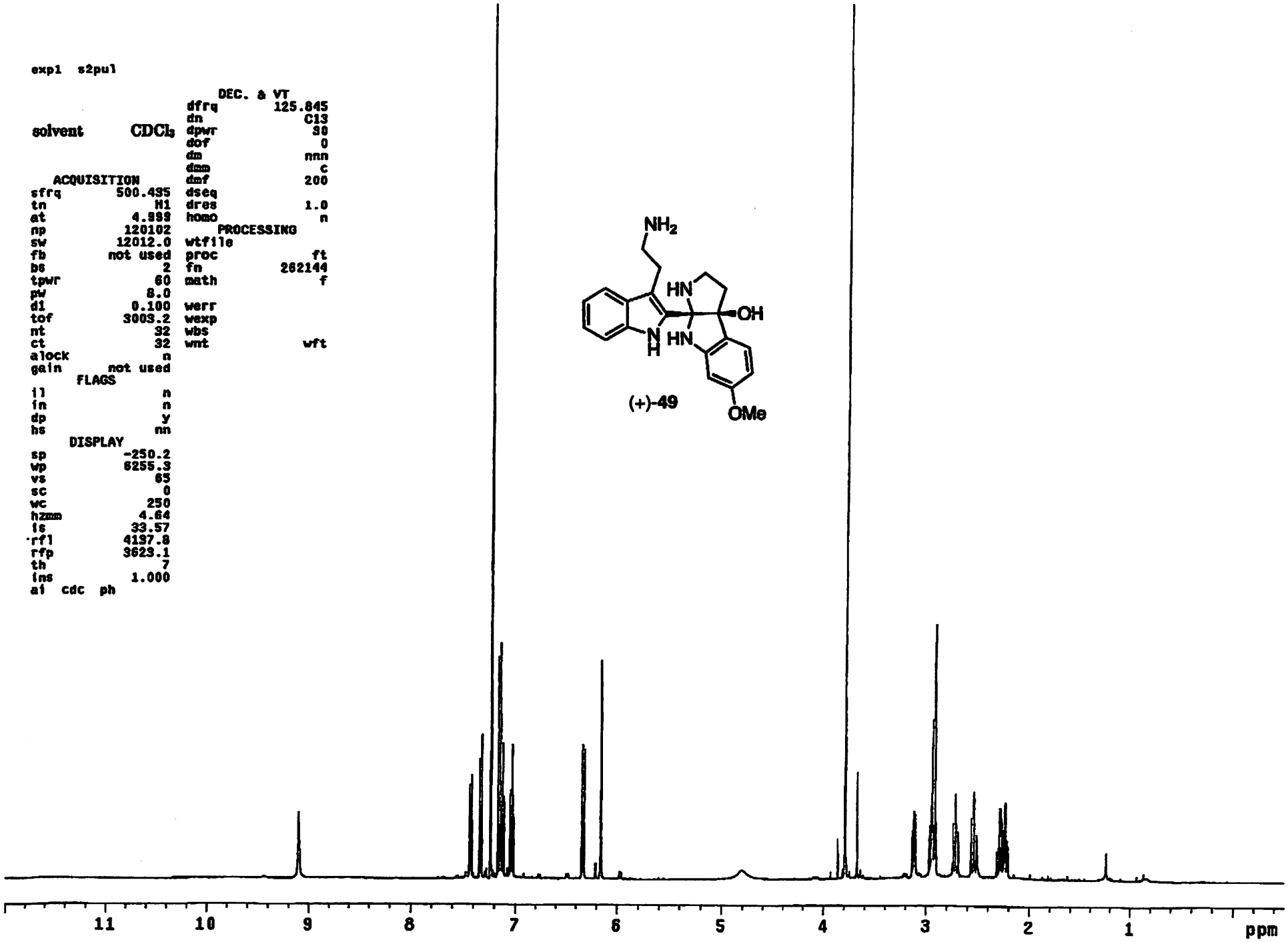
```
==========================================================================
Injection Date  :                                   Seq. Line :   2
Sample Name     :                                    Location : Vial 92
Acq. Operator   : SH                                     Inj :   1
                                                  Inj Volume : 0 µl
Different Inj Volume from Sequence !     Actual Inj Volume : 5 µl
Acq. Method     :
Last changed    :

Analysis Method :
Last changed    :

==========================================================================
```




```
==========================================================================
                        Area Percent Report
==========================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 B, Sig=220,16 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  14.921 BB    0.3776 3.41137e4  1364.64807  89.3473
   2  24.798 BB    0.6212 4067.29736   91.39735  10.6527

Totals :                  3.81810e4  1456.04542

 Results obtained with enhanced integrator!
==========================================================================
                        Summed Peaks Report
==========================================================================

Signal 1: DAD1 B, Sig=220,16 Ref=360,100
```


100.0
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0.0
%T
4000.0
3000
2000
1500
1000
500
400.0
cm-1
O
OTBS
N
H
O2N

(–)-66


exp1 s2pul
solvent CDCl3
ACQUISITION
sfrq 500.435
tn H1
at 4.999
np 120102
sw 12012.0
fb not used
bs 2
tpwr 60
pw 8.0
d1 0.100
tof 3003.2
nt 32
ct 32
alock n
gain not used
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -250.2
wp 6255.3
vs 65
sc 0
wc 250
hzmm 4.64
is 33.57
rf1 4197.8
rfp 3623.1
th 7
ins 1.000
ai cdc ph
DEC. & VT
dfrq 125.845
dn C13
dpwr 30
dof 0
dm nnn
dmm c
dmf 200
dseq
dres 1.0
homo n
PROCESSING
wtfile
proc ft
fn 262144
math f
werr
wexp
wbs
wnt wft
NH2
HN
OH
N
H
HN
(+)-49
OMe
11
10
9
8
7
6
5
4
3
2
1
ppm

exp2 s2pul

solvent	$CDCl_3$

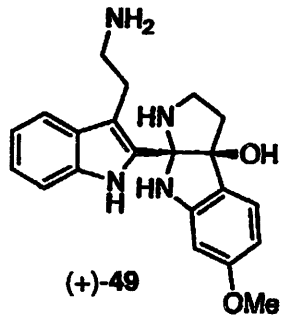
ACQUISITION	
sfrq	125.795
tn	C13
at	1.736
np	131010
sw	37735.8
fb	not used
bs	2
ss	1
tpwr	53
pw	6.9
d1	0.763
tof	631.4
nt	100000
ct	86
alock	n
gain	60

FLAGS	
il	n
in	n
dp	y
hs	nn

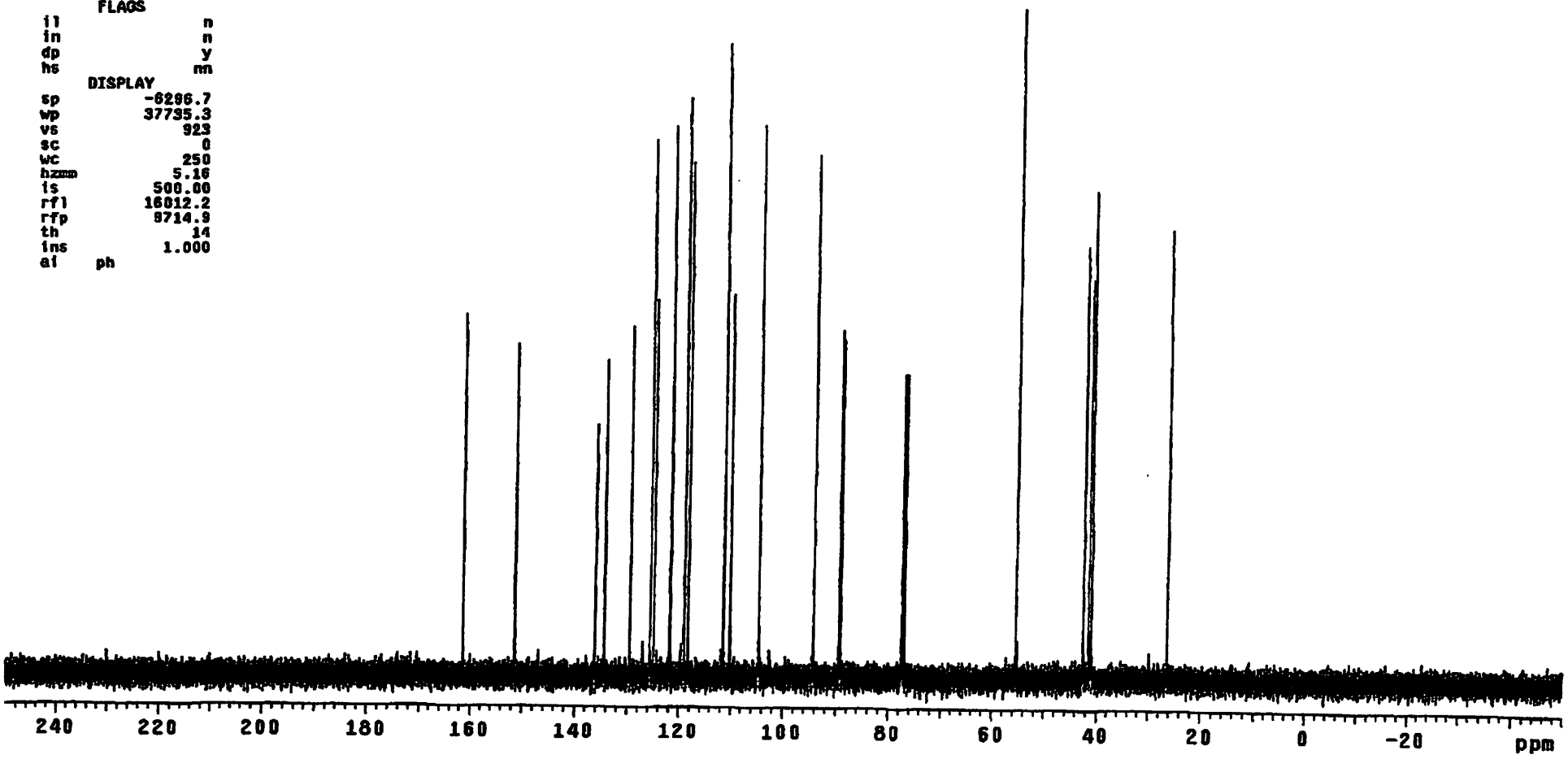
DISPLAY	
sp	-6296.7
wp	37735.3
vs	923
sc	0
wc	250
hzmm	5.16
is	500.00
rfl	16012.2
rfp	9714.9
th	14
ins	1.000
al	ph

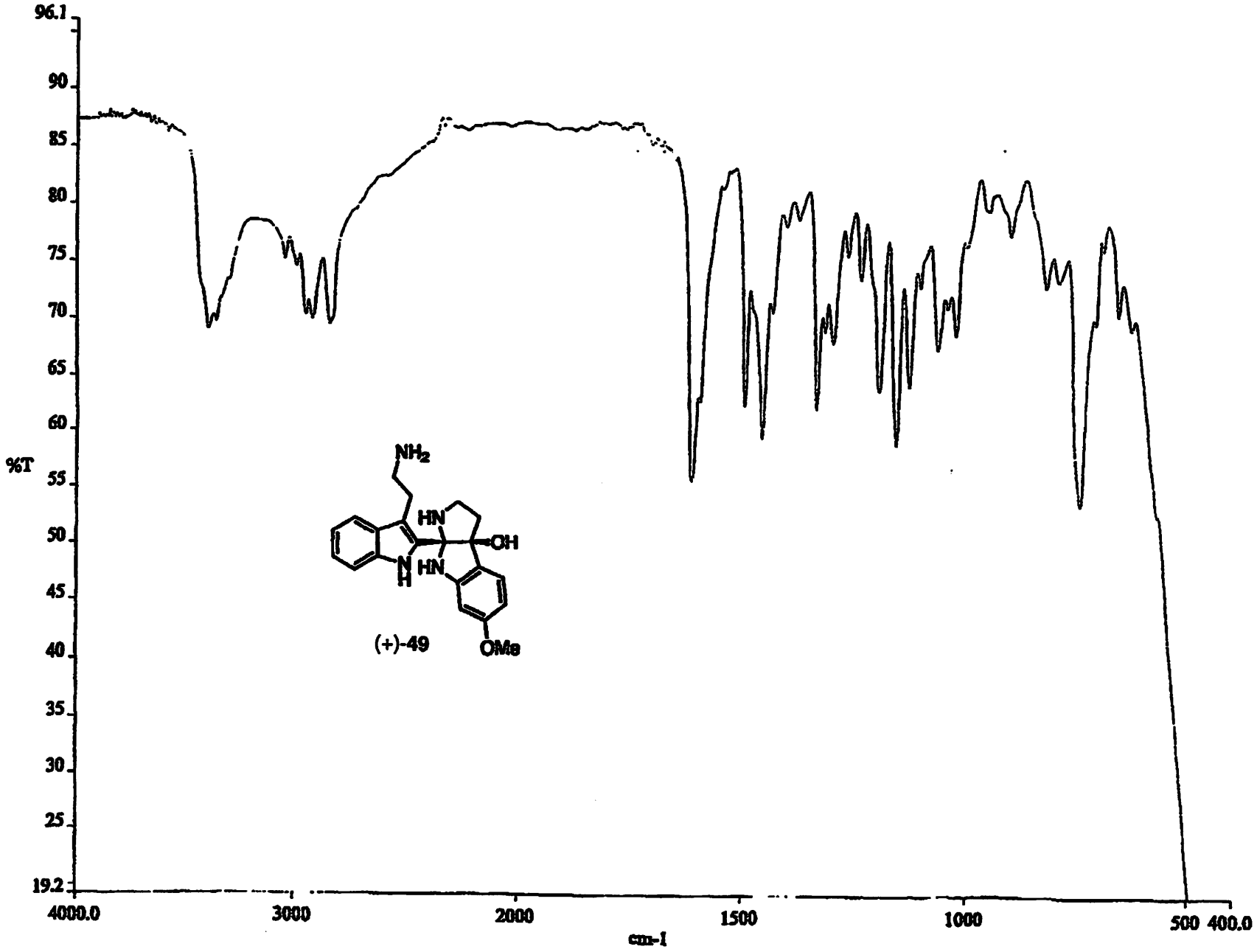
DEC. & VT	
dfrq	500.229
dn	H1
dpwr	37
dof	-500.0
dm	y
dmm	w
dmf	10000
dseq	
dres	1.0
homo	n

PROCESSING	
lb	0.30
wtfile	
proc	ft
fn	131072
math	f
werr	
wexp	
wbs	
wnt	



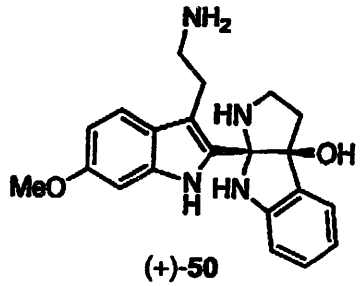
(+)-49



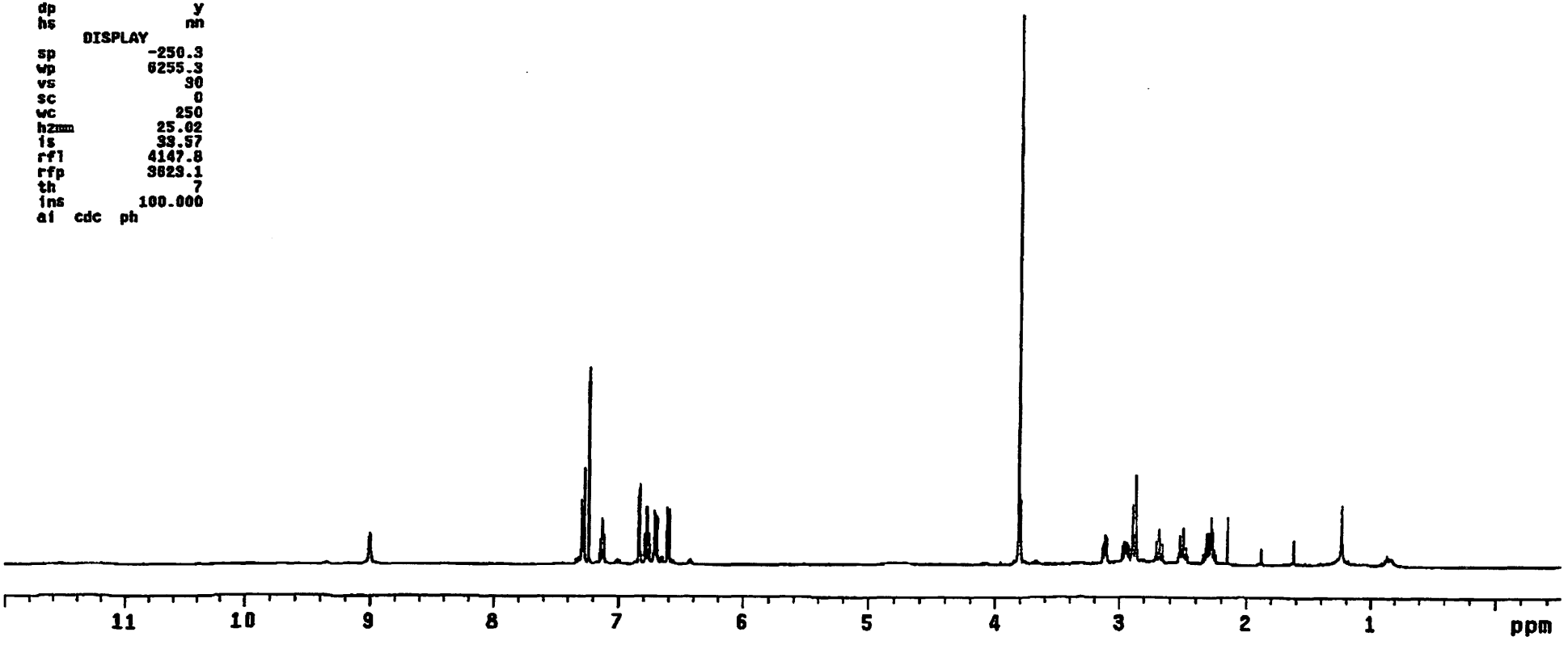

96.1
90
85
80
75
70
65
60
55
50
45
40
35
30
25
19.2
%T
4000.0
3000
2000
1500
1000
500
400.0
cm-1
NH2
HN
OH
N
H
HN
(+)-49
OMe

exp1 s2pul

solvent	CDCl3		
		DEC. & VT	
		dfrq	125.844
		dn	C13
		dpwr	30
		dof	0
		dm	nnn
		dmm	c
ACQUISITION		dmf	200
sfrq	500.431	dseq	
tn	H1	dres	1.0
at	4.999	homo	n
np	120102	PROCESSING	
sw	12012.0	wtfile	
fb	not used	proc	ft
bs	2	fn	262144
tpwr	60	math	f
pw	8.0		
d1	0.100	werr	
tof	3003.2	wexp	
nt	32	wbs	
ct	10	wnt	wft
alock	n		
gain	not used		
FLAGS			
il	n		
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-250.3		
wp	6255.3		
vs	30		
sc	0		
wc	250		
hzmm	25.02		
is	38.57		
rfl	4147.8		
rfp	3829.1		
th	7		
ins	100.000		
ai cdc ph			



(+)-50



exp2 s2pul

solvent $CDCl_3$

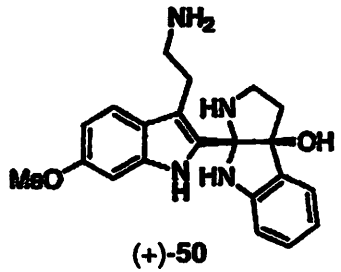
ACQUISITION	
sfrq	125.795
tn	C13
at	1.736
np	131010
sw	37735.8
fb	not used
bs	2
ss	1
tpwr	53
pw	6.9
d1	0.763
tof	631.4
nt	10800
ct	420
alock	n
gain	60

FLAGS	
il	n
in	n
dp	y
hs	nn

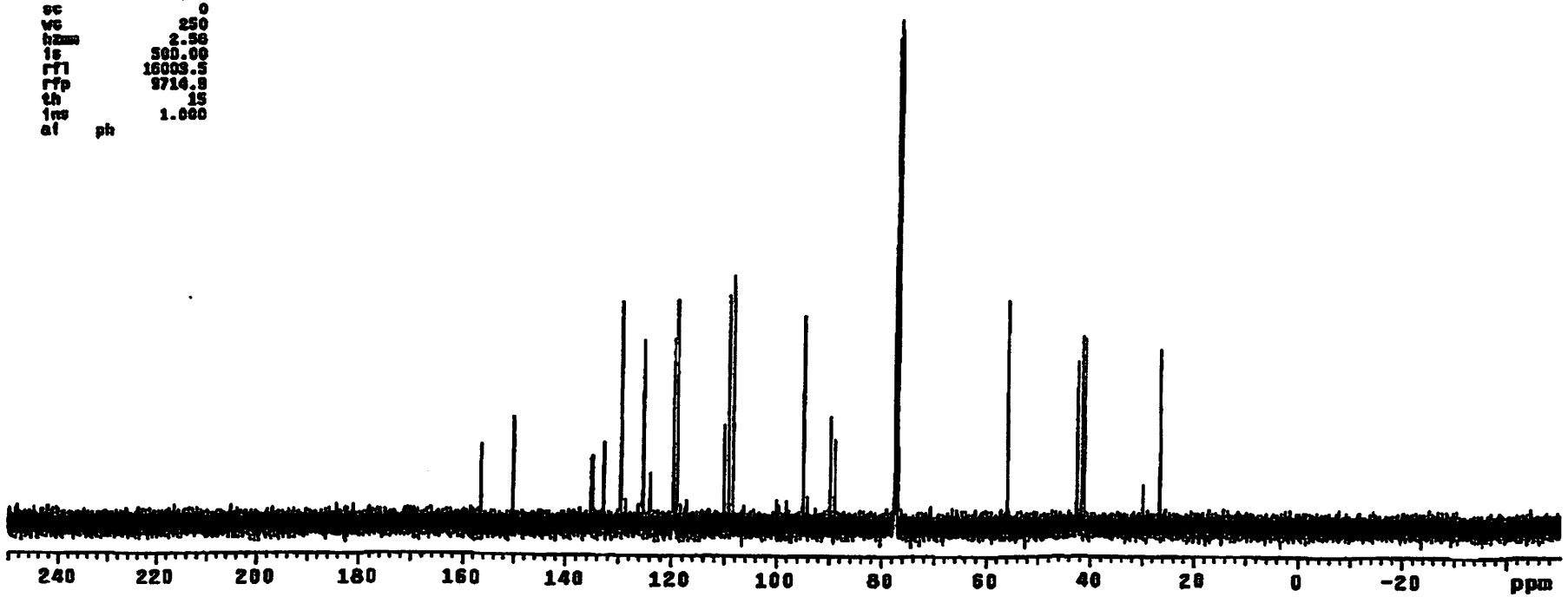
DISPLAY	
sp	-3288.1
wp	37735.9
vs	1781
sc	0
vc	250
hzmm	2.56
is	500.00
rfl	16009.5
rfp	9714.8
th	15
ins	1.000
ai	ph

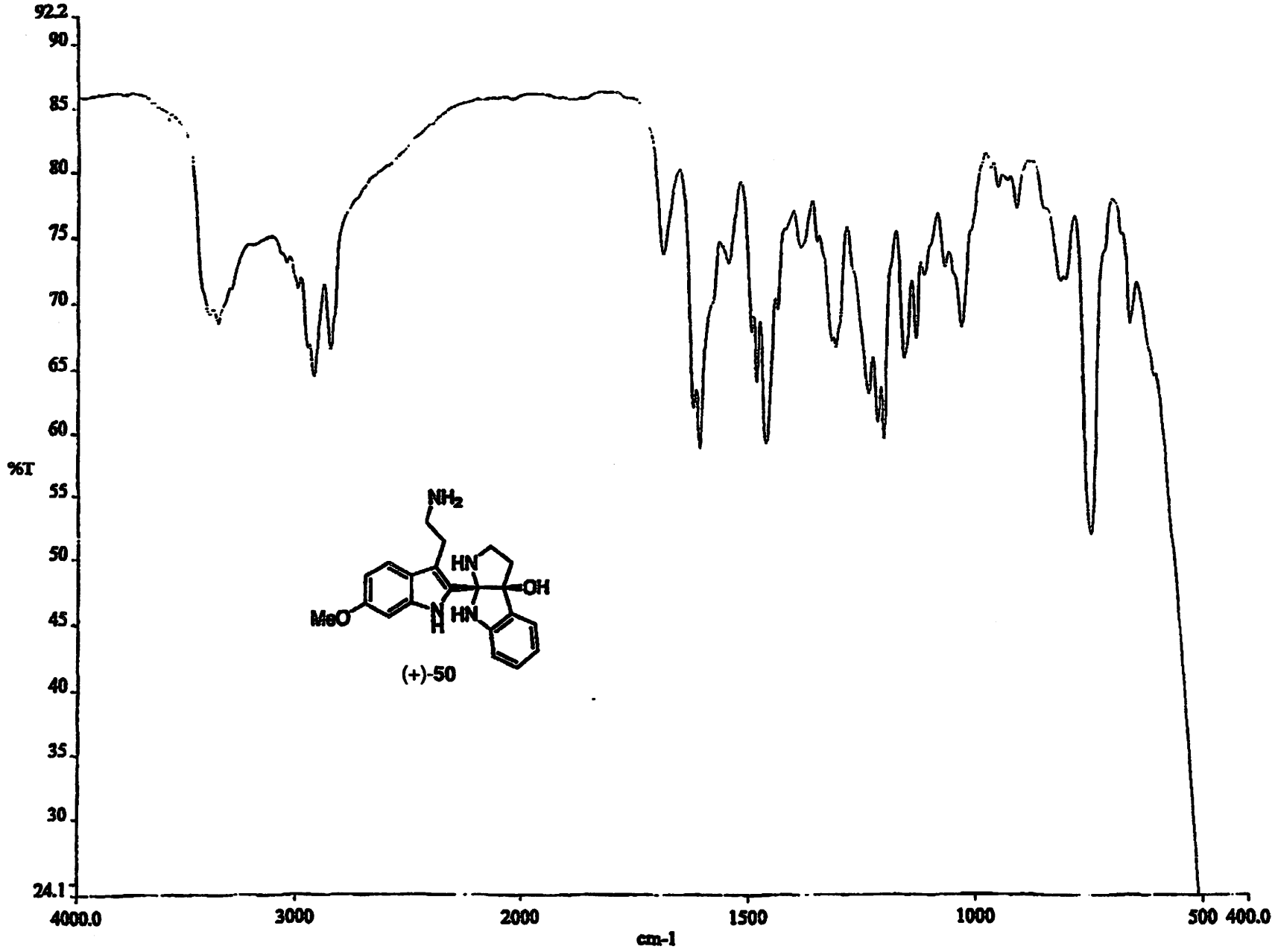
DEC. & VT	
dfrq	500.229
dn	H1
dpwr	37
dof	-500.0
dm	y
dmm	w
dmf	10000
dseq	
dres	1.0
homo	n

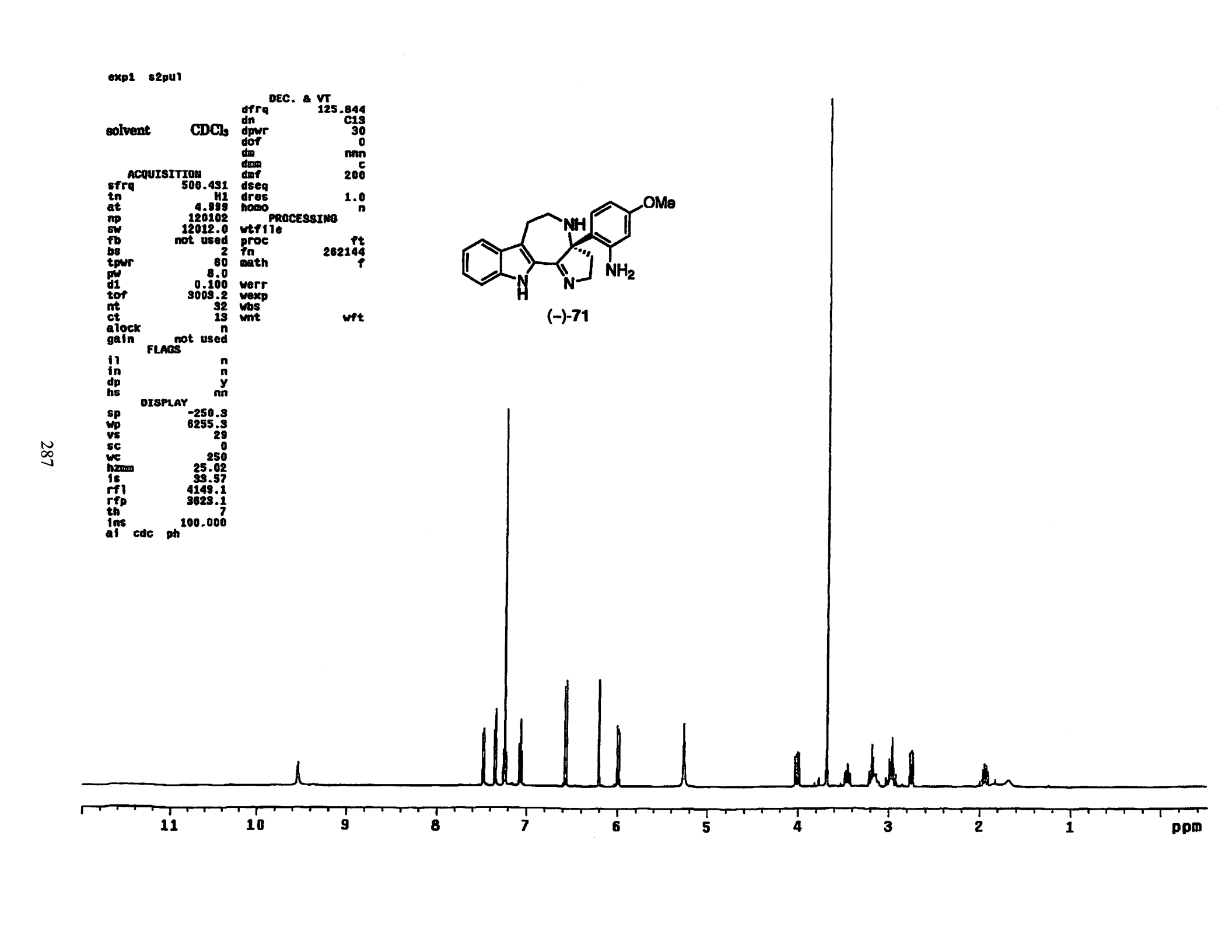
PROCESSING	
lb	0.30
wtfile	
proc	ft
fn	131072
math	f
werr	
wexp	
wbs	
wnt	



(+)-50




92.2
90
85
80
75
70
65
60
%T
55
50
45
40
35
30
24.1
4000.0
3000
2000
1500
1000
500 400.0
cm-1
NH2
HN
OH
MeO
N
H
HN
(+)-50


exp1 s2pul
solvent CDCl3
ACQUISITION
sfrq 500.431
tn H1
at 4.999
np 120102
sw 12012.0
fb not used
bs 2
tpwr 60
pw 8.0
d1 0.100
tof 3009.2
nt 32
ct 13
alock n
gain not used
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -250.3
wp 6255.3
vs 29
sc 0
wc 250
hzmm 25.02
is 39.57
rfl 4149.1
rfp 3629.1
th 7
ins 100.000
ai cdc ph
DEC. & VT
dfrq 125.844
dn C13
dpwr 30
dof 0
dm nnn
dmm c
dmf 200
dseq
dres 1.0
homo n
PROCESSING
wtfile
proc ft
fn 262144
math f
werr
wexp
wbs
wnt wft
OMe
NH
NH2
N
N
H
(-)-71
11
10
9
8
7
6
5
4
3
2
1
ppm

exp2 s2pul

solvent $CDCl_3$

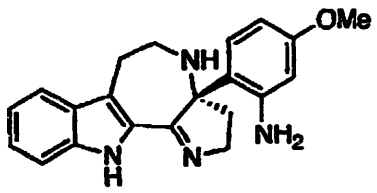
ACQUISITION	
sfrq	125.795
tn	C13
at	1.736
np	131010
sw	37735.8
fb	not used
bs	2
ss	1
tpwr	53
pw	6.9
d1	0.763
tof	631.4
nt	100000
ct	2952
alock	n
gain	60

FLAGS	
il	n
in	n
dp	y
hs	nn

DISPLAY	
sp	-6285.8
wp	37735.3
vs	19720
sc	0
wc	250
hzmm	3.97
is	500.00
rf1	18001.2
rfp	9714.8
th	10
ins	1.000
ai	ph

DEC. & VT	
dfrq	500.229
dn	H1
dpwr	37
dof	-500.0
dm	y
dmm	w
dmf	10000
dseq	
dres	1.0
homo	n

PROCESSING	
lb	0.30
wtfile	
proc	ft
fn	131072
math	f
werr	
wexp	
wbs	
wnt	



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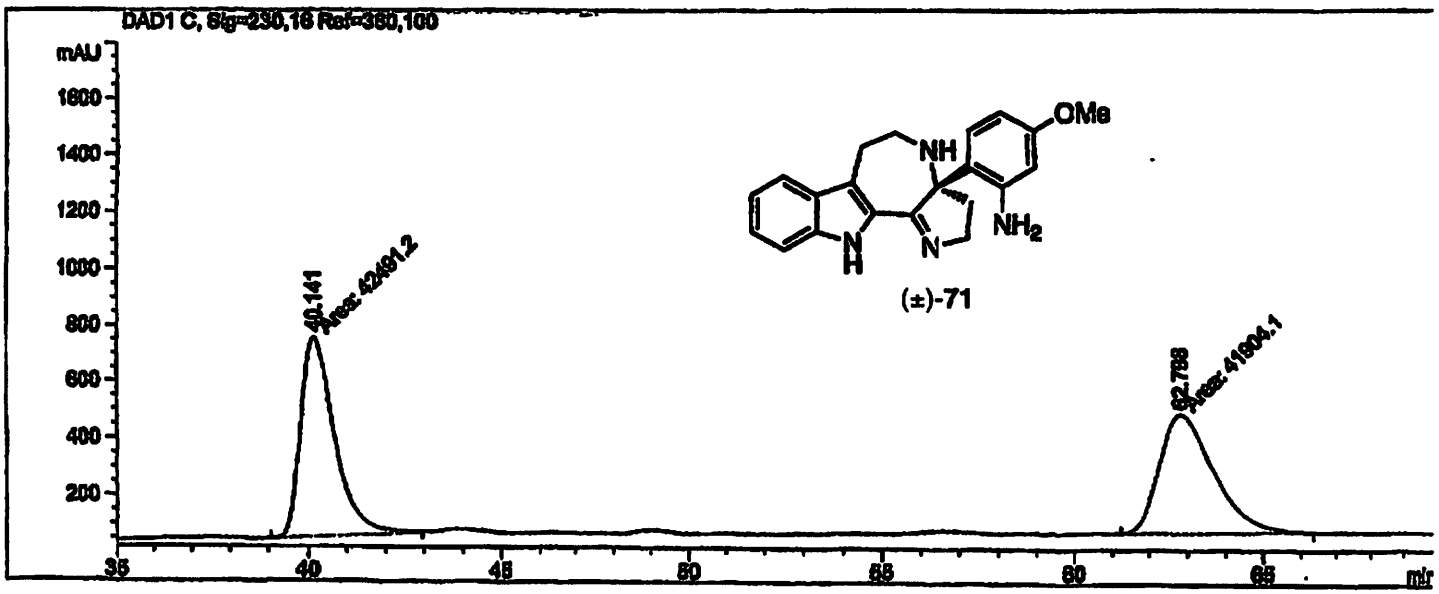
Chiralcell OD-H 0.5mL/min, 100% Hexane -> 80:20=iPrOH:H
x in 80 min

Injection Date	:	Seq. Line	: 6
Sample Name	:	Location	: Vial 27
Acq. Operator	:	Inj	: 1
		Inj Volume	: 0 µl
Different Inj Volume from Sequence !		Actual Inj Volume	: 10 µl
Acq. Method	:		
Last changed	:		
Analysis Method	:		
Last changed	:		



Area Percent Report

Sorted By	:	Signal
Multiplier	:	1.0000
Dilution	:	1.0000

Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 C, Sig=230,16 Ref=360,100

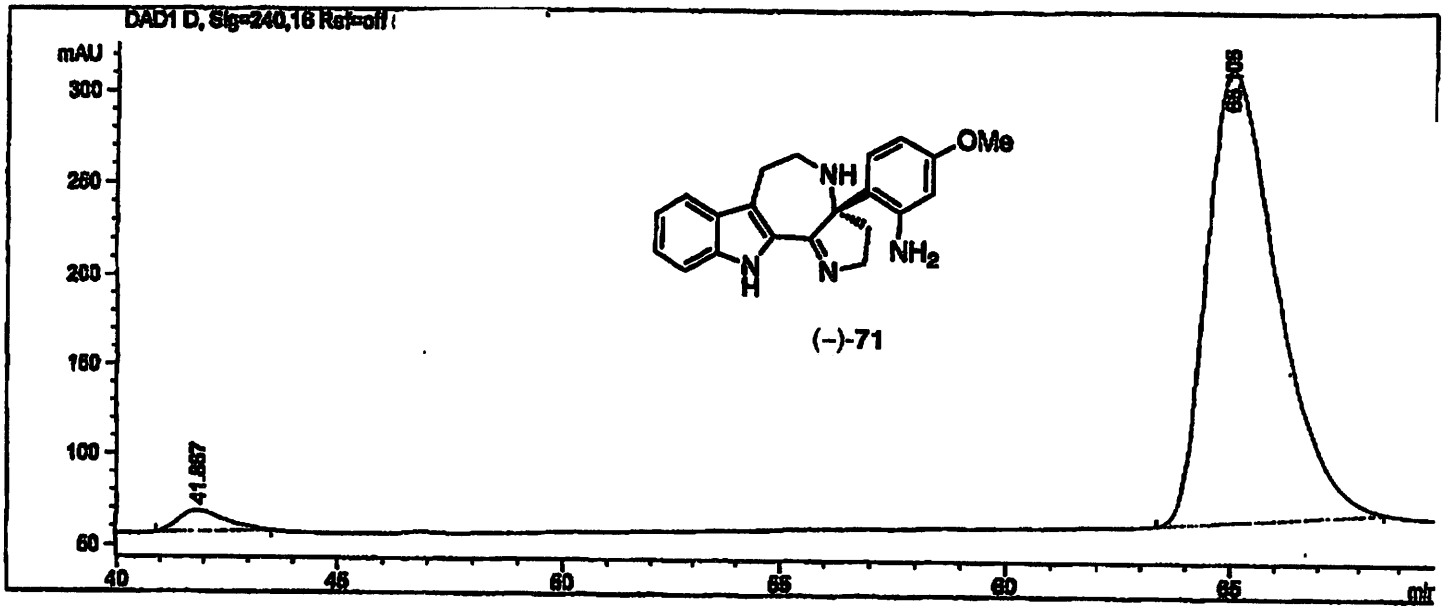
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	40.141	MM	1.0038	4.24912e4	705.52020	50.3479
2	62.798	MM	1.6881	4.19041e4	413.71451	49.6521
Totals :				8.43953e4	1119.23471	

Results obtained with enhanced integrator!

*** End of Report ***

chiralpak OD-H 100%Hexanes to 80% IPrOH over 80 min

Injection Date	:	Seq. Line	: 1
Sample Name	:	Location	: Vial 24
Acq. Operator	:	Inj	: 1
		Inj Volume	: 0 µl
Different Inj Volume from Sequence !		Actual Inj Volume	: 3 µl
Acq. Method	:		
Last changed	:		
Analysis Method	:		
Last changed	:		



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Area Percent Report

Sorted By	:	Signal
Multiplier	:	1.0000
Dilution	:	1.0000

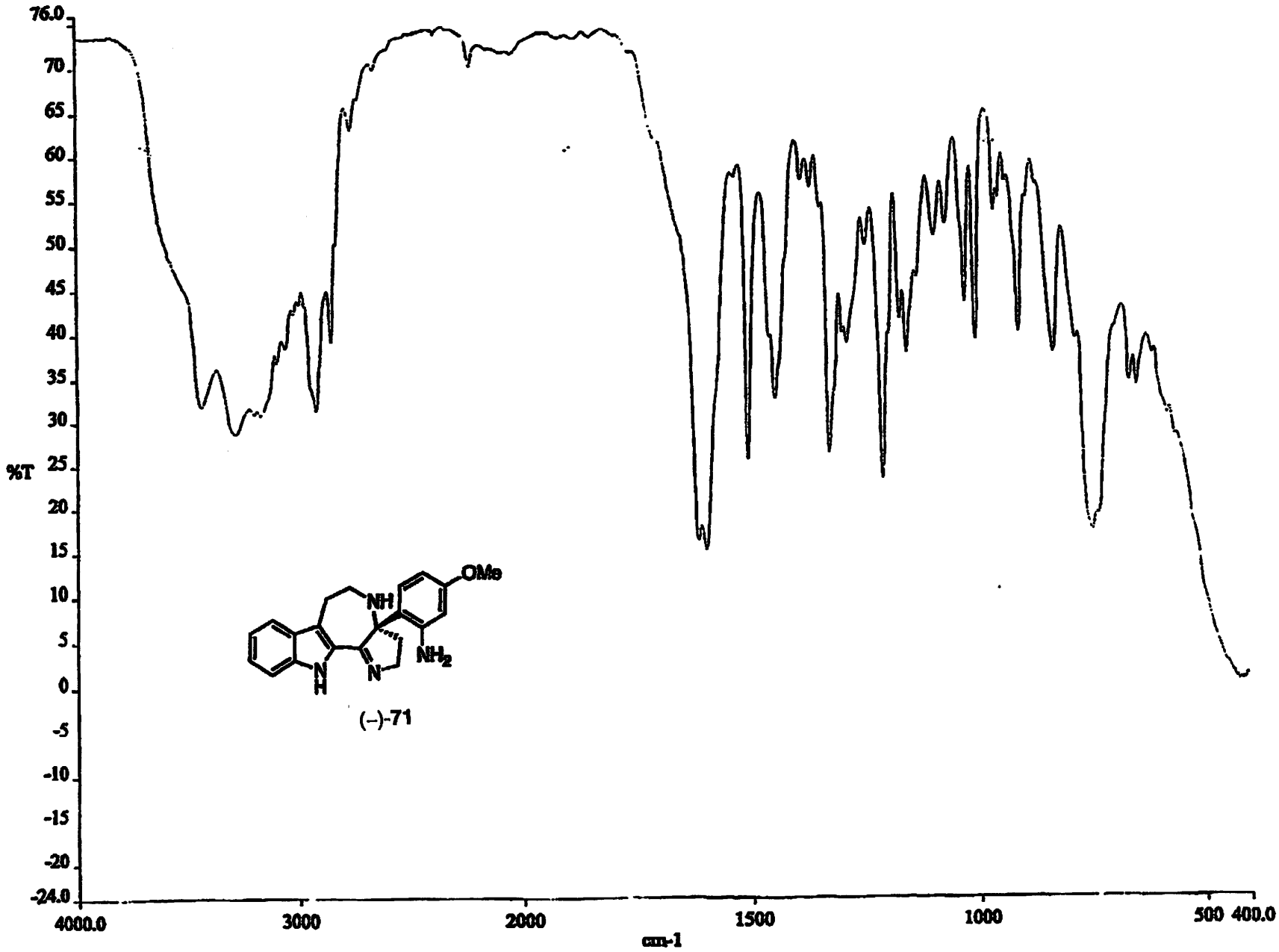
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 D, Sig=240,16 Ref=off

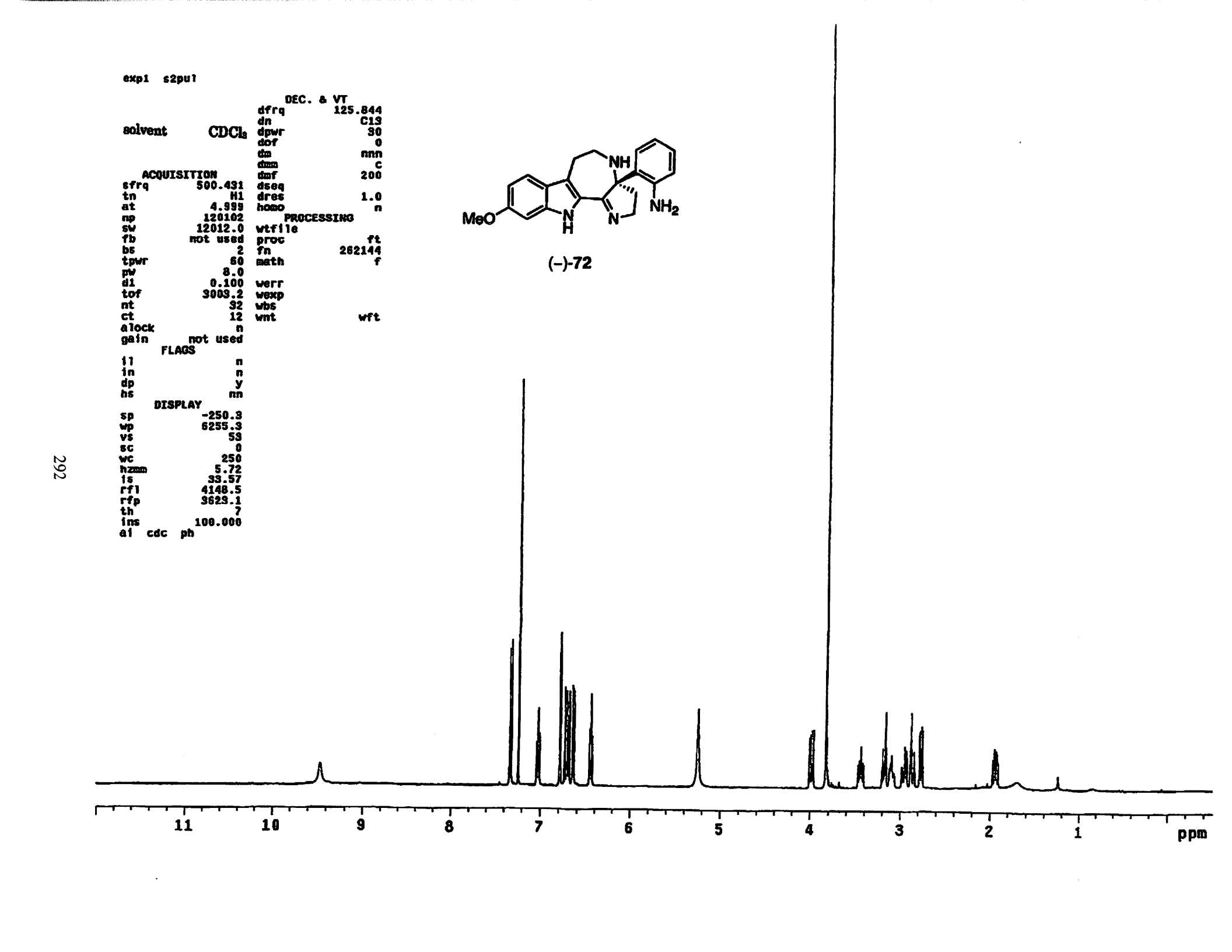
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	41.867	BB	0.8883	854.34039	11.46530	3.0007
2	65.106	BB	1.5928	2.76173e4	247.50766	96.9993
Totals :				2.84717e4	258.97296	

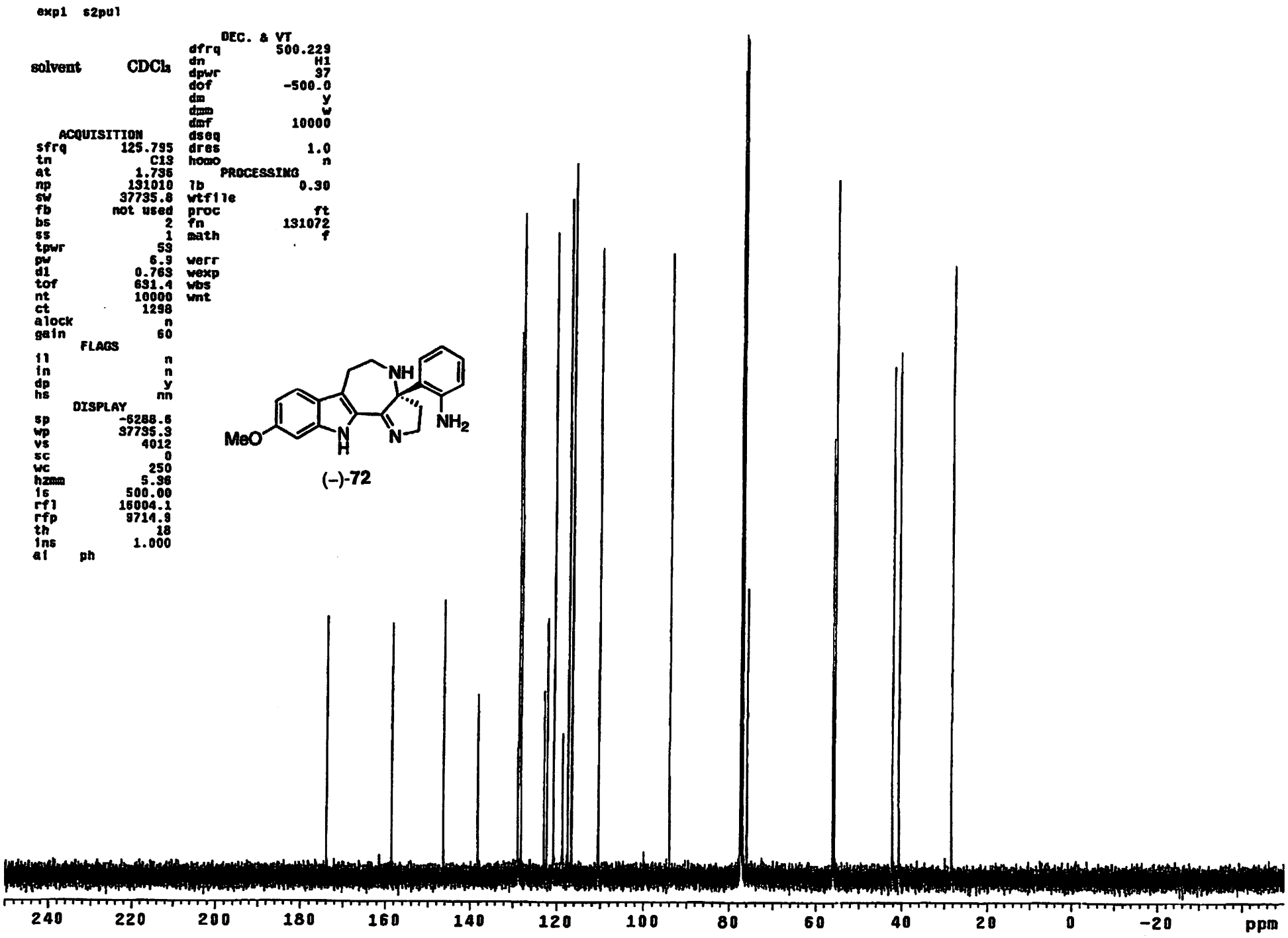
Results obtained with enhanced integrator!

*** End of Report ***


76.0
70
65
60
55
50
45
40
35
30
%T 25
20
15
10
5
0
-5
-10
-15
-20
-24.0
4000.0
3000
2000
1500
1000
500 400.0
cm-1
OMe
NH
NH2
N
H
N

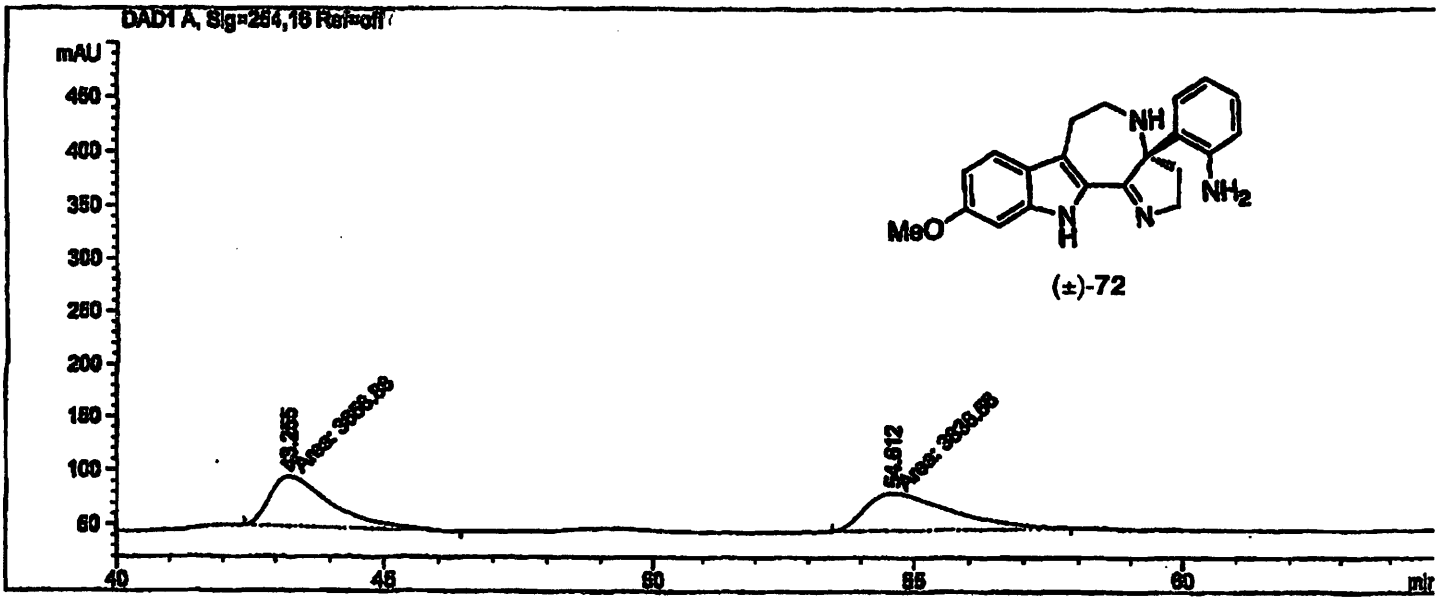
(–)-71


exp1 s2pul
solvent CDCl3
ACQUISITION
sfrq 500.431
tn H1
at 4.999
np 120102
sw 12012.0
fb not used
bs 2
tpwr 60
pw 8.0
d1 0.100
tof 3003.2
nt 32
ct 12
alock n
gain not used
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -250.3
wp 6255.9
vs 53
sc 0
wc 250
hzmm 5.72
is 33.57
rfl 4148.5
rfp 3623.1
th 7
ins 100.000
ai cdc ph
DEC. & VT
dfrq 125.844
dn C13
dpwr 30
dof 0
dm nnn
dmm c
dmf 200
dseq
dres 1.0
homo n
PROCESSING
wtfile
proc ft
fn 262144
math f
werr
wexp
wbs
wnt wft
MeO
NH
N
H
N
NH2
(-)-72
11
10
9
8
7
6
5
4
3
2
1
ppm


exp1 s2pul
solvent CDCl3
ACQUISITION
sfrq 125.795
tn C13
at 1.736
np 131010
sw 37735.8
fb not used
bs 2
ss 1
tpwr 53
pw 6.9
d1 0.763
tof 631.4
nt 10000
ct 1298
alock n
gain 60
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -6288.6
wp 37735.3
vs 4012
sc 0
wc 250
hzmm 5.96
is 500.00
rf1 16004.1
rfp 9714.9
th 18
ins 1.000
ai ph
DEC. & VT
dfrq 500.229
dn H1
dpwr 37
dof -500.0
dm y
dmm w
dmf 10000
dseq
dres 1.0
homo n
PROCESSING
lb 0.30
wtfile
proc ft
fn 131072
math f
werr
wexp
wbs
wnt
NH
NH2
MeO
N
N
H
(-)-72
240
220
200
180
160
140
120
100
80
60
40
20
0
-20
ppm

OD-H 100%Hexanes->80%IPA:20%Hxns over 80 min

Injection Date	:	Seq. Line	: 1
Sample Name	:	Location	: Vial 23
Acq. Operator	:	Inj	: 1
		Inj Volume	: 0 µl
Different Inj Volume from Sequence !		Actual Inj Volume	: 10 µl
Acq. Method	:		
Last changed	:		
Analysis Method	:		
Last changed	:		



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Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 A, Sig=254,16 Ref=off

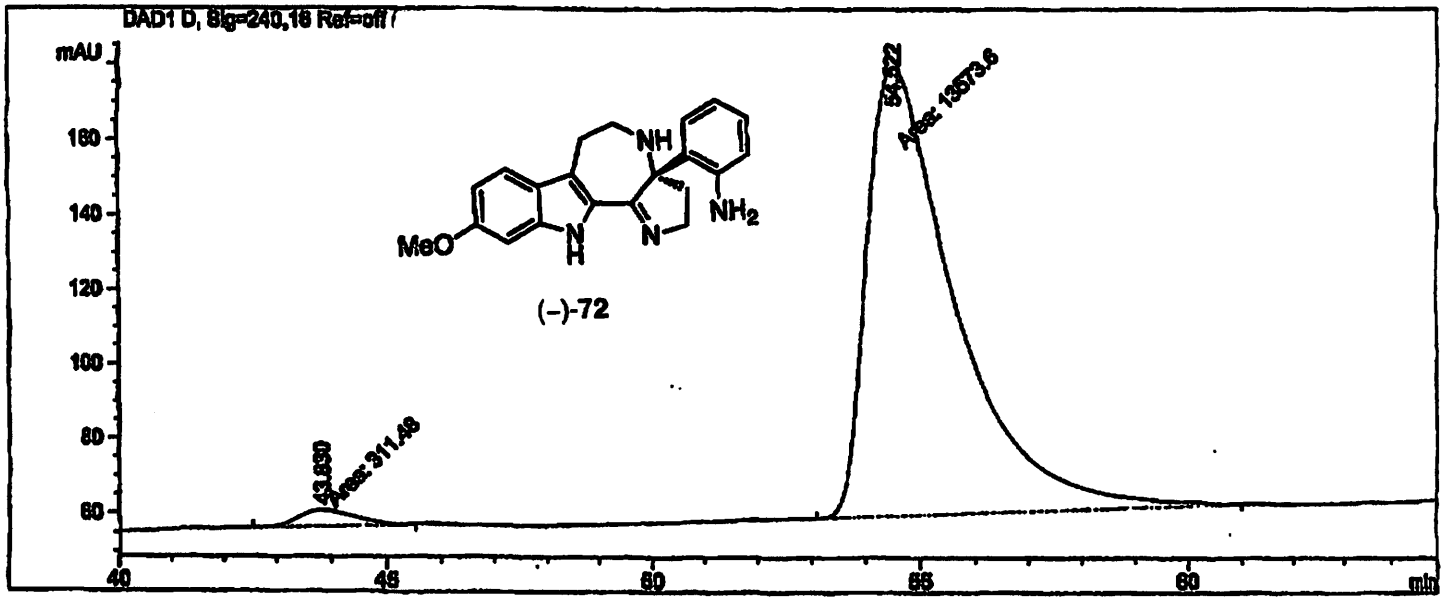
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	43.255	MM	1.3339	3656.88037	45.69140	48.8011
2	54.612	MM	1.8544	3836.56177	34.48214	51.1989
Totals :				7493.44214	80.17355	

Results obtained with enhanced integrator!

*** End of Report ***

chiralpak OD-H 100%Hexanes to 80% IPrOH over 80 min

Injection Date	:	Seq. Line	: 1
Sample Name	:	Location	: Vial 26
Acq. Operator	:	Inj	: 1
		Inj Volume	: 0 µl
Different Inj Volume from Sequence !		Actual Inj Volume	: 10 µl
Acq. Method	:		
Last changed	:		
Analysis Method	:		
Last changed	:		



Area Percent Report

Sorted By	:	Signal
Multiplier	:	1.0000
Dilution	:	1.0000

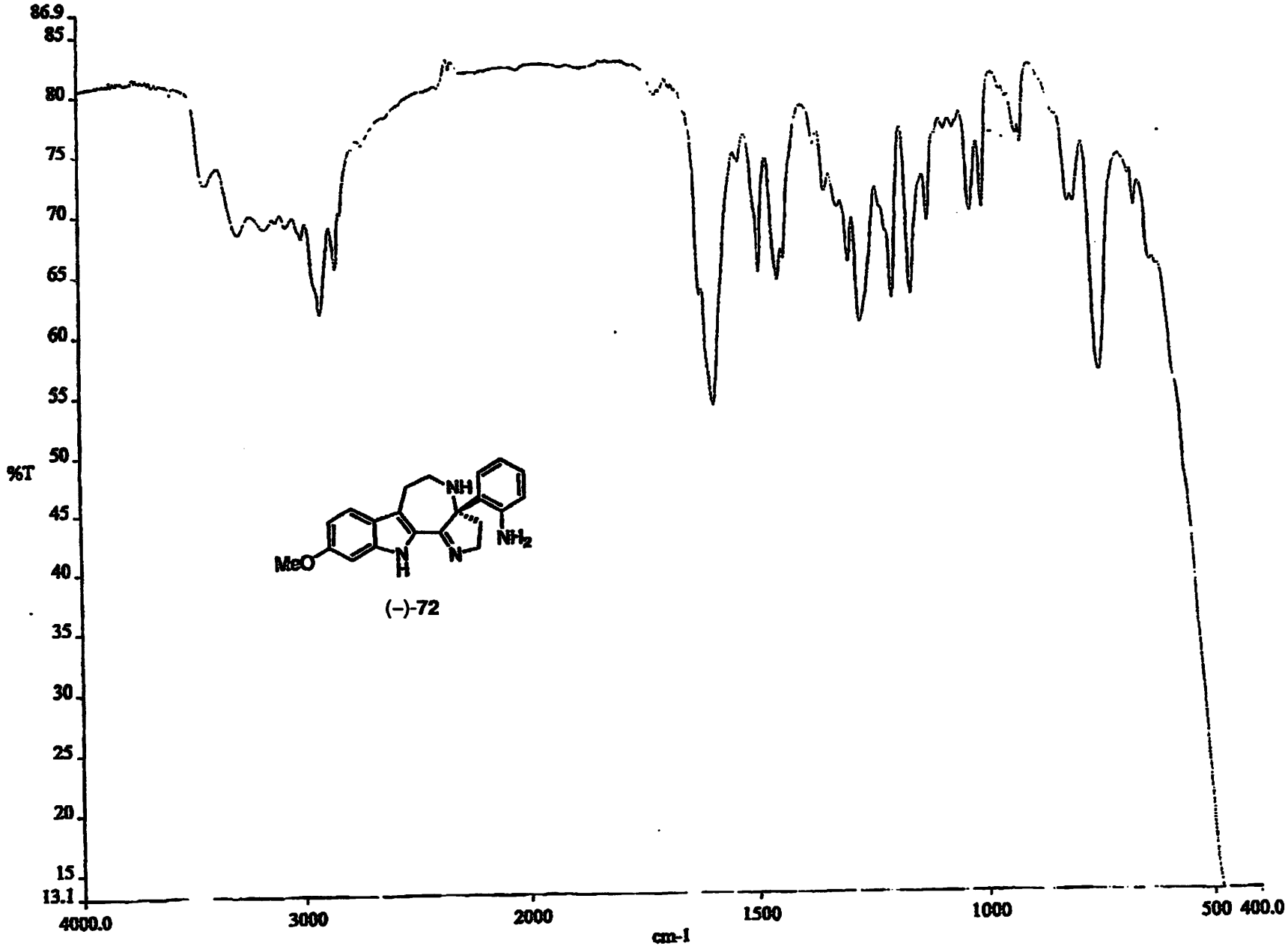
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 D, Sig=240,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	43.830	MM	1.2124	311.47989	4.28179	2.2433
2	54.522	MM	1.8907	1.35736e4	119.65495	97.7567
Totals :				1.38851e4	123.93674	

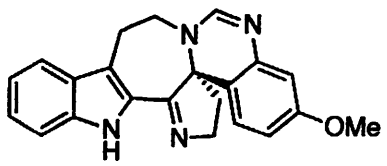
Results obtained with enhanced integrator!

*** End of Report ***


86.9
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
13.1
%T
4000.0
3000
2000
1500
1000
500 400.0
cm-1
NH
NH2
MeO
N
H
N

(–)-72

```
exp1  s2pul

                                DEC. & VT
                          dfrq        125.845
solvent          DMSO     dn              C13
                          dpwr             30
                          dof               0
                          dm              nnn
                          dmm               c
                          dmf             200
   ACQUISITION            dseq
sfrq          500.433     dres            1.0
tn                H1      homo              n
at             4.999          PROCESSING
np           120102     wtfile
sw           12012.0     proc              ft
fb         not used      fn           262144
bs                2      math              f
tpwr             60
pw              8.0      werr
d1            0.100      wexp
tof          3003.2      wbs
nt               32      wnt             wft
ct               16
alock             n
gain       not used
      FLAGS
il                n
in                n
dp                y
hs               nn
     DISPLAY
sp           -250.2
wp           6255.3
vs               48
sc                0
wc              250
hzmm          25.02
is            33.57
rfl           1756.3
rfp           1251.1
th                7
ins          100.000
ai  cdc  ph
```



(–)-trigonoliimine A (1)

exp1 s2pul

ACQUISITION	
sfrq	500.433
tn	H1
at	4.999
np	120102
sw	12012.0
fb	not used
bs	2
tpwr	60
pw	8.0
d1	0.100
tof	3003.2
nt	32
ct	10
alock	n
gain	not used

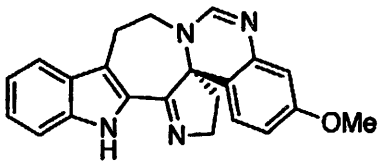
FLAGS	
il	n
in	n
dp	y
hs	nn

DISPLAY	
sp	-250.2
wp	6255.3
vs	50
sc	0
wc	250
hzmm	25.02
is	33.57
rfl	2170.5
rfp	1656.4
th	7
ins	100.000

ai cdc ph

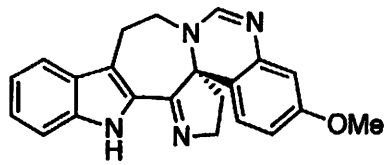
DEC. & VT	
dfrq	125.844
dn	C13
dpwr	30
dof	0
dm	nnn
dmm	c
dmf	200
dseq	
dres	1.0
homo	n

PROCESSING	
wtfile	
proc	ft
fn	262144
math	f
werr	
wexp	
wbs	
wnt	wft

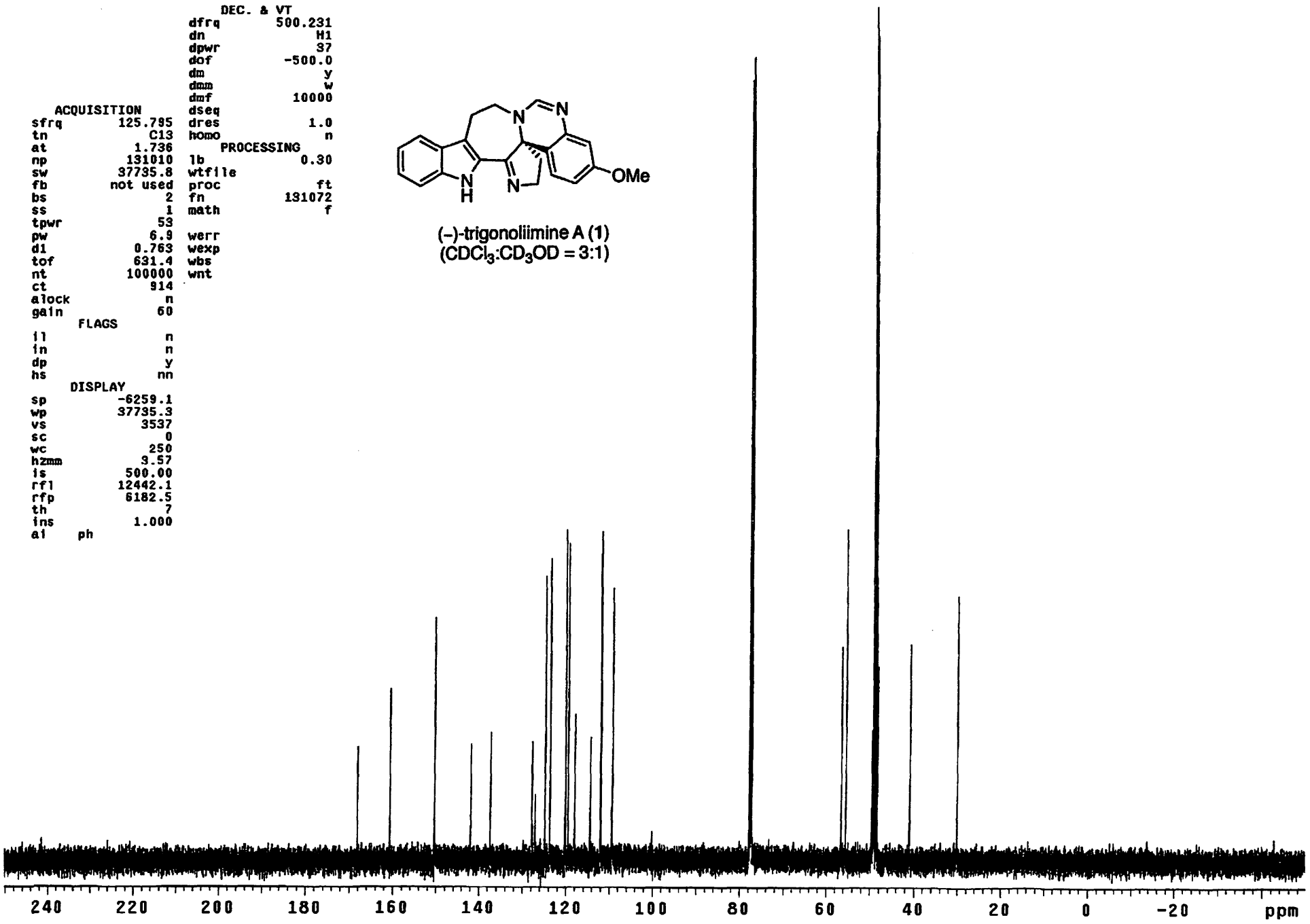


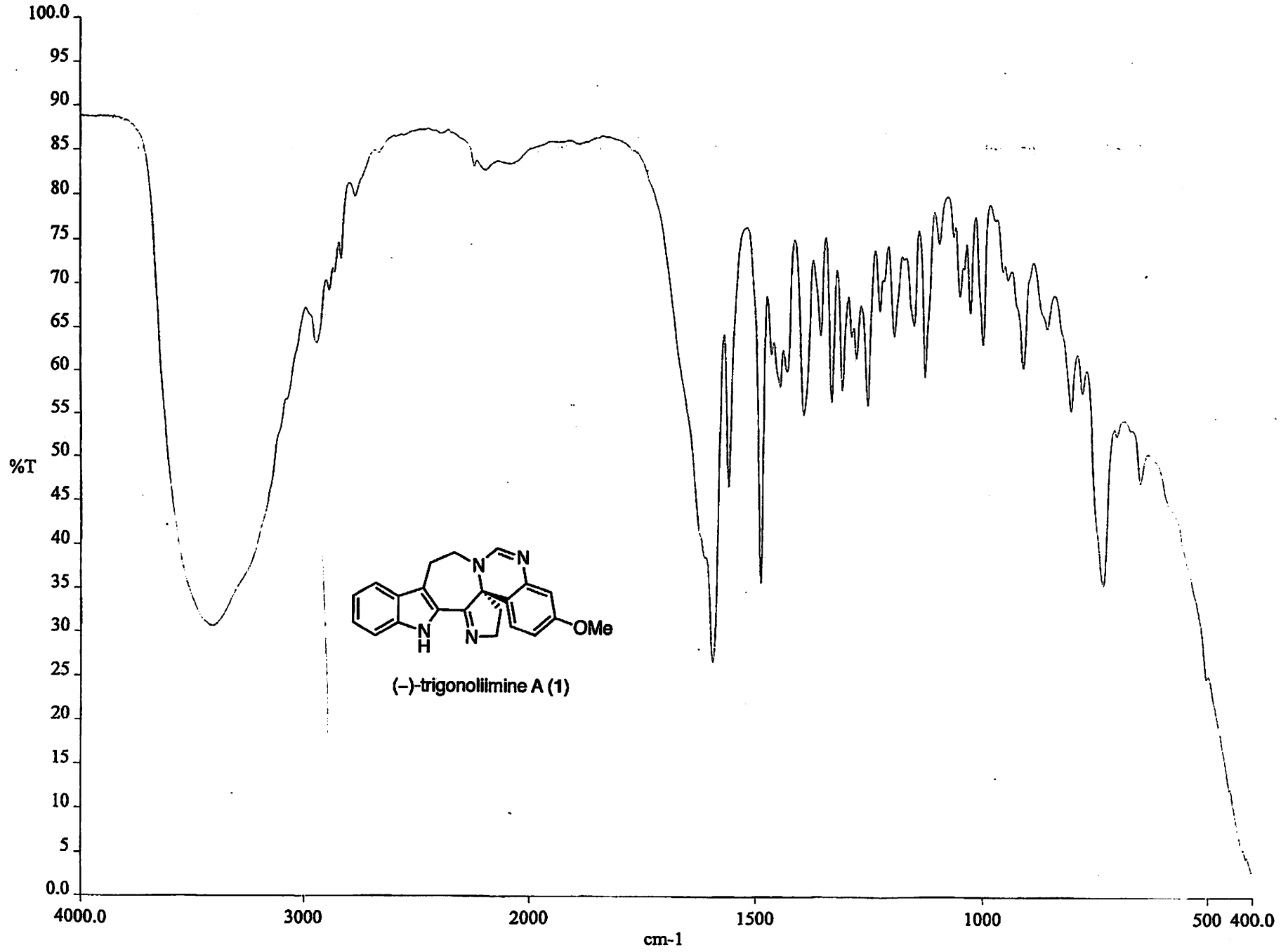
(–)-trigonoliimine A (1)
($CDCl_3$:CD_3OD = 3:1)

```
exp1  s2pul

                                  DEC. & VT
                              dfrq        500.232
solvent          DMSO         dn               H1
                              dpwr              37
                              dof           -500.0
                              dm                 y
                              dmm                w
                              dmf           10000
   ACQUISITION                dseq
sfrq          125.795         dres             1.0
tn                C13         homo               n
at               1.736            PROCESSING
np            131010          lb              0.30
sw           37735.8          wtfile
fb         not used           proc               ft
bs                2           fn            131072
ss                1           math               f
tpwr             53
pw              6.9           werr
d1            0.763           wexp
tof           631.4           wbs
nt           100000           wnt
ct              832
alock             n
gain             18
      FLAGS
il                n
in                n
dp                y
hs               nn
     DISPLAY
sp          -6370.7
wp          37735.3
vs       1.09664e+06
sc                0
wc              250
hzmm           2.58
is           500.00
rfl         11341.2
rfp          4969.9
th              20
ins          1.000
ai     ph
```



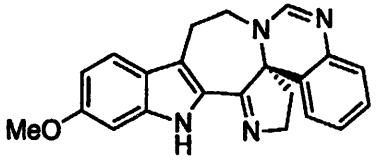
(–)-trigonoliimine A (1)


exp1 s2pul
ACQUISITION
sfrq 125.795
tn C13
at 1.736
np 131010
sw 37735.8
fb not used
bs 2
ss 1
tpwr 53
pw 6.9
d1 0.763
tof 631.4
nt 100000
ct 914
alock n
gain 60
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -6259.1
wp 37735.3
vs 3537
sc 0
wc 250
hzmm 3.57
is 500.00
rfl 12442.1
rfp 6182.5
th 7
ins 1.000
ai ph
DEC. & VT
dfrq 500.231
dn H1
dpwr 37
dof -500.0
dm y
dmm w
dmf 10000
dseq
dres 1.0
homo n
PROCESSING
lb 0.30
wtfile
proc ft
fn 131072
math f
werr
wexp
wbs
wnt
N
N
N
H
OMe
(–)-trigonoliimine A (1)
(CDCl3:CD3OD = 3:1)
240
220
200
180
160
140
120
100
80
60
40
20
0
-20
ppm

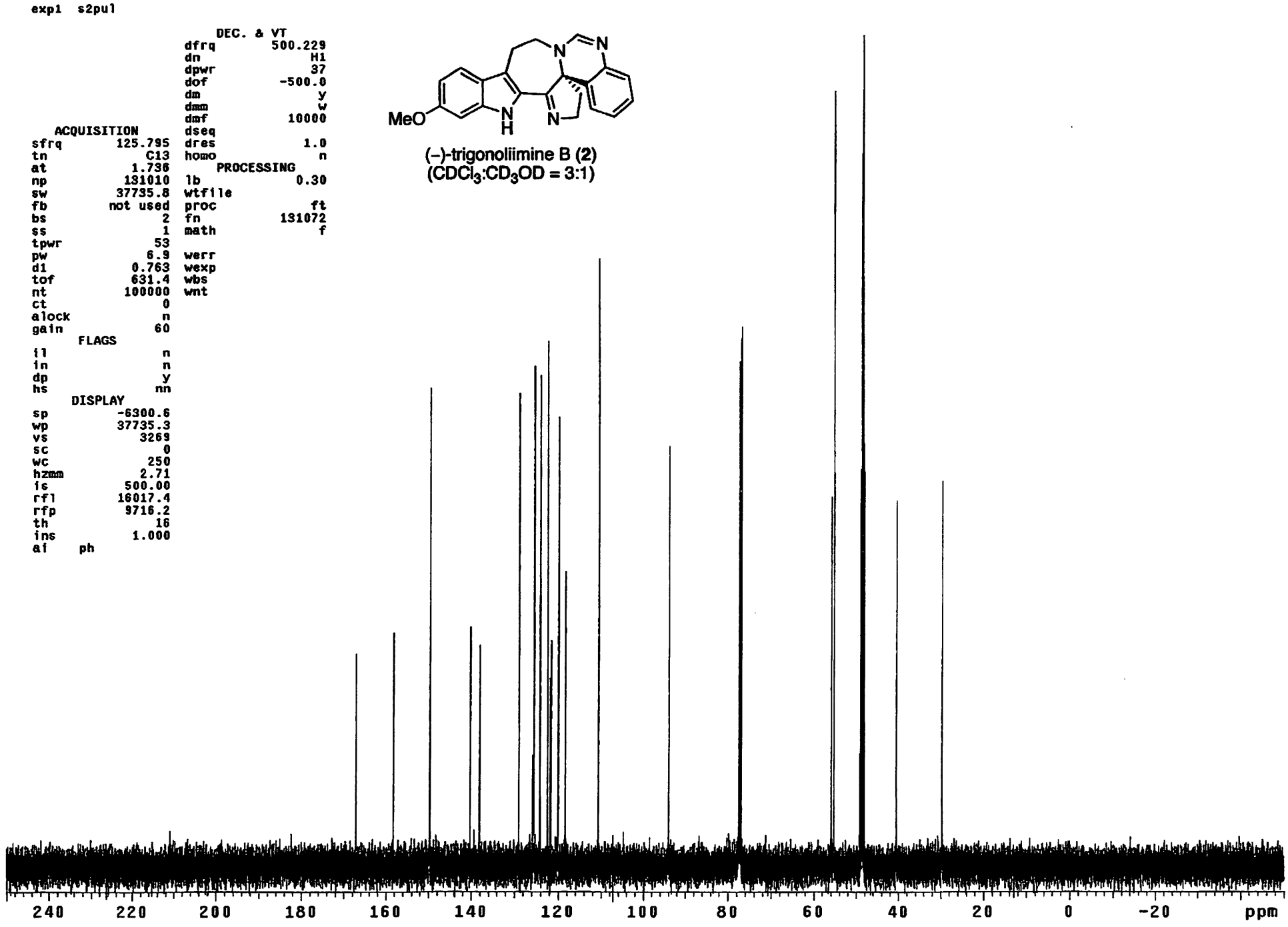


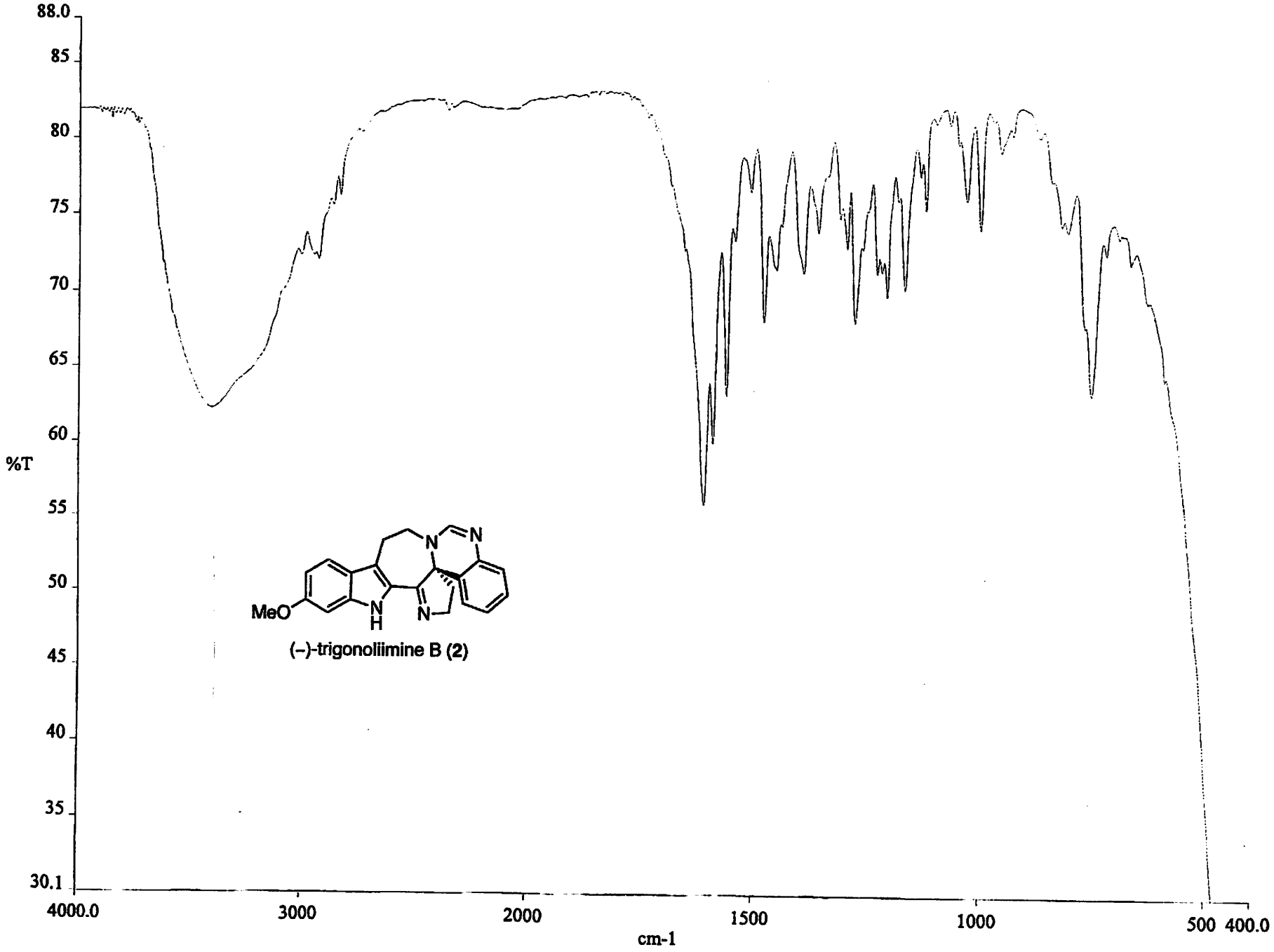
(–)-trigonoliimine A (1)

```
exp1  s2pul

                    DEC. & VT
                dfrq        125.673
                dn              C13
                dpwr             30
                dof               0
                dm              nnn
                dmm               w
                dmf           10000
                dseq
                dres            1.0
                homo              n
    ACQUISITION     PROCESSING
sfrq        499.748 wtfile
tn               H1 proc             ft
at            3.001 fn           262144
np            63050 math              f
sw         10504.2  werr
fb        not used  wexp
bs                2  wbs
tpwr             56  wnt            wft
pw              8.6
d1            2.000
tof          1519.5
nt               16
ct               14
alock             n
gain      not used
      FLAGS
il                n
in                n
dp                y
hs               nn
     DISPLAY
sp           -249.9
wp           6246.7
vs               34
sc                0
wc              250
hzmm          24.99
is            33.57
rfl          2889.9
rfp          1654.2
th                7
ins         100.000
ai  cdc  ph
```



(–)-trigonoliimine B (**2**)
($CDCl_3$:CD_3OD = 3:1)

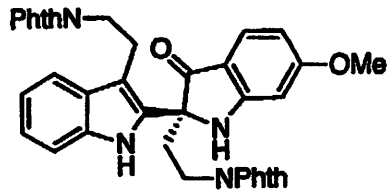

exp1 s2pul
ACQUISITION
sfrq 125.795
tn C13
at 1.736
np 131010
sw 37735.8
fb not used
bs 2
ss 1
tpwr 53
pw 6.9
d1 0.763
tof 631.4
nt 100000
ct 0
alock n
gain 60
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -6300.6
wp 37735.3
vs 3269
sc 0
wc 250
hzmm 2.71
is 500.00
rfl 16017.4
rfp 9716.2
th 16
ins 1.000
ai ph
DEC. & VT
dfrq 500.229
dn H1
dpwr 37
dof -500.0
dm y
dmm w
dmf 10000
dseq
dres 1.0
homo n
PROCESSING
lb 0.30
wtfile
proc ft
fn 131072
math f
werr
wexp
wbs
wnt
MeO
N
H
N
N
N
(–)-trigonoliimine B (2)
(CDCl3:CD3OD = 3:1)
240
220
200
180
160
140
120
100
80
60
40
20
0
-20
ppm


88.0
85
80
75
70
65
60
%T
55
50
45
40
35
30.1
4000.0
3000
2000
1500
1000
500
400.0
cm-1
MeO
N
H
N
N
(–)-trigonoliimine B (2)

exp1 s2pul

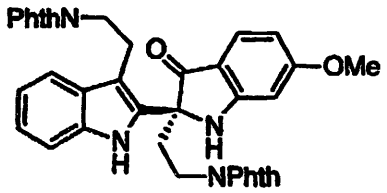
		DEC. & VT	
solvent	CDCl3	dfrq	125.845
		dn	C13
		dpwr	30
		dof	0
		dm	nnn
		dmm	c
ACQUISITION		dmf	200
sfrq	500.435	dseq	
tn	H1	dres	1.0
at	4.985	homo	n
np	120102	PROCESSING	
sw	12012.0	wtfile	
fb	not used	proc	ft
bs	2	fn	262144
tpwr	57	math	f
pw	8.0		
d1	0.100	werr	
tof	3003.2	wexp	
nt	16	wbs	
ct	14	wnt	wft
alock	n		
gain	not used		
FLAGS			
il	n		
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-250.2		
wp	6255.3		
vs	48		
sc	0		
wc	250		
hzmm	25.02		
is	33.57		
rfl	4138.9		
rfp	3623.1		
th	7		
ins	100.000		

ai cdc ph

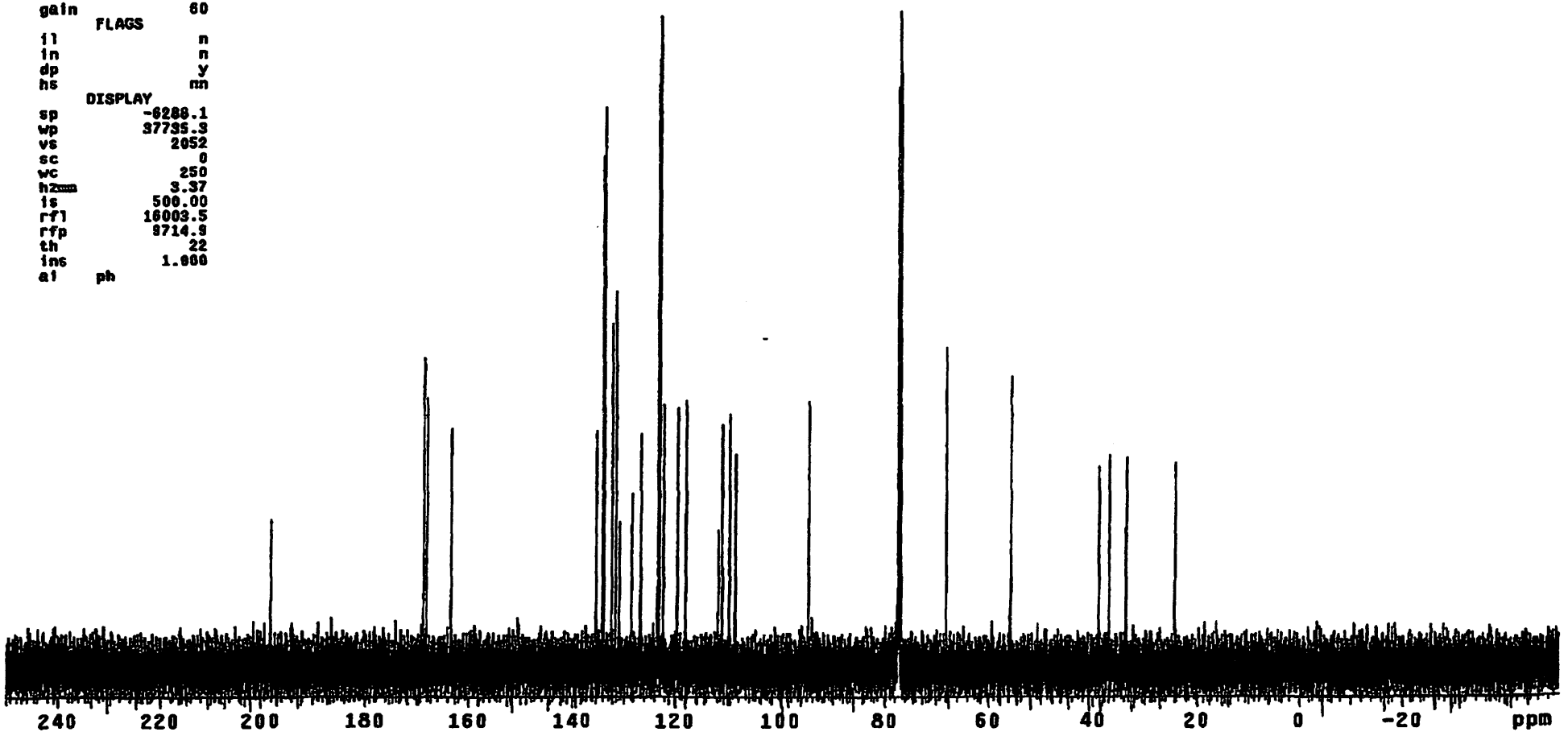


(–)-76

```
exp1  s2pul

                                    DEC. & VT
                                dfrq        500.229
solvent        CDCl3            dn              H1
                                dpwr              37
                                dof           -500.0
                                dm                y
                                dmm               w
                                dmf           10000
   ACQUISITION                  dseq
sfrq          125.795           dres             1.0
tn               C13            homo              n
at             1.736                PROCESSING
np           131010             lb              0.30
sw          37735.8             wtfile
fb        not used              proc              ft
bs               2              fn           131072
ss               1              math              f
tpwr            53
pw             6.9              werr
d1           0.763              wexp
tof          631.4              wbs
nt           10000              wnt
ct             126
alock            n
gain            60
      FLAGS
il               n
in               n
dp               y
hs              nn
      DISPLAY
sp          -6288.1
wp          37735.3
vs             2052
sc                0
wc              250
hzmm           3.37
is           500.00
rfl          16003.5
rfp           9714.9
th                22
ins           1.000
ai     ph
```

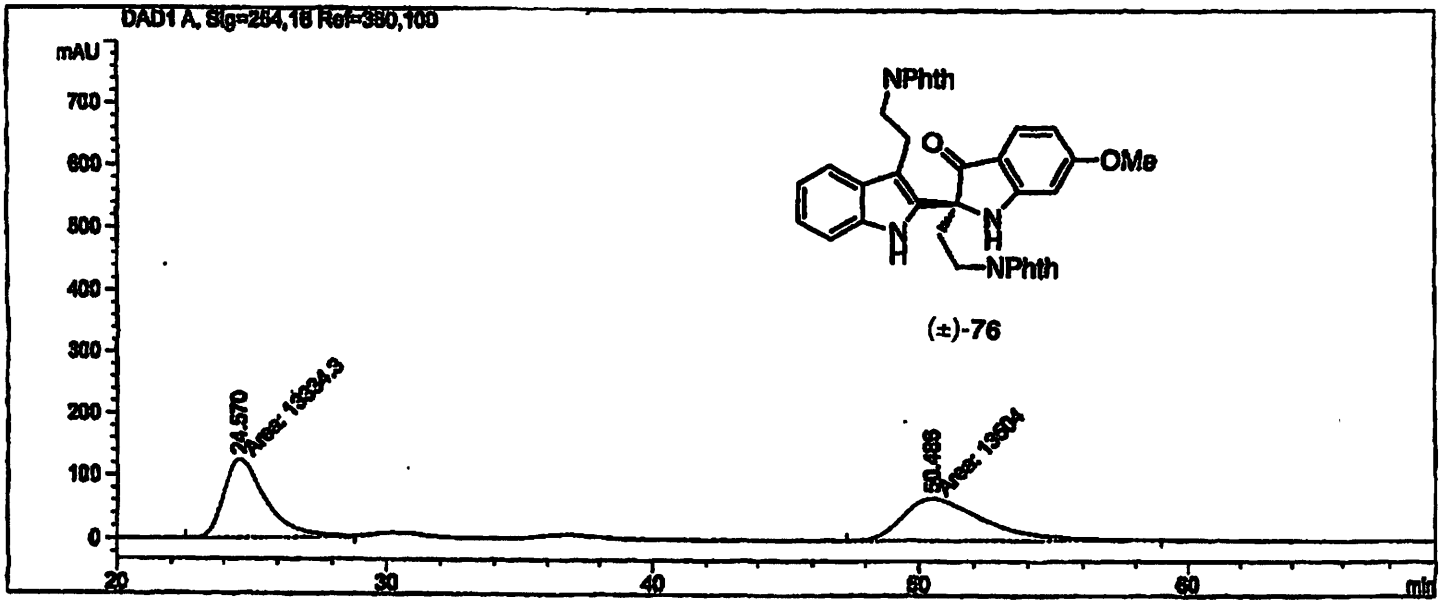


(–)-76



ChiralPak IC 0.7mL/min, 55:45=iPrOH:Hexane

Injection Date	:	Seq. Line	: 1
Sample Name	:	Location	: Vial 23
Acq. Operator	:	Inj	: 1
		Inj Volume	: 0 µl
Different Inj Volume from Sequence !		Actual Inj Volume	: 10 µl
Acq. Method	:		
Last changed	:		
Analysis Method	:		
Last changed	:		



Area Percent Report

Sorted By	:	Signal
Multiplier	:	1.0000
Dilution	:	1.0000

Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 A, Sig=254,16 Ref=360,100

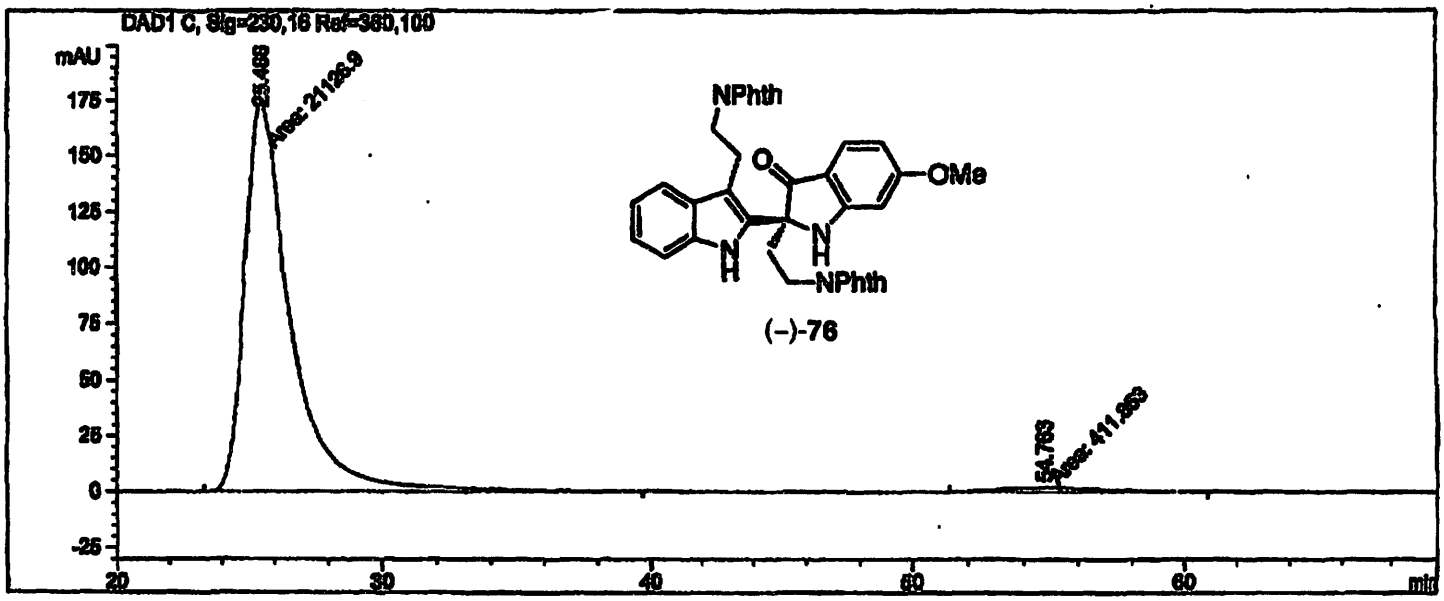
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	24.570	MM	1.7985	1.33343e4	123.56780	49.6839
2	50.486	MM	3.4308	1.35040e4	65.60233	50.3161
Totals :				2.68383e4	189.17013	

Results obtained with enhanced integrator!

*** End of Report ***

chiralpak IC 45%Hexanes:55%IPA; 0.7 mL/min

Injection Date	:	Seq. Line	: 2
Sample Name	:	Location	: Vial 25
Acq. Operator	:	Inj	: 1
		Inj Volume	: 0 µl
Different Inj Volume from Sequence !		Actual Inj Volume	: 10 µl
Acq. Method	:		
Last changed	:		
Analysis Method	:		
Last changed	:		



Area Percent Report

Sorted By	:	Signal
Multiplier	:	1.0000
Dilution	:	1.0000

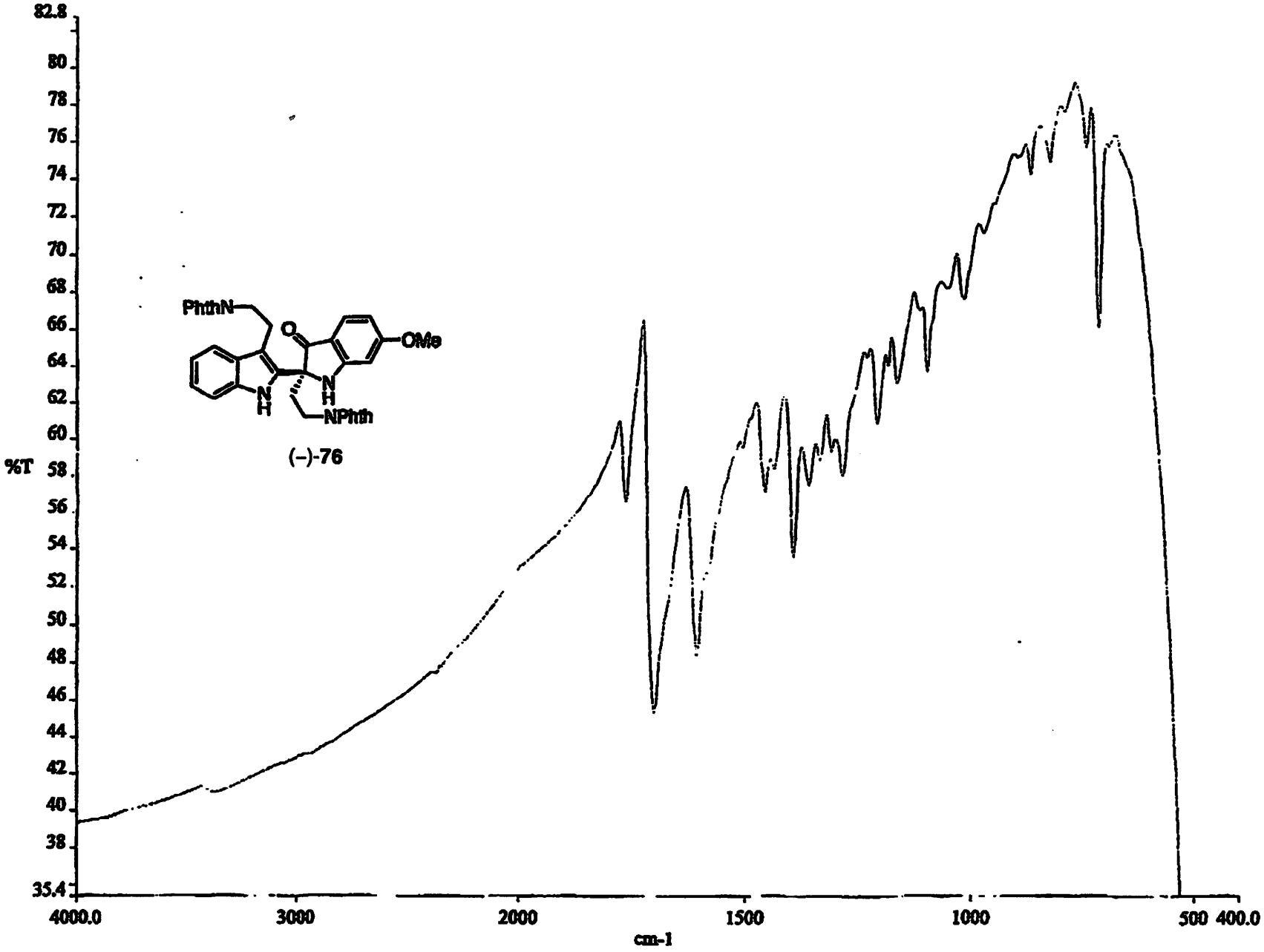
Use Multiplier & Dilution Factor with ISTDs

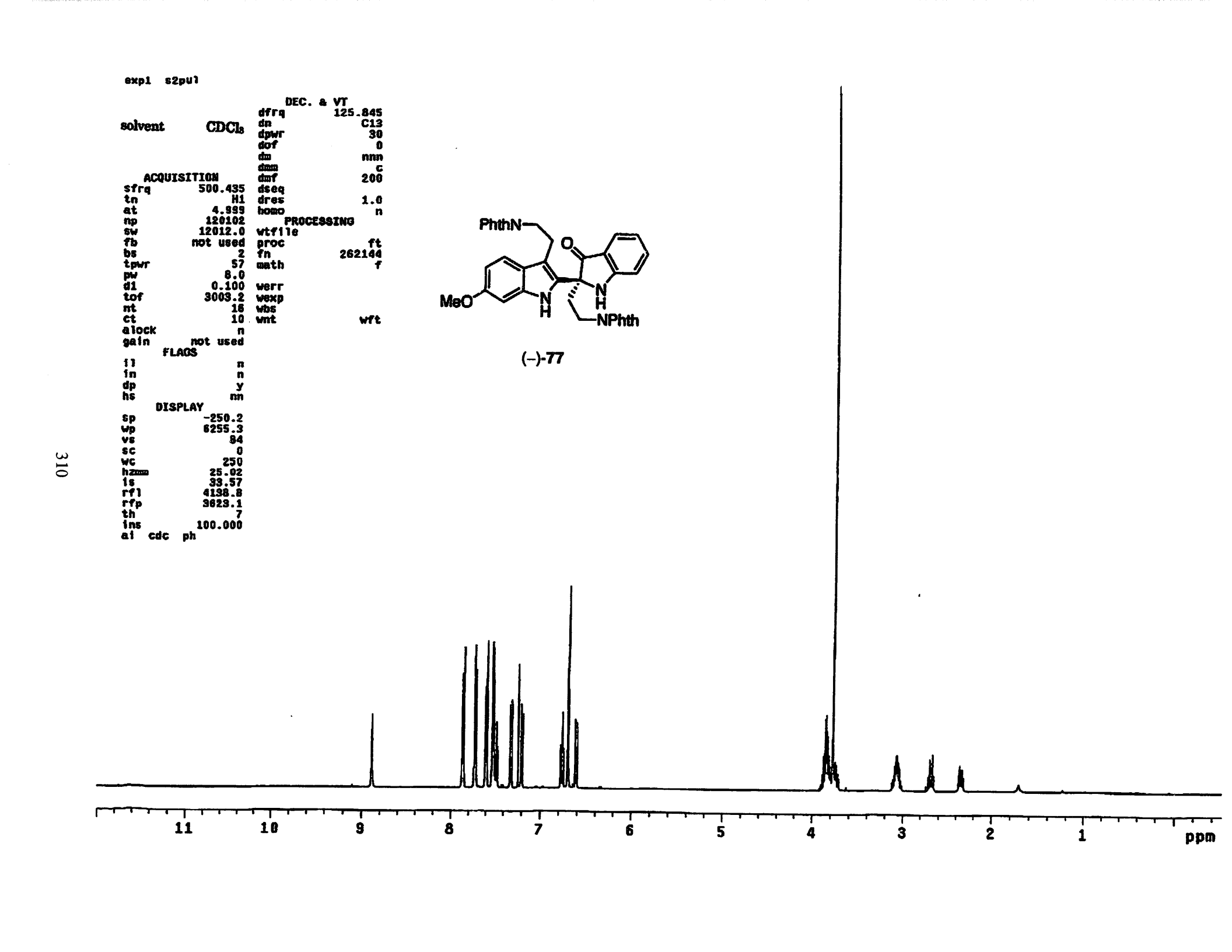
Signal 1: DAD1 C, Sig=230,16 Ref=360,100

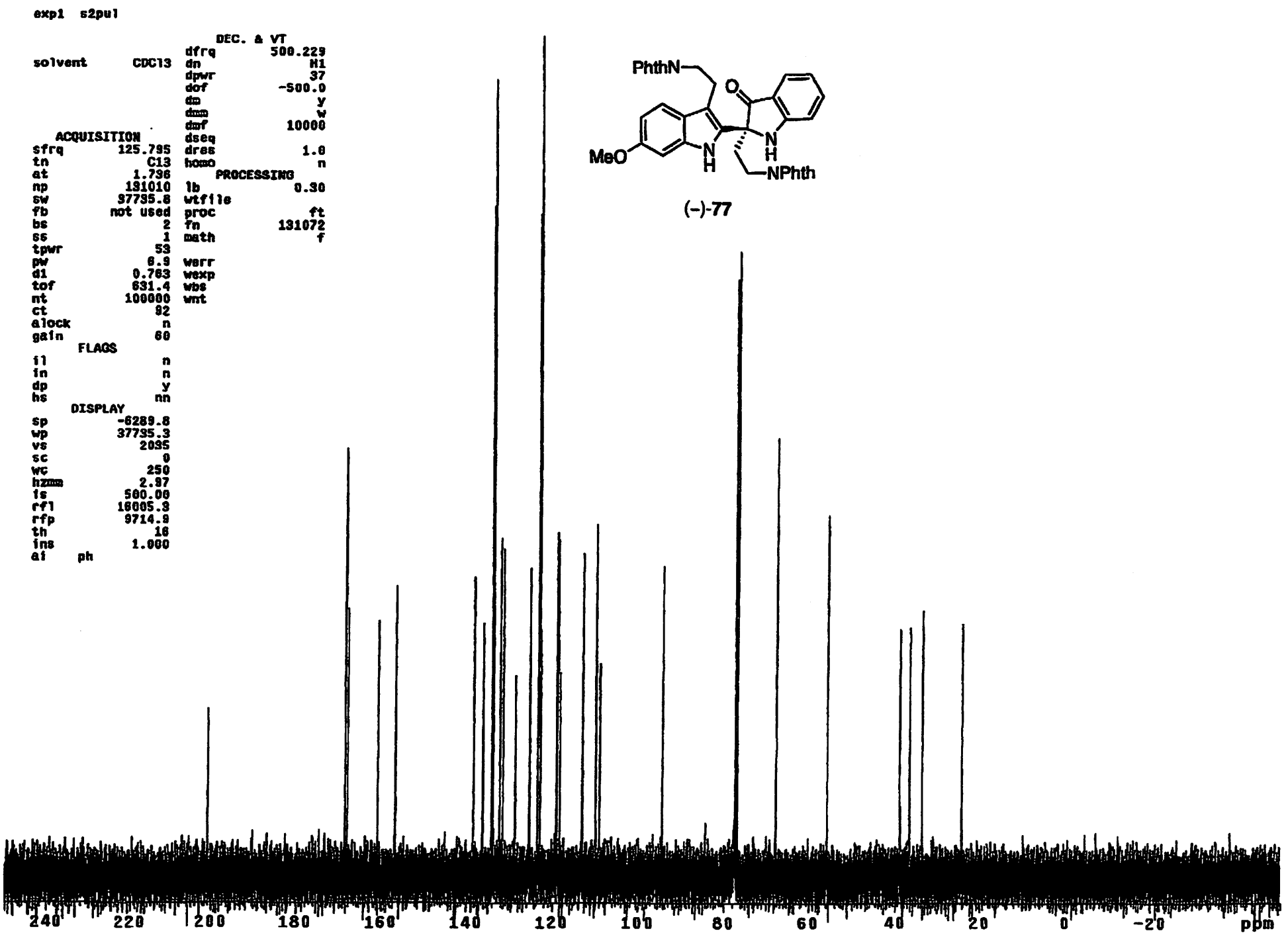
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	25.486	MM	2.0268	2.11269e4	173.72997	98.0878
2	54.763	MM	4.0101	411.85291	1.71173	1.9122
Totals :				2.15387e4	175.44169	

Results obtained with enhanced integrator!

*** End of Report ***


82.8
80
78
76
74
72
70
68
66
64
62
60
58
56
54
52
50
48
46
44
42
40
38
35.4
%T
4000.0
3000
2000
1500
1000
500 400.0
cm-1
PhthN
O
OMe
N
H
N
H
NPhth
(–)-76


expl s2pul
solvent CDCl3
ACQUISITION
sfrq 500.435
tn H1
at 4.999
np 120102
sw 12012.0
fb not used
bs 2
tpwr 57
pw 8.0
d1 0.100
tof 3003.2
nt 16
ct 10
alock n
gain not used
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -250.2
wp 6255.3
vs 84
sc 0
wc 250
hzmm 25.02
is 33.57
rfl 4138.8
rfp 3623.1
th 7
ins 100.000
ai cdc ph
DEC. & VT
dfrq 125.845
dn C13
dpwr 30
dof 0
dm nnn
dmm c
dmf 200
dseq
dres 1.0
homo n
PROCESSING
wtfile
proc ft
fn 262144
math f
werr
wexp
wbs
wnt wft
PhthN
O
MeO
N
H
N
H
NPhth
(–)-77
11
10
9
8
7
6
5
4
3
2
1
ppm


exp1 s2pul
solvent CDCl3
ACQUISITION
sfrq 125.795
tn C13
at 1.796
np 131010
sw 37735.8
fb not used
bs 2
ss 1
tpwr 53
pw 8.9
d1 0.763
tof 631.4
nt 100000
ct 92
alock n
gain 60
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -6289.8
wp 37735.3
vs 2035
sc 0
wc 250
hzmm 2.97
fs 500.00
rfl 16005.9
rfp 9714.9
th 16
ins 1.000
ai ph
DEC. & VT
dfrq 500.229
dn H1
dpwr 37
dof -500.0
dm y
dmm w
dmf 10000
dseq
drss 1.0
homo n
PROCESSING
lb 0.30
wtfile
proc ft
fn 131072
math f
werr
wexp
wbs
wnt
PhthN
O
MeO
N
H
N
H
NPhth
(-)-77
240
220
200
180
160
140
120
100
80
60
40
20
0
-20
ppm

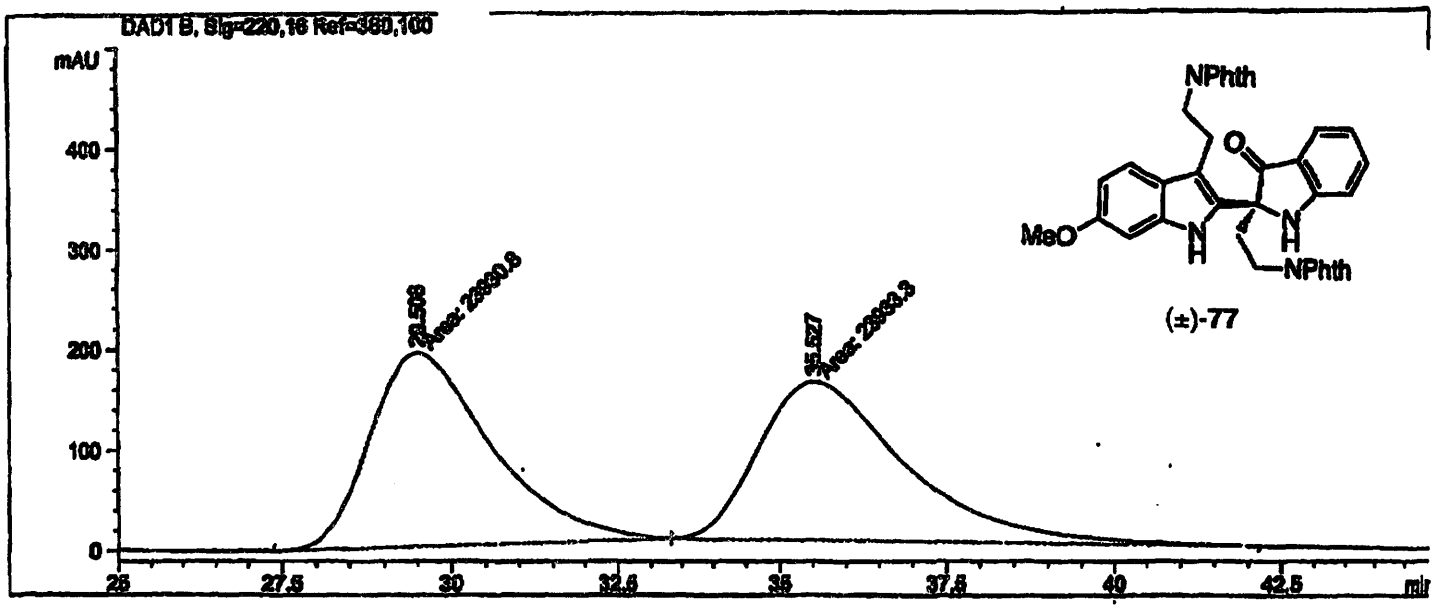
ChiralPak IC 0.7mL/min, 55:45=iPrOH:Hexane

Injection Date :
Sample Name :
Acq. Operator :

Seq. Line : 1
Location : Vial 27
Inj : 1
Inj Volume : 0 µl

Different Inj Volume from Sequence ! Actual Inj Volume : 10 µl

Acq. Method :
Last changed :
Analysis Method :
Last changed :



Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 B, Sig=220,16 Ref=360,100

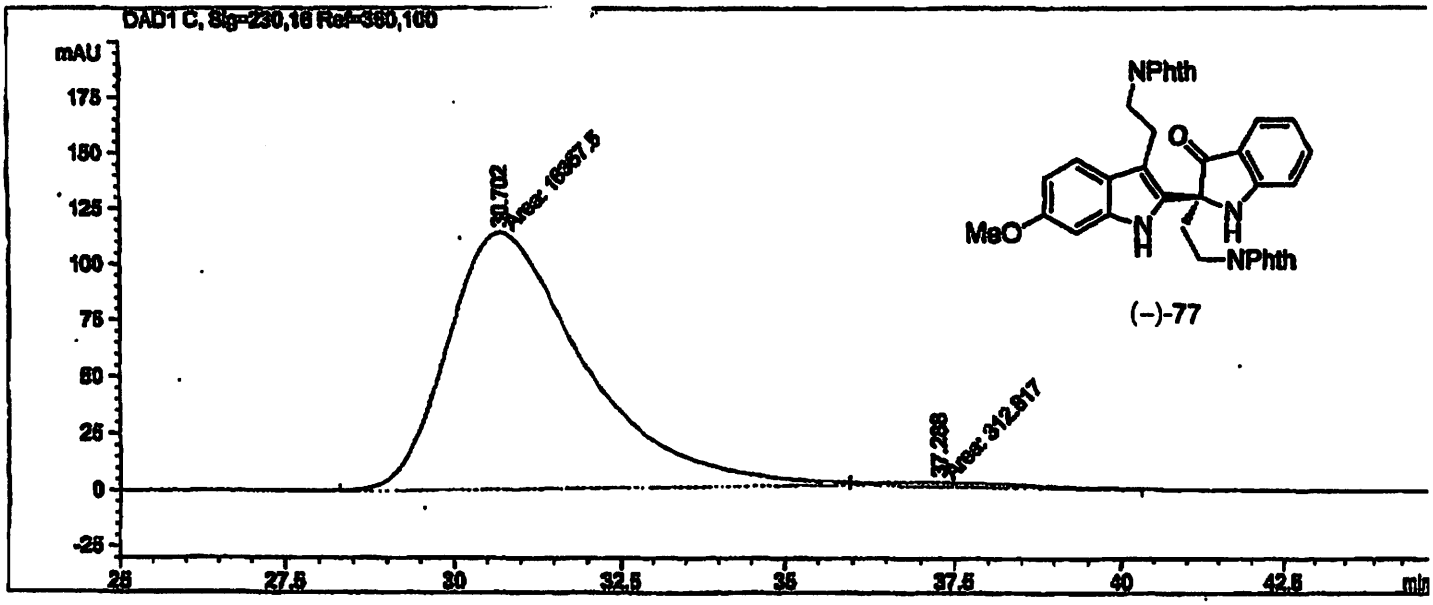
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	29.506	MM	2.0782	2.39308e4	191.91936	49.9974
2	35.527	MM	2.5518	2.39333e4	156.31505	50.0026
Totals :				4.78641e4	348.23441	

Results obtained with enhanced integrator!

*** End of Report ***

chiralpak IC 45%Hexanes:55%IPA; 0.7 mL/min

Injection Date	:	Seq. Line	: 1
Sample Name	:	Location	: Vial 24
Acq. Operator	:	Inj	: 1
		Inj Volume	: 0 µl
		Actual Inj Volume	: 10 µl
Acq. Method	:		
Last changed	:		
Analysis Method	:		
Last changed	:		



Area Percent Report

Sorted By	:	Signal
Multiplier	:	1.0000
Dilution	:	1.0000

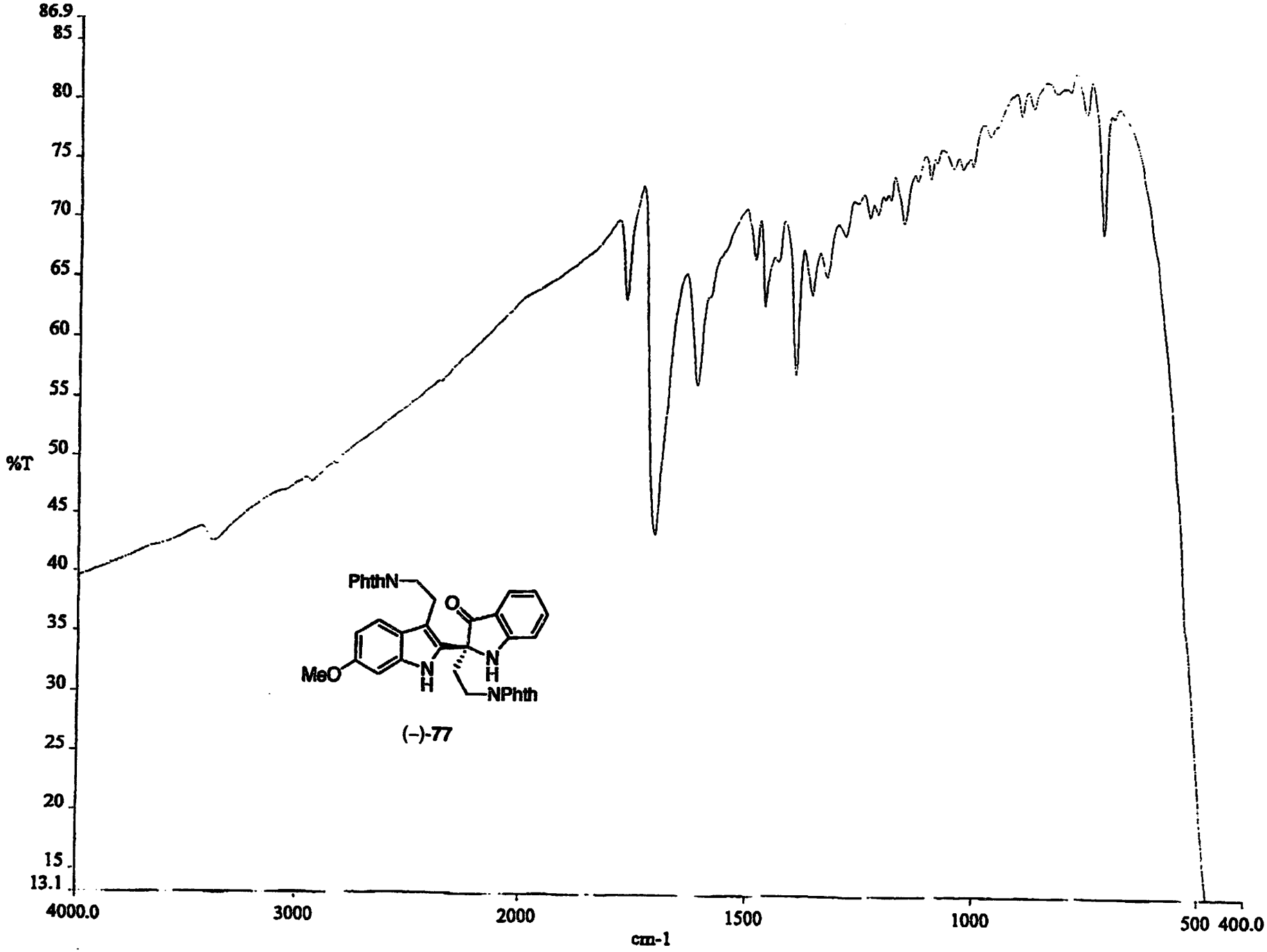
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 C, Sig=230,16 Ref=360,100

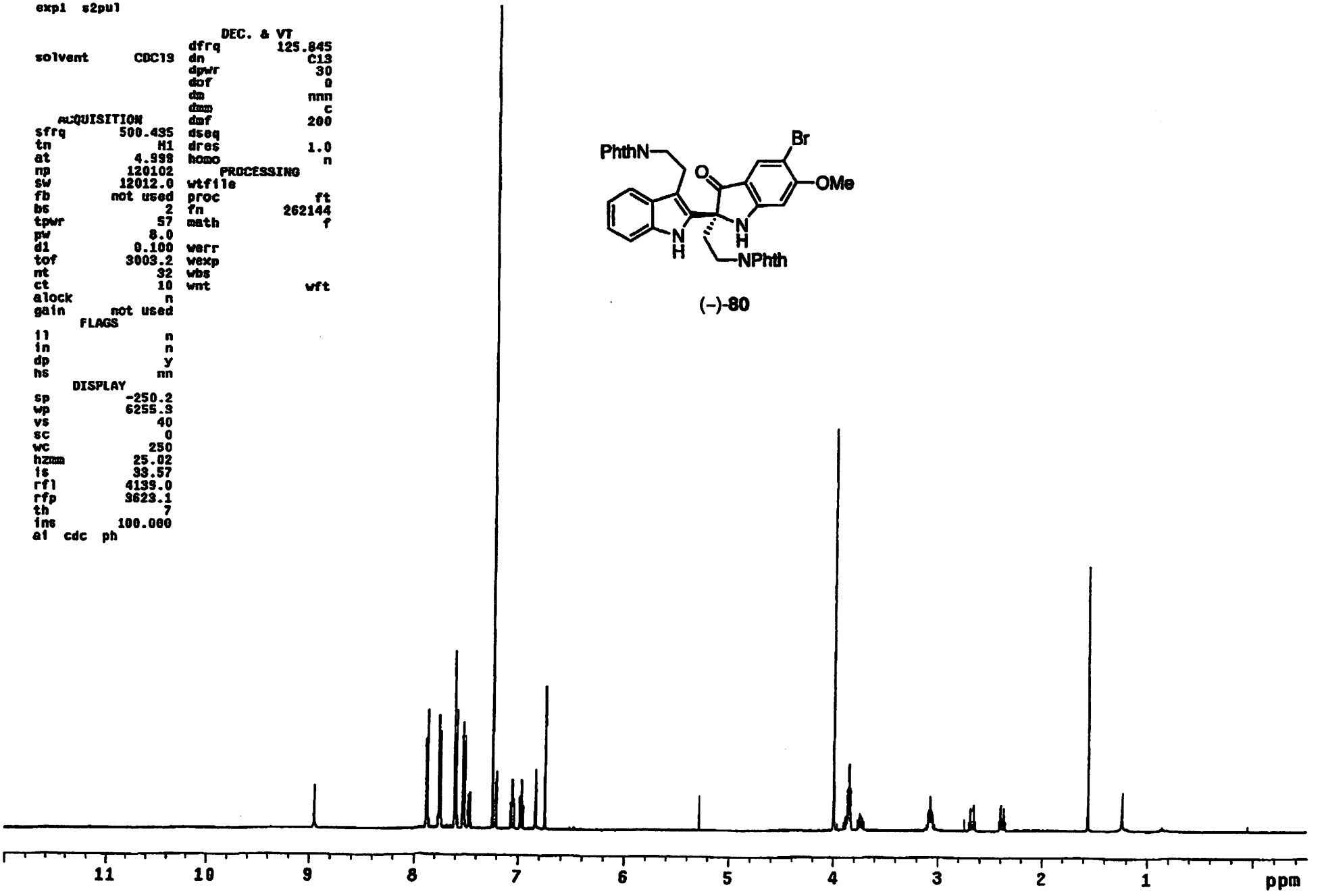
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	30.702	MM	2.3934	1.63575e4	113.90890	98.1235
2	37.288	MM	3.0133	312.81677	1.73019	1.8765
Totals :				1.66703e4	115.63909	

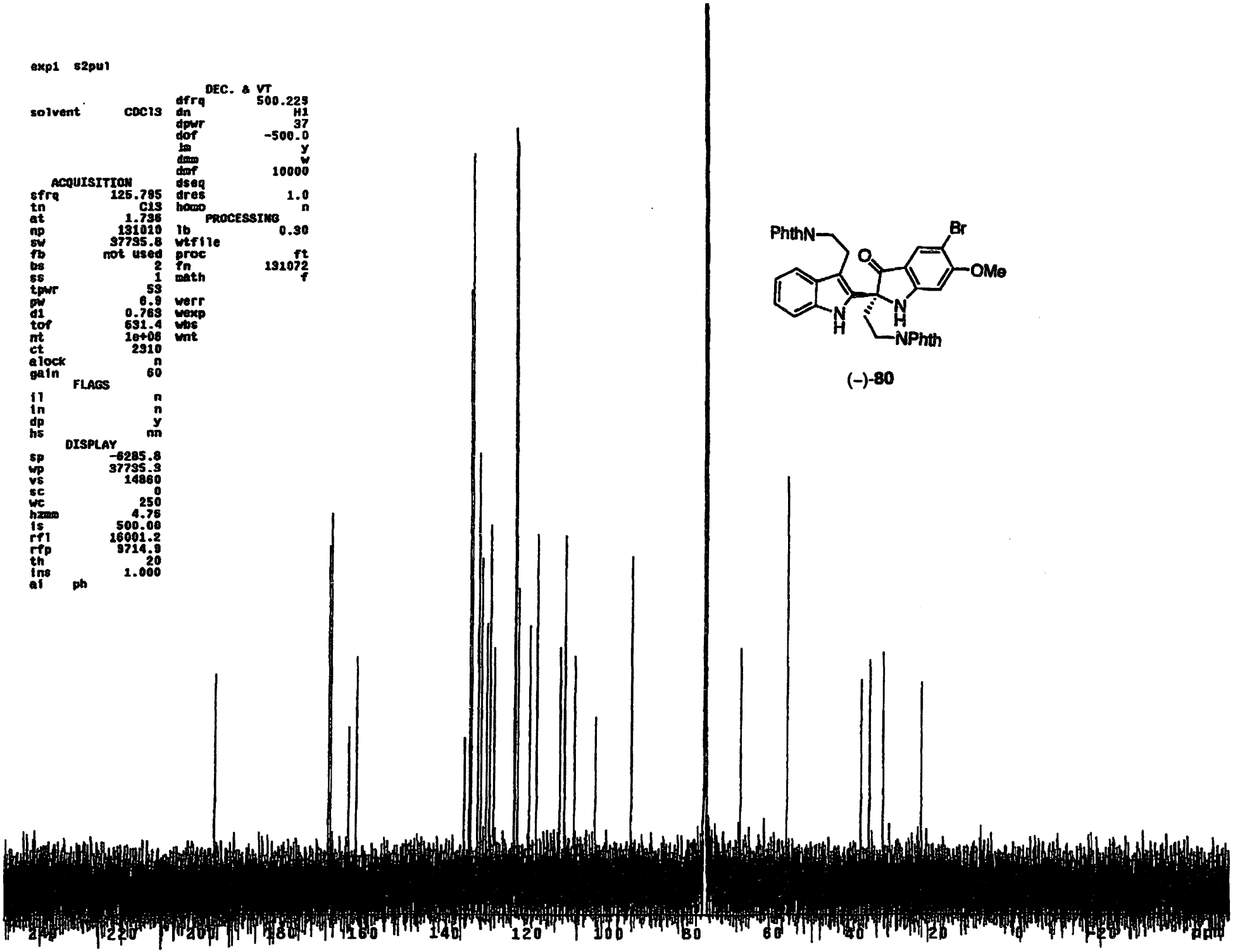
Results obtained with enhanced integrator!

*** End of Report ***


86.9
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
13.1
%T
4000.0
3000
2000
1500
1000
500 400.0
cm-1
PhthN
O
MeO
N
H
N
H
NPhth

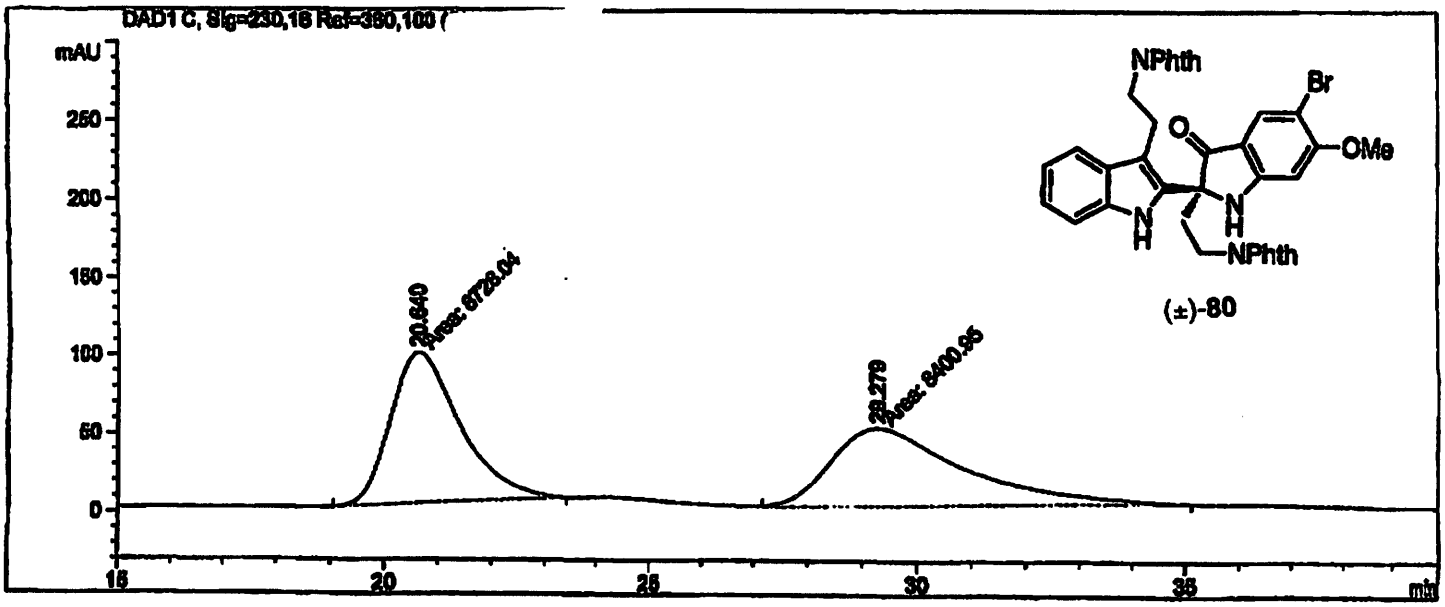
(–)-77


expl s2pul
solvent CDCl3
ACQUISITION
sfrq 500.435
tn H1
at 4.998
np 120102
sw 12012.0
fb not used
bs 2
tpwr 57
pw 8.0
d1 0.100
tof 3003.2
nt 32
ct 10
alock n
gain not used
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -250.2
wp 6255.3
vs 40
sc 0
wc 250
hzmm 25.02
is 33.57
rfl 4139.0
rfp 3623.1
th 7
ins 100.000
al cdc ph
DEC. & VT
dfrq 125.845
dn C13
dpwr 30
dof 0
dm nnn
dmm c
dmf 200
dseq
dres 1.0
homo n
PROCESSING
wtfile
proc ft
fn 262144
math f
werr
wexp
wbs
wnt wft
PhthN
Br
O
OMe
N
H
N
H
NPhth
(-)-80
11
10
9
8
7
6
5
4
3
2
1
ppm


exp1 s2pul
solvent CDCl3
ACQUISITION
sfrq 125.785
tn C13
at 1.736
np 131010
sw 37735.8
fb not used
bs 2
ss 1
tpwr 53
pw 6.8
d1 0.768
tof 631.4
nt 1e+06
ct 2310
alock n
gain 60
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -6285.8
wp 37735.3
vs 14860
sc 0
wc 250
hzmm 4.76
is 500.08
rfl 16001.2
rfp 9714.9
th 20
ins 1.000
ai ph
DEC. & VT
dfrq 500.225
dn H1
dpwr 37
dof -500.0
lm y
dmm w
dmf 10000
dseq
dres 1.0
homo n
PROCESSING
lb 0.30
wtfile
proc ft
fn 131072
math f
werr
wexp
wbs
wnt
PhthN
Br
O
OMe
N
H
N
H
NPhth
(-)-80
200
180
160
140
120
100
80
60
40
20
0
-20
ppm

ChiralPak IC 0.7mL/min, 55:45=iPrOH:Hexane

Injection Date	:	Seq. Line	: 1
Sample Name	:	Location	: Vial 23
Acq. Operator	:	Inj	: 1
		Inj Volume	: 0 µl
Different Inj Volume from Sequence !		Actual Inj Volume	: 20 µl
Acq. Method	:		
Last changed	:		
Analysis Method	:		
Last changed	:		



Area Percent Report

Sorted By	:	Signal
Multiplier	:	1.0000
Dilution	:	1.0000

Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 C, Sig=230,16 Ref=360,100

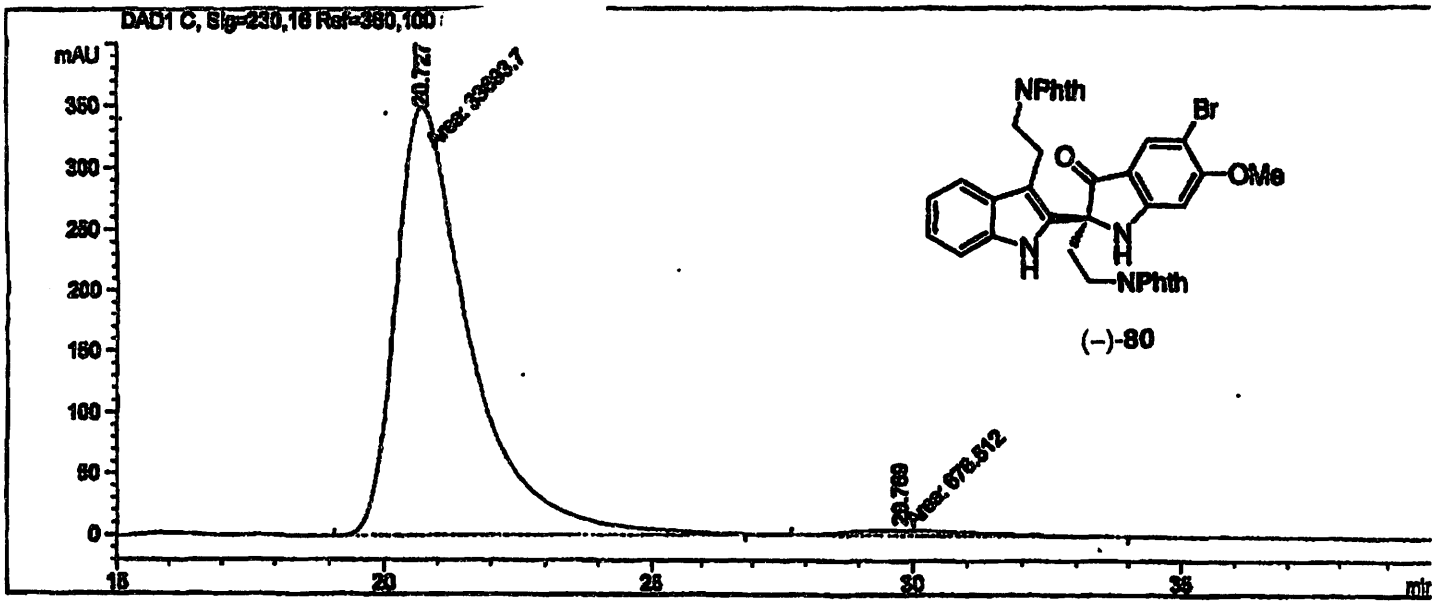
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.640	MM	1.5072	8728.03906	96.51717	50.9548
2	29.279	MM	2.8044	8400.94922	49.92635	49.0452
Totals :				1.71290e4	146.44352	

Results obtained with enhanced integrator!

*** End of Report ***

ChiralPak IC 0.7mL/min, 55:45=iPrOH:Hexane

Injection Date	:	Seq. Line	: 1
Sample Name	:	Location	: Vial 27
Acq. Operator	:	Inj	: 1
		Inj Volume	: 0 µl
Different Inj Volume from Sequence !		Actual Inj Volume	: 10 µl
Acq. Method	:		
Last changed	:		
Analysis Method	:		
Last changed	:		



(–)-80

Area Percent Report

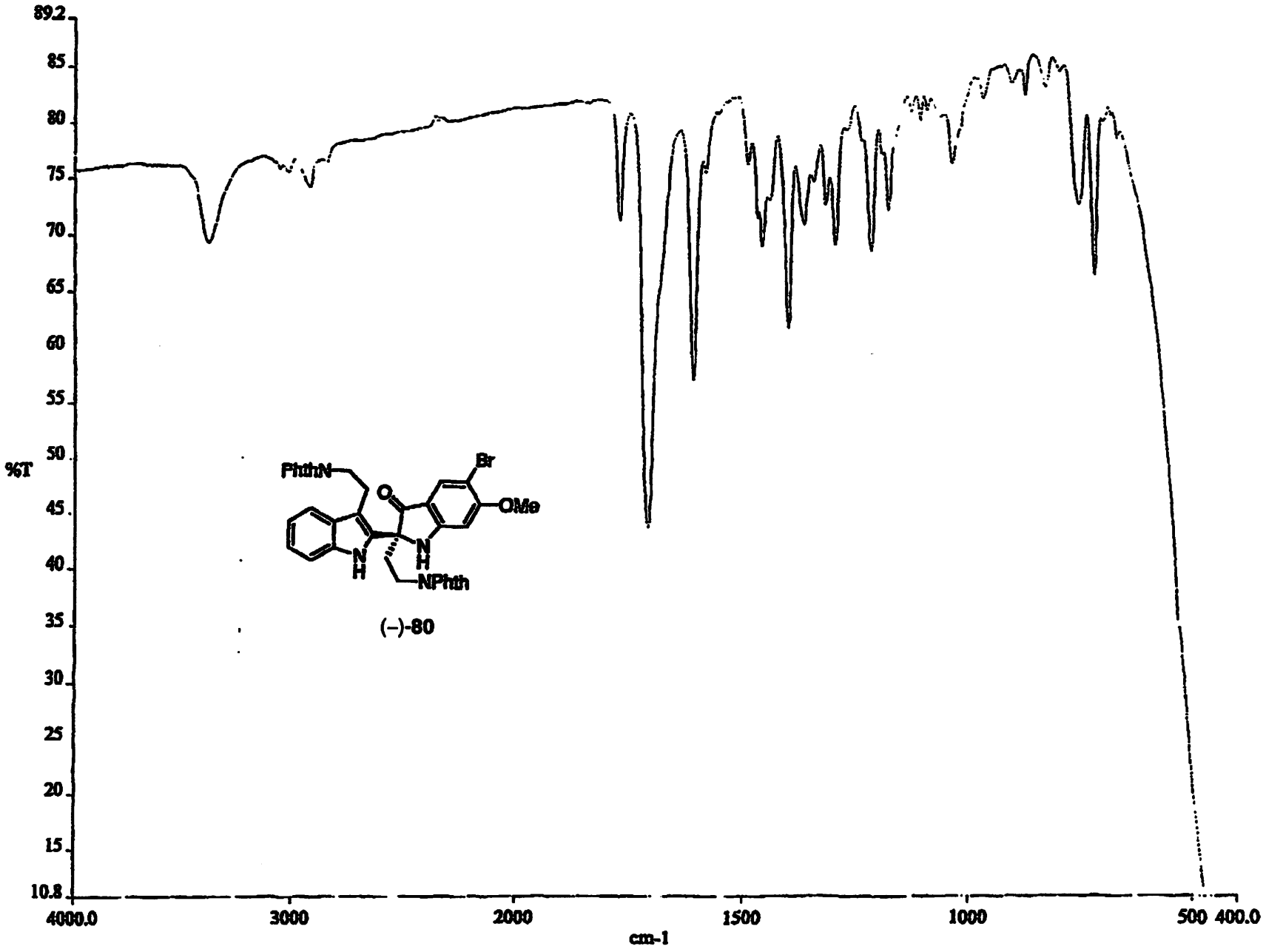
Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 C, Sig=230,16 Ref=360,100

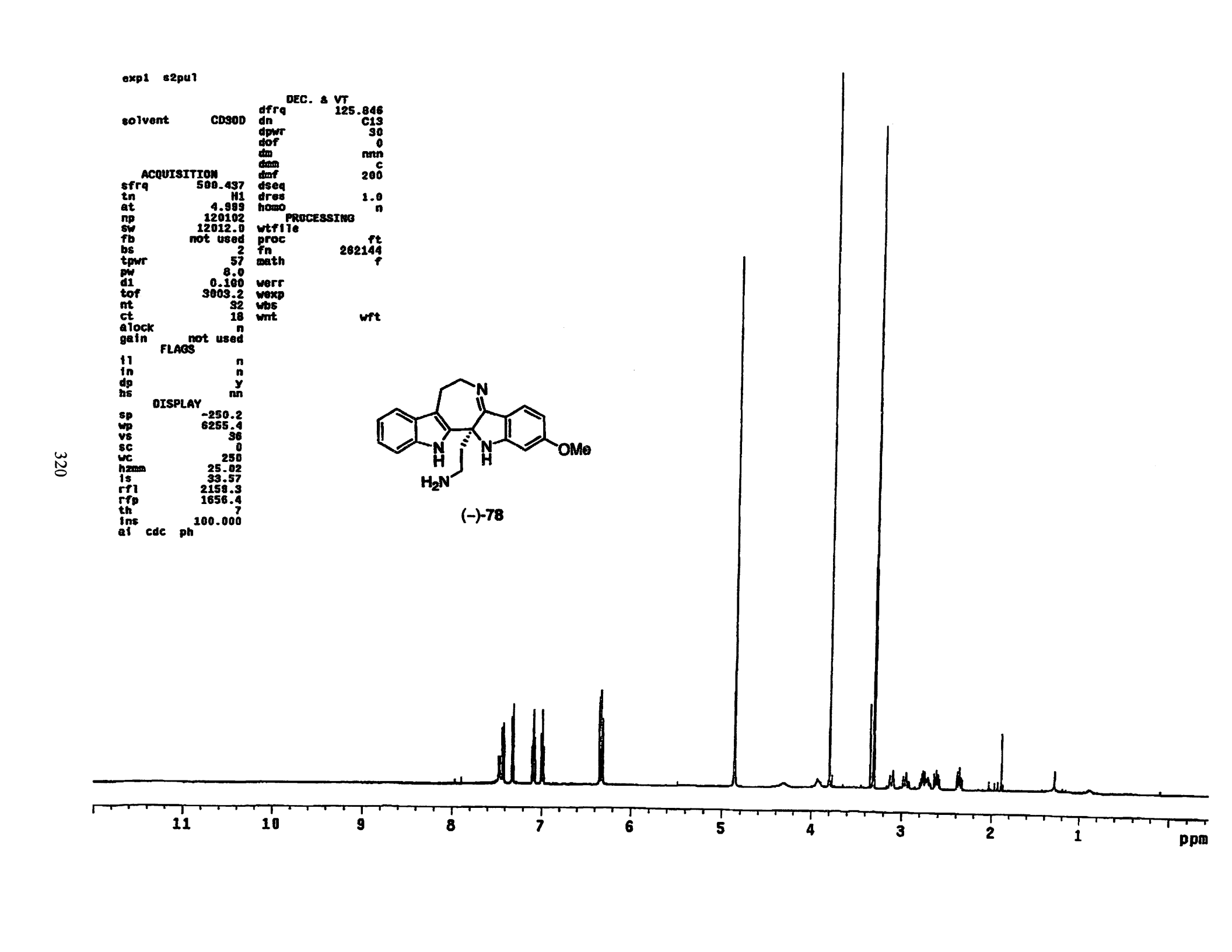
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.727	MM	1.6073	3.36937e4	349.37302	98.0317
2	29.769	MM	2.7526	676.51196	4.09626	1.9683
Totals :				3.43702e4	353.46927	

Results obtained with enhanced integrator!

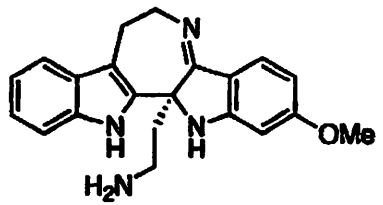
*** End of Report ***


89.2
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10.8
%T
4000.0
3000
2000
1500
1000
500
400.0
cm-1
PhthN
Br
OMe
O
N
H
N
H
NPhth

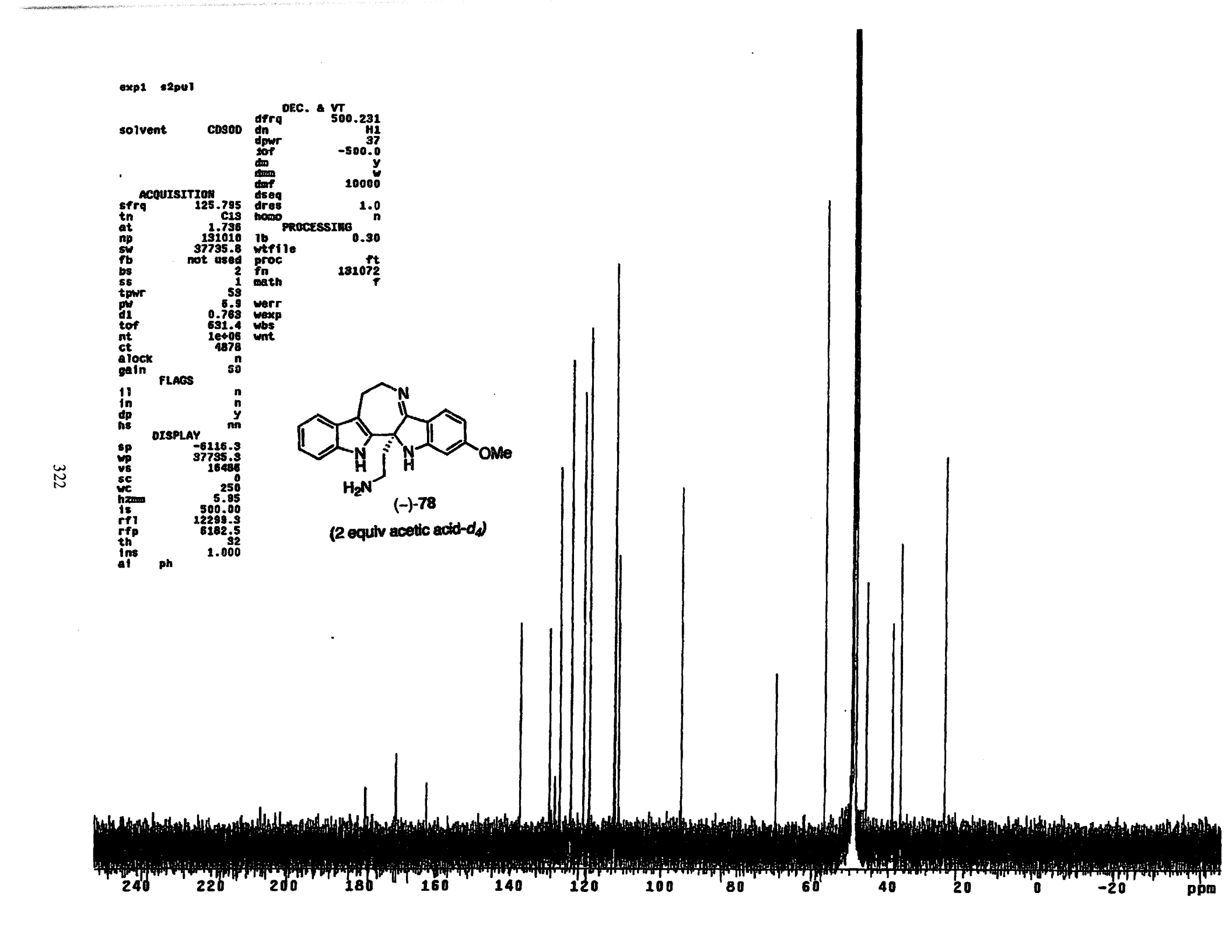
(–)-80

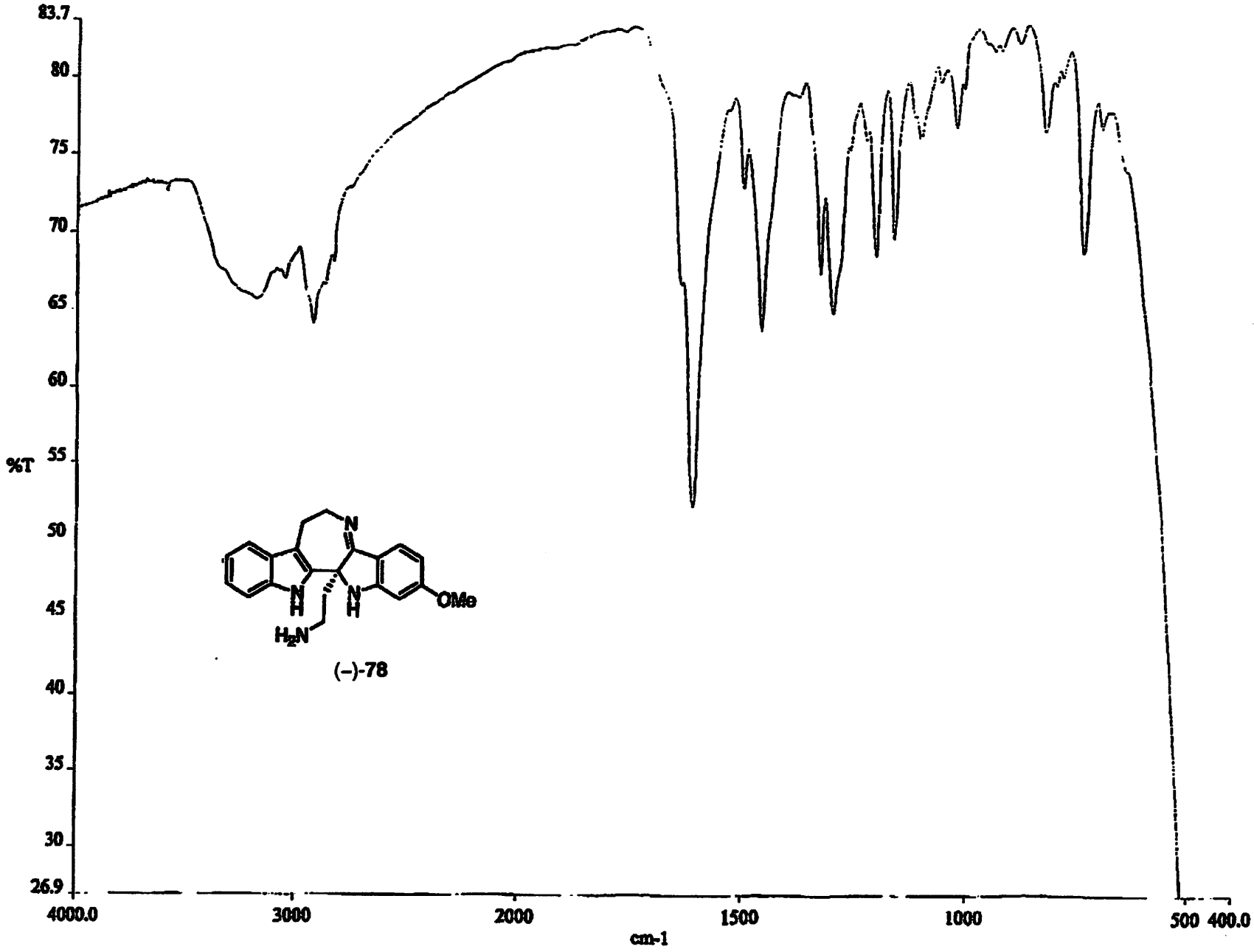

exp1 s2pul
solvent CDSOD
ACQUISITION
sfrq 500.437
tn H1
at 4.999
np 120102
sw 12012.0
fb not used
bs 2
tpwr 57
pw 8.0
d1 0.100
tof 3003.2
nt 32
ct 18
alock n
gain not used
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -250.2
wp 6255.4
vs 36
sc 0
wc 250
hzmm 25.02
is 33.57
rfl 2158.3
rfp 1656.4
th 7
ins 100.000
ai cdc ph
DEC. & VT
dfrq 125.846
dn C13
dpwr 30
dof 0
dm nnn
dmm c
dmf 200
dseq
dres 1.0
homo n
PROCESSING
wtfile
proc ft
fn 262144
math f
werr
wexp
wbs
wnt wft
N
N
H
N
H
OMe
H2N
(-)-78
11
10
9
8
7
6
5
4
3
2
1
ppm

```
exp1  s2pul

                                DEC. & VT
                          dfrq          125.846
solvent        CD3OD      dn                C13
                          dpwr               30
                          dof                 0
                          dm                nnn
                          dmm                 c
                          dmf               200
   ACQUISITION            dseq
sfrq          500.497     dres              1.0
tn                 H1     homo                n
at              4.999        PROCESSING
np             120102     wtfile
sw           12012.0      proc                ft
fb         not used       fn             262144
bs                 2      math                f
tpwr              60
pw               8.0      werr
d1             0.100      wexp
tof           3003.2      wbs
nt                32      wnt               wft
ct                10
alock              n
gain       not used
      FLAGS
il                 n
in                 n
dp                 y
hs                nn
     DISPLAY
sp             -250.2
wp             6255.4
vs                 43
sc                  0
wc                250
hzmm            25.02
is              33.57
rf1           2159.7
rfp           1656.4
th                  7
ins           100.000
ai  cdc  ph
```

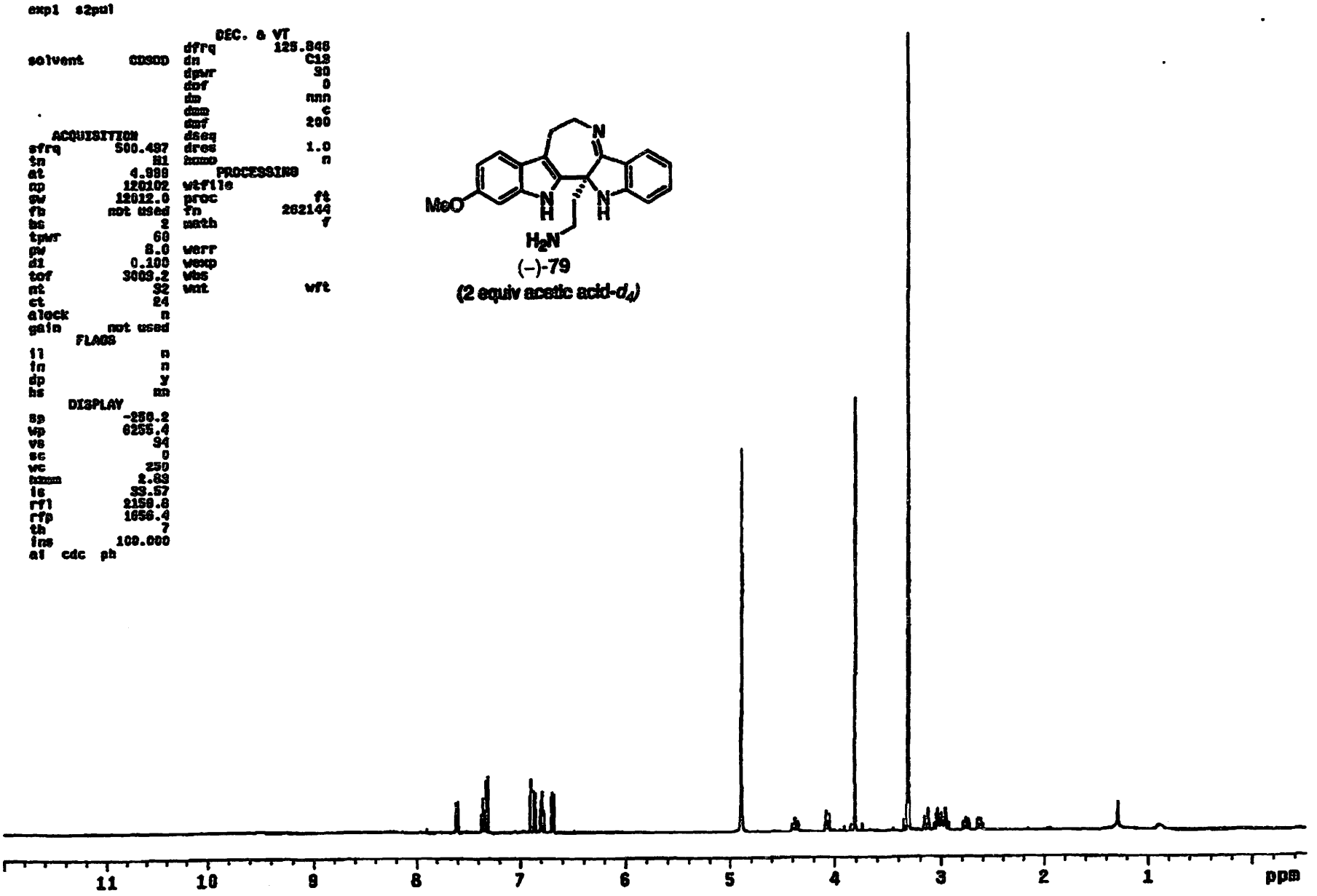


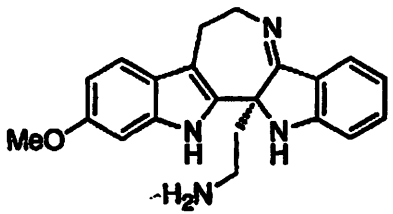
(–)-78
(2 equiv acetic acid-d_4)


exp1 s2pul
solvent CDSOD
ACQUISITION
sfrq 125.795
tn C13
at 1.736
np 131010
sw 37735.8
fb not used
bs 2
ss 1
tpwr 53
pw 5.9
d1 0.763
tof 631.4
nt 1e+06
ct 4878
alock n
gain 50
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -6116.3
wp 37735.3
vs 16486
sc 0
wc 250
hzmm 5.85
is 500.00
rfl 12299.3
rfp 6182.5
th 32
ins 1.000
ai ph
DEC. & VT
dfrq 500.231
dn H1
dpwr 37
tof -500.0
dm y
dmm w
dmf 10000
dseq
dres 1.0
homo n
PROCESSING
lb 0.30
wtfile
proc ft
fn 131072
math f
werr
wexp
wbs
wnt
N
N
H
N
H
OMe
H2N
(–)-78
(2 equiv acetic acid-d4)
240
220
200
180
160
140
120
100
80
60
40
20
0
-20
ppm


83.7
80
75
70
65
60
55
50
45
40
35
30
26.9
%T
4000.0
3000
2000
1500
1000
500 400.0
cm-1
N
N
H
N
H
H2N
OMe

(–)-78

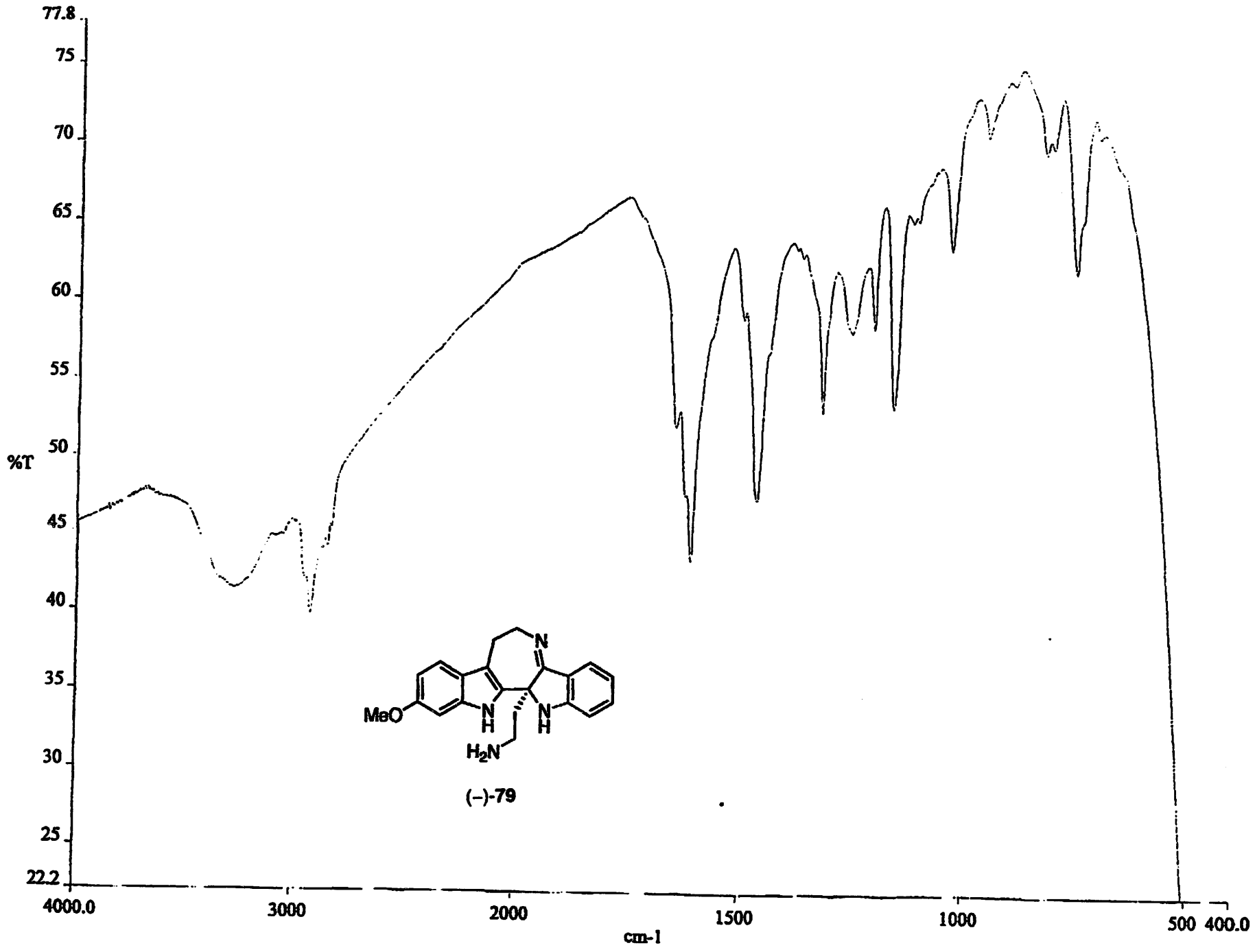

expl s2pul
solvent CDSOD
ACQUISITION
sfrq 500.497
tn H1
at 4.988
np 120102
sw 12012.0
fb not used
bs 2
tpwr 60
pw 8.0
d1 0.100
tof 3003.2
nt 32
ct 24
alock n
gain not used
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -259.2
wp 6255.4
vs 94
sc 0
vc 250
mmm 2.69
is 33.57
rfl 2158.8
rfp 1856.4
th 7
ins 100.000
ai cdc ph
DEC. & VT
dfrq 125.848
dn C13
dpwr 30
dof 0
dm nnn
dmm c
dmf 200
dseq
dres 1.0
homo n
PROCESSING
wtfile
proc ft
fn 262144
math f
werr
wexp
wbs
wnt wft
MeO
N
H
N
H
H2N
(–)-79
(2 equiv acetic acid-d4)
11
10
9
8
7
6
5
4
3
2
1
ppm



(–)-79

(2 equiv acetic acid-d_4)


```
Current Data Parameters
NAME
EXPNO
PROCNO                       1

F2 - Acquisition Parameters
Date_
Time
INSTRUM                   spect
PROBHD     5 mm BRO BB-1H
PULPROG                zgpg30
TD                      65536
SOLVENT                 CDCl3
NS                       2820
DS                          2
SWH                23980.814 Hz
FIDRES             0.365918 Hz
AQ                 1.3664756 sec
RG                   14596.5
DW                    20.850 usec
DE                     6.00 usec
TE                     296.2 K
D1                2.00000000 sec
d11               0.03000000 sec
DELTA             1.89999998 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                      13C
P1                     8.75 usec
PL1                   -3.00 dB
SFO1           100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2              waltz16
NUC2                      1H
PCPD2                 90.00 usec
PL2                   -1.00 dB
PL12                  14.52 dB
PL13                  18.00 dB
SFO2           400.1316005 MHz

F2 - Processing parameters
SI                       65536
SF             100.6126115 MHz
WDW                         EM
SSB                          0
LB                    1.00 Hz
GB                           0
PC                    1.40
```


77.8
75
70
65
60
55
50
45
40
35
30
25
22.2
%T
4000.0
3000
2000
1500
1000
500
400.0
cm-1
MeO
N
H
N
H
H_2N

(–)-79

exp1 s2pul

solvent	DMSO

ACQUISITION	
sfrq	500.437
tn	H1
at	4.999
np	120102
sw	12012.0
fb	not used
bs	2
tpwr	57
pw	8.0
d1	0.100
tof	3003.2
nt	32
ct	12
alock	n
gain	not used

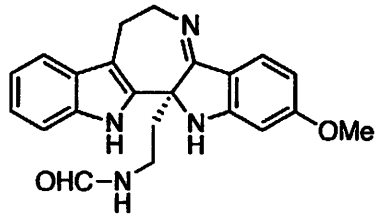
FLAGS	
il	n
in	n
dp	y
hs	nn

DISPLAY	
sp	-250.2
wp	6255.4
vs	54
sc	0
wc	250
hzmm	25.02
is	33.57
rfl	1748.6
rfp	1251.1
th	7
ins	100.000

ai cdc ph

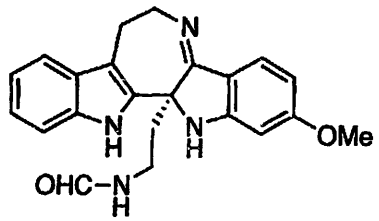
DEC. & VT	
dfrq	125.846
dn	C13
dpwr	30
dof	0
dm	nnn
dmm	c
dmf	200
dseq	
dres	1.0
homo	n

PROCESSING	
wtfile	
proc	ft
fn	262144
math	f
werr	
wexp	
wbs	
wnt	wft



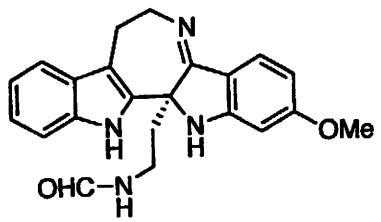
(–)-trigonoliimine C (3)

```
exp1  s2pul

                          DEC. & VT
                      dfrq          125.846
solvent       CD3OD   dn                C13
                      dpwr               30
                      dof                 0
                      dm                nnn
                      dmm                 c
   ACQUISITION        dmf               200
sfrq          500.437 dseq
tn                 H1 dres               1.0
at              4.999 homo                n
np             120102     PROCESSING
sw           12012.0  wtfile
fb          not used  proc              ft
bs                 2   fn            262144
tpwr              57   math               f
pw               8.0
d1             0.100   werr
tof           3003.2   wexp
nt                 3   wbs
ct                 3   wnt              wft
alock              n
gain        not used
      FLAGS
il                 n
in                 n
dp                 y
hs                nn
     DISPLAY
sp            -250.2
wp            6255.4
vs                25
sc                 0
wc               250
hzmm           25.02
is             33.57
rfl            2159.4
rfp            1656.4
th                 7
ins           100.000
ai  cdc  ph
```



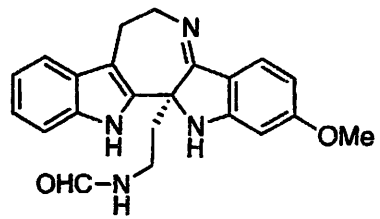
(–)-trigonoliimine C (**3**)

```
exp1  s2pul

                    DEC. & VT
                dfrq        125.846
                dn              C13
                dpwr             30
                dof               0
                dm              nnn
                dmm               c
                dmf             200
   ACQUISITION  dseq
sfrq        500.437 dres            1.0
tn               H1 homo             n
at            4.999     PROCESSING
np           120102 wtfile
sw         12012.0  proc             ft
fb         not used fn           262144
bs               2  math             f
tpwr            57
pw             8.0  werr
d1           0.100  wexp
tof         3003.2  wbs
nt              32  wnt            wft
ct              24
alock            n
gain     not used
     FLAGS
il               n
in               n
dp               y
hs              nn
    DISPLAY
sp          -250.2
wp          6255.4
vs              56
sc               0
wc             250
hzmm         25.02
is           33.57
rfl         2160.1
rfp         1656.4
th               7
ins        100.000
ai  cdc  ph
```

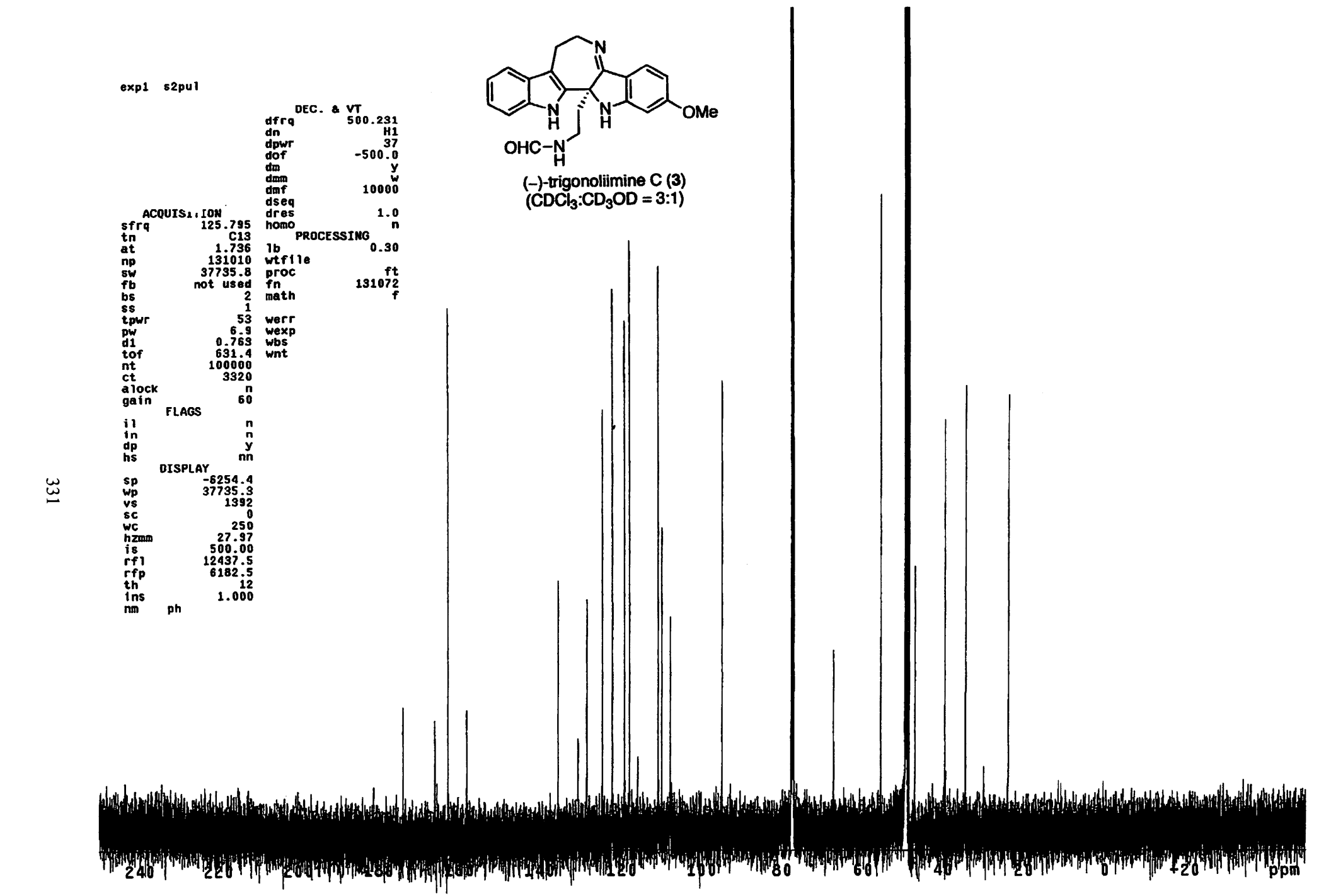


(-)-trigonoliimine C (3)
($CDCl_3$:CD_3OD = 3:1)

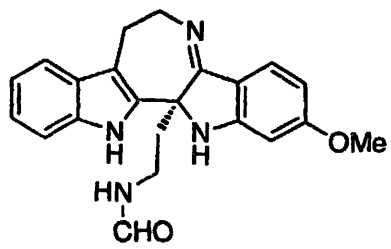
```
exp1  s2pul

                              DEC. & VT
                          dfrq        500.232
solvent          DMSO     dn               H1
                          dpwr             37
                          dof          -500.0
                          dm                y
                          dmm               w
                          dmf           10000
   ACQUISITION            dseq
sfrq          125.795     dres             1.0
tn                C13     homo              n
at               1.736        PROCESSING
np            131010      lb             0.30
sw           37735.8      wtfile
fb         not used       proc             ft
bs                   2    fn           131072
ss                   1    math              f
tpwr                53
pw                 6.9    werr
d1               0.763    wexp
tof              631.4    wbs
nt               1e+07    wnt
ct                4114
alock                n
gain                60
        FLAGS
il                   n
in                   n
dp                   y
hs                  nn
       DISPLAY
sp           -6370.7
wp           37735.3
vs             19795
sc                 0
wc               250
hzmm            4.36
is            500.00
rfl          11341.2
rfp           4969.9
th                20
ins            1.000
ai     ph
```



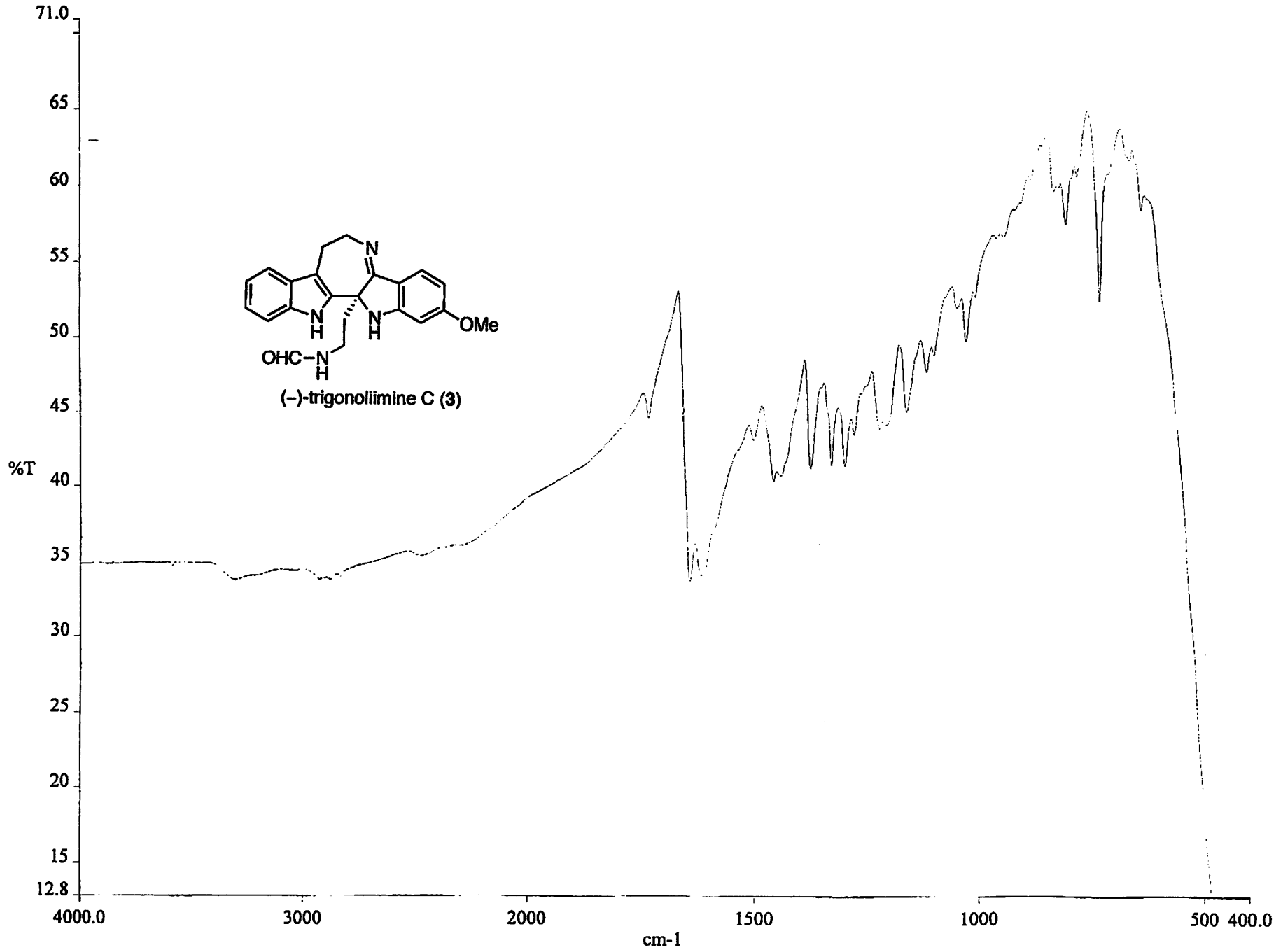
(–)-trigonoliimine C (3)


exp1 s2pul
DEC. & VT
dfrq 500.231
dn H1
dpwr 37
dof -500.0
dm y
dmm w
dmf 10000
dseq
dres 1.0
homo n
PROCESSING
lb 0.30
wtfile
proc ft
fn 131072
math f
werr
wexp
wbs
wnt
ACQUISITION
sfrq 125.795
tn C13
at 1.736
np 131010
sw 37735.8
fb not used
bs 2
ss 1
tpwr 53
pw 6.9
d1 0.768
tof 631.4
nt 100000
ct 3320
alock n
gain 60
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -6254.4
wp 37735.3
vs 1392
sc 0
wc 250
hzmm 27.97
is 500.00
rfl 12437.5
rfp 6182.5
th 12
ins 1.000
nm ph
OMe
OHC–N
(–)-trigonoliimine C (3)
(CDCl3:CD3OD = 3:1)
240
220
200
180
160
140
120
100
80
60
40
20
0
-20
ppm

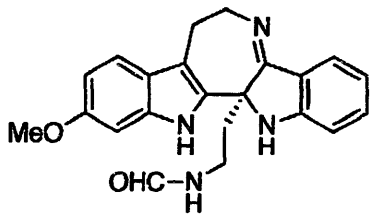
```
exp1  s2pul

                                    DEC. & VT
                                dfrq          500.231
solvent          CD3OD          dn                 H1
                                dpwr                37
                                dof           -500.0
                                dm                  y
                                dmm                 w
                                dmf           10000
   ACQUISITION                  dseq
sfrq          125.795           dres             1.0
tn                C13           homo                n
at              1.736               PROCESSING
np             131010           lb              0.30
sw           37735.8            wtfile
fb         not used             proc               ft
bs                 2             fn            131072
ss                 1             math               f
tpwr              53
pw               6.9            werr
d1             0.763            wexp
tof            631.4            wbs
nt             1e+06            wnt
ct              2794
alock              n
gain              60
      FLAGS
il                 n
in                 n
dp                 y
hs                nn
     DISPLAY
sp           -6116.9
wp           37735.3
vs              9011
sc                 0
wc               250
hzmm          150.94
is            500.00
rfl         12299.7
rfp          6182.2
th                17
ins            1.000
ai    ph
```



(–)-trigonoliimine C (**3**)

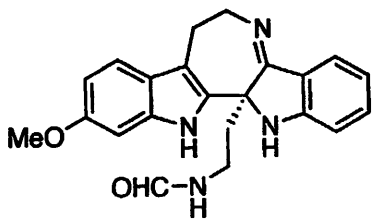

71.0
65
60
55
50
45
%T
40
35
30
25
20
15
12.8
4000.0
3000
2000
1500
1000
500
400.0
cm-1
N
N
H
N
H
OMe
OHC–N
H
(–)-trigonoliimine C (3)

```
exp2  s2pul

                          DEC. & VT
                      dfrq          125.844
solvent       CD3OD   dn                C13
                      dpwr               30
                      dof                 0
                      dm                nnn
                      dmm                 c
   ACQUISITION        dmf               200
sfrq          500.433 dseq
tn                 H1 dres              1.0
at              4.999 homo               n
np             120102     PROCESSING
sw             12012.0 wtfile
fb           not used  proc              ft
bs                  2  fn            262144
tpwr               60  math               f
pw                8.0
d1              0.100  werr
tof            3003.2  wexp
nt                 32  wbs
ct                 32  wnt              wft
alock               n
gain         not used
      FLAGS
il                  n
in                  n
dp                  y
hs                 nn
     DISPLAY
sp             -250.2
wp             6255.3
vs                110
sc                  0
wc                250
hzmm            25.02
is              33.57
rfl             2169.2
rfp             1656.4
th                  7
ins            100.000
ai  cdc  ph
```

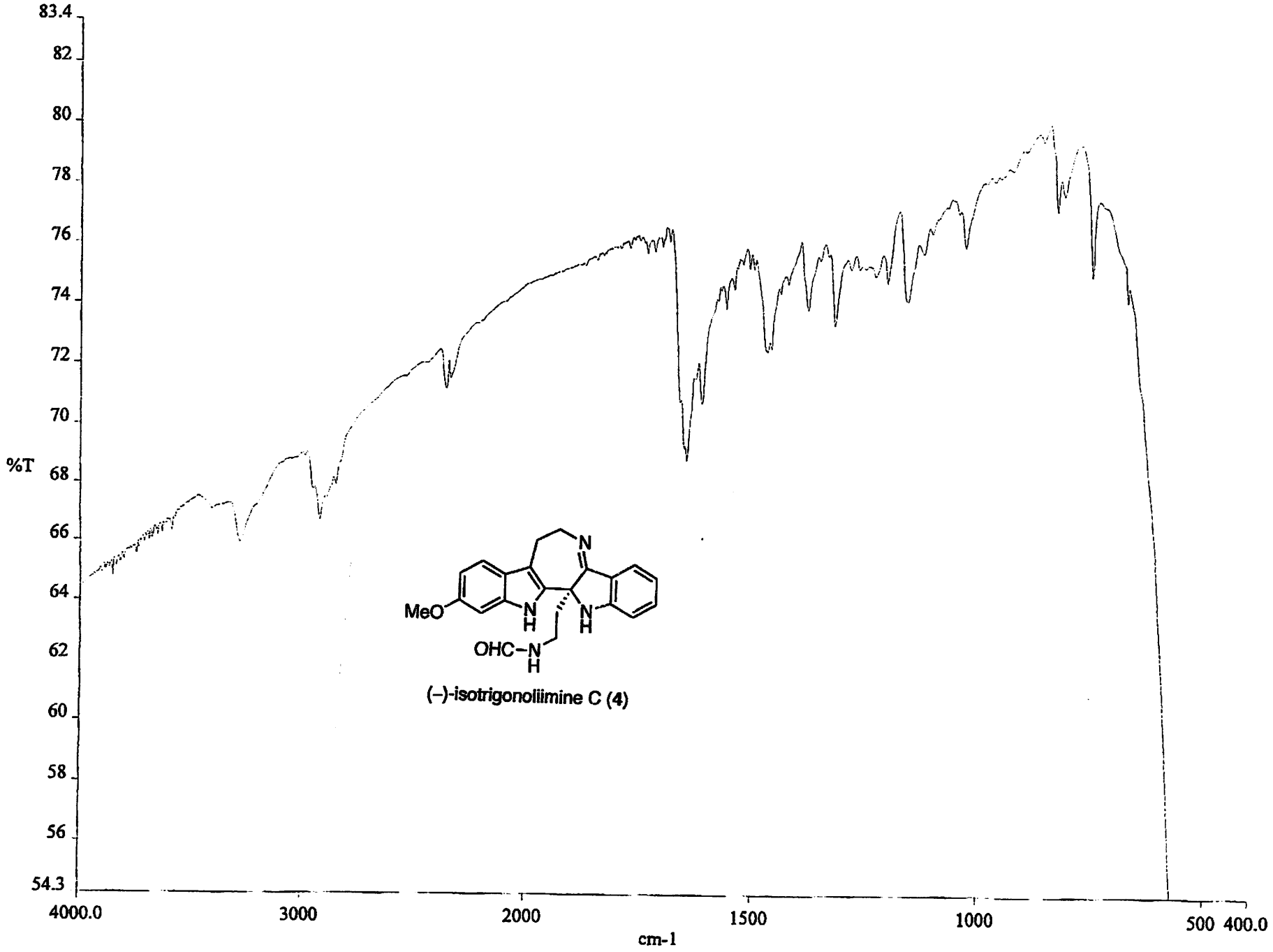


(–)-isotrigonoliimine C (4)

```
exp2  s2pul

                          DEC. & VT
                      dfrq          500.231
solvent       CD3OD   dn                 H1
                      dpwr               57
                      dof            -500.0
                      dm                  y
                      dmm                 w
                      dmf             10000
   ACQUISITION        dseq
sfrq          125.795 dres              1.0
tn                C13 homo                n
at               1.736      PROCESSING
np            131010  lb                0.30
sw           37735.8  wtfile
fb         not used   proc              ft
bs                2   fn            131072
ss                1   math               f
tpwr             53
pw              6.9   werr
d1            0.763   wexp
tof           631.4   wbs
nt           100000   wnt
ct            18494
alock             n
gain             60
      FLAGS
il                n
in                n
dp                y
hs               nn
     DISPLAY
sp          -6115.1
wp          37735.3
vs            15690
sc                0
wc              250
hzmm           2.78
is           500.00
rfl         12298.2
rfp          6182.5
th                20
ins            1.000
al    ph
```



(–)-isotrigonoliimine C (**4**)



(–)-isotrigonoliimine C (4)

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617-519-6782 (cell)

PERSONAL DATA

Born in July 17th, 1982, Pisa, Italy (residence in Italy from 1982 to 1990).

EDUCATION

Massachusetts Institute of Technology
Ph.D. candidate, Organic Chemistry (September 2006 – present)
Advisor: Professor Mohammad Movassaghi

Korea Advanced Institute of Science and Technology
B.S. Chemistry, *summa cum laude*, 2nd out of 412 (February 2006).
Thesis title: "An asymmetric alkylation of the amidine and intramolecular multi-component reaction for the synthesis of cyclic amidine."
Advisor: Professor Sukbok Chang

RESEARCH

Massachusetts Institute of Technology Cambridge, MA
Graduate Research Assistant, Professor Mohammad Movassaghi
November 2006-present
- Completed the enantioselective total synthesis of all trigonoliimine alkaloids.
- Completed the enantioselective total synthesis of all agelastatin alkaloids.

Korea Institute of Science and Technology Seoul, Korea
Research Scientist, Dr. Hee-Sup Shin and Dr. Changjoon Justin Lee
March 2006-July 2006
- Designed and synthesized selective blockers for Ca^{2+}-activated Cl^- channel.
- Tested biological activity of Ca^{2+}-activated Cl^- channel blockers using *Xenopus laevis* oocytes. .

Korea Advanced Institute of Science and Technology Daejon, Korea
Undergraduate Research Assistant, Professor Sukbok Chang
January 2005-February 2006
- Conducted research on asymmetric induction of amidine.
- Designed and synthesized aminoalkynes for copper catalyzed cyclic amidine formation.

Undergraduate Research Assistant, Professor Jie-oh Lee
September 2001-December 2002
- Conducted cloning, protein expression, purification and crystallization for BAFF–BAFF-R complex.

Kyonggi Science High School Suwon, Korea
Student Researcher, Mr. Jungheang Park
March 1998-February 2000
- Conducted research on "The optimal condition of clay court based on the moisture content the clay."

FELLOWSHIPS & AWARDS

- Kenneth M. Gordon Summer Graduate Fellowship in Organic Chemistry (MIT, 2011)
- EMD Serono Summer Graduate Fellowship (MIT, 2010)
- The Korea Foundation for Advanced Studies Scholarship. (presented to 30 Korean university students in all fields of studies including humanities, social sciences, engineering, and natural sciences, KAIST, 2005)
- ARCOM (Army Commendation Medal), awarded by Brigadier General Richard W. Mills (Special Operations Command Korea (SOCKOR), 2004).

- GE Foundation Scholar-Leaders Award (presented to 7 Korean Undergraduate students in the fields of engineering and natural sciences, KAIST, 2002)
- Departmental Scholarship for academic excellence (KAIST, 2001, 2002, 2005).
- Gold Prize (1st place) in the 6th Samsung Humantech Thesis Prize, thesis: "The Optimal Condition of Clay Court Based on the Moisture Content the Clay." (Kyonggi Science High School, 2000)

PUBLICATIONS

- Han, S.; Siegel, D. S.; Movassaghi, M. "Lithiation and Electrophilic Substitution of Dimethyl Triazones" *Tetrahedron Lett.* **2012**, *in press*.
- Han, S.; Movassaghi, M. "Concise Total Synthesis and Stereochemical Revision of all (–)-Trigonoliimines." *J. Am. Chem. Soc.* **2011**, *133*, 10768 *(Most Read Paper on July, 2011 in the J. Am. Chem. Soc)*.
- Movassaghi, M.; Han, S. "Total Synthesis of all (–)-Agelastatin Alkaloids." *Asymmetric Synthesis–The Essentials 2* Wiley-VCH, **2011**, *submitted*.
- Movassaghi, M.; Siegel, D. S.; Han, S. "Total Synthesis of all (–)-Agelastatin Alkaloids." *Chem. Sci.* **2010**, *1*, 561.
- Oh, S.; Park, J.; Han, S.; Lee, J.; Roh, E.; Lee, C. J. "Development of Selective Blockers for Ca^{2+}-Activated Cl^- Channel Using *Xenopus laevis* oocytes with an Improved Drug Screening Strategy." *Molecular Brain*, **2008**, *1*, 14.
- Chang, S.; Lee, M.; Jung, D.; Yoo, E.; Cho, S.; Han, S. "Catalytic One-pot Synthesis of Cyclic Amidine by Virtue of Tandem Reactions Involving Intramolecular Hydroamination Under Mild Condition." *J. Am. Chem. Soc.* **2006**, *128*, 12366.

PRESENTATIONS

- Gordon Research Conference (Natural Products) Poster Presentation (Jul, 2011).
- AstraZeneca Excellence In Chemistry Symposium Poster Presentation (Oct, 2010).
- EMD Serono Science Day Symposium Oral Presentation (Sep, 2010).
- MIT Graduate Research Symposium Oral Presentation (May, 2010).

EXPERIENCES & SKILLS

- Head Teaching assistant for an undergraduate level second semester organic chemistry course (MIT, 5.13, Professor Mohammad Movassaghi, Fall 2011).
- Teaching assistant for an undergraduate level first semester organic chemistry course (MIT, 5.12, Professor Rick Danheiser and Professor Timothy Jamison, Spring 2009).
- Teaching assistant for an undergraduate level first semester organic chemistry course (MIT, 5.12, Professor Sarah E. O'Connor and Dr. Kimberly Berkowski, Spring 2007).
- Teaching assistant for an undergraduate level organic chemistry laboratory (MIT, 5.310, Dr. Mircea Gheorghiu and Dr. Janet Schrenk, Fall 2006).
- Constitutional Military Services as a KATUSA (Korean Augmentee to the United States Army, SOCKOR, December 2002–December 2004)
- Korean (native), English (fluent), Italian (conversational).