Investigations on the Radical Chemistry of Thionocarbonates of Alcohols and Acyl Derivatives of Hydroxamic and Thiohydroxamic Acids.

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Abstract.

The radical deoxygenation of primary alcohols has been achieved using derivatives of perhalophenyl chlorothionocarbonates. Following the tradition of the Barton-McCombie reaction the deoxygenation proceeds *via* an organotin radical attack at the thiocarbonyl group. This forms an intermediate radical which rapidly decomposes to furnish the primary carbon radical. This is smoothly reduced by tributyltin hydride and forms the chain carrying organotin radical. This is a clean and fast reaction and deoxygenation is achieved in a matter of minutes with high yields.

Utilizing organotin radicals, a radical chain has been achieved with acyl derivatives of hydroxamic acids. This is the first example of a chain reaction *via* decarboxylation for these derivatives. Encouraging results were also obtained when the hydrogen source and chain carrier radical was replaced by an organosilane. These acyl derivatives of hydroxamic acids are not photoactive to visible light the same way their thiohydroxamic counterparts are.

A new class of acyl derivatives of 2-aryl-3-hydroxy-3,4-dihydroquinazoline-4(3*H*)-thione and its benzoquinazoline analogue has been introduced which were found to be more photolabile than their N-hydroxy-2-thiopyridone counterpart. In preliminary results of trapping experiments these new derivatives compare well with the N-hydroxy-2-thiopyridone counterpart and are even less sensitive to lower temperatures.

Quantum yields with various traps (CCl_4, $CBrCl_3$, CBr_4, $(PhS)_2$, $(PhSe)_2$ and CH_2=$CHSO_2Ph$) were determined for primary, secondary and tertiary radicals produced by the action of light on the corresponding acyl derivatives of N-hydroxy-2-thiopyridone. These were in the range expected

(10-30) for good radical chain reactions . Values for the new acyl derivatives were much higher (with $CBrCl_3$ as a trap), sometimes even double. This corresponds to lower half-life values, which are an order of magnitude lower for these new acyl derivatives.

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Experimental

Abbreviations

The following abbreviations are used

Ar	aryl
Ac	acetyl
^{t}Bu	*t*-butyl
^{i}Bu	*i*-butyl
^{n}Bu	n-butyl
Bu	butyl
iPr	iso-propyl
Et	ethyl
Me	methyl
Ph	phenyl
Py	pyridine
SPy	2-thiopyridyl
CN	nitrile
THF	tetrahydrofuran
ether	diethyl ether
AIBN	azobisisobutyronitrile
DCC	N, N'-dicyclohexylcarbodiimide
DMAP	4-(dimethylamino) pyridine
NHS	N-hydroxysuccinimide
BDMAP	1,6-*bis*(dimethylamino)pyrene
IR	infra-red
GC-MS	gass chromatography-mass spectrum
m/e	mass per unit charge
NMR	nuclear magnetic resonance

UV-vis	ultra-violet-visible
tlc	thin layer chromatography
glc	gass liquid chromatography
h	hour
min	minute
sec	second
anal.	analysis
calcd.	calculated
init	initiator
HOMO	highest occupied molecular orbital
SOMO	singly occupied molecular orbital
LOMO	lowest unoccupied molecular orbital

Chapter 1

Radical Chain Reactions.

Review

Chapter 1

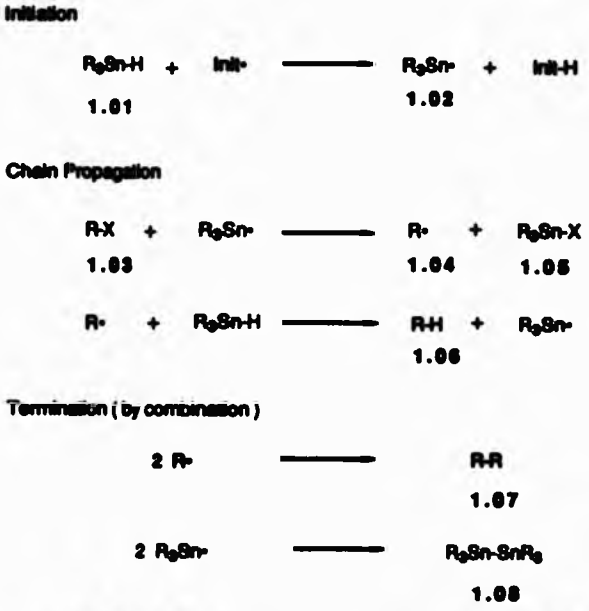
1.0 INTRODUCTION

Radical chemistry has become an important tool in synthetic organic chemistry during the past ten to fifteen[1-6] years. The ability to discipline a radical with a suitable functional group has enabled synthetic chemists to utilize radical chemistry successfully[6]. Undisciplined radicals give many unwanted products and thus are not useful for organic synthesis.

Radical reactions have an enormous importance in polymer chemistry, these reactions are similar to synthetic radical reactions. Both reactions proceed *via* a carbon chain mechanism and have initiation, propagation, and termination steps. However, they differ in their chain length, polymerization with free radicals can give chain lengths at the start of the reaction in excess of 150.[10] Synthetic radical chemistry must have chain lengths considerably lower,[11] as discussed in chapter 5. This is evidenced by polymerization reactions being extremely sensitive to termination steps for example with molecular oxygen. Shorter chain lengths allow less sensitivity to termination reactions but require periodic initiation.

An example of a synthetically useful chain reaction is the facile reduction of an alkyl halide with a trialkyltin hydride[12] (Scheme 1.01). This proceeds through an initiation step where the initiator radical, Init•, generated by thermal decomposition of azobisisobutyronitrile (AIBN) or benzoyl peroxide for example, abstracts a hydrogen atom from the tin hydride 1.01. This produces the corresponding tin radical 1.02. This tin radical then has the option of abstracting a halide atom (I or Br) from the alkyl halide 1.03, in a

chain propagating step to form the alkyl radical 1.04. Two tin radicals can combine in a chain termination step to form the hexaalkyiditin compound 1.06. The alkyl radical formed in the chain propagating step can be reduced in another chain propagating step with the tin hydride to give 1.06, or the alkyl radical can end the chain by combination or disproportionation.



Scheme 1.01

For the reduction of the alkyl halide 1.03 to be synthetically useful, the rate of reaction of the alkyl radical 1.04 with the tin hydride 1.01 must be greater than all the other potential reactions. Likewise the tin radical 1.02 must have a greater rate of reaction with the alkyl halide 1.03 than with the other species

present in the reaction. If this is not the case then the radical chain reaction breaks down and the yields of desired products are low. A way to overcome a possible lower rate of reaction between the alkyl radical **1.04** and the tin hydride **1.01** is to increase the concentration of the tin hydride relative to the alkyl halide.

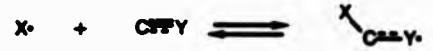
The last thirty five years has provided a detailed understanding of reactivity, selectivity, and stability of many types of organic radicals.[13,14] Despite this, only recently has there been a rapid growth in the application of free radicals to organic synthesis. This rapid growth has mainly been due to the increased understanding of the advantages in synthetic applications as compared with ionic processes. Radical reactions are often highly chemoselective and proceed in neutral conditions. In contrast, ionic reactions are generally carried out in basic or acidic conditions which are often not compatible with the various functional groups present in a compound. This is particularly important in carbohydrate chemistry where the pH of the reaction medium is critical for retention of protecting groups. The application of heat is usually only required for initiation purposes in radical reactions, this can be overcome, however, by photolytic methods of initiation if heat sensitive compounds are involved. Virtually all oxygenated functional groups are tolerated by radical reactions. Thus O-H or N-H groups require no protection since these are amongst the strongest bonds to hydrogen, again a strong advantage in carbohydrate chemistry. Radical reactions are little influenced by remote substituent effects or steric crowding. For example tertiary butyl radicals often add to alkenes with rates similar or faster than that of the corresponding reaction with less substituted radicals (for an explanation see Section 1.3.1- page 14). Radicals are free of ionic complications such as anion kinetics, ion-pairing, aggregation and large solvent effects. Techniques

usually applied in ionic chemistry, such as solvent, temperature, and counter ion changes do not generally effect the outcome of a radical reaction. In addition, product ratios often cannot be altered for reactions that exhibit low stereo- or regioselectivity. Concentration ratios however can have dramatic effects on product ratio when one or more second order reactions are involved. Nearly all the useful reactions of free radicals can be grouped into two broad classes:

a) Atom (or group) abstraction;

Although this reaction is formally reversible, in practice this never occurs on the radical chain reaction time scale. The most commonly abstracted groups are when X = halogen, hydrogen, or SR, SeR. The direction is determined by relative bond strengths of the forming and breaking bonds, hence the rate of reaction is under thermodynamic control.

b) Addition to multiple bonds;



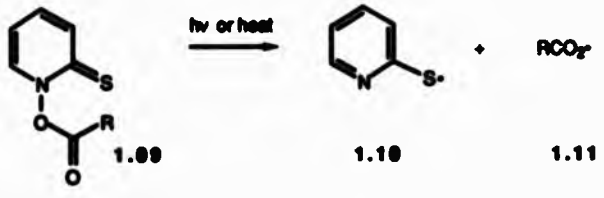
This review deals only with addition to carbon-carbon multiple bonds. This addition is reversible and the equilibrium is controlled by relative bond strengths and stabilities of radicals involved. Generally the addition of a carbon centred radical to a carbon-carbon multiple bond is a favourable process because a carbon-carbon σ-bond is formed at the expense of a weaker π--bond. This is why addition does not take place to a carbon-oxygen double bond; the carbon-oxygen π-bond is as strong as a carbon-carbon σ-bond. Frontier molecular orbital considerations have provided a basis for understanding the diverse collection of results of the radical carbon-carbon addition reaction (see page 15). These exothermic reactions are typically thought to have early transition states and thus frontier orbital theory can be

used to describe these reactions. The reverse of addition is elimination and this occurs with groups X that form stable radicals and weak bonds to carbon such as RSe-, RS-, R_3Sn-, and epoxides.

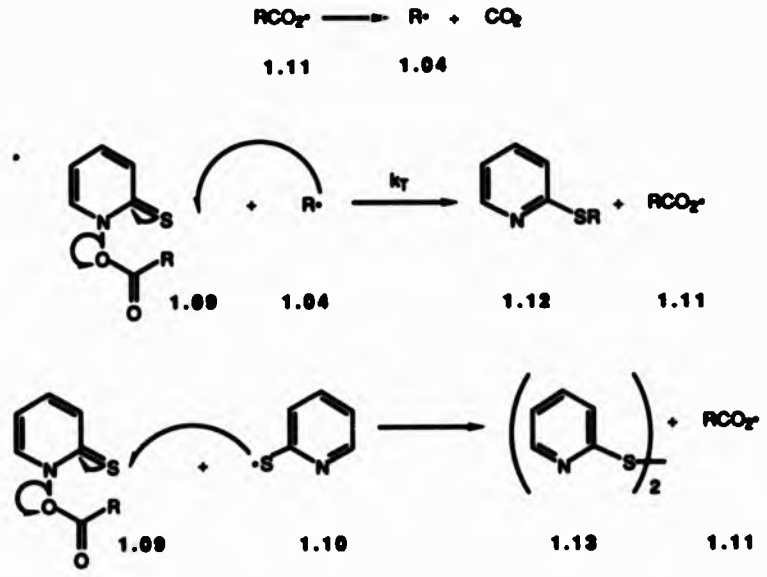
Thus, it is the aim of this review to give a general outline of the usefulness of radical reactions for the generation of carbon centred radicals, used in synthetically valuable transformations. Carbon-carbon bond formation including substituent effects is discussed. The importance of rate constants in synthetic planning as well as the understanding of the criteria needed for a successful chain reaction is also briefly discussed.

1.1 Rate Constants in Synthetic Planning.

Examples of how knowledge of rate constants can help in the synthetic planning are well documented[1,2,3]. Newcomb and Kaplan[15] have shown how knowledge of the rate constant for an alkyl radical attacking the thiohydroxamate derivative 1.09[16] can be applied to the synthetic planning of a radical chain reaction involving this radical precursor. Scheme 1.02 shows a simple radical chain reaction involving this group of light sensitive compounds.



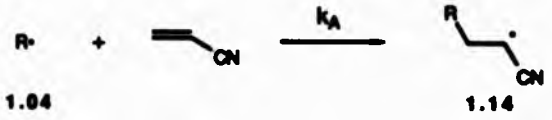
1.09 1.10 1.11



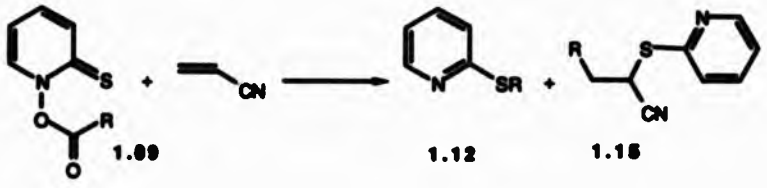
Scheme 1.02

The N-hydroxypyridine-2-thione derivative **1.09** can be fragmented by either heat or visible light to give to radicals **1.10** and **1.11**. Clearly, the weakness of the N-O bond and the aromatisation of the pyridine ring provide a powerful driving force for this process. Decarboxylation of the carboxylate radical **1.11** to give the carbon centred radical **1.04** occurs spontaneously if R does not effect stabilization of **1.11** (see page 44). Radical **1.04** can then attack the thiocarbonyl group of its precursor forming the alkyl-2-thiopyridine **1.12** (the rearranged product). This reaction also forms **1.11** thus allowing the chain to continue, the formation of **1.13** is also a chain propagating step and involves the attack of the thiopyridyl radical **1.10** formed during initiation. Newcomb and Kaplan[15] have determined the rate constant for the attack of **1.04** (R = octyl) on its precursor **1.09** and found $k_T = 1.36 \times 10^6\ M^{-1}s^{-1}$ at 25°C.[17] The

addition of the primary radical 1.04 to acrylonitrile has a known rate constant (Scheme 1.03; k_A = $1x10^6$ $M^{-1}s^{-1}$ at 25°C[18]). Knowing this Newcomb predicted the product ratio of 1.12 and 1.15 for the reaction depicted in Scheme 1.04 to be 45:55[19] respectively (R = octyl). This is in good agreement to the value he finds experimentally (40:60, 0°C).[15]



Scheme 1.03



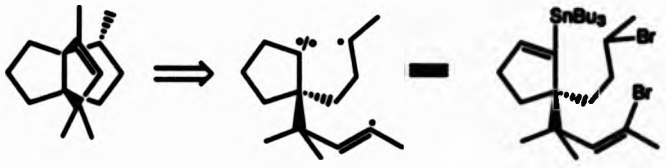
Scheme 1.04

From a purely qualitative stand point one can predict that the product ratio between 1.12 and 1.15 would be almost equal, since the rate constants k_T and k_A are of the same order of magnitude. The fact that the value of k_T is slightly larger is compensated for in the reaction by the acyl derivative 1.09 decreasing in concentration faster than the acrylonitrile hence favouring the radical addition onto the relatively higher concentrated alkene. For example when the concentrations are increased to 1.0 M for acrylonitrile and to 0.1 M for that of 1.09 it has been predicted[15] that the product ratio can change such that the desired product is favoured, 12:88 for 1.12:1.15. This again compares favourably with the experimental facts where only 10% of 1.12 was

reported and 59% of **1.15** with only a five fold excess of acrylonitrile.[20] This shows that an understanding of the rate constant for a radical reaction can be useful in predicting product distributions.

1.2 Criteria for Synthetically Useful Chain Reactions.

Reterosynthetic analysis,[21] often used in ionic chemistry, can also be applied to radical chemistry. Curran[22] has proposed new symbols that represent radical disconnections. An example is shown in Figure 1.01 with the retrosynthetic analysis of modhephene **1.16**.



Modhephene

1.16 **1.17** **1.18**

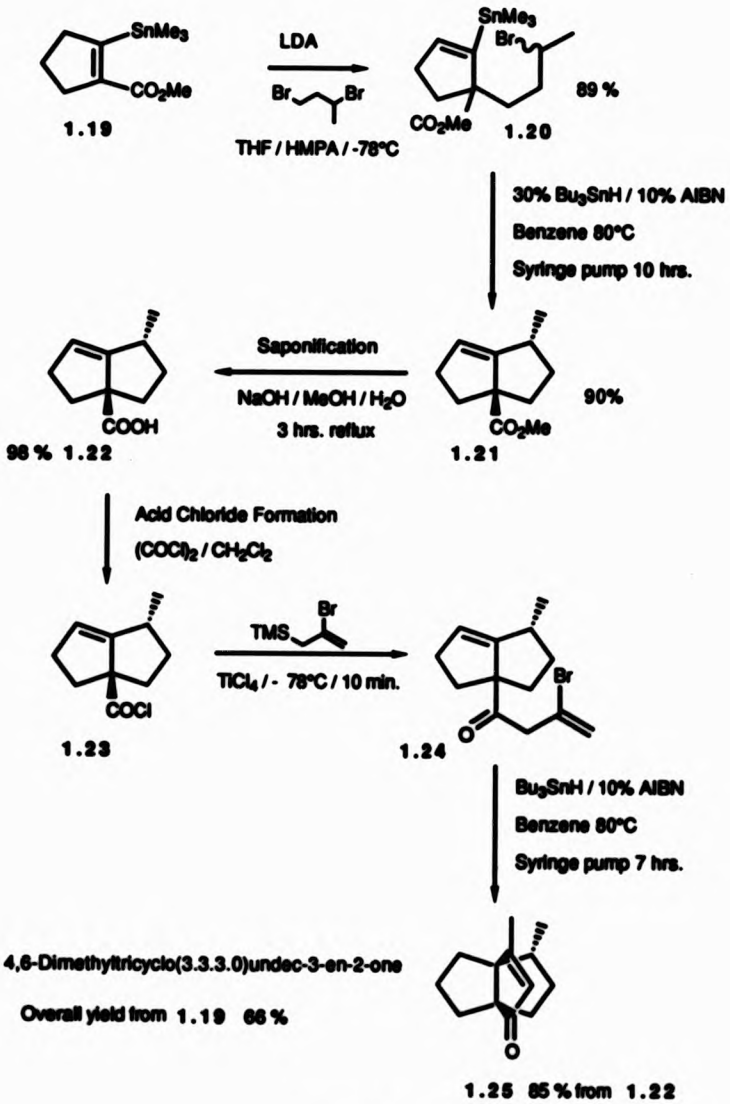
° = Radical acceptor

• = Radical donor

Figure 1.01

In **1.17** the radical acceptors (°) are represented by the carbon-carbon double bond and the tributyltin moiety as shown in **1.18**. The radical donors (•) in **1.17** are represented by the bromine-carbon bonds as in **1.18**. With these new notations radical reactions can add a new dimension to retrosynthetic analysis. Radical disconnection methods can give rise to synthons not previously available with ionic retrosynthetic analysis. Noteworthy is the functional group economy that often results from strategies based on radical

cyclizations. For example Curran and Jasperse[23] in studies towards their successful radical synthesis of modhephene **1.16** also reported the use of an efficient radical process in the synthesis of the propellane **1.25**, distinctive by its functional group economy. Curran was able to form the propellane **1.25** with only two traditional functional group interconversions, namely saponification and acid chloride formation. No protecting groups were used and there were no oxidations. The only reductions being the key tin hydride cyclizations (Scheme 1.05).

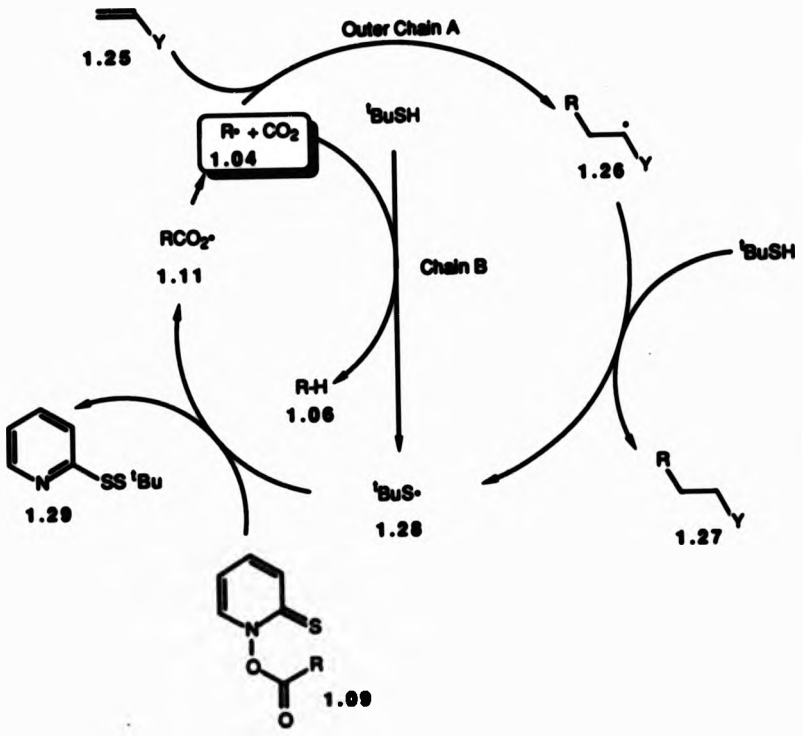

SnMe3
CO2Me
1.19
LDA
Br
Br
THF / HMPA / -78°C
SnMe3
Br
CO2Me
1.20
89 %
30% Bu3SnH / 10% AIBN
Benzene 80°C
Syringe pump 10 hrs.
Saponification
NaOH / MeOH / H2O
3 hrs. reflux
COOH
98 % 1.22
CO2Me
1.21
90%
Acid Chloride Formation
(COCl)2 / CH2Cl2
COCl
1.23
TMS
Br
TiCl4 / - 78°C / 10 min.
Br
O
1.24
Bu3SnH / 10% AIBN
Benzene 80°C
Syringe pump 7 hrs.
4,6-Dimethyltricyclo(3.3.3.0)undec-3-en-2-one
Overall yield from 1.19 66 %
O
1.25 85 % from 1.22

Scheme 1.05

There are two different ways to conduct multiple radical reactions, either individually or in a tandem process. Whilst an individual radical reaction allows synthetic flexibility, a tandem process can be more powerful. In a tandem process very complex systems can be assembled from simple precursors.

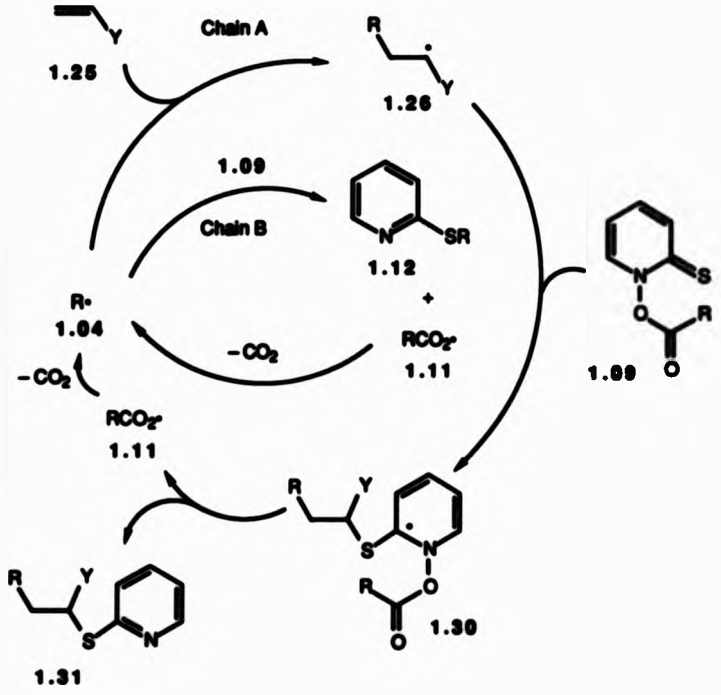
For synthetic transformations to take place a radical reaction must have a reasonable chain length otherwise the reaction becomes prohibitively slow. In a useful chain reaction radicals must have sufficient lifetime to react. Free radicals react with themselves, unlike cations and anions, by combination and disproportionation at rates approaching the diffusion controlled limit.[30] Hence, if the life-times of the radicals are too long they may engage in destructive chain-termination steps as mentioned above. This is generally not a problem as the concentration of radicals is usually very small. Their reaction with non radical chain carrying traps is usually not diffusion controlled, and so selectivities can be influenced by variation of the concentration of these non radicals.

The rate of a radical reaction determines which reactions will or will not occur. Thus for a radical chain to be successful the selectivities of the radicals involved in that chain must differ from each other. The rate of reaction between non-radical chain carriers and radicals must be faster than the rate of radical-radical reaction. This principle is illustrated in Schemes 1.06 and 1.07.


1.25
Y
Outer Chain A
R
1.26
Y
tBuSH
R• + CO2
1.04
RCO2•
1.11
Chain B
tBuSH
R-H
1.06
N
SS tBu
1.29
tBuS•
1.28
R
Y
1.27
N
S
O
R
O
1.09

Scheme 1.06

For the chain reaction shown in Scheme 1.06 to take place the alkyl radical 1.04 must react faster with the olefin 1.25 (outer chain A) than with the thiol (inner chain B). This reaction was conceived by Barton *et al* [24] but in practice the radical 1.04 was reduced to 1.06 faster than it could react with the electron deficient olefin 1.25. The Barton group then examined the same reaction in the absence of the thiol as shown in Scheme 1.07. This worked well and gave fair to good yields depending on the electron withdrawing group Y present in the olefin 1.25 as seen in Table 1.01.



Scheme 1.07

Table 1.01[24]

Radical additions to electron deficient olefins.

Examples for Scheme 1.07		
R=	Y= (eq.)	Yield % 1.31
$C_{10}H_{21}$	CN (5)	57
$C_{10}H_{21}$	CO_2Me (2)	83
$C_{10}H_{21}$	NO_2 (1.1)	83
C_6H_{11}	NO_2 (1.2)	46
$CHMe_2$	NO_2 (1.2)	82
Adamantyl	CO_2Me (2)	35

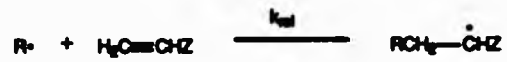
The competing chain in this case involves the alkyl radical reacting with its thiohydroxamate precursor **1.09** to form the rearranged compound **1.12** (Scheme 1.07).

1.3 Carbon-Carbon Bond Formation

1.3.1 Theoretical Considerations

In the copolymerization of styrene and methyl methacrylate Mayo[25] observed in 1944 that the polymeric benzyl radical had a marked preference for the methyl methacrylate monomer over the styrene monomer. This led to the interpretation that the rate of addition of the polymeric benzyl radical increases when alkenes bear electron withdrawing substituents.[26]

Thus for the reaction outlined in Scheme 1.06 where R• = C_6H_{11}• one obtains the relative rates of reaction shown in Table 1.02 for various substituents Z.



Scheme 1.08

Table 1.02[14]

Relative rates of radical additions to olefins.

Alkene Z=	k_{rel} 20°C
CHO	34
CN	24
$COCH_3$	13
CO_2CH_3	6.7
$CONH_2$	1.0
C_6H_5	1.0
Cl	0.12
$OCOCH_3$	0.016
H	(0.015)[a]
nC_4H_9	0.004

a: Extrapolated value from Hammett relationship

Hammett plots indicate that alkyl radicals have nucleophilic character.[14] This remarkable result is explained by frontier orbital theory. The highest occupied molecular orbital (HOMO) and the singly occupied molecular orbital (SOMO) are approximately given by the ionization potentials of the substrate and free radicals.[28,29] The SOMO-LUMO interaction is the energetically important one in reactions of nucleophilic alkyl radicals since electron donating groups, serve to increase the energy of the SOMO.[28] As the SOMO-LUMO energy

difference is decreased the rate of nucleophilic addition increases. The nucleophilic reactivity of these radicals increases as electron donating substituents are incorporated into the radical, decreasing the SOMO-LUMO energy difference as shown in Figures 1.02 and 1.03.

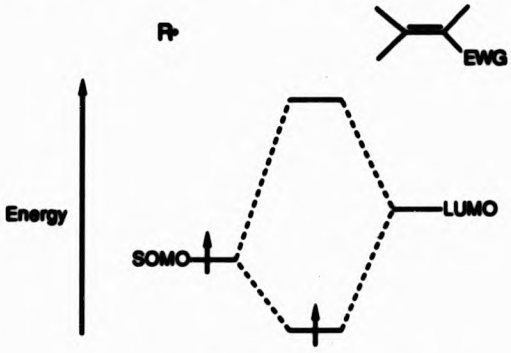


Figure 1.02: Orbital interaction between a nucleophilic radical and an electron-poor alkene.

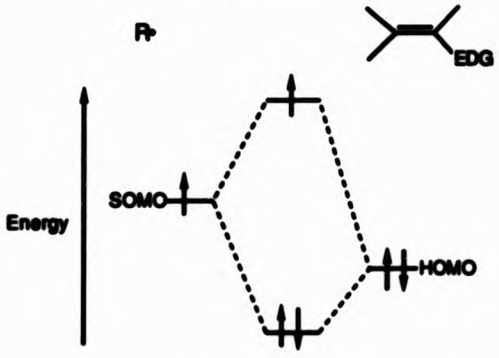


Figure 1.03: Orbital interaction between an electrophilic radical and an electron-rich alkene.

Thus, the increase in SOMO energy in going from primary to tertiary radicals has a larger effect on the rate than the associated decrease in the strength of bond being formed. For example secondary alkyl radicals are generally considered to be more stabilised than primary alkyl radicals. However due to the secondary alkyl radical being more nucleophilic it is more reactive towards electron deficient olefins.[29] In contrast, the SOMO-HOMO interaction dominates in reactions of electrophilic radicals because the SOMO energy is lowered by the electron withdrawing substituents at the radical centre.

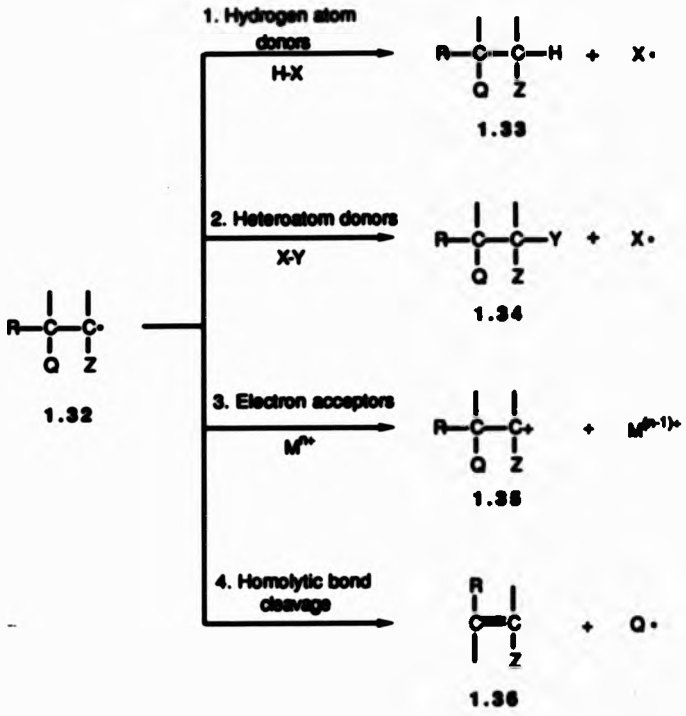
The LUMO of alkynes lie higher and the HOMO lower than in alkenes therefore the interaction between the SOMO of the alkyl radical and the π-system of the alkyne is smaller than for alkenes. Thus alkyl radicals react faster with alkenes than with alkynes, this applies to both nucleophilic and electrophilic radicals.

1.3.2 Radical Additions

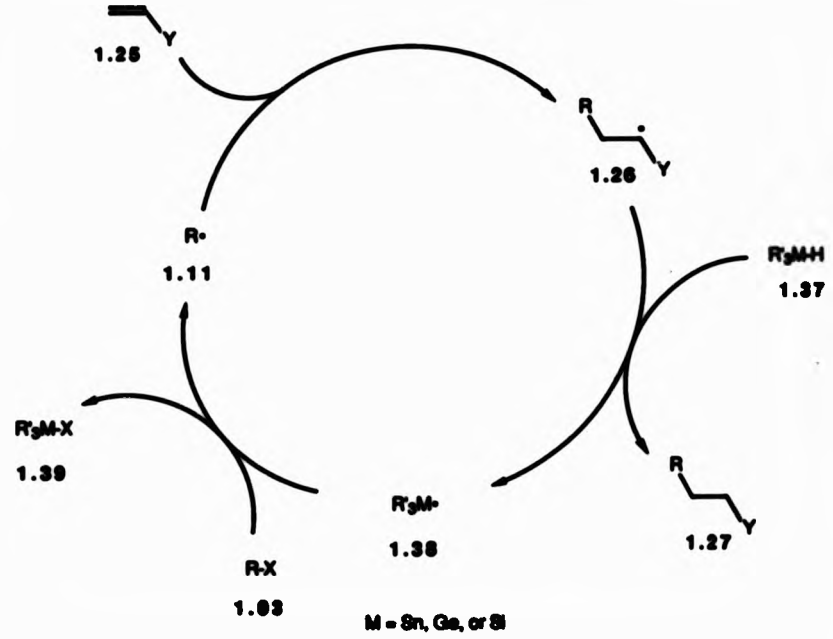
The addition of alkyl radicals to alkenes (Scheme 1.08) is the most important method of generating carbon-carbon bonds in radical chemistry. The radical thus generated will polymerize unless radicophilic traps are present or there is a substituent present which will allow homolytic cleavage to form another alkene. The principles of this process are outlined in Scheme 1.09.

As was examined in section 1.3.1 the substituents present on the alkene can have a dramatic effect on the reaction products. The principle of rate constants as applied to radical reactions has also already been covered in sections 1.1 and 1.2. Thus, with the correct selectivities and rates of

reaction the four systems outlined in Scheme 1.09 can work well to produce carbon-carbon bonds in reasonable yields.



Scheme 1.09


1.25
Y
R
Y
1.26
R'3M-H
1.37
R
Y
1.27
R'3M•
1.38
R-X
1.03
R'3M-X
1.39
R•
1.11
M = Sn, Ge, or Si

Scheme 1.10

Table 1.03

Radical addition to olefins *via* organotin; germanium; or silicon hydrides.

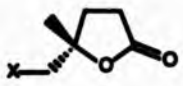
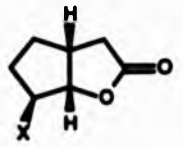
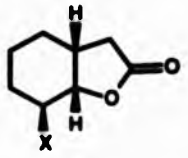
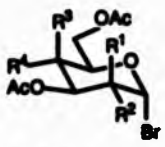
R-X	R'_3M-H	CH_2=CH-Y	Addition product	
1.03	1.37	1.25	1.27 %	(Ref.)
		Y= CO_2Me		
X= I	n-Bu_3SnH	12 eq.	45	(31)
X= SePh	n-Bu_3SnH	20 eq.	69	(31)
			(exo only)	
X= I	n-Bu_3SnH	10 eq.	54	(31)
X= SePh	n-Bu_3SnH	10 eq.	70	(31)
			3:1 (exo:endo)	
X= I	n-Bu_3SnH	10 eq.	58	(31)
X= SePh	n-Bu_3SnH	10 eq.	80	(31)
			(axial addition only)	
X= SePh, X'= H	n-Bu_3SnH	10 eq.	41	(32)
X= H, X'= Br	n-Bu_3SnH	10 eq.	35	(32)

Table 1.03 (Contd.)

R-X	R'_3M-H	CH_2=CH-Y	Addition product	
1.03	1.37	1.25	1.27 %	(Ref.)
				
R_1=R_3=H, R_2=R_4=OAc	n-Bu_3SnH	Y= CN	72	(33)
R_1=R_4=H, R_2=R_3=OAc	n-Bu_3SnH	10-20 eq.	70	(33)
R_2=R_3=H, R_1=R_4=OAc	n-Bu_3SnH		65	(33)
n-$C_{11}H_{23}I$	Bu_3GeH	Y= CN	63	(34)
n-$C_{11}H_{23}I$	Bu_3SnH	1.5 eq.	41	(34)
$PhCH_2I$	Bu_3GeH		76	(34)
$PhCH_2I$	Bu_3SnH		33	(34)
c-$C_6H_{11}I$	$(Me_3Si)_3SiH$	Y= CN	81	(35)
c-$C_6H_{11}Br$	$(Me_3Si)_3SiH$	1.1 eq.	64	(35)
c-$C_6H_{11}NC$	$(Me_3Si)_3SiH$		70	(35)
c-$C_6H_{11}C(S)SMe$	$(Me_3Si)_3SiH$		45	(35)
c-$C_6H_{11}SePh$	$(Me_3Si)_3SiH$		46	(35)

One cannot mention carbon-carbon bond formation without mentioning organotin hydrides. As seen in Scheme 1.10 a useful radical chain reaction can be set up to form carbon-carbon bonds. Examples of the use of organotin hydrides have already been described in Scheme 1.05. In Table 1.03 are some more examples including some exciting new alternatives to tin hydride

reagents. Tin containing compounds are toxic and due to their high molecular weight one needs to use large amounts. This can lead to difficulties in the isolation of reaction products. Organogermanium hydrides are expensive and somewhat less reactive than their tin analogues. Due partly to their expense, their use is not commonly encountered in the literature. On many occasions where organogermanium hydrides could be of use organotin hydrides are used instead, either in catalytic amounts or in dilute solutions added *via* a syringe pump. In contrast, organosilicon hydrides are cheaper than their germanium counter parts and as such are utilized more, they are generally non-toxic and easier to remove from the reaction. Their lower molecular weight is also an advantage. Table 1.03 shows that in many reactions organosilicon hydrides represent an attractive alternative to organotin hydrides.

1.4 Thiocarbonyl as a Radicophilic Group.

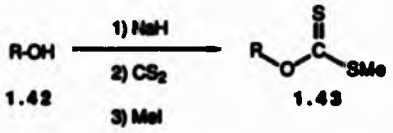
1.4.1 Deoxygenation

The Barton-McCombie reaction[36] was first introduced in 1975 for the deoxygenation of secondary alcohols and utilized the the thiocarbonyl group as a radicophilic centre for trialkyltin radical reactions. Scheme 1.11 illustrates this process.

1.40 1.41 1.06

Scheme 1.11

Scheme 1.12 & Table 1.04 show the preparation of a xanthate used for deoxygenation and the accompanying yields of some examples of deoxygenation using xanthate derivatives.



Scheme 1.12

Table 1.04[36]

Deoxygenation of various xanthates with tributyltin hydride.

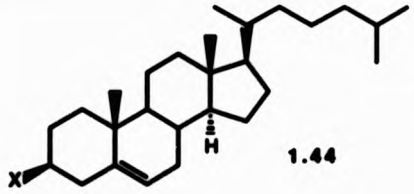
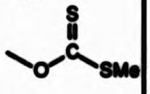
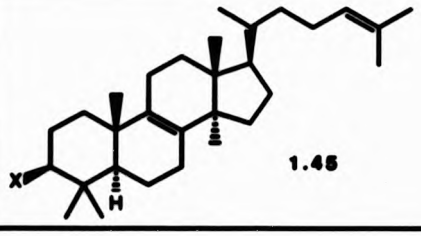
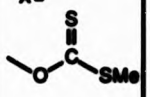
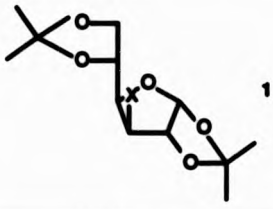
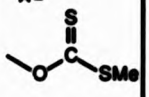
Examples	Xanthate Yield 1.43	Deoxygenation Yield 1.06
 1.44	X=  92%	X= H 78%

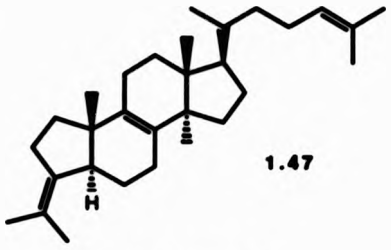
Table 1.04 (Contd.)

Examples	Xanthate Yield 1.43	Deoxygenation Yield 1.06
 1.45	X=  85%	X= H 83%
 1.46	X=  –	X= H 85%

Xanthates are not the only group that allow clean deoxygenation and ease of preparation. Thionocarbonates,[37,38] 1-imidazolyl,[36] 1-pyrrolyl[39] and 1-(1H) pyridin-2-onyl[40] derivatives also give good yields in deoxygenation.

The introduction of the Barton-McCombie reaction was prompted by the desire for an alternative to the ionic methods of deoxygenation, and the need for a method which will work under mild conditions where unwanted ionic eliminations are prone to occur. Ionic methods work well for primary and are possible for tertiary alcohols but secondary alcohols are susceptible to β-elimination and neighbouring group effects. Thus the deoxygenation of lanosterol 1.45 represents an important challenge because under ionic

conditions isolanostatriene 1.47 is formed through a carbocation intermediate.

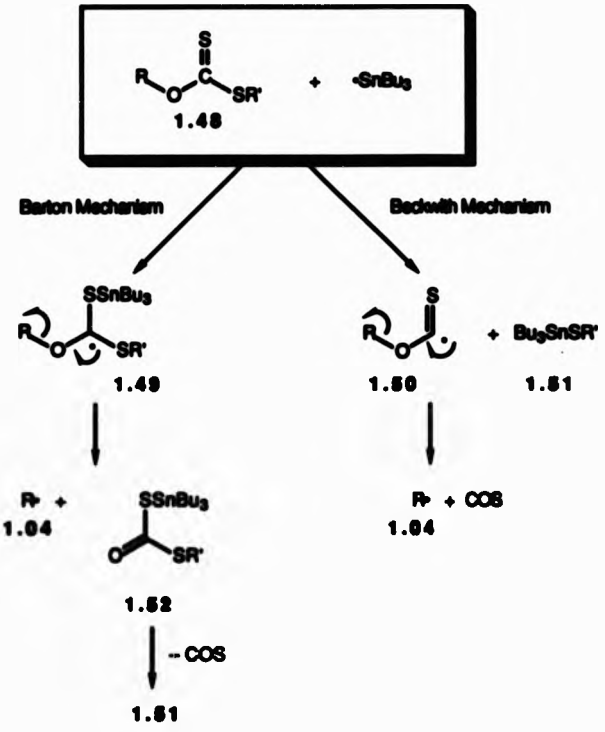


1.47

Structure 1.01

Under the conditions employed the Barton-McCombie deoxygenation of the xanthate derivative of lanosterol 1.45 gave no isolanostriene 1.47. Showing that there is no formation of any carbocation intermediate under these conditions.

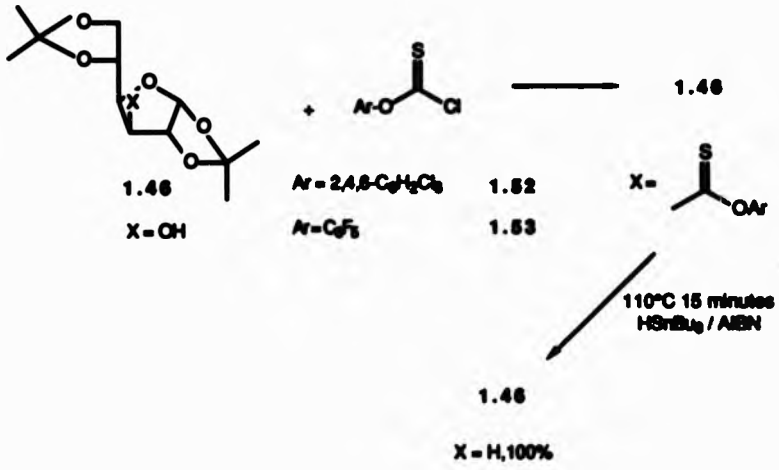
Until recently the exact mechanism of xanthate reduction with organotin hydride was uncertain. The two proposed mechanisms are outlined in Scheme 1.13. They involved either attack of the organotin radical to the thiocarbonyl, as originally proposed by Barton,[36] or attack at the thiomethyl moiety as proposed by Beckwith and Barker.[41] The use of triethylborane/oxygen as a low temperature radical initiator allowed Barton[42] to investigate this mechanism. An intermediate believed to be the dithiocarbonate 1.52 was detected by low temperature ^{119}Sn NMR. This intermediate is stable at -20°C but when the temperature is raised to +20°C the intermediate peak (at 66 ppm) disappeared and a new peak appearing at 83-84 ppm was observed. This new peak was assigned to the structure 1.51 by comparison with an authentic specimen. If the Beckwith mechanism was correct then the intermediate 1.52 would not exist, and 1.51 should be formed and observed at -20°C from the beginning of the reaction.



Scheme 1.13

Recently, these methods of deoxygenation have been applied to halophenylthionocarbonate derivatives of alcohols.[43] These derivatives possess activity comparable with the xanthates and thus can be employed where xanthate synthesis becomes difficult[36] (see Chapter 2: introduction). The diacetoneglucofuranoside 1.46 (X = OH) was used as a model and acylated with various halophenoxythiocarbonyl chlorides (152, 153 Scheme 1.14). These derivatives deoxygenated quantitatively in a matter of a few

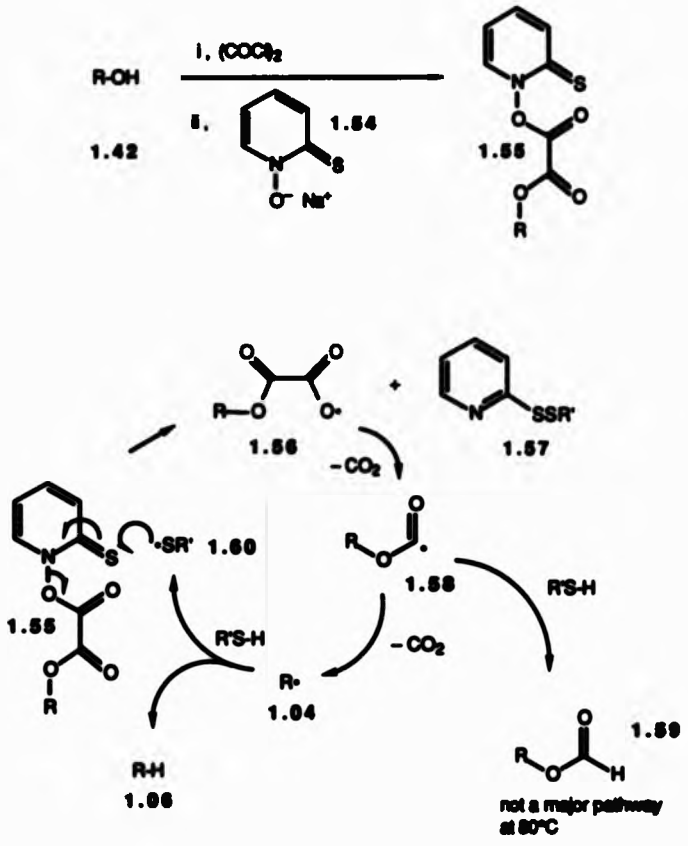
minutes at 110°C with no by-products unlike the phenoxythiocarbonyl derivative. A more comprehensive study of these new reagents has been carried out using both primary and secondary alcohols[44] (see Chapter 2).



Scheme 1.14[43]

Tertiary alcohols have also been deoxygenated *via* radical methods using the thioformates and tributyltin hydride.[45] A better method which does not use tin hydrides uses the half ester of oxalic acid with the tertiary alcohol and N-hydroxypyridine-2-thione.[46,47] The deoxygenation proceeds as shown in Scheme 1.15. The double decarboxylation (1.56–1.58–1.04) proceeds stepwise with the loss of one carbon dioxide first, the intermediate thus formed can then be trapped with the thiol at room temperature. It is important that a suitably hindered thiol be used otherwise reduction of the radical 1.56 occurs.

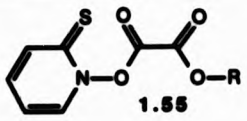
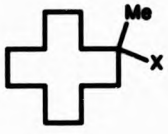
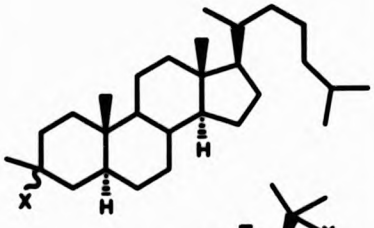
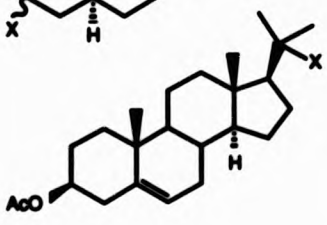
Good yields of the hydrocarbon 1.06 can be obtained under action of heat as shown in Table 1.05.[46,47]



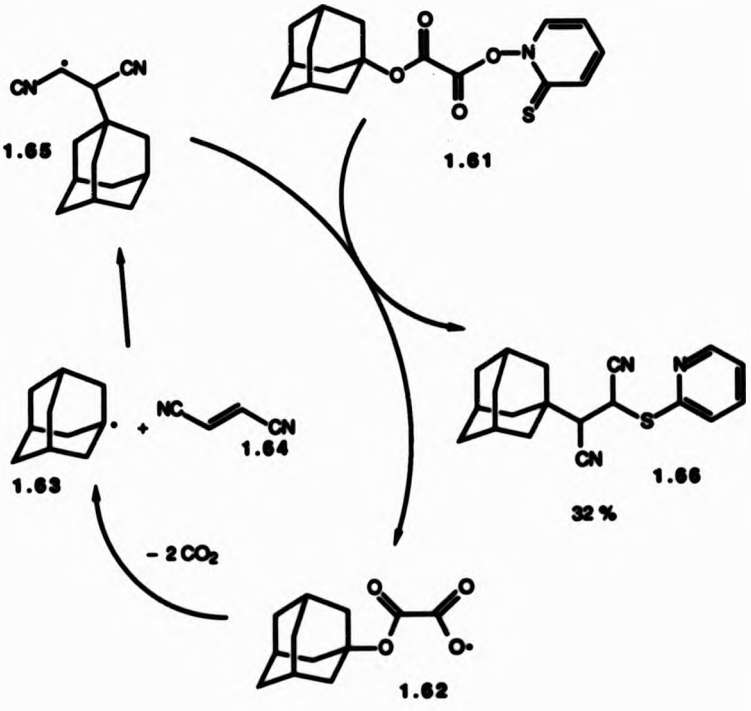
Scheme 1.15

Table 1.05[46,47]

Deoxygenation of tertiary alcohols utilizing N-hydroxypyridine-2-thione.

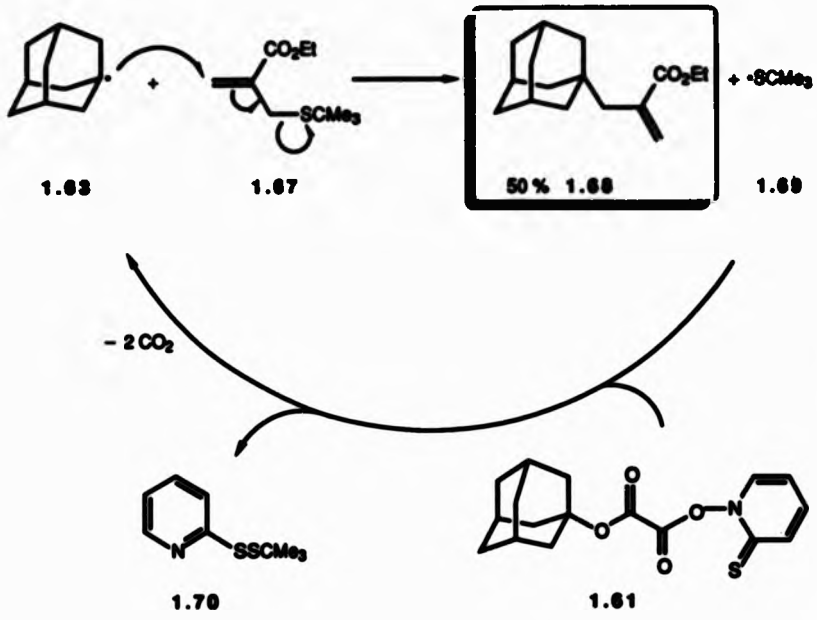
 1.55 R=	1.06 R-H Yield %
$Me(CH_2)_{16}CMe_2X$	81
	70
	79
	90

The carbon radicals formed in this manner can also undergo addition to electron deficient olefins.[47] In this case the thiol must be absent from the reaction. Reasonable yields (32-54%) of the addition product can be obtained. A representative example is given in Scheme 1.16. Thus the adamantyl radical **1.63** adds to fumarodinitrile **1.64** to give the intermediate radical **1.65**. This radical **1.65** is then quenched by its precursor **1.61** to furnish the addition product **1.66**, and after double decarboxylation the adamantyl radical **1.63** which then continues the radical chain.



Scheme 1.16[47]

The yield is increased to 50% when the olefin contains a 2-thioether (1.67).[47] This then allows homolytic bond cleavage producing the olefin 1.68 and the sulphide radical 1.69 which allows continuation of the radical chain. This is shown in Scheme 1.17.

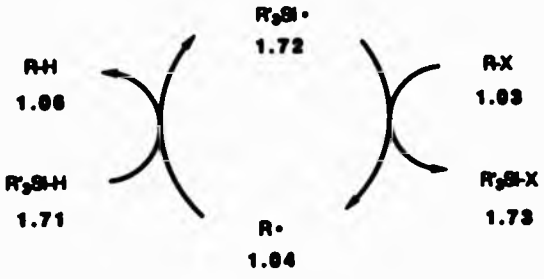


Scheme 1.17[47]

Although the Barton-McCombie deoxygenation of alcohols is extremely wide ranging, a major disadvantage of this process is the use of toxic tin containing compounds. In addition difficulties arise in the removal of the non-

polar non-volatile tin residues from the reaction. Barton[48a,b], Schummer[49] and Chatgilialoglu[35,50] have recently applied organosilanes to this field of deoxygenation (Scheme 1.18). Table 1.06 shows some useful examples. As can be seen from Table 1.06 use of the silane reagents gives comparable yields to the tin hydride reagents.

All the deoxygenations appear to have short radical chain lengths. This is evidenced by the fact that in all cases the radical initiator needs to be added at regular intervals. If this were not the case then the initiator would need only to be added at the start of the reaction. It is interesting to note that these deoxygenations can be carried out at room temperature with the aid of triethylborane and air as initiators. Even using such initiators the reaction is clean and easy to work up as the silane residues can be easily oxidized with hydrogen peroxide. This forms polar silicon compounds which are non-toxic and can be easily removed by column chromatography. The mechanism is thought to be similar to that involving the tin hydride with attack by the silyl radical on the radicophilic thiocarbonyl group.



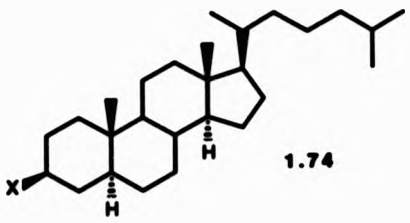
Scheme 1.18

Table 1.06

Deoxygenation of alcohols with organo silicon reagents.

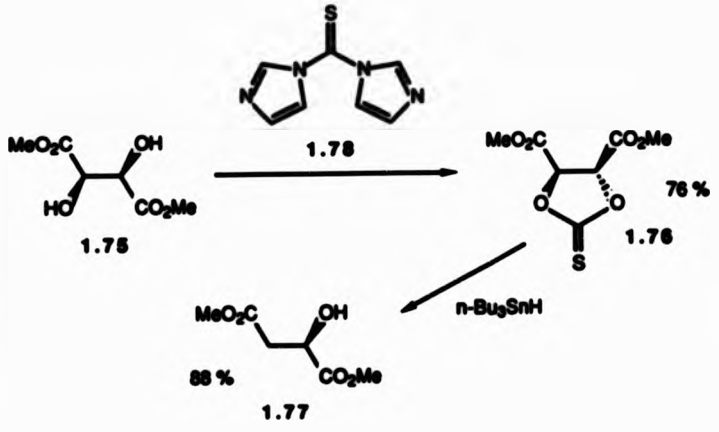
R-X 1.03	Silane 1.71 (Method)	R-H 1.05 Yield % (Ref.)
R= c-C_6H_{11}		
X= OC(S)SMe	$(MeS)_3SiH$ (a)	97 (50)
	$(iPrS)_3SiH$ (a)	98 (50)
	$(Me_3Si)_3SiH$ (a)	86 (35)
X= OC(S)-N-Imidazole	$(Me_3Si)_3SiH$ (a)	95 (35)
R= 1.44		
X= OC(S)OPh	$(Me_3Si)_3SiH$ (a)	94 (49)
R= 1.45		
X= OC(S)OPh	$(Me_3Si)_3SiH$ (a)	80 (49)
R= 1.46		
X= OC(S)OPh	$(Me_3Si)_3SiH$ (a)	81 (49)
X= OC(S)O-4-C_6H_4F	$PhSiH_3$ (a)	100 (48a)
X= OC(S)O-4-C_6H_4F	Ph_2SiH_2 (b)	83 (48b)
R= c-$C_{12}H_{23}$		
X= OC(S)SMe	$PhSiH_3$ (a)	100 (48a)
X= OC(S)SMe	Ph_2SiH_2 (b)	81 (48b)
R= 1.74		
X=OC(S)O-4-C_6H_4F	$PhSiH_3$ (a)	87 (48a)
X=OC(S)O-4-C_6H_4F	Ph_2SiH_2 (b)	82 (48b)

Method: (a) Boiling toluene or benzene with initiator (b) Room temperature with triethyl borane-air as initiator.



Structure 1.02

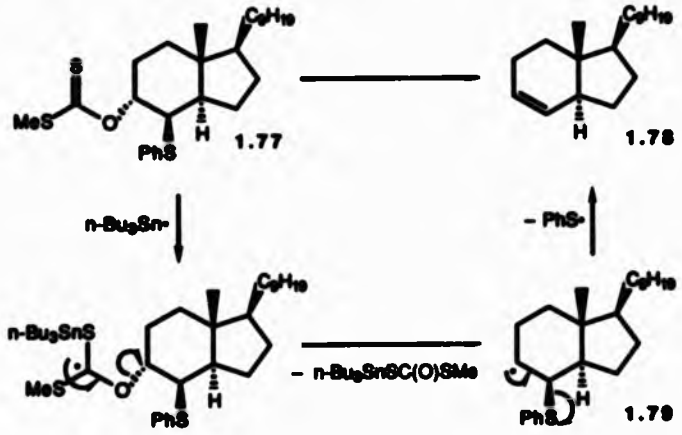
Cyclic thionocarbonates can also be utilized for radical deoxygenation reactions. An good example of the utility of this class of compounds has been described by Hanessian *et al* [51] in the synthesis of dimethyl-*R*-malate **1.77** from *R,R*-dimethyl tartrate **1.75**. The tartrate **1.75** is treated with thiocarbonyl diimidazole **1.78** forming the cyclic thiocarbonate **1.76** which when treated with tributyltin hydride is reduced to alcohol **1.77**.



Scheme 1.19

The use of cyclic thionocarbonates was first reported by Barton and Subramanian[52] and later Stick and co-workers[53] carried out a systematic investigation in this area.

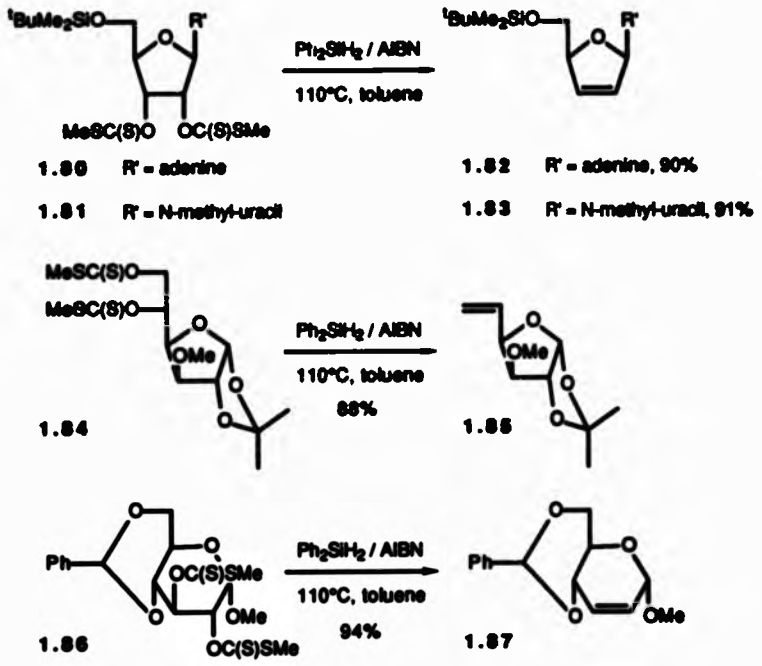
Olefination has also been reported *via* cyclic thionocarbonates.[54] An alternative method, however, makes use of a neigbouring group to afford homolytic bond cleavage resulting in formation of olefin and a more stable radical (β-elimination). Thus when Lythgoe[55] treated **1.77** with tributyltin hydride (Scheme 1.20) the formation of olefin **1.78** was detected (65%). This was presumed to occur through the intermediate radical **1.79** which loses the phenylsulphide radical to furnish the olefin **1.78**.



Scheme 1.20

Barton[56] and later Hayashi[57] have extended this methodology to include dixanthates and showed that discrete radical intermediates are likely[58a] because the dixanthates of both meso and (±)-dihydrobenzoin form exclusively the more stable trans-stilbene. Recently the dixanthate method of

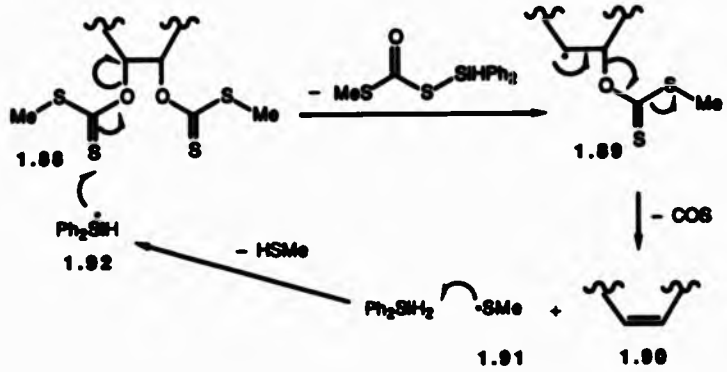
olefination has been applied successfully with diphenylsilane as the radical source.[58b] Thus, in boiling toluene with diphenylsilane and AIBN the dixanthates **1.80**, **1.81**, **1.84**, and **1.86** undergo fragmentation as shown in Scheme 1.21 to furnish the respective olefin **1.82**, **1.83**, **1.85** and **1.87** in high yield.



Scheme 1.21

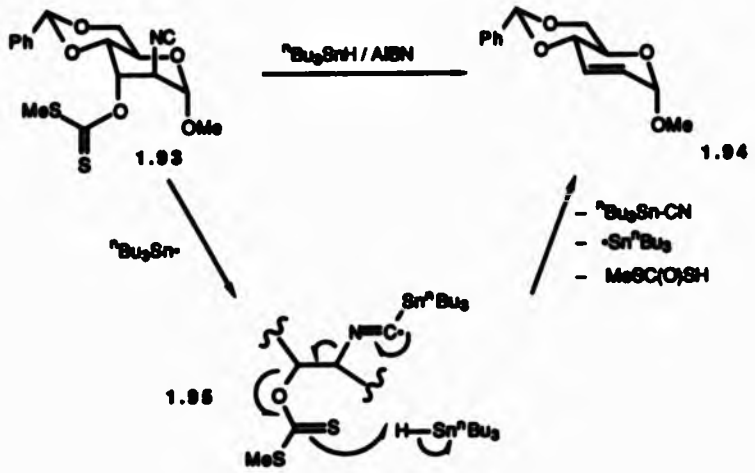
A possible mechanism is outlined in Scheme 1.22. The attack of the silyl radical **1.92** on the dixanthate **1.88** forms the monoxanthate radical **1.89**.

This radical **1.89** forms the desired olefin **1.90** by homolytic rupture of the second xanthate with evolution of carbonyl sulphide and formation of the methylthio radical **1.91**. The methylthio radical **1.91** continues the radical chain reaction by reacting with the diphenylsilane.



Scheme 1.22

This type of radical olefination has also been applied to β-isocyano xanthate esters.[59] It has been shown that the tributyltin radical attacks the isocyano group in **1.93** preferentially which then causes radical fragmentation of the xanthate **1.95**, as shown in Scheme 1.23, forming the olefin **1.94** in 90% yield.



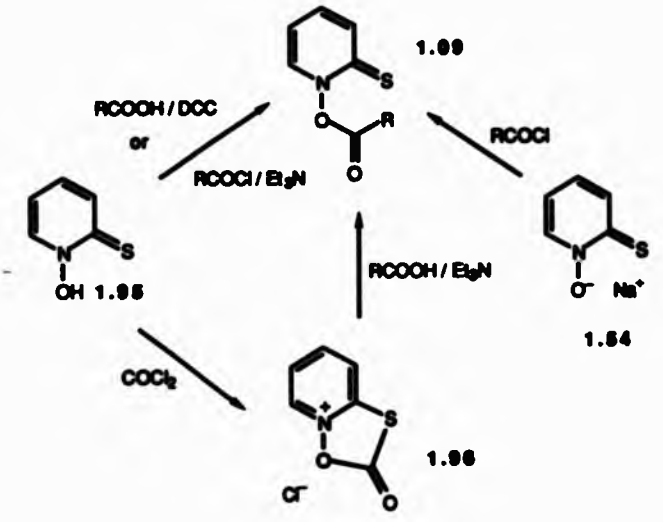
Scheme 1.23

The original Barton-McCombie reaction has evolved to include a large range of possible deoxygenation precursors. The most important step, however, in this evolution is the replacement of organotin hydrides by non-toxic organosilicon hydrides. Thus, the only major limiting factor in the Barton-McCombie reaction has been removed.

1.4.2 Thiohydroxamic Acids and their Derivatives.

In 1983 Barton and co-workers[16] reported that acyl derivatives of N-hydroxypyridine-2-thione **1.95** undergo decarboxylation with heat in a radical chain process. It was also noted that an organotin hydride need not exclusively be used for reduction of the resulting alkyl radical. Replacement with tertiary butylthiol gave similarly high yields. During the course of these

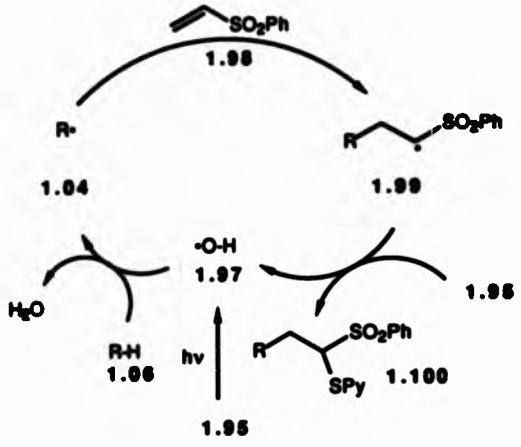
investigations it was also reported that the reaction is accelerated by irradiation with a tungsten lamp. These obeservations led to the discovery that acyl derivatives such as 1.09 can undergo N-O bond cleavage using visible light at room temperature (Scheme 1.02, page 5). Thus visible light can be used to furnish alkyl radicals. Scheme 1.24 shows the various routes to acylate the thiohydroxamic acid. 1.95 can be directly acylated using an acid activator such as N,N'-dicyclohexylcarbodiimide (DCC) with the acid, or the use of the acid chloride and base is just as effective. Equally effective is use of the sodium salt of N-hydroxypyridine-2-thione 1.54 and the acid chloride. The reaction of 1.95 with phosgene forms the cyclic salt 1.96 which can be used directly with the acid and base to form the acyl derivative 1.09 (Scheme 1.24).



Scheme 1.24

The mild methods employed in forming the acyl derivatives **1.09** are a great advantage to this system.[60]

The photochemistry of **1.95** has been investigated by Zard *et al*[61] who found that irradiation using a tungsten lamp produced hydroxy radicals **1.97** (Scheme 1.25). These hydroxy radicals can be used to create carbon centred radicals **1.04** by abstraction of a hydrogen atom from a weak carbon-hydrogen bond in a molecule. In this way Zard was able to add this resulting carbon centred radical **1.04** to phenyl vinyl sulphone **1.98**, forming the radical **1.99** as shown in Scheme 1.25. Radical **1.99** then reacts with **1.95** to furnish the addition product **1.100** and the hydroxy radical **1.97** which then continues the radical chain reaction. Table 1.07 shows yields of the addition product **1.100**.



Scheme 1.24

Table 1.07[61]

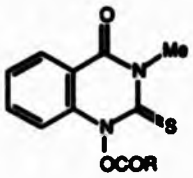
Carbon centred radical addition to phenyl vinyl sulphone *via* hydroxy radicals derived from N-hydroxy-2-thiopyridone.

R-H, 1.04 as solvent	Addition products 1.100 Yield %
Tetrahydrofuran	65
1,3-Dioxolane	68
1,4-Dioxane	77

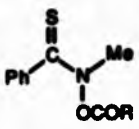
The Barton group has also investigated the radical properties of other thiohydroxamic acids[62,24] (1.101-1.105, Structures 1.03). However of the compounds studied, none were as efficient as the N-hydroxypyridine-2-thione acyl derivatives in their ability to form radicals.

1.101 X=Me

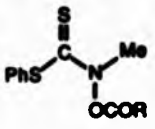
1.102 X=Ph



1.103



1.104

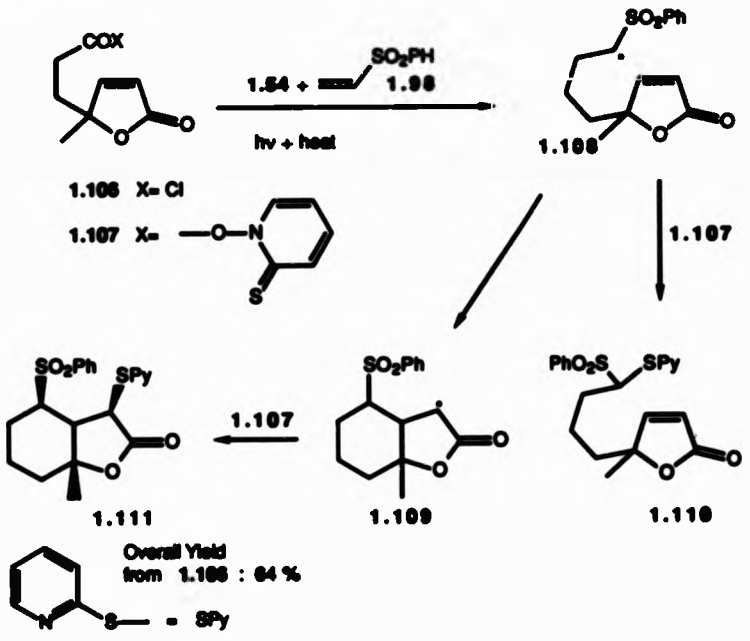


1.105

Structures 1.03

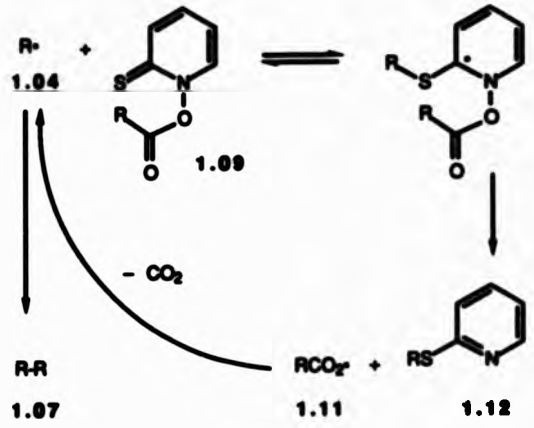
The simplest reaction of 1.09 is decarboxylative rearrangement to give the sulphide 1.12 by either photolysis or heat (Scheme 1.02 page 5). Photolysis is generally the method of choice as studies[62] have indicated that

under the action of heat a partial cage mechanism may be involved. Visible light, however, shows no sign of a cage type mechanism. Moreover it has been reported recently by Zard and co-workers[63] that yields are increased substantially when 1.09 is subjected to both heat and light. Thus, in the formation of the bicyclic lactone 1.111 (Scheme 1.26) the overall yield was improved dramatically from 16% to 64%. In this way Zard avoided the competition to cyclization of the radical 1.108 reacting with its precursor 1.107, only a minimal formation of an unwanted uncyclized product 1.110 was reported.



Scheme 1.26[63]

When acyl derivatives of **1.95** are photolyzed at room temperature or below without a reactive trap dimerization of the carbon radicals occurs.[64] Thus, even at 0-10°C up to 20% of triacontane is formed along with dipyridyldisulphide in the photolysis of the palmitic acid derivative of **1.95** Scheme 1.27. At higher temperatures (80°C) there is no trace of dimerization and the sulphide is formed in almost quantitative yield.



Scheme 1.27

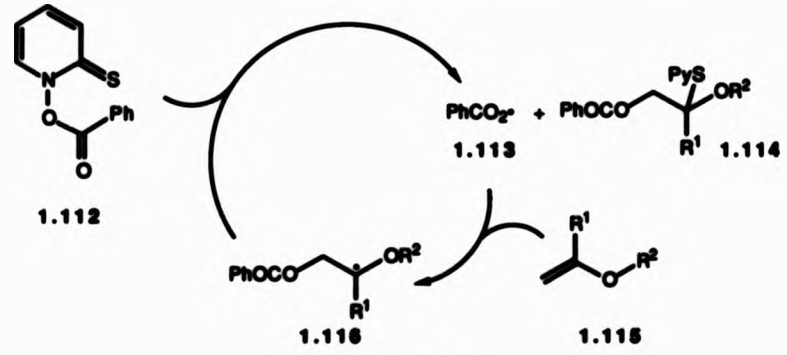
At low temperatures N-O bond cleavage is comparatively slow which slows down the radical chain reaction. Thus long irradiation times are necessary at low temperatures. The slow chain reaction keeps the radical concentration relatively high thus allowing dimerization to take place. This is a non reversible process. Some typical examples are given in Table 1.08.

Table 1.08[64]

Low temperature radical dimerization.

R	R-R Yield % 1.97
$CH_3(CH_2)_{14}$–	75
Ph_2CH–	69
$PhCH_2$–	57
CH_2–$CH(CH_2)_6$–	42
Reaction temperature = –64°C	

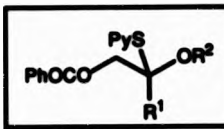
When aromatic or vinylic acyl derivatives of N-hydroxy-2-thiopyridone are subjected to irradiation the corresponding oxygen centred radical is formed.[65] Thus when the benzoic acid derivative **1.112** is photolysed the corresponding benzoyloxy radical **1.113** is formed. This radical can be trapped with suitable electron rich olefins such as vinyl ethers[66] **1.115** (Scheme 1.28) to furnish good yields of the addition product **1.114**. Table 1.09 gives some examples of such addition.



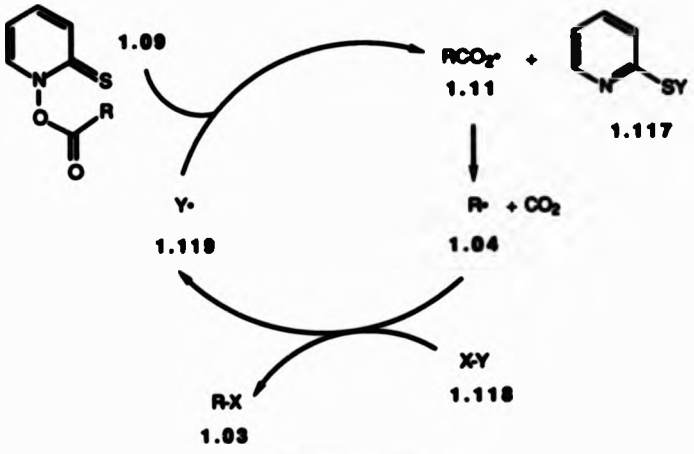
Scheme 1.28

Table 1.09[66]

Benzoyloxy radical addition to vinyl ethers.

	Yield % 1.114
R^1=H, R^2=Et	74
R^1=H, R^2=^{n}Bu	67
R^1=H, R^2=^{t}Bu	62
R^1=R^2=Me	54

Alkyl halides can be formed from the acid *via* their N-hydroxy-2-thiopyridone derivatives.[67,68,69] This is an alternative to the classical Hunsdiecker reaction[70] with the advantage of not needing any heavy metal salts. The reaction proceeds as a radical chain as shown in Scheme 1.29.



Scheme 1.29

Table 1.10[67,69]

Formation of alkyl halides by radical chain reaction.

R	Trap X-Y 1.118			
	Cl-CCl_3	Br-CCl_3	I-CH_2I	
$CH_3(CH_2)_{14}$–	70	95	74	Yield R-X
1-adamantyl	95	98	—	1.03
$(PhCH_2)_2CH$–	72	90	60	%

The results collected in Table 1.10 are obtained when the acyl derivative is refluxed in the halogenating solvent. Similar results are obtained when the acyl derivative is photolyzed at room temperature.[68]

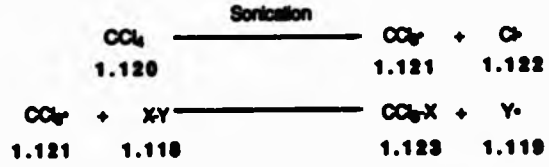
Sulphides, selenides and tellurides can also be obtained in good yields, the mechanism is similar to that shown in Scheme 1.29 (where X-Y = diaryl disulphides ,diselenides or ditellurides). Table 1.11 summarizes some results where the acyl derivative is either heated[71] or photolysed[72] with the chalcogen. The advantages of photolysis over heat are clearly seen. When diphenyl disulphide is used as a trap, 30 equivalents are needed to effect good yields (74%) when the reaction is heated (120°C).[71] However, under photolytic conditions only two equivalents of the disulphide are necessary to give a good yield (82%) of the same sulphide.[64]

Table 1.11[71,72,84]

Formation of alkyl chalcogenides by radical chain reaction.

R	Temperature (equivalents of trap X-Y)		Yield of R-X 1.03 using trap X-Y 1.118		
	hν	Δ	PhSSPh	PhSeSePh	$(PhOC_6H_4O\text{-}Te)_2$
$CH_3(CH_2)_{14}$–	0°C (2)	120 °C (30)	74%		
		110°C (10)	82%		
	0 °C (2)			75%	
	35 °C (2)			85%	
					69%
1-adamantyl	0°C (2)			93%	
	35°C (2)				79%
$(PhCH_2)_2CH$–	0°C (2)			97%	

Sonication has also been used with some success for reductive decarboxylation of acyl derivatives of N-hydroxy-2-thiopyridone.[73] The mechanism involves a radical chain process in which initiation proceeds through the sonication of carbon tetrachloride 1.120 present as solvent. This produces the trichloromethyl radical 1.121 which starts the chain reaction by attacking the thiocarbonyl of 1.09 or reacting with the disulphide or diselenide trap (X-Y 1.118, Scheme 1.30). If a thiol is present in the reaction medium the the corresponding nor-alkane is formed. Yields are summarized in Table 1.12.



Either Y• can carry the chain or CCl_3• can by reacting with acyl derivative 1.09 as seen earlier.

Scheme 1.30

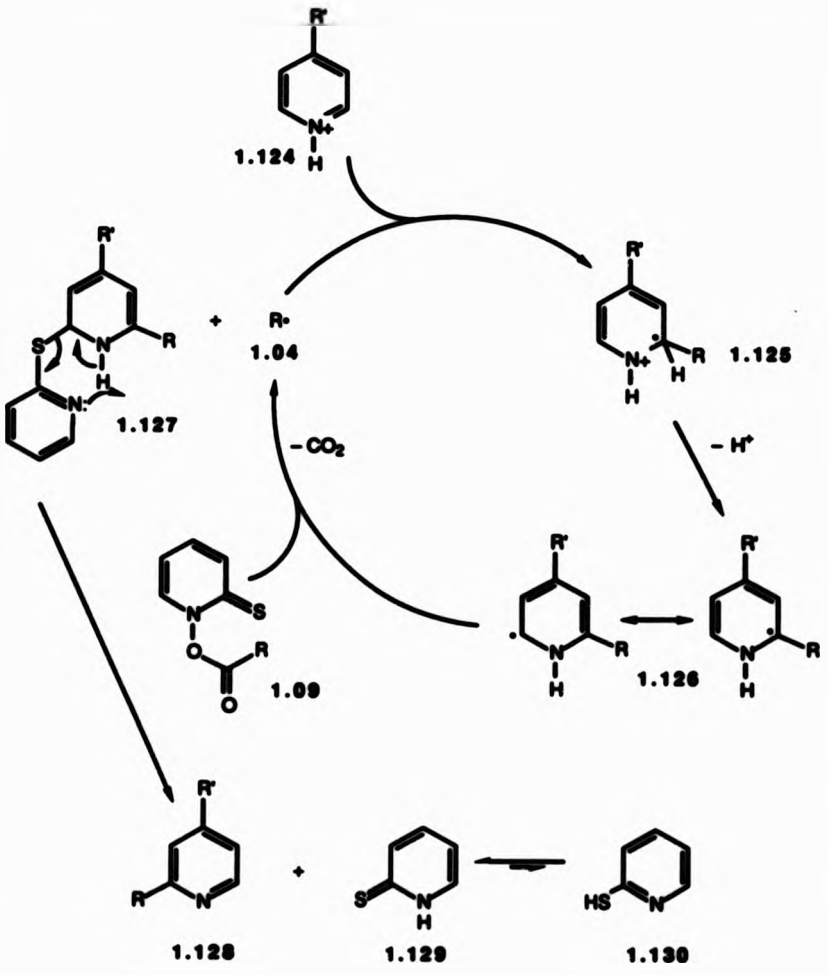
Table 1.12[73]

Radical reaction using sonication for initiation.

	X-Y 1.118 (equivalents)	R-X 1.03 yield %
$R = C_{10}H_{21}$ Solvent = CCl_4	H-SPh (3) $(PhSe)_2$ (2) $(PhS)_2$ (5)	85 80 8*
	* In this case 80 % of the alkyl chloride was formed	

The alkyl radical 1.04 produced from the photolysis of the acyl derivatives of N-hydroxypyridine-2-thione 1.09 can also be trapped with sulphur dioxide[74] or oxygen.[75,69] This results in the formation the corresponding thiosulphonates or the nor-alkyl hydroperoxides respectively. In a similar radical chain reaction alkyl radicals can undergo addition to protonated heteroaromatic compounds[76] 1.124 which contain a basic nitrogen. Scheme 1.31 shows this chain reaction. The heteroaromatic radical intermediate 1.126 adds on to the thiocarbonyl of the radical precursor 1.09 forming the sulphide 1.127 and the alkyl radical 1.04 which continues the radical chain. The sulphide 1.127 decomposes as shown in Scheme 1.31 forming the 2-thiopyridone 1.129 and the addition product 1.128. Yields for some of the addition products are shown in Table 1.13. In the absence of acid, addition products were formed but the yield was poor, 30 % for methyl nicotinate as compared to 79 % in acidic conditions. Pyridine was reported to show no reaction except in the presence of acid. The tautomeric equilibrium between 2-thiopyridone 1.129 and the thiol 1.130 lies strongly in favour of the thiolactam 1.129. This is evidenced by the fact that if large amounts of the

thiol was present in the reaction the alkyl radical would have been preferentially reduced to the corresponding alkane.



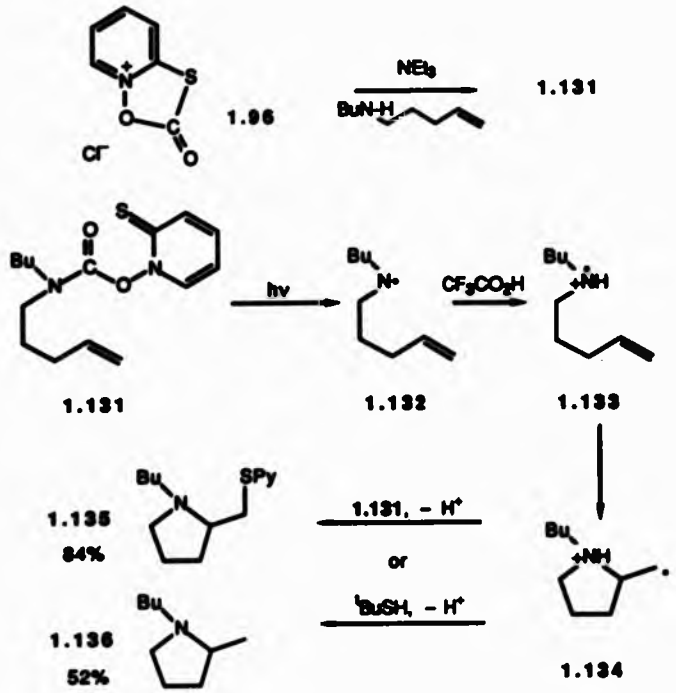
Scheme 1.31

Table 1.13[76]

Adamantyl radical additions to protonated substituted pyridines.

	R'			
	H	Me	Ph	CN
R= 	84%*	65%	67%	72%
	Yields of the addition product 1.128			
	*43 % of the 2- substituted 41 % of the 4- substituted			

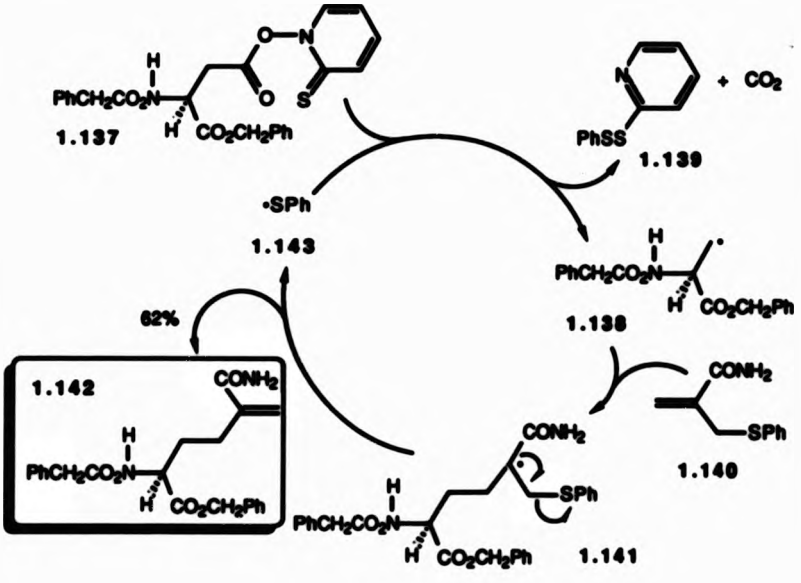
The generation of nitrogen centred radicals has also been achieved[77] using N-hydroxypyridine-2-thione carbamates for example 1.131 (Scheme 1.32). These carbamates are easly formed from 1.96, triethylamine and a secondary amine. The nitrogen centred radicals 1.132 produced from the photolysis of these derivatives can be intramolecularly trapped if the aminyl radical is protonated[78]. If not uncyclized reduction products are formed. Reaction of 1.132 with its precursor 1.131 does not take place, thus a chain reaction is not possible unless the radical 1.132 is protonated. Protonation of radical 1.132 forms 1.133, this dialkylaminium radical cation can then cyclize to give 1.134. This radical reacts with its precursor 1.131 to form after deprotonation 1.135 in 84% isolated yield.[77] If tertiary butylthiol is present in the reaction medium 1.134 is reduced to 1.136 after deprotonation in 52% isolated yield. When the thiol is present the formation of the sulphide 1.135 is not detected. Without trifluoroacetic acid, cyclization occurs only sluggishly and in poor yields.



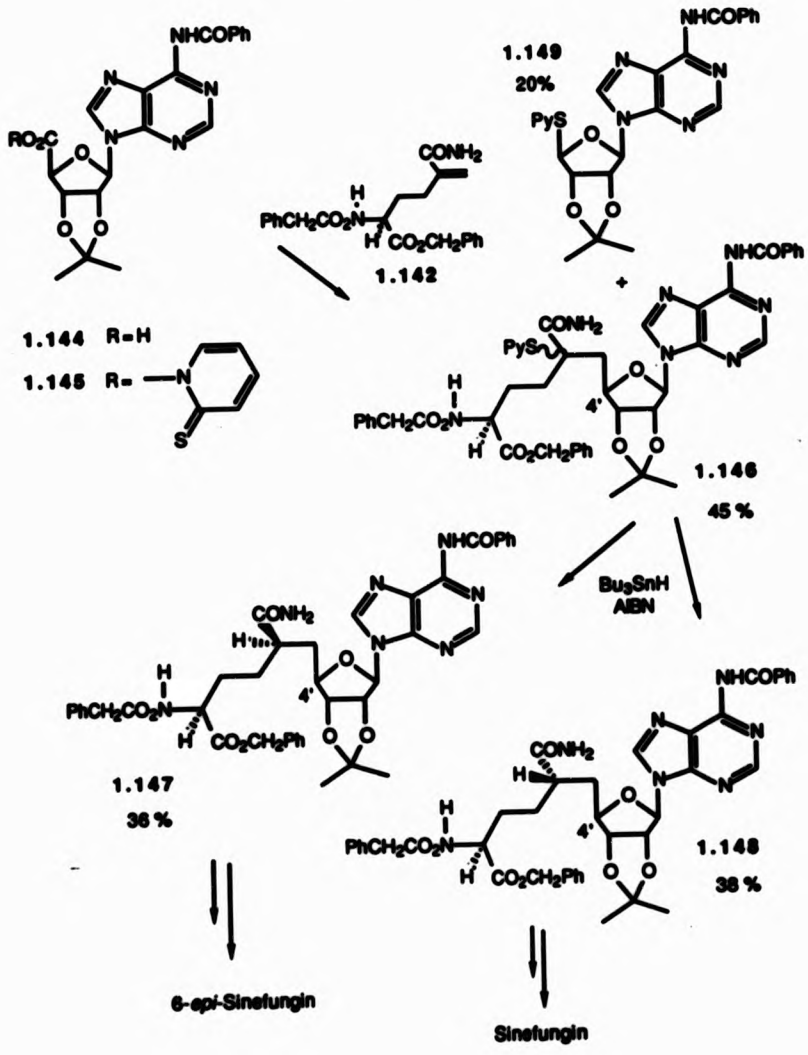
Scheme 1.32

There is an increasing interest in the diastereoselectivity associated with free radical chemistry.[79,80] Great progress has been made by the groups of Curran[81] and Porter.[82] The use of acyl derivatives of N-hydroxypyridine-2-thione to produce radicals for diastereoselective synthesis has also been investigated.[83,84,85] Of particular note are Barton's synthesis of sinefungin and 6-*epi*-sinefungin which use two key radical reactions.[83] The first involves the synthesis of the radical trap **1.142**. The known derivative of L-aspartic acid **1.137** was added to olefin **1.140** which contains a phenylsulphide group. After radical addition and homolytic cleavage of the carbon sulphur

bond the olefin **1.142** is formed (62%), and the phenyl sulphide radical **1.143** which continues the radical chain. The N-hydroxypyridine-2-thione derivative **1.145** is made *in situ* from the sodium salt of N-hydroxypyridine-2-thione **1.54** and the acid **1.144**. The radical trap **1.142** was added and the solution was photolyzed giving 45 % of the desired product **1.146** and 20 % of the non-addition product **1.149**. Thus the radical at the C-4' position reacts stereospecifically. The addition product **1.146** is easily converted to **1.147** and **1.148** by tributyltin hydride and AIBN in a combined yield of 74%.



Scheme 1.33


NHCOPh
RO2C
1.144 R=H
1.145 R=
1.142
1.149
20%
PyS
1.146
45 %
Bu3SnH
AIBN
1.147
36 %
1.148
38 %
6-epi-Sinefungin
Sinefungin

Scheme 1.34

Review

The thiocarbonyl is a versatile functional group which easily undergoes reaction with various radical species as has been illustrated in this review. The most useful reaction to organic chemists is the formation of carbon-carbon bonds. The radical precursor **1.09** has been shown to be of use in a variety of transformations including that of carbon-carbon bond formation.

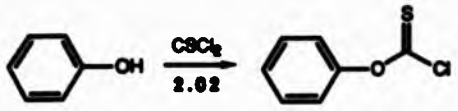
Chapter 2

Deoxygenation of Primary Alcohols *via* their Thionocarbonate Derivatives.

Chapter 2

2.0 INTRODUCTION

The deoxygenation of alcohols by the Barton-McCombie method[36] is an efficient and wide ranging process as shown in the previous chapter. However the basic conditions that are required for the introduction of xanthates are often incompatible with certain protecting groups.[36] Robins and Wilson in 1981 introduced a thiocarbonyl reagent that could be generated by simple acylation[38] (2.03 Scheme 2.01).



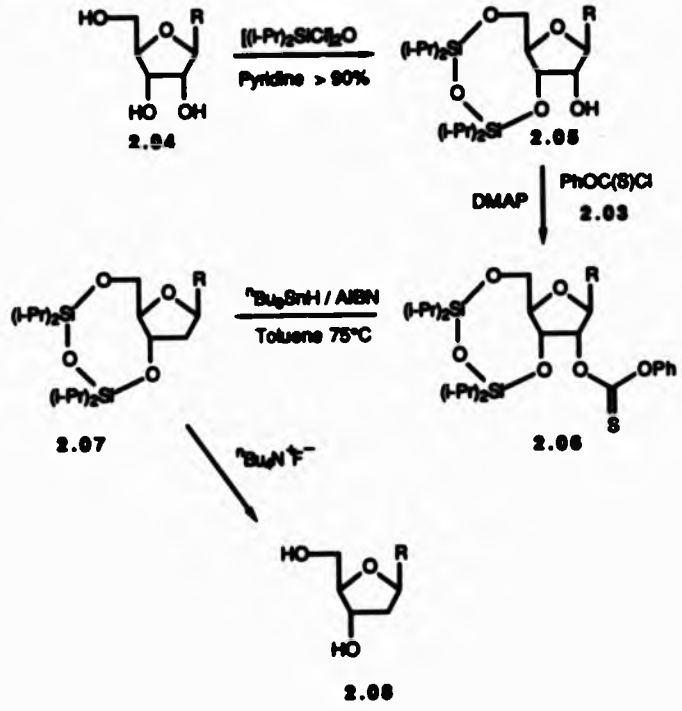
2.01 2.03

Scheme 2.01

When Robins and Wilson treated phenol 2.01 with thiophosgene 2.02 they obtained phenyl chlorothionocarbonate 2.03.[38a] When reagent 2.03 is reacted with alcohols in the presence of pyridine, or with hindered alcohols in the presence of N,N-dimethylaminopyridine, smooth conversion to the respective phenoxythiocarbonyl derivative is effected.

When the derivative 2.06 is treated with tributyltin hydride and AIBN radical deoxygenation occurs giving high yields (see Scheme 2.02) of the 2'-deoxy compound 2.07. Table 2.01 shows the overall yields of three

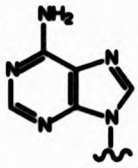
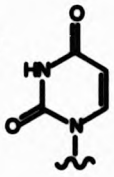
examples. Of particular note are the nucleosides **2.04a** and **2.04b**. In contrast, conventional introduction of the xanthate group in these nucleosides would require protection of the acidic hydrogens present in the heterocyclic base.



Scheme 2.02

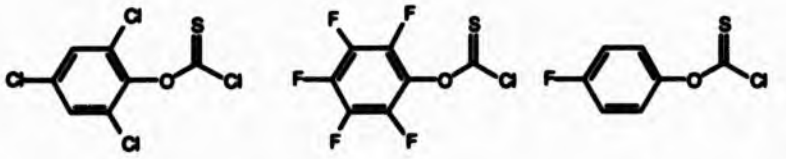
Table 2.01[38a]

Deoxygenation of alcohols utilizing derivatives of phenyl thionocarbonates.

2.04 R=	2.08	Overall yield from 2.04
2.04a 	2.08a	78%
2.04b 	2.08b	68%
2.04c 	2.08c	58%

An extension of the Robins reagent has been the introduction of electron withdrawing groups on the phenyl ring to enhance the radicophilicity of the thiocarbonyl.[43] Thus, Barton and Jaszberenyi examined 2,4,6-trichlorophenyl chlorothionoformate 1.52 and pentafluorophenyl chlorothionoformate 1.53 as reagents that could acylate alcohols and effect deoxygenation.[43] More recently this methodology has been extended to include 4-fluorophenyl chlorothionoformate 2.09 as the acylating agent and

diphenylsilane as the hydrogen source and chain carrier[48b] (Chapter 1, page 33). The ease of acylation by these new compounds together with their short reaction times, minutes rather than hours, represents an advantage over the existing methods for the formation of xanthates and phenyl thionocarbonates.



1.52 1.53 2.09

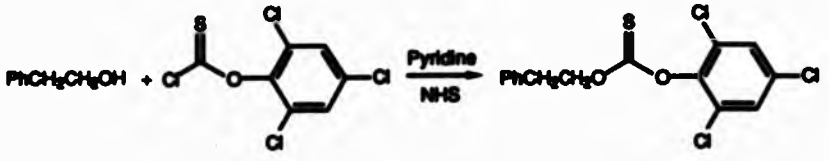
Structures 2.01: Chlorothionoformates

2.1 Discussion

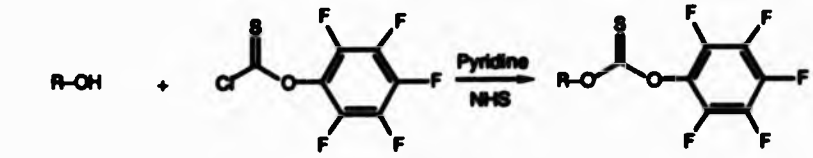
It was decided to extend the work of Barton and Jaszberenyi[43] to include deoxygenation of primary alcohols.

The model alcohol β-phenylethanol **2.10** was acylated with trichlorophenyl chlorothionoformate **1.52** to give the thionocarbonate intermediate **2.14** (97%) Scheme 2.03. Yields for acylation are shown in Table 2.02. Similary tetradecanol **2.11** was acylated in toluene in the presence of dry pyridine and N-hydroxysuccinimide (NHS) with pentafluorophenyl chlorothionoformate **1.53** . The acylation was complete in five minutes at room temperature. The pyridinium chloride was then removed by filtration. The intermediate thionocarbonate **2.15** can be isolated if desired by column chromatography (89%) or deoxygenation can be effected on the crude product, thus allowing a one pot synthesis of the hydrocarbon. Thus,

treatment of 2.14 or 2.15 with tributyltin hydride and AIBN at 110°C under nitrogen for five minutes gave ethylbenzene 2.18 or tetradecane 2.19 in 97% or 95% overall yield, respectively (Scheme 2.02). Good yields were also obtained for octane 2.20 and octadecane 2.21 using the same method as described above. The results obtained are summarized in Table 2.03.



2.16 1.52 2.14

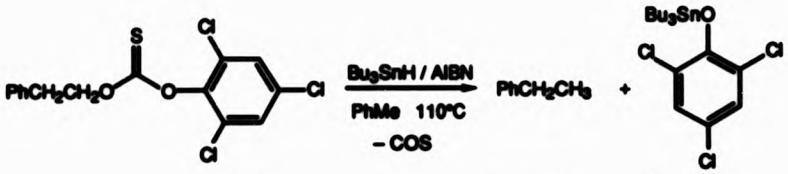


$R = C_{14}H_{29}$	2.11	1.53	$R = C_{14}H_{29}$ 2.15
$R = C_8H_{17}$	2.12		$R = C_8H_{17}$ 2.16
$R = C_{18}H_{37}$	2.13		$R = C_{18}H_{37}$ 2.17

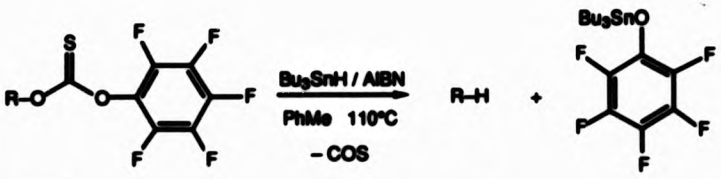
Scheme 2.03

Without the presence of initiator no thermal or photolytic (tungsten light) decomposition of the intermediates (2.14–2.17) was observed. Deoxygenation was also found to take place in boiling benzene. Using a one pot procedure with the acyl derivative of tetradecanol and pentafluorophenyl thionocarbonate, tetradecane was formed in 90% overall yield. In contrast ,

the reported yield of the tributyltin hydride – triethylborane deoxygenation of the tetradecanol methyl xanthate was only 18% (at room temperature).[86]



2.14 2.18 2.22



R = $C_{14}H_{29}$	2.15	R = $C_{14}H_{29}$	2.19	2.23
R = C_8H_{17}	2.16	R = C_8H_{17}	2.20	
R = $C_{18}H_{37}$	2.17	R = $C_{18}H_{37}$	2.21	

Scheme 2.04

Table 2.02

Acylation of primary alcohols.

Alcohol	Solvent	Time (minutes)	Chlorothiono--formate	Yield[a] (%)
2.10	PhMe	330	1.52	97
2.11	PhMe	240	1.53	89
2.11	PhMe	5	1.53	b
2.11	PhH	10	1.53	b
2.12	PhMe	10	1.53	b
2.13	PhMe	18	1.53	97
2.13	PhMe	720	1.53	b

Table 2.03

Deoxygenation of primary alcohols.[c]

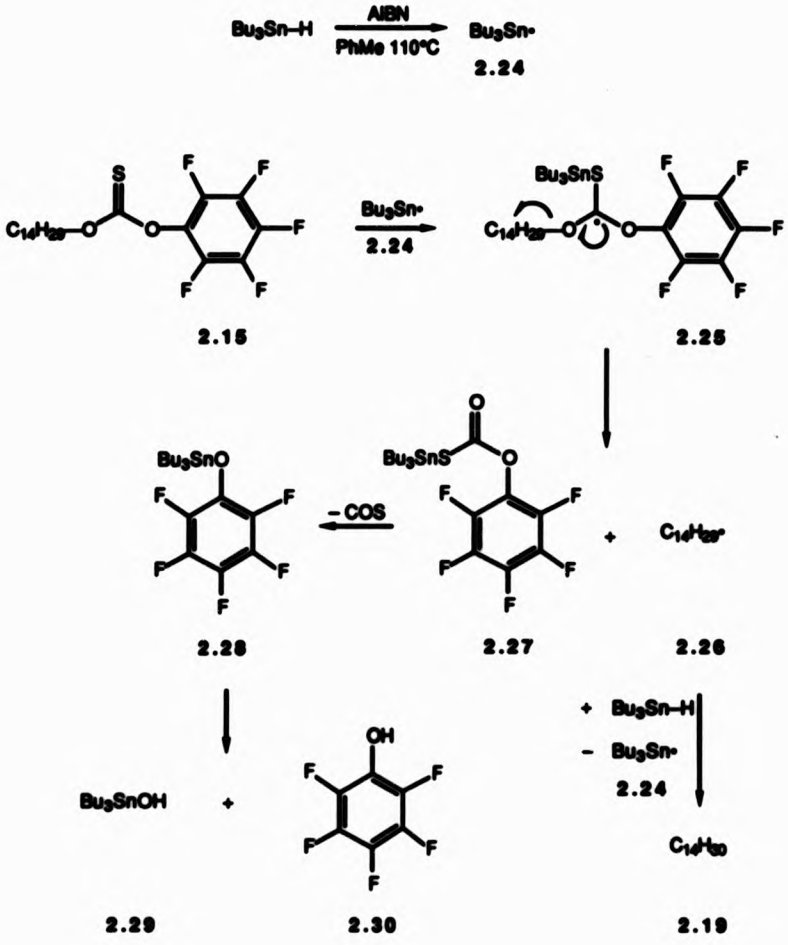
Alcohol	Solvent	Time (minutes)	Yield (%)	Overall Yield (%)
2.10	PhMe	10	100	97[d]
2.11	PhMe	5	95	95[b,d]
2.11	PhH	20	90	90[b,d,e]
2.12	PhMe	15	97	97[b,d]
2.13	PhMe	12	86	83[d]
2.13	PhMe	10	72	72[a, b]

Notes to Tables 2.02 and 2.03

a: Preparative yield; b: One pot procedure; c: All deoxygenations used tributyltin hydride and AIBN and were carried out in the boiling solvent; d: Yield measured by glc; e: 10% of alcohol was also measured by glc.

The mechanism of this deoxygenation is assumed to be similar to the reduction of xanthates with tributyltin hydride (Chapter 1, page 26). Thus, in boiling toluene and in the presence of AIBN tributyltin hydride forms the tin radical **2.24** (Scheme 2.05). In the presence of thionocarbonate **2.15** this tin radical **2.24** attacks the thiocarbonyl forming the intermediate tertiary radical **2.25**. Fragmentation of this intermediate tertiary radical **2.25** gives the tetradecyl radical **2.26** and the thiocarbonate **2.27**. The tetradecyl radical **2.26** reacts with the tributyltin hydride to furnish the hydrocarbon, tetradecane **2.19**, and another tributyltin radical **2.24** which continues the radical chain reaction. The thiocarbonate **2.27** is unstable and decomposes to the phenolate **2.28** and carbonyl sulphide spontaneously. Subsequent hydrolysis, upon work up or upon standing, gives rise to the formation of pentafluorophenol **2.30** and the hydroxide **2.29**.

Thionocarbonates



Scheme 2.05

2.2 Conclusion

It has been shown that primary alcohol derivatives of **1.52** and **1.53** can easily be deoxygenated under mild conditions yielding the respective hydrocarbon in good yields. The ease of acylation of the alcohols is particulary noteworthy as strong bases are not necessary. Reaction times for deoxygenation have been dramaticaly reduced from four hours for alcohol derivatives of **2.03** to under half an hour for alcohol derivatives of **1.52** and **1.53**.

Chapter 3

Decarboxylation of Acyl Derivatives of Hydroxamic Acids.

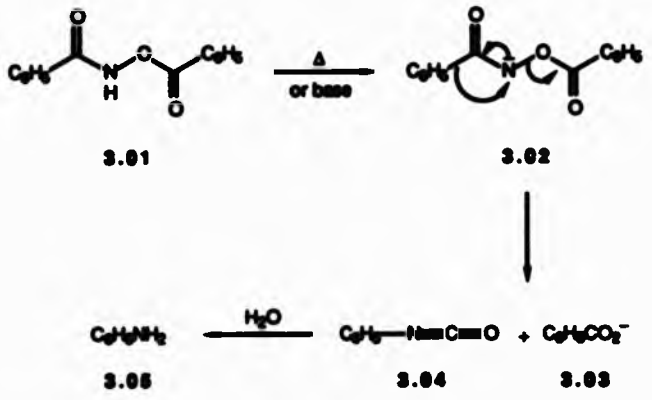
Chapter 3

3.0 INTRODUCTION

The radical chemistry of acyl derivatives of the thiohydroxamic acid N-hydroxy-2-thiopyridone has already been covered in Chapter 1 (page 38). As was also mentioned earlier Barton and co-workers[24,60,62] have extended the family of radical reactions based on acyl derivatives to several thiohydroxamic acids (page 39). The success of this chemistry is due to the disciplinary action of the thione function on carbon and other radicals and to the weakness of the nitrogen-oxygen bond. It was thus of interest to compare the radical chemistry of acyl derivatives of thiohydroxamic and hydroxamic acids. The latter still contains the weak nitrogen-oxygen bond.

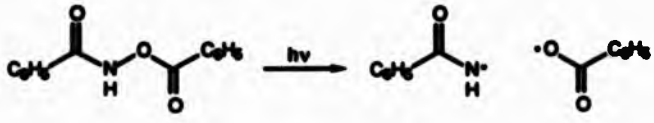
Acyl derivatives of acyclic hydroxamic acids are known to undergo decomposition with the action of heat in the well known Lossen rearrangement.[87, 88] However this reaction is generally considered to proceed *via* polar paths.[89] Hence, under the action of heat or base dibenzoylhydroxylamine 3.01 forms the anion 3.02. This anion 3.02 can then undergo rearrangement to form the isocyanate 3.04 and the benzoate anion 3.03. In the presence of water the isocyanate decomposes to give aniline 3.05. In contrast to this the products of photolysis of acyclic[90] and cyclic[91, 92, 93, 94] acyl derivatives of hydroxamic acids are consistent with homolytic nitrogen-oxygen bond fission. Thus, Walling and Naglieri[90] confirmed the presence of free radicals in the photolysis (ultraviolet light) of dibenzoylhydroxylamine (3.01, Scheme 3.02) by successfully polymerizing methyl methacrylate. This polymerization was only 1% as effective under

thermal conditions. This shows that some homolytic nitrogen-oxygen bond cleavage occurs under the action of heat but the main pathway is by polar intermediates (Loesen rearrangement).



3.01 3.02 3.05 3.04 3.03

Scheme 3.01: Loesen rearrangement.

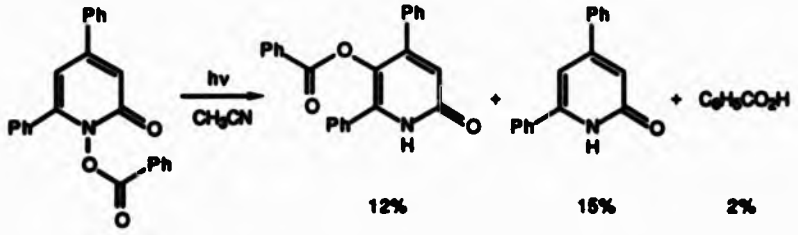


3.01 3.06 1.113

Scheme 3.02

Katritzky and co-workers[82] have reported photolysis of acyl derivatives of the type **3.07**, Scheme 3.03, which resulted in the formation of the

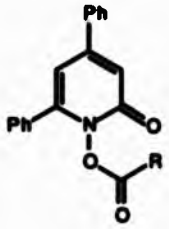
rearranged ester **3.08** (12%) and 4,6-diphenyl-2-pyridone **3.09** (15%) and benzoic acid **3.10** (2%).



Scheme 3.03[92]

The photolysis reported were carried out at 350nm (medium pressure mercury lamp). Compound **3.07** is known to have a λ_{max} at 250nm and 330nm although the extinction coefficients were not reported. Examples of trapping benzoyloxy radicals have already been seen (page 44-45) and the ester **3.08** seems to be a product of this sort of trapping. The benzoic acid is the product of quenching of the benzoyloxy radical by the solvent. No other products are reported except the pyridone **3.09** again probably from solvent quenching of the nitrogen radical. Here it can be clearly seen that the benzoyloxy radical has no affinity for the lactam carbonyl. This also applies to carbon centred radicals as Katritzky *et al* [92] only reported a black tar as product when either **3.11** or **3.12** were photolyized at 250nm (Structure 3.01). However they do not report the results of photolyses at 350nm.

Hydroxamic Acid Derivatives

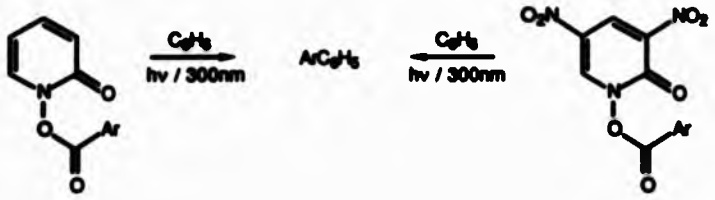


R = Me 3.11

R = CH_2Ph 3.12

Structure 3.01

Taylor *et al*[93] photolysed aryl-acyl derivatives of 2-pyridones **3.13** or 3,5-dinitro-2-pyridones **3.14** (Scheme 3.04) and trapped the corresponding aryl radicals with benzene to yield unsymmetrical biphenyls in low to moderate yield as shown in Table 3.01. The other product being the corresponding pyridone **3.16** or **3.17** (Structure 3.02).



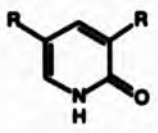
3.13 **3.15** **3.14**

Scheme 3.03

Table 3.01[93]

Aryl radical substitution on benzene.

Ar	Yield of 3.15 %	
	From 3.13	From 3.14
C_6H_6	40	57
$m\text{-}BrC_6H_4$	30	58
$p\text{-}CH_3C_6H_4$	44	57

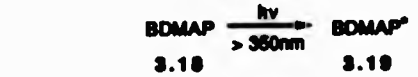


R = H 3.16
R = NO_2 3.17

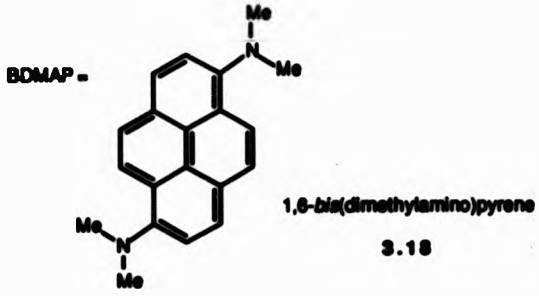
Structure 3.02

In an attempt to make synthetic use of this nitrogen-oxygen bond homolysis Okada and co-workers[94] have successfully used the photosensitizer 1,6-*bis*(dimethylamino)pyrene (BDMAP) 3.18 to excite the carbonyl of the acyl derivative of N-hydroxyphthalimide (3.20, Scheme 3.05). Thus when BDMAP is photolyzed with visible light (350-450nm) in the presence of the acyl derivative 3.20 the radical anion 3.22 is produced. Okada suggested two possible mechanisms by which this radical anion 3.22 can decompose to give the acyloxy radical 1.11 and phthalimide 3.25. These two possible pathways are shown in Scheme 3.06.

Hydroxamic Acid Derivatives

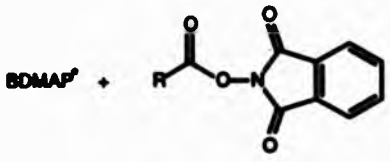


3.18 3.19

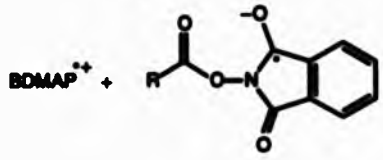


1,6-*bis*(dimethylamino)pyrene

3.18

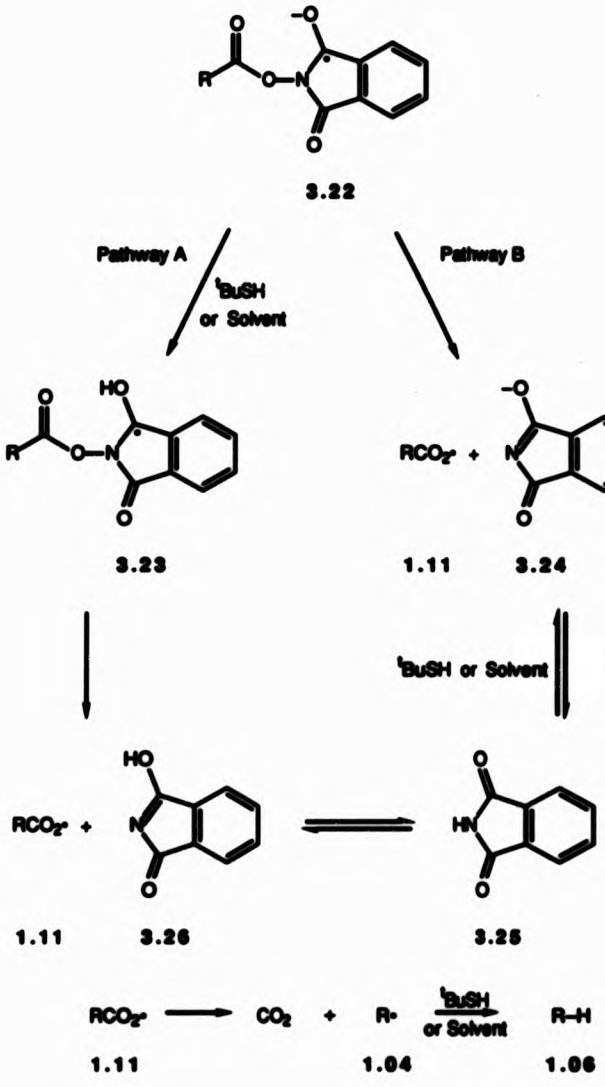


3.19 3.20



3.21 3.22

Scheme 3.05



3.22

3.23

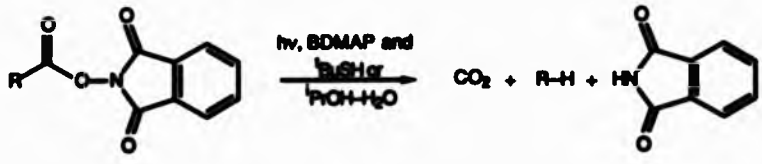
1.11 3.24

1.11 3.26 3.25

1.11 1.04 1.06

Scheme 3.06

The two pathways A and B differ in the sequence which the phthalimide anion abstracts a proton from the proton source (tert-butyl thiol or the solvent). In pathway A the radical anion **3.22** abstracts a proton to form the radical intermediate **3.23** which then fragments to the acyloxy radical **1.11** and phthalimide **3.25** *via* **3.26**. Pathway B involves homolytic cleavage of the nitrogen-oxygen bond in the radical anion **3.22** to form the acyloxy radical and the phthalimide anion **3.24** which can the abstract a proton to furnish phthalimide **3.25**. The acyloxy radical **1.11** then loses carbon dioxide giving the alkyl radical **1.04** which is quenched by the tert-butyl thiol or the solvent thus forming the hydrocarbon **1.06**. The general equation is shown in Scheme 3.07 and representative yields are given in Table 3.02.



3.20 **1.06** **3.25**

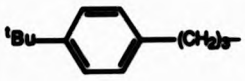
Scheme 3.07

This is a non radical chain reaction which is reflected in the low quantum yields observed, approximately 0.1 at 366nm.

Hydroxamic Acid Derivatives

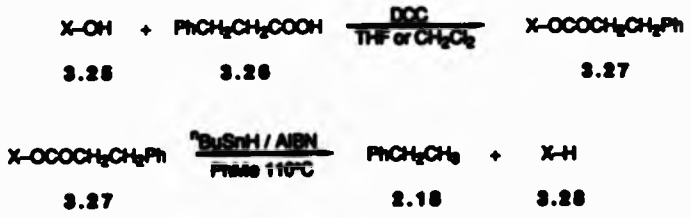
Table 3.02[94]

Reduction of acyl derivatives of N-hydroxyphthalimide.

R =	Yield of R–H 1.06
	88%
$(PhCH_2)_2CH$–	98%
9-triptycyl	84%

3.1 DISCUSSION

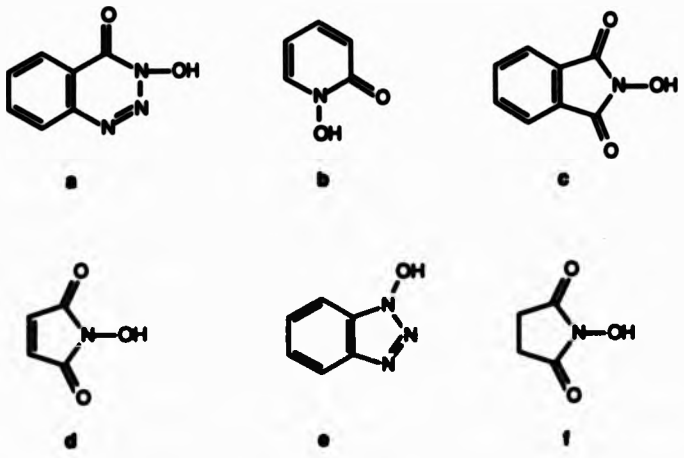
Thus, it was envisaged that a radical chain process with acyl derivatives of hydroxamic acids would give high yields of the corresponding reduction product. This was in fact the case as can be seen from Scheme 3.08 and Table 3.03.



Scheme 3.08

Hydroxamic Acid Derivatives

X-OH 3.25a–f



Structures 3.03: Hydroxamic Acids

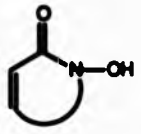
Table 3.03

Radical reductions of acyl derivatives of hydroxamic acids with tributyltin hydride.

Hydroxamic Acid 3.25	Acyl Derivative Yield 3.27	Decarboxylation Time (hours)	Ethylbenzene Yield 2.18
a	100%	3.00	97%
b	100%	2.50	73%
c	88%	1.50	62%
d	30%	1.25	49%
e	93%	3.00	0%
f	48%	1.50	2%

Hydroxamic Acid Derivatives

Table 3.03 shows that certain rules apply for the radical reaction shown in Scheme 3.08 to be efficient. It was thus shown that for efficient radical chain propagation the hydroxamic acid must contain a conjugated enone directly adjacent to the nitrogen-oxygen bond undergoing homolysis **3.29** (Structure 3.04).

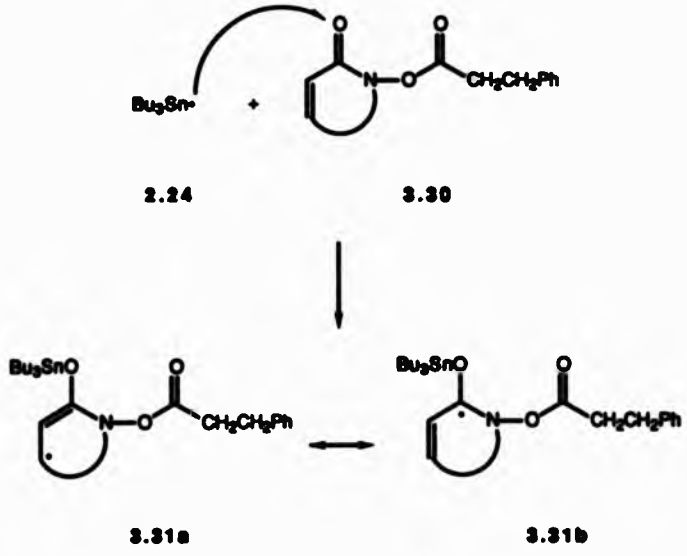


3.29

Structure 3.04

For convenience comparative experiments were carried out using dihydrocinnamic acid. The acyl derivatives **3.27** were easily prepared using N,N'-dicyclohexylcarbodiimide (DCC) in a suitable solvent (Scheme 3.08). These derivatives were then decarboxylated with tributyltin hydride in boiling toluene. A catalytic amount of AIBN was used to initiate the reaction and was injected in the reaction with the tributyltin hydride. The reactions were monitored by glc and tlc. When no further increase in ethylbenzene **2.18** was observed the reaction was stopped. In the case of **3.27e** and **3.27f** tlc showed the presence of the starting material. Using N-hydroxybenzotriazin-4-one acyl derivative **3.27a** an excellent yield of hydrocarbon was obtained. In the absence of initiator and tributyltin hydride no reaction took place and the acyl derivative was recovered unchanged. The acyl derivative of N-hydroxy-2-pyridone **3.27b** also gave good yields of hydrocarbon. In contrast N-hydroxybenzotriazole **3.27e** and N-hydroxysuccinimide **3.27f** gave

derivatives that showed no sign of fragmentation. The hydroxamic acids **3.25a-d** of which their acyl derivatives all showed fragmentation have in common the possible addition of the tin radical to the oxygen of a carbonyl group to give a allylically stabilized radical. This is illustrated in Scheme 3.09.



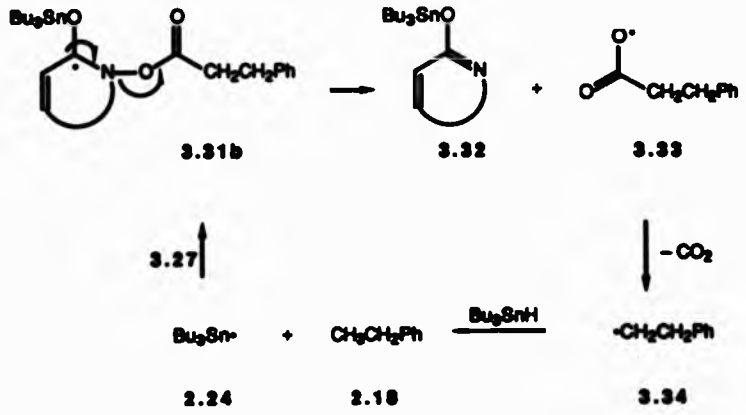
2.24 **3.30**

3.31a **3.31b**

Scheme 3.09

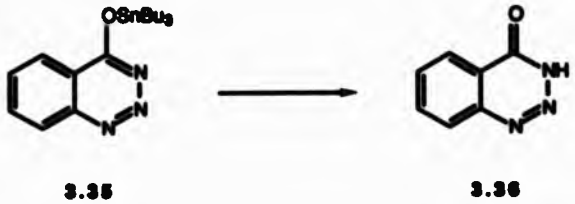
This radical **3.31** can then fragment to give the acyloxy radical **3.33** and thence after decarboxylation the β-phenylethyl radical **3.34**. This radical can then be reduced by the tributyltin hydride to furnish ethylbenzene **2.18** and another tin radical. This tin radical is then capable of continuing the radical chain reaction (Scheme 3.10).

Hydroxamic Acid Derivatives



Scheme 3.10

Upon work up of the reaction (silica gel) the stannyl imidate **3.32** is hydrolysed to form the respective lactam. Thus in the case of the acyl derivative **3.27** after decarboxylation under the conditions already mentioned a quantitative amount of the benzotriazin-4-one **3.36** was formed, presumably from the hydrolysis of **3.35**.

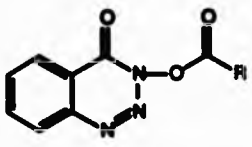


Scheme 3.11

Hydroxamic Acid Derivatives

Attempts to substitute dodecylthiol for tributyltin hydride as the hydrogen source and chain carrier failed. This was due to the lack of affinity of the thiyl radical for the carbonyl group. Thus when dodecylthiol and **3.27a** were refluxed in toluene and AIBN was added slowly no ethylbenzene was detected and the acyl derivative was recovered from the reaction unchanged.

Similar experiments were undertaken to utilize diphenylsilane as the chain carrier/hydrogen source. Although silicon has a large affinity for oxygen and there has been reports of silyl radicals adding to carbonyl[95,95,96] no successful replacement was possible. Thus when acyl derivatives of N-hydroxybenzotriazin-4-one **3.27a** or **3.37** (Scheme 3.12) were boiled in various solvents with diphenylsilane and a radical initiator the best yield of hydrocarbon that was obtainable was 25%. The remaining mass balance was unreacted starting material either **3.27a** or **3.37**, which crystallized out of the cooling solvent. These results are summarized in Table 3.04.



Ph_2SiH_2 / Solvent
AIBN or $(PhCOO)_2$

R–H

R = CH_2CH_2Ph	**3.27a**	1.86
R = $(CH_2)_{14}CH_3$	**3.37**	

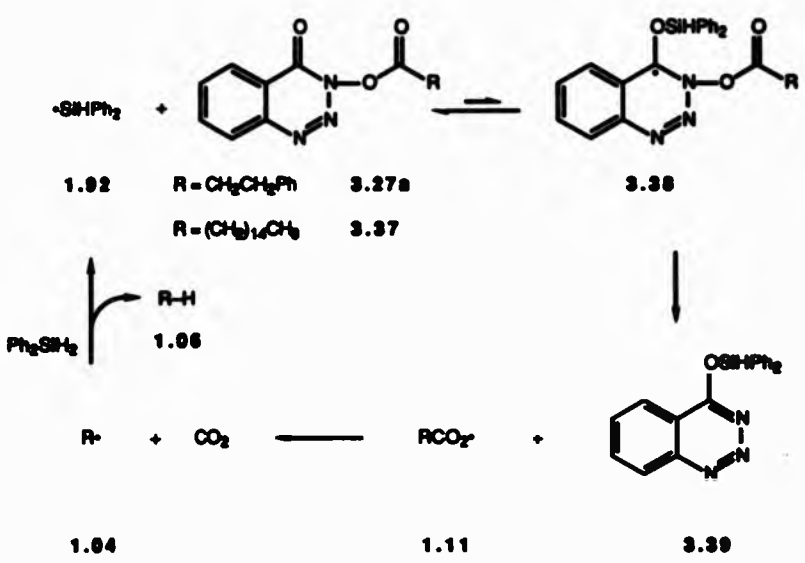
Scheme 3.12

Table 3.04

Reduction of acyl derivatives of [illegible]benzotriazin-4-one with diphenylsilane.

Compound	Ph_2SiH_2 (equivalents)	Solvent (temp.)	AIBN or $(PhCO_2)_2$ (equivalents)	Reaction time	Yield R–H 1.06
3.27a	2	PhMe 110°C	AIBN (0.1)	20 mins	0%
3.27a	4	PhMe 110°C	AIBN (0.2)	3 hr.	11%
3.27a	2	PhH 80°C	$(PhCO_2)_2$ (1.0)	4 hr.	20%
3.37	2	PhMe 110°C	$(PhCO_2)_2$ (1.0)	4 hr.	25%
3.37	2	p-Cymene 180°C	$(PhCO_2)_2$ (1.0)	4 hr.	5%

A possible reason for the lack of reduction is that the aromatic solvent is competing for the silyl radical 1.92, as the addition of silyl radicals to aromatic rings is a well known phenomenon.[97] A better choice of solvent might have been a high boiling hydrocarbon. However the reactions reported of silyl radical attack upon carbonyls were actually carried out in refluxing toluene.[95] There seems little doubt that the choice of solvent had no significant effect in the reduction of the acyl derivatives of the hydroxamic acids. The silyl radical probably adds reversibly to the carbonyl giving the radical 3.38 (Scheme 3.13) which can then undergo nitrogen-oxygen bond cleavage to give the acyloxy radical 1.11. Thus, if the silyl radical 1.92 is more stabilized and of lower energy than the carbon centred radical 3.38 the equilibrium will lie to the left in favour of 3.27a or 3.37 and radical 1.92 (Scheme 3.13).



Scheme 3.13

The dihydrocinnamyl derivative **3.27a** was stable to tungsten light and the tin hydride reduction was not effected by such irradiation.

3.2 CONCLUSION

Clearly the thiocarbonyl group is very important for carrying a radical chain. Hence, under the same conditions using the acyl derivative of N-hydroxy-2-thiopyridone the tributyltin hydride can be substituted by a thiol which will then give good yields of the nor-alkane (Chapter 1 page 38).

Despite the disadvantages however, this is the only example of a radical chain mechanism for acyl derivatives of hydroxamic acids.[98]

The derivative 3-(1-oxo-3-phenylpropoxy)-1,2,3-benzotriazin-4(3*H*)-one **3.27a** was tested for *in-vitro* anti-HIV activity and was found to be inactive.

Lipczynska-Kochany[99] has published a short review on the environmental effects of hydroxamic acids and their derivatives which are used as flotation agents, herbicides, fungicides, or insecticides. The photochemistry of these acids or their derivatives has not been extensively investigated. There is considerable evidence that on exposure to direct sunlight both hydroxamic acids and their derivatives may form highly carcinogenic compounds. Thus these hydroxamic acids and their derivatives should be handled with care.

Chapter 4

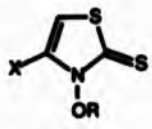
Synthesis and Radical Reactions of 2-Aryl-3-acyloxy-3,4-dihydroquinazoline-4(3*H*)-thiones and its Benzoquinazoline Analogue.

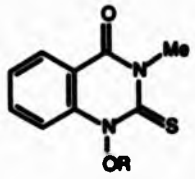
Chapter 4

4.0 INTRODUCTION

The extensive radical chemistry of acyl derivatives of N-hydroxy-2-thiopyridone (1.09) has been reviewed in Chapter 1 (page 38). As was mentioned this chemistry is not only restricted to acyl derivatives of N-hydroxy-2-thiopyridone (1.09) but is generally applicable to acyl derivatives of thiohydroxamic acids[24,62,100] and to some extent hydroxamic acids (Chapter 3 page 73).

Acyl derivatives of the thiohydroxamic acids 4.01-4.05 (Structures 4.01) were found to have similar chemistry as that of 1.09.[24,62,100] For example all the palmitoyl derivatives of the hydroxamic acids 4.01-4.05 can be converted to their nor-alkyl sulphides Structures 4.02 (as in the reaction of 1.09, Chapter 1 page 5, Scheme 1.02). Table 4.01 shows the conditions for such transformations and the respective yields.

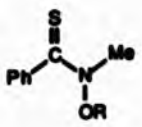




4.01	X = Me, R = H	4.03	R = H
4.02	X = Ph, R = H	4.04	R = $CO(CH_2)_{14}CH_3$
4.06	X = Me, R = $CO(CH_2)_{14}CH_3$		
4.07	X = Ph, R = $CO(CH_2)_{14}CH_3$		

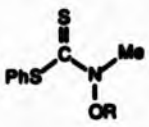
Structures 4.01

Thiohydroxamic Acid Derivatives



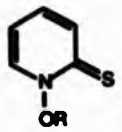
4.04 R=H

4.09 R=$CO(CH_2)_{14}CH_3$



4.05 R=H

4.10 R=$CO(CH_2)_{14}CH_3$

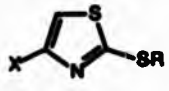


1.95 R=H

4.11 R=$CO(CH_2)_{14}CH_3$

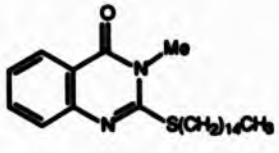
Thiohydroxamic acids and their palmitoyl derivatives.

Structures 4.01 (contd.)

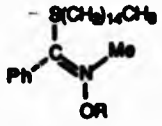


4.12 X=Me, R=$(CH_2)_{14}CH_3$

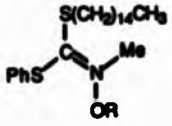
4.13 X=Ph, R=$(CH_2)_{14}CH_3$



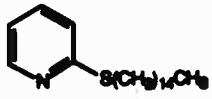
4.14



4.15



4.16



4.17

Non-alkyl sulphides.

Structures 4.02

Table 4.01

Conversion of thiohydroxamates to their respective nor-alkyl sulphides.

Acyl Derivative	Reaction Conditions	Time (hr)	Sulphide (Yield)	(Ref.)
4.06	25°C(hv, 300W, W)	1	N. R.	(24)
4.06	25°C(hv, 100W, Hg)	0.5	4.12(70%)	(24)
4.06	80°C(benzene)	2	4.12(84%)	(24)
4.07	25°C(hv, 100W, Hg)	2	4.13(50%)	(24)
4.07	80°C(benzene)	2	4.13(82%)	(24)
4.08	25°C(hv, 100W, Hg)	a	4.14(85%)	(62)
4.08	140°C(xylene)	40	4.14(54%)	(24)
4.09	140°C(neat)	3	4.15(60%)	(24)
4.10	25°C(hv, 100W, Hg)	a	4.16(100%)	(62)
4.11	25°C(hv, 250W, W)	0.5	4.17(90%)	—
4.11	81°C(cyclohexane)	2	4.17(92%)	(69)

Notes to Table 4.01: Hg = high pressure mercury lamp; W = tungsten lamp; N. R. = no reaction; a: time not quoted in in reference;

Table 4.01 shows that although the chemistry of the various acyl derivatives are similar there is a marked difference in their thermal and photolytic rearrangement reactions. Acyl derivative 4.11 can be both photolyzed (white light) and thermolyzed to produce the respective nor-alkyl sulphide 4.17 in high yield. The only other acyl derivative which can be rearranged by the use of tungsten light is 4.07, but this is dramatically slower. Thus, only 50% of the rearranged sulphide 4.13 is detected after two hours (the remainder being the starting acyl derivative 4.07). In contrast, 90% of 4.17 is formed after only half an hour. The only difference between 4.06 and 4.07 is a phenyl group

rather than a methyl group at the 4-position. This difference, however, leads to the acyl derivative 4.06 being inactive to visible light. Both the 3-palmitoyloxy-4-phenylthiazolin-2(3*H*)-thione (4.07) and 4-methylthiazolin-2(3*H*)-thione (4.08) can be thermolyzed to produce the nor-alkyl sulphides (4.12 and 4.13) in high yield. The time required for these transformations is the same as that for the thermolysis of 4.11 (2 hours). From Table 4.01 it is seen that photolytic (high pressure mercury lamp) transformations to the respective nor-alkyl sulphide are more efficient and result in higher yields than the corresponding thermal rearrangement. Thus when 4.08 is subjected to light from a high pressure mercury lamp rearrangement to the corresponding sulphide 4.14 (85%) takes place. To effect the same transformation in lower yield (54%) 4.08 must be boiled in xylene for 40 hours. Derivatives 4.09 and 4.10 are able to form the corresponding sulphides 4.15 and 4.16, either by thermal or photolytic (light from a high pressure mercury lamp) conditions respectively. High yields are generally attained *via* either tungsten light or high pressure mercury light (UV) to the corresponding nor-alkyl sulphide. This is not the case when rearrangement is brought about by thermolysis. Therefore aromatization is less important as a driving force in these photochemical rearrangements. Thus, 4.11 becomes fully aromatized when converted to sulphide 4.17, however the same is not true of 4.08 which does not become aromatic when converted to sulphide 4.14.

The acyl derivatives 4.06-4.09 and 4.11 were also thermally or photochemically decomposed in the presence of bromotrichloromethane to form pentadecyl bromide (except 4.08 where no reaction is observed).

Table 4.02

Trapping with bromotrichloromethane of radicals derived from palmitoyl derivatives of various thiohydroxamic acids.

Acyl Derivative	Conditions, Temp, Solvent(eq of $BrCCl_3$)	Time (hr)	Brompentadecane (Yield)	(Ref.)
4.06	80°C, PhH, (15)	1	92%	(24)
4.07	25°C, hv, PhH, (34)	2	96%	(24)
4.08	25°C, hv, PhH, (34)	5	N. R.	(24)
4.09	110°C, PhMe, (13)	0.75	77%	(24)
4.11	105°C, $BrCCl_3$, (50)	1.5	95%	(69)
4.11	20°C, hv*, CCl_4, (5)	5 mins	98%	(68)

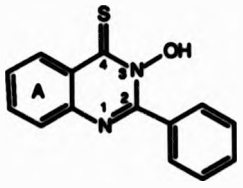
Notes to Table 4.02: hv = 300W tungsten lamp * 250W tungsten lamp; N. R. = no reaction.

Good yields are reported for both thermolytic or photolytic (tungsten light) conversion to the nor-alkyl bromide from derivative 4.11. These yields are in the same range as those for the conversion to the nor-alkyl sulphide. The yield of pentadecyl bromide is high for the reaction of 4.06 (92%) or 4.07 (96%) with bromotrichloromethane. This is significantly higher than the corresponding yield of the nor-alkyl sulphides under the same reaction conditions, 84% for conversion to 4.12 and 50% for conversion to 4.13. This result implies that the thiocarbonyl in either 4.06 or 4.07 is less reactive towards the nucleophilic pentadecyl radical than the electrophilic trichloromethyl radical. With these conclusions it can also be stated that the thiocarbonyl of 4.11 is more reactive towards pentadecyl radicals than the thiocarbonyl in molecules 4.06 or 4.07.

Thiohydroxamic Acid Derivatives

4.1 Discussion

Thus, it was of interest to investigate other thiohydroxamic acids which form acyl derivatives which are more active to visible light than that of acyl derivatives of **4.02**, but contain a thiocarbonyl with similar reactivity of that of **4.02**.



4.18

2-Phenyl-3-hydroxy-3,4-dihydroquinazoline-4(3*H*)-thione.

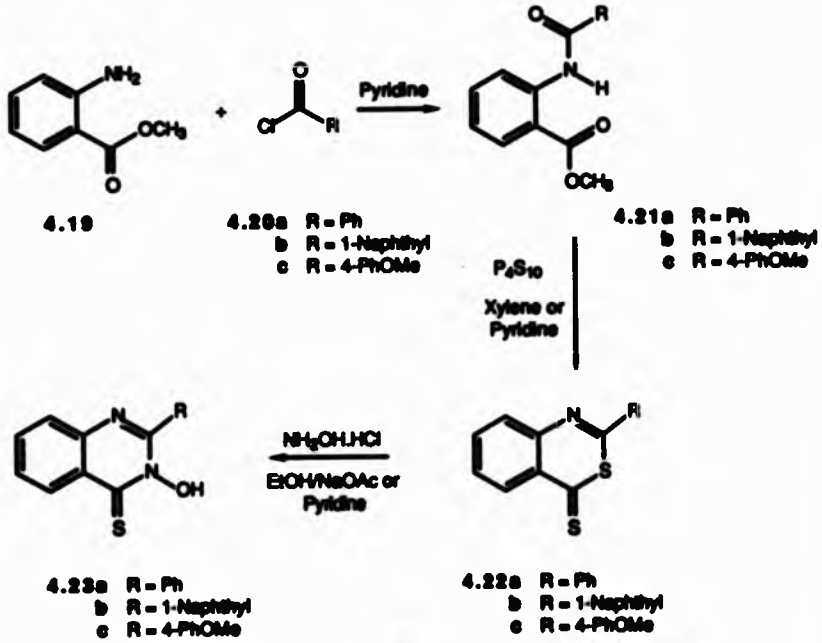
Structure 4.03

The known thiohydroxamic acid **4.18**[101,102] complies with all the criteria laid down by the hydroxamic acid work (Chapter 3 page 74) and that demonstrated by Barton *et al*[24] (Chapter 4: Introduction). An advantage of the 3-hydroxy-3,4-dihydroquinazoline-4(3*H*)-thione system was that their synthesis enabled access to a range of compounds that differed only in their 2-substituent. This has led to an understanding of the structural-chemical relationship of differing substituents.

4.1.1 Synthesis

The thiohydroxamic acids **4.23a-c** were synthesized from readily available methyl anthranilate **4.19** as described by Legrand.[101, 103] The

anthraniate **4.19** was N-acylated with the appropriate acid chloride **4.20** (Scheme 4.01). The choice of acid chloride enables variation of substituents at the 2-position in the resulting 2-aryl-3-hydroxy-3,4-dihydroquinazoline-4(3*H*)-thiones **4.23**. Thionation and cyclization with phosphorus pentasulphide in a high boiling solvent results in the formation of the benzothiazine **4.22** in reasonable yield (see Table 4.03). Treatment of **4.22** with hydroxylamine hydrochloride in the presence of a mild base gives the required thiohydroxamic acid **4.23**. Isolation of the 3,1-benzothiazine-4-thiones **4.22a-c** reported by Legrand involved the use of undesirable mercury salts.



4.19

4.20a R = Ph
b R = 1-Naphthyl
c R = 4-PhOMe

4.21a R = Ph
b R = 1-Naphthyl
c R = 4-PhOMe

4.23a R = Ph
b R = 1-Naphthyl
c R = 4-PhOMe

4.22a R = Ph
b R = 1-Naphthyl
c R = 4-PhOMe

Synthesis of 2-aryl-3-hydroxy-3,4-dihydroquinazoline-4(3*H*)-thiones.

Scheme 4.01

Table 4.03[101]

Overall yields for synthesis of 2-aryl-3-hydroxy-3,4-dihydroquinazoline-4(3*H*)-thiones.

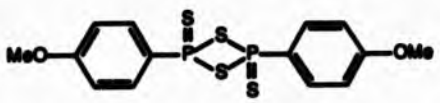
Compound 4.23	Lawesson's reagent 4.24	P_4S_{10} in boiling xylene	P_4S_{10} in boiling pyridine	Reported yield[101]
a	40%	33%	61%	35%
b	—	41%	—	50%
c	—	37%	—	37%

The same overall yield as was reported was attained without isolation of the intermediate 3,1-benzothiazine-4-thione 4.22 as shown in Table 4.03. The use of pyridine as a solvent for the thionation step (4.21a-4.22a) greatly improved the yield (resulting in 61% overall yield of 4.23a) and allowed easy isolation of the 2-phenyl-3,1-benzothiazine-4-thione 4.22a, by simple repeated crystallization yielding 73% of pure 4.22a.

The use of readily available, cheap starting materials (anthranilic acid) and easily available inexpensive thionating agents makes the radical precursors 4.23a-c an inexpensive alternative to N-hydroxy-2-thiopyridone (1.95).

There are a tremendous range of thionating reagents available today in addition to the classical phosphorus pentasulphide (P_4S_{10}).[104, 105] Most notably Lawesson's reagent 4.24[106, 107] conveniently prepared from anisole and P_4S_{10} (50% yield). Other useful reagents include H_2S/HCl[108], Scheeren's reagent ($P_4S_{10}/NaHCO_3$)[109], S_8/HMPA[110], Davy's reagent 4.25[111], and P_4S_{10}/Et_3N.[112] The general reason for making organic analogues to P_4S_{10} is to increase its solubility thus allowing lower temperatures to be used.

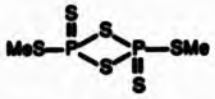
Thiohydroxamic Acid Derivatives



2,4-bis(4-methoxyphenyl)-1,3-dithiadiphosphetane-2,4-disulphide

"Lawesson's Reagent"

4.24



4.25

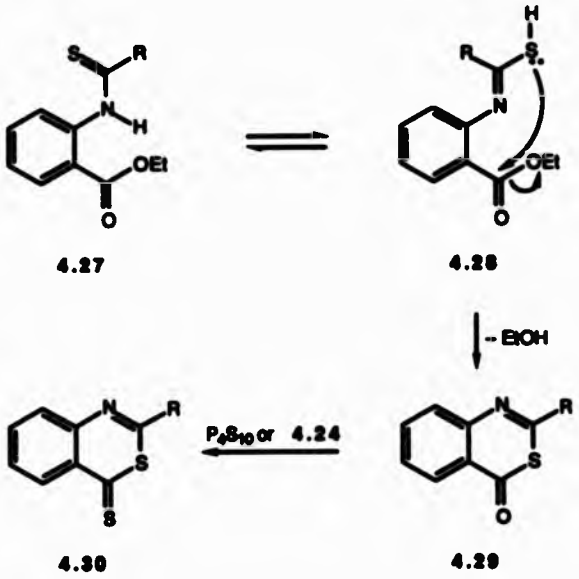
Structures 4.04

Lawesson's reagent has been used for the conversion of 4.21 to 4.22 and high yields were obtained[113], however, the isolation required the use of chromatography which is undesirable in large scale reactions. When Lawessons reagent is used and chromatography avoided similar yields are attained as that of the corresponding P_4S_{10} reaction (Table 4.03).

The mechanism of the thionation/cyclization reaction (Scheme 4.02) first proposed by Legrand[103] has been proven by Lawesson.[113] High temperatures were shown to be needed to effect cyclization. Thus, when 4.26 is treated with either P_4S_{10} or 4.24 at 80°C a mixture of 4.27, 4.29, and 4.30 is obtained. However if the temperature of the reaction is raised to 140°C only 4.30 is detected, Scheme 4.02 and Table 4.04.

4.26 4.27

Scheme 4.02



Scheme 4.02 (contd.)

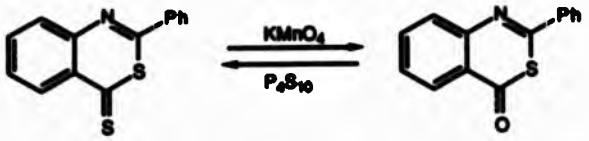
Table 4.04[113]

Product distribution for the thionation of ethyl-N-benzoylanthranilate with Lawesson's reagent.

R =	Time hours	Temperature °C	Products		
			4.27	4.28	4.30
i-propyl	5	80	44%	8%	32%
phenyl	10	80	67%	—	30%
t-butyl	72	80	2%	—	96%
phenyl	2.5	140	—	—	90%

When Legrand[103] treated 4.22a with potassium permanganate ($KMnO_4$) 4.31 was obtained (Scheme 4.03) and when 4.31 was treated with P_4S_{10}

4.22a was recovered. This also confirms the intermediary of 4.29 in the reaction.



4.22a 4.31

Scheme 4.03

Further evidence that cyclization requires high temperature was provided by Panda *et al.*[112] Thus, when 4.32, the oxo-analogue of 4.30 is treated with P_4S_{10}/Et_3N at room temperature for 24 hours 4.22a is obtained in 90% yield without the need for chromatography (Scheme 4.04).

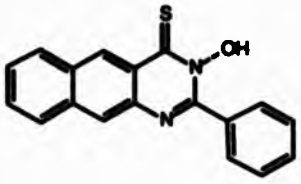
4.32 4.22a

Scheme 4.04

The problem with Lawesson's reagent is that the organic ligands increase the solubility of the thionating species in organic solvents and thus make purification by crystallization difficult. As P_4S_{10} is completely soluble in

boiling pyridine there is no need of using Lawesson's reagent or any others that increase the thionating agents solubility.

With the synthesis well established and good yields attainable it was of interest to prepare the 2-phenyl-3-hydroxy-3,4-dihydrobenzoquinazoline-4(3*H*)-thione 4.33.

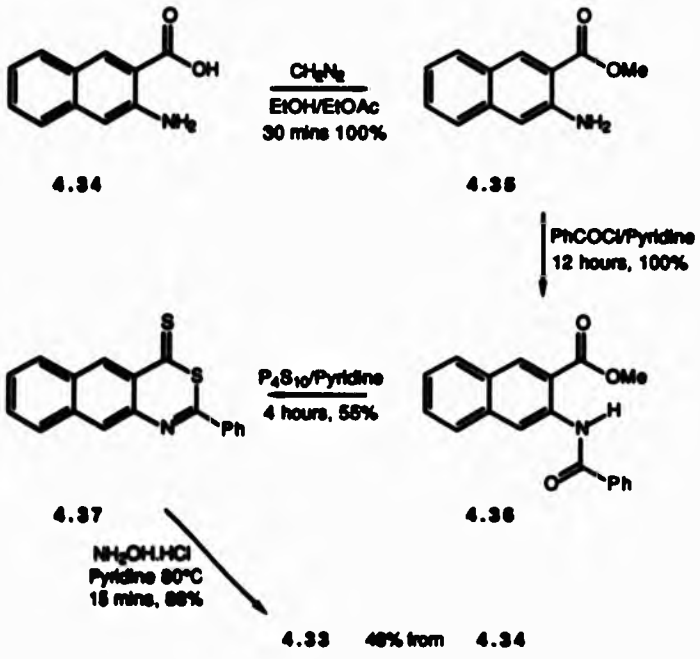


4.33

Structure 4.05

This would enable comparison of the structural and physical properties of its acyl derivative with those of the acyl derivatives of the thiohydroxamic acids 4.23a-c. Thus, 4.33 was prepared in a similar manner starting from 3-amino-2-naphthoic acid 4.34 which was O-methylated using diazomethane yielding the amino ester 4.35 (Scheme 4.05). When 4.35 was treated with benzoylchloride 4.36 was isolated which reacted with phosphorus pentasulphide in boiling pyridine to give the naphthothiazine 4.37. Hydroxylamine in hot pyridine reacted with 4.37 and formed 4.33 after 15 minutes in an overall yield of 48% from 4.34.

Thiohydroxamic Acid Derivatives

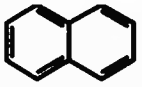


Scheme 4.05

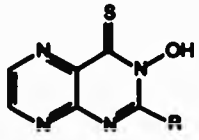
Table 4.05 shows the λ_{max} for various aromatic and heteroaromatic compounds. As can be seen from Table 4.05 the λ_{max} of an aromatic compound has a bathochromic shift as nitrogens are introduced. It was thus thought that the λ_{max} related to the thiocarbonyl would also correspondingly shift towards the visible, this was in fact not the case as will be seen in Section 4.1.2, Physical Properties.

Table 4.05[114]

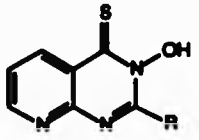
Absorption maxima for benzene, naphthalene, pyridine, pyrazine, and pyridazine.

Compound					
λ_{max1}(logε)	204(3.9)	286(3.97)	251(3.30)	260(3.8)	246(3.11)
λ_{max2}(logε)	256(2.3)	312(2.46)	270(2.65)	327(2.0)	340(2.50)

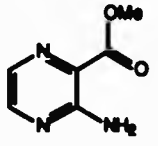
The synthesis of compounds of the type 4.37 and 4.38 was attempted but failed. N-Acylation of 2-methyl-3-aminopyrazine carboxylate only resulted in di-N-N-benzoylation. The 2-aminonicotinic acid 4.40 was readily converted to its methyl ester quantitatively with diazomethane giving 4.41, which was then N-benzoylated with benzoyl chloride to give 4.42 in 74% yield.



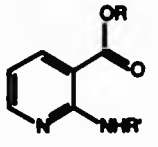
4.37



4.38



4.39

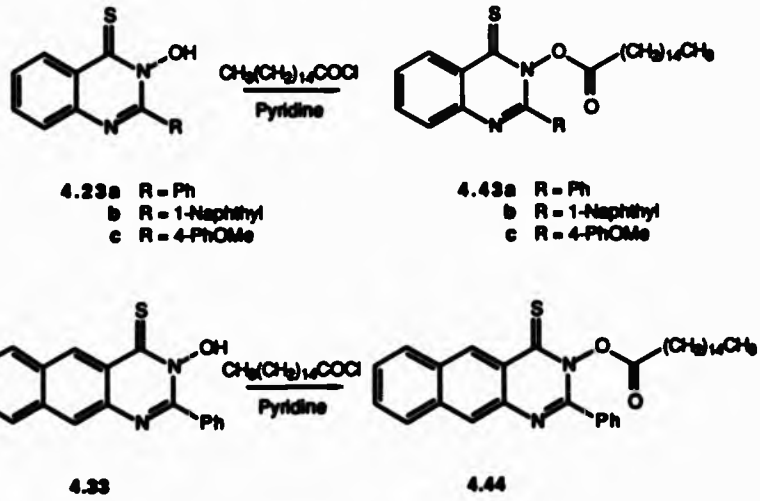


4.40 R' = R = H
4.41 R' = H, R = CH_3
4.42 R' = Ph, R = CH_3

Structures 4.06

Attempts to thionate and cyclize failed with P_4S_{10} in refluxing toluene or xylene and only a black tar resulted. When P_4S_{10} and pyridine was used however, a reddish brown gum was isolated. This was then treated immediately with hydroxylamine in ethanol to form **4.38** (11%) which was too unstable to characterize fully except by proton and carbon NMR. The conditions of thionation/cyclization were seemingly too vigorous to synthesize these compounds *via* the P_4S_{10} method.

When the thiohydroxamic acids **4.23a-c** and **4.33** are allowed to react with palmitoyl chloride in the presence of pyridine, Scheme 4.06, acyl derivatives **4.43a-c** and **4.44** are formed in almost quantitative yield. This is the first example of acylation of these thiohydroxamic acids.



4.23a R = Ph
b R = 1-Naphthyl
c R = 4-PhOMe

4.43a R = Ph
b R = 1-Naphthyl
c R = 4-PhOMe

4.33

4.44

Scheme 4.06

Compounds of type 4.23 are known to possess analgesic antiinflammatory, hypnotic, antibacterial, and antifungal activity.[115] Indeed compounds 4.23a-c and 4.33 have been tested for their antifungal activity and found to be active.

4.1.2 PHYSICAL PROPERTIES

a) UV-Visible

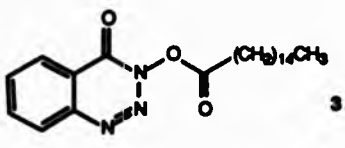
It was the aim of this study to determine the effects of the various 2-substituents in 4.43 on its UV-visible absorption. It was also of interest to discover the effect of extending the conjugation of the quinazoline aromatic ring, which is present in compound 4.44, on the thiocarbonyl λ_{max}. Thus, it is clear from Table 4.06 that differing substituents at the two position have no real effect on the λ_{max}(C=S) which is equal to approximately 356nm for 4.43a-c.

Table 4.06

UV-Visible data of O-acyl-hydroxamic and thiohydroxamic acid derivatives.

Compound	4.11	4.43a	4.43b	4.43c	4.44	4.07	3.37
λ_{max1}(nm)	367	356	355	358	325	324	283
ε ($l\ mol^{-1}cm^{-1}$)	7,000	14,290	15,000	12,540	21,810	10,900	7,019

Thiohydroxamic Acid Derivatives

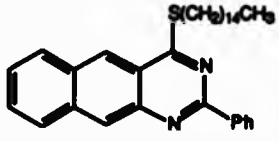


3.37

Structure 4.07

The molar extinction coefficient is double that of the N-hydroxy-2-thiopyridone derivative 4.11, ε = 12,500-15,000 as opposed to that of ε = 7,000 for 4.11. It is also of interest to note that the benzotriazine-4(3*H*)-one derivative 3.37 has a molar extinction coefficient of only ε = 7,019, similar to that of 4.11. Thus, it could be tentatively assumed that 2-aryl substituents increase the molar extinction coefficient of the quinazoline system.

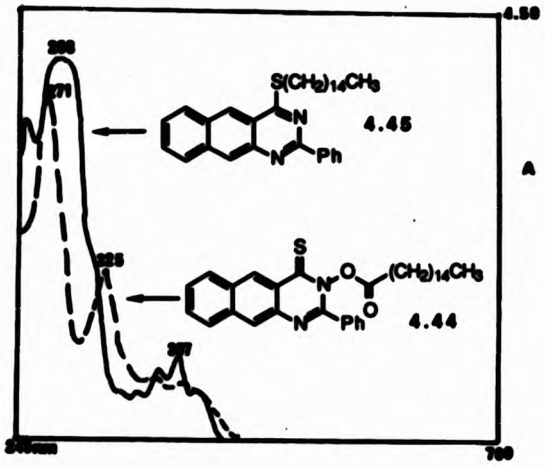
When conjugation on the parent aromatic ring (ring A, Structure 4.03) in the quinazoline-4-thione system is increased as it is in 4.44 the λ_{max} for the thiocarbonyl absorption shifts towards the ultraviolet (λ_{max} = 325nm). This is also accompanied by an increase in the molar extinction coefficient (ε = 21,810). The compound 4.44 is strongly yellow due to a tail at λ_{max} = 400nm (ε = 7,000) but this tail remains when the compound undergoes decarboxylative rearrangement to form the nor-alkyl sulphide 4.45.



4.45

Structure 4.08

The absorption at 325nm disappears however as can be seen from Figure 4.01 which shows the UV-visible absorption of 4.44 and 4.45 overlaid.

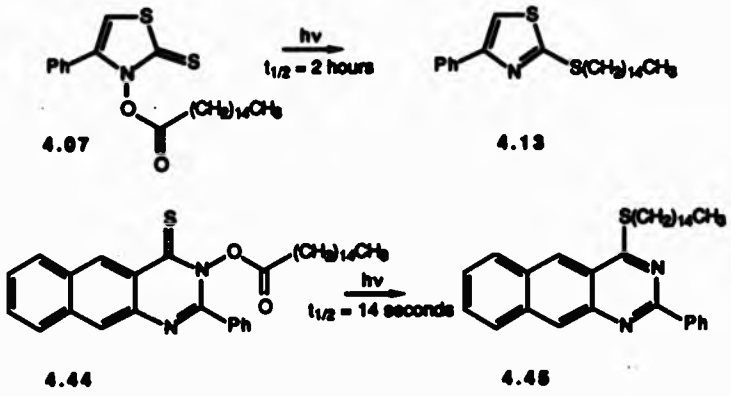


UV-Visible absorption spectra for 2-phenyl-3-palmitoyloxy-3,4-dihydrobenzoquinazoline-4(3*H*)-thione 4.44 and its rearranged derivative 4.45.

Figure 4.01

The dramatic difference that the molar extinction coefficient can have upon a compounds ability to absorb light is exemplified when acyl derivatives 4.44 and 4.07 are compared. Table 4.06 shows that the λ_{max} (C=S) for 4.07 is 324nm, similar to that of 4.44, however, the molar extinction coefficient of 4.07 is almost half that of 4.44 Scheme 4.07. Hence, whereas the thiazole 4.07 can be photolyzed with a tungsten light (300W) for two hours and only 50% of the nor-alkyl sulphide 4.13 is formed[24] (Table 4.01). In contrast to this the half life of 4.44 is 14 seconds.

Thiohydroxamic Acid Derivatives



Scheme 4.07

All of the new acyl derivatives 4.23a-c and 4.44 follow the general rule that the thiocarbonyl absorption maximum is generally greater than 320nm, the carbonyl group is usually transparent in this region.[116]

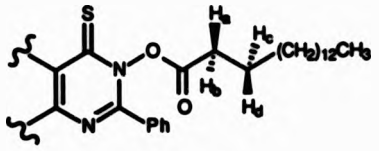
b) NMR

Another interesting feature of these new acyl derivatives is their structure as assigned by ^1H and ^{13}C NMR. In the ^1H NMR spectrum acyl derivatives 4.43a, 4.43c, and 4.44 have a ten line signal appearing at δ 2.23-2.60 ppm as seen in figure 4.02.

Multiplet arising from the coupling of protons α to the carbonyl in 4.43a.

Figure 4.02

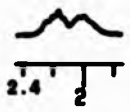
This multiplet was assigned to the methylene α to the carbonyl on the basis of its chemical shift and its integral. This multiplet stems from the differing magnetic environments of H_a and H_b and that of H_c and H_d as shown in Figure 4.03.



4.46

Figure 4.03

This implies that free rotation about the CO—CH_2 bond is restricted. This is probably due to the aliphatic chain lying over the aryl group at the 2–position. In comparison to this effect acyl derivative **4.43b**, which contains the α-naphthalyl group at the 2–position, seems to have only semi-restricted rotation of the aliphatic palmitoyl group. This is evidenced by the broad signal appearing a δ 1.90-2.30 ppm in the ^1H NMR spectrum for the methylene α to the carbonyl, as shown in Figure 4.04.

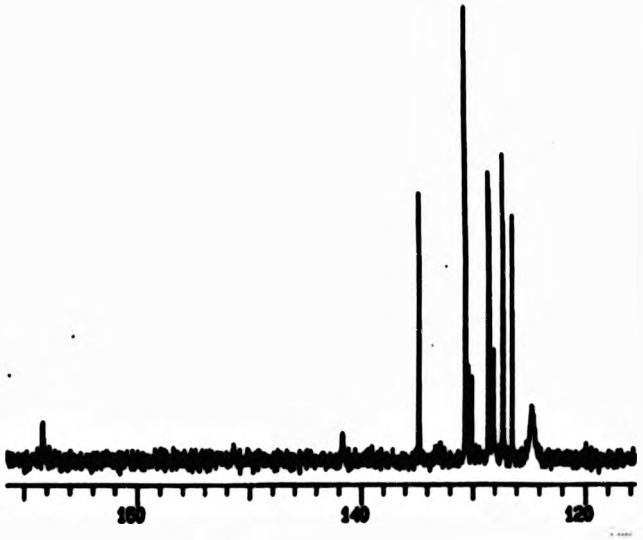


Expanded ^1H NMR spectrum of **4.43b**.

Figure 4.04

Thus, the NMR time scale is not fast enough to observe the individual rotomers in the case of compound **4.43b**. When the temperature was lowered to –60°C and a ^1H NMR spectrum was recorded there was no

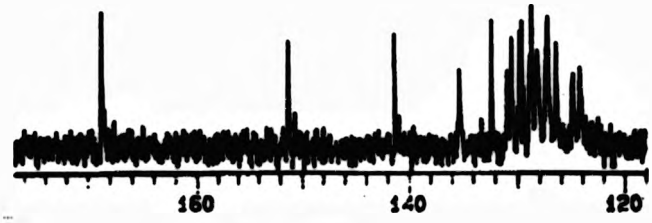
significant change observed. However, the same was not true for the ^{13}C NMR spectrum as at 25°C several broad peaks appeared, most notably that at 124-126 ppm, as shown in Figure 4.05.



Expanded ^{13}C NMR of acyl derivative 4.43b at 25°C.

Figure 4.05

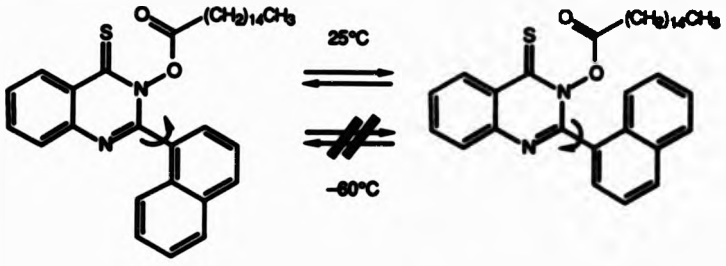
When the temperature was lowered to –60°C this broad peak was resolved into two distinct lines, as shown in Figure 4.06.



Expanded ^{13}C NMR of acyl derivative 4.43b at –60°C.

Figure 4.06

Indeed the ^{13}C NMR spectrum at –60°C showed extra peaks which could represent signals from both rotomers, thus the rotation was frozen out enough for the ^{13}C NMR time scale to observe both rotomers (Scheme 4.08).



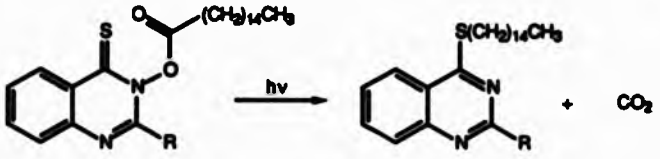
Scheme 4.08

4.1.3 REACTIVITY

Quantum yields have been determined for the trapping of alkyl radicals derived from the acyl derivatives 4.43a-c with bromotrichloromethane. These will be described in Chapter 5.

Thiohydroxamic Acid Derivatives

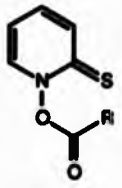
The simplest radical reaction that the O-acyl derivatives **4.43a-c** and **4.44** can undergo is decarboxylative rearrangement leading to the nor-alkyl sulphides, Schemes 4.07 (page 100) and 4.09. The yields and conditions are summarized in Table 4.07 and are compared with those of the acyl derivatives of **1.95** and **4.02** (Structures 4.01 and 4.10).

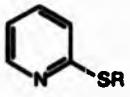


4.43a R = Ph
b R = 1-Naphthyl
c R = 4-PhOMe

4.47a R = Ph
b R = 1-Naphthyl
c R = 4-PhOMe

Scheme 4.09





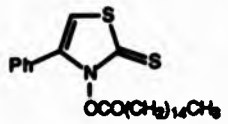
4.11 **4.13** R = $-(CH_2)_{14}CH_3$

4.48a **4.49a** R =

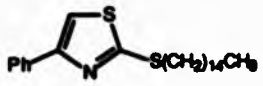
4.48b **4.49b** R =

Structures 4.10

Thiohydroxamic Acid Derivatives



4.07



4.13

Structures 4.10 (Contd.)

Table 4.07

Yields of decarboxylative rearrangement for O-acyl derivatives of thiohydroxamic acids.†

Acyl Derivative	Time	Nor-Alkyl Sulphide (yield%)	m.p. °C	lit. m.p °C. Ref
4.07	8 hrs	4.13(70)	52-54	53[24]
4.11	30 min	4.17(90)	50-53	48-55[72,117]
4.48a	30 min	4.49a(87)	oil	—[117]
4.48b	30 min	4.49b(86)	oil	—[118]
4.43a*	10 min	4.47a(96)	53	—
4.43b	10 min	4.47b(94)	80	—
4.43c	10 min	4.47c(90)	79-80	—
4.44	5 min	4.45(98)	89-90	—

Notes to Table 4.07; †: All photolysis carried out in 0.1 M CH_2Cl_2 solutions under argon with a 250 W tungsten lamp; *: In this case the CH_2Cl_2 was rigorously degassed (liquid nitrogen) prior to use.

As is shown in Table 4.07 yields for the decarboxylative rearrangement to the corresponding nor-alkyl sulphide are similar. However, the time needed for completion of the reaction is less for the new acyl derivatives 4.43a-c and

4.44 than for compounds 4.07, 4.11, 4.43a, and 4.43b. This was further investigated and the half-lives of this rearrangement were determined. The results are summarized in Table 4.06. There is a dramatic difference between the half-lives of the quinazoline-4(3*H*)-thione acyl derivatives and the corresponding N-hydroxy-2-thiopyridone acyl derivative. Thus, the half-life of acyl derivatives 4.23a-c is an order of magnitude less than that of derivative 4.11. The half-life of 4.44 is lower still (14 seconds) and probably reflects the increase in the molar extinction coefficient.

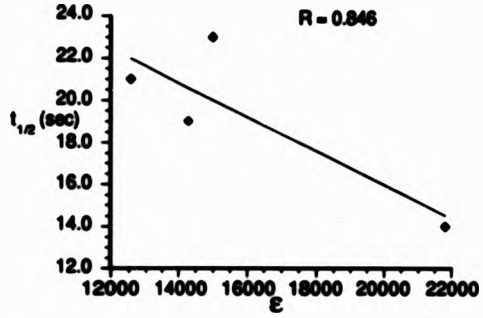
Table 4.06*

Half-lives of palmitoyloxy derivatives of the thiohydroxamic acids.

Compound	4.07	4.11	4.43a	4.43b	4.43c	4.44
$t_{1/2}$(sec)	7,200†	200	19	23	21	14

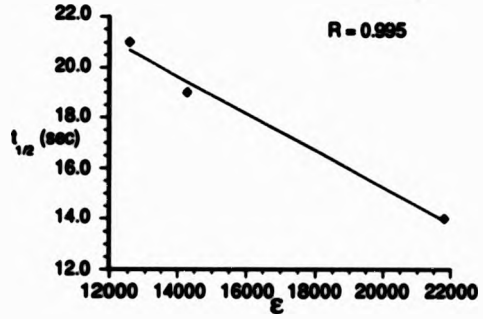
Notes to Table 4.06; *: Half-lives determined in 0.1 M $CDCl_3$ solutions with a 250W tungsten lamp at 0°C; †: Reference 24.

When the half-lives of the 2-arylquinazoline derivatives are plotted against their respective molar extinction coefficients a straight line with a poor fit results (regression value of 0.846, Figure 4.07). If however only 2-phenylquinazoline derivatives (4.43a, 4.43c, and 4.44) are considered a straight line is again obeserved but with a better fit (regression value of 0.995) as shown in Figure 4.08.



Plot of half-life versus the molar extinction coefficient of the 2-aryiquinazoline derivatives 4.43a-c and 4.44.

Figure 4.07



Plot of half-life versus the molar extinction coefficient of the 2-phenylquinazoline derivatives 4.43a, 4.43c and 4.44.

Figure 4.08

Thus for every one second decrease in the half-life there must be a corresponding increase of 1,400 in the molar extinction coefficient.

Photolysis of 4.11 in the presence of 4.43a-c gave corresponding increases in the respective half-lives of 4.43a-c (36-40 sec) as summarized

in Table 4.09. This is probably due to a filter effect, i.e. the light being absorbed inefficiently by 4.11 instead of 4.43a-c.

Table 4.09*

Competition of photolysis of acyl derivatives of thiohydroxamic acids.

Compound	4.11 + 4.43a	4.11 + 4.43b	4.11 + 4.43c	4.11 + 4.07
$t_{1/2}$ of 4.11	196	200	198	253
$t_{1/2}$ of 4.43 or 4.07	37	36	40	399

Notes to Table 4.09; *: 0.1 M in both components of $CDCl_3$ solutions, 250 W tungsten lamp, $t_{1/2}$ values reported in seconds.

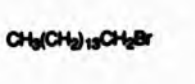
In all the cases there was no 4.17 observed until approximately 80-90% of 4.43a-c had been consumed. This shows the preferential attack of the alkyl radical on the thiocarbonyl of acyl derivatives 4.43a-c rather than on the thiocarbonyl of acyl derivative 4.11. When 4.11 and 4.07 were photolysed together the $t_{1/2}$ value of 4.11 was increased by 50 seconds. This increase is probably due to interference of the thiocarbonyl of 4.07 leading to an inefficient radical chain thus retarding the reaction slightly. These results suggest that the thiocarbonyl of the quinazoline-4(3*H*)-thione system (4.43a-c and 4.44) is more reactive towards alkyl radicals than that of either the thiocarbonyl in 4.11 or 4.07.

Table 4.10*

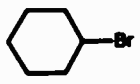
Trapping of the alkyl radical derived from acyl derivatives of thiohydroxamic acids with bromotrichloromethane.

Acyl derivative	Reaction time (minutes)	Alkyl bromide (yield%)	Thioether (yield%)	Sulphide (yield%)
4.11	20	4.50(90)	4.53(80)	4.17(4)
4.48a	20	4.51(80)	4.53(73)	4.49a(15)
4.48b	20	4.52(75)	4.53(50)	4.49b(20)
4.43a	5	4.50(82)	4.54a(85)	—
4.43b	5	4.50(78)	4.54b(81)	—
4.43c	5	4.50(95)	4.54c(97)	—

Notes to Table 4.10; *: Photolyses were conducted with 0.1 M solutions of the acyl derivative in CH_2Cl_2 containing 5 equivalents of $BrCCl_3$ under argon with a 250 W tungsten lamp.

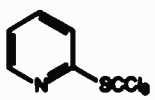


4.50

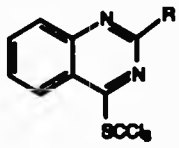


4.51

4.52



4.53



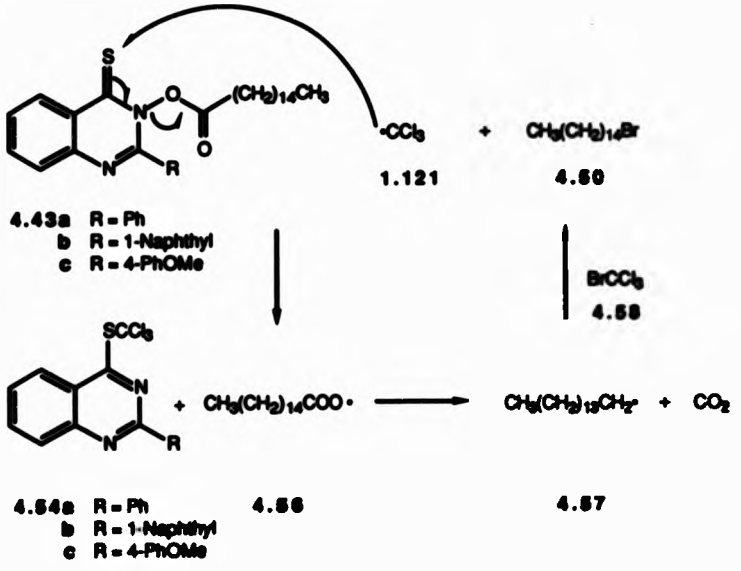
4.54a R = Ph
b R = 1-Naphthyl
c R = 4-PhOMe

Structures 4.11

To determine the synthetic utility of these new acyl derivatives 4.43a-c an efficient radical trap, bromotrichloromethane, was employed. Results are

summarized in Table 4.10 and compared to those of the corresponding reaction of acyl derivatives 4.11, 4.48a, and 4.48b.

As can be seen from Table 4.10 the yields of alkyl bromide derived from the new acyl derivatives 4.43a-c compare favourably with the yields obtained from acyl derivatives 4.11, 4.48a, and 4.48b. The isolation of the trichlorothioether 4.54a-c (Structures 4.11) in comparable yields to that of the bromide confirms this to be a radical chain process as outlined in Scheme 4.10.



Scheme 4.10

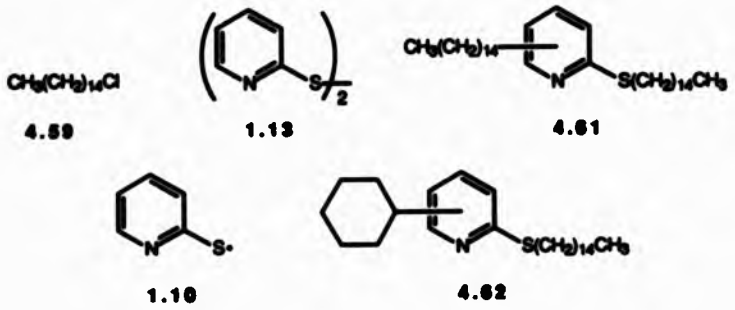
Thus, the trichloromethyl radical 1.121 attacks the thiocarbonyl of the acyl derivative 4.43, which after cleavage of the nitrogen-oxygen bond forms the trichlorothioether 4.54 and the acyloxy radical 4.56. After loss of carbon

dioxide from the acyloxy radical 4.56 the alkyl radical 4.57 is formed. Attack by the alkyl radical 4.57 on the bromine atom in bromotrichloromethane 4.58 forms the desired pentadecyl bromide 4.50 and generates the trichloromethyl radical 1.121. This radical 1.121 then can continue the radical chain reaction.

A further example of the reactivity of the thiocarbonyl in acyl derivatives 4.43a-c towards radicals was shown by a low temperature photolysis experiment. Thus, comparison of the photolysis of the thiohydroxamic acid acyl derivatives 4.11 and 4.43b at –60°C with the trap bromotrichloromethane, clearly demonstrated the superiority of this new group of compounds as a source of carbon radicals at such low temperatures. Hence, photolysis of 4.11 (0.1 M, $CDCl_3$, $CBrCl_3$ 5 equivalents) at –60°C for twenty minutes resulted in the formation of only 15% of the trapped product (bromopentadecane, 4.50). The rearranged product 4.17 was also formed , 8%, the remainder being the unreacted acyl derivative 4.11 (77%). In contrast, when 4.43b or 4.43c (0.1 M, $CDCl_3$, $CBrCl_3$ 5 equivalents) was photolyzed under the same conditions (–60°C, 20 minutes) there was a quantitative conversion to the trapped product bromopentadecane 4.50. No rearranged product 4.47b or 4.47c was observed. This is an important result because as noted in Chapter 1 (page 43, Scheme 1.27) low temperature photolysis (–64°C) of 4.11 results in up to 75% dimerization of the pentadecyl radical. The fact that this was not seen in the case of 4.47b or 4.47c further supports the proposal that the thiocarbonyl group in these compounds 4.43a-c is more reactive towards chain carrying radicals than that of the thiocarbonyl of 4.11. High yielding low temperature photolysis could be important synthetically. At low temperatures rotational barriers are more important and thus the thermodynamically most favoured conformer is present in a higher

concentration. Thus, this may allow stereoselective radical reactions at low temperatures.

An experiment to determine the products of chain termination in a radical chain reaction was undertaken. Thus, photolysis of N-hydroxy-2-thiopyridone palmitoate **4.11** with visible light (tungsten) in carbon tetrachloride solution gives (the expected) pentadecyl chloride **4.59**, 83% (Structures 4.15). The corresponding chain-carrier radical $\cdot CCl_3$, **1.121** reacts with **4.11** giving a similar amount (82%) of 2-trichloromethylthiopyridine **4.53**. The presence of dipyridyl disulphide **1.13** indicates the role played by the photolytic initiation step. Its amount (0.7%), however, shows clearly that the radical chain, once initiated, is carried effectively by the chain-carrier trichloromethyl radical **1.121**.



Structures 4.12

The presence of the expected rearrangement product, the thioether **4.17** (9%) indicates that the trap is not good enough, i.e. the thiocarbonyl group of **4.11** competes for the carbon radical **4.57** formed by the decarboxylation process from the acyloxy radical **4.56**. This thioether, **4.17**, in turn, can also act as a

trap for carbon radicals giving a ring-alkylated derivative of the nor-alkyl sulphide, **4.61** in 4% yield. The rearranged compound **4.17** is an unwanted, but chain-carrier by-product.

Photolysis of **4.48a** in $CDCl_3$ solution without any reactive trap results in a more complicated picture. In the absence of other effective chain-carriers the contribution of the photoproduct thiyl radical **1.10** increases, indicating very short radical chains. Consequently, the yield of dipyridyl disulphide **1.13** increases to 34%, an almost 50-fold increase. The rearranged product thioether **4.49a** is present in 32% yield. The presence of the trichloromethylthiopyridine **4.53** (3.6%), cyclohexanol (3.7%), cyclohexanone (4.2%), cyclohexane (trace), and cyclohexyl-(2-cyclohexylthio)pyridine **4.62** (0.22%) all indicate possible termination steps. The oxygenated products are formed by the reaction of the carbon radical generated, with traces of oxygen dissolved in the $CDCl_3$ solution. The reaction itself was carried out under argon, but the solvent was not degassed. The ring alkylated products **4.61**, and **4.62** presumably arise *via* a similar mechanism to that shown in Chapter 1 (page 49, Scheme 1.31).

4.2 Conclusion

The clean reaction mixtures associated with the acyl derivatives **4.43a-c** and **4.44** indicate a delicately balanced reactivity of the disciplinary thiocarbonyl group of these new radical precursors. However, their photolytic half-lives (14-23 seconds) reflect their great reactivity as well as their approach to the limit where light sensitivity still allows careful synthetic manipulations. Of particular note is the ability of the thiocarbonyl group to still discipline the radical at low temperatures (–60°C) in contrast to that of the

thiocarbonyl group of acyl derivatives 1.09. The differences between 4.43a-c and 4.44 to 4.11 as generators of radicals reside firstly in their two fold greater molar extinction coefficients. Secondly, it is due to the greater reactivity of the thiocarbonyl in 4.43a-c and 4.44 towards carrier radicals.

Chapter 5

Quantum Yield Determination of the Radical Reactions Associated with Acyl Derivatives of N-Hydroxy-2-thiopyridone and 2-Aryl-3-hydroxy-3,4-dihydroquinazoline-4(3*H*)-thione.

Chapter 5

5.0 INTRODUCTION

In the last seventy years an understanding of photochemical processes has developed. Only after the concept of quantization of energy had been established has a logical pattern of the interaction between light and matter emerged. The theory of black body radiation, developed by Planck, postulates that radiation possessed particulate properties. These particles (photons) of radiation with a specific frequency ν have associated with them a fixed energy E[119], Equation 5.01.

$$E = h\nu$$

Equation 5.01: Relationship between energy and frequency, where $h = 6.6256 \times 10^{-34}$ J s (Planck's constant).

The frequency ν can be expressed in terms of wavelength, Equation 5.02.

$$\nu = c/\lambda$$

Equation 5.02: Relationship between frequency and wavelength, where $c = 2.9979 \times 10^{8}$ m s^{-1} (speed of light).

For a molecule the energy of excitation equals hc/λ whilst for one mole the energy of excitation is given by Equation 5.03.[120]

$$\frac{N h c}{\lambda} = \frac{6.023 \times 10^{23} \times 6.6256 \times 10^{-34} \times 2.9979 \times 10^{8}}{\lambda(nm) \times 10^{-9}}$$

(N = Avogadro's number)

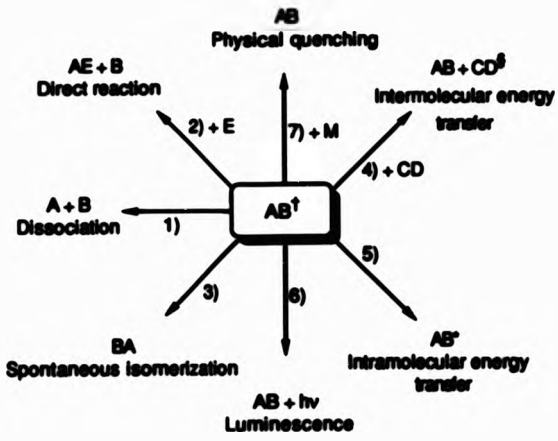
$$= \frac{1.20 \times 10^{5}}{\lambda(nm)} \quad k J mol^{-1}$$

Equation 5.03

Thus, absorption by a molecule of radiation in the ultraviolet (200-400 nm) or visible (400-800 nm) region of the spectrum may result in an excited state of sufficient energy that the energy absorbed is comparable in magnitude to bond dissociation energies. Hence, using Equation 5.03, if absorption occurs at 250 nm, then the energy associated with this transition (E = 480 k J mol^{-1}) is greater than the bond dissociation energy of a carbon-carbon σ-bond (D ~ 347 k J mol-1).[120]

It must be noted however that not every photon (hν) absorbed by a molecule will produce a chemical change. Figure 5.01 shows the general process which an excited species can undergo and Figure 5.02 shows the Jablonski diagram for the possible excitation and deactivation routes.

Quantum Yields



Notes: †; §; °; indicate the presence of electronic excitation and not necessarily differences in states. One or both of the products in processes 1-3 may be excited.

Figure 5.01: General processes that excited species can undergo.

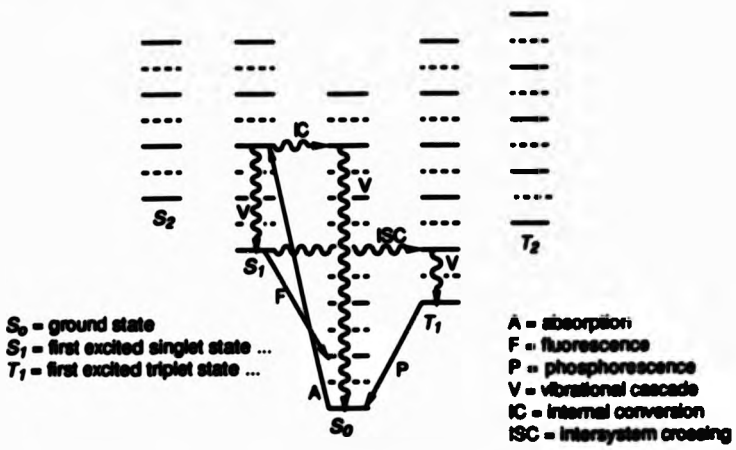


Figure 5.02: A Jablonski diagram showing excitation and deactivation routes.

Quantum Yields

The thiocarbonyl group can undergo four general excitations, all of which involve promotion of an electron from one molecular orbital to another of higher energy. These four are, $\sigma^* \leftarrow \sigma$, $\sigma^* \leftarrow n$, $\pi^* \leftarrow \pi$, and $\pi^* \leftarrow n$. Figure 5.03 illustrates these processes.

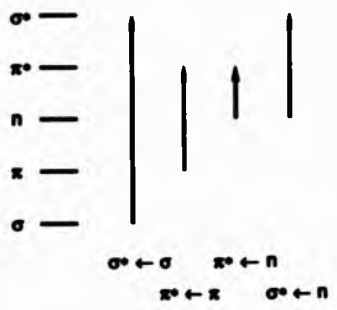


Figure 5.03: Electronic excitation from one molecular orbital to another.

Excitation of an electron from either $\sigma^* \leftarrow \sigma$ or $\sigma^* \leftarrow n$ generally requires too high an energy to be of interest to organic chemists, (>150 nm and 200 nm, respectively). Using the definitions of S_0, S_1 and T_1 in Figure 5.02 it is possible to show the differing states for $\pi^* \leftarrow \pi$ and $\pi^* \leftarrow n$ excitations (Figure 5.04). Although the $\pi^* \leftarrow n$ excitation is energetically more favoured than the $\pi^* \leftarrow \pi$ excitation for the thiocarbonyl group, the latter generally has a molar extinction coefficient (a measure of transition probability, ε) of 10^2-10^4 $m^2\ mol^{-1}$, indicating a high probability of excitation, while for the former ε is usually in the range of 1-5 $m^2\ mol^{-1}$.[120, 121]

Quantum Yields

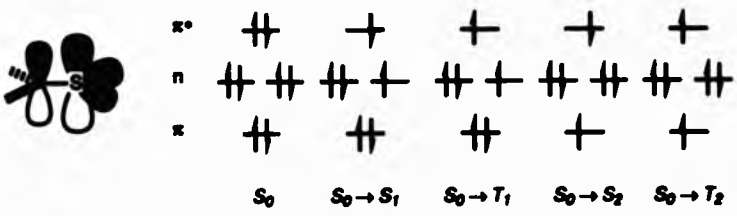


Figure 5.04[122]

The low transition probability for the π* ← n excitation reflects the fact that it is a symmetry forbidden transition.

The excited state most responsible for chemical reactions in organic photochemistry is the triplet state. This is because the triplet state has the longest lifetime, as, in order for the excited electron to fall back to the ground state (S_0), an inversion of electron spin is required. Direct excitation of $S_0 \rightarrow T_1$ or $S_0 \rightarrow T_2$ is rare because the transition is spin-forbidden. Therefore, triplet states are usually formed from $S_1 \rightarrow T_1$ (intersystem crossing, see Figure 5.02) which is efficient when singlet and triplet states are of comparable energy.[123] Using the arguments above, it is possible to explain the thiocarbonyl excitation processes for derivatives of the type 1.09, 4.43a-c, and 4.44. The extinction coefficients (ε) of these derivatives which are assignable to the thiocarbonyl group are in the order of 7-21 x 10^2 m^2 mol^{-1} which can be assigned to a π* ← π transition.[120, 121, 123] Initially this is a $S_0 \rightarrow S_2$ excitation which rapidly undergoes internal conversion (IC) and/or vibrational cascade to form an S_1 excited state. This excited state can then further undergo intersystem crossing (ISC) and vibrational cascade (V) forming the longer lived T_1 state. The life time of the

singlet excited state, given by Equation 5.04, is in the range of 10^{-9} to 10^{-5} seconds.

$$\text{life time of } S_1 \text{ state, } \tau = \frac{10^{-5}}{\varepsilon_{max}\ (m^2\ mol^{-1})} \text{ seconds}$$

Equation 5.04[120]

For comparison as mentioned earlier, triplet states are much longer lived and have life times in the range of 10^{-5} to 10^{-3} seconds.[120]

When a molecule is irradiated, absorption of a single photon normally occurs. The excited species can then undergo competition between radiative and non-radiative deactivation and chemical reaction, as shown earlier in Figures 5.01 and 5.02. However, not every photon that is absorbed is necessarily effective in bringing about a chemical reaction. Specifically in the case of thiocarbonyls, quenching of the triplet excited state by the ground-state thione is observed. In the case of thiobenzophenone the bimolecular quenching constant is close to that expected of diffusion control.[123]

The efficiency of a photochemical process is therefore of fundamental importance in chemistry. The quantum yield, Φ, defines the efficiency of a photochemical process in relation to either a product molecule or the decomposition of the starting molecule. The quantum yield for a given outcome, x, of a reaction Φ_x is defined by Equation 5.05.[120]

$$\Phi_x = \frac{\text{number of molecules reacting to produce a given outcome, x, per unit volume per unit time}}{\text{number of photons absorbed per unit volume per unit time}}$$

Equation 5.05[120, 124, 125]

Quantum Yields

The nature and complexity of a reaction determines its quantum yield. The quantum yield of the formation of a specific product may or may not be the same as the quantum yield of the decomposition of the starting material. In most photochemical reactions the quantum yield ranges from zero to unity. A quantum yield greater than unity implies a chain reaction. In such cases the quantum yield value may be several powers of ten, for example the formation of hydrogen chloride by the photolysis of highly pure chlorine and hydrogen gases results in quantum yields in the range of $1x10^6$-10^7 at room temperature.[124] Similarly, the quantum yield for the reaction of bromine with alkanes is also large, approximately $1x10^5$.[124] The quantum yield for the photoinduced polymerization of methyl methacrylate was found to be in the range of 150-341 for conversions of nearly 5% to polymer.[10]

5.01 ACTINOMETRY

Determination of the quantum yield for a given reaction depends on the measurement of the reaction product and measurement of the light intensity. Chemical analysis can be used to determine the former and is not discussed here. Light intensity, I, the number of photons per second, has been measured by three main methods by photochemists. Firstly, by the thermopile-galvanometer system, secondly by a chemical actinometer, and thirdly by the phototube approach.[124] The simplest and most available method is chemical actinometry, which is explained here. Information concerning the remaining methods can be found in Calvert and Pitts.[124] The most widely used liquid-phase actinometer consists of a sulphuric acid solution of potassium trisoxalatoferrate.[120, 124, 126] The ferrioxalate

actinometer is an ideal choice because of its thermal stability, availability, reproducibility, and uniform response over a large wavelength range (250-450 nm). This actinometer, used in aqueous solutions, does not require degassing and reacts with light as shown in Equation 5.06.

$$[Fe^{III}(C_2O_4)_3]^{3-} \xrightarrow{h\nu} [Fe^{II}(C_2O_4)_2]^{2-} + C_2O_4^{\bullet-} \quad (a)$$

$$C_2O_4^{\bullet-} + [Fe^{III}(C_2O_4)_3]^{3-} \longrightarrow C_2O_4 + [Fe^{III}(C_2O_4)_3]^{2-} \quad (b)$$

$$[Fe^{III}(C_2O_4)_3]^{2-} \longrightarrow [Fe^{II}(C_2O_4)_2]^{2-} + 2CO_2 \quad (c)$$

Equation 5.06[126]

It can be seen from Equation 5.06 that although only one photon is absorbed the oxalyl radical anion produces, *via* the dark reactions, (b) and (c) another molecule of potassium ferrous oxalate. Hence, the observed quantum yield is twice the quantum yield of the primary photochemical process (a). The iron(II) oxalate complex does not absorb radiation in the range of the actinometer (250-450 nm). The concentration of the iron(II) can be measured by forming the iron(II) 1,10-phenanthroline complex which can be analyzed spectrophotometrically at 510 nm by virtue of its high molar extinction coefficient ($\varepsilon = 1.11 \times 10^4$ l/mole-cm). The light intensity can be expressed by Equation 5.07.

$$I = \frac{M^{Fe2+} \times V_1 \times 10^{-3} \times 6.023 \times 10^{23}}{t_1 \times \Phi_{Fe2+}} \quad \text{quanta/second}$$

M^{Fe2+} = molarity of the iron(II) formed during the photolysis
V_1 = volume of the cell photolyzed (cm^3)
Φ_{Fe2+} = quantum yield of Fe^{2+} at specific wavelength
t_1 = time the cell containing the iron actinometer was irradiated (seconds)

Equation 5.07[114, 127]

Quantum Yields

Knowing the light intensity I, the quantum yield for a given reaction at a given wavelength can be determined by Equation 5.08.

$$\Phi = \frac{M^P \times V_1 \times 10^{-3} \times 6.023 \times 10^{23}}{I \times t_1}$$

M^P = molarity of product whose quantum yield is to be determined
V_1 = volume of the cell photolyzed (cm^3)
I = light intensity (quanta per second)
t_1 = time the cell containing the sample was irradiated (seconds)

Equation 5.08[114, 127]

5.03 EQUIPMENT

Monochromatic light is essential for the measurement of quantum yields. Mercury vapour arc lamps are the usual source of such light, providing radiation in the ultraviolet and visible regions of the spectrum (200 nm, 599 k J mol-1 to 750 nm, 159 k J mol^{-1}). The three main types of mercury lamps are low, medium and high pressure with each having different characteristics. Low pressure mercury lamps (~ 0.005 torr) mainly emit at 184.9 nm and 253.7 nm and the former is only transmitted if ultra-pure quartz is used. Medium pressure mercury lamps (1-10 atmosphere) work at higher temperatures and thus need a few minutes to warm up before operational stability is attained. The wavelengths which medium lamps emit are 184.9 nm, 253.7 nm (in diminished intensity due to the higher pressures), 265.4 nm, 310 nm and 365 nm. High pressure mercury lamps operate further in the visible region but the high pressure (200 atmosphere) results in considerable line broadening and thus is not really applicable to the determination of quantum yields.

Quantum Yields

Isolation of particular lines is easily attained using suitable filters.[126] Pyrex does not allow light under 280 nm and interferes with light below 320 nm.

There are several different ways of measuring light intensity and one of the most popular is the so called "merry-go-round" method.[126, 127] This method requires the solution under investigation to have a high optical density to enable all light hitting the cell to be absorbed. Another method involves splitting the beam so that direct measurement of the light intensity is possible while determining the quantum yield.[124, 126] Neither of these methods were used in this study and Figure 5.05 shows the set up used for quantum yield and light intensity determination. The light intensity was measured before and after a sample was investigated but not during.

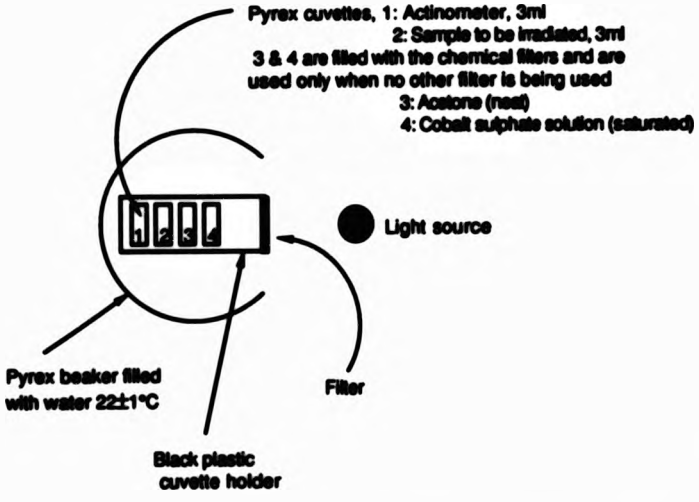


Figure 5.05

Quantum Yields

5.1 Discussion

The actinometer used in the present investigation was potassium trisoxalatoferrate $K_3[Fe(C_2O_4)_3]$ which was prepared from iron(III) chloride and potassium oxalate by a standard procedure.[124] A 0.006 M solution of the above complex was prepared and was stable indefinitely in the dark. This solution absorbs 99% of all light up to 390 nm with a quantum yield (Φ_{Fe2+}) of 1.21 at 366 nm. As suggested,[124] the spectrophotometer was calibrated prior to in all measurements of quantum yields. This was achieved by making standard solutions of the iron(II) phenanthroline complex in water and then checking the molar extinction coefficient at various complex concentrations. The results obtained are shown in Figure 5.06.

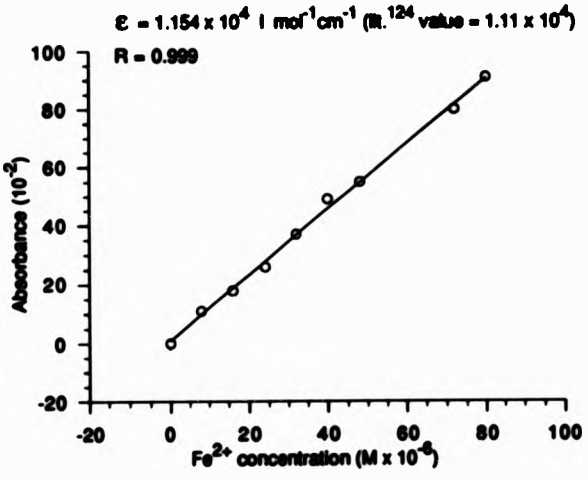
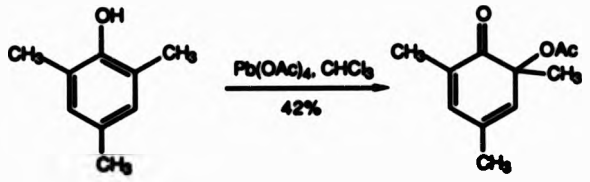


Figure 5.06: Calibration of spectrophotometer.

Quantum Yields

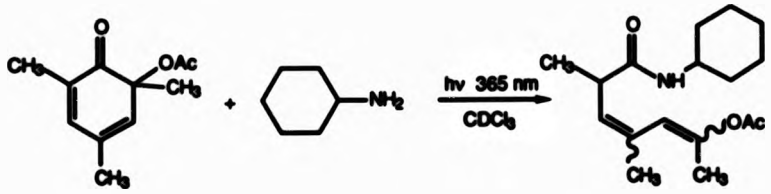
The value obtained for the molar extinction coefficient was within ±3% of that quoted in the literature[124] ($\varepsilon = 1.11 \times 10^4$ l mol^{-1} cm^{-1}).

The system used for quantum yield determination was checked by the use of a 365±5 nm interference filter.[128] The compound studied was 2,4,6-trimethyl-6-acetoxycyclohexa-2,4-dienone **5.02** which was made by treating 2,4,6-trimethylphenol **5.01** with lead tetraacetate in chloroform,[129, 130, 131] Scheme 5.01. This compound **5.02** has a well documented history of photochemistry[132] and, once excited, the ketene formed can be trapped by good nucleophiles such as cyclohexylamine **5.03**, Scheme 5.02, with a known quantum yield ($\Phi = 0.53$, 365 nm, 20°C [133, 134]). The quantum yield was reproduced in this study ($\Phi = 0.52$, 365 nm, 22°C).



5.01 **5.02**

Scheme 5.01



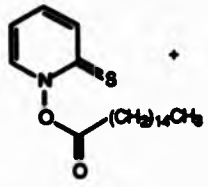
5.02 **5.03** **5.04**

$\Phi = 0.52$ (lit.[133, 134] 0.53)

Scheme 5.02

Quantum Yields

Two types of filters were used to isolate the mercury line at 366 nm. The first filter was a chemical filter consisting of acetone (neat) and a saturated solution of cobalt sulphate,[126] both in Pyrex glass photometer cuvettes. This gave a quantum yield of 29 for the formation of bromopentadecane 4.50 with the radical reaction of 4.11 with bromotrichloromethane 4.58, Scheme 5.03. The second filter used was a band pass filter 360 nm[135] which gave, under the same conditions as above, bromopentadecane 4.50 with a quantum yield of 27. The quantum yields are the average of five measurements. The use of two differing filter systems provides another check for the system used to measure the quantum yields.



$CBrCl_3$ $\xrightarrow[22\pm1°C]{h\nu,\ CDCl_3}$ $CH_3(CH_2)_{14}Br$

Chemical filter Φ = 29±7%
Band pass filter Φ = 27±7%

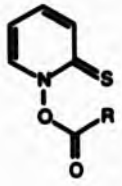
4.11 4.58 4.50

Scheme 5.03

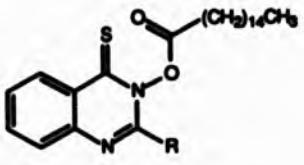
With these checks, quantum yields of trapped products were determined with five differing traps, namely carbon tetrachloride, bromotrichloromethane, carbon tetrabromide, diphenyldisulphide, diphenyldiselenide, and phenyl vinyl sulphone. The pentadecyl-, cyclohexyl-, and *tert*-butyl-radicals were chosen to represent primary, secondary, and tertiary radicals, respectively. All the radicals were formed from light initiation of their respective acyl derivatives with N-hydroxy-2-thiopyridone 1.95.

Quantum Yields

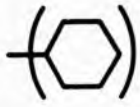
Conversions to the trapped product were kept low (generally 5-20%) so as not to upset the concentrations of the starting compounds. Results of the experiments are given in Tables 5.01, 5.02 and 5.03. Five parallel samples were run and the yield of the trapped product was determined by ^{1}H NMR or glc with the appropriate internal standard (propyl acetate or tetradecane). All of the trapped products are known compounds and were identified in the reaction mixtures by comparison with ^{1}H NMR data available in the literature references given in Table 5.04.



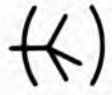
4.11 R = $-(CH_2)_{14}CH_3$



4.43a R = Ph
b R = 1-Naphthyl
c R = 4-PhOMe



4.48a R =



4.48b R =

Structures 5.01

Quantum Yields

Table 5.01

Quantum yields of photolysis products of thiopyridone derivatives 4.11, 4.48a, and 4.48b.

		Quantum Yields[a, b] (Φ)		
Entry	Trap (5 eq.)	4.11[c]	4.48a[c]	4.48b[d]
1	CCl_4	6	23[d]	13
2	$CBrCl_3$	29	31	8
3	CBr_4	32	28	24
4	$(PhS)_2$	24	27	11
5	$(PhSe)_2$	14	19	10
6	CH_2=$CHSO_2Ph$	35	34	22

a: Average of five experiments with a chemical filter; b: Unless otherwise stated, data obtained in 0.1 M solutions of the thiopyridone derivatives in the given solvents at 22±1°C; c: Solvent = CH_2Cl_2; d: Solvent = $CDCl_3$.

Table 5.02

Quantum yields of photolysis products of 4.11.

Entry	Trap	Quantum Yield[a] (Φ)
1	CCl_4	24[b]
2	$CBrCl_3$	24[b](55[c])
3	$(PhS)_2$	8[d]
4	$(PhSe)_2$	27[d]

a: Average of five experiments with a chemical filter with all solutions at 22±1°C; b: Trap as solvent, for CCl_4 this means 102.91 equivalents of trap in the case of a 0.1 M solution of 4.11 in CCl_4. For $CBrCl_3$ this means 101.47 equivalents of trap related to the 0.1 M solution of 4.11 in $CBrCl_3$ solution; c: Saturated solution of 4.11 (0.771 M) in $CBrCl_3$ as solvent and trap. This means 13.16 equivalents of the trap; d: CH_2Cl_2 solution of 4.11 (0.1 M) + 2 equivalents (0.2 M) of trap.

Quantum Yields

Table 5.03

Quantum yields of photolysis products 4.11 and 4.43a-c using a band pass 360 nm filter.[135]

Trap 5 (eq)[b]	Quantum Yields[a] (Φ)			
	4.11	4.43a	4.43b	4.43c
$CBrCl_3$	27	60	32	54

a: Data given are for 0.1 M solutions in $CDCl_3$ at 22±1°C; b: Concentration of trap in the reaction mixture before photolysis (0.5 M).

Table 5.04

Photolysis products of acyl derivatives 4.11, 4.48a, 4.48b, and 4.43a-c.

	Substituent		
Product type[a]	R = $-(CH_2)_{14}CH_3$	R = $-C(CH_3)_3$	R = $-cyclo C_6H_{11}$
RCl	4.59[136]	5.05[136]	5.06[136]
RBr	4.50[137]	4.52[139]	4.51[138]
RSPh	5.07[138]	5.08[140]	5.09[142]
RSePh	5.10[138]	5.11[141]	5.12[143]
$RCH_2CH(SPy)SO_2Ph$	5.13[139]	5.14[139]	5.15[139]

a: The products are all known compounds. ^1H NMR, glc and GC-MS were used to identify these products. The data obtained was compared with the data present in the literature or with authentic samples.

From Table 5.01 it is seen that the quantum yield is generally in the range of 10-30 for primary, secondary and tertiary radicals derived from the respective acyl derivative of N-hydroxy-2-thiopyridone. These quantum yields can be related directly to the chain length of the reaction. For example, in the reaction of 4.11 with bromotrichloromethane, the quantum yield of

bromopentadecane 4.50 is 29, that is, one photon causes twenty-nine product molecules, therefore the chain length is said to be 29. The values obtained for the halogenated traps generally obey the order of reactivity CCl_4 < $CBrCl_3$ < CBr_4 determined from the rate constants of radical abstraction of a halogen from the trap.[144] The relatively larger values obtained for the reaction of 4.48a and 4.48b probably stem from solvent interactions with the radical as these values were determined in $CDCl_3$ solutions. It has been determined that the carbon-chlorine bond in chloroform is ten times more reactive towards carbon radicals than the carbon-chlorine bond in carbon tetrachloride.[145, 146] Hence, the radical probably abstracts a chlorine atom from the solvent, present in much higher concentrations, than from the trap.

The bond strength of the selenium-selenium bond is weaker than that of the sulphur-sulphur bond.[147] Thus, diphenyldiselenide would be expected to be a better trap and therefore have a larger quantum yield than diphenyldisulphide. However, this is not what is observed as the quantum yields for entries 4 and 5 in Table 5.01 show the light filtering effect the diphenyldiselenide has, thus retarding the initiation of the acyl derivative. This is not seen in the case of diphenyldisulphide which does not absorb light in the same region. This effect diminishes when only two equivalents of the diphenyldiselenide is used as seen in Table 5.02, entry 5. Here the quantum yield is seen to increase from 14 to 27 for the acyl derivative of 4.11.

The quantum yields for the addition of a primary, secondary or tertiary radical to the electron deficient olefin phenyl vinyl sulphone is relatively high. This shows this to be a facile process which is in accordance with rate constants determined for the addition of radicals to electron deficient olefins.[14]

There is a dramatic increase in radical chain length from 29 to 55 when a saturated solution (0.771 M) of the acyl derivative 4.11 in $BrCCl_3$ is

photolyzed, Table 5.02. This is due to the relative increase in concentration of the thiocarbonyl towards the trichloromethyl radical which increases the radical chain length.

When acyl derivative 4.11 is compared to derivatives 4.43a-c under the same reaction conditions (5 equivalents of $CBrCl_3$ trap, 0.1 M, 22°C, Band pass filter[135]), a dramatic difference in the quantum yield is seen, Table 5.03. This is in accordance with the differences in half-lives of these compounds (Chapter 4 page 110 Table 4.08).

5.2 Conclusion

Quantum yields have been determined for N-acyl derivatives of some thiohydroxamic acids and were generally found to be in the range of 10-30. These values are consistent with a radical chain mechanism and give an insight into the differing reactivities of the new acyl derivatives 4.43a-c and the acyl derivatives 4.11, 4.48a, and 4.48b.

A system for the measurement of quantum yields was designed which, when checked with differing filters produced consistent results.

Chapter 6

Experimental.

Chapter 6

6.0 EXPERIMENTAL

E0 General Procedures and Starting Materials.

Melting points were determined with a Kofler hot-stage melting point apparatus and are uncorrected. IR spectra were recorded on a Perkin Elmer 881 spectrophotometer either as solution cells (solvent specified) or on sodium chloride discs. UV-vis spectra were recorded on a Beckman DU-7 spectrometer with solvent as specified, molar extinction coefficients are expressed in l mol^{-1} cm^{-1}. ^{1}H, and ^{13}C NMR spectra were determined for solutions in deuterochloroform (unless specified otherwise) with TMS internal reference on Varian Gemini 200, Varian XL 200E, Varian XL 200. Gas chromatography (glc) measurements were performed on a Chrompack Packard Model 439 gas chromatograph on 30 m capillary columns. GC-MS data were obtained on a Hewlett-Packard 5890 GC-MS system. Mass spectra were obtained on a VG Analytical 70S high resolution double focusing magnetic sector mass spectrometer with attached VG 11/250J data system in the EI or FAB mode. FAB spectra were obtained neat or in glycerol matrix. Microanalyses were performed by Atlantic Microlab, Inc., Norcross, Georgia. Separations by column and flash chromatograph were performed using Merck Kieselgel 60 (Art. 7734) and 60 (230-400 mesh ASTM), respectively. Merck precoated Kieselgel $60F_{254}$ was used for thin layer chromatography and Merck Kieselgel $PF_{254+336}$ for preparative layer chromatography. Solvents were used either as purchased or dried and purified by standard methodology under dry, pure argon. 2,4,6-Trichlorophenyl chlorothionoformate and

pentafluorophenyl chlorothionoformate were kind gifts from Dr. Cs. Jaszberenyi and are now available from Aldrich Chemical Co.. Acid chlorides where not commercially available were synthesized by the action of thionyl chloride or oxalyl chloride on the respective acid. Other reference compounds and starting materials were purchased from Aldrich Chemical Co., Inc., Milwaukee, Wisconsin.

E 1 β-Phenylethyl (2,4,6-trichlorophenyl) thionocarbonate 2.14.

β-Phenylethanol (0.6138 g, 5 mmol), dry pyridine (1 ml, 12.3 mmol) and dry benzene (9 ml) were placed in a round bottom flask and sealed with a rubber septum. To this stirred solution was added 2,4,6-trichlorophenoxythiocarbonyl chloride. The resulting solution was stirred for five and a half hours. The solvent was removed under reduced pressure and the remaining residue was dissolved in methylene dichloride. This solution was then washed with saturated sodium hydrogen carbonate solution and brine. The organic layer was then dried with anhydrous magnesium sulphate and evaporated.

The pure β-phenylethyl (2,4,6-trichlorophenyl)thionocarbonate 2.14 (1.762 g, 97% yield, oil) was obtained by column chromatography on silica (dichloromethane : ether = 10:1; Rf: 0.79); IR ($CHCl_3$, cm^{-1}): 3081, 1742, 1430, 1298, 1193; ^1H NMR ($CDCl_3$) δ 3.16 (t, 2H), 4.78 (t, 2H), 7.2-7.4 (m, 7H); MS m/e: 181 (M^+-$C_6H_2Cl_3$); 241, 239 (M^+-$PhCH_2CH_2O$). FAB $(M+H)^+$ 361 ($^{35}Cl_2{}^{37}Cl$) (Found: Cl, 30.27; S, 8.54 Calcd. for $C_{15}H_{11}Cl_3O_2S$: Cl, 29.41; S, 8.87%).

E 2 Tetradecyl pentafluorophenyl thionocarbonate 2.15.

Tetradecanol (0.9647 g, 4.5 mmol), dry pyridine (0.25 ml, 3 mmol), dry benzene (1.75 ml) and 4-dimethylaminopyridine (0.0750 g, 0.6 mmol) were placed in a round bottom flask and the flask was then sealed with a rubber septum. To this stirred solution was added pentafluorophenyl chlorothionoformate 1.53 (0.8 ml, 5 mmol). The resulting solution was stirred for four hours and then filtered. The filtrate yielded pure tetradecyl pentafluorophenyl-thionocarbonate 2.15 (1.4124 g, 3.2 mmol, 71%) upon removal of the benzene under reduced pressure.

The reaction flask and the precipitate were washed with dichloromethane which was then washed with sodium bicarbonate and brine. The resulting organic layer was dried with anhydrous magnesium sulphate, the pure tetradecyl pentafluorophenyl thionocarbonate 2.15 (0.349 g, 18%; total yield 89%) was recovered upon reduced pressure evaporation. Rf: 0.61 (dichloromethane: ether 10:1); IR ($CHCl_3$, cm^{-1}): 2928, 2857, 1744, 1660, 1520, 1311, 1157, 995; ^1H NMR ($CDCl_3$) δ 0.85 (m, 3H), 1.3 (m, 22H), 1.83 (m, 2H), 4.55 (t, 2H); MS m/e: 257 (M^+-OC_6F_5), 197 (M^+-$OCSOC_6F_5$). FAB $(M+H)^+$ 439. (Found: S, 6.99: Calcd. for $C_{21}H_{29}F_5O_2S$: S, 7.28%).

E 3 Octadecyl pentafluorophenyl thionocarbonate 2.17.

Octadecanol (0.1352 g, 0.5 mmol), dry pyridine (0.0514 g, 0.65 mmol), dry toluene (0.5 ml) and N-hydroxysuccinimide (0.0057 g, 0.05 mmol) were placed in a round bottom flask and sealed with a rubber septum. To this stirred solution was added pentafluorophenyl chlorothionoformate (105 ml, 0.65 mmol). The solution was then stirred for 18 minutes.

Then the solution was filtered and washed with toluene (0.2 ml) yielding pure octadecyl pentafluorophenyl thionocarbonate 2.17 (0.2107 g,

85% yield); mp: 31-32°C; Rf: 0.68 (dichloromethane : hexanes 3:1); IR: ($CHCl_3$, cm^{-1}) 2927, 2856, 1519, 1161; ^1H NMR ($CDCl_3$) δ 0.87 (t, 3H), 1.27 (m, 30H), 1.85 (m, 2H), 4.55 (t, 2H); MS m/e: 313 (M^+-OC_6F_5); 252 (M^+-$OCSOC_6F_5$). FAB $(M+H)^+$ 497, $(M-H)^+$ 495; (Found: S, 6.34. Calcd. for $C_{25}H_{37}F_5O_2S$: S, 6.46%).

A further experiment was undertaken where the reaction was stirred for 14 hours. The solution was then filtered and the toluene evaporated under reduced pressure resulting in an oil. (Crude yield of octadecyl pentafluorophenylthionocarbonate 2.17: 100%). This was then purified by column chromatography on silica gel (dichloromethane : hexanes = 3:1) to give a yield of 97% of pure crystalline 2.17.

E4 Octane and tetradecane: General procedure for one pot deoxygenation.

The alcohol (0.1 mmol), the internal standard, N-hydroxysuccinimide (0.0023 g, 0.02 mmol) and the dry solvent (0.5 ml) were placed in a two-neck flask equipped with a magnetic stirrer bar. The flask was sealed with rubber septa, then dry pyridine (21 µl, 0.26 mmol) and pentafluorophenyl chlorothionoformate (25 µl, 0.15 mmol) were injected, in sequence. The reaction mixture was stirred at room temperature, the precipitate formed was removed by reduced pressure filtration (caution was taken to prevent condensation of water vapor) and the reaction flask was washed twice with the dry solvent (0.2 ml, 0.1 ml). The filtrate was transferred to another flask fitted with a condenser which was attached to an oil bubbler. Dry nitrogen was passed through the system to give an inert atmosphere, then the solution was brought to boil, followed by the addition of a solution of AIBN (1.6 mg, 0.01 mmol), tributyltin hydride (80 µl, 0.3 mmol) in the dry solvent (0.1 ml).

Aliquots were removed every five minutes and the hydrocarbon formation measured by glc. Hydrocarbons were compared to the authentic sample.[137]

Tetradecanol in toluene gave 95% of tetradecane.

Tetradecanol in benzene gave 90% of tetradecane.

Octanol in toluene gave 64% of octane, a blank experiment was carried out using the same conditions and 66% of octane was recorded. Therefore the adjusted yield of octane based on the blank experiment is 97%.

E 5 Ethylbenzene

β-Phenylethyl (2,4,6-trichlorophenyl) thionocarbonate **2.14** (0.0036 g, 0.01 mmol), the internal standard and dry toluene (0.6 ml) were placed in a flame dried two neck flask fitted with a condenser attached to a bubbler. The system was sealed with a rubber septum and flushed with nitrogen to provide an inert atmosphere. The nitrogen source was removed and the solution was stirred and brought to boil.

A solution of AIBN (0.3 mg, 0.002 mmol), tributyltin hydride (4 µl, 0.015 mmol) in dry toluene was then added to the flask. After ten minutes an aliquot was removed and the formation of ethylbenzene measured by glc 97% as compared with the authentic sample.[137]

E 6 Octadecane

Octadecyl pentafluorophenylthionocarbonate **2.17** (0.0090 g, 0.02 mmol) the internal standard and dry toluene (0.3 ml) were placed in a flame dried two neck-flask connected to a condenser equipped with a bubbler and sealed with a rubber septum. The system was flushed with dry nitrogen to provide an inert atmosphere. The nitrogen source removed and the contents of the flask brought to reflux (oil bath temperature: 125°C).

To this boiling solution was added in three portions a solution of tributyltin hydride (27 µl, 0.10 mmol), AIBN, (0.0128 g, 0.8 mmol) in dry toluene (273 µl) (t = 0 min, 120 µl ; t = 3 min, 60 µl; t = 6 min, 120 µl). An aliquot was removed after a further 6 minutes and the octadecane formed measured by glc 83% as compared with the authentic sample.[137]

E7 Preparative deoxygenation of 2.17.

Octadecanol (1.08 g, 4 mmol), N-hydroxysuccinimide (0.046 g, 0.4 mmol) and dry toluene (10 ml) were placed in a two-neck flask equipped with a magnetic stirrer bar. The flask was sealed with rubber septa, then dry pyridine (0.42 ml, 5.2 mmol) was added. The flask was then placed into a warm bath (60°C) until the octadecanol completely dissolved (5 minutes). Once this was achieved the pentafluorophenyl chlorothionoformate (0.84 ml, 5.2 mmol) was injected into the reaction flask. The reaction mixture was stirred at room temperature overnight and the precipitate formed was removed by reduced pressure filtration, the reaction flask being washed twice with dry toluene (2 ml, 2 ml).

The filtrate was then transferred to another flask fitted with a condenser which was connected to an oil bubbler. Dry nitrogen was passed through the system to give an inert atmosphere, the solution was brought to boil, followed by the addition of a solution of AIBN (0.1956 g, 1.2 mmol) tributyltin hydride (3.2 ml, 12 mmol) in dry toluene (2 ml).

After ten minutes a sample was removed and a proton NMR spectrum recorded. Deoxygenation was deemed complete from the absence of the methylene triplet at δ 4.5 ppm. Then the reaction mixture was cooled and the toluene removed by reduced pressure evaporation. The residue was refluxed for three hours in carbon tetrachloride (60 ml). After evaporation, iodine/ether

solution was added until the iodine colour remained, the solution was then diluted with more ether (100 ml) and shaken with 10% potassium fluoride solution (70 ml), filtered and separated. This procedure was repeated until no precipitate was detected. Drying and evaporation gave the crude product which was filtered down a silica gel column to give octadecane (0.73 g, 71.8%, mp: 28°C (lit.[59] 29°C).

E8 3-(1-Oxo-3-phenylpropoxy)-1,2,3-benzotriazin-4(3*H*)-one **3.27a**.

A two neck flask was charged with dihydrocinnamic acid (1.5 g, 10 mmol), 3-hydroxy-1,2,3-benzotriazin-4(3*H*)-one (1.63 g, 10 mmol) and THF (15 ml). The resulting homogeneous solution was cooled (ice bath) and a solution of dicyclohexylcarbodiimide (2.06 g, 10 mmol) in THF (20 ml) was added dropwise over a period of five minutes. The precipitate of dicyclohexylurea was removed by vacuum filtration and the THF of the filtrate evaporated under reduced pressure. The crude product was crystallized from methylene dichloride and pentane to give pure 3-(1-oxo-3-phenylpropoxy)-1,2,3-benzotriazin-4(3*H*)-one (**3.27a**) (2.95 g, 100%); mp 87-90°C; IR ($CHCl_3$, cm^{-1}) 3020, 1811, 1714, 1073; ^1H NMR ($CDCl_3$) δ 3.0-3.2 (m, 4H), 7.2-7.4 (m, 5H), 7.8-7.9 (m, 1H), 7.95-8.05 (m, 1H), 8.2-8.3 (m, 1H), 8.35-8.45 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 30.7, 33.2 (CH_2-s), 126.2, 127.3 (CH-s), 128.9 (2 x CH), 129.3 (2 x CH), 129.5, 133.3, 136.0 (CH-s), 122.7, 139.8, 144.9, 150.9, 169.5 (C_q-s); MS m/e 295 (M^+); Mass Calcd. for $C_{16}H_{13}N_3O_3$ 295.0957, found 295.0982.

E9 (1-Oxo-3-phenylpropoxy)-2-pyridone **3.27b**.

Prepared as for **3.27a**, (100% yield); mp 76-79°C; IR ($CHCl_3$, cm^{-1}) 3006, 1806, 1673, 1595, 1532, 1079; ^1H NMR ($CDCl_3$) δ 2.90-3.15 (m, 4H),

6.08-6.18 (m, 1H), 6.40-6.52 (m, 1H), 7.1-7.4 (m, 7H); ^{13}C NMR ($CDCl_3$) δ 30.6, 33.0 (CH_2-s), 105.2, 122.9, 126.8 (CH-s), 128.4 (2 x CH), 128.7 (2 x CH), 135.4 (CH), 139.4 (C_q), 139.5 (CH), 157.1 (CO-N), 168.8 (COO); MS m/e 243 (M^+); Mass Calcd. for $C_{14}H_{13}NO_3$ 243.0895, found 243.0888.

E10 2-(1-Oxo-3-phenylpropoxy)-1*H*-isoindole-1,3(2*H*)-dione **3.27c.**

Prepared as for **3.27a**, (88% yield); mp 79-80°C (lit.[148] 83-84°C); IR ($CHCl_3$, cm^{-1}) 3025, 1800, 1788, 1745, 1214, 782; ^1H NMR ($CDCl_3$) δ 2.90-3.20 (m, 4H), 7.15-7.40 (m, 5H), 7.65-8.00 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 30.6, 32.8 (CH_2-s), 124.0 (2 x CH), 126.8 (2 x C_q), 128.4 (2 x CH), 128.8 (2 x CH), 129.0 (CH), 134.8 (2 x CH), 139.2 (C_q), 161.9 (COO), 168.9 (2 x CO-N); MS m/e 295 (M^+); Mass Calcd. for $C_{17}H_{13}NO_4$ 295.0845, found 295.0818.

E11 1-(1-Oxo-3-phenylpropoxy)-1*H*-pyrrole-2,5-dione **3.27d.**

Prepared as for **3.27a**, (30% yield); mp 97-99°; IR ($CHCl_3$, cm^{-1}) 3025, 1810, 1746, 1369, 1164, 1079, 811; ^1H NMR ($CDCl_3$) δ 2.88-3.12 (m, 4H), 6.80 (s, 2H), 7.2-7.4 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 30.5, 32.6 (CH_2-s), 126.8 (2 x CH), 128.3 (2 x CH), 128.8 (CH), 132.4 (2 x CH), 139.1 (C_q), 164.2 (COO), 169.1 (2 x CO-N); MS m/e 245 (M^+); Mass Calcd. for $C_{13}H_{11}NO_4$ 245.0688, found 245.0685.

E12 1-(1-Oxo-3-phenylpropoxy)-1*H*-benzotriazole **3.27e.**

Prepared as for **3.27a**, (93% yield); mp 88-91°C; IR ($CHCl_3$, cm^{-1}) 3020, 1734, 1686, 1500, 1213, 759; UV-vis ($CHCl_3$) λ_{max1} = 342 nm, ε = 9 560, λ_{max2} = 328 nm, ε = 10 480; ^1H NMR ($CDCl_3$) δ 3.16 (t, J = 7 Hz, 2H), 3.47 (t, J =7 Hz, 2H), 7.3 (m, 5H), 7.5-7.6 (m, 1H), 7.7-7.8 (m, 1H), 7.98 (d, J = 8.3 Hz, 1H), 8.38 (d, J = 8.3 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 25.6, 32.7

(CH_2-s), 115.6, 116.2, 126.7, 126.9 (CH-s), 125.0 (C_q), 128.5 (2 x CH), 128.7 (2 x CH), 132.8 (C_q), 133.1 (CH), 139.6 (C_q), 169.2 (C=O); MS m/e 267 (M^+); Mass Calcd. for $C_{15}H_{13}N_3O_2$ 267.1008, found 267.1013.

E13 1-(1-Oxo-3-phenylpropoxy)-2,5-pyrrolidinedione **3.27f**.

Prepared as for **3.27a**, (48% yield); mp 108-110°C (lit.[149] 112-115°C); IR ($CHCl_3$, cm^{-1}) 3012, 1809, 1780, 1732, 1210, 907, 776; ^1H NMR ($CDCl_3$) δ 2.75 (s, 4H), 2.85-2.95 (m, 2H), 2.97-3.10 (m, 2H), 7.17-7.35 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 25.6 (2 x CH_2), 30.4, 32.6 (CH_2-S), 126.9 (CH), 128.5 (2 x CH), 128.9 (2 x CH), 139.4 (C_q), 168.2 (COO), 169.5 (2 x CO-N); MS m/e 247 (M^+); Mass Calcd. for $C_{13}H_{13}NO_4$ 247.0845, found 247.0853.

E14 Decarboxylation of **3.27a**.

3-(1-Oxo-3-phenylpropoxy)-1,2,3-benzotriazin-4(3*H*)-one (**3.27a**) (0.0295 g, 0.1 mmol), the internal standard and dry toluene (1.0 ml) were placed in a flame dried two neck flask fitted with a condenser attached to a bubbler. The system was sealed with a rubber septum and flushed with argon to provide an inert atmosphere. The argon source was removed and the solution was stirred and brought to boil.

A solution of AIBN (1.6 mg, 0.01 mmol), tributyltin hydride (0.08 ml, 0.3 mmol) in dry toluene was then added to the flask. After ten minutes an aliquot was removed and the formation of ethylbenzene measured by glc. In this way the reaction was followed. After three hours the yield of ethylbenzene remained constant, 97% as compared with the authentic sample.[137]

E15 Decarboxylation of 3.27b.

Procedure was as for **3.27a**, after two and a half hours 73% of ethylbenzene was recorded (glc) as compared with the authentic sample.[137]

E16 Decarboxylation of 3.27c.

Procedure was as for **3.27a**, after one and a half hours 62% of ethylbenzene was recorded (glc) as compared with the authentic sample.[137]

E17 Decarboxylation of 3.27d.

Procedure was as for **3.27a**, after one and a quarter hours 49% of ethylbenzene was recorded (glc) as compared with the authentic sample.[137]

E18 Decarboxylation of 3.27e.

Procedure was as for **3.27a**, after three hours no ethylbenzene was detected.

E19 Decarboxylation of 3.27f.

Procedure was as for **3.27a**, after one and a half hours 2% of ethylbenzene was recorded (glc) as compared with the authentic sample.[137]

E20 1,2,3-Benzotriazin-4(3*H*)-one 3.36.

3-(1-Oxo-3-phenylpropoxy)-1,2,3-benzotriazin-4(3*H*)-one (**3.27a**) (0.295 g, 1.0 mmol), the internal standard and dry toluene (10 ml) were placed in a flame dried two neck flask fitted with a condenser attached to a bubbler. The system was sealed with a rubber septum and flushed with argon to provide an inert atmosphere. The argon source was removed and the solution was stirred and brought to boil.

Experimental

A solution of AIBN (16.4 mg, 0.10 mmol), tributyltin hydride (0.80 ml, 3.0 mmol) in dry toluene was then added to the flask. After three hours an aliquot was removed and the formation of ethylbenzene measured by glc (90%).

Evaporation of the solvent and ethylbenzene resulted in a yellow oil. This yellow oil was passed down a silica gel column (CH_2Cl_2 : Et_2O, 10 : 1) and gave 1,2,3-benzotriazin-4(3*H*)-one **3.36** (134 mg, 90%); mp 208-211°C (lit.[150] 210°C); IR ($CHCl_3$, cm^{-1}) 3020, 1705, 1780, 1656, 1635, 1538, 1214; ^1H NMR ($CDCl_3$) δ 7.78-7.90 (m, 1H), 7.95-8.05 (m, 1H), 8.15-8.25 (m, 1H), 8.30-8.40 (m, 1H); GC-MS m/e 147 (M^+).

E21 3-(1-Oxo-hexadecoxy)-1,2,3-benzotriazin-4(3*H*)-one **3.37**.

Prepared as for **3.27a**, (92% yield); mp 78°C; IR ($CHCl_3$, cm^{-1}) 2928, 2855, 1809, 1714, 1601, 1443, 1249, 1127; UV-vis ($CHCl_3$) λ_{max} = 283 nm, ε = 7 020; ^1H NMR ($CDCl_3$) δ 0.8-1.0 (m, 3H), 1.20-1.60 (m, 24H), 176-196 (m, 2H), 2.77 (t, J = 8.0 Hz, 2H), 7.80-7.90 (m, 1H), 7.96-8.06 (m, 1H), 8.20-8.29 (m, 1H), 8.36-8.44 (m, 1H), ^{13}C NMR ($CDCl_3$) δ 14.1 (CH_3), 22.6, 24.5, 28.8, 29.1, 29.3, 29.5 (CH_2-s), 29.6 (6 x CH_2), 31.2, 31.9 (CH_3-s), 122.2 (C_q), 125.6, 128.9, 132.6, 135.2 (CH-s), 144.3 (C=O), 150.2 (C_q, C-N=N), 169.5 (C=O-N); Anal. Calcd. for $C_{23}H_{35}N_3O_3$: C, 68.80; H, 8.79; N, 10.46. Found: C, 68.80; H, 8.74; N, 10.50.

E22 Decarboxylation of **3.27a** with diphenylsilane in toluene with 0.1 equivalents of AIBN.

3-(1-Oxo-3-phenylpropoxy)-1,2,3-benzotriazin-4(3H)-one (**3.27a**) (0.2953 g, 1.0 mmol), the internal standard and dry toluene (2.0 ml) were placed in a flame dried two neck flask fitted with a condenser attached to a

bubbler. The system was sealed with a rubber septum and flushed with argon to provide an inert atmosphere. The argon source was removed and the solution was stirred and brought to boil.

A solution of AIBN (0.0164 g, 0.1 mmol), diphenylsilane (0.280 ml, 2.3 mmol) in dry toluene (2.0 ml) was added to the flask. After twenty minutes no ethylbenzene was detected and the reaction was stopped.

E23 Decarboxylation of 3.27a with diphenylsilane in toluene with 0.2 equivalents of AIBN

3-(1-Oxo-3-phenylpropoxy)-1,2,3-benzotriazin-4(3*H*)-one (3.27a) (0.0295 g, 0.1 mmol), the internal standard and dry toluene (0.2 ml) were placed in a flame dried two neck flask fitted with a condenser attached to a bubbler. The system was sealed with a rubber septum and flushed with argon to provide an inert atmosphere. The argon source was removed and the solution was stirred and brought to boil.

A solution of AIBN (0.010 g, 0.06 mmol), diphenylsilane (0.028 ml, 0.23 mmol) in dry toluene (0.2 ml) was added to the flask. Every twenty minutes an aliquot was removed and the formation of ethylbenzene was measured by glc. In this way the reaction was followed. After three hours the amount of ethylbenzene remained constant (11%) and the reaction was stopped.

E24 Decarboxylation of 3.27a with diphenylsilane in benzene with one equivalent of benzoylperoxide

3-(1-Oxo-3-phenylpropoxy)-1,2,3-benzotriazin-4(3*H*)-one (3.27a) (0.2953 g, 1.0 mmol), the internal standard and dry benzene (10.0 ml) were placed in a flame dried two neck flask fitted with a condenser attached to a

bubbler. The system was sealed with a rubber septum and flushed with argon to provide an inert atmosphere. The argon source was removed and the solution was stirred and brought to boil.

0.1 ml of a solution of benzoylperoxide (0.242 g, 1.0 mmol), diphenylsilane (0.369 ml, 2.0 mmol) in dry toluene (2 ml) was added to the flask every half hour. Every twenty minutes an aliquot was removed and the formation of ethylbenzene measured by glc. After four hours the amount of ethylbenzene remained constant (20%) and the reaction was stopped.

E25 Decarboxylation of **3.37** with diphenylsilane in toluene with one equivalent of benzoylperoxide.

3-(1-Oxo-hexadecoxy)-1,2,3-benzotriazin-4(3*H*)-one (**3.37**) (0.1004 g, 0.25 mmol), the internal standard tetradecane and dry toluene (1.0 ml) were placed in a flame dried two neck flask fitted with a condenser attached to a bubbler. The system was sealed with a rubber septum and flushed with argon to provide an inert atmosphere. The argon source was removed and the solution was stirred and brought to boil.

0.1 ml of a solution of benzoylperoxide (0.0606 g, 0.25 mmol), diphenylsilane (0.092 ml, 0.5 mmol) in dry toluene (1 ml) was added to the flask every half hour. Every half hour an aliquot was removed and the formation of ethylbenzene measured by glc. After four hours the amount of ethylbenzene remained constant (25%) and the reaction was stopped.

E26 Decarboxylation of **3.37** with diphenylsilane in *p*-cymene with one equivalent of benzoylperoxide.

3-(1-Oxo-hexadecoxy)-1,2,3-benzotriazin-4(3*H*)-one (**3.37**) (0.1004 g, 0.25 mmol), the internal standard and dry *p*-cymene (1.0 ml) were placed in a

flame dried two neck flask fitted with a condenser attached to a bubbler. The system was sealed with a rubber septum and flushed with argon to provide an inert atmosphere. The argon source was removed and the solution was stirred and brought to boil.

0.1 ml of a solution of benzoylperoxide (0.0606 g, 0.25 mmol), diphenylsilane (0.092 ml, 0.5 mmol) in dry toluene (1 ml) was added to the flask every half hour. Every half hour an aliquot was removed and the formation of ethylbenzene measured by glc. After four hours the amount of ethylbenzene remained constant (5%) and the reaction was stopped.

E27 N-Benzoyl methyl anthranilate 4.21a.

To a solution of methyl anthranilate (6.47 ml, 50.2 mmol) in pyridine (40 ml, 10 equivalents) cooled to 0°C was added slowly benzoyl chloride (5.8 ml, 50.0 mmol). After the contents of the flask were stirred overnight at room temperature the resulting solution was poured onto crushed ice. The ice was allowed to melt and the precipitate formed was filtered and dried (CH_2Cl_2/anhydrous $MgSO_4$) crystallization from ethanol yielded white crystals of the title compound (12.15 g, 95%); mp 99°C (lit.[103, 151] 100°C); IR ($CHCl_3$, cm^{-1}) 3313, 1671, 1586, 1525, 1444, 1299; ^1H NMR ($CDCl_3$) δ 3.96 (s, 3H), 7.12 (m,1H), 7.55 (m, 4H), 8.07 (m, 3H), 8.93 (m, 1H), 12.04 (s, 1H); MS m/e 255 (M^+), 223 (M^+–OMe); Mass Calcd. for $C_{15}H_{13}NO_3$ 255.0895, found 255.0895.

E28 N-(α-Naphthoyl) methyl anthranilate 4.21b.

Prepared as for 4.21a, (84% yield); mp 120-121°C (lit.[103] 120°C); ^1H NMR ($CDCl_3$) δ 3.80 (s, 3H), 7.02-7.18 (m,1H), 7.44-7.66 (m, 4H), 7.80-7.96 (m, 3H), 8.03 (dd, J = 1.6, 8.0 Hz, 1H), 8.50-8.60 (m, 1H), 8.99-9.06 (m, 1H),

11.70 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 52.8 (CH_3), 115.9 (C_q), 121.0 (CH), 123.4, 125.4, 126.0, 126.1, 127.0, 127.7, 128.9 (7 x CH), 130.9 (C_q), 131.5, 131.9 (2 x CH), 134.4, 134.9 (2 x C_q), 135.5 (CH), 142.3 (C_q), 168.4 (C=O), 169.1 (C=O); MS m/e 305 (M^+); Mass Calcd for $C_{19}H_{15}NO_3$ 305.1052 found 305.1086.

E29 N-(*o*-Methoxybenzoyl) methyl anthranilate 4.21c.

Prepared as for 4.21a, (81% yield); mp 114°C (lit[103] 114°C); ^1H NMR ($CDCl_3$) δ 3.87 (s, 3H), 3.96 (s, 3H), 6.98-7.14 (m,3H), 7.54-7.66 (m, 1H), 7.98-8.12 (m, 3H), 8.93 (dd, J = 1.1, 8.6 Hz, 1H), 11.80 (s, 1H); MS m/e 285 (M^+), 254 (M^+–OCH_3); Mass Calcd for $C_{16}H_{15}NO_4$ 285.1001 found 285.1016.

E30 3-Benzoylamino-2-methyl naphthoate 4.36.

3-Amino-2-naphthoic acid (4.2 g, 80% tech., 17.9 mmol) was suspended in methanol (400 ml) at 0°C and treated with a diazomethane solution in ether (~80 mmol) prepared earlier.[152] Once the yellow colour of diazomethane persisted and there was no precipitate present the ice bath was removed and the solution was allowed to attain room temperature. The methanol and ether were evaporated under reduced pressure and a ^1H NMR spectrum was recorded which showed complete esterification. The resulting solid was dissolved in dry pyridine and the flask was sealed and cooled to 0°C with an ice bath. Benzoyl chloride (2.6 ml, 22 mmol) was then added to the sealed solution by syringe over a period of ten minutes. The resulting mixture was stirred over night after which the contents of the flask were poured onto crushed ice. Once the ice had melted the precipitate was filtered and then dried (CH_2Cl_2/anhydrous $MgSO_4$). Filtration and evaporation yielded the crude solid which was crystallized from CH_2Cl_2/hexanes to give 4.33 g

(1st crop) and 1.133 g (2nd crop) 99% yield of the title compound; mp 150-151°C; IR ($CHCl_3$, cm^{-1}) 3312, 3006, 1685, 1539, 1294; UV-vis ($CHCl_3$) λ_{max1} = 384 nm, ε = 3 025, λ_{max2} = 269(310)nm, ε = 24 610(9 224); ^1H NMR ($CDCl_3$) δ 4.01 (s, 3H), 7.40-7.62 (m, 5H), 7.80-7.96 (t, 2H), 8.02-8.20 (m, 2H), 8.65 (s, 1H), 9.40 (s, 1H), 12.02 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 52.7 (CH_3), 115.7 (C_q), 117.5, 125.5 (2 x CH), 127.2 (2 x CH), 127.8 (CH), 128.4 (C_q), 128.8 (2 x CH), 128.9 (C_q), 129.3, 131.8, 133.4 (3 x CH), 134.9, 136.4, 136.6 (3 x CH), 165.6, 169.0 (2 x C=O); MS m/e 305 (M^+), 273 (M^+–OCH_3+H), 246 (M^+–CO_2CH_3). Analyzed as 4.37.

E31 2-Phenyl benzothiazine-4-thione **4.22a.**

N-Benzoyl methyl anthranilate **4.21a** (10.3601 g, 40.5 mmol), phosphorus pentasulphide (18 g, 1 equivalent) and freshly distilled dry pyridine (150 ml) were placed in a round bottom flask equipped with a condenser and drying tube. The stirred solution was then immersed into an oil bath preheated to 140°C and boiled for 18 hours. Then the heating was stopped and the reaction mixture was poured on crushed ice. Once the ice melted, the precipitate was filtered, redissolved in methylene dichloride and dried with anhydrous magnesium sulfate. The solvent was then removed in vacuum and the resulting solid crystallized from methylene dichloride/ethyl alcohol. The first two crops gave **4.22a** (9.0179 g, 73%); mp 122°C, lit. mp 128°C from benzene[103];.IR ($CHCl_3$, cm^{-1}) 3059, 2992, 1564, 1536, 1458, 1323, 1244, 1154, 1019, 941, 688, 649; UV-vis ($CHCl_3$) λ_{max1} = 410 nm, ε = 8 350, λ_{max2} = 325 nm, ε = 9 470, λ_{max3} = 271.5 nm, ε = 33 020; ^1H NMR ($CDCl_3$) δ 7.56 (m, 4H), 7.89 (m, 2H), 8.09 (m, 2H), 8.80 (d, 1H); MS m/e 255 (M^+), 223 (M^+–S); Mass Calcd. for $C_{14}H_9NS_2$ 255.0176 found 255.0191.

E32 2-Phenyl-[α]-naphthothiazine-4-thione **4.37.**

3-Benzoylamino-2-methyl naphthoate **4.36** (4.07 g, 13.3 mmol), phosphorus pentasulphide (12 g, 2 equivalents) and freshly distilled dry pyridine (150 ml) were placed in a round bottom flask equipped with a condenser and drying tube. The stirred solution was then immersed into an oil bath preheated to 140°C and boiled. The reaction was followed by tlc and after four hours the reaction was deemed complete. The heating was stopped and the hot reaction mixture was poured on crushed ice. Once the ice melted, the precipitate formed was filtered, redissolved in methylene dichloride and dried with anhydrous magnesium sulphate. After removal of the solvent in vacuum the resulting solid was crystallized from methylene dichloride and ethanol. The first two crops gave the title compound 2.2456 g, 55.3%; mp 180-181°C; IR ($CHCl_3$, cm^{-1}) 3033, 1599, 1550, 1201, 1013; UV-vis ($CHCl_3$) λ_{max1} = 460 nm, ε = 3 800, λ_{max2} = 354 nm, ε = 15 780, λ_{max3} = 305(273)nm, ε = 37 740(23 380); ^1H NMR ($CDCl_3$) δ 7.50-7.60 (m, 5H), 7.98-8.60 (d, 1H), 8.10-8.20 (m, 3H), 8.40 (s, 1H), 9.36 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 125.5 (C_q), 126.8 (2 x CH), 127.7, 128.0, 128.1 (3 x CH), 129.1 (2 x CH), 129.7, 130.5, 130.6, 132.0 (4 x CH), 133.1, 135.9, 137.2, 138.1 (4 x C_q), 158.6 (N=C–), 212.6 (C=S); MS m/e 305 (M^+), 273 (M^+–S); Anal. Calcd. for $C_{18}H_{11}NS_2$: C, 70.79; H, 3.63; N, 4.59; S, 21.00. Found: C, 70.72; H, 3.60; N, 4.60; S, 20.88.

E33 2-Phenyl-3-hydroxy-3,4-dihydroquinazoline-4-thione **4.23a** from **4.22a.**

2-Phenyl benzothiazine-4-thione **4.22a** (2 g, 7.8 mmol) was dissolved in boiling pyridine (10 ml) to which was added cautiously hydroxylamine hydrochloride (0.6 g, 8.6 mmol). After 15 minutes no **4.22a** was observed (tlc) and the pyridine solution was allowed to cool. Pure **4.23a** crystallized

out of this solution and was recovered by filtration to give fluffy pale yellow needles 1.745 g, 88%; mp 143-144°C (lit.[101] 148°C); IR ($CHCl_3$, cm^{-1}) 3019, 2957, 2863, 1726, 1558, 1502, 1463, 1301, 1123, 965; UV-vis ($CHCl_3$) λ_{max1} = 365 nm, ε = 9 530, λ_{max2} = 349 nm, ε = 11 550, λ_{max3} = 259 nm, ε = 22 770; ^1H NMR ($CDCl_3$) δ 7.55 (m, 4H), 7.85 (m, 2H), 8.03 (m, 2H), 8.53 (dd, 1H), 12.00 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 126.8 (C_q), 128.2 (2 x CH), 128.5, 128.7, 129.6 (3 x CH), 129.7 (2 x CH), 131.2 (CH), 131.6 (C_q), 134.3 (CH), 142.3, 146.9 (2 x C_q), 179.4 (C=S); MS m/e 254 (M^+), 238 (M^+–O); Mass Calcd. for $C_{14}H_{10}N_2OS$ 254.0513 found 254.0509; Anal. Calcd. for $C_{14}H_{10}N_2OS$: C, 66.12; H, 3.96; N, 11.01; S, 12.61. Found: C, 66.32; H, 3.89; N, 10.94; S, 12.50.

E34 2-Phenyl-3-hydroxy-3,4-dihydroquinazoline-4-thione **4.23a** from **4.21a**.

Freshly distilled dry *p*-xylene (300 ml), N-benzoyl methyl anthranilate **4.21a** (12.15 g, 47.6 mmol) and phosphorus pentasulphide (24.3 g, 54.7 mmol) were added into a two-neck round bottom flask, previously flushed with dry argon and equipped with a reflux condenser connected to a calcium chloride drying tube. The solution was then brought to boil and the reaction followed by tlc. After 10 h the solution was allowed to cool to room temperature. The solution was filtered and the flask washed with benzene (300 ml) that was then also filtered. The organic solutions were combined and washed with sodium hydroxide solution (5%, 800 ml) two times and water (800 ml) also two times. The solvents were then evaporated and the resulting solid dried in vacuum over P_2O_5. The solid (**4.22a**) was then dissolved in a minimal amount of boiling ethanol and treated with hydroxylamine hydrochloride (3.5 g, 50 mmol) and sodium acetate (3.5 g, 25 mmol), both

dissolved in the minimal amount of water. The red colour of the solution changed to yellow in about 15 min and tlc indicated that there was no more 4.22a present. Then the ethyl alcohol was evaporated in vacuum and 4.23a was filtered and purified by repeated crystallization from ethyl alcohol; overall yield from 4.21a: 33%

E35 2-(1'-Naphthyl)-3-hydroxy-3,4-dihydroquinazoline-4-thione 4.23b.

Prepared as for 4.23a (E34) from 4.21b. Overall yield: 41%; mp 181-182°C (lit.[101] 183°C); UV-vis ($CHCl_3$) λ_{max1} = 348 nm, ε = 13 643, λ_{max2} = 283 nm, ε = 14 775; ^1H NMR ($CDCl_3$) δ 7.44-8.00 (m, 9H), 8.02-8.10 (m, 1H), 8.60-8.65 (m, 1H), 11.64 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 124.7, 125.0, 126.5, 127.2, 127.3, 127.6, 128.6, 128.8, 128.9, 129.4, 129.7, 130.5, 131.1, 133.4, 134.5, 142.3, 146.9, 176.3 (C=S); MS m/e 304 (M^+), 287 (M^+–OH); Mass Calcd. for $C_{18}H_{12}N_2OS$ 304.0670 found 304.0655.

E36 2-(o-Methoxyphenyl)-3-hydroxy-3,4-dihydroquinazoline-4-thione 4.23c.

Prepared as for 4.23a (E34) from 4.21c. Overall yield: 37%; mp 174°C (lit.[101] 173°C); MS m/e 284 (M^+), 268 (M^+–O), 252 (M^+–S).

E37 2-Phenyl-3-hydroxy-3,4-dihydro-[g]-benzoquinazoline-4-thione 4.33.

2-Phenyl-[g]-naphthothiazine-4-thione 4.37 (258 mg, 0.84 mmol) was dissolved in the minimum amount of boiling ethanol (2 ml) to which was added hydroxylamine hydrochloride (64 mg, 1.1 equivalents) and sodium acetate (96 mg). Following the immediate colour change the solution was allowed to cool and the resulting crystals were filtered. Recrystallization from ethanol gives the title compound as bright yellow needles 225 mg, 88%; mp

183-184°C; IR ($CHCl_3$, cm^{-1}) 3062, 1588, 1563, 1506, 1478, 1333, 1260; UV-vis ($CHCl_3$) λ_{max1} = 430 nm, ε = 3 740, λ_{max2} = 408 nm, ε = 6 275, λ_{max3} = 389 nm, ε = 6 150, λ_{max4} = 335 nm, ε = 12 560, λ_{max5} = 280 nm, ε = 35 100; ^1H NMR ($CDCl_3$) δ 7.50-7.70 (m, 5H), 7.99-8.19 (m, 4H), 8.42 (s, 1H), 9.14 (s, 1H), 11.90 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 124.6 (C_q), 127.2 (2 x CH), 128.1 (CH), 128.3 (2 x CH), 128.8, 129.3 (2 x CH), 129.8 (2 x CH), 130.9, 131.1 (2 x CH), 131.9, 132.5, 136.4, 137.8 (4 x C_q), 145.8 (C=N), 177.7 (C=S); Anal. Calcd. for $C_{18}H_{12}N_2OS$: C, 71.03; H, 3.97; N, 9.20; S, 10.53. Found: C, 70.97; H, 3.98; N, 9.13; S, 10.43.

E38 2-(N-Benzoylamino)-3-methyl nicotinate 4.42.

Prepared as for 4.36, 74% yield; mp 155-156°C; IR (CH_2Cl_2, cm^{-1}) 3287, 3037, 2956, 1700, 1600, 1485, 1238, 1137, 902; UV-vis ($CHCl_3$) λ_{max1} = 273 nm, ε = 8 016; ^1H NMR ($CDCl_3$) δ 3.98 (s, 3H), 7.08-7.15 (m, 1H), 7.48-7.64 (m, 3H), 8.06-8.14 (m, 2H), 8.33-8.39 (m, 1H), 8.71-8.75 (m, 1H), 11.80 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 52.7 (CH_3), 111.2 (C_q), 118.2 (CH), 127.4 (2 x CH), 128.6 (2 x CH), 132.0 (CH), 134.6 (C_q), 139.7 (CH), 152.8 (C_q), 153.4 (CH), 164.1 (O-C=O), 167.4 (N-C=O); Anal. Calcd. for $C_{14}H_{12}N_2O_3$: C, 65.62; H, 4.72; N, 10.93. Found: C, 65.56; H, 4.73; N, 10.90.

E39 2-Phenyl-3-hydroxy-3,4-dihydro-8-azaquinazoline-4-thione 4.38.

Prepared as for 4.33, 11% yield, too unstable to characterize fully. ^1H NMR ($CDCl_3$) δ 7.52-7.70 (m, 4H), 8.18-8.26 (m, 2H), 8.87-8.95 (m, 1H), 9.14-9.17 (m, 1H), 11.70 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 122.3 (C_q), 123.6 (CH), 128.3 (2 x CH), 130.3 (2 x CH), 130.9 (C_q), 132.0, 139.1 (2 x CH), 151.6 (C_q), 157.1 (CH), 177.8 (C_q), 222.6 (C=S).

E40 2-Phenyl-3-palmitoyloxy-3,4-dihydroquinazoline-4-thione **4.43a.**

To a sealed covered flask containing 2-phenyl-3-hydroxy-3,4-dihydroquinazoline-4-thione **4.23a** (4.5 g, 17.7 mmol) and dry pyridine (16 ml) which was cooled to 0°C was added palmitoyl chloride (5.25 ml, 17.7 mmol). Once the reaction was complete (15 minutes, tlc) the contents of the flask were poured on crushed ice and kept in the dark while the ice was allowed to melt. The precipitate formed was filtered and dried at the pump, further drying using high vacuum may be necessary. The pale yellow powder recovered 7.59 g, 87%, may be crystallized from methylene dichloride and hexanes or if further purification is necessary passed down a short column (SiO_2, CH_2Cl_2:hexanes, 1:1); mp 58°C (CH_2Cl_2/hexanes); IR ($CHCl_3$, cm^{-1}) 2927, 1803, 1582, 1455, 1355, 1291, 1226, 1131, 863; UV-vis ($CHCl_3$) λ_{max1} 356 nm, ε = 14 290, λ_{max2} 279 nm, ε = 15 000; ^1H NMR ($CDCl_3$) δ 0.85 (m, 3H), 1.2 (m, 24H), 2.5 (m, 2H), 2.2-2.6 (m, 2H), 7.4-7.9 (m, 8H), 8.75 (d, 1H); ^{13}C NMR ($CDCl_3$) δ 14.02 (CH_3), 22.57, 23.97, 28.52, 28.90, 29.17, 29.24, 29.41 (CH_2-groups), 29.58 (5 x CH_2), 31.33 (CH_2), 31.80 (CH_2), 128.19 (2 x CH), 128.38 (CH), 128.44 (CH), 128.86 (2 x CH), 129.97 (C_q), 130.64 (CH), 130.70 (CH), 131.81 (C_q), 134.71 (CH), 141.74 (C_q), 151.86 (C_q), 168.48 (C=O), 182.38 (C=S); Anal. Calcd. for $C_{30}H_{40}N_2O_2S$: C, 73.13; H, 8.18; N, 5.69; S, 6.51. Found: C, 73.23; H, 8.20; N, 5.70; S, 6.48.

E41 2-(α-Naphthyl)-3-palmitoyloxy-3,4-dihydroquinazoline-4-thione **4.43b.**

Prepared as for **4.43a**, (96% yield); mp 65°C (CH_2Cl_2/hexanes); IR ($CHCl_3$, cm^{-1}) 2928, 2855, 1805, 1589, 1463, 1346, 1319, 1296, 1262, 1049; UV-vis ($CHCl_3$) λ_{max1} = 355 nm ε = 15 000, λ_{max2} = 286 nm, ε = 15 740; ^1H NMR ($CDCl_3$) δ 0.8-1.4 (m, 29 H), 1.9-2.3 (m, 2H), 7.4-8.0 (m, 10H), 8.79 (d, 1H); ^{13}C NMR ($CDCl_3$) δ 14.0, 22.6, 23.7, 28.3 (broad), 28.8, 29.0, 29.3,

29.4, 29.5, 29.6, 29.7, 31.1, 31.8, 124.7 (broad), 126.5, 127.3, 127.4, 128.2, 128.6, 128.7, 130.2, 130.5, 130.7, 134.8, 141.7, 168.4, 182.3; Anal. Calcd. for $C_{34}H_{42}N_2O_2S$: C, 75.24; H, 7.80; N, 5.16; S, 5.91. Found: C, 75.34; H, 7.86; N, 5.12; S, 6.02.

E42 2-(*p*-Methoxyphenyl)-3-palmitoyloxy-3,4-dihydroquinazoline-4-thione **4.43c.**

Prepared as for 4.43a, (95% yield); mp 61-62°C (CH_2Cl_2/hexanes); IR ($CHCl_3$, cm^{-1}) 2928, 2854, 1805, 1587, 1463, 1253; UV-vis ($CHCl_3$) λ_{max1} = 358 nm, ε = 12 540, λ_{max2} = 279 nm, ε = 19 719; ^1H NMR ($CDCl_3$) δ 0.80-1.00 (m, 3H), 1.10-1.65 (m, 26H), 2.29-2.64 (m, 2H), 3.87 (s, 3H), 6.70-7.02 (m, 2H), 7.49-7-59 (m, 1H), 7.70-7.82 (m, 4H), 8.68-8.76 (m, 1H). Analyzed as 4.47c.

E43 2-Phenyl-3-palmitoyloxy-3,4-dihydro-[*a*]-benzoquinazoline-4-thione **4.44.**

Prepared as for 4.43a, (94% yield); mp 63°C; IR ($CHCl_3$, cm^{-1}) 3062, 2927, 1803, 1588, 1492, 1449, 1351, 1322, 1244, 1188, 1042; UV-vis ($CHCl_3$) λ_{max1} = 400 nm, ε = 7 245, λ_{max2} = 369 nm, ε = 7 680, λ_{max3} = 325 nm ε = 21 810, λ_{max3} = 271 nm, ε = 43 900; ^1H NMR ($CDCl_3$) δ 0.80-1.00 (m, 3 H), 1.05-1.60 (m, 26H), 2.24-2.60 (m, 2H), 7.40-7.70 (m, 5H), 7.72-7.80 (m, 2H), 7.94-7.99 (d, 1H), 8.07-8.11 (d, 1H), 8.30 (s, 1H), 9.29 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 14.1 (CH_3), 22.7, 24.1, 28.6, 29.0, 29.2, 29.3, 29.5 (7 x CH_2), 29.6 (5 x CH_2), 31.4, 31.9 (2 x CH_2), 126.9, 127.1 (2 x CH), 127.5 (C_q), 127.9 (CH), 128.3 (2 x CH), 128.9 (CH), 129.0 (2 x CH), 129.6, 130.7 (2 x CH), 132.1 (C_q), 132.5 (CH), 132.6, 136.7, 137.5 (3 x C_q), 150.3 (–C=N), 168.8 (C=O), 183.9 (C=S); Anal. Calcd. for $C_{34}H_{42}N_2O_2S$: C, 75.24; H, 7.80; N, 5.16; S, 5.91. Found: C, 75.29; H, 7.84; N, 5.12; S, 6.00.

E44 3-Palmitoyloxy-4-phenylthiazolin-2(3*H*)-thione 4.07.

Prepared as for 4.43a from 3-hydroxy-4-phenylthiazolin-2-thione[153] (71% yield); mp 60-62°C (lit.[24] 61-62°C); UV-vis (CH_2Cl_2) λ_{max1} = 324 nm, ε = 10 900, λ_{max2} = 242 nm, ε = 7 600; ^1H NMR ($CDCl_3$) δ 0.50-1.90 (m, 29H), 2.50 (m, 2H), 6.60 (s, 1H), 7.60 (m, 5H); MS m/e 403 (M^+–CO_2).

E45 N-Hydroxy-2-thiopyridone 1.95.

To a solution of sodium 2-thiopyridine-N-oxide[154] (1 000 ml) was added 600 ml of water and the resulting solution cooled to 10°C. To this cooled solution was added 350 ml of concentrated hydrochloric acid over a period of twenty minutes. The solution was stirred for a further twenty minutes (mechanical stirrer). The precipitate formed was filtered and washed with cold water (2 000 ml). After further drying at the pump the solid was dried in vacuum over potassium hydroxide (24-48 hours). The dry solid was then recrystallized from ethanol, 953 g, 90%; mp 69°C (lit.[155] 68-70°C). Care was taken through out not to allow the solution or the resulting solid to come in contact with any metal objects. The reaction and subsequent work-up was carried out in a semi-dark room.

E46 1-(1-Oxohexadecanoxy)-2(1*H*)-pyridine thione 4.11.

Prepared as for 4.43a from N-hydroxy-2-thiopyridone 1.95, (90% yield); mp 50-53°C (lit.[72] 48-55°C); IR ($CHCl_3$, cm^{-1}) 3020, 2980, 1810, 1730, 1645, 1540, 1220; UV-vis ($CHCl_3$) λ_{max} = 366 nm, ε = 7 000; ^1H NMR (C_6D_6) δ 0.8-0.95 (m, 3H), 1.10-1.40 (m, 26H), 1.6-1.8 (m, 2H), 2.56 (t, J = 7.5 Hz, 2H), 6.15-6.22 (m, 1H), 6.70-6.85 (m, 1H), 7.09-7.15 (m, 1H), 7.40-7.50 (m, 1H); MS m/e 365 (M^+), 321 (M^+–CO_2).

E47 1-(Cyclohexyl-1'-carboxyl)-2(1*H*)-pyridine thione **4.48a**.

Prepared as for **4.11**, (80% yield); mp 109-111°C (lit.[72] 110°C); IR ($CHCl_3$, cm^{-1}) 1805, 1745, 1610, 1110, 1045, 690; ^1H NMR ($CDCl_3$) δ 1.23-1.45 (m, 3H), 1.63-1.90 (m, 5H), 2.18 (d, 2H), 2.75 (m, 1H), 6.62 (t, 1H), 7.19 (t, 1H), 7.53 (d, 1H), 7.68 (d, 1H); MS m/e 193 ($M^{+\cdot}-CO_2$).

E48 1-Oxo-2,2-dimethylpropanoxy-2(1*H*)-pyridine thione **4.48b**.

Prepared as for **3.27a**, from N-hydroxy-2-thiopyridone **1.95**, (87% yield); mp 110-112°C (lit.[72] 113°C); IR ($CHCl_3$, cm^{-1}) 2920, 1795, 1745, 1610, 1140, 980; ^1H NMR ($CDCl_3$) δ 1.44 (s, 9H), 6.60 (td, J = 1.8, 6.9 Hz, 1H), 7.12 (td, J = 1.8, 6.9 Hz, 1H), 7.50 (dd, J = 1.8, 8.8 Hz, 1H), 7.65 (dd, J = 1.8, 8.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 27.6 (3 x CH_3), 39.4 (C_q), 113.0, 133.7 (2 x CH), 138.1 (2 x CH), 174.1 (C=O), 176.5 (C=S); MS m/e 167 ($M^{+\cdot}-CO_2$).

E49 2-Phenyl-4-pentadecylthioquinazoline **4.47a**.

2-Phenyl-3-palmitoyloxy-3,4-dihydroquinazoline-4-thione **4.43a** (246 mg, 0.5 mmol) was placed in a flame dried covered flask which was sealed and the dry argon was passed through for twenty minutes (Semi-darkness is required for the manipulation of **4.43a**). To this was injected methylene dichloride (5 ml) which had been rigorously degassed (liquid nitrogen) before hand. The resulting solution was then irradiated with light from a tungsten lamp (250 W) for ten minutes, tlc showed the reaction to be complete. The solvent was evaporated and the resulting solid crystallized from methylene dichloride and hexanes to give the title compound 215 mg (96% yield); mp 53°C; IR (CH_2Cl_2, cm^{-1}) 2927, 2854, 1611, 1532, 1480, 1339, 1305, 1125, 686; UV-vis (CH_2Cl_2) λ_{max} = 264 nm ε = 34,100; ^1H NMR ($CDCl_3$) δ 0.80-1.00 (m, 3H), 1.20-1.70 (m, 24H), 1.80-2.00 (m, 2H), 3.45-3.52 (t, 2H),

7.45-7.60 (m, 4H), 7.76-7.86 (m, 1H), 7.96-8.12 (m, 2H), 8.59-8.68 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 14.10 (CH_3), 22.69, 29.17, 29.20, 29.29, 29.35, 29.60, 29.68, 31.91 (CH_2 groups) 122.66 (C_q), 123.82, 126.53, 128.43, 128.50, 129.03, 130.43, 133.44 (CH-s), 138.20 (C_q), 148.91 (C_q), 158.82 (C_q), 171.72 (C_q); MS m/e 448 (M^+); Anal. Calcd. for $C_{29}H_{40}N_2S$: C, 77.63; H, 8.99; N, 6.24; S, 7.15. Found: C, 77.64; H, 8.99; N, 6.19; S, 7.14.

E50 2-(α-Naphthyl)-4-pentadecylthioquinazoline 4.47b.

2-(α-Naphthyl)-3-palmitoyloxy-3,4-dihydroquinazoline-4-thione 4.43b (271 mg, 0.5 mmol) was dissolved in methylene dichloride (5 ml) in a covered flask. The resulting solution was the irradiated (250 W tungsten lamp) for ten minutes after which the solvent was evaporated. The solid formed was crystallized from methylene dichloride and pentane to give 234 mg. (94% yield);mp 80°C; IR ($CHCl_3$, cm^{-1}) 2927, 1524, 1471; UV-vis ($CHCl_3$) λ_{max} = 312 nm ε = 19,650; ^1H NMR ($CDCl_3$) δ 0.80-0.90 (m, 3H), 1.0-1.5 (m, 24H), 1.70-1.80 (m, 2H), 3.35-3.45 (t, 2H), 7.48-7.68 (m, 4H), 7.80-8.20 (m, 6H), 8.75-8.90 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 14.19 (CH_3), 22.76, 29.09, 29.27, 29.44, 29.47, 29.60, 29.65, 29.71, 29.75, 32.00 (CH_2 groups),122.30 (C_q), 123.93, 125.26, 125.83, 126.44, 126.56, 127.04, 128.47, 129.14, 129.56, 130.31 (CH-s), 131.43 (C_q), 133.67 (CH), 134.25 (C_q), 136.56 (C_q), 148.76 (C_q), 161.55 (C_q), 171.37 (C_q); Anal. Calcd. for $C_{33}H_{42}N_2S$: C, 79.48; H, 8.49; N, 5.62; S, 6.43. Found: C, 79.37; H, 8.50; N, 5.62; S, 6.42.

E51 2-(o-Methoxyphenyl)-4-pentadecylthioquinazoline 4.47c.

Prepared as for 4.47b from 4.43c, (90% yield); mp 79°C; IR ($CHCl_3$, cm^{-1}) 2928, 2854, 1603, 1246; ^1H NMR ($CDCl_3$) δ 0.8-0.95 (m, 3H), 1.2-1.6 (m, 24H), 1.80-2.00 (m, 2H), 3.46-3.53 (t, 2H), 3.92 (s, 3H), 7.02-7-10 (d, 2H),

7.44-7.54 (m, 1H), 7.74-7.86 (m, 1H), 7.93-8.01 (m, 1H), 8.04-8.12 (m, 1H), 8.56-8.64 (d, 2H); Anal. Calcd. for $C_{30}H_{42}N_2OS$: C, 75.27; H, 8.84; N, 5.85; S, 6.70. Found: C, 75.41; H, 8.90; N, 5.90; S, 6.82.

E52 2-Phenyl-4-pentadecylthio-[a]-benzoquinazoline 4.45.

Prepared as for 4.47b from 4.44, (98% yield); mp 89-90°C; IR ($CHCl_3$, cm^{-1}) 2927, 2854, 1597, 1509, 1460, 1319, 1125; UV-vis ($CHCl_3$) λ_{max} (ε): 418 nm (4 160), 397 nm (6 790), 378 nm (5 795), 288 nm (30 425), 252 nm (25 810); ^1H NMR ($CDCl_3$) δ 0.80-1.00 (m, 3H), 1.1-1.7 (m, 24H), 1.8-2.0 (m, 2H), 3.52 (t, J = 7 Hz, 2H), 7.4-7.6 (m, 5H), 7.96-8.04 (m, 2H), 8.51 (s, 1H), 8.60-8.74 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 14.1 (CH_3), 22.7, 29.1, 29.2, 29.31, 29.35 (5 x CH_2), 29.6 (6 x CH_2), 29.9 (CH_2),121.0 (C_q), 123.8, 126.2, 126.6, 127.8, 128.1 (5 x CH), 128.4 (2 x CH), 128.6 (2 x CH), 128.9, 130.4 (2 x CH), 131.5, 136.3, 138.2, 143.9, 157.3, 172.7 (6 x C_q); Anal. Calcd. for $C_{33}H_{42}N_2S$: C, 79.48; H, 8.49; N, 5.62; S, 6.43. Found: C, 79.38; H, 8.51; N, 5.61; S, 6.35.

E53 n-Pentadecyl thioether-2-phenyl-4-thiazole 4.13.

Prepared as for 4.47b from 4.07, (70% yield); mp 52-54°C (lit.[24] 53°C); IR ($CHCl_3$, cm^{-1}) 1065, 1035, 915, 840, 770, 725, 715, 690; ^1H NMR ($CDCl_3$) δ 0.65-2.30 (m, 29H), 3.28 (t, 2H), 7.10-8.20 (m, 6H); MS m/e 403 (M^+).

E54 (n-Pentadecyl thioether)-2-pyridine 4.17.

Prepared as for 4.47b from 4.11, (90% yield); mp 53-55°C (lit.[72] 52-54°C); IR ($CHCl_3$, cm^{-1}) 1570, 1550, 1320; ^1H NMR ($CDCl_3$) δ 0.80-0.90 (m, 3H), 1.10-1.50 (m, 24H), 1.60-1.80 (m, 2H), 3.10 (t, J = 7 Hz, 2H), 6.7-7.4 (m, 3H), 8.30 (d, J = 5 Hz, 1H); MS m/e 321 (M^+).

E55 (Cyclohexyl thioether)-2-pyridine **4.48a**.[117]

Prepared as for 4.47b from 4.48a except purified by chromatography (SiO_2, CH_2Cl_2/hexanes 1:2, 87% yield); IR ($CHCl_3$, cm^{-1}) 1580, 1125, 960; ^1H NMR ($CDCl_3$) δ 1.20-2.00 (m, 8H), 2.00-2.22 (m, 2H), 3.70-3.90 (m, 1H), 6.94 (td, J = 1.0, 1.0 Hz, 1H), 7.14 (dd, J = 1.0, 7.0 Hz, 1H), 7.45 (td, J = 2.0, 6.0 Hz, 1H), 8.42 (dd, J = 2.0, 5.0 Hz, 1H); MS m/e 193 (M^+).

E56 (t-Butyl thioether)-2-pyridine **4.48b**.[118]

Prepared as for 4.47b from 4.48b except purified by chromatography (SiO_2, CH_2Cl_2/hexanes 1:2, 87% yield); IR ($CHCl_3$, cm^{-1}) 3002, 2910, 1554, 1370, 1210, 870; ^1H NMR ($CDCl_3$) δ 1.54 (s, 9H), 7.10-7.77 (m, 3H), 8.50-8.56 (m, 1H); MS m/e 167 (M^+).

E57 2-Phenyl-4-trichlorothioquinazoline **4.54a**.

2-Phenyl-3-palmitoyloxy-3,4-dihydroquinazoline-4-thione **4.43a** (96.5 mg, 0.2 mmol) was placed in a covered flask which was then sealed and flushed with argon. Methylene dichloride (2 ml) and bromotrichloromethane (0.1 ml, 1.0 mmol) were then injected into the reaction flask. Irradiation of the resulting solution with light from a tungsten lamp (250 W) for five minutes caused the orange-yellow colour to fade to pale yellow. Evaporation of the solvent and excess bromotrichloromethane followed by chromatography (SiO_2, CH_2Cl_2/hexanes 1:2) gave bromopentadecane[156] **4.51**, {47.8 mg, (82% yield); IR (NaCl, cm^{-1}) 2925, 1460, 1370, 1260, 720, 650; ^1H NMR ($CDCl_3$) δ 0.9 (t, 3H), 1.3 (m, 26H), 3.45 (t, J = 7 Hz, 2H)} and the title compound as colourless needles 60.4 mg, (85% yield) which could be recrystallized from chloroform; mp 107-108°C; IR ($CHCl_3$, cm^{-1}) 3053, 1532, 1329, 980; UV-vis ($CHCl_3$) λ_{max1} = 331 nm, ε = 5,350, λ_{max2} = 264 nm ε =

33,470; ^{1}H NMR ($CDCl_3$) d 7.48-7.60 (m, 4H), 7.80-7.90 (m, 2H), 8.02-8.10 (m, 1H), 8.72-8.80 (m, 2H); ^{13}C NMR ($CDCl_3$) d 93.5 (CCl_3), 121.3 (C_q), 122.2 (CH), 127.3 (CH), 128.6 (2 x CH), 128.9 (2 x CH), 129.5 (CH), 131.0 (CH), 134.3 (CH), 137.2 (C_q), 149.8 (C_q), 159.3 (C_q), 165.8 (C-S); Anal. Calcd. for $C_{15}H_9Cl_3N_2S$: C, 50.65; H, 2.55; N, 7.88; Cl, 29.90, S, 9.02. Found: C, 50.92; H, 2.61; N, 7.82; Cl, 29.75; S, 8.90.

E58 2-(α-Naphthyl)-4-trichloromethioquinazoline 4.54b.

Prepared as for 4.54a from 4.43b, bromopentadecane yield: 78%; 4.54b yield: 81%; mp 126°C; IR ($CHCl_3$, cm^{-1}) 3009, 1609, 1541, 1479, 1316, 795; UV-vis ($CHCl_3$) λ_{max} = 317 nm ε = 13,720; ^{1}H NMR ($CDCl_3$) δ 7.5-7.70 (m, 4H), 7.9-8.10 (m, 4H), 8.14-8.22 (m, 1H), 8.50-8.60 (m, 1H), 9.14-9.24 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 93.64 (CCl_3), 121.12 (C_q), 112.52, 125.26, 125.90, 126.42, 126.90, 127.82, 128.48, 129.51, 130.91, 131.07 (CH-s), 131.24 (C_q), 134.21 (C_q), 134.46 (CH), 134.79 (C_q), 149.53 (C_q), 161.49 (C_q), 165.83 (C_q); Anal. Calcd. for $C_{19}H_{11}N_2Cl_3S$: C, 56.25; H, 2.73; N, 6.91; Cl, 26.21; S, 7.90. Found: C, 56.33; H, 2.74; N, 6.92; Cl, 26.15; S, 7.81.

E59 2-(*p*-Methoxyphenyl)-4-trichloroquinazoline 4.54c.

2-(*p*-Methoxyphenyl)-3-palmitoyloxy-3,4-dihydroquinazoline-4-thione 4.43c (104.5 mg, 0.2 mmol) was placed in a covered flame dried flask which was then sealed and flushed with dry argon (20 minutes). To this was injected degassed methylene dichloride (2 ml) and bromotrichloromethane (0.1 ml, 1.0 mmol), irradiation for five minutes with light from a tungsten lamp (250 W) followed by evaporation of the solvent and excess trap resulted in an oil. To this oil was added hexanes which gave a precipitate which was isolated as the title compound 74.7 mg, 97%. This gave fluffy needles when recrystallized

from ether; mp 152°C; IR ($CHCl_3$, cm^{-1}) 3016, 1602, 1538, 1247, 1205, 719, 665; UV-vis ($CHCl_3$) λ_{max} = 300 nm ε = 26,090; ^1H NMR ($CDCl_3$) δ 3.91 (s, 3H), 7.05-7.11 (d, 2H), 7.50-7.60 (m, 1H), 7.85-7.95 (m, 2H), 8.05-8.13 (m, 1H), 8.69-8.77 (d, 2H); Anal. Calcd. for $C_{18}H_{11}Cl_3N_2OS$: C, 49.83; H, 2.87; N, 7.26; Cl, 27.58; S, 8.31. Found: C, 49.77; H, 2.89; N, 7.20; Cl, 27.64; S, 8.25. The filtrate gave bromopentadecane 4.50 55 mg, 95% yield, upon evaporation of the combined hexanes.

E60 2-Trichloromethylthiopyridine 4.53.[157]

Prepared as for 4.54a from 4.11, bromopentadecane yield: 90%; 4.17 yield: 4%; 4.53 yield: 80%; IR (NaCl, cm^{-1}) 2930, 1565, 1450, 1050, 960, 765, 720, 690; ^1H NMR ($CDCl_3$) δ 7.30 (m, 2H), 7.75 (d, J = 4.0 Hz, 1H), 8.65 (d, J = 4.0 Hz, 1H); MS m/e 227, 229, 231 (M^+).

E61 Cyclohexyl bromide 4.51.[137]

Prepared as for 4.51 from 4.48a, 4.53 yield: 73%; 4.49a yield: 15%; 4.51 yield: 80%; IR (NaCl, cm^{-1}) 2934, 1450, 1250, 1190, 990, 885, 810, 687, 658; ^1H NMR ($CDCl_3$) δ 1.00-2.50 (m, 10H), 3.90-5.50 (m, 1H).

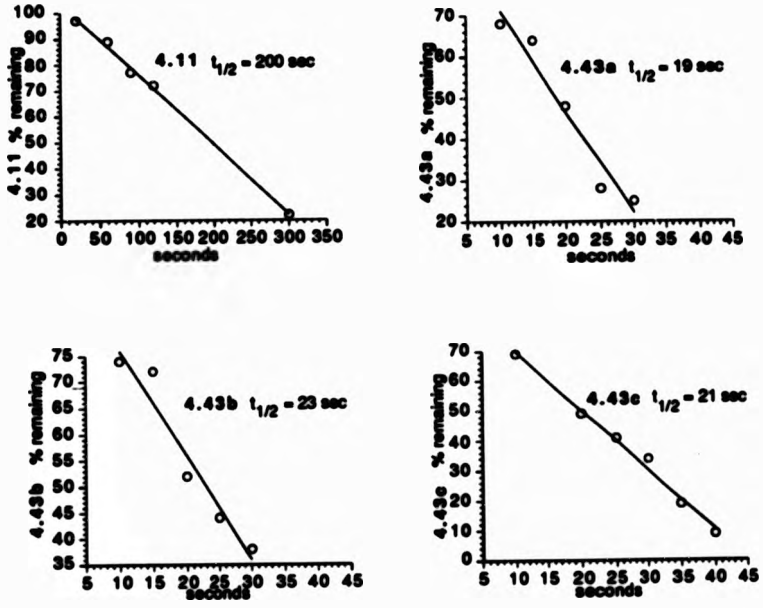
E62 2-Bromo-2-methyl propane 4.52.[137]

Prepared as for 4.51 from 4.48b, 4.53 yield: 50%; 4.49b yield: 20%; 4.52 yield: 75%; IR ($CHCl_3$, cm^{-1}) 2990, 1450, 1360, 1180, 800; ^1H NMR ($CDCl_3$) δ 1.81 (s, 3 x CH_3).

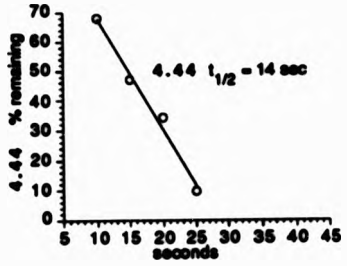
E63 Half-life determination for 4.11, 4.43a-c and 4.44.

A standard 0.1 M solution of the acyl derivative in $CDCl_3$ (5 ml) with propyl acetate as the internal standard was made. Then seven 0.7 ml

fractions were removed and injected into NMR tubes which had previously been sealed and flushed with argon. The NMR tubes were then placed in a 400 ml beaker covered three quarters of the way round with aluminium foil and containing 0°C water. The 250 W tungsten lamp was then placed next to the glass of the beaker and switched on at the same time as a stop clock. During the course of irradiation the samples were removed after set periods of time and the decomposition of the acyl derivative measured by ^1H NMR spectroscopy. The half-life values ($t_{1/2}$) were then calculated and are shown below.



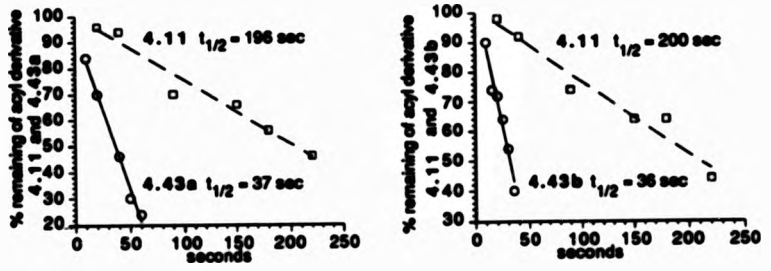
Plot of % acyl derivative (4.11, 4.43a-c) against photolysis time (seconds).



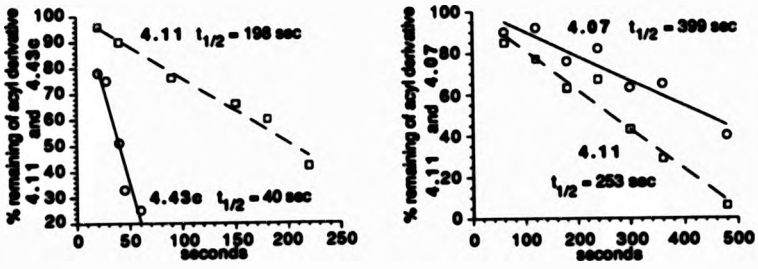
Plot of % acyl derivative remaining (4.44) against photolysis time (seconds).

E64 Competition photolysis of acyl derivatives 4.07, 4.11 and 4.43a-c.

As for **E63** except that the standard solution contained both acyl derivatives and the concentration was 0.1 M in both components. The results are shown below.



Plot of the percentage of the acyl derivatives (either 4.11 + 4.43a or 4.11 + 4.43b) remaining against time (seconds) to determine the respective half-lives.



Plot of percentage of acyl derivatives (either 4.11 + 4.43c or 4.11 + 4.07) remaining against time (seconds) to determine the respective half-lives.

E65 Low temperature photolysis of 4.11, 4.43b and 4.43c.

Individual standard solutions (0.1 M) of **4.11**, **4.43b** and **4.43c** were made in $CDCl_3$ (1 ml) with propyl acetate as the internal standard and bromotrichloromethane (0.5 M). These were then transferred to 3 NMR tubes and cooled to –60°C ($CO_{2(s)}$ / $CHCl_3$) after ten minutes of cooling the samples were subjected to irradiation from a tungsten lamp (250 W) for twenty minutes. ^1H NMR spectra were then recorded and the formation of products determined from their distinctive ^1H NMR signals.

Compound	Starting material remaining (%)	Pentadecyl bromide (%)	Nor-alkyl sulphide (%)
4.11	**4.11(77%)**	**4.50(15%)**	**4.17(8%)**
4.43b	**4.43b(0%)**	**4.50(100%)**	**4.47b(0%)**
4.43c	**4.43c(0%)**	**4.50(100%)**	**4.47c(0%)**

E66 Experiment to determine chain termination products for the photolysis of 4.11 and 4.48a.

Standard 0.1 M solutions of 4.11 and 4.48a were made in CCl_4 and $CDCl_3$, respectively (5 ml for each). These solutions were then transferred to sealed flask which had been flushed previously with argon and then irradiated with light from a tungsten lamp (250 W) for twenty minutes. A sample from each of the resulting solutions was injected into the GC-MS machine which had attached a library facility and the mass spectra recorded. Results of analysis of these spectra are given below with compound number (relative intensity).

Experiment using compound 4.11: 4.59 (83%); 4.53 (82%); 1.13 (0.7%); 4.17 (9%); 4.61 (4%).

Experiment using compound 4.48a: 4.49a (32%); 4.53 (3.6%); cyclohexanol (3.7%); cyclohexanone (4.2%); cyclohexane (trace); 4.62 (0.22%).

E67 General procedure for quantum yield determination.

A standard solution of the acyl derivative was made in the particular solvent (0.1 M, usually 25 ml). Three ml samples were removed by syringe and injected into five 1 cm x 1 cm Pyrex photometer cells. These cells had already been flushed with argon (99.998% pure) (20 min) and were sealed with rubber septa and parafilm. A cell filled with a solution of iron(III)oxalate (0. 006 M) was placed behind the sample cell. Before each set of measurements the light source was warmed up for 20 minutes so as to ensure a consistent light intensity value. The light intensity was also measured before and during a given set of quantum yield measurements using the iron oxalate actinometer. Five parallel samples were run and the

yield of the trapped product determined by ^1H NMR or glc with an appropriate internal standard. The conversion to the given trapped product was kept low (generally 5-20%) so as to not upset the concentrations of the starting compounds.

E68 Photochemistry: equipment and filters.

Filters:

Two types of filters were used for the photolysis experiments. The first filter was a chemical filter: a saturated aqueous solution of cobalt sulfate and an acetone (neat) filter,[126] both in 1 cm Pyrex glass photometer cuvettes. The other filter used was obtained from the Oriel Corporation, Stratford, CT. This was a band pass filter 360 nm (Model No. 59810). The quantum yields were determined at 22°C with a medium pressure mercury lamp light source in a Rayonet apparatus (obtained from the Southern New England Ultraviolet Co.). The system used for quantum yield determination was checked by the use of an Optometrics Corporation, Inc. Ayer, Ma. 365±5 nm interference filter (Catalog No. 02_3652, central wavelength 365 nm). The compound studied was 2,4,6-trimethyl-6-acetoxycyclohexa-2,4-dienone 5.02, see E72.

Equipment:

Figure 5.05, Chapter 5 page 124 shows the equipment used for light intensity and quantum yield determination (also see E73).

E69 Potassium trisoxalatoferrate trihydrate $K_3[Fe(C_2O_4)_3].3H_2O$ [124]

Prepared in a semi-dark room. Two standard solutions both 1.5 M were prepared the first of potassium oxalate (69.0693 g) in water (250 ml) and the second of iron(III) trichloride hexahydrate (40.5442 g) in water (100 ml). To the iron trichloride (80 ml) solution was added the potassium oxalate (240 ml)

solution, with vigorous stirring. After 40 minutes the precipitate was then filtered and recrystallized four times from warm water and dried at the pump with the action of a hair dryer. This gave pure green crystals of the title compound 40 g, 68%.

This was characterized by making a standard 0.006 M solution using 2.947 g, in 800 ml of water to which 100 ml of 0.5 M sulphuric acid was added. The resulting solution was then diluted to one litre with distilled water and mixed. Ten samples (10 ml) were then removed from this solution and photolyzed with light from a tungsten lamp (250 W) for one hour at 25°C. From each of these irradiated solutions was taken 1 ml samples and one 1 ml sample from the standard solution of the iron(III) oxalate solution. These samples were placed in eleven 50 ml volumetric flasks. To these flasks was added 12 ml of a 0.1% (weight) 1,10-phenanthroline solution (water, 0.00555 M, 11 equivalents = *solution b*) and 30 ml of a buffer solution (*solution c*). The buffer solution was prepared from mixing a 600 ml 1N solution of sodium acetate and 360 ml of 0.5 M sulphuric acid solution. This was then diluted to one litre with distilled water

The contents of the 50 ml volumetric flasks was further diluted to the mark with distilled water. These solutions were left for one hour in the dark and then the absorbance at 510 nm was recorded using the standard iron(III) oxalate solution, which had been treated similar except that it was not photolyzed, as a reference. Using the literature value for the molar extinction coefficient for an iron(II) phenanthroline solution (1.11×10^4 l $mol^{-1}cm^{-1}$) the concentration of the iron in the original 10 ml sample of potassium trisoxalatoferrate solution (0.006 M) was calculated. This was found to be 6×10^{-3} M ± 4%.

E70 Calibration of the Spectrophotometer.

A standard solution (0.1 M of iron(II) sulphate was prepared. Then in a 250 ml volumetric flask was added 1 ml of this iron(II) sulphate solution. This was then diluted to the mark with 0.05 M sulphuric acid solution to give a 0.0004 M solution of iron(II) sulphate (0.4×10^{-6} moles of Fe^{2+} per ml) and 0.05 M in sulphuric acid. To a series of eleven 25 ml volumetric flasks was added, by pipette, 0, 0.5, 1.0, 1.5, ..., 4.5, 5.0 ml of the 0.0004 M iron(II) sulphate solution. Then to each flask was added 10, 9.5, 8.0, 7.5, ..., 5.5, 5.0 ml of 0.05 M sulphuric acid solution, respectively. Then 2 ml of *solution b* and 5 ml of *solution c* was added (see E67). The flasks were diluted to the mark with distilled water and left in the dark for one hour. The absorbance of each solution at 510 nm was then determined using the blank iron-free solution as a reference. A linear plot of absorbance *versus* the molar concentration of the Fe^{2+} complex was found and gave the gradient equal to the molar extinction coefficient of 1.154×10^4 l $mol^{-1}cm^{-1}$ which is 3% different from the literature value[124] of 1.11×10^4 l $mol^{-1}cm^{-1}$.

Table of Fe^{2+} concentration *versus* absorbance at 510 nm.

Fe^{2+} concentration ($M \times 10^{-6}$)	Absorbance ($\times 10^{-2}$)	Fe^{2+} concentration ($M \times 10^{-6}$)	Absorbance ($\times 10^{-2}$)
X	Y	X	Y
0	0	49	40
11	8	55	48
18	16	80	72
26	24	91	80
37	32		

E71 Standard method for light intensity determination.

From the irradiated cell containing the standard iron(III) oxalate solution was taken by pipette a 1 ml sample which was placed in a 50 ml volumetric flask. To this was added 12 ml of *solution b* and *solution c* (see **E70**). The contents were then further diluted to the mark with distilled water. A sample was also taken from the non irradiated solution of the iron(III) oxalate (0.006 M) standard solution and prepared as for the irradiated solution above. This solution is used as a reference in the spectrophotometer. All these solutions were then allowed to stand in the dark for one hour and then the absorbance was recorded at 510 nm. Using the molar extinction coefficient calculated in **E70** (1.154×10^4 l mol^{-1} cm^{-1}) the concentration of iron(II) oxalate in the radiated sample can be calculated using the Beer-Lambert absorption law. This then allows the light intensity to be calculated using the equation below.[114, 127]

$$I = \frac{M^{Fe2+} \times V_1 \times 10^{-3} \times 6.023 \times 10^{23}}{t_1 \times \Phi_{Fe2+}} \quad \text{quanta/second}$$

M^{Fe2+} = molarity of the iron(II) formed during the photolysis
V_1 = volume of the cell photolyzed (cm^3)
Φ_{Fe2+} = quantum yield of Fe2+ at specific wavelength (1.21 at 365 nm)
t_1 = time the cell containing the iron actinometer was irradiated (seconds)

E72 2,4,6-Trimethyl-6-acetoxycyclohexa-2,4-dienone **5.02**.

To a solution of mesitol (2.724 g, 20 mol) in chloroform (100 ml) was added lead tetraacetate (13.301 g, 30 mmol) and the resulting solution stirred overnight. The precipitate that was formed was isolated by reduced pressure filtration and then was washed twice with water (30 ml) and a saturated solution of sodium bicarbonate (30 ml). After drying (anhydrous $MgSO_4$) and

evaporation the solid was recrystallized from petroleum ether (bp 60-120°C) and then recrystallized from ethanol to give the title compound 1.55 g, 40%; mp 82-83°C (lit.[129, 130] 82-84°C); IR ($CHCl_3$, cm^{-1}) 2940, 1730, 1670, 1440; UV-vis ($CHCl_3$) λ_{max} = 312, ε = 4 000 ; ^1H NMR ($CDCl_3$) δ 1.35 (s, 3H), 1.93 (m, 6H), 2.06 (s, 3H), 5.79-5.80 (m, 1H), 6.65-6.67 (m, 1H).

E73 Quantum yield of decomposition of **5.02** in the presence of cyclohexylamine.

2,4,6-Trimethyl-6-acetoxycyclohexa-2,4-dienone **5.02** (84.5 mg) was placed in a 50 ml volumetric flask which was then filled to the mark with $CDCl_3$. A sample (1 ml) was removed and diluted to 10 ml ($CDCl_3$, volumetric flask), from this solution was taken a 5 ml sample and was added to a 25 ml volumetric flask. To this was then added freshly distilled cyclohexylamine (2 µl) and then $CDCl_3$ was added to the mark. This provides a 1.74 x 10^{-4} M solution of **5.02** with cyclohexylamine (1.18 x 10^{-3} M, 6.8 equivalents) from which five 3 ml samples were removed and photolyzed as described in **E67** with an interference filter (365±5 nm).[128] The decrease in concentration of **5.02** was checked by ^1H NMR and UV-vis spectroscopy.

A blank run to determine light intensity was under taken (see **E71**, **E68** and Chapter 5 page 124 Figure 5.05) cell 3 and cell 4 were not used as the interference filter was employed.[128]

1st run cell 1: empty cell 2: actinometer, I = 1.445 x 10^{14} q/s

2nd run cell 1: actinometer, I = 0.875 x 10^{14} q/s cell 2: empty

Therefore correction factor due to distance for cell 1 = 1.39

This means that any light intensity measurements determined for the light passing through the sample solution into the actinometer solution in cell 1

must be corrected due to distance by a factor of 1.39 (i.e. $I_{cell\ 1} \times 1.39 = I_{absorbed}$ in cell 2).

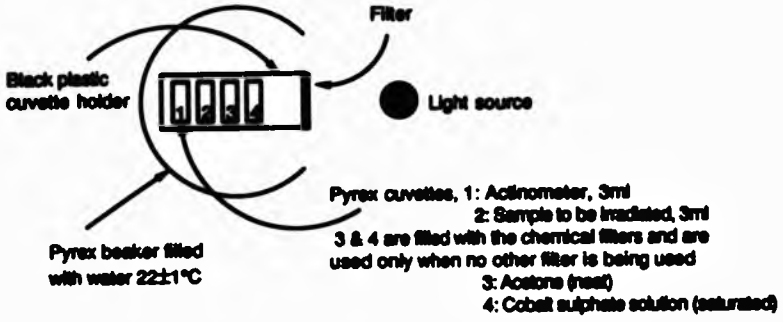


Diagram of equipment for the measurement of light intensity and quantum yields.

Table of light intensity and quantum yield of decomposition of 5.02.

Number	I^1 (x 10^{13} q/s)	I^{corr} (x 10^{13} q/s)	$I^2 - I^{corr}$ (x 10^{13} q/s)	conversion 5.02 (%)	Φ
1	6.2	8.62	5.83	34.7	0.52
2	5.34	7.42	7.03	27.5	0.34
3	6.38	8.87	5.58	34.8	0.545
4	6.49	9.02	5.43	37.3	0.599
5	6.33	8.799	5.65	32.9	0.508

I^1 – light intensity cell 1. I^2 = light intensity cell 2. I^{corr} = corrected light intensity of cell 2 = $I^1 \times 1.39$. $I^2 - I^{corr}$ = actual light absorbed by sample cell.
Quantum yield Φ is given by the equation below[114, 127] (see Chapter 5 page 123 Equation 5.06):

$$\Phi = \frac{M^P \times V_1 \times 10^{-3} \times 6.023 \times 10^{23}}{I \times t_1}$$

M^P = molarity of product whose quantum yield is to be determined
V_1 = volume of the cell photolyzed (cm^3)
I = light intensity (quanta per second)
t_1 = time the cell containing the sample was irradiated (seconds)

Thus, the average quantum yield of decomposition of 5.02 (not including the low or high values, entries 2 and 4) is given below:

$\Phi = 0.52$

(365 nm; 22±1°C; c for 5.02 = 1.74×10^{-4} M; 6.8 equivalents of cyclohexylamine).

The literature[133] value for the quantum yield of decomposition is given below:

$\Phi = 0.53$

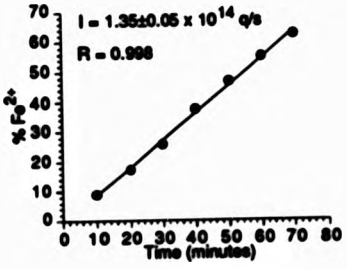
(365 nm; 20°C; c for 5.02 = 1.62×10^{-4} M[134]; 5.4 equivalents of cyclohexylamine).

E74 Light intensity determination for the 360 nm band pass filter.[135]

Seven 3 ml samples of the actinometer solution were irradiated for 10-70 minutes respectively by the medium pressure mercury lamp through the band pass filter.[135] After irradiation the percentage conversion of the Fe^{III} to Fe^{II} was measured in the usual way (see E71). Results are shown below.

Table of irradiation time, percentage formation of Fe^{II} and light intensity.

Number	Irradiation time (minutes)	% Fe^{2+} formed	Light intensity I (x 10^{15} q/s)
1	10	9	1.35
2	20	17.2	1.29
3	30	25.8	1.28
4	40	37.5	1.40
5	50	46.8	1.40
6	60	55.2	1.37
7	70	62.5	1.33



Plot of % Fe^{2+} formed against time of irradiation.

E75 Quantum yield of n-pentyldecyl chloride 4.59 from 4.11 and CCl_4.

The general procedure for quantum yield determination is given in **E67**. In this case chemical filters were used, see **E68**. The trapped product **4.59**[136] was identified from its GC-MS spectrum and its ^1H NMR spectrum; MS m/e 248, 246 (M^+); ^1H NMR ($CDCl_3$) δ 0.8-1.0 (m, 3H), 1.0-2.1 (m, 26H), 3.58 (t, 2H).

Solvent	Trap (equivalents)	Irradiation time (seconds)	Light intensity (x 10^{15}q/s)	Trapped product (%)	Φ
CH_2Cl_2	CCl_4(5)	600	2.265	1.77	2.36
CH_2Cl_2	CCl_4(5)	600	2.265	4.6	6.13
CH_2Cl_2	CCl_4(5)	600	2.265	4.1	5.46
CH_2Cl_2	CCl_4(5)	600	2.265	4.8	6.40
CH_2Cl_2	CCl_4(5)	600	2.265	7.1	9.46

Φ = 6 (rejecting high and low values)

Solvent	Trap (equivalents)	Irradiation time (seconds)	Light intensity (x 10^{15}q/s)	Trapped product (%)	Φ
CCl_4	CCl_4(102.9)	900	1.89	20	21
CCl_4	CCl_4(102.9)	900	1.89	21.3	22.6
CCl_4	CCl_4(102.9)	900	1.89	24.4	25.9
CCl_4	CCl_4(102.9)	900	1.89	28.8	30.6
CCl_4	CCl_4(102.9)	900	1.89	23	24.4

Φ = 24 (rejecting high and low values)

E76 Quantum yield of n-pentyldecyl bromide 4.50 from 4.11 and $CBrCl_3$.

The general procedure for quantum yield determination is given in E67. In this case chemical filters were used, see E68. The trapped product 4.50[137] was identified from its ^1H NMR spectrum; ^1H NMR ($CDCl_3$) δ 0.9 (t, 3H), 1.3 (m, 26H), 3.45 (t, J = 7 Hz, 2H).

Solvent	Trap (equivalents)	Irradiation time (seconds)	Light intensity (x 10^{15}q/s)	Trapped product (%)	Φ
CH_2Cl_2	$CBrCl_3$(5)	600	2.3	21.5	28.1
CH_2Cl_2	$CBrCl_3$(5)	600	2.3	21.0	27.5
CH_2Cl_2	$CBrCl_3$(5)	600	2.3	24.2	31.4
CH_2Cl_2	$CBrCl_3$(5)	600	3.5	36.4	31.3
CH_2Cl_2	$CBrCl_3$(5)	600	3.5	32.5	28.0

Φ = 29

Solvent	Trap (equivalents)	Irradiation time (seconds)	Light intensity (x 10^{15}q/s)	Trapped product (%)	Φ
$CBrCl_3$	$CBrCl_3$(101)	360	2.0	9	22.6
$CBrCl_3$	$CBrCl_3$(101)	360	2.0	11.3	28.4
$CBrCl_3$	$CBrCl_3$(101)	480	2.0	10.1	19
$CBrCl_3$	$CBrCl_3$(101)	480	2.0	13.8	26
$CBrCl_3$	$CBrCl_3$(101)	480	2.0	12.7	23.9

Φ = 24 (rejecting low and high values)

Quantum yield for pentadecyl bromide using a saturated solution of 4.11 (0.771 M).

Solvent	Trap (equivalents.)	Irradiation time (seconds)	Light intensity (x 10^{15}q/s)	Trapped product (%)	Φ
$CBrCl_3$	$CBrCl_3$(13)	600	3.66	7.4	47.0
$CBrCl_3$	$CBrCl_3$(13)	600	3.66	8.4	53.3
$CBrCl_3$	$CBrCl_3$(13)	600	3.66	10	64.0

Φ = 55

E77 Quantum yield of n-pentyldecyl bromide 4.50 from 4.11 and CBr_4.

The general procedure for quantum yield determination is given in **E67**. In this case chemical filters were used, see **E68**. The trapped product **4.50**[137] was identified from its ^1H NMR spectrum see **E76**.

Solvent	Trap (equivalents)	Irradiation time (seconds)	Light intensity (x 10^{15}q/s)	Trapped product (%)	Φ
CH_2Cl_2	CBr_4(5)	600	2.2	22	30.1
CH_2Cl_2	CBr_4(5)	600	2.2	23	31.5
CH_2Cl_2	CBr_4(5)	600	2.2	22	30.1
CH_2Cl_2	CBr_4(5)	600	2.2	25	34.2
CH_2Cl_2	CBr_4(5)	600	2.2	24	32.8

Φ = 32

E78 Quantum yield of n-pentyldecyl phenyl sulphide 5.07 from 4.11 and $(PhS)_2$.

The general procedure for quantum yield determination is given in **E67**. In this case chemical filters were used, see **E68**. The trapped product **5.07**[138] was identified from its ^1H NMR spectrum; ^1H NMR ($CDCl_3$) δ 0.89 (m, 3H), 1.30 (m, 26H), 2.84 (t, 2H), 7.00-7.60 (m, 5H).

Solvent	Trap (equivalents)	Irradiation time (seconds)	Light intensity (x 10^{15}q/s)	Trapped product (%)	Φ
CH_2Cl_2	$(PhS)_2$(5)	1200	2.2	29.9	20.5
CH_2Cl_2	$(PhS)_2$(5)	1200	2.2	34.6	23.7
CH_2Cl_2	$(PhS)_2$(5)	1200	2.2	36.6	25.05
CH_2Cl_2	$(PhS)_2$(5)	600	2.0	18.2	27.4
CH_2Cl_2	$(PhS)_2$(5)	600	2.0	15.8	23.8

Φ = 24 (rejecting the low and high values)

Solvent	Trap (equivalents)	Irradiation time (seconds)	Light intensity (x 10^{15}q/s)	Trapped product (%)	Φ
CH_2Cl_2	$(PhS)_2$(2)	600	1.99	5.8	8.8
CH_2Cl_2	$(PhS)_2$(2)	600	1.99	3.6	5.4
CH_2Cl_2	$(PhS)_2$(2)	900	1.99	7.6	7.7
CH_2Cl_2	$(PhS)_2$(2)	600	1.99	5.4	8.2
CH_2Cl_2	$(PhS)_2$(2)	600	1.99	6.2	9.4

Φ = 8 (rejecting the low and high values)

E79 Quantum yield of n-pentyldecyl phenyl selenide 5.10 from 4.11 and $(PhSe)_2$.

The general procedure for quantum yield determination is given in **E67**. In this case chemical filters were used, see **E68**. The trapped product **5.10**[136] was identified from its GC-MS spectrum and its ^{1}H NMR spectrum; MS m/e 366, 368 (M^+); ^{1}H NMR ($CDCl_3$) δ 0.88 (m, 3H), 1.28 (m, 26H), 2.95 (t, J = 7 Hz, 2H), 7.35 (m, 5H).

Solvent	Trap (equivalents)	Irradiation time (seconds)	Light intensity (x 10^{15}q/s)	Trapped product (%)	Φ
CH_2Cl_2	$(PhSe)_2$(5)	1200	2.3	17.1	12.1
CH_2Cl_2	$(PhSe)_2$(5)	600	2.3	10	14.1
CH_2Cl_2	$(PhSe)_2$(5)	600	2.3	10.1	14.3
CH_2Cl_2	$(PhSe)_2$(5)	600	2.3	10.3	14.6
CH_2Cl_2	$(PhSe)_2$(5)	600	2.3	9.3	13.2

Φ = 14 (rejecting the low and high values)

Solvent	Trap (equivalents)	Irradiation time (seconds)	Light intensity (x 10^{15}q/s)	Trapped product (%)	Φ
CH_2Cl_2	$(PhSe)_2$(2)	600	1.91	16.3	25.7
CH_2Cl_2	$(PhSe)_2$(2)	600	1.91	20.1	31.7
CH_2Cl_2	$(PhSe)_2$(2)	600	1.91	16.4	25.9
CH_2Cl_2	$(PhSe)_2$(2)	600	1.91	15.1	23.8
CH_2Cl_2	$(PhSe)_2$(2)	660	1.91	20	26.7

Φ = 27 (rejecting the low and high values)

E80 Quantum yield of (1-(2'-thiopyridine)-n-heptadecyl) phenyl sulphone 5.13 from 4.11 and CH_2=$CHSO_2Ph$.

The general procedure for quantum yield determination is given in E67. In this case chemical filters were used, see E68. The trapped product 5.13[139] was identified from its GC-MS spectrum and its ^{1}H NMR spectrum; MS m/e 348 (M^+–SO_2Ph); ^{1}H NMR ($CDCl_3$) δ 0.88 (m, 3H), 1.27 (m, 26H),

1.43-1.99 (m, 3H), 2.20-2.55 (m, 1H), 5.70 (m, 1H), 6.82-7.03 (m, 2H), 7.20-7.48 (m, 4H), 7.86 (m, 2H), 8.20 (m, 1H).

Solvent	Trap (equivalents)	Irradiation time (seconds)	Light intensity (x 10^{15}q/s)	Trapped product (%)	Φ
CH_2Cl_2	CH_2=$CHSO_2Ph$(5)	1200	2.5	57	34.3
CH_2Cl_2	CH_2=$CHSO_2Ph$(5)	1200	2.5	58	34.9
CH_2Cl_2	CH_2=$CHSO_2Ph$(5)	1200	2.5	59.5	35.8
CH_2Cl_2	CH_2=$CHSO_2Ph$(5)	1200	2.19	55.7	38
CH_2Cl_2	CH_2=$CHSO_2Ph$(5)	1200	2.19	48.8	33.5

Φ = 35 (rejecting low and high values)

E81 Quantum yield of cyclohexyl chloride 5.06 from 4.48a and CCl_4.

The general procedure for quantum yield determination is given in **E67**. In this case chemical filters were used, see **E68**. The trapped product **5.06**[138] was identified from its GC-MS spectrum and its ^{1}H NMR spectrum; MS m/e 118, 120 (M^+); ^{1}H NMR ($CDCl_3$) δ 1.0-2.5 (m, 10H), 3.7-4.30 (m, 1H).

Solvent	Trap (equivalents)	Irradiation time (seconds)	Light intensity (x 10^{15}q/s)	Trapped product (%)	Φ
$CDCl_3$	CCl_4(5)	1200	1.87	36	29
$CDCl_3$	CCl_4(5)	1200	1.87	24	19.3
$CDCl_3$	CCl_4(5)	1200	1.87	30	24.1
$CDCl_3$	CCl_4(5)	1080	1.87	25.4	22.7
$CDCl_3$	CCl_4(5)	1200	1.87	27	21.7

Φ = 23 (rejecting high and low values)

E82 Quantum yield of cyclohexyl bromide 4.51 from 4.48a and $CBrCl_3$.

The general procedure for quantum yield determination is given in **E67**. In this case chemical filters were used, see **E68**. The trapped product **4.51**[138] was identified from its ^1H NMR spectrum; ^1H NMR ($CDCl_3$) δ 1.00-2.50 (m, 10H), 3.9-4.5 (m, 1H).

Solvent	Trap (equivalents)	Irradiation time (seconds)	Light intensity (x 10^{15}q/s)	Trapped product (%)	Φ
$CDCl_3$	$CBrCl_3$(5)	1200	2.39	52	32.8
$CDCl_3$	$CBrCl_3$(5)	1380	2.39	55	30.1
$CDCl_3$	$CBrCl_3$(5)	1200	2.39	65	40.95
$CDCl_3$	$CBrCl_3$(5)	1200	2.39	50	31.5
$CDCl_3$	$CBrCl_3$(5)	1200	2.39	48.7	30.24

Φ = 31 (rejecting the high value)

E83 Quantum yield of cyclohexyl bromide 4.51 from 4.48a and CBr_4.

The general procedure for quantum yield determination is given in **E67**. In this case chemical filters were used, see **E68**. The trapped product **4.51**[138] was identified from its ^1H NMR spectrum see **E82**.

Solvent	Trap (equivalents)	Irradiation time (seconds)	Light intensity (x 10^{15}q/s)	Trapped product (%)	Φ
$CDCl_3$	CBr_4(5)	1200	2.4	46.7	29.3
$CDCl_3$	CBr_4(5)	1200	2.4	46.7	29.3
$CDCl_3$	CBr_4(5)	1440	2.4	53.0	27.7
$CDCl_3$	CBr_4(5)	1200	2.4	43.5	27.3
$CDCl_3$	CBr_4(5)	1200	2.4	42.5	26.7

Φ = 28

E84 Quantum yield of cyclohexyl phenyl sulphide **5.09** from **4.48a** and $(PhS)_2$.

The general procedure for quantum yield determination is given in **E67**. In this case chemical filters were used, see **E68**. The trapped product **5.09**[142] was identified from its GC-MS spectrum and its ^1H NMR spectrum; MS m/e 192 (M^+); ^1H NMR ($CDCl_3$) δ 1.10-2.10 (m, 10H), 3.08-3.24 (m, 1H), 7.15-7.40 (m, 5H).

Solvent	Trap (equivalents)	Irradiation time (seconds)	Light intensity (x 10^{15}q/s)	Trapped product (%)	Φ
CH_2Cl_2	$(PhS)_2$(5)	900	3.0	39.8	26.6
CH_2Cl_2	$(PhS)_2$(5)	900	3.0	42.0	28.1
CH_2Cl_2	$(PhS)_2$(5)	900	3.0	35.5	23.7
CH_2Cl_2	$(PhS)_2$(5)	900	3.0	40.1	26.8
CH_2Cl_2	$(PhS)_2$(5)	900	3.0	39.9	26.7

Φ = 27 (rejecting the low and high values)

E85 Quantum yield of cyclohexyl phenyl selenide **5.12** from **4.48a** and $(PhSe)_2$.

The general procedure for quantum yield determination is given in **E67**. In this case chemical filters were used, see **E68**. The trapped product **5.12**[143] was identified from its GC-MS spectrum and its ^1H NMR spectrum; MS m/e 240, 238 (M^+); ^1H NMR ($CDCl_3$) δ 1.45 (m, 10H), 3.08-3.24 (m, 1H), 7.26 (m, 5H).

Solvent	Trap (equivalents)	Irradiation time (seconds)	Light intensity (x 10^{15}q/s)	Trapped product (%)	Φ
CH_2Cl_2	$(PhSe)_2$(5)	1200	2.2	33.1	22.6
CH_2Cl_2	$(PhSe)_2$(5)	900	2.2	21.0	19.1
CH_2Cl_2	$(PhSe)_2$(5)	1200	2.2	27.4	18.75
CH_2Cl_2	$(PhSe)_2$(5)	900	2.2	21.5	19.6
CH_2Cl_2	$(PhSe)_2$(5)	1200	2.2	26.5	18.14

Φ = 19 (rejecting the low and high values)

E66 Quantum yield of (2-cyclohexyl-1-(2'-thiopyridine) ethyl) phenyl sulphone 5.15 from 4.48a and CH_2=$CHSO_2Ph$.

The general procedure for quantum yield determination is given in **E67**. In this case chemical filters were used, see **E68**. The trapped product 5.15[139] was identified from its GC-MS spectrum and its ^{1}H NMR spectrum; MS m/e 361 (M^+), 221 (M^+–SO_2Ph); ^{1}H NMR ($CDCl_3$) δ 0.75-1.32 (m, 5H), 1.47-1.95 (m, 7H), 2.06-2.34 (m, 1H), 5.70-5.91 (m, 1H), 6.79-6.99 (m, 2H), 7.19-7.45 (m, 4H), 7.90 (m, 2H), 8.20 (m, 1H).

Solvent	Trap (equivalents)	Irradiation time (seconds)	Light intensity (x 10^{15}q/s)	Trapped product (%)	Φ
CH_2Cl_2	CH_2=$CHSO_2Ph$(5)	600	2.67	29.2	32.9
CH_2Cl_2	CH_2=$CHSO_2Ph$(5)	600	2.67	27.5	31.0
CH_2Cl_2	CH_2=$CHSO_2Ph$(5)	600	2.67	32.0	36.1
CH_2Cl_2	CH_2=$CHSO_2Ph$(5)	600	2.67	30.0	33.8
CH_2Cl_2	CH_2=$CHSO_2Ph$(5)	720	2.67	36.7	34.5

Φ = 34 (rejecting low and high values)

E67 Quantum yield of *t*-butyl chloride 5.05 from 4.48b and CCl_4.

The general procedure for quantum yield determination is given in **E67**. In this case chemical filters were used, see **E68**. The trapped product 5.05[138] was identified from its GC-MS spectrum and its ^1H NMR spectrum; MS m/e 92, 94 (M^+); ^1H NMR ($CDCl_3$) δ 1.62 (s, 9H).

Solvent	Trap (equivalents)	Irradiation time (seconds)	Light intensity (x 10^{15}q/s)	Trapped product (%)	Φ
$CDCl_3$	CCl_4(5)	1200	1.75	15.8	13.5
$CDCl_3$	CCl_4(5)	1200	1.75	23.6	20.1
$CDCl_3$	CCl_4(5)	1200	1.75	17.0	14.5
$CDCl_3$	CCl_4(5)	1200	1.75	12.6	10.8
$CDCl_3$	CCl_4(5)	1260	1.75	16.5	14.0

Φ = 13 (rejecting the high value)

E68 Quantum yield of *t*-butyl bromide 4.52 from 4.48b and $CBrCl_3$.

The general procedure for quantum yield determination is given in **E67**. In this case chemical filters were used, see **E68**. The trapped product 4.52[139] was identified from its ^1H NMR spectrum; ^1H NMR ($CDCl_3$) δ 1.81 (s, 9H).

Solvent	Trap (equivalents)	Irradiation time (seconds)	Light intensity (x 10^{15}q/s)	Trapped product (%)	Φ
$CDCl_3$	$CBrCl_3$(5)	900	1.95	6.6	6.8
$CDCl_3$	$CBrCl_3$(5)	900	1.95	8.6	8.8
$CDCl_3$	$CBrCl_3$(5)	1200	1.95	8.0	8.2
$CDCl_3$	$CBrCl_3$(5)	900	1.95	6.7	6.9
$CDCl_3$	$CBrCl_3$(5)	900	1.95	9.5	10

Φ = 8 (rejecting high and low values)

E89 Quantum yield of t-butyl bromide 4.52 from 4.48b and CBr_4.

The general procedure for quantum yield determination is given in **E67**. In this case chemical filters were used, see **E68**. The trapped product **4.52**[139] was identified from its ^{1}H NMR spectrum, see **E88**

Solvent	Trap (equivalents)	Irradiation time (seconds)	Light intensity (x 10^{15}q/s)	Trapped product (%)	Φ
$CDCl_3$	CBr_4(5)	900	2.0	25.5	25.6
$CDCl_3$	CBr_4(5)	900	2.0	25.9	25.6
$CDCl_3$	CBr_4(5)	900	1.75	21.2	24
$CDCl_3$	CBr_4(5)	780	1.75	13.9	18.4
$CDCl_3$	CBr_4(5)	780	1.75	16.8	22.2

Φ = 24 (rejecting low value)

E90 Quantum yield of *t*-butyl phenyl sulphide **5.08** from **4.48b** and $(PhS)_2$.

The general procedure for quantum yield determination is given in **E67**. In this case chemical filters were used, see **E68**. The trapped product **5.08**[140] was identified from its GC-MS spectrum and its ^1H NMR spectrum; MS m/e 166 (M^+); ^1H NMR ($CDCl_3$) δ 1.27 (s, 9H), 7.1-7.5 (m, 5H).

Solvent	Trap (equivalents)	Irradiation time (seconds)	Light intensity (x 10^{15}q/s)	Trapped product (%)	Φ
$CDCl_3$	$(PhS)_2$(5)	900	1.82	6.5	7.2
$CDCl_3$	$(PhS)_2$(5)	900	1.82	8.6	9.5
$CDCl_3$	$(PhS)_2$(5)	900	1.82	10.5	11.6
$CDCl_3$	$(PhS)_2$(5)	900	1.82	13.0	14.3
$CDCl_3$	$(PhS)_2$(5)	900	1.75	9.2	10.6

Φ = 11 (rejecting the low and high values)

E91 Quantum yield of *t*-butyl phenyl selenide **5.11** from **4.48b** and $(PhSe)_2$.

The general procedure for quantum yield determination is given in **E67**. In this case chemical filters were used, see **E68**. The trapped product **5.11**[141] was identified from its GC-MS spectrum and its ^1H NMR spectrum; MS m/e 212, 214 (M^+); ^1H NMR ($CDCl_3$) δ 1.39 (s, 9H), 7.19-7.60 (m, 5H).

Solvent	Trap (equivalents)	Irradiation time (seconds)	Light intensity (x 10^{15}q/s)	Trapped product (%)	Φ
$CDCl_3$	$(PhSe)_2$(5)	1200	1.77	12.6	10.7
$CDCl_3$	$(PhSe)_2$(5)	1200	1.77	12.6	10.2
$CDCl_3$	$(PhSe)_2$(5)	1200	1.77	11.5	9.8
$CDCl_3$	$(PhSe)_2$(5)	1200	1.77	10.2	8.7
$CDCl_3$	$(PhSe)_2$(5)	1200	1.77	14.3	12.1

Φ = 10 (rejecting the low and high values)

E92 Quantum yield of (3,3-dimethyl-1-(2'-thiopyridine) butyl) phenyl sulphone 5.14 from 4.48b and CH_2=$CHSO_2Ph$.

The general procedure for quantum yield determination is given in E67. In this case chemical filters were used, see E68. The trapped product 5.14[139] was identified from its GC-MS spectrum and its ^1H NMR spectrum; MS m/e 335 (M^+), 320 (M^+–CH_3); ^1H NMR ($CDCl_3$) δ 0.99 (s, 9H), 1.82 (m, 1H), 2.35 (d, 1H), 5.80 (m, 1H), 6.91 (m, 1H), 7.28-7.36 (m, 5H), 7.88 (m, 2H), 8.22 (m, 1H).

Solvent	Trap (equivalents)	Irradiation time (seconds)	Light intensity (x 10^{15}q/s)	Trapped product (%)	Φ
$CDCl_3$	CH_2=$CHSO_2Ph$(5)	900	1.8	20.4	22.8
$CDCl_3$	CH_2=$CHSO_2Ph$(5)	960	1.8	20.6	23
$CDCl_3$	CH_2=$CHSO_2Ph$(5)	900	1.8	20.5	22.9
$CDCl_3$	CH_2=$CHSO_2Ph$(5)	900	1.8	18.5	20.6
$CDCl_3$	CH_2=$CHSO_2Ph$(5)	900	1.8	19.5	21.8

Φ = 22

E93 Quantum yield of pentadecyl bromide 4.50 from a 0.1 M solution of 4.11 and $CBrCl_3$ using the band pass filter.[135]

The general procedure for quantum yield determination is given in **E67**. In this case the band pass filter[135] was used, see **E68**. The trapped product **4.50**[137] was identified from its ^1H NMR spectrum see **E76**.

Solvent	Trap (equivalents)	Irradiation time (seconds)	Light intensity (x 10^{15}q/s)	Trapped product (%)	Φ
$CDCl_3$	$CBrCl_3$(5)	300	1.35	5	22.3
$CDCl_3$	$CBrCl_3$(5)	300	1.35	6.7	29.9
$CDCl_3$	$CBrCl_3$(5)	900	1.35	18.4	27.4
$CDCl_3$	$CBrCl_3$(5)	900	1.35	16.6	31.3
$CDCl_3$	$CBrCl_3$(5)	900	1.35	22.2	25.1

Φ = 27 (rejecting low and high values)

E94 Quantum yield of pentadecyl bromide 4.50 from a 0.1 M solution of 4.49a and $CBrCl_3$ using the band pass filter.[135]

The general procedure for quantum yield determination is given in **E67**. In this case the band pass filter[135] was used, see **E68**. The trapped product **4.50**[137] was identified from its ^1H NMR spectrum see **E76**.

Solvent	Trap (equivalents)	Irradiation time (seconds)	Light intensity (x 10^{15}q/s)	Trapped product (%)	Φ
$CDCl_3$	$CBrCl_3$(5)	900	1.35	46.4	69.0
$CDCl_3$	$CBrCl_3$(5)	900	1.35	39.6	58.9
$CDCl_3$	$CBrCl_3$(5)	900	1.35	40.36	60.2

Φ = 60 (rejecting high value)

E95 Quantum yield of pentadecyl bromide 4.50 from a 0.1 M solution of 4.43b and $CBrCl_3$ using the band pass filter.[135]

The general procedure for quantum yield determination is given in **E67**. In this case the band pass filter[135] was used, see **E68**. The trapped product 4.50[137] was identified from its ^1H NMR spectrum see **E76**.

Solvent	Trap (equivalents)	Irradiation time (seconds)	Light intensity (x 10^{15}q/s)	Trapped product (%)	Φ
$CDCl_3$	$CBrCl_3$(5)	900	1.35	33.8	33.8
$CDCl_3$	$CBrCl_3$(5)	900	1.35	31.7	31.7
$CDCl_3$	$CBrCl_3$(5)	900	1.35	33.0	33.0
$CDCl_3$	$CBrCl_3$(5)	900	1.35	32.3	32.3
$CDCl_3$	$CBrCl_3$(5)	900	1.35	30.7	30.7

Φ = 32

E96 Quantum yield of pentadecyl bromide 4.50 from a 0.1 M solution of 4.43a and $CBrCl_3$ using the band pass filter.[135]

The general procedure for quantum yield determination is given in **E67**. In this case the band pass filter[135] was used, see **E68**. The trapped product 4.50[137] was identified from its ^1H NMR spectrum see **E76**.

Solvent	Trap (equivalents.)	Irradiation time (seconds)	Light intensity (x 10^{15}q/s)	Trapped product (%)	Φ
$CDCl_3$	$CBrCl_3$(5)	900	1.35	36.05	53.6

Φ = 54

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