SOME NEW ASPECTS OF RADICAL TRAPPING USING AN AMINOXYL RADICAL TRAP
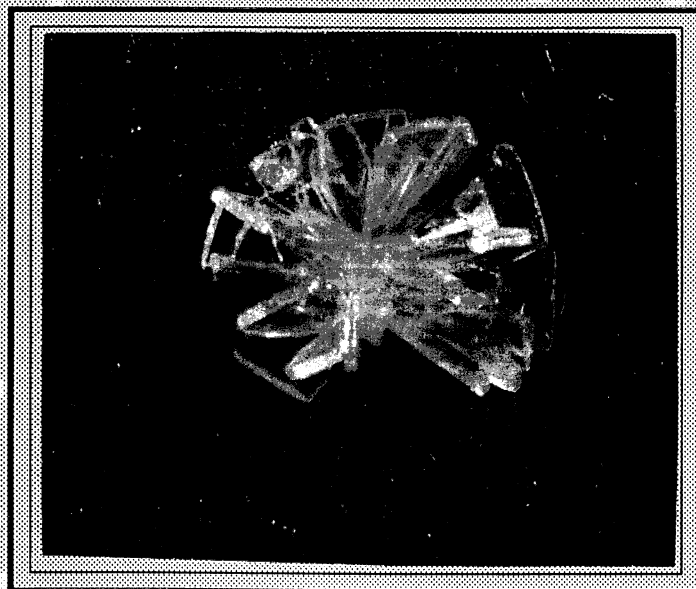
A Thesis submitted for the Degree of Doctor of Philosophy

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1,1,3,3-Tetramethyl-2,3-dihydro-1H-isoindol-2-yloxyl
Aminoxyl Trap

Acknowledgements

Summary

An investigation of the initiation mechanism in the free radical copolymerisation of acrylonitrile and vinyl acetate using the aminoxyl radical trapping technique, employing 1,1,3,3-tetramethyl-2,3-dihydro-1H-isoindol-2-yloxyl is reported. Based upon the experimental results, the mechanism of initiation is suggested as proceeding via the 'free monomer' mechanism. Additionally, the effect of Lewis acids on the initiation mechanism is reported.

A study of the addition of phosphorus-centred radicals to alkenes and phenylacetylene, utilising the aminoxyl radical trapping technique is reported. The results indicate a decreased rate of addition by both diphenylphosphinyl and dimethoxyphosphinyl radicals to cyclic versus acyclic alkenes. In contrast to cyclic alkenes, both these phosphorus-centred radicals add readily to the triple bond of phenylacetylene. The stereochemistry of the addition of diphenylphosphinyl and dimethoxyphosphinyl radicals and of the aminoxyl trap is discussed.

The stereochemistry of the addition of benzoyloxyl radicals to a conformationally rigid alkene, trans-Δ^2-octalin is reported.

Attempts to examine the initiation mechanism in the free radical copolymerisation of styrene/maleic anhydride and of styrene/tetracyanoethylene utilising the aminoxyl radical trapping technique are described. Also described are attempts to synthesise some new phosphorus radical initiators.

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CHAPTER ONE

GENERAL INTRODUCTION

CHAPTER ONE

1.0 Historical Background

"Science moves, but slowly slowly, creeping on from point to point"(Lord Alfred Tennyson 1809-1892). Free radical chemistry most certainly followed this path.

In the early 1800's the term 'radical' meant a part of a molecule[1], and most chemists believed these parts to be capable of independent, separate existence. However, with Mendeleef's periodic system of classification of the elements it was recognised that valency was a periodic property of the elements, making it clear that many species formerly assumed to be radicals were actually molecules.

During the first quarter of the twentieth century, physicists, unaware of the concept of valence, were busily studying free radicals produced in flames and by electrical excitation; at the same time chemists were steadfastly denying the very possibility of the existence of free radicals. Interestingly during the mid-nineteenth century there was active research in many laboratories on free radicals. Frankland[2](1849) said that he had proof beyond doubt for the existence of ethyl radicals. Kolbe[3] in the same year felt he also had proof for the existence of methyl radicals. Both Frankland and Kolbe's work was immediately questioned, in particular by Laurent[4](1850). Kolbe energetically protested Laurent's claims, but finally in 1864 Schorlemmer[5] seemingly settled the matter claiming to have proven that methyl radicals produced by Kolbe were actually ethane. There was a deathly silence in the literature on free radicals for several decades following. The conclusion seems to have been drawn that there were no organic "free radicals".

In 1892 Nef[6] initiated a resurgence of interest in free radicals. He challenged the idea of the constant valency of carbon and tried to interpret the mechanism of a wide variety of organic reactions as proceeding through bivalent carbon. His ideas proved to be largely incorrect but no doubt he influenced chemical thinking so that Gomberg's discovery of the triphenyl methyl radical was certainly more palatable.

Moses Gomberg[7] in 1900, by accident, prepared the first free radical. Gomberg produced triphenyl methyl radicals by the action of metallic silver on triphenylchloromethane.

$$2(C_6H_5)_3CCl + 2Ag \longrightarrow 2AgCl + (C_6H_5)_3C\text{-}C(C_6H_5)_3$$

He expected an inert colourless hydrocarbon, but obtained highly coloured yellow solutions that were decolourised very rapidly by air, iodine and a number of other materials now known to react with radicals. Gomberg correctly proposed that he was dealing with triphenylmethyl(trityl) radicals produced by the dissociation of the dimeric species into two free radicals.

$$(C_6H_5)_3C\text{-}C(C_6H_5)_3 \rightleftharpoons 2(C_6H_5)_3\overset{\bullet}{C}$$
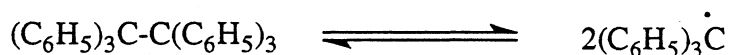
These 'radicals' were still regarded as having little relevance to organic chemistry, and for many years Gomberg's radical was considered as merely a chemical novelty. In the 1920's evidence for free radical intermediates began to accumulate. The discovery of the methyl radical was achieved by Paneth and Hofeditz[8] in 1929. By pyrolising tetramethyl lead in a flowing system at pressures of a few tenths of a millimetre not only would a lead mirror be deposited on the walls of the pyrolysis tube but a short lived intermediate was also generated capable of removing a similar mirror previously deposited down-stream. This result was interpreted in terms of the temperature-dependent equilibrium:

$$(CH_3)_4Pb \rightleftharpoons 4\overset{\bullet}{C}H_3 + Pb$$
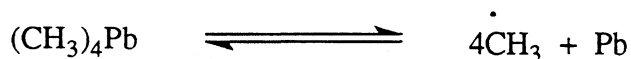
This "mirror" test was to become an important method for the detection of small transient gas phase radicals[9]. Although this work was of interest at the time, it apparently had no great influence on either fundamental chemical thought or practical chemical experimentation. The general consensus is illustrated by the following quote by Bennett and Chapman[10] in 1930 "The possibility of free radicals being formed as intermediate products in the course of chemical reactions whilst always admissible, is only occasionally supported by the experimental evidence".

The recognition of free radicals as participating reactive entities in chemical reactions dates from 1937, following the publication of three papers. The first was an influential review by Hey and Waters[11] in England, who provided detailed radical mechanisms for some reactions which until then had been difficult to explain. The second was a formulation by Kharasch, Engelmann and Mayo[12] in America who identified the radical mechanism for the anti-Markovnikov addition of hydrogen bromide to olefins, as a radical chain reaction in its modern form.

$$\dot{Br} + CH_2=CHR \longrightarrow BrCH_2\dot{C}HR$$

$$BrCH_2\dot{C}HR + HBr \longrightarrow BrCH_2CH_2R + \dot{Br}$$
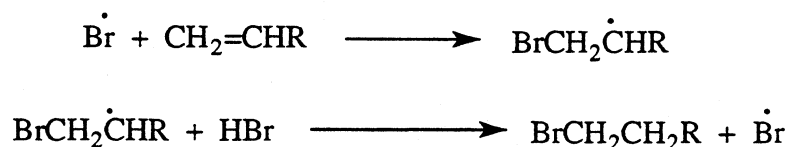
The third paper in the same year by Flory[13] introduced the now accepted radical mechanism for addition polymerisation, and the concept of chain transfer.

These three publications made radical intermediates 'respectable' and in fact marked the stage at which the organic chemist's interest in radicals was aroused. The modern history of radical chemistry had begun and had aptly been christened the 'New Organic Chemistry'[14]. Not so much new in the sense of newly discovered, but new in the sense of recognition now that many reactions involved free radicals.

This 'New Organic Chemistry' rocketed into prominence with the outbreak of the second world war in 1939. By 1942 Japan occupied southeast Asia and so cut off supplies of rubber to the Allies, and this demanded the development of a synthetic rubber industry, virtually from scratch (The synthetic rubber industry had its start in what was essentially a reversal of these conditions, when in the Second World War Germany was starved of its rubber suplies. They made 'methyl rubber' from dimethyl butadiene). Many of these synthetic materials were produced by radical vinyl polymerisation processes, and therefore radical chemistry became very important industrially.

The advances in understanding of radical chemistry made at this time were awesome, especially where it was related to polymerisation processes. The polymer industry has continued to flourish and by 1982 polymer production was greater by volume than the output of steel[15]. Although the polymer

industry continued to flourish, academic interest in radical chemistry after the second world war centred mainly on small molecule reactions.

To demonstrate their presence and to study their structure and reactivity, new techniques had to be developed, including various trapping techniques, and spectroscopic techniques such as ESR(electron spin resonance, also called EPR-electron paramagnetic resonance), NMR spectroscopy and mass spectrometry.

Despite their slow humble beginnings, today free radicals have gained unquestionable recognition as playing a significant part not only in organic chemistry, but chemistry as a whole. They are known to participate in atmospheric chemistry: ozone chemistry in the stratosphere, the formation and the destruction of pollutants in the lower atmosphere[9]. They are also important in biological chemistry, in metabolic and enzymatic processes, in pathological processes eg, ageing, cancer, cataracts, radiation injury and diabetes[16] to name but a few.

Free radicals are fast becoming as well known as the kangaroo, with progress being made in leaps and bounds.

1.1 Techniques used in the Study of Free Radicals

There are two main techniques used in the detection and study of free radical intermediates, particularly as they pertain to free radical polymerisation processes. These are the well known esr/spin trapping[17] technique and the more recently developed 'radical trapping technique'[18]. Both methods rely on intercepting and trapping the radicals formed in the early stages of polymerisation, i.e the initiation stage. For example, addition of the initiating radical I· to the monomer results in a carbon-centred radical (scheme 1). Both the spin-trapping and the radical trapping techniques result in trapping of this carbon-centred radical before significant propagation can occur.

scheme 1

Initiation

a. Initiator $\longrightarrow$ 2 x I$^\bullet$

b. I$^\bullet$ + $CH_2{=}C{\overset{A}{\underset{B}{\diagup}}}$ $\longrightarrow$ $I{-}CH_2{-}\overset{\overset{A}{|}}{\underset{\underset{B}{|}}{C}}^\bullet$

Propagation

c. $I{-}CH_2{-}\overset{\overset{A}{|}}{\underset{\underset{B}{|}}{C}}^\bullet$ + $n(CH_2{=}C{\overset{A}{\underset{B}{\diagup}}})$ $\longrightarrow$ $I{-}[CH_2{-}\overset{\overset{A}{|}}{\underset{\underset{B}{|}}{C}}]_{n+1}$

Termination

d. Combination $RCH_2{-}\overset{\overset{A}{|}}{\underset{\underset{B}{|}}{C}}^\bullet + {}^\bullet\overset{\overset{A}{|}}{\underset{\underset{B}{|}}{C}}{-}CH_2R$ $\longrightarrow$ $RH_2C{-}\overset{\overset{A}{|}}{\underset{\underset{B}{|}}{C}}{-}\overset{\overset{A}{|}}{\underset{\underset{B}{|}}{C}}{-}CH_2R$

e. Disproportionation $RCH_2{-}\overset{\overset{A}{|}}{\underset{\underset{B}{|}}{C}}^\bullet + {}^\bullet\overset{\overset{A}{|}}{\underset{\underset{B}{|}}{C}}{-}CH_2R$ $\longrightarrow$ $RH_2C{-}\overset{\overset{A}{|}}{\underset{\underset{B}{|}}{C}}{-}H$

$+$ $R{-}CH{=}C{\overset{A}{\underset{B}{\diagup}}}$

f. Chain Transfer $R^\bullet + A_c{-}R'$ $\longrightarrow$ $R{-}A_c + R'^\bullet$
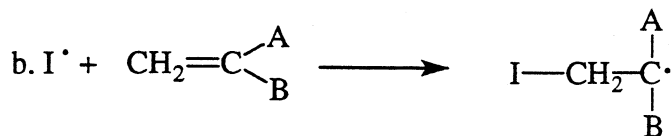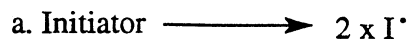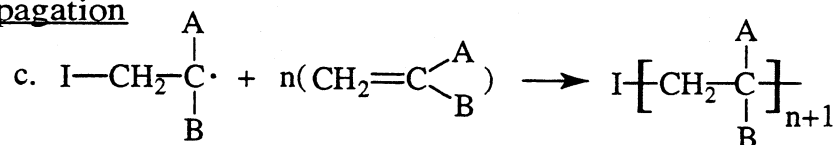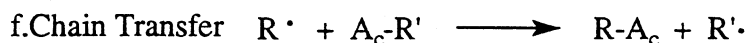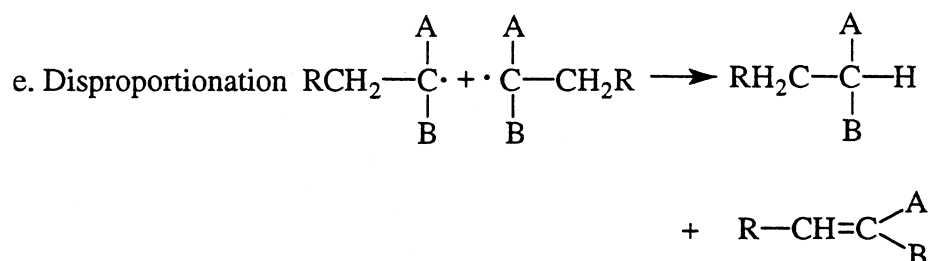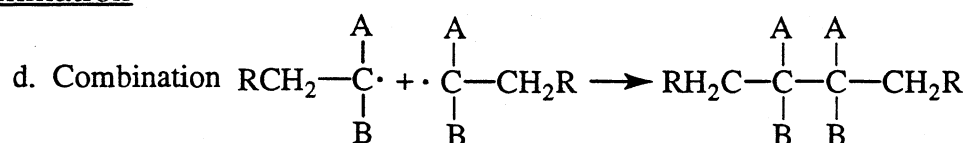
1.1.0 ESR/Spin Trapping

Spin trapping[17] in conjunction with esr is generally accepted as being a powerful weapon in the chemist's armoury for investigating free-radical reaction mechanisms. Spin trapping is the process of transforming short-lived transient or reactive free radicals into more persistent paramagnetic species. This process depends upon reacting the transient radical with a small quantity of a diamagnetic substance ('spin trap') to produce the more persistent 'spin adduct' (often an aminoxyl). This spin adduct can then be detected by esr.

$$R^\bullet + ST \longrightarrow (\dot{S}T{-}R) \qquad\qquad I$$

spin trap   spin adduct
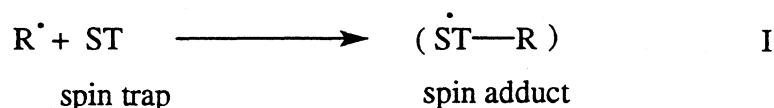
The following features need to be taken into consideration, when designing spin-trapping experiments or interpreting results.

(a) Can the spin-trapping agent participate in any reactions other than those with reactive radicals generated during the experiment? If so, can these alternative reactions yield paramagnetic species which will hamper spectrum interpretation?

(b) How readily can the esr spectrum of the spin adduct be interpreted, and is the identity of R·, the radical which has been trapped according to I, readily discerned from the spectrum?
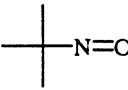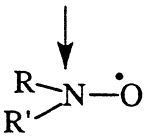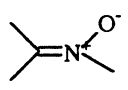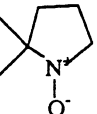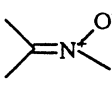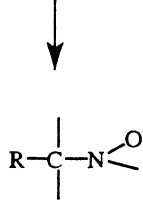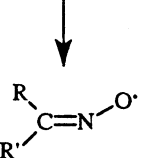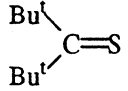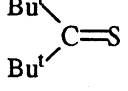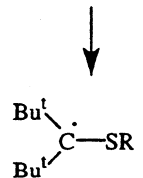
(c) How fast is the trapping reaction, and how persistent are the various spin adducts which may be formed during the experiment?

(d) Does the formation of a spin adduct really signify a major reaction pathway, or could it merely reveal the incursion of some minor side reaction?[17d].

The majority of work with spin-trapping appears to have been done with two main types of organic substances acting as diamagnetic scavengers- C-nitroso compounds and nitrones, although other types are also employed(see table 1).

An example of this technique is the study of the reaction of t-butoxyl radicals(generated by the thermolysis of di-t-butyl peroxyoxalate-DTBP)[23] with styrene using t-nitrosobutane(MNP) as the spin-trap (scheme 2)[24]. The only radical observed was the aminoxyl (1).

Table 1 Spin traps (diamagnetic scavengers)

Types	Example/formula	Reaction
C-Nitroso E.g.	$R'N = O$ MNP t- nitrosobutane[19]	$R^{\cdot} + R'N = O$
Nitrones E.g.	DMPO- 5,5-dimethyl-pyrroline-N-oxide[20]	
Nitrile oxides	$R'C \equiv N^{\pm}\!-\!O^{-}$ [21]	$R^{\cdot} + R'C \equiv N^{\pm}\!-\!O^{-}$
Thio alkyls E.g.	$R_2C = S$ di-t-butylthioketone[22]	

Scheme 2

$$\text{{}^tBu-O-O-C(=O)-C(=O)-O-O-{}^tBu} \quad \xrightarrow{\Delta} \quad 2\ {}^\bullet O-{}^tBu + 2\ CO_2$$

(DTBP)

$${}^\bullet O-{}^tBu \quad + \quad CH_2=CH\text{-}(C_6H_5)$$

$$\downarrow$$

$${}^tBu-O-CH_2-\overset{\bullet}{C}H\text{-}(C_6H_5)$$

$$\downarrow \quad {}^tBu-N=O$$

$${}^tBu-O-CH_2-\underset{(C_6H_5)}{CH}-N({}^tBu)-O^\bullet$$

(1) - (100%)
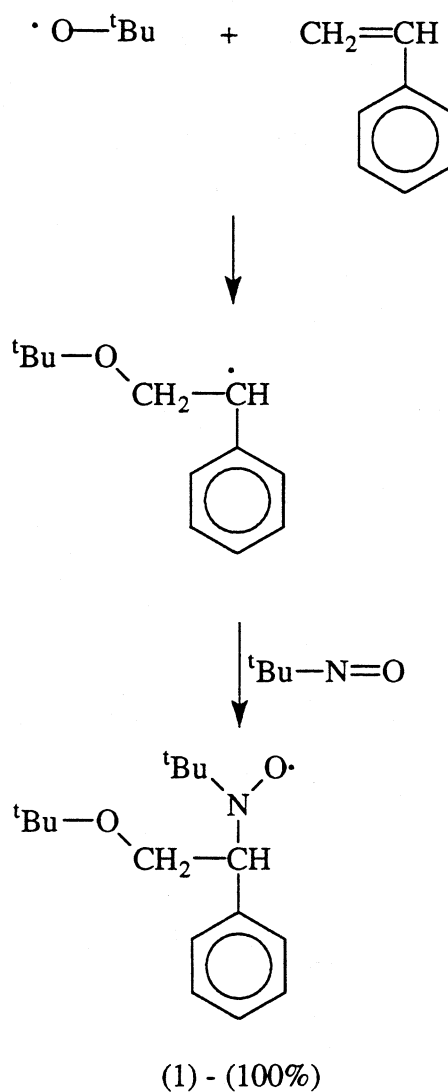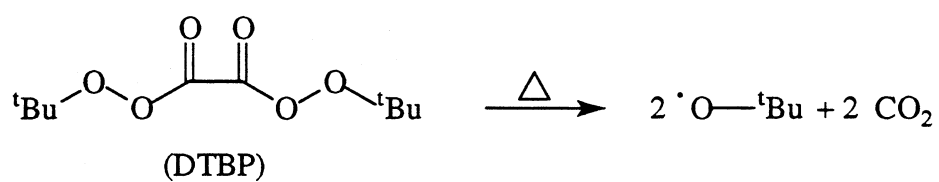
1.1.1 Radical Trapping

A little over a decade ago Rizzardo and Solomon[18] developed a new technique for trapping and investigating radical mechanisms in radical induced polymerisation processes. The technique utilizes the very fast (almost

diffusion controlled) reaction of stable aminoxyls[*] such as (10) with carbon-centred radical species(R·)(scheme 3)($k_T = 10^8 - 10^9$ M^{-1} s^{-1})[25](solvent effects can slow this rate of trapping quite dramatically[25b]), which effectively inhibits the propagation step in vinyl polymerisations (see scheme 1)($k_{prop} = 10 - 10^4$ M^{-1} s^{-1}). This results (in most cases) in the formation of stable alkoxyamine adducts that can be quantitatively isolated, purified and their structures determined by nmr in the normal way. Aminoxyls have a very low reactivity towards oxygen-centred radicals, therefore no combination reaction occurs with alkoxyl or acyloxyl radicals. Nor do aminoxyls dimerise by oxygen-oxygen bond formation above room temperature[26].

Rizzardo and Solomon[18a] initially used 2,2,6,6-tetramethylpiperidine-1-yloxyl(6) as the radical trapping agent, however it was recognised that to have a detectable UV chromophore on the trapping agent would be a distinct advantage; facilitating the chromatographic resolution of complex alkoxyamine mixtures. So 1,1,3,3-tetramethyl-2,3-dihydro-1H-isoindol-2-yloxyl(10) was designed and synthesised[18b]. However, there are many other

Scheme 3

$$ I\cdot + M \xrightarrow{k_1} R\cdot \xrightarrow{k_2} \sum_{i=1}^{n} R_iM_i \longrightarrow Polymer $$

propagating radicals

$$ T \Big| k_T $$

$$ R{\diagup}^{O-NR_2} $$

stable alkoxyamines
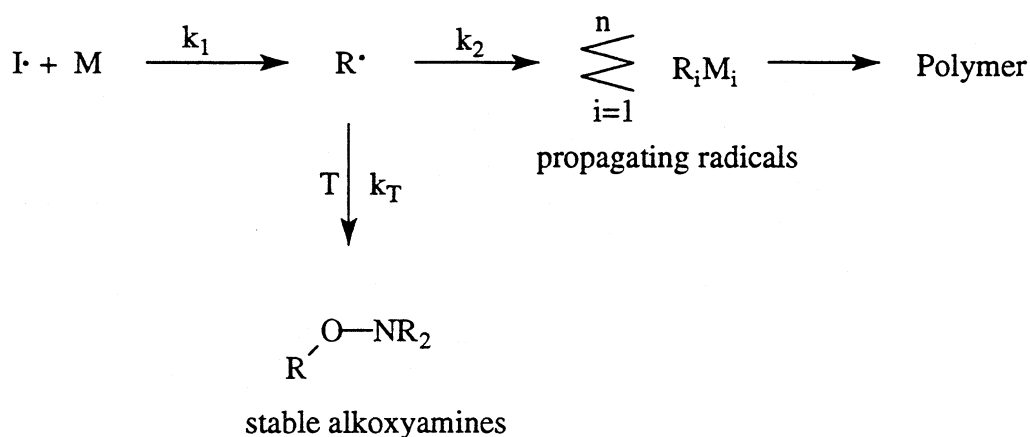
currently available for use (see table 2). The aminoxyl(10) has been utilised for the research described in this thesis. It is superior to the six-membered ring nitroxide (6), due to the presence of the UV chromophore, and also because of its symmetry, which greatly simplifies the nmr spectra of the alkoxyamine adducts. Also the five-membered ring bearing the amine is a lot more rigid

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[*] The more commonly used name is 'nitroxide', however Aminoxyl is the IUPAC name and will be used throughout this thesis.

Table 2 Stable Organic Free Radicals

Pyrrolidine series('proxyls')

2,2,5,5-Tetramethylpyr-
rolidin-1-yloxyl(2)

(3) X=OH
(4) X=CO$_2$H

('Doxyls')
(5)

Piperidine series

2,2,6,6-Tetramethylpiperidin-
1-yloxyl
(TEMPO) (6)

(TEMPONE)
(7)

(8) X=OH (4-Hydroxy tempo)
(9) X=PhCO$_2$ (4-Benzoyl-
oxy-TEMPO)

Isoindoline series

1,1,3,3-Tetramethyl-2,3-di-
hydro-1H-isoindol-2-yloxyl
(10) = (T)

(11)

(12)
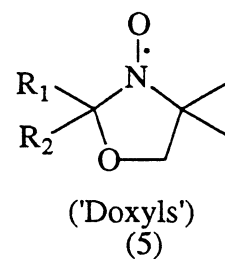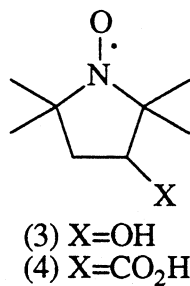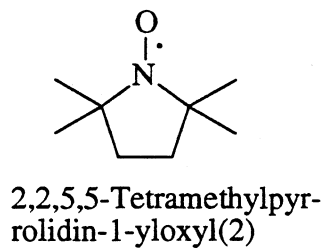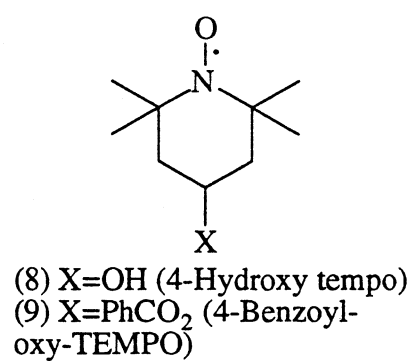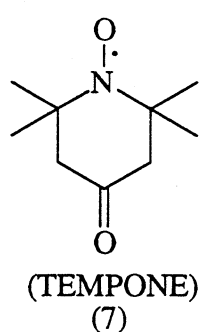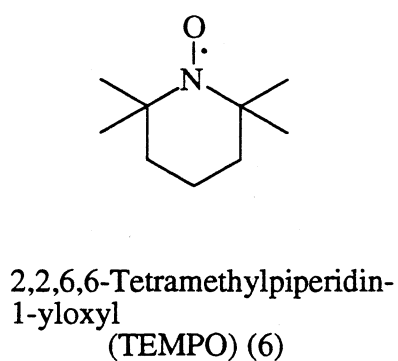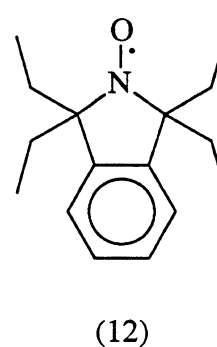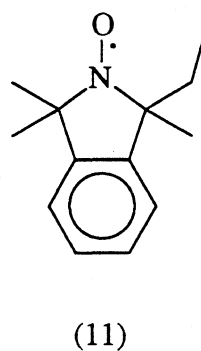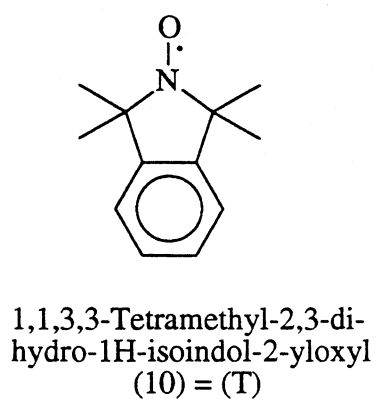
Other stable free radicals

Di-t-butylnitroxide(13)
(DBNO)

'Galvinoxyl'
(14)

Diphenylnitroxide
(15)

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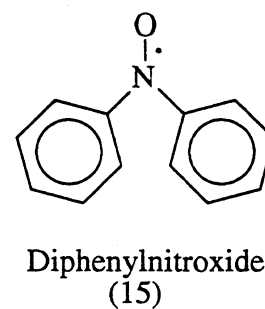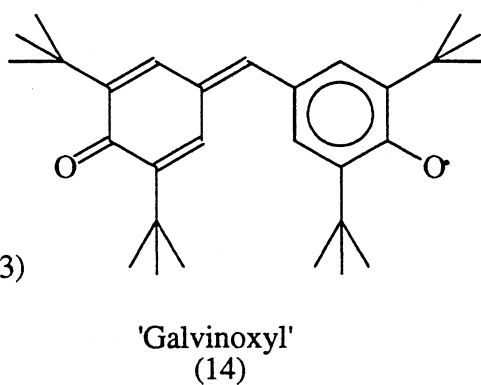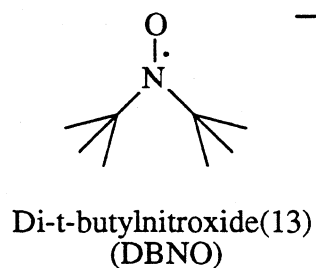
than in the corresponding six-membered ring . This results in much sharper line shapes in the nmr spectra of the resulting alkoxyamines($R'-ONR_2$)[27].

The superiority of the 'radical trapping technique' over esr/'spin trapping' is that it not only provides qualitative, but accurate quantitative detail about the system under study.

A disadvantage of the esr/spin trapping technique, is that nitrones and C-nitroso compounds are known to be very susceptible to nucleophilic attack[28]. Producing hydroxylamines which can easily be oxidised to unwanted aminoxyls[26]. These aminoxyls not necessarily derived from initiator radicals, can complicate the esr spectra produced. There is a further limitation with C-nitroso compounds. Due to their photolability to produce di-t-butyl aminoxyls, it is necessary to exclude daylight during spin-trapping experiments. It is noteworthy also that nitrones are less useful than C-nitroso compounds, because the radical fragment is further from the radical centre, therefore contributing less to the splitting pattern.

An examination of the two techniques (scheme 2 cf scheme 4)[#] highlights the advantages of the radical trapping technique. The esr study shows only the major pathway, leading to the formation of (1) (scheme 2). In contrast the radical trapping technique (scheme 4) produced three initiator derived products[31]. So even very minor initiation pathways (e.g leading to the formation (17)) can be successfully detected, due to the sensitivity of the 'radical trapping technique'. In polymers where only tiny amounts of defect groups can result in polymer degradation, these minor pathways can be all important.

Therefore the radical trapping technique is much more sensitive than the spin trapping/esr technique, at least in the case of oxygen-centred radical initiators. It is generally acknowledged[18,31,32] that in the study of the initiation stages of the polymerisation process, the radical-trapping technique is the method of choice.

See also the esr/spin-trapping study of N-Vinylcarbazole with benzoyloxy radicals by Sato et al.[29] versus the corresponding study using the 'radical trapping technique' by Bottle et al.[30]

In chapters three and four of this thesis an investigation of the usefulness of this technique in the study of phosphorus-centred radical initiation and phosphorus radical reactions is presented.

Scheme 4

^{t}Bu—O$^\bullet$ + H$_2$C=CH

Styrene

^{t}Bu—O—CH$^\bullet$

R$_2$NO$^\bullet$ = Aminoxyl(10)

(10)

^{t}Bu—O—CH—O—NR$_2$

(16) (98.7%)

H$_3$C—O—NR$_2$

(22) (1.1%)

^{t}Bu—O$^\bullet$ ⟶ $\rangle$=O + $^\bullet$CH$_3$ $\xrightarrow[\text{(10)}]{\text{Styrene}}$

H$_3$C—CH—O—NR$_2$

(17) (0.2%)

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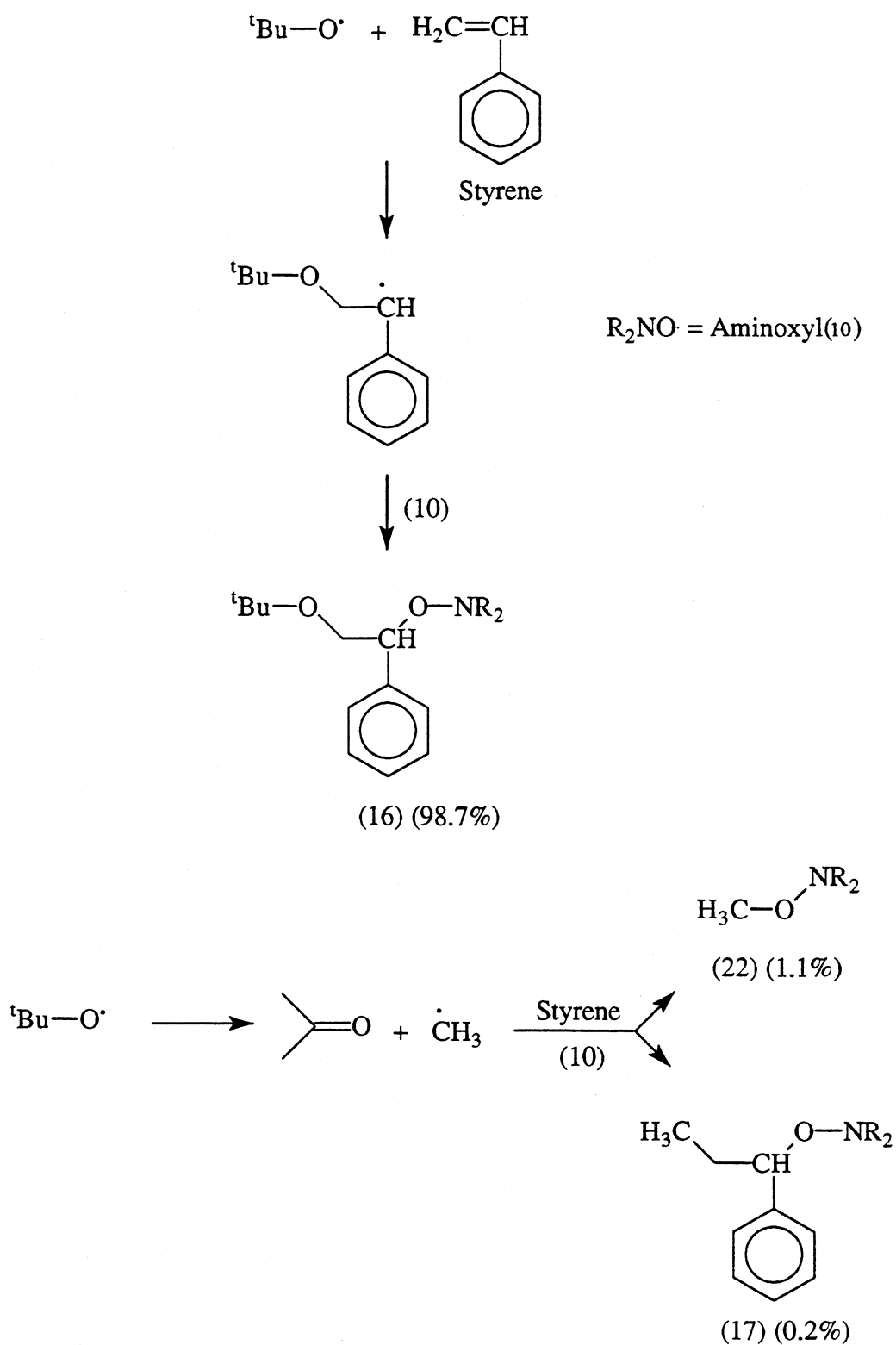
1.2 Structure and stability of Aminoxyls

The aminoxyl function is often represented as a hybrid of the two main forms (19a) and (19b). The spin density in dialkyl aminoxyls is reportedly[33,34]

$$\overset{\cdot\cdot}{\underset{/}{\overset{\backslash}{N}}}-\overset{\cdot}{O} \quad \rightleftharpoons \quad \overset{\cdot\cdot+}{\underset{/}{\overset{\backslash}{N}}}-\overset{-}{O} \quad \equiv\equiv\equiv \quad \overset{\cdot}{\underset{/}{\overset{\backslash}{N}}}\!\!\rightarrow O$$

(19a)   (19b)
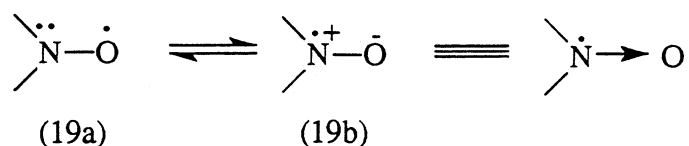
divided almost equally between the nitrogen and oxygen centres. The NO bond has a high delocalisation energy also, and is estimated as 127 kJ mol^{-1} for TEMPO(6)[35]. The aminoxyl radicals are π-radicals, the unpaired electron occupying a π* orbital between the oxygen and the nitrogen atoms. There is also an NO σ−bond, and two electrons fill a π-bonding orbital between these atoms, the effective NO bond order is 1.5[36].
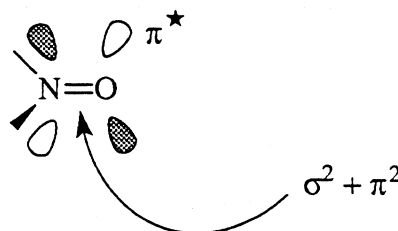
The dipole moment of an aminoxyl bond is 3.0 Debye, being calculated from a typical bond length of 1.25 Å; this dipole moment is similar to that of acetone, 2.9 Debye[37].

The majority of aminoxyl free radicals are chemically stable, i.e they can be purified, stored and handled like normal organic compounds. Certainly electron delocalisation contributes to this stability but there are some other rather special structural features that are important for the stability of aminoxyls.

Self dimerization may seem like the most likely reaction for aminoxyls, but as mentioned previously stable aminoxyls do not measureably dimerize by O-O bond formation in the solid state or in solution[38]. This is not surprising when we consider that the calculated bond formation energy is 117 kJ mol^{-1} i.e an endothermic process[39].

Also, the vast majority of stable aminoxyls are secondary amine N-oxides where there are no hydrogens attached to the α-carbon atoms. When the α-carbon atoms have one or more hydrogen atoms attached, the radicals will typically undergo a disproportionation reaction possibly via the O-O dimer (scheme 5) resulting in production of a nitrone(20) and a N-hydroxyamine(21),
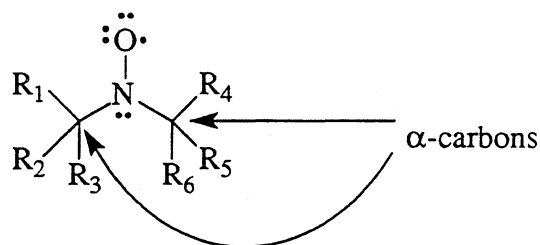
both of which are capable of undergoing further reaction. Scheme 5 however has only been proposed tentatively by Ingold[40]. The presence of substituents

Scheme 5

(20)   (21)
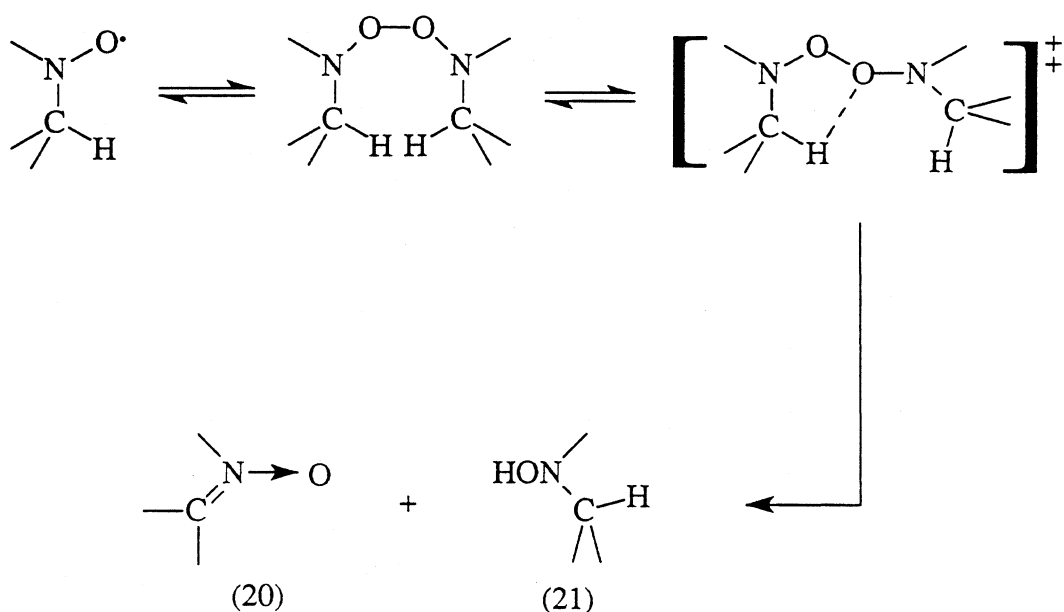
on the α-carbon atoms prevents the above disproportionation reaction but also suppresses the proclivity towards dimerization in solution. There are exceptions towards this disproportionation reaction, however where molecules bearing hydrogen on the α-carbon atom are still stable to disproportionation. This is the case with adamantyl aminoxyl where disproportionation to produce a nitrone

(18)
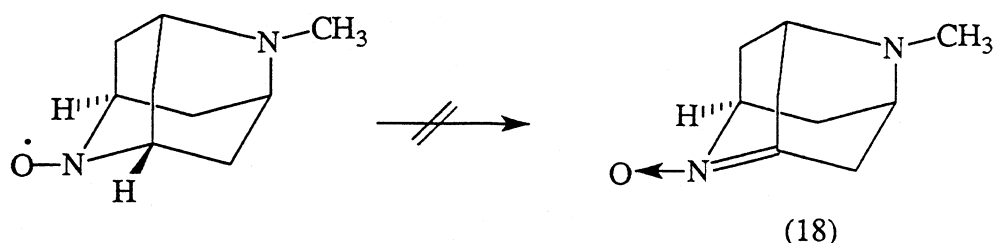
(18) would involve the bridgehead carbon atom, and be in violation of Bredt's rule[41]. Steric hindrance at the reaction centre also affects the stability of aminoxyls towards disproportionation. For example (a) is stable whereas the analogous cyclic radical (b) is unstable[42].

(a)

(b)
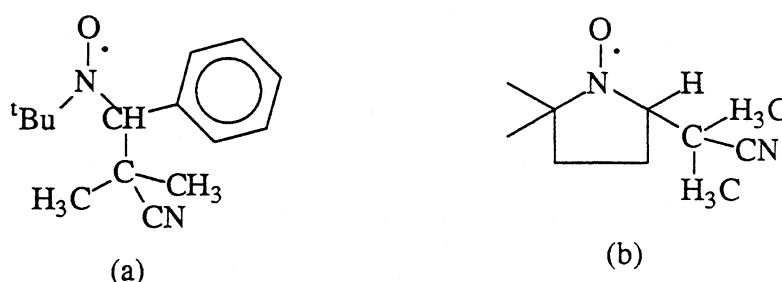
With the isoindoline aminoxyl(10), as with di-tert-alkyl aminoxyls in general, stability is due to (1) no readily abstractable hydrogens, and (2) steric hindrance to dimerization. The aminoxyl (10) is a yellow crystalline solid, stable indefinitely at room temperature and remarkably inert in the common organic solvents. It can bring about hydrogen abstraction however. For example, prolonged reflux in cyclohexene results in allylic hydrogen abstaction[43]. Also aminoxyls react with acyl and alkyl halides. The suggested mechanism involves transfer of a single electron(SET) in what is termed 'homosolvolysis'[44]. Another relevant example of the SET reaction is the aminoxyl induced decomposition of diacyl peroxides[45].

Some features of relevance to the reactivity of the aminoxyl (10) are: The five-membered N-bearing ring is flat about the N-centre and throughout the ring, which is in contrast to the piperidine series which have a distinctly pyramidal aminoxyl centre with an out of plane angle of 16°. (10) has a smaller CNC angle than does (6) by 10°. Also, the N-O bond length in (10) is 1.24 Å, 0.05 Å shorter than in (9)[37] (see figure 1).

Figure 1 Structure of Aminoxyls (6) & (10)

(6)

(planar)
(10) = (T)
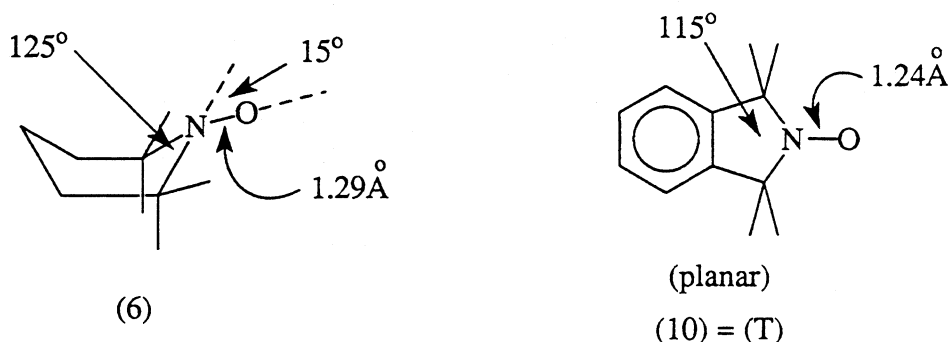
These factors suggest a more favourable geometry for the N-O π bond in the isoindoline series than for the piperidine series of aminoxyls.

The trapping of carbon-centred radicals by aminoxyls is highly exothermic (ΔH = -D(NO-C) = -125 to -146 kJ mol^{-1} and has only a very small energy barrier ($\leq$ 6.3 kJ mol^{-1})[46]. In contrast to the aminoxyl (10), which is flat, the trapped radical species, the alkoxyamines, contain a distinctly pyramidal nitrogen. For example, an X-ray structure has been published for the N-vinylpyrrolidone adduct shown in figure 2[37].

Figure 2 Schematic of Aminoxyl trapped product

<NOR = 112°

(T-R)
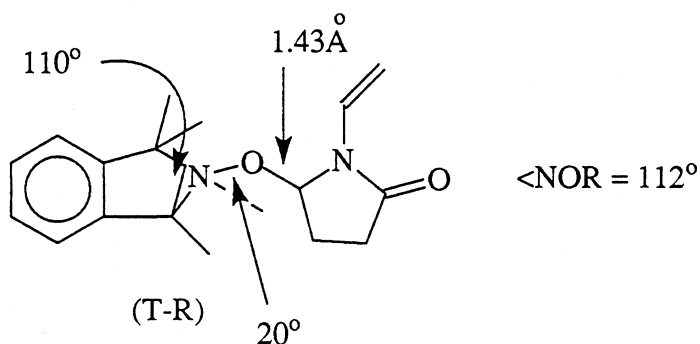
The C-O bond length of 1.43 Å and an N-O-C bond angle of 112° is in line with a normal ether. The nitrogen bearing ring is now similar to normal isoindoline compounds having a puckered ring and a discernibly pyramidal nitrogen centre.

In the ^{1}H nmr spectra of R'ONR$_2$ adducts, non-chiral adducts (i.e the oxygen of the aminoxyl is bound to a non-chiral carbon) occurs as one or two broad singlets for the methyl groups, in contrast to chiral alkoxy adducts which result in three or four signals for the methyl groups of the aminoxyl[32].

1.3 Synopsis of Thesis

The 'radical trapping technique' as developed by Rizzardo et al.[47], has been extended to new and more complex systems.

Chapter 2 utilises the radical trapping technique to investigate the initial stages in the free radical copolymerisation of monomer pairs with differing polarities. The results have given information on the mechanism of these copolymerisations. In chapters 3 and 4, the use of the radical trapping technique to study the addition of phosphorus-centred radicals to alkenes and alkynes is reported. Prior to this work, the use of the radical trapping technique had been confined to systems involving only oxygen-centred radicals as initiators.

The stereochemistry of the addition of benzoyloxy radicals to a conformationally rigid alkene trans-Δ^2-octalin, is reported in chapter 5.

We have also applied the radical trapping technique to the mixed systems styrene/maleic anhydride and styrene/tetracyanoethylene. These (inconclusive) studies are reported in appendices 1 and 2 respectively.

The attempted synthesis of some phosphorus-radical initiators is also reported in appendix 3.

1.4 Summary of MPhil Research

As my MPhil research was closely related to my PhD work, a summary of the main findings are included here for the sake of completeness.

The radical trapping technique was employed to study the reaction of t-butoxyl radicals with cyclic and acyclic ethers. Rate constants for hydrogen abstraction were determinded by analysing reaction mixtures ((appropriate

ether plus internal standard, either THF or cyclohexane), di-tert-butyl peroxyoxalate(DTBP) and (10)) which had been heated at 60°C for 68 minutes.

For acyclic ethers[48] it was found that:

(I) Oxygen α to C-H strongly promotes H-abstraction. This had been well documented previously[49], and explained in terms of overlap between a P-type lone-pair on oxygen and the radical centre. Confromational effects appeared to have little importance on abstraction rates.

(II) Oxygen β to C-H inhibits abstraction, probably as a consequence of polar factors. t-Butoxyl radicals, being electrophilic are presumably less likely to attack at the β site due to the electron attracting effect of the ethereal O (presumably this is also true at the α-position, but this inductive effect is clearly outweighed by the mesomeric effect).

(III) Oxygen γ to C-H slightly promotes abstraction.

(IV) Two oxygens α to C-H are less effective than one in promoting H-abstraction. There is a medium range attractive interaction between O atoms in the 1,3 positions (anomeric effect); this it seems reduces the conjugation potential of the O non-bonding orbitals to assist radical formation at the methine group. Malatesta and Scaiana have reported a similar result[49a].

(V) Methyl α to C-H inhibits abstraction.

(VI) Abstraction at CH_2 occurs at about the same rate as at CH.

$$ \overset{\diagdown}{\underset{\diagup}{\diagup}}CH \; \simeq \; \overset{\diagdown}{\underset{\diagup}{}}CH_2 \; \gg \; \overset{\diagdown}{}CH_3 $$
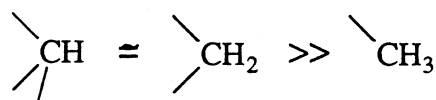
(VII) Abstraction at CH_3 is significantly slower than at CH_2 or CH. This may primarily be due to the loss of the methyl internal rotational mode of motion in the formation of the transition state.

(VIII) Hydroxyl α to C-H very strongly promotes abstraction. This is likely due to the H-atom enhancing the ability of the non-bonding electron pairs of the O atom to stabilise an unpaired electron on the α-carbon atom during free radical formation.

For <u>Cyclic ethers</u>[50]:

(I) As with acyclic ethers the presence of O α to C-H strongly promotes abstraction- relative to cylic hydrocarbons. The product radical stabilisation is strongly dependant upon the amount of orbital overlap (maximum if dihedral angle-0°, minimum-90°). So in cyclic ethers, the extent of stereoelectronic control is very much more dependant upon conformational factors.

(II) O β to C-H generally inhibits abstraction, with respect to the α position.

(III) In cyclic mono-ethers the influence of ring size on abstraction rate α to ethereal O is:

$$5 > 7 \gg 6 > 4$$

The apparent explanation is that 5 and 7 membered rings are much less rigid than 6 and 4 membered rings, hence have sufficient conformational freedom for conjugative stabilisation to be maximised. In general as the ring size decreases, polar effects at the β and γ positions become more effective.

(IV) Two O atoms α to C-H promote abstraction in both 5 and 6 membered rings, compared to corresponding monoethers. This is in contrast to acyclic ethers.

(V) With O's in 1, 3 and 5 positions of a 6 membered ring, the hydrogen abstraction rate is much reduced.

(VI) Abstraction at CH is much greater than at the corresponding methylene position in unsubstituted cyclic ethers. This is presumably due to more favourable overlap in the conformationally constrained cyclic systems.

(VII)(a) Introduction of a double bond into the 6 membered ring mono-ether results in allylic H abstraction being 10 times faster than at the position α to oxygen in the same molecule.

(b) The allylic abstraction product is trapped twice as fast γ to the oxygen as α to oxygen. Presumably this is due to polar effects[18c].

Publications arising from MPhil work

1. "Reaction of t-Butoxy Radicals with Cyclic Alkenes Studied by the Nitroxide Radical-Trapping Technique". Busfield, W.K., Grice, D.I., Jenkins, I.D., and Thang, S.H., Aust. J. Chem., 44, 1407-1415(1991).

2. "Reactions of Tert-Butoxyl Radicals with Cyclic Ethers Studied by the Radical Trapping Technique". Busfield, W.K., Grice, D.I., and Jenkins, I.D., J. Chem. Soc., Perkin Trans. II, in preparation.

3. "Reactions of Tert-Butoxyl Radicals with Acyclic Ethers Studied by the Radical Trapping Technique". Busfield, W.K., Grice, D.I., Jenkins, I.D., and Montiero, M., J. Chem. Soc., Perkin Trans. II, in preparation.

Publications arising from PhD work

1. "Free Radical Initiation Mechanisms in Copolymerisation Studied by the Nitroxide Trapping Technique". Busfield, W.K., Grice, D.I., and Jenkins, I.D., Polymer International., 27, 119-123(1992).

2. "The Reaction of Organophosphorus Radicals with Alkenes in the Presence of an Aminoxyl Radical Scavenger". Grice, D.I., and Jenkins, I.D., Paper in preparation.

CHAPTER TWO

THE INITIATION MECHANISM OF FREE RADICAL COPOLYMERISATION OF ACRYLONITRILE AND VINYL ACETATE

CHAPTER TWO

2.0. Introduction

Free radical copolymerisation is of great industrial importance. It could be said that copolymers to polymer science are like alloys to metallurgy.

Copolymerisation provides a convienient method of synthesising new polymeric structures with a wide range of properties. These properties can often be closely controlled by adjusting the compostion and monomer sequence in the copolymer chain. Understanding the factors that control and influence these features in copolymers is important; from this understanding comes the ability to predict why one monomer tends to react with another, therefore producing these properties.

When two monomers M_1 and M_2 are mixed together in the presence of a free radical initiator, the monomers may combine together in a number of different ways. The resulting copolymer may be (a). a mixture of homopolymers formed exclusively from either M_1 or M_2; (b). a statistically random mixture of M_1 and M_2 units in the chain, incorporated in the same proportions as that in the feed; (c). a regular alternation of M_1 and M_2 units along the chain; (d). structures intermediate, between the extreme cases of (b) and (c). In reality however, copolymerisations lead to copolymers with intermediate structures to those listed above. The composition being determinded by the relative reactivities (tendency of each monomer to enter the chain during propagation) of the two monomers. Dostal[51] was probably the first person to try and quantify this relative reactivity of a monomer. He assumed the rate of addition of a monomer to a radical is independant of the size and nature of the radical chain, being influenced only by the nature of the radical end group. Dostal proposed four reactions in his 'terminal' model:

$$\sim\sim\sim\dot{M_1} + M_1 \xrightarrow{\ k_{11}\ } \sim\sim\sim\dot{M_1} \qquad\qquad (I)$$

$$\sim\sim\sim\dot{M_1} + M_2 \xrightarrow{\ k_{12}\ } \sim\sim\sim\dot{M_2} \qquad\qquad (II)$$

$$\sim\sim\sim\dot{M_2} + M_2 \xrightarrow{\ k_{22}\ } \sim\sim\sim\dot{M_2} \qquad\qquad (III)$$

$$\sim\sim\sim\dot{M_2} + M_1 \xrightarrow{\ k_{21}\ } \sim\sim\sim\dot{M_1} \qquad\qquad (IV)$$
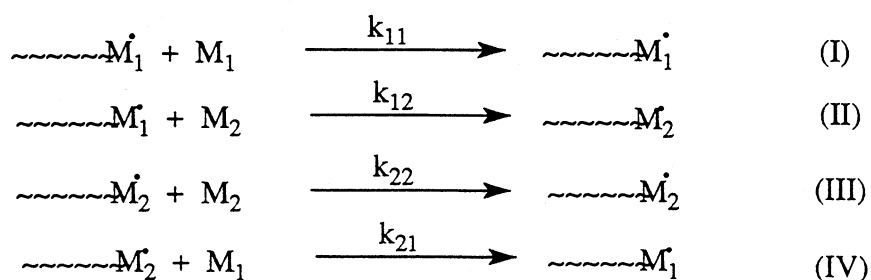
An alternation of monomer units occurs in the chain when k_{12} and k_{21} are much larger than k_{11} and k_{22}.

The assumption of steady-state conditions[52] for the reactions (I)-(IV) leads to the copolymer composition equation(instantaneous):

$$\frac{m_1}{m_2} = \frac{[M_1]}{[M_2]} \left\{ \frac{r_1[M_1]}{r_2[M_2]} + \frac{[M_2]}{[M_1]} \right\} \qquad (V)$$

(m_1/m_2) is the instantaneous composition of the copolymer when the ratio of monomer composition in the reaction mixture is $([M_1]/[M_2])$. Monomer reactivity ratios r_1 and r_2 indicate a monomer radical's preference for reacting with its own monomer rather than with the comonomer in the mixture. Small values of r indicate a tendency towards alternation. The extent of alternation approaches a maximum as r_1r_2 approaches zero.

$$r_1 = \frac{k_{11}}{k_{12}} \qquad\qquad r_2 = \frac{k_{22}}{k_{21}}$$

Resonance stabilisation[53,54] and polarity[55,56] have been shown to affect alternation. A high degree of alternation is achieved in copolymers when notable differences in the polarity of the double bond exist[57].

To predict the behaviour of pairs of monomers, taking into account resonance stabilisation and polarity effects, Alfrey and Price[58] developed the 'Q-e' scheme (a modification of the Hammett equation). The relation they suggested for the cross propagation reaction:

$$\sim\sim\sim\sim\sim M_1^{\bullet} + M_2 \quad\xrightarrow{\ k_{12}\ }\quad \sim\sim\sim\sim\sim M_2^{\bullet}$$
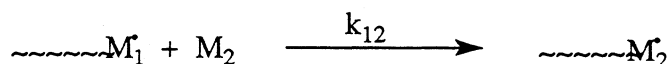
was:

$$k_{12} = P_1Q_2 \exp(-e_1e_2)$$

where P characterizes the radical state, Q is a measure of the monomer reactivity, and e_1 and e_2 describe the polarization characteristics of the radical and reacting monomer, respectively. Styrene was chosen as a standard (Q=1, e= -0.8) for the Q-e scheme, and all other monomers were related to it. Monomer pairs with similar Q values, and high e values of opposite sign will favour alternation (see for example acrylonitrile (A) and styrene, table 3). The tendency towards alternation can be expressed by the following relationship:

$$(r_1 r_2) = \exp[-(e_1 - e_2)^2]$$

This is in line with $r_1 r_2 \approx 0$, for an alternating system.

Table 3. Some representative Donor and Acceptor monomers with their Q and e values

Donor	Acceptor	Q	e
α-Methylstyrene		0.980	-1.27
Styrene		1.000	-0.80
Vinyl acetate(V)		0.026	-0.25
	Acrylonitrile(A)	0.600	1.20
	Fumaronitrile	0.800	1.96
	Maleic anhydride	0.230	2.25

Calculations indicate that the electron donor monomer has the HOMO (highest occupied molecular orbital) and that the electron acceptor monomer has the LUMO (lowest unoccupied molecular orbital). It is the SOMO (singularly occupied molecualr orbital or frontier orbital) in any radical that reacts with the HOMO and the LUMO of the incoming monomer[57]. Flemming[57b] puts forth an interesting proposal for alternating copolymerisation in that it proceeds because radicals with a high energy SUMO (nucleophilic radicals) will react at a fast rate with molecules having a low energy LUMO, and radicals with a low-energy SUMO (electrophilic radicals) will react at a fast rate with molecules having a high energy HOMO.

Alternating copolymerisations are characterised by the fact that from a wide variety of comonomer mole fractions in the feed, a nearly 1:1 molar ratio of the comonomers is found in the copolymers produced. Why this alternation is quite strictly adhered to has been the subject of much debate[59]. Possible pathways to achieve this alternation are shown in scheme 6[60], and two main mechanisms have been proposed.

Scheme 6

$$ED + EA \; \underset{}{\overset{K}{\rightleftharpoons}} \; \text{Charge Transfer Complex}$$

$$\sim\sim\{-ED\text{-}EA\}_x\sim\sim$$

Alternating Copolymer
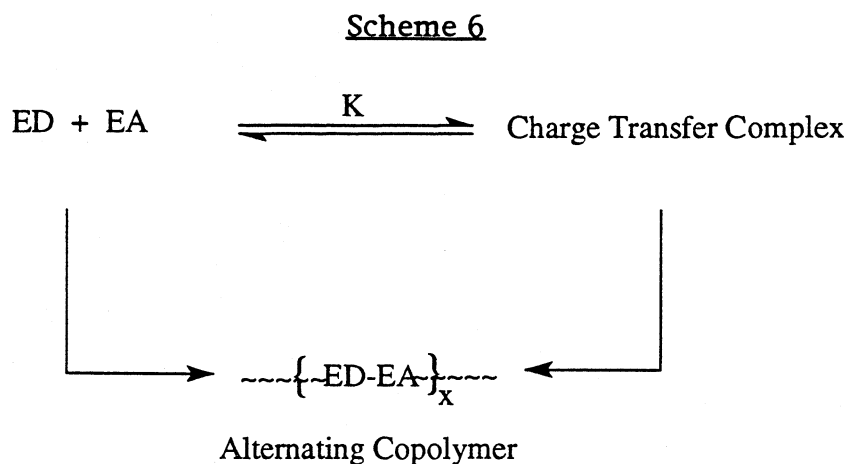
The first, called the 'free monomer' mechanism, may be divided into two types (a). (proposed by Mayo and Walling[61]) Charge transfer complexes(CTC's) are formed between chain radicals and monomers; (b). (proposed by Alfrey and Price[62]) The inherent reactivities of the monomers towards propagating radicals is a function of resonance and polar effects.

The second mechanism, termed the 'Complex' mechanism, was first proposed by Bartlett and Nozaki[63]. They suggested that copolymerisation occurs via a stable monomer complex composed of the ED and EA monomer units, which acts as a kind of new monomer unit capable of reacting with chain radicals. Despite being of low concentration in the system, they have a much higher reactivity. This mechanism has been supported by the work of Butler and co-workers[64,65](maleic anhydride-divinyl ether and maleic anhydride-furan copolymers), Caze and Loucheaux[66](maleic anhydride-vinyl acetate co-polymer) and Gaylord et al.[67,68](maleic anhydride-conjugated diene copolymers).

With regard to the involvement of vinyl acetate and acrylonitrile in alternating copolymerisation, it is reported by Sato et al.[69] and Yabumoto et

al.[70] that the copolymerisation of acrylonitrile with styrene involves the active participation of CTC's. In contrast, Butler and Chen[59] suggest that copolymerisation of electron-donor dienes and acrylonitrile proceeds under their reaction conditions by the free monomer mechanism. However, Li et al.[71] suggest active CTC involvement in the copolymerisation of vinyl acetate and maleic anhydride. Previous work on the copolymerisation of vinyl acetate and acrylonitrile includes that by Kharatova et al.[72], on radical copolymerisation of vinyl acetate and acrylonitrile, and Wu and Hseieh[73] on solubility parameters and I.R composition of vinyl acetate/acrylonitrile copolymers. Additionally work by Ziyaev et al.[74] on synthesis and study of properties of copolymers of acrylonitrile and vinyl acetate with fluoroethylenes and Mokhtar et al.[75] on the influence of stannic chloride on the copolymerisation behaviour of vinyl acetate with acrylonitrile. The copolymer sequence analysis technique has been employed by Hill et al.[77] to test these mechanisms for the copolymerisation of vinyl acetate and acrylonitrile. But as to the elucidation of the mechanism of formation of this important copolymer (it is used for the manufacture of membranes[76] and for preparing fibrous activated carbon of high adsorption capacity and strength[78]), until now, it has remained speculative.

The aim of the work presented in this chapter was to investigate the mechanism by which vinyl acetate (V-ED monomer) and acrylonitrile (A-EA monomer) undergo copolymerisation when initiated by t-butoxyl radicals (R•). The 'radical trapping' technique using (10) was employed to identify the participating species and the pattern of reactivity in the early stages of the reaction. Although this method does not provide any information about later stages (i.e, the main propagation step involving addition of an oligomeric radical to a monomer unit), it was considered that useful information might be obtained by studying the initiation stage of the copolymerisation. It is interesting to note that there is considerable interest in kinetic information on the early stages of copolymerisation, although in general it has not been easy to obtain[79].

2.1.The reaction of Vinyl acetate(V) and of Acrylonitrile(A) with t-butoxyl radicals

In a previous study of the reaction pathway for the attack of t-butoxyl radicals on vinyl monomers, Griffiths et al.[80] isolated four reaction products

Scheme 7 The reaction of t-butoxyl radicals with Vinyl acetate
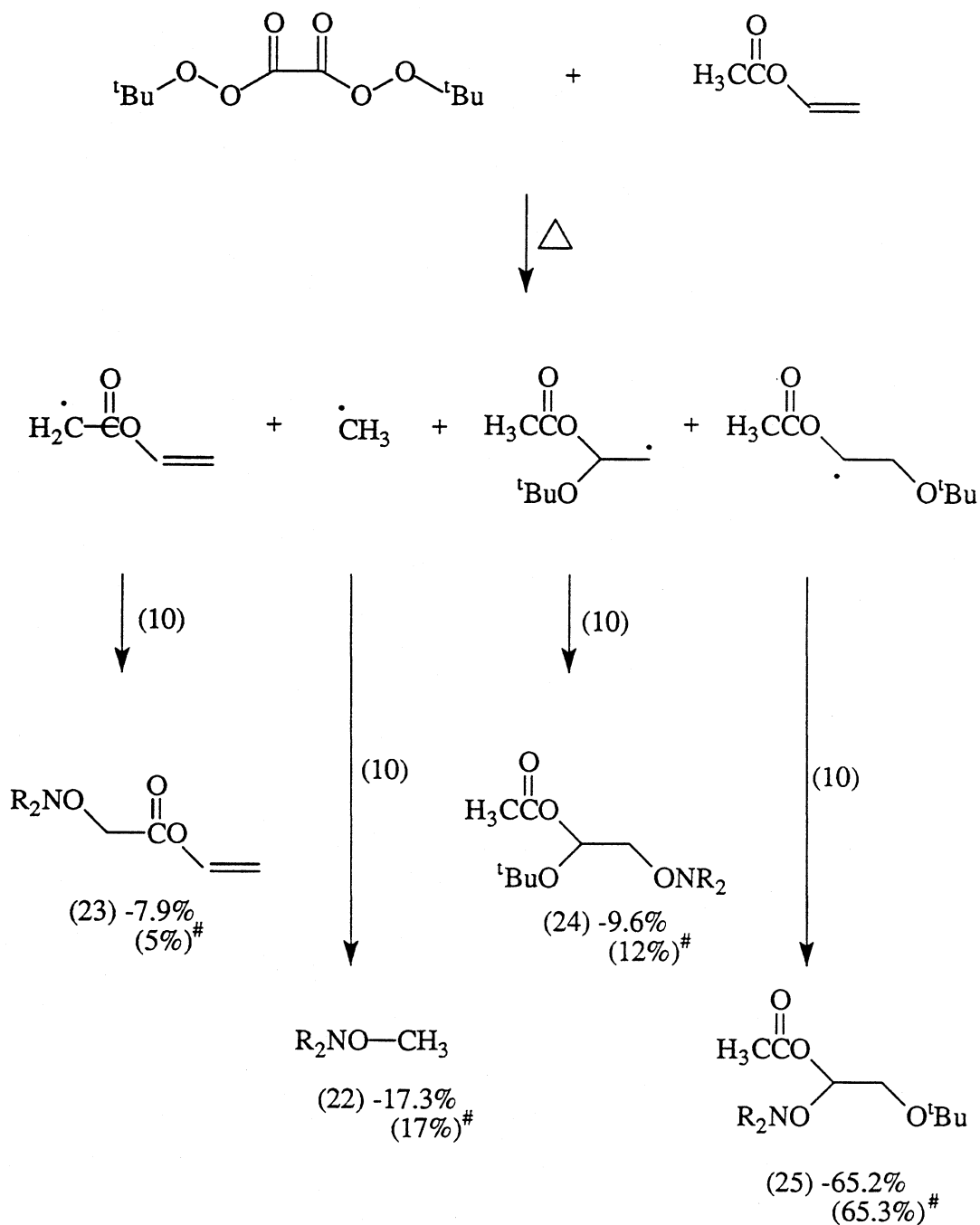
Griffiths et al.[80]

Scheme 8 The reaction of t-butoxyl radicals with Acrylonitrile

$$\text{}^t\text{Bu} - \text{O} - \text{O} - \overset{\text{O}}{\underset{}{\text{C}}} - \overset{\text{O}}{\underset{}{\text{C}}} - \text{O} - \text{O} - \text{}^t\text{Bu} \quad + \quad NC \diagdown\diagup$$

(A)

$$\downarrow \triangle$$

$$\overset{\bullet}{CH_3} \quad + \quad NC\diagdown\diagup\overset{\bullet}{\diagdown}\diagup O^t Bu$$

(A),(10)   (10)   (10)

$$CH_3\diagdown\underset{CN}{\overset{ONR_2}{\diagup}} \qquad R_2NO{-}CH_3 \qquad NC\diagdown\underset{R_2NO}{\overset{}{\diagup}}\diagup O^t Bu$$

(26) -1.3%   (22) -9.5%   (27) -89.2%
(-)[#]   (19%)[#]   (81%)[#]
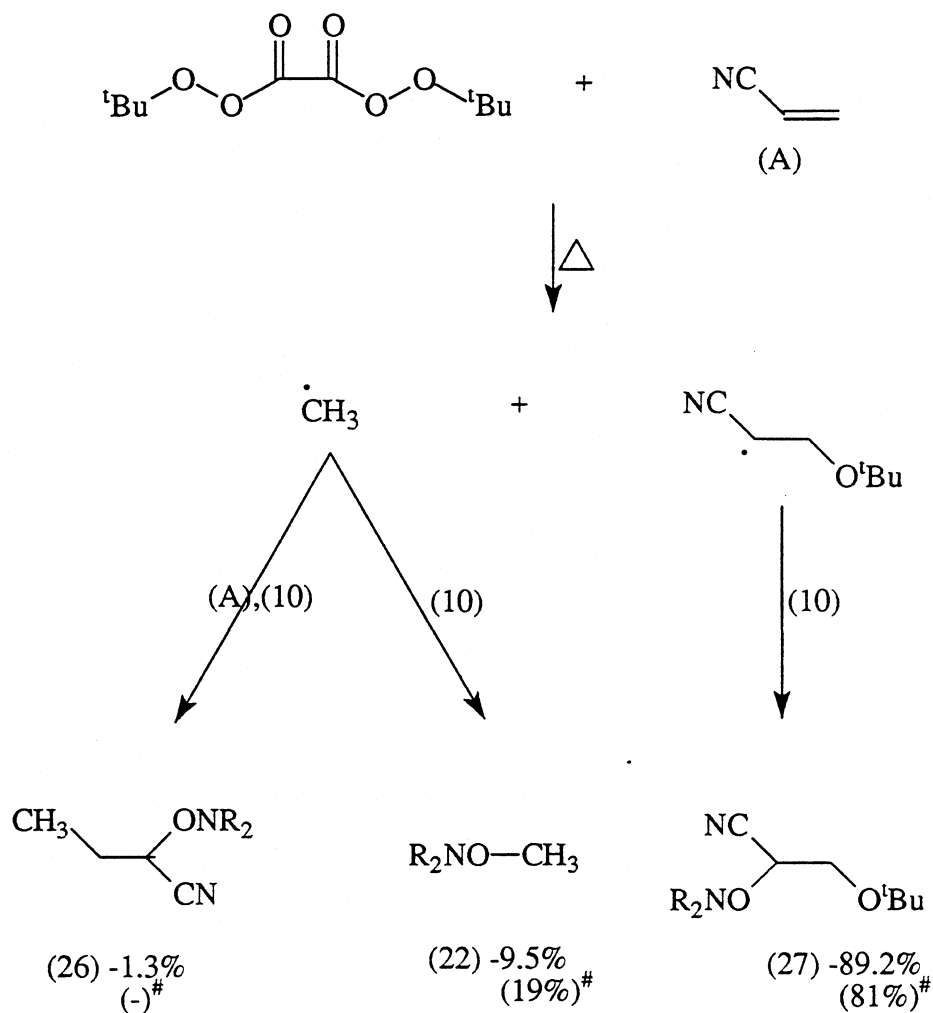
[#] Griffiths et al.[80]

(22)-(25), when studying vinyl acetate (scheme 7), and three reaction products (22),(26) and (27) when studying acrylonitrile (scheme 8). They used the 'radical trapping' technique, generating t-butoxyl radicals (R•) by the thermolysis of di-t-butylperoxyoxalate (DTBP) at 60°C. Their work with the separate monomers was repeated in this research; in addition to the reactions with various mixtures of the two monomers. The results for the separate monomers are shown in schemes 7 and 8. These results are consistent with those reported by Griffiths et al.[80]

Product (22) arises from the methyl radicals produced by β–fragmentation of the t-butoxyl radicals (R•), and the amount of (22) present in a reaction mixture is an indication of the rate of the reaction of t-butoxyl radicals with monomer and serves as an internal free radical clock[83]. While we see both head and tail addition are observed with vinyl acetate, no head addition is detected with acrylonitrile. This may be due to the electrophilic[81] nature of the t-butoxyl radical or to polar factors. Hydrogen abstraction from vinyl acetate to give (23), while small, is also not unexpected as t-butoxyl radicals are known to be good hydrogen abstractors[48].

2.2. The reaction of mixtures of Vinyl acetate(V) and Acrylonitrile(A) with t-butoxyl radicals

2.2.1. Results

The reaction mixtures of V and A with t-butoxyl radicals in the presence of (10) were studied over a wide range of concentrations. The percentage yields of the reaction products as a function of the concentrations of V, A, DTBP and (10) are given in table 4. The structures of the reaction products are given in figure 3. The reaction products formed ((23), (26), (22), (27), (24)* and (25)) were the same as those observed by Griffiths et al.[80] from the reaction of t-butoxyl radicals with the separate monomers in the presence of (10) (see 2.1). In addition to these products, two new products were formed, (28) and (29). These were separated by HPLC and their structures determinded by ^{1}H and ^{13}C nmr. Although it was not possible to distinguish unequivocally between the two it was clear that (28) and (29) were diastereomers and that they contained both monomer units. NMR assignments should be regarded as tentative and could be reversed.

The mechanism of formation of the reaction products excluding the two diastereomers (28) and (29) is shown in scheme 9.

---

* (24) was observed, but data for it is not included in this study.

Figure 3 Products from the reaction of t-butoxyl radicals with Acrylonitrile and Vinyl acetate in the presence of (10)

=RVAT=

R = O ^{t}Bu
T = ONR$_2$
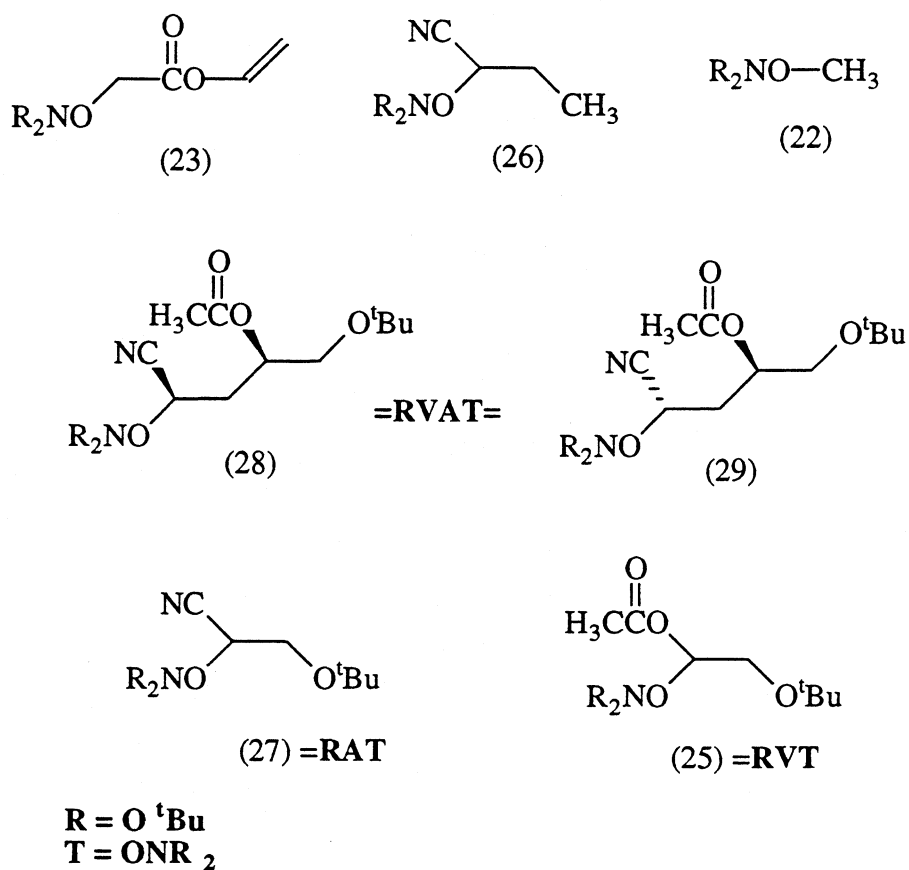
Scheme 9
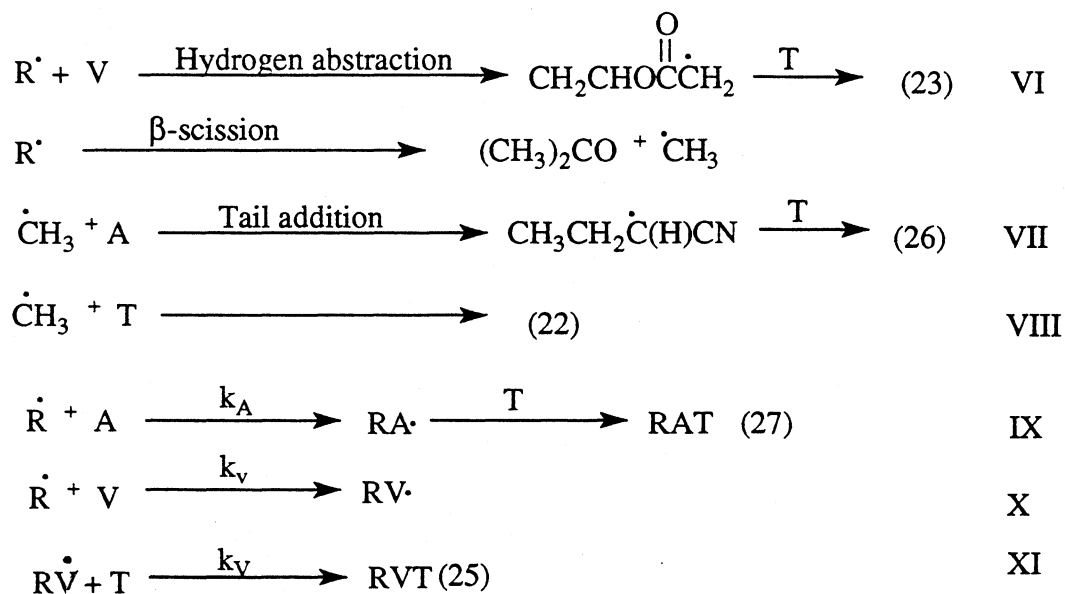
Table 4 Reactant concentrations and product ratios

Reactants(mol litre^{-1})				Products (%)[a]						
[V]	[A]	[T] $\times 10^{-2}$	[I]^b $\times 10^{-2}$	(23)	(26)	(22)	(28)	(29)	(27)	(25)
3.37	3.37	2.90	1.33	0.4	3.2	15.3	5.9	6.5	50.5	18.0
5.14	2.57	2.20	1.01	-	3.5	16.7	9.9	10.7	36.7	22.3
3.10	6.20	1.90	0.87	-	7.0	29.6	5.5	6.3	47.2	4.3
3.37	3.37	3.00	1.30	0.4	3.5	15.8	6.3	7.0	51.2	16.8
3.37	3.37	10.0	1.50	0.8	1.7	24.2	1.8	2.1	47.2	22.2
3.23	1.61	12.7	0.63	-	1.2	22.1	2.1	1.6	36.9	36.0
4.22	1.41	11.1	0.55	0.2	1.0	15.3	1.2	1.2	31.0	50.3
4.49	4.49	10.0	4.50	-	0.9	16.7	3.9	3.0	51.1	24.4
3.46	6.93	7.60	0.34	-	1.8	16.1	4.7	3.5	60.9	12.9
2.11	6.33	8.30	0.42	-	1.4	13.6	2.5	1.7	72.4	8.4
-	solvent	14.0	0.71	-	1.6	16.9	-	-	81.5	-
solvent	-	14.0	0.71	4.8	-	18.3	-	-	-	76.8

a. Only products containing the moiety T(10) are included.
b. Concentration of initiator.

2.2.2. Discussion

The two diastereomers (28) and (29) may be formed in two different ways in line with the two main accepted mechanisms of formation(see 2.0). Firstly, in accordance with the 'free monomer' mechanism it may be formed by the reaction of A with RV· followed by trapping with T.

$$A + RV\cdot \xrightarrow{\text{k}_X} RV\overset{\bullet}{A} \xrightarrow{\text{T}} RVAT \ ((28) \& (29)) \qquad XII$$
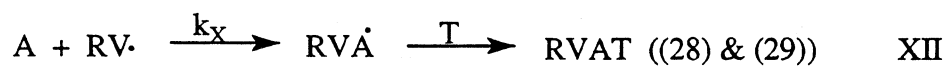
Or secondly, by reaction of R· (t-butoxyl radicals) with a preformed charge transfer complex of V and A followed by trapping (the 'complex' mechanism).

$$A + V \; \underset{}{\overset{K}{\rightleftharpoons}} \; AV$$

$$R^{\textbf{·}} + AV \; \xrightarrow{k_{VA}} \; RV\dot{A} \; \xrightarrow{T} \; RVAT \;\; ((28) \, \& \, (29)) \quad XIII$$
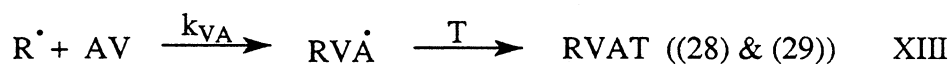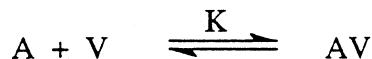
The concentration of T, A and V are relatively constant throughout the reaction, i.e they are in excess over the initiator concentration. If the first mechanism is exclusive, then the ratio of rates of formation is equal to the ratio of total amounts of products formed, i.e

$$\left(\frac{d[RVT]}{dt} \middle/ \frac{d[RVAT]}{dt} = \frac{[RVT]_T}{[RVAT]_T} \right) = \frac{(25)}{(28)+(29)} \qquad (i)$$

Where the subscript T refers to the total amount of product formed. Also since

$$\frac{d[RVT]}{dt} = k_y \, [RV\text{·}][T] \quad \text{from (XI) and}$$

$$\frac{d[RVAT]}{dt} = k_x[RV\text{·}][A] \quad \text{from (XII)}$$

we have

$$\frac{d[RVT]}{d[RVAT]} = \frac{k_y[RV\text{·}][T]}{k_x[RV\text{·}][A]} = \frac{k_y \, [T]}{k_x \, [A]} \qquad (ii)$$

From (i) and (ii)

$$\frac{k_y[T]}{k_x[A]} = \frac{(25)}{(28) + (29)}$$

as long as equations X, XI and XII are the only sources of these products. Thus the ratio of formation of these products is strongly dependant on $[T]/[A]$.

However if the second mechanism ('complex' mechanism) is exclusively followed then we have (in line with equations IX, X and XIII):

$$\frac{d[RVT]}{dt} = k_V[V][R\text{·}] \quad \text{from X and} \quad \frac{d[RVAT]}{dt} = k_{VA}[AV][R\text{·}] \quad \text{from XIII}$$

giving:

$$\frac{d[RVT]}{d[RVAT]} = \frac{k_V[V][R\text{·}]}{K_{VA}[AV][R\text{·}]} = \frac{k_V[V]}{k_{VA}[VA]}$$

$$= \frac{k_V[V]}{k_{VA}[A][V]K} = \frac{k_V}{k_{VA}[A]K} \qquad (iii)$$

Where K is the equilibrium constant for the formation of complex,

$$K = [VA]/[V][A]$$

Thus the product ratio $[RVT]_T / [RVAT]_T$ over the whole reaction is given by:

$$\frac{[RVT]_T}{[RVAT]_T} = \frac{k_V}{k_{VA}K[A]} = \frac{(25)}{(28) + (29)}$$

i.e. independant of T, in strong contrast with (ii).

The result of plotting $([RVT] \times [A])/[RVAT]$ against [T] over a six-fold variation in [T] is shown in figure 4. The ratio of $([RVT] \times [A])/[RVAT]$ increases with increasing [T], clearly precluding the complex mechanism.

Figure 4 Influence of trap concentrations on product yields
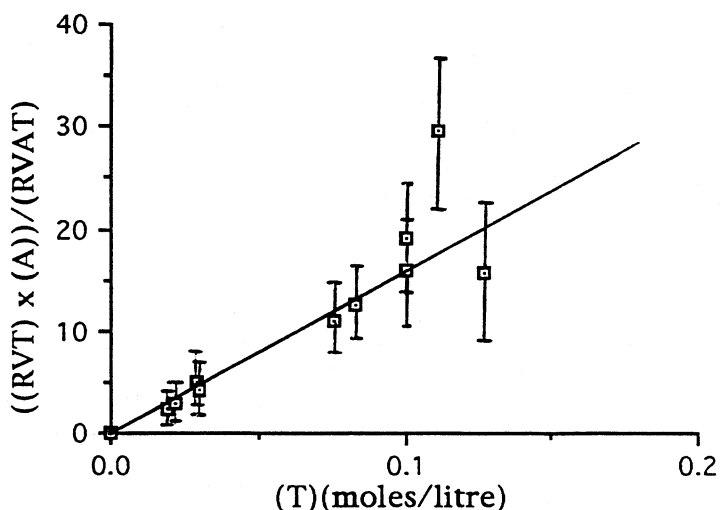
This leads to the conclusion that a charge transfer complex plays little or no part in the initiation step in the copolymerisation of V and A with t-butoxyl radicals.

Assuming the 'free monomer' mechanism is exclusive, the slope of the graph gives the result:

$$k_Y/k_X = 160$$

T(10) reacts 160 times faster with RV· than A.

Examining further the relationship between the products (25)(RVT) and (27)(RAT) and the concentrations of V and A, a less compelling test of the

mechanism can be made. If the first mechanism(free monomer mechanism) is exclusive the relative rates of production of RVT and RAT, (in line with equations IX and XI) will be:

$$\frac{d[RVT]/dt}{d[RAT]/dt} = \frac{k_Y[RV\cdot][T]}{k_A[R\cdot][A]} \qquad (iv)$$

By the steady state principle, applied to the active intermediate RV• in reactions X and XI we have :

$$\frac{d[RV\cdot]}{dt} = k_V[V][R\cdot] - k_X[A][RV\cdot] - k_Y[T][RV\cdot] = 0$$

i.e. $k_V[V][R\cdot] = k_X[A][RV\cdot] + k_Y[T][RV\cdot]$

Therefore $[RV] = \dfrac{k_V[V][R]}{k_X[A] + k_Y[T]}$ \qquad (v)

and from (iv)

$$\frac{d[RVT]/dt}{d[RAT]/dt} = \frac{[V]}{[A]} \cdot \frac{k_V}{k_A\,(1 + k_X[A]/k_Y[T])} \qquad (vi)$$

If the second mechanism('complex' mechanism) is exclusive we have from reactions IX, X and XI:

$$\frac{d[RVT]/dt}{d[RAT]/dt} = \frac{k_V[V][R\cdot]}{k_A[A][R\cdot]} = \frac{k_V[V]}{k_A[A]} \qquad (vii)$$

Taking the total accumulated product ratio to be equal to the ratio of production rates over the whole reaction, i.e.

$$\frac{[RVT]_T}{[RAT]_T} = \frac{d[RVT]/dt}{d[RAT]/dt}$$

The ratio $[RVT]_T/[RAT]_T$ is plotted against $[V]/[A]$ in figure 5. The points are best represented by a curve; hence $[RVT]_T/[RAT]_T$ is not directly proportional to $[V]/[A]$. This demonstrates again that the data is not consistent with the exclusive operation of the'complex' mechanism.

On the other hand for the 'free monomer' mechanism a linear relationship should exist for the product function $([RVT]_T + [RVAT]_T)/[RAT]_T$. And the reactant ratio $[V]/[A]$ according to the following analysis(in line with equation vi):

we have
$$\frac{[RVT]_T + [RVAT]_T)}{[RAT]_T} = \frac{k_y[RV\cdot][T] + k_x[RV\cdot][A]}{k_A[R\cdot][A]}$$

$$= \frac{[RV\cdot](k_y[T] + k_x[A])}{[R\cdot]k_A[A]}$$

$$= \frac{k_V[V]}{k_A[A]} \qquad \text{(viii)}$$

Figure 5 Graph to test 'complex' mechanism
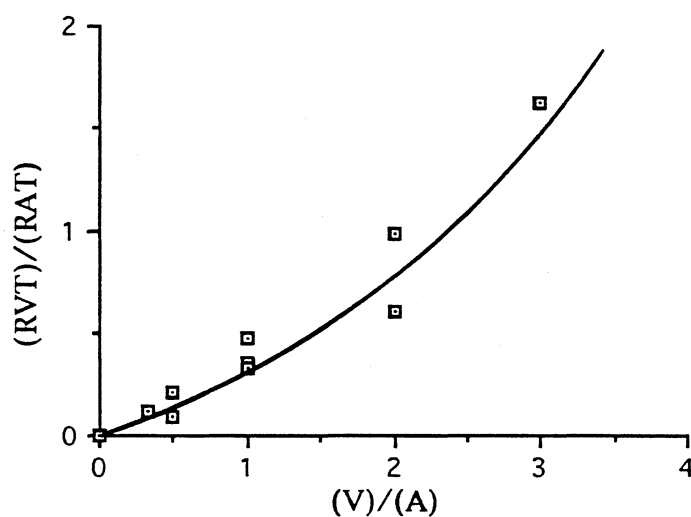
The 'complex' mechanism gives the following relationship for the same product to monomer ratio:

$$\frac{([RVT]_T + [RVAT]_T)}{[RAT]_T} = \frac{k_V[V][R\cdot] + k_{VA}[VA][R]}{k_A[A][R]}$$

$$= \frac{k_V[V] + k_{VA}[VA]}{k_A[A]} = \frac{k_V V + k_{VA} VA}{k_A A}$$

substituting for [VA] = K[V][A] we get

$$\frac{([RVT]_T + [RVAT]_T)}{[RAT]_T} = \frac{k_V[V]}{k_A[A]} + \frac{k_{VA}K[V]}{k_A} \qquad (ix)$$

i.e. the product ratio is not directly proportional to [V]/[A]. Plotting data for (ix)(figure 6) shows the points to lie on a good straight line passing through the origin with a slope of 0.58.

Figure 6 Graph to test 'free monomer' mechanism
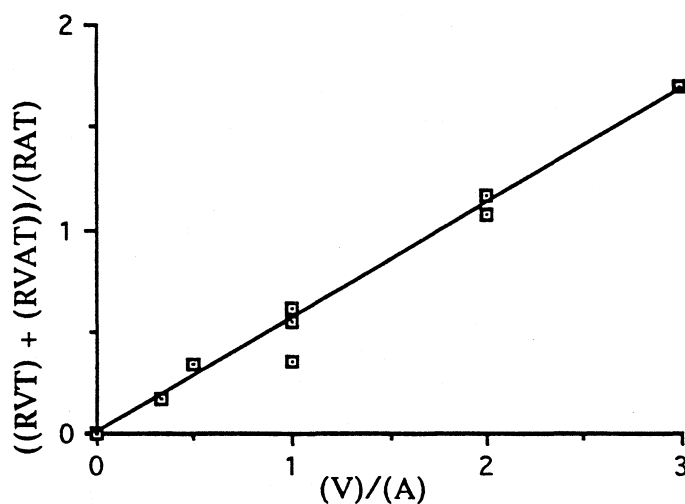
According to the 'free monomer' mechanism, the slope of the plot $([RVT]_T + [RVAT]_T)/[RAT]_T$ vs [V]/[A] is the ratio of the rate constants k_V/k_A(equation ix).

$$k_V/k_A = 0.58$$

A value can also be estimated from the results of similar experiments involving the separate monomers, which has been carried out in previous work and also in this work (see table 4). The calculation involves a comparision of the amount of trapped tail addition product, RVT and RAT in the V and A systems respectively, with the products derived from methyl radicals in each case

(methyl radicals as mentioned previously serve as a so-called free radical clock).

$$H_3C-\overset{\overset{\displaystyle CH_3}{|}}{\underset{\underset{\displaystyle CH_3}{|}}{C}}-O\cdot \xrightarrow{\quad k_1 \quad} \cdot CH_3 \xrightarrow{\quad T \quad} CH_3T \qquad \qquad XIII$$
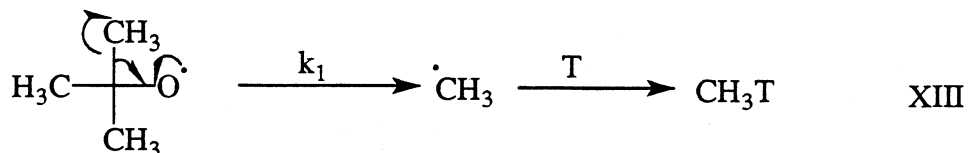
In line with equations X, XI, XII and XV, and assuming that vinyl acetate(V) is in excess (i.e [V] is constant) and k_1 is independant of solvent, we have:

$$\left[\int_{start}^{finish} \frac{d[CH_3^{\cdot}]}{dt} \, dt = \sum ([\text{all products formed from } \dot{C}H_3]) \right.$$

$$= (22) \text{ in pure V}$$

$$= (22) + (26) \text{ in pure A}$$

$$\frac{d[CH_3^{\cdot}]}{dt} = k_1[tBuO\cdot]$$

$$\frac{d[CH_3T]/dt}{d[RVT]/dt} = \frac{k_1}{k_V[V]} \qquad \text{(in pure V)}$$

similarly $\qquad \dfrac{d[CH_3T]/dt + d[26]/dt}{d[RAT]/dt} = \dfrac{k_1}{k_A[A]} \qquad$ (in pure A)

Eliminating k_1 from the equations and assuming the ratio of total product yields is equal to the ratio of the rates of product formation

$$\frac{[RVT]_{T,N}}{[RAT]_{T,N}} = \frac{k_V[V]}{k_A[A]}$$

Where the subscript T refers to the total yield and the subscript N refers to normalised yield, i.e.

$$[RVT]_{T,N} = \frac{[RVT]_T}{[CH_3T]_T} \qquad \text{and } [RAT]_{T,N} = \frac{[RAT]_T}{[CH_3T]_T + [26]_T}$$

This gives values for k_V/k_A of 1.26 from previous work[80] and 1.36 from this work.

Although these two values are in themselves in good agreement, they are over twice the value obtained from the mixed monomer systems(0.58). The anomalous difference here is most likely due to the assumption that the rate of decomposition of R is independant of solvent in the normalisation of product yields from separate monomer experiments. Therefore the most reliable value for k_V/k_A at 60°C is 0.58. This indicates that under similar reaction conditions i.e in a direct competition experiment t-butoxyl radicals react faster with acrylonitrile than with vinyl acetate. As previously mentioned t-butoxyl radicals are reported to be 'electrophilic' in character[81], which makes this result somewhat surprising. The findings here are in line though with more recent work by the CSIRO[84] group who suggest that t-butoxyl radicals exhibit nucleophilic behaviour. This apparent 'ambiphilic' behaviour of t-butoxyl radicals may be a consequence of a late transition state for addition to alkenes.

The ratio of the diastereomers was about 1:1. A similar result was obtained by Ivin and Navratil[85] in the free radical polymerisation of propene with sulphur dioxide, at 60°C. They observed cis and trans addition in almost equal proportions. However, the diastereomeric formation of (28) and (29) may not be strictly analogous, as both (28) and (29) could be the result of exclusive trans addition (see scheme 10). Hence, pyramidal inversion of the intermediate radicals is not necessary to explain the formation of (28) and (29).

With regard to the two diastereomers, there is an interesting trend, in that when there is a slight excess of T(10) over t-butoxyl radicals, the ratio of (29):(28) is 1.1:1.0(see table 4). However, when T(10) is in about a 10 fold excess over t-butoxyl radicals the result is reversed and the ratio of (29):(28) decreases to 0.7:1.0. The elution order of (28) and (29) from the reverse phase HPLC (namely (28) is eluted before (29)) suggests that (28) is more polar than (29). Hence, (28) is likely the diastereomer posessing the acetate and nitrile group on the same side of the molecule (assuming the most stable conformation contains the bulky aminoxyl moiety anti to the $CH(OAc)CH_2O\text{-}t\text{-}Bu$ group as shown-scheme 10).

Perhaps (as suggested in scheme 10) the radical once formed undergoes a bond rotation; it is possible that the initially formed conformation is destabilised by polar factors.

Scheme 10
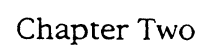
2.2.3. Influence of lewis acids on the copolymerisation behaviour of Vinyl acetate and Acrylonitrile

In 1957, Bamford[86] reported that when acrylonitrile was polymerised in dimethylformamide the rate could be enhanced significantly (up to twofold) by the addition of small amounts of lithium chloride. Ensuing studies showed this to be a general phenomenon for polymerisations involving in particular acrylic monomers and vinyl heteroaromatic compounds, in the presence of lewis acids[87].

The addition of lewis acids is now known to be effective in enhancing the tendency towards alternation in copolymerisation of certain monomer pairs[88]. It has also been shown[89] that equimolar alternating copolymers of high molecular weight can be synthesised with the aid of lewis acids from monomers which were previously not considered polymerisable.

Mokhtar et al.[75] report that the presence of $SnCl_4$ results in an increase in the reactivity of vinyl acetate and acrylonitrile towards the alternating copolymerisation reaction. Bamford et al.[86] also report that the presence of LiCl brings about a change in the reactivity ratio of the monomers in the copolymerisation reaction.

Mokhtar[75], Gaylord et al.[90] and Moad and Solomon[91] suggest that when a lewis acid is present in the reaction mixture it forms a binary complex with the functional group of the acceptor monomer (EA). The electron deficiency of the double bond is thus enhanced (conjugation energy of the π electrons of the double bond is increased), due to complexation with the lewis acid. They suggest that this enhances its reactivity towards nucleophilic radicals. In terms of this work acrylonitrile should have an enhanced reactivity towards vinyl acetate, when in the presence of a lewis acid.

2.2.3.1. Results and Discussion

$ZnCl_2$ and $FeCl_3$ were added in varying amounts to reaction mixtures of vinyl acetate and acrylonitrile(see table 5), the objective being to increase the percentages of comonomer products (28) and (29) in the reaction mixtures. When $ZnCl_2$ (or $FeCl_3$) was added to the reaction mixture (reactions IV-XI, table 5) the hydrogen abstraction product (23) was one of the main reaction products.

Interestingly the inclusion of $ZnCl_2$ (or $FeCl_3$) in the reaction gave no detectable formation of the products (28), (29), (27) and (25), although (27) was detected when the concentration of $ZnCl_2$ was very low (4% w.r.t. the number of moles of vinyl acetate).

In a blank reaction (to check that the lewis acid is responsible for this increased percentage of (23) present in the reaction mixtures) (reaction I, table 5) with no lewis acid present, the hydrogen abstraction product (23) is not produced in sufficient quantities to be detected by HPLC analysis(under certain reaction conditions, (23) is detected although in minor amounts-see table 4). Repeating this reaction, but excluding DTBP from the reaction mixture(to determine whether the aminoxyl (10) is responsible for the increased percentage of (23) in the reaction mixtures), and incorporating an internal standard, (23) is still undetected(see reaction II, table 5).

In order to check that the products (28), (29), (27) and (25) were not decomposing under the reaction conditions, the following experiments were performed. A blank reaction (reaction I, table 5) was carried out (minus benzene), then $ZnCl_2$ (60% w.r.t. the number of moles of vinyl acetate) was added and the reaction mixture heated at 30°C for two and one half hours. Analysis of this reaction mixture showed there had been no change in the amounts of products (28), (29), (27) and (25) formed compared with the original blank reactions (reaction I, table 5). To check also, that these products if formed were not then decomposing when in contact with aqueous methanol (in the presence of $ZnCl_2$) a reaction mixture(reaction V, table 5) had sufficient triethylamine added to it to neutralize the $ZnCl_2$ present, prior to contact with methanol/water. This reaction mixture was then filtered prior to HPLC analysis. This reaction mixture also showed products (28), (29), (27) and (25) to be present in percentages consistent with the standard blank reaction(reaction I, table 5). Clearly then these products((28), (29), (27) and (25)) are not being formed in the presence of $ZnCl_2$ (or $FeCl_3$).

Large amounts of (23) are produced when $ZnCl_2$ (or $FeCl_3$), DTBP, (V) and (A) are reacted in the presence of (10). Hydrogen abstraction by (10) is not observed in the absence of lewis acids (reaction II, table 5). Also, a comparision of reactions (III) and (IV) (table 5) indicates no appreciable hydrogen abstraction by t-butoxyl radicals. This suggests that when (10) is complexed to $ZnCl_2$, it becomes a very effective hydrogen abstraction agent (scheme 11).

Table 5 Effect of lewis acids on reaction products

Experiments→ Products↓	Blank	Blank	ZnCl2^D							FeCl3^D	
	I^A,B,F %	II^A,C,G ratio	III^A,C,G ratio	IV^A,B,G %/ratio	V^A,B %	VI^E %	VII^A,B %	VIII^A,B %/ratio	IX^A,B %	X^A,B %	XI^A,B %
(23)	-	<0.003	0.41	24 (0.42)	5	24	26	28 (0.46)	25	6	72
(26)	0.9			20	22	15	22	16	1	10	3
(22)	16.7			57	57	62	53	56	74	84	25
(28)(RVAT)	3.9			-	-	-	-	-	-	-	-
(29)(RVAT)	3.0			-	16	-	-	-	-	-	-
(27)(RAT)	51.1		-	-	-	-	-	-	-	-	-
(25)(RVT)	24.4			-	-	-	-	-	-	-	-
Internal standard^G		1.00	1.00	(1.00)				(1.00)			

A. 1.0 ml vinyl acetate(1Eq):0.714ml acrylonitrile(1Eq).
B. [Trap(10)] = 10 x [^{t}BuO·]. Trap-40mg, DTBP-2.5mg.
C. Trap-40mg, NO DTBP.
D. % lewis acid with repect to vinyl acetate moles.
E. [Trap] = 2.1 x [^{t}BuO·]. Trap(10)-18mg, DTBP-10mg, 2.0ml vinyl acetate(8 M):0.714ml acrylonitrile(4 M).
F. 0.7ml Benzene.
G. Plus internal standard.-1,1,3,3-tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy diphenylphosphinate(32).

Interestingly, FeCl3 appears to be even more effective than ZnCl2 in this regard.

Presumably complexation of (10) to a lewis acid results in a more localised (less stable) radical which increases the propensity towards H-abstraction. This would be consistent with the higher H-abstracting ability of acyl aminoxyls:

$$[\,R-\overset{\overset{\displaystyle O}{\|}}{C}-\underset{\underset{\displaystyle R'}{|}}{N}-O\cdot\,]$$
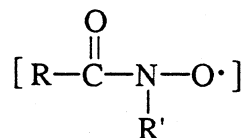
compared with dialkyl nitroxides[92].

Scheme 11
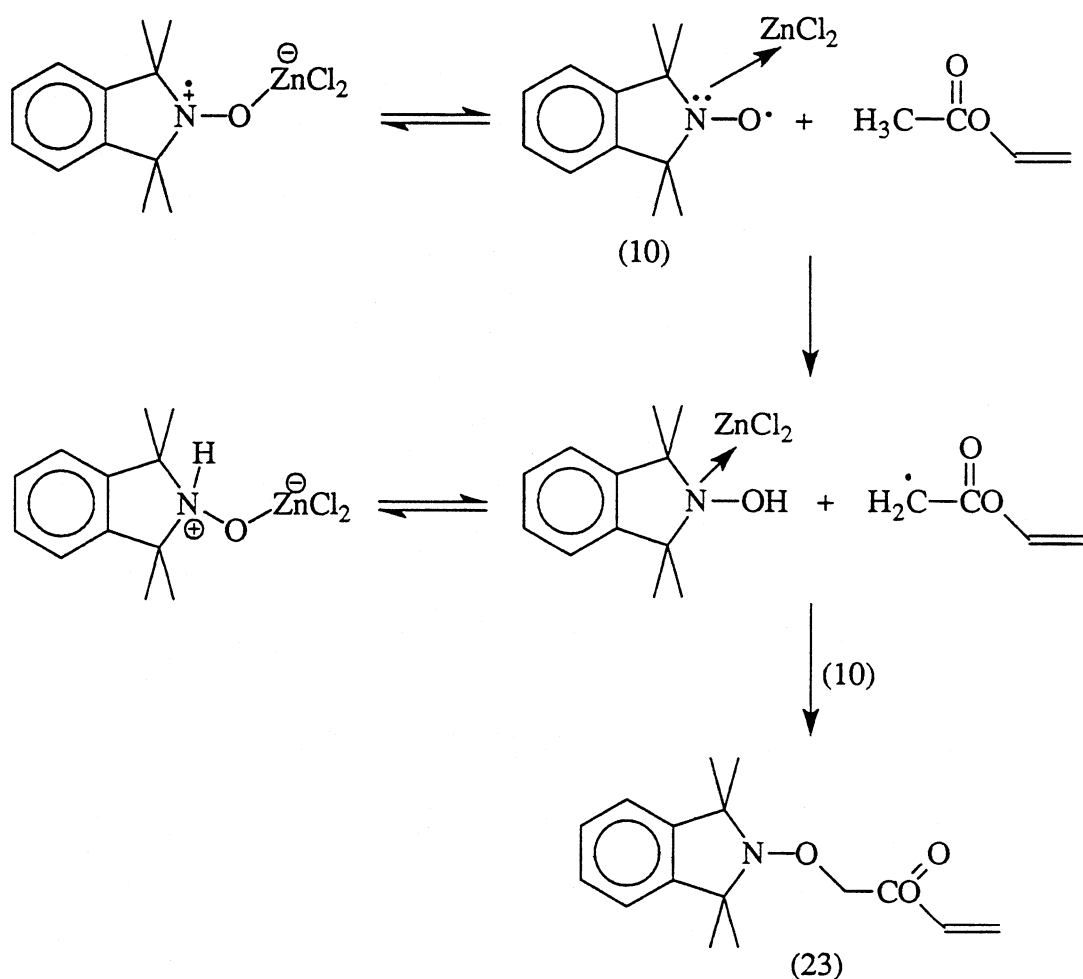
Another interesting feature of these reactions is the change in the ratio of the methyl radical addition product (26) to the directly trapped product (22). Addition of ZnCl2 (4-20%) increases the relative proportion of radical addition

product (26)*. This is consistent with the suggestion of Mokhtar[75], Gaylord et al.[90] and Moad and Solomon[91] that $ZnCl_2$ complexes to acrylonitrile which enhances the rate of addition of the methyl radical (from β scission of the t-butoxyl radical) to the now more electron deficient tail end of the double bond.
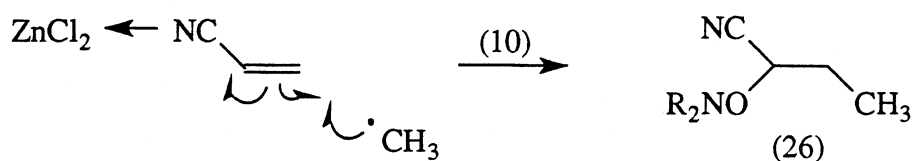
When the amount of added $ZnCl_2$ was increased to 60-80%, the relative proportion of radical addition product decreased drammatically. Possibly this was due to removal of (A) from the system by lewis acid-catalysed reactions with vinyl acetate (eg, ionic polymerisation). In contrast, $FeCl_3$ had little effect on the ratio of (26):(22), suggesting that it was behaving as a much weaker lewis acid towards (A).

An unexpected finding in this study was the absence of the t-butoxyl addition products (28), (29), (27) and (25), when $ZnCl_2$ or $FeCl_3$ were present. The reason for this is not entirely clear. It may be that, the lewis acid complexes to the nitrile group on (A), as previously mentioned and also to the carbonyl of (V), Mokhtar et al.[75] suggest that this is what occurs. This would then result in an electron depleted double bond on both monomers: thus reducing the propensity towards attack by the electrophilic[81] t-butoxyl radical.

2.2.3.2. Conclusion

The results indicate that the 'charge transfer' mechanism plays little or no part in the initiation step in the free radical copolymerisation of acrylonitrile and vinyl acetate with t-butoxyl radicals. The initiation step does however appear to proceed via the 'free monomer' mechanism.

Inclusion of $ZnCl_2$ (or $FeCl_3$) in these reaction mixtures results in the hydrogen abstraction product (23) becoming one of the major reaction products. This is in contrast to reactions carried out in the absence of $ZnCl_2$ (or

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* Note that the apparently anomalous result for 10% $ZnCl_2$ is presumably due to the lower acrylonitrile concentration used in that experiment.

FeCl3) where (23) in general is not detected. This dramatic increase in (23) is attributed to the aminoxyl (10) forming a complex with the lewis acid and therefore becoming an effective hydrogen abstracting agent.

The presence of ZnCl2 or FeCl3 also eliminates addition of the t-butoxyl radical to either monomer (i.e no formation of (28), (29), (27) and (25)). It is not directly clear as to why this is the case. However, lewis acid complexation to both monomers and therefore decreased double bond reactivity towards the electrophilic t-butoxyl radical, is suggested.

It appears that ZnCl2 complexation to acrylonitrile is responsible for an increase in methyl radical addition to acrylonitrile, with respect to amount of methyl radical trapped directly by (10).

These results indicate that the 'radical trapping' technique employing (10) has limitations when attempting to employ it as a tool to study the effect of lewis acids on the initiation mechanism in the free radical copolymerisation of vinyl acetate and acrylonitrile.

The aminoxyl (10) does not act as a non-intrusive radical trap under these conditions.

CHAPTER THREE

THE REACTION OF DIPHENYLPHOSPHINE OXIDE AND OF DIPHENYLPHOSPHINE WITH t-BUTOXYL RADICALS

CHAPTER THREE

3.0 Introduction

Phosphorus radicals have played a large part in the history of phosphorus chemistry[93]. It seems likely, that in 1681 A.D. when Robert Boyle observed a glow accompanying the oxidation of phosphorus in air phosphorus radicals were involved[94].

Kharasch however, was first to propose a chain reaction involving radicals with an unpaired electron on phosphorus. This came from his studies in 1945, on the reaction of phosphorus trichloride with 1-octene in the presence of acetyl peroxide[95]. Following this proposal by Kharasch, phosphorus radicals were frequently proposed as transient (although not observable) intermediates in many reactions[96]. It was almost 25 years later, that Kochi provided proof of the existence of phosphorus radicals with the observation of the esr spectrum of $Me_3P \cdot OBu^t$[97].

However there is much yet to be learned about phosphorus centred radicals and there are yet some important reasons for gaining knowledge in this area. For instance, free radicals are known to be responsible for the induction of certain types of cancer. Cancer is basically the mutation of a normal cell, and therfore any interaction of radicals with DNA or RNA could, theoretically initiate the mutation. Understanding phosphorus radical chemistry becomes important because the backbone of the nucleic acids in DNA and RNA is composed of phosphate ester moieties[16,98].

There are *two* main types of phosphorus radical. The *first*, has seven electrons (one unpaired) in the valence shell of the phosphorus atom. Examples of this type are the phosphinyl* radical, $R_2 \cdot P=O$, the phosphino radical, $R_2P \cdot$, and the phosphinium radical cation, $R_3P \cdot \oplus$. The *second* radical type has nine electrons (one unpaired) around the phosphorus atom, and is illustrated by the phosphoranyl radical, $R_4P \cdot$, or $(RO)_4P \cdot$ and by the phosphonium radical anion, $R_3P \cdot^-$. The first class of phosphorus radicals, and in particular (30) and (31) are the subject of the research work presented in this chapter.

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* It should be noted that this type of radical is also referred to as the phosphonyl radical[100,101]. However in line with more recent work[105], this radical type is reffered to throughout this thesis as phosphinyl.

(30)
Diphenylphosphinyl
radical

(31)
Diphenylphosphino
radical
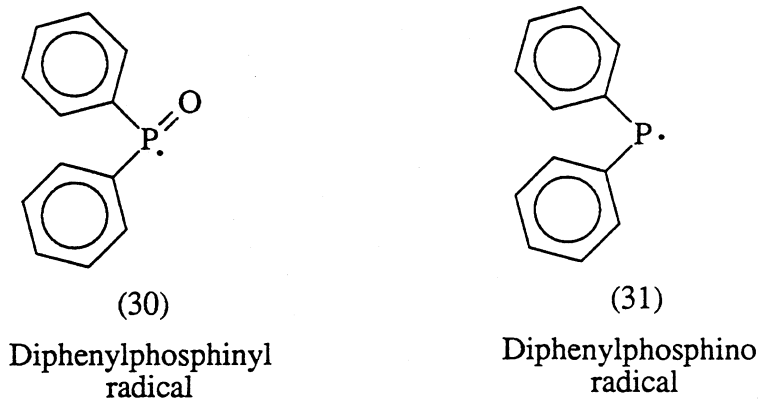
There is a certain amount of double bond character in the phosphorus oxygen bond of phosphinyl radicals, such as the diphenylphosphinyl radical, and therefore these radicals could well be regarded as nine-electron radicals. However because they demonstrate a similar type of reactivity to the phosphino radical they are classed with the seven electron radicals. The correct representation of the phosphinyl radical should be denoted by resonance hybrids:

$$R_2\overset{\oplus}{\overset{\bullet}{P}}\!\!-\!\!\overset{\ominus}{O} \rightleftharpoons R_2\overset{\bullet}{P}\!\!=\!\!O \rightleftharpoons R_2\overset{\bullet\bullet}{P}\!\!-\!\!\overset{\bullet}{O}$$
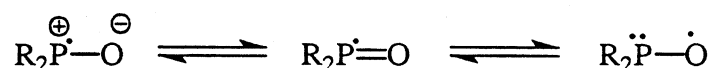
Phosphinyl radicals in general are generated by hydrogen abstraction from secondary dialkyl (or diacyl) phosphine oxides[99], $R_2P(=O)H$, or by photolysis of secondary acyl phosphine oxides[100]. There has been some recent work on UV irradiation of acyl-diphenylphosphine oxides

$$R_2\overset{\overset{\textstyle O}{\|}}{P}H \xrightarrow{\quad h\nu \ or \ R\cdot \quad} R_2\overset{\overset{\textstyle O}{\|}}{P}\cdot$$
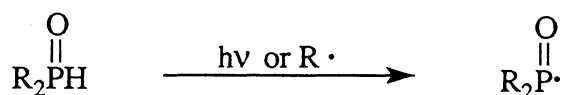
to produce diphenylphosphinyl radicals. These radicals are generated by α-scission of compounds such as TMDPO(2,4,6-trimethylbenzoyl diphenylphosphine oxide)(scheme 12), and have been shown to be suitable initiators for photocuring compositions, photo-polymerisations in TiO_2-pigmented coatings[101] and free radical polymerisations of olefinic compounds in general[100].

Scheme 12 Laser flash photolysis of an acyl phosphine oxide
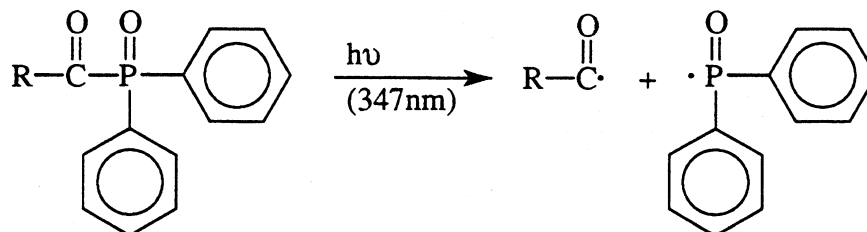
The diphenylphosphinyl radical (30) (and phosphinyl radicals in general) is pyramidal and configurationally stable, exhibiting high reactivity towards olefins (see chapter four) adding with retention of configuration at phosphorus[98,100]. The pyramidal structure is thought to
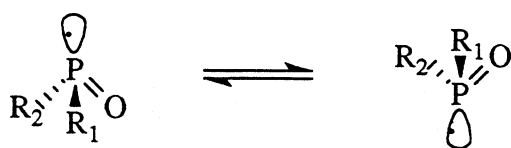
contribute to the high reactivity of phosphorus radicals[101].

The nature of the substituents on phosphorus determines whether the pyramidal structure of the radical is more or less pronounced. Esr studies by Kerr et al.[102] and Geoffroy and Lucken[103], found that spin densities in 3p and 3s orbitals of phosphorus in dialkoxyphosphinyl radicals is $\rho 3p/\rho 3s \cong 3$ and in diphenylphosphinyl radicals $\rho 3p/\rho 3s \cong 5.5$. The rather low value of $\rho 3p/\rho 3s$ for dialkoxyphosphinyl radicals (eg $(MeO)_2P\cdot O$) indicates a pronounced delocalisation of the unpaired electron in the sp^3 orbitals, in contrast to the case of the diphenylphosphinyl radical where a higher value indicates little or negligible delocalisation. This indicates a rather flattened tetrahedral (pyramidal) structure of $Ph_2P\cdot(O)$ relative to $(MeO)_2P\cdot(O)$. So increasing the oxyl substitution by more electropositive groups (eg. replacing OCH_3 with phenyl) produces a change from pyramidal to a more planar configuration about the phosphorus radical.

Spin trapping in conjunction with esr has been employed to study phosphinyl radicals. For example, t-nitrosobutane was employed[104] as a radical scavenger in the following manner:

$$(C_2H_5O)_2\overset{\overset{\displaystyle O}{\|}}{P}H \xrightarrow{R^\bullet} [\ (C_2H_5O)_2\overset{\overset{\displaystyle O}{\|}}{P}{\bullet}\ ] \xrightarrow{{}^tBuN=O} (C_2H_5O)_2\overset{\overset{\displaystyle O}{\|}}{P}-N\overset{\diagup O^\bullet}{\diagdown {}^tBu}$$
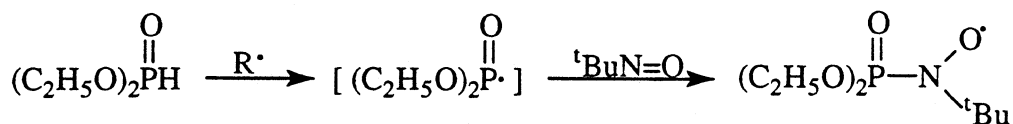
More recently, aminoxyl radical scavenging ('radical trapping') has been used by Baxter et al.[105] to trap the diphenylphosphinyl radical produced from photo-induced α-cleavage of a number of acyl diphenylphosphine oxides. TEMPO(6) was employed as the aminoxyl trap, and Baxter et al. reported solvent independant, efficient trapping of (30) by (6).

Phosphino radicals are generated also by radical initiated hydrogen atom abstraction from PH_3, RPH_2 or R_2PH[99,106], for example:

$$Ph_2PH \xrightarrow{R^\bullet} Ph_2P^\bullet + RH$$
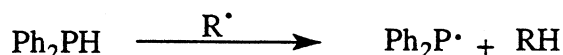
or by, photolysis of phosphines (PH_3, RPH_2 or R_2PH) or bisphosphines (R_2PPR_2, etc)[98], for example:

$$Ph_2P-PPh_2 \xrightarrow{h\upsilon} 2Ph_2P^\bullet$$
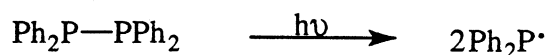
Once formed these radicals are known to abstract hydrogen themselves or add rapidly to unsaturated systems[98].

The diphenylphosphino radical (31) has also been produced by the X-irradiation of single crystals of triphenylphosphine oxide and diphenylphosphine sulphide[107]. The diphenylphosphino radical is relatively stable and has a half life of 20 minutes at 173 K[98].

Like the phosphinyl radical, the phosphino radical has also been spin-trapped by radical scavengers such as t-nitrosobutane, and the resultant, relatively stable nitroso radicals studied by esr spectroscopy[104,108].

$$\begin{array}{c}Ph_3P,\ Ph_2PH \\ or\ Ph_2PPPh_2\end{array} \longrightarrow [\ Ph_2P^\bullet\ ] + {}^tBuN=O \longrightarrow Ph_2PN\overset{\diagup {}^tBu}{\diagdown O^\bullet}$$
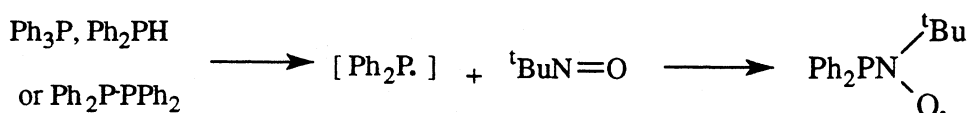
Kochi and Krusic's[109] esr study of the reactions of t-butoxyl radicals with phosphines provided the first spectroscopic report of a phosphoranyl radical ($R_4P^\bullet$), and demonstrated that the t-butoxyl radical will add to phosphines.

Chapter Three

$^tBuO^\bullet$ + $(CH_3)_3P$ $\longrightarrow$ [phosphoranyl radical structure] $\rightleftharpoons$ [phosphoranyl radical structure]
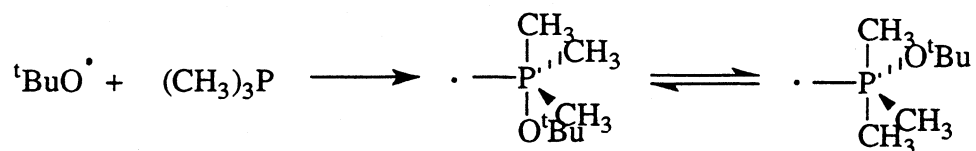
There is a 22 kJ. mol^{-1} energy barrier reported for the above pseudo-rotation in phosphoranyl radicals[110]. It is also interesting to note that the addition of t-butoxyl radicals to the phosphite $P(O^tBu)_3$ proceeds more rapidly than β–fragmentation of the t-butoxyl radical; as methyl radicals are not observed in this reaction[111].

As has already been mentioned there are reports of 'spin-trapping'/ esr studies of both diphenylphosphino and diphenylphosphinyl radicals[104,110] a method which sometimes fails to establish unambiguously the structure of transient radicals[36]. There is however only one reported study using the 'radical trapping' technique to trap and study phosphorus radicals(the diphenylphosphinyl radical)[105]. There are nevertheless, other reports of aminoxyls reacting with phosphorus bearing substrates. For example, bis(trifluoromethyl)aminoxyl gives oxidation reactions with tris(pentafluorophenyl)phosphine[112],
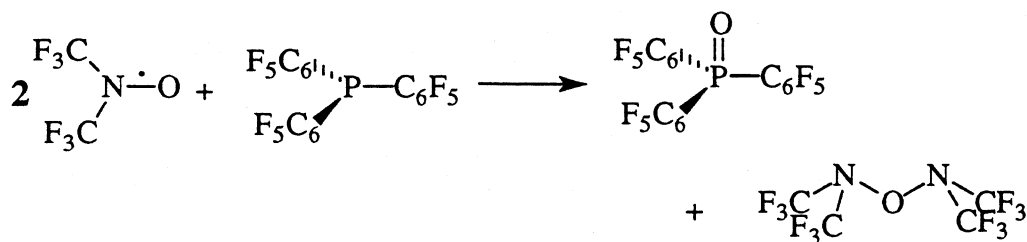
addition reactions with $(CH_3O)P$[113] and hydrogen abstraction with $(CF_3)_2PH$[114].

The 'radical trapping' technique has not been applied to the study of the reactions of diphenylphosphine oxide and of diphenylphosphine with t-butoxy radicals. It is the purpose of the work presented in this chapter to examine such reactions by employing the aminoxyl (10). As with the aminoxyl-trapping of carbon-centred radicals (see chapter one), it is believed that the aminoxyl-trapping of phosphorus-centred radicals may be the method of choice to study phosphorus radical reactions. This is suggested by the preliminary work of Baxter et al.[105](diphenylphosphinyl radicals) and by the work presented in this thesis. Based on the high P-O bond

strength, phosphorus-centred radical trapping by an aminoxyl such as (10), would be expected to occur readily.

3.1 Results and Discussion

3.1.1 The reaction of Diphenylphosphine oxide with t- butoxyl radicals in the presence of (10)

Diphenylphosphine oxide(DPPO), di-tert-butyl peroxyoxalate(DTBP) and (10) were combined with benzene in a reaction vessel in the amounts shown in scheme 13. The reaction mixture was then subjected to successive freeze/evacuation/thaw cycles under high vacuum. Following this the reaction mixture was heated at 60°C for 68 minutes.

The reaction products produced and unreacted starting materials were isolated by reverse-phase HPLC and characterised in the standard way by ^{1}H, ^{13}C and ^{31}P nmr. These components along with their respective amounts are given in scheme 13 (left to right, in order of elution from the HPLC column).

The isolation of diphenylphosphinic acid(DPPA) from the reaction mixture, suggests oxidation of diphenylphosphine oxide(DPPO) possibly by the peroxalate, as oxidations of this type are known[115,116]. However, diphenylphosphinic acid could also be produced during the reaction work up, either by hydrolysis of (32) or by aerial oxidation of diphenylphosphine oxide. The higher recovery of diphenylphosphine oxide from the reaction with DTBP (versus the blank reaction- without DTBP) is admittedly strange, although this in part may be due to the highly hygroscopic nature of diphenylphosphine oxide. It is admissible that high atmospheric humidity when weighing the DTBP reaction sample is responsible for this anomally.

In a separate experiment where (32) was left in contact at room temperature with the solvent used for HPLC analysis (water/methanol, 50:50), analysis by HPLC after one hour showed that 1% of the initial amount of (32) had been hydrolysed to diphenylphosphinic acid, after 29 hours 10% had been hydrolysed. The aminoxyl (10) is also generated during the hydrolysis experiment, by partial oxidation of the corresponding hydroxylamine.

Scheme 13 Isolated material from the reaction of Diphenylphosphine oxide with t-butoxyl radicals in the presence of (10)

O O
‖ ‖
ᵗBu–O–O–C–C–O–O–ᵗBu

(DTBP)
(58mg)/(0mg)

+

Ph   O
  \\ ‖
   P
  / \
Ph   H

(DPPO)
(100mg)/(100mg)

Δ (60°)
Benzene (2ml)/(2ml)
(10) (103mg)/(94mg)

Ph   O
  \\ ‖
   P
  / \
Ph   OH

(DPPA)
(10mg)/(4.1mg)

Ph   O
  \\ ‖
   P
  / \
Ph   H

(DPPO)
(46mg)/(38mg)

· ONR₂

(10)
(70mg)/(69mg)

Ph   O
  \\ ‖
   P
  / \
Ph   ONR₂

(32)
(62mg)/(45mg)
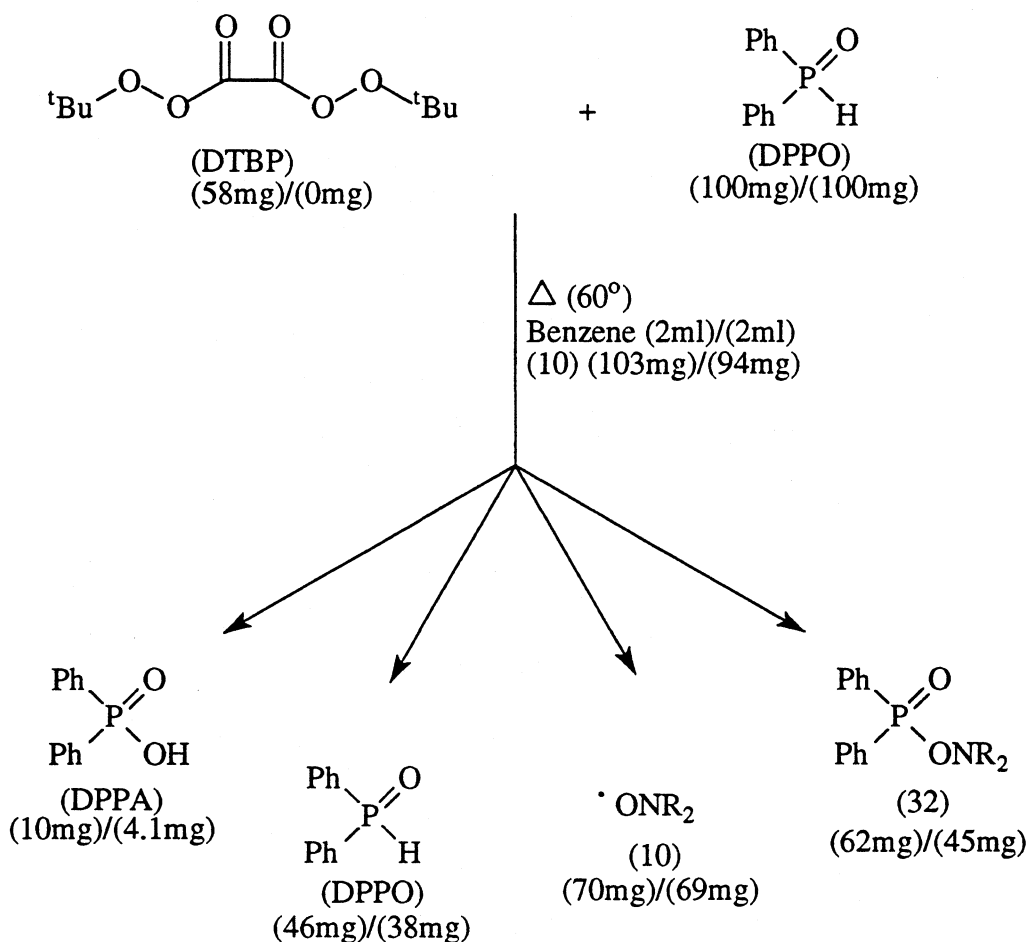
Ph = Phenyl

note: The amounts shown in the second brackets correspond to yields obtained in a separate 'blank' reaction between diphenylphosphine-oxide(DPPO) and the aminoxyl (10) in the absence of di-t-butyl peroxy-oxalate(DTBP).

The blank reaction (no DTBP-scheme 13), indicates that most of the diphenylphosphinic acid is being formed when the peroxyoxalate is present in the reaction mixture. It is not clear though whether the oxidation process is radical, or ionic or a combination of both.

The other reaction product isolated is the diphenylphosphinate (32). Hydrogen abstraction from secondary diaryl phosphine oxides such as diphenylphosphine oxide(DPPO) is known to occur[99], and therefore the formation of (32) under these reaction conditions (scheme 14) appears likely.

Scheme 14
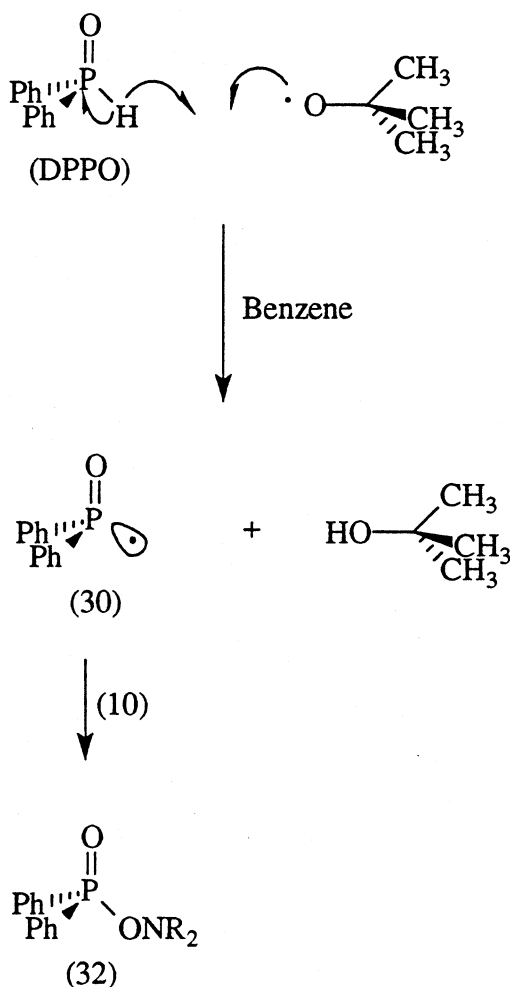
However, (32) is also formed in the absence of DTBP (blank reaction-scheme 13). Comparing the two reactions in scheme 13 (both with and without DTBP) indicates that at 60°C when [DTBP] = 0.124M, [(10)] = 0.271M and [DPPO] = 0.248M about 75% of (32) is formed not via t-butoxyl hydrogen-abstraction, but via hydrogen-abstraction by the aminoxyl (10). The aminoxyl (10) is known to be a hydrogen-abstraction agent under certain conditions[43]. Further analytical experiments were carried out to determine whether concentration affects altered the relative propensity of either the t-butoxyl radical or (10) to abstract hydrogen from diphenylphosphine oxide.

The first, a reaction identical to that with DTBP in scheme 13, except [DTBP] = 0.012M, [[diphenylphosphine oxide] = 0.026M and [(10)] = 0.026M; the second experiment identical to the blank in scheme 13, except that [diphenylphosphine oxide] = 0.026M and [(10)] = 0.026M, HPLC indicated that after 90 minutes at 60°C approximately 5% of (32) present in the reaction mixture was due to hydrogen-abstraction from diphenylphosphine oxide by (10). The remaining 95% of (32) being due to hydrogen-abstraction by t-butoxyl radicals. In a third reaction where the concentration of diphenylphosphine oxide was 0.013M and (10) was 0.026M, HPLC showed no discernable increase or decrease in the amount of (32) formed in relation to the first analytical reaction where the concentration of diphenylphosphine oxide and (10) were equimolar.

This reaction system is complex as hydrogen-abstraction by (10) followed by trapping effectively removes two equivalents of (10) from the system, one as the product (32), the other as the hydroxylamine R_2N-OH. However, R_2N-OH can subsequently be re-oxidised to (10) by t-butoxyl radicals. The concentration experiments carried out above, suggest that hydrogen-abstraction by (10) can be minimised by employing high-dilution conditions. Slow addition of (10) (via syringe-pump) could also be employed.

3.1.2 The reaction of Diphenylphosphine with t-butoxyl radicals in the presence of (10)

Aminoxyl (10) and DTBP were combined with benzene in a reaction vessel. The vessel was evacuated and filled with dry N_2, the cooled diphenylphosphine was then slowly added (see section 6.9.0). This precaution was taken to avoid neat contact of diphenylphosphine and DTBP (powerful reducing and oxidising agents respectively).

The reaction products were isolated by HPLC and characterised by ^{1}H, ^{13}C and ^{31}P nmr. They are shown, along with the amounts isolated, in scheme 15 (numbering is in order of elution from the reverse phase HPLC column).

As with the diphenylphosphine oxide reactions, where some oxidation (to diphenylphosphinic acid) is observed, so too with diphenylphosphine, oxidation to both diphenylphosphine oxide and diphenylphosphinic acid is seen.

Scheme 15 Isolated material from the reaction of Diphenylphosphine with t-butoxyl radicals in the presence of (10)
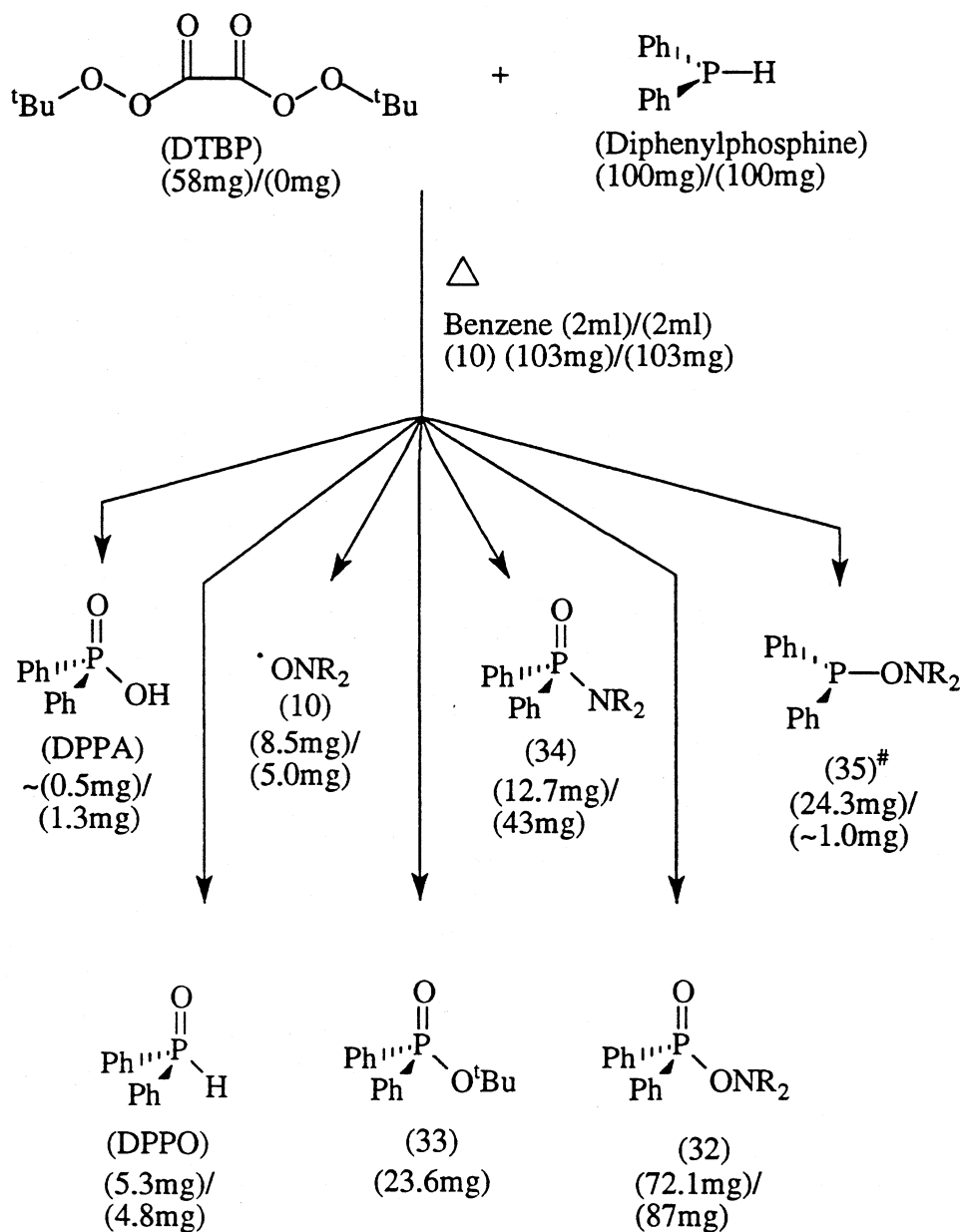
#. Unstable- minimum amount produced.

Note: The amounts shown in the second brackets relate to a separate 'blank' reaction - i.e. reaction between diphenylphosphine and the aminoxyl (10) in the absence of DTBP.

Phosphines are known to react with peroxides such as DTBP (as also are phosphites) by a radical mechanism[115].

$$\text{HPPh}_2 + \text{Bu}^t\text{O}-\text{O}-\overset{\overset{\text{O}}{\|}}{\text{C}}-\overset{\overset{\text{O}}{\|}}{\text{C}}-\text{O}-\text{O}^t\text{Bu} \xrightarrow{60°\text{C}} \overset{\overset{\text{O}}{\|}}{\text{Ph}_2\text{P}}-\text{H} + {}^t\text{Bu}-{}^t\text{Bu}$$

$$\text{(DTBP)}$$

$$+ \ 2\text{CO}_2$$
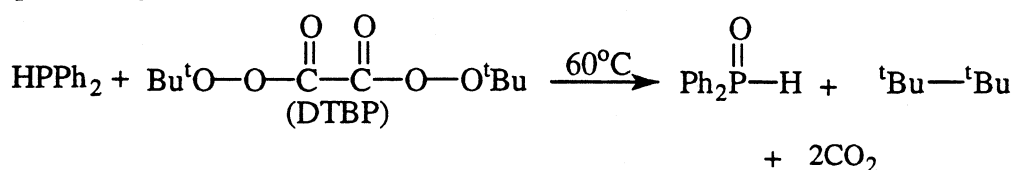
By analogy with phosphites it is likely that phosphines combine irreversibly with t-butoxyl radicals. The combining of t-butoxyl radicals with phosphines is known to occur very rapidly, in fact just below diffusion controlled rates as shown by rate constants for attack on PPh3 of 1.9×10^9 mol^{-1} s^{-1} and 8.1×10^8 mol^{-1} s^{-1} for t-butoxyl attack on P(OC2H5)3 at room temperature[117]. This suggests that t-butoxyl radicals will combine with diphenylphosphine at a similar rate to the rate of aminoxyl trapping of carbon-centred radicals[25]. The activation energy (E_a) for β-scission of the t-butoxyl radical is reported as being 34-42 kJ. mol^{-1} [117].

Although a possible mechanism for the formation of diphenylphosphine oxide would involve phosphoranyl radicals which undergo β-scission to produce diphenylphosphine oxide (scheme 16). There was no evidence to indicate the formation of t-butyl radicals in this system, therefore this mechanism seems unlikely.

Scheme 16
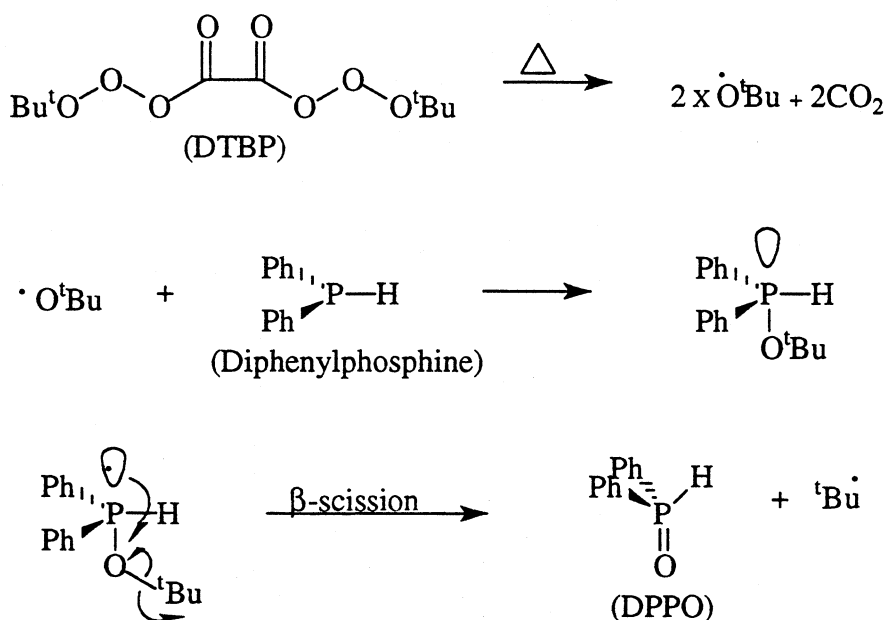
Diphenylphosphine oxide and diphenylphosphinic acid are also isolated (in the amounts shown- scheme 15) when DTBP is absent from the reaction mixture. This indicates that the aminoxyl (10) must therefore be actively involved in oxidising diphenylphosphine to diphenylphosphine oxide in a like manner to that suggested for t-butoxyl radicals. Once added, the aminoxyl (10) likewise being eliminated by β-scission (as suggested for the t-butoxyl radical in scheme 16) to produce diphenylphosphine oxide. Diphenylphosphine oxide and diphenylphosphinic acid were isolated in about the same amounts from the two reactions (scheme 15), indicating (10) to be almost solely responsible for this oxidation. The reason why β-scission is such a favourable process for phosphinyl radicals is that the gain in enthalpy on forming a phosphoryl group (P=O) is of the order of 630 kJ. mol^{-1}.

or
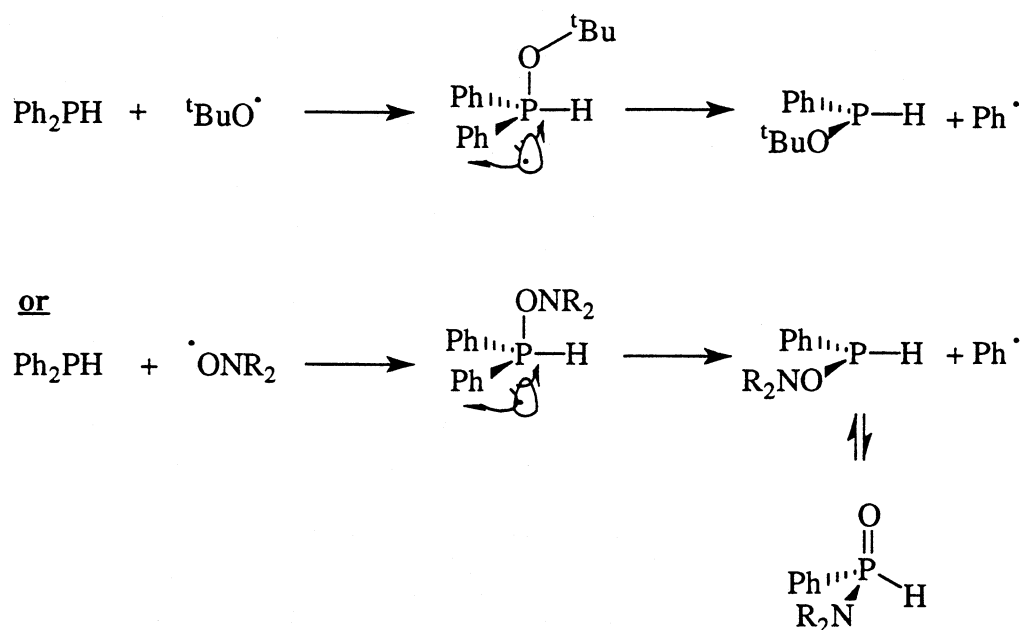
When phosphines react with alkoxy radicals they may undergo α-scission[117], although this is less likely, and apparently is not occuring under these reaction conditions as phenyl radicals were not detected in the reaction mixture (i.e. no phenyl-aminoxy (36) product was isolated).
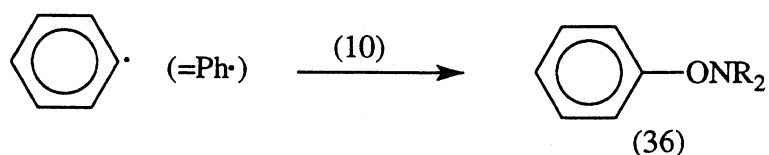
Although the indications are that t-butoxyl radicals play little or no part in the oxidation of diphenylphosphine to diphenylphosphine oxide, t-butoxyl addition to diphenylphosphine does occur under these reaction conditions as is evidenced by the formation of (33). A likely mechanism for the formation of (32) and (33) involves the participation of the phosphorane (37), as shown in scheme 17. The isolated quantities of these two products suggest that this process (scheme 17) is the main reaction pathway. The intermediate phosphoranyl radical is probably resonance stabilised by the attached phenyl groups[118,119].

Scheme 17
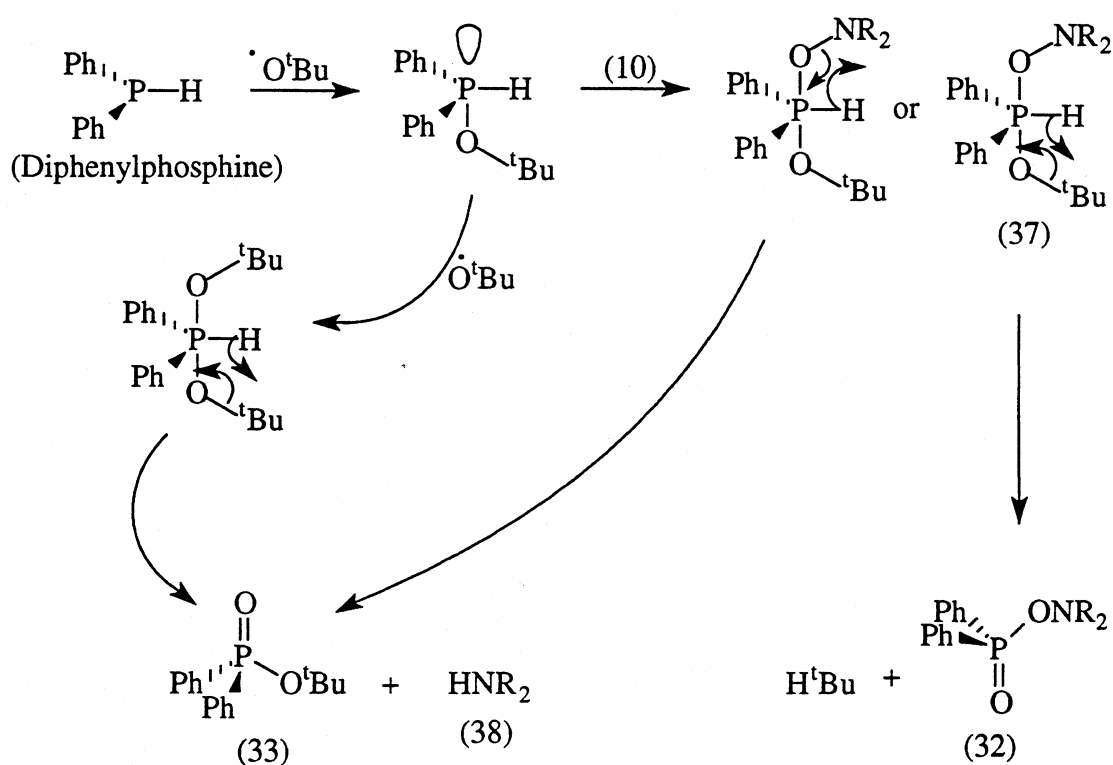
This mechanism (scheme 17) cannot however be the only mechanism by which (32) is produced, as it is also formed in the absence of DTBP. An additional mechanism (scheme 18) is therefore proposed for the formation of (32), as well as (34) and (35); this involves the phosphorane (39), produced by the addition of two moles of aminoxyl to diphenylphosphine. The phosphorane (39) may then decompose to (35), eliminating the hydroxylamine (38). Rearrangement of (35) to the more stable (34) must then occur. The hydroxylamine (38) was not detected in the reaction mixture by HPLC analysis; this is not unexpected as (38) is quite unstable, especially in air, or in a water/methanol solution where oxidation to (10) occurs rapidly.

The amine (HNR$_2$) was however detected by HPLC (using a very low solvent flow rate) following washing with sodium bicarbonate solution and re-extraction with ether. This was carried out as it was likely that the amine was present as a salt with diphenylphosphinic acid.

Scheme 18
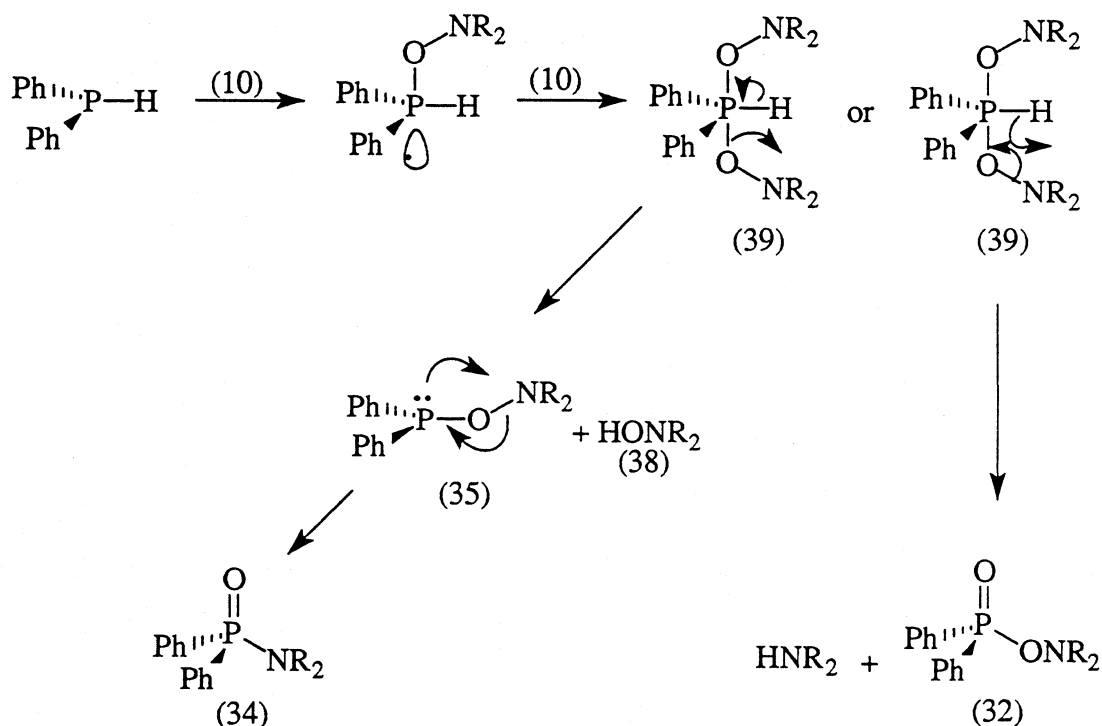
The blank reaction of diphenylphosphine (no DTBP) produces (32) and (34) as the two main products; the fact that almost twice as much (32) as (34) is isolated suggests that elimination of HNR$_2$ is more favourable than HONR$_2$ (38) elimination. However, it is also possible that the phosphorane intermediate (39) undergoes hydrogen-abstraction (by either t-butoxyl or (10)) followed by β-fragmentation to give (32) and R$_2$N• and that (34) arises from a sequential (chain) reaction of R$_2$N• with diphenylphosphine.

A mass balance of the DTBP/diphenylphosphine reaction and the blank reaction shows incomplete recovery of (10), for both reactions. While formation of (33), seems to necessitate the mechanism indicated in scheme 17, the quantity of (10) unaccounted for(almost an equivalent number of moles as the total number of moles of (32) produced) may well be present as HNR$_2$; being formed when (32) is produced according to scheme 18. If the total amount unaccounted for is to be attributed to the formation of HNR$_2$ (hence

(32))- which is in line with (32) being formed solely by the suggested mechanism in scheme 18, then this indicates only a very small percentage of (32) is being produced via (37)(scheme 17). This is supported by the consistency of the ratio of products [((34) + (35)) : (32)] produced in the DTBP/diphenylphosphine reaction [(9.86 X 10^{-5} moles) : (1.84 X 10^{-4} moles)- (1.87 : 1.00)] and in the blank reaction [(1.17 X 10^{-4} moles) : (2.24 X 10^{-4} moles)- (1.91 : 1.00)]. The ratio of the amounts of (32) and (35) formed are, in the presence and absence of DTBP consistent- indicating further that (32) is produced almost solely via the phosphorane (39). Our inability to isolate and fully characterise (the unstable) (35) however makes accurate quantitation difficult.

It is interesting to note that the reaction of tetraphenyldiphosphine with (10) at 60°C also produces (32) and (34)[120], however under the same reaction conditions tetraphenyldiphosphine dioxide does not react with (10).
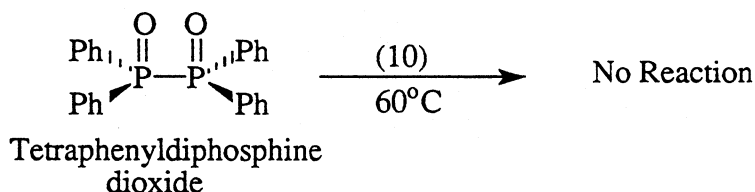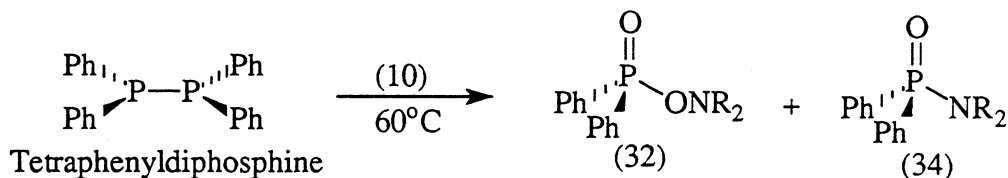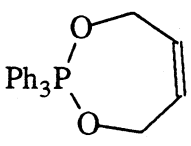
Evidence for the existence of (39) comes from the ^{31}P nmr analysis of several blank reactions (no DTBP), where diphenylphosphine(1 equivalent) and (10)(1 equivalent) were combined in benzene. One of these was heated at 60°C for 68 minutes, the other left at room temperature for 43 hours prior to analysis. Both reactions were evacuated and flushed with N_2 several times prior to heating. Reactions were not exposed to the atmosphere/water or methanol prior to ^{31}P nmr analysis.

For the room temperature experiment peaks were detected at -40.1(6.6), -39.9(5.4), 17.8(5.0), 24.8(2.0) and 32.6(12.0)(ppm, relative integral in brackets), for the 60°C experiment identical peaks were detected with

slightly different ratios -40.1(7.7), -39.9(6.3), 17.8(3.0), 24.8(1.0) and 32.6(11.0). The peak at 32.6ppm is due to (32), -40.1ppm to diphenylphosphine and the -39.9ppm peak is assigned to the phosphorane (39)(although these last two assignments could likely be the reverse). Phosphoranes of this type are known to have similar ^{31}P nmr shifts (see table 6).

<u>Table 6</u> ^{31}P nmr shifts of some representative phosphoranes

Structure	Shift (ppm)
$Ph_3P(O^iPr)_2$	-49.6[121]
	-45.4[121]
$Ph_2(H)P[O(2,5-^tBu_2C_6H_6)O]$	-30.8[122]
$nBu_3P(OC_2H_6)_2$	-38.0[98]
$Ph_2(H)P(ONR_2)_2$	-39.9

Due to the instability of (35) complete characterisation could not be achieved by elemental analysis. Several attempts were also made to obtain a definitive mass mass spectrum, however a parent ion could not be obtained. The ^{31}P nmr shift for (35) of 86.9ppm is in the accepted region for this type of three-coordinate phosphorus compound. For example $Ph_2P(OC_2H_5)$ -δ 109.8ppm[121]. Interestingly the peak at 86.9ppm was only seen in the latter stages of the reaction. Upon HPLC separation it was isolated and partially characterised. It is suggested that (35) is formed via the phosphorane (39) which by ^{31}P nmr was present in the reaction mixture in good quantity. Workup it seems them must produce the suggested rearrangement to form (35).

The ^1H nmr spectrum of (35) has only one peak upfield at 1.36ppm (12H) due to the four methyl groups on the aminoxyl, and two multiplets downfield at 7.18-7.30ppm(8H) and 7.40-7.47ppm(6H). These multiplets

containing 14 hydrogens in total, 10H from the two phenyl groups and 4H from the aminoxy aromatic ring. When warmed in aqueous THF, decomposition occuried immediately giving the characteristic yellow colouration of the aminoxyl (10). This was verified by HPLC which showed the formation of diphenylphosphine oxide, further supporting the structure proposed for (35). Distinctive infrared absorptions at 1460 cm^{-1} due to P-Ph and 1170 cm^{-1} due to P-ON in the I.R spectrum also support this structure.

Further confirmation of the structure of (32) was achieved by X-ray crystal structure determination of the analogous compound (40), obtained by substituting (10) with (12), in the reaction of diphenylphosphine oxide, DTBP and (10).

Figure 7 X-ray crystal structure of (40)
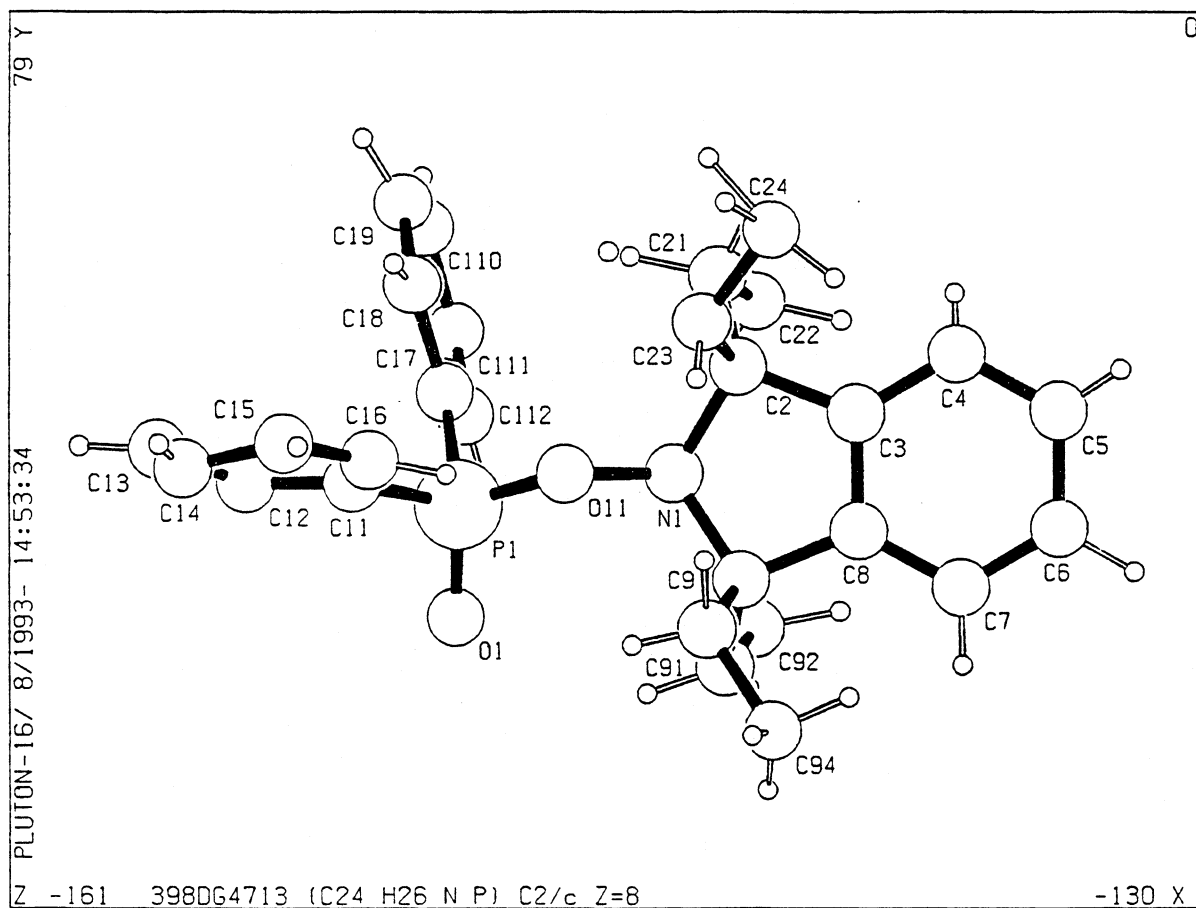
The structures of (33) (34) have been confirmed also by x-ray crystal structure determination (see figures 8 and 9).

<u>Figure 8</u> X-ray crystal structure of (33)
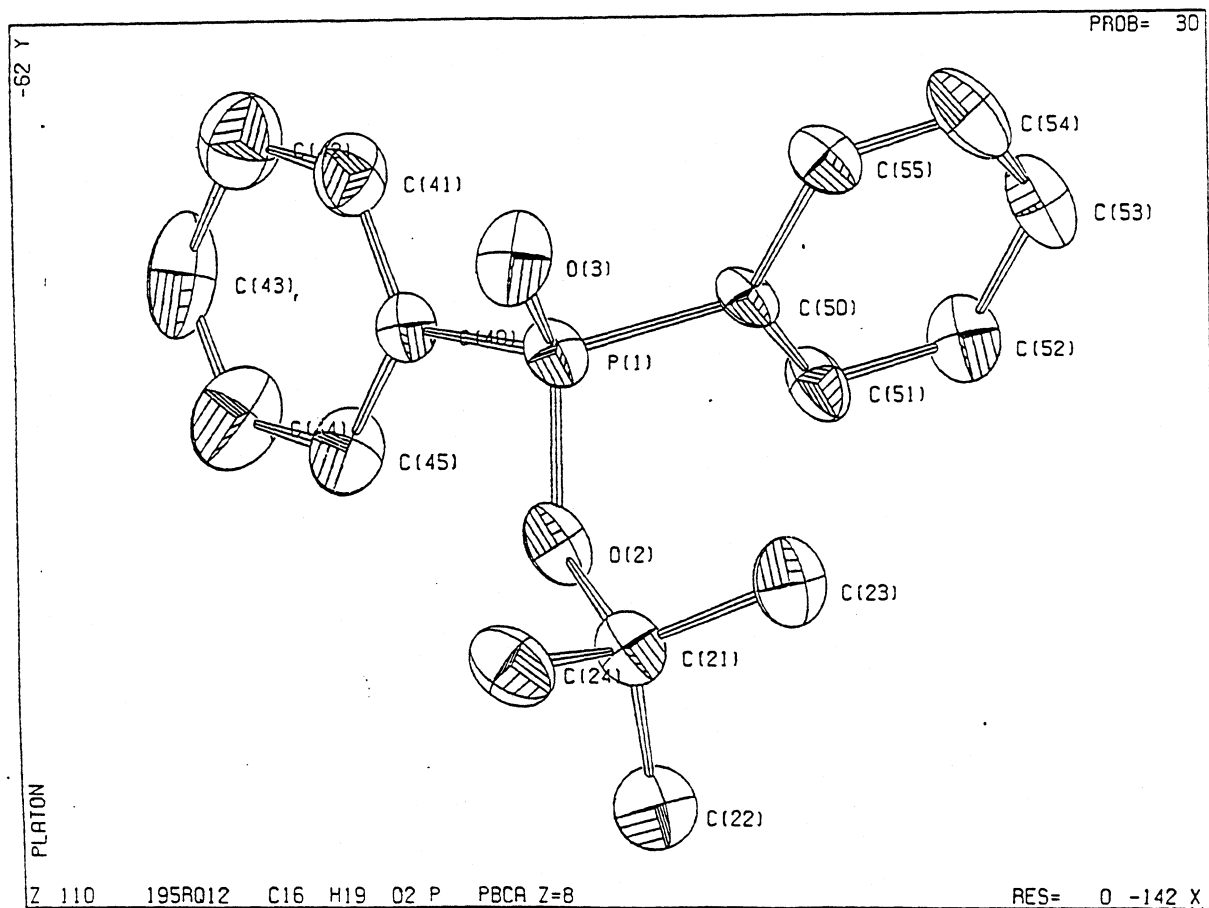
<u>Figure 9</u> X-ray crystal structure of (34)
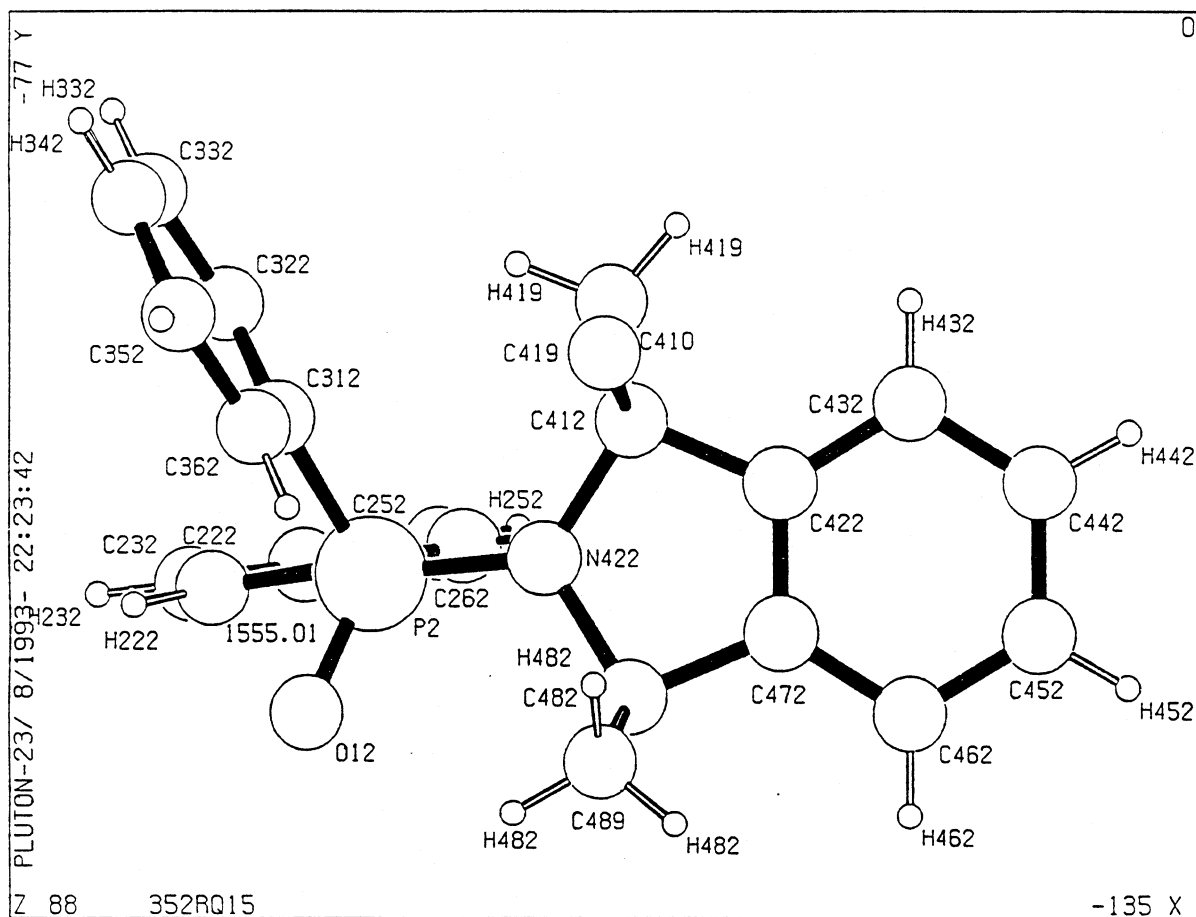
Examination of the x-ray crystal structures shows that compounds (32)
(by analogy with (40)), (33) and (34) all have a tetrahedral phosphorus atom.

Chapter Three

3.2.0 Conclusion

At low concentrations of (10), t-butoxyl will hydrogen-abstract from diphenylphosphine oxide to produce diphenylphosphinyl radicals, which are then trapped by (10). However, at high concentrations of (10), (10) itself will hydrogen abstract from diphenylphosphine oxide. To eliminate this intrusive involvement by (10), high dilution conditions need to be employed. One way to achieve this is by syringe-pump addition of (10).

The aminoxyl (10) is also responsible, at least in part for the oxidation of diphenylphosphine oxide.

While trapping of the diphenylphosphinyl radical by (10) appears to be quite straightforward, where addition to the phosphorus species is quite favourable as in the diphenylphosphine, the involvement of (10) is not so simple. However, the 'radical trapping' technique is certainly a valuable technique to study reactions such as those between diphenylphosphine oxide and of diphenylphosphine with t-butoxyl radicals; although (10) does not act as a totally non-intrusive phosphorus-radical trap under all situations.

CHAPTER FOUR

THE REACTIONS OF DIPHENYLPHOSPHINYL AND DIMETHOXYPHOSPHINYL RADICALS WITH VARIOUS ALKENES AND PHENYLACETYLENE

CHAPTER FOUR

4.0 Introduction

The reaction of oxygen-centred radicals with vinylic and acrylic monomers have been studied extensively by the radical trapping technique[27], the carbon-centred radicals so formed being efficiently trapped by (10) yielding stable and isolable alkoxyamine adducts.

Previous work[123,124,125] has shown that when oxy-radicals (particularly t-butoxyl radicals) react with cyclic olefins hydrogen-abstraction of allylic hydrogens is a major reaction. For example cyclohexene reacted with t-butoxyl radicals via allylic hydrogen-abstraction to give greater than 94% of the reaction product[18c]. There have been few detailed studies however, of the reaction of phosphorus-centred radicals with alkenes.

Phosphinyl radicals, which are pyramidal and configurationally stable are known to add to olefins with retention of configuration at phosphorus[98], and the rate of addition is very fast(10^6-10^8 l mol^{-1} s^{-1})[100,101]. For example, (31) reacts with styrene, with a rate constant of 6 x 10^7 lmol^{-1}sec^{-1}, a value 1-2 orders of magnitude higher than that for the addition of carbon-centred radicals to styrene[126,127] (and of similar magnitude for the addition of benzoyl radicals to styrene[100], 5.0 x 10^5 l mol^{-1} s^{-1}).

In the absense of radical scavengers Schnabel et al.[100] report the following rate constants for the reaction of the diphenylphosphinyl radical(31) and the dimethoxyphosphinyl radical(41) (generated by hydrogen-abstraction from dimethyl phosphite), with acrylonitrile(A) and vinyl acetate(V)(table 7).

$$H_3CO \diagdown \diagup O$$
$$P$$
$$H_3CO \diagup \diagdown H$$

(Dimethyl phosphite)
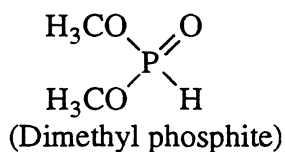
Trapping by (10) would be expected to be only 2-3 orders of magnitude faster than this, so that at low concentrations of (10), and in the presence of

Table 7 Bimolecular rate constants for the reactions of phosphinyl radicals with Acrylonitrile and Vinyl acetate in Cyclohexane at room temperature

Monomer(M)	$k_{R\cdot + M}$(Rate constants $(l\ mol^{-1}\ s^{-1})$)	
	$\overset{O}{\overset{\|\|}{Ph_2P\cdot}}$ (31)	$\overset{O}{\overset{\|\|}{(H_3CO)_2P\cdot}}$ (41)
Acrylonitrile	$(2.0 \pm 0.1) \times 10^7$	$(5.8 \pm 0.2) \times 10^6$
Vinyl acetate	$(1.6 \pm 0.1) \times 10^6$	$(2.9 \pm 0.2) \times 10^6$

an excess of the olefin R-CH=CH$_2$, trapping of the phosphinyl radicals would be expected to be competitive with trapping of the carbon-centred radicals formed by addition to the olefin, i.e. R-C·H-CH$_2$-P(O)R'$_2$.

The relatively high reactivity of (31) and (41) towards olefinic compounds has been explained in terms of the pyramidal structure of the phosphinyl radicals (as previously mentioned- see chapter 3). The pyramidal shape permits easy site approach to the unpaired electron by reactants. Radical (41) has a pronounced tetrahedral structure and pronounced electron delocalisation, in contrast to (31) which has a flattened tetrahedral structure and negligible electron delocalisation. These differences in (41) with respect to (31) are reflected in their variation of reactivity towards olefins[100].

Although phosphinyl radical addition to olefins is known, detection of the resulting carbon-centred radicals seems only to have been studied by laser flash photolysis techniques. Aminoxyl trapping of the carbon-centred radicals formed following phosphinyl addition to olefins, has apparently not been carried out before.

While laser flash photolysis techniques rely upon the assignment of absorption bands to the appropriate radical, and provide little information about the stereochemistry of addition, the 'radical trapping' technique has the demonstrated ability[47] to provide a large amount of information regarding stereochemistry of oxy radical additions and therefore the

potential to provide similar information for phosphinyl radical addition to olefins.

The importance of stereochemistry should not be underestimated. By understanding the nature of radical additions to olefinic and acetylenic groups and the factors that influence the stereo- and regioselectivity of addition, the polymer chemist can more easily control the properties of the synthetic macromolecule produced. Moreover, polymer end groups can greatly influence the properties and stability of polymers. A phosphinoyl end group may also provide a novel way to attach the polymer chain to another polymer chain or surface aldehyde or ketone function via the Horner-Wadsworth-Emmons modification of the Wittig reaction[128].

The usefulness of phosphinyl radicals as initiators of free radical polymerisation reactions is increasingly being appreciated[129,130,131]. Too, in organic synthesis, phosphorus radical chemistry has become increasingly accepted as a useful technique, being applied to such areas as heterocyclic synthesis[132]. Hence knowledge of the regioselectivity and stereochemistry of phosphorus radical additions to olefins and acetylene is tremendously valuable.

We have therefore used the 'radical trapping' technique to investigate the reactions of the diphenylphosphinyl(31) and dimethoxyphosphinyl(41) radicals with various olefins and with phenyl acetylene. The phosphorus radicals were produced by thermolysis of a mixture of di-t-butyl-peroxyoxalate(DTBP) and either the phosphine oxide or phosphine, as it is known that t-butoxyl radicals produce phosphinyl radicals by hydrogen-abstraction. The olefins studied in this chapter were acrylonitrile(A), vinyl acetate(V), cyclopentene(43), cyclohexene(44), 3,4-dihydro-2H-pyran(45) and 4-t-butylcyanocyclohexene(46).

Figure 10

(A) (V) (43)

(44) (45) (46)
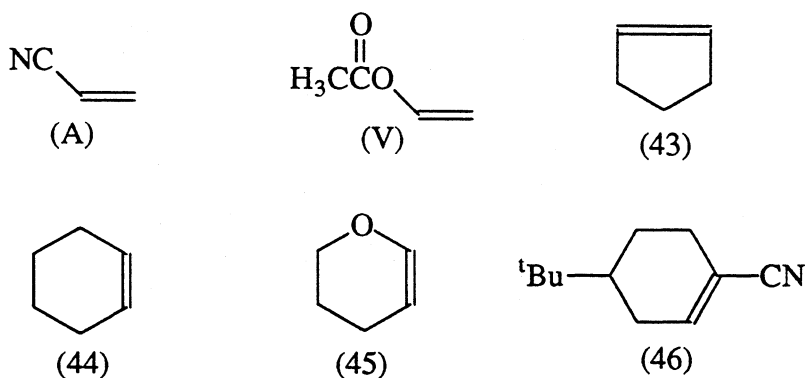
RESULTS AND DISCUSSION

4.1 Acyclic Olefins

4.1.0 The reaction of Diphenylphosphine oxide and t-butoxyl radicals with Acrylonitrile in the presence of (10)

As with previous experiments, t-butoxyl radicals were generated by thermolysis of DTBP[23]. The trapping experiment was carried out by heating DTBP(0.235M) and diphenylphosphine oxide(0.524M) with an excess of (10)(0.597M) in neat acrylonitrile for 68 minutes at $60^{o}C$.

The reaction products were separated and quantified by HPLC(reverse-phase) and characterised by ^{1}H, ^{13}C and ^{31}P nmr. The structures, relative yields(ratios) and reaction pathway for the formation of products are given in figure 11 and scheme 19.

<u>Figure 11</u> Products formed in the reaction of Acrylonitrile with t-butoxyl radicals and Diphenylphosphine oxide in the presence of (10)

$$\begin{array}{ccc}
\text{(42)} & \text{(32)} & \text{(27)} \\
\text{(0.81)} & \text{(1.00)} & \text{(0.20)}
\end{array}$$
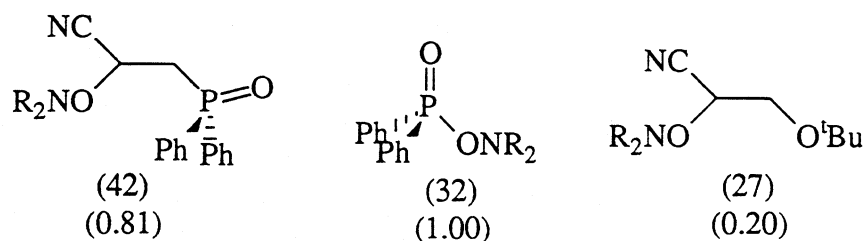
As expected, with a low relative concentration of (10)(2.4 equivalents) with respect to diphenylphosphine oxide (2.2 equivalents) and DTBP(1.0 equivalent) and an excess of acrylonitrile (reaction I), trapping of the diphenylphosphinyl radical(31) by (10) is competitive with addition of (31) to acrylonitrile. The fact that the phosphorus-trapped product (32) is still the major product, shows that the trapping of phosphorus-centred radicals by the aminoxyl (10) is very fast.

Scheme 19 Reaction of Acrylonitrile with t-butoxyl radicals and
Diphenylphosphine oxide in the presence of (10)
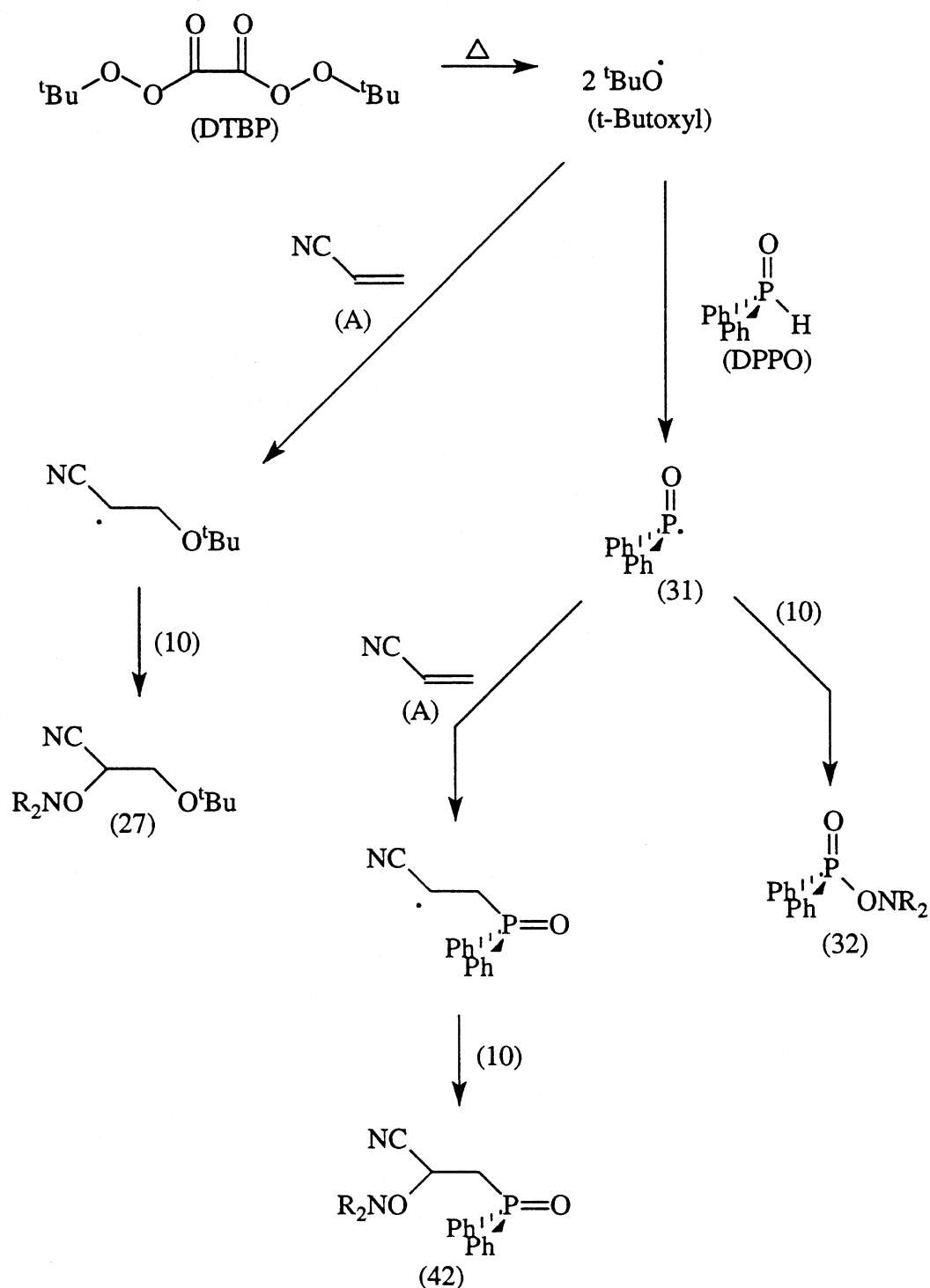
Under these conditions, addition of (31) to acrylonitrile is four times
more favourable than t-butoxyl addition to acrylonitrile, ((42)(0.81):(27)
(0.20)). The t-butoxyl radical is known to be electrophilic[81] in character.

From this result we deduce that (31) is more nucleophilic than the t-butoxyl radical.

An analytical scale reaction with the following concentrations: (10)(0.03M, 2.2 equivalents), DTBP(0.014M, 1.0 equivalent) and diphenylphosphine oxide(0.03M, 2.2 equivalents) in neat acrylonitrile (reaction II), resulted in the following ratio of reaction products: (42)(5.55):(32)(1.00):(27)(6.11). As expected, lowering the concentration of aminoxyl(10) led to an increase in addition of the diphenylphosphinyl radical to acrylonitrile and a decrease in the relative amount of (32). The relative amount of (27) increased as a result of the lower concentration of diphenylphosphine oxide. Examining this concentration affect further, another analytical reaction was carried out where 10 equivalents of (10)(0.05M) were combined along with diphenylphosphine oxide(0.01M, 2.0 equivalents) and DTBP(0.005M, 1.0 equivalent) in neat acrylonitrile(reaction III). The above reactant concentrations and product ratios are summarised in table 7b. Under these last conditions, the ratio of (32):(42) (phosphorus-trapping:phosphorus addition) has decreased with the use of an increased number of equivalents of (10), also, now diphenylphosphinyl addition to acrylonitrile occurs twice as often as t-butoxyl addition to acrylonitrile(reaction III).

Table 7b demonstrates, that under these conditions, the relative concentration of (10) is all-important in determining the ratio of (42):(32) and therefore, (42):(27).

It is also interesting to note that only tail addition of (31) to acrylonitrile was seen under these reaction conditions, this being analogous to t-butoxyl addition to acrylonitrile[80,82].

As the number of equivalents of (10) is increased with respect to diphenylphosphine oxide and DTBP, the trapping of (31) with respect to addition to acrylonitrile increases (c.f reaction II with III-table 7b).

<u>Table 7b</u> Reactant concentrations influence on product ratios in
neat Acrylonitrile

Reaction	(10) (DPPO) (DTBP) M(moles.l^{-1})/equivalents			(42)	(32) (ratio)	(27)
I	0.597 (2.4)	0.524 (2.2)	0.235 (1.0)	0.81	1.00	0.20
II	0.030 (2.2)	0.030 (2.2)	0.014 (1.0)	5.55	1.00	6.11
III	0.050 (10.0)	0.010 (2.0)	0.005 (1.0)	1.47	1.00	0.75

DPPO-Diphenylphosphine oxide.

4.1.1 The Reaction of Vinyl acetate with Diphenylphosphine oxide and t-butoxyl radicals in the presence of (10)

t-Butoxyl radicals were again generated by thermolysis of DTBP[23]. The trapping experiment was also carried out by heating DTBP(0.168M, 1.0 equivalent) and diphenylphosphine oxide(0.335M, 2.0 equivalents) with an excess of (10)(0.351M, 2.1 equivalents) in neat vinyl acetate for 68 minutes at 60°C.

The reaction products were separated and quantified by HPLC (reverse-phase), and characterised by ^{1}H, ^{13}C and ^{31}P nmr. For ease of comparision to reaction III(section 4.1.0), relative yields(ratios) are given for the following analytical reaction: DTBP(0.005M, 1.0 equivalent), diphenylphosphine oxide(0.01M, 2.0 equivalents) with an excess of (10)(0.05M, 10.0 equivalents)in neat vinyl acetate (reaction IV). Structures and relative yields(ratios) for reaction IV are given in figure 12. Reaction pathways for the formation of products are given in scheme 20.

Addition of the electrophilic t-butoxyl radical[81] to vinyl acetate (to form (24) and (25)) accounts for 45% of the reaction products detected under these reaction conditions (the corresponding figure for acrylonitrile was 10%). This is to be expected when consideration is given to the polarisation of

the two monomers-vinyl acetate is an electron donor(ED), whereas acrylonitrile is an electron acceptor(EA).

Figure 12 Products formed in the reaction of Vinyl acetate with Diphenylphosphine oxide and t-butoxyl radicals in the presence of (10)

(43)
(0.32)

(32)
(1.00)

(24)
(0.14)

(25)
(0.96)
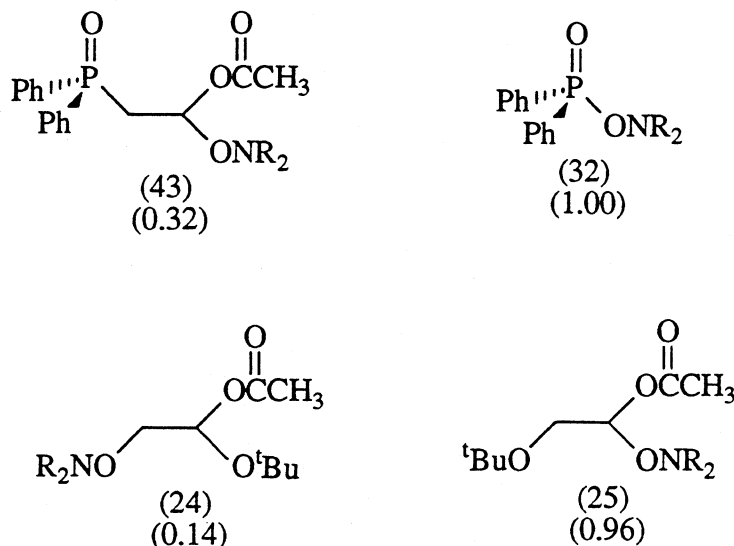
However 12.7% of this addition by t-butoxyl is to the 'head' of vinyl acetate, an unusual result, that has been observed previously[80]. There are in fact very few reports of head addition by t-butoxyl to olefins to be found in the literature, one example though is the case of vinylidene fluoride, where head addition occurs to the exclusion of addition to the unsubstituted end of the monomer[133].

In contrast to the t-butoxyl radical, (31) adds exclusively to the tail of vinyl acetate (and acrylonitrile-4.1.0), under these reaction conditions. A reason for why t-butoxyl gives some head addition, but (31) does not, is not readily obvious. Possibly though the addition of t-butoxyl involves an earlier transition state, so that stabilisation of the developing radical centre is less important. It is expected that steric effects would be of little importance, therefore suggesting that polar factors would likely be of importance.

Reaction IV with vinyl acetate had the same reactant concentrations as rection III for acrylonitrile(4.1.0), and while a direct comparison cannot be made here because of solvent effects, the ratio of products (42):(32) and (43):(32) is interesting to examine. The ratios are (1.47):(1.00) and

Scheme 20 Reaction of Vinyl acetate with t-butoxyl radicals and Diphenylphosphine oxide in the presence of (10)
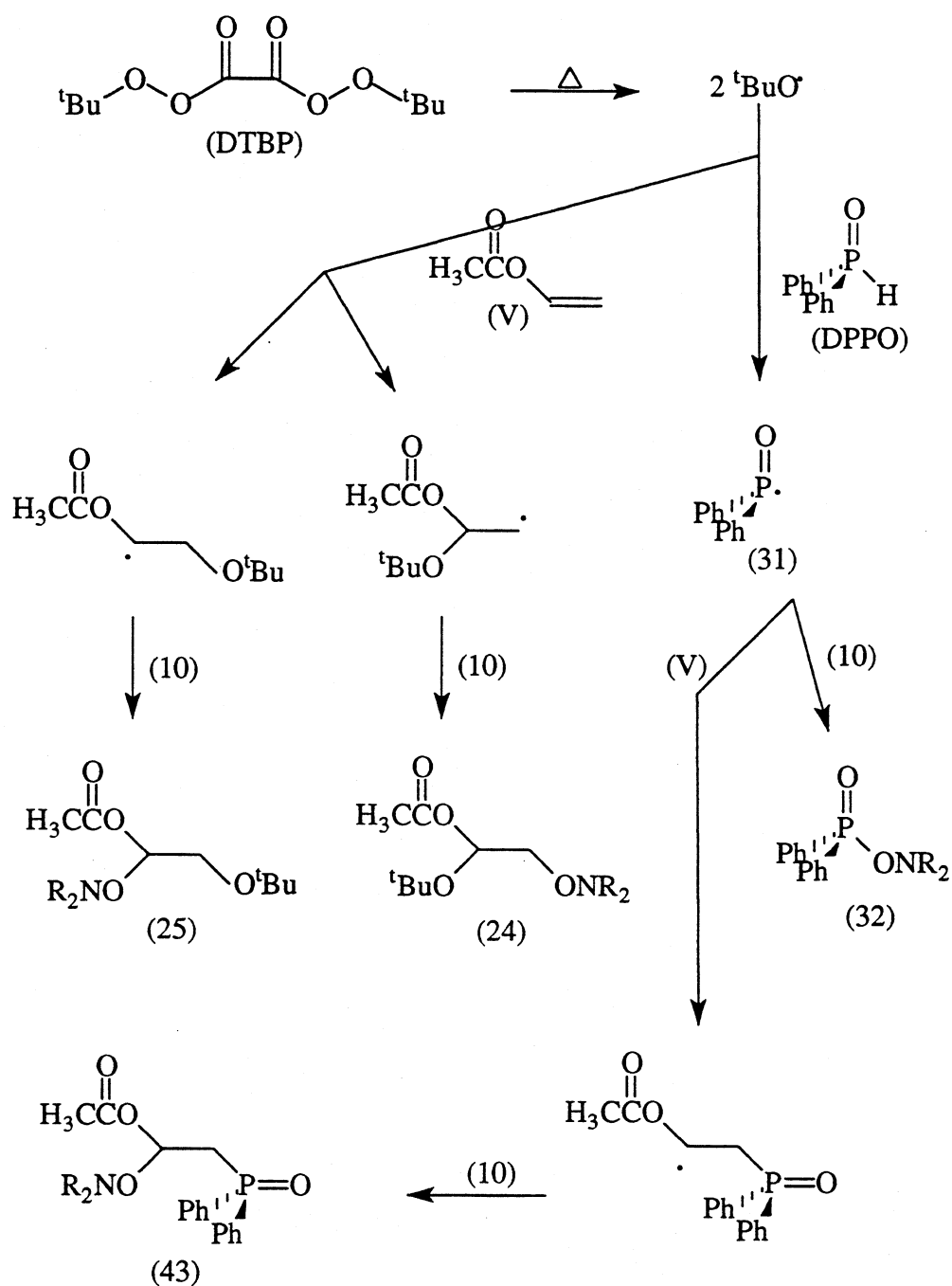
(0.32):(1.00) respectively; and these indicate that there is a strong preference for (31) to add to acrylonitrile over vinyl acetate. The rate constant for addition of (31) to acrylonitrile is indicated as being approximately 4.5 times greater than for addition to vinyl acetate. A competitive addition reaction combining both vinyl acetate and acrylonitrile together was carried out

(section 4.1.2) to provide a more accurate result for the relative rate of addition by (31) to acrylonitrile versus vinyl acetate.

t-Butoxyl addition to vinyl acetate(reaction IV) is 3.4 times greater than addition of (31) to vinyl acetate in contrast with the identical reaction (reaction III, 4.1.0) with acrylonitrile, where t-butoxyl addition to acrylonitrile was only 0.5 that of addition by (31) to acrylonitrile. Demonstrating again the more nucleophilic character of (31) with respect to the t-butoxyl radical.

4.1.2 The Reaction of Diphenylphosphine oxide and t-butoxyl radicals with Acrylonitrile(A) and Vinyl acetate(V) in the presence of (10)

Reaction mixtures of acrylonitrile and vinyl acetate with DTBP and diphenylphosphine oxide in the presence of (10) were studied over a range of concentrations. The reaction mixtures were all heated at 60°C for 68 minutes. The t-butoxyl radicals were produced by thermolysis of DTBP[23].

The products formed((24),(25),(27),(32),(42) and (43) see figure 13) were all previously produced in either of the respective separate reactions with acrylonitrile or vinyl acetate.

The yields(ratios) of the reaction products as a function of the concentrations of acrylonitrile, vinyl acetate, diphenylphosphine oxide, DTBP and (10) are given in table 8, and are listed in order of elution from the reverse-phase HPLC column.

In reaction V, where the concentration of vinyl acetate is double that of acrylonitrile, and 10 equivalents of (10) were used with respect to DTBP, no t-butoxyl addition to vinyl acetate and negligible addition to acrylonitrile were detected. Rather, the main products ((42), (43) and (32)) all arise from generation of (31). The majority(58%) of (31) formed escapes direct trapping by (10), and adds to either acrylonitrile or vinyl acetate to produce (42) and (43), respectively. Taking into account the number of moles of vinyl acetate with respect to acrylonitrile, (31) adds to acrylonitrile 12 times faster than to vinyl acetate (i.e. the bimolecular rate constant under these conditions, for

Table 8 Reactant concentrations and product ratios

Reaction	Reactants(mol.l^{-1})					Products(ratios)					
	[A]$^{\#}$	[V]$^{\#}$	DPPO $\times 10^{-3}$	DTBP $\times 10^{-3}$	(10) $\times 10^{-2}$	(42)	(43)	(32)	(27)	(24)	(25)
V	4.0	8.0	7.09	3.56	3.56	1.20	0.20	1.00	0.01	n.d	n.d
VI	1.9	9.5	14.9	7.48	1.64	0.96	0.52	1.00	0.55	0.16	1.50
VII	1.01	10.1	4.00	2.00	2.00	0.21	0.25	1.00	0.03	0.02	0.16

n.d. Not detected.

Figure 13 Products from the reaction of Acrylonitrile and Vinyl acetate with t-butoxyl radicals and Diphenylphosphine oxide in the presence of (10)
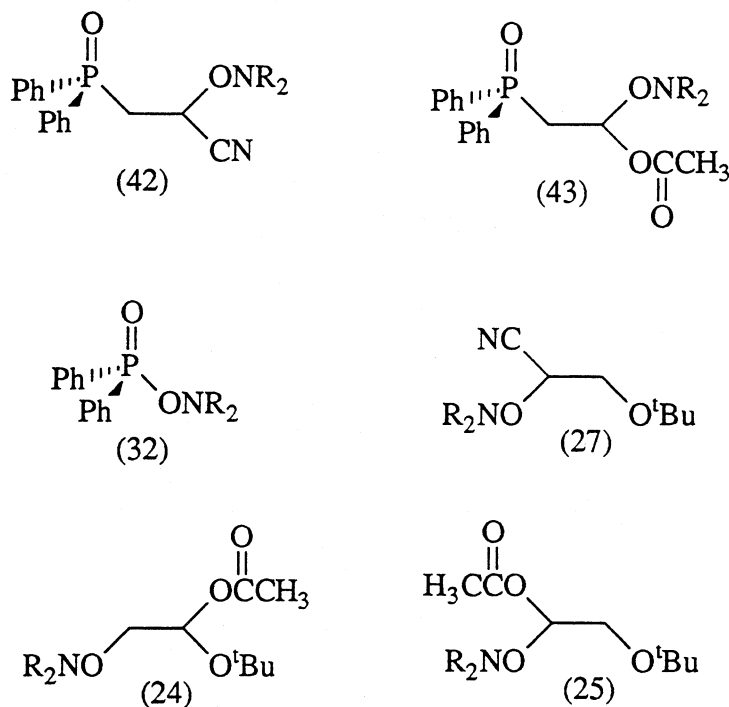
the reaction of (31) with acrylonitrile is 12 times greater than for vinyl acetate). This ratio of rate constants is very similar to the result obtained from laser flash photolysis studies by Schnabel et al.[100], who reported (table 7) bimolecular rate constants corresponding to a rate ratio of 12.5.

Reduction of reactant concentrations (diphenylphosphine oxide, DTBP and (10), reaction VII) and with a large excess of vinyl acetate (10 times the number of moles of vinyl acetate with respect to acrylonitrile), 31% of the (31) formed escapes direct trapping by (10). Adjusting for the molar concentrations of vinyl acetate and acrylonitrile, (31) adds 8.4 times faster to acrylonitrile than to vinyl acetate. This is a significant change from the figure of 12 obtained above (reaction V) and reflects the importance of solvent and cage affects on these reactions.

<u>Table 9</u> Reactant concentrations and product ratios for solvent affect study*

Reaction	Reactants(mol.l^{-1})					Products(ratios)					
	[A]#	[V]#	DPPO	DTBP	(10)	(42)	(43)	(32)	(27)	(24)	(25)
	x10^{-3}	x10^{-3}			x10^{-2}						
VIII	3.0#	-	4.26	2.14	2.10	1.10	-	1.00	0.22	-	-
IX	-	3.0#	3.93	1.97	1.94	-	0.22	1.00	-	n.d	0.22
X	0.27	2.73#	3.93	1.97	1.94	0.10	0.30	1.00	n.d	0.04	0.36

n.d. Not detected.
*. Reactions VIII-X include 4.0ml of cyclohexane(eg, reaction X contained 0.1ml acrylonitrile, 1.38ml vinyl acetate and 4.0ml cyclohexane).
#. Equivalent to 15mmol.

Once again, t-butoxyl addition to acrylonitrile and vinyl acetate in reaction VII, was relatively unimportant. The amount of tail addition of t-butoxyl radicals to vinyl acetate was approximately half that of addition of (31) to vinyl acetate.

In reaction VI, reactant concentrations (diphenylphosphine oxide and DTBP) were increased compared with reaction V, although the number of equivalents of (10) was decreased to 2.1 with respect to DTBP, and five times the number of moles of vinyl acetate as acrylonitrile were used. This resulted in an increase in the t-butoxyl addition products, namely (27), (24) and (25), relative to (31). This is reasonable as the concentration of t-butoxyl radicals in the system has increased while proportionally there is less (10) (i.e. reaction VI- (42)(0.96):(32)(1.00) c.f reaction VII (42)(0.21):(32)(1.00)). In

reaction VI, allowing for the difference in concentration between acrylonitrile and vinyl acetate, (31) adds 9.2 times faster to acrylonitrile than to vinyl acetate; this is consisitent with the values obtained in reactions V and VII, this figure being closer to the value of 8.4 where vinyl acetate is the dominant solvent.

In an examination of solvent effects, table 9 shows that very similar results were obtained for reactions VIII and X, i.e. acrylonitrile and cyclohexane and acrylonitrile, vinyl acetate and cyclohexane- (42):(32):(27)- reaction VIII (1.10):(1.00):(0.27); reaction X (allowing for the concentration of acrylonitrile being one tenth that of vinyl acetate) (1.00):(1.00):(n.d). It is likely that (27) may have been formed, but due to the low concentration of vinyl acetate, the amount was below the detection limits of the experiment. The result for vinyl acetate in reaction IX (table 9) is however not so consistent. The ratios of the products (43):(32):(24):(25) for reactions IX and X may be directly compared, and this comparison shows a variation, in the increased amounts of (31) and t-butoxyl addition to vinyl acetate in X (relative to (32)). Addition by (31) has increased by 26% and t-butoxyl addition by 45% over reaction IX. These variations may once again reflect solvent effects.

Beckwith et al.[25b] have shown that in polar solvents (eg., acrylonitrile) the aminoxyl radical trapping reaction of carbon-centred radicals is slowed compared to the same reaction in non-polar solvents, such as saturated hydrocarbons (eg., cyclohexane). The rate of trapping is slowed because a polar solvent will stabilize the substantial dipole moment aminoxyls are known to have. In the valence bond representation of the three-electron bond, the two canonical forms A and B make about equal contributions to

Scheme 21
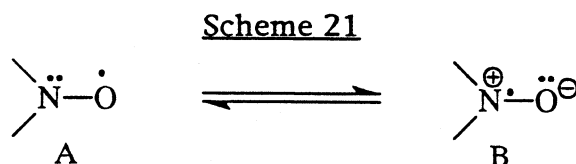
the overall electron distribution. Therefore a polar solvent will substantially stabilize the dipolar form B and form like a cage around the aminoxyl. Acrylonitrile is more polar (e value of 1.2) than vinyl acetate (e, -0.25), hence when appreciably more acrylonitrile is present we would expect to see

a slower aminoxyl radical trapping rate. This may be the reason for the increase of addition products (relative to (32)) observed in reaction X compared to reaction IX.

<u>Table 10</u> Comparison of reactions VII and X

Reaction	Reactants(mol.l^{-1})					Products(ratios)					
	[A]	[V]	DPPO $\times10^{-3}$	DTBP $\times10^{-2}$	(10)	(42)	(43)	(32)	(27)	(24)	(25)
VII	1.01	10.1	4.00	2.00	2.00	0.21	0.25	1.00	0.03	0.02	0.16
X[#]	0.27	2.73	3.93	1.97	1.97	0.10	0.30	1.00	n.d	0.04	0.36

#.Includes 4.0ml of cyclohexane.
DPPO. Diphenylphosphine oxide.

The only obvious conclusion that can be drawn from the comparison of reaction VII with X (table 10) is that the transition state for addition of (31) to acrylonitrile is more polar than the transition state for addition of (31) to vinyl acetate(the ratio of (43):(32) is about the same in VII and X, but the ratio of (42):(32) decreases in the non-polar solvent. The same is true for the addition of t-butoxyl to acrylonitrile and vinyl acetate (c.f ratio of (27):(25) for the two experiments).

4.1.3 The Reaction of Dimethyl phosphite and t-butoxyl radicals with Acrylonitrile in the presence of (10)

t-Butoxyl radicals were again generated by thermolysis of DTBP[23]. The trapping experiment was carried out by combining dimethyl phosphite(0.3ml) and acrylonitrile(0.3ml) in a round-bottomed flask at 60°C. This solution had previously been flushed with N_2, it was then sealed with a septum cap. To this mixture, a solution containing (10)(4.26mg), DTBP(2.5mg) and acrylonitrile(0.5ml) was added slowly (over 200 minutes) via a motor driven syringe. This solution had also been previously flushed with N_2. The combination of these two solutions produced the total concentrations for reactants given in table 11 (see section 4.1.5- reaction XI).

The reason for employing the syringe pump is that it enables the maintenance of low concentrations of both (10) and DTBP throughout the experiment, i.e the concentrations of both dimethyl phosphite and acrylonitrile are kept high. These conditions were expected to enhance the relative amount of dimethoxyphosphinyl addition to the alkenes under study.

The reaction products were identified and quantified by reverse-phase HPLC. These reaction products were all isolated and fully characterised (see section 4.1.5). The structures (given in order of elution from the HPLC column) and yields (ratios) of reaction products are given in figure 14, while the reaction pathway for the formation of these products is given in scheme 22.

Figure 14 Products formed in the reaction of Acrylonitrile with Dimethyl phosphite and t-butoxyl radicals in the presence of (10)
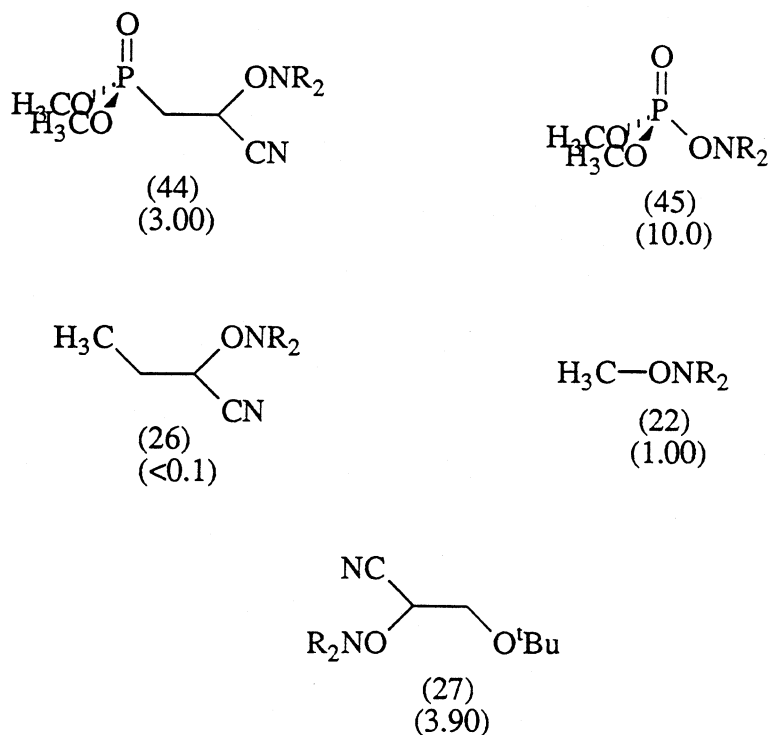
Scheme 22 Reaction of Acrylonitrile and Dimethyl phosphite with t-butoxyl radicals in the presence of (10)
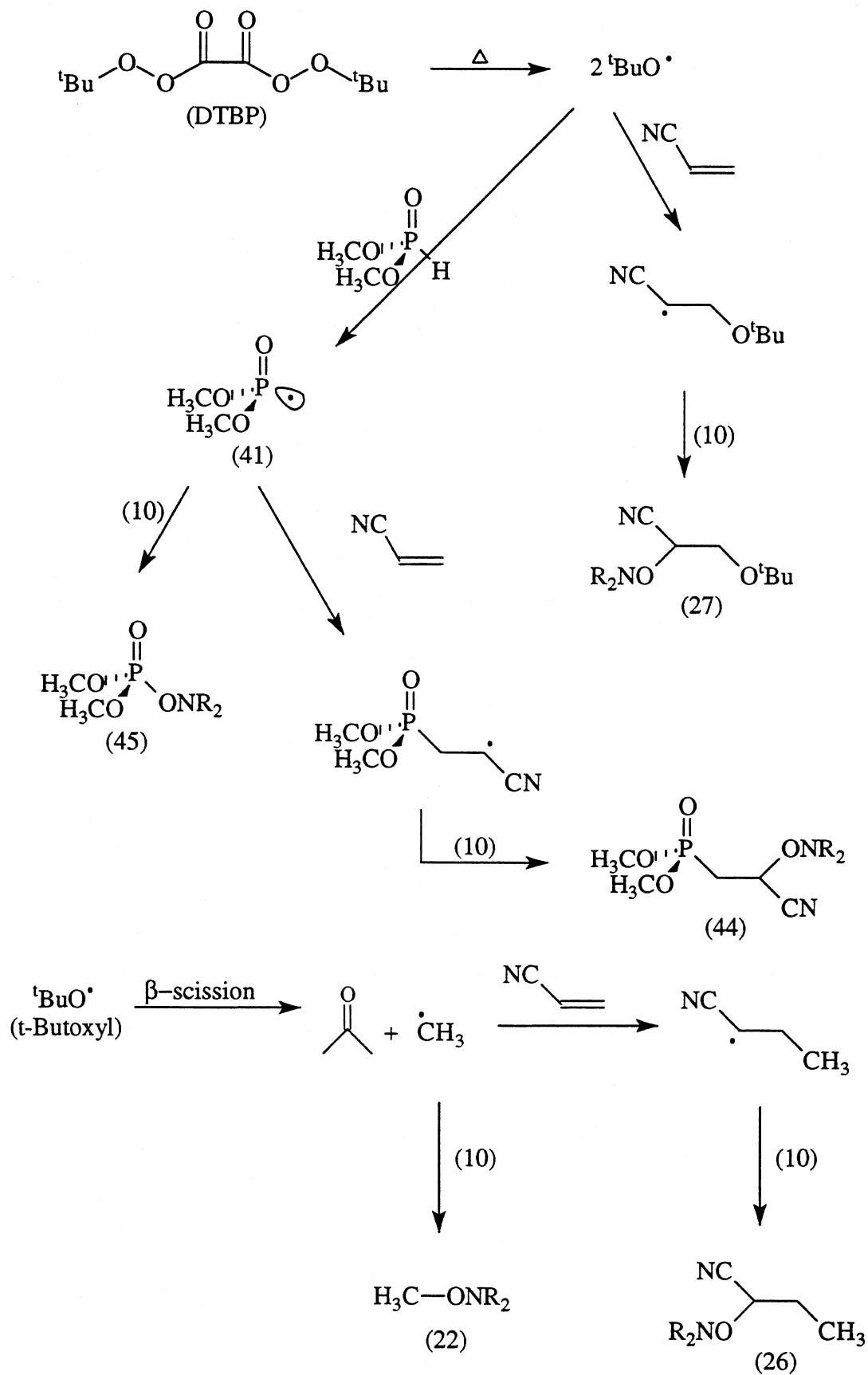
The formation of the methyl radical derived products (26) and (22) indicate that the addition of the dimethoxyphosphinyl radical (41) to acrylonitrile is appreciably slower than addition of (31) to acrylonitrile, where (22) was not detected. As previously mentioned, the amount of (22) formed serves as an internal free radical clock[83].

Under these conditions (i.e. very low concentration of (10)-reaction XI) 23% of (41) formed adds to acrylonitrile to produce (44), the remaining 77% is trapped by (10) to form (45).

Also, t-butoxyl radicals add to acrylonitrile faster than does (41), as shown by the ratio of (44):(27), (3.00):(3.90). Although this result is similar to that obtained in the analogous reaction (reaction II) with diphenylphosphinyl radicals (42):(27), (5.55):(6.11), it must be remembered that in the latter reaction, the concentration of (10) was very much higher. This means that dimethoxyphosphinyl radicals are considerably less reactive towards acrylonitrile than are diphenylphosphinyl radicals, consistent with the kinetic data of Schnabel (table 7)[100].

4.1.4 The reaction of Dimethyl phosphite and t-butoxyl radicals with Vinyl acetate in the presence of (10)

In a similar manner to 4.1.3, dimethyl phosphite($9.8\mu l$) and vinyl acetate(0.3ml) were combined in a round-bottomed flask at $60^\circ C$ and sealed with a septum cap following flushing with N_2. To this solution, was added(via a motor driven syringe) over 200 minutes, (10)(4.3mg), DTBP(2.5mg) dissolved in vinyl acetate(0.8ml). This solution had likewise been flushed with N_2. The combination of these two solutions produced the total concentrations of reactants given for reaction XII in table 11 (see section 4.1.5).

The reaction products were identified and quantified by reverse-phase HPLC (see 4.1.5 for characterisation). The structures (given in order of elution from the HPLC column) and yields(ratios) of the reaction products are given in Figure 15, with reaction pathway for product formation given in scheme 23.

Scheme 23 Reaction of Dimethyl phosphite and t-butoxyl radicals with Vinyl acetate in the presence of (10)
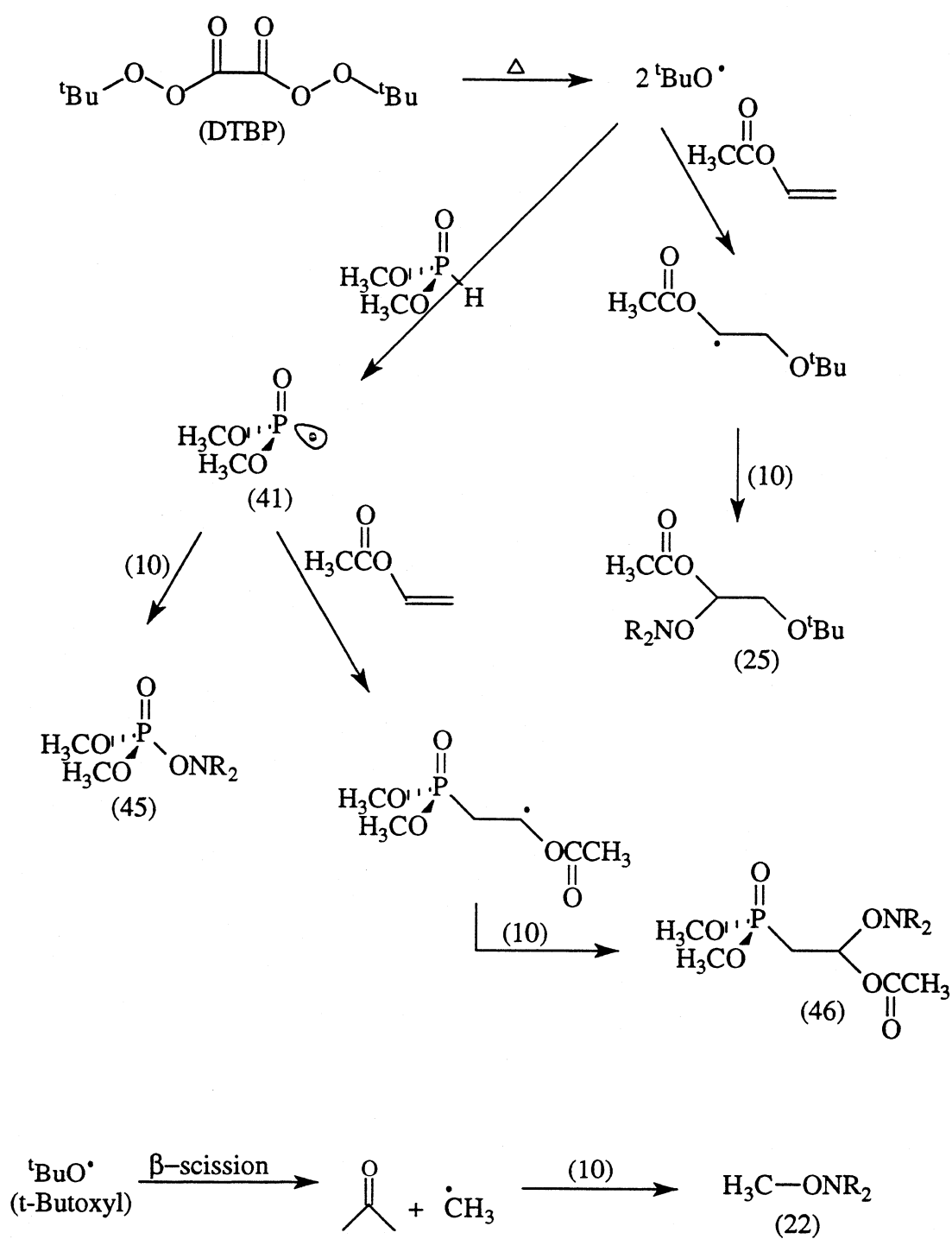
Figure 15 Products formed in the reaction of Dimethyl phosphite
and t-butoxyl radicals with Vinyl acetate in the presence of (10)
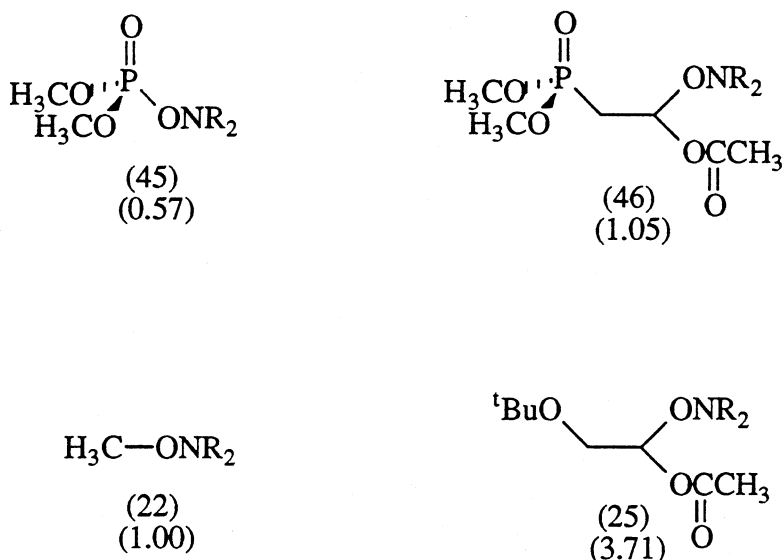
Even with the relatively low concentration of dimethyl phosphite in reaction XII (see 4.1.5, table 11), 64% of (41) formed adds to vinyl acetate to produce (46), with the remaining 36% is trapped by (10) to form (45).

The low concentration of dimethyl phosphite in reaction XII (compared to reaction XI (see 4.1.5, table 11)), results reasonably in much less of (41) being produced and therefore much less of (45) and (46) with respect to (22). With less dimethyl phosphite in the system, the t-butoxyl radical reacts preferentially with vinyl acetate or undergoes β-fragmentation to produce (25) and (22) respectively.

4.1.5 The reaction of Dimethyl phosphite and t-butoxyl radicals with Acrylonitrile and Vinyl acetate in the presence of (10).

In a similar manner to 4.1.3 and 4.1.4 the following reactants with the stated initial concentrations were combined; dimethyl phosphite(1.91M), acrylonitrile(4.0M), vinyl acetate(6.0M) and acetonitrile(0.6ml- as solvent), in a round-bottomed flask at 60°C, sealed with a septum cap, following flushing with N_2. To this solution was added via a motor driven syringe over 200 minutes the following solution, containing:(initial concentrations in brackets), (10)(1.68M), DTBP(0.8M), acrylonitrile(1.94M), vinyl

acetate(2.95M) and acetonitrile(solvent-0.6ml), this solution also having been previously flushed with N_2. This produced the total theoretical concentrations of reactants and monomers given in table 11 (reaction XIII).

The reaction products were isolated and quantified by reverse-phase HPLC and then characterised by ^1H, ^{13}C and ^{31}P nmr. Yields (ratios) of the reaction products as a function of the reactant concentrations are given in table V, products are in order of elution from the HPLC column. All reaction products formed in reaction XIII were previously formed in either of the respective separate reactions with acrylonitrile or vinyl acetate. Their structures are given in figures 14 and 15, reaction pathways for formation of these reaction products are given in schemes 22 and 23.

Table 11 Reactant concentrations and product ratios for the reactions of Acrylonitrile and Vinyl acetate with Dimethyl phosphite in the presence of (10)

Reaction	Reactants(mol.l^{-1})					Products(ratios)						
	[A]$^#$	[V]$^#$	DMP x10^{-3}	DTBP	(10) x10^{-2}	(44)	(45)	(46)	(26)	(22)	(27)	(25)
XI	11.1	-	2.97	9.71	2.04	3.00	10.0	-	0.10	1.00	3.90	-
XII	-	10.9	0.09	9.71	2.04	-	0.57	1.05	-	1.00	-	3.71 *
XIII	3.53	5.37	1.48	181	38.1	2.64	4.55	1.95	0.04	1.00	1.36	1.00
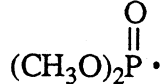
#.Total theoretical concentration of solutions combined(mol.l^{-1}).
DMP. Dimethyl phosphite.
*.Includes head addition product.

Of most interest is the relative rate of addition by (41) to acrylonitrile and vinyl acetate, to produce (44) and (46). This ratio of (44):(46) is (2.64):(1.95) (table 11, reaction XIII). When this ratio is adjusted however, for the amount of acrylonitrile with respect to vinyl acetate, the rate ratio becomes (4.01):(1.95), i.e the bimolecular rate constant for the reaction of (41) with acrylonitrile is 2.05 times larger than for reaction of (41) with vinyl acetate. This ratio of rate constants is in good agreement with the results reported by Schnabel et al.[100] (table 7), who report $k_{R^\bullet + A} = 5.8 \times 10^6$ l mol^{-1} s^{-1} for (41) with acrylonitrile and $k_{R^\bullet + V} = 2.9 \times 10^6$ l mol^{-1} s^{-1} for

(41) with vinyl acetate, i.e. a rate constant 2.0 times larger for the reaction of (41) with acrylonitrile than for (41) with vinyl acetate.

We have also examined the relative rates of formation of (31) and (41) produced by t-butoxyl radicals, relative to each other and to tetrahydrofuran(THF)(see table 12).

Table 12 Relative rates of formation of (31) and (41)*

	(THF)	$(CH_3O)_2\overset{O}{\overset{\|}{P}}$ • (41)	$Ph_2\overset{O}{\overset{\|}{P}}$ • (31)
Relative molar rate	1.00	0.29	0.85
Relative rate per hydrogen atom	1.00	1.14	3.4

*. Rates are determinded by the relative amounts of the respective radicals trapped by (10).

These figures come from a combined reaction of THF(1.33×10^{-1}M), diphenylphosphine oxide(6.63×10^{-2}M), dimethyl phosphite(6.63×10^{-2}M), (10)(4.63×10^{-2}M), DTBP(2.14×10^{-2}M) and acetonitrile(1.0ml-cosolvent), which was heated at 60°C for 68 minutes according to the standard trapping procedure (6.5.0). Figures given in table 12 are concentration and extinction coefficient adjusted, and are derived from HPLC quantified amounts of the respective aminoxyl trapped products, i.e (32),(45) and (47).

(47)
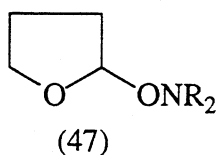
Table 12 indicates that under these reaction conditions, the hydrogen atom of diphenylphosphine oxide and the hydrogen atom of dimethyl phopsphite are abstracted 3.40 and 1.14 , respectively, times faster than an α-hydrogen atom on THF by t-butoxyl, i.e diphenylphosphine oxide undergoes

hydrogen abstraction by t-butoxyl radicals 2.98 times faster than dimethyl phosphite.

4.2 Cyclic Alkenes

4.2.1 Cyclopentene

4.2.1.0 The reaction of Diphenylphosphine oxide and t-butoxyl radicals with Cyclopentene in the presence of (10)

According to the standard radical trapping procedure, DTBP(0.022M), diphenylphosphine oxide(0.044M), (10)(0.047M) and cyclopentene(1.0ml) were combined and heated for 68 minutes at 60°C.

The reaction products were isolated and quantified by reverse-phase HPLC and characterised by ^{1}H and ^{13}C nmr. Structures and yields(percentages) are given in figure 16 (in order of elution from the HPLC column, left to right); reaction pathways for product formation are given in scheme 24.

Figure 16 Products formed in the reaction of Diphenylphosphine oxide and t-butoxyl radicals with Cyclopentene in the presence of (10)

Scheme 24 Reaction of Diphenylphosphine oxide and t-butoxyl radicals with Cyclopentene in the presence of (10)
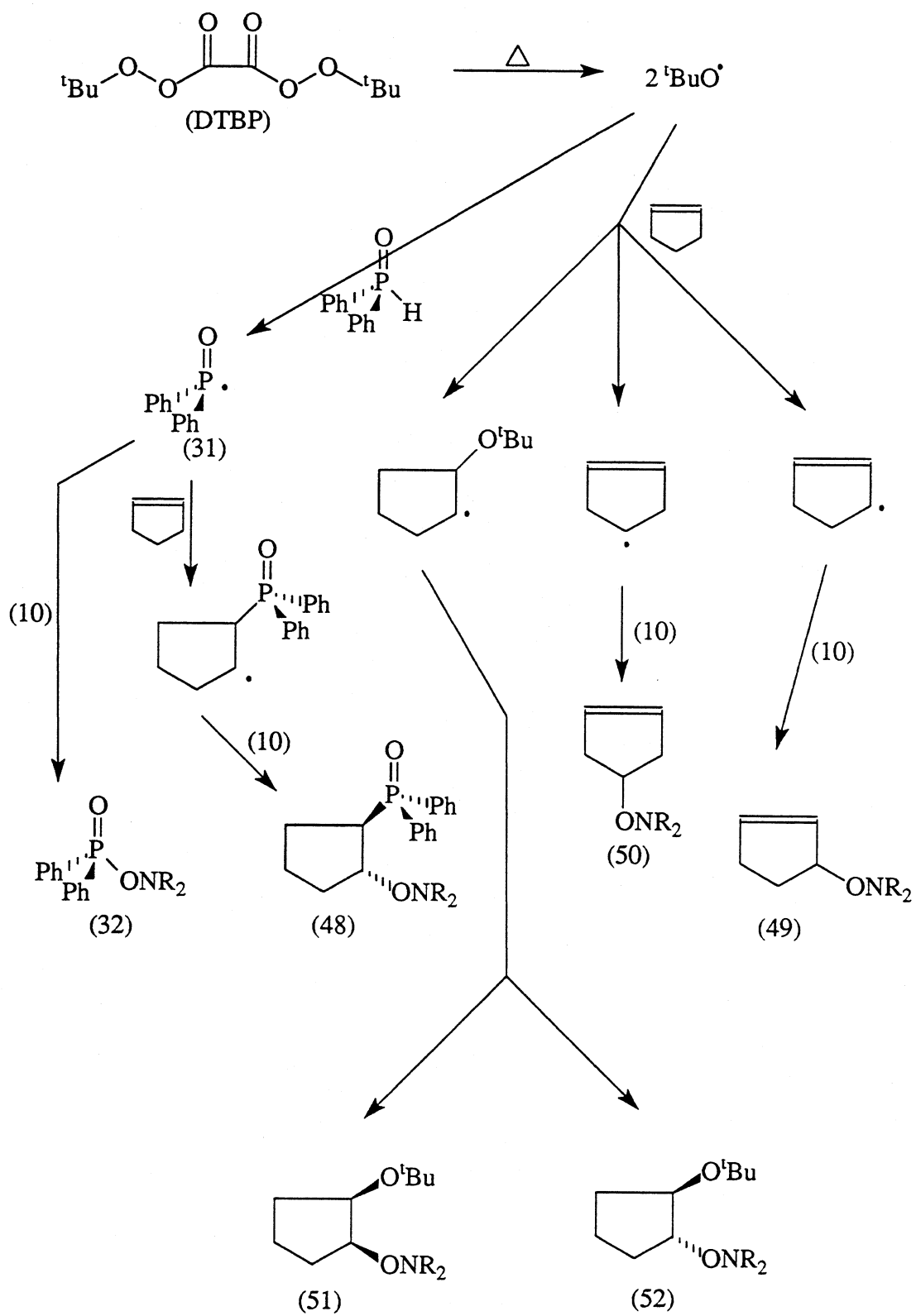
With cyclopentene in large excess and (10) in slight excess over diphenylphosphine oxide, hydrogen abstraction from cyclopentene (α and β to the double bond) account for the majority(78.4%) of the reaction products.
The rate of hydrogen abstraction from cyclopentene is approximately a factor of five times faster than for hydrogen abstraction from diphenylphosphine oxide to produce (31) (and therefore (32) and (48)); ((49)+(50)):((32)+(48)) = 78.4:14.8.

Addition by (31) to cyclopentene is markedly slower than addition by t-butoxyl to cyclopentene, where we see both cis and trans trapping by (10); (48):((51)+(52)), 1.5:7.2.

The ratio of abstraction products to addition by t-butoxyl obtained from this reaction is in reasonable agreement with results obtained by Thang[18c], where a ratio of (α):(β):(cis+trans) = (42.3):(1.00):(6.7) was found. From figure 16 the corresponding ratio is (38.2):(1.0):(3.6).

The stability of (32) was investigated by heating it with excess cyclopentene for two hours at 80°C. Analysis of this mixture after two hours by HPLC established that (48) was not being formed and therefore the regeneration of (31) and (10) according to scheme 25 followed by addition to cyclopentene was not taking place.

Scheme 25

4.2.1.1 The reaction of Dimethyl phosphite and t-butoxyl radicals with Cyclopentene in the presence of (10)

In an identical manner to 4.2.1.0 DTBP(0.036M), dimethyl phosphite(0.749M), (10)(0.079M) and cyclopentene(1.2ml), were combined and heated for 68 minutes at 60°C.

The products were identified and quantified by HPLC. Isolation and characterisation was not carried out, as all products formed had been fully characterised previously. Structures and yields(percentages) though are given in figure 17 (in order of elution from the HPLC column- left to right), reaction pathway for formation of (45) is given in scheme 23 and for products (49)-(52) in scheme 24. No products of phosphorus radical addition to cyclopentene were observed.

Even with 10 equivalents of dimethyl phosphite (a relatively high concentration) and 2.1 equivalents of (10) (a relatively low concentration) with respect to t-butoxyl radicals, there is no addition by (41) to cyclopentene detected. It would be expected that this addition product would only be present in very small amounts as even with (31), the amount of addition product was very low(1.5%) and we have previously shown that the rate of formation of (41) is slower than (31). Moreover, (41) is less reactive towards alkenes than is (31) (see section 4.1). The amount of (41) formed (c.f (45)) in this reaction is low, compared to the formation of (31) in the analogous reaction with diphenylphosphine oxide(section 4.2.1.0). Table 12 suggested formation of (31) to be approximately 3 times faster than formation of (41), in acetonitrile solution, whereas the present results suggest that approximately 10 times more (31) is produced in 4.2.1.0 than the corresponding amount of (41) produced in 4.2.1.1 (based on (49) as an internal standard). It appears that once again, solvent effects are important, and apparently the differential reactivity between diphenylphosphine oxide and dimethyl phosphite towards hydrogen abstraction is much greater in non-polar solvents. Clearly this effect requires further investigation.

The ratio of abstraction products to addition products in the reaction of t-butoxyl radicals with the cyclopentene is in good agreement with the result from the analogous diphenylphosphine oxide reaction (4.2.1.0), namely

Figure 17 Products formed in the reaction of Dimethyl phosphite and t-butoxyl radicals with Cyclopentene in the presence of (10)
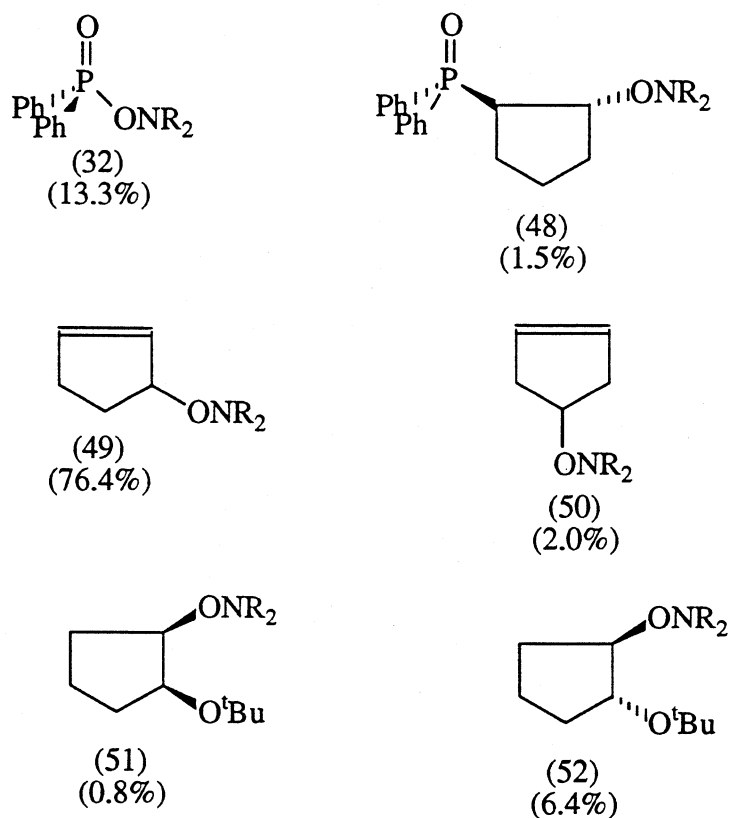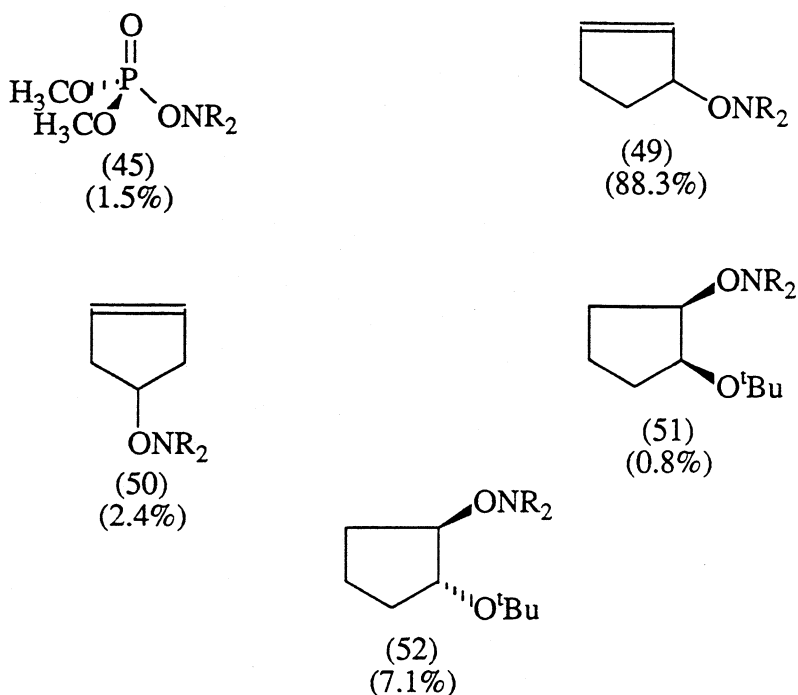

(49):(50):((51)+(52))=36.8:1.0:3.3.

4.2.2 Cyclohexene

4.2.2.0 The Reaction of Diphenylphosphine oxide and t-butoxyl radicals with Cyclohexene in the presence of (10)

A solution of DTBP(0.022M), diphenylphosphine oxide(0.044M), (10)(0.047M) and cyclohexene(10.0ml), was heated at $60^{\circ}C$ for 68 minutes according to the standard radical trapping procedure(see 6.5.0).

Isolation of the reaction components by reverse-phase HPLC produced five products, which were identified by ^1H and ^{13}C nmr. The structures and quantities isolated (as percentages) are given in figure 18 (from left to right in order of elution from the HPLC column); the reaction pathways for product formation are given in scheme 26.

Figure 18 Products formed in the reaction of Diphenylphosphine oxide and t-butoxyl radicals with Cyclohexene in the presence of (10)

$$\begin{array}{c}\text{O}\\ \|\\ \text{P}\\ \text{Ph}\diagdown\diagup\diagdown\text{ONR}_2\\ \text{Ph}\end{array}$$

(32)
(18.4%)

(53)
(76.5%)

(54)
(3.7%)

(55)
(0.3%)

(56)
(0.9%)
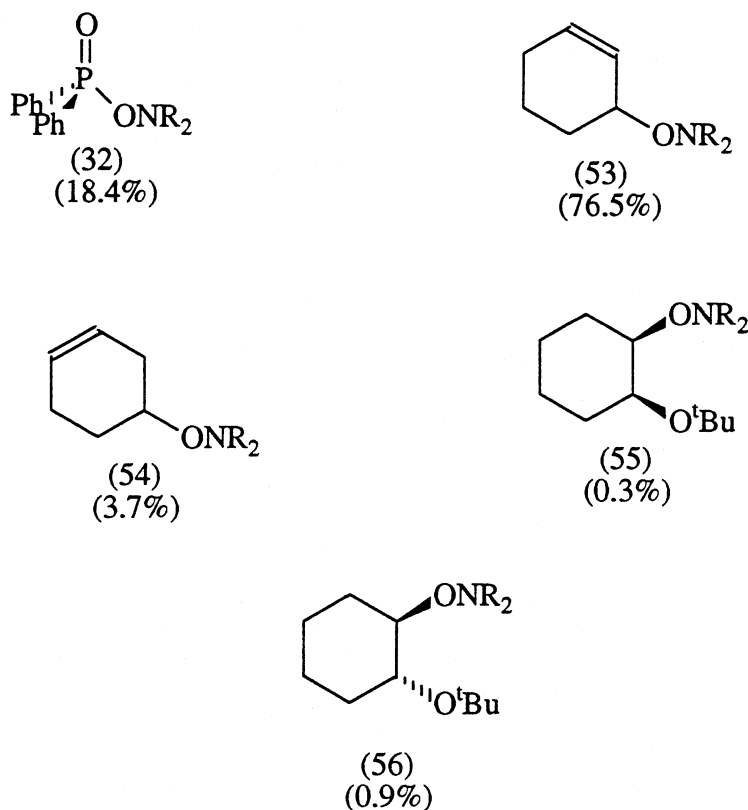
No addition of (31) to cyclohexene was detected under these reaction conditions, although (32) makes up 18.4% of the reaction product, in comparison to cyclopentene where (32) makes up 13.3% of the reaction product. Repeating this experiment (with 20 equivalents of diphenylphosphine oxide) made very little differnece to the percentage of (32) in the total reaction product, and still no products of addition (of(31)) to cyclohexene were detected.

Comparing the two equivalents (of diphenylphosphine oxide) reaction with the analogous cyclopentene reaction(4.2.1.0) where addition of (31) to cyclopentene was detected, the results indicate a reduced double bond reactivity in cyclohexene compared to cyclopentene towards (31). A similar result to this is reported for t-butoxyl radicals by Shelton et al.[135] (t-butoxyl generated from di-t-butyl peroxide), Walling et al.[136] (generated from t-butyl hypochlorite) and Busfield et al.[18c] (generated from DTBP) and is also supported by this work (abstraction:addition by t-butoxyl), cyclopentene

Scheme 26 Reaction of Diphenylphosphine oxide and t-butoxyl
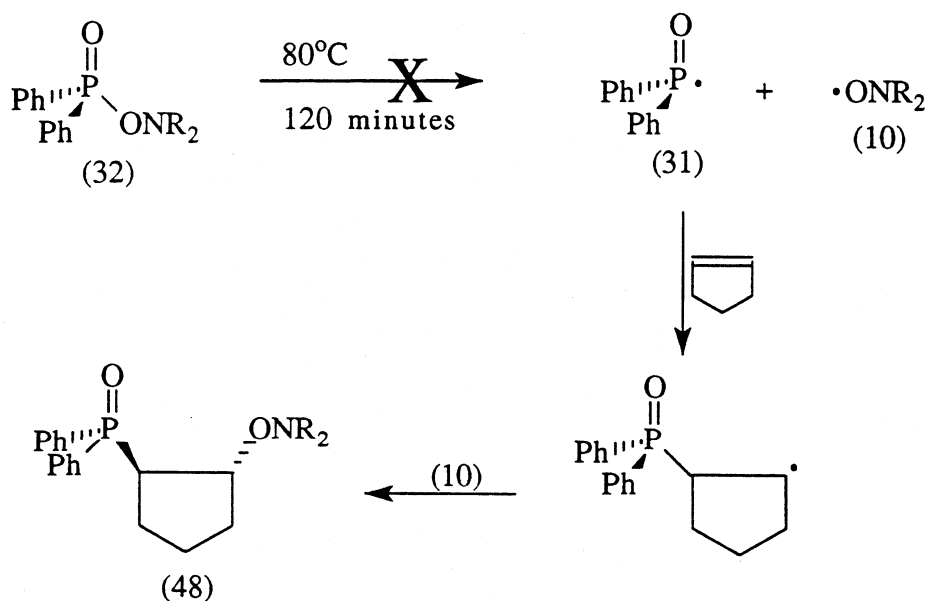radicals with Cyclohexene in the presence of (10)
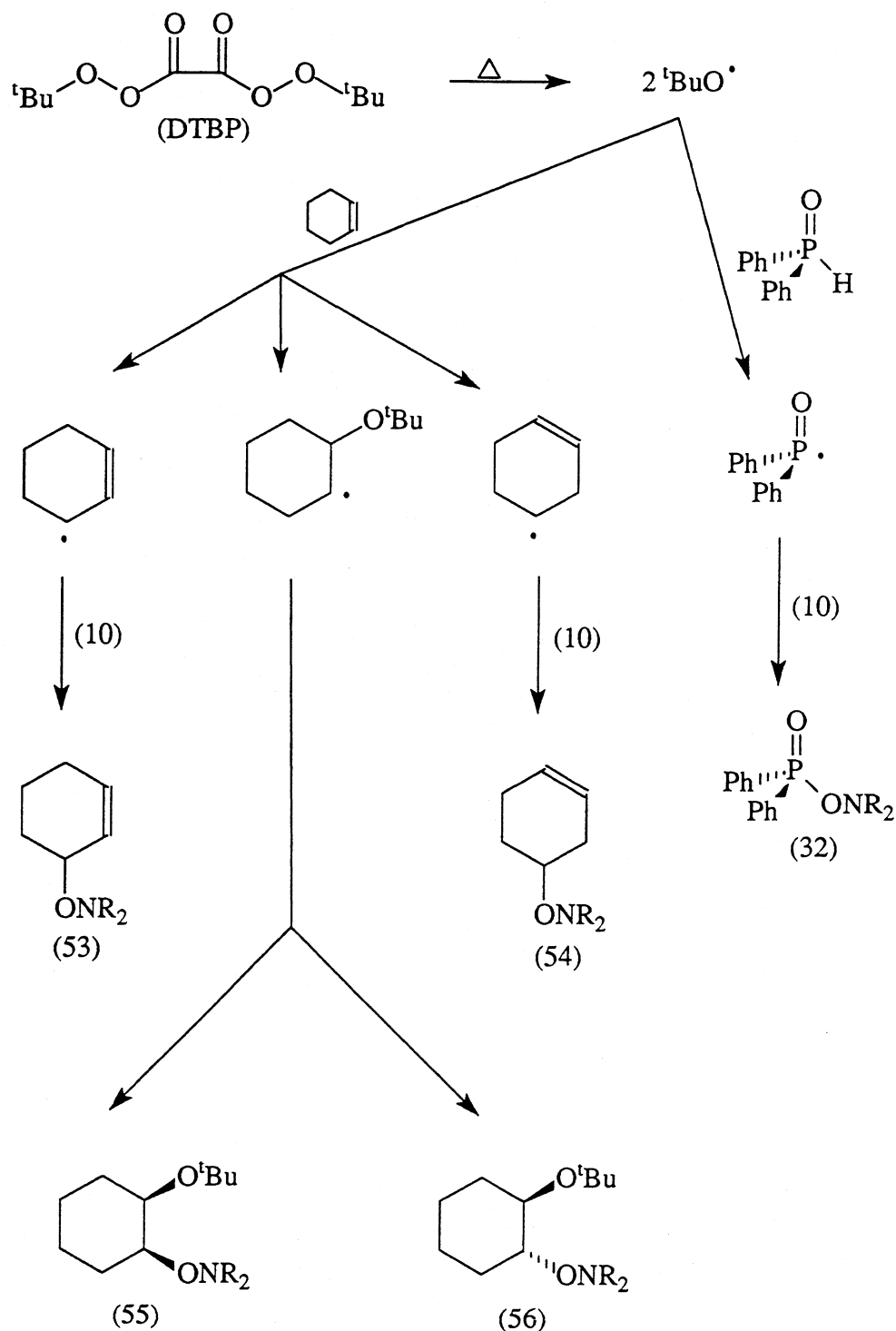
(10.9:1.0) c.f cyclohexene (66.8:1.0). This difference in propensity for
addition by t-butoxyl may not necessarily be due to an enhanced rate of
addition in cyclopentene, but may be due to a decreased rate of abstraction at
the allylic position in cyclopentene. Allylic abstraction from cyclopentene to

give a resonance stabilized radical would result in three of the five carbons being sp^2-hybridised, thus resulting in an increase in ring(angle) strain.

In both cyclopentene and cyclohexene the higher proportion of trans adducts to cis is likely accounted for by steric effects[18c,72](8:1 and 3:1, trans:cis adducts), respectively.

It is suggested however, that the reason for seeing addition of (31) to cyclopentene and not to cyclohexene is most likely due to steric effects. Cyclopentene is closer to planarity[135] than the semi-chair conformation of cyclohexene, hence approach by (31) would be somewhat easier than pseudo-axial approach to the double-bond of cyclohexene which would suffer pseudo 1,3-diaxial repulsions.

Methyl trap(22), an indicator of the life time of t-butoxyl radicals in the system[83] was not detected in this reaction, nor in the analogous cyclopentene reaction(4.2.1.0). This supports fast allylic hydrogen abstraction by t-butoxyl radicals in both cyclohexene and cyclopentene, as observed.

4.2.2.1 The reaction of Dimethyl phosphite and t-butoxyl radicals with Cyclohexene in the presence of (10)

In a like manner to 4.2.2.0, DTBP(0.0103M), dimethyl phosphite(5.191M), (10)(0.023M) and cyclohexene(1.1ml) were combined and heated for 68 minutes at 60°C.

The reaction products were identified and quantified by HPLC. All products isolated had previously been characterised. Structures and yields (percentages) are given in figure 19 (left to right in order of elution from the HPLC column); reaction pathways for formation of (45) and for products (53)-(56) are given in schemes 23 and 26 respectively.

From the results of the reaction of cyclopentene with dimethyl phosphite it seemed necessary to use a very high concentration of dimethyl phosphite in order to observe addition of (41) to cyclohexene. Using 260 equivalents of dimethyl phosphite and 2.1 equivalents of (10) with respect to t-butoxyl, still no addition to cyclohexene was observed.

Figure 19 Products formed in the reaction of Dimethyl phosphite and t-butoxyl radicals with Cyclohexene in the presence of (10)
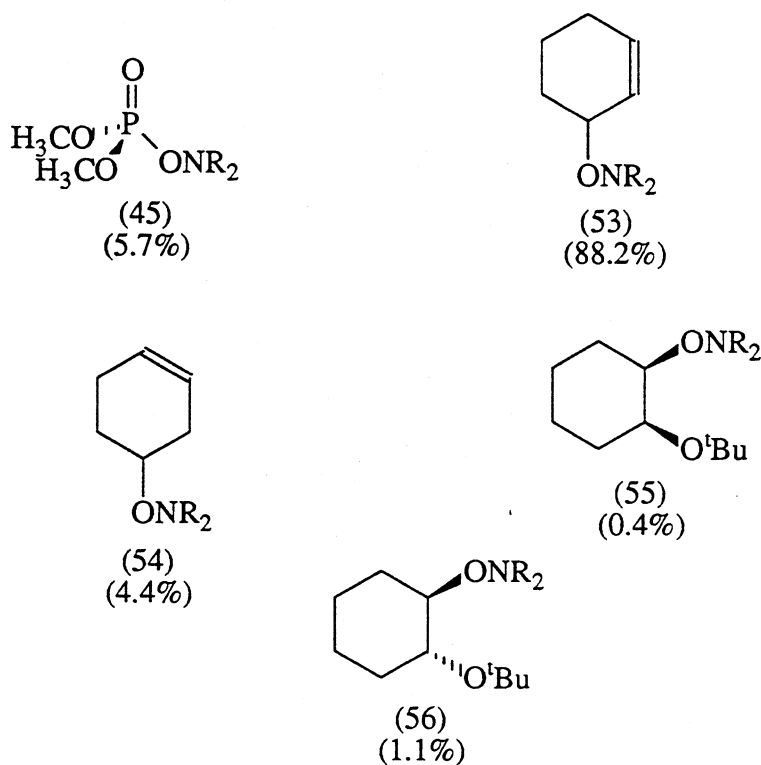
4.2.3 3,4-Dihydro-2H-pyran

4.2.3.0 The reaction of Diphenylphosphine oxide and t-butoxyl radicals with 3,4-Dihydro-2H-pyran in the presence of (10)

In a similar manner to 4.3.2.0 DTBP(0.022M), diphenylphosphine oxide (0.044M), (10)(0.047M) and 3,4-dihydro-2H-pyran(10.0ml) were combined and heated at 60°C for 68 minutes.

Reverse-phase HPLC isolation afforded seven products, which were identified by ^{1}H and ^{13}C nmr. The structures and quantities isolated (as percentages) are given in figure 20 (left to right in order of elution from the HPLC column). Reaction pathways for product formation are shown in scheme 27.

Compared to the analogous cyclohexene reaction(4.2.2.0) the presence of the ethereal oxygen α to the double bond in 3,4-dihydro-2H-pyran increases, quite markedly the relative amount of addition by t-butoxyl (ratio abstraction to addition = 7.7:1.0 for 3,4-dihydro-2H-pyran and 67.0:1.0 for cyclohexene). This is almost certainly due to an enhanced rate of addition to 3,4-dihydro-2H-pyran rather than a reduced rate of hydrogen abstraction as ethereal oxygen generally enhances the rate of hydrogen abstraction[48,50].

Figure 20 Products from the reaction of Diphenylphosphine oxide and t-butoxyl radicals with 3,4-Dihydro-2H-pyran in the presence of (10)

(32)
(26.7%)

(57)
(0.5%)

(58)
(18.0%)

(59)
(0.3%)

(60)
(40.3%)

(61)
(5.8%)

(62)
(8.3%)
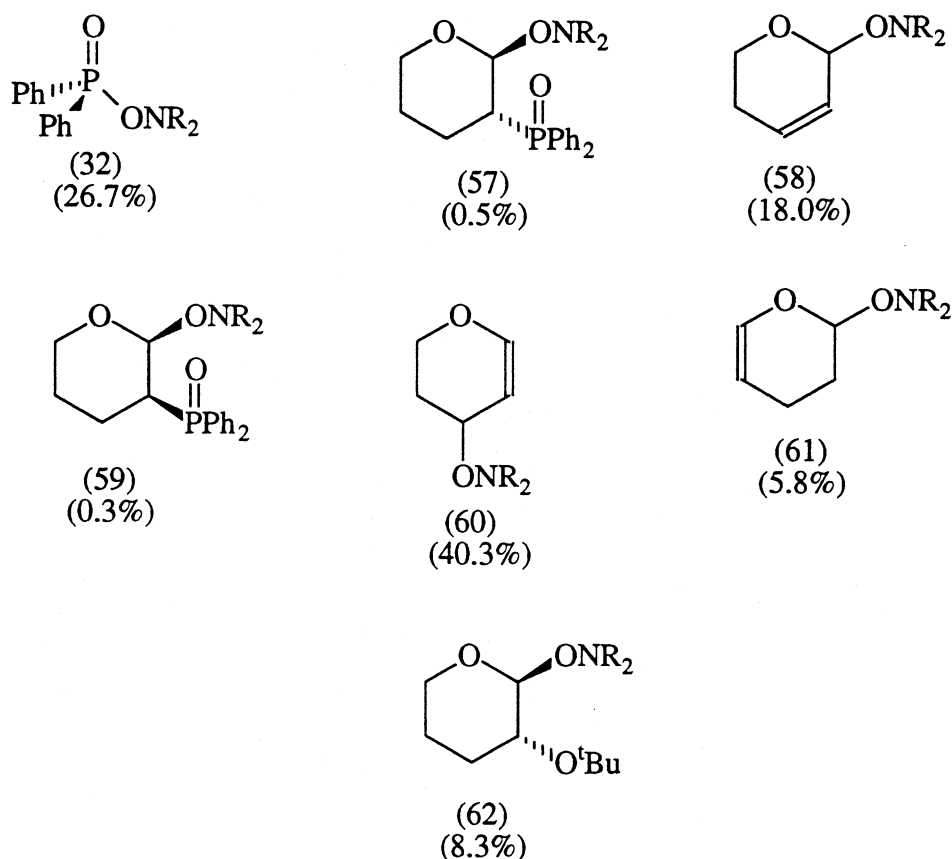
Interestingly, with the ethereal oxygen present in the ring (i.e 3,4-dihydro-2H-pyran, versus cyclohexene) we see addition by (31) to the double bond at both α and β positions (with respect to oxygen). The larger amount of β–addition is presumably due to stabilisation of the resulting radical by the α-oxygen[25]. The amounts α and β which result in products (57) and (59) are however

Scheme 27 Reaction of Diphenylphosphine oxide and t-butoxyl radicals with 3,4-Dihydro-2H-pyran in the presence of (10)
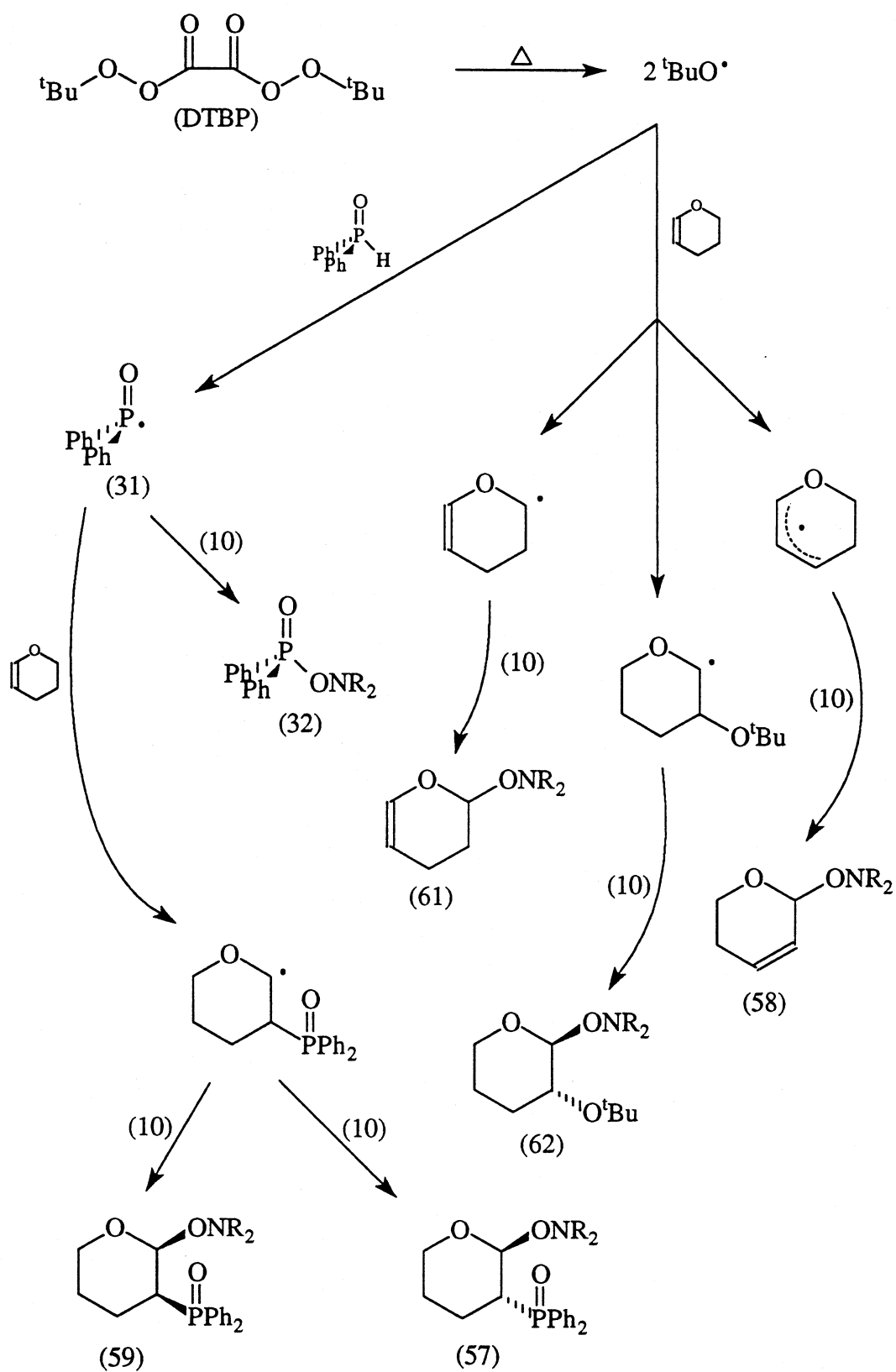
minor($\leq$0.05%). Because of insufficient quantities of these two minor products ((57) and (59)) microanalyses could not be obtained. High resolution mass spectrometry failed to give parent ions on (57) and (59), however low resolution mass spectra recorded for positive ion chemical ionisation produced MH$^+$ of 476 for both (see section 6.10.2.4).

Assignment of stereochemistry was possible by comparision of the data from a series of similar compounds (although not phosphorus bearing)[18c]. In the ^{1}H nmr spectrum of (57) the narrowest (non-aromatic) multiplet was the furthest downfield(5.23ppm, dd), consistent with it being an equatorial anomeric proton(equatorial-equatorial coupling of ^{3}J=3.6Hz). This shows the stereochemistry of (57) to be trans (phosphinoyl/aminoxyl). The proton on C2'(geminal to the diphenylphosphinoyl moiety)(2.69ppm) is further indicated as being equatorial by the peak width, which is also narrow, suggesting no axial-axial coupling. The proposed structure (57) is consisitent with the expected anomeric effect effect.

(57)
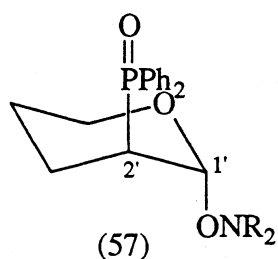
Product (59), of which there was appreciably less isolated than product (57), had a resonance of narrow band width at 4.82ppm. This resonance (doublet of doublets) had couplings of 2.2 and 2.3Hz, one due to a phosphorus-hydrogen coupling the other due to either an equatorial-equatorial, or equatorial-axial coupling with H$_b$. This shift and couplings suggest the structure vide infra for (59).

(59)
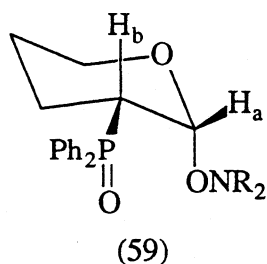
Little other information can be determinded from ring multiplets in the spectrum obtained due to a poor signal to noise ratio, a result of minimal sample quantity.

Characteristic aromatic resonances at 6.92 and 7.07ppm, each corresponding to 2H, along with peak integration for 12H in the 1-2ppm region indicate the presence of the aminoxyl. Additional aromatic resonances at 7.51, 7.68 and 7.86, corresponding to 6H, 2H and 2H, respectively are characteristic of the diphenylphosphinoyl moiety (see section 6.8.0). Hence, the structure of (59) is not definite, but is likely the structure given.

Addition of t-butoxyl to 3,4-dihydro-2H-pyran occurs exclusively at the position β to ethereal oxygen. This is to be expected as a radical sited α to ethereal oxygen is known to be stabilised by stereoelectronic interaction with the neighbouring lone-pair orbitals[50]. Additionally, radical formation at the position β to the ethereal oxygen is hindered by polar effects[137]. This result is identical to that for t-butoxyl addition to 3,4-dihydro-2H-pyran in the absence of diphenylphosphine oxide, where the ratio for the products (58):(60):(61):(62) is 3.3:6.8:1.0:1.7. From 4.2.3.0 with diphenylphosphine oxide present, we have the following ratio for the same products. 3.1:6.9:1.0:1.4.
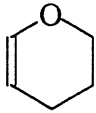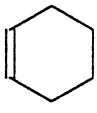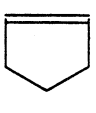
A competitive 'radical trapping' reaction (without diphenylphosphine oxide) between cyclopentene, cyclohexene and 3,4-dihydro-2H-pyran was carried out to provide relative abstraction/addition information for t-butoxyl radicals. The results are given in table 13. Thus, cyclopentene, cyclohexene and 3,4-dihydro-2H-pyran (in equimolar amounts, producing a total volume of 3.06ml) were combined with (10)(0.066M) and DTBP(0.029M). From table 13, it can be seen that the rate of allylic abstraction (per hydrogen) by t-butoxyl radicals is slightly decreased in the dihydropyran ring due to the presence of the ethereal oxygen (1.04:1.16 for 3,4-dihydro-2H-pyran versus cyclohexene, respectively).

Abstraction at non-allylic positions occurs to a small extent in the case of cyclopentene, cyclohexene and 3,4-dihydro-2H-pyran (c.f products (50), (54) and (61)). The most reactive non-allylic position is at C2 in 3,4-dihydro-2H-pyran (α to ethereal oxygen). This is no real surprise as radical formation is aided by favourable interaction between the orbitals of the radcial and the lone pairs on the adjacent oxygen[18c]. These effects are known in acyclic[48] and cyclic[50] ethers and are known to be subject to stereoelectronic control[49]. It has been previously observed that allylic hydrogens are much more easily abstracted by t-butoxyl radicals than those sited α to an oxygen atom under comparable conditions[138]. Even in the presence of (31) the

results here for 3,4-dihydro-2H-pyran bear out this observation; the allylic hydrogens are abstracted 10 times faster than those α to oxygen. The relative amounts of t-butoxyl addition to cyclopentene, cyclohexene and 3,4-dihydro-2H-pyran (table 13) show decreased addition to cyclohexene relative to cyclopentene and 3,4-dihydro-2H-pyran (although another product, likely the cis addition product, was formed but was unstable and therefore characterisation could not be carried out. The relative amount of total addition to the double bond then given in table 13 is likely a minimum value).

The addition of (31) to the same substrates showed a similar trend, in that addition was seen to cyclopentene and 3,4-dihydro-2H-pyran but not to cyclohexene (although reactant concentrations did vary slightly), for reasons suggested previously. Also, only the trans addition products formed from (31) were detected for cyclopentene and 3,4-dihydro-2H-pyran.

Table 13 Competitive abstraction/addition reaction by t-butoxyl radicals to Cyclopentene, Cyclohexene and 3,4-Dihydro-2H-pyran

Total allylic abstraction per hydrogen(ratio)	0.58 1.04	1.16 1.16	1.00 1.00
Total abstraction-non allylic per hydrogen(ratio)	0.024 8.00	0.006 1.00	0.003 1.00
Total addition to double bond (ratio)	>0.011# >1.00#	0.002 0.20	0.011 1.00

#. It is suggested that another unstable product isolated was the cis-addition product. Hence this would be a minimum value.

4.2.4 4-t-Butyl-1-1-cycanocyclohexene

4.2.4.0 The reaction of Diphenylphosphine oxide and t-butoxyl radicals with 4-t-Butyl-1-cyanocyclohexene in the presence of (10)

In a similar manner to 4.1.3, diphenylphosphine oxide(0.89M) and 4-t-butyl-1-cyanocyclohexene(1.71M) were combined in a round-bottomed flask at 60°C. This solution had been previously flushed with N_2 and was then sealed with a septum cap. To this solution was added as acetonitrile solution(1.4ml), (10)(0.94M) and DTBP(0.45M), via a motor driven syringe pump over 540 minutes.

Four products were isolated and their structures determinded by ^{1}H nmr. The structures and quantities (as percentages) are given in figure 21 (left to right in order of elution from the reverse-phase HPLC column). Reaction pathways for product formation are given in scheme 28.

Figure 21 Products formed in the reaction of Diphenylphosphine oxide and t-butoxyl radicals with 4-t-Butyl-1-cyanocyclohexene in the presence of (10)
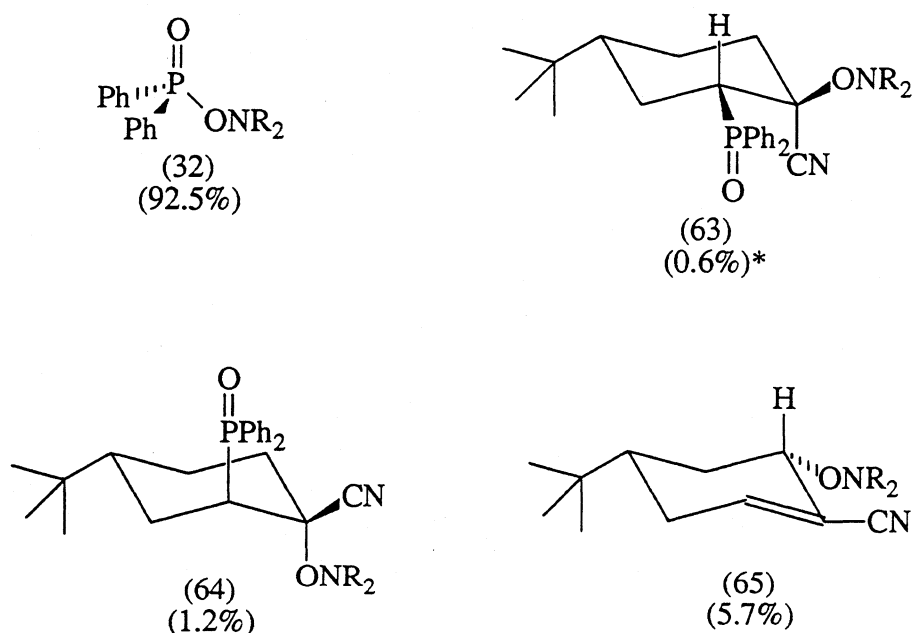
*. Structures (63) and (64) are tentative.

When the above reaction was repeated with more dilute solutions [diphenylphosphine oxide(0.07M), 4-t-butyl-1-cyanocyclohexene(0.72M), (10)

Scheme 28 Reaction of Diphenylphosphine oxide and DTBP with 4-t-Butyl-1-cyanocyclohexene(46) in the presence of (10)
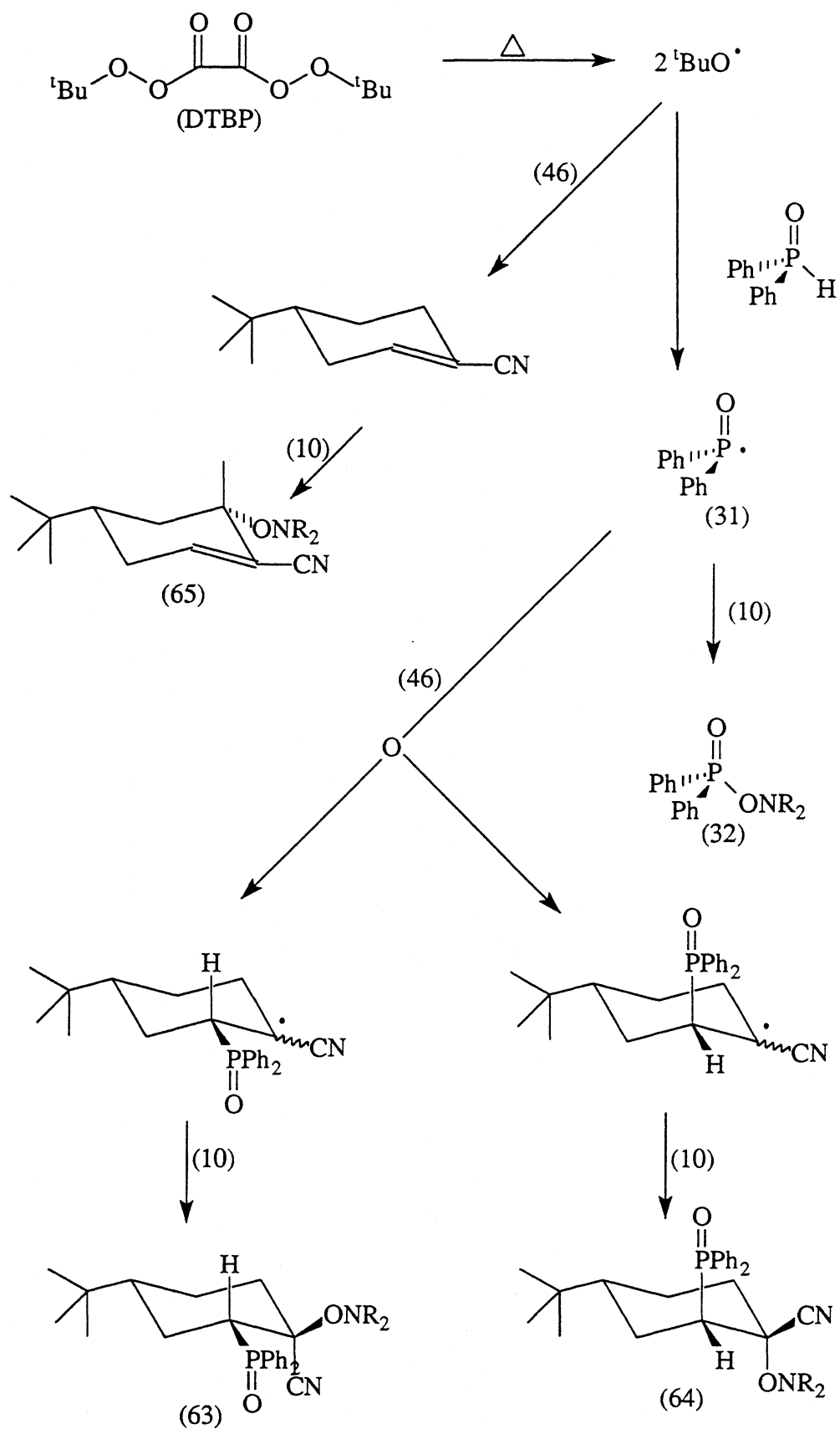
(0.04M), DTBP(0.02M) and acetonitrile(0.9ml)] an increase in the percentages of (63), (64) and (65)[to 3.2%, 3.9% and 12.2% of the total reaction product, respectively] was observed. Numerous atempts to improve on this result, proved unsuccessful.

Isolation of (63), (64) and (65) yielded very small quantities, insufficient to obtain elemental analyses. Attempts to obtain high resolution EI(electron impact) and CI(chemical ionisation) mass spectra were also unsucessful (on all three samples); although FAB(fast atom bombardment) did provide an MH^+ peak for (63). The structures given in figure 21 are therefore tentative, assignment is based on the following ^1H nmr features.

(63)
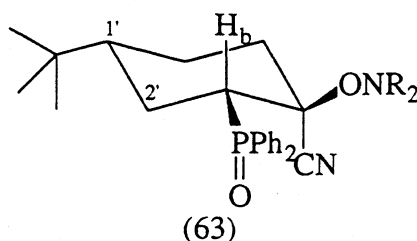
A 250.122MHz spectrum of (63) showed a singlet (0.72ppm) corresponding to 9H from the t-butyl group. Also four 3H singlets (1.11, 1.23, 1.38 and 1.68ppm) from the aminoxyl methyl groups were present. A multiplet at 2.93ppm is assigned to the proton geminal to the diphenylphosphinoyl moiety. This resonance was rather broad (~18Hz) and is therefore indicative of at least one diaxial coupling (typically 10Hz[139]), and an accompanying axial-equatorial coupling (typically 0-5Hz[139]). This resonance (2.93ppm-H_b) is further upfield than the corresponding equatorial H(H_b) in (64), which is also a further indication of H_b on (63) being axial. Further support for the assignment of H_b to the proton geminal to the diphenylphosphoryl group, is that the preferred orientation of addition by a nucleophilic radical (diphenylphosphinyl) to an olefin is to the least substituted end of the double bond[140]. The intermediate free radical being sited on the more substituted carbon, therefore producing the more stable intermediate radical[141] (it is also stabilised by resonance interaction with the nitrile group).

Some of the methylene ring resonances (0.75-1.79ppm) were submerged beneath the aminoxyl methyl resonances, this coupled with a poor signal to noise ratio (due to insufficient sample) made further structural analysis virtually impossible.

Aromatic resonances at 6.95 and 7.15ppm likewise confirmed the presence of the aminoxyl. The aminoxyl is more likely to be equatorial as the orientation of addition should be governed predominantly by steric factors. Equatorial attack by (10) would be consistent with the results reported by Bottle et al[142].

Resonances at 7.30 and 7.44ppm each corresponding to 3H and resonances at 7.75 and 7.86ppm corresponding to 2H each confirm the presence of the diphenylphosphoryl moiety, in (63).

The ^{1}H nmr spectrum of (64) also displayed the characteristic aminoxyl methyl signals (1.18, 1.34, 1.49 and 1.71ppm) and aromatic peaks (7.02 and 7.18ppm). Aromatic signals at 7.42, 7.79 and 7.94ppm equivalent to 10H are consistent with the presence of the diphenylphosphinoyl group. A singlet(0.54ppm) corresponding to 9H from the t-butyl group on the cyclohexane ring was also present.

The signal at 3.30ppm (assigned to H_b-geminal to the diphenylphosphinoyl moiety) was the futhest downfield 1H multiplet, and was seen as a signal of narrow band width ($\leq$12Hz). This indicates no large diaxial couplings to be present, but does allow for one equatorial-axial coupling (typically 0-5Hz[139]), one equatorial-equatorial coupling (typically 0-5Hz[139]) and one proton-phosphorus coupling (PCH typically 10-13Hz[139]) consistent with the equatorial assignment to H_b.
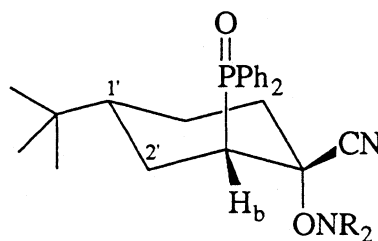
(64)

The structures given for (64) and (63) are in agreement with Bohm and Abell's[143] results, that addition generally proceeds by a trans mechanism.

The last product isolated from the HPLC column was the result of allylic hydrogen abstraction (65). The ^{1}H nmr spectrum displayed four distinctive methyl signals from the aminoxyl moiety (1.30, 1.39, 1.50 and 1.57ppm), indicating the aminoxyl to be bound to a chiral carbon. Also present were

the aromatic proton signals of the aminoxyl ring (7.04 and 7.17ppm). No other aromatic resonances were present in the spectrum, indicating the absence of the diphenylphosphinoyl group. The vinylic proton(H_C) of the cyclohexene ring was present as a doublet of doublets (J=4.9 and 2.2Hz) at 6.82ppm, demonstrating that the aminoxyl is on C5' and not on C2' (where H_C would be evidenced as a doublet).

(65)
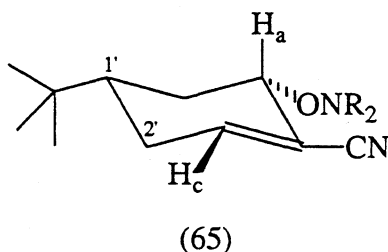
A ^1H multiplet at 4.49ppm is assigned to the proton geminal to the aminoxyl(H_a). This resonance had a band width of (>10Hz), which allows for one small diaxial coupling plus one equatorial-axial coupling (typically 2-3Hz[139]). A 9H singlet at 0.87ppm corresponds to the t-butyl group on the cyclohexane ring. The ^{13}C nmr spectrum confirmed these features.

Although the structures for (63) and (64) are tentative, the ratio of axial:equatorial addition of approximately 2:1 is consistent with the general trends reported in the literature for addition of radicals to cyclohexenes. For example, for addition of benzoyloxyl radicals[142] it was 3:2, for bromine radicals(Br·)[144] ≥ 20:1 and for thiyl radicals(RS·)[145] it was 2-4:1.

While it was known[140] that an electron-withdrawing group such as the cyano group facilitates addition of (nucleophilic) radicals to olefins, it is interesting to compare directly the rate of addition by diphenylphosphinyl radicals to acrylonitrile and to its corrsponding cyclic counterpart 4-t-butyl-1-cyanocyclohexene(45). 4-t-Butyl-1-cyanocyclohexene(0.43M), acrylonitrile(0.42M), diphenylphosphine oxide(0.21M), DTBP(0.02M), (10)(0.05M) and acetonitrile(solvent-2.0ml) were combined and submitted to the general trapping reaction procedure. Figure 22 contains the products formed and their relative percentages.

From figure 22 it can be seen that the diphenylphosphinyl radical adds 6.2 times faster to the terminal end of the double-bond of acrylonitrile than it adds to the corresponding position on 4-t-butyl-1-cyanocyclohexene, i.e. (42):((63)+(64)) ~ (20.3:(3.3).

Figure 22 Products formed in the Diphenylphosphinyl competitive addition reaction between Acrylonitrile and 4-t-Butyl-1-cyanocyclohexene in the presence of (10)

(42)
(20.3%)

(32)
(70.8%)

(63)
(0.5%)

(64)
(2.8%)

(65)
(5.6%)
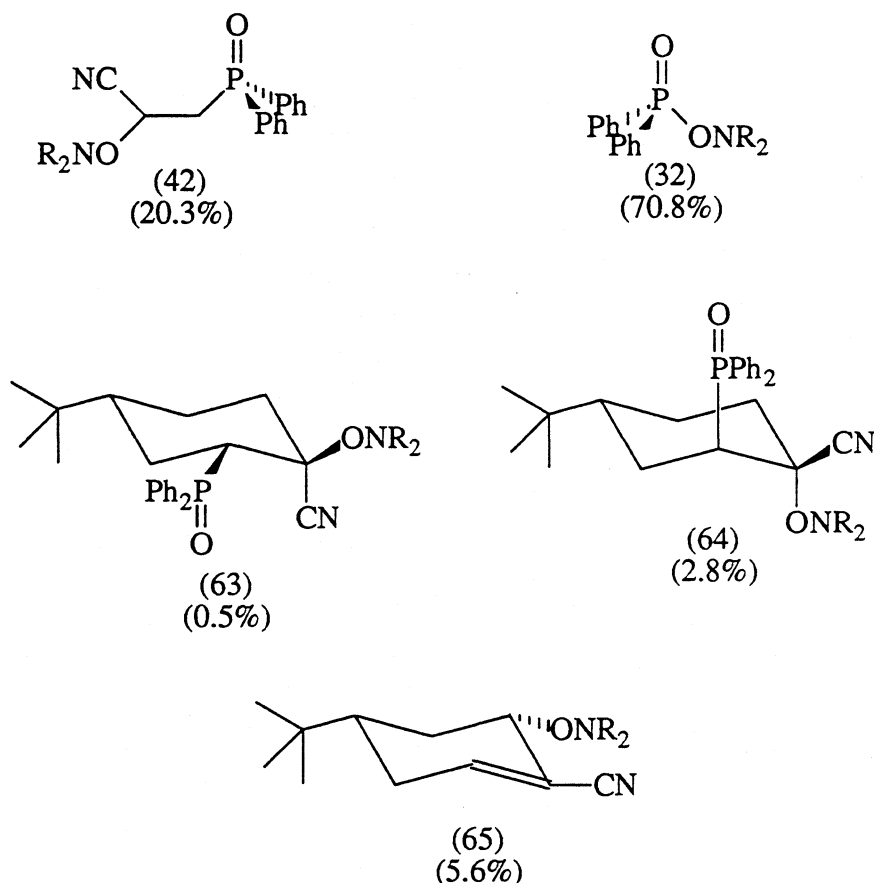
As mentioned previously, it is well recognised that in free radical addition to olefins stric effects are very important[146]. The difference in reactivity of 6.2:1.0, acyclic:cyclic can probably be attributed largely to steric factors that the diphenylphosphinyl radical encounters when approaching the double bond of 4-t-butyl-1-cyanocyclohexene (figure 23).

In 4-t-butyl-1-cyanocyclohexene the addition to C2' from above the plane leads to an unfavoured 1,2-hydrogen/initiator eclipsing interaction. Acrylonitrile in contrast (being planar) does not have such unfavourable interactions when diphenylphosphinoyl radicals (and radical initiators in general) approach its double bond.

Figure 23
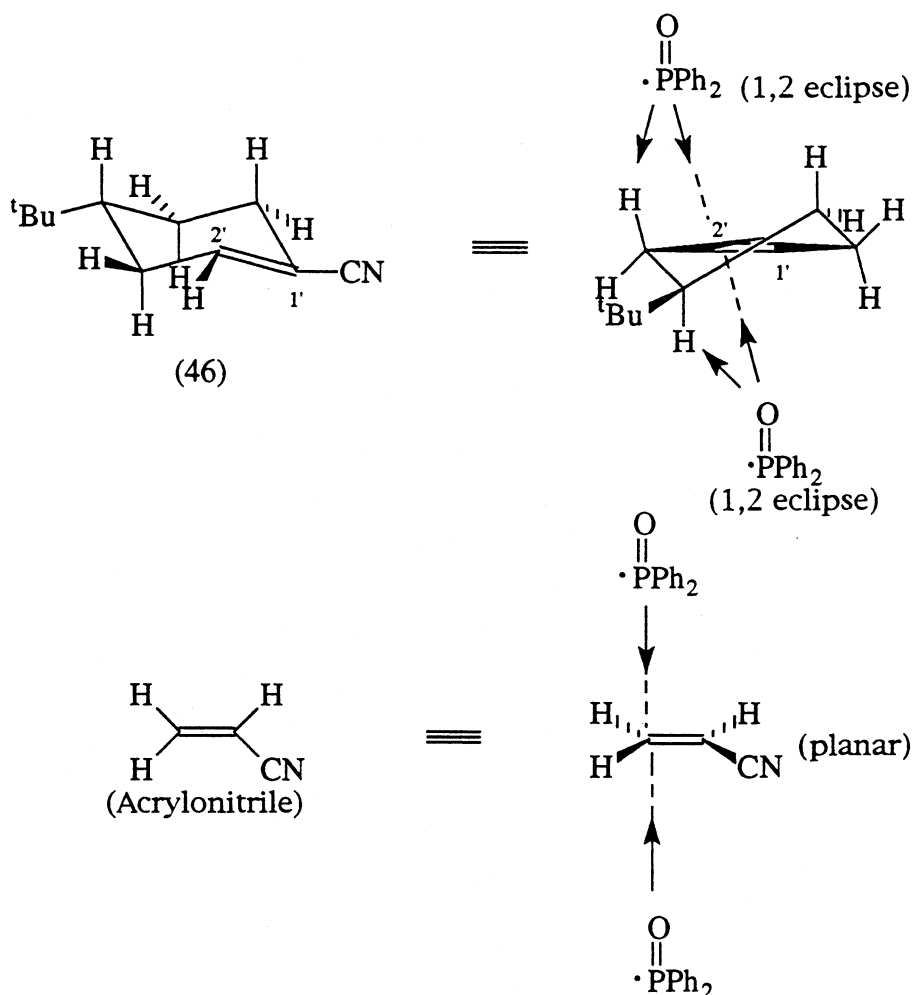
4.3 Phenylacetylene(42)

4.3.1 The reaction of Diphenylphosphine oxide and t-butoxyl radicals with Phenylacetylene(42) in the presence of (10)

DTBP(0.08M), diphenylphosphine oxide(0.16M), (10)(0.18M) and phenylacetylene(9.1M) were combined, then subjected to three/evacuation/thaw cycles on the high vacuum line. Following this, the solution was heated at 60°C for 68 minutes (10 half lives of the initiator). Excess phenylacetylene was then removed, and the reaction mixture separated by reverse-phase HPLC. Two products were detected, (32) and (66). Their structures and relative yields are given in scheme 29.

Scheme 29 The reaction of Diphenylphosphine oxide and t-butoxyl radicals with Phenylacetylene in the presence of (10)
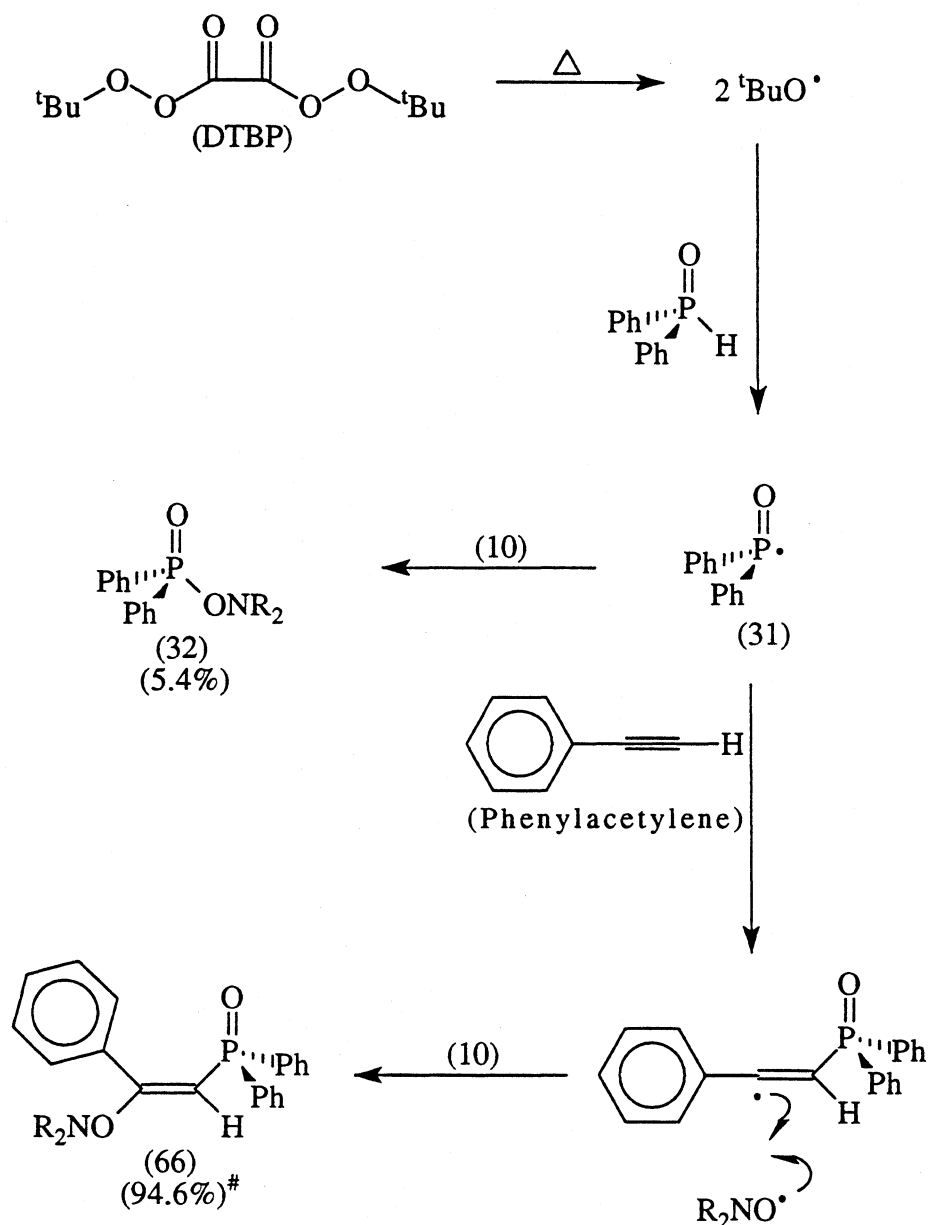
#. 29% yield with respect to initiator.

Compound (66) arises from addition of diphenylphosphinyl radicals (generated via hydrogen abstraction by t-butoxyl radicals) to the triple bond of phenylacetylene, then exclusive trans (relative to the diphenylphosphoryl moiety) trapping by (10).

The addition of t-butoxyl radicals to phenylacetylene apparently is not competitive with addition by diphenylphosphinyl radcials. Bloodworth et

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al.[147] have reported a similar result, detecting no t-butoxyl addition to alkynes by esr. Under acidic conditions however protonated t-butoxyl radicals are reported[147-149] to behave atypically and add to alkynes.

The formation of (66) is not unexpected and contrasts with the unusual result reported by Bottle et al.[150]. Bottle et al.[150] also report only two products, (67) and methyl trap(22), in the percentages given in scheme 30. Product (67) is most unusual and so to it seems, is the mechanism for its formation. No mechanism is confidently put forward for its formation, although the mechanism in scheme 31 is suggested. This mechanism does involve the addition of t-butoxyl radicals to the triple bond.

Scheme 30 The reaction of Phenylacetylene with t-butoxyl
radicals in the presence of (10)
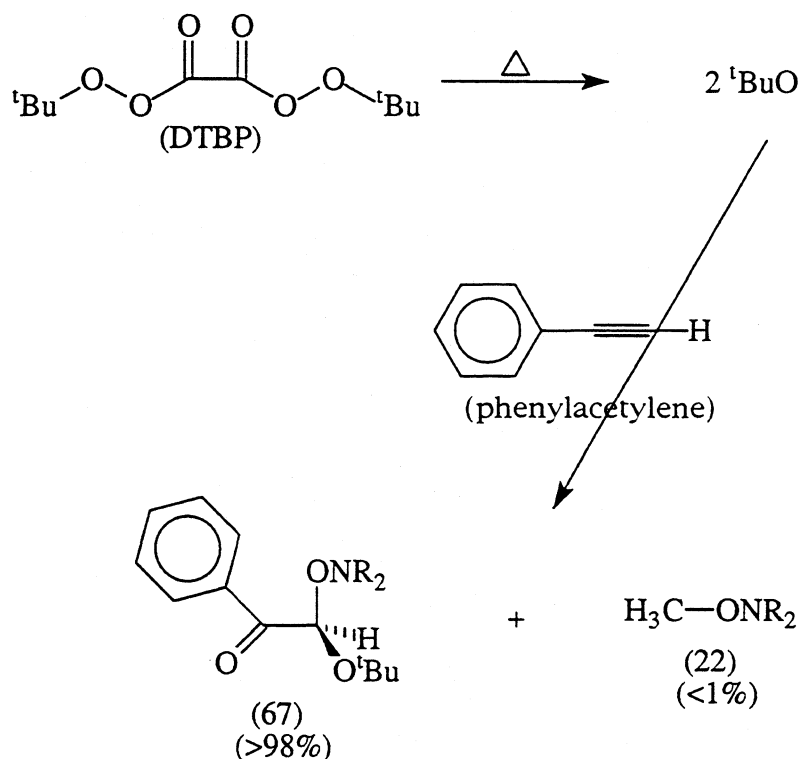
Judging by the amount of diphenylphosphinyl radicals that escape trapping by (10) and add to the triple bond, addition to phenylacetylene is very much faster than to cyclopentene, cyclohexene, 3,4-dihydro-2H-pyran and 4-t-butyl-1-cyanocyclohexene and is appreciably faster than to acrylonitrile and vinyl acetate (see table 14). This result is interesting because Giese[151,152] and Nagase[153] state that radicals add more slowly (in

general) to alkynes than to similar alkenes. Although results for diphenylphosphinyl addition to styrene (the equivalent alkene to phenylacetylene) are not available, a rough equivalent would be vinyl acetate (both electron donors, although their Q and e values are different-see table 3, chapter two). Comparing the result for vinyl acetate to phenylacetylene, and making allowance for a concentration effect(see table14), it seems safe to conclude that diphenylphosphinyl radical addition to phenylacetylene occurs appreciably faster than to the alkene (vinyl acetate).

Scheme 31
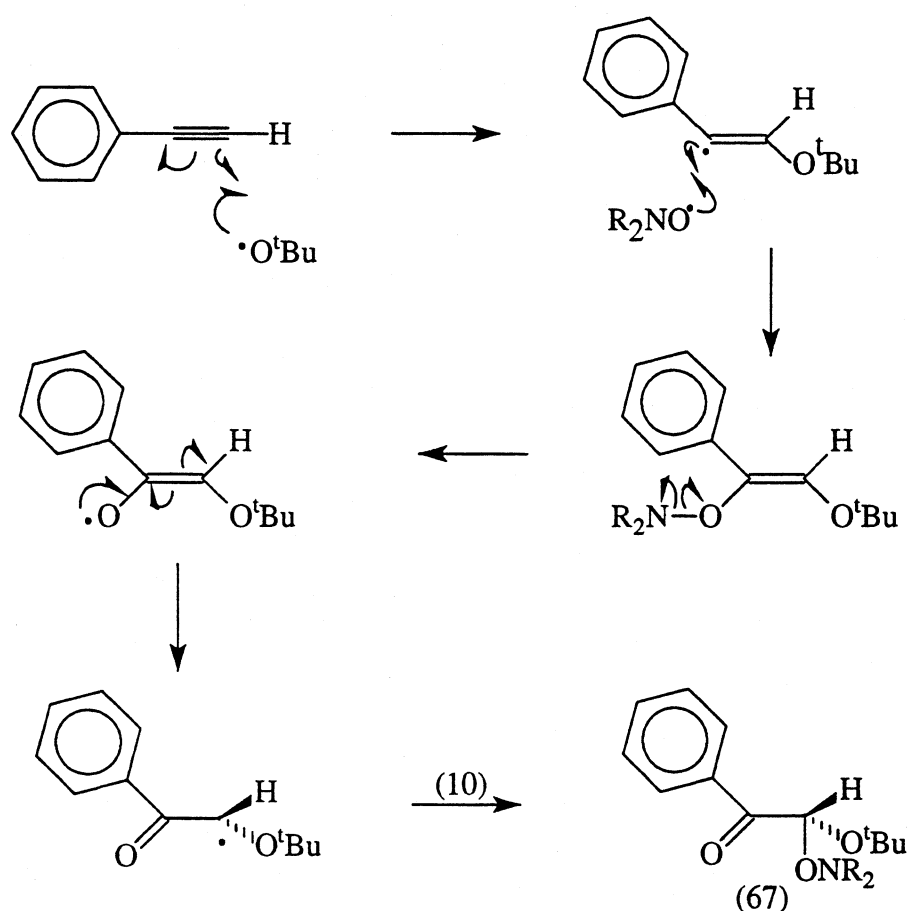
The suggested stereochemistry of (66) seems reasonable on steric grounds: following addition by diphenylphosphinyl (nucleophilic in character-see 4.1.0) to the least crowded end of the double bond (the terminal end) the phenyl group is then forced cis to the diphenylphosphinoyl moiety

Table 14 Monomer addition versus trapping by (10), for the
Diphenylphosphinyl radical(31)

Monomer		Ratio trapping:addition[#]	Reactant Concentration (M)(ratio of equivalents)		
	conc(M)	(32):(DB orTB)	(10)	DPPO	DTBP
Acrylonitrile	15.2	1.00:0.81	0.60 (2.4)	0.52 (2.2)	0.24 (1.0)
Vinyl acetate	10.8	1.00:0.32	0.35 (2.1)	0.34 (2.0)	0.17 (1.0)
Cyclopentene	11.4	1.00:0.11	0.05 (2.4)	0.04 (2.2)	0.02 (1.0)
Cyclohexene	9.9	1.00:n.d	0.05 (2.4)	0.04 (2.2)	0.02 (1.0)
3,4-Dihydro-2H-pyran	11.0	1.00:0.03	0.05 (2.4)	0.04 (2.2)	0.02 (1.0)
4-t-Butyl-1-cyanocyclohexene*	1.7	1.00:0.02	0.94 (2.1)	0.90 (2.0)	0.45 (1.0)
Phenylacetylene	9.1	1.00:17.5	0.18 (2.1)	0.16 (2.0)	0.08 (1.0)

#. Total addition to double bond.
*. Syringe pump addition of DTBP and (10)(see 4.3.4.0).
DB or TB. Addition to double or triple bond.
DPPO. Diphenylphosphine oxide.

by the bulkier incoming aminoxyl. This stereochemistry places the two bulkiest groups (initiator and aminoxyl) trans to each other.

The stereochemistry of (66) is strongly supported by analogy with (68)(4.3.2) (the equivalent product to (66), where the dimethoxyphosphinoyl moiety replaces the diphenylphosphinoyl moiety), where an X-ray crystal structure (see figure 24) confirmed the trans stereochemistry. Unfortunately, numerous attempts to grow a suitable crystal of (66) for X-ray crystal structure analysis were unsuccessful, at best producing twinned crystals. The product (66) appeared to be quite stable. After (66) was heated at

60°C for 105 minutes with two equivalents of (10) in acetonitrile (following three freeze/evacuation/thaw cycles), HPLC analysis showed no fragmentation of (66) to produce (32) or the bis aminoxyl product (69) (see scheme 32).

Scheme 32
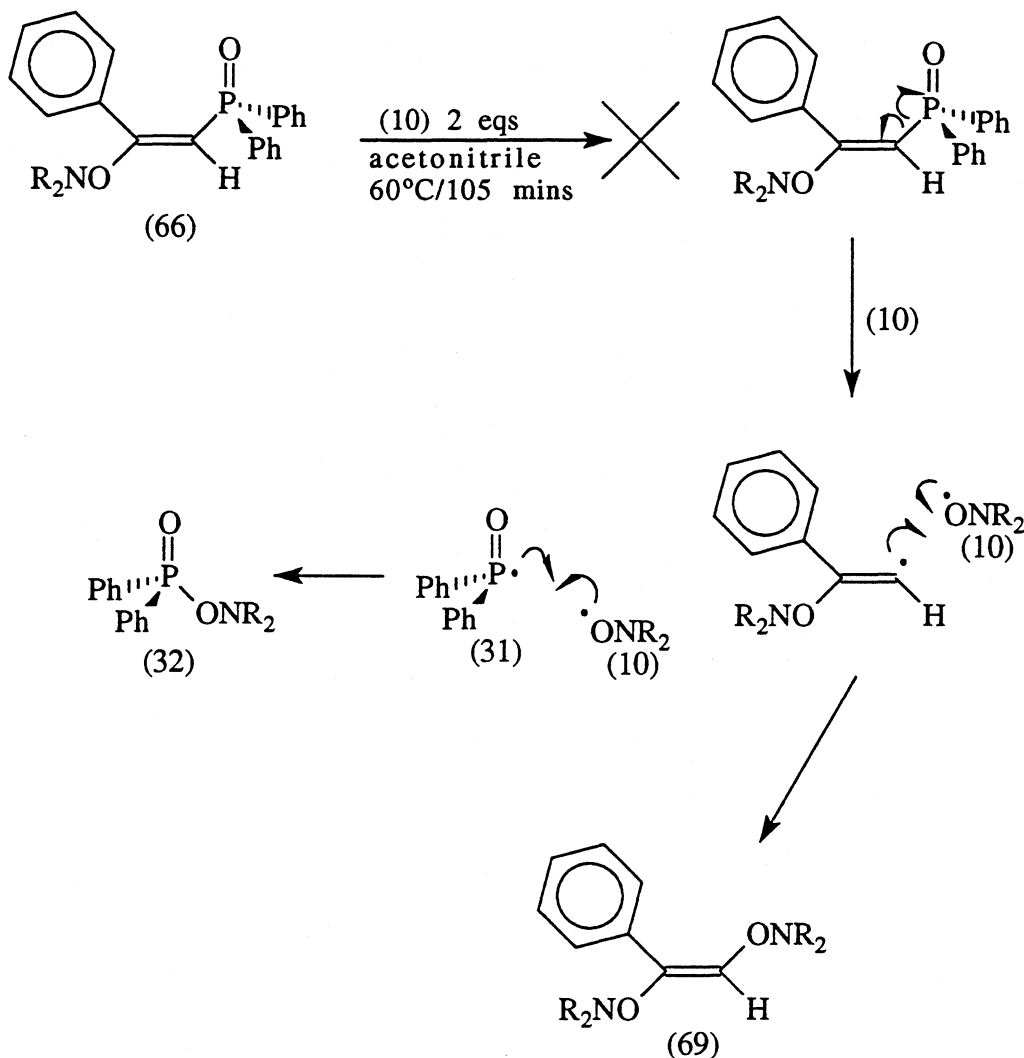
4.3.2 The reaction of Dimethyl phosphite and t-butoxyl radicals with Phenylacetylene in the presence of (10)

In a similar manner to 4.3.1., DTBP(0.16M), dimethyl phosphite(1.60M), (10)(0.33M) and phenylacetylene(7.8M) were combined and heated for 68 minutes at 60°C.

Reverse-phase HPLC separation of the reaction mixture produced two products, namely (45) and (68). Their structures and relative yields are given in scheme 33.

Scheme 33 The reaction of Dimethyl phosphite and t-butoxyl radicals with Phenylacetylene in the presence of (10)
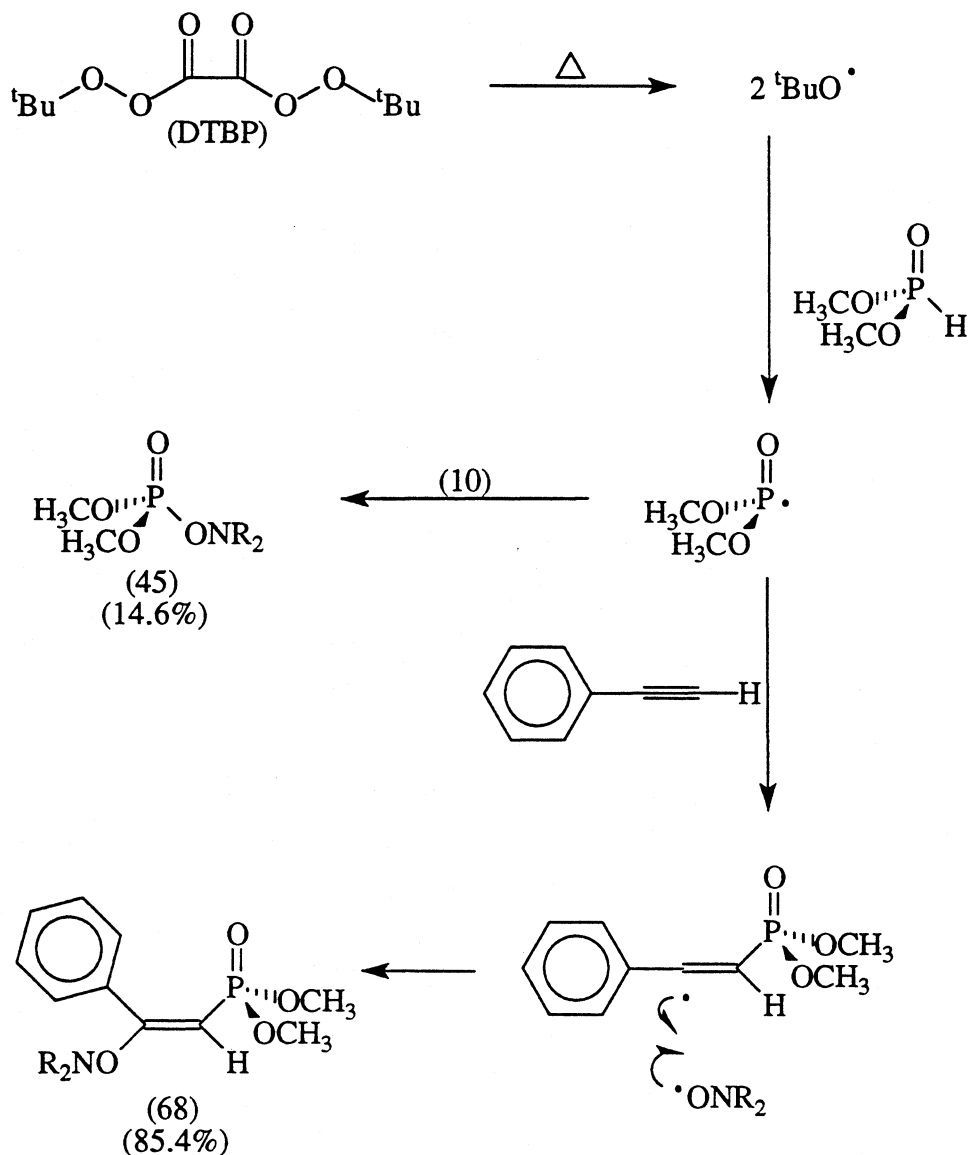
From previous work described in this chapter it was known that the dimethoxyphosphinyl radical adds more slowly to olefins than does the diphenylphosphinyl radical. To enhance the amount of dimethoxyphosphinyl addition (relative to t-butoxyl addition) to phenylacetylene (as a similar trend with alkynes was expected) an increased number of equivalents of dimethyl phosphite was used in the reaction (5:1, dimethyl phosphite:t-butoxyl, compared to 1:1 in 4.3.1).

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Conclusive evidence for the structure of (68) was obtained when a crystal was grown from methanol and analyses by X-ray crystallography (see figure 24).

Figure 24 X-ray crystal structure of (68)
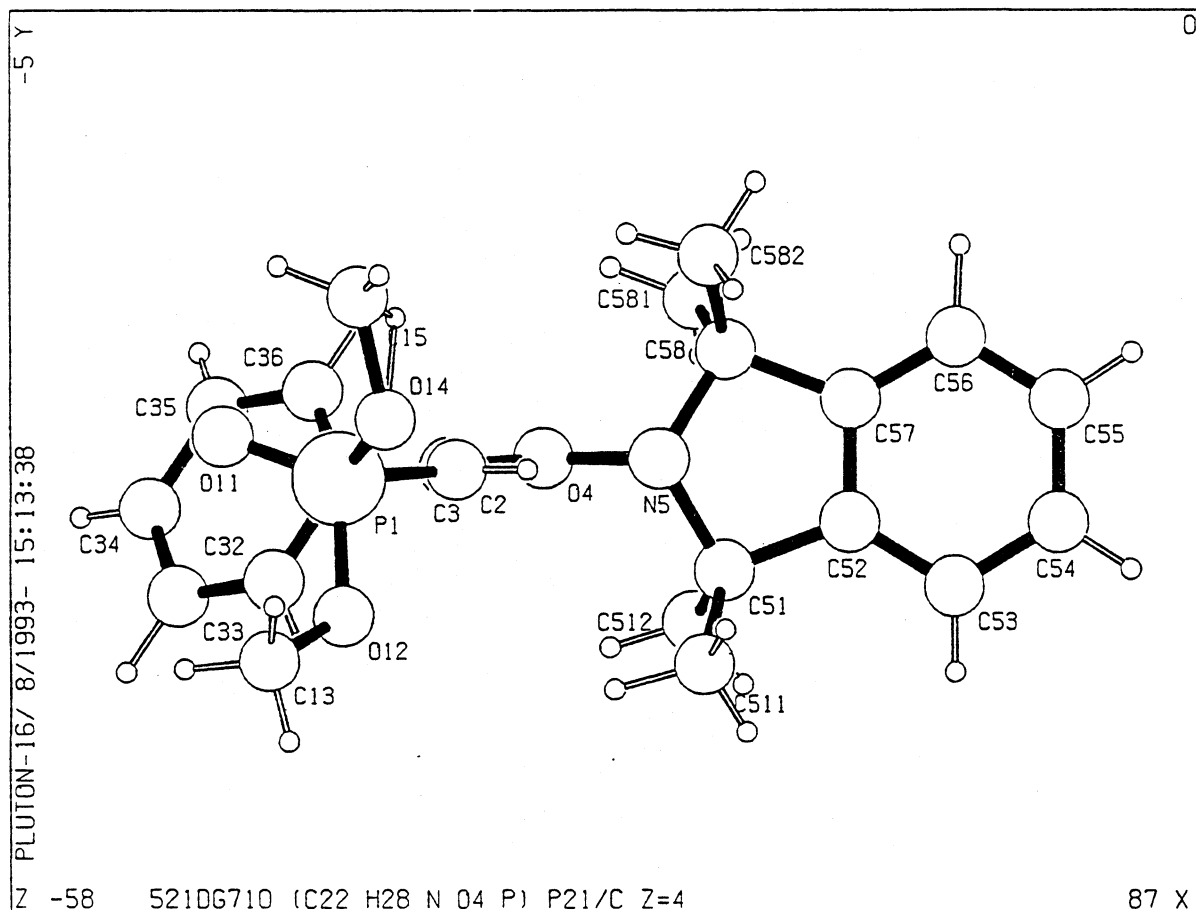
4.4 Conclusions

To maximise addition of diphenylphosphinyl(31) and dimethoxy-phosphinyl radicals(41) [rather than interception by (10)] the concentration of (10) needs to be kept low and the monomer concentration high.

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The use of t-butoxyl radicals to generate phosphinyl radicals was accompanied by side-reactions involving t-butoxyl radicals with acrylonitrile, vinyl acetate or any of the cyclic olefins under the reaction conditions studied. t-Butoxyl radicals either hydrogen abstracted from the monomer or added to the double bond in these cases (with the exception of 4-t-butyl-1-cyanocyclohexene where no t-butoxyl addition was detected).

Acrylonitrile and vinyl acetate

Diphenylphosphinyl and dimethoxyphosphinyl radicals add efficiently to both acrylonitrile and vinyl acetate, although dimethoxyphosphinyl has a lower rate constant for this addition reaction. Both phosphinyl radicals exhibit a slower rate of addition to vinyl acetate than to acrylonitrile therefore demonstrating their nucleophilic character.

Cyclic Olefins

With cyclopentene, 11.3% of the diphenylphosphinyl radicals generated were found to add to the double bond and the trapping of this resultant radical was exclusively trans. However, this product constituted only 1.5% of the total reaction product. Addition of dimethoxyphosphinyl radicals to cyclopentene was not detected. The major reaction product in both of these reactions was the product arising from allylic hydrogen abstraction by the t-butoxyl radical. Likewise with cyclohexene, the major reaction product in both the diphenylphosphinyl and dimethoxyphosphinyl radical reactions was the product arising from allylic hydrogen abstraction by the t-butoxyl radical. Addition of both the diphenylphosphinyl and dimethoxyphosphinyl radicals to the double bond of cyclohexene was not detected. This total absence of addition by phosphinyl radicals in cyclohexene compared to cyclopentene is explained by steric differences. The result indicates that the rate of phosphinyl radical trapping is much faster than the rate of addition to the double bond of cyclohexene.

With 3,4-dihydro-2H-pyran only a very small proportion(3%) of the diphenylphosphinyl radicals formed were found to add to the double bond. Allylic hydrogen abstraction by t-butoxyl radicals comprised 65% of the reaction product. Therefore the presence of the ethereal oxygen in the six-membered ring α to the double bond does enhance diphenylphosphinyl radical addition. In the conformationally biased 4-t-butyl-1-cyanocyclohexene, again only a very low percentage(2%) of

diphenylphosphinyl radicals generated were found to add to the double bond. However allylic abstraction constituted only 5.7% of the reaction product.

The very low (and in some cases not at all) percentages of phosphinyl radical addition to the cyclic olefins studied suggests that an alternate method of generation of phosphinyl radicals not involving t-butoxyl radicals is needed. Studies[154] recently carried out at Griffith University suggest that photolysis of acyl phosphine oxides, in conjunction with the radical trapping technique is a superior method for generation of phosphinyl radicals for studies such as those reported here.

Phenylacetylene

In contrast to cyclic olefins, both diphenylphosphinyl and dimethoxyphosphinyl radicals readily add to the triple bond of phenylacetylene. Exclusive trans (with respect to the phosphinoyl moiety) trapping of these resultant radicals by the aminoxyl occurs. Also no t-butoxyl addition to the triple bond was detected. Therefore the radical trapping technique in conjunction with t-butoxyl, phosphinyl radical generation is a useful tool for the stereochemical studies of phosphinyl radical additions to phenylacetylene and probably acetylenes in general. Although exclusive trans addition of phosphinyl radicals to phenylacetylene has been attributed to steric factors, it is also possible that the addition process (to give the least stable vinyl radical) may be for electronic reasons. This feature clearly warrants further investigation.

CHAPTER FIVE

THE STEREOCHEMISTRY OF ADDITION OF BENZOYLOXYL RADICALS TO TRANS-Δ^2-OCTALIN

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5.0 Introduction

Just as stereochemistry is crucial to biological activity, so too does it determine the properties of a polymer.

In the polymerisation reaction of an alkene $RCH=CH_2$, and assuming standard head to tail addition, the relative stereochemistry of the R groups will affect the properties of the polymer. The R groups may be positioned all on one side of the polymer chain (termed isotactic), on different sides of the chain alternately (syndiotactic), or arranged randomly (atactic). Each isomer having drastically different properties, eg polypropylene[155].

In organic synthesis the stereoselective control of free radical reactions is becoming increasingly important[156]. Free radical chemistry is increasingly being utilised as a useful synthetic technique, due to its ability to modify functional groups and to form carbon-carbon bonds under often mild and selective conditions. The main factors known to affect stereo and regio-selectivity in free radical addition reactions, and therefore of importance to both polymer and synthetic organic chemistry, are polar effects, bond strength terms and steric effects[140,156-158].

Some free radical addition reactions are highly stereoselective. For example, the free radical addition of hydrogen bromide to cyclohexenes, affording almost exclusively (95-100%) diaxial addition[144,145]. In general addition to cyclic alkenes is selective, affording predominantly the trans adduct[143].

The radical trapping technique as mentioned previously (chapters one to four) is a convienient technique[142,159] to study regio- and stereo-selectivity in the reactions of oxyl radicals with cyclic olefins. In this chapter results are reported for the reaction of benzoyloxyl radicals with trans-Δ^2-octalin(70) in the presence of (10).

(70)
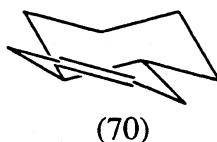
In contrast to the t-butoxyl radical which shows a strong propensity towards allylic hydrogen abstraction[125,136] rather than to addition, the benzoyloxyl radical has a much diminished propensity towards hydrogen abstraction. For example, hydrogen atom abstraction from cyclohexene by benzoyloxyl radicals is ~7 times slower than addition at $60^{\circ}C$[142], while hydrogen atom abstraction from cyclohexene by t-butoxyl radicals is 47 times faster than addition at $60^{\circ}C$[18c]. Interestingly though the ratio of cis:trans addition products in the above studies was very similar (approximately 1:3) for both t-butoxyl and benzoyloxyl radicals. When more hydrogen abstraction is occuring, the percentages of addition products in the total reaction product must decrease. Hence choice of the benzoyloxyl radical over the t-butoxyl radical in the present study.

Benzoyloxyl radicals were generated by thermal decomposition of benzoyl peroxide(71). Once generated the benzoyloxyl radicals may however fragment to phenyl radicals (see scheme 34), which may be trapped by (10) to produce (72). Whether this process occurs or not though depends upon the rate of benzoyloxyl radical addition to the substrate under study.

Scheme 34
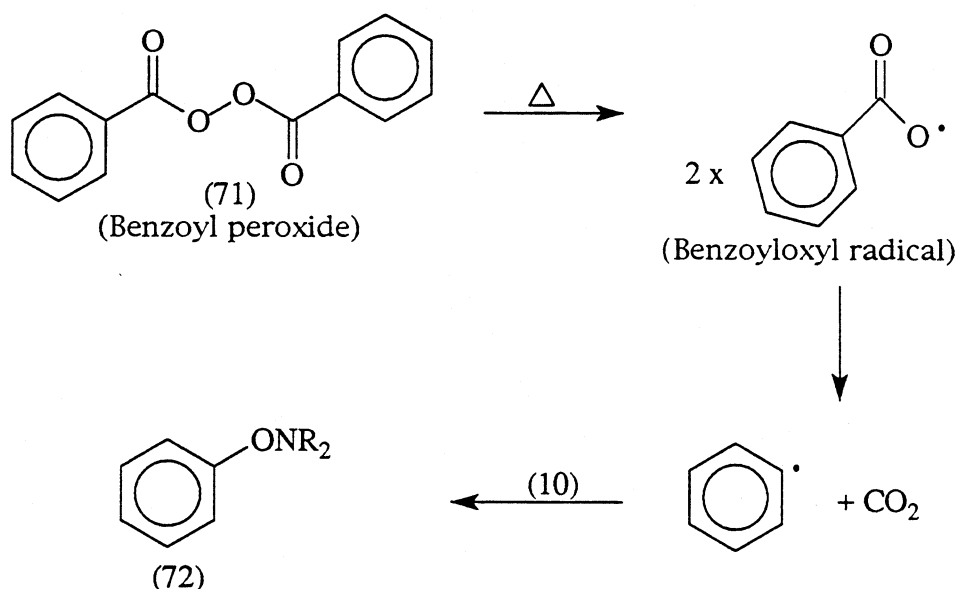
The only other study known on the stereochemistry of addition of oxyl radicals to cyclohexenes has been carried out by Bottle et al.[142]. Their experiments on the addition of benzoyloxyl radicals to cyclohexene show clearly that trans addition is favoured over cis addition by a factor of 3-4:1.

Their results for cyclohexene do not however indicate whether the addition of benzoyloxyl radicals is stereospecific (i.e whether the trans product (73) is a result of axial addition followed by axial trapping, or equatorial addition followed by equatorial trapping, etc, -scheme 35). The ratio of cis:trans is governed not only by the mode of the addition and trapping processes but also by the rate of ring inversion. The rate of ring inversion can be affected by a number of factors, such as concentration, solvent polarity and temperature. Therefore changes in these will alter the ratio of cis:trans adducts. Also the rate of ring inversion will be affected by the nature of the initiator. It is known[160,161] that an alkyl group has greater preference for equatorial orientation than do polar groups, and as the size of the alkyl group increases, so does this preference.

Scheme 35
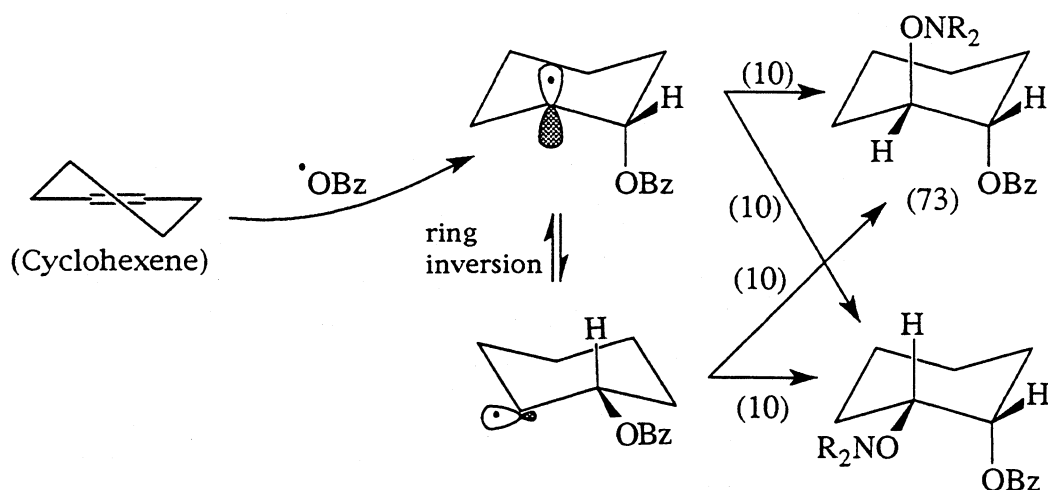
To gain some indication as to whether the addition of benzoyloxyl radicals to cyclohexenes was in fact stereospecific, Bottle et al.[142] analysed the reaction of benzoyloxyl radicals with the conformationally biased 4-t-butyl-cyclohexene. The 'locked' conformation of 4-t-butyl-cyclohexene eliminates the problem of ring flipping (inversion). This study afforded eight addition products, comprising ~90% of the total reaction products (scheme 36). They concluded that the addition of benzoyloxyl radicals to cyclohexenes proceeds with only modest stereoselectivity; axial addition being favoured over equatorial addition by approximately 3:2. This modest preference they attributed to steric factors. Trapping of the resultant radical adducts by the aminoxyl(10) occured with slightly greater stereoselectivity; axial trapping being favoured over equatorial by approximately 4:1. Both

Scheme 36 The reaction of benzoyloxyl radicals with 4-t-Butyl-cyclohexene in the presence of (10)

(4-t-butylcyclohexene)

(74)
(26.7%)

(75)
(4.7%)

(76)#

(77)#

(78)
(25.0%)

(79)
(4.7%)

(80)
(11.9%)

(81)
(5.2%)

#. (76) and (77) were unable to be separated. Combined percentage was 21.6%.
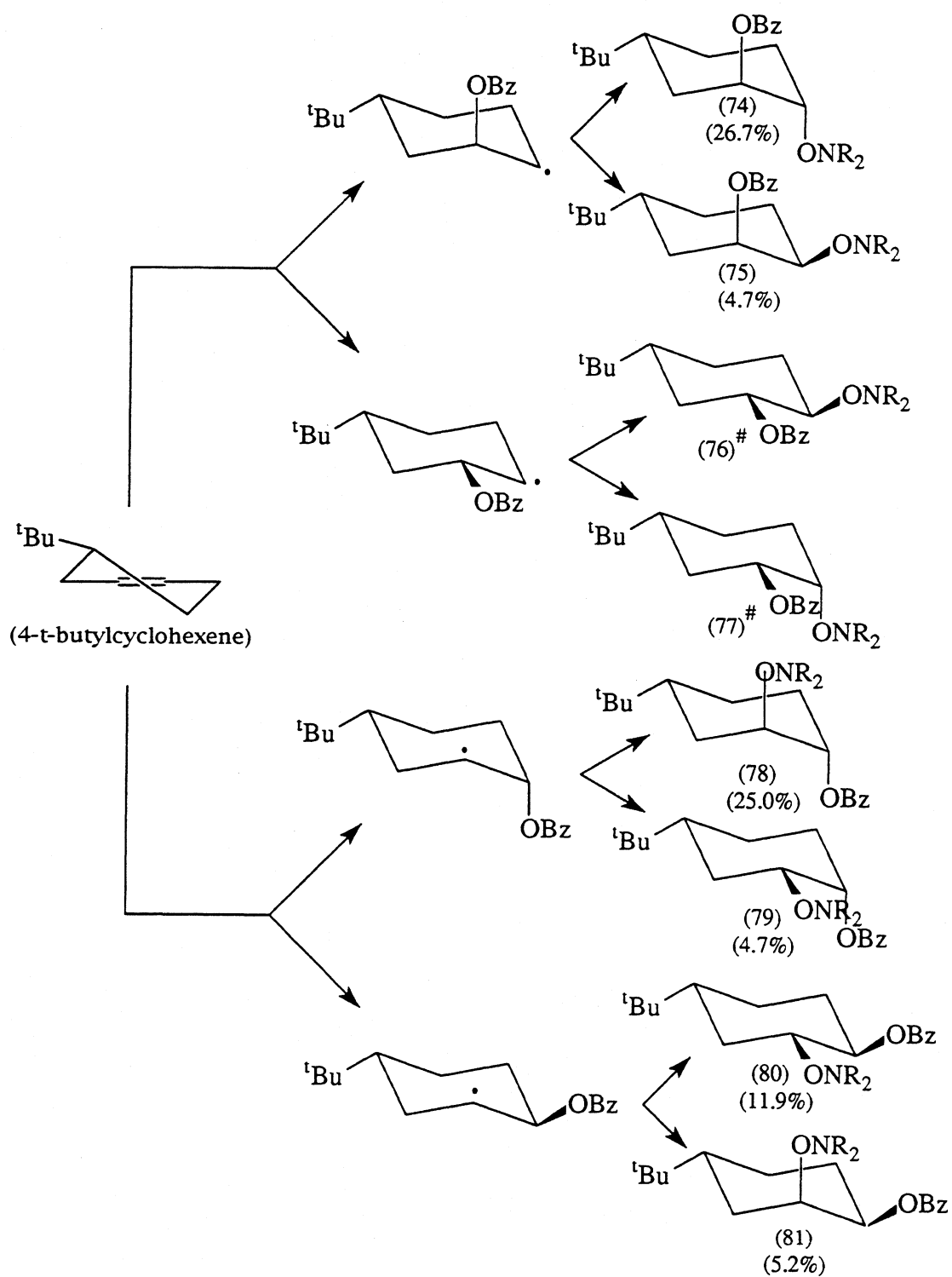
steric and polar factors are suggested as being responsible for the preferred overall trans product[142].

The results presented in this chapter are for the reaction of benzoyloxyl radicials with trans-Δ^2-octalin. The advantage of the octalin over 4-t-butyl-cyclohexene is that the symmetry of the former means that only four addition products are possible, compared with the eight for the latter alkene. The disadvantage is that the octalin is more difficult to synthesise. The benzoyloxyl radical study was intended as a prelude to an investigation of the stereochemistry of addition of phosphinyl radicals to conformationally locked alkenes.

5.1 The reaction of benzoyloxyl radicals with Trans-Δ^2-octalin in the presence of (10)

Benzoyl peroxide(0.182g, 0.11M, 1.0 equivalents) and (10)(0.3g, 0.23M, 2.1 eqivalents) were dissolved in a trans-Δ^2-octalin/acetone mixture(7.0mls, 30:70) and then heated for 27 hours at 60°C, following successive freeze/evacuation/thaw cycles under high vacuum.

Reverse-phase HPLC isolation of the reaction mixture gave seven products, which were identified (all except an unidentified product (84)), by ^{1}H and ^{13}C nmr. Their structures and percentage yields (ratios) are given in figure 25 (left to right in order of elution from the HPLC column). The reaction pathway for product formation is given in scheme 37.

In the ^{1}H nmr spectra of all the products (85)-(88), the characteristic methyl signals (occuring as four singlets, ranging from 1.16-1.60ppm) from the aminoxyl trap moiety were displayed. Also present were the aromatic proton signals from the isoindoline ring (6.99-7.21ppm) of the aminoxy and resonances from the benzoate moieties (7.43-8.11ppm). The most important signals for the structural elucidation of these compounds were the two 1H multiplets that occured in the ranges 3.91-4.34ppm and 5.08-5.61ppm. Previous results[18c,31] have shown that protons geminal to the aminoxy moiety have chemical shifts that lie in the range 3.6-4.7ppm (see table 15). Protons attached geminally to the benzoyloxy group have resonances that lie in the range 5.02-5.68ppm[142].

Figure 25 Products formed in the reaction of benzoyloxy radicals
with Trans-Δ^2-octalin in the presence of (10)

(82)
(3.41)

(83)*
(1.62)

(85)
(1.00)

(86)
(3.45)

(87)
(1.47)

(88)
(7.41)
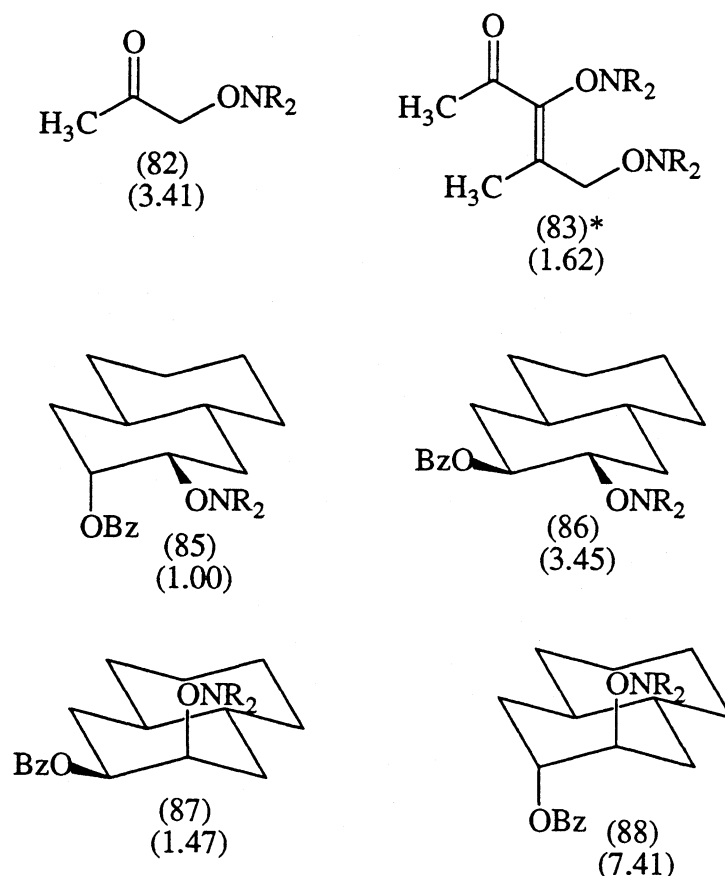
*.Structure (83) is tentative.

It is concievable that (83) is the result of a self aldol type condensation reaction on (82)(vide infra) (see section 6.11.0).

(82)   Aldol condensation   (83)
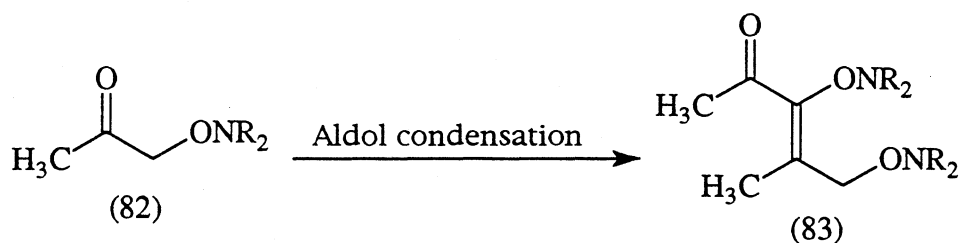
At 250.12MHz product (85) had a 1H ddd resonance at 3.91ppm which was assigned as the proton geminal to the aminoxyl group(H_a). The coupling constants (2.9Hz, 4.1Hz and 11.7Hz) correspond to two axial/equatorial couplings (typically 2-3Hz)[139] and one diaxial coupling (typically 8-10Hz)[139]. The 1H resonance at 5.61ppm could not be resolved but was of narrower band-width than the signal at 3.91ppm. The resonance was assigned to H_b (geminal to the benzoate group), its narrow (~7.0Hz) bandwidth being indicative of H_b being equatorial, i.e. no diaxial couplings.

Scheme 37 Reaction of benzoyloxyl radicals with Trans-Δ²-octalin in the presence of (10)
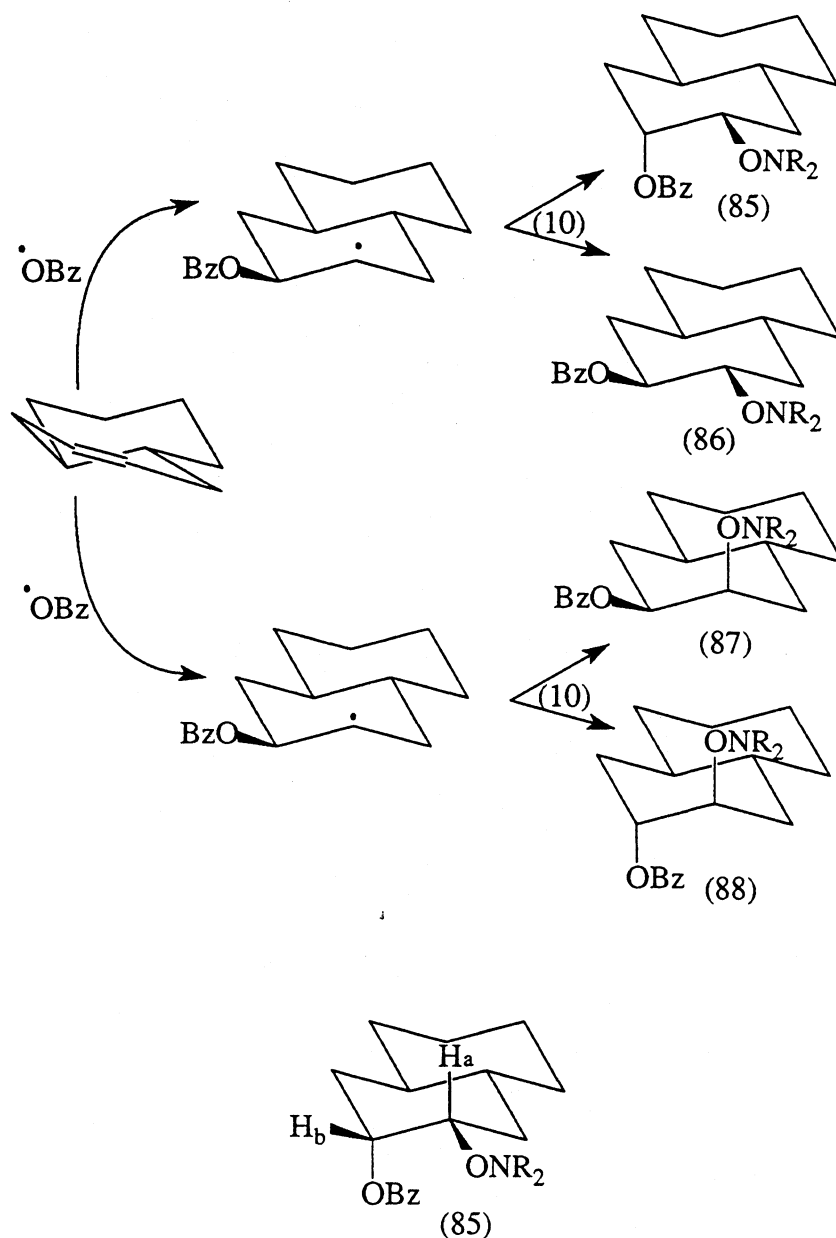
Therefore the aminoxyl group is equatorial and the benzoate group is axial in line with structure (85).

The 300.06MHz spectrum of (86) showed a 1H, ddd resonance at 4.0ppm. Couplings of 10.1Hz, 10.1Hz and 5.0Hz correspond to two diaxial couplings (typically 8-10Hz)[139] and one equatorial/axial coupling (typically 2-3Hz)[139],

(86)
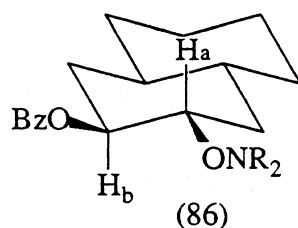
hence the assignment of this resonance to Ha (geminal to the aminoxy group); Ha being axial. The signal at 5.11ppm (1H, ddd) had couplings of 10.1Hz, 10.1Hz and 5.3Hz, corresponding to two diaxial couplings and one equatorial/axial coupling, indicating that this proton, assigned to Hb is also axial, hence structure (86).

Table 15 Typical α proton shifts for some alkoxyamines

Structure • ONR$_2$ = (10)	Shift R$_2$NOCH$_a$ (ppm)
H$_3$C—ONR$_2$ (22)	3.80[18c]
	4.06[18c]
	3.88[18c]
	4.42[142]
	4.69[18c]

At 250.12MHz the signals at 4.34 and 5.08ppm from (87) could be resolved into a broad singlet and an eight-line doublet of doublet of doublets

(3.2, 5.04 and 11.9Hz). The signal at 4.34ppm was assigned as the proton geminal to the aminoxy(H_a) and its narrow band width (13.7Hz) indicates that it is equatorial (i.e no large diaxial couplings-typically 8-10Hz[139]). The

(87)
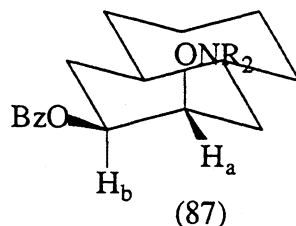
signal at 5.08ppm is assigned to the proton geminal the benzoate group (Hb), and the couplings indicate one diaxial coupling (11.9Hz) and two axial/equatorial couplings (3.2 and 5.0Hz-typically 2-3Hz[139]) in line with structure (87).

The 250.12MHz spectrum of (88) showed the methine hydrogens, geminal to the aminoxy group(H_a-4.08ppm) and geminal to the benzoate group (H_b-5.49ppm) to have very narrow band width resonances (~11Hz). Both signals could be resolved into doublets with a splitting of 2.0Hz each being indicaitve of an equatorial/equatorial coupling (typically 2-3Hz)[139]. These narrow band widths indicate H_a and H_b to be equatorial, therefore placing the aminoxyl and benzoate groups axial, hence the structure given for (88).

(88)
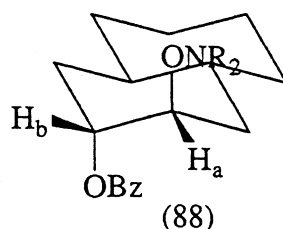
In an attempt to confirm the stereochemical configuration of (88), Mitsunobu methodology was employed[162,163], whereby the benzoate was to be hydrolysed from (88) to give the free hydroxy compound (89). This alcohol (89) was then to be re-esterified by the Mitsunobu reaction (scheme 38), utilizing triphenylphosphine(TPP), diisopropylazodicarboxylate(DIAD) and benzoic acid. Inversion of configuration should result in the formation of the product (87).

This reaction on (88) was however unsuccessful. Interestingly Bottle[164] had a similar problem, in that he could not convert his

corresponding diaxial product(74) to (77) by Mitsunobu methodology when using THF as solvent or in dilute solutions.

The structure of (87) was confirmed though by an X-ray crystal structure analysis, the result of which is shown in figure 26.

<u>Scheme 38</u>
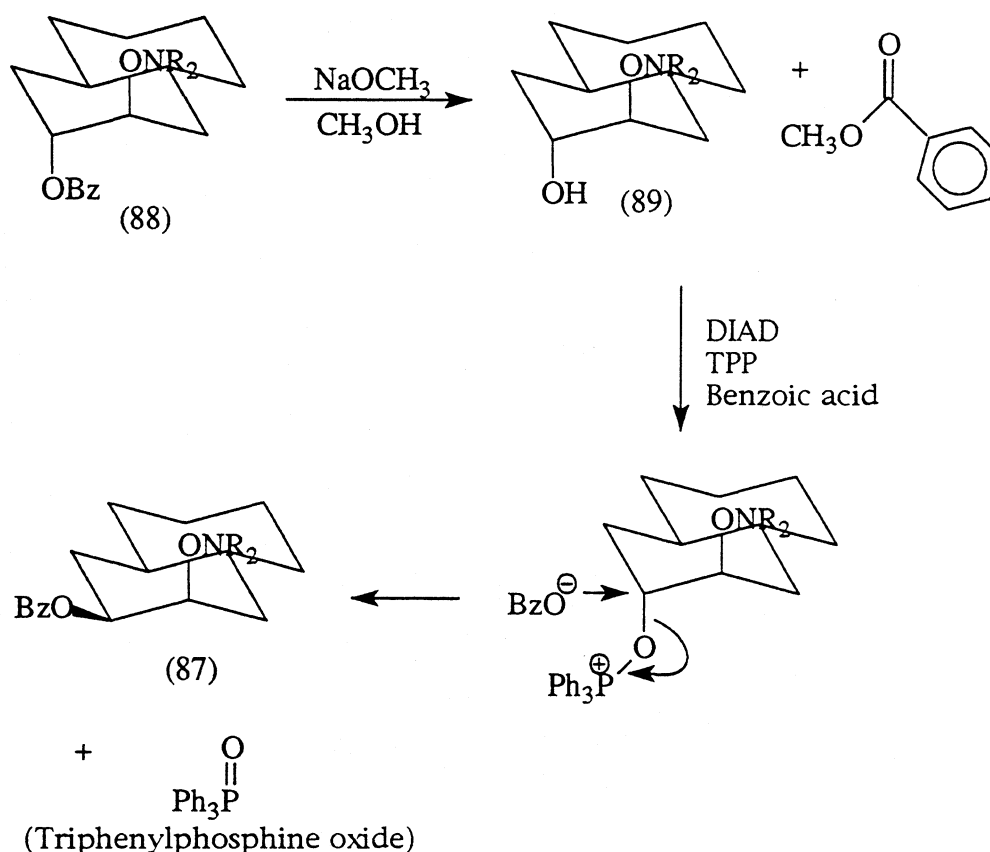
From the amounts of the various addition products in figure 25, it can be seen that axial addition by the benzoyloxyl radical to the double bond of trans-Δ^2-octalin is the major type of addition (ratio, 60:40, axial:equatorial). This result is in very good agreement with the result of Bottle et al.[142], and in agreement with other studies such as the addition of thiols to cyclohexenes[165] (about 70-90%, diaxial addition), and addition of HBr to substituted cyclohexenes[144].

5.1.1 The Benzoyloxyl radical addition step

It has been suggested[144,165] that the stability of the adduct radical will govern the mode of addition (i.e axial or equatorial). Therefore this preference for axial addition could be explained on the basis of axial addition producing a more stable intermediate radical than equatorial addition. For bromine radical addition (axial:equatorial, $\geq$ 20:1) the high stereoselectivity

Figure 26 X-ray crystal structure of (88)
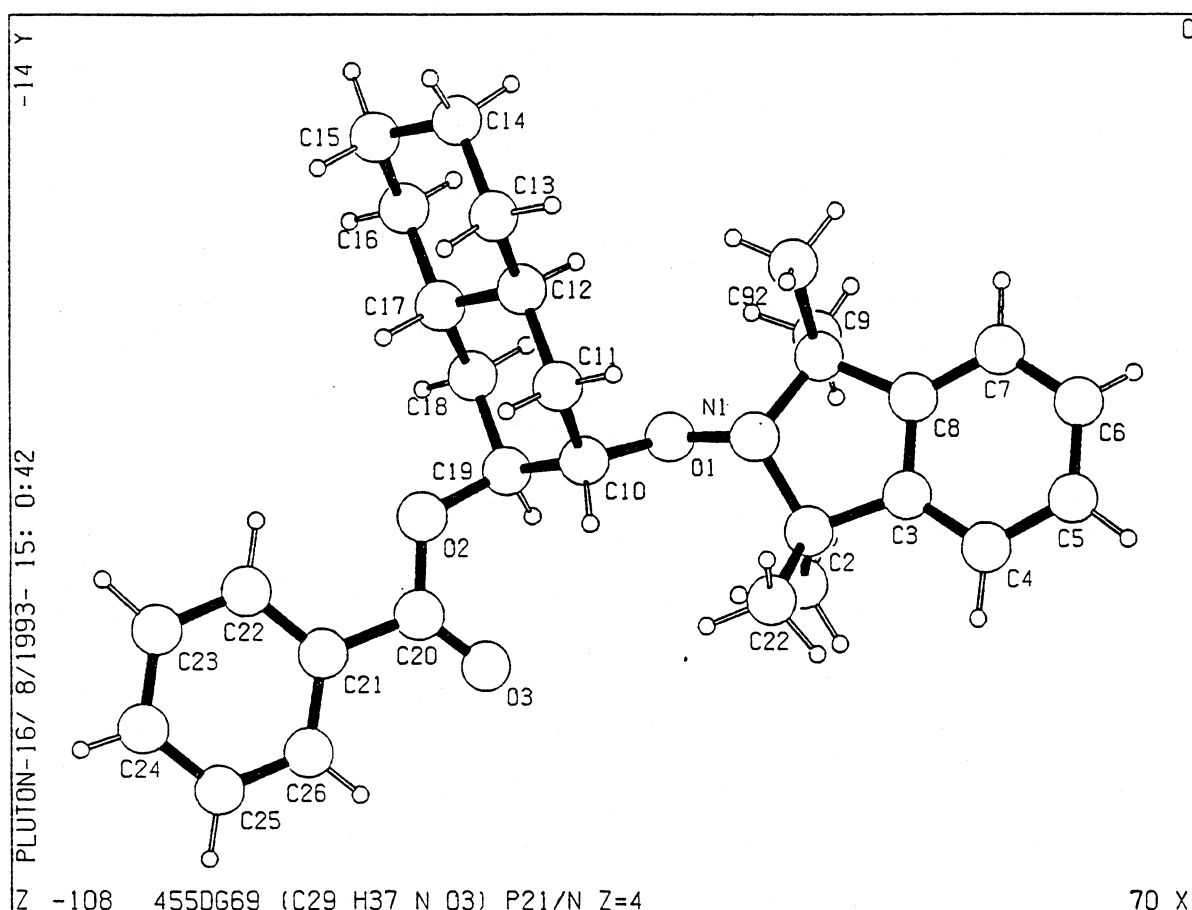
was attributed to the formation of a bromine bridged radical intermediate[144] (figure 27). The preferred axial addition by thiyl radicals on 2-chloro-4-t-butylcyclohexene (initial preference is $\geq$ 9:1.0) LeBel et al.[145] argues is due

Figure 27
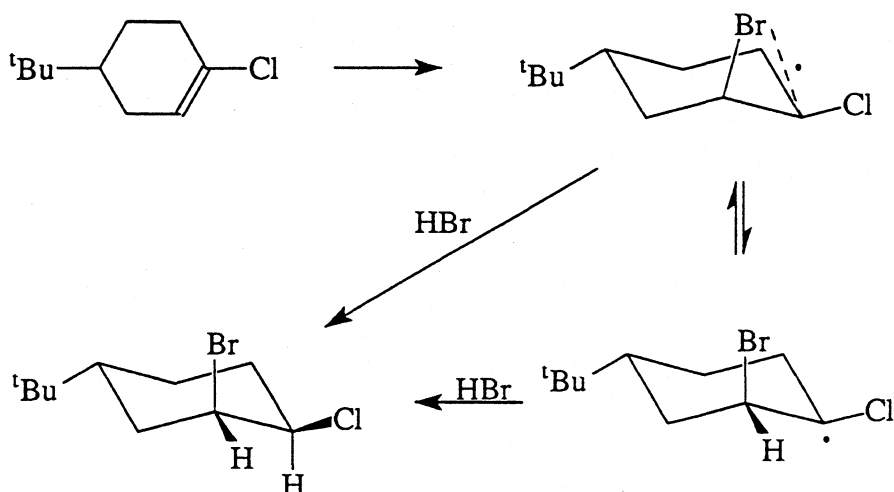
to the fact that axial attack produces a cyclohexyl radical having a chair conformation. Alternatively attack from the other side ('equatorial') direction, must give a twist-boat radical (higher energy) intermediate. The energy difference between these two conformations is reflected in the varying rates of formation of these two intermediates (scheme 39). They suggest therefore that torsional effects determine the preferred mode of addition. Reversibility of the thiyl addition step, they point out does however decrease the overall selectivity for addition (ca 2-4:1). The rate determining step in the radical addition of thiols to alkenes is recognised as being chain transfer[145]. Hence the nature of the product is governed by the rapidity of the addition of the hydrogen and this is facilitated by reduced steric crowding in the intermediate, i.e (92) [it is very likely that (91) is converted to the lower energy chair conformation (92), which would be more stable than (90)].

Following this rationalisation, attack from above the plane on C2 or below the plane on C1 of (70) leads to the energetically unfavourable twist-boat conformer[166] (ultimately equatorial addition). Alternatively attack from above on C1 or below on C2 produces the more favourable chair conformation, leading to axial addition (see scheme 40). This is a possible explanation for the preference of axial addition by benzoyloxyl radicals.

Chapter Five

Scheme 39

a-axial addition
e-equatorial addition
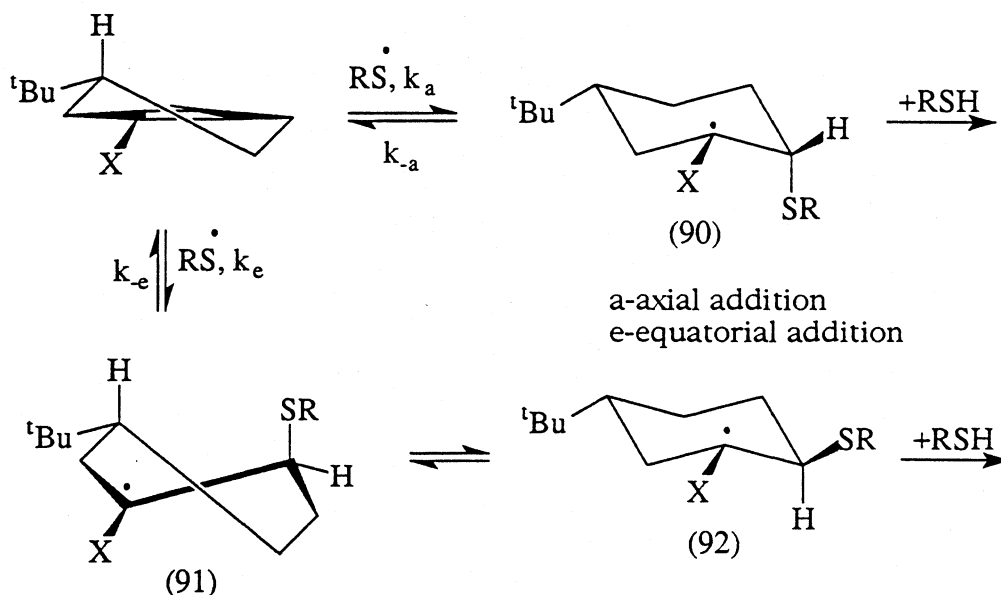
However as Bottle[164] has pointed out, recent papers by Tedder[140,158] remind us how small the effects of resonance stabilisation are, on the rate of radical formation, compared to steric and polar factors in radical reactions. In support of this the addition of acyloxyl radicals to alkenes is suggested[142] to be strongly exothermic, as the C-O bond being formed(~359 kJ mol^{-1}) is

Scheme 40
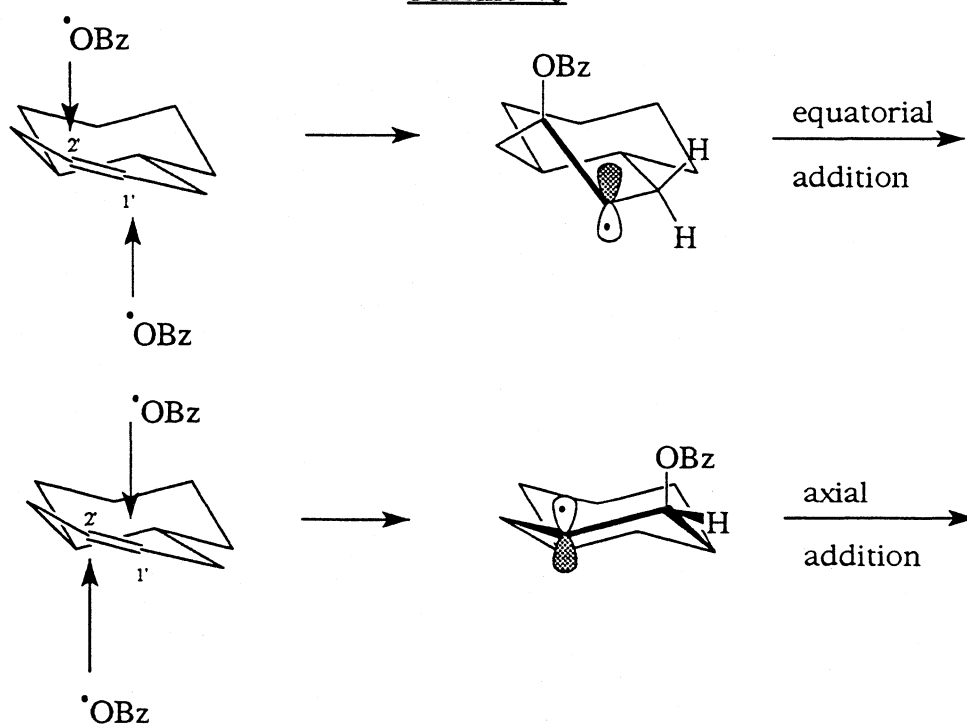
much stronger than the π bond being broken (-263 kJ mol^{-1}). For such exothermic additions, according to the Hammond postulate[167] the transition state should lie early on the reaction coordinate, where the partial bonds are still long. Hence the stability of the cyclohexyl radical intermediate is indicated as having little effect in determining the preferential attack (axial:equatorial) by the benzoyloxyl radical. Bottle et al.[142] cite evidence for this early transition state, coming from the reaction of styrene with benzoyloxyl radicals. In this reaction a good percentage of the head addition product was obtained, demonstrating that adduct radical stability (primary versus secondary benzylic) did not affect in any appreciable way the addition process. In contrast, bromine and thiyl radical addition will have a later transition state, resulting in higher stereoselectivity and therefore torsional effects should predominate over steric effects to control the preferred mode of addition.

Another process that could have bearing on the axial:equatorial ratio is 1,2-benzoyloxy migration (scheme 41). These rearrangements are well known[168], and have been suggested by LeBel et al.[145], but shown to be unlikely for thiol-acetoxy additions to cyclohexenes. Giese et al.[168] have also shown that acyloxyl migrations do not occur in 1,3-dioxolan-2-yl radical ring

Scheme 41
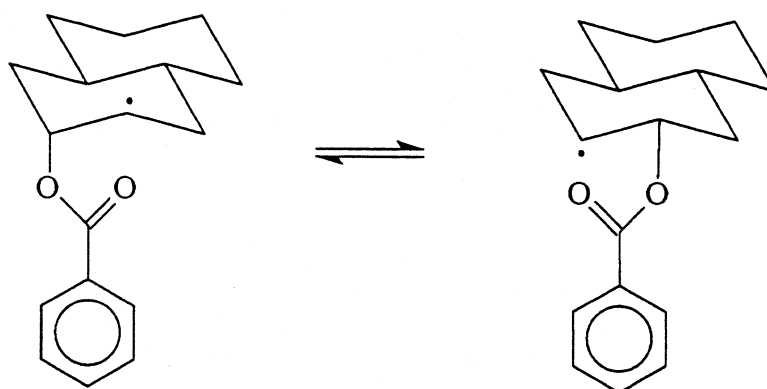
systems. These group migrations are reported as occuring at quite slow rates ($k = 10^2$-10^4 s^{-1} at 75°C)[169,170]. This rate of migration is however much slower than tha almost diffusion controlled rate ($k_T = 10^8$-10^9 M^{-1} s^{-1})[172] at which the radical trapping process occurs under these reaction conditions. Therefore, this migratory process would not be expected to compete under these reaction conditions. Further evidence that benzoyloxy group migration

is unlikely to be occuring here, are the results from non-acyl radical additions to cyclohexenes[144,145,171,172], where very similar results to that with acyloxyl radicals were obtained. It seems therefore that 1,2-benzoyloxy group migrations would not be contributing here to the preferential axial addition by benzoyloxyl radicals to trans-Δ^2-octalin.

The most likely explanation for this preference of axial addition, is based upon steric interactions between the pseudo-axial hydrogens H_a and H_b and the incoming benzoyloxyl radical (figure 28).It is suggested that this modest steric effect controls the orientation of addition. Addition to C1 from below the plane and addition to C2 from above the plane results in 1,2-hydrogen/benzoyloxyl radical eclipsing interactions, i.e unfavourable steric repulsion. Bordwell et al.[173] and Bottle et al.[142] have also shown the importance of steric approach factors. This implies then that attack occurs

Figure 28

1,2-eclipse

1,2-eclipse
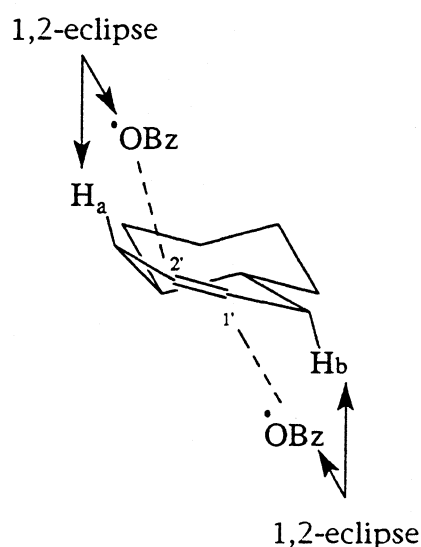
not because this is activated over equatorial attack but rather that equatorial addition is sterically impeded, i.e deactivated.

Interestingly, no phenyl trap(72) was isolated from this reaction (phenyl radicals were evidently not produced by the decomposition of benzoyloxyl radicals). This seems to indicate that the rate of addition by benzoyloxyl radicals to the double bond of trans-Δ^2-octalin(70) proceeds at a rate faster than the rate of decomposition of the benzoyloxyl radical at 60°C[#].

[#] It should be noted that although (72) was not observed under the reaction

5.1.2 The Aminoxyl radical trapping step

Scheme 37 shows that the stereoselectivity of trapping by the aminoxyl and of addition by the benzoyloxyl radical together determine the overall stereochemistry of the products formed. When the benzoyloxy group is axial, axial trapping by (10) is favoured (7.4:1.0). Interestingly though, when the benzoyloxy group is equatorial, equatorial trapping by (10) is favoured over axial trapping (2.3:1.0). This value is virtually identical to that reported by Bottle et al[142] for 4-t-butylcyclohexene when the benzoyloxy group is equatorial (equatorial:axial, 2.2:1.0). They also report a ratio for overall trans:cis addition of 4.4:1.0 for 4-t-butylcyclohexene and 4.3:1.0 for cyclohexene in acetone. Both these figures are in exceptionally good agreement with the present results for trans-Δ^2-octalin in acetone (4.4:1.0).

Both steric and torsional affects are known[142,156] to determine the preferred attack on the cyclohexyl radical. Examining steric factors, it becomes obvious (figure 29) that in the radical adduct, trapping by (10) is least hindered when approach is from above, which leads to equatorial trapping. Whereas trapping axially (approach from below the ring) is hindered by 1,3-steric interactions with the axial hydrogens. While this

Figure 29

Axial addition   **Equatorial addition**

Less hindered   More hindered   Less hindered   More hindered

---
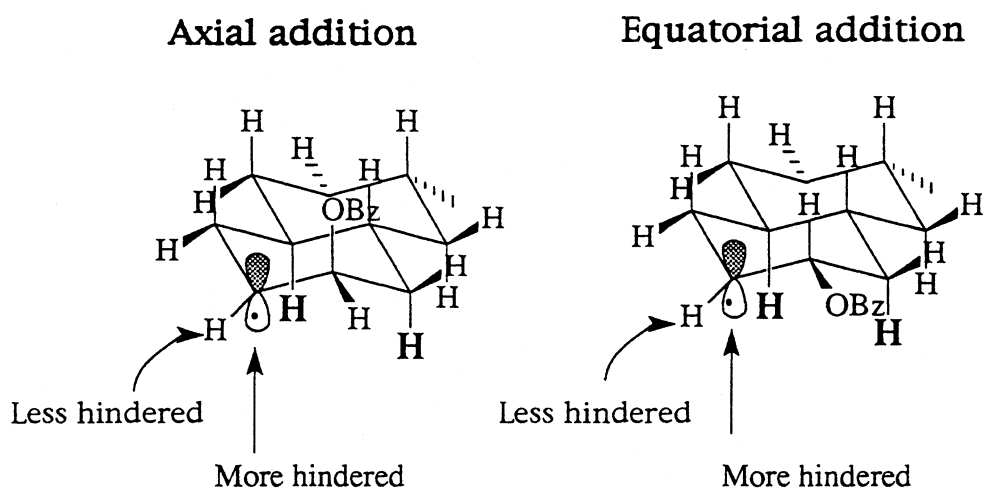
conditions reported here, it is not a very stable compound and may well have decomposed; i.e some fragmentation of benzoyloxyl radicals may have occured although no evidence for phenyl radical formation was obtained.

is a reasonable explanation when the benzoyloxy group is equatorial as preferred trapping by (10) is also equatorial ((86):(87), 2.3:1.0) it seems that other factors overide this effect when the benzoyloxy group is axial.

When the benzoyloxy group is axial and the aminoxyl approaches in such a way as to produce equatorial trapping(85), a 1,2-eclipsing interaction occurs (figure 30). Along with this unfavourable 1,2-eclipsing interaction encountered with equatorial trapping is the likewise unfavourable dipolar repulsion that would be experienced when this synperiplanar conformation was forming in the transition state (figure 31). This effect of dipolar repulsion it seems would also enhance the preference for equatorial trapping when the benzoyloxy group is equatorial. Attack from above the ring leading to axial trapping would result in a synclinal-transition state where dipolar repulsion would be experienced. Whereas attack from below

Figure 30

1,2-eclipse
(unfavourable)
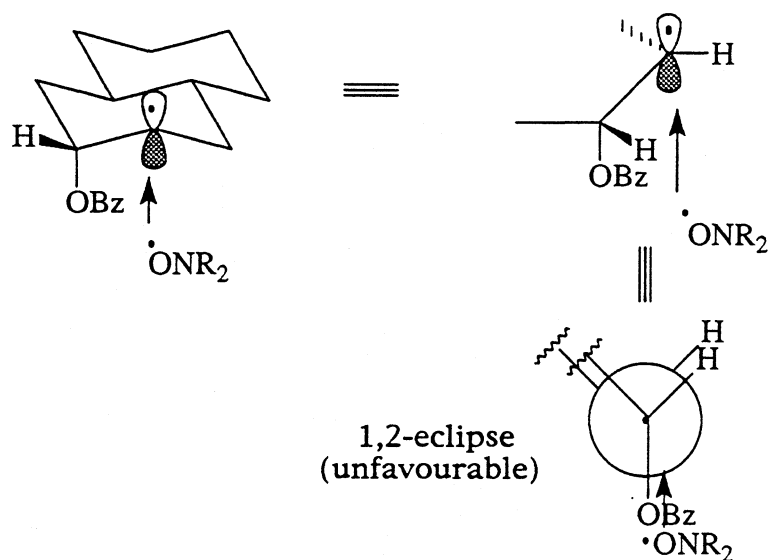
the plane leading to equatorial trapping results in an anti-clinal conformation, where little dipolar repulsion would be experienced (figure 33). It seems reasonable then that these two factors namely, 1,2-eclipsing and 1,2-dipolar repulsion explain the preference for axial trapping by (10) when the benzoyloxy group is axial. These two factors overide the 1,3-diaxial steric interaction.

133
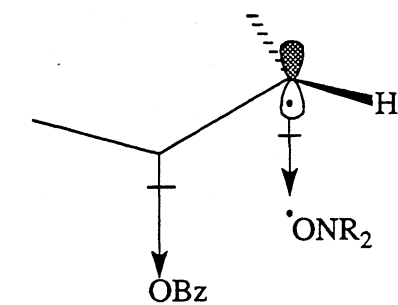
Figure 31

Synperiplanar conformer

Figure 32

(axial trapping)
ONR₂

(equatorial trapping)

axial

Synclinal conformer

equatorial

Anticlinal conformer
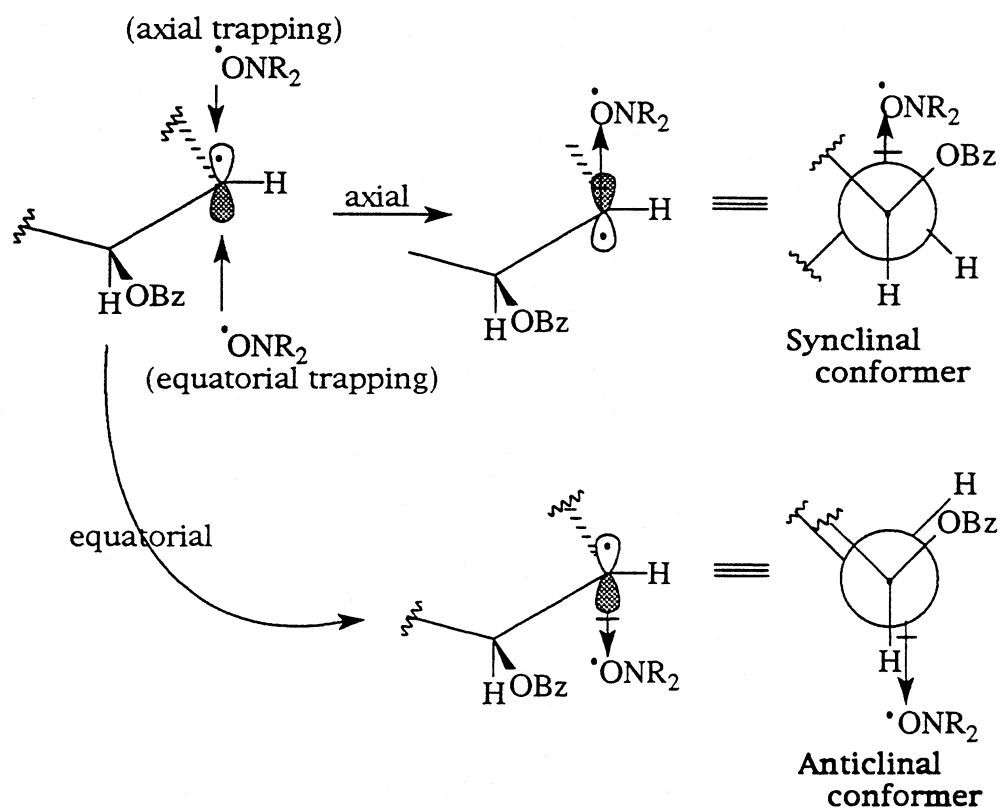
5.1.3 Acetone as Cosolvent

It is known[31,174] that the aminoxyl (10) induces the decomposition of benzoyl peroxide. This results in oxidation of the aminoxyl to the oxoammonium benzoate (93), and production of benzoyloxyl radicals (scheme

43). Product (93) may then undergo fragmentation to give the unsaturated nitroso compound (94) and benzoic acid. The nitroso compound (94) may then undergo further reactions[175] such as trapping radical species in competition with the aminoxyl (10). This is known to result in very complex mixtures of reaction products[31], making HPLC analysis difficult.

However employing acetone as a cosolvent in the reaction has been shown[31] to eliminate these nitroso side reactions. Acetone reacts rapidly with the oxoammonium benzoate to give quantitatively the acetone-trap product (82), plus benzoic acid (see scheme 44).

Scheme 43

(71)

(10)

(Benzoyloxyl radical)

(93)

PhCO$_2$

(94)

PhC—OH
(Benzoic acid)
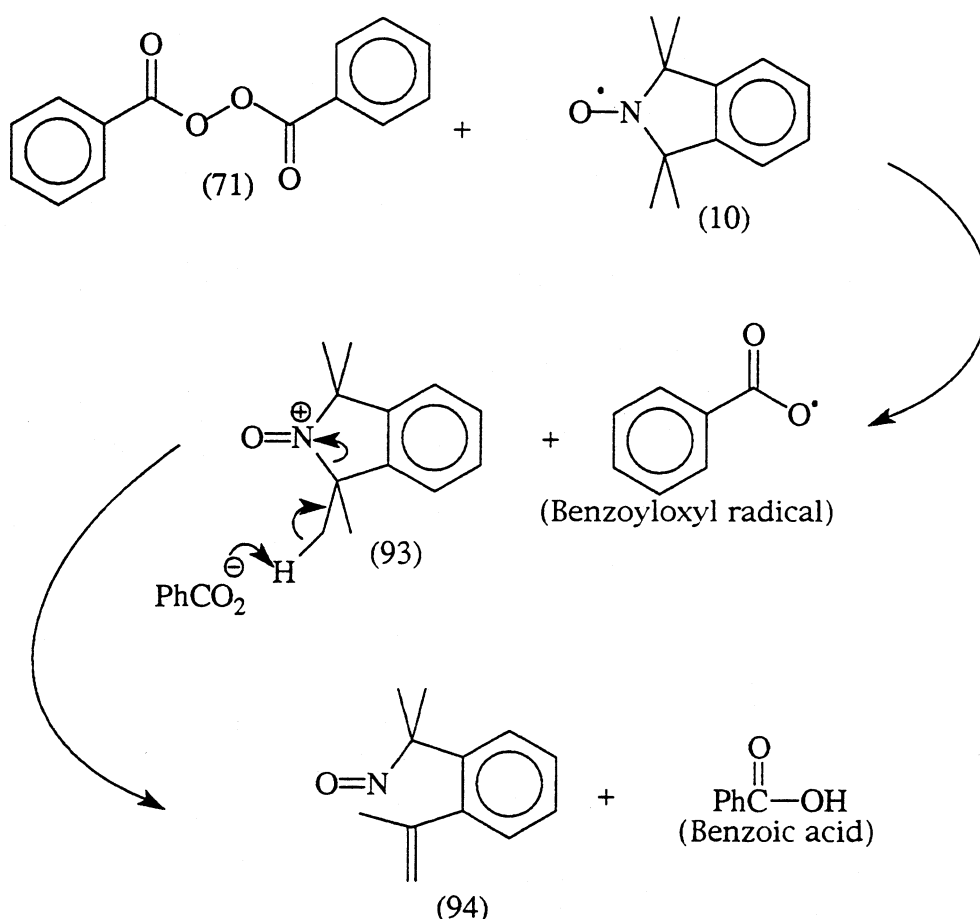
Compound (82) was isolated from the reaction of trans-Δ^2-octalin with benzoyloxyl radicals in contrast to the reactions by Bottle et al.[142] on cyclohexene and 4-t-butylcyclohexene, where (82) was reportedly not produced. So the aminoxyl (10), did, in the present study with trans-Δ^2-

octalin, induce some decomposition of benzoyl peroxide and this reaction occurs in competition with simple thermolysis of benzoyl peroxide (71).

<u>Scheme 44</u>

(93) → Acetone → (82) + PhC—OH (Benzoic acid)
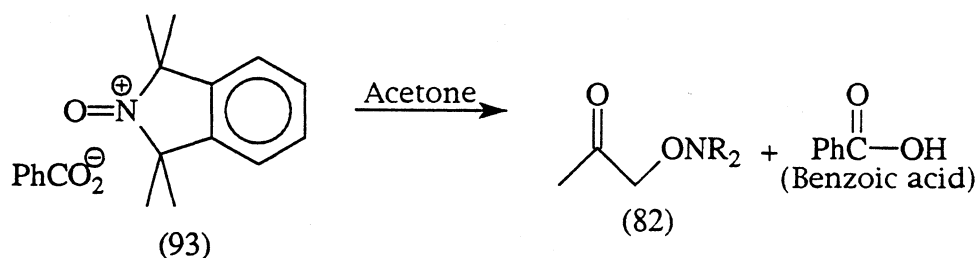
The ratio of total addition products (85)-(88) to the acetone-trap (82) was 3.9:1.0. This implies that aminoxyl decomposition versus thermal decomposition of benzoyl peroxide is occuring at a rate ratio of 2.0:2.9 respectively. The rate of aminoxyl (10)-induced decomposition of benzoyl peroxide is known to be polarity, solvent, and viscosity dependent[176].

5.2 Conclusion

Axial addition of the benzoyloxyl radical to trans-Δ^2-octalin is favoured over equatorial addition with modest selectivity (axial:equatorial, 3:2), probably as a result of steric factors. Trapping of the resultant radical by (10) however has greater selectivity, with a trans:cis ratio of 4.4:1.0 being obtained. Both steric and polar factors are suggested as being responsible for this preference.

This study shows that the aminoxyl 'radical trapping' technique, employing (10), is a very useful tool to obtain quantitative stereochemical information about radical addition reactions.

CHAPTER SIX

EXPERIMENTAL

Apparatus used for the synthesis of Aminoxyl Trap

Chapter Six

6.0 General

6.0.1 Solvents

Common solvents were distilled through a vacuum-jacketed column (2 x 40cm) filled with Fenske helices. Methanol (AR grade) was distilled through a vacuum-jacketed column (2 x 55cm) fitted with a reflux ratio head, and filled with Fenske helices. The distilled methanol was then filtered through 0.22μm millipore filters before use on the HPLC system. Distilled water was combined with the filtered methanol in varying proportions and re-filtered through 0.22μm millipore filters. Absolute ethanol (AR grade) was purchased from M & B Australia Pty. Ltd., and used without further drying or purification, unless otherwise stated. Acetonitrile (UNICHROM) HPLC grade was used as purchased.

6.0.2 Evaporation

Organic solvents were evaporated on a Buchi rotary evaporator under water pump reduced pressure. This was carried out at temperatures less than 40°C. Final traces of solvents were removed on a high vacuum line system (~0.1 Torr).

6.0.3 Melting Points

Melting points were determind on either a Buchi "Tottoli" silicone oil-bath melting point apparatus or a Gallenkamp electronic melting point machine, and are uncorrected.

6.0.4 Spectra
6.0.4.1 Infra-red Spectra

Infra-red spectra were determind on a Jasco IR-810, or on a Perkin Elmer 1600 series FT-IR spectrophotometer. For solids, KBr disks were used, for oils and liquids smears on NaCl disks were used. Spectra were calibrated against a standard polystyrene film.

6.0.4.2 Ultra-violet Spectra

Ultra-violet spectra were run in methanol (HPLC grade) on either a Varian series 634 or Hitachi series u-3200 spectrophotometer.

6.0.4.3 Nuclear Magnetic Resonance Spectra

^{1}H and ^{13}C n.m.r. spectra (proton noise decoupled; off resonance decoupled) were recorded by the author using as indicated either a Bruker WM-250 spectrometer at 250.12MHz and 62.80MHz, respectively or a Bruker CXP-300 spectrometer at 300.06MHz and 75.46MHz, respectively. ^{31}P n.m.r. spectra were recorded on the Bruker CXP 300 spectrometer at 121.5MHz, relative to 85% phosphoric acid. Tetramethyl silane (TMS) was used as the internal standard, chemical shifts are reported in δ(ppm) relative to TMS. Deuterated solvent for n.m.r. was $CDCl_3$ unless otherwise stated. Where necessary proton decoupling experiments were performed to confirm assignments.

The following abbreviations are used to describe signals:

s	singlet
d	doublet
t	triplet
q	quartet
dd	doublet of doublets
dt	doublet of triplets
dq	doublet of quartets
ddd	doublet of doublets of doublets
m	complex multiplet, no coupling information
brs	broad singlet
vbrs	very broad singlet

The attachment of the nitroxide trap(10) to a primary carbon atom resulted in the observance of a broad hump in the proton spectra for the isoindoline methyl groups. For the ^{13}C n.m.r spectra of alkoxyamines, the four methyl carbon atoms also occur as a broad hump and are often barely discernible in spectra recorded at room temperature[27]. However when attached to a chiral carbon the isoindoline methyl protons occured as three or four sharp signals. This is believed to be due to slow nitrogen inversion and N-O bond rotation in these compounds[177].

6.0.4.4 Mass Spectra

Low resolution and high resolution mass spectra were recorded by Dr Greame M^{ac} Farlane at the Organic Mass Spectrometry unit in the Chemistry department of The University of Queensland on a Kratos MS 25RFA mass spectrometer. High resolution mass spectra were obtained when products were unstable, non-crystalline or obtained in small quantities. Unless otherwise stated these compounds were shown to be pure by n.m.r spectroscopy and HPLC.

6.0.4.5 Chromatography
6.0.4.5.1 Thin-layer Chromatography (TLC)

TLC was performed on glass slides (20 x 70mm) which were coated with Merck GF $_{254}$ silica-gel, or on aluminium sheets (Merck) coated with aluminium oxide 60 F$_{254}$. Spots were detected by U.V. fluorescence (chromatavue model CC20-ultra-violet Products Inc) and/or with iodine vapour.

6.0.4.5.2 Silica Column Chromatography

Liquid column chromatography on silica-gel was carried out routinely in glass columns fitted with teflon taps or glass scinters using Merck Kieselgel-60 (70-230 mesh). Basic or neutral alumina (activity 1) from Waelm or Ajax chemicals were also used in some instances.

6.0.4.5.3 Reverse Phase High Pressure Liquid Chromatography

Analytical HPLC runs were carried out with either an analytical Rainin Instruments Dynamax-60A 8μm 250 x 4.6mm C$_{18}$ column, or a semi-preparative Whatman Partisil 10-ODS-3 500 x 10mm C$_{18}$ column. Either an ETP Kortec K35M dual piston HPLC pump or an ICI LC1110 HPLC pump was coupled to the column. The output of the column was then coupled to either a Soma S-310A-11, ETP Kortec K95 or an ICI LC1200 variable wavelength UV/Vis detector set at 270nm. The columns were protected with Uptight 2cm guard columns (filled with Whatman 30-38μm glass beads coated with C$_{18}$ groups) and an in-line solvent filter (fitted with a 0.5μm PTFE frit).

Preparative isolation of reaction products was carried out using a reverse phase Ranin Instruments Dynamax-60A 8μm 250 x 21.4mm C$_{18}$ preparative

column. In the cases of vinyl acetate and acrylonitrile preparative isolation was carried out on an Altec Ultrasphere ODS Semi-preparative column. Compounds were detected by either an ICI LC1200 or Soma (fitted with a 1mm preparative cell) UV/Vis detector. Solvents were pumped by either a Gilson 330 pump fitted with a 25ml/min preparative head and a 803c manometric module or by the ICI LC1110 pump. Solvents were pumped at pressures less than 2000p.s.i.

Isolated products were futher purified by passing through a preparative Dynamax-60A column with solvent of a higher percentage water, and/or slower flow rates.

6.0.4.6 Microanalysis

Microanalyses were carried out by the Microanalytical service, Department of Chemistry, University of Queensland, or by the Australian Microanalytical Service, National Analytical Laboratories, Pty, Ltd, Melbourne.

6.0.4.7. X-Ray Crystal Structure Determination

X-Ray crystal structure determination was carried out on a ENRAF-NONIUS CAD-4, four circle computer-controlled diffractometer, by Professor Colin Kennard, Dr Karl Byriel and Mr Daniel Lynch in the Small Molecule X-Ray Crystal Structure Laboratory, Department of Chemistry at the University of Queensland.

6.1 Purification of Monomers

Acrylonitrile was fractionally distilled through Fenske helices and then stored over 4Å sieves.

Benzene was obtained from Aldrich as HPLC grade and stored over sodium wire under N_2 gas.

Butadiene was obtained from Aldrich as 99% + and used as was.

Cyclohexene was obtained from Aldrich and distilled fractionally through helices then strored over sodium wire.

Cyclopentene was obtained from Aldrich and distilled fractionally through helices, then stored over sodium wire.

3,4-Dihydro-2H-pyran was obtained from Aldrich as 99%, then dried over $MgSO_4$ followed by refluxing over $LiAlH_4$, followed by fractional distillation through helices and then stored over 3Å sieves.

Diphenylphosphine was obtained from Aldrich and used without further purification.

Dimethyl phosphite, obtained from Aldrich as 99%, was dried over molecular sieves and kept from the light.

Maleic anhydride was recrystallised twice from AR grade chlorform. (Mpt-54-56°C. Lit Mpt-54-56°C[178]).

Phenyl acetylene was obtained from Aldrich as 98% pure and used without further purification.

Styrene was obtained from Aldrich, passed twice through a short column of neutral alumina (activity 1) then distilled under reduced pressure (B.pt 40°C/16 mmHg).

Tetracyanoethylene was obtained from Aldrich, purified by recrystallisation from Ar grade chlorobenzene (Mpt-199-202°C. Lit Mpt-197-199°C[178]).

Vinyl acetate was fractionally distilled through Fenske helices and then stores over 4Å sieves.

6.2 Synthesis of Monomers

6.2.1 Trans-Δ^2-Octalin(70)

6.2.1.1 Cis-5,8,9,10-tetrahydro-1,4-napthoquinone(95)

This compound was synthesised via the general method of Henbest et al.[193]

(95)
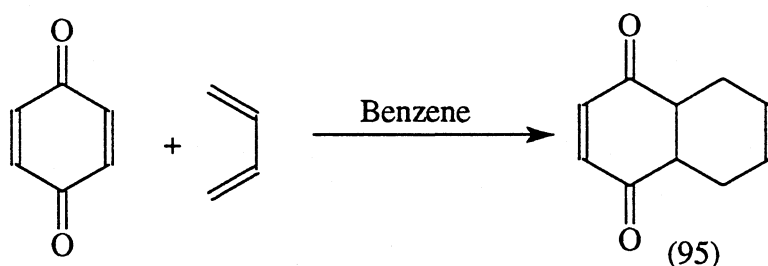
p-Benzoquinone (100g) and benzene (dried over CaCl$_2$, fractionally distilled and then stored over 3Å sieves, 720ml) were combined, flushed with nitrogen then frozen in ethanol/dry-ice bath. 1,3-Butadiene (100g) was then condensed into the flask, the flask then sealed and kept at approximately 20°c for 18 days. The solution was then filtered, the solvent removed, and the residue recrystallised from hexane/benzene, to give the diketone (95)(101g, 67%, Mpt-57°C. Lit Mpt-58°C[179]).

This material was also synthesised according to the procedure of Ramo Rao et al.[180]; this however produced dismally low yields.

In line with the reported[181] successful use of 3-sulfolene instead of 1,3-butadiene, this reaction was attempted with 3-sulfolene. Eliminating the use of butadiene gas would certainly have been advantageous. However, over a range of solvents, temperatures and reaction times 5,8-dihydro-1,4-naphtho-hydroquinone(96)(Mpt 207-210°C. Lit Mpt 208-209°C[182]) was obtained in very good yield on each occasion.
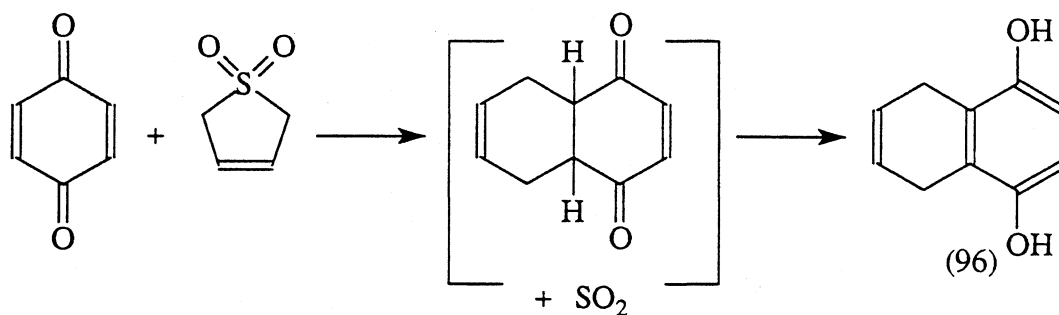
6.2.1.2 cis-2,3,5,8,9,10-Hexahydro-1,4-naphtho-quinone

The procedure of Johnson et al.[183] was followed in the synthesis of this compound.
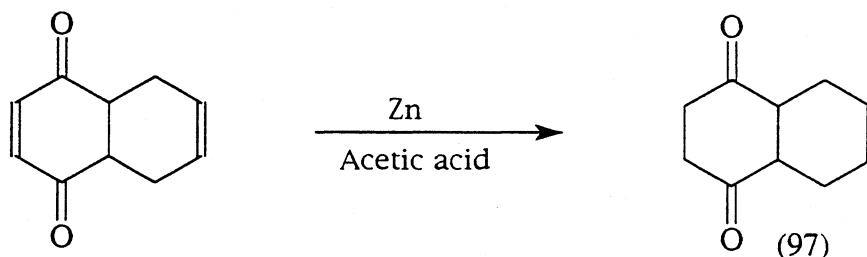
A solution of 43.1g (0.26moles) of cis-5,8,9,10-tetrahydro-1,4-naphthoquinone(95) in 500ml of acetic acid (99%) was treated with small portions of Zn dust (AR-Mallinchrodt). The temperature of the reaction which was exothermic was kept below 25°C (majority of the time- below 10°C) with an ice/rock-salt bath. Addition of Zn continued until the temperature ceased to rise upon its addition. Then acetone (500ml) was added and the mixture allowed to stir for one hour. The suspension was then filtered through filter aid and the solvent removed under vacuum. The solid residue was taken up in chloroform, and washed with aqueous sodium bicarbonate and water. The organic layer was then dried over $MgSO_4$. Removal of the solvent at reduced pressure afforded the title compound(97)(38g, 87%, Mpt 98.9-101.8°C. Lit Mpt 108°C[184]).

6.2.1.3 Δ^2-Octalin Mixture(98)

The Huang-Minlon modification of the Wolff-Kishner reduction procedure was employed[185].
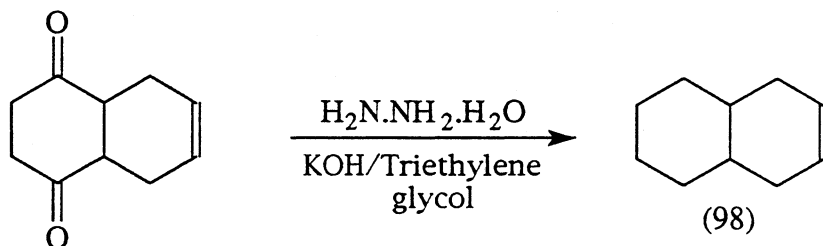
A solution of cis-2,3,5,8,9,10-hexahydro-1,4-naphthoquinone(97)(21g, 0.128 moles) and KOH pellets (23.3g) in 200ml of ethylene glycol was swirled for 5 minutes. Then 29.2ml of hydrazine hydrate was added and the mixture was refluxed for 1.5 hours. The temperature was then gradually raised (170-190°C, destroys the hydrazine hydrate), and the distillate which separated into two layers, was collected in a water separator, diluted with water and extracted with ether. The ether layer was then dried over MgSO4. Removal of the solvent followed by distillation afforded (26.2g, 83%) a colourless liquid(98), bpt-80°C, 20mm/Hg. Lit bpt 80°C-20mm/Hg[183]).

6.2.1.4 Trans-Δ^2-Octalin Dibromide(99)

Bromine(30.6g) in 40 ml of dry chloroform was added dropwise with stirring and ice-bath cooling to a solution of crude Δ^2-Octalin mixture(98) (26.2g) in 60ml of chloroform. The solution was then diluted with 80ml of chlorofrom, extracted with 50ml of 10% aqueous sodium bisulfite, washed with water , and dried over anhydrous magnesium sulfate. Solvent was then removed at reduced pressure and the residual material was allowed to crystallize in the freezer. Recrystallization from absolute ethanol yielded 14.5g of colourless crystals(99)(m.pt 83.5-84°C. Lit m.pt 85°C[183]. Yield of 26%).

(99)

(Removed by recrystallisation)
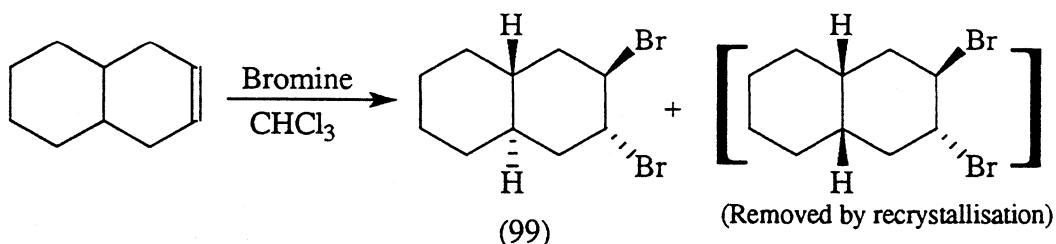
6.2.1.5 Trans-Δ^2-Octalin(70)

This compound was synthesised following the procedure of Johnson et al.[183]

H

Br

$\underset{\text{Absolute ethanol}}{\xrightarrow{\text{Zn}}}$

H

(99)

(70)
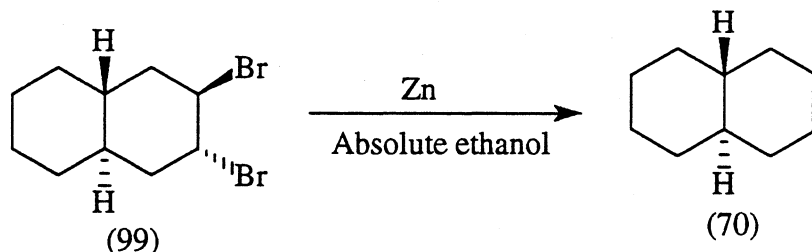
To a slurry of zinc dust (25.6g) in 130ml of absolute ethanol was added trans-Δ^2-Octalin dibromide(99)(14.5g). The mixture was then stirred at room temperature for 90 minutes and at 65^0C for 150 minutes. Ether (90ml) was added, the mixture was filtered through filter-aid, and the filter cake was then washed with ether(50ml). The filtrate was washed with water and saturated salt solution, then dried over $CaCl_2$. Solvent was removed at reduced pressure and the residual yellow liquid was fractionally distilled affording 4.5mls of colourless liquid(70)(b.pt 47^0C(3.5mmHg), n_D^{25} 1.481. Lit b.pt 59^0C[183](8 mmHg), n_D^{25} 1.479).

6.2.2 4-t-Butyl-1-cyanocyclohexene(46)

6.2.2.1 4-t-Butylcyclohexanone cyanohydrin(100)

This compound was synthesised from 4-t-butylcyclohexanone, via the method of Abramovitch and Struble[186].

Concentrated HCl (29.2ml) was added dropwise to a cooled(10^0C) mixture of 4-t-butylcyclohexanone(20g) and powdered NaCN(96%, 9.8g) in ether(47ml) and water(10ml). Stirring at 0^0C was continued for 150 minutes after which the ether layer was decanted and washed with saturated $NaHSO_3$(2 x 50ml) and dried over $MgSO_4$. Evaporation of the solvent gave the cyanohydrin as an oil, which cyrstallised on cooling to give 10.8g(100) (M.pt 53-56^{0}C. Lit M.pt 53-54^{0}C[187]).

=O $\underset{\text{NaCN}}{\xrightarrow{\text{HCl}}}$ OH CN

(100)
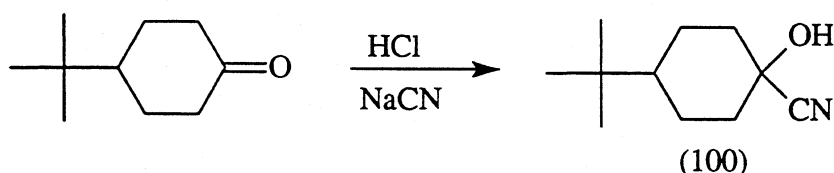
6.2.2.2 4-t-Butyl-1-cyanocyclohexene(46)

This compound was synthesised using phosphorus oxychloride via the method of Wheeler and Lerner[188].
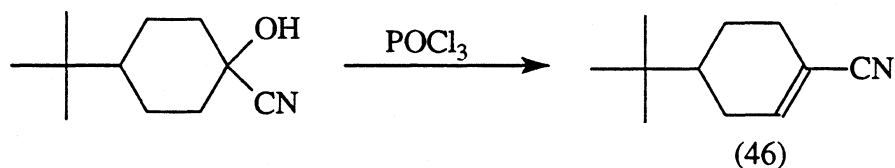
To a vigorously stirred solution of 4-t-butylcyclohexanone cyanohydrin(100)(10.8g) in pyridine (15ml) and benzene(15ml) at 0^0C, was added a solution of $POCl_3$(19.5ml) in pyridine(18ml) dropwise. A white precipitate separated. The mixture was then heated slowly and eventually boiled under reflux for 35 minutes. The wine/orange coloured solution was poured onto ice(300g), extracted with ether(3 x 50ml) and combined extracts dried over $MgSO_4$. Evaporation of the solvent gave 4-t-butyl-1-cyanocyclohexene as an oil which solidified in the freezer(-30^0C). Two recrystallisations from ethanol afforded colourless crystals(46)(6.71g, M.pt 45.5-46.9^{0}C. Lit M.pt 45-46^{0}C[188]. IR spectrum(NaCl disc): 2200(m), 1632(m) and 1365cm^{-1}(s). IR spectrum(KBr disc): 2200(m), 1632(m) and 1365cm^{-1}(s)[188].

6.3.0 Preparation of radical precursors

6.3.1. Di-t-butylperoxyoxalate(DTBP)

DTBP was prepared from t-butyl hydroperoxide and oxalyl chloride following the procedure of Bartlett et al.[23](65% yield, M.pt 51-52^{0}C(dec), Lit M.pt 50.5-51.5^{0}C[23]).
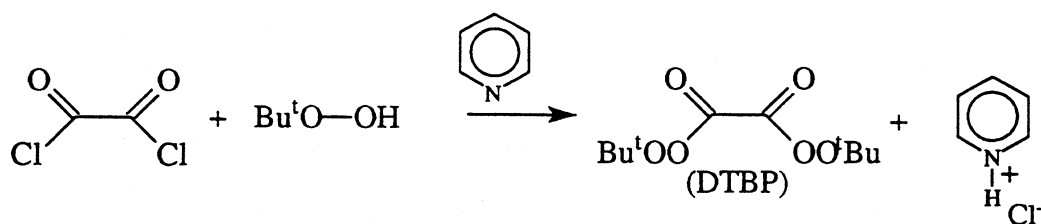
6.3.2. Benzoyl peroxide

This commercially available material which was stabilised with water was purified by recrystallising twice from chloroform/methanol(1:1). (M.pt 106-107^{0}C. Lit M.pt 104-106^{0}C[178]).

6.3.3 Diphenylphosphine oxide

Diphenylphosphinous chloride(30g, 25.12ml) in carbon tetrachloride (150ml) was treated with water(2.5ml, added dropwise over 90 minutes) under nitrogen. The mixture was stirred at room temperature for a further 6 hours and allowed to stand overnight. The white, precipitated solid was removed by filtration and dissolved in chloroform. The solution was extracted with NaHCO$_3$, washed with water, dried and evaporated to leave an oil which solidified after being left in the fridge for several hours. This crude product was recystallised from ether to afford 19.2g (70%, M.pt 53-56^{0}C. Lit M.pt 53-56^{0}C[189]).

6.3.4 Tetraphenyldiphosphine oxide

Tetraphenyldiphosphine oxide was prepared according to the method of Quin and Anderson[190].

Diphenylphosphinous chloride(5g) in ether(25ml) was added over 45 minutes to a chilled(-10^{0}C) solution of N,N-diethylaniline(3.39g) and water(0.245g) in ether(30ml). The solution was stirred in air for 1 hour then over night under a drying tube and a further 90 minutes in air before filtering. The white solid was then washed with ether, then water and dried to yield 3.33g. The product contained some diphenylphosphinic acid, hence the solid was washed with NaHCO$_3$ solution then water and recrystallised from dry acetone(M.pt 166-169^{0}C. Lit M.pt 167-169^{0}C[190]).

6.4.0 Preparation of the Aminoxyl Radical Scavenger

6.4.1 1,1,3,3-Tetramethyl-2,3-dihydro-1H-isoindol-2-yloxyl(10)

(10)
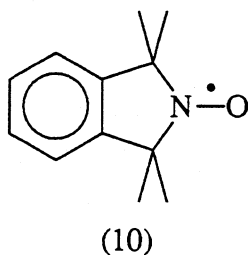
The title compound was synthesised via the literature procedure[191](M.pt 128-129^{0}C. Lit M.pt 128-129^{0}C[191]). Prior to use it was analysed by HPLC and shown to be of purity >99%.

6.4.2 1-Ethyl-1,3,3-trimethyl-2,3-dihydro-1H-isoindol-2-yloxyl(11)

(11)
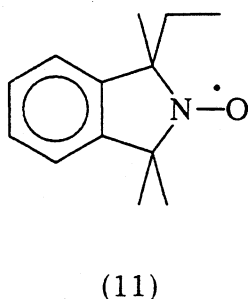
This compound was formed in about 2-3% yield during the preparation of compound (1)[191]. (M.pt 70-72^{0}C. Lit M.pt 71-73^{0}C).

6.4.3 1,1,3,3-Tetraethyl-2,3-dihydro-1H-isoindol-2-yloxyl(12)

(12)
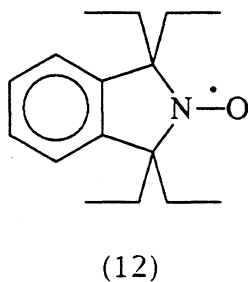
The title compound was prepared via the literature procedure[191](M.pt 54-55^{0}C. Lit M.pt 54.5-55.5^{0}C[191]).

6.4.4 2-Methoxy-1,1,3,3-tetramethyl-2,3-dihydro-1H-isoindol(22)

The title compound was prepared by utilising the literature procedure of Minisci et al.[192] whereby hydrogen peroxide was reacted with DMSO at room temperature in the presence of a ferrous salt catalyst to produce methyl
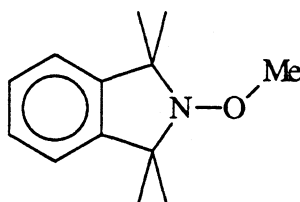
(22)

radicals, which in the presence of (10) were efficiently trapped in good yield(>90%) to produce the title compound(22).

6.5.0 General Procedure for Radical Trapping Experiments

An appropriate amount (at most 45% of the aminoxyl concentration) of the initiator was added to a solution of the aminoxyl in purified monomer or monomer/cosolvent (eg, benzene, acetonotrile, acetone). For the phosphorus radical experiments the appropriate phosphorus-bearing species was also included in this solution.

This solution was degased using repeated freezing/evacuating/thawing cycles (three cycles in general) on a high vacuum line, sealed in vacuo in glass vessels, then heated for a period of not less than 10 half lives at 60^0C (DTBP- 68 minutes, benzoyl peroxide-22 hours). The exceptions to this were the reactions involving 4-t-butyl-1-cyanocyclohexene(46)(see 6.10.2.5), vinyl acetate and acrylonitrile with dimethyl phosphite (see 6.10.1.5). In these reactions the aminoxyl trap(10), DTBP and appropriate cosolvent were injected over longer periods of time (by a motor driven syringe) to a heated solution (60^0C) of monomer and appropriate phosphorus-bearing substrate.

Analytical reaction mixtures were analysed by reverse phase HPLC using methanol/water for elution and UV detection at 270nm. Preparative reaction mixtures were concentrated by the removal of the majority of monomer (where the monomer was volatile) under reduced pressure, before isolation of the reaction products. Peak areas were determind by integration of the HPLC

chromatogram, then converted directly into relative yields for those products where only the aminoxyl contributes to the UV chromophore. Allowance for the differing chromophores was made by either determining the extinction coefficients(at 270nm), of these individual products, or by reinjection of solutions of known concentration to determine peak response ratios for the UV detector. The adjusted peak areas were converted into relative yields and normalised to 100%.

6.6 Characterisation of Alkoxyamine products by nmr.spectroscopy

^{1}H nmr and ^{13}C nmr spectroscopy were primarily used to elucidate the structure of the alkoxyamine products. The following are the spectral data of the isoindoline ring system for all the compounds isolated:

^{1}H nmr (ppm), δ 0.75-1.60, 4 x s, 12H, ring methyl protons; 7.05-7.15, m, 2H, H4, H7; 7.17-7.31, m, 2H, H5, H6.

^{13}C nmr (ppm) δ 25.0-30.0, ring methyl carbons; 67.0-70.4, C1, C3; 121.1-122.6, C4, C7; 127.1-127.6, C5, C6; 143.8-145.5, C3a, C7a.

6.7 The reaction of t-butoxyl radicals with Vinyl acetate and Acrylonitrile

A typical analytical scale reaction was:

DTBP(2.5mg, 1.068 x 10^{-5}moles)

Trap(10)(40.0mg, 2.136 x 10^{-4}moles)

Vinyl acetate(1.0ml, 1 equivalent)

Acrylonitrile(0.714ml, 1 equivalent)

Benzene(1.0ml-solvent)

Preparative reaction:

DTBP(234mg, 1.0 x 10^{-3}moles)

Trap(10)(400mg, 2.1 x 10^{-3}moles)

Vinyl acetate(2.0ml, 1 equivalent)

Acrylonitrile(1.43ml, 1 equivalent)

Benzene(2.0ml-solvent)

Reaction time: 68 minutes at 60^0C.

The reaction mixture was concentrated down to approximately 10%, under high vacuum and then separated via semi-preparative HPLC. Semi-preparative HPLC conditions: 75% methanol in water, flow rate-1.8ml/min. This produced the following compounds which were isolated and characterised as follows (in order of elution from the HPLC column).

Vinyl (1,1,3,3-tetramethyl-2,3-dihydro-1H-isoindolin-2-yloxy)acetate(23)
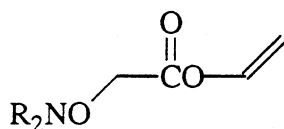
(23)

This material was identical to an authentic sample by HPLC and [1]H n.m.r.[80].

2-(1,1,3,3-Tetramethyl-2,3-dihydro-1H-isoindolin-2-yloxy)butyronitrile(26)

(Found: 258.173. $C_{16}H_{22}N_2O$ requires 258.173).

[1]H n.m.r.(CDCl$_3$, 250.122MHz, shifts in ppm, couplings in Hz):

1.30, 1.31, 1.46, 1.59, 4 x s, 12H,
4 x CH$_3$

7.01, m, 2H

1.91, ddq, 2H, ^3J,7.2, ^3J,6.3, ^2J,14.6

1.11, t, 3H, ^3J,7.2

7.17, m, 2H

4.55, t, 1H, ^3J,6.3

NC

N—O

CH$_3$

H

2-Methoxy-1,1,3,3-tetramethyl-2,3-dihydro-1H-isoindole(22)

R$_2$NO—CH$_3$
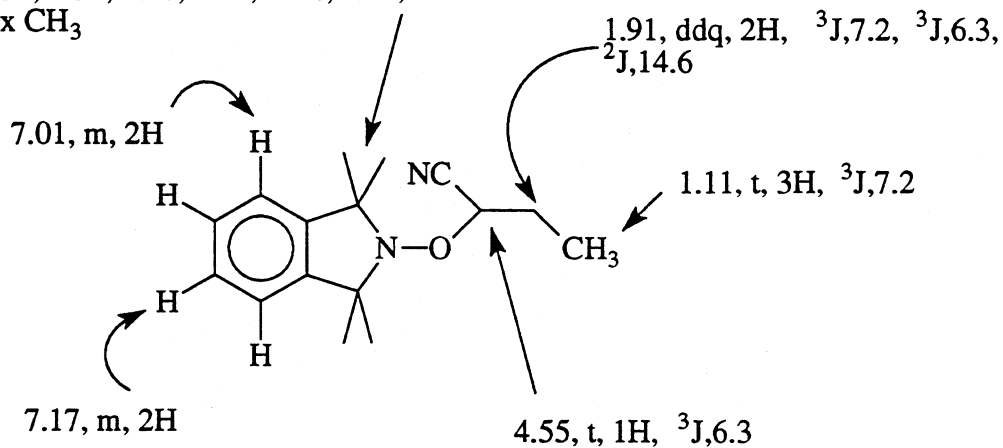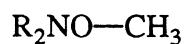
(22)

This material was identical to an authentic sample by HPLC and [1]H
n.m.r.[80].

Experimental

4-Acetoxy-5-t-butoxy-2-(1,1,3,3-tetramethyl-2,3-dihydro-1H-isoindolin-2-yloxy)pentyronitrile(28)*

(Found: 387.224. $C_{23}H_{34}N_2O_4$ requires 402.252. Loss of CH_3 requires 387.228).

^{1}H n.m.r(CDCl$_3$, 250.122MHz, shifts in ppm, couplings in Hz):
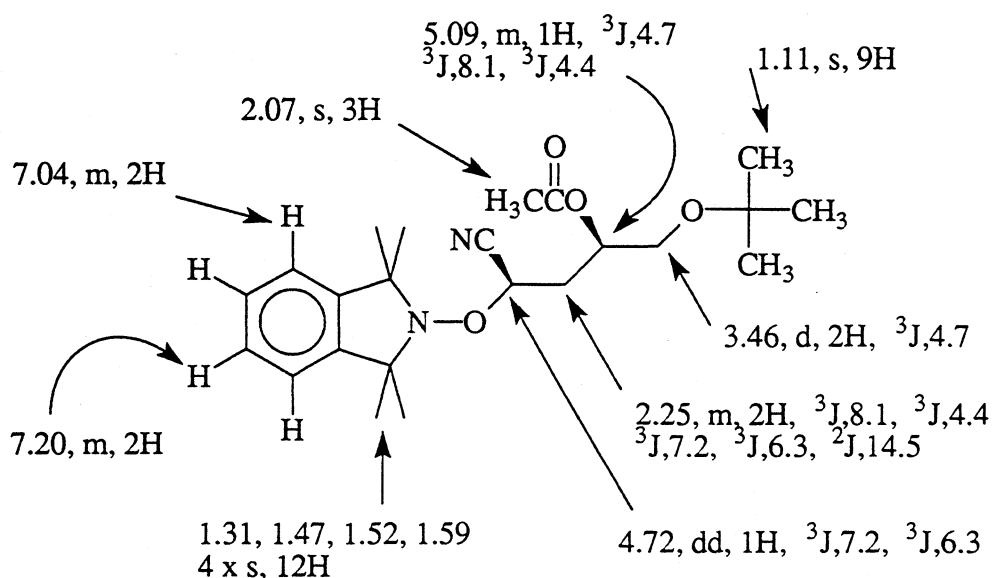
^{13}C n.m.r.(CDCl$_3$, 62.8MHz, shifts in ppm)$^{\#}$:

---
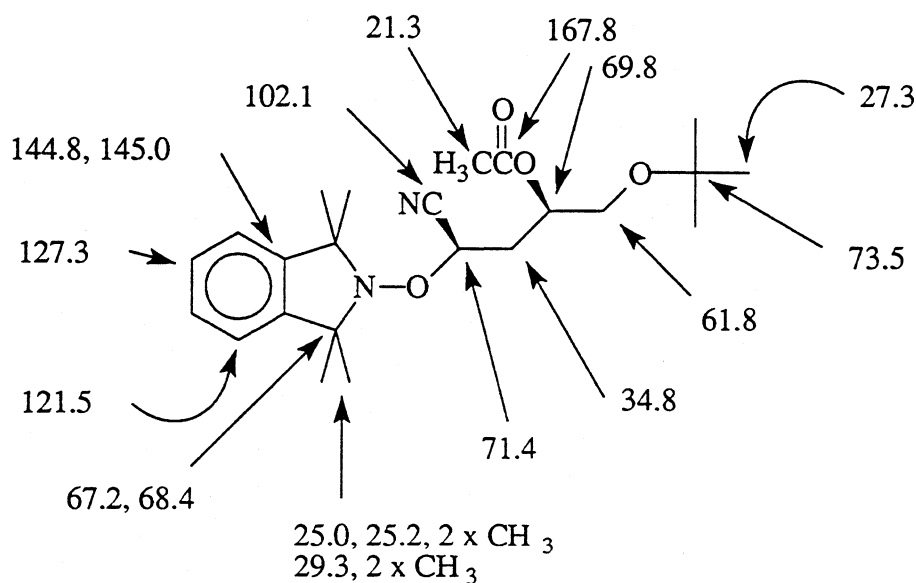
* It was not possible to distinguish unequivocally between the two diastereomers((28) & (29)), therefore these assignments should be regarded as tentative and may be reversed.

The shifts at 69.8 & 71.4ppm are tentative and therefore are interchangeable.

4-Acetoxy-5-t-butoxy-2-(1,1,3,3-tetramethyl-2,3-dihydro-1H-isoindolin-2-yloxy)- pentyronitrile(29)

(Found: 387.224. $C_{23}H_{34}N_2O_4$ requires 402.252. Loss of CH_3 requires 387.228)..

^{1}H nmr(CDCl$_3$, 250.122MHz, shifts in ppm, couplings in Hz):

5.14, m, 1H

1.12, s, 9H

2.05, s, 3H

7.03, m, 2H

CH_3

O

H_3CCO

NC

O—C—CH$_3$

CH$_3$

H

H

N—O

H

H

3.39, 2x dd, 2H, ^{3}J,4.4, ^{2}J,9.8, ^{3}J,5.7

7.19, m, 2H

2.26, m, 2H, ^{3}J,7.3, ^{3}J,4.3 ^{3}J,7.5, ^{3}J,5.2, ^{2}J,14.5

1.30, s, 6H 1.47, 1.57, 2 x s, 6H

4.71, dd, 1H, ^{3}J,7.3, ^{3}J,5.2
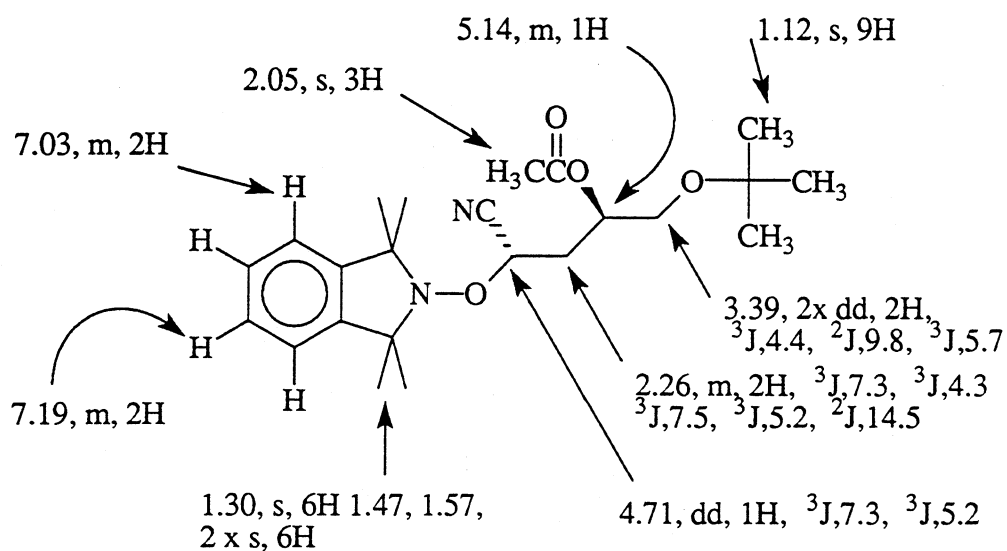
^{13}C nmr(CDCl$_3$, 62.8MHz, shifts are in ppm)* :

20.9

119.3

170.4

144.8, 145.2

69.1

27.3

O

127.6

H_3CCO

CN

O

73.4

121.6

N—O

62.6

71.6

34.4

66.1

25.1, 29.5, 4 x CH$_3$

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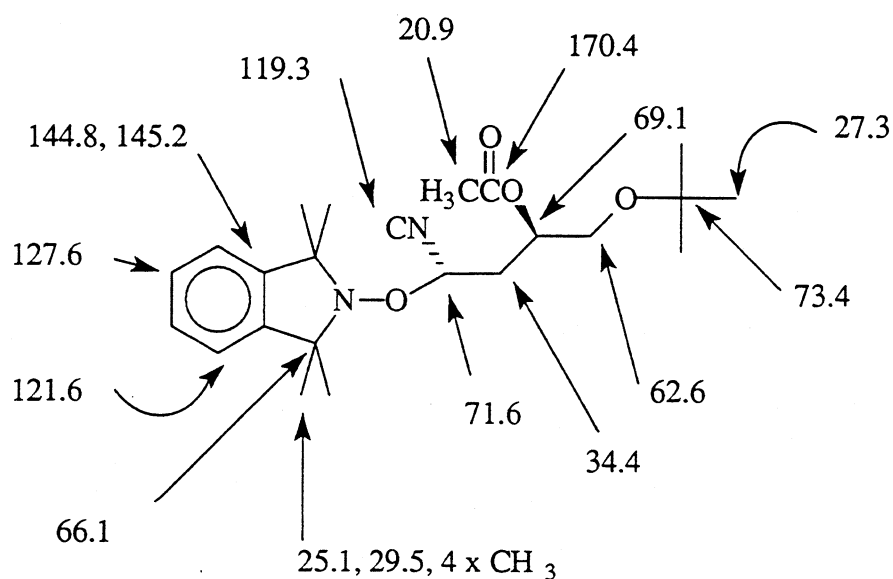
* The shifts at 69.1 & 71.6ppm are tentative and therefore are interchangeable.

Experimental

PANIC (Parameter Adjustment in N.M.R. by Iteration Calculation-Bruker) was performed with Aspect 3000 n.m.r. software(Bruker- version 830731) to simulate the ^{1}H n.m.r. spectrum of (29) using the determined coupling constants, and thereby verify these assignments.

Assigned shifts of signals occuring between 2.0ppm(500Hz) and 5.5ppm (1376Hz):

α_1 – 3.37ppm(842.91Hz)

α_2 –3.39ppm(850.41Hz)

β_3 -5.14ppm(1285.63Hz)

γ_4 -2.27ppm(567.78Hz)

γ_5 -2.31ppm(577.78Hz)

δ_6 -4.71ppm(1178.08Hz)

Assigned coupling constants(Hz):

$J_{1,2}$ =9.8Hz

$J_{1,3}$=5.7Hz

$J_{2,3}$=4.4Hz

$J_{3,4}$=7.5Hz

$J_{3,5}$=7.3Hz

$J_{4,5}$=14.5Hz

$J_{4,6}$=5.2Hz

$J_{5,6}$=7.3Hz
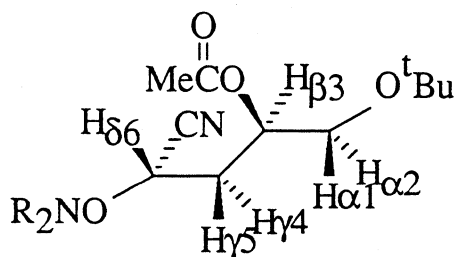
(29)

Figure 33 ^{1}H nmr spectrum of (28)
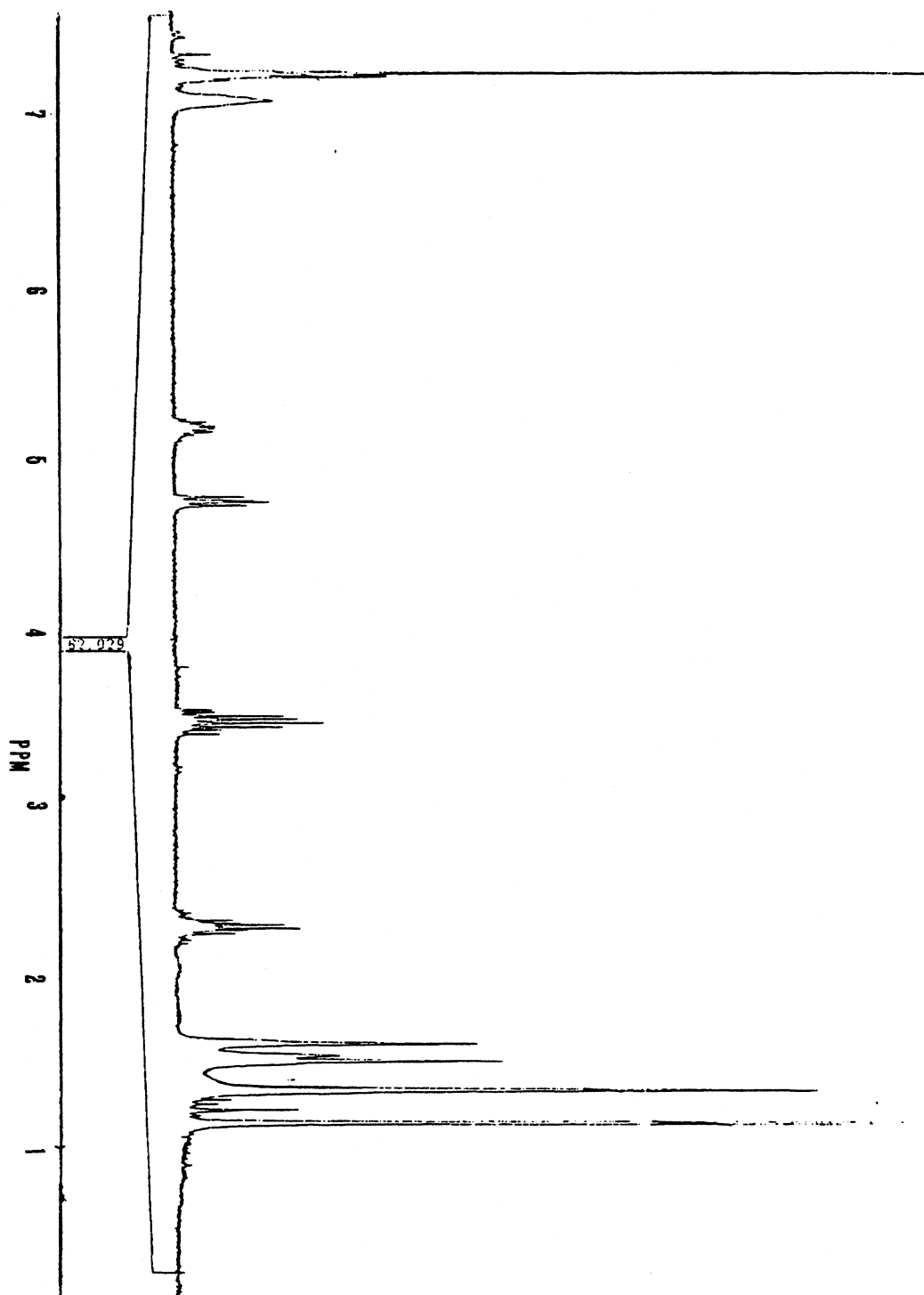
Figure 35 PANIC simulation of (29) in the region 500-1340Hz
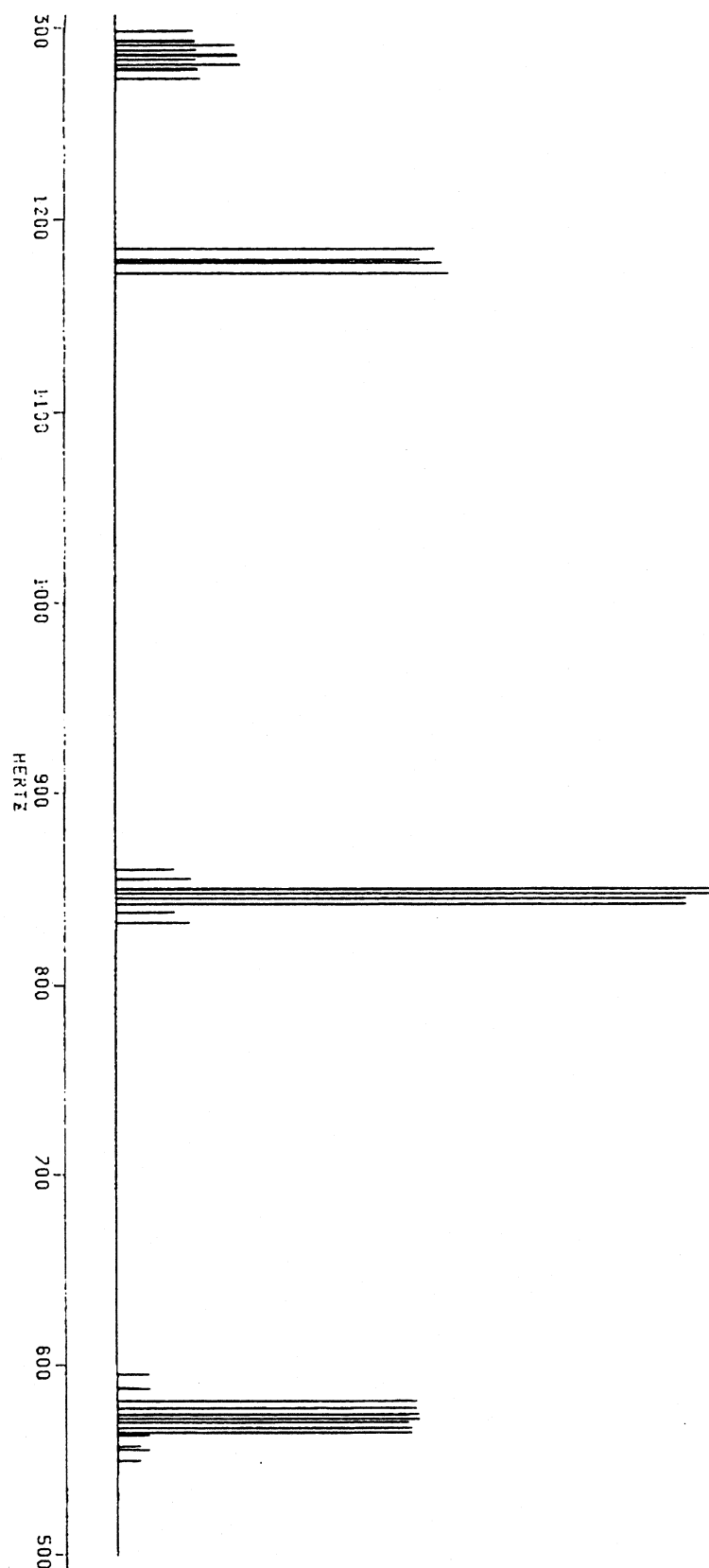
Experimental

Figure 34 ^{1}H nmr spectrum of (29)
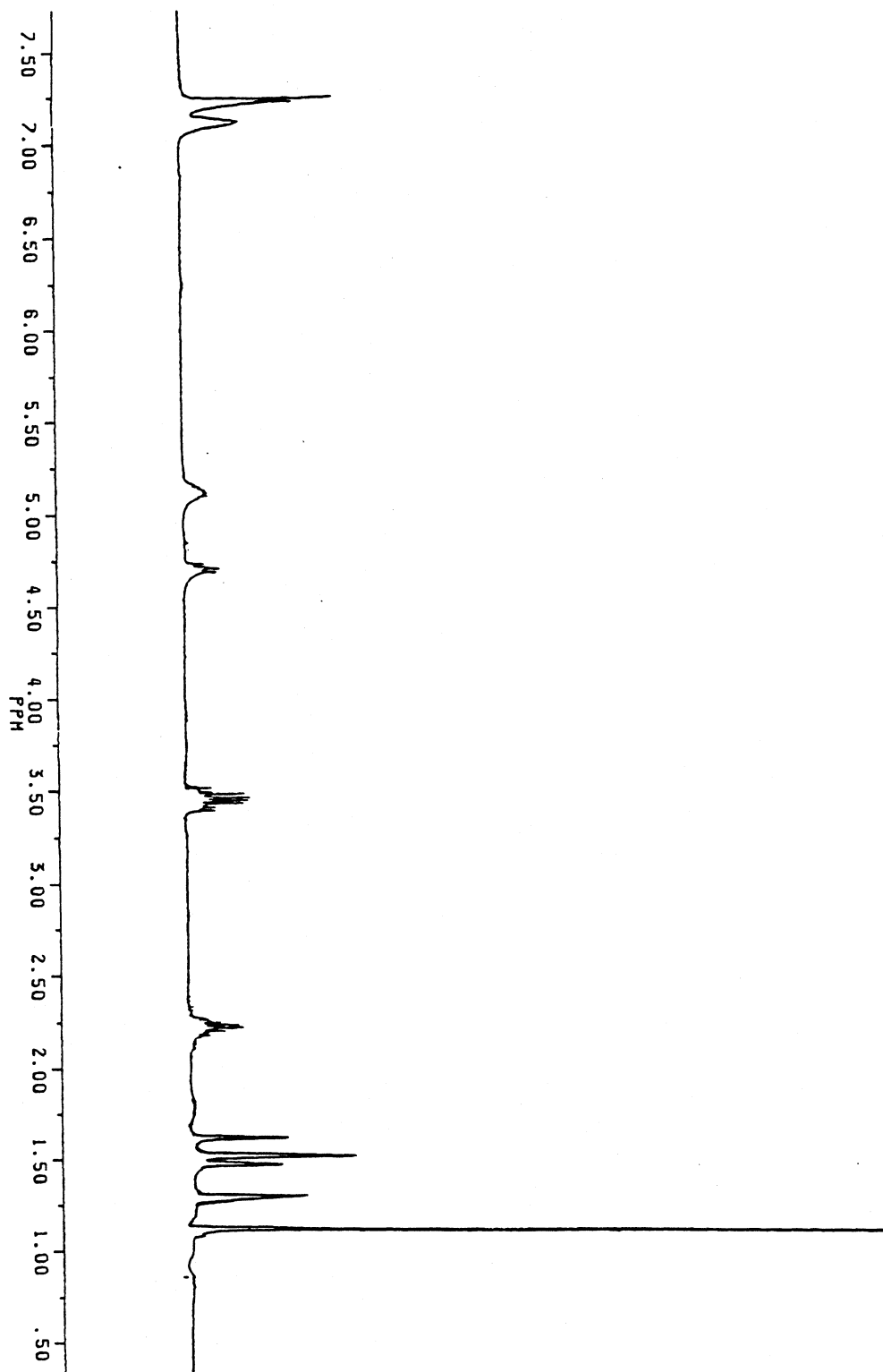
2-t-Butoxy-1-cyano-1-(1,1,3,3-tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy)-ethane(27)

(Found: M 316.213. $C_{19}H_{28}N_2O_2$ requires 316.215).

^1H n.m.r.(CDCl$_3$, 250.122MHz, shifts in ppm, couplings in Hz):
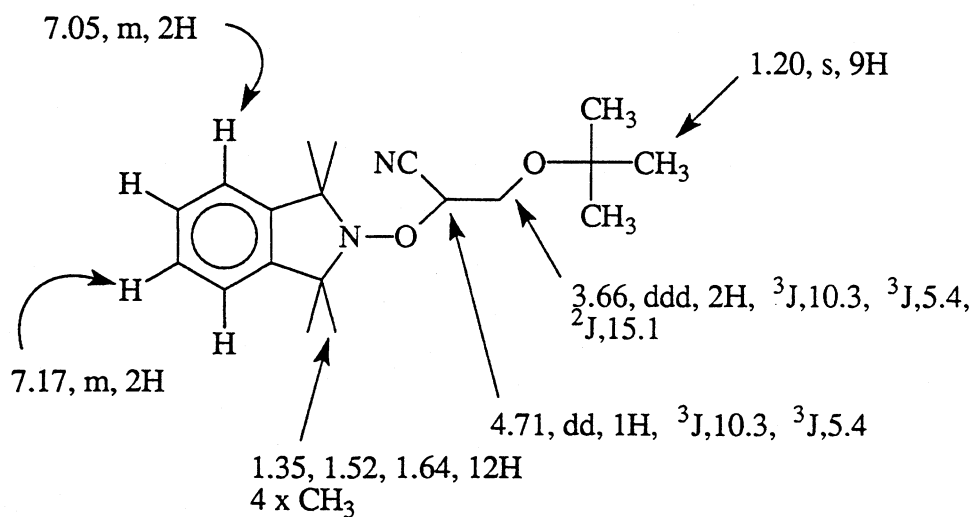
7.05, m, 2H

1.20, s, 9H

3.66, ddd, 2H, ^3J,10.3, ^3J,5.4, ^2J,15.1

7.17, m, 2H

4.71, dd, 1H, ^3J,10.3, ^3J,5.4

1.35, 1.52, 1.64, 12H
4 x CH$_3$

^{13}C n.m.r.(CDCl$_3$, 62.8MHz, shifts in ppm):

144.4

118.6

27.2

127.5

74.2

63.0

122.0

76.03

68.0, 68.5

25.1, 29.0, 29.9, 30.2,
4 x CH$_3$

Experimental
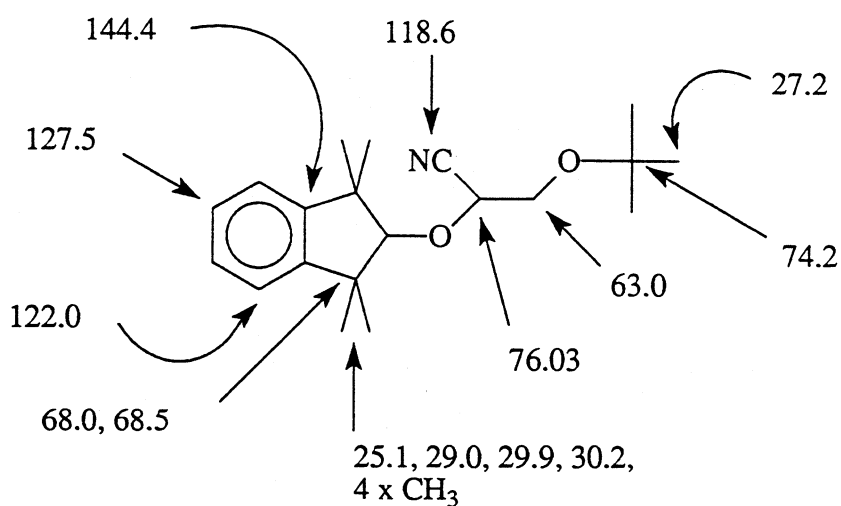
2-t-Butoxy-2-acetoxy-1-(1,1,3,3-tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy)-ethane(24)

^{1}H n.m.r.(CDCl3, 250.122MHz, shifts in ppm, couplings in Hz):

3.78, s, 3H

4.09, m, 2H

7.03-7.26, m, 4H

4.33, dd, 1H
J,5.5, J,6.5

1.25, s, 9H

1.42, brs, 3H, 3 x CH$_3$
1.58, 3H, CH$_3$
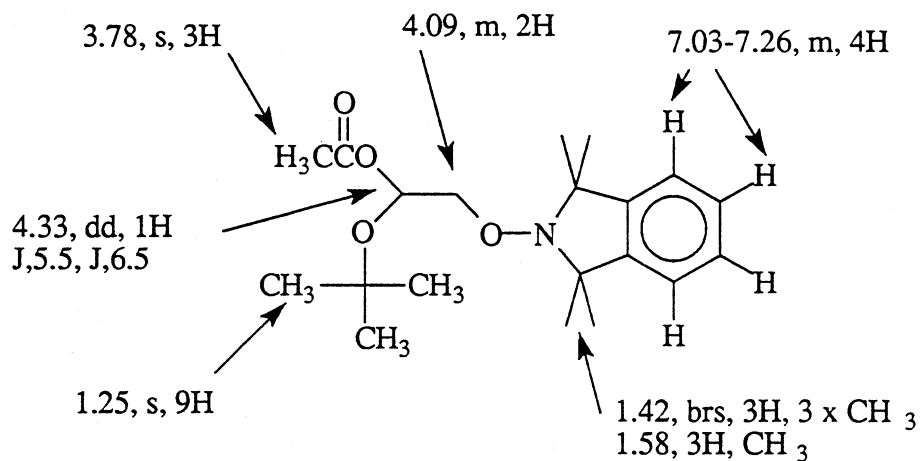
Identical to an authentic sample by ^{1}H n.m.r.[80].

2-t-Butoxy-1-acetoxy-1-(1,1,3,3-tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy)-ethane(25)

(Found: MH$^+$ 350.227. C$_{20}$H$_{31}$NO$_4$H$^+$ requires 350.233).

^{1}H n.m.r.(CDCl3, 250.122MHz, shifts in ppm, couplings in Hz):

2.11, s, 3H

6.16, dd, 1H, ^{3}J,7.8,
^{3}J,7.1

1.23, s, 9H

1.37, 1.43, 1.48, 1.58,
4 x CH$_3$

3.46, ddd, 2H, ^{3}J,7.8,
^{3}J,7.1, ^{2}J,14.4

7.20, m, 2H

7.06, m, 2H

Experimental
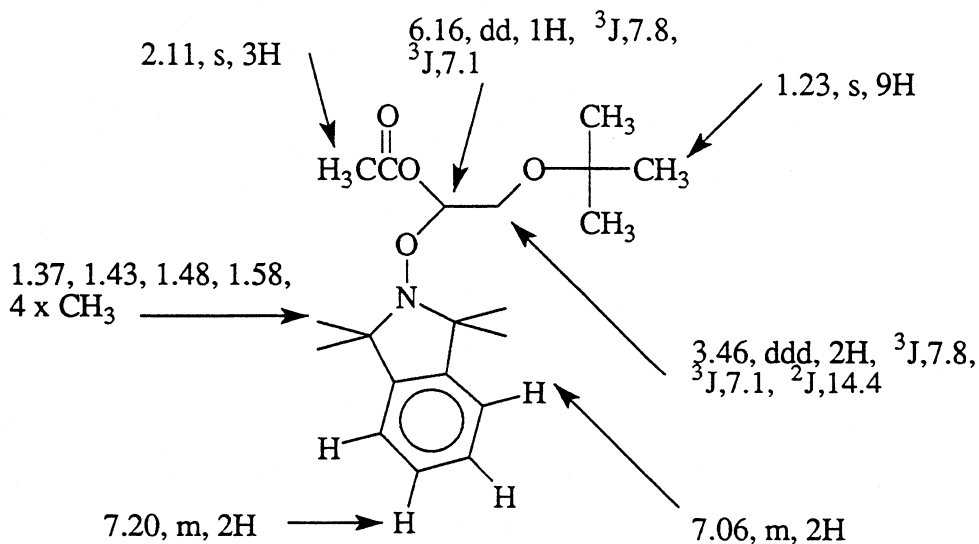
^{13}C n.m.r.(CDCl3, 62.8MHz, shifts in ppm):
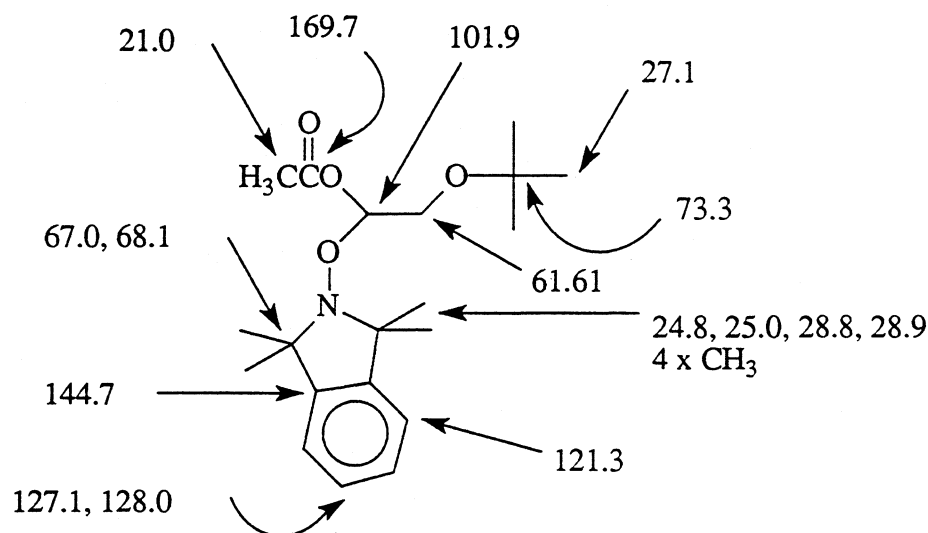
6.8.0   The reaction of Diphenylphosphine oxide with t-butoxyl radicals

Reaction time: 68 minutes

DTBP (85mg, 3.63 x 10^{-4}moles)

Trap(10) (145mg, 7.63 x 10^{-4}moles)

DPPO (140mg, 6.93 x 10^{-4}moles)

Benzene 2.5mls

(Combining DTBP and diphenylphosphine oxide neat was avoided as this leads to an explosion). The reaction mixture was concentrated to approximately 30% of the original volume under high vacuum prior to separation.

HPLC conditions: 80% methanol in water, 4.0 ml/min preparative separation. Isolation of reaction components gave the following compounds (in order of elution from the HPLC column).

Diphenylphosphinic acid(DPPA)

(DPPA)

Experimental
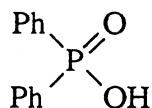
This was identical to an authentic sample by HPLC. M.pt 193-195°C. Lit M.pt 191-192°C[193].

1,1,3,3-Tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy diphenylphosphinate(32)

(Found: C, 73.3; H, 6.9; N, 3.4. $C_{24}H_{26}NO_2P$ requires C, 73.6; H, 6.7; N, 3.5). White solid (Methanol). M.pt 141-145°C.

^{1}H n.m.r.(CDCl$_3$, 250.122MHz, shifts in ppm, couplings in Hz):

7.04, m, 2H

7.22, m, 2H

7.47, m, 6H
7.89, m, 4H
Aromatic H

1.3, brs, 12H, 4 x CH$_3$

^{13}C n.m.r.(CDCl$_3$, 62.8MHz, shifts in ppm):

128.1, $^3J_{P,C}$,12.9

132.4

70.0

121.5

132.4, $^2J_{P,C}$,34.8

127.5

131.1, J$_{P,C}$,135.4

144.4

27.4, brs, 4 x CH$_3$
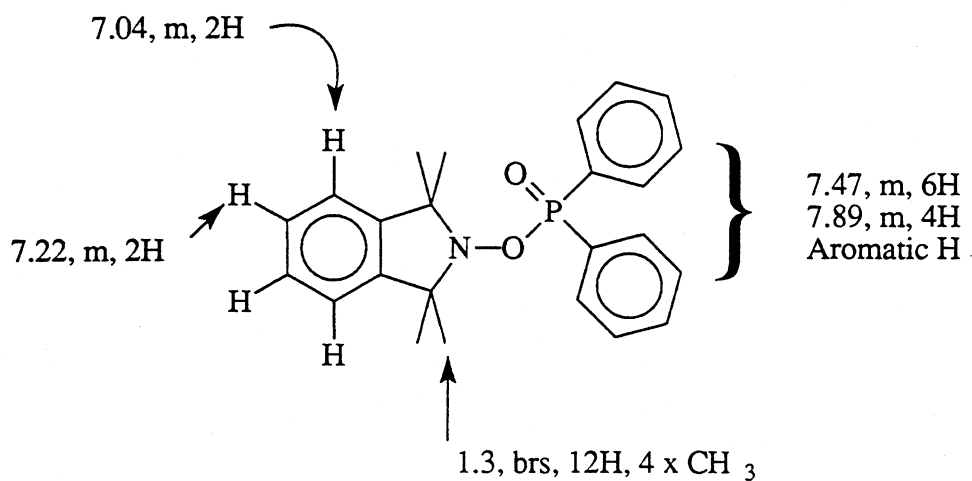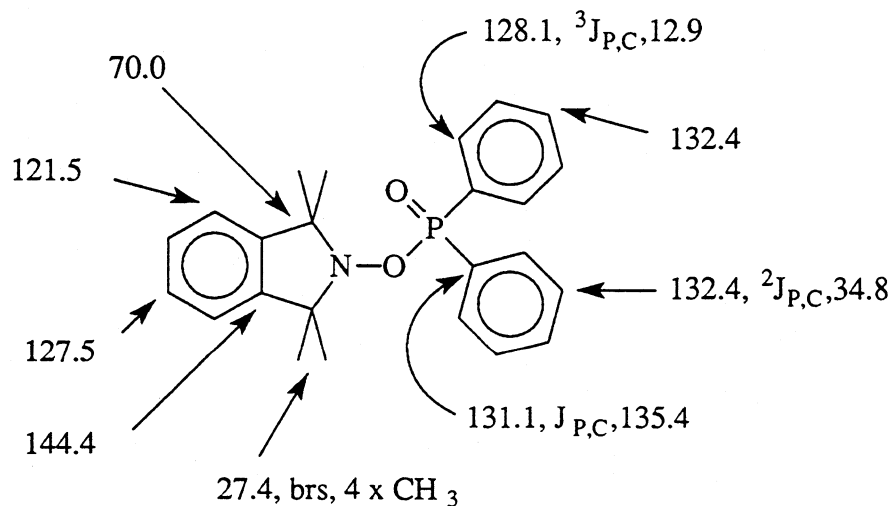
^{31}P n.m.r. 32.51ppm. ξ_{270} = 51956 lmol^{-1}cm^{-1}.

6.8.1 The reaction of Diphenylphosphine oxide and Trap(10)(blank reaction)

Reaction Time: 120 minutes

Trap(10) (130mg, 6.84×10^{-4} moles)

Diphenylphosphine oxide (140mg, 6.93×10^{-4} moles)

Benzene (2.5mls)

The reaction mixture was concentrated to approximately 30% of original volume under high vacuum prior to separation. HPLC conditions: 80% methanol in water, 0.4ml/min. Preparative HPLC isolation gave identical products to 6.8.0, namely (in order of elution from the HPLC column):
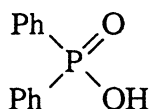
Diphenylphosphinic Acid(DPPA)

$$\begin{array}{c} Ph \\ \diagdown \\ P \\ \diagup \diagdown \\ Ph \end{array} \begin{array}{c} O \\ \diagup\diagup \\ \diagdown \\ OH \end{array}$$

(DPPA)

Identical to an authentic sample by HPLC(see 6.8.0).

1,1,3,3-Tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy diphenylphosphinate(32)

$$\begin{array}{c} Ph \\ \diagdown \\ P \\ \diagup \diagdown \\ Ph \end{array} \begin{array}{c} O \\ \diagup\diagup \\ \diagdown \\ ONR_2 \end{array}$$

(32)
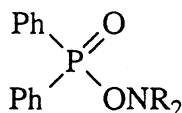
Identical to an authentic sample by HPLC and ^{1}H n.m.r.(see 6.8.0).

6.9.0 The reaction of Diphenylphosphine with t-butoxyl radicals

Reaction Time: 68 minutes

DTBP (58mg, 2.47 x 10^{-4} moles)

Trap(10) (103mg, 5.42 x 10^{-4} moles)

Diphenylphosphine (100mg, 5.37 x 10^{-4} moles)

Benzene (2.5mls)

Trap(10), DTBP and benzene were added to the reaction vessel, which was then evacuated, followed by filling with N_2. The solution was then cooled (water/ice bath) and diphenylphosphine added under N_2, it was then allowed to warm to room temperature. This was followed by heating at 60°C.

This procedure was followed as a safety precaution. The reaction mixture was concentrated to approximately 30% of original volume under high vacuum prior to separation. HPLC conditions: 80% methanol in water, 4.0 ml/min.flow rate Isolation gave the folowing compounds (in order of elution from the HPLC column):

Diphenylphosphinic Acid(DPPA)

$$\begin{array}{c} Ph \\ \diagdown \\ \diagup \\ Ph \end{array} P \begin{array}{c} \diagup O \\ \diagdown \\ OH \end{array}$$
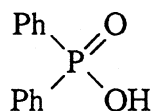
(DPPA)

This was identical to an authentic sample by HPLC (see 6.8.0).

t-Butyldiphenylphosphinate(33)

^{1}H n.m.r.(CDCl$_3$, 250.122MHz, shifts in ppm, couplings in Hz):

7.42, m, 6H

7.79, m, 4H

Aromatic H

1.51, s, 9H

^{13}C n.m.r.(CDCl$_3$, 62.8MHz, shifts in ppm):

128.2, ^{3}J$_{P,C}$, 13.2

134.8, J$_{P,C}$,138.5

30.8, ^{3}J$_{P,C}$,18.5

83.4

129.1

131.3, ^{2}J$_{P,C}$,10.7
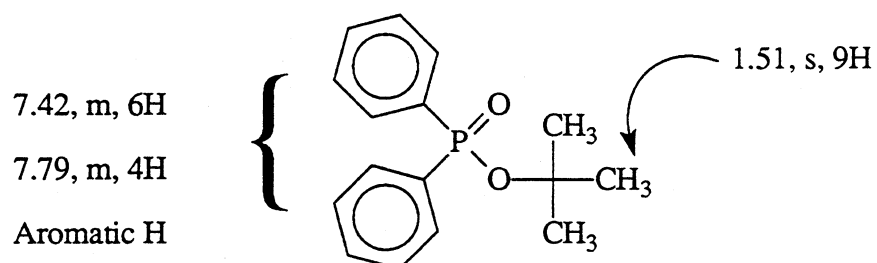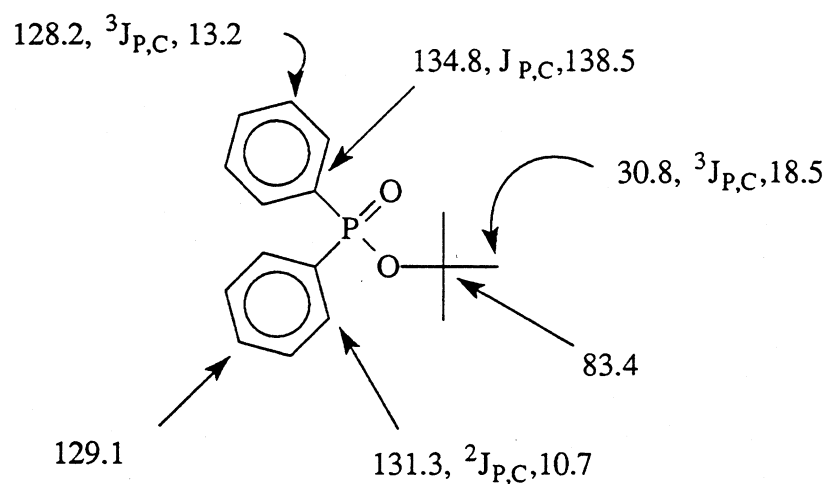
The above structure(33) was confirmed by an X-ray diffraction structural analysis (see 3.1.2).

^{31}P n.m.r. 9.94ppm.

1,1,3,3-Tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy diphenylphosphine Oxide(34)

(Found: C, 77.3; H, 6.5; N, 3.6. C$_{24}$H$_{26}$NOP requires C, 76.8; H, 6.9; N, 3.7%). M.pt 185-188°C.

^{1}H n.m.r.(CDCl$_3$, 250.122MHz, shifts in ppm, couplings in Hz):

7.04, m, 2H

1.56, s, 12H, 4 x CH$_3$

7.44, m, 6H
7.83, m, 4H
Aromatic H

7.23, m, 2H

^{13}C n.m.r.(CDCl$_3$, 62.8MHz, shifts in ppm):

32.2, 4 x CH$_3$

68.6

127.8, J$_{P,C}$,15.7

127.5

131.5

133.7, J$_{P,C}$,138.1

120.9

133.4, J$_{P,C}$,10.67

145.9
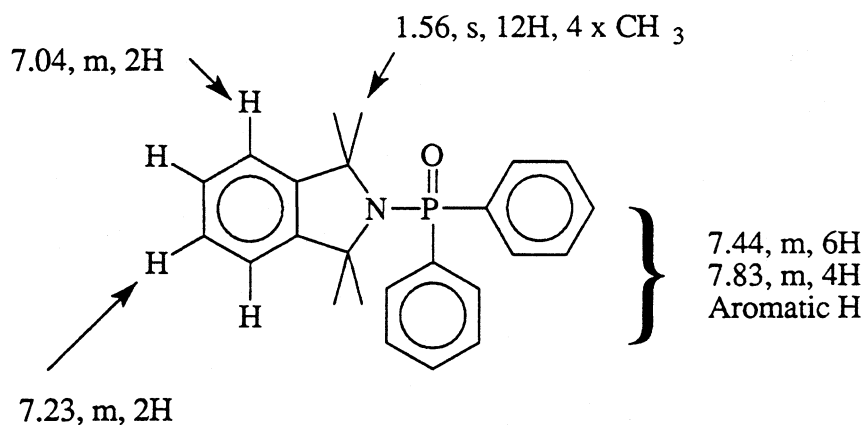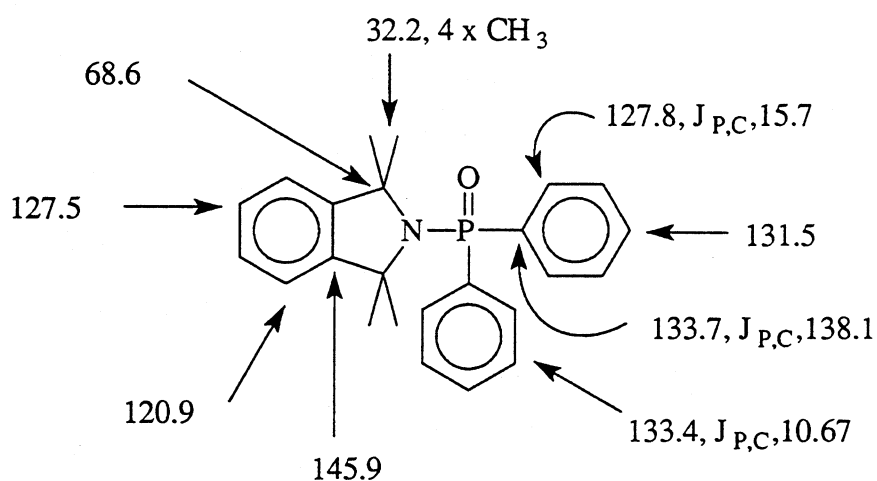
^{31}P n.m.r. 9.70ppm. An X-ray diffraction analysis was done on this compound (see chapter three).

1,1,3,3-Tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy diphenylphosphinate(32)

Ph O
   P
Ph   ONR$_2$

(32)
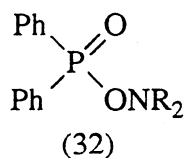
This was identical to an authentic sample by HPLC and ^{1}H n.m.r. (see 6.8.0).

1,1,3,3-Tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy diphenylphosphinite(35)

^{1}H n.m.r.(CDCl₃, 250.122MHz, shifts in ppm):

7.18-7.30, m, 4H

7.18-7.30, m, 4H
7.47, m, 6H
Aromatic H

1.36, s, 12H, 4 x CH₃

^{13}C n.m.r.(CDCl₃, 62.8MHz, shifts in ppm):

120.0

128.1, J$_{P,C}$,6.97

130.0, J$_{P,C}$,22.1

128.6

143.7, 144.0

29.9, 30.0, 4 x CH₃
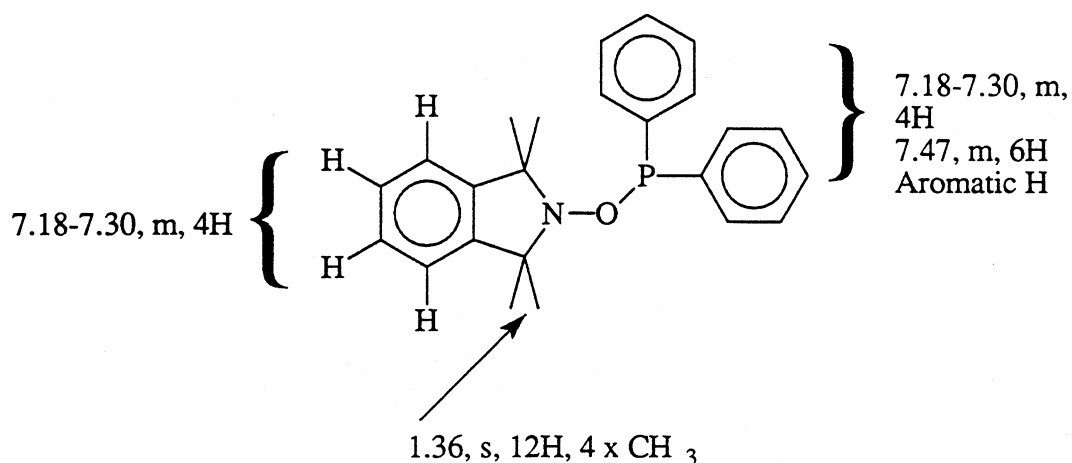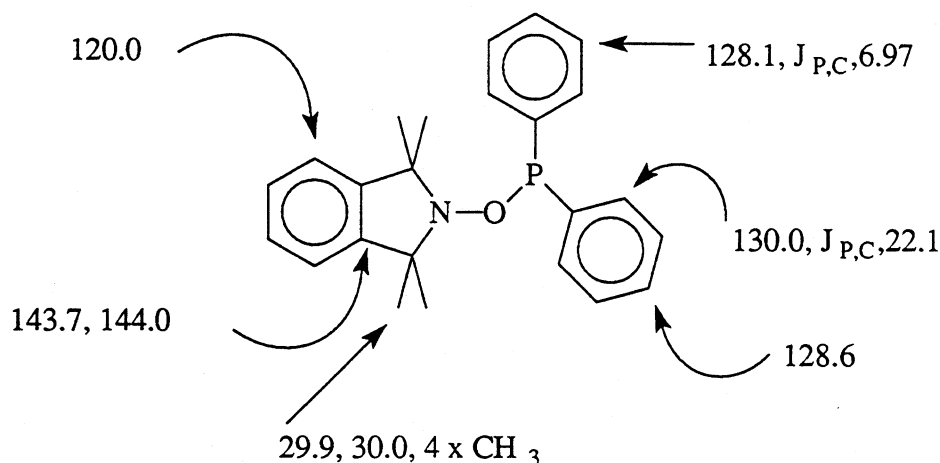
^{31}P n.m.r. 86.90ppm.

C1, C3, C5 and C6 from the trap moiety and the two ipso carbons of the phenyl rings were not detected in the ^{13}C n.m.r. spectrum.

This material was unstable, decomposing in warmed aqueous THF almost instantly to give by HPLC, trap(10) and diphenylphosphine oxide. While still in the reaction mixture and in the presence of methanol some of this material apparently was oxidised to the phosphinate(32). High resolution mass spectrometry failed to give a parent ion, and it was too unstable for an elemental analysis to be obtained.

6.9.1 The reaction of Diphenylphosphine and Trap(10)-(Blank reaction)

Reaction Time: 120 minutes

Trap(10) (103mg, 5.42×10^{-4}moles)

Diphenylphosphine (100mg, 5.37×10^{-4}moles)

Benzene (2.5mls)

The reaction mixture was concentrated to approximately 30% of the original volume under high vacuum prior to separation. HPLC conditions: 80% methanol in water, 4.0 ml/min. Isolation of the reaction components gave the following:

Diphenylphosphinic Acid(DPPA)
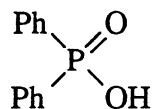
Ph_ /O
  \\P//
 / \\
Ph' OH

(DPPA)

Identical to an authentic sample by HPLC (see 6.8.0).

1,1,3,3-Tetramethyl-2,3-dihydro-1H-isoindol-2-diphenylphosphine oxide(34)
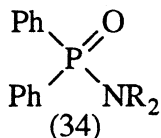
Ph_ /O
  \\P//
 / \\
Ph' NR$_2$
 (34)

Identical to an authentic sample by and HPLC (see 6.9.0).

Experimental

1,1,3,3-Tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy diphenyl-phosphinate(32)

$$\text{Ph} \diagdown \kern-0.5em \underset{\text{Ph} \diagup}{\overset{\diagup \kern-0.4em O}{P}} \diagdown \text{ONR}_2$$

(32)

Identical to an authentic sample by HPLC (see 6.8.0).

1,1,3,3-Tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy diphenyl-phosphinite(35)

$$\text{Ph} \diagdown \kern-0.3em \underset{\text{Ph} \diagup}{P} \kern-0.3em - \text{ONR}_2$$
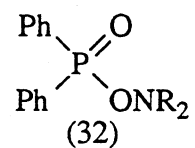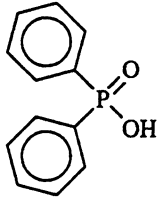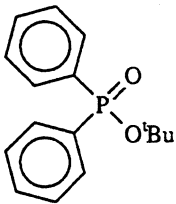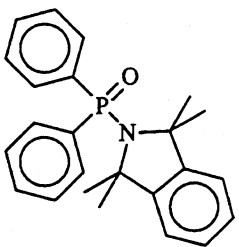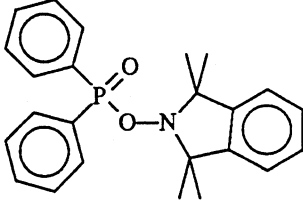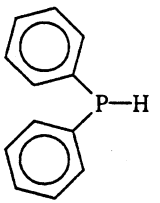
(35)
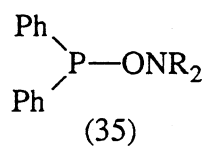
Identical to an authentic sample by HPLC (see 6.9.0).

Experimental

Table 16 [31]P n.m.r. chemical shifts of compounds from the reaction of Diphenylphosphine with t-butoxyl radicals in the presence of (10).

compound	chemical shifts (ppm)
(Diphenylphosphinic acid)	15, 25.5 [194]
(33)	9.94
(34)	9.70
(32)	32.51
(Diphenylphosphine)	-41, -43.8 [194]
(35)	86.9

Experimental

6.10 The addition of Diphenylphosphinyl(31) and Dimethoxy phosphinyl(41) radicals to various alkenes and Phenylacetylene

6.10.1.0 The reaction of Diphenylphosphine oxide with t-butoxyl radicals and Acrylonitrile in the presence of (10)

Reaction time: 68 minutes

DTBP (133mg, 0.45 equivalents)

Trap(10) (227mg, 1.1 equivalents)

Diphenylphosphine oxide (212mg, 1.0 equivalent)

Acrylonitrile (3.0 ml)

In addition, a number of different reactions were carried out, where the amount of trap(10) used was varied. The number of equivalents used ranged between one and five.

The reaction mixture was concentrated to approximately 30% of the original volume under high vacuum prior to separation. HPLC conditions: 80% methanol in water, 2.5 ml/minute- flow rate. Preparative isolation by HPLC gave the following compounds in order of elution from the reverse-phase HPLC column.

2-Cyano-2-(1,1,3,3-tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy)ethyl diphenylphosphine oxide(42)

(Found: C, 73.0; H, 6.7; N, 6.1. $C_{27}H_{29}N_2O_2P$ requires C, 73.0; H, 6.6; N, 6.3%).

^{1}H n.m.r.(CDCl$_3$, 250.122MHz, shifts in ppm, couplings in Hz):

7.03, m, 2H

5.30, ddd, 1H, ^{3}J,4.4, ^{3}J,8.8, ^{3}J$_{P,H}$,8.4

7.19, m, 2H

7.48, m, 6H
7.80, m, 4H
Aromatic H

2.84, ddd, 1H, ^{3}J,4.4, ^{2}J,15.3, J$_{P,H}$,13.4

3.13, ddd, 1H, ^{3}J,8.8, ^{2}J,15.3, J$_{P,H}$,6.9

1.05, 1.12, 1.58, 1.59, 12H, 4 x CH$_3$

^{13}C n.m.r.(CDCl$_3$, 62.8MHz, shifts in ppm):

143.7

127.2 →

121.1

118.7, ^{3}J$_{P,C}$,13.0

CN

128.3*, ^{2}J$_{P,C}$,13.1

130.2*, ^{3}J$_{P,C}$,9.4

131.7*

132.4*, J$_{P,C}$,136.9

130.6*, ^{3}J$_{P,C}$,9.4

131.9*

128.6*, ^{2}J$_{P,C}$,11.9

33.4, J$_{P,C}$,70.3

131.9*, J$_{P,C}$,136.9

67.9

25.0, 29.2, 30.3,
4 x CH$_3$
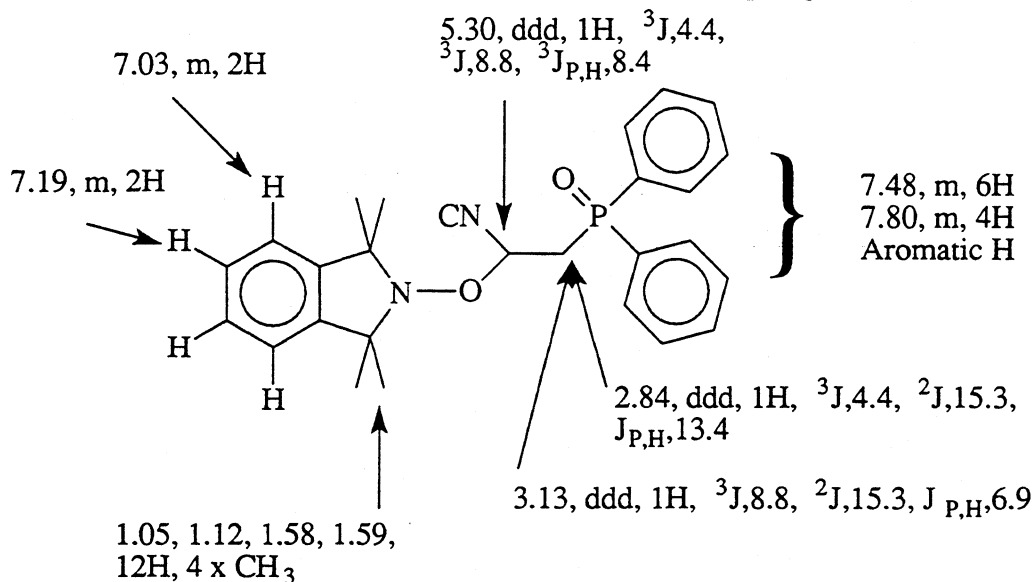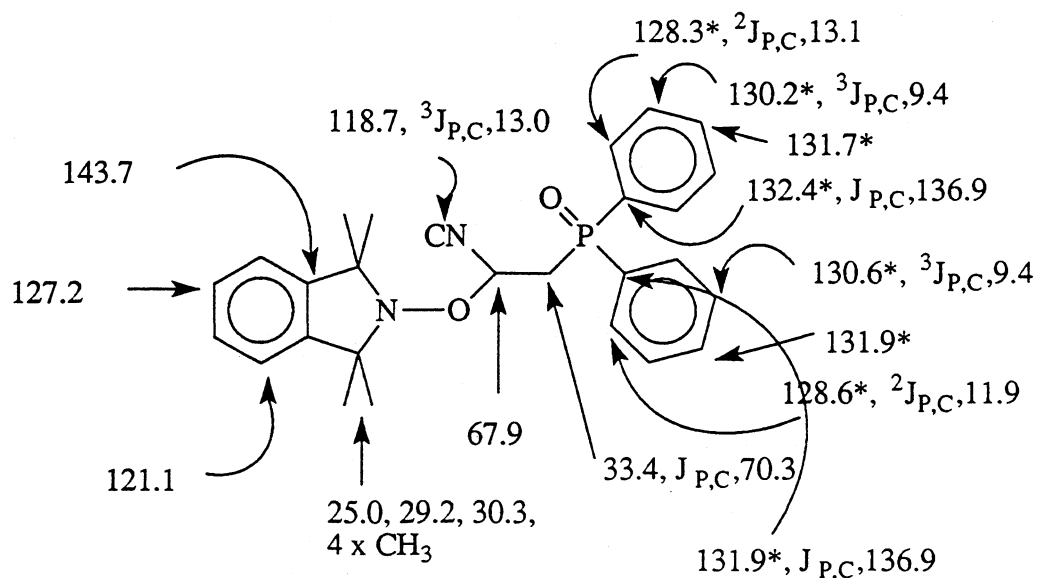
* Assignments are not absolute and are interchangeable with the corresponding carbon.

1,1,3,3-Tetramethyl-2,3-dihydro-1H-isoindol diphenylphosphinate(32)
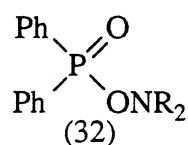
Ph\
P\
Ph

O

ONR$_2$

(32)

Identical to an authentic sample by ^{1}H nmr and HPLC(see 6.8.0).

2-t-Butoxy-1-cyano-1-(1,1,3,3-tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy)-ethane(27)

CN

R$_2$NO   O^{t}Bu

(27)
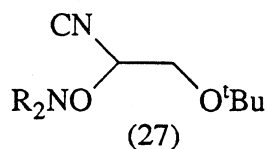
Identical to authentic sample by ^{1}H nmr and HPLC (see 6.7).

Experimental

6.10.1.1 The reaction of Diphenylphosphine oxide, t-butoxyl radicals and Vinyl acetate in the presence of (10)

Reaction time: 68 minutes

DTBP (133mg, 0.45 equivalents)

Trap(10) (227mg, 1.1 equivalents)

Diphenylphosphine oxide (212mg, 1.0 equivalent)

Vinyl acetate (3ml)

The reaction mixture was concentrated to approximately 30% of the original volume under high vacuum prior to separation. HPLC conditions: 80% methanol in water, flow rate- 2.5 ml/minute. Preparative isolation by HPLC gave the following compunds (in order of elution from the HPLC column).

2-Acetoxy-2-(1,1,3,3-tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy)ethyl diphenylphosphine oxide(43)

(Found: C,70.7; H,7.1; N,3.1. $C_{28}H_{32}NO_4P$ requires C,70.4; H,6.8; N,2.9%).
^{1}H n.m.r.(CDCl$_3$, 250.122MHz, shifts in ppm, couplings in Hz):

6.56, q, 1H, ^{3}J,5.8

1.88, s, 3H

1.23, s, 6H, 2 x CH$_3$
1.40, s, 3H, CH$_3$
1.42, s, 3H, CH$_3$

7.49, m, 6H
7.82, m, 4H
Aromatic H

2.92, 14 line multiplet, 2H, ^{3}J,5.8, J,3.8

7.03, m, 2H

7.19, m, 2H

^{13}C n.m.r.(CDCl$_3$, 62.8MHz, shifts in ppm):

128.5*, $^2J_{P,C}$,11.3

130.9*, $^3J_{P,C}$, 5.6

133.3*, $J_{P,C}$,101.1

133.6*, $J_{P,C}$,108.0

128.6*, $^2J_{P,C}$,11.3

131.0*, $^3J_{P,C}$,5.02

169.3

21.0

96.2

25.3, 29.1, 29.3, 4 x CH$_3$

34.5, $J_{P,C}$,70.4

144.3, 144.7

67.3, 68.1

121.4

127.3

H$_3$CCO

O

P

O

N
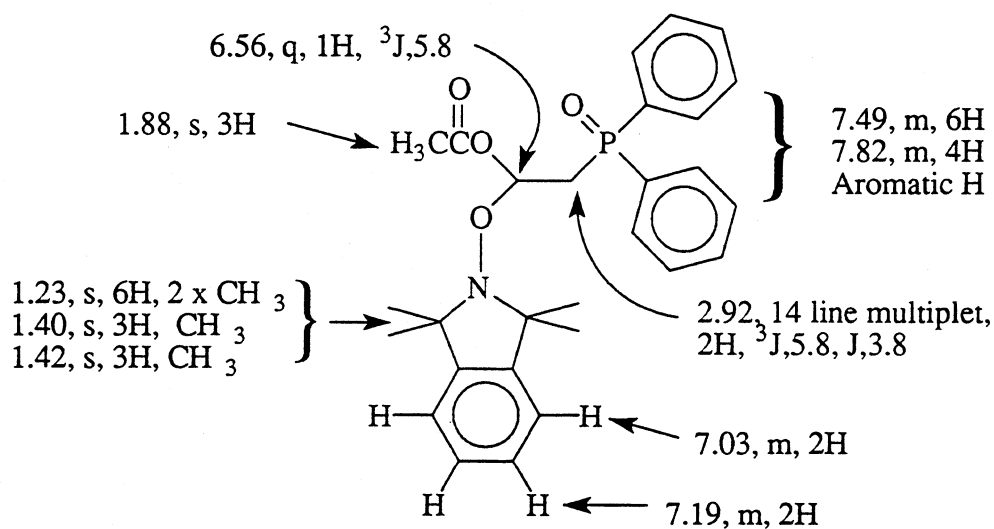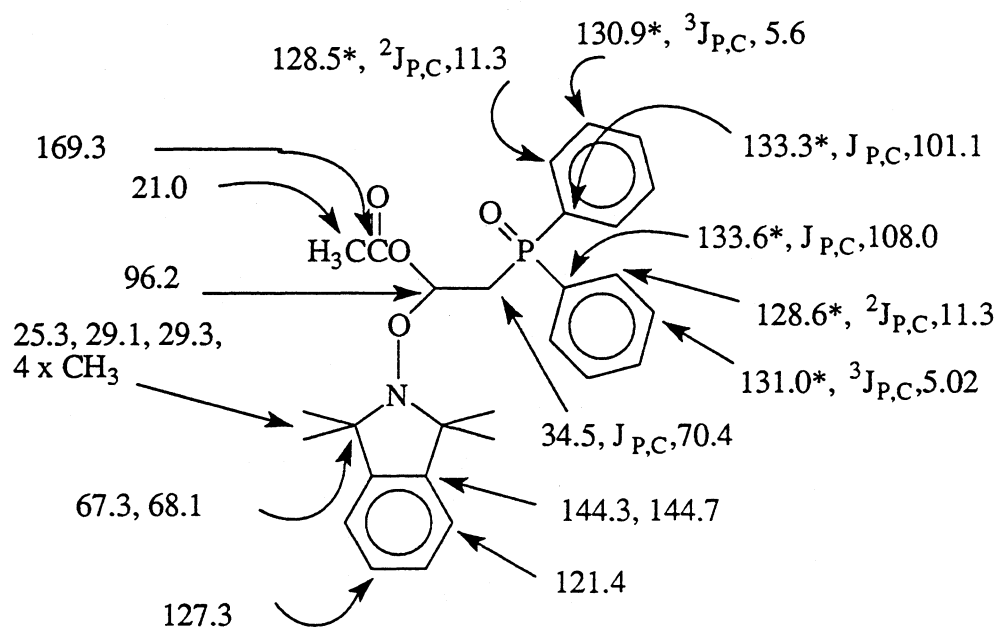
*. Corresponding assignments are interchangeable. Also the para aromatic carbon resonances were not observed.

1,1,3,3-Tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy diphenylphosphinate(32)
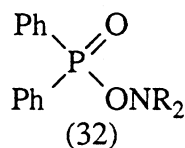
Ph
Ph—P=O
ONR$_2$
(32)

Identical to an authentic sample by ^{1}H n.m.r. and HPLC(see 6.8.0).

2-t-Butoxy-1-acetoxy-1-(1,1,3,3-tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy)ethane(25)

O
H$_3$CCO   O^{t}Bu
R$_2$NO
(25)
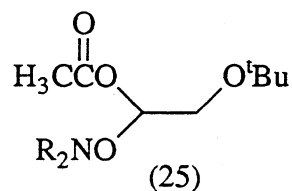
Identical to an authentic sample by HPLC and ^{1}H n.m.r.(see 6.7).

Experimental

6.10.1.2 The reaction of Diphenyphosphine oxide, t-butoxyl radicals, Acrylonitrile and Vinyl acetate in the presence of (10)

Reaction time: 68 minutes

DTBP (2.5mg, 1.0 equivalent)

Trap(10) (20.3mg, 10.0 equivalents)

Diphenylphosphine oxide (4.3mg, 2.0 equivalents)

Vinyl acetate (5.0ml, 10.13M)

Acrylonitrile (0.357ml, 1.01M)

Being an analytical reaction, the reaction mixture was injected into the HPLC column as is. Using methanol/water, 70/30 at a flow rate of 0.5ml/minute the products were eluted from the column in the following order.

2-Cyano-2-(1,1,3,3-tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy)ethyl-diphenylphosphine oxide(42)

(42)
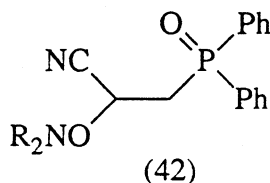
Identical to an authentic sample by HPLC(see 6.10.1.0).

2-Acetoxy-2-(1,1,3,3-tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy)ethyl-diphenylphosphine oxide(43)

(43)
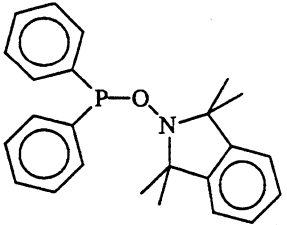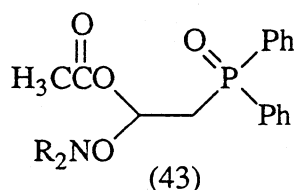
Identical to an authentic sample by HPLC(see 6.10.1.1).

1,1,3,3-Tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy diphenylphosphinate(32)

$$Ph \quad O$$
$$\overset{Ph}{\underset{Ph}{\diagdown}} P \diagup \quad ONR_2$$
$$(32)$$
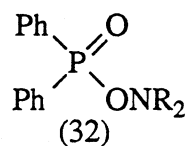
Identical to an authentic sample by HPLC(see 6.8.0).

2-t-Butoxy-1-cyano-1-(1,1,3,3-tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy)ethane(27)

$$NC$$
$$R_2NO \qquad O^tBu$$
$$(27)$$
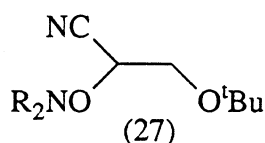
Identical to an authentic sample by HPLC (see 6.7).

2-t-Butoxy-2-acetoxy-1-(1,1,3,3-tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy)ethane(24)
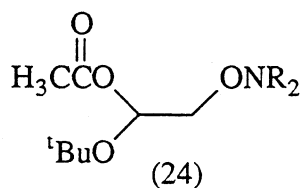
$$O$$
$$\parallel$$
$$H_3CCO \qquad ONR_2$$
$$^tBuO$$
$$(24)$$

Identical to an authentic sample by HPLC(see 6.7).

2-t-Butoxy-1-acetoxy-1-(1,1,3,3-tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy)ethane(25)

$$O$$
$$\parallel$$
$$H_3CCO$$
$$R_2NO \qquad O^tBu$$
$$(25)$$

Identical to an authentic sample by HPLC(see 6.7).

Experimental
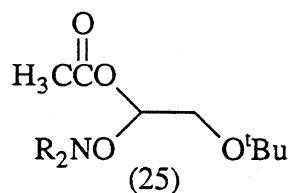
6.10.1.3 The reaction of Dimethyl phosphite with t-butoxyl radicals and Acrylonitrile in the pressence of (10)

Reaction time: 200 minutes
>   DTBP (2.5mg,1.0 equivalent)
>   Trap(10) (4.3mg, 2.1 equivalents)
>   Dimethyl phosphite (300μl, 306 equivalents)
>   Acrylonitrile (800μl)

The trap, initiator(DTBP) and 500μl of acrylonitrile were added to dimethyl phosphite and acrylonitrile(300μl) at 60°C, over 200 minutes, via a motor driven syringe. Both the solutions were degassed with N_2 (see 6.5.0).

This was an analytical scale reaction, with the following HPLC conditions: 70% methanol in water, flow rate of 0.25ml/minute. The products were separated and characterised however in 6.10.1.5. The products were eluted from the HPLC column in the following order.

Dimethyl 2-cyano-2-(1,1,3,3-tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy)ethyl-phosphonate(44)

(44)
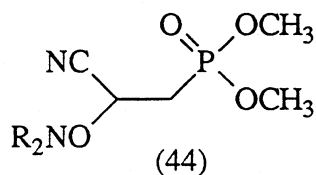
Identical to an authentic sample by HPLC (see 6.10.1.5).

Dimethyl (1,1,3,3-tetramethyl-2,3-dihydo-1H-isoindol-2-yloxy) phosphate(45)
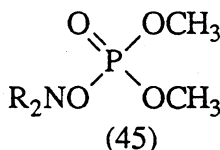
(45)

Identical to an authentic sample by HPLC (see 6.10.1.5).

Experimental

2-(1,1,3,3-Tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy) butyronitrile(26)

(26)
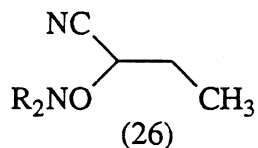
Identical to an authentic sample by HPLC (see 6.7).

2-Methoxy-1,1,3,3-tetramethyl-2,3-dihydro-1H-isoindol(22)
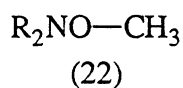
$$R_2NO-CH_3$$
(22)

Identical to an authentic sample by HPLC (see 6.7).

2-t-Butoxy-1-cyano-1-(1,1,3,3-tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy)ethane(27)

(27)
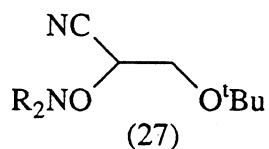
Identical to an authentic sample by HPLC (see 6.7).

6.10.1.4 The reaction of Dimethyl phosphite with t-butoxyl radicals and Vinyl acetate in the presence of (10)

Reaction time: 200 minutes

DTBP (2.5mg, 1.0 equivalent)

Trap(10) (4.3mg, 2.1 equivalents)

Dimethyl phosphite (11.7mg, 10 equivalents)

Vinyl acetate (1.1ml)

Experimental

The aminoxyl trap(10), initiator(DTBP) and vinyl acetate(800μl) were added to dimethyl phosphite and 300μl of vinyl acetate at 60°C over 200 minutes, via a motor driven syringe. Both the solutions were degased with N_2 (see 6.5.0).

HPLC conditions were: 70% methanol in water, with a 0.25ml/minute flow rate. The products were separated and characterised in 6.10.1.5, in a preparative scale reaction. However the products were eluted from the HPLC column in the following order.

Dimethyl (1,1,3,3-tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy) phosphate(45)

$$\begin{array}{c} O \diagdown \diagup OCH_3 \\ P \\ R_2NO \diagup \diagdown OCH_3 \end{array}$$
(45)
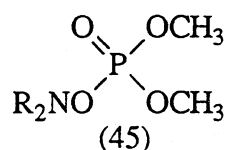
Identical to an authentic sample by HPLC (see 6.10.1.5).

Dimethyl 2-acetoxy-2-(1,1,3,3-tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy)ethylphosphonate(46)

$$\begin{array}{c} O \\ \parallel \\ H_3CCO \\ R_2NO \diagup \diagdown P(OCH_3)_2 \\ \parallel \\ O \end{array}$$
(46)
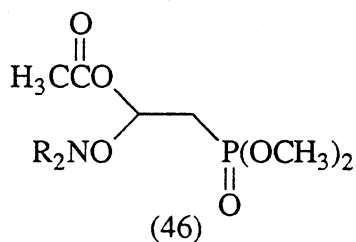
Identical to an authentic sample by HPLC (see 6.10.1.5).

2-Methoxy-1,1,3,3-tetramethyl-2,3-dihydro-1H-isoindol(22)
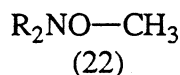
$$R_2NO{-}CH_3$$
(22)

Identical to an authentic sample by and HPLC (see 6.7).

Experimental

2-t-Butoxy-1-acetoxy-1-(1,1,3,3-tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy)ethane(25)

$$\underset{\underset{\displaystyle R_2NO}{|}}{\overset{\displaystyle \overset{O}{\underset{||}{H_3CCO}}}{\diagdown}}\diagup\diagdown O^tBu$$

(25)
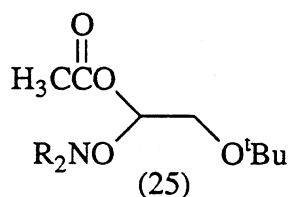
Identical to an authentic sample by HPLC (see 6.7).

6.10.1.5 The reaction of Dimethyl phosphite with t-butoxyl radicals, Acrylonitrile and Vinyl acetate in the presence of (10)

Reaction time: 240 minutes

DTBP (188mg, 1.0 equivalent)

Trap(10) (320mg, 2.1 equivalents)

Dimethyl phosphite (600μl, 8.3 equivalents)

Acrylonitrile (3.5M)

Vinyl acetate (7.0M)

Acetonitrile-cosolvent (600μl)

Likewise to 6.10.1.3 and 6.10.1.4 the trap(10), initiator(DTBP), acrylonitrile(128μl) and vinyl acetate(272μl) were added to the dimethyl phosphite, acrylonitrile(900μl) and vinyl acetate(1920μl) at 60°C over 240 minutes, via a motor driven syringe. Both solutions were degassed with N_2 (see 6.5.0).

The reaction mixture was concentrated to approximately 30% of the original volume under high vacuum prior to separation. Preparative HPLC at 75/25, methanol/water and a flow rate of 4.0 ml/minute produced the following compounds in order of elution from the reverse-phase HPLC column.

Dimethyl 2-cyano-2-(1,1,3,3-tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy)-ethylphosphonate(44)

(Found: M 352.159. $C_{17}H_{25}N_2O_4P$ requires 352.160).

^1H n.m.r.(CDCl$_3$, 250.122MHz, shifts in ppm, couplings in Hz):
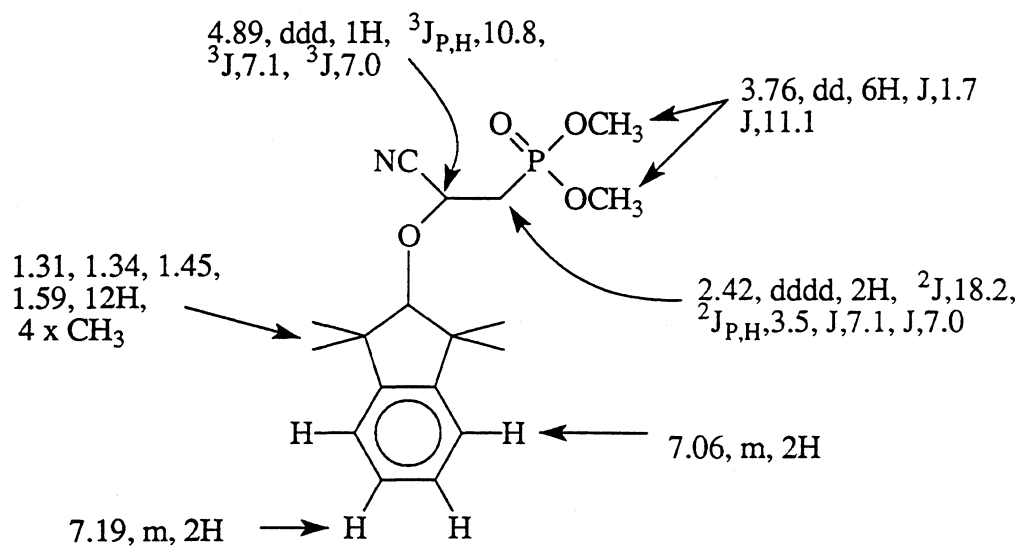
4.89, ddd, 1H, $^3J_{P,H}$,10.8, ^3J,7.1, ^3J,7.0

3.76, dd, 6H, J,1.7 J,11.1

2.42, dddd, 2H, ^2J,18.2, $^2J_{P,H}$,3.5, J,7.1, J,7.0

1.31, 1.34, 1.45, 1.59, 12H, 4 x CH$_3$

7.06, m, 2H

7.19, m, 2H

^{13}C n.m.r.(CDCl$_3$, 62.8MHz, shifts in ppm):

120.2, $^3J_{P,C}$,12

98.6

52.7, $^2J_{P,C}$,7.5

29.1, J$_{P,C}$,143.9

25.1, 29.9, 4 x CH$_3$

69.2, 69.6

121.5

127.6

Experimental
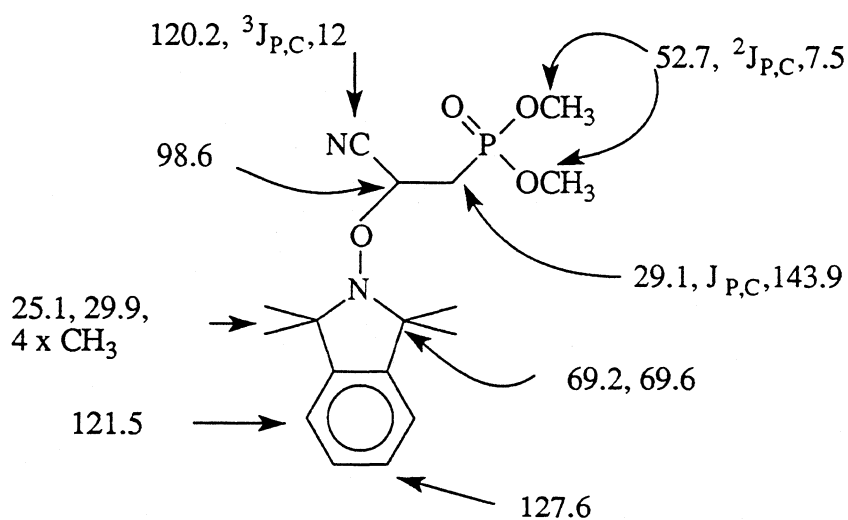
Dimethyl (1,1,3,3-tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy) phosphate(45)

(Found: C, 56.3; H, 7.5; N, 4.6. $C_{14}H_{22}NO_4P$ requires C, 56.2; H, 7.5; N, 4.6%).

^{1}H n.m.r.(CO(CD$_3$)$_2$, 250.122MHz, shifts in ppm, couplings in Hz):

7.23, m, 2H

3.81, d, 6H, $^3J_{P,H}$,10.0

7.31, m, 2H

1.53, brs, 12H
4 x CH$_3$
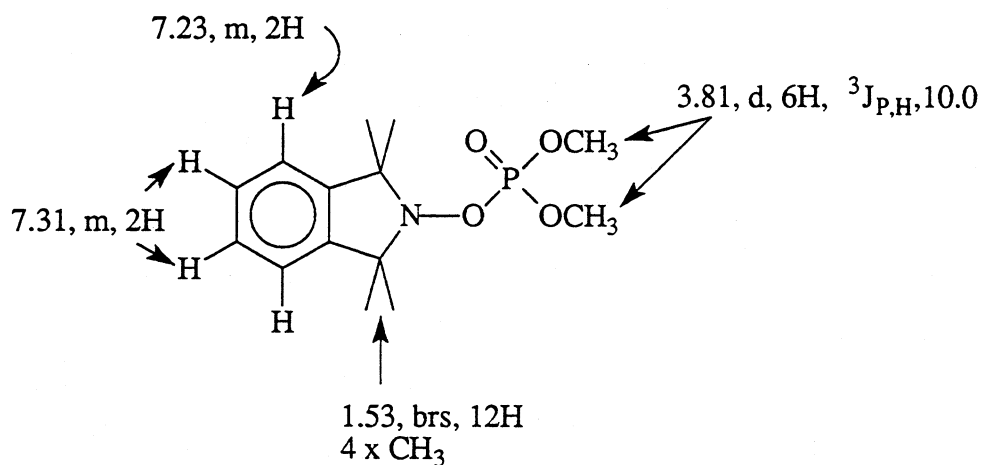
^{13}C n.m.r.(CO(CD$_3$)$_2$, 62.8MHz, shifts in ppm):
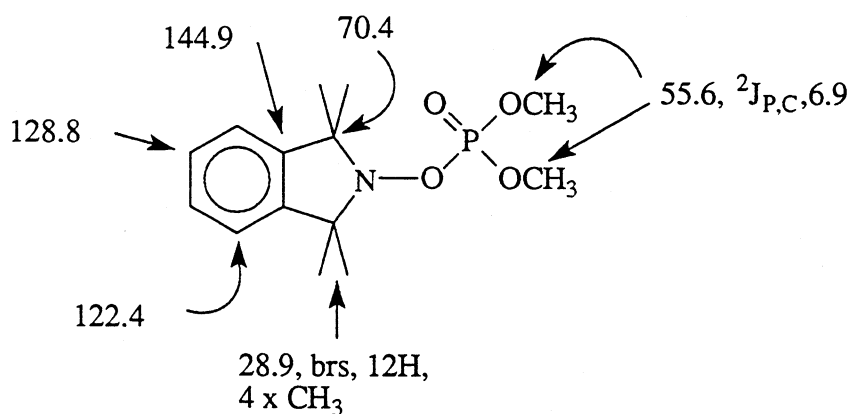
144.9   70.4

128.8

55.6, $^2J_{P,C}$,6.9

122.4

28.9, brs, 12H,
4 x CH$_3$

^{31}P n.m.r 4.94ppm.

Experimental

Dimethyl 2-acetoxy-2-(1,1,3,3-tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy)-ethylphosphonate(46)

(Found: MH$^+$ 386.173. C$_{18}$H$_{28}$NO$_6$PH$^+$ requires 386.175).

^{1}H n.m.r.(CDCl$_3$, 250.122MHz, shifts in ppm, couplings in Hz):
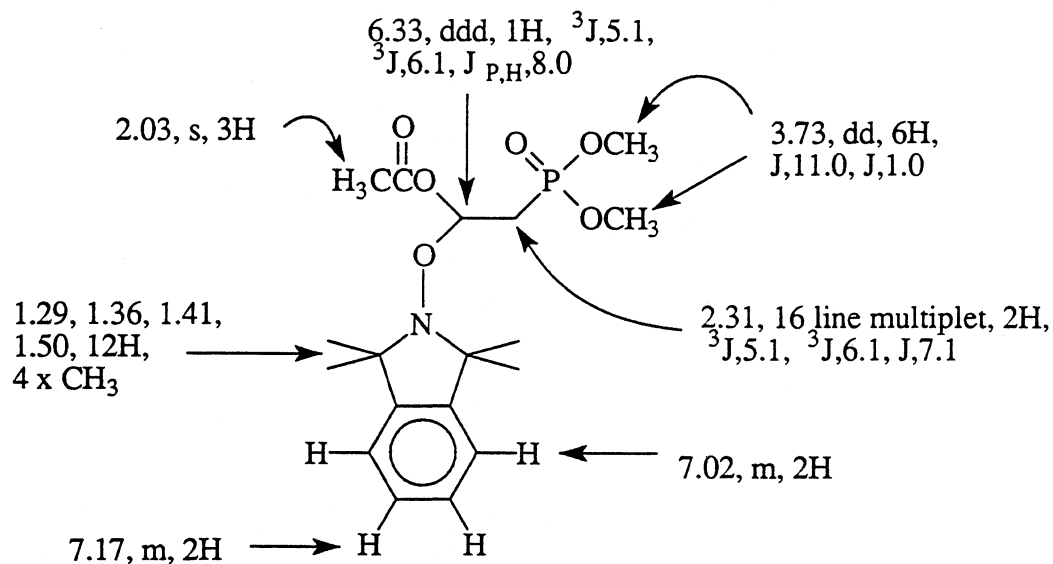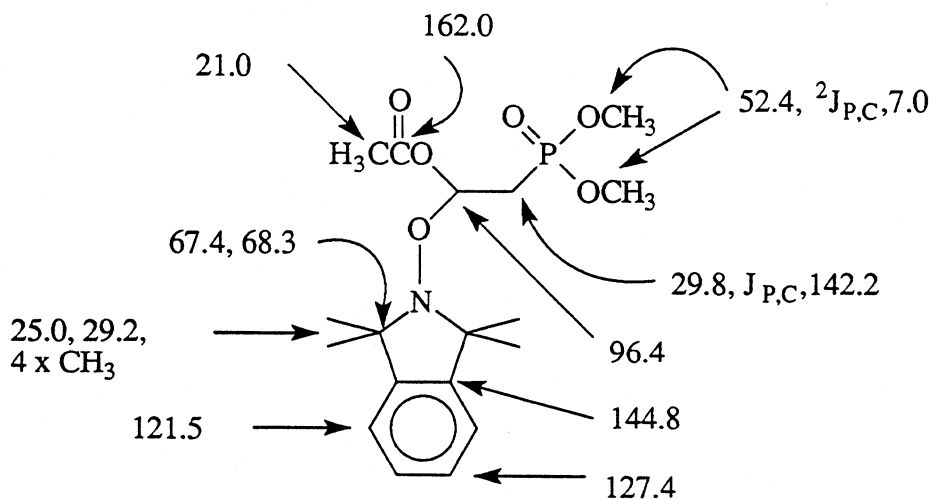
6.33, ddd, 1H, ^{3}J,5.1, ^{3}J,6.1, J$_{P,H}$,8.0

2.03, s, 3H

3.73, dd, 6H, J,11.0, J,1.0

1.29, 1.36, 1.41, 1.50, 12H, 4 x CH$_3$

2.31, 16 line multiplet, 2H, ^{3}J,5.1, ^{3}J,6.1, J,7.1

7.02, m, 2H

7.17, m, 2H

^{13}C n.m.r.(CDCl$_3$, 62.8MHz, shifts in ppm):

21.0

162.0

52.4, ^{2}J$_{P,C}$,7.0

67.4, 68.3

29.8, J$_{P,C}$,142.2

25.0, 29.2, 4 x CH$_3$

96.4

144.8

121.5

127.4

^{31}P n.m.r. 27.29.

Experimental

<u>2-Methoxy-1,1,3,3-tetramethyl-2,3-dihydro-1H-isoindol(22)</u>

$$R_2NO-CH_3$$
(22)

Identical to an authentic sample by ^{1}H nmr and HPLC (see 6.7).

<u>2-t-Butoxy-1-cyano-1-(1,1,3,3-tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy)ethane(27)</u>

NC
R₂NO   OᵗBu
(27)

Identical to an authentic sample by ^{1}H nmr and HPLC (see 6.7).

<u>2-t-Butoxy-1-acetoxy-1-(1,1,3,3-tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy)ethane(25)</u>

O
‖
H₃CCO
R₂NO   OᵗBu
(25)
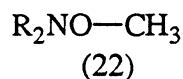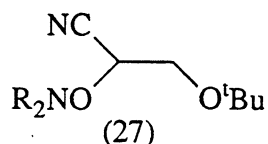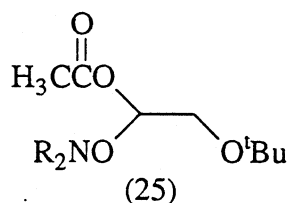
Identical to an authentic sample by ^{1}H nmr and HPLC (see 6.7).

6.10.2 Addition to Cyclic Alkenes

6.10.2.0 The reaction of Diphenylphosphine oxide, Cyclopentene, and t-butoxyl radicals in the presence of (10)

Reaction time: 68 minutes
DTBP (56mg, 1.0 equivalent)
Trap(10) (225mg, 5.0 equivalents)
Diphenylphosphine oxide (97mg, 2.0 equivalents)
Cyclopentene (5.0 ml)

Experimental

The reaction mixture was concentrated to approximately 30% of the original volume under high vacuum, prior to separation.

HPLC conditions: 90% methanol in water, flow rate of 6.5 ml/minute. Preparative isolation by HPLC gave the following compounds (in order of elution from the reverse-phase HPLC column).

1,1,3,3-Tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy diphenyl-phosphinate(32)
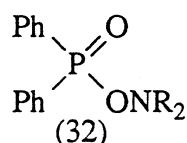
Identical to an authentic sample by ^{1}H nmr and HPLC (see 6.8).

trans-1-(1,1,3,3-Tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy)-2-diphenyl-phosphinoylcyclopentane(48)

(Found: M 459.230. $C_{29}H_{34}NO_2P$ requires 459.232).

[1]H n.m.r.(CDCl$_3$, 250.122MHz, shifts in ppm, couplings in Hz):
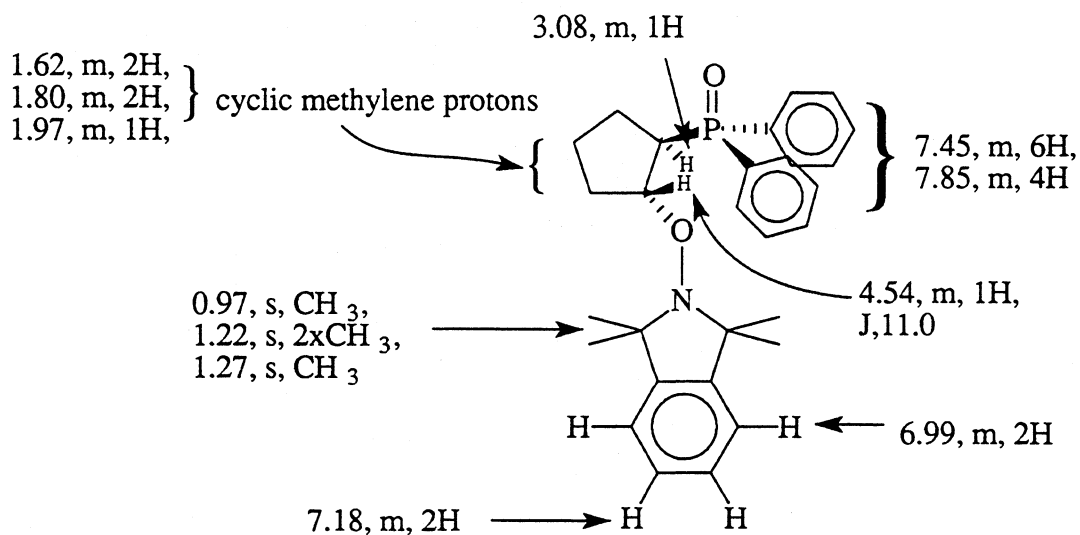
3-(1,1,3,3-Tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy)cyclopentene(49)

^{1}H n.m.r.(CDCl$_3$, 250.122MHz, shifts in ppm):

1.95, m, 1H,
2.28, m, 2H,
2.51, m, 1H
cyclic methylene
protons

6.01, m, 2H

7.10, m, 2H

5.05, m, 1H

1.37, 1.54, vbrs, 4 x CH$_3$

7.22, m, 2H
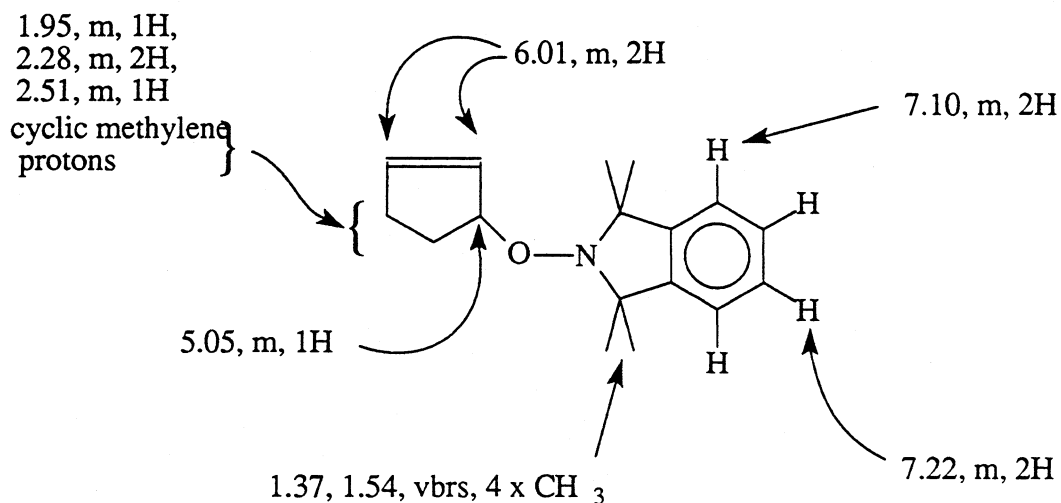
Identical to an authentic sample by ^{1}H nmr[18c] and HPLC.

4-(1,1,3,3-Tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy)cyclopentene(50)

^{1}H nmr(CDCl$_3$, 250.122MHz, shifts in ppm):

1.62, m, 1H, 2.07-2.25,unresolved multiplets,
4H, 2.42, m, 1H,cyclic methylene protons
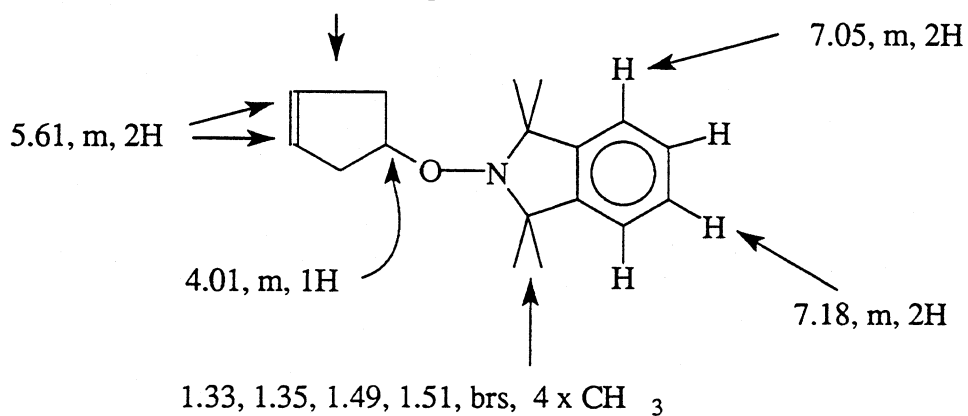
7.05, m, 2H

5.61, m, 2H

4.01, m, 1H

1.33, 1.35, 1.49, 1.51, brs, 4 x CH$_3$

7.18, m, 2H

Identical to an authentic sample by ^{1}H nmr[18c] and HPLC.

Experimental

cis-1-(1,1,3,3-Tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy)-2-t-butoxy-
cyclopentane(51)

^{1}H nmr(CDCl$_3$, 250.122MHz, shifts in ppm):

1.36, 1.47, 1.52, 1.57,
s, 4 x CH$_3$

7.17, m, 2H

3.88, m, 1H

1.30-1.87, m, 7H,
2.10, m, 1H,
cyclic methylene
protons

3.50, m, 1H

7.05, m, 2H

1.24, s, 9H, 3 x CH$_3$
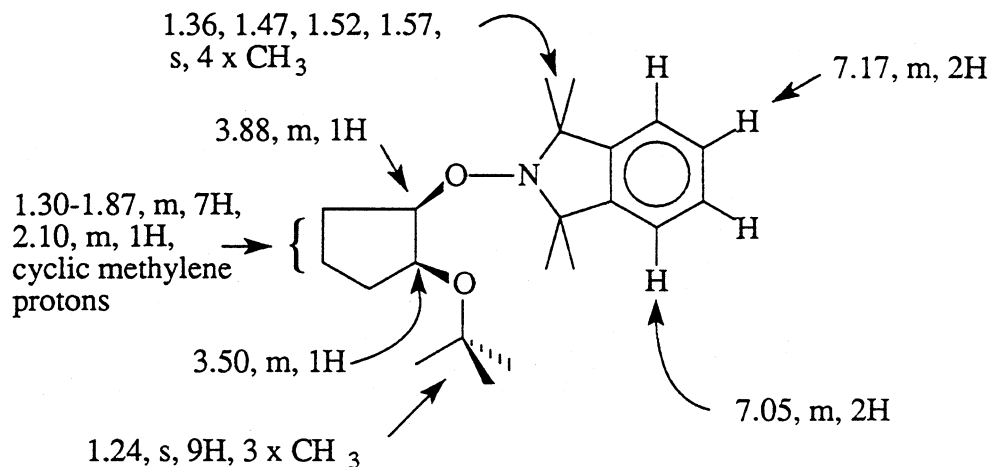
Identical to an authentic sample by ^{1}H nmr[18c] and HPLC.

trans-1-(1,1,3,3-Tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy)-2-t-butoxy-
cyclopentane(52)

^{1}H nmr(CDCl$_3$, 250.122MHz, shifts in ppm):

1.30, 1.54, 2 x s,
12H, 4 x CH$_3$

3.64, m, 1H

1.30-1.70, m, 4H,
1.82, m, 1H,
2.27, m, 1H,
cyclic methylene
protons

3.53, m, 1H

7.18, m, 2H

7.04, m, 2H

1.20, s, 9H

Identical to an authentic sample by ^{1}H nmr[18c] and HPLC.

Experimental
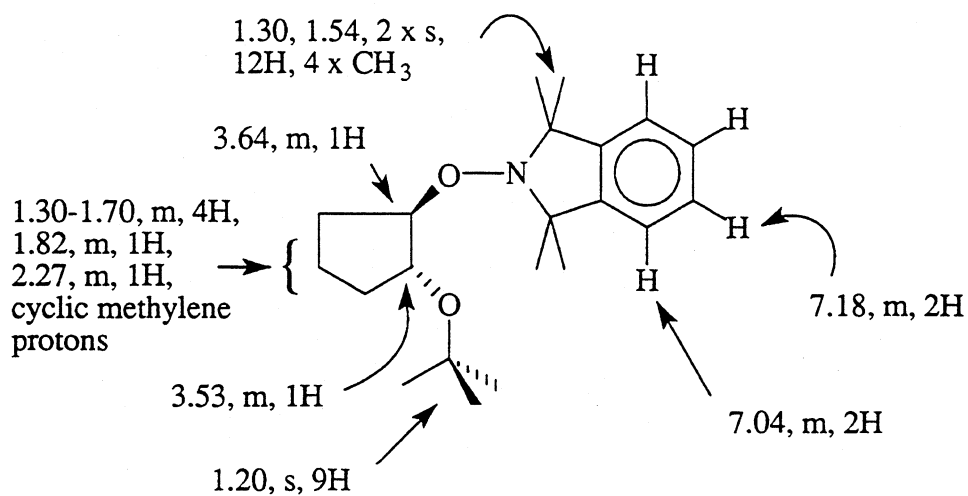
6.10.2.1 The reaction of Cyclopentene, with t-Butoxyl radicals and Dimethyl phosphite in the presence of (10)

Reaction time: 68 minutes

DTBP (10mg, 1.0 equivalent)

Trap(10) (18mg, 2.1 equivalents)

Dimethyl phosphite (119μl, 20.0 equivalents)

Cyclopentene (1.2ml)

Acetonitrile (co-solvent-0.5ml)

This was an analytical reaction which by HPLC showed no dimethoxy phosphinyl radical addition products to be present in the reaction mixture. The reaction mixture was analysed using 85% methanol in water with a flow rate of 0.5ml/minute. Products were eluted in the following order from the reverse-phase HPLC column.

Dimethyl (1,1,3,3-tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy) phosphate(45)

$$\begin{array}{c} H_3CO \diagdown \quad \diagup O \\ P \\ H_3CO \diagup \quad \diagdown ONR_2 \\ (45) \end{array}$$
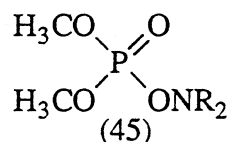
Identical to an authentic sample by HPLC (see 6.10.1.5).

3-(1,1,3,3-Tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy)cyclopentene(49)

(49)

Identical to an authentic sample by HPLC (see 6.10.2.0).

Experimental
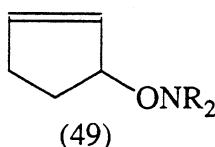
4-(1,1,3,3-Tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy)cyclopentene(50)

(50)
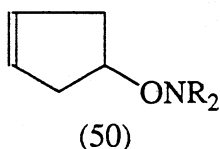
Identical to an authentic sample by HPLC (see 6.10.2.0).

cis-1-(1,1,3,3-Tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy)-2-t-butoxycyclopentane(51)

(51)
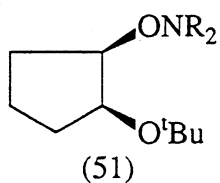
Identical to an authentic sample by HPLC (see 6.10.2.0).

trans-1-(1,1,3,3-Tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy)-2-t-butoxy-cyclopentane(52)

(52)
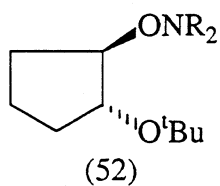
Identical to an authentic sample by HPLC (see 6.10.2.0).

6.10.2.2 The reaction of Diphenylphosphine oxide, t-Butoxyl radicals and Cyclohexene in the presence of (10)

Reaction time: 68 minutes

DTBP (56.6 mg, 1.0 equivalent)

Trap(10) (100mg, 2.1 equivalents)

Diphenylphosphine oxide (98.8mg, 2.0 equivalents)

Cyclohexene (1.0ml)

The reaction mixture was analysed using 85% methanol in water, with a flow rate of 3.5ml/minute. Products were eluted in the following order from the reverse-phase HPLC column.

1,1,3,3-Tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy diphenylphosphinate(32)

(32)
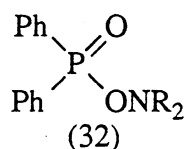
Identical to an authentic sample by ^{1}H nmr[18c] and HPLC (see 6.8.0).

3-(1,1,3,3-Tetramethyl-2,3-dihydo-1H-isoindol-2-yloxy)cyclohexene(53)

[1]H n.m.r.(CDCl3, 250.122MHz, shifts in ppm):
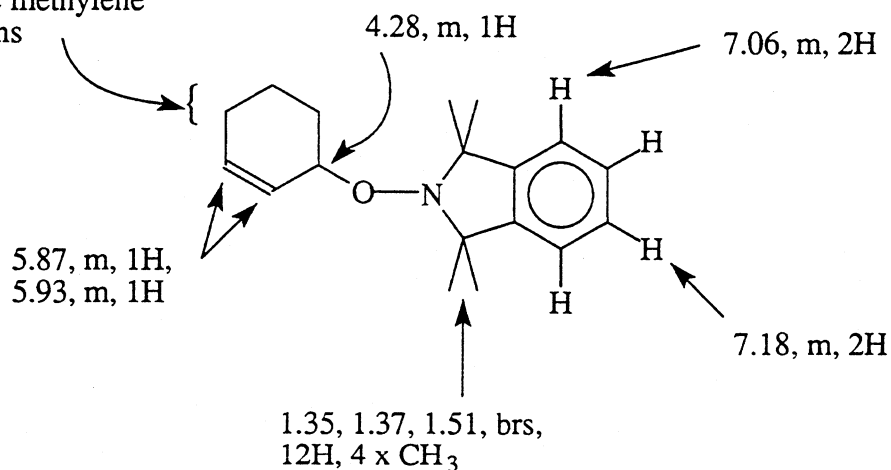
Identical to an authentic sample by ^{1}H nmr[18c] and HPLC.

Experimental

4-(1,1,3,3-Tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy)cyclohexene(54)

^{1}H n.m.r(CDCl$_3$, 250.122MHz, shifts in ppm):

1.62, m, 1H, 2.07-2.25, m,4H,
2.42, m, 1H,cyclic methylene protons

7.05, m, 2H

5.61, m, 2H

4.01, m, 1H

1.33, 1.35, 1.49, 1.51,
brs, 4 x CH$_3$

7.18, m, 2H
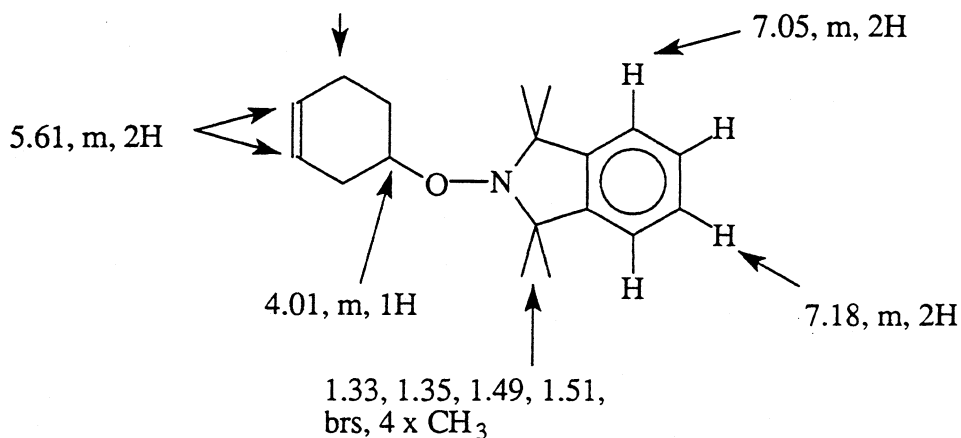
Identical to an authentic sample by ^{1}H nmr[18c] and HPLC.

cis-1-(1,1,3,3-Tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy)-2-t-butoxy-cyclohexane(55)

^{1}H n.m.r(CDCl$_3$, 250.122MHz, shifts in ppm):
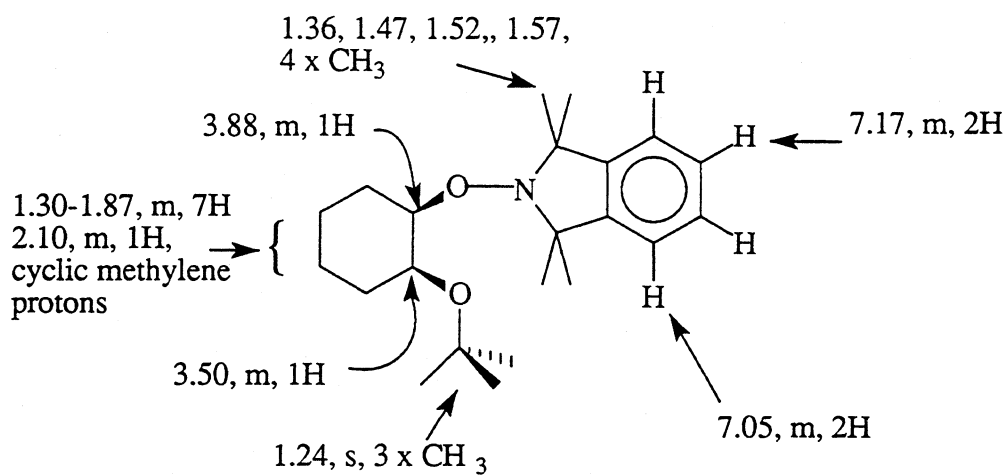
1.36, 1.47, 1.52,, 1.57,
4 x CH$_3$

3.88, m, 1H

7.17, m, 2H

1.30-1.87, m, 7H
2.10, m, 1H,
cyclic methylene
protons

3.50, m, 1H

1.24, s, 3 x CH$_3$

7.05, m, 2H

Identical to an authentic sample by ^{1}H nmr[18c] and HPLC.

Experimental

<u>trans-1-(1,1,3,3-Tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy)-2-t-butoxy-cyclohexane(56)</u>

^{1}H n.m.r(CDCl3, 250.122MHz, shifts in ppm):
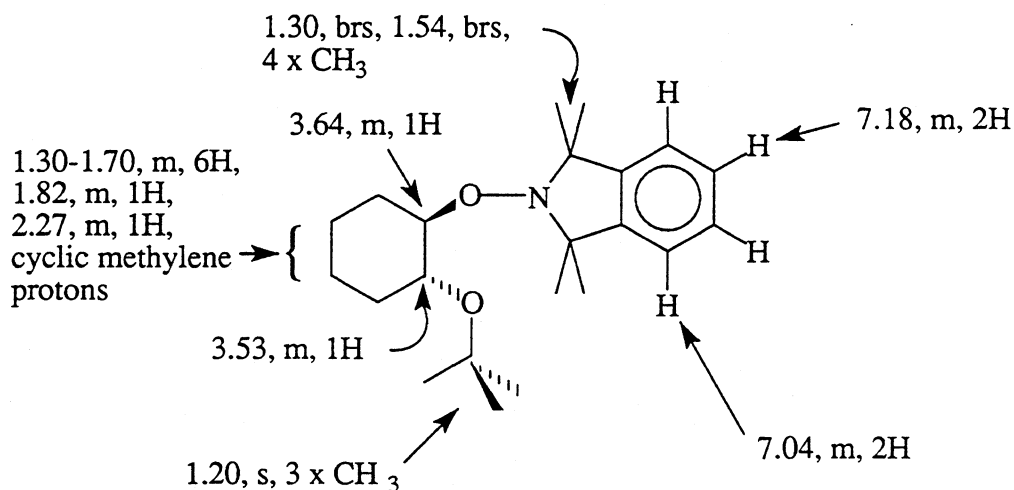
Identical to an authentic sample by ^{1}Hnmr[18c] and HPLC.

6.10.2.3 The reaction of Cyclohexene with t-butoxyl radicals and Dimethyl phosphite in the presence of (10)

Reaction time: 68 minutes

DTBP (5.1mg, 1.0 equivalent)

Trap(10) (9.0mg, 2.1 equivalents)

Dimethyl phosphite (1.0ml, 230 equivalents)

Cyclohexene (1.1ml)

This was an analytical scale reaction, due to no addition products being detected by HPLC, even though 230 equivalents of dimethyl phosphite was used. The reaction mixture was analysed as is with the following HPLC conditions: 85% methanol in water. Flow rate, 0.5ml/minute. Products were eluted in the following order from the reverse-phase HPLC column.

Dimethyl (1,1,3,3-tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy) phosphate(45)

$$H_3CO \quad O$$
$$H_3CO \diagdown P \diagup$$
$$H_3CO \diagup \diagdown ONR_2$$

(45)

Identical to an authentic sample by HPLC (see 6.10.1.5).

3-(1,1,3,3-Tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy)cyclohexene(53)

ONR$_2$

(53)
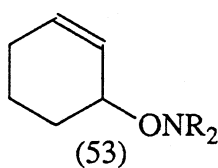
Identical to an authentic sample by HPLC (see 6.10.2.2).

4-(1,1,3,3-Tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy)cyclohexene(54)

ONR$_2$

(54)
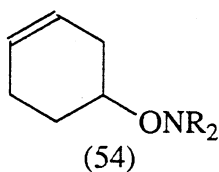
Identical to an authentic sample by HPLC (see 6.10.2.2).

trans-1-(1,1,3,3-Tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy)-2-t-butoxy-cyclohexane(55)

ONR$_2$

O^tBu

(55)

Identical to an authentic sample by HPLC (see 6.10.2.2.).

Experimental
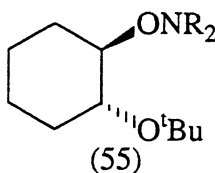
6.10.2.4 The reaction of 3,4-Dihydro-2H-pyran with t-butoxyl radicals and Diphenylphosphine oxide in the presence of (10)

Reaction time: 68 minutes

DTBP (140mg, 1.0 equivalent)

Trap(10) (250mg, 2.1 equivalents)

Diphenylphosphine oxide (238mg, 2.0 equivalents)

3,4-Dihydro-2H-pyran (3.0ml)

The reaction mixture was concentrated to approximately 30% of its original volume under high vacuum, prior to separation. The reaction products were separated using the following HPLC conditions: 80% methanol in water, 2.5-5.0ml/minute flow rate over 260 minutes. Preparative isolation gave the following products (in order of elution from the reverse-phase HPLC column).

1,1,3,3-Tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy diphenylphosphinate(32)

$$\text{Ph} \diagdown \underset{\text{Ph}}{\overset{\diagup}{P}} \diagup \overset{O}{\diagup} \diagdown \text{ONR}_2$$
(32)
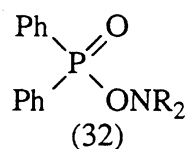
Identical to an authentic sample by ^{1}H nmr and HPLC (see 6.8.0).

trans-2-(1,1,3,3-Tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy)-3-diphenyl-phosphinoyltetrahydropyran(57)

(Found: MH$^+$ 476. C$_{29}$H$_{35}$NO$_3$P requires MH$^+$ 476)[#].

^{1}H n.m.r(CDCl$_3$, 250.122MHz, shifts in ppm, couplings in Hz):

7.15, m, 2H

6.99, m, 2H

3.70, ddd, J $_{ax/ax}$,9.2, J$_{eq/eq}$,3.6, J$_{gem}$,11.6

0.87, vbrs, 1.23-1.90, m, 16H,(4 x CH$_3$, 4H cyclic methylene protons)

2.69, m, ^{2}J$_{gem}$,11.6

4.16, m

5.23, dd, ^{3}J$_{P,H}$,5.4, ^{3}J$_{eq/eq}$,3.6

7.46, m, 6H, 7.68, m, 2H, 7.91, m, 2H

2-(1,1,3,3-Tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy)-5,6-dihydro-2H-pyran(58)

^{1}H n.m.r(CDCl$_3$, 250.122MHz, shifts in ppm, couplings in Hz):

1.38, s, 2 x CH$_3$, 1.48, s, CH$_3$, 1.58, s, CH$_3$

7.12, m, 2H

3.85, ddt, 1H, ^{2}J,11.1, J,6.1, J,1.1

4.04, td, 1H, ^{2}J,11.1, J,3.4

7.23, m, 2H

2.36, m, 1H

5.27, m,1H

1.93, dddt, 1H, ^{2}J,17.8, ^{3}J,5.7, J,3.4, J,1.0

6.13, dddt, J,10.1, J,5.7, J,1.5, J,0.6

5.87, dtd, J,10.1, J,2.9, J,1.2

Identical to an authentic sample by 1H nmr[18c] and HPLC.

[#] Several attempts at obtaining a parent ion from accurate mass mass spectrometry were unsuccesful for (57) and (59). However the values given for ((57) & (59)) come from low resolution mass spectra.

Experimental

cis-2-(1,1,3,3-Tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy)-3-diphenyl-phosphinoyltetrahydropyran(59)

(Found: MH$^+$ 476. $C_{29}H_{34}NO_3PH^+$ requires 476).

^{1}H n.m.r(CDCl$_3$, 250.122MHz, shifts in ppm, couplings in Hz):

7.07, m, 2H

4.17-4.37[#], m, 2H

1.05, m, 1.46-2.20, m,
4 x CH$_3$ plus 4 cyclic
methylene protons

6.92, m, 2H

7.51, m, 6H,
7.68, m, 2H,
7.86, m, 2H

3.75[#], m

4.82, dd, J,2.4, J,2.2
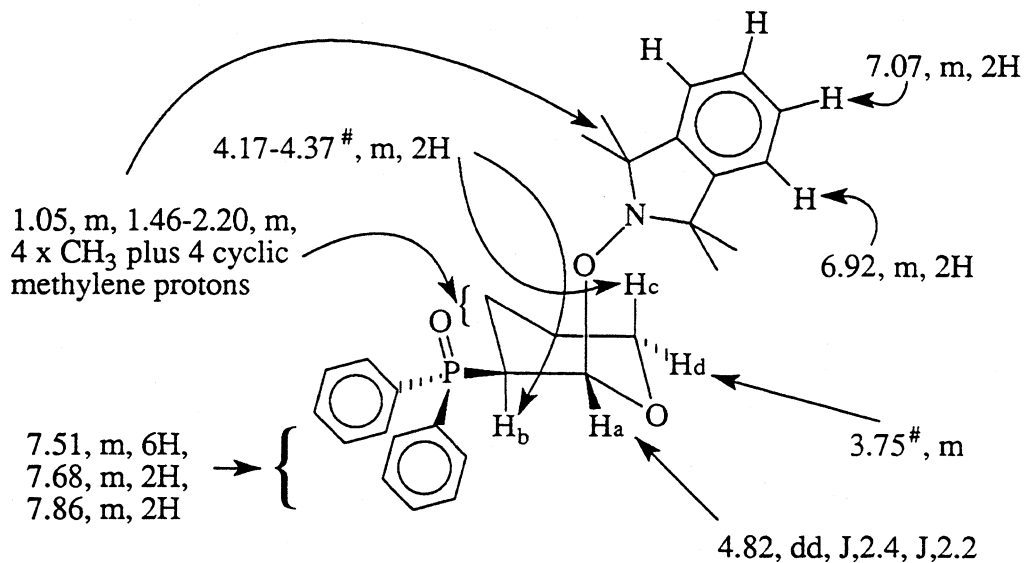
[#] Tentative assignment, H$_c$ interchangeable with H$_d$.

4-(1,1,3,3-Tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy)-5,6-dihydro-2H-pyran(60)

^{1}H n.m.r(CDCl$_3$, 250.122MHz, shifts in ppm, couplings in Hz):
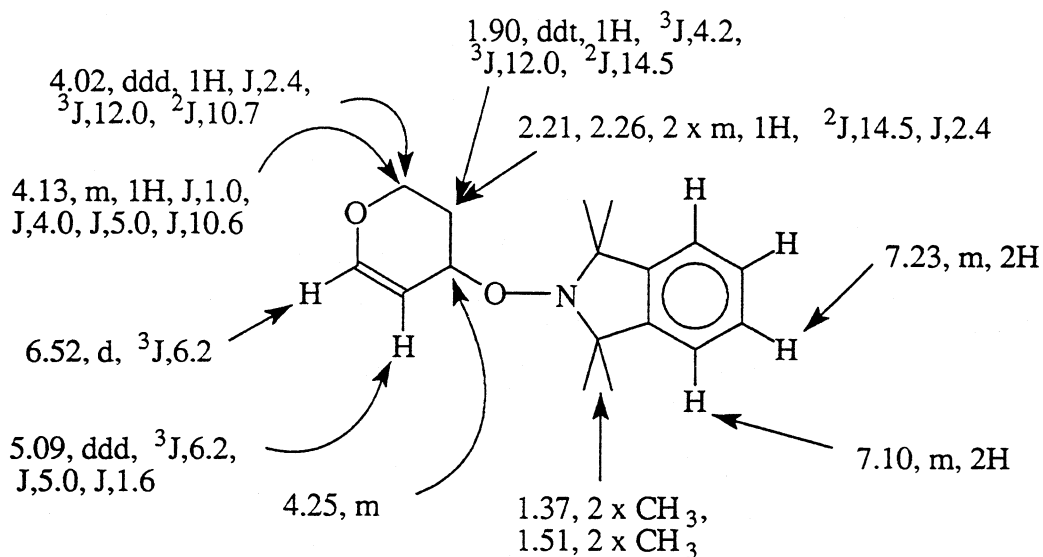
1.90, ddt, 1H, ^{3}J,4.2,
^{3}J,12.0, ^{2}J,14.5

4.02, ddd, 1H, J,2.4,
^{3}J,12.0, ^{2}J,10.7

2.21, 2.26, 2 x m, 1H, ^{2}J,14.5, J,2.4

4.13, m, 1H, J,1.0,
J,4.0, J,5.0, J,10.6

7.23, m, 2H

6.52, d, ^{3}J,6.2

7.10, m, 2H

5.09, ddd, ^{3}J,6.2,
J,5.0, J,1.6

4.25, m

1.37, 2 x CH$_3$,
1.51, 2 x CH$_3$

Identical to an authentic sample by ^{1}H nmr[18c] and HPLC.

Experimental

2-(1,1,3,3-Tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy)-3,4-dihydro-2H-pyran(61)

^{1}H n.m.r(CDCl$_3$, 250.122MHz, shifts in ppm, couplings in Hz):

6.33, d, J,6.2

4.81, ddd, ^{3}J$_{cis}$,6.2, ^{3}J,4.3, ^{3}J,4.3

1.35, 2 x CH$_3$,
1.51, 2 x CH$_3$

7.23, m, 2H

1.8-2.3, m, 4H, cyclic methylene protons

5.35, dd, ^{3}J,2.7, ^{3}J,2.7

7.1, m, 2H
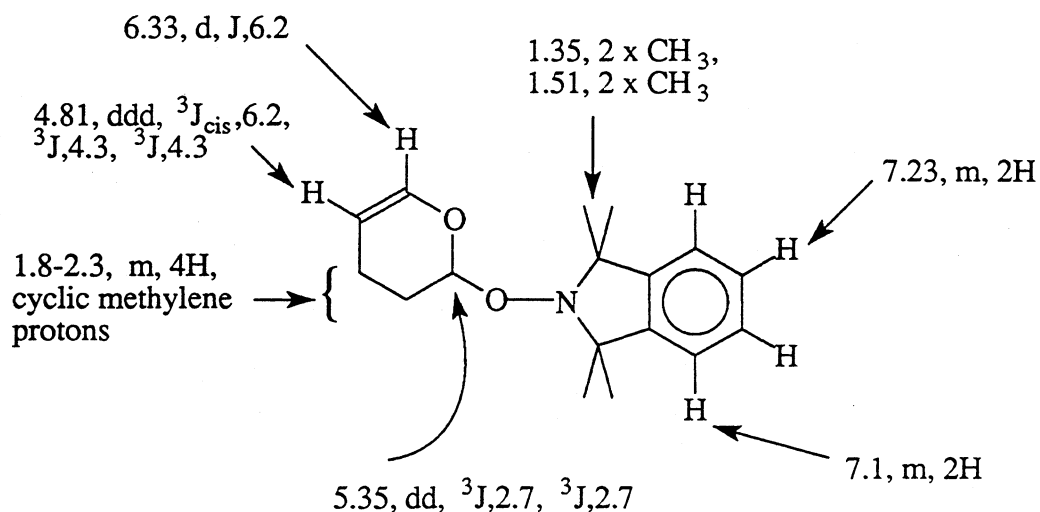
Identical to an authentic sample ^{1}H nmr[18c] and HPLC.

trans-2-(1,1,3,3-Tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy)-3-t-butoxy-tetrahydropyran(62)

^{1}H n.m.r(CDCl$_3$, 250.122MHz, shifts in ppm, couplings in Hz):

3.91, ddd, 1H, ^{2}J,11.3, ^{3}J$_{trans}$,8.9, ^{3}J$_{cis}$,3.2

3.54, m, 1H

7.03, m, 2H

4.69, d, ^{3}J$_{eq/eq}$,2.0

7.17, m, 2H

1.87, m, 2H

3.53, m

1.18, s, 3 x CH$_3$

1.26-1.53, m, 4 x CH$_3$, plus 2H cyclic methylene protons

Identical to an authentic sample by ^{1}H nmr[18c] and HPLC.

Experimental
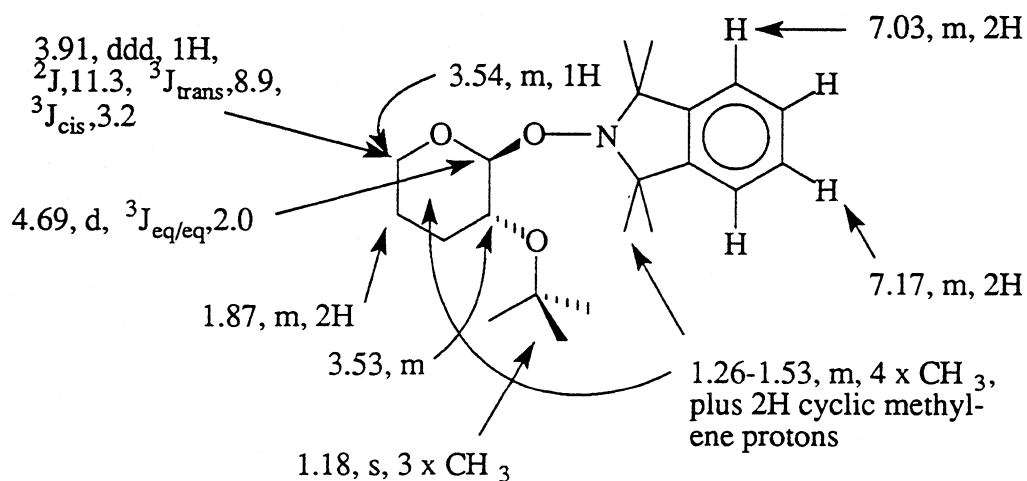
6.10.2.5 The reaction of 4-t-Butylcyanocyclohexene with t-butoxyl radicals and Diphenylphosphine oxide in the presence of (10)

Reaction time: 555 minutes

DTBP (147mg, 1.0 equivalent)

Trap(10) (250mg, 2.1 equivalents)

Diphenylphosphine oxide (252mg, 2.0 equivalents)

4-t-Butylcyanocyclohexene (390mg, 3.8 equivalents)

Acetonitrile (co-solvent, 1.4ml)

The initiator(DTBP), trap(10) and acetonitrile were added to the 4-t-butylcyanocyclohexene(Mpt 45-46°C) and diphenylphosphine oxide at 60°C over 555 minutes via a motor driven syringe. Both the solutions were previously degassed with N_2(see 6.5.0).

The quantities of 4-t-butylcyanocyclohexene and diphenylphosphine oxide were varied in numerous reactions in an attempt to improve the very low yield of phosphinyl radical addition products. This was carried out with little success.however. HPLC conditions: 80% methanol in water, with a 5.5 ml/minute flow rate. Preparative isolation by HPLC gave the following compunds (in order of elution from the reverse-phase HPLC column).

1,1,3,3-Tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy diphenylphosphinate(32)

$$\begin{array}{c} Ph \\ \diagdown \\ P \\ \diagup \quad \diagdown \\ Ph \qquad ONR_2 \\ (32) \end{array}$$
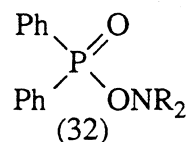
Identical to an authentic sample by ^{1}H nmr and HPLC (see 6.8.0).

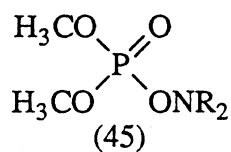4-cis-Cyano-4-trans-(1,1,3,3-tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy)-3-cis-(diphenylphosphinoyl)-4-t-butylcyclohexane(63)

(Found: MH$^+$ 555. C$_{35}$H$_{43}$N$_2$O$_2$PH$^+$ requires 555).

^{1}H n.m.r(CDCl$_3$, 250.122MHz, shifts in ppm):

0.75-1.79, m, 5H,1.93, m, 1H, 2.59, m, 1H, cyclic methylene protons

1.11, 1.23, 1.38, 1.68, 4 x CH$_3$

0.72, s

2.93, m

6.95, m, 2H

7.30, m, 3H,
7.44, m, 3H,
7.75, m, 2H,
7.86, m, 2H

7.15, m, 2H
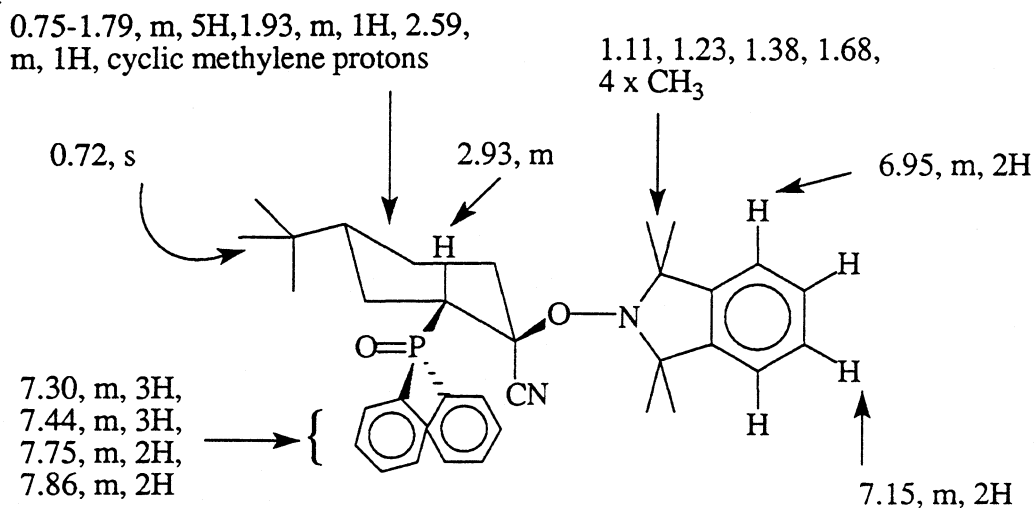
4-trans-Cyano-4-cis-(1,1,3,3-tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy)-3-trans-(diphenylphosphinoyl)-t-butyl-cyclohexane(64)

^{1}H n.m.r(CDCl$_3$, 250.122MHz, shifts in ppm):

0.54, s,
3 x CH$_3$

7.42, m, 6H,
7.79, m, 2H,
7.94, m, 2H

0.72-1.75, m, 5H,
2.32, m, 1H, 2.86,
m, 1H, cyclic methyl-
ene protons7

3.30, m

1.18, 1.34, 1.49, 1.71,
4 x CH$_3$

H ← 7.02, m, 2H

7.18, m, 2H

Experimental
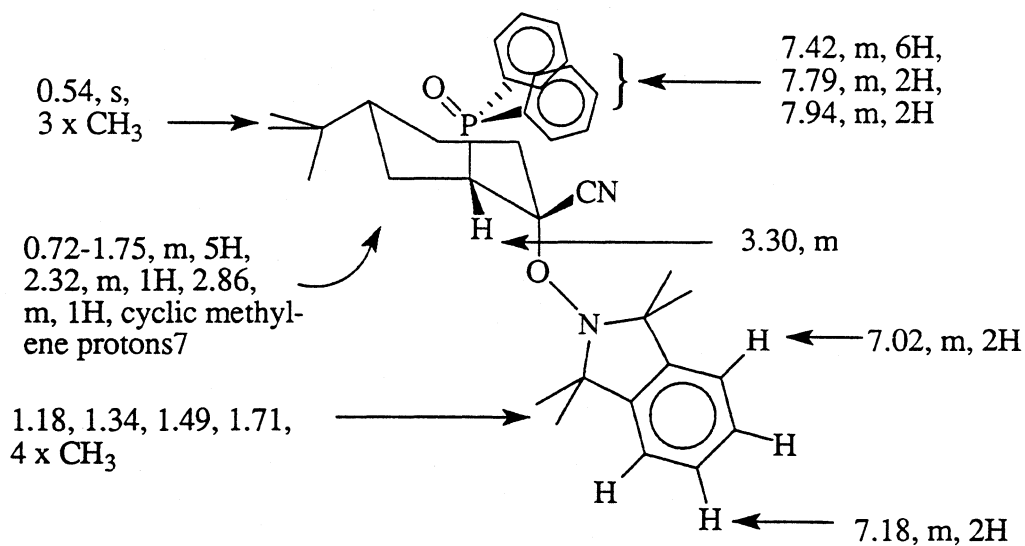
5-(1,1,3,3-Tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy)-4-cyano-t-butyl-cyclohex-3-ene(65)

^{1}H n.m.r(CDCl3, 250.122MHz, shifts in ppm, couplings in Hz):

0.87,s, 3 x CH$_3$

4.49, m

1.30, 1.39, 1.50, 1.57, 4 x CH$_3$

7.17, m, 2H

1.49-1.68, m, 2H, 1.90 1H, 2.28, m, 1H, 2.34, m, 1H, cyclic methylene protons

6.82, dd, ^{3}J,4.9, ^{3}J,2.2

7.04, m, 2H

^{13}C n.m.r(CDCl3, 62.8MHz, shifts in ppm):

26.9   27.2   41.9   67.6   25.6, 27.3, 4 x CH$_3$ 121.5

30.1

36.4   127.8   113.1   68.7   145.1   127.3
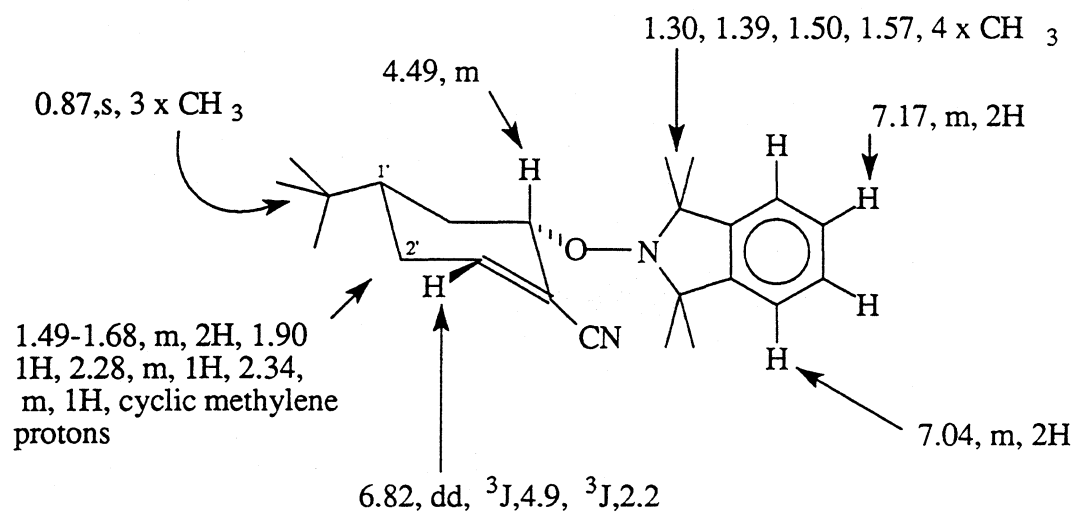
The vinylic carbon(C3') was not observed.

Experimental

6.10.2.6 The reaction of Diphenylphosphine oxide with t-butoxyl radicals and Phenylacetylene in the presence of (10)

Reaction time: 68 minutes

> DTBP (63mg, 1.0 equivalent)
> Trap(10) (113mg, 2.1 equivalents)
> Diphenylphosphine oxide (110mg, 2.0 equivalents)
> Phenyl acetylene (3.5mls)

The reaction mixture was concentrated to approximately 30% of the original volume under high vacuum, prior to separation.

HPLC conditions: 80% methanol in water, with a flow rate of 4.5ml/minute. Preparative isolation by HPLC gave the following products (in order of elution from the HPLC column).

1,1,3,3-Tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy diphenylphosphinate(32)

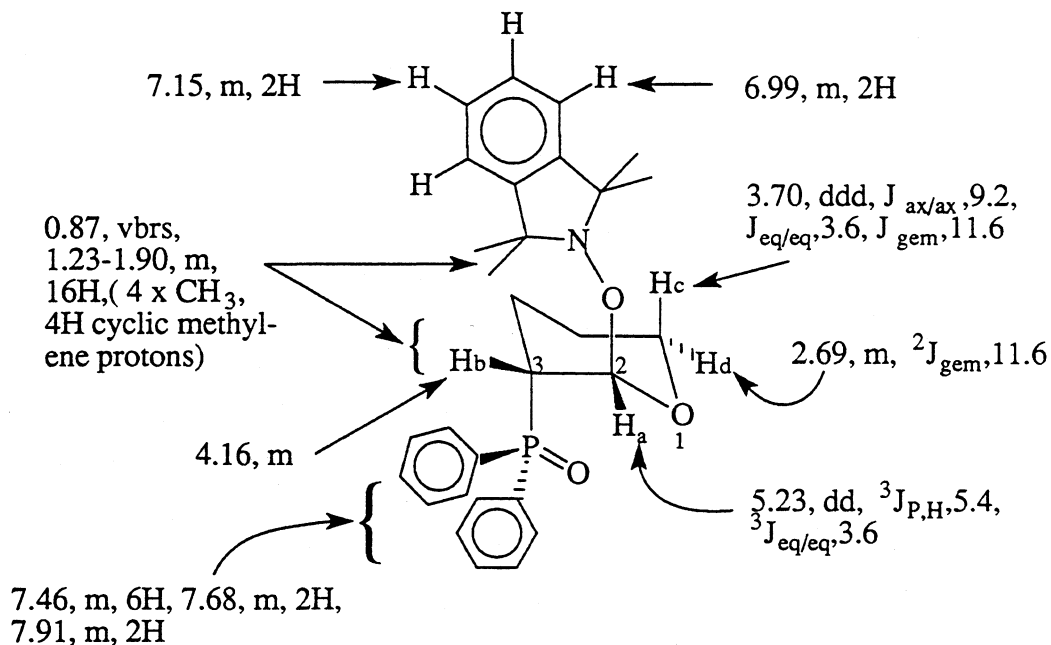$$Ph\diagdown P\diagup O$$
$$Ph\diagup P\diagdown ONR_2$$
(32)
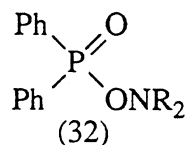
Identical to an authentic sample by ^{1}H nmr and HPLC (see 6.8.0).

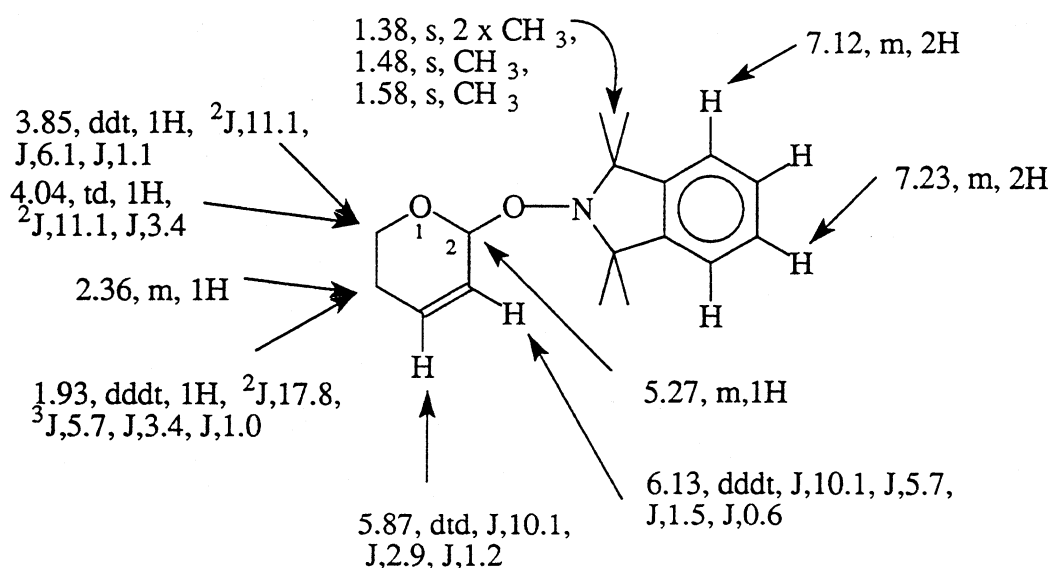### trans-1-(1,1,3,3-Tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy)-2-diphenyl-phosphinoyl-1-phenylethene(66)

The structure of this material is confirmed by analogy with the corresponding dimethylphosphite product(68) (see 4.3.2). An X-ray crystal structure obtained on this material gave structural confirmation. Attempts to grow suitable crystals for an X-ray crystal structure analysis of (66) were unsuccessful and at best produced only twinned crystals..

This material when in contact with CDCl3 decomposed immediately.

(Found M: 493.219. $C_{32}H_{32}NO_2P$ requires 493.217).

(Found: C, 77.6; H, 6.7; N, 3.1. $C_{32}H_{32}NO_2P$ requires C, 77.8; H, 6.5; N, 2.9).

^{1}H n.m.r(CD$_3$OD, 250.122MHz, shifts in ppm, couplings in Hz):

7.17-7.37, m, 9H,
7.66-7.79, m, 6H

7.17-7.37, m, 4H

6.74, d, $^2J_{P,H}$,13.5

1.48, 2 x CH$_3$,
1.66, 2 x CH$_3$

^{13}C n.m.r(CD$_3$OD, 62.8MHz, shifts in ppm):

129.4, J$_{P,C}$,33.0

131.65

128.6

128.3

138.4

130.5, J$_{P,C}$,126.2

132.3, J$_{P,C}$,42.0

25.9, 2 x CH$_3$,
30.2, 2 x CH$_3$

92.9, J$_{P,C}$,119.3

69.9

122.7

129.1
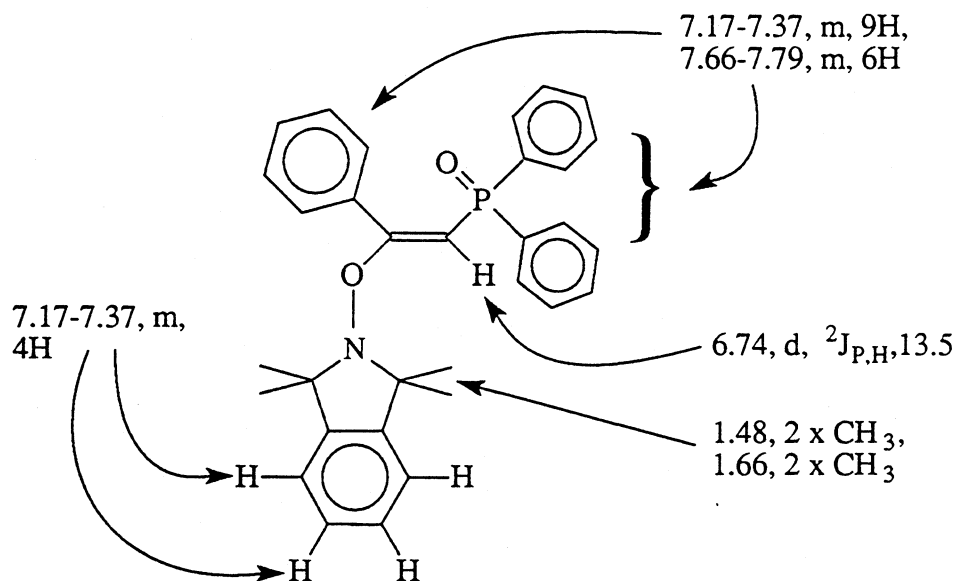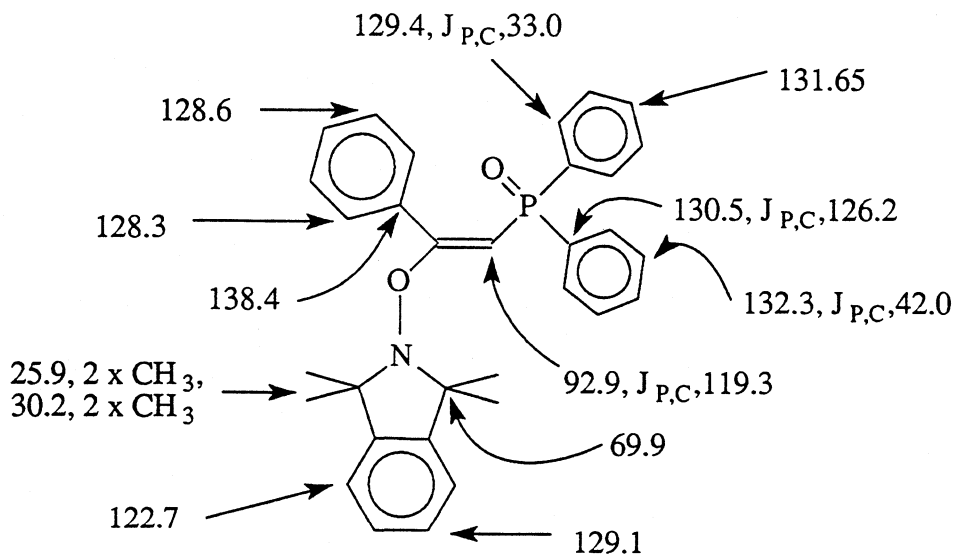
One vinylic carbon and the C$_{para}$ on the phenyl group attached to this vinylic carbon were undetected.

^{31}P n.m.r 16.7ppm.

Experimental

6.10.2.7 The reaction of Dimethyl phosphite with t-butoxyl radicals and Phenylacetylene in the presence of (11)

Reaction time: 68 minutes

DTBP (86mg, 1.0 equivalent)

Trap(11) (160mg, 2.1 equivalents)

Dimethyl phosphite (337μl, 10 equivalents)

Phenyl acetylene (2.0ml)

The reaction mixture was concentrated to approximately 30% of the original volume under high vacuum prior to separation.

HPLC conditions: 80% methanol in water, with a flow rate of 6.0 ml/minute. Preparative isolation by HPLC gave the following products (in order of elution from the HPLC column).

Dimethyl (1-ethyl-1,3,3-trimethyl-2,3-dihydro-1H-isoindol-2-yloxy) phosphate(45b)

$$H_3CO \diagdown \underset{H_3CO \diagup}{\overset{\diagup O}{P}} \diagdown ONR''_2$$

(45b)
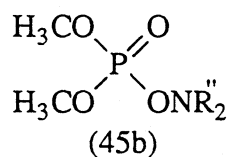
Equivalent by HPLC to an authentic sample of (45) (see 6.10.1.5).

trans-1-(1-Ethyl-1,3,3-trimethyl-2,3-dihydro-1H-isoindol-2-yloxy)-2-dimethoxy-phosphinoyl-1-phenylethene(68)[#]

Pale dusty pink solid. An X-ray diffraction structural analysis confirmed the above structure (see 4.3.2).

^{1}H n.m.r(CD$_3$OD, 250.122MHz, shifts in ppm, couplings in Hz):

7.45, m, 3H,
7.64, m, 2H

0.83, t, ^{3}J,7.3

1.88, q, ^{3}J,7.3

1.42, 1.43, 1.61,
3 x CH$_3$

7.20, m, 1H

4.91, s, 6H

6.03, d, J$_{P,C}$,9.7

7.11, m, 1H

7.29, m, 2H

^{13}C n.m.r(CD$_3$OD, 62.8MHz, shifts in ppm):

129.9

123.3

134.8

131.6

129.0, J$_{P,C}$,3.1

9.6

26.5

25.8, 30.0, 33.5,
3 x CH$_3$

129.3

51.3, J$_{P,C}$,172.0

86.0, J$_{P,C}$,210.0

70.4

146.2

122.7
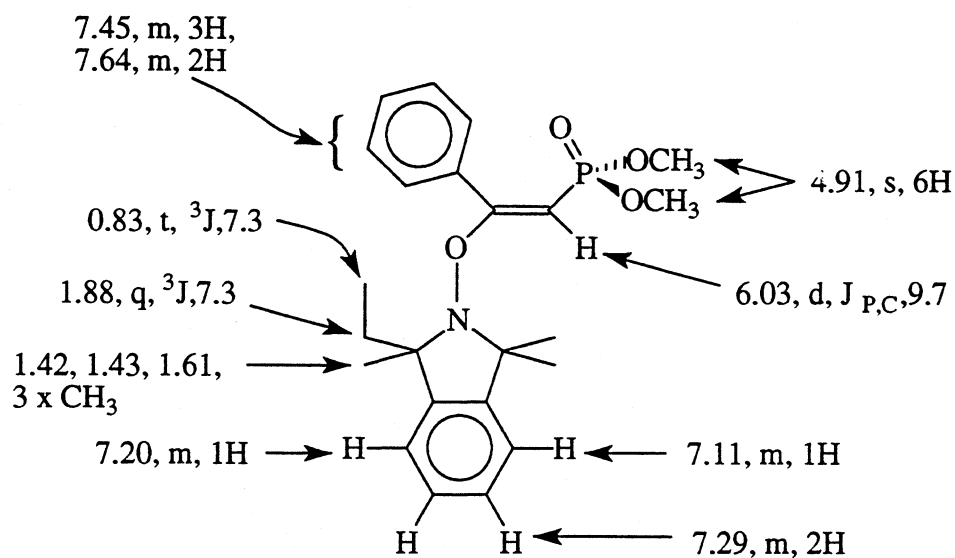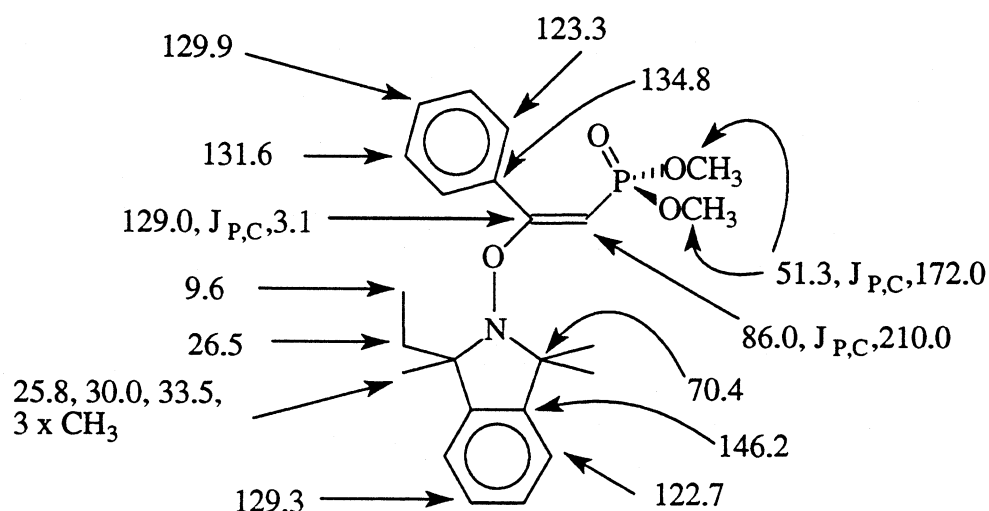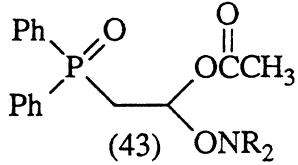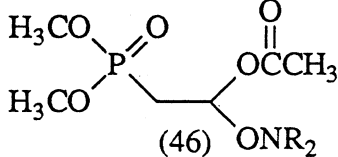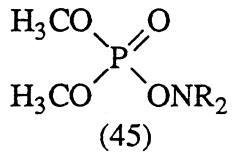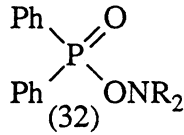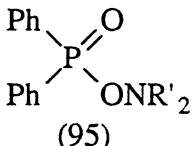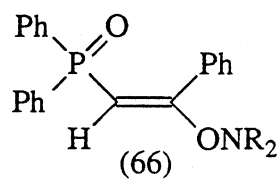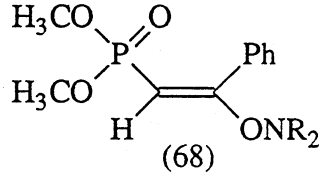
^{31}P n.m.r. 24.03ppm.

[#] [*] The substitution of (11) for (10) is known to make no discernible difference to the rate of trapping[25b].

Table <u> </u> ^{31}P n.m.r. Chemical shifts of various phosphorus bearing compounds

Compound	Chemical shift(ppm)
(43)	10.65
(46)	27.29
(45)	4.94
(32)	32.51
(95)	30.10
(66)	16.73
(68)	24.03

Ph-Phenyl.

ONR_2 = Tetramethyl aminoxyl(10)

ONR'_2 = Tetraethyl aminoxyl(12)

Experimental

6.11.0 The reaction of Trans-Δ²-Octalin with benzoyloxyl radicals in the presence of (10)

Reaction time: 27 hours

    Benzoyl peroxide (182mg, 1.0 equivalent)

    Trap(10) (300mg, 2.1 equivalents)

    Trans-Δ²-Octalin (2.0ml)

    Acetone-(co-solvent 5.0ml)

The reaction mixture was concentrated to approximately 30% of the original volume under high vacuum, prior to separation. HPLC conditions: 90% methanol in water, with a flow rate of 5.0-8.5ml/minute over 210 minutes.

Isolation gave the following products(in order of elution from the reverse-phase HPLC column):

1,1,3,3-Tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy propanone(82)

^{1}H n.m.r(CDCl$_3$, 250.122MHz, shifts in ppm):
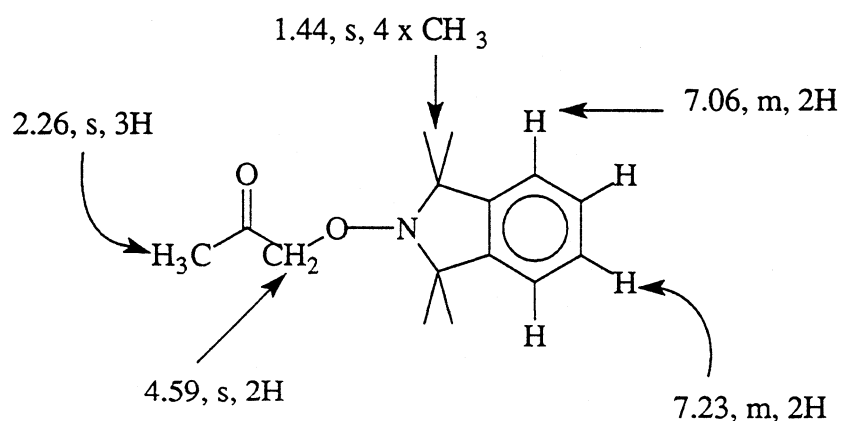
Identical to an authentic sample by ^{1}H nmr[31].

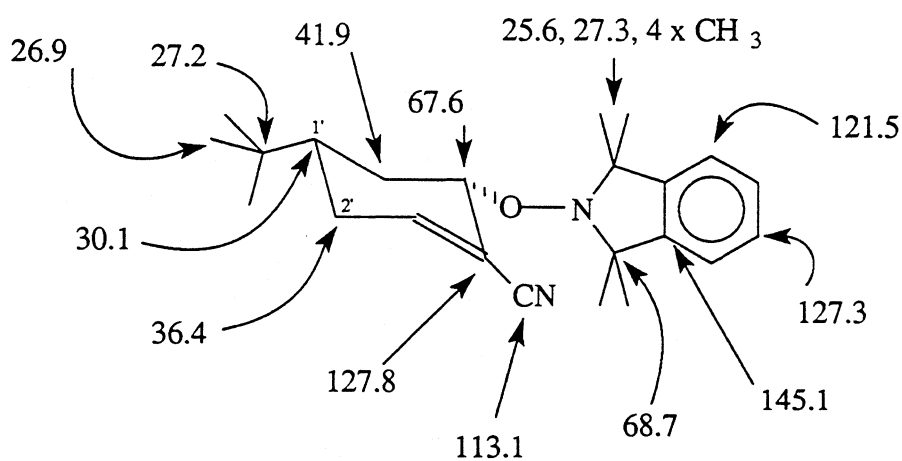## trans-4-Methyl-3,5-di-(1,1,3,3-tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy)-pent-3-ene-2-one(83)

^{1}H n.m.r.(CDCl$_3$, 250.122MHz, shifts in ppm, couplings in Hz):

0.57, m, 1.15, s, 1.23, s, 1.43, s,
1.62, s, 1.80, s, 1.88, s, 8 x CH$_3$-trap

2.30, s

2.91, s

4.14, d, J,8.0

4.28, d, J,8.0

6.95, m, 2H,
7.14, m, 2H,
7.30, m, 1H,
7.42, m, 2H,
7.58, m, 1H,
Aromatic H
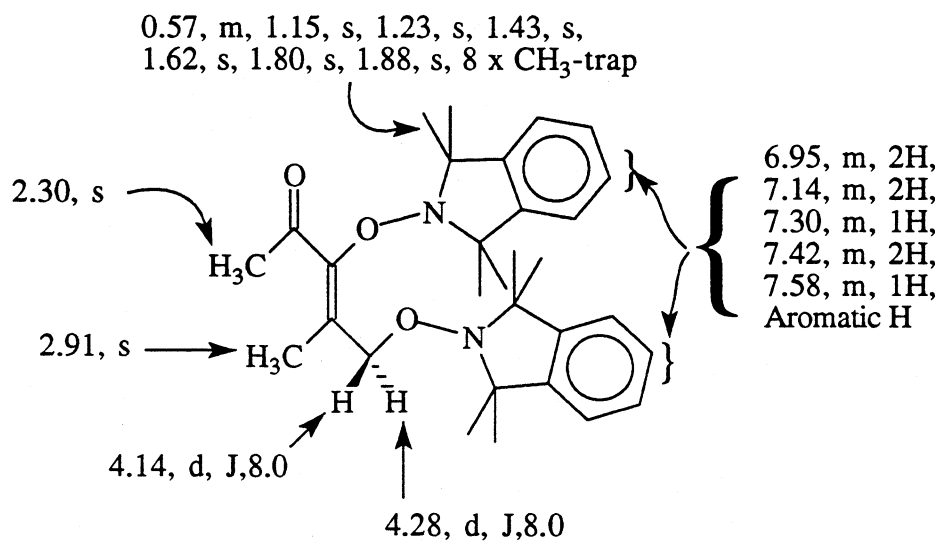
A low resolution mass mass spectrum gave no parent ion, however it did confirm the presence of the aminoxyl(10). The above structure is tentative.

An unidentified material (84) was also obtained in low yield.

^{1}H n.m.r.(CDCl$_3$, 250.122MHz, shifts in ppm, couplings in Hz, integration is given as a ratio):

0.54, m, 2; 0.61, m, 2; 1.10, s, 1.13, s, 2 x ring methyls-trap; 1.39, m, 3; 1.76, 1.83, 2 x s, 6, ring methyls-trap; 2.34, s, 3; 2.90, s, 3; 4.09, d, 1, J,8.0; 4.23, d, 1; 7.24, m, 1, aromatic H; 7.38, m, 2, aromatic H; 7.49, m, 1, aromatic H; 7.98, m, 2, aromatic H.

2(ax)-Benzoyloxy-3(eq)-(1,1,3,3-tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy)-trans-decalin(85)

(Found: M 447.277. $C_{29}H_{37}NO_3$ requires 447.277).

[1]H n.m.r(CDCl₃, 250.122MHz, shifts in ppm, couplings in Hz):

0.78-1.79, m, 12H, 2.07, m, 2H, cyclic methylene protons

3.91, ddd, J,2.9, J,4.1, J,11.7

5.61, m,

1.21, 1.23, 1.42, 1.49, 4 x CH₃

7.45, t, 2H, J,6.9,
7.55, d, 1H, J,7.4,
8.11, d, 2H, J,8.1

7.04, m, 2H

7.18, m, 2H

[13]C n.m.r(CDCl₃, 62.8MHz, shifts in ppm):

26.3, 29.3, 29.6, 33.9, 34.4, 36.5, 41.5, cyclic carbons

83.5

72.1

132.9

129.7

128.4

130.1

25.1, 30.1, 4 x CH₃

67.9

145.4

121.6

127.2
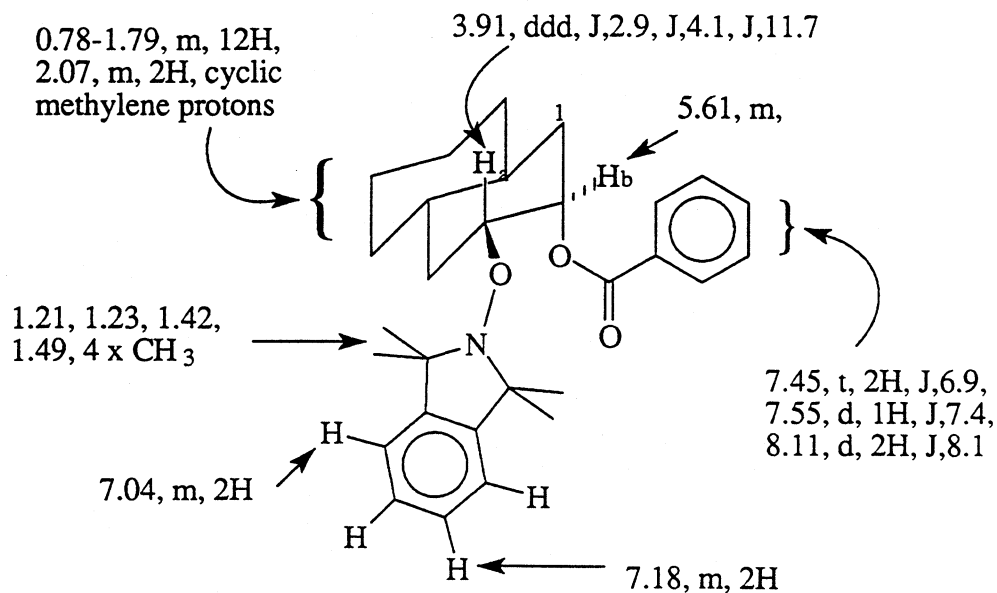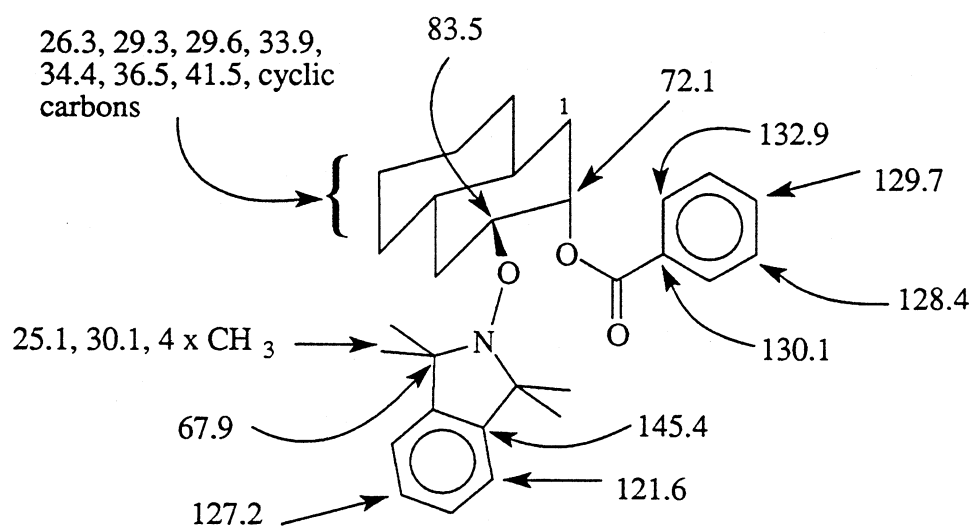
The ester carbon was not observed.

Experimental

<u>2(eq)-Benzoyloxy-3(eq)-(1,1,3,3-tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy)-trans-decalin(86)</u>

(Found: M 447.277. C$_{29}$H$_{37}$NO$_3$ requires 447.277).

^{1}H n.m.r(CDCl$_3$, 300.06MHz, shifts in ppm, couplings in Hz):

0.83-1.75, m, 12H, cyclic protons

4.00, ddd, J,10.1, J,10.1, J,5.0

2.08, ddd, J,2.3, J,5.0, J,11.7

2.47, dd, J,11.1, J,5.0

1.16, 1.25, 1.48, 1.60, 4 x CH$_3$

5.11, ddd, J,10.1, J,10.1, J,5.3

7.43, m, 2H,
7.53, m, 1H,
8.09, m, 2H

7.02, m, 2H

7.16, m, 2H

^{13}C n.m.r(CDCl$_3$, 62.8MHz, shifts in ppm);

26.0, 26.1, 32.9, 33.1, 37.9, 39.0, 40.4, cyclic carbons

80.2

166.3

128.2

129.8

132.7

131.0

75.3

24.7, 25.1, 29.9, 30.3, 4 x CH$_3$

66.9, 68.2

121.3, 121.65

145.7

127.1

Experimental
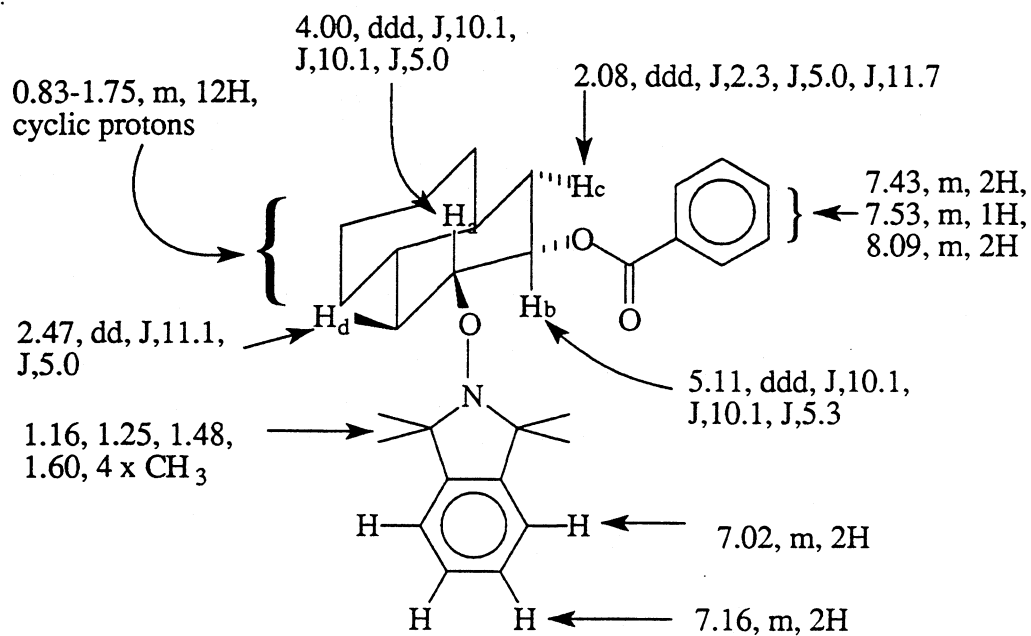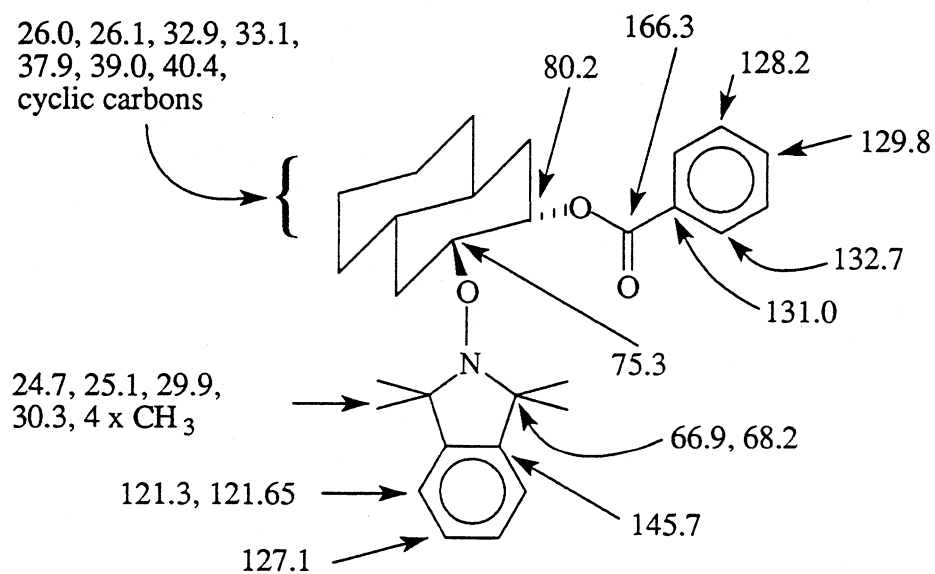
2(eq)-Benzoyloxy-3(ax)-(1,1,3,3-tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy)-trans-decalin(87)

(Found: M 447.277. $C_{29}H_{37}NO_3$ requires 447.277).

^{1}H n.m.r(CDCl$_3$, 250.12MHz, shifts in ppm, couplings in Hz):

7.18, m, 2H

7.08, m, 1H

6.99, m, 1H

7.43, t, 2H, J,7.2, J,7.2,
7.55, tt, 1H J,7.3, J,7.3,
J,2.5, J,2.5,
8.11, dd, 2H, J,8.6, J,1.5

1.23, 1.36, 1.40,
1.46, 4 X CH$_3$

0.83-1.83, m, 13H,
cyclic protons

2.28, ddd, J,3.6,
J,3.6, J,14.1

5.08, ddd, J,3.2,
J,5.0, J,11.9

4.34, vbrs

^{13}C n.m.r(CDCl$_3$, 62.8MHz, shifts in ppm):

127.2

145.7

25.2, 29.6, 4 x CH$_3$

121.3, 121.7

41.4

67.8, 68.6

132.8

128.3

26.2, 26.7, 30.1, 32.6,
33.5, 36.1, 36.4,
cyclic carbons

79.5

129.9

75.5
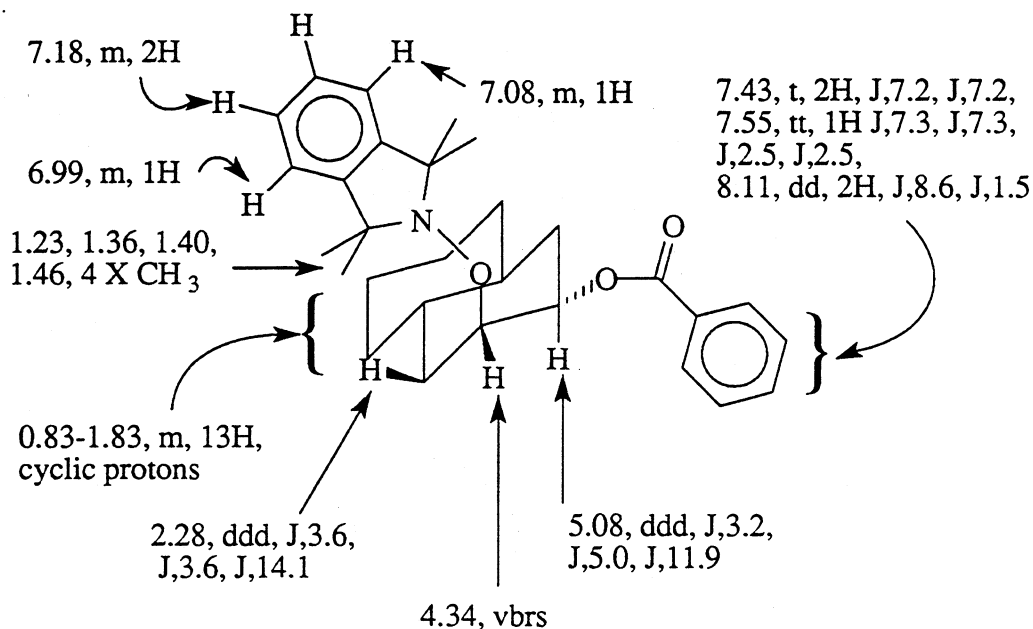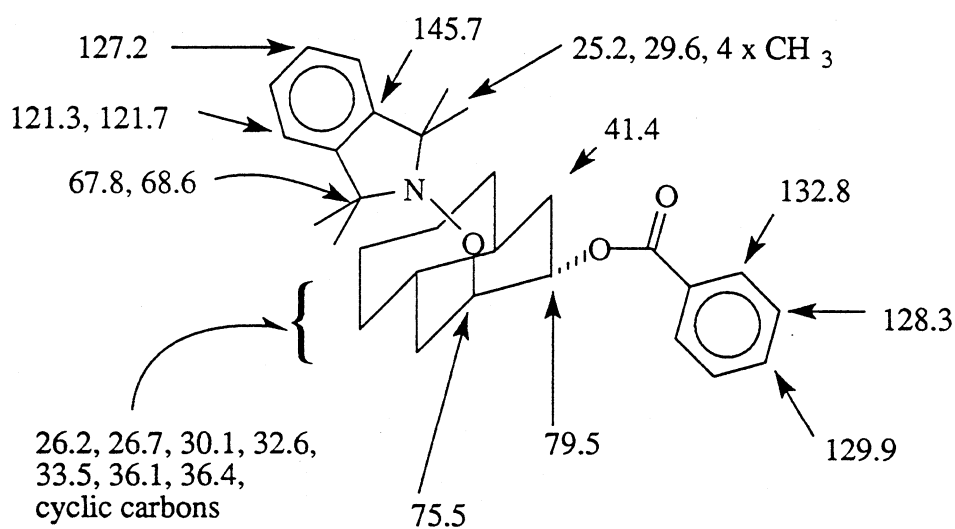
The benzoate ipso and ester carbons were not observed after 24000 scans.

Experimental

2(ax)-Benzoyloxy-3(ax)-(1,1,3,3-tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy)-trans-decalin(88)

(Found: M 447.277. $C_{29}H_{37}NO_3$ requires 447.277).

An X-ray diffraction structural analysis was also carried out on this material-confirming structure (88) (see 5.1).

^1H n.m.r(CDCl$_3$, 250.12MHz, shifts in ppm, couplings in Hz):

7.21, m, 2H

1.38, 1.40, 1.49, 1.58, 4 x CH$_3$

7.09, m, 2H

5.49, d, ^3J,2.0

1.03, m, 2H,
1.24-1.86, m, 11H,
cyclic protons

1.99$^\#$, d, ^3J,10.1

4.08$^\#$, d, ^3J,2.0

7.44, t, 2H, J,7.7, J,7.7,
7.55, t, 1H, J,7.3, J,7.3,
8.04, d, 2H, J,8.4

^{13}C n.m.r(CDCl$_3$, 62.8MHz, shifts in ppm):

145.2

25.4, 4 x CH$_3$

127.3

121.6

67.8

79.3

165.7

128.4

132.9

26.5, 33.4, 33.5, 33.6,
33.9, 36.9, 37.2,
cyclic carbons

131.0

71.0

129.6
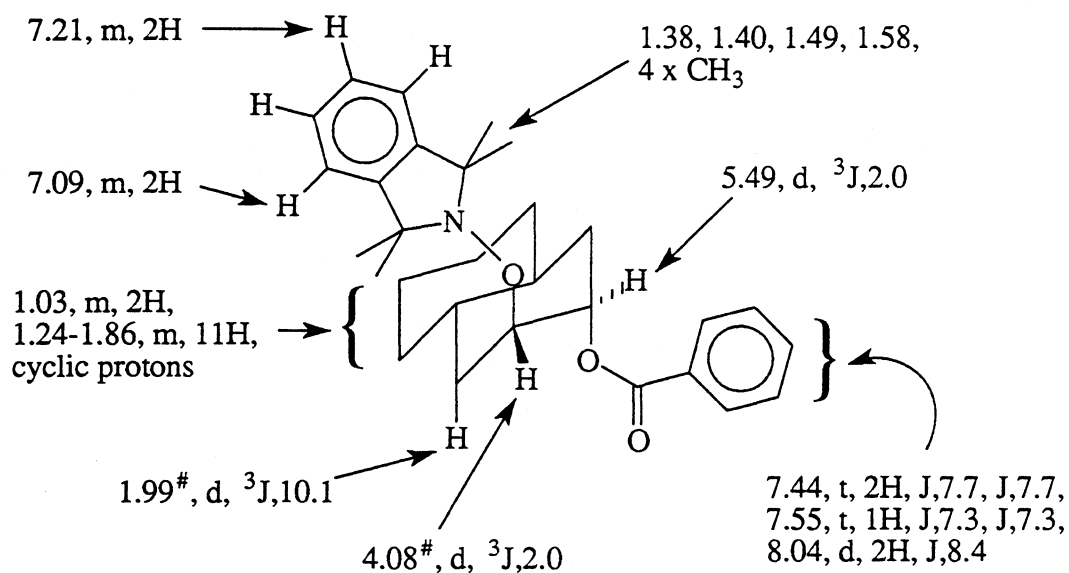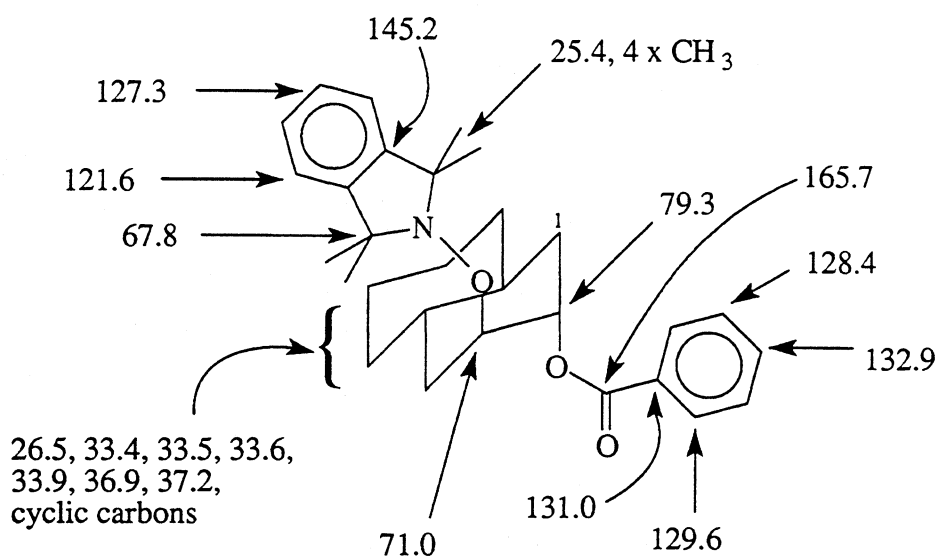
$^\#$. The X-ray crystal structure suggests that the angle between these two neighbouring protons is 90° (therefore J=0).

Experimental

6.12.0 The reaction of Styrene and Maleic anhydride with t-butoxyl radicals (see appendix one)

Reaction time:68 minutes
  DTBP (220mg, 1.0 equivalent)
  Trap (10) (500mg, 2.8 equivalents)
  Styrene (5.0ml, 8.1M)
  Maleic anhydride (4.22g, 8.1M)

The reaction mixture was concentrated to approximately 40% of the original volume, under high vacuum prior to separation.

HPLC conditions: 75% methanol in water, with a flow rate of 6.25ml/minute for 33 minutes, then 90% methanol in water at a flow rate of 7.5ml/minute for 120 minutes. Products were eluted in the following order from the revers-phase HPLC column.

2-Methoxy-1,1,3,3-tetramethyl-2,3-dihydro-1H-isoindol (22)

$$H_3C—ONR_2$$
(22)
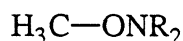
Identical to an authentic sample by [1]H n.m.r.[31].

1-(1,1,3,3-Tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy)-1-phenylpropane(105)

[1]H n.m.r.(CDCl$_3$, 250.122MHz, shifts in ppm, couplings in Hz);

4.61, dd, ^{3}J,6.0, ^{3}J,8.0

0.89, t, ^{3}J,7.5

6.90-7.40, m

1.80, qdd, 1H, ^{2}J,13.5,
^{3}J,7.5, ^{3}J,8.0,
2.17, qdd, 1H, ^{2}J,13.5,
^{3}J,7.5, ^{3}J,6.0

0.73, 1.22, 1.45,
1.62, 4 x CH$_3$
6.9-7.4, m, aromatic H
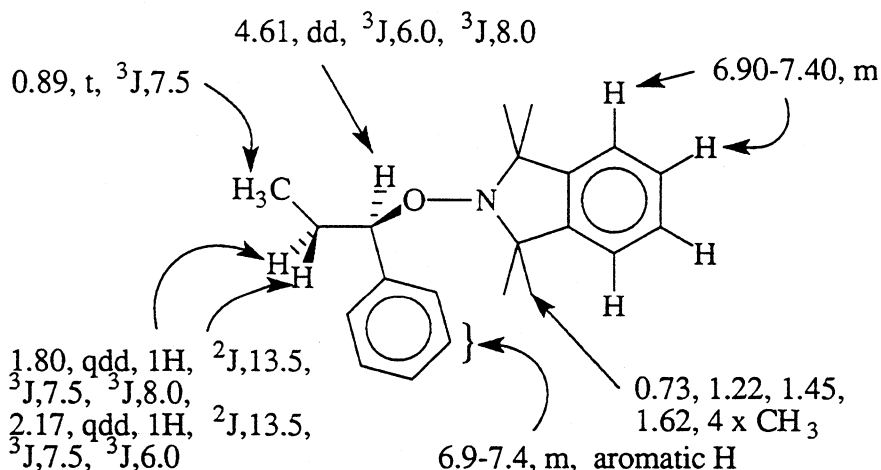
Identical to an authentic sample by ^{1}H nmr[31].

2-t-Butoxy-1-phenyl-1-(1,1,3,3-tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy)-ethane(106)

^{1}H n.m.r.(CDCl$_3$, 250.122MHz, shifts in ppm, couplings in Hz):

1.22, s

4.86, dd, ^{3}J,4.0, ^{2}J,8.5

0.77, 1.26, 1.51, 1.69, 4 x CH$_3$

3.40, dd, ^{2}J,10.0, ^{3}J,4.0

3.79, dd, ^{3}J,8.5, ^{2}J,10.0

6.8-7.5, m, aromatic H

6.8-7.5, m, aromatic H
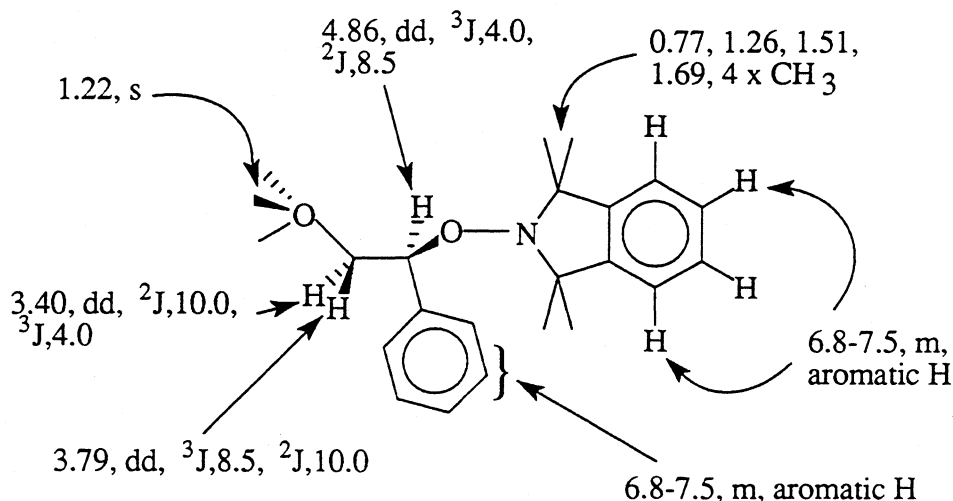
Identical to an authentic sample by ^{1}H nmr[31].

6.13.0 The reaction of Tetracyanoethylene with t-butoxyl radicals in the presence of (10) (see appendix two)

Reaction time: 68 minutes

DTBP (66mg, 1.0 equivalent)

Trap(10) (120mg, 2.2 equivalents)

Tetracyanoethylene (564mg, 15.4 equivalents)

Acetone (co-solvent 3.6ml)

Benzene (co-solvent 2.4ml)

The reaction mixture was concentrated to approximately 30% of the original volume, under high vacuum prior to separation.

HPLC conditions: 70% methanol in water, with a flow rate of 3.8ml/minute. Products were eluted in the following order from the reverse-phase HPLC column.

4-Dicyano-5-dicyano-5-(1,1,3,3-tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy)propan-2-one(108)

(Found: C, 67.1; H, 5.7; N, 18.8. $C_{21}H_{21}N_5O_2$ requires C, 67.1; H, 5.6; N, 18.7%).

^{1}H n.m.r(CDCl$_3$, 250.12MHz, shifts in ppm):
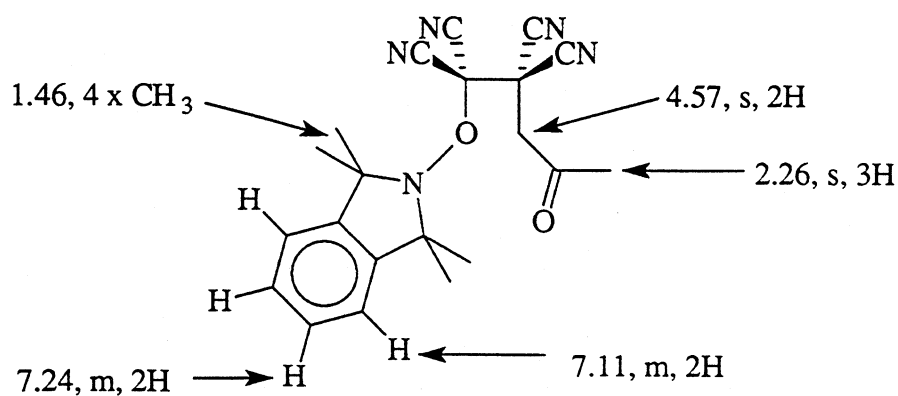
^{13}C n.m.r(CDCl$_3$, 62.8MHz, shifts in ppm):
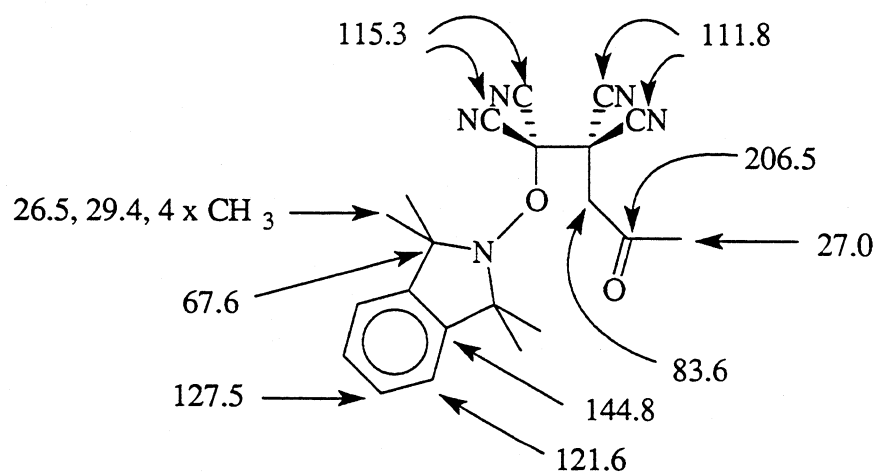
The quarternary carbons(C$_4$ and C$_5$) were not observed.

<u>2-Methoxy-1,1,3,3-tetramethyl-2,3-dihydro-1H-isoindol (22)</u>

$$H_3C-ONR_2$$
(22)

Identical to an authentic sample by ^1H nmr and HPLC (see 6.7).

6.13.1 The reaction of Tetracyanoethylene and Styrene with t-butoxyl radicals in the presence of (10) (see appendix two)

Reaction time: 68 minutes

DTBP (2.5mg, 1.0 equivalent)

Trap(10) (15mg, 7.4 equivalents)

Tetracyanoethylene (966mg, 696 equivalents)

Styrene (500μl, 696 equivalents)

Acetone (4.0ml)

Benzene (6.0ml)

This was an analytical scale reaction. The reaction was not carried out preparatively as samples of the following compounds were available for coinjection to verify the styrene reaction products. There were no new products (bearing both monomers, tetracyanoethylene/styrene) detected in the reaction mixture. Because of this, the study of this system was discontinued.

However the products were eluted from the reverse-phase HPLC column in the following order (HPLC conditions: 70% methanol in water. flow rate, 1.0 ml/minute-Whatman semi-preparative column).

<u>4-Dicyano-5-dicyano-5-(1,1,3,3-tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy)propan-2-one(108)</u>

NC   CN
NC   CN

R$_2$NO   CH$_3$

(108) O

Identical to an authentic sample by HPLC (see 6.12.0).

2-Methoxy-1,1,3,3-tetramethyl-2,3-dihydro-1H-isoindol (22)

$$H_3C-ONR_2$$

(22)

Identical to an authentic sample by HPLC (see 6.7).

1-Phenyl-1-(1,1,3,3-tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy)-propane(105)

$$H_3C \diagdown \diagup ONR_2$$

(105) Ph
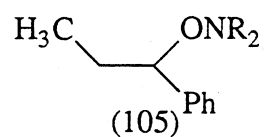
Identical to an authentic sample[31] by HPLC.

2-t-Butoxy-1-phenyl-1-(1,1,3,3-tetramethyl-2,3-dihydro-1H-isoindol-2-yloxy)ethane(106)

$$^tBuO \diagdown \diagup Ph$$

(106) ONR_2

Identical to an authentic sample[31] by HPLC.

Experimental
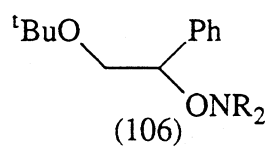
APPENDIX ONE

On the Initiation Mechanism of Free Radical Copolymerisation of Styrene and Maleic anhydride

Copolymers of styrene and maleic anhydride have been around since the 1940's. They have been used as textile assistants, dye pastes[195], polyesters[196] and engineering plastics[197], and consequently this is one of the most extensively studied copolymer systems. It was first studied by Mayo et al.[54], and later by Bamford and Barb[198], Tsuchida et al[199], Makuda and Abe[200] and Dodgson and Ebdon[201]. When styrene and maleic anhydride are copolymerised there is a strong tendency towards alternation. The mechanism of alternation has been the subject of much speculation and controversy[54,198-201].

Hence, the desire here was to employ the aminoxyl 'radical trapping" technique to investigate the mechanism of initiation and therefore determine whether the 'free monomer' mechanism (see 2.0) or the 'charge transfer complex' mechanism (see 2.0) was being adhered to in the free radical initiated copolymerisation of styrene and maleic anhydride.

Otsu et al.[202,203], employed the 'spin trapping' technique in an attempt to identify the initiating species. When 2-methyl-2-nitroso-propane(BNO) was added to the styrene-maleic-anhydride system, Otsu et al.[202,203] found two radical adducts could be identified, (101) and (102) (see scheme 45). This suggests that styrene is active as an initiating species. Otsu et al.[202,203] also found that when initiating the copolymerisation with t-butoxyl radicals (which interestingly are unreactive towards maleic anhydride) that again only two adducts were obtained, (103) and (104). This work produced no conclusive results on the mechanism of initiation.

(103)

(104)

Scheme 45

(101)

(102)

+ BNO
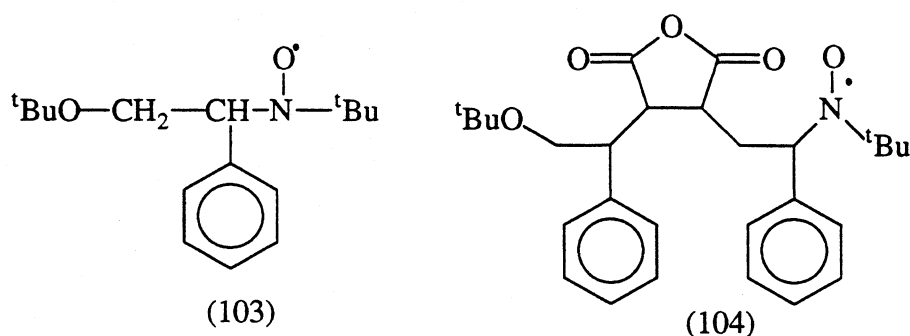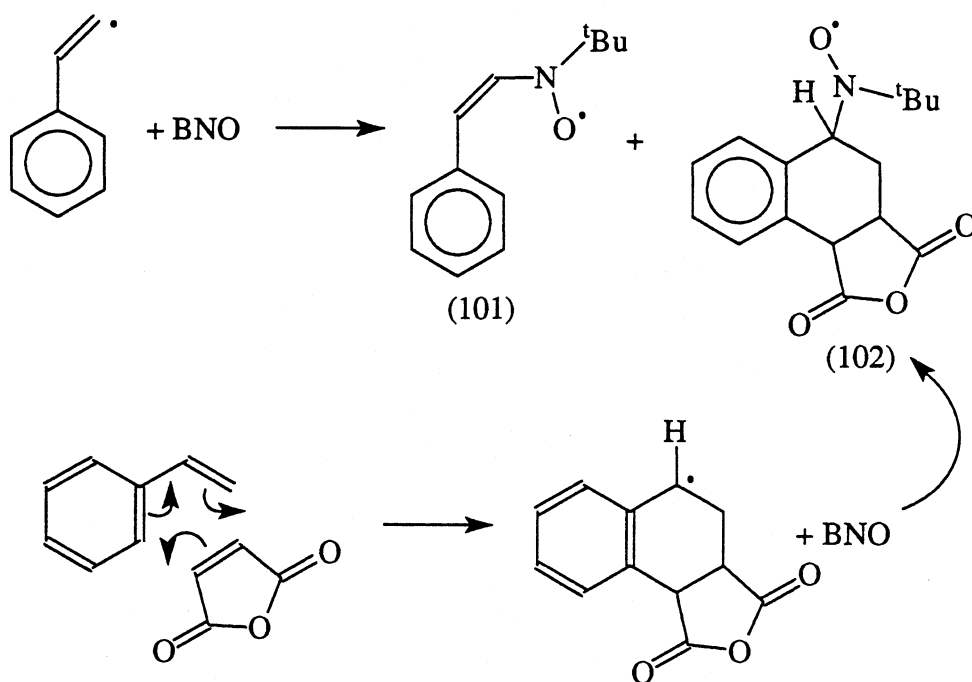
The 'copolymerisation' reaction was carried out following the standard procedure for the 'radical trapping' technique (see section 6.5.0). A typical preparative reaction was as follows: styrene(2.0ml, 1.62×10^{-3} moles), maleic anhydride(1.59g, 1.62×10^{-2} moles), trap(10)(436mg, 2.3×10^{-3} moles), DTBP(240mg, 1.02×10^{-3} moles) and benzene(5.0ml-solvent) were combined. The reaction mixture was subjected to three freeze/evacuation/thaw cycles, followed by heating at 60°C for 68 minutes. This afforded three isolable products (see scheme 46). Two other compounds were detected in the reaction mixture by analytical HPLC, however these both started to decompose immediately upon contact with aqueous methanol. Strenuous efforts min-imizing contact time with aqueous methanol, varying reaction times and varying reaction work up procedure were directed at trying to isolate the two decomposing reaction products; but to no avail. The products (22), (105) and (106) were isolated when styrene alone was reacted with t-butoxyl radicals in the presence of (10). Moad et al.[31] also obtained these same products in the identical reaction with styrene (i.e no maleic anhydride).

So, no comonomer products were isolated; whether the two unstable products did contain both monomers or not, is not known.

Scheme 46 The reaction of t-butoxyl radicals with Maleic anhydride and Styrene in the presence of (10)

(DTBP) $\xrightarrow{\Delta}$ 2 ^{t}BuȮ +

β-fragmentation

ĊH₃

(10)

H₃C—ONR₂
(22)
(1.8%)

—CH₃

(10)

ONR₂
—CH₃
(105)
(2.1%)

—OᵗBu

(10)

ONR₂
—OᵗBu
(106)
(95.9%)
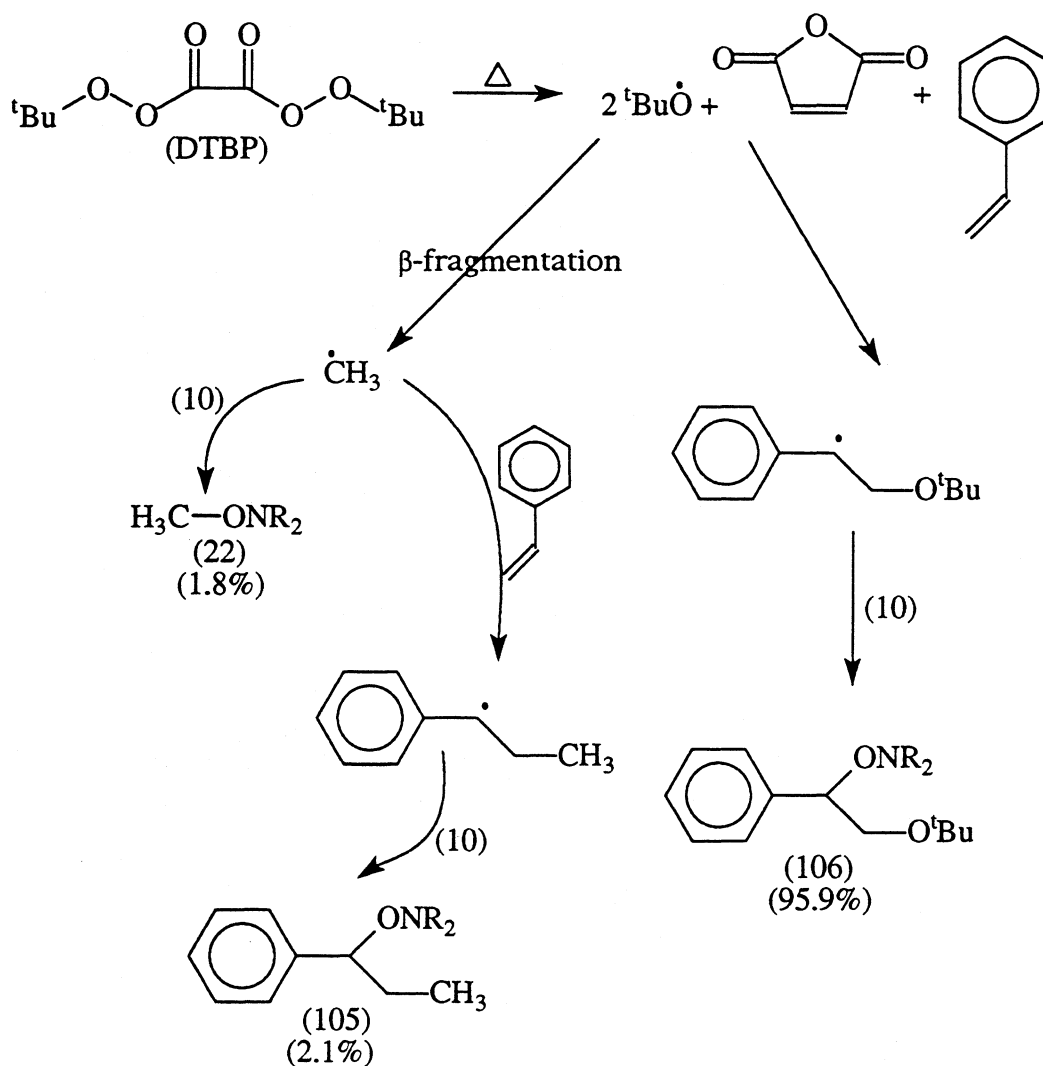
(Percentages pertain only to isolated products)

It seems unlikely that either of these products could have been the product corresponding to (104), i.e (107) identified by Otsu et al.[203] The stability of (107) would surely be no less than (104).

The presence of methyl radicals to produce (22) and (105) indicates that the tail addition of t-butoxyl radicals to styrene to produce (106) is slow. The rate of trapping by (10) however, is fast (close to diffusion controlled-see section 1.1.1), evidently faster than the rate of addition of the untrapped radical of product (106) to maleic anhydride, as (107) was not isolated.

(107)
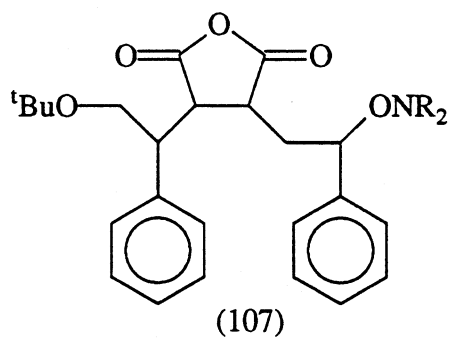
The reason therefore for no comonomer products being isolated, may be due to the rate of trapping by the aminoxyl(10) being faster than the rate of addition of the styrene-t-butoxyl radical to the double bond of maleic anhydride.

APPENDIX TWO

On the Initiation Mechanism of Free Radical copolymerisation of Styrene and Tetracyanoethylene

Styrene is known to produce a copolymer displaying alternating tendency with acrylonitrile (particularly in the presence of lewis acids and at temperatures $\sim 50^\circ C$[204]) and fumaronitrile[205].

It seemed reasonable that tetracyanoethylene (a more powerful electron acceptor monomer in this series) when copolymerised with styrene may also form a copolymer of high alternation. This being the case the aminoxyl 'radical trapping' technique could be employed (in like manner to acrylonitrile/vinyl acetate-see chapter two) to provide information on the mechanism of initiation.

Thus, tetracyanoethylene, DTBP, (10), benzene and acetone(co-solvent) were combined in the normal manner. This reaction afforded only two products, namely (108) and (22)(see figure 36). Product (108) is

Figure 36 Products formed in the reaction of Tetracyanoethylene and Styrene with t-butoxyl radicals in the presence of (10) and acetone
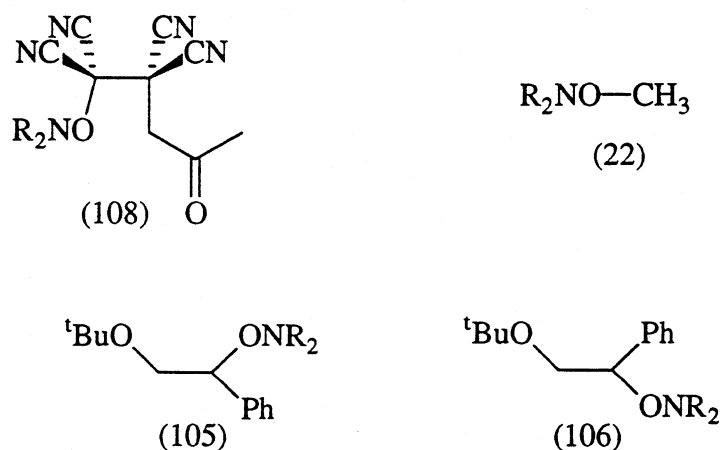
solvent derived, arising from hydrogen-abstraction (by t-butoxyl radicals) on acetone, followed by addition to tetracyanoethylene, then trapping by (10) (see scheme 47). The presence of (22) indicates (see 2.1) that the formation of (108) to occurs at a relatively slow rate.

The inclusion of styrene in this reaction mixture afforded four reaction products (see figure 36), namely (108), (22), (105) and (106), i.e. there were no comonomer products isolated. Products (22), (105) and (106) are produced when styrene alone is reacted with DTBP and (10) (see scheme 46).

Scheme 47
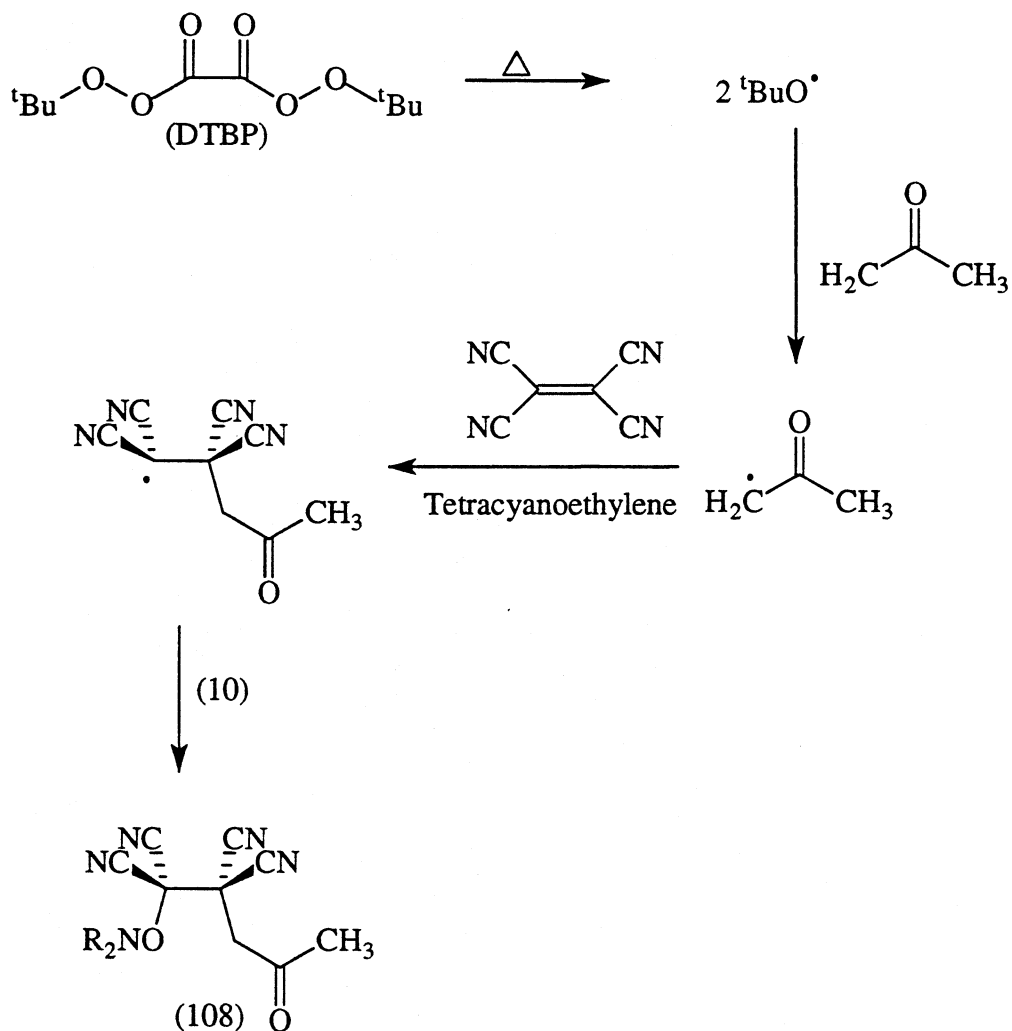
Several variations on the amounts of reactants used were tried, in an attempt to foster the formation of products containing both monomers, this was however unsuccessful. The study of this system was discontinued.

APPENDIX THREE

Attempted Synthesis of some Phosphorus Radical Initiators

The work presented in chapter four on olefins has shown that the use of t-butoxyl radicals to generate phosphinyl radicals is accompanied by side reactions involving t-butoxyl radicals reacting with the particular monomer.

The low (and in some cases not at all) percentages of phosphinyl radical addition to the olefin (particularly cyclic olefins) studied, suggested that an alternative method of generation of phosphinyl radicals, not involving t-butoxyl radicals was needed. With this in mind it was the intention to synthesise via the hydrazines, several phosphorus bearing azo compounds, namely azo-1,2-bis(diphenylphosphine oxide)(109) and azo-1,2-bis-(diphenylphosphine)(110).

$$
\begin{array}{cc}
\text{O} & \text{O} \\
\| & \| \\
\text{Ph}-\text{P}-\text{N}=\text{N}-\text{P}-\text{Ph} \\
/ & \backslash \\
\text{Ph} & \text{Ph} \\
(109) &
\end{array}
\qquad
\begin{array}{c}
\text{Ph} \backslash \quad \quad /\text{Ph} \\
\text{P}-\text{N}=\text{N}-\text{P} \\
\text{Ph}/ \quad \quad \backslash\text{Ph} \\
(110)
\end{array}
$$
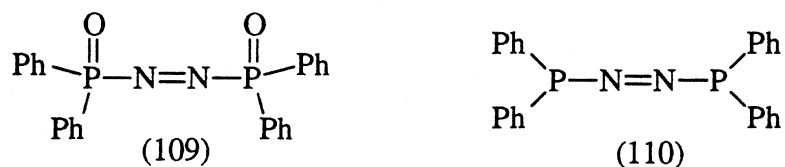
Disubstituted azo compounds are known[206] to undergo thermal decomposition, affording N_2 and radical fragments (eg, disubstituted azo-cumenes-see figure 37). In line with this, it was hoped that (109) and (110) would behave similarly, affording diphenylphosphinyl (or diphenyl-phosphino in the case of (110)) radicals and N_2 (scheme 48). This would effectively eliminate the need to employ the t-butoxyl radical in such studies.

Figure 37

$$
\begin{array}{ccc}
\text{CH}_3 & \text{CH}_3 & \text{CH}_3 \\
| & | & \xrightarrow{\Delta} \quad 2 \text{ x Ph}-\overset{|}{\underset{|}{\text{C}}}\cdot + \text{N}_2 \\
\text{Ph}-\overset{|}{\underset{|}{\text{C}}}-\text{N}=\text{N}-\overset{|}{\underset{|}{\text{C}}}-\text{Ph} & & \\
\text{H} & \text{H} & \text{H}
\end{array}
$$

Scheme 48

$$\text{Ph}\!-\!\underset{\underset{\text{Ph}}{|}}{\overset{\overset{O}{\|}}{P}}\!-\!N\!=\!N\!-\!\underset{\underset{\text{Ph}}{|}}{\overset{\overset{O}{\|}}{P}}\!-\!\text{Ph} \quad\xrightarrow{\Delta}\quad 2\,x\ \ \text{Ph}\!-\!\underset{\underset{\text{Ph}}{|}}{\overset{\overset{O}{\|}}{P}}\!\cdot\ +\,N_2$$

(109)

$$\underset{\text{Ph}}{\overset{\text{Ph}}{>}}P\!-\!N\!=\!N\!-\!P\underset{\text{Ph}}{\overset{\text{Ph}}{<}} \quad\xrightarrow{\Delta}\quad 2\,x\ \ \underset{\text{Ph}}{\overset{\text{Ph}}{>}}P\!\cdot\ +\,N_2$$

(110)
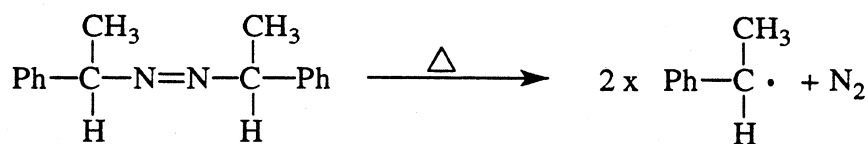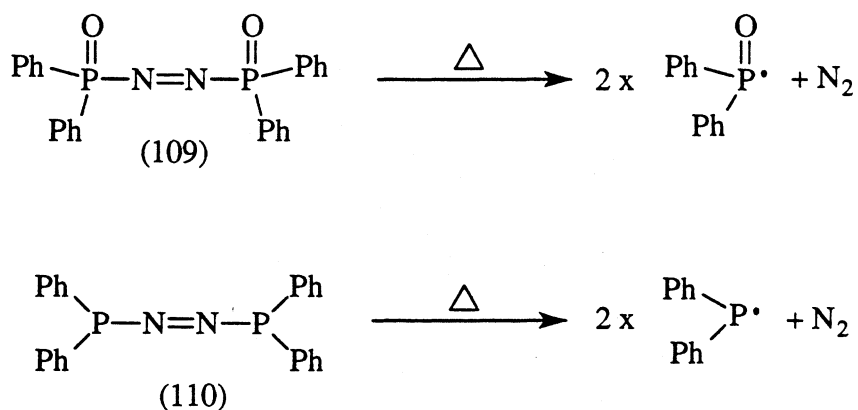
The method of Bock and Rudolph[207] being the only literature procedure found for the synthesis of 1,2-bis-(diphenylphosphine oxide)-hydrazine was followed to produce (111) (scheme 49). This afforded a white crystalline solid(111)(67%, Mpt 258-260°C. Lit Mpt 253-256°C[207]. I.R(NaCl disk) 1440cm^{-1}, s, P-Phenyl; 1179cm^{-1},(m-s), P=O; 1121cm^{-1},(m-s), Phenyl (near P=O); 968cm^{-1}, (m-s), N-N.

Scheme 49

$$\underset{\text{Ph}}{\overset{\text{Ph}}{>}}P\underset{\text{Cl}}{\overset{O}{<}} \quad\xrightarrow[\text{Et}_3\text{N/CHCl}_3]{\overset{H_2NNH_2}{\text{(anhydrous)}}}\quad \text{Ph}\!-\!\underset{\underset{\text{Ph}}{|}}{\overset{\overset{O}{\|}}{P}}\!-\!NH\,NH\!-\!\underset{\underset{\text{Ph}}{|}}{\overset{\overset{O}{\|}}{P}}\!-\!\text{Ph} \quad\xrightarrow[\text{Pyridine}]{\text{NBS}}$$

(111)

$$\text{Ph}\!-\!\underset{\underset{\text{Ph}}{|}}{\overset{\overset{O}{\|}}{P}}\!-\!N\!=\!N\!-\!\underset{\underset{\text{Ph}}{|}}{\overset{\overset{O}{\|}}{P}}\!-\!\text{Ph} \quad\longleftarrow$$

(109)
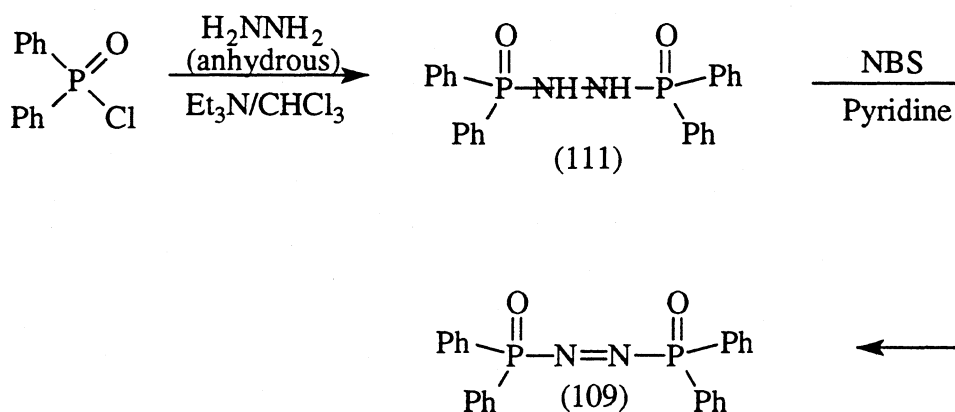
Numerous attempts at the procedure of Bock and Rudolph[207] using NBS(N-bromosuccinimide) and pyridine in methylene chloride for the conversion of (111) to (109) were unsuccessful. As were also varied attempts using yellow and red mercuric oxide in benzene.

The procedure of Nielson and Sisler[208] was used for the synthesis of 1,2-bis-(diphenylphosphino)-hydrazine(112). Product (112) was obtained as a white crystalline solid(Mpt 128-130°C. Lit Mpt 129-129.5°C[208]). I.R(NaCl disk) 1438cm^{-1}, s, P-Phenyl; 950cm^{-1}, w, N-N.

$$Ph \diagdown \!\!\!\!\diagdown P\!-\!Cl \xrightarrow[\text{Et}_3\text{N/CHCl}_3]{\begin{array}{c}H_2NNH_2\\ \text{(anhydrous)}\end{array}} Ph \diagdown \!\!\!\!\diagdown P\!-\!NH\!-\!NH\!-\!P \diagup \!\!\!\!\diagup Ph$$

$$\underset{Ph}{}\qquad\qquad\qquad\qquad\qquad \underset{Ph}{}\ \ (112)\ \ \underset{Ph}{}$$
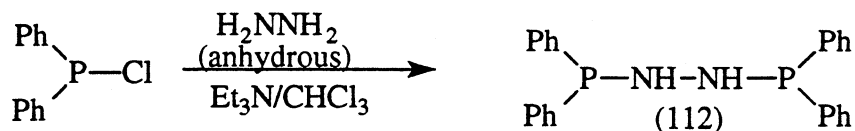
The procedure of Bock and Rudolph[207] using NBS and pyridine for the conversion of (111) to (109) was employed under various reaction conditions to attempt the conversion of (112) to (110). Other oxidants such as KMnO4 were also employed, however all attempts were unsuccessful. Further work is obviously required to obtain (109) and (110).

Additionally, thermolysis of (113) may yield diphenylphosphinyl radicals. Future work on a synthesis of (113) could well be justified.

$$Ph\diagdown \underset{Ph}{\overset{O}{\underset{\|}{P}}}\diagdown O \diagdown \underset{}{\overset{O\ \ O}{\underset{\|\ \ \|}{C\!-\!C}}} \diagdown O \diagdown \underset{Ph}{\overset{O}{\underset{\|}{P}}}\!-\!Ph$$

$$(113)$$
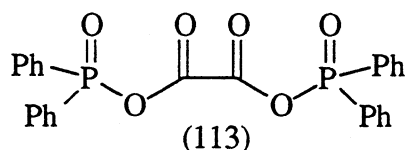
A possible synthesis of (113) could be achieved by reacting two equivalents of diphenylphosphinic acid with one equivalent of oxalyl chloride in the presence of pyridine(see scheme 50).

<u>Scheme 50</u>
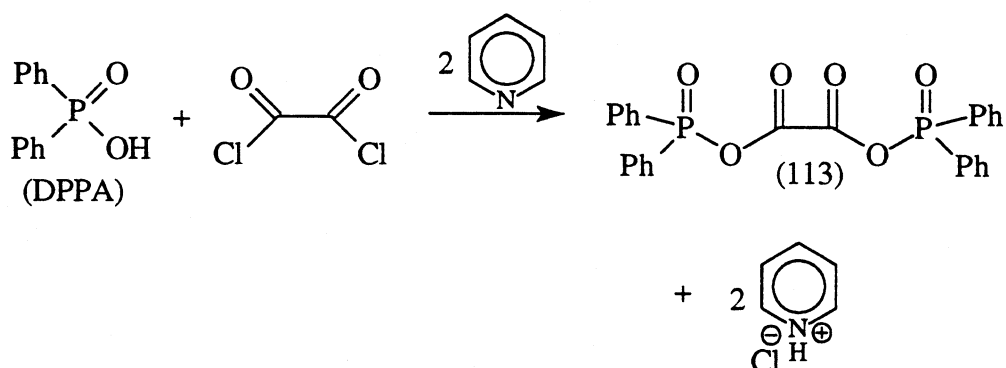
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