AZO-ANIONS IN ORGANIC SYNTHESIS

A Thesis submitted to the Board
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Doctor of Philosophy in the
University of Oxford.

by

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Michaelmas 1985

Abstract :- Azo-Anions in Organic Synthesis

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Novel synthetic applications of ambident azo-anions derived from hindered hydrazones have been investigated. Reaction with electrophiles occurred predominantly at carbon as the N-addition pathway was sterically retarded. Trityl,diphenyl-4-pyridylmethyl (DPP) benzhydryl,and t-butyldiphenylmethyl (BDP) hydrazones of various aldehydes and ketones were prepared in good yields from the corresponding hydrazines and carbonyls in aqueous methanol. The lithium salts derived from trityl and DPP hydrazones,by treatment with methyl lithium at -55°C,reacted with aldehydes and ketones to generate azo-alkoxides. These could be diverted to alcohols,by sequential protonation and spontaneous homolysis (about -20°C) in the presence of ethanethiol,or to alkenes,by treatment with phosphorus trichloride at -78°C followed by azo-homolysis. The reactions enabled efficient reductive cross-coupling of aldehydes and ketones. The mechanism of the alkene forming reaction was investigated. Anions of benzhydryl hydrazones were found to react inefficiently by a C-addition pathway giving mainly N-addition products.

Anions of BDP hydrazones conveniently gave excellent yields of azo-alkanes upon treatment with alkyl halides,but no products were obtained on reaction with carbonyl electrophiles. The azo-alkanes could be isolated and purified and acted as key intermediates for several synthetically useful transformations. Homolysis in refluxing benzene with thiophenol gave alkanes in good yields. Phenylselenenyl-,bromo-, and chloro-alkanes,and β-alkylstyrenes were generated when thiol was replaced by diphenyl diselenide,N-bromosuccinimide,N-chlorosuccinimide and β-nitrostyrene respectively.

Treatment of the azo-alkanes with trifluoroacetic acid generated benzophenone alkylhydrazones. These were dissolved in ethanol with concentrated hydrochloric acid,thereafter hydrolysis yielded alkylhydrazines or treatment with hydrogen (1 atm., 50°C, 20h) over 10% Pd/C generated primary amines by a novel use of carbonyls as α-aminocarbanion equivalents.

"Great are the works of the Lord;
they are pondered on by all
who delight in them."

Psalm 111:2

Acknowledgements

I should like to thank my supervisor Professor J.E.Baldwin for his input to and interest in this project.

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I must also thank all in Room 30 for providing an enjoyable working atmosphere over the past 2 years. Especial thanks go to Matthew Perry,my co-conspirator in the "Azo-Anions Group", for many useful discussions,and general nattering.

I must also acknowledge financial support from my wife,Alyson, who has put up with me whilst this thesis was in preparation.

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Common Abbreviations Used in this Thesis

trityl	= triphenylmethyl
DPP	= diphenyl-4-pyridylmethyl
BDP	= t-butyldiphenylmethyl
Me	= methyl
Et	= ethyl
Bu^t	= t-butyl
Ph	= phenyl
THF	= tetrahydrofuran
TMEDA	= N,N,N',N'-tetramethylethylenediamine
TFA	= trifluoroacetic acid
AIBN	= azobisisobutyronitrile
m.p.	= melting point
b.p.	= boiling point
^oC	= degrees Celsius
t.l.c.	= thin layer chromatography
p.l.c.	= preparative layer chromatography
i.r.	= infra-red
n.m.r.	= nuclear magnetic resonance
p.s.i.	= pounds per square inch
h	= hours
min	= minutes

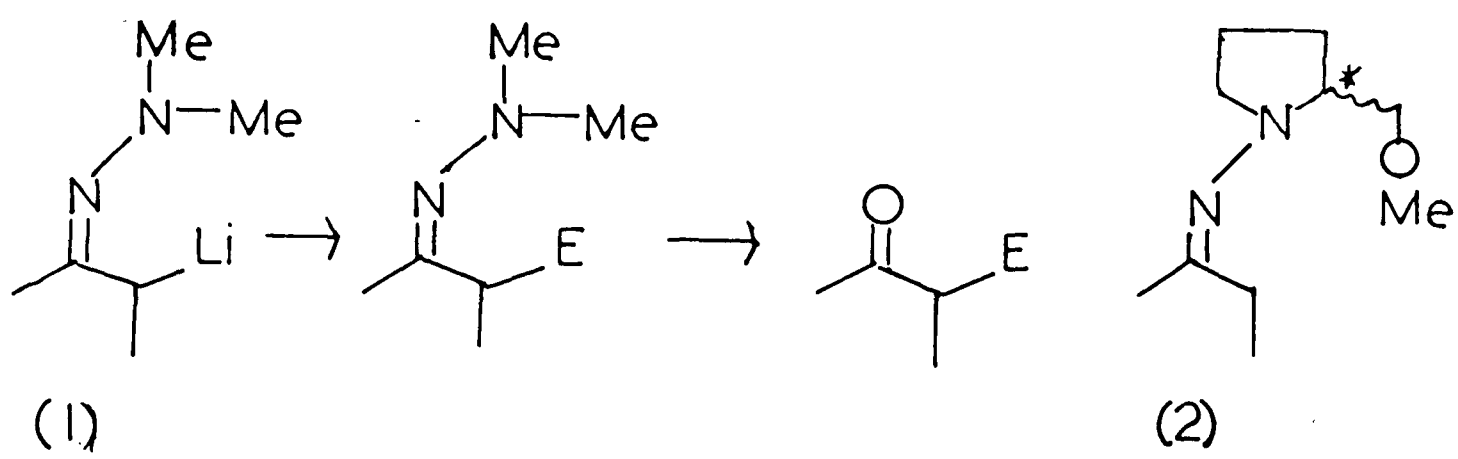
CONTENTS

CHAPTER I - INTRODUCTION

The results described in this thesis are concerned with the reactions of anions derived from hindered hydrazones - herein referred to as azo-anions - with a variety of electrophiles and the further reactions of the intermediate azo-species thus generated.

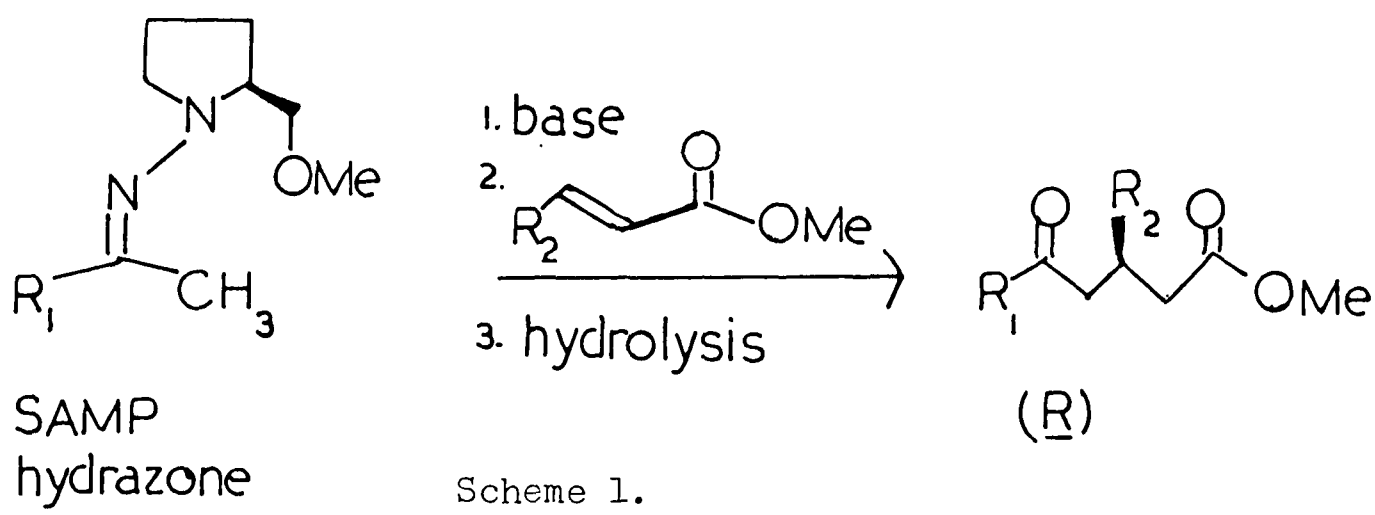
A. Hydrazones in Synthesis

Hydrazones have been used synthetically in a number of useful reactions. In particular, the generation of anions from hydrazones has received recent attention. Corey and Enders[1] have developed the use of anions (1) derived from dimethylhydrazones as versatile enolate equivalents.



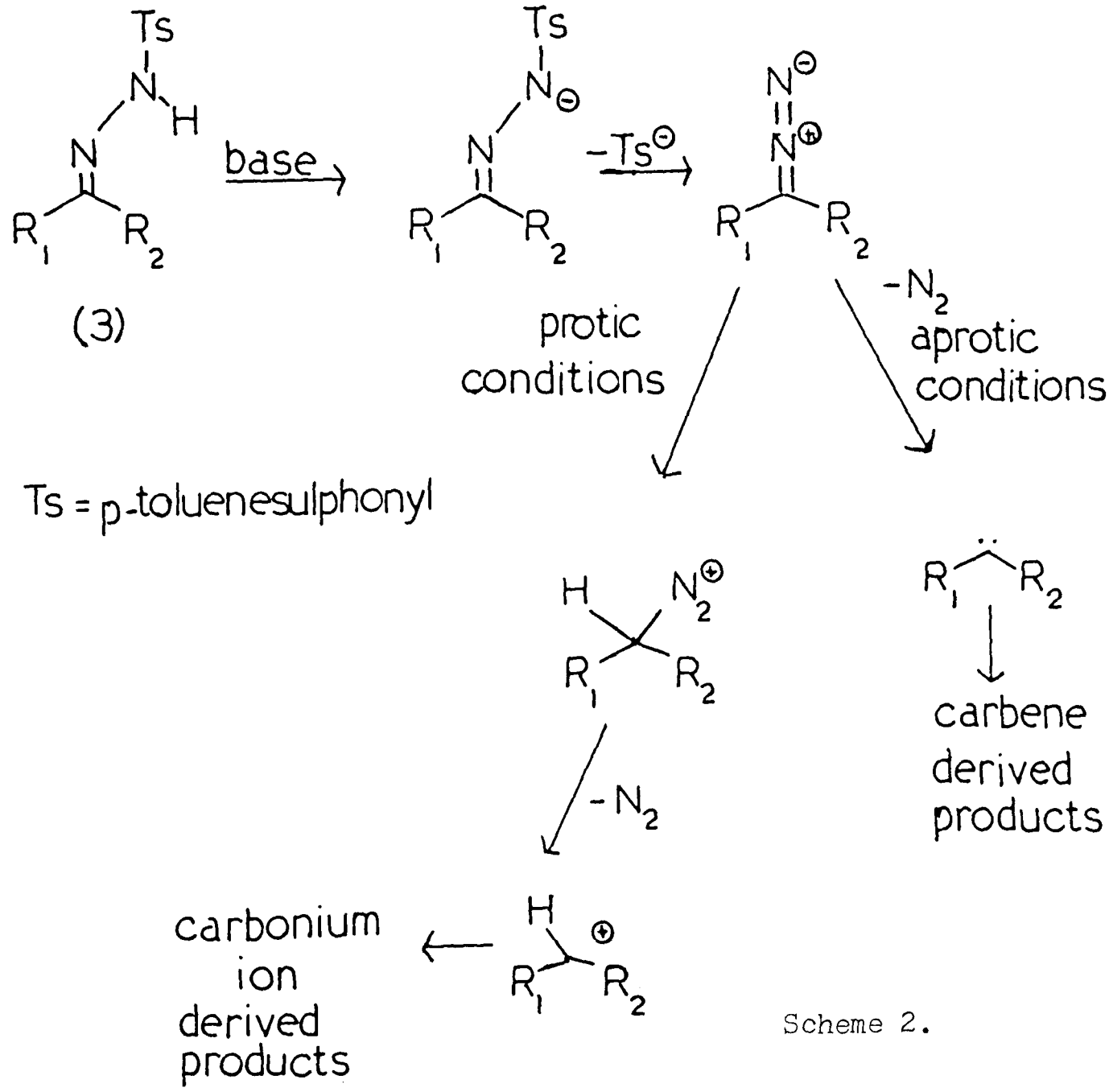
(1) (2)

Enders has further developed this idea to produce the so-called SAMP and RAMP hydrazones (2), the anions of which are useful chiral enolate equivalents (Scheme 1).[1b,2]

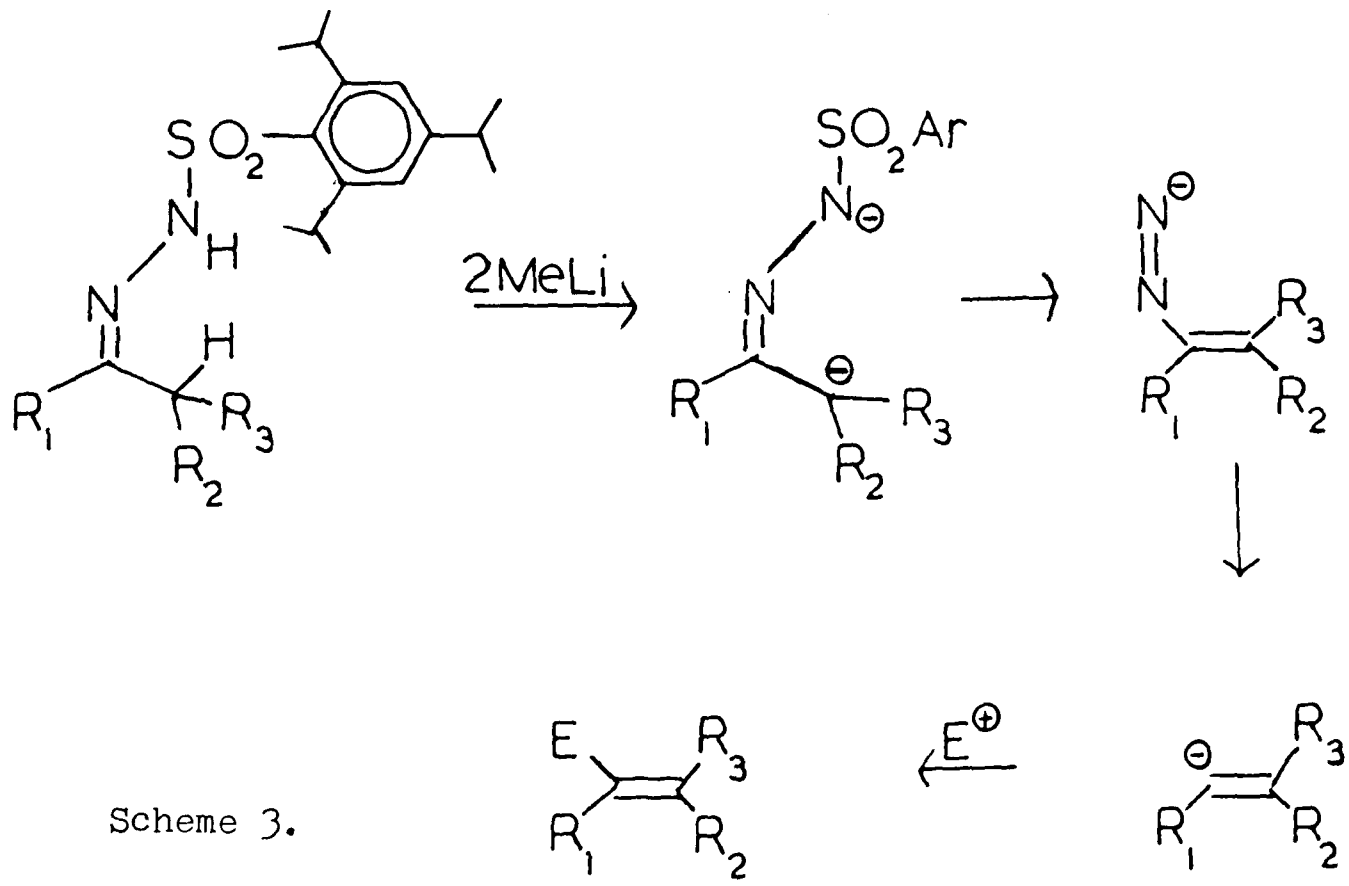


Scheme 1.

Toluenesulphonyl hydrazones (3) have long been known to undergo the Bamford-Stevens reaction[3] (Scheme 2) and, more recently, developments by Shapiro[4] and others[5] have extended the versatility of these hydrazones (Scheme 3).

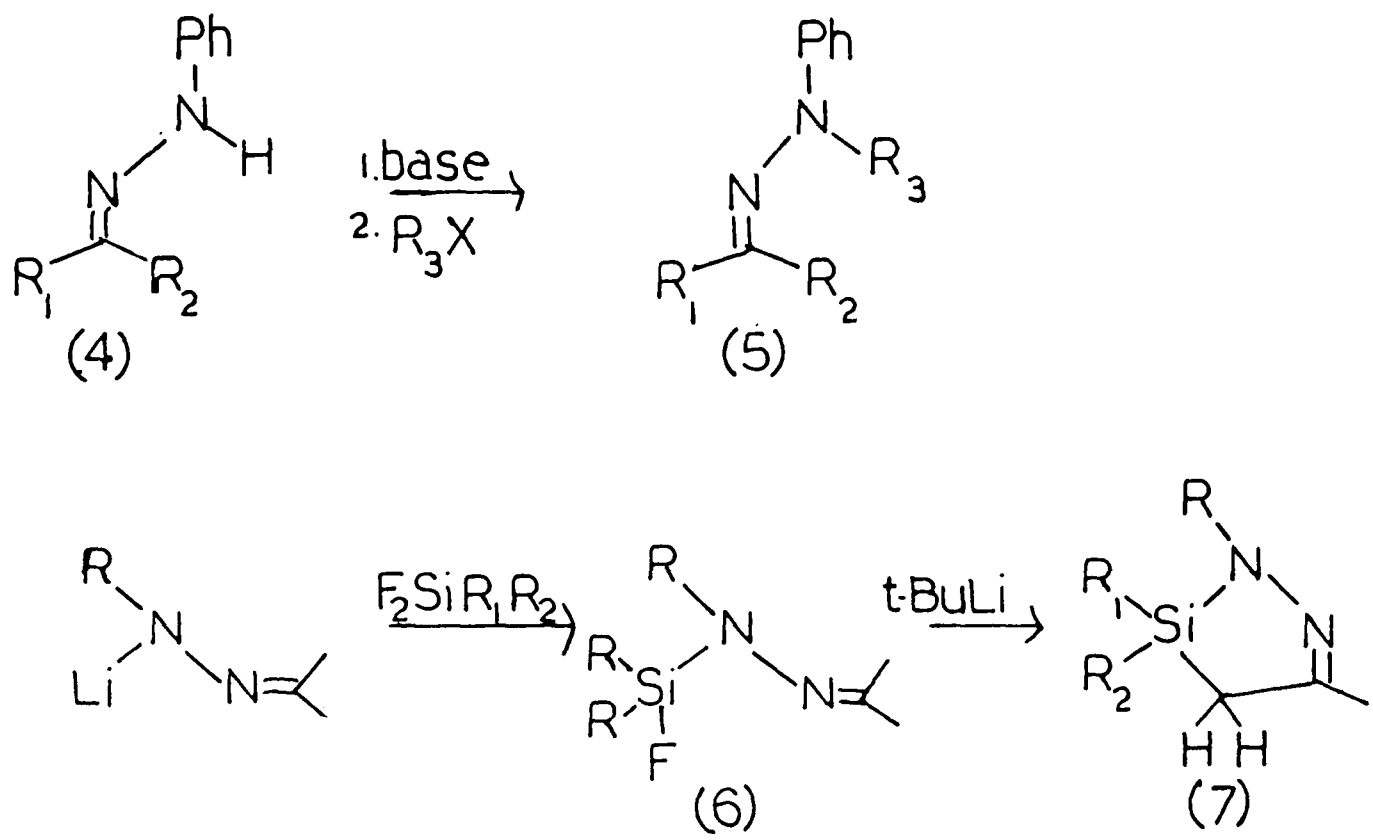


Scheme 2.

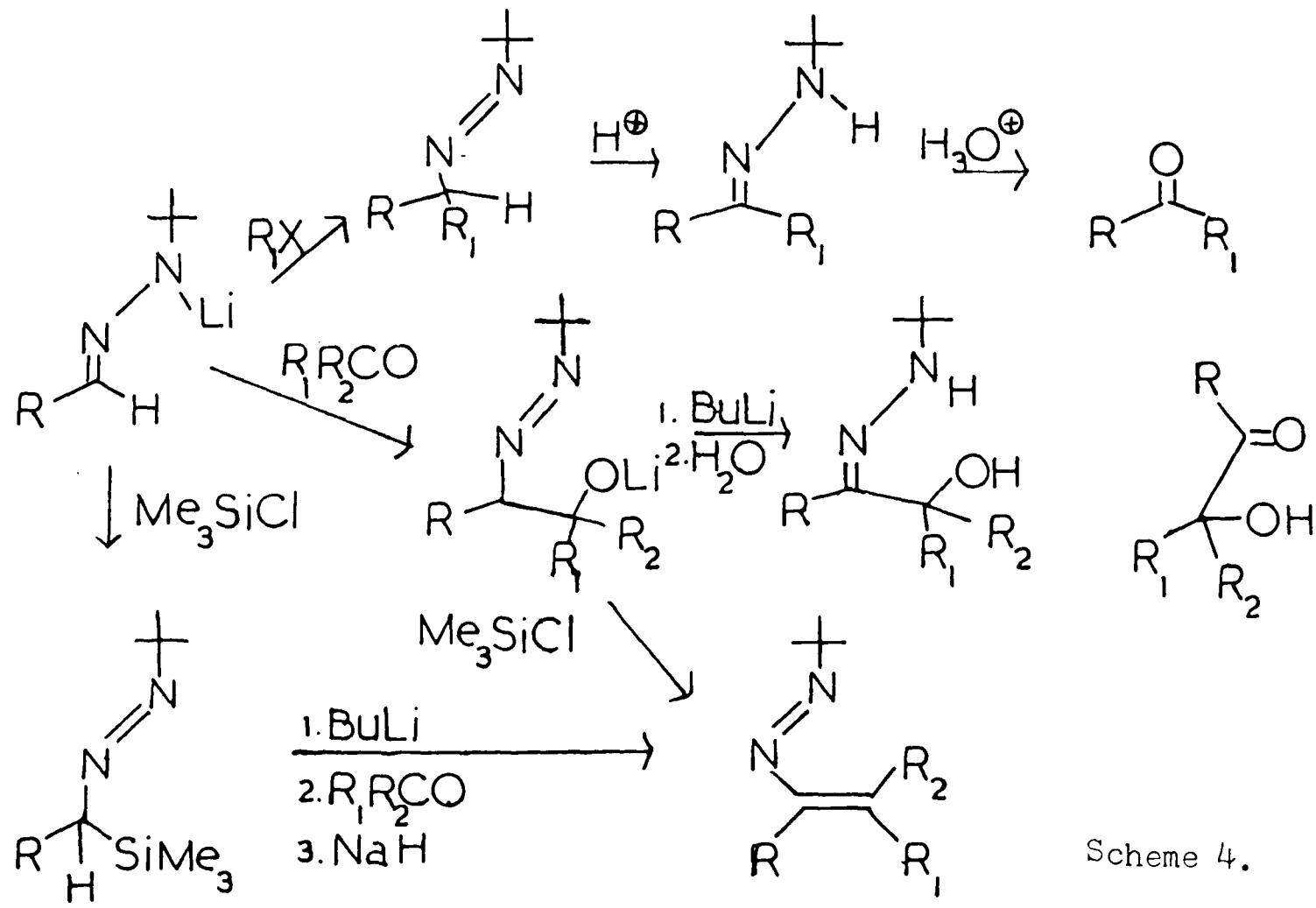


Scheme 3.

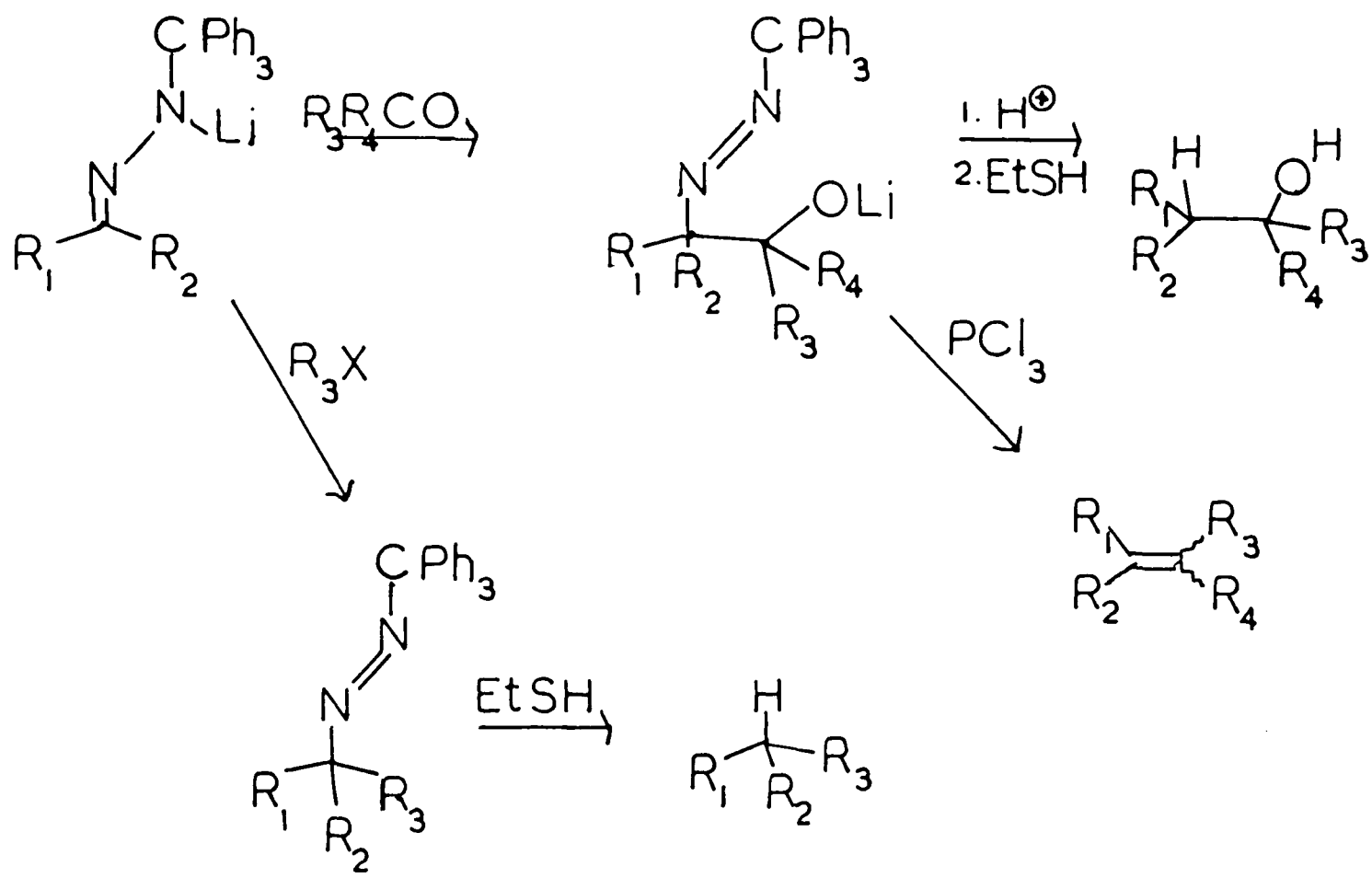
Other synthetic uses of hydrazones include N-alkylation of phenylhydrazones (4) as a synthesis of disubstituted hydrazones (5)[6] ; ∝-alkylation of phenylhydrazone dianions[7]; N-silylation of various hydrazones to give products (6) which can be cyclised to siladiazenes (7)[8];and resolution of ∝-substituted aldehydes via their diastereoisomeric (S)-aminosiloxymethylpyrrolidines (SASP-hydrazones).[9]



More recently some interesting synthetic applications of hindered hydrazones have been discovered[10,11] (Schemes 4 and 5).



Scheme 4.

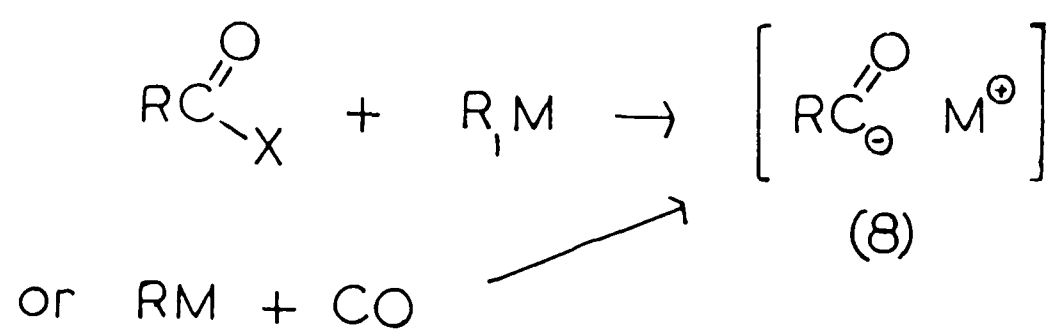


Scheme 5.

B Acylanions

The t-butylhydrazones in scheme 4 react as 'acylanions',an example of polarity reversal (umpolung) of the carbonyl group.Such acylanions are of significant synthetic potential.[12]

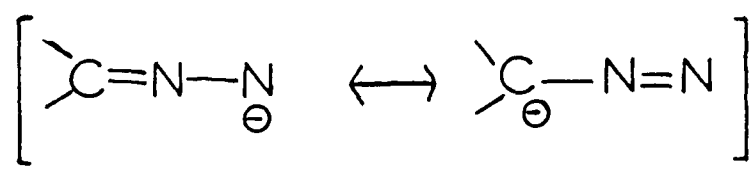
Generation of the naked acylanion (8) by metallation of acyl halides,or carbonylation of alkyl metal species,has not proved synthetically useful for metals of Groups Ia,IIa,or IIIa,[12a] but some transition metal acyl species and carbonyl complexes [e.g.$Na_2Fe(CO)_4$] have proved valuable.[13] Some synthetic utility has for example been attained with samarium acyls.[14]



Protection of carbonyls, especially as dithioacetals,[12a,15] has found significant use in the generation of acylanion equivalents. Other examples of 'masked' acylanions (that is a species which can, after reaction, be converted to a carbonyl) include cyanohydrins and protected cyanohydrins,[12a,16] metallated enols,[17] nitronates,[18] acetylide anions,[12a] Reissert compounds,[19] some hydrazones,[20] dihaloalkyllithiums,[21] isonitriles,[22] α-silylsulphones,[23] α-amino-nitriles,[24] and t-butylhydrazones.[10]

C. Azo-Anions as Ambident Nucleophiles

Anions generated from hydrazones can be represented by two resonance canonicals (9) which reveal the possibility of electrophilic reaction at carbon or nitrogen.



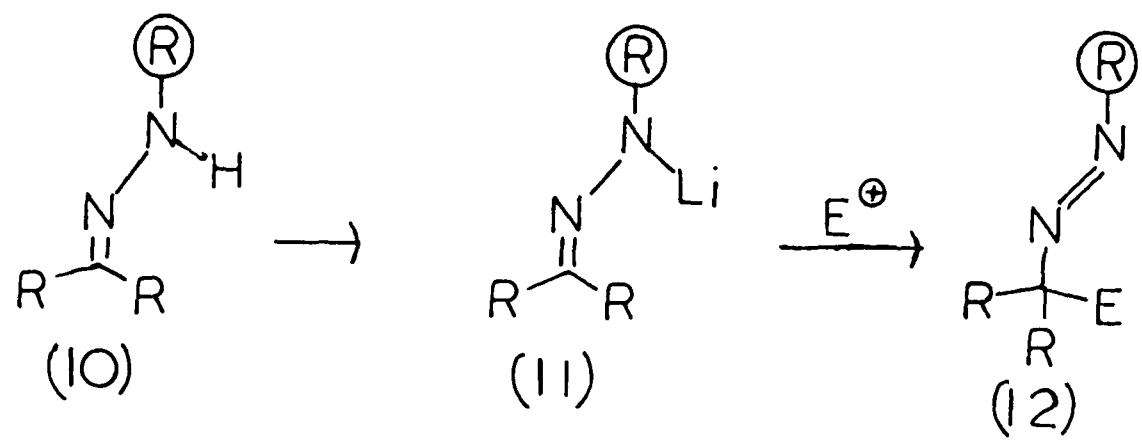
(9)

Most reactions with electrophiles occur from the nitrogen anion. That canonical is the major contributor to the structure,[25] but there are reports of carbon reactivity.[20] Reaction of benzaldehyde phenylhydrazone lithium salt with aldehydes and ketones gave some C-addition products.[26] Hydrazones with electron-withdrawing substituents on the carbonyl carbon also undergo reaction at carbon with acrylates and acrylonitrile.[27] Hydrazones themselves, as opposed to their anions, have been shown to react at carbon with aryldiazonium salts and bromine.[28]

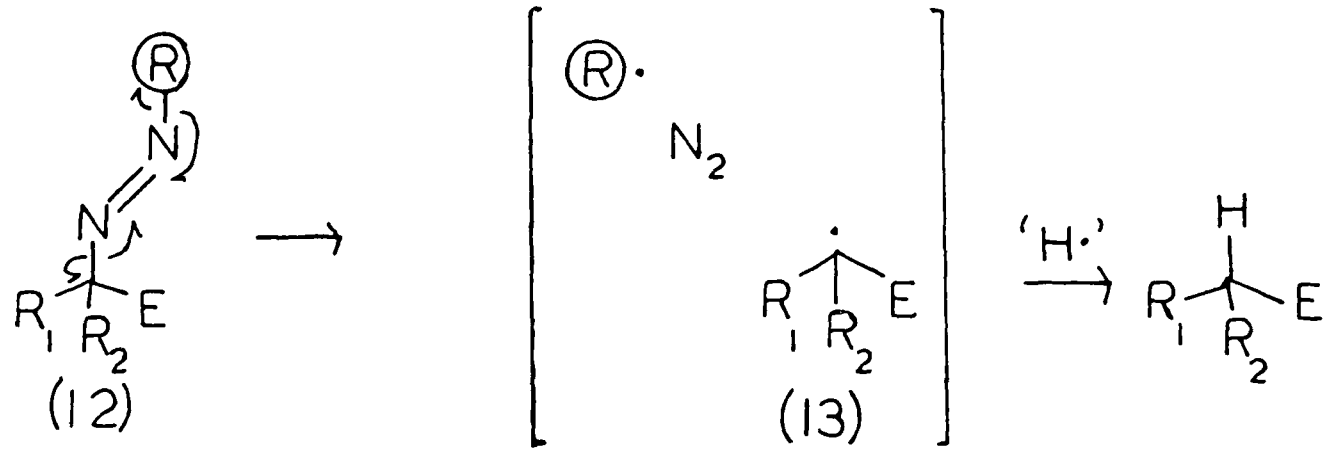
D. Rationale for Azo-Anion Methodology

The basis of the work described in this thesis is that anions

(11) derived from hydrazones (10) where R is sufficiently hindered, react with electrophiles at the carbon centre.This is because the reaction rate at the severely sterically hindered nitrogen site is significantly lower than that at the relatively unhindered carbon. The azo-species (12) is thus generated.[10,11]



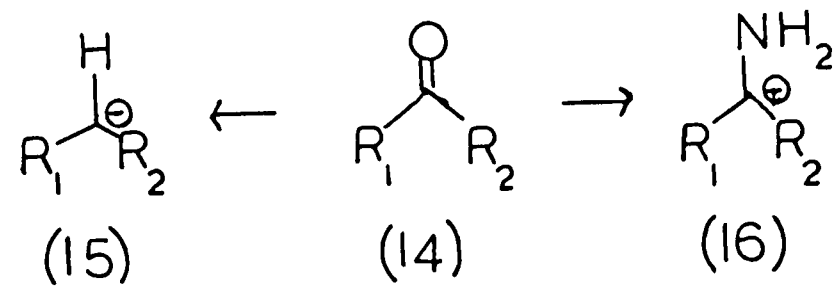
It was considered that if R were chosen so that it could exist as a stabilised radical,the thermal decomposition of (12)[29] would be enhanced.The radical (13) thus generated could then be trapped by a hydrogen donor (e.g. a thiol) (Scheme 6).



Scheme 6.

The resultant transformation would involve a carbonyl (14) being equivalent to anion (15). Another target of synthetic potential would be to cleave the nitrogen-nitrogen bond of the C-trapped

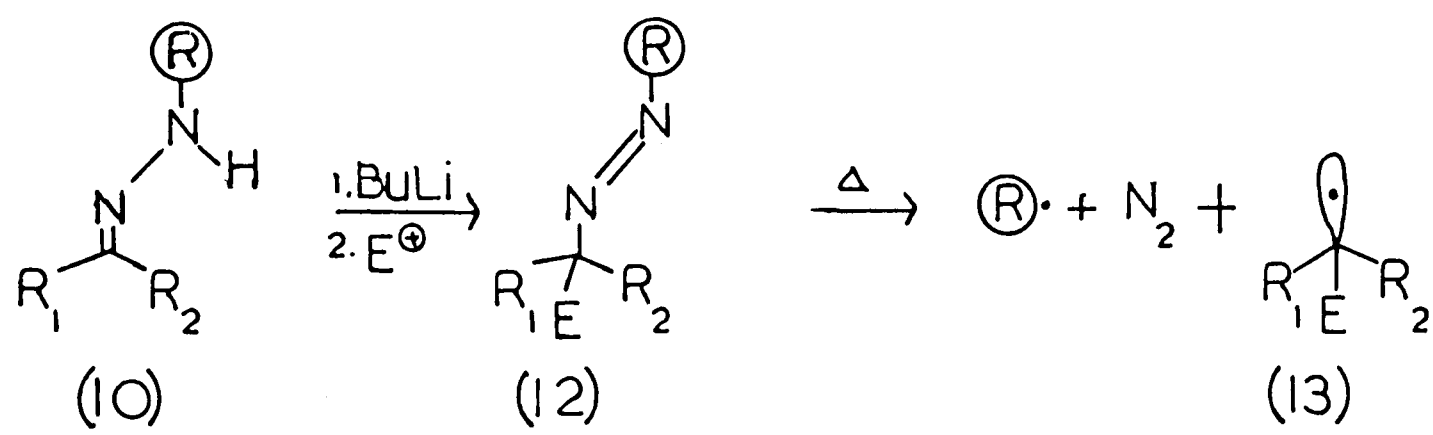
azo-adduct (12) to generate an amine. This would yield an α-amino-carbanion equivalent (16).[30]



The remainder of this thesis will demonstrate the approaches to and achievements of these goals.

CHAPTER II - THE PREPARATION AND DEPROTONATION OF HYDRAZONES

The development of the methodology discussed in this thesis depends on the use of sterically hindered hydrazones (10).The thermal stability of the azo products (12) has played an important part in the exploitation of the method.Initial work has been carried out on t-butylhydrazones (10,R = t-Bu) whose derived azo products (12,R = t-Bu) were shown to be stable to refluxing xylene (150°C).[10]



(10) (12) (13)

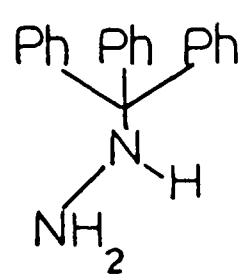
Alternatively,tritylhydrazones (10,R = CPh_3) gave azo compounds which decomposed homolytically at about -20°C.The decomposition (see Chap.IV) generates a radical (13) and it is the fate of these radicals and their synthetic use which has enabled the development of this aspect of azo-anion methodology.

In order to fully investigate both the steric requirements of (10,R variable) and the thermal stability of compounds (12),a range of hydrazones has been prepared.Perry has prepared isopropyl, 2,4 - dimethyl - 3 - pentyl,cyclohexyl,and 3,3 - dimethyl - 2 - butyl hydrazones.[31] In this thesis preparation and reactions of trityl, diphenyl - 4 - pyridylmethyl (hereafter called DPP),benzhydryl,and t-butyldiphenylmethyl (hereafter called BDP) hydrazones are discussed.

A. Preparation of Hydrazines

For a synthetic method to be widely applicable it is important

for the starting materials to be readily available,or at least simple to prepare.Hydrazines - the precursors of hydrazones - can be prepared in a number of ways,[32] but all those discussed here have been made by the same general method.This has involved the alkylation of hydrazine, or its monohydrate,with the appropriate alkyl chloride.The following hydrazines were thus prepared : tritylhydrazine (17); DPP hydrazine (18); benzhydrylhydrazine (19); and BDP hydrazine (20).All were isolated as their hydrochloride salts.



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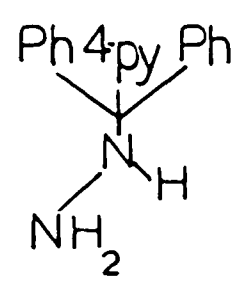

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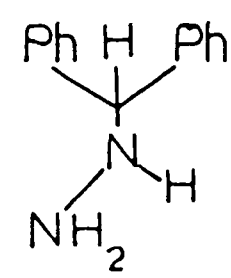

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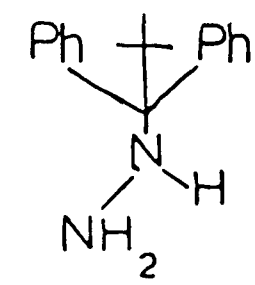
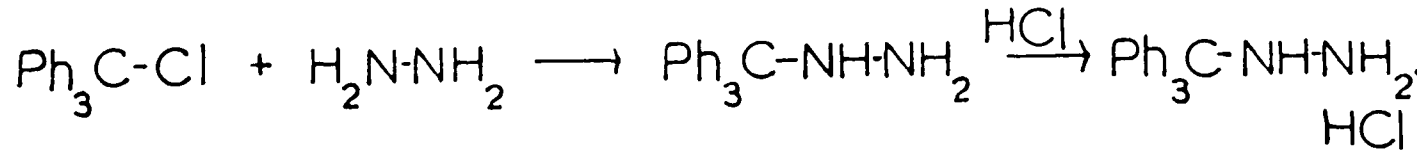


(20)

i) Tritylhydrazine (17)

Tritylhydrazine (17) has long been known [33] and the method chosen for preparation was based on that of Senior[34] (Scheme 7). Trityl chloride was treated with hydrazine hydrate in THF under reflux for 6h.The product was isolated as its hydrochloride salt (86%) by addition of methanolic hydrogen chloride to an ether extract of the reaction mixture.

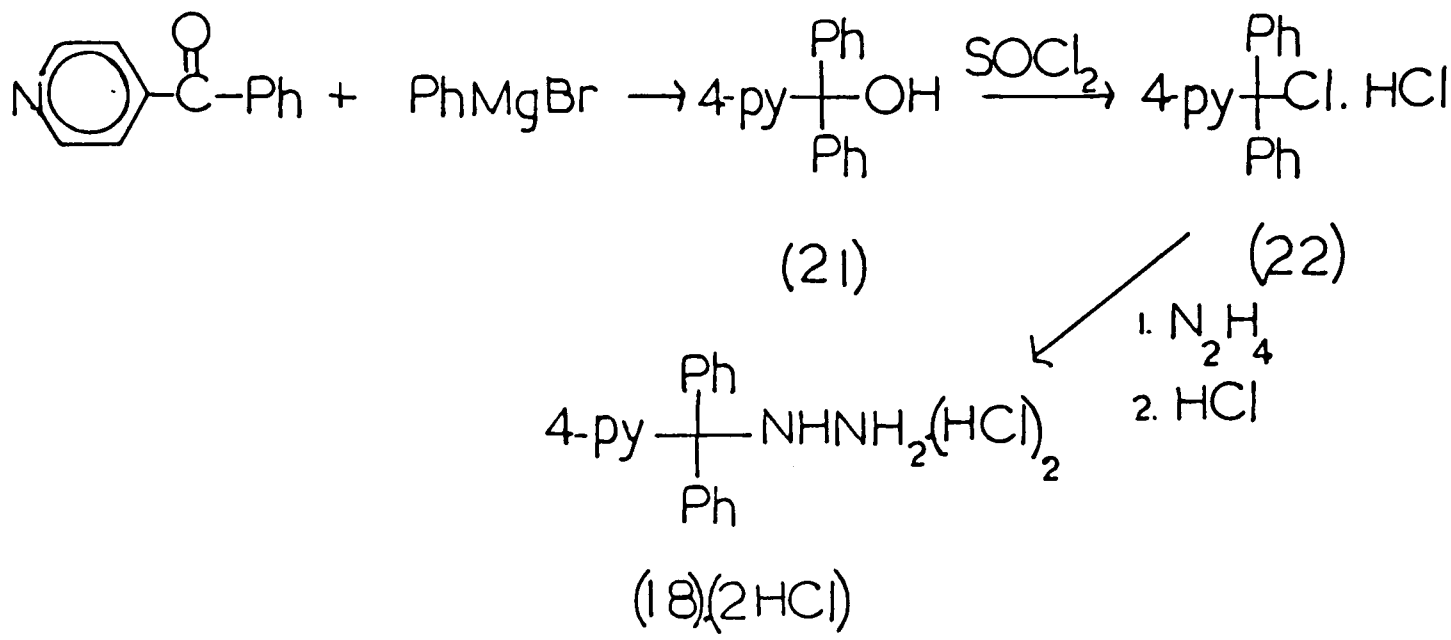


Scheme 7.

ii) DPP hydrazine (18)

DPP hydrazine (18) was prepared similarly with anhydrous

hydrazine, the reactant chloride being derived from 4 - benzoylpyridine by a Grignard reaction and subsequent chlorination (Scheme 8). The alcohol (21) was isolated in good yield (82%) and its spectral data compared with the literature.[35] Treatment with thionyl chloride, according to precedent,[36] gave the chloride as a hydrochloride salt (22). The melting point (174 - 176°C) obtained for this material was inexplicably higher than the literature value (134 - 135°C).[36] Other (spectral) data confirmed the structure, as did the conversion into the hydrazine (18), isolated as a dihydrochloride salt (96% from alcohol).



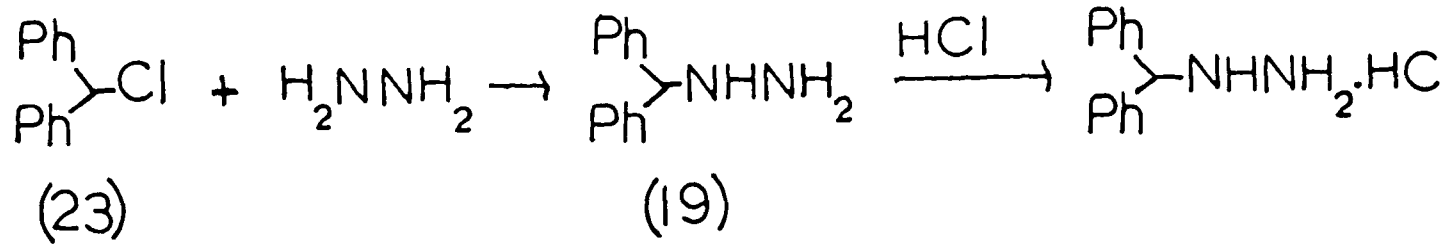
Scheme 8.

The dihydrochloride was confirmed by the pyridine doublets in the proton n.m.r. [8.33 (d, J 7Hz), 8.85 (d, J 7Hz)] . If less than two equivalents of hydrogen chloride were used in the preparation of the salt a mixture of two compounds was observed by n.m.r., with the dihydrochloride (18).(2HCl) and another species (either free base or monohydrochloride) which possessed a set of pyridine doublets [8.27 (d, J 7Hz), 8.77 (d, J 7Hz)] . The overall yield was also lowered in this case.

iii) Benzhydrylhydrazine (19)

Benzhydrylhydrazine (19) was prepared from chlorodiphenyl

methane (23) and anhydrous hydrazine in THF in acceptable yield (46%). The method (Scheme 9) was a slight variation of an existing procedure involving DMSO as solvent.[37]

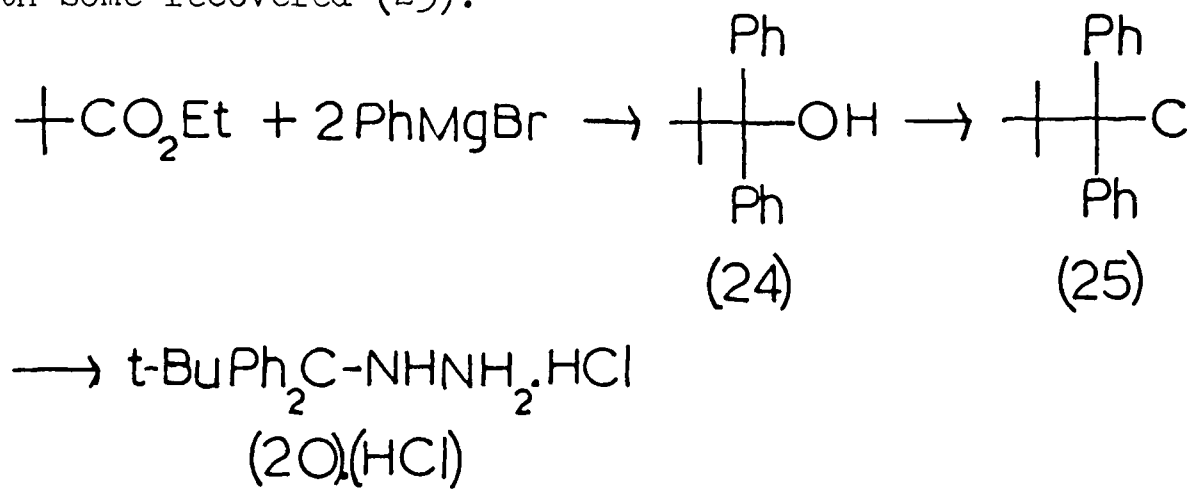


(23) (19)

Scheme 9.

iv) BDP hydrazine (20)

BDP hydrazine (20) was prepared according to scheme 10. Schlenk's method for preparation of carbinol (24) was employed.[38] The chlorination, with thionyl chloride, proceeded well, but the chloride (25) was very hindered and slow to react with nucleophiles in further reaction. (25) could be recrystallised from light petroleum and reaction with anhydrous hydrazine in dioxan, at reflux for 3.5 d, gave a moderate yield of hydrazine (20). This was isolated as a hydrochloride salt (60%) with some recovered (25).



(24) (25) (20).(HCl)

Scheme 10.

All of these hydrazine hydrochlorides were stored at 4°C without serious degradation over periods up to a year.

B. Preparation of Hydrazones

All four classes of hydrazone described in this thesis were accessible by one simple,convenient route.The hydrazine hydrochloride in methanol solution was neutralised with aqueous sodium formate and the carbonyl component was added.After stirring for two hours under an inert argon atmosphere,in darkness,the product was isolated.Most of the hydrazones precipitated out as solids which were isolated by filtration and washed with water before drying under high vacuum. Highly unsymmetrical ketones,and aldehydes other than acetaldehyde or benzaldehyde,gave hydrazone products which were isolated as viscous oils by extraction into dichloromethane.

Further purification of the solids was not performed as initial attempts to recrystallise the crude products led to decomposition. The oils could be purified,with loss of yield,by very rapid chromatography on silica gel but were routinely used in the purity obtained from extraction.

The hydrazones of all classes were unstable to autoxidation.[39] They could be stored without significant decomposition for periods of up to two months if kept cold ($-18^{o}C$) under argon in the dark.Table 1 shows the hydrazones prepared and the yields obtained.

C. Deprotonation of Hydrazones

The azo-anion methodology requires generation of anions (11) by treatment of hydrazones (10) with a base.The pKa for these hydrazones is expected to be around 30 - 35,[40] so strong bases are required.

Lithium diisopropylamide (LDA) could be used but,as its pKa is similar to the hydrazone,methyl or n-butyl lithium are to be preferred.

A slight excess (10%) of base was added to a solution of the

Carbonyl \ Hydrazone	Yield (%) Trityl (26)	DPP (27)	Benzhydryl (28)	BDP (29)
a) Acetaldehyde	81	-	90	70
b) 2 - Methyl propanal	81	-	-	-
c) Pentanal	87[a]	-	-	95[a]
d) 3 - Methyl butanal	-	-	-	100[a]
e) Benzaldehyde	-	-	71	-
f) Acetone	90	65	71	82
g) 2 - Octanone	36[b]	57	-	-
h) Butanone	49	47	-	-
i) Cyclohexanone	58	57	-	73
j) Cyclo-dodecanone	87	81	-	96

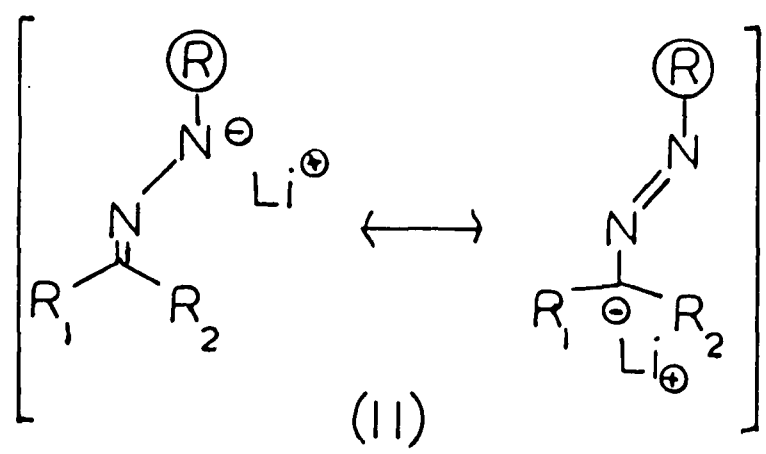
a - isolated as oil by extraction

b - columned material

Table 1.

hydrazone,normally in THF,at about -40°C.The solution was left for 20 min to allow complete anion formation.The solutions were generally coloured at this stage,varying from yellow to deep red.Whether the colour results from the so-formed azo-anion or from impurities is uncertain.

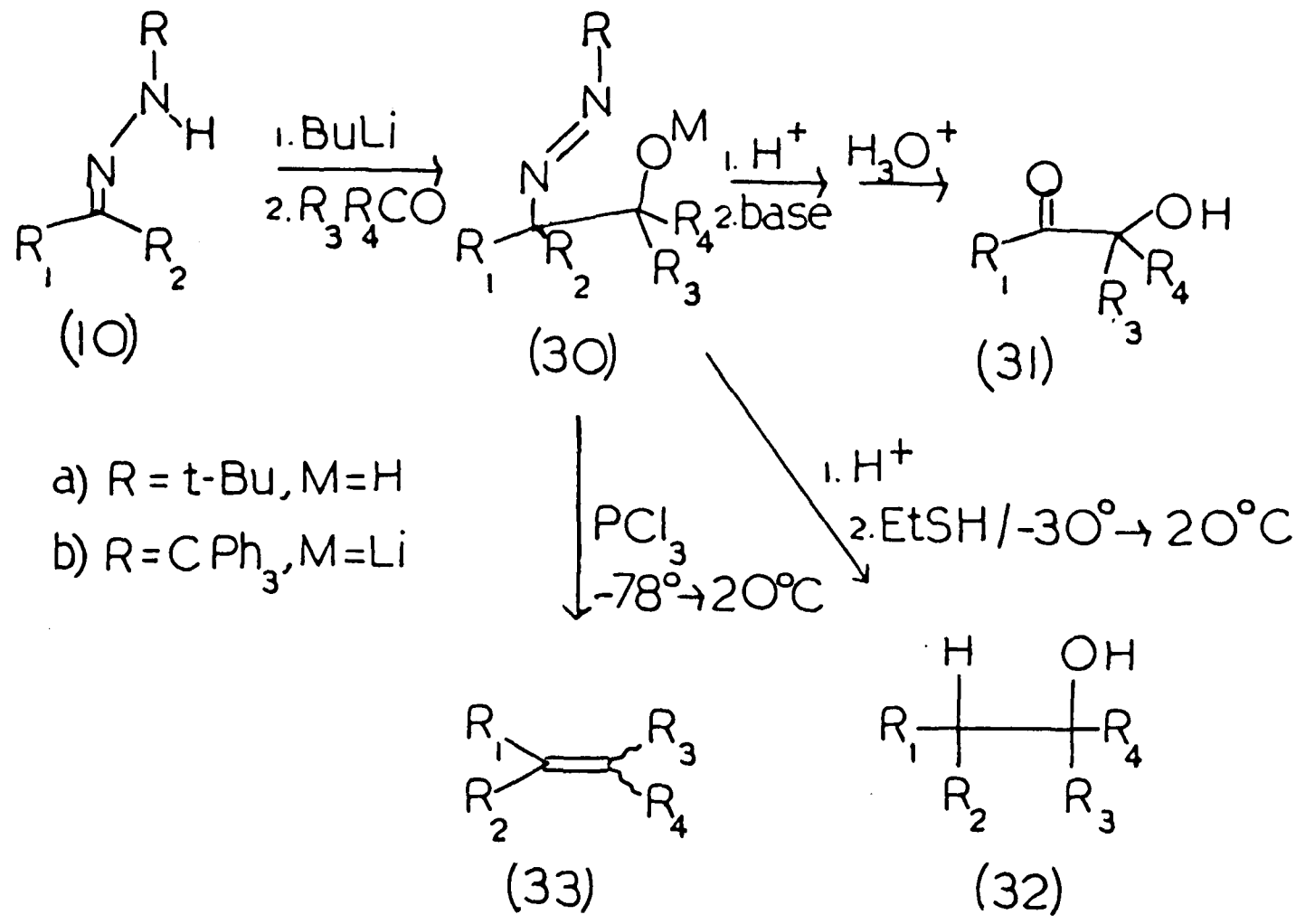
Two resonance stabilised canonical forms can be written for anions (11) and this methodology requires reaction through the azo-carbanion form.



(11)

CHAPTER III - REACTIONS OF AZO-ANIONS WITH CARBONYL ELECTROPHILES

The lithium anions generated from t-butylhydrazones (10, R = t-Bu) react with aldehydes and ketones to generate azoalcohols (30a) (Scheme 11). These intermediates (R_2 = H) were isomerised and hydrolysed to give ∝-hydroxyketones (31).[10] It was subsequently shown that tritylhydrazones (26) underwent a similar reaction to give the alkoxides (30b) which could be diverted to produce alcohols (32) or alkenes (33).[11] The latter two transformations are the equivalent of a reductive coupling of two carbonyl compounds.

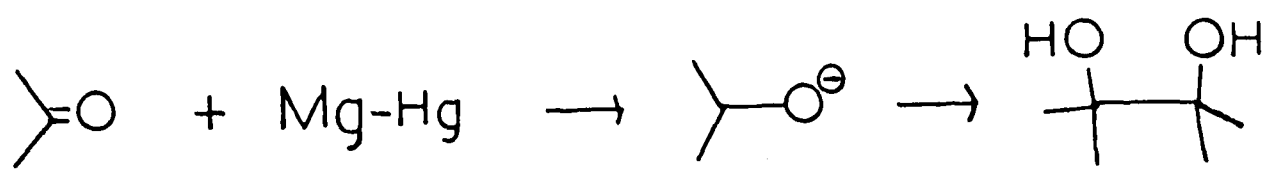


Scheme 11.

A. Reductive Coupling of Carbonyl Compounds

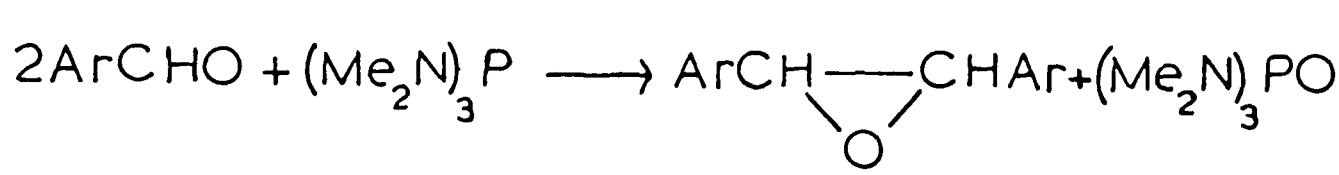
There are a number of reactions known in the literature to accomplish the reductive coupling of two carbonyl compounds. The pinacol reaction, used to prepare vicinal diols (34) from aldehydes and ketones,

is a well known,long standing,example.[41] The reaction proceeds via one electron reduction to give radical intermediates which couple to give the products.[41] A similar reaction is the acyloin reaction which couples carboxylic acid esters.[42]



(34)

Aromatic aldehydes can be coupled to form epoxides (35) by using hexamethylphosphorus triamide.[43] Horner also found a method for reductive coupling of aromatic aldehydes using diphenylphosphinoyl-sodium at 200°C.[44]

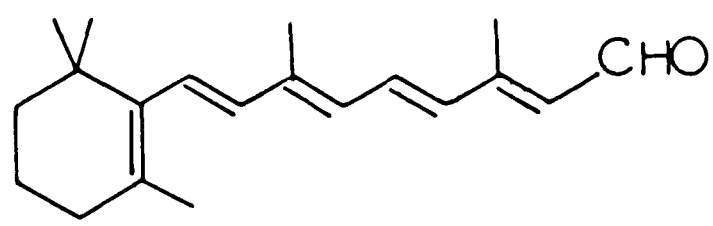


(35)

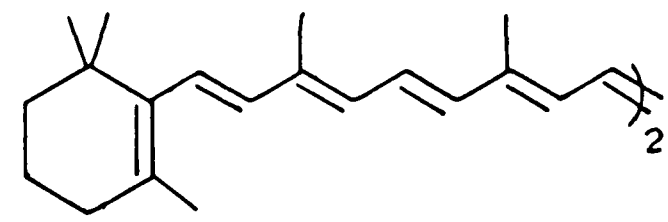
More recently Sharpless has used low valent tungsten compounds to couple aldehydes and ketones to generate alkenes.[45] Fujiwara has also prepared similar tungsten and molybdenum reagents.[46] The reactions using these reagents were,however,only useful for aryl substrates.

The most synthetically useful reagents developed for the coupling of carbonyl compounds to date are the titanium based reagents originally discovered by Tyrlik[47] and Mukaiyama[48] and principally developed by McMurry.[49] McMurry found that a reagent prepared from titanium trichloride and lithium aluminium hydride would effect the coupling of carbonyls to alkenes,for alkyl as well as aryl aldehydes and ketones. The synthetic utility of this reaction was demonstrated

by coupling retinal (36) to give β-carotene (37) in 85% yield.[49a]

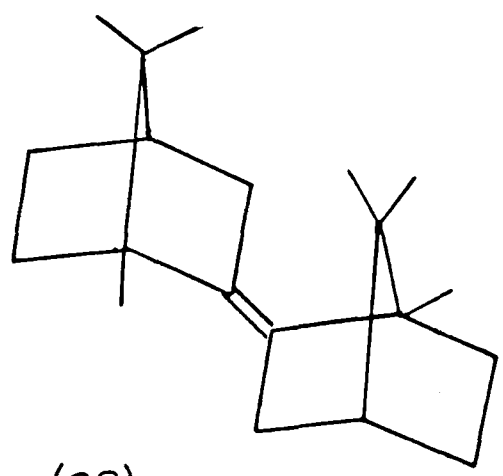


(36)

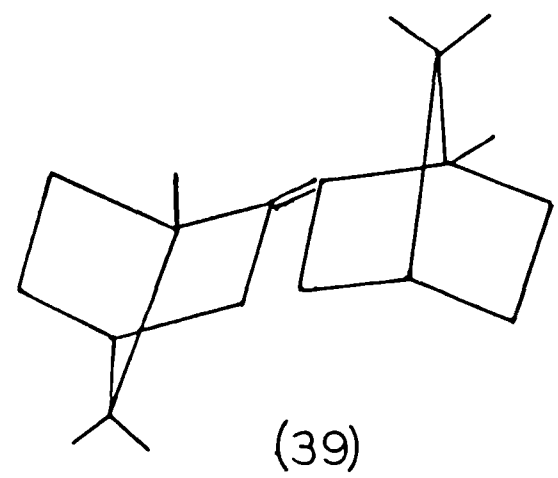


(37)

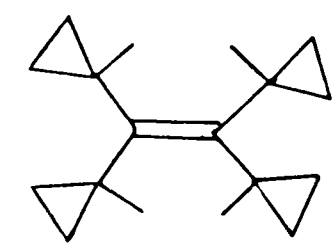
There were some problems with the reproducibility of the transformation (36) to (37) owing to batches of reagent of varying quality. To overcome this another reagent was prepared by treating titanium trichloride with potassium, lithium, or best of all a zinc-copper couple in THF according to a method developed by Rieke.[50] This reagent was found to be very convenient for alkene preparation and some interesting examples have been reported. For example, camphor was dimerised to give isomers (38) and (39),[51] 4,4'-homoadamantylidenehomoadamantane (40) was prepared [52] as were tetraisopropylethylene (41)[53] and the highly hindered alkene (42).[54]



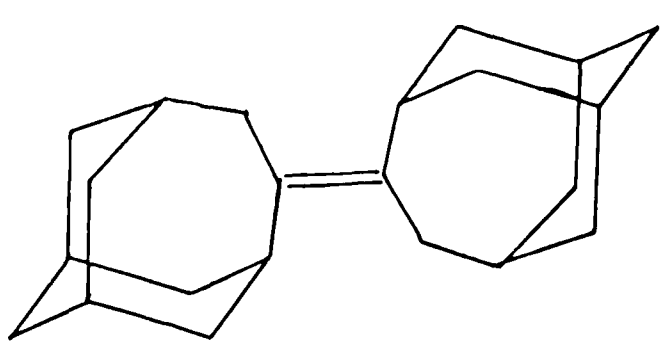
(38)



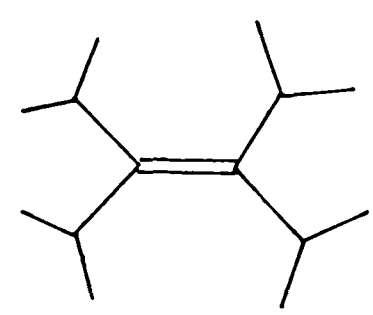
(39)



(42)



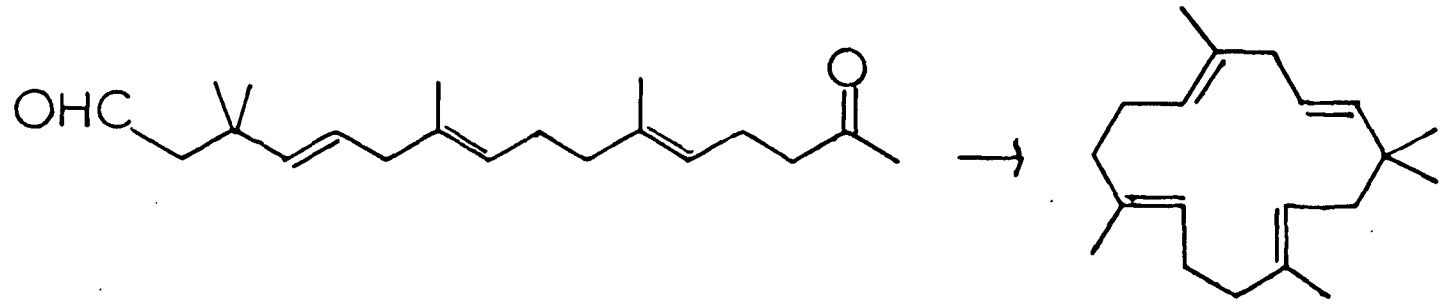
(40)



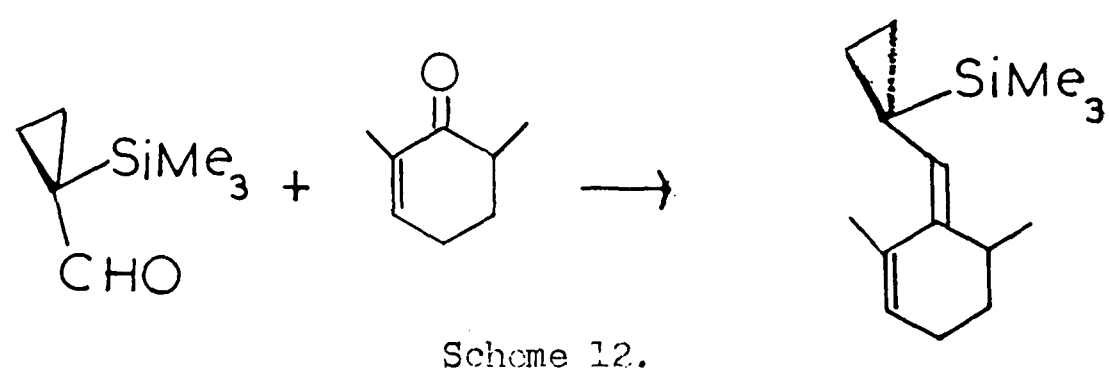
(41)

Intramolecular coupling has also proved an efficient method for cycloalkene synthesis. A synthesis of flexibilene (43) used this method as the crucial ring closing step.[49b]

One of the drawbacks of this methodology is that in <u>inter</u>-molecular reactions only symmetrical alkenes are produced. Only in limited cases can unsymmetrical alkenes be prepared by cross-coupling. McMurry has achieved this goal by using a large excess of one reaction partner,usually a volatile ketone. Alternatively,when a diaryl ketone was used as one partner very good yields of cross-coupled products were obtained with a 1:1 ratio of reagents. This results from a change of mechanism,from radical to anionic,owing to the ready reducibility of diaryl ketones.[55] An example of cross-coupling using an $\alpha\beta$-unsat--urated partner has recently been published by Paquette (Scheme 12) as part of a spirosesquiterpene synthesis.[56]



(43)

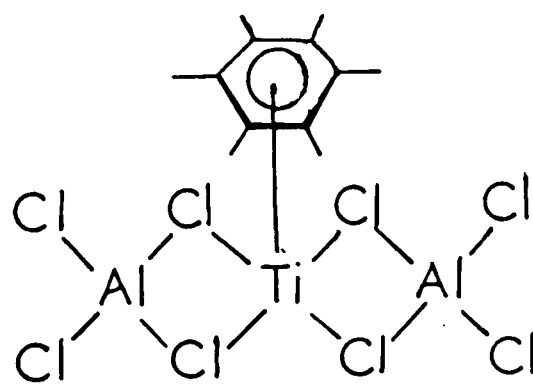


Scheme 12.

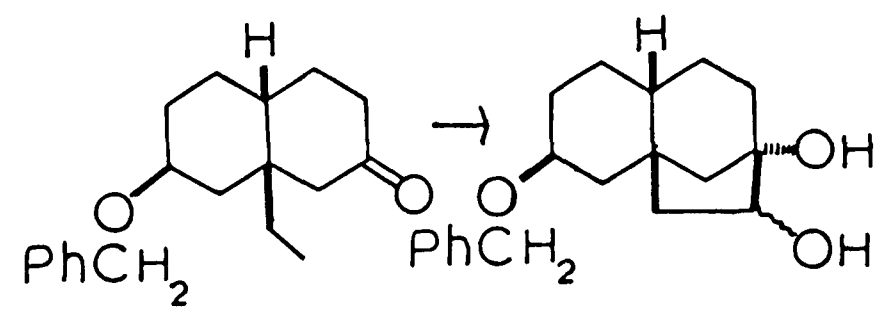
The structure and mechanism of action of these low valent titanium reagents has been thoroughly investigated by Geise.[57] This revealed a pinacol-type process,proceeding by an initial one electron reduction. The intermediate pinacol products could be isolated if the reaction was worked up before complete consumption of starting material.

Mixed pinacol couplings have been carried out by Corey using titanium tetrachloride - magnesium, cyclopentadienyltitanium trichloride-

lithium aluminium hydride or complex (44).[58] A gibberellic acid intermediate (45) was prepared by an intramolecular example of this process.



(44)



(45)

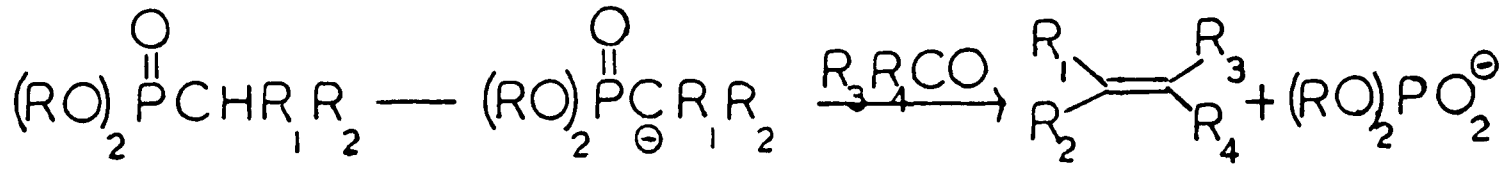
Clerici and Porta have developed aqueous titanium trichloride as a convenient cross-coupling pinacol reagent for carbonyls with electron-withdrawing groups attached to the carbonyl carbon.[59] $\alpha\beta$-unsaturated carbonyls give allylic diols by this method. There is also a cerium reagent,prepared from cerium triiodide and potassium, which is both mild and compatible with ester,nitrile,vinyl or aryl halide functionality and which gives pinacol coupled products.[60] Samarium diiodide can also be used to cross-couple aldehydes and ketones.[61]

McMurry's method appears to be the most useful system for reductive carbonyl coupling but he concludes that,"the mixed titanium induced carbonyl coupling reaction is not of general synthetic use." The results presented in this chapter will show that a convenient mixed reductive carbonyl coupling can be achieved by the application of azo-anion chemistry.

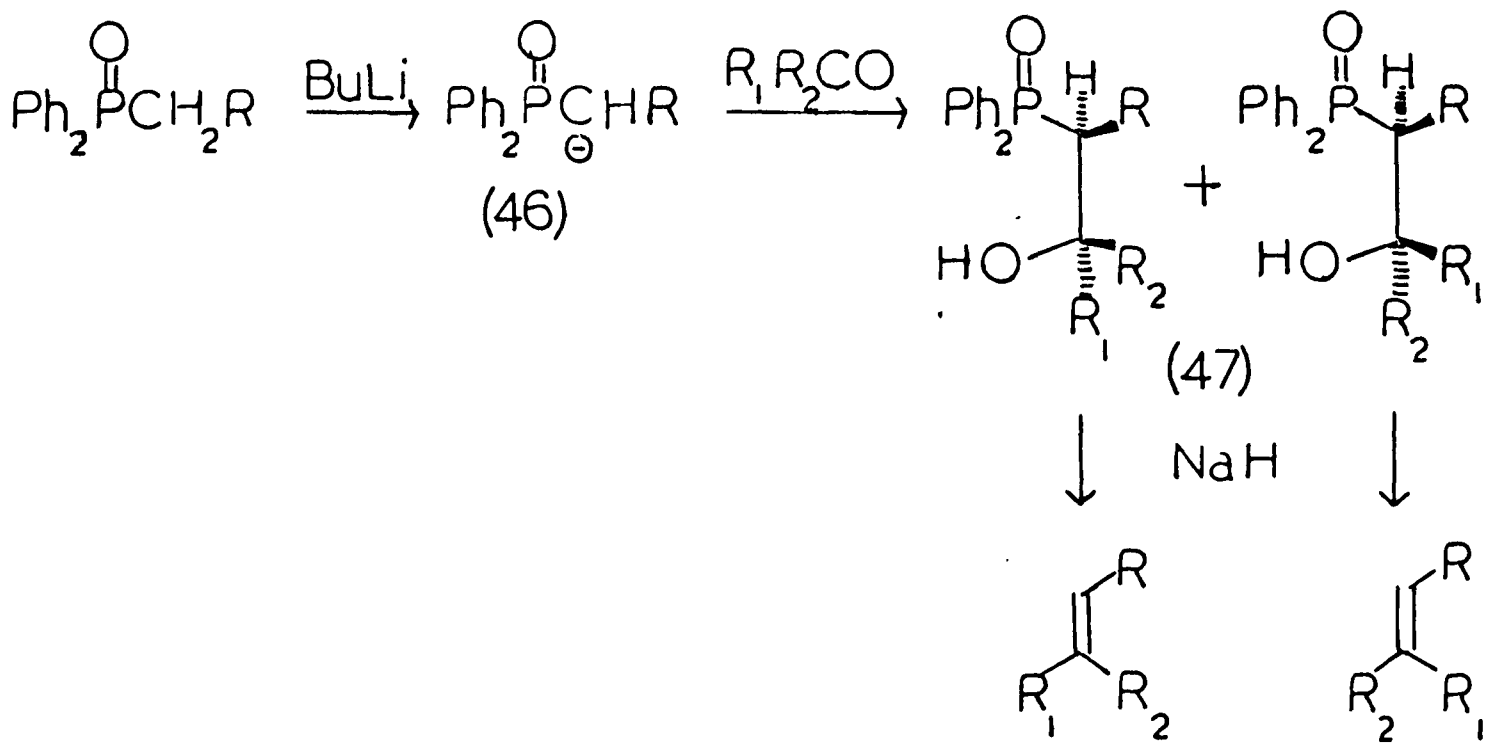
B. Alkene Forming Reactions

Although McMurry's method has enabled the reductive coupling

of two carbonyl compounds to form an alkene, the literature contains many other methods for alkene generation when only one partner is a carbonyl compound. Probably the most well known of these is the Wittig reaction,[62] where phosphorus ylides are used in reaction with aldehydes and ketones. The stereochemistry of the product alkene can be controlled to some extent by the choice of reaction conditions.[63] There are more recent variations of this reaction which offer some advantages. For example, the Horner-Emmons reaction (Scheme 13) which generates water soluble by-products.[64] More recently a variant using diphenylphosphin--oyl anions (46) has been extensively developed by Warren.[65] In this reaction the intermediates (47) are isolable and the diastereoisomers can be easily separated to give geometrically pure alkenes on further reaction (Scheme 14).

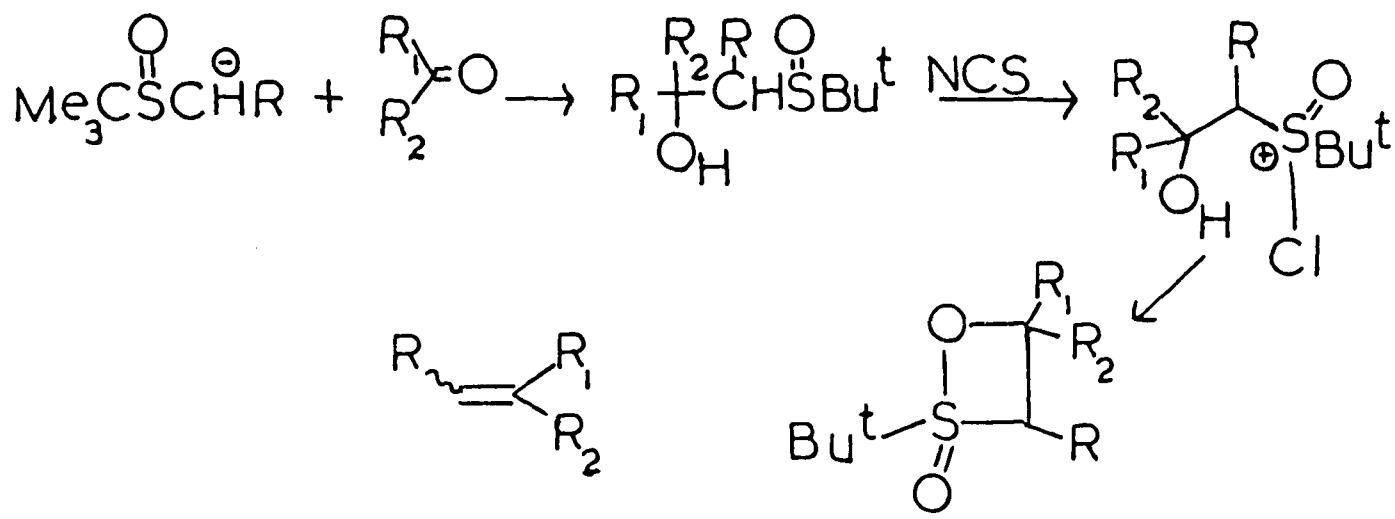


Scheme 13.

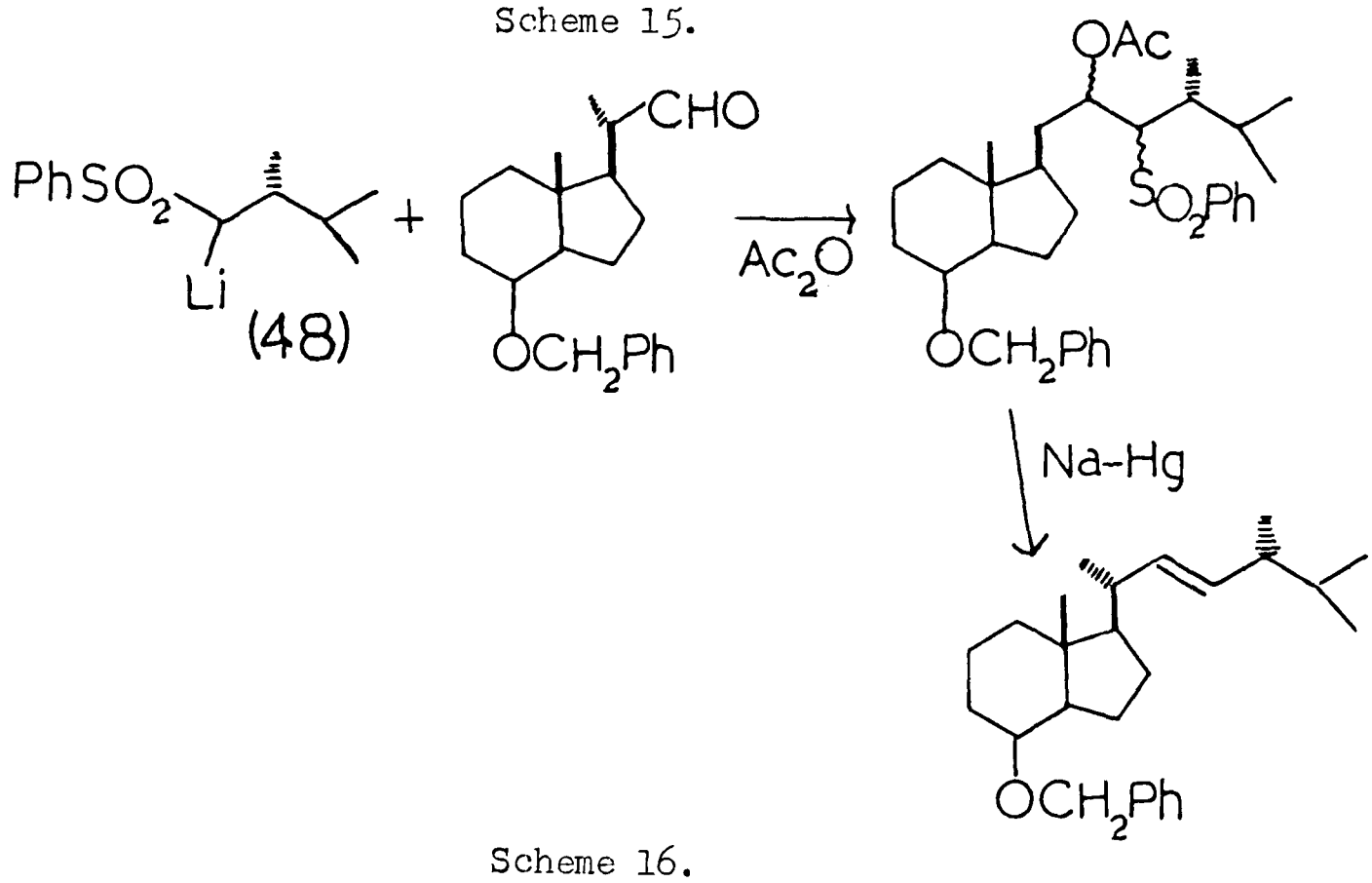


Scheme 14.

There is a sulphur analogue of the Wittig reaction which has been developed by Durst (Scheme 15).[66] Julia has also developed a sulphur based alkene synthesis using ∝-lithiosulphones (e.g. 48).[67] These sulphones give <u>trans</u>-alkenes on elimination (Scheme 16) but are not applicable to tetrasubstituted alkenes and give poorer yields of trisubstituted alkenes owing to the reversibility of the initial addition to the carbonyl.



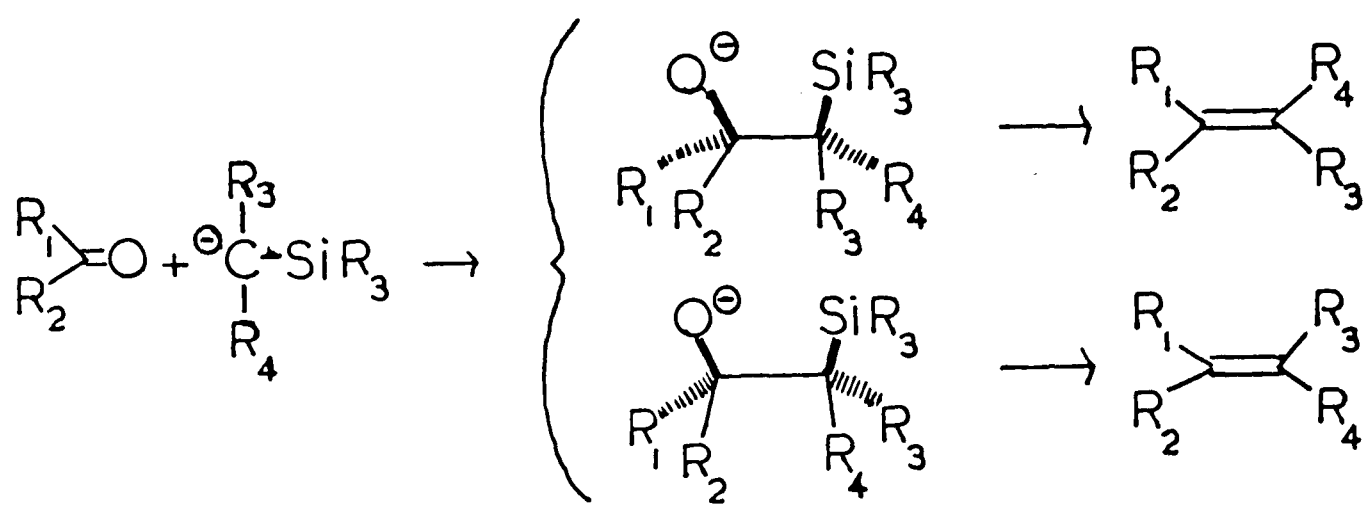
Scheme 15.



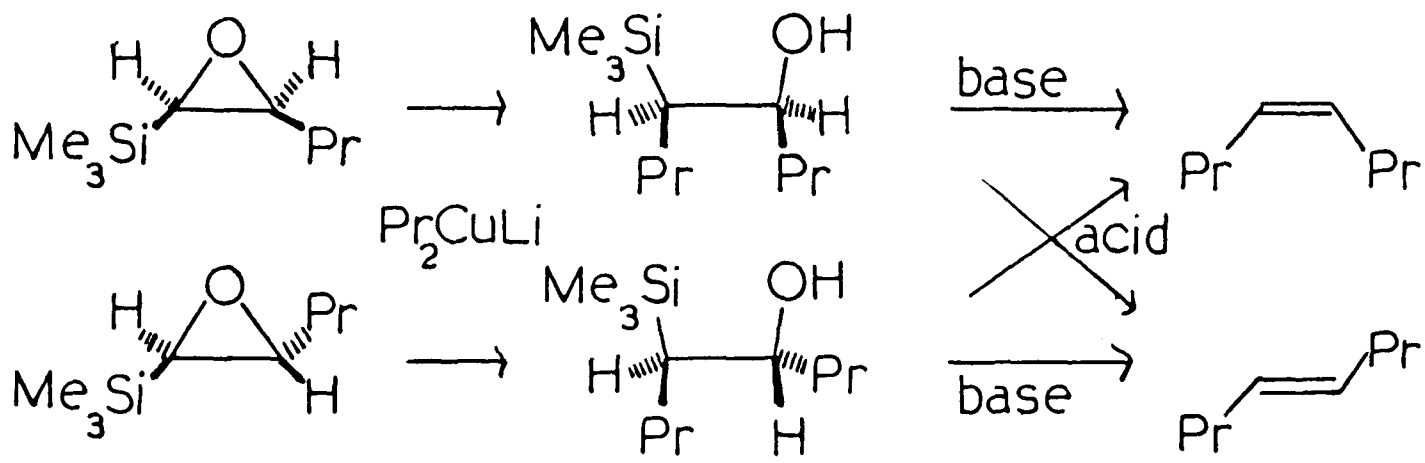
Scheme 16.

The Peterson reaction is also another general alkene forming reaction,[68] involving elimination from β-hydroxysilanes. The overall

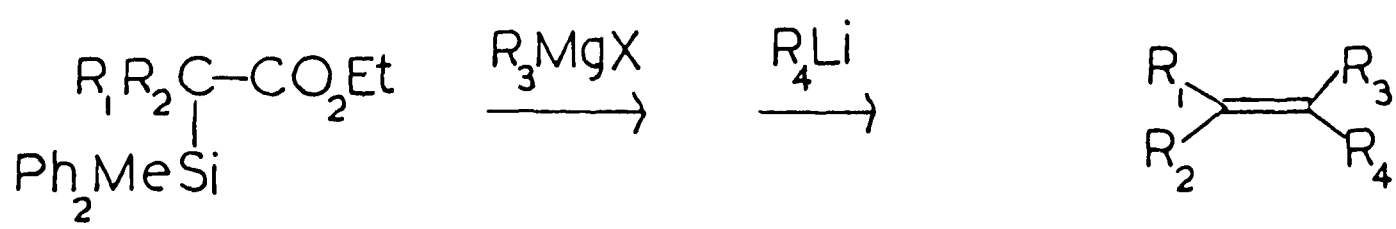
reaction proceeds without stereocontrol (Scheme 17) but, as the elimination can be carried out stereospecifically syn- (basic conditions) or anti- (acidic conditions), alkenes can be generated with controlled geometry (Scheme 18). A recent variant of the reaction allows a good synthesis of tri- and tetra-substituted alkenes (Scheme 19).[69]



Scheme 17.

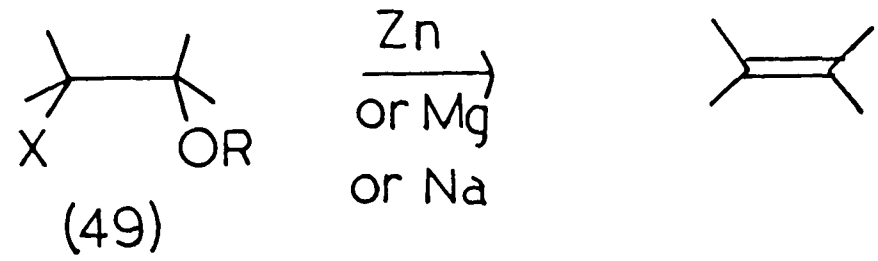


Scheme 18.



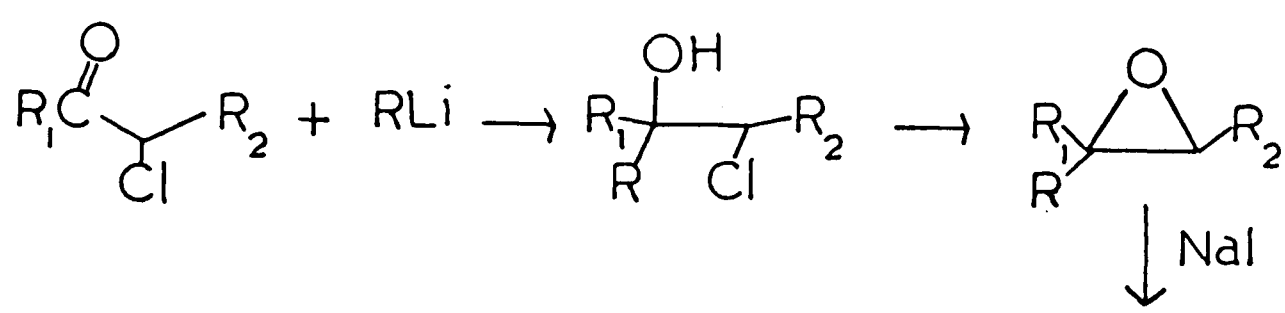
Scheme 19.

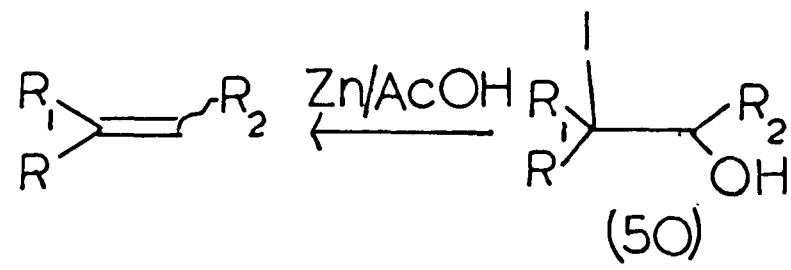
In a similar vein, β-haloethers (e.g. 49) eliminate to give alkenes in a general reaction known as the Boord reaction.[70]



(49)

The Cornforth method [71] is another process for alkene formation. This proceeds from an α-chloroketone via the iodohydrin (50, Scheme 20).

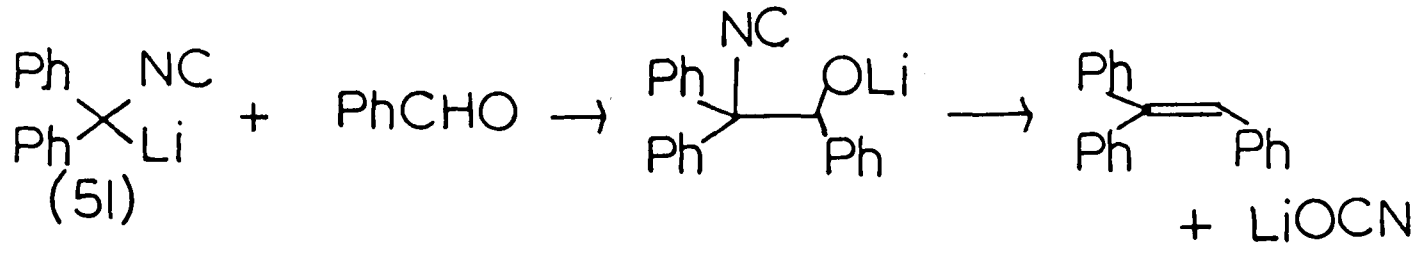


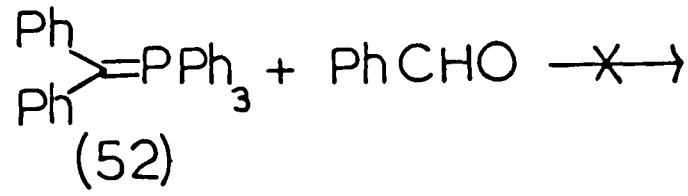


(50)

Scheme 20.

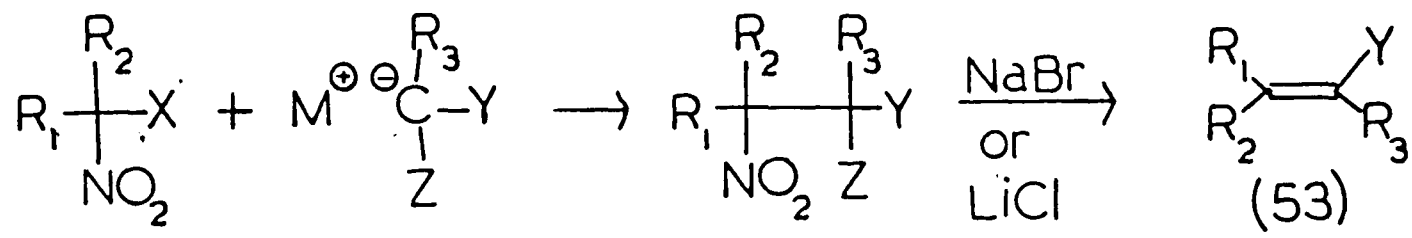
α-Lithioisonitriles can be used to form alkenes [72] by reaction with aldehydes and ketones and offer some advantages over the Wittig method. For example, benzhydryl isonitrile anion (51) added to benzaldehyde to give triphenylethylene, whilst the corresponding phosphorus ylide (52) did not react.





(52)

Ono has developed an interesting coupling reaction[73] based on nitro compounds for the preparation of activated alkenes (53, Scheme 21).

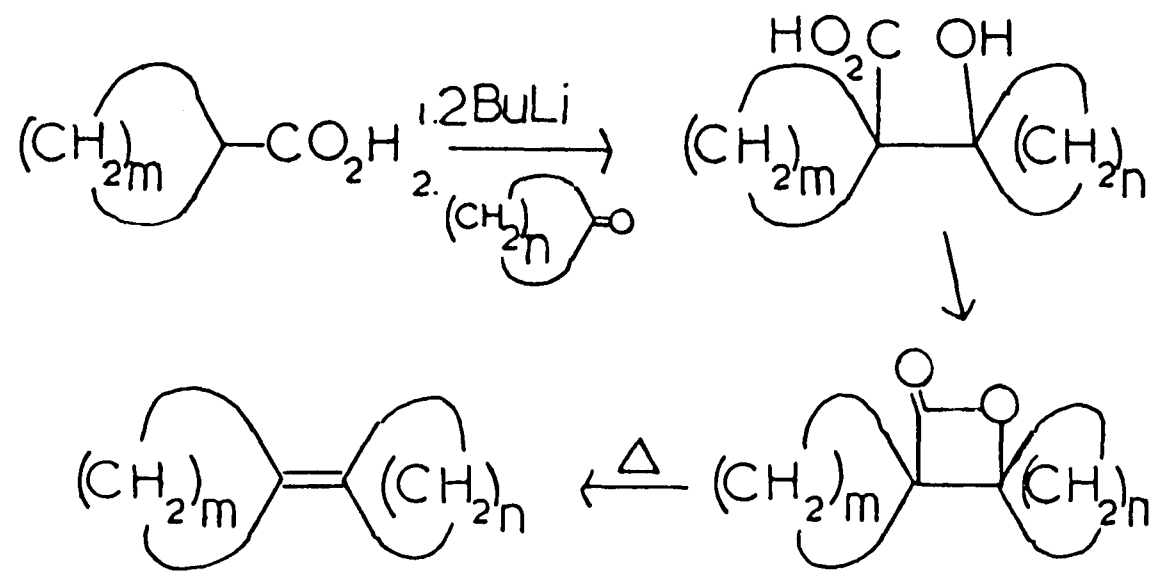


Y = CN, CO_2Et, C(O)Me, SO_2Ar

Z = CO_2Et, C(O)Me

Scheme 21.

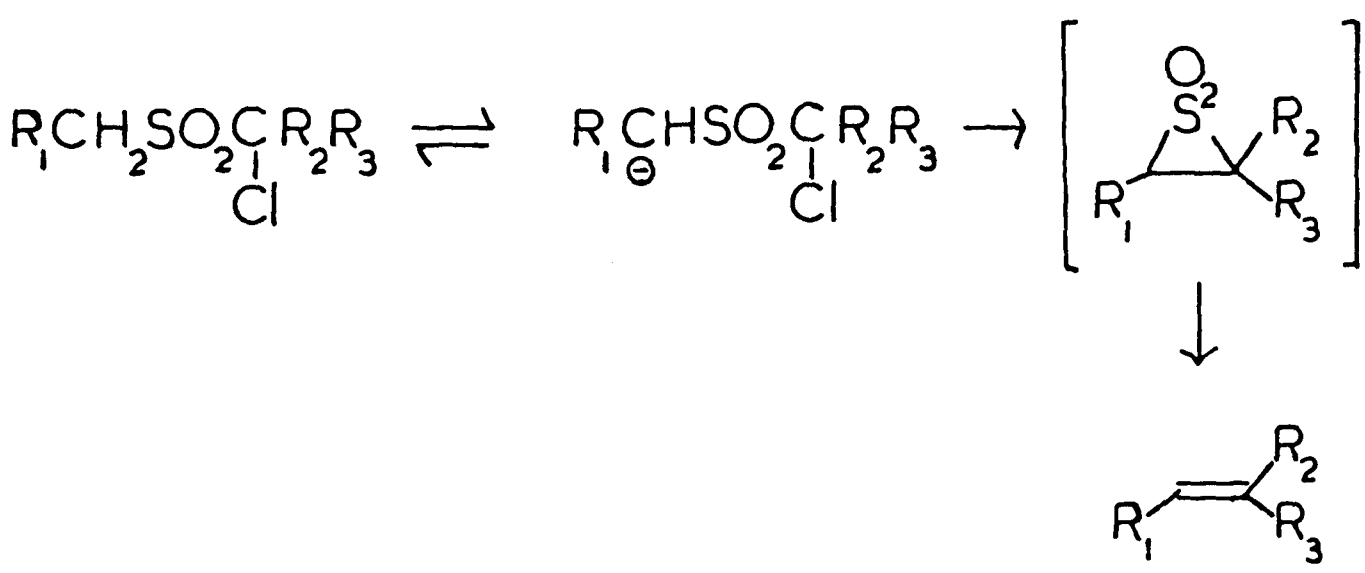
Elimination of carbon dioxide from β-lactones [74] has given rise to a good yielding cycloalkylidenecycloalkane synthesis (Scheme 22).[75]



Scheme 22.

More traditional coupling reactions, such as the Knoevenagel, Perkin, Darzens and Reformatsky reactions, give rise to activated alkenes.[76] Simple treatment of carbonyls with metal alkyls followed by elimination of water is also available as a method for alkene synthesis. However, this can give rise to mixtures of regio- and stereo-isomers. Use of aldol products also suffers from this drawback.

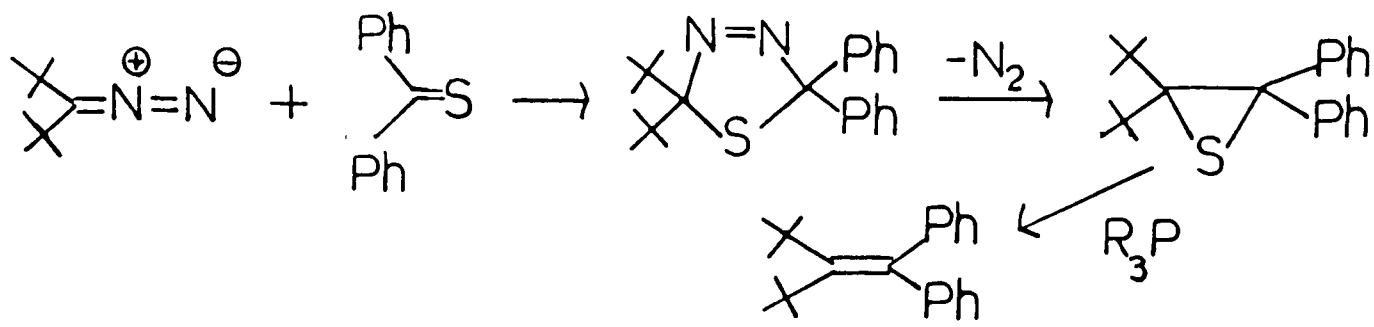
There are extrusion processes which give rise to alkenes, such as the Ramberg - Bäcklund reaction.[77] Here an ∝-chlorosulphone undergoes rearrangement and loss of sulphur dioxide on base treatment (Scheme 23). Z - alkene isomers predominate in this process.

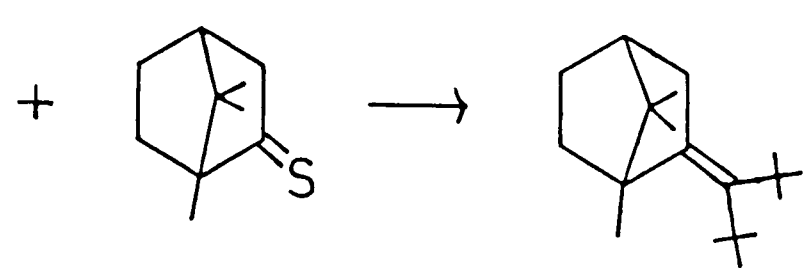


Scheme 23.

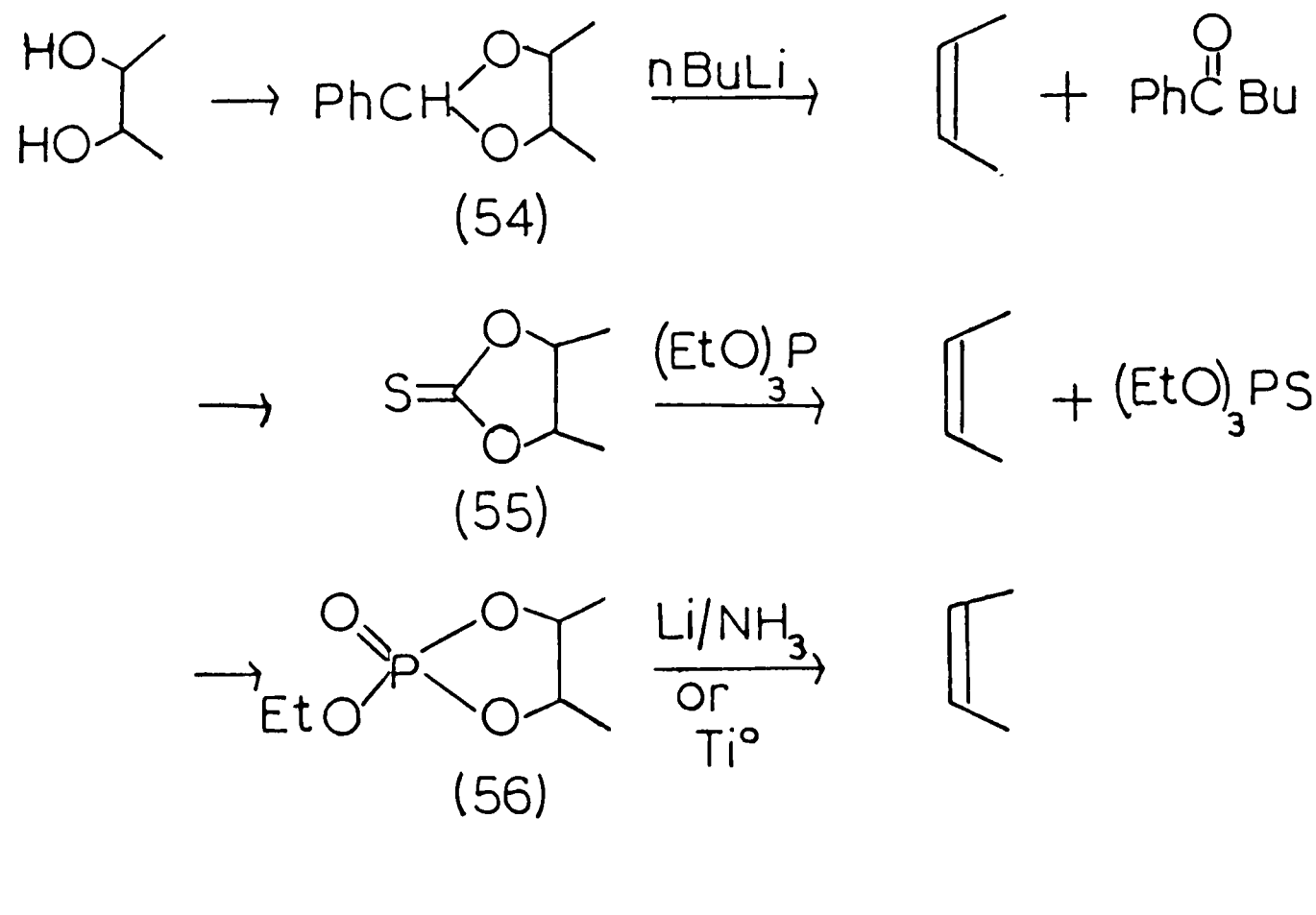
Barton has developed some twofold extrusion processes,[78] the most useful of which is the thiadiazoline method.[78a] This has been used to generate some very hindered alkenes (Scheme 24).

There are a number of methods for bisdehydroxylation of 1,2-diols, which can be generated by the pinacol-type processes discussed (vide supra). These usually involve formation of a cyclic derivative such as benzaldehyde acetal (54),[79] 1,3-dioxalane-2-thione (55),[80] 2-ethoxy-1,3-dioxalane ,[81] or phosphate (56).[82]

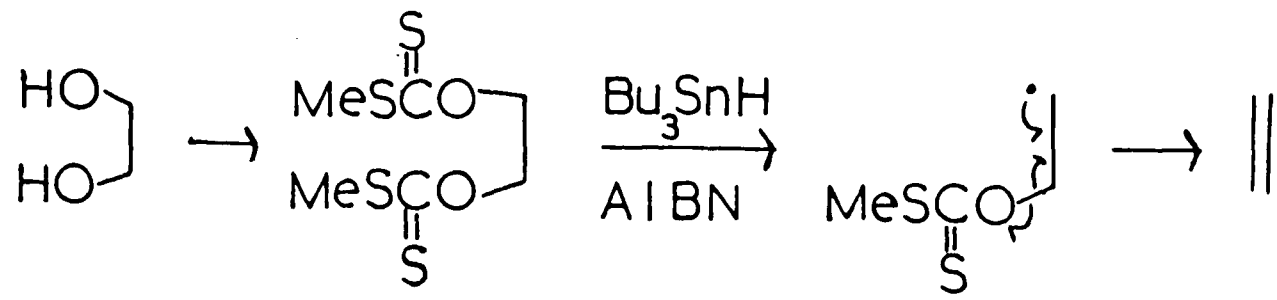

Ph
Ph
N=N
Ph
Ph
S
$-N_2$
Ph
Ph
S
Ph
Ph
R_3P


S

Scheme 24.


HO
HO
PhCH
O
O
nBuLi
PhC
O
Bu
(54)
S=
O
O
$(EtO)_3P$
$(EtO)_3PS$
(55)
O
P
EtO
O
O
Li/NH_3
or
Ti°
(56)

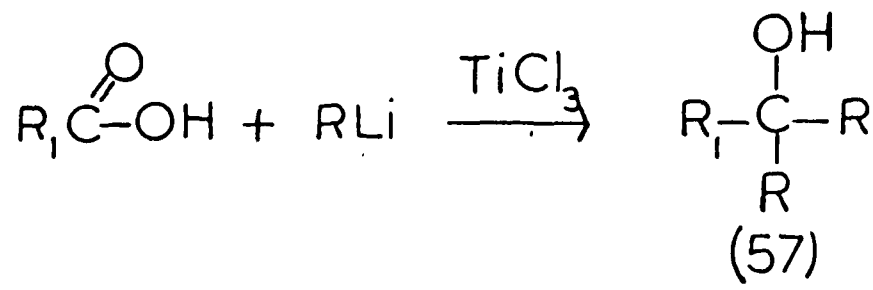
Barton has also developed a bisxanthate radical fragmentation (Scheme 25).[83] The final step of this process is similar to that envisaged for an azo-anion based route to alkenes (sect. E).[11]



Scheme 25.

C. Alcohols by Reductive Coupling Methods

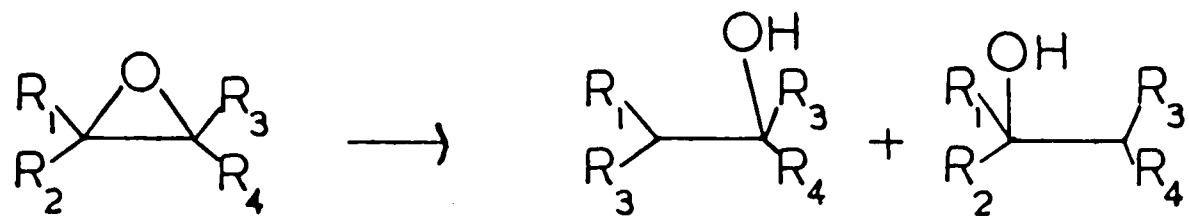
As well as alkenes azo-anions can be used to generate alcohols (32).[11] This reaction has fewer alternatives than the alkene forming synthesis. Clearly,the addition of an alkyl metal species to an aldehyde or ketone will yield an alcohol,which is the most direct route if the appropriate alkyl metal is available. Similarly,treatment of carboxylic acids with alkyl lithium and titanium trichloride gives alcohols (57).[84]



(57)

Epoxides (58) are reduced to alcohols (59) with aluminium or boron hydride reagents.[85] It is not always possible to efficiently obtain the required regioisomer,however. The epoxides (58) can be obtained from pinacols,which makes the overall process a reductive

coupling of two carbonyls.



(58) (59)

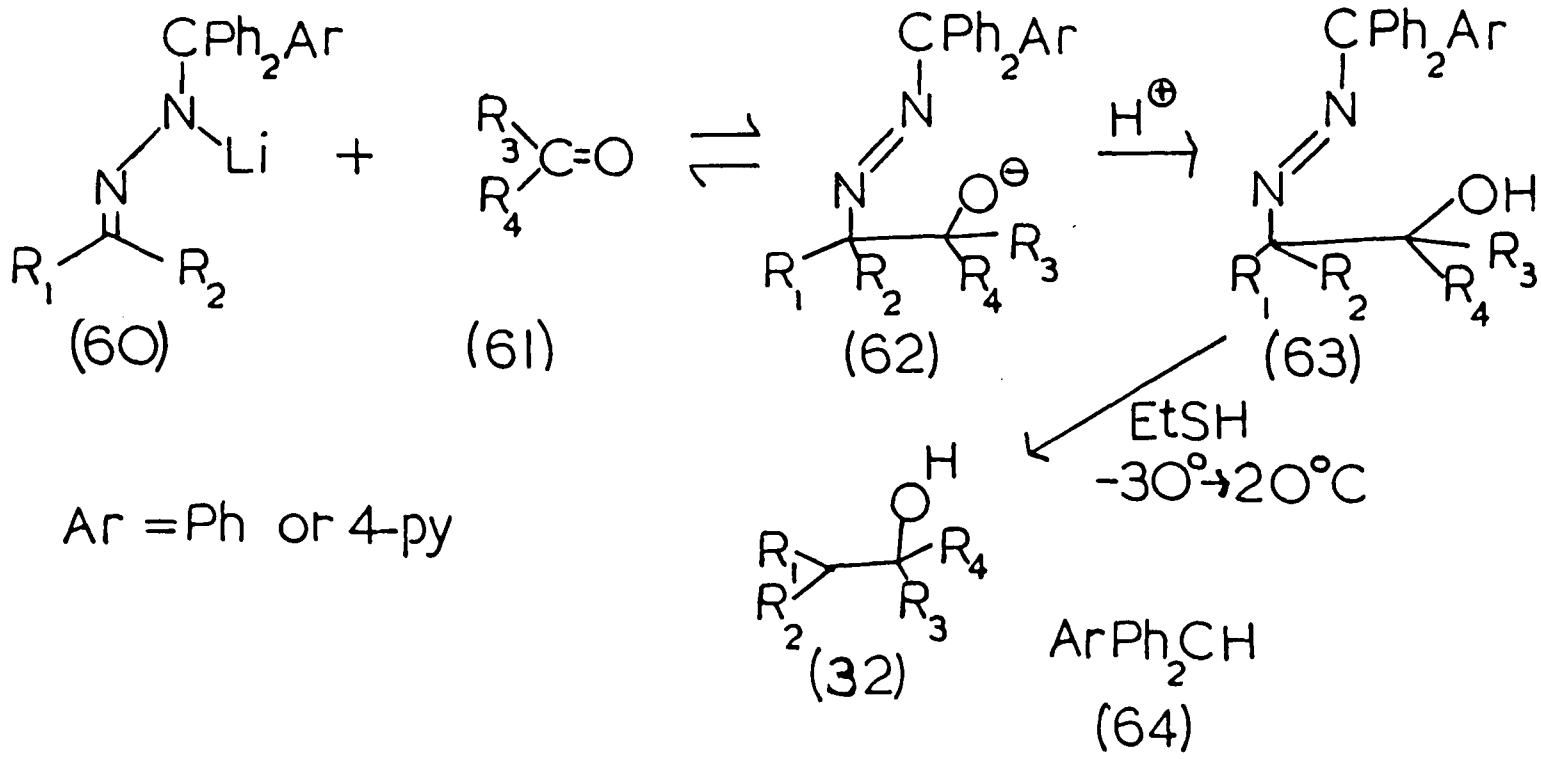
The results now presented will demonstrate an efficient reductive carbonyl coupling reaction allowing either alcohol (32) or alkene (33) production from a common first-formed azo-adduct (30). 1,4 - Addition to crotonates is also discussed as is a reductive carboxylation process.

D. Synthesis of Alcohols (32) from Azo-Anions

A synthesis of alcohols (32) was performed as depicted in scheme 26. Thus the lithium anions (60) - derived from trityl-(26) or DPP-(27) hydrazones - were treated with an aldehyde or a ketone (61) at -55°C to generate the azo-alkoxide (62) which upon protonation gave the azoalcohol (63). (63) decomposed homolytically at about -20°C with the evolution of nitrogen (equivalent to alcohol yield) and the radicals thus generated were trapped with ethanethiol to allow a convenient general synthesis of alcohols (32).

i) Reaction Conditions

a) Choice of base Methyl lithium was chosen as base rather than the cheaper n-butyl lithium as the products formed by the reaction of any excess base with excess carbonyl component (61) would be either more volatile (for small R_3 and R_4) or different in Rf values on silica gel (for larger R_3 and R_4) than the butyl equivalents.



Scheme 26.

b) Choice of solvent The reaction method involves cooling the preformed azo-anion solution to -55°C. In some cases this caused the precipitation of the lithium salt (60). Thus it was found beneficial to use a mixture of THF and TMEDA (4:1), rather than simply THF, to enhance the anion solubility at low temperature.

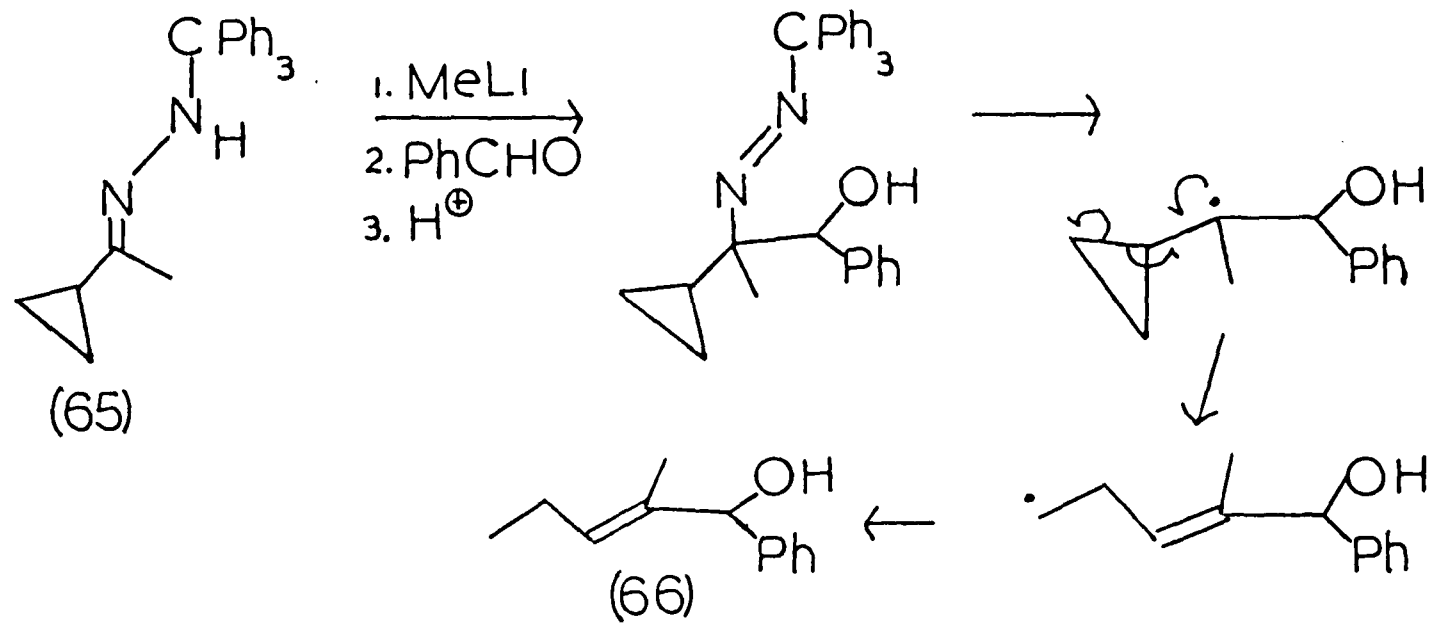
c) Work-up The reaction of azo-anion (60) with carbonyl (61) was fast and after 15 - 20 min the initial azo-adduct (62) was quenched with acetic acid. It was found advantageous to quench the alkoxide (62) prior to the azo decomposition step as yields of alcohols (32) were improved. Ethanethiol was added (in excess), immediately after the acetic acid quenching, and the cold bath was removed.

When the evolution of nitrogen had ceased diethyl ether was added and the resulting solution washed with aqueous sodium hydroxide (2M) to remove excess thiol, then with aqueous hydrochloric acid (2M) to remove TMEDA, then the organic solution was dried and evaporated.

d) Purification The concentrated residue was purified first by flash column chromatography on silica gel then by p.l.c. or by rotating disc chromatography. DPP hydrazone anions (60, Ar = 4-py) gave products that were easier to purify as the triarylmethane residue (64) was removed by the acid wash.

ii) The Radical Fragmentation

The fragmentation of azo-alcohols (63) has been shown to involve a radical intermediate by conducting the reaction with cyclopropylmethylketone tritylhydrazone (65). This gave the ring-opened homoallylic alcohol (66) expected from a radical process (Scheme 27).[86]



Scheme 27.

iii) Alcohols (32) Prepared

Table 2 shows the alcohols (32) prepared and the yields obtained. It was notable that the yields of alcohol (32) were lower when enolisable carbonyls (61) were employed. This was not surprising in view of the basicity of the lithiated hydrazones (60). Attempts to reduce the basicity by preparing the magnesium, zinc or titanium salts resulted in lower overall yields of the alcohols (32).

Hydrazone	R_3	R_4	Yield (32) (%)
a) 26a	Ph	H	74
b) 26a	Ph	CH_3	54
c) 26a	$-(CH_2)_5-$		39
d) 26c	Ph	H	40
e) 26c	Ph	CH_3	51
f) 26c	$-(CH_2)_5-$		42
g) 26f, 27f	Ph	H	65[a]
h) 27f	Ph	CH_3	46
i) 27g	Ph	H	63
j) 27g	i-C_3H_7	H	65
k) 26h, 27h	Ph	H	49[b]
l) 27h	Ar*	H	15[b]
m) 26i, 27i	Ph	H	64
n) 26i	Ph	CH_3	50
p) 27i	i-C_3H_7	H	40
q) 26i	$-(CH_2)_5-$		40
r) 26j, 27j	Ph	H	82

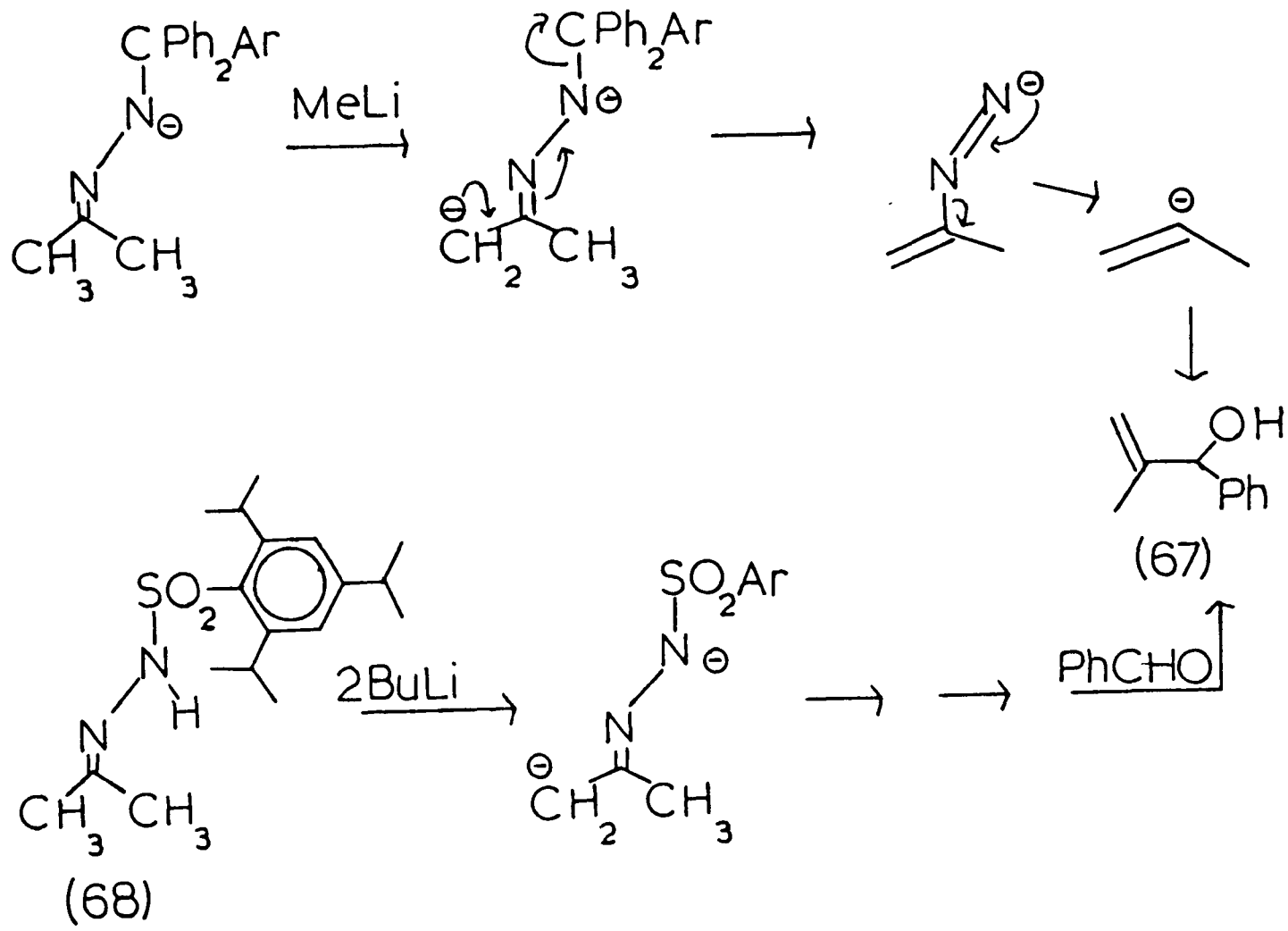
a - after bromine wash during work-up.
b - small-scale preparation.
* - Ar = 2,4,6-trimethylphenyl.

Table 2.

iv) By-Products

In the reaction of hydrazone (26f) or (27f) with benzaldehyde the proton n.m.r. of the product showed an unsaturated impurity which was not removed by chromatography. N.m.r. data suggested that this was 2-methyl-1-phenylprop-2-en-1-ol (67). The proportion was about 6% from (26f) and 15% from (27f) of the total product. It was considered that

a Shapiro - type pathway could account for this by-product (Scheme 28)[5] as the diphenyl-4-pyridylmethyl anion would be a better leaving group than the trityl anion, thus rationalising the difference in proportion of unsaturated and saturated alcohols from the two hydrazones (26f) and (27f).



Scheme 28.

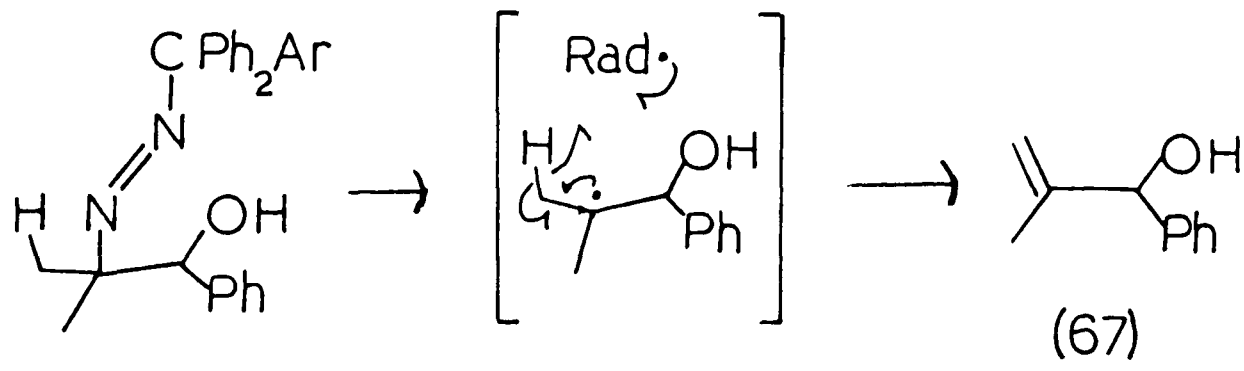
To verify the nature of the product an authentic Shapiro reaction was carried out, with acetone 2,4,6-triisopropylphenylsulphonyl hydrazone (68) and benzaldehyde to give alcohol (67). The by-product of the azo-anion reaction was shown to be identical to this material (by n.m.r., m/e, and i.r.) and co-ran on t.l.c. with alcohol (32g).

Alcohol (32g) was independently prepared by reaction of isopropropylmagnesium bromide with benzaldehyde to verify its structure.

In order to determine the pathway for formation of alcohol (67) the reaction between hydrazone (27f) and benzaldehyde was conducted under a variety of conditions. Lower temperature, less than one mole equivalent of base, and two mole equivalents of base all failed to change the proportion of (32g) : (67).

When the azo-alcohol intermediate was allowed to warm up in the absence of ethanethiol the ratio changed dramatically from 85 : 15 (32g) : (67) to $<5 : >95$. The overall yield was also lowered to about 50%. A slower warming up of the reaction with thiol present failed to reduce the proportion of alcohol (67).

As the ratio (32g) : (67) seemed to be unaffected by changes in the reactions, even with greater than thirty mole equivalents of thiol, it seemed reasonable to postulate either a cage process for hydrogen abstraction (Scheme 29) to generate (67) from (27f) and benzaldehyde, or that the abundance of radicals available in solution is enough to cause this reaction to be significant. The difference between the proportion of (67) generated from (26f) and that from (27f) could presumably result from differences in the temperature of the azo homolysis; the DPP azo compounds undergoing decomposition at a lower temperature leading to a higher proportion of 'cage' products (see chap IV).



Scheme 29.

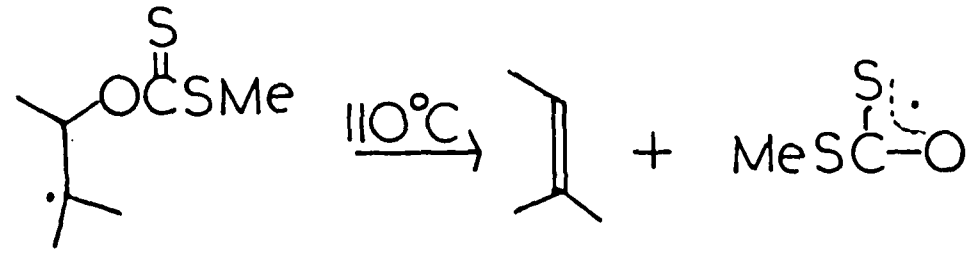
Although the allylic alcohols were noticed in several of the alcohol (32) reactions as by-products they were only significant for reactions of methyl ketone hydrazones. The product mixtures in these examples could be purified by shaking with bromine prior to the final p.l.c. purification, although this did result in some loss of yield due to reaction of bromine with the alcohols (32) containing phenyl groups.

v) Other Hydrazones

Attempts to use benzhydrylhydrazones (28) resulted in very poor yields of azo-alcohols due to extensive N-addition (chap IV, sect E). BDP hydrazones (29) also failed to generate products. The reason for this latter failure probably reflects the fact that the azo-alkoxides, generated by the initial addition, were in equilibrium with the azo-anion and carbonyl. The steric requirements for the t-butyldiphenylmethyl group cause the equilibrium to lie in favour of the starting materials. Attempts to trap the intermediate alkoxides as trimethylsilyl or methyl ethers failed to yield significant amounts of C-trapped azo products.

E. Synthesis of Alkenes (33) from Azo-Anions

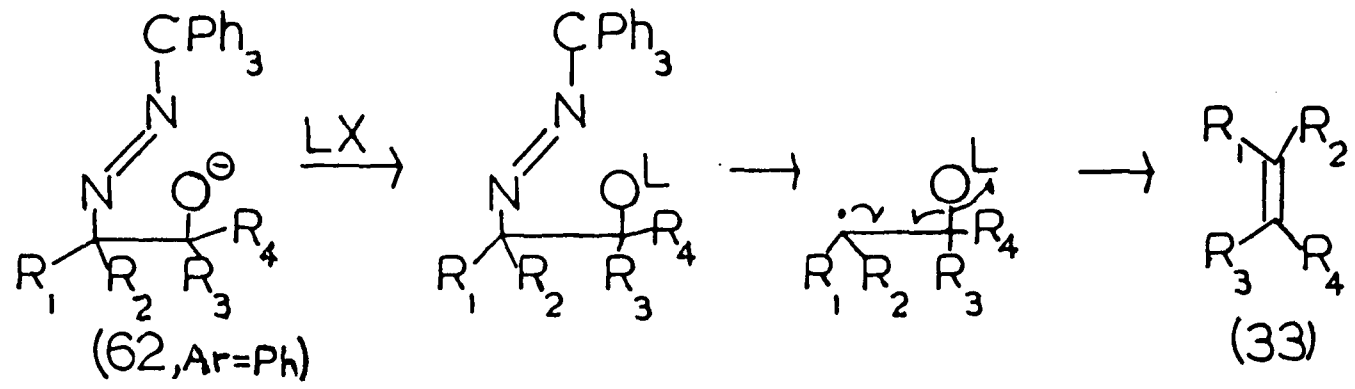
Barton has developed a procedure for alkene formation involving a radical intermediate (69) which eliminated a stabilised radical at refluxing toluene temperature (110°C).[87] As trityl azo compounds generate radicals by thermolysis, it was considered that a radical stabilising leaving group attached to the alkoxide (62, Ar = Ph) would give rise to an alkene on fragmentation (Scheme 30) in a similar manner. However, our attempts concentrated on the generation of alkenes at the lowest possible temperature, namely as close as possible to the azo fragmentation temperature (-20°C).



(69)

i) Reaction Conditions

a) Procedure The procedure adopted involved following the alcohol (32) preparation route to generate alkoxides (62). At this stage the reaction was cooled to -78°C and the chosen reagent (LX) to promote alkene formation was added in slight excess. The reaction was then allowed to warm slowly (2 - 3h) to ambient temperature. After work up, alkenes (33) were readily isolated by flash column chromatography on silica gel. DPP hydrazones (27) offered no advantages over trityl hydrazones (26) in terms of ease of product purification as the alkenes (33) were much less polar than all other products and easily separated from them on silica gel.



Scheme 30.

b) Reagents LX Table 3 shows the variety of reagents tried in this reaction. The yields given are for the reaction of cyclohexanone tritylhydrazone (26i) with benzaldehyde, which was chosen as a test system.

PCl_3 was found to be the best reagent for the process described. The series of reagents obtained by replacing the chlorine atoms in PCl_3 by phenyl groups gave an interesting series of results. These may have a bearing on the mechanism of the reaction (sect. E ii).

c) Alkenes (33) Prepared Using PCl_3 a series of alkenes (33) was prepared (Table 4). The overall yields generally varied from about two-thirds to three-quarters of the yield of the corresponding reaction

to give alcohols (32) (Table 2). In unsymmetrical cases mixtures of E and Z isomers were produced with slightly more production of the E isomers. The ratio of isomers (33) was obtained by an n.O.e. experiment.[86]

Reagent	Yield (33) (%)
PCl_3	48
$PO.Cl_3$	39
$PhPCl_2$	25
PBr_3	12
$(EtO)_2PO.Cl$	6
Ph_2PCl	0
CS_2/MeI	26
$Cl.CS_2Et$	26
$Cl.CS_2Et$/EtSH	25
$Cl.CS_2Et$, then reflux in THF	20
$Im_2C=S$ [a]	0
$SnCl_4$	0
$SOCl_2$	10

a - Im = imidazole

Table 3.

ii) Mechanism

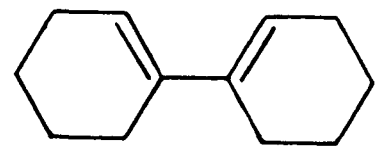
The attempt to produce cyclohexylidene cyclohexane (33f) resulted in concomitant formation of the 1,3-diene (70). This unexpected result led to speculation concerning the mechanism of the elimination (sect. E ii b).

a) Alcohol Diastereoisomers It had been observed that the alcohol (32i) was produced as a mixture of diastereoisomers (about 6:5). Inspection of the literature revealed that n.m.r. data was available for the diastereoisomers of alcohols (32k) and (32l).[88] This revealed

Hydrazone	R_3	R_4	Yield (33) (%)
a) 26a	Ph	H	20
b) 26f	Ph	H	52
c) 27g	Ph	H	60 (E:Z,65:35)
d) 26i	Ph	H	48
e) 26i	Ph	CH_3	34
f) 26i	$-(CH_2)_5-$		23 + [(70), 18%]
g) 26i	CH_3	CH_3	36
h) 26j	Ph	H	37

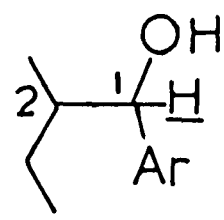
$R_3.CO.R_4$

Table 4.



(70)

that $\delta_{1S2R} > \delta_{1R2R}$ and $J_{IR2R} > J_{1S2R}$ (δ = chemical shift, J = coupling constant) for the benzylic protons of a series of alcohols (71).



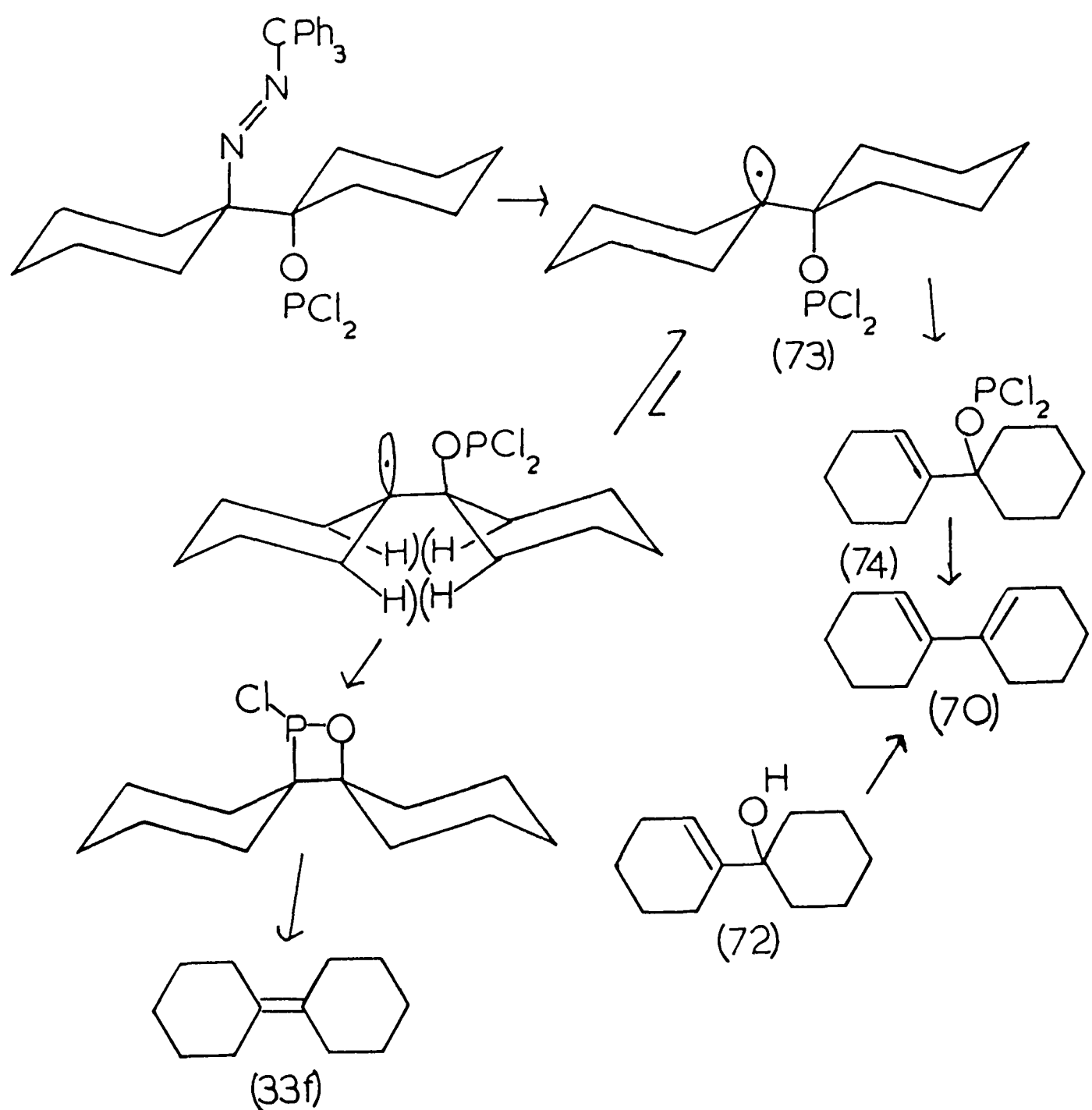
(71)

Ar Ph(32k), o tolyl, mesityl(32l)

The alcohols (32k) and (32l) were thus prepared by the azo-anion route. Although there was clear preference for one diastereoisomer in each case, the values for δ and J obtained did not correspond to those in the literature.[88] It was therefore not possible to compare the

diastereoisomer ratio of alcohols (32) with the E:Z ratio of the alkenes (33) to see if there was evidence of stereospecific elimination during the conversion of alkoxides (62) to alkenes (33).

b) Origin of Diene (70) Indirect evidence for the mechanism has resulted from investigation of the origin of diene (70). The allylic alcohol (72) was produced by a thiol-free alcohol procedure (sect. D iv) and this was treated with n-butyl lithium and phosphorus trichloride,in sequence,in a solution of THF : TMEDA (4:1) under the same conditions used for the alkene (33) synthesis. The result was conversion of alcohol (72) to diene (70).



Scheme 31.

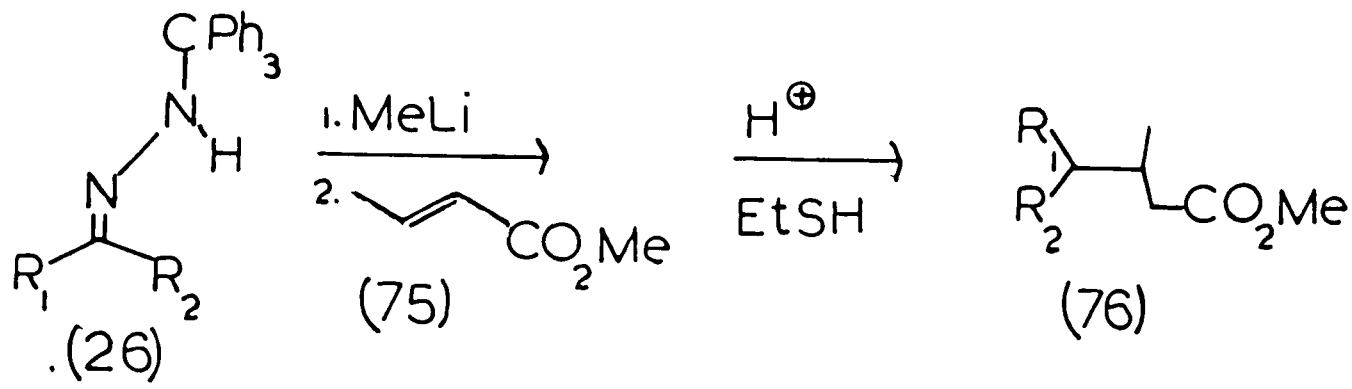
It is proposed that a possible pathway for alkene (33) production involves a four-membered ring intermediate similar to the intermediate of the Wittig reaction. This would explain the reactivity of phenylphosphorusdichloride in the alkene (33) synthesis and the failure of diphenylphosphoruschloride to give alkenes (33), as the latter reagent has only one leaving group and cannot then form the intermediate. In the case of the cyclohexylidene cyclohexane synthesis the syn-elimination pathway involved in this proposed mechanism would be hindered by the steric requirements of the two rings (Scheme 31). The trans-intermediate (73), presumably the thermodynamically more stable, and also set up for anti-elimination, would fail to eliminate and undergo instead a hydrogen abstraction to give the allyl species (74).

In summary, a syn-elimination pathway, possibly via a four membered ring intermediate could account for the production of alkenes (33).

F. 1,4 - Addition Reactions

If $\alpha\beta$-unsaturated carbonyl compounds were to be used as electrophiles there is the possibility of a Michael addition pathway occurring.[89] This was investigated using anions of tritylhydrazones (26). DME was chosen as the solvent for these reactions to aid complexation of the lithium counter ions.

Reaction of hydrazone (26i) with methyl acrylate gave only a 6% yield of the ester produced by 1,4-addition, after thermolysis in the presence of thiol. $\beta\beta$-dimethylacrylate gave no product, and acrylonitrile simply polymerised. Methyl crotonate (75) was the only $\alpha\beta$-unsaturated system found to give yields worth investigating. The esters (76) prepared are shown in table 5.



Hydrazone (26)	Yield (76) (%)
b	23
c	20
i	35

Table 5.

i)_ Reaction_Conditions

The optimum procedure that was developed for these reactions was to form the azo-anion with methyl lithium at -40°C in DME . The solution was then cooled to -55°C and methyl crotonate (1.5 mole equivalents) was added via a syringe pump over 1h. The reaction was quenched,after a further 1h,with trifluoroacetic acid and ethanethiol was added. After warming to ambient temperature the reaction was worked up and the products purified by Kugelrohr distillation followed by p.l.c..The use of DPP hydrazones (27) rather than tritylhydrazones (26) resulted in very poor yields.

ii) _Problems Arising from_Azo-Anion_Basicity

The major problem with the 1,4-addition reactions appeared to be the basicity of the lithium anion of the hydrazone used for the reaction. This resulted in competing deprotonation of the crotonate (75) and hydrazones (26) could be recovered from the reaction mixtures.

In fact, when hydrazone (26j) was used, the hydrazone (26j) was observed to precipitate out of solution as the methyl crotonate was added.

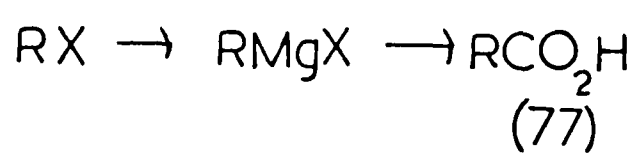
An attempt was made to use the cuprate derivative of the hydrazones (26), by treatment of the lithium anions with a copper (I) species, but this gave no improvement in yield upon attempted reaction with Michael electrophiles.

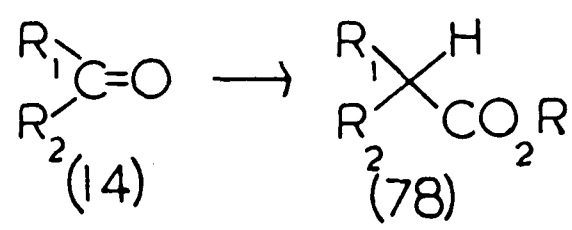
iii) Other Hydrazones

BDP hydrazones (29) failed to undergo reaction with Michael type electrophiles, possibly because of the increased steric requirements of the t-butyldiphenylmethyl group compared to the trityl group. t-Butylhydrazones have been shown to undergo anionic 1,4-addition in moderate yields with methyl crotonate.[90]

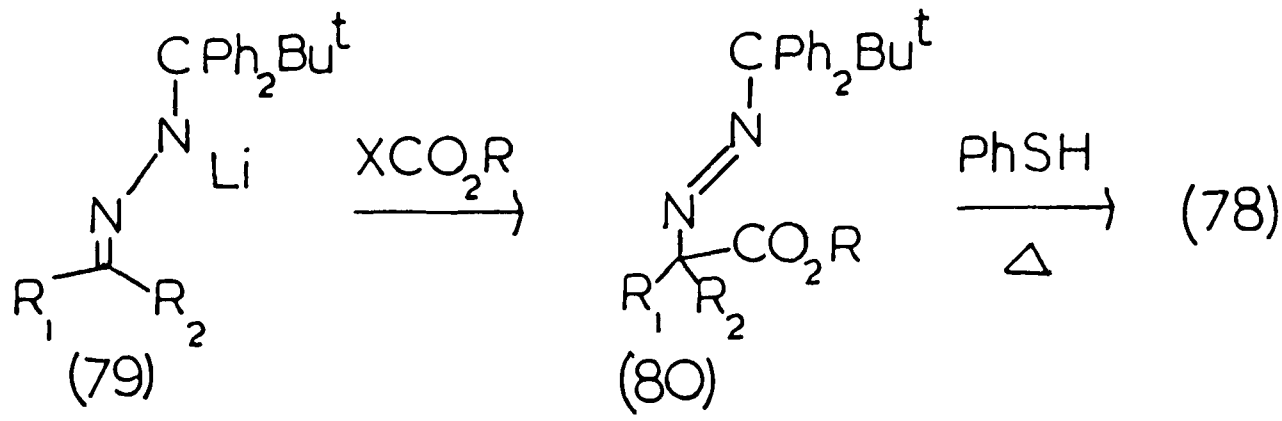
G. Reductive Carboxylation with Azo-Anions

Alkyl halides can be converted to Grignard reagents which react with carbon dioxide to give the corresponding homologated acids (77). In view of the reductive nature of the azo-anion methodology carboxylation of azo-anions would convert carbonyl (14) to an acid derivative (78).





This conversion was accomplished in modest yield using trityl hydrazones (26) and methyl chloroformate by Perry.[31] Use of BDP hydrazones (29) also gave modest yields of some carboxylated products.

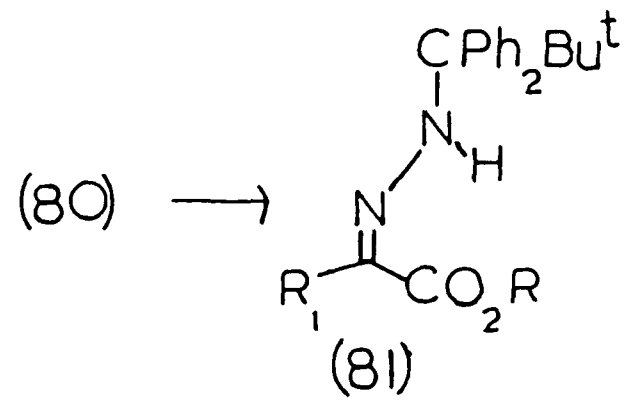


Hydrazone	X	R	Yield (78) (%)
a) 29i	Cl	CH_3	50
b) 29i	CN	C_2H_5	50
c) 29j	Cl	CH_3	45

Table 6.

Reaction of azo-anion (79) with methyl chloroformate or ethyl cyanoformate at -78°C in THF gave rise to azo compound (80). This was thermally decomposed, after isolation, by refluxing benzene in the presence of thiophenol (chap. IV) to generate ester (78).

Aldehyde hydrazones (29, R_2 = H) cannot be used in this reaction as the azo-adduct (80) has a very acidic proton and under the basic reaction conditions isomerisation to a hydrazone of an ∝-ketoester (81) occurs.



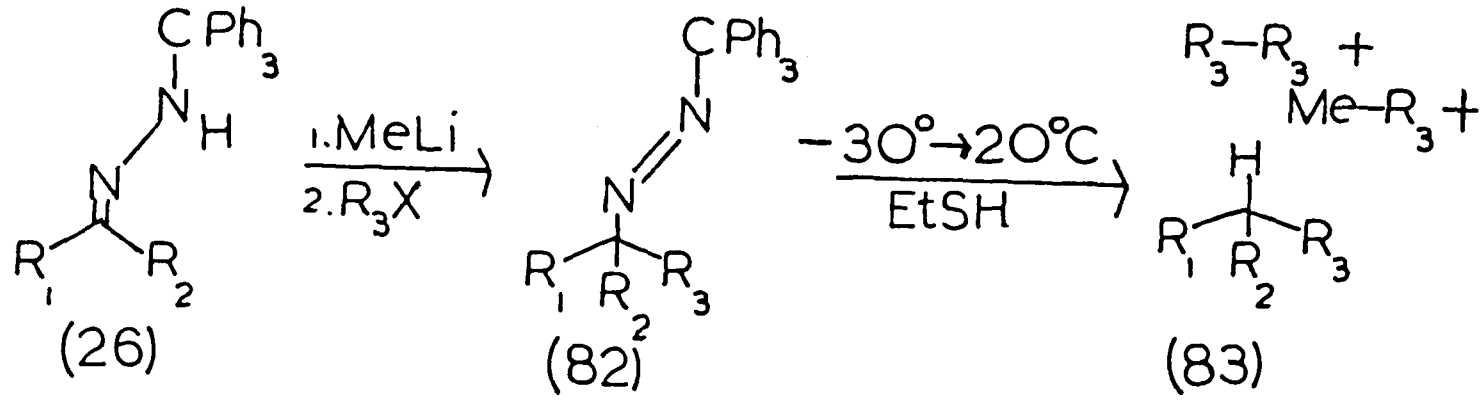
H. Summary

Azo-anions reacted with various carbonyl electrophiles to give azo-adducts which have been diverted to give synthetically useful

products. A synthesis of alcohols (32) and alkenes (33) has been achieved in addition to a modest reductive carboxylation of ketones. Michael additions of the anions of hydrazones (26), (27), and (29) do not appear to be synthetically useful.[90]

CHAPTER IV - PREPARATION AND REACTIONS OF AZO-ALKANES

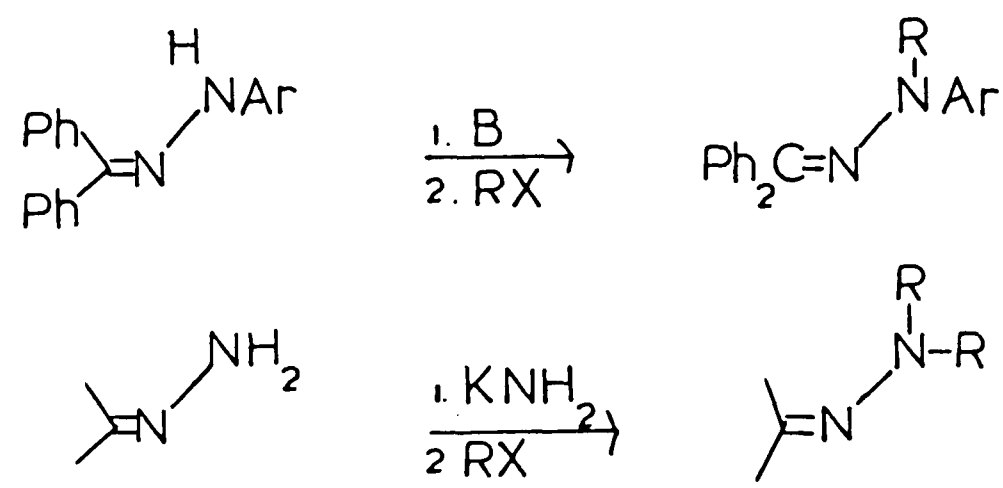
Alkyl halides are among the most widely used electrophiles in organic synthesis and therefore an obvious choice for reaction with azo-anions. Related efforts have given rise to a synthesis of alkanes from tritylhydrazones (26).[31] The procedure for this synthesis,however, was somewhat inconvenient owing to the need to conduct the alkylation reaction at -30°C due to homolysis of the azo-adducts (82) above this temperature. There were co-produced by-products,from Wurtz-type coupling of the alkyl halides,and olefinic products (chap. III, sect. D.iv) which made the purification of the alkanes (83) difficult and tedious (Scheme 32). The use of BDP hydrazones (29) would be expected to give rise to more stable azo-alkanes (see sect. B) and thus allow a more convenient higher temperature alkylation procedure.



As previously reported (chap. I) the reactions of hydrazones or their anions with electrophiles usually resulted in reaction at nitrogen. In the case of alkyl halides this resulted in the formation of new hydrazones. Indeed,this has been demonstrated as a synthetic method (Scheme 33).[91]

Alkylation at carbon has resulted in azo-alkanes (84, R = trityl, t-butyl). The trityl azo intermediates (84, R = trityl) have been used in an alkane synthesis (83).[11,31] The azo-alkanes

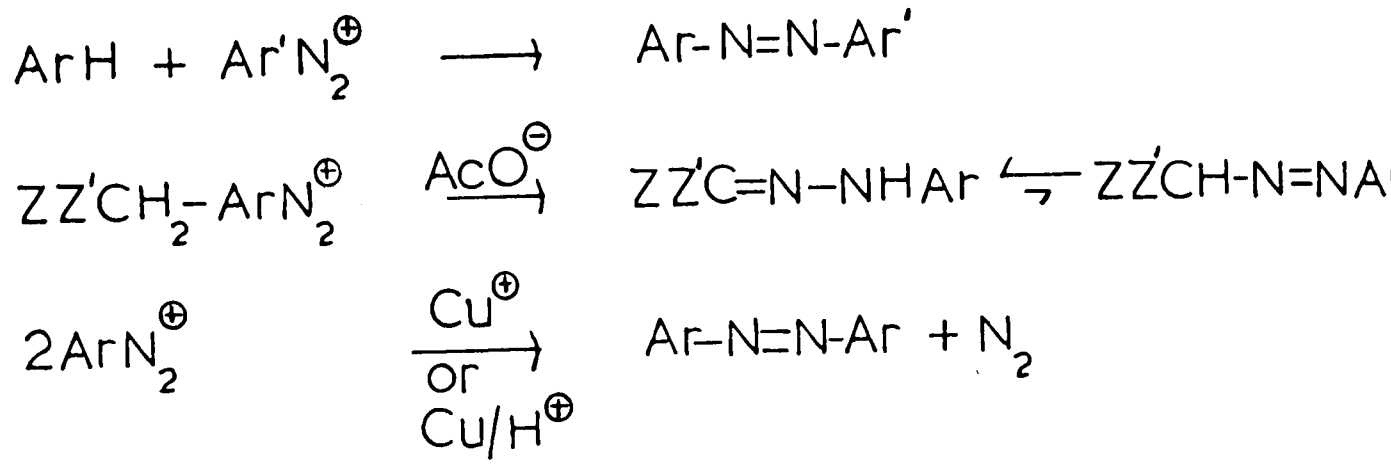
(84, R = trityl) were too thermally unstable to isolate. The results presented in this chapter will show that for azo-anions (11, R = t-butyl-diphenylmethyl) the azo-alkanes (84) generated by alkylation are stable enough to be isolated and purified. They are shown to be key intermediates for the synthesis of a number of types of compounds via radical processes.



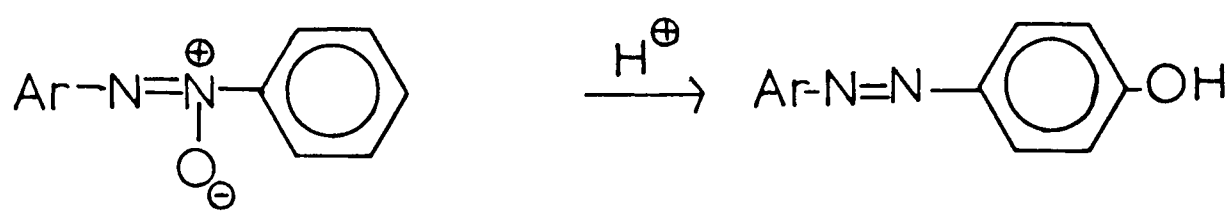
Scheme 33.

A. Azo-Compounds

Azo-compounds have been generated in a number of ways. One of the most widely reported is the diazonium coupling reaction,[92] where activated aromatic rings couple to diazonium salts. Diazonium salts can also be coupled to activated methylene compounds but the resultant products exist as their hydrazo tautomers. Self-coupling, catalysed by copper (I), is also possible if the aromatic nucleus of the diazonium salt has electron-withdrawing groups attached.[93]

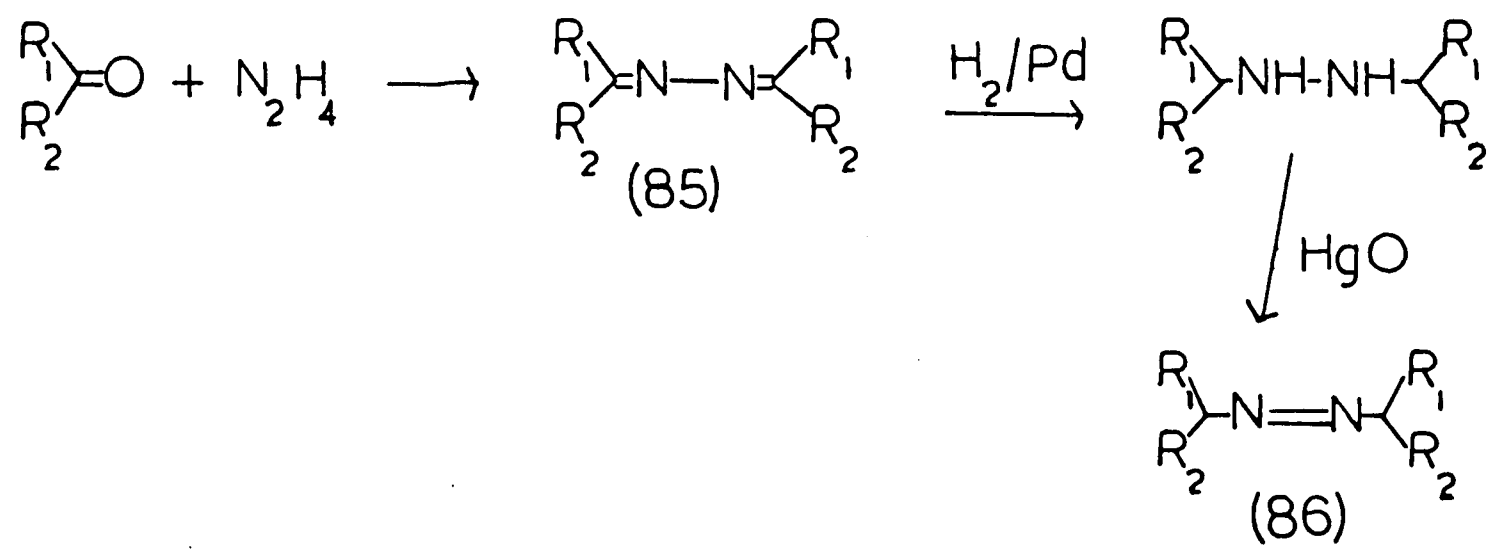


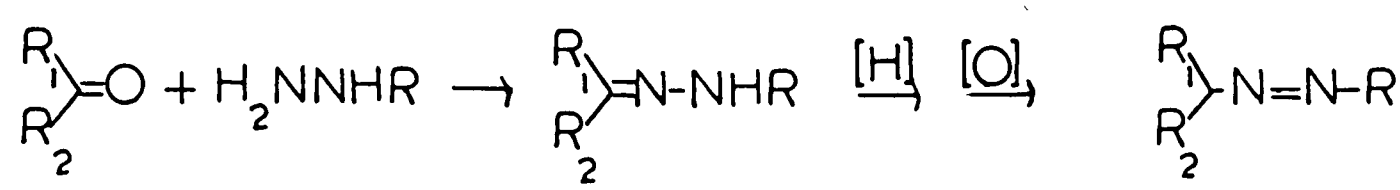
The Wallach rearrangement [94] also generates azo-species :



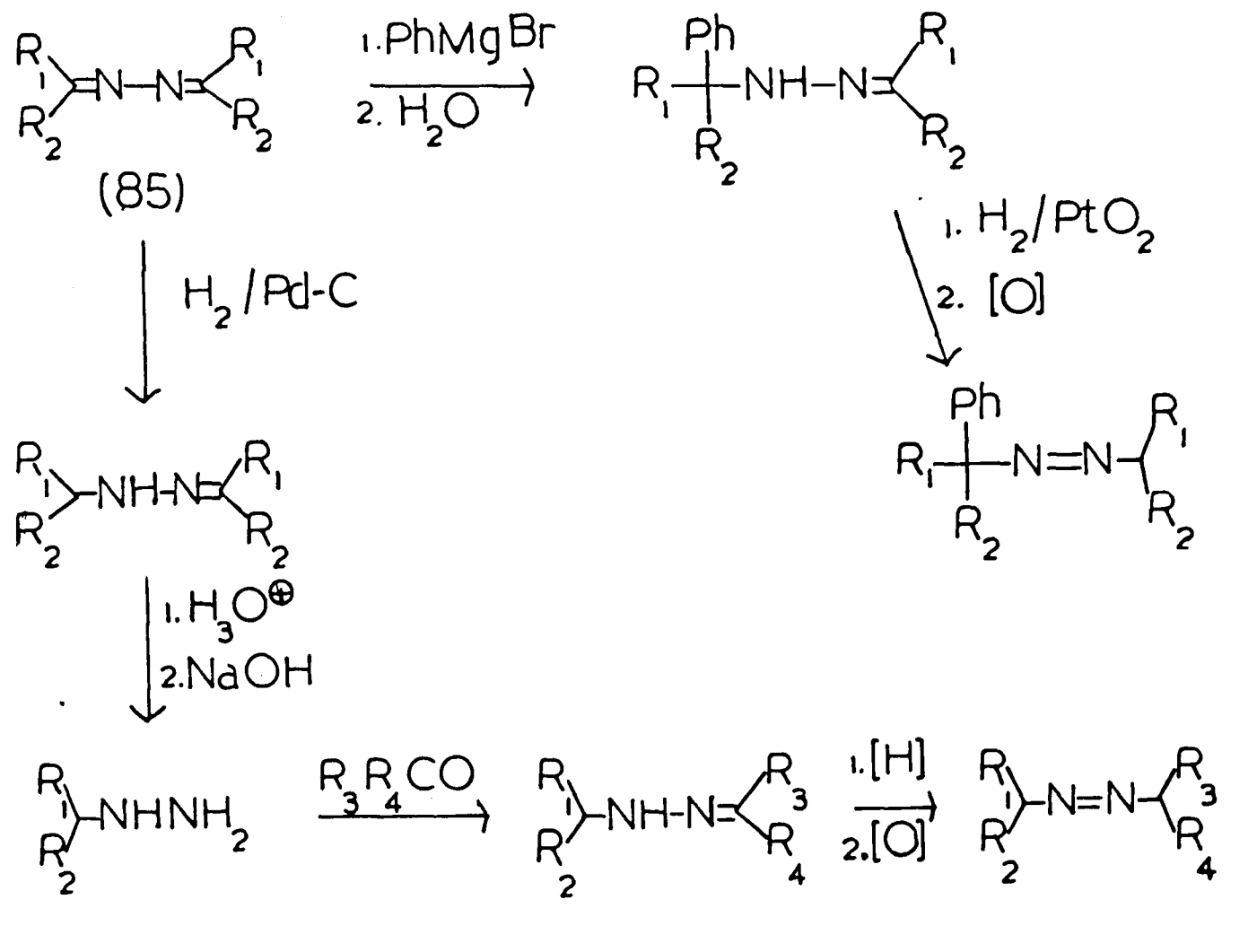
and coupling of amino and nitroso benzenes gives azo-compounds.[95]

The oxidation of hydrazines with a variety of reagents[96] has become the basis for a range of synthetic methods used for the preparation of symmetrical (86)[97] and unsymmetrical[98] azo-alkanes.

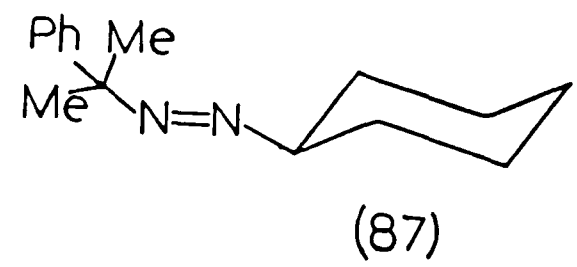




Overberger developed a very useful method (Scheme 34)[99] which has been used to generate some interesting azo-alkanes (e.g.87).[100]

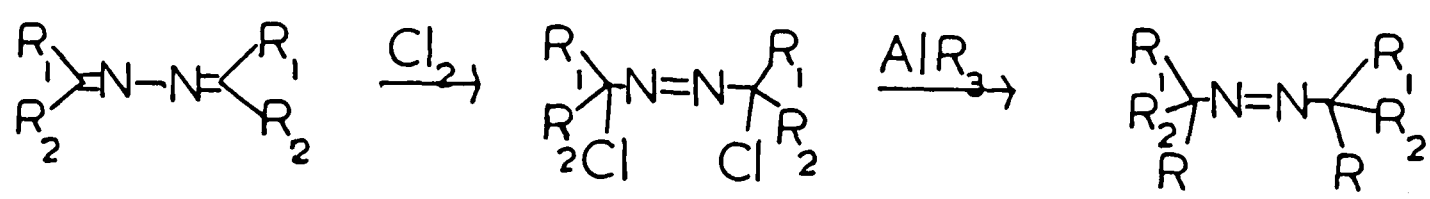


Scheme 34.



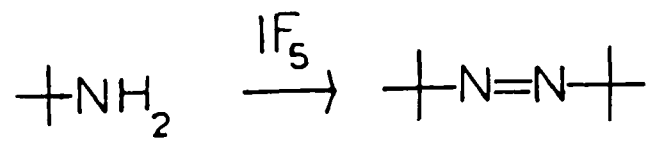
(87)

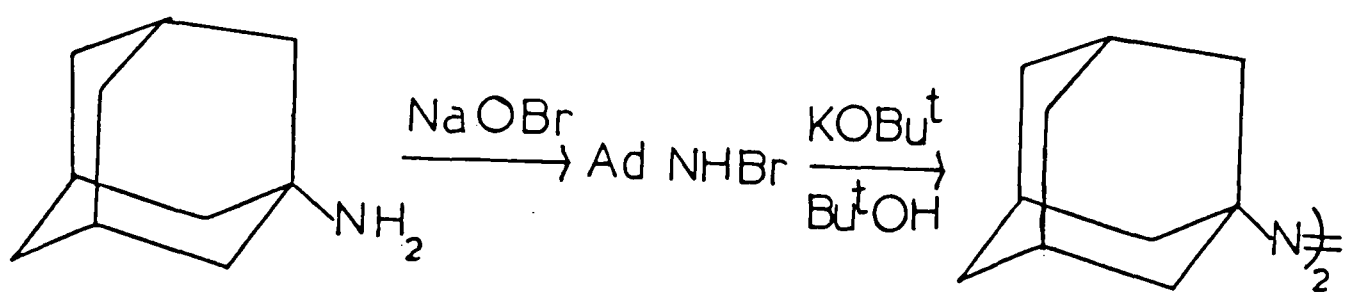
1.4 - Dichloroazo-alkanes (88) which are readily available from azines (85) are substituted straightforwardly by alanes.[101]



(85) (88)

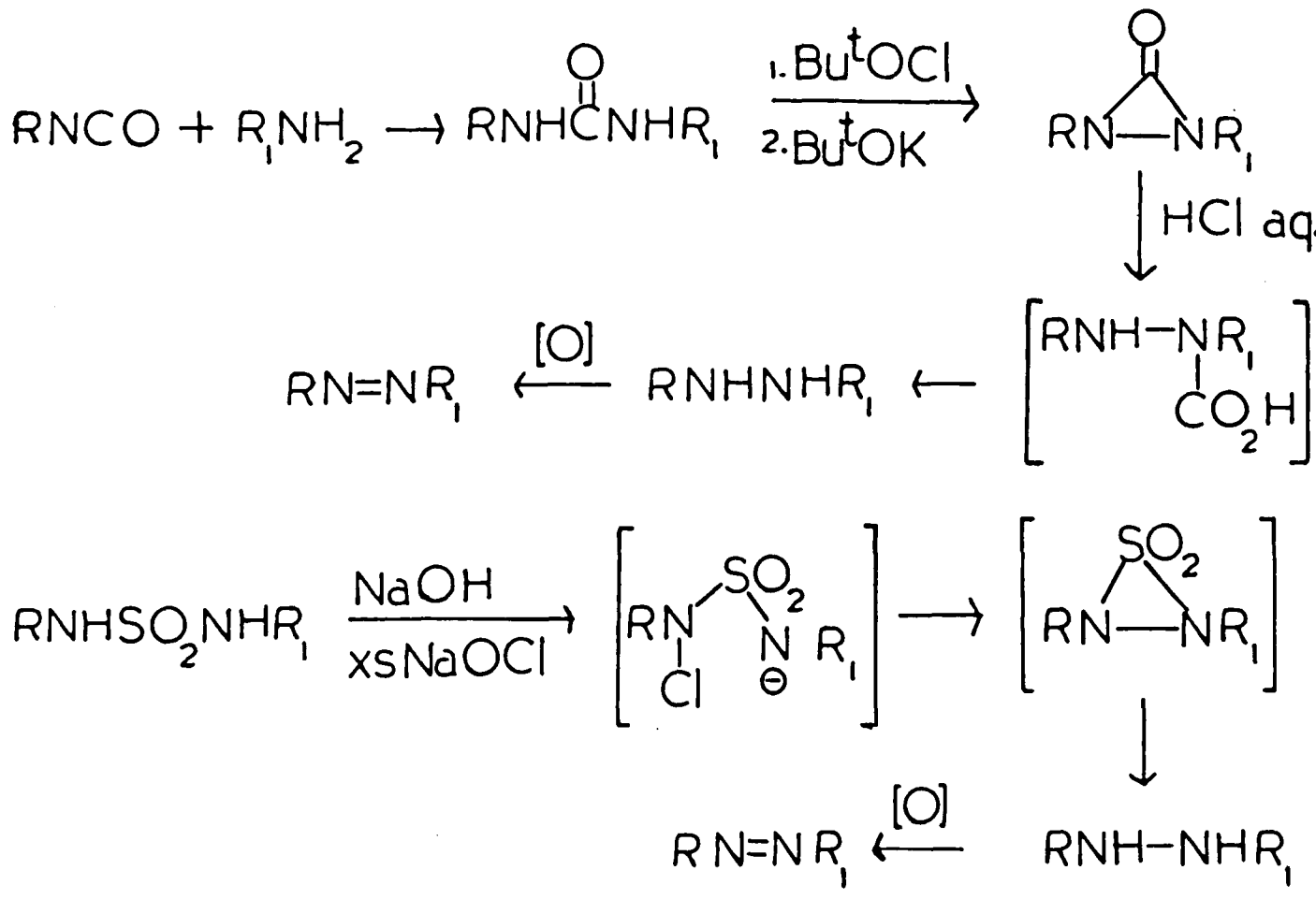
For symmetrical azo-alkanes the oxidative coupling of amines is an available route (Scheme 35)[102] but this is limited in its application.





Scheme 35.

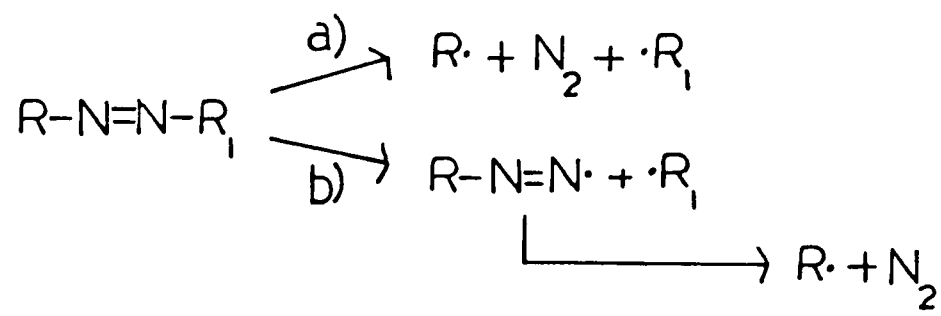
More useful for general preparations of unsymmetrical azo-alkanes are methods involving three-membered ring intermediates, generated from ureas[103] or sulphonamides[104] (Scheme 36).



Scheme 36.

B. Thermolysis of Azo-Alkanes

Once prepared, azo-alkanes have been used as a source of alkyl radicals in thermal or photochemical studies. They decompose to give two alkyl radicals and a molecule of nitrogen, the mechanism of this reaction having been the subject of much debate.[29] Two pathways (a) and (b) (Scheme 37) have been proposed which represent either concerted two bond scission or stepwise one bond scission followed by diazenyl radical decomposition respectively.

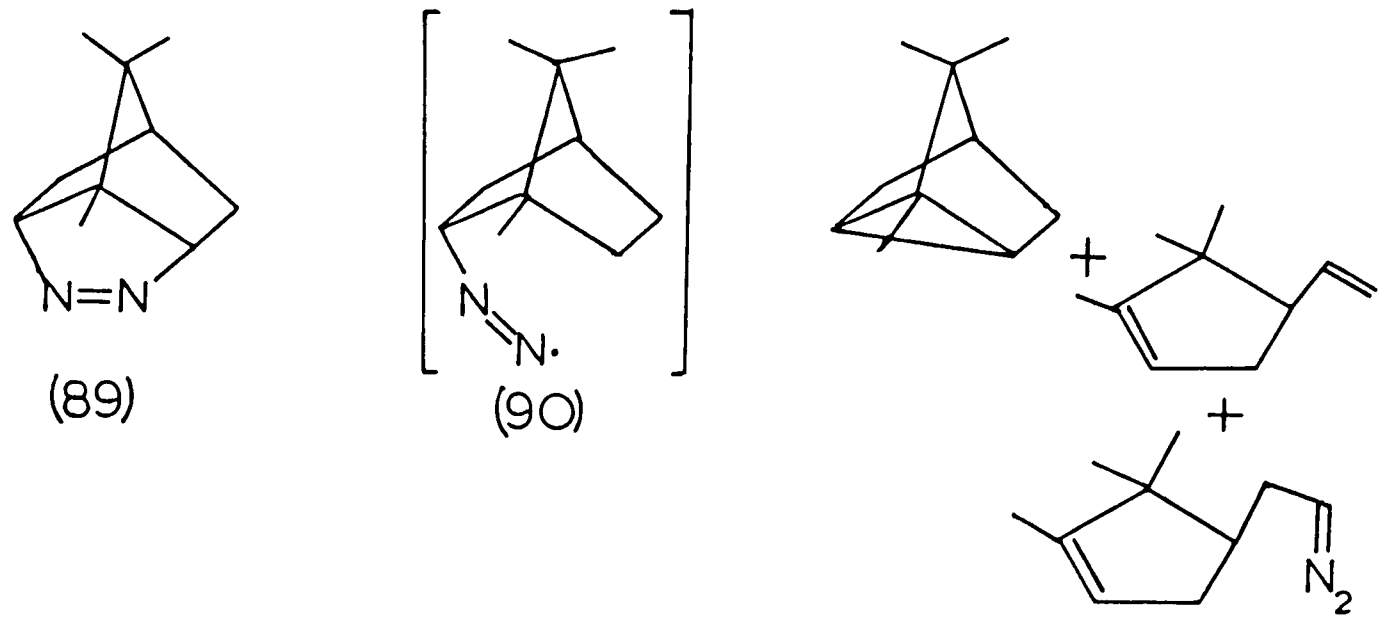


Scheme 37.

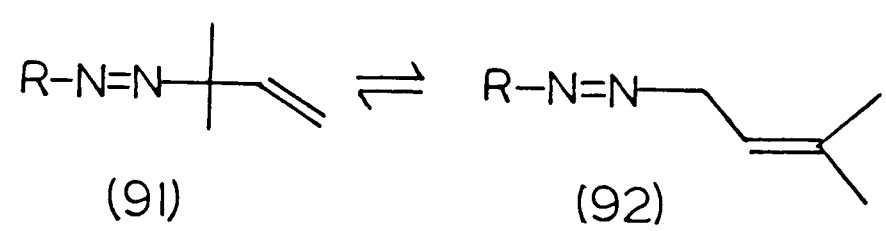
Many experiments have been carried out and kinetic,[97a,105] product isolation,[106] solvent viscosity effect,[107] direct spectroscopic,[108] and calculational[109] data have all been gathered in attempts to ellucidate the mechanism. The first proposal, for concerted two bond rupture, was based on calculation of activation energies for homolysis based on the observed reaction rates for thermal decomposition of azomethane, isopropylazomethane and azoisopropane.[110] More recently, Engel ended his review of this reaction [29] by stating that there is a spectrum of mechanism from (a) to (b) depending on the structure of the azo-alkane.

The most recent views[106,107b,108,109,111] based on modern techniques and mathematical models for calculations are in agreement

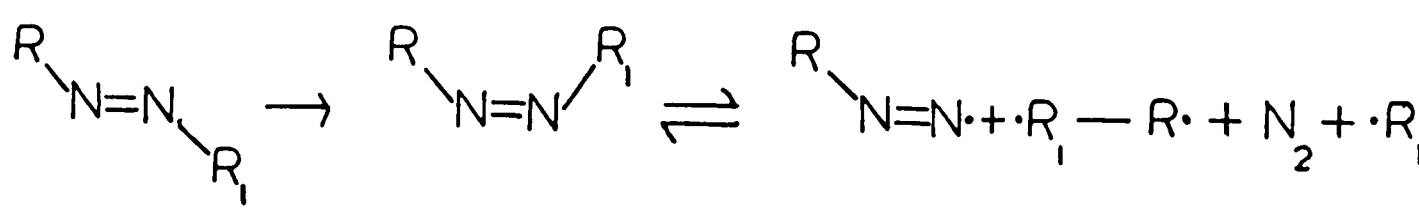
with path (b), with a reversible first step, as being the best way to explain all the observations.



Scheme 38.



Symmetrical cyclic azo-compounds (e.g. 89) gave thermolysis products which can only be straightforwardly explained by a diazenyl radical intermediate (e.g. 90)[106a] (Scheme 38), and 3,3-dimethyl-3-allyl azo-alkanes (91) gave 'turnaround' products (92) when the reaction was analysed before completion,[107b] even in the symmetrical case (91, R = 3,3-dimethyl-3-allyl). The probable mechanism now proposed[107b] involves a reversible first step (Scheme 39) and it has also been proposed that the cis-azo-alkane is formed initially.



Scheme 39.

Whatever the mechanism, the factors affecting the thermal stability of azo-alkanes are well documented. Clearly, the ability of the alkyl group to exist as a stable radical affects the rate of decomposition markedly.[29,107a] Resonance stabilising groups α to the azo group accelerate the decomposition as do sulphur substituents in this position.

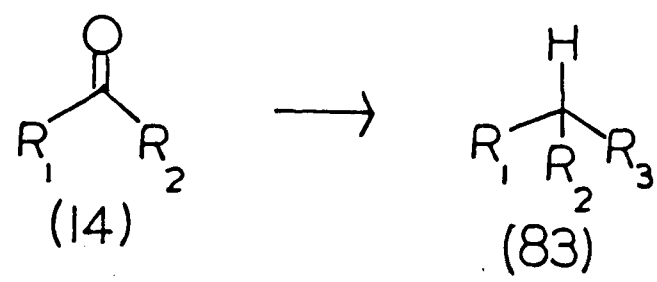
Steric factors also play a significant role. Ruchardt pointed out that as the transition state is late in the reaction pathway, so the planarity of the radical centre is nearly reached before bond cleavage.[112] Therefore there is a loss of B-strain as the reaction proceeds towards the transition state and more bulky alkyl groups lower the activation energy of the process. The rate of azo decomposition has been compared to the rate of solvolysis of the corresponding alkyl p-nitrobenzoate esters and alkyl chlorides;[113] cycloalkyl compounds have also been compared.[29] These experiments revealed a good correlation between the rates of the different processes suggesting a planar transition state for the decomposition. β-Branching was also found to increase the reaction rate for thermolysis despite the trans-configuration normally adopted in the ground state.[105,114]

C. Alkane Preparation

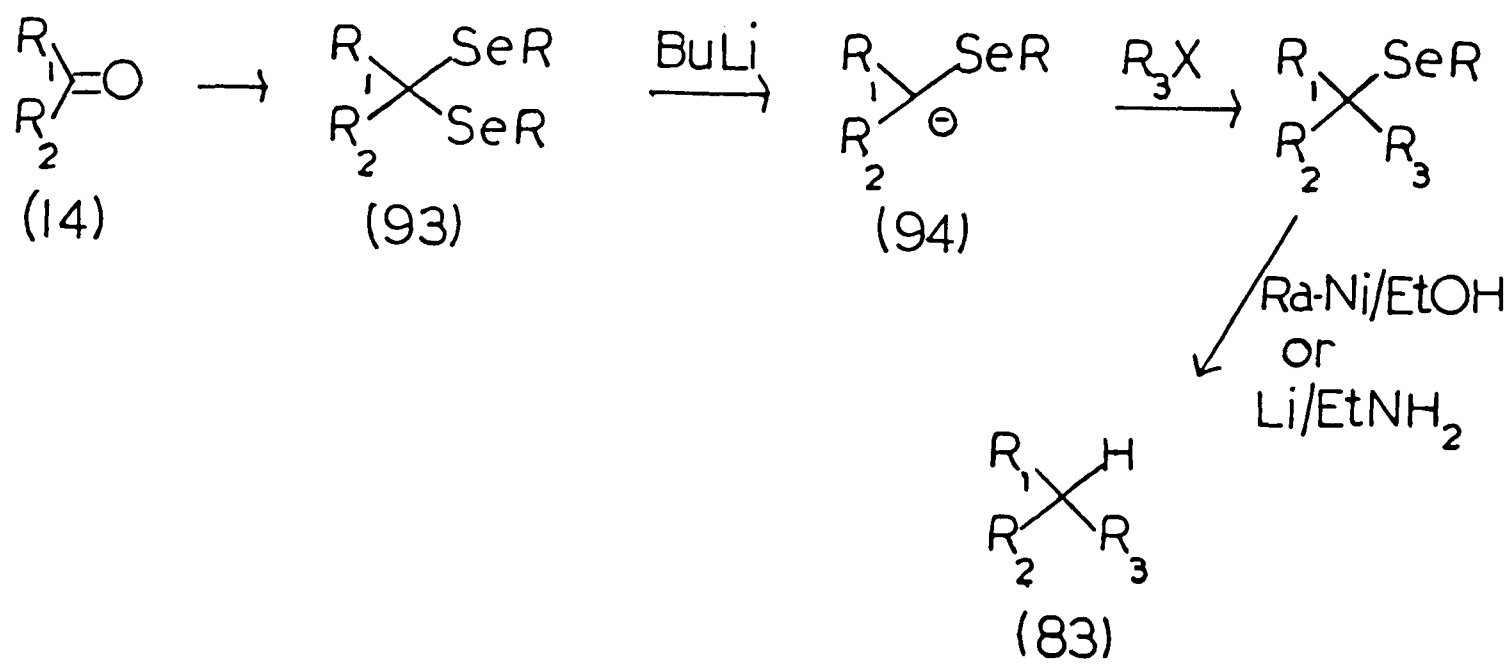
The azo-alkanes (84, R = t-BuPh_2C-), derived from BDP hydrazones (29), should upon homolysis give a t-butyldiphenylmethyl radical. This would be both a resonance stabilised and a hindered radical. Thus the homolysis of azo-alkanes (84, R = t-BuPh_2C-) should be facile and thermolysis in the presence of thiol would generate alkanes. Thus by this method a carbonyl (14) could be transformed to an alkane (83) via a reductive alkylation.

This reductive alkylation of carbonyl compounds is not a very

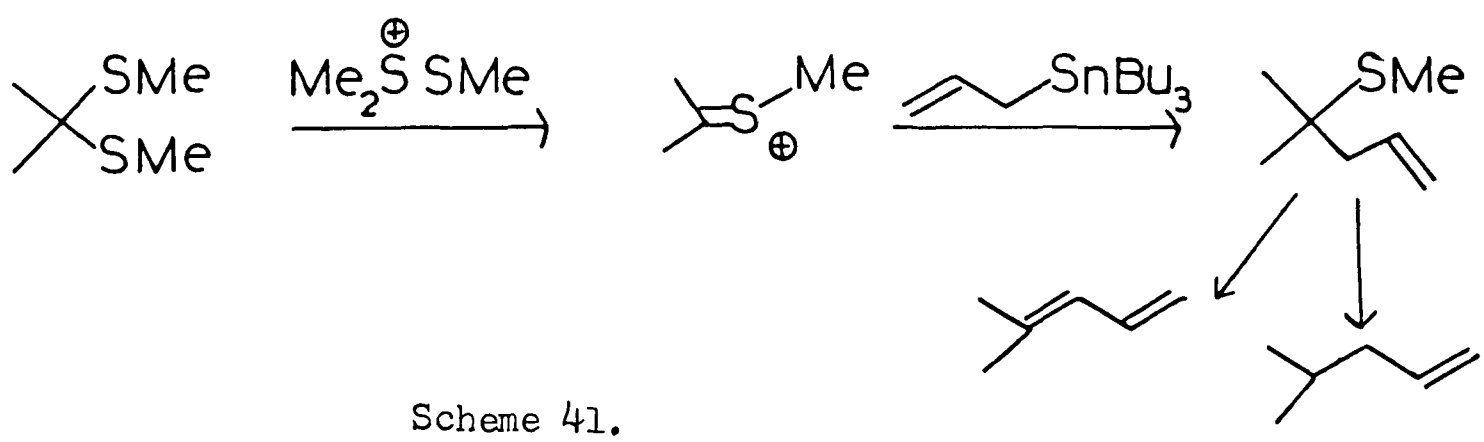
well documented reaction. In contrast the reaction of carbonyl compounds with alkyl metal species to give alcohols,technically a reductive alkylation,is well known.



One general method for this process involves selenoacetals (93) as a synthon.[115] These compounds were treated with alkyl lithium reagents to generate the anions (94),then with alkyl halides. Removal of the selenium moiety gave alkanes (83) (Scheme 40).



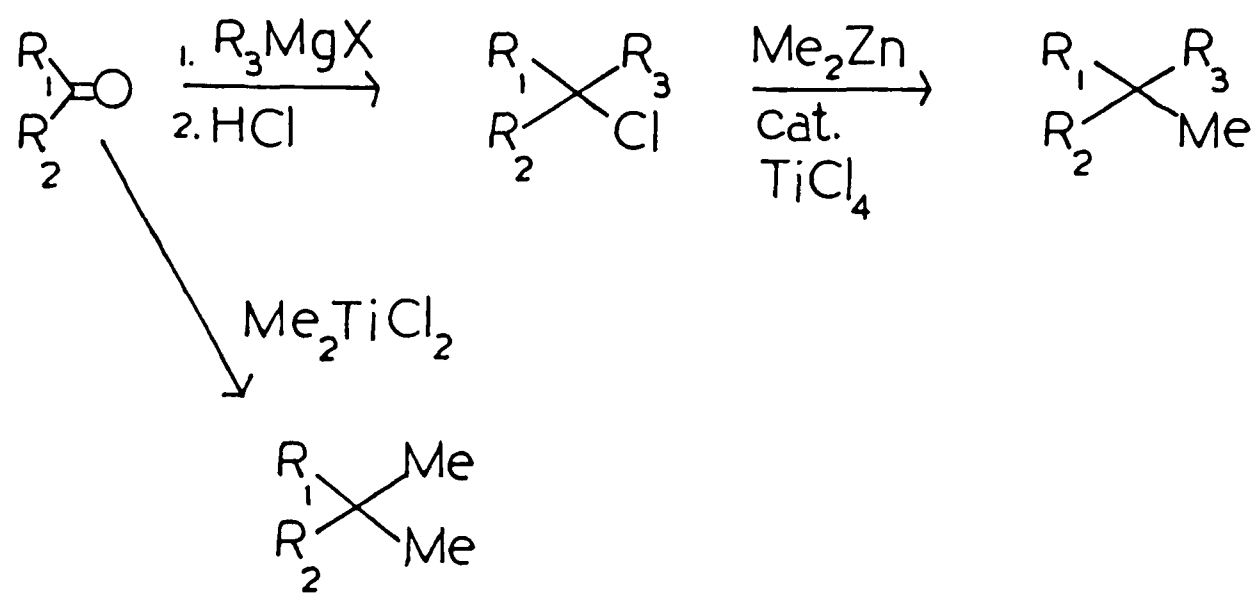
Scheme 40.



Scheme 41.

Recently Trost made use of thioacetals with allyl tin reagents in what represented a reductive allylation (Scheme 41).[116]

Gem dialkylation is also known using titanium alkyls (Scheme 42).[117]



Scheme 42.

Alkanes can be prepared in a large number of ways. These can be divided into three main categories : catalytic procedures,which are often used industrially and give mixtures of products,or to saturate carbon - carbon multiple bonds on small as well as large scale; replacement of functional groups by hydrogen,as in the Wolff-Kishner reaction; and coupling reactions.

Catalytic reduction of alkenes and alkynes is a very useful synthetic procedure. Reductive replacement of functionality is also very important and many methods have been developed. For the carbonyl to alkane conversion there are Clemmensen,[118] Wolff-Kishner,[119] dithiane desulphurisation,[120] and hydride reduction of tosylhydrazones[121] as common methods. Aldehydes can also be decarbonylated with tristriphenylphosphine rhodium chloride (Wilkinsons catalyst).[122]

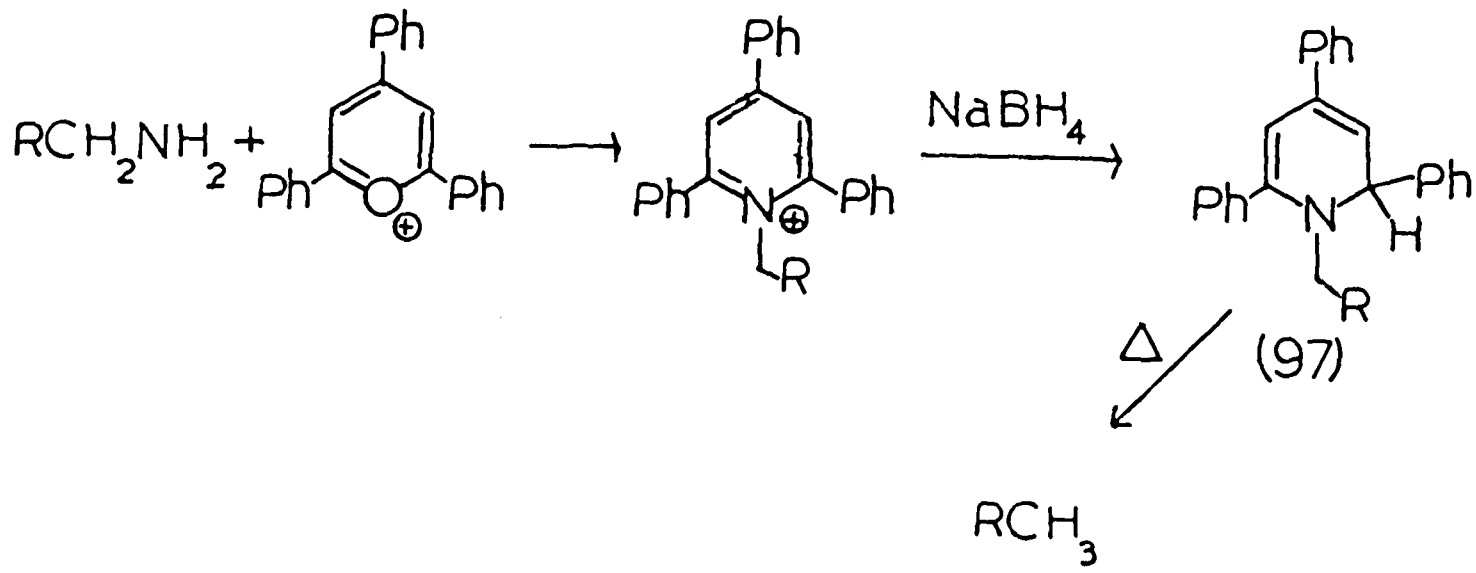
Decarboxylation of acids is well established as an alkane synthesis and new mild methods have been developed, such as that by Barton via pyridylthione N-esters[123] and another by Fristad, Fry and Klang[124] with silver nitrate and persulphate. Both procedures generate an alkyl radical (95) as an intermediate.

$$RCO_2H \longrightarrow \underset{(95)}{R\cdot} \longrightarrow RH$$

Other carboxylic acid derivatives can be converted to alkanes such as amides,[125] acyl chlorides,[126] and esters[127] as also can nitriles.[128]

Reduction of alkyl halides or tosylates and tetraalkylammonium salts with hydride reagents,[129] of nitriles with metal in ammonia systems,[130] and of alcohols, either directly with hydrogen and a catalyst or indirectly, via thioformates[131] or chloroformates,[132] with silanes, are all known reactions. Amines can be reduced after conversion to isonitriles (96)[133] or dihydropyridines (97).[134]

$$R\text{-}NH_2 \longrightarrow \underset{(96)}{R\text{-}NC} \xrightarrow[AIBN]{Bu_3SnH} RH$$



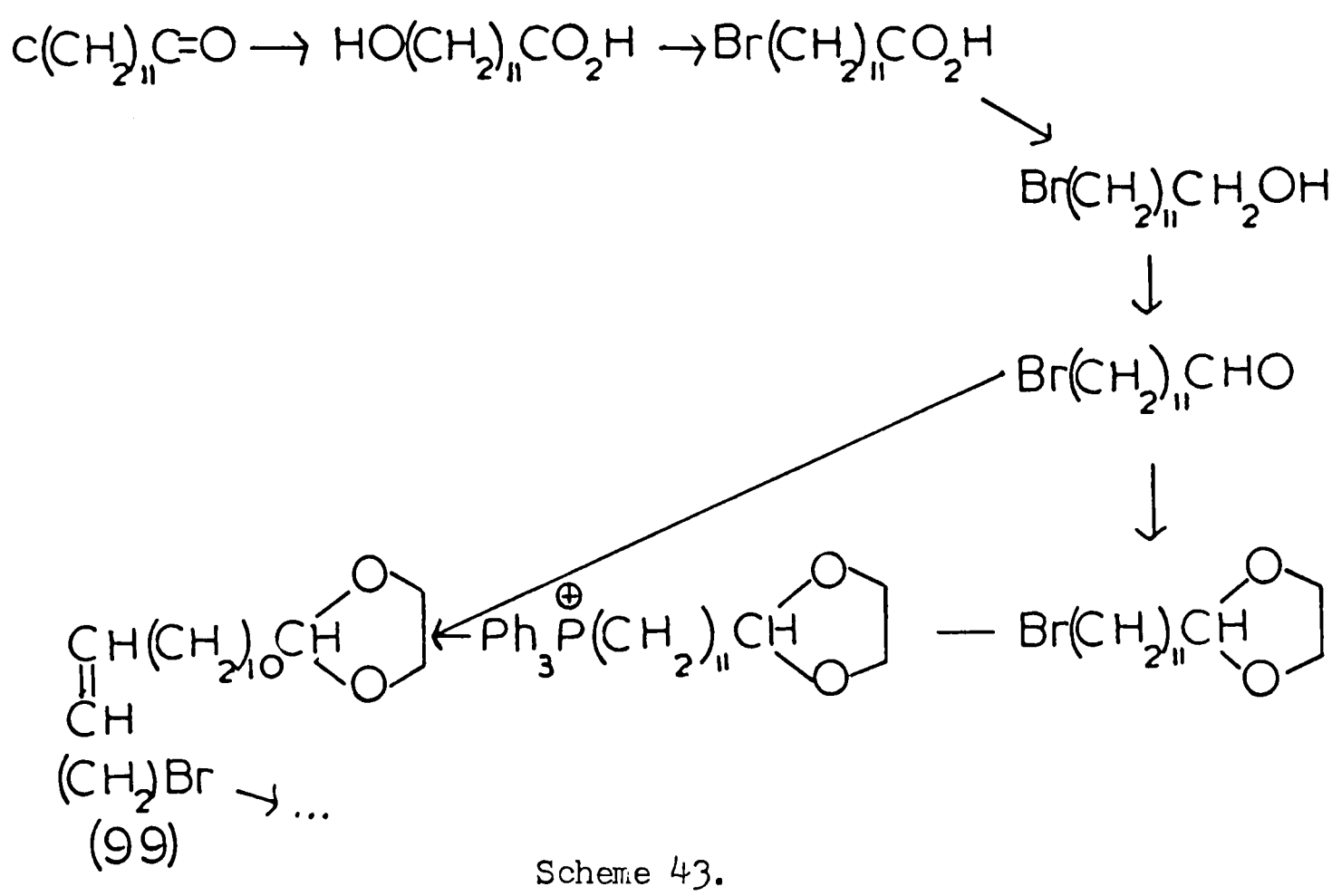
There are many well known coupling reactions that give rise to alkanes,of which the Wurtz coupling is probably the most well known.

$$2RX + Na \longrightarrow R{-}R$$

However,this method is not very synthetically useful due to side reactions and the inability to cross-couple effectively. Cuprates couple with alkyl halides to give cross-coupled products (98).[135] Allylic and benzylic alcohols can be symmetrically coupled with methyl lithium and titanium trichloride,[136] carboxylate salts by the Kolbe reaction,[137] Grignard reagents with thallium (I) bromide,[138] and boranes with silver nitrate and a base.[139]

$$RX + R'_2CuLi \longrightarrow \underset{(98)}{R{-}R'}$$

An interesting recently published procedure[140] generated very long straight chain alkanes from cyclododecanone (Scheme 43). The bromoalkene (99) can be hydrogenated or reacted further with more phosphonium salt. Chains of up to 104 carbon atoms have been prepared.



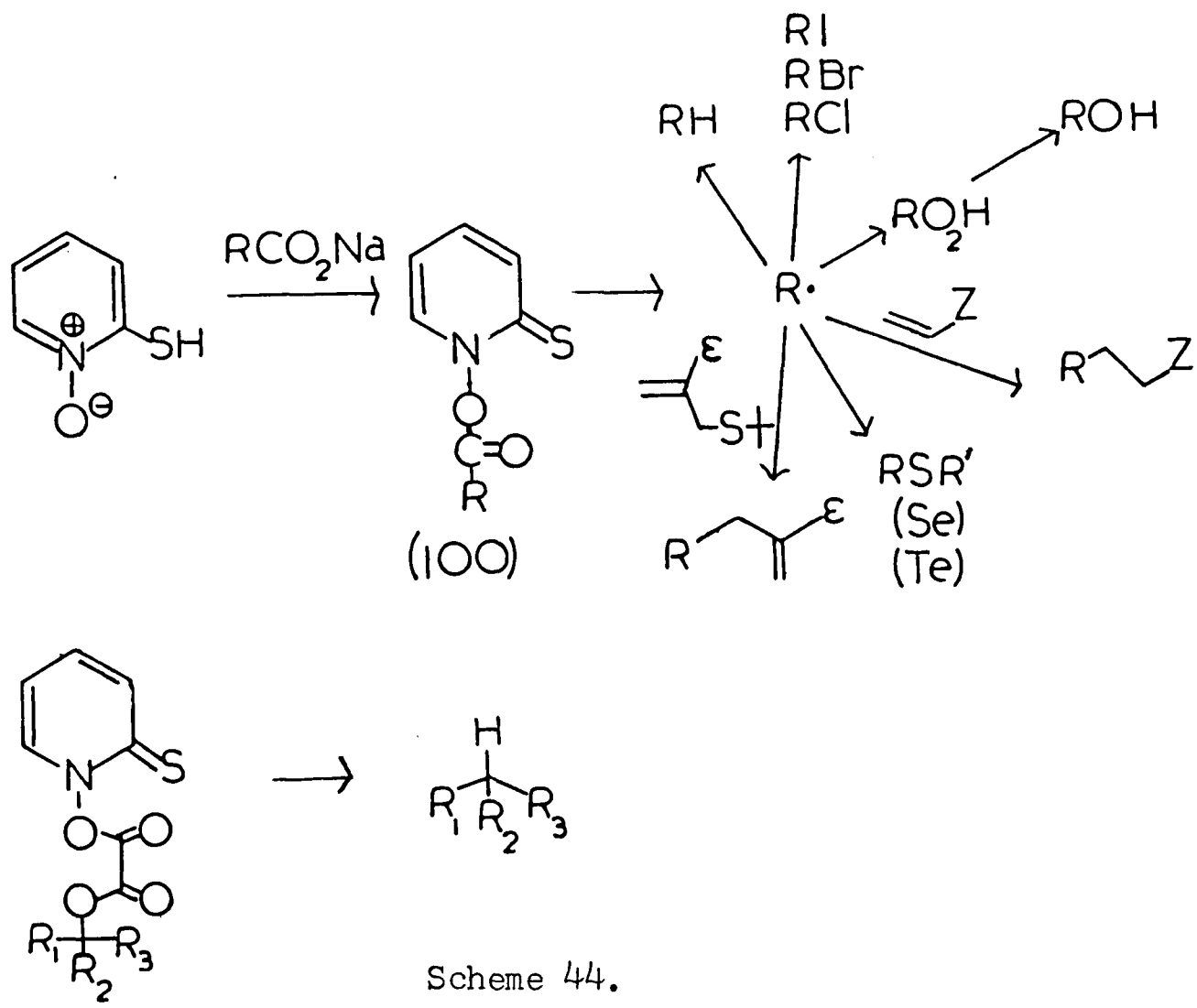
Scheme 43.

D. Radicals in Synthesis

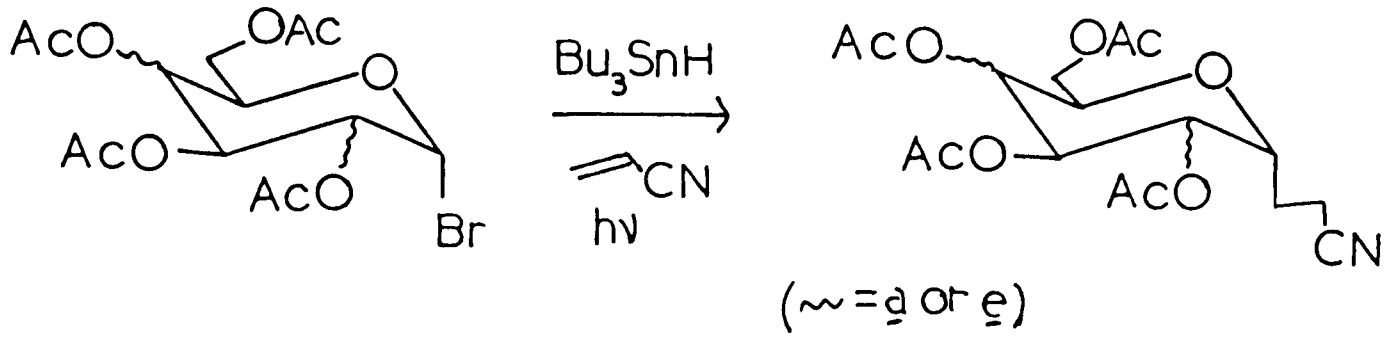
The alkane synthesis developed using tritylhydrazone anions,[31] involving a radical intermediate, led to consideration of means to utilise these radicals in synthetically useful ways. This was enhanced by recent developments in the mild generation and use of radicals by several other workers.[141 - 146]

For example, Barton[141] has developed the use of esters of thiohydroxamic acids (e.g. 100) to generate radicals which were then used in a series of synthetically useful transformations (Scheme 44).

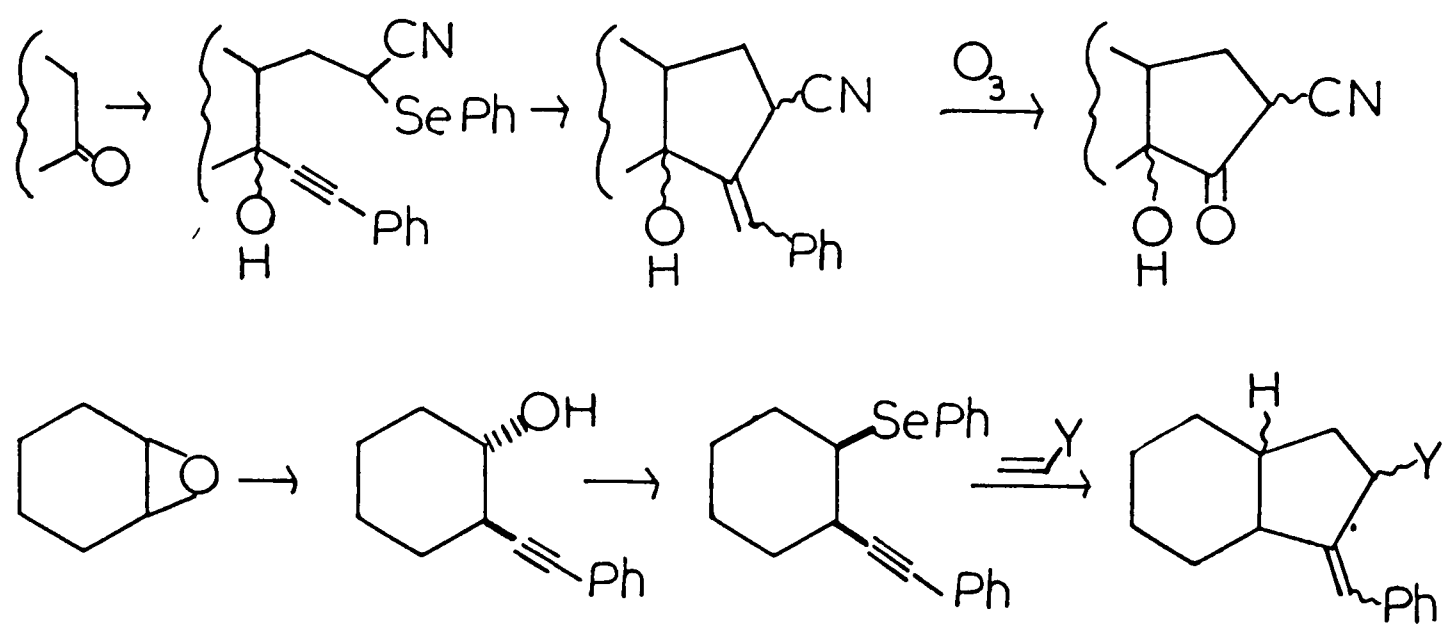
Baldwin has developed methods of allene transfer[142a] and methods of addition of glucosyl and β-alanyl radicals to alkenes.[142b] Giese has reviewed radical addition to alkenes[143] and has also shown useful stereocontrolled reactions of glucosyl radicals (Scheme 45).[144] Clive has developed some interesting cyclisations[145] including a new annulation procedure (Scheme 46).[145c] Stork has also developed a number of synthetically useful reactions which exhibit stereocontrol (Scheme 47).[146]



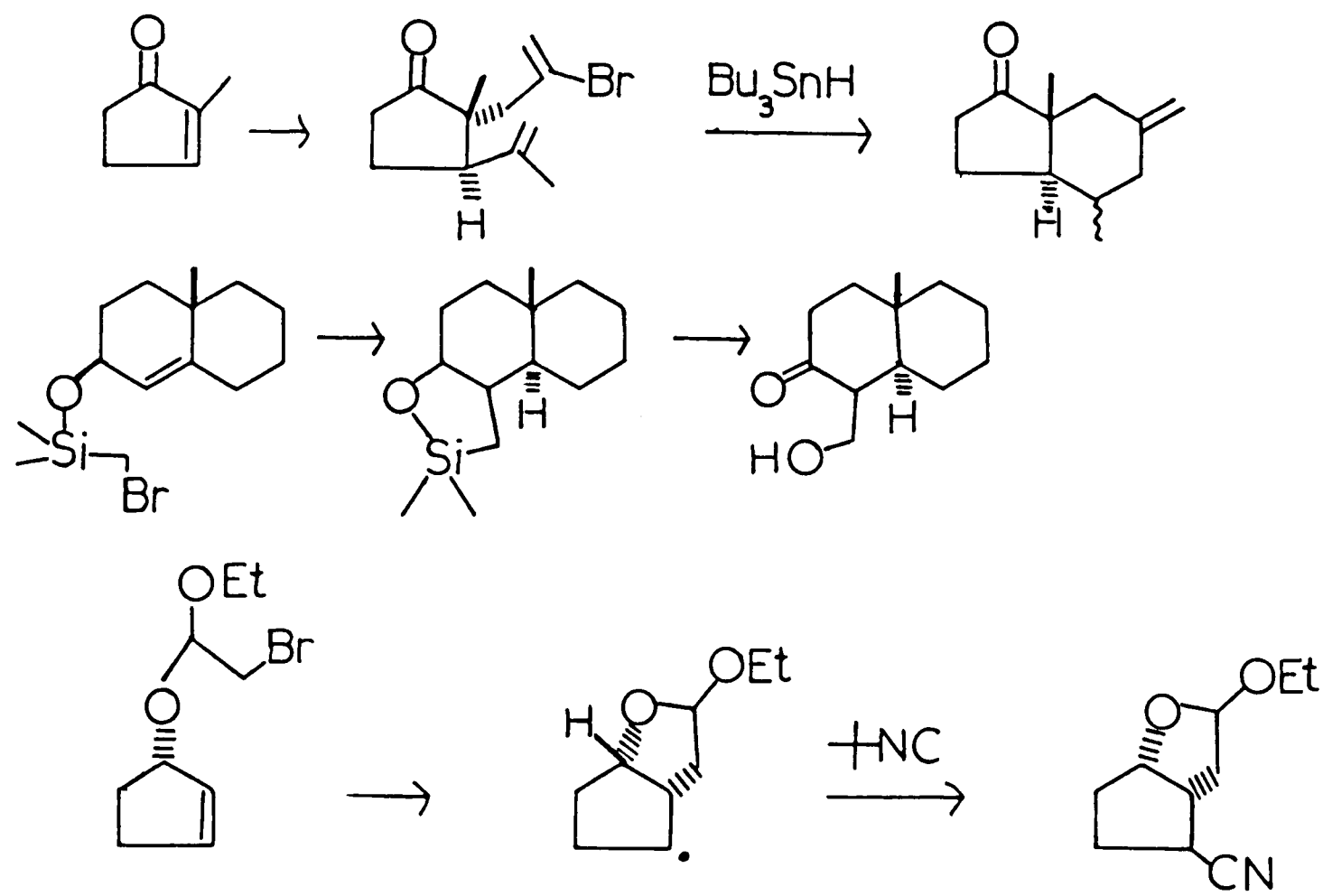
Scheme 44.



Scheme 45.

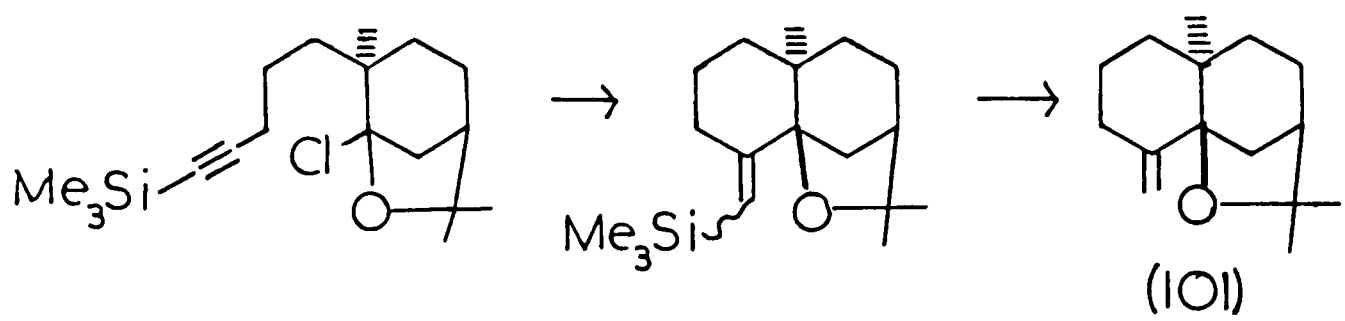


Scheme 46.

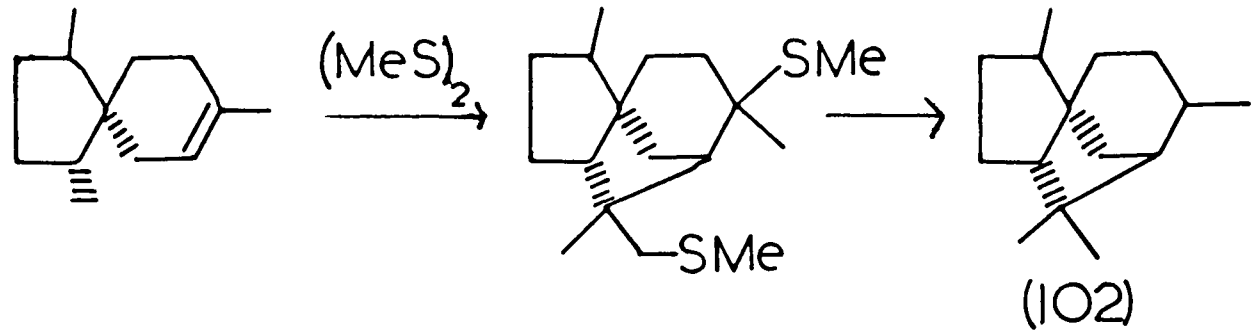


Scheme 47.

Radical reactions offer a number of advantages to synthetic chemists, the principal one is that the radical reagents are compatible with a wide variety of functionality. Of prime importance is the formation of carbon - carbon bonds ; radical methods to achieve this have been recently reviewed.[147] A number of complex molecules have been synthesised using radical reactions as key steps, such as β-agarofuran (101),[148] cedrane (102),[149] and some alkaloid skeletons (e.g. 103, 104).[150,151]



(101)



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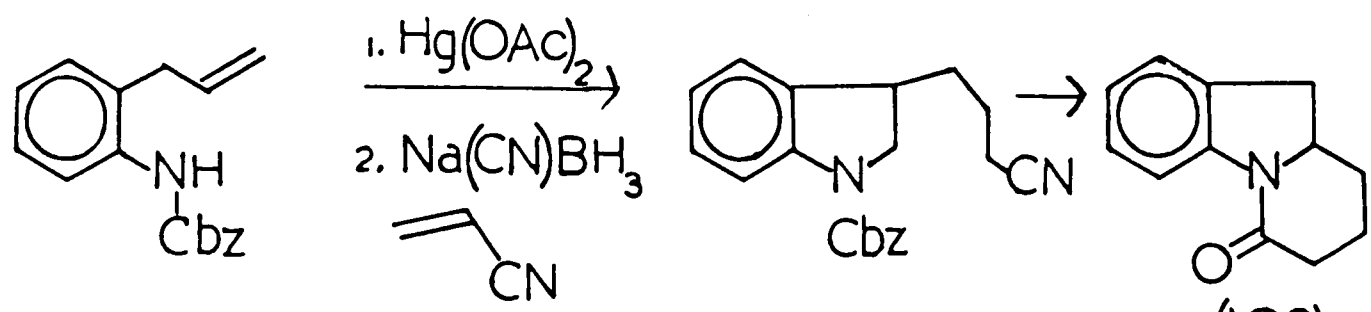

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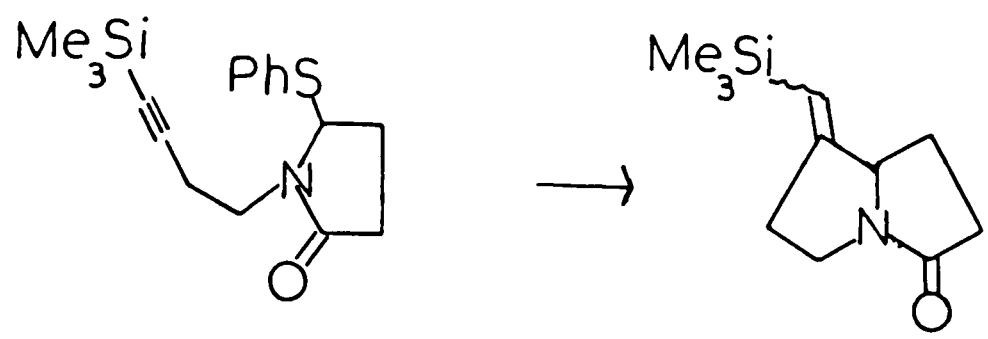


(104)

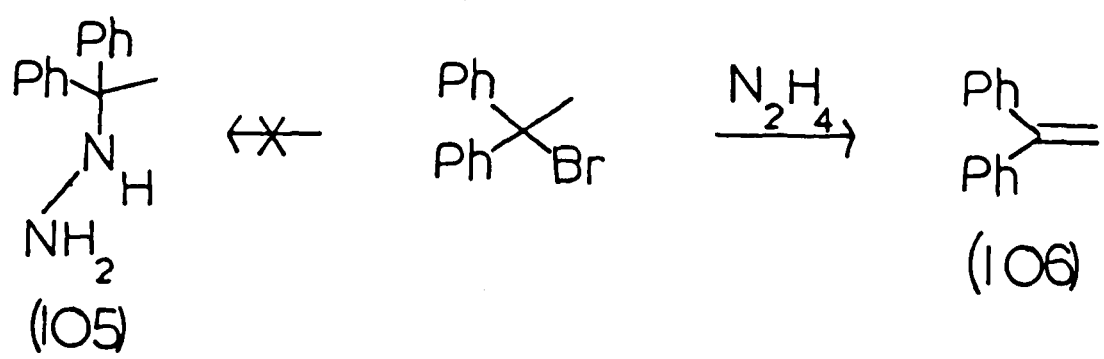
E. Benzhydryl Hydrazone Reactions

The azo-compounds generated from t-butylhydrazones were thermally stable when refluxed in xylene[31] which resulted in limitations to the method. The azo-compounds generated from trityl (26) or DPP (27) hydrazones were thermally unstable to homolysis above about -20°C. This resulted in virtually uncontrolled generation of radicals in the presence of complex reaction mixtures. We were therefore led to consider the use of alternative hydrazones that would generate azo-compounds of intermediate homolytic cleavage reactivity.

i) Choice of Hydrazone

The hydrazone required would need to be sufficiently hindered to ensure good C vs. N reactivity of its derived anions, and the substituent group should exist as a moderately stabilised radical. Replacement of the phenyl groups of trityl azo-compounds by an alkyl, or other non-resonance stabilising group, is known to increase the activation energy for homolysis (by about 6 - 7 kcal mol^{-1}).[107a] This led us to consider alkyldiphenylmethylhydrazones for our purpose. A problem became immediately apparent in that if the alkyl substituent possessed β hydrogen atoms then preparation of the hydrazines would not be easy. This problem arises as elimination would become competitive with hydrazine substitution of the alkyl chloride.

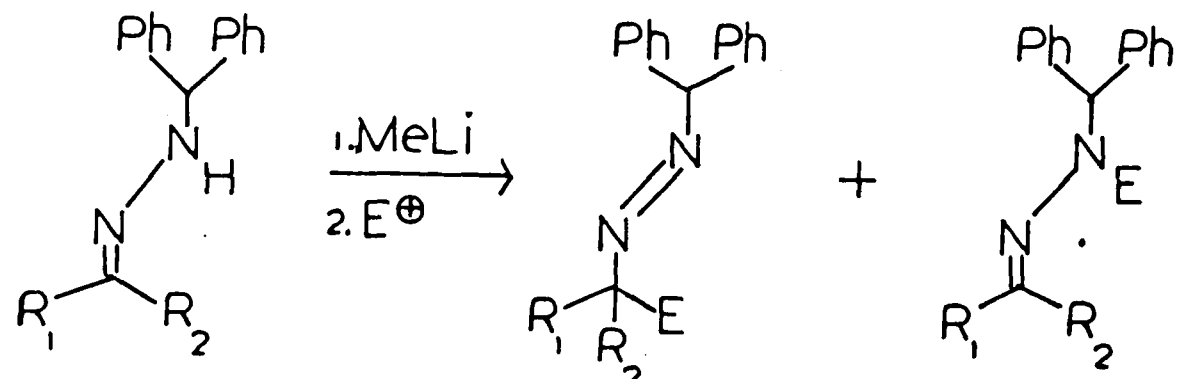
Indeed, attempts to prepare methyldiphenylmethylhydrazine (105) failed and only 1,1-diphenylethylene (106) was recovered.



(105) (106)

ii) Results

Although hydrazines with disubstituted carbon substituents had not been used for azo-anion methodology, benzhydryl hydrazine (19) was prepared by treatment of chlorodiphenylmethane with hydrazine in THF (chap. II). This represented a use of hydrogen rather than alkyl as a phenyl replacement in tritylhydrazine (17) (giving a ΔE_a for homolysis of the corresponding azo-compounds of about 4 kcal mol^{-1}).[107a] Benzhydrylhydrazones (28) were prepared by the standard route (chap. II) and reactions of their lithium salts with electrophiles were carried out. The results are depicted in table 7.



(28) (107) (108)

Hydrazone (28)	E^+	Yield (%)	(107):(108)
a	$PhCH_2Br$	70	1 : 7.5
e	PhCHO	-	-
e	$PhCH_2Br$	70	2 : 3
e	nC_4H_9I	60	1 : 1
f	PhCHO	-	-
f	$PhCOCH_3$	-	-
f	$PhCH_2Br$	-	-

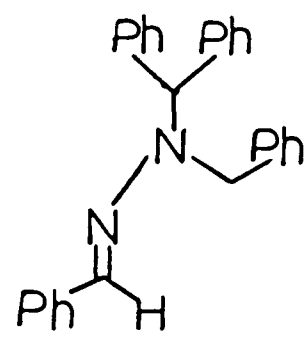
Table 7.

a) Procedure Under the established conditions for alcohol synthesis (chap. III, sect. D i) no azo-alcohols were isolated and only

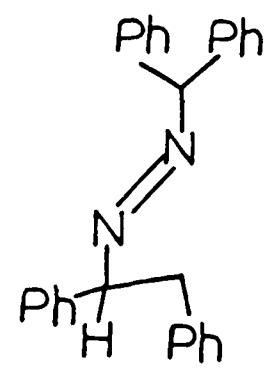
hydrazones (28) were recovered from the reaction mixture in high yield. Alkylation was conducted as for t-butylhydrazones [10] by addition of the alkyl halide to a solution of the azo-anion at -78°C, allowing the reaction mixture to warm to ambient temperature and stirring for 18h before work-up.

b) Analysis of Results The crude product mixtures were analysed by high field proton n.m.r. to determine the N : C addition ratios. Acetone hydrazone (28f) gave no C-alkylated products (107). Benzaldehyde hydrazone (28e) gave the best C : N ratio, probably due to electronic biasing of the reaction pathway.

The N-alkylated product (109) was isolated and identified by its spectral data [δ_H 4.51 (2H, s, $C\underline{H}_2Ph$), 5.88 (1H, s, $C\underline{H}Ph_2$), 7.14 - 7.49 (20H, m, phenyl-$\underline{H}$) ; m/e (E.I.) 376 (M^+, 21%), 167 (100) ; (Found : 376.1939 ; $C_{27}H_{24}N_2$ requires : 376.1939)]. The C-alkylated product (110) was also identified by spectroscopic data [δ_H 3.37 - 3.48 (2H, m, $C\underline{H}_2Ph$), 4.89 - 4.98 (1H, m, $PhC\underline{H}N$), 5.70 (1H, s, $C\underline{H}Ph_2$), 6.97 - 7.50 (20H, m, phenyl-$\underline{H}$) ; m/e (NH_3 D.C.I.) 377 (MH^+, 49%), 181 ($C_{14}H_{13}^+$, 31), and 167 (100)]. The N-alkylated products from these reactions decomposed readily by hydrolysis on attempted chromatography on silica gel.



(109)



(110)

The conclusion to be drawn from these results is that hydrazones (28) are not sufficiently hindered for effective C-reaction. The thermal stability of azo-compounds (107) was not investigated as

only low levels of material were synthetically available.

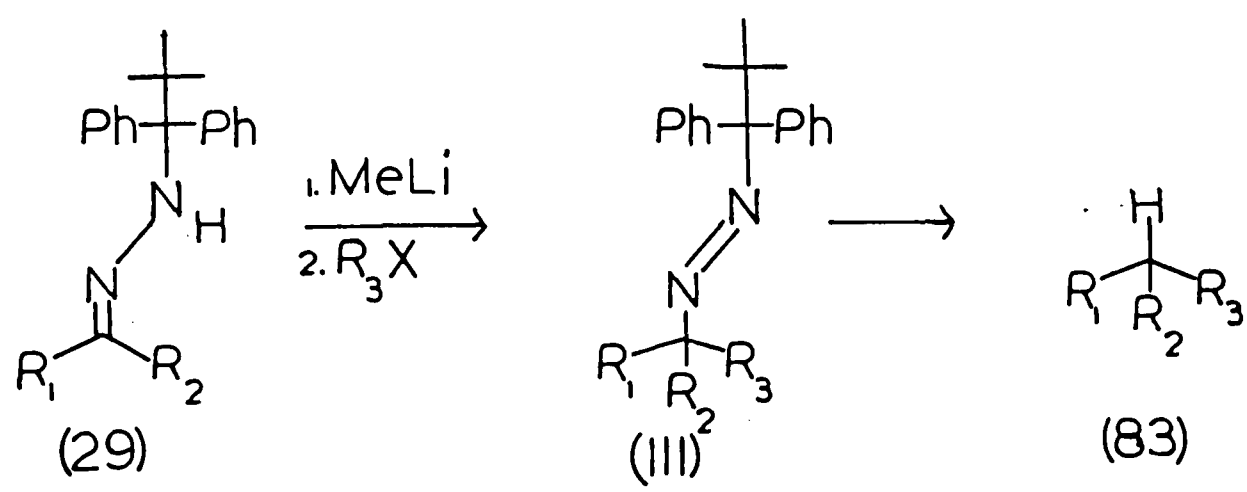
F. Alkylation of BDP Hydrazones (29)

The t-butyl group was chosen next as the alkyl group for the synthesis of an alkyldiphenylmethylhydrazine in order i to allow for ease of synthesis without elimination problems (sect. E ii) ; ii to generate a highly hindered system for good C-reactivity ; and iii to allow formation of more stable azo intermediates than was possible from tritylhydrazone (26) reactions.

BDP hydrazones (29) were readily prepared as described in chapter II by reaction of phenylmagnesium bromide with ethyl pivalate, chlorination of the resultant alcohol,and hydrazine substitution to give t-butyldiphenylmethyl (BDP) hydrazine (20) which was treated with aldehydes and ketones to generate the hydrazones (29).

i) Preparation of Azo-Alkanes

a) Reaction Conditions Alkylation of BDP hydrazones (29) provided very good yields of azo-alkanes (111). The procedure adopted was that used for t-butylhydrazone alkylation[10] namely,to treat an azo-anion solution at -78°C with the alkyl halide and allow the mixture to warm to ambient temperature over 2 - 3h before stirring for a further 18h. The reactions were then quenched with acetic acid and diluted with diethyl ether before washing with water,drying and evaporating off the solvent to give a crude product.



(29) (111) (83)

b) Purification The concentrated residue was purified by flash column chromatography on silica gel. The azo-alkanes (111) were obtained as viscous yellow oils which were thermally unstable above about 50 - 60°C. They were stored at 4°C in darkness. Table 8 shows the azo-alkanes (111) prepared and the yields obtained. Compounds (111) proved too unstable for satisfactory elemental analysis giving lower than calculated nitrogen percentage, but full spectroscopic data were obtained.

Hydrazone (29)	R_3X	Product(111)	Yield (%)
a	$nC_{10}H_{21}I$	a	95
a	CH_3I	b	76
a	$PhCH_2Br$	c	99
a	nC_4H_9I	d	89
c	$nC_{10}H_{21}I$	e	70
c	$nC_7H_{15}I$	f	48
c	$PhCH_2Br$	g	77
d	$nC_{10}H_{21}I$	h	79
d	CH_3I	i	71
d	$Br(CH_2)_5Br$	j	89
f	CH_3I	k	84
f	$PhCH_2Br$	l	100
i	$nC_7H_{15}I$	m	88
i	$PhCH_2Br$	n	100
i	allyl-Br	p	52
j	nC_4H_9I	q	93
j	CH_3I	r	85
j	$PhCH_2Br$	s	85

Table 8.

ii) Preparation of Alkanes (83)

a) Reaction Conditions Azo-alkane (111a) was dissolved in benzene and a large excess of thiophenol was added. The solution was heated under reflux and the disappearance of starting material was monitored by t.l.c.. After 2h t.l.c. showed complete consumption of the azo-alkane (111a). Dodecane was isolated in 95% yield. Benzene was replaced with THF in another experiment to determine whether the lower temperature and different solvent would offer any advantages. The result was a less clean reaction with a lower alkane yield. The amount of thiophenol was then varied and it was discovered that for optimum alkane yields not less than 5 mole equivalents were necessary.

b) General Procedure A general alkane (83) synthesis developed from the above results. Azo-alkanes (111) were refluxed in benzene for 2h with 5 - 6 mole equivalents of thiophenol. The cooled solution was diluted with diethyl ether,washed with sodium hydroxide solution (2M) and the solvents evaporated. The residue was purified by flash column chromatography on silica gel with light petroleum as eluant. Further purification could be achieved by p.l.c. if required.

The alkanes (83) prepared and the yields obtained are recorded in table 9.

c) Tritylhydrazone (26) Alkylation Alkylation of trityl hydrazone (26) anions was carried out by Perry[31] and the yields obtained are shown in table 9 for comparison. His procedure involved maintaining a temperature of -30°C for at least 3h to avoid premature homolysis and allow maximum alkylation. The procedure developed with BDP hydrazones (29) is clearly higher yielding and more convenient. The other notable advantage here is that any Wurtz-type coupling products,produced from excess alkyl halide,are removed during the azo-alkane (111) purification and so do not cause separation difficulties

in purifying the alkanes (83). Thermolysis of azo-alkanes (111) also appears to avoid any alkene production which had been noticed in the tritylhydrazone (26) system[31] (e.g. Scheme 29).

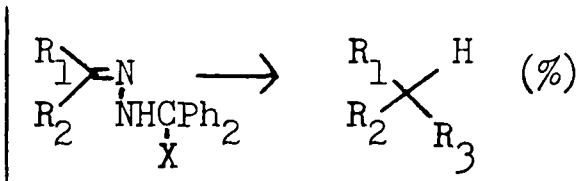
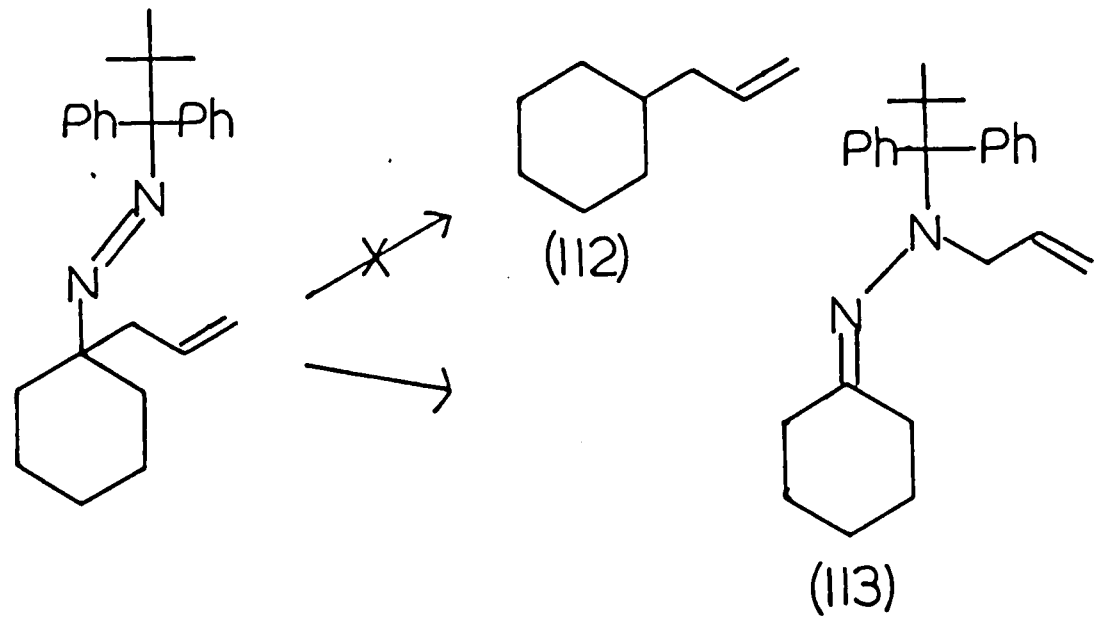
			 (%)	
(111)	Product (83)	Yield (%)	X = t-Bu	X = Ph
a	a	94	89	39
e	b	93	65	-
g	c	56	43	-
h	d	84	66	38
m	e	64	54	69
n	f	71	71	69
q	g	72	70	51
r	h	87	74	-
s	i	78	66	45

Table 9.

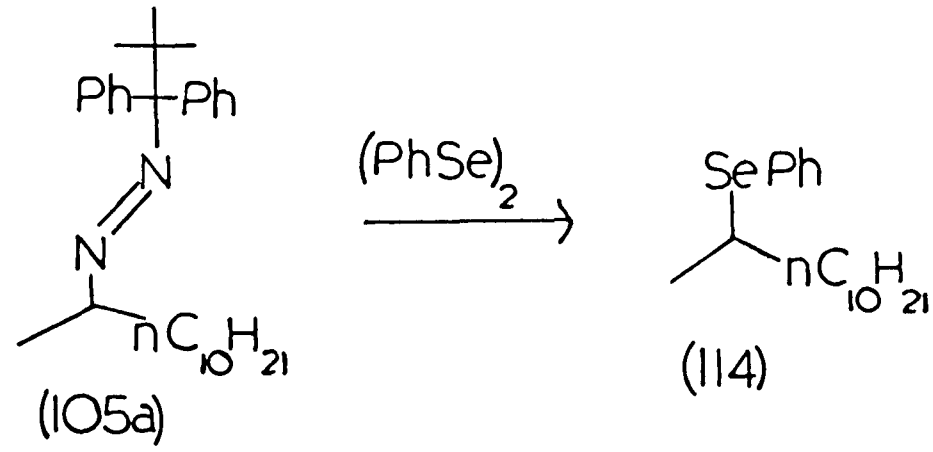
d) A Rearrangement The azo-alkane (111p) formed by addition of allyl bromide to cyclohexanone BDP hydrazone (29i) did not give allylcyclohexane (112) on thermolysis. Instead it appeared, by inspection of the proton n.m.r. spectrum of the crude reaction mixture, to have undergone a [3,3]-diaza-Cope rearrangement to give hydrazone (113). This compound was not isolated owing to decomposition during the work-up and purification.



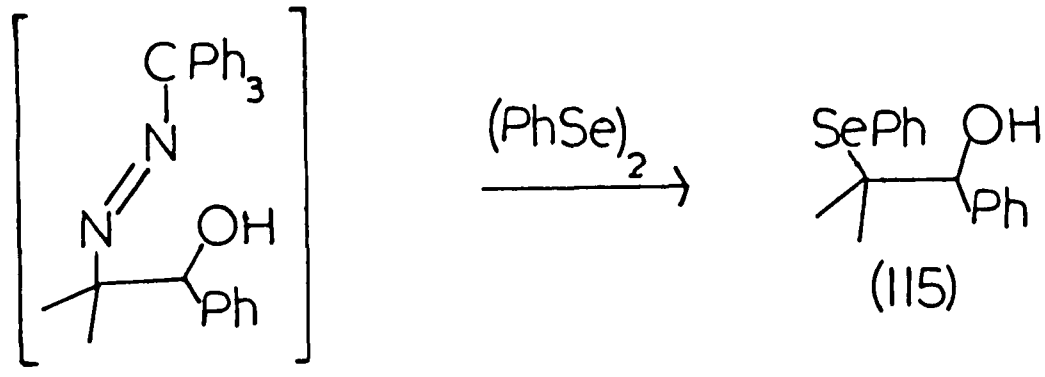
iii) Radicals from Azo-Alkanes (111)

In view of the fact that radicals were generated by thermolysis of the azo-alkanes (111),it seemed reasonable to attempt to trap them with reagents other than thiols. This would then allow the introduction of additional functionality and extend the scope of the azo-anion alkylation methodology.

Disulphides and diselenides are well known as good trapping agents for radicals,so diphenyl diselenide was added to a benzene solution of azo-alkane (111a) and the solution heated under reflux for 2h. After work-up and chromatography 2-phenylselenenyldodecane (114) was isolated in 77% yield.



A similar reaction had been attempted during an alcohol synthesis with tritylhydrazones (26). However,the products from this low temperature homolysis were complex,although proton n.m.r. did indicate that a β-hydroxyselenide such as (115) had been produced in poor yield (Scheme 48).

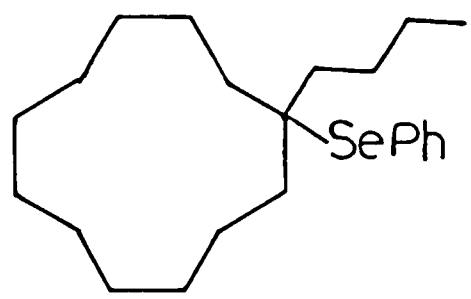


Scheme 48.

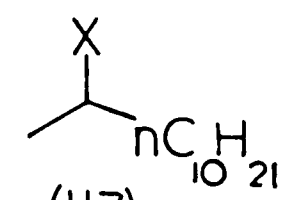
a) Reaction Conditions The general procedure adopted was similar to the alkane (83) synthesis (sect. ii b). At least five mole equivalents of trapping reagent were found necessary for the reaction. Disulphides gave moderate yields of trapped products but these were difficult to separate from the excess disulphide reagent by chromatography.

Azo-Alkane (111)	Trap	Product	Yield (%)
a	$(PhSe)_2$	114	77
q	$(PhSe)_2$	116	54
a	NBS	117a	50
a	NCS	117b	50
b	β-nitrostyrene	118	48
f	β-nitrostyrene	119	28
h	β-nitrostyrene	120	25

Table 10.



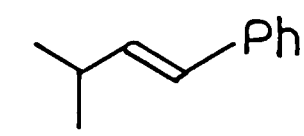
(116)



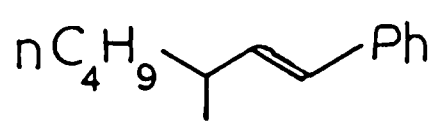
(117)

a) X = Br

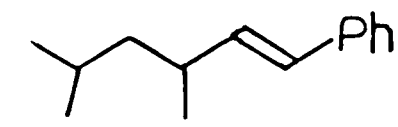
b) X = Cl



(118)

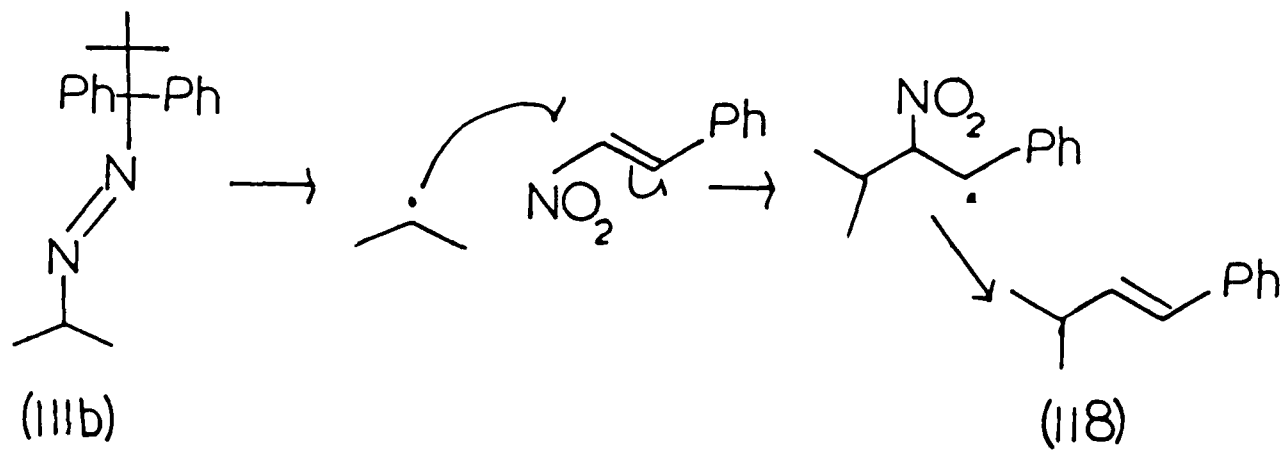


(119)



(120)

Table 10 shows the products and yields obtained using several trapping reagents. An alkyl bromide (117a) and an alkyl chloride (117b) were prepared using N-bromo- and N-chloro-succinimide respectively. An interesting reaction to generate styrenes (118) - (120) involved a radical addition - elimination pathway (Scheme 49).

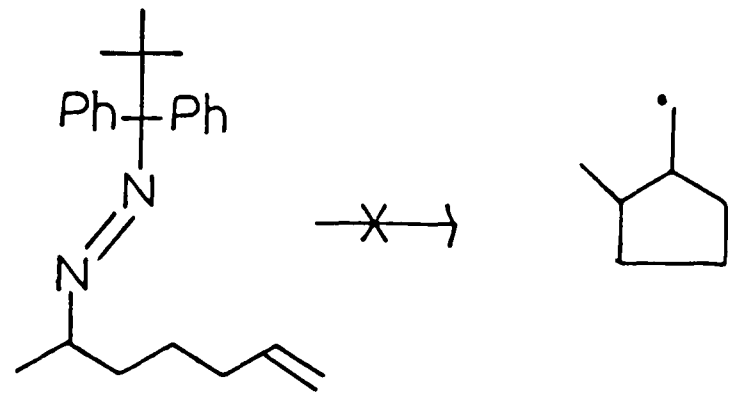


Scheme 49.

The styrenes were formed as the E isomers by this proximal addition - elimination. This type of addition - elimination reaction has been achieved with tin reagents.[152]

It was found that most tertiary radicals generated from azo-alkanes (111, $R_1, R_2, R_3 \neq H$) gave much poorer yields of trapped products than the secondary examples.

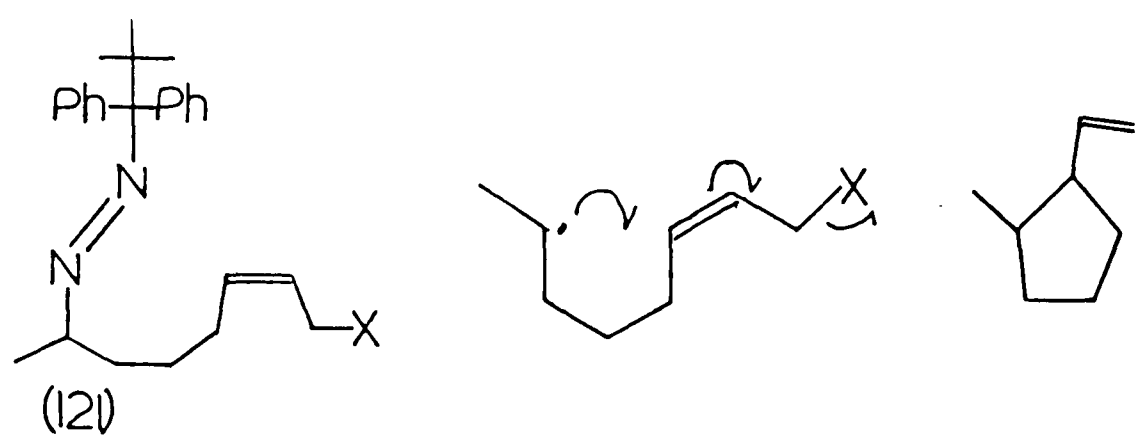
b) Cyclisation Radical cyclisation reactions have received recent attention.[145] and attempts were made to achieve cyclisation using azo-anion methodology. Alkylation with ω-haloalkenes or alkynes and subsequent thermolysis did not generate the cyclised products,however (Scheme 50).



Scheme 50.

The problem associated with this radical generation procedure is that high concentrations of radicals are produced in a non chain process. All the reported reactions for radical cyclisations are chain processes whilst the BDP method gives rise to a complex mixture of radicals in solution, with the result that the product mixture is also complex and the reactions are not synthetically viable.

Cyclisations could perhaps be achieved by an addition - elimination process if an azo-adduct such as (121) were produced (Scheme 51).[153]



(121)

$X = NO_2$ or SnR_3

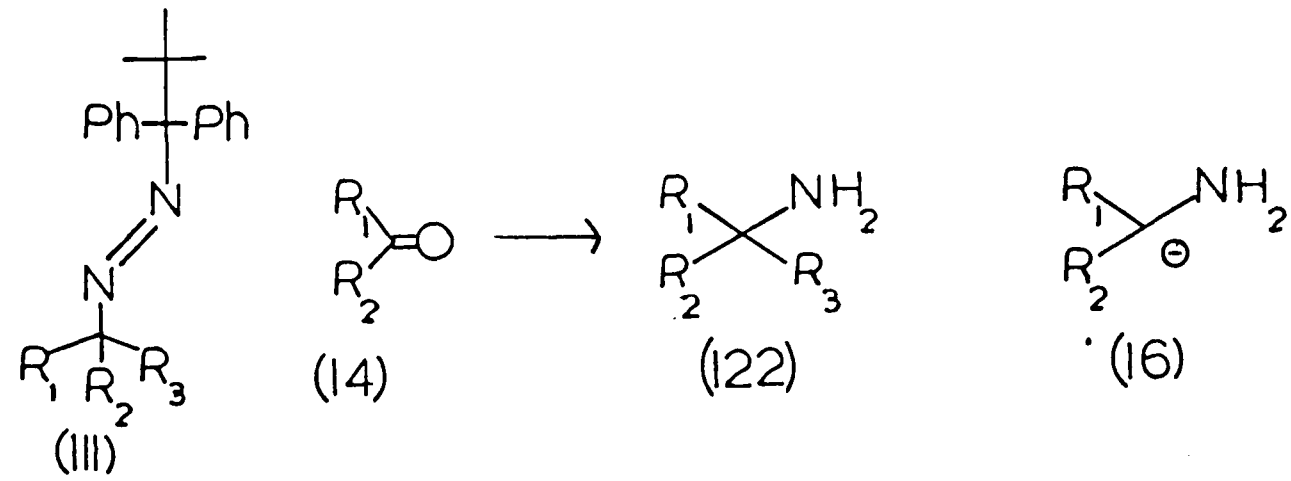
Scheme 51.

G. Summary

Alkylation of BDP hydrazones (29) has given rise to a useful synthesis of azo-alkanes (111). These can be usefully diverted to give alkanes (83) or alternatively they can be functionalised by thermolysis in the presence of radical trapping reagents.

CHAPTER V - AN α - AMINOCARBANION EQUIVALENT

The azo-alkanes (111), produced in generally excellent yields (Table 8) by azo-anion methodology, were sufficiently stable to thermal decomposition to allow chemistry other than azo-homolysis to be attempted. Methods do exist for reductive cleavage of the nitrogen - nitrogen bond of azo-compounds to generate amines.[154] If these could be applied to azo-adducts (111) then this would result in the conversion of a carbonyl (14) to an amine (122) and would represent the use of a carbonyl as an α-aminocarbanion equivalent (16).

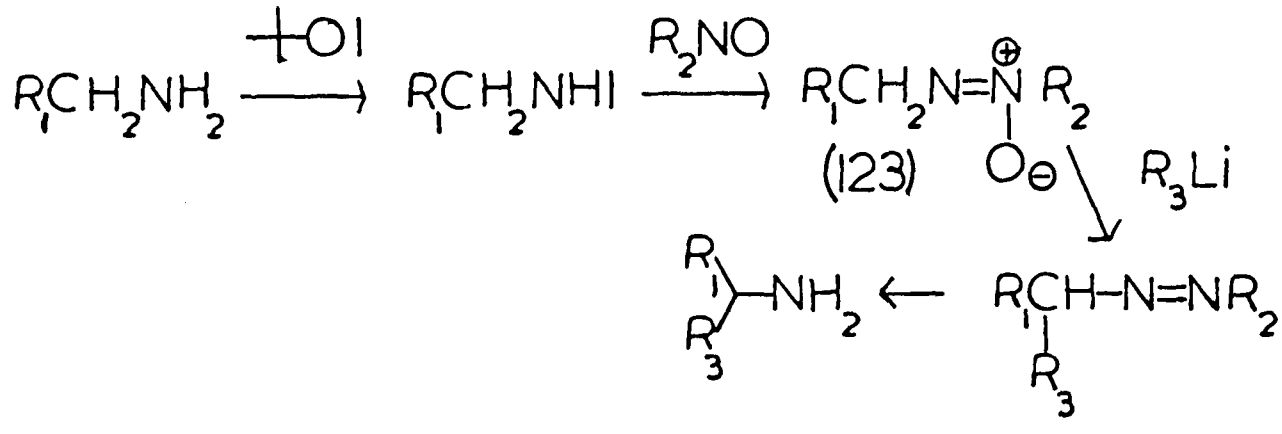


This transformation would be a useful addition to the existing range of methods for generation of a nucleophilic centre α to an amino group, particularly in view of the ubiquitous nature of the carbonyl group. This example of reactivity umpolung is an important one owing to the large number of natural and unnatural products containing amine functionality.

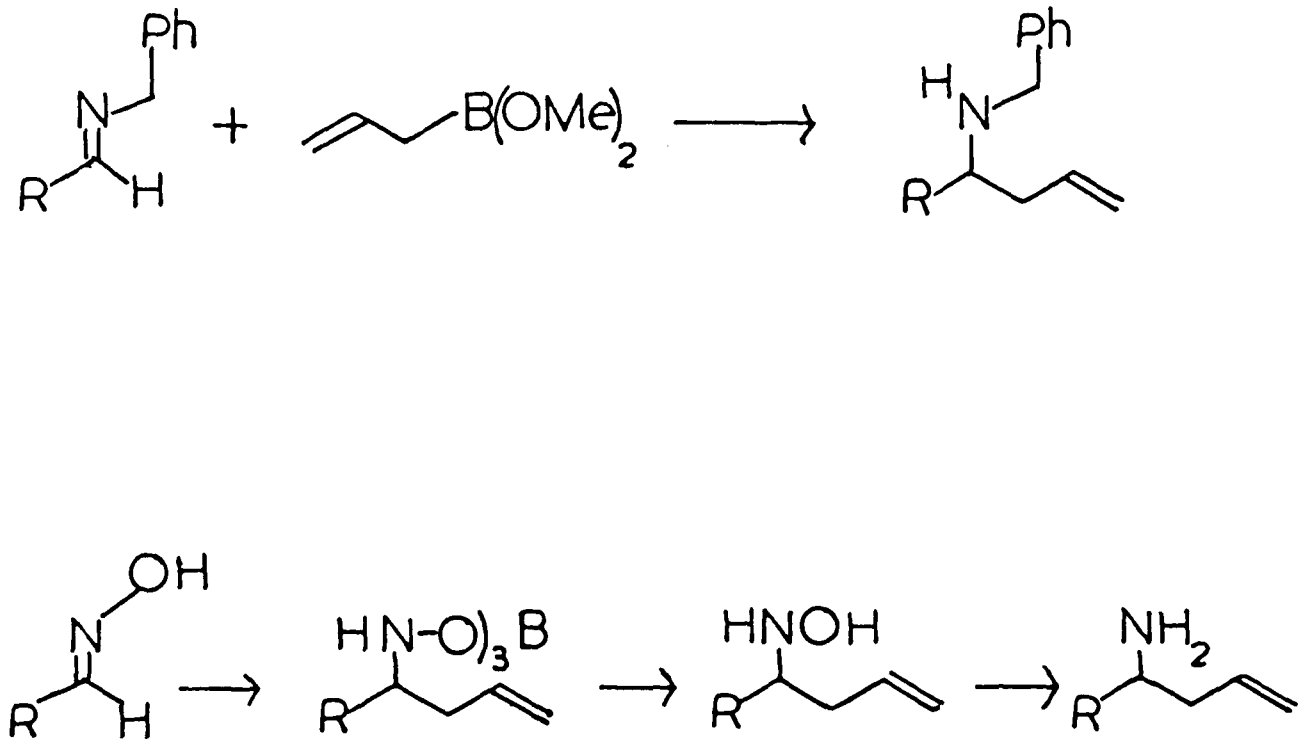
A. α - Aminoalkylation

Nature has developed ways of achieving electrophilic α-aminoalkylation and the organic chemist also has a number of methods at his disposal. Standard methods include the Mannich,[155] Vilsmeier - Haak,[156] Bischler - Napieralski and Pictet - Spengler reactions.[157] Other examples of methods for α-aminoalkylation include Barton's

reaction via the azoxy - intermediate (123) (Scheme 52),[158] and an interesting allylboronate reaction with imines or hydroxylamines (Scheme 53).[159]



Scheme 52.

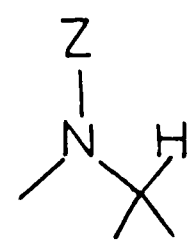


Scheme 53.

However, until relatively recently there were few methods available for nucleophilic α-aminoalkylation. A recent review[30] has covered the major methods available up to 1983.

The principle involved in the main class of these methods is that of activation of the nitrogen by a group Z (124) to enhance

the acidity of the ∝ proton. Table 11 lists the compound types that have been used. These methods all depend on the removal of the group Z, to reveal the amine, after reaction. This has proved a major limitation of these methods.



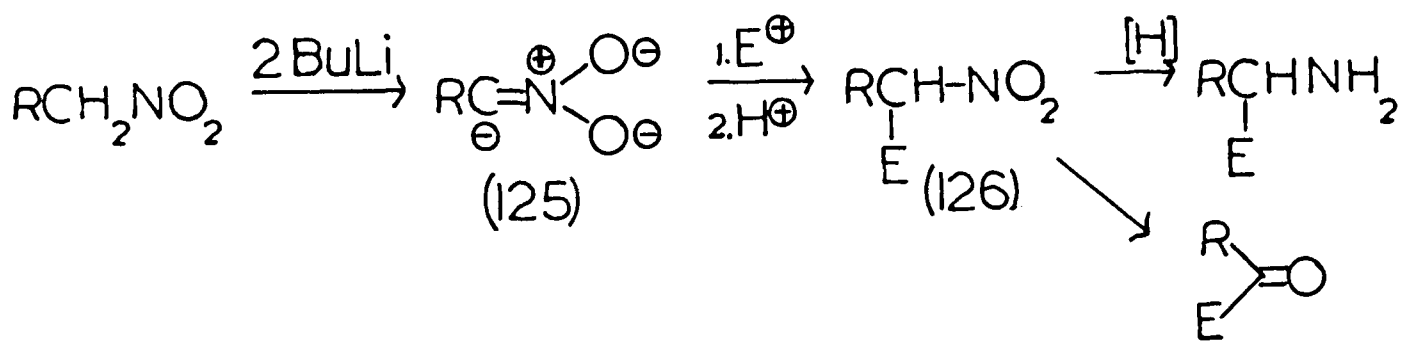
(124)

Compound Type	Z
amide	-C(O)R
thioamide	-C(S)R
imide	$-(CO.R)_2$
urea	$-C(O)NR_2$
carbamate	$-CO_2R$
phosphoramide	$-PO.(NMe_2)_2$
nitrosamine	-NO
isonitrile	=C:
formamidine	-C=NR
imine	$=CR_2$
isothiocyanate	=C=S
sulphinylamine	-SO
amine oxide	-O

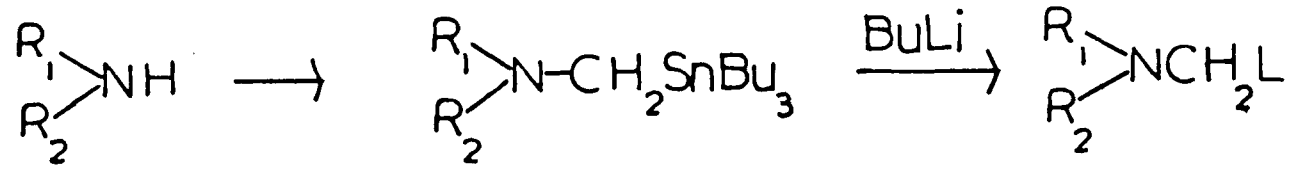
Table 11.

There are also methods outside this general class, perhaps the most obvious being the use of nitro-compounds. It was found that the dianions (125) were much better than their corresponding monoanions

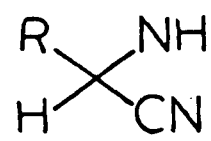
in reactions with electrophiles such as aldehydes,ketones,carbonates, anhydrides and alkyl halides.[160] The nitro-products (126) can be reduced to amines or converted to carbonyl compounds (Nef reaction).



Direct α-aminoanion formation has been achieved by a transmetallation using tin species (e.g. 127).[161] α-Aminonitriles (128) also allow deprotonation α to the amine group and the nitrile group can be removed or transformed readily.[30]



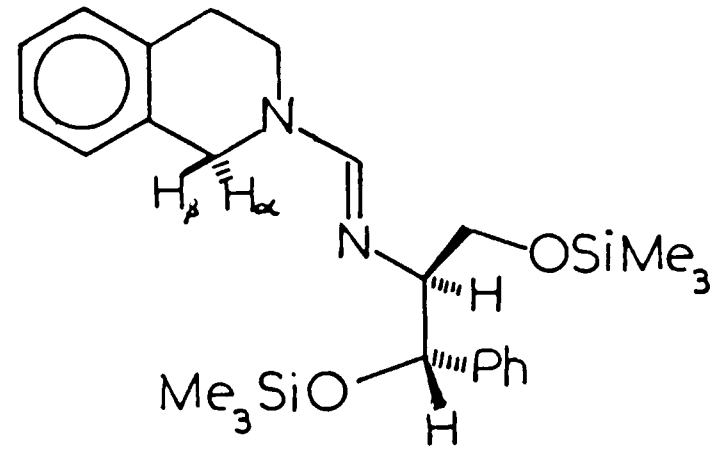
(127)



(128)

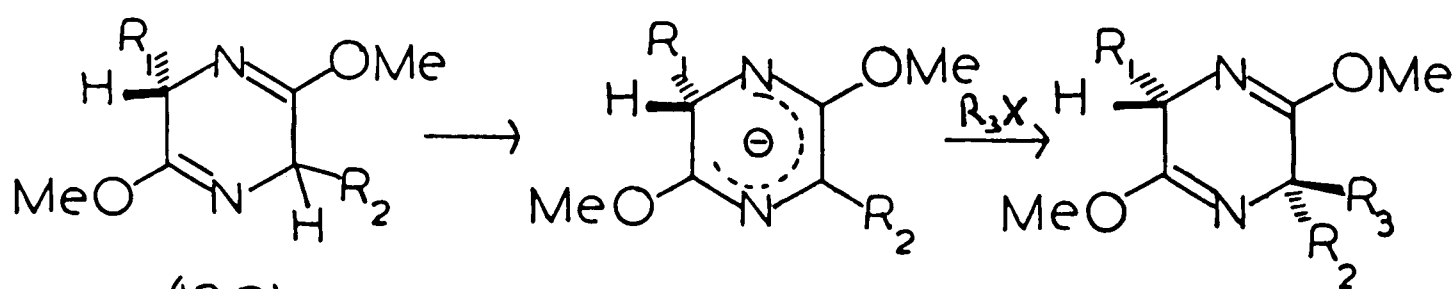
Of all these methods the use of nitrosamines probably has the broadest scope. Primary,secondary,and tertiary amines can all be used and the only major drawback is the removal of the nitroso group. There are now mild methods for achieving this[162] and a one-pot procedure is now available to avoid handling the carcinogenic nitrosamines.[163]

The formamidine method developed extensively by Meyers[164] has become a powerful means of achieving asymmetric α-aminoalkylation. A chiral auxiliary is used to form the formamidine (e.g. 129) and this can be regenerated after the alkylation reaction. This allows specific proton removal from the substrate (129, either H_α or H_β).

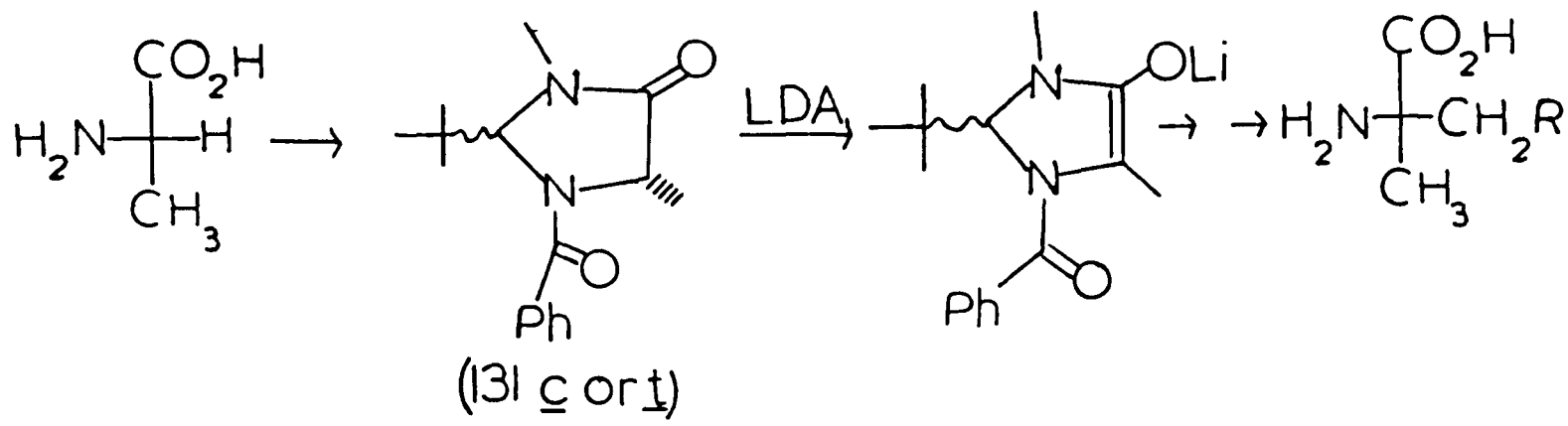


(129)

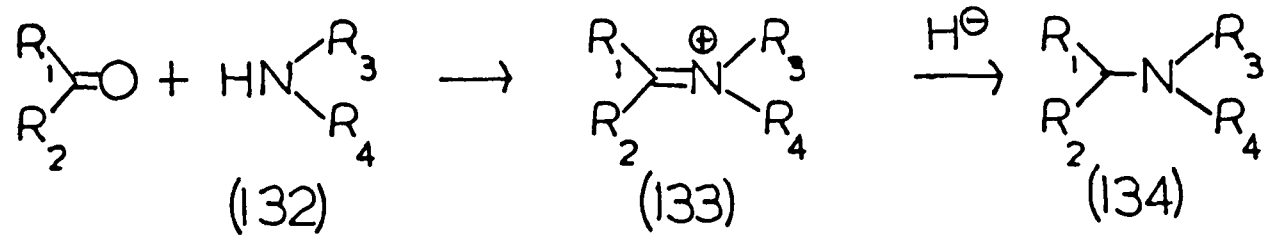
Amongst chiral synthetic targets the α-amino acids, and unusual variants of them, are increasingly important. Methods for their α-alkylation have been developed other than application of the methods discussed above. For example, Schöllkopf has developed the use of the bislactim ethers (130) of the 2,5-diketopiperazines formed by the condensation of two amino acids.[165] The best enantiomeric excesses were obtained for R_1 = t-butyl or isopropyl. Both product enantiomers can be synthesised by choice of the appropriate co-coupling amino acid isomer. Seebach has also developed a method based on pivaldehyde N,N - acetals (131) which allow retention or inversion of the acid stereochemistry by using the <u>cis</u>- or <u>trans</u>- isomers (131) respectively.[166]



(130)



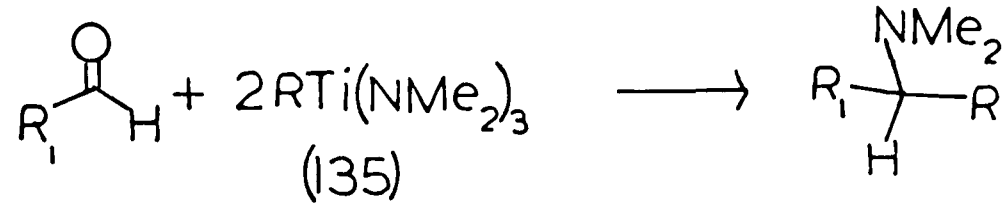
None of these methods involves the transformation of a carbonyl (14) to an amine (122). There is a method which achieves a similar transformation giving rise to amines (122, R_3 = H). This is reductive amination where the carbonyl (14) reacts with an amine (132) to generate an iminium ion (133). This is then reduced to give the amine (134) by using hydrogen and a catalyst, formic acid (Wallach reaction), or in situ sodium cyanoborohydride.[167] The Leuckart reaction involves direct reaction between the carbonyl and a formamide[168] instead of the sequential reaction with an amine followed by formic acid.



Reduction of other nitrogen containing species has also been used to prepare amines. Nitro-compounds have been mentioned, but oximes, hydrazones and semicarbazones are all reducible with zinc in acid or with hydrogen over Raney-nickel.[169]

The proposed transformation of carbonyl (14) to amine (122) by azo-anion methodology involves geminal alkylative amination. There is

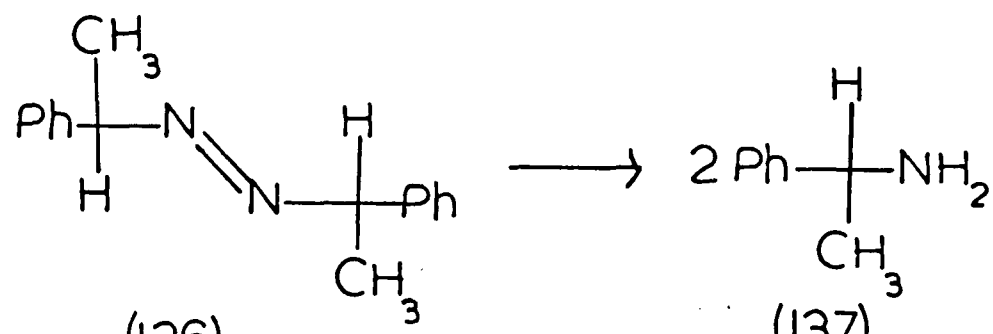
a known method to accomplish this but it is only applicable to non - enolisable aldehydes.[170] This method involves alkylaminotitanium reagents (135).



(135)

B. Reductive N - N Bond Cleavage

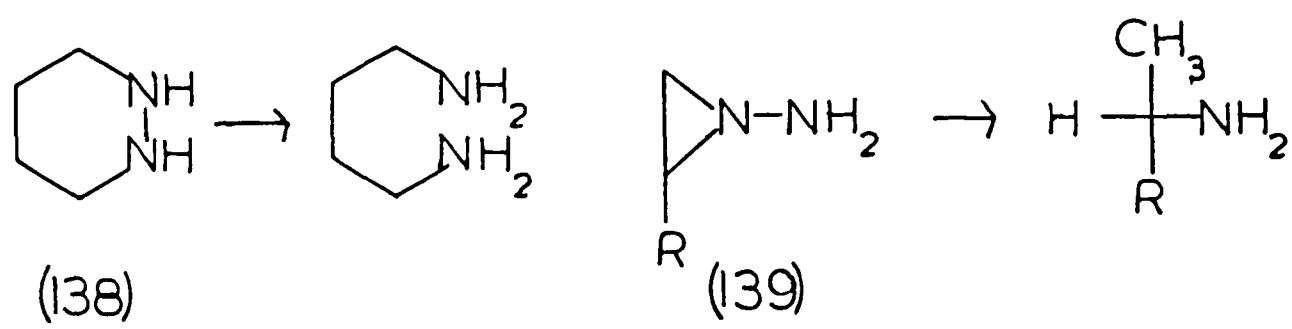
As reductive cleavage of the nitrogen - nitrogen bond of azo-compounds is known,[154,158] this procedure appeared to offer the most straightforward way of achieving conversion of azo-adducts (111) to amines (122). It was,however,clear that most of these reported reductive cleavages had been achieved with azo-benzene substrates and not with azo-alkanes. An exception was described by Greene who reduced azo-alkane (136) to the amine (137) with zinc in aqueous ethanol and glacial acetic acid.[171]



(136) (137)

As the azo double bond is readily reduced to the hydrazo single bond,methods for cleavage of hydrazines would also be applicable to the proposed methodology.[154] Mellor has recently investigated this reaction for activated hydrazines such as 1,2-diacyl- or 1,2-disulphonyl-hydrazines and obtained acceptable N - N cleavage with sodium,in liquid

ammonia or ethanol, aluminium amalgam, zinc in acetic acid or Raney-nickel depending on the actual hydrazine used.[172] For unactivated substrates more vigorous conditions are usually necessary. Feuer has used excess borane (10 fold, 65°C) to cleave cyclic 1,2-dialkylhydrazines (e.g. 138) to the amines.[173] Catalytic reduction has been successfully employed in some cases[174] and Raney-nickel with hydrazine has been used to cleave 1,1-dialkylhydrazines (e.g. 139) to an amine.[175]



(138) (139)

With this broad range of methods available we considered that azo-anion methodology was well suited for amine production via the application of a novel ∝ -aminocarbanion equivalent.

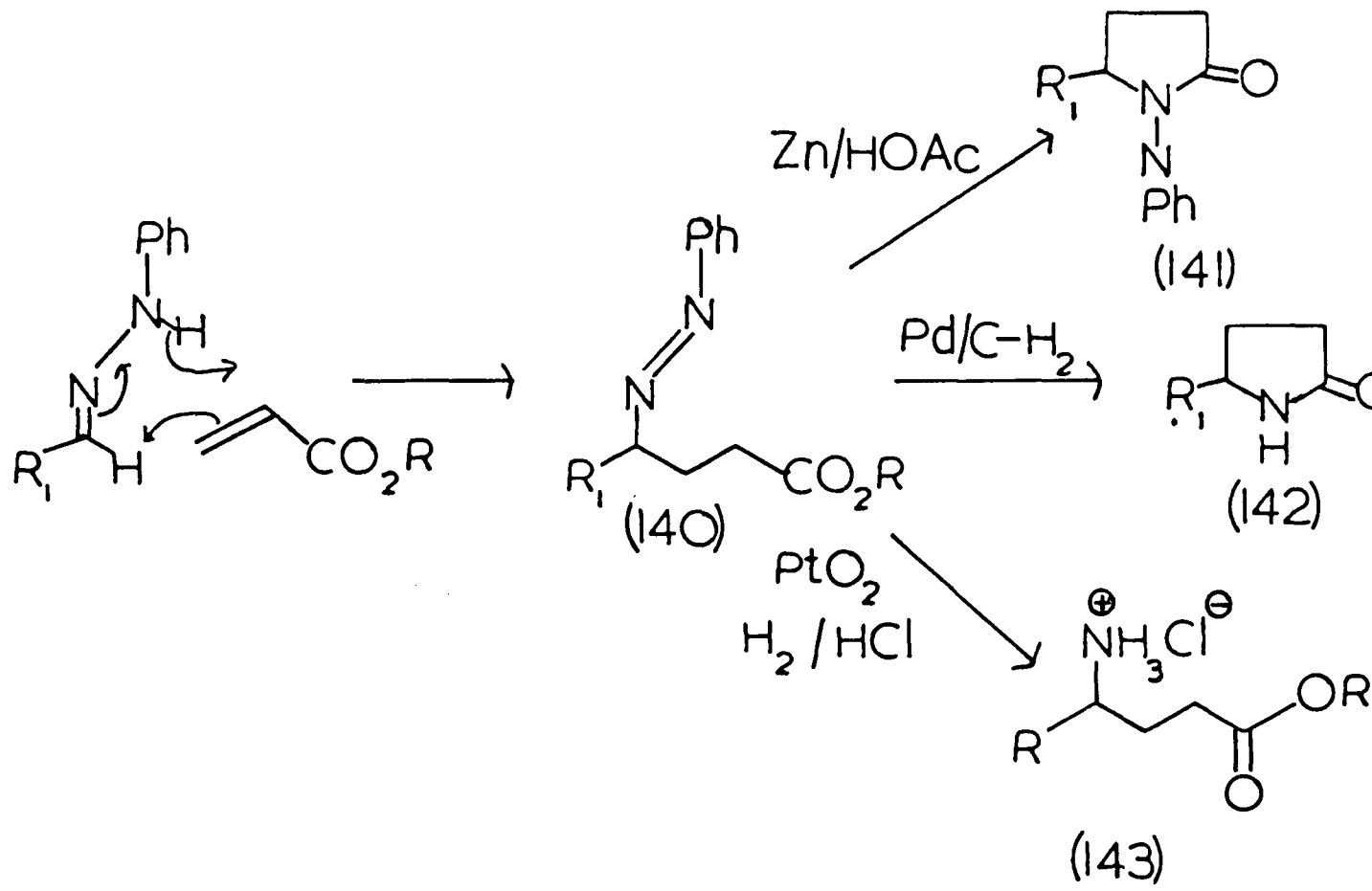
C. Some Reductive Cleavages of Azo-Compounds

i) Benzhydryl Azo-Compound (110)

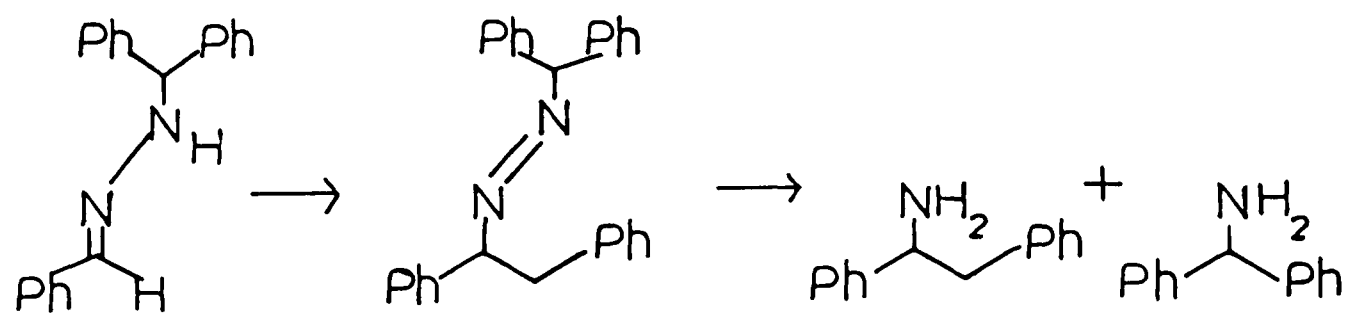
Phenylhydrazones of aldehydes undergo thermal ene reactions with acrylates and acrylonitrile.[90,176] The resulting azo-adducts (140) were found to be reducible to give products (141 - 143) which depended on the exact conditions used (Scheme 54).[90]

The azo-compound (110) generated by benzylation of benzaldehyde benzhydrylhydrazone (28e) was isolated in low yield (chap. IV, sect.E iia) but sufficient material was available to attempt an N - N cleavage reaction. The azo-alkane (110) was dissolved in methanolic hydrogen chloride and treated with Adam's catalyst and hydrogen (1 atm., 20°C, 24h).

That the amines (144) and (145) were produced was suggested by mass spectral evidence [m/e(NH_3 D.C.I.) 197 {MH^+(144), 23%}, and 183 {MH^+(145), 70}] and by observation of the product n.m.r. spectrum [δ_H (CD_3OD, $C\underline{H}D_2OD$ = 3.305 p.p.m.) (144) 2.80 - 3.05 (m,$C\underline{H}_2$), 3.95 - 4.25 (m, $C\underline{H}N$) ; (145) 5.45 (s, $C\underline{H}N$)] .



Scheme 54.



Separation of the two amines was not achieved and,owing to the small amounts of material available,derivatisation was not attempted. As the C-alkylation of benzhydrylhydrazones (28) proceeded in only low yield no further work was carried out on this type of azo-adduct cleavage reaction.

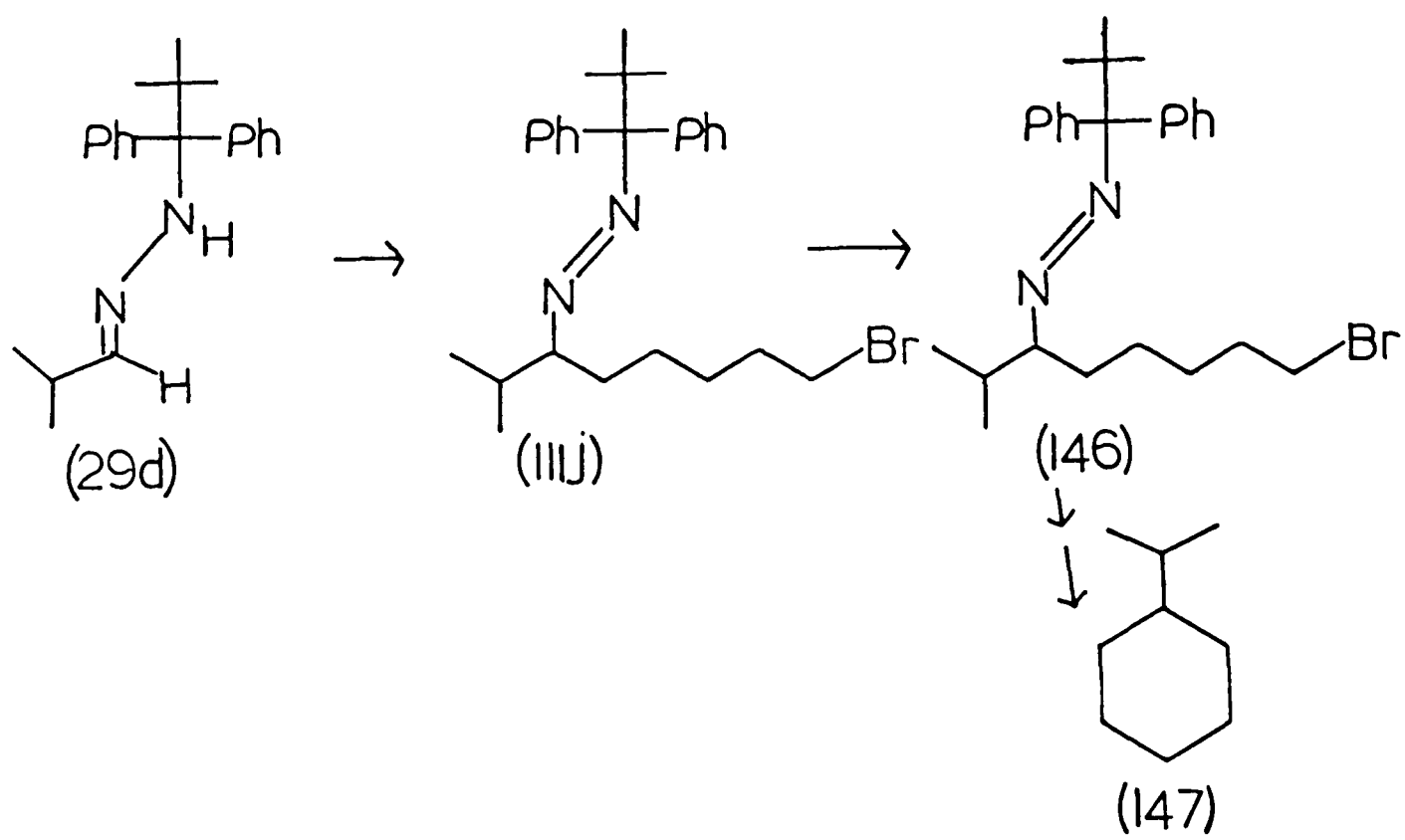
ii) BDP Azo-Alkanes (111)

BDP hydrazones (29) gave good yields of azo-alkanes (111) by a C-addition pathway (chap. IV). The azo-alkane (111a) was dissolved in methanolic hydrogen chloride with Adam's catalyst and treated with hydrogen (1 atm., 20°C, 24h). No amine products were found,however, and the spectroscopic evidence suggested that some starting material was still present.

Perry had also attempted reductive cleavage of azo-compounds derived from various hindered hydrazones and met with little success.[31]

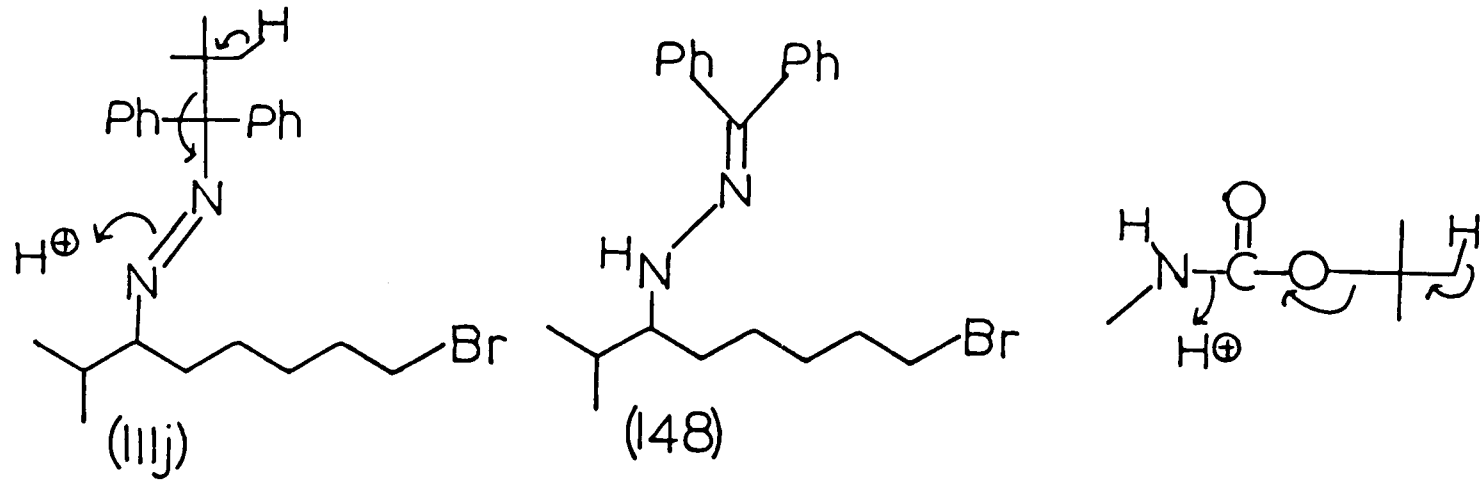
D. Benzophenone Alkylhydrazones

Alkylation of BDP hydrazone (29d) with 1,5-dibromopentane gave a good yield of the bromoazo-alkane (111j) (Table 8). It was hoped to isomerise this azo-alkane (111j) to generate the hydrazone (146) which could then undergo intramolecular alkylation to give the cycloalkane (147) after thermolysis.



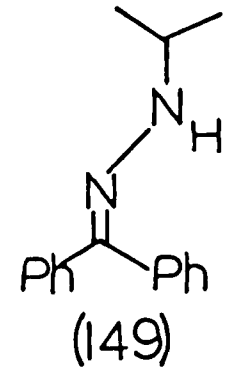
However,when the azo-alkane (111j) was treated with neat trifluoroacetic acid (6h, 20°C) under an inert argon atmosphere (the conditions used to isomerise t-butylazo-compounds[10]) an unexpected reaction took place. The product isolated after evaporation of the residual TFA appeared to have lost the t-butyl group when examined by proton n.m.r. and mass spectroscopy also revealed this loss [m/e (NH_3 D.C.I.) 403/401 (MH^+,4%), 167(100),105 (8), and 91 (28)

Formulation of the product as benzophenone 3-(8-bromo-2-methyl)octylhydrazone (148) was consistent with the data. Presumably this was formed by a reaction similar to that for removal of the t-butyloxycarbonyl protecting groups from amines (Scheme 55).



Scheme 55.

To verify this result azo-alkane (111b) was treated similarly with TFA and benzophenone isopropylhydrazone (149) was isolated. Purification of the concentrated residue was achieved by dissolving in dichloromethane and neutralising remaining traces of TFA with an aqueous sodium bicarbonate wash. The resulting product was essentially pure and good spectroscopic data were obtained.

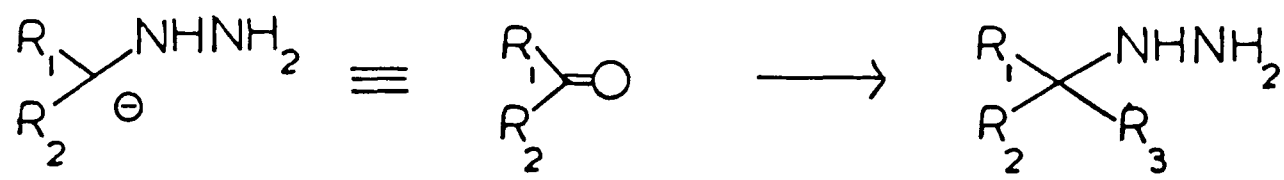


(149)

The benzophenone alkylhydrazones generated by this method were unstable and readily decomposed in air. Storage at -18°C under argon was possible for short periods (3 - 5d) before significant decomposition occurred.

E. An ∝-Hydrazinocarbanion Equivalent

With the availability of benzophenone alkylhydrazones from azo-alkanes (111) by a simple procedure it seemed reasonable to attempt to hydrolyse these compounds and isolate the alkylhydrazines. The overall transformation thus achieved would result in the use of a carbonyl (14) as an ∝-hydrazinocarbanion (150).



(150) (14)

Hydrolysis conditions for t-butylhydrazones had been developed[10] and these utilised oxalic acid in diethyl ether : water (1:1) for 24h at 20°C. These conditions were found to be insufficient for the hydrolysis of the benzophenone alkylhydrazones generated as described. Aqueous hydrochloric acid (2M) in THF failed to effect complete conversion and heating to reflux caused extensive decomposition before complete consumption of starting material occurred.

Concentrated hydrochloric acid in ethanol (1:2) at 20°C had been used for the hydrolysis of a benzophenone alkylhydrazone[177]. After 18h of hydrolysis under these conditions benzophenone isopropyl hydrazone (149) had been completely consumed. The ethanol was evaporated and the aqueous layer extracted with diethyl ether then evaporated.

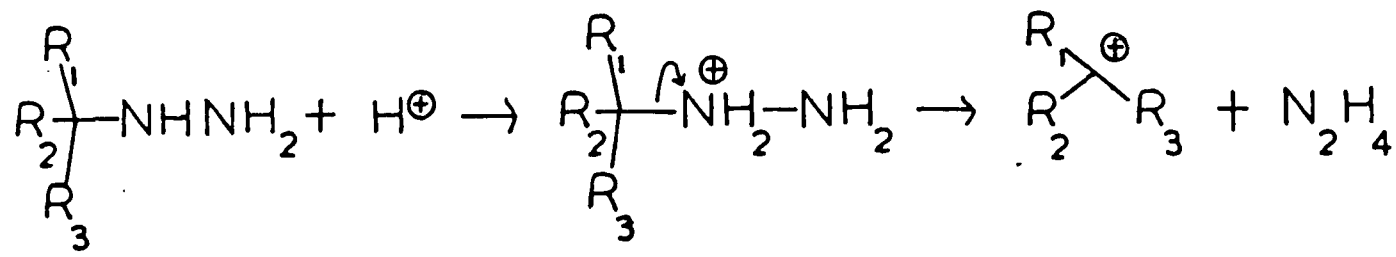
The crude product was recrystallised from ethanol to give isopropyl hydrazine hydrochloride. The diethyl ether layer upon evaporation was shown to contain mainly benzophenone. Table 12 shows the hydrazines prepared by this method and the yields obtained.

R_1	R_2	R_3	Hydrazine	Yield (% from 111)
CH_3	H	CH_3	(149)	60
CH_3	H	$PhCH_2$		74
CH_3	CH_3	CH_3		25[a]
CH_3	CH_3	$PhCH_2$		25

a) t-butylhydrazine has been reported in 60% yield by this procedure.[177] This reaction was only performed on a small scale.

Table 12.

For α-trisubstituted hydrazones the product yields were found to be significantly lower than for α-disubstituted cases. This is because some decomposition of the product hydrazines occurs under the acidic reaction conditions (Scheme 56) and the former hydrazines are particularly susceptible as they give rise to more stable carbonium ions.[177]



Scheme 56.

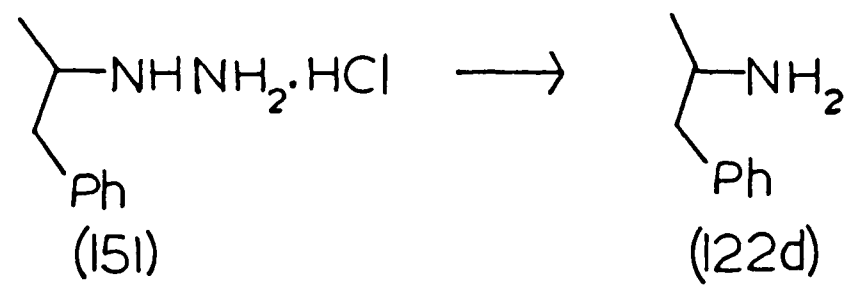
The hydrazines were isolated as their hydrochloride salts from the adopted procedure.

F. An ∝-Aminocarbanion Equivalent

i) Amines from Hydrazines

The goal of an ∝-aminocarbanion equivalent from a carbonyl could be achieved now by simply cleaving the hydrazo bond of the hydrazines produced by the above procedure (sect. E). Raney-nickel and hydrazine in combination had been recently reported to effect this transformation[178] and therefore was attempted.

Thus (1-benzylethyl)hydrazine (151), as a hydrochloride salt, was added to a methanol suspension of Raney-nickel with hydrazine and after 4 - 5h the starting material was observed to have been consumed (t.l.c. monitoring). The nickel was filtered off and the volume reduced before partitioning between ethyl acetate and water. Amphetamine (122d) was isolated in moderate yield from the organic layer.



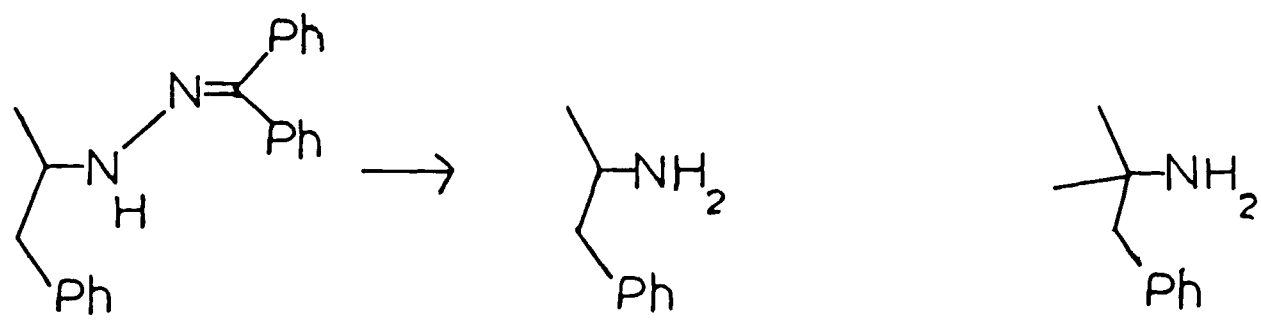
(151) (122d)

ii) A One-Pot Amine Synthesis

As the required reductive cleavage had been achieved in acceptable yield we considered that use of hydrogen over palladium might achieve a similar reaction. Also, the acid conditions used to avoid catalyst problems with the substrate could achieve the hydrolysis of the benzophenone alkylhydrazones at the same time. If the reductive cleavage of the alkylhydrazine to the amine was faster than the reduction of the benzophenone alkylhydrazone to an N,N'-alkylbenzhydrylhydrazine, a one-pot reaction should be feasible.

When the benzophenone alkylhydrazone (152) was dissolved in

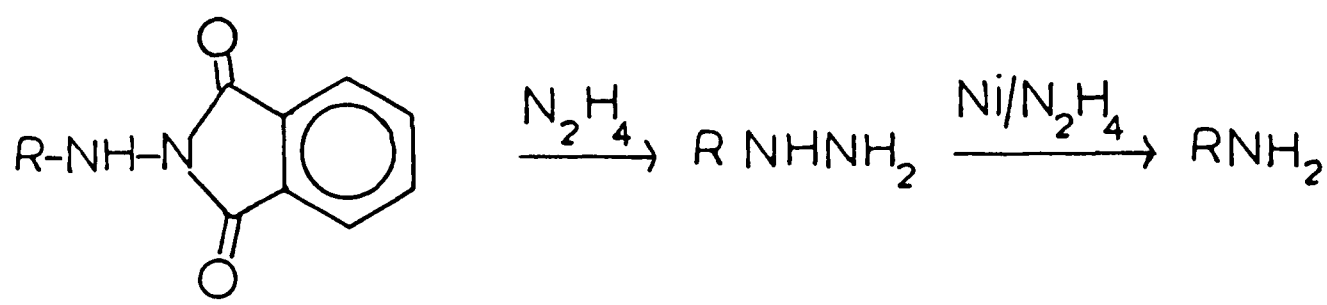
ethanol and concentrated hydrochloric acid and treated with 10% palladium on charcoal under hydrogen (50 p.s.i., 45°C, 20h) the amine (122d) was indeed produced. 2-Methyl-1-phenyl-2-propylamine (122a) was also prepared in good yield by this procedure.



(152) (122d) (122a)

The work-up involved filtration through Celite, evaporation then partitioning between diethyl ether and water. The aqueous layer was evaporated and the residue recrystallised from ethyl acetate to yield the amine (122). The organic layer was found to contain mainly diphenylmethane, presumably from benzophenone by reduction.

The mechanism postulated for this reaction was for a hydrolysis to the hydrazine and subsequent reductive cleavage to the amine. This has literature precedent in the reductive cleavage of N-phthalimido-amines (Scheme 57).[178]



Scheme 57.

It was found that some reactions gave poor yields of amines by the above procedure. This was attributed to a poor hydrolysis relative to hydrogenolysis rate. If this is so, a lower pressure of hydrogen

should work better. Indeed the reaction at one atmosphere of hydrogen (50°C, 20h) gave amines (122) in respectable yields. This was adopted as the standard procedure and both the amines prepared by the higher pressure route were shown to give equally good yields by the new procedure. Table 13. shows the amines (122) prepared by this procedure and the yields obtained. The yields for the overall conversion of carbonyl (14) to amine (122) are also given.

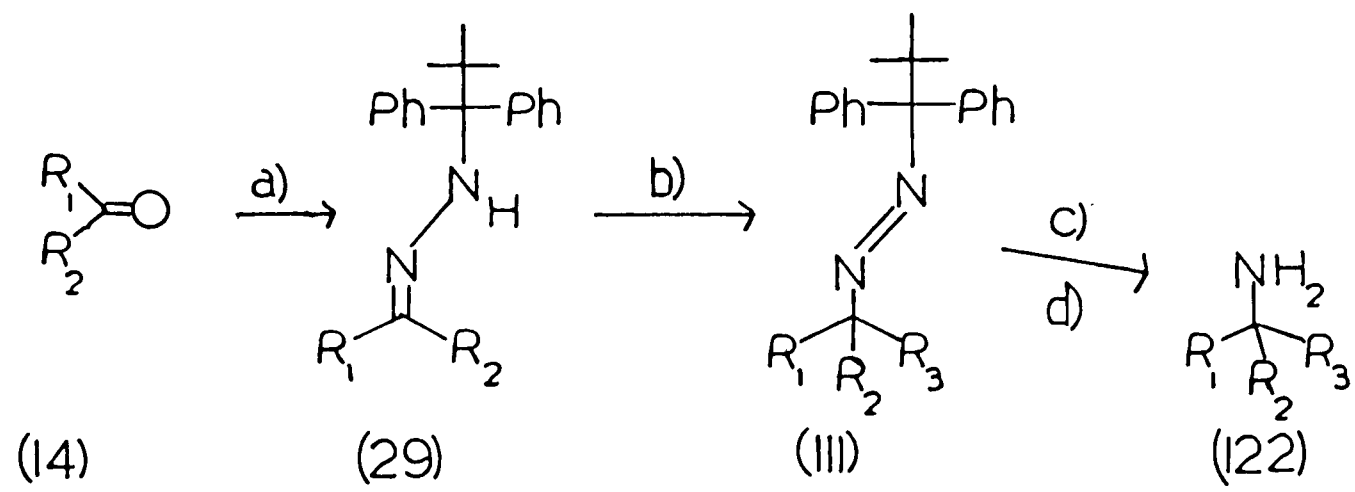
	R_1	R_2	R_3	Yield (122)(%)	(14)-(122)(%)
a)	CH_3	CH_3	$PhCH_2$	67[a]	54
b)	$-(CH_2)_5-$		$PhCH_2$	71[a]	52
c)	$-(CH_2)_{11}-$		CH_3	38[a]	31
d)	CH_3	H	$PhCH_2$	68[b]	47
e)	CH_3	H	$nC_{10}H_{21}$	68[a]	45

a) isolated as hydrochloride salt ; b) isolated as oxalate salt.

Table 13.

In order to prove that the hydrazines were the direct precursors of the amines (122) 1-phenyl-2-propylhydrazine (151) was treated under the standard amine-forming conditions. Amphetamine (122d) was indeed produced and isolated as its oxalate salt, the hydrochloride being too hygroscopic to handle easily.

The overall conversion of a carbonyl (14) to an amine (122) has therefore been achieved. The yields shown in the table demonstrate the reasonable efficiency of this procedure. Only one step in the sequence (Scheme 58) required chromatography and the final product was simply purified by recrystallisation of a hydrochloride salt.



(14) (29) (111) (122)

a) chap. 2 ; b) chap. 4, chromatography ; c) TFA
d) H_2–Pd/C

Scheme 58.

CHAPTER VI - EXPERIMENTAL

General Procedures

Reactions involving air or water sensitive reagents were carried out under an atmosphere of dry nitrogen unless otherwise stated. The nitrogen was dried by passage through a column closely packed with anhydrous calcium chloride and anhydrous silica gel.

Reagents were purified by literature procedures[179] unless otherwise stated. Aldehydes were distilled from anhydrous calcium chloride, ketones from phosphorus pentoxide, and stored over 4Å molecular sieves. Alkyl halides were dried over anhydrous calcium chloride, then distilled and stored over 4Å molecular sieves in darkness.

Alkyl lithium reagents (n-butyl lithium in hexane, Aldrich ; methyl lithium in diethyl ether, Aldrich) were titrated against 1,3-diphenylacetone tosylhydrazone (J.Organomet.Chem., 1980, 186, 155) and added to reaction mixtures via syringe.

Diethyl ether and light petroleum (b.p. 30 - 40°C) were distilled prior to use for chromatography.

THF for organometallic reactions was dried by refluxing with potassium and benzophenone and distilled. Diethyl ether for Grignard reactions was dried over sodium wire (>24h).

Reaction mixtures were concentrated by evaporation on a Büchi Rotavapor R ; further traces of solvent were removed from involatile materials by evaporation at lower pressure (<2 mmHg).

T.l.c. was carried out on Merck 5554 aluminium backed Si_{F254} plates, eluants are given in parenthesis. Visualisation was by u.v. light and acid charring [dodecamolybdophosphoric acid in ethanol (5% w/v)].

Column chromatography was carried out using Merck flash silica gel 40 - 63 um in a 4 cm diameter column.

P.l.c. was carried out on Merck Kieselgel 60_{F254} 20 x 20 x 0.1

cm glass plates prepared by Mr R.F.Prior of the Dyson Perrins Laboratory, Oxford.

Temperatures were recorded in degrees Celsius and low temperatures were recorded as equilibrium coolant bath temperatures.

Melting points (m.p.) were determined by use of a Büchi 510 capillary melting point apparatus and are uncorrected.

Infra-red ($\nu_{max.}$) spectra were recorded on a Perkin-Elmer 681 instrument and are referenced to polystyrene (1602 cm^{-1}). Broad (br), medium (m), strong (s) and significant weak (w) bands are reported and quoted to $\pm$ 5 cm^{-1} (4000 - 2000 cm^{-1}) and $\pm$ 2 cm^{-1} (2000 - 600 cm^{-1}).

Proton n.m.r. spectra (δ_H) were recorded on Bruker WH 300 or Perkin-Elmer R 24B spectrometers operating at 300 MHz and 60 MHz respectively. The spectra were recorded in deuteriochloroform ($CDCl_3$) unless otherwise stated. Residual protiated solvent was used as a reference ($C\underline{H}Cl_3$ = 7.27 p.p.m.) and chemical shifts are expressed in p.p.m. on the δ scale relative to tetramethylsilane. Coupling constants ($\underline{J}$) are quoted to $\pm$ 0.5Hz. Each δ is followed by integral,spin multiplicity, $\underline{J}$ (if applicable) and assignment of signal (if known) all in parenthesis. Multiplicities are recorded as br (broad peak), s (singlet), d (doublet), t (triplet), q (quartet), and m (multiplet).

Carbon - 13 n.m.r. (δ_C) spectra were recorded on a Bruker AM 250 spectrometer operating at 62.7 MHz. Spectra were recorded in deuteriochloroform ($CDCl_3$) in broad band decoupled and continuous wave modes,unless otherwise stated. Solvent was used as reference ($\underline{C}DCl_3$ about 77.00 p.p.m.) and chemical shifts are expressed in p.p.m. on the δ scale relative to tetramethylsilane. δ is followed by the continuous wave multiplicity (if available) and the assignment,both in parenthesis.

Mass spectra (m/e) were recorded by the Mass Spectrometry Service,Dyson Perrins Laboratory,on V.G. Analytical 16F, 30F, or ZAB 1F

spectrometers. High resolution mass spectra were recorded on the ZAB 1F instrument.

Elemental Microanalysis were carried out by Dr F.B.Strauss of the Dyson Perrins Laboratory,or by the Microanalysis Service of Manchester University. Solids were recrystallised,liquids distilled, and oils purified by p.l.c. prior to microanalysis.

Preparation of Tritylhydrazine (17) Hydrochloride

Triphenylmethyl chloride (100g, 0.35 mol) was added to a solution of hydrazine hydrate (120 ml, excess) in THF (500 ml) and the mixture stirred under reflux for 6 - 18 h. The solution was cooled to 25°C,concentrated to half volume,and extracted into diethyl ether (2 x 150 ml). The organic layer was washed with brine (2 x 30 ml), dried (Na_2SO_4),filtered and treated with a solution prepared from hydrogen chloride (g) in methanol (55 ml, 6.5 M, 1.0 equiv.). The solution was cooled to 0°C for 24h,and the solid filtered off and washed with diethyl ether to give tritylhydrazine (17) hydrochloride (96.0g, 86%),m.p. 109 - 112°C (Lit.,[34] 108 - 113°C).

Preparation of Diphenyl-4-pyridylmethylhydrazine (18) Hydrochloride

A solution of 4-benzoylpyridine (25.0g, 0.13 mol) in dry diethyl ether (330 ml) was added to a solution of phenylmagnesium bromide from bromobenzene (0.28 mol) and magnesium (0.26 mol) in diethyl ether (150 ml) at a rate to maintain reflux. The solution was then refluxed for 2h,stirred at 20°C for 10h,then poured into ice-cold hydrochloric acid (110 ml,1.3 mol). The aqueous layer was separated, then basified to pH 9 with 0.88 ammonia. The solid product was filtered off,washed with water and benzene then dried to give diphenyl-4-pyridyl methanol (21) (29.3g, 82%),m.p. 230 - 232°C (Lit.,[35] 235°C) ; ν_{max} (nujol) 3150 m (O-H) cm^{-1}.

Diphenyl-4-pyridylmethanol (21) (25.0g, 96 mmnol) was converted to diphenyl-4-pyridylmethylchloride hydrochloride (22) (25.4g, 84%) by a modification to the procedure of Young[36] in which a shorter reaction time (16h) was employed,m.p. 174 - 176°C (Lit.,[36] 134 - 135°C) ; δ_H (D_2O, HOD = 4.60 p.p.m.) 7.10 - 7.15 (4H,m,phenyl-H), 7.22 - 7.25 (6H,m,phenyl-H), 7.86 (2H,d,J 7Hz,pyridyl-H), and 8.53 (2H,d,J 7Hz, pyridyl-H).

Diphenyl-4-pyridylmethylchloride hydrochloride (22) (24.0g, 76 mmol) was dissolved in dry THF (250 ml) and excess anhydrous hydrazine (24 ml) added.The mixture was stirred at 65°C for 12h,cooled and extracted into diethyl ether (2 x 100 ml). The organic layer was washed with brine (2 x 30 ml),dried (Na_2SO_4),and treated with a solution prepared from hydrogen chloride (g) (175 mmol) in diethyl ether. The white solid was filtered off,washed with diethyl ether (200 ml) and dried to yield diphenyl-4-pyridylmethylhydrazine (18) dihydrochloride (25.4g, 96%) ; m.p. 182 - 184°C ; $\nu_{max.}$(nujol) 3400 wbr, 3090 m, 3060 m, 3020 m, 1600 m, 765 m, and 700 m cm^{-1} ; δ_H (CD_3OD, $C\underline{H}D_2OD$ = 3.305 p.p.m.) 7.39 - 7.56 (10H, m, phenyl-H), 8.32 (2H,d, J 6Hz, pyridyl-H), 8.86 (2H,d, J 6Hz, pridyl-H) ; m/e (positive argon F.A.B.) 276 ($C_{18}H_{18}N_3^+$, 17%), 262 (75), and 246 (100).

Preparation of Benzhydrylhydrazine (19) Hydrochloride

Chlorodiphenylmethane (50 ml, 280 mmol) was added to a solution of hydrazine hydrate (50 ml, excess) in dry THF (400 ml) and the mixture stirred at 50°C under argon for 16h,then heated under reflux for 5h. The solution was cooled,reduced to half volume,and extracted into diethyl ether (2 x 200 ml). The organic layer was washed with brine (2 x 20 ml),dried (Na_2SO_4),filtered and a solution of hydrogen chloride (g) in methanol (50 ml, 6.0 M, 1.1 equiv.) was added. The product was filtered off,washed with diethyl ether and dried under vacuum to give the title compound (30.3g, 46%) as a white solid,m.p. 207 - 208°C (Lit.,[180] 211°C) ; $\nu_{max.}$ (nujol) 3230 s (N-H), 3080 m, 3060 m, 3030 m, 1595 s, 1535 s, 745 m, and 700 s cm^{-1}; δ_H (CD_3OD, $C\underline{H}D_2OD$ = 3.305 p.p.m.) 3.34 (1H, s, $C\underline{H}Ph_2$), 7.28 - 7.37 (6H, m, phenyl-H), 7.45 - 7.53 (4H, m, phenyl-H) ; m/e (NH_3 D.C.I.) 199 ($C_{13}H_{15}N_2^+$, 6%), 167 (Ph_2CH^+, 100), 165 (15).

Preparation of t-Butyldiphenylmethylhydrazine (20) Hydrochloride

A solution of ethyl pivalate (57.7 ml, 380 mmol) in dry diethyl ether (400 ml) was added to a solution of phenylmagnesium bromide [from bromobenzene (82.6 ml, 800 mmol) and magnesium (18.8g, 780 mmol) in diethyl ether (500 ml)] over 1h at reflux. The mixture was heated under reflux for a further 1h then stirred at 20°C for 18h. Saturated ammonium chloride solution was added to neutralise and the residue was extracted into diethyl ether (3 x 200 ml). The organic layer was dried ($MgSO_4$), filtered, and evaporated. The residue was distilled to give t-butyldiphenylmethylcarbinol (24) (65g, 70%) as a colourless liquid, b.p. 150 - 152°C at 3 mmHg (Lit.,[38] 148 - 150°C at 2.5 mmHg); $\nu_{max.}$ (film) 3500 mbr, (O-H), 3090 w, 3060 m, 3030 m, 2990 s, 2910 m, 2880 m, 1600 m, 1490 m, 1450 s, 755 s, 705 s, and 640 m cm^{-1}; δ_H 1.13 (9H, s, t-Bu), 2.23 (1H, s, OH), 7.10 - 7.70 (10H, m, phenyl-H).

Thionyl chloride (17 ml, 230 mmol) was added dropwise to a stirred solution of t-butyldiphenylmethylcarbinol (24) (50g, 210 mmol) in chloroform (50 ml) and the solution was then heated under reflux for 1h and cooled over 2h. The solvent was evaporated and the residual yellow oil used without further purification. [A small sample was recrystallised from light petroleum to give large colourless crystals of t-butyldiphenylmethylchloride (25), m.p. 70.0 - 71.5°C (Lit.,[181] 70.5 - 71.5°C).]

The crude chloride (25) was dissolved in dioxan (400 ml) with anhydrous hydrazine (50 ml, excess) and heated under reflux for 3.5d. The solution was cooled, reduced to half volume and extracted into diethyl ether (2 x 150 ml). The organic layer was dried (Na_2SO_4), filtered, and a solution of hydrogen chloride (g) in diethyl ether (50 ml, 6 M, 300 mmol) was added. After 20 min the precipitate was

filtered off,washed with diethyl ether and dried under vacuum to yield t-butyldiphenylmethylhydrazine (20) hydrochloride (36.1g, 60%) as a white solid,m.p. 170 - 171°C ; $\nu_{max.}$ (nujol) 3340 m, 3320 m, 3260 m (N-H), 3050 m, 3040 m, 3020 m, 1605 m, 1590 m, 1148 m, 1132 m, 780 m, 772 m, 750 s, and 710 s cm^{-1}; δ_H (CD_3OD, $C\underline{H}D_2OD$ = 3.305 p.p.m.) 1.15 (9H, s, t-Bu), 7.34 - 7.61 (10H, m, phenyl-H) ;m/e (NH_3 D.C.I.) 255 ($C_{17}H_{23}N_2^+$, 49%), 238 (69), 223 ($C_{17}H_{19}^+$, 96), 197 (55), 182 (100), 105 (70), and 57 (50).

General procedure for the preparation of Tritylhydrazones (26)

The following procedure for the preparation of acetone tritylhydrazone (26f) is typical.

Tritylhydrazine (17) hydrochloride (10.0g, 32 mmol) was dissolved in methanol (200 ml) and a solution of sodium formate (3.28g, 48 mmol) in water (15 ml) was added. Acetone (2.60 ml, 35 mmol) was added and the mixture stirred under argon for 2h in the dark. The solid precipitate was filtered off,washed with water and light petroleum (10 ml) in sequence,then dried under vacuum to yield acetone tritylhydrazone (26f) (9.10g, 90%) as a white solid,m.p.119 - 120°C ; $\nu_{max.}$ ($CHCl_3$) 3060 w, 2960 s, 2930 s, 2860 s, 1597 m, 1487 m, 1445 s, 760 s, 720 s, and 705 s cm^{-1}; δ_H 1.74 (3H, s, Me), 1.80 (3H, s, Me), 5.38 (1H, br, N$\underline{H}$), and 7.19 - 7.46 (15H, m, Ar-H) ; δ_C 15.63 (q,Me), 25.30 (q, Me), 75.50 (s, $\underline{C}Ph_3$), 126.43, 127.60, 129.16 (3 x d, phenyl $\underline{C}$-H), 145.66, 146.17 (2 x s, phenyl-ipso-$\underline{C}$, $\underline{C}$=N) ; m/e (NH_3 C.I.) 315 (MH^+, 11%), 243 (Ph_3C^+, 100), and 165 (27) ; (E.I.) 243 (100%), and 165 (60).

Those hydrazones which did not crystallise were extracted into dichloromethane,dried (Na_2SO_4),and evaporated to give oily products. Further purification could be achieved by rapid flash chromatography on silica gel.

Acetaldehyde tritylhydrazone (26a) was prepared from tritylhydrazine hydrochloride (10.0g, 32 mmol) and acetaldehyde (2.35 ml, 42 mmol) as a white solid (7.80g, 81%), m.p. 112 - 114°C as a mixture of isomers (1:1) ; $\nu_{max.}$ (nujol) 3090 s, 3060 s, 3025 s, 1597 m, 760 s, and 705 s cm^{-1}; δ_H 1.75, 1.77 (3H,2 x d, J 5.5Hz, Me), 6.70, 7.00 (1H, 2 x q, J 5.5Hz, N=CH), 7.22 - 7.40 (15H, m, Ar-H) ; δ_C 12.27, 18.00 (2 x q, Me), 72.54, 72.58 (2 x s, CPh_3), 126.43,126.57,127.61, 127.71,128.93,and 129.05 (6 x d, phenyl-C), 137.79, 140.06 (2 x d, CH=N), 145.51, and 145.78 (2 x s, ipso-C) ; m/e(NH_3 C.I.)301 (MH^+, 38%), 243 (Ph_3C^+, 100), 183 (10), 165 (19), and 59 (15).

2-Methylpropanal tritylhydrazone (26b) was prepared from tritylhydrazine hydrochloride (2.50g, 8.0 mmol) and 2-methylpropanal (0.75 ml, 9.0 mmol) as a yellow oil (2.15g, 81%) by extraction into dichloromethane,as a mixtures of isomers (17:3). $\nu_{max.}$ (film) 3085 m, 3060 s, 3020 m, 2960 s, 2930 s, 2870 s, 1598 m, 1490 m, 1448 m, 900 m, 760 m, 745 m,and 700 s cm^{-1}; δ_H 0.87, 1.16 (6H, 2 x d, J 7.5Hz, CMe_2), 2.25 -2.39, 2.53 - 2.70 (1H, m, $CHMe_2$), 6.82, 6.37 (1H, 2 x d, J 7.5Hz, CH=N), 7.18 - 7.44 (15H, m, Ar-H) ; δ_C 20.08 (q, Me), 30.98 (d, CH), 72.89 (s, CPh_3), 126.42, 127.56, 129.17 (3 x d, phenyl-C), 145.56 (s, ipso-C), 150.10 (d, CH=N) ; m/e (NH_3 D.C.I.) 329 (MH^+, 2%), 243 (Ph_3C^+, 100).

Pentanal tritylhydrazone (26c) was prepared from tritylhydrazine hydrochloride (10.0g, 32 mmol) and pentanal (3.72 ml, 35 mmol) as a waxy solid (9.58g, 87%) by extraction,as a mixture of isomers (2:1). $\nu_{max.}$ (nujol) 3090 s, 3055 s, 3030 s, 3020 s, 1597 m, 760 s, 745 s, 720 s, and 705 s cm^{-1}; δ_H 0.83, 0.96 (3H, 2 x t, J 7.5Hz, Me), 1.10 - 1.64 (4H, brm, 2 x CH_2), 2.05 - 2.20 (2H, m, CH_2), 6.95, 6.57 (1H, 2 x t, J 6Hz, CH=N), 7.20 - 7.50 (15H, m, phenyl-H) ; δ_C 13.78 (q, Me), 21.83, 22.45, 25.83, 28.25, 28.94, 31.61 (6 x t, CH_2), 72.73 (s, CPh_3),

126.43, 126.57, 127.61, 127.73, 128.96, 129.11 (6 x d, phenyl-C), 143.89, 144.85 (2 x d, CH=N), 145.52, 145.78 (2 x s, ipso-C) ; m/e (NH_3 C.I.) 343 (MH^+, 10%), and 243 (Ph_3C^+, 100).

2-Octanone tritylhydrazone (26g) was prepared from trityl hydrazine hydrochloride (5.00g, 16 mmol) and 2-octanone (2.80 ml, 19 mmol) as a pale yellow viscous oil (2.25g, 36%) after flash chromatography on silica gel (diethyl ether - light petroleum / 3:17). $\nu_{max.}$ (film) 3060 w, 2965 s, 2930 s, 2850 s, 1597 w, 1486 w, 760 s, and 700 s cm^{-1}; δ_H 0.85 (3H, t, Me), 1.02 - 1.36 (8H, m, 4 x CH_2), 1.71 (3H, s, Me), 2.07 (2H, t, J 7Hz, CH_2), 5.40 (1H, br, NH), 7.13 - 7.55 (15H,m, Ar-H) ; δ_C 14.10 (q, Me), 14.34 (q, Me), 22.57, 26.48, 28.56, 31.78, 38.80 (5 x t, CH_2), 72.64 (s, CPh_3), 126.38, 127.54, 129.23 (3 x d, phenyl-C) ; m/e (NH_3 C.I.) 385 (MH^+, 12%), 243 (Ph_3C^+, 100), and 165 (23).

Butanone tritylhydrazone (26h) was prepared from trityl hydrazine hydrochloride (5.00g, 16 mmol) and butanone (1.73 ml, 18 mmol) as a white solid (2.60g,49%),m.p. 128 - 130°C, as a mixture of isomers (4:1) ; $\nu_{max.}$ (nujol) 3090 s, 3060 s, 3025 s, 1598 m, 1445 m, 760 s, 720 s, and 705 s cm^{-1}; δ_H 0.89, 1.06 (3H, 2 x t, J 8Hz, Me), 1.75, 1.80 (3H, 2 x s, Me), 2.09 - 2.19 (2H, m, CH_2), 5.46, 5.54 (1H, 2 x brs, NH), 7.22 - 7.47 (15H, m, Ar-H) ; δ_C 11.04 (q, Me), 14.19 (q, Me), 32.07 (t, CH_2), 72.68 (s, CPh_3), 126.35, 127.49, 127.54, 127.85, 128.84, 129.20 (6 x d, phenyl-C), 142.40, 146.16, 149.57 (3 x s, ipso-C, C=N) ; m/e (NH_3 C.I.) 243 (Ph_3C^+, 100%).

Cyclohexanone tritylhydrazone (26i) was prepared from tritylhydrazine hydrochloride (20.0g, 64 mmol) and cyclohexanone (7.26 ml, 70 mmol) as a white solid (19.5g, 86%) m.p. 135 - 137°C ; $\nu_{max.}$ ($CHCl_3$) 3061 w, 3005 s, 2940 s, 2830 s, 1598 w, 1488 w, and 698 s cm^{-1}; δ_H 1.41 - 1.70 (6H, br, 3,4,5-CH_2), 2.12, 2.33 (4H, 2 x t, J 6Hz, 2,6-CH_2), 5.60 (1H, br, NH), 7.19 - 7.38 (15H, m, Ar-H) ; δ_C 25.13

(t, $\underline{C}H_2$), 25.94 (2 x t, unresolved, $\underline{C}H_2$), 27.19, 35.62 (2 x t, $\underline{C}H_2$), 72.30 (s, $Ph_3\underline{C}$), 126.38, 127.58, 129.20 (3 x d, phenyl-$\underline{C}$), 146.02, 152.01 (2 x s, ipso-$\underline{C}$, $\underline{C}$=N) ; m/e (NH_3 C.I.) 355 (MH^+, 17%), 243 (Ph_3C^+, 100), and 165 (18) ; (E.I.) 243 (100%), and 165 (52).

Cyclododecanone tritylhydrazone (26j) was prepared from tritylhydrazine hydrochloride (10.0g, 32 mmol) and cyclododecanone (6.37g, 32 mmol) as a white solid (12.3g, 87%), m.p. 142 - 143°C ; $\nu_{max.}$ ($CHCl_3$) 3061 w, 3010 s, 2920 s, 2850 s, 1565 m, 1468 m, 1448 m, 910 s, and 705 s cm^{-1}; δ_H 0.85 - 0.94 (2H, m, $C\underline{H}_2$), 1.15 - 1.60 (16H, br, 8 x $C\underline{H}_2$), 2.15, 2.24 (4H, 2 x t, J 7Hz, 2,12-$C\underline{H}_2$), 5.55 (1H, br, N$\underline{H}$), 7.20 - 7.33 (10H, m, Ar-$\underline{H}$), 7.43 - 7.57 (5H, m, Ar-H) ; δ_C 22.40, 22.74, 23.27, 23.42 (4 x t, $\underline{C}H_2$), 23.53 (2 x t, unresolved, $\underline{C}H_2$), 24.83, 25.89, 26.30, 27.66, 31.94 (5 x t, $\underline{C}H_2$), 72.54 (s, $\underline{C}Ph_3$), 126.17, 127.52, 129.20 (3 x d, phenyl-$\underline{C}$), 146.43, 151.14 (2 x s, ipso-$\underline{C}$, $\underline{C}$=N) ; m/e (NH_3 C.I.) 439 (MH^+, 9%), 243 (100), 184 (20), and 165 (18).

General procedure for the preparation of DPP Hydrazones (27)

The following method for the preparation of acetone DPP hydrazone (27f) is typical.

Diphenyl -4- pyridylmethylhydrazine(18) dihydrochloride (10.0g, 29 mmol) was dissolved in methanol (100 ml) and a solution of sodium formate (4.80g, 73 mmol) in water (20 ml) was added. Acetone (2.60 ml, 35 mmol) was added and the mixture stirred under argon for 2h in the dark. The resultant solid was filtered off, washed with water (50 ml) and light petroleum (10 ml) in sequence to give acetone DPP hydrazone (27f) (5.88g, 65%) as a white solid m.p. 124 - 125°C ; $\nu_{max.}$ (nujol) 3200 m, 1595 s, 760 m, and 700 s cm^{-1}; δ_H 1.74 (3H, s, Me), 1.80 (3H, s, Me), 5.30 (1H, brs, N-$\underline{H}$), 7.24 - 7.33 (12H, m, Ar-$\underline{H}$), 8.50 (2H, d, J 6Hz, pyridyl-$\underline{H}$) ; δ_C 15.63 (q, Me), 25.22 (q, Me),

72.02 (s, $\underline{C}Ar_3$), 124.29, 126.93, 127.88, 128.75 (4 x d, aryl-$\underline{C}$), 144.72, 146.81 (2 x s), 149.26 (d, aryl-$\underline{C}$), and 154.66 (s) ; m/e(NH_3 C.I.) 316 (MH^+, 10%), 244 (Ar_3C^+, 100), and 165 (10).

2-Octanone DPP hydrazone (27g) was prepared from DPP hydrazine dihydrochloride (10.0g, 29 mmol) and 2-octanone (5.50 ml, 35 mmol) as a white solid (6.31g, 57%) m.p. 114 - 115°C ; $\nu_{max.}$ (nujol) 3200 m, 3080 w, 3060 w, 3040 w, 3020 w, 1595 s, 775 m, 755 m, 725 m, and 700 s cm^{-1} ; δ_H 0.85 (3H, t, $\underline{J}$ 7Hz, Me), 1.04 - 1.33 (8H, brm, 3,4,5,6-$C\underline{H}_2$), 1.71 (3H, s, Me), 2.07 (2H, t, $\underline{J}$ 7Hz, 2-$C\underline{H}_2$), 5.31 (1H, brs, N-$\underline{H}$), 7.23 - 7.35 (12H, m, Ar-$\underline{H}$), 8.51 (2H, d, $\underline{J}$ 5HZ, pyridyl-$\underline{H}$) ; δ_C 14.07 (q, Me), 14.45 (q, Me), 22.51, 26.30, 28.50, 31.68, 38.71 (5 x t, $\underline{C}H_2$), 72.12 (s, $\underline{C}Ar_3$), 124.31, 126.90, 127.85, 128.79 (4 x d, aryl-$\underline{C}$), 144.78 (2 x s, unresolved), 149.11 (d, pyridyl-$\underline{C}$), 149.81,154.69 (2 x s) ; m/e(NH_3 C.I.) 386 (MH^+, 7%), 244 (Ar_3C^+, 100).

Butanone DPP hydrazone (27h) was prepared from DPP hydrazine dihydrochloride (5.00g, 14 mmol) and butanone (1.60 ml, 18 mmol) as a white solid (2.31g, 47%) m.p. 118 - 120°C ; $\nu_{max.}$ (nujol) 3090 m, 3060 m, 3030 m, 3020 w, 1595 s, 770 m, 760 s, 730 m, and 705 s cm^{-1}; δ_H 0.83 (3H, t, $\underline{J}$ 7Hz, Me), 1.71 (3H, s, Me), 2.07 (2H, q, $\underline{J}$ 7Hz,$C\underline{H}_2$), 5.30 (1H, brs, N-$\underline{H}$), 7.22 - 7.36 (12H, m, Ar-$\underline{H}$), 8.48 (2H, d, $\underline{J}$ 6Hz, pyridyl-$\underline{H}$) ; δ_C 10.95 (q, Me), 14.40 (q, Me), 32.11 (t, $\underline{C}H_2$), 72.29 (s, $\underline{C}Ar_3$), 124.44, 126.99, 127.90, 128.90 (4 x d, aryl-$\underline{C}$), 144.81 (s), 149.11 (d, pyridyl-$\underline{C}$), 150.70, 154.81 (2 x s) ; m/e (NH_3 C.I.) 244 (Ar_3C^+, 14%), 243 (37), 183 (100) and 105 (36).

Cyclohexanone DPP hydrazone (27i) was prepared from DPP hydrazine dihydrochloride (10.0g, 29 mmol) and cyclohexanone (3.63 ml, 35 mmol) as a white solid (5.81g, 57%) m.p. 127 - 129°C ; $\nu_{max.}$ (nujol) 3070 m, 3040 m, 3020 w, 1590 s, 760 m, and 705 s cm^{-1}; δ_H 1.35 - 1.53 (6H, m, 3,4,5-$C\underline{H}_2$), 2.09 (2H, t, $\underline{J}$ 6Hz, $C\underline{H}_2$), 2.17 (2H, t, $\underline{J}$ 6Hz, $C\underline{H}_2$),

5.49 (1H, brs, N-H), 7.15 - 7.29 (12H, m, Ar-H), 8.51 (2H, d, J 6Hz, pyridyl-H) ; δ_C 25.16, 25.83, 25.92, 27.16, 35.53 (5 x t, $\underline{C}H_2$), 72.23 (s, $\underline{C}Ar_3$), 124.31, 126.88, 127.84, 128.81 (4 x d, aryl-C), 144.61 (s), 149.13 (d, pyridyl-C), 153.60, 154.51 (2 x s) ; m/e (NH_3 C.I.) 356 (MH^+, 10%), 244 (Ar_3C^+, 100).

Cyclododecanone DPP hydrazone (27j) was prepared from DPP hydrazine dihydrochloride (5.00g, 14 mmol) and cyclododecanone (2.50g, 14 mmol) as a white solid (5.10g, 81%) m.p. 139.5 - 140.5°C ; $\nu_{max.}$ (nujol) 3090 m, 3060 m, 3035 m, 1600 w, 770 m, 750 s, and 708 s cm^{-1} ; δ_H 0.85 - 1.65 (18H, brm, 3 - 11-$\underline{C}H_2$), 2.09 (2H, t, J 6Hz, $\underline{C}H_2$), 2.18 (2H, t, J 6Hz, $\underline{C}H_2$), 5.43 (1H, brs, N-H), 7.18 - 7.47 (12H, m, Ar-H), 8.53 (2H, d, J 7.5Hz, pyridyl-H) ; m/e (NH_3 D.C.I.) 440 (MH^+, 10%), and 244 (Ar_3C^+, 100).

General procedure for the preparation of Benzhydrylhydrazones (28)

The following procedure for the preparation of acetone benzhydrylhydrazone (28f) is typical.

Benzhydrylhydrazine (19) hydrochloride (10.0g, 43 mmol) was dissolved in methanol (120 ml) and a solution of sodium formate (2.17g, 64 mmol) in water (15 ml) was added. Acetone (3.80 ml, 52 mmol) was added and the mixture stirred under argon for 2h in the dark. The product was extracted into dichloromethane (2 x 35 ml) after addition of water (100 ml). The organic layer was dried (Na_2SO_4), filtered and evaporated to yield acetone benzhydrylhydrazone (28f) (7.20g, 71%) as a waxy solid ; $\nu_{max.}$ (nujol) 3280 m (N-H), 3090 w, 3060 w, 3040 w, 1600 m, 775 m, 750 s, and 700 s cm^{-1}; δ_H 1.83 (3H, s, Me), 1.95 (3H, s, Me), 5.06 (1H, brs, N-H), 5.61 (1H, s, $\underline{C}HPh_2$), 7.27 - 7.35 (10H, m, phenyl-H) ; δ_C 15.77 (q, Me), 25.09 (q, Me), 67.71 (d, $\underline{C}HPh_2$), 126.87, 127.60, 128.23 (3 x d, phenyl-C), 142.85, 146.87 (2 x s) ;

m/e (NH_3 C.I.) 239 (MH^+, 6%), 220 (1), 182 (19), 167 (Ph_2CH^+, 34), and 58 (100).

Acetaldehyde benzhydrylhydrazone (28a) was prepared from benzhydrylhydrazine (19) hydrochloride (5.00g,21 mmol) and acetaldehyde (1.50 ml, 26 mmol) as a yellow oil (4.33g, 90%) as a mixture of isomers (1.4 : 1) ; $\nu_{max.}$ (nujol) 3280 m (N-H), 3065 w, 3050 w, 3030 w, 1600 s, 765 s, 750 s, and 700 s cm^{-1}; δ_H 1.78, 1.84 (3H, 2 x d, J 4.5Hz, Me), 5.45, 5.61 (1H, s, C<u>H</u>Ph_2), 6.73, 6.98 (1H, q, J 4.5Hz, C<u>H</u>N), 7.26 - 7.39 (10H, m, phenyl-<u>H</u>) ; δ_C 12.34 (q, Me), 18.22 (q, Me), 66.88, 67.72 (2 x d, <u>C</u>HPh_2), 127.11, 127.49, 127.55, 128.92 (4 x d, phenyl-<u>C</u>), 138.30, 138.34 (2 x d, <u>C</u>HN), 142.02, 142.38 (2 x s, ipso-<u>C</u>) ; m/e (NH_3 C.I.) 225 (MH^+, 8%), and 167 (Ph_2CH^+, 100).

Benzaldehyde benzhydrylhydrazone (28e) was prepared from benzhydrylhydrazine (19) hydrochloride (5.00g, 21 mmol) and benzaldehyde (2.38 ml, 23 mmol) as a white solid by filtration from the reaction mixture (4.35g, 71%) m.p. 76 - 78°C ; $\nu_{max.}$ (nujol) 3275 m (N-H), 3060 m, 3050 m, 3030 m, 1600 s, 755 s, 750 s, and 700 s cm^{-1}; δ_H 5.66 (1H, s, C<u>H</u>Ph_2), 5.97 (1H,brs, N-<u>H</u>), 7.22 - 7.57 (15H, m, phenyl-<u>H</u>) ; δ_C 66.77 (d, <u>C</u>HPh_2), 125.93, 127.38, 127.67, 127.96, 128.37, 128.61 (6 x d, phenyl-<u>C</u>), 135.86 (s, ipso-<u>C</u>), 137.69 (d, <u>C</u>HN), 141.67 (s, ipso-<u>C</u>) ;m/e (NH_3 C.I.) 287 (MH^+, 2%), 182 (35), 167 (91), and 108(100).

General procedure for the preparation of BDP Hydrazones (29)

The following procedure for the preparation of acetone BDP hydrazone (29f) is typical.

t-Butyldiphenylmethylhydrazine (20) hydrochloride (4.00g, 14 mmol) was dissolved in methanol (70 ml) and a solution of sodium formate (1.40g, 21 mmol) in water (10 ml) was added. Acetone (2.00 ml, 17 mmol) was added and the mixture stirred under argon for 2h in darkness.

The product was filtered off,washed with water and dried under high vacuum to yield acetone BDP hydrazone (29f) as a white solid (3.30g, 82%) m.p. 116.5 - 118°C ; $\nu_{max.}$ (nujol) 3290 w (N-H), 3090 w, 3060 m, 3030 m, 1598 w, 1380 m, 1365 s, 1265 m, 1120 m, 940 m, 908 m, 756 s, 705 s, and 648 s cm^{-1}; δ_H 1.25 (9H, s, t-Bu), 1.75 (3H, s, Me), 1.82 (3H, s, Me), 5.34 (1H, brs, N-H), 7.20 - 7.45 (10H, m, phenyl-H) ; δ_C 15.36 (q, Me), 25.30 (q, Me), 29.07 (q, t-Bu), 38.77 (s, $\underline{C}Me_3$), 73.00 (s, $\underline{C}Ph_2Bu^t$), 125.81, 126.52, 130.58 (3 x d, phenyl-C), 143.14, 144.95 (2 x s, ipso-C, C=N) ; m/e (NH_3 D.C.I.) 295 (MH^+, 100%), 237 (43), 223 ($t\text{-}BuPh_2C^+$, 35), 182 (11), and 56 (13).

Acetaldehyde BDP hydrazone (29a) was prepared from BDP hydrazine (20) hydrochloride (6.00g, 21 mmol) and acetaldehyde (1.50 ml, 26 mmol) as a white solid (4.05g, 70%) as a mixture of isomers (2:1), m.p. 90 - 92°C ; $\nu_{max.}$ (nujol) 3300 w (N-H), 3090 w, 3055 m, 3025 m, 1598 m, 1100 m, 1032 m, 775 m, 758 s, 728 s, 705 s, and 642 m cm^{-1}; δ_H 1.25, 1.27 (9H, 2 x s, t-Bu), 1.76, 1.78 (3H, 2 x d, J 5.5Hz, Me), 5.63, 5.86 (1H, 2 x brs, N-H), 6.61, 6.90 (1H, 2 x q, J 5.5Hz, CH=N), 7.18 - 7.49 (10H, m, phenyl-H) ; δ_C 12.19 (q, Me), 18.10 (q, Me), 28.89 (q, t-Bu), 38.50, 39.00 (2 x s, $\underline{C}Me_3$), 73.03, 73.27 (2 x s, $\underline{C}Ph_2Bu^t$), 125.88, 126.05, 126.51, 126.79, 130.29, 130.78 (6 x d, phenyl-C), 135.33, 137.70 (2 x d, CHN), 144.20, 144.58 (2 x s, ipso-C) ; m/e (NH_3 D.C.I.) 281 (MH^+, 0.5%), 223 ($tBuPh_2C^+$, 18), 200 (16), 183 (100), 182 (10), and 105 (10).

Pentanal BDP hydrazone (29c) was prepared from BDP hydrazine (20) hydrochloride (2.00g, 7 mmol) and pentanal (0.80 ml, 8 mmol) as a yellow oil (2.11g, 95%) by extraction into dichloromethane,as a mixture of isomers (1.7:1) ; $\nu_{max.}$ (film) 3090 w, 3060 m, 3030 w, 3020 w, 2960 s, 2930 s, 2875 s, 1600 m, 1580 w, 1495 m, 1480 m, 1465 m, 1448 m, 1280 m, 765 m, 755 m, 705 s, and 640 m cm^{-1}; δ_H 0.84, 0.97

(3H, 2 x t, J 7Hz, Me), 1.15 - 1.58 (4H, m, $C\underline{H}_2$), 1.26 (9H, s, t-Bu), 2.06 - 2.17 (2H, m, $C\underline{H}_2$), 5.88 (1H, brs, N-H), 6.47, 6.84 (1H, 2 x t, J 5.5Hz, CHN), 7.17 - 7.33 (6H, m, phenyl-H), 7.41 - 7.49 (4H, m, phenyl-H) ; δ_C 13.81 (q, Me), 21.98, 22.54, 25.75, 28.36 (4 x t, $\underline{C}H_2$), 28.92 (q, t-Bu), 29.04, 31.74 (2 x t, $\underline{C}H_2$), 38.56, 38.60 (2 x s, $\underline{C}Me_3$), 73.31, 73.35 (2 x s, $\underline{C}Ph_2Bu^t$), 125.86, 126.05, 126.52, 126.78, 130.33, 130.79 (6 x d, phenyl-C), 141.40, 142.28 (2 x d, CHN), 144.19, 144.55 (2 x s, ipso-C) ; m/e (NH_3 D.C.I.) 323 (MH^+, 100%), 265 (52), 223 ($t\text{-}BuPh_2C^+$, 90), 183 (45), and 169 (11).

3-Methylbutanal BDP hydrazone (29d) was prepared from BDP hydrazine (20) hydrochloride (2.00g, 7 mmol) and 3-methylbutanal (0.80 ml, 8 mmol) as a viscous yellow oil (2.26g, 100%) by extraction into dichloromethane, as a mixture of isomers (1.7 :1) ; $\nu_{max.}$ (film) 3300 w (N-H), 3090 w, 3060 m, 3030 m, 2960 s, 2930 s, 2880 m, 1600 m, 1580 m, 1495 m, 1480 m, 1460 m, 1280 m, 765 s, 755 m, 705 s, and 640 m cm^{-1}; δ_H 0.78, 1.02 (6H, 2 x d, J 6.5Hz, Me), 1.24, 1.25 (9H, 2 x s, t-Bu), 1.59 - 1.71, 1.87 - 1.97 (1H, 2 x m, $C\underline{H}Me_2$), 1.91 - 2.03 (2H, m, $C\underline{H}_2$), 6.49, 6.83 (1H, 2 x t, J 6Hz, CHN), 7.19 - 7.46 (10H, m, phenyl-H) ; δ_C 22.28, 22.51, 22.66 (4 x t, one unresolved, Me), 26.36, 26.95 (2 x d, $\underline{C}HMe_2$), 28.93 (q, t-Bu), 35.04 (t, $\underline{C}H_2$), 38.59, 38.99 (2 x s, $\underline{C}Me_3$), 41.13 (t, $\underline{C}H_2$), 73.18, 73.30 (2 x s, $\underline{C}Ph_2Bu^t$), 125.87, 126.03, 126.56, 126.76, 130.22, 130.75 (6 x d, phenyl-C), 140.43, 141.31 (2 x d, CHN), 144.12, 144.55 (2 x s, ipso-C) ; m/e (NH_3 D.C.I.) 323 (MH^+, 100%), 265 (53), 223 ($t\text{-}BuPh_2C^+$, 35), and 182 (13).

Cyclohexanone BDP hydrazone (29i) was prepared from BDP hydrazine (20) hydrochloride (6.00g, 21 mmol) and cyclohexanone (2.10 ml, 23 mmol) as a white solid (5.04g, 73%) m.p. 90 - 92°C ; $\nu_{max.}$ (nujol) 3300 m (N-H), 3100 m, 3050 m, 1620 m, 1598 m, 1110 s, 1095 s, 1078 s, 905 s, 790 m, 760 s, 705 s, 680 m, and 652 s cm^{-1}; δ_H 1.26 (9H, s, t-Bu),

1.43 - 1.59 (6H, brm, 3,4,5-C$\underline{H}_2$), 2.07 - 2.23 (4H, m, 2,6-C$\underline{H}_2$), 7.16 - 7.32 (6H, m, phenyl-$\underline{H}$), 7.40 - 7.50 (4H, m, phenyl-$\underline{H}$) ; δ_C 24.91 25.77, 26.04, 27.15 (4 x t, $\underline{C}H_2$), 29.13 (q, t-Bu), 35.59 (t, $\underline{C}H_2$), 38.77 (s, $\underline{C}Me_3$), 73.18 (s, $\underline{C}Ph_2Bu^t$), 125.74, 126.46, 130.64 (3 x d, phenyl-$\underline{C}$), 144.81, 150.17 (2 x s, ipso-$\underline{C}$, $\underline{C}N$) ; m/e (NH_3 D.C.I.) 355 (MH^+, 100%), 277 (13), and 223 ($t\text{-}BuPh_2C^+$, 9).

Cyclododecanone BDP hydrazone (29j) was prepared from BDP hydrazine (20) hydrochloride (6.00g, 21 mmol) and cyclododecanone (3.57g, 21 mmol) as a white solid (8.31g, 96%) m.p. 103°-105°C ; $\nu_{max.}$ (nujol) 3350 w (N-H), 3100 w, 3090 w, 3060 m, 3030 m, 3020 m, 1620 w, 1600 w, 1490 m, 1445 s, 1398 m, 1092 w, 1068 m, 895 m, 755 s, and 710 s cm^{-1}; δ_H 1.08 - 1.24 (2H, brm, 7-C$\underline{H}_2$), 1.24 - 1.37 (12H, brm, 4,5,6,8,9,10-C$\underline{H}_2$), 1.34 (9H, s, t-Bu), 1.38 1.74 (4H, m, 3,11-C$\underline{H}_2$), 2.15 - 2.27 (4H, m, 2,12-C$\underline{H}_2$), 5.61 (1H, brs, N-$\underline{H}$), 7.22 - 7.38 (6H, m, phenyl-$\underline{H}$), 7.49 - 7.55 (4H, m, phenyl-$\underline{H}$) ; δ_C 22.75, 23.48, 23.54, 23.74, 24.93, 26.04, 26.51, 27.67 (8 x t, $\underline{C}H_2$), 29.19 (q, Me), 32.40 (t, $\underline{C}H_2$), 38.48 (s, $\underline{C}Me_3$), 73.24 (s, $\underline{C}Ph_2Bu^t$), 125.62, 126.34, 130.84 (3 x d, phenyl-$\underline{C}$), 145.37, 148.46 (2 x s, ipso-$\underline{C}$, $\underline{C}$=N) ; m/e (NH_3 D.C.I.) 419 (MH^+, 100%), 361 (55), and 223 ($t\text{-}BuPh_2C^+$, 50).

General procedure for the preparation of Alcohols (32)

The following procedure for the preparation of 1-cyclododecyl-1-phenylmethanol (32r) is typical for the preparation of alcohols (32) from trityl- (26) or DPP- (27) hydrazones.

Hydrazone (27j) (4.0 mmol) was dissolved in THF:TMEDA (4:1, 50 ml) and the solution cooled to -40°C. Methyl lithium (5.3 mmol in diethyl ether) was added and the solution stirred for 20 min before cooling to -55°C and adding benzaldehyde (5.3 mmol). After 20 min the reaction was quenched with acetic acid (5.3 mmol) and ethanethiol added.

The mixture was warmed to 20°C over 30 min,during which time nitrogen evolution occurred. The mixture was extracted into diethyl ether (100 ml) washed with sodium hydroxide solution (2M, 2 x 20 ml),hydrochloric acid (2M, 2 x 20 ml),dried (Na_2SO_4),filtered and evaporated to yield a crude product. Purification by flash column chromatography on silica gel and p.l.c. using diethyl ether : light petroleum (3:17) as eluant gave 1-cyclododecyl-1-phenylmethanol (899 mg, 82%); m.p. 82 - 83°C ; t.l.c. [diethyl ether : light petroleum (3:17)] Rf 0.35 ; $\nu_{max.}$ (nujol) 3400 m (O-H), 3085 w, 3060 w, 3030 w, 765 s, and 705 s cm^{-1}; δ_H 1.17 - 1.57 (22H, m, C$\underline{H}_2$), 1.74 - 1.94 (1H, m, C$\underline{H}$), 4.55 (1H, d, $\underline{J}$ 5Hz, C$\underline{H}$OH), 7.20 - 7.41 (5H, m, phenyl-$\underline{H}$); δ_C 21.77, 22.10, 23.23, 23.58, 24.24, 24.80, 24.89, 25.71, 25.80 (9 x t, $\underline{C}H_2$), 41.64 (d, $\underline{C}$H), 77.10 (d, $\underline{C}$HOH), 126.55, 127.27, 128.18 (3 x d, phenyl-$\underline{C}$), 144.08 (s, ipso-$\underline{C}$); m/e (E.I.) 274 (M^+,1%), 257 (22), 107(100), 79 (36), 77 (21), 55 (15), 41 (20), and 39 (11); (Found : C,83.41; H,11.00%. $C_{19}H_{30}O$ requires : C, 83.15, H, 11.02%).

For alcohols (32) derived from methyl ketone hydrazones a brief bromine wash was employed prior to the final p.l.c. purification (to facilitate separation from olefinic by-products).

The following alcohols (32) were similarly prepared :-

1-Phenylpropan-1-ol (32a)[182] was prepared from hydrazone (26a) (5.0 mmol) and benzaldehyde (5.3 mmol) as a colourless liquid (503mg, 74%) ; t.l.c. [diethyl ether : light petroleum (3:17)] Rf 0.2 ; $\nu_{max.}$ (film) 3370 m br (OH), 3090 w, 3065 w, 3035 w, 2970 s, 2935 s, 2880 s, 750 m, and 705 s cm^{-1}; δ_H (0.85 (3H, t, $\underline{J}$ 7.5Hz, Me), 1.63 - 1.81 (2H, m, C$\underline{H}_2$), 1.96 (1H, brs, O-$\underline{H}$), 4.52 (1H, t, $\underline{J}$ 6.5Hz, C$\underline{H}$OH), 7.16 - 7.34 (5H, m, phenyl-$\underline{H}$) ; δ_C 10.10 (q, Me), 31.86 (t, $\underline{C}H_2$), 75.98 (d, $\underline{C}$HOH), 125.93, 127.42, 128.34 (3 x d, phenyl-$\underline{C}$), 144.56 (s, ipso-$\underline{C}$) ; m/e (E.I.) 136 (M^+, 9%), 107 (100), 79 (50), 77 (26),

51 (11) ; (Found : 136.0888 ; $C_9H_{12}O$ requires : 136.0888).

2-Phenylbutan-2-ol (32b)[183] was prepared from hydrazone (26a) (5.0 mmol) and acetophenone (5.3 mmol) as a colourless liquid (405mg, 54%) ; t.l.c. [diethyl ether : light petroleum (3:17)] Rf 0.3 ; $\nu_{max.}$ (film) 3400 m br (O-H), 3090 w, 3060 w, 3030 w, 2980 s, 2940 s, 2885 s, 765 m, and 705 s cm^{-1}; δ_H 0.81 (3H, t, J 7.5Hz, Me), 1.56 (3H, s, Me), 1.83 (1H, brs, O-H), 1.79 - 1.90 (2H, m, CH_2), 7.22 - 7.46 (5H, m, phenyl-H) ; δ_C 8.25 (q, Me), 29.56 (q, Me), 36.65 (t, CH_2), 74.85 (s, COH), 124.82, 126.41, 128.02 (3 x d, phenyl-C), 147.72 (s, ipso-C) ; m/e (E.I.) 151 (M^+, 1.5%), 122 (100), 77 (15), 57 (11) and 43 (90).

1-Ethylcyclohexan-1-ol (32c)[184] was prepared from hydrazone (26a) (5.0 mmol) and cyclohexanone (5.3 mmol) as a colourless liquid (250mg, 39%) ; t.l.c. [diethyl ether : light petroleum (3:17)] Rf 0.25; $\nu_{max.}$ (film) 3380 m br (O-H), 2970 m, 2935 s, 2860 m, 1460 w, 1450 w, and 955 m cm^{-1}; δ_H 0.90 (3H, t, J 9Hz, Me), 1.20 - 1.67 (12H, m, CH_2); δ_C 7.19 (q, Me), 22.25, 25.90, 34.74, 36.94 (4 x t, CH_2), 71.41 (s, COH) ; m/e (E.I.) 128 (M^+, 4%), 99 ($M^+-C_2H_5$, 94), and 43 (100).

1-Phenylhexan-1-ol (32d)[185] was prepared from hydrazone (26c) (4.5 mmol) and benzaldehyde (4.7 mmol) as a colourless liquid (320mg, 40%) ; t.l.c. [diethyl ether : light petroleum (3:17)] Rf 0.2 ; $\nu_{max.}$ (film) 3350 m br (O-H), 3090 w, 3065 w, 3035 w, 2960 s, 2935 s, 2860 s, 755 s, and 702 s cm^{-1}; δ_H 0.89 (3H, t, J 6.5Hz, Me), 1.22 - 1.46 (6H, m, CH_2), 1.66 - 1.97 (3H, m), 4.67 (1H, t, J 6.5Hz, CHOH), 7.22 - 7.39 (5H, m, phenyl-H) ; δ_C 14.01 (q, Me), 22.57, 25.51, 31.74, 39.08 (4 x t, CH_2), 74.74 (d, CHOH), 125.87, 127.46, 128.40 (3 x d, phenyl-C), 144.90 (s, ipso-C) ; m/e (E.I.) 178 (M^+, 3%), 161 (M^+-OH,1), 107 (100), 79 (56), 77 (22), and 37 (9) ; (Found : 178.1357 ; $C_{12}H_{18}O$ requires : 178.1357).

2-Phenylheptan-2-ol (32e)[186] was prepared from hydrazone (26c) (4.5 mmol) and acetophenone (4.7 mmol) as a colourless liquid (441mg, 51%) ; t.l.c. [diethyl ether : light petroleum (3:17)] Rf 0.4 ; $\nu_{max.}$ (film) 3400 m br (O-H), 3090 w, 3060 w, 3030 w, 2960 s, 2930 s, 2860 s, 765 m, and 700 s cm^{-1}; δ_H 0.89 (3H, t, J 7.5Hz, Me), 1.10 - 1.40 (6H, m, $C\underline{H}_2$), 1.61 (3H, s, Me), 1.75 - 1.91 (2H, m, $C\underline{H}_2$), 7.25 - 7.53 (5H, m, phenyl-H) ; δ_C 13.98 (q, Me), 22.51, 23.63 (2 x t, $\underline{C}H_2$), 30.11 (q, Me), 32.16, 44.17 (2 x t, $\underline{C}H_2$), 74.70 (s, COH), 124.73, 126.40, 128.05 (3 x d, phenyl-C), 148.10 (s, ipso-C) ; m/e (E.I.) 177 (M^+-CH_3, 3%), 175 (M^+-H_2O, 1), 121 (99), and 42 (100) ; (Found : C, 81.34; H, 10.34%. $C_{13}H_{20}O$ requires : C, 81.12 ; H, 10.48%).

1-Pentylcyclohexan-1-ol (32f)[187] was prepared from hydrazone (26c) (4.5 mmol) and cyclohexanone (4.7 mmol) as a colourless liquid (321mg, 42%) ; t.l.c. [diethyl ether : light petroleum (3:17)] Rf 0.25; $\nu_{max.}$ (film) 3390 m br (O-H), 2930 s, 2860 s cm^{-1}; δ_H 0.90 (3H, t, J 7.5Hz, Me), 1.14 - 1.67 (18H, m) ; δ_C 14.07 (q, Me), 22.30, 22.57, 22.70, 25.89, 32.51, 37.45, 42.43 (7 x t, $\underline{C}H_2$), 71.46 (s, COH) ; m/e (E.I.) 170 (M^+ ,0.5%), 127 (23), 99 ($C_6H_{11}O^+$, 100), 81 (33), 41 (30) ; (Found : 170.1670 ; $C_{11}H_{22}O$ requires : 170.1671).

2-Methyl-1-phenylpropan-1-ol (32g)[188] was prepared from hydrazone (26f) or (27f) (5.0 mmol) and benzaldehyde (5.3 mmol) as a colourless liquid (488mg, 65%) ; t.l.c. [diethyl ether : light petroleum (3:17)] Rf 0.3 ; $\nu_{max.}$ (film) 3400 m br (O-H), 3090 w, 3070 w, 3030 w, 2965 s, 2935 s, 2880 s, 760 s, and 705 s cm^{-1}; δ_H 0.80 (3H, d, J 7Hz, Me), 1.01 (3H, d, J 7Hz, Me), 1.91 - 2.02 (1H, m, $C\underline{H}Me_2$), 4.36 (1H, d, J 7Hz, C<u>H</u>OH), 7.23 - 7.37 (5H, m, phenyl-H) ; δ_C 18.19 (q, Me), 18.96 (q, Me), 35.21 (d, $\underline{C}HMe_2$), 79.97 (d, CHOH), 126.50, 127.32, 128.10 (3 x d, phenyl-C), 143.59 (s, ipso-C) ; m/e (E.I.) 150 (M^+,4%), 132 (21), 117 (31), 115 (12), 107 (100), 91 (17), 79 (51), 77 (28), 51 (13),

40 (17), and 39 (13) ; (Found : 150.1044 ; $C_{10}H_{14}O$ requires : 150.1045); together with 2-Methyl-1-phenylprop-2-en-1-ol (67) (86mg, 11%) ; t.l.c. (light petroleum) Rf 0.6 ; $\nu_{max.}$ (film) 3360 m br (O-H), 3060 m, 3030 m, 2970 m, 1450 s, 1045 s, 1025 s, 905 s, and 700 s cm^{-1}; δ_H 1.63 (3H, s, Me), 2.09 (1H, brs, O-H), 4.97 (1H, multiplet s, vinyl-H), 5.14 (1H, s, CHOH), 5.22 (1H, multiplet s, vinyl-H), 7.27 - 7.41 (5H, m, phenyl-H) ; m/e (E.I.) 148 (M^+, 100%), 133 (70), 105 (86),and 79 (96); (Found : 148.0886 ; $C_{10}H_{12}O$ requires : 148.0888).

2-Methyl-1-phenylpropan-1-ol (32g) was also prepared from isopropyl magnesium bromide and benzaldehyde and shown to have identical spectral properties.

2-Methyl-1-phenylprop-2-en-1-ol (67) was also prepared from acetone triisopropylbenzenesulphonylhydrazone (68) and benzaldehyde by a Shapiro reaction procedure[5] and shown to have identical spectral properties. These data also corresponded to literature data[189].

Preparation of 2-Methyl-1-phenylprop-2-en-1-ol (67) in the absence of ethanethiol

The standard procedure for alcohol (32) formation was employed using hydrazone (27f) (1.5 mmol) and benzaldehyde (1.5 mmol) except that the ethanethiol addition was omitted at the work up stage. Standard isolation and chromatography gave (67) (110mg, 49%) ; t.l.c., n.m.r. as before along with minor amounts (<5%) of (32g).

3-Methyl-2-phenylbutan-2-ol (32h)[190] was prepared from hydrazone (26f) (4.5 mmol)and acetophenone (4.7 mmol) as a colourless liquid (339mg, 46%) ; t.l.c. [diethyl ether : light petroleum (3:17)] Rf 0.3 ; $\nu_{max.}$ (film) 3460 m br (O-H), 3090 m, 3060 m, 3030 m, 2970 s, 2940 s, 2880 s, 765 m, and 710 s cm^{-1}; δ_H 0.83 (3H, d, J 7Hz, Me), 0.91 (3H, d, J 7Hz, Me), 2.02 - 2.09 (1H, m, $CHMe_2$), 7.22 - 7.46 (5H, m, phenyl-H) ;m/e (E.I.) 146 (M^+-H_2O, 24%), 131 (54), 121 (69), 103 (18),

91 (25), 77 (24), 51 (16), 43 (100), 40 (21), and 39 (12).

2-Methyl-1-phenyloctan-1-ol (32i)[191] was prepared from hydrazone (27g) (4.5 mmol) and benzaldehyde (4.7 mmol) as a colourless liquid (624mg, 63%) ; mixture of diastereoisomers (1.1 : 1) ; t.l.c. [diethyl ether : light petroleum (3:17)] Rf 0.35 ; $\nu_{max.}$ (film) 3400 m br (O-H), 3090 m, 3070 m, 3035 m, 2960 s, 2930 s, 2860 s, 760 s, and 700 s cm^{-1}; δ_H 0.76, 0.92 (3H, 2 x d, J 7Hz, Me), 0.85 - 0.94 (3H, m, Me), 1.10 - 1.43 (10H, m, CH_2), 4.44 (0.48H, d, J 7Hz, CHOH), 4.54 (0.52H, d, J 6Hz, CHOH), 7.25 - 7.38 (5H, m, phenyl-H) ; δ_C 14.07, 14.33, 15.66 (3 x q, Me), 22.64, 26.98, 27.13, 29.45, 29.62, 31.83, 32.24, 33.15 (8 x t, CH_2), 40.14 (d, CH), 78.18, 79.06 (2 x d, CHOH), 126.31, 126.66, 128.11 (3 x d, phenyl-C), 143.55, 143.87 (2 x s, ipso-C); m/e (E.I.) 220 (M^+, 1%), 107 (100), and 79 (20).

2,4-Dimethyldecan-3-ol (32j) was prepared from hydrazone (27g) (4.5 mmol) and 2-methylpropanal (4.7 mmol) as a colourless liquid (544mg, 65%) ; mixture of diastereoisomers (undetermined ratio) ; t.l.c. [diethyl ether : light petroleum (3:17)] Rf 0.3 ; $\nu_{max.}$ (film) 3400 m br (O-H), 2960 s, 2920 s, 2870 s, 2860 s cm^{-1}; δ_H 0.85 - 0.98 (12H, 4 x Me), 1.21 - 1.37 (8H, m, CH_2), 1.50 - 1.70 (2H, m, CH_2), 1.71 - 1.90 (2H, m, 2 x CH), 3.06 - 3.12 (1H, m, CHOH); δ_C 13.01, 14.05, 16.43, 16.48, 18.46, 19.42, 19.97 (8 x q, one unresolved, Me), 22.65, 27.10, 27.15, 29.57, 29.71 (5 x t, CH_2), 30.15, 30.86 (2 x d, CH), 31.05 (t, CH_2), 31.89 (2 x t, unresolved, CH_2), 34.16 (t, CH_2), 34.97, 35.97 (2 x d, CH); m/e (E.I.) 185 (M^+-1, 4%), 169 (M^+-OH, 100), 143 (9), 113 (10), 99 (10), 83 (14), 73 (21), 69 (16), 55 (12), 43 (14), and 41 (13) ; (Found : 185.1907 ; $C_{12}H_{25}O$ requires : 185.1905).

1-Cyclohexyl-1-phenylmethanol (32m)[192] was prepared from hydrazones (26i) and (27i) (5.0 mmol) and benzaldehyde (5.3 mmol) as a colourless liquid (608mg, 64%) ; t.l.c. [diethyl ether : light petroleum

(3:17)] Rf 0.25 ; $\nu_{max.}$ (film) 3380 m br (O-H), 3090 w, 3060 w, 3030 w, 2950 s, 2860 s, 760 s, and 702 s cm^{-1}; δ_H 0.90 - 1.80 (11H, brm), 2.00 (1H, brs, O-H), 4.35 (1H, d, J 7Hz, CHOH), 7.09 - 7.31 (5H, m, phenyl-H) ; δ_C 26.01, 26.09, 26.42, 28.81, 29.31 (5 x t, CH_2), 44.96 (d, CH), 79.35 (d, CHOH), 126.58, 127.34, 128.13 (3 x d, phenyl-C), 143.60 (s, ipso-C) ; m/e (E.I.) 190 (M^+, 11%), 107 ($PhCHOH^+$, 100), 79 (42), and 77 (14) ; (Found : 190.1357 ; $C_{13}H_{18}O$ requires : 190.1358).

1-Cyclohexyl-1-phenylethanol (32n)[193] was prepared from hydrazone (26i) (3.0 mmol) and acetophenone (3.2 mmol) as a colourless liquid (285mg, 50%) ; t.l.c. [diethyl ether : light petroleum (3:17)] Rf 0.2 ; $\nu_{max.}$ (film) 3455 m br (O-H), 3085 w, 3060 w, 3025 w, 2930 s, 2855 s, 765 s, and 705 s cm^{-1}; δ_H 0.85 - 1.21 (6H, m, CH_2), 1.47 (3H, s, Me), 1.47 - 1.81 (5H, m), 7.10 - 7.47 (5H, m, phenyl-H) ; δ_C 26.37 (t, CH_2), 26.62 (2 x t, unresolved, CH_2), 26.74 (q, Me), 27.16, 27.34 (2 x t, CH_2), 48.95 (s, COH), 125.26, 126.29, 127.76 (3 x d, phenyl-C), 147.67 (s, ipso-C) ; m/e (E.I.) 187 (M^+-OH, 6%), 147 (9), 121 ($PhMeCOH^+$, 100), 105 (13), 77 (11), and 43 (18) ; (NH_3 C.I.) 204 (M^+, 4%).

1-Cyclohexyl-2-methylpropan-1-ol (32p)[194] was prepared from hydrazone (27i) (5.0 mmol) and 2-methylpropanal (5.3 mmol) as a colourless liquid (312mg, 40%) ; t.l.c. [diethyl ether : light petroleum (3:17)] Rf 0.35 ; $\nu_{max.}$ (film) 3380 m br (O-H), 2960 s, 2920 s, 2850 s. cm^{-1}; δ_H 0.90 - 1.00 (6H, m, 2 x Me), 1.00 - 1.90 (12H, brm), 3.05 (1H, t, J 6Hz, CHOH) : δ_C 16.52, 19.89 (2 x q, Me), 26.16, 26.43, 26.54, 27.66 (4 x t, CH_2), 29.77 (d, CH), 40.62 (d, CH), 81.03 (d, CHOH); m/e (E.I.) 139 (M^+-OH, 100%), 95 (86), and 83 (28) ; (NH_3 C.I.) 156 (M^+, 15%).

1-Cyclohexylcyclohexan-1-ol (32q)[195] was prepared from hydrazone (26i) (4.5 mmol) and cyclohexanone (4.7 mmol) as a white solid

(328mg, 40%) ; m.p. 61 - 65°C (Lit.[195] 53 - 54°C) ; t.l.c. [diethyl ether : light petroleum (3:17)] Rf 0.25 ; $\nu_{max.}$ (nujol) 3460 m br (O-H) cm^{-1}; δ_H 0.95 - 1.90 (brm) ; δ_C 21.95, 26.05, 26.57, 26.62, 26.89, 34.36 (6 x t, $\underline{C}H_2$), 48.27 (d, $\underline{C}H$), 72.98 (s, $\underline{C}OH$) ; m/e (E.I.) 183 (MH^+, 100%), 182 (M^+, 21), 165 (M^+-OH, 69) ; (Found : 182.1671 ; $C_{12}H_{22}O$ requires : 182.1671).

2-Methyl-1-phenylbutan-1-ol (32k) was prepared on a small scale [to determine their n.m.r. spectrum] from hydrazone (26h) or (27h) (2.7 mmol) and benzaldehyde (3.0 mmol) as a colourless liquid (220mg, 49%) ; t.l.c. [diethyl ether : light petroleum (3:17)] Rf 0.35 ; $\nu_{max.}$ (film) 3400 m br (O-H), 3090 m, 3065 m, 3030 m, 2960 s, 2930 s, 2865 s, 760 s, and 700 s cm^{-1}; δ_H 0.92 (1.71H, d, J 7.5Hz, Me), 1.03 - 1.16 (4.29H, d + 2 x t, unresolved, Me), 1.80 - 2.00 (3H, m, $C\underline{H}$, $C\underline{H}_2$), 2.07 (1H, brs, O-$\underline{H}$), 4.60 (0.57H, d, J 8Hz, $C\underline{H}OH$), 4.69 (0.43H, d, J 6.5Hz, $C\underline{H}OH$), 7.40 - 7.57 (5H, m, phenyl-H).

2-Methyl-1-(2,4,6-trimethylphenyl)butan-1-ol (32l) was also prepared on a small scale for n.m.r. data as a mixture of diastereomers (1.4 : 1) from hydrazone (27h) (3.0 mmol) and mesitaldehyde (3.3 mmol) as a colourless liquid (95mg, 15%) ; t.l.c. [diethyl ether : light petroleum (3:17)] Rf 0.4 ; $\nu_{max.}$ (film) 3380 m br (O-H), 3090 m, 3060 m, 3025 m, 2960 s, 2925 s, 2860 s, 745 s, and 705 s cm^{-1}; δ_H 0.66 (1.74H, d, J 7.5Hz, Me), 0.83 (1.26H, t, J 7.5Hz, Me), 1.02 (1.74H, t, J 7.5Hz, Me), 1.17 (1.26H, d, J 7.5Hz, Me), 1.15 - 1.40 (3H, m, $C\underline{H}$, $C\underline{H}_2$), 1.72 (1H, brs, O-$\underline{H}$), 2.28 (3.75H, s, Ar-Me), 2.43 (5.25H, s, Ar-Me), 4.76 (0.42H, d, J 10Hz, $C\underline{H}OH$), 4.82 (0.58H, d, 9Hz, $C\underline{H}OH$), 6.83 (2H, s, phenyl-$\underline{H}$).

General procedure for the preparation of Alkenes (33)

The following procedure for the preparation of ββ-dimethyl styrene (33b) is typical.

Acetone tritylhydrazone (26f) (5.0 mmol) was dissolved in THF : TMEDA (4:1, 50ml) and the solution cooled to -55°C. Methyl lithium (5.3 mmol) was added, the solution stirred for 20 min, then treated with benzaldehyde (5.3 mmol). After 20 min the solution was cooled to -78°C and phosphorus trichloride (6.3 mmol) was added. The mixture was allowed to warm to 20°C over 90 min then stirred for a further 60 min. Diethyl ether (100ml) was added, the solution washed with sodium hydroxide solution (1M, 2 x 20ml), hydrochloric acid (1M, 2 x 20ml), dried ($MgSO_4$), filtered, and evaporated to give a viscous oil (3.2g). Purification by flash chromatography on silica gel (75g) using light petroleum as eluant gave ββ-dimethylstyrene (343mg, 52%)[196] as an oil ; t.l.c. (light petroleum) Rf 0.6 ; $\nu_{max.}$ (film) 3080 w, 3060 w, 3020 w, 2970 s, 2930 s, 2910 s, 2850 s, 1650 m (C=C), 745 s, and 700 s cm^{-1}; δ_H 1.90 (3H, s, Me), 1.94 (3H, s, Me), 6.31 (1H, s, vinyl-H), and 7.25 - 7.37 (5H, m, phenyl-H) ; δ_C 19.36 (q, Me), 28.84 (q, Me), 125.11, 125.72, 127.96, 128.69 (4 x d, vinyl,phenyl-C), 135.37, 138.66 (2 x s, CMe_2, ipso-C) ; m/e (E.I.) 132 (M^+, 80%), 117 (100), 115 (21), and 91 (22) ; (Found : 132.0939 ; $C_{10}H_{12}$ requires : 132.0938).

The following alkenes (33) were similarly prepared :-

β-Methylstyrene (33a)[197] was prepared from hydrazone (26a) (3.3 mmol) and benzaldehyde (3.7 mmol) as a colourless liquid (80mg, 20%) ; t.l.c. (light petroleum) Rf 0.7 ; δ_H 1.85 (3H, d, J 6Hz, Me), 6.15 - 6.35 (2H, m, vinyl-H), 7.00 - 7.40 (5H, m, phenyl-H).

This data was compared with literature data to show that the compound was indeed β-methylstyrene.

2-Methyl-1-phenyloct-1-ene (33c) was prepared from hydrazone (27g) (4.0 mmol) and benzaldehyde (4.4 mmol) as a colourless oil (485mg, 60%, E : Z = 65 : 35) ; t.l.c. (light petroleum) Rf 0.65 ; $\nu_{max.}$ (film) 3085 w, 3060 w, 3030 w, 2960 s, 2930 s, 2860 s, 1650 m (C=C), 745 m, and 700 s cm^{-1}; δ_H 0.89 - 0.96 (3H, m, $CH_2\underline{Me}$), 1.30 - 1.39 (6H, m, $C\underline{H}_2$), 1.52 - 1.55 (2H, m, $C\underline{H}_2$), 1.88 and 1.91 (3H, 2 x multiplet s, ratio 65:35, vinyl-Me), 2.17 - 2.27 (2H, m, allylic-$C\underline{H}_2$), 6.30 (1H, s, vinyl-$\underline{H}$), 7.17 - 7.38 (5H, m, phenyl-$\underline{H}$) ; δ_C 14.09 (q, Me), 17.72 (q, Me), 22.65 (t, $\underline{C}H_2$), 24.09 (q, Me), 27.99, 28.10, 29.01, 29.36, 31.71, 31.81, 32.54, 40.76 (8 x t, $\underline{C}H_2$), 124.67, 125.29, 125.67, 127.94, 128.52, 128.78 (6 x d, vinyl-$\underline{C}$H, phenyl-$\underline{C}$), 138.72, 139.34, 139.79 (3 x s, CH=$\underline{C}$, ipso-$\underline{C}$) ; m/e (E.I.) 202 (M^+, 49%), 131 (100), 117 (21), 115 (11), 91 (57), 69 (11), and 55 (9) ; (Found : C, 89.29 ; H, 11.16% ; 202.1721. $C_{15}H_{22}$ requires : C, 89.04 ; H, 10.96% ; 202.1721).

Benzylidenecyclohexane (33d)[198] was prepared from hydrazone (26i) (5.0 mmol) and benzaldehyde (5.3 mmol) as a colourless oil (413mg, 48%); t.l.c. (light petroleum) Rf 0.75 ; $\nu_{max.}$ (film) 3080 w, 3055 w, 3020 w, 2920 s, 2850 s, 1650 m (C=C), 736 m, and 700 s cm^{-1}; δ_H 1.61 - 1.68 (6H, m, 3,4,5-$C\underline{H}_2$), 2.30 (2H, t, $\underline{J}$ 5.5Hz, $C\underline{H}_2$), 2.42 (2H, t, $\underline{J}$ 5.5Hz, $C\underline{H}_2$), 6.28 (1H, s, C=C$\underline{H}$), 7.23 - 7.34 (5H, m, phenyl-$\underline{H}$) ; δ_C 26.69, 27.88, 28.63, 29.45, 37.66 (5 x t, $\underline{C}H_2$), 121.92 (d, C=$\underline{C}$H), 125.72, 127.94, 128.87 (3 x d, phenyl-$\underline{C}$), 138.37, 143.35 (2 x s, CH=$\underline{C}$, ipso-$\underline{C}$) ; m/e (E.I.) 172 (M^+, 100%), 171 (12), 129 (24), 126 (12), 115 (23), 104 (19), 91 ($PhCH_2^+$, 22), and 81 (14) ; (Found : C, 90.41 ; H, 9.51% ; 172.1253 . $C_{13}H_{16}$ requires : C, 90.64 ; H, 9.36 ; 172.1252).

1-Phenylethylidenecyclohexane (33e)[199] was prepared from hydrazone (26i) (4.5 mmol) and acetophenone (4.7 mmol) as a colourless oil (285mg, 34%) ; t.l.c. (light petroleum) Rf 0.7 ; $\nu_{max.}$ (film) 3080 w, 3060 w, 3025 w, 2965 s, 2925 s, 2860 s, 1600 m, 768 s, and

705 s cm^{-1}; δ_H 1.43 - 1.50 (2H, m, $C\underline{H}_2$), 1.55 - 1.68 (4H, m, $C\underline{H}_2$), 1.99 (3H, s, Me), 2.03 (2H, t, J 6Hz, $C\underline{H}_2$), 2.34 (2H, t, J 6Hz, $C\underline{H}_2$), 7.14 - 7.34 (5H, m, phenyl-H) ; δ_C 20.19 (q, Me), 26.88, 28.08, 28.48, 30.60, 31.92 (5 x t, $\underline{C}H_2$), 125.63 (d, phenyl-C), 126.67 (s, C=C), 127.90, 128.35 (2 x d, phenyl-C), 135.40 (s, C=C), 145.31 (s, ipso-C) ; m/e (NH_3 C.I.) 186 (M^+, 100%), and 172 (53).

Cyclohexylidenecyclohexane (33f)[200] was prepared from hydrazone (26i) (4.5 mmol) and cyclohexanone (5.0 mmol) as a white solid (170 mg, 23%) m.p. 55 - 56°C (Lit.,[200] 53°C) ; t.l.c. (light petroleum) Rf 0.75 ; $\nu_{max.}$ (nujol) 1265 w, 1240 w, 1015 w, 890 m, and 850 m cm^{-1}; δ_H 1.43 - 1.65 (12H, br, $C\underline{H}_2$), 2.13 - 2.27 (8H, br, allylic-$C\underline{H}_2$) ; δ_C 27.30, 28.71, 30.13 (3 x t, $\underline{C}H_2$), and 129.40 (s, C=C) ; m/e (E.I.) 164 (M^+, 73%), 135 (12), 121 (20), 107 (17), 93 (23), 91 (15), 82 (100), 81 (66), 79 (40), 67 (75), 55 (41), 39 (40), and 37 (22) ; (Found : 164.1565 ; $C_{12}H_{20}$ requires : 164.1565), along with the diene (70) (131mg, 18%) as an oil ; t.l.c. (light petroleum) Rf 0.8 ; $\nu_{max.}$ (film) 2930 s, 2860 s, 2835 s, 1450 m, 1435 m, 1335 w, 1135 w, 925 w, and 795 m cm^{-1}; δ_H 1.50 - 1.63 (4H, m), 2.05 - 2.26 (8H, m), 5.80 (2H, br s) ; δ_C 22.54, 23.16, 25.54, 25.86 (4 x t, $\underline{C}H_2$), 121.30 (d, vinyl-CH), 136.82 (s, vinyl-C) ; m/e (E.I.) 162 (M^+, 100%), 147 (14), 133 (30), 119 (30), 105 (32), 94 (60), 91 (70), 79 (75), 65 (18), 51 (19), 41 (45), and 39 (41).

Isopropylidenecyclohexane (33g)[201] was prepared from hydrazone (26i) (2.8 mmol) and acetone (3.0 mmol) as a colourless oil (125mg, 36%); t.l.c. (light petroleum) Rf 0.8 ; $\nu_{max.}$ (film) 2970 m, 2955 s, 2860 m, and 1655 m (C=C) cm^{-1}; δ_H 1.44 - 1.60 (6H, m, 3,4,5-$C\underline{H}_2$), 1.68 (6H, s, Me), 2.13 - 2.22 (4H, m, 2,6-$C\underline{H}_2$) ; m/e (E.I.) 124 (M^+, 44%), 109 (M^+-CH_3, 42), 105 (13), 81 (100), 67 (39), 55 (18), and 41 (22).

Benzylidenecyclododecane (33h) was prepared from hydrazone

(26j) (3.0 mmol) and benzaldehyde (3.2 mmol) as a colourless oil (284mg, 37%) ; t.l.c. (light petroleum) Rf 0.7 ; $\nu_{max.}$ (film) 3080 w, 3055 w, 3025 w, 2930 s, 2860 s, 2850 s, 1650 m (C=C), 1600 m, 1470 m, 750 m, 720 s, and 700 s cm^{-1}; δ_H 1.38 - 1.56 (16H, m), 1.58 - 1.71 (2H, m, $C\underline{H}_2$), 2.24 (2H, t, J 7Hz, $C\underline{H}_2$), 2.32 (2H, t, J 7Hz, $C\underline{H}_2$), 6.42 (1H, s, C=C$\underline{H}$), 7.21 - 7.41 (5H, m, phenyl-$\underline{H}$) ; δ_C 22.56, 23.10, 23.98, 24.19, 24.28, 24.33, 24.48, 24.94, 25.24, 28.01, 32.68 (11 x t, $\underline{C}H_2$), 125.62, 125.72, 127.93, 128.62 (4 x d, vinyl-$\underline{C}$H, phenyl-$\underline{C}$), 138.87 (s, CH=$\underline{C}$), 142.55 (s, ipso-$\underline{C}$) ; m/e (E.I.) 256 (M^+, 93%), 143 (29), 129 (100), 128 (29), 117 (54), 105 (52), 104 (40), 91 (74), 83 (33), 81 (17), 67 (17), 55 (34), 40 (57), and 38 (26) ; (Found : C, 89.24 ; H, 11.20% ; 256.2190 . $C_{19}H_{28}$ requires : C, 88.99 ; H, 11.01% ; 256.2191).

Preparation of the Allylic alcohol (72)

The standard procedure for alcohol (32) formation was employed using hydrazone (26i) (4.5 mmol) and cyclohexanone (5.0 mmol) except that the ethanethiol addition was omitted. Standard work up and p.l.c. [on silica using diethyl ether : light petroleum (3:17)] gave (72) (303mg, 37%) ; t.l.c. [diethyl ether : light petroleum (3:17)] Rf 0.3 ; m.p. 64 - 65°C (Lit.,[202] 69°C) ; $\nu_{max.}$ (nujol) 3280 s, 3220 s (O-H), 1295 m, 1195 m, 1055 s, 960 s, 925 m, 905 m, and 855 s cm^{-1}; δ_H 1.22 - 1.32 (2H, m), 1.45 - 1.71 (12H, m), 2.00 - 2.05 (4H, m), 5.75 - 5.81 (1H, m) ; m/e (E.I.) 180 (M^+, 24%), 137 (100), 119 (18), 109 (25), 91 (21), 81 (37), 67 (21), and 55 (22) ; (Found : 180.1514 ; $C_{12}H_{20}O$ requires : 180.1514).

Conversion of the Allylic alcohol (72) to the Diene (70)

The allylic alcohol (72) (1.3 mmol) was dissolved on THF:TMEDA (4:1, 15ml) and the solution cooled to -78°C. Methyl lithium (1.4 mmol) was added, the solution stirred for 10 min, then treated with phosphorus

trichloride (1.6 mmol). The mixture was warmed to 20°C over 90 min and stirred for 30 min. Diethyl ether (30ml) was added, the solution washed with hydrochloric acid (2M, 10ml), brine (2 x 10ml), dried, filtered, and evaporated. Purification by chromatography on silica gel [(70g) using light petroleum as eluant] gave the diene (70) (132mg, 62%) ; t.l.c., n.m.r. as before.[203]

General procedure for the preparation of Saturated Esters (76)

The following procedure for the preparation of methyl-3-cyclohexylbutanoate (76c) is typical.

Cyclohexanone tritylhydrazone (26i) (5.0 mmol) was dissolved in dry DME (60ml) and the solution cooled to -55°C. n-Butyl lithium (4.9 mmol) was added, the solution stirred for 20 min, and a solution of methyl crotonate (10 mmol) in DME (8ml) was added over 1h. Trifluoroacetic acid (5.0 mmol) was added followed by ethanethiol (5ml), the solution warmed to 20°C and evaporated. The residue was triturated with light petroleum (4 x 20ml) and the extracts evaporated to give an oil (1.40g). Kügelrohr distillation b.p. ca 150°C at 20mmHg (Lit.,[204] 149 - 150°C at 25 mmHg) gave a colourless oil (640mg) which was purified by p.l.c. [using diethyl ether : light petroleum (3:17) as eluant] to give methyl-3-cyclohexylbutanoate (76c) (323mg, 35%) as an oil ; t.l.c. diethyl ether : light petroleum (3:17) Rf 0.75 ; $\nu_{max.}$ (film) 2965 s, 2860 s, 1745 s (C=O), 1450 m, and 1140 m cm^{-1}; δ_H 0.88 (3H, d, J 7Hz, Me), 0.88 - 1.24 (6H, m, CH_2), 1.57 - 1.80 (5H, m, CH_2 and C(4)H), 1.80 - 1.91 (1H, m, C(3)H), 2.03 - 2.15 (1H, m, AB part of ABX, CH_2CO), 2.33 - 2.43 (1H, m, AB part of ABX, CH_2CO), 3.66 (3H, s, OMe); δ_C 16.52 (q, Me), 26.66, 28.98, 30.30 (3 x t, CH_2), 35.39 (d, CH), 39.05 (t, CH_2CO), 42.63 (d, CHMe), 51.33 (q, OMe), 174.23 (s, C=O) ; m/e (E.I.) 185 (MH^+, 5%), 153 (17), 111 (100), 101 (95),

87 (62), 74 (72), 55 (90), and 41 (76) ; (Found : C, 71.83 ; H, 10.92%. $C_{11}H_{20}O_2$ requires : C, 71.63 ; H, 10.93%).

The following esters (76) were similarly prepared :-

Methyl-3,5-dimethylhexanoate (76a)[205] was prepared from hydrazone (26b) (6.5 mmol) and methyl crotonate (13 mmol) as a colourless oil (236mg, 23%) ; t.l.c. [diethyl ether : light petroleum (3:17)] Rf 0.65 ; $\nu_{max.}$ (film) 2960 s, 2930 s, 2875 s, 1740 s (C=O) cm^{-1}; δ_H 0.84 - 0.93 (9H, m, 3 x Me), 1.06 - 1.12 (2H, m, C$\underline{H}_2$), 1.57 - 1.66 (1H, m, C$\underline{H}$Me$_2$), 2.00 - 2.09 (1H, m, C$\underline{H}$), 2.05 - 2.11 (1H, m, AB part of ABX, C$\underline{H}_2$), 2.24 - 2.31 (1H, m, AB part of ABX, C$\underline{H}_2$), 3.65 (3H, s, OMe); δ_C 19.81, 22.13, 23.19 (3 x q, Me), 25.24, 28.10 (2 x d, $\underline{C}$H), 41.98, 46.29 (2 x t, $\underline{C}H_2$), 51.25 (q, O$\underline{C}H_3$), 173.65 (s, $\underline{C}$=O) ; (Found : C, 68.60 ; H, 11.35%. $C_9H_{18}O_2$ requires : C, 68.31 ; H, 11.47%).

Methyl-3-methyloctanoate (76b) was prepared from hydrazone (26c) (4.0 mmol) and methyl crotonate (8.0 mmol) as a colourless oil (138mg, 20%) ;t.l.c. [diethyl ether : light petroleum (3:17)] Rf 0.7 ; $\nu_{max.}$ (film) 2960 s, 2930 s, 2860 s, 1742 s (C=O) cm^{-1}; δ_H 0.88 (3H, t, $\underline{J}$ 7.5Hz, Me), 0.92 (3H, d, $\underline{J}$ 7Hz, Me), 1.13 - 1.33 (8H, m, C$\underline{H}_2$), 1.91 - 1.99 (1H, m, C$\underline{H}$), 2.06 - 2.14 (1H, m, AB part of ABX, C$\underline{H}_2$), 2.26 - 2.34 (1H, m, AB part of ABX, C$\underline{H}_2$), 3.66 (3H, s, OMe) ; δ_C 14.02 (q, Me), 19.75 (q, Me), 22.62, 26.57 (2 x t, $\underline{C}H_2$), 30.36 (d, $\underline{C}$H), 31.95, 36.71, 41.68 (3 x t, $\underline{C}H_2$), 51.27 (q, O$\underline{C}H_3$), 173.72 (s, $\underline{C}$=O) ; m/e (E.I.) 172 (M^+, 1%), 157 (M^+-CH_3, 2), 141 (7), 129 (2), 115 (3), 101 (30), 74 (100), 55 (13), and 40 (19) ; (Found : C, 69.92 ; H, 11.67%. $C_{10}H_{20}O_2$ requires : C, 69.72 ; H, 11.70%).

Preparation of Carboxylate Esters (78) from BDP Hydrazones (29)

The following preparation of methylcyclohexanecarboxylate (78a) is typical.

Cyclohexanone BDP hydrazone (29i) (1.5 mmol) was dissolved in dry THF (25ml) and the solution cooled to -40°C. Methyl lithium (1.7 mmol) was added and after 20 min the solution was cooled to -78°C. Methyl chloroformate (2.3 mmol) was added, the solution warmed to 20°C over 4h, stirred for 16h, quenched with acetic acid (1.7 mmol), and partitioned between diethyl ether (100ml) and water. The organic layer was dried ($MgSO_4$), filtered, and evaporated to give a crude product. Purification by flash chromatography on silica gel gave 1-(t-butyl diphenylmethylazo)-1-carbomethoxycyclohexane as a viscous yellow oil (400mg, 68%) ; t.l.c. [diethyl ether : light petroleum (1:19)] Rf 0.4 ; δ_H(60 MHz) 1.15 (9H, s, t-Bu), 1.00 - 2.10 (10H, m, C$\underline{H}_2$), 3.70 (3H, s, OMe), 7.07 - 7.23 (10H, m, phenyl-$\underline{H}$).

This azo compound (0.9 mmol) was dissolved in benzene (30ml) with thiophenol (1.5ml) and the solution heated under reflux for 2h. Diethyl ether (80ml) was added and the solution washed with sodium hydroxide solution (2M, 2 x 20ml), brine (2 x 15ml), dried ($MgSO_4$), filtered and evaporated to give a crude product. Purification by flash chromatography on silica gel followed by p.l.c. [diethyl ether : light petroleum (1:9)] gave methylcyclohexanecarboxylate (85mg, 65%, overall from hydrazone 50%) as a colourless liquid ; t.l.c. [diethyl ether : light petroleum (1:9)] Rf 0.6 ; $\nu_{max.}$ (film) 2980 m, 2930 s, 2860 s, 1735 s (C=O), 1450 m, 1375 m, 1325 m, 1248 m, 1172 m, 1132 m, and 1045 m cm^{-1}; δ_H (60 MHz) 0.95 - 2.20 (10H, m, C$\underline{H}_2$), 2.30 - 2.40 (1H, m, C$\underline{H}$CO$_2$Me), 3.70 (3H, s, OMe) ; m/e (E.I.) 142 (M^+, 55%), 113 (25), 111 (M^+-OCH_3, 24), 110 (31), 101 (15), 87 (89), 83 ($C_6H_{11}^+$, 95), 82 (26), 81 (22), 74 (39), 68 (24), 67 (22), 55 (100), 40 (58), and 38 (31) ; (Found : 142.0993 ; $C_8H_{14}O_2$ requires : 142.0994).

The following esters (78) were prepared in a similar way from BDP hydrazones (29):-

Ethylcyclohexanecarboxylate (78b) was prepared from cyclohexanone BDP hydrazone (29i) (1.5 mmol) and ethyl cyanoformate (2.3 mmol) via 1-(t-butyldiphenylmethylazo)-1-carboethoxycyclohexane {(385mg, 63%) ; t.l.c. [diethyl ether : light petroleum (1:19)] Rf 0.4 ; δ_H (60 MHz) 0.85 - 1.85 (11H, m), 1.15 (9H, s, t-Bu), 1.87 - 1.94 (2H, m), 4.15 (2H, q, J 8Hz, $OC\underline{H}_2Me$), 7.07 - 7.24 (10H, m, phenyl-H)} as a colourless liquid (99mg, 50% overall) ;t.l.c. [diethyl ether : light petroleum (1:9)] Rf 0.6 ; $\nu_{max.}$ (film) 2980 m, 2930 s, 2860 s, 1735 s (C=O), 1450 m, 1375 m, 1250 m, 1170 m, 1132 m, and 1046 m cm^{-1}; δ_H (60 MHz) 0.85 - 2.25 (10H, m, $C\underline{H}_2$), 1.35 (3H, t, J 8Hz, Me), 2.31 - 2.39 (1H, m), 4.20 (2H, q, J, 8Hz, $OC\underline{H}_2Me$) ; m/e (E.I.) 156 (M^+, 59%), 111 (M^+-OEt, 29), 110 (17), 101 (50), 83 (100), 81 (22), 67 (17), 55 (80), 40 (51), and 38 (29) ; (Found : 156.1149 ; $C_9H_{16}O_2$ requires : 156.1150).

Methylcyclododecanecarboxylate (78c) was prepared from hydrazone (29j) (1.2 mmol) and methyl chloroformate (1.8 mmol) via 1-(t-butyldiphenylmethylazo)-1-carbomethoxycyclododecane{(350mg, 61%) ; t.l.c. [diethyl ether : light petroleum (1:19)] Rf 0.7 ; δ_H (60 MHz) 0.90 - 1.50 (22H, m, $C\underline{H}_2$), 1.05 (9H, s, t-Bu), 3.55 (3H, s, OMe), 7.05 (10H,brs, phenyl-H).} as a colourless liquid (122mg, 45% overall) ; t.l.c. [diethyl ether : light petroleum (1:9)] Rf 0.65 ; $\nu_{max.}$ (film) 2980 m, 2930 s, 2865 s, 1735 s (C=O), 1450 m, 1375 m, 1250 m, 1174 m, 1130 m, and 1044 m cm^{-1}; δ_H (60 MHz) 1.10 - 1.80 (22H, m, $C\underline{H}_2$), 2.10 - 2.65 (1H, m, $C\underline{H}CO_2Me$), 3.60 (3H, s, OMe); m/e (NH_3 D.C.I.) 227 (MH^+, 100%), and 167 (77). These data were compared with data available in the literature[206] and the compound shown to be authentic.

General procedure for the preparation of Azo-Alkanes (111)

The following procedure for the preparation of 2-(t-butyl diphenylmethylazo)dodecane (111a) is typical.

Acetaldehyde BDP hydrazone (29a) (5.4 mmol) was dissolved in dry THF (30ml) and the solution cooled to -40°C. Methyl lithium (5.9 mmol) was added and the solution stirred for 20 min before cooling to -78°C. 1-Iododecane (8.0 mmol) was added, the mixture allowed to warm to 20°C over 4h, stirred for 16h, then quenched with acetic acid (5.9 mmol). The solution was partitioned between diethyl ether (100ml) and water (30ml), the organic layer dried ($MgSO_4$), filtered, and evaporated (water bath <40°C) to yield a crude product. Purification by flash chromatography on silica gel gave 2-(t-butyldiphenylmethylazo)dodecane (111a) as a viscous yellow oil (2.13g, 95%) ; t.l.c. [diethyl ether : light petroleum (1:19)] Rf 0.8 ; δ_H 0.92 (3H, t, J 7Hz, Me), 1.20 - 1.36 (19H, m), 1.24 (9H, s, t-Bu), 1.51 - 1.57 (1H, m, AB part of ABX, $C\underline{H}_2$), 1.76 - 1.80 (1H, m, AB part of ABX, $C\underline{H}_2$), 3.82 - 3.88 (1H, m, X part of ABX, $C\underline{H}N$), 7.18 - 7.37 (10H, m, phenyl-$\underline{H}$) ; δ_C 14.13 (q, Me), 18.48 (q, Me), 22.71, 26.25 (2 x t, $\underline{C}H_2$), 28.29 (q, t-Bu), 29.36, 29.61, 31.94, 34.80 (4 x t, $\underline{C}H_2$), 38.30 (s, $\underline{C}Me_3$), 73.27 (d, $\underline{C}HN$), 86.14 (s, $\underline{C}Ph_2Bu^t$), 125.85, 125.90, 126.42, 131.44, 131.67 (6 x d, one unresolved ,phenyl-$\underline{C}$), 144.96, 145.14 (2 x s, ipso-$\underline{C}$) ; m/e (NH_3 D.C.I.) 421 (MH^+, 15%), 365 (81), 223 ($t\text{-}BuPh_2C^+$, 100), 167 (30), 147 (45), and 105 (13).

The following azo-alkanes (111) were similarly prepared :-

2-(t-Butyldiphenylmethylazo)propane (111b) was prepared from hydrazone (29a) (4.4 mmol) and iodomethane (6.6 mmol) as a viscous yellow oil (0.98g, 76%) ; t.l.c. [diethyl ether : light petroleum (1:19)] Rf 0.85 ; δ_H 1.25 (9H, s, t-Bu), 1.28 (6H, d, J 7.5Hz, $CH\underline{Me}_2$), 4.07 - 4.11 (1H, m, $C\underline{H}Me_2$), 7.22 - 7.34 (10H, m, phenyl-$\underline{H}$) ; δ_C 20.09 (q, Me),

28.21 (q, t-Bu), 38.37 (s, $\underline{C}Me_3$), 68.41 (d, $\underline{C}HN$), 85.82 (s, $\underline{C}Ph_2Bu^t$), 125.90, 126.40, 131.50 (3 x d, phenyl-$\underline{C}$), 144.99 (s, ipso-$\underline{C}$) ; m/e (NH_3 D.C.I.) 295 (MH^+, 5%), 239 (59), 223 (t-$BuPh_2C^+$, 100), 167 (26), and 105 (29).

2-(t-Butyldiphenylmethylazo)-1-phenylpropane (111c) was prepared from hydrazone (29a) (7.1 mmol) and benzyl bromide (10.7 mmol) as a viscous yellow oil (2.63g, 99%) ; t.l.c. [diethyl ether : light petroleum (1:19)] Rf 0.75 ; δ_H 1.19 (9H, s, t-Bu), 1.23 (3H, d, 7Hz, Me), 2.84 - 2.89 (1H, m, $PhC\underline{H}_2$), 3.11 - 3.18 (1H, m, $PhC\underline{H}_2$), 4.17 - 4.28 (1H, m, $C\underline{H}N$), 7.11 - 7.28 (15H, m, phenyl-$\underline{H}$) ; δ_C 18.15 (q, Me), 28.30 (q, t-Bu), 38.33 (s, $\underline{C}Me_3$), 41.03 (t, $Ph\underline{C}H_2$), 74.29 (d, $\underline{C}HN$), 86.37 (s, $\underline{C}Ph_2Bu^t$), 125.90, 125.96, 126.40, 126.46, 128.14, 129.46, 131.36, 131.55 (8 x d, phenyl-$\underline{C}$), 138.87, 144.64 (2 x s, ipso-$\underline{C}$) ; m/e (NH_3 D.C.I.) 323 (M^+-tBu, 4%), 315 (10), 239 (10), 223 (t-$BuPh_2C^+$, 63), 208 (23), 182 (16), 167 (100), 165 (37), 105 (48), and 91 ($PhCH_2^+$, 70).

2-(t-Butyldiphenylmethylazo)hexane (111d) was prepared from hydrazone (29a) (3.4 mmol) and 1-iodobutane (5.1 mmol) as a viscous yellow oil (1.0g, 89%) ; t.l.c. [diethyl ether : light petroleum (1:19)] Rf 0.7 ; δ_H 0.86 (3H, t, J 7Hz, Me), 1.17 (2H, d, J 7Hz, $C\underline{H}_2$), 1.15 - 1.38 (4H, m, $C\underline{H}_2$), 1.23 (9H, s, t-Bu), 1.50 - 1.64 (1H, m, AB part of ABX, $C\underline{H}_2$), 1.73 - 1.84 (1H, m, AB part of ABX, $C\underline{H}_2$), 3.81 - 3.94 (1H, m, X part of ABX, $C\underline{H}N$), 7.17 - 7.33 (10H, m, phenyl-$\underline{H}$) ; δ_C 13.98 (q, Me), 18.45 (q, Me), 22.63 (t, $\underline{C}H_2$), 28.27 (q, t-Bu), 28.42, 34.42 (2 x t, $\underline{C}H_2$), 38.29 (s, $\underline{C}Me_3$), 73.22 (d, $\underline{C}HN$), 86.13 (s, $\underline{C}Ph_2Bu^t$), 125.85, 125.90, 126.40, 131.43, 131.67 (6 x d, one unresolved, phenyl-$\underline{C}$), 144.96, 145.13 (2 x s, ipso-$\underline{C}$) ; m/e (NH_3 D.C.I.) 337 (M^+, 3%), 281 (29), 223 (t-$BuPh_2C^+$, 100), 183 (29), 167 (32), and 105 (33).

5-(t-Butyldiphenylmethylazo)pentadecane (111e) was prepared from hydrazone (29c) (2.4 mmol) and 1-iododecane (3.6 mmol) as a viscous yellow oil (780mg, 70%) ; t.l.c. [diethyl ether : light petroleum (1:19)] Rf 0.85 ; $\nu_{max.}$ (film) 3090 w, 3060 w, 2960 m, 2930 s, 2880 m, 2860 m, 1602, w, 1495 w, 1465 w, 1455 w, 1446 w, 1115 w, 912 s, 737 s, and 710 m cm^{-1}; δ_H 0.87 (3H, t, J 7Hz, Me), 0.92 (3H, t, J 7Hz, Me), 1.03 - 1.43 (20H, m), 1.30 (9H, s, t-Bu), 1.51 - 1.64 (2H, m, CH_2), 1.63 - 1.76 (2H, m, CH_2), 3.58 - 3.70 (1H, m, CHN), 7.18 - 7.42 (10H, m, phenyl-H) ; δ_C 13.98 (q, Me), 14.13 (q, Me), 22.72, 26.13, 28.30 (3 x t, CH_2), 28.45 (q, t-Bu), 29.36, 29.64, 31.95, 32.71, 33.04 (5 x t, CH_2), 38.20 (s, CMe_3), 78.10 (d, CHN), 86.62 (s, CPh_2Bu^t), 125.87, 126.35, 131.66 (3 x d, phenyl-C), 145.07 (s, ipso-C) ; m/e (NH_3 D.C.I.) 463 (MH^+, 1%), 435 (8), 407 (11), 223 ($t\text{-}BuPh_2C^+$, 100), 208 (13), 167 (40), 147 (44), and 105 (17).

5-(t-Butyldiphenylmethylazo)dodecane (111f) was prepared from hydrazone (29c) (2.4 mmol) and 1-iodoheptane (3.6 mmol) as a viscous yellow oil (484mg, 48%) ; t.l.c. [diethyl ether : light petroleum (1:19)] Rf 0.8 ; δ_H 0.87 (3H, t, J 7Hz, Me), 0.91 (3H, t, J 7Hz, Me), 1.01 - 1.41 (14H, m, CH_2), 1.28 (9H, s, t-Bu), 1.52 - 1.63 (2H, m, CH_2), 1.66 - 1.77 (2H, m, CH_2), 3.61 - 3.75 (1H, m, CHN), 7.15 - 7.41 (10H, m, phenyl-H) ; δ_C 13.98 (q, Me), 14.18 (q, Me), 22.68, 25.36 (2 x t, CH_2), 28.41 (q, t-Bu), 28.69, 29.31, 29.73, 30.07, 31.84, 32.51, 34.11 (7 x t, CH_2), 38.27 (s, CMe_3), 77.97 (d, CHN), 86.58 (s, CPh_2Bu^t), 125.86, 126.28, 131.64 (3 x d, phenyl-C), 145.03 (s, ipso-C) ; m/e (NH_3 D.C.I.) 421 (MH^+, 5%), 223 ($t\text{-}BuPh_2C^+$, 100), 167 (37), and 105 (21).

2-(t-Butyldiphenylmethylazo)-1-phenylhexane (111g) was prepared from hydrazone (29c) (3.2 mmol) and benzyl bromide (4.8 mmol) as a viscous yellow oil (980mg, 77%) ; t.l.c. [diethyl ether : light petroleum (1:19)] Rf 0.8 ; $\nu_{max.}$ (film) 3090 w, 3060 w, 3030 w, 2960 m,

2935 m, 2880 m, 1603 w, 1495 m, 1455 m, 912 m, 736 s, and 708 s cm^{-1}; δ_H 0.90 (3H, t, J 7Hz, Me), 1.14 - 1.47 (4H, m, CH_2), 1.25 (9H, s, t-Bu), 1.57 - 1.71 (1H, m), 1.71 - 1.83 (1H, m), 2.95 - 3.14 (2H, m, AB part of ABX, CH_2), 4.03 - 4.13 (1H, m, X part of ABX, CHN), 7.13 - 7.36 (10H, m, phenyl-H) ; δ_C 13.92 (q, Me), 22.60, 28.18 (2 x t, CH_2), 28.38 (q, t-Bu), 32.35 (t, CH_2), 38.21 (s, CMe_3), 39.44 (t, CH_2), 78.96 (d, CHN), 86.85 (s, CPh_2Bu^t), 125.81, 125.92, 126.32, 126.37, 128.14, 129.49, 131.52, 131.60 (9 x d,one unresolved, phenyl-C), 138.96, 144.63, 144.82 (3 x s, ipso-C) ; m/e (NH_3 D.C.I.) 413 (MH^+, 2%), 385 (4), 357 (27), 223 ($t\text{-}BuPh_2C^+$, 100), 208 (14), 167 (33), 91 (17).

4-(t-Butyldiphenylmethylazo)-2-methyltetradecane (111h) was prepared from hydrazone (29d) (1.6 mmol) and 1-iododecane (2.4 mmol) as a viscous oil (580mg, 79%) ; t.l.c. [diethyl ether : light petroleum (1:19)] Rf 0.85 ; δ_H 0.93 - 1.03 (9H, complex, 3 x Me), 1.10 - 1.76 (21H, brm), 3.70 - 3.78 (1H, m, CHN), 7.15 - 7.31 (10H, m, phenyl-H) ; δ_C 14.10, 22.07 (2 x q, Me), 22.69 (t,CH_2), 23.31 (d, $CHMe_2$), 24.71 (q, Me), 26.06 (t, CH_2), 28.44 (q, t-Bu), 29.33, 29.54, 29.63, 33.48 (4 x t, CH_2), 38.18 (s, CMe_3), 42.07 (t, CH_2), 76.24 (d, CHN), 86.64 (s, CPh_2Bu^t), 125.87, 126.34, 131.64 (3 x d, phenyl-C), 145.06 (s, ipso-C) ; m/e (NH_3 C.I.) 452 (2%), 393 (4), 223 ($t\text{-}BuPh_2C^+$, 30), 200 (29), 183 (100), and 105 (13).

2-(t-Butyldiphenylmethylazo)-4-methylpentane (111i) was prepared from hydrazone (29d) (1.6 mmol) and iodomethane (2.4 mmol) as a viscous yellow oil (370mg, 71%) ; t.l.c. [diethyl ether : light petroleum (1:19)] Rf 0.75 ; δ_H 0.87 (6H, 2 x d, unresolved , J 7Hz, Me), 1.18 (3H, d, J 7.5Hz, Me), 1.23 (9H, s, t-Bu), 1.26 - 1.33 (1H, m, AB part of ABX, CH_2), 1.47 - 1.54 (1H, m, AB part of ABX, CH_2), 1.71 - 1.79 (1H, m, $CHMe_2$), 3.89 - 4.02 (1H, m, X part of ABX, CHN), 7.22 - 7.29 (10H, m, phenyl-H) ; m/e (NH_3 D.C.I.) 337 (MH^+, 3%), 223 ($t\text{-}BuPh_2C^+$,

35), 200 (19), 183 (100), and 105 (9).

9-Bromo-4-(t-butyldiphenylmethylazo)-2-methylnonane (111j) was prepared from hydrazone (29d) (1.5 mmol) and 1,5-dibromopentane (2.3 mmol) as a viscous yellow oil (660mg, 89%) ; t.l.c. [diethyl ether : light petroleum (1:19)] Rf 0.75 ; δ_H 0.85, 0.88 (6H, 2 x d, J 7Hz, $CH\underline{Me}_2$), 1.24 (9H, s, t-Bu), 1.13 - 1.97 (11H, m), 3.36 (2H, t, J 7.5Hz, $C\underline{H}_2Br$), 3.67 - 3.79 (1H, m, C<u>H</u>N), 7.12 - 7.32 (10H, m, phenyl-<u>H</u>) ; δ_C 22.67 (q, Me), 23.24 (q, Me), 24.66 (d, $\underline{C}HMe_2$), 25.10, 28.12 (2 x t, $\underline{C}H_2$), 28.43 (q, t-Bu), 31.86, 32.65, 33.21 (3 x t, $\underline{C}H_2$), 38.15 (s, $\underline{C}Me_3$), 41.98 (t, $\underline{C}H_2$), 75.91 (d, <u>C</u>HN), 86.73 (s, $\underline{C}Ph_2Bu^t$), 125.89, 126.33, 131.57 (3 x d, phenyl-<u>C</u>), 144.91 (s, ipso-<u>C</u>) ; m/e (NH_3 D.C.I.) 473/471 (MH^+, 1%), 417/415 (8), 403/401 (4), 223 ($t\text{-}BuPh_2C^+$, 100), 147 (30), and 105 (10).

2-(t-Butyldiphenylmethylazo)-2-methylpropane (111k) was prepared from hydrazone (29f) (6.8 mmol) and iodomethane (10.5 mmol) as a viscous yellow oil (1.76g, 84%) ; t.l.c. [diethyl ether : light petroleum (1:19)] Rf 0.85 ; δ_H 1.23 (9H, s, t-Bu), 1.28 (9H, s, t-Bu), 7.18 - 7.35 (10H, m, phenyl-<u>H</u>) ; δ_C 26.77 (q, t-Bu), 28.21 (q, t-Bu), 38.30 (s, $\underline{C}Me_3$), 68.88 (s, $\underline{C}Me_3$), 85.59 (s, $\underline{C}Ph_2Bu^t$), 125.82, 126.40, 131.54 (3 x d, phenyl-<u>C</u>), 145.16 (s, ipso-<u>C</u>) ; m/e (NH_3 C.I.) 309 (MH^+, 3%), 239 (25), 223 ($t\text{-}BuPh_2C^+$, 47), 200 (10), 183 (57), 182 (22), 167 (100), 105 (31), 91 (15), and 57 (10).

2-(t-Butyldiphenylmethylazo)-2-methyl-1-phenylpropane (111l) was prepared from hydrazone (29f) (3.4 mmol) and benzyl bromide (5.1 mmol) as a viscous yellow oil (1.30g, 100%) ; t.l.c. [diethyl ether : light petroleum (1:19)] Rf 0.8 ; δ_H 1.16 (6H, s, 2 x Me), 1 19 (9H, s, t-Bu), 2.90 (2H, s, $PhC\underline{H}_2$), 6.92 - 6.96 (2H, m, phenyl-<u>H</u>), 7.15 - 7.27 (13H, m, phenyl-<u>H</u>) ; δ_C 24.71 (q, Me), 28.39 (q, t-Bu), 38.39 (s, $\underline{C}Me_3$), 46.81 (t, $\underline{C}H_2Ph$), 71.71 (s, $\underline{C}Me_2CH_2Ph$), 86.29 (s, $\underline{C}Ph_2Bu^t$), 125.87, 126.40,

127.57, 130.75, 131.56 (6 x d, one unresolved, phenyl-C), 138.15, 144.87 (2 x s, ipso-C) ; m/e (NH_3 C.I.) 355 (3%), 315 (40), 223 (t-BuPh_2C^+, 79), 208 (100), 193 (24), 167 (38), 165 (22), 133 (23), 115 (24), 105 (26), and 91 (36).

1-(t-Butyldiphenylmethylazo)-1-heptylcyclohexane (111m)

was prepared from hydrazone (29i) (4.5 mmol) and 1-iodoheptane (6.8 mmol) as a viscous yellow oil (1.80g, 88%) ; t.l.c. [diethyl ether : light petroleum (1:19)] Rf 0.85 ; δ_H 0.89 (3H, t, J 7Hz, Me), 1.04 - 1.84 (22H, brm, CH_2), 1.22 (9H, s, t-Bu), 7.17 - 7.34 (10H, m, phenyl-H) ; δ_C 14.10 (q, Me), 22.39, 22.67, 23.04 (3 x t, CH_2), 28.47 (q, t-Bu), 29.25, 30.41, 31.86, 33.96, 38.13 (5 x t, CH_2), 39.77 (s, CMe_3), 72.82 (s, C-N), 86.88 (s, CPh_2Bu^t), 125.78, 126.26, 131.72 (3 x d, phenyl-C), 145.26 (s, ipso-C) ; m/e (NH_3 D.C.I.) 433 (MH^+, 0.5%), 403 (49), 363 (100), and 223 (t-BuPh_2C^+, 9).

1-Benzyl-1-(t-butyldiphenylmethylazo)cyclohexane (111n)

was prepared from hydrazone (29i) (4.5 mmol) and benzyl bromide (6.8 mmol) as a viscous yellow oil (1.90g, 100%) ; t.l.c. [diethyl ether : light petroleum (1:19)] Rf 0.8 ; δ_H 1.42 (9H, s, t-Bu), 1.14 - 1.59 (6H, m, 3,4,5-CH_2), 1.71 - 1.90 (4H, m, 2,6-CH_2), 2.83 (2H, s, PhCH_2), 6.96 - 7.05 (2H, m, phenyl-H), 7.16 - 7.36 (13H, m, phenyl-H) ; δ_C 22.30, 25.66 (2 x t, CH_2), 28.57 (q, t-Bu), 33.48 (t, CH_2), 38.34 (s, CMe_3), 44.17 (t, CH_2Ph), 73.38 (s, C-N), 87.17 (s, CPh_2Bu^t), 125.81, 125.92, 126.37, 127.58, 130.93, 131.70 (6 x d, phenyl-C), 138.08, 144.96 (2 x s, ipso-C) ; m/e (NH_3 D.C.I.) 397 (31%), 395 (22), 355 (100), 223 (t-BuPh_2C^+, 50), 173 ($C_{13}H_{17}^+$, 26), 147 (32), and 91 ($PhCH_2^+$, 10).

1-Allyl-1-(t-butyldiphenylmethylazo)cyclohexane (111p)

was prepared from hydrazone (29i) (3.1 mmol) and allyl bromide (4.6 mmol) as a viscous yellow oil (600mg, 52%) ; t.l.c. [diethyl ether : light petroleum (1:19)] Rf 0.75 ; δ_H 1.08 - 1.93 (10H, m, CH_2), 1.33

(9H, s, t-Bu), 2.40 (2H, d, J 8Hz, allyl-$C\underline{H}_2$), 5.04 - 5.17 (2H, m, $=C\underline{H}_2$), 5.63 - 5.80 (1H, m, $=C\underline{H}$), 7.13 - 7.44 (10H, m, phenyl-H) ; δ_C 22.16, 25.80 (2 x t, $\underline{C}H_2$), 28.49 (q, t-Bu), 33.83 (t, $\underline{C}H_2$), 38.18 (s, $\underline{C}Me_3$), 42.27 (t, allyl-$\underline{C}H_2$), 72.73 (s, $\underline{C}$-N), 87.08 (s, $\underline{C}Ph_2Bu^t$), 117.14 (t, $=\underline{C}H$), 125.85, 126.32, 131.70 (3 x d, phenyl-$\underline{C}$), 134.55 (d, $=\underline{C}H$), 145.12 (s, ipso-$\underline{C}$) ; m/e (NH_3 D.C.I.) 345 (29%), 305 (100), 263 (45), 223 ($t\text{-}BuPh_2C^+$, 30), 167 (20), and 105 (37).

1-(t-Butyldiphenylmethylazo)-1-butylcyclododecane (111q)

was prepared from hydrazone (29j) (2.4 mmol) and 1-iodobutane (3.6 mmol) as a viscous yellow oil (1.10g, 97%) ; t.l.c. [diethyl ether : light petroleum (1:19)] Rf 0.85 ; δ_H 0.81 (3H, t, J 7Hz, Me), 0.86 - 0.95 (3H, m), 1.09 - 1.81 (28H, brm, $C\underline{H}_2$), 1.25 (9H, s, t-Bu), 7.14 - 7.35 (10H, m, phenyl-H) ; δ_C 13.95 (q, Me), 22.54, 22.98, 23.42, 25.28, 26.22, 27.10 (6 x t, $\underline{C}H_2$), 28.66 (q, t-Bu), 31.18, 37.84 (2 x t, $\underline{C}H_2$), 38.04 (s, $\underline{C}Me_3$), 76.38 (s, $\underline{C}$-N), 87.15 (s, $\underline{C}Ph_2Bu^t$), 125.76, 126.17, 131.73 (3 x d, phenyl-$\underline{C}$), 145.08 (s, ipso-$\underline{C}$) ;m/e (NH_3 D.C.I.) 405 (100%), 223 ($t\text{-}BuPh_2C^+$, 3), and 105 (26).

1-(t-Butyldiphenylmethylazo)-1-methylcyclododecane (111r)

was prepared from hydrazone (29j) (1.2 mmol) and iodomethane (1.8 mmol) as a viscous yellow oil (440mg, 85%) ; t.l.c. [diethyl ether : light petroleum (1:19)] Rf 0.85 ; δ_H 1.00 - 1.80 (25H, brm), 1.20 (9H, s, t-Bu), 7.13 - 7.34 (10H, m, phenyl-H) ; m/e (NH_3 D.C.I.) 433 (MH^+, 2%), 403 (2), 363 (26), 242 (22), 223 ($t\text{-}BuPh_2C^+$, 56), 183 (80), 167 (100), and 105 (29).

1-Benzyl-1-(t-butyldiphenylmethylazo)cyclododecane (111s)

was prepared from hydrazone (29j) (2.4 mmol) and benzyl bromide (3.6 mmol) as a viscous yellow oil (1.17g, 96%) ; t.l.c. [diethyl ether : light petroleum (1:19)] Rf 0.85 ; δ_H 0.83 - 0.94 (2H, m, 7-$C\underline{H}_2$), 1.07 - 1.61 (18H, brm, $C\underline{H}_2$), 1.15 (9H, s, t-Bu), 1.74 - 1.87 (2H, m), 2.91

(2H, s, C$\underline{H}_2$Ph), 6.69 - 6.74 (2H, m, phenyl-$\underline{H}$), 6.97 - 7.11 (3H, m, phenyl-$\underline{H}$), 7.12 - 7.31 (10H, m, phenyl-$\underline{H}$) ; δ_C 20.07, 23.13, 23.25, 26.31, 27.22 (5 x t, $\underline{C}H_2$), 28.60 (q, t-Bu), 29.33, 31.13 (2 x t, $\underline{C}H_2$), 38.36 (s, $\underline{C}Me_3$), 44.80 (t, $\underline{C}H_2$), 64.47 (s, $\underline{C}$-N), 87.58 (s, $\underline{C}Ph_2Bu^t$), 125.88, 126.20, 127.43, 129.84, 130.93, 131.79 (6 x d, phenyl-$\underline{C}$), 137.84, 144.49 (2 x s, ipso-$\underline{C}$) ; m/e (NH_3 D.C.I.) 498 (31%), 439 (100), 223 (t-BuPh_2C^+, 4), 105 (24), 91 ($PhCH_2^+$, 14).

General procedure for the preparation of Alkanes (83)

The following procedure for the preparation of n-dodecane (83a) is typical.

Azo-alkane (111a) (2.4 mmol) was dissolved in benzene (50ml) and thiophenol (3ml, excess) was added. The solution was heated under reflux for 2h,cooled, and diluted with diethyl ether (100ml). The solution was washed with aqueous sodium hydroxide (2M, 2 x 30ml), brine (2 x 15ml),dried ($MgSO_4$),filtered and evaporated to yield a crude product. Purification by flash chromatography on silica gel followed by p.l.c. (light petroleum) gave n-dodecane (83a) as a colourless liquid (379mg, 94%) b.p.76 - 78°C at 2.0 mmHg (Lit.[207] 79 - 81°C at 3.8 mmHg) ; t.l.c. (light petroleum) Rf 0.5 ; $\nu_{max.}$ (film) 2960 s, 2930 s, 2855 s, 1468 m, and 1450 m cm^{-1}; δ_H 0.91 (6H, t, $\underline{J}$ 7Hz, 2 x Me), 1.20 - 1.40 (20H, brm) ; m/e (E.I.) 170 (M^+, 5%), 85 ($C_6H_{13}^+$, 25), 71 (46), 57 (100), and 43 (89).

The following alkanes (83) were similarly prepared :-

Pentadecane (83b)[208] was prepared from azo-alkane (111e) (1.0 mmol) as a colourless liquid (197mg, 93%); t.l.c. (light petroleum) Rf 0.5 ; $\nu_{max.}$ (film) 2960 s, 2930 s, 2850 s, 1470 m, 1450 m, and 1380 m cm^{-1}; δ_H 0.91 (6H, t, $\underline{J}$ 7Hz, 2 x Me), 1.19 - 1.31 (26H, brm) ; m/e (E.I.) 212 (M^+, 2%), 183 (1), 169 (1), 155 (1), 141 (1), 127 (3),

113 (4), 99 (7), 85 (32), 71 (53), 57 (100), and 43 (98).

Hexylbenzene (83c)[209] was prepared from azo-alkane (111g) (2.4 mmol) as a colourless liquid (220mg, 56%) ; t.l.c. (light petroleum) Rf 0.4 ; $\nu_{max.}$ (film) 3090 w, 3065 w, 3030 w, 2960 s, 2930 s, 2860 s, 1606 w, 1496 w, 1456 m, 748 s, and 700 s cm^{-1}; δ_H 0.86 (3H, t, J 7Hz, Me), 1.21 - 1.35 (6H, m, $C\underline{H}_2$), 1.52 - 1.64 (2H, m, $C\underline{H}_2$), 2.58 (2H, t, J 8Hz, $C\underline{H}_2Ph$), 7.10 - 7.33 (5H, m, phenyl-H) ; m/e (E.I.) 162 (M^+,22%), 105 (10), 91 ($PhCH_2^+$, 100), 65 (11), 43 (15), and 39 (9).

2-Methyltetradecane (83d) was prepared from azo-alkane (111h) (0.6 mmol) as a colourless liquid (107mg, 84%) ; t.l.c. (light petroleum) Rf 0.5 ; $\nu_{max.}$ (film) 2960 s, 2925 s, 2860 s, 1466 m, 1386 w, and 1368 w cm^{-1}; δ_H 0.87 (6H, d, J 6.5Hz, $CH\underline{Me}_2$), 0.89 (3H, t, J 7Hz, Me), 1.23 - 1.30 (22H, m, $C\underline{H}_2$), 1.50 - 1.56 (1H, m, $C\underline{H}Me_2$) ; δ_C 14.07 (q, Me), 22.64 (q, 2 x Me), 22.69, 27.42, 27.98, 29.36, 29.66 (5 x t, $\underline{C}H_2$), 29.70 (t, 3 x $\underline{C}H_2$ unresolved), 29.73, 29.96, 31.93 (3 x t, $\underline{C}H_2$), 39.09 (d, $\underline{C}HMe_2$) ; m/e (E.I.) 212 (M^+,1%), 197 (M^+-CH_3, 5), 169 (24), 168 (11), 155 (1), 141 (3), 127 (6), 113 (9), 99 (16), 85 (46), 71 (57), 57 (100), 56 (20), 55 (10), 43 (59), and 41 (14) ; (Found : C, 84.78 ; H, 15.31%. $C_{15}H_{32}$ requires : C, 84.82 ; H, 15.18%).

Heptylcyclohexane (83e) was prepared from azo-alkane (111m) (1.9 mmol) as a colourless liquid (240mg, 64%) ; t.l.c. (light petroleum) Rf 0.7 ; $\nu_{max.}$ (film) 2960 s, 2930 s, 2855 s, 1466 m, 1450 m, and 1380 w cm^{-1}; δ_H 0.89 (3H, t, J 6.5Hz, Me), 1.11 - 1.38 (20H, brm), 1.60 - 1.87 (3H, m) ; δ_C 14.13 (q, Me), 22.74 (t, $\underline{C}H_2Me$), 26.52, 26.84, 26.95, 29.44, 30.04, 31.98, 33.54, 37.62 (8 x t, $\underline{C}H_2$), 37.77 (d, $\underline{C}H$) ; m/e (E.I.) 182 (M^+, 10%), 83 (100), 82 (73), 57 (34), 55 (68), 43 (50), and 41 (64) ; (Found : 182.2033 ; $C_{13}H_{26}$ requires : 182.2034).

Benzylcyclohexane (83f) was prepared from azo-alkane (111n) (2.0 mmol) as a colourless liquid (257mg, 71%); t.l.c. (light petroleum)

Rf 0.4 ; $\nu_{max.}$ (film) 3090 w, 3065 w, 3030 m, 2920 s, 2855 m, 1608 w, 1496 w, 1450 m, 744 m, and 698 s cm^{-1}; δ_H 0.92 - 1.37 (5H, m), 1.51 - 1.89 (6H, m), 2.56 (2H, d, J 7Hz, $C\underline{H}_2Ph$), 7.17 - 7.41 (5H, m, phenyl-H) ; δ_C 26.33, 26.60, 33.17 (3 x t, 2,3,4,5,6-$\underline{C}H_2$), 39.78 (d, $\underline{C}H$), 44.14 (t, $\underline{C}H_2Ph$), 125.52, 127.99, 129.14 (3 x d, phenyl-$\underline{C}$), 141.33 (s, ipso-$\underline{C}$); m/e (E.I.) 174 (M^+, 24%), 92 (100), 91 (39), 83 (40), 82 (12), 67 (12), 65 (11), 55 (60), and 41 (24) ; (Found :C, 89.35 ; H, 10.15% ; 174.1408. $C_{13}H_{18}$ requires : C, 89.59 ; H, 10.41% ; 174.1408).

Butylcyclododecane (83g) was prepared from azo-alkane (111q) (2.0 mmol) as a colourless liquid (377mg, 72%) ; t.l.c. (light petroleum) Rf 0.7 ; $\nu_{max.}$ (film) 2960 s, 2940 s, 2860 s, 1472 m, 1450 m, and 1380 w cm^{-1}; δ_H 0.93 (3H, t, J 7Hz, Me), 1.15 - 1.49 (29H, brm) ; δ_C 14.16 (q, Me), 21.81, 23.10, 23.44, 24.25, 24.91, 29.20, 29.71, 34.82 (8 x t, $\underline{C}H_2$), 33.98 (d, $\underline{C}H$); m/e (E.I.) 224 (M^+, 19%), 125 (18), 111 (36), 97 (67), 83 (82), 69 (80), 55 (100), 43 (67), and 41 (72) ; (Found : 224.2505 ; $C_{16}H_{32}$ requires : 224.2504).

Methylcyclododecane (83h)[210] was prepared from azo-alkane (111r) (0.65 mmol) as a colourless liquid (102mg, 87%) ; t.l.c. (light petroleum) Rf 0.75 ; $\nu_{max.}$ (film) 2960 s, 2930 s, 2855 s, 1476 m, 1444 m, and 1380 w cm^{-1}; δ_H 0.82 (3H, d, J 8.5Hz, Me), 0.97 - 1.64 (23H, brm) ; δ_C 21.30 (q, Me), 22.30, 23.76, 24.35 (3 x t, $\underline{C}H_2$), 28.30 (d, $\underline{C}H$), 31.89 (t, $\underline{C}H_2$) ; m/e (E.I.) 182 (M^+, 39%), 154 (10), 125 (16), 111 (31), 97 (54), 83 (77), 69 (73), 55 (100), and 41 (59) ; (Found : 182.2033 ; $C_{13}H_{26}$ requires : 182.2034).

Benzylcyclododecane (83i) was prepared from azo-alkane (111s) (1.9 mmol) as a colourless liquid (410mg, 78%) ; t.l.c. (light petroleum) Rf 0.65 ; $\nu_{max.}$ (film) 3090 w, 3065 w, 3030 w, 2930 s, 2910 s, 2860 s, 2850 m, 1606 w, 1494 w, 1470 m, 1446 w, 756 s, and 700 s cm^{-1}; δ_H 1.19 - 1.58 (22H, brm), 1.78 - 1.86 (1H, m), 2.54 (2H, d, J 7Hz, $C\underline{H}_2Ph$),

7.16 - 7.37 (5H, m, phenyl-H) ; δ_C 21.75, 23.36, 23.45, 24.30, 24.86, 28.78 (6 x t, 2-12-CH_2), 36.32 (d, CH), 41.63 (t, CH_2Ph), 125.48, 128.04, 129.08 (3 x d, phenyl-C), 141.87 (s, ipso-C) ; m/e (E.I.) 258 (M^+, 25%), 166 (89), 111 (35), 97 (66), 92 (46), 91 ($PhCH_2^+$, 100), 83 (60), 69 (48), 55 (53), and 40 (36) ; (Found : C, 88.60 ; H, 11.92% ; 258.2347. $C_{19}H_{30}$ requires : C, 88.30 ; H, 11.70%; 258.2347).

General procedure for radical trapped products

The following procedure for the preparation of 2-phenyl selenenyldodecane (114) is typical.

The azo-alkane (111a) (0.47 mmol) was dissolved in benzene (30ml) with diphenyl diselenide (2.4 mmol) and the solution heated under reflux for 2h. The solvent was evaporated and the residue purified by flash chromatography on silica gel to give 2-phenylselenenyl-dodecane (120mg, 77%) as a low melting white solid ; t.l.c. (light petroleum) Rf 0.8 ; $\nu_{max.}$ (film) 3070 w, 3055 w, 2955 m, 2925 s, 2855 s, 1580 m, 1478 m, 1460 m, 1378 m, 740 m, and 692 m cm^{-1}; δ_H 0.90 (3H, t, J 7Hz, Me), 1.21 - 1.36 (16H, brm), 1.41 (3H, d, J 7Hz, Me), 1.42 - 1.70 (2H, m, CH_2), 3.25 - 3.34 (1H, m, CHSePh), 7.26 - 7.32 (3H, m, phenyl-H), 7.51 - 7.60 (2H, m, phenyl-H) ; δ_C 14.10, 22.19 (2 x q, Me), 22.69, 27.83, 29.33, 29.39, 29.54, 29.60, 31.92, 37.59 (8 x t, CH_2), 39.84 (d, CHSePh), 127.20, 128.79, 134.84 (3 x d, phenyl-C), 129.55 (s, ipso-C) ; m/e (E.I.) 326 (M^+, 17%), 158 (100), 156 (51), 154 (22), 71 (40), 69 (24), 57 (87), 55 (55), 43 (90), 41 (68), and 39 (18) ; (Found : 326.1511 ; $C_{18}H_{30}Se$ requires : 326.1513).

The following compounds were prepared similarly :-

1-Butyl-1-phenylselenenylcyclododecane (116) was prepared from azo-alkane (111q) (0.53 mmol) and diphenyl diselenide (2.7 mmol) as a viscous liquid (108mg, 54%) ; t.l.c. (light petroleum) Rf 0.9 ;

$\nu_{max.}$ (film) 3070 w, 3055 w, 2960 s, 2910 s, 2860 s, 1578 w, 1468 s, 1446 m, 1022 m, 740 s, and 694 s cm^{-1}; δ_H 0.93 (3H, t, J 7Hz, Me), 1.18 - 1.71 (28H, brm), 7.25 - 7.36 (3H, m, phenyl-H), 7.56 - 7.62 (2H, m, phenyl-H) ; δ_C 14.25 (q, Me), 20.31, 22.69, 22.98, 26.10, 26.75, 27.16, 33.74, 38.48 (8 x t, $\underline{C}H_2$), 57.97 (s, $\underline{C}$SePh), 127.82 (s,ipso-C), 128.16, 128.50, 137.81 (3 x d, phenyl-C) ; m/e (E.I.) 380 (M^+, 4%), 222 (55), 157 (25), 110 (35), 96 (83), 94 (31), 82, (96), 77 (53), 68 (82), 66 (37), 57 (64), 55 (100), 41 (38), and 39 (63) ; (Found : 380.1981 ; $C_{22}H_{36}Se$ requires : 380.1982).

2-Bromododecane (117a)[211] was prepared from azo-alkane (111a) (0.49 mmol) and N-bromosuccinimide (2.5 mmol) in a solution of THF : benzene (1:1, 25ml) as a colourless liquid (50mg, 50%) ; t.l.c. (light petroleum) Rf 0.65 ; $\nu_{max.}$ (film) 2960 s, 2925 s, 2860 s, 1466 m, and 1380 w cm^{-1}; δ_H 0.86 (3H, t, J 7Hz, Me), 1.14 - 1.34 (18H, brm), 1.68 (3H, d, J 7Hz, Me), 3.90 - 4.30 (1H, m, CHBr) ; m/e (NH_3 C.I.) 250/248 (M^+, 1%), 208/206 (7), 194/192 (11), 169 (6), 111 (13), 97 (20), 85 (37), 83 (21), 71 (55), 69 (39), 57 (100), 55 (70), 43 (89), 41 (78), and 39 (16).

2-Chlorododecane (117b)[212] was prepared from azo-alkane (111a) (0.35 mmol) and N-chlorosuccinimide (1.8 mmol) as a colourless liquid (35mg, 50%) ; t.l.c. (light petroleum) Rf 0.6 ; $\nu_{max.}$ (film) 2960 m, 2925 s, 2855 s, 1460 m, and 1378 m cm^{-1}; δ_H 0.85 (3H, t, J 7Hz, Me), 1.15 - 1.34 (18H, brm), 1.47 (3H, d, J 8Hz, Me), 3.95 - 4.14 (1H, m, CHCl) ; δ_C 14.10 (q, Me), 22.69 (t, $\underline{C}H_2$), 25.36 (q, Me), 26.69, 29.16, 29.33, 29.42, 29.54, 29.60, 31.92, 40.45 (8 x t, $\underline{C}H_2$), 58.92 (d, CHCl) ; m/e (E.I.) 168 (18%), 140 (7), 126 (10), 125 (10), 111 (20), 105 (11), 97 (39), 83 (45), 82 (22), 69 (67), 55 (81), 43 (93), 41 (100), and 39 (29).

3-Methyl-1-phenylbut-1-ene (118)[213] was prepared from azo-alkane (111b) (2.6 mmol) and β-nitrostyrene (13 mmol) as a colourless oil (183mg, 48%) ; t.l.c. (light petroleum) Rf 0.85 ; $\nu_{max.}$ (film) 3080 w, 3060 w, 3025 w, 2960 s, 2930 m, 2870 w, 1598 w, 968 m, 748 s, and 696 s cm^{-1}; δ_H 1.11 - 1.20 (6H, 2 x d, J 7Hz, Me), 2.45 - 2.60 (1H, m, C<u>H</u>Me_2), 6.21 - 6.28 (1H, m, vinyl-C<u>H</u>), 6.40 (1H, d, J 16Hz, C<u>H</u>Ph), 7.23 - 7.42 (5H, m, phenyl-<u>H</u>) ; δ_C 22.46 (2 x q, unresolved, Me), 31.54 (d, <u>C</u>HMe_2), 125.96, 126.73, 128.63 (3 x d, phenyl-<u>C</u>), 133.69 (d, =<u>C</u>H), 137.96 (s+d, unresolved, ipso-<u>C</u>, =<u>C</u>HPh) ; m/e (E.I.) 146 (M^+, 36%), 145 (34), 131 (100), 91 (43) ; (Found : 146.1094 ; $C_{11}H_{14}$ requires : 146.1095).

3-Butyl-1-phenyldec-1-ene (119) was prepared from azo-alkane (111f) (1.4 mmol) and β-nitrostyrene (7.0 mmol) as a colourless oil (109mg, 28%) ; t.l.c. (light petroleum) Rf 0.75 ; $\nu_{max.}$ (film) 3080 w, 3060 w, 3030 w, 2960 s, 2930 s, 2855 s, 1598 w, 970 m, 748 s, and 696 m cm^{-1}; δ_H 0.89 (6H, t, J 7Hz, 2 x Me), 1.23 - 1.34 (16H, brm, C<u>H</u>$_2$), 1.40 - 1.51 (2H, m, C<u>H</u>$_2$), 2.08 - 2.17 (1H, m, allyl-<u>H</u>), 5.95 - 6.04 (1H, m, =C<u>H</u>), 6.33 (1H, d, J 16Hz, =C<u>H</u>Ph), 7.21 - 7.41 (5H, m, phenyl-<u>H</u>) ; m/e (E.I.) 272 (M^+, 14%), 215 (24), 173 (48), 131 (16), 129 (16), 117 (100), 105 (36), 104 (40), 91 (94), 85 (21), 77 (24), 69 (37), 58 (31), 57 (61), 56 (23), 55 (35), 42 (51), 40 (63), and 37 (17) ; (Found : C, 87.90 ; H, 11.90%. $C_{20}H_{32}$ requires : C, 88.16 ; H, 11.84%).

3-(2-Methylpropyl)-1-phenyltridec-1-ene (120) was prepared from azo-alkane (111h) (0.4 mmol) and β-nitrostyrene (2.0 mmol) as a colourless oil (31.5mg, 25%) ; t.l.c. (light petroleum) Rf 0.8 ; $\nu_{max.}$ (film) 3080 w, 3060 w, 3025 w, 2960 s, 2930 s, 2855 m, 1600 w, 968 m, 750 m, and 696 m cm^{-1}; δ_H 0.85 - 0.95 (9H, complex, 3 x Me), 1.20 - 1.34 (20H, brm, C<u>H</u>$_2$), 1.59 - 1.69 (1H, m, C<u>H</u>Me_2), 2.17 - 2.25

(1H, m, allyl-H), 5.88 - 6.00 (1H, m, =CH), 6.33 (1H, d, J 15Hz, =CHPh), 7.15 - 7.42 (5H, m, phenyl-H) ; m/e (E.I.) 314 (M^+, 13%), 257 ($M^+-C_4H_9$, 15), 173 (31),117 (100), 105 (23), 91 (35), 57 (10), 55 (10), 42 (33), and 40 (26) ; (Found : C, 87.80 ; H, 12.50% . $C_{23}H_{38}$ requires : C, 87.82 ; H, 12.18%).

General procedure for the preparation of Hydrazines

The following procedure for the preparation of isopropyl hydrazine hydrochloride (149) is typical.

Azo-alkane (111b) (2.7 mmol) was dissolved in trifluoroacetic acid (5ml) and the solution stirred under argon at 20°C for 6h. The solvent was evaporated to give crude benzophenone isopropylhydrazone[214] [δ_H 1.19, 1.22 (6H, 2 x d, J 6.5Hz, Me), 3.56 - 3.69 (1H, m, CHMe$_2$), 7.28 - 7.33 (5H, m, phenyl-H), 7.48 - 7.56 (5H, m, phenyl-H) ; m/e (NH_3 D.C.I.) 239 (MH^+, 57%), 237 (100), 200 (30), 183 (30), 182 (19), 167 (10), and 105 (19)]. This was dissolved in ethanol (10ml) with concentrated hydrochloric acid (5ml) and the solution stirred at 20°C for 12 - 15h. The solvent was partially evaporated,water (15ml) added and the solution washed with diethyl ether (2 x 10ml) and the aqueous layer evaporated to give a crude product. Purification by recrystalli--sation from ethanol gave isopropylhydrazine hydrochloride (149) as a white crystalline solid (210mg, 60%) m.p. 111 - 113°C (Lit.,[215] 114°C) ; δ_H (CD_3OD, CHD_2OD = 3.305 p.p.m.) 1.30 (6H, d, J 7.5Hz, Me), 3.30 - 3.38 (1H, m, CHMe$_2$) ; m/e (NH_3 C.I.) 75 ($C_3H_{11}N_2^+$, 100%), and 59 (10).

The following hydrazines were similarly prepared :-

(1-Phenylmethyl)ethylhydrazine (151)[216] was prepared from azo-alkane (111c) (4.0 mmol) via benzophenone (1-phenylmethyl)ethyl hydrazine [δ_H 1.46 (3H, d, J 6.5Hz, Me), 2.88 - 2.95 (1H, m, PhCH$_2$), 3.10 - 3.17 (1H, m, PhCH$_2$), 3.85 - 4.00 (1H, m, CHN), 7.09 - 7.60

(15H, m, phenyl-H) ; m/e (NH_3 D.C.I.) 315 (MH^+, 100%), 223 (48), 180 (38), and 91 (17)], as a white crystalline solid hydrochloride (550mg, 74%) m.p. 119 - 120.5°C from ethanol (Lit.,[216] 122 - 124°C) ; δ_H [$(CD_3)_2SO$, $C\underline{H}D_2S(O)CD_3$ = 2.50 p.p.m.] 1.04 (3H, d, J 7Hz, Me), 2.44 - 2.57 (1H, m, $PhC\underline{H}_2$), 3.16 - 3.24 (1H, m, $PhC\underline{H}_2$), 3.27 - 3.37 (1H, m, C<u>H</u>N), 7.18 - 7.33 (5H, m, phenyl-H) ; m/e (NH_3 C.I.) 151 ($C_9H_{15}N_2^+$, 100%), 91 (22), and 59 (62).

t-Butylhydrazine was prepared from azo-alkane (111k) (3.6 mmol) via benzophenone t-butylhydrazone [δ_H 1.48 (9H, s, t-Bu), 7.26 - 7.61 (10H, m, phenyl-H) ; m/e (NH_3 D.C.I.) 253 (MH^+, 100%), 252 (24), 237 (38), 195 (10), 180 (20), and 167 (17)] , as a white crystalline solid hydrochloride (110mg, 25%) m.p. 188 - 190°C from ethanol (Lit.,[177] 189°C) ; δ_H [$(CD_3)_2SO$, $C\underline{H}D_2S(O)CD_3$ = 2.50 p.p.m.] 1.22 (s) ; m/e (NH_3 C.I.) 89 ($C_4H_{13}N_2^+$, 100%), 47 (57), and 46 (14).

(2-Methyl-1-phenyl)-2-propylhydrazine was prepared from azo-alkane (1111) (1.4 mmol) via benzophenone (2-methyl-1-phenyl)-2-propylhydrazone [δ_H 1.48 (6H, s, Me), 3.11 (2H, s, $PhC\underline{H}_2$), 7.08 - 7.63 (15H, m, phenyl-H)], as an unstable white crystalline solid hydrochloride (70mg, 25%) m.p. 137 - 139°C from ethanol (Lit.,[217] 139 - 141°C) ; δ_H (CD_3OD, $C\underline{H}D_2OD$ = 3.305 p.p.m.) 1.26 (6H, s, Me), 2.96 (2H, s, $PhC\underline{H}_2$), 7.23 - 7.39 (5H, m, phenyl-H) ; δ_C 22.12 (q, Me), 43.54 (t, $PhC\underline{H}_2$), 62.91 (s, <u>C</u>N), 128.35, 129.52, 131.74 (3 x d, phenyl-<u>C</u>), 136.02 (s, ipso-<u>C</u>) ; m/e (NH_3 D.C.I.) 165 ($C_{10}H_{17}N_2^+$, 100%), and 73 (26).

General procedure for the preparation of Amines (122)

The following procedure for the preparation of 1-benzyl cyclohexylamine (122b) is typical.

Azo-alkane (111n) (3.3 mmol) was dissolved in trifluoroacetic acid (5ml) and stirred under argon at 20°C for 6h. The solvent was

evaporated and the residue dissolved in a suspension of palladium on charcoal (10%, 30mg) in ethanol (35ml) with concentrated hydrochloric acid (5ml). The mixture was stirred under an atmosphere of hydrogen (1 atm.) at 50°C for 15h. The catalyst was removed by filtration through Celite, the Celite washed with ethanol (60ml) and the combined washings evaporated. Water (30ml) was added and the mixture was extracted with diethyl ether (2 x 20ml). The aqueous layer was evaporated to give a crude product which was purified by recrystallisation from ethyl acetate to give 1-benzylcyclohexylamine hydrochloride (528mg, 71%) as a white crystalline solid, m.p. 288 - 289°C (Lit.[218] 285 - 290°C) ; δ_H (CD_3OD, $C\underline{H}D_2OD$ = 3.305 p.p.m.) 1.41 - 1.58 (2H, m, 4-$C\underline{H}_2$), 1.58 - 1.85 (8H, m, 2,3,5,6-$C\underline{H}_2$), 3.01 (2H, s, $PhC\underline{H}_2$), 7.23 - 7.40 (5H, m, phenyl-$\underline{H}$) ; δ_C (CD_3OD, $\underline{C}D_3OD$ =49 .30 p.p.m.) 22.24, 25.84, 34.74, 43.37 (4 x t, $\underline{C}H_2$), 57.82 (s, $\underline{C}N$), 128.55, 130.20, 131.78 (3 x d, phenyl-$\underline{C}$), 135.54 (s, ipso-$\underline{C}$) ; m/e (NH_3 C.I.) 190 ($C_{13}H_{20}N^+$, 8%), 167 (100), and 106 (14).

The following amines (122) were prepared similarly :-

(2-Methyl-1-phenyl)-2-propylamine (122a)[219] was prepared from azo-alkane (1111) (3.2 mmol) as a white crystalline solid hydrochloride (400mg, 67%) m.p. 194 - 195°C from ethyl acetate (Lit.,[219] 195 - 197°C) ; δ_H (CD_3OD, $C\underline{H}D_2OD$ = 3.305 p.p.m.) 1.33 (6H, s, Me), 2.92 (2H, s, $PhC\underline{H}_2$), 7.21 - 7.42 (5H, m, phenyl-$\underline{H}$) ; δ_C (CD_3OD, $\underline{C}D_3OD$ =49 .30 p.p.m.) 25.61 (q, Me), 46.84 (t, $PhC\underline{H}_2$), 55.68 (s, $\underline{C}N$), 128.49, 129.65, 131.66 (3 x d, phenyl-$\underline{C}$), 136.08 (s, ipso-$\underline{C}$) ; m/e (NH_3 D.C.I.) 150 ($C_{10}H_{16}N^+$, 100%), and 58 (61).

1-Methylcyclododecylamine (122c) was prepared from azo-alkane (111r) (1.4 mmol) as a white crystalline solid hydrochloride (125mg, 38%) m.p. 215 - 219°C from ethyl acetate ; δ_H (CD_3OD, $C\underline{H}D_2OD$ = 3.305 p.p.m.) 1.29 (3H, s, Me), 1.29 - 1.57 (18H, brm, $C\underline{H}_2$), 1.57 - 1.77 (4H, m,

2,12-C$\underline{H}_2$) ; δ_C (CD_3OD, $\underline{C}D_3OD$ = 49.30 p.p.m.) 20.00 (t, $\underline{C}H_2$), 22.97 (q, Me), 23.53, 25.45, 27.02, 27.15, 33.79 (5 x t, $\underline{C}H_2$), 58.20 (s, $\underline{C}N$) ; m/e (E.I.) 197 ($C_{13}H_{27}N^+$, 3%), 182 (6), 168 (3), 154 (6), 126 (4), 106 (17), 105 (10), 70 (100), and 58 (45); (Found : 197.2146 ; $C_{13}H_{27}N$ requires : 197.2143).

Amphetamine (122d) was prepared from azo-alkane (111c) (3.0 mmol) as a white crystalline oxalate salt (450mg, 68%) m.p. 167 - 171°C from ethyl acetate ; δ_H (CD_3OD, $C\underline{H}D_2OD$ = 3.305 p.p.m.) 1.23 (3H, d, J 6.5Hz, Me), 2.73 - 2.80 (1H, m, Ph$C\underline{H}_2$), 3.00 - 3.06 (1H, m, Ph$C\underline{H}_2$), 3.47 - 3.55 (1H, m, $C\underline{H}N$), 7.20 - 7.45 (5H, m, phenyl-$\underline{H}$) ; δ_C (CD_3OD, $\underline{C}D_3OD$ = 49.30 p.p.m.) 18.21 (q, Me), 41.79 (t, $\underline{C}H_2$), 50.37 (d, $\underline{C}HN$), 128.21, 129.86, 130.34 (3 x d, phenyl-$\underline{C}$), 137.57 (s, ipso-$\underline{C}$) ; m/e (NH_3 C.I.) 136 ($C_9H_{14}N^+$, 100%), and 102 (7). The amine was initially isolated as its hydrochloride salt m.p. 143.- 145°C (Lit.,[220] 145 - 147°C) but this proved very hygroscopic.

2-Dodecylamine (122e)[221] was prepared from azo-alkane (111a) (3.9 mmol) as a white crystalline hydrochloride (600mg, 69%) m.p.89 - 91°C (Lit.,[221] 91 - 92°C) from ethyl acetate ; δ_H (CD_3OD, $C\underline{H}D_2OD$ = 3.305 p.p.m.) 0.91 (3H, t, J 7Hz, Me), 1.21 - 1.47 (19H, bm), 1.47 - 1.73 (2H, m, CH_2), 3.18 - 3.33 (1H, m, $C\underline{H}N$) ; δ_C (CD_3OD, $\underline{C}D_3OD$ = 49.30 p.p.m.) 14.40, 18.70 (2 x q, Me), 23.68, 26.47, 30.41, 30.47, 30.63, 33.03, 35.85 (7 x t, $\underline{C}H_2$), 59.47 (d, $\underline{C}HN$) ; m/e (NH_3 C.I.) 186 ($C_{12}H_{28}N^+$, 100%), 167 (15), and 43 (46).

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APPENDIX

PUBLICATIONS

Michael Additions of Hydrazones for Carbon–Carbon Bond Formation

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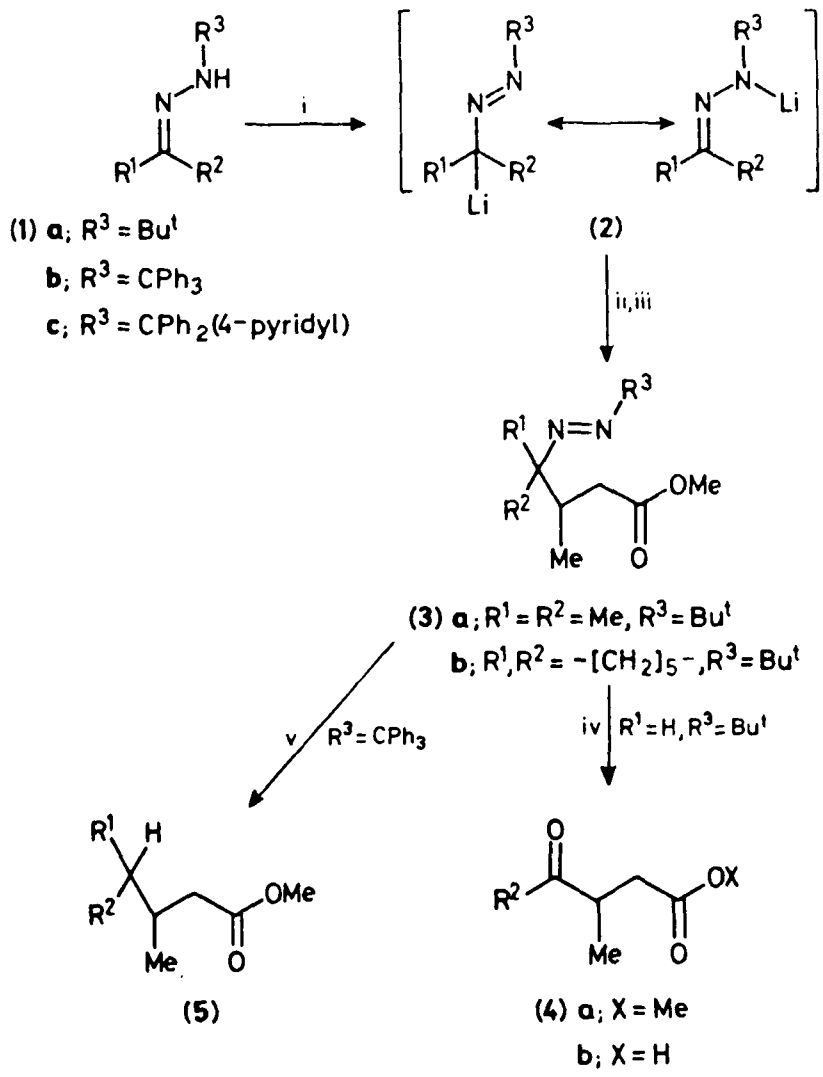
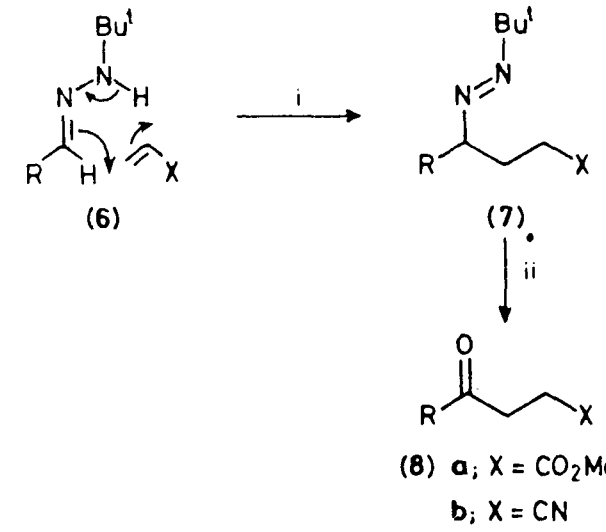
The lithium salts of t-butyl- and trityl-hydrazones react with methyl crotonate to form *C*-trapped azo-esters and similar products were observed from a thermal ene-reaction of aldehyde t-butylhydrazones with methyl acrylate or acrylonitrile, and aldehyde phenylhydrazones with methyl acrylate; these products can be diverted into synthetically useful γ-keto-esters, γ-keto-nitriles, saturated esters, γ-alkyl-2-pyrrolidones, and γ-amino-esters.

Recently we described the use of t-butylhydrazones (**1a**) as acyl anion equivalents,[1] and the use of trityl (**1b**) and diphenyl-4-pyridylmethyl (**1c**) hydrazones for reductive C–C bond formation from aldehydes and ketones.[2] Herein we report C–C bond forming reactions by the reaction of these hydrazones with Michael type electrophiles in both ionic (Scheme 1) and thermal (Schemes 2 and 3) type pathways.

Thus treatment of the t-butylhydrazones (**1a**) with n-butyl-lithium (0.95 equiv.) in tetrahydrofuran (THF) at 0 °C gave the azo-anion (**2**) which was cooled to −78 °C and treated with methyl crotonate (1.0 equiv., −78 °C, 30 min) (Scheme 1). Acetic acid (1.0 equiv.) was added, and in the case of ketone t-butylhydrazones, the stable azo-esters [(**3a**), 58%; (**3b**), 53%] were isolated by chromatography.† The azo-esters (**3**) derived from aldehyde t-butylhydrazones were not isolated, but directly isomerised [trifluoroacetic acid (TFA), 5 h, 20 °C] to their hydrazone forms. Thereafter hydrolysis [$(CO_2H)_2$–H_2O–diethyl ether, 12 h, 20 °C] and chromatography gave the γ-keto-esters (**4a**) (50—60%, Table 1). With trityl (**1b**) or diphenyl-4-pyridylmethyl (**1c**) hydrazones a lower yielding *C*-addition pathway *via* the azo-anion (**2**) was observed. Thus treatment of the tritylhydrazone (**1b**) with n-butyl-lithium (0.95 equiv.) in dimethoxyethane at −78 °C gave the azo-anion (**2**) which was warmed to −50 °C and treated with methyl crotonate (2.0 equiv. added over 1 h, −50 °C). TFA (1.0 equiv.) and ethanethiol (5 equiv.) were added in sequence and the solution warmed to 20 °C. Purification by chromatography gave the saturated esters (**5**) (20—35%, Table 1).‡



Scheme 1. *Reagents:* i, n-butyl-lithium (0.95 equiv., −78 or −50 °C); ii, methyl crotonate; iii, HOAc or TFA (1.0 equiv.); iv, TFA, 5 h, 20 °C; $(CO_2H)_2$–H_2O–diethyl ether, 12 h, 20 °C; v, EtSH.



Scheme 2. *Reagents:* i, methyl acrylate or acrylonitrile (2–3 equiv.), toluene or xylene, reflux, 24 h; ii, TFA, 1.5 h, 20 °C; $(CO_2H)_2$–H_2O–diethyl ether, 20 °C, 12 h (X = CO_2Me) or 3 h (X = CN).

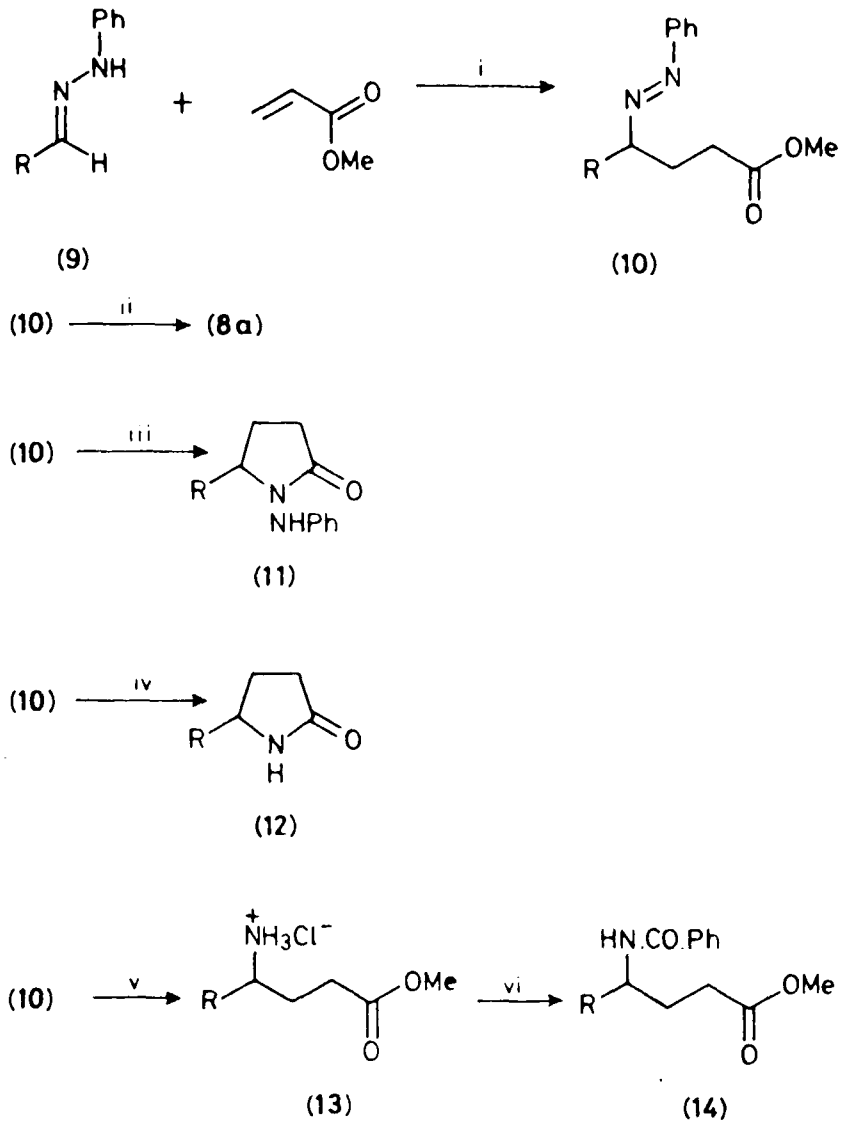
Table 1

Hydrazone (1)			Product, %			
R^1	R^2	R^3				
Me	Me	But	(**3a**)	58		
	-[CH_2]$_5$-	But	(**3b**)	53		
H	Me	But	(**4a**)	58		
H	Bun	But	(**4a**)	60[a]		
H	Bui	But	(**3**)	55	(**4b**)	47[b]
H	n-C_7H_{15}	But	(**4a**)	50		
H	Ph	But	(**3**)	68	(**4b**)	47[b]
	-[CH_2]$_5$-	$C(Ph)_3$	(**5**)	35		
H	Bun	$C(Ph)_3$	(**5**)	20		
H	Bui	$C(Ph)_3$	(**5**)	23		

[a] If a deficiency of methyl crotonate (0.5 equiv.) was used in this reaction, then the yield of (**4a**) was 76% based upon methyl crotonate. [b] These hydrazones proved resistant to hydrolysis at 20 °C. γ-Keto-acids were isolated after more forcing hydrolysis [2 M HCl in H_2O: THF (1 : 1), reflux, 15 h].

† All known compounds were characterised by comparison to literature data. All new compounds were characterised by full spectral and analytical data. Yields refer to isolated and purified products from the hydrazone starting material.

‡ The major pathway in these examples appears to be a basic deprotonation of methyl crotonate by the azo-anion (**2**) to give a recovered hydrazone (**1b**).



Scheme 3. *Reagents:* i, xylene, reflux, 24 h; ii, TFA, 20 °C, 5 h then $(CO_2H)_2$–H_2O–diethyl ether, 20 °C, 12 h; iii, Zn, HOAc, 60 °C, 1.5 h; iv, Pd/C, H_2 (1 atm), 50 °C, 12—24 h; v, PtO_2, H_2 (1 atm), 20 °C, 24 h, MeOH–HCl; vi, C_5H_5N, PhCOCl.

Table 2

Hydrazone (6) R		Product, %		
Me	(8a)	80[a]	—	
Bu[i]	(8a)	77[b]	(8b)	20[b]
Bu[n]	(8a)	75[b]	(8b)	47[b]
n-C_7H_{15}	(8a)	90[b]	(8b)	60[b]

[a] Thermal reaction in toluene solvent. [b] Thermal reaction in xylene solvent.

Under these ionic conditions with either t-butyl (**1a**) or trityl (**1b**) hydrazones, substitution of methyl crotonate by methyl acrylate, methyl β,β-dimethylacrylate, or acrylonitrile gave negligible *C*-addition to the azo-anions (**2**). However under thermal conditions (reflux in toluene or xylene) the aldehyde t-butylhydrazones (**6**) reacted with methyl acrylate (2 equiv.) or acrylonitrile (3 equiv.) in high yield *via* *C*-addition to yield the t-butyl-azo compounds (**7**) in an ene-type reaction. These azo-species (**7**) were not isolated but were directly isomerised (TFA, 5 h, 20 °C) and subsequently hydrolysed [$(CO_2H)_2$–H_2O–diethyl ether, 20 °C]. Work up and chromatography gave the γ-keto-esters and γ-keto-nitriles (**8**) (20—90%, Scheme 2, Table 2). The thermal reaction of aldehyde t-butylhydrazones with methyl crotonate or methyl β,β-dimethylacrylate gave negligible *C*-addition to azo-esters (**7**), as did a reaction of cyclohexanone t-butylhydrazone with methyl acrylate.

Table 3

Phenyl hydrazone (9) R	Product (%) from (9) (10)	(8a)	(11)	(12)	(14)
H	60	—	48	51	33
Me	56	41	45	48	34
Et	57	44	45	46	34
Pr[i]	56	52	52	45	38

Unfortunately these azo-adducts (**3**) and (**7**) derived from t-butylhydrazones could not be reductively cleaved to yield the potentially valuable amino functions. However the reported[3] thermal reaction of aldehyde phenylhydrazones (**9**) with methyl acrylate to yield the phenylazo-esters (**10**) offered a solution to this problem and provides thereby a convenient route to protected γ-amino-acids.§ Thus treatment of the aldehyde phenylhydrazones (**9**) with methyl acrylate (2.0 equiv.) under reflux in xylene gave the γ-phenylazo-esters (**10**) in reasonable yields (55—60%). As before these azo-esters (**10**) could be isomerised (TFA, 20 °C, 5 h) and hydrolysed [$(CO_2H)_2$–H_2O–diethyl ether, 20 °C, 12 h] to the γ-keto-esters (**8a**) (41—52%). Alternatively the azo-esters (**10**) were reduced under mild conditions (Zn, HOAc, 60 °C, 1.5 h) to hydrazo-esters, which upon work up cyclised to the 5-alkyl-1-(phenylamino)-2-pyrrolidones (**11**) (45—52%). Under more forcing conditions [Pd/C, H_2 (1 atm), 50 °C, 12—24 h] the azo-esters (**10**) gave the 5-alkyl-2-pyrrolidones (**12**) (45—51%) arising from reductive cleavage of the azo function. With Adam's catalyst [PtO_2, H_2 (1 atm), 20 °C, 24 h, MeOH–HCl] in the presence of hydrochloric acid, the azo-esters (**10**) gave the hydrochloride salts of γ-amino-esters (**13**)¶ which were isolated as their *N*-benzoyl derivatives (**14**) (Scheme 3, Table 3).

In summary, the azo-anions have now been extended to conjugate additions to α,β-unsaturated systems. Similar types of product may be reached more economically by a purely thermal ene reaction of aldehyde t-butyl- or phenylhydrazones. The derived phenylazo-esters (**10**) allow reductive azo-bond cleavage and thus offer an operational equivalent of an α-aminocarbanion.

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§ Although the thermal ene reaction of aliphatic aldehyde phenylhydrazones with methyl acrylate or acrylonitrile to give phenylazoalkanes has been described,[3] the potential to use such adducts as amine synthons was not exploited.

¶ This reduction gave a mixture (*ca.* 1 : 1) of the hydrochloride salts of γ-amino-esters (**13**) and cyclohexylamine in high yield (>90%) from the azo-esters (**10**).

Azo Anions in Synthesis: α-Amino carbanion equivalents from t-Butyldiphenylmethylhydrazones.

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Abstract

α-Amino carbanion equivalents ($\overset{\ominus}{C}$-NH_2) and α-hydrazino anion equivalents ($\overset{\ominus}{C}$-NH-NH_2) are readily accessible for the C-alkylation products of t-Butyldiphenylmethylhydrazones. These azo-alkanes can be efficiently transformed into amines, hydrazines and also alkanes under mild reaction conditions.

Recently we described the use of azo stabilized anions 1 for the synthesis of ketones[1], acyloins[1], alcohols[2], alkanes[2], alkenes[2], and esters[3]. These products were derived by tautomerisation and hydrolysis (in the case of ketones or acyloins, Scheme 1) or via low temperature C- azo homolysis (in the case of alcohols, alkanes, or esters, Scheme 2) of the initial C-trapped azo products 2 and 3 respectively. However, these hindered azo products, 2 and 3, proved resistant to reductive cleavage to the amino compounds† thereby denying us access to a very general α-amino anion equivalent 4.[4] We have now found a simple solution to this problem by use of t-butyldiphenylmethylhydrazones 5 whose derived azo products 7 on treatment with acid (TFA, 25°) gave the hydrazones 8 which we readily converted to primary amines 9 or hydrazines 10 (Scheme 3). Thus, azo anion 6 derived from t-butyldiphenylmethylhydrazones (5)‡ reacted smoothly with alkyl iodides under standard conditions[1] to give the isolable C-trapped azo species 7 (Table 1). Noteworthy is the reaction with methyl iodide to give high yields (61 - 85%) of C-trapped azo products 7, whereas in the case of the less hindered t-butylhydrazones, the N-methylation pathway was predominant.[1] The product 7 could be diverted to alkanes 12 and t-butyldiphenylmethane (Table 2, Scheme 4) via radical 11 by simple thermolysis in the presence of thiol [benzene, reflux, for 2h., PhSH (>5 equiv.)] or alternatively 11 could be intercepted by alternative radical trapping reagents (X-Y) to products 13 (Table 3, Scheme 4).

The primary amines or hydrazines were accessible in a simple fashion. Thus, upon treatment with TFA at room temperature, the azo products 7 derived from both ketone and aldehyde t-butyldiphenylmethylhydrazones 5 underwent clean dealkylation to form benzophenone hydrazones 8. These hydrazones have been reported elswhere [5] as readily converted to hydrazine products. Thus acidic hydrolysis (EtOH, conc. HCl, 25°, 15h.) of 8 gave good yields of secondary hydrazines and moderate yields of tertiary hydrazines 10 (Scheme 4, Table 4). Alternatively, in acid media, the hydrazones 8 could be catalytically reduced (EtOH, conc. HCl, 10% Pd on C, H_2, 50°) to the amines 9 (Table 5).

In summary, the t-butyl group serves to bias the electrophilic attack on 6 along the desired C-alkylation pathway at the same time as providing a labile functionality in the C-trapped azo product 7 which operationally provides efficient α-amino and α-hydrazino carbanion equivalents. The two step alkane synthesis via the isolated azo product 7 also represents a more convenient method than the low temperature route from tritylhydrazones previously described.[2]

Footnotes

† Although reduction of the azo function to hydrazo species can be achieved[6], the cleavage of N,N' - dialkylhydrazo species to amines has proved difficult. Such reductions are commonly achieved by high pressure catalytic hydrogenation methods [7] which are not compatable with sterically hindered azo products.

‡ t-Butyldiphenylhydrazones (5) were prepared from t-butyldiphenylhydrazine by standard methods[1]. The hydrazine was prepared by treatment of ethyl pivalate with phenylmagnesium bromide (2.2 equivs.) to give t-butyldiphenylcarbinol (70%) which was chlorinated ($SOCl_2$, $CHCl_3$, reflux, 1h.) and reacted with excess hydrazine in refluxing dioxane (3.5d.) The hydrazine was isolated as its hydrochloride salt (69%), mp.144-8°C.

‡‡ Tertiary hydrazines are reported to be labile to acidic conditions[5].

‡‡ Diphenylmethane has been isolated as the by-product in this reaction. We have also shown that hydrazines (10) give amines (9) under these hydrogenation conditions. Thus it is probable that the reduction of (8) to the amine (9) proceeds <u>via</u> formation <u>in situ</u> of the hydrazine (10).

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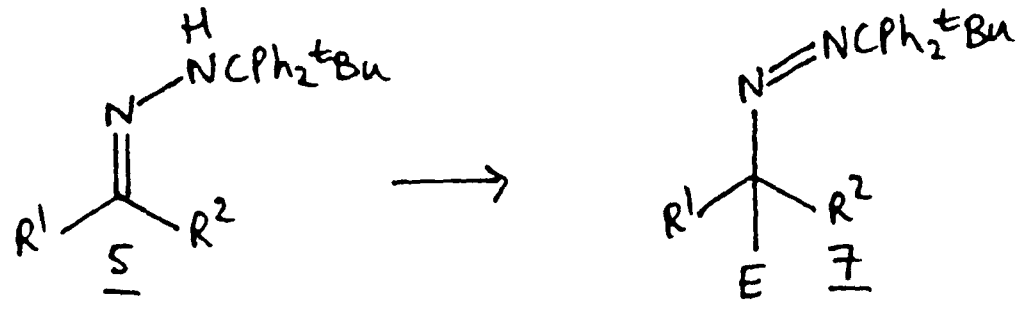
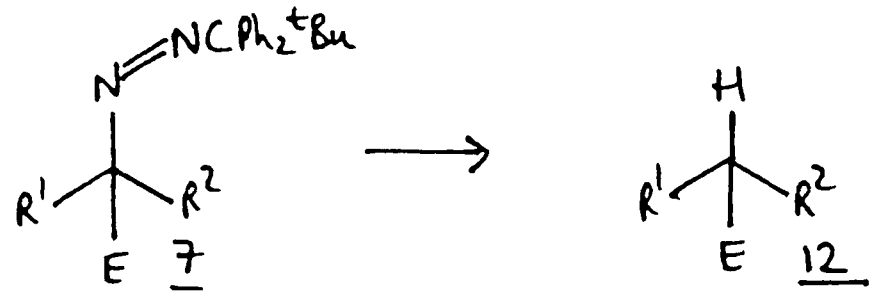


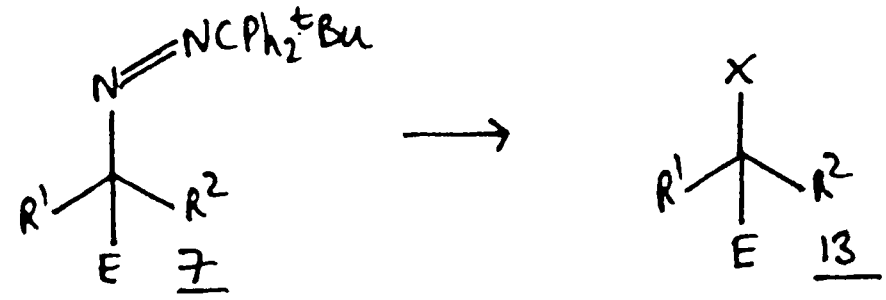
R^1	R^2	E	Yield 7 (%)
CH_3	H	n-$C_{10}H_{21}I$	95
CH_3	H	CH_3I	76
CH_3	H	$PhCH_2Br$	99
CH_3	H	n-C_4H_9I	89
CH_3	CH_3	CH_3I	84
CH_3	CH_3	$PhCH_2Br$	100
i- C_4H_9	H	n-$C_{10}H_{21}I$	79
i- C_4H_9	H	$BrC_5H_{10}Br$	89
i- C_4H_9	H	CH_3I	61
n- C_4H_9	H	$PhCH_2Br$	77
n- C_4H_9	H	n-$C_{10}H_{21}I$	70
$-(CH_2)_5-$		$PhCH_2Br$	100
$-(CH_2)_5-$		n-$C_7H_{15}I$	88
$-(CH_2)_{11}-$		$PhCH_2Br$	96
$-(CH_2)_{11}-$		n-C_4H_9I	97
$-(CH_2)_{11}-$		CH_3I	85

Table 1



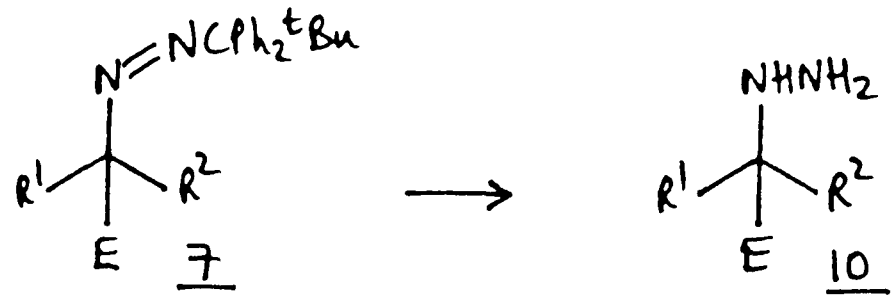
R^1	R^2	E	Yield 12 (% from 7)
CH_3	H	n-$C_{10}H_{21}$	94
i-C_4H_9	H	n-$C_{10}H_{21}$	84
n-C_4H_9	H	n-$C_{10}H_{21}$	93
$-(CH_2)_5-$		$PhCH_2$	71
$-(CH_2)_5-$		n-C_7H_{15}	64
$-(CH_2)_{11}-$		$PhCH_2$	78
$-(CH_2)_{11}-$		n-C_4H_9	72
$-(CH_2)_{11}-$		CH_3	87

Table 2



R^1	R^2	E	XY	Yield 13 (% from 7)
CH_3	H	n-$C_{10}H_{21}$	$(PhSe)_2$	77
$-(CH_2)_{11}-$		n-C_4H_9	$(PhSe)_2$	54
CH_3	H	n-$C_{10}H_{21}$	NBS	50
CH_3	H	n-$C_{10}H_{21}$	NCS	50
CH_3	H	CH_3	β-Nitrostyene	48

Table 3

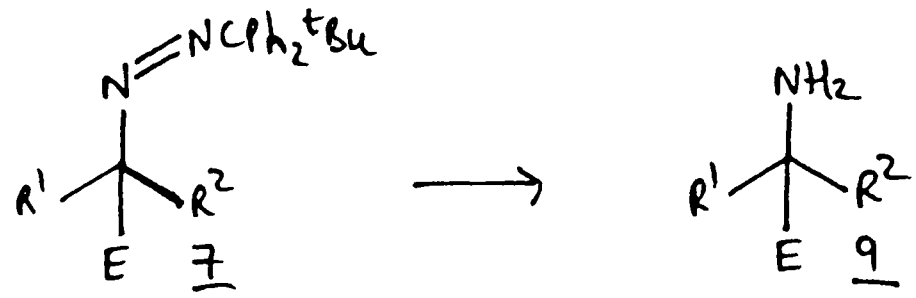


R^1	R^2	E	Yield (% from 7)		m.p. °C[a]
CH_3	H	CH_3	10	60	111-3
CH_3	H	$PhCH_2$	10	74	119-120.5
CH_3	CH_3	CH_3	8	80[b]	189-91
CH_3	CH_3	$PhCH_2$	10	25	137-9

a) M.p.'s are in agreement with literature values

b) Hydrolysis of this hydrazone to t-butylhydrazine hydrochloride (60%) has been reported[5].

Table 4



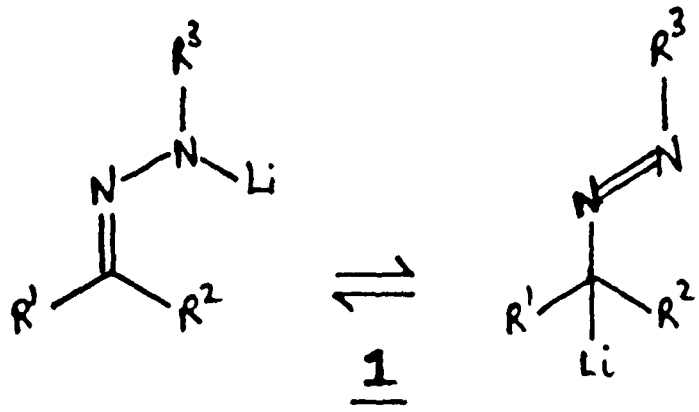
R^1	R^2	E	Yield 9 (% from 7)	m.p.°C[a]
CH_3	CH_3	$PhCH_2$	67[b]	194-5
$-(CH_2)_5-$		$PhCH_2$	71[b]	288-9
$-(CH_2)_{11}-$		CH_3	38[b]	215-9
CH_3	H	$PhCH_2$	68[c]	167-71
CH_3	H	n-$C_{10}H_{21}$	68[b]	89-91

a) M.p.'s are in agreement with literature values

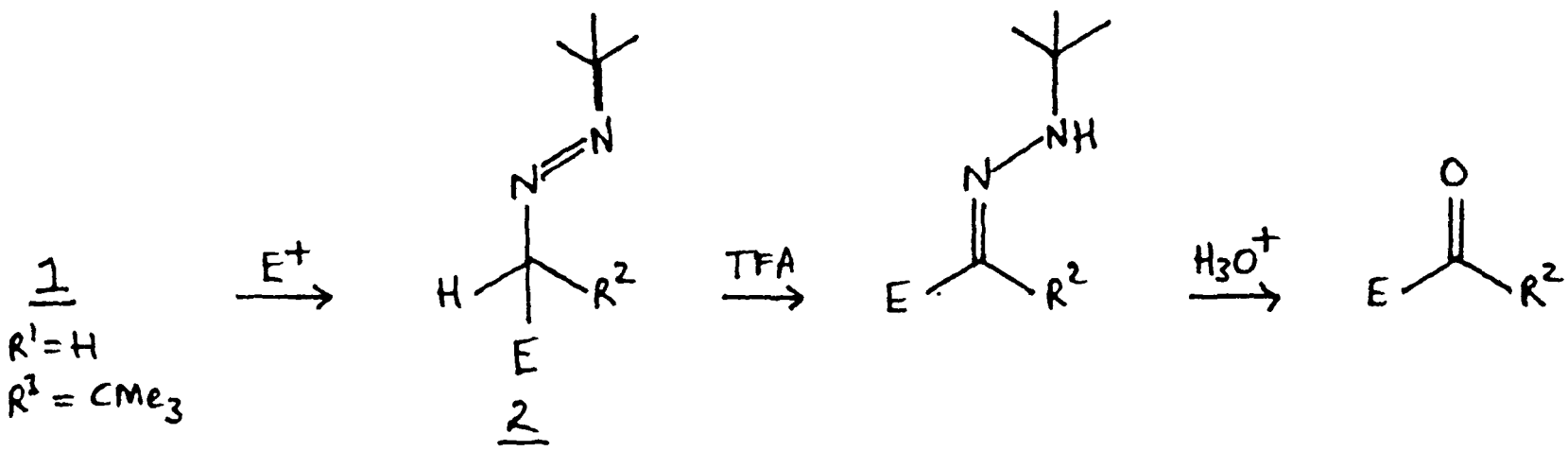
b) Isolated as hydrochloride salt

c) Isolated as oxalate salt

Table 5



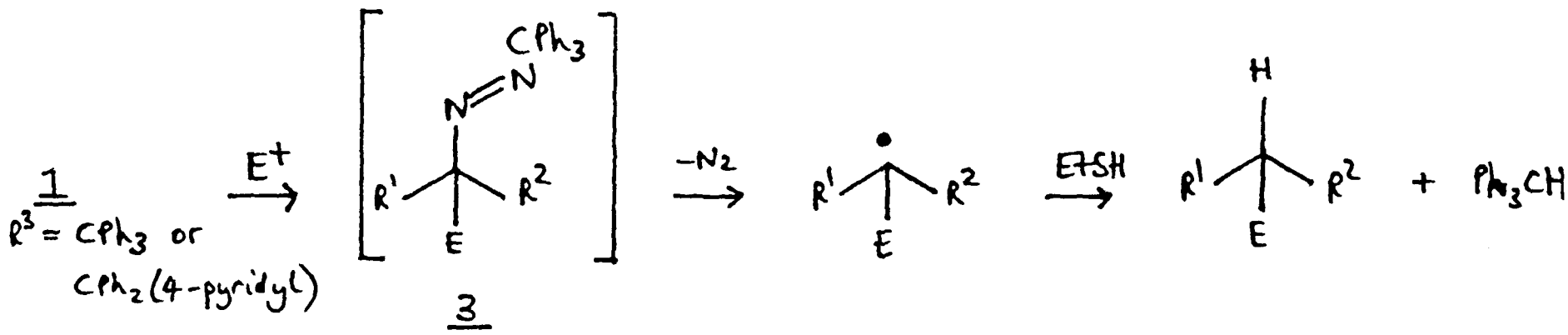
1



1
R¹ = H
R³ = CMe₃

2

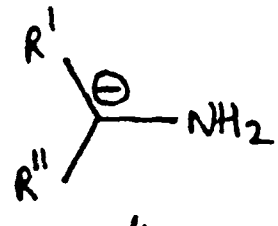
Scheme 1



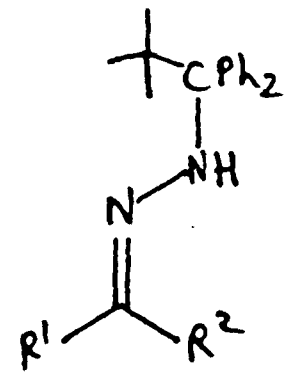
1
R³ = CPh₃ or
CPh₂(4-pyridyl)

3

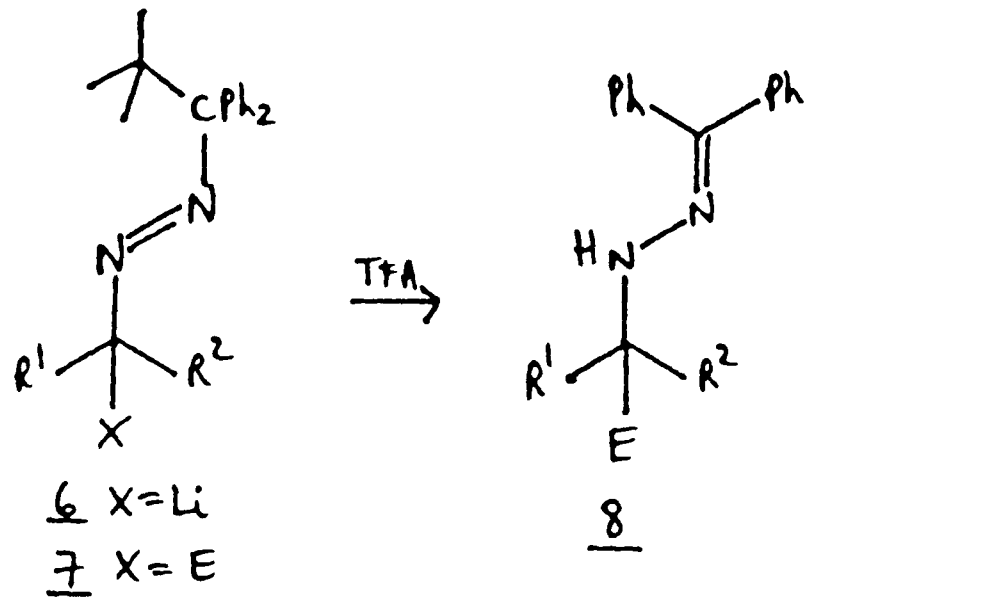
Scheme 2



4



5



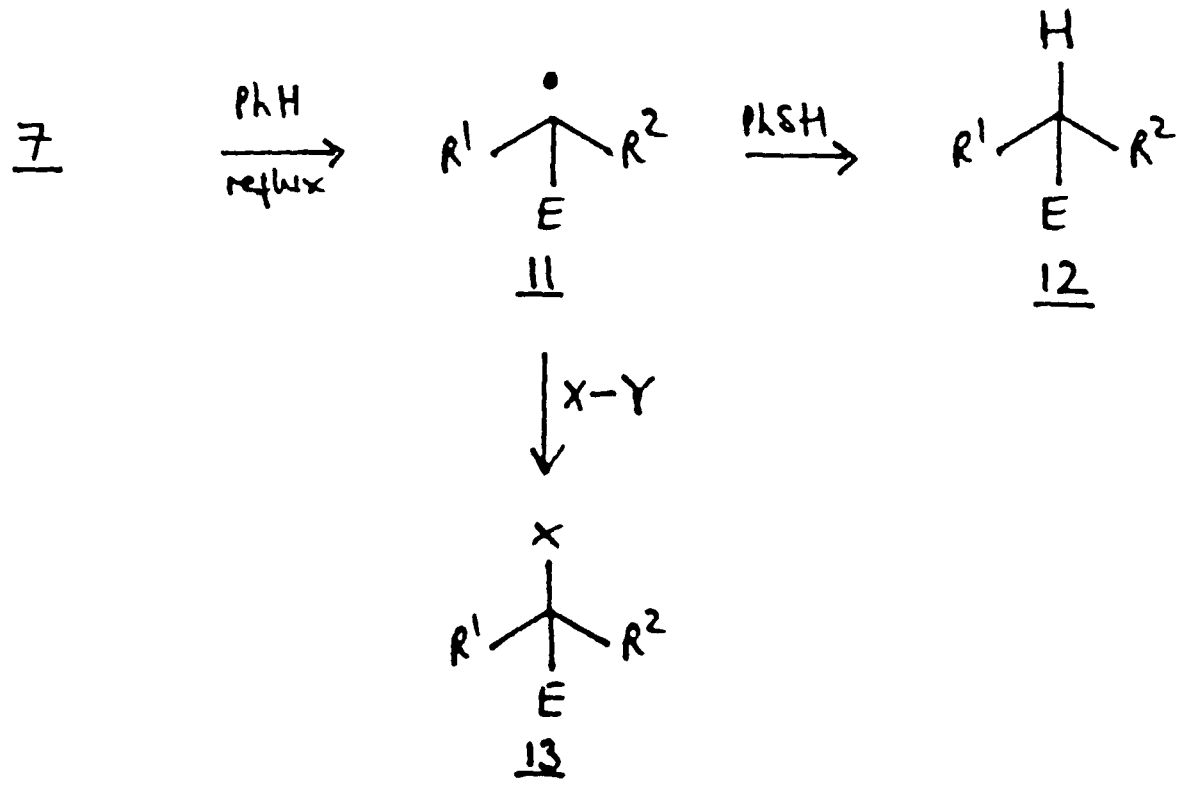
6 X=Li
7 X=E

8

9

10

Scheme 3



11

12

13

Scheme 4

AZO ANIONS IN SYNTHESIS. USE OF TRITYL- AND DIPHENYL-4-PYRIDYLMETHYLHYDRAZONES FOR REDUCTIVE C-C BOND FORMATION.

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Abstract: The lithium salts of trityl- and diphenyl-4-pyridylmethyl-hydrazones of both aldehydes and ketones react with electrophiles (alkyl halides, aldehydes, ketones, crotonates) at low temperature to form C-trapped azo compounds; these intermediates decompose homolytically with loss of nitrogen below room temperature and can be diverted in a synthetically useful way to alkanes, alkenes, alcohols or saturated esters.

Recently we demonstrated that the lithium salts of hindered hydrazones, e.g. t-butylhydrazones, undergo reaction with electrophiles at carbon.[1] The so-formed azo- products from aldehyde t-butylhydrazones could be tautomerised, and thereafter hydrolysed, to yield ketonic products, thus illustrating the potential of hindered hydrazones as a new acyl anion equivalent (Scheme 1). The use of such hindered hydrazones was advanced by the development of trityl- and diphenyl-4-pyridylmethyl-(DPP)hydrazones. The lithium anions of these hydrazones could also be trapped on carbon to produce thermally labile azo- products which decomposed homolytically, below room temperature, with evolution of nitrogen gas forming a radical pair. Quenching of these radicals with thiols led to a reductive carbon-carbon bond forming sequence (Scheme 2).[2] This methodology was developed [1c,2] using various electrophiles ($E^{\oplus}$) to create new practical methods for the preparation of alkanes (1)(path a), alcohols (2)(path b), olefins (3)(path c), and saturated esters (4)(path d)(Scheme3). Herein we describe details of these novel reductive carbon-carbon bond forming procedures.

Preparation of Trityl- and Diphenyl-4-pyridylmethylhydrazones

Tritylhydrazones (5) were prepared from tritylhydrazine hydrochloride, which itself was prepared[3] from tritylchloride and hydrazine hydrate (Scheme 4). Diphenyl-4-pyridylmethylhydrazones (DPP)(6) were prepared by analogous methods from diphenyl-4-pyridylmethylchloride[4] (Scheme 5). Typically the solid hydrazone derivatives (5),(6) precipitated from the reaction mixtures (Table 1). They were filtered off, dried at room temperature under vacuum (18hrs.), and used without further purification.$^{\theta}$ Those that could not be precipitated were extracted into organic solvent (e.g. CH_2Cl_2), dried over sodium sulphate (s), and concentrated to give oils. Further purification could be achieved by rapid flash chromatography on silica gel.

θ These compounds are metastable at room temperature in the absence of air.

Preparation of Alkanes (1)

For an alkane synthesis, the lithium anions of the tritylhydrazones were reacted with an alkyl halide (1.2 equivs.) at -30^{o} for 3h. Thereafter treatment with acetic acid (1.2 equivs.) and ethanethiol (excess) in sequence followed by warming to room temperature led to nitrogen evolution at -10^{o} to $+20^{o}$C (equivalent to the alkane yield) and alkane production (Scheme 3, path a, table 2). These optimal conditions probably reflect a need for extensive azo-anion alkylation (at -30^{o}

C)

prior to radical fragmentation at (-10°C), which itself requires thiol quenching to avoid undesired olefin forming [see preparation of alcohols (2)] and possible radical coupling pathways. Reactions in which alkylation was attempted at higher temperatures gave lower yields of alkanes, as did the use of DPP-hydrazones (6) under the optimal conditions.

Longer reaction times were not tried due to experimental inconvience.

Preparation of Alcohols (2)

For the reductive coupling of carbonyls to form alcohols (2), the azo-anion from a tritylhydrazone (5) or DPP- hydrazone (6) was treated with an aldehyde or ketone ($R^3.CO.R^4$, 1.1 equiv.) at -40° to -25°C followed by the addition of acetic acid (1.1 equiv.) and ethanethiol (>10 equiv.) at -25°C in sequence. Warming to room temperature led to nitrogen evolution and alcohol (2) production (Scheme 3, path b, Table 3). In Table 3, the results of a comparison between the use of trityl-(5)- or DPP-hydrazone(6)-are given. In general yields from the two methods are comparable but the DPP-hydrazones offer the advantage that basic residues obtained from the reaction can be removed with a dilute acid wash . Like the azo-anions from t-butylhydrazones[1], the azo-anions from (5) or (6) formed from alkyl lithium reagents are significantly basic and lower yields of alcohols (2) were obtained with enolisable carbonyl electrophiles.

When attempts were made to exchange the lithium counter ion of such azo-anions [eg. from (5b)] with other metal counter ions (eg. Zn^{2+}, Ti^{4+}, and $BF_3.Et_2O$) which were then tried as azo anions for an alcohol synthesis with acetophenone, these procedures gave lower yields of the desired alcohol than the standard conditions.

Direct evidence for the free radical intermediate postulated in the decomposition of the azo adduct (Scheme 2) was obtained from the reaction of the anion of cyclopropylmethylketone tritylhydrazone (7) with benzaldehyde. Warming (-35°→ +20°) of the so-formed azo-adduct (8) in the presence of ethanethiol gave the ring opened alcohol (11)(52%, E :Z 93:7). The intermediate radical (9) would, as is known [5], be expected to undergo rapid ring opening to the isomeric homoallylic radical (10), which was then trapped by thiol to give (11) (Scheme 6).

The preparation of 2-methyl-1-phenylpropan-1-ol (2, R^1=R^2=Me,R^3,R^4=Ph,H) from the tritylhydrazone (5b) and benzaldehyde followed by acid quench and a standared ethanethiol work up led to the production of 2-methylene-1-phenylpropan-1-ol (12) as a minor by-product (ca 5%). This by-product, which could be obtained by Shapiro reaction methodology from acetone 2,4,6-tri-isopropylbenzenesulphonylhydrazone [6], was more significant when the DPP- hydrazone (6b) was used (ca 15%). As the diphenyl-4-pyridylmethyl carbanion is a potentially better leaving group than its trityl counterpart, it could be argued that a Shapiro type pathway accounted for the by-product (12) formation (Scheme 7). However, treatment of the intermediate (13) with excess base (MeLi, 1.1 equivs.) gave not only lower overall alcohol yields, but did not change the ratio of (2, R^1=R^2=Me,R^3,R^4= Ph,H) to the allylic alcohol (12). The origin of the allylic by-product (12) was found when the reaction was warmed to room temperature without addition of ethanethiol. In this reaction the ratio of (2,R^1=R^2=Me,R^3,R^4= Ph,H) : (12) changed dramatically to <5 : >95.ϕ A possible mechanism for the by-product formation is given in Scheme 8. This undesired olefinic by-product forming reaction was only found to be significant when hydrazones from methyl ketones were used, and in these reactions and in the case of the alkane (1) synthesis (path a, Scheme 3), a bromine wash was employed in the work up procedure to aid product purification.

ϕ The overall yield of combined (12) and (2, R^1=R^2=Me,R^3,R^4=Ph,H) was also lowered by this procedure (ca 50%).

Preparation of Alkenes (3)

For an alkene synthesis, the lithium anions (14) formed from the adduct of the tritylhydrazones (5) with carbonyl electrophiles were treated with phosphorous trichloride. Thus addition at -78°C to the adduct (14) in THF: TMEDA (4:1) of PCl_3 (1.2 equivs.) gave, upon warming to +20°C, the alkenes (3) (path c, Scheme 3, Table 4). The DPP-hydrazones (6) offer no advantage over the tritylhydrazone (5) in this synthesis, as the alkene products are readily separated from the trityl residues by silica gel chromatography. Using the preparation of benzylidene cyclohexane from (5f) and benzaldehyde as a model reaction, reagents other than PCl_3 were tried for alkene preparation. However, in all cases lower yields were obtained than with PCl_3 (Table 5). The mechanism of the PCl_3 mediated olefin formation is uncertain, but a possible mechanism is given in Scheme 9. Thus the intermediate radical (15) could close to the 4 membered ring (16) which could cis-eliminate to the olefin (3) in a similar manner to the Wittig reaction. Evidence for 4 membered ring (16) follows from the following observations. Firstly, the preparation of cyclohexylidene cyclohexane (17)(23%) gave as a by-product, the diene (18)(18%). Secondly, whereas the standard alcohol preparation from (6f) and cyclohexanone gave the alcohol (2, R^1,R^2,and R^3,R^4=-$(CH_2)_5$-(40%), if the thiol work-up was omitted, then the allylic alcohol (19)(37%) was obtained. Treatment of the allylic alcohol (19) with PCl_3 and TMEDA gave the diene (18). These observations are consistent with the following explanation (Scheme 10). During the olefin forming sequence, the first formed radical intermadiate as (20) can only form the olefin (17) from a cis-elimination process, via (21). As this requires four membered ring formation from a sterically demanding conformation as cis-(20), then a low yield of the olefin (17) would be expected. Alternatively, the sterically favoured conformation as trans-(20) could generate the allylic species (22)(via a method similar to that in Scheme 8) which under the reaction conditions (TMEDA as base) could generate the observed diene (18).

It should be noted that whereas phenylphosphorous dichloride can be used to generate olefin by this methodology, diphenylphosphorous chloride can not. Clearly the phosphorous based reagents are required to possess at least two potential leaving groups to allow olefin formation.

This general method for olefin formation enables the discriminated coupling of two different carbonyl compounds as opposed to the pinacol related processes [7] which necessarily yield both symmetrically coupled and cross-over products. The coupling of two ketones to give a tetrasubstituted olefin is also noteworthy.

Preparation of Saturated Esters (4)

The lithium anions of tritylhydrazones (5) could also be quenched with methyl crotonate to give a C- addition product. Thus treatment of (5) with n-butyl lithium (0.95 equiv.) in 1,2-dimethoxyethane at -78° gave an azo-anion which was warmed to -50° and treated with methyl crotonate (2.0 equiv. added over 1h., -50°C). TFA (1.0 equiv.) and ethanethiol (5 equiv.) were added in sequence and the solution warmed to 20°C. Purification by chromatography on silica gel gave the saturated esters (4, Scheme 3, path d, table 6). The yields in this sequence were disappointingly low and the major reaction pathway in these processes appeared to be a basic deprotonation of methyl crotonate by the azo-anions to give recovered tritylhydrazone (5). The DPP- hydrazones (6) gave lower yields than the corresponding tritylhydrazones (5) with methyl crotonate. Substitution of methyl crotonate by methyl acrylate, methyl β,β-dimethylacrylate, or acrylonitrile led to negligible yields of C-addition products.

			Tritylhydrazone (5)		DPP- hydrazone (6)	
Entry	R^1	R^2	Yield(%)	m.p.(°C)	Yield	m.p. (°C)
a	Me	H	81	112-114	-	-
b	Me	Me	90	119-120	65	124-5
c	i-Pr	H	81	oil	-	-
d	n-Bu	H	87	wax	-	-
e	$-(CH_2)_4-$		83	127-130.5	-	-
f	$-(CH_2)_5-$		86	135-137	57	127-9
g	$n-C_6H_{13}$	Me	-	-	57	114-5
h	$-(CH_2)_{11}-$		87	142-143	81	139.5-140.5
(7)	c-C_3H_5	Me	88	55		

Table 1

Hydrazone (5)	Alkyl halide (R_2X)	Yield of (1) (%)
a	n-$C_{12}H_{25}I$	27
b	$PhCH_2Br$	42
b	n-$C_{12}H_{25}I$	38
d	n-$C_{12}H_{25}I$	47
e	n-$C_{12}H_{25}I$	27
f	n-C_4H_9I	40
f	n-$C_7H_{15}I$	67
f	$PhCH_2Br$	68
h	n-C_4H_9I	51*
h	$PhCH_2Br$	44

* : Yield estimated by g.c. analysis

Table 2

Hydrazone (5) or (6)	$R^3 \cdot CO \cdot R^4$		Yield of (2) (%)	
	R^3	R^4	Tritylhydrazone (5)	DPP-hydrazone (6)
a	Ph	H	60	-
a	Ph	Me	54	-
a	$-(CH_2)_5-$		39	-
b	Ph	H	<72	65
b	Ph	Me	46	-
d	Ph	H	40	-
d	Ph	Me	51	-
d	$-(CH_2)_5-$		42	-
f	Me_2CH	H	-	40
f	$-(CH_2)_5-$		35	40
f	Ph	H	63	72
f	Ph	Me	50	-
g	Ph	H	-	63
g	Me_2CH	H	-	65
h	Ph	H	82	82

Table 3

Hydrazone	$R^3.CO.R^4$		Yield of (3) (%)
	R^3	R^4	
5a	Ph	H	20
5b	Ph	H	52
5f	Ph	H	48
5f	Ph	Me	34
5f	$-(CH_2)_5-$		23 + (18, 18%)
6g	Ph	H	60 (E:Z 65:35)
6g	$n-C_7H_{15}$	H	55 (E:Z 60:40)
5h	Ph	H	37

Table 4

Reagent	Yield (%)
PCl_3	48
$PO.Cl_3$	39
$PhPCl_2$	25
PBr_3	12
$(EtO)_2PO.Cl$	6
Ph_2PCl	0

CS_2/MeI	26
Cl.CS_2Et	26
Cl.CS_2Et/EtSH	25
Cl.CS_2Et, then reflux in THF	20
	0
$SnCl_4$	0

Table 5

Hydrazone (5)	Ester (4) (%)
c	23
d	20
f	35

Table 6

General Experimental

Standard laboratory practice as previously described[8] was observed. All ^1H N.M.R. spectra were recorded at 300MHz upon a Bruker WH 300 N.M.R. spectrometer using deuteriochloroform as solvent referenced to residual $CHCl_3$ = 7.27 p.p.m. unless otherwise stated. Coupling constants J were measured to the nearest ±0.5Hz. All ^{13}C N.M.R. spectra were recorded at 62.85 MHz on a Bruker AM 250 spectrometer using deuteriochloroform as solvent, referenced to $CDCl_3$ = 77.00 p.p.m. unless otherwise stated. Some ^{13}C peaks (especially in the case of geometric isomers) are unresolved. Only selected I.R., ^1H, and ^{13}C N.M.R. signals are assigned. Accurate mass measurements were recorded from the electron impact (E.I.) mode only. G.L.C. was run on a Pye series 104 chromatograph with a 5'x 0.25" I.D., 3% OV1 on gas chrome Q (100-120 mesh) column.

Compounds reported in tables 1 - 4 but not described in the experimental section gave satisfactory spectral and analytical data consistant with their structures; this data has been omitted in order for brevity in the presentation of this manuscript.

Preparation of Tritylhydrazine Hydrochloride

Triphenylmethyl chloride (100g, 0.35 mol.) was added to a solution of hydrazine hydrate (120 ml, excess) in THF (500ml.) and the mixture stirred under reflux for 6-18 h. The solution was cooled to 25°, concentrated to half volume, and extracted into diethyl ether (2 x 150ml.). The organic layer was washed with brine (2 x 30ml.), dried (Na_2SO_4), filtered and treated with a solution prepared from hydrogen chloride (g) in methanol (55ml, 6.5M, 1.0 equiv.). The solution was cooled to 0° for 24h., and the solid filtered off and washed with diethyl ether to give tritylhydrazine hydrochloride (96.0g, 86%), m.p. 109-112°C (Lit.,[3] 108-113°C).

General procedure for the preparation of Tritylhydrazones (5)

The following procedure for the preparation of acetone tritylhydrazone (5b) is typical.

Tritylhydrazine hydrochloride (10.0g, 32 mmol.) was dissolved in methanol (200ml.) and a solution of sodium formate (3.28g, 48 mmol) in water (15ml) was added. Acetone (2.60ml, 35 mmol) was added and the mixture stirred under argon for 2h. in the dark. The solid precipitate was

filtered off, washed with water and light petroleum (10ml) in sequence, then dried under vacuum to yield acetone tritylhydrazone (5b) as a while solid (9.10g, 90%), m.p. 119-120°C; νmax. ($CHCl_3$) 3060 w, 2960 s, 2930 s, 2860 s, 1597 m, 1487 m, 1445 s, 760 s, 720 s, and 705 s cm^{-1}. δH 1.74 (3H, s, Me), 1.80 (3H, s, Me), 5.38 (1H, br, NH), and 7.19 - 7.46 (15H, m, Ar-H); δC 15.63 (q, Me), 25.30 (q, Me), 75.50 (s, $\underline{C}Ph_3$), 126.43, 127.60, 129.16 (3 x d, phenyl CH), 145.66, 146.17 (2 x s, phenyl-ipso-$\underline{C}$, $\underline{C}$=N); m/e ($\overline{NH_3}$ C.I.) 315 (MH^+, 11%), 243 ($Ph_3C^{\oplus}$, 100), and 165 (27); (E.I.) 243 (100%), 165 (60).

Those hydrazones which did not crystallise were extracted into dichloromethane, dried (Na_2SO_4), and evaporated to give oily products. Further purification could be achieved by rapid flash chromatography on silica gel.

Preparation of Diphenyl-4-pyridylmethylhydrazine dihydrochloride

A solution of 4-benzoylpyridine (25.0g, 0.13 mol) in dry diethyl ether (330ml) was added to a solution of phenylmagnesium bromide [from bromobenzene (0.28 mol.) and magnesium (0.26 mol.) in diethyl ether (150ml)] at a rate to maintain reflux. The solution was then refluxed for 2h., stirred at 20° for 10h., then poured into ice-cold, hydrochloric acid (110ml, 0.65 mol.). The aqueous layer was seperated, then basified to pH 9 with 0.880 ammonia. The solid product was filtered off, washed with water and benzene then dried to give diphenyl-4-pyridylmethanol (29.3g, 82%), m.p. 230-232°C. (Lit.[9] 235°C), νmax. (nujol) 3150 m (O-H) cm^{-1}.

Diphenyl-4-pyridylmethanol (25.0g, 96 mmol) was converted to diphenyl-4-pyridylmethylcholoride hydrochloride (25.40g, 84%) by a modification to the procedure of Young[4] in which a shorter reaction time (16h.) was employed, m.p. 174-6°C (Lit., [4] 134-5°C), δH (D_2O, $\underline{H}OD$ = 4.60 p.p.m.) 7.10 - 7.15 (4H,m, phenyl-H), 7.22 - 7.25 (6H,m, phenyl-H), 7.86 (2H,d,$\underline{J}$ 7Hz,pyridyl-H), and 8.53 (2H,d,$\underline{J}$ 7Hz, pyridyl-H).

Diphenyl-4-pyridylmethylchloride hydrochloride (24.0g, 76 mmol) was dissolved in dry THF (250ml) and excess anhydrous hydrazine (24ml) added. The mixture was stirred at 65° for 12h., cooled and extracted into diethyl ether (2 x 100ml). The organic layer was washed with brine (2 x 100ml), dried (Na_2SO_4), and treated with a solution prepared from hydrogen chloride (g) (175 mmol) in diethyl ether. The white solid was filtered off, washed with diethyl ether (200ml) and dried to yield diphenyl-4-pyridylmethylhydrazine dihydrochloride (25.40g, 96%); m.p. 182-4° C; νmax. (nujol) 3400 wbr, 3090 m, 3060 m, 3020 m, 1600 m, 765 m, and 700 m cm^{-1}; δH (CD_3OD, $\underline{C}H\overline{D_2}OD$=3.305 p.p.m.) 7.39 - 7.56 (10H,m, phenyl-H), 8.32 (2H,d,$\underline{J}$ 6Hz, pyridyl-H), 8.86 (2H,d,$\underline{J}$ 6Hz, pyridyl-H), m/e (positive argon F.A.B.) 276 ($C_{18}H_{18}N_3^+$, 17%), 262 (75), and 246 (100).

General procedure for the preparation of Diphenyl-4-pyridylmethylhydrazones (6)

The following method for the preparation of acetone diphenyl-4-pyridylmethylhydrazone (6b) is typical.

Diphenyl-4-pyridylmethylhydrazine dihydrochloride (10.0g, 29 mmols.) was dissolved in methanol (100ml) and a solution of sodium formate (4.80g, 72.5 mmols) in water (20ml.) was added. Acetone (35 mmol.) was added and the mixture stirred under argon for 2h. in the dark. The resultant solid was filtered off, washed with water (50ml.), and light petroleum (10ml) in sequence to give acetone diphenyl-4-pyridylmethylhydrazone (6b) (5.88g, 65%); as a white solid m.p. 124-5°C; νmax. (nujol) 3200 m, 1595 s, 760 m, and 700 s cm^{-1}; δH 1.74 (3H,s,Me), 1.80 (3H,s,Me), 5.30 (1H,s,NH), 7.24 -7.33 (12H,m,aryl-H), 8.50 (2H,d, $\underline{J}$ 6Hz, pyridyl-H); δC 15.63 (q, Me), 25.22 (q, Me) 72.02 (s, $\underline{C}Ar_3$), 124.29, 126.93, 127.88, 128.75 (4 x d, aryl CH), 144.72, 146.81 (2 x s), 149.26 (d, aryl $\overline{C}H$), and 154.66 (s); m/e (NH_3 C.I.) 316 (MH^+, 10%), 244 (Ar_3C^+, 100) and 165 (10).

General procedure for the preparation of Alkanes (1)

The following procedure for the preparation of alkanes (1) from tritylhydrazones (5) is typical.

To a solution of tritylhydrazone (5f) (5.0 mmol) in THF (30ml) at -40°C was added methyl lithium (5.5 mmol). After 20 min., benzyl bromide (6.5 mmol) was added, the reaction warmed to -30°C and stirred for 3h. The reaction was quenched with acetic acid (5.5 mmol), then ethanethiol (2ml) was added and the reaction warmed to 20°C over 30 min. during which nitrogen evolution occurred. Diethyl ether (40ml) was added and the solution washed with aqueous sodium hydroxide (2M, 2 x 100ml), brine (60ml), dried, filtered, and evaporated. The crude product was then initially purified by filtration through silica gel (50g) using light petroleum as eluant. The product was dissolved in dichloromethane (20ml), reacted briefly with bromine until present in excess, washed with saturatured sodium thiosulphate solution (2 x 15ml.),dried, filtered, and evaporated. Final purification by p.l.c. (Merck Kieselgel 60. P254 20 x 20 x 0.1 cm plates, using light petroleum as eluant) gave benzylcyclohexane (594 mg, 68%); b.p. 129° at 14 mm Hg; g.c. retention time 5.6 min at 155°; νmax. (film) 3090 w, 3065 w, 3025 w, 2925 s, 1285 m, 1607 w, 1496 w, 1450 m, 743 m, and 698 m cm^{-1}; δH 0.98 - 1.73 (11H, m, C_6H_{11}), 2.51 (2H, d, $\underline{J}$ 7Hz, CH_2Ph), and 7.11 - 7.37 (5H, m, aryl-H); δC 26.33, 26.60, 33.17 (3 x t, CH_2), 39.78 (d, CH), 44.14 (t, CH_2Ph), 125.52, 127.99, 129.14 (3 x d, aryl CH), and 141.33 (s, aryl-ipso-C); m/e (E.I.) 174 (M^+, 24%), 92 (100), 91 (39), 83 (40), 82 (12), 67 (12), 65 (11), 55 (60), and 41 (24); (Found : C, 89.4%; H, 10.2%; 174.1408. $C_{13}H_{18}$ requires C, 89.6%; H, 10.4%; 174.1408.).

General procedure for the preparation of Alcohols (2)

The following procedure is typical for the preparation of alcohols (2) from trityl-(5) or DPP-(6) hydrazones.

Hydrazone (6h.) (4.0 mmol) was dissolved in THF:TMEDA (4:1, 50ml.) and the solution cooled to -55°C. Methyl lithium (5.25 mmol in diethyl ether) was added and the solution stirred for 20 min. before addition of benzaldehyde (5.25 mmol.). After 20 min. the reaction was quenched with acetic acid (5.25 mmol) and ethanethiol (5ml) added. The mixture was warmed to 20° over 30 min., during which time nitrogen evolution occured. The mixture was extracted into diethyl ether (100ml.), washed with sodium hydroxide solution (1M, 2 x 20ml.), hydrochloric acid (2M, 2 x 20ml.), dried (Na_2SO_4), filtered, and evaporated to yield a crude product. Purification by flash column chromatography on silica gel and p.l.c. [using diethyl ether : light petroleum (3:17) as eluant] gave 1-cyclododecyl-1-phenylmethanol (899 mg, 82%); m.p. 82-3°; t.l.c. [diethyl ether : light petroleum (3:17)] Rf 0.35; νmax. (nujol) 3400 m (O-H), 3085 w, 3060 w, 3030 w, 765 s, and 705 s cm^{-1}; δH 1.17 - 1.57 (22H, m, CH_2), 1.74 - 1.94 (1H, m, CH), 4.55 (1H, d, $\underline{J}$ 5Hz, $\underline{C}HOH$), 7.20 -7.41 (5H, m, phenyl-H); δC 21.77, 22.10, 23.23, 23.58, 24.24, 24.80, 24.89, 25.71, 25.80 (9 x t, CH_2

), 41.64 (d, CH), 77.10 (d, CHOH), 126.55, 127.27, 128.18 (3 x d, phenyl CH), 144.08 (phenyl-ipso-C); m/e (E.I.) 274 (M^+, 1%), 257 (22), 107 (100), 79 (36), 77 (21), 55 (15), 41 (20), 39 (11); (Found : C, 83.41%; H, 11.00%. $C_{19}H_{30}O$ requires C, 83.15%; H, 11.02%).

For alcohols derived from methyl ketone hydrazones, a brief bromine wash was employed prior to final p.l.c. purification (to facilitate seperation from olefinic by-products).

Also prepared 2-methyl-1-phenylpropan-1-ol [from (6b, 5.0 mmol) and benzaldehyde] (488 mg, 65%); t.l.c. [diethyl ether : light petroleum (3:7)] Rf 0.3; νmax. (film) 3400m (O-H), 3090 w, 3070 w, 3030 w, 2965 s, 2935 s, 2880 s, 760 s, 705 s cm^{-1}; δH 0.80 (3H, d, J 7Hz, Me), 1.01 (3H, d, J 7Hz, Me), 1.91 - 2.02 (1H, m, $CHMe_2$), 4.36 (1H, d, J 7Hz, CHOH), 7.23 - 7.37 (5H, m, phenyl-H); δC 18.19 (q, Me), 18.96 (q, Me), 35.21 (d, $CHMe_2$) 79.97 (d, CHOH), 126.50, 127.32, 128.10 (3 x d, phenyl CH), 143.59 (s, phenyl-ipso-C); m/e 150 (M^+, 4%), 132(21), 117(31), 115(12), 107(100), 91 (17), 79(51), 77(28), 51(13), 40(17), 39(13); (Found : 150.1044. $C_{10}H_{14}O$ requires 150.1045) along with 2-Methylene-1-phenylpropan-1-ol (12); (111 mg, 15%); t.l.c. [SiO_2, light petroleum (4:1)] Rf 0.6; νmax. (film) 3360 br (O-H), 3060 m, 3030 m, 2970 m, 1450 s, 1045 s, 1025 s, 905 s, and 700 s cm^{-1}; δH 1.63 (3H, s, Me), 2.09 (1H, br s, OH), 4.97 (1H, multiplet s, vinyl-H), 5.14 (1H,s, CHOH), 5.22 (1H, multiplet S, vinyl-H), and 7.27 - 7.41 (5H, m, phenyl-H), m/e (E.I.) 148 (MH^+, 100%), 133(70), 105(86), and 79(96).

2-Methyl-1-phenylpropan-1-ol was also prepared from isopropyl magnesium bromide and benzaldehyde and shown to have identical spectral properties.

An authentic sample of 2-methylene-1-phenylpropan-1-ol (12) was prepared *via* acetone 2,4,6-tri-isopropylbenzenesulphonylhydrazone [6] and benzaldehyde and shown to have identical spectral properties.

Preparation of 2-Methyl-1-phenylpent-2-en-2-ol (11)

(7) (1.50g, 4.41 mmol.) was dissolved in dry THF (15ml), the solution cooled to -35° and treated with n-butyl lithium (5.0 mmol). The solution was stirred for 20 min. at -35°C, quenched with benzaldehyde (5.0 mmol) then stirred for 5 min. Ethanethiol (4ml) was then added and the solution warmed slowly to 20° during which nitrogen evolution was observed. The solution was evaporated, extracted into diethyl ether (100ml), washed with water (50ml), dried, filtered, and evaporated. Purification by chromatography on flash silica gel [60g, using dichloromethane as eluant] gave the title compound (11) (404mg, 52%); as an oil; E:Z = 93:7; t.l.c. (dichloromethane) Rf 0.3; νmax. (neat film) 3380 br m (O-H), 3090 w, 3060 w, 3030 w, 2960 m, 2930 m, 2870 m, 1605 w, 1490 m, 1450 m, 1190 w, 1020 s, 915 w, 870 w, 740 m, and 700 s cm^{-1}; δH 1.05 (3H,d, J 7Hz,$MeCH_2$), 1.47 and 1.56 (3H, 2 x multiplet s, ratio 93:7, vinyl Me), 2.00 - 2.20 (3H,m, CH_2Me and OH), 5.10 (1H,s, CHOH), 5.65 (1H,t, J 5Hz, vinyl-H), 7.20 - 7.40 (5H,m, phenyl-H); m/e (E.I.) 176 (M^+, 40%), 147(90), 129(40), 107(60), 105(60), 79(100), 77(95), 69(40), and 41(60) (Found : 176.1200. $C_{12}H_{16}O$ requires 176.1201). In a n.O.e experiment irradiation of the vinyl methyl group at δH 1.47 gave n.O.e of the CH_2Me protons, δH 2.0 - 2.2 (3%) but not to the vinylic proton δH 5.65 (< 0.5%), whereas irradiation of the vinyl proton, δH 5.65 gave n.O.e of the CHOH proton, δH 5.10 (6%) but not to the vinyl methyl group, δH 1.47 (< 0.1%).

Preparation of 2-Methylene-1-phenylpropen-1-ol (12) in the absence of ethanethiol

The standard procedure for alcohol (2) formation was employed using (6b) (1.5 mmol) and benzaldehyde (1.5 mmol) except that the ethanethiol addition was omitted. Standard work up and chromatography gave (12) (110mg, 49%) t.l.c., n.m.r. as before along with minor (< 5%) ammounts of 2-Methyl-1-phenylpropan-1-ol.

General procedure for the preparation of Alkenes (3)

The following procedure for the preparation of β,β-dimethylstyrene is typical.

(5b) (5.0 mmol) was dissolved in THF:TMEDA (4:1, 50ml.) and the solution cooled to -55°C. Methyl lithium (5.25 mmol in diethyl ether) was added, the solution stirred for 20 min., then treated with benzaldehyde (5.25 mmol). After 20 min the solution was cooled to -78°C and phosphorous trichloride (6.25 mmol.) was added. The mixture was allowed to warm to 20° over 90 min., then stirred for a further 60 min. Diethyl ether (100ml.) was added, the solution washed with sodium hydroxide solution (1M, 2 x 20ml.), hydrochloric acid (1M, 2 x 20ml), dried ($MgSO_4$), filtered, and evaporated to give a viscous oil (3.2g). Purification by flash chromatography on silica gel (75g) using light petroleum as eluant gave β,β-dimethylstyrene (343mg, 52%); as an oil; t.l.c. (light petroleum) Rf 0.6; νmax (film) 3080 w, 3060 w, 3020 w, 2970 s, 2930 s, 2910 s, 2850 s, 1650 m (C=C), 745 s, and 700 s cm^{-1}; δH 1.90 (3H,s, Me), 1.94 (3H,s, Me), 6.31 (1H,s, vinyl-H), and 7.25 - 7.37 (5H,m, phenyl-H), δC 19.36 (q,Me), 28.84 (q,Me), 125.11, 125.72, 127.96, 128.69 (4 x d, vinyl, phenyl CH), 135.37, 138.66 (2 x S, CMe_2, phenyl-ipso-C); m/e (E.I.) 132 (M^+., 80%), 117(100), 115(21), 91(22); (Found 132.0939. $C_{10}H_{12}$ requires 132.0938).

Also thus prepared cyclohexylidene cyclohexane [from (5f, 4.5 mmol.) and cyclohexanone] (170 mg, 23%); m.p. 55-6° (lit., [10] 53°) t.l.c. (light petroleum) Rf 0.75; νmax (nujol) 1265 w, 1240 w, 1015 w, 890 m, and 850 m cm^{-1}; δH 1.43 - 1.65 (12H, br, CH_2), 2.13 - 2.27 (δH, br, allylic CH_2); δC 27.30, 28.71, 30.13 (3 x t, CH_2), and 129.40 (s, C=C); m/e (E.I.) 164 (M^+., 73%), 135(12), 121(20), 107(17), 93(23), 91(15), 82(100), 81(66), 79(40), 67(75), 55(41), 39(40), 37(22); (Found 164.1565. $C_{12}H_{20}$ requires 164.1565) along with the diene (18) (131mg, 18%) as an oil; t.l.c. (light petroleum) Rf 0.8; νmax (film) 2930 s, 2860 s, 2835 s, 1450 m, 1435 m, 1335 w, 1135 w, 925 w, and 795 m cm^{-1}, δH 1.50 - 1.63 (4H,m), 2.05 - 2.26 (8H,m), 5.80 (2H, br s); δC 22.54; 23.16, 25.54, 25.86 (4 x t, CH_2), 121.30 (d, vinyl CH), 136.82 (s, vinyl C); m/e (E.I.) 162 (M+, 100%), 147(14), 133(30), 119(30), 105(32), 94(60), 91(70), 79(75), 65(18), 51(19), 41(45), and 39(41).

Also thus prepared 2-Methyl-1-phenyloct-1-ene [from (6g, 4.0 mmol.) and benzaldehyde] [485mg, 60%, E : Z = 65:35] as an oil; t.l.c. (light petroleum) Rf 0.65; νmax (film) 3085 w, 3060 w, 3030 w, 2960 s, 2930 s, 2860 s, 1650 m (C=C),745 m, and 700 s cm^{-1}; δH 0.89 - 0.96 (3H,m, CH_2Me), 1.30 -1.39 (6H,m, CH_2), 1.52 - 1.55 (2H,m, CH_2), 1.88 and 1.91 (3H, 2 x multiplet s, ratio 65:35, vinyl-Me), 2.17 - 2.27 (2H,m, allylic CH_2), 6.30 (1H,s, vinyl-H), 7.17 - 7.38 (5H,m, phenyl-H); δC 14.09 (q, Me), 17.72 (q, Me), 22.65 (t, CH_2), 24.09 (q, Me), 27.99, 28.10, 29.01, 29.36, 31.71, 31.81, 32.54, 40.76, (8 x t, CH_2), 124.67, 125.29, 125.67, 127.94, 128.52, 128.78 (6 x d, vinyl CH, phenyl CH), 138.72, 139.34, 139.79 (3 x S, C=C, phenyl-ipso-C); m/e (E.I.) 202 (M^+, 49%), 131(100), 117(21), 115(11), 91(57) 69(11), and 55(9), (Found : C, 89.29; H, 11.16; 202.1721. $C_{15}H_{22}$ requires 89.04; H, 10.96%; 202.1721).

C,

In an n.O.e experiment, irradiation of the vinyl proton, δH 6.30 gave n.O.e of the vinyl resonances δH 1.91 (2.2%) and δH 1.88 (< 0.5%).

Preparation of the Allylic alcohol[12](19)

The standard procedure for alcohol (2) formation was employed using (5f) (4.5 mmol) and cyclohexanone except that the ethanethiol addition was omitted. Standard work up and p.l.c. [SiO_2, using light petroleum : diethyl ether (17:3)] gave (19) (303mg, 37%), t.l.c. [light petroleum : diethyl ether (17:3] Rf 0.3; m.p. 64-5°c (Lit.[12] 69°c); νmax 3280 s, 3220 s (O-H), 1295 m, 1195 m, 1055 s, 960 s, 925 m, 905 m, 855 s; δH 1.22 - 1.32 (2H, m), 1.45 - 1.71 (12H, m), 2.00 - 2.05 (4H, m), 5.75 -5.81 (1H, m); m/e (E.I.) 180 (M^+, 24%), 137(100), 119(18), 109(25), 91(21), 81(37), 67(21), and 55(22) [Found 180.1514. $C_{12}H_{20}O$ requires 180.1514].

Conversion of the Allylic alcohol (19) to the Diene (18)

The allylic alcohol (19) (1.3 mmol) was dissolved in THF:TMEDA [(4:1), 15ml] and cooled to -78°. Methyl lithium (1.4 mmol) was added, the solution stirred for 10 min, and treated with phosphorous trichloride (1.6 mmol). The mixture was warmed to 20° over 90 min, and stirred for 30 min. Diethyl either (50ml) was added, the solution washed with hydrochloric acid (2M, 10ml), brine (2 x 10ml), dried, filtered, and evaporated. Purification by chromatography on silica gel [(70g); using light petroleum as eluant] gave the diene (18) (132mg, 62%), t.l.c., n.m.r. as before.

General procedure for the preparation of Saturated Esters (4)

The following procedure for the preparation of methyl-3-cyclohexylbutanoate is typical.

(5f) (5.0 mmol.) was dissolved in dry 1,2-DME (60ml) and the solution cooled to -55°. n-Butyl lithium (4.75 mmol in hexane) was added, the solution stirred for 20 min., and a solution of methyl crotonate (10.0 mmol) in 1,2-DME (8ml) was added over 1h. Trifluoroacetic acid (5.0 mmol) was added, followed by ethanethiol (5ml), the solution warmed to 20° and evaporated. The residue was triturated with light petroleum (4 x 20ml), and the extracts evaporated to give an oil (1.40g). Kügelrohr distillation b.p. ca 150° at 20 mmHg, (Lit.[13], 149-50° at 25 mmHg) gave a colourless oil (640mg) which was purified by p.l.c. [using diethyl ether : light petroleum (3:17) as eluant] to give methyl-3-cyclohexylbutanoate[13] (323mg, 35%) as an oil, t.l.c. [diethyl ether : light petroleum (3:17)] Rf 0.75; νmax (film) 2965 s, 2860 s, 1745 s (C=O), 1450 m, and 1140 m, cm^{-1}; δH 0.88 (3H,d, J 7Hz,Me), 0.88 - 1.24 (6H, m, CH_2), 1.57 - 1.80 (5H,m, CH_2 and C(4)H), 1.80 - 1.91 (1H,m, C(3) H), 2.03 - 2.15 (1H,m, AB part of ABX, CH_2CO), 2.33 - 2.43 (1H,m, AB part of ABX, CH_2CO), 3.66 (3H,s, OMe); δC 16.52 (q, Me), 26.66, 28.98, 30.30 (3 x t, CH_2), 35.39 (d, CH), 39.05 (t, CH_2CO), 42.63 (d, CHMe), 51.33 (q, OMe), 174.23 (s, CO); m/e (E.I.) 185 (MH^+, 5%), 153(17), 111(100), 101(95), 87(62), 74(72), 55(90), and 41(67); (Found; C, 71.83%; H, 10.92%). $C_{11}H_{20}O_2$ requires C, 71.63%; H, 10.93%).

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