IONIC AND RADICAL REACTIONS OF SOME NITRO COMPOUNDS

A thesis submitted in partial fulfilment of the requirements for admission to the degree of

DOCTOR OF PHILOSOPHY

by

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PREFACE

Unless otherwise stated, the results recorded in this thesis are those of the author. The work described in this thesis was carried out under the supervision of Dr R.K. Norris during the period February 1979 to February 1983. Some of the work described in Part II of this thesis was carried out in 1978 and has been included for completeness.

I wish to thank Dr R.K. Norris for his patient guidance and enthusiastic encouragement through the course of this work. I would also like to thank Professor S. Sternhell and all members of the Department of Organic Chemistry for their friendship and support.

The support I have received from my wife Susan and my family has been invaluable.

I thank the Australian Government for a Commonwealth Postgraduate Research Award.

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Norris, R.K., and Wright, T.A., *Aust. J. Chem.*, 1982, 35, 2161.

ABSTRACT

The thesis deals with substitution and elimination reactions of some nitro compounds.

The reactions of *p*-(1-chloro-2,2-dimethylpropyl)-nitrobenzene and *p*-(2,3-dimethyl-1-nitropropyl)nitrobenzene with ambident nucleophiles of the type $(Z)(Y)RC^-$ where Z,Y are electron withdrawing substituents (e.g. CN, CO_2Et, Ac) were examined. The substitution reactions at the benzylic carbon proceed by the $S_{RN}1$ mechanism. Increased steric hindrance favours an alternate reduction process and so does the presence of acyl groups in the nucleophile. In the absence of severe steric hindrance good yields of *C*-alkylated products are obtained. The reversibility of the association step of the $S_{RN}1$ reaction was studied. The dissociation of *C*-alkylated products is extremely slow and it is also clear that the association step in most of the $S_{RN}1$ reactions studied is not reversible. The dynamic ^1H n.m.r. behaviour of derivatives of the *C*-alkylates formed in the above $S_{RN}1$ reactions was examined. There is no correlation between the yield and reaction time in $S_{RN}1$ reactions and the energy parameters, determined by dynamic ^1H n.m.r., for rotation around the aryl-benzylic carbon bond. Useful information on the conformational changes involved in rotation about the sp^2-sp^3 bond was obtained, however.

The mechanisms of elimination of nitrous acid from *p*-(2-methyl)-2-nitropropyl)nitrobenzene and 1-chloro-2-methyl-2-nitro-1-(*p*-nitrophenyl)propane and their deuterated analogues were studied. Deuterium isotope effects and the stereochemistry of elimination from *p*-(2,3,3-trimethyl-2-nitrobutyl)nitrobenzene show the elimination from *p*-(2-methyl-2-nitropropyl)nitrobenzene in 50% dimethylsulfoxide - methanol with sodium methoxide as base is occurring by an *E*2 mechanism. Comparison of the rate of elimination from this compound with the analogous compounds in which bromide and chloride are the nucleofuges allows nitrite to be ranked as intermediate in nucleofugacity between the two halides. Determination of activation parameters show that this increased nucleofugacity of nitrite is due to a more positive entropy of activation for the nitrous acid elimination. Deuterium isotope effects and isotopic exchange experiments show that the mechanism of elimination for 1-chloro-2-methyl-2-nitro-1-(*p*-nitrophenyl)propane in methanol with sodium methoxide as base tends to *E*1cB with an irreversible first step. The electrophilic addition of hydrogen halides and mercury(II) to β,β-dimethylstyrene and its *p*-OMe and *p*-NO_2 derivatives gave products that can be rationalized as arising from the tertiary cation rather than a benzylic cation.

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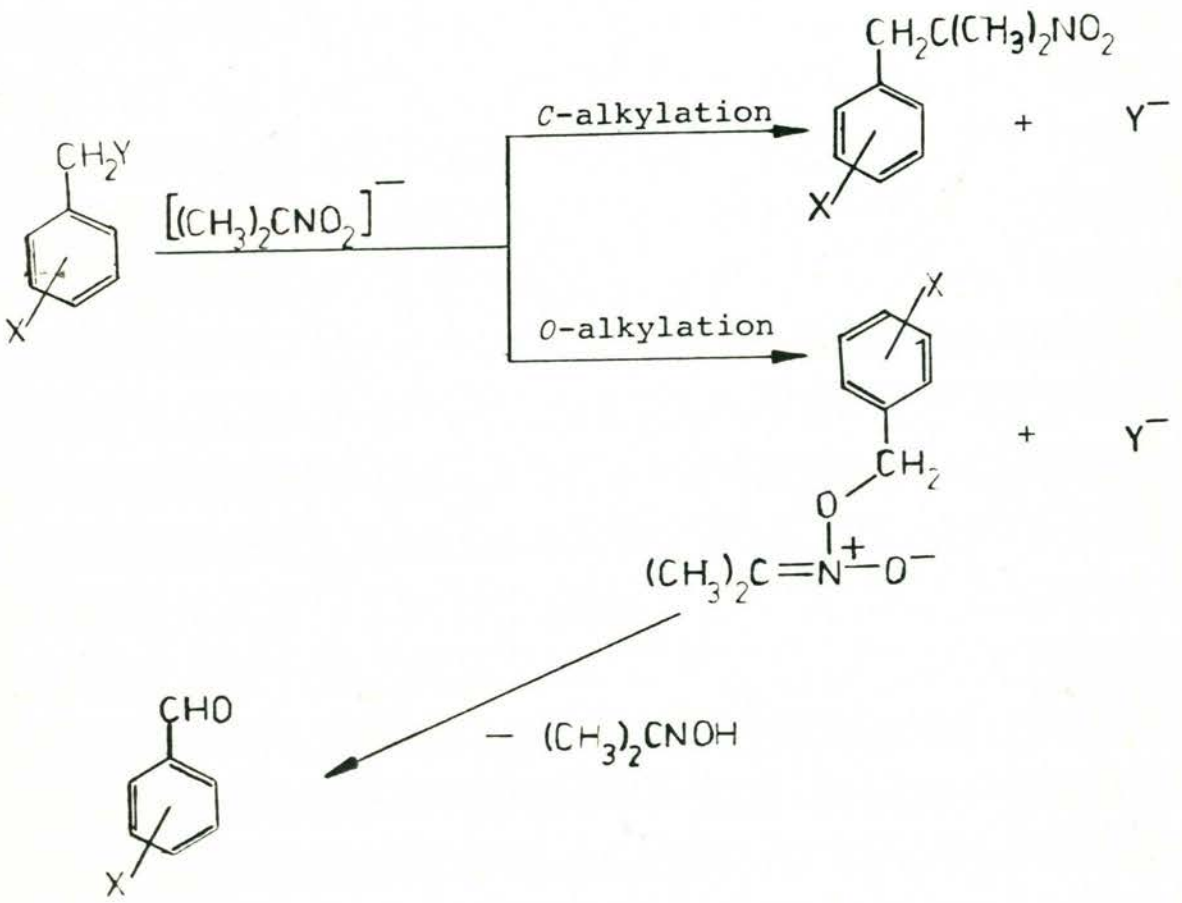
PART I

PART II

INTRODUCTION

INTRODUCTION

Ambident *aci*-nitronate ions formed from primary and secondary nitroalkanes give, upon reaction with alkyl halides, products that arise from either *C*-alkylation (*C*-*C* bond formation) or *O*-alkylation (*C*-*O* bond formation). This duality of behaviour for benzyl halides is shown in Scheme 1. *O*-Alkylation (proceeding by an S_N2 mechanism) is the favoured pathway for most substrates[1,2] and yields a nitronate ester which then reacts further. Hass and Bender[2] studied the reactions of a



Scheme 1

series of *p*-substituted benzyl halides with the sodium salt of 2-nitropropane and found that all except one gave high yields of the corresponding benzaldehydes derived from the unstable intermediate nitronate esters. The notable exception was *p*-nitrobenzyl chloride which gave almost exclusive *C*-alkylation (83 - 95%).[2,3] In subsequent work,[4] it was found that *o*-nitrobenzyl chloride gave a 46% yield of *C*-alkylate whilst *m*-nitrobenzyl chloride gave only *m*-nitrobenzaldehyde.

The *o*- or *p*-nitro group's effect was found not to be the sole influence on the mode of alkylation of nitronate anions. If the leaving group is more easily displaced than chloride there is a decrease in the amount of *C*-alkylation and an increase in the yield of products derived from *O*-alkylation. For example, *p*-nitrobenzyl iodide affords an 81% yield of *p*-nitrobenzaldehyde (Scheme 1; X = *p*-NO_2, Y = I).[3] *C*-Alkylation is inhibited by triplet oxygen[5] and by the presence of small amounts of readily reduced nitroaromatics such as *p*- and *m*-dinitrobenzene.[6] The efficacy of this inhibitory effect is proportional to the ease of one-electron reduction of the nitroaromatics.[7] Thus *p*-dinitrobenzene is a more efficient inhibitor of *C*-alkylation than is *m*-dinitrobenzene and nitrobenzene has minimal inhibitory effect.[6] *C*-Alkylation is catalysed by white light;[8] for example *p*-nitrobenzyl chloride and the lithium salt of 2-nitropropane do not react at all in ethanol in five hours in the dark whereas with irradiation the reaction proceeds to more than 90% completion in under three hours.[8] When reaction occurs in the *p*-nitrobenzylic system

to give *C*-alkylation, the reaction rate is at least one hundred times faster than for the denitro benzylic compound, which gives *O*-alkylation.

The above phenomena led to the proposal of a radical chain mechanism involving radical anion intermediates and is summarized in Scheme 2[†] [R = H, X = Cl, $Y^- = (Me_2CNO_2)^-$].[8,9]

$$ArCR^1R^2X + Y^- \rightarrow [ArCR^1R^2X]^{-\cdot} + Y\cdot \quad (1)$$

$$[ArCR^1R^2X]^{-\cdot} \rightarrow Ar\dot{C}R^1R^2 + X^- \quad (2)$$

$$Ar\dot{C}R^1R^2 + Y^- \rightarrow [ArCR^1R^2Y]^{-\cdot} \quad (3)$$

$$[ArCR^1R^2Y]^{-\cdot} + ArCR^1R^2X \rightarrow ArCR^1R^2Y + [ArCR^1R^2X]^{-\cdot} \quad (4)$$

Scheme 2

Bunnett found that a similar mechanism operated in the photo-initiated substitutions of aryl iodides and designated it $S_{RN}1$ to stand for radical-nucleophilic-substitution, unimolecular.[10]

This reaction has been extensively reviewed.[11-14] Some facets of particular importance to *p*-nitrobenzylic systems are discussed below.

It was found that α,*p*-dinitrocumene, which cannot undergo S_N1 or S_N2 substitutions, reacted *via* the $S_{RN}1$ mechanism

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[†] Throughout this thesis the abbreviation Ar stands specifically for *p*-$O_2NC_6H_4$.

with a wide variety of nucleophiles [Scheme 2; R = Me, X = NO_2, Y^- = PhS^-, N_3^-, NO_2^-, $(EtO_2C)_2\bar{C}H$, $PhSO_2^-$, etc.].[15,16,17] These reactions were catalysed by light, and inhibited by radical scavengers such as galvinoxyl and di-t-butyl nitroxide.[11] Some of the reactions required entrainment with the lithium salt of 2-nitropropane when the relevant anion was not a sufficiently powerful electron donor.[11,18]

In the reactions of ambident nucleophiles with *p*-nitrocumyl chloride† or α,*p*-dinitrocumene, bond formation always occurred at the more hindered site: the nitrogen of nitrite,[16] the carbon of diethyl malonate and the sulfur of benzenesulfinate.[17] It was also found that *p*-nitrocumyl chloride[11,16] and α,*p*-dinitrocumene[11] reacted with lithium 2-nitropropan-2-ide to afford 65 - 90% yields of the highly branched carbon alkylate *p*-(2-nitro-1,1,2-trimethylpropyl)nitrobenzene. As a consequence of these results, it was stated[11,16] that steric hindrance has but minimal opportunity to exert itself in the reaction sequence of Scheme 2.

The effect of steric hindrance on the reaction of *aci*-nitronates with a series of benzylic chlorides ($ArCHR^1$; R^1 = Me, Et, Pr^i, Bu^t) has been studied.[19,20] The reaction of lithium 2-nitropropan-2-ide in dimethyl sulfoxide at 20° with *p*-(1-chloroethyl)nitrobenzene afforded a 70% yield of the carbon alkylate $S_{RN}1$ product and a 15% yield of *p*-nitroaceto-

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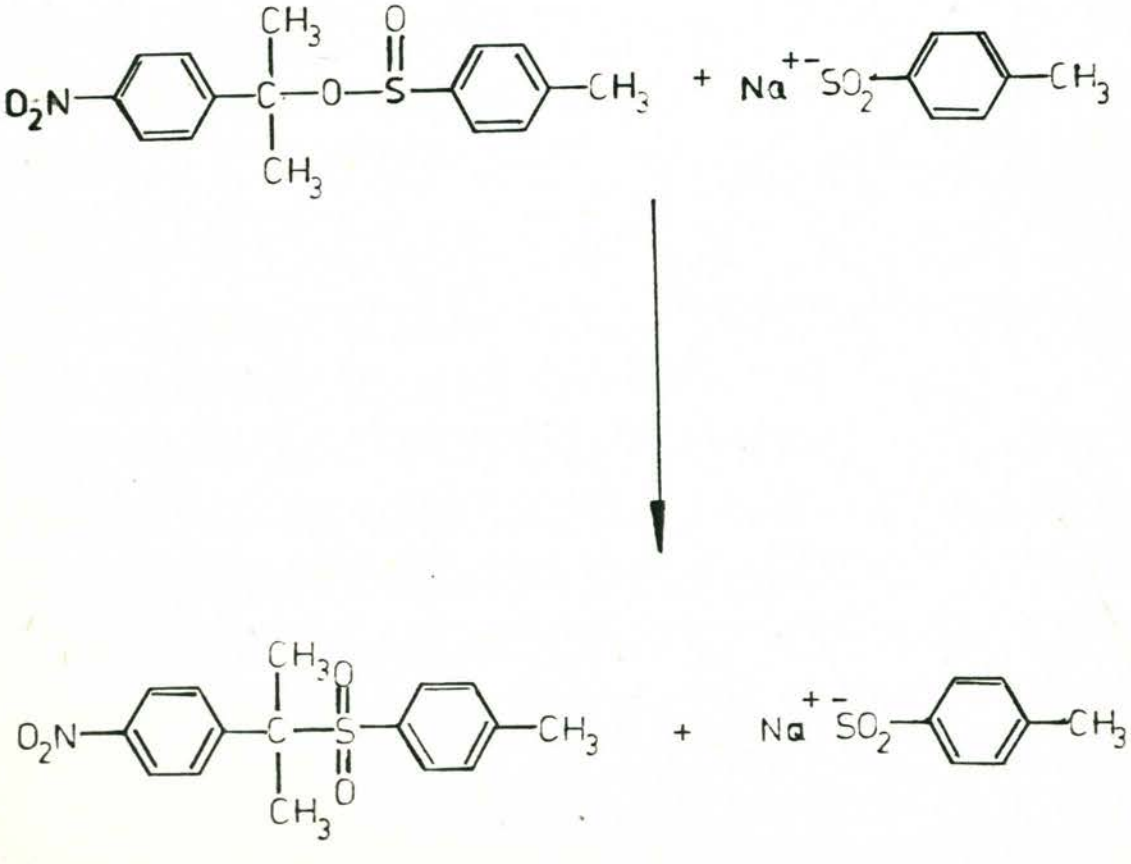
† Throughout this thesis the traditional term *p*-nitrocumyl has been preferred to the unwieldy, but systematic, term 1-methyl-1-(*p*-nitrophenyl)ethyl.

phenone which probably arose by an S_N2 process.[19] A less likely source of *p*-nitroacetophenone would be an $S_{RN}1$ process with oxygen alkylation.[19] When *p*-(1-chloro-2,2-dimethylpropyl)-nitrobenzene (1) was treated in the same manner, but for a longer time, *p*-nitropivalophenone was the sole product in 95% yield.[19] The pathway of this latter reaction was demonstrated to be an $S_{RN}1$ reaction with exclusive *O*-alkylation,[19] and it was assumed to be the kinetically favoured process.[20] Kornblum objected to this interpretation of these results, claiming that the *C*- and *O*-alkylation processes were reversible.[21]

In support of the proposal of reversibility in the association step [Scheme 2, eqn (3)] of $S_{RN}1$ reactions, the reaction shown in Scheme 3 was examined.[21] This clearly

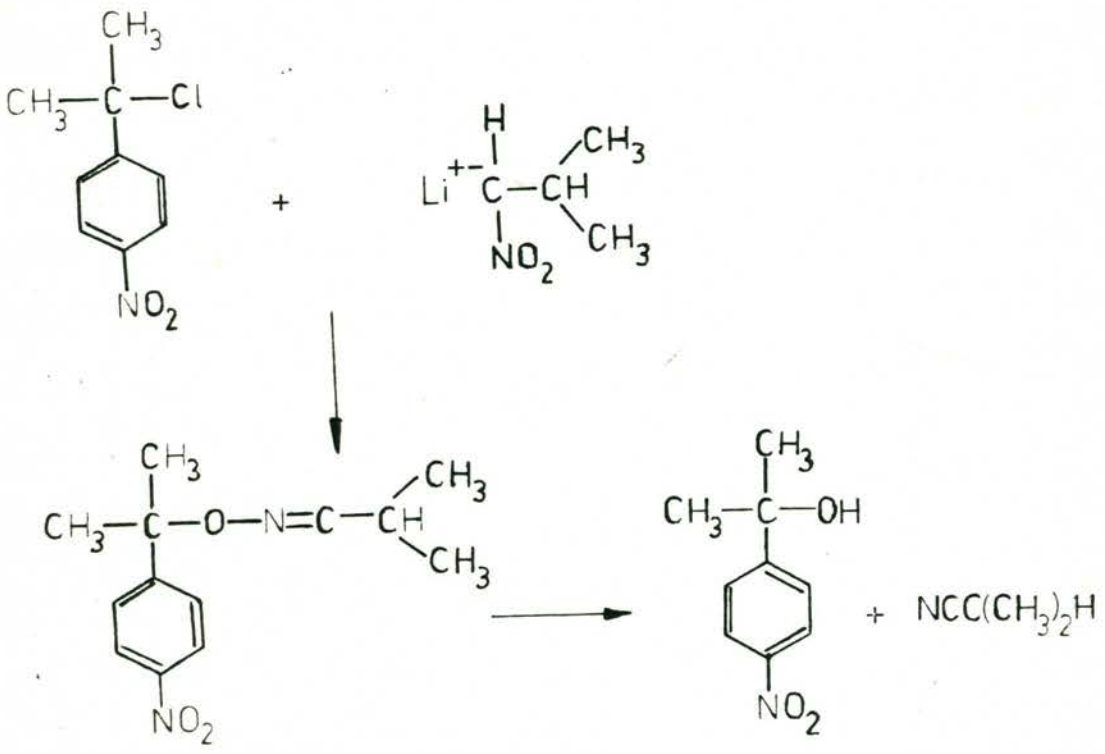


Scheme 3

demonstrated that sulfinate esters could be converted to sulfones rapidly under $S_{RN}1$ conditions. It was subsequently argued that if the sulfinate ester were initially formed in the association step [Scheme 2, eqn (3)] of an $S_{RN}1$ process in the reaction of a *p*-nitrocumyl radical and *p*-toluenesulfinate ion it would rearrange to the sulfone under the reaction conditions. It should be noted, however, that sulfinate esters were neither isolated from, nor detected in, the reactions forming sulfones under $S_{RN}1$ conditions.

Tolbert and Siddiqui have commented[22] that the rearrangement of the sulfinate ester in Scheme 3 provides "chemical evidence for the feasibility of this pathway and its corresponding mechanistic rationale, (although) the existence of reversibility of itself is not *prima facie* proof for the pathway followed in the actual reaction." In this paper evidence was presented that the $S_{RN}1$ arylation of indene and isoindene occurs under kinetic control.

Further evidence[23] has been published to support the argument that the regiochemistry of the association step [Scheme 2, eqn (3)] is a kinetically controlled, irreversible process. For example, *p*-nitrocumyl chloride reacts with the salt of 2-methyl-1-nitropropane to give the oxime ether (derived irreversibly from the nitronate ester), which further reacts to give *p*-nitrocumyl alcohol. This process is shown in Scheme 4.

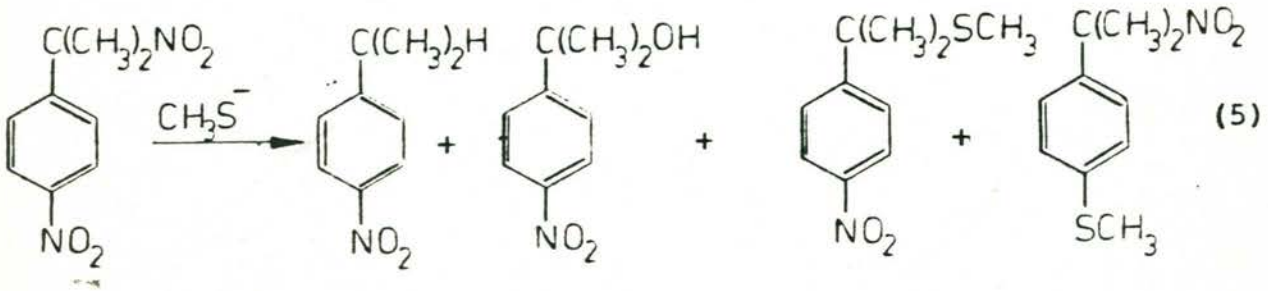


Scheme 4

Extensive studies on other sterically hindered substrates ($ArCMeR^1NO_2$; R^1 = Me, Et, Pr^i, CH_2Bu^t)[24] as well as the previously mentioned results,[19,20,23] led to the proposal of definitive rules which predict when *O*-alkylation would be favoured in the association of *aci*-nitronates with *p*-nitrobenzylic substrates. β-Branching in either the *aci*-nitronates or the benzylic substrate favours *O*-alkylation at the expense of *C*-alkylation.[24]

Although the association of *aci*-nitronates with these benzylic substrates appears to be kinetically controlled there

is some limited evidence that *C*-alkylates may dissociate. This evidence is presented in Scheme 5, eqn (5).[25] Presumably the formation of the first three products involves the dissociation step in eqn (6). The reaction conditions involve the use of the powerful nucleophile and one-electron-transfer reagent, methanethiolate ion, in the excellent solvent hexamethylphosphoramide. There are other clear cut examples of reversible $S_{RN}1$ processes, for example the sulfone-sulfinate system referred to above, and those involving azide, nitrite and naphthyloxides as leaving groups.[11,26]



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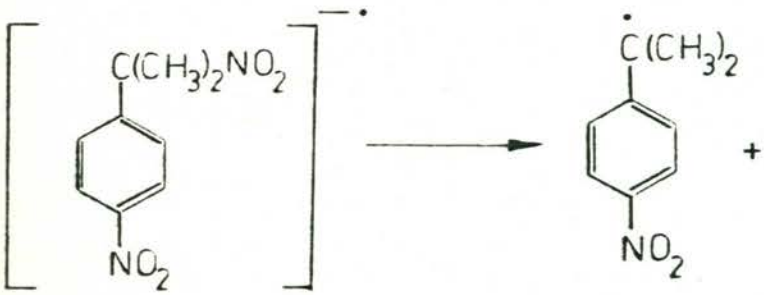

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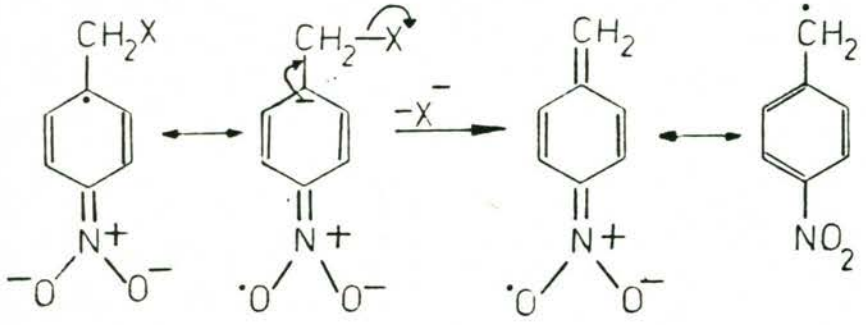
Scheme 5



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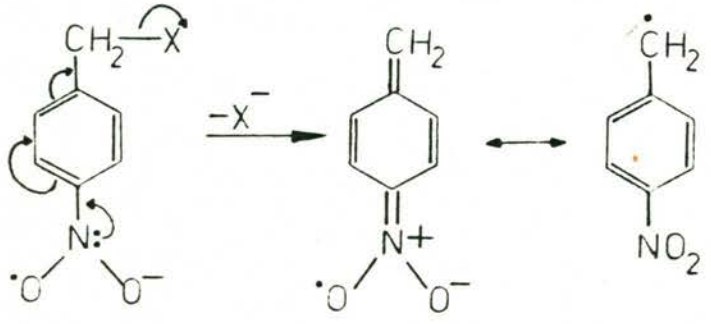

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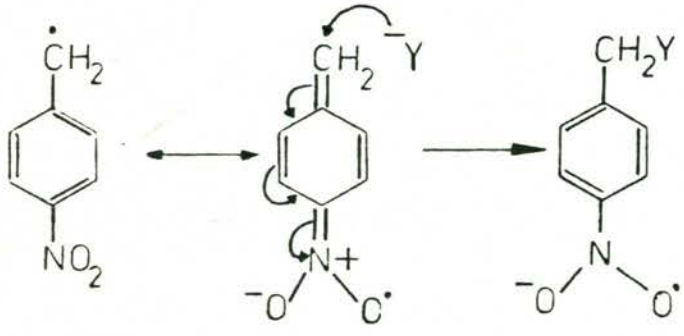


(9)

Scheme 6

Two different modes for the mechanism of dissociation (and the reverse reaction, association) of radical anions have been proposed. The first mode is shown in Scheme 6.[11,21] Dissociation [Scheme 6, eqn (7)] is formally an E_{1cB} elimination. This process may also be represented as a retro-Michael reaction [Scheme 6, eqn (8)] in which the lone pair on the nitrogen assists the displacement of the leaving group to form a planar intermediate radical. Association [Scheme 6, eqn (9)]

is a Michael-type addition. Since Michael reactions are classic examples of reversible processes, if $S_{RN}1$ reactions did proceed through such a process it would be reasonable to assume that *in general* they were reversible, as are Michael addition processes involving nitro compounds.

The alternative approach to the mode of dissociation and association in $S_{RN}1$ reactions that has been proposed[14,26] is shown in general form in Scheme 7. Dissociation [Scheme

$$\cdot^{-}R - X(\pi^{*}) \rightarrow R - X^{-}\cdot(\sigma^{*}) \qquad (10)$$

$$\cdot^{-}R - X(\sigma^{*}) \rightarrow R^{\cdot} + X^{-} \qquad (11)$$

$$R^{\cdot} + Y^{-} \rightarrow R - Y^{-}\cdot(\sigma^{*}) \qquad (12)$$

$$R\text{-}Y^{-}\cdot(\sigma^{*}) \rightarrow R - Y^{-}\cdot(\pi^{*}) \qquad (13)$$

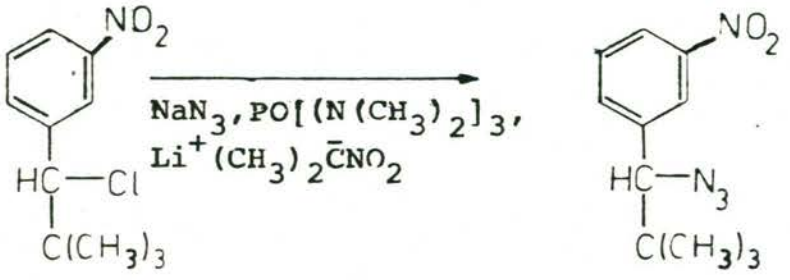
Scheme 7

7, eqns (10) and (11)] involves an initially formed π^{*} radical anion undergoing intramolecular electron transfer to a σ^{*} orbital of the C - X bond, which then dissociates. Association [Scheme 7, eqns (12) and (13)] is the reverse process, but in a benzylic system the radical intermediate could be pyramidal (i.e. sp^3), since the unpaired electron resides in the σ^{*} orbital. The processes of Scheme 7 have been independently proposed for both aromatic[27] and benzylic[28] systems.

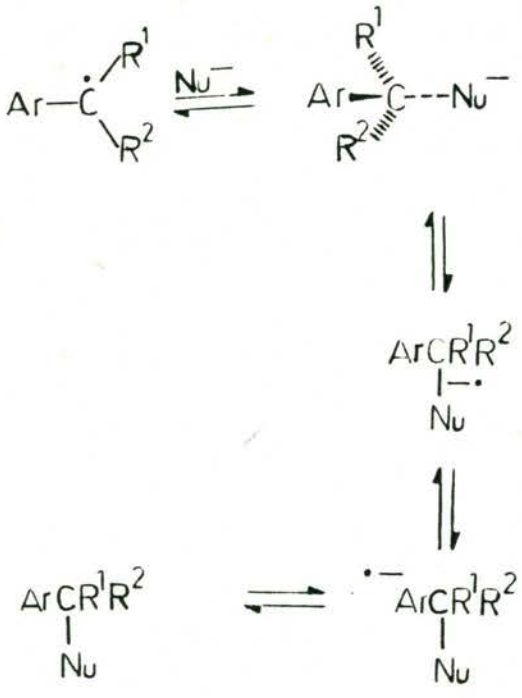
The fact that optically active *p*-(1-methyl-1-nitropropyl)nitrobenzene (Scheme 2, R^1 = Me, R^2 = Et, X = NO_2)

gives racemic products when treated with a range of anions has been taken as evidence for the processes shown in Scheme 6.[11] However, the results are not necessarily definitive,[26] and can also be rationalized in the context of the processes in Scheme 7. If the essentially ionic Michael process occurs in benzylic systems, clearly a different mechanism must hold for aromatic $S_{RN}1$ reactions, in which such a mechanism cannot operate. Indeed, this duality has been proposed.[29]

Recently, however, intramolecular electron transfer has been reported to occur in the dissociation of radical anions of *p*-nitrobenzyl halides.[30] The stereospecific trapping, in a *p*-nitrobenzylic system, of an sp^3 radical before epimerization could occur also provides supporting evidence for the processes of Scheme 7.[26,31] Studies in the α-t-butyl-*m*-nitrobenzyl systems[28] show that $S_{RN}1$ reactions occur such as that shown in eqn (14). The Michael-type process cannot be drawn for these reactions.



(14)



Scheme 8

Kinetic control of the regiochemistry of the association step [Scheme 2, eqn (3)] in benzylic $S_{RN}1$ processes can be explained by the sequence described in Scheme 8.[28] The "planar" (or rapidly inverting) benzylic radical becomes "pyramidal" on the approach of a nucleophile and a σ^* radical anion results. This undergoes intramolecular electron transfer to the π^* radical anion, in which the free electron is delocalized over the *p*-nitrophenyl system. The distortion in shape as the nucleophile approaches could explain the marked effect of steric hindrance on the regiochemistry of association of benzylic radicals and *aci*-nitronates in which β-branching is present. The pyramidalization increases the

steric crowding around the reaction site, favouring the formation of the less sterically demanding *O*-alkylates.

The regiochemistry of the association step in the reaction of other non-*aci*-nitronate, ambident anions with sterically hindered *p*-nitrobenzylic substrates might also display significant steric effects. Two such substrates, the chloride (1) and *p*-(1,2-dimethyl-1-nitropropyl)nitrobenzene (2), had been studied with *aci*-nitronates and sulfinate salts.[19,20,23,24,32] The reactions of the chloride (1) had also been studied with the sodium salts of ethylmalononitrile, which gave the *C*-alkylate, and diethyl methylmalonate which gave the *C*-alkylate and products believed to arise from *O*-alkylation.[20] It was hoped that these hindered substrates would react with a range of ambident anions and that results of these studies would allow a correlation of steric size with *C*-alkylation and other reactions. It was decided to attempt to make a correlation between the steric bulk of derivatives of the products (determined by dynamic ^{1}H n.m.r. spectroscopy) with the proportion of *C*-alkylation. In addition a study of reversibility in some $S_{RN}1$ reactions was undertaken.

$ArCH(Cl)Bu^{t}$ (1)

$ArC(Me)(Pr^{i})NO_2$ (2)

RESULTS AND DISCUSSION

(Structures in fold-out section
at end of thesis)

1. Reactions of Sterically Hindered *p*-Nitrobenzylic Substrates with Nucleophiles

(a) Reactions of the α-t-Butyl Chlorides (1) and (3)

(i) *Enumeration of Products*

The results of reactions of the sterically hindered *p*-nitrobenzylic chloride (1), and its denitro analogue (3), with the salts (4) - (17) and quinuclidine (18) are given in Table 1. The products comprised the azides (20) and (21), the *C*-alkylates (22) - (30), the *O*-alkylates (31) and (32), the sulfone (33), the ketone (34), the alcohol (35) and the reduced compound (36) in which the chlorine atom was replaced by hydrogen. The assignment of structure to these products, and their spectroscopic properties are discussed below [Section 1 (d)].

(ii) *Mechanism of the Substitution Reactions*

The chlorides (1) and (3) are both extremely hindered neopentylic compounds, and therefore one would expect any S_N2 substitution at the benzylic carbon to be slow. In fact only sodium azide (4) gave any detectable reaction with the denitro chloride (3) (Table 1, expt 5), at a rate at least eight thousand times slower than the reaction between the *p*-nitrobenzylic chloride (1) and the salt (4) (Table 1, expt 1). Treatment of the denitro chloride (3) with other nucleophiles [see entries in Table 1 after reactions of the *p*-nitrobenzylic

Table 1. Reactions of the α-t-butyl chlorides (1) and (3) with nucleophiles

Unless otherwise stated reactions were performed[A] on substrate (2.5 mmol) and the salt (10.0 mmol) in $(Me_2N)_3PO$ (10.0 ml) under nitrogen with irradiation by white light from a 500-W GE lamp 20 cm from the reaction vessel. Yields in normal type are isolated yields, those in italics are estimated[B] yields.

Experiment	Substrate	Salt	Temperature[C] (°)	Time (h)	Products:yield %
1	(1)	(4)[D]	60	<0.15	(20):89
2[E,F]	(1)	(4)[D]	20	2.5	(20):*90*; (1):*7*
3[E,F,G]	(1)	(4)[D]	20	2.5	(1):*95*
4[E,H]	(1)	(4)[D]	20	2.5	(1):*94*
5	(3)	(4)[D]	65	72	(3):*90*; (21) < *4*
6	(1)	(5)	55	<0.3	(22):*98*, 97
7[G,I]	(1)	(5)	55	2.5	(1):*34*; (34):*27*; (35):*8*
8	(3)	(5)	65	120	(3):*91*
9	(1)	(6)	60	2	(36):*2*; (23):59

Table 1 continued

Experiment	Substrate	Salt	Temperature[C] (°)	Time (h)	Products:yield %
10	(1)	(7)	65	24	(36):*8*; (1):*4*; (34):*23*
11	(1)	(8)	65	0.3	(24):41; (25):51
12	(3)	(8)	65	192	(3):*79*
13	(1)	(9)	65	10	(36):*14*;(26):19; (27):17
14	(1)	(10)	65	1.3	(1):*2*; (28)*73*; (35):*6*
15[J]	(1)	(10)	65	1.3	(36):*3*; (28)*73*,73; (35):*1.5*
16[K]	(1)	(10)	65	2	(1):*5*; (28):*57*;(35):*34*
17[G]	(1)	(10)	65	2.5	(1):*2*; (34):31; (35):55
18	(3)	(10)	65	144	(3):*88*
19[J]	(1)	(11)	65	6	(36):*5*; (29):54
20[L]	(1)	(12)	65	28	(36):*7*; (34):*10*; (35):*17*
21[M]	(1)	(13)	65	48	(36):9; (34)*16*
22	(1)	(14)	65	7.5	(36):45; (1):*8*; (31) and (32):7; (30): 2

Table 1 continued

Experiment	Substrate	Salt	Temperature[C] (°)	Time (h)	Product:yield %
23	(3)	(14)	65	168	(3):*64*
24	(1)	(15)	65	1.5	(36):56
25[N]	(1)	(15)	65	6	(36):*76*
26	(1)	(16)	50	2	(1):*90*
27[L]	(1)	(16)	50	0.85	(34):*4*; (33):68
28	(3)	(16)	50	192	(3):*94*
29[L]	(3)	(16)	50	24	(3):*87*
30[O]	(1)	(17)	60	120	(1):*31*; (34):*12*; (35)*9*
31[O]	(1)	(18)	60	72	(1):*37*; (34):*11*
32[O]	(1)		65	24	(1):*82*

A Full details in experimental p. 95.

B Yields were estimated by ^{1}H n.m.r. spectroscopy with 2,4,6-trinitrotoluene as internal standard.

C The variation in the temperature in the range 50 - 65° was ±3° and at 20° was ±1°.

D Saturated solution of sodium azide (approximately 0.25 M).

Table 1 continued

E Reaction scale 1.0 mmol substrate, 4.0 ml hexamethylphosphoramide.

F Irradiation with 250-W GE lamp.

G Under oxygen (see Experimental).

H Reaction performed in dark (see Experimental) and with 1.0 mmol of di-t-butyl nitroxide.

I Reaction scale 0.625 mmol substrate, 2.5 ml solvent.

J Quenched with degassed water.

K Under dry air (see Experimental).

L Entrained with 0.13 mmol lithium 2-nitropropan-2-ide (19).

M Entrained with 0.40 mmol lithium 2-nitropropan-2-ide (19).

N 20.0 ml of hexamethylphosphoramide.

O Reaction scale 1.25 mmol substrate, 5.0 mmol salt, 5.0 ml hexamethylphosphoramide.

chloride (1) with the appropriate nucleophiles] gave reasonable to good recoveries of starting material (3) and no detectable amounts of substitution products (< 5%). These results clearly show that the denitro chloride (3) does not react to any significant extent by S_N1 or S_N2 mechanisms. The *p*-nitrobenzylic chloride (1) was quite stable under the standard reaction conditions in the absence of nucleophiles (Table 1, expt 32), affording only starting material (1) after 24 hours. This result precludes any S_N1-type reactions, i.e. ionization followed by rearrangement and elimination, on the time scale of most reactions in Table 1. The general observation that the denitro chloride (3) did not react with nucleophiles, while the *p*-nitrobenzylic chloride (1) did, is *prima facie* evidence that the chloride (1) undergoes substitution by an $S_{RN}1$ process.

The reaction of the *p*-nitrobenzylic chloride (1) with the salt (4) was sensitive to oxygen and di-t-butyl nitroxide (compare expts 3 and 4 with expt 2 in Table 1); both completely inhibited reaction in the presence of an excess of the salt. These observations are evidence for the occurrence of radical processes. The absence of products derived from oxygenation of the intermediate benzylic radical (37) (see below) was attributed to the poor electron transfer capacity of the azide anion,[11] which gave rise to a very low steady state concentration of radical anions which were destroyed by oxygen before significant dissociation could take place.

The reactions of the chloride (1) with the sodium salts (5) and (10) of ethylmalononitrile and diethyl methylmalonate

(Table 1, expts 6, 14 and 15) gave good yields of *C*-alkylates with little or no formation of the alcohol (35), especially when deoxygenated water (see Experimental) was employed in workup (Table 1, expt 15). The reaction of the chloride (1) with the salts (5) and (10), when performed under oxygen (Table 1, expts 7 and 17), gave no *C*-alkylated products and the ketone (34) and alcohol (35) were the only products. Under an atmosphere of dry air, the chloride (1) reacted with the salt (10) to give a reduced yield of the *C*-alkylate (28) and a significant amount of the alcohol (35) (Table 1, expt 16). The formation of the ketone (34)[†] and the alcohol (35) in the reaction of the chloride (1) with the salt (10) in dimethyl sulfoxide has been observed previously by Randles.[20] These products had been presumed to arise from *O*-alkylation processes in the same way as *O*-alkylation products formed in the reaction of (1), and related substrates, with *aci*-nitronate salts.[19,20] Kornblum, as an alternative to *O*-alkylation by the potentially ambident malonic ester anions, has suggested that the formation of these products should be attributed to the trapping of benzylic radicals by the oxygen atom of the dimethyl sulfoxide, with subsequent fragmentation.[21] Without entrainment by the salt (19), the reaction of (1) and the salt (10) in dimethyl sulfoxide took 11 days and, since the nitrogen atmosphere which was used was found to contain traces

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[†] Whenever the salt, lithium 2-nitropropan-2-ide, (19), was employed to entrain reactions in Table 1 the ketone (34) was formed. The formation of the ketone (34) under these conditions can be attributed at least in part to a sterically hindered *O*-alkylation process.[19,20]

of oxygen,† formation of the ketone (34) and alcohol (35) in Me_2SO probably arises not by *O*-alkylation but by oxygen trapping processes. In this work, with the careful exclusion of oxygen, the use of very pure nitrogen and much shorter reaction times in hexamethylphosphoramide only minor formation of alcohol (35) and ketone (34) occurred. The use of hexamethylphosphoramide also avoids the possibility of solvent participation of the type suggested by Kornblum. It can be concluded, therefore, that the ketone (34) and the alcohol (35) arose, not from *O*-alkylation processes, but from oxygenation of the intermediate benzylic radical (37). The relative ratios of the ketone (39) and alcohol (35) will depend in part on the amount of oxygen present, since it was demonstrated (see Experimental) that oxygen in the presence of the salt (10) was capable of slowly oxidizing the alcohol (35) to the ketone (34). This latter conversion did not, however, take place quickly enough for it to be the sole process by which the ketone (34) was formed. The ketone (34) and the alcohol (35) must both form from redox processes involving a common peroxy intermediate as shown in Scheme 9.

The very low reactivity of the denitro chloride (3), the inhibitory effects of oxygen and di-t-butyl nitroxide in the azide system and the effect of oxygen on the nature of the products in the reaction of (1) with the salts (5) and (10) lead to the conclusion that all the substitution reactions involving the chloride (1) are $S_{RN}1$ processes.

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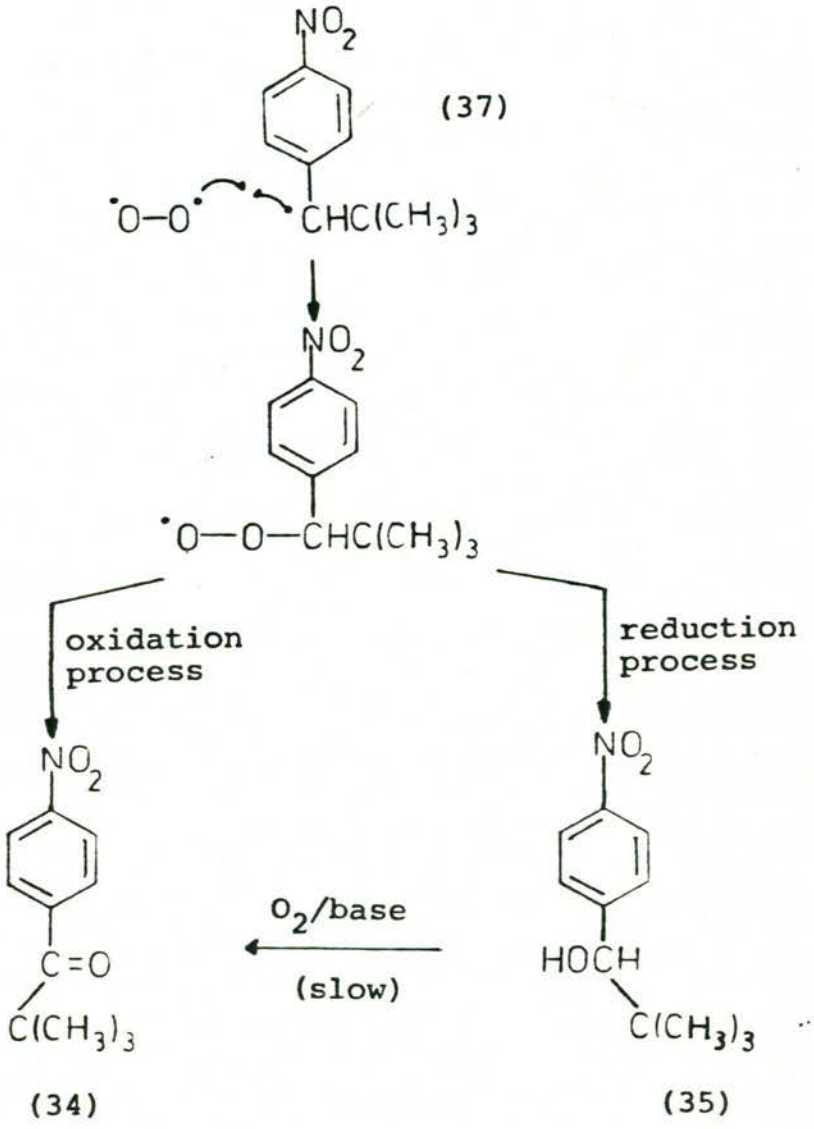
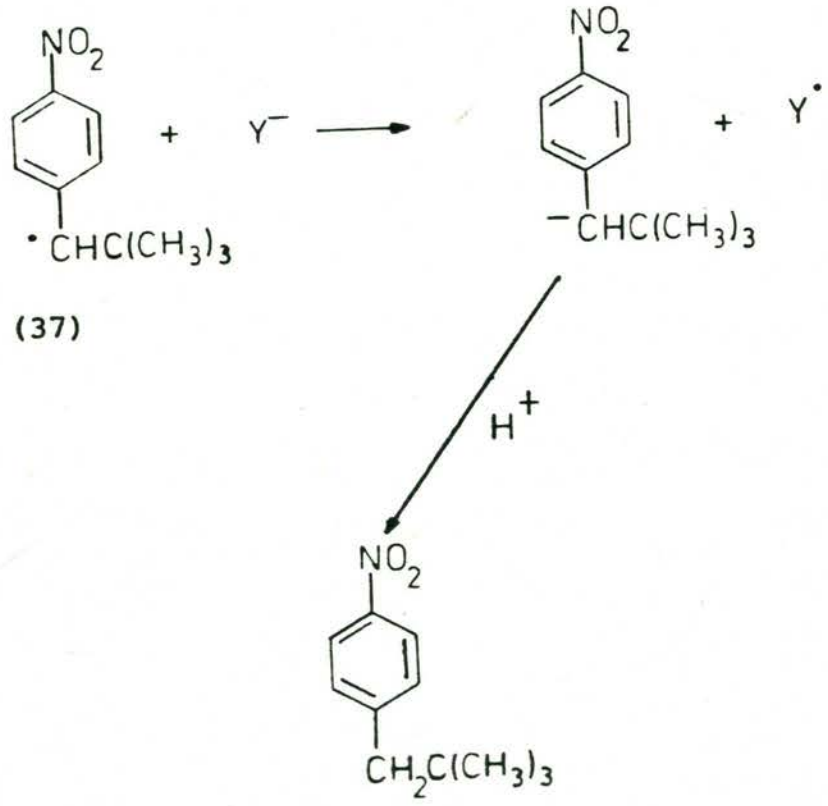
† See footnote p. 1488 of reference.[20]


NO2
(37)
O–O
CHC(CH3)3
NO2
O–O–CHC(CH3)3
oxidation process
reduction process
NO2
C=O
C(CH3)3
O2/base
(slow)
NO2
HOCH
C(CH3)3
(34)
(35)

Scheme 9

(iii) *Steric and Electronic Effects on Reaction Rates and Product Yields*

The tertiary nucleophilic carbon atoms in the anions (5a), (8a), (10a), 14a) and (15a) from the salts (5), (8), (10), (14) and (15) each bear either a methyl or ethyl group, and two anion-stabilizing substituents. Inspection of space-filling models of these anions seems to indicate that the anion (5a) is the least encumbered, followed by (8a), and that the anions (10a), (14a) and (15a) have much the same steric requirements. In the reactions of the chloride (1) with these anions a large decrease in the proportion of *C*-alkylation is observed (see Table 1, expts 6, 11, 15, 22 and 24), and the yields of *C*-alkylates from the above salts are 98, 92, 73, 2 and 0 % respectively. The sharp discontinuity in the yield of *C*-alkylate in the reaction of chloride (1) with the anions (10a) and (14a) is particularly striking. Only in the reaction with the salt (14) were *O*-alkylation products isolated, and even these, (31) and (32), are formed in poor yield (7%; Table 1, expt 22). The yield of the reduction product (36) inversely reflects this trend. The compound (36) is the major product in reactions of the chloride (1) with the salts (14) and (15) (Table 1, expts 22 and 24), is formed in low yield with the salt (10) (Table 1, expt 15) and is undetectable when the salts (8) and (5) (Table 1, expts 6 and 11) are used. This reduction product (36) was formed in some of the reactions of the chloride (1) with very sterically hindered *aci*-nitronates.[20,32] A proposed sequence for this reduction process is outlined in Scheme 10.[24]



(37)

(36)

Scheme 10

Whenever the reduction product (36) was formed in significant quantities there was a corresponding increase in the amount of an extremely polar, intractable mixture of products. The highly-coloured, base-line (t.l.c.) products probably result from reduction of the nitro groups in the starting material (1) and/or products followed by various condensation processes.

This sharp discontinuity in behaviour, i.e. the change from *C*-alkylation to reduction and other processes may be electronic rather than steric in origin, since the carbanions (14a) and (15a) do not appear to differ significantly in steric demand from the anion (10a) and may even be smaller. The carbanions (14a) and (15a) have one and two simple ketone functions respectively, as anion-stabilizing substituents, however, and it may be that the presence of these groups facilitates the reduction process (Scheme 10) and/or decreases the ability of the carbanion to trap the sterically hindered intermediate benzylic radical (37). It should be noted that the carbanion (15a) does trap hindered radicals [see Section 1 (c)]. The differences in the rate of reaction of the salts (5), (8) and (10) also may be partly attributable to electronic effects but inspection of space-filling models indicates that the encumberance of the tertiary carbanions increases in the order (5a), (8a), (10a) while the reaction rate decreases in the same order. Not insignificantly, the times for reaction of (1) with (10) and with (15), wherein the major processes are *C*-alkylation and reduction respectively, are effectively identical (Table 1, expts 15 and 24).

When steric hindrance at the tertiary carbon in the nucleophiles was increased by varying the alkyl group, while at the same time the anion-stabilizing substituents were kept the same, the reaction rate decreased, the proportion of *C*-alkylation decreased and the amount of reduced product increased. For example the *p*-nitrobenzylic chloride (1) reacted rapidly

with the salt (5) from *ethyl*malononitrile (Table 1, expt 6) to give a quantitative yield of the *C*-alkylate (22) while the more hindered salt (6) from *isopropyl*malononitrile (Table 1, expt 9) reacted more slowly to give a lower yield of *C*-alkylate and some of the reduction product (36). The extremely hindered salt (7) from *t-butyl*malononitrile (Table 1, expt10) gave no *C*-alkylate in its reaction with (1). In similar fashion, the salt (8) reacted more rapidly with the chloride (1) (Table 1, expt 11) than did the more hindered analogue (9) (Table 1, expt 13) and gave more *C*-alkylation and less reduction product (36); the salt (11) (Table 1, expt 19) reacted much more slowly than did (10) (Table 1, expt 15) and gave less *C*-alkylate and more reduction product (36). The extremely hindered salts (12) and (13) (Table 1, expts 20 and 21) failed to give any *C*-alkylate.

The phosphonate salt (17) and quinuclidine (18) (Table 1, expts 30 and 31) gave no substitution products in contrast with their reactions with less hindered *p*-nitrobenzylic substrates.[33,34]

(b) Reactions of the α,*p*-Dinitro Compound (2)

The α,*p*-dinitro compound (2) was studied to see if the benzylic radical (38) derived from it was more sterically demanding than the isomeric radical (37).

(i) *Enumeration of Products*

The results of reactions of the α,*p*-dinitro compound (2) with the salts (4) - (6), (8), (10), (14) and (15)

are given in Table 2. The products comprised the azide (39), the *C*-alkylates (40 - 44), *p*-nitroacetophenone (45), the alcohol (46) and the reduced compound (47) in which the benzylic nitro group had been replaced by hydrogen. The structure and spectroscopic properties of these products are discussed below [Section 1 (d)].

(ii) *Mechanism of the Substitution Reactions*

The benzylic carbon in the α,*p*-dinitro compound (2) is tertiary and therefore (2) cannot react by an S_N2 mechanism. An S_N1 mechanism can be ruled out because the leaving group is nitrite, and the *p*-nitro group will destabilize the intermediate benzylic cation. These general comments, together with the clearly demonstrated $S_{RN}1$ substitution of less sterically hindered α,*p*-dinitrotoluenes[11, 23, 24] support the conclusion that (2) undergoes substitution by the $S_{RN}1$ mechanism. Nevertheless some confirmatory experiments were performed. For example, the α,*p*-dinitro compound (2) did not react with sodium azide (4) unless the reaction was entrained with the salt (19) (Table 2, expts 1 and 2), typical behaviour for substrates reacting by the $S_{RN}1$ process.[11,14] The reaction of the α,*p*-dinitro compound (2) with the salt (5), under nitrogen (Table 2, expt 3), gave a good yield of the *C*-alkylate (40), but when performed under oxygen (Table 2, expt 4) gave only a low yield of (40), some *p*-nitroacetophenone (45) and a significant amount of the alcohol (46). The latter two products may be rationalized as arising from oxygenation of the intermediate benzylic radical (38). The peroxide

Table 2. Reactions of the α,*p*-dinitro compound (2) with nucleophiles

Unless otherwise stated reactions were performed under the conditions specified in Table 1.

Experiment	Salt	Temperature[A]	Time (h)	Products:yield %
1[B,C]	(4)	20	5	(2):*90*
2[B,C,D]	(4)	20	3.3	(39):*81*, 75
3	(5)	60	2	(47):*3*; (2)*18*; (40):60
4[E,F]	(5)	60	2	(40):*6*; (45):8; (46):29
5[G]	(6)	60	72	(47):26; (41)18
6	(8)	60	7	(47):*10*; (42):13; (43):18
7	(10)	60	13	(47):*13*; (2)*9*; (44):19
8[F]	(14)	60	20	(47):*29*
9[F]	(15)	60	24	(47):*36*; (46):*5*

A Variation in temperature for 60° was ±3°, for 20° was ±1°.

B Reaction scale 1.0 mmol substrate, 4.0 mmol salt, 4.0 ml hexamethylphosphoramide.

Table 2 continued

C Saturated solution of sodium azide (approximately 0.25 M).

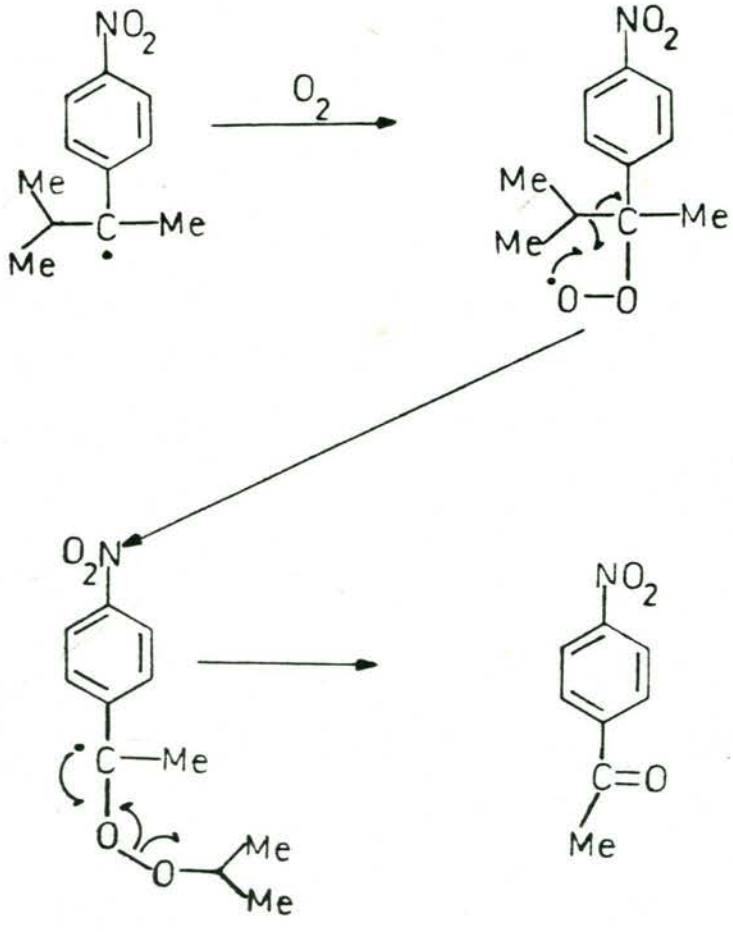
D Entrained with 0.1 mmol of lithium 2-nitropropan-2-ide.

E Under oxygen.

F Reaction scale 0.625 mmol substrate, 2.5 mmol salt, 2.5 ml hexamethylphosphoramide.

G Reaction scale 1.25 mmol substrate, 5 ml hexamethylphosphoramide.

undergoes an alkyl shift and the resulting intermediate can fragment to give *p*-nitroacetophenone (45) (Scheme 11).



Scheme 11

These experiments confirm that (2) does react with nucleophiles by an $S_{RN}1$ mechanism.

(iii) *Effect of Steric Hindrance on Reaction Rate and Product Yields*

These reactions follow the same general trends as those found for reactions of the chloride (1) (see Table 1). There is a decrease in the yield of *C*-alkylation products from 60 to 31 to 19% in the reactions of (2) with the salts (5), (8) and (10) (see Table 2, expts 3, 6 and 7) respectively. In the reaction of (2) with the salt (14) (Table 2, expt 8) no substitution products are formed. Only the reduction product (47) was isolated from the reactions of (2) with the salts (14) and (15) (Table 2, expts 8 and 9). The decreasing yield of *C*-alkylation products was accompanied by increasing yields of the reduced compound (47) and the accompanying polar intractable products. The compound (47) was formed to a greater extent in the reaction with the salts (14) and (15) but it was present in the reactions of (2) with the salts (5) and (8) (Table 2, expts 3 and 5), although only in low yield. A comparison of the reactions of the salts (5) and (6) with the α,*p*-dinitro compound (2) (Table 2, expts 3 and 5) shows a marked increase in reaction time for the more hindered salt (6), and an equally marked decrease in the yield of *C*-alkylate, again confirming the effect of increased steric hindrance.

Comparison of expts 3, 5, 6, 7, 8 in Table 2 with expts 6, 9, 11, 15, 22 in Table 1 shows that the α,*p*-dinitro compound (2) reacts with nucleophiles more slowly and gives lower yields of *C*-alkylates than the *p*-nitrobenzylic chloride

(1). Direct conclusions about the effect that differences in steric hindrance between (1) and (2) have on rate are not possible because the leaving groups in the two substrates are different. However, because both the substitution process and the reduction process compete for the appropriate benzylic radical, it is clear that conclusions may be drawn from product distributions. For example, the salt (5) reacts with the α,*p*-dinitro compound (2) to give some reduction product (47) and the *C*-alkylate (40) in moderate yield (Table 2, expt 3). This same salt, (5), reacts with the chloride (1) to give a quantitative yield of the *C*-alkylate (22) (Table 1, expt 6). Clearly the association step [Scheme 2, eqn (3)] is slower for the benzylic radical (38), allowing reduction to compete. Similar comparisons may be made for the other anions. The only difference between the two benzylic radicals (37) and (38) is the substitution pattern on the benzylic carbon, and, on the basis of the above results, it must be concluded that (38) is more hindered. In previous work the substrate (2) has also been found to give lower yields of *C*-alkylates than (1) in reaction with *aci*-nitronates.[19,20,24]

(c) Reactions of Other Substrates

Since the salt (15) gave only reduction products in its reaction with the substrates (1) and (2) it was treated with α,*p*-dinitrocumene (48) and *p*-nitrobenzyl chloride (49) to see if *C*-alkylates could be formed. The α-isopropyl

chloride (50) was treated with the salts (7) and (12) because (50) is less hindered than (1) and it was hoped these salts would give *C*-alkylates in the reaction with (50).

The results of these reactions are given in Table 3. The products comprised the *C*-alkylates (51) - (54), the reduced compounds (55) and (56), β,β-dimethyl-*p*-nitrostyrene (57), the ketone (58) and the alcohol (59). α,*p*-Dinitrocumene (48) and the α-isopropyl chloride (50) were assumed on the basis of the results obtained with the chloride (1) and the nitro compound (2) above [see Sections 1(a) and (b)] , and previous results[11,19,20,23] to react by $S_{RN}1$ processes. α,*p*-Dinitrocumene (48), on reaction with the salt (15), gave the *C*-alkylate (51) and the reduction product *p*-nitrocumene (55) (Table 3, expt 1).

The α-isopropyl chloride (50) reacted with the salt (7) to give the *C*-alkylate (54) and the reduced compound (56) (Table 3, expt 4). With the salt (12), however, the chloride (50) gave only the alcohol (59), the ketone (58) [at least partially arising from the salt (19)[19,20]] and the styrene (57) (Table 3, expt 5).

p-Nitrobenzyl chloride (49) reacted with the salt (15) to give the *C*-alkylates (52) and (53). The compound (53) was derived from (52) by an acyl cleavage.[35] These products were produced with equal facility under conditions which favoured operation of $S_{RN}1$ (Table 3, expt 2) or S_N2 (Table 3, expt 3) processes. It would appear that the $S_{RN}1$ reaction between (49) and (15) occurs too rapidly to be suppressed, and/or the

Table 3. Reactions of the substrates α,*p*-dinitrocumene (48), *p*-nitrobenzyl chloride (49) and *p*-(1-chloro-2-methylpropyl)nitrobenzene (50) with nucleophiles.

Reactions were performed on substrate (2.5 mmol) and the salt (5.0 mmol) in either hexamethylphosphoramide or dimethylformamide (10.0 ml). Other conditions are specified in Table 1 and Experimental.

Experiment	Substrate	Salt	Temperature[A] (°)	Time (h)	Products:yield %
1[B]	(48)	(15)	50	2	(55):2; (51):31
2[C,D]	(49)	(15)	5	1.5	(52):49; (53):23
3[C,E]	(49)	(15)	5	1.5	(52):53; (53):14
4[B,F]	(50)	(7)	55	4	(56):10; (54):52
5[B,G,H]	(50)	(12)	65	14	(57):5; (58):9; (59)14

A Temperature variation 50 - 65° was ±3°, 5° has ±1°.

B Solvent was hexamethylphosphoramide.

C Solvent was dimethylformamide.

Table 3 continued

D Reaction was performed under normal room light.

E Reaction in dark (see Experimental), in presence of 2.5 mmol of di-t-butylnitroxide.

F Salt (10.0 mmol).

G Substrate (1.25 mmol), 5.0 ml hexamethylphosphoramide.

H Entrained with 0.2 mmol lithium 2-nitropropan-2-ide (19).

chloride (49) undergoes rapid *C*-alkylation under both $S_{RN}1$ and S_N2 conditions or the chloride (49) reacts by a rapid S_N2 *C*-alkylation process under both sets of conditions. Since only *C*-alkylation occurred the reaction was not studied further.

(d) The Determination of Structure for the Products in Tables 1, 2 and 3

A number of the products which appear in Tables 1 - 3 are known compounds and these were identified by comparison with independently synthesized samples (see Experimental). The discussion below deals with new compounds synthesized in this work, with particular emphasis, where relevant, on their assignment as *C*- or *O*-alkylates.

The presence of the *p*-nitrophenyl group in all of the reaction products was confirmed by inspection of the aromatic region of their ^1H n.m.r. data. Either AA'XX' or broad complex four-spin systems which exhibited absorptions from two downfield protons near δ 8.1, *ortho* to the nitro group, were present. The *C*-alkylates[†] (22) - (30) and (54) exhibited dynamic exchange broadened spectra in the aromatic region for all field strengths from 60 - 400 MHz, for the protons *meta* to the nitro group. This is due to restricted rotation around the benzylic carbon-phenyl group bond (see Section 3). In the

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[†] Derivatives of five of these *C*-alkylates were synthesized and dynamic n.m.r. studies were carried out on them (see Section 3 below).

C-alkylates (40) - (44) derived from the α,*p*-dinitro compound (2) the protons *meta* to the nitro group appeared as part of a normal AA'XX' system at 90 MHz, but at 400 MHz (going to higher field is equivalent to lowering temperature) they were exchange broadened.

The presence of the aromatic nitro group was confirmed by the sharp absorptions at 1520 - 1495 cm^{-1} in the i.r. spectra of all products. All compounds derived from the *p*-nitrobenzylic chloride (1) had strong peaks at 57 ($C_4H_9^+$- from the t-butyl group) in their mass spectra. Similarly the *C*-alkylate (54) and products derived from the α,*p*-dinitro compound (2) had a peak at 43 ($C_3H_7^+$). The *C*-alkylates (40) - (44) were all stable to dilute acid, which should not be the case were they *N*- or *O*-alkylates.

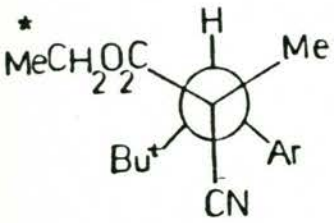
All compounds had the expected analytical and/or high resolution mass spectral parameters.

The azides (20) and (39) had strong absorptions at 2105 cm^{-1} in their i.r. spectra, characteristic of the azido group.[36] The chemical shift of the benzylic proton in (20) was δ 4.37 which was upfield from the benzylic resonance of the chloride (1) at δ 4.80 ppm. The azide (21) was not isolable (see Experimental), but the i.r. spectrum of the total reaction product showed a very weak absorption at 2105 cm^{-1}, and the ^1H n.m.r. spectrum of the reaction product had a weak resonance at δ 4.59. This absorption was attributed to the benzylic proton of the azide (21) and the maximum yield of *c.* 4% for (21) (see Table 1, expt 5) was calculated on this assumption.

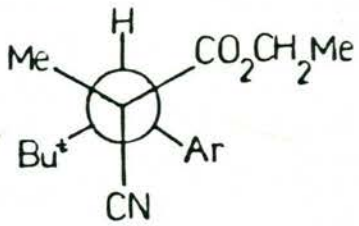
The structure of the *C*-alkylate (23) was readily determined from the ^{1}H n.m.r. chemical shift of the benzylic proton at δ 3.12, which confirmed that *C*-alkylation had taken place. The *C*-alkylate (23) had a weak absorption at 2250 cm^{-1} (C ≡ N) in its i.r. spectrum.

The reaction of the *p*-nitrobenzylic chloride (1) with the salt (8) (Table 1, expt 11) gave two diastereomeric *C*-alkylates (24) and (25) which both had weak absorptions at 2245 cm^{-1} (C ≡ N) and strong carbonyl absorptions at 1735 cm^{-1} in their i.r. spectra. Their relative stereochemistries were assigned by ^{1}H n.m.r. spectroscopy and conformational analysis, as follows. The Newman projections (60) and (61) show the diastereomers in their most populated conformations, in which the two smallest groups (the benzylic proton and the cyano group) are in an *anti*-periplanar configuration thus minimizing unfavourable steric interactions. The choice of the cyano group as the smallest group on the quaternary carbon is based on van der Waals radii.[37]

Further support for this preliminary assumption of most populated conformations was based on the absence of any significant ^{1}H n.m.r. long-range coupling between the benzylic proton and the methyl group β to the aromatic ring. Irradiation of the benzylic proton at δ 3.39 in the less polar diastereomer resulted in no detectable narrowing of the quaternary methyl resonance. The corresponding irradiation of the benzylic proton at δ 3.12 in the more polar diastereomer resulted in a reduction of the width-at-half-height ($W_{h/2}$) of the quaternary



(60)



(61)

methyl resonance of only 0.26 Hz. A larger reduction would have occurred were the proton and the methyl group in an *anti*-periplanar arrangement.[38] The ^{1}H n.m.r. spectra of the diastereomers (24) and (25) are shown in Figure 1 (a) and (b) respectively. The quaternary methyl groups in the less polar and more polar diastereomers resonate at δ 1.24 and 1.87 respectively. The less polar diastereomer was assigned the structure (60) wherein the methyl group is shielded by the aromatic ring. A quaternary methyl group in this environment, in the absence of specific shielding effects, would normally resonate near δ 1.5. The more polar diastereomer

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† This value was calculated from substituent addivity tables, ignoring the effect of the aromatic ring.[39,40]

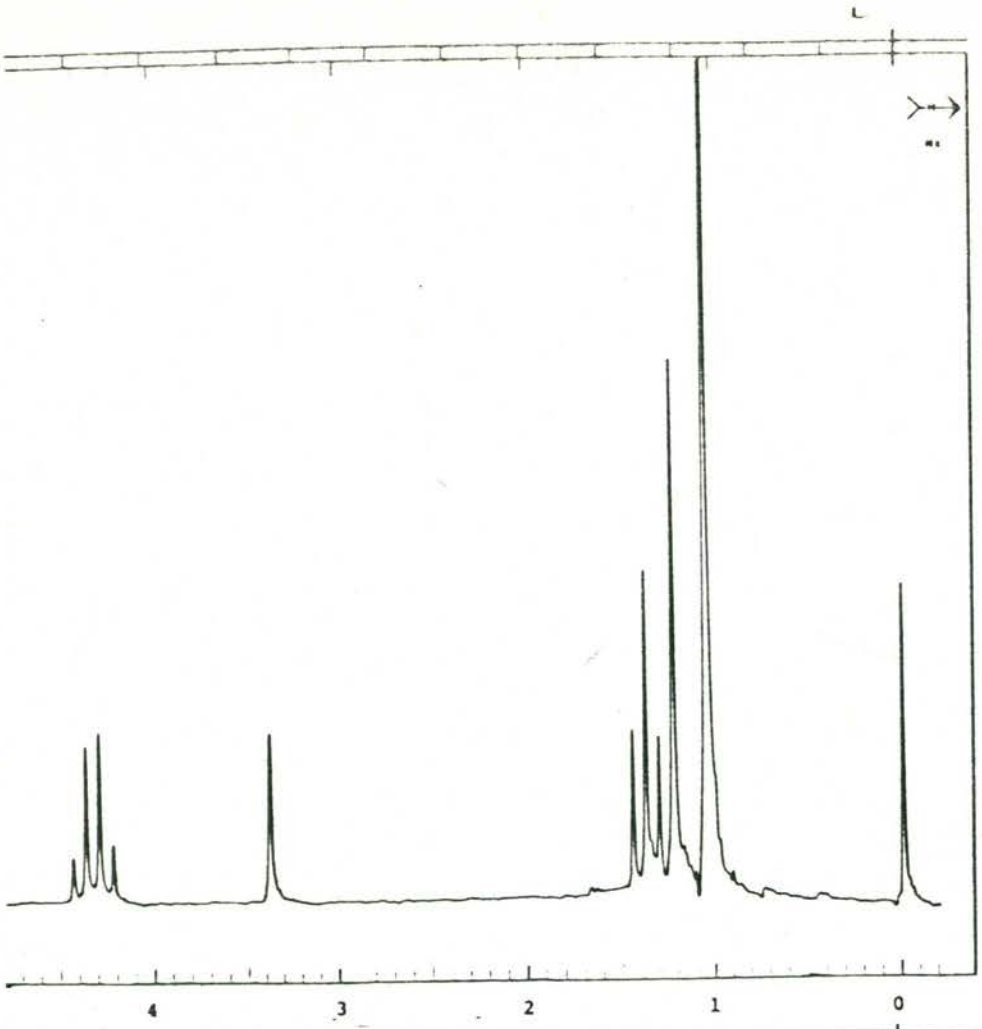

Fig. 1(a)

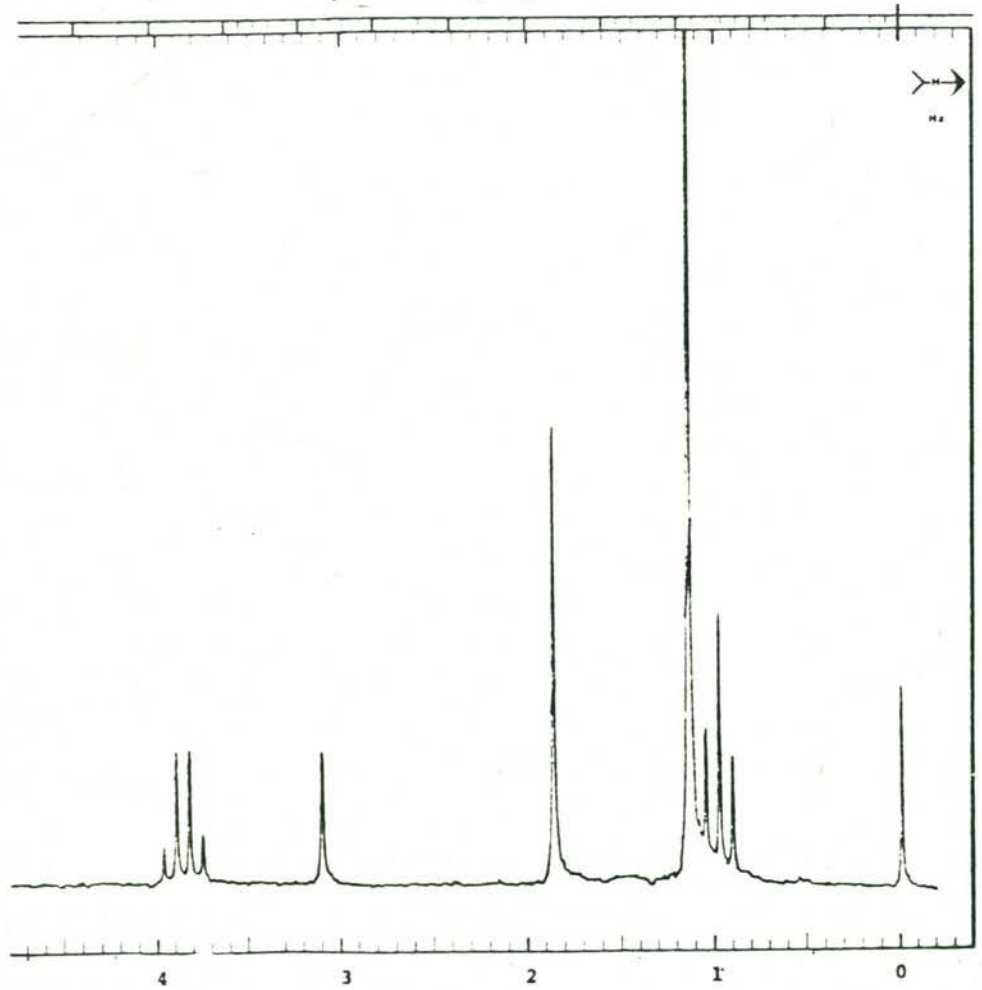

Fig. 1(b)

Fig. 1. The aliphatic 100 MHz ^{1}H n.m.r. spectra of the diastereomers (24) (top) and (25) (bottom). Scale in ppm.

was assigned the structure (61) since in this conformation the methyl group is away from the aromatic ring. Consequently the less polar isomer is the (2*RS*, 3*RS*) diastereomer (24) and the more polar isomer is the (2*RS*, 3*SR*) diastereomer (25). The methyl groups (triplets) [marked by asterisks in structures (60) and (61)] in the diastereomers (24) and (25) resonated at δ 1.46 and 0.99 respectively, further confirming the assignment of relative stereochemistry. The appropriate methyl group in (25) is shielded by the aromatic ring. A methyl group in this environment, in the absence of the aromatic ring, would resonate near δ 1.3.[39]

The more hindered salt (9) also reacted with the *p*-nitrobenzylic chloride (1) (Table 1, expt 13) to give two diastereomeric *C*-alkylates (26) and (27), whose benzylic protons had chemical shifts of δ 3.51 and 3.29 respectively. Both (26) and (27) had weak absorptions at 2240 cm^{-1} (C ≡ N) and strong carbonyl absorptions at 1735 cm^{-1} in their i.r. spectra. The relative stereochemistries of the diastereomers were assigned by ^{1}H n.m.r. spectroscopy. The Newman projections (62) and (63) show the most populated conformations of the two diastereomers. The isopropyl group doublets in the less polar diastereomer resonate at δ 0.73 and 1.04 whereas the isopropyl doublets in the more polar diastereomer resonate at δ 0.96 and 1.01. The less polar diastereomer was assigned the structure (62) wherein one of the methyl groups of the isopropyl group is shielded by the aromatic ring.[†] The more

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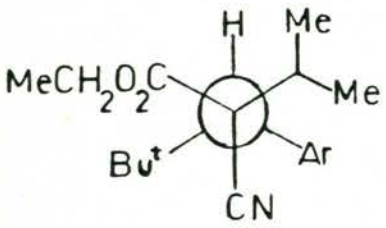
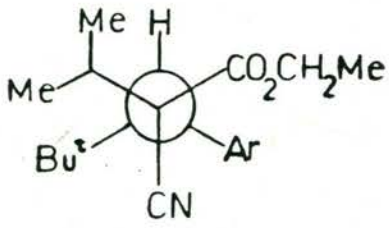
[†] This is particularly clear from consideration of a space-filling model of the conformation (62) of compound (26).



(62)



(63)

polar diastereomer was assigned the structure (63) since both the methyl groups in the isopropyl group in conformation (63) are well removed from the shielding region of the aromatic ring. Hence the less polar isomer is the (2*RS*, 3*RS*) diastereomer (26) and the more polar isomer is the (2*RS*, 3*SR*) diastereomer (27). The chemical shift of the methyl triplet of the ethoxy carbonyl group in (26) was δ 1.39 and in (27) this peak was at δ 1.33. The methylene signal of (26) appeared at δ 4.33 and in (27) the methylene signal appeared at δ 4.25. This similarity in chemical shifts indicated that in (27) the ethyl group of the ester is twisted away from the aromatic ring, unlike the ester group in conformation (61) of the *C*-alkylate (25). This change in conformation of

the ester function is not surprising since the quaternary methyl group in (61) has been replaced by the far more sterically demanding isopropyl group in (63).

The *C*-alkylate (29) had a strong carbonyl absorption at 1725 cm^{-1} in its i.r. spectrum and had a chemical shift of δ 3.67 for its benzylic proton. The 400 MHz ^1H n.m.r. spectrum is shown in Figure 2. There were three ABX_3 systems, corresponding to the three ethyl groups of the molecule. Irradiation of the upfield triplet at δ 0.67 resulted in simplification of the AB system centred at δ 1.5 (J_{AB} 14.0 Hz) confirming that this is the methyl triplet of the ethyl group α to the ester functions. The chemical shift of this methyl triplet shows that it is in the shielding zone of the ring. The two AB systems of the ester methylene protons overlapped and were not fully resolved at 400 MHz.

Reaction of the *p*-nitrobenzylic chloride (1) with the salt (14) (Table 1, expt 22) yielded two *O*-alkylates which could not be separated. The constitutions of these *O*-alkylates were assigned by ^1H n.m.r. spectroscopy as the (*Z*)- and (*E*)-isomers (31) and (32). The major isomer had a t-butyl peak at δ 0.988,† a methoxyl at δ 3.665 and a benzylic peak at

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† The chemical shifts for the protons in (31) and (32) are quoted to three decimal places as it is only in the third place that some of the chemical shifts differ. The third decimal place is only of relative significance since reproducibility of chemical shifts (as a result of temperature and concentration variation) was usually ± 0.01 ppm.

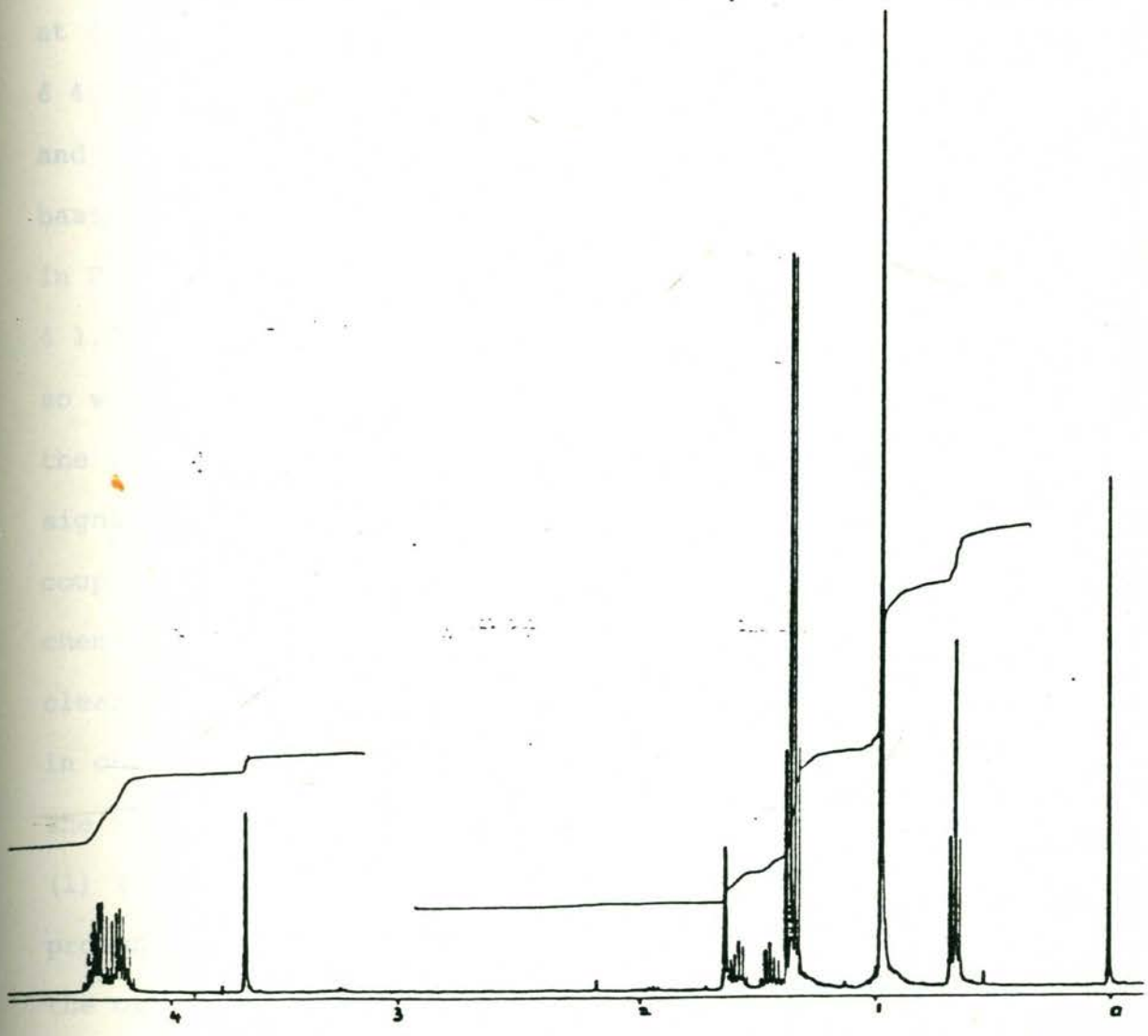
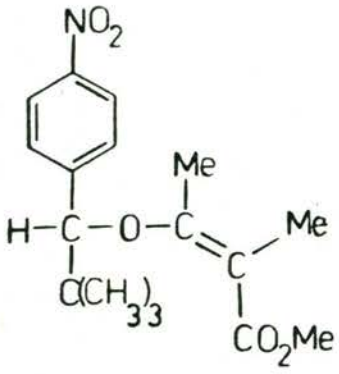


Fig. 2. Aliphatic region of the 400 MHz ^{1}H n.m.r. spectrum of (29) scale in ppm.

δ 4.918, the chemical shift of which clearly confirms the presence of a C-O bond. The minor isomer had a t-butyl peak at δ 0.992, a methoxyl at δ 3.662 and its benzylic peak at δ 4.929. The compounds could be assigned the structures (31) and (32) rather than the structures (64) and (65) on the basis of the methyl region of the ^{1}H n.m.r. spectrum, shown in Figure 3. The two methyl groups of the major isomer, δ 1.995 and 2.139, were coupled to one another *J* 1.5 Hz and so were those of the minor isomer at δ 2.014 and 2.160. If the *O*-alkylates had the structures (64) and (65), these methyl signals would have been singlets or have very small coupling constants. The assignment of the *relative* stereochemistries (31) and (32) to the major and minor isomers was clearly not possible on account of the negligible differences in chemical shifts. A *C*-alkylate (30) was also isolated from the reaction of the salt (14) with the *p*-nitrobenzylic chloride (1) (Table 1, expt 22), albeit in very low yield. The benzylic proton resonated at δ 4.09 in the ^{1}H n.m.r. spectrum and all the other aliphatic peaks were singlets. The M-15 peak (corresponding to methyl loss) gave a good mass match; the parent ion was too weak.

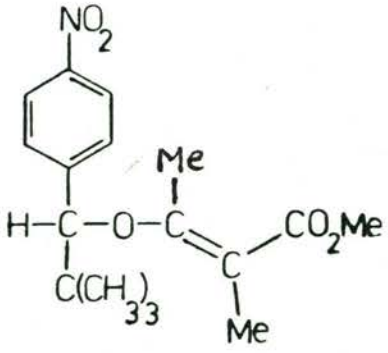
The *C*-alkylate (40) had a weak absorption at 2245 cm^{-1} (C ≡ N) in the i.r. spectrum. The ethyl group appears as an AXY_3 system in the ^{1}H n.m.r. spectrum (Figure 4). One proton (δ 1.07) of the methylene AX system is actually upfield of the triplet at δ 1.21 and the other methylene proton was partially masked by the benzylic methyl group at δ 1.63. The large difference in chemical shift for the methylene protons

Figure 3. The olefinic methyl group region in the 400 MHz ^{1}H n.m.r. spectrum for the *O*-alkylates (31) and (32). Scale is in ppm.



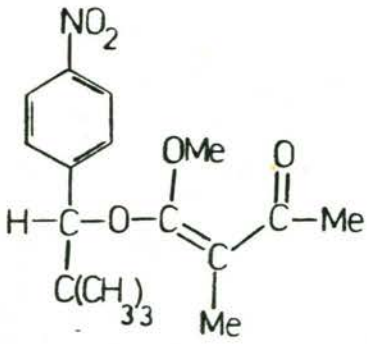
Z

(31)



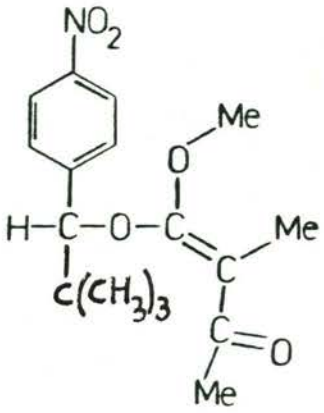
E

(32)



E

(64)



Z

(65)

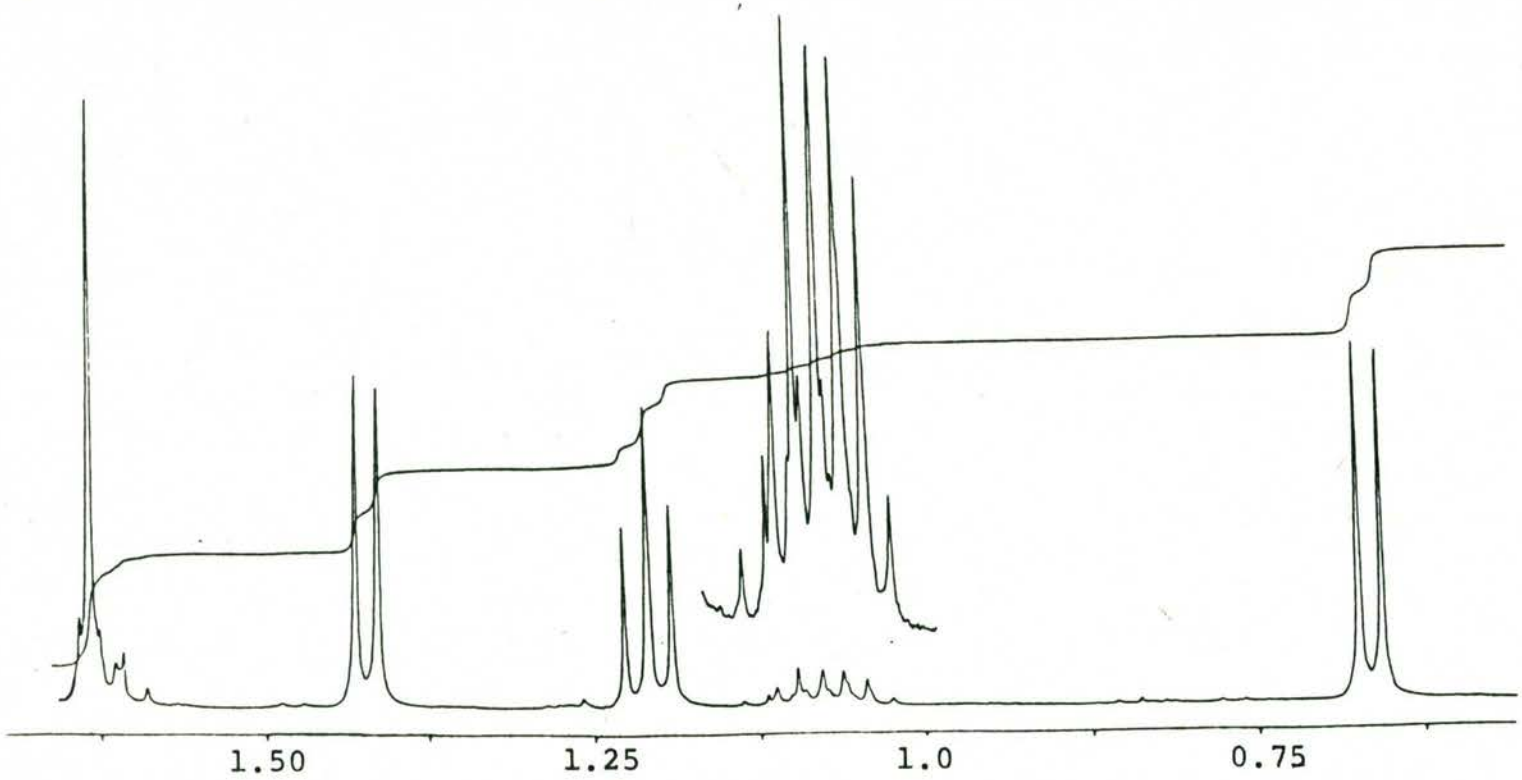
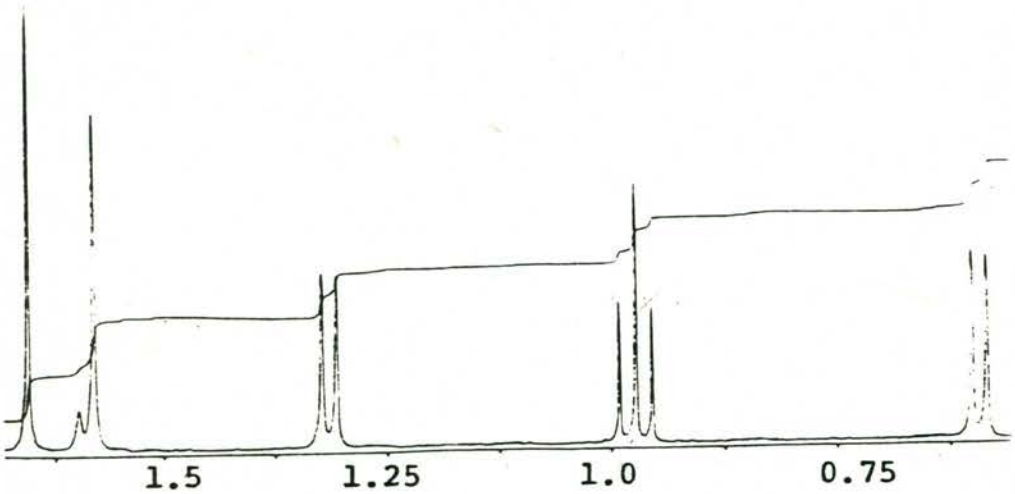


Figure 4. The upfield region of the 400 MHz ^{1}H n.m.r. spectrum of (40). The expanded multiplet is one second order wing of the AB system. The other wing is under the benzylic methyl. Scale is in ppm.

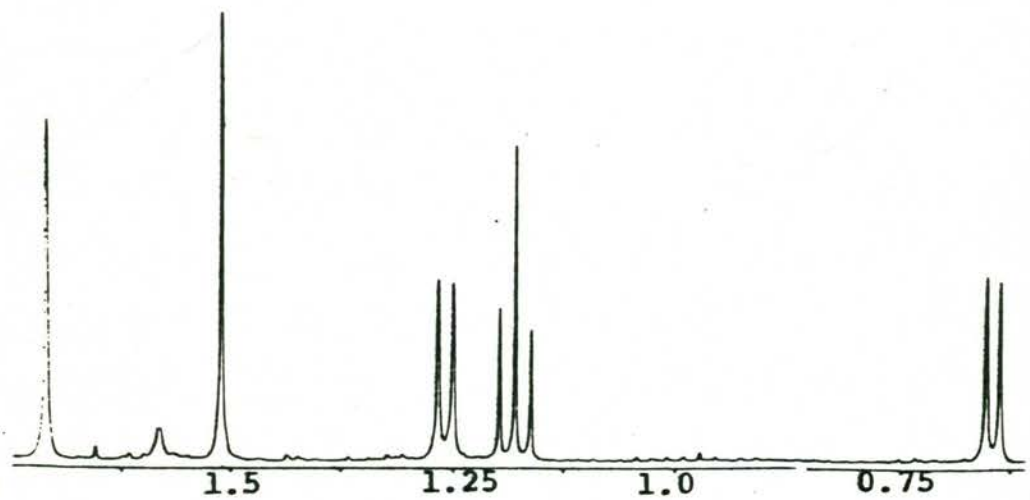
is caused by one methylene proton being strongly shielded by the aromatic ring. Also evident from Figure 4 is the large chemical shift difference between the isopropyl methyls, at δ 0.67 and 1.42. This was again due to the shielding effects of the aromatic ring; one methyl was shielded and the other deshielded. The benzylic methyl group resonated at δ 1.63.

The extremely crowded *C*-alkylate (41) had a weak absorption at 2250 cm^{-1} (C ≡ N), and displayed a large chemical shift difference for the methyl groups of the isopropyl group on the benzylic carbon; one appeared at δ 0.59 and the other at δ 1.40. The benzylic methyl appeared at δ 1.70, a typical value for all the *C*-alkylated (40) - (44).

The reaction of the α,*p*-dinitro compound (2) with the salt (8) (Table 2, expt 6) yielded two diastereomeric *C*-alkylates (42) and (43) which had weak C ≡ N absorptions at 2245 cm^{-1} and 2240 cm^{-1} respectively and strong carbonyl absorptions at 1735 cm^{-1} in their i.r. spectra. The relative stereochemistry of these diastereomers was assigned by ^{1}H n.m.r. spectroscopy, as follows. The most populated conformations were assigned in the usual way with the two smallest groups (the benzylic methyl and the cyano group) in an *anti*-periplanar arrangement as shown in the Newman projections (66) and (67). The upfield aliphatic ^{1}H n.m.r. spectra of the diastereomers appear in Figure 5. The quaternary methyl group in the less polar and more polar isomers resonated at δ 1.66 and 1.51 respectively. The more polar isomer was assigned structure (67) wherein this methyl group is shielded

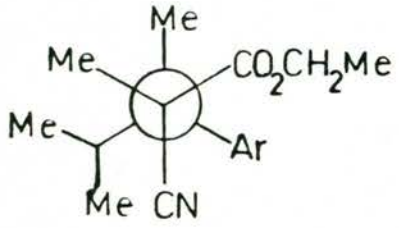


5(a)

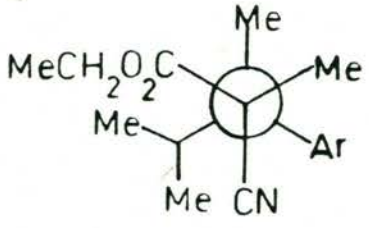


5(b)

Figure 5. The upfield aliphatic region of the 400 MHz ^{1}H n.m.r. spectra of (42) (top) and (43). Scale is in ppm.



(66)



(67)

by the aromatic ring. The less polar isomer was assigned structure (66). Consequently, the more polar isomer is the (2*RS*, 3*RS*) diastereomer (43) and the less polar isomer is the (2*RS*, 3*SR*) diastereomer (42). The chemical shifts of the methyl groups (triplets) in the ethoxy carbonyl groups of the diastereomers (42) and (43) were δ 0.97 and 1.18 respectively. The former methyl group is shielded in structure (66). The benzylic methyl groups were distinguished from the quaternary methyl groups by $W_{h/2}$ measurements. In (40) the benzylic methyl δ 1.58 is 0.5 Hz broader than the quaternary methyl. This broadening is due to the long-range (across 4 bonds) coupling of the benzylic methyl to the proton of the isopropyl group and the aromatic protons. The quaternary methyl protons are 5 bonds from the closest protons.

Whereas in the related compounds (24)-(27) the methylene protons of the ester groups appeared as deceptively

simple 'quartets' the methylene protons of the ester groups in (42), (43) appeared as fully resolved AB sections of ABX_3 systems, as shown in Figure 6.

The structure of the *C*-alkylate (42) was confirmed by the presence of two carbonyl peaks in its fully-decoupled ^{13}C n.m.r. spectrum at δ 171.0 and 170.7. The ^{1}H n.m.r. spectrum of this compound showed two ABX_3 systems resulting from the two ester groups in which the AB sections overlapped considerably. The isopropyl group methyls showed the expected large chemical shift difference, one resonating at δ 0.57 and the other at δ 1.10. The benzylic methyl appeared at δ 1.67 and had a $W_{h/2}$ 0.3 Hz larger than that of the quaternary methyl at 1.47. Irradiation of the isopropyl proton produces a 0.2 Hz narrowing of $W_{h/2}$ in the benzylic methyl and no change in the quaternary methyl.

The *C*-alkylate (51) had three sharp methyl signals in the ^{1}H n.m.r. spectrum at δ 1.50, 1.63, 1.93 in the ratio 3:6:6, which corresponded to the expected pattern of the *C*-alkylate. The *C*-alkylate (52) was readily identified by the chemical shift of the benzylic protons at δ 3.27.

The *C*-alkylate (53) had a benzylic doublet at δ 3.21 in the ^{1}H n.m.r. spectrum which confirmed that *C*-alkylation had taken place.

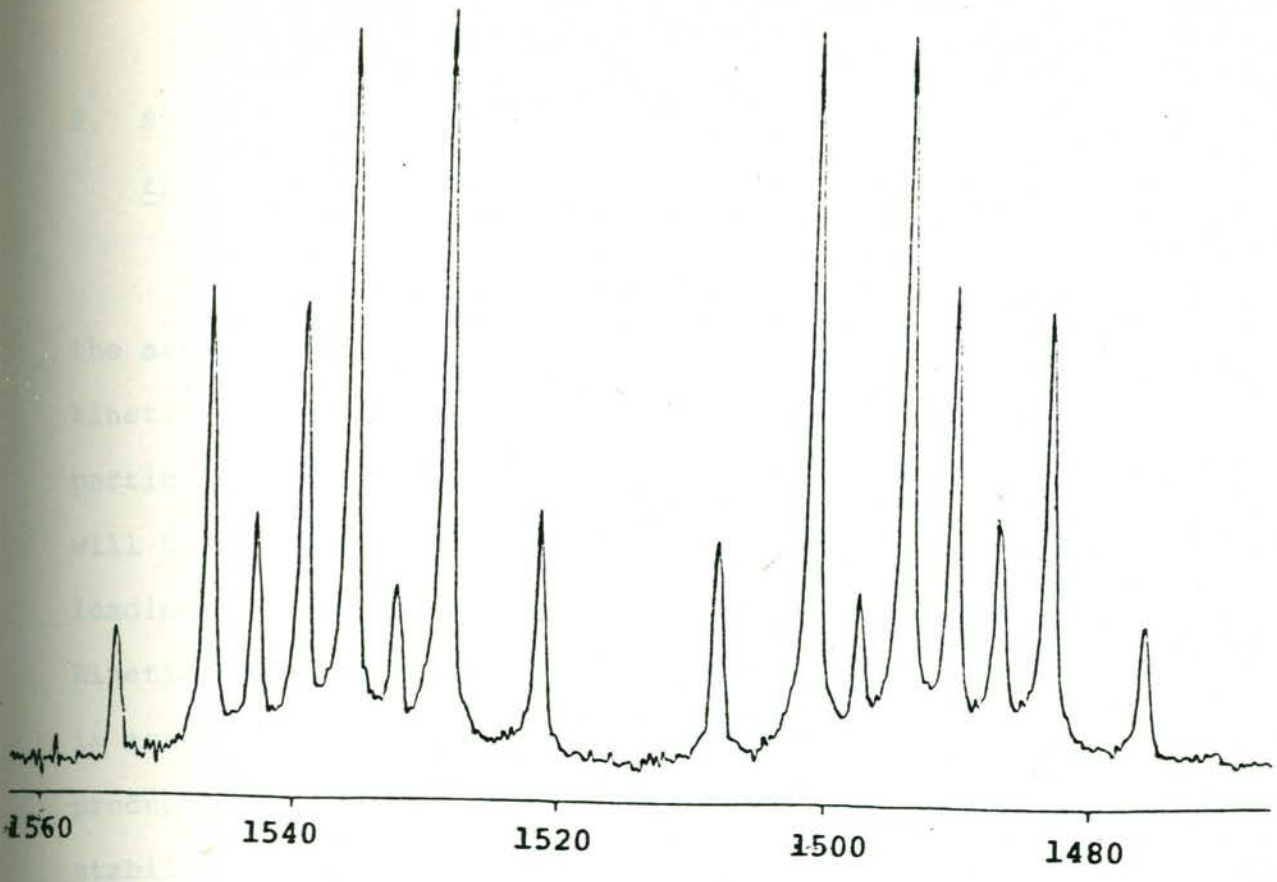


Figure 6(a). The 400 MHz ^{1}H n.m.r. spectrum of the methylene protons of (42). Scale in Hz ex TMS.

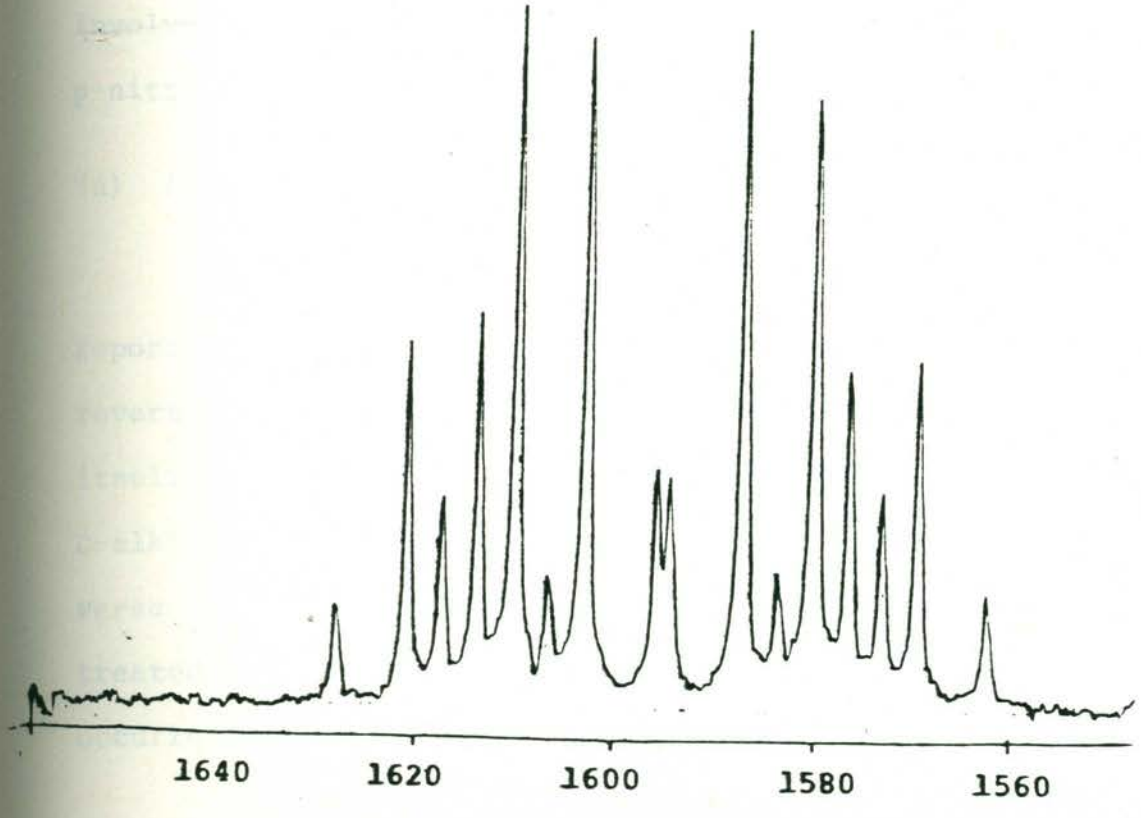


Figure 6(b). The 400 MHz ^{1}H n.m.r. spectrum of the methylene protons of (43). Scale in Hz ex TMS.

2. Studies on the Reversibility of the Association Step in the $S_{RN}1$ Reaction, and some Competitive Studies

The products formed in $S_{RN}1$ reactions may result from the association step [Scheme 2, eqn (3)] taking place under kinetic or thermodynamic control. If the products in a particular $S_{RN}1$ reaction are thermodynamically controlled it will have an association step that is readily reversible, leading in time to the most thermodynamically stable product. Kinetic control, however, requires an association step that is essentially irreversible; that is, the most quickly formed product predominates regardless of its relative thermodynamic stability. In order to investigate the reversibility of the association step, two systems were studied. The first involved an investigation of exchange between *C*-alkylates derived from the *p*-nitrocumyl system and *aci*-nitronates; the second involved exchange between *O*- and *C*-alkylates in the simple *p*-nitrobenzylic system.

(a) *Exchange Reactions Between* C-*Alkylates and* aci-*Nitronates*

The *C*-alkylates (68) and (69) had previously been reported by Kornblum.[11,41] A simple method of studying the reversibility of the association step consequently presented itself. Would the *C*-alkylate (68) be converted to the *C*-alkylate (69) when treated with the anion (71a), and *vice versa* would the *C*-alkylate (69) be converted to (68) when treated with the anion (19a)? If such transformations occurred then they might indicate that the radical anions

$(68)^{-\cdot}$ and $(69)^{-\cdot}$ dissociate to the *p*-nitrocumyl radical (70) and the corresponding *aci*-nitronate ions (19a) and (71a). The original preparation of the *C*-alkylates (68) and (69) had been performed with α,*p*-dinitrocumene (48) and the salts lithium 2-nitropropan-2-ide (19) and lithium 2-nitrobutan-2-ide (71).[41,42] These reactions were carried out in hexamethylphosphoramide at 25 °C, with irradiation and were complete in 2 and 6 hours respectively. In this work the tetrabutylammonium salts (72) and (73) were employed because they are much more reactive than lithium salts.[43] For example the S_RN1 reaction in eqn (15) is complete in less than 5 minutes whereas the lithium salt (19) in dimethyl sulfoxide reacts over thirty times more slowly. Another example

$$ArNO_2 + \overset{+}{N}Bu_4\overset{-}{C}Me_2NO_2 \xrightarrow[C_6H_6]{} ArCMe_2NO_2 + \overset{+}{N}Bu_4\overset{-}{N}O_2 \qquad (15)$$

of this enhanced reactivity is found in the S_RN1 reaction of *p*-(1-methyl-1-nitropropyl)nitrobenzene with the salt (72),[23] The reaction was complete in 30 minutes (in Me_2SO), but with the lithium salt (19) (in the more effective solvent $(Me_2N)_3PO$) the reaction took 3 hours to reach completion.

Under the conditions outlined in Table 4 the *C*-alkylate (68) was formed in less than 3 minutes in 79% yield, and the *C*-alkylate (69) was formed in 4 minutes in 73% yield (Table 4, expts 1 and 2 respectively).

The *C*-alkylate (68) was treated with the tetrabutylammonium salt (73) and, after 210 minutes, gave *p*-nitrocumene (55) and starting material (68) (Table 4, expt 3). The recip-

Table 4. Reactions of α,*p*-dinitrocumene (48) and the *C*-alkylates (68), (69) with *aci*-nitronates

All reactions performed on substrate (1.0 mmol) with salt (2.0 mmol) in hexamethylphosphoramide (6.0 ml) at 60° under nitrogen. Irradiated by a 500-W GE lamp 20 cm from the reaction flask. All yields are isolated yields.

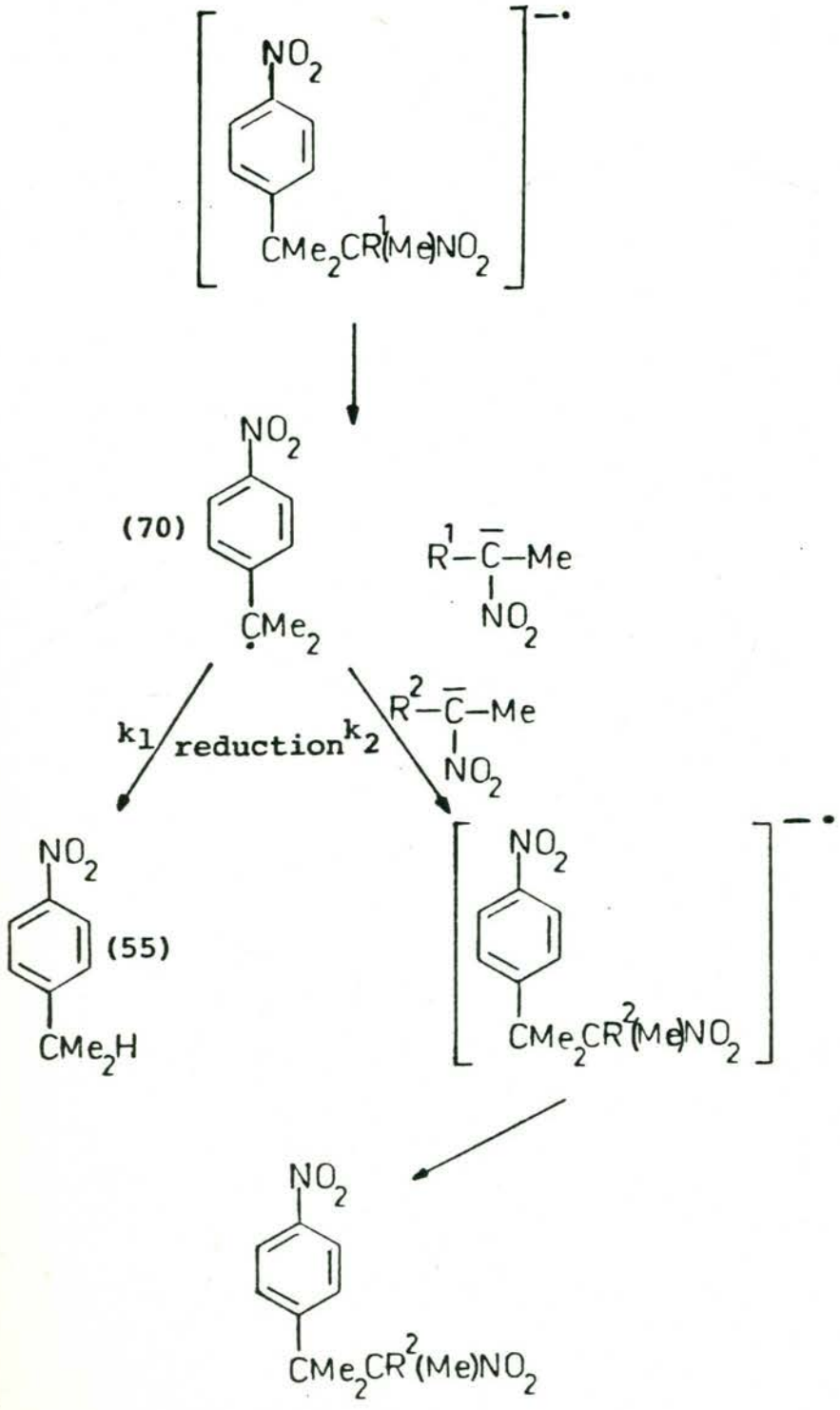
Experiment	Substrate	Salt	Time (min)	Product:yield %
1	(48)	(72)	3	(68):79
2	(48)	(73)	4	(69):73
3	(68)	(73)	210	(55):13; (68):81
4	(69)	(72)	210	(55):18; (69):51; (68):3
5	(69)	(19)	210	(69):95

rocal reaction, in which the *C*-alkylate (69) was treated with the tetrabutylammonium salt (72), also proceeded slowly to give *p*-nitrocumene (55), the starting material (69) and the other *C*-alkylate (68) after 210 minutes (Table 4, expt 4). The reaction of the *C*-alkylate (69) with the lithium salt (19) (Table 4, expt 5) gave nothing but starting material, demonstrating not only that the dissociation of such a *C*-alkylate is extremely slow, but also the greater reactivity of the tetrabutylammonium salts.

These results appear to show that, under extreme conditions and protracted reaction times, it is possible to reverse the association step in the $S_{RN}1$ reaction of *aci*-nitronates with *p*-nitrocumyl radicals. However, since 210 minutes is at least 200 times the half-lives for the normal *C*-alkylation reactions (Table 4, expts 1 and 2), it is clear that dissociation of *C*-alkylates occurs at a rate which is negligible relative to association and hence the association step is effectively irreversible. Since it has also been shown in the reaction given in Scheme 4[23] that *O*-alkylation processes are usually irreversible it can be concluded that the association step is kinetically controlled in reactions involving *aci*-nitronates.

The formation of the *p*-nitrocumene (55) in both exchange reactions (Table 4, expts 3 and 4), and the formation of the crossed product (68) in expt 4, may be explained by the dissociation of the *C*-alkylate radical anion to the *p*-nitrocumyl radical (70) and the appropriate *aci*-nitronate. The radical

(70) may be reduced to the anion, which gives rise to *p*-nitrocumene (55), or recombine with the "opposite" anion to give the crossed product. This sort of process is outlined in Scheme 12.

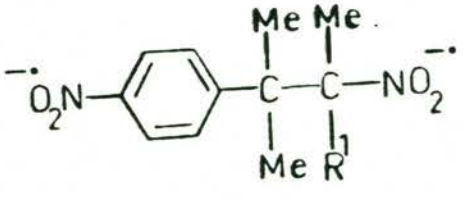


Scheme 12

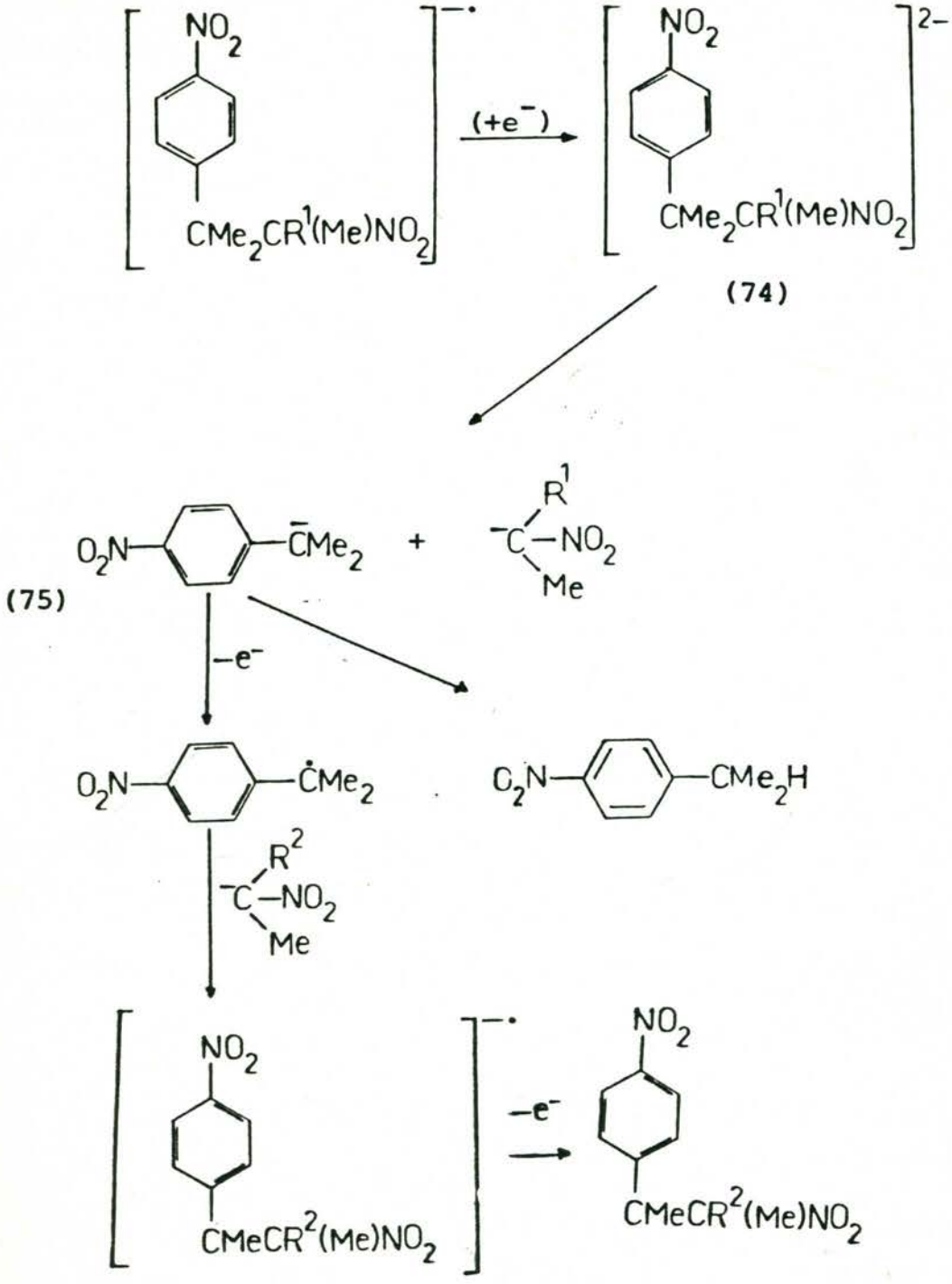
However, the reduction product is found in both reactions but only becomes apparent by t.l.c. (approximately 1% or greater) after about 20 minutes. *C*-alkylation is very fast relative to this, which indicates that the combination of the anion with the *p*-nitrocumyl radical (70) is fast. Since exchange is negligible in both reactions it would appear that the *p*-nitrocumyl radical (70) is not formed in significant amounts, as it would be expected that *C*-alkylation would compete more effectively for the radical (70) (Scheme 12, $k_2 > k_1$). If $k_2 < k_1$ reduction would be apparent earlier.

An alternative mechanism is shown in Scheme 13 and involves the conversion of the radical ion of the *C*-alkylate into the corresponding dianion. The dianion† (74) can dissociate to the *aci*-nitronate anion and the benzylic anion (75).

†This species may be alternatively described as the triplet (76).



(76)


NO2
CMe2CR1(Me)NO2
(+e−)
2−
(74)
(75)
O2N
CMe2
R1
C
NO2
Me
−e−
CMe2H
R2
CMeCR2(Me)NO2

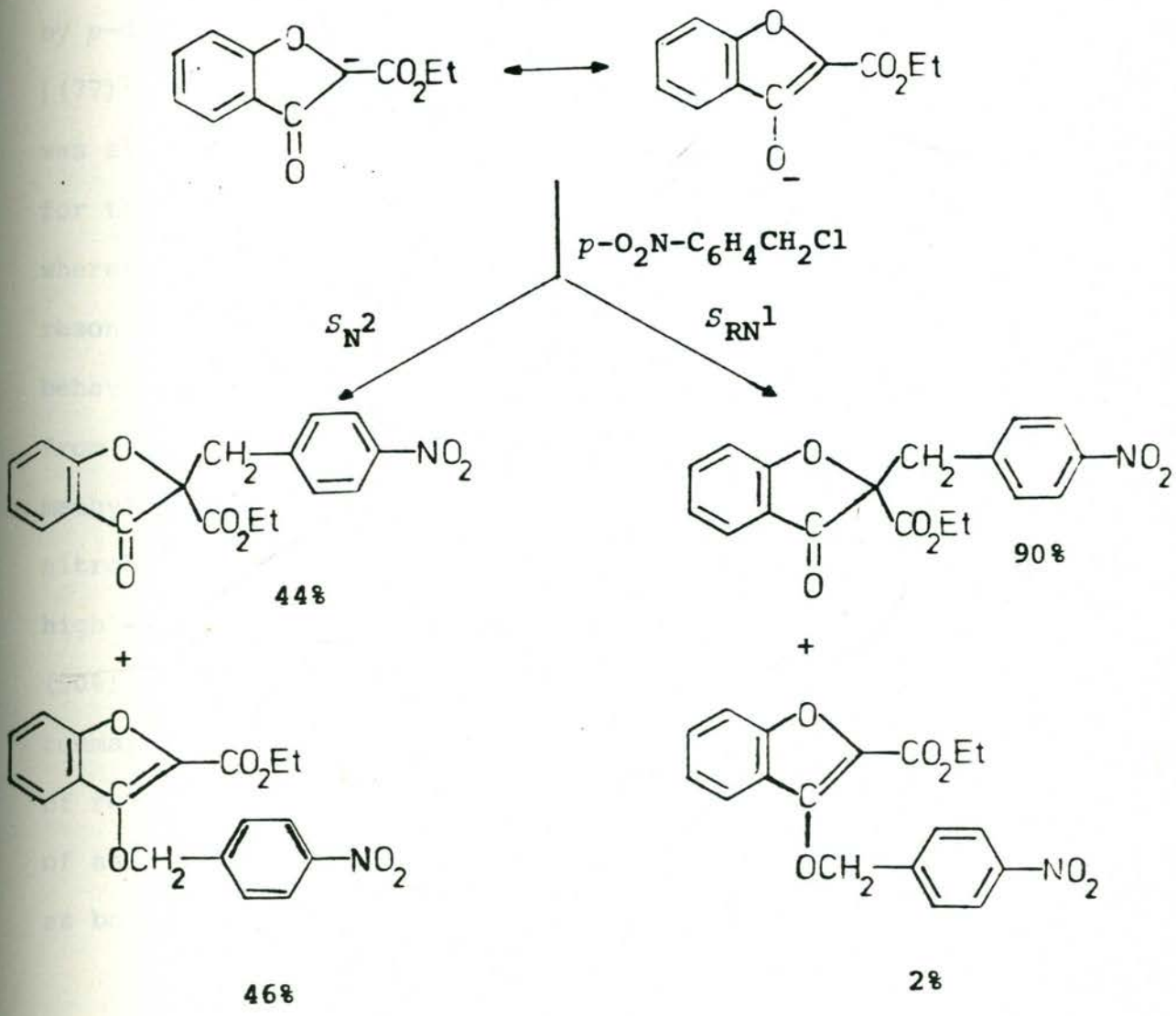
Scheme 13

The benzylic anion (75) may be protonated (the method of preparation of the tetrabutylammonium salts inevitably leaves water in the reaction solution) to give *p*-nitrocumene (55), or it may lose an electron (e.g. by transfer to a neutral molecule of substrate) to give the *p*-nitrocumyl radical (70) which then reacts to give the crossed *C*-alkylate.

Some of the products of the reaction shown in Scheme 5 involving the powerful reductant methanethiolate could also be rationalized by a similar process, involving dianions. Hence it may well be that the radical ions of *C*-alkylates in *p*-nitrobenzylic substrates do not dissociate at an appreciable rate even under the extreme reaction conditions employed here, and that an alternative pathway involving dianions is operating. However, it is clear that in related compounds which have electron-withdrawing substituents other than a *p*-nitro group (e.g. *p*-cyano-, 3,5-bis(trifluoromethyl)) fragmentations proceeding by way of radical ions do occur.[44]

(b) C- *and* O-*Alkylates Derived from a* β-*Ketoester*

The anions from β-ketoesters are potentially ambident and, indeed, in the $S_{RN}1$ reactions of the chloride (1) with nucleophiles the only *O*-alkylates isolated were derived from the anion (14a) (Table 1, expt 22). The coumaranone system shown in Scheme 14 has also been studied.[9] This work was in fact one of the earliest papers published that confirmed a radical anion mechanism for the reaction of *p*-nitrobenzylic systems with certain nucleophiles under conditions which favour radical processes. No further details or extensions



Scheme 14

of this particular system have been reported. Under $S_{RN}1$ conditions the main product was reported to be the *C*-alkylate (77) (90%), with very small amounts of the *O*-alkylate (78) (2%). Under S_N2 conditions (the $S_{RN}1$ process was inhibited by *p*-dinitrobenzene) the products were more evenly distributed [(77):(78) = 44:46 %] but the fact that the *C*-alkylate (77) was still formed in significant amounts is worthy of note for the *O*-alkylate (78) is a fully aromatic benzofuran system whereas the *C*-alkylate (77) lacks not only some of the aromatic resonance stabilization but is also quite hindered. The behaviour of the β-ketoester anion (83a) is quite different from that found with the anion (85a) derived from ethyl 2-methylacetoacetate. The reaction of the salt (85) with *p*-nitrobenzyl chloride (49) gave only the *C*-alkylate (86) in high yield under conditions which would favour either $S_{RN}1$ (90%) or S_N2 (86%) processes[†] (see Experimental). The coumaranone system should provide a probe for the investigation of reversibility (particularly with regard to regiochemistry of association) in the association step of the $S_{RN}1$ reaction, as both *C*- and *O*-alkylates are stable, isolable compounds.

Both the ethyl ester (81) and the methyl ester (82) were synthesized and their sodium salts (83) and (84) were treated with *p*-nitrobenzyl chloride (49) in dimethylformamide (Table 5, expts 1 - 4), under both $S_{RN}1$ and S_N2 conditions. The very high yields (> 90%) of the original work could not

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[†] Both reactions were performed in dimethyl formamide at 5°. Di-t-butyl nitroxide was used to suppress the $S_{RN}1$ process.

be duplicated [the yields (64 - 80%) in Table 5 are isolated yields] but the overall import with regard to occurrence of $S_{RN}1$ and S_N2 processes of the results was the same. The reaction products were readily identified by ^1H n.m.r. and were all fully characterised.

The *O*-alkylate (78) was treated with the sodium salt (84) under $S_{RN}1$ reaction conditions (Table 5, expt 5). The *O*-alkylate (78) did not rearrange to either *C*-alkylate (77) or (79) after 24 hours and only the *O*-alkylate was recovered. In no case did t.l.c. of the reaction mixture (the *O*-alkylates are much less polar than the *C*-alkylates) reveal a component corresponding to the *C*-alkylates. Similarly ^1H n.m.r. revealed no triplet at δ 1.22 for (77) (the *O*-alkylate's triplet appears at δ 1.43) or any AB system near δ 3.60 for (77) or (79) at amplitudes which would detect these products at 1% of the product mixture. When the same *O*-alkylate (78) was treated with the salt (84), but in the presence of *p*-nitrobenzyl chloride (49), the only products were the methyl *C*-alkylate (79) and the *O*-alkylate (78) (Tables 5, expt 5). This latter experiment demonstrates that the *O*-alkylate (78) does not rearrange in conditions under which an $S_{RN}1$ process is demonstrably taking place. The formation of the *C*-alkylate (79) in 61% yield clearly shows that an $S_{RN}1$ reaction is occurring under the latter reaction conditions. The possibility of "losing" trace amounts of the *C*-alkylate (77) in workup is minimal as this *C*-alkylate is much more soluble than the *C*-alkylate (79).

Table 5. Reactions of the sodium salts (83) and (84) derived from coumaranone esters

Reactions performed on substrate (1.00 mmol), salt (1.4 mmol) in dimethylformamide (10.0 ml) at 30° under nitrogen. Irradiation performed with a 250-W GE lamp at 10 cm from the reaction vessel. Yields are isolated yields.

Experiment	Substrate	Salt	Time (h)	Products:yield %
1	(49)	(83)	4.5	(78): < 2; (77):77
2[A]	(49)	(83)	48	(78):33 ; (77):36
3	(49)	(84)	4	(80): < 2; (79):74
4[A]	(49)	(84)	48	(80):30 ; (79):34
5	(78)	(84)	24	(78):80
6	(78), (49)[B]	(84)	24	(78):80 ; (79):61

[A] In dark (see Experimental), in presence of 2.0 mmol *p*-dinitrobenzene.

[B] 1 mmol of each substrate.

These last two experiments demonstrate that the regiochemistry of association is not readily reversible in this system.

(c) *Competitive Studies*

The results of reactions of the *p*-nitrobenzylic chloride (1) with nucleophiles (Table 1) indicated that some nucleophiles trapped the benzylic radical (37) more quickly and more efficiently than others. However, direct comparisons of the reactivity of nucleophiles with the benzylic radical (37) are best made from the results of competitive reactions. The $S_{RN}1$ reaction of aryl halides with various nucleophiles has been studied by such methods[29] and the reactions yielded mixtures of products. These results were interpreted as evidence that the association step in this system was relatively independent of the nucleophile. In similar fashion competition studies involving the reaction of the system shown in Scheme 15 and similar systems showed a marked dependence of product ratios depending on the leaving group X.[45] This may be interpreted as evidence for an $S_{RN}2$ mechanism[45,46] which implies that the anion is implicated in the dissociation step [Scheme 2, eqn (2)] in this reaction. It was thought that competitive reactions involving the chloride (1) would be a direct measure of the sensitivity of the association step [Scheme 2, eqn (3)] of the $S_{RN}1$ reaction to the steric size of the anion. Some reactions of this type were performed and the results of these reactions are shown in Table 6.

Table 6. Competitive reactions of the *p*-nitrobenzylic chloride (1) with nucleophiles at 60°

Reactions were performed as in Table 1. Yields in italics are estimated.

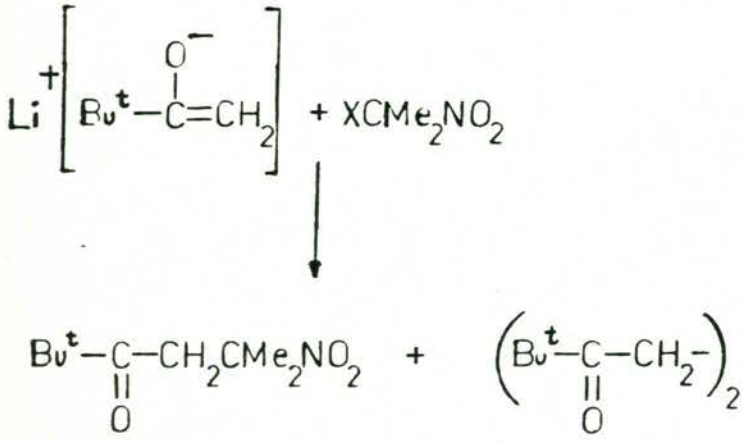
Experiment	Salts	Time (h)	Products: yield
1[A]	(4), (5)	3	(20):*55*
2[A]	(5), (10)	3[B]	(22):*100*
3	(10), (11)[C]	4.5	(36):*5*; (29):17; (28):36; (35):*8*

[A] Reaction scale 0.625 mmol substrate, 1.25 mmol each salt.

[B] Reaction complete by t.l.c. in 0.7 h.

[C] 5.0 mmol of each salt employed.

The reaction of the chloride (1) with an equimolar solution of the salts (4) and (5) yielded only the azide (20) (by ^{1}H n.m.r.) (Table 6, expt 1) after 3 hours. The formation of the azide (20) might be expected to be reversible, since azide has been shown to be an effective nucleofuge in $S_{RN}1$ reactions,[11,26] but even so it is the only product. The dinitrile (22) does not react with sodium azide (4) to give the azide (20), even when entrained with the salt† (19) (see Experimental). This result rules out the possibility of formation of the dinitrile (22) followed by rapid dissociation and eventual formation of the azide (20) as a more thermodynamically stable product. The low yield of the azide (20) can be attributed to its decomposition under the vigorous reaction conditions (even when refrigerated in the dark the azide (20) decomposed on standing; the process was accelerated at higher temperatures).



Scheme 15

† This result is evidence that this association step is also irreversible.

The reaction of (1) with an equimolar solution of the salts (5) and (10) afforded only the dinitrile (22) (Table 6, expt 2) in quantitative yield.

The reaction of the chloride (1) with an equimolar solution of the salts (10) and (11) gave both *C*-alkylates, but the *C*-alkylate (28) derived from the smaller anion (10) predominated (Table 6, expt 3).

It is clear from the above results that in every reaction the least encumbered anion gave the predominant product.

In two of the reactions (Table 6, expts 1 and 2) the smaller anion reacts with the radical (37) exclusively; in both these reactions there is a large difference in the steric hindrance of the competing anions. In one reaction, however, relatively small differences in steric bulk led to marked selectivity by the radical (37) (Table 6, expt 3). This last reaction shows that the association step [Scheme 2, eqn (3)] of the $S_{RN}1$ reaction in *p*-nitrobenzylic systems is indeed sensitive to steric hindrance.

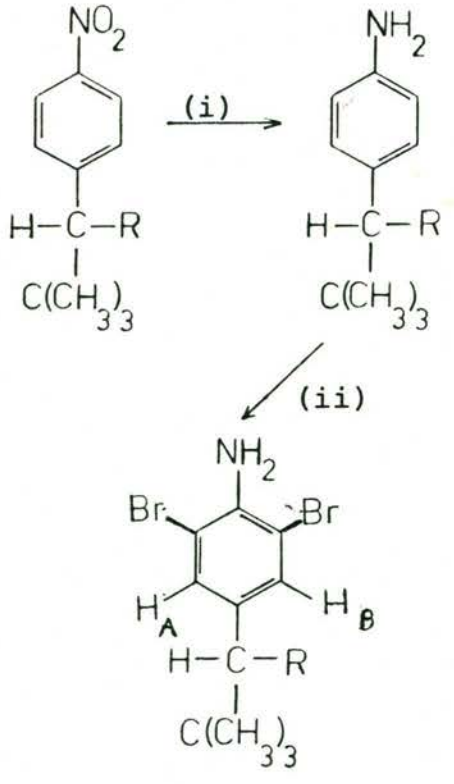
3. Dynamic N.M.R. Properties of $S_{RN}1$ Products and their Derivatives

Dynamic nuclear magnetic resonance spectroscopy concerns the n.m.r. behaviour of any nucleus, or group of nuclei, which is exchanging between two or more magnetically distinct environments at a rate detectable by the spectrometer. The range of processes for which kinetic data can be obtained by this technique typically have free energies of activation ($\Delta G^{\ddagger}$) which lie between 40 and 120 kJ mol^{-1}.[47]

The *C*-alkylates (22-30) derived from the chloride (1) and those (40-44) derived from the dinitro compound (2) all displayed dynamic n.m.r. (d.n.m.r.) effects in the aromatic region of their ^{1}H n.m.r. spectra, caused by restricted rotation around the aryl carbon-benzylic carbon, sp^2-sp^3, bond. It was hoped that on determination of the energy parameters for the rotation about the sp^2-sp^3 bond in these systems a correlation could be found between the size of the substituents on the benzylic carbon (as reflected in the energy parameters) and the yield and reaction time in the $S_{RN}1$ processes in which these products are formed.

In this work derivatives of the sulfone (33), the dinitriles (22) and (23), the two diastereomeric cyano esters (24) and (25) and the diester (28) were studied. The sulfone (33) had been studied previously.[20,32] It was decided to simplify the experimental spectra and subsequent computations (see below) by reduction of the number of spins in the exchanging system from four to two. This transformation was readily achieved by conversion

of the nitro group to an amine function followed by bromination of the positions *ortho* to the amino group, as shown in Scheme 16 and gave the expected products (87)-(92) whose constitutions were confirmed by their analytical and spectral parameters.

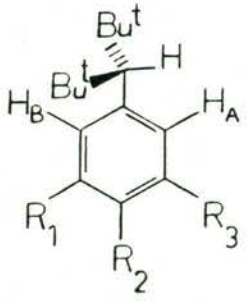


(i) H_2/Pd (ii) $Br_2/CH_3CO_2H/CCl_4$

Scheme 16

At slow exchange the resonance pattern of the two aromatic protons [H_A and H_B in Scheme (16)] appears as a simple AB system, i.e. the signals for each of H_A and H_B appear as 'doublets', broadened slightly by benzylic coupling (see below). This pattern collapses to a singlet as the rate of rotation

increases. The assignment of H_A and H_B in the ^1H n.m.r. spectra was performed by analogy with the systems studied by Landman,[48] which had the general form (93). Landman



(93)

found that for the aromatic proton *cis* to the benzylic proton (H_A) the benzylic coupling constant lay in the range 0.33-0.53 Hz. The proton *trans* to the benzylic proton had a coupling constant in the range 0.0-0.35 Hz. In the compounds in this study the benzylic couplings could not be resolved. The width-at-half-height ($W_{h/2}$) for each of H_A and H_B could be measured. The ^1H n.m.r. spectra of the aromatic region of the dinitrile (89) and the cyano ester (90) are shown in Fig. 7. The differences in $W_{h/2}$ for the aromatic peaks of the five compounds (87)-(91) are listed in Table 7. The $W_{h/2}$ values for each

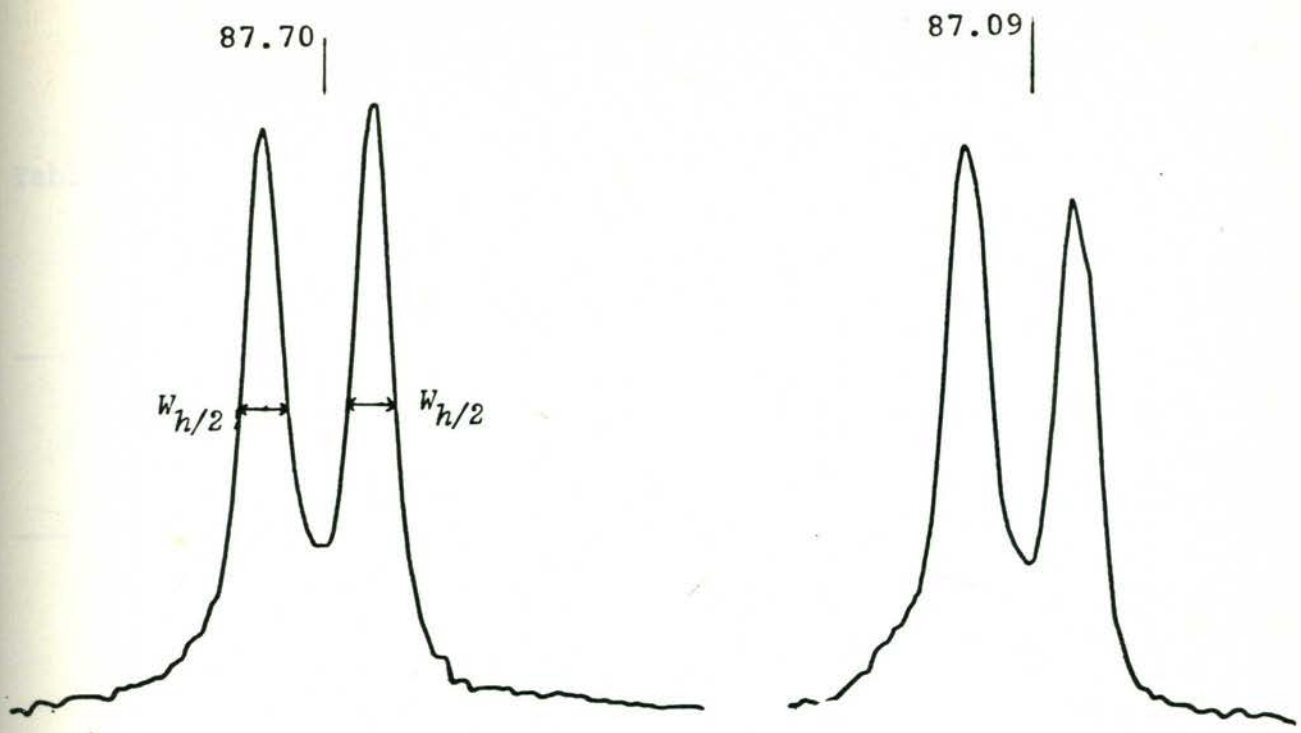


Figure 7(a). The aromatic region of the 100 MHz ^{1}H n.m.r. spectrum of (89). Scale is 1 cm = 2Hz.

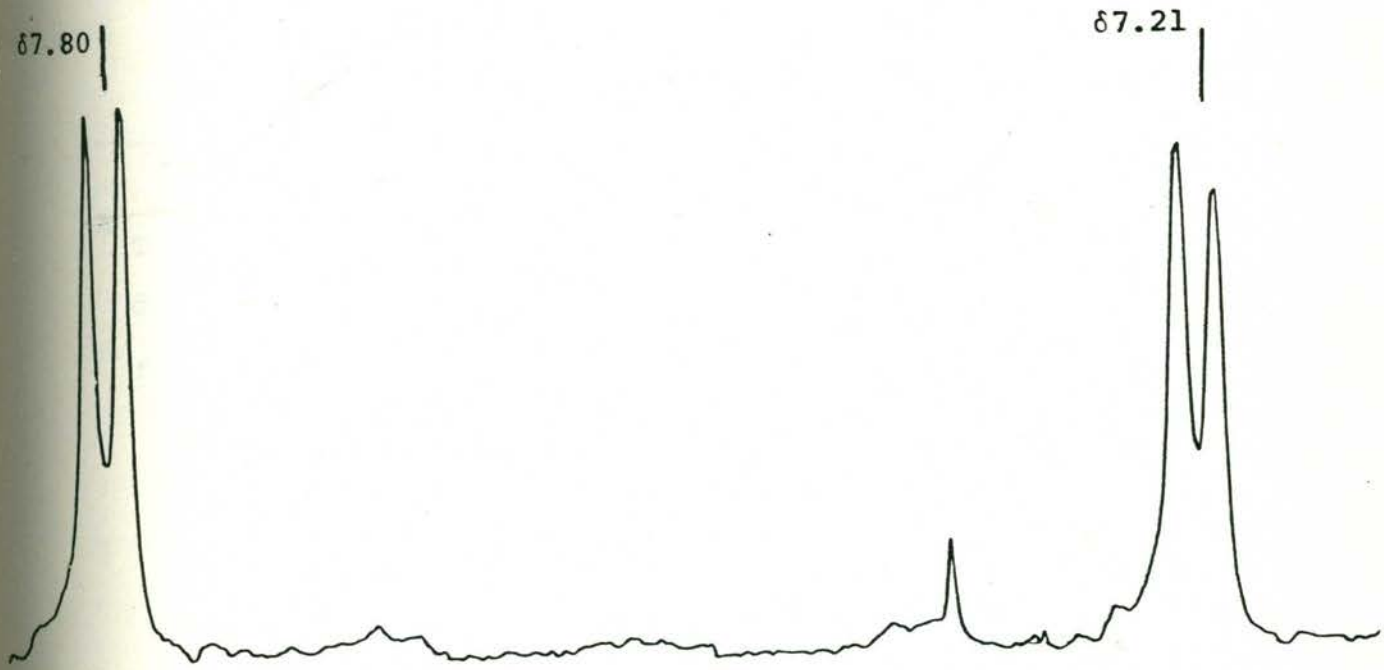


Figure 7(b). The aromatic region of the 100 MHz ^{1}H n.m.r. spectrum of (90). Scale is 1 cm = 5.33 Hz.

Table 7. Differences in total $W_{h/2}$ measurements for the aromatic protons in (87)-(91).

Compound	Chemical shift of aromatic protons (δ)	Difference in $W_{h/2}$ (Hz)[A]
(87)	6.51, 7.94	0.16
(88)	7.07, 7.64	0.18
(89)	7.09, 7.70	0.23
(90)	7.21, 7.80	0.34
(91)	7.03, 7.76	0.36

[A] The average $W_{h/2}$ for the individual components of the downfield signal was substracted from the average $W_{h/2}$ for that from the upfield signal (see Fig. 7).

doublet were obtained by measuring the $W_{h/2}$ of each component of the doublet; this is illustrated in Fig. 7. A nuclear Overhauser effect (n.O.e.) experiment on the dinitrile (88) showed an 11% n.O.e. between the benzylic proton and the upfield aromatic proton at δ 7.07. The upfield proton signal was broader than the downfield signal for each of the compounds (87)-(91) and consequently the upfield aromatic proton was assigned as *cis* to the benzylic proton in the compounds (87)-(91).

The diester (92), however, had very broad peaks for H_A and H_B at 304 K, and a low temperature spectrum (243 K) at 400 MHz showed effectively no difference in the $W_{h/2}$ for the peaks at δ 7.25 and 7.40. A low temperature (243 K) n.O.e. experiment showed a 14% n.O.e. between the upfield aromatic proton and the benzylic proton, which was in agreement with the general observation that the upfield proton is *cis* to the benzylic proton for the compounds (87)-(91).

Each compound, except the sulfone (87)[†], was examined by d.n.m.r. spectroscopy. In all experiments the benzylic proton was irradiated so that all benzylic couplings were removed. Spectra were recorded over a range of temperatures and rate constants were determined by lineshape analysis with the program DNMR 3[49] which had been locally modified.[47]

The lineshape of the signal arising from a nucleus (or nuclei) involved in an exchange process is a function of the following variables:[47]

[†] The sulfone (87) could not be studied because the aromatic protons of the *p*-toluenesulfinate group masked the exchanging protons in the region of fast exchange.

(i) the chemical shift difference between the sites ($\Delta\nu_s$);

(ii) the linewidth of the resonance line ($W_{h/2}$);

(iii) the scalar coupling between nuclei (J);

(iv) the rate of exchange between the sites (k).

For a specific system, given an experimental lineshape, the set(s) of variables ($\Delta\nu_s$, $W_{h/2}$, J and k) which define it can be obtained. In this work $\Delta\nu_s$, $W_{h/2}$ and J were determined experimentally and k was determined by matching experimental with computer simulated spectra. The determination of these parameters is outlined below.

The chemical shift difference ($\Delta\nu_s$)

The true chemical shift difference between exchanging sites varies with the temperature, independently of the exchange process. In the systems studied in this work the difference increased with temperature for all compounds. The value of this difference ($\Delta\nu_s$) for the spectra where rapid exchange was occurring was obtained by extrapolation from regions where exchange has no observable effect on the chemical shift. Several points were obtained for each compound and the resultant straight lines extrapolated to the region of fast exchange.

The linewidth of the resonance ($W_{h/2}$)

In an exchanging system the effective linewidth of the resonance of any nucleus can be expressed as the sum of three

contributions, as expressed in eqn (16).[47]

$$W_{h/2} = \frac{1}{\pi T_2^{eff}} = \frac{1}{\pi T_2^{inh}} + \frac{1}{\pi T_2^{sc}} + \frac{1}{\pi T_2^{dd}} \qquad (16)$$

T_2^{eff} is the effective tranverse relaxation time of the nucleus. The term T_2^{inh} is the contribution to linewidth due to inhomogeneity. It was estimated by measuring the linewidth of hexamethyldisilane which was present as an internal reference with each spectrum. T_2^{sc} is the contribution from small scalar couplings to other nuclei, assumed to be negligible in the systems studied here and T_2^{dd} is that contribution from dipole-dipole interactions between individual protons in the molecule and is effectively zero above 300 K.[47]

The meta *coupling constant* (J)

The coupling constant between *meta* protons has been found to usually lie in the range 1.2 - 3.1 hz.[50] In the series of compounds studied J_{AB} was determined at temperatures where the AB system was fully resolved (slow exchange). The benzylic proton was irradiated and the AB coupling constant measured. It was assumed that the coupling constant did not vary with temperature.

The rate constant k *and measurement of temperature*

Using the values of J, $W_{h/2}$ and $\Delta\nu_s$ determined experimentally spectra were computed, varying the value of k until the calculated spectrum gave a visual match with the experimental one. The final calculated spectra for the aromatic

region of the dinitrile (89) are shown with the experimental spectra in Fig. 8.

Temperature was determined using a secondary standard whose chemical shift varies with temperature, usually ethylene glycol (calibrated according to the curve of Kaplan[51]) or methanol (calibrated according to the curve of van Geet[52]). A temperature accuracy of ±2 K was assumed for all measured temperatures.

Determination of kinetic parameters

The measurement of exchange rate (k) as a function of temperature permits the calculation of activation parameters ($\Delta G^{\ddagger}$, $\Delta H^{\ddagger}$, $\Delta S^{\ddagger}$, E_a etc) for the exchange process. The values of the free energy of activation ($\Delta G^{\ddagger}$), the enthalpy of activation ($\Delta H^{\ddagger}$) and the entropy of activation ($\Delta S^{\ddagger}$) are most accurately determined from the Eyring equation[53] given in eqn (17) where k is the rate constant, t is the transmission factor

$$k = t\, k_B \frac{T}{h} \exp(-\Delta G^{\ddagger}/RT) = t\, k_B \frac{T}{h} \exp(-\Delta H^{\ddagger}/RT) \exp(\Delta S^{\ddagger}/R) \qquad (17)$$

(taken as 1), k_B is the Boltzmann constant, T is the absolute temperature, h is Planck's constant and R is the gas constant.

Rate constants at a number of different temperatures can be related to the Arrhenius activation energy (E_a) by the Arrhenius equation (18) where A is the pre-exponential factor.

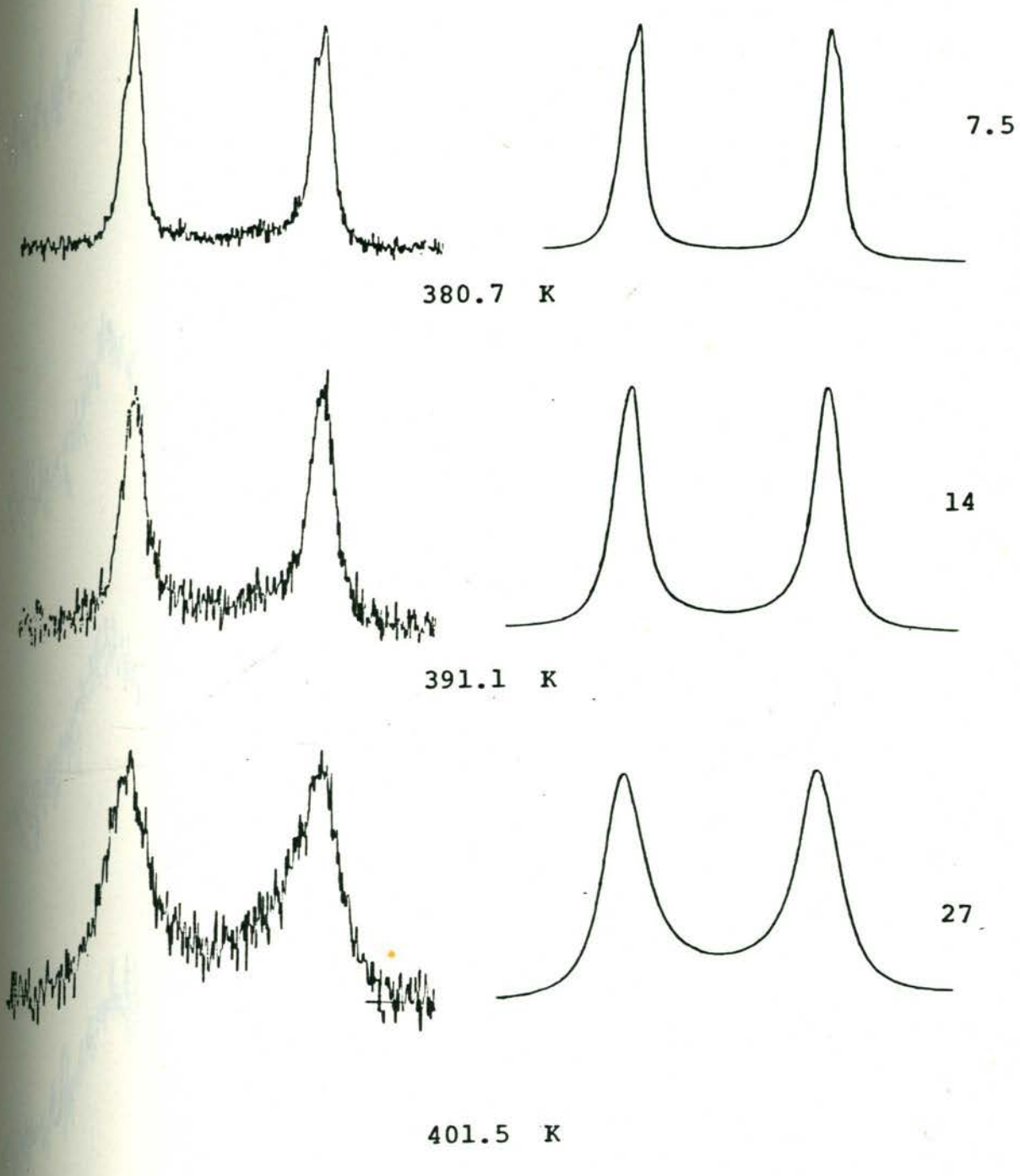


Figure 8. The computed spectra (right hand column) and experimental spectra (left hand column) for the exchange process of (89). The value of the rate constant used for generation of the computed spectra is also given.

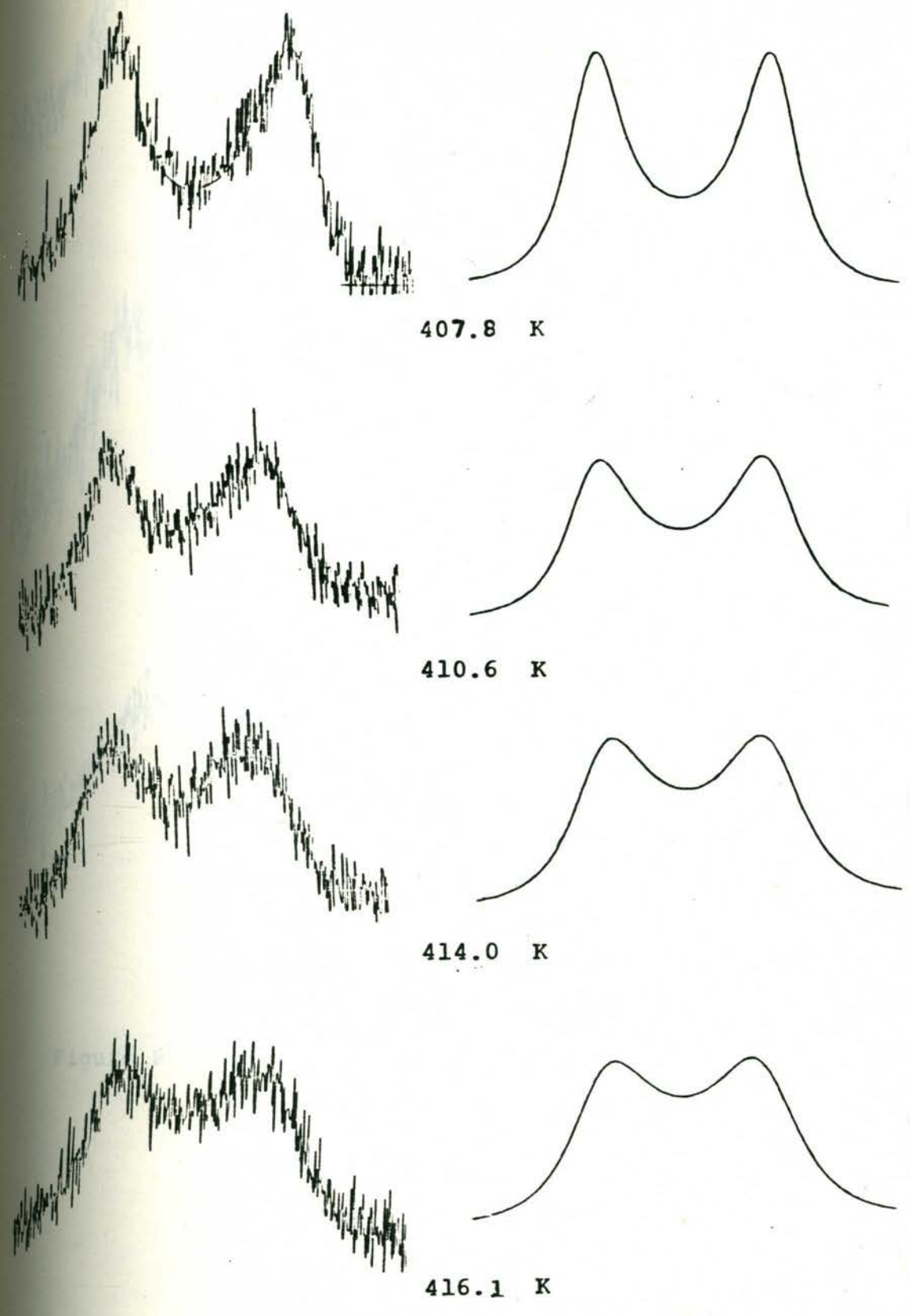


Figure 8 continued.

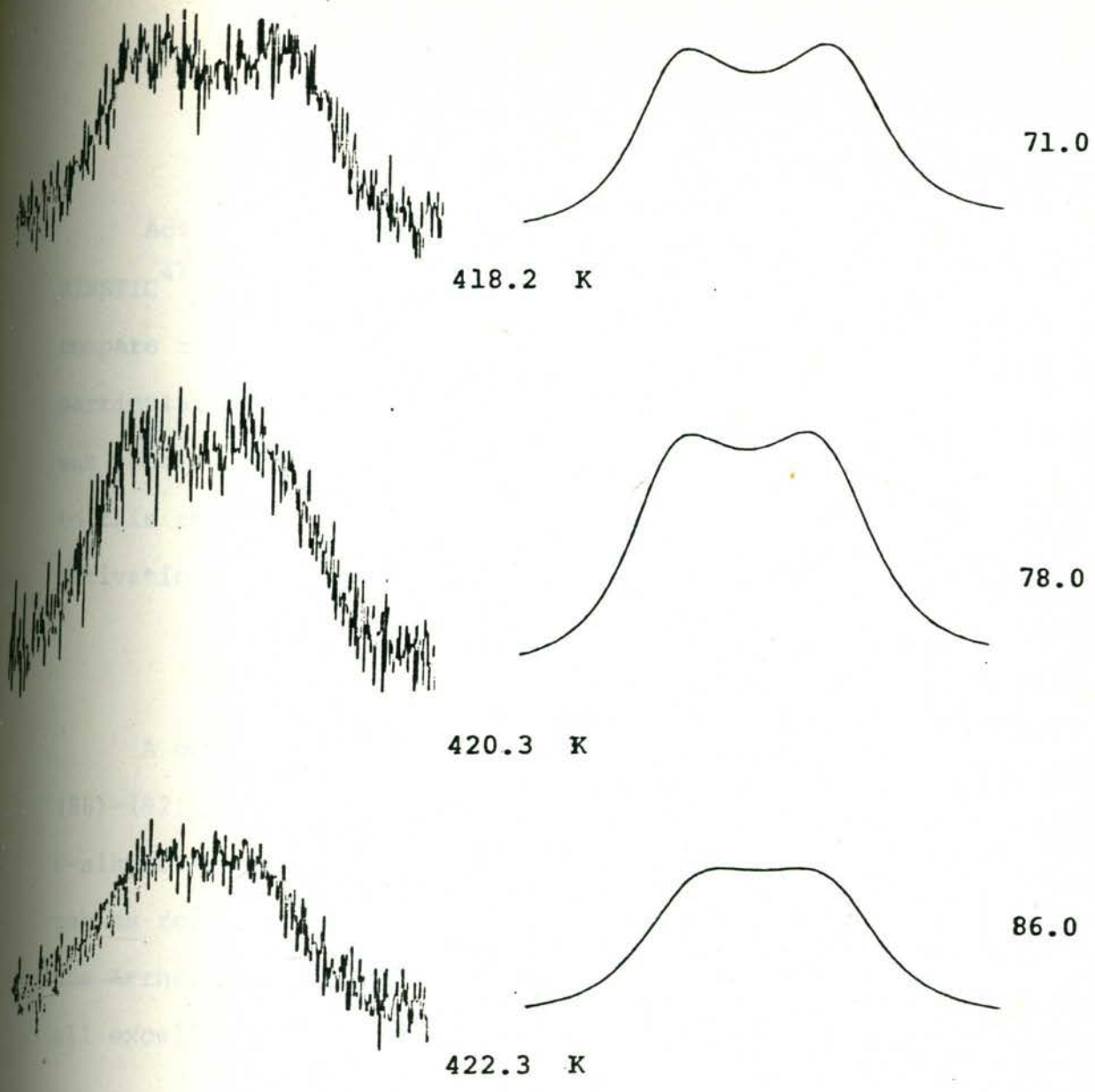


Figure 8 continued.

$$k = A \exp(-E_a/RT) \qquad (18)$$

Activation parameters were calculated with the program KINETIC[47] which also performs an error analysis. In order to compare rotational barriers, $\Delta G^{\ddagger}$ values were calculated at a particular temperature for all compounds. In this work 380 K was chosen, as most compounds had experimental points close to this temperature $\Delta G_{380}^{\ddagger}$ was calculated from the Eyring activation parameters by eqn (19).

$$\Delta G_{380}^{\ddagger} = \Delta H^{\ddagger} - 380\Delta S^{\ddagger} \qquad (19)$$

A comparison of activation parameters for the compounds (88)-(92) with the yields of formation of the corresponding *C*-alkylates (22)-(25) and (28) can be made from Table 8 (Full tables for the compounds (88)-(92) are given in appendix 1). The Arrhenius plots (ln k against $1/RT$) shown in Fig. 9 are all excellent straight lines.

The rotational barriers in the two dinitriles (88) and (89) correlate as expected with the yields of the parent compounds (22) and (23); i.e. the dinitrile (88) has a lower rotational barrier than (89) and the *C*-alkylate (22) is formed more rapidly and in higher yield than (23). Similarly, the diastereomers (90) and (91) have a small difference in their $\Delta G^{\ddagger}_{380}$ values which reflects the difference in yield of the two compounds (24) and (25). However, they have a marginally lower rotational barrier than the dinitrile (88). The diester (92) has the lowest rotational barrier of all but its parent diester (28) is formed more slowly and in lower yield than

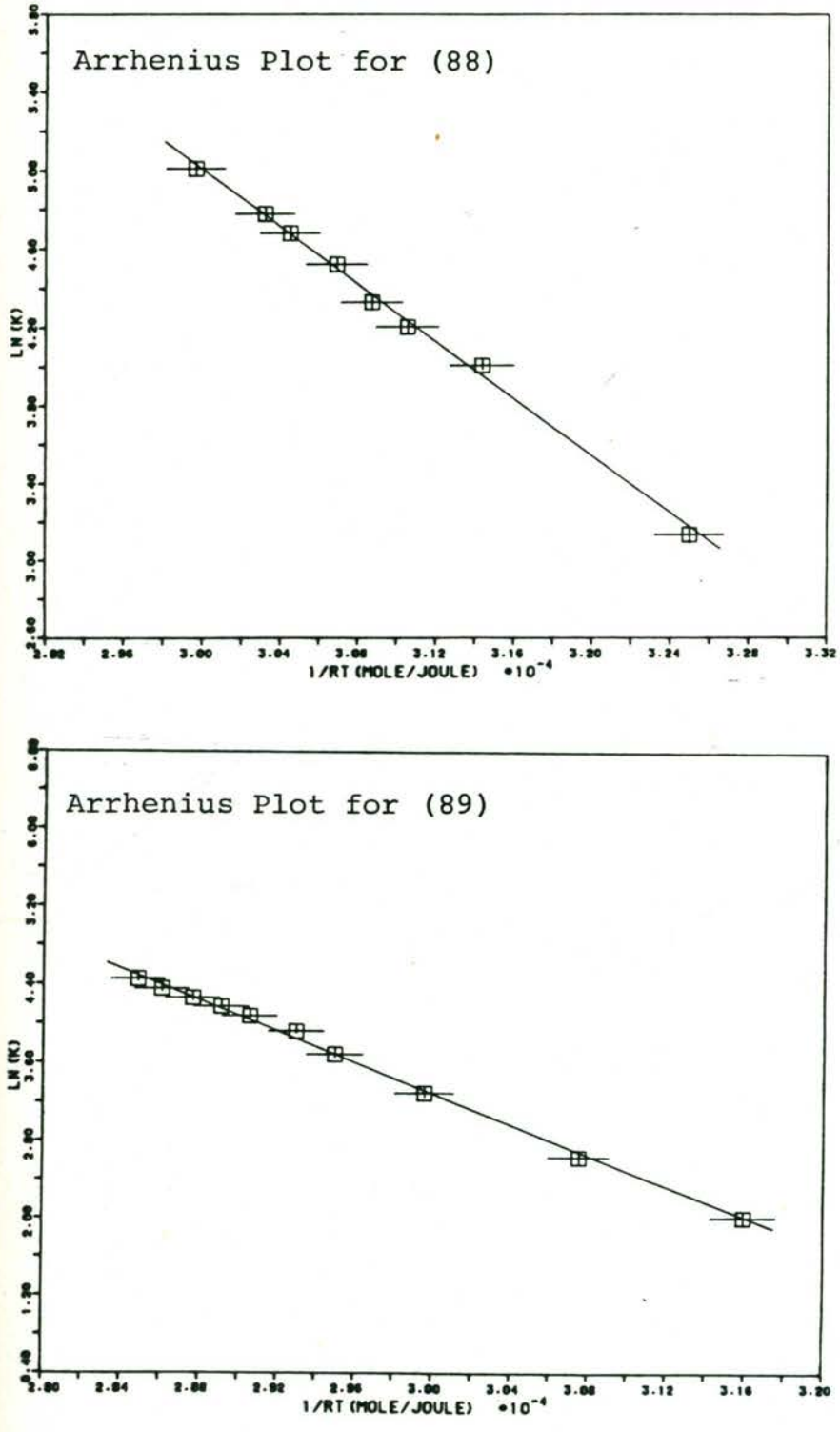
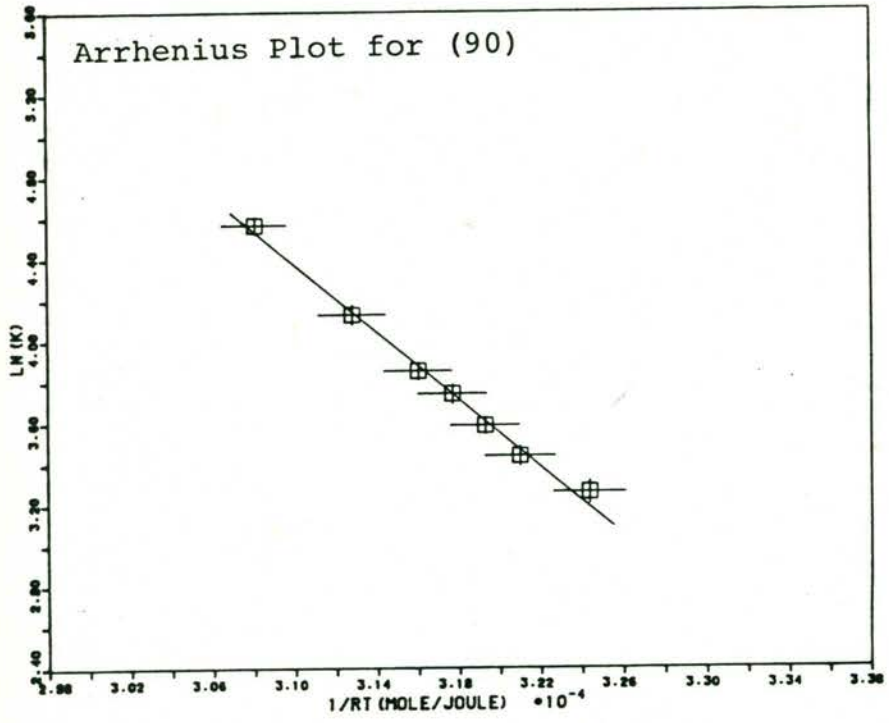
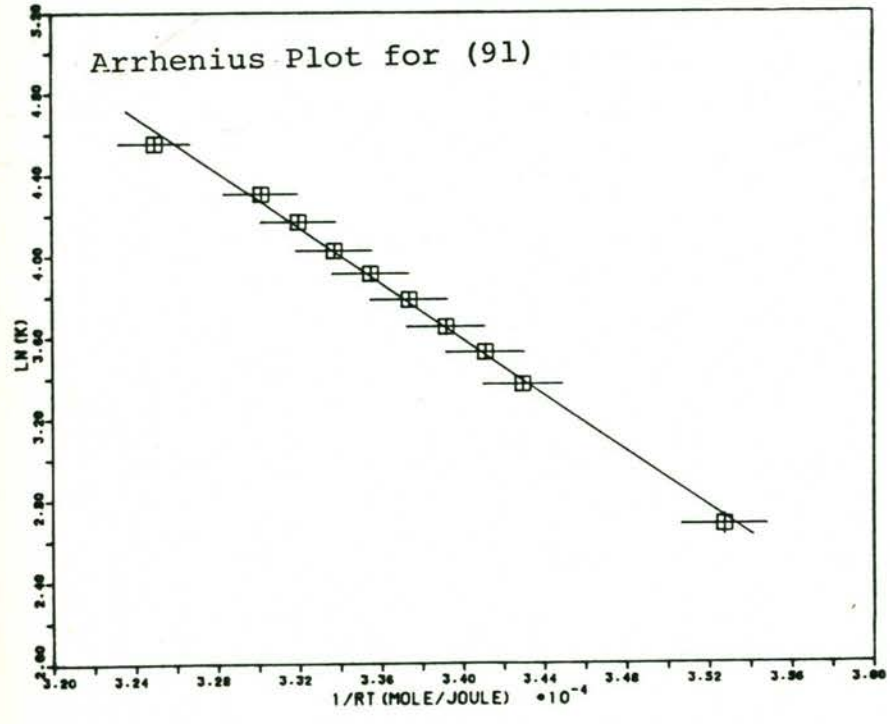


Figure 9. Arrhenius Plots for the exchange processes in (88) - (92).





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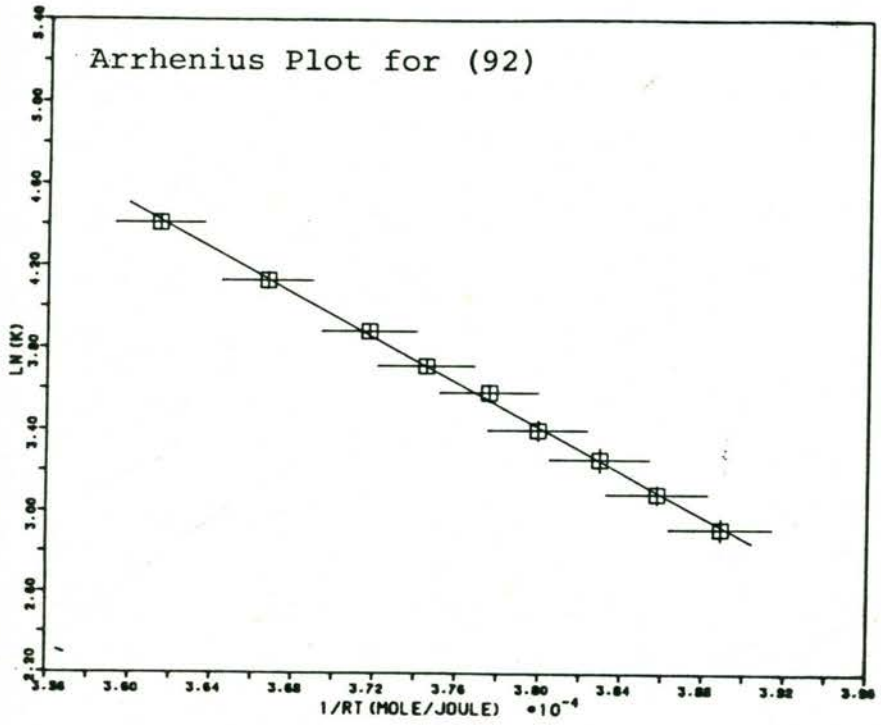


Figure 9 continued.

Table 8. Activation parameters for intramolecular rotation about the *C*-aryl-*C*-benzylic bond in compounds (88) - (92), and yields and reaction times for the radical coupling reactions for the parent compounds (22) - (25) and (28)[A]

Compound	$\Delta G^{\ddagger}_{380}$ [B] kJ mol^{-1}	$\Delta H^{\ddagger}$ [B] kJ mol^{-1}	$\Delta S^{\ddagger}$ [B] J K^{-1} mol^{-1}	E_a [C] kJ mol^{-1}	ln A [C]	Parent compound, % yield and reaction time
(88)	81.8±1.7	70.6±0.9	-29.6±2.2	73.1±1.8	27.0±0.3	(22), 98, 20 min
(89)	87.6±1.4	65.5±0.7	-29.2±1.7	79.3±0.7	27.1±0.2	(23), 59, 120 min
(90)	81.7±3.0	78.8±1.5	-7.6±4.0	82.6±1.6	30.0±0.5	(24), 41, 20 min
(91)	77.4±1.6	66.2±0.8	-29.5±2.1	68.8±0.7	27.0±0.3	(25), 51, 20 min
(92)	72.1±1.2	51.6±0.4	-54.0±1.2	54.2±0.4	24.0±0.1	(28), 73, 80 min

[A] Full tables for each compound appear in Appendix A.

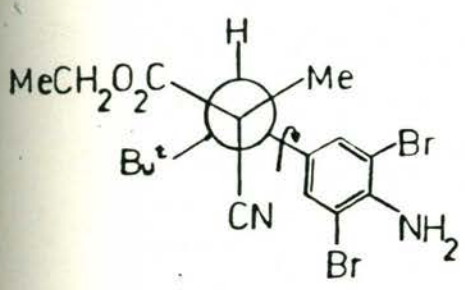
[B] Values calculated from the Eyring equation.

[C] Values calculated from the Arrhenius equation.

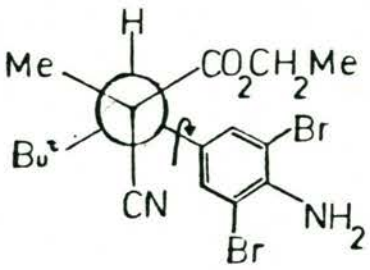
the dinitrile (22) or the cyano esters (24) and (25) (combined yield 92%). Clearly, there is no simple correlation between the rotational energy barriers and the yield and reaction times for the appropriate $S_{RN}1$ reaction. The energy parameters for the rotational processes can be rationalized, however, and are discussed immediately below.

Molecular models indicate that the diester (92) is extremely crowded, much more so than either of the diastereomers (90) and (91) or the dinitrile (88). This crowding may destabilize the ground state conformation, therefore raising it in energy, without affecting the transition state to the same degree, hence lowering the effective barrier. Thus groups which differ markedly in their chemical nature or steric size may not be satisfactorily compared with this system, and it is consequently not surprising that the reaction parameter against energy parameter correlation does not exist.

The values of $\Delta S^{\ddagger}$ given in Table 8 show that the two diastereomers (90) and (91) have significantly different changes in entropy between their ground and transition states. This observation can be rationalized in the following manner. Assuming that (90) and (91) exist in their most stable conformations [(95) and (96) respectively], it is apparent that rotation of the phenyl group about the aryl carbon - benzylic carbon bond [as indicated in (95) and (96)] involves interaction of the *ortho* hydrogen atoms with a cyano and a methyl group in (90) and with a cyano and a carboethoxy group in (91).



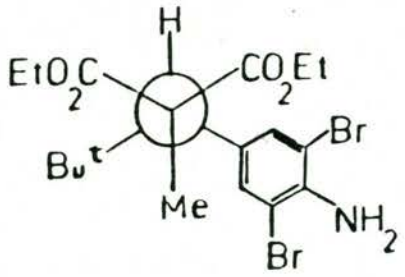
(95)



(96)

The higher $\Delta S^{\ddagger}$ in (91) can be ascribed to greater loss of rotational freedom of the ester group in a crowded transition state compared to that loss experienced by the methyl group in (90). The 2*RS*, 3*RS* diastereomer (90) has to rotate through the methyl group, which has a larger effective van der Waals radius than the carbonyl of the ester[37] and consequently the higher enthalpy change is seen in this compound.

The two dinitriles have virtually identical $\Delta S^{\ddagger}$ values, the substitution difference being reflected most clearly in the $\Delta H^{\ddagger}$ values. However the diester (97) has an extremely high value of $\Delta S^{\ddagger}$ when compared to the four other compounds in Table 8. From the Newman projection in (97) it can be seen that rotation about the *C*-aryl-*C*-benzylic bond necessitates forcing the ester function to "swing" back into the



(97)

sidechain, resulting in a rotational freedom loss for *both* ester groups as well as the t-butyl group.

All the rotational barriers are large compared with the value for "free rotation", taken as 12.5 kJ mol^{-1} for the *C-C* bond in ethane.[54] The compounds in this study have rotational barriers 6 - 7 times greater than this value, and the high yields that the parent compounds are formed in is a reflection of the capacity of the $S_{RN}1$ reaction to proceed in spite of steric hindrance.

4. General Conclusions

A number of conclusions may be drawn from Sections 1 - 3 of this work.

1. *The $S_{RN}1$ Reaction and Steric Hindrance*

The $S_{RN}1$ reaction in benzylic systems is sensitive to steric hindrance. Less hindered salts, for example (5), react more quickly and give more *C*-alkylate with a given substrate than do their more hindered analogues, for example (6); the most sterically hindered salts failed to give *C*-alkylates. This observation implies that the initiation and/or association steps [Scheme 2, eqns (1) and (3)] are sensitive to steric effects, as these are the stages at which the anion is involved in the reaction process. There is no need to postulate a $S_{RN}2$ mechanism in this system,[29,45,46] as the observed differences in rate may be explained in terms of factors affecting the initiation and association steps. Electron transfer may be slower between bulky reactants compared with unencumbered reactants and hence more hindered substrates will cause a reduction in the rate of the initiation step [Scheme 2, eqn (1)]. The association step [Scheme 2, eqn (3)] requires that the two reactants form a bond and clearly steric hindrance will affect the rate of this bond formation. Differences in product yields from reactions of analogous salts [for example (5) and (6), (8) and (9), (10) and (11)] with a given substrate can be attributed to differences in the rate of association, as the major reactions (oxygenation, reduction and *C*-alkylation)

all proceed through the benzylic radicals (37) or (38). Thus bulkier anions associate more slowly with a given radical intermediate and allow the other processes to compete more efficiently. Steric-effects are also apparent from a comparison of the chloride (1) with the dinitro compound (2) in their reactions with identical anions. Both substrates react by $S_{RN}1$ mechanisms, and so differences in yields of *C*-alkylates (both in this and other work[19,20,24]) between these substrates are most readily explained by the greater steric hindrance of the radical (38) compared to (37).

Competitive reactions in this work, where the association step was kinetically controlled, between anions always led to the formation of the product derived from the less hindered anion. Again this indicates that the association step is sensitive to steric hindrance.

Collaborative work with Professor P. Neta undertaken in connection with this study provided direct evidence that the dissociation step [Scheme 2, eqn (2)] is also sensitive to steric hindrance. Measurements of the rate of dissociation of the radical anions of (1) and (49) were made in aqueous 2-propanol. The radical anion of *p*-nitrobenzyl chloride (49) decayed at 4×10^3 s^{-1} and that of the chloride (1) decayed at 4×10^2 s^{-1}.

2. *Side Reactions*

The sensitivity of the association step [Scheme 2, eqn (3)] to steric hindrance allows other reactions to compete

with *C*-alkylation. In the case of *aci*-nitronates reacting with the chloride (1) the major competing reaction is *O*-alkylation by an $S_{RN}1$ mechanism.[19,20] With the anions studied in this work, reduction is the main alternative to *C*-alkylation. However, an inert atmosphere is imperative, as these reactions are extremely sensitive to oxygen.

3. *Reversibility*

The association step of the reaction between benzylic radicals and *aci*-nitronates has been shown to be under kinetic control.[23] The failure of the *C*-alkylates (68) and (69) to rapidly exchange in the experiments in Table 4 shows that the association step is effectively irreversible. This clearly supports the conclusion that the *O*-alkylation products result from direct $S_{RN}1$ *O*-alkylation,[19,20,23] and are not derived from the *C*-alkylates by equilibration.[21] Similarly the failure of the *O*-alkylate (78) to rearrange under conditions which favour $S_{RN}1$ processes clearly shows that the regiochemistry of association in the coumaranone system (Table 5) is irreversible. The fact that the sulfinate-sulfone interconversion[21] (Scheme 4) occurs cannot be generalized to imply that all $S_{RN}1$ association steps are reversible. Although this work does not establish which of the representations in Schemes 5 and 8 more accurately describe the association step, it is clear that neither has a *readily* reversible association step for the reactions studied in this work.

4. *The Utility of the $S_{RN}1$ Reaction*

The sensitivity of the benzylic $S_{RN}1$ reaction to steric hindrance must be placed in perspective. The $S_{RN}1$ reaction is amongst the most useful reactions for *C-C* bond formation between hindered sites; the successful synthesis of the crowded *C*-alkylates in this work, and the high rotational barriers of some of their derivatives (see Section 3 above) is evidence of this. The ability of the reaction to introduce synthetically labile groups (e.g. cyano and ester groups) α to the new *C-C* bond is of great importance for the further chemical manipulation of the products.

5. *The Use of Hexamethylphosphoramide*

The use of hexamethylphosphoramide in the $S_{RN}1$ reactions of sterically hindered substrates is worthy of note. The solvent dramatically reduces reaction times, which in turn avoids oxygenation side reactions, and increases yields. For example in Me_2SO the salt (10) takes 11 days to reach 85% reaction with the chloride (1) and gives a low yield of the *C*-alkylate (28),[20,32] at least partially due to oxygenation reactions. The reaction of (1) with (10) in $(Me_2N)_3PO$ is complete in 1.3 hours. The use of hexamethylphosphoramide also precludes oxygenation by the solvent such as that claimed elsewhere.[21]

EXPERIMENTAL

GENERAL

Melting points were determined thermoelectrically on a Kofler melting point apparatus and are uncorrected. ^{1}H n.m.r. spectra were determined on a Jeol FX-60Q, Varian Associates EM-390, HA-100 or XL-100, or a Bruker WM-400 spectrometer, with $SiMe_4$ as internal standard on *c.* 10% w/v solutions in $CDCl_3$. ^{13}C n.m.r. spectra were determined on a Jeol FX-60Q spectrometer on 10 - 30% w/v solutions in $CDCl_3$, with $SiMe_4$ as internal standard. Chemical shifts are quoted in ppm downfield of $SiMe_4$. Infrared spectra were recorded in $CHCl_3$ or as liquid films on a Perkin-Elmer 221 spectrophotometer, and ultraviolet spectra were recorded on a Perkin-Elmer 402 spectrophotometer. Mass spectra were recorded on an A.E.I. MS-9 spectrometer at 70 eV. Analyses were carried out at the Australian Microanalytical Service, Melbourne.

Preparative layer chromatography (p.l.c.) was performed on Merck Kieselgel 60 $PF_{254+366}$. Thin layer chromatography (t.l.c.) was performed on Merck Kieselgel $HF_{254+366}$ (type 60). Column chromotagraphy was performed on Merck silica gel (70 - 230 mesh). H.p.l.c. was performed on a Waters Associate Prep LC/system 500 instrument with a Prep Pak-500 silica gel cartridge.

Solvents were dried and purified in the usual manner.[55] Light petroleum refers to the fraction of b.p. 65 - 70°.

1. REACTIONS OF STERICALLY HINDERED SUBSTRATES

A. Preparation of Nucleophilic Reagents

(1) The sodium salts (5) - (17)

The sodium salts were prepared by addition of excess sodium hydride to a solution of the appropriate conjugate acid† in hexamethylphosphoramide or *N*,*N*-dimethylformamide, in a dry atmosphere. After 10 minutes the solution was filtered through sintered glass to remove excess sodium hydride and the clear solution was used immediately.

(2) Lithium 2-nitropropan-2-ide (19)

Lithium 2-nitropropan-2-ide (19) was prepared by the method of Kornblum.[6]

B. Preparation of Starting Materials

p-(1-chloro-2,2-dimethylpropyl)nitrobenzene (1),[19] *p*-(1,2-dimethyl-1-nitropropyl)nitrobenzene (2),[62] 1-chloro-2,2-dimethylpropylbenzene (3),[63] α,*p*-dinitrocumene (48)[42,62] and *p*-(1-chloro-2-methylpropyl)nitrobenzene (50),[19] were all

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† Ethylmalononitrile,[56] isopropylmalononitrile,[56] t-butylmalononitrile,[57] ethyl 2-cyanopropionate (Fluka), ethyl 2-cyano-3-methylbutyrate,[58] diethyl t-butylmalonate,[59] methyl 2-methylacetoacetate (Aldrich), 3-methyl-2,4-pentanedione,[60,61] and diethyl phosphite (Fluka) were prepared by the indicated literature method or were commercially available.

prepared by the indicated literature procedures and had physical and spectroscopic values in agreement with the literature values. The separation of *p*-(1-chloro-2,2-dimethylpropyl)nitrobenzene (1) from the corresponding *ortho* isomer was performed by h.p.l.c. with 1% ethyl acetate/light petroleum as eluent.

C. Preparation of Authentic Reaction Products

p-Nitropivalophenone (34),[19] 2,2-dimethyl-1-(*p*-nitrophenyl)propan-1-ol (35),[20] *p*-(2,2-dimethylpropyl)nitrobenzene (36),[64] *p*-(1,2-dimethylpropyl)nitrobenzene,[65] 3-methyl-2-(*p*-nitrophenyl)butan-2-ol,[23] *p*-(2-methylpropyl)nitrobenzene (56),[20] β,β-dimethylstyrene (57)[66], *p*-nitroisobutyrophenone (58)[67] and 2-methyl-1-*p*-nitrophenylpropanol (59)[19] had been synthesized by the indicated procedures during earlier work[32] in this department or were synthesized in the course of the present work. Whenever one of the above compounds was isolated as a reaction product it was compared with an authentic sample by appropriate spectroscopic (^{1}H n.m.r., i.r.) or physical (m.p., t.l.c.) methods.

D. Reactions of Substrates with Nucleophiles

The salt was dissolved or prepared *in situ* (see A above) in the appropriate solvent (as stated in the relevant Table) and the solution was deoxygenated by passage of dry nitrogen for *c*. 15 minutes. The appropriate substrate was added, with stirring, and the reaction temperature was maintained in a constant temperature oil or water bath. Reactions performed with irradiation were carried out by placing a 500-W GE sunlamp 20 cm from the reaction vessel. Reactions performed

under oxygen were carried out with oxygen bubbling through the solution. Reactions were performed for the times, at the temperatures and under the conditions stated in the Tables. The reaction mixtures were worked up by dilution with water, addition of excess sodium chloride, and threefold extraction with ether. The ether layers were washed three times with water, then with brine, and dried ($MgSO_4$). The solvent was removed and if the conjugate acid of the anion was still present it was removed by distillation (kugelrohr). The crude reaction product was purified by p.l.c. The products are listed in order of increasing polarity.

(1) Reactions of *p*-(1-chloro-2,2-dimethylpropyl)nitrobenzene (1) with Nucleophiles (Table 1)

(i) Reactions of *p*-(1-chloro-2,2-dimethylpropyl)-nitrobenzene (1) with sodium azide (4) (expts 1 - 4)

Under Nitrogen at 60° (expt 1)

The crude product was purified by p.l.c. with light petroleum as eluent to afford p-*(1-azido-2,2-dimethylpropyl)-nitrobenzene* (20) (520 mg, 89%), a pale yellow oil (Found: C, 56.2; H, 6.0; N, 23.7. $C_{11}H_{14}N_4O_2$ requires C, 56.4; H, 6.0; N, 23.9 %). ^1H n.m.r.: δ 0.94, s, Bu^t; 4.37, s, benzylic H; AA'XX' system: 7.46, m, 2H *meta* to NO_2; 8.22, m, 2H *ortho* to NO_2; $J_{AX} + J_{AX'}$ 8.7 Hz. ν_{max} (liquid film) 2915, 2105, 1605, 1520, 1400, 1300, 870 cm^{-1}. λ_{max} (ethanol) 268 nm (ε 9730). *m/z* 206 ($M-N_2$; 0.4%), 191 (8), 150 (30), 149 (17), 133 (26), 103 (29), 77 (14), 76 (30), 75 (12), 58 (23), 57 (100), 51 (14), 50 (21), 43 (11), 41 (75), 39 (24).

Under nitrogen at 20° (expt 2)

The crude product was purified by p.l.c. with light petroleum as eluent to yield starting material (1) (16 mg, 7%) and *p*-(1-azido-2,2-dimethylpropyl)nitrobenzene (20) (211 mg, 90%), identical with that prepared above.

Under oxygen at 20° (expt 3)

The only product was starting material (1) (217 mg, 95%).

In the dark with di-t-butyl nitroxide at 20° (expt 4)

The only product was starting material (1) (214 mg, 94%).

(ii) Reactions of *p*-(1-chloro-2,2-dimethylpropyl)nitrobenzene (1) with the sodium salt (5) of ethylmalononitrile (expts 6,7)

Under nitrogen (expt 6)

The only product was 2-[2,2-dimethyl-1-(*p*-nitrophenyl)-propyl]-2-ethylmalononitrile (22) (691 mg, 97%), identical with an authentic sample.[32]

Under oxygen (expt 7)

The crude product was purified by p.l.c. with 15% ethyl acetate/light petroleum as eluent to afford starting material (1) (48 mg, 34%), *p*-nitropivalophenone (34) (35 mg,

27%) and 2,2-dimethyl-1-(*p*-nitrophenyl)propan-1-ol (35) (11 mg, 8%).

(iii) Reaction of *p*-(1-chloro-2,2-dimethylpropyl)nitrobenzene (1) with the sodium salt (6) of isopropylmalononitrile (expt 9)

The crude product was purified by p.l.c. with 15% ethyl acetate/light petroleum as eluent to afford *p*-(2,2-dimethylpropyl)nitrobenzene (36) (10 mg, 2%) and *2-[2,2-dimethyl-1-(p-nitrophenyl)propyl]-2-isopropylmalononitrile* (23) (441 mg, 59%), which was recrystallized from pentane to give pale yellow needles, m.p. 133-135° (Found: C, 68.0; H, 6.9; N, 13.7. $C_{17}H_{21}N_3O_2$ requires C, 68.2; H, 7.1; N, 14.0%). ^{1}H n.m.r.: δ 1.00, d, *J* 6.5 Hz, CHMeMe; 1.23, s, Bu^t; 1.28, d, *J* 6.5 Hz, CHMeMe; 1.82, m, CHMeMe; 3.12, s, benzylic H; 7.30, m, H *meta* to NO_2; 7.93, m, H *meta* to NO_2; 8.25, m, 2H *ortho* to NO_2. ν_{max} 2920, 2250, 1600, 1520, 1390, 865 cm^{-1}. λ_{max} (ethanol) 267 nm (ε 9740). *m/e* 284 (M-Me; 0.5%), 57 (100), 43 (20), 41 (22).

(iv) Reaction of *p*-(1-chloro-2,2-dimethylpropyl)nitrobenzene (1) with the sodium salt (7) of t-butylmalononitrile (expt 10)

The crude product was purified by p.l.c. with 15% ethyl acetate/light petroleum as eluent to afford *p*-(2,2-dimethylpropyl)nitrobenzene (36) (39 mg, 8%), starting material (1) (23 mg, 4%), *p*-nitropivalophenone (34) (120 mg,

23%) and a compound (20 mg), which could not be definitely identified and which had m.p. 98-101° (Found: C, 65.2; H, 7.8; N, 4.6% which corresponds to an average constitution $C_{16.3}H_{23.4}NO_2$). ^{1}H n.m.r.: δ 0.96, s, 9H; 1.25, s, 9H; 5.49, s, 1H; AA'XX' system: 7.44, m, 2H *meta* to NO_2; 8.20, m, 2H *ortho* to NO_2; $J_{AX} + J_{AX'}$ 8.8 Hz. ν_{max} 2920, 1735, 1610, 1520, 1480, 1400, 1325, 1170, 860 cm^{-1}. λ_{max} (ethanol) 269 nm. *m/z* 237 (2%), 135 (18), 85 (14), 57 (100).

(v) Reaction with the sodium salt (8) of ethyl 2-cyanopropionate (expt 11)

The crude product was purified by repetitive p.l.c. with 5% diethyl ether/light petroleum as eluent to afford *ethyl (2RS, 3RS)-2-cyano-3-(p-nitrophenyl)-2,4,4-trimethylpentanoate* (24) (326 mg, 41%), which was recrystalliaed from light petroleum to give white needles, m.p. 95-96° (Found: C, 63.9; H, 7.1; N, 8.9. $C_{17}H_{22}N_2O_4$ requires C, 64.1; H, 7.0; N, 8.8%). ^{1}H n.m.r.: δ 1.06, s, Bu^t; 1.24, s, C(CN)(CO_2Et)Me; 1.46, t, *J* 7.1 Hz, CO_2CH_2Me; 3.39, s, benzylic H; 4.34, m†, CO_2CH_2Me; 7.32, m, H *meta* to NO_2; 7.95, H *meta* to NO_2; 8.23, m, 2H *ortho* to NO_2. ν_{max} 2920, 2245, 1735, 1600, 1515, 1390, 1275-1230 (br), 1140, 870 cm^{-1}. λ_{max} (ethanol) 272 nm (ε 10750). *m/z* 318 (M; 0.2%), 262 (35), 201 (18), 190 (10), 189 (30), 173 (18), 172 (22), 115

† This multiplet has the appearance of a simple quartet, *J* 7.1 Hz.

(12), 57 (100), 41 (26) and *ethyl (2RS, 3SR)-2-cyano-3-(p-nitrophenyl)-2,4,4-trimethylpentanoate* (25) (405 mg, 51%) which was recrystallized from light petroleum to give white needles, m.p. 112 - 113° (Found: C, 64.4; H, 7.2: N, 8.5. $C_{17}H_{22}N_2O_4$ requires C, 64.1; H, 7.0; N, 8.8%). ^{1}H n.m.r.: δ 0.99, t, *J* 7.2 Hz, $CO_2CH_2\underset{\sim}{\sim}CH_3$; 1.15, s, Bu^t; 1.87, s, $C(CN)(CO_2Et)\underset{\sim}{\sim}Me$; 3.12, s, benzylic H; 3.87, m† , $CO_2\underset{\sim}{\sim}CH_2Me$; 7.18, m, H *meta* to NO_2; 7.96, m, H *meta* to NO_2; 8.16, m, 2H *ortho* to NO_2. ν_{max} 2920, 2245, 1735, 1600, 1515, 1395, 1515, 1280 - 1240 (br), 1140, 870 cm^{-1}. λ_{max} (ethanol) 277 nm (ε 10670). *m/z* 318 (M; 0.2%), 262 (29), 201 (17), 190 (10), 189 (30), 173 (16), 172 (20), 115 (10), 57 (100), 41 (27).

(vi) Reaction with the sodium salt (9) of ethyl 2-cyano-3-methylbutyrate (expt 13)

The crude product was purified by p.l.c. with 15% ethyl acetate/light petroleum as eluent to afford *p*-(2,2-dimethylpropyl)nitrobenzene (36) (68 mg, 14%), and a band which was further purified by repetitive p.l.c. with 5% ethyl acetate/light petroleum as eluent to give *ethyl (2RS, 3RS)-2-cyano-2-isopropyl-4,4-dimethyl-3-(p-nitrophenyl)pentanoate* (26) (164 mg, 19%), which was recrystallized from methanol to give white needles, m.p. 126 - 128° (Found: C, 66.0; H, 7.8; N, 8.3. $C_{19}H_{26}N_2O_4$ requires C, 65.9; H, 7.6; N, 8.1%). ^{1}H n.m.r.: δ 0.73, d, *J* 6.5 Hz, $Me\underset{\sim}{\sim}CHMe$; 1.04, d, *J* 6.5 Hz,

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† This multiplet has the appearance of a simple quartet, *J* 7.2 Hz.

MeCHMe; 1.05, s, Bu^t; ABX_3 system: 1.39, t, *J* 7.2 Hz, CO_2CH_2Me, 4.33, m, CO_2CH_2Me; 1.89, septet, *J* 6.8 Hz MeCHMe; 3.51, s, benzylic H; 7.35, m, H *meta* to NO_2; 8.03, m, H *meta* to NO_2; 8.20, m, 2H *ortho* to NO_2. ν_{max} 2920, 2240, 1735, 1610, 1520, 1400, 1270 - 1250 (br), 870 cm^{-1}. λ_{max} (ethanol) 273 nm (ε 10930). *m/z* 346 (M; 0.1%), 218 (23), 176 (18), 57 (100), 43 (20), 41(26) and *ethyl (2RS, 3SR)-2-cyano-2-isopropyl-4,4-dimethyl-3-(p-nitrophenyl)pentanoate* (27) (147 mg, 17%), which was recrystallized from methanol to give white needles, m.p. 110 - 112° (Found: C, 65.9; H, 7.3; N, 8.0. $C_{19}H_{26}N_2O_4$ requires C, 65.9; H, 7.6; N, 8.1%). ^1H n.m.r.: δ 0.96, d, *J* 6.5 Hz, MeCHMe; 1.01, d, *J* 6.5 Hz, MeCHMe; 1.07, s, Bu^t; ABX_3 system: 1.33, t, *J* 7.3 Hz, CO_2CH_2Me; 4.25, m, CO_2CH_2Me; 2.17, septet, *J* 6.5 Hz, MeCHMe; 3.29, s, benzylic H; 7.29, m, H *meta* to NO_2; 8.13, m, H *meta* to NO_2; 8.21, m, 2H *ortho* to NO_2. ν_{max} 2920, 2240, 1735, 1605, 1520, 1400, 1270 - 1250 (br), 870 cm^{-1}. λ_{max} (ethanol) 273 nm (ε 9310). *m/z* 346 (M; 0.1%), 248 (21), 218 (10), 57 (100), 43 (14), 41 (23).

(vii) Reaction with with sodium salt (10) of diethyl methylmalonate (expts 14 - 17)

The crude product was purified by p.l.c. with 20% ethyl acetate/light petroleum as eluent to afford *p*-(2,2-dimethylpropyl)nitrobenzene (26) (10 mg, 2%), diethyl 2-[2,2-dimethyl-1-(*p*-nitrophenyl)propyl]-2-methylmalonate (28) (667 mg, 73%) identical with an authentic sample[20] and 2,2-dimethyl-1-(*p*-nitrophenyl)propan-1-ol (35) (31 mg, 6%).

Work up with deoxygenated water (expt 15)

The reaction solution was quenched with freshly boiled water and the crude product was purified by p.l.c. with 20% ethyl acetate/light petroleum as eluent to afford *p*-(2,2-dimethylpropyl)nitrobenzene (36) (14 mg, 3%), diethyl 2-[2,2-dimethyl-1-(*p*-nitrophenyl)propyl]-2-methylmalonate (28) (666 mg, 73%) m.p. and m.m.p. 67 - 68° (lit.[20] 67.5 - 68°) and 2,2-dimethyl-1-(*p*-nitrophenyl)propan-1-ol (35) (8 mg, 1.5%).

Reaction under a dry air atmosphere (expt 16)

The reaction solution was prepared without degassing, and the flask was stoppered with a drying tube (silica gel). The crude product was purified by p.l.c. with 20% ethyl acetate/light petroleum as eluent to afford starting material (1) (28 mg, 5%), diethyl 2-[2,2-dimethyl-1-(*p*-nitrophenyl)-propyl]-2-methylmalonate (28) (520 mg, 57%) and 2,2-dimethyl-1-(*p*-nitrophenyl)propan-1-ol (35) (178 mg, 34%).

Under oxygen (expt 17)

The crude product was purified by p.l.c. with 20% ethyl acetate/light petroleum as eluent to afford starting material (1) (11 mg, 2%), *p*-nitropivalophenone (34) (160 mg, 31%) m.p. and m.m.p. 64 - 65° (lit.[19] 64 - 65°) and 2,2-dimethyl-1-(*p*-nitrophenyl)propan-1-ol (35) (287 mg, 55%) m.p. and m.m.p. 88 - 89° (lit.[20] 87.5 - 88°).

(viii) Reaction with the sodium salt (11) of diethyl ethylmalonate (expt 19)

The reaction mixture was quenched with freshly boiled water and the crude product was purified by p.l.c. with 20% ethyl acetate/light petroleum as eluent to afford *p*-(2,2-dimethylpropyl)nitrobenzene (36) (24 mg, 5%) and *diethyl 2-[2,2-dimethyl-1-(p-nitrophenyl)propyl]-2-ethylmalonate* (29) (512 mg, 54%) a pale yellow oil (Found: C, 63.6; H, 7.7; N, 4.0. $C_{20}H_{29}NO_6$ requires C, 63.3; H, 7.7; N, 3.7%). ^{1}H n.m.r.: ABX_3 system [$C(CO_2Et)_2CH_2Me$]: δ 0.67, t, Me; 1.43, m, H_A; 1.57, m, H_B: $J_{AX} = J_{BX}$ 7.2 Hz, J_{AB} 13.6 Hz; 0.97, s, Bu^t; ABX_3 system (CO_2CH_2Me): 1.33, t, Me; 4.21, m, H_A; 4.23, m, H_B; $J_{AX} = J_{BX}$ 7.2 Hz, J_{AB} 11.0 Hz; ABX_3 system (CO_2CH_2Me): 1.35, t, Me; 4.31, m, H_A; 4.34, H_B; $J_{AX} = J_{BX}$ 7.2 Hz, J_{AB} 10.8 Hz; 3.67, s, benzylic H; 7.31, m H *meta* to NO_2; 7.53, m, H *meta* to NO_2; 8.13, m, 2H *ortho* to NO_2. ν_{max} 2920, 1730, 1600, 1515, 1390, 1270 (br), 1140, 1040, 870 cm^{-1}. λ_{max} (ethanol) 275 nm (ε 10500). *m/z* 379 (M; 0.1%), 320 (18), 249 (12), 181 (29), 57 (100), 41 (25).

(ix) Reaction with the sodium salt (12) of diethyl isopropylmalonate (expt 20)

The crude product was purified by p.l.c. with 15% ethyl acetate/light petroleum as eluent to afford *p*-(2,2-dimethylpropyl)nitrobenzene (36) (34 mg, 7%), *p*-nitropivalophenone (34) (53 mg, 10%) and 2,2-dimethyl-1-(*p*-nitrophenyl)-propan-1-ol (35) (88 mg, 17%).

(x) Reaction with the sodium salt (13) of diethyl t-butylmalonate (expt 21)

The crude product was purified by p.l.c. with 15% ethyl acetate/light petroleum as eluent to afford *p*-(2,2-dimethylpropyl)nitrobenzene (36) (43 mg, 9%) and *p*-nitropivalophenone (34) (83 mg, 10%).

(xi) Reaction with the sodium salt (14) of methyl 2-methylacetoacetate (expt 22)

The crude product was purified by p.l.c. with 15% ethyl acetate/light petroleum as eluent to afford *p*-(2,2-dimethylpropyl)nitrobenzene (36) (216 mg, 45%), starting material (1) (45 mg, 8%), a band which could not be further purified and which contained *methyl* (E)- and (Z)-*2-methyl-3-[2',2'-dimethyl-1'-(p-nitrophenyl)propanoxy]butenoate* (31) and (32) (56 mg, 7%) (Found: C, 63.6; H, 7.2; N, 4.0. $C_{17}H_{23}NO_5$ requires C, 63.5; H, 7.2; 4.4%). ^{1}H n.m.r.: (major isomer) δ 0.988, s, Bu^t; 1.995, q, *J* 1.5 Hz, Me; 2.139, q, *J* 1.5 Hz, Me; 3.665, s, OMe; 4.918, s, benzylic H; 7.38, m, 2H *meta* to NO_2; 8.45, m, 2H *ortho* to NO_2. ^{1}H n.m.r.: (minor isomer) δ 0.992, s, Bu^t; 2.014, q, *J* 1.5 Hz, Me; 2.160, q, *J* 1.5 Hz, Me; 3.662, s, OMe, 4.929, s, benzylic H; 7.53, m, 2H *meta* to NO_2; 8.45, m, 2H *ortho* to NO_2. Ratio of major to minor isomer 1.9:1. ν_{max} 2890, 1695, 1625, 1520, 1400, 1300 - 1220 (br), 1160, 870 cm^{-1}. λ_{max} (ethanol) 256 nm (ε 19600). *m/z* 321 (M; 0.08%), 192 (17), 153 (45), 150 (61), 136 (29), 135 (33), 131 (14), 130 (72), 115 (11),

99 (13), 98 (27), 91 (11), 77 (11), 73 (18), 59 (12), 57 (89), 55 (11), 45 (10), 44 (15), 43 (100), 41 (46), 39 (16). and *methyl 2-acetyl-2,4,4-trimethyl-3-(p-nitrophenyl) pentanoate* (30) (16 mg, 2%), a pale yellow oil (High resolution mass spectrum: M^+ - Me 306.1334. $C_{16}H_{20}NO_5$ requires 306.1341). ^1H n.m.r.: δ 0.97, s, Bu^t; 1.89, s, C(Ac)-(CO_2Me)Me; 2.23, s, COMe; 3.19, s, CO_2Me; 4.09, s, benzylic H; 7.48, m, 2H *meta* to NO_2; 8.12, m, 2H *ortho* to NO_2. ν_{max} 2910, 1715, 1390, 1130, 865 cm^{-1}. λ_{max} (ethanol) 275 nm (ε 9270). *m/z* 321 (M; 0.1%), 306 (1), 223 (64), 222 (41), 206 (29), 205 (43), 190 (10), 130 (14), 116 (12), 115 (20), 57 (100), 43 (93), 41 (38).

(xii) Reaction with the sodium salt (15) of 3-methyl-2,4-pentanedione (expts 24 and 25)

The crude product was purified by p.l.c. with 10% ethyl acetate light petrol as eluent to give *p*-(2,2-dimethylpropyl)nitrobenzene (36) [270 mg, 56% (expt 24); 367 mg, 76% (expt 25)]

(xiii) Reaction with the sodium salt (16) of *p*-toluenesulfonic acid (expts 26 and 27)

Without entrainment (expt 26)

The reaction gave only unchanged starting material (1) (512 mg, 90%).

Entrained with lithium 2-nitropropan-2-ide (expt 27)

The crude reaction product was purified by p.l.c. with 15% ethyl acetate/light petroleum as eluent to afford *p*-nitropivalophenone (34) (21 mg, 4%) and 2,2-dimethyl-1-(*p*-nitrophenyl)propyl *p*-tolyl sulfone (33) (591 mg, 68%), m.p. and m.m.p. 139 - 140° (lit.[20] 139 - 140°).

(xiv) Reaction with the sodium salt (17) of diethyl phosphite (expt 30)

The crude reaction product was purified by p.l.c. with 10% ethyl acetate/light petroleum as eluent to afford starting material (1) (88 mg, 31%), *p*-nitropivalophenone (34) (31 mg, 12%) and 2,2-dimethyl-1-(*p*-nitrophenyl)propan-1-ol (35) (24 mg, 9%).

(xv) Reaction with quinuclidine (18) (expt 31)

The crude reaction product was purified by p.l.c. with 10% ethyl acetate/light petroleum as eluent to give starting material (1) (105 mg, 37%) and *p*-nitropivalophenone (34) (28 mg, 11%).

(xvi) Reaction of *p*-(1-chloro-2,2-dimethylpropyl)nitrobenzene (1) in the absence of nucleophiles (expt 32)

p-(1-Chloro-2,2-dimethylpropyl)nitrobenzene (1) was dissolved in hexamethylphosphoramide (5.0 ml) at 65°. The solution was degassed in a stream of nitrogen for 15 minutes and sealed under a nitrogen atmosphere. The reaction vessel

was irradiated with a 500-W GE sunlamp placed 20 cm from the flask. After 24 hours the solution was worked up to give starting material (1) (233 mg, 82%).

E. Reactions of 1-Chloro-2,2-dimethylpropylbenzene (3) with Nucleophiles

These reactions were performed under the conditions and for the times given in Table 1.

(i) Reaction with sodium azide (4) (expt 5)

The reaction product could not be separated from the starting material by p.l.c. in light petroleum. The yields of chloride (90%) and the presumed product *1-azido-2,2-dimethylpropylbenzene* (21) ($\leq$ 4%) were estimated by ^{1}H n.m.r. spectroscopy. The following parameters for the azide (21) were obtained. ν_{max} 2105 cm^{-1}. ^{1}H n.m.r.: δ 4.59, s, benzylic H.

(ii) Reaction with the sodium salts (5), (8), (10), (14) and (16) (expts 8, 12, 18, 23, 28, 29)

All these reactions afforded moderate to good recoveries of starting material (3) only.

F. Reactions of *p*-(1,2-Dimethyl-1-nitropropyl)nitrobenzene (2) with Nucleophiles

These reactions were performed under the conditions and for the times given in Table 2.

(i) Reactions-with sodium azide (4) (expts 1 and 2)

Without entrainment (expt 1)

The reaction gave only unchanged starting material (2) (214 mg, 90%).

Entrained with lithium 2-nitropropan-2-ide (expt 2)

The crude reaction product was purified by p.l.c. with light petroleum as eluent to afford p-*(1-azido-1,2-dimethylpropyl)nitrobenzene* (39) (176 mg, 75%), a pale yellow oil (Found: C, 56.4, H, 6.1; N, 23.7. $C_{11}H_{14}N_4O_2$ requires C, 56.4; H, 6.0; N, 23.9%). ^{1}H n.m.r.: δ 0.84, d, J 6.7 Hz, MeCHMe; 0.87, d, J 6.7 Hz, MeCHMe; 1.73, s, CH_3; 2.04, m, MeCHMe; AA'XX' system: 7.57, m, 2H *meta* to NO_2; 8.22, m, 2H *ortho* to NO_2; $J_{AX} + J_{AX'}$ 9.0 Hz. ν_{max} 2960, 2105, 1600, 1520, 1400, 1290, 870 cm^{-1}. λ_{max} (ethanol) 273 nm (ε 9630). *m/z* 206 ($M-N_2$; 2%), 192 (10), 191 (13), 164 (18), 163 (62), 150 (27), 149 (17), 147 (14), 118 (19), 117 (90), 103 (15), 77 (18), 76 (68), 75 (20), 51 (16), 50 (32), 43 (100), 42 (30), 41 (52), 39 (23).

(ii) Reactions with the sodium salt (5) of ethylmalononitrile (expts 3 and 4)

Under nitrogen (expt 3)

The crude reaction product was purified by p.l.c. with 20% ethyl acetate/light petroleum as eluent to afford *p*-(1,2-dimethylpropyl)nitrobenzene (47) (15 mg, 3%), starting material (2) (107 mg, 18%) and *2-[1',2'-dimethyl-1'-(p-nitrophenyl)propyl]-2-ethylmalononitrile* (40) (425 mg, 60%), which was recrystallised from pentane to give pale yellow needles, m.p. 94-96° (Found: C, 67.0; H, 6.8; N, 14.5. $C_{16}H_{19}N_3O_2$ requires C, 67.3; H, 6.7; N, 14.7%). ^{1}H n.m.r.: δ 0.67, d, *J* 6.8 Hz, MeCHMe; ABC_3 system (CH_2Me): 1.07, m, H_A; 1.21, t, Me; 1.63, m, H_B; $J_{AC} = J_{BC}$ 7.2 Hz; 1.42, d, *J* 6.8 Hz, MeCHMe; 1.63, s, benzylic Me; 2.94, septet, *J* 6.8 Hz; 7.73, m, 2H *meta* to NO_2; 8.26, m, 2H *ortho* to NO_2. ν_{max} 2960, 2245, 1600, 1515, 1390, 870 cm^{-1}. λ_{max} (ethanol) 267 nm (ε 11230). *m/z* 285 (M; 2%), 243 (33), 217 (14), 216 (100), 214 (67), 199 (18), 192 (66), 169 (16), 168 (27), 155 (18), 150 (99), 146 (15), 140 (11), 136 (17), 131 (17), 130 (10), 129 (10), 128 (11), 115 (20), 104 (12), 91 (13), 77 (13), 70 (42), 43 (98), 41 (37), 39 (13).

Under oxygen (expt 4)

The crude reaction product was purified by p.l.c. with 20% ethyl acetate/light petroleum as eluent to afford 2-[1',2'-dimethyl-1'-(*p*-nitrophenyl)propyl]-2-ethylmalononitrile (40) 11 mg, 6%), identical with the sample prepared above, *p*-nitroacetophenone (45) (8 mg, 8%), m.p. 76-78° (lit.[68] 81°), and 1,2-dimethyl-1-(*p*-nitrophenyl)propan-1-ol (46) (38 mg, 29%), m.p. 49-50° (lit.[32] 48-49°).

(iii) Reaction with the sodium salt (6) of isopropylmalononitrile (expt 5)

The crude reaction product was purified by p.l.c. with 20% ethyl acetate/light petroleum as eluent to afford *p*-(1,2-dimethylpropyl)nitrobenzene (47) (63 mg, 26%) and *2-[1',2'-dimethyl-1'-(p-nitrophenyl)propyl]-2-isopropylmalononitrile* (41) (67 mg, 18%), m.p. 121-122° (Found: C, 68.3; H, 7.0; N, 14.3. $C_{17}H_{21}N_3O_4$ requires C, 68.2; H, 7.1; N, 14.0%). ^{1}H n.m.r.: δ 0.59, d, *J* 6.6 Hz, benzylic MeCHMe; 0.98, d, *J* 6.6 Hz, MeCHMe; 1.22, d, *J* 6.6 Hz, MeCHMe; 1.40, d, *J* 6.6 Hz, benzylic MeCHMe; 1.66, septet, *J* 6.6 Hz, MeCHMe; 1.70, s, benzylic Me; 2.90, septet, *J* 6.6 Hz, benzylic MeCHMe; 7.79, m, 2H *meta* to NO_2; 8.27, m, 2H *ortho* to NO_2. ν_{max} 2970, 2250, 1600, 1520, 1400, 870 cm^{-1}. λ_{max} (ethanol) 268 nm (ε 10000). *m/z* 299 (M; 0.5%), 256 (5), 230 (11), 214 (27), 197 (14), 192 (13), 176 (14), 150 (26), 130 (13), 43 (100), 41 (38), 39 (13).

(iv) Reaction with the sodium salt (8) of ethyl 2-cyanopropionate (expt 6)

The crude product was purified by p.l.c. with 20% ethyl acetate/light petroleum as eluent to give *p*-(1,2-dimethylpropyl)nitrobenzene (47) (50 mg, 10%), and a band which was further purified by repetitive p.l.c. with 5% ethyl acetate/light petroleum as eluent to afford:

Ethyl (2RS, 2SR)-2-cyano-2,3,4-trimethyl-3-(p-nitrophenyl)pentanoate (42) (100 mg, 13%) a pale yellow oil

(Found: C, 63.9; H, 7.0; N, 8.8. $C_{17}H_{22}N_2O_4$ requires C, 64.1; H, 7.0; N, 8.8%). ^{1}H n.m.r.: δ 0.59, d, *J* 6.7 Hz, MeCHMe; ABX_3 system (CO_2CH_2Me): 0.97, t, Me; 3.72, m, H_A: 3.85, m, H_B; $J_{AX} = J_{BX}$ 7.8 Hz, J_{AB} 11.9 Hz; 1.32, d, *J* 6.7 Hz, MeCHMe; 1.54, s, C(CN)(CO_2Et)Me; 1.66, s, benzylic Me; 2.87, septet, *J* 6.7 Hz, MeCHMe; 7.70, m, 2H *meta* to NO_2; 8.17, m, 2H *ortho* to NO_2. ν_{max} 2970, 2250, 1745, 1600, 1520, 1395, 1290 - 1260 (br), 875 cm^{-1}. λ_{max} (ethanol) 272 nm (ε 10820). *m/z* 318 (M; 0.7%), 249 (11), 245 (20), 204 (25), 203 (99), 193 (11), 192 (86), 186 (20), 177 (13), 157 (18), 151 (12), 150 (100), 146 (15), 136 (14), 131 (17), 130 (18), 129 (14), 128 (12), 104 (10), 91 (12), 77 (10), 55 (14), 43 (43), 41 (24), 39 (10).

Ethyl (2RS, 3RS)-2-cyano-2,3,4-trimethyl-3-(p-nitro phenyl)pentanoate (43) (142 mg, 18%), a pale yellow oil (Found: C, 63.9; H, 6.9; N, 8.8. $C_{17}H_{22}N_2O_4$ requires C, 64.1; H, 7.0; n, 8.8%). ^{1}H n.m.r.: δ 0.65, d, *J* 6.7 Hz, MeCHMe; ABX_3 system (CO_2CH_2Me): 1.18, t, Me, 3.96, m, H_A; 4.04, m, H_B; $J_{AX} = J_{BX}$ 7.2 Hz, J_{AB} 11.0 Hz; 1.26, d, *J* 6.7 Hz, MeCHMe; 1.51, s, C(CN)(CO_2Et)Me; 1.71, s, benzylic Me; 2.84, septet, *J* 6.7 Hz, MeCHMe; 7.63, m, 2H *meta* to NO_2; 8.19, m, 2H *ortho* to NO_2. ν_{max} 2970, 2240, 1735, 1610, 1525, 1400, 1275, 1170, 875 cm^{-1}. λ_{max} (ethanol) 271 nm (ε 10570). *m/z* 318 (M; 0.8%), 245 (13), 204 (15), 203 (61), 193 (10), 192 (83), 186 (22), 166 (16), 157 (12), 150 (82), 146 (13), 136 (14), 131 (13), 130 (12), 129 (11), 115 (13), 91 (11), 88 (11), 88 (11), 86 (63), 84 (100), 77 (10), 55 (14), 51 (10), 49 (17), 47 (21), 43 (50), 41 (23), 39 (10).

(v) Reaction with the sodium salt (10) of diethyl methylmalonate (expt 7)

The crude reaction product was purified by p.l.c. with 20% ethyl acetate/light petroleum as eluent to give *p*-(1,2-dimethylpropyl)nitrobenzene (47) (63 mg, 13%), starting material (2) (54 mg, 9%) and *diethyl 2-[1',2'-dimethyl-1'-(p-nitrophenyl)propyl]-2-methylmalonate* (44) (174 mg, 19%), a pale yellow oil (Found: C, 62.5; H, 7.3; N, 4.2. $C_{19}H_{27}NO_6$ requires C, 62.5; H, 7.5; N, 3.8%). ^{1}H n.m.r.: δ 0.57, d, *J* 6.6 Hz, MeCHMe; 1.10, d, *J* 6.6 Hz, MeCHMe; ABX_3 system (CO_2CH_2Me): 1.10, t, Me; 3.93, m, H_A; 3.99, m, H_B; $J_{AX} = J_{BX}$ 7.2 Hz, J_{AB} 10.8 Hz; ABX_3 system (CO_2CH_2Me): 1.19, t, Me; 4.06, m, H_A and H_B; $J_{AX} = J_{BX}$ 7.2 Hz; 1.47, s, $C(CO_2Et)_2Me$; 1.67, s, benzylic Me; 3.13, septet, *J* 6.6 Hz, MeCHMe; 7.69, m, 2H *meta* to NO_2; 8.11, m, 2H *ortho* to NO_2. ^{13}C n.m.r. (fully decoupled): δ 13.6, 16.1, 18.8, 19.4, 20.1, 33.4, 37.9, 50.5, 61.1, 122.2, 129.3, 146.1, 153.4, 170.7, 171.0. ν_{max} (liquid film) 2975, 1745, 1540, 1420, 1310, 1152, 900 cm^{-1}. λ_{max} (ethanol) 275 nm (ε 9360). *m/z* 365 (M; 0.5%), 323 (31), 277 (14), 250 (15), 249 (27), 248 (10), 232 (12), 230 (10), 220 (20), 204 (27), 203 (11), 202 (10), 192 (48), 175 (14), 174 (100), 151 (11), 150 (65, 146 (14), 136 (12), 131 (17), 130 (29, 129 (58), 115 (17), 100 (15), 91 (11), 44 (25), 43 (31), 41 (18).

G. Reactions of α,*p*-Dinitrocumene (48), *p*-Nitrobenzyl chloride (49) and *p*-(1-Chloro-2-methylpropyl)nitrobenzene (50) with Nucleophiles

These reactions were performed under the conditions and for the times given in Table 3.

(i) Reaction of α,*p*-dinitrocumene (48) with the sodium salt (15) of 3-methyl-2,4-pentanedione (expt 1)

The crude reaction product was purified by p.l.c. with 20% ethyl acetate/light petroleum as eluent to afford *p*-nitrocumene (55) (10 mg, 2%) and *3-methyl-3-(p-nitrocumyl)-2,4-pentanedione* (213 mg, 31%), which was recrystallized from light petroleum to give pale yellow needles, m.p. 100-101° (Found: C, 65.1; H, 6.9; N, 5.1. $C_{15}H_{19}NO_4$ requires C, 65.0: H, 6.9; N, 5.1%). ^{1}H n.m.r.: δ 1.50, s, Me; 1.63, s, $ArC\underset{\sim\sim}{Me}_2$; 1.93, s, $C(CO\underset{\sim\sim}{Me})_2Me$; AA'XX' system: 7.60, m, 2H *meta* to NO_2; 8.14, m, 2H *ortho* to NO_2; $J_{AX} + J_{AX'}$ 9.1 Hz. ν_{max} 2970, 1710, 1600, 1510, 1390, 865 cm^{-1}. λ_{max} (ethanol) 274 nm (ε 10800). *m/z* 277 (M; 0.5%), 220 (6), 164 (24), 114 (10), 99 (10), 43 (100).

(ii) Reaction of *p*-nitrobenzyl chloride (49) with the sodium salt (15) of 3-methyl-2,4-pentanedione (expts 2 and 3)

Under nitrogen (expt 2)

The crude reaction product was purified by p.l.c. with 20% ethyl acetate/light petroleum as eluent to afford *3-methyl-3-(p-nitrobenzyl)-2,4-pentanedione* (52) (305 mg, 49%), a pale yellow oil (Found: C, 62.5; H, 62.6; N, 5.7. $C_{13}H_{15}NO_4$ requires C, 62.6; H, 6.1: n, 5.6%). ^{1}H n.m.r.: δ 1.31, s, $C(COMe)_2\underset{\sim\sim}{Me}$; 2.15, s, $C(\underset{\sim\sim}{COMe})_2Me$; 3.27, s, benzylic CH_2; AA'XX' system: 7.28, m, 2H *meta* to NO_2; 8.12, m, 2H *ortho* to NO_2; $J_{AX} + J_{AX'}$ 8.8 Hz. ν_{max} (liquid film) 1700, 1600, 1520, 1400, 870 cm^{-1}. λ_{max} (ethanol) 274 nm (ε 10100). *m/z* 249 (M; 0.4%), 207 (15), 43 (100), and 3-(*p*-nitrobenzyl)-2-butanone (53) (119 mg, 23%), which was recrystallized from pentane to give colourless prisms, m.p. 57.5-59° (lit.[35] 54°). ^{1}H n.m.r.: $ABMX_3$ system [$CH_2C(Me)H$]: δ 1.15, d, CH_3; 2.67, m, H_A; 2.88, m, H_M; 3.13, m, H_B; $J_{AM} = J_{BM}$ 7.3 Hz, J_{AB} 13.8 Hz, J_{MX} 7.2 Hz; 2.14, s, $\underset{\sim\sim}{COMe}$; AA'XX' system; 7.34, m, 2H *meta* to NO_2; 8.15, m, 2H *ortho* to NO_2; $J_{AX} + J_{AX'}$ 8.8 Hz.

In the dark with di-t-butyl nitroxide (expt 3)

The crude reaction product was purified by p.l.c. with 20% ethyl acetate/light petroleum as eluent to give 3-methyl-3-(*p*-nitrobenzyl)-2,4-pentanedione (52) (330 mg, 53%), identical with the sample prepared above and 3-(*p*-nitrobenzyl)-2-butanone (53) (72 mg, 14%), m.p. 57.5 - 59° (lit.[35] 54°).

(iii) Reaction of *p*-(1-chloro-2-methylpropyl)nitrobenzene (50) with the sodium salt (7) of t-butylmalononitrile (expt 4)

The crude reaction product was purified by p.l.c. with 15% ethyl acetate/light petroleum as eluent to afford *p*-(2-methylpropyl)nitrobenzene (56) (45 mg, 10%) and *2-[2'-methyl-1'-(p-nitrophenyl)propyl]-2-t-butylmalononitrile* (54) (390 mg, 52%), which was recrylstallized from pentane to give pale yellow needles, m.p. 105 - 106° (Found: C, 68.0; H, 7.0; N, 13.9. $C_{17}H_{21}N_3O_2$ requires C, 68.2; H, 7.1; N, 14.0%). ^1H n.m.r.: δ 0.86, d, *J* 6.8 Hz, MeCHMe; 1.12, s, Bu^t; 1.16, d, *J* 6.8 Hz, MeCHMe; 2.73, m, MeCHMe; 3.21, d, *J* 3.7 Hz; 7.64, m, 2H *meta* to NO_2; 8.24, m, 2H *ortho* to NO_2. ν_{max} 2970, 1610, 1525, 1400, 870 cm^{-1}. λ_{max} (ethanol) 268 nm (ε 11440). *m/z* 299 (M; 0.7%), 242 (24), 201 (15), 200 (37), 178 (16), 57 (100), 43 (47), 41 (30).

(iv) Reaction of *p*-(1-chloro-2-methylpropyl)nitrobenzene (50) with the sodium salt (12) of diethyl isopropylmalonate (expt 5)

The crude reaction product was purified by p.l.c. with 15% ethyl acetate/light petroleum as eluent to afford β,β-dimethyl-*p*-nitrostyrene (57) (22 mg, 5%), *p*-nitroisobutyrophenone (58) (43 mg, 9%) and 2-methyl-1-(*p*-nitrophenyl)propan-1-ol (57) (70 mg, 14%)

H. Oxidation of 2,2-Dimethyl-1-(*p*-nitrophenyl)propan-1-ol (35)

2,2-Dimethyl-1-(*p*-nitrophenyl)propan-1-ol (35) (45 mg, 0.22 mmol) was added to a solution of the sodium salt (10) of diethyl methylmalonate (0.186 mg, 1 mmol) in hexamethyl-

phosphoramide (10.0 ml) at 60°. A stream of oxygen was passed through the solution for 5 hours and the reaction was worked up. The crude reaction product was purified by p.l.c. with 20% ethyl acetate/light petroleum as eluent to afford *p*-nitropivalophenone (34) 5 mg, 11%) and starting material (35) (18 mg, 40%).

I. Attempted Hydrolysis of the *C*-alkylates (40) - (44)

Each of these *C*-alkylates (0.5 mmol) was shaken in an acidic aqueous ethanol solution made by adding ethanol (10 ml) to a hydrochloric acid solution (3 M; 5 ml) for 15 min. In every case unchanged starting material was recovered.

2. REVERSIBILITY AND COMPETITIVE STUDIES

A. Reversibility Studies Involving Reactions of *Aci*-Nitronates and *p*-Nitrobenzylic Substrates

The results of these reactions are shown in Table 4. The tetrabutylammonium salts[62] (72) and (73) (2.0 mmol) of 2-nitropropane and 2-nitrobutane were dissolved in hexamethylphosphoramide (6.0 ml) and deoxygenated in a stream of nitrogen for 15 minutes. The substrate (1.0 mmol) was added and the reactions maintained at 60 °C under nitrogen with irradiation from a 500-W GE lamp placed at 20 cm from the flask. Yields are isolated yields

(i) Reaction of α,*p*-dinitrocumene (48) with the tetrabutylammonium salt (72) of 2-nitropropane (expt 1)

The reaction yielded *p*-(1,1,2-trimethyl-2-nitropropyl)-nitrobenzene (68) (200 mg, 79%) which was recrystallized from ethyl acetate to give white needles, m.p. 208 - 210 (lit.[32] 209 - 210°). ^{1}H n.m.r.: δ 1.55, s, $C\underset{\sim\sim}{Me}_2C\underset{\sim\sim}{Me}_2$; AA'XX' system: 7.49, m, 2H *meta* to NO_2; 8.17, m, 2H *ortho* to NO_2; $J_{AX} + J_{AX'}$ 9.1 Hz.

(ii) Reaction of α,*p*-dinitrocumene (48) with the tetrabutyl ammonium salt (73) of 2-nitrobutane (expt 2)

The reaction yielded *p*-(1,1,2-trimethyl-2-nitrobutyl) nitrobenzene (69) (193 mg, 73%) which was recrystallized from methanol to give white needles, m.p. 108 - 109° (lit.[41] 105.5 - 106°). ^{1}H n.m.r.: ABX_3 system (CH_2Me): δ 0.82, t, Me; 1.62, m, H_A; 2.44, m, H_B; $J_{AX} = J_{BX}$ 7.0 Hz, J_{AB} 14.0 Hz; 1.44, s, Me; 1.55, s, CMe_2; AA'XX' system: 7.50, m, 2H *meta* to NO_2; 8.16, m, 2H *ortho* to NO_2; $J_{AX} + J_{AX'}$ 9.1 Hz.

(iii) Reaction of *p*-(1,1,2-trimethyl-2-nitropropyl)-nitrobenzene (68) with the tetrabutylammonium salt (73) of 2-nitrobutane (expt 3)

The reaction was worked up (ethyl acetate was chosen as the extraction solvent) and the crude reaction product was purified by p.l.c. with 30% ethyl acetate/light petroleum as eluent to afford *p*-nitrocumene (55) (22 mg, 13%) identical with a commercial sample (Fluka) and starting material (68) (204 mg, 81%) m.p. 208 - 210°.

(iv) Reaction of *p*-(1,1,2-trimethyl-2-nitrobutyl)-nitrobenzene (69) with the tetrabutylammonium salt (72) of 2-nitropropane (expt 4)

The crude reaction product was purified by p.l.c. with 30% ethyl acetate/light petroleum as eluent to afford *p*-nitrocumene (55) (30 mg, 18%), starting material (69) (135 mg, 51%), m.p. 108 - 109° and *p*-(1,1,2-trimethyl-2-nitropropyl)-nitrobenzene (68) (8 mg, 3%), m.p. 208 - 210°.

(v) Reaction of *p*-(1,1,2-trimethyl-2-nitrobutyl)-nitrobenzene (69) with the lithium salt (19) of 2-nitropropane (expt 5)

The reaction product was isolated and shown to be starting material (69) (253 mg, 96%), m.p. 108 - 109°.

B. Reactions of the Sodium Salts (83) and (84) of the Coumaranone Esters

o-Carboxyphenoxyacetic acid (98)[69] was esterified by standard procedures to yield ethyl *o*-carboethoxyphenoxy-acetate (99) and methyl *o*-carbomethoxyphenoxyacetate (100). Both were cyclised by the method of Friedlander[70] to give ethyl coumaranone-2-carboxylate (81), m.p. 63 - 65° (lit.[70] 65°) and methyl coumaranone-2-carboxylate (82), m.p. 102 - 103° (lit.[70] 105°). Excess sodium hydride was added to a solution of the appropriate ester (1.4 mmol) in dimethyl-formamide (10.0 ml), stirred for 5 minutes and filtered through sintered glass. The solution was deoxygenated in a stream of nitrogen for 15 minutes. The substrate (1.0 mmol) was added and the solution maintained at 30° under nitrogen with irradiation from a 250-W GE lamp at 10 cm from the flask. Yields are isolated yields.

(i) Reactions of *p*-nitrobenzyl chloride (49) with with sodium salt (83) of ethyl coumaranone-2-carboxylate (81)

Under Nitrogen (expt 1)

The crude reaction product was purified by p.l.c. with 50% ethyl acetate/light petroleum as eluent to afford *ethyl 3-p-nitrobenzyloxybenzofuran-2-carboxylate* (78) (< 2%), identical with that prepared below and *ethyl 2-p-nitrobenzyl-3-coumaranone-2-carboxylate* (77) (263 mg, 77%) which was recrystallized from ethanol to give white plates m.p. 108.5 - 110° (Found: C, 63.1; H, 4.7; N, 4.2 $C_{18}H_{15}NO_6$ requires C, 63.3; H, 4.4; N, 4.1%). ^1H n.m.r.: δ 1.22, t, *J* 7.2 Hz $CH_2\underset{\sim\sim}{Me}$; AB system (benzylic CH_2): 3.51, m, H_A; 3.69, m, H_B; J_{AB} 14.4 Hz; 4.22, q, *J* 7.2 Hz $\underset{\sim\sim}{CH_2}Me$; 6.96 - 7.70, m, 2H *meta* to NO_2 and 4H of coumaranone system, 8.05 2H *ortho* to NO_2, $J_{AX} + J_{AX'}$ 8.8 Hz. ν_{max} 1750, 1725, 1610, 1520, 1465, 1395, 1280 (br), 1170, 870 cm^{-1}. λ_{max} (ethanol) 260 nm (ε 14180) 330 nm (ε 4190). *m/z* 342 (M + 1; 11%), 341 (M; 51), 269 (57), 268 (100), 252 (29), 240 (29), 222 (28), 219 (30), 212 (10), 194 (13), 166 (12), 165 (25), 149 (21), 147 (17), 133 (18), 121 (71), 120 (17), 106 (12), 104 (11), 102 (12), 93 (14), 92 (18), 90 (17), 89 (21), 77 (13), 76 (41), 65 (19), 50 (12).

In the dark with p-*dinitrobenzene (expt 2)*

The crude reaction product was purified by p.l.c. with 30% ethyl acetate/light petroleum as eluent to afford *ethyl 3-p-nitrobenzyloxybenzofuran-2-carboxylate* (78) (114 mg, 33%), which was recrystallized from ethanol to give white needles, m.p. 144 - 145° (Found: C, 63.7; H, 4.5; N, 4.2. $C_{18}H_{15}NO_6$

requires C, 63.3; H, 4.4; N, 4.1%). ^{1}H n.m.r.: δ 1.43, t, *J* 7.1 Hz, $CH_2\underset{\sim}{Me}$; 4.46, q, *J* 7.1 Hz, $\underset{\sim}{CH_2}Me$; 5.59, s, benzylic CH_2; 7.17 - 7.80, m, 2H *meta* to NO_2 and 4H of benzofuran system; 8.25, m, 2H *ortho* to NO_2; $J_{AX} + J_{AX'}$ 8.8 Hz. ν_{max} 1710, 1600, 1520, 1395, 1190, 865 cm^{-1}. λ_{max} (ethanol) 282 nm (ε 25070). *m/z* 341 (M; 29%), 269 (17), 268 (26), 221 (14), 161 (11), 149 (100), 136 (40), 133 (78), 121 (48), 106 (24), 105 (11), 104 (15), 90 (36), 89 (28), 78 (31), 77 (16), 76 (25), 65 (12), 63 (12), 51 (13), 50 (10) and ethyl 2-*p*-nitrobenzyl-3-coumaranone-2-carboxylate (77) (123 mg, 36%), identical with that prepared above.

(ii) Reactions of *p*-nitrobenzyl chloride (49) with the sodium salt (84) of methyl coumaranone-2-carboxylate (82)

Under nitrogen (expt 3)

The crude reaction product was purified by p.l.c. with 50% ethyl acetate/light petroleum as eluent to afford *methyl 3-p-nitrobenzyloxybenzofuran-2-carboxylate* (80) (< 2%), identical with that prepared below and *ethyl 2-p-nitrobenzyl-3-coumaranone-2-carboxylate* (79) (242 mg, 74%), which was recrystallized from methanol to give white plates, m.p. 192 - 193° (Found: C, 62.1; H, 4.1; N, 4.2. $C_{17}H_{13}NO_6$ requires C, 62.4; H, 4.0; N, 4.3%). ^{1}H n.m.r.: AB system (benzylic CH_2): δ 3.52, m, H_A; 3.69, m, H_B; J_{AB} 14.0 Hz; 3.75, s, OMe; 6.95 - 7.70, m, 2H *meta* to NO_2 and 4H of coumaranone system; 8.05, m, 2H *ortho* to NO_2; $J_{AX} + J_{AX'}$

8.8 Hz. ν_{max} 1760, 1725, 1615, 1520, 1465, 1395, 1300 (br), 1180, 875 cm^{-1}. λ_{max} (ethanol) 258 nm (ε 13740) 330 nm (ε 3530). *m/z* 328 (M + 1; 12%), 327 (M; 68), 284 (24), 269 (17), 268 (100), 240 (28), 222 (22), 221 (28), 212 (15), 206 (13), 205 (99), 194 (13), 173 (11), 166 (19), 165 (33), 164 (11), 163 (61), 161 (14), 136 (24), 135 (30), 123 (20), 121 (96), 120 (24), 110 (13), 106 (37), 104 (22), 102 (13), 93 (16), 92 (33), 91 (11), 90 (27), 89 (34), 85 (21), 78 (24), 77 (38), 76 (64), 75 (14), 71 (30), 69 (12), 65 (24), 64 (18), 63 (26), 59 (31), 57 (55), 56 (14), 55 (17), 51 (19), 50 (26), 44 (13), 43 (42), 41 (30), 39 (27).

In the dark with p-*dinitrobenzene (expt 4)*

The crude reaction product was purified by p.l.c. with 30% ethyl acetate/light petroleum as eluent to afford *methyl 3-*p-*nitrobenzyloxybenzofuran-2-carboxylate* (80) (98 mg; 30%), which was recrystallized from methanol to give white plates, m.p. 183 - 184° (Found: C, 62.3; H, 4.0; N, 4.4. $C_{17}H_{13}NO_6$ requires C, 62.4; H, 4.0; N, 4.3%). ^1H n.m.r.: δ 4.10, s, OMe; 5.60, s, benzylic CH_2; 7.14 - 7.80, m, 2H *meta* to NO_2 and 4H of benzofuran system; 8.25, m, 2H *ortho* to NO_2; $J_{AX} + J_{AX'}$ 8.8 Hz. ν_{max} 1720, 1610, 1530, 1450, 1400, 1200, 870 cm^{-1}. λ_{max} (ethanol) 282 nm (ε 23800). *m/z* 327 (43), 284 (12), 268 (38), 207 (27), 205 (41), 164 (11), 163 (100), 136 (54), 135 (66), 121 (26), 120 (23), 106 (51), 105 (12), 104 (24), 92 (24), 90 (45), 89 (43), 79 (13), 78 (58), 77 (61), 76 (42), 71 (13), 64 (11), 63 (20), 59 (11), 57 (23), 51 (15), 50 (20), 43 (20), 41 (10), 39 (16) and

ethyl 2-*p*-nitrobenzyl-3-coumaranone-2-carboxylate (79) (110 mg, 34%), identical with that prepared above.

(iii) Reactions of ethyl 3-*p*-nitrobenzyloxybenzofuran-2-carboxylate (78) with the sodium salt (84) of methyl coumaranone-2-carboxylate (82)

(Expt 5)

The reaction afforded only starting material (78) (273 mg, 80%)

In the presence of p-*nitrobenzyl chloride (49)*

(expt 6)

The crude reaction product was purified by p.l.c. with 30% ethyl acetate/light petroleum to afford starting material (78) (246 mg; 72%) and methyl 2-*p*-nitrobenzyl-3-coumaranone-2-carboxylate (79) (200 mg, 61%), identical with that prepared above.

C. Reactions of *p*-Nitrobenzyl chloride (49) with the sodium salt (85) of ethyl 2-methylacetoacetate

Under Nitrogen

The sodium salt (85) (10 mmol) was prepared by a similar method to that described for reactions in 1 above and dissolved in dimethylformamide (10.0 ml). The reaction was deoxygenated in a stream of nitrogen for 15 minutes and *p*-nitrobenzyl chloride (49) (0.86 g, 5 mmol) added. The reaction solution

was maintained under nitrogen at 5° C for ten minutes and worked up. The crude reaction product was purified by p.l.c. with 15% ether/light petroleum as eluent to give *ethyl 2-methyl-2-p-nitrobenzylacetoacetate* (86) (1.26 g, 90%), which was recrystallized from ethanol to give white needles, m.p. 56 - 57°, (Found: C, 60.5; H, 6.5; N, 4.8. $C_{14}H_{17}NO_5$ requires C, 60.2; H, 6.1; N, 5.0%). ^1H n.m.r.: δ 1.25, t, $\underset{\sim\sim}{CH_2}Me$, *J* 7.1 Hz; 1.32, s, Me; 2.18, s, COMe; AB system (benzylic CH_2): 3.13, m, H_A; 3.37, m, H_B; J_{AB} 13.6 Hz; 4.19, m, CH_2Me; AA'XX' system: 7.30, 2H *meta* to NO_2; 8.15, 2H *ortho* to NO_2; $J_{AX} + J_{AX'}$ 8.8 Hz. ν_{max} 2940, 1715 (br), 1605, 1515, 1390, 870 cm^{-1}. λ_{max} (ethanol) 273 nm (ε 9380). *m/z* 279 (M; 2%) 237 (25), 236 (11), 164 (10), 43 (100).

In the presence of di-t-butyl nitroxide

The reaction was performed as above in the presence of di-t-butyl nitroxide (1.4 g, 10 mmol) and worked up after 30 minutes to give ethyl 2-methyl-2-*p*-nitrobenzylacetoacetate (86) (1.21 g, 86%) identical with that prepared above.

D. Competitive Reactions of *p*-(1-chloro-2,2-dimethylpropyl)-nitrobenzene (1) with Nucleophiles

The results of these reactions are shown in Table 6. The anionic solution for expt 1 was made by adding excess sodium hydride to a solution of ethylmalononitrile (120 mg, 1.25 mmol) in hexamethylphosphoramide (5.0 ml). The solution was filtered through sintered glass and sodium azide (4)

(80 mg, 1.25 mmol) was added. The reaction solution was deoxygenated in a stream of nitrogen for 15 minutes. The solution was then treated as set out in the Table.

The anionic solutions for expts 2 and 3 were made by dissolving equimolar amounts of the conjugate acids in hexamethylphosphoramide which were then treated as set out in the Table.

(i) Reaction with sodium azide (4) and the sodium salt of ethylmalononitrile (expt 1)

The reaction yielded only *p*-(1-azido, 2,2-dimethyl propyl)nitrobenzene (20) (80 mg, 55%), identical with that prepared above.

(ii) Reaction with the sodium salts (5) and (10) of ethylmalononitrile and diethyl methylmalonate (expt 2)

The reaction yielded only 2-[2',2'-dimethyl-1'-(*p*-nitrophenyl)propyl]-2-ethylmalononitrile (22) (180 mg, 100%).

(iii) Reaction with the sodium salts (10) and (11) of diethyl methylmalonate and diethyl ethylmalonate (expt 3)

The crude reaction product was purified by p.l.c. with 10% ethyl acetate/light petroleum as eluent to afford *p*-(2,2-dimethylpropyl)nitrobenzene (36) (24 mg, 5%) identical

with an authentic sample, diethyl 2-[2',2'-dimethyl-1'-(*p*-nitrophenyl)propyl]-2-ethylmalonate (29) (161 mg, 17%), identical with that prepared above, diethyl 2-[2',2'-dimethyl-1'-(*p*-nitrophenyl)propyl]-2-methylmalonate (28) (329 mg, 36%), identical with an authentic sample and 2,2-dimethyl-1-(*p*-nitrophenyl)propan-1-ol (35) (42 mg, 8%), identical with an authentic sample.

(iv) Reaction of (22) with sodium azide (4)

2-[2',2'-dimethyl-1'-(*p*-nitrophenyl)propyl]-2-ethylmalononitrile (22) (180 mg, 0.63 mmol) was dissolved in hexamethylphosphoramide (10.0 ml), and the solution was deoxygenated with a stream of nitrogen. Sodium azide (160 mg, 2.5 mmol) was added with lithium 2-nitropropan-2-ide (6 mg, 0.063 mmol) with stirring. The reaction was maintained at 60^{o} under nitrogen with irradiation from a 500 W-GE sunlamp 20 cm from the reaction vessel for six hours. Workup gave unchanged starting material (22) (164 mg, 91%).

3. DYNAMIC ^{1}H N.M.R. SPECTROSCOPY

A. Synthesis of Compounds

General Procedure

The nitro compound was dissolved in ethanol (10 ml) and hydrogenated over 10% palladium on charcoal (150 mg) at atmospheric pressure. When hydrogen uptake was complete, the reaction mixture was filtered through sintered glass and the solvent was removed to afford the amine which was immediately dissolved in carbon tetrachloride (10 ml). Acetic acid (17 M, 1 ml) and bromine (2.2 equivalents) were added and the reaction mixture stirred overnight at room temperature. The reaction solution was poured into water and methylene chloride (100 ml) was added. The organic phase was washed with sodium bicarbonate solution (10%, 3 x 100 ml), water (3 x 100 ml) and dried ($MgSO_4$). The solvent was evaporated to yield the crude product.

(i) 1-(4'-amino-3',5'-dibromophenyl)-2,2-dimethylpropyl *p*-tolyl sulfone (87)

2,2-Dimethyl-1-(*p*-nitrophenyl)propyl *p*-tolyl sulfone (33) (800 mg, 2.3 mmol) was treated as above to give, after recrystallization from methanol, pale needles of *1-(4'-amino-3',5'-dibromophenyl)-2,2-dimethylpropyl* p-*tolyl sulfone* (87) (400 mg, 37%), m.p. 184-185.5^o (Found: C, 46.0; H, 4.4; N, 3.3. $C_{18}H_{21}Br_2NO_2S$ requires C, 45.5; H, 4.5; N, 3.0%).

^{1}H n.m.r.: δ 1.26, s, Bu^t; 2.34, s, Me; 3.71, s, benzylic H; 4.54, br S, NH_2; AB system (2H *meta* to NH_2): 6.51, d, H_A; 7.93, d, H_B; J_{AB} 2.1 Hz; AA'XX' system: 7.11, m, 2H *meta* to SO_2; 7.40, m, 2H *ortho* to SO_2; $J_{AX} + J_{AX'}$ 8.4 Hz. ν_{max} 3490, 3385, 1610, 1470, 1355, 1170 cm^{-1}. λ_{max} (ethanol) 254 nm (ε 9740), 306 nm (ε 2840). *m/z* 477 (M + 4; 0.2%), 475 (M + 2; 0.4) 473 (M; 0.2), 322 (49), 320 (100), 318 (50), 264 (12), 91 (12), 69 (20), 41 (20).

(ii) 2-[1'-(4"-amino-3",5"-dibromophenyl-2',2'-dimethylpropyl]-2-ethylmalonitrile (88)

2-[2',2'-dimethyl-1'-(*p*-nitrophenyl)propyl]-2-ethylmalononitrile (22) (850 mg, 3.0 mmol) was treated as above to yield, after recrystallization from pentane, white needles of *2-[1'-(4"-amino-3",5"-dibromophenyl)-2',2'-dimethylpropyl]-2-ethylmalononitrile* (88) (450 mg, 36%) m.p. 141-143° (Found: C, 46.6; H, 4.7; N, 10.0. $C_{16}H_{19}Br_2N_3$ requires C, 46.5; H, 4.6; N, 10.2%). ^{1}H n.m.r.: δ 1.21, s, Bu^t; 1.21, m, $CH_2\underset{\sim}{Me}$; 1.67, m, $\underset{\sim}{CH_2}Me$; 2.71, s, benzylic H; 4.45, br s, NH_2; AB system (2H *meta* to NH_2): 7.06, d, H_A; 7.64, d, H_B; J_{AB} 2.1 Hz. ν_{max} 3485, 3385, 2250, 1615, 1475 cm^{-1}. λ_{max} (ethanol) 306 nm (ε 3060). *m/z* 415 (M + 4, 1%), 413 (M + 2, 3), 411 (M, 1), 330 (18), 328 (11), 320 (25), 318 (13), 57 (100), 41 (22).

(iii) 2-[1'-(4"-amino-3",5"-dibromophenyl)-2',2'-dimethylpropyl]-2-isopropylmalononitrile (89)

2-[2',2'-dimethyl-1'-(*p*-nitrophenyl)propyl]-2-isopropylmalononitrile (23) (400 mg, 1.3 mmol) was treated as above to give, after recrystallization from pentane, white needles of *2-[1'-(4"-amino-3",5"-dibromophenyl)-2',2'-dimethylpropyl]-2-isopropylmalononitrile* (89) (225 mg, 41%), m.p. 156 - 158° (Found: C, 48.0; H, 5.2; N, 9.6. $C_{17}H_{21}Br_2N_3$ requires C, 47.8; H, 5.0; N, 9.8%). ^{1}H n.m.r.: δ 1.01, d, *J* 6.5 Hz MeCHMe; 1.21, s, Bu^t; 1.27, d, *J* 6.5 Hz, MeCHMe; 1.93, m, MeCHMe; 2.78, s, benzylic H; 4.4, br s, NH_2; AB system (2H *meta* to NH_2): 7.09, d, H_A; 7.70, d, H_B; J_{AB} 2.25 Hz. ν_{max} 3480, 3380, 2245, 1620, 1475 cm^{-1}. λ_{max} (ethanol) 306 nm (ε 250). *m/z* 429 (M + 4, 1.5%), 427 (M + 2, 3%), 425 (M, 1.5%), 346 (12), 344 (26), 342 (13), 328 (13), 322 (14), 320 (29), 318 (14), 264 (10), 57 (100), 43 (31), 41 (40).

(iv) Ethyl (2*RS*, 3*RS*)-3-(4'-amino-3',5'-dibromophenyl)-2-cyano-2,4,4-trimethylpentanoate (90)

Ethyl (2*RS*, 3*RS*)-2-cyano-2,4,4-trimethyl-3-(*p*-nitrophenyl)pentanoate (24) (250 mg, 0.79 mmol) was treated as above to give, after recrystallization from ethanol, white needles of *ethyl (2RS, 3RS)-3-(4'-amino-3',5'-dibromophenyl)-2-cyano-2,4,4-trimethylpentanoate* (90) (160 mg, 45%), m.p. 150 - 152° (Found: C, 45.9; H, 4.9; N, 6.5. $C_{17}H_{22}Br_2N_2O_2$ requires C, 45.8; H, 5.0; N, 6.3%). ^{1}H n.m.r.: δ 1.09, s, Bu^t; 1.34, s, C(CO_2Et)(CN)Me; ABX_3 system (CO_2CH_2Me): 1.42, t, Me; 4.37, m, CH_2Me; $J_{AX} = J_{BX}$ 7.1 Hz; 3.1, s, benzylic H; 4.60, br s, NH_2; AB system (2H *meta* to NH_2): 7.21, d, H_A;

7.80, d, H_B; J_{AB} 2.22 Hz. ν_{max} 3490, 3390, 2255, 1745, 1620, 1480, 1280 - 1240 (br), 1150 cm^{-1}. λ_{max} (ethanol) 306 nm (2310). *m/z* 448 (M + 4, 7%) 446 (M + 2, 14), 444 (M, 7%), 391 (14), 389 (28), 387 (14), 365 (47), 364 (19), 363 (100), 361 (51), 322 (29), 310(62), 319 (21), 318 (47), 317 (32), 316 (25), 315 (15), 314 (10), 266 (26), 264 (42), 262 (17), 239 (12), 238 (48), 236 (51), 223 (11), 156 (22), 155 (22), 144 (12), 130 (20), 69 (17), 57 (94), 41 (47).

(v) Ethyl (2*RS*, 3*SR*)-3-(4'-amino-3',5'-dibromophenyl)-2-cyano-2,4,4-trimethylpentanoate (91)

Ethyl (2*RS*, 3*SR*)-2-cyano-2,4,4-trimethyl-3-(*p*-nitrophenyl)pentanoate (25) (250 mg, 0.79 mmol) was treated as above to give, after recrystallization from ethanol, white needles of *ethyl (2*RS, *3*SR*)-3-(4'-amino-3',5'-dibromophenyl)-2-cyano-2,4,4-trimethylpentanoate* (91) 150 mg, 43%), m.p. 121 - 123° (Found: C, 45.9; H, 5.1; N, 6.6. $C_{17}H_{22}Br_2N_2O_2$ requires C, 45.8; H, 5.0; N, 6.3%). ^1H n.m.r.: ABX_3 system (CO_2CH_2Me): δ 1.07, t, Me; 3.96, m, $\underset{\sim}{CH_2}Me$; $J_{AX} = J_{BX}$ 7.2 Hz; 1.12, s, $C(CO_2CH_2Me)(CN)\underset{\sim}{Me}$; 2.78, s, benzylic H; 4.38, br s, NH_2; AB system (2H *meta* to NH_2): 7.03, d, H_A; 7.76, d, H_B; J_{AB} 2.05 Hz. ν_{max} 3485, 3385, 2245, 1738, 1615, 1475, 1280 - 1230 (br), 1140 cm^{-1}. λ_{max} (ethanol) 306 nm (ε 2870). *m/z* 448 (M + 4; 6%), 446 (M + 2; 14%), 444 (M; 7), 391 (12), 389 (25), 387 (12), 365 (37), 363 (80), 361 (40), 322 (44), 320 (100), 319 (24), 318 (47), 317 (28), 316 (28), 315 (18), 266 (20), 264 (32), 262 (16), 239 (15), 238 (45), 237 (11), 236 (53), 156 (20), 155 (20), 144 (13), 120 (19), 69 (14), 57 (95), 43 (17), 41 (57).

(vi) Diethyl 2-[1'-(4"-amino-3",5"-dibromophenyl)-2',2'-dimethylpropyl]-2-methylmalonate (92)

Diethyl 2-[2',2'-dimethyl-1'-(*p*-nitrophenyl)propyl]-2-methylmalonate (28) (600 mg, 1.58 mmol) was treated as above to give, after recrystallization from pentane, white needles of *diethyl 2-[1'-(4"-amino-3",5"-dibromophenyl)-2',2'-dimethylpropyl]-2-methylmalonate* (92) (380 mg, 49%), m.p. 86.5 - 88° (Found: C, 46.6; H, 5.6; N, 2.6. $C_{19}H_{27}Br_2NO_4$ requires C, 46.3; H, 5.6; N, 2.8%). ^{1}H n.m.r.: δ 0.98, s, Bu^t; ABX_3 system (CO_2CH_2Me): 1.06, t, Me; 3.54, m, H_A; 3.62, m, H_B; $J_{AX} = J_{BX}$ 7.1 Me, J_{AB} 11.0 Hz; ABX_3 system (CO_2CH_2Me): 1.29, t, Me; 4.17, m, H_A; 4.25, m, H_B; $J_{AX} = J_{BX}$ 7.1 Hz, J_{AB} 7.1 Hz, J_{AB} 11.5 Hz; 1.64, s, $C(CO_2CH_2Me)_2\underset{\sim\sim}{Me}$; 3.62, s, benzylic H; 4.48, br s, NH_2; 7.24, m, 1 H *meta* to NH_2; 7.41, m, 1 H *meta* to NH_2.† ν_{max} 3480, 3380, 1725, 1610, 1460, 1270 (br), 1125 cm^{-1}. λ_{max} (ethanol) 300 nm (ε 3700). *m/z* 495 (M + 4; 2%), 493 (M + 2; 4), 491 (M, 2), 439 (24), 438 (54), 437 (52), 436 (100), 435 (26), 434 (48), 365 (13), 364 (11), 363 (26), 361 (12), 322 (17), 320 (60), 318 (63), 316 (21), 311 (11), 310 (33), 308 (63), 306 (36), 289 (11), 266 (26), 264 (54), 262 (28), 255 (11), 239 (23), 237 (20), 227 (13), 225 (12), 211 (16), 210 (14), 209 (15), 208 (11), 144 (17), 131 (18), 130 (81), 129 (16), 128 (11), 102 (14), 77 (13), 69 (16), 57 (95), 55 (12), 43 (38), 41 (90), 39 (18).

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† A low temperature (243 K) enabled the determination of the *meta* coupling constant, 1.95 Hz.

B. Variable Temperature ^{1}H n.m.r. Runs

All spectra were determined in (1,2-D_2)-1,1,2,2-tetrachloroethane with hexamethyldisilane as internal reference. The benzylic proton was decoupled for each spectrum and the probe temperature calibrated with ethylene glycol or methanol. The parameters $\Delta\nu_s$, J, $W_{h/2}$ were determined and the rate constants evaluated as detailed in the text (pp 139-148) values and full activation parameters for each compound are tabulated in Appendix I.

Appendix A

The tables 9 - 13 contain the full details of the n.m.r. stucies performed on the compounds (88) - (92). The value T(set) refers to the setting of the variable temperature control of the spectrometer.

Table 9(a). Lineshape analysis and kinetic parameters for 2-[1'-(4"-amino-3",5"-dibromopheny1)-2',2'-dimethylpropyl]-2-ethylmalononitrile (88). J_{AB} 2.1 Hz.

T(set)±2	T(K)±2	$\Delta\nu_s$ (Hz)	T_2^{eff} (s)	Rate (s^{-1})	$(RT)^{-1}x10^4$	ln k (exptl)	ln k (calc)	$\Delta H^{\ddagger}$ (kJ mol^{-1})	$\Delta S^{\ddagger}$ (J mol^{-1} K^{-1})	$\Delta G^{\ddagger}$ (kJ mol^{-1})
100	370.1	60.9	0.740	23.0 ± 1	3.250	3.135	3.179	70.1	-31.0	81.7 ± 0.6
110	382.6	62.1	0.579	55.0 ± 1	3.144	4.007	3.956	70.0	-31.3	81.8 ± 0.5
114	387.3	62.6	0.579	67.0 ± 2	3.105	4.205	4.235	69.9	-31.4	82.2 ± 0.6
116	389.6	62.8	0.568	76.0 ± 2	3.087	4.331	4.369	69.9	-31.4	82.3 ± 0.5
118	391.9	63.0	0.482	92.0 ± 2	3.069	4.522	4.502	69.9	-31.5	82.1 ± 0.5
120	394.0	63.3	0.388	108.0 ± 3	3.045	4.682	4.678	69.9	-31.5	82.3 ± 0.5
122	396.7	63.5	0.354	119.0 ± 3	3.032	4.779	4.773	69.8	-31.6	82.3 ± 0.5
126	401.4	64.0	0.335	150.0 ± 5	2.996	5.011	5.033	69.8	-31.7	82.6 ± 0.6

Eyring Parameters: $\Delta H^{\ddagger}$ = 70.6 ± 0.9 kJ mol^{-1}; $\Delta S^{\ddagger}$ = -29.6 ± 2.4 J mol^{-1} K^{-1}; $\Delta G^{\ddagger}_{380}$ = 81.8 ± 1.7 kJ mol^{-1}

Table 9(b). $\Delta\nu_s$ values at temperature ranges for slow exchange.

T(set)	$\Delta\nu_s$(exptl) Hz
50	54.9
60	56.25
70	57.45
80	58.5
90	59.7

Table 10(a). Lineshape analysis and kinetic parameters for 2-[1'-(4''-amino-3'',5''-dibromophenyl)-2,2'-dimethylpropyl]-2-isopropylmalononitrile (89). J_{AB} 2.25 Hz.

T(set)±2	T(K)±2	$\Delta\nu^s$ (Hz)	T_2^{eff} (s)	Rate (s^{-1})	$(RT)^{-1}\times10^4$	ln k (exptl)	ln k (calc)	$\Delta H^{\ddagger}$ kJ mol^{-1}	$\Delta S^{\ddagger}$ J mol^{-1} K^{-1}	$\Delta G^{\ddagger}$ kJ mol^{-1}
100	380.7	38.73	0.424	7.5 ± 0.5	3.159	2.015	2.028	76.1	-30.2	87.6 ± 0.7
110	391.1	39.38	0.430	14.0 ± 1.0	3.075	2.639	2.694	76.0	-30.4	88.1 ± 0.7
120	401.5	40.03	1.183	27.0 ± 1.0	2.996	3.296	3.325	75.9	-30.6	88.3 ± 0.6
126	407.8	40.42	0.637	40.0 ± 1.0	2.949	3.689	3.692	75.9	-30.8	88.4 ± 0.6
130	410.6	40.68	0.509	50.5 ± 1.0	2.929	2.922	3.852	75.8	-30.8	88.3 ± 0.5
132	414.0	40.81	0.485	59.0 ± 1.5	2.905	4.078	4.042	75.8	-30.9	88.5 ± 0.6
134	416.1	40.94	0.637	65.0 ± 1.5	2.891	4.174	4.158	75.8	-31.0	88.6 ± 0.5
136	418.2	41.07	0.707	71.0 ± 2.0	2.876	4.263	4.274	75.8	-31.0	88.8 ± 0.6
138	420.5	41.20	0.637	78.0 ± 2.0	2.860	4.357	4.398	75.8	-31.0	89.0 ± 0.6
140	422.3	41.33	0.796	86.0 ± 2.0	2.848	4.454	4.495	75.8	-31.1	89.0 ± 0.5

Eyring Parameters: $\Delta H^{\ddagger}$ = 76.5 ± 0.7 kJ mol^{-1}; $\Delta S^{\ddagger}$ = -29.2 ± 1.7 J mol^{-1} K^{-1}; $\Delta G^{\ddagger}_{380}$ = 87.6 ± 1.4 kJ mol^{-1}

Table 10(b). $\Delta\nu_s$ values at temperature ranges for slow exchange.

T(set)	$\Delta\nu_s$(exptl)
50	35.50
60	36.13
70	36.75
80	37.38
90	38.13

Table 11(a). Lineshape analysis and kinetic parameters for ethyl (2*RS*, 3*RS*)-3-(4'-amino-3',5'-dibromophenyl) 2-cyano 2,4,4-trimethylpentanoate (90). J_{AB} 2.22 Hz.

T(set)	T(K)±2	$\Delta\nu_s$ (Hz)	T_2^{eff}(s)	Rate (s^{-1})	$(RT)^{-1}x10^4$	ln k (exptl)	ln k (calc)	$\Delta H^{\ddagger}$ (kJ mol^{-1})	$\Delta S^{\ddagger}$ (J $mol^{-1}K^{-1}$)	$\Delta G^{\ddagger}$ (kJ mol^{-1})
90	370.8	35.66	0.835	26.0 ± 1.5	3.244	3.258	3.186	79.5	-5.9	81.4 ± 0.7
94	374.7	35.82	0.545	31.0 ± 1.5	3.210	3.434	3.465	79.5	-5.9	81.8 ± 0.6
96	376.7	35.91	0.545	36.0 ± 1.5	3.193	3.584	3.606	79.4	-6.0	81.8 ± 0.6
98	378.6	35.99	0.559	42.0 ± 2.0	3.177	3.738	3.738	79.4	-6.0	81.7 ± 0.6
100	380.6	35.08	0.863	47.0 ± 2.0	3.160	3.850	3.876	79.4	-6.1	81.8 ± 0.6
104	384.5	36.24	0.717	62.0 ± 3.0	3.128	4.127	4.140	79.4	-6.2	81.8 ± 0.6
110	390.4	36.50	0.585	96.0 ± 4.0	3.081	4.564	4.531	79.3	-6.3	81.7 ± 0.6

Eyring Parameters: $\Delta H^{\ddagger}$ = 78.8 ± 1.5 kJ mol^{-1}; $\Delta S^{\ddagger}$ = -7.6 ± 4 J mol^{-1} K^{-1}; $\Delta G^{\ddagger}_{380}$ = 81.7 ± 3.0 kJ mol^{-1}

Table 11(b). $\Delta\nu_s$ values at temperature ranges for slow exchange.

T(set)	$\Delta\nu$
30	33.13
40	33.55
50	34.00
60	34.38
70	34.63

Table 12(a). Lineshape analysis and kinetic parameters for ethyl (2*RS*, 3*SR*)-3-(4'-amino-3',5'-dibromophenyl)-2-cyano-2,4,4-trimethylpentanoate (91). J_{AB} 2.05.

T(set)	T(K)	$\Delta\nu_s$ (Hz)	T_2^{eff} (s)	Rate (s^{-1})	$(RT)^{-1}x10^4$	ln k (exptl)	ln k (calc)	$\Delta H^{\ddagger}$ (kJ mol^{-1})	$\Delta S^{\ddagger}$ (J $mol^{-1}K^{-1}$)	$\Delta G^{\ddagger}$ (kJ mol^{-1})
60	341.0	40.91	0.652	14.5 ± 0.75	3.527	2.674	2.715	65.9	-30.1	76.3 ± 0.6
70	350.7	41.28	0.435	29.0 ± 1.0	3.430	3.367	3.386	65.9	-30.3	76.5 ± 0.6
72	352.6	41.36	0.629	34.0 ± 1.0	3.411	3.526	3.513	65.8	-30.4	76.5 ± 0.6
74	354.6	41.43	0.364	38.5 ± 1.5	3.392	3.651	3.645	65.8	-30.4	76.6 ± 0.6
76	356.5	41.51	0.476	44.0 ± 1.5	3.374	3.784	3.770	65.8	-30.4	76.6 ± 0.6
78	358.5	41.58	0.443	50.0 ± 1.5	3.355	3.912	3.899	65.8	-30.5	76.7 ± 0.6
80	360.4	41.66	0.467	56.0 ± 2.0	3.337	4.025	4.021	65.8	-30.5	76.8 ± 0.6
82	362.3	41.73	0.519	64.5 ± 2.0	3.320	4.167	4.141	65.8	-30.6	76.8 ± 0.6
84	364.3	41.81	0.509	74.0 ± 2.5	3.302	4.304	4.267	65.8	-30.6	76.8 ± 0.6
90	370.1	42.03	0.549	95.0 ± 3.0	3.250	4.554	4.622	65.7	-30.8	77.3 ± 0.6

Eyring Parameters: $\Delta H^{\ddagger}$ = 66.2 ± 0.8 kJ mol^{-1}; $\Delta S^{\ddagger}$ = -29.5 ± 2.1 J mol^{-1} K^{-1}; $\Delta G^{\ddagger}_{380}$ = 77.4 ± 1.6 kJ mol^{-1}

Table 12(b). $\Delta\nu_s$ values at temperature ranges for slow exchange.

T(set)	$\Delta\nu$
30	39.80
34	39.95
36	40.00
40	40.15
44	40.33

Table 13(a). Lineshape analysis and kinetic parameters for diethyl 2-[1'-(4"-amino-3",5"-dibromophenyl)-2',2'-dimethylpropyl]-2-methylmalonate (92). J_{AB} 1.95 Hz.

T(K) ± 2	$\Delta\nu_s$ (Hz)	T_2^{eff} (s)	Rate (s^{-1})	$(RT)^{-1}x10^4$	ln k (exptl)	ln k (calc)	$\Delta H^{\ddagger}$ (kJ mol^{-1})	$\Delta S^{\ddagger}$ (J $mol^{-1}K^{-1}$)	ΔG (kJ mol^{-1})
309.3	17.57	0.522	18.5 ± 1.0	3.889	2.918	2.932	51.7	-53.8	68.3 ± 0.6
311.8	17.73	0.388	22.0 ± 1.0	3.857	3.091	3.102	51.6	-53.9	68.5 ± 0.6
314.1	17.89	0.379	26.0 ± 1.5	3.829	3.258	3.255	51.6	-53.9	68.6 ± 0.6
316.6	18.06	0.455	30.0 ± 1.5	3.799	3.401	3.419	51.6	-54.0	68.7 ± 0.6
318.6	18.19	0.461	36.0 ± 1.5	3.775	3.584	3.548	51.6	-54.0	68.7 ± 0.6
321.2	18.36	0.505	41.0 ± 1.5	3.745	3.714	3.714	51.6	-54.1	68.9 ± 0.6
323.6	18.52	0.383	48.5 ± 1.5	3.717	3.882	3.864	51.5	-54.2	69.0 ± 0.6
328.0	18.81	0.342	62.0 ± 2.5	3.667	4.127	4.135	51.5	-54.3	69.3 ± 0.6
332.8	19.14	0.346	82.0 ± 3.0	3.614	4.407	4.422	51.5	-54.4	69.6 ± 0.6

Eyring Parameters: $\Delta H^{\ddagger}$ = 51.6 ± 0.35 kJ mol^{-1}; $\Delta S^{\ddagger}$ = -54.0 ± 1.2 J mol^{-1} K^{-1}; $\Delta G^{\ddagger}_{380}$ = 72.1 ± 1.2 kJ mol^{-1}

Table 13(b). $\Delta\nu_s$ values of temperature ranges for slow exchange.

T(K)	$\Delta\nu_s$(exptl) Hz
248.8	13.6
256.0	14.00
260.4	14.44
273.8	15.20
285.4	16.00

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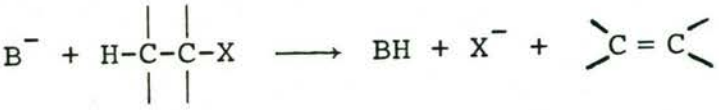
PART II

INTRODUCTION

INTRODUCTION

β-Elimination Reactions[1a]

Elimination reactions are amongst the earliest reactions whose mechanisms were systematically studied and established.[2] Ionic β-eliminations, of the general form shown in eqn (1), are the most widely known and studied.[1a]

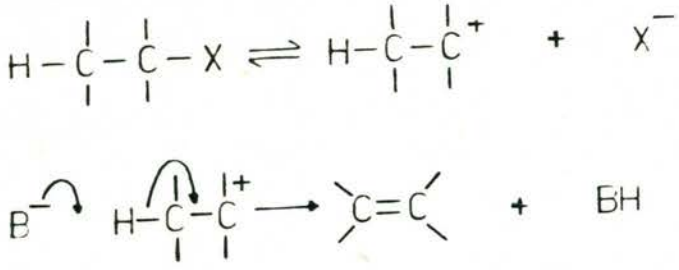


(1)

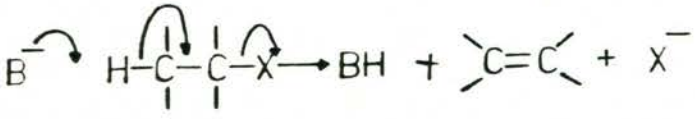
These β-eliminations are base- or solvent-promoted and are classified by the mechanism by which they proceed. There are three basic types of mechanism, which are shown in Scheme 1.[1a,3,4a]

It is now generally accepted[3] that these three types of mechanism are not totally discrete, but are 'snapshots' in a continuum[5] of mechanisms which vary from the pure *E*1 (elimination, unimolecular) through *E*2 (elimination, bimolecular) to the *E*1cB (elimination, unimolecular from the conjugate base) type of mechanism.

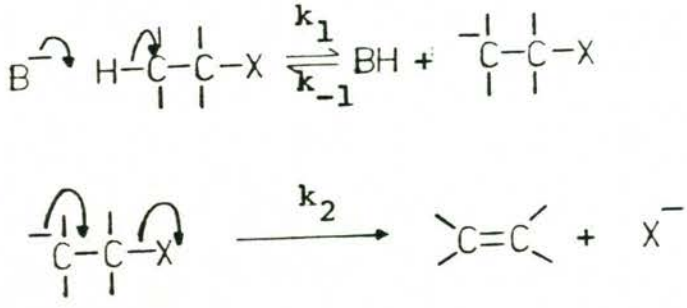
One of the factors influencing the elimination mechanism which operates in a particular reaction is the nature of the leaving group X. When X is an exceptionally good leaving group such as iodide, bromide or methanesulfonate the mechanism is *E*1 or *E*2 with a large amount of *E*1 character i.e., an *E*1-like *E*2 mechanism. With intermediate leaving groups, such as chloride, the mechanism is close to the *E*2 type. Poorer



*E*1



*E*2



*E*1cB

Scheme 1

leaving groups such as trimethylamine and dimethyl sulfide favour an *E*1cB-like *E*2 or an *E*1cB mechanism.[3]

Another factor which determines the mechanism of an elimination process is the acidity of the proton(s) β to the leaving group X. Very acidic protons, particularly when the leaving group is intermediate or poor, favour an *E*1cB mechanism,[3] whilst much less acidic protons favour the *E*2 or *E*1 processes.

The assignment of mechanistic type may be made on a number of criteria, the most important of which are reaction kinetics, isotopic effects and stereochemical product studies.

Reaction kinetics of β-eliminations

The rate of the *E*1 process shows a first order dependence on the substrate alone, whilst for the *E*2 process the rate is first order with respect to both substrate and base, and second order overall. The *E*1cB case is more complex[1a] and can be subdivided into three kinetic types. The rate equation can be shown to be that of eqn (2).[1a] If $k_1 >> k_{-1}$ the rate law

$$\text{rate} = k_1 k_2[\text{substrate}][\text{base}]/(k_1[\text{BH}] + k_2) \qquad (2)$$

becomes the relationship shown in eqn (3), which is indistinguishable from that for the *E*2 mechanism. If

$$\text{rate} = k_1[\text{substrate}][\text{base}] \qquad (3)$$

k_{-1} is greater than or approximately equal to k_1 there is an inverse dependence of the rate on the conjugate acid of the base. However, the detection of this process under these circumstances ($k_1 \approx k_{-1}$) is usually made by isotopic (usually deuterium) exchange between solvent and the intermediate carbanion. When decomposition of the carbanion is the rate determining step, a process rarely found, a third type of *E*lcB mechanism occurs in which the reaction rate is first order in substrate and zero order in base.[1b,3] In this latter process the carbanion is quantitatively formed before any appreciable loss of the nucleofuge occurs.

Isotope effects

In any reaction in which the rate determining step involves the cleavage of a carbon-hydrogen bond, there is a reduction in reaction rate when the hydrogen is replaced by deuterium.[1c,6] The zero-point energy of the *C-D* bond, E_0^D, is lower than that of the *C-H* bond, E_0^H: at 20 °C the difference is about 4.8 kJ mol^{-1}.[1c] If the bond is unaffected in the transition state there will be no observed isotope effect as the zero-point energy difference of the bond in the transition state will be identical to that same difference in the reactants. If the bond is completely broken before the transition state, once again there will be no primary isotope effect observed. It has been shown[1c] that the effect will be a maximum in an elimination process when the transition state is symmetrical, as shown in Figure 1.

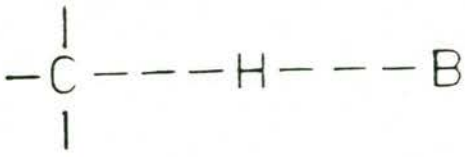


Figure 1

The value of k_H/k_D (where k_H is the rate of elimination of HX and k_D is the rate of elimination of DX) at 20 °C usually lies between 2 and 8.[3] For elimination reactions with second-order kinetics, k_H/k_D rises from low values for an E_1-like transition state [Figure 2(a)] to a maximum for an $E2$ transition state [Figure 2(b)] and then decreases for an $E1cB$-like transition state [Figure 2(c)].

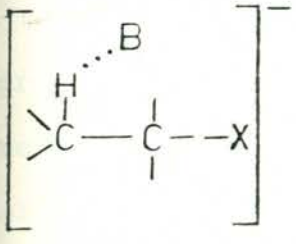


Figure 2(a)

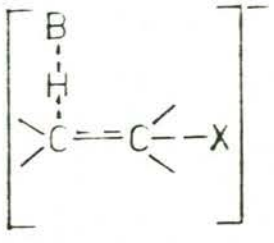


Figure 2(b)

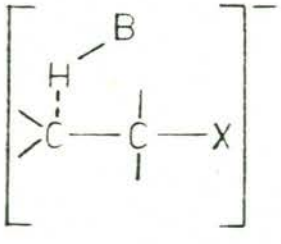


Figure 2(c)

From orbital arguments it is generally accepted that bimolecular eliminations will proceed most readily if the molecule is in, or close to, *syn*- or *anti*-periplanar conformations.[1d,3] Many *E*2 reactions proceed by an *anti*-periplanar conformation, and a number of theoretical reasons have been proposed to explain this observation.[1d,3] *Syn*-eliminations for such reactions are known but are rarer. There have been a number of reports of processes proceeding by both pathways.[7,8,9] Strong *anti*-stereospecificity has been in the past taken as virtual proof of an *E*2 mechanism. However, *E*1cB reactions may be stereospecific in an *anti*-periplanar sense, and so other factors must be considered.

Elimination of the Elements of Nitrous Acid. Nitrite Ion as a Nucleofuge

Although the nitrite ion has been known as a leaving group in S_NAr reactions for a considerable time, it is only recently that it has been reported as a leaving group in aliphatic systems. In fact, it has been stated that it 'generally fails to serve as a leaving group in substitution or elimination reactions by *ionic*[†] processes.'[10] The potent nucleophile *p*-$MeC_6H_4S^-$ has been reported to displace nitrite ion in an S_N2 reaction with nitromethane,[14] albeit slowly, and there has been a report of an intramolecular S_N2 displace-

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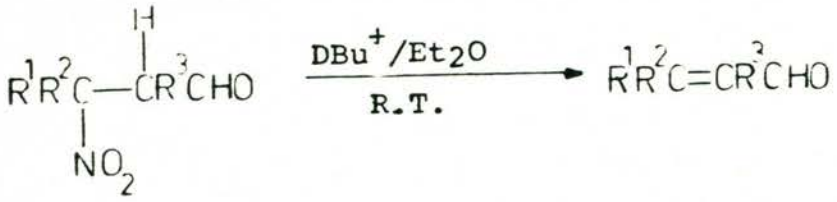
[†] Nitrite is a good leaving group in radical substitution ($S_{RN}1$) and elimination ($E_{RC}1$) processes.[11,12,13]

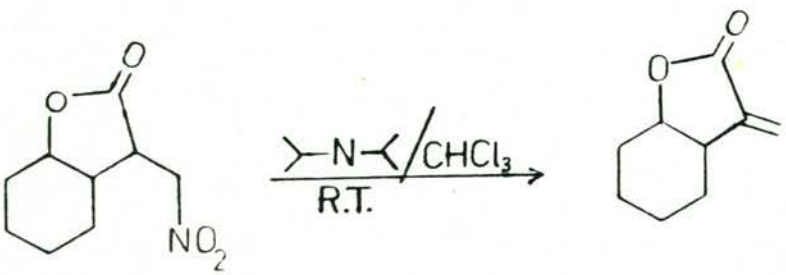
ment of nitrite ion.[15] Elimination reactions involving nitrite are somewhat more common. The necessity for a group which stabilizes developing negative charge β to the nitro group, however, is well recognized. When such a stabilizing (electron-withdrawing) group is present 'elimination of nitrous acid takes place readily to give olefins in good yield.'[10] A selection of these reactions, mostly taken from the more recent literature,[10,16-18] are given in eqns (4) - (7). Other examples are known,[19 - 26] but these also have an electron withdrawing group on the β-carbon. The absence of a large number of these elimination processes, particularly as a general synthetic method, is probably due to the competing ionization shown in eqn (8), which occurs when the nitro group is attached to a carbon which is primary or secondary and the β-electron-withdrawing substituent is absent.

$$B^- + R^1R^2CHNO_2 \longrightarrow \left[R^1R^2CNO_2\right]^- + HB \qquad (8)$$

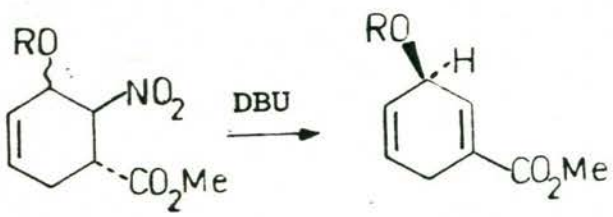
It might be expected that nitrite ion would be a poor leaving group, as nitrous acid is a relatively weak acid (*p*Ka 3.14),[27] and traditionally the nucleofugality of a group has been linked to the acidity of its conjugate acid.[4b] That is, the stronger the conjugate acid, the better the leaving



(4)[10]



(5)[16]



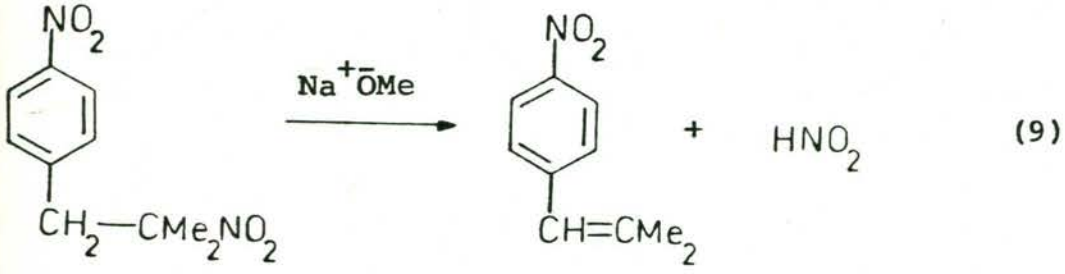
(6)[17]

$$R^1CCH(R)CMe_2NO_2 + B^- \longrightarrow R^1CC(R)=CMe_2 + \bar{N}O_2 + HB$$

(7)[18]

group. However, this correlation is not reliable in elimination processes, and indeed it has been stated that "Ranks of leaving groups (≡ nucleofugalities) in alkene forming eliminations are not related to the *pK*a of the conjugate acid ...',[28]

No quantitative studies on nitrous acid eliminations, except for indirect measurements on sequential elimination and addition reactions in 1,1,1-trinitroalkanes,[29] have been reported. The elimination of nitrous acid from the nitroalkane (1) [eqn (9)] had been observed,[13] and so it was decided to study this system further. Preliminary kinetic studies[30] of the elimination of nitrous acid from (1)



(1) (9)

indicated that the process was bimolecular and could be easily followed by u.v. spectroscopy. In this work it was decided to investigate the reaction of deuterated analogues of (1) in order to determine isotope effects, and to study analogous compounds with bromide and chloride as the leaving group to enable some ranking of nitrite as a nucleofuge in elimination processes. Studies of compounds with unsymmetrical substitution α to the aliphatic nitro group were also undertaken to determine the stereochemistry of elimination.

It was also decided to study elimination reactions of (2) and related compounds to determine what effect replacement of one of the benzylic hydrogens by a carbanion-stabilizing chlorine would have on the mechanism of the elimination process.

RESULTS AND DISCUSSION

RESULTS AND DISCUSSION

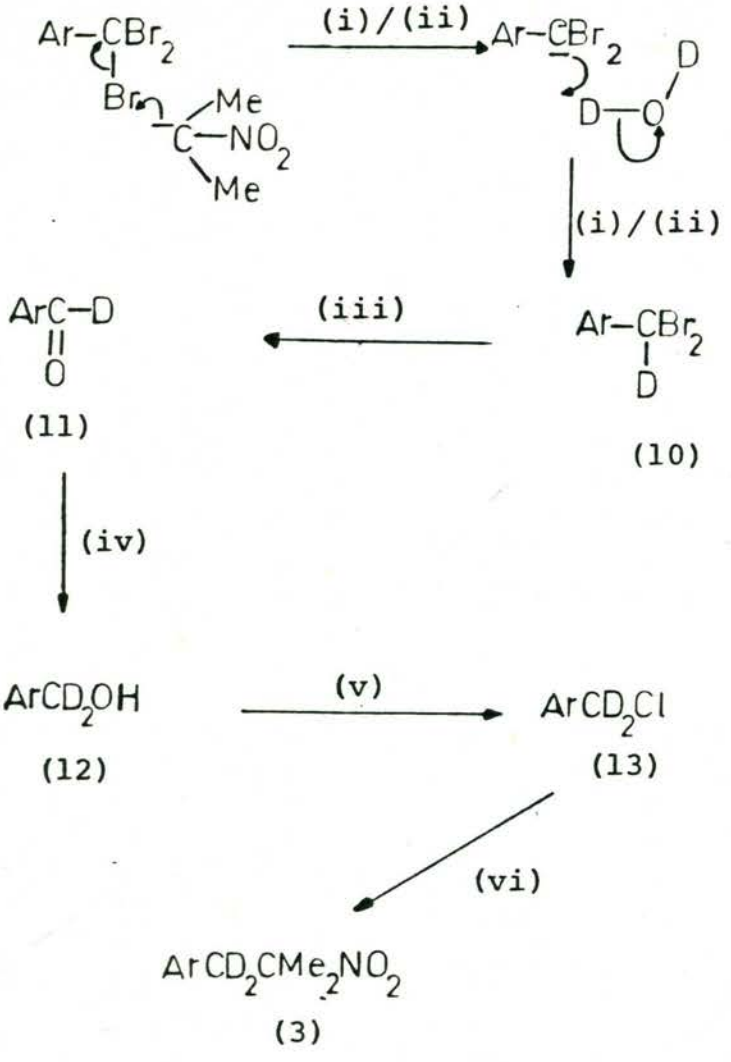
1. Preparation of Compounds and a Study of some Addition Reactions to β,β-Dialkylstyrenes

(a) Synthesis of Substrates

The compounds (3)-(8) required for kinetic studies were made as outlined below and in the Experimental.

The (D_2) compound (3) was prepared by the method outlined in Scheme 2. The tribromide (9) was converted to the α-deuterio dibromide (10) by a phase-transfer process. The anion of 2-nitropropane removes bromine from (9) and the resultant carbanion is deuterated.[32] Hydrolysis of the dibromide (10) was performed in the presence of silver(I) ion to give the aldehyde (11), which was reduced to the alcohol (12) with sodium cyanoborodeuteride. Treatment of the alcohol (12) with thionyl chloride gave the chloride (13) which was treated with lithium 2-nitropropan-2-ide (14) to give the (D_2) compound (3).

Reduction of *p*-nitrobenzaldehyde (16) to the alcohol (17), followed by chlorination gave (18) and an $S_{RN}1$ reaction of the salt (14) with (18) gave the monodeuterated compound (4). The preparation of the compounds (19a) and (19b) was performed by an $S_{RN}1$ reaction of the chloride (18) with lithium 2-nitrobutan-2-ide (15), under the same conditions employed in the synthesis of the undeuterated compound (8).[12]



(i) $NBu_4^+\bar{C}Me_2NO_2/CH_2Cl$; (ii) D_2O; (iii) $Ag^+/EtOH/H_2O$;

(iv) 1. $NaB(CN)D_3$/pH3-4/ MeOD, 2. H_2O; (v) $SOCl_2$;

(vi) $Li^+\bar{C}Me_2NO_2/HCONMe_2$

Scheme 2

The chloride (6) was prepared by addition of anhydrous hydrogen chloride to β,β-dimethyl-*p*-nitrostyrene (5) in the presence of iron(III) chloride. In similar fashion, the

bromide (7) was conveniently prepared by addition of anhydrous hydrogen bromide to the styrene (5) but, in contrast to the preparation of (6), no Lewis acid catalyst was required.

The α-deuterated compound (20) was synthesised by a straightforward $S_{RN}1$ reaction of the salt (14) with the dichloride (21).[13]

An attempt to synthesize the dichloro compound (22) by addition of chlorine to the styrene (5) under a variety of conditions (see Experimental) resulted in the isolation of a mixture of products (by mass spectroscopy) containing *three* or more chlorine atoms. ^1H N.m.r. also showed signals from methyl groups with one or two chlorine atoms present. Addition of chlorine to the unsubstituted styrene (23) gave a similar result. The dichloro compound (22) was successfully made by addition of anhydrous hydrogen chloride to the α-chlorostyrene (24) in the presence of iron(III) chloride.

The addition of deuterium chloride to the styrene (5) in the presence of iron(III) chloride proceeded smoothly to give a monochlorinated compound, which was homogeneous by t.l.c. and which had an R_f identical with the chloride (6). Examination of this product by ^1H n.m.r., however, showed it to be a mixture of products with varying amounts of deuterium incorporated into the methyl groups and the benzylic position and it was not the desired monodeuterated chloride (25). The benzylic signal in the ^1H n.m.r. spectrum of the product, at δ 3.13, comprised a triplet (ArCHD-) and a broad singlet ($ArCH_2$-) in the approximate ratio 1.45:1 [Figure 3 (a)].

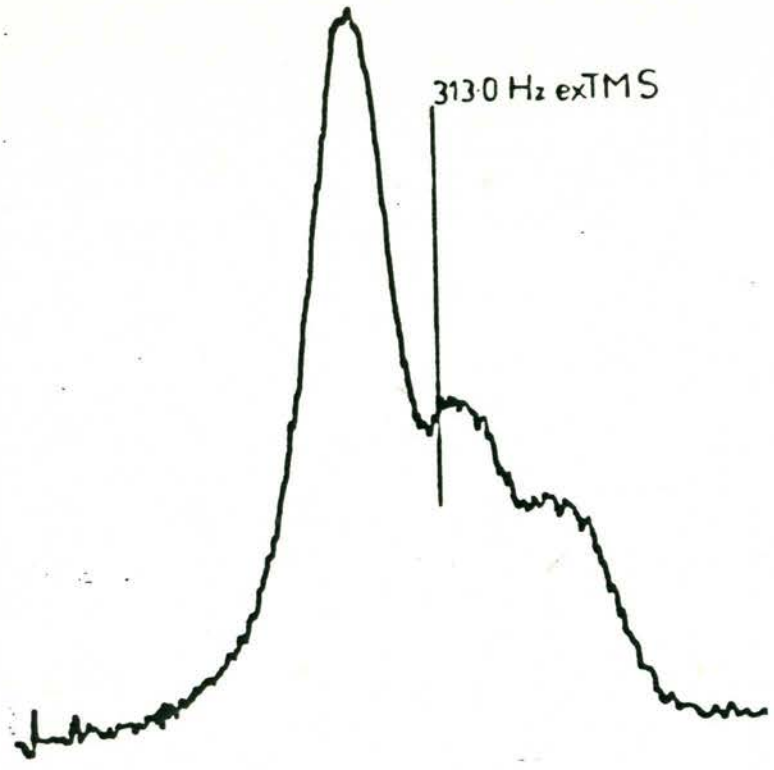


Figure 3(a). Expansion of the benzylic signal from the 100 MHz ^{1}H n.m.r. spectrum of the products resulting from the addition of DCl to the styrene (5). 1 cm = 1.38 Hz.

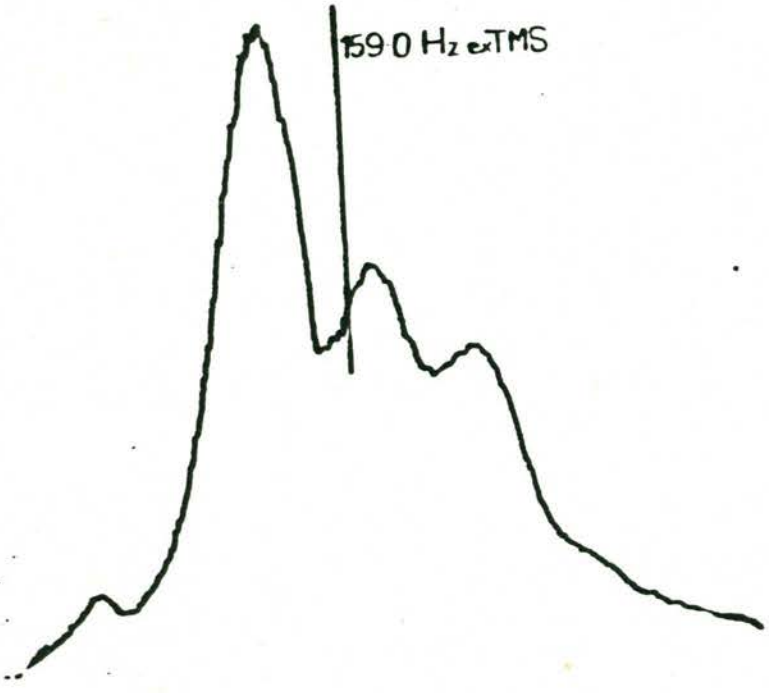
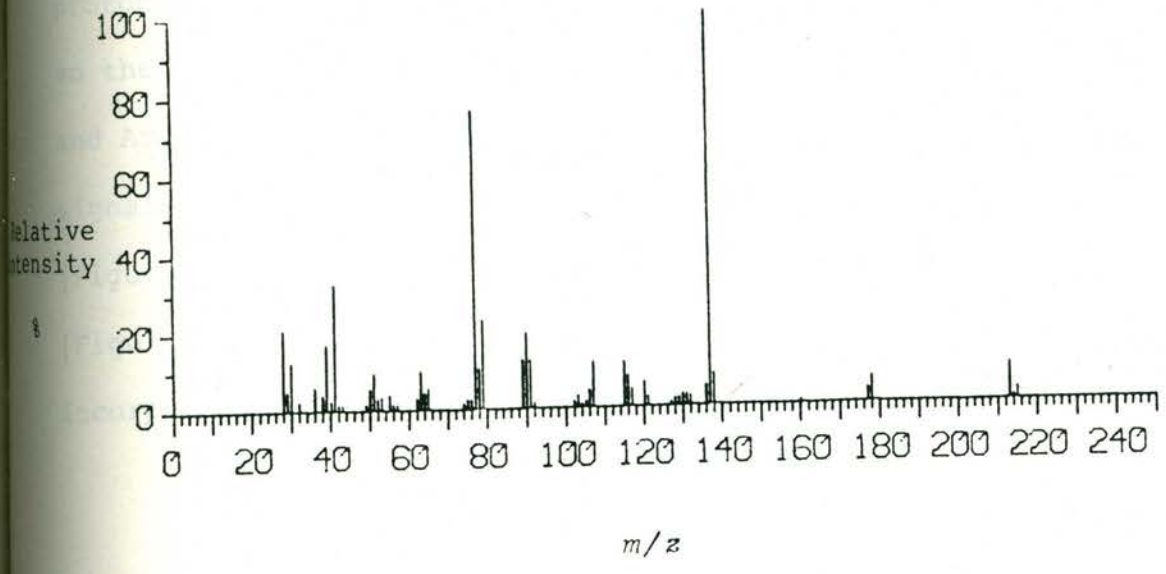
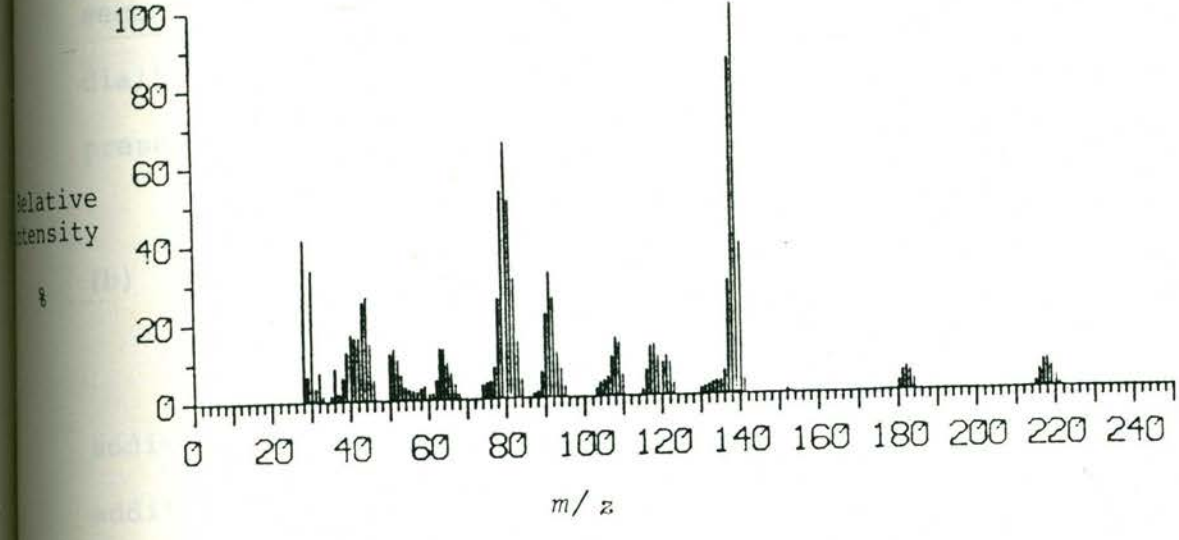


Figure 3(b). Expansion of the methyl signal from the 100 MHz ^{1}H n.m.r. spectrum of the reaction products resulting from the addition of DCl to the styrene (5). 1 cm = 1.38 Hz.



Mass spectrum of the chloro compound (6).



Mass spectrum of the reaction products resulting from the addition of DCl to the styrene (5).

Figure 3(c)

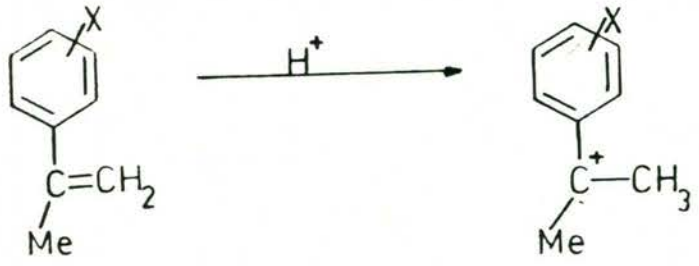
The integral of the benzylic signal was equivalent to 0.76 protons (normalized with respect to the aromatic protons) and so the approximate proportions of $ArCD_2CMe_2Cl$, $ArCHDCMe_2Cl$ and $ArCH_2CMe_2Cl$ were 40%, 45% and 15% respectively. The methyl signal at δ 1.58 was a multiplet equivalent to 3.16 protons [Figure 3 (b)]. The mass spectrum of this product mixture [Figure 3 (c)] shows species with up to eight deuterium atoms incorporated in the molecule.

The formation of the overchlorinated products on treatment of (5) with chlorine and the randomization of deuterium in the addition of deuterium chloride to (5), as well as the general observation of preference for the negative end of adducts to become attached to the tertiary carbon of the β,β-dimethyl-*p*-nitrostyrene (5) rather than the benzylic (but secondary) carbon led to further studies of addition to β,β-dialkyl (mainly dimethyl) styrenes and these studies are presented immediately below.

(b) Addition Reactions of β,β-Dialkylstyrenes

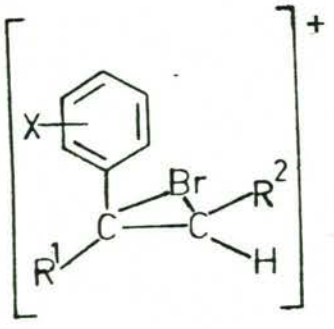
There have been extensive studies of electrophilic addition to styrenes and α- and β-monoalkyl styrenes. The addition of hydrogen bromide to nitrostyrenes,[33] deuterium bromide to (*E*)- and (*Z*)-β-t-butylstyrene,[34] trifluoroacetic acid to several ring substituted styrenes and (*E*)- and (*Z*)-1-phenylpropenes[35] and other protic additions[35 - 38] all

proceed by initial protonation to give the benzylic cation for both the styrenes themselves and the α- and β-monalkylated styrenes [an example is shown in eqn (10)]. Extensive studies

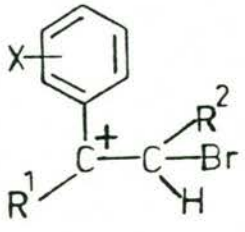


(10)

of the bromination of similar systems[39 - 47] seem to indicate that the reactive intermediate may be an unsymmetrical bridged bromonium ion (26) or an open benzylic cation (27),



(26)



(27)

depending on substituents.[43] In these cases the benzylic carbon bears considerable positive charge.

The addition of arenesulfenyl chlorides to styrene and (*E*)-1-phenylpropene proceeds by a bridged intermediate,[38,43] and the addition of chlorine to styrenes proceeds by an open β-chlorobenzyl cation with a tightly held chloride counterion.[48]

In contrast to the body of work touched upon above, little work has been carried out on β,β-dialkylstyrenes. However, hydrogen chloride adds to β,β-dimethylstyrene (23) to give (28),[49] which suggests the cation (29) is the intermediate. The addition of hydrogen chloride and hydrogen bromide to the styrene (5) also can be rationalised by the formation of an intermediate tertiary cation (30). However the possibility

$PhCH_2CMe_2Cl$

(28)

$PhCH_2\overset{+}{C}Me_2$

(29)

$ArCH_2\overset{+}{C}Me_2$

(30)

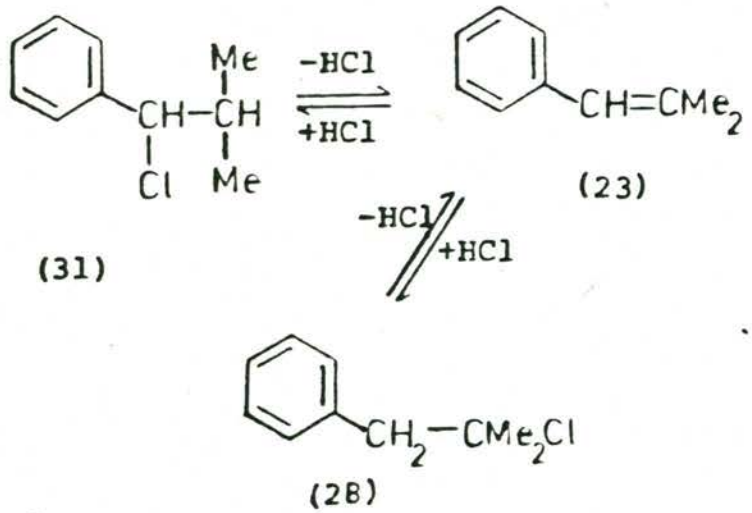
$PhCHClCMe_2H$

(31)

$ArCHClCMe_2H$

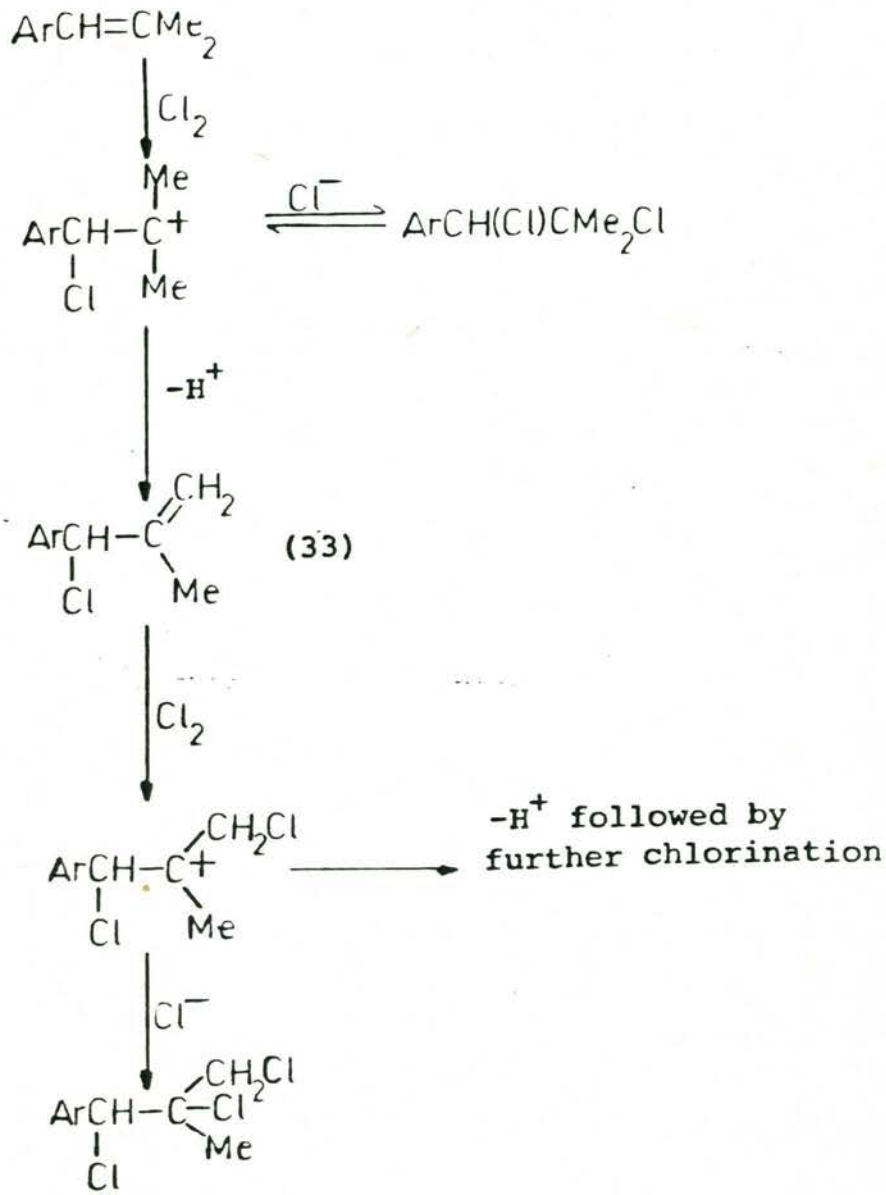
(32)

of (28) being the thermodynamic product and the regioisomer (31) being the kinetic product cannot be ruled out. Equilibration of the type shown in Scheme 3 may be occurring; indeed, it has been shown that when the benzylic chloro compound (32) is treated with hydrogen chloride it isomerises to the chloride

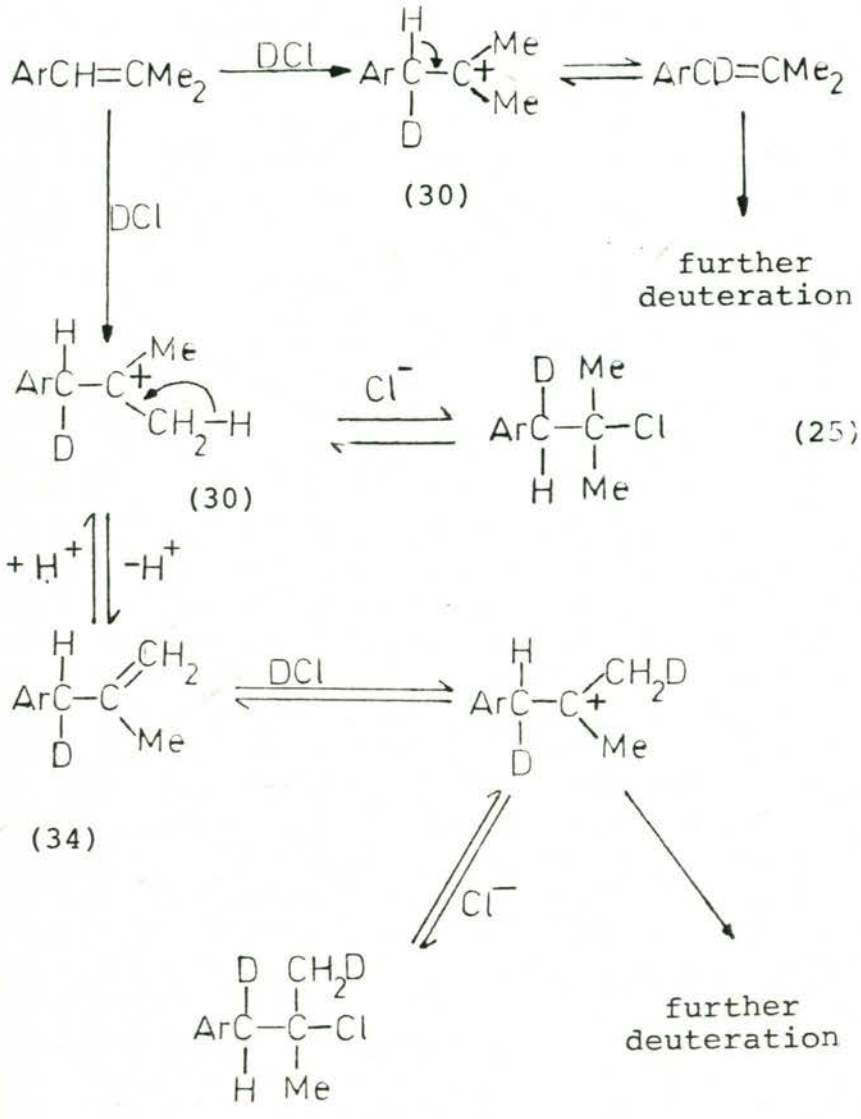


Scheme 3

(6).[50] The overchlorination and scrambling of deuterium discussed in Section 1(a) above can be rationalised by the processes shown in Schemes 4 and 5 in which tertiary cations are formed. These processes require that deconjugated olefins, e.g. (33) and (34) are intermediate in the addition reactions. The olefin (35) was in fact isolated from an addition reaction of hydrogen chloride with the styrene (5) which was quenched at approximately 50% completion. The compound (35) was separated from (5) by preparative gas chromatography. It was demonstrated that (5) did not rearrange to (35) under the chromatography conditions and (35) was easily observed in the ^{1}H n.m.r. spectrum of the crude reaction product. The deconjugated olefin (35) had spectroscopic properties in agreement with the literature,[51] and its ^{1}H n.m.r. spectrum especially confirms its structure


ArCH=CMe2
Cl2
Me
ArCH–C+
Cl
Me
Cl−
ArCH(Cl)CMe2Cl
-H+
CH2
ArCH–C
Cl
Me
(33)
Cl2
CH2Cl
ArCH–C+
Cl
Me
-H+ followed by
further chlorination
Cl−
CH2Cl
ArCH–C–Cl
Cl
Me

Scheme 4

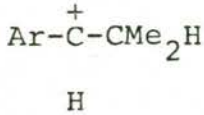

ArCH=CMe2
DCl
ArCD=CMe2
(30)
further deuteration
Cl⁻
(25)
+H⁺
-H⁺
DCl
(34)
further deuteration

Scheme 5

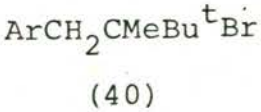
(see Experimental). The isolation of this compound is evidence for the type of processes outlined in Scheme 5.

Some further additions to β,β-dialkylstyrenes were carried out to further investigate the generality of cation formation at the tertiary carbon.

When the styrene (5) was dissolved in methanol which was saturated with hydrogen chloride gas, with ferric chloride as catalyst, only the chloride (6) and the ether (36) were formed. No trace of the benzylic ether (37) was detected. Although this result clearly shows that the cation (30) is the predominant intermediate, it does not totally preclude the benzylic cation (38) as a possible intermediate.

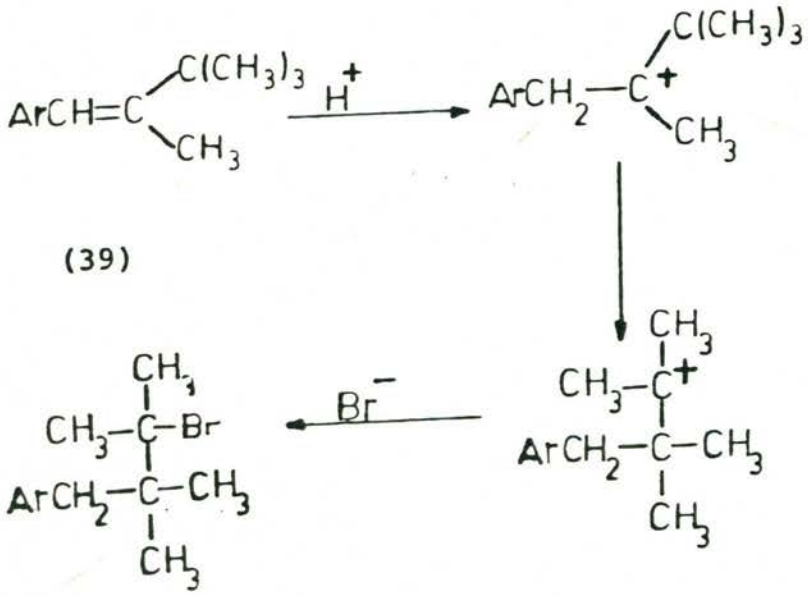


(38)



(40)

If the tertiary cation (30) is an intermediate in electrophilic reactions then replacement of one of the methyl groups with a t-butyl group may lead to methyl shifts and rearrangements as shown in Scheme 6. This possibility was examined by performing the addition of hydrogen bromide to the styrene (39). The bromide (40) (53% yield) was isolated but no detectable amount of (41) could be found.



(39)

(41)

Scheme 6

In order to remove any problems of isomerisation of products under protic conditions the addition reactions of mercury salts with β,β-dimethylstyrenes were investigated. Addition of mercury salts to olefins in the presence of nucleophiles has been shown to proceed in a highly selective fashion to give the Markovnikov product.[52 - 54] The demercuration of the intermediate adducts with alkaline borohydride[55] proceeds smoothly and the overall procedure is an extremely

useful synthetic process. Mercuration of styrene in aqueous[56] or methanolic[54,57] solutions gives almost exclusive formation of the 2-alkoxy-2-phenylethylmercury(II) derivatives (42) and (43). The methoxymercuration of (*Z*) and (*E*)-1-phenylpropene (44) and (45) respectively give mixtures of the regioisomers (46) and (47).[58] Methoxymercuration of β,β-dimethylstyrene (23) with mercury(II) acetate (48) in methanol followed by exchange of chloride for acetate gave the product (49).[59] Upon reduction with hydrazine hydrate, (49) gave the two diastereomers of the dimer (50) in 76% yield and the reduced compound (51) in 9% yield. A recent systematic study of the methoxymercuration of *para*-substituted styrenes has revealed that the reactions proceed regiospecifically and give the Markovnikov products in every case over a range of *para* substituents from nitro to methoxy.[57] In order to examine whether β,β-dimethylstyrenes exhibited a similar regiospecificity over a range of *p*-substituents, methoxy mercuration reactions of the styrenes (5), (23) and (52) followed by alkaline borohydride workup were studied.

The reaction of the styrene (23) with two equivalents of (48) in methanol was complete, by t.l.c., in less than 30 minutes. Subsequent demercuration[55] gave poor isolated yields of the reduced compound (51) (23%) and the dimers (50a) (10%) and (50b) (9%).[†] No trace (<3%) of products arising from

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[†] Assignment of relative stereochemistry to (50 a,b) was not performed in the original study.[59] The ^{1}H n.m.r. data obtained in this work, although quite different for each isomer, did not allow a distinction to be made.

methoxymercuration with the opposite regiochemistry could be detected by ^{1}H n.m.r. inspection of the crude reaction product or the various fractions produced during the fairly inefficient (small-scale) separation of (50 a,b) and (51). This result, combined with the previous report,[59] confirms the regiochemistry of methoxymercuration of (23). It is also clear that, even with the normally superior alkaline borohydride demercuration procedure,[55] considerable (presumably radical[59]) dimerization occurs in the demercuration step.

The methoxymercuration-demercuration process when applied to the styrene (5) proceeded smoothly to give a reasonable yield of the ether (36). The regioisomer (37) could not be detected (< 3%).

The reaction of the *p*-methoxy compound (52) with which reverse regiochemistry is a possibility† (*p*-methoxybenzyl and secondary against tertiary cation), proceeded in an unexpected fashion. The styrene (52), when treated with 2 equivalents of the salt (48) in methanol, had completely disappeared (by t.l.c.) after 30 minutes. After 5 minutes, however, a white crystalline material began to precipitate. The reaction mixture was stirred for 1.5 hours to ensure complete precipitation of the solid, which was identified as mercury(I) acetate (53) (86% yield). The mother liquor on workup, *without* the demercuration step, gave an excellent yield (87%) of the

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† The *p*-methoxy group favours the open benzylic cation intermediate in the bromination of (*E*)-1-phenylpropene.[39]

vicinal dimethyl ether (54), whose constitution was quite readily deduced from its ^{1}H n.m.r. parameters and elementary composition.

In similar fashion, a good yield (76%) of (54) was obtained on treatment of (52) with 1 equivalent of (48). In this case, a white precipitate of salt (53) formed initially and then metallic mercury began to appear. After 24 hours, the white solid had been completely replaced by elementary mercury. Reaction of (52) with 2 equivalents of (48), in a more dilute solution in methanol, so that the reaction took *c.* 1 hour to reach completion, was undertaken, and aliquots taken at various time intervals were quenched with alkaline borohydride. Mixtures of starting material (52), the sole monomethoxylated derivative (55) with no trace (< 3%) of regioisomer (56), and the vicinal dimethyl ether (54) were isolated, and the product distribution was estimated by ^{1}H n.m.r. A plot of product distribution with time is given in Figure 4.

From the above result, it is clear that styrene (52) methoxymercurates regiospecifically to give the intermediate (57), which can be demercurated, without dimer formation, to give (56). The intermediate (57), however, is quite reactive and undergoes reaction with methanol, with production of salt (53) or metallic mercury, and the anomalous product (54). Although the solvolysis of alkylmercury(II) salts in strongly acidic solutions is known to produce mercury and results in nucleophilically substituted products, and although a recent

report has shown that β-aminoalkylmercury(II) tetrafluoroborates will react with amines to produce vicinal diamines and mercury,[60] the nucleophilic displacement of mercury in covalent mercury(II) derivatives, such as acetoxy compounds, is quite rare; however, some cases have been reported.[61]

Two pathways are possible for the displacement of mercury, in the reaction of (57) with methanol. One is direct attack of methanol at the benzylic carbon. The other involves neighbouring group participation by the methoxy group as shown in Scheme 7. The driving force for substitution, either

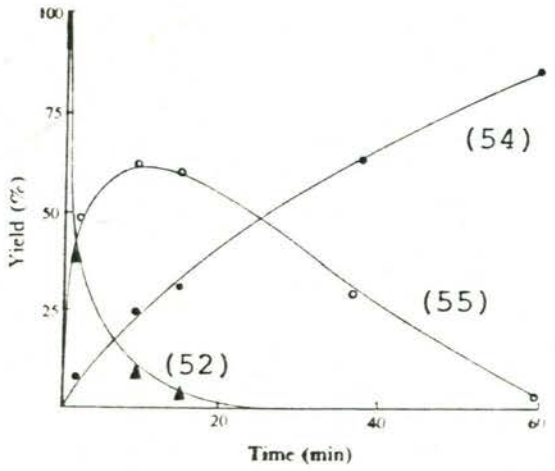
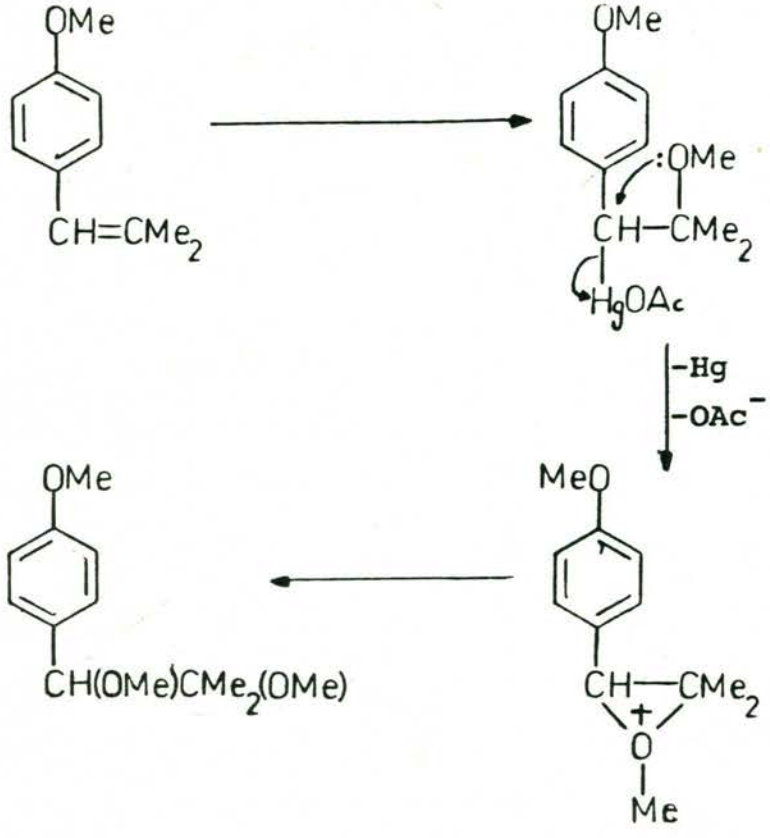


Figure 4. Yields of products, 2-methoxy-1-(*p*-methoxyphenyl)-2-methylpropane (55) and 1,2-dimethoxy-1-(*p*-methoxyphenyl)-2-methylpropane (54), from reaction of *p*-methoxy-β,β-dimethylstyrene (52) with mercury(II) acetate in methanol followed by demercuration with alkaline borohydride.


OMe
CH=CMe2
OMe
:OMe
CH—CMe2
HgOAc
-Hg
-OAc⁻
MeO
CH—CMe2
O
Me
OMe
CH(OMe)CMe2(OMe)

Scheme 7

externally or internally, is presumably the stabilizing effect of the *p*-methoxy group on any positive charge that develops on the benzylic carbon during attack by a nucleophile. Two factors which cause the suggestion of the pathway given in Scheme 7, as an alternative to direct attack by methanol, are the presence of the geminal methyl groups, which would facilitate formation of a three-membered ring, and the reported participation by vicinal alkoxy groups in the reactions of some β-alkoxyalkylmercury(II) tetrafluoroborates.

Clearly the styrenes (5), (23) and (52) undergo initial regiospecific methoxymercuration, implicating a tertiary cation as the reactive intermediate. The intermediate mercury derivatives from (5) and (52), but not (23), cleanly demercurate, although the intermediate (57) reacts readily to give (54), making monomethoxylation impractical.

All the available evidence indicates that the *p*-nitro styrene (5) undergoes electrophilic addition through the cation (30).

2. Kinetics and Mechanism of Nitrous Acid Elimination from the Nitroalkanes (1) and (2), and Some Related Reactions

The β-eliminations of nitrous acid from (1), hydrochloric acid from (6) and hydrobromic acid from (7) to give the styrene (5) proceeded smoothly and at a convenient rate for kinetic measurement when performed in 50% v/v dimethyl sulfoxide-methanol with sodium methoxide as base, at 20.0 °C.

The reactions were monitored by ultraviolet spectroscopy, by the method fully outlined in the experimental (p. 214). The data thus obtained were treated by the eqn (11)[63,64a] for bimolecular reactions in which a and b are initial concentrations in mol l^{-1} of base and substrate respectively, x is the concentration of product, t is the time elapsed in seconds and k_2 is the second-order rate constant in l mol^{-1} s^{-1}. When the right hand

$$tk_2 = \frac{1}{a - b} \left\{ \ln \left[\frac{b(a - x)}{a(b - x)} \right] \right\} \qquad (11)$$

expression of eqn (11) was evaluated and plotted against time for each individual run a good linear plot was obtained. The slopes of the lines were determined by linear regression analysis and these slopes were the value of k_2. All lines had correlation coefficients in excess of 0.99. In some of the initial experiments the lines did not pass through the origin but had a small positive intercept. This was attributed

to a mixing effect. A methanol solution of base at 20.0 °C was added to an equal volume of a solution of substrate in dimethyl sulfoxide in these experiments. The reaction proceeds more quickly at the higher concentration of dimethyl sulfoxide and when the order of mixing was reversed so was the effect. Later runs were performed by having the base and substrate in separate 50% v/v solutions prior to mixing. The rate constants so determined were well within experimental error of those determined earlier.

The rates of β-elimination in (1), (6) and (7) were determined at several other temperatures and plots of ln k (k is the rate constant) against $1/T$ (T is the absolute temperature) gave the straight lines of Fig. 5 . The activation parameters for the three elimination processes were determined from the eqns. (12) - (15).

$$\ln k = \frac{-E_a}{RT} + \ln A \qquad (12)^{64b}$$

$$E_a = \Delta H^{\ddagger} + RT \qquad (13)^{64b}$$

$$\Delta S^{\ddagger} = 19.128\left(\log k_2 - 10.753 - \log T + \frac{E_a}{19.128T}\right) \qquad (14)^{64b\dagger,65}$$

$$\Delta G^{\ddagger} = \Delta H^{\ddagger} - T\Delta S^{\ddagger} \qquad (15)^{66}$$

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† This equation differs from that derived by Bunnett in that the constants have been changed to give values in SI units.

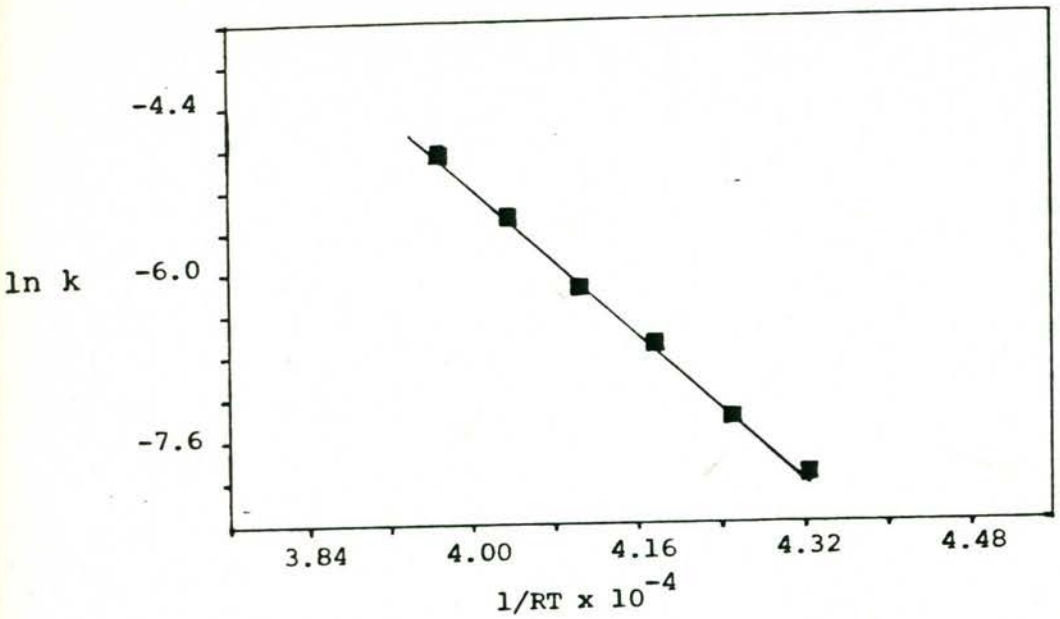

Figure 5(a). Arrhenius plot for (1)

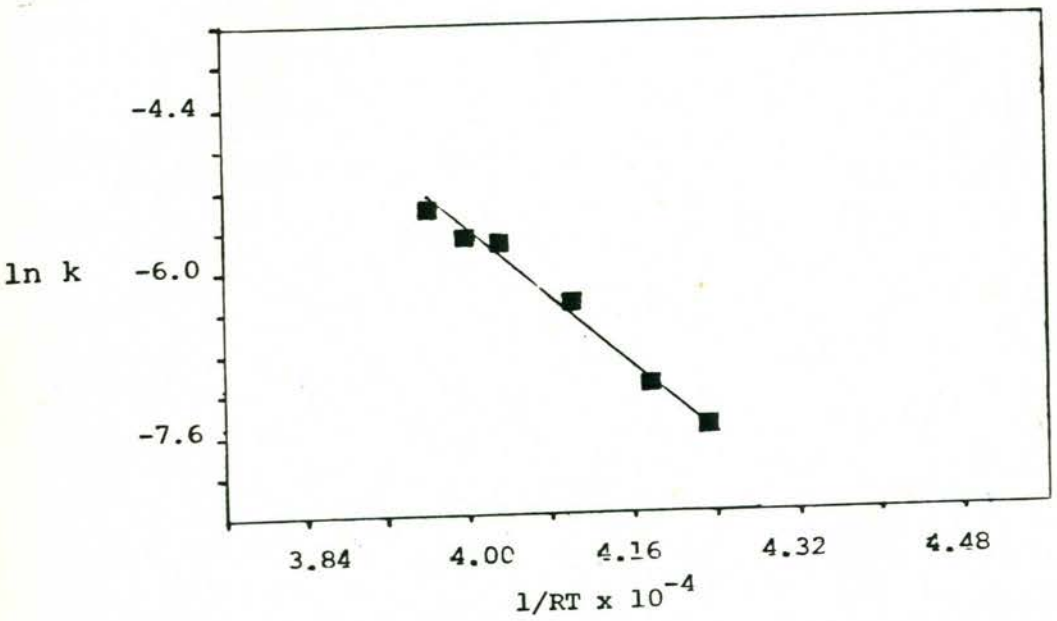

Figure 5(b). Arrhenius plot for (6)

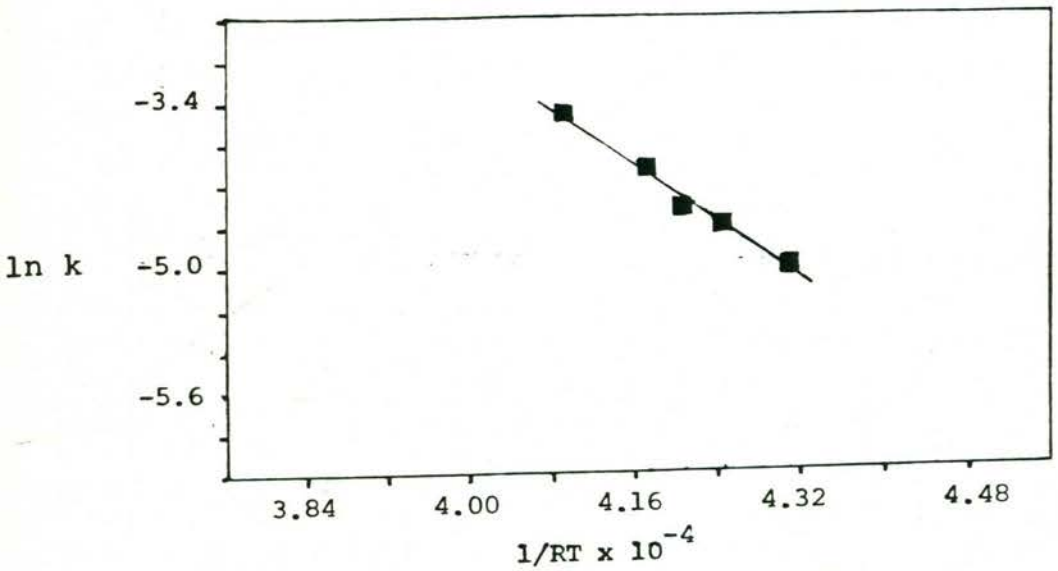

Figure 5(c). Arrhenius plot for (7)

Table 1. Kinetic and activation energy parameters for the elimination reactions of (1), (6) and (7) at 20.0 °C. Reactions performed in 50% v/v methanol-dimethyl sulfoxide with sodium methoxide as base.

Compound	Rate constant[A,B] $\times 10^3$ ($l\,mol^{-1}\,s^{-1}$)	E_a $kJ\,mol^{-1}$	$ln\,A$	$G^{\ddagger C}$ $kJ\,mol^{-1}$	$H^{\ddagger C}$ $kJ\,mol^{-1}$	$S^{\ddagger C}$ $J\,mol^{-1}K^{-1}$
(1)	3.17 ± 0.07	90 ± 2	31.1±0.8	85.7±4	87.5±2	6±7
(6)	1.12 ± 0.03	78 ± 5	25±2	90.6±10	75.5±5	-43±17
(7)	31 ± 2.4	73 ± 5	26±2	82.4±10	70.5±5	-32±16

[A] The individual kinetic runs for which these values are the means are tabulated in Appendix 1.

[B] Errors are standard deviations

[C] Errors are maximum deviations.

where R is the gas constant, A is the frequency factor, E_a is the Arrhenius activation energy, $\Delta H^{\ddagger}$ is the enthalpy of activation, $\Delta S^{\ddagger}$ is the entropy of activation and $\Delta G^{\ddagger}$ is the free energy of activation.

The kinetic and activation parameters for the three elimination processes at 20.0 °C are tabulated in Table 1. The elimination of nitrous acid from (1) is intermediate in rate between the β-eliminations from (6) and (7), and the $\Delta G^{\ddagger}$ value follows the same pattern. Nucleofugality, as measured by reaction rate, is not directly related to the pK_a [†] of the conjugate acids of the nucleofuges in this system. However, $\Delta H^{\ddagger}$, which is a reflection of the energy cost in breaking bonds, does follow the expected order of pK_a values. The two halides do reflect the traditional nucleofugality order.

The reason for the "enhanced" nucleofugality of nitrite appears to lie in the $\Delta S^{\ddagger}$ value. Bunnett has determined $\Delta S^{\ddagger}$ and $\Delta S^{\ddagger}$ values for 2-halohexanes undergoing bimolecular elimi-

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[†] It is not really valid to compare pK_a values for hydrobromic and hydrochloric acids in aqueous solutions, as both are virtually entirely dissociated, and therefore water has a strong levelling effect. However, it is generally accepted that hydrobromic acid is the stronger acid.[67] Measurements of pK_a for these acids have been made in ethylenediamine[68] and hydrobromic acid is the stronger. Although no measurement of acid strength in methanol-dimethyl sulfoxide has been made, there is no reason to expect the order of acid strength to change for the three acids, hydrobromic, hydrochloric and nitrous.

nation, with sodium methoxide as base, in methanol.[65] These values are of the same order and sign as those determined for (6) and (7) in this work. Bunnett has also determined the value of $\Delta S^{\ddagger}$ in the elimination of hydrochloric acid from (6) to give (5) in methanol to be -20.1 ± 5 kJ mol^{-1}.[51] The change in solvent from methanol to 50% v/v methanol/dimethyl sulfoxide in the present work has made this value more negative and this implies a more highly ordered (solvated) transition state. The elimination of $S(CH_3)_2$ from $PhCH_2C(CH_3)_2\overset{+}{S}(CH_3)_2ClO_4^-$ to give (23) has a $\Delta S^{\ddagger}$ value of $+71 \pm 17$ J K^{-1} mol^{-1},[69] and this positive value was attributed to release of solvent molecules in the transition state. Generally, in solution kinetics, relatively low values of $\Delta S^{\ddagger}$ are attributed to greater solvation of the transition state,[70] and higher $\Delta S^{\ddagger}$ values reflect a release of solvent molecules in the transition state. The higher $\Delta S^{\ddagger}$ value for (1) as compared with those for (6) and (7) can be attributed to such a solvent effect.[†] The developing negative charge on the nucleofuge is delocalized over the group in the case of the nitrite group whereas with chloride and bromide it is more localized. This may mean that solvent molecules (particularly methanol) may be more tightly bound for (6) and (7). Alternatively this entropy effect may be due to the methoxide anion being less solvated for (1) than for (6) and (7): if the transition state has a large degree of methoxide-β-hydrogen bond formation in (1) then the methoxide anion

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[†] Although the errors for $\Delta S^{\ddagger}$ are large the trend is clear.

charge is more dissipated than if the mechanism is *E1*-like and therefore does not need to be as tightly solvated.

Isotope effects in the β-elimination reactions of (1) at 20.0 °C

The isotope effects were determined from the dideuterated compound (3) and the monodeuterated compound (4). The rates of elimination from these compounds are shown in Table 2. The isotope effect was calculated directly by comparison of the rate of elimination of HNO_2 from (1) with the rate of elimination of DNO_2 from (3). The value of k_H/k_D is 6.5 ± 0.3. Since compound (3) contained 13% of (4) and its presence would increase the measured rate of k_D, this value of k_H/k_D may be low. At the latter state of reaction this effect would be diminished and since the experiments gave good straight lines, the influence on k_D is slight. This method of determination of k_H/k_D is the one usually employed.[1e]

β-Elimination in the monodeuterated nitroalkane (4) in 50% v/v dimethyl sulfoxide/methanol gave a value of k_H/k_D based on product distribution. The elimination of HNO_2 from (4) proceeds to give (58). Similarly the elimination of DNO_2 gives (5). The ratio of (58):(5) gives the value of k_H/k_D. This ratio was determined by ^1H n.m.r. and mass spectroscopy. The mass spectrum of (5) is shown in Figure 6 and the parent ion peak (*m/z* 177) and M+1 peak (*m/z* 178) in this spectrum are shown enlarged in Figure 6 (b). A similar enlargement of the parent ion peaks of one of the product

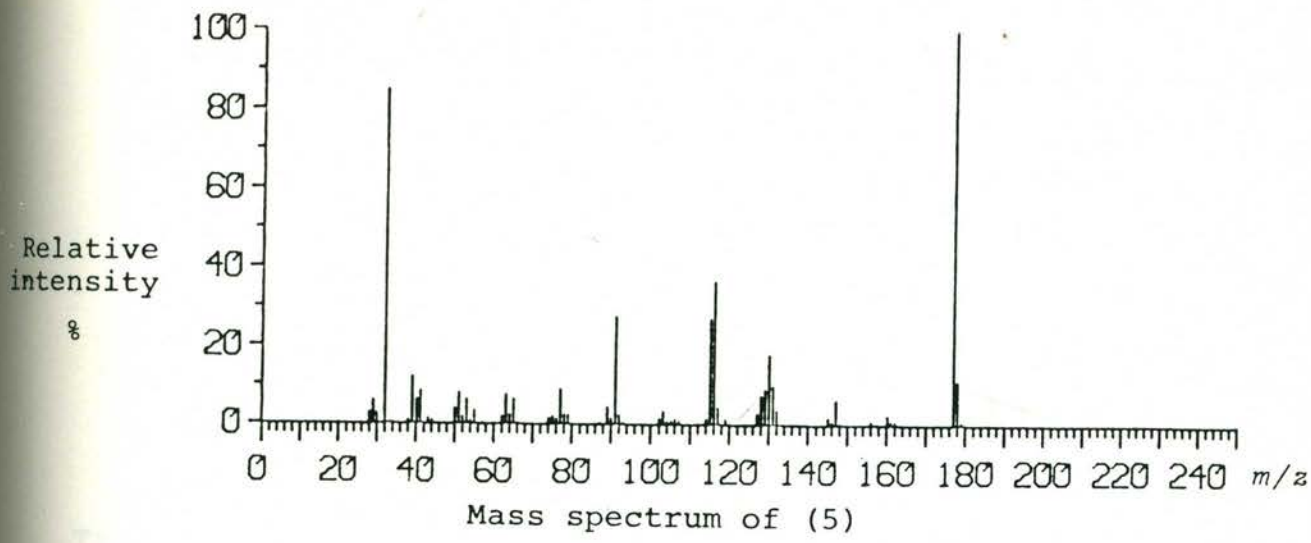
Table 2. Rate of β-elimination in the compounds (3) and (4) at 20.0 °C.

Compound	Rate of elimination[A,B] $\times 10^3$ l mol^{-1} s^{-1}
(3)	0.49 ± 0.02
(4)	1.78 ± 0.05

Mean value of k_H/k_D = 6.5 ± 0.3.

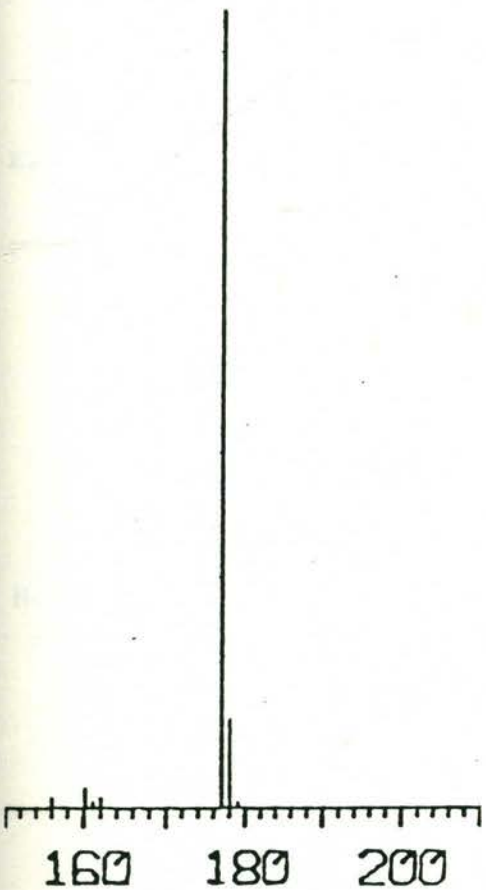
[A] The individual kinetic runs for which these are the means are tabulated in Appendix 2.

[B] Errors are standard deviations.



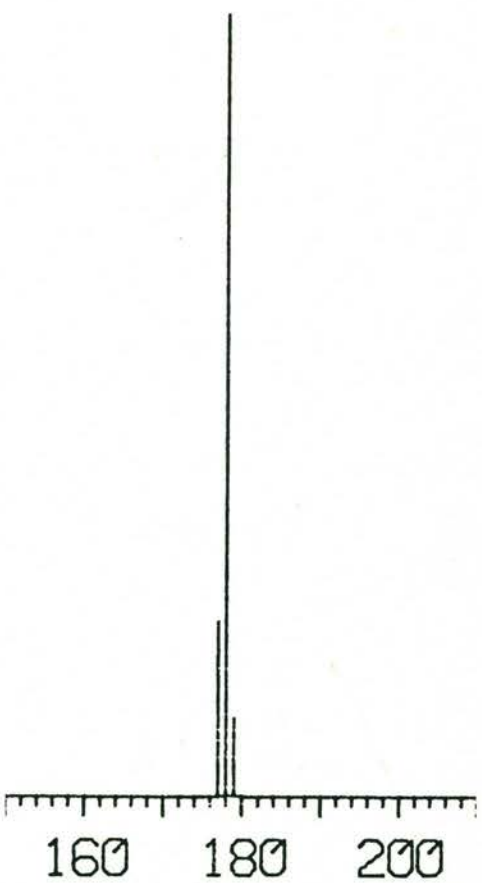
Mass spectrum of (5)

Figure 6(a)



Parent ion of (5)

Figure 6(b)



Parent ions of the product mixture

Figure 6(c)

Table 3. Values of (58)/(5) (k_H/k_D) determined by ^1H n.m.r. and mass spectroscopy. All β-eliminations performed in 50% v/v methanol-dimethyl sulfoxide with sodium methoxide as base, at 20.0 °C.

Experiment	Ratio of (58)/(5) by: ^1H n.m.r.	Mass Spectral analysis
(1)	5.21	5.43
(2)	5.02	5.24

Mean value of (k_H/k_D) = 5.2 ± 0.2

mixtures is shown in Figure 6(c). The M^+ peak for the styrene (5) appears at m/z 177 in Figure 6 (c) and the peak at m/z 178 is due to both the M+1 peak of (5), for which appropriate corrections were made, and the deuterated styrene (58). The ratios determined for (58)/(5), i.e. k_H/k_D, are given in Table 3.

Since the rate for the elimination of nitrous acid from (4), which was 1.78×10^{-3} l mol^{-1} s^{-1}, is equal to $(k_H + k_D)/2$ the absolute values of k_H and k_D may be calculated for (4). The value of k_H is $(3.0 \pm 0.2) \times 10^{-3}$ l mol^{-1} s^{-1} and k_D is equal to $(0.57 \pm 0.05) \times 10^{-3}$ l mol^{-1} s^{-1}.

Comparing the sets of values for k_H/k_D obtained above it can be seen that they differ quite markedly. This was attributed to the operation of a secondary α-isotope effect.

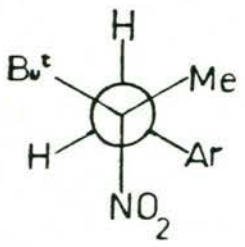
The origin of the secondary isotope effect is vibrational[71] and a deuterium atom α to a C-H (or C-D) bond which is being broken in the transition state reduces the value for k_H (or k_D). The effect observed on the values of k_H and k_D for the monodeuterated compound (4) is of the correct order of magnitude and direction, i.e. k_H in compound (4) is less than k_H in (1) and k_D in (4) is greater than k_D in the compound (4). However, it is clear from both sets of results that the elimination of nitrous acid from (1) proceeds through a transition state of the type in Figure 2 (b); i.e. an *E*2 type of elimination is taking place with substantial C-H and C-NO_2 bond breaking. Examples of *E*2 eliminations in which

similar isotope effects are observed are the elimination of hydrobromic acid and *p*-toluenesulfonic acid from 2-phenylethyl substrates.[le]

Stereochemistry of the nitrous acid elimination

In order to establish the stereochemistry of elimination it is necessary to have a system in which a correlation can be made between starting material conformation and the stereochemistry or either the product or residual starting material, that is, the starting material must be unsymmetrical.

The compound (8) is shown in its preferred conformation in the Newman projection (59) in which the large t-butyl

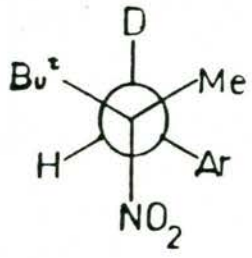


(59)

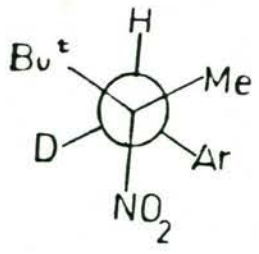
and *p*-nitrophenyl groups are *anti* to one another. The ^1H n.m.r. spectrum of (8) confirms that (59) is the conformation of lowest energy. There is a doublet at δ 2.91 for the proton *anti* to the nitro group (J = 14.2 Hz) and a doublet of quartets at δ 4.00 which was assigned to the proton *anti* to the methyl group (J = 0.9 Hz) on the basis of long-range coupling.[72]

The elimination of nitrous acid from the compound (8) proceeds stereospecifically to give (*E*)-*p*-(2,3,3-trimethylbutenyl)nitrobenzene (39) in a bimolecular process with a rate constant k_2 of $(3.7 \pm 0.4) \times 10^{-4}$ l mol^{-1} s^{-1} (Appendix 2). This rate constant is nearly one tenth of that for (1), and presumably the t-butyl hinders the approach of methoxide ion. If this elimination is concerted (as the bimolecularity of the process indicates), a method of conveniently determining the stereochemistry of this elimination consequently presents itself.

The monodeuterated diastereomers (19a) and (19b) are shown below in their preferred conformations. Assuming that there is an isotope effect operating in the elimination of nitrous acid from (19a) and (19b) then the following predictions may be made. If the elimination of nitrous acid in this system is *syn*-periplanar the diastereomer (19a) will eliminate more quickly than the diastereomer (19b), since (19a) is already in a favourable *syn*-clinal conformation for the elimination of HNO_2. *Anti*-periplanar elimination will



19 (a)



19 (b)

give the converse result. The course of the reaction can be followed by ^1H n.m.r., by comparing the relative intensities of the two benzylic proton signals in the mixture of starting materials (19a) and (19b). A series of these experiments were performed and the results appear in Table 4. It is immediately apparent that (19b) reacts more quickly than (19a).

The results clearly show that not only is the reaction proceeding by an *anti*-periplanar transition state but also that a substantial deuterium isotope effect is operating. Presumably the less hindered substrate (1) also eliminates nitrous acid by an *anti*-periplanar transition state.

Table 4. Distribution of isomers (19a) and (19b) after elimination of nitrous acid. All reactions were performed in 50% v/v methanol-dimethyl sulfoxide with sodium methoxide as base, at 20.0 °C.

Percent reaction	Value of (19a)/(19b)	Percent deuterium in product by ^{1}H n.m.r.
0	1.08	-
11	1.29	-
18	1.94	81
48	3.23	83

Mechanism of β-elimination in (1)

The large isotope effect, the *anti*-periplanar stereoselectivity of the elimination in (8) and the fact that the elimination of HNO_2 from (1) is bimolecular all support the conclusion that (1) eliminates by a concerted, *anti*-periplanar *E*2 mechanism.

β- Elimination in (2), (20) and (22)

The presence of the benzylic chlorine atom in (2) should make the benzylic hydrogen more acidic than those of (1) because of the electron withdrawing effect of the chlorine atom. When the β-hydrogen is made more acidic, it would be expected that the elimination mechanism would be more like the *E*1cB process.[1a]

The β-eliminations of nitrous acid from (2), DNO_2 from (20) and hydrochloric acid from (22) were studied, and the rate constants derived by the method fully outlined in the Experimental (p. 214). The rate constants at 20.0 ^{o}C in methanol[†] are shown in Table 5. All reactions gave >95% of (24).

The deuterium isotope effect for the elimination of nitrous acid from (2) is 1.6 ± 0.3 which is relatively low.

[†] These reactions occur too rapidly in 50% v/v methanol/dimethyl sulfoxide to be followed conveniently; they proceed much faster than the eliminations in (1), (6) and (7).

Consequently it can be concluded that the mechanism of the elimination was close to an *E*1cB type.

If the reaction does proceed by an *E*1cB mechanism, the first step may be reversible (Scheme 1, $k_{-1} \approx k_1$), and deuterium exchange may occur between (2) and MeOD. Three such reactions were performed at 20.0 °C, and allowed to proceed to 21%, 28% and 67% completion. No deuterium incorporation was detected in any of the recovered starting material. An elimination of (20) with methanol at 20.0 °C also failed to show any hydrogen incorporation in recovered (20). Therefore the elimination of nitrous acid from (2) is not an *E*1cB with a reversible first step.

The rate of elimination of nitrite in (2) is approximately the same as the loss of chloride from (22), and there is therefore a slight levelling of rate. The loss of nitrite proceeds at a rate comparable to chloride and this enhanced nucleofugality of the nitrite group is presumably again due to an entropy factor.

Stereochemistry of the elimination of nitrous acid from the diastereomers (60) and (61)

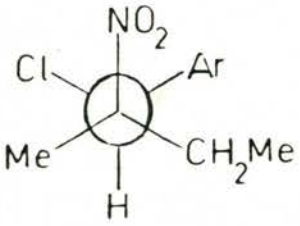
The diastereomers (60) and (61) are separable. They are described in the subsequent discussion as the "less polar" and "more polar" isomers (by t.l.c.) respectively. No assignment could be made (e.g. by ^{1}H n.m.r.). These isomers are represented by conformations (62) and (63).

Table 5. Rate constants for bimolecular elimination from (2), (20) and (22) in methanol with sodium methoxide as base, at 20.0 °C.

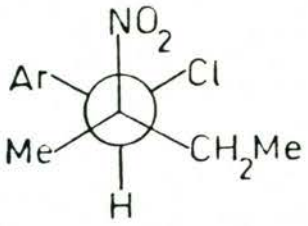
Compound	Rate constants[A,B] $\times 10^4$ l mol^{-1} s^{-1}
(2)	2.1 ± 0.1
(20)	1.3 ± 0.2
(22)	2.7 ± 0.2

[A] The individual kinetic runs for which these values are the means are tabulated in Appendix 3.

[B] Errors are standard deviations.



(62)



(63)

If the elimination of nitrous acid is stereospecific, in either an *anti*- or a *syn*- periplanar sense, then each diastereomer should eliminate to give a single alkene, either (64) or (65), and the alkene product will be different for the diastereomers (60) and (61).

Each alkane was treated with sodium methoxide in methanol at 20.0 ^{o} and the reactions allowed to proceed to completion. The less polar (t.l.c.) diastereomer (60) (benzylic H at δ 5.57) proceeded to give a 1:1 mixture of the *(E)*- and *(Z)*-alkenes (64) and (65) in quantitative yield. The more polar (t.l.c.) diastereomer (61) (benzylic H at δ 5.70) gave a quantitative yield of 1.6 ± 0.1:1 mixture of the alkenes (no relative stereochemistry was assigned to the alkenes). When similar reactions were quenched before completion, only the original starting diastereomer was present, indicating that the mixture of alkenes was not due

to epimerization of the starting material. This result confirms the result from the isotope exchange experiments that deprotonation is irreversible.

The lack of stereospecificity in the eliminations from (60) and (61) is consistent with development of considerable carbanion character in the transition state and consequent rotation around the benzylic carbon-tertiary sp^3 carbon bond in the transition state, or elimination occurring by both *syn*- and *anti*- periplanar pathways. Both possibilities are consistent with an *E*1cB mechanism or an *E*2 process with very high carbanion-character development.

Mechanism of elimination in (2)

The low isotope effect, the lack of stereospecificity in the eliminations from (60) and (61) and the bimolecularity imply a carbanion-like *E*2 or an *E*1cB reaction in which attack by base is rate determining and with an irreversible first step.

Nitrite as a leaving group under S_N1 (E_1) *conditions*

S_N1 and *E*1 reactions of tertiary alkyl halides are very well known, but such processes are rare for tertiary nitroalkanes.[†] In order to confirm that nitrite was not a

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[†] One such S_N1 reaction has been reported.[74]

nucleofuge in such processes a comparison of *relative* rates of methanolysis for t-butyl bromide (66), t-butyl chloride (67) and 2-methyl-2-nitropropane (68) was undertaken under conditions known to methanolyse the alkyl halides by an S_N1 mechanism.[73] All the reactions were performed with 1 M solutions of reactant in methanol at 64° and were followed by ^1H n.m.r. The t-butyl bromide (66) solvolysed completely within half an hour, and 60% of the t-butyl chloride (67) had reacted after 5 hours. After 24 hours the 2-methyl-2-nitropropane (68) showed no detectable amount of the t-butyl methyl ether (69) which was the observed product of the methanolysis of the halides (66) and (67), and (68) was recovered quantitatively.

A similar methanolysis of the chloro compound (6) at 58.0° has been reported.[32] The products were the ether (36) (53.1%), the styrene (5) (25.5%), and the deconjugated olefin (35) (21.3%). A methanolysis at 64° of the bromo compound (7) was complete within 5 hours to give the ether (36) (67%), the styrene (5) (14%) and the olefin (35) (16%). The nitro compound (1) was indefinitely stable under these conditions.

Other Reactions

In order to eliminate the possibility that (1) may react by an E_2C mechanism,[75-77] (1) was treated with a saturated solution of sodium iodide in dimethyl sulfoxide. No reaction occurred. When treated with a solution of sodium thiophenoxide in 50%

methanol/dimethyl sulfoxide, (1) eliminated nitrous acid slowly to give the styrene (5), with an approximate rate constant of 5×10^{-7} l mol^{-1} s^{-1}, much less than that for methoxide.

The *p*-iodo compound (70) and the *p*-phenyl compound (71) both fail to eliminate nitrous acid under the standard conditions, which combined with the inability of nitroalkanes to undergo S_N1 reactions clearly show that the nucleofugality of nitrite is substrate/mechanism dependent.

Conclusions

Clearly, the eliminations of nitrous acid from the substrates (1) and (2) are explicable in terms of traditional elimination mechanisms. In the case of (1) it appears that the process is a concerted, *anti*-periplanar *E*2 elimination. An *E*2 mechanism with a large amount of carbanion character or an irreversible *E*1cB mechanism is operating in the β-elimination of nitrous acid from (2).

In these systems the nucleofugality of nitrite is similar to the halides, and for (1) this has been demonstrated to be largely due to the positive entropy of activation.

The nucleofugality of nitrite is substrate/mechanism dependent, as nitrite is not a good leaving group under conditions which would allow only operation of S_N1 or $E1$ processes. A facilitating factor in the elimination of nitrous acid from (1) and (2) is the presence of electron-withdrawing substituents on the β-carbon

[a *p*-nitrophenyl group in both (1) and (2) and a chlorine atom in (2)] which makes the benzylic β-hydrogens acidic and promote the elimination process. The presence of the nitro group, which is the nucleofuge, also would assist proton removal. The importance of the presence of these substituents can be seen from the failure of other phenyl groups to promote elimination in analogues of (1).

As nitrite is a good leaving group in S_NAr and $S_{RN}1$ reactions[11-13] it is likely that it acts as a nucleofuge only when there is a strong driving force present (the rearomatization in the S_NAr process, dissociation of the radical anion in the $S_{RN}1$ process and the presence of electron-withdrawing substituents in elimination reactions).

Although acid strength for the conjugate acids of the leaving groups values do not reflect nucleofugalities in this work the $\Delta H^{\ddagger}$ values do follow the pK_a trend for the

conjugate acids of the leaving groups.

EXPERIMENTAL

For general experimental procedures see Part I of this thesis (p. 98).

1. Preparation of Compounds and Addition Studies

A. Preparation of Compounds

β,β-Dimethyl-*p*-nitrostyrene (5) and lithium 2-nitropropan-2-ide (14) were prepared in Part I of this thesis. *p*-(2-Methyl-2-nitropropyl)nitrobenzene (1),[78] *p*-(1-chloro-2-methyl-2-nitropropyl)nitrobenzene (2),[13] *p*-(2,3,3-trimethyl-2-nitrobutyl)nitrobenzene (8),[12] *p*-nitrobenzylidyne tribromide (9),[79] lithium 3,3-dimethyl-2-nitrobutan-2-ide (15),[12] *p*-nitrobenzaldehyde (16) (Merck), 1-(D)-*p*-nitrobenzylidene dichloride (21),[80] *p*-nitrobenzylidene dichloride,[80] β,β-dimethylstyrene (23),[81] α-chloro-β,β-dimethyl-*p*-nitrostyrene (24),[13] (*E*)-*p*-(2,3,3-trimethylbutenyl)nitrobenzene (39),[12] both diastereomers of 1-chloro-2-methyl-2-nitro-1-*p*-nitrophenylbutane (60) and (61),[82] t-butyl bromide (66) (Fluka), t-butyl chloride (67) (Fluka) and 2-methyl-2-nitropropane (68),[83] *p*-(2-methyl-2-nitropropyl)iodobenzene (70)[30] and 2-methyl-2-nitro-2-phenylpropane (71)[30] were commercially available or were synthesized by the indicated literature procedure. All had physical constants in agreement with the literature.

(i) *p*-[1,1-(D_2)-2-methyl-2-nitropropyl]nitrobenzene (3)

(a) Synthesis of the undeuterated *p*-(2-methyl-2-nitropropyl)nitrobenzene (1)

p-Nitrobenzylidyne tribromide (9) (11.2 g, 30 mmol) was dissolved in dichloromethane (100 ml). To this solution tetrabutylammonium perchlorate (5.1 g, 15 mmol), lithium 2-nitropropan-2-ide (9 g, 0.1 mol) and water (18 g, 1 mol) were added. The reaction was stirred for twenty four hours and worked up by dilution with water, acidification with dilute hydrochloric acid (3 M), and threefold extraction with ether.† The combined ether extracts were washed with water, brine and dried ($MgSO_4$). The solvent was removed and the volatile byproduct, 2-bromo-2-nitropropane, was removed at 3 mm. Successive recrystallizations from ethanol gave *p*-nitrobenzylidene dibromide (72) (8.8 g, 57%), m.p. 81-82° (lit.[84] 82°). ^1H n.m.r.: δ 6.8, s, benzylic H; 7.9, m, 2H *meta* to NO_2; 8.4, m, 2H *ortho* to NO_2.

p-Nitrobenzylidene dibromide (150 mg, 0.51 mmol) was dissolved in ethanol (5 ml) and heated. A solution of silver nitrate (3 g) in water (5 ml) was added. When t.l.c. indicated the reaction was complete (*c* 3 h) the reaction mixture was worked up and the crude product was recrystallized

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† This basic procedure is implied by the term worked up in this section of the thesis.

from ethanol to give yellow needles of *p*-nitrobenzaldehyde (16) (45 mg, 58%) m.p. 107-108° (lit.[85] 106°).

p-Nitrobenzaldehyde (16) (10.0 g, 66 mmol) was suspended in dry methanol (25 ml) and sodium cyanoborohydride (2.5 g) was added. The reaction mixture was maintained at pH 3-4 by addition of a solution of sulfuric acid in methanol (*c* 3 M) with bromocresol green as indicator. The reaction was complete after 5 hours (t.l.c.) Hydrochloric acid (3 M, 20 ml) was added to the reaction mixture which was then worked up. The crude *p*-nitrobenzyl alcohol was dissolved in thionyl chloride (45 ml) and heated for five hours. The reaction mixture was diluted with ice water (400 ml) and worked up. Recrystallization from light petroleum gave needles of *p*-nitrobenzyl chloride (6.3 mg, 56%) m.p. 70-71° (lit.[86] 71°). ^{1}H n.m.r.: δ 4.7, benzylic CH_2; 7.58, m, 2H *meta* to NO_2; 8.23, m, 2H *ortho* to NO_2.

p-Nitrobenzyl chloride (4 g, 23 mmol) in dimethylformamide (20 ml) was added to a solution of lithium 2-nitro-2-ide (14) (5 g, 53 mmol) in dimethylformamide (100 ml) at 20 °C under nitrogen. The reaction was complete in approximately twenty four hours (t.l.c.). The reaction mixture was worked up. The combined ether extracts were washed with hydrochloric acid (3 M, 50 ml) and a bisulfite solution (10%, 2 x 50 ml). The crude product was recrystallized from aqueous ethanol to give pale plates of *p*-(2-methyl-2-nitropropyl)nitrobenzene (1) (4.92 g, 95%) m.p. 66-67° (lit.[78] 67-68°).

(b) Synthesis of the deuterated compound (3)

p-Nitrobenzylidyne tribromide (9) (11.2 g, 30 mmol) was dissolved in dry dichloromethane (100 ml) in a dry, stoppered flask. To this solution tetrabutylammonium perchlorate (5.1 g, 15 mmol), lithium 2-nitropropan-2-ide (14) (9 g, 0.1 mol) and deuterium oxide (>97% deuterated, 20 g, 1 mol) were added. After twenty four hours the reaction mixture was worked up and the 2-bromo-2-nitropropane was removed at 3 mm. The crude product was chromatographed on silica gel with 50% ether/light petroleum as eluent. The product, α-(D)-*p*-nitrobenzylidene dibromide (10) (7.8 g) (9% H by ^{1}H n.m.r.) contained some 2,3-dinitro-2,3-dimethylbutane impurity (about 15%) and was used without further purification. ^{1}H n.m.r.: δ 7.9, m, 2H *meta* to NO_2; 8.4, m, 2H *ortho* to NO_2. *m/z* 298 (M + 4, 0.5%), 296 (M + 2, 1), 294 (M, 0.5), 217 (100), 215 (98), 159 (10), 157 (11), 90 (38), 82 (36), 80 (38).

The crude α-(D)-*p*-nitrobenzylidene dibromide (10) (7.8 g) was dissolved in ethanol (35 ml) and heated. Silver nitrate (40 g, 0.235 mol) in distilled water (58 ml) was added and heated for five hours. The reaction mixture was worked up to yield crude α-(D)-*p*-nitrobenzaldehyde (11) (4.24 g) which was used without further purification.

The crude α-(D)-*p*-nitrobenzaldehyde (11) (4.24 g) was suspended in methanol-*o*-(D)^{87} (12 ml) and sodium cyanoborodeuteride (1 g) was added. The reaction mixture

was maintained at pH 3-4 by addition of a solution of D_2SO_4 in methanol-*O*-(D), prepared by heating dimethyl sulfate (10 ml) with deuterium oxide (15 ml) in a sealed vessel at 100 ^{o} for three hours, with bromocresol green as indicator. The reaction was complete after five hours. Hydrochloric acid (3 M, 20 ml) was added and the reaction mixture worked up. The crude product 1,1-(D_2)-*p*-nitrobenzyl alcohol (12) (4.37 g) was used without further purification.

The crude 1,1-(D_2)-*p*-nitrobenzyl alcohol (12) (4.37 g) was dissolved in thionyl chloride (20 ml) and heated for five hours. The reaction mixture was worked up and the crude product was purified by p.l.c. with 10% ethyl acetate/light petroleum as eluent. This product, α,α-(D_2)-*p*-nitrobenzyl chloride (13), still contained 2,3-dimethyl-2,3-dinitrobutane and was used without further purification.

Impure α,α-(D_2)-*p*-nitrobenzyl chloride (13) (1.8 g) was dissolved in dimethylformamide (20 ml) and added to a solution of lithium 2-nitropropan-2-ide (14) (2.3 g, 25 mmol) in dimethylformamide (60 ml) at 20 ^{o} under nitrogen. After twenty four hours the reaction mixture was worked up and the crude product was recrystallized from ethanol. This product was purified by p.l.c. with 20% ethyl acetate/light petroleum as eluent. Final recrystallization from benzene - light petroleum gave pale plates of *p*-[1,1-(D_2)-2-methyl-2-nitropropyl)nitrobenzene (250 mg) m.p. 66-67^{o} (lit.[78] of undeuterated compound 67-68^{o}). ^{1}H n.m.r.: δ 1.63, s, $C\underset{\sim\sim}{Me}_2NO_2$;

AA'XX' system: 7.38, m, 2H *meta* to NO_2; 8.21, m, 2H *ortho* to NO_2; $J_{AX} + J_{AX'}$ 9 Hz. This product contained 13% (by ^1H n.m.r. integral) of *p*-[1-(D)-2-methyl-2-nitropropyl]-nitrobenzene (4).

(ii) *p*-[1-(D)-2-Methyl-2-nitropropyl]nitrobenzene (4)

p-Nitrobenzaldehyde (10 g, 66 mmol) was reduced and chlorinated by the same method as in (i) above to give, after recrystallization from light petroleum, needles of α-(D)-*p*-nitrobenzyl chloride (18) (6.4 g, 56%), m.p. 71° (lit.[86] of undeuterated compound 71°). ^1H n.m.r.: δ 4.67, t, benzylic H, J_{HD} 1.8 Hz; AA'XX' system: 7.58, m, 2H *ortho* to NO_2; 8.23, m, 2H *meta* to NO_2; $J_{AX} + J_{AX'}$ 9 Hz.

α-(D)-*p*-Nitrobenzyl chloride (18) (2 g, 12 mmol) was dissolved in anhydrous dimethylformamide (80 ml) and added to a solution of lithium 2-nitropropan-2-ide (14) (2.5 g, 29 mmol) in dimethylformamide (20 ml). The reaction was allowed to proceed for twenty four hours, under nitrogen. The reaction mixture was diluted. The crude product was purified by two recrystallizations from ethanol to give pale plates of *p*-[1-(D)-2-methyl-2-nitropropyl]nitrobenzene (4) (2.1 g, 80%), m.p. 66-67° (lit.[78] of undeuterated compound 67-68°). ^1H n.m.r.: δ 1.63, s, $C\underset{\sim\sim}{Me}_2NO_2$; 3.35, t, benzylic H, J_{HD} 1.75 Hz; AA'XX' system: 7.38, m, 2H *meta* to NO_2; 8.21, m, 2H *ortho* to NO_2; $J_{AX} + J_{AX'}$ 9 Hz.

(iii) 1-(D)-*p*-Nitrobenzyl chloride (18) (1.9 g, 11 mmol) was dissolved in anhydrous dimethylformamide (60 ml) and added to a solution of lithium 3,3-dimethyl 2-nitrobutan-2-ide in dimethylformamide (20 ml) at 20 °C under nitrogen. The reaction was complete after twenty four hours (t.l.c.) and was worked up. The crude product was purified by p.l.c. with 10% ethyl acetate/light petroleum as eluent. The product was recrystallized from ethanol to give *p*-[1-(D)-2,3,3-trimethyl-2-nitrobutyl]nitrobenzene (19a and b) (0.52 g, 18%), m.p. 141-143° (lit.[12] 142-143°). ^{1}H n.m.r.: δ 1.14, s, Bu^t; 1.32, d, Me, *J* 0.9 Hz; 2.90, m, 0.48 H; 3.98, m, 052 H; AA'XX' system: 7.26, m, 2H *meta* to NO_2; 8.10, m, 2H *ortho* to NO_2; $J_{AX} + J_{AX'}$ 9 Hz.

(iv) *p*-(2-Chloro-2-methylpropyl)nitrobenzene (6)

β,β-Dimethyl-*p*-nitrostyrene (21.4 g, 0.12 mol) was dissolved in dry dichloromethane (50 ml) in the presence of anhydrous iron(III) trichloride (2 g). Anhydrous hydrogen chloride was passed through the solution until reaction was complete by t.l.c. (*c.* three hours). The reaction mixture was worked up by dilution with water and threefold extraction with dichloromethane. The organic phases were dried ($MgSO_4$) and the solvent removed to give the crude product which was distilled three times to give an oil which solidified to white needles of *p*-(2-chloro-2-methylpropyl)nitrobenzene (6) (8 g, 31%) b.p. 126.5°/0.5 mm, m.p. 42-44° (lit.[51] 42.5-44°).

(v) *p*-(2-Bromo-2-methylpropyl)nitrobenzene (7)

β,β-Dimethyl-*p*-nitrostyrene (0.34 g, 1.9 mmol) was dissolved in dry dichloromethane (8 ml). Anhydrous hydrogen bromide was passed through the solution until reaction was complete by t.l.c. (*c.* one hour). The reaction mixture was poured into water (40 ml) and extracted into dichloromethane (2 x 20 ml). The organic layers were combined, dried ($MgSO_4$) and the solvent removed. The crude product was recrystallized twice from light petroleum (b.p. 30-40°) to give colourless prisms of p-*(2-bromo-2-methylpropyl)nitrobenzene* (7) (0.21 g, 42%), m.p. 45-46° (Found: C, 46.5; H, 4.6; Br, 31.1; N, 5.3. $C_{10}H_{12}BrNO_2$ requires C, 46.5; H, 4.7; Br, 30.9; N, 5.4%). ^1H n.m.r.: δ 1.79, s, CMe_2Br; 3.25, s, benzylic CH_2; AA'XX' system: 7.46, m, 2H *meta* to NO_2; 8.18, m, 2H *ortho* to NO_2; $J_{AX} + J_{AX'}$ 9 Hz. ν_{max} 1605, 1510, 1365, 860 cm^{-1}. λ_{max} (cyclohexane) 262 nm (ε 11550). *m/z* 259 (M + 2, 1%), 257 (M, 1), 179 (11), 178 (100), 137 (11), 136 (21), 132 (12), 130 (11), 117 (14), 116 (21), 115 (19), 91 (20), 90 (15), 89 (10), 41 (19).

(vi) 1-(D)-*p*-(1-Chloro methyl-2-nitropropyl)nitrobenzene (20)

1-(D)-*p*-Nitrobenzylidene chloride (21) (3 g, 14.5 mmol) was dissolved in anhydrous dimethyl sulfoxide (10 ml) and added to a solution of lithium 2-nitropropan-2-ide (14) (2 g, 21 mmol) in dimethyl sulfoxide (10 ml) at 20 ° under

nitrogen. The reaction was monitored by t.l.c. and when the proportion of 1-(D)-*p*-1-chloro-2-methyl-2-nitropropyl)-nitrobenzene (20) was maximized with respect to the $E_{RC}1$ product (5)[13] (*c.* one hour) the reaction mixture was worked up. Purification by flash chromatography with 30% dichloromethane/light petroleum as eluent and recrystallization from light petroleum gave 1-(D)-*p*-(1-chloro-2-methyl-2-nitropropyl)nitrobenzene (20) (0.8 g, 21%) as pale needles m.p. 125-126° (lit.[13] of undeuterated compound 126°) ^{1}H n.m.r.: δ 1.59, s, Me; 1.78, s, Me; AA'XX' system: 7.65, m, 2H *meta* to NO_2; 8.27, m, 2H *ortho* to NO_2; $J_{AX} + J_{AX'}$ 8.8 Hz. This material contained 11% of (2) by ^{1}H n.m.r. and mass spectroscopy.

(vii) *1,2-Dichloro-2-methyl-1-*p*-nitrophenylpropane*

(a) α-Chloro-β,β-dimethyl-*p*-nitrostyrene (24) (1.2 g, 5.7 mmol) was dissolved in dichloromethane (25 ml) in the presence of anhydrous iron(III) chloride (0.5 g). Anhydrous hydrogen chloride was passed through for twenty four hours. The reaction mixture was worked up to give, after recrystallization from pentane, white prisms of *1,2-dichloro-2-methyl-1-*p*-nitrophenylpropane* (22) (0.48 g, 34%), m.p. 42-43° (Found: C, 48.6; H, 4.4; N, 5.7. $C_{10}H_{11}Cl_2NO_2$ requires C, 48.4; H, 4.5; N, 5.7%). ^{1}H n.m.r.: δ 1.68, s, C(Cl)MeMe; 1.74, s, C(Cl)MeMe; 5.07, s, benzylic H; AA'XX' system: 7.67, m, 2H *meta* to NO_2; 8.22, m, 2H *ortho* to NO_2; $J_{AX} + J_{AX'}$ 8.9 Hz. ν_{max} 1610, 1522, 1395, 1140, 880 cm^{-1}. λ_{max} (cyclohexane) 260 nm (ε 10940). *m/z* 249 (M + 2; 1.2%), 247 (M, 2), 212

(5), 173 (45), 172 (14), 171 (83), 154 (13), 141 (12), 130 (12), 124 (13), 115 (28), 91 (13), 89 (30), 79 (58), 77 (100), 63 (18), 51 (14), 41 (71).

(b) An attempt to make 1,2-dichloro-2-methyl-1-*p*-nitrophenylpropane (22) by addition of chloride to a solution of β,β-dimethyl-*p*-nitrostyrene (5) (2 g, 11.2 mmol) in carbon tetrachloride (30 ml) gave a mixture of products which contained at least three chlorine atoms. *m/z* 285 (M + 4, 2%), 283 (M + 2, 6), 281 (M, 6), 210 ($M-Cl_2$, 21), 173 ($M-Cl_3$, 28), 172 (11), 171 (93), 166 (20), 164 (73), 130 (18), 129 (100).

An addition of chlorine to a solution of β,β-dimethyl-*p*-nitrostyrene in tetrahydrofuran saturated with lithium chloride gave a similar result.

(viii) p-*Methoxy*-β,β-*dimethylstyrene (52)*

Butyllithium in hexane (1.23 M, 49.0 ml; 0.06 mol) was added to a stirred suspension of isopropylidenetriphenylphosphonium iodide (21.7 g, 0.05 mol) in anhydrous tetrahydrofuran (100 ml), under nitrogen. After 5 min, *p*-anisaldehyde (6.8 g, 0.05 mol) was slowly added. The reaction mixture was heated under reflux for 48 h and then cooled; light petroleum (500 ml) was added to complete the precipitation of triphenylphosphine oxide. The organic solvents were decanted, and the solid residues of triphenylphosphine oxide and lithium iodide were washed by suspension in light

petroleum followed by decanting and filtration. The solvents were removed and the residue was distilled with a Kugelrohr apparatus at 135°/20 mm (lit.[88] 81°/1 mm) to yield *p*-methoxy-β,β-dimethylstyrene (6.2 g, 77%).

(ix) *2-Methoxy-1-(*p*-methoxyphenyl)-2-methylpropane (55)*

p-Methoxy-β,β-dimethylstyrene (52) (0.81 g, 5.0 mmol) was dissolved in anhydrous methanol (15.0 ml) with 3 drops of sulfuric acid (18 M). The reaction mixture was heated for 3 days, quenched in water and extracted with ether. The ether phase was washed with brine, dried ($MgSO_4$), and the solvent removed. The product was separated by preparative g.l.c. from residual starting material (13) to give 2-methoxy-1-(*p*-methoxyphenyl)-2-methylpropane (55) (0.31 g, 32%) (High-resolution mass spectrum: M^+, 194.1306. Calc. for $C_{12}H_{18}O_2$: M^+, 194.1306). ^1H n.m.r.:[51] δ 1.11, s, CMe_2; 2.70, s, CH_2; 3.27, s, OMe; AA'XX' system: 6.80, aryl H *ortho* to OMe; 7.11, aryl H *meta* to OMe; $J_{AX} + J_{AX'}$ 8.8 Hz.

(x) *Addition of dueterium chloride to β,β-dimethyl-*p*-nitrostyrene (5)*

Anhydrous deuterium chloride was generated by adding deuterium oxide (2 ml) slowly to a stirred suspension of anhydrous phosphorous pentachloride (10 g) in dry dichloromethane (50 ml). The deuterium chloride was passed through a solution of β,β-dimethyl-*p*-nitrostyrene (2 g, 11 mmol) in

dry dichloromethane (10 ml), in the presence of anhydrous iron(III) chloride (0.5 g). The reaction was allowed to proceed until complete by t.l.c. after ninety minutes. The reaction mixture was worked up by dilution with water and threefold extraction with dichloromethane (3 x 50 ml). The crude product (2.44 g) was purified by p.l.c. with 20% ethyl acetate/light petroleum as eluent. The purified product was shown to consist of a mixture of compounds containing up to eight deuterium nuclei by mass spectral and ^{1}H n.m.r. analysis. The mass spectrum had peaks at *m/z* 221 (1%), 220 (3), 219 (5), 218 (8), 217 (7), 216 (4.5) and 215 (2) whereas the undeuterated chloride (6) had peaks at *m/z* 215 (M + 2, 3%), 213 (M, 9) and 137 (100). ^{1}H n.m.r.: δ 1.59, m, CH_3, CH_2D, CHD_2; 3.13, m, CH_2, CHD; AA'XX' system: 7.46, m, 2H *meta* to NO_2; 8.18, m, 2H *ortho* to NO_2; $J_{AX} + J_{AX'}$ 9 Hz.

B. Addition Studies

(i) Isolation of 2-methyl-3-p-nitrophenylbutene (35)

Anhydrous hydrogen chloride was passed through a solution of β,β-dimethyl-*p*-nitrostyrene (5) (5.2 g, 29 mmol) in dry dichloromethane (20 ml) in the presence of anhydrous iron(III) chloride (0.5 g). The reaction was quenched by pouring into water when about 50% complete by t.l.c. The reaction mixture was extracted with dichloromethane (3 x 50 ml) and the combined organic phases were dried ($MgSO_4$) and

evaporated to give a mixture (5 g) of starting material (5), *p*-(2-chloro-2-methylpropyl)nitrobenzene (6) and 2-methyl-3-*p*-nitrophenylbutene (35) in the ratio 5:3:6 by ^{1}H n.m.r. A portion of this mixture was purified by preparative gas chromatography with a Hewlett Packard 402 gas chromatograph using a carbowax 2 μM 5.7% column to give 2-methyl-3-*p*-nitrophenyl-1-butene (35),[51] a yellow oil (Found: C, 68.0; H, 6.4; N, 7.8. $C_{10}H_{11}NO_2$ requires C, 67.8; H, 6.3; N, 7.9%). ^{1}H n.m.r.: δ ABM_2X_3 system: δ 1.68, m, Me; 3.42, m, benzylic 2H; 4.74, m, H_A; 4.89, m, H_B; J_{AB} 1.85 Hz; J_{AM} 1.35 Hz; J_{BM} 0.7 Hz; J_{AX} 0.75 Hz; J_{BX} 1.6 Hz; AA'XX' system: 7.35, m, 2H *meta* to NO_2; 8.15, m, 2H *ortho* to NO_2; $J_{AX} + J_{AX'}$ 8.9 Hz. ν_{max} 1645, 1510, 1360 cm^{-1}. λ_{max} (cyclohexane) 265 nm (ε 7185).

(ii) Addition of hydrogen bromide to (E)-p-*(2,3,3-trimethylbutyl)nitrobenzene (39)*

Anhydrous hydrogen bromide was passed through a solution of *(E)-p*-(2,3,3-trimethylbutyl)nitrobenzene (39) (0.55 g, 2.5 mmol) in dry dichloromethane (10 ml) until reaction was complete by t.l.c. (*c.* two hours). The reaction was worked up as in (i) above to give a crude product which was recrystallized from cyclohexane to give white needles of p-*(2-bromo-3,3-dimethylbutyl)nitrobenzene* (40) (0.4 g, 53%) m.p. 114-116° (Found: C, 52.3; H, 5.9; Br, 27.0; N, 4.7. $C_{13}H_{18}BrNO_2$ requires C, 52.0; H, 6.0; Br, 26.6; N, 4.7%). ^{1}H n.m.r.: δ 1.24, s, Bu^t; 1.57, d, Me, *J* 0.8 Hz;

Mercury(II) acetate (1.28 g, 4.0 mmol) was added, and the solution was stirred for 35 min. A solution of sodium hydroxide (3 M, 4.0 ml) was added and then the alkaline borohydride reagent (4.0 ml). The solution was extracted into ether; the combined ether phases were washed with water, brine, dried ($CaCl_2$), and the ether was removed. The crude product was purified by p.l.c. with 5% ethyl acetate/light petroleum as eluent to give 2-methoxy-2-methyl-1-(*p*-nitrophenyl)propane[51] (36) (0.280 g, 67%), a pale yellow oil (Found: C, 63.3; H, 6.9; N, 6.7. Calc. for $C_{11}H_{15}NO_3$: C, 63.2; H, 7.2; N, 6.7%). ^1H n.m.r.: δ 1.15, s, CMe_2; 2.86, s, CH_2; 3.26, s, OMe; AA'XX' system: 7.37, aryl H *meta* to nitro; $J_{AX} + J_{AX'}$, 8.6 Hz. ν_{max} (chloroform) 1510, 1360, 1080 cm^{-1}. λ_{max} (cyclohexane) 266 nm (ε 11300). *m/z* 209 (M; 0.1%), 73 (100).

(b) Reaction of β,β-dimethylstyrene (23)

β,β-Dimethylstyrene (1.32 g, 10.0 mmol) was dissolved in anhydrous methanol (20.0 ml) at 20°. Mercury(II) acetate (6.38 g, 20.0 mmol) was added and the solution stirred for 30 min. A solution of sodium hydroxide (3 M, 20.0 ml) was added, followed by the alkaline borohydride reagent (20.0 ml). The solution was extracted into ether, and the combined ether phases were washed with water, brine, and dried ($CaCl_2$); the ether was then removed. The crude mixture of products was distilled with a Kugelrohr apparatus to yield 2-methoxy-2-methyl-1-phenylpropane (51) (0.37 g, 23%), b.p. 110-115°/

AB system (benzylic CH_2): 3.05, d, H_A; 3.48, dq, H_B; J_{AB} 13.9 Hz; AA'XX' system: 7.50, m, 2H *meta* to NO_2; 8.82, m, 2H *ortho* to NO_2; $J_{AX} + J_{AX'}$ 8.9 Hz. ν_{max} 1512, 1365, 865 cm^{-1}. λ_{max} (ethanol) 263 nm (ε 10 000). *m/z* 220 (M-Br, 4%), 219 (9), 164 (50), 158 (40), 143 (38), 83 (100), 57 (88), 55 (51), 41 (72).

(iii) *Addition of hydrogen chloride to* β,β-*dimethyl* -p-*nitrostyrene (5) in methanol*

Anhydrous hydrogen chloride was slowly passed through a solution of β,β-dimethyl-*p*-nitrostyrene (5) (2 g, 11 mmol) in dry methanol (20 ml) in the presence of iron(III) chloride (0.5 g). The reaction flask was cooled in ice until the methanol was saturated with hydrogen chloride. The reaction was complete by t.l.c. in two hours. The reaction mixture was worked up and the crude product purified by p.l.c. in 5% ethyl acetate/light petroleum to give *p*-(2-chloro-2-methylpropyl)nitrobenzene (6) (2.2 g, 94%) and 2-methoxy-2-methyl-1-(*p*-nitrophenyl)propane (36) (0.12 g, 5%) identical with that prepared below.

(iv) Methoxymercuration reactions of the styrenes (5), (23) and (52)

(a) Reaction of β,β-dimethyl-*p*-nitrostyrene (5)

β,β-Dimethyl-*p*-nitrostyrene (5) (0.354 g, 2.0 mmol) was dissolved in anhydrous methanol (4.0 ml) at 20°.

25 mm (lit.[59] 87-93°/15 mm). ^{1}H n.m.r.: δ 1.10, s, CMe_2; 2.76, s, CH_2; 3.35, s, OMe; 7.17, br, s, Ph. Upon cooling, the residue partly crystallized. The crystals were separated by centrifugation, followed by removal of the oily diastereomer, and were crystallized from methanol to give white needles of one of the diastereoisomers (50a) of [1'-2'-bis-{(1"-methoxy-1"-methyl)ethyl}ethane-1'-2'-diyl]bisbenzene (0.165 g, 10%), m.p. 137.5-138° (lit.[59] 139-139.8°). ^{1}H n.m.r.: δ 0.58, s, CMeMe; 0.95, s, CMeMe; 2.80, s, CH; 3.45, s, OMe; 7.28, m, Ph. The oil separated by the above centrifugation was distilled with the Kugelrohr apparatus to give the diastereoisomer (50b) of [1',2'-bis{(1"-methoxy-1"-methyl)ethyl}ethane-1',2'-diyl]bisbenzene (0.140 g, 9%), b.p. 215-220°/25 mm (lit.[59] 200-210°/13 mm). ^{1}H n.m.r.: δ 1.02, s, CMeMe; 1.14, s, CMeMe; 3.20, s, CH; 3.49, s, OMe; 7.25, m, Ph.

(c) Reactions of *p*-methoxy-β,β-dimethylstyrene (52)

(A) *p*-Methoxy-β,β-dimethylstyrene (52) (1.62 g, 10.0 mmol) was dissolved in anhydrous methanol (20.0 ml) at 20°. Mercury(II) acetate (48) (6.38 g, 20 mmol) was added, and the reaction mixture was stirred. After 5 min. white flakes began to precipitate. After 30 min. the reaction was complete by t.l.c., but stirring was continued for a further hour. The reaction mixture was diluted with light petroleum to complete precipitation, and the precipitate was filtered off. The white solid was washed with light petroleum to complete precipitation, and the precipitate

was filtered off. The white solid was washed with light petroleum, cold water, ethanol and ether, and dried under vacuum to yield white micaceous plates (4.49 g, 86%) of a solid which was shown to be mercury(I) acetate (53) as follows.

A sample (10.0 mg) was dissolved readily in nitric acid (4 M, 0.5 ml) and a white precipitate formed on addition of several drops of concentrated hydrochloric acid. Ammonia solution (4 M, 2 ml) was added. This precipitate turned black; this indicated the presence of Hg^1 ion.

The original organic filtrates were dissolved in ether; the solution was washed with aqueous sodium bicarbonate, water, and dried ($CaCl_2$). The solvents were removed and the crude product distilled with a Kugelrohr apparatus to yield *1,2-dimethoxy-1-(p-methoxyphenyl)-2-methylpropane* (54) (1.94 g, 87%), b.p. $100^{o}/0.01$ mm, a colourless liquid (Found: C, 69.7; H, 9.0. $C_{13}H_{20}O_3$ requires C, 69.6; H, 9.0%). ^1H n.m.r.: δ 1.05, s, CMeMe; 1.15, s, CMeMe; 3.22, s, OMe; 3.26, s, OMe; 3.80, s, OMe; 4.01, s, CH; AA'XX' system: 6.86, aryl H *ortho* to OMe; 7.24, aryl H *meta* to OMe; $J_{AX} + J_{AX'}$, 8.8 Hz. ν_{max} (chloroform) 1720, 1590, 1580, 1490, 1440, 1330-1150br, 1150-1050br cm^{-1}. λ_{max} (ethanol 235 (ε 3267), 274 (1493), 280 nm (1296). *m/e* 224 (M; 0.5%), 151 (84), 135 (10), 73 (100).

(B) *p*-Methoxy-β,β-dimethylstyrene (52) (10.162 g, 1.0 mmol) was dissolved in anhydrous methanol (5.0 ml) at

20°; mercury(ii) acetate (48) (0.319 g, 1.0 mmol) was added and the reaction mixture was stirred. After 15 min, a white solid began forming, and metallic mercury became obvious after 2 h. After the reaction was complete (24 h, t.l.c.), the methanol solution was decanted from the mercury and the mercury washed with ether. The organic phases were combined and washed with water, brine, and dried ($CaCl_2$). The solvent was removed and the residue distilled with a Kugelrohr apparatus to yield 1,2-dimethoxy-1-(*p*-methoxyphenyl)-2-methylpropane (54) (0.17 g, 76%), identical with the sample prepared above.

(c) A solution of *p*-methoxy-β,β-dimethylstyrene (52) (1.62 g, 10.0 mmol) in anhydrous methanol (25.0 ml) was added to a solution of mercury(II) acetate (48) (6.38 g, 20.0 mmol) in anhydrous methanol (100 ml), both solutions being at 20.0°. The temperature was maintained, and 20.0 ml aliquots were taken and worked up with the alkaline borohydride as in (i) above. The products in each of these samples were identified and estimated by ^1H n.m.r. and g.l.c. comparison with authentic samples, and were shown to be starting material (52), 2-methoxy-1-(*p*-methoxyphenyl)-2-methylpropane (55) (see below) and 1,2-dimethoxy-1-(*p*-methoxyphenyl)-2-methylpropane (54). The proportions of the components (52), (54) and (55) in these samples were estimated and are plotted in Fig. 4.

2. Elimination Studies

A. Kinetic experiments for the substrates (1), (3), (4), (6), (7) and (8) (Tables 1 and 2)

The substrates were recrystallized to constant m.p. before use. The elimination reactions for (1), (3), (4), (6), (7) and (8) were all performed in anhydrous 50% v/v dimethyl sulfoxide/methanol solutions. The reactions were maintained at the appropriate temperature in the water bath of a Colora Kryothermostat WK 5.

Some experiments were performed by adding with stirring a known volume of a sodium methoxide solution in methanol to a solution of the substrate in dimethyl sulfoxide; both solutions were equilibrated at the appropriate temperature prior to mixing. The sodium methoxide solution was titrated with standard sulfuric acid with phenolphthalein as indicator. Allowance was made for a 1.5% volume contraction upon mixing the methanol and dimethyl sulfoxide solutions at 20.0 ^{o}C. This factor was determined by mixing equal volumes of a solution of known sodium methoxide concentration in methanol and dimethyl sulfoxide at 20.0 ^{o}C, and the change in methoxide concentration on mixing allowed determination of the volume change.

Most experiments were performed by mixing solutions of base and substrate which were 50% v/v dimethyl sulfoxide/ methanol prior to mixing at the appropriate temperature.

Both methods gave rate constants within experimental error of each other.

The reactions were monitored by u.v. spectroscopy in the following manner: aliquots of known volume were taken at appropriate time intervals and quenched in water (10 - 15 ml), then shaken in a stoppered flask with cyclohexane (50.00 ml). An aliquot of the cyclohexane extract was diluted appropriately and analysed by u.v. spectroscopy. From this spectrum, using appropriate simultaneous equations, the concentration of reactant and product were calculated. For example, in the reaction of (1) to give (5), the equations were

$$[(5)] = \left[\frac{(A_{307}\varepsilon_1 262) - (A_{262}\varepsilon_1 307)}{(\varepsilon_1 262\varepsilon_5 307) - (\varepsilon_1 307\varepsilon_5 262)} \right] q$$

$$[1] = \left[\frac{(A_{262}\varepsilon_5 307) - (A_{307}\varepsilon_5 262)}{(\varepsilon_1 262\varepsilon_5 307) - (\varepsilon_1 307\varepsilon_5 262)} \right] q$$

where $\varepsilon_y z$ is the extinction coefficient of (y) at z nm, A_x is the measured absorbance at x nm, and q is a factor allowing for dilution and u.v. cell path length. The extinction coefficients used for the runs were: (1), (3) and (4) at 262 nm ε 11300, at 307 nm ε 380; (6) at 262 nm ε 11600, at 307 nm ε 630; (7) at 262 nm ε 11550, at 307 nm ε 510; (8) at 262 nm ε 12100, at 295 nm ε 1400; (39) at 262 nm ε 3700, at 295 nm 10600; (5) and (58) at 262 nm ε 3700, at 307 nm ε 13400. All elimination processes proceeded to give

quantitative (>94%) yields of alkenes. The rate constants were determined as outlined in the discussion and appear in the Appendices.

B. Kinetic experiments for the substrates (2), (20) and (22) (Table 5)

These experiments were performed in anhydrous methanol.[89] The aliquots for the experiments with (22) were treated in exactly the same way as outlined in A above. However, because of the low solubility of (2) and (20) in cyclohexane, the aliquots from these runs were diluted with chilled methanol (5 ^{o}) to 250.0 ml and then promptly analysed by u.v. spectroscopy. The extinction coefficients used for calculation of rate constants were: (2), (20) at 260 nm ε 11300, at 303 nm ε 1330; (22) at 260 nm ε 10940, at 303 nm ε 1270.

C. Other miscellaneous mechanistic experiments

(i) Competitive elimination of HNO_2 and DNO_2 from the monodeuterated compound (4) (Table 3)

These reactions were carried out in anhydrous 50% v/v dimethyl sulfoxide/methanol, using sodium methoxide as base at 20.0 ± 0.1 ^{o} . The reactions were allowed to proceed to completion. The product mixture of (5) and (58) was purified by p.l.c. and the mixture was analysed by ^{1}H n.m.r. and mass spectrometry to determine the ratio of (5):(58).

(ii) Elimination of HNO_2 from the diastereomers (19a) and (19b) (Table 4)

These elimination reactions were carried out in 50% v/v dimethyl sulfoxide/methanol with sodium methoxide as base at 20.0 ± 0.1 °. A series of identical reactions were set up and allowed to proceed for varying periods of time. The reactions were worked up and the reaction products separated by p.l.c. with 20% ethyl acetate/light petroleum as eluent. The remaining starting material was then analysed by ^1H n.m.r. to determine the relative proportions of (19a) and (19b).

(iii) Exchange reactions of (2) and (20)

Three portions of *p*-(1-chloro-2-methyl-2-nitropropyl)-nitrobenzene (2) (each 129 mg, 0.5 mmol) were dissolved separately in sodium methoxide solutions in *O*-(D)-methanol[87] (0.1 M, 10.0 ml) and allowed to react at 20.0 °. The reactions were allowed to proceed to 21, 28 and 67% completion respectively and worked up. The reaction product was purified by p.l.c. with 15% ethyl acetate/light petroleum as eluent and the remaining starting material examined by ^1H n.m.r. No incorporation of deuterium was detectable.

A similar experiment in which 1-(D)-*p*-(1-chloro-2-methyl-2-nitropropyl)nitrobenzene (130 mg, 0.5 mmol) was dissolved in a sodium methoxide solution in methanol (0.1 M, 10.0 ml) at 20.0 ° and allowed to proceed to 60% reaction. No proton/deuterium exchange had occurred.

(iv) Elimination of nitrous acid from the diastereomers (60) and (61)

The less polar diastereomer (60) (410 mg, 1.5 mmol) was dissolved in a sodium methoxide in methanol solution (0.42 g of sodium in 50.0 ml methanol) at 20.0 °C. The reaction was complete in eight hours and upon work up a 1.1 mixture by ^{1}H n.m.r. the alkenes (64) and (65) (340 mg, 100%) was recovered (Found: C, 58.4; H, 5.6; N, 6.4. $C_{11}H_{12}ClNO_2$ requires C, 58.4; H, 5.4; N, 6.2%). ^{1}H n.m.r.: δ 1.03, t, $CH_2\underset{\sim}{Me}$, *J* 7.4 Hz; 2.02, s, Me; 2.08, q, $\underset{\sim}{CH_2}Me$, *J* 7.4 Hz. AA'XX' system: 7.50, m, 2H *meta* to NO_2; 8.22, m, 2H *ortho* to NO_2; δ 1.14, t, $CH_2\underset{\sim}{Me}$, *J* 7.4 Hz; 1.77, s, Me; 2.44, q, $\underset{\sim}{CH_2}Me$, *J* 7.4 Hz; AA'XX; system: 7.51, m, 2H *meta* to NO_2; 8.22, m, 2H *ortho* to NO_2. *m/z* 227 (M + 2, 17%), 225 (M, 65), 210 (10), 208(15), 190 (14), 178 (10), 166(11), 164(39), 145(14), 144(72), 143(25), 130(12), 129(100), 128(62), 127 (23), 116(12), 115(34), 89(11), 77(15), 63(23), 51(21).

A similar reaction of (60) (210 mg, 0.77 mmol) which was worked up before completion and purified by p.l.c. with 10% ethyl acetate/light petroleum as eluent gave starting material (60) (74 mg, 35%) and the 1:1 mixture of alkenes (82 mg, 47%). No trace of the more polar diastereomer was detected by ^{1}H n.m.r. or t.l.c.

The more polar diastereomer (61) (410 mg, 1.5 mmol) was dissolved in a sodium methoxide in methanol solution (0.42 g of sodium in 50.0 ml of methanol) at 20.0 °. Upon work up

the reaction mixture gave a 1.7:1 mixture by ^{1}H n.m.r. of the alkenes (64) and (65) (300 mg, 88%). A similar reaction gave a 1.5:1 mixture.

A similar reaction of (61) (170 mg, 0.62 mmol) which was worked up before completion and purified by p.l.c. with 10% ethyl acetate/light petroleum as eluent gave starting material (61) (105 mg, 62%) and a 1.6:1 mixture of alkenes (47 mg, 33%). No trace of the more polar diastereomer was detected by ^{1}H n.m.r. or t.l.c.

(v) Solvolysis of t-butyl bromide (66), t-butyl chloride (67) and 2-methyl-2-nitropropane (68)

Methanol solutions of the appropriate substrate (1 M, 50.0 ml) were heated at 64 °. The progress of reaction was followed by ^{1}H n.m.r. The t-butyl bromide (66) solvolysed completely within thirty minutes and 60% of the t-butyl chloride had reacted after five hours. The 2-methyl-2-nitropropane showed no change after twenty four hours.

(vi) Solvolysis of p-*(2-bromo-2-methylpropyl)nitrobenzene (7) and* p-*(2-methyl-2-nitropropyl)nitrobenzene (1)*

Methanol solutions of the appropriate substrate (0.1 M, 50.0 ml) were heated at 64 °. The progress of reaction was followed by t.l.c. After five hours the *p*-(2-bromo-2-methylpropyl)nitrobenzene (7) had solvolysed and the proportions of (5), (35) and (36) were determined,

after work up, by ^{1}H n.m.r. The *p*-(2-methyl-2-nitropropyl)-nitrobenzene (1) was indefinitely stable under these conditions.

(vii) Attempted elimination of nitrous acid from p-(2-methyl-2-nitropropyl)iodobenzene (70) and p-(2-methyl-2-nitropropyl)phenylbenzene (71)

p-(2-Methyl-2-nitropropyl)iodobenzene (70) (305 mg, 1 mmol) was dissolved in a solution of sodium methoxide in 50% v/v dimethyl sulfoxide/methanol (0.3 M, 10.0 ml). After one month no detectable reaction had occurred. A similar reaction of (71) (180 mg, 1 mmol) also gave no reaction.

(viii) Reaction of (1) with sodium

A solution of *p*-toluenethiol (4 g) in anhydrous dimethyl sulfoxide was added to a solution of sodium methoxide in methanol. The resulting solution was titrated against standard sulfuric acid and the concentration of base determined as 0.193 M. *p*-(2-Methyl-2-nitropropyl)nitrobenzene (1) (1.12 g, 5 mmol) was dissolved in 10.0 ml of this solution at 30.0 ^{o}, under nitrogen. After 123.3 hours the reaction was quenched and the ratio of (5):(1) determined by ^{1}H n.m.r. was 1:3.9.

APPENDIX 1

Rates of bimolecular β-elimination in (1), (6) and (7). All reactions in 50% v/v Me_2SO/MeOH. All rate constants are quoted with standard deviations.

Table 6. Rates of elimination from (1) at 20.0 ± 0.1 °.

Initial Concentrations (1)	$^{-}$OMe	k_2 (x 10^3)^A l mol^{-1} s^{-1}	Correlation Coefficient	k_2 (x 10^3)^B l mol^{-1} s^{-1}	Correlation Coefficient
0.0121 M	0.0398 M	3.09 ± 0.05	.9999	3.11 ± 0.03	.9997
0.0121 M	0.0398 M	3.25 ± 0.02	.9999	3.09 ± 0.04	.9999
0.0165 M	0.0665 M	3.15 ± 0.04	.9995		
0.0165 M	0.0665 M	3.18 ± 0.04	.9993		

Mean rate constant^A = (3.17 ± 0.07) x 10^{-3} l mol^{-1} s^{-1}

^{A} Based on appearance of (5).

^{B} Based on disappearance of (1).

Table 7. Rates of elimination from (1) at 5.2, 10.0, 15.0, 25.0 and 30.0 °.
Rates are based on appearance of (5).

Temperature °C	Initial Concentrations (1)	$^-$OMe	k_2 ($\times 10^3$) l mol^{-1} s^{-1}	Correlation Coefficients	Mean rates $\times 10^3$ l mol^{-1} s^{-1}
5.2 ± 0.2	0.0398 M	0.1231 M	0.488 ± 0.019	.9969	
	0.0398 M	0.1231 M	0.545 ± 0.012	.9991	0.52 ± 0.04
10.0 ± 0.1	0.0194 M	0.051 M	0.902 ± 0.01	.9997	
	0.0194 M	0.051 M	0.888 ± 0.01	.9993	0.895± 0.01
15.0 ± 0.1	0.0230 M	0.0313 M	1.83 ± 0.03	.9986	
	0.0230 M	0.0313 M	1.80 ± 0.01	.9999	1.82 ± 0.02
25.0 ± 0.1	0.01238 M	0.0378 M	6.01 ± 0.04	.9999	6.2 ± 0.03
	0.01238 M	0.0378 M	6.45 ± 0.04	.9951	
30.0 ± 0.1	0.00548 M	0.0125	11.8 ± 0.02	.9994	
	0.00548 M	0.0125	11.3 ± 0.01	.9997	11.6 ± 0.4

Table 8. Rates of elimination from (6) at 20.0 ± 0.1 °. Rates are based on appearance of (5).

Initial Concentrations		k_2 (x 10^3)	Correlation
(6)	$^-$OMe	1 mol^{-1} s^{-1}	Coefficient
0.00625 M	0.01805 M	1.17 ± 0.02	.9994
0.00625 M	0.06018 M	1.10 ± 0.05	.9951
0.0118 M	0.06018 M	1.10 ± 0.02	.9991
0.0118 M	0.06018 M	1.11 ± 0.01	.9998

Mean rate constant = (1.12 ± 0.03) x 10^{-3} 1 mol^{-1} s^{-1}

Table 9. Rates of elimination from (6) at 10.0, 15.0, 25.2, 27.5 and 30.0 °.
Rates are based on appearance of (5).

Temperature ±0.1 °	Initial Concentrations (6)	$^-$OMe	k_2 (x 10^3) 1 mol^{-1} s^{-1}	Correlation Coefficients	Mean rates x 10^3 1 mol^{-1} s^{-1}
10.0	0.01286 M	0.10550 M	0.371 ± 0.005	.9996	
	0.01957 M	0.10550 M	0.353 ± 0.033	.9999	0.362 ± 0.012
15.0	0.01140 M	0.0945 M	0.549 ± 0.006	.9997	
	0.03966 M	0.0510 M	0.500 ± 0.02	.9968	0.525 ± 0.03
25.2	0.01270 M	0.0845 M	2.09 ± 0.02	.9996	
	0.01170 M	0.0845 M	2.24 ± 0.04	.9990	2.17 ± 0.1
27.5	0.01757 M	0.0245 M	2.25 ± 0.04	.9994	
	0.01992 M	0.0245 M	2.31 ± 0.03	.9996	2.28 ±0.07
30.0	0.01865 M	0.0245 M	3.02 ± 0.03	.9998	
	0.01290 M	0.0745 M	3.09 ± 0.09	.9977	3.06 ± 0.1

Table 10. Rates of elimination from (7) at 20.0 ± 0.1 °. Rates are based on appearance of (5).

Initial Concentrations (7)	$^-$OMe	k_2 (x 10^3) 1 mol^{-1} s^{-1}	Correlation Coefficient
0.0042 M	0.0208 M	32.5 ± 0.4	.9997
0.0042 M	0.0208 M	33.1 ± 0.5	.9998
0.0031 M	0.0124 M	29.6 ± 0.2	.9999
0.0031 M	0.0124 M	27.4 ± 0.6	.9992
0.0039 M	0.0053 M	32.2 ± 0.4	.9997

Mean rate constant = 31.0 ± 2.4 1 mol^{-1} s^{-1}

Table 11. Rates of elimination from (7) at 6.0, 10.05, 12.4 and 14.9 °.

Rates are based on appearance of (5).

Temperature ±0.1 °	Initial Concentrations (7)	$^-$OMe	k_2 (x 10^3) l mol^{-1} s^{-1}	Correlation Coefficients	Mean rates x 10^3 l $mol^{-1}s^{-1}$
6.0	0.00789 M	0.04131 M	7.21 ± 0.08	.9996	6.82 ± 0.5
	0.00751 M	0.04131 M	6.42 ± 0.1	.9994	
10.05	0.00734 M	0.05750 M	12.0 ± 0.4	.9982	12.1 ± 0.5
	0.00652 M	0.05750 M	12.2 ± 0.3	.9989	
	0.00652 M	0.05750 M	12.2 ± 0.1	.9997	
12.4	0.00664 M	0.02375 M	12.8 ± 0.1	.9997	12.8 ± 0.5
	0.00881 M	0.01400 M	12.8 ± 0.3	.9986	
14.9	0.00578 M	0.02625 M	17.2 ± 0.6	.999	18.6 ± 2.0
	0.00578 M	0.02625 M	18.5 ± 0.4	.998	
	0.00592 M	0.02625 M	20.2 ± 0.7	.999	

APPENDIX 2

Rates of bimolecular elimination in (3), (4) and (8). All reactions in 50% v/v Me_2SO/MeOH. All rate constants are quoted with standard deviations.

Table 12. Rates of elimination from (3) at 20.0 ± 0.1 °.

Initial Concentrations (3)	^-OMe	k_2 (x 10^3) l $mol^{-1}s^{-1}$	Correlation Coefficient
0.0165 M	0.0992 M	0.504 ± 0.008	.9993
0.0165 M	0.0992 M	0.471 ± 0.009	.9990

Mean rate constant = (0.49 ± 0.02) x 10^{-3} l mol^{-1} s^{-1}

Table 13. Rates of elimination from (4) at 20.0 ± 0.1 °.

Initial Concentrations (4)	^-OMe	k_2 (x 10^3) l $mol^{-1}s^{-1}$	Correlation Coefficient
0.0244 M	0.1825 M	1.81 ± 0.02	.9997
0.0244 M	0.1825 M	1.74 ± 0.04	.9990

Mean rate constant = (1.79 ± 0.05) x 10^{-3} l mol^{-1} s^{-1}

Table 14. Rates of elimination from (8) at $20.0 \pm 0.1\ ^{o}$.
Rates based on appearance of (39).

Initial Concentrations (8)	$^{-}$OMe	k_2 (x 10^3) $1\ mol^{-1}s^{-1}$	Correlation Coefficient
0.119 M	0.2423 M	0.312 ± 0.014	.9993
0.119 M	0.2423 M	0.386 ± 0.005	.9998
0.0257 M	0.0992 M	0.407 ± 0.022	.993
0.0257 M	0.0992 M	0.379 ± 0.018	.997

Mean rate constant = $(0.37 \pm 0.04) \times 10^{-3}\ 1\ mol^{-1}\ s^{-1}$

APPENDIX 3

Rates of elimination from (2), (20) and (22). All reactions in MeOH at 20.0 ± 0.1 ^{o}C. Rates based on disappearance of substrate.

Table 15. Rate of elimination from (2).

Initial Concentrations (20)	$^{-}$OMe	k_2 (x 10^3) l $mol^{-1}s^{-1}$	Correlation Coefficient
0.02429 M	0.09406 M	0.205 ± 0.002	.9996
0.02429 M	0.09406 M	0.215 ± 0.001	.9999
0.02610 M	0.12226 M	0.212 ± 0.002	.9998

Mean rate = (0.21 ± 0.01) x 10^{-3} l mol^{-1} s^{-1}

Table 16. Rate of elimination from (20).

Initial Concentrations (20)	$^{-}$OMe	k_2 (x 10^3) l $mol^{-1}s^{-1}$	Correlation Coefficient
0.03153 M	0.1416 M	0.143 ± 0.006	.9994
0.03153 M	0.1416 M	0.122 ± 0.006	.9991

Mean rate = (0.13 ± 0.02) x 10^{-3} l mol^{-1} s^{-1}

Table 17. Rate of elimination from (22).

Initial Concentrations (22)	-OMe	k_2 (x 10^3) $1\ mol^{-1} s^{-1}$	Correlation Coefficient
0.02557 M	0.0942 M	0.260 ± 0.005	.9999
0.02557 M	0.0942 M	0.284 ± 0.01	.9999

Mean rate = (0.27 ± 0.02) x 10^{-3} $1\ mol^{-1}\ s^{-1}$

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STRUCTURES FOR PART I

$ArCH(Cl)Bu^t$ (1)

$ArC(Me)(Pr^i)NO_2$ (2)

$PhCH(Cl)Bu^t$ (3)

NaN_3 (4)

$Na^+\bar{C}(CN)_2R$

(5) R = $^\dagger Et$

(6) R = $^\dagger Pr^i$

(7) R = $^\dagger Bu^t$

$Na^+\bar{C}(CN)(CO_2Et)R$

(8) †R = Me

(9) †R = Pr^i

$Na^+\bar{C}(CO_2Et)_2R$

(10) †R = Me

(11) †R = Et

(12) †R = Pr^1

(13) †R = Bu^t

$Na^+\bar{C}(CO_2R)(COMe)Me$

(14) †R = Me

†R = Et

$Na^+\bar{C}(COMe)_2Me$ (15)†

$Na^+p\text{-}\bar{S}O_2C_6H_4Me$ (16)†

$Na^+\bar{P}O(OEt)_2$ (17)†

(18)

$[Li^+ MeC(R)NO_2]^-$

(19)† R = Me

(71)† R = Et

$ArCH(N_3)Bu^t$ (20)

$Ph(CH(N_3)Bu^t$ (21)

$ArCH(R)Bu^t$

---

(22) R = $C(CN)_2Et$

(23) R = $C(CN)_2Pr^i$

(24) *2RS, 3RS* R = $C(CN)(CO_2Et)Me$

(25) *2RS, 3SR* R = $C(CN)(CO_2Et)Me$

(26) *2RS, 3RS* R = $C(CN)(CO_2Et)Pr^i$

(27) *2RS, 3SR* R = $C(CN)(CO_2Et)Pr^i$

(28) R = $C(CO_2Et)_2Me$

(29) R = $C(CO_2Et)_2Et$

(30) R = $C(CO_2Me)(COMe)Me$

(31) R = $-O-C(Me)=C(Me)CO_2Me$

(32) R = $-O-C(Me)=C(CO_2Me)Me$

(33) R = $p\text{-}SO_2C_6H_4Me$

(35) R = OH

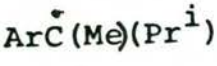
(36) R = H

---

† For these structures a number with the (a), such as 5(a), indicates the anion of a salt e.g. 10(a)= $^-C(CO_2Et)_2Me$.

(34)

(37)



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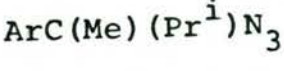

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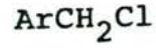
(45)

(48)



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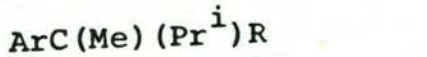


(40) R = $C(CN)_2Et$

(41) R = $C(CN)_2Pr^i$

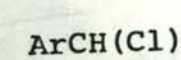
(42) 2*RS*, 3*SR* R = $C(CN)(CO_2Et)Me$

(43) 2*RS*, 3*RS* R = $C(CN)(CO_2Et)Me$

(44) R = $C(CO_2Et)_2Me$

(46) R = OH

(47) R = H



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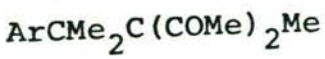

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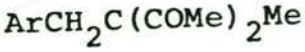

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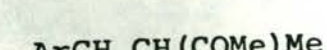

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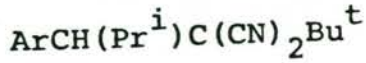

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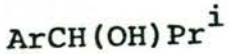
(57)

(58)

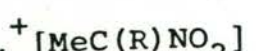


(59)

(68) R = Me

(69) R = Et

(70)

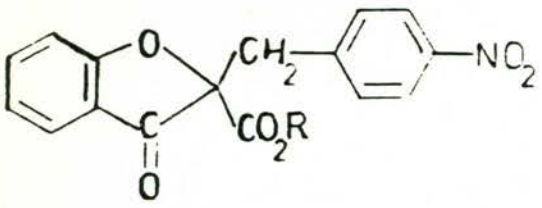


(72) R = Me

(73) R = Et

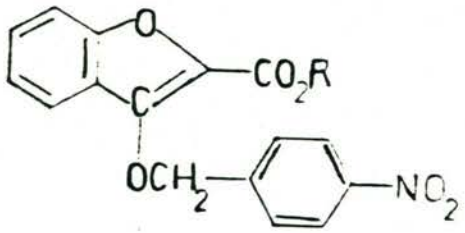
(19) R = Me

(71) R = Et



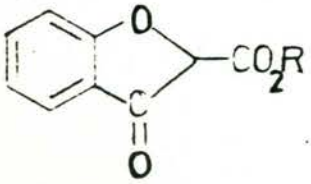
(77) R = Et

(79) R = Me



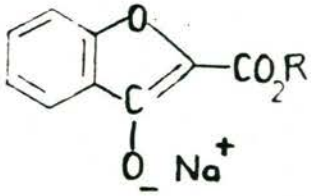
(78) R = Et

(80) R = Me



(81) R = Et

(82) R = Me



(83) R = Et

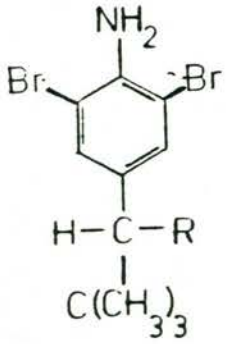
(84) R = Me

$Na^{+-}C(CO_2Et)(COMe)Me$

(85)

$ArCH_2C(CO_2Et)(COMe)Me$

(86)



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(87) R = p-$SO_2C_6H_4Me$

(88) R = $C(CN)_2Et$

(89) R = $C(CN)_2Pr^i$

(90) 2*RS*, 3*RS* R = $C(CN)(CO_2Et)Me$

(91) 2*RS*, 3*R* R = $C(CN)(CO_2Et)Me$

(92) R = $C(CO_2Et)Me$

STRUCTURES FOR PART II

$ArCH_2CMe_2X$

(1) X = NO_2

(6) X = Cl

(7) X = Br

$ArCHClCMe_2NO_2$

(2)

$ArCD_2CMe_2NO_2$

(3)

$ArCHDCMe_2NO_2$

(4)

$ArCH=CMe_2$

(5)

$ArCH_2CMe(Bu^t)NO_2$

(8)

$ArCBr_3$

(9)

$ArCDBr_2$

(10)

ArCDO

(11)

$ArCD_2OH$

(12)

$ArCD_2Cl$

(13)

$Li^{+-}CMe(R)NO_2$

(14) R = Me

(15) R = Et

ArCHO

(16)

ArCHDOH

(17)

ArCHDCl

(18)

$ArCHDCMeBu^tNO_2$

(19a) 1*RS*, 2*SR*

1*RS*, 2*SR*

$ArCDClCMe_2NO_2$

(20)

$ArCDCl_2$

(21)

$ArCHClCMe_2Cl$

(22)

$PhCH=CMe_2$

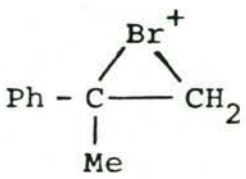
(23)

$ArCDClCMe_2Cl$

(24)

$ArCHDCMe_2Cl$

(25)



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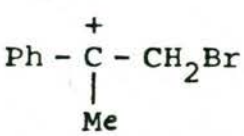

(27)

$PhCH_2CMe_2Cl$

(28)

$PhCH_2-\overset{+}{C}Me_2$

(29)

$ArCH_2\overset{+}{C}Me_2$

(30)

$PhCHClCMe_2H$ (31)

$ArCHClCMe_2H$ (32)

$ArCHClC(Me)=CH_2$ (33)

$ArCHDC(Me)=CH_2$ (34)

$ArCH_2C(Me)=CH_2$ (35)

$ArCH_2CMe_2OMe$ (36)

$ArCH(OMe)CMe_2H$ (37)

$ArCHCMe_2H$ (38)

E-$ArCH=CMeBu^t$ (39)

$ArCH_2CMeBu^tBr$ (40)

$PhCH(OR)CH_2HgX$

(42) R = H

(43) R = Me

$PhCH=CHMe$

(44) (*Z*)

(45) (*E*)

$PhCH(OMe)CH(HgX)Me$ (46)

$PhCH(HgX)CH(OMe)Me$ (47)

$Hg(OAc)_2$ (48)

$PhCH(HgCl)CMe_2OMe$ (49)

$PhCH(CHMe_2OMe)_2$ (50)

p-$MeOC_6H_4CH=CMe_2$ (52)

$PhCH_2CMe_2OMe$ (51)

$Hg_2(OAc)_2$ (53)

p-$MeOC_6H_4CH(OMe)CMe_2OMe$ (54)

p-$MeOC_6H_4CH_2CMe_2OMe$

(55)

p-$MeOC_6H_4CH(OMe)CMe_2H$

(56)

p-$MeOC_6H_4CH(HgOAc)CMe_2OMe$

(57)

$ArCD = CMe_2$

(58)

$ArCHClCMeEtNO_2$

(60) less polar

(61) more polar

$ArCH = CMeEt$

(64) (E)-

(65) (Z)-

Me_3CX

(66) X = Br

(67) X = Cl

(68) X = NO_2

(69) X = OMe

p-$IC_6H_4CH_2CMe_2NO_2$

(70)

p-$PhC_6H_4CH_2CMe_2NO_2$

(71)