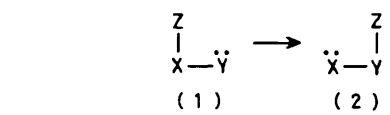
Base Catalysed Rearrangements involving Ylide Intermediates. Part 15.[1] The Mechanism of the Stevens [1,2] Rearrangement

W. David Ollis,* Max Rey, and Ian O. Sutherland
Department of Chemistry, The University, Sheffield S3 7HF

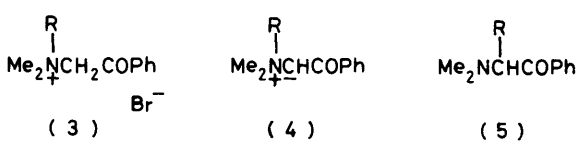
The Stevens [1,2] rearrangement of acyl-stabilised ammonium ylides has been investigated with regard to stereoselectivity, intramolecularity and the formation of products in addition to the [1,2] rearrangement product. A detailed study of the effects of reaction conditions upon the rearrangement of the ylide derived from the salt (13) has shown that the stereoselectivity (retention of the configuration of the chiral migrating group) and intramolecularity decrease as solvent viscosity decreases. The rearrangement of the salt (13) in water at 0 °C is essentially intramolecular with virtually complete retention of the configuration of the migrating group. These results, together with the isolation of products that can be rationalised on the basis of random free-radical coupling, indicate that the [1,2] rearrangement of acyl-stabilised ammonium ylides normally involves a radical pair mechanism.

The Stevens rearrangement [2,3] of the ammonium ylides (1) ⟶ (2) ($X = \overset{+}{N}R_2$, $Y = \overset{-}{C}R_2$, $Z = CR_3$) is one example of the wide range [4] of anionic sigmatropic rearrangements represented by the general reaction (1) ⟶ (2). The mechanism of these reactions has been a topic of investigation and discussion for many years and the mechanistic investigation of the Stevens rearrangement is typical. Thus, the reaction was first recognised [3] as a base catalysed transformation of the ammonium salt (3a), later shown by Stevens [5] to involve the ylide intermediate (4a) [6] which rearranged to give the observed reaction product (5a). The reaction has been reviewed [2] and its scope and limitation and some evidence for reaction mechanism have been discussed. The important experimental facts, established prior to the investigation reported in this paper, are (i) the rearrangement is intramolecular,[7] (ii) for a chiral migrating group R (for example R = CHMePh) the product is formed with almost complete retention of the configuration of R,[8–10] and (iii) in suitable cases [11] chirality can be transferred from nitrogen to carbon. Two principal mechanisms can be envisaged for the reaction: (a) a concerted [1,2] sigmatropic rearrangement,[12] with retention of configuration of the migrating group and simultaneous bond breaking and making, or (b) a process in which bond breaking precedes bond making which must, therefore, involve initial homolysis to give a radical pair [9,13,14] or heterolysis to give an ion pair [15,16] followed by rapid pair recombination. The first possibility, a concerted mechanism, requires a process with suprafacial use of the π-bonding between atoms X and Y in the transition state and would be symmetry forbidden by the Woodward–Hoffmann rules. However, on the basis of calculations,[17] it has been suggested that such processes may occur in highly favoured, strongly exothermic cases, although it is difficult to extrapolate from these calculations to reactions of highly polar species, such as ylides, in solution.

In view of our interest in the [3,2] sigmatropic rearrangements [1,18] closely related to the Stevens rearrangement and the first isolation [6] of ammonium ylides such as (4), we decided to re-investigate the mechanism of the Stevens rearrangement.[19] We chose as reaction probes (*a*) the structures of reaction products additional to the rearrangement product (5), (*b*) the intramolecularity of the rearrangement, and (*c*) the stereoselectivity of the rearrangement of a chiral ylide (4b) ⟶ (5b). The investigation was also conducted in the light of a number of reports [9,14,20,21] of the observation of CIDNP during Stevens rearrangements and other related [1,2] anionic rearrangements. A further method of investigation using ambident migrating groups has been described in preliminary communications [22] and will be discussed fully in future papers in this series.



(1) (2)



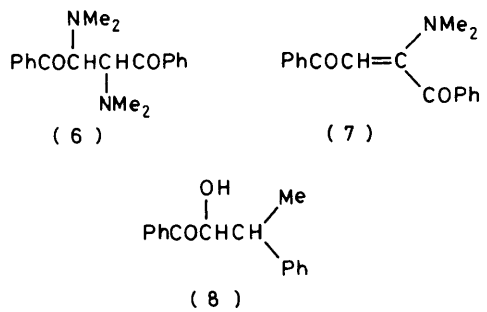
(3) (4) (5)

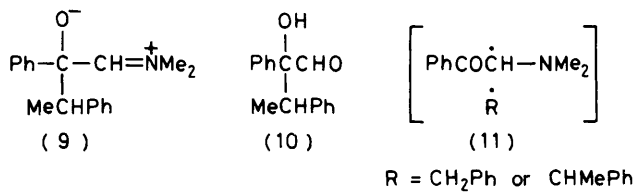
In (3) – (5): a, R = CH_2Ph; b, R = CHMePh.

The Structures of Reaction Products.—The ylide (4a) was prepared [6] by the action of aqueous sodium hydroxide on the ammonium salt (3a) as a crystalline monohydrate, m.p. 75—82 °C, which could be stored at 0 °C for one year without noticeable decomposition. Thermal rearrangement of the ylide (4a) in chloroform at 60 °C gave the [1,2] rearrangement product (5a) as the major product together with 1,2-diphenylethane, the diastereoisomeric diamines (6), and *N*,*N*-dimethylbenzylamine. A similar set of products was obtained under a variety of reaction conditions in yields that depended upon the conditions used (see Table 6, Experimental section) and these products accounted for >95% of the total reaction product. The diamine (6) was synthesised, as the single diastereoisomer *A*, m.p. 156—158 °C, by the reaction of (*E*)-1,2-dibenzoylethylene with dimethylamine in the presence of iodine; a low yield of the vinylogous amide (7) was also obtained from this reaction. Equilibration of the diastereoisomer *A* of the diamine (6) in hot methanol followed by fractional crystallisation of the product gave diastereoisomer *B*, m.p. 94—95 °C. The relative configurations of these two diastereoisomers could not be established with certainty, but we note that although diastereoisomer *B* is thermodynamically favoured in methanol solution it could be reconverted into diastereoisomer *A* by heating to its melting point.

The rearrangement of the related ylide (4b) was investigated in a similar manner, but it was found in this case that treatment of the quaternary salt (3b) with aqueous sodium hydroxide at 0 °C gave only rearrangement products since the ylide (bb) is evidently unstable under these conditions. The reaction was therefore investigated by treating the ammonium salt

(3b) with base. In methanol at 55 °C, using sodium methoxide as the base, the salt (3b) gave the [1,2] rearrangement product (5b) as the major product as a mixture of both diastereoisomers (1 : 1 ratio), together with small quantities of both diastereoisomers of 2,3-diphenylbutane (1 : 1 ratio), and diastereoisomers *A* and *B* of the diamine (6) (3 : 1 ratio). The rearrangement of the salt (3b) in water at 0 °C, using sodium hydroxide as the base, gave the [1,2] rearrangement product (5b) as a mixture of diastereoisomers (5 : 4 ratio) and small quantities of 1-phenylethanol and both diastereoisomers of the acyloin (8) (5 : 3 ratio). The origin of (8) was not clear from this work, but subsequent work [23a] showed that hydroxyketones may be formed during Stevens rearrangements in aqueous solution by a competing [1,3] rearrangement of the ylide (4b) to give a betaine (9). Hydrolysis of (9), to give an acyloin (10), followed by a base catalysed [1,2] acyloin rearrangement [24] (10) ⟶ (8) would account for the formation of this product (8). The small quantity of 1-phenylethanol obtained from the reaction of the salt (3b) is presumably a consequence of a nucleophilic





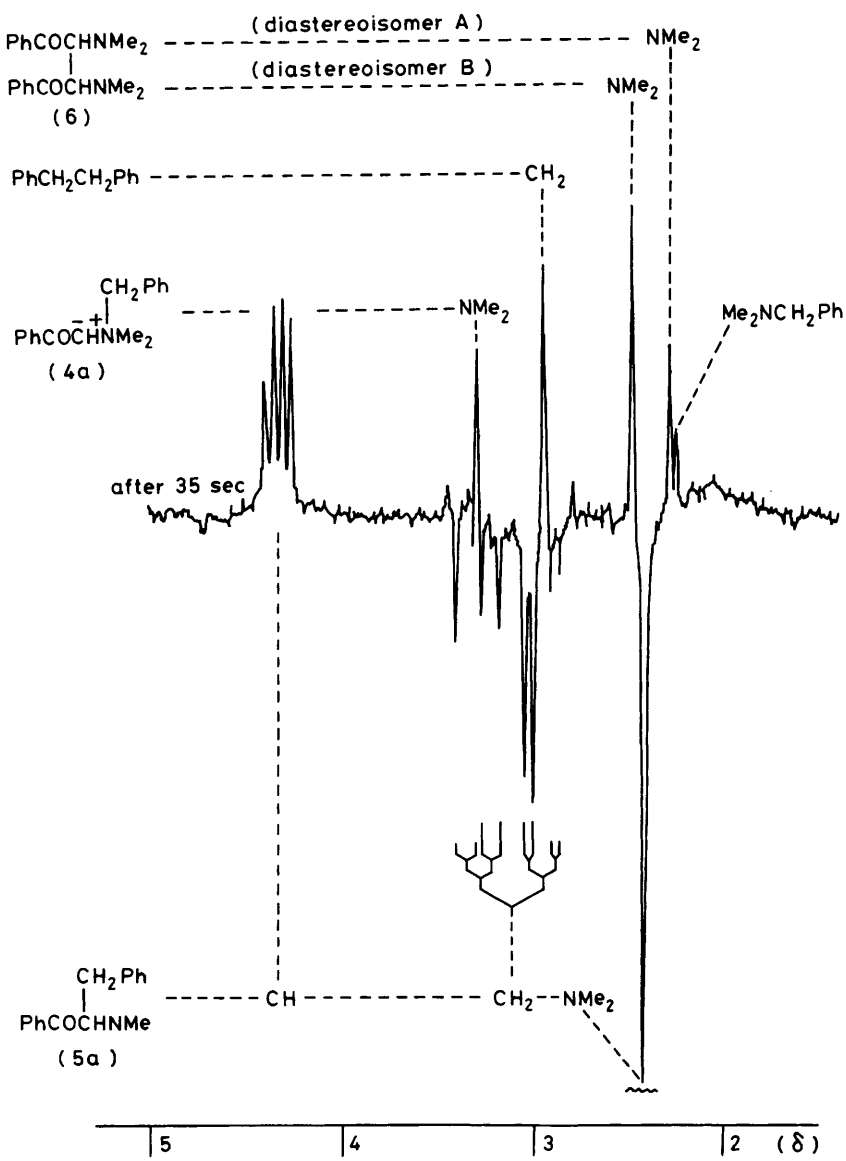


Figure 1. CIDNP effects during the rearrangement (4a) ⟶ (5a) in $CDCl_3$ at 60 °C

displacement reaction. The rearrangement of the salt (3b) in water at 50 °C gave, in addition to the rearrangement product (5b), a low yield of both diastereoisomers of 2,3-diphenylbutane (1 : 1 ratio).

In addition to the direct pathway for the [1,2] rearrangement (4) ⟶ (5) two alternative but indirect pathways can be envisaged. These alternative pathways are (i) a [1,3] rearrangement to give a betaine intermediate [*cf.* (9)] which could then undergo a subsequent [1,2] rearrangement and (ii) a [1,4] sigmatropic rearrangement giving an enol ether as an intermediate which could then undergo a subsequent [1,3] sigmatropic rearrangement. These alternative pathways (i) and (ii) are both excluded by experimental evidence. Pathway (i) can be excluded because in competing [1,2] and [1,3] rearrangements of chiral ylides, the stereoselectivity of the [1,3] rearrangement has been shown to be *less* then the stereoselectivity of the [1,2] rearrangement.[23a] Pathway (ii) has also been discounted [23b] and it has been firmly excluded by the experimental result [23c] that the thermal [1,3] rearrangement of enol ethers is much too slow for them to function as intermediates in the [1,2] rearrangement of ylides.

The above investigation of products is totally consistent with a mechanism for the rearrangement (4) ⟶ (5) involving initial homolysis to give the radical pair (11) followed by intramolecular recombination to give the amine (5) as the major reaction product. The minor products, including the diamine (6) and 1,2-diphenylethane [from (4a)] or 2,3-diphenylbutane [from (3b)], are the expected products from intermolecular recombination of radicals [25] which escape from the solvent caged radical pair (11). This conclusion was provided with strong support by the observation that the rearrangement of the ylide (4a) (in $CDCl_3$ at 60 °C) in the probe of an n.m.r. spectrometer (100 MHz) gave a ^1H spectrum of the initially formed reaction products that showed strong CIDNP associated with the signals of the [1,2] rearrangement product (5a), 1,2-diphenylethane, and both diastereoisomers

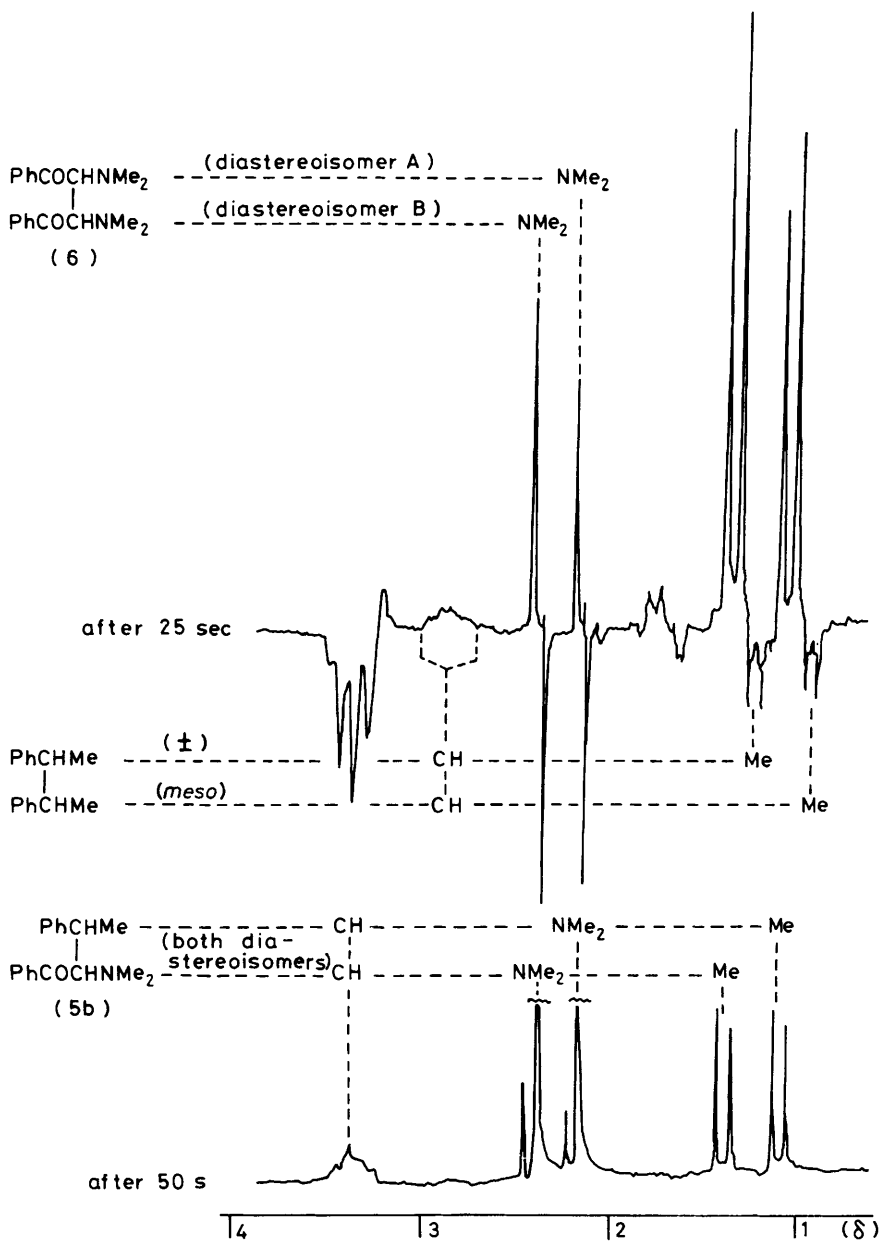
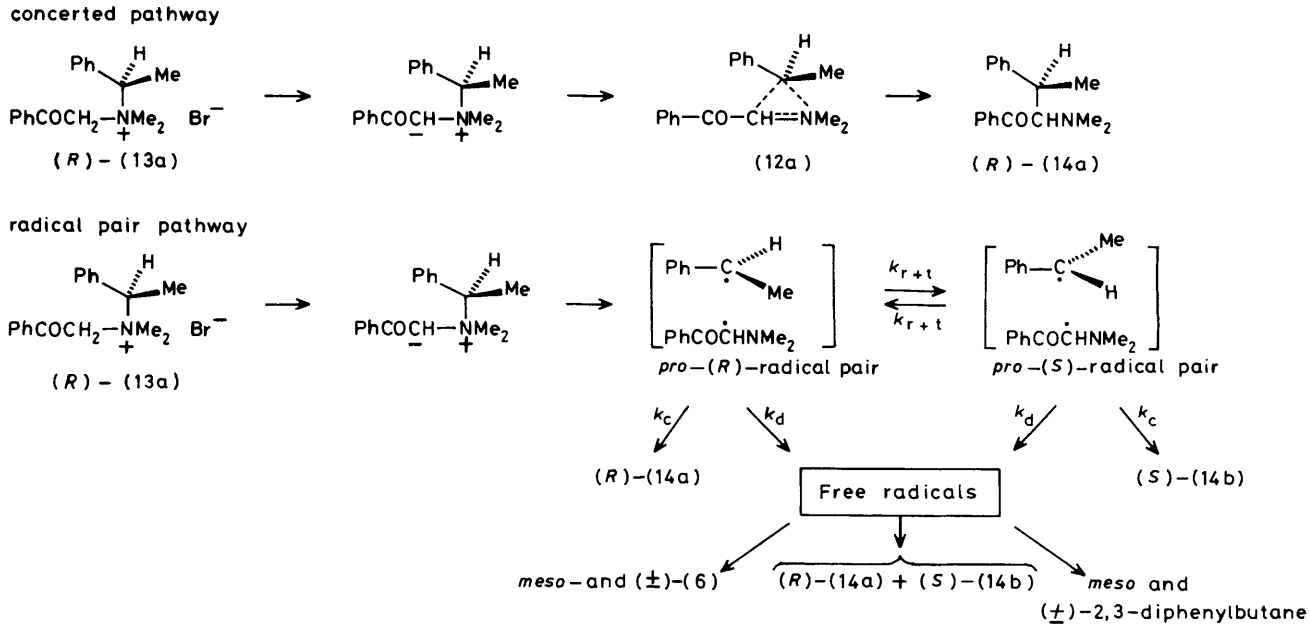


Figure 2. CIDNP effects during the rearrangement (3b) ⟶ (5b) in CD_3OD–$NaOCD_3$ at 60 °C



Scheme 1. Concerted and radical pair pathways for the thermal transformation of the ylide derived from the (*R*)-(+)-salt (13a).

Table 1. CIDNP during rearrangement of ylide (4a) and salt (3b)

Reaction conditions	Product	Signals [a,b]
Ylide (4a) at 60 °C in $CDCl_3$	$PhCOCH(CH_2Ph)NMe_2$	CH(A), CH_2(E), NMe_2(E)
	$PhCH_2CH_2Ph$	CH_2(A)
	$PhCOCH(NMe_2)CH(NMe_2)COPh$ (Both diastereoisomers)	NMe_2(A)
Salt (3b) at 60 °C in CD_3OD + CD_3ONa	$PhCOCH(CHMePh)NMe_2$ (Both diastereoisomers)	PhCOC*H*,[c] C*H*Me(E), CH*Me*(A), NMe_2(E)
	PhCHMe·CHMePh (Both diastereoisomers)	CH(A), Me(E)
	$PhCOCH(NMe_2)CH(NMe_2)COPh$ (Both diastereoisomers)	NMe_2(A)

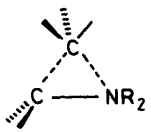
[a] The letters A and E in parentheses refer to enhanced adsorption and emission respectively (see Figures 1 and 2). [b] Product signals observed after 35 s for the ylide (4a) and 25 s for the salt (3b) using a JEOL PFT 100 n.m.r. spectrometer. [c] Signal not observed.

of the diamine (6) (see Table 1 and Figure 1). The rearrangement of the salt (3b) (with $NaOCD_3$ in CD_3OD at 60 °C) under similar conditions also gave a ^1H n.m.r. spectrum of the initially formed reaction products that showed strong CIDNP (see Table 1 and Figure 2). These CIDNP effects are indicative of the operation of radical pair processes,[20,25] but leave open the question of whether the [1,2] rearrangement proceeds uniquely by a radical pair pathway, (4) ⟶ (11) ⟶ (5), or involves competing radical pair and concerted processes (Scheme 1) because the development of spin polarisation [26] is necessarily a relatively slow process as compared with the rotation and diffusion of the component radicals of the pair (11).

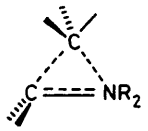
*Stereoselectivity.**—In 1951 Hauser and Kantor [27] suggested that the Stevens rearrangement involves an intramolecular nucleophilic displacement (S_Ni) with a three-membered cyclic transition state (12a). Such a reaction necessarily involves retention of the configuration of a chiral migrating group and, in accord with this view, the rearrangement of the optically active salt (13a)† was shown [8-10] to give the product (14a) in which the migrating 1-phenylethyl group largely retains its configuration [for (13a) ⟶ (14a) >90% retention and for (13c) ⟶ (14c) >90% retention [10]]. The transition state pro-

* The term stereoselectivity in this section relates only to the chiral centre of the migrating group and not to the formation of diastereoisomers.

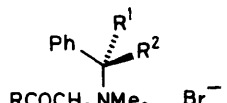
† Throughout this paper, formulae analogous to (13) will be used for chiral compounds which are (*R*,*S*)-racemates, (*R*)-enantiomers, or (*S*)-enantiomers. The use of the unqualified description (13) will refer to the (*R*,*S*)-racemate whereas (13a), (13b), *etc.*, will refer to particular (*R*)- or (*S*)-enantiomers which are determined by the nature of the substituents R^1 and R^2.



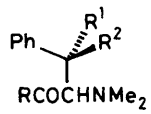
(12a)



(12b)

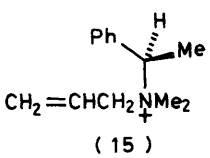


(13)

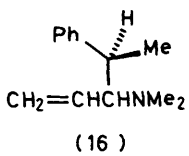


(14)

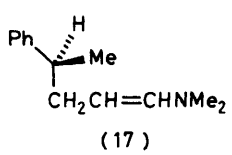
In (13) and (14): a, R = Ph, R^1 = H, R^2 = Me; b, R = Ph, R^1 = Me, R^2 = H; c, R = Me, R^1 = H, R^2 = Me



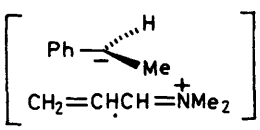
(15)



(16)



(17)

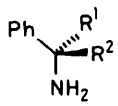


(18)

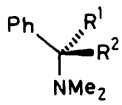
posal (12a) is clearly at variance with the established stereochemical requirements of an intramolecular S_N displacement, but the recognition of the generality of sigmatropic rearrangements by Woodward and Hoffmann [12] allows (12a) to be regarded as (12b), the transition state of a concerted [1,2] sigmatropic rearrangement with *s r* geometry and the development of pericyclic π-bonding. This is the transition state of a symmetry-forbidden process.

The optically active salt (15) rearranged on treatment with sodamide to give the [1,2] rearrangement product (16) (>90% retention of configuration) and the [1,4] rearrangement product (17) (>80% retention of configuration) but in this case the authors [15] interpreted their results in terms of a tight ion pair intermediate (18). The ion pair hypothesis received further support from other workers [16] but, on the basis of results that we have reported in preliminary form,[23a] it is probable that the rearrangement (15) ⟶ (16) + (17) involves the formation of the radical pair analogous to (18) followed by fast intramolecular radical coupling to give the observed products with, largely, retention of configuration of the migrating phenylethyl group.

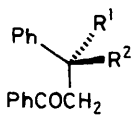
These results and conclusions prompted us to examine the stereoselectivity of the Stevens rearrangement in greater detail and, in particular, to attempt to explain the apparently conflicting observations of CIDNP and the reported intramolecularity and high stereoselectivity. The optically active (*R*)-(+)-salt (13a) (100% e.e.) was prepared from (*R*)-(+)-1-phenylethylamine (19a) by methylation (formaldehyde–formic acid) and quaternisation with phenacyl bromide. The enantiomeric excess * of the (*R*)-(+)-salt (13a) ($[\alpha]_D^{22}$ +83.5°) was checked by reductive cleavage (zinc–acetic acid) to regenerate (*R*)-(+)-*NN*-dimethyl-1-phenylethylamine (20a) with a



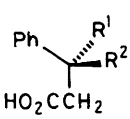
(19)



(20)



(21)



(22)

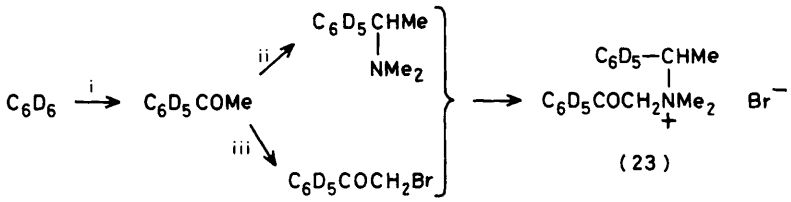
In (19) – (22): a, R^1 = H, R^2 = Me; b, R^1 = Me, R^2 = H

slightly higher optical rotation (α_D^{22} +65.8°) than that of a sample (α_D^{22} +62.5°) obtained by methylating the (*R*)-(+)-amine (19a), with 99% enantiomeric excess based on the highest value in the literature [28] for α_D. The enantiomeric excess of the (*R*)-(+)-salt (13a) ($[\alpha]_D^{22}$ +83.5°) is therefore considered to be 100% and enantiomer fractionation must have occurred during recrystallisation. The (*S*)-(−)-salt (13b), ($[\alpha]_D^{22}$ −82.3°; 98.6% e.e.), was prepared in a similar manner.

The base catalysed rearrangement of the (*R*)-(+)-salt (13a) (99.9% e.e.) by methanolic sodium methoxide at 55 °C gave three products including the [1,2] rearrangement product (14) (yield 80%), the diamine (6) (yield 11%), and 2,3-diphenylbutane (yield 5%). The diamine (6) was *racemic*, and by n.m.r. spectral comparison with synthetic compounds, was shown to be a mixture (ratio 1 : 1) of the (±)- and *meso*-forms. The 2,3-diphenylbutane was also *racemic* ($[\alpha]_D^{22}$ 0.00°) and was shown to be a mixture of the (±)- and *meso*-forms. In contrast with these two products, but in accord with earlier results,[3,8–10] the [1,2] rearrangement product was shown to be a mixture ($[\alpha]_D^{22}$ −27.6°) (1 : 1 ratio) of two diastereoisomers (14) which were *optically active*. These additional experimental observations provided a basis for our consideration of possible mechanistic routes which could lead to the formation of *racemic* and *optically active* products (see Scheme 1). This naturally encouraged the investigation which is now reported [19] of the influence of reaction conditions upon the stereoselectivity of the [1,2] rearrangement (13) ⟶ (14) using the (*S*)-(−)-salt (13b). The rearrangement of the (*S*)-(−)-salt (13b) was carried out under a variety of reaction conditions (see Table 2), in each case by the addition of base to a solution of the salt (13b) (98.6% e.e.) at the appropriate temperature. The enantiomeric excess of the product (14b) was established by reduction (zinc–acetic acid) to (*R*)-(−)-1,3-diphenylbutan-1-one (21b). The results of this investigation are summarised in Table 2. The stereoselectivities of the rearrangement (13b) ⟶ (14b) are based upon (i) the observed specific rotations of the ketone (21b), (ii) the absolute rotation of the (*R*)-(−)-ketone (21b) ($[\alpha]_D^{22}$ −14.0°), and (iii) the optical purity of the starting (*S*)-(−)-salt (13b) (98.6% e.e.).

The absolute rotation and configuration of (*S*)-(+)-1,3-diphenylbutan-1-one (21a), prepared by a sequence of rearrangement and reduction from the optically pure (*R*)-(+)-salt (13a) (100% e.e.), were checked by correlation with (*S*)-(+)-3-phenylbutyric acid (22a) of known absolute rotation.[29] Baeyer–Villiger oxidation of the (*S*)-(+)-ketone (21a) ($[\alpha]_D^{22}$ +13.3°, $[\alpha]_{578}^{22}$ +14.2°) followed by hydrolysis gave the (*S*)-(+)-acid (22a) with $[\alpha]_D^{22}$ +55.7°. This specific rotation for the (*S*)-(+)-acid (22a) corresponds to 95.2% enantiomeric excess based upon the highest literature value [29] for its specific rotation ($[\alpha]_D^{25}$ +58.5°). The observed specific rotation for the ketone, therefore, also corresponds to 95.2% enantiomeric excess and confirms that the rearrangement (13) ⟶ (14)

* The term ' enantiomeric excess ' will be used in the usual way to indicate the percentage excess of the major enantiomer over the minor enantiomer.



Scheme 2. Reagents: i, CH_3COCl; ii, Me_2NCHO–HCO_2H; iii, Br_2

proceeds with high retention of configuration of the migrating chiral phenylethyl group.

It should be noted that the previously reported stereoselectivities for the rearrangement (13) ⟶ (14) require correction, since they were based upon incorrect values for the absolute rotations of the acid (22) and the ketone (21). The reported stereoselectivities of 99 [8] and 95% [9] should be corrected to 79 and 87% respectively. The conclusion, based upon these earlier investigations, that the rearrangement (13) ⟶ (14) can proceed with a high degree of stereoselectivity has been supported by the results reported in Table 2. The highest degree of stereoselectivity (99%) is, however, restricted to the reaction in water at low temperatures and, in general, a high degree of stereoselectivity requires a solvent of high viscosity.

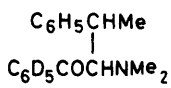
Intramolecularity.—It was necessary to establish the intramolecularity of the rearrangement (13) ⟶ (14) for all the reaction conditions reported in Table 2 so that the stereoselectivity of the intramolecular component of the reaction could be determined. The [$^2H_{10}$]salt (23) was, therefore, prepared from [$^2H_6$]benzene using the reactions outlined in Scheme 2. The synthetic intermediates were analysed for their deuterium content by mass and n.m.r. spectra to confirm that no appreciable hydrogen–deuterium exchange had occurred at any stage during the synthesis of the [$^2H_{10}$]salt (23).

An intimate mixture of the (*R*,*S*)-salt (13) and the (*R*,*S*)-[$^2H_{10}$]salt (23) in a 1 : 1 ratio was rearranged under the same reaction conditions as those used to examine the stereoselectivity of the rearrangement (13b) ⟶ (14b) (see Table 2).

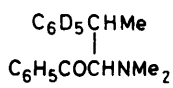
The isotopic composition ([$^2H_0$], [$^2H_5$], and [$^2H_{10}$]) of the rearrangement product (14) was determined by mass spectrometry (see Table 8, Experimental section) and this information was used to provide quantitative information on the percentage intramolecularity * and intermolecularity * of the reaction (13) ⟶ (14) using the relations: % intermolecularity 2 × [% crossover products (24) + (25)]. % intramolecularity = 100 − % intermolecularity.

These results (Table 8, Experimental section) and those obtained in the previous section (Table 2) could then be used to estimate the stereoselectivity of the intramolecular component of the reaction (13b) ⟶ (14b) (Table 3).

The Mechanism of the [1,2] *Rearrangement.*—The intermolecularity and intramolecular stereoselectivity for the [1,2] rearrangement (13) ⟶ (14), carried out under various reaction conditions, are summarised in Table 3. These results lead to two general conclusions. (*a*) The intramolecular stereoselectivity shows a strong dependence on solvent viscosity and decreases with decreasing viscosity; there are in addition smaller effects due to changes in reaction temperature, but there is no obvious relation with solvent polarity. (*b*) The intermolecularity of the rearrangement also shows a strong dependence on solvent viscosity and increases as viscosity decreases; in addition, intermolecularity increases as reaction temperature increases.



(24)



(25)

These trends in stereoselectivity and intramolecularity together with the observation of CIDNP (Table 1 and Figures 1 and 2) and the isolation of the typical radical coupling products, (6) and 1,2-diphenylethane [from (4a)] or 2,3-diphenylbutane [(from (3b)] strongly support a reaction mechanism involving homolytic dissociation to give a radical pair (11) followed by recombination of geminate and free radicals. Such processes have often been characterised by the ratio (k_c/k_{r+t}) of rate constants for radical pair recombination (k_c) and rotation or tumbling processes that lead to loss of stereochemical characteristics (k_{r+t}), and the ratio (k_c/k_d) of rate constants for radical pair recombination (k_c) and diffusion from the radical pair to give free radicals (k_d) (Scheme 1). If it is assumed that the recombination of free radicals randomly involves the deuteriated and undeuteriated species and that it is also associated with the formation of racemic products, then: k_c/k_{r+t} = 2 × intramolecular stereoselectivity/(100-intramolecular stereoselectivity) and k_c/k_d = intramolecularity/2 × intermolecularity.

The values of these ratios are recorded in Table 3 and it is interesting to compare the values obtained for the rearrangement (13) ⟶ (14) with those obtained by other workers for the recombination of radical pairs obtained from different types of precursors. Thus, values of k_c/k_{r+t} for the recombination of radicals formed by the thermal cleavage of azo-compounds, peroxyesters, and hyponitrites are typically very low.[31] These processes are rather unsuitable as models for the rearrangement (13) ⟶ (14), however, because the radical pairs are formed from precursors in which the two molecular fragments from which the radicals are derived are separated by a developing nitrogen and/or a carbon dioxide molecule. The homolysis and racemisation of the azo-compound (27) to give the radical pair (28) is a closer analogue of the process (13) ⟶ (11) ⟶ (14) and in this case [32] the value of k_c/k_{r+t} (*ca.* 1.5) in a solvent of viscosity *ca.* 1 cP is comparable with the value of the k_c/k_{r+t} (*ca.* 5) for the reaction (13) ⟶ (14) in a solvent of similar viscosity (Table 3). The high stereoselectivity observed for the Stevens rearrangement is not, therefore, quite so exceptional for a radical pair process as we had supposed at the beginning of this investigation.

* Unfortunately we have repeated the same error in three footnotes of three Tables associated with three of our preliminary communications.[19,23a] The statements given in these three footnotes that Intramolecularity = 4*z*% and Intermolecularity = 100 − 4*z*% are incorrect; they must be replaced by the correct statements that Intermolecularity = 4*z*% and Intramolecularity = 100 − 4*z*% (see Table 3 of this paper). We apologise for the careless repetition of this error but we emphasise that the figures given in the Tables in our preliminary communications are all correct because they were calculated on the basis of the correct statements for Intermolecularity = 4*z*% and Intramolecularity = 100 − 4*z*%.

Table 2. Stereoselectivity [a] of the rearrangement (13b) ⟶ (14b) under various reaction conditions

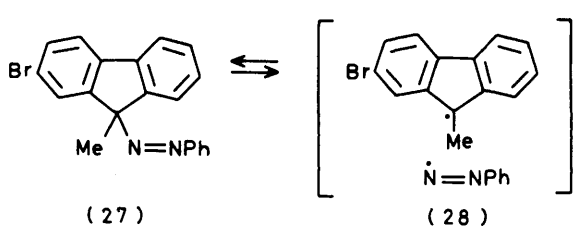
Reaction conditions			$[\alpha]_D^{22}$ of (21b) [a]	Stereoselectivity [b]
Solvent	Base	Temp. (±2 °C)	(±0.1°)	(±2%)
Methanol	NaOMe	0	−9.77	71
Methanol	NaOMe	40	−8.03	58
t-Butyl alcohol	NaOMe	50	−9.23	67
Cyclohexanol	NaOMe	50	−10.50	76
Glycerol	NaOH	50	−12.42	90
Water	NaOH	0	−13.67	99
Water	NaOH	50	−10.80	78

[a] Further details are given in the Experimental section, Table 7. [b] Stereoselectivity = 100% − percentage racemisation of the migrating group during the rearrangement (13b) ⟶ (14b). The percentage racemisation is based upon enantiomeric excess of 98.6% for starting (*S*)-(−)-salt (13b) and absolute value for rotation of the (*R*)-(−)-ketone (21b), $[\alpha]_D^{22}$ −14.0°.

Table 3. Intramolecular stereoselectivity and intermolecularity for the rearrangement (13) ⟶ (14) under various conditions

Solvent	Base	Temp. (±2 °C)	Solvent viscosity [a] (cP)	Intermolecularity [b] (%)	Intramolecular stereoselectivity [c] (%)	k_c/k_{r+t}	k_c/k_d
Methanol	NaOMe	0	0.8	6.9	76	6.3	6.7
Methanol	NaOMe	40	0.5	16.7	70	4.7	2.5
Methanol	NaOMe	60	0.3	22.9	—	—	1.7
t-Butyl alcohol	NaOMe	50	1.4	10.5	75	6.0	4.3
Cyclohexanol	NaOMe	50	13	5.5	81	8.5	8.6
Glycerol	NaOH	50	142	2.5	92	23.0	19.5
Water	NaOH	0	1.8	0.1	99	198	>100
Water	NaOH	50	0.6	4.3	82	9.1	11.1

[a] Taken from ref. 30. [b] Intramolecularity = 100 − percentage intermolecularity and intermolecularity = 2 × [percentage crossover products (24) + (25)] = 2 × percentage [$^2H_5$] species (24) + (25) obtained from an approximately equimolar mixture of (13) and (23). For details of the isotopic composition of products (14) see Experimental section, Table 8. [c] Intramolecular stereoselectivity = (stereoselectivity)/(intramolecularity) × 100%.



(27) (28)

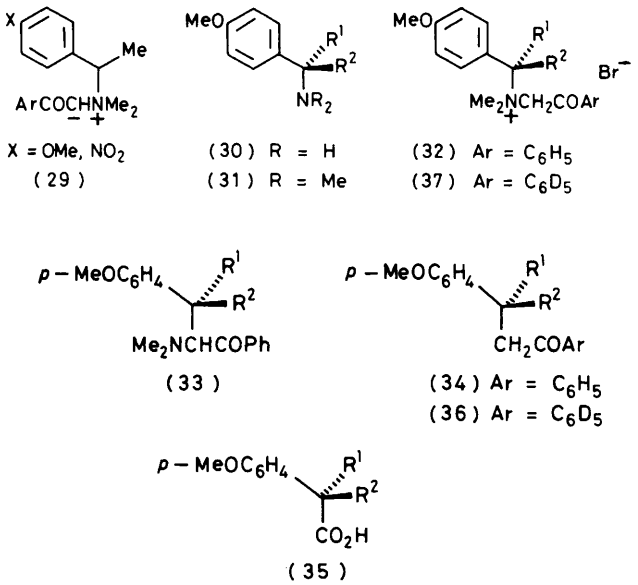
The values of k_c/k_{r+t} and k_c/k_d for the reaction (13) ⟶ (14) in water are unusually large (Table 3), but this is presumably a consequence of the highly structured nature of water, particularly at 0 °C. Furthermore, if one assumes that the value of k_{r+t} for the radical pair involved in the reaction (13) ⟶ (14) is *ca.* 10^{11} s^{-1}, by analogy with the correlation rates of molecules of similar size and shape, then the value of k_c may be estimated as *ca.* 10^{12} s^{-1}. This is quite close to the values of k_c estimated for the decomposition of peroxyesters and hyponitrites [31] and suggests that the Stevens [1,2] rearrangement does not involve unusual radical pairs.

It is not, therefore, necessary to invoke a contribution to the reaction mechanism from a competing, concerted process to account for the observed stereoselectivity and intramolecularity. Furthermore, it is not necessary to consider that the Stevens [1,2] rearrangement requires a novel mechanistic description.

[1,2] *Rearrangements of Substituted Ammonium Ylides* (29). —(*R*)-(+)-1-*p*-Methoxyphenylethylamine (30a) was obtained by resolution of the (*R,S*)-amine (30) [33a] using (+)-tartaric acid. The resolution was repeated four times and the amine liberated at each stage showed a progressive increase in optical rotation. Eventually (*R*)-(+)-1-*p*-methoxyphenylethylamine (30a) (100% e.e.) was obtained with the optical rotation α_D^{22} +36.1° (neat). The absolute configuration of the (*R*)-(+)-amine (30a) has been established [33b] and its optical rotation α_D^{22} +36.1° (neat) correlates excellently with one reported value [33c] [α_D +21.62° (neat) (60% e.e.) = α_D +36.0° (100% e.e.)]. These values for the optical rotation of the *R*-(+)-amines (30a) and (31a) are different in magnitude from other reports.[33a,33d] Our values have received independent confirmation by the determination of the enantiomeric excess of a partially resolved sample of (*S*)-(−)-1-*p*-methoxyphenylethylamine (30b) by the use of the chiral lanthanide shift reagent, tris-[(3-trifluoromethylhydroxymethylene)-(+)-camphorato]europium(III). The result (40% e.e.) was in satisfactory agreement with the figure (38% e.e.) based upon the optical rotation α_D^{22} −13.8° (neat) for the partially resolved amine (30b).

The (*R*)-(+)-tertiary amine (31a) [α_D^{22} +56.7° (neat) (100% e.e.)] was quaternised with phenacyl bromide to yield the (*R*)-(+)-salt (32a). It was established that no racemisation occurred during the quaternisation reaction [(31a) ⟶ (32a)] because zinc–acetic acid reduction of the (*R*)-(+)-salt (32a) {$[\alpha]_D^{22}$ +67.6° (ethanol) (100% e.e.)} gave the (*R*)-(+)-tertiary amine (31a) (100% e.e.). If the (*R,S*)-salt (32) was heated above 120 °C or if the quaternisation of the *R*-(+)-amine (31a) was carried out in acetonitrile or acetone some decomposition occurred to give *p*-methoxystyrene and *NN*-dimethylphenacylammonium bromide, presumably a result of heterolysis of the $ArC^{+}\!-\!N$ bond facilitated by the *p*-methoxy-substituent.

The (*R,S*)-salt (32) was prepared by quaternisation of the (*R,S*)-amine (31) [33a] with phenacyl bromide in acetone solution. Rearrangement of the (*R,S*)-salt (32) in water at 0 °C, using sodium hydroxide as base, gave the [1,2] rearrangement



In (30)—(37): a, R^1 = H, R^2 = Me; b, R^1 = Me, R^2 = H

product (33) as a mixture of diastereoisomers, the diamine (6) (3—4% yield of both diastereoisomers in a 3 : 1 ratio), 2,3-di-*p*-methoxyphenylbutane (4% yield of both diastereoisomers in a 5 : 4 ratio), 1-*p*-methoxyphenylethanol (1.1% yield), and *p*-methoxystyrene (0.4% yield). The formation of the dimeric products, (6) and 2,3-di-*p*-methoxyphenylbutane, are indicative of a radical pair mechanism for the rearrangement (32) ⟶ (33). It is noteworthy that dimeric products of this type, which represent some of the products formed by non-geminate recombination, were not formed under these conditions from the salt (13) which lacked the *p*-methoxy-substituent. It was, therefore, of importance to determine the stereoselectivity of the rearrangement (32) ⟶ (33).

The (*R*)-(+)-salt (32a) (100% e.e.) was rearranged under the conditions summarised in Table 4, in each case base was added to a solution of the salt which was maintained at the appropriate temperature until the reaction was complete. The isolated rearrangement product (33) was reduced to the (*S*)-(+)-ketone (34a) which had the specific rotations recorded in Table 4. The use of these experimental results to determine the stereoselectivity of the rearrangement (32) ⟶ (33) required the determination of the absolute optical rotation of the (*S*)-(+)-ketone (34a). Our initial approach was a modified Barbier-Wieland degradation of the (*S*)-(+)-ketone (34a) to give (*R*)-(−)-*p*-methoxyhydratropic acid (35a) {$[\alpha]_D^{22}$ −61.5° (ethanol)}. The (*R*)-absolute configuration of the laevorotatory *p*-methoxyhydratropic acid is firmly established.[34] However, there is an inconsistency for the values of the absolute rotations in ethanol which have been published ($[\alpha]_D^{19}$ −58°,[34a] $[\alpha]_D^{22}$ −88.8°,[34c] $[\alpha]_D^{27}$ −64.0°[34d]) for the (*R*)-acid (35a), so that the calculation of the enantiomeric excess corresponding to $[\alpha]_D^{22}$ −61.5° was impossible. It was, therefore, necessary to adopt a different method to determine the absolute rotation of (*S*)-(+)-3-*p*-methoxyphenyl-1-phenylbutan-1-one (34a). This was achieved using the isotope dilution method[35,36] developed by Berson and Ben-Efraim.[35a] Various isotopes (^{14}C, ^{36}Cl, ^{2}H, and ^{15}N) have been used for the determination of absolute rotations using the isotope dilution method.[36] However, so far as we are aware, only one result has been previously reported using deuterium labelling. In this case, Gerlach[35b] determined the absolute rotation of *N*-benzyl-4-phenyloxazolidine-2-thione by mixing known amounts of the

Table 4. Stereoselectivity for the rearrangement (32a)[a] ⟶ (33a) under various conditions

Solvent	Base	Temp. (±2 °C)	Observed $[\alpha]_D^{22}$ of ketone (34)	Stereoselectivity[b] (%)
Methanol	NaOMe	0	+13.3	61
Methanol	NaOMe	40	+10.8	50
Water	NaOH	0	+18.9	87

[a] Using the (*R*)-(+)-salt (32a) $[\alpha]_D^{22}$ +67.6° (100% e.e.). [b] Based upon the absolute rotation for ketone (34a) $[\alpha]_D^{22}$ +21.64° determined by isotope dilution analysis (see Experimental section).

labelled racemic thione and the *unlabelled partially resolved* thione. Crystallisation yielded a *partially deuteriated optically active* re-isolated sample which, by deuterium assay and specific rotation measurement, enabled the absolute rotation of *N*-benzyl-4-phenyloxazolidine-2-thione to be determined. A different but complementary approach was used for the determination of the absolute rotation of (*S*)-(+)-3-*p*-methoxyphenylbutan-1-one (34a). Known amounts of the *unlabelled racemic* ketone (34) and the *labelled partially resolved* ketone (36a) were mixed and recrystallisation yielded a re-isolated sample as a *partially deuteriated racemate*. Measurement of the isotopic composition of this re-isolated sample by deuterium analysis (see Experimental section) enabled the absolute rotation of (*S*)-(+)-3-*p*-methoxyphenyl-1-phenylbutan-1-one (34a) to be determined.

Raban and Mislow[36] have derived the general equation (1) for the calculation of absolute rotations from the results of isotope dilution analyses.

$$[\alpha]_{max.} = \sqrt{\frac{I_i n^2[\alpha]^2 - I_o mn[\alpha][\alpha_i]}{I_i(m+n)^2 - I_o m(m+n)}} \qquad (1)$$

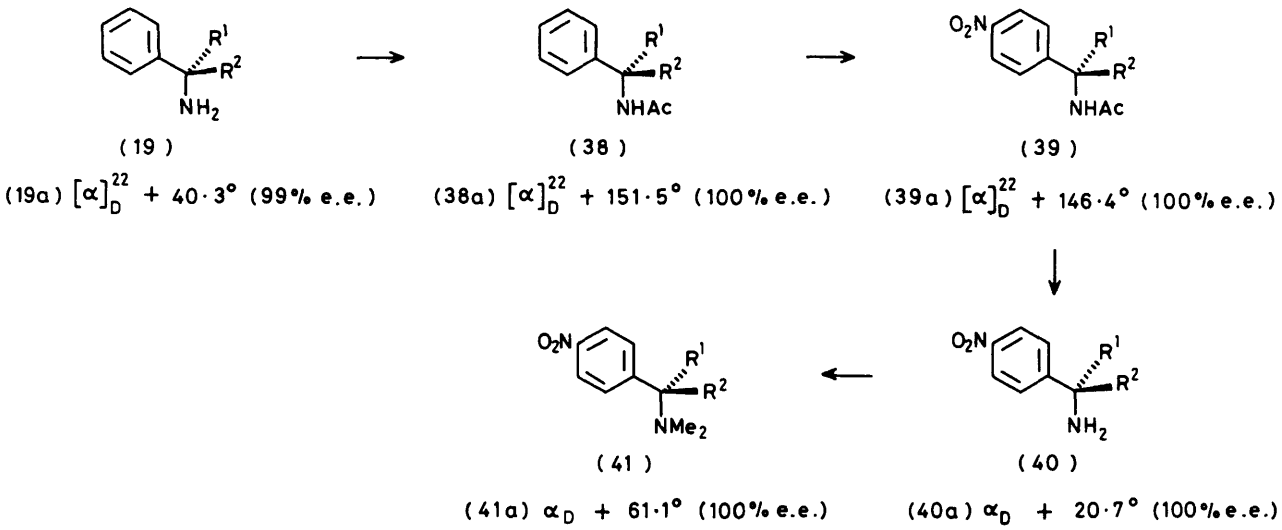
$[\alpha]_{max.}$ = Absolute rotation of the enantiomer; m = weight (g) of labelled racemate added to test sample; I_o = isotope content of labelled racemate added to test sample; n = weight (g) of test sample; $[\alpha]$ = specific rotation of test sample; I_i = isotope content of re-isolated sample; $[\alpha_i]$ = specific rotation of re-isolated sample.

In the isotope dilution analysis described above, the unlabelled racemate (34) was added to the labelled partially resolved test sample (36a) and the re-isolated sample was *racemic*. Equation (1) is then reducible to equation (2) because $[\alpha_i] = 0°$ and $I_o = 1$.

$$[\alpha]_{max.} = \sqrt{\frac{I_i n^2[\alpha]^2}{I_i(m+n)^2 - m(m+n)}} \qquad (2)$$

$[\alpha]_{max.}$ = Absolute rotation of the enantiomer; m = weight (g) of unlabelled racemate added to test sample; I_o = percentage ($\times 10^{-2}$) of undeuteriated species in unlabelled racemate ($I_o = 100 \times 10^{-2} = 1$); n = weight (g) of labelled (95% of $[^2H_5]$- and 5% of $[^2H_4]$-species) test sample; $[\alpha]$ = specific rotation of labelled test sample; I_i = percentage ($\times 10^{-2}$) of undeuteriated $[^2H_0]$ species in re-isolated racemate; $[\alpha_i]$ = specific rotation of re-isolated racemate, $[\alpha_i] = 0$.

The application of an isotope dilution analysis required the synthesis of the unlabelled racemate (34) as the carrier and the partially resolved pentadeuterio-derivative (36a) as the test sample. The racemic ketone (34) was prepared by reduction with zinc and acetic acid of the mixture of diastereoisomeric ketones (33) prepared from the (*R,S*)-salt (32). The optically active $[^2H_5]$-ketone (36a) ($[\alpha]_D^{22}$ +18.7°) was prepared from



Scheme 2. a, R^1 = H, R^2 = Me; b, R^1 = Me, R^2 = H

the (*R*)-[$^2H_5$]-salt (37a) by the sequence of rearrangement (aqueous sodium hydroxide at 0 °C) and zinc–acetic acid reduction. The (*R*)-[$^2H_5$]-salt (37a) (100% e.e.) was obtained by reaction of the (*R*)-(+)-amine (31a) ($[\alpha]_D^{22}$ +56.7°; 100% e.e.) with [$^2H_5$]-phenacyl bromide. Fractional crystallisation of the derived (*S*)-(+)-[$^2H_5$]-ketone (36a) ($[\alpha]_D^{22}$ +18.7°) gave two samples of differing enantiomeric excess ($[\alpha]_D^{22}$ +20.34° and $[\alpha]_D^{22}$ +15.96°). The two samples in each case consisted of only the [$^2H_5$] (95%) and the [$^2H_4$] (5%) species. These figures originate from the isotopic composition of the benzene starting material (^2H >99%) and do not affect the isotope dilution analysis. Known amounts (*n* in grams) of each of the two samples of the (*S*)-(+)-[$^2H_5$]-ketone (36a) ($[\alpha]_D^{22}$ +20.34° and $[\alpha]_D^{22}$ +15.96°) were separately mixed with known amounts (*m* in grams) of the unlabelled racemic ketone (34). Determination of the isotopic composition ([$^2H_0$], [$^2H_4$], and [$^2H_5$]) of each re-isolated racemate ($[\alpha_i]_D^{22}$ = 0°) and substitution in equation (2) gave two values for the absolute rotation ($[\alpha]_D^{22}$ +21.56 and +21.72°) which were in excellent agreement. With this knowledge of the average value, $[\alpha]_D^{22}$ +21.64°, for the absolute rotation of the (*S*)-(+)-ketone (34a), it was then possible to determine how the stereoselectivity of the base catalysed rearrangement (32a) ⟶ (33a) was influenced by reaction conditions (Table 4).

Although the stereoselectivities for the [1,2] rearrangement [(32a) ⟶ (33a); Table 4], are lower than those observed for the analogous [1,2] rearrangement [(13b) ⟶ (14b); Table 2], the striking fact is that the ratios of the stereoselectivities for the two [1,2] rearrangements under corresponding reaction conditions show a remarkable correspondence. This strongly suggests that both rearrangements proceed by radical pair intermediates. The association of the second rearrangement [(32a) ⟶ (33a); Table 4] with increased racemisation under similar conditions (see Table 2) is exactly in accord with expectation because the 1-*p*-methoxyphenylethyl radical would have a relatively longer lifetime than the 1-phenylethyl radical (see Scheme 1).

It may be mentioned parenthetically that having determined the absolute rotation of the (*S*)-(+)-ketone (34a) {$[\alpha]_D^{22}$ +21.64° (100% e.e.)}, it followed that the (*S*)-(+)-ketone (34a) ($[\alpha]_D^{22}$ +18.9°), which was transformed into the (*R*)-(−)-acid (35a) {$[\alpha]_D^{22}$ −61.5° (ethanol} had an enantiomeric excess of 87.3%. Assuming that the Barbier-Wieland degradation [(34a) ⟶ (35a)] proceeded without racemisation then the absolute rotation may be calculated for (*R*)-(−)-*p*-methoxyhydratropic acid (35a) {$[\alpha]_D^{22}$ −61.5° (87.3% e.e.) ≡ $[\alpha]_D^{22}$ −70.4° (ethanol) (100% e.e.)}. This value for the absolute rotation may be compared with the three values previously reported [34a,34c,34d] and discussed above.

Having examined the effect of the electron-releasing methoxy-substituent upon the mechanism of the Stevens [1,2] rearrangement of the ylide (29; X = OMe), it was of interest to examine the effects of an electron-attracting nitro-group [see (29; X = NO_2)]. Optically pure (*R*)-(+)-*NN*-dimethyl-1-*p*-nitrophenylethylamine (41a) was prepared from (*R*)-(+)-1-phenylethylamine (19a) by the route outlined in Scheme 2. The enantiomeric excess of the intermediates (38a) and (39a) was established by comparison of the observed specific rotations with reported absolute values.[37] It is assumed that no racemisation takes place during the interconversion (39a) ⟶ (40a) ⟶ (41a) and that the product (41a) is the optically pure (*R*)-amine (41a). The (*R*,*S*)-amine (41) was prepared by a similar route from (*R*,*S*)-1-phenylethylamine. Quaternisation of the (*R*,*S*)-amine (41) with phenacyl bromide gave the (*R*,S)-salt (42).

The rearrangement of the (*R*,*S*)-salt (42) in aqueous sodium hydroxide at 0 °C gave three major products identified as the [1,2] rearrangement product (44), the diamine (6), and 2,3-di-*p*-nitrophenylbutane. Each of these three products was produced as a mixture of diastereoisomers which was analysed by n.m.r. spectrometry (see Table 5). The molar ratio (46 : 21 : 33) of the relative yields of the three products is very close to the molar ratio (50 : 25 : 25) which would have been expected for completely random recombination of free radicals derived from the initial radical pair (47).

This remarkable result demanded further enquiry by an investigation of the stereoselectivity of the base catalysed rearrangement of the optically active (*R*)-(+)-salt (42a). Unfortunately, this salt (42a) could not be obtained crystalline, but the corresponding crystalline *R*-(+)-salt (43a) ($[\alpha]_D^{22}$ +83.7°; 100% e.e.) was obtained by quaternisation of the (*R*)-(+)-*NN*-dimethyl-1-*p*-nitrophenylethylamine (41a) ($[\alpha]_D^{22}$ +61.1°; 100% e.e.) with *p*-methoxyphenacyl bromide.

The base catalysed rearrangement of the (*R*)-(+)-salt (43a) (100% e.e.) gave three products (Table 5) including the [1,2] rearrangement product (45), the diamine (46), and 2,3-di-*p*-nitrophenylbutane. Again the molar ratio (66—68 : 12—16 : 22—26) of these three products is approximately related

Table 5. Products from the base catalysed rearrangement of salts (42) and (43a) (mol %)

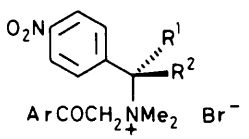
Salt	Solvent	Base	Temp. (±2 °C)	Product composition (mol %) [1,2] Product [a,d]	Diamine [b,d]	Diarylbutane [c,d]
(42)	Water	NaOH	0	46	21	33
(43a)	Methanol	NaOMe	0	66	12	22
(43a)	Water	NaOH	0	58	16	26

[a] Both diastereoisomers of amine (44) from (42) in a 4 : 3 ratio and optically active samples of both diastereoisomers of (45) from (43a) in a 1 : 1 ratio. [b] Both diastereoisomers of diamine (6) from (42) in a 2 : 1 ratio and both diastereoisomers of diamine (46) from (43a) in a 1 : 1 ratio. [c] (±) and *meso*-Diastereoisomers of 2,3-di-*p*-nitrophenylbutane in a 5 : 1 ratio from (42) and a 4 : 1 ratio from (43a). [d] The [1,2] rearrangement product, the diamine, and the diarylbutane were shown by n.m.r. spectra to account for 80—90% of the total isolated product (92—97%).

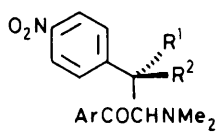
to the molar ratio (50 : 25 : 25) which could be associated with random recombination of free radicals produced by homolysis of the ylide (29; X = NO_2; Ar = *p*-methoxyphenyl). The diamine (46) was *racemic* and was shown to be a mixture (1 : 1 ratio) of (±)- and *meso*-forms. The 2,3-di-*p*-nitrophenylbutane was *racemic* and was shown to be a mixture (4 : 1 ratio) of (±)- and *meso*-forms. The [1,2] rearrangement product (46) was also a mixture of diastereoisomers *which were both optically active* (diastereoisomer A, $[\alpha]_D^{22}$ −73.7°; diastereoisomer B, $[\alpha]_D^{22}$ −62.0°). This is a remarkable result. Although the [1,2] rearrangement (43a) ⟶ (45) is associated with the retention of optical activity, an iron-clad mechanistic interpretation of this result is not possible until the influence of the nitro-substituent on the stereoselectivity and the intramolecularity of the process (43a) ⟶ (45) has been quantitatively established. The dilemma, which is not yet resolved, is that for the formation of the three products derived from the (*R*)-(+)-salt (43a), the observed product ratio apparently requires extensive random recombination of free radicals, whereas the observed retention of optical activity in the diastereoisomeric [1,2] rearrangement products (45) apparently requires cage recombination of geminate radical pairs.

Adequate experimental evidence supports our interpretation of the results for the base catalysed rearrangement of the optically active salts (13b) and (32a). However, a more extensive experimental investigation is necessary to resolve the interesting mechanistic problems which have been raised by our initial examination of the base catalysed rearrangement of the (*R*)-(+)-salt (43a).

Conclusions.—The results described in this paper establish the following experimental facts that are relevant to the mechanism of the Stevens [1,2] rearrangement. (i) The rearrangements of the ylide (4a) and the ylides derived from the salts (3b) ≡ (13), (32), (42), and (43) give, in addition to the product(s) of a [1,2] rearrangement, 2,3-diarylbutanes and 1,2-bis(dimethylamino)-1,3-diaroylethanes derivable by random coupling of free radicals formed by escape from the radical pairs analogous to (11) (Scheme 1). (ii) The rearrangements of the optically active salts (13b), (32a), and (43a) give [1,2] rearrangement products in which the optical activity is retained. In the cases of (13b) and (32a), it has been shown that this is associated with high retention of the configuration of the migrating group. (iii) The stereoselectivity of the [1,2] rearrangement associated with the migrating group is dependent upon solvent and temperature, in the case of the salt (13b), it has been shown that stereoselectivity decreases as solvent viscosity decreases. (iv) The intramolecularity of the rearrangement of the salt (13b) decreases as solvent viscosity decreases or reaction temperature increases. (v) In water at 0 °C the [1,2] rearrangement of the salt (13b) is essentially intramolecular (99.9%) with almost complete retention (99%)

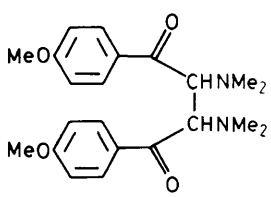


(42) Ar = Ph
(43) Ar = *p*-$MeOC_6H_4$

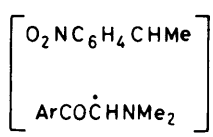


(44) Ar = Ph
(45) Ar = *p*-$MeOC_6H_4$

in (42)–(45): a, R^1 = H, R^2 = Me; b, R^1 = Me, R^2 = H



(46)



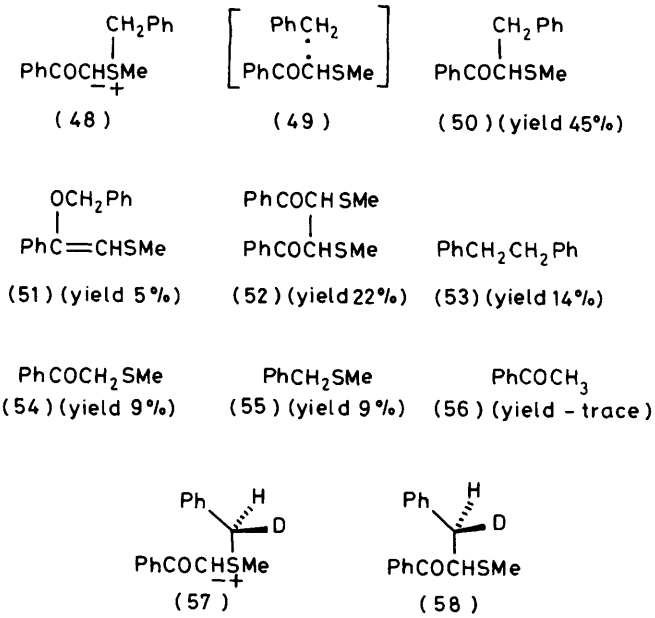
(47)

of the configuration of the migrating group. (vi) Under certain reaction conditions, particularly for high reaction temperatures, the [1,2] rearrangement and the associated reactions may show CIDNP.

It is clear from the observations (i)—(iv) that the isolated, apparently conflicting, observations (v) and (vi) represent the mechanistic extremes of the rearrangement. Thus, analysis of the data summarised by observations (ii) and (iv) shows that the [1,2] rearrangement exhibits stereoselectivity and intramolecularity that are consistent with a reaction proceeding *via* a radical pair in which the two components are formed initially in close proximity. It is not unreasonable to conclude that other [1,2] anionic rearrangements of the general type (1) ⟶ (2) also proceed by a radical pair mechanism. It is not possible, on the basis of the results cited in this paper, to exclude the possibility that a [1,2] anionic rearrangement may proceed, at least to some extent, by a ' concerted ' mechanism, but it is not necessary to make this proposal in order to account for our observations. The distinction between ' concerted ' and ' radical pair ' mechanisms was discussed * in the first paper of this series [18a] and on the basis of the distinction proposed at that time, the [1,2] rearrangement is a non-concerted process involving a radical pair intermediate.

There are instructive similarities between the thermal [1,2] rearrangements of ammonium ylides and sulphonium ylides. Thus the sulphonium ylide (48) [38] was shown, in an important investigation by Baldwin, Erickson, Hackler, and Scott,[14b] to rearrange in boiling toluene to give the products (50)—(56) in the indicated yields. The products (50)—(53) were rationalised

* Footnote to p. 1437 of reference 18a.



as arising from dissociation-recombination processes involving either the caged radical pair (49) or the corresponding free radicals and coupling modes analogous to those reported in this paper and elsewhere [23a] for analogous ammonium ylides. The products (54)—(56) could also arise from processes involving radicals, but alternative derivations can also be envisaged.

Furthermore the rearrangement product (50) shows CIDNP effects when it is formed [14b] from the ylide (48) in diphenyl ether at 130 °C (CH signals show enhanced absorption, CH_2 signals show emission) in satisfying correspondence with the CIDNP effects observed for the thermal rearrangement of the ylide (4a) (Table 1 and Figure 1). The common mechanism for the [1,2] rearrangement of ammonium and sulphonium ylides is also demonstrated by comparison of the stereoselectivity and intramolecularity of the two rearrangements. Thus, the rearrangement (48) ⟶ (50) is substantially intramolecular [14b] (82 ± 6%) and the reaction (57) ⟶ (58) was shown [14b] to proceed with net retention of configuration (36 ± 11%), corresponding with intramolecular stereoselectivity of 44 ± 13%. These results were interpreted [14b] in the terms of a radical pair pathway for the rearrangement of the ylide (48) and they correspond with the results now reported for ammonium ylides (Tables 2, 3, and 4).

The [1,2] rearrangements of ylides are members of a family of reactions in which there is currently great interest. These are non-concerted reactions which show high stereoselectivity, although they involve intermediates (radical pairs or diradicals) which could provide an opportunity for stereochemical equilibration. The prediction and rationalisation of the stereospecificity of concerted reactions is one of the many triumphs of the Woodward-Hoffmann generalisations [12] but it was explicitly emphasised by Woodward and Hoffmann that the experimental observation of stereospecificity or high stereoselectivity must not be regarded as other than a necessary, but not sufficient, criterion for concertedness. The association of high stereoselectivity with a two-step non-concerted process usually means that the second step is too fast to permit stereorandomisation, as in the case of [1,2] rearrangements of ylides.

Impressive progress is now being made towards an understanding of the structural and electronic factors which are responsible for the high stereoselectivity of reactions involving diradical intermediates.[39-42] Those rearrangements which show high stereoselectivity, which contradict the predictions of the Woodward-Hoffmann rules for concerted processes, are of particular interest. Examples include [1,3] sigmatropic rearrangements with suprafacial-retention stereochemistries [39,43] and [1,5] sigmatropic rearrangements that exhibit suprafacial-inversion stereochemistries.[44,45] Factors other than frontier orbital interaction must be involved but explanations range from ' a process of minimal obstruction of orbital overlap along the path to the biradical intermediate ' [42] to ' closure by the least motion pathway '.[45] Reactions involving diradical intermediates must be intramolecular, but the spectrum of mechanistic pathways is increased for reactions involving radical pair intermediates. The present investigation provides a firm foundation for the belief that there could be many reactions which are highly stereoselective or regioselective although they involve radical pair intermediates but the assignment of reactions to this group requires careful experimental validation. Attention must also be directed towards the question of whether there is or is not an interaction between the components of the radical pair which is responsible for the retention of configuration or chirality in radical pair intermediates.

Experimental

For general directions see Part 1.[18a] ^{1}H N.m.r. spectra showing CIDNP effects were recorded using a JEOL PFT100 Fourier Transform spectrometer: spectra were recorded at intervals using a single radio frequency pulse and disc storage of the time domain spectrum. ^{1}H N.m.r. chemical shifts are given in p.p.m. (δ) relative to tetramethylsilane as an internal reference.

Rearrangement of α-Benzyl(dimethyl)ammoniophenacylide (4a)*: Formation of* NN-*Dimethylbenzylamine*, 1,2-*Diphenylethane*, 2-*Dimethylamino-3-phenylpropiophenone* (5a), *and* 1,2-*Bis(dimethylamino)-1,2-dibenzoylethane* (*Isomers* A *and* B) (6).—The ylide (4a) was prepared as a monohydrate, m.p. 75—82 °C (lit.,[6] m.p. 70—71 °C) as described previously.[6] A solution of the ylide (6.00 g) in ethanol-free chloroform was heated at 60 °C for 30 min. The resulting yellow solution was dried (Na_2SO_4) and evaporated, the residue was heated at 60 °C (12 Torr) and volatile compounds were collected in a trap cooled by liquid N_2. The contents of the trap were distilled in a Kugelrohr apparatus at 80—100 °C (12 Torr) to give *NN*-dimethylbenzylamine (0.132 g, 4.4%) identical (n.m.r. spectrum) with an authentic sample. The less volatile residue was dissolved in ether (200 ml) and the ether solution extracted with 3% hydrochloric acid. The ether layer was washed with water, dried (Na_2SO_4), and evaporated; distillation of the residue at 80—100 °C (0.01 Torr, Kugelrohr) gave 1,2-diphenylethane (0.158 g, 7.9%), m.p. 48—49 °C, identical (n.m.r. spectrum, m.p.) with an authentic sample. The hydrochloric acid extracts were made basic (Na_2CO_3) and extracted with ether; the ether extract was dried (Na_2SO_4) and evaporated to give 2-dimethylamino-3-phenylpropiophenone (5a) (3.83 g, 69%) as a pale yellow solid, shown by n.m.r. examination to be contaminated with *ca.* 7% of both diastereoisomers of 1,2-bis(dimethylamino)-1,2-dibenzoylethane (6; isomer *A*: δ 4.93, 2.24; isomer *B*: δ 4.93, 2.45). The aminoketone (5a) was recrystallised from methanol to give a pure sample as pale yellow needles, m.p. 74—75 °C (lit.,[3a] 77—79 °C); δ 7.94—7.80 (m, 2 aryl H), 7.52—6.98 (m, 8 aryl H), ABX system, δ_A 3.26, δ_B 2.90, δ_X 4.29 (J_{AB} 13.2, J_{AX} 9.5, J_{BX} 4.0 Hz, $CH_X{-}CH_AH_B$), and 2.36 (s, NMe_2). The rearrangement of the ylide (4a) was conducted under a number of different conditions and the total product isolated and analysed for the

Table 6. Products from α-benzyl(dimethyl)ammoniophenacylide (4a)

Reaction conditions	Product composition (mol %) (5a)	(6) Isomers *A* and *B*	1,2-Diphenylethane	*NN*-Dimethylbenzylamine
$CHCl_3$, 60 °C	80	7.5	7.5	5
$CHCl_3$, 20 °C	85	5	4.5	5.5
MeOH, 60 °C	94	2	2.5	1.5
Neat, 110 °C	96.5	1	2	0.5

above products using n.m.r. spectroscopy. The following signals were assigned to specific compounds and the assignments were checked by the addition of a small quantity of the compound: δ 2.88 (1,2-diphenylethane); δ 4.93 and 2.45 [1,2-bis(dimethylamino)-1,2-dibenzoylethane (6; isomer *B*)]; δ 4.93 and 2.24 [1,2-bis(dimethylamino)-1,2-dibenzoylethane (6; isomer *A*)], δ 3.43 and 2.22 (*NN*-dimethylbenzylamine); the other signals in the spectrum were assignable to 2-dimethylamino-3-phenylpropiophenone (5a). The compositions of the product mixture are given in Table 6 for rearrangements under the conditions stated.

1,2-*Bis*(*dimethylamino*)-1,2-*dibenzoylethane* (6).—(a) *Diastereoisomer* A. Iodine (10.8 g) in benzene (100 ml) was added in one portion to a stirred solution of (*E*)-1,2-dibenzoylethylene (10.0 g) and dimethylamine (7.7 g) in benzene (100 ml). The mixture was stirred at room temperature for 14 h, the white precipitate removed by filtration, and the filtrate evaporated. The residual dark semi-solid was triturated with methanol (50 ml) to give the crude product (5.07 g, 37%) as pale yellow crystals; recrystallisation from 1,2-dimethoxyethane (without excessive heating) gave 1,2-*bis*(*dimethylamino*)-1,2-*dibenzoylethane* (6; diastereoisomer *A*) as pale yellow needles, m.p. 156—158 °C. Excessive heating during the recrystallisation or attempted recrystallisation from other solvents resulted in decomposition (Found: C, 73.8; H, 7.6; N, 8.6. $C_{20}H_{24}N_2O_2$ requires C, 74.0; H, 7.5; N, 8.6%), $\nu_{max.}$ 1 670 cm^{-1}; δ 8.09—7.95 (m, 4 aryl H), 7.65—7.36 (m, 6 aryl H), 4.93 (s, CH⁻CH), and 2.24 (s, 2 × NMe_2). The methanol filtrate from the above preparation deposited a brown crystalline solid (4.35 g) after standing overnight at 0 °C. Work-up for basic material (2% HCl, Na_2CO_3) and crystallisation from ethanol gave 1-dimethylamino-1,2-dibenzoylethylene (7) (1.41 g, 12%) as a pale yellow solid, m.p. 163—165 °C (lit.,[46] m.p. 160—162 °C); $\nu_{max.}$ 1 677 cm^{-1}; δ 8.04—7.76 (m, 4 aryl H), 7.54—7.20 (m, 6 aryl H), 5.94 (s, C=CH), and 2.94 (s, NMe_2).

(b) *Diastereoisomer* B. A solution of 1,2-bis(dimethylamino)-1,2-dibenzoylethane (6; diastereoisomer *A*) was heated at 50—60 °C for 10 min. The solution was evaporated and the residue triturated with light petroleum; the solution was then decanted from the insoluble solid and kept overnight at 0 °C. The large pale yellow needles (0.4—1.5 cm long) which separated were sorted from smaller crystals of a different type and dried to give 1,2-bis(dimethylamino)-1,2-dibenzoylethane (6; diastereoisomer *B*), m.p. 94—95 °C (83 mg, 33%). The melt solidified at 96—101 °C and re-melted at 137—145 °C (Found: C, 73.8; H, 7.5; N, 8.7%), $\nu_{max.}$ 1 670 cm^{-1}; δ 8.03—7.89 (m, 4 aryl H), 7.60—7.32 (m, 6 aryl H), 4.93 (s, CH⁻CH), and 2.45 (s, 2 × NMe_2).

(c) *Equilibration of the diastereoisomers* A *and* B *of the diamine* (6). A sample of the diastereoisomer *A* (100 mg) was heated under reflux in methanol (5 ml) for 10 min. The solvent was evaporated and the residue shown (n.m.r.) to consist of 72% diastereoisomer *B*, 18% diastereoisomer *A*, and 10% unidentified products of decomposition. The diastereoisomer *B* (20 mg), when heated slowly, melted at 95 °C and resolidified on heating to 110 °C. After a further 10 min at 110 °C the solid obtained was shown (n.m.r.) to consist of 90% diastereoisomer *A*, 5% diastereoisomer *B*, and 5% unidentified products of decomposition.

NN-*Dimethyl*-1-*phenylethylamine* (20).—(*R*,*S*)-1-Phenylethylamine (19) (48.5 g) was added to 90% formic acid (102 g) with ice cooling and 40% aqueous formaldehyde (85 ml) was then added; the mixture was heated at 100 °C for 8 h. The mixture was cooled, acidified (200 ml; 4M-HCl) and evaporated to dryness. The residual solid was dissolved in water (150 ml) and the solution made basic (K_2CO_3) and extracted with benzene. The benzene extract was dried (Na_2SO_4) and evaporated and the residue distilled to give (*R*,*S*)-*NN*-dimethyl-1-phenylethylamine (20) (41.2 g, 69%), b.p. 65 °C at 12 Torr (lit.,[47] b.p. 92—94 °C at 30 Torr); δ 7.34—7.14 (m, 5 aryl H), 3.21 (q, *J* 6.5 Hz, C*H*Me), 2.16 (s, NMe_2), and 1.34 (d, *J* 6.5 Hz, CH*Me*). The (*S*)-isomer (20b),[48] prepared by a similar method from (*S*)-(−)-1-phenylethylamine (19b) (60% yield), b.p. 62 °C) at 11 Torr (lit.,[8] 65 °C at 8 Torr) had α_D^{22} −60.0° (neat) [lit. α_D^{24} −65.3° (neat),[8] α_D^{28} −63.1° (neat)[49]]. The (*R*)-(+)-isomer (20a), prepared by a similar method from (*R*)-1-phenylethylamine (19a) (67% yield), b.p. 64 °C at 11 Torr had α_D^{22} +62.5° (neat).

[$^2H_5$]*Phenacyl Bromide*.—Acetyl chloride (26.7 g) was added during 15 min to a suspension of anhydrous aluminium chloride (56.6 g), which had been treated with one drop of D_2O, in carbon disulphide (25 ml). The suspension was heated under reflux for 5—10 min and a solution of [$^2H_6$]benzene (28.5 g, >99 atom % D) in carbon disulphide (18 ml) was added dropwise with stirring. The mixture was heated under reflux for 6 h, cooled, poured into ice–water (300 ml) and the product extracted into dichloromethane. The extracts were washed with water, dried (Na_2SO_4), and evaporated. The residue was distilled to give [$^2H_5$]acetophenone (28.8 g, 68%), b.p. 83 °C at 12 Torr. The n.m.r. spectrum showed no signals assignable to aryl H indicating >99 atom % D in the phenyl group. Bromine (16.0 g) was added to a stirred and cooled solution of [$^2H_5$]acetophenone (12.52 g) in acetic acid (20 ml) at such a rate that the temperature of the reaction mixture remained below 20 °C. The mixture was poured into ice–water (120 ml) and the precipitated solid collected and dissolved in ether (250 ml). The ethereal solution was washed with water, dried (Na_2SO_4), and evaporated and the residue distilled to give [$^2H_5$]phenacyl bromide (14.8 g, 73%), b.p. 78—79 °C at 0.1 Torr. The product crystallised from ether–light petroleum as plates, m.p. 48—49 °C; the n.m.r. spectrum showed no signals assignable to aryl H indicating >99 atom % D in the phenyl group.

(*RS*)-NN-*Dimethyl*-1-[$^2H_5$]*phenylethylamine*.—A mixture of [$^2H_5$]acetophenone (6.26 g), 90% formic acid (6.4 g), and dimethylformamide (11.0 g) was heated in a glass-lined auto-

clave at 190 °C for 16 h. The reaction mixture was extracted with ether and 10% HCl and the organic layer separated and discarded. The aqueous layer was washed with ether, concentrated to a small volume, made basic (K_2CO_3), and extracted with ether. The ethereal extracts were dried (Na_2SO_4) and evaporated and the residue distilled to give (*R,S*)-NN-*dimethyl*-1-[$^2H_5$]*phenylethylamine* (3.32 g, 43%), b.p. (Kugelrohr) 80—100 °C at 12 Torr. This product showed no detectable signals in the n.m.r. spectrum in the range δ 10—5 indicating a label of >99 atom % deuterium at each position of the phenyl group.

NN-*Dimethyl*-N-*phenacyl*-1-*phenylethylammonium Bromide* (13).—(*R,S*)-*NN*-Dimethyl-1-phenylethylamine (15.0 g) and phenacyl bromide (21.0 g) in acetone (150 ml) were kept at room temperature for 3 h. The precipitated solid was washed with hot acetone, dissolved in the minimum quantity of ethanol, and ether (300 ml) added. The precipitate was collected and dried to give the (*R,S*)-salt (13) (28.6 g, 82%) as a microcrystalline solid, m.p. 153—154 °C (lit., m.p. 155—157 °C,[3b] 100—102.5 °C [8]), δ 8.17—8.03 (m, 2 aryl H), 7.69—7.32 (m, 8 aryl H), AB system, δ_A 5.92, δ_B 5.51 (*J* 17.5 Hz, $COCH_AH_B\overset{+}{N}$), 5.81 (q, *J* 7 Hz, C*H*Me), 3.63 (s, $\overset{+}{N}$Me), 3.48 (s, $\overset{+}{N}$Me), and 1.95 (d, *J* 7 Hz, C*H*Me). The (*S*)-salt (13b), prepared in a similar manner from (*S*)-(−)-*NN*-dimethyl-1-phenylethylamine (63% yield), was recrystallised from ethyl methyl ketone–ethanol to give large colourless prisms which were dissolved in ethanol and precipitated by the addition of ether. The (*S*)-salt (13b) was obtained as a microcrystalline solid, m.p. 126—127 °C (lit.,[8] m.p. 119.5—120 °C), $[\alpha]_D^{22}$ −82.3° (*c* 7.02 in ethanol) (98.6% e.e.); lit.,[8] $[\alpha]_D^{26}$ −79.9° (*c* 7.108 in 95% ethanol).

The (*R*)-salt (13a), prepared in a similar manner from (*R*)-(+)-*NN*-dimethyl-1-phenylethylamine (60% yield), was recrystallised twice from acetone–ethanol and then from ethanol by the addition of ether. The (*R*)-salt (13a) was a microcrystalline solid, m.p. 126—127 °C (lit.,[8] m.p. 119.5—120 °C), $[\alpha]_D^{22}$ +83.5° (*c* 7.1 in ethanol) {lit.,[8] $[\alpha]_D^{29}$ +80.3° (*c* 6.989 in 95% ethanol)}. The (*R*)-salt (13a) (2.5 g) in acetic acid (20 ml) at 70 °C was treated portionwise with zinc dust (1.0 g) during 10 min. The mixture was cooled, treated with 5% HCl, and unchanged zinc removed by filtration. The filtrate was washed with ether, made basic (Na_2CO_3), and extracted with dichloromethane. The extract was dried (Na_2SO_4) and evaporated and the residue distilled to give (*R*)-(+)-*NN*-dimethyl-1-phenylethylamine (0.75 g, 70%), b.p. (Kugelrohr) 60—80 °C at 12 Torr, α_D^{22} +65.8° (neat) (100% e.e.).

(R,S)-NN-*Dimethyl*-N-[$^2H_5$]*phenacyl*-1-[$^2H_5$]*phenylethylammonium Bromide*. Compound (23) was prepared from *NN*-dimethyl-1-[$^2H_5$]phenylethylamine (1.54 g) and [$^2H_5$]phenacyl bromide by a similar method to that used for the undeuteriated salt (13). The deuteriated salt (23) (57% yield) had m.p. 148—150 °C.

Base Catalysed Rearrangement of NN-*Dimethyl*-N-*phenacyl*-1-*phenylethylammonium Bromide* (13)*: Formation of* 2-*Dimethylamino*-1,3-*diphenylbutan*-1-*one* (14), 2-*Hydroxy*-1,3-*diphenylbutan*-1-*one* (8), *and* 1-*Phenylethanol*.—(a) A solution of (*R,S*)-*NN*-dimethyl-*N*-phenacyl-1-phenylethylammonium bromide (13) (17.41 g) in water (200 ml) at 0 °C containing ice (100 g) was treated with aqueous sodium hydroxide at 0 °C (1.4 M; 50 ml) and left overnight at 0 °C. The mixture was extracted with ether and the ethereal extract was extracted with 2% HCl, dried (Na_2SO_4), and evaporated. The residue was separated into three components by t.l.c. using light petroleum–di-isopropyl ether as the solvent. The first fraction was identified as 2-hydroxy-1,3-diphenylbutan-1-one (8; diastereoisomer *A*) (174 mg, 1.5%); $\nu_{max.}$ 3 480 and 1 682 cm^{-1}; δ 7.96—7.81 (m, 2 aryl H), 7.63—7.01 (m, 8 aryl H), and $ABCX_3$ system, δ_A 5.22, δ_B 3.81, δ_C 3.19, δ_X 1.05 [J_{AB} 6, J_{AC} 2, J_{CX} 7 Hz, $H_BOCH_ACH_CC(H_X)_3$]. The second fraction was identified as 2-hydroxy-1,3-diphenylbutan-1-one (8; diastereoisomer *B*) (111 mg, 0.9%), $\nu_{max.}$ 3 480 and 1 684 cm^{-1}; δ 7.83—6.81 (m, 10 aryl H), and $ABCX_3$ system, δ_A 5.19, δ_B 3.54, δ_C 3.30, δ_X 1.50 [J_{AB} 7, J_{AX} 3, J_{CX} 7 Hz, $H_BOCH_ACH_CC(H_X)_3$]. The third fraction was identified (n.m.r. comparison) as 1-phenylethanol (87 mg, 1.4%). The hydrochloric acid extract was made basic (Na_2CO_3) and extracted with ether. The ethereal solution was dried (Na_2SO_4) and evaporated to give pure 2-dimethylamino-1,3-diphenylbutan-1-one (14) as a pale yellow mixture of 2 diastereoisomers (11.2 g, 84%) in a 4 : 5 ratio, m.p. 81—99 °C (lit.,[8] m.p. 75—84 °C); major diastereoisomer, δ 8.04—7.90 (m, 2 aryl H), 7.58—7.14 (m, 8 aryl H), ABX_3 system, δ_A 4.42, δ_B 3.44, δ_X 1.11 [J_{AB} 10, J_{BX} 6.5 Hz, $CH_ACH_BC(H_X)_3$], and 2.15 (s, NMe_2); minor diastereoisomer, δ 7.64—6.90 (m, 10 aryl H), ABX_3 system, δ_A 4.32, δ_B 3.40, δ_X 1.41 [J_{AB} 10, J_{BX} 6.5 Hz, $CH_ACH_BC(H_X)_3$], and 2.35 (s, NMe_2).

(b) 3M-Sodium hydroxide (10 ml) at 50 °C was added to a solution of the (*R,S*)-salt (13) (7.00 g) at 50 °C in water (50 ml). After 30 min at 50 °C (±2°) the mixture was extracted with ether. The ether extract was washed with 2% HCl, dried (Na_2SO_4), and evaporated to give a semi-solid residue (153 mg) consisting of *ca.* 50% 2,3-diphenylbutane (3—4% yield, 1 : 1 mixture of diastereoisomers), on the basis of n.m.r. comparison with an authentic sample, and *ca.* 50% unidentified products. The hydrochloric acid extract was worked up as in the previous experiment to give 2-dimethylamino-1,3-diphenylbutan-1-one (14) as a pale yellow mixture of diastereoisomers (4.68 g, 87%), m.p. 70—92 °C (lit.,[8] 75—84 °C).

(c) Methanolic sodium methoxide (1.6M; 5 ml) was added to a solution of the (*R*)-salt (13a) {2.00 g $[\alpha]_D^{22}$ +83.4° (*c* 6.7 in ethanol)} (99.9% e.e.) at 55 °C in methanol (10 ml). The mixture was kept at 55—60 °C for 5 min, allowed to cool to room temperature, diluted with ether (100 ml), and washed with water. The organic layer was evaporated to give a pale yellow solid (1.41 g) which was dissolved in 2% HCl and extracted with ether. The ether extract was evaporated and the residue (62 mg) shown by n.m.r. and t.l.c. to consist largely (>70%) of 2,3-diphenylbutane. Purification by t.l.c. (light petroleum) followed by distillation (Kugelrohr) at 70—90 °C (0.3 Torr) gave pure 2,3-diphenylbutane as a 1 : 1 mixture of diastereoisomers (29 mg, 5%); $[\alpha]_D^{22}$ 0.00° (*c* 2.9 in CCl_4) {lit.,[50] $[\alpha]_D^{24}$ −108.6° (*c* 0.433 in $CHCl_3$) for the pure (−)-diastereoisomer}; δ(CCl_4) 7.25—6.81 (m, 10 aryl H), 3.03—2.57 (m, CH⁻CH), 1.26 (d, *J* 6.5 Hz, CH*Me*), and 1.00 (d, *J* 6 Hz, CH*Me*). These data are in agreement with those reported for the authentic compounds.[51] The hydrochloric acid extract was made basic (Na_2CO_3), extracted with ether, and the ether extract dried (Na_2SO_4) and evaporated to give 2-dimethylamino-1,3-diphenylbutan-1-one (14) (1.22 g, 80%) as a pale yellow solid, m.p. 74—93 °C (lit.,[8] 75—84 °C) consisting of a 1 : 1 mixture of two diastereoisomers. The total crude rearrangement product also contained *ca.* 6% of 1,2-bis(dimethylamino)-1,2-dibenzoylethane (6) (*ca.* 11% yield of both diastereoisomers in a 3 : 1 ratio) which could not be isolated but which was identified by comparison of the n.m.r. spectra of the total product and authentic samples of the diamines (6).

(S)-(+)-1,3-*Diphenylbutan*-1-*one* (21a).—Aqueous sodium hydroxide (10 ml; 2M), at 0 °C was added during 3 min to a stirred solution of (*R*)-(+)-*NN*-dimethyl-*N*-phenacyl-1-phenylethylammonium bromide (13a) (5.00 g) {$[\alpha]_D^{22}$ +83.5° (*c* 7.1 in ethanol); 100% e.e.} in water (110 ml) at 0 °C. The mixture was kept overnight at 0 °C, allowed to warm to room temp-

Table 7. Rearrangement of (*S*)-(−)-*NN*-dimethyl-*N*-phenacyl-1-phenylethylammonium bromide (13b) under various reaction conditions

Rearrangement conditions						Details of 1,3-diphenylbutan-1-one (21b)	
Solvent	Base	Temp. (°C)	Reaction time (h)	Yield of (21b) (%)	Yield of (14b) (%)	M.p. (°C)	Specific rotation in CCl_4, $[\alpha]_D^{22}$ (°) (*c*)
Methanol	NaOMe	0	50	79	81	45—65	−9.77 (5.17)
Methanol	NaOMe	40	30	81	74	44—67	−8.03 (5.18)
t-Butyl alcohol	NaOMe	50	1	76	77	46—66	−9.23 (5.18)
Cyclohexanol	NaOMe [a]	50	1	81	71	45—65	−10.50 (5.17)
Glycerol	NaOH	50	2	96	83	46—57	−12.42 (5.23)
Water	NaOH	0	60	87	83	46—48	−13.67 (5.14)
Water	NaOH	50	30	84	81	46—62	−10.80 (5.15)

[a] Base added as a solution in methanol (1 ml).

erature and extracted with ether. The ether extract was dried (Na_2SO_4) and evaporated to give the crude aminoketone (14a) (3.38 g) as a pale yellow solid, m.p. 66—108 °C (lit.,[8] 65—85 °C), $[\alpha]_D^{22}$ −27.6° (*c* 1.65 in methanol) {lit.,[8] $[\alpha]_D$ −24.9° (*c* 1.69 in methanol), which was a mixture of diastereoisomers (n.m.r., ratio 4 : 5). This product (2.67 g) in acetic acid (30 ml) was treated portionwise with zinc dust (1.30 g) during 15 min at 100 °C. The cooled mixture was diluted with hydrochloric acid (40 ml, 1%), unchanged zinc removed, and the mixture extracted with ether. The ether extract was washed (water and aqueous $NaHCO_3$), dried, and evaporated to give the crude (*S*)-(+)-ketone (21a) (2.10 g, 94%) as a solid, m.p. 37—43 °C. A sample was purified by t.l.c. (light petroleum–ether 4 : 1) and distilled (Kugelrohr) at 90—120 °C (0.01 Torr) to give the pure ketone (21a), m.p. 45—48 °C (lit.,[8] 48—70 °C), $[\alpha]_D^{22}$ +13.3°, $[\alpha]_{578}^{22}$ +14.2° (*c* 5.00 or 6.95 in CCl_4) {lit.,[8] $[\alpha]_D^{28}$ +10.6° (*c* 2.78 in CCl_4); lit.,[9] absolute rotation $[\alpha]_{578}^{25}$ +13.68 (*c* 6.905 in CCl_4)}; $\nu_{max.}$ 1 696 cm^{-1}; δ 7.98—7.81 (m, 2 aryl H), 7.55—7.05 (m, 8 aryl H), and $ABCX_3$ system, δ_A 3.51, δ_B 3.31, δ_C 3.11, δ_X 1.31 [J_{AB} 5.5, J_{AC} 8.5, J_{BC} 16, J_{AX} 6.5 Hz, $CH_BH_CCH_AC(H_X)_3$]. The enantiomeric excess of this product was shown to be 95.2% by degradation to (*S*)-(+)-3-phenylbutyric acid (22a).

(S)-(+)-3-*Phenylbutyric Acid* (22a).—A mixture of (*S*)-(+)-1,3-diphenylbutan-1-one (21a) (1.90 g) {$[\alpha]_D^{22}$ +13.3° (*c* 5.0 in CCl_4); 95.2% e.e.} and *m*-chloroperoxybenzoic acid (2.00 g) was heated under reflux in 1,2-dichloroethane (20 ml) for 6 h. The cooled mixture was washed with saturated aqueous $NaHCO_3$, dried, and concentrated. The residual oil (1.95 g) was stirred with a solution of sodium hydroxide (1.0 g) in aqueous ethanol (25 ml, 60%) for 16 h, concentrated to a volume of 10 ml, washed with ether, acidified, and extracted with ether. The ether extract was dried and evaporated to give a 2 : 1 mixture (n.m.r.) of 3-phenylbutyric acid and benzoic acid. (*S*)-(+)-3-Phenylbutyric acid (22a) (0.4 g, 34%), isolated from this mixture by t.l.c. (chloroform–methanol 85 : 15) and distillation (Kugelrohr) at 80—100 °C (0.2 Torr), was obtained as an oil $[\alpha]_D^{22}$ +55.7° (*c* 2.975 in benzene) (95.2% e.e.) {lit.,[29] $[\alpha]_D^{25}$ +58.5° (*c* 3 in benzene), lit.,[52] $[\alpha]_D$ +57.23° (*c* 8.8 in benzene), lit.,[53] $[\alpha]_D$ +56.7°, configuration (S)-(+)}; $\nu_{max.}$ 3 500—2 300br and 1 710 cm^{-1}; δ 7.37—7.07 (m, 5 aryl H), and $ABCX_3$ system, δ_A 3.27, δ_B 2.70, δ_C 2.53, δ_X 1.30 [J_{AB} 6.5, J_{AC} 8.5, J_{BC} 16, J_{AX} 7 Hz, $CH_BH_CCH_AC(H_X)_3$].

Base Catalysed Rearrangement of (S)-(−)-NN-*Dimethyl*-N-*phenacyl*-1-*phenylethylammonium Bromide* (13b)*: Determination of Stereoselectivity under Various Conditions.*—The rearrangements were conducted, in each case, under the conditions recorded in Table 7 by adding the appropriate base (1.5—2 molar equivalents) in solvent (2 ml) to a stirred solution of the (*S*)-(−)-salt (13b) (0.520 g) {$[\alpha]_D^{22}$ −82.3° (*c* 7.02 in ethanol); 98.6% e.e.} in the same solvent (10 ml). Both solutions were first adjusted to the appropriate temperature which was maintained (±2 °C) during the addition of base and the subsequent reaction. The rearrangement product (14) was isolated as a pale yellow solid by a method similar to that used in the previous experiments, and it was then degraded to 1,3-diphenylbutan-1-one (21) by the following procedure. Zinc dust (0.25 g) was added portionwise to a stirred solution of the rearrangement product (14) (0.30—0.38 g) in acetic acid (6 ml) during 10—20 min, the mixture being kept at 80 °C. The mixture was cooled, diluted with water (6 ml), and the product extracted into ether. The ether extract was washed (water and $NaHCO_3$ solution), dried (Na_2SO_4), and evaporated. The residual oil was purified by t.l.c. (light petroleum–ether 2 : 1) and distilled (Kugelrohr) at 120—130 °C (0.1 Torr) to give 1,3-diphenylbutan-1-one (21) as a colourless oil which solidified with time. The yields, melting points, and specific rotations are listed in Table 7.

Base Catalysed Rearrangement of (R,S)-NN-*Dimethyl*-N-*phenacyl*-1-*phenylethylammonium Bromide* (13)*: Determination of Intramolecularity under Various Conditions.*—The rearrangements were conducted in each case under the conditions indicated in Table 8 by adding the appropriate base (1.5—2.5 molar equivalents) in solvent (1 ml) to a stirred solution of a 1 : 1 mixture of (*R*,*S*)-*NN*-dimethyl-*N*-phenacyl-1-phenylethylammonium bromide (13) and (*R*,*S*)-*NN*-dimethyl-*N*-[$^2H_5$]phenacyl-1-[$^2H_5$]phenylethylammonium bromide (23) (0.177 g) in the same solvent (3 ml). The reaction was carried out and the product isolated as in the previous experiment. The isotopic compositions of the rearrangement product (14) {[$^2H_0$],[$^2H_5$], and [$^2H_{10}$]} were determined by mass spectral analysis based upon peaks heights (averaged over several spectra) of the $(M)^+$, $(M + 5)^+$, and $(M + 10)^+$ ions. The results are recorded in Table 8.

(R)-(+)-1-p-*Methoxyphenylethylamine* (30a).—The (*R*,*S*)-amine (30) (121 g), prepared using the procedure described for the preparation of 1-*p*-chlorophenylethylamine,[33] was added to a boiling solution of (+)-tartaric acid (122 g) in methanol (1.1 l) and the hot solution filtered and left overnight. The crystals which were deposited were collected (111 g, m.p. 167—173 °C) and dissolved in water (500 ml); the solution was treated with 5M-NaOH solution (230 ml) and the liberated amine extracted with dichloromethane. The extract was dried (Na_2SO_4) and evaporated and the residue distilled to give the partly resolved amine (55 g), b.p. 72 °C (0.5 Torr), α_D^{22} +14.7° (neat). This amine was treated again with (+)-tartaric acid (58.5 g) in methanol (600 ml) to give a salt, m.p. 175—178 °C, from which the amine (38.7 g) was liberated with α_D^{22} +24.7° (neat).

A further treatment of this amine with (+)-tartaric acid

Table 8. Rearrangement of a mixture of [$^2H_0$]- and [$^2H_{10}$]-*NN*-dimethyl-*N*-phenacyl-1-phenylethylammonium bromide (13) and (23). Isotopic composition of the products {(14), [$^2H_0$], [$^2H_5$], [$^2H_{10}$]} under various reaction conditions

Reaction conditions					Product (14) Isotopic composition (%)		
Solvent	Base	Temp. (°C)	Time (h)	Yield (%)	[$^2H_0$]	[$^2H_5$]	[$^2H_{10}$]
Methanol	NaOMe	0	92	72	53.37	3.46	43.17
Methanol	NaOMe	40	3	76	50.95	8.33	40.72
Methanol	NaOMe	60	1	74	48.68	11.48	39.85
t-Butyl alcohol	NaOMe	50	2	67	51.41	5.27	43.32
Cyclohexanol	NaOMe	50	2	71	54.43	2.75	42.82
Glycerol	NaOH	50	3	82	54.81	1.24	43.95
Water	NaOH	0	106	83	56.84	<0.10	43.06
Water	NaOH	50	2	87	53.99	2.15	43.86

(40 g) in methanol (500 ml) gave a salt (56 g) (m.p. 179—182 °C, raised to 181—183 °C by recrystallisation from methanol (600 ml). The liberated amine (20.2 g) had α_D^{22} +32.4° (neat) and was again treated with (+)-tartaric acid (21 g) in methanol (500 ml) to give a salt (28 g), m.p. 183—185 °C. (*R*)-(+)-1-*p*-Methoxyphenylethylamine (30a) (12.7 g, 21%) was liberated from this salt with α_D^{22} +36.1° (neat) (100% e.e.) {lit.,[33d] α_D +21.62° (neat) for the amine of 60% enantiomeric excess; this corresponds with α_D +36.0° (100% e.e.)}. The original methanol mother liquor was concentrated and the residue suspended in methanol (400 ml) and treated with 5M-NaOH solution (300 ml). The liberated amine was extracted with dichloromethane and distilled to give a sample (63 g), b.p. 72 °C (0.5 Torr), with α_D^{22} −13.8° (neat) (38.2% e.e.). The enantiomeric composition of this sample was determined by n.m.r. spectroscopy using the chiral lanthanide shift reagent [Eu(tfc)$_3$] at a molar ratio [Eu(tfc)$_3$] : amine of 0.5 : 1 and a 0.27M-solution of the amine in $CDCl_3$. All signals, except the CH_3O singlet, showed different chemical shifts for the (*R*)- and (*S*)-enantiomers and the enantiomeric excess of the sample of the (*S*)-amine (30b) was determined as 40.4%. The (*R*)-amine (30a) α_D^{22} +36.1° (neat) was shown to be enantiomerically pure within the limits of n.m.r. detection.

NN-*Dimethyl*-1-p-*methoxyphenylethylamine* (31).—(a) (*R*)-(+)-1-*p*-Methoxyphenylethylamine (30a) (12.00 g) [α_D^{22} +36.1° (neat)] was dissolved in 98—100% formic acid (18.3 g) with ice cooling. Aqueous formaldehyde (19.4 g, 37—40%) was added and the mixture was heated under reflux for 9 h. The cooled reaction mixture was acidified (10M-HCl), washed with ether, evaporated to a small volume, and made basic (6M-KOH). The liberated amine was extracted into dichloromethane and the extracts were dried (Na_2SO_4) and evaporated and the residue distilled to give the (*R*)-(+)-amine (31a) (6.78 g, 47%), b.p. 68 °C (0.5 Torr); α_D^{22} +56.7 (neat) (100% e.e.); δ, AA′BB′ system, δ_A 7.18, δ_B 6.81 (J_{AB}, $J_{A'B'}$ 9 Hz, C_6H_4), 3.74 (s, OMe), AX_3 system, δ_A 3.20, δ_X 1.32 [J_{AX} 6.5 Hz, $CH_AC(H_X)_3$], and 2.15 (s, NMe_2).

(b) (*S*)-(−)-1-*p*-Methoxyphenylethylamine (30a) [α_D^{22} −13.8° (neat)] by a similar procedure gave the (*S*)-(−)-amine (31b) with α_D^{22} −22.8° (neat) (40.2% e.e.).

NN-*Dimethyl*-N-*phenacyl*-1-p-*methoxyphenylethylammonium Bromide* (32).—(a) A solution of (*R,S*)-*NN*-dimethyl-1-*p*-methoxyphenylethylamine (31)[33a] (8.96 g) and phenacyl bromide (10.3 g) in acetone (60 ml) was kept for 16 h at room temperature and then 4 days at 0 °C. The precipitated solid was collected, washed with acetone, and dried to give the (R,S)-*salt* (32) (10.6 g, 56%), m.p. 122—123 °C (followed by solidification and remelting at 180—190 °C) (Found: C, 60.6; H, 6.6; Br, 21.0; N, 3.6. $C_{19}H_{24}BrNO_2$ requires C, 60.3; H, 6.4; Br, 21.1; N, 3.7%), $\nu_{max.}$ 1 687 cm^{-1}; δ 8.19—8.05 (m, 2 aryl H), 7.63—7.31 (m, 5 aryl H), 7.93 (d, *J* 9.5 Hz, 2 aryl H), AB system, δ_A 5.91, δ_B 5.50 (*J* 18.5 Hz, NCH_AH_BCO), AX_3 system, δ_A 5.78, δ_X 1.89 [J_{AX} 6.5 Hz, $CH_AC(H_X)_3$], 3.79 (s, OMe), 3.62 (s, $\overset{+}{N}Me$), and 3.45 (s, $\overset{+}{N}Me$).

(b) A solution of (*R*)-(+)-*NN*-dimethyl-1-*p*-methoxyphenylethylamine (31a) [α_D^{22} +56.7° (neat); 100% e.e.] and phenacyl bromide (7.00 g) in methanol (50 ml) was kept for 4 h at room temperature and then overnight at 0 °C. The solution was concentrated and the residual gum washed several times with ether and dried at 0.1 Torr. The resulting foam was triturated with ether to give a solid which was washed with ether and dried to give the (*R*)-(+)-salt (32a) (12.9 g, 100%) as a non-crystalline hygroscopic solid; {$[\alpha]_D^{22}$ +67.6°(*c* 9.81 in ethanol); 100% e.e.}. A stirred solution of this (*R*)-salt (32a) (2.4 g) in acetic acid (15 ml) was treated portionwise with zinc dust during 20 min at 70—80 °C. The mixture was cooled and decanted and the solution acidified (5M-HCl; 6 ml), concentrated to a small volume, diluted with water (10 ml), and made basic (2M-NaOH). The ether extract of this basic solution was dried (Na_2SO_4) and evaporated and the residue distilled (Kugelrohr) at 90—110 °C (12 Torr) to give (*R*)-(+)-*NN*-dimethyl-1-*p*-methoxyphenylethylamine (31a) (0.95 g, 81%) with α_D^{22} +56.7° (100% e.e.) identified by comparison with an authentic sample.

Base Catalysed Rearrangement of NN-*Dimethyl*-N-*phenacyl*-1-p-*methoxyphenylethylammonium Bromide* (32): *Formation of* 2-*Dimethylamino*-3-p-*methoxyphenyl*-1-*phenylbutan*-1-*one* (33), p-*Methoxystyrene*, 2,3-*Bis*(p-*methoxyphenyl*)*butane*, 1-p-*Methoxyphenylethanol*, *and* 1,2-*Bis*(*dimethylamino*)-1,2-*dibenzoylethane* (6) (*Isomers* A *and B*).—Cold aqueous sodium hydroxide (10 ml; 2.25M) was added to a stirred solution of the (*R,S*)-salt (32) (5.67 g) in ice–water (100 ml). The mixture was kept at 0 °C for 14 h, allowed to warm to room temperature and extracted with dichloromethane. The extract was dried (Na_2SO_4) and evaporated and the residual semi-solid (4.50 g) dissolved in 2% HCl and the solution extracted with ether. The ether extract was evaporated and the residue (0.38 g) separated by t.l.c. (light petroleum–di-isopropyl ether, 11 : 9) to give three products. The first product was identified as *p*-methoxystyrene (8 mg, 0.4%) by comparison (n.m.r.) with an authentic sample. The second product was obtained as a solid, identified as a mixture of diastereoisomeric 2,3-bis(*p*-methoxyphenyl)butanes (83 mg, 4.0%) in a 4 : 5 ratio; δ 7.12—6.64 (m, 8 aromatic H of each isomer), 3.75 and 3.69 (s, 2 × OMe of each isomer), 3.00—2.52 (m, CH−CH), and 1.21 and 0.98 (d, *J* 6.5 Hz, 2 × CH*Me* of each isomer). The third product was identified as 1-*p*-methoxyphenylethanol (26 mg, 1.1%); δ, AA′BB′ system, δ_A 7.23, δ_B 6.85 (J_{AB}, $J_{A'B'}$ 9 Hz, C_6H_4), AX_3

system, δ_A 4.85, δ_X 1.47 [J_{AX} 6.5 Hz, $CH_AC(H_X)_3$], 3.77 (s, OMe), and 3.5br (s, OH). The hydrochloric acid solution was made basic (Na_2CO_3) and extracted with dichloromethane. The extract was dried and evaporated to give 2-*dimethylamino*-3-p-*methoxyphenyl*-1-*phenylbutan*-1-*one* (33) (3.86 g, 87%) as a yellow semi-solid mixture of two diastereoisomers in a 4 : 5 ratio. Crystallisation from methanol gave a single diastereoisomer as pale yellow needles, m.p. 123—126 °C (Found: C, 76.9; H, 7.8; N, 4.9. $C_{19}H_{23}NO_2$ requires C, 76.7; H, 7.8; N, 4.7%); $\nu_{max.}$ 1 675 cm^{-1}; δ 7.65—7.53 (m, 2 aryl H), 7.46—7.18 (m, 3 aryl H), AA′BB′ system, δ_A 7.11, δ_B 6.66 (J_{AB}, $J_{A'B'}$, 9 Hz, C_6H_4), ABX_3 system, δ_A 4.27, δ_B 3.33, δ_X 1.38 [J_{AB} 11, J_{BX} 7 Hz, $CH_ACH_BC(H_X)_3$], 3.62 (s, OMe), and 2.34 (s, NMe_2). The other diastereoisomer was not obtained pure, but was identified by its n.m.r. spectrum; δ 8.04—7.92 (m, 2 aryl H), 7.6—7.4 (m, 3 aryl H), AA′BB′ system, δ_A 7.21, δ_B 6.83 (J_{AB}, $J_{A'B'}$, 9 Hz, C_6H_4), ABX_3 system, δ_A 4.38, δ_B *ca.* 3.35, δ_X 1.09 [J_{AB} 10, J_{BX} 7 Hz, $CH_ACH_BC(H_X)_3$], 3.72 (s, OMe), and 2.17 (s, NMe_2). The total crude rearrangement product contained 3—4% of 1,2-bis(dimethylamino)-1,2-dibenzoylethane (6; diastereoisomers *A* and *B* in a 3 : 1 ratio) which could not be isolated, but which was identified in the mixture on the basis of n.m.r. comparison with authentic samples (singlets at δ 4.93, 2.45, and 2.24).

Base Catalysed Rearrangement of (R)-(+)-NN-*Dimethyl*-N-*phenacyl*-1-p-*methoxyphenylethylammonium Bromide* (32a)*: Formation of* 2-*Dimethylamino*-3-p-*methoxyphenyl*-1-*phenylbutan*-1-*one* (33a) *and its Degradation to* (S)-(+)-3-p-*Methoxyphenyl*-1-*phenylbutan*-1-*one* (34a).—(a) A solution of the (*R*)-(+)-salt (32a) (8.32 g) (100% e.e.) in ice–water (160 ml) was treated with ice-cold aqueous sodium hydroxide (2M; 17 ml). The mixture was stirred for 30 min and kept overnight at 0 °C, allowed to warm to room temperature, and extracted with ether. The ethereal solution was extracted with 3% HCl; the extract was washed with ether, made basic (Na_2CO_3), and extracted with ether. The extract was dried (Na_2SO_4) and evaporated to give the aminoketone (33a) (5.51 g, 84%) as a yellow semi-solid. This product was dissolved in acetic acid (50 ml) and the solution treated portionwise with zinc dust (3.0 g) during 20 min at 80—90 °C. The mixture was allowed to cool to room temperature, diluted with water (100 ml), and extracted with ether. The ether extract was washed with water and saturated aqueous $NaHCO_3$, dried (Na_2SO_4), and evaporated. Distillation of the residue (Kugelrohr) at 130—150 °C (0.01 Torr) gave the (*S*)-(+)-ketone (34a) (4.12 g, 88%) as an oil which solidified with time. Further purification by t.l.c. (ether–light petroleum) followed by distillation gave the (*S*)-(+)-ketone (34a), m.p. 33—48 °C, $[\alpha]_D^{22}$ +18.9° (*c* 5.09 in CCl_4) (87.3% e.e.).

(b) A solution of the (*R*)-(+)-salt (32a) (0.95 g) (100% e.e.) in methanol (15 ml) was treated with methanolic sodium methoxide (4 ml; 1M) at 0 °C. The solution was kept at 0 °C for 50 h, the solvent evaporated, and the residue dissolved in 3% HCl (15 ml). Work-up for basic material as before gave the aminoketone (33a) (0.52 g, 70%) which was reduced with zinc dust–acetic acid to give the (*S*)-(+)-ketone (34a) (0.36 g, 80%), m.p. 34—60 °C, $[\alpha]_D^{22}$ +13.3° (*c* 5.19 in CCl_4) (61.4% e.e.).

(c) A solution of the (*R*)-(+)-salt (32a) (0.95 g) (100% e.e.) in methanol (15 ml) was treated with methanolic sodium methoxide (4 ml; M) at 40 °C. The solution was kept at 40 °C for 90 min and the aminoketone (33a) isolated (0.51 g, 69%) and degraded to give the (*S*)-(+)-ketone (34a) (0.35 g, 80%), m.p. 33—61 °C, $[\alpha]_D^{20}$ +10.8° (*c* 5.31 in CCl_4) (49.9% e.e.).

(R,S)-3-p-*Methoxyphenyl*-1-*phenylbutan*-1-*one* (34).—The aminoketone (33) (0.75 g), prepared from the (*R,S*)-salt (32), was reduced using zinc dust (0.50 g) and acetic acid (10 ml) at 80—90 °C. The (*R,S*)-ketone (34) was extracted from the reaction mixture as before and recrystallised from methanol to give the pure (R,S)-*ketone* (34) (0.46 g, 72%) as needles, m.p. 64—66 °C (Found: C, 80.4; H, 7.4. $C_{17}H_{18}O_2$ requires C, 80.3; H, 7.1%), $\nu_{max.}$ 1 690 cm^{-1}; δ 7.90—7.76 (m, 2 aryl H), 7.52—7.20 (m, 3 aryl N), AA′BB′ system, δ_A 7.06, δ_B 6.69 (J_{AB}, $J_{A'B'}$ 8.5 Hz, C_6H_4), 3.70 (s, OMe), and $ABCX_3$ system, δ_A 3.16, δ_B 3.16, δ_C 2.96, δ_X 1.26 [J_{AB} 5.5, J_{AC} 9, J_{AX} 7, J_{BC} 17 Hz, $CH_BH_CCH_AC(H_X)_3$].

(S)-(+)-3-p-*Methoxyphenyl*-1-[$^2H_5$]*phenylbutan*-1-*one* (36a).—A solution of (*R*)-(+)-*NN*-dimethyl-1-*p*-methoxyphenylethylamine (31a) (1.00 g) (100% e.e.) and [$^2H_5$]phenacyl bromide (1.20 g) in methanol (10 ml) was kept at room temperature for 4 h and then at 0 °C overnight. The solution was evaporated, the residual gum dissolved in water (20 ml), and the aqueous solution washed with ether, and concentrated to a volume of 15 ml. The resulting clear solution was cooled to 0 °C by the addition of ice (24 g) and treated with ice-cold aqueous sodium hydroxide (5 ml; 2M). The mixture was stirred for 30 min and stored overnight at 0 °C, allowed to warm to room temperature, and extracted with ether. The ether extract was extracted with 2% HCl and the acid extract washed with ether, made basic (Na_2CO_3), and extracted with ether. The ethereal extract was dried (Na_2SO_4), and evaporated and the residual semi-solid (1.38 g) dissolved in acetic acid (15 ml) and treated portionwise with zinc dust (1.0 g) during 20 min at 80—90 °C. The mixture was cooled, diluted with water (30 ml), and extracted with ether. The ether extract was washed (water and saturated aqueous $NaHCO_3$), dried (Na_2SO_4), and evaporated and the residual oil distilled (Kugelrohr) at 130—150 °C (0.01 Torr) to give (*S*)-(+)-3-*p*-methoxyphenyl-1-[$^2H_5$]phenylbutan-1-one (36a) (0.99 g, 68%) as a solid, $[\alpha]_D^{22}$ +18.7° (*c* 5.12 in CCl_4). Recrystallisation from light petroleum–di-isopropyl ether (4 : 1) at 0 °C gave colourless needles (0.30 g), m.p. 31—56°, $[\alpha]_D^{22}$ +15.96° (*c* 5.37 in CCl_4). The mother liquor was evaporated and the residue crystallised from methanol at 0 °C to give a second crop (0.29 g), m.p. 37—58 °C, $[\alpha]_D^{22}$ +20.34° (*c* 4.97 in CCl_4). Both samples had an isotopic composition 95 ± 0.2% [$^2H_5$] and 5 ± 0.2% [$^2H_4$] by mass spectrometric analysis.

Determination of the Absolute Rotation of (S)-(+)-3-p-*Methoxyphenyl*-1-*phenylbutan*-1-*one* (34a) *by the Isotope Dilution Method.*[36]—(a) A solution of (*S*)-(+)-3-*p*-methoxyphenyl-1-[$^2H_5$]phenylbutan-1-one (36a) (244.0 mg) {$[\alpha]_D^{22}$ +20.34° (*c* 4.97 in CCl_4)} and (*R,S*)-3-*p*-methoxyphenyl-1-phenylbutan-1-one (34) (119.4 mg) in carbon tetrachloride (5 ml) was evaporated and the residue crystallised from methanol (5 ml). The product was recrystallised from light petroleum–di-isopropyl ether (4 : 1) at 0 °C to give colourless prisms (46 mg), m.p. 64—66 °C, $[\alpha]_D^{22}$ 0.00° (*c* 3.0 in CCl_4) which consisted * of the [$^2H_0$] ketone (54.89%) and a mixture of the [$^2H_4$]- and [$^2H_5$]-ketones (45.11%).

(b) A similar experiment using the (*S*)-(+)-[$^2H_5$]ketone (36a) (264.0 mg) {$[\alpha]_D^{22}$ +15.96° (*c* 5.37 in CCl_4)} and the (*R,S*)-ketone (34) (131.2 mg) gave a product (102 mg), m.p. 64—66 °C $[\alpha]_D^{22}$ 0.00 (*c* 9.3 in CCl_4 which consisted * of the

* The isotopic composition was determined by mass spectral analysis on the averaged peak heights [$(M)^+$ *etc.* from 15 and 12 spectra] using equation (3).

$$\%\ [^2H_0]\ \text{species} = 100\ (M)^+/[(M)^+ + (M+5)^+ + (M+4)^+ - 0.19\ (M+4)^+] \quad (3)$$

The factor 0.19 in equation (3) is necessary to correct for the contribution made to the (M + 5) peak height by the natural abundance of isotopes associated with $C_{17}{}^1H_{14}{}^2H_4O_2$ (M + 4).

[$^2H_0$]-ketone (43.74%) and the [$^2H_4$]- and [$^2H_5$]-ketones (56.26%).

The above results were used to derive values of $[\alpha]_D^{22}$ +21.56° and $[\alpha]_D^{22}$ +21.72° for the pure (*S*)-(+)-ketone (34a) by using equation (2) giving the average value, $[\alpha]_D^{22}$ = +21.64°.

Conversion of (S)-(+)-3-p-*Methoxyphenyl*-1-*phenylbutan*-1-*one* (34a) *into* (R)-(−)-p-*Methoxyhydratropic Acid* (35a).—The (*S*)-(+)-ketone (34a) (3.90 g) {$[\alpha]_D^{22}$ +18.9° (*c* 5.09 in CCl_4); 87.3% e.e.} in ether (12 ml) was added during 20 min to a stirred solution of phenylmagnesium bromide [from bromobenzene (3.93 g) and magnesium (0.61 g) in ether (20 ml)]. The mixture was heated under reflux for 4 h, and hydrolysed by the addition of ice (1.5 g) and saturated aqueous NH_4Cl. The organic layer and ether extracts were washed with water, dried (Na_2SO_4), and evaporated. The residual oil (5.15 g) was dissolved in pyridine (40 ml) and treated with thionyl chloride (10 ml) at 0 °C. After 20 min at 0 °C the mixture was allowed to warm to room temperature and kept at 40 °C for 30 min, poured into ice-cold HCl and extracted with ether and benzene. The organic layers were combined, washed with water and saturated aqueous $NaHCO_3$, dried (Na_2SO_4), and evaporated. The residual solid was triturated with methanol (10 ml) and dried to give (*S*)-(+)-3-*p*-methoxyphenyl-1,1-diphenylbut-1-ene (3.81 g, 79%), m.p. 102—108 °C, $[\alpha]_D^{22}$ +106.6° (*c* 5.13 in C_6H_6); recrystallisation from methanol gave a sample, m.p. 108—110 °C (Found: C, 88.1; H, 7.3. $C_{23}H_{20}O$ requires C, 87.9; H, 7.05%), δ 7.38—7.01 (m, 12 aryl H), 6.78 (d, *J* 9 Hz, 2 aryl H), AMX_3 system, δ_A 6.14, δ_M 3.58, δ_X 1.31 [J_{AB} 10, J_{MX} 7 Hz, $CH_ACH_MC(H_X)_3$], and 3.71 (s, OMe). A solution of chromium trioxide (3.5 ml) [prepared by the addition of sulphuric acid (1.60 g) to chromium trioxide (1.00 g) in water (2 ml) and diluting the mixture with water to 3.5 ml] was added over 20 min to a vigorously stirred solution of the above (*S*)-but-1-ene derivative (0.63 g) in acetone (12 ml). The mixture was stirred for a further 15 min, isopropyl alcohol (2 ml) was added carefully, and the solution decanted. The precipitate was washed several times with ether and the combined acetone and ether solutions were washed with water, dried (Na_2SO_4), and evaporated. The residual oil (0.67 g) was dissolved in ether (10 ml) and the solution extracted with 3% aqueous Na_2CO_3. The extract was washed with ether, acidified (HCl), and extracted with ether. The ethereal extract was dried (Na_2SO_4) and evaporated and the residual oil distilled (Kugelrohr) at 100—110 °C (0.01 Torr) to give (*R*)-(−)-*p*-methoxyhydratropic acid (35a) (0.188 g, 52%) as a colourless solid (pure on the basis of t.l.c. and n.m.r.), m.p. 55—70 °C, $[\alpha]_D^{22}$ −55.9° (*c* 1.38 in ethanol). A sample was recrystallised from light petroleum to give colourless needles, m.p. 74—77 °C (lit.,[34d] 77—79 °C), $[\alpha]_D^{22}$ −61.5° (*c* 1.15 in ethanol) (87.3% e.e.) {lit [34d] $[\alpha]_D^{27}$ − 64.0° (*c* 1.06 in ethanol) and [34c] $[\varphi]_D$ 111.8° in ethanol for a sample with 70% enantiomeric excess}; $\nu_{max.}$ 1710 cm^{-1}; δ, AA′BB′ system, δ_A 7.21, δ_B 6.83 ($J_{A'B'}$, J_{AB} 8.5 Hz, C_6H_4), 3.75 (s, OMe), and AX_3 system, δ_A 3.65, δ_X 1.45 [J_{AX} 7.5 Hz, $CH_AC(H_X)_3$].

NN-*Dimethyl*-1-p-*nitrophenylethylamine* (41).—(a) Aqueous formaldehyde (61 g, 37—40%) was added to a solution of (*R,S*)-1-*p*-nitrophenylethylamine (40) (41.5 g) in formic acid (57.5 g) at 0 °C. The mixture was heated under reflux for 10 h, cooled, acidified (11M-HCl), washed with ether, and concentrated. The residue was made basic (30% aqueous KOH) and extracted with dichloromethane. The extract was dried and evaporated and the residual oil distilled to give (*R,S*)-*NN*-dimethyl-1-*p*-nitrophenylethylamine (41) (39.4 g, 81%) as a pale yellow liquid, b.p. 82—86 °C (0.01 Torr) (lit.,[54] b.p. 106—109 °C at 1 Torr); δ AA′BB′ system, δ_A 8.15, δ_B 7.49 (J_{AB}, $J_{A'B'}$ 9 Hz, C_6H_4), AX_3 system, δ_A 3.35, δ_X 1.35 [J_{AX} 6.5 Hz, $CH_AC(H_X)_3$], and 2.19 (s, NMe_2).

(b) (*R*)-(+)-1-*p*-Nitrophenylethylamine * (40a) (33.2 g) [α^{22} +20.7° (neat)] was converted by a similar method into (*R*)-(+)-*NN*-dimethyl-1-*p*-nitrophenylethylamine (41a) (33.1 g, 85%), b.p. 82—86 °C (0.01 Torr); α_D^{22} +61.1° (neat) (lit.,[46] $[\alpha]_D$ +55.30°).

(R,S)-*NN-Dimethyl*-N-*phenacyl*-1-p-*nitrophenylethylammonium Bromide* (42).—A solution of (*R,S*)-*NN*-dimethyl-1-*p*-nitrophenylethylamine (41) (1.94 g) and phenacyl bromide (2.10 g) in acetone (10 ml)) was kept at room temperature for 2 days. The precipitated solid was collected and recrystallised from ethanol to give the (*R,S*)-salt (42) (1.59 g, 40%), m.p. 168—169 °C. The salt could also be obtained (20—25% yield) using ethanol as solvent but an attempted preparation in acetonitrile was not successful (Found: C, 54.7; H, 5.5; Br, 20.4; N, 7.3. $C_{18}H_{21}BrN_2O_3$ requires C, 55.0; H, 5.4; Br, 20.3; N, 7.1%), $\nu_{max.}$ (KBr) 1685 cm^{-1}; δ (CD_3OD) 8.37—7.43 (m, 9 aryl H); AX_3 system, δ_A 5.65, δ_X 1.92 [J_{AX} 7 Hz, $CH_AC(H_X)_3$], AB system, δ_A 5.39, δ_B 5.09 (*J* 18 Hz, $\overset{+}{N}CH_AH_BCO$), 3.44 (s, $\overset{+}{N}Me$), and 3.35 (s, $\overset{+}{N}Me$). Attempts to prepare the (*R*)-salt (42a) by a similar method failed to yield crystalline material.

Base Catalysed Rearrangement of (R,S)-NN-*Dimethyl*-N-*phenacyl*-1-p-*nitrophenylethylammonium Bromide* (42)*: Formation of* meso- *and* (±)-2,3-*Di*-p-*nitrophenylbutane*.—A suspension of the powdered salt (42) (2.95 g) in ice–water (190 ml) was treated with ice-cold aqueous sodium hydroxide (10 ml; 1 5M) (N_2 atmosphere). The mixture was stirred for 90 min at 0 °C and the products extracted into ethyl acetate. The extract was dried and evaporated and the semi-solid residue (2.25 g, 96%) triturated with hot methanol and kept at 0 °C overnight to give a pale yellow solid (0.74 g) and a methanol soluble oil (1.51 g). Both fractions were examined by n.m.r. to determine their composition (Table 5). The solid fraction was triturated again with hot methanol (6 ml) and the insoluble material recrystallised from benzene to give *meso*-2,3-di-*p*-nitrophenylbutane, m.p. 258—259 °C (lit.,[55] m.p. 256 °C); δ, AA′BB′ system, δ_A 8.17, δ_B 7.33 (J_{AB}, $J_{A'B'}$ 8.5 Hz, 2 × C_6H_4), 3.09—2.93 (m, CHCH) and 1.07 (d, *J* 6.5 Hz, 2 × $CHCH_3$). The methanol mother liquor was evaporated and the residue extracted with hot ether (25 ml). The ethereal extract was evaporated and the residue recrystallised from ethanol to give (±)-2,3-di-*p*-nitrophenylbutane, m.p. 129—131 °C (lit.,[55] m.p. 133 °C).

(R)-(+)-N-p-*Methoxyphenacyl*-NN-*dimethyl*-1-p-*nitrophenylethylammonium Bromide* (43a).—A solution of (*R*)-(+)-*NN*-dimethyl-1-*p*-nitrophenylethylamine (41) α_D^{22} +61.1°) (7.00 g) (100% e.e.) and *p*-methoxyphenacyl bromide (9.00 g) in methanol (100 ml) was kept at room temperature for 2 days. The solvent was evaporated and the residual solid triturated with acetone (150 ml), collected, and recrystallised from ethanol to give the (*R*)-(+)-salt (43a) (5.31 g, 35%), m.p. 152—154 °C (Found: C, 54.2; H, 5.3; Br, 18.9; N, 6.5. $C_{19}H_{23}BrN_2O_4$ requires C, 53.9; H, 5.5; Br, 18.9; N, 6.6), $[\alpha]_D^{22}$ +83.7° (*c* 1.63 in methanol); $\nu_{max.}$ 1685 cm^{-1}; δ (CF_3CO_2H) AA′BB′ system, δ_A 8.37, δ_B 7.90 (J_{AB}, $J_{A'B'}$ 9 Hz, 4 aryl H), AA′BB′ system, δ_A 8.02, δ_B 7.06 (J_{AB}, $J_{A'B'}$ 9 Hz, 4 aryl H), AX_3 system, δ_A 5.86, δ_X 2.04 [J_{AX} 7 Hz, $CH_AC(H_X)_3$], AB system, δ_A

* Prepared by hydrolysis (HCl) of (*R*)-(+)-*N*-1-*p*-nitrophenylethylacetamide (39a) {$[\alpha]_D^{22}$ +146.4° (*c* 2.974 in ethanol)} {lit.,[37] $[\alpha]_D^{21}$ +146.9° (in ethanol)}.

5.28, δ_B 4.94 (J_{AB} 18 Hz, $CH_AH_B\overset{+}{N}$), 3.97 (s, OMe), 3.61 (s, $\overset{+}{N}$Me), and 3.50 (s, $\overset{+}{N}$Me).

Base Catalysed Rearrangement of (R)-(+)-N-p-*Methoxyphenacyl*-NN-*dimethyl*-1-p-*nitrophenylethylammonium Bromide* (43a)*: Formation of* (−)-2-*Dimethylamino*-1-p-*methoxyphenyl*-3-p-*nitrophenylbutan*-1-*one* (*Diastereoisomers* A *and* B) (45), 1,2-*Bis*(*dimethylamino*)-1,2-*di*-p-*methoxybenzoylethane* (46), *and* 2,3-*Di*-p-*nitrophenylbutane* [(±)- *and* meso-*Diastereoisomers*].—(i) *Isolation of rearrangement product* (45). Cold (0 °C), methanolic potassium hydroxide (5ml; 1.4M) was added to a stirred, ice-cooled, suspension of the powdered (*R*)-(+)-salt (43a) (2.12 g) in methanol (20 ml). The mixture was stirred for 1 h at 0 °C, saturated with hydrogen chloride gas, evaporated, and the solid residue extracted with boiling acetone (30 ml). The acetone extract was evaporated and the residue extracted with water. The aqueous solution was washed with ethyl acetate, made basic (Na_2CO_3), and extracted with ether. The ether extract was dried (Na_2SO_4) and evaporated and the residual oil separated by t.l.c. (isopropyl ether–ethanol, 2 : 1) to give two fractions. The first fraction yielded (−)-2-dimethylamino-1-*p*-methoxyphenyl-3-*p*-nitrophenylbutan-1-one (45; diastereoisomer *A*) (171 mg, 10%), as a pale yellow gum, $[\alpha]_D^{22}$ −73.7° (*c* 8.55 in chloroform) which crystallised from isopropyl ether at 0 °C as yellow prisms, m.p. 95—97 °C (Found: C, 66.8; H, 6.7; N, 7.9. $C_{19}H_{22}N_2O_4$ requires C, 66.65; H, 6.48; N, 8.2%), $\nu_{max.}$ 1 662 cm^{-1}; δ, AA′BB′ system, δ_A 8.13, δ_B 7.45 (J_{AB}, $J_{A'B'}$ 8.5 Hz, 4 aryl H), AA′BB′ system, δ_A 8.01, δ_B 6.96 (J_{AB}, $J_{A'B'}$ 8.5 Hz, 4 aryl H), ABX_3 system δ_A 4.44, δ_B 3.53, δ_X 1.12 [J_{AB} 10.5, J_{BX} 7 Hz, $CH_ACH_BC(H_X)_3$], 3.88 (s, OMe), and 2.17 (s, NMe_2). The second fraction gave (−)-2-dimethylamino-1-*p*-methoxyphenyl-3-*p*-nitrophenylbutan-1-one (45; diastereoisomer *B*) (78 mg, 5%) as a pale yellow gum, $[\alpha]_D^{22}$ −62.0° (*c* 7.8 in chloroform); $\nu_{max.}$ 1 662 cm^{-1}; δ, AA′BB′ system, δ_A 7.97, δ_B 7.35 (J_{AB}, $J_{A'B'}$ 8.5 Hz, 4 aryl H), AA′BB′ system, δ_A 7.66, δ_B 6.88 (J_{AB}, $J_{A'B'}$ 8.5 Hz, 4 aryl H), ABX_3 system, δ_A 4.32, δ_B 3.51, δ_X 1.42 [J_{AB} 10.5, J_{BX} 7 Hz, $CH_ACH_BC(H_X)_3$], 3.77 (s, OMe), and 2.40 (s, NMe_2).

(ii) *Quantitative determination of product composition.* The rearrangement of the (*R*)-(+)-salt (43a) (1.06 g) was carried out (a) in water (20 ml) at 0 °C using aqueous sodium hydroxide (5 ml; 0.8M) as the base and (b) in methanol (10 ml) at 0 °C using methanolic potassium hydroxide (4 ml; 1.0M) as the base. After 60 min at 0 °C ethyl acetate was added and the organic layer dried and evaporated to give the reaction products as a yellow gum [0.79 g, 92% from method (a) and 0.83 g, 97% from method (b)].

The residue from both experiments was analysed by comparing its n.m.r. spectrum with those of authentic samples of the diastereoisomeric diamines (46), and the 2,3-di-*p*-nitrophenylbutanes and with the n.m.r. spectrum of the diamines (6), analogous to the diamines (46). The diamines (46) could not be obtained sufficiently pure from the product mixture for full characterisation, but n.m.r. spectroscopic assignments could be made as follows: diastereoisomer *A*, δ, AA′BB′ system, δ_A 7.95, δ_B 6.90 (J_{AB}, $J_{A'B'}$ 8.5 Hz, 2 × 4 aryl H), 4.91 (s, CHCH), 3.87 (s, 2 × OMe), and 2.26 (s, 2 × NMe_2); diastereoisomer *B*, δ, AA′BB′ system, δ_A 8.02, δ_B 6.93 (J_{AB}, $J_{A'B'}$ 8.5 Hz, 2 × 4 aryl H), 4.91 (s, CHCH), 3.84 (s, 2 × OMe), and 2.46 (s, 2 × NMe_2). The results of this analysis are recorded in Table 5.

References

1 Part 14, S. Mageswaran, W. D. Ollis, R. Somanathan, and I. O. Sutherland, *J. Chem. Soc., Perkin Trans. 1*, 1982, 893.

2 T. S. Stevens, *Prog. Org. Chem.*, 1968, **7**, 48; S. H. Pine, *Org. React.*, 1970, **18**, 403; A. R. Lepley and A. G. Giumanini in ' Mechanisms of Molecular Migration,' ed. B. S. Thyagarajan, Interscience, New York, 1971, vol. 3, p. 297; T. S. Stevens and W. E. Watts, ' Selected Molecular Rearrangements,' van Nostrand-Reinhold, London, 1973, p. 81.

3 (*a*) T. S. Stevens, E. M. Creighton, A. B. Gordon, and K. MacNicol, *J. Chem. Soc.*, 1928, 3193; (*b*) T. S. Stevens, *J. Chem. Soc.*, 1930, 2107.

4 For examples of [1,2] rearrangements with the X, Y, and Z centres cited see: C, C^-, C; E. Grovenstein and G. Wentworth, *J. Am. Chem. Soc.*, 1963, **85**, 3305; H. E. Zimmerman and A. Zweig, *J. Am. Chem. Soc.*, 1961, **83**, 1196. $\overset{+}{N}$, C^-, O; S, C^-, O; G. A. Russell and G. J. Mikol in ' Mechanisms of Molecular Migration,' ed. B. S. Thyagarajan, Interscience, New York, 1968, vol. 1, p. 157. N, C^-, C; W. F. Cockburn, R. A. W. Johnstone, and T. S. Stevens, *J. Chem. Soc.*, 1960, 3340, 3346. N, C^-, Si; A. G. Brook and J. M. Duff, *J. Am. Chem. Soc.*, 1974, **96**, 4692. O^+, C^-, Si; S^+, C^-, Si; W. Ando, *J. Am. Chem. Soc.*, 1974, **96**, 1601. O, C^-, C; U. Schöllkopf, *Angew. Chem., Int. Ed. Engl.*, 1970, **9**, 763. O, C^-, Si; R. West, R. Lowe, H. F. Steward, and A. Wright, *J. Am. Chem. Soc.*, 1971, **93**, 282. S^+, C^-, C; G. M. Blackburn, W. D. Ollis, J. D. Plackett, C. Smith, and I. O. Sutherland, *Chem. Commun.*, 1968, 186; J. E. Baldwin, R. E. Hackler, and D. P. Kelly, *Chem. Commun.*, 1968, 537, 538, S^+, C^-, N; E. Vilsmaier, K. H. Dittrich, and W. Sprugel, *Tetrahedron Lett.*, 1974, 3601. S, C^-, C; T. J. Wallace, H. Pobiner, J. E. Hofmann, and A. Schrieshem, *Proc. Chem. Soc.*, 1963, 137. As^+, C^-, C; Sb^+, C^-, C; G. Wittig and H. Laib, *Liebigs Ann. Chem.*, 1953, **580**, 57. O, N^-, Si; R. West and P. Boudjouk, *J. Am. Chem. Soc.*, 1973, **95**, 3987. N, N^-, C; R. West, H. F. Stewart, and G. R. Husk, *J. Am. Chem. Soc.*, 1967, **89**, 5050. S^+, N^-, C; T. S Stevens and J. L. Dunn, *J. Chem. Soc.*, 1952, 2796. C, O^-, Si; R. West, *Pure Appl. Chem.*, 1969, **19**, 291. N^+, O^-, C; R. A. W. Johnstone in ' Mechanisms of Molecular Migrations,' ed. B. S. Thyagarajan, Interscience, New York, 1969, vol. 2, p. 249. S^+, O^-, C; D. R. Rayner, E. G. Miller, P. Bickart, A. J. Gordon, and K. Mislow, *J. Am. Chem. Soc.*, 1966, **88**, 3138, 3139; P. Bickart, F. W. Carson, J. Jacobus, E. G. Miller, and K. Mislow, *J. Am. Chem. Soc.*, 1968, **90**, 4869. O, S, C; E. G. Miller, D. R. Rayner, H. T. Thomas, and K. Mislow, *J. Am. Chem. Soc.*, 1968, **90**, 4861. O, P, C; V. Mark in ' Mechanisms of Molecular Migration,' ed. B. S. Thyagarajan, Interscience, New York, 1969, vol. 2, p. 319.

5 T. Thomson and T. S. Stevens, *J. Chem. Soc.*, 1932, 55.

6 R. W. Jemison, S. Mageswaran, W. D. Ollis, S. E. Potter, A. J. Pretty, I. O. Sutherland, and Y. Thebtaranonth, *Chem. Commun.*, 1970, 1201; R. W. Jemison, S. Mageswaran, W. D. Ollis, I. O. Sutherland, and Y. Thebtaranonth, *J. Chem. Soc., Perkin Trans. 1*, 1981, 1154.

7 R. A. W. Johnstone and T. S. Stevens, *J. Chem. Soc.*, 1955, 4487; E. Grovenstein, jun., and G. Wentworth, *J. Am. Chem. Soc.*, 1967, **89**, 1852.

8 A. Campbell, A. H. J. Houston, and J. Kenyon, *J. Chem. Soc.*, 1947, 93; J. H. Brewster and M. W. Kline, *J. Am. Chem. Soc.*, 1952, **74**, 5179.

9 U. Schöllkopf, U. Ludwig, G. Ostermann, and M. Patsch, *Tetrahedron Lett.*, 1969, 3415.

10 B. J. Millard and T. S. Stevens, *J. Chem. Soc.*, 1963, 3397.

11 R. K. Hill and T. H. Chan, *J. Am. Chem. Soc.*, 1966, **88**, 866; G. Wittig and H. Zimmermann, *Chem. Ber.*, 1953, **86**, 629; H. Joshua, R. Gans, and K. Mislow, *J. Am. Chem. Soc.*, 1968, **90**, 4884; J. H. Brewster and R. S. Jones, jun., *J. Org. Chem.*, 1969, **34**, 354.

12 R. B. Woodward and R. Hoffmann, *Angew. Chem., Int. Ed. Engl.*, 1969, **8**, 781.

13 U. Schöllkopf and U. Ludwig, *Chem. Ber.*, 1968, **101**, 2224.

14 (*a*) A. R. Lepley, *J. Am. Chem. Soc.*, 1969, **91**, 1237; (*b*) J. E. Baldwin, W. F. Erickson, R. E. Hackler, and R. M. Scott, *Chem. Commun.*, 1970, 576.

15 E. F. Jenny and J. Druey, *Angew. Chem., Int. Ed. Engl.*, 1962, **1**, 155.

16 E. F. Jenny and K. Schenker, *Angew. Chem., Int. Ed. Engl.*, 1965, **4**, 441; E. F. Jenny and A. Melzer, *Tetrahedron Lett.*,

1966, 3507; S. H. Pine, B. A. Catto, and F. G. Yamagishi, *J. Org. Chem.*, 1970, **35**, 3663.
17 M. J. S. Dewar and C. A. Ramsden, *J. Chem. Soc., Perkin Trans. 1*, 1974, 1839.
18 (*a*) R. W. Jemison, T. Laird, W. D. Ollis, and I. O. Sutherland, *J. Chem. Soc., Perkin Trans. 1*, 1980, 1436; (*b*) R. W. Jemison, T. Laird, W. D. Ollis, and I. O. Sutherland, *J. Chem. Soc., Perkin Trans. 1*, 1980, 1450; (*c*) S. Mageswaran, W. D. Ollis, and I. O. Sutherland, *J. Chem. Soc., Perkin Trans. 1*, 1981, 1953; (*d*) W. D. Ollis, I. O. Sutherland, and Y. Thebtaranonth, *J. Chem. Soc., Perkin Trans. 1*, 1981, 1963; (*e*) W. D. Ollis, I. O. Sutherland, and Y. Thebtaranonth, *J. Chem. Soc., Perkin Trans. 1*, 1981, 1981; (*f*) W. D. Ollis, R. Somanathan, and I. O. Sutherland, *J. Chem. Soc., Perkin Trans. 1*, 1981, 2930; *J. Chem. Soc., Chem. Commun.*, 1981, 573.
19 Preliminary communication: W. D. Ollis, M. Rey, I. O. Sutherland, and G. L. Closs, *J. Chem. Soc., Chem. Commun.*, 1975, 543.
20 D. Bethell and M. R. Brinkman, *Adv. Phys. Org. Chem.*, 1973, **10**, 53.
21 S. H. Pine, *J. Chem. Educ.*, 1971, **49**, 99; U. H. Dolling, G. L. Closs, A. H. Cohen, and W. D. Ollis, *J. Chem. Soc., Chem. Commun.*, 1975, 545.
22 K. Chantrapromma, W. D. Ollis, and I. O. Sutherland, *J. Chem. Soc., Chem. Commun.*, 1977, 97; 1978, 673; M. Rey, W. D. Ollis, and I. O. Sutherland, *J. Chem. Soc., Chem. Commun.*, 1978, 675.
23 (*a*) K. Chantrapromma, W. D. Ollis, and I. O. Sutherland, *J. Chem. Soc., Chem. Commun.*, 1978, 670 and 672; (*b*) S. H. Pine and J. Cheney, *J. Org. Chem.*, 1975, **40**, 870; (*c*) W. D. Ollis and M. Rey, forthcoming publication.
24 W. von E. Doering and R. S. Urban, *J. Am. Chem. Soc.*, 1956, **78**, 5938; W. D. Ollis, R. Somanathan, and I. O. Sutherland, *J. Chem. Soc., Chem. Commun.*, 1974, 494.
25 ' Free Radicals,' ed. J. K. Kochi, Interscience, New York, 1973, Vol. 1.
26 G. L. Closs, *J. Am. Chem. Soc.*, 1969, **91**, 4552; G. L. Closs and L. E. Closs, *J. Am. Chem. Soc.*, 1969, **91**, 4549, 4550; G. L. Closs and A. D. Trifunac, *J. Am. Chem. Soc.*, 1969, **91**, 4554; 1970, **92**, 2183; R. Kaptein and L. J. Oosterhof, *Chem. Phys. Lett.*, 1969, **4**, 195, 214; R. Kaptein, *Chem. Commun.*, 1971, 732; G. L. Closs, *J. Am. Chem. Soc.*, 1971, **93**, 1546; R. G. Lawler, *Acc. Chem. Res.*, 1972, **5**, 25; H. R. Ward, *Acc. Chem. Res.*, 1972, **5**, 18.
27 C. R. Hauser and S. W. Kantor, *J. Am. Chem. Soc.*, 1951, **73**, 1437.
28 B. Holmberg, *Chem. Ber.*, 1912, **45**, 999.
29 D. J. Cram, *J. Am. Chem. Soc.*, 1952, **74**, 2138.
30 Landolt-Börnstein, Springer, Berlin, 1969, 6th Edn., vol. 2, Part 5, p. 92.
31 F. D. Greene, M. A. Berwick, and J. C. Stowell, *J. Am. Chem. Soc.*, 1970, **92**, 867; K. R. Kopecky and T. Gillan, *Can. J. Chem.*, 1969, **47**, 2371; T. Koenig and J. M. Owens, *J. Am. Chem. Soc.*, 1973, **95**, 8486; 1974, **96**, 4052.
32 R. A. Johnson and S. Seltzer, *J. Am. Chem. Soc.*, 1973, **95**, 938.
33 (*a*) R. A. Moss and W. L. Sunshine, *J. Org. Chem.*, 1974, **39**, 1083; (*b*) J. H. Brewster and S. F. Osman, *J. Am. Chem. Soc.*, 1960, **82**, 5754; (*c*) W. H. Pirkle, T. G. Burlinghame, and S. D. Beare, *Tetrahedron Lett.*, 1968, 5849; (*d*) G. Gottarelli and B. Samori, *J. Chem. Soc. B*, 1971, 2418.
34 (*a*) W. D. Ollis, M. V. J. Ramsay, and I. O. Sutherland, *Aust. J. Chem.*, 1965, **18**, 1787; (*b*) J. W. Clark-Lewis and R. W. Jemison, *ibid.*, 1965, **18**, 1791; (*c*) A. J. deGee, J. W. Verhoeven, I. P. Dirkx, and T. J. deBoer, *Tetrahedron*, 1969, **25**, 3407; (*d*) D. J. Collins and J. J. Hobbs, *Aust. J. Chem.*, 1970, **23**, 119.
35 (*a*) J. A. Berson and D. A. Ben-Efraim, *J. Am. Chem. Soc.*, 1959, **81**, 4083; (*b*) H. Gerlach, *Helv. Chim. Acta*, 1966, **49**, 2481.
36 M. Raban and K. Mislow, *Top. Stereochem.*, 1967, **2**, 199.
37 F. Nerdel, H. Goetz, and M. Fenske, *Annalen*, 1963, **665**, 21.
38 K. W. Ratts and A. N. Yao, *J. Org. Chem.*, 1966, **31**, 1185; 1968, **33**, 70.
39 J. A. Berson, ' Rearrangements in Ground and Excited States,' ed. P. de Mayo, Academic Press, New York, 1980, **1**, 311.
40 J. J. Gajewski, *Acc. Chem. Res.*, 1980, **13**, 142.
41 J. J. Gajewski, *Isr. J. Chem.*, 1981, **21**, 169.
42 J. J. Gajewski and J. Salazar, *J. Am. Chem. Soc.*, 1981, **103**, 4145.
43 J. A. Berson, *Acc. Chem. Res.*, 1972, **5**, 406.
44 F.-G. Klarner and B. J. Brassel, *J. Am. Chem. Soc.*, 1980, **102**, 2469; R. F. Childs, *Tetrahedron*, 1982, **38**, 567.
45 W. T. Borden, J. G. Lee, and S. D. Young, *J. Am. Chem. Soc.*, 1980, **102**, 4841.
46 R. E. Lutz, T. Amacker, S. M. King, and N. H. Shearer, *J. Org. Chem.*, 1951, **15**, 151.
47 R. N. Icke, B. B. Wisegarver, and G. A. Alles, *Org. Synth.*, 1945, **25**, 89.
48 J. C. Craig, R. P. K. Chan, and S. K. Roy, *Tetrahedron*, 1967, **23**, 3573.
49 A. C. Cope, E. Ciganek, L. J. Fleckenstein, and A. P. Meisinger, *J. Am. Chem. Soc.*, 1960, **82**, 4651.
50 N. D. Berova and B. J. Kurtev, *Tetrahedron*, 1969, **25**, 2301.
51 P. Bonn and G. Weill, *J. Chim. Phys.*, 1967, **64**, 253; P. Singh, *J. Chem. Soc. C*, 1971, 714.
52 H. Rupe, *Annalen*, 1909, **369**, 311.
53 P. Weyerstahl, R. Zielke, and F. Nerdel, *Annalen*, 1970, **731**, 18.
54 V. M. Potapov, V. M. Demyanovich, and A. P. Terentev, *J. Gen. Chem., USSR*, 1965, **35**, 1541.
55 G. F. Wright, *J. Am. Chem. Soc.*, 1939, **61**, 2106; H. H. Richmond, E. J. Underhill, A. G. Brook, and G. F. Wright, *J. Am. Chem. Soc.*, 1947, **69**, 937.

Received 11*th June* 1982; *Paper* 2/982