The Mechanism of the Stevens Rearrangement

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Summary The influence of solvent viscosity and reaction temperature upon the stereoselectivity and intramolecularity of the Stevens [1,2] rearrangement of the ylide (**1**) has been examined; the results are compatible with two possible mechanisms: (i) a radical pair mechanism with an average geminate recombination rate which is exceptionally fast, or (ii) dual pathways involving concurrent radical pair and concerted processes.

THE radical pair mechanism (Scheme, pathway b) for the Stevens [1,2] rearrangement[1] and related [1,2] anionic rearrangements has been widely accepted.[1-5] This opinion has been based upon (a) qualitative CIDNP results[2-4] and (b) the isolation of compounds[3,5] regarded as escape products formed from radical pair intermediates. These results, however, do not establish that these rearrangements proceed solely by radical pair pathways.[6] Furthermore, radical pair mechanisms are not easily compatible with the observed high stereoselectivity (80—90% retention of configuration at the terminus of the migrating group†) for the thermal rearrangement (**1** → **2**) of the chiral ylide (**1**).[4,7-9] We have now re-investigated the stereoselectivity

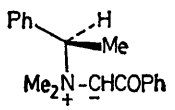
† The reported stereoselectivities[7] are based upon incorrect values for the specific rotations of the degradation products (**4**) and (**5**). The figures given above are corrected for these errors.

TABLE

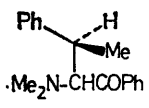
Solvent–base	Temp./°C ±2°C	Solvent viscosity (cp)	Stereoselectivity[a] % (±2%)	Intermolecularity[b] %	Intramolecular stereoselectivity[c] %	k_c^d/k_{r+t}	k_c^d/k_d
Glycerol–NaOH	50	142	91	2·5	93	26·5	19·5
Cyclohexanol–NaOH ..	50	13	77	5·5	82	9·1	8·6
Bu^{t}OH–NaOH	50	1·4	67	10·5	75	6·0	4·3
MeOH–NaOMe	0	0·8	71	6·9	76	6·3	6·7
MeOH–NaOMe	40	0·5	59	16·7	71	4·9	2·5
MeOH–NaOMe	60	0·3	—	22·9	—	—	1·4
H_2O–NaOH	0	1·8	99	0·1	99	198	>100
H_2O–NaOH	50	0·6	79	4·3	83	9·7	11·5

[a] Stereoselectivity = $[(x - y)/(x + y)] \times 100\%$ where in the reaction (1) → (2) the reaction (1) → *R*-(2) proceeds $x\%$ with retention and the reaction (1) → *S*-(2) proceeds $y\%$ with inversion. [b] Intramolecularity = $4z\%$ and intermolecularity = $100 - 4z\%$ where an equimolecular mixture of racemic (3) and (8) gives the following relative proportions of non-deuteriated and deuteriated products (2): [$^2H_0$]-(2), $50 - z\%$; [$^2H_5$]-(2), $2z\%$; [$^2H_{10}$]-(2), $50 - z\%$. [c] Intramolecular stereoselectivity = (stereoselectivity)/(intramolecularity) × 100%. [d] The rate constants, k_c, k_d, and k_{r+t}, are defined in the Scheme. k_c/k_d = Intramolecularity/2 × Intermolecularity; k_c/k_{r+t} = 2 × Intramolecular stereoselectivity/(100 − Intramolecular stereoselectivity).

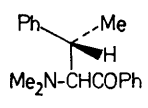
and intramolecularity of the base-catalysed rearrangement of the salt (3) using a variety of solvents and reaction temperatures (Table). The stereoselectivity of the reaction has been determined using transformations based upon the correlation[7] of the chiral amine *R*-(2) with the known chiral ketone (4)[4] and the known chiral acid (5):[5,10] the chiral acid (5) is formed by the Baeyer–Villiger oxidation of the chiral ketone (4) followed by hydrolysis.



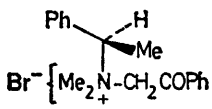
(1)



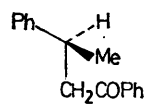
R-(2)



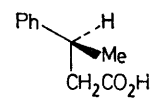
S-(2)



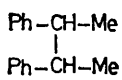
(3)



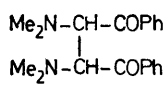
(4)



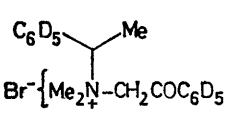
(5)



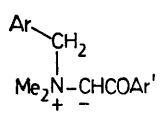
(6)



(7)

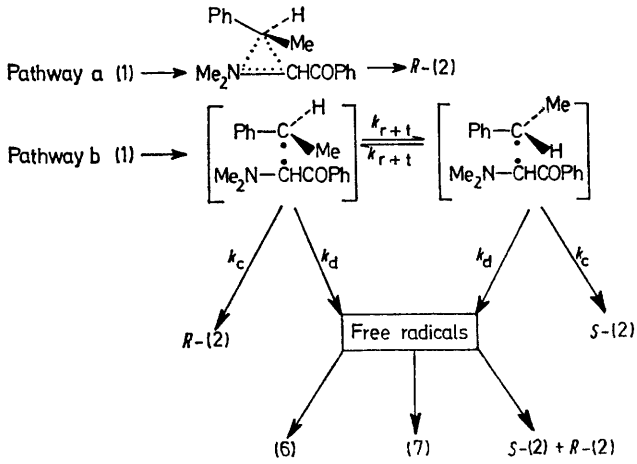


(8)



(9)

Two extreme results require particular discussion. The *R*-ammonium salt (3) with H_2O–NaOH (0°) gave the rearrangement product (2) [89% isolated yield of two diastereomers (4:3 ratio)] which was degraded *via* the ketone (4) to the acid (5) whose specific rotation[10] showed that in H_2O–NaOH (0°) the rearrangement (1 → 2) proceeds with 99 ± 1% net retention of configuration [*R*-(2)] and 1 ± 1% racemisation [*R*-(2) + *S*-(2)] at the chiral centre of the migrating α-phenylethyl group. In contrast, in MeOH–NaOMe (55°) (*cf.* ref. 9 for discussion of CIDNP effects observed under these conditions), the *R*-ammonium salt (3) rearranges with 56 ± 2% net retention [*R*-(2)] and 44 ± 2% racemisation [*R*-(2) + *S*-(2)]. Furthermore, additional products from (3) with MeOH–NaOMe (55°) include the optically inactive 2,3-diphenylbutanes (6) [6% yield of two diastereomers (1:1 ratio)] and the amines (7) [6% yield of two diastereomers (3:1 ratio)]. These escape products (6) and (7) were not detected in the [1,2] rearrangement of the salt (3) using H_2O–NaOH (0°).



SCHEME. Concerted and radical pair pat ways for the thermal transformations of the ylide (1).

Thus, a correlation between the stereoselectivity of the Stevens rearrangement (1 → 2), the observation of CIDNP effects,[11] the formation of escape products (6) and (7), and reaction conditions (Table) was beginning to emerge. The need to determine the extent to which stereoselectivity was associated with intramolecular recombination was met by determining the intermolecularity of the rearrangement (1 → 2). Mass spectral examination of the reaction product from an equimolecular mixture of the racemic salt (*cf.* 3) and its racemic decadeuterio-derivative (8) gave

quantitative information (see Table, footnote b) on the percentage intermolecularity and intramolecularity for the rearrangement (**1** → **2**). The Table summarises the influence of reaction temperature and solvent viscosity upon overall stereoselectivity (footnote a), intermolecularity (footnote b), and intramolecular stereoselectivity (footnote c). If it is assumed that the rearrangement (**1** → **2**) is a radical pair process then the ratios of the rate constants (k_c/k_{r+t}) and k_c/k_d) may be evaluated (footnote d) assuming that racemisation is an obligatory consequence of diffusion followed by intermolecular radical recombination.

The data summarised in the Table lead to the following conclusions. The stereoselectivity of the Stevens rearrangement [(**1**) → *R*-(**2**) + *S*-(**2**)] shows a strong dependence upon solvent viscosity (low viscosity—decrease in stereoselectivity), small temperature effects, but no direct relation with solvent polarity. The intramolecularity of the Stevens rearrangement [(**1**) → *R*-(**2**) + *S*-(**2**)] showed strong dependence upon solvent viscosity (low viscosity—decrease in intramolecularity) and large temperature effects (decrease in intramolecularity at higher temperatures). These trends are highly suggestive of a reaction pathway involving radical pair intermediates[12] (Scheme, pathway b), but the ratios (k_c/k_{r+t}) and (k_c/k_d) are unusually large (*cf.* ref. 12). Thus, if we assume that k_{r+t} is *ca.* 10^{11} s^{-1} based upon correlation rates for molecules of a similar size and shape as the components of the radical pair, then k_c is *ca.* 10^{12} s^{-1} This very high rate for radical pair recombination may be a consequence of the proximity of the components of the initially formed radical pair.

Although it is not possible to exclude some contribution from a competing concerted process (Scheme, pathway a) to the observed intramolecularity and stereoselectivity of the rearrangement (**1** → **2**), this would still require unusually high values of k_c/k_d and k_c/k_{r+t} for the radical pair component (Scheme, pathway b) of the reaction mechanism. Either view of the reaction mechanism would be compatible with the quantitative study[11] of the CIDNP effects observed during the rearrangement of the ylides (**9**).

The Stevens [1,2] rearrangement obviously can proceed with a high degree of stereoselectivity and intramolecularity, although a radical pair pathway is at least an important or even exclusive‡ contributor to the reaction mechanism. Such stereoselective and intramolecular recombination of radicals has been observed[13] for other 'forbidden' sigmatropic rearrangements, and may apply generally to reactions of this type which proceed at relatively low temperatures. These views are related to current opinions about reactions involving radical pair intermediates,[12] symmetry-forbidden transformations,[14] and pericyclic reaction mechanisms.[15]

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‡ Our unpublished results[13] require an exclusive radical pair pathway for some examples of anionic [1,2] sigmatropic rearrangements.

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