Solvent Effects on Stereochemistry of Eliminations from Quaternary Ammonium Salts

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ELIMINATION reactions of open-chain[1] and cyclic[2-5] quaternary ammonium salts have recently been shown to involve *syn*-loss of trimethylamine and hydrogen much more frequently than was formerly supposed. We report results bearing on the conditions under which *syn*-eliminations can be expected to occur.

erythro- and *threo*-1-Ethyl[2-^{2}H]butylamine were prepared by deuterioboration of *cis*- and *trans*-hex-3-ene, respectively, followed by treatment with hydroxylamine-*O*-sulphonic acid.[6] The amines were then converted to the corresponding *erythro*- and *threo*-1-ethyl[2-^{2}H]butyltrimethylammonium iodides by standard procedures.[7,8] These compounds and undeuteriated 1-ethylbutyltrimethylammonium iodide were subjected to elimination reactions in five different alcohol–alkoxide solutions. The product percentages are recorded in Table 1.

The k_H/k_D values in Table 1 are calculated from product percentages.[1,2] One can anticipate three extreme possibilities: (1) all *anti*-elimination, (2) all *syn*-elimination, and (3) *syn-anti*-elimination (*trans*-olefin *via syn*-elimination and *cis*-olefin *via anti*-elimination).[1] The consequences of these possibilities are outlined in Scheme 1. Since those reactions occurring with deuterium loss would be expected to show substantial isotope effects while those occurring with hydrogen loss should at most show small secondary isotope effects, the k_H/k_D values in Table 1 should distinguish among the possibilities.

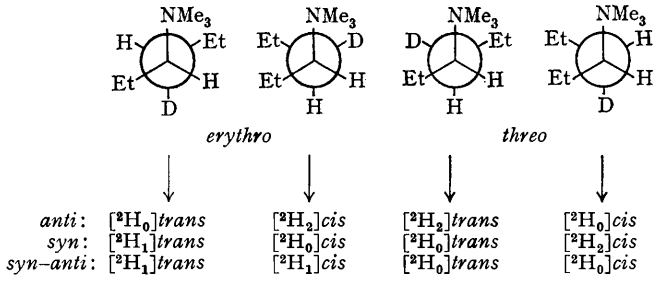
The results in methanol–methoxide and n-butanol–butoxide clearly fit best a predominant or exclusive *anti*-mechanism, while the results in t-butyl alcohol-t-butoxide and t-pentyl alcohol–t-pentoxide equally clearly suggest a *syn–anti* mechanism as the major path. The results in butan-2-ol–s-butoxide appear intermediate. Isotopic analyses of the products in n-butanol-n-butoxide and t-pentyl alcohol–t-pentoxide were performed and are given in Table 2. The deuterium contents of the olefin mixtures are in qualitative agreement with the conclusions from k_H/k_D

TABLE 1

Olefin proportions and k_H/k_D *values in eliminations from* erythro- *and* threo-1-*ethyl*[2-^{2}H]*butyltrimethylammonium and* 1-*ethylbutyltrimethylammonium iodides*

Reaction Conditions	Reactant	Hexene[a,b] *trans*-2 (%)	*cis*-2 (%)	*trans*-3 (%)	k_H/k_D[c]	*cis*-3 (%)	k_H/k_D[c]
MeOH–MeOK(135°)	H	19·3	55·3	6·4	—	19·1	—
	[4-^{2}H]*erythro*	22·3	56·1	3·4	2·1	18·2	1·1
	[4-^{2}H]*threo*	22·7	65·3	6·0	1·2	6·0	3·6
Bu^{n}OH–Bu^{n}OK (85°)	H	17·5	58·5	6·1	—	18·0	—
	[4-^{2}H]*erythro*	19·6	62·3	2·1	3·2	16·0	1·2
	[4-^{2}H]*threo*	20·4	69·5	5·5	1·3	4·6	4·5
Bu^{s}OH–Bu^{s}OK (85°)	H	25·5	50·1	12·6	—	11·7	—
	[4-^{2}H]*erythro*	27·7	51·8	9·5	1·4	11·1	1·1
	[4-^{2}H]*threo*	32·0	56·4	8·7	1·7	2·9	4·7
Bu^{t}OH–Bu^{t}OK (70°)	H	33·5	40·8	17·4	—	8·7	—
	[4-^{2}H]*erythro*	36·0	41·2	14·4	1·3	8·4	1·1
	[4-^{2}H]*threo*	39·9	45·2	11·4	1·8	3·6	2·8
$EtMe_2COH$–$EtMe_2COK$ (85°)	H	35·4	39·5	18·3	—	6·5	—
	[4-^{2}H]*erythro*	35·5	41·1	15·6	1·2	7·8	0·8
	[4-^{2}H]*threo*	42·7	45·5	9·8	2·2	2·0	3·8

[a] Corrected for 5% of undeuteriated starting material.
[b] Determined by g.l.p.c. on a column of 20 ft. of 20% adiponitrile on Chromosorb P plus 1·5 ft. of silver nitrate–ethylene glycol on Chromosorb P.
[c] Calculated with both *trans*-hex-2-ene and *cis*-hex-2-ene as references and averaged. Estimated error *ca.* ± 10%.



SCHEME 1

TABLE 2

Deuterium loss in eliminations from erythro- *and* threo-1-*ethyl*[2-^{2}H]*butyltrimethylammonium iodides*[a]

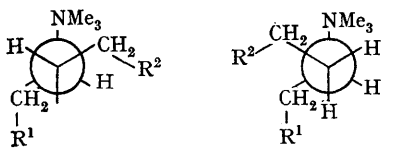
Reaction conditions	Reactant	% [$^2H_0$] calculated[b] for *anti*	*syn–anti*	% [$^2H_0$] observed
Bu^{n}OH–Bu^{n}OK (85°)	[4-^{2}H]*erythro*	10·8	5·2	8·2
	[4-^{2}H]*threo*	20·3	38·1	20·1
$EtMe_2COH$–$EtMe_2COK$ (85°)	[4-^{2}H]*erythro*	31·9	5·2	6·8
	[4-^{2}H]*threo*	8·9	26·9	20·3

[a] *cis*-Hex-2-ene was separated by g.l.p.c. on a 20-ft. column of 20% adiponitrile on Chromosorb P and the remaining three olefins analyzed on an Atlas CH-4 mass spectrometer at an ionizing voltage of 15 e.v. There was no appreciable P-1 peak.
[b] Using predictions from Scheme 1 and percentages from Table 1, allowing for 5% of undeuteriated starting material.

values. The large deviations from clean stereochemistry with *erythro*-reactant in butanol and *threo*-reactant in t-pentyl alcohol may be real, or may result from contamination of the material analyzed by [^{2}H]*cis*-hex-2-ene, which is eluted very soon after it and which would consistently lower the percentage of [$^2H_0$]-product. The trimethylamine in both cases was isotopically normal, which excludes any appreciable contribution from the α-β mechanism.[9]

A plausible steric hypothesis can accommodate the results so far available on open-chain systems. First, one assumes that the stereo-electronic preference for *anti*-elimination becomes weaker as the transition state becomes more reactant-like, *e.g.* on increase in strength on the attacking base from n-alkoxide to t-alkoxide,[10] giving the *syn*-mechanism a better chance to compete.

There are two possible reasons why the *syn*-mechanism becomes an important route for production of *trans*-, but not *cis*-, olefin. The bulk of the trimethylammonio-group can be expected to force the α- and β-alkyl groups as far away as possible (Scheme 2). The *anti*-β-hydrogen



SCHEME 2

will then be effectively shielded on both sides in the conformation leading to *trans*-olefin, particularly when R^1 is a t-butyl group as it was in the work of Pánková, Sicher, and Závada.[1] In the conformation leading to *cis*-olefin, the *anti*-β-hydrogen is still hindered on one side, but relatively open on the other. If non-linear approach of the base is energetically feasible, *cis*- should form faster than *trans*-olefin, especially with the bulkier bases. This argument assumes that eclipsing effects on *trans* : *cis* ratios are small for *anti*-elimination from a reactant-like transition state.

We can expect the *syn*-mechanism to produce *trans* faster than *cis*-olefin if the transition state possesses an eclipsed or nearly eclipsed conformation. The alkyl–alkyl *vs.* alkyl–hydrogen interactions might lead to substantial rate differences. The predominance of *syn*- over *anti*-elimination in some circumstances might arise from electrostatic attraction between the oppositely-charged base and leaving group, or from greater accessibility of the *syn*- than the *anti*-hydrogen (careful examination of models offers some support for this seemingly unlikely idea).

This hypothesis explains the preference for *cis*-olefin in some eliminations of quaternary ammonium salts, as well as the decrease in *cis*-olefin with the more branched alkoxides.[11,12]

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