Mechanisms of Elimination Reactions. XVII. The Relationship between Stereochemistry and Trans:Cis Ratios in Eliminations from Open-Chain Quaternary Ammonium Salts[1]

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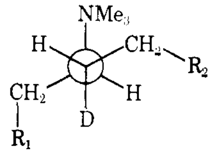
Abstract: Eliminations from 2- and 3-hexyltrimethylammonium ions show an excellent correlation between the stereochemistry of the elimination and the trans:cis ratio of the 2- and 3-hexene produced. As the importance of syn elimination increases, the percentage of *cis*-ene decreases. This relationship is expected from the steric theory of the syn–anti dichotomy which we have advanced. The magnitude of the decrease in per cent *cis*-ene can be used to estimate the importance of syn elimination in cases where the stereochemistry has not been determined. The application of this reasoning to a series of *sec*-alkyltrimethylammonium ions is discussed. The 2-butyltrimethylammonium ion is not expected by our theory to show an appreciable propensity for syn elimination, and in fact shows practically no variation in per cent *cis*-2-butene under different conditions.

The trans:cis ratios of olefins obtained in eliminations from quaternary ammonium salts vary with reactant structure and reaction conditions in a complex and interesting manner. In many open-chain systems, a predominance of *cis*- over *trans*-olefin is observed,[4–9] but in others the reverse is true.[6,10,11] In the medium rings, very high trans:cis ratios can be found.[12–14] This wide variability in trans:cis ratios makes it evident that a factor or factors other than the relative stabilities of the *trans*- and *cis*-olefins must be operating.

We recently presented a theory of the stereochemistry of elimination reactions of quaternary ammonium salts[7,15] which explains the occurrence of the syn–anti dichotomy[9,10] in open-chair systems. Our theory postulates that formation of *trans*-olefin by anti elimination is sterically hindered, and that formation of *trans*-olefin by syn elimination becomes more important as the hindrance increases and as the strength of the attacking base increases. An obvious consequence of the theory is a close relationship between trans:cis ratio and stereochemistry. In this paper we demonstrate the relationship and explore its consequences.

Table I contains our previously reported data[15] arranged in order of decreasing per cent *cis*-ene. Except for the data in dilute aqueous solution and one pyrolysis of a quaternary hydroxide, there is a good correlation between the decrease in per cent *cis*-ene and the increase in the per cent of syn elimination to give *trans*-olefin. Table II reports the per cent *cis*-ene from elimination reactions of various *sec*-alkyltrimethylammonium salts, partly from the present work and partly from the literature. Except for the 5-decyl[9] and the 2- and 3-hexyl cases, the reactions are of undetermined stereochemistry under the conditions reported. There is, with the exception of 2-butyl, a decrease in per cent *cis*-ene on going from the reactions involving a primary to those involving a tertiary alkoxide–alcohol. The magnitude of the decrease depends upon the reactant, however, being larger for the longer chain reactants.

Our theory of syn elimination postulates that the bulky trimethylammonio group forces the alkyl groups attached to the β' and γ positions of the alkyl chain into positions where they can hinder access to the anti β-hydrogen.[7,15] This is illustrated by means of Newman projections in **1** and **2**, which are the conformations leading to *trans*- and *cis*-olefin, respectively. As the strength of the attacking base increases and the transition state becomes more reactant like,[16] steric hindrance to attack on the β-hydrogen becomes greater, but is more serious in **1** than in **2** because the β-hydrogen is shielded on both sides in **1** but on only one in **2**. The syn → trans route becomes easier than the anti → trans, but the anti → cis remains preferable to the syn → cis route, both because of the lesser steric hindrance in **2** and the severe eclipsing interactions in the syn → cis route. Furthermore, it appeared from models that the β' substituent (R_1) exerts a greater steric



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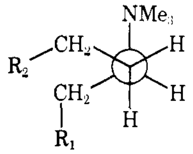

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Table I. Percentages of *cis*-Olefin and Syn Elimination in Reactions of 2- and 3-Hexyltrimethylammonium Iodides

Reaction condn	Reaction[a]	*cis*-Ene, %[b]	Syn elim, %[c]
n-BuOH–*n*-BuOK (85°)	2 → 2-ene	77.6	0
n-BuOH–*n*-BuOK (85°)	3 → 2-ene	75.0	9.5 ± 1.1
MeOH–MeOK (130°)	3 → 3-ene	74.9	20
n-BuOH–*n*-BuOK (85°)	3 → 3-ene	73.8	16.6 ± 0.7
tert-BuOH–*tert*-BuOK (85°)	2 → 2-ene	70.2	15
H_2O–NaOH (190°)	3 → 2-ene	67.2	2.2 ± 0.1
H_2O–NaOH (190°)	3 → 3-ene	65.3	9.4 ± 1.1
Pyrol $RNMe_3OH$[d]	3 → 2-ene	55.9	43.7 ± 5.3
62% DMSO–H_2O–NaOH (130°)[e]	3 → 3-ene	54.5	53.0 ± 1.5
tert-PeOH–*tert*-PeOK (85°)	3 → 2-ene	51.1	69.5 ± 0.5
sec-BuOH–*sec*-BuOK (85°)	3 → 3-ene	48.8	67.5 ± 2.5
Pyrol $RNMe_3OH$[d]	3 → 3-ene	45.7	59.8 ± 5.2
tert-BuOH–*tert*-BuOK (70°)	3 → 3-ene	33.3	80
tert-PeOH–*tert*-PeOK (85°)	3 → 3-ene	27.0	83.0 ± 2.0

[a] 2 → 2-ene refers to production of 2-hexene from 2-hexyltrimethylammonium iodide, and so on. [b] Our of cis plus trans total of the position isomer referred to. [c] Numbers with deviations are averages from deuterium analyses on products from the threo and erythro β-deuterated reactants, corrected for assumed $(k_H/k_D)_{syn} = 2.2$ and $(k_H/k_D)_{anti} = 3.0$ (see ref 15). Numbers without deviations are estimated from apparent isotope effects, calculated from product proportions as in ref 7 and 10. [d] Aqueous solution of quaternary hydroxide concentrated by distillation until olefin distilled (usual Hoffmann conditions). [e] Solvent was 62 mol % dimethyl sulfoxide in water.

Table II. Per Cent *cis*-Alkene from Elimination Reactions of Alkyltrimethylammonium Salts

	Class								
	IV[a]	IV	IV	IV	III	III	II	II	I
	Reactant								
	5-Decyl	5-Nonyl	4-Heptyl	3-Hexyl	3-Hexyl	3-Pentyl	2-Hexyl	2-Pentyl	2-Butyl
	Product								
Reaction condn	4-Ene[b]	4-Ene[c]	3-Ene	3-Ene	2-Ene	2-Ene	2-Ene	2-Ene[g]	2-Ene
MeOH–MeOK (130°)	79.0	81		74.9	74.1				
EtOH–EtOK (110°)		74				77.7			63.7[d]
n-BuOH–*n*-BuOK (85°)			74.6	73.8	75.0	74.6	77.6	80.1	69.2
i-PrOH–*i*-PrOK (85°)			55.8						
sec-BuOH–*sec*-BuOK (85°)			48.4	48.2	66.3	66.3	73.3	75.8	68
tert-BuOH–*tert*-BuOK (*ca.* 85°)	28.0	26	35.2	33.3	55.0	58.5	70.2	70.9	70.9
tert-PeOH–*tert*-PeOK (85°)			26.0	27.0	50.9				69.1[d]
Pyrolysis[e]	29.0			45.7	55.9	55.5[d]			59[f]

[a] See text. [b] Reference 9. [c] Reference 4. [d] D. H. Froemsdorf, unpublished results at 55°. [e] Aqueous solution of quaternary ammonium hydroxide concentrated by distillation until olefin distilled (usual Hoffmann conditions). [f] Reference 11. [g] Reference 6.

hindrance to the anti → trans route than the γ substituent (R_2).[15]

The reactions in Table II can be divided into four structural classes depending on the nature of R_1 and R_2: I, neither β'- nor γ-methyl or methylene substitution (2-butyl → 2-butene is the only representative of this class); II, methyl or methylene group on the γ but not the β' position (2-hexyl → 2-hexene, 2-pentyl → 2-pentene); III, methyl or methylene group on the β' but not the γ position (3-hexyl → 2-hexene, 3-pentyl → 2-pentene); IV, methyl or methylene substitution at both the β' and γ positions (3-hexyl → 3-hexene, 4-heptyl → 3-heptene, 5-nonyl → 4-nonene, 5-decyl → 4,5-decene). According to our theory, the order of decreasing steric congestion about the anti β-hydrogen should be IV > III > II > I.

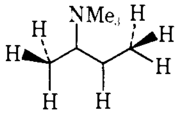
With very few exceptions, the values of per cent cis with a given base-solvent pair and within a given class are all similar, and increase in the order IV < III < II < I, which is expected to be the order of decreasing syn elimination.[15] If our analysis of the results is correct, we should be able to predict per cent syn elimination to a good approximation by assuming that it will be constant within a given group. One comparison is possible, between 3-hexyl → 3-hexene[15] and 5-decyl → 5-decene.[9] With methoxide–methanol, there is 20% syn elimination for the former and 32% for the latter, with *tert*-butoxide–*tert*-butyl alcohol, 80 and 87%, and for pyrolysis of the quaternary hydroxide, 60 and 95%. The agreement is good under the first two sets of conditions in spite of different methods of determining stereochemistry and different detailed reaction conditions between the two investigations. The effective basicity of the reaction mixture in the pyrolysis depends strongly on how concentrated the syrupy hydroxide is, and this in turn depends on rate and intensity of heating, so the greater discrepancy in that case is not surprising. While the magnitude of this difference is probably exaggerated, it is likely that the consistently greater per cent syn elimination with the 5-decyl → 5-decene reactions is real. Here both R_1 and R_2 are *n*-propyl, while in the 3-hexyl → 3-hexene reactions they are methyl, and it would not be surprising if the longer alkyl groups exerted somewhat more steric hindrance.

The 2-butyl → 2-butene reactions require separate comment, for there is no significant change in the per cent *cis*-2-butene, with the possible exception of the pyrolysis and the ethoxide–ethanol reaction, and certainly no trend with changing base strength. We can conclude from these observations that there is little or no syn elimination from 2-butyltrimethylammonium ion under any of the experimental conditions. The one reported study of stereochemistry in this system, using ethoxide in dimethyl sulfoxide, bears out this prediction.[8] Furthermore, the tendency toward syn elimination is expected to be small in this system, for it lacks alkyl substitution at the β' and γ positions to provide steric hindrance to abstraction of the anti β-hydrogen.

These results also support our contention that the necessary condition for syn elimination in open-chain systems or medium rings is a transition-state conformation which shields the anti β-hydrogen.[15] While the strength and steric requirements of the base,[15] and a solvent system which favors ion pairing[14] may all create conditions favorable to syn elimination, they are not alone sufficient to cause it.

Although the cause of syn elimination in smaller (four- to seven-membered) rings cannot be the same in detail, the effect is again probably basically conformational: difficulty in attaining a precisely anti arrangement of the leaving group and the β-hydrogen.[17,18]

In conclusion, a few more comments on the 2-butyl → 2-butene reactions are needed. Although the β'- and γ-alkyl groups which are postulated to hinder the anti → trans route are absent, the preference for *cis*- over *trans*-2-butene remains nearly as strong as in the other reactions. One is at first tempted to invoke an additional effect (we had previously suggested greater ease of solvation of the cis transition state[6]), but it is preferable to see if the conformational argument can be adapted to these circumstances. Examination of models reveals considerable restriction to free rotation even in 2-butyltrimethylammonium ion, and a conformation of the anti → trans transition state like that in **3** is definitely favored, with a β' carbon–hydrogen bond forced into a 1,3 interaction,



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and a γ carbon–hydrogen bond into a 1,2 interaction, with the anti β-hydrogen. These hydrogens can thus provide hindrance to abstraction of the anti β-hydrogen similar in character to that from alkyl groups at the same positions, though much less in magnitude. The hindrance again appears less for the anti → cis route. Thus, a similar preference for the anti → cis over the anti → trans route is not unreasonable because a difference between two degrees of steric hindrance may be similar, even though the absolute magnitude of each is much smaller than in the longer chain cases. The eclipsing effects which hinder the syn routes, however, will be almost as large in the 2-butyl as in the longer chain systems, so anti remains of lower energy than syn elimination under all reaction conditions with the 2-butyl system.

Experimental Section

4-Heptyl-*p*-toluenesulfonate was prepared by the method of Tipson.[19] The crude tosylate was taken up in ligroin, filtered through activated charcoal, and recrystallized at *ca.* −80°. The product had $n^{20}\mathrm{D}$ 1.4935 (lit.[20] $n^{20}\mathrm{D}$ 1.4967).

4-Heptyldimethylamine was prepared by the procedure of Cram, *et al.*,[21] as described for the hexylamines.[15]

4-Heptyltrimethylammonium iodide was prepared by the addition of a twofold excess of methyl iodide to a solution of heptyldimethylamine in acetonitrile.[22] The product was precipitated by addition to ether, then recrystallized from ethanol–ether. The product had mp 228–230° dec.

2-Butyltrimethylammonium bromide was prepared from 2-butyl-*p*-toluenesulfonate as above by Feit.[6] The product had mp 145–149° dec. *Anal.* Calcd for $C_7H_{18}NI$: C, 42.86; H, 9.25; N, 7.14. Found: C, 42.74; H, 9.24; N, 7.01.

3-Pentyltrimethylammonium Iodide. 3-Pentyldimethylamine, prepared by reduction of the corresponding oxime[23] followed by the Eschweiler–Clark reaction[7] was provided by Feit prior to conversion to the corresponding ammonium iodide.[22] The product had mp 231–232° dec (lit.[23,24] 233–234° dec).

Elimination Product Studies. The reaction procedures are those given previously.[15] The products of elimination of 2-butyl-, 3-pentyl-, and 4-heptyltrimethylammonium salts were analyzed on a 20 ft × 0.25 in. column of 20% adiponitrile on Chromosorb P-AW.[24–26] In the 3-pentyl and 4-heptyl compounds no other olefinic products were detected[26] indicating the absence of any positional isomers of the ammonium salts. The elimination reaction mixtures of the 2-butyl- and 3-pentyltrimethylammonium salts were analyzed directly. The 4-heptyltrimethylammonium salt eliminations were extracted into pentane prior to analysis.[15] All product studies are the result of at least two independent reactions, each analyzed by multiple glpc injections.

Reagents. Purification of solvents and preparation of base solutions were performed as described previously.[15]

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