Mechanisms of Elimination Reactions. XII. Hydrogen Isotope Effects and the Nature of the Transition State in Eliminations from Alicyclic Quaternary Ammonium Salts[1]

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Abstract: *trans*-Cyclohexyl-2-*d*-trimethylammonium, *trans*-cyclopentyl-2-*d*-trimethylammonium, and 3-pentyl-2,2-d_2-trimethylammonium *p*-toluenesulfonates were prepared. Intramolecular isotope effects were determined for their base-promoted decomposition by measuring the deuterium contents of the product olefins in the mass spectrometer. With hydroxide ion in water at 191°, k_H/k_D ran cyclohexyl, 4.33; cyclopentyl, 3.99; 3-pentyl, 3.22. The latter two compounds were also run in ethoxide–ethanol, isopropoxide–isopropyl alcohol, and *t*-butoxide–*t*-butyl alcohol. In all cases, k_H/k_D was larger for cyclopentyl than for 3-pentyl. Kinetics and products were determined for the undeuterated compounds and rates of elimination calculated. The cyclohexyltrimethylammonium salt reacted more slowly than the other two under all conditions. These results are consistent with an explanation previously advanced for Saytzev-rule products from cyclic quaternary ammonium salts. Steric strain is assumed to make the carbon–nitrogen bond easier to break in the cyclic reactants, necessitating less assistance from concomitant carbon–hydrogen cleavage. This results in an extent of hydrogen transfer in the transition state in the order 3-pentyl > cyclopentyl > cyclohexyl. Evidence is adduced that *syn* elimination is probably not a significant complication in the interpretation of our results.

Although E2 reactions of quaternary ammonium salts normally give the less-substituted (Hofmann-rule) olefin where there is a choice, there are numerous examples of alicyclic quaternary ammonium salts giving the more substituted (Saytzev-rule) product. These include neomenthyltrimethylammonium,[3–5] *cis*-2-methylcyclohexyl- and *cis*-2-methylcyclopentyltrimethylammonium,[6] and 6-β-cholestanyltrimethylammonium[7] salts. Since the *trans*-4-*t*-butylcyclohexyltrimethylammonium ion yields only product of displacement on methyl when treated with *t*-butoxide, while the *cis* isomer gives an excellent yield of 4-*t*-butylcyclohexene,[8] the favored stereochemistry for elimination from cyclohexyltrimethylammonium salts appears to be *trans-anti*, with both trimethylammonio and the β-hydrogen in axial positions. It was argued[5,6] that steric compression in the transition state lengthens the carbon–nitrogen bond, resulting in considerable double-bond character instead of the carbanion character normally found in quaternary ammonium salt eliminations.[9]

Although this explanation is plausible, we desired additional evidence. Relative rates, deuterium isotope effects, and nitrogen isotope effects were all expected to be helpful. Because the low yield of elimination product from cyclohexyltrimethylammonium ion (see below) makes the study of the nitrogen isotope effect difficult, we chose to study rates and deuterium isotope effects first, even though the evidence they afford is less direct.

The quaternary ammonium salts used were cyclohexyl-, cyclopentyl-, and 3-pentyltrimethylammonium, the latter to give an acyclic comparison close in structure to the two cyclic systems. The products of reaction were determined by glpc analysis. In each case the only significant reactions were elimination or displacement on a methyl group. The proportions of elimination are recorded in Table I. Over-all rates of reaction were determined by acid–base titration, using thymolphthalein as indicator with added pyridine to repress interference from the tertiary amines present.[10] These data were combined with the product studies to obtain the rates of elimination and substitution given in Table II.

Table I. Product Studies in Elimination Reaction of Quaternary Ammonium Salts

Base/solvent, °C[a]	% Elimination[b] from $RNMe_3^+$ for Cyclohexyl	Cyclopentyl	3-Pentyl
HO^-/H_2O, 192	15[c]	26[d]	36[d]
$EtO^-/EtOH$, 115	4.0	35.2	67.5
i-PrO^-/*i*-PrOH, 96	7.6	37.4	59.1
t-BuO^-/*t*-BuOH, 70	7.9	69.6	65.6

[a] In Pyrex ampoules in a constant-temperature bath at ±0.1°, except for runs in water which were done in an oven at ±5°. [b] Only other products were those of displacement on methyl of $RNMe_3^+$. Except as otherwise noted, each figure is the average of two or more runs with average deviation <2%. [c] In a Pyrex ampoule. Two runs in stainless steel ampoules gave 8 and 11%. [d] Erratic results. Runs in stainless steel ampoules gave much lower figures. Five runs each were done in Pyrex ampoules. Since errors were likely to be in the direction of loss of olefin, the two lowest figures (13 and 18% for cyclopentyl, 21 and 21% for 3-pentyl) were discarded and the remaining three figures averaged. Average deviations were then ±2%.

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Table II. Rate Constants for Elimination and Substitution Reactions of Quaternary Ammonium Salts

Conditions,[a] R in $RNMe_3^+$	10^4k_E,[b] l. mol^{-1} sec^{-1}	10^4k_S,[b] l. mol^{-1} sec^{-1}
	$NaOH/H_2O$, 191.2°	
Cyclohexyl	0.164[c]	0.926[c]
Cyclopentyl	0.346[c]	0.984[c]
3-Pentyl	2.83[c]	5.03[c]
	EtONa/EtOH, 114.8°	
Cyclohexyl	0.286 ± 0.027	6.86 ± 0.04
Cyclopentyl	2.30 ± 0.04	4.24 ± 0.05
3-Pentyl	12.4 ± 0.03	5.96 ± 0.18
	i-PrOK/*i*-PrOH, 96.3°	
Cyclohexyl	2.48 ± 0.17	30.1 ± 0.6
Cyclopentyl	10.5 ± 0.3	17.5 ± 0.3
3-Pentyl	4.36 ± 0.10	3.02 ± 0.10
	t-BuOK/*t*-BuOH, 69.8°	
Cyclohexyl	0.75 ± 0.05	8.74 ± 0.05
Cyclopentyl	15.6 ± 0.4	6.81 ± 0.38
3-Pentyl	4.28 ± 0.26	2.24 ± 0.16

[a] Temperature constant to ±0.1° below 100°, ±0.2° above 100°. [b] Reaction followed by titration of unreacted base (see Experimental Section). k_E and k_S calculated from k_2 and product proportions given in Table I. $k_2 = k_E + k_S$. Error given is square root of sum of squares of errors in both k_2 and product analysis. [c] No error quoted because of erratic product analyses (footnote *d*, Table I). Error in k_2 ran 5% or less, estimated over-all error 10–15%.

Because these compounds are unactivated quaternary ammonium salts, the conditions needed for measurable rates of reaction are rather severe, involving sealed ampoules for all except the reactions in *t*-butyl alcohol. Furthermore, the low yields of elimination product in most of the reactions contribute another source of imprecision in determining the rate constants. The changes in deuterium isotope effects, which we wished to measure, were expected to be sufficiently small that they probably would not exceed the combined experimental errors of the rate and product determinations. Consequently, we decided to determine intramolecular deuterium isotope effects with appropriately labeled reactants.

Cyclohexene was subjected to deuterioboration[11,12] and the product converted to *cis*-cyclohexyl-2-*d* *p*-toluenesulfonate. Treatment with trimethylamine in nitromethane yielded *trans*-cyclohexyl-2-*d*-trimethylammonium *p*-toluenesulfonate. In order to determine whether this reaction was the expected SN2 displacement, a sample of *trans*-cyclohexanol-2-*d* from the action of lithium aluminum deuteride on cyclohexene oxide was tosylated and treated with trimethylamine in nitromethane. The resulting quaternary ammonium salt was converted to the hydroxide and subjected to the usual conditions for Hofmann elimination. Examination of the cyclohexene in the mass spectrometer revealed 5% of dideuterated material, which can be explained as arising from reaction of aluminum deuteride with the alkoxide intermediate from the opening of the epoxide.[11,13] Once this complication is allowed for, however, the *cis* deuterium is found to be retained completely within experimental error. Since the elimination has been demonstrated to be almost entirely *anti*,[14] the substitution must have proceeded cleanly with inversion.

The preparation of *trans*-cyclopentyl-2-*d*-trimethylammonium *p*-toluenesulfonate followed the same sequence as above, starting with deuterioboration of cyclopentene. The 3-pentyl-2,2-d_2-trimethylammonium *p*-toluenesulfonate was obtained in the same manner from 3-pentanol-2,2-d_2, which in turn resulted from the reaction of ethyl-1,1-d_2 bromide[15] with magnesium to give a Grignard reagent which was treated with propionaldehyde.

Isotope effects were then determined by carrying out the elimination reactions on the deuterated quaternary ammonium salts, isolating the alkene from the reaction mixture, and determining its deuterium content in the mass spectrometer. This method assumes, of course, that the eliminations are entirely *trans-anti* (see below for discussion of this point). Given this assumption, k_H/k_D is simply the ratio of deuterated to undeuterated olefin from the cyclic reactants, and dideuterated to monodeuterated olefin from the acyclic reactant. The results are given in Table III. The *cis*-cyclohexyl-2-*d*-trimethylammonium salt was run only in water because of difficulties in isolating the low yields of cyclohexene from the other solvents.

Table III. Deuterium Isotope Effects in Elimination Reactions of Quaternary Ammonium Salts

Base/solvent, °C[a]	k_H/k_D for Cyclohexyl	Cyclopentyl	3-Pentyl[d]
$NaOH/H_2O$, 191.2	4.33 ± 0.03[b]	3.99 ± 0.03[b]	3.22 ± 0.02
EtONa/EtOH, 114.8		4.66 ± 0.05[c,e]	3.92 ± 0.27
i-PrOK/*i*-PrOH, 96.8		5.56 ± 0.08[c]	4.19 ± 0.02
t-BuOK/*t*-KuOH, 69.8		6.71 ± 0.01[c]	4.33 ± 0.06

[a] Base/substrate ratio *ca.* 2/1. [b] Mass spectrum determined at an ionizing potential of 70 eV and the composition determined from a calibration curve prepared using known mixtures of the isotopic species (see Experimental Section). [c] Determined at an ionizing potential of 9.0 eV, with correction for natural abundance of ^{13}C. [d] Determined at an ionizing potential of 11.0 eV, with correction for natural abundance of ^{13}C. [e] This sample was also analyzed by the method of footnote *b*, which gave a value of 4.56.

Discussion

The cyclohexyl system stands out from the others in two respects. Elimination competes very poorly with substitution and the elimination is slower than for the other two systems. Both of these effects undoubtedly result from the necessity of forcing the trimethylammonio group into an axial position for the elimination.[8] The substitution, by contrast, can occur with this group in an unhindered equatorial position.

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The comparison of elimination rates between cyclopentyl and 3-pentyl is less clear. Here conflicting effects must be operating. The high carbanion character in the transition state for the acyclic system means its reactions are decelerated by β-alkyl substitution, whereas the reverse is true for the cyclic systems.[5,6] The acyclic system, on the other hand, can avoid most of the steric strain in the transition state which affects cyclopentyl and, to an even greater extent, cyclohexyl. Considerations of steric strain alone, in fact, would lead one to predict a more drastic slowing than is observed in the elimination reactions of the cyclohexyl system.

Not a great deal can be made of the substitution rates. The equatorial trimethylammonio group in the cyclohexyl system should be least hindered to SN2 attack on methyl, while the trimethylammonio group of the acyclic system should be most hindered because the alkyl group is not "tied back" as in the cyclic systems. Most of the results are consistent with these ideas, but the high rate of substitution with the 3-pentyl compound in water is difficult to account for.

The elimination rates as discussed above fit well our hypothesis of steric strain leading to more double-bond character in the transition states for elimination from the cyclic reactants. They do not, however, demonstrate unequivocally that there is a difference in transition-state structure between the reactions of the cyclic and acyclic systems. For direct evidence on this point, it is necessary to refer to the isotope effects (Table III).

The k_H/k_D values evidently vary with structure of reactant over a much wider range than the experimental error. To determine the meaning of this variation with respect to changes in transition-state structure, one must remember that primary hydrogen isotope effects have been predicted theoretically[16] and shown experimentally[17–19] to reach a maximum when the proton is half-transferred. Evidence that the proton transfer is past the half-way point in elimination reactions of 2-arylethyltrimethylammonium ion has been presented.[9] If this conclusion applies generally to alkyltrimethylammonium ions, then the extent of proton transfer in the transition state runs 3-pentyl > cyclopentyl > cyclohexyl. Since acyclic quaternary ammonium salts obey the Hofmann rule while the cyclic ones obey the Saytzev rule,[5–7] the order of extent of proton transfer is in line with the expected order of carbanion character. No reliable conclusions can be drawn from the changes in k_H/k_D with the solvent–base system because of concomitant temperature changes.

Although the k_H/k_D values give no direct information on the extent of carbon–nitrogen cleavage in the transition state, one can make a plausible argument for the consistency of our results with the hypothesis[5,6] used to explain orientation effects in the cyclic system. If cleavage of the carbon–nitrogen bond is aided by steric strain in the transition state with cyclohexyl (and, to a lesser extent, with cyclopentyl), then less assistance will be needed from the carbon–hydrogen bonding electrons to "displace" the trimethylammonio group. Our picture of the transition state, then, is that the extent of proton transfer increases, and the extent of carbon–nitrogen cleavage decreases, in the order cyclohexyl, cyclopentyl, 3-pentyl. We hope to be able to test this conclusion with nitrogen isotope effects.

The design and interpretation of our experiments are based on the assumption that all of the elimination reactions studied have *anti* stereochemistry, an assumption which seemed perfectly safe when this work was initiated in 1962. Since then, however, substantial *syn* elimination has been observed in Hofmann elimination from four-, five-, and seven-membered (but not six-membered) cyclic quaternary ammonium salts.[14] In addition, a mechanistic dichotomy in which *cis*-olefin is formed by *anti* elimination but *trans*-olefin by *syn* elimination from acyclic quaternary ammonium salts has been reported.[20] These developments cast suspicion on all of our isotope effects except that for the cyclohexyl system.

Recent work in these laboratories by Bailey[21] partially rescues the significance of the results on the 3-pentyl system. He found that a closely similar open-chain reactant, 3-hexyl-4-*d*-trimethylammonium ion (stereospecifically deuterated), gives both *cis*- and *trans*-3-hexene predominantly by an *anti* mechanism in water–hydroxide, methanol–methoxide, and 1-butanol–*n*-butoxide. The *syn–anti* dichotomy[20] prevailed in *t*-butyl alcohol–*t*-butoxide, and *sec*-butyl alcohol–*sec*-butoxide gave intermediate results. Thus, our isotope effects in water–hydroxide and ethanol–ethoxide are probably reliable values for *anti* elimination, but those in isopropyl alcohol–isopropoxide and *t*-butyl alcohol–and *t*-butoxide may be weighted averages of the values for the *syn* and *anti* mechanisms.

It appeared unlikely that the cyclopentyltrimethylammonium ion under our conditions could be giving nearly as much *syn* elimination as was reported by Coke[14] under Hofmann conditions. The occurrence of *syn* elimination with our reactant, since it produces deuterated olefin, would raise the apparent k_H/k_D above $(k_H/k_D)_{trans}$.

$$\left(\frac{k_H}{k_D}\right)_{\text{apparent}} = \frac{(k_H)_{trans} + 2(k_H)_{cis}}{(k_D)_{trans}}$$

A $(k_H)_{cis}$ comparable to that observed by Coke should have given a $(k_H/k_D)_{\text{apparent}}$ two or three times as large as $(k_H/k_D)_{trans}$, reducing the latter to the improbably low value of 1.3–2.0.

Consequently, we prepared *cis*-cyclopentyl-2-*d*-trimethylammonium ion to determine the stereochemistry of its elimination reactions under our experimental conditions.[22] While this investigation is not yet complete, it is evident that there is little or no *syn* elimination with hydroxide ion in dilute aqueous solution. Two experiments with different samples gave 99.3 and and 97.2% retention of *cis* deuterium. Since the isotope effect is unknown under our conditions, a precise correction for it cannot be made. Even assuming the value Coke[14] reported for a lower temperature, however, these figures would correspond to 10% or less of *syn* elimination. Slightly more deuterium loss is ob-

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served with *t*-butoxide in *t*-butyl alcohol at 70°. Even so, the 95.3% retention of deuterium could correspond to no more than 15–20% *syn* elimination, again assuming Coke's[14] isotope effects. A complete account and discussion of these investigations of stereochemistry will be published at a later date.

We conclude that the isotope effects in Table III for the reactions with hydroxide ion in water are almost certainly reliable, since all three reactions are essentially entirely *anti* eliminations. At the other end of the list, there is apparently some *syn* elimination with both the cyclopentyl and 3-pentyl compounds in *t*-butoxide–*t*-butyl alcohol. Until we can dissect the relative amounts of *syn* and *anti* elimination, and determine k_H/k_D for both, these results should be treated with caution. It is somewhat encouraging that the apparent k_H/k_D values for the 3-pentyl and cyclopentyl compounds are in the same order in all solvent–base systems, which suggests that *syn* elimination may not be extensive enough to distort seriously the qualitative picture even in *t*-butoxide–*t*-butyl alcohol.

Experimental Section[23]

3-Pentyltrimethylammonium Bromide. To a methanolic solution of 5.2 g of N,N-dimethyl-3-pentylamine[24] was added 20.0 g of cold methyl bromide. The mixture was refluxed under a Dry Ice condenser for 2 hr, the methanol removed, and the white hygroscopic solid recrystallized from ethanol–acetone, mp 246–247° dec. *Anal.* Calcd for $C_8H_{20}BrN$: C, 45.70; H, 9.60; N, 6.67. Found: C, 45.66; H, 9.59; N, 7.05.

3-Pentyltrimethylammonium Iodide. An ethereal solution of 7.4 g of N,N-dimethyl-3-pentylamine and 10.5 g of methyl iodide deposited 11.3 g of solid on standing. Recrystallization from acetone gave product of mp 233–234° dec (lit.[24] 233.3–234.0° dec). *Anal.* Calcd for $C_8H_{20}IN$: C, 37.36; H, 7.84. Found: C, 37.47; H, 7.97.

N,N-Dimethylcyclopentylamine was prepared in 39% yield from cyclopentylamine[25] by treatment with formic acid and formaldehyde.[26] The product had bp 131–132° (lit.[27] 135–137°).

Cyclopentyltrimethylammonium bromide was prepared by treating an ethereal solution of 7.1 g of N,N-dimethylcyclopentylamine with 18.2 g of methyl bromide. The product (12.8 g) was recrystallized from acetone, mp 280–281° dec (lit.[28] 280–281° dec). *Anal.* Calcd for $C_8H_{18}BrN$: C, 46.16; H, 8.72. Found: C, 46.05; H, 8.75.

Cyclopentyltrimethylammonium iodide was prepared by treating a methanolic solution of 7.3 g of N,N-dimethylcyclopentylamine with 15.9 g of methyl iodide. Removal of the methanol (rotary evaporator), followed by recrystallization from fresh methanol, gave product of mp 266–268° dec. *Anal.* Calcd for $C_8H_{18}IN$: C, 37.66; H, 7.11. Found: C, 37.73; H, 7.25.

Cyclohexyltrimethylammonium bromide was prepared from N,N-dimethylcyclohexylamine (Eastman Kodak) and methyl bromide. Recrystallization from 95% ethanol gave white needles, mp 270–273° dec (lit.[29] 308–311° dec). *Anal.* Calcd for $C_9H_{20}BrN$: C, 48.63; H, 9.07; N, 6.37. Found: C, 48.76; H, 9.07; N, 6.66.

Cyclohexyltrimethylammonium *p*-Toluenesulfonate. A solution of 36.7 g of cyclohexyl *p*-toluenesulfonate and 25 g of trimethylamine in 25 ml of nitromethane was heated in a sealed tube at 55° for 66–72 hr. The resulting mixture was filtered, ether added to the filtrate to precipitate the remaining salt, and the product (85% yield) recrystallized from ethanol to give material of mp 244.5–246.5°. *Anal.* Calcd for $C_{16}H_{27}NO_3S$: C, 61.30; H, 8.68; N, 4.47. Found: C, 61.67; H, 8.84; N, 4.38.

Cyclopentyltrimethylammonium *p*-toluenesulfonate was prepared from 10 g of cyclopentyl *p*-toluenesulfonate and 10 g of trimethylamine in 10 ml of nitromethane as described above. Removal of solvent (rotary evaporator) and treatment of the residue with ether gave 70% of crystalline solid which was recrystallized from ethanol to give product of mp 209–210°. *Anal.* Calcd for $C_{15}H_{25}NO_3S$: C, 60.17; H, 8.42; N, 4.68. Found: C, 60.34; H, 8.58; N, 5.24.

3-Pentyltrimethylammonium *p*-toluenesulfonate was prepared as described above in 34% crude yield. Recrystallization from ethanol–ether gave a very hygroscopic white solid, mp 138.5–141°. *Anal.* Calcd for $C_{15}H_{27}SO_3N$: C, 59.76; H, 9.03. Found: C, 59.48; H, 9.06.

***cis*-Cyclohexyl-2-*d*-trimethylammonium *p*-toluenesulfonate** was prepared in the same manner as the undeuterated material, using *trans*-cyclohexyl-2-*d* *p*-toluenesulfonate.[11] There was obtained 79% of product which was recrystallized from ethanol–acetone to give material of mp 246–247°, 0.995 atom of D/molecule.

***trans*-Cyclohexyl-2-*d*-trimethylammonium *p*-toluenesulfonate** was prepared as above, starting with *cis*-cyclohexyl-2-*d* *p*-toluenesulfonate. Recrystallization from ethanol–acetone gave white plates, mp 244.5–247°, 0.978 atom of D/molecule.

cis*-Cyclopentanol-2-*d was prepared by deuterioboration of cyclopentene by the procedure described for the preparation of *cis*-cyclohexanol-2-*d*.[11] The product (68% yield) had bp 137–139° (lit.[30] 139°).

***cis*-Cyclopentyl-2-*d* *p*-toluenesulfonate** was prepared by treatment of *cis*-cyclopentanol-2-*d* with *p*-toluenesulfonyl chloride in dry pyridine.[31] The product had mp 27–28° (lit.[32] 28°). It kept indefinitely if refrigerated, but slowly decomposed on standing at room temperature.

***trans*-Cyclopentyl-2-*d*-trimethylammonium *p*-toluenesulfonate** was prepared from *cis*-cyclopentyl-2-*d* *p*-toluenesulfonate in the same manner as the undeuterated material. Recrystallization from acetone–ethanol gave material of mp 212–213°, 0.975 atom of D/molecule.

3-Pentanol-2,2-d_2. A Grignard reagent was prepared from 17.5 g of ethyl-1,1-d_2 bromide[15] in 40 ml of dry ether and 3.9 g of magnesium in 75 ml of dry ether. It was then treated with 9.2 g of freshly distilled propionaldehyde at −10° and the mixture left standing for 19 hr. It was then treated with saturated ammonium chloride, the ether solution filtered, and the inorganic residue washed well with ether. The combined extracts were dried over magnesium sulfate and fractionated to give 6.0 g (42%) of 3-pentanol-2,2-d_2, bp 110–114° (lit.[33] 111–113°).

3-Pentyl-2,2-d_2 *p*-Toluenesulfonate. Reaction of 3-Pentanol-2,2-d_2 and *p*-toluenesulfonyl chloride in dry pyridine[31] gave 63% of 3-pentyl-2,2-d_2 *p*-toluenesulfonate, mp 44–45° (lit.[32] 43.2–44°), 1.97 atoms of D/molecule.

3-Pentyl-2,2-d_2-trimethylammonium *p*-toluenesulfonate was obtained in 32% yield in the same manner as the undeuterated material. Recrystallization from acetone gave a hygroscopic product of mp 141–143.5°, 1.85 atoms of D/molecule.

Cyclohexene-1-*d* was obtained by heating a solution of 5.0 g of potassium hydroxide and 7.4 g of cyclohexyl-1-*d* *p*-toluenesulfonate[11] in 25 ml of ethylene glycol to 140–150°, with collection of the distillate in a Dry Ice trap. The olefin was separated from the water and dried over sodium sulfate to give 1.12 g (46%) of cyclohexene-1-*d*, 99% monodeuterated by nmr and mass spectra.

Cyclopentene-1-*d* was prepared in the same manner as cyclohexene-1-*d*, using cyclopentyl-1-*d* *p*-toluenesulfonate.[30] The mass spectrum showed it to be >99% monodeuterated.

Ethers for Product Studies. Ethyl, isopropyl, and *t*-butyl methyl ethers were prepared from the appropriate sodium or potassium alkoxide and methyl iodide. Analysis by glpc showed them to be free of contaminants except for the corresponding alcohol.

Solvents and Reagents. Absolute ethanol was refluxed over and then distilled from magnesium ethoxide. Isopropyl alcohol (99%) was treated with sodium metal and then distilled. The treatment was repeated. *t*-Butyl alcohol was treated with potassium metal and distilled. The treatment was repeated. Alkoxide solutions were prepared by dissolving the clean metal (sodium or

(23) Melting points and boiling points are uncorrected. Elemental analyses were done by Micro-Tech Laboratories, and deuterium analyses on solid compounds by Mr. J. Németh, Urbana, Ill.

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potassium) in the appropriate alcohol. The resulting solutions were stored under nitrogen in polyethylene bottles and the concentration was determined by titration prior to each use. For the acid–base titrations, sodium hydroxide solutions were standardized against potassium acid phthalate, and hydrochloric acid solutions were standardized against the sodium hydroxide solutions.

Kinetics of Reactions. A constant-temperature bath capable of maintaining the temperature within ±0.1° below 100° and ±0.2° above 100° was used. The bath liquid was a polyglycol ether, 50 HB-280-X (Union Carbide). Reactions with ethoxide, isopropoxide, and hydroxide were carried out in stainless steel ampoules. These consisted of 11–13 cm no. 304 (5/8 in. o.d.) stainless steel tubing closed at one end by a heli-arc weld to a stainless steel disk, and at the other by a heli-arc weld to a no. 6WC SSP stainless steel fitting (SSP Fittings Corp., Bedford, Ohio) with Teflon rings. Sodium hydroxide heated in these ampoules at 175° did not change in molarity over 5 days. The reactions with *t*-butoxide were carried out in a Pyrex volumetric flask with side arm and sample bulb closed by an ampoule stopper.[34]

Each run in the stainless steel ampoules used 12 of them containing about 5.8 ml each of reaction mixture. The fitting was closed firmly with two box wrenches and the ampoules immersed in the bath. When the temperature of the bath had remained constant for 5–10 min, two ampoules were withdrawn and quenched in Dry Ice–acetone (bath below 130°) or ice water (bath above 130°). The remaining tubes were withdrawn and quenched at appropriate intervals. A sample was withdrawn from each with a calibrated pipet (4.98 ml) and titrated with standard hydrochloric acid using three to five drops of 1% thymolphthalein in pyridine. For reactions in water 5 ml of pyridine was added before titration, and for reactions in ethanol 25 ml of pyridine and 25 ml of isopropyl alcohol were added prior to titration.

For the reactions in *t*-butyl alcohol, solutions of the quaternary ammonium salt and the base were equilibrated separately and mixed. Aliquots were withdrawn with a calibrated 5-ml syringe, quenched in excess hydrochloric acid, and titrated with standard base using thymolphthalein as indicator. The titration procedure used in the kinetic runs is based on that of Siggia.[10] All reactions were followed through at least one half-life. Rate constants are not corrected for thermal expansion of the solvent.

Product Studies. A 10-ml sample of a solution 0.1 *M* in base and 0.05 *M* in substrate was heated at the same temperature as the kinetic runs in a sealed Pyrex ampoule for at least ten half-lives. The aqueous reaction mixture was extracted with five 1-ml portions of carbon disulfide and the solution analyzed on a 10 ft × 1/8 in. column of 15% Carbowax 20M and 4% potassium hydroxide on Chromosorb P 45–60. The mixture from reaction in ethanol was diluted with 15 ml of 5% potassium hydroxide and extracted as above. Analyses of the reaction mixtures from cyclohexyltrimethylammonium and cyclopentyltrimethylammonium salts were performed on the Chromosorb column. The reaction mixture from the 3-pentyltrimethylammonium salts was analyzed for 2-pentene and methyl ethyl ether on a 6 ft × 1/8 in. column of 28% Flexol plasticizer 8N8 on Chromosorb P. Determination of the *cis*/*trans* ratio for 2-pentene was complicated by overlapping of the peaks for *cis*-2-pentene and methyl ethyl ether under the usual conditions (20 ft × 1/8 in. column of 20% adiponitrile on Chromosorb P). Diluting the reaction mixture with five to ten volumes of water, extracting with carbon disulfide, and washing the extracts well with water removed the ether without affecting the *cis*/*trans* ratio. Analyses for total olefin and methyl ether for all reactions in isopropyl and *t*-butyl alcohols were performed directly on the cooled reaction mixtures using a 10 ft × 1/8 in. column of 15% tri-*o*-cresyl phosphate on Chromosorb P 45–60. Analyses for *cis*- and *trans*-2-pentene were performed on the adiponitrile column either by direct injection of the reaction mixture or by acidification and extraction by carbon disulfide, followed by injection of the extract. The instrument was an Aerograph A-600 B Hy-Fi with flame ionization detector.

Control Experiments. Known mixtures of the appropriate olefin, tertiary amine, and alkyl methyl ether were analyzed by glpc and then subjected to the reaction conditions for the appropriate period of time. These simulated reaction mixtures were then analyzed again. Results are shown in Table IV.

Olefin Samples for Mass Spectrometry. Reactions in aqueous solution were run in stainless steel ampoules for at least five half-lives. The mixture was neutralized with 85% phosphoric acid and degassed on a high vacuum line, the stopcock to the vacuum closed, and the olefin distilled from the mixture at −25° (carbon tetrachloride slush) to a tube at −78° (Dry Ice–acetone) containing 4A molecular sieves. The olefin was then distilled three times between this tube and a mass spectrum sample tube. Reactions in sodium ethoxide were run in sealed glass ampoules. 2-Pentene was isolated and purified as above. Cyclopentene was isolated by neutralizing the reaction mixture with hydrochloric acid and distilling through a 3-in. column packed with steel wool until 0.5 ml was collected. This was purified by glpc on a 15 ft × 0.25 in. column of 15% tri-*o*-cresyl phosphate on Chromosorb P 45–60 using an Aerograph A-100 instrument and collecting the cyclopentene in a spiral trap cooled with liquid nitrogen. About five to eight injections of 70 μl each gave sufficient material for a good mass spectrum. Both 2-pentene and cyclopentene from the reactions in isopropyl and *t*-butyl alcohols were isolated in the same manner.

All mass spectrometric samples were degassed on a high vacuum line using at least three freeze–thaw cycles, and then distilled into sample tubes. About 15 mm of sample in a volume of 10 ml gave good mass spectra.

Standard mixtures of cyclohexene–cyclohexene-1-*d* and cyclopentene–cyclopentene-1-*d* were prepared on a vacuum line by allowing the cyclohexene at 0° (−40° for cyclopentene, using diethyl ketone slush) to expand into an evacuated manifold, followed by condensation (liquid nitrogen) into the sample tube. The process was repeated the appropriate number of times with each olefin to obtain the desired ratio in the mixture. The samples were degassed as above.

Determination of Mass Spectra. An Atlas CH-4 instrument was used. Background was checked prior to each sample. Two procedures were used. With spectra run at an ionizing potential of 70 eV, the ratio parent/(parent + 1) (82/83 for cyclohexene, 68/69 for cyclopentene) was referred to a plot of peak height ratio *vs.* composition obtained from mass spectra of the standard mixtures. In the other procedure mass spectra were determined at an ionizing potential of 9.0 eV (11.0 eV for 2-pentene) where fragmentation is negligible. The contribution from ^{13}C was subtracted from the parent + 1 peak,[35] and the peak ratio taken as the ratio of isotopic products. Where both procedures were used on the same sample, the results agreed within experimental error.

Hofmann Elimination Reaction on *cis*-Cyclohexyl-2-*d*-trimethylammonium *p*-Toluenesulfonate. A column of 50–60 mequiv of Dowex 2X-4 strong base resin (as hydroxide) was washed well with water and then with methanol. *cis*-Cyclohexyl-2-*d*-trimethylammonium *p*-toluenesulfonate in 50 ml of anhydrous methanol was passed through the column and the column washed with an additional 100 ml of methanol. The methanol solution was concentrated to an oil on a rotary evaporator. The oil was washed with 5 ml of water into a 25-ml distilling flask fitted with a nitrogen inlet. The flask was heated in an oil bath at 135° and the products were carried by the N_2 stream into a trap at −78°. The organic products were separated from the aqueous layers and dried over sodium sulfate. The cyclohexene (9%) was separated from the N,N-di-

Table IV. Control Experiments for Product Analyses

Base/solvent, °C[a]	% Olefin before and after[b] Cyclohexene	Cyclopentene	2-Pentene
HO^-/H_2O, 192	9.6	26.4	41.8
	9.6	19.8	26.0
$EtO^-/EtOH$, 115	12.4[c]	88.0	91.6
	12.6[c]	84.1	88.2
i-PrO^-/*i*-PrOH, 96	18.2	56.2	64.2
	19.1	55.3	63.5
t-BuO^-/*t*-BuOH, 70	16.6	52.4	67.0
	13.7	50.6	58.2

[a] Simulated reaction mixtures of olefin, tertiary amine, and alkyl methyl ether were heated with the appropriate base/solvent under the same conditions as the reactions reported in Table I. [b] Top figure in each entry gives analysis of the simulated product mixture before treatment under the reaction conditions; lower figure gives the results after. [c] No heating. This run was to test product extraction procedure.

(34) W. H. Saunders, Jr., and R. A. Williams, *J. Am. Chem. Soc.*, **79**, 3712 (1957).

(35) K. Biemann, "Mass Spectrometry: Organic Chemical Applications," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, p 63.

methylcyclohexylamine (91%) by glpc on a 10 ft × 0.25 in. column of 15% Carbowax 20M and 4% KOH on Chromosorb P 45–60.

The cyclohexene was prepared for mass spectrometric analysis as above. The isotopic composition was calculated from the mass spectrum as follows. Assuming identical ionization efficiencies for isotopic species and statistical loss of hydrogen and deuterium, (P − 1)/P should be identical for deuterated and undeuterated species. Then

$$\% \, d_1 = [((P - 1)/P)_{d_0}/((P - 1)/P)_{d_1}] \times 100$$

In this manner, 94.2% d_1 was found for the cyclohexene. In a control experiment, a known sample of cyclohexene-1-*d* (99% d_1 by nmr) was found to contain 99.1% d_1. The (P + 1)/P ratio was higher for the cyclohexene obtained in this elimination reaction than for either undeuterated cyclohexene or cyclohexene-1-*d*, suggesting the presence of d_2 species. After subtraction of the natural abundance of ^{13}C (6.71%), the intensities of the P + 1 and P peaks indicated 5.0% of $C_6H_8D_2$ and 95.0% of C_6H_9D, in good agreement with the 94.2% d_1 calculated from the (P − 1)/P ratio.

Alternative Electrocyclic Pathways. Photolysis and Thermolysis of Dimethylallene Dimers

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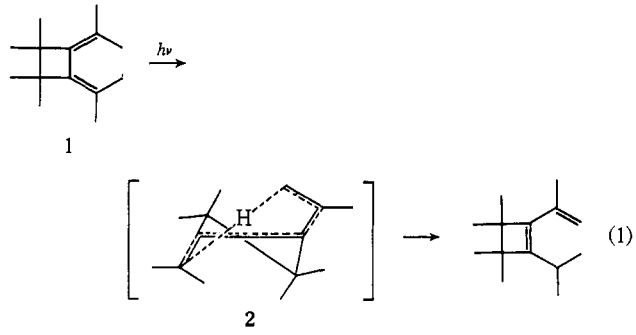
Abstract: The thermal and photochemical isomerizations of 1,2-diisopropylidenecyclobutane and 1-isopropylidene-2-methylene-3,3-dimethylcyclobutane are discussed. The results for both compounds can be interpreted in terms of a concerted 1,5-hydrogen shift, followed in the thermal case by electrocyclic opening of the resulting cyclobutene ring to give a cross-conjugated triene. The relative rates of the thermal and photochemical processes suggest that the initial sigmatropic rearrangement proceeds *via* an antarafacial transition state in the latter case, as predicted by orbital symmetry rules.

In spite of the widespread interest in electrocyclic reactions generated by the Woodward–Hoffmann orbital symmetry rules,[2] certain key points in the general theory have not yet been substantiated.[3] One of these concerns the stereochemistry of sigmatropic rearrangements, in which a σ-bonded substituent migrates from one position in a π-electron system to another.[4] In the absence of an available antisymmetric orbital in the migrating group, only antarafacial transfer is "allowed" for thermal 1,3 and 1,7 and photochemical 1,5 rearrangements (*i.e.*, those rearrangements having π components characterized by antisymmetric frontier orbitals). Among these three possibilities, 1,3 and 1,7 rearrangements are unattractive for testing purposes: concerted antarafacial transfer appears to be sterically impossible for the former and quite possibly preferred on simple steric grounds for the latter in acyclic systems.[5] 1,5 shifts, however, present a meaningful challenge to the theory. The antarafacial transition state in this case clearly must possess significantly higher strain energy than the suprafacial—in fact, the former has been dismissed as effectively "unachievable."[3] A demonstration of its existence would thus carry considerable quantitative significance.

Recently, we reported an exceptionally facile photochemical 1,5-hydrogen shift in tetramethylallene dimer (**1**), and suggested that steric influences in this compound should strongly favor an antarafacial process.[6]



We now wish to describe a study of the thermal and photochemical behavior of dimethylallene dimers **3** and **4** which lends further support to the feasibility of 1,5-antarafacial transition states, as well as presenting a stark contrast to the behavior of unsubstituted allene dimer.[7,8]

Results

Diene **3**, the major product from thermal dimerization of 1,1-dimethylallene,[9] displayed unexpected thermal stability; it was recovered essentially unchanged after several hours at 200°. However, at 260–270° it was slowly converted to a single volatile product, with surprisingly little polymer. The 100-MHz nmr spectrum of this product showed only an isopropyl group (τ 8.98, 6 H, d, J = 7 Hz; τ 7.62, 1 H, septet, J = 7 Hz, verified by double resonance), a vinyl methyl group

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