Steric Effects in Elimination Reactions. XII. The Reaction of Potassium *t*-Butoxide with Cyclic Tosylates. The Effect of Structure on the Rate and Direction of Eliminations in Cyclic Systems[1]

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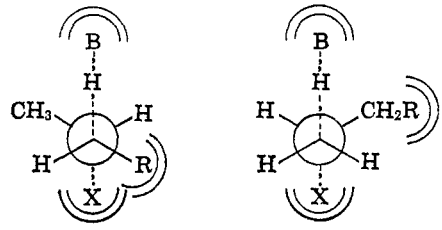
Abstract: Rates and isomer distributions in the elimination reactions of potassium *t*-butoxide in *t*-butyl alcohol at 50° with representative cycloalkyl and *trans*-2-methylcycloalkyl tosylates were determined in order to examine this reaction as a suitable probe for structural effects in E2 reactions and to test the relative advantages of the electronic and steric theories in accounting for the results. The rates of the simple cycloalkyl tosylates reveal only a modest change in the second-order rate constants with ring size ($k_2 \times 10^4$ mole^{-1} sec^{-1}): cyclopentyl, 7.81; cyclohexyl, 2.14; cycloheptyl, 2.34; cyclooctyl, 1.28. *trans*-2-Methylcycloalkanols were synthesized *via* the hydroboration of the 1-methylcycloalkenes and the tosylates were subjected to elimination. The 99% 3-, 1% 1-distribution in the first three members reveals stereoelectronic control requiring the usual *trans* coplanar arrangement of the atoms involved in the elimination stage. However, a 50–50 formation of the two olefins was observed in the cyclooctyl derivative, presumably a result of the greater flexibility of the eight-membered ring. Finally, the rates of elimination of *trans*-2-methylcyclopentyl (1.10) and -cycloheptyl tosylate (0.84) are only moderately slower than those of the parent compound, but the rate constant for the corresponding cyclohexyl compound, 0.024, is markedly depressed from the rate constant for the parent structure, 2.14. The slow rate in cyclohexyl system can be attributed to the energy required to place both the methyl and the tosyl groups in the axial position.

The observation that a regular and systematic shift from Saytzeff toward Hofmann eliminations can be achieved by an increase in the steric requirements of (a) the attacking base B, (b) the alkyl group R on the incipient double bond, and (c) the leaving group X, is readily understandable in terms of two transition states for the elimination reaction, I and II.[4,5] It is



I II

proposed that in the absence of major steric interactions, the reaction will proceed through transition state I to give the thermodynamically more stable of the two possible olefins. However, as the steric effects due to any one or combination of these three centers of steric interactions increase, the stability of transition state I will decrease to a greater extent than II, resulting in an increasing fraction of the reaction which will proceed through the latter to give the less stable of the two possible olefins.

This interpretation has been questioned, especially with regard to the ability of the leaving group X to influence the direction of elimination through its steric requirements. Instead it is argued that the change from Saytzeff to Hofmann elimination is controlled only by the electronic characteristics of the leaving group as they influence the amounts of bond breaking and bond making in the transition state.[6]

Surprising as it may seem, in view of the amount of discussion of the topic, there has been almost no systematic effort devoted to testing the electronic theory in its application to the problem of directive effects in eliminations involving simple acyclic and alicyclic systems by varying the polar characteristics of the leaving group while maintaining its steric requirements constant. Indeed, the one effort along that line which has appeared[7] established that there was no significant change in the direction of elimination by ethoxide of a number of 2-pentyl *para*-substituted benzenesulfonates, in spite of large variations in the rate of the elimination caused by the substituents.

Accordingly, we decided to undertake a study of the effect on the direction of elimination in both acyclic and alicyclic systems of varying the polar characteristics of the leaving group while maintaining its steric requirements constant, and of varying the steric requirements of the leaving group while maintaining its polar characteristics essentially constant. To this end the substituted benzenesulfonates appeared highly adaptable.[8]

The use of potassium *t*-butoxide in *t*-butyl alcohol[9] offers many advantages over the corresponding sodium or potassium ethoxide in ethanol. The *t*-butoxide

(1) Based on a thesis submitted by Richard L. Klimisch in partial fulfillment of the requirements for the degree of Doctor of Philosophy.
(2) Research assistant, 1961–1962, on a grant (G-6273) supported by the National Science Foundation.
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(4) H. C. Brown and I. Moritani, *J. Am. Chem. Soc.*, 78, 2203 (1956).
(5) H. C. Brown and R. L. Klimisch, *ibid.*, 88, 1425 (1966).
(6) For a detailed presentation of the electronic theory with pertinent literature references, see J. F. Bunnett, *Angew. Chem. Intern. Ed. Engl.*, 1, 225 (1962).
(7) A. K. Colter and R. D. Johnson, *J. Am. Chem. Soc.*, 84, 3289 (1962).
(8) Actually, our work in this direction had been initiated before the publication of the study by Colter and Johnson.[7] Fortunately, communication with Professor Colter revealed no significant overlap in our respective efforts.
(9) H. C. Brown and I. Moritani, *J. Am. Chem. Soc.*, 76, 455 (1954).

system is much faster, proceeding rapidly at 50°. Moreover, the incursion of the undesirable E1 reaction is far less than in the corresponding ethoxide system.[7]

On the other hand, the kinetic and stereochemical characteristics of the ethoxide system have been well explored.[6] It appeared desirable, therefore, that we examine these characteristics of the *t*-butoxide system before embarking upon an intensive study involving the primary goal of our investigation. Accordingly, we undertook a study of the rates and isomer distributions in the elimination reactions of potassium *t*-butoxide in *t*-butyl alcohol with representative cycloalkyl and *trans*-2-methylcycloalkyl tosylates.

Results

Rates of Cycloalkyl Tosylates. The rates were followed by mixing aliquots of standard solutions in *t*-butyl alcohol of the cycloalkyl tosylates and the *t*-butoxide, preequilibrated at 50.0°. At appropriate time intervals, aliquots were removed and titrated for residual base. The reactions followed simple second-order kinetics. The observed rate constants are summarized in Table I.

Table I. Rate Constants for the Reaction of Potassium *t*-Butoxide in *t*-Butyl Alcohol at 50.0° with the Cycloalkyl Tosylates

Tosylate	Rate constant, $k_2 \times 10^4$ l. mole^{-1} sec^{-1}
Cyclopentyl	7.81
Cyclohexyl	2.14
Cycloheptyl	2.34
Cyclooctyl	1.28

Synthesis of *trans*-2-Methylcycloalkanols. The hydroboration–oxidation of 1-methylcyclopentene and -cyclohexene provided a convenient synthesis of these pure *trans*-2-methylcycloalkanols.[10] In the case of 1-methylcycloheptene, the desired alcohol also was obtained, but there was present about 2–3% of an isomeric alcohol. This difficulty is greatly magnified in the hydroboration of 1-methylcyclooctene. Hydroboration–oxidation by the usual techniques[10] yielded a mixture of at least four products, whose similarity in properties and retention times indicated that they were isomeric secondary alcohols. This difficulty had been encountered previously.[10] Hydroboration with disiamylborane[11] was slower and the reaction was incomplete. Moreover, the product was also a mixture of the same isomeric alcohols. It was considered probable that the addition takes place in the normal *cis* manner, but that the isomerization reaction to which organoboranes are subject[12] takes the place with remarkable ease in the cyclooctyl system, placing the boron at different points around the ring. It follows from this interpretation that very short hydroboration times might circumvent the difficulty. Indeed, a total reaction time of 4 min for the hydroboration stage at −15° yielded 30% residual olefin, but the alcohol product exhibited a single peak in the gas chromatogram.

(10) H. C. Brown and G. Zweifel, *J. Am. Chem. Soc.*, **83**, 2544 (1961).
(11) H. C. Brown and G. Zweifel, *ibid.*, **83**, 1241 (1961).
(12) H. C. Brown and B. C. Subba Rao, *ibid.*, **81**, 6434 (1959); H. C. Brown and G. Zweifel, *ibid.*, **82**, 1504 (1960).

Products and Rates of the E2 Elimination. The *trans*-2-methylcyclooctanols were converted into the tosylates and subjected to the elimination procedure under the standard kinetic conditions. The products were analyzed by gas chromatographic analysis for the formation of isomeric 1- and 3-methylcycloalkenes. Within the limits of the gas chromatographic analysis, the yields were quantitative. The results are summarized in Table II.

Table II. Rate Constants and Product Distributions for the Reaction of Potassium *t*-Butoxide in *t*-Butyl Alcohol at 50.0° with the *trans*-2-Methylcycloalkanols

Tosylate	Methylcycloalkene, % 1-	Methylcycloalkene, % 3-	Rate constant, $k_2 \times 10^4$ l. mole^{-1} sec^{-1}
trans-2-Methylcyclopentyl	1	99	1.10
trans-2-Methylcyclohexyl	1	99	0.024
trans-2-Methylcycloheptyl	1[a]	99[b]	0.84
trans-2-Methylcyclooctyl	50	50	

[a] Observed, 2.5%. Correction estimated for presence of 3% of an isomeric alcohol in the starting material. [b] Structure assumed.

The rates of the elimination reactions were run under the same conditions used for the parent compounds. The available rate constants are listed in Table II.

Discussion

Perhaps the most unexpected feature of the rate data are the very minor differences in the relative reactivities of the parent ring compounds. In the acetolysis of the tosylates the observed rates at 25° exhibit a change in relative rate from a low of 1.00 for cyclohexyl to a high of 583 for the cyclooctyl.[13] Similarly, in the reaction of this range of cyclic ketones with sodium borohydride, the rates at 0° reveal a maximum of 1.00 for cyclohexanone to a low of $^1/_{2000}$ for cyclooctanone.[14] Finally, in the addition of disiamylborane to cycloalkenes, cycloheptene is 550 times as reactive as cyclohexene, with cyclopentene intermediate.[15]

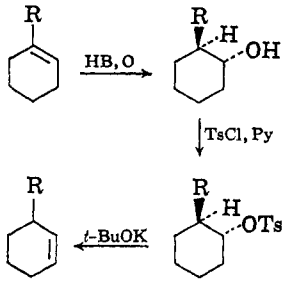
It may be that the relatively slight change in reactivity observed for the elimination reaction in the present study is merely a reflection of the enormous base strength of the system employed. In other words, the *t*-butoxide–*t*-butyl alcohol system may be one of low selectivity. Unfortunately, there do not appear to be any data for related E2 eliminations of this series of derivatives with which the results could be compared.

It should be pointed out that these eliminations are quite facile, being complete in several hours at 50°. This should contribute to the utility of this elimination procedure in synthetic work.

We had previously carried out the elimination reactions of *trans*-2-methylcyclopentyl and -cyclohexyl tosylates with isoamyloxysodium and diglyme at elevated temperatures.[10] The reactions proceeded to give the corresponding 3-methylcycloalkenes predominantly, but the reactions were much less stereoselective than the present system, possibly because of the higher temperatures and some competitive E1 reaction. It

(13) H. C. Brown and G. Ham, *ibid.*, **78**, 2735 (1956).
(14) H. C. Brown and K. Ichikawa, *Tetrahedron*, **1**, 221 (1957).
(15) H. C. Brown and A. W. Moerikofer, *J. Am. Chem. Soc.*, **83**, 3417 (1961).

appears, therefore, that the present system provides an unusually simple procedure for converting the 1-alkylcycloalkenes into the corresponding 3-alkylcycloalkenes for the five-, six-, and seven-membered ring systems (III).



III

The clean stereochemistry is important in establishing that eliminations in this system must possess the usual stereoelectronic preference for *trans* elimination, involving a transition state in which the hydrogen atom, the tosyl group, and the two carbon atoms of the incipient double bond all lie in a single plane (I and II).

Our study of the bimolecular elimination reaction in *trans*-2-methylcyclooctyl tosylate was greatly delayed by the initial synthetic difficulties. After these were solved, time did not permit a detailed study of the kinetics and mechanism. Indeed, we include our preliminary results here primarily as a warning to those who may wish to apply the reaction for synthetic applications that the clean stereoelectronic preference for *trans* eliminations exhibited by the five-, six-, and seven-membered ring systems is apparently lost in the cyclooctyl derivative. Possibly this is due to the flexibility of the larger ring and may be related to the ability of cyclooctyldimethylamine oxide to undergo elimination in two directions to give both *cis*- and *trans*-cyclooctene.[16] We plan to make a more detailed study of this phenomenon.

Even though the rate differences are small, it might be of interest to consider possible physical causes for the observed differences. Since the reaction evidently involves a clean *trans* elimination, this will require a 1,2-diaxial conformation in the cyclohexyl derivative for the groups undergoing elimination. The difference in energy between axial and equatorial tosylates has been estimated to be about 0.6 kcal mole^{-1},[17,18] entirely adequate to explain the observed rate difference.

The very slow rate observed for *trans*-2-methylcyclohexyl tosylate, as compared with the parent compound, may be accounted for similarly in terms of the combined energy (2.1 kcal/mole) required to place both the methyl group (1.5 kcal/mole)[19] and the tosyl group (0.6 kcal/mole) in the axial position. Also, there is a statistical factor of 2 arising from the presence of two *trans* hydrogens in cyclohexyl tosylate capable of undergoing elimination, whereas there is only one such hydrogen in the derivative.

The cycloheptane and cyclooctane rings are relatively strained, attributed to the severe crowding of the carbon–hydrogen moeities. Such crowding should be reduced in the corresponding olefins, so that on the basis of this consideration a rate enhancement might have been predicted. Possibly, if we were dealing with a reaction in which the rate were determined by the thermodynamic stability of the product, this might be observed. However, elimination of tosylate by *t*-butoxide is a reaction which is over on the Hofmann side.[20] Therefore, its rate is controlled primarily by factors other than the thermodynamic stability of the product.

Finally, in the case of *trans*-2-methylcycloheptyl tosylate, the statistical factor of 2 largely accounts for the observed decrease from the parent compound.

Experimental Section

Materials. The simple cyclanols were available from earlier studies.[13] The *trans*-2-methylcycloalkanols were prepared by hydroboration–oxidation, as described below, of the 1-methylcycloalkenes, readily prepared by the dehydration of the tertiary alcohols, prepared from the ketones and methylmagnesium iodide. The alcohols were converted into the tosylates by the usual pyridine technique. The identity of the compounds was confirmed by agreement of the melting point or n^{20}D values with the literature, or by elementary analysis.

The purification of the *t*-butyl alcohol and the preparation of the solutions of potassium *t*-butoxide in *t*-butyl alcohol were carried through as described earlier.[5]

***trans*-2-Methylcycloalkanols.** The hydroboration of 1-methylcyclopentene and 1-methylcyclohexene has been described previously.[10]

1-Methylcycloheptene (10 g, 0.104 mole) in tetrahydrofuran cooled to 0° was treated with 40 ml of 1.6 *M* borane in tetrahydrofuran (0.064 mole). Water was added to decompose excess hydride and the product was oxidized by adding 13.5 ml of 3 *N* sodium hydroxide, followed by 13.5 ml of 30% of hydrogen peroxide. There was obtained 9.5 g (0.074 mole, 71%) of *trans*-2-methylcycloheptanol, bp 95° (25 mm), n^{20}D 1.4721. Gas chromatographic analysis showed the presence of 2–3% of an isomeric alcohol.

1-Methylcyclooctene was purified carefully until gas chromatographic examination indicated its homogeneity, n^{20}D 1.4670. Application of the above hydroboration procedure yielded a product whose gas chromatogram indicated the presence of four isomeric alcohols: A, 12%; B, 60%; C, 4%; D, 24%. From the similarity in their properties and retention times, it was concluded that these must be isomers. (The presence of the tertiary was excluded by direct comparison.) The following modified procedure yielded the desired product in essentially pure state. 1-Methylcyclooctene (3.86 g, 14.8 mmoles) was dissolved in dry tetrahydrofuran and cooled to −15°. Then 8.2 ml of 1.92 *M* borane–tetrahydrofuran solution was added rapidly within 2 min. The

Table III. Representative Rate Data for the Second-Order Reactions of Cycloalkyl Tosylates with Potassium *t*-Butoxide in *t*-Butyl Alcohol at 50.0°

Cyclopentyl tosylate[a]		Cyclooctyl tosylate[b]	
a, 0.191 *M* b, 0.456 *M*		a, 0.176 *M* b, 0.455 *M*	
Time, min	*x*	Time, min	*x*
0	0.000	0	0.000
24	0.038	18	0.011
31	0.051	41	0.018
41	0.071	67	0.036
48	0.088	85	0.042
56	0.099	121	0.066
∞	0.191	155	0.087
		∞	0.176

[a] $k_2 = 7.51 \times 10^{-4}$ l. mole^{-1} sec^{-1}. [b] $k_2 = 1.28 \times 10^{-4}$ l. mole^{-1} sec^{-1}.

(16) A. C. Cope, R. A. Pike, and C. F. Spencer, *J. Am. Chem. Soc.*, 75, 3212 (1953).
(17) E. L. Eliel and R. S. Ro, *ibid.*, 79, 5995 (1957).
(18) S. Winstein and N. J. Holness, *ibid.*, 77, 5562 (1955).
(19) E. L. Eliel and M. N. Rerick, *ibid.*, 82, 1367 (1960).
(20) For example, 2-pentyl tosylate yields 73% 1-, 27% 2-pentene.[4]

vigorous reaction slowed noticeably after an additional 2 min. The reaction mixture then was hydrolyzed immediately by the injection of 5 ml of water in 10 ml of tetrahydrofuran. Oxidation in the usual manner yielded a product whose gas chromatogram showed the presence of 30% residual olefin and 70% of a single peak, corresponding to the isomer B above. (Since the individual peaks were not well resolved, we cannot exclude the possibility that small quantities of the isomeric alcohols were present.) Distillation yielded 1.0 g of olefin, bp 55° (60 mm), n^{20}D 1.4690, 25%, and 1.1 g of alcohol, bp 85° (12 mm), n^{20}D 1.4807. Gas chromatographic examination of the olefin indicated the presence of 5% of an isomeric material, corresponding to the 3-methylcyclooctene indicated in the elimination.

Product Studies. The elimination reactions were carried out as reported earlier for the halides.[5] The isomeric compositions were established by gas chromatographic analysis. Authentic samples of 1- and 3-methylcyclopentene and -cyclohexene were available. In the higher members, authentic samples of 1-methylcycloheptene and 1-methylcyclooctene were available. It was assumed that the second peak in the elimination product was the 3- isomer.

Rate Studies. The sulfonate was weighed in a 20-ml reaction flask. Ten milliliters of pure *t*-butyl alcohol at 50° was added, and the solution was equilibrated at 50°. The 1.0 *M* *t*-butoxide solution also was equilibrated at this temperature. The reaction was initiated by introducing 10.0 ml of the base solution into the ampoule and mixing by vigorous shaking. Thus the initial concentrations were 0.5 *M* in base and 0.15 to 0.25 *M* in the tosylate. At appropriate intervals of time, 2.00-ml aliquots were removed and quenched in 15 ml of acetone containing 1.00 ml of 1.00 *M* hydrochloric acid to neutralize the original quantity of base. The excess acid present was then titrated with saturated 0.1 *M* sodium hydroxide. Several aliquots were allowed to go to completion and the infinity titers obtained. Tests indicated that the observed rate constants were reproducible to ±3%.

The rates were determined graphically, using the expression

$$k_t = \frac{1}{b - a} \ln \frac{a(b - x)}{b(a - x)}$$

where a is the initial concentration of the sulfonate ester, b is the initial concentration of *t*-butoxide, and x is the amount reacted in time t. Representative rate data are reported in Table III.

Organoboranes. III. Isomerization of Organoboranes Derived from the Hydroboration of Acyclic Olefins

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Contribution from the Richard B. Wetherill Laboratory of Purdue University, Lafayette, Indiana. *Received October 16, 1965*

Abstract: Organoboranes prepared from internal acyclic olefins *via* hydroboration with the usual slight excess of reagent undergo rapid isomerization at temperatures of 100 to 160° to place the boron atom predominantly at the terminal position. It was established that the isomerization reaction is markedly catalyzed by a small excess of diborane in the reaction mixture. The scope and rate of the isomerization reaction was explored with a number of representative acyclic olefins. It was established that the boron atom readily moves down the chain past a single branch, but not past a quaternary carbon atom. Hydroboration–isomerization of the organoboranes from 2-methyl-1-butene, 2-methyl-2-butene, and 3-methyl-1-butene yields the same equilibrium mixture of organoboranes with 59% 3-methyl-1-bora- and 39% 2-methyl-1-borabutane moeities. The preference of the boron atom for the less crowded of the two primary positions is attributed to the operation of steric effects. A mechanism is proposed for the isomerization reaction involving successive *cis* eliminations of boron–hydrogen moeities from the organoborane at relatively moderate temperatures, followed by additions, rapidly achieving thermodynamic equilibrium among the possible organoboranes (except where the isomerization involves moving the boron atom past a quaternary carbon). The boron atom ends up preferentially in the least sterically crowded position of the alkyl group. Internal olefins are synthesized readily from tertiary alcohols prepared *via* the Grignard reaction. Application of the hydroboration–isomerization reaction to such olefins makes possible a number of promising syntheses of primary alcohols, amines, and related derivatives.

Organoboranes, readily accessible *via* hydroboration of olefins, are finding considerable application as useful intermediates in organic synthesis.[1] Thus, oxidation of organoboranes with alkaline hydrogen peroxide yields alcohols whose stereochemistry can be deduced in a predictable manner.[2] The noncatalytic hydrogenation of olefins *via* protonolysis of organoboranes with organic acids takes place without rearrangement, even in the case of terpenes.[3] Moreover, the reaction permits the introduction of one or two deuterium atoms in sterically defined positions.[4] Treatment of organoboranes with silver nitrate under alkaline conditions provides a versatile new procedure for the formation of carbon-to-carbon bonds.[5] Finally, the reaction of organoboranes with hydroxylamine-*O*-sulfonic acid provides a convenient synthetic procedure to proceed from a particular olefin to the corresponding amine.[6]

It was previously observed that organoboranes undergo isomerization on heating.[7,8] However, isomeri-

(1) For a review with pertinent references, see H. C. Brown, "Hydroboration," W. A. Benjamin, Inc., New York, N. Y., 1962.
(2) H. C. Brown and G. Zweifel, *J. Am. Chem. Soc.*, 83, 2544 (1961).
(3) H. C. Brown and K. Murray, *ibid.*, 81, 4108 (1959), and unpublished observations of G. Zweifel.
(4) H. C. Brown and K. J. Murray, *J. Org. Chem.*, 26, 631 (1961).
(5) H. C. Brown and C. H. Snyder, *J. Am. Chem. Soc.*, 83, 1003 (1961).
(6) H. C. Brown, W. R. Heydkamp, E. Breuer, and W. S. Murphy, *ibid.*, 86, 3565 (1964).
(7) G. F. Hennion, P. A. McCusker, E. C. Ashby, and A. J. Rutkowski, *ibid.*, 79, 5190 (1957).
(8) H. C. Brown and B. C. Subba Rao, *J. Org. Chem.*, 22, 1136 (1957); H. C. Brown and B. C. Subba Rao, *J. Am. Chem. Soc.*, 81, 6434 (1959).