phenylcyclobutene, along with other olefinic resonances. No transient abnormalities were apparent in the position of the 1-phenylcyclobutene absorption.

Reactions with Tri-*n*-butyltin Hydride.—In an nmr tube, there were placed 0.55 ml of a 1.2 *M* stock solution of tri-*n*-butyltin hydride in benzene, 0.144 g (0.59 mmol) of 1-chloro-4-bromo-1-phenyl-1-butene, 0.0016 g of azobisisobutyronitrile, and 0.020 ml of tetrahydrofuran (as an internal reference). The sample was heated at 85° until the nmr spectrum showed complete disappearance of the Sn–H band (δ 2.24 ppm upfield from benzene). The nmr spectrum showed partial disappearance of the chlorobromide olefinic triplet δ 1.32 ppm upfield from benzene, and replacement by a new triplet at δ 1.28 ppm. By gas chromatography, components of the mixture were separated and identified as *cis*-1-phenyl-1-butene (by retention time), *trans*-1-phenyl-1-butene (by nmr), *cis*-1-chloro-1-phenyl-1-butene (by nmr), *trans*-1-phenyl-1-chloro-1-butene (by nmr), and cis and *trans* isomers of the starting halide (by retention time). The ratio of *trans*-1-phenyl-1-butene to *trans*-1-chloro-1-phenyl-1-butene was about 0.1. Reactions at lower concentrations gave less complete reduction and apparent side reactions.

A similar attempt at reduction of 1-phenyl-1-butene led to no disappearance of either hydride or alkene, based on nmr observation. With 1-chloro-1-phenyl-1-butene, disappearance of the hydride occurred, and a product was formed which was identified by nnr and by its retention time as *n*-butylbenzene. 1-Phenyl-1-butene was formed in less than 10% of the amount of *n*-butylbenzene.

A competitive reaction was carried out with 1-bromobutane and 1-phenyl-1-chloro-1-butene. No 1-phenyl-1-butene was found by gas chromatography.

Registry No.—**1b**, 28273-63-4; 4,4-dideuterio-**1b**, 28273-64-5; **2**, 3365-26-2; *cis*-**3**, 28273-67-8; *trans*-**3**, 3365-30-8; *cis*-**4**, 1560-0-94; *trans*-**4**, 1005-64-7.

Conformational Analysis. LXXII. Solvolysis Studies with the 5-Phenylcyclooctanol System[1-3]

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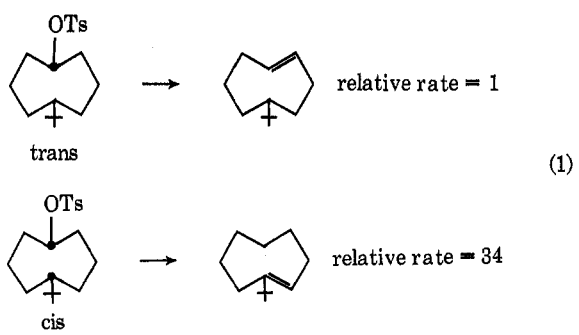
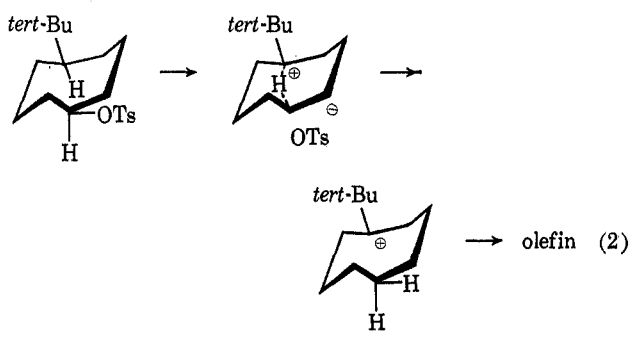
A rate and product study has been carried out on the solvolysis in aqueous ethanol of *cis*- and *trans*-5-phenylcyclooctanol tosylate and the corresponding *p*-anisyl derivatives. The results indicate that in these compounds, and by inference other cyclooctyl derivatives, neighboring group participation is not of importance in determining solvolysis rates. The rather fast rates observed, and rate differences between isomers, are attributed to steric effects.

Transannular hydride shifts across medium rings have been known for almost 20 years.[5] In an effort to understand the stereochemical features of these shifts, the solvolyses of a number of different stereoisomers of three- and five-substituted cyclooctane compounds were studied.[6-10] It was found that *cis*-5-*tert*-butylcyclooctyl tosylate solvolyzed much more rapidly than did the trans isomer, and the product obtained from the cis isomer was mostly rearranged olefin, while that from the trans isomer was mostly the olefin corresponding to simple elimination[6-8] (eq 1). From



(1)

examination of the probable conformations of the molecules, participation by the transannular hydrogen of the cis isomer in the rate-determining step appeared to be indicated (eq 2). Only the cis isomer has a geometry



(2)

which will permit such participation. The trans isomer reacts without participation, and without much rearrangement. However, the difference in rate between the cis and trans isomers was only a factor of 34, and not large enough to be convincingly attributed to neighboring group participation. Since the *tert*-butyl group is obviously quite bulky, it may well deform appreciably the cyclooctane ring to which it is attached, and hence the earlier experiments did not conclusively rule out the possibility that the unusual rate for the cis isomer was a result of conformational distortion of the ring by the *tert*-butyl group, rather than of neighboring group participation in the usual sense. The rearranged product in that case would have to be formed by a trans-

(1) Paper LXXI: M. T. Tribble, M. A. Miller, and N. L. Allinger, *J. Amer. Chem. Soc.*, in press.

(2) Abstracted in part from the Ph.D. Dissertation of C. L. N., presented to Wayne State University, Sept 1966.

(3) Supported in part by Grant No. GP 15263 from the National Science Foundation.

(4) Correspondence regarding this paper should be directed to this author at the Department of Chemistry, University of Georgia.

(5) (a) A. C. Cope, S. W. Fenton, and C. F. Spencer, *J. Amer. Chem. Soc.*, **74**, 5884 (1952); (b) V. Prelog and K. Schenker, *Helv. Chim. Acta*, **35**, 2044 (1952). For reviews, see E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill, New York, N. Y., 1962, p 252; A. C. Cope, M. M. Martin, and M. A. McKervey, *Quart. Rev., Chem. Soc.*, **20**, 119 (1966).

(6) N. L. Allinger and S. Greenberg, *J. Amer. Chem. Soc.*, **84**, 2394 (1962).

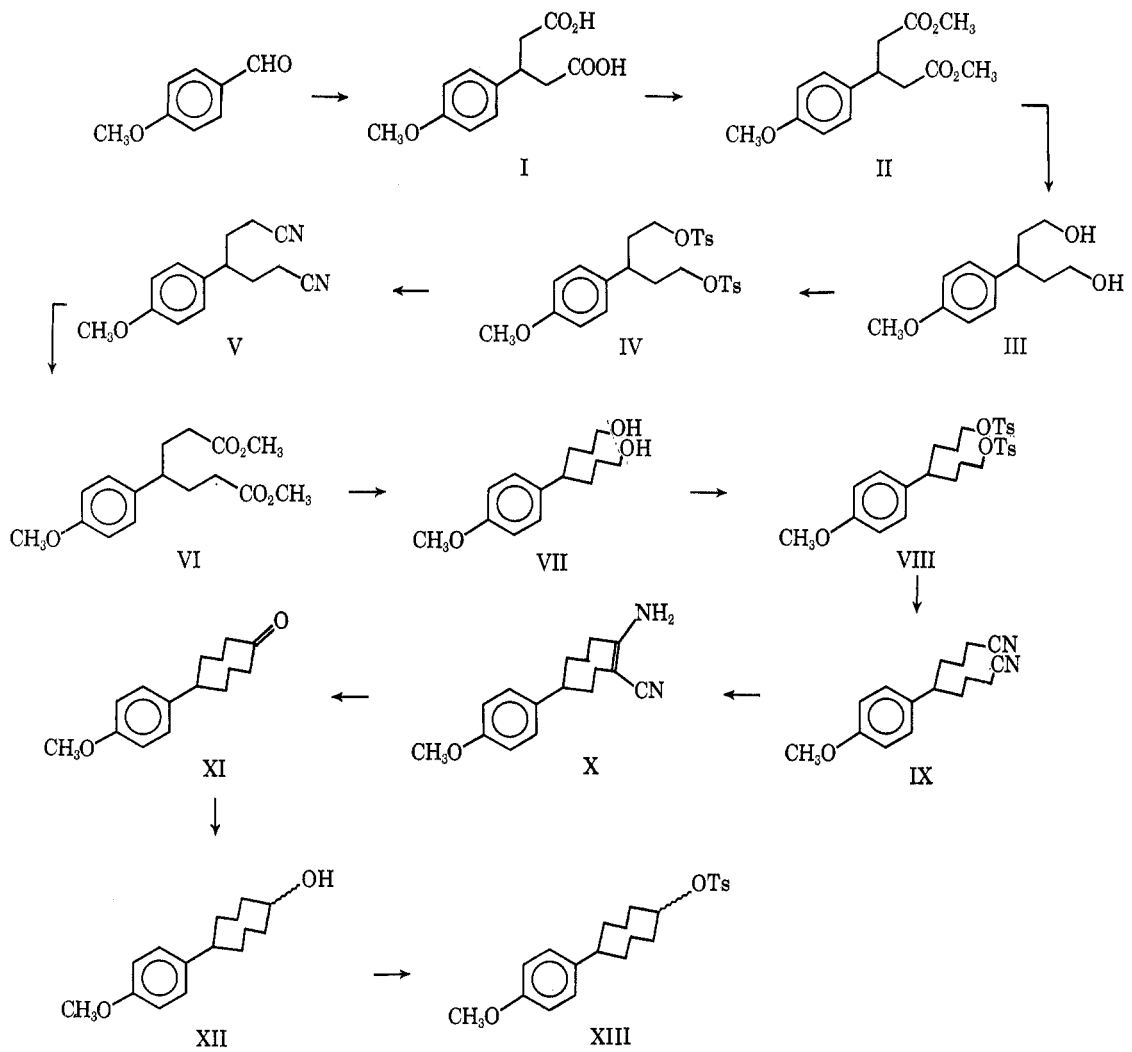
(7) N. L. Allinger and W. Szkrybalo, *Tetrahedron*, **24**, 4699 (1968).

(8) N. L. Allinger, I. Lillien, C. L. Neumann, H. Sugiyama, and N. A. Pamphilis, *J. Org. Chem.*, **35**, 1255 (1970).

(9) A. C. Cope and R. B. Kinnel, *J. Amer. Chem. Soc.*, **88**, 752 (1966).

(10) A. C. Cope and D. M. Gale, *ibid.*, **85**, 3743 (1963).

CHART I



annular hydride ion transfer subsequent to the rate-determining step.

In order to differentiate steric and electronic effects in such a case, a convenient method involves carrying out parallel experiments on a phenyl compound, and on the *p*-anisyl derivative. The steric effects are essentially the same for these two, but the *p*-anisyl compound is able to supply electrons to a much higher degree if required to do so by an electronic demanding transition state. One might therefore predict that since a phenyl group has approximately the same, or somewhat smaller, bulk as a *tert*-butyl group[11] (depending on how it is measured), the 5-phenylcyclooctyl derivatives would solvolyze at rates similar to those of the corresponding *tert*-butyl compounds if neighboring group participation were unimportant in the transition state, but the cis isomer should be much faster if it were important. The *cis*-5-*p*-anisyl compound should either solvolyze at the same rate as the phenyl derivative, which would indicate no participation, or at a greatly accelerated rate, which would indicate a high degree of participation, or somewhere in between, while the trans isomer should have a rate similar to *trans*-phenylcyclooctyl tosylate in any case.

Synthesis

During the early stages of this work, a paper by Cope[9] appeared, in which the syntheses of the isomeric 5-phenylcyclooctyl tosylates were described. We prepared a mixture of the two isomers by substantially the method described by Cope. There was no particular need to separate them; so we determined the rates of the two isomers directly from the mixture. Since the cis isomer solvolyzes over five times as fast as the trans isomer, this was easy to do experimentally. The analogous 5-anisylcyclooctyl tosylates were then prepared, by the scheme outlined on Chart I. Anisylaldehyde was converted to 3-anisylglutaric acid (I) *via* a Knovenagel reaction with ethyl acetoacetate, followed by basic cleavage (a reverse Claisen reaction) which yielded the acid. The acid I was esterified and reduced to 3-anisylpentane-1,5-diol (III) with lithium hydride. Chain extension of this diol *via* the tosylate IV and treatment with cyanide yielded 4-anisylpimelonitrile (V), which was converted to the ester VI, which was in turn reduced to 4-anisylheptane-1,7-diol (VII). Another chain extension *via* the tosylate VIII gave 5-anisylazelanitrile (IX). This compound was cyclized to yield 2-cyano-5-anisylcyclooctenylamine (X) by means of a Thorpe–Ziegler cyclization. Hydrolysis and decarboxylation furnished 5-anisylcyclooctanone (XI). The ketone was reduced with lithium aluminum hydride to give a mixture of the *cis*- and *trans*-5-*p*-anisylcyclooctanols (XII). The tosylates XIII were pre-

(11) J. A. Hirsch, *Top. Stereochem.*, **1**, 207 (1967).

TABLE I

THE PRODUCT ANALYSIS FROM THE SOLVOLYSIS OF TOSYLATES IN 80% ETHANOL

Compound solvolyzed	Rearranged products, % Olefin	Rearranged products, % Alcohol	Unrearranged products, % Olefin	Unrearranged products, % Alcohol	Other products, %
cis-5-*tert*-Butylcyclooctyl tosylate	100	0	0	0	0
trans-5-*tert*-Butylcyclooctyl tosylate[a]	5–10	0	45–50	42	3
5-Phenylcyclooctyl tosylate (cis/trans ratio 1.32)	34	8	46	9	3
5-Anisylcyclooctyl tosylate (cis/trans ratio 2.3)	28	23	42	3	4
cis-3-*tert*-Butylcyclooctyl tosylate	10			40% *cis*-3-*tert*-butylcyclooctanol	50% ether
Cyclooctyl tosylate			53	47	

[a] Shown to contain 8% of the cis isomer during solvolysis.

pared and solvolyzed in the usual way; the solvolysis products are given in Table I. For comparison purposes, a number of other cyclooctyl tosylates were solvolyzed, or had previously been solvolyzed,[8] under identical conditions (in 80% ethanol, 25°, and pH 8.4). The relative rates of these compounds are summarized in Table II.

TABLE II

RATES OF SOLVOLYSIS OF CYCLOOCTYL TOSYLATES IN 80% ETHANOL–20% WATER AT 25° AND pH 8.4

Compound	Absolute rate, sec^{-1}	Rel rate
Cyclooctyl tosylate	1.26×10^{-4}	39[b]
cis-5-*tert*-Butylcyclooctyl tosylate	9.97×10^{-4}	312[b]
trans-5-*tert*-Butylcyclooctyl tosylate	2.92×10^{-5}	9.1[b]
cis-5-Phenylcyclooctyl tosylate	7.06×10^{-5}	22
trans-5-Phenylcyclooctyl tosylate	1.32×10^{-5}	4.1
cis-5-*p*-Anisylcyclooctyl tosylate	8.01×10^{-5}	25
trans-5-*p*-Anisylcyclooctyl tosylate	9.25×10^{-6}	2.9
cis-3-*tert*-Butylcyclooctyl tosylate	5.46×10^{-4}	171[b]
2-Pentyl tosylate[a]	3.2×10^{-6}	1[b]

[a] A rate of 2.94×10^{-6} sec^{-1} has been found under similar conditions: S. H. Liggero, J. J. Harper, P. v. R. Schleyer, A. P. Krapcho, and D. E. Horn, *J. Amer. Chem. Soc.*, **92**, 3789 (1970). [b] Reference 8.

Results and Discussion

The products of the solvolysis of *cis*- and *trans*-5-phenylcyclooctyl tosylate (in formic acid) were studied earlier by Cope and Kinnel.[9] They found that various alcohols were obtained as minor products; the cis isomer gave mostly the olefin obtained by hydride migration from C-5, while the trans isomer gave mostly unrearranged olefin, analogous to what was found earlier with the 5-alkylcyclooctyl tosylates.[6–8,10] In general our results seem to agree with Cope's, although our alcohol/olefin ratio was a little larger, as would be expected from the higher nucleophilicity of the solvent we employed. We did not separate our isomeric tosylates for separate study, but the products obtained are consistent with the cis isomer yielding mostly rearranged olefin and the trans isomer yielding mostly olefin without rearrangement (Table I).

The relative solvolysis rates of the tosylates are more informative than the reaction products. Looking now at Table II, we might first compare the relative rates of *trans*-5-*tert*-butylcyclooctyl tosylate (9.1) with the corresponding phenyl compound (4.1). The rates differ by only about a factor of 2, indicating that the steric effects are similar and the electronic effect is negligible, or there is some fortuitous cancellation of the two effects. Looking at the corresponding cis isomers, the 5-*tert*-butylcyclooctyl tosylate has a solvolysis rate of 312, compared to a *cis*-5-phenylcyclooctyl tosylate rate of 22. Any participation by the phenyl would be expected to accelerate the rate, and since the phenyl compound solvolyzes *more slowly* by a factor of 14, any acceleration must be pretty small, and more than counterbalanced by a steric or inductive effect. Looking only at the rates of the phenylcyclooctyl tosylates, then, one would conclude that there is no evidence for neighboring group participation by the phenyl.

If we now compare the *p*-anisylcyclooctyl tosylates with the corresponding *p*-phenyl compound, we notice that for the trans isomers the phenyl (rate 4.1) is just slightly faster than the *p*-anisyl (rate 2.9), a difference too small to be of much importance. Looking at the corresponding cis isomers, the *p*-anisyl (rate 25) is just slightly faster than the *p*-phenyl (rate 22). We thus conclude that there is no detectable neighboring group participation in the transition state in any of these phenyl- or anisyl-substituted cyclooctyl tosylates.

It might be argued that perhaps the phenyl group cannot achieve planarity with the carbonium ion being generated by hydride migration, and therefore it is unable to become involved in neighboring group participation in the transition state. While proof that this is not the case is lacking, it seems improbable that at least a small effect would not be observed if hydride migration is concerted with the solvolysis. For it not to occur, the phenyl would have to remain at almost exactly 90° to the plane of the carbonium ion being generated by hydride migration. This seems highly improbable. The large rate acceleration (34 times) brought about by the *cis*-5-*tert*-butyl group therefore seems best interpreted as a steric effect, that is, a relief of strain of some sort in the transition state. It might be noted that the *cis*-3-*tert*-butyl group also brings about a substantial rate acceleration (although not so large as in the 5-*tert*-butyl case), but here participation by hydride is unlikely, as the product obtained shows no hydride migration from the 3 position.

Since we conclude that neighboring group participation is negligible in the transition state, we must also conclude that the *cis*- and *trans*-cyclooctyl derivatives do not go through a common intermediate, since they give different products. The cis isomer is geometrically more favorably disposed toward transannular hydride transfer, and it undergoes such transfer in a fast

step subsequent to the rate-determining step. The corresponding trans isomer does not undergo much hydride transfer, and ordinary elimination–substitution is observed.

Experimental Section

3-*p*-Anisylglutaric Acid (I).—To a mixture of 119.9 g of anisaldehyde and 225 g of ethyl acetoacetate was added dropwise 20 ml of piperidine, with stirring. After standing overnight the mixture had solidified. A solution of 200 g of sodium hydroxide in 1 l. of absolute ethanol was added to the solid product. After the solid had dissolved, the solution was heated under reflux with stirring for 24 hr. The majority of the ethanol was then evaporated, and 1 l. of ether was added to the cooled residue. The precipitate was filtered, washed with ether, and dissolved in 500 ml of water. Acidification with concentrated hydrochloric acid yielded the crude product, 165 g, mp 160–162°. Recrystallization from ethyl acetate gave crystals, mp 165–167° (lit.[12] mp 165°).

Anal. Calcd for $C_{12}H_{14}O_5$: C, 60.50; H, 5.92. Found: C, 60.71; H, 6.02.

Dimethyl 3-*p*-Anisylglutarate (II).—A mixture of 165 g of crude acid I, 500 ml of methanol, 1 l. of benzene, and 20 ml of concentrated sulfuric acid was heated under reflux for 72 hr. After the reaction mixture was cooled, 1 l. of water was added, the organic layer was separated, and the aqueous layer was extracted with benzene. The combined organic portions were washed again with water and dried over magnesium sulfate. The benzene was evaporated and the product was distilled, bp 164–165° (1 mm), yield 151 g, $n^{25}D$ 1.5073 [lit.[12] 205–210° (20 mm), mp 42°].

Anal. Calcd for $C_{14}H_{18}O_5$: C, 63.15; H, 6.81. Found: C, 63.41; H, 6.85.

3-*p*-Anisylpentane-1,5-diol (III).—To a stirred solution of 38 g of lithium aluminum hydride in 1 l. of dry ether was added dropwise 151 g of II in 450 ml of dry ether. The reaction mixture was refluxed for 2 hr, cooled, and treated with 500 ml of saturated aqueous ammonium chloride with stirring and cooling. The precipitate was filtered and washed with ether. The ether layer was separated and the aqueous layer was extracted with ether. The combined ether solutions were dried over magnesium sulfate and the solvent was evaporated. The residual solid was washed with a small amount of benzene to give crystals, mp 69–70°, yield 114 g. Recrystallization from benzene gave crystals, mp 70–71°.

Anal. Calcd for $C_{12}H_{18}O_3$: C, 68.55; H, 8.63. Found: C, 68.57; H, 8.90.

3-*p*-Anisylpentane-1,5-diol Bis(*p*-toluenesulfonate) (IV).—To an ice-cooled solution of 2 g of III in 10 ml of dry pyridine was added 2 g of *p*-toluenesulfonyl chloride in 5 ml of pyridine. The reaction mixture was stirred in an ice bath for 2 hr. To the reaction mixture was then added 30 ml of ice water and 30 ml of ether. The ether layer was separated and washed with ice-cold 2 *N* hydrochloric acid, water, and saturated sodium bicarbonate solution. After drying over magnesium sulfate, the ether was removed, and the residue was recrystallized from methanol to yield 2.3 g of product, mp 64.5–65°.

Anal. Calcd for $C_{26}H_{30}O_7S_2$: C, 60.21; H, 5.83. Found: C, 60.46; H, 5.96.

4-*p*-Anisylpimelonitrile (V).—A mixture of 80 g of IV, 20 g of potassium cyanide, and 200 ml of 95% ethanol was heated under reflux with stirring for 16 hr. After most of the ethanol had been removed by distillation, 200 ml of water was added to the mixture, which was then extracted with ether. The ether layer was washed with water and dried over magnesium sulfate, and the ether was removed under reduced pressure. The oily residue was recrystallized from ethanol twice to yield 30 g of crystals, mp 60.5–61°.

Anal. Calcd for $C_{14}H_{16}ON_2$: C, 73.66; H, 7.06; N, 12.27. Found: C, 73.57; H, 7.21; N, 12.11.

Dimethyl 4-*p*-Anisylpimelate (VI).—A mixture of 30 g of V, 200 ml of methanol, and 10 ml of concentrated sulfuric acid was heated under reflux for 7 days. After most of the methanol was evaporated, the residual oil was poured into water and extracted with ether. The ether layer was washed with water and saturated sodium bicarbonate and dried over magnesium sulfate. After concentration, the residue was distilled, bp 163–164° (0.7 mm), $n^{25}D$ 1.5031, yield 34 g.

Anal. Calcd for $C_{16}H_{22}O_5$: C, 65.29; H, 7.53. Found: C, 65.31; H, 7.71.

4-*p*-Anisylheptane-1,7-diol (VII).—A solution of 34 g of VI in 170 ml of dry tetrahydrofuran was added dropwise to a stirred solution of 10 g of lithium aluminum hydride in 600 ml of dry ether. The reaction mixture was heated under reflux for 3 hr, cooled, and treated with 200 ml of saturated ammonium chloride with cooling and stirring. The precipitate was filtered and washed with ether. The organic layer was separated, and the aqueous layer was extracted with ether. The combined ether extracts were dried over magnesium sulfate and concentrated, yield 24.1 g, mp 41–42°. Recrystallization from ether in a Dry Ice–acetone bath gave mp 51–52°.

Anal. Calcd for $C_{14}H_{22}O_3$: C, 70.56; H, 9.30. Found: C, 70.81; H, 9.31.

5-*p*-Anisylazelanitrile (IX).—To a stirred solution of 1 g of VII in 10 ml of dry pyridine, in an ice–salt bath, 1.8 g of toxyl chloride was slowly added. The reaction mixture was stirred for 2 hr at 0° and treated with 20 ml of water. The aqueous solution was extracted with ether. The ether layer was washed with ice-cold 2 *N* hydrochloric acid, water, and saturated sodium bicarbonate and was dried over magnesium sulfate. After concentration, 2 g of the oily ditosylate VIII, which failed to crystallize, was obtained. A solution of 2 g of the tosylate and 4 g of potassium cyanide in 40 ml of 95% ethanol was refluxed with stirring for 17 hr. The reaction mixture was treated with 200 ml of water and extracted with ether. The ether layer was washed with water and dried over magnesium sulfate. After concentration, 0.9 g of crude crystal was obtained, mp 53–60°. Recrystallization several times from methanol gave crystals, mp 78–79°.

Anal. Calcd for $C_{16}H_{20}ON_2$: C, 74.97; H, 7.86; N, 10.93. Found: C, 74.73; H, 8.02; N, 11.14.

2-Cyano-5-*p*-anisylcyclooctenylamine (X).—To a well-stirred, boiling solution of sodium methylanilide, which was prepared from 12 g of sodium, 40.4 g of naphthalene, and 70 g of *N*-methylaniline in 800 ml of ether, a solution of 10.6 g of IX in 1.9 l. of dry ether was added dropwise through the high-dilution apparatus[13] over a period of 3 days. The reaction mixture was heated under reflux for 3 hr, cooled, and treated with 500 ml of water with stirring and cooling. The ether layer was separated and the aqueous layer was extracted with ether. After evaporation of solvent from the combined ether layers, the residue was steam distilled to remove methylaniline and dihydronaphthalene. The material remaining was extracted with chloroform, and the chloroform solution was dried over magnesium sulfate. Evaporation of the solvent gave a residue, mp 85–90°. Recrystallization from methanol gave 7.2 g of crystals, mp 136–137°.

Anal. Calcd for $C_{16}H_{20}ON_2$: C, 74.97; H, 7.86; N, 10.93. Found: C, 74.85; H, 8.01; N, 10.79.

5-*p*-Anisylcyclooctanone (XI).—The ketone was prepared by heating under reflux 4.8 g of X in 200 ml of 30% (volume) sulfuric acid for 17 hr with stirring. After cooling, the reaction mixture was extracted with chloroform, and the chloroform layer was washed with water. After drying over magnesium sulfate, the solution was evaporated to yield the crude ketone. Careful sublimation of this residue at 60° and 0.02 mm yielded white crystals, mp 35°, yield 2 g.

Anal. Calcd for $C_{15}H_{20}O$: C, 77.55; H, 8.68. Found: C, 77.44; H, 8.62.

5-*p*-Anisylcyclooctanol (XII).—To a slurry of 80 mg of lithium aluminum hydride in 25 ml of dry ether was added 275 mg of XI dissolved in a minimum amount of dry ether, at 0–10°. The reaction was allowed to warm and was stirred at 25° for 24 hr. The reaction was again cooled in an ice bath, and saturated aqueous ammonium chloride solution was carefully added until gas evolution ceased. The reaction was stirred for an additional half-hour, and 5 ml more of the ammonium chloride solution was added. The solid was filtered and washed with ether. The washings were combined and dried over magnesium sulfate, and the solvent was evaporated under reduced pressure. Sublimation at 70–90° and 0.02 mm yielded crystals, mp 50–59°.

Anal. Calcd for $C_{15}H_{22}O$: C, 76.88; H, 9.47. Found: C, 76.76; H, 9.21.

5-*p*-Anisylcyclooctyl *p*-Toluenesulfonate (XIII).—To a solution of 240 mg of XII in 5 ml of pyridine, cooled in Dry Ice–acetone so that the solution was slushy, was added with stirring 330 mg

(12) J. G. Jackson and J. Kenner, *J. Chem. Soc.*, 1657 (1928).

(13) D. J. Cram and M. F. Antar, *J. Amer. Chem. Soc.*, **80**, 3103 (1958).

of *p*-toluenesulfonyl chloride in 5 ml of pyridine. The reagent was added as fast as consistent with maintaining the reaction temperature. The resulting solution was then stored at −20° for 2 days. The flask was removed from the freezer, five drops of water were added to the reaction, and the solution was allowed to warm to 0°. The reaction was then poured into 30 ml of ice-cold 5% hydrochloric acid, and the solution was extracted with 30 ml of ether. The ether solution was washed with cold 5% acid and with sodium bicarbonate and was dried over magnesium sulfate. The solution was evaporated to dryness under reduced pressure, and the residue was recrystallized from ether–pentane at −20° to yield crystals, mp 77.5–82°. Kinetic runs were made on this product and showed different batches to be a mixture of epimers of variable composition.

5-Phenylcyclooctyl *p*-Toluenesulfonate.—This compound was prepared following the procedure used for XIII and gave crystals, from ether–pentane (−20°), mp 68–70° [lit.[9] 69.5–70.5 (cis isomer) and 70–71.5° (trans isomer)]. Kinetic runs were made on the mixture of epimers, and these runs showed the composition to be 1.3 parts cis epimer to one part trans.

1-Phenylcyclooctene (XV).—The preparation of this compound was accomplished by the dehydration of XIV in ether solution with iodine. This product was shown to be the olefin by thin layer chromatography, gas chromatography, and tetranitromethane tests.

1-*p*-Anisylcyclooctanol.—The method of preparation of this compound was identical with that described for the preparation of XIV, and the preparation of **1-*p*-anisylcyclooctene** was similarly analogous to the preparation of XV. Both compounds were used as ether solutions for the product analysis. Thin layer chromatography and gas chromatography were consistent with the above structures.

Kinetic Experiments.—The rates of solvolysis were measured on a Sargeant recording pH-Stat, as discussed earlier.[8]

Preparation of Solvents and Reagents.—The aqueous ethanol used in the kinetic runs was prepared all at once, and the same solvent was used for the base titrant and the solutions of tosylate. It was stored under dry nitrogen when not being used. Preparation consisted of dilution of commercial 95% ethanol with enough distilled water to make the solvent 80% ethanol by volume. Physical constants of the solution were as follows: $n^{25}D$ 1.3624, density 0.84985 g/ml at 25°. The basic titrant was prepared by dissolving reagent potassium hydroxide (0.65 g) in 500 ml of the above solvent. Titration against standard hydrochloric acid showed it to be 0.0182 *N*. An indicator consisting of 12 parts of cresol red to 36 parts of thymol blue was used in this titration, and also was used in the kinetic runs as a visual check of pH constancy.

Treatment of Kinetic Data.—The data obtained from the machine consisted of a graph of the milliliters of titrant used *vs.* time and was more or less smooth, depending on the rate of stirring, speed of reaction, etc. These graphs were smoothed out by means of a French curve, and then the points on the graph put in tabular form for each run. At least 10 points were taken, and in some cases as many as 75 were used. The factors that introduced the largest uncertainty in the treatment of these data were, first, that the infinity titer was uncertain in some cases, owing to errors inherent in the machine, and also because the weight of tosylate was known only to an accuracy of ±0.05 mg; second, when mixtures of two epimers were solvolyzed, the rate of solvolysis of the faster epimer may be determined accurately only if the rate of the slower one is known accurately.

For pure isomers then, when the infinity titer could be determined accurately, the rate was determined by plotting the logarithm of the concentration *vs.* time in seconds. When the infinity titer was not known, either the method developed by Guggenheim[14] was used, or the infinity titer was varied until the plot of log [ROTs] *vs.* time gave the straightest line, which corresponds to the correct infinity titer, within experimental error. The above methods, when they could be used on the same run, gave consistent results.

In the case of mixtures of epimers, one of the above-mentioned methods gave the absolute rate of the slower isomer. The absolute rate of the faster isomer was determined by extrapolating the concentration of the slower isomer back to zero time, and then subtracting the concentrations of the slower isomer away from the total concentrations of the isomers, thus obtaining the concentration of the faster, and, hence, the rate of disappearance of the faster isomer, uncontaminated with the slower. As a further check on this method of obtaining the rates of a mixture, synthetic mixtures of *cis*- and *trans*-5-*tert*-butylcyclooctyl *p*-toluenesulfonate of known composition were made and the individual rates determined from the mixture. These rates compared very favorably with those obtained on the pure epimers.

It should be noted that, since concentration does not enter into the rate equation for first-order kinetics, any convenient concentration units may be used. Here, 1 mm of chart paper is proportional to 1 mmol of alkyl toluenesulfonate remaining, and this is the most convenient measure of concentration. A sample run is reported in Table III.

TABLE III

SOLVOLYSIS OF *cis*- AND *trans*-5-PHENYLCYCLOOCTYL *p*-TOLUENESULFONATES IN 80% ETHANOL AT 25 ±0.05° [a]

Time, hr	[ROTs], mm of chart	Log [ROTs]	Time, hr	[ROTs], mm of chart	Log [ROTs]
0	207.8	1.3177	21	34.4	0.537
1	178.2	1.251	22	32.9	0.517
2	153.4	1.186	23	30.4	0.483
3	134.3	1.128	24	29.9	0.476
4	119.0	1.076	25	28.4	0.453
5	106.0	1.025	26	27.2	0.435
6	94.5	0.975	27	26.3	0.420
7	84.6	0.927	28	25.4	0.405
8	77.1	0.887	29	24.1	0.382
9	70.7	0.849	30	23.3	0.367
10	65.5	0.816	31	22.3	0.348
11	61.0	0.785	32	20.5	0.312
12	56.8	0.754	33	19.7	0.295
13	53.8	0.731	34	18.8	0.274
14	49.6	0.696	35	18.4	0.265
15	46.7	0.669	36	17.6	0.246
16	44.1	0.644	37	16.9	0.228
17	40.9	0.612	38	16.5	0.218
18	39.9	0.601	39	15.7	0.196
19	37.8	0.578	40	15.1	0.179
20	36.0	0.556	41	14.5	0.161

$k_{cis} = 7.07 \times 10^{-5}$ sec^{-1}; $k_{trans} = 1.24 \times 10^{-5}$ sec^{-1}
Ratio of cis/trans = 1.34

[a] Run no. 3: 13.50 mg of *p*-toluenesulfonate in 15 ml of 80% ethanol maintained at pH 8.4 ± 0.4.

Product Analysis.—Product analyses of the tosylate solvolyses were done by gas chromatography, and the results were checked by thin layer chromatography. The actual solvolysis runs were used for the analysis, rather than separate runs. This eliminated any uncertainty due to variable composition of epimers in the mixtures, which appears to occur with the *p*-anisyl derivative. A typical work-up of a solvolysis for analysis follows.

The reaction vessel was removed from the titrator, excess base was added to the solution, and the solution was transferred to a stoppered flask and stored at 25° until work-up was convenient. (In the case of the slower reactions, the reaction was left for several more half-lives to ensure complete reaction.) The reaction mixture was then diluted with 50 ml of pentane and extracted twice with 50 ml of distilled water. The water extracts were washed with pentane, and the organic fractions were combined and dried over magnesium sulfate. The pentane was then distilled carefully, using a 12-in. column packed with stainless steel gauze, and equipped with a head in which the reflux ratio could be varied. Distillation was continued until only 0.5–1 ml of liquid remained in the pot. This solution was stored in the freezer until needed.

The actual analyses were done on an aluminum column, 4 m × 0.25 in., packed with 10% SE-60 on 40–60 mesh Chromosorb B. One other column was used for the separation of the olefins obtained from the 5-*tert*-butylcyclooctyl tosylate solvolysis. It was a 20-ft dual column, the first half packed with XE-60 on 60–80 mesh firebrick, and the second half packed with tricresyl phos-

(14) E. A. Guggenheim, *Phil. Mag.*, **2**, 538 (1926).

phates on 60–80 mesh firebrick. This column separated the olefins but would not allow elution of the alcohols. The resuts are summarized in Table I.

Registry No.—III, 28252-86-0; IV, 28252-87-1; V, 28252-88-2; VI, 28252-89-3; VII, 28252-90-6; IX, 28252-91-7; X, 28252-92-8; XI, 28252-93-9; *cis*-XII, 28252-94-0; *trans*-XII, 28256-86-2; *cis*-XIII, 28252-95-1; *trans*-XIII, 28252-96-2; *cis*-5-phenylcyclooctyl *p*-toluenesulfonate, 7286-93-3; *trans*-5-phenylcyclooctyl *p*-toluenesulfonate, 7368-50-5.

Base-Induced Rearrangement of Epoxides to Allylic Alcohols. III. Alkylidenecycloalkane Oxides[1]

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The lithium diethylamide induced rearrangement of a series of propylidenecycloalkane oxides to allylic alcohols exhibits marked regioselectivity, with endocyclic olefin product being formed preferentially. An exception is propylidenecyclohexane oxide which gives 95% of the alternate, tertiary allylic alcohol. A series of ethylidenecycloalkane oxides, where preference for endocyclic elimination competes with proton abstraction from primary carbon, was also examined. The results of both series support a syn elimination mechanism, with very specific cis-coplanar transition state geometrical requirements.

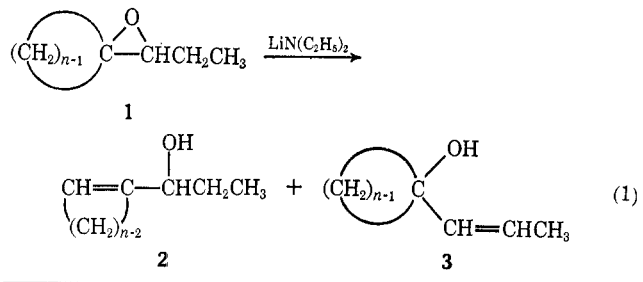
Cope and Tiffany[2] were apparently the first workers to observe an unusual base-catalyzed rearrangement of an epoxide when dealing with cyclooctatetraene oxide. Subsequent work with phenyl-substituted ethylene oxides,[3] medium-ring cycloalkene oxides,[4] and open-chain epoxides[5] established several novel reaction pathways on treatment with strong base. The extensive work of Crandall and his coworkers[6] amplified these and brought to light additional reactions.

This paper deals with our continuing[1,7] study of the lithium diethylamide induced rearrangement of epoxides to allylic alcohols. Formally an elimination, this reaction is remarkable for its very high selectivity, *e.g.*, stereoselectivity (exclusive formation of trans olefin in open-chain systems[5,7]) and regioselectivity[8] (exclusive, or nearly so, abstraction of proton from least substituted carbon[6,7]). Recently deuterium labeling studies[1] have established that syn elimination is the preferred pathway in cyclohexene oxide rearrangements.

The factors which influence the regioselectivity of the base-induced reaction are incompletely understood. We have undertaken a systematic study of substituted epoxides to examine this question; the results obtained with alkylidenecycloalkane oxides are presented here.

Results and Discussion

A series of propylidenecycloalkane oxides (**1**) was prepared by standard procedures and treated with lithium diethylamide in refluxing ether–hexane (eq 1). The course of the reaction was followed by vpc, and the mixture quenched with water when the epoxide was consumed. The results are shown in Table I.



(1)

1 **2** **3**

TABLE I

PRODUCT DISTRIBUTION FROM THE REACTION OF PROPYLIDENECYCLOALKANE OXIDES (1) WITH LITHIUM DIETHYLAMIDE

1	*n*	Time, hr[a]	2	3
a	4	6	77	15[b]
b	5	1	100	0
c	6	49[c]	5	95
d	7	5	98	2
e	8	2	100	0
f	12	22	≥84	...[d]

[a] The reactions were followed by vpc; this is the time required for effective complete loss of starting epoxide. [b] The product mixture in this case contained 5% cyclobutyl ethyl ketone and 3% unidentified material. [c] At this time 9% unreacted epoxide remained. [d] Not directly determined; see Experimental Section.

In this series, proton abstraction from secondary cyclic carbon competes with that from a secondary acyclic center. The data in Table I show not only high selectivity depending on ring size, but a striking reversal in the direction of elimination in the series cyclopentyl (endocyclic), cyclohexyl (acyclic), and cycloheptyl (endocyclic olefin preferred).

It is apparent that subtle conformational effects can significantly diminish the activation energy for elimination into the carbocyclic ring. The propylidenecyclohexane oxide **1c** serves as a basis for comparison; reaction to form the acyclic double bond (as strongly favored in **1c**) requires in excess of 49 hr for complete conversion. All other systems shown in Table I react more rapidly, from a great deal faster in the completely

(1) Part II: R. P. Thummel and B. Rickborn, *J. Amer. Chem. Soc.*, **92**, 2064 (1970).

(2) A. C. Cope and B. D. Tiffany, *ibid.*, **73**, 4158 (1951).

(3) A. C. Cope, P. A. Trumbull, and E. R. Trumbull, *ibid.*, **80**, 2844 (1958).

(4) (a) A. C. Cope, H. Lee, and H. E. Petree, *ibid.*, **80**, 2849 (1958); (b) A. C. Cope, M. Brown, and H. Lee, *ibid.*, **80**, 2855 (1958); (c) A. C. Cope, G. A. Berchtold, P. E. Peterson, and S. H. Sharman, *ibid.*, **82**, 6370 (1960).

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(6) (a) J. K. Crandall, *J. Org. Chem.*, **29**, 2830 (1964); (b) J. K. Crandall and L. Chang, *ibid.*, **32**, 435 (1967); (c) *ibid.*, **32**, 532 (1967); (d) J. K. Crandall and L. C. Lin, *J. Amer. Chem. Soc.*, **89**, 4526, 4527 (1967); (e) *J. Org. Chem.*, **33**, 2375 (1968).

(7) B. Rickborn and R. P. Thummel, *ibid.*, **34**, 3583 (1969).

(8) The terminology suggested by A. Hassner, *ibid.*, **33**, 2685 (1968).