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CONFORMATIONAL ANALYSIS. LXII. SOLVOLYSIS AND DEAMINATION STUDIES OF THE 5-*t*-BUTYLCYCLOOCTYL SYSTEM.[1,2]

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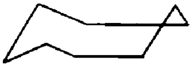
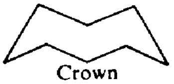
Abstract—The solvolyses of *cis*- and *trans*-5-t-butylcyclooctyl tosylates in acetic acid have been studied, and the rates and products are reported. The fast rate and rearranged product from the *cis* isomer are interpreted in terms of neighboring group participation by hydride. Improved syntheses of the compounds are given. Deamination reactions of the corresponding amines were also studied, and a product study is described and interpreted in terms of the accepted mechanism of the reaction.

INTRODUCTION

THE cyclooctane ring shows marked differences in many of its physical and chemical properties from those characteristic of cyclohexyl or acyclic systems, and most of these differences are directly attributable to the conformation of the ring. While the latter is known with certainty in only one case,[3] the available (extensive) experimental data appears to indicate[4] that there are two general types of conformations which are most likely to exist, and these may be referred to as the boat and crown.[5] The boat is the form found in the crystal of *cis*-1,2-dicarboxycyclooctane,[3] and it appears to be the principal form in cyclooctane itself from the NMR spectrum of the compound.[6] Calculations of the Westheimer type indicate that the boat and crown (possibly distorted) are preferred over other possible conformations.[7–9]

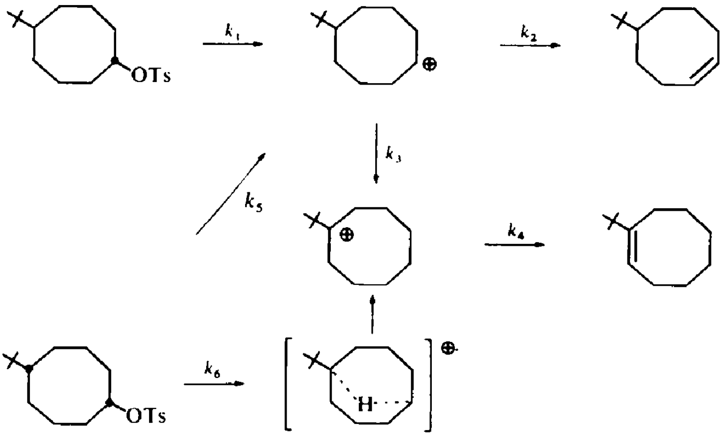

Boat


Crown

In an earlier paper, the solvolysis of the *cis* and *trans*-isomers of 5-t-butylcyclooctyl tosylate in acetic acid was described.[10] One of the isomers gave mainly 5-t-butylcyclooctene by way of a simple elimination reaction, while the other yielded primarily 1-t-butylcyclooctene from hydride migration. The isomer which yielded the rearranged product was assigned the *cis*-configuration, and the assignment would be equally valid for migration occurring in either a crown or a boat form. More recently Cope[11] was able to assign unambiguously the *cis* and *trans* configurations to the 5-methylcyclooctanols, and here too, the *cis* isomer is the one which shows mainly a transannular hydride migration.

The earlier work[10] indicated that some hydride migration occurred with the *trans*-5-t-butylcyclooctyl tosylate, while some of the 1,2-elimination product also resulted from the solvolysis of the *cis* isomer. It was shown that the products were stable under the reaction conditions. The most simple (not necessarily the correct) mechanistic scheme consistent with the solvolysis products is shown in Chart I. The first objective

CHART I



of the present work was to examine this scheme more closely, and to determine some of the rate constants. The solvolysis of a tosylate is related to, but different from, the nitrous acid deamination of an amine, and the latter type of reaction was also investigated.

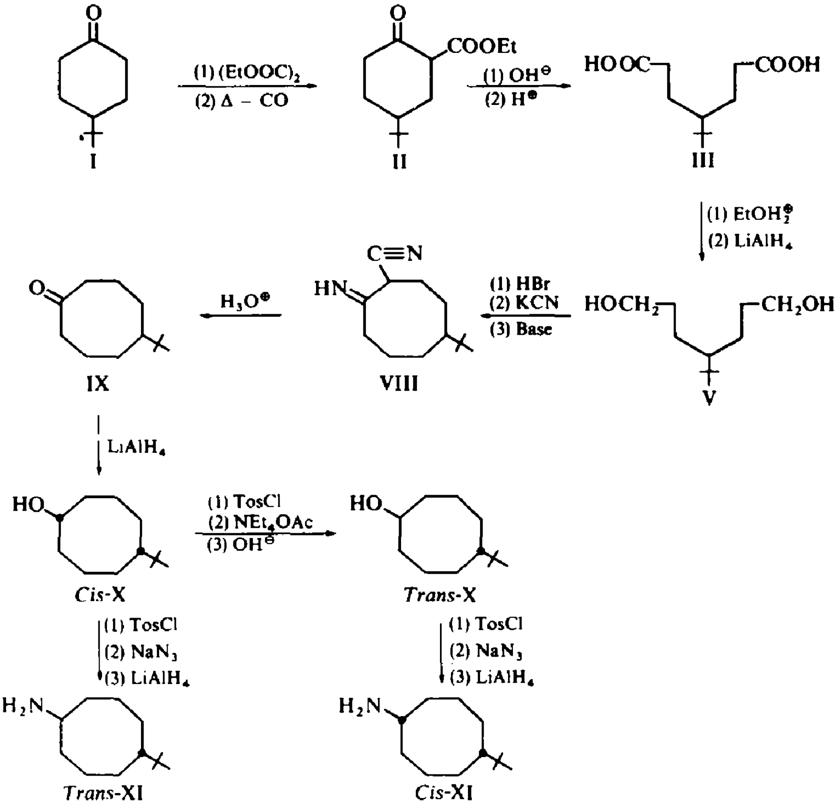
SYNTHESIS

The *cis* and *trans*-isomers of 5-t-butylcyclooctanol were reported earlier.[10] The original synthesis involved a Friedel–Crafts reaction on phenol to give the 4-t-butyl derivative. Hydrogenation of the latter to the cyclohexanol, followed by chromic acid oxidation gave 4-t-butylcyclohexanone (I), a compound which has subsequently became available commercially. Upon oxidation with peroxytrifluoroacetic acid the ketone was converted to a lactone, which was opened to the omega-bromo acid with hydrogen bromide. Reaction of the bromide with cyanide gave the nitrile, which upon alcoholysis yielded diethyl γ-t-butylpimelate (IV).

Compound IV is more easily prepared from 4-t-butylcyclohexanone by the sequence shown in Chart II. A Claisen condensation of I with diethyl oxylate, followed by decarbonylation gave the β-ketoester II,[12] which was submitted to a reverse Claisen reaction with base to give the diacid III. Esterification of III followed by hydride reduction gave diol V, which was converted to the corresponding dibromide (VI) with hydrogen bromide. The dibromide was chain extended with cyanide to give the dinitrile (VII), which underwent a Thorpe–Ziegler cyclization to the imino-nitrile (VIII), which was hydrolyzed to 5-t-butylcyclooctanone (IX, in 73% yield from the dinitrile). Hydride reduction of IX gave largely the *cis* alcohol X. The *trans* isomer was obtained by converting the *cis* isomer to its tosylate, and allowing the latter to react with tetraethylammonium acetate. The resulting acetate was saponified to the alcohol (*trans*-X) in an overall yield of 82% from the *cis* alcohol.

The corresponding amines (XI) were obtained from the alcohols (with inversion of configuration) by conversion of the appropriate alcohol to the tosylate, and conversion of the tosylate to the azide with azide ion. The azide was then reduced to the amine with hydride.

CHART II



TOSYLATE SOLVOLYSIS

The solvolysis of either *cis* or *trans*-5-t-butylcyclooctyl tosylate in acetic acid–sodium acetate gave a mixture of olefins which was at least 99% 1-t-butylcyclooctene in the former case and 90% of the 5-isomer in the latter. Traces of other olefins were also detected. Earlier it had been found[10] that solvolysis of the crude *cis*-tosylate gave the 1- and 5-olefins in the ratio of 4:1. In the present work the tosylate was carefully recrystallized from pentane at −20° before solvolysis, and under these circumstances the ratio increased to at least 99:1. The acetolysis of the pure *cis*-tosylate then, gives substantially complete rearrangement. The mixture of olefins obtained from the crude tosylate[10] is now believed to be a result of acid-catalyzed decomposition of tosylate in the crystal. A similar phenomenon has been reported for cyclodecyl tosylate.[13]

The pure *trans*-tosylate (from X) gave 10–12% of the 1-olefin (with hydride migration) and 88–90% of the normal elimination product. These values are summarized in Table 1, along with the rate constants for the solvolyses. The original interpretation was that the 5-hydrogen participated in the solvolysis of the *cis*- but not the *trans*-isomer, which is consistent with the observed products and with either a boat or a crown conformation for the cyclooctane ring in each case. The rate constants for the solvolysis constitute a test for neighboring group participation as follows.

TABLE 1. PRODUCT ANALYSIS AND RATE CONSTANTS FOR ACETOLYSIS OF CYCLOOCTYL-*p*-TOLUENESULFONATES AT 25·00°

Compound	Rate constant k_1 (sec^{-1})	Products[a]
Cyclooctyl-*p*-toluenesulfonate[b]	$2{\cdot}81 \times 10^{-5}$	*cis*-Cyclooctene (52 %) Cyclooctyl acetate (48 %)
cis-5-t-Butylcyclooctyl-*p*-toluenesulfonate	$6{\cdot}10 \times 10^{-4}$	1-t-Butylcyclooctene (99 %)[c]
	$5{\cdot}92 \times 10^{-4}$	1-t-Butylcyclooctene (99·5 %)[c]
trans-5-t-Butylcyclooctyl-*p*-toluenesulfonate	$1{\cdot}17 \times 10^{-5}$	5-t-Butylcyclooctene (88 %) 1-t-Butylcyclooctene (12 %)
	$1{\cdot}11 \times 10^{-5}$	5-t-Butylcyclooctene (90 %) 1-t-Butylcyclooctene (10 %)

[a] The products were determined in runs separate from the kinetic runs. Exactly the same conditions were used, the only exception being a scale-up for the product analysis.

[b] The literature (R. Heck and V. Prelog, *Helv. Chem. Acta* **38**, 1541 (1955); and Ref. 30) report values of 2·66 and $2{\cdot}82 \times 10^{-5}$ sec^{-1}.

[c] Small traces of other olefins probably arising from premature decomposition in the solid state account for the remaining percentage.

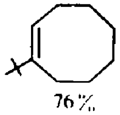
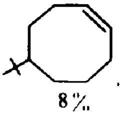
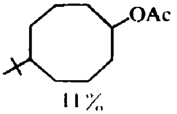
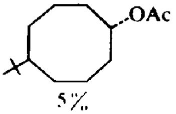
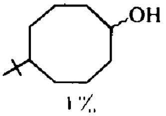
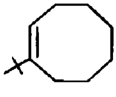
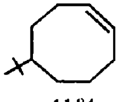
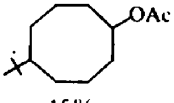
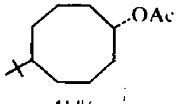
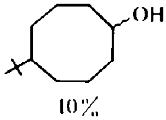
The 5-t-butylcyclooctanols have been equilibrated, and the *cis* is more stable by 0·4 kcal/mole.[10] The rate constants k_1 and k_5 lead to the same carbonium ion (to the extent that it is "free" at least), and by the Evans–Polanyi Principle, therefore, k_1 should be slightly greater than k_5. (In the analogous 4-t-butylcyclohexanol system the *trans* isomer is more stable by 0·9 kcal/mole under the same conditions,[14] and it solvolyzes more slowly by a factor of 3 under similar conditions.[15]) As indicated in Table 1, the observed rate of the *cis* isomer is 50 times greater than that of the *trans*, and consequently $(k_6 + k_5) = 50\ k_1$. Thus if $k_5 < k_1$, k_6 is some fifty times greater than k_1; and this factor appears to be a measure of the effect of neighboring group participation. Cyclooctyl tosylate itself solvolyzes some two times faster than does the *trans*-isomer. Deuterium experiments have shown[16] that cyclooctyl brosylate undergoes 1,5-hydride transfer under similar conditions to the extent of about 50 %. These relatively small factors are taken to indicate that neighboring group participation is of minor importance in the unsubstituted case. This situation is not unexpected, since when participation occurs in the *cis*-5-t-butyl system, the positive charge is being transferred from a secondary to a tertiary carbon. This transfer will obviously be a more favorable change than in the unsubstituted case where the charge would be moved from one secondary carbon to another.

THE DEAMINATION REACTION

The deamination of an alkyl amine with nitrous acid is a reaction which has been extensively studied, but which is still not thoroughly understood. The earlier work has been summarized and discussed by Streitwieser.[17] His general mechanistic scheme involves the generation of a diazonium ion, which can undergo substitution, elimination or rearrangement, or it can loose nitrogen and form a carbonium ion, which in turn can undergo the same types of processes. The activation energy for the loss of nitrogen by the diazonium ion is considered to be small, perhaps 3–5 kcal/mole,[17] as compared to perhaps 25 kcal/mole for tosylate solvolysis. Since the activation energy is so small, Streitwieser suggests that the differences between the activation energies for the different reactions which involve loss of nitrogen from the ion should be small too, and hence the reactions should not be clean, but should lead to product mixtures containing reaction products not ordinarily observed in solvolyses, and this is what is observed. For the cyclohexyl system, the axial amine tends to give a large amount of elimination, and the alcohol and acetate found are largely inverted. An equatorial amine gives relatively less elimination, and the alcohol and acetate are largely of retained configuration. The most glaring exception to these general trends was that reported by Shoppee,[18] but a repetition of this work, with what appear to be better analytical techniques, indicates that Shoppee's original conclusions were in error, and in fact those systems also follow the usual pattern.[19]

Stereochemical studies of the deamination reaction in simple medium ring compounds have not been reported previously.[20] It was hoped that the results of such a reaction in the 5-t-butylcyclooctyl system might shed some light on the stereochemistry of the molecules or on the reaction, or both. The deaminations of the *cis* and *trans* isomers were carried out in glacial acetic acid, and the products were studied by gas chromatography. As expected, olefins, alcohols and acetates were obtained. The 5-olefin (from ordinary 1,2-elimination) was a minor product in each case. The *trans*-isomer also gave a small amount of the 1-olefin, which would result from a transannular 1,5-hydride transfer. The 2- and 3-olefins were also found, indicating the possibility of series of 1,2-shifts here, which is not the case in the tosylate solvolysis. We interpret the formation of these olefinic products as proceeding through the free carbonium ion. The *cis* amine gave mostly the 1-olefin upon deamination. Hence the transannular hydride transfer is the preferred reaction here, as it was in the tosylate solvolysis. These data are summarized in Table 2. These results are consistent with Streitwiesers mechanism, where most of the reaction occurs on the diazonium ion, but some of it goes through a carbonium ion.

TABLE 2. PRODUCT ANALYSIS[a] FROM DEAMINATION OF CYCLOOCTYL AMINES IN GLACIAL ACETIC ACID SODIUM ACETATE SOLUTION AT 25–27°

Compound	Products[a, d]				
Cyclooctyl-Amine	*cis*-Cyclooctene (33%). Cyclooctyl Acetate (64%). Cyclooctanol (3%)				
cis-XI	 76%	 8%	 11%	 5%	 1%
trans-XI[b, c]	 11%	 11%	 15%	 41%	 10%

[a] Because of the closeness of peaks and analysis on different columns, percentages are believed to be ±5%.

[b] In addition, 8% of a mixture of 3- and 4-t-butylcyclooctene with the isomer of higher retention time predominating was obtained.

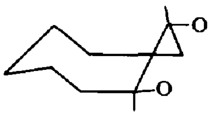
[c] Approximately 3% of another acetate having the same retention time as 3-t-butylcyclooctyl acetate was obtained.

[d] It was noted that 1-t-butylcyclooctyl acetate was not stable under the deamination conditions, but was converted to the 1-olefin. The amount of the latter which is formed via the 1-acetate is not known.

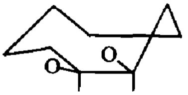
A small amount of alcohol was formed in the deamination, and this is presumed to result from the water from the nitrous acid in the usual way. Acetates accounted for the remainder of the reaction product. Retention of configuration predominated over inversion in both cases, but only by a factor of 2 or 3 to 1, so the stereoselectivity of the reaction is not very great.

DISCUSSION AND CONCLUSIONS

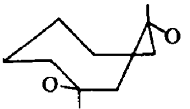
If the boat form of cyclooctane is tentatively accepted as the more stable, a number of facts which were previously explicable only with the aid of considerable imagination now become straightforward. The fact that appropriate 1,2-disubstituted cyclooctanes can form intramolecular hydrogen bonds about equally well from the *cis* or *trans* isomer,[4] and the fact that 1,3-dimethylcyclooctane is about equally stable in the *cis* or *trans*-form,[21] for example, follow from the fact that all of these isomers have available at least one low-energy diequatorial conformation, as the examples given below illustrate.



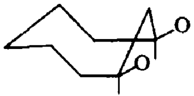
1,2-*trans*-Diequatorial



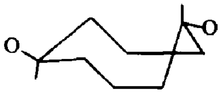
1,2-*cis*-Diequatorial



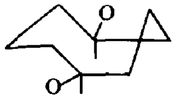
1,3-*trans*-Diequatorial



1,3-*cis*-Diequatorial



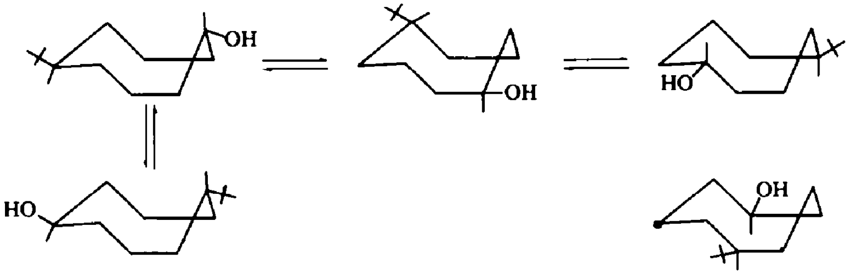
1,5-*trans*-Diequatorial



1,5-*cis*-Diequatorial

Doubt has recently been raised[6] concerning the validity of our assignment of stereochemistry to the 5-t-butylcyclooctanols. The stereochemistry originally assigned was based on the assumption of a crown conformation,[10] since the available evidence at the time seemed to indicate a crown, rather than a boat, form was of lower energy.[5] The assignment made use of, but did not require, the assumption of a crown form. If we accept the boat form as the stable one, the diequatorial conformation shown for a 1,5-disubstituted cyclooctane would appear to be the most important one. It is clear that only the *cis*-isomer has the proper geometry to transfer a hydride across the ring without introducing excessive deformation of some sort into the ring. It is important to note, however, that the hydroxyl is equatorial in both the *cis* and *trans* isomers. The similarity of the hydroxyls in the *cis* and *trans* isomers, as determined[10] by their relative energies, or by the rates of chromic acid oxidation or phathalate hydrolysis, is also now understandable.

Cope has recently reported that the proton magnetic spectra of 1,5-substituted cyclooctanes give characteristic methylene regions; a very complex broad multiplet for the *cis*, and a simple broad singlet for the *trans*. The interpretation of these facts was that the *cis*- was relatively flexible, while the *trans*- was a rapidly equilibrating mixture of conformers. We agree with this view, and can amplify it as follows. If we accept that a boat form of the ring with both substituents equatorial is a prerequisite to a conformer contributing appreciably to the molecular population, then the *trans* isomer is a mixture of four conformations, while the *cis* isomer is but one (neglecting mirror images) as illustrated. The *cis* isomer should therefore show a



highly complex methylene region. The spectrum of the *trans* isomer is not predictable in any simple obvious way, but since the axial and equatorial protons loose their identity upon pseudorotation, greater equivalence of the methylene protons would seem to be a reasonable result.

The activation energy of the deamination reaction is low, as shown by the fact that the cyclohexyl carbonium ion generated mostly reacts before the ring can invert.[23] The barrier to inversion of the cyclohexyl cation is not known, but it may be presumed to be smaller than that of cyclohexane (10·3 kcal/mole[24]), and probably similar to those of the geometrically similar cyclohexanone (which is known experimentally only to be < 8 kcal/mole[25] and which has been calculated to be 4·8 kcal[25]), or cyclohexyl radical (4·9 kcal[26]). The cyclooctane ring can therefore probably pseudorotate, but not invert, during the lifetime of the cyclooctyl cation, as the barriers are believed to be about 8 and 3 kcal/mole for these two processes respectively.[6, 7] Since both the *cis*- and *trans*-isomers of the 5-t-butylcyclooctylamines appear to have diequatorial conformations as discussed earlier, neither has an optimum geometry for a 1,2-diaxial elimination. Such a geometry is available by a low-energy pseudorotation, however, hence the 1,2-elimination is an easy process, and such products are formed.

The acetates formed by deamination constitute an epimeric mixture, with retention of configuration pedominating with either isomer. The amount of alcohol obtained was always small, and its stereochemistry was not examined. In general, in cyclohexyl systems the equatorial acetate appears to predominate regardless of the configuration of the starting material. In the cyclooctyl systems, either configuration can result from substitution at an equatorial position on a suitable pseudorotational conformer. An S_N2 attack on the cyclooctane ring is in general quite unfavorable for steric reasons, and it seems likely that it will also be unfavorable (relative to other alternatives) in the deamination reactions. The best interpretation of the results, therefore, seems to be that the *cis* isomer reacts mainly by hydride transfer (neighboring group participation) while the *trans* isomer reacts mainly via a carbonium ion. The ion obtained from the *trans* isomer is not the same as that from the *cis* isomer without participation, because they react to give quantitatively different products. The carbonium ion generated from either isomer is one from a conformation with an equatorial leaving group, and these react preferentially with retention of configuration, analogous to the equatorial cyclohexyl case. Pseudorotation is expected to occur, but not to be sufficiently fast to completely erase the ancestry of the carbonium ion before the subsequent reaction. Hence the acetates show an excess of retained configuration, but they are largely epimerized.

EXPERIMENTAL

4-t-Butylpimelic acid (III). The procedure followed was similar to that described for the preparation of pimelic acid[27] from 2-carboethoxy 4-t-butylcyclohexanone (II).[12]

In a 2-liter 3-necked flask equipped with a dropping funnel, a reflux condenser, and a special[27] wire stirrer was placed 100 g NaOH and 300 ml MeOH. The stirred mixture was heated for 1 hr in an oil bath held at 120° in order to effect soln of most of the NaOH. Stirring and heating were continued while 130 g 2-carbethoxy-4-t-butylcyclohexanone was added during 2 hr. After stirring for 1 hr longer, 600 ml water was added and the mixture was extracted several times with ether. Subsequent removal of the ether gave recovered 4-t-butylcyclohexanone. The basic aqueous layer was acidified and the crude acid was extracted with seven 200 ml portions ether. The ether was removed by distillation, and benzene was added to remove any water from the crude acid. Distillation of the crude acid at 173–175° at about 0·2 mm gave 103 (80%) of III, m.p. 62·5–64·5° (after immediate solidification). After recrystallization from an ether–pentane mixture, the product had m.p. 78·5–79·5°. (Found: C, 61·18; H, 9·49. Calc. for $C_{11}H_{20}O_4$: C, 61·09; H, 9·32%).

Diethyl-4-t-butylpimelate (IV). In a 1-liter distilling flask was placed 184 g acid III, 160 ml toluene, 306 ml abs EtOH, and 0·7 ml conc H_2SO_4 [28] A distillation head, reflux condenser, and thermometer were attached and the flask was immersed in an oil bath and was heated to 135°. An azeotropic mixture of alcohol, toluene, and water began to distil at 75° and was removed. Distillation was continued until the thermometer in the neck of the flask rose to 78°.

The distillate was collected in a 1-liter flask containing 156 g of anhyd K_2CO_3. It was shaken well and after filtration returned to the distillation flask. The flask was again heated until the temp rose to 78–80° when distillation was discontinued. The residual liquid was emptied into a 300 ml flask and distilled at 1·7 mm, at 127–133°, yield, 195 g (84%), n_D^{25} 1·4430 (lit.[29] b.p. 134–136° (5 mm), n_D^{25} 1·4428).

5-t-Butylcyclooctanone (IX). The ester IV was reduced to diol V, which was converted through the dibromide to the dicyanide as indicated on the flow sheet and previously described. The cyclization procedure and special equipment is outlined by Greenberg.[10,29]

Under a N_2 atm 78 g of bromobenzene was added with stirring over approximately 2 hr to 7 g Li metal suspended in 1500 ml refluxing anhyd ether, followed by the dropwise addition of 68 g N-methylaniline. To this mixture was added 20·6 g of VIII in 900 ml anhyd ether with continuous stirring over a 48 hr period. Following this the mixture was hydrolyzed by the addition of 250 ml water. The ether layer was separated, dried with $MgSO_4$, and the ether was removed over a steam bath. The residue partially crystallized. Upon filtration of a portion of this material and recrystallization from an ether–pentane mixture a stable white crystalline product was obtained, m.p. 172–174°. The product was identified as 1-cyano-5-t-butylcyclooctylimine. (Found: C, 75·97; H, 10·75; N, 13·69. Calc. for $C_{13}H_{22}N_2$: C, 75·67; H, 10·75; N, 13·58%).

Treatment of the imine with dilute acid gave the known cyano ketone.

The residues from 3 such experiments were combined and mixed with 400 ml of 33% H_2SO_4 by volume. The mixture was stirred under gentle reflux for 24 hr and then steam distilled using a liquid-liquid extractor for use with solvents heavier than water. The ketone which was formed collected at the top of the separator and the water was returned back into the reaction flask.

When no more ketone appeared to distil, the 2-phase system was separated and the aqueous portion was extracted 5 times with 50 ml portions of ether. The ether extracts were combined, dried over $MgSO_4$ and the mixture was filtered. The filtrate was concentrated by evaporation on the steam bath, and the residue was distilled *in vacuo* through a short Vigreux column to give 40·0 g (73% based on the dinitrile) of IX, b.p. 111–117° at 6·5–7·5 mm, n_D^{25} 1·4716 (lit.[29] b.p. 113–115° at 7 mm, n_D^{25} 1·4714).

cis-5-*t-Butylcyclooctanol* (X). To a stirred slurry of 2 g LAH in 100 ml ether was added 20·3 g of IX dropwise, so as to maintain a gentle reflux. Following the addition, the mixture was heated to reflux for 24 hr. The mixture was then hydrolyzed by the careful addition of water followed by 6M HCl. The ether layer was separated and washed with water and $NaHCO_3$aq. After the removal of the ether by distillation over a steam bath using a Vigreux column (to prevent loss of product), the remaining alcohol was dissolved in pentane and recrystallized at least 7 times at −20° under a dry N_2. The yield of purified X was 4·8 g (24%), m.p. 60·2–61·2 (lit.^{29} 60–60·5°).

The pentane was removed from the mother liquors, and the alcohol (consisting of both isomers) was oxidized directly to the starting ketone IX with Jones' reagent.^{30} The crude IX recovered in this manner was reduced again with LAH to obtain more X and the entire procedure repeated. In this manner, a greater than 75% conversion of IX to *cis* X could be realized.

cis-5-*t-Butylcyclooctyl acetate.* A mixture of 0·92 g of *cis*-X and 10 ml acetyl chloride was heated to reflux for 5 hr. The excess acetyl chloride was removed under aspirator vacuum and water was added to the crude acetate. The mixture was extracted with five 10 ml portions of ether and the ether extracts were combined and washed with 5% $NaHCO_3$aq and then with water. The ether extract was dried with $MgSO_4$ and the ether (after filtration) was removed over a steam bath. The product was distilled at 138–139° at 10 mm, n_D^{25} 1·4615, yield: 1 g (88%). (Found: C, 74·20; H, 11·67. Calc. for $C_{14}H_{26}O_2$: C, 74·28; H, 11·58%).

trans-5-*t-Butylcyclooctanol* (X). A soln of 8·25 g of *p*-toluenesulfonyl chloride in 25 ml anhyd pyridine at 0° was added to 5·45 g of *cis*-X in 25 ml pyridine at 0°. The mixture was then kept at −20° from 24 to 48 hr. After this time 1 ml water was added and the mixture was allowed to warm to about 0°. The mixture was then poured into 150 ml cold 5% HClaq and the soln was extracted immediately with 125 ml ether. The ether extract was washed at least twice with 50 ml portions cold 5% HClaq in order to completely remove the pyridine, followed by one washing with water and a 5% $NaHCO_3$aq. The ether phase was then dried over $MgSO_4$ and filtered. The ether was removed *in vacuo* at room temp.

To the crude tosylate was added 30 g of tetraethylammonium acetate in 125 ml of anhyd acetone. The resultant soln was stirred at room temp for 12 days. The acetone was removed over a steam bath and the ester was saponified by heating to reflux for 2 hr with 12 g KOH in 100 ml 95% EtOH. The EtOH was removed *in vacuo* and water was added to the residue. The mixture was then extracted with five 20 ml portions ether. The ether extracts were combined and were washed with dilute acid followed by water. After drying, the ether was distilled over a steam bath through a Vigreux column and the crude inverted alcohol(*trans*-X) was recrystallized 6 times from pentane at −20° under dry N_2. The crude yield of product (after one recrystallization) containing about 2% *cis*-X was 4·5 g (82·5%), m.p. 59–61°. The yield of product almost entirely free of *trans*-X was 2·5 g or 46%, m.p. 61–62° (lit.^{10} m.p. 58·5–59·5°).

trans-5-*t-Butylcyclooctyl acetate.* The *trans*-acetate was prepared in a similar manner as the *cis*-acetate. From the reaction of 0·92 g of *trans*-X and 10 ml of acetyl chloride 1 g of product (88%), b.p. 138–141° (10 mm), n_D^{25} 1·4625 was obtained. (Found: C, 74·23; H, 11·34. Calc. for $C_{14}H_{26}O_2$: C, 74·28; H, 11·58%).

trans-5-*t-Butylcyclooctylamine hydrochloride.* A soln of 5·72 g *p*-toluenesulfonyl chloride in 15 ml anhyd pyridine at 0° was added to a soln of 3·68 g *cis*-X in 15 ml pyridine at 0°. The resultant soln was kept at about −20°. Precipitated pyridine hydrochloride began to appear about 3 to 6 hr after mixing. After about 36 hr, 2 ml water was added and the mixture was allowed to warm to 0°. The mixture was then poured into 150 ml ice-water and the resultant 2-phase system was immediately extracted with 200 ml cold ether. The ether extract was quickly extracted with 3–4 50 ml portions of cold 5% HClaq, followed by one extraction with 25 ml ice-water and finally one extraction with a 5% $NaHCO_3$aq.

The ether layer was then dried over $MgSO_4$, filtered, and the ether was removed by distillation *in vacuo*. The residue was immediately dissolved in 25 ml cold dimethylformamide and the resulting soln was added all at once to a stirred soln of 7·80 g of sodium azide, 20 ml water and 150 ml dimethylformamide. The resultant soln was stirred for 24 hr at room temp and then was heated to 80° with an oil bath with further stirring for 5 hr.

The reaction mixture was then cooled to room temp and poured into 1000 ml water. The mixture was extracted with five 100 ml portions ether and the ether extracts were combined and washed portionwise with a NaClaq (ca. 100 ml) to remove dimethylformamide.

The ether soln containing *trans* azide was dried over $MgSO_4$, filtered, and was added dropwise to a stirred slurry of 4 g of LAH in 100 ml anhyd ether. After the addition had been completed the mixture was heated to reflux for 24 hr. Hydrolysis of the excess LAH was accomplished by the dropwise addition of water. Only that amount of water which would bring about a precipitation of the basic salts was added. The ppt was filtered and washed well with ether. The ether filtrate was then dried over $MgSO_4$ overnight. The following day the drying agent was removed by filtration and the ether filtrate containing the amine was concentrated to about 400 ml.

Anhyd HCl was passed over the stirred ether soln under slight press and the amine hydrochloride precipitated out. The product was filtered and dried and finally was sublimed at approximately 165° under full vacuum press. The yield was 0·75 g or 17% based on the *cis*-X alcohol, m.p. 283–286° (d) in a sealed capillary tube under N_2. (Found: C, 65·33; H, 11·91. Calc. for $C_{12}H_{26}NCl$: C, 65·57; H, 11·92%).

cis-*5-t-Butylcyclooctylamine hydrochloride*. The *cis*-isomer was prepared in a similar manner to that described for the *trans* isomer. The tosylate was prepared by the reaction of 1·84 g of *trans*-X and 2·86 of *p*-toluenesulfonyl chloride. The appearance of pyridine hydrochloride did not occur until after 10 hr at −20°. The crude tosylate was dissolved in 25 ml dimethylformamide and the soln was added all at once to a stirred soln of 4 g sodium azide, 100 ml dimethylformamide and 10 ml water. The crude azide was reduced with 4 g LAH. The yield of sublimed product was 1·4 g (64% based on the starting alcohol XIV), m.p. 291–293° (d) in a sealed capillary tube under N_2. (Found: C, 65·36; H, 12·11. Calc. for $C_{12}H_{26}NCl$: C, 65·57; H, 11·92%).

Cyclooctanol. Cyclooctanol was prepared by the reduction of 20 g of the commercially available cyclooctanone by 3·8 g LAH. The yield of product was 17·6 g, 87%, b.p. 99–100° at 17 mm, n_D^{25} 1·4820 (lit.[31] b.p. 99° at 16 mm, n_D^{25} 1·4835).

Cyclooctyl acetate. Cyclooctyl acetate was prepared in the same manner as the other acetates. From 1·28 g cyclooctanol and 10 ml acetyl chloride 1·3 g (88%) cyclooctyl acetate was obtained, b.p. 93–96° at 9 mm, n_D^{25} 1·4580 (lit.[32] b.p. 95–96° at 11 mm, n_D^{20} 1·4593).

1-t-*Butylcyclooctene*. The dehydration of 1·6 g 1-t-butylcyclooctanol with 40 mg I_2 in 20 ml toluene was accomplished by refluxing the soln for 24 hr and removing the water formed with a Stark water separator. The organic layer was washed with dil $Na_2S_2O_3$aq, and after drying with Na_2SO_4, the toluene soln was filtered and distilled. After a forerun of mostly toluene was removed at atmospheric press, the product was distilled at 84–88° (11 mm) n_D^{25} 1·4750 (lit.[10] b.p. 88–89°, n_D^{25} 1·4750), yield 1 g (70%).

Product analysis from solvolysis of cis-5-*t-Butylcyclooctyl*-p-*toluenesulfonate*. A soln of 249 mg of *p*-toluenesulfonyl chloride in 1 ml pyridine at 0° was added to 200 mg *cis*-X in 1 ml pyridine at 0°. After the general workup, the dried ether extract was concentrated *in vacuo* and the residue was dissolved in 25 ml pentane (redistilled from LAH). The pentane soln was filtered into a 50 ml Erlenmeyer flask and the pentane was removed slowly under aspirator vacuum. When the tosylate began to crystallize out and about 5 ml pentane remained, the temp of the mixture was about −20°. The mother liquor was drawn off with a thin drawn-out pipette and the crude tosylate was dissolved again in 25 ml pentane. The pentane was again removed slowly under aspirator vacuum until crystallization occurred and 5 ml pentane remained in the flask. Again the liquor was drawn off and the remaining crystalline tosylate was again dissolved in 25 ml pentane. This procedure was carried out a total of 8 times. At this point the tosylate was obtained as small plates, m.p. 54° (d).

The tosylate was immediately solvolyzed in 100 ml 0·02167 M NaOAc in glacial AcOH soln containing 1% Ac_2O for 48 hr at 25°. At the end of this period the solvolysis mixture was poured into 200 ml cold water and the entire mixture was extracted with five 50 ml portions pentane. The pentane extracts were combined and washed once with water. After drying, the solution was concentrated by distillation through a 12 in. Vigreux column.

The residue was analyzed by gas chromatography on column C. Only one component was present, namely 1-t-butylcyclooctene, which was established by having the same retention time as authentic 1-t-butylcyclooctene and augmentation of the VPC peak when the residue was mixed with authentic olefin. Small traces (ca. 1%) of other olefins were detected in one sample but are believed to arise from decomposition of the tosylate prior to solvolysis.

Analysis of the unknown mixture on column A showed only olefins to be present; no acetates were detected.

Product analysis from solvolysis of trans-5-*t-butylcyclooctyl*-p-*toluenesulfonate*. The same procedure as described for the *cis* isomer was followed. The purified tosylate had m.p. 67° (d).

Gas chromatography on column C showed the mixture to contain 88% of 5-t-butylcyclooctene and 12% of 1-t-butylcyclooctene. Both peaks had the same retention times as authentic olefins and both were augmented when the respective olefin was added to the unknown mixture. When the unknown mixture was analyzed on column A no acetates were detected.

Product analysis from solvolysis of cyclooctyl-p-*toluenesulfonate*. Essentially the same procedure was followed as described for *cis*-5-t-butylcyclooctyl-*p*-toluenesulfonate. The tosylate was prepared from 128 mg of cyclooctanol and 249 mg of *p*-toluenesulfonyl chloride. Purification was accomplished in the same manner as described with the exception that the tosylate was crystallized out at dry-ice temp. The tosylate obtained in this manner was a liquid and had n_D^{25} 1·5280 (lit.[31] n_D^{20} 1·5276).

Analysis on column A showed the mixture to contain 52% of *cis*-cyclooctene and 48% of cyclooctyl acetate. The retention times were identical to an authentic mixture of *cis*-cyclooctene and cyclooctyl acetate. A small amount of *trans*-cyclooctene was present (ca. 1 %) in all the mixtures analyzed.

Kinetic experiments. Published procedures were used in the study of the kinetics of the acetolysis of the tosylates. From the freezing point of Baker and Adamson glacial AcOH, the amount of water present was estimated and the equivalent amount of Ac_2O was added.[33] After a brief refluxing period, the anhyd AcOH was distilled under dry N_2. Ac_2O was added to make up a 1 % by wt soln. (11·10 ml Ac_2O per 1 l. of anhyd AcOH). This soln was used throughout the kinetic studies.

Standard solns of perchloric acid and NaOAc were prepared as described.[34] Perchloric acid (0·01526 M) containing a 1 % excess Ac_2O, was prepared by diluting 1·08 g 70 % perchloric acid and 5·40 ml Ac_2O to 500 ml with anhyd AcOH. NaOAc (0·02167 M) containing a 1 % excess Ac_2O was prepared by diluting 0·5725 g reagent grade Na_2CO_3 and 5·14 ml Ac_2O to 500 ml anhyd AcOH. The perchloric acid soln was standardized against 100–200 mg samples of primary standard potassium acid phthalate using one drop of a 0·2 % soln of crystal violet in glacial AcOH as the indicator. The end point was marked by a change from a deep blue to an aqua color.

The reaction for all of the kinetics were carried out in a 25 ml volumetric flask immersed in a constant temp water bath maintained at 25·00 ± 0·005°. The tosylates were prepared and purified as described in the product analysis experiments. After weighing the tosylates, the standard NaOAc soln was added (brought to constant temp of 25·00° beforehand) and the solvolysis began.

Aliquots (3 ml) were taken at the various times and titrated immediately (usually within 1·5 min). In the case of *cis*-5-t-butylcyclooctyl *p*-toluenesulfonate, the aliquots were quenched immediately by addition to a flask which had been cooled to − 80° containing 6 ml pentane. Titrations were carried out at about 0°.

In the case of *trans*-5-t-butylcyclooctyl *p*-toluenesulfonate, a small amount of the faster solvolyzing *cis* isomer was present. This was apparent as a larger rate constant was observed for the beginning of the reaction. If zero time was called 5 min after the solvolysis had begun, first order kinetics and a non-drifting rate constant were obtained.

The purity of all the tosylates was greater than 95 % based on titration. The final rate constants reported were calculated by the method of least squares. A sample run is given in Table 3.

TABLE 3. ACETOLYSIS OF CYCLOOCTYL *p*-TOLUENESULFONATES AT 25·00 ± 0·01°

Run No. 1: 0·14489 g *p*-toluenesulfonate in 25 ml of 0·02 M NaOAc–HOAc

t, sec	ml $HClO_4$-infinity titer (0·01526 M)	$[\mathrm{ROTs}]_t \times 10^2$	$-\log[\mathrm{ROTs}]_t$	$k_t \times 10^{-5}\ \mathrm{sec}^{-1}$
0	3·703	1·884	1·7249	
3805	3·332	1·695	1·7708	2·77
10965	2·717	1·382	1·8595	2·83
21583	1·995	1·015	1·9935	2·87
32519	1·496	0·761	2·1186	2·79
43326	1·085	0·5519	2·2581	2·83
87388	0·315	0·1602	2·7953	2·82

$t_{\frac{1}{2}}$ = 24,580 sec $k_1 = 2{\cdot}81 \times 10^{-5}\ \mathrm{sec}^{-1}$

Deamination of cyclooctyl amine in glacial acetic acid. To 327 mg of cyclooctyl amine hydrochloride in 20 ml glacial AcOH containing 164 mg NaOAc was added 138 mg $NaNO_2$ with stirring. The mixture was stirred for 24 hr at room temp after which time another 138 mg $NaNO_2$ was added portionwise over a 3 hr period. After stirring another 24 hr at room temp the mixture was poured into 200 ml of ice–water and extracted immediately with five 20 ml portions pentane. The pentane extracts were combined and washed with 5 % $NaHCO_3$aq and finally with water. After drying the pentane soln with $MgSO_4$ and filtering, the pentane was removed by distillation through a 12 in. Vigreux column. The residue was analyzed directly by gas chromatography.

Gas chromatographic analysis on column A showed the presence of 3 components: Cyclooctyl acetate, 64 %; *cis*-cyclooctene, 33 %; cyclooctanol, 3 %. The components of the unknown mixture were identified by having identical retention times when compared to authentic samples of cyclooctyl acetate; *cis*-cyclooctene and cyclooctanol. Reinforcement of the GC peaks was observed when these known compounds were added to the unknown mixture.

In another run where the reaction mixture was poured into a $NaHCO_3$aq to neutralize the AcOH, and then worked up in the described manner, all of the ratios of products remained essentially unchanged.

It was noted that *trans*-cyclooctene is isomerized to *cis*-cyclooctene under deamination conditions by submitting *trans*-cyclooctene under identical reaction conditions as described above and worked up in the same manner. The product was then analyzed by GC. The GC conditions would not isomerize *trans*-cyclooctene.

Deamination of cis-*5-t-butylcyclooctylamine.* The same procedure was used as described for the deamination of cyclooctylamine. In a 25 ml Erlenmeyer flask with magnetic stirrer, 220 mg of *cis*-XI was dissolved in 10 ml glacial AcOH containing 82 mg NaOAC. With stirring, 69 mg $NaNO_2$ was added. Another 69 mg $NaNO_2$ was added portionwise after 24 hr. After workup the residue was analyzed by GC.

GC analysis on column A showed the presence of 4 components: 84% olefins, 16% acetates, and about 1% alcohols. The acetates present had retention times identical with those of authentic samples. Analysis on Column C showed the olefins to consist of 76% of 1-t-butylcyclooctene and 8% of 5-t-butylcyclooctene.

Another sample submitted to a neutralizing workup gave the same ratio of products. A small amount (ca. 1%) of 5-t-butylcyclooctanol of unknown stereochemistry was obtained in both cases.

It was noted that 5-t-butylcyclooctene did not isomerize under the deamination conditions.

Deamination of trans-*5-t-butylcyclooctylcyclooctylamine.* The same procedure was followed with the *trans*-amine as with the *cis*-amine. Gas chromatographic analysis on column A showed 8 components to be present in the deamination mixture: 30% olefins; 41% *trans*- and 15% *cis*-acetate; 10% of 5-t-butylcyclooctanol of unknown stereochemistry and about 3% of an acetate believed to be 3-t-butylcyclooctyl acetate (retention time identical with authentic 3-t-butylcyclooctyl acetate. Analysis of the olefin portion using column C showed the mixture to contain: 11% of 1-t-butylcyclooctene, 11% of 5-t-butylcyclooctene, and 8% of a mixture of 3- and 4-t-butylcyclooctene.

TABLE 4. TYPICAL RETENTION TIMES IN MINUTES AND SECONDS

Compound	Column		
	A[a]	B[b]	C[c]
3-t-Butylcyclooctene*	1:40 or 2:14		12:30 or 21:24
1-t-Butylcyclooctene	1:55		15:00
5-t-Butylcyclooctene	2:02	2:06	18:07
4-t-Butylcyclooctene*	1:40 or 2:14		12:30 or 21:24
3-t-Butylcyclooctyl Acetate*	10:20		
cis-5-t-Butylcyclooctyl Acetate	11:22	11:18	
trans-5-t-Butylcyclooctyl Acetate	12:27	12:24	
5-t-Butylcyclooctanol†	15:37	15:30	
cis-Cyclooctene	1:20		9:00
trans-Cyclooctene	—		10:42
Cyclooctyl Acetate	7:35		
Cyclooctanol	9:10		

* I. Lillian (unpublished results), obtained by pyrolysis of 3-t-butylcycloctyl acetate. The position of the double bond (2 or 3) is not known with certainty at present.

† Stereochemistry could not be determined by GC because the isomers were inseparable under all conditions tried.

[a] The temperature of Column A was 190° with a flow rate of 120–130 ml of He/min for the t-butyl compounds and 180° for the cyclooctyl compounds.

[b] The column temperature was 203° at 120 ml of He/min.

[c] The temp of column C was 136° for t-butyl compounds and 130° for the cyclooctyl compounds.

Description of vapor phase chromatography. Three standard columns were employed in the analysis of the mixtures obtained from the solvolysis and deamination reactions. Column A was an 8-foot stainless steel column packed with 10% carbowax 20 M on 60–80 mesh firebrick and was used to determine the ratio of olefins to acetates and the ratio of the isomers of the acetates. Column B, an 8-foot × 8 mm Pyrex column packed with 20% polyglycol E 20,000 on 35–80 mesh firebrick, was used to determine the ratio of olefins to acetates. Column C was a 16 ft × 8 mm Pyrex column packed with 20% γ-nitro- γ-methylpimelonitrile suspended on 35–80 mesh firebrick and was used to determine the ratio of the isomeric olefins Table 4 records typical retention times.

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