intermediate. The necessity for the appearance of anhydride as an obligatory intermediate could be determined readily by isotope experiments of the type reported by Bender and co-workers[25] for the hydrolysis of phthalamic acid. Another likely mechanism is (7), specific acid catalysis with nucleophilic attack by carboxyl anion. We have excluded the possibility of a change in mechanism with temperature in the case of the methyl ester. Thus, the ratio of the observed rates at pH 4.0 and 3.0 at 100° was 0.39 (0.1 *M* citrate buffer) while the ratio under otherwise identical conditions at 70° was 0.41.

The activation parameters obtained for methyl hydrogen phthalate are those expected for an intramolecular reaction and are strikingly similar to those reported by Gaetjens and Morawetz for the hydrolyses of phenyl acid succinates and glutarates which proceed with participation by the neighboring carboxylate group.[5b] It has been demonstrated that the molecularity of a nucleophilic displacement reaction (for phenyl acetates) can be multiplied by approximately 5 kcal/mole in order to obtain the $T\Delta S^{\neq}$ value.[26] The present study of an intramolecular, first-order reaction has an experimentally determined $T\Delta S^{\neq}$ value of -4.6 kcal/mole, in good agreement with the conclusions of Bruice and Benkovic.[26] The large slope of the log k_{rel} *vs.* pK_a' plot for COO^- participation (Figure 5) is anticipated since electron withdrawal should favor the intramolecular nucleophilic attack. The large decrease in sensitivity to electronic effects observed for the cases of COOH participation also is anticipated on the basis that electron withdrawal should favor nucleophilic attack but disfavor protonation of the ester function (mechanisms 3 to 7).

We are unable to explain the total disagreement between our results for methyl hydrogen phthalate and those of Bender, *et al.*,[10] who report COO^- participation in the hydrolysis of this compound under similar conditions. In support of our data, we cite the results of Ågren and co-workers[7] and of Eberson[8] who present evidence for COOH participation in the hydrolysis of ethyl hydrogen phthalate and methyl hydrogen 3,6-dimethyl phthalate, respectively. A complete change in mechanism between the above-named compounds and methyl hydrogen phthalate is not readily conceivable on the basis of polar and/or steric factors.

It should be added that the k_{rate} for ethyl hydrogen phthalate (calculated from Ågren's data[7]) falls almost exactly on the line drawn in the Brønsted plot (Figure 5).

Acknowledgments. This work was supported by a grant from the National Institutes of Health. We should like to express our thanks to Mr. Clark Newcomb for his skilled technical assistance in collecting many of the rate data.

(26) T. C. Bruice and S. J. Benkovic, *J. Am. Chem. Soc.*, **86**, 418 (1964).

Proximity Effects. XLIV. Stereospecific Synthesis and Solvolysis of *cis*- and *trans*-5-Phenylcyclooctyl and *cis*- and *trans*-5-Phenylcyclooctyl-1,2,2,8,8-d_5 Tosylates[1]

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Abstract: The isomeric *cis*- and *trans*-5-phenylcyclooctyl tosylates, whose structures have been verified by a stereospecific synthesis, were prepared and solvolyzed in anhydrous formic acid. The *cis* isomer gave mostly products from a transannular 1,5 hydride shift whereas the *trans* compound afforded mostly direct substitution or elimination products. Corresponding deuterated tosylates were prepared and solvolyzed. Degradation of the deuterated products established that no transannular phenyl migration had occurred.

The occurrence of hydride shifts during solvolytic reactions of medium-ring compounds is well documented.[3] The facility of this reaction led to speculation on the possibility of transannular alkyl or aryl migration. Earlier efforts to find phenyl or methyl migration in nine-membered rings[4] proved fruitless, but the recent observation of 1% phenyl migration during solvolysis of 5,5-diphenylcyclooctyl tosylate[5] spurred new interest in the problem. Two earlier cases of solvolysis of isomeric 5-substituted cyclooctyl tosylates have been reported.[6a,b]

The symmetrical phenonium ion (Figure 1) presented a very attractive hypothetical intermediate; this type of ion has been described for the case of 1,2 aryl participation.[7] Furthermore, a 5-phenylcyclooctyl tosylate is free from the possibly deleterious *gem*-dialkyl effect found in the 5,5-diphenyl derivative, which would force C-1 and C-5 apart.

The isomeric 5-phenylcyclooctyl tosylates also offer

(1) Supported in part by a research grant (NSF-GP-1587) from the National Science Foundation.

(2) National Institutes of Health Fellow, 1963–1964; Procter and Gamble Fellow, 1962–1963.

(3) For a general discussion see E. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, p 252 ff, and references contained therein; A. C. Cope, M. M. Martin, and M. A. McKervey, to be published.

(4) A. T. Blomquist and Y. C. Meinwald, *J. Am. Chem. Soc.*, **80**, 630 (1958); A. T. Blomquist and B. F. Hallam, *ibid.*, **81**, 676 (1959).

(5) A. C. Cope, P. E. Burton, and M. L. Caspar, *ibid.*, **84**, 4855 (1962).

(6) (a) A. C. Cope and D. M. Gale, *ibid.*, **85**, 3743 (1963); (b) N. L. Allinger and S. Greenberg, *ibid.*, **84**, 2394 (1962).

(7) E. S. Gould, "Mechanism and Structure in Organic Chemistry," Henry Holt and Co., Inc., New York, N. Y., 1959, p 457 ff.

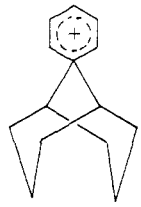


Figure 1.

some basis for comparing phenyl migration to hydride migration. The occurrence of phenyl migration could be demonstrated by labeling the 1,2,2,8,8 positions with deuterium. Degradation of the products from solvolysis would then show whether or not phenyl migration had occurred.

Synthesis and Proof of Structure. The synthesis of 5-phenylcyclooctanone by Thorpe ring closure of 5-phenylazelanitrile[8] was improved by utilization of dimethyl sulfoxide in the displacement steps and the use of tetrahydrofuran as a solvent in the lithium aluminum hydride reductions; the over-all yield of the ketone was 13%. 5-Phenylcyclooctanone was reduced with lithium aluminum hydride, yielding a crystalline mixture of isomers which, upon repeated crystallization, gave a sharply melting eutectic containing approximately two-thirds of the *cis* isomer. Formation of such a mixture with approximately the same isomeric composition was observed with the 4-phenylcyclohexanols.[9]

The isomeric mixture was converted to the 3,5-dinitrobenzoates by the procedure of Brewster and Ciotti[10] and repeated fractional recrystallization led to isolation of the *cis* isomer in 27% yield; alkaline hydrolysis afforded the free alcohol. The *cis* isomer was converted to the *trans* isomer in 46% yield by tosylation, inversion with tetraethylammonium acetate, and reduction of the resulting acetate with lithium aluminum hydride. A by-product in the inversion reaction was 5-phenylcyclooctene.

The configuration of the alcohols was established by three methods. Examination of the trifluoroacetates of the mixture and of the *cis* isomer by gas chromatography revealed that the *cis* isomer was formed preferentially upon lithium aluminum hydride reduction of the ketone; this is in accord with the preferential formation of *cis* isomers on reduction of other 5-alkylcyclooctanones.[6a,b] The nuclear magnetic resonance (nmr) spectra of the pure isomeric alcohols provided further proof of the correctness of the original assignment. The *cis* isomer gave rise to a very complex methylene absorption consisting of a broad multiplet centered at δ 1.80 with side bands at 2.03 and 1.47. The methylene signal for the *trans* isomer was much simpler, consisting of a broad singlet at δ 1.78. This was interpreted as an indication of the relative inflexibility of the ring in the *cis* isomer because it is able to accommodate both substituents in a pseudo-equatorial position stabilizing the conformation. This is exemplified in Figure 2 utilizing the crown conformation; several other conformations also show relatively unstrained equatorial forms. The *trans* isomer can have both substituents in a pesudo-equatorial position only in a strained twist form of the ring; in the other conformations one of the substituents

(8) A. C. Cope and R. J. Cotter, *J. Org. Chem.*, **29**, 3467 (1964).
(9) H. E. Ungnade, *ibid.*, 13, 361 (1948).
(10) J. H. Brewster and R. Ciotti, *J. Am. Chem. Soc.*, 77, 6214 (1955).

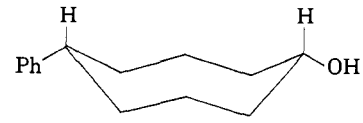


Figure 2.

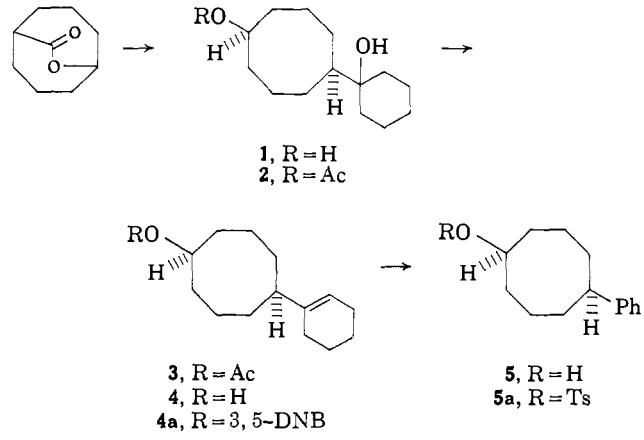


Figure 3.

is pseudo-axial. Thus the *trans* isomer probably exists in solution as a rapidly equilibrating mixture of conformers, causing the methylene protons to have approximately the same chemical shift. The isomeric 5-methylcyclooctanols also exhibit this behavior.[6a]

The third method by which the configuration was established was a stereospecific synthesis (Figure 3). The availability of 5-hydroxycyclooctanecarboxylic acid ε-lactone,[6a] of known stereochemistry, made it an attractive starting material. Treatment of the lactone with the Grignard reagent prepared from pentamethylene dibromide[11] in three molar excess gave the glycol **1** in 40% yield. Dehydration of the hydroxyacetate **2** with phosphorus oxychloride in pyridine[12] gave 90% pure **3** in 98% yield. In its nmr spectrum **3** exhibited absorption for one olefinic hydrogen, indicating a trisubstituted double bond; the possibility that the double bond had migrated into the cyclooctane ring was excluded by the coupling of the olefinic proton. The signal was a broad, ill-defined multiplet, much the same as that described for systems having a 1-alkylcyclohexene unit.[13] A 1-alkyl- and a 1-arylcyclooctene have been measured[14] and each exhibited the olefinic proton as a cleanly separated triplet, J = 8 cps.

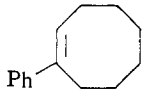
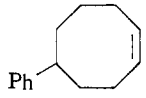
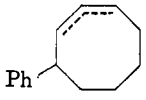
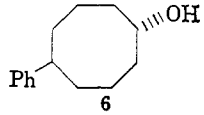
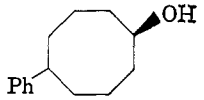
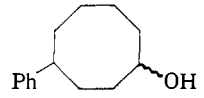
The crude acetate **3** was reduced to the alcohol **4** which was converted directly to the 3,5-dinitrobenzoate **4a** for purification. Upon hydrolysis the crystalline olefinic alcohol **4** was obtained in 64% over-all yield from the glycol **1**. Attempted dehydrogenation of the olefinic acetate **3** under mild conditions failed; refluxing in *p*-cymene in the presence of platinum did result in aromatization, but the product was shown by gas chromatography (vpc) to be a mixture of configurational isomers.

(11) A. Murray, III, and D. L. Williams, "Organic Syntheses with Isotopes," Interscience Publishers, Inc., New York, N. Y., 1958, p 102.
(12) K. L. Rinehart and E. G. Perkins, *Org. Syn.*, 37, 37 (1957).
(13) "Tables of NMR Spectra," Varian Associates, Palo Alto, Calif., 1962.
(14) See ref 6a. Other more complicated cyclooctenes with this same grouping show a clean triplet: A. C. Cope and J. M. McIntosh, unpublished results.

The stereospecific synthesis was accomplished by allylic bromination of **3** with N-bromosuccinimide followed by dehydrohalogenation with lithium carbonate in dimethylformamide. This procedure led to a mixture of polyunsaturated acetates from which *cis*-5-phenylcyclooctyl acetate could be isolated by chromatography on alumina. This acetate was essentially free of the *trans* isomer as shown by vpc. During the dehydrohalogenation the aromatic product presumably is formed by a disproportionation mechanism. The acetate was reduced with lithium aluminum hydride; the product was a crystalline alcohol which was identical with material which on other grounds had been designated as the *cis* isomer.

Solvolysis. The alcohols were converted to their respective tosylates (**5a** and **5b**) which were solvolyzed in anhydrous formic acid 0.25 *M* in sodium formate. After reduction of the formates with lithium aluminum hydride, the products were isolated where it was possible and identified by comparison of the infrared spectra and retention times with those of authentic materials. Table I indicates the composition of the solvolysis products.

Table I. Products of Solvolysis of *cis*- and *trans*-5-Phenylcyclooctyl Tosylate (**5a** and **6a**)

Products	Formed on solvolysis of *cis* tosylate **5a**	Formed on solvolysis of *trans* tosylate **6a**
	81.2	19.0
	11.0	47.5
	...	2.6
 **6**	1.4	8.1
 **5**	1.4	2.3
	2.5	18.8
Unknowns	2.5[a]	1.8[b]

[a] Includes 2.2% of a material which gives the same decomposition peaks on vpc analysis as does 1-phenylcyclooctanol. [b] Includes 0.5% of a methylphenylcycloheptene (see text).

The olefin fraction was isolated by column chromatography and 1- and 5-phenylcyclooctene were isolated by collection from vpc. It was not possible to isolate either 3- or 4-phenylcyclooctene, but the formation of either one or both from the *trans* tosylate was inferred from two pieces of information: there was a peak on vpc of the olefin fraction which corresponded to the retention time of authentic material; when the total olefin fraction was hydrogenated, the product was 99% of phenylcyclooctane. Thus, the component was a phenylcyclooctene.

From solvolysis of a mixture of isomers (61:39 *cis*:*trans*) 0.08% of a material was isolated which has been identified tentatively as a methylphenylcycloheptene. It was shown by vpc analysis that the product arises during solvolysis of **6a** but not during solvolysis of **5a**. The amount of material isolated precluded positive identification, but the presence of a methyl group and an olefinic bond was clearly demonstrated by the infrared spectrum and the mass spectrum of the material.

An alcoholic fraction from solvolysis of each pure isomer was obtained by column chromatography and the composition was estimated by indirect methods. Preparative thin layer chromatography was used to isolate a mixture of the 4- and 5-phenylcyclooctanols, which were oxidized quantitatively to the respective ketones and identified as such. Another sample of the secondary alcohol mixture was coverted to trifluoroacetates in 97% crude yield. Vpc analysis of this material disclosed two peaks; the latter was identified as *trans*-5-phenylcyclooctyl trifluoroacetate (**6b**). The first peak had a retention time and an infrared spectrum consistent with a mixture of the isomeric 4-phenylcyclooctyl trifluoroacetates and *cis*-5-phenylcyclooctyl trifluoroacetate (**5b**). An estimate of the amount of **5b** in the mixture from either isomeric tosylate could be made by difference, however, knowing the amounts of positional isomers from oxidation to the ketones.

Authentic samples were synthesized for comparison with the solvolysis products. 5-Phenylcyclooctene (**7**) was prepared by pyrolysis of 5-phenylcyclooctyl xanthate. 1-Phenylcyclooctanol was prepared by addition of phenylmagnesium bromide to cyclooctanone. Dehydration with iodine in benzene gave the known 1-phenylcyclooctene (**8**).[15] Epoxidation of **7** followed by lithium aluminum hydride reduction gave a mixture of 4- and 5-phenylcyclooctanols in a ratio of 52.5:47.5 as determined by vpc analysis of the ketones formed upon Jones oxidation of the mixture. The alcohols were treated with phosphorus oxychloride in pyridine,[12] yielding a mixture of olefins and another product which was presumably a mixture of chlorides. The olefin mixture was subjected to preparative vpc; it was found to contain 59.0% **7**, 26.6% 4-phenylcyclooctene, and 14.5% 1-phenylcyclooctene. Since 4-phenylcyclooctene was not separated from 3-phenylcyclooctene (see below) the only criterion for the purity of the olefin was the nmr spectrum, which displayed exactly five allylic and benzylic protons. Since this material was different from 5-phenylcyclooctene by vpc it must be 4-phenylcyclooctene.

Authentic 3-phenylcyclooctene was prepared by coupling of phenylmagnesium bromide with 3-bromocyclooctene.[16] The nmr spectrum of this material was distinguished by the low-field position of the benzylic proton at δ 3.65 and the resonance for only two allylic protons at 2.14. This material could not be separated from 4-phenylcyclooctene by vpc.

(15) A. C. Cope and A. A. D'Addieco, *J. Am. Chem. Soc.*, **73**, 3419 (1951).

(16) A. C. Cope and G. L. Woo, *ibid.*, **85**, 3601 (1963).

Treatment of cyclooctane-1,4-dione with less than 1 equiv of phenyllithium gave 4-hydroxy-4-phenylcyclooctanone as the hemiketal. Hydrogenolysis in the presence of palladium on carbon in the presence of a trace of perchloric acid yielded 4-phenylcyclooctanone. Hydroboration of 1-phenylcyclooctene followed by hydrogen peroxide oxidation gave a mixture of secondary alcohols which was separated by chromatography on alumina. The fractions were oxidized separately to two ketones different from 4- and 5-phenylcyclooctanone.[17]

The formation of 1-phenylcyclooctene, almost to the exclusion of other products, during solvolysis of the *cis* tosylate is in accord with the earlier results with 5-alkylcyclooctyl tosylates. The stereochemistry of the *cis* tosylate is such that the back side of C-1 is especially vulnerable to attack by migrating hydride; in these 5-substituted derivatives the formation of a tertiary carbonium ion makes 1,5 hydride shift especially favorable. However, the presence of either 3- or 4-phenylcyclooctene indicates that 1,3 or 1,2 hydride shifts also occurred. While this was not observed for the 5-alkylcyclooctanols, a 1,3 shift was observed when deuterated cyclooctyl brosylate was solvolyzed,[18] but no 1,2 hydride shift was found. Formation of other products during the present solvolysis, however, indicates that it is probably a 1,2 shift that accounts for this minor product.

The small amount of the methylphenylcycloheptene that was formed probably arose from a Wagner–Meerwein rearrangement of the initially formed carbonium ion. Ring contractions, while not observed during the solvolysis of other 5-substituted cyclooctyl tosylates, have been observed in other reactions of medium-sized ring compounds.[19]

The formation of 4-phenylcyclooctanol during the solvolyses of both the *cis* and *trans* tosylates (**5a** and **6a**) was unexpected. This product presumably arises by a 1,2 hydride shift followed by attack of solvent.[20] The fact that one-half of the secondary alcohols formed from **5a** and two-thirds of those from **6a** arise from 1,2 hydride shift points to a significant role played by the phenyl group during the solvolysis. This hypothesis is strengthened by the 4:1 ratio of retention to inversion in the alcohol fraction from **6a**.

To determine whether or not phenyl migration had occurred, a labeling scheme was employed (Figure 4). Phenylcyclooctanone was labeled in the α positions by equilibration in deuterium oxide both alone and with added inert solvents, such as tetrahydrofuran and dioxane, in the presence of potassium carbonate. After eight equilibrations the mass spectrum indicated 82.20% d_4 species. Reduction with lithium aluminum deuteride gave an alcohol mixture from which *cis*-5-phenylcyclooctanol-d_5 could be isolated by conversion to the 3,5-dinitrobenzoates, fractional crystallization, and liberation of the alcohol by basic hydrolysis; combustion analysis indicated 4.79 atoms of deuterium per molecule. The *trans* isomer was obtained by Walden inversion as with the nondeuterated compound.

(17) For details see R. B. Kinnel, Ph.D. Thesis, Massachusetts Institute of Technology, 1964.

(18) A. C. Cope and D. M. Gale, *J. Am. Chem. Soc.*, **85**, 3747 (1963).

(19) A. C. Cope and M. J. Youngquist, *ibid.*, **84**, 2411 (1962); A. C. Cope and J. K. Hecht, *ibid.*, **84**, 4872 (1962); A. C. Cope, P. Scheiner, and J. M. McIntosh, unpublished results.

(20) Both 5-phenylcyclooctene and 5-phenylcyclooctyl formate were found to be stable to solvolysis conditions.

Table II. Solvolysis of Deuterated 5-Phenylcyclooctyl Tosylates

	Product compn			
Isomer	1-Phenylcyclooctene d_5	5-Phenylcyclooctene-d_4	4- and 5-Phenylcyclooctanol-d_5	Others
cis tosylate-d_5	91.2	5.8	2.2	0.8[a]
trans tosylate-d_5	15.3	46.5	34.7	3.6[b]

[a] Includes 0.5% of a material which has the same decomposition pattern on vpc as 1-phenylcyclooctanol. [b] Includes 1.7% of 1-phenylcyclooctanol.

The pure alcohols were converted to their tosylates and solvolyzed separately. The products are shown in Table II.

A mixture of 4- and 5-phenylcyclooctanols was isolated from the alcoholic fraction from solvolysis of the *trans* tosylate; the material was oxidized to 4- and 5-phenylcyclooctanone and the deuterium α to the ketone was removed by equilibration with sodium methoxide in methanol.[21] Measurement of the mass spectrum of this material exhibited no peak at *m/e* 207, indicating that no phenyl migration had occurred in formation of the secondary alcohols. It was estimated that 1.5% of d_5 species could have been detected. Peaks were observed at *m/e* 202 and 204 for the molecular ions of the two ketones (see Figure 4). The peak at *m/e* 204 was 59.2% of the total, which corroborates the estimate of 4-phenylcyclooctanone found during solvolysis of the nondeuterated compound.

The possibility remained that phenyl migration had occurred during formation of 5-phenylcyclooctene. The olefin was isolated from the solvolysis product of the deuterated *trans* tosylate by preparative vpc. Oxidation with potassium permanganate–sodium metaperiodate, followed by esterification with diazomethane, afforded a deuterated dicarboxylic ester in 66% crude yield. A sample of authentic dimethyl 4-phenylsuberate was obtained from 5-phenylcyclooctene in a similar manner. The deuterated dicarboxylic ester was equilibrated with sodium methoxide in methanol to remove the α-deuterium; the ester with four α deuterons was prepared in analogous fashion from dimethyl 4-phenylsuberate, sodium methoxide, and methanol-O-*d*.

In their respective mass spectra, all four of the esters lost the elements of methanol, affording a strong peak at 32 *m/e* units below the molecular ions. There were also present moderate peaks for the molecular ions. Examination of the spectrum from the unknown deuterated ester revealed 10.6% of a peak at *m/e* 251, indicating a d_5 species; however, there was no corresponding peak in the molecular ion region at *m/e* 283. It was estimated that 5% or less could have been detected using the molecular ion. Furthermore, after equilibration, the peak was shifted to *m/e* 249 and no[22] peak was observed at *m/e* 251. No peak was observed at *m/e* 283 (d_5) or *m/e* 281 (d_3) in the equilibrated ester. The remainder of the spectrum was virtually identical with that of dimethyl 4-phenylsuberate.

(21) An experiment run on labeled 5-phenylcyclooctanone indicated that 99.9% of the deuterium was removed.

(22) There could have been as much as 1% of a peak at *m/e* 251, but it is considered part of the isotopic content of the peak at 249.

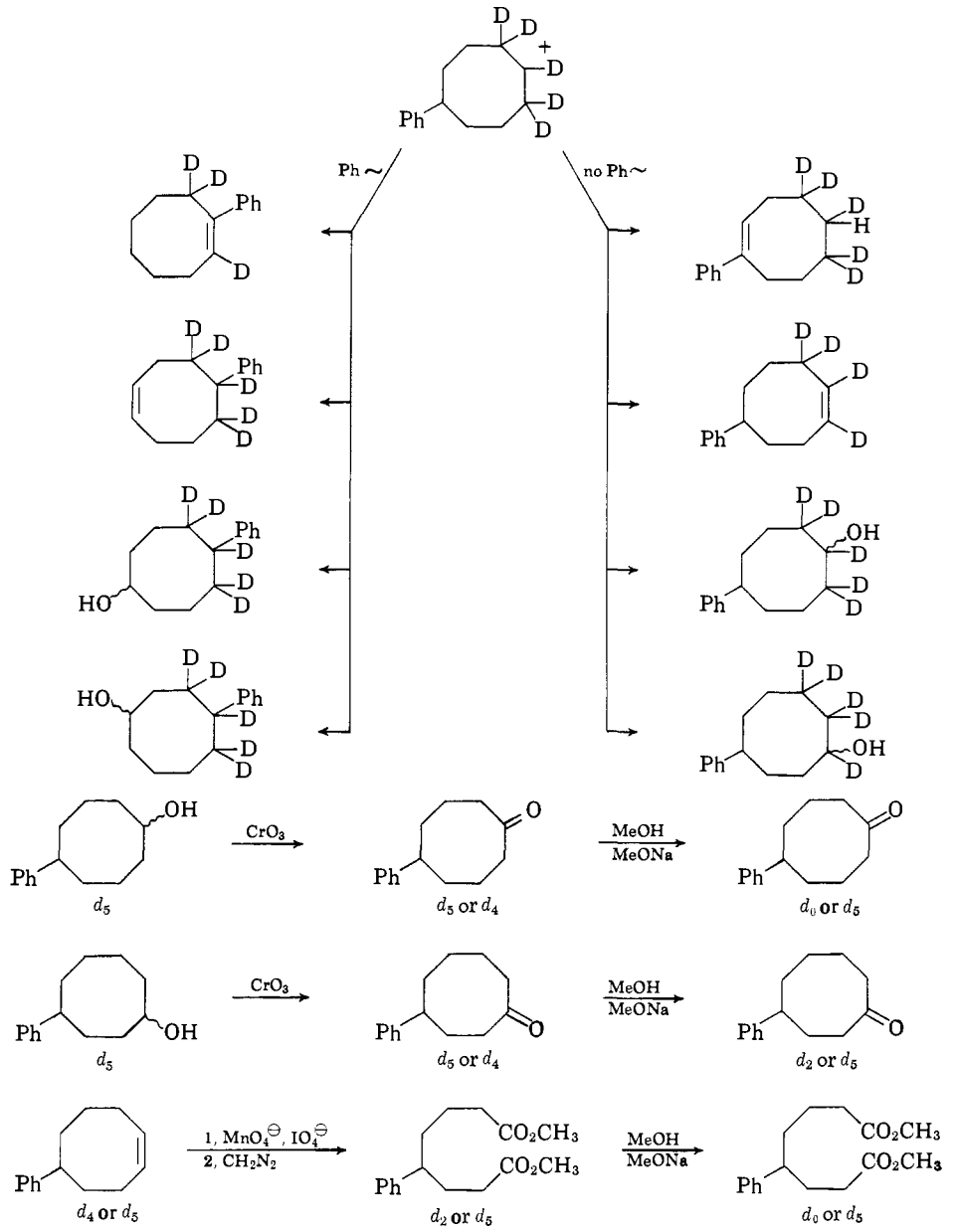


Figure 4. Scheme for determination of phenyl migration.

The foregoing data indicate that no direct 1,5 phenyl migration has occurred leading to 5-phenylcyclooctene (see Figure 4). The presence of the spurious peak at *m/e* 251 in the spectrum of the deuterated ester from solvolysis is most easily accounted for by contamination of the 5-phenylcyclooctene with 3-phenylcyclooctene, which is separated only with difficulty by vpc. (One of the isomeric cylooctenes was observed during solvolysis of the *trans* tosylate.) The deuterated 3-phenylcyclooctene would then have been converted to a d_5 dimethyl 2-phenylsuberate and subsequently to a d_3 dimethyl 2-phenylsuberate by equilibration, as shown in Figure 5.

An examination of Dreiding models reveals a possible reason why phenyl migration does not occur during solvolysis of the *trans* tosylate. During formation of the bridged ion (Figure 1) which is at least a transition state for phenyl migration, there develop severe interactions between the *o*-hydrogens and the methylene hydrogens β to the bridging group.

The ratio of 1-phenylcyclooctene to 5-phenylcyclooctene from solvolysis of the deuterated and nondeuterated *cis* tosylate was quite different (8:1 and 15:1, respectively). This was interpreted as indicative of a true E2 elimination leading to 5-phenylcyclooctene, since the rate of transannular hydride migration should be essentially the same for the deuterated and nondeuterated tosylates. The elimination, if it proceeded by an E2 mechanism, should be considerably slower in the deuterated *cis* tosylate.

Experimental Section[23]

5-Phenylazelanitrile. A solution of 101 g of 4-phenylheptane-1,7-diol ditosylate[8] and 19.5 g of sodium cyanide in 500 ml of dimethyl sulfoxide was stirred at room temperature for 6 days.

(23) All melting points were taken on a Kofler hot stage and are corrected; boiling points are uncorrected. Vpc analyses were carried out on an F and M Model 720 gas chromatograph, utilizing the following columns: column A, 4 ft × 0.25 in. XF-1150 (G.E. experimental nitrile silicone fluid), 15% on 80–100 mesh Chromosorb W; column B, 2 ft ×

The solution was poured into 2.5 l of cold water and extracted with two portions of ether. The combined ether layers were washed with five portions of water and dried. Removal of the solvent gave 41.7 g (95%) of crude dinitrile. Recrystallization at −20° from 100 ml of methanol gave 33.6 g of the dinitrile, mp 31–35°, (lit.[8] mp 34.0–34.6°), in two crops.

1-Amino-2-cyano-5-phenylcyclooctene. To 40.4 g of naphthalene dissolved in 1 l. of anhydrous ether under nitrogen was added 12 g of sodium wire cut into small pieces. Freshly distilled N-methylaniline (70.0 g) was added at once and the mixture was refluxed until the sodium had disappeared. Addition of a solution of 11.8 g of 5-phenylazelanitrile in 1 l. of ether through a simple dilution apparatus was begun and continued for 22 hr. After an additional 2-hr reflux period the mixture was cooled and 1.5 l. of cold water was added. The layers were separated and the aqueous phase was extracted with four portions of ether. The ether was removed and the residue was steam distilled to remove the by-products. The aqueous residue was extracted with methylene chloride and the organic layer was dried. *n*-Hexane was added and slow evaporation yielded 10.49 g (89%) of the enamine in three crops, mp 85–99°. A sample which was recrystallized repeatedly from ethanol melted at 96–98°; $\lambda_{max}^{CHCl_3}$ 264 mμ (log ε 4.02); nmr δ 7.17 (5 H), 4.65 (broad, 2 H), 2.58 (broad shoulder, 1 H), 2.33 (multiplet, 4 H), 1.77 (multiplet, 6 H).

5-Phenylcyclooctanol. 5-Phenylcyclooctanone[8] (1.434 g) in 15 ml of ether was added dropwise to a solution of 0.135 g of lithium aluminum hydride in 15 ml of anhydrous ether at a rate sufficient to maintain reflux. The mixture was refluxed for 1 additional hr, then 5 ml of water was added, followed by 50 ml of 10% hydrochloric acid. The layers were separated and the aqueous phase was extracted with two additional portions of ether. The combined organic phases were dried and the solvent was removed. Trituration with pentane and removal of the solvent gave 1.443 g of the crude crystalline alcohol. Four recrystallizations from pentane afforded 1.129 g (78%) of a mixture of the *cis* and *trans* isomers, mp 65.0–67.5°.

Anal. Calcd for $C_{14}H_{20}O$: C, 82.30; H, 9.86. Found: C, 82.19; H, 9.75.

***cis*-5-Phenylcyclooctyl 3,5-Dinitrobenzoate.** To 2.20 g of 3,5-dinitrobenzoic acid dissolved in 125 ml of dry pyridine was added 3.96 g of *p*-toluenesulfonyl chloride. The solution was chilled to 0° and 2.10 g of the above mixture of *cis*- and *trans*-5-phenylcyclooctanols, mp 64.5–66.5°, was added. The mixture was swirled in an ice bath until solution occurred, and allowed to warm to room temperature during the next hour. The solution was poured into 700 ml of ice–water with stirring; the product soon crystallized. Filtration and air drying yielded 3.55 g (86%) of crude ester, mp 126–140°. Fractional crystallization of the material from chloroform–ethanol yielded 1.062 g (27%) of the *cis* isomer, mp 140–142°, in the two least soluble fractions after 15 stages.

Anal. Calcd for $C_{21}H_{22}N_2O_6$: C, 63.30; H, 5.57. Found: C, 63.10; H, 5.52.

***cis*-5-Phenylcyclooctanol (5).** *cis*-5-Phenylcyclooctyl 3,5-dinitrobenzoate (437 mg) was hydrolyzed by refluxing overnight with a mixture of 15 ml of methanol and 5 ml of 10% potassium hydroxide solution. The mixture was diluted with water and extracted with ether. Removal of ether from the dried extracts afforded 197 mg (88%) of the crude alcohol, mp 69.5–70.5°. Several recrystallizations from pentane furnished an analytical sample: mp 70.0–71.0°; infrared (KBr) 1470, 1455, 1447 (sh), 1350, 1084, 1072, 1047 (sh), 1038, 989, 976 cm^{-1}; nmr δ 1.83 (multiplet, side bands at δ 1.48 and 2.03, 12 H), 2.62 (broad, 1 H), 3.12 (singlet, 1 H), 3.95 (broad, 1 H), 7.17 (singlet, 5 H).

Anal. Calcd for $C_{14}H_{20}O$: C, 82.30; H, 9.87. Found: C, 82.28; H, 9.91.

***trans*-5-Phenylcyclooctanol (6).** Hydrolysis of *cis*-5-phenylcyclooctyl 3,5-dinitrobenzoate (1.937 g), mp 139.0–142.3°, gave 914 mg (92%) of crude *cis*-5-phenylcyclooctanol. It was dissolved in 10 ml of pyridine, 3.81 g (100% excess) of *p*-toluenesulfonyl chloride was added, and the resulting solution was allowed to stand at −10° for 18 hr. The mixture was poured into 75 ml of ice–water. Stirring and scratching yielded crystals; they were collected and air dried, and amounted to 1.769 g (99%).

The tosylate was dissolved in 80 ml of anhydrous acetone and 6.3 g of tetraethylammonium acetate monohydrate[24] was added. The solution was refluxed for 53 hr, cooled, and evaporated. The residual oil was diluted with 75 ml of water and extracted with two portions of ether. The ether layers were washed with water and dried, and the solvent volume was adjusted to about 50 ml by evaporation. To this solution 100 mg of lithium aluminum hydride was added in small portions over a period of 10 min with stirring. Stirring was continued for 3 hr. Water (0.5 ml) was added slowly; after the mixture was stirred for 0.5 hr, magnesium sulfate was added and, after stirring for an additional 0.5 hr, the dried solution was filtered.[25] Removal of the solvent gave 943 mg of oily crystals. The mixture was dissolved in 5 ml of methylene chloride and diluted with 70 ml of pentane. Chilling at −8° gave 355 mg of *trans*-5-phenylcyclooctanol. The mother liquors were evaporated to an oil and chromatographed over 12 g of alumina (Woelm, activity III). Elution with pentane yielded 457 mg of 5-phenylcyclooctene (50.6%), while elution with ether yielded 180 mg of crystalline **6**, which was combined with the crystalline product previously obtained by cooling. Crystallization from methylene chloride–pentane gave 425 mg (41.5% from the 3,5-dinitrobenzoate) of the *trans* alcohol, mp 82.0–84.0°. An analytical sample, prepared by three more recrystallizations, melted at 83.5–84.5°; infrared (KBr) 1482 (m), 1465 (sh), 1450 (s), 1375, 1340, 1308, 1277, 1223, 1209,

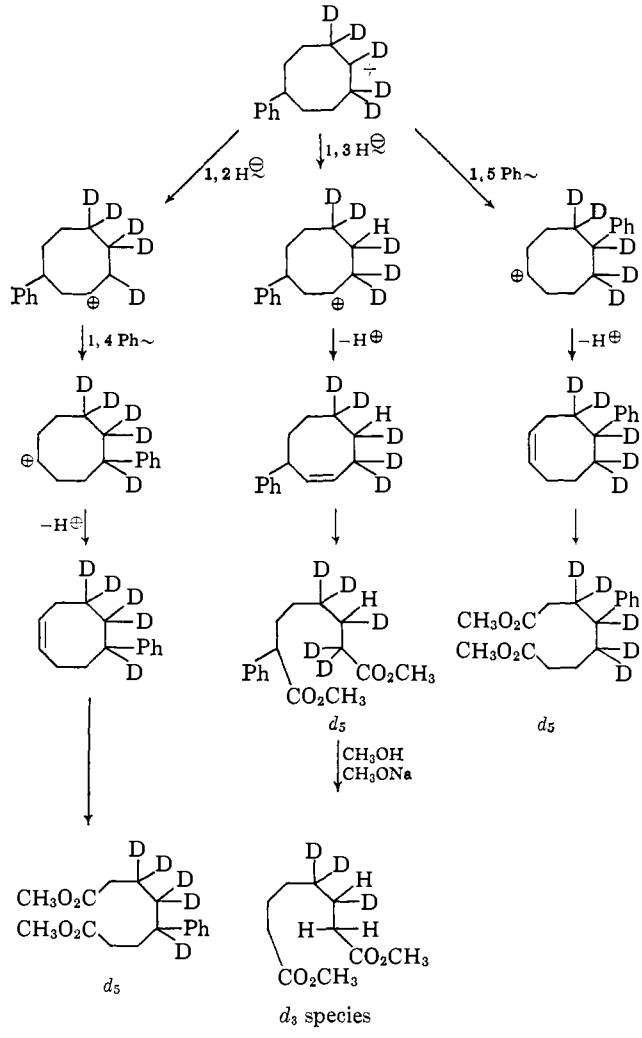


Figure 5. Possible pathways for phenyl migration.

0.25 in. 20% SE-30 (silicone rubber) on 60–80 mesh Chromosorb W; column C, the same as column B except at a concentration of 10%; column D, 10 ft × 0.25 in. Versamid 900 (General Mills), 5% on 60–80 mesh Diatoport S; column E, 12 ft × 0.25 in. Versamid 900, 10% on 60–80 mesh Diatoport S. Compositions of mixtures were measured by tracing the curves obtained from vpc and cutting out and weighing the peaks. Nmr spectra were recorded on a Varian Associates A-60 instrument and absorptions are expressed in δ units relative to tetramethylsilane as the internal standard. Except as noted the drying agent employed was magnesium sulfate and solvents were removed under reduced pressure.

(24) A. C. Cope and M. Fournier, *J. Am. Chem. Soc.*, **79**, 3896 (1957).

(25) This method of isolation is designated hereafter by ref 25.

1165, 1155 (all w), 1063 (sh), 1059 (s), 1056 (w), 1051 (s), 1002 (w), 988 (s), 976 (sh), 915–920 (w), 868 (w) cm^{-1}; nmr δ 1.78 (broad, singlet, 12 H), 2.72 (broad, 1 H), 2.90 (singlet, 1 H), 3.79 (broad, 1 H), 7.11 (singlet, 5 H).

Anal. Calcd for $C_{14}H_{20}O$: C, 82.30; H, 9.87. Found: C, 82.22; H, 9.94.

***trans*-5-Phenylcyclooctyl 3,5-Dinitrobenzoate.** The ester was prepared as above in 81% crude yield from 50 mg of *trans*-5-phenylcyclooctanol. Three recrystallizations from methylene chloride–pentane furnished an analytical sample, mp 141.5–142.5°. The melting point of a mixture with the *cis* isomer was 126–140°

Anal. Calcd for $C_{21}H_{22}N_2O_6$: C, 63.30; H, 5.57. Found: C, 63.21; H, 5.58.

***cis*-5-Phenylcyclooctyl Trifluoroacetate (5b).** To a solution of 9.6 mg of *cis*-5-phenylcyclooctanol in 0.1 ml of dry pyridine was added 0.01 ml of trifluoroacetic anhydride. Water (2 ml) was added and the mixture was extracted with two portions of ether. The combined ether extracts were washed with water, two portions of 10% hydrochloric acid, water, and 5% sodium bicarbonate. Drying and removal of the solvent yielded 13.5 mg (95%) of *cis*-5-phenylcyclooctyl trifluoroacetate as a colorless oil exhibiting no OH absorption in the infrared and a strong peak at 1775 cm^{-1}. A sample collected from column B (200°) for analysis had $n^{29.3}D$ 1.4771.

Anal. Calcd for $C_{16}H_{19}O_2F_3$: C, 63.99; H, 6.38. Found: C, 64.29; H, 6.48.

***trans*-5-Phenylcyclooctyl Trifluoroacetate (6b).** The ester was prepared in 97% crude yield from 10.3 mg of **6**. The analytical sample, collected in the same way as the *cis* isomer, had $n^{30.6}D$ 1.4758.

Anal. Calcd for $C_{16}H_{19}O_2F_3$: C, 63.99; H, 6.38. Found: C, 64.37; H, 6.42.

***cis*-5-Phenylcyclooctyl Acetate.** The compound was obtained in 92% crude yield from the alcohol and acetic anhydride by the procedure used for preparing the trifluoroacetates. Collected material (column B, 200°) had $n^{30.6}D$ 1.5181.

Anal. Calcd for $C_{16}H_{22}O_2$: C, 78.01; H, 9.00. Found: C, 77.86; H, 9.12.

***trans*-5-Phenylcyclooctyl Acetate.** A collected sample (column B, 195°) had $n^{29.1}D$ 1.5197.

Anal. Calcd for $C_{16}H_{22}O_2$: C, 78.01; H, 9.00. Found: C, 77.93; H, 8.98.

***trans*-5-Phenylcyclooctyl Tosylate (6a).** To a solution of 91 mg of **6** dissolved in 1 ml of pyridine was added 179 mg of *p*-toluenesulfonyl chloride. The resulting solution was allowed to stand at −20° for 15 hr. The mixture was poured into 25 ml of ice–water and stirred for 20 min, during which time the ester crystallized. Filtration and air drying gave 149 mg (94%) of the ester, which was used without purification for solvolysis, since the infrared spectrum displayed no OH absorption. Two recrystallizations from pentane–methylene chloride gave an analytical sample,[26] mp 70.0–71.5°.

Anal. Calcd for $C_{21}H_{26}O_3S$: C, 70.35: H, 7.31. Found: C, 70.01; H, 7.61.

***cis*-5-Phenylcyclooctyl Tosylate (5a).** The ester was prepared in 97% crude yield by the procedure described for the *trans* isomer. One recrystallization from pentane gave the unstable tosylate, mp 69.5–70.5° dec.

Anal. Calcd for $C_{21}H_{26}O_3S$: C, 70.35; H, 7.31. Found: C, 70.20; H, 7.48.

Solvolysis Runs. A sample of tosylate was slurried in an amount of formic acid (anhydrous,[27] 0.049 *M* in sodium formate[28]) such that the resulting mixture was 0.015 *M* in tosylate, and was placed in an oil bath maintained at 50 ± 2° and stirred for 24.0 hr. The reaction mixture was quenched with ten volumes of cold water and the product was extracted with two portions of ether. The combined ethereal extracts were washed with five portions of water and one portion of saturated sodium bicarbonate. Drying and removal of the solvent yielded the crude solvolysis product (93–97%); it was analyzed on column B (program 120–220° at 2°/min) and the olefin to formate ratio was determined. The crude solvolysis product was dissolved in 10–20 volumes of ether and stirred for 2–3 hr with excess lithium aluminum hydride. Quantitative recovery of a mixture of olefins and alcohols resulted after the usual work-up.[25] The mixture was chromatographed over alumina (Woelm, activity III); elution with pentane gave the olefin fraction, while elution with ether gave the alcohol fraction.

Identification of Olefins. The olefin fraction was subjected to analysis by vpc on column E (175°) and column B (160°). The peaks were collected from column E and then recollected from column B (200°). The 1- and 5-phenylcyclooctenes were identified by comparison of their retention times and infrared spectra with authentic specimens. A third material, present in the olefins from solvolysis of **6a**, had the same retention time as 3- and 4-phenylcyclooctene but could not be isolated.

Phenylcyclooctane from Olefins Obtained by Solvolysis. A sample of 46 mg of olefins from solvolysis of the *trans* tosylate **6a** was added to 3 ml of ethanol containing 27 mg of prereduced 10% palladium on carbon. The mixture absorbed 100% of the theoretical amount of hydrogen. It was filtered and the filtrate was diluted with 30 ml of water and extracted with two portions of ether. Drying and removal of the solvent yielded 36 mg of oil. Vpc analysis (column E, 175°) indicated 99.0% of phenylcyclooctane. A collected sample exhibited an infrared spectrum identical with authentic material.[29]

A Methylphenylcycloheptene. An olefin fraction (1.456 g) from solvolysis of a mixture of the *cis* and *trans* tosylates **5a** and **6a** was processed by preparative vpc on an 8-ft 20% silicone rubber column at 187°; this gave material enriched in the most volatile component. This had been shown to arise only from the *trans* tosylate **6a**. Collection from column E (180°) followed by re-collection from column B (160°) gave 1.2 mg (0.08%) of hydrocarbon. The infrared spectrum of this material had peaks due to a phenyl group (3030, 1600 cm^{-1}), unsaturation (1600 cm^{-1}), and a methyl group (2970, 1380 cm^{-1}). The mass spectrum indicated a molecular weight of 186 and exhibited a moderate peak at M − 15.

Identification of the Alcohols. The alcohol fraction was analyzed on column B (200°). The peak which corresponded to 5-phenylcyclooctanol comprised 75–90% of this mixture of alcohols. A sample (12 mg) was subjected to thin layer chromatography and the material having R_f 0.55–0.65 (ethyl acetate–hexane, 1:1) was recovered by elution with methylene chloride, giving 9 mg of alcohols, which were oxidized with Jones reagent;[30] work-up gave 8 mg of the ketone mixture. Analysis on column B (200°) showed only one peak. Analysis on column E (180°) showed two peaks; they had retention times, mass spectra, and infrared spectra identical with those of 4- and 5-phenylcyclooctanone, respectively.

A second sample of the alcohol mixture was acylated with trifluoroacetic anhydride in 90–96% yield. The infrared spectrum of the crude material exhibited no hydroxyl bands and a strong band at 1776 cm^{-1}. Analysis on column D (160°) disclosed two peaks, one of which corresponded in its retention time and infrared spectrum to *trans*-5-phenylcyclooctyl trifluoroacetate. The faster moving component had a retention time of a mixture of the two 4-phenylcyclooctyl trifluoroacetates and *cis*-5-phenylcyclooctyl trifluoroacetate (**5b**). The infrared spectrum was different from that of either a mixture of the 4-phenylcyclooctyltrifluoroacetates or of **5b**, but closely resembled a composite spectrum.

***cis*-5-(1-Hydroxycyclohexyl)cyclooctanol (1).** To 1.20 g of magnesium overlaid with 20 ml of anhydrous ether was added 5.705 g of pentamethylene dibromide under nitrogen. The reaction started soon after commencing stirring, at which time 20 ml of ether was added as a moderator. The reaction had completely subsided after 1 hr. The mixture was cooled in an ice bath and a solution of 1.288 g of 5-hydroxycyclooctanecarboxylic acid ϵ-lactone[6a] in 10 ml of ether was added over a period of 10 min. The mixture was allowed to stand overnight and then it was refluxed for 1 hr. After addition of 12 ml of 25% ammonium chloride solution to the mixture it was stirred for 1 hr. The ether solution was decanted and the residue was washed with two portions of ether. The combined ether solutions were washed with three portions of water and one portion of 5% sodium bicarbonate. After drying and removal of the solvent 1.825 g of a waxy solid was obtained. Five crystallizations from chloroform–hexane gave 466 mg (25%) of *cis*-5-(1-hydroxycyclohexyl)cyclooctanol in two crops, mp 122.0–125.5°, with infrared bands at 3585 and 3420 cm^{-1}. An analytical sample was prepared by recrystallization from chloroform at −20°, mp 130.8–131.4°.

Anal. Calcd for $C_{14}H_{26}O_2$: C, 74.28; H, 11.58. Found: C, 74.52; H, 11.48.

(26) The material decomposed within 10 min on drying over silica gel under high vacuum. Air drying was found to be adequate.

(27) S. Winstein and H. Marshall, *J. Am. Chem. Soc.*, 74, 1120 (1952).

(28) S. Winstein and R. Heck, *ibid.*, 78, 4801 (1956).

(29) A. C. Cope and E. C. Hermann, *ibid.*, 72, 3405 (1950).

(30) A. Bowers, T. G. Halsall, E. R. H. Jones, and A. J. Lemin, *J. Chem. Soc.*, 2548 (1953).

cis-**5-(1-Hydroxycyclohexyl)cyclooctyl Acetate (2).** To a solution of 824 mg of **1** in 8 ml of dry pyridine was added 1 ml of acetic anhydride. The solution was allowed to stand overnight; work-up in the usual manner afforded 921 mg (98%) of **2** which had infrared absorption at 3505, 1720, 1355, and 1220–1250 cm^{-1}. Thin layer chromatographic analysis (silica gel, 1:1 etyhl acetate–pentane) revealed only one spot, R_f 0.645. A collected sample (column B, 200°) was analyzed.

Anal. Calcd for $C_{16}H_{28}O_3$: C, 71.60; H, 10.52. Found: C, 71.90; H, 10.32.

cis-**5-Cyclohex-1-enylcyclooctyl Acetate (3).** To a solution of 921 mg of **2** in 10 ml of dry pyridine chilled to 0° was added 0.4 ml of phosphorus oxychloride. A precipitate soon formed. The mixture was allowed to stand overnight at room temperature and then was heated on a steam bath for 1 hr. The mixture was poured onto 100 g of ice and extracted with two portions of hexane. The combined extracts were washed with water and dried; removal of solvent yielded 842 mg (98%) of crude **3.** Vpc analysis on column A (190°) indicated that it was 90% pure. In its nmr spectrum the crude olefinic acetate exhibited peaks at δ 5.36 (broad, 1 H), 4.88 (broad, 1 H), 2.12 (singlet, 3 H), and 1.55 (broad, 20 H), while in the infrared spectrum peaks at 3010 (sh), 1725, 1650, and 1250 cm^{-1} were observed. A collected sample was analyzed.

Anal. Calcd for $C_{16}H_{26}O_2$: C, 76.75; H, 10.47. Found: C, 76.90; H, 10.39.

cis-**5-Cyclohex-1-enylcyclooctyl 3,5-Dinitrobenzoate (4a).** To a solution of 842 mg of **3** in 25 ml of ether was added 200 mg of lithium aluminum hydride in small portions. The slurry was stirred for 15 min and then was worked up by the usual method.[25] The oil which remained after removal of the solvent was esterified with 709 mg of 3,5-dinitrobenzoic acid and 1.291 g of *p*-toluenesulfonyl chloride in 30 ml of pyridine.[10] Work-up as usual yielded 1.302 g (96%) of crude ester, mp 95–108°, from which 973 mg of **4a**, mp 106.5–108.5°, was obtained by recrystallization from ethanol.

Anal. Calcd for $C_{21}H_{26}N_2O_6$: C, 62.67; H, 6.51. Found: C, 62.38; H, 6.59.

cis-**5-Cyclohex-1-enylcyclooctanol (4).** A mixture of 730 mg of **4a**, 25 ml of methanol, and 10 ml of 5 *N* sodium hydroxide was stirred overnight. The mixture was worked up by dilution with water (125 ml) and extraction with two portions of ether. Drying and removal of the solvent yielded 362 mg (96%) of crude **4**, an oil which solidified after a time, mp 53–65°. An analytical sample was prepared by three recrystallizations from pentane, mp 64.8–66.2°.

Anal. Calcd for $C_{14}H_{24}O$: C, 80.71; H, 11.61. Found: C, 80.35; H, 11.64.

cis-**5-Phenylcyclooctanol (5).** To a solution of 720 mg of acetate **3** in carbon tetrachloride was added 340 mg of N-bromosuccinimide. The suspension was refluxed for 1.5 hr. The mixture was cooled and filtered and the solvent was removed from the filtrate. The resulting oil was dissolved in 10 ml of dimethylformamide and 1 g of lithium carbonate was added. The mixture was heated on a steam bath for 14 hr, cooled, diluted with 100 ml of water, and extracted with two portions of hexane. The hexane solution was washed with five portions of water, two portions of 10% hydrochloric acid, water, and saturated sodium bicarbonate. Drying and removal of the solvent gave 434 mg (61%) of a yellow oil, which after standing for 3 days was extracted with pentane.[31] The resulting 225 mg of material was chromatographed over 8 g of alumina (Woelm, activity IV). Elution with pentane (10 ml) yielded 113 mg of a mixture of the unsaturated acetate **3** and 5-phenylcyclooctyl acetate. In the next 20 ml was eluted 39 mg of 5-phenylcyclooctyl acetate which was shown to be 83% pure by vpc (column A, 190°). This material was cleaved with lithium aluminum hydride; work-up by the usual method[25] afforded 18 mg of crude *cis*-5-phenylcyclooctanol after one recrystallization from pentane, mp 55.8–68.5°. Four recrystallizations gave the alcohol **5**, mp 67–70°, displaying an infrared spectrum identical with that of material which had been obtained previously by the reduction of 5-phenylcyclooctanone.

5-Phenylcyclooctene Oxide. A solution of 931 mg of 5-phenylcyclooctene was oxidized with perbenzoic acid[32] at 8° for 72 hr. Work-up as usual followed by distillation gave 871 mg (86%) of an oil, bp 115–120° (0.43 mm), $n^{25.5}D$ 1.5410. A sample was collected (column B, 200°) for analysis.

Anal. Calcd for $C_{14}H_{18}O$: C, 83.12; H, 8.97. Found: C, 83.07; H, 9.21.

4-Phenylcyclooctene. A mixture of 809 mg of 5-phenylcyclooctene oxide, 200 mg of lithium aluminum hydride, and 25 ml of ether was refluxed for 20 hr. Work-up by the usual method[25] gave 792 mg (97%) of a mixture of 4- and 5-phenylcyclooctanols. A sample which was oxidized to the ketones with Jones reagent was analyzed on column E (180°) and disclosed a 52.5:47.5 ratio of 4- to 5-phenylcyclooctanone.

To 768 mg of the alcohol mixture dissolved in 10 ml of pyridine at 0° was added 600 mg of phosphorus oxychloride. The mixture was allowed to stand for 16 hr at room temperature and then was heated for 1 hr on a steam bath. Work-up as described for the preparation of the olefinic acetate **3** gave 586 mg of an oil. Analysis on column B (200°) disclosed 50% of material having the retention time of the olefins, 48% of presumed chlorides (no OH absorption, positive silver nitrate test), and 2% unknowns. Collection from column E (175°) gave 39.5 mg (5.6%) of 4-phenylcyclooctene, having a retention time different from 5- and 1-phenylcyclooctene; nmr δ 7.12 (5 H), 5.67 (triplet, 2 H), 2.0–2.8 (multiplet, 5 H), 1.3–2.0 (multiplet, 6 H). A sample which was re-collected from column B (175°) had $n^{30.4}D$ 1.5419 and was analyzed.

Anal. Calcd for $C_{14}H_{18}$: C, 90.26; H, 9.74. Found: C, 89.98; H, 9.77.

3-Phenylcyclooctene. To a solution of phenylmagnesium bromide in 150 ml of ether, prepared from 7.2 g of magnesium and 47.2 g of bromobenzene, under nitrogen, was added 15.53 g of 3-bromocyclooctene[33] in 25 ml of ether over a period of 25 min. The mixture became warm and maintained a gentle reflux during the addition. It was stirred for 18 hr at room temperature, then was poured onto 400 g of ice, and solid ammonium sulfate was added until a two-phase system was obtained. The layers were separated and the aqueous phase was extracted with two 100-ml portions of ether. The combined ether layers were washed with saturated ammonium chloride, 10% ammonium hydroxide solution, and saturated sodium chloride solution. Drying and removal of the solvent followed by distillation gave 10.68 g (69%) of 3-phenylcyclooctene, bp 63–65° (0.02 mm), which was shown by vpc on column E (175°) to be 93% pure. A sample which was redistilled had $n^{25}D$ 1.5433; nmr δ 7.13 (singlet, 5 H), 5.57 (multiplet, 2 H), 3.65 (broad, 1 H), 2.14 (broad, 2 H), 1.62 (broad singlet with shoulder, 8 H).

Anal. Calcd for $C_{14}H_{18}$: C, 90.26; H, 9.74. Found: C, 89.94; H, 9.85.

1-Phenylcyclooctanol. Phenylmagnesium bromide was prepared from 8.73 g of magnesium turnings and 56.5 g of bromobenzene in 300 ml of ether. A solution of 15.4 g of cyclooctanone in 75 ml of ether was added over a period of 45 min. The dark mixture was refluxed for 1.5 hr, allowed to stand overnight, and then cooled in ice while 100 ml of 25% ammonium chloride solution was added dropwise. The ethereal solution was decanted, and the gummy residue was rinsed well with additional portions of water. The combined ether layers were washed with two portions of ice–water, twice with saturated sodium bicarbonate solution, and then with two portions of water. The ether solution was dried over potassium carbonate and the ether was removed; 25.3 g (92%) remained. Pentane was added and from the solution at −20° 1-phenylcyclooctanol (15.44 g, 56%), mp 40–56°, was deposited in three crops. Further recrystallization yielded the hydrated crystals, mp 42.3–45.0°. Upon drying the material became an oil with the following infrared spectrum (CCl_4): 3540, 3500, 3010, 1600, 1055, 855, 700 cm^{-1}.

Anal. Calcd for $C_{14}H_{20}O$: C, 82.30; H, 9.84. Found: C, 81.93; H, 9.68.

1-Phenylcyclooctene (25).[15] 1-Phenylcyclooctanol (1.012 g) was dissolved in 35 ml of benzene and a crystal of iodine was added. The solution was refluxed for 16 hr under a Dean–Stark trap and cooled to room temperature. The benzene solution was washed with two 20-ml portions of 5% sodium thiosulfate solution and 20 ml of water. The benzene layer was dried over sodium sulfate and the benzene was removed. There remained 0.791 g (85%) of a brown oil which was distilled in a short-path still (0.2 mm, bath temperature 110°) yielding 541 mg (59%) of a colorless oil, $n^{25}D$ 1.5628 (lit.[15] 1.5612), with nmr absorption at δ 5.92 (1 H, triplet, J = 8 cps). Vpc analysis (Viton A-HV[5] at 233°) indicated 96% purity.

(31) Some of the material apparently polymerized.

(32) A. Vogel, "Practical Organic Chemistry," 3rd ed, Longmans, Green and Co., London, 1956, p 893.

(33) A. C. Cope and L. L. Estes, Jr., *J. Am. Chem. Soc.*, **72**, 1128 (1950).

5-Phenylcyclooctene.[34] A mixture of 5-phenylcyclooctanol (202 mg), sodium hydride (293 mg), and benzene (10 ml) was refluxed for 2 days. Then 1.6 ml of carbon disulfide was added and the mixture was refluxed for 1 day. After cooling, 1.54 ml of methyl iodide was added and the mixture again was refluxed for 1 day. Water (2 ml) was added cautiously after cooling to room temperature and then the mixture was poured into 20 ml of water. The bright orange benzene solution was washed with water and dried, and the solvent was removed; 0.319 g (99%) of a red-orange oil remained. The crude xanthate was heated to 140° where decomposition began; it was heated at 140–150° for 1 hr, and the temperature then was raised to 200° over a period of 30 min and held there for 15 min. After the residue was cooled to room temperature ether was added and the ethereal solution was washed with 5% sodium hydroxide, dried, treated with charcoal, and filtered. Removal of the solvent afforded 167 mg (90%) which was dissolved in pentane and passed through alumina, yielding 139 mg of a yellow oil which on vpc (30% Viton A-HV, 240°) was 75% pure. A collected sample (column B, 170°) had $n^{27.7}$D 1.5393; infrared (CS_2) 1647, 1600, 755, 725, 700 cm^{-1}.

Anal. Calcd for $C_{14}H_{18}$: C, 90.26; H, 9.74. Found: C, 90.33; H, 9.71.

5-Phenylcyclooctanone-2,2,8,8-d_4 (8). A solution of 5-phenylcyclooctanone (9.148 g) in methanol-O-*d* and deuterium oxide (1:1) containing a trace of potassium carbonate was refluxed for 2 days. The methanol was removed and the residue was extracted with three portions of pentane. Drying and removal of the solvent gave a quantitative recovery of ketone. Two additional treatments under these conditions gave material whose mass spectrum indicated 77.5% d_4 species. Several treatments using other solvent systems (deuterium oxide–tetrahydrofuran, deuterium oxide–dioxane) resulted in little increase in the amount of d_4 species. The material was distilled through a semimicro column yielding 7.687 g (82.3%) of **8**, n^{25}D 1.5365, bp 93–95° (0.07 mm). The mass spectrum of the material indicated 82.2% d_4 species or 3.78 D/molecule.

Anal. Calcd for $C_{14}H_{14}D_4O$: C, 81.50; H, 8.79. Found: C, 81.43; H, 9.10.

***cis*-5-Phenylcyclooctyl-1,2,2,8,8-d_5 3,5-Dinitrobenzoate (9a).** A sample of 3.269 g of **8** was reduced with 600 mg of lithium aluminum deuteride in the standard fashion. Work-up by the usual[25] method gave 3.318 g (quantitative) of crude, crystalline alcohol displaying no carbonyl absorption in its infrared spectrum. This material was converted directly to the 3,5-dinitrobenzoate, using 3.38 g of 3,5-dinitrobenzoic acid, 6.07 g of *p*-toluenesulfonyl chloride, and 100 ml of pyridine; 6.4 g of ester was obtained. Fractional crystallization as above gave 900 mg (14%) of **9a**, mp 140.5–141.5°.

Anal. Calcd for $C_{21}H_{17}D_2N_2O_6$: C, 62.52; H, 5.50; N, 6.94. Found: C, 62.37; H, 5.63; N, 7.40. Average number of D/molecule, 4.78 (falling drop).

***cis*-5-Phenylcyclooctanol-1,2,2,8,8-d_5 (9).** A sample of 845 mg of **9a** was hydrolyzed as described for the undeuterated compound; 388 mg (88%) of **9**, mp 70.0–71.0°, was obtained after one recrystallization from pentane. An additional recrystallization gave an analytical sample with the same melting point.

Anal. Calcd for $C_{14}H_{15}D_5O$: C, 80.32; H, 9.63. Found: C, 80.43; H, 9.87. Average number of D/molecule, 4.79 (falling drop).

***trans*-5-Phenylcyclooctanol-1,2,2,8,8-d_5 (10).** A sample of 5-phenylcyclooctanol-1,2,2,8,8-d_5 (1.368 g) containing 83% of the *cis* isomer was esterified in the usual manner with 2.5 g of *p*-toluenesulfonyl chloride in 10 ml of pyridine. Work-up by dilution and extraction with ether gave 2.322 g (98%) of crystalline tosylate. The tosylate was boiled with 6.1 g of tetraethylammonium acetate in 60 ml of acetone for 70 hr. Work-up as before yielded 1.598 g of oil. Reductive cleavage with lithium aluminum hydride gave 1.307 g of oily crystals, which upon crystallization from 25 ml of pentane gave 702 mg of crude **10**. The mother liquors were evaporated and the residual oil was chromatographed over 20 g of alumina. Elution with pentane yielded 266 mg (21%) of 5-phenylcyclooctene-1,2,2,8,8-d_5, n^{25}D 1.5377, one peak on column E (180°), no vinyl H in nmr; infrared 2100–2250 (C–D), 1617 cm^{-1} (olefin).

Anal. Calcd for $C_{14}H_{14}D_4$: C, 88.35; H, 9.54. Found: C, 88.15; H, 9.88. Average number of D/molecule, 3.82 (falling drop).

Drying and removal of the solvent left 294 mg of semicrystalline oil which was recrystallized from pentane, yielding 110 mg (7%) of **12**: mp 89.0–92.0°; infrared 3590, 3400, 1000–1100 cm^{-1} (the range includes a series of five bands), no carbonyl absorption. An analytical sample, obtained by two additional recrystallizations from pentane, melted at 90.0–91.8°.

Anal. Calcd for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31. Found: C, 77.06; H, 8.09.

4-Phenylcyclooctanone. A solution of 93.5 mg of **12** in 10 ml of ethanol containing 0.1 ml of 4% perchloric acid was reduced in the presence of 25 mg of 10% palladium on charcoal. In 44 hr the mixture absorbed 14.6 ml of hydrogen (138% of theory). It was filtered and the filtrate was diluted with 30 ml of water. Extraction with two portions of pentane followed by drying and removal of the solvent gave 82.5 mg (95%) of crude 4-phenylcyclooctanone: infrared (CCl_4) 1703 cm^{-1} (no OH); nmr δ 1.50–2.58 (multiplet, 12 H), 2.70 (broad, 1 H), 7.09 (singlet, 5 H). An analytical sample was prepared by collection from column B (200°), n^{25}D 1.5413.

Anal. Calcd for $C_{14}H_{18}O$: C, 83.12; H, 8.97. Found: C, 82.98; H, 9.06.

A small sample (38 mg) of this ketone was reduced with lithium aluminum hydride in the usual fashion giving a mixture of isomeric alcohols (94%) which partially solidified after standing for 1 week, mp 35–55°. These were converted to their trifluoroacetates in 70% crude yield, infrared (CCl_4) 1775 cm^{-1} (no OH). Vpc analysis on column D (160°) showed one peak having the retention time of **5b**.

Dimethyl 4-Phenylsuberate. A solution of 52 mg of 5-phenylcyclooctene in 30 ml of acetone was oxidized[35] with a mixture of 5.4 mg of potassium permanganate, 112 mg of potassium carbonate, and 461 mg of sodium metaperiodate in 50 ml of water. Upon standard work-up 68 mg (97%) of oily acid was obtained. Esterification with diazomethane yielded 63 mg (81%) of crude dimethyl ester. Preparative vpc (8 ft, 20% SE-30, 220°) gave 25.3 mg (32%) of pure ester; infrared (CCl_4) 1735, 1600, 1490, 700 cm^{-1}.

Anal. Calcd for $C_{16}H_{22}O_4$: C, 69.04; H, 7.97. Found: C, 69.23; H, 7.91.

Determination of Phenyl Migration. A. Alcohol Fraction. The alcohol fraction from solvolysis of the tosylate of **10** was subjected to preparative thin layer chromatography (1:1 ethyl acetate–hexane), from which 3 mg of alcohols, R_f 0.55–0.65, was obtained. This material was oxidized with 2 drops of Jones reagent. After drying the acetone solution, the solvent was removed under a stream of nitrogen. The residue, shown to be free of the alcohol by vpc on column B (200°), was dissolved in 3 ml of methanol and a trace of sodium methoxide was added. The solution was allowed to stand overnight, and then the solvent was removed under a stream of nitrogen. Methanol was added and the solution was allowed to stand once again. Three more equilibrations were done; water (2 ml) was added to the residue after evaporation of the methanol and the mixture was extracted with two 1-ml portions of pentane. Drying and removal of the solvent left 2 mg which was collected from column B (200°). The mass spectrum of this material exhibited molecular ion peaks at *m/e* 202 and 204 (40.3:59.7 peak height ratio) in addition to M + 1 peaks at *m/e* 203 and 205. No peak was observed at *m/e* 207.

B. **5-Phenylcyclooctene.** The olefins from solvolysis of the deuterated *trans* tosylate were subjected to preparative vpc on column E (180°). The recovered 5-phenylcyclooctene (50 mg) was oxidized as above with 5.4 mg of potassium permanganate, 461 mg of sodium metaperiodate, and 112.6 mg of potassium carbonate, and yielded 65 mg of crude acid which was esterified with diazomethane. The ether solution was filtered through alumina and the solvent was removed yielding 49 mg (66%) of the dimethyl ester. Vpc analysis indicated that this material was 85% pure and had the same retention time as dimethyl 4-phenylsuberate. A sample was collected from column B (190°) for mass spectrometry. Significant peaks were observed at *m/e* 280, 251, 250, 249, 248, 207, 206, 199, 190, 175, 161, 146, 131, 117, 91. The spectrum of undeuterated dimethyl 4-phenylsuberate had major peaks at *m/e* 278, 248, 247, 246, 205, 204, 197, 190, 173, 159, 144, 131, 117, 91.

A 10.4-mg sample of the crude deuterated ester was dissolved in 2 ml of methanol (distilled from magnesium methoxide) and a trace of sodium methoxide was added; the solution was refluxed under a drying tube for 16 hr. The solvent was removed under a stream of nitrogen and a second portion (2 ml) of anhydrous

(34) Procedure of A. T. Blomquist and A. Goldstein, *J. Am. Chem. Soc.*, 77, 1001 (1955).

(35) R. U. Lemieux and E. v. Rudloff, *Can. J. Chem.*, 33, 1701 (1955).

methanol was added. The solution was refluxed overnight and the solvent was removed under a stream of nitrogen. The residue was extracted with 1 ml of ether and the solvent was removed leaving 4 mg. A sample was collected from column B (190°); the major peaks in its mass spectrum were at *m/e* 278, 249, 246, 228, 215, 205, 204, 197, 190. A sample of dimethyl 4-phenylsuberate which had been treated similarly with methanol-O-*d* contained >95% d_4 species by mass spectrometric analysis.

Molecular Asymmetry of Olefins. V. Resolution of *cis,trans*-1,5-Cyclooctadiene[1]

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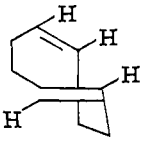
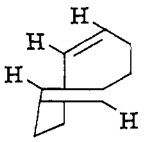
Abstract: Resolution of *cis,trans*-1,5-cyclooctadiene has been accomplished through platinum complexes containing optically active α-methylbenzylamine. Fractional crystallization of (+)-*trans*-dichloro(*cis,trans*-1,5-cyclooctadiene)(α-methylbenzylamine)platinum(II) to constant rotation and decomposition of this complex with sodium cyanide yielded optically active (−)-*cis,trans*-1,5-cyclooctadiene, $[\alpha]^0D$ −152°.

The labile 1,5-cyclooctadiene obtained from N-methylgranatanine by two successive Hofmann exhaustive methylation reactions has been shown unequivocally to be *cis,trans*-1,5-cyclooctadiene.[4] Because of the rigid structure of the ring and the nonbonded hydrogen interactions which prevent rotation of the *trans*-olefinic bond with respect to the rest of the ring, the molecule should exist in two enantiomeric forms, **1a** and **1b**. Evidence that this is the case



1a

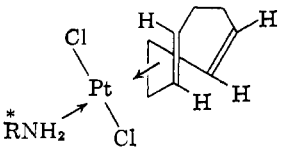


1b

has been obtained by the asymmetric synthesis of *cis,trans*-1,5-cyclooctadiene from resolved N,N-dimethyl-*cis*-4-cycloocten-1-ylamine[5] and by partial resolution of the racemic diene *via* a platinum complex containing optically active (+)-α-methylphenethylamine (Dexedrine).[6]

For the resolution of *trans*-cyclooctene, (+ or −)-α-methylbenzylamine was found to be more suitable as the optically active ligand in the platinum complex.[7] This paper reports the resolution of *cis,trans*-1,5-cyclooctadiene *via* the platinum complex containing optically active α-methylbenzylamine.

Unlike *trans*-cyclooctene, *cis,trans*-1,5-cyclooctadiene may form a bond with platinum in more than one way, since both ethylenic linkages are available as ligands.[8]



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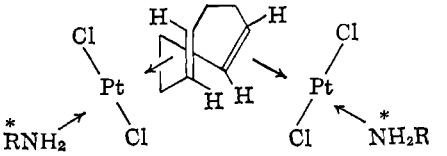

3

The *trans*-olefinic bond may form a coordination bond with one platinum as shown in the complex *trans*-dichloro(*cis,trans*-1,5-cyclooctadiene)(α-methylbenzylamine)platinum(II) (**2**), or both the *cis*- and *trans*-olefinic linkages may bond to two separate platinum atoms forming the bridged complex μ-(*cis,trans*-1,5-cyclooctadiene)-*trans,trans*-tetrachlorobis(α-methylbenzylamine)diplatinum(II) (**3**).

Displacement of ethylene from the complex (+)-*trans*-dichloro(ethylene)(α-methylbenzylamine)platinum(II) by *cis,trans*-1,5-cyclooctadiene in methylene chloride solution afforded as a less soluble fraction a material having the elemental composition expected for complex **2**. After fractional crystallization to constant rotation from methylene chloride, this material had $[\alpha]^{28}D$ +97.2°.

Attempts to repeat the preparation of this complex and its enantiomer containing (−)-α-methylbenzylamine gave only the other complex **3**, characterized by elemental analysis, thin layer chromatographic properties, and lack of the infrared absorption at *ca.* 725 cm^{-1} associated with *cis* olefins. After fractional crystallization to constant rotation from methylene chloride–*n*-hexane, the complex **3** had $[\alpha]^{28}D$ −94°.

It was possible to prepare complex **2** by cleavage of the bridged complex, di-μ-chloro-1,3-dichloro-2,4-bis(*cis,trans*-1,5-cyclooctadiene)diplatinum(II) with (+)-α-

(1) Supported in part by the Army Research Office (Durham) under Grant No. DA-AROD 31-124-G404.

(2) National Science Foundation Summer Fellow, 1962; National Institutes of Health Predoctoral Fellow, 1962–1963.

(3) National Science Foundation Science Faculty Fellow, 1960–1961.

(4) A. C. Cope, J. E. Bowers, C. F. Howell, and R. C. Lord, to be published.

(5) A. C. Cope, C. F. Howell, and A. Knowles, *J. Am. Chem. Soc.*, 84, 3190 (1962).

(6) A. C. Cope, C. R. Ganellin, and H. W. Johnson, Jr., *ibid.*, 84, 3191 (1962).

(7) A. C. Cope, C. R. Ganellin, H. W. Johnson, Jr., T. V. Van Auken, and H. J. S. Winkler, *ibid.*, 85, 3276 (1963).

(8) The asterisk above RNH_2 indicates that (+ or −)-α-methylbenzylamine was used.