2 hr until a dark orange solution was obtained. To this a solution of 3.16 g of 9-benzonorbornenone in 50 ml of tetrahydrofuran was added and the mixture refluxed for 10 hr. The tetrahydrofuran was evaporated; the residue was extracted with ether, washed with water, dried, and evaporated, leaving an oil. Distillation of the oil followed by elution chromatography over Florisil yielded 1.1 g (35%) of 9-methylenebenzonorbornene, bp 76–78° (5 mm), n^{25}D 1.5680.

Anal. Calcd for $C_{12}H_{12}$: C, 92.26; H, 7.74. Found: C, 92.44; H, 7.88.

6,7-Dinitrobenzonorbornen-9-*anti*-ol. To a solution of 656 mg of 6-nitrobenzonorbornen-9-*anti*-ol acetate[2b] in 8 g of 98% H_2SO_4 was added a mixture containing 225 mg of fuming HNO_3 (*d* 1.5) and 450 mg of 98% H_2SO_4 at about 0°. The usual work-up gave 480 mg of the crude dinitro acetate. This compound was hydrolyzed by heating for 4 hr on a steam bath in a solvent composed of 70 ml of 20% H_2SO_4 and 30 ml of dioxane. The work-up yielded 6,7-dinitrobenzonorbornen-9-*anti*-ol, mp 130–131°.

Anal. Calcd for $C_{11}H_{10}O_5N_2$: C, 52.80; H, 4.03; N, 11.20. Found: C, 52.96; H, 4.26; N, 10.81.

The brosylate was prepared by the standard procedure and had mp 195°.

Anal. Calcd for $C_{17}H_{13}O_7SBrN_2$: C, 43.51; H, 2.79; N, 5.97. Found: C, 43.54; H, 2.85; N, 6.03.

6,7-Dinitrobenzonorbornen-9-*syn*-ol, mp 148–149°, was similarly prepared by the nitration of 6-nitrobenzonorbornen-9-*syn*-ol acetate,[2b] followed by hydrolysis.

Anal. Calcd for $C_{11}H_{10}O_5N_2$: C, 52.80; H, 4.03; N, 11.20. Found: C, 52.88; H, 4.09; N, 11.03.

The acetate had mp 216–217°.

Anal. Calcd for $C_{13}H_{12}O_6N_2$: C, 53.43; H, 4.14. Found: C, 53.42; H, 4.02.

The brosylate had mp 204–205°.

Anal. Calcd for $C_{17}H_{13}O_7SBrN_2$: C, 43.51; H, 2.79. Found: C, 43.46; H, 2.84.

Vpc analyses of solvolysis products were carried out on a Hitachi gas chromatograph Model F-6, equipped with a 1 × 3 mm stainless steel column packed with 10% SE 30 on 60–80 mesh Chromosorb W. Helium was used at a pressure of 1 kg/cm² as a carrier gas. Retention times of *anti*- and *syn*-2-benzo[3,4]bicyclo[3.2.0]heptenol at 150° were 20.2 and 23.1 min, respectively. Those of 9-methylenebenzonorbornene, III-OAc, and IV-OAc at 120° were 9.5, 38.4, and 35.3 min, respectively.

Proximity Effects. XLVI. Stereospecific Synthesis of *cis*- and *trans*-4-Phenylcyclooctanol[1]

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Abstract: The stereospecific synthesis of *cis*- and *trans*-4-phenylcyclooctanol *via* transannular reactions involving oxygen-bridged ring precursors is described. A number of alternative paths involving cyclizations with lead tetraacetate, mercuric acetate, and mercuric oxide and iodine have been investigated and several products have been identified. An improved synthesis of *cis*-5-phenylcyclooctanol is described.

Previous papers in this series describe the synthesis of cyclooctane derivatives as part of a general study of proximity effects and transannular reactions in medium-ring compounds.[4] Our interest in such systems includes the use of transannular reactions to develop convenient stereospecific routes to the less accessible phenylcyclooctanols. The general approach was to synthesize cyclooctyl compounds with suitably constituted oxygen bridges which could subsequently be severed by hydrogenolysis. Thus, in principle, bridge scission[5] of 1-phenyl-9-oxabicyclo[4.2.1]nonane (**1a**) and 1-phenyl-9-oxabicyclo[3.3.1]nonane (**1b**) at the benzylic carbon–oxygen bonds would give rise to 4-phenylcyclooctanol and 5-phenylcyclooctanol, respectively. The utility of this approach depends on the hydrogenolysis occurring exclusively at the benzylic position and on the ring-opening process being stereospecific. There was ample evidence that the former condition would hold; the latter condition appeared less certain. As an initial exploration of this idea this paper describes the synthesis and hydrogenolysis of the cyclic ethers **1a** and **b**.

Many examples of the formation of cyclic ethers on treatment of steroidal alcohols with lead tetraacetate have been reported.[6] The reaction has been extended to saturated acyclic,[7] unsaturated acyclic,[8] and saturated bicyclic[9] alcohol systems. The cyclic ethers formed usually have been five membered rather than six membered although in some cases mixtures of the two have been isolated. For example, treatment of cyclooctanol with lead tetraacetate in benzene gave 9-oxabicyclo[4.2.1]nonane; no detectable amount of the 1,5 isomer could be found in the product.[10] Under similar conditions, 1-methylcyclooctanol gave a mixture (1:3) of 1-methyl-9-oxabicyclo[4.2.1]nonane and 1-methyl-9-oxabicyclo[3.3.1]nonane.[10] Thus, introduction of a methyl group may alter the conformation of the cyclooctane ring so as to favor the formation of the 1,5 over

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(1) Supported in part by Research Grant GP-1587 from the National Science Foundation.

(2) Deceased, June 4, 1966.

(3) (a) To whom enquiries may be addressed at the Department of Chemistry, Queens University, Belfast, Ireland. (b) National Institutes of Health Fellow 1965–1966.

(4) For a general discussion see A. C. Cope, M. M. Martin, and M. A. McKervey *Quart. Rev.* (London), 20, 119 (1966).

(5) Removal of the carbonyl bridge in compounds containing the bicyclo[3.3.1]nonan-9-one system offers a promising method for the synthesis of a variety of substituted cyclooctanes and cyclooctapolyenes. See A. C. Cope, F. S. Fawcett, and G. Munn, *J. Am. Chem. Soc.*, 72, 3399 (1950); A. C. Cope, E. S. Graham, and D. J. Marshall, *ibid.*, 76, 6159 (1954); A. C. Cope and D. M. Gale, *ibid.*, **85**, 3743 (1963); G. L. Buchanan, M. McKillop, and R. A. Raphael, *J. Chem. Soc.*, 833 (1965).

(6) Summarized in "Steroid Reactions," C. Djerassi Ed., Holden-Day, Inc., San Francisco, Calif., 1963, Chapter 8.

(7) V. W. Micovic, R. I. Mamuzic, D. Jeremic, and M. Lj. Mihailovic, *Tetrahedron Letters*, 2091 (1963).

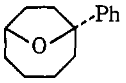
(8) S. Moon and J. M. Lodge, *J. Org. Chem.*, **29**, 3453 (1964).

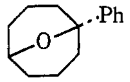
(9) K. Kitahonoki and A. Matsuura, *Tetrahedron Letters*, 2263 (1964).

(10) A. C. Cope, M. Gordon, S. Moon, and C. H. Park, *J. Am. Chem. Soc.*, **87**, 3119 (1965).

the 1,4 oxide. Other reagents which effect cyclic ether formation from monohydric alcohols include mercuric oxide and iodine, lead tetraacetate and iodine, silver oxide and bromine, and N-iodosuccinimide. These reactions have been reviewed by Heusler and Kalvoda.[11] Bordwell[12] has described the mercuration of 4-cycloocten-1-ol with mercuric acetate in the presence of sodium acetate. Reduction of the resulting 5-acetoxymercuri-9-oxabicyclo[4.2.1]nonane with sodium borohydride gave 9-oxabicyclo[4.2.1]nonane uncontaminated by the [3.3.1] isomer.

In the present study, 1-phenyl-4-cycloocten-1-ol (**2**), prepared from 4-cycloocten-1-one and phenylmagnesium bromide, was treated with lead tetraacetate in boiling chloroform for 10 hr. Gas chromatographic and infrared analysis of the crude product indicated the presence of a saturated acetate (97%) in addition to two minor components (3%). One of the minor components[13] appeared to be a mixture of phenylcyclooctadienes formed presumably by dehydration of the starting alcohol during the reaction or during the gas chromatographic analysis. The saturated acetate fraction, which could be obtained pure by distillation, had significant infrared absorption[14] at 1730, 1070, and 1025 cm^{-1}. It was further resolved by gas chromatography into the isomers **3a** and **b** (present in about equal amounts). It was not necessary at this stage to determine the stereochemistry of the acetoxy substituent since the asymmetry at this position was to be removed in a subsequent step. It follows however from analogy with a similar reaction with 4-cycloocten-1-ol.[15] The acetate mixture was reduced with lithium aluminum hydride to give a mixture of the secondary alcohols **4a** and **b** (approximately equal amounts). Oxidation with chromium trioxide in pyridine gave the corresponding ketones **5a** and **b**. Wolff–Kishner reduction of the ketone mixture afforded the ethers **1a** (60%) and **b** (40%) in 95% yield. Partial separation of the ether mixture was achieved by crystallization from pentane at −78°. Isomer **1b** separated as a crystalline solid, mp 47–47.5°, and the filtrate, which was enriched (70–75%) with isomer **1a**, could be further purified by chromatography on alumina. In this way **1a** was obtained 90% isomerically pure.


1a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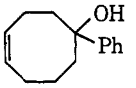
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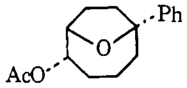
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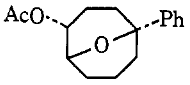
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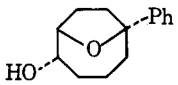
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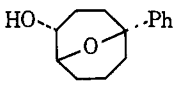
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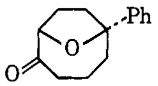
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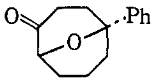
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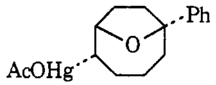
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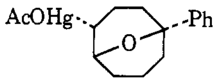
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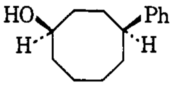
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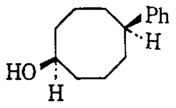
9b

The method of oxymercuration followed by reduction is of synthetic value for ethers, alcohols, and lactones.[12,16] This route was chosen in an attempt to increase the amount of the [4.2.1] isomer initially present in the mixture. Addition of the mercuri group was also chosen in the hope that a crystalline product would be obtained. Mercuration of 1-phenyl-4-cycloocten-1-ol with mercuric acetate in the presence of sodium acetate proceeded rapidly at room temperature to give a mixture of 1-phenyl-5-acetoxymercuri-9-oxabicyclo-[4.2.1]nonane (**6a**) and 1-phenyl-4-acetoxymercuri-9-oxabicyclo[3.3.1]nonane (**6b**) as a crystalline solid. The isomeric composition could not be determined directly but sodium borohydride reduction[12] of the mixture gave the ethers **1a** (70%) and **b** (30%). In addition it was found that fractional crystallization of **6** gave the [4.2.1] isomer **6a** as the less soluble fraction and in this way the purity of this isomer was increased to >95%. Reduction of **6a** with sodium borohydride gave **1a** in 62% yield. The formation of the acetoxymercuri ethers **6a** and **b** indicates that a functional group such as hydroxyl can participate in a transannular reaction as an internal nucleophile. The stereochemistry of the oxymercuration products was not determined but the relative configurations of the oxygen atom and the acetoxymercuri substituent in the product will be *trans* as shown on the basis of the normal *trans* addition to the olefinic bond.[12,16–18]

We also undertook a study of the photochemically induced reaction of 1-phenylcyclooctanol with mercuric oxide and iodine to determine whether the 1-phenylcyclooctyloxy radical would undergo a transannular rearrangement of the type observed in the photochemical decomposition of 1-methylcyclooctyl hypochlorite.[19] The action of such reagents as mercuric oxide and iodine or mercuric acetate and iodine on monohydric alcohols may also involve transannular hydrogen abstraction through the decomposition of the *in situ* produced hypoiodites. Unlike hypochlorites, these hypoiodites have not been isolated or characterized.[20] A complex mixture of products was obtained on ir-

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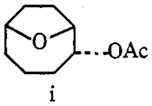
[11] K. Heusler and J. Kalvoda, *Angew. Chem. Intern. Ed. Engl.*, **3**, 525 (1964), and references contained therein.

[12] F. G. Bordwell and M. L. Douglass, *J. Am. Chem. Soc.*, **88**, 993 (1966).

[13] Comparison based only on retention time on gas chromatography.

[14] 9-Oxabicyclo[4.2.1]nonane and 9-oxabicyclo[3.3.1]nonane have distinguishing infrared bands at 1065 and 1022 cm^{-1}, respectively.

[15] We observed initially that the reaction of 4-cycloocten-1-ol with lead tetraacetate gave a mixture of the acetoxy ethers i and ii in high yield. The configuration of the acetoxy substituent in both isomers was established to be as shown: A. C. Cope and M. A. McKervey, unpublished results.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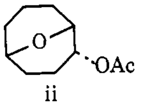

ii

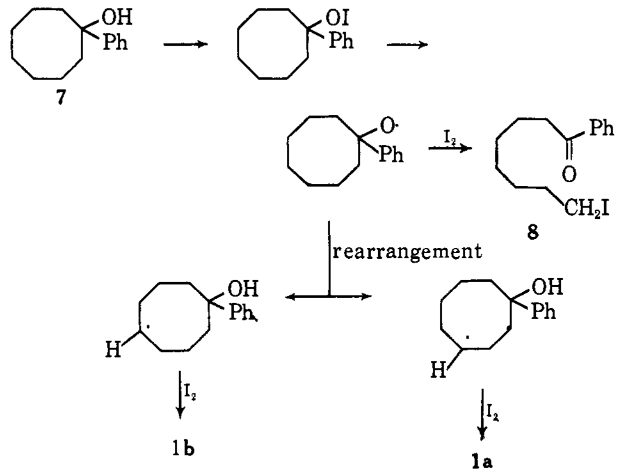
[16] H. B. Henbest and B. Nicholls, *J. Chem. Soc.*, 227 (1959).

[17] T. G. Traylor, *J. Am. Chem. Soc.*, **86**, 244 (1964).

[18] M. M. Kreevoy and F. R. Kowitt, *ibid.*, **82**, 739 (1960).

[19] A. C. Cope, R. S. Bly, M. M. Martin, and R. C. Petterson, *ibid.*, **87**, 3111 (1965).

[20] M. Akhtar and D. R. H. Barton, *ibid.*, **86**, 1528 (1964).



radiation of 1-phenylcyclooctanol (**7**) in cyclohexane containing mercuric oxide, iodine, and calcium carbonate. Two of the major products, isolated in ~30% yield by chromatography and distillation, were identified as the desired ethers **1a** and **b**. 8-Iodo-1-phenyloctan-1-one (**8**), the product of the type of ring-opening rearrangement predominating in the decomposition of five- and six-membered cyclic tertiary hypohalites,[21,22] was also isolated. Thus a total of at least 30% of the photochemical reaction proceeded *via* transannular radical rearrangements involving both the 4 position (~15%) and the 5 position (~15%) of the cyclooctane ring.[23] Three methods for the preparation of the ethers **1a** and **b** were thus in hand.

In order to establish the stereochemistry of the hydrogenolysis of **1a** and **b**, a number of points were considered. First, we expected cleavage to occur exclusively at the benzylic position and indeed when the hydrogenolysis was carried out in ethanol containing a trace of perchloric acid[24] using palladium as catalyst the ethers gave products which were clearly the desired secondary alcohols. Second, the availability of *cis*- and *trans*-5-phenylcyclooctanol from another synthetic sequence[25] provided a direct check on the stereospecificity of hydrogenolysis of isomer **1b**. This isomer gave an alcohol **9b** which was identical in melting point and infrared spectrum with a sample of *cis*-5-phenylcyclooctanol prepared by Cope and Kinnel.[25,26] The hydrogenolysis proceeds therefore with inversion of configuration at the benzylic carbon atom.[27] A similar reaction with isomer **1a** gave a crystalline alcohol, mp 79–80.5°, to which we assign the *cis* configuration **9a**. For comparative purposes **9a** was converted to *trans*-4-phenylcyclooctanol by tosylation, inversion with tetraethylammonium acetate, and reduction of the resulting *trans*-4-phenylcyclooctyl acetate with lithium aluminum hydride. The *trans* alcohol[28] thus obtained had mp 63–64.5°. The infrared spectra of the *cis* and *trans* alcohols showed significant differences; in particular, the *cis* isomer had a strong band at 985 cm^{-1} which was absent in the spectrum of the *trans* isomer.[29] Lithium aluminum hydride reduction of 4-phenylcyclooctanone gave a crystalline product, mp 44–52°, which was shown by infrared to be a mixture of the *cis* and *trans* alcohols.

Experimental Section[30]

1-Phenyl-4-cycloocten-1-ol (2). A solution of 4-cycloocten-1-one (25 g) in anhydrous ether (100 ml) was added dropwise during 45 min to a stirred solution of phenylmagnesium bromide prepared from bromobenzene (34.8 g) and magnesium (5.3 g) in anhydrous ether (250 ml). The mixture was stirred for an additional 30 min and was then treated with saturated ammonium chloride solution. The solids were removed by filtration, and the solvent was evaporated to give a yellow oil (41 g). A 34-g fraction was distilled through a 6-in. Vigreux column to yield a main fraction of 25.7 g (75.7%) of the pure alcohol, bp 106–109° (0.02 mm).

Anal. Calcd for $C_{14}H_{18}O$: C, 83.12; H, 9.01. Found: C, 83.30; H, 8.97.

1-Phenyl-5-acetoxy-9-oxabicyclo[4.2.1]nonane (3a) and 1-Phenyl-4-acetoxy-9-oxabicyclo[3.3.1]nonane (3b). Commercial lead tetraacetate[31] (20 g) was dried at 25° (0.05 mm) for 1 hr. A solution of 1-phenyl-4-cycloocten-1-ol (**2**) (5 g) in reagent grade chloroform (100 ml) was added to the lead tetraacetate, and the mixture was heated under reflux for 10 hr. (In larger scale preparations it was necessary to use mechanical stirring and to add the alcohol slowly to a solution of lead tetraacetate in chloroform as the initial reaction was exothermic.) The reaction mixture was cooled and excess lead tetraacetate was destroyed by the addition of ethylene glycol (10 ml). The solution was poured into a large volume of water and the chloroform layer was separated and washed with two 5-ml portions of 10% sodium thiosulfate solution and water. After drying, the solvent was removed to give a viscous oil (6.55 g). Distillation yielded 5.05 g (77%) of a mixture of the acetoxy ethers **3a** and **b**, bp 131–135° (0.22 mm). Gas chromatographic analysis on a 5 ft × 0.25 in. i.d. 5% XF-1150 column at 180° showed the presence of the two isomers in the ratio 49.5:50.5. A sample from a similar preparation was redistilled at 135–136° (0.4 mm) and was analyzed. The infrared spectrum showed no olefinic or hydroxyl absorption but had significant bands at 1730, 1070, and 1025 cm^{-1}. In a series of preparations the yields ranged from 60 to 84% after distillation.

Anal. Calcd for $C_{16}H_{20}O_3$: C, 73.82; H, 7.74. Found: C, 74.13; H, 7.80.

1-Phenyl-5-hydroxy-9-oxabicyclo[4.2.1]nonane (4a) and 1-Phenyl-4-hydroxy-9-oxabicyclo[3.3.1]nonane (4b). A solution of the acetoxy ether mixture **3a** and **b** (20 g) in anhydrous ether (50 ml) was added dropwise to a stirred slurry of lithium aluminum hydride (2.25 g) in anhydrous ether (200 ml). The mixture was stirred for

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(21) F. D. Greene, M. L. Savitz, H. H. Lau, F. D. Osterholtz, and W. N. Smith, *J. Am. Chem. Soc.*, **83**, 2196 (1961).

(22) (a) T. L. Cairns and B. E. Englund, *J. Org. Chem.*, **21**, 140 (1956); (b) J. W. Wilt and J. W. Hill, *ibid.*, **26**, 3523 (1961).

(23) About 60% of the decomposition of 1-methylcyclooctyl hypochlorite proceeded *via* transannular rearrangement involving both the 4 position (35%) and the 5 position (24%); see ref 19.

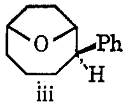
(24) In the absence of perchloric acid the hydrogenolysis proceeds much more slowly.

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

(26) The earlier synthesis involved a tedious fractional crystallization of a mixture of *cis*- and *trans*-5-phenylcyclooctyl 3,5-dinitrobenzoates, the *cis* isomer being the less soluble in chloroform–ethanol.

(27) For a discussion of the stereochemistry of hydrogenolysis of some benzyl ethers see S. Mitsui, Y. Senda, and K. Konno, *Chem. Ind.* (London), 1354 (1963), and references contained therein.

(28) Our stereochemical assignments were supported in the following way: reaction of *trans*-4-phenylcyclooctanol with lead tetraacetate gave back the ether **1a** as the major product whereas the *cis* isomer gave a mixture of products which contained no detectable amount of **1a**. A similar reaction with *trans*-5-phenylcyclooctanol gave the ether **1b** in high yield whereas the *cis* isomer gave compound iii as the major product: A. C. Cope, R. B. Kinnel, M. A. McKervey, and N. M. Weinshenker, unpublished results.



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(29) Both isomers had identical retention times on all the gas chromatography columns available; the corresponding acetates and trifluoroacetates were also inseparable by gas chromatography. A mixture melting point diagram for the alcohols showed that less than 5% of either isomer in a mixture produced a measurable depression of the melting point (see Experimental Section).

(30) Melting points were taken on a Thomas–Hoover melting point apparatus and are uncorrected; boiling points are uncorrected. Gas chromatographic analyses were carried out using an F & M Model 720 gas chromatograph. Nmr spectra were recorded on a Varian Associates A-60 instrument. Microanalyses were performed by Dr. S. M. Nagy and his associates. Except as noted the drying agent employed was sodium sulfate and solvents were removed under reduced pressure.

(31) Aceto Chemical Co. Inc., Flushing, N. Y.

an additional 1.5 hr and was then treated cautiously with cold water. The precipitate was separated and the ether solution evaporated to give 16.8 g (100%) of a viscous oil which partially solidified on standing. The infrared spectrum of this material showed strong hydroxyl absorption and the absence of acetate absorption. Gas chromatographic analysis (10-ft, 10% XF-1150 column at 198°) showed that **4a** and **b** were present in about equal amounts. A sample was recrystallized several times from benzene–pentane and was then sublimed at 70° (0.1 mm). The highest melting point obtained was 73–74.5°; gas chromatography showed that this material still contained both isomers.

Anal. Calcd for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31. Found: C, 76.92; H, 8.46.

1-Phenyl-5-oxo-9-oxabicyclo[4.2.1]nonane (5a) and 1-Phenyl-4-oxo-9-oxabicyclo[3.3.1]nonane (5b). A solution of the alcohol mixture **4a** and **b** (23.3 g) in pyridine (50 ml) was added to the complex[32] prepared from chromium trioxide (25 g) and pyridine (250 ml). The resulting brown mixture was stirred at room temperature for 15 hr and was then diluted with ether (200 ml). The solids were removed by filtration through Celite, and the filtrate was diluted with cold water (1 l.) and the organic layer separated. The aqueous layer was extracted five times with ether (total volume 1500 ml), and the combined organic extracts were washed repeatedly with cold, dilute hydrochloric acid. The dried ether solution was evaporated to give an oil (22.5 g). Distillation gave 18.1 g(78.5%), bp 133–139° (0.55 mm). Gas chromatographic analysis on a 10-ft, 5% XF-1150 column at 220° showed the presence of the two isomers in unequal amounts (*ca.* 37:63). A sample collected from silicone rubber at 200° was analyzed.

Anal. Calcd for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46. Found: C, 77.22; H, 7.44.

1-Phenyl-9-oxabicyclo[4.2.1]nonane (1a) and 1-Phenyl-9-oxabicyclo[3.3.1]nonane (1b). The above ketone mixture (18 g), 95% anhydrous hydrazine (8.7 g), potassium hydroxide (35 g), and ethylene glycol (200 ml) were heated at 130° for 1 hr. The temperature was slowly raised to 175° and maintained for 2.5 hr. The mixture was cooled and diluted with water (500 ml). The aqueous solution was extracted with three 150-ml portions of ether, and the combined extracts were washed with water and dried. Removal of the solvent gave 15.8 g (95%) of a colorless oil which was shown by gas chromatography on a 5-ft 5% XF-1150 column at 175° to contain 95% of a mixture of the [4.2.1] isomer **1a** (60%) and the [3.3.1] isomer **1b** (40%). Partial separation of the two isomers was achieved by crystallization from pentane at −78°. Isomer **1b** separated as a crystalline solid. Recrystallization from pentane gave needles, mp 47–47.7°.

Anal. Calcd for $C_{14}H_{18}O$: C, 83.12; H, 8.97. Found: C, 82.98; H, 9.04.

The filtrate from the above fractional crystallization was enriched (*ca.* 70–75%) with the isomer **1a**. Further fractionation was achieved by chromatography on Merck acid-washed alumina. In this way isomer **1a** was obtained in about 90% isomeric purity.

1-Phenyl-5-acetoxymercuri-9-oxabicyclo[4.2.1]nonane (6a). To a rapidly stirred solution of mercuric acetate (32.2 g) and sodium acetate (9 g) in distilled water (200 ml) was added 1-phenyl-4-cycloocten-1-ol (**2**) (20.4 g) in methanol (50 ml). The solid which was deposited after 1 hr was isolated by filtration and washed with water. There was obtained 34 g of a mixture which contained 70% of the [4.2.1] isomer **6a** and 30% of the [3.3.1] isomer **6b**. Fractional crystallization from benzene–pentane (1:1) gave 13.5 g of material, mp 140–142.5°, containing 91.5% of isomer **6a**. An additional 6.5 g, mp 140–141.5°, was obtained by similar treatment of the filtrate residues. These two fractions were combined and recrystallized from a mixture of benzene (125 ml) and pentane (75 ml) to give 15.5 g, mp 141–143°. This material contained >95% of the isomer **6a**.

Anal. Calcd for $C_{16}H_{20}HgO_3$: C, 41.69; H, 4.37. Found: C, 41.54; H, 4.15.

The distribution in the above organomercurials was determined by adding 5 mg of the solid to 0.25 ml of a sodium hydroxide solution of sodium borohydride. The mixture was shaken for a few minutes and extracted with pentane. The pentane solution was then analyzed by gas chromatography on an 8-ft 20% LAC-728 column at 210°.

1-Phenyl-9-oxabicyclo[4.2.1]nonane (1a). The mercurial **6a** (15 g) was suspended in 0.5 *M* sodium hydroxide solution (200 ml) and stirred rapidly while a solution of sodium borohydride (1 g) in 2.5 *M* sodium hydroxide (30 ml) was added over 30 min. Pentane (50 ml) was added, and stirring was continued for 2 hr. The pentane layer was separated, and the aqueous layer was extracted with two 100-ml portions of pentane. The combined pentane solutions were washed with water and dried. Removal of the solvent followed by distillation gave 3.95 g (61.5%) of **1a**, bp 89–92° (0.25 mm). Gas chromatographic analysis showed that the product contained less than 3% **1b**.

Anal. Calcd for $C_{14}H_{18}O$: C, 83.12; H, 8.97. Found: C, 83.01; H, 9.05.

In a similar experiment the yield was 77%. The residue from the distillation contained mostly the fragmentation product 1-phenyl-4-cycloocten-1-ol.

***cis*-4-Phenylcyclooctanol (9a).** A solution of **1a** (3.0 g) in absolute ethanol (30 ml) containing 10% palladium on charcoal (0.75 g) and two drops of perchloric acid was hydrogenated at atmospheric pressure until hydrogen uptake had ceased. The catalyst was removed by filtration, and the solvent was evaporated to leave an oil which soon crystallized. Recrystallization from hexane gave 2.25 g of *cis*-4-phenylcyclooctanol as needles, mp 76–78.5°. An analytical sample, mp 79–80.5°, was obtained by several recrystallizations from hexane. The molecular weight obtained by mass spectrometry was 202. The infrared spectrum (KBr) showed bands at 1092, 1075, 1054, 985, 897, 759, and 703 cm^{-1}.

Anal. Calcd for $C_{14}H_{20}O$: C, 82.30; H, 9.87. Found: C, 81.94; H, 9.92.

***cis*-4-Phenylcyclooctyl Tosylate.** *cis*-4-Phenylcyclooctanol (5 g) was dissolved in pyridine (50 ml), and *p*-toluenesulfonyl chloride (9.3 g) was added. The solution was kept at 5° for 16 hr. Crushed ice was added to bring the total volume to 100 ml, and an oil separated. Addition of an additional 100 ml of cold water with stirring caused the oil to crystallize. The solid was collected and dissolved in methylene chloride. After drying, the solvent was removed to leave an oil which solidified on standing. There was obtained 8.6 g (98%), mp 63–65.5°. Two crystallizations from pentane gave an analytical sample, mp 67–67.5°.

Anal. Calcd for $C_{21}H_{26}O_3S$: C, 70.35; H, 7.31. Found: C, 70.11; H, 7.22.

***trans*-4-Phenylcyclooctanol.** Crude *cis*-4-phenylcyclooctyl tosylate (7.45 g) was added to a solution of tetraethylammonium acetate (35 g) in reagent grade acetone (300 ml) containing Linde Molecular Sieves. The mixture was heated under reflux for 24 hr, and most of the solvent was then removed under reduced pressure. The residue was dissolved in water and extracted with ether. The ether solution was washed with water and dried. Removal of the solvent gave an oil (4.0 g). Gas chromatographic analysis on a 2-ft 20% SE 30 column at 190° showed the presence of *trans*-4-phenylcyclooctyl acetate (63%) and a mixture of 4- and 5-phenylcyclooctene (37%). The total reaction product was dissolved in ether (50 ml), and lithium aluminum hydride (0.5 g) was added in small portions with stirring. The mixture was heated under reflux for 1 hr and then treated cautiously with cold water and 10% hydrochloric acid. The ether layer was separated and dried. Removal of the solvent gave an oil (3.5 g). The oil was dissolved in pentane (30 ml) and was allowed to stand at −5° for 24 hr. The crystals obtained (1.7 g) had mp 60–62°. Crystallization from hexane gave 1.55 g (36.5%), mp 61–62°. An analytical sample, mp 63–64.5°, was obtained by recrystallization from hexane. The infrared spectrum (KBr) showed bands at 1049, 1035, 1010, 915, 759, and 703 cm^{-1}.

Anal. Calcd for $C_{14}H_{20}O$: C, 82.30; H, 9.87. Found: C, 82.24; H, 9.62.

4-Phenylcyclooctanone. *cis*-4-Phenylcyclooctanol (1.0 g) in acetone (5 ml) was oxidized with an excess of Jones reagent[33] at room temperature for 24 hr. The mixture was poured into water and extracted with three 25-ml portions of ether. The combined extracts were washed with saturated sodium bicarbonate solution and dried. Removal of the solvent gave 0.9 g (91%) of an oil which was shown by gas chromatography on a 2-ft 20% SE 30 column at 190° to be 98% pure. A sample collected from the same column was analyzed.

Anal. Calcd for $C_{14}H_{18}O$: C, 83.12; H, 8.97. Found: C, 82.75; H, 8.93.

The tosylhydrazone prepared in ethanol and recrystallized from the same solvent had mp 128–130°.

Anal. Calcd for $C_{21}H_{26}N_2O_2S$: C, 68.07; H, 7.07; N, 7.56. Found: C, 67.65; H, 7.11; N, 7.55.

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

***cis*-5-Phenylcyclooctanol (9b).** A solution of 1-phenyl-9-oxabicyclo[3.3.1]nonane (**1b**) (3.25 g) in absolute ethanol (35 ml) containing 10% palladium on charcoal (1.0 g) and six drops of perchloric acid was hydrogenated until hydrogen uptake had ceased. The catalyst was removed by filtration through Celite, and the filtrate was treated with ten drops of saturated potassium bicarbonate solution and then concentrated at reduced pressure. The residual semisolid was dissolved in ether, and the ether solution was washed with water and dried. Removal of solvent gave a white solid (3.2 g), mp 66–68°. Two crystallizations from hexane gave crystals, mp 69.5–70.5° (lit.[25] mp 70–71°). The infrared spectrum of the product was identical with that of *cis*-5-phenylcyclooctanol described by Cope and Kinnel.[25]

Lithium Aluminum Hydride Reduction of 4-Phenylcyclooctanone. Lithium aluminum hydride (100 mg) was added to the ketone (200 mg) in ether (5 ml). The mixture was allowed to stand at room temperature for 1 hr. Cold water and dilute hydrochloric acid were added, and the ether layer was separated, washed with water, and dried. Removal of solvent gave an oil (*ca.* 220 mg). This material crystallized in part from pentane at −5° after 6 weeks. The crystals obtained had mp 44–52°. The infrared spectrum showed that the product was a mixture of *cis*- and *trans*-4-phenylcyclooctanol.

Mixtures of *cis*- and *trans*-4-phenylcyclooctanol were prepared and their melting point ranges were determined (see Table I).

Table I

% *cis*	Mp, °C	% *cis*	Mp, °C
0.0	61.5–62.5	76.8	56.5–71.0
7.55	55.5–59.5	85.3	68.5–75.5
21.9	50.0–56.5	95.4	72.5–78.0
35.0	45.0–47.0	100.0	79–79.5
51.5	44.0–52.0		

1-Phenylcyclooctanol. The white crystalline hydrate, prepared by the method of Cope and Kinnel,[25] could be distilled at 125.5–127° (1.0 mm) to give the anhydrous product as a viscous oil.

Anal. Calcd for $C_{14}H_{20}O$: C, 82.30; H, 9.87. Found: C, 82.40; H, 9.83.

Reaction of 1-Phenylcyclooctanol with Mercuric Oxide and Iodine. Anhydrous 1-phenylcyclooctanol (25 g) was dissolved in cyclohexane (500 ml) in a 1-l. flask fitted with a stirrer and a condenser set for reflux. Calcium carbonate (50 g) and red mercuric oxide (150 g) were added, and the mixture was stirred and heated to boiling with a GE 274-w sunlamp. Iodine (100 g) was added in small portions through the condenser over a period of 45 min. The mixture was stirred and irradiated for an additional 3 hr. After cooling, the solids were removed by filtration, and the filtrate was washed with 10% sodium thiosulfate solution (350 ml) and dried. Removal of solvent gave a yellow oil (35 g). The oil was dissolved in pentane and chromatographed on acid-washed alumina (350 g). Elution with pentane (1200 ml) gave an oil (11.7 g) in several fractions. Distillation afforded 7.25 g (29.3%) of a mixture of **1a** and **b**, bp 101–115° (0.75 mm). Gas chromatographic analysis indicated that the two ethers were present in about equal amounts. The mixture was dissolved in pentane (65 ml), and the solution was cooled at −75° for 30 min. The crystals were isolated to give 2.1 g of **1b** uncontaminated with **1a**. The filtrate yielded an oil containing **1a** (65%) and **1b** (35%). The yield of the ether mixture varied from 20 to 35% in similar runs.

Further elution of the column during the chromatography yielded a third product which was shown to be 8-iodo-1-phenyloctan-1-one (**8**). After several recrystallizations from pentane it had a melting point of 41.5–42°.

Anal. Calcd for $C_{14}H_{19}IO$: C, 50.92; H, 5.79; I, 38.43. Found: C, 51.21; H, 5.79; I, 38.18.

Reduction of 8-Iodo-1-phenyloctan-1-one (8). The iodide (0.5 g) was dissolved in glacial acetic acid (7 ml), and zinc dust (1.0 g) was added. The mixture was heated on a steam bath with occasional stirring for 20 min. The solution was decanted, and the residual solid was washed several times with pentane. Water was added to the acetic acid–pentane mixture, and the organic layer was separated. The pentane solution was washed several times with saturated sodium bicarbonate solution and dried. Removal of the solvent gave an oil (300 mg) which was 90% pure by gas chromatography. The infrared spectrum of a sample collected from a 2-ft 20% SE 30 column at 200° was identical with that of heptyl phenyl ketone described below.

A portion was converted to the dinitrophenylhydrazone which had mp 113–115° after recrystallization.

Heptyl Phenyl Ketone. Octanoic acid (5.0 g) and thionyl chloride (7 ml) were heated on a steam bath for 1 hr. The excess thionyl chloride was removed at reduced pressure, and the residue was dissolved in benzene (10 ml). The benzene solution was added slowly (caution) to a suspension of aluminum chloride (10.0 g) in benzene (50 ml). When the addition was complete, the mixture was heated on a steam bath for 1 hr and then was poured onto crushed ice. The benzene layer was separated, washed with 10% sodium bicarbonate solution and water, and dried. Removal of the solvent left an oil which was purified by dissolution in pentane and addition of activated charcoal. The pentane solution was filtered and cooled to −10°. The crystals which could be obtained by rapid filtration melted at room temperature. A pure sample of heptyl phenyl ketone (a band appeared in the infrared at 1685 cm^{-1}) was obtained by preparative gas chromatography on a 2-ft 10% SE 30 column at 200°.

The 2,4-dinitrophenylhydrazone had mp 113–116° after recrystallization from ethanol. It showed no melting point depression when mixed with the 2,4-dinitrophenylhydrazone of heptyl phenyl ketone prepared by reduction of the iodide described above.

Anal. Calcd for $C_{20}H_{24}N_4O_4$: C, 62.48; H, 6.29; N, 14.58. Found: C, 62.18; H, 6.33; N, 14.84.