identical conditions. The enol of **6** appeared to form, similar to the reaction of **4**, but not of **5**; no other products were observed.

The substrate **9**, in the same period of time, isomerized to other materials of a larger R_f, but no **8** was evident by tlc. The product mixture was worked up by extraction into ether, and dried ($MgSO_4$). The nmr spectrum did not show the characteristic absorptions of **8**.

Preparation and Reaction of 10.—This material was prepared by the procedure of Ruheman:[31] mp 129–130°, lit. 131°; nmr (100 MHz, pyridine) δ *ca.* 7.5 (m, 15, aromatic protons), 5.86 (d, 1, J = 8.6 Hz, H_1 or H_3), 5.67 (d, 1, J = 9.3 Hz, H_3 or H_1), δ 5.30 (doublet of doublets, 1, H_2), *ca.* 3.9 (interspersed quartets, 4, O—CH_2—CH_3), *ca.* 0.9 (superposed triplets, 6, O-CH_2-CH_3). Treatment with *t*-butylamine in deuteriochloroform this material rapidly changes in part to two other materials with nmr absorptions in the same general regions as starting material. However no change in integration was evident during the period which **4** readily formed **8**. Upon work-up by adding to ether, extracting three times with H_2O, drying ($MgSO_4$), and evaporating, the same materials were evident, in the same proportions. Thus ethanol was not formed and no decarboxylation had occurred.

In pyridine at 100 MHz, the resonances of the three isomers were well separated: nmr of the major *meso* isomer, δ 5.72 (superposed d, 2, J = 7.8 Hz, H_1 and H_3), δ 5.18 (d of d, 1, H_2); minor *meso* isomer, δ 5.88 (superposed d, 2, J = 9.2 Hz, H_1 and H_3), 5.17 (d of d, 1, H_2).

Preparation of 11.—This material was prepared by the method of Erlenmeyer:[32] mp 205–206°, lit. 206°; nmr (60 MHz, $CDCl_3$) δ 7.09 (m, 15, aromatic protons), 4.57 (d, 1, J = 12.5 Hz, H_1), 4.08 (d, 1, J = 13.5 Hz, H_2), 4.02 (9, 2, J = 7.0 Hz, OCH_2–CH_3), *ca.* 3.87 (m, 1, H_{4e}), 3.53 (d of d, 1, $J_{4e,4a}$ = 14 Hz, H_{3a}), 3.92 (d of d, 1, $J_{3,4e}$ = 1.5 Hz, $J_{3,4a}$ = 12.5 Hz, H_3), 0.98 (t, 3, J = 7 Hz, O–CH_3–CH_3). Upon treatment of 0.25 g of **11** with 0.1 g of *t*-butylamine in chloroform at 69° for 3 weeks, followed by evaporation to dryness and very slow crystallization, 0.203 g of starting material was recovered. The remainder was a tar.

Preparation of 13.—A solution of 5.0 g of **4** and 1.4 g of ethanedithiol in 50 ml of methylene chloride was treated with 0.5 ml of 47% boron trifluoride–ether complex. An immediate precipitate was observed, but the mixture was allowed to stand for 2 wks. The solvent was evaporated and the mixture was mixed with water and methylene chloride. The organic extract was washed with dilute base twice, dilute HCl, and water and dried ($MgSO_4$). Upon evaporation needles of **13** were deposited, mp 180°. These were recrystallized from methylene chloride and from ethanol: mp 202–203°, mmp 180–190° with **4**; 2.89 g; nmr (60 MHz, $CDCl_3$) δ 7.18 (s, 5, aromatic protons), 3.87, (d, 1, J = 1.9 Hz, hydroxyl), 3.77 (*t*, 1, J = 11.7, H_3), 3.28 (s, 6, methoxyl), 3.17 (broad s, 4, ethylene bisthioketal protons), 3.16 (d, 1, J = 11.7, H_4), 2.66 (d, 1, J = 11.7, H_2), 2.62 (d, 1, J = −14.3, H_{6e}), 2.35 (d of d, 1, J = −14.3, J = 1.9, H_{6a}).

Anal. Calcd for $C_{19}H_{24}O_5S_2$: C, 57.55; H, 6.10. Found: C, 57.51; H, 5.98.

Registry No.—**4**, 24904-00-5; **5**, 24904-01-6; **6**, 24961-35-1; **7**, 24904-02-7; **8** (R = CH_3), 24904-03-8; **9**, 24904-04-9; **13**, 24904-05-0.

Acknowledgment.—Initial support (to C. A. K.) by the National Science Foundation was greatly appreciated. C. A. K. wishes to thank Abbott Laboratories for making their HA-100 available for this study.

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(32) (a) E. Erlenmeyer, Jr., *Chem. Ber.*, **32**, 2008 (1900). (b) S. Avery and G. McDole, *J. Amer. Chem. Soc.*, **30**, 596 (1908).

Proximity Effects. Reactions of Lead Tetraacetate with 4- and 5-Phenylcyclooctanol[1]

A. C. COPE,[2a] M. A. MCKERVEY,[2b] N. M. WEINSHENKER,[2c] AND R. B. KINNEL[2d]

Contribution from the Department of Chemistry, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139

Received October 14, 1969

The reactions of lead tetraacetate with the *cis* and *trans* isomers of 4- and 5-phenylcyclooctanol were examined in order to establish the magnitude of the directive effect of the phenyl substituent on the direction of transannular cyclization leading to bicyclic ethers. As compared with 5-phenylpentanol previously reported, there is observed a marked enhancement in the amount of cyclization at the benzylic position with the *trans* isomers. Thus *trans*-5-phenylcyclooctanol yields 1-phenyl-9-oxabicyclo[3.3.1]nonane in 72% yield. Although cyclization at the benzylic position in the *cis* isomers is not possible, the products obtained with *cis*-4-phenylcyclooctanol suggest that the phenyl group is exerting a directive effect here also. The structures of the new compounds isolated in this study were established by synthesis.

A large amount of data is available on features of the lead tetraacetate oxidation of alcohols such as the effect of solvent and structural variations in the alcohol. One process which has been particularly well examined with acyclic and steroidal substrates involves the formation of cyclic ethers from alcohols containing methyl or methylene groups at the δ and ϵ positions relative to the hydroxyl group. Indeed this particular reaction has contributed greatly to the solution of certain problems in steroid synthesis such as the introduction of functionality into angular methyl groups.[3] The products are usually five-membered rather than six-membered cyclic ethers, although in some cases mixtures of the two have been isolated. The important step in the cyclization process is the transfer of a hydrogen atom from a nonactivated methylene or methyl group to the oxygen atom within an alkoxy radical intermediate *via* a six- or seven-membered transition state. There are some indications that the subsequent steps may involve the oxidation of the resulting carbon radical to a carbonium ion *via* a one-electron transfer to lead followed by a cyclization of the hydroxy group onto the carbonium ion to give the cyclic ethers (Scheme I).[3–5] A competing fragmentation reaction, formulated as proceeding from the same precursor as in the cyclization reaction, gives rise to carbonyl compounds, olefins, and acetates.

The reactions of some medium-ring alcohols with lead tetraacetate have been examined since it was of interest to determine what effect the proximity of the δ and ϵ methylene groups to the hydroxyl group would

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(2) (a) Deceased June 4, 1966. (b) To whom inquiries should be addressed at the Department of Chemistry, Queen's University, Belfast, Northern Ireland. (c) NIH Fellow, 1964–1968. (d) NIH Fellow, 1960–1964.

(3) *Cf.* the review by K. Heusler and J. Kalvoda, *Angew. Chem., Int. Ed. Engl.*, **3**, 525 (1964).

(4) M. Lj. Mihailovic, Z. Cekovic, Z. Maksimovic, D. Jeremic, Lj. Lorenc, and R. I. Mamvzic, *Tetrahedron*, **21**, 2799 (1965).

(5) M. Lj. Mihailovic, S. Konstantinovic, A. Milovanovic, J. Jankovic, Z. Cekovic, and D. Jeremic, *Chem. Comm.*, 236 (1969).

SCHEME I

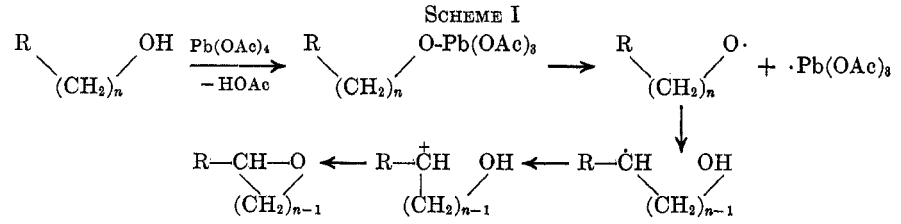
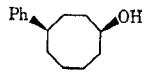
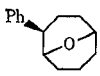
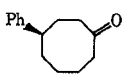
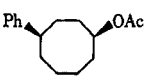
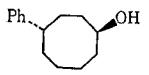
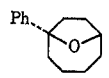
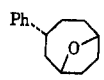
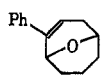
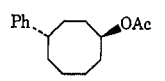
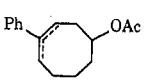
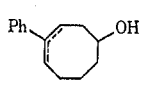
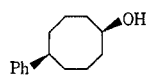
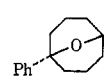
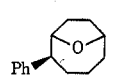
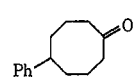
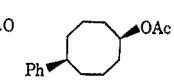
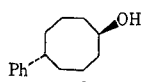
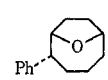
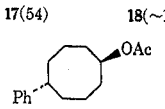


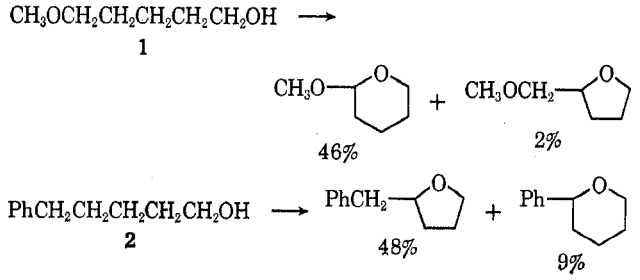
TABLE I

Alcohol	Products[a] (yield %)								
					3				
3	4(13)	5(20)	6(44)	7(5)	(15)				
							6	8	
8[b]	9(18)	10(8.5)	11(6)	12(5)	13(3.5)	14(15)	(10)	(28)	
					15				
15[c]	16(~1)	17(54)	18(~15)[d]	19(7)	(13)				
	16			18	20				
20[c]	(72)	21[e](5)	22(0.2)	(15)	(5)				

[a] Product distributions by vpc analysis. [b] Two unidentified compounds (3% each) were also formed in this reaction. [c] A compound with the infrared characteristics of an α-acetoxy ketone was also formed in this reaction. [d] This component was contaminated with a product having the same vpc retention time as 5-phenylcyclooctene oxide. [e] Identification based only on comparison of the vpc retention time with that of an authentic sample.

have on the direction and extent of the cyclization reaction. Cyclooctanol gave the 1,4-bridged ether, 9-oxabicyclo[4.2.1]nonane, in up to 36% yield together with a trace (0.8%) of the 1,5 isomer, 9-oxabicyclo-[3.3.1]nonane.[6,7] On the other hand, 1-methylcyclooctanol, under similar reaction conditions, gave a mixture of bicyclic ethers (23%) containing a preponderance of 1-methyl-9-oxabicyclo[3.3.1]nonane.[6a] Thus, introduction of the 1-methyl substituent may alter the conformation of the cyclooctane ring so as to favor the formation of a seven-membered transition state for hydrogen abstraction. Cyclodecanol is reported to give several bicyclic ethers (27.5%) although only one of these, *trans*-1,2-epoxycyclodecane, has been identified.[7] Irrespective of the direction of cyclization in this limited series, the yields are comparable with those obtained in the cyclization of simple acyclic alcohols with lead tetraacetate, suggesting that the proximity effects which play such a dominant role in transannular reactions are not important in the cyclization of medium-ring alcohols with lead tetraacetate.

Another feature of the reaction which is pertinent to the results presented in this paper emerges from an investigation of the influence of remote substituents on the direction of cyclization of acyclic alcohols. Placement of an ether grouping in the alcohol (as in **1**) greatly enhances the amount of cyclization at the methylene group adjacent to the ether oxygen atom.[8] However, a phenyl substituent, similarly placed, appears to have little influence on the direction of cyclization as shown by the product distribution in the reaction of 5-phenyl-1-pentanol (**2**) with lead tetraacetate.[9,10]



In order to examine the directive effects of a phenyl group on the transannular cyclization of a medium-ring alcohol, we have studied the reactions of 4- and 5-phenylcyclooctanol with lead tetraacetate in benzene. The *cis* and *trans* isomers of each alcohol were prepared by the published methods[11,12] and the results are summarized in Table I. It is immediately clear that the phenyl substituent has a pronounced effect on both the direction and extent of transannular cyclization. For the case of *trans*-5-phenylcyclooctanol (**20**), abstraction of the ε (benzylic) hydrogen atom occurs much more readily than does abstraction of the δ hydrogen atom, in spite of the 2:1 statistical advantage of the latter and the requirement of a seven-membered transition state. In addition, the total yield of cyclized product (77%) is more than twice the highest yield

(6) (a) A. C. Cope, M. Gordon, S. Moon, and C. H. Park, *J. Amer. Chem. Soc.*, **87**, 3119 (1965); (b) R. Moriarty and H. G. Walsh, *Tetrahedron Lett.*, 465 (1965).

(7) M. Lj. Mihailovic, Z. Cekovic, V. Andrejevic, R. Matic, and D. Jeremic, *Tetrahedron*, **24**, 4947 (1968).

(8) M. Lj. Mihailovic and M. Miloradovic, *ibid.*, **22**, 723 (1966).

(9) S. Moon and P. R. Clifford, *J. Org. Chem.*, **32**, 4017 (1967).

(10) M. Lj. Mihailovic, L. Zivkovic, Z. Maksimovic, D. Jeremic, Z. Cekovic, and R. Matic, *Tetrahedron*, **23**, 3095 (1967).

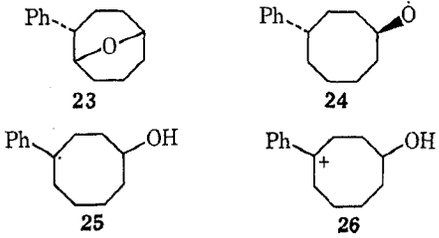
(11) A. C. Cope, M. A. McKervey, and N. M. Weinshenker, *J. Amer. Chem. Soc.*, **89**, 2932 (1967).

(12) A. C. Cope and R. B. Kinnel, *ibid.*, **88**, 752 (1966).

recorded for cyclooctanol. The yield of the bicyclic ether **17** obtained from *cis*-5-phenylcyclooctanol (**15**) is also good and the product results from abstraction of the δ hydrogen atom only; the ε hydrogen atom is inaccessible since it is *trans* to the oxygen atom in the alkoxy radical (the 1% of cyclization at the ε position is probably due to a trace of **20** present in **15** as an isomeric impurity). Both alcohols also give substantial amounts of the simple oxidation product, 5-phenylcyclooctanone (**18**).

The possibilities for cyclization with *cis*- and *trans*-4-phenylcyclooctanol are greater owing to their unsymmetrical structures; the *trans* isomer **8** possesses two types of δ hydrogen atoms, one of which is also benzylic. The ratio of the products **9** and **10** again demonstrates that the benzylic position is favored by a factor of 2:1 although the preference is much less than that shown with the *trans*-5 isomer. Although *endo*-2-phenyl-9-oxabicyclo[3.3.1]nonane (**23**), the product anticipated from cyclization at the ε position, had the same vpc retention time as **10**, it was judged to be present in not more than 0.85% yield on the basis of infrared and mass spectral evidence. The infrared spectrum of an authentic sample of **23** (*vide infra*) has a very strong absorption band at 1040 cm^{-1} which was not present in the spectrum of a sample of **10** collected from the crude reaction mixture. The mass spectrum of **23** had a peak at *m/e* 85 of intensity (55%) equal to that of a peak at *m/e* 91; the mass spectrum of **10**, on the other hand, contained a peak (100%) at *m/e* 91 and only a 10% peak at *m/e* 85. The interpretative difficulties with these reactions are well illustrated by the behavior of the *cis*-4 isomer **3**; in this case, the 1,5-bridged ether **4** constitutes 39% of the total amount of cyclized product. 4-Phenylcyclooctanone (**6**) is also formed in 44% yield.

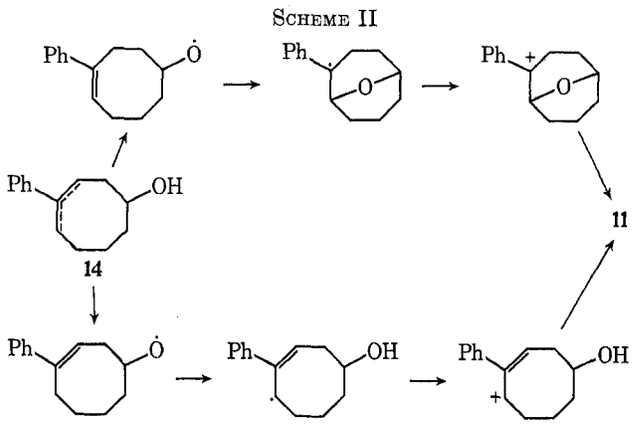
Three other products obtained from alcohol **8** can be rationalized in terms of transannular rearrangement of the alkoxy radical **24** to the carbon radical **25**. Oxidation of this latter species to the carbonium ion **26** fol-



lowed by proton elimination could give the hydroxy-olefin mixture **14**. Further reaction of **14** with lead tetraacetate could then give the corresponding acetate mixture **13**. When a sample of **14** was subjected to the reaction conditions the product isolated was a mixture of **13**, two unidentified compounds, and the unsaturated bicyclic ether **11**; two possible mechanisms for the conversion of **14** into **11** are shown in Scheme II.[13] These secondary reactions consume lead tetraacetate and, therefore, the relatively large amount (28%) of the starting material in the product mixture is understandable.

(13) These mechanisms are derived from our earlier observation that transannular oxygen bridging occurs with great ease with various cyclooctenols; see ref 11 and literature cited therein. Yet another possibility, suggested by a referee, is that the unsaturated ether **11** is produced by reaction of **23** with lead tetraacetate. This possibility was not investigated.

SCHEME II

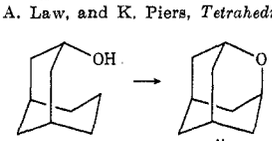


While it is not yet possible to interpret these results in conformational terms in the manner suggested for steroidal alcohols by Heusler and Kalvoda,[3,14] certain facts do emerge. The first of these is the demonstration that a phenyl substituent has a marked effect, at least with cyclooctanol, on the type of ether formed. This is most clearly seen by comparing the behavior of cyclooctanol, which gives only a trace of the 1,5-bridged ether, with *cis*-4-phenylcyclooctanol where the 1,5-bridged product constitutes 39% of the total amount of cyclization. Secondly, these results give the qualitative impression that the effects of the phenyl group depend on its position relative to the hydroxyl group. For example, nearly half of the total product from alcohol **8** are olefins, whereas no olefinic products are formed from the other three alcohols. It appears also that cyclization at the benzylic position is a much more facile process with alcohol **20** than with alcohol **8** in spite of the requirement of a seven-membered transition state in the former case. Proximity effects may play an important role here emphasizing the differences in behavior of medium-ring and acyclic alcohols.[15]

Identification of Products.—Compounds **6, 9, 16, 18, 19,** and **22** were identified by vpc and spectral comparisons with authentic samples; *cis*- and *trans*-4-

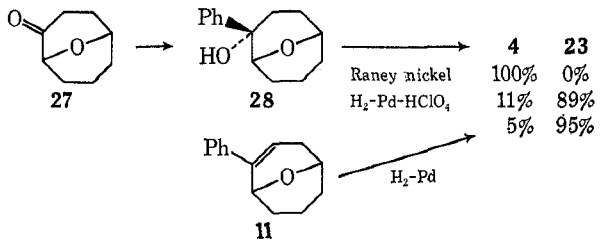
(14) These authors have compiled a considerable amount of data concerning the conformational requirements for intramolecular hydrogen abstraction by alkoxy radicals. They concluded that a six-membered chair form is the most favorable transition state. From studies involving steroidal alcohols, in which rigid conformations hold the internuclear distances nearly constant, certain trends could be discerned. These distances, as measured on Dreiding models, show that the optimum separation between the oxygen atom and the carbon bearing the hydrogen atom undergoing abstraction (called the C–O distance) in the alkoxy radical consistently lies between 2.5 and 2.7 Å. Within this range the rate of intramolecular abstraction far exceeds the rate of fragmentation or intermolecular reaction. As the C–O distance approaches 2.8 Å these trends tend to be reversed.

(15) (a) In certain favorable cases proximity effects may be responsible for the exclusive formation of 1,5-bridged ethers. For example, oxidation of *endo*-bicyclo[3.3.1]nonan-3-ol (i) with lead tetraacetate gives oxaadamantane (ii) in almost quantitative yield: M. Fisch, S. Smallcombe, J. C. Gramain, M. A. McKervy, and J. E. Anderson, *J. Org Chem.*, **35**, 1886 (1970). See also W. A. Ayer, D. A. Law, and K. Piers, *Tetrahedron Lett.*, 2959 (1965).



(b) The photochemically induced decomposition of 1-methylcyclooctyl hypochlorite proceeds *via* transannular radical rearrangements involving both the δ position (35%) and the ε position (24%). The hydrogen atoms at the single ε position are therefore about 1.4 times as reactive as those at the two δ positions in spite of the requirement of a seven-membered transition state for hydrogen abstraction from C–ε. A. C. Cope, R. S. Bly, M. M. Martin, and R. C. Petterson, *J. Amer. Chem. Soc.*, **87**, 3111 (1967). For similar effects in the transannular rearrangement of the 1-phenylcyclooctyloxy radical, see ref 11.

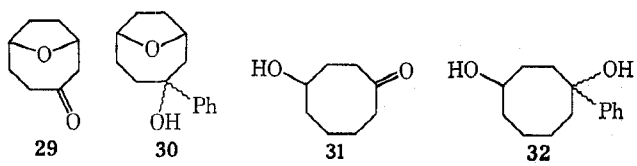
phenylcyclooctyl acetate (**7**) and (**12**) were prepared from the corresponding alcohols. The synthesis of *exo*- and *endo*-2-phenyl-9-oxabicyclo[3.3.1]nonane (**4**) and (**23**) was accomplished by the sequence outlined below. Treatment of 9-oxabicyclo[3.3.1]nonan-2-one



27 28 11

(**27**)[16] with phenyllithium in ether gave the crystalline tertiary alcohol **28**, mp 86–87.5°, which appeared to be homogeneous on vpc analysis. The phenyl group in **28** is assigned the *exo* configuration since addition of the organometallic reagent should occur from the less hindered side of the carbonyl group; the bridging oxygen atom may also play a part in controlling the direction of addition. Hydrogenolysis of **28** with Raney nickel in hot ethanol afforded a single product which was identical (vpc retention time and infrared spectrum) with the bicyclic ether **4** produced in 13% yield in the reaction of alcohol **3** with lead tetraacetate. This result is consistent with the known stereochemical tendencies of Raney nickel[17] in hydrogenolysis of benzyl alcohols and confirms the assignment of structure **28** to the tertiary alcohol. Compound **4** was also produced using palladium on carbon in ethyl acetate containing a trace of perchloric acid as the catalyst for hydrogenolysis of **28**. It was, however, the minor product. The major product was the epimeric bicyclic ether **23**. Dehydration of **28** with iodine in hot benzene gave a product which proved to be identical with the unsaturated bicyclic ether **11** isolated from the oxidation of alcohol **8**. Hydrogenation of **11** over palladium on carbon also gave the bicyclic ethers **4** and **23**.

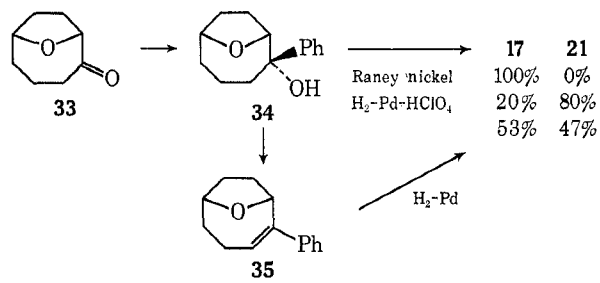
A similar scheme was used in the identification of *exo*- and *endo*-3-phenyl-9-oxabicyclo[4.2.1]nonane (**5**) and (**10**). Treatment of 9-oxabicyclo[4.2.1]nonan-3-one (**29**)[16,18] with phenyllithium in ether gave what



29 30 31 32

appeared to be a mixture of the epimeric alcohols **30**. These compounds were unstable to vpc analysis (dehydration occurred on an SE-30 column). Hydrogenolysis of the crude mixture employing Raney nickel in ethanol gave a monodeoxygenated product in excellent yield. Assuming that this reaction proceeded with retention of configuration (cf the hydrogenolysis of **28**), the product was expected to be a mixture of the *exo* and *endo* isomers. Efforts to achieve a separation by vpc analysis were unsuccessful although infrared analysis of the mixture did show the presence of both bicyclic ethers **5** and **10** which had been isolated from the lead tetraacetate oxidations of alcohols **3** and **8**, respectively. On the other hand, hydrogenolysis of **30** using palladium on carbon and perchloric acid gave a product which had an infrared spectrum identical with that of **5**. The remaining products from the reaction of *trans*-4-phenylcyclooctanol with lead tetraacetate were prepared from 4-hydroxycyclooctanone (**31**).[19] Treatment of this ketone with a large excess of phenylmagnesium bromide gave the diol mixture **32** which was subsequently dehydrated in benzene in the presence of iodine, yielding a mixture containing 90% **14** and 10% **9**. The unsaturated alcohol mixture **14** was identical (infrared and vpc analysis) with that obtained from alcohol **8**. Acteylation of **14** employing acetic anhydride in pyridine gave the acetate mixture **13**. Unlike the alcohols, these acetates could be resolved by vpc analysis (isomer ratio, 23:77).

The final synthetic sequence used in this work commenced with the preparation of the crystalline alcohol **34**, mp 93–93.5°, from 9-oxabicyclo[4.2.1]nonan-2-one (**33**)[16] and phenyllithium. Like alcohol **28**, the phenyl substituent in **34** is assigned the *exo* configuration and support for this was obtained from its behavior on Raney nickel hydrogenolysis. The product, which was



33 34 35

homogeneous on vpc analysis, had an infrared spectrum identical with that of the bicyclic ether **17** isolated in 54% yield from the lead tetraacetate reaction of alcohol **15**. Hydrogenolysis of **34** employing palladium on carbon and perchloric acid gave a mixture of bicyclic ethers containing **17** (20%) and **21** (80%) and these two compounds were also formed in about equal amounts when the unsaturated bicyclic ether **35**, obtained from **34** by dehydration, was hydrogenated on palladium.

Experimental Section

Melting points, determined using a Thomas–Hoover melting point apparatus, are uncorrected. Infrared data were obtained with a Perkin-Elmer Model 237 spectrophotometer. Vapor phase chromatography was performed using an F & M Model 720 instrument fitted with $^1/_4$-in. o.d. copper or stainless steel columns. The mass spectra were recorded using an Hitachi Perkin-Elmer Model RMU-6D mass spectrometer. Microanalyses were performed by Dr. S. M. Nagy and associates at Massachusetts Institute of Technology.

***exo*-2-Phenyl-9-oxabicyclo[3.3.1]nonan-2-ol (28).**—A solution of ketone **27** (525 mg) in ether (2 ml) was added to a stirred solution of phenyllithium prepared from bromobenzene (740 mg) and lithium (50 mg) in dry ether (10 ml) under nitrogen and the mixture was heated under reflux for 30 min. The cooled mixture was treated with saturated ammonium chloride solution and filtered. The ether solution was dried ($MgSO_4$) and concentrated, giving 470 mg of an oil. Vpc analysis (2 ft × 20% SE-30 at 195°) showed that the product was 95% pure. An analytical

(16) A. C. Cope, M. A. McKervey, and N. M. Weinshenker, *J. Org. Chem.*, **34**, 2229 (1969).

(17) For a discussion of the sterochemistry of hydrogenolysis of some benzyl-type alcohols, see S. Mitsui, Y. Kudo, and M. Kobayashi, *Tetrahedron*, 1921 (1969), and references contained therein.

(18) A. C. Cope and B. C. Anderson, *J. Amer. Chem. Soc.*, **79**, 3892 (1957).

(19) We thank Badische Anilin und Soda Fabrik, Ludwigshafen, Germany, for a gernous gift of this material.

sample, obtained by preparative vpc, had mp 86–87.5° after crystallization from pentane; infrared (neat melt) 3375, 1035, 960, 900, 860, 760, and 690 cm^{-1}.

Anal. Calcd for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31. Found: C, 77.47; H, 8.52.

2-Phenyl-9-oxabicyclo[3.3.1]non-2-ene (11).—A sample of the crude alcohol **28** (189 mg) in benzene (2.5 ml) containing a small crystal of iodine was heated under reflux for 6 hr. The cooled solution was washed with 10% sodium thiosulfate solution and dried ($MgSO_4$). Removal of the solvent gave 136 mg of **11** as an oil, *ca.* 90% pure by vpc analysis (2 ft × 20% SE-30 at 200°). An analytical sample was obtained by preparative vpc (8 ft × 10% Carbowax 20M at 245°): infrared (film) 1590, 1105, 1075, 1030, 1000, 915, 870, 865, 855, 750, and 690 cm^{-1}; mass spectrum (70 eV) *m/e* (rel intensity) 200 (100, parent ion), 157 (36), 156 (38), 139 (30), 138 (38), 110 (31), 91 (27).

Anal. Calcd for $C_{14}H_{16}O$: C, 83.96; H, 8.05. Found: C, 83.91; H, 8.18.

***endo*-2-Phenyl-9-oxabicyclo[3.3.1]nonane (23).**—To a solution of **11** (21.5 mg) in ethyl acetate (0.5 ml), 10% palladium on carbon (5 mg) was added. The solution was hydrogenated at atmospheric pressure for 1 hr. The catalyst was removed by filtration and the solution was analysed by vpc (5 ft × 5% XF-1150 at 175°). Two components, in the ratio 5:95, were present. A sample of the major component, assigned structure **23**, was obtained by preparative vpc: infrared (film) 1040, 990, 905, 870, and 690 cm^{-1}; mass spectrum (70 eV) *m/e* (rel intensity) 104 (100), 91 (56), 85 (55), 39 (37).

Anal. Calcd for $C_{14}H_{18}O$: C, 83.01; H, 8.97. Found: C, 83.58; H, 8.79.

Hydrogenolysis of *exo*-2-Phenyl-9-oxabicyclo[3.3.1]nonan-2-ol (28). (a) **On Palladium.**—To a solution of **28** (10.6 mg) in ethyl acetate (250 μl) was added a few mg of 10% palladium on carbon. The solution was hydrogenated at atmospheric pressure for 2.5 hr. Vpc analysis indicated that little or no reaction had taken place. One drop of 70% perchloric acid was added to the solution and the hydrogenation was repeated. After 30 min the reaction was complete and vpc analysis (8 ft × 20% LAC-728 at 210°) of the solution showed the presence of the *endo* isomer **23** and the *exo* isomer **4** in the ratio of 89:11.

(b) **Raney Nickel.**—The alcohol (13 mg) was dissolved in absolute ethanol (0.5 ml) and commercial Raney nickel (100 mg) was added. The mixture was heated under reflux for 2 hr after which time vpc analysis (2 ft × 20% SE-30 at 195°) showed that reaction was complete. The cooled mixture was decanted into cold water and extracted with pentane. The pentane solution was washed with water, dried ($MgSO_4$), and concentrated, yielding an oil which contained a single component by vpc analysis (8 ft × 20% LAC-728 at 210°). A sample collected by preparative vpc was identical (infrared, retention time) with compound **4** obtained from the lead tetraacetate oxidation of *cis*-4-phenylcyclooctanol (**3**): infrared (film) 1500, 1470, 1080, 1030, 900, 865, 750, and 700 cm^{-1}; mass spectrum (70 eV) *m/e* (rel intensity) 202 (15, parent ion), 120 (12), 105 (38), 104 (100), 91 (18), 85 (15), 78 (10), 77 (31), 51 (16), 44 (44), 43 (10), 41 (14), 38 (11).

Anal. Calcd for $C_{14}H_{18}O$: C, 83.01; H, 8.97. Found: C, 82.87; H, 9.02.

***exo*- and *endo*-3-Phenyl-9-oxabicyclo[4.2.1]nonane (5) and (10).**—9-Oxabicyclo[4.2.1]nonan-3-one (**29**) (51.8 mg) in ether (3 ml) was added to a stirred solution of phenyllithium prepared from lithium (15 mg) and bromobenzene (300 mg) in ether (3 ml). After 30 min the reaction mixture was processed in the usual way, yielding the tertiary alcohol **30** (76.7 mg) as a viscous oil. Trituration of a portion of the product with pentane at −78° gave a solid which, after recrystallization from hexane, had mp 105–108°. The product was not stable to vpc analysis and the crude material was used in the following hydrogenolysis experiments:

(a) **Raney Nickel.**—The crude alcohol **30** (25.5 mg) was dissolved in absolute ethanol (0.5 ml) and Raney nickel (~500 mg) was added. The mixture was heated under reflux for 1 hr. The cooled mixture was filtered and the ethanol solution was concentrated, yielding an oil (22 mg). Comparison of the infrared spectrum (film) of an analytical sample, obtained by preparative vpc (2 ft × 20% SE-30 at 190°), with the spectra of the two compounds **5** and **10** showed the product of hydrogenolysis with Raney nickel was a mixture of these two isomers. Their vpc retention times were identical on all available columns.

Anal. Calcd for $C_{14}H_{20}O$: C, 83.01; H, 8.97. Found: C, 83.42; H, 8.81.

A sample of isomer **10**, isolated from the lead tetraacetate oxidation of alcohol **8**, had principal infrared (film) bands at 1490, 1450, 1100, 1065, 1045, 1025, 750, 700 cm^{-1}; mass spectrum (70 eV) *m/e* (rel intensity) 202 (47), 174 (13), 158 (13), 156 (28), 145 (10), 144 (21), 143 (28), 131 (12), 130 (27), 129 (38), 128 (16), 119 (16), 118 (68), 117 (56), 116 (56), 115 (45), 105 (30), 104 (90), 103 (31), 91 (100), 85 (10), 78 (31), 77 (35), 65 (19), 63 (13), 55 (19), 54 (10), 51 (13), 44 (11), 43 (10), 41 (37), 39 (37).

Anal. Calcd for $C_{14}H_{18}O$: C, 83.01; H, 8.97. Found: C, 83.42; H, 8.81.

(b) **Palladium on Carbon.**—The crude alcohol **30** (19.6 mg) was dissolved in ethylacetate (0.5 ml) containing 70% perchloric acid (15 ml) and 10% palladium on carbon (25 mg) was added. The mixture was hydrogenated until hydrogen uptake had ceased. Work-up in the usual way gave an oil (17.4 mg). A sample of the product was purified by preparative vpc. The infrared spectrum which was identical with that of isomer **5** isolated from the lead tetraacetate oxidation of alcohol **3**, had principal bands at 1500, 1465, 1110, 1075, 1045, 1035, 1010, 750, and 700 cm^{-1}; mass spectrum (70 eV) *m/e* (rel intensity) 203 (10), 202 (60), 158 (19), 145 (12), 143 (38), 131 (31), 105 (29), 128 (12), 118 (50), 117 (48), 116 (13), 115 (31), 105 (29), 104 (100), 103 (19), 98 (10), 92 (10), 91 (66), 83 (10), 80 (17), 79 (10), 78 (18), 77 (24), 71 (10), 65 (12), 55 (14), 51 (19), 44 (29), 42 (29).

Anal. Calcd for $C_{14}H_{18}O$: C, 83.01; H, 8.97. Found: C, 83.27; H, 8.98.

1-Phenyl-1,4-cyclooctanediol (32).—A solution of 4-hydroxycyclooctanone (5.0 g) in tetrahydrofuran (25 ml) was added dropwise with stirring to a solution of phenylmagnesium bromide (prepared from 2.4 g of magnesium and 15.7 g of bromobenzene) in tetrahydrofuran (75 ml). The mixture was stirred for a further 30 min and then was treated with saturated ammonium chloride solution. The solids were removed by filtration and the filtrate was concentrated, yielding a viscous liquid. This material was dissolved in ether, dried ($MgSO_4$), and concentrated to a semicrystalline solid. Crystallization from chloroform gave 3.1 g (40%) of **32**, mp 116–118°. An analytical sample, mp 122–124°, was obtained by recrystallization from ethyl acetate.

Anal. Calcd for $C_{14}H_{20}O_2$: C, 76.32; H, 9.15. Found: C, 76.37; H, 9.05.

Dehydration of Diol 32.—A crystal of iodine was added to a solution of **32** (2.5 g) in benzene (20 ml) and the mixture was heated under reflux for 24 hr with continuous removal of water in a Dean–Stark apparatus. The cooled solution was washed with aqueous sodium thiosulfate solution, dried ($MgSO_4$), and concentrated, yielding 1.9 g of an oil. Vpc analysis (8 ft × 10% Carbowax 20M at 245°) indicated the presence of the hydroxy–olefin mixture **14** (82.5%) and 1-phenyl-9-oxabicyclo[4.2.1]-nonane (**9**) (17.5%). The hydroxy–olefin mixture was purified by preparative vpc using the same column; the individual isomers were not separated under these conditions. An analytical sample had principal infrared bands at 3350, 2910, 2840, 1590, 1035, 1025, 760, and 690 cm^{-1}.

Anal. Calcd for $C_{14}H_{18}O$: C, 83.01; H, 8.97. Found: C, 83.14; H, 8.53.

Acetoxy–Olefin Mixture 13.—A portion of the crude alcohol mixture **14** was treated with acetic anhydride in pyridine. Vpc analysis (8 ft × 10% Carbowax 20M at 245°) of the product showed the presence of the two isomers in the ratio of 23:77. A sample of the mixture, purified by preparative vpc, had infrared (film) absorptions at 2920, 1735, 1235, 1020, 950, 850, 760, 690 cm^{-1}.

Anal. Calcd for $C_{16}H_{20}O_2$: C, 78.65; H, 8.25. Found: C, 78.26; H, 8.52.

Reaction of Hydroxy–Olefin Mixture 14 with Lead Tetraacetate.—A sample of crude **14** (179 mg) containing 17.5% 1-phenyl-9-oxabicyclo[4.2.1]nonane (**9**) was dissolved in dry benzene (5 ml) and lead tetraacetate (350 mg) was added. The mixture was heated under reflux for 1 hr, cooled, washed with aqueous sodium thiosulfate, and dried ($MgSO_4$). Removal of the solvent yielded an oil (186 mg). Vpc analysis (8 ft × 10% Carbowax 20M at 245°) showed the presence of six components; relative retention times (rrt) 0.85, 1.00, 1.23, 1.59, 2.59, 3.28. The component with rrt 1.00 (20%) was identified as the 1-phenyl-9-oxabicyclo[4.2.1]nonane present in the starting material. Excluding this compound, the other products were (1) rrt 0.85 (9%), an unidentified compound which was also detected in the product mixture from the reaction of *trans*-4-phenylcyclo-

octanol with lead tetraacetate; (2) rrt 1.23 (9%), unidentified product also present in the product mixture from **8**; (3) rrt 1.59 (24.8%), 2-phenyl-9-oxabicyclo[3.3.1]non-2-ene (**11**); (4) rrt 2.59 (4.0%), the acetates **13** of the starting alcohols; (5) rrt 3.28 (53.2%), unreacted starting material **14**. These components were identified by their infrared spectra and vpc retention times.

trans-**4-Phenylcyclooctyl Acetate** (**12**).—*trans*-4-Phenylcyclooctanol (**8**) (100 mg) was dissolved in pyridine (1 ml) and acetic anhydride (5 drops) was added. The solution was allowed to stand at room temperature for several days and was then poured into cold water. Extraction with ether in the usual way gave ~100 mg of an oil. An analytical sample was obtained by preparative vpc (2 ft × 20% SE-30 at 210°): infrared spectrum (film) 1725, 1235, 1020, 750, and 690 cm^{-1}.

Anal. Calcd for $C_{16}H_{22}O_2$: C, 78.01; H, 9.00. Found: C, 78.33; H, 9.07.

cis-**4-Phenylcyclooctyl Acetate** (**7**).—A sample of *cis*-4-phenylcyclooctanol (**3**) was treated with acetic anhydride as described above for the *trans* isomer. A pure sample of the product had principal infrared absorptions at 1735, 1250, 1035, 755, and 690 cm^{-1}.

Anal. Calcd for $C_{16}H_{22}O_2$: C, 78.01; H, 9.00. Found: C, 78.19; H, 8.98.

exo-**2-Phenyl-9-oxabicyclo[4.2.1]nonan-2-ol** (**34**).—To a solution of phenyllithium (prepared from 0.17 g lithium and 1.7 g bromobenzene) in dry ether was added 9-oxabicyclo[4.2.1]-nonan-2-one (1.3 g) in ether (10 ml). The mixture was stirred for 30 min and then was treated with saturated ammonium chloride solution. The ether layer was separated and the aqueous layer was extracted twice with ether. The combined extracts were washed with water and dried ($MgSO_4$). Removal of the solvent gave 1.6 g (80%) of **34** as a white solid. Recrystallization of a sample from hexane–ethanol gave material of mp 92.5–94°.

Anal. Calcd for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31. Found: C, 76.91; H, 8.22.

Dehydration of 34.—A sample of 34 (1.3 g) was dissolved in benzene (30 ml) containing a crystal of iodine. The solution was heated under reflux for 24 hr with continuous removal of water. The cooled solution was washed with sodium thiosulfate solution, water, and dried ($MgSO_4$). Removal of the solvent gave *ca.* 1.3 g of an oil which was distilled, yielding 0.9 g (75%) of **35**: bp 111–113° (0.5 mm); infrared (film) 1590, 1500, 1474, 1450, 1190, 1110, 1070, 1020, 1000, 965, 925, 915, 855, 845, 755, and 695 cm^{-1}.

Anal. Calcd for $C_{14}H_{16}O$: C, 83.96; H, 8.05. Found: C, 83.91; H, 8.18.

Hydrogenolysis of 34. (a) **Raney Nickel.**—To a solution of **34** (30 mg) in ethanol (5 ml) was added Raney nickel (*ca.* 100 mg). The mixture was heated under reflux for 1 hr and the catalyst was then removed from the cooled mixture by filtration. The ethanol solution was diluted with water and extracted with ether. The ether extract was washed with water, dried ($MgSO_4$), and concentrated, yielding an oil. Vpc analysis (5 ft × 5 ft XF-1150 at 180°) under conditions which cleanly separated isomers **17** and **21** showed that the product contained a single component with the same retention time and infrared spectrum as the compound **17** isolated from the lead tetraacetate oxidation of *cis*-5-phenylcyclooctanol. The infrared spectrum of a sample of **17** collected by preparative vpc had principal absorptions at 1600, 1100, 1085, 1070, 980, 935, 925, 753, and 700 cm^{-1}.

Anal. Calcd for $C_{14}H_{18}O$: C, 83.01; H, 8.97. Found: C, 83.26; H, 9.05.

(b) **Palladium on Carbon.**—A sample of **34** (20 mg) was dissolved in ethyl acetate (5 ml) containing 10% palladium on carbon (10 mg) and perchloric acid (1 ml), and the mixture was hydrogenated at atmospheric pressure until hydrogen uptake ceased. The catalyst was removed by filtration and the filtrate was concentrated. Vpc analysis (5 ft × 5% XF 1150 at 180°) indicated the presence of two components in the ratio of 20:80. The minor component was identified as the bicyclic ether **17** and the major component **21**.

Hydrogenation of 2-Phenyl-9-oxabicyclo[4.2.1]non-2-ene (**35**). —A sample of **35** (300 mg) in ethanol (30 ml) containing 10% palladium on carbon (100 mg) was hydrogenated at atmospheric pressure. After 1 hr, the theoretical amount of hydrogen had been taken up. The catalyst was removed by filtration and the ethanol solution was concentrated, yielding ~300 mg of an oil. Vpc analysis (5 ft × 5% XF-1150 at 180°) showed the presence of two components in the ratio 53:47. Pure samples of both components were obtained by preparative vpc. The major component was identical in retention time and infrared spectrum with the bicyclic ether **17**, and the minor component **21** had the same retention time as the compound formed in 5% yield in the reaction of *trans*-5-phenylcyclooctanol with lead tetraacetate. The infrared spectrum of **21** had principal absorptions at 1600, 1065, 980, 925, 750, and 700 cm^{-1}.

Anal. Calcd. for $C_{14}H_{18}O$: C, 83.01; H, 8.97. Found: C, 82.83; H, 9.00.

Lead Tetraacetate Reactions. (a) *cis*-**5-Phenylcyclooctanol** (**15**).—Commercial lead tetraacetate was dried at 0.3 mm and room temperature immediately before use. To a solution of *cis*-5-phenylcyclooctanol (1.5 g) in dry benzene (65 ml) was added lead tetraacetate (4.5 g) and the mixture was heated under reflux for 42 hr with stirring. The cooled solution was treated with ethylene glycol (8 ml) and stirring was continued for 10 min. The layers were then separated and the ethylene glycol layer was diluted with water and extracted three times with ether. The ether extracts and the main benzene solution were combined, washed successively with water, 10% sodium thiosulfate, and saturated sodium chloride solution, and dried ($MgSO_4$). Removal of the solvent gave 1.7 g of an oil which was distilled, yielding a fraction (1.5 g), bp 113–145° (0.6 mm). Partial separation of the products was achieved by chromatography on Merck acid washed alumina (70 g). Elution with pentane followed by pentane–methylene chloride mixtures (from 10% methylene chloride up to 50%) gave partial separation. Ten fractions, containing a total of 1.49 g of material, were collected. Each fraction was examined by vpc (5 ft × 5% XF-1150 at 180°) and the individual components were isolated by preparative vpc using the same column. Final purification was achieved in some cases by recollection from a 2 ft × 20% SE-30 column.

(b) *trans*-**5-Phenylcyclooctanol** (**20**).—This reaction was carried out using 100 mg of the alcohol and the products were isolated as described above except that the distillation of the crude product was omitted.

(c) *cis*- **and** *trans*-**4-Phenylcyclooctanols** (**3**) **and** (**8**).—These reactions were conducted on a 1.5-g scale. In each case, the products were isolated by a combination of distillation, column chromatography, and vapor phase chromatography.

In all cases, the identifications are based on comparison of retention times and infrared spectra with those of authentic samples. Compounds **6**, **9**, **16**, **18**, **19**, and **22** were available from earlier studies.[11,12]

Registry No.—Lead tetraacetate, 546-67-8; **3**, 14573-36-5; **5**, 25090-54-4; **7**, 25090-55-5; **8**, 14573-37-6; **10**, 25090-57-7; **11**, 25090-58-8; **12**, 25090-59-9; **13a**, 25090-60-2; **13b**, 25090-37-3; **14a**, 25090-61-3; **14b**, 25090-38-4; **15**, 7286-96-6; **17**, 25096-34-8; **20**, 7286-64-8; **21**, 25096-36-0; **23**, 25096-37-1; **28**, 25096-38-2; **32**, 25096-39-3; **34**, 25096-40-6; **35**, 25096-41-7.