TpT segment of DNA. The use of *o*-xylylene dibromide to link conjoined bases having proximate nitrogens may find further application in structure establishment and modification.

Acknowledgment. We thank Mrs. Carlyn R. Peterson for her assistance in the preparation of the stereoscopic drawings which were plotted with ORTEP written by C. K. Johnson, Oak Ridge National Laboratory. Computations were carried out on the IBM 1800, 7094, and 360-75 at the University of Illinois. We are grateful to Dr. John Occolowitz of the Lilly Research Laboratories, Eli Lilly and Co., Indianapolis, Ind., for determination of the high-resolution mass spectrum (compound **4**).

The Structural and Stereochemical Course of *in Vitro* Epoxy Olefin Cyclization. Diterpenoid Intermediates[1]

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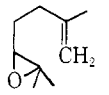
Abstract: The cyclization of unsaturated epoxides to tricyclic systems is shown to be a stereospecific process. Boron fluoride etherate treatment of an epoxy olefin with a central *trans*-substituted double bond, *trans*-**7**, leads to two tricyclic alcohols, **12** and **14**, both of which have *trans*-fused A/B rings. The corresponding *cis* compound, *cis*-**7**, produces an A/B *cis*-fused alcohol, **20**. These reactions also yield monocyclized products of specific geometry depending on the stereochemistry of the original double bond and the conformational folding of the epoxy olefin chain. The stereochemistry of these products suggests that cyclization occurs *via* intermediate cations of fixed geometry rather than as a "nonstop" process.

The first cyclization of an acyclic epoxy olefin, geraniolene monoepoxide, **1**, was reported[3] by us as a model system for the biosynthesis of cholesterol. Subsequent biochemical experimentation[4] has shown this type of cyclization to be the actual pathway used by cholesterol synthesizing enzymatic systems. A number of *in vitro* cyclizations of unsaturated oxiranes have also been reported[5] including one leading to the synthesis of the naturally occurring farnesiferol series of sesquiterpenoids. These studies have been patterned on the "biogenetic" process producing, as exemplified by our cyclization of **1** → **2** + **3**, 3-hydroxy-4,4-dimethylcyclohexyl systems. In this paper we wish to report the application of epoxide cyclization to "nonbiogenetic" systems with the object of preparing intermediates for diterpene acid synthesis, and the obtaining of the first definitive evidence for the stereospecificity of epoxy olefin cyclization.[1]



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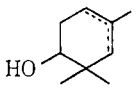

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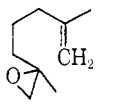
In order to produce useful intermediates for diterpene acid synthesis it was necessary to employ an unsaturated epoxide which would lead to a product having a potential C_4-carboxyl group. We chose, therefore, to investigate the reactivity of terminal epoxides. In one of our initial model studies[6] we found that treatment of terminal epoxide **4** with boron fluoride etherate in benzene gave two monocyclic products, **5** and **6**, with the desired structural features: a cyclohexane ring system with an oxygenated carbon substituent at the potential C_4 position of a diterpene acid.



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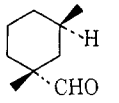

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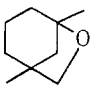

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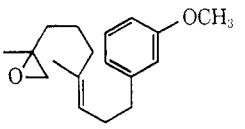
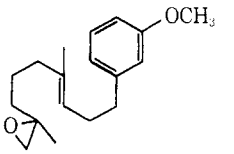
As a result of this successful monocyclic case, we turned our attention to the preparation of potential tricyclic substances. The epoxy olefins we chose for study are the *cis* and *trans* isomers of **7**. As discussed in the sequel, we expected the cyclizations of both *cis*- and *trans*-double bond isomers to yield information on the stereochemical course of epoxide cyclization as well as to lead to synthetically useful intermediates.



cis-**7**



trans-**7**

(1) (a) This work was submitted but not published as a Communication to the Editor of *J. Am. Chem. Soc.* in June 1968. It constituted at that time the first demonstration of *stereospecific in vitro* epoxy olefin cyclization. The results and conclusions incorporated in that communication and this paper have been subsequently supported by a recently published communication: E. E. van Tamelen and J. P. McCormick, *J. Am. Chem. Soc.*, **91**, 1847 (1969). (b) This work was supported in part by a grant (GM-11729) from the Public Health Service. (c) Steroid numbering is used throughout the text of this paper.

(2) Trainee, 1967–1969, NIH Training Grant GM-01394.

(3) D. J. Goldsmith, *J. Am. Chem. Soc.*, **84**, 3913 (1962).

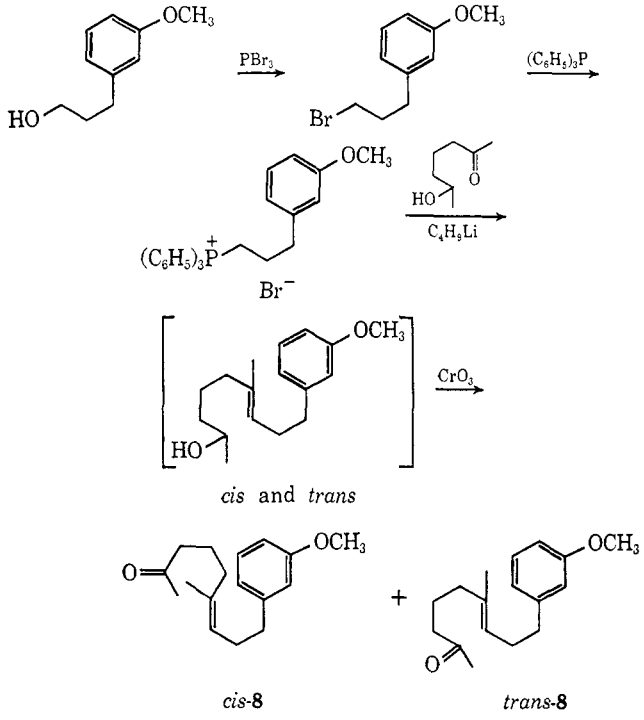
(4) (a) E. J. Corey, W. E. Russey, and P. R. Ortiz de Montellano, *ibid.*, **88**, 4750 (1966); (b) E. E. van Tamelen, J. D. Willett, R. B. Clayton, and K. E. Lord, *ibid.*, **88**, 4752 (1966).

(5) For a review of this work, see E. E. van Tamelen, *Accounts Chem. Res.*, **1**, 11 (1968).

(6) D. J. Goldsmith and B. C. Clark, Jr., *Tetrahedron Letters*, 1215 (1967).

Two methods of synthesis were employed for the preparation of the necessary epoxy olefins. One of these methods produced both isomers and the other yielded only the *trans* material. In the first sequence, shown in Scheme I, a Wittig reaction was employed to

Scheme I

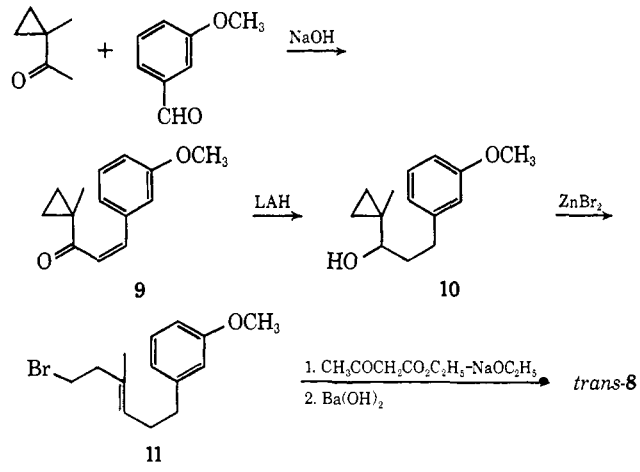


introduce the olefinic linkage. As expected the olefin formed in this manner was a mixture of *cis* and *trans* isomers. Complete separation of these hydroxy olefins from triphenylphosphine oxide could not be effected. The crude reaction product was therefore oxidized and the resulting ketones, *cis*- and *trans*-**8**, were purified by column chromatography. Gas chromatographic analysis of the mixture of ketones showed that one of the double bond isomers predominated in a ratio of 2:1. Separation of these isomers was effected by preparative glpc but the major isomer continued to be contaminated by about 8% of the minor component. The stereochemistry of the unsaturated ketones was assigned on the basis of their nmr spectra. *cis*-**8**, the major compound, displayed a vinyl methyl signal at 1.64 ppm while the lesser component, *trans*-**8**, showed the equivalent signal at 1.53 ppm. The appearance of a resonance position for a vinyl methyl group on a *trans*-substituted double bond at about 0.1 ppm higher field than that of the corresponding *cis* analog has been reported by Bates.[7] Our values for *cis*- and *trans*-**8** are in agreement with those found by Bates for the *cis*- and *trans*-farnesols.

Treatment of the individual ketones, *cis*- and *trans*-**8**, with dimethyloxosulfonium methylide afforded the epoxy *cis*-olefin, *cis*-**7**, in 50% yield and the epoxy *trans*-olefin, *trans*-**7**, in 64% yield. The spectral characteristics of both of these compounds were in accord with both their structural and stereochemical assignments.

For the synthesis of the *trans*-epoxy olefin alone we employed the method of Julia as modified by Johnson[8] for acid-catalyzed ring opening of a cyclopropylcarbinol. As shown in Scheme II condensation of α-methyl-

Scheme II



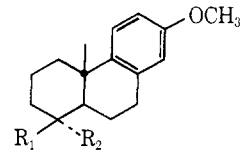
cyclopropyl methyl ketone with *m*-methoxybenzaldehyde afforded the unsaturated ketone **9**. When **9** was treated with an excess of lithium aluminum hydride reduction of both the carbonyl group and the olefinic bond occurred yielding the saturated alcohol **10**. Johnson[8b] has shown that secondary cyclopropylcarbinols like **10** when subjected to zinc bromide catalyzed ring opening yield *trans*-olefins. This finding was borne out in our case also when **19** yielded the *trans*-bromide **11** contaminated by less than 2% of the *cis* isomer. Conversion of **11** to the *trans*-ketone **8** was effected by alkylation with acetoacetic ester followed by barium hydroxide catalyzed hydrolysis and decarboxylation. The over-all yield of *trans*-**8** from the cyclopropyl ketone was 19%. Despite the number of steps involved this last route is better suited for the preparation of large quantities of the epoxy olefin *trans*-**7** than is the Wittig reaction sequence. The latter is limited by the inefficient glpc separation of *cis*- and *trans*-**8**.

We examined the cyclizing propensities of *cis*- and *trans*-**7** employing a variety of acid catalysts and reaction media. The greatest yields of tricyclic material were obtained with boron fluoride etherate in methylene chloride and we shall report here our results with this particular set of reaction conditions only. Treatment of *trans*-**7** with boron fluoride etherate afforded a complex mixture of transformation products. Chromatography of this mixture yielded two crystalline tricyclic alcohols. One of these, mp 109–111°, obtained in 24% yield was assigned structure **12** on the basis of spectroscopic and chemical evidence. The nmr spectrum of **12** reveals the presence of two methyl groups on saturated carbon atoms. One of these methyl groups displays a signal at 0.89 ppm and the other at 1.20 ppm. These peak positions correlate with the reported[9] values for the C_4-methyl group and the angular methyl group of the *trans*-A/B series of C-ring aromatic diterpenoids. The nmr spectrum also shows the presence of the C_4-hydroxymethyl group of **12** by the appearance of an AB quartet centered at 3.36 ppm. The aromatic portion of the nmr spectrum, moreover, integrates for three hydrogens and displays a pattern consistent with the substitution of the benzenoid ring of formula **12**.

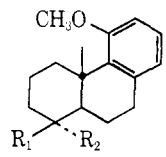
(7) R. B. Bates, D. M. Gale, and B. J. Gruner, *J. Org. Chem.*, **28**, 1086 (1963).

(8) (a) M. Julia, S. Julia, and R. Guegan, *Bull. Soc. Chim. France*, 1072 (1960); (b) S. F. Brady, M. A. Ilton, and W. S. Johnson, *J. Am. Chem. Soc.*, **90**, 2882 (1968).

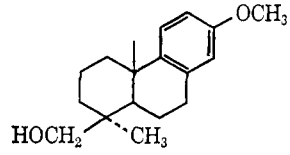
(9) E. Wenkert, A. Afonso, P. Beak, R. W. J. Carney, P. W. Jeffs, and J. D. McChesney, *J. Org. Chem.*, **30**, 713 (1965).



12, $R_1 = CH_3$; $R_2 = CH_2OH$
13, $R_1 = CH_3$; $R_2 = CO_2H$



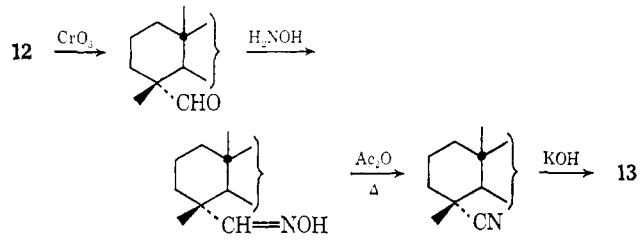
14, $R_1 = CH_3$; $R_2 = CH_2OH$
16, $R_1 = CH_3$; $R_2 = CHO$



15

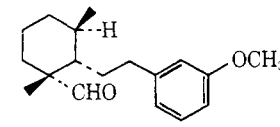
Chemical confirmation of the structure of **12** was obtained by conversion to the tricyclic acid **13**, as shown in Scheme III.[10] This acid has been prepared recently by Pelletier and coworkers[11] by an independent synthesis. The physical and spectroscopic properties of **13** obtained in our conversion were identical with those found by the previous workers.

Scheme III

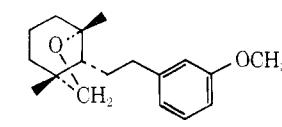


The second tricyclic alcohol, obtained in 9% yield from *trans*-**7**, was also found to be an A/B *trans*-fused system. This alcohol, **14**, mp 154–156°, shows three significant differences from **12** in its nmr spectrum. The signal for the angular methyl group of **14** occurs at 1.35 ppm compared to 1.20 ppm for the corresponding group in **12**. This difference cannot be accounted for by assuming that the angular methyl group of **14** is deshielded by a β-oriented C_4-hydroxymethyl group as, for example, in the alternate structure **15**. Wenkert and coworkers have shown that the effect of a C_4-hydroxymethyl group on the chemical shift of the C_{10} angular methyl substituent is a negligible one. Second, one of the aliphatic ring proton signals which occur in the 1.5–2-ppm region in the spectrum of **12** is shifted to approximately 3.0 ppm in the spectrum of the second alcohol. The only protons in **12** which fall in this region are the benzylic ones and the hydroxymethylene pair. Finally, the aromatic region of the nmr spectrum of **14** is significantly different from that of **12**. This region in the spectrum of the latter alcohol correlates both in chemical shift positions and coupling pattern to similarly substituted aromatic rings, *e.g.*, ring A of 17-α-ethynylestradiol.[12] In contrast, analysis of the aromatic region of the nmr spectrum of **14** shows that the three ring C protons for this compound have a serial relationship to the methoxy group rather than flanking it two on one side and one on the other as in **12**. Computation[13] of the theoretical spectrum for a 2,3-dialkyl-substituted anisole produces a spectrum in close agreement with the observed one. Thus the second tricyclic alcohol obtained from the cyclization of *trans*-**7** must have the assigned structure **14**. This structure also accounts for the previously described characteristics of the nmr spectrum. Both the angular methyl group and at least one of the C_1 hydrogens would be expected to be deshielded by the methoxyl group at C_{11} and therefore appear in the nmr at lower field than they do in the spectrum of **12**. Additional evidence for the steric disposition of the C_4-hydroxymethyl group of **14** was obtained by converting the alcohol to the corresponding aldehyde. This latter compound **16** produced by chromic acid oxidation of **14** revealed no shift to higher field of the nmr signal of the angular methyl group. If the aldehyde group of **16** were β oriented, then shielding of the angular methyl by the carbonyl would in fact produce such a shift.[9]

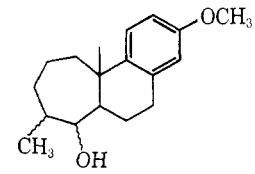
The reaction mixture from acid treatment of *trans*-**7** yields, in addition to the crystalline tricyclic alcohols described above, a number of noncrystalline components. The first fractions from chromatography of this mixture yield a number of hydrocarbons in which the epoxide oxygen has been lost.[14] We have been unable to isolate any individual compounds from this hydrocarbon mixture but the aromatic region of the nmr spectra of these fractions suggest that they contain some tricyclic materials. Following these hydrocarbons an aldehyde was obtained in 7% yield. This substance on the basis of its nmr spectrum which shows signals for two methyl groups on saturated carbon, one as a singlet and the other as a doublet, as well as the presence of four aromatic protons is assigned structure **17**. The stereochemical assignment for **17** is based on evidence found for the epimeric compound obtained in the cyclization of *cis*-**7**.



17



18



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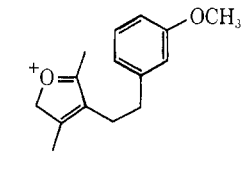


i

A second product resulting from monocyclization of *trans*-**7** is the bridged ether **18** which we obtained in a yield of 15%. The demonstration of the structure of this material is also based on spectroscopic evidence. The two methyl group resonances which appear in the nmr spectrum of **18** are singlets indicative of substitution at quaternary centers. In addition one of these methyl groups is located in the grouping CH_3C–O since its signal occurs at lower field (1.21 ppm) than that of any of the other saturated methyl groups occurring in this series of compounds with the exception of the an-

(10) R. E. Ireland and R. C. Kierstead, *J. Org. Chem.*, **31**, 2543 (1966).

(11) A. Ogiso and S. W. Pelletier, *Chem. Commun.*, 94 (1967). We wish to thank Dr. Pelletier for supplying us with spectra of **13**.

(12) N. S. Bhacca, L. F. Johnson, and J. N. Shoolery, "NMR Spectra Catalog," Varian Associates, Palo Alto, Calif., 1962, spectrum no. 343.

(13) We wish to thank Dr. Roger M. Crecely of these labs for carrying out this computation an an IBM 1620 computor employing the Prospect-1 program for a three-spin system.

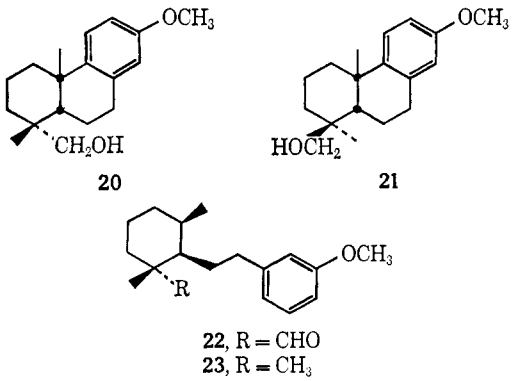
(14) Short reactions times, *e.g.*, 1 min, lead to a dimunition of the hydrocarbon yield. Increased amounts of **14** and the saturated aldehyde **17** were noted under these conditions.

gular methyl group of **14**. The infrared spectrum of **18** shows the absence of either hydroxyl or carbonyl groups and the mass spectrum shows a fragment at *m/e* 231, i, for the loss of the methylene groups at carbons 1, 2, and 3 plus one additional proton. This type of fragmentation pattern is characteristic of bridged bicyclic ethers corresponding in structure to **18**.[15] Our assignment of the stereochemistry of **18** is a tentative one and is based on the apparent stereochemical course of these cyclizations which will be discussed below.

Finally we obtained in 3% yield a mixture of substances, **19**, which appear to be tricyclic but which contain a seven-membered ring A. We found in previous work[6] with model systems that seven-membered ring products were formed in epoxide cyclizations by opening of the epoxide ring to an aldehyde followed by cyclization of the latter.[16]

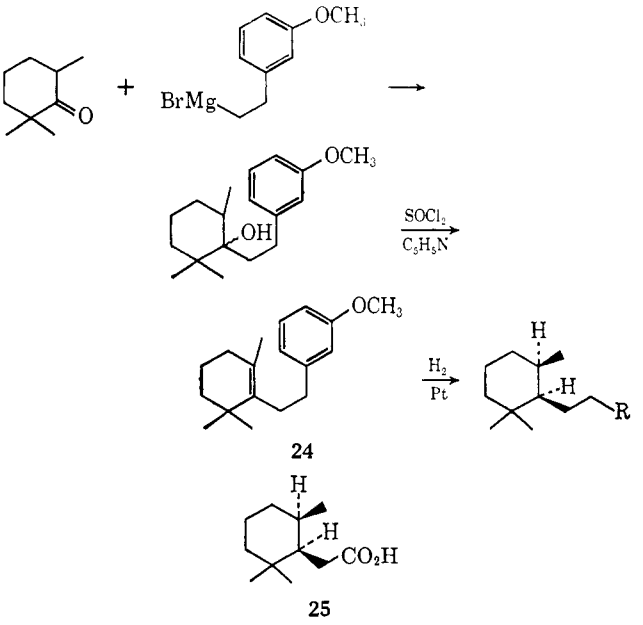
The cyclization of *cis*-**7** was carried out in the same manner as that of the *trans* isomer. In this case a much lower percentage of tricyclic material was obtained. Chromatography of the reaction mixture afforded only one pure tricyclic alcohol, **20**, as an oil in 10% yield. The nmr spectrum of **20** revealed the *cis* nature of the A/B ring fusion. The $C_{4\alpha}$ substituents of ring C aromatic diterpenoids are shifted to abnormally high field when rings A and B are *cis* fused.[9] In these cases the α substituent lies in the shielding portion of the aromatic ring's magnetic anisotropy. In the case of **20** the protons of the C_4-hydroxymethylene group occur as an AB quartet centered at 2.84 ppm. By comparison the equivalent protons in the spectra of the *trans* materials **12** and **14** give rise to signals centered at 3.36 and 3.35 ppm, respectively. The remainder of the nmr spectrum of **20** as well as its infrared and mass spectra are also consistent with the assigned structure and stereochemistry.

Two additional fractions containing tricyclic alcohols were also obtained from the cyclization of *cis*-**7**. Nmr analysis of one of these fractions obtained in 2% yield indicated that it contained a mixture of **12** and a second *cis*-fused product, **21**. The occurrence of the latter alcohol was indicated by the appearance of a signal at 0.32 ppm. This high-field position for a methyl group is consistent with the values reported by Wenkert[9] for an α-oriented C_4-methyl group in a A/B *cis*-fused system with an aromatic C ring. The *cis*-epoxy olefin, *cis*-**7**, does not appear to be, however, the precursor of the second component of this mixture, **12**. All of this *trans*-fused product can be accounted for by the presence of 8–10% of *trans*-**7** in the *cis*-epoxy olefin used for cyclization studies. The final tricyclic material obtained from *cis*-**7** is an oily substance which resembles **19** in its spectroscopic properties. This substance obtained in 2% yield is not identical with **19**, but whether it differs in its ring junction stereochemistry or only in the stereochemistry of the A ring substituents is not known with certainty at present.



cis-**7** like its *trans* isomer yields a complex mixture of hydrocarbons (36%) and a monocyclic saturated aldehyde, **22** (21%). The latter resembles **17** in its spectroscopic properties but is clearly isomeric. Since the mode of formation[6] of either **17** or **22** requires that the two methyl substituents have a *cis* relationship, these two aldehydes must differ only in the relative stereochemistry of the *m*-methoxphenyl chain. In order to determine this stereochemistry, we chose aldehyde **22** obtained from *cis*-**7** for study. Wolff–Kishner reduction of **22** produced the hydrocarbon **23**. An independent synthesis of **23**, shown in Scheme IV, was then attempted. In the last step of this correlation we attempted the catalytic reduction of **24**. Palladium-on-charcoal-catalyzed hydrogenation of **24** led to a mixture of both **23** and its *trans* isomer. When platinum was employed partial reduction of the aromatic ring occurred. Since this latter method has been shown to lead predominantly to the production of *cis* isomers in the reduction of 1,2-disubstituted cyclohexenes we subjected **23** to the same reaction conditions. The hydroaromatic material obtained in this way was identical with the substances produced *via* the independent synthesis of Scheme IV. Comparison of the nmr spectrum to that reported by Cason[17] for **25** demonstrated that reduction has indeed occurred to yield a *cis* product and that the relative stereochemistry of **17** and **22** is as shown.

Scheme IV



The cyclization reactions of a variety of unsaturated compounds have been extensively studied. Both

(15) Unpublished results of these laboratories.

(16) J. A. Marshall and N. H. Anderson, *Tetrahedron Lett.*, 1219 (1967).

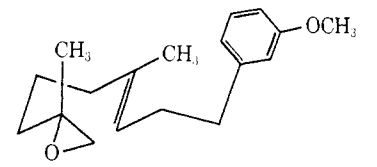
(17) J. Cason and K. Liauw, *J. Org. Chem.*, **30**, 1763 (1965).

Stork[18] and Eschenmoser[19] have found that the acid-catalyzed cyclizations of polyenic acids are nonstereospecific and that the geometry of the products (*trans*-decalins) depends on factors other than the stereochemistry of the original olefinic bonds. In contrast, Johnson[20] has shown that the cyclization reactions of olefinic acetals, sulfonate esters, and allylic alcohols are highly stereospecific. Although a variety of unsaturated epoxides have also been induced to undergo cyclization, all of the reported[1,5] cases have concerned the use of *trans*-olefins. The cyclizations of *cis*- and *trans*-**7** reported here constitute the first demonstration that epoxy olefin cyclization is a stereospecific process.

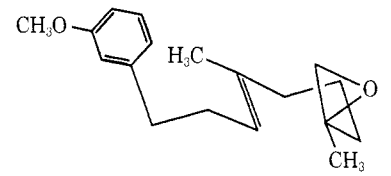
This stereospecificity does not demonstrate, however, that epoxy olefin cyclization must necessarily be a fully synchronous event. Indeed the structural and stereochemical nature of the products which we have obtained from the reactions of *cis*- and *trans*-**7** suggest that cationic intermediates of fixed geometry may intervene in the cyclization process. The reaction of *trans*-**7** with boron fluoride produces tricyclic alcohols, **12** and **14**, that have an α-C_4-methyl group only. We find no equivalent tricyclic products with the hydroxymethyl group in the β configuration. Consideration of the conformational requirements for cyclization suggests that both types of products *ought* to be possible. The two foldings of the alkyl chain of *trans*-**7** required for cyclization, ii and iii, differ only by rotations about single bonds, rotamer ii leading to α-hydroxymethyl products, and rotamer iii leading to β-hydroxymethyl products. A significant difference between these two modes of cyclization appears, however, if one considers the stereochemistry of the possible π-complexed cations iv and v. Cation iv cannot yield a bicyclic ether or a saturated aldehyde unless it reverts to an uncomplexed cyclohexyl carbonium ion. Cation v, on the other hand, may undergo several competing reactions—conversion to a σ complex followed by proton loss to form a tricyclic alcohol, hydride transfer to form a saturated aldehyde, or oxygen bridging to form a bicyclic ether. The same types of intermediates and reaction pathways may be described for the cyclization of *cis*-**7**.

It is noteworthy that these conformationally fixed cations dictate a specific stereochemistry for the products of monocyclization, **17**, **18**, and **22**, as well as for the tricyclic alcohol ring junctions. Uncomplexed, conformationally mobile cyclohexyl cations, on the other hand, would most likely produce stereochemically mixed products from both *cis*- and *trans*-**7**.

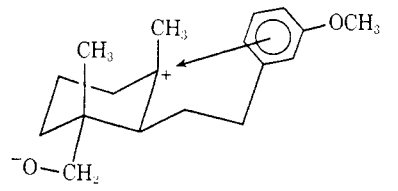
Experimentally we find that the stereochemistry of the products from both *cis*- and *trans*-**7** fits the picture of intermediate cations of fixed geometry. Thus *trans*-**7** yields an aldehyde, **17**, derived from iii, and *cis*-**7** yields an isomeric compound, **22**, which must arise from a cation, vi, that also has an axial C_4-oxymethylene group. It is also not surprising that partitioning of iii along the three reaction pathways described above is exclusively in the direction of **17** and **18**. The formation of these products relieves the "diaxial" interaction of the "angular" methyl group and the oxymethylene group present in iii and any tricyclic products derived from it.



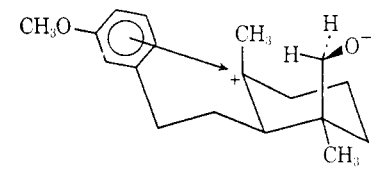
ii



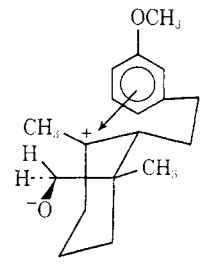
iii



iv



v



vi

Finally two other stereochemical results from the cyclization of *cis*-**7** are explicable in terms of these intermediate cations. *cis*-**7** produces no bridged ether. This is understandable on the basis of the conformational energy of the intermediate cation vi. Since free rotation of a C_4 β-hydroxymethyl substituent in an aromatic diterpenoid is known to be restricted, the additional conformational energy of a *cis* system over that of a *trans* one may completely preclude the rotation of the oxygenated group necessary for ether formation. Thus hydride transfer predominates in the further reactions of vi. In addition it is noteworthy that cyclization of *cis*-**7** produces no *ortho*-substituted tricyclic alcohol analogous to **16**. The transition state leading to such a product from *cis*-**7** has a strong nonbonded interaction between the angular methyl group and the "*ortho*" methoxyl substituent. The energy of this interaction is apparently great enough to preclude formation of the *ortho* product, and we have observed similar results with other epoxy olefin cyclizations.[21]

The tricyclic alcohols reported here are potentially useful in the synthesis of terpenoid systems with either *cis* or *trans* A/B ring junctions. At present, however,

(18) (a) G. Stork and A. W. Burgstahler, *J. Am. Chem. Soc.*, 77, 5068 (1955); (b) P. A. Stadler, A. Eschenmoser, H. Schinz, and G. Stork, *Helv. Chim. Acta*, 40, 2191 (1957).

(19) A. Eschenmoser, D. Felix, M. Gut, J. Meier, and P. A. Stadler in "Ciba Foundation Symposium on the Biosynthesis of Terpenes and Sterols," G. E. Wolstenholme and M. O'Conner, Ed., J. and A. Churchill, Ltd., London, 1959.

(20) W. S. Johnson, *Accounts Chem. Res.*, 1, 1 (1968).

(21) J. E. Evans, unpublished results.

the yields of these products are lower than desirable for protracted synthetic efforts. We are continuing to explore the pathways of these reactions in order to increase the efficiency of the cyclization process.

Experimental Section

Infrared spectra were recorded on Perkin-Elmer Models 137, 137G, and 257 spectrophotometers and run as neat liquids unless otherwise stated. Analyses by gas–liquid partition chromatography (glpc) were done with Hewlett-Packard 720 and 776 instruments with 0.25-in. diameter columns. Nuclear magnetic resonance spectra were recorded on Varian Models A60, A60-A, or T60 spectrometers in carbon tetrachloride unless otherwise stated. The coupling constants are accurate to 0.5 Hz. Mass spectra were recorded on a Varian M66 spectrometer at 70 eV. Refractive indices were measured on an Abbe-3L Bausch & Lomb instrument. All melting points were taken on a Thomas–Hoover melting point apparatus or a Fisher-Johns melting point apparatus and are uncorrected. Microanalyses were performed by either Midwest Microlab, Inc., or Spang Microanalytical Laboratory.

3-(*m*-Methoxyphenyl)propyl Bromide. 3-(*m*-Methoxyphenyl)-propanol, 20 g (Aldrich), was dissolved in 30 ml of benzene and the solution was cooled in an ice bath. A mixture of 13.7 g of phosphorus tribromide in 22 ml of benzene was added dropwise. The reaction mixture was warmed at 70° for 19 hr and then cooled in an ice bath. The solution was poured over cracked ice and the organic layer was decanted off. This layer was washed three times with sodium hydroxide (5% solution), hydrochloric acid (5% solution), then brine, and dried over sodium sulfate. Removal of the solvent at reduced pressure yielded 25.8 g of clear oil. Fractionation at 71° (0.2 mm) produced 22.5 g of bromide. Glpc (6-ft SE 30, 175°, Chromosorb 45–60 W) showed the product to be at least 96% homogeneous: n^{22}D 1.5494 (lit.[22] n^{18}D 1.5497); ir ($CHCl_3$) 970, 929, 828 cm^{-1}; nmr δ 2.14 (m, 2), 2.70 (t, 2), 3.30 (t, 2), 3.74 (s, 3).

3-(*m*-Methoxyphenyl)propyltriphenylphosphonium Bromide. The bromide, 22.5 g, and 21.7 g of triphenylphosphine in 120 ml of nitromethane (dried over Drierite) were refluxed 17 hr. The solvent was removed under reduced pressure leaving a viscous residue. Addition of benzene and nitromethane helped induce crystallization. The crystals were removed, washed with four 50-ml portions of benzene, and dried 12 hr in a vacuum desiccator over phosphorus pentoxide at 85°. The 39.6 g of product was used without further purification in the Wittig reaction: ir ($CHCl_3$) 1437, 1112 cm^{-1}.

***cis*- and *trans*-1-(*m*-Methoxyphenyl)-4-methyl-3-nonen-8-ol.** In a flask fitted with a stirrer and under nitrogen was suspended 106.9 g of the phosphonium salt in 850 ml of anhydrous ether. Butyllithium, 274 ml (Foote Mineral Co., 1.6 *N* in hexane), in 250 ml of ether was slowly added. This produced an intensely orange ylide. After 2 hr of stirring 22.6 g of heptan-6-ol-2-one[23] in 700 ml of ether was slowly added. A white precipitate immediately formed. After stirring the solution overnight under nitrogen, the ether was replaced, under nitrogen, with 1500 ml of dry tetrahydrofuran and the mixture was refluxed overnight. After removing roughly 80% of the tetrahydrofuran, 1000 ml of water was added and the organic phase was taken up in ether. The ether solution was washed three times with water and brine, and dried over sodium sulfate, yielding 105 g of residue after solvent removal. Because of the difficulty in removing triphenylphosphine oxide from the product, the crude reaction mixture was used to make ketone **8**.

An analytical sample was prepared by thick layer chromatography on silica gel G (Brinkmann) followed by preparative glpc (2-ft DC710, 170°, Chromosorb 45–60 W): ir ($CHCl_3$) 3550, 3400, 1590, 1480 cm^{-1}; nmr δ 1.07 (d, 3, J = 6 Hz), 1.49 and 1.60 (unresolved multiplets, total of three, vinyl methyl protons for *cis* and *trans*), 3.74 (s, 3), 5.10 (m, 1).

Anal. Calcd for $C_{17}H_{26}O_2$: C, 77.82; H, 9.99. Found: C, 77.7; H, 10.0.

***cis*- and *trans*-1-(*m*-Methoxyphenyl)-4-methyl-3-nonen-8-one (8).** A solution of the crude alcohol, 105 g, in 500 ml of acetone was oxidized with 25 ml of 8 *N* chromic acid solution.[24] The solution was stirred at room temperature 30 min and diluted with water. This mixture was partitioned between water and ether. The ether solution was washed with water and brine and dried over sodium sulfate. The ketone mixture, 81.9 g after solvent removal, was chromatographed on 1200 g of neutral alumina (Woelm, activity grade III). Elution with 5% ether in petroleum ether (bp 60–90°) yielded 24.9 g of pure ketone. An analytical sample was prepared by preparative glpc (2-ft DC710, 200°, Chromosorb 45–60 W).

Anal. Calcd for $C_{17}H_{24}O_2$: C, 78.41; H, 9.29. Found: C, 78.6; H, 9.2.

Ketones *cis*- and *trans*-**8** were separated by preparative glpc (0.75 × 80 in., 7% Versamid 900 on Chromosorb WAW-DMCS, 45–60 mesh, 214°). The *cis* ketone had the shorter retention time—21 min compared to that of the *trans*, 25 min. Aerosoling and poor separation resulted in only a 20% recovery of the separated ketones.

Analytical glpc (8-ft Apiezon L, 245°, 60–80 S) showed that the original ketone mixture was 3 parts *cis* to two parts *trans*. Under the same conditions *cis*-ketone **8** contained 8% *trans*-**8** and the *trans*-ketone contained 1% *cis*-**8**.

Spectral data of *cis*-**8** were as follows: ir 1715 cm^{-1}; nmr δ 1.64 (unresolved multiplet, 3), 1.94 (s, 3), 3.76 (s, 3), 5.25 (m, 1).

Spectral data of *trans*-**8** were as follows: ir 1715 cm^{-1}; nmr δ 1.53 (unresolved multiplet, 3), 2.00 (s, 3), 3.75 (s, 3), 5.14 (m, 1).

***trans*-2,6-Dimethyl-1,2-epoxy-9-(*m*-methoxyphenyl)-6-nonene (7).** Following Corey's method,[25] 1.67 g of a 52.6% dispersion of sodium hydride in mineral oil (Metal Hydrides, Inc.) was placed in a vessel under nitrogen. The mineral oil was removed by adding pentane, stirring, letting the sodium hydride settle, and subsequently withdrawing the solution through a gas dispersion tube. This process was repeated two additional times. Dimethyl sulfoxide, 25 ml (distilled from calcium hydride), and 8.5 g of trimethyloxosulfonium iodide[25] were added to the sodium hydride and the resulting mixture was stirred 1 hr to form the ylide. *trans*-Ketone **8** (9.11 g) in 10 ml of dimethyl sulfoxide was then added dropwise. The solution was stirred 15 min at room temperature and 1 hr at 50°. The mixture was cooled, water was added, and the organic part was partitioned into ether. The ether layers were washed with water and brine and dried over sodium sulfate yielding 7.00 g after solvent removal. The product was chromatographed on 70 g of Mallinckrodt silica gel (100–200 mesh) and eluted with 12% ether in hexane yielding 6.13 g of *trans*-epoxide **7**: ir 3100, 900 cm^{-1}; nmr δ 1.20 (s, 3), 1.52 (unresolved multiplet, 3), 2.36 (s, 2), 5.12 (m, 1). An analytical sample of a mixture of *cis*- and *trans*-**7** was collected on a 2-ft Apiezon L column at 210° (Chromosorb 60–80 W).

Anal. Calcd for $C_{18}H_{26}O_2$: C, 78.79; H, 9.55. Found: C, 78.5; H, 9.5.

***cis*-2,6-Dimethyl-1,2-epoxy-9-(*m*-methoxyphenyl)-6-nonene (*cis*-7).** *cis*-Epoxide **7** was made the same way as *trans*-**7**: ir 3150, 900 cm^{-1}; nmr δ 1.23 (s, 3), 1.64 (unresolved multiplet), 2.38 (s, 2), 5.12 (m, 1); mass spectrum *m/e* (relative intensitity) 121 (100), 122 (75), 134 (68), 202 (58), 274 (8).

3-(*m*-Methoxyphenyl)-1-methylcyclopropyl-2-propenone (9). A 32.5-g sample of 1-acetyl-1-methylcyclopropane,[8] 63.3 g of *m*-methoxybenzaldehyde, 154 ml of ethanol, 42 ml of water, and 32.5 ml of a 10% sodium hydroxide solution were placed on a shaker for 96 hr. The mixture was then diluted with an equal volume of water and extracted with ether. The ether solution was washed with water. The solution, diluted to 1.5 l. with ether, was shaken for 4 hr with 168 g of sodium bisulfite dissolved in 1710 ml of water and The ether layer was decanted and the aqueous layer was extracted with ether. The combined organic phase was washed with water and brine and dried over sodium sulfate yielding 50.7 g of aldol product. Glpc showed no starting materials present (6-ft SE 30, programmed at 10°/min, start 120°, Chromosorb 45–60 W): ir 3070, 2998, 1668, 1085, 1043, 1010 cm^{-1}; nmr δ 0 68 (m, 2), 1.27 (m, 2), 1.58 (s, 3), 3.80 (s, 3); uv max (methanol) 221 mμ (ϵ 11,100), 240 (9810), 290 (15,600). An analytical sample was prepared by preparative glpc.

Anal. Calcd for $C_{14}H_{16}O_2$: C, 77.74; H, 7.46. Found: C, 77.7; H, 7.4.

3-(*m*-Methoxyphenyl)-1-methylcyclopropylpropanol (10). To 19 g of lithium aluminum hydride in 460 ml of anhydrous ether was added 99.6 g of **9** dropwise over 5 hr. The mixture was refluxed 2 hr. Hydrochloric acid, 10%, was added to the cooled solution until a clear liquid resulted. The water layer was extracted with ether. The combined ether layers were washed with water and brine

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(23) R. G. Fargher and W. H. Perkin, *ibid.*, 1355 (1914).
(24) A. Bowers, T. G. Halsall, and E. R. H. Jones, *ibid.*, 2548 (1953).
(25) E. J. Corey and M. Chaykovsky, *J. Am. Chem. Soc.*, **87**, 1353 (1965).

and dried over sodium sulfate yielding 96.4 g of **10**. Glpc (6-ft SE 30, programmed at 10°/min, start 120°, Chromosorb 45–60 W) showed the product to be 84% homogeneous. The alcohol **10** was used without purification in the following reaction: ir 3420 cm^{-1}; nmr δ 0.27 (m, 4), 1.02 (s, 3), 1.83 (m, 2), 2.70 (m, 2), 3.74 (s, 3). An analytical sample was prepared by chromatography on silica gel (100–200 mesh, Mallinckrodt) and eluted with 20% ether in hexane.

Anal. Calcd for $C_{14}H_{20}O_2$: C, 76.31; H, 9.16. Found: C, 76.2; H, 9.2.

***trans*-1-Bromo-6-(*m*-methoxyphenyl)-3-methyl-3-hexene (11).** The following is a modification of a published procedure.[8] A mixture of 96.4 g of **10**, 60.6 ml of collidine, 129.2 g of anhydrous lithium bromide (weighed under dry conditions), and 660 ml of anhydrous ether was cooled to −40° and vigorously stirred. Phosphorus tribromide, 81.2 g (28.8 ml), was added dropwise. The solution was warmed to 0° and stirred 2 hr after which 113 ml of collidine and 111 ml of water were added to destroy the excess phosphorus tribromide. The solution was poured into water and extracted with pentane. The combined organic layers were washed with water, cold 10% hydrochloric acid, sodium bicarbonate solution and brine and dried over sodium sulfate. This residue, 81.0 g, in 70 ml of anhydrous ether was added dropwise to a rapidly stirred solution of anhydrous zinc bromide, 34.0 g, in 50 ml of ether (cooled to −40°). After stirring for 2.3 hr at 0°, pentane and brine were added and the mixture was stirred 15 min. The organic part was partitioned into pentane. The pentane solution was washed with brine and dried over sodium sulfate. The residue was chromatographed with pentane through 500 g of Merck acid-washed alumina yielding 75.8 g of bromide **11**: nmr δ 1.53 (unresolved multiplet, 3), 3.32 (t, 2), 3.72 (s, 3), 5.23 (m, 1). An analytical sample was prepared by chromatography on silica gel (100–200 mesh, Mallinckrodt) followed by short-path distillation at 0.001 mm.

Anal. Calcd for $C_{14}H_{19}OBr$: C, 59.56; H, 6.79; Br, 27.98. Found: C, 59.7; H, 6.8; Br, 27.9.

***trans*-Ethyl 2-Acetyl-8-(*m*-methoxyphenyl)-5-methyl-5-octenoate.** Sodium, 6.2 g, was added to 300 ml of ethanol (distilled from sodium under nitrogen directly into the reaction vessel). After the sodium had reacted, 43.5 g of ethyl acetoacetate (purified by extraction with sodium bicarbonate and distillation) was slowly added and the mixture was refluxed 10 min. After cooling the vessel to room temperature 75.8 g of bromide **11** was added dropwise over 1 hr. The mixture was refluxed 22 hr. After cooling the solution water was added and the solution was extracted with ether. The ether solution was washed with water and brine and dried over sodium sulfate yielding 75.7 g of crude alkylated product. Chromatography in three portions on 300 g of silica gel (100–200 mesh, Mallinckrodt) and elution with 32% ether in hexane yielded 51.2 g of keto ester: ir 1736, 1712 cm^{-1}; nmr δ 1.25 (t, 3), 1.55 (unresolved multiplet, 3), 1.77 (s, 3) 3.75 (s, 3), 4.15 (q, 2, J = 7 Hz), 5.15 (m, 1); precise M^+ measurement, 332.1919 (calcd 332.1885); mass spectrum 121 (66), 187 (72), 188 (50), 202 (100), 287 (19), 332 (10).

***trans*-Ketone 8 *via* Decarboethoxylation.** The keto ester was refluxed under nitrogen 19 hr with 80 ml of ethanol, 200 ml of water, and 64.3 g of barium hydroxide. After cooling the vessel, water was added and the barium hydroxide was dissolved with cold 10% hydrochloric acid. The organic material was extracted into ether. The ether solution was washed with water, sodium bicarbonate solution, and brine and dried over sodium sulfate yielding 8.6 g of *trans*-**8**. The product was identical in every respect with *trans*-ketone prepared *via* the Wittig reaction. Glpc analysis on an 8-ft Apiezon L column at 245° (60–80 S) showed the product to be greater than 98% *trans* isomer.

Cyclization of *trans*-2,6-Dimethyl-1,2-epoxy-9-(*m*-methoxyphenyl)-6-nonene (*trans*-7) with Boron Fluoride Etherate. *trans*-Epoxide, 0.80 g, and 20 ml of distilled methylene chloride were cooled to 0° under nitrogen. Distilled boron fluoride etherate (0.2 mole equiv, 0.074 ml) was added. The ice bath was removed and stirring was continued 15 min. Water was added and the mixture was extracted with ether. The ether solution was washed with water, sodium bicarbonate solution, and brine and dried over sodium sulfate yielding 0.81 g. The products were chromatographed on 95 g of silica gel (200–325 mesh, Mallinckrodt).

A. Nonpolar Fractions. Elution with 10% ether in hexane yielded 112 mg of a mixture of compounds as shown with 6-ft SE 30 column, 230°, 60–80 S: ir 1430–1630 cm^{-1}, several peaks.

B. 1-*trans*-3-Dimethyl-*cis*-2-(*m*-methoxyphenethyl)cyclohexanecarboxaldehyde (17). Further elution with the same solvent mixture gave 57 mg of **17**: ir 2717, 1712 cm^{-1}; nmr δ 1.01 (s, 3), 1.02 (d, 3), 3.74 (s, 3), 6.7 (center of aromatic protons, 4), 9.60 (s, 1); precise M^+ measurement, 274.1925 (calcd 274.1933); mass spectrum 121 (64), 122 (100), 134 (61), 135 (50), 246 (21), 274 (27), 290 (3).

C. *syn*-8-(*m*-Methoxyphenethyl)-1,5-dimethyl-6-oxabicyclo[3.2.1]octane (18). Elution with 25% ether in hexane yielded 123 mg of **18**. ir 1049, 1149 cm^{-1}; nmr δ 1.01 (s, 3), 1.21 (s, 3), 3.45 (AB quartet, 2, J = 7 Hz, $\Delta\nu$ = 7 Hz); mass spectrum 121 (52), 122 (32), 134 (46), 153 (100), 231 (91), 274 (65).

Anal. Calcd for $C_{18}H_{26}O_2$: C, 78.79; H, 9.55. Found: C, 78.7; H, 9.5.

D. 5,6,6aα,7a-Tetrahydro-8,11aβ-dimethyl-14-methoxycyclohepta[*a*]naphthalen-7-ol (19) from Cyclization of *trans*-7. Elution with 50% ether in hexane yielded 20 mg of a mixture of two or more tricyclic alcohols containing a seven-membered A ring: ir 3510, 1440, 1630 cm^{-1}; nmr δ 0.90 (d, 3), 1.18 and 1.21 (two singlets, 3), 3.70 (s, 3).

E. 1,2,3,4,4a,9,10,10aα-Octahydro-1α-hydroxymethyl-1,4aβ-dimethyl-5-methoxyphenanthrene (14). Further elution with 50% ether yielded 74 mg of **14**: ir 3340, 3290, 1594, 1571 cm^{-1}; nmr δ ($CDCl_3$) 0.85 (s, 3), 1.31 (s, 3), 3.75 (s, 3); aromatic proton peaks 6.61, 6.66, 6.75, 6.97, 7.06, 7.10, and 7.21; using a disubstituted anisole as a model, H-6 6.69, H-8 6.72, H-7 7.05, $J_{6,7}$ = 8.3, $J_{6,8}$ = 1.1, $J_{7,8}$ = 7.4 Hz; mass spectrum 147 (89), 161 (85), 173 (46), 241 (53), 259 (38), 274 (100). The product was recrystallized from carbon tetrachloride for analysis. The crystals melted at 154–156°.

Anal. Calcd for $C_{18}H_{26}O_2$: C, 78.79; H, 9.55. Found: C, 78.6; H, 9.3.

Oxidation of Alcohol 14 with Jones Reagent. Alcohol **14**, 160 mg, was oxidized in 7 ml of acetone with 0.22 ml of Jones reagent.[24] The reaction was initiated at 0° and stirred 20 min at ambient temperature. Water was added and the organic part was partitioned into ether. The ether solution was washed with water and brine and dried over sodium sulfate yielding 101 mg of an oil. This oil was chromatographed on 7 g of silica gel (100–200 mesh, Mallinckrodt) and the aldehyde **16**, 61 mg, was eluted with 5% ether in hexane as a crystalline compound: mp 107–108.5°; ir (KBr) 2820, 2762, 2680, 1720, 1652, 1630 cm^{-1}; nmr δ ($CDCl_3$) 1.18 (s, 3), 1.36 (s, 3), 3.79 (s, 3), 9.32 (s, 1).

Anal. Calcd for $C_{18}H_{24}O_2$: C, 79.36; H, 8.89. Found: C, 79.4; H, 8.9.

Additional chromatographic elution yielded a crystalline carboxylic acid: mp 200–214°; ir (KBr) 2400–3600, 1684, 1590, 1570 cm^{-1}.

F. 1,2,3,4,4a,9,10,10aα-Octahydro-1α-hydroxymethyl-1,4aβ-dimethyl-7-methoxyphenanthene (12) from Epoxide *trans*-7. Further elution with 50% ether in hexane yielded 194 mg of another tricyclic alcohol: ir (KBr) 3240, 1605, 1578, 1492, 1460, 1448, 1430 cm^{-1}; nmr δ ($CDCl_3$) 0.89 (s, 3), 1.20 (s, 3), 3.28 (AB quartet, 2, J = 11 Hz, $\Delta\nu$ = 16 Hz), 3.78 (s, 3), aromatic protons, H-8 6.61, H-6 6.70, H-5 7.19, $J_{5,6}$ = 9 Hz, $J_{5,8}$ = 1 Hz, $J_{6,8}$ = 3 Hz; mass spectrum 147 (26), 161 (24), 173 (18), 241 (84), 259 (88), 274 (100). The product was recrystallized from ether–hexane for an analysis, mp 190–111°.

Anal. Calcd for $C_{18}H_{26}O_2$: C, 78.79; H, 9.55. Found: C, 78.7; H, 9.5.

Cyclization of *cis*-2,6-Dimethyl-1,2-epoxy-9-(*m*-methoxyphenyl)-6-nonene (*cis*-7) with Boron Fluoride Etherate. *cis*-Epoxide **7**, 1.32 g, in 30 ml of methylene chloride was treated with 0.2 mole equiv (0.12 ml) of boron fluoride etherate in the same way as *trans*-**7** to yield 1.33 g of a mixture of products. They were separated in part on 95 g of silica gel (200–325 mesh, Mallinckrodt).

A. Nonpolar Fractions. Elution with 10% ether in hexane resulted in 473 mg of a mixture of compounds as shown by ir and a 6-ft SE 30 column, 230°, 60–80 S.

B. 1-*trans*-3-Dimethyl-*trans*-2-(*m*-methoxyphenethyl)cyclohexanecarboxaldehyde (22). Elution with the same solvent mixture resulted in 285 mg of aldehyde **22**: ir 2681, 1718 cm^{-1}; nmr δ 0.92 (d, 3, J = 6 Hz), 0.93 (s, 3), 3.74 (s, 3), 9.25 (s, 1; precise M^+ measurement, 274.1915 (calcd 275.1933); mass spectrum 121 (57), 122 (100), 134 (31), 135 (21), 274 (22).

***cis*-1-(*m*-Methoxyphenethyl)-2,2,6-trimethylcyclohexane (23).** Aldehyde **22** was reduced Cram's method.[26] The aldehyde, 830 mg, was dissolved in 40 ml of absolute ethanol. Hydrazine (97%, Fairmount, 0.55 ml) was added and the mixture was refluxed under nitrogen 24 hr. The solvent was then removed under reduced

(26) D. J. Cram, M. R. V. Sahyun, and G. R. Knox, *J. Am. Chem. Soc.*, **84**, 1734 (1962).

pressure. This hydrazine in 1 ml of dry dimethyl sulfoxide was added over a period of 4 hr to 1 g of freshly sublimed potassium *t*-butoxide in 2.5 ml of dimethyl sulfoxide. The orange mixture was stirred until nitrogen evolution ceased. The organic part was partitioned between methylene chloride and water. The methylene chloride layer was washed with water and brine and dried over sodium sulfate. After solvent removal there was 720 mg of an oily residue. Chromatography on 29 g of silica gel (200–325 mesh, Mallinckrodt) and elution with 10% ether in hexane yielded 541 mg of a mixture of hydrocarbons as shown by nmr and ir spectra. The mixture was rechromatographed on Woelm neutral alumina (activity grade I) and elution with 2% ether in hexane yielded 157 mg of **23**: ir 1381, 1363 cm^{-1}; nmr δ 0.83 (unresolved half of doublet, 1.5), 0.95 (*gem*-dimethyl and low-field half of doublet), 3.75 (s, 3); mass spectrum 121 (36), 122 (100), 134 (16), 135 (19), 146 (34), 160 (19), 161 (14), 260 (18). An analytical sample was purified by short-path distillation at 0.01 mm, 100°.

Anal. Calcd for $C_{18}H_{28}O$: C, 83.02; H, 10.84. Found: C, 82.9; H, 10.6.

Hydrogenation of Wolff–Kishner Product 23. A sample of **23** was hydrogenated with platinum oxide in acetic acid at 1 atm for 1 hr at 20°. The solution was filtered through Celite and the solvent was removed under reduced pressure. All aromaticity and part of the methoxyl group absorption was lost in the process as demonstrated by nmr examination. Glpc on an 8-ft Apiezon L column (270°, 60–80 S) showed a peak at 8 min, 70%, and a peak at 13 min, 30%; nmr δ 0.83 (d, 2, J = 8 Hz), 0.86 and 0.94 (*gem*-dimethyl group).

C. 5,6,6aβ,11a-Tetrahydro-8,11aβ-dimethyl-3-methoxycyclohepta[*a*]naphthalen-7β-ol. Elution with 70% ether in hexane yielded 25 mg of an oil: nmr δ 0.95 (d, 3, J = 6 Hz), 1.27 (s, 3), 3.72 (s, 3), aromatic protons, H-4 6.42, H-2 6.58, H-1 7.03, $J_{1,2}$ = 8.5 Hz, $J_{1,4}$ = 1 Hz, $J_{2,4}$ = 3 Hz; precise M^+ measurement, 274.1951 (calcd 274.1933); mass spectrum 203 (27), 241 (24), 259 (100), 274 (26).

D. 1,2,3,4,4a,9,10,10aβ-Octahydro-1β,4aβ-dimethyl-1-hydroxymethyl-7-methoxyphenanthrene (20). Further elution with 70% ether in hexane yielded 133 mg of noncrystalline **20**: ir 3425 cm^{-1}; nmr δ ($CDCl_3$) 1.02 (s, 3), 1.17 (s, 3), 2.98 (AB quartet, 2, J = 10.5 Hz, $\Delta\nu$ = 7 Hz), 3.76 (s, 3), aromatic protons, H-8 6.61, H-6 6.78, H-5 7.19, $J_{5,6}$ = 9 Hz, $J_{5,8}$ = 1 Hz, $J_{6,8}$ = 3 Hz; mass spectrum 147 (40), 161 (30), 173 (26), 241 (33), 259 (100), 274 (56). A sample for analysis was purified by short-path distillation at 0.01 mm, 130°.

Anal. Calcd for $C_{18}H_{26}O_2$: C, 78.79; H, 9.55. Found: C, 79.0; H, 9.6.

E. 1,2,3,4,4a,9,10,10aβ-Octahydro-1β,4aβ-dimethyl-1-hydroxymethyl-7-methoxyphenanthrene (21) and 12. Elution with pure ether yielded 20 mg of a mixture of **21** and **12** as demonstrated by nmr analysis. The nmr signals of **21** were extracted from the spectrum: δ 0.20 (s, 3), 1.13 (s, 3), 3.24 (AB quartet, 2, J = 11 Hz, $\Delta\nu$ = 18 Hz), 3.71 (s, 3); precise M^+ measurement on mixture, 274.1908 (calcd 274.1933).

1,2,3,4,4a,9,10,10aα-Octahydro-1β,4aβ-dimethyl-7-methoxyphenanthrene-1-carboxaldehyde. Alcohol **12**, 450 mg, was dissolved in 5 ml of acetone and cooled to 0°. The alcohol was oxidized with 0.42 ml of 8 *N* chromic acid solution.[24] The mixture was stirred 30 min at 0°, water was added, and the mixture was extracted with ether. The ether solution was washed with water and brine and dried over sodium sulfate. Solvent removal under reduced pressure yielded 444 mg of crystalline aldehyde. An analytical sample was recrystallized three times from hexane: mp 118–120°; ir 2682, 1725 cm^{-1}; nmr δ ($CHCl_3$) 1.15 (s, 3), 1.22 (s, 3), 3.77 (s, 3), 9.31 (s, 1).

Anal. Calcd for $C_{18}H_{24}O_2$: C, 79.36; H, 8.89. Found: C, 79.1; H, 8.9.

1,2,3,4,4a,9,10,10aα-Octahydro-1α-cyano-1,4aβ-dimethyl-7-methoxyphenanthrene. This is an adaptation of a procedure of Ireland.[10] The aldehyde, 382 mg, and 465 mg of hydroxylamine hydrochloride in 6.7 ml of pyridine and 11.2 ml of absolute ethanol were refluxed under nitrogen 2 hr. Most of the solvents were removed by warming the vessel under a stream of nitrogen. The residue was partitioned between water and ether. The combined ether layers were washed with water, cold 2% sulfuric acid, water, and brine and dried with sodium sulfate yielding after solvent removal 335 mg of oxime.

The oximes and 20 ml of acetic anhydride were heated at reflux under nitrogen 5 hr. The solvent was removed under reduced pressure. The residue was chromatographed on 20 g of Florisil (60–100 mesh, Fisher). The nitrile was eluted as an oil with 10% ether in hexane. The oil was crystallized and recrystallized from petroleum ether (bp 60–90°) yielding 231 mg of product: mp 97.5–98.5°; ir 2220 cm^{-1}; nmr δ 1.14 (s, 3), 1.34 (s, 3), 3.71 (s, 3).

Anal. Calcd for $C_{18}H_{23}NO$: C, 80.24; H, 8.61; N, 5.20. Found: C, 80.4; H, 8.9; N, 5.3.

1,2,3,4,4a,9,10,10aα-Octahydro-7-methoxy-1β,4aβ-dimethylphenanthrene-1-carboxylic Acid (13) and Dimethoxylated Carboxylic Acid. The nitrile, 160 mg, and 3 g of powdered potassium hydroxide in 20 ml of diethylene glycol was refluxed 24 hr under nitrogen. After cooling the mixture, water was added and the solution was acidified with cold dilute sulfuric acid. Ether extraction was followed by washing of the ether layers with water and brine and drying the solution over sodium sulfate. This yielded 156 mg of a yellow oil after solvent removal. Chromatography on 10 g of silica gel (100–200 mesh, Mallinckrodt) and elution with 10% ether in hexane yielded 101 mg of crystalline acid **13**. Recrystallization from acetone–hexane afforded 71 mg of carboxylic acid, identical in every respect with the same acid prepared by Pelletier:[11] mp 150–152.5° (lit.[11] mp 152–155°); ir (mull) 3115, 1706, 1653, 1605 cm^{-1}; nmr δ ($CDCl_3$) 1.19 (s, 3), 1.28 (s, 3), 3.75 (s, 3); mass spectrum 227 (28), 273 (100), 288 (40).

Anal. Calcd for $C_{18}H_{24}O_3$: C, 74.97; H, 8.39. Found: C, 74.9; H, 8.6.

Further elution with 20% ether in hexane yielded 40 mg of demethoxylated carboxylic acid. Recrystallization from acetone–hexane yielded 27 mg of product: ir (mull) 3220, 1720, 1660, 1620, 1580 cm^{-1}; nmr δ ($CDCl_3$) 1.18 (s, 3), 1.28 (s, 3); mass spectrum 213 (76), 259 (100), 274 (69); precise M^+ measurement, 274.1567 (calcd 274.1524).

***m*-Methoxyphenethyl Bromide.** Lithium aluminum hydride, 11.2 g, in 300 ml of anhydrous tetrahydrofuran was stirred under nitrogen as 459 g of *m*-methoxyphenyl acetate acid (Columbia) in 200 ml of tetrahydrofuran was added dropwise. Stirring was continued for 30 min after addition. A saturated solution of sodium potassium tartrate was added dropwise until the ether cleared. The ether solution was filtered. The ether was removed under reduced pressure yielding 39.7 g of clear oil. The alcohol was greater than 99% homogeneous by glpc analysis on a 2-ft Versamid 900 column (160° 45–60 W).

This crude alcohol was brominated using Bachmann's procedure for the same compound[27] giving 33.4 g of bromide. The bromide was 98% homogeneous by glpc (2-ft DC 710, 120°, Chromosorb 45–60 W; 2-ft Versamid 900, 140°, 45–60 W); nmr δ 3.0 (m, 2), 3.5 (m, 2), 3.67 (s, 3).

1-(*m*-Methoxyphenethyl)-2,2,6-trimethylcyclohexanol. The bromide, 8.17 g, was added dropwise to 0.87 g of magnesium turnings in 7 ml of tetrahydrofuran (dried over sodium wire) under nitrogen. The reaction was initiated by warming the vessel. After the Grignard reagent had formed, 2,2,6-trimethylcyclohexanone, 5 g, was added dropwise. The resulting mixture was refluxed 6 hr. Saturated ammonium chloride solution (6.25 ml) was added. This mixture was stirred 15 min. The precipitate was filtered from the ether solution and the solvent was removed under reduced pressure yielding 10.55 g of a clear oil. All volatile products and starting materials were removed by distillation at 0.1 mm, 117°. The residue, 1.63 g, was chromatographed on 40 g of silica gel (200–325 mesh, Mallinckrodt). Elution with 5% ether in hexane gave the tertiary alcohol, 1.02 g. A center fraction, shown to be homogeneous by glpc (2-ft DC 710, programmed at 10°/min, start 150°, Chromosorb 45–60 W), was submitted to analysis: ir 3580, 1600, 1594, 1586, 1578, 1379, 1369, 1360 cm^{-1}; nmr δ 0.96 (unresolved methyls, 9), 3.74 (s, 3).

Anal. Calcd for $C_{18}H_{27}O_2$: C, 78.21; H, 10.21. Found: C, 78.2; H, 10.3.

1-(*m*-Methoxyphenethyl)-2,2,6-trimethylcyclohexene (24). The cyclohexanol, 377 mg, and 30 ml of anhydrous ether were put in a flask fitted with a drying tube. Thionyl chloride (0.6 ml) was added dropwise followed by 1.2 ml of pyridine. A white precipitate formed. After the mixture was stirred for 12 hr the vessel was cooled in ice and water was added. The organic part was extracted into ether. The ether solution was washed with water and brine and dried over sodium sulfate. Removal of the ether under reduced pressure yielded 300 mg of product which was chromatographed on silica gel (100–200 mesh, Mallinckrodt). Elution with 4% ether in hexane yielded 274 mg of **24**, 96 % pure by glpc (2-ft DC 710, programmed at 10°/min, start 90°, Chromosorb 45–60 W): ir 1375, 1369, 1352 cm^{-1}; nmr δ 1.04 (s, 6), 1.67 (m, 3), 3.70 (s, 3).

(27) W. E. Bachmann and D. G. Thomas, *J. Am. Chem. Soc.*, **64**, 94 (1942).

An analytical sample was obtained by preparative glpc (2-ft SE 30, programmed at 10°/min, start 100°, Chromosorb 45–60 W).

Anal. Calcd for $C_{18}H_{26}O$: C, 83.67; H, 10.14. Found: C, 83.7; H, 10.1.

23 *via* Hydrogenation of 24. Olefin **24**, 166 mg, was hydrogenated in 4 ml of acetic acid with 30 ml of 5% palladium on charcoal at 2 atm, 20°, for 16 hr. Removal of the catalyst by filtration through Celite and evaporation of the solvent at reduced pressure yielded an oil which was chromatographed on 20 g of alumina (Woelm, activity grade I). Elution with 16% benzene in hexane yielded 156 mg of **23**. A mixture of this and the Wolff–Kishner product **23** from aldehyde **22** had identical retention times on two columns: 6-ft Carbowax 20M, 250°, 60–80 S and 8-ft Apiezon L, 270°, 60–80 S. The nmr spectrum had minor peaks presumably due to product from *trans* hydrogenation: ir 1380, 1360 cm^{-1}; nmr δ 0.82 (resolved half of doublet), 0.95 (*gem*-dimethyl group and low-field half of doublet), 3.74 (s, 3), 0.78, 0.87, 1.02 (extraneous peaks).

Anal. Calcd for $C_{18}H_{28}O$: C, 83.02; H, 10.84. Found: C, 82.9; H, 10.8.

Hydrogenation of 24 with Platinum Oxide. A sample of **24** was hydrogenated in the same manner as the Wolff–Kishner product. A similar ratio (3:2) of the methoxylated and demethoxylated compounds was observed. A mixture of the products obtained from the two different routes had the same glpc retention times as each injected separately (8-ft Apiezon L, 270°, 60–80 S).

Communications to the Editor

Arene–Metal Complexes. I. Thermodynamic Stabilities of Substituted Benzyl Cations Complexed with Tricarbonylchromium[1]

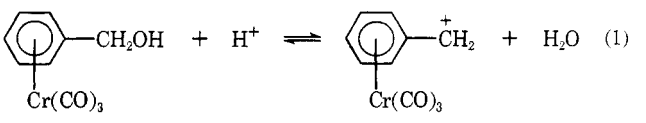
Sir:

The rapid rate of solvolysis of (benzyl chloride)tricarbonylchromium compared to the uncomplexed benzyl chloride has led Holmes, Jones, and Pettit to postulate that the complexed benzyl cation is extraordinarily stable.[2] It is reported, however, that the complexed cation cannot be isolated since rapid decomposition occurs when (benzyl alcohol)tricarbonylchromium is treated with strong acids.[2] We have found that the electronic spectrum of the complexed cation can be measured in sulfuric acid if two precautions are taken. First, the sulfuric acid must be thoroughly purged with nitrogen before use since the complexed cation is sensitive to oxygen. Second, only dilute solutions of the cation must be generated since the cation decomposes by a higher than first order process. In this communication we report the results of a study of the pK_{R^+} values of substituted benzyl cations complexed with tricarbonylchromium. These pK_{R^+} values were measured in aqueous sulfuric acid by Deno's method.[3]

Upon adding an ethanol or acetic acid solution of the substituted (benzyl alcohol)tricarbonylchromiums[4] to moderately (>80%) concentrated sulfuric acid solutions, new absorption bands appear in the ultraviolet–visible spectrum. For example, the spectrum of (benzyl alcohol)tricarbonylchromium in 95% ethanol is 217 (25,800),[7] 254 (6410), and 316 (9650). In 41.0% H_2SO_4, this spectrum is 216 (26,600), 253 (6020), and 313 (9800). In 85–87% H_2SO_4, however, the spectrum that complexed benzyl alcohol gives rise to is 201 (27,800), 278 (11,500), 348 (1500), and 514 (365).

Two experiments were performed which indicate that the formation of the species responsible for the spectrum in the concentrated sulfuric acid can be reversed. A solution of the complex in 82.6% sulfuric acid (violet) was poured onto ice to give a 52.5% sulfuric acid solution (yellow). The λ_{max} values and absorbances of the electronic spectrum of this yellow solution agreed within 2 mμ and about 10% in absorbance to the electronic spectrum of the (benzyl alcohol)tricarbonylchromium in 41.0% sulfuric acid. Another solution of the complex in 85% sulfuric acid was poured onto ice and an ether extraction and conventional work-up gave a 58% isolated recovery of the starting material (verified by nmr, ir, melting point, and mixture melting point). The 58% recovery is a high recovery since using the same procedure only 63% of (*p*-methylbenzyl alcohol)tricarbonylchromium was recovered from 51% sulfuric acid in which it is in the alcohol form.

Since the spectrum of (benzene)tricarbonylchromium is essentially the same in 95% ethanol and 41–97% sulfuric acid mixtures, the spectral changes for the complexed benzyl alcohols cannot be a result of protonation of the aromatic ring or the tricarbonylchromium moiety. Thus we believe that the spectrum of (benzyl alcohol)tricarbonylchromium in concentrated sulfuric acid is that of the benzyl cation complexed with tricarbonylchromium and that the equilibrium shown in eq 1 exists in aqueous sulfuric acid mixtures.



(1) (a) This work was partially supported by Public Health Service Grant GM 13799 from the National Institute of General Medical Sciences; (b) based on work by D. K. W. in partial fulfillment of the requirements for the Ph.D. degree at Iowa State University.

(2) J. D. Holmes, D. A. K. Jones, and R. Pettit, *J. Organometal. Chem.*, 4, 324 (1965).

(3) N. C. Deno, J. J. Jaruzelski, and A. Schriesheim, *J. Am. Chem. Soc.*, 77, 3044 (1955).

(4) The (benzyl alcohol)tricarbonylchromium complexes were prepared from (triacetonitrile)tricarbonylchromium and benzyl alcohol following the procedure of King.[5] The complexes were purified by chromatography on silica gel, sublimation, and/or recrystallization (melting points: parent, 92.5–94° (lit.[6] 95.5–96.5°); *p*-methoxy, 60–62°; *p*-methyl, 80–82°; *p*-chloro, 88–89°, 2,4,6-trimethyl, 101–103°). The nmr spectra of the complexes were consistent with their structures and all had signals at δ 5.3 which are characteristic of protons on benzene rings complexed with tricarbonylchromium. Acceptable elemental analyses were obtained for the new tricarbonylchromium complexes.

(5) R. B. King, *J. Organometal. Chem.*, 8, 139 (1967).

(6) B. Nicholls and M. C. Whiting, *J. Chem. Soc.*, 551 (1959).

(7) The wavelength is in mμ and the molar extinction coefficient is given in parentheses.