Cyclopropyl Participation in the Carane System

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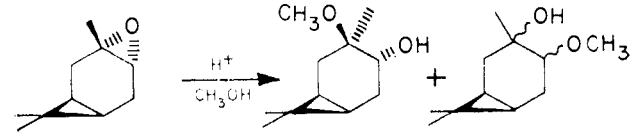
Abstract: The first examples of cyclopropyl participation in the carane series and of the rearrangement of a carane derivative to another bicyclic system are reported. From these and other data it is concluded that electrophilic attack on 3-carene (**1**) occurs stereoselectively *trans* to the three-membered ring, possibly because of transannular cyclopropyl participation. Dehydration of the *cis*-hydroxy acetate **3** with phosphorus oxychloride–pyridine proceeded selectively to give the exocyclic olefin **4.** The *trans*-hydroxy acetate **9** likewise gave the exocyclic olefin **4,** but accompanied by the novel rearranged product **11.** Similar dehydration of the epimeric 3-caranols **13** and **16** afforded principally (+)-3- (**1**) and (+)-2-carene (**14**), accompanied by only small amounts of the (+)-3(10) isomer **15** and no rearranged product. Treatment of "(+)-α-3,4-epoxycarane" (**7**) with boron trifluoride etherate provided a mixture of (−)-4-caranones (**25**) and the unexpected menthenone **26,** which was shown not to arise *via* a secondary rearrangement of **25**; the β-epoxide **17** gave principally the (−)-4-caranones (**25**), accompanied by only a trace amount of the menthenone **26.** Acid-catalyzed cleavage of the β-epoxide **17** in aqueous media afforded a mixture of the *trans* diol **19** and the *cis* diol **18,** whereas in methanolic solution the *trans*-methoxy alcohol **27** and the *cis*-methoxy alcohol **28** were obtained. Support of the *trans* assignment **7** for the (+)-α-epoxide is adduced from nmr data. The mechanistic and stereochemical implications of these results are discussed.

Despite its early isolation[1] and rather wide abundance as a constituent of terpentine,[2] the monoterpene hydrocarbon (+)-3-carene (**1**) and its derivatives have been the subject of surprisingly few chemical studies.[3] One important question which lay open at the inception of the present work was that of the stereochemistry of "(+)-α-3,4-epoxycarane" (**7**),[4] the product of direct, peracid epoxidation of (+)-3-carene (**1**), for which both the *trans* (**7**)[5] and *cis* (**17**)[6] structures have been proposed.[7] Since almost all known carane derivatives have been, or could be, related to this epoxide stereochemically, it holds a cardinal position in the carane system; hence, the stereochemical assignments of all but a few carane derivatives were in dispute.

One reason for the paucity of exacting stereochemical data in the carane system has been the general lack of any behavior, such as rearrangement to other bicyclic systems or transannular cyclopropyl participation,[8] which would have obvious stereoelectronic requirements. We wish now to report the first examples of such phenomena and to discuss their stereochemical implications.

Results

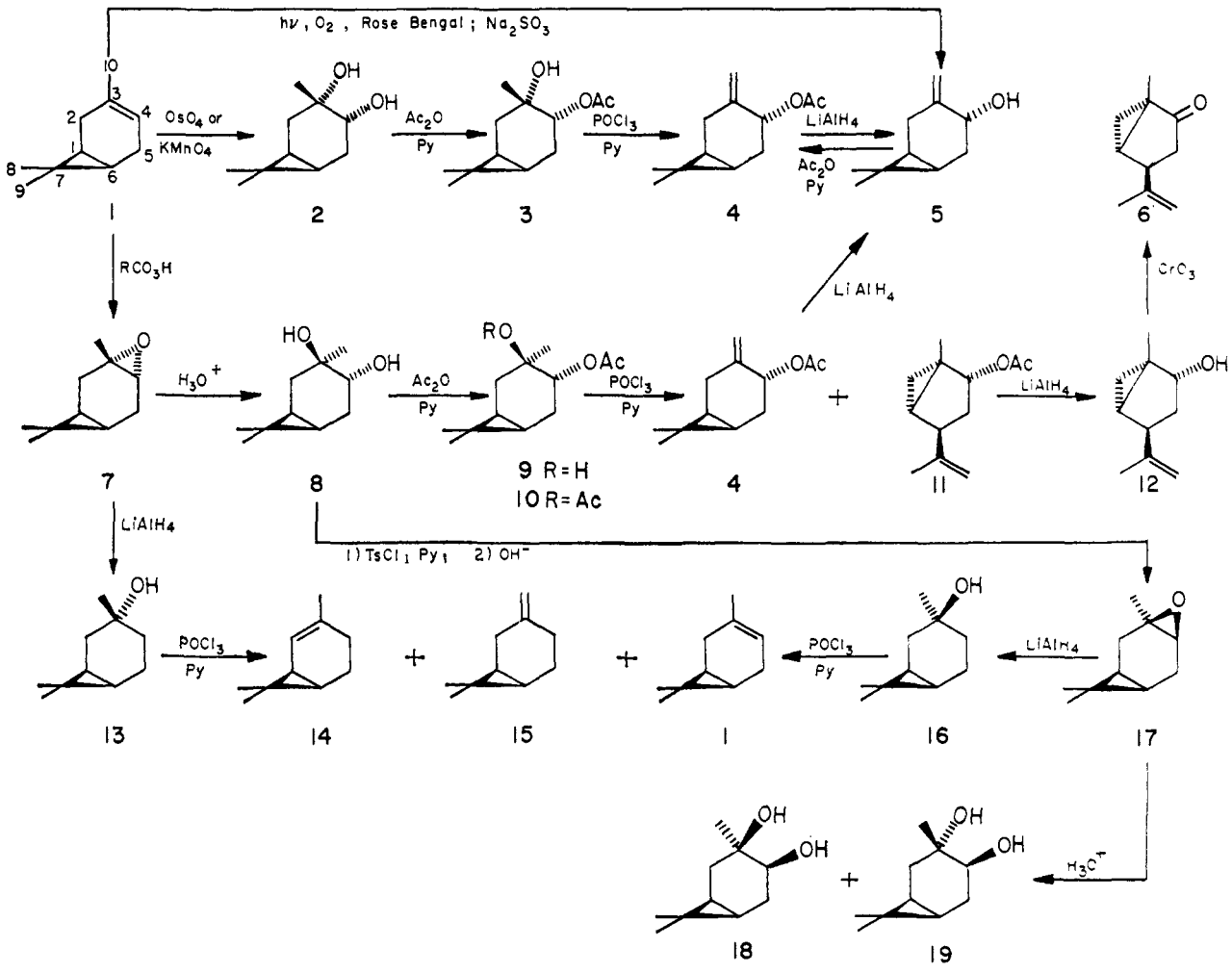
Dehydration Studies. Epoxidation of (+)-3-carene (**1**) with *m*-chloroperbenzoic acid followed by acidic hydrolysis of the resulting "(+)-α-epoxide" (**7**)[4] provided in good over-all yield a 3,4-diol, mp 88–89°.[9,10] Epoxides of cyclic olefins normally open with inversion of configuration to give *trans* diols,[11] and a *trans* assignment (**8**) for this diol is confirmed by a number of its properties[7,12–14]—including its resistance to cleavage by lead tetraacetate,[7b] its proclivity for forming a hydrate,[13] and its ready conversion to the epimeric β-epoxide **17**.[14] It is also known that acid-catalyzed opening of the α-epoxide (**7**) involves, as expected, cleavage of the more highly substituted C_3–O bond, since treatment of **7** in acidic methanol affords principally a 3-methoxy-4-caranol (I) accompanied by only trace amounts of the opposite 4-methoxy-3-caranol (II).[15] If the *trans* stereochemical assignment **7** is accepted for the α-epoxide, as will be discussed below, the stereochemical assignment **8** (and, by analogy, I) follows.



7 I 75 % II 6 %

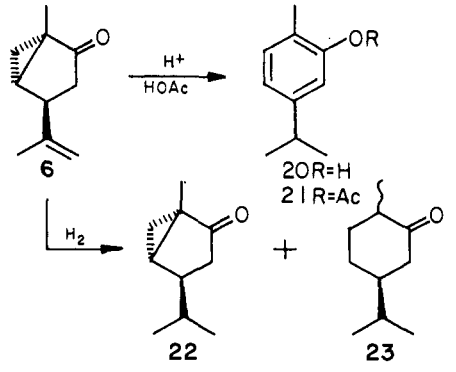
(1) J. L. Simonsen, *J. Chem. Soc.*, **117**, 570 (1920).
(2) See, for example, B. D. Sully, *Chem. Ind.* (London), 263 (1964).
(3) For a recent review of the chemistry of 3-carene see J. Verghese, *Perfumery Essent. Oil Record*, **56**, 438 (1965).
(4) B. A. Arbuzov and B. M. Mikhailov, *J. Prakt. Chem.*, **127**, 1 (1930); *Chem. Abstr.*, **24**, 4285 (1930).
(5) (a) G. O. Schenck, S. Schroeter, and G. Ohloff, *Chem. Ind.* (London), 459 (1962); (b) K. Gollnick, S. Schroeter, G. Ohloff, G. Schade, and G. O. Schenck, *Ann.*, **687**, 14 (1965).
(6) (a) B. A. Arbuzov, Y. Y. Samitov, and Z. G. Isaeva, *Dokl. Akad. Nauk SSSR*, **150**, 1036 (1963); (b) B. A. Arbuzov, V. A. Naumov, and L. F. Shatrukov, *ibid.*, **163**, 355 (1965).
(7) In addition, assignments of *conformational* preferences for substituents at C-3 and C-4 have been suggested for a number of carane derivatives related to the (+)-α-epoxide, but *without the establishment of configurational assignments at these positions:* (a) Z. Chabudziński and H. Kuczyński, *Roczniki Chem.*, **36**, 1173 (1962); (b) H. Schmidt, P. Richter, and M. Mühlstädt, *Chem. Ber.*, **96**, 2636 (1963).
(8) For examples of transannular cyclopropyl participation in other ring systems see, among others, (a) S. Winstein and J. Sonnenberg, *J. Am. Chem. Soc.*, **83**, 3235, 3244 (1961); (b) T. Norin, *Tetrahedron Letters*, 37 (1964); (c) S. Winstein, P. Bruck, P. Radlick, and R. Baker, *J. Am. Chem. Soc.*, **86**, 1867 (1964); (d) A. C. Cope, S. Moon, and C. H. Park, *ibid.*, **84**, 4850 (1962); (e) D. H. R. Barton, R. Bernasconi, and J. Klein, *J. Chem. Soc.*, 511 (1960). However, note also E. J. Corey and R. L. Dawson, *J. Am. Chem. Soc.*, **85**, 1782 (1963), and E. J. Corey and H. Uda, *ibid.*, **85**, 1788 (1963).
(9) P. P. Pillay and J. L. Simonsen, *J. Chem. Soc.*, 359 (1928).
(10) For the numbering system and stereochemical designations employed, see "Nomenclature for Terpene Hydrocarbons," Advances in Chemistry Series, No. 14, American Chemica Society, Washington, D. C., 1955.
(11) R. E. Parker and N. S. Isaacs, *Chem. Rev.*, **59**, 737 (1959).
(12) B. A. Arbuzov and B. M. Mikhailov, *J. Russ. Phys. Chem. Soc.*, **62**, 607 (1930); *Chem. Abstr.*, **24**, 4775 (1930).
(13) H. H. Hatt, *Rev. Pure Appl. Chem.*, **6**, 153 (1956); *Chem. Ind.* (London), 48 (1957).
(14) H. Kuczyński and Z. Chabudziński, *Roczniki Chem.*, **34**, 177 (1960).
(15) (a) Z. G. Isaeva and B. A. Arbuzov, *Zh. Obshch. Khim.*, **19**, 893 (1949); *Chem. Abstr.*, **44**, 3467 (1950); (b) Z. G. Isaeva and I. S. Andreeva, *Dokl. Akad. Nauk SSSR*, **152**, 106 (1963); *Chem. Abstr.*, **59**, 15314 (1963).

Chart I



Treatment of diol **8** with acetic anhydride–pyridine provided the hydroxy acetate **9**, which was resistant to dehydration in refluxing acetic anhydride—giving only the diacetate **10**.[16] However, dehydration of **9** with phosphorus oxychloride–pyridine proceeded smoothly, affording the two olefinic acetates **4**[17] (34–42%) and **11** (31–35%) as the only major products.[18] A control run revealed that **11** does not arise *via* secondary rearrangement of **4** under the reaction conditions and is most likely a primary product. (See Chart I.)

Both **4** and **11** exhibit absorption in the regions 11.1–11.2 μ and τ 5.1–5.3, typical of exocyclic olefins. Lithium aluminum hydride cleavage of **4** provided the alcohol **5**,[5,17,19] which was identical with a specimen prepared by photosensitized oxidation of (+)-3-carene (**1**).[5] Similar reduction of acetate **11** followed by chromic acid oxidation of the resulting alcohol **12** according to the Jones procedure[20] gave the cyclopropyl ketone **6**, which has the appropriate infrared absorption at 5.79 μ. The secondary cyclopropyl protons of **11** and **12**, which appear at τ 9.58, are shifted downfield to τ 8.95 in **6**, demonstrating conjugation (and hence juxtaposition) of the cyclopropane ring and carbonyl group. On treatment with acetic–sulfuric acid, **6** underwent exclusive rearrangement to a mixture of carvacrol (**20**) and carvacrol acetate (**21**). Hydrogenation of **6** over palladium-on-charcoal invariably resulted in the absorption of more than 1 molar equiv of hydrogen to provide a mixture of ketone **22**, λ_{max} 5.78 μ, and (+)-*p*-menthan-2-one (**23**).



(16) (a) B. A. Arbuzov and Z. G. Isaeva, *Zh. Obshch. Khim.*, 24, 1250 (1954); *Chem. Abstr.*, **49**, 12378 (1955); (b) *Dokl. Akad. Nauk SSSR*, **122**, 73 (1958); *Chem. Abstr.*, **53**, 1397 (1959).

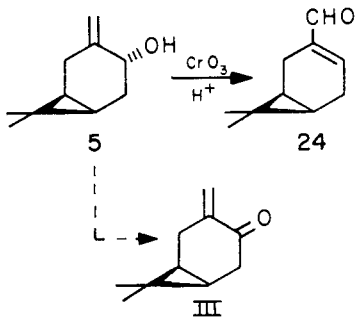
(17) Apparently obtained previously in an impure form by the reaction of epoxide **7** with acetic anhydride; see ref 16 and B. A. Arbuzov, Z. G. Isaeva, and I. P. Povodyreva, *Dokl. Akad. Nauk SSSR*, **159**, 827 (1964).

(18) Also observed were gas chromatographic peaks corresponding to lower molecular weight material (13–17%) and additional unidentified olefinic acetates (6–7%). From among the former were isolated fractions having retention times and infrared and nmr spectra identical with *p*-cymene, α,*p*-dimethylstyrene, and 1,1,4-trimethylcycloheptatriene.

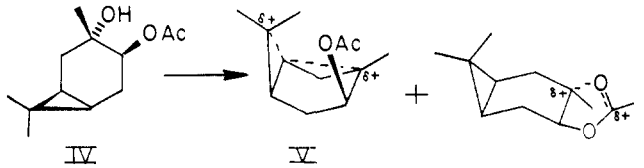
(19) B. A. Arbuzov, Z. G. Isaeva, and V. V. Ratner, *Dokl. Akad. Nauk SSSR*, **134**, 583 (1960); *Chem. Abstr.*, **55**, 6516 (1961).

(20) K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon, *J. Chem. Soc.*, 39 (1946).

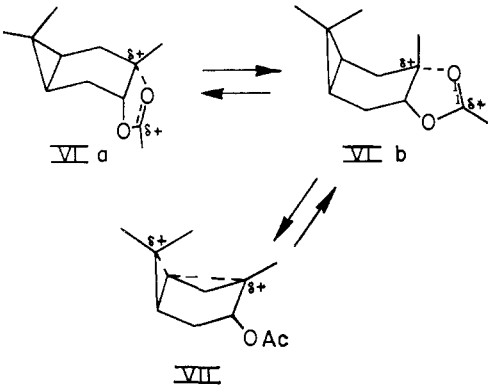
In practice it was more convenient to conduct the Jones oxidation on a mixture of alcohols **5** and **12**, afforded by dehydration of the *trans*-hydroxy acetate **9** followed by hydride reduction. In addition to the ketone **6** a second major oxidation product was isolated which clearly does not possess the structure III, as recently proposed[17] for a product obtained by oxidation of **5** by the Brown procedure,[21] since it exhibits typical aldehydic absorptions at 3.66 μ and τ 0.82 and only a single, endocyclic vinylic proton resonance at τ 3.52. However, the presence of two cyclopropyl protons (multiplet centered at τ 9.18) implies that the carane skeleton is still intact, and the structure **24** is proposed, even though the physical properties do not correlate well with those reported for a product obtained by a chromium trioxide catalyzed photooxidation of (+)-3-carene and also assigned the structure **24**.[22,23]



The formation of the rearranged bicyclo[3.1.0]hexene derivative **11** from **9** represents, to the best of our knowledge, the first example of a transformation of the carane skeleton into that of another bicyclic system. Likewise, it is the first documented example of transannular participation by the cyclopropane ring in carane chemistry. At first thought it is tempting to assume that participation by the cyclopropane ring accompanies cleavage of the C_3–O bond and is a direct consequence of the C_3-hydroxyl group being situated *trans* to the cyclopropane ring in the starting hydroxy acetate (*cf.* IV). Proton loss from the resulting homocyclopropylcarbinyl intermediate V[24] at either C_8 or C_{10} would then provide the two olefinic products **4** and **11**. It would thereby be inferred that the C_4–acetoxyl group is *cis* to the cyclopropane ring and, hence, that the α-epoxide has the *cis* stereochemistry **17**.



However, generation of the intermediate V would require a severe interaction of the C_4–acetoxyl substituent with the 8-CH_3 group. Moreover, the situation is complicated by the fact that the neighboring acetoxyl group is known to be positioned *trans* to the C_3-hydroxyl substituent and would surely itself participate in bond cleavage at C_3 and compete with cyclopropyl participation. Indeed, the stereochemical assignment IV is neither satisfying nor compelling. In the case of the stereoisomer **9**, on the other hand, acetoxyl participation would afford the acetoxonium ion VI. This intermediate would be constrained to exist in either of the two boat conformations VIa and VIb, the latter of which is particularly well disposed for subsequent participation by the cyclopropane ring in the form of the homocyclopropylcarbinyl intermediate VII.



To gain further insight into the influence of stereochemical features on the course of dehydration in this system and the involvement, or lack of involvement, of the cyclopropyl and acetoxyl groups, the *cis*-hydroxy acetate **3** was prepared by osmium tetroxide hydroxylation of (+)-3-carene (**1**), followed by acetylation of the resulting *cis* diol **2**.[25] Dehydration of **3** under conditions identical with those employed with the *trans*-hydroxy acetate **9** afforded the allylic acetate **4** as the only major product (42–49%).[26] The rearranged olefin **11**, if formed, was present in less than 2% yield, and no evidence for cyclopropyl participation could be detected.

For comparison of their behavior, the epimeric 3-caranols **13**[27] and **16**,[14] prepared by lithium aluminum hydride cleavage of the corresponding α- and β-epoxides, were subjected to the same dehydration conditions as **3** and **9**. Although slightly different product distributions were obtained from the two alcohols, in each case (+)-2- (**14**, 31–44%) and (+)-3-carene (**1**, 50–57%) were obtained as the major products, accompanied by only trace amounts of the exocyclic (+)-3(10) isomer **15** (6–12%).[28] Again, no evidence for any rearranged products analogous to **11** could be detected.

(21) H. C. Brown and C. P. Garg, *J. Am. Chem. Soc.*, **83**, 2952 (1961).

(22) W. Zacharewicz, J. Krupowicz, and L. Borowiecki, *Roczniki Chem.*, **33**, 87 (1959); *Chem. Abstr.*, **53**, 16194 (1959); W. Zacharewicz, L. Borowiecki, and B. Januszewska, *Roczniki Chem.*, **36**, 173 (1962); L. Borowiecki and W. Zacharewicz, *ibid.*, **37**, 1143 (1963). Repetition of this oxidation in our hands has afforded none of the aldehyde **24**.

(23) Recently K. Gollnick and G. Schade, *Tetrahedron*, **22**, 133 (1966), have likewise assigned the structure **24** to a product obtained by oxidation of alcohol **5** with chromic acid in benzene and having properties identical with those observed in the present work and have rejected the previous assignment of ref 22.

(24) The representation of ions in nonclassical form is for simplicity in presentation and does not necessarily have mechanistic significance.

(25) Obtained previously by potassium permanganate oxidation of (+)-3-carene; see ref 1.

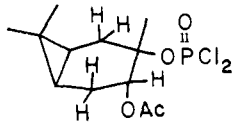
(26) Also obtained were *p*-cymene (4–7%), 1,1,4-trimethylcycloheptatriene (7–11%), α,*p*-dimethylstyrene (7%), additional unidentified low molecular weight products (18–27%), and additional unidentified olefinic acetates (17–19%).

(27) H. Kuczyński and K. Piatkowski, *Roczniki Chem.*, **31**, 59 (1957).

(28) It was previously reported that dehydration of **13** with *p*-toluenesulfonyl chloride–pyridine gave 3-carene (**1**) contaminated with 2-carene (**14**) (ref 27) and that dehydration of **16** gave 3-carene (**1**) (ref 14).

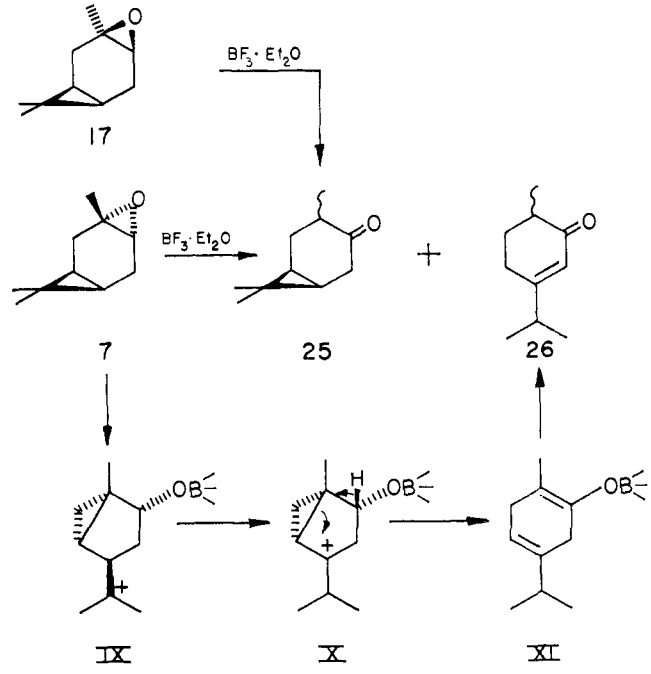
Since in one member of the epimeric pair **13** and **16** the hydroxyl group and cyclopropane ring must be *trans* oriented, regardless of whether the stereochemistry is identical with, or opposite to, that depicted in Chart I, it is apparent that the mere presence of a *trans*-hydroxyl group at C_3 is, in itself, not sufficient to ensure cyclopropyl participation. This confirms the suggestion that in the case of **9** participation is facilitated by the occurrence of a preliminary acetoxyl participation which preserves asymmetry at C_3 and conformationally freezes the six-membered ring of VI in a boat form. This is further seen in the *cis*-hydroxy acetate **3**, in which the *cis* orientation of the C_3 and C_4 substituents precludes acetoxyl participation and no rearranged olefin **11** is formed, even though the hydroxyl group is *trans* to the cyclopropane ring.

The selective formation of the exocyclic isomer **4** from the hydroxy acetate **9**, in preference to the possible endocyclic products, is most likely a consequence of the involvement of intermediate VII, in which only the hydrogen atoms of the freely rotating 10-CH_3 group are capable of achieving the preferred *trans*-antiparallel relationship to the C_3–O bond. In the case of the *cis*-hydroxy acetate **3**, in which such participation is structurally inhibited, selective formation of the exocyclic isomer **4** is also observed. In this case the selectivity is probably attributable to the preferred conformation VIII for the phosphorodichloridate intermediate, in which, again, only the C_{10}-hydrogen atoms are capable of assuming a *trans* orientation. The unsubstituted 3-caranols **13** and **16** are more flexible conformationally and can undergo the generally more favored endocyclic elimination.



VIII

Epoxide Cleavages. Since the two 3,4-epoxides are rather rigidly held in the boat conformations **7a**, **7b**, **17a**, and **17b**, it seemed likely that a study of C_3–O cleavage, particularly in the *trans* isomer **7**, would reveal a further example of cyclopropyl participation. That this is indeed the case was evident when it was found that treatment of the α-epoxide **7** with boron trifluoride etherate in ether solution provided a mixture of (−)-4-caranone (**25**, 43%) and (−)-*p*-menth-3-en-2-one (**26**, 28%). The rearrangement of **7** to **25**, which has also been effected using mineral acids,[26] has extensive analogy, but the formation of **26** is without apparent precedent. Since the necessary control experiments revealed that **26** does not arise from (−)-4-caranone (**25**) under the reaction conditions, it can be assumed that **26** is a primary product coming[29,32] directly from



IX X XI

cleavage of **7**. The formation of **26**, which can be depicted as IX → XI, undoubtedly involves cyclopropyl participation analogous to that encountered in the dehydration of **9**. However, in the absence of a strongly basic solvent, the initially formed homocyclopropylcarbinyl intermediate IX can undergo rearrangement to the cyclopropylcarbinyl cation X, which then suffers proton loss to give XI. Hydrolysis and migration of the double bond into conjugation then provides the menthenone **26**.[33] As expected from this interpretation, treatment of the isomeric epoxide **17**, in which the two three-membered rings are now assumed to be *cis* oriented, under identical conditions provided principally the (−)-4-caranone product **25** (66%) accompanied by only a trace amount of the menthenone **26** (2%).[34] These results represent strong support for the stereochemical assignments **7** and **17**.

Finally, there is one report in the literature regarding the β-epoxide **17** which has stereochemical implications and requires further comment. In contrast with the α-epoxide (**7**)—which gives only one major product (**8**) on acid-catalyzed hydrolysis—the β-epoxide (**17**) was noted to give both the expected *trans* diol **19** and a second diol, in unstated yields.[7a] Since this latter diol is not identical with either the *cis* diol **2** or the *trans* diol **8**, it must have the *cis* stereochemistry **18**.[35] In our hands this hydrolysis provided the *cis* diol **18** in 26% and the *trans* diol **19** in 53% yield. Repetition of the

(29) Isomerization of the α- (**7**) and β-epoxides (**17**) to a (−)-4-caranone (**25**) has previously been effected in the presence of sodium (ref 14 and 30) and of the α-epoxide (**7**) with both mineral acids and acetic acid (ref 15b and 31). In the latter case, the formation of an unidentified monocyclic ketone was also noted; this material was quite possibly the menthenone **26**.

(30) H. Kuczyński and Z. Chabudziński, *Roczniki Chem.*, **29**, 437 (1955).

(31) (a) H. Kuczyński and A. Hendrich, *ibid.*, **33**, 293 (1959); *Chem. Abstr.*, **53**, 22059 (1959); (b) Z. Chabudziński and H. Kuczyński, *Roczniki Chem.*, **33**, 871 (1959); *Chem. Abstr.*, **54**, 3486 (1960).

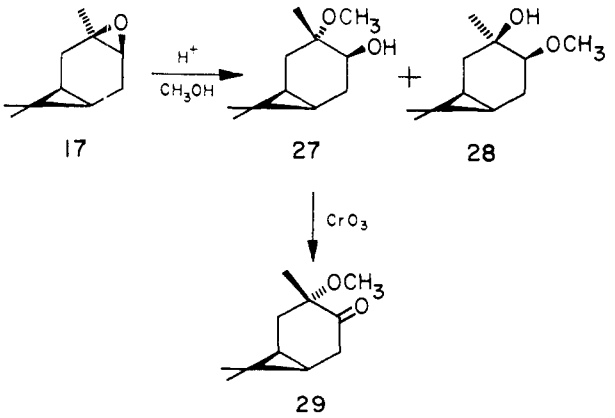
(32) However, rearrangement of **25** to **26** is reported to occur in the presence of dilute sulfuric acid (ref 30).

(33) If a mechanism involving the intermediate VI does indeed obtain, the resulting menthenone **26** should consist of an equilibrium mixture of C_1 epimers. This is consistent with the low optical activity (−6°) observed for the rearrangement product.

(34) Since the Lewis acid catalyzed rearrangement of epoxides to ketones is known, at least in some cases, to proceed stereospecifically with *cis*-hydrogen shifts [see, for example, H. B. Henbest and T. I. Wrigley, *J. Chem. Soc.*, 4596 (1957)], the α-epoxide **7** would be expected to provide the 4-caranone **25** having an α-oriented C_3-methyl substituent, and the β-epoxide **17** the 3-β isomer. Although the optical rotations of the (−)-4-caranones obtained from **7** and **17** were somewhat different (−120 and −82°), it is apparent that neither product was stereochemically homogeneous (see Experimental Section).

(35) The *cis* diol **18** has been further characterized through conversion to the *trans* diol **8** by tosylate displacement at C_4 (see ref 7a).

experiment in acidic methanol gave two hydroxy ethers in yields of 10 and 70%. Since these two products have the same order of elution from silica gel and exhibit nmr spectra virtually superimposable in the appropriate regions with those for the diols **18** and **19**, they are assigned the *cis* and *trans* structures **28** and **27**, respectively. The presence of a secondary alcohol function in **27** was demonstrated by the appearance of the hydroxyl proton in dimethyl sulfoxide as a doublet at τ 5.12 (J = 4.4 cps) which collapsed to a singlet on irradiation of the band at τ 6.39 due to the C_4 proton.[36] This was confirmed by oxidation to the methoxy ketone **29**, which has spectral properties quite different from those observed for the oxidation product from the methoxy alcohol I.[15b] By contrast, no coupling could be observed for the hydroxyl proton of the *cis* product, and the structure **28** is tentatively assigned.

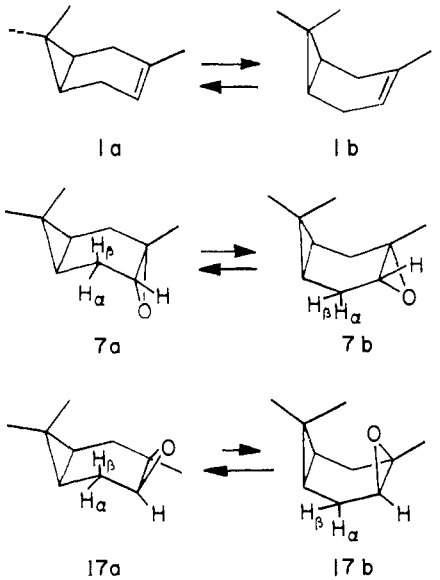


17 27 28

29

The occurrence of *cis* cleavage in the case of the β-epoxide **17** is another manifestation of the *cis* relationship between the two three-membered rings. Of the two conformations available to the epoxide (see Chart II), **17b** can be dismissed as a significant form because of a severe interaction of the oxygen atom with the 8-CH_3 group. In the case of **17a**, the rear side of C_3 is shielded by a large portion of the molecule, and nucleophilic attack is retarded. Thus the normally less favorable *cis* cleavage can effectively compete.

Chart II



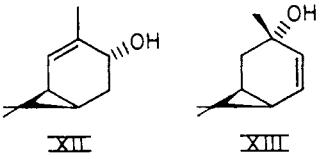
1a 1b 7a 7b 17a 17b

(36) See O. L. Chapman and R. W. King, *J. Am. Chem. Soc.*, **86**, 1256 (1964).

Discussion

Through the common intermediacy of the alcohol **5**, as outlined in Chart I, it is clear that peracid epoxidation, osmium tetroxide hydroxylation, and photosensitized oxidation of 3-carene all involve initial attack by an electrophile from the same side of the molecule. Moreover, the high yields of these reactions indicate that the attack is highly stereoselective in each case. However, it is not evident *a priori* which direction of attack should be so highly favored. 3-Carene, like the epoxides **7** and **17**, is conformationally restricted to two boat forms, **1a** and **1b**; the former appears to be readily susceptible to electrophilic attack *cis* to the cyclopropane ring and the latter to *trans* attack. As discussed above, the present results, particularly those relating to the behavior of the epoxides **7** and **17**, point to a preferred *trans* attack.[37]

Quite recently the *trans* assignments XII and XIII for the two products which are obtained along with **5** from the photosensitized oxidation of (+)-3-carene[5] have been apparently well established by degradation to compounds having previously assigned configurations, thereby indirectly confirming the stereochemical assignment **7** for the α-epoxide.[39,40]



XII XIII

However, there has not been unanimous agreement on stereochemical assignments in this area, as the opposite conclusion has been reached on the basis of the nmr spectra of epoxides **7** and **17**.[6a] In this regard it is helpful to note first that in the spectra of 2- (**14**) or 3-carene (**1**) and most of their derivatives one of the cyclopropyl methyl groups appears at a fairly constant position, close to τ 9.0, whereas the second cyclopropyl methyl group appears at a higher frequency (see Table I). It is likely that the shielded protons are those of

Table I. Chemical Shifts of 8- and 9-Methyl Groups of Some Representative Carane Derivatives

Compound	Chemical shift, τ 9-CH_3	Chemical shift, τ 8-CH_3	Δ ppm
2-Carene (**14**)	8.90	9.10	0.20
3-Carene (**1**)	8.97	9.23	0.26
3-Caren-10-al (**24**)	8.94	9.30	0.36
3(10)-Carene (**15**)	9.05	9.11	0.06
cis-Carane[a]	9.02	9.07	0.05
α-Epoxide (**7**)	9.02	9.29	0.27
β-Epoxide (**17**)	9.06	9.10	0.04

[a] Reference 41.

the 8-CH_3 group, which is oriented *syn* to the six-membered ring and lies in close proximity to the double

(37) Evidence has recently been adduced that hydroboration of 3-carene involves *cis* addition to the α side (ref 38). However, in view of the possibility of reaction *via* the open-boat form **1a**, we do not *a priori* consider attack on the β face as being "unlikely" because it is "sterically hindered."

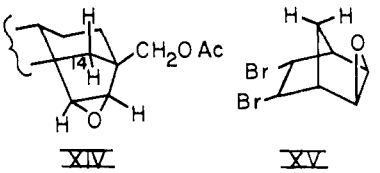
(38) W. Cocker, P. V. R. Shannon, and P. A. Staniland, *Tetrahedron Letters*, 1409 (1966).

(39) G. Ohloff, *ibid.*, 3795 (1965).

(40) K. Gollnick, *ibid.*, 327 (1966).

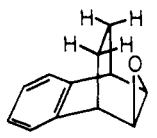
bond. By contrast, the two cyclopropyl methyl groups of (−)-*cis*-carane, obtained by hydrogenation of (+)-3-carene, display no significant shielding.[41] The large magnitude of the shielding in the case of 3-carene suggests that the folded form **1b** makes a substantial contribution to the equilibrium mixture, despite the obviously serious interaction of the 8-CH_3 group with the π orbitals of the double bond. A similar strong shielding of one of the methyl groups is also seen in the spectrum of the α-epoxide but not in that of the β-epoxide (Table I). Assuming that the shift in this case is attributable to an anisotropic ring-current shielding of the 8-CH_3 protons by the three-membered ring, Arbuzov and co-workers assigned the *cis* stereochemistry **17** to the α-epoxide.[6a,42]

However, there are few clear-cut precedents on which to base a stereochemical conclusion from such chemical shift data. The several documented examples of long-range shielding by an epoxide ring suggest that extreme caution must be exercised in extrapolating to other systems. For example, *one* of the C_{14} protons in ring C of the diterpene byerol (partial structure XIV) is found at high field,[43] whereas *both* the 7-*syn* and -*anti* protons of XV are considerably shielded relative to those of the corresponding dibromobicyclo[2.2.1]-hexene.[44] On the other hand, the *exo* epoxides XVI, XVII, and XVIII display a *shielding* of the C_7 or C_7 and C_8-*anti* protons and a *deshielding* of the *syn* protons relative to those in benzobicyclo[2.2.2]octene, benzonorbornene, or bornane, respectively.[45] Thus it is obvious that subtle stereochemical factors, not yet fully delineated, can influence the long-range anisotropic effects of the epoxide group.

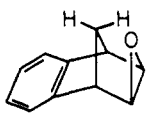


XIV

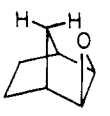
XV



XVI



XVII



XVIII

Although the chemical shift data fail to provide a reliable basis for assigning stereochemistry to the carane epoxides, the nmr spectra are nevertheless revealing in that the C_4-epoxy protons are clearly distinguishable. In the α-epoxide this proton appears as an unresolved triplet at τ 7.22 (width at half-height, 5 cps *vs.* 1 cps for TMS) and in the β isomer as a sharp doublet at τ 7.18 (J = 5 cps). This latter pattern is consistent with the *cis* structure **17**, since that compound is compelled to exist principally in the conformation **17a** because of the severe C_8–O interaction in **17b**. In **17a** the dihedral angle between H_4 and $H_{5\alpha}$ ($\theta_{4,5\alpha}$) $\approx$ 3°, whereas $\theta_{4,5\beta} \approx 107°$; hence $J_{4,5\alpha} \approx 5$ and $J_{4,5\beta} \approx 0$ cps, and a sharp doublet should result.[46] By contrast, the *trans* isomer **7** can exist with somewhat more equal probability in the two conformational forms **7a** and **7b**. In **7b** $\theta_{4,5\alpha} = \theta_{4,5\beta} \cong 55°$ and $J_{4,5\alpha} = J_{4,5\beta} \approx$ 1.5 cps; in **7b** $\theta_{4,5\alpha} \approx 107°$, $\theta_{4,5\beta} \approx 3°$, $J_{4,5\alpha} \approx 0$, and $J_{4,5\beta} \approx 5$ cps. Since both conformational forms should contribute significantly to the equilibrium, the observed broadened triplet is in agreement with expectation for the *trans* isomer.

There remains the key question of why electrophilic attack on 3-carene is so highly favored from the *trans* side. One tenable explanation is that cyclopropyl participation is involved, which selectively facilitates *trans* attack. This is made particularly attractive by the present results, since 3-carene is conformationally restricted to the two boat forms **1a** and **1b**, which are analogous to those available to the epoxide **7** and the acetoxonium ion VI. Unfortunately, details of the charge distribution during electrophilic attack by peracids, osmium tetroxide, and singlet oxygen[47] (or a sensitizer–oxygen complex[48]) on double bonds are still obscure, but such reactions are aided by alkyl substitution on the double bond and should be subject to facilitation by cyclopropyl participation.[49] Moreover, the strong shielding of the 8-CH_3 group suggests that 3-carene exists to a considerable extent in the folded form **1b**, despite the apparently severe interaction between the 8-CH_3 group and the π orbitals of the double bond—perhaps implying stabilization of the ground-state molecule through π overlap with the three-membered ring.[49a] Future studies will explore the generality of cyclopropyl participation in the chemistry and stereochemistry of 3-carene.

Experimental Section[50]

(−)-3β,4α-Caranediol 4-Acetate (9). A. Preparation. As previously described by Schmidt, *et al.*,[7b] (+)-3β,4α-caranediol (**8**), mp 88–89°, was prepared by acidic hydrolysis of (+)-α-3,4-epoxy-

(41) W. Cocker, P. V. R. Shannon, and P. A. Staniland, *J. Chem. Soc., Sect. C.*, 41 (1966).

(42) A gas-phase electron diffraction study of the α- and β-epoxides has also been recently reported by Arbuzov, *et al.* (ref 6b), but it does not provide any insight into the question of *cis–trans* stereochemistry since the calculations were based on an initial premise that the α-epoxide has the *cis* structure **17**.

(43) P. R. Jefferies, R. S. Rosich, and D. E. White, *Tetrahedron Letters*, 1853 (1963).

(44) P. M. Subramanian, M. T. Emerson, and N. A. LeBel, *J. Org. Chem.*, 30, 2624 (1965).

(45) K. Tori, K. Kitahonoki, Y. Takano, H. Tanida, and T. Tsuji, *Tetrahedron Letters*, 559 (1964). The *syn* and *anti* assignments as listed here have been interchanged from those originally given in light of the recent revision of these assignments in norbornene and benzonorbornene; see K. Tori, K. Aono, Y. Hata, R. Muneyuki, T. Tsuji, and H. Tanida, *ibid.*, 9 (1966).

(46) (a) K. Tori, T. Komeno, and T. Nakagawa, *J. Org. Chem.*, **29**, 1136 (1964); (b) A. D. Cross, *J. Am. Chem. Soc.*, **84**, 3206 (1962).

(47) C. S. Foote and S. Wexler, *ibid.*, **86**, 3879 (1964).

(48) See discussion by K. Gollnick and G. O. Schenck, *Pure Appl. Chem.*, **9**, 507 (1964).

(49) Stereochemical control in the case of photosensitized oxidation may also be controlled by the accessibility of a quasi-axial allylic hydrogen; see A. Nickon and J. F. Bagli, *J. Am. Chem. Soc.*, **83**, 1498 (1961).

(49a) NOTE ADDED IN PROOF. After this paper had been submitted a report appeared in which S. P. Acharya, *Tetrahedron Letters*, 4117 (1966), similarily concluded from nmr data that 3-carene exists principally in the folded form **1b**. A possible steric explanation was suggested involving the nonbonded interactions in **1a** between the 8-CH_3 group and the 2β and 5β hydrogen atoms and between the cyclopropyl and 2α and 5α hydrogen atoms. These latter interactions are only slightly alleviated in **1b**. Since it is difficult to assess the relative importance of the former interaction in **1a** and the severe interaction of the 8-CH_3 group with the double bond in **1b**, the intriguing question of the degree to which steric and electronic factors play a role in determining the preferred conformation of 3-carene requires further study.

(50) Ultraviolet spectra were determined in absolute ethanol with a Cary Model 14 spectrophotometer, and infrared spectra were obtained on neat samples with a Perkin-Elmer Infracord spectrophotometer unless otherwise indicated. Optical rotations were measured in absolute ethanol. Melting points were determined on a micro hot stage and are

carane (7).[1] Treatment of **8** with pyridine–acetic anhydride for 16 hr at 25° gave the acetate **9** as a colorless oil which crystallized on refrigeration. Recrystallization from ether–petroleum ether gave colorless prisms, mp 73–73.5°; $[\alpha]^{25}D$ −13° (*c* 1.75); $\lambda_{max}^{CH_2Cl_2}$ 2.75 and 5.75 μ; nmr spectrum: τ 5.42 (q, 1, CH-4), 7.94 (s, 3, $-OCOCH_3$), 8.73 (s, 3, CH_3-10), 8.97 and 9.00 (2s, 6, CH_3-8 and -9), and 9.26 (m, 2, CH-1 and -6);[51a] *m/e* 152, 134, 109, 93, 82, 60, 43, and 41.[51b]

Anal. Calcd for $C_{12}H_{20}O_3$: C, 67.89; H, 9.50. Found: C, 67.8; H, 9.3.

B. Acetylation. Treatment of 1.69 g of hydroxy acetate **9** with 5 ml of acetic anhydride containing 5 drops of pyridine under reflux in an atmosphere of nitrogen for 3.7 hr followed by distillation gave the diacetate **10** as a colorless liquid, bp 50–52° (0.2 mm); $[\alpha]^{25}D$ −22° (*c* 1.88); λ_{max} 5.78 μ; nmr spectrum: τ 5.04 (t, 1, CH-4), 7.98 and 8.10 (2s, 6, $-OCOCH_3$), 8.42 (s, 3, CH_3-10), 8.96 and 9.01 (2s, 6, CH_3-8 and -9), and 9.28 (m, 2, CH-1 and -6); *m/e* 195, 152, 134, 119; lit.[16a] bp 120–121° (4 mm).

Anal. Calcd. for $C_{14}H_{22}O_4$: C, 66.11; H, 8.72. Found: C, 66.1; H, 8.7.

C. Dehydration. A solution containing 9.70 g (45.6 mmoles) of hydroxy acetate **9** and 82.6 ml of phosphorus oxychloride in 826 ml of pyridine (distilled from barium oxide) was maintained at 100° under an atmosphere of nitrogen for 3 hr. The resulting brown solution was poured over ice water and exhaustively extracted with ether. The combined ether extracts were washed with 10% hydrochloric acid and dried over saturated sodium chloride solution followed by anhydrous sodium sulfate. Removal of the solvent by distillation gave 6.88 g of amber residue which was shown by gas chromatography to contain the acetates **4** (34%) and **11** (31%), which were purified by preparative gas chromatography. In a total of four runs, **4** and **11** were obtained in yields of 34–42% and 31–35%, respectively. Also observed were peaks corresponding to lower molecular weight material (13–17%) and additional unidentified olefinic acetates (6–7%). From among the former fractions, peaks were isolated having retention times, infrared, and nmr spectra identical with *p*-cymene, α,*p*-dimethylstyrene, and 1,1,4-trimethylcycloheptatriene.[52]

(−)-1-Methyl-2-*endo*-hydroxy-4-*exo*-isopropenylbicyclo[3.1.0]-hexane acetate (11) was obtained as a colorless oil, bp 72–74° (1.2 mm); $[\alpha]^{25}D$ −18° (*c* 1.38); λ_{max} 5.80, 6.08, and 11.24 μ; nmr spectrum: τ 4.82 (d, 1, *J* = 4.5 cps, CH-2), 5.26 (d, 2, $=CH_2$), 6.96 (m, 1, CH-4), 7.94 (s, 3, $-OCOCH_3$), 8.26 (s, 3, $=CCH_3$), 8.86 (s, 3, CH_3-1), and 9.58 (m, 2, CH_2-6); *m/e* 152, 137, 134, 119.

Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 74.0; H, 9.3.

The acetate **4** was obtained as a colorless oil which showed identical infrared and nmr spectra and gas chromatographic retention time with a specimen obtained by acetylation of the alcohol **5** as described below.

D. Control Run. A solution containing 112 mg of acetate **4** and 368 mg of pyridine hydrochloride in 5.6 ml of pyridine (distilled from barium oxide) was maintained at 100° under an atmosphere of nitrogen for 3 hr. Isolation as described above gave 123 mg of an amber oil which showed only one peak by gas chromatography and was identical in retention time and infrared spectrum with the starting material.

(−)-3(10)-Caren-4α-ol Acetate (4). Acetylation of a specimen of (−)-3(10)-caren-4α-ol (**5**), prepared by photosensitized oxidation of (+)-3-carene (**1**),[5,53] with pyridine–acetic anhydride in the usual manner gave the acetate **4** as a colorless oil, bp 80–82° (1.2 mm); $[\alpha]^{25}D$ −12° (*c* 1.38); λ_{max} 5.75, 6.06, and 11.14 μ; nmr spectrum: τ 4.86 (t, 1, CH-4), 5.15 (m, 2, CH_2-10), 7.96 (s, 3, $-OCOCH_3$), 8.98 (s, 3, CH_3-9), and 9.08 (s, 3, CH_3-8); lit.[16b] bp 86.5° (3.5 mm); $[\alpha]D$ −44.01°.

Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 74.4; H, 9.3.

(+)-3α,4α-Caranediol (2). The general procedure of Baran[54] was followed. To a solution of 1.09 g of (+)-3-carene (**1**)[53] in 25 ml of anhydrous pyridine was added with cooling 2.00 g (7.87 mmoles) of osmium tetroxide, and the resulting solution was maintained at 25° under an atmosphere of nitrogen for 4 hr. A solution of 3 g of sodium bisulfite in a mixture of 25 ml of pyridine and 50 ml water was then added, and the reaction mixture was allowed to stand an additional 0.5 hr. Isolation by extracting with ether, washing with 10% hydrochloric acid, and drying over saturated sodium chloride solution followed by anhydrous sodium sulfate gave, after removal of solvent by distillation, 1.45 g of an amber oil which crystallized on seeding. Recrystallization from petroleum ether gave 758 mg of colorless needles, mp 69–71°, and a second crop, 77 mg, mp 70–72°. Chromatography of the mother liquors on 10 g of silica gel gave, on elution with 1:3 ether–benzene, an additional 137 mg of colorless crystals, giving a total yield of 972 mg (70%). Repeated recrystallization of a portion from petroleum ether gave long colorless needles, mp 71–72°; $[\alpha]^{25}D$ +15° (*c* 1.00, acetone); nmr spectrum: τ 6.63 (q, 1, CH-4), 8.82 (s, CH_3-10), 9.02 and 9.14 (2s, 6, CH_3-8 and -9), and 9.38 (m, 2, CH-1 and -6); lit. mp 69–70°;[1] $[\alpha]D$ +16.05°,[1] +12.8°.[7b]

(−)-3β,4β-Carandiol 4-Acetate (3). A. Preparation. Treatment of 971 mg of diol **2** with 2.5 ml of anhydrous pyridine and 1.25 ml of acetic anhydride for 16 hr at 10° followed by isolation in the usual manner gave 1.68 g of an amber oil which was purified by chromatography through 50 g of silica gel. Elution with 1:19 ether–benzene gave 1.20 g of a colorless liquid which was given final purification by short-path distillation at 83.5–84° (0.2 mm); $[\alpha]^{25}_{5461}$ −37.5° (*c* 1.79); λ_{max} 2.82, 5.72, and 5.78 (sh) μ; nmr spectrum: τ 5.43 (q, 1, CH-4), 7.88 (s, $-OCOCH_3$), 8.94 (s, 3, CH_3-10), 9.04 and 9.07 (2s, 6, CH_3-8 and -9), and 9.2 (m, 2, CH-1 and -6); *m/e* 194, 152, 136, 134, 132, 120, and 119.

Anal. Calcd for $C_{12}H_{20}O_3$: C, 67.89; H, 9.50. Found: C, 67.8; H, 9.7.

B. Dehydration. A solution containing 958 mg (4.51 mmoles) of hydroxy acetate **3** and 2 ml of phosphorus oxychloride in 20 ml of pyridine (distilled from barium oxide) was maintained at 100° under an atmosphere of nitrogen for 3 hr. Isolation as described above for **9** gave 860 mg of amber residue which was shown by gas chromatography to consist of 1,1,4-trimethylcycloheptatriene (7% yield, nmr spectrum identical with that of an authentic sample prepared by dehydration of eucarvol[52]), *p*-cymene (7%), α,*p*-dimethylstyrene (7%), additional unidentified low molecular weight products (27%), acetate **4** (42%, identical in all respects with the samples described above), and additional unidentified olefinic acetates (17%). A peak which appeared at the position corresponding to acetate **11** amounted to less than 2% of the total material. In another run the products described above were obtained in yields of 11, 4, 7, 18, 49, and 19%, respectively.

Reduction of Acetates 4 and 11. A. From Dehydration of 9. A solution containing 3.54 g (18.2 mmoles) of a 27:24 mixture of the acetates **4** and **11** in 20 ml of ether was added dropwise with cooling to a solution of 2.96 g (78.2 mmoles) of lithium aluminum hydride in 20 ml of ether. After 2 hr, isolation in the usual fashion gave 3.32 g of a pale yellow oil. Further purification by preparative gas chromatography followed by short-path distillation at 71.5–72° (1.0 mm) gave **1-methyl-2-*endo*-hydroxy-4-*exo*-isopropenylbicyclo-[3.1.0]hexane (12)** as a colorless oil, λ_{max} 2.90, 6.04, and 11.22 μ; nmr spectrum: τ 5.24 (d, 2, $=CH_2$), 5.88 (d, 1, *J* = 4.8 cps, CH-2), 6.92 (m, 1, CH-4), 8.26 (s, 3, $=CCH_3$), 8.74 (s, 3, CH_3-1), and 9.6 (m, 2, CH_2-6); *m/e* 152, 150, 148, 137, 135, and 134.

Anal. Calcd for $C_{10}H_{16}O$: C, 78.89; H, 10.59. Found: C, 78.9; H, 10.3.

Also obtained was **(−)-3(10)-caren-4α-ol (5)** as a colorless oil which crystallized on seeding with an authentic sample;[5] λ_{max} 2.75, 6.06, and 11.12 μ; nmr spectrum: τ 5.23 (d, 2, CH_2-10), 5.94 (t, 1, CH-4), 8.98 and 9.11 (2s, 6, CH_3-9 and -8), and 9.22 (m, 2, CH-1 and -6).

B. From Dehydration of Acetate 3. Reduction of 96 mg of acetate **4** obtained by dehydration of **3** with 19 mg of lithium alu-

calibrated and corrected. Gas chromatographic analyses were performed on an Aerograph Model A-90P instrument using 5 ft or 10 ft × 0.25 in. columns packed with (A) 20% Carbowax 20M on 60–80 mesh Firebrick or (B) 20% SE-30 on 60–80 mesh Chromosorb W. The elution order used in column chromatography was hexane, benzene, ether, ethyl acetate. Nuclear magnetic resonance spectra were determined in deuterated chloroform solution with a Varian Model HA-100 or A-60 spectrometer, using tetramethylsilane as an internal standard. Mass spectra were obtained using an Atlas Model CH-4 spectrometer. Microanalyses were performed by Spang Microanalytical Laboratories, Ann Arbor, Mich.

(51) (a) Indicates multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, and m = unresolved multiplet) and integration; (b) the mass spectral data reported include the parent ion peak, if present, and other significantly large peaks appearing above the lowest *m/e* value listed.

(52) E. J. Corey, H. J. Burke, and W. A. Remers, *J. Am. Chem. Soc.*, **78**, 180 (1956).

(53) Generously suppplied by Waldorf-Hoerner Paper Products Co., Missoula, Mont.

(54) J. S. Baran, *J. Org. Chem.*, **25**, 257 (1960).

minum hydride as described above gave 77 mg of a colorless oil which crystallized on seeding with an authentic specimen of alcohol **5**.[5] Sublimation gave long colorless needles, mp 43.5–44°; mp 43–44° on admixture with the authentic specimen.

Oxidation of Alcohols 5 and 12. Titration of a solution of 744 mg of the mixture of alcohols **5** and **12** obtained as described above in 20 ml of acetone with 1 equiv of 2.67 *M* chromic acid solution[20] gave 772 mg of a yellow oil. Isolation of the major component, present in 52% yield, by preparative gas chromatography (column A) followed by short-path distillation at 84–85° (1.5 mm) gave (+)-**1-methyl-4-*exo*-isopropenylbicyclo[3.1.0]hexan-2-one** (**6**) as a colorless liquid, $[\alpha]^{25}_{5461}$ +137.5° (*c* 2.38); λ_{max} 5.78, 6.06, and 11.22 μ; λ_{max} 251 mμ (ϵ 166); nmr spectrum: τ 5.14 (s, 2, $=CH_2$), 6.98 (m, 1, CH-4), 8.19 (s, 3, $=CCH_3$), 8.76 (s, 3, CH_3-1), and 8.95 (m, 3, CH_2-6 and CH-5); *m/e* 150, 134, and 122.

Anal. Calcd for $C_{10}H_{14}O$: C, 79.95; H, 9.39. Found: C, 79.9; H, 9.6.

Also isolated was a second component, present in 42% yield, which was separated into two equal fractions by rechromatography (column B). Collection of the first fraction gave recovered alcohol **12**, and isolation of the second fraction followed by short-path distillation at 85–85.5° (0.3 mm) afforded (−)-**3-caren-10-al** (**24**) as a colorless liquid, $[\alpha]^{25}D$ −26° (*c* 1.46); λ_{max} 3.66, 5.97, 6.08, and 12.42 μ; λ_{max} 227 mμ (ϵ 8400); nmr spectrum: τ 0.82 (s, 1, −CHO), 3.52 (m, 1, CH-4), 8.92 (s, 3, CH_3-9), 9.18 (m, 2, CH-1 and -6), and 9.30 (s, 3, CH_3-8); *m/e* 150, 148, 146, 145, 135, 133, 131, and 121.

Acid-Catalyzed Cleavage of Ketone 6. A solution containing 154 mg of ketone **6** and 4 drops of concentrated sulfuric acid in 2 ml of glacial acetic acid was maintained at 100° under an atmosphere of nitrogen for 2 hr. Neutralization with sodium bicarbonate followed by extraction with ether and removal of the solvent by distillation gave 172 mg of a brown oil. Isolation by preparative gas chromatography gave samples of carvacrol (**20**, 85% yield) and carvacrol acetate (**21**, 18%) which had infrared and nmr spectra identical with those of authentic specimens.

Hydrogenation of Ketone 6. A solution of 229 mg of ketone **6** in 15 ml of absolute ethanol was stirred with 10 mg of 10% palladium on charcoal in the presence of hydrogen at atmospheric pressure. After 1.1 molar equiv of hydrogen had been adsorbed, the rate of uptake diminished and the reaction was terminated. Filtration of the reaction mixture followed by distillation to remove solvent gave 209 mg of a colorless liquid which was shown by gas chromatography to contain ketone **22** (57% yield) and ketone **23** (38%).

Isolation by preparative gas chromatography followed by short-path distillation at 89–90° (2.1 mm) gave (+)-**1-methyl-4-*exo*-isopropylbicyclo[3.1.0]hexan-2-one** (**22**) as a colorless liquid which crystallized on standing to give colorless prisms, mp 26–27°; $[\alpha]^{25}_{5461}$ +80° (*c* 3.07); λ_{max} 5.78μ; nmr spectrum: τ 8.78 (s, 3, CH_3-1), and 9.02 and 9.09 (2d, J = 7.2 cps, CH_3-isopropyl); *m/e* 152, 137, 110.

Anal. Calcd for $C_{10}H_{16}O$: C, 78.89; H, 10.59. Found: C, 79.1; H, 10.8.

Similarly, gas chromatographic isolation followed by short-path distillation at 97° (1.5 mm) gave (−)-*p*-**menthan-2-one** (**23**) as a colorless liquid, λ_{max} 5.82 μ. This material was identical in all respects with an authentic specimen prepared by catalytic hydrogenation of (−)-dihydrocarvone.

Dehydration of (+)-3α-caranol (**13**). A solution containing 1.02 g of alcohol **13** (bp 62–64° (2.5 mm); $[\alpha]^{27}D$ +18° (*c* 1.49); *p*-nitrobenzoate, mp 112.5–113.5°; prepared by lithium aluminum hydride reduction of epoxide **7**[21]) and 2.5 ml of phosphorus oxychloride in 25 ml of anhydrous pyridine was maintained at 100° under an atmosphere of nitrogen for 3 hr. Isolation as described above for hydroxy acetate **9** gave 920 mg of an amber oil which was separated by gas chromatography into two fractions, which were present in equal amounts. The infrared and nmr spectra of one fraction showed that it was pure (+)-3-carene (**1**, 49% yield). Analysis of the infrared and nmr spectra of the second fraction revealed that it was a mixture of (+)-2-(**14**, 43%) and (+)-3(10)-carene (**15**, 5%).

Dehydration of (+)-3β-caranol (**16**). A solution containing 509 mg of alcohol **16** (mp 71.5–72.5°; $[\alpha]^{25}D$ +10° (*c* 1.79); prepared by lithium aluminum hydride reduction of epoxide **17**[14]) and 1.25 ml of phosphorus oxychloride in 12.5 ml of anhydrous pyridine was maintained at 100° under an atmosphere of nitrogen for 3 hr. Isolation as described above for hydroxy acetate **9** gave 500 mg of a yellow liquid which was separated by gas chromatography into two principal components. Isolation of the major component gave a colorless liquid which exhibited infrared and nmr spectra identical with those of (+)-3-carene. The spectra of the second fraction were consistent with a superimposition of the spectra for (+)-2- (**14**) and (+)-3(10)-carene (**15**). Analysis of the nmr spectrum of the material obtained by collecting the two components together revealed that the carene isomers were isomers present in yields of 51, 28, and 11%, respectively.

Acid-Catalyzed Rearrangement of (+)-α-3,4-Epoxycarane (**7**). A solution containing 1.00 g of epoxide **7** and 4 drops of boron trifluoride etherate in 20 ml of ether was heated under reflux in an atmosphere of nitrogen for 45 min. The resulting solution was diluted with 150 ml of ether and was washed with three 50-ml portions of water. The combined ether extracts were dried over two 50-ml portions of saturated sodium chloride solution followed by anhydrous sodium sulfate. Removal of the solvent by distillation gave a pale yellow oil which was separated by gas chromatography into three major components, present in yields of 14%, 43%, and 28%. The first fraction had a retention time characteristic of C_{10} aromatic hydrocarbons and was not further investigated.

Final purification of the middle fraction by short-path distillation at 82–83° (5 mm) gave (−)-**4-caranone** (**25**) as a colorless liquid, $[\alpha]^{25}D$ −120° (*c* 1.50); λ_{max} 5.82 μ; nmr spectrum: τ 8.97 and 9.16 (2s, 6, CH_3-9 and -8) and 9.05 (d, J = 6.0 cps, CH_3-10). The infrared spectrum was similar to that published by Ohloff, *et al.*, for a similar mixture obtained by ozonization of (−)-$\Delta^{4,\alpha}$-caranemethanol acetate:[55] semicarbazone, fine colorless needles from ethanol, mp 197–198°; $[\alpha]^{25}D$ −76° (*c* 1.11, chloroform), $[\alpha]^{25}D$ −20° (*c* 0.96, pyridine).[56]

Final purification of the last fraction by short-path distillation at 88° (3 mm) gave (−)-*p*-**menth-3-en-2-one** (**26**) as a colorless liquid, $[\alpha]^{25}D$ −6° (*c* 1.88); λ_{max} 6.00 and 6.16 μ; λ_{max} 233 mμ (ϵ 14,000); nmr spectrum: τ 4.18 (s, 1, CH–3), 8.87 (d, J = 6.0 cps, CH_3-7), and 8.93 (d, J = 6.0 cps, CH_3-8 and -9); 2,4-dinitrophenylhydrazone, long red prisms, mp 166.5–168°; lit. $[\alpha]^{21}D$ +45.4 (*c* 10.16), λ_{max} 234 mμ (ϵ 14,700),[54] 2,4-dinitrophenylhydrazone, mp 165[57] and 167°.[58]

Anal. Calcd for $C_{10}H_{16}O$: C, 78.89; H, 10.59. Found: C, 78.6; H, 10.3.

Control Runs. A solution containing 158 mg of (−)-4-caranone (**25**), obtained from the reaction above, and 1 drop of boron trifluoride etherate in 5 ml of ether was heated under reflux in an atmosphere of nitrogen for 45 min. Isolation as described above gave a colorless liquid which was shown by gas chromatography to consist of recovered starting material with no detectable amount of ketone **26**. Similar treatment of a solution of 24 mg of the major (−)-4-caranone isomer obtained above and 1 drop of boron trifluoride etherate in 5 ml of ether gave, on isolation, 26 mg of a yellow liquid which was shown by gas chromatography to consist of the starting isomer with no detectable amount of the minor (−)-4-caranone isomer obtained above.

Acid-Catalyzed Cleavage of (−)-β-3,4-Epoxycarene (**17**). **A. With Boron Trifluoride.** A solution containing 1.00 g of epoxide **17** and 4 drops of boron trifluoride etherate in 20 ml of ether was heated under reflux in an atmosphere of nitrogen for 45 min, The resulting solution was diluted with 150 ml of ether and was washed with three 50-ml portions of water. The combined ether extracts were dried over two 50-ml portions of saturated sodium chloride solution followed by anhydrous sodium sulfate. Removal of the solvent by distillation gave 1.10 g of a pale yellow oil. Isolation by gas chromatography followed by short-path distillation gave (−)-4-caranone (**25**, 66% yield) as a colorless liquid, $[\alpha]^{25}D$ −82° (*c* 1.48), which exhibited infrared and nmr spectra identical with those described above: semicarbazone, colorless needles from ethanol, mp 197–198° dec and 196.5–198° on admixture with the material obtained from epoxide **7**; $[\alpha]^{25}D$ −64° (*c* 0.81, chloroform), $[\alpha]^{25}D$ −11° (*c* 0.70, pyridine). Also isolated was *p*-menth-3-en-2-one (**26**, 2%) as a colorless liquid, λ_{max} 233mμ (ϵ 14,000), which had an infrared spectrum and gas chromatographic retention

(55) G. Ohloff, H. Farnow, and W. Philipp, *Ann.*, **613**, 43 (1958).

(56) Lit. for *cis*-4-caranone: $[\alpha]^{23}D$ −148.65° (*c* 2.5, benzene); semicarbazone, mp 200–201°, $[\alpha]^{23}D$ −86.0° (*c* 1.8, chloroform), $[\alpha]^{26}D$ ±0° (*c* 0.6, pyridine); for *trans*-4-caranone: $[\alpha]^{22}D$ −91.4° (*c* 3.8, benzene); semicarbazone, mp 213–214°, $[\alpha]^{26}D$ +87.75° (*c* 0.5, pyridine).[5b, 40]

(57) H. Pines and H. E. Eschinazi, *J. Am. Chem. Soc.*, 77, 6314 (1955).

(58) K. Fujita, *Bull. Chem. Soc. Japan*, **34**, 968 (1961).

time identical with that for the material described above. At least eight additional minor products were also detected.

B. With Aqueous Acid. A mixture of 1.22 g of epoxide **17** and 25 ml of 4% sulfuric acid was stirred at 0° for 90 min under an atmosphere of nitrogen and then saturated with sodium chloride and extracted with ether. Drying of the resulting ether extracts over saturated sodium chloride solution followed by anhydrous sodium sulfate and subsequent removal of the solvent by distillation gave 1.40 g of colorless wet crystals which was chromatographed on 45 g of silica gel. Elution with 1:3 ether–benzene gave 665 mg (53% yield) of (+)-**3α,4β-carandiol (19)** as a colorless oil which was further purified by short-path distillation at 103–104° (0.2 mm), $[\alpha]^{25}_{5461}$ +87° (*c* 1.25); nmr spectrum: τ 6.50 (m, 1, CH–4), 8.82 (s, 3, CH_3-10), 8.94 and 8.98 (2s, 6, CH_3-8 and -9), and 9.34 (m, 2, CH-1 and -6); lit.[7a] mp 30°, $[\alpha]^{20}D$ +84.15° (*c* 6, chloroform).

Further elution with 1:1 ether–benzene gave 318 mg (26% yield) of (+)-**3β,4β-carandiol (18)**; colorless needles from ethyl acetate, mp 138.5–139.5°; $[\alpha]^{25}D$ +64° (*c* 1.49); lit.[7a] mp 137°, $[\alpha]^{20}D$ +61.25° (*c* 4).

C. With Methanolic Acid. A solution containing 341 mg of epoxide **17** in 15 ml of 4% methanolic sulfuric acid was stirred at 0° for 90 min under an atmosphere of nitrogen. The resulting mixture was diluted with saturated sodium chloride solution and extracted with ether. The combined ether extracts were washed with saturated sodium bicarbonate solution and dried over saturated sodium chloride solution followed by anhydrous sodium sulfate. Removal of the solvent by distillation gave 450 mg of a colorless liquid which was chromatographed on 20 g of silica gel. Elution with 1:19 ether–benzene gave 283 mg (70% yield) of (−)-**3α-methoxy-4β-caranol (27)**, mp 57.5–63°. Sublimation gave long colorless needles, mp 63.5–64.5°; $[\alpha]^{25}_{5461}$ −69° (*c* 1.25); $\lambda^{CH_2Cl_2}_{max}$ 2.75 μ; nmr spectrum: τ 6.20 (t, 1, CH–4), 6.60 (s, 3, $-OCH_3$), 8.72 and 8.80 (2s, 9, CH_3–8, –9, and –10), and 9.2 (m, 2, CH–1 and –6); *m/e* 184, 152, 137, 134, 125, 123, and 119.

Anal. Calcd for $C_{11}H_{20}O_2$: C, 71.69; H, 10.94. Found: C, 71.4; H, 11.0.

Elution with 1:3 ether–benzene gave 41 mg (10% yield) of (+)-**4β-methoxy-3β-caranol (28)** as a colorless liquid which was further purified by short-path distillation at 82° (0.5 mm); λ_{max} 2.90 μ; $[\alpha]^{27}D$ +53° (*c* 1.74); nmr spectrum: τ 5.96 (t, 1, CH–4), 6.90 (s, 3, $-OCH_3$), and 8.86, 8.92, and 8.98 (3s, CH_3–8, –9, and –10); *m/e* 166, 152, 151, 150, 137, 135, 134, 132, and 123.

Anal. Calcd for $C_{11}H_{20}O_2$: C, 71.69; H, 10.94. Found: C, 71.8; H, 10.9.

(+)-**3α-Methoxy-4-caranone (29).** Titration of a solution of 75 mg of alcohol **27** in 5 ml of acetone with 1 molar equiv of 2.67 *M* chromic acid solution[20] gave, on isolation, 75 mg of ketone **29** as a pale yellow liquid. Further purification by gas chromatography followed by short-path distillation at 88–89° (3.5 mm) gave a colorless liquid, λ_{max} 5.80 μ; $[\alpha]^{27}D$ +21° (*c* 2.08); nmr spectrum: τ 6.70 (s, 3, CH_3O–), 8.74 (s, 3, CH_3–3), and 8.83 and 9.04 (2s, 6, CH_3-9 and -8); *m/e* 182, 153, 150, 148, 139, 135, 122. This material exhibited spectral and gas chromatographic behavior quite distinct from that of a specimen of (+)-3β-methoxy-4-caranone.[16b]

Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.96 Found: C, 72.6; H, 10.1.

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The Rates of Methoxyl Exchange of Camphor and Norcamphor Dimethyl Ketals in Methanol-d_4

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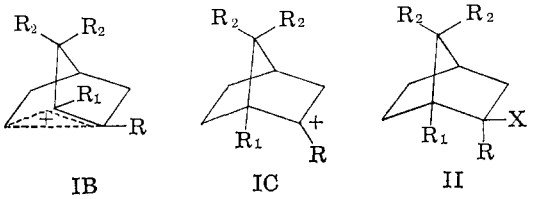
Abstract: In methanol-d_4, methoxyl exchange in camphor and norcamphor dimethyl ketals (III) proceeds through the *classical* 2-methoxybicyclo[2.2.1]heptyl-2 cations (IV). The *exo/endo* rate ratios for ionization to IV and for reaction of IV with solvent to give labeled III are identical. The observed *exo/endo* ratios are 0.10 for camphor dimethyl ketal (IIIb) and 16 for norcamphor dimethyl ketal (IIIa). Reaction of the cations (IV) with hydrides gives *exo/endo* rate ratios very close to those for the exchange reaction (0.13 and 20). These results define the behavior of *classical* bicycloheptyl systems and provide a basis for estimating the importance of steric effects and anchimeric assistance in other bicycloheptyl systems. In particular we conclude that bicyclo[2.2.1]heptyl-2 cations having no 2-substituent are not classical.

Considerable interest and controversy have arisen over the structure of 2-bicyclo[2.2.1]heptyl cations.[1,2] The large *exo/endo* rate ratios in solvolysis and the high stereospecificity for formation of *exo* products have been interpreted[1,3] as evidence for neighboring group participation, leading to bridged ions IB.



It has also been suggested[2b] that if this interpretation is correct, substitution of methyl, phenyl, or *p*-anisyl groups at the 2-position (II, R = Me, C_6H_5, *p*-Me-OC_6H_4) should lead to stabilization of the classical ion IC relative to the bridged ion IB; such stabilization should diminish the necessity for participation and

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(2) (a) H. C. Brown, F. C. Chloupek, and M.-H. Rei, *ibid.*, **86**, 1246 (1964); (b) *ibid.*, **86**, 1247 (1964); (c) *ibid.*, **86**, 1248 (1964); (d) H. C. Brown and H. M. Bell, *ibid.*, **86**, 5003 (1964); (e) *ibid.*, **86**, 5006 (1964); (f) *ibid.*, **86**, 5007 (1964); (g) H. C. Brown and M.-H. Rei, *ibid.*, **86**, 5004 (1964); (h) *ibid.*, **86**, 5008 (1964); (i) H. C. Brown and H. M. Bell, *ibid.*, **85**, 2324 (1963).

(3) For a historical summary of this concept see J. A. Berson, "Molecular Rearrangements," P. de Mayo, Ed., Interscience Publishers, Inc., New York, N. Y., 1963, Chapter 3.