Hydroboration of Terpenes. IV. Hydroboration of (+)-3-Carene (Δ^3-Carene). Configuration Assignments for the 4-Caranols and 4-Caranones. An Unusual Stability of 4-Isocaranone with a *cis* Relationship of the Methyl and *gem*-Dimethyl Groups

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Abstract: (+)-3-Carene (**1**) on hydroboration–protonolysis yields *cis*-carane. Consequently, hydroboration of (+)-3-carene occurs from the side away from the *gem*-dimethyl group and the hydroboration–oxidation product must be (−)-4-isocaranol (**2**) and not 4-neocaranol (**6**) as reported in the literature. Chromic acid–ether oxidation of (−)-4-isocaranol yields (−)-4-isocaranone (**3**), reduced by lithium trimethoxyaluminohydride to (+)-4-neoisocaranol (**5**). In contrast to the corresponding ketones from α-pinene and 2-carene, (−)-4-isocaranone, with an assigned *cis* relationship of the 3-Me and *gem*-dimethyl groups, is only slightly (10%) epimerized by base to (−)-4-caranone (**4**). The same equilibrium distribution was realized with 4-caranone. It is proposed that all of the earlier configurational assignments for the isomeric 4-caranols and 4-caranones must be revised, with the earlier assignments in error, in part because of this unusual stability of the ketone with a *cis* relationship between the 3-Me and *gem*-dimethyl groups. This unusual stability can be accounted for on the basis of the conformational preference of both 4-isocaranone (**3**) and 4-caranone (**4**) in the half-chair form. The proposed reassignments are supported by the formation of *cis*-carane in the reduction of the tosylhydrazone of 4-isocaranone (**12**) by sodium borohydride and in the hydrogenation of *cis*-4-carene (**16**) from the elimination reaction of the tosylates from 4-isocaranol (**14**) and 4-neoisocaranol (**15**). Ketonization studies of the enol acetates **17** and **18** from 4-isocaranone also support the proposed *cis* relationship. Finally, the nmr spectra of the ketones, alcohols, and epoxides are subjected to detailed analysis and shown to support the proposed reassignments.

The report in 1960 that the hydroboration–oxidation of (+)-3-carene (**1**) yields (−)-4-neocaranol (**6**),[2,3] with a *trans* addition of the elements of water to the double bond, was startling (Figure 1, I). This proposed exception to the generalization that hydroboration–oxidation involves a *cis* addition of the elements of water to the double bond[4] persuaded us to undertake a study of this hydroboration reaction and a reexamination of the configurational assignments[5] for the 4-caranols and 4-caranones. Their assignment of the configuration of (−)-4-caranone (**4**) relied on the assumption that the formation of the ketone from α-(3,4)-epoxycarane (**8**) involves the formation of a thermodynamically more stable species such as (**8B**) in which the methyl and *gem*-dimethyl groups must necessarily be *trans* related. Further, they assigned the configuration[6] of 4-neocaranol (**6**) on the basis of their results on hydrolysis of the phthalate esters and the elimination reactions of the tosylates.

Initially, our studies went very smoothly, paralleling our earlier study of α-pinene[7] (Figure 1, III). Thus (+)-3-carene (**1**) underwent hydroboration readily with diborane in tetrahydrofuran. Oxidation as usual, with alkaline hydrogen peroxide, gave in 98% yield a single pure alcohol, confirmed by glpc on four different 150-ft Golay capillary columns, which was tentatively assigned the structure of (−)-4-isocaranol (**2**). Oxidation by the ether–chromic acid procedure[8] produced (−)-4-isocaranone (**3**) in 98% yield.

Reduction of the ketone with lithium trimethoxyaluminohydride[9] yielded the epimeric alcohol, (+)-4-neoisocaranol (**5**), and the hydroboration–oxidation alcohol, (−)-4-isocaranol (**2**), in a ratio of 79:21 (Figure 1, II). The properties of these compounds, including their derivatives, were comparable with those reported for Kuczynski's 4-neocaranol,[6] 4-caranone,[10] and 4-caranol,[6] respectively.

Attempts to epimerize the ketone, 4-isocaranone (**3**), *resulted in a surprise. This ketone, with a postulated cis arrangement for the 3-Me and the gem-dimethyl substituents, proved to be more stable than its epimer, 4-caranone* (**4**), *yielding a 90:10 equilibrium distribution.*

A sample of 4-caranone (**4**)[11] was prepared by converting the α-epoxide (**8**) (Figure 2) *via* the glycol (**9**) and monotosylate (**10**) to the β-epoxide (**11**). It yielded the same equilibrium distribution.

These early experiments by Drs. Nagraj Ayyangar, Takashi Munekata, and G. Zweifel were completed some time ago. However, we delayed publication un-

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(1) Postdoctoral Research Associate, 1963–1965, on Contract No. 12-14-100-7152(72) supported by the Southern Utilization Research and Development Division of the U. S. Department of Agriculture.

(2) (a) W. Kuczynski and A. Andrzejak, *Roczniki Chem.*, **34**, 1189 (1960). (b) More recently it was proposed that this alcohol is (−)-4-neoisocaranol (**5**), also involving a *trans* addition of the elements of water: K. Piatkowaski, H. Kuczynski, and A. Kubik, *ibid.*, **40**, 213 (1966).

(3) Kuczynski, *et al.*,[2a] report this compound under the name *l*-3-caranol. The numbering system followed in this paper is in accordance with that used in *Chemical Abstracts*. The prefix iso is used to indicate that the cyclopropyl and the 3-Me are *cis* to each other, and neo is used to indicate that the hydroxyl and 3-Me are *cis* to each other. See also S. H. Schroeter and E. L. Eliel, *J. Org. Chem.*, **30**, 1 (1965).

(4) H. C. Brown and G. Zweifel, *J. Am. Chem. Soc.*, **83**, 2544 (1961).

(5) H. Kuczynski and Z. Chabudzinski, *Roczniki Chem.*, **29**, 437 (1955).

(6) H. Kuczynski and Z. Chabudzinski, *ibid.*, **32**, 49 (1958).

(7) G. Zweifel and H. C. Brown, *J. Am. Chem. Soc.*, **86**, 393 (1964).

(8) H. C. Brown and C. P. Garg, *ibid.*, **83**, 2952 (1961).

(9) H. C. Brown and H. R. Deck, *ibid.*, **87**, 5620 (1965).

(10) H. Kuczynski and Z. Chabudzinski, *Roczniki Chem.*, **35**, 227 (1961).

(11) H. Kuczynski and Z. Chabudzinski, *ibid.*, **34**, 117 (1960).

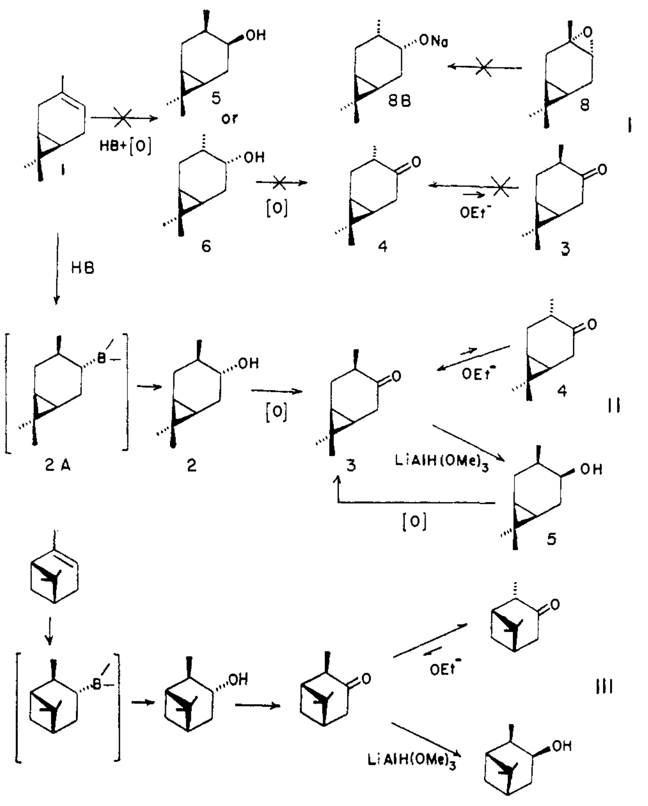

Figure 1. Comparison of the hydroboration–oxidation of (+)-3-carene and α-pinene with subsequent reactions of the original alcohols.

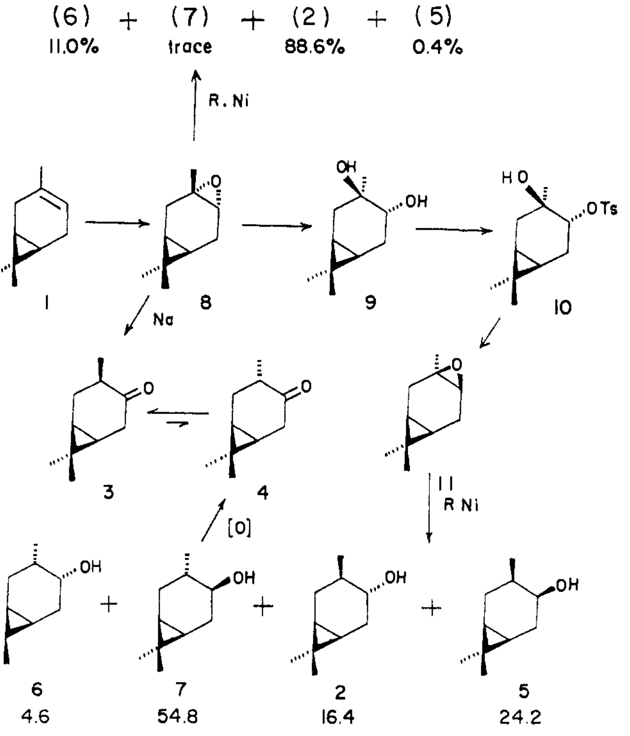

Figure 2. Syntheses of 4-caranols *via* the epoxides.

til we could obtain independent confirmation of the unusual stability of 4-isocaranone with a proposed *cis* relationship of the 3-Me and *gem*-dimethyl groups.

Hydroboration–protonolysis of (+)-3-carene and sodium borohydride reduction of the tosylhydrazone of 4-isocaranone both yielded (−)-*cis*-carane (Figure 3), identical with a sample prepared from 2-carene.[12] Consequently, there could be no question about the new assignments.

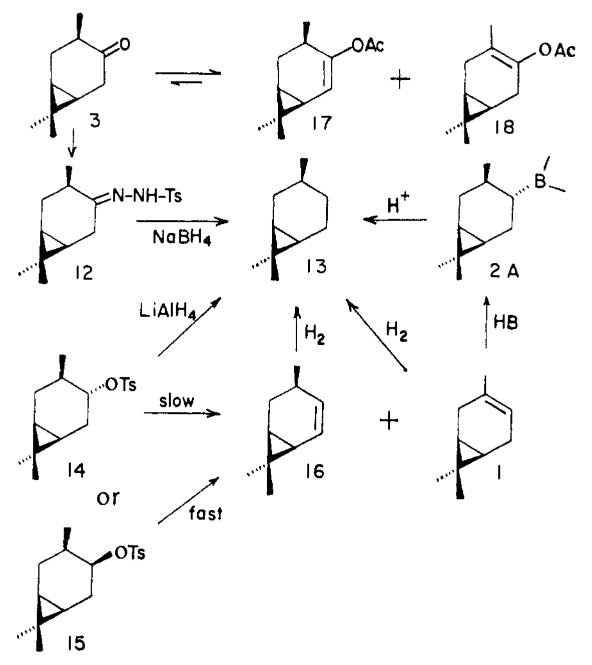

Figure 3. Conversions to *cis*-carane and other reactions supporting the reassignments.

While this work was in progress, Schenck, *et al.*,[13] subjected (+)-3-carene (**1**) to a photosensitized oxygen-transfer reaction. The allylic alcohols so obtained were reduced to the corresponding 4-caranols. Their assignments for these compounds agree *in toto* with our results. Gollnick[14] recently established unequivocally the absolute configuration of 4-isocaranol (**2**) by degradation to a known compound, (+)-(3*R*)-3-methyladipic acid, and by the pyrolysis of the xanthate ester of 4-isocaranol (**2**) to 3-carene (**1**), 35%, and *cis*-4-carene (**16**), 65% yield, and that of 4-neocaranol (**6**) to entirely *trans*-4-carene. Cocker, *et al.*,[15] and Gollnick[14] subjected the tosylate of 4-isocaranol (**14**) to lithium aluminum hydride reduction to obtain *cis*-carane (**13**) (Figure 3), which was readily distinguishable from *trans*-carane obtained by Wolff–Kishner reduction of 2-caranone[12,15] and by lithium aluminum hydride reduction of the tosylate of 4-caranol (**7**).[16]

Consequently, there is now agreement between three different groups that the previous assignments must be revised, confirming our previous generalization that hydroboration–oxidation involves a *cis* hydration of a double bond from the less hindered side. Fortunately, there is a little overlap in the experimental approaches we adopted and those published recently.[13-16] Finally, we wish to report a detailed analysis of the nmr spectra which confirms the assignments and permits conclusions as to the conformational preferences for the various derivatives.

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[12] S. P. Acharya and H. C. Brown, *J. Am. Chem. Soc.*, **89**, 1925 (1967).

[13] K. Gollnick, S. Schroeter, G. Ohloff, G. Schade, and G. O. Schenck, *Ann.*, **687**, 14 (1965).

[14] K. Gollnick, *Tetrahedron Letters*, 327 (1966).

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

[16] K. Gollnick and G. Schade, *Tetrahedron Letters*, 2335 (1966).

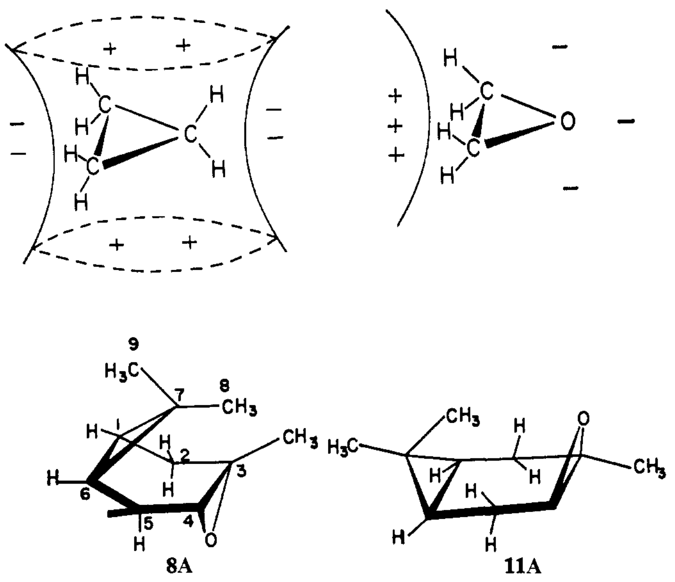

Figure 4. Anisotropic effects of the cyclopropane and epoxide rings and the preferred conformations of α- and β-epoxycaranes.

The two possible epoxides from (+)-3-carene (**1**) were prepared by Kuczynski, *et al.*,[10,11] who assigned the structures α-(3,4)-epoxycarane (**8**) for the compound obtained by direct epoxidation and β-(3,4)-epoxycarane (**11**) for the other which was obtained by a series of reactions involving the opening of the α-epoxide to a glycol (**9**) and the conversion of the monotosylate of the glycol (**10**) to the β-epoxide (**11**) (Figure 2).

These two epoxides have been subjected to vigorous examination by various physical methods.[17-19] These workers concluded from the nmr study[17] that the α-epoxide has the epoxide and the cyclopropane rings *cis* to each other, whereas the β-epoxide has these groups *trans* to each other. Indeed, in the inverted boat conformation of (+)-3-carene,[20] attack from both sides appears feasible. An electron diffraction study,[19] although it did not rule out these configurational assignments of α- and β-epoxycaranes, also failed to provide support.

The above configurational assignments were apparently based on the belief that the epoxide ring should exert a diamagnetic effect. However, recent studies on the nmr of epoxides[21] revealed that this is incorrect. It is probable that the anisotropic distribution of an epoxide ring will be paramagnetic around the oxygen and diamagnetic at the neighboring carbon atoms, unlike the influence of the cyclopropane ring[22] as shown in Figure 4.

Assuming the favorable conformation for the α-epoxide to be **8A** and the β-epoxide to be **11A** (Figure 4), and considering the various nonbonded interactions, which are similar in nature to the two conformations of (+)-3-carene,[20] the 8-Me group is subjected to various diamagnetic anisotropic effects of bonds 1–2, 3–4, 4–5, 5–6, and the paramagnetic anisotropic effects of the oxygen atom. Apparently, these happen to oppose each other equally in the β-epoxide. Hence there is no chemical shift difference between the 8-Me and the 9-Me groups (Table II). In the case of α-epoxycarane (**8A**), the paramagnetic shift is no longer present. However, the 8-Me is subjected to diagmagnetic anisotropic effects of the epoxide ring as well as the C_3–C_{10} bond over and above that due to bonds 1–2, 3–4, 4–5, and 5–6. Hence the 8-Me is shifted upfield even more than in 3-carene.[20]

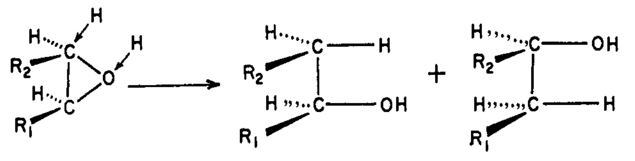

Figure 5. The stereospecific nature of the catalytic hydrogenation of an epoxide ring.

On this basis the nmr results can be considered to be consistent with the original assignment by Kuczynski and co-workers.[10,11] The result also supports the conclusion that the side away from the *gem*-dimethyl group is less hindered and provides the preferred direction of attack.

Support for this assignment for the α- (**8**) and β-epoxide (**11**) is obtained by the products obtained during high-pressure hydrogenation of the epoxides over Raney nickel. The results of the glpc analysis of only the secondary alcohols thus obtained are given in Figure 2. Catalytic hydrogenation of an epoxide is considered to proceed by a *cis* opening of the carbon–oxygen bond,[23a-c] as shown in Figure 5. On this basis, 4-isocaranol (**2**) should be the preferred product from the α-epoxide and 4-caranol (**7**) from the β-epoxide. This was observed.

Mention may be made here of earlier references on the higher pressure hydrogenation of the α- and β-epoxycaranes (**8** and **11**) over Raney nickel catalyst.[24] Thus Arbuzov, *et al.*, mention that the secondary alcohol they obtained had the same properties as those mentioned by Kuczynski, *et al.*,[10] who had reported that the α-epoxide gave 4-neoisocaranol (**5**) and 4-neocaranol (**6**), whereas the β-epoxide gave 30% 4-neocaranol (**6**) and 70% 4-isocaranol (**2**). Gollnick, *et al.*,[13] report that they obtained 82% isocaranol (**2**) and 13% neocaranol (**6**) from the α-epoxide and a 50:50 mixture of 4-neoisocaranol (**5**) and 4-caranol (**7**) from the β-epoxide.[13] This result indicates that there is no stereoselectivity in the hydrogenation process of the β-epoxide, whereas we realized satisfactory stereoselectivity with both epoxides.

The chromic acid oxidation of these epimeric alcohols should assist in confirming the configurational assignments. In the absence of a competing side reaction, the alcohol with a more hindered hydroxyl group should oxidize more rapidly.[25] Accordingly, if our

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(17) B. A. Arbuzov, Z. G. Isaeva, and Y. Y. Samitov, *Proc. Acad. Sci. USSR, Chem. Sect.*, **137**, 296 (1961); **150**, 475 (1963).

(18) B. A. Arbuzov, Y. Y. Eframov, and V. L. Tal'roze, *ibid.*, **158**, 990 (1964).

(19) B. A. Arbuzov, V. A. Naumov, and L. F. Shatrukov, *ibid.*, **163**, 646 (1965).

(20) S. P. Acharya, *Tetrahedron Letters*, 4117 (1966).

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(22) T. Norin, *Svensk Kem. Tidskr.*, **76**, 118 (1964).

(23) (a) S. Mitsui and S. Imaizumi, *J. Chem. Soc. Japan*, **86**, 219 (1965); (b) M. Shiota, T. Ogihara, and Y. Watanabe, *Bull. Chem. Soc. Japan*, **34**, 40 (1961); (c) A. Fürst and P. A. Plattner, *Helv. Chim. Acta*, **32**, 275 (1949).

(24) (a) Z. G. Isaeva and B. A. Arbuzov, *Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1013 (1959); (b) B. A. Arbuzov and Z. G. Isaeva, *Chem. Abstr.* **54**, 4652 (1960); (c) *Proc. Acad. Sci. USSR, Chem. Sect.*, 121–123, 507 (1958).

(25) H. O. House, "Modern Synthetic Organic Reactions," W. A. Benjamin, Inc., New York, N. Y., 1965, p 83.

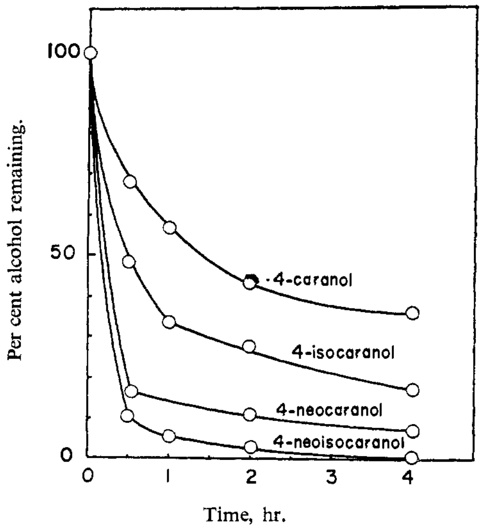

Figure 6. Comparison of the oxidation rates of the 4-caranols.

reassignments are correct, chromic acid oxidation should be fastest for 4-neoisocaranol (**5**), slowest for 4-caranol (**7**), and intermediate for 4-neocaranol (**6**) and 4-isocaranol (**2**). Indeed, this was observed (Figure 6, Table V).

cis-Carane (**13**) which can be readily distinguished from *trans*-carane, by analysis on a 150-ft Golay squalene column, was obtained by the following methods, which readily establish α attack during the hydroboration.

Hydrogenation[26] of (+)-3-carene (**1**) at room temperature over borohydride reduced platinum on carbon gave (−)-*cis*-carane (**13**) with minor amounts of two other components, *trans*-carane and either 1,1,4-trimethylcycloheptane or 1-methyl-4-isopropylcyclohexane (Figure 3). Even more significant, the protonolysis of the hydroboration intermediate (**2A**) yielded pure (−)-*cis*-carane. Reduction of the tosylhydrazone of 4-isocaranone (**12**) by Caglioti's method[27] also gave pure *cis*-carane (**13**), without any evidence for the formation of *trans* isomer, confirming the absence of any epimerization in these reactions.

When the tosylates of 4-neoisocaranol (**15**) and 4-isocaranol (**14**) were subjected to elimination, using potassium *t*-butoxide in *t*-butyl alcohol at 50°, the former gave *cis*-4-carene (**16**) (Δ^2-*carene*) and 3-carene (**1**) in the ratio 95:5, whereas the latter compound gave them in the ratio 81:17. These results are very different from the highly stereoselective *trans* eliminations observed under these conditions in the cyclohexane series.[28] Clearly, the cyclohexane ring cannot be utilized as a satisfactory model for the carane system. Rates of elimination were determined by analyzing aliquots at regular intervals by glpc. The rate was very much faster for 4-neoisocaranol (**15**) than for 4-isocaranol (**14**) (Table VI). The rate data may be considered to be in agreement with the more crowded environment of the hydroxyl group in 4-neoisocaranol (**5**), as compared to 4-isocaranol (**2**). Hence 4-neoisocaranol was assigned the all-*cis* configuration. *cis*-4-Carene so obtained was purified by glpc and the structure confirmed by infrared and nmr analysis. The infrared spectrum showed $\nu_{\max}$ 6.10, 7.11, and 4.06 μ (endocyclic double bond). The nmr spectrum showed 338 ($CH{=}CH$) and 54 cps (3-Me, J = 7 cps) from TMS. Hydrogenation of the compound yielded pure *cis*-carane (**13**).

Recent studies on ketonization of enol acetates lead to the conclusion that ketonization proceeds by protopic attack from the less hindered side of the enolic double bond. Isopropenyl acetate reacts with all enolizable carbonyl groups to form enol acetates in good yield in the presence of an acid catalyst.[29] But acids are known to open the cyclopropane ring of the carane molecule.[30] Indeed, in the absence of isopropenyl acetate, *p*-tolylsulfonic acid does open the cyclopropane ring as indicated by the spectra data of the product [infrared spectrum: 3.22, 6.06, and 11.2 μ ($>C{=}CH_2$); nmr spectrum: 276 (broad singlet, vinylic protons) and 102 cps (methyl on a double bond)] from TMS. But in the presence of isopropenyl acetate, two enol acetates (86.2% yield by vpc), readily distinguished by their retention times, were obtained. Unfortunately, they could not be separated by preparative glpc. Nmr spectra of the mixture indicated that the product was a 50:50 mixture of 4-acetoxy-3-carene (**18**) and 4-acetoxy-*cis*-4-carene (**17**). When this mixture was subjected to ketonization at 50° in the presence of *n*-propylamine, 98% 4-isocaranone (**3**) and 2% 4-caranone (**4**) were obtained. Since the equilibrium mixture contains considerably more 4-caranone, this must mean that 4-isocaranone is the preferred product from both enol acetates and both of these must undergo protonation from the side away from the *gem*-dimethyl group.

All of the chemical evidence is consistent with the conclusion that the side of 3-carene away from *gem*-dimethyl groups is least hindered, that both epoxidation and hydroboration take place from that direction, and that the hydroboration–oxidation product involves a *cis* addition of the elements of water from that direction, resulting in the formation of 4-isocaranol (**2**), and not 4-caranol (**6**) or 4-neoisocaranol (**5**) as previously reported. In Table I are summarized our data for the ketones, alcohols, and their derivatives and epoxycaranes derived from (+)-3-carene.

Spectroscopic Evidence for the Configurational Assignments of the 4-Caranols and 4-Caranones

There are in all four possible conformations (Figure 7) for the 4-caranones, one pair being derived from the two possible boat forms III C_1 and III C_2 and the other pair from two possible half-chair forms III C_3 and III C_4.

When the 10-Me has a β configuration, the conformations III C_1, III C_2, and III C_3 are to be neglected because of severe nonbonded interactions between the 8-Me and the 2,5-β-H atoms in the case of III C_1[31] or the 8-Me and the β-10-Me in the case of III C_2 or III C_3. On these considerations, 4-isocaranone should exist preferentially in the conformation shown in III C_4.

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(26) C. A. Brown and H. C. Brown, *J. Am. Chem. Soc.*, **84**, 2929 (1962).

(27) (a) L. Caglioti, *Tetrahedron*, **22**, 487 (1966); (b) M. Fischer, Z. Pelah, D. H. Williams, and C. Djerassi, *Ber.*, **98**, 3236 (1965).

(28) H. C. Brown and R. L. Klimisch, *J. Am. Chem. Soc.*, **88**, 1425 (1966).

(29) H. J. Hagenmeyer and D. C. Hull, *Ind. Eng. Chem.*, **41**, 2920 (1949).

(30) (a) L. Borowieki, *Roczniki Chem.*, **39**, 107 (1965); (b) J. Verghese, *Perfumery Essent. Oil Record*, **56**, 438 (1965).

(31) These interactions are exactly similar to those present in 3-carene in its inverted boat form, which is an unstable conformation.[20]

Table I. Physical Properties of 4-Caranols and 4-Caranones and Other Derivatives of Carane

Compound	Bp (mm) or mp, °C	$n^{20}D$	d^{20}_4	α^tD, neat, 1 dm, deg
(−)-4-Isocaranol (**2**)	89–90 (3.5)	1.4816	0.9517	-69.1^{20}
p-Nitrobenzoate	62	...	...	...
3,5-Dinitrobenzoate	130–131.5	...	...	...
(+)-Neoisocaranol (**5**)	67 (2)	1.4820	0.9543	$+36.3^{20}$
p-Nitrobenzoate	78–79.5	...	...	...
3,5-Dinitrobenzoate	104–105.5	...	...	...
(+)-4-Caranol (**7**)	42.5–43.5	...	...	$+65.4^{20}$
Monophthalate	128–129	...	...	...
(−)-4-Neocaranol (**6**)[a]	82–83 (2.5)	1.4831	0.9501	-6.3^{20}
p-Nitrobenzoate	129.5–130	...	...	...
(−)-4-Isocaranone (**3**)	80–81 (5.3)	1.4703	0.9510	-152.5^{20}
Semicarbazone	208–209	...	...	...
2,4-DNP	160–162	...	...	...
Tosylhydrazone (**12**)	133	...	...	...
(−)-4-Caranone (4)	...	1.4706	0.9523	-88^{20}
(−)-*cis*-Carane (**13**)	166 (755)	1.4542	...	-17.8^{c}
α-(+)-3,4-Epoxycarane (**8**)	92–93 (23)	1.4668	...	$+13.35^{26.5}$
β-(−)-3,4-Epoxycarane (**11**)	101–103 (36)	1.4690	...	-2.36^{28}
(−)-*cis*-4-Carene (**16**)	...	1.4662	...	$-141.7^{29\ b}$

[a] As reported by Kuczynski, *et al.*[10] [b] In chloroform. [c] In benzene.

When the 10-Me group has an α configuration, interactions between 8-Me and 3-β-H in III C_3 are severe, the interatomic distance being 0.4 A, and the molecule will tend to exist in a conformation between III C_2 and III C_4. That is to say, the methyl group will be neither completely axial, as in III C_4, nor completely equatorial, as in III C_2. If these conclusions, which are based on a close inspection of Dreiding models, are correct, *4-isocaranone will have an equatorial 10-Me group and 4-caranone will have a quasi-axial 10-Me group, thereby providing an unusual stability for 4-isocaranone*, since it has been recently observed that the 2-alkyl ketone effect[32,33] no longer exists when the alkyl group is methyl.

Nmr and ORD provides a valuable tool to test these conclusions. It has been recently reported that an axial methyl group adjacent to a ketonic function will suffer an appreciable upfield shift, 15–18 cps, on passing from carbon tetrachloride to benzene.[34] However, the equatorial methyl suffers a small downfield shift, 1–2 cps. Indeed, as shown in Table II the 10-Me of 4-caranone, which is quasi-axial according to the proposed conformation, has suffered an upfield shift of 8.5 cps, whereas the 10-Me of 4-isocaranone, with an equatorial 10-Me according to the proposed conformation, has suffered an upfield shift of 1 cps.

Owing to the diamagnetic anisotropic effects of the ketonic group,[35] the 8-Me in conformation III C_4, a favorable conformation for 4-isocaranone, is expected to have a higher upfield shift compared to that in III C_2 ~ III C_4, a favorable conformation for 4-caranone. The chemical shift difference between the 8-Me and the 9-Me for 4-isocaranone in CCl_4 is 11.4 cps and that for 4-caranone is 7.8 cps (Table II).

The octant diagram[36] (Figure 8) for the favorable conformation of 4-isocaranone (III C_4) predicts that it should have a lower amplitude as compared to 4-caranone in its most favorable conformation (III C_2–

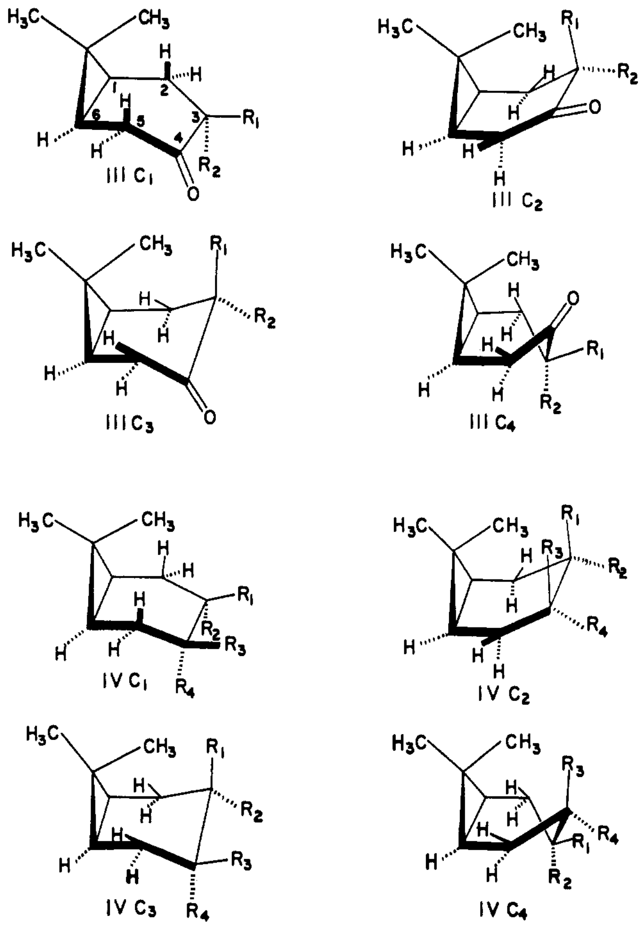

Figure 7. Possible conformations for the 4-caranones and 4-caranols.

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(34) N. S. Bhacca and D. H. Williams, "Applications of Nmr Spectroscopy in Organic Chemistry," Holden-Day Inc., San Francisco, Calif., 1964, p 158.

(35) L. M. Jackman, "Applications of Nmr Spectroscopy in Organic Chemistry," Pergamon Press Inc., New York, N. Y., 1962, p 124.

(36) W. Moffit, R. B. Woodward, A. Moscowitz, W. Klyne, and C. Djerassi, *J. Am. Chem. Soc.*, **83**, 4013 (1961).

Table II. Chemical Shifts of the 8-, 9-, and 10-Me Groups and the Hydroxyl Proton[a]

Compound	8-Me	9-Me	10-Me	(δ 8-Me) − (δ 9-Me)	OH/proton
4-Neoisocaranol	65	59	52	+6	151
4-Isocaranol	55	59	47.5	−4	246
4-Isocaranone	51.5	63	55	−11.5	...
b	43	53	56.5	−10	...
c	+8.5	+10	−1.5	...	...
4-Caranone	57	65	71	−8	...
b	44	52	62.5	−8	...
c	+13	+13	+8.5	...	...
α-(3,4)-Epoxycarene	43	60	70	−17	...
β-(3,4)-Epoxycarane	58 (59)	59 (58)	73	...	...

[a] All spectra were determined as 25% solution in carbon tetrachloride unless otherwise stated. [b] Spectra, determined in benzene as a 25% solution. [c] Difference in chemical shift, when determined in carbon tetrachloride and benzene.

Table III. Chemical Shift[a] of the Carbinyl Proton and the Coupling Constant

Compound	Peak position, cps	Preferred conformation	Coupling atoms	Dihedral angle, deg	Coupling constant Calcd	Obsd
4-Neoisocaranol	221[b]	IV C$_1$–IV C$_4$	$H_{5\beta}$–$H_{4\alpha}$	90–110	0–2	2
			$H_{5\alpha}$–$H_{4\alpha}$	10–30	7.5–9	7
			$H_{3\alpha}$–$H_{4\alpha}$	70–90	0–2	2
4-Isocaranol	176[c]	IV C$_1$–IV C$_4$	$H_{5\beta}$–$H_{4\beta}$	10–30	7.5–9	8
			$H_{5\alpha}$–$H_{4\beta}$	90–110	0–2	2
			$H_{3\alpha}$–$H_{4\beta}$	145–160	11–14	8

[a] Shift from TMS in cps. [b] Broad sextet. [c] Broad quartet.

III C$_4$) and that they should exhibit positive Cotton effects. Indeed, this was observed. The amplitude of 4-isocaranone was −122 and that of 4-caranone was −136. But the reversal of the sign of the Cotton effect suggests that the absolute configuration of these compounds should be (1*R*,3*S*,6*S*) for 4-isocaranone and (1*R*,3*R*,6*S*) for 4-caranone. This contradicts our assignments for the absolute configuration of (+)-2-carene,[12] as (1*S*,6*R*), and thereby that of (+)-3-carene, which are based on sound bases. However, recently such a reversal of the sign of the Cotton effect[37] was observed for the ketones in conjugation with the cyclopropyl group. In that case, this may be the first example wherein a reversal of the sign of the Cotton effect for a homoconjugated cyclopropyl ketone has been observed.

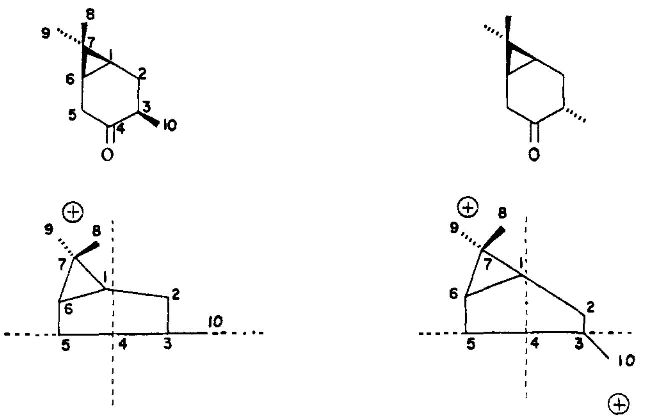

Figure 8. Octant diagrams for the favorable conformations of 4-isocaranone and 4-caranone.

There are in all four possible conformations for the 4-caranols, one pair being derived from the boat forms, as in IV C$_1$ and IV C$_2$, the other pair being derived from two possible half-chair forms, as in IV C$_3$ and IV C$_4$. The most favorable conformation for 4-caranols would be those where neither two boat forms nor half-chair forms exist. In half-chair forms, in order to avoid severe nonbonded interactions between the 8-Me and R$_1$, as in IV C$_3$ or the 8-Me and R$_3$, as in IV C$_4$, R$_1$ and R$_3$ will not be perfectly axial, but they will be quasi-axial. These considerations, based on Dreiding molecular models, are supported by the nmr study.

In an α-alkylcyclohexanol, the alkyl group is known to have a preference for the equatorial position.[38] The favorable conformation for 4-isocaranol would be IV C$_4$ and that for 4-neoisocaranol would be IV C$_2$–IV C$_1$. If this assumption is correct, the carbinyl proton in 4-neoisocaranol, being equatorial, should shift more downfield compared to that in 4-isocaranol, which has an axial disposition, according to the general observation of Eliel, *et al.*[39] (Table III). Moreover a downfield shift for the 8-Me in 4-neoisocaranol should be greater than that for 4-isocaranol, because of the greater proximity of the hydroxyl group in 4-neoisocaranol (Table II).

Further, the coupling constants between the carbinyl proton and the neighboring methine and methylene protons also support the assignment of the preferred conformations for 4-isocaranol and 4-neoisocaranol. Table III gives the coupling constants calculated according to the modified Karplus equation[40] together with the observed coupling constant on the basis of the preferred conformations for 4-isocaranol and 4-neoiso-

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(37) C. Djerassi, W. Klyne, T. Norin, G. O loff, and E. Klein, *Tetrahedron*, **21**, 163 (1965).

(38) M. Hanack, "Conformation Theory," Academic Press Inc., New York, N. Y., 1965, p 112.

(39) E. L. Eliel, M. H. Gianni, T. H. Williams, and J. B. Stothers, *Tetrahedron Letters*, 741 (1962).

(40) K. L. Williamson and W. S. Johnson, *J. Am. Chem. Soc.*, **83**, 4623 (1961).

caranol. The agreement between the calculated and observed coupling constants strongly supports the structural assignments for the various caranols and caranones.

Experimental Section

Purification of (+)-3-carene and other materials was done as described earlier.[12] Unless otherwise mentioned all glpc analysis were done on a Perkin-Elmer 226 or 154, using 150-ft Golay capillary columns; UCON LBX 550, A; Carbowax 20M, B; 1,1,1-tricyanoethoxypropane (TCEP), C; squalene, D; *m*-bis(*m*-phenoxyphenoxy)benzene (MBMA), E; and Apeizon L, F.

(−)-4-Isocaranol (2). In a 500-ml, three-necked flask equipped with a thermometer, condenser, pressure-equalizing dropping funnel, and a side arm with a serum cap, were placed (+)-3-carene (20.4 g, 150 mmoles) and tetrahydrofuran (to make a total volume of 60 ml). The mixture was cooled to 0° and, under stirring, a diborane solution in tetrahydrofuran (35.7 ml, 2.17 *M* in BH_3, 230 mmoles of H^-) was added dropwise. During the addition, hydrogen (162 ml) was evolved at 29° (750 mm). The mixture was stirred at 0° for 3 hr. Water (7.5 ml) in tetrahydrofuran (15 ml) was added dropwise by syringe for 30 min. After complete addition of water, the reaction mixture was allowed to stand for 1 hr, during which period hydrogen [2120 ml, 28° (750 mm)] was evolved. To the mixture, sodium hydroxide (3 *N*, 18 ml) was added, followed by hydrogen peroxide (30%, 18 ml) added dropwise for 50 min, carefully maintaining the reaction temperature at 44–45°. The reaction mixture was stirred for 3 hr at room temperature. The alcohol was extracted with ether (three 70-ml portions), and the extracts were mixed and dried over $MgSO_4$. When analyzed by glpc on A and B columns, only one peak was obtained. After removal of the solvent, the alcohol was distilled under reduced pressure, bp 89–90° (35 mm), $n^{20}D$ 1.4816, $d^{20}{}_4$ 0.9517, $\alpha^{20}D$ −69.1°.

Anal. Calcd for $C_{10}H_{18}O$: C, 77.87; H, 11.76. Found: C, 77.92; H, 11.71.

3,5-Dinitrobenzoate of 4-Isocaranol. A mixture of 3,5-dinitrobenzoic acid (1.06 g) and pyridine (8 ml) was cooled to 0°. Recrystallized *p*-toluenesulfonyl chloride (1.9 g) was added and the mixture shaken. 4-Isocaranol (0.8 g) was added at 0°. The mixture was stirred for 1 hr, then poured over crushed ice, and the separated product, 1.3 g, was collected. Crystallized from alcohol, it had mp 130–131.5°, $[\alpha]^{25}D$ −75.05°.

Anal. Calcd for $C_{17}H_{20}N_2O_6$: C, 58.61; H, 5.79; N, 8.04. Found: C, 58.77; H, 6.07; N, 8.33.

***p*-Nitrobenzoate of 4-Isocaranol.** This was prepared as above from *p*-nitrobenzoic acid (from methanol–water), mp 68.5–69.5°.

Anal. Calcd for $C_{17}H_{21}O_4$: C, 67.31; H, 6.98; N, 4.62. Found: C, 67.10, H, 6.99; N, 4.62.

Acid Phthalate of 4-Isocaranol. A mixture of 4-isocaranol, phthalic anhydride (2 g), and pyridine (5 ml) was heated at 100° for 30 min. The reaction mixture was poured into aqueous sodium carbonate; the unreacted anhydride was extracted with ether, and the aqueous layer was neutralized with hydrochloric acid (3 *N*). The product, 2.29 g, exhibited mp 161–162° (from methanol).

Anal. Calcd for $C_{18}H_{22}O_4$: C, 71.50; H, 7.33. Found: C, 71.32; H, 7.45.

Tosylate of 4-Isocaranol (14). To a solution of 4-isocaranol (4 g) in pyridine (6 ml) was added at 0° recrystallized *p*-tolylsulfonyl chloride, and the reaction mixture was allowed to stand at 0° for 2 days. The mixture was poured over crushed ice and extracted with ether (three 30-ml portions). The combined ether extracts were washed with sulfuric acid (1 *N*, two 25-ml portions) and with water (three 25-ml portions) and dried over $MgSO_4$. The solvent was pumped off and the residue cooled below −70°. The separated product, 5–6 g, exhibited mp 54–55° (from petroleum ether, bp 35–37°). The tosylate decomposed at room temperature to a dark brown, viscous oil.

Anal. Calcd for $C_{17}H_{24}O_3S$: C, 66.21; H, 7.85. Found: C, 66.10; H, 7.91.

(−)-4-Isocaranone (3) from Alcohol. (−)-4-Isocaranol (7.7 g, 50 mmoles) and ether (20 ml) were placed in a 100-ml flask fitted with a condenser and a dropping funnel. The chromic acid solution, prepared from sodium dichromate dihydrate (5.0 g, 16.8 mmoles) and sulfuric acid (93%, 3.7 ml) diluted to 25 ml, was added to the stirred solution for 1.5 hr maintaining the temperature at 25°. After the addition, stirring was continued for 1 hr. The upper organic layer was separated, and the aqueous phase was extracted with ether (two 35-ml portions). The combined ether extracts were washed with water, saturated bicarbonate, and water and dried over $MgSO_4$. Glpc on column A indicated only one peak, and the yield was 97.6%. The ketone was distilled under reduced pressure, yield 6.3 g (82.9%), bp 80–81° (5.3 mm), $n^{20}D$ 1.4703, $d^{20}{}_4$ 0.9510, $\alpha^{20}D$ −152.5°.

Anal. Calcd for $C_{10}H_{16}O$: C, 78.89; H, 10.59. Found: C, 79.15; H, 10.48.

The semicarbazone of 4-isocaranone had mp 208–209°, $[\alpha]D$ −90.22°.

Anal. Calcd for $C_{11}H_{19}N_3O$: C, 63.12; H, 9.15; N, 20.08. Found: C, 63.23; H, 9.29; N, 20.17.

The 2,4-dinitrophenylhydrazone of 4-isocaranone had mp 160–162°.

Anal. Calcd for $C_{16}H_{20}N_4O_4$: C, 57.83; H, 6.07; N, 16.85. Found: C, 57.58; H, 5.91; N, 17.00.

***p*-Tolylsulfonylhydrazone of 4-Isocaranone (12).** 4-Isocaranone (3 g, 19.7 mmoles) was added to a solution of *p*-tolylsulfonylhydrazine (5.1 g, 27.4 mmoles) in 120 ml of dry methanol and the mixture refluxed for 4 hr. When most of the methanol was removed and the residue cooled to −70°, there was obtained 3 g of the product, mp 133° (from methanol).

Anal. Calcd for $C_{17}H_{24}O_2N_2S$: C, 63.73; H, 7.55. Found: C, 63.94; H, 7.41.

α-(+)-3,4-Epoxycarane (8). A solution of (+)-3-carene (68 g, 500 mmoles) in chloroform (750 ml) was taken in a 3-l. four-necked flask fitted with a mechanical stirrer, thermometer, condenser, and a graduated dropping funnel. *m*-Chloroperbenzoic acid (109 g, 85% pure, 540 mmoles) in chloroform (1200 ml) was added over a 75-min period at 23–27°. After complete addition, stirring was continued at that temperature for 1 hr. The progress of the reaction was followed by glpc examination of 1-ml aliquots immediately following complete addition of the peracid. This revealed a 100% conversion of 3-carene to the epoxide within 5 min. The excess of perbenzoic acid was destroyed by slow addition of sodium bisulfite (10%) until a test with starch–iodide was negative. The mixture was transferred to a separatory funnel, and the organic layer was washed with sodium bicarbonate (10%) and saturated brine and dried over Na_2SO_4. The solvent was removed and the residue distilled under reduced pressure to obtain the product, yield 64.5 g (84.9%), bp 92–93° (23 mm), $n^{20}D$ 1.4664, $\alpha^{26.5}D$ +13.35°.

Anal. Calcd for $C_{10}H_{16}O$: C, 78.89; H, 10.59. Found: C, 78.88; H, 11.19.

(−)-4-Isocaranone from α-(+)-3,4-Epoxycarane. In a 100-ml flask equipped with a condenser and a side arm with a serum cap, were placed α-(+)-3,4-epoxycarane (7.6 g, 50 mmoles), powdered sodium (2.3 g, 0.1 g-atom), and benzene (30 ml). The mixture was refluxed under stirring. Periodically, 1 ml of the solution was removed and analyzed by glpc on column B. The progress of the reaction was as follows: 10 min, 57.3%; 40 min, 85.2%; 120 min, 96.2%; 190 min, 97.4%. The last sample analyzed for 6.1%, 3-carene; 57.8%, 4-isocaranone; 8.2%, 4-caranone; 5.4%, 4-isocaranol; 1.4%, 4-caranol; and 21.1%, unknown peak. It was worked up, and the crude material was distilled using a 30-cm Vigreux column to yield 4.1 g of the ketone, bp 98–100° (20 mm). A pure sample of 4-isocaranone was obtained by preparative glpc on a 4-ft column of Carbowax 20M (25%) on firebrick (60–80), and it had the following properties: $n^{20}D$ 1.4702, $[\alpha]^{26}D$ −140.6° (*c* 4.5, $CHCl_3$). The semicarbazone of this ketone did not depress the melting point on admixture with that obtained *via* hydroboration.

(+)-4-Neoisocaranol (5). In a three-necked flask equipped with a magnetic stirrer, thermometer, serum cap on a side arm, and a condenser with a nitrogen inlet was placed a solution of lithium aluminum hydride in tetrahydrofuran (1.20 *M*, 91.7 ml, 110 mmoles). Under stirring at 22–23°, dry methanol (13.3 ml, 330 mmoles) in tetrahydrofuran (15 ml) was added dropwise for 4.5 hr. When a little gel appeared, the addition of methanol was stopped, and the mixture was vigorously stirred until the gel dissolved. During the addition, hydrogen [8260 ml, 23° (74 mm), corresponding to 335 mmoles of hydrogen] was evolved.

4-Isocaranone (7.61 g, 50 mmoles) in tetrahydrofuran (15 ml) was then added for 15 min at 0.5° under stirring. The mixture was then stirred at room temperature for 2 hr. Water (10 ml) in tetrahydrofuran (10 ml) was then added carefully to destroy an excess of the reagent. The thick white precipitate of aluminum hydroxide was dissolved with a saturated solution of sodium potassium tartarate. The upper layer of tetrahydrofuran was removed, and the lower aqueous layer was extracted with ether. The combined extracts were washed with saturated brine solution and dried over Na_2SO_4. Removal of the solvent and distillation of the residue gave 6.8 g of the alcohol mixture. Glpc analysis on column B indicated the isomer distribution of 4-neoisocaranol to 4-isocaranol was 79:21. A pure product of 4-neoisocaranol, obtained by preparative glpc, had the following properties: bp 67° (2 mm), n^{20}D 1.4820, $d^{20}{}_4$ 0.9543, α^{20}D +36.29°.

3,5-Dinitrobenzoate of 4-Neoisocaranol. Prepared as described above, 3-neoisocaranol (0.38 g) gave 3,5-dinitrobenzoate (0.69 g), mp 104–105.5° (from aqueous ethanol), $[\alpha]$D +3.51°.

Anal. Calcd for $C_{17}H_{20}N_2O_6$: C, 58.61; H, 5.79; N, 8.04. Found: C, 58.54; H, 5.88; N, 8.08.

The **p-nitrobenzoate of 4-neoisocaranol** was prepared as described above; mp 78–79.5°.

Anal. Calcd for $C_{17}H_{21}NO_4$: C, 67.31; H, 6.98; N, 4.62. Found: C, 67.59; H, 6.82; N, 4.55.

Tosylate of 4-Neoisocaranol (15). Prepared as described above, 4-neoisocaranol (4 g) gave the tosylate (3.6 g), mp 39–42° (from petroleum ether at −70°).

Anal. Calcd for $C_{17}H_{25}NO_3S$: C, 66.21; H, 7.85. Found: C, 65.12; H, 7.93.

Reduction of 4-Isocaranone with Lithium Tri-*t*-butoxyaluminohydride. (−)-4-Isocaranone (7.6 g, 50 mmoles) was added to lithium tri-*t*-butoxyaluminohydride in tetrahydrofuran (100 ml, 107.6 mmoles) at 0° under stirring. It was periodically tested by analyzing aliquots of the reaction mixture for the content of ketones and alcohols by glpc on column A. Reduction was complete in a matter of minutes. There was obtained 7.0 g of crude alcohols, 41.4% 4-neoisocaranol and 58.6% 4-isocaranol.

Oxidation of 4-Neoisocaranol. 4-Neoisocaranol was oxidized by the ether–chromic acid procedure, as described above, to yield 4-isocaranone. A purified sample by glpc on Carbowax 20M showed n^{20}D 1.4703, $[\alpha]^{25}$D −148.7° (c 5.1, $CHCl_3$). Glpc analysis on column C gave a single peak, and the peak height increased when admixed with the ketone obtained by the oxidation of 4-isocaranol. The semicarbazone, mp 208–209°, showed no depression with the semicarbazone of the hydroboration–oxidation ketone.

(+)-4-Caranol (7) was prepared by the hydrogenation of β-(−)-3,4-epoxycarane.[41] The latter compound was prepared by the epimerization procedure utilized by Kuczynski:[10,11] α-(+)-3,4-epoxycarane → 3β,4α-dihydroxy-*trans*-carane-4-tosylate → β-(−)-3,4-epoxycarane.

The solution of the β-epoxide (7.61 g, 50 mmoles) in ethanol (20 ml) was charged in a 100-ml autoclave, and Raney nickel (W-4) catalyst[42] was added. Hydrogenation was carried out at 100° with an initial pressure of 115 atm. Glpc analysis on column A revealed that only 31% of the reaction was over in 4 hr. Therefore, the hydrogenation was continued for further 19 hr. After removal of the catalyst by filtration and solvent by evaporation, the reaction product was analyzed by glpc on column A. It was a mixture of the composition 79.3% alcohols, 3.1% ketones, 11.5% β-epoxide, and 6.1% others. The alcoholic fraction was separated by preparative glpc on a 6-ft column of Carbowax 20M–firebrick (60–80). The alcoholic portion when analyzed by glpc on column A gave the composition 4.6% 4-neoisocaranol, 24.2% 4-neoisocaranol, 16.4% 4-isocaranol, and 54.8% 4-caranol. Similarly, when α-(−)-3,4-epoxycarane was reduced with Raney nickel, 11% of 4-neocaranol, traces of 4-isocaranol, 88.6% of 4-caranol, and 0.4% of 4-neoisocaranol were obtained.

Acid Phthalate of 4-Caranol. The mixture of crude caranols (12.9 g), freshly distilled phthalic anhydride (11.9 g), and dry pyridine (15 ml) was heated at 100° for 5 hr. It was poured into sodium carbonate (5%, 150 ml), and the neutral compounds were extracted three times with petroleum ether (bp 35–37°). The clear aqueous layer was then acidified with H_2SO_4 (30%) to congo red. The separated, gum-like product was extracted three times with ether. The combined ether extracts were washed with brine, dried over Na_2SO_4, and evaporated to a viscous liquid which solidified after 5 days at room temperature. The solid was separated by filtration and washed with petroleum ether (bp 35–37°). Crystallized from methanol–petroleum ether, it had mp 128–129°, yield 4.2 g.

Anal. Calcd for $C_{18}H_{22}O_4$: C, 71.50; H, 7.33. Found: C, 71.27; H, 7.35.

(+)-4-Caranol (7). Hydrolysis with potassium hydroxide in ethanol gave (+)-4-caranol, purified by preparative glpc on Carbowax 20M (20%)–firebrick (60–80) to give a sample having the properties mp 42.5–43.5°, α^{20}D +65.4°.

Anal. Calcd for $C_{10}H_{18}O$: C, 77.87; H, 11.76. Found: C, 77.72, H, 11.75.

(−)-4-Caranone (4). 4-Caranol was oxidized to the ketone by the ether–chromic acid procedure. There was realized a 98% yield of ketone of composition 96.2% 4-caranone and 3.8% 4-isocaranone. Some epimerization occurred during preparative glpc yielding a product (83.3% 4-caranone and 16.7% 4-isocaranone) with n^{20}D 1.4705, $d^{20}{}_4$ 0.9523, $[\alpha]^{20}$D −88°.

Anal. Calcd for $C_{10}H_{16}O$: C, 78.87; H, 10.59. Found: C, 79.07; H, 10.84.

Equilibration of 4-Isocaranone and 4-Caranone. 4-Isocaranone was dissolved in dilute sodium ethoxide in ethanol at 25°. Aliquots were removed, and the ketone was isolated and analyzed by glpc. The results were (time in hours, per cent of 4-isocaranone): 0, 99.8; 0.5, 89.9; 1.0, 90.3; 2.0, 90.6; 5.0, 90.1; 17, 90.2. A similar experiment was carried out with 4-caranone: 0, 86.6; 0.5, 9.3; 1.0, 8.4; 2.0, 9.4; 5.0, 9.4; 17, 9.8.

Under the same conditions, but at 74°, the equilibrium distribution was 84% 4-isocaranone to 16% 4-caranone.

(−)-*cis*-4-Carene (16). A mixture of the tosylate of 4-isocaranol (3.08 g, 10 mmoles) and potassium *t*-butoxide (60 ml of 1 *M*) in *t*-butyl alcohol was heated at 80° for 29 hr. After separation of the precipitated potassium salt, water was added and the hydrocarbon extracted with *n*-pentane. Preparative glpc on a 6-ft column of Carbowax 20M (25%)–firebrick (60–80) separated the *cis*-4-carene (81%) from the 3-carene (19%). The *cis*-4-carene exhibited the properties n^{20}D 1.4662, $[\alpha]^{29.7}$D −141.75° (c 4, $CHCl_3$).

(−)-*cis*-Carane from Hydroboration–Protonolysis. In a 300-ml flask was placed (+)-3-carene (13.6 g, 100 mmoles), diglyme (40 ml), and a standard solution of $NaBH_4$ in diglyme (46.9 ml of 0.96 *M*). In the mixture, immersed in an ice bath, was added boron trifluoride (3.65 *M*, 16.4 ml, 60 mmoles) in diglyme over 40 min with stirring. After 2 hr at 25°, the excess of hydride was destroyed by addition of glycerol (3 ml), followed by propionic acid (11 ml, 15 mmoles). The flask was heated for 6 hr at 150–152°. After cooling to room temperature, the reaction mixture was diluted with NaOH (3 *N*, 75 ml). The upper layer was separated, washed with cold water to remove diglyme, and dried over $MgSO_4$. The analysis of the product by glpc on columns C and D indicated that it is essentially pure *cis*-carane. The crude product was purified by preparative glpc using Carbowax 20M (25%)–firebrick (60–80). It had the properties n^{20}D 1.4542, $[\alpha]$D −17.8° (c 2.92, benzene).

(−)-*cis*-Carane from Hydrogenation of (+)-3-Carene. The procedure was similar to that described for the hydrogenation of (+)-2-carene.[12] After complete hydrogenation, the catalyst was separated by filtration, dichloromethane and water were added, and the organic layer was separated, washed with bicarbonate solution (10%) and saturated brine solution, and dried over $MgSO_4$. The solvent was removed, and the residue was distilled. There was obtained 12.1 g (90%) of the product, bp 166° (755 mm). The glpc analysis on column D indicated that it was a mixture: 94% *cis*-carane, 4% *trans*-carane, and 2% an unidentified product possibly, 1,1,4-trimethylcycloheptane. The product, purified by preparative glpc on Carbowax 20M–firebrick (60–80), had the properties n^{20}D 1.4535, $[\alpha]$D −13.0° (c 3.7, benzene).

(−)-*cis*-Carane from Reduction of *p*-Tolylsulfonylhydrazone of 4-Isocaranone. To a solution of the *p*-tosylhydrazone of 3-isocaranone (0.32 g, 1 mmole) in dioxane (40 ml) was added sodium borohydride (2 g, 53 mmoles), and the mixture was boiled under reflux. Periodically, 1-ml aliquots were removed and analyzed by glpc on column D. *cis*-Carane (23%) was obtained within 45 min, and there was no improvement in the yield over an additional 6 hr. The product was 100% pure. It was identical with the *cis*-carane from hydroboration–protonolysis and the *cis*-carane from 2-carene.[21] The absence of *trans*-carane or 1,1,4-trimethylcycloheptane was established.

(−)-*cis*-Carane from Hydrogenation of *cis*-4-Carene. The usual hydrogenation procedure was followed.[26] (−)-*cis*-4-Carene (0.06 g, 0.044 mmole) was converted into *cis*-carane, identical with the previous samples.

Enol Acetates (17 and 18) from 4-Isocaranone. In a 10-ml flask, 4-isocaranone (0.152 g, 10 mmoles), isopropenyl acetate (1.5 g, 15 mmoles), and *p*-toluenesulfonic acid (0.019 g, 1 mmole) were placed and heated at 100° to reflux under a Vigreux column. The acetone formed was distilled off gradually. At different times, a portion (10 μl) of the reaction mixture was removed, extracted, and analyzed for the content of enol acetates. The results are summarized in Table IV. After 4 hr, the mixture was cooled and diluted with ether, and the product was fractionated by preparative glpc. Fractions C and D, the enol acetates, were not well separated and

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[41] A detailed study of the hydrogenation of several terpene epoxides over Raney nickel has been carried out and will shortly be reported.

[42] R. P. Linstead, J. A. Elvidge, and M. Whalley, "A Course in Modern Techniques of Organic Chemistry," Butterworth and Co., Ltd., London, 1955, p 91.

Table IV. Conversion of 4-Isocaranone to Enol Acetates

Reaction time, hr	Conversion, %	Product compn, % B	C	D
1	51.4	21.5	36.8	41.7
2	74.2	12.9	41.3	45.8
3	88.1	12.9	42.6	44.5
4	99.4	13.8	41.9	44.3

were collected together. Fractions A and B were 4-caranone and 4-isocaranone, respectively, yield 1.3 g, n^{20}D 1.4727, $\alpha^{32.4}$D −27.00°.

Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 73.91; H, 9.33.

Glpc analysis of the fraction showed that it is a mixture of two enol acetates, 4-acetoxy-3-carene and 4-acetoxy-*cis*-4-carene, in the ratio of 49:51. Nmr analysis of the mixture confirmed the conclusion. (In the absence of isopropenyl acetate, the catalyst, *p*-toluenesulfonic acid, opens the cyclopropane ring of 4-isocaranone.)

Ketonization of the Enol Acetates. A mixture of the two enol acetates of 4-isocaranone (0.097 g, 0.5 mmole), composed of 50% 4-acetoxy-3-carene and 50% 4-acetoxy-*cis*-4-carene, and *n*-propylamine, was heated at 50°. At different times, aliquots were removed and analyzed by glpc using E and F columns. Under identical conditions another blank experiment with 4-isocaranone (instead of enol acetates) was also conducted to ensure that there is no epimerization of 4-isocaranone in the presence of *n*-propylamine. The results are summarized in Table V.

Table V. Ketonization of Enol Acetates

		Composition of ketones, %			
				Blank	
Time, hr	Ketone yield, %	4-Iso-caranone	4-Car-anone	4-Iso-caranone	4-Car-anone
0	0	0	0	98.1	1.9
0.17	38.3	98.3	1.7	97.9	2.1
1.0	74.8	97.9	2.1	98.3	1.7
2.0	89.3	98.1	1.9	98.6	1.4
3.0	94.1	98.0	2.0	98.1	1.9

Oxidation of the Alcohol Mixture by Beckmann's Procedure. The alcohol mixture (0.175 g), containing the four alcohols, 4.6% 4-neocaranol, 24.2% 4-neoisocaranol, 16.4% 4-isocaranol, and 54.8% 4-caranol, and ether (1.5 ml) were placed in a 10-ml flask equipped with a condenser and a dropping funnel. The chromic acid solution prepared from potassium dichromate (0.154 g), concentrated sulfuric acid (0.115 g), and water (1.73 ml) was added to the stirred solution. At different times, aliquots were removed and analyzed by glpc on column B. The results are summarized in Table VI.

Table VI. Chromic Acid Oxidation of Alcohols

Reaction time, hr	Ketone yield, %	Compn of caranones, % 4-Iso	4-	Compn of caranols, % 4-Neo	4-Neoiso	4-Iso	4-
0	0	0	0	4.6	24.2	16.4	54.8
0.5	51.7	64.7	35.3	1.2	5.5	16.4	76.9
1.0	61.7	65.4	34.6	1.3	3.3	14.4	81.0
2.0	70.7	64.9	35.1	2.3	1.9	15.5	80.3
4.0	76.9	62.4	37.6	2.2	0	12.3	85.5
6.5	76.8	60.4	39.6	...	...	...	...
23.0	83.8	57.7	42.3	...	...	...	...

Elimination Reactions of the Tosylates of 4-Isocaranol and 4-Neoisocaranol. The reaction mixture of the respective tosylate (0.308 g, 1 mmole), potassium *t*-butoxide (7 mmoles) in *t*-butyl alcohol (7 ml), and 81.35 μl of *n*-nonane as an internal standard was immersed in a thermostat 50.3°. Aliquots (0.2 ml) were tested periodically by glpc on column A. The results are summarized in Table VII.

Table VII. Elimination Reactions

Reaction time, hr	Carene yield, %	Composition of carenes, % 3-	4-
	Tosylate of 4-Isocaranol		
0.5	0.6	...	...
1.0	1.6	...	...
2.5	13.3	17.4	82.6
5.0	21.2	16.7	83.3
8.0	38.3	20.8	79.2
12.0	49.5	20.6	79.4
27.0	74.6	19.2	80.8
33.0	77.0	19.6	80.4
Av	...	(19.0)	(81.0)
	Tosylate of 4-Neoisocaranol		
0.17	69.4	4.9	95
0.5	71.1	4.4	95.6
1.0	73.2	5.6	94.4
2.5	76.1	5.3	94.7
Av	...	(5.0)	(95.0)

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