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STEREOCHEMISTRY OF ELECTROPHILIC SUBSTITUTION OF (+)-3-CARENE

PRINS AND FRIEDEL–CRAFTS-ACETYLATION REACTIONS

P. J. KROPP, D. C. HECKERT and T. J. FLAUTT

The Procter & Gamble Company, Miami Valley Laboratories, Cincinnati, Ohio 45239

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Abstract—Evidence is presented that the previously studied Prins and Friedel–Crafts-acetylation reactions of (+)-3-carene (IV) each involve electrophilic attack *trans* to the cyclopropyl ring to give the products I and IX, having the newly introduced C-4 substituents in an α-orientation. Through oxidation, I and IX were converted to a common intermediate, the ester VI. Analysis of the NMR spectra of the epimeric esters VI and VII and ketones IX and X with the aid of double decoupling techniques permitted assignment of the 4α and 4β configurations, respectively. Additional support for the assignments I and IX is provided by examination of the NMR spectra of the epoxides XII and XIII.

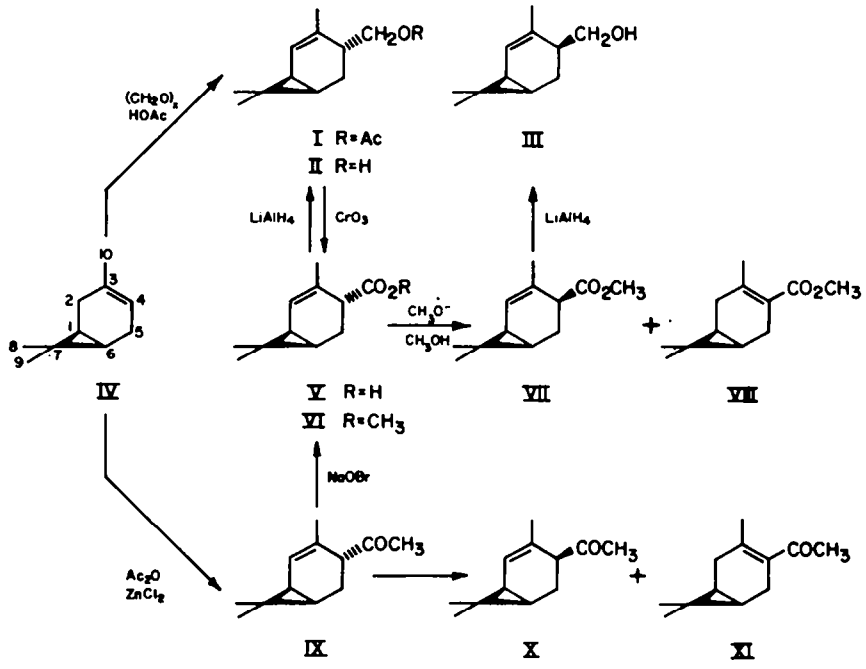
IT RECENTLY has been demonstrated that with (+)-3-carene (IV) peracid epoxidation,[1] osmium tetroxide hydroxylation,[1] photosensitized oxidation,[2] and hydroboration[3] all proceed selectively via attack *trans* to the cyclopropane ring, and both steric and electronic effects have been considered as possible controlling stereochemical factors.[1] However, since relatively little is known about the extent or distribution of charge separation during the course of each of these four particular reactions, which are generally considered to proceed via cyclic mechanisms, it was of interest to examine the behavior of (+)-3-carene (IV) toward other types of electrophilic reagents, such as those which involve attack by a cationic species. Evidence is now presented that the Prins and Friedel–Crafts-acetylation reactions of IV likewise involve attack *trans* to the cyclopropane ring, affording the 4α derivatives I and IX, respectively.

RESULTS

As has previously been reported, treatment of (+)-3-carene (IV) with paraformaldehyde in acetic acid affords a single principal product,[4,*] for which convincing evidence in support of the structural assignment I (except for stereochemistry) has been presented.[4,†] The analogous 2-carene structure IX has also been assigned to the principal product from treatment of (+)-3-carene (IV) with acetic anhydride in the presence of Lewis acids, but the stereochemistry at C-4 was not elucidated

* In our hands a mixture consisting principally of acetate I (82%) accompanied by at least 4 minor products, as evidenced by gas chromatographic analysis, was obtained. On the basis of spectral data one of the minor products obtained, after saponification, is assigned the structure (−)-3(10)-carene-4-methanol.[5]

† The 4α stereochemical assignment II for the corresponding alcohol has previously been depicted, but without supporting comment.[6]



and, indeed, little evidence to support the structural assignment IX was presented.[8]

In an effort to interrelate the products I and IX, it was found that both chromic acid oxidation[9] of the alcohol II[4] and sodium hypobromite oxidation of IX afforded the carboxylic acid V, which was characterized as the methyl ester VI. From the NMR spectrum of VI, which is discussed in detail below, it is clear that the cyclopropane ring and double bond remained intact during the oxidation. LAH reduction of VI regenerated the alcohol II, both confirming the structural assignment VI and verifying that epimerization at C-4 had not occurred during oxidation of II. These data also corroborate the basic 4-acetyl-2-carene structural assignment IX and establish that I and IX have the same configuration, whether α or β, at C-4.

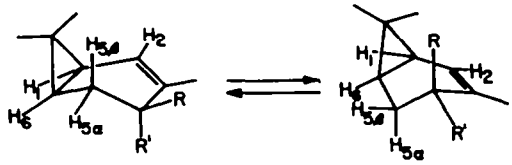
Since stereochemical assignments are usually facilitated by the availability of data for both members of an epimeric pair, the ester VI was treated with methanolic sodium methoxide. This afforded two isomeric esters, in addition to recovered starting material. The first isomer is assigned the epimeric structure VII on the basis of the NMR spectrum, which again shows the presence of an unaltered cyclopropane ring and double bond (see below). LAH reduction of VII generated an alcohol isomeric with I, but having an NMR spectrum almost identical with that of I, and hence assigned the structure III.

The major product of the base-catalyzed isomerization of ester V is assumed to be the corresponding conjugated ester VIII. This assignment is attested to by the absence of any absorption in the NMR spectrum attributable to a vinylic proton but the presence of peaks corresponding to a vinylic methyl group (τ 8·08) and two cyclopropyl protons (9·25). Also consistent with the assignment VIII are the appearance of IR and UV absorptions typical of an α,β-unsaturated ester (5·80 and 6·06 μ and 224 mμ).

Products analogous to the esters VII and VIII were obtained by similar treatment

of the acetyl derivative IX with methanolic sodium methoxide or, preferably, sodium hydride–benzene.* Assignment of these products as the 4β epimer X and the conjugated isomer XI was facilitated by the close similarity of their spectral data with those of the esters VII and VIII.† With authentic specimens of the epimeric alcohol III and ketone X each available for reference, it could be shown that no detectable amount of either of these isomers is formed during the preparation of II or IX, respectively, from (+)-3-carene.

With the epimeric esters VI and VII both in hand, as well as the epimeric ketones IX and X, it was possible to make stereochemical assignments at C-4 by analysis of their NMR spectra. This will be discussed in detail for the ester series. Examination of Dreiding models indicates that only the two conformations A and B are available to the esters. In the conformation B there is a severe interaction between the 8-Me group and the 4β substitutent which precludes any significant contribution by that form. Hence the NMR splitting patterns are assumed to be governed principally by the spatial relationships of conformations VIA and VIIA.



VI R=$H_{4\beta}$, R'=CO_2CH_3

VII R=CO_2CH_3, R'=$H_{4\alpha}$

TABLE 1. ESTIMATION OF DIHEDRAL ANGLES FOR VIA AND VIIA

x, y	$\theta_{x,y}$ (°)
2, 4α	100
2, 4β	20
4α, 5α	57
4α, 5β	175
4β, 5α	63
4β, 5β	56

Estimation from a model of conformation A gave the dihedral angles listed in Table 1. From these relationships it would be expected that $H_{4\alpha}$ of the β-ester VII will couple with the two adjacent protons $H_{5\alpha}$ and $H_{5\beta}$ with a "small" ($J_{4\alpha,5\alpha}$) and a "large" coupling constant ($J_{4\alpha,5\beta}$), respectively.‡ It should also couple with the vinylic proton H_2 with a relatively large allylic coupling constant ($J_{2,4\alpha}$) of 2–3 Hz

* Although the latter method afforded higher yields of the β epimer X, two additional products were obtained which are tentatively assigned the structures α-methyl-2-carene-4-methanol and 2-acetyl-*p*- or 6-acetyl-*m*-cymene.[10]

† The isomers X and XI were also obtained as by-products of the sodium hypobromite oxidation of IX. However, the close spectral similarity between the acetyl series IX–XI and ester series VI–VIII assures that a configurational assignment at C-4 based on this oxidation is not invalidated by an epimerization of the ketone prior to oxidation.

‡ In the case of steroids "large" is 8–14 and "small" 1–7 Hz.[11]

because the C_4—$H_{4\alpha}$ bond is parallel to the π orbitals of the double bond.[13] On the other hand, $H_{4\beta}$ of the α-ester VI would be expected to display two relatively small couplings with the H_5 protons and a small allylic coupling with H_2.

The NMR spectra of the esters VI and VII are summarized in Table 2, and the results of spin-coupling analysis for the two isomers are given in Table 3. It is possible to analyze the $H_{4\beta}$ band of VI directly for the coupling constants $J_{4\beta,5\alpha}$ and $J_{4\beta,5\beta}$ (Fig. 1). However, the corresponding $H_{4\alpha}$ band for the isomer VII is so broad and complicated (Fig. 2E) that spin decoupling techniques were employed. Decoupling the vinylic proton H_2 from $H_{4\alpha}$ permitted analysis of this band for $J_{4\alpha,5\alpha}$ and $J_{4\alpha,5\beta}$ (Fig. 2F). It was not possible to measure the value of the allylic coupling constant

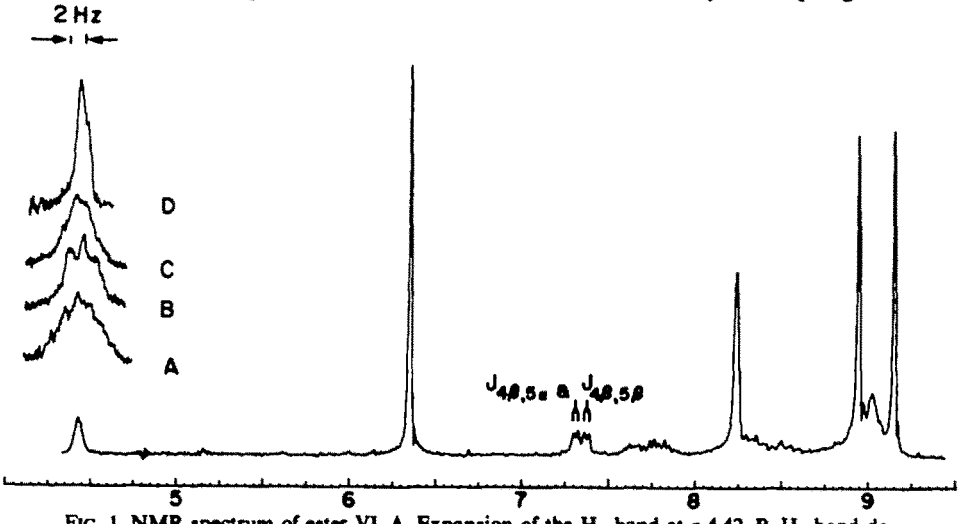


FIG. 1. NMR spectrum of ester VI. A. Expansion of the H_2 band at τ 4·42. B. H_2 band decoupled from Me-10. C. H_2 band decoupled from H_1 and H_6. D. H_2 band decoupled simultaneously from Me-10, H_1, and H_6.

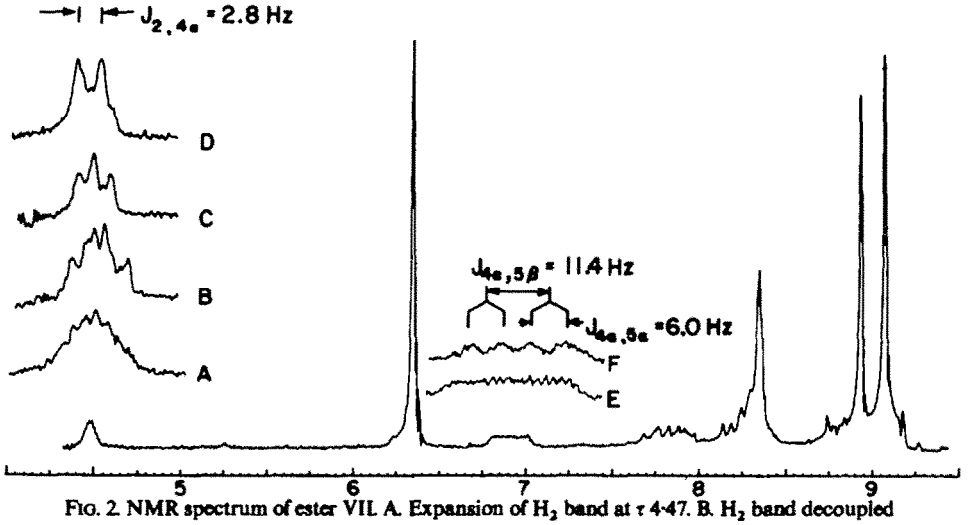


FIG. 2. NMR spectrum of ester VII. A. Expansion of H_2 band at τ 4·47. B. H_2 band decoupled from Me-10. C. H_2 band decoupled from H_1 and H_6. D. H_2 band decoupled simultaneously from Me-10, H_1, and H_6. E. Expansion of $H_{4\alpha}$ band at τ 6·90. F. $H_{4\alpha}$ band decoupled from H_2.

$J_{2,4\alpha}$ directly by decoupling $H_{4\alpha}$ from the two H_5 protons, however, because one of these latter bands is not sufficiently far removed from the band for $H_{4\alpha}$. Instead, an indirect method was used which consisted of decoupling all of the protons from the vinylic proton H_2 except for $H_{4\alpha}$. For this experiment it was necessary to decouple the Me-10 protons and the two cyclopropyl protons H_1 and H_6. Since the latter two protons appear to have the same chemical shift, a total of only two decoupling frequencies was required. When the Me-10 and H_1 and H_6 protons were irradiated simultaneously, the broad H_2 band collapsed to a relatively sharp doublet displaying $J_{2,4\alpha} = 2{\cdot}8$ Hz (Fig. 2D). When the same experiment was performed with isomer VI, the vinyl absorption became a sharp singlet, displaying residual coupling of less than 1·0 Hz (Fig. 1D). From these data the stereochemical assignments VI and VII can be confidently assigned. A similar analysis of the spectra of ketones IX and X is summarized in Tables 2 and 3. It can be seen that the two series of compounds display almost identical spectra.

TABLE 2. NMR SPECTRA OF ESTERS VI–VII AND KETONES IX–X[a]

Assignment	4α Isomer		4β Isomer	
	VI	IX	VII	X
H_2	4·42	4·41	4·47	4·41
MeO—	6·34	—	6·34	—
H_4	7·33	7·38	6·90	6·78
H_5	7·72	~7·8[b]	7·84	~7·8[b]
Ac—	—	7·86	—	7·87
Me-10	8·25	8·29	8·34	8·36
H_5	~8·4[c]	~8·3[c]	~8·2[c]	~8·35[c]
Me-9	8·95	8·92	8·93	8·92
Me-8	9·14	9·14	9·07	9·07
H_1 and H_6	9·03	9·02	9·13[d,e]	~9·10[d]

[a] τ-values.
[b] Obscured by Ac—band.
[c] Obscured by Me-10 band.
[d] Obscured by Me-8 band.
[e] Measured indirectly by the spin decoupling frequency necessary to sharpen the H_2 band.

TABLE 3. SPIN COUPLING CONSTANTS DETERMINED FROM NMR SPECTRA OF ESTERS VI–VII AND KETONES IX–X (Hz)

Coupling constant	4α Isomer		4β Isomer	
	VI	IX	VII	X
$J_{2,4}$	<1·0	<1·0	2·8	2·7
$J_{4,5\alpha}$	2·8[a]	~2·0[a]	6·0	6·4
$J_{4,5\beta}$	5·8[a]	6·4[a]	11·4	10·6

[a] Assignments may be reversed.

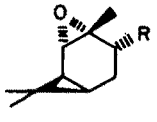
It has recently been noted that the difference in chemical shifts of the 8- and 9-Me groups is useful in characterizing 2- and 3-carenes.[1,13] The parent hydrocarbons display differences of 0·19–0·20 and 0·26–0·27 ppm, respectively. As can be seen in Table 4, the 3-carenes VIII and XI and the 2-carene 4α derivatives I, II, VI, and IX display differences close to these values. The 4β-methanol derivative III is also in line, but the differences are a little low for the 4β-acetyl derivative X and the 4β ester VII, principally because of a paramagnetic shift of the 8-methyl group relative to that of the corresponding 4α isomers. This perhaps reflects some deshielding of the 8-Me protons by the carbonyl groups of the 4β substituents and indicates that caution must be exercised in applying this criterion to 4β-substituted 2-carenes.

TABLE 4. DIFFERENCES IN CHEMICAL SHIFTS OF 8- and 9-Me GROUPS OF 2- AND 3-CARENES

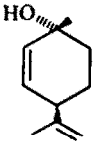
Compound	Difference (ppm)
3-Carene (IV)	0·26,[a] 0·27[b]
4-Carboxylic acid, methyl ester (VIII)	0·29
4-Acetyl- (XI)	0·28
2-Carene	0·19,[b] 0·20[a]
-4α-Methanol (II)	0·19
-4α-Methanol acetate (I)	0·19
-4α-Carboxylic acid, methyl ester (VI)	0·19
4α-Acetyl- (IX)	0·22
-4β-Methanol (III)	0·18
-4β-Carboxylic acid, methyl ester (VII)	0·14
4β-Acetyl- (X)	0·15

[a] Ref. 1. [b] Ref. 14.

Additional evidence for the 4α assignment in the case of the acetyl derivative IX was afforded by treatment of IX with *m*-chloroperbenzoic acid to afford the epoxide XIII, which displays in the NMR spectrum a clean triplet at τ 7·31 (J = 5·5 Hz) for $H_{4\beta}$. Such a triplet is characteristic for an equatorial-type proton which experiences small, approximately equal coupling with each of a pair of adjacent protons.[11] A second one-proton band which appears as a sharp singlet at τ 7·14 (width at half-height 2·6 Hz *vs.* 0·8 Hz for TMS) is assumed to be the epoxy proton H_2. This assignment is supported by the fact that a similar one-proton singlet at τ 7·16 is displayed by the epoxide XII, obtained by similar peracid treatment of acetate I. That this proton appears as a singlet in both cases suggests an α configuration for the epoxide group in XII and XIII. For, if it is assumed that the epoxides exist preferentially in a



XII R = CH_2OAc
XIII R = $COCH_3$
XIV R = H

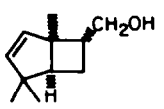


XV

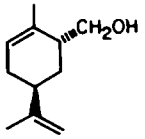
type-A conformation, $\theta_{1,2\beta} \approx 78°$ in the α-epoxy isomers and $J_{1,2\beta}$ should be ≈ 0,[14] whereas $\theta_{1,2\alpha} \approx 28°$ in the β isomers and $J_{1,2\alpha}$ should be ≈ 4 Hz.[14,*]

DISCUSSION

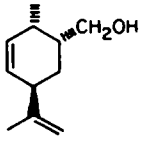
It is seen from the foregoing data that the Prins and Friedel–Crafts-acetylation reactions, which presumably involve attack by a positively charged species, each proceed selectively via attack from the α side of 3-carene—a selectivity exactly analogous to that previously observed with peracid epoxidation,[1] osmium tetroxide hydroxylation,[1] photosensitized oxidation,[2] and hydroboration[3] of 3-carene (IV). With the 4α configuration of alcohol II confirmed, the stereochemical assignments previously advanced for the photochemical (XVI and XVII)[16] and thermal (XVIII)[7] transformation products of II are thus now corroborated. At the same time, however, the intriguing question of why attack occurs selectively from the α side is again raised.



XVI



XVII



XVIII

3-Carene is conformationally restricted to two boat forms, IVA and B. Because of top side shielding by the 8-Me group, conformation IVB can undergo electrophilic attack only *trans* to the cyclopropane ring, whereas the open form IVA appears from an examination of Dreiding models to be susceptible to both *cis* and *trans* attack. However, NMR studies have recently led to the surprising conclusion that 3-carene exists preferentially in the folded form IVB,[1,13] despite the rather severe interaction in this form of the 8-Me group with the π orbitals of the double bond.† This predominant existence in conformation IVB could in itself account for the high preference for *trans* attack.

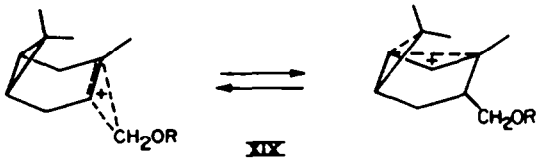
IV A IV B

In addition, however, it might also be noted from previous studies that electrophilic attack on 3-carene might be further facilitated by assistance of the cyclopropane ring,[1] a factor which could only be available in the case of α-side approach to IVB. It is generally agreed that attack in the Prins reaction involves a cyclic transition state,[17,18] such as that shown in XIX,[18] and it has previously been demonstrated that a bridged intermediate of this type, in which the 6-membered ring is constrained to a boat form, is favorably disposed toward involvement by the cyclopropane ring.[1] However,

* The preparation of epoxides XII and XIII is of additional interest in light of the recent report that attempted preparation of the epoxide XIV by treatment of 2-carene with peracetic acid gave only the rearranged alcohol XV.[15]

† The center-to-center distance between the methyl group and double bond is estimated from Dreiding models to be 2·2 A.

no products resulting from rearrangement of the cyclopropane ring, which would lend support to such an argument, were detected in this case. It is hoped that additional studies will answer more clearly the question of which factors are involved in controlling the stereochemical behaviour of 3-carene.



XIX

EXPERIMENTAL

Optical rotations were measured in abs EtOH, and IR spectra were obtained on neat samples with a Perkin–Elmer Infracord spectrophotometer. M.p.s were determined on a microhotstage and are calibrated and corrected. Gas chromatographic analyses were performed on an Aerograph model 90P or 202B instrument using 10-ft × 0·25-in columns packed with 20% Carbowax 20M or 20% diethylene glycol succinate on 60/80 mesh Chromosorb W. NMR spectra were determined in $CDCl_3$ soln with a Varian model HA-100 spectrometer using TMS as an internal standard. Spin decoupling was achieved by audio modulation of the magnetic field with two oscillators and amplifiers matched by a transformer to the spectrometer probe. The details of this apparatus will be given elsewhere. Mass spectra were obtained using an Atlas CH-4 or SM-1 spectrometer.

(+)-2-Carene-4α-carboxylic acid (V)

In a typical reaction a soln containing 2·00 g of II[4] in 100 ml acetone was titrated with 6·0 ml 4N CrO_3 according to the Jones procedure.[9] Isolation in the usual manner followed by chromatography through 30 g of silica gel gave, on elution with 1:1 benzene–hexane, 625 mg (29% yield) of V as a colorless liquid which was further purified by short-path distillation at 100° (0·3 mm); $[\alpha]_D^{27}$ +252° (*c* 1·05); λ_{max} 5·88 μ; λ_{max} 206 mμ (ε, 5800); NMR spectrum: τ 4·44 (1, m, CH-2), 7·32 (1, m, CH-4), 8·21 (3, s, Me-10), 8·95 (3, s, Me-9), and 9·15 (3, s, Me-8);* *m/e*: 180, 135, 134 and 119. Treatment of similar material from another run with diazomethane followed by short-path distillation at 82° (1·5 mm) gave the *methyl ester* VI as a colorless liquid, $[\alpha]_{5461}^{27}$ +314° (*c* 1·23); λ_{max} 5·74 μ; λ_{max} 206 mμ (ε, 5700). (Found: C, 74·6; H, 9·4. $C_{12}H_{18}O_2$ requires: C, 74·2; H, 9·3%.)

Base-catalyzed isomerization of ester VI

A soln containing 659 mg of VI and a small piece Na metal in 5 ml MeOH was heated under reflux in an atmosphere of N_2 for 24 hr. After cooling, the mixture was poured onto 150 ml sat. NaCl aq, acidified with conc HCl and extracted with three 100-ml portions ether. The combined ether extracts were washed with 150 ml sat. NaCl aq, dried over Na_2SO_4, and concentrated by distillation to give 807 mg of a dark brown oil which was shown by gas chromatography to consist of recovered ester VI (40%) and two additional principal products (8 and 49%).

Isolation of the minor product by preparative gas chromatography gave *(+)-2-carene-4β-carboxylic acid, methyl ester* (VII) as a colorless liquid which was further purified by short-path distillation at 87° (1·5 mm); $[\alpha]_{5461}^{27}$ +151° (*c*, 1·52); λ_{max} 5·74 μ. (Found: C, 74·6; H, 9·7. $C_{12}H_{18}O_2$ requires: C, 74·2; H, 9·3%).

Similar isolation of the major product followed by short-path distillation at 85–86° (1·0 mm) gave *(+)-3-carene-4-carboxylic acid, methyl ester* (VIII) as a colorless liquid, $[\alpha]_{5461}^{27}$ +25° (*c*, 1·36); λ_{max} 5·80 and 6·06 μ; λ_{max} 224 mμ (ε, 5090); NMR spectrum: τ 6·34 (s, 3, MeO—), 8·08 (s, 3, Me-10), 8·99 (s, 3, Me-9), and 9·28 (m, 5, Me-8, CH-1 and -6); *m/e*: 194, 179, 163, 151, 147, 138, 137, 135 and 119. (Found: C, 74·4; H, 9·4. $C_{12}H_{18}O_2$ requires: C, 74·2; H, 9·3%.)

(+)-2-Carene-4α-methanol (II) *and (−)-3(10)-Carene-4-methanol*

To a soln containing 16 mg LAH in 15 ml anhyd ether was added 83 mg of VII, and the resulting

* Indicates multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, and m = unresolved multiplet), integration, coupling constant (Hz), and assignment; *m/e* values reported include the parent ion peak, if present, and other significantly large peaks appearing above the lowest value listed.

mixture was stirred at 27° for 24 hr under an atmosphere of N_2. Isolation in the usual manner gave 81 mg of a pale yellow oil. Purification by preparative gas chromatography followed by short-path distillation at least 4 minor products as evidenced by gas chromatography, Isolation of the principal component (m, 1, CH-2), 6·34 (m, 2, —CH_2O—), 8·24 (s, 3, Me-10), 8·90 (s, 3, Me-9), and 9·08 (s, 5, Me-8 and CH-1 and -6). (Found: C, 79·3; H, 11·0. $C_{11}H_{18}O$ requires: C, 79·5; H, 10·9%.)

(+)-2-Carene-4α-methanol (II) *and (−)-3(10)-Carene-4-methanol*

Treatment of IV with paraformaldehyde in AcOH followed by saponification of the resulting acetate mixture as described previously[4] afforded a mixture which consisted principally of II accompanied by at least 4 minor products as evidenced by gas chromatography. Isolation of the principal component by distillation at 94–96° (1 mm) afforded II as a colorless oil, $[\alpha]_D^{27}$ +137° (*c*, 1·98); 3,5-DNB long colorless needles, m.p. 105·5–106·5°; NMR spectrum: τ 4·52 (m, 1, CH-2), 6·42 (d, 2, J = 6 Hz, —CH_2O—), 8·32 (s, 3, Me-10), 8·95 (s, 3, Me-9) and 9·14 (s, 5, Me-8 and CH-1 and -6); lit.: $[\alpha]_D^{20}$ +126·5[4] and +145°;[2b] 3,5-DNB m.p. 102° (dec).[4]

Isolation of one of the minor components by preparative gas chromatography followed by sublimation at 73° (67 mm) afforded colorless needles, m.p. 50–51·5°, for which the structure (−)-3(10)-carene-4-methanol is proposed; $[\alpha]_D^{27}$ −51° (*c*, 1·49); λ_{max} 2·90, 6·06 and 11·26 μ; NMR spectrum: τ 5·23 (m, 2, CH_2-10), 6·18 (m, 2, —CH_2O—), and 9·00 and 9·06 (2s, 6, Me-9 and -8). (Found: C, 79·5; H, 10·9. $C_{11}H_{18}O$ requires: C, 79·5; H, 10·9%.)

(+)-4α-Acetyl-2-carene (IX)

A. *Preparation.* The procedure employed was essentially that of Alder *et al.*[8] A stirred soln containing 220 ml (2·33 mole) Ac_2O and 136 g (1·00 mole) of IV was heated to 50° under an atmosphere of N_2. A total of 24 g (0·18 mole) of anhyd $ZnCl_2$ was then added portionwise over a period of 2 hr. The mixture was maintained at 50° for an additional 3 hr and then poured into 300 ml water. The resulting soln was extracted with three 150-ml portions of ether, and the combined ether extracts were washed with sat. $NaHCO_3$ aq until there was no further evolution of gas. The organic layer was separated, dried over $MgSO_4$, and distilled through an 18-in spinning band column at 48–51° (0·2 mm) to yield 125 g of IX as a colorless liquid, λ_{max} 272 mμ (ε, 330, hexane). Gas chromatographic analysis indicated that the product was 98% pure.

B. *Oxidation.* A soln containing 8·50 g of IX in 40 ml THF was added to a soln prepared from 4·8 ml Br_2, 13 g NaOH, and 100 ml water. The 2-phase mixture was heated to 60° with stirring for 16 hr, poured into 150 ml water, and extracted with three 50-ml portions ether. The ether extracts were dried and distilled, yielding 6·73 g (79% recovery) of a colorless liquid, b.p. 76–80° (2·1 mm), which was shown by gas chromatography to consist of recovered IX (51%), accompanied by X (9%) and XI (32%). The aqueous layer from the above extraction was acidified with conc HCl, saturated with NaCl, and extracted with five 50-ml portions of ether. The combined ether extracts were washed with three 30-ml portions of sat. NaCl aq and dried over $MgSO_4$. An ether soln of diazomethane was added, and the ether was removed by distillation. The product was isolated from the remaining yellow oil by preparative gas chromatography and further purified by a short-path distillation at 90° (2·1 mm) to give 0·32 g (3·5% yield) of VI. The NMR and IR spectra of this material were identical in all respects with those of the specimen of ester VI obtained as described above.

C. *Treatment with sodium hydride.* To 2·46 g of a NaH dispersion (59·5% in mineral oil, washed once with 50 ml benzene) was added 50 ml freshly distilled benzene and 4·25 g of IX. After 16 hr of reflux, a total of 580 ml (110%) H_2 had been evolved. The soln was cooled and poured onto a mixture of 100 g ice and 200 ml 5% HCl. The aqueous layer was saturated with NaCl and extracted with eight 100-ml portions ether. The combined extracts were dried over $MgSO_4$ and distilled to yield 3·32 g (78%) of a colorless oil, b.p. 80–85° (1·8 mm) which consisted of 5 major components: recovered IX (43%), the epimer X (19%), the conjugated isomer XI (20%), an alcohol (3%), and an aromatic ketone (10%).

Treatment of IX with methanolic MeONa also afforded mixtures of ketones IX, X and XI; however, since this gave very low yields of X, it was found better for preparative purposes to use the sodium hydride method described above.

Isolation by gas chromatography followed by short-path distillation at 80° (2·0 mm) gave (+)-4β-*acetyl-2-carene* (X) as a colorless liquid, $[\alpha]_D^{27}$ +100° (*c*, 1·88); λ_{max} 5·83 μ. (Found: C, 80·8; H, 10·1. $C_{12}H_{18}O$ requires: C, 80·85; H, 10·18%.)

Isolation of a second fraction by gas chromatography followed by short-path distillation at 78° (1·8 mm) gave (+)-4-*acetyl-3-carene* (XI) as a colorless liquid, $[\alpha]_D^{27}$ +29° (*c*, 1·54); λ_{max} 5·92 μ; λ_{max} 298 (ε, 165)

and 247 mμ (ε, 5400); NMR spectrum: τ 7·79 (3, s, Ac—), 8·20 (3, s, Me-10), 8·97 (3, s, Me-9), and 9·25 (5, m, Me-8, CH-1 and CH-6). (Found: C, 80·6; H, 10·2. $C_{12}H_{18}O$ requires: C, 80·85; H, 10·18%.)

Similar isolation by gas chromatography followed by sublimation at 85° (2·1 mm) afforded an alcohol, tentatively assigned the structure α-methyl-2-carene-4-methanol, as a colorless crystalline solid, m.p. 86–86·5°; λ_{max} 2·75 and 7·29 μ; NMR spectrum: τ 4·50 (1, m, CH-2), 6·10 (1, m, J = 6 Hz, —CHOH), 7·90 (1, m, CH-4), 8·31 (3, s, Me-10), ~8·45 (2, m, CH_2-5), 8·82 (3, d, J = 6 Hz, CH_3CH—), 8·98 (3, s, Me-9), and 9·17 (5, m, Me-8, CH-1 and CH-6). (Found: C, 79·9; H, 11·25. $C_{12}H_{20}O$ requires: C, 79·94; H, 11·18%.)

Isolation of the last component by gas chromatography followed by short-path distillation at 87° (2·3 mm) gave a colorless liquid which is tentatively identified as either 2-acetyl-*p*- or 6-acetyl-*m*-cymene; λ_{max} 5·93 μ; λ_{max} 292 (ε, 1200), 246 (ε, 6300), and 209 mμ (ε, 19,000); NMR spectrum: τ 2·55 (1, s, aromatic H), 2·85 (2, m, aromatic H), 7·09 (1, m, J = 7 Hz, isopropyl CH), 7·44 (3, s, —Ac), 7·53 (3, s, aromatic Me), and 8·76 (6, d, J = 7 Hz, isopropyl Me); *m/e* 176, 161, 133, 117, 105, 91 and 77. (Found: C, 81·8; H, 9·2. $C_{12}H_{16}O$ requires: C, 81·77; H, 9·15%.)

(+)-2α,3α-*Epoxycarane*-4α-*methanol acetate* (XII)

Preparation of a specimen of I as described previously[4] afforded a colorless liquid, b.p. 67–69° (0·45 mm); λ_{max} 5·74 μ; NMR spectrum: τ 4·56 (m, 1, CH-2), 6·00 (τ, 2, —CH_2O—), 7·96 (s, 3, —Ac), 8·32 (s, 3, Me-10), 8·93 (s, 3, Me-9), and 9·12 (s, 5, Me-8 and CH-1 and -6).

To a cooled soln of 1·84 g of I in 50 ml CH_2Cl_2 was added 1·99 g *m*-chloroperbenzoic acid, and the resulting mixture was stirred at 25° overnight under an atmosphere of N_2. The resulting soln was diluted with 100 ml CH_2Cl_2, washed with two 20-ml portions of sat. $NaHCO_3$ aq and two 20-ml portions of sat. NaCl aq. The organic layer was separated and dried over Na_2SO_4. After removal of solvent, the remaining oil was distilled through a short-path column to yield 1·63 g (82% yield) of a colorless liquid, b.p. 87–90° (0·35 mm); $[\alpha]_D^{27}$ +8·35° (*c*, 1·34); λ_{max} 5·72 μ; NMR spectrum: τ 5·99 (2, m, —CH_2O—), 7·16 (1, s, CH-2), 7·96 (3, s, MeO—), 8·70 (3, s, Me-10), 8·92 (3, s, Me-9), and 8·98 (3, s, Me-8). (Found: C, 69·9; H, 8·9. $C_{13}H_{20}O_3$ requires: C, 69·61; H, 8·99%.)

(+)-4α-*Acetyl*-2α,3α-*epoxycarane* (XIII)

To a cooled soln of 3·00 g of IX[6] in 20 ml CH_2Cl_2 was added 3·48 g of *m*-chloroperbenzoic acid in 45 ml CH_2Cl_2. The resulting mixture was stirred overnight at 25° under an atmosphere of N_2. After dilution with 100 ml CH_2Cl_2, the soln was washed with four 100-ml portions of 5% NaOH aq, one 120-ml portion 5% $NaHSO_3$ aq, and one 100-ml portion sat. NaCl aq. The organic layer was dried over $MgSO_4$ and distilled to yield 1·63 g (50% yield) of the epoxide as a colorless oil, b.p. 58–63° (0·13 mm); $[\alpha]_D^{27}$ +17° (*c*, 1·98); λ_{max} 5·87 μ; NMR spectrum: τ 7·14 (1, s, CH-2), 7·31 (1, t, CH-4), 7·81 (3, s, MeO—), 8·59 (3, s, Me-10), 8·93 (3, s, Me-9), and 9·01 (3, s, Me-8). (Found: C, 74·3; H, 9·35. $C_{12}H_{18}O_2$ requires: C, 74·19; H, 9·34%.)

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Note added in proof—Mühlstädt and Richter have recently presented evidence in support of the structural and stereochemical assignment IX for the Friedel–Crafts-acetylation product of 3-carene.[19]