phosphate ester might be induced to migrate to a position from which cleavage might occur. To test this possibility the diethyl 5-pent-1-enyl phosphate (IX) was prepared and subjected to the standard conditions of hydrogenolysis. Unlike the result observed with VI, also an alkyl ester, with IX it is found that cleavage to yield pentane does occur at 1 atm pressure of hydrogen, albeit to a relatively low extent (5%), the remaining material being the reduced phosphate ester; complete reaction is obtained within 6 hr. Only reduction is observed at 4 atm pressure of hydrogen over extended periods of time.

Moreover, these results raise questions concerning the required location of the site of unsaturation if cleavage is to occur. The capability of a vinyl phosphate ester to undergo cleavage *without* isomerization is shown by the hydrogenolysis of compound I and the lack of deuterium incorporation into the unreacted vinyl phosphate esters. This does not eliminate the possibility that a more distant olefinic site might also be subject to hydrogenolysis; allylic and benzylic phosphate linkages are subject to hydrogenolysis over palladium catalysts, and in the present effort have been found to be subject to cleavage over Adams catalyst as well. Efforts to investigate the nature of allylic and benzylic ester cleavage over Adams catalyst have not proven fruitful; with the ester linkage being primary or secondary they are capable of undergoing hydrogen exchange (and isomerization) both prior to and after hydrogenolysis yielding no data of significance (for the current question) from their cleavage with or without deuterium. Tertiary esters would be unsatisfactory as they cleave by other routes.[13]

## Summary

Vinyl phosphate esters undergo hydrogenolysis over Adams catalyst to yield the phosphoric acid and the alkene, the latter being reduced to the alkane. Olefinic linkages in other positions can undergo migration to the vinylic (or allylic) site by hydrogen exchange on the catalytic surface; once the site of unsaturation is in the vinylic ester position no further hydrogen exchange occurs. Benzylic, but not homobenzylic, phosphate esters also undergo hydrogenolysis over Adams catalyst.

**Acknowledgment.** This work was performed under support from a CUNY FRAP research grant.

**Registry No.**—I, 5954-28-9; II, 4452-32-8; III, 30842-23-0; IV, 31327-27-2; V, 1021-45-0; VI, 7301-86-2; VII, 884-90-2; VIII, 56830-42-3; IX, 56830-43-4; 1-chloro-2-propanone, 78-95-5; 2-chlorocyclohexanone, 822-87-7; 2-chlorocyclopentanone, 694-28-0; 2-chlorocycloheptanone, 766-66-5; 2-chloro-1-phenyl-1-ethanone, 532-27-4; triethyl phosphite, 122-52-1; cyclohexanol, 108-93-0; benzyl alcohol, 100-51-6; benzeneethanol, 60-12-8; 4-penten-1-ol, 821-09-0; diethyl phosphorochloridate, 814-49-3.

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# Addition of Trichloroacetic Acid to 8-Methylcamphene

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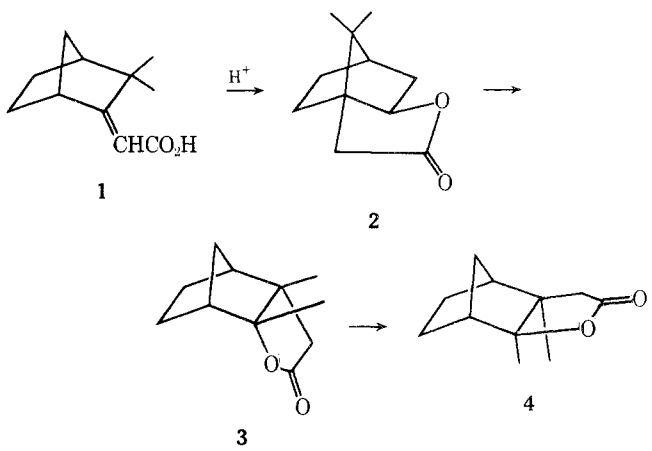
*Received July 25, 1975*

The reaction of 8-methylcamphene (**5**) with haloacetic acids gives a mixture of isobornyl esters which on hydrolysis followed by dehydration with phosphorus oxychloride in pyridine affords a mixture of 8-methylcamphene (**5**), 9-methylcamphene (**8**), and 10-methylcamphene (**7**). Authentic samples of 8-methylisoborneol (**15**) and 10-methylisoborneol (**19**) on dehydration with phosphorus oxychloride in pyridine gave 10-methylcamphene (**7**) and 8-methylcamphene (**5**), respectively, demonstrating that dehydration occurs by way of a Wagner–Meerwein shift without the intervention of 3,2-alkyl shifts.

The facile and sequential conversion of 8-camphenecarboxylic acid (**1**) to lactone **2**, endo lactone **3**, and exo lactone **4**[2] led us to investigate the action of acids on 8-methylcamphene (**5**) in order to determine whether similar alkyl shifts would provide a simple entry to the $\beta$-santalene ring system.[3]

A mixture of 8-methylcamphenes **5** and **6**[4] was obtained in 36% overall yield by the sequence shown in Chart I. Gas chromatographic analysis indicated the presence of *anti*-**5** and *syn*-**6** in a ratio of 93:7.[5]

The action of stannic chloride on **5** and **6** gave recovered starting material or polymer depending on conditions, while sulfuric acid produced polymers. Oxalic acid or cupric acetate in acetic acid[6] gave no rearrangement,[7] while pyruvic acid at 160° for 6 hr afforded 7% of isomerized olefins.[7] Subsequent to the completion of this work Vaughan[8]




1 2 3 4

Chart I

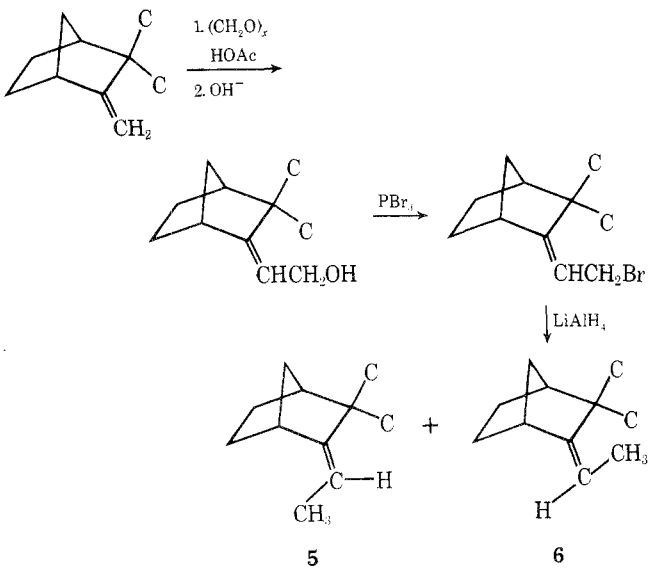



Table I
Reaction of 8-Methylcamphene with Organic Acids Followed by Hydrolysis and Dehydration[a]

| Acid | Conditions | % 5 and 6 | % 7 and 8 |
|---|---|---|---|
| $CH_3CO_2H$ + 0.5% $H_2SO_4$ | 60°, 30 hr | 75 | 25 |
| $ClCH_2CO_2H$ | 100°, 24 hr | 80 | 20 |
| $Cl_3CCO_2H$ 1 equiv | 100°, 24 hr | 64 | 36 |
| 5 equiv | 100°, 24 hr | 50 | 50 |
| 10 equiv | 100°, 24 hr | 42 | 58 |

[a] NMR analysis by comparison of peak areas of the overlapping quartets at 4.90 ppm for olefins 5 and 6 and the pair of identical singlets at 4.42 and 4.66 ppm for olefins 7 and 8.

reported a 4% conversion of 5 to 10-methylcamphene (7) after heating with pyruvic acid for 7 hr in acetonitrile and that pure 7 gave 38% of 5 under the same conditions.

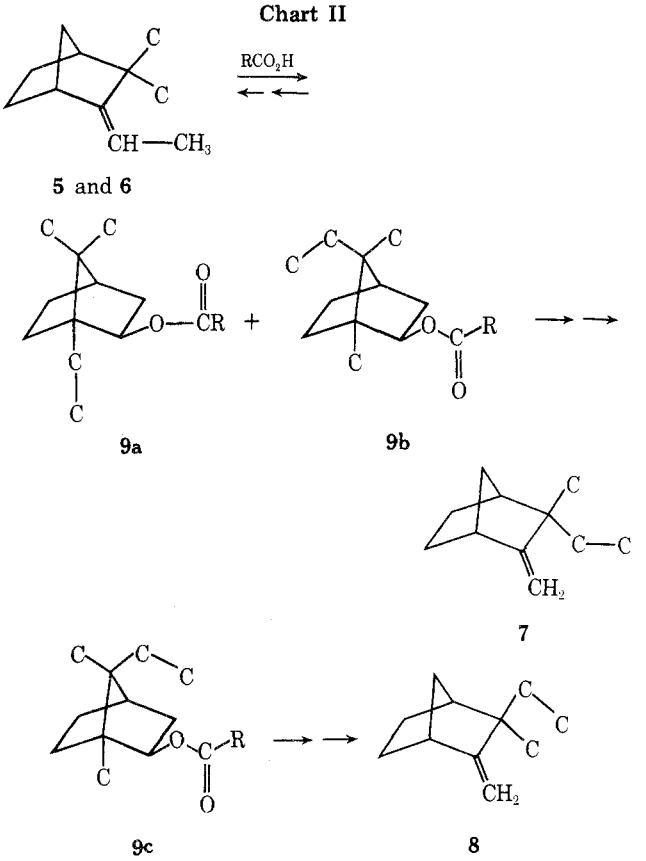
The action of strong organic acids such as trichloroacetic acid on 5 and 6 gave a mixture of isobornyl esters 9a–c for which a convenient method of separation was not found. The ester mixture was hydrolyzed and the resulting alcohols were dehydrated with phosphorus oxychloride in pyridine to a mixture of olefins 5, 6, 7, and 8 (See Chart II and Table I). It was independently established that dehydration of isoborneol derivatives with phosphorus oxychloride in pyridine proceeds by way of a Wagner–Meerwein shift without the intervention of 6,2-hydride or 3,2-methyl or ethyl shifts; consequently, the proportion of each olefin formed by dehydration provides a measure of the amount of the corresponding isoborneol derivative present in the original mixture.

Treatment of 9-methylcamphene (8) with trichloroacetic acid gave an ester mixture which was hydrolyzed and dehydrated to a mixture of 40% 5, 30% 7, and 30% 8.

A mixture of isobornyl esters was also obtained by heating pure trifluoroacetate 9b with a small amount of trifluoroacetic acid.

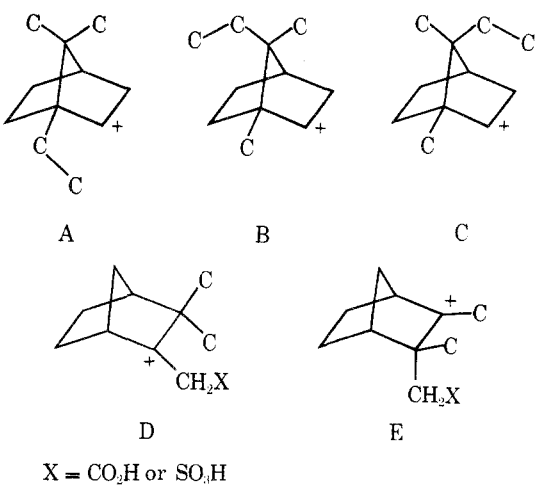
It is apparent that Wagner–Meerwein, 6,2-hydride, and 3,2-alkyl shifts occur competetively when the methylcamphenes or methylisobornyl trihaloacetates are heated in a haloacetic acid and that an acid-catalyzed isomerization of an 8-alkylcamphene derivative as a selective entry to the β-santalene system must fail since there appears to be little difference in stability between ions A, B, or C which are likely intermediates in these transformations. These results

Chart II



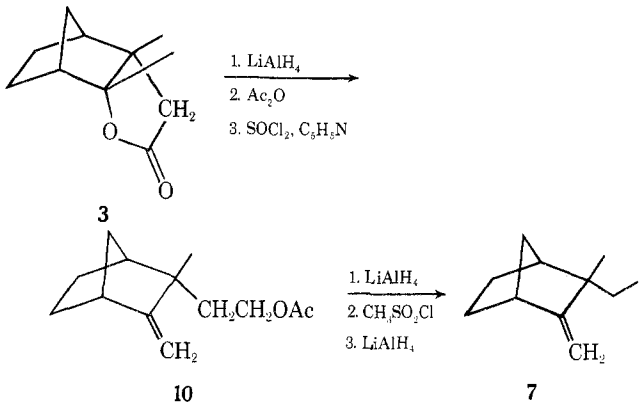

are in sharp contrast to those observed with pyruvic acid. Pyruvic acid apparently avoids trapping ions A, B, or C and favors the formation of the more thermodynamically stable 8-methylcamphene (5 and 6). The lack of rearrangement of the 8-alkylcamphenes claimed by Ritter[9] is suspect, since hydrogen chloride addition followed by base-catalyzed dehydrochlorination should parallel the behavior of trichloroacetic acid and afford rearranged olefins.

Finally, the difference in behavior of olefin 5, lactone 2, and camphene sultone[10] in strong acids derives from the proximity of the electron-withdrawing substituents to the carbonium ion center in the latter cases (ion D) which raises their energy considerably by comparison with that of ion E.




To confirm the stereochemical assignments of the isoborneols and characterize their mode of dehydration, authentic samples of 10-methylcamphene (7), 8-methylisoborneol (15), and 10-methylisoborneol (19) were prepared as illustrated in Charts III and IV.

Chart III




8-Cyanocamphor (**12**) was prepared from 8-bromocamphor (**11**)[11] in 40% yield by heating with potassium cyanide in $Me_2SO$. Hydrolysis of **12** gave camphor-8-carboxylic acid (**13**), which was reduced with lithium aluminum hydride in THF to 8-hydroxymethylisoborneol (**14**) which was freed of a small amount of 8-hydroxymethylborneol by recrystallization. Diol **14** was converted to a monotosylate derivative which was transformed into 8-methylisoborneol (**15**) by reduction with lithium aluminum hydride.

A variety of attempts to prepare 10-methylisoborneol (**19**) were unsuccessful. For example, hydride reduction of monomesylate **16a** or its acetate derivative **16b** afforded tricyclic ether **17**. 10-Methylisoborneol (**19**) was finally obtained by sulfonation of 8-methylcamphene (**5**) followed by aluminum hydride reduction of sultone **18**.[12]

Dehydration of 8-methylisoborneol (**15**) with phosphorus oxychloride in pyridine gave 10-methylcamphene (**7**), while dehydration of 10-methylisoborneol (**19**) afforded 8-methylcamphene (**5**). Further evidence[13] for the absence of 6,2-hydride or 3,2-alkyl shifts in these dehydrations was provided by the formation of optically active camphene on dehydration of (−)-isoborneol. It is reasonable to assume that dehydration of 9-methylisoborneol would lead exclusively to 9-methylcamphene (**8**), although a sample was not prepared to check this.

## Experimental Section[14]

**8-Methylcamphene (5 and 6).** To a stirred slurry of 5 g (0.13 mol) of lithium aluminum hydride in 50 ml of dry ether at 0° was added (0.5 hr) a solution of 11.0 g (0.046 mol) of 8-bromomethylcamphene[2] [bp 68–72° (0.5 mm), $n^{20}D$ 1.5282] in 20 ml of ether. The mixture was stirred at ambient temperature for 48 hr and the excess hydride was destroyed by the addition of 25 ml of ethyl acetate. The salts were removed and washed with ether and the ether solution was washed with water, dried ($MgSO_4$), and evaporated to yield 5.6 g (85%) of 8-methylcamphene: ir 5.96 and 11.35 $\mu$; NMR ($CDCl_3$) 0.98 and 1.00 (s, 6, $CH_3CCH_3$), 1.60 (d, 3, $J$ = 7 Hz, C=CHC**H**$_3$), 2.92 (m, 1), and 4.96 ppm (q, 1, $J$ = 7 Hz, -C=C**H**CH$_3$); mass spectrum *m/e* (rel intensity) 150 (39), 135 (100), 121 (42), 107 (89), 93 (43), 91 (17), 79 (23), 67 (20), and 41 (23).

GLC using a 6-ft 15% Carbowax 20M column at 95° indicated the presence of two isomers in a ratio of 13:1. The minor isomer was collected (retention time 28 min vs. 23 min for **5**) and exhibited ir ($CHCl_3$) 5.98 $\mu$; NMR ($CDCl_3$) 1.13 and 1.18 (s, 6, $CH_3CCH_3$), 1.62 (d, 3, $J$ = 6.5 Hz, C=CHC**H**$_3$), 2.49 (m, 1), and 5.12 ppm (q, 1, $J$ = 6.5 Hz, C=C**H**CH$_3$).

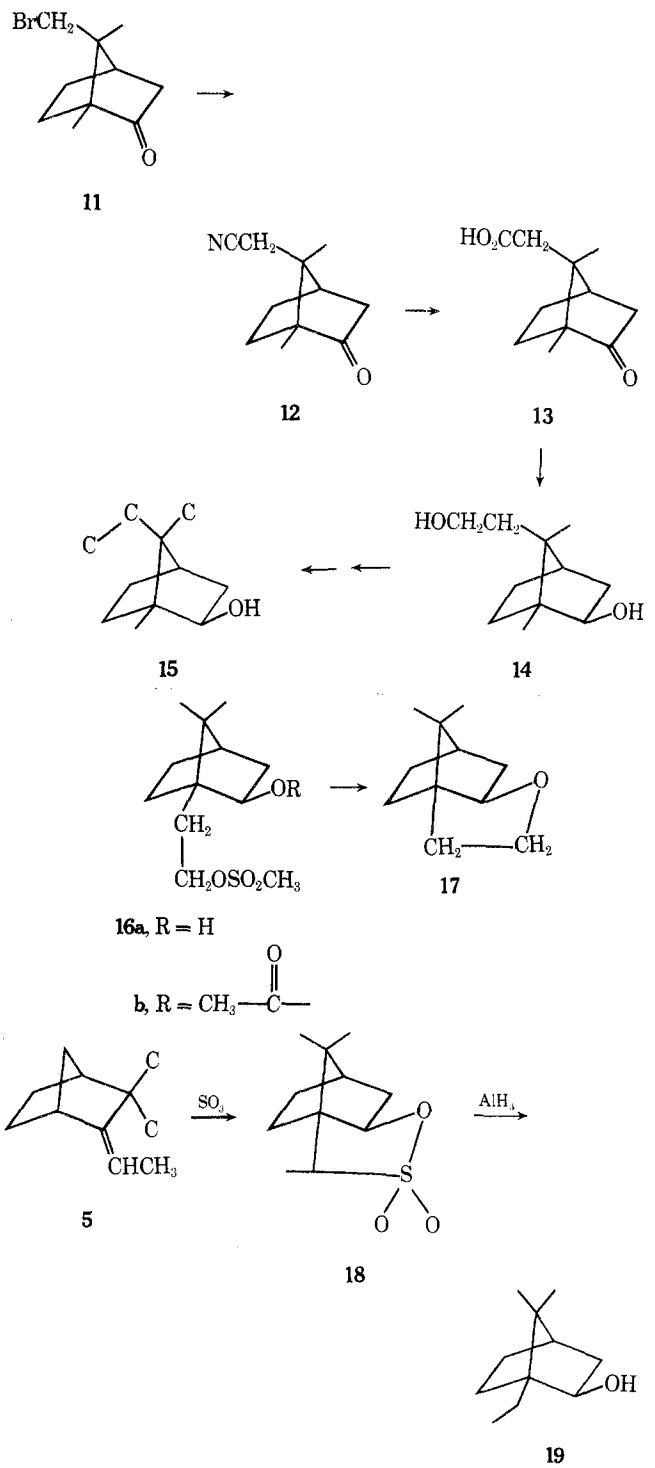
**10-Acetoxymethylcamphene (10).** A solution of 2.0 g (11.1 mol) of endo lactone **3**[2] was reduced with 0.6 g (15.8 mmol) of lithium aluminum hydride in ether. Work-up in the usual manner and recrystallization from hexane afforded 1.22 g of *exo,exo*-2,3-dimethyl-*endo*-3-(2-hydroxyethyl)-*endo*-2-norbornanol: mp 78–81°; NMR ($CDCl_3$) 0.95 (t, 3, $CH_3C$–), 1.18 (s, 3, $CH_3CO$–), 4.58 (m, 2, -$CH_2O$–), and 5.0–5.5 ppm (m, 2, -OH).

A solution of 1.20 g of the diol in 30 ml of acetic anhydride containing 0.3 ml of pyridine was kept at 50° overnight. Water (20 ml) was added and the mixture was heated for 1 hr, cooled, and extracted with ether. The ether solution was dried ($MgSO_4$) and evaporated, and the residue was taken up in methylene chloride, cooled to 0°, and treated with 10 ml of thionyl chloride in 10 ml of pyridine. The mixture was stirred for 30 min, poured over ice, and extracted with ether. The ether was washed with dilute hydrochloric acid and water, dried ($MgSO_4$), and evaporated to yield 1.18 g of crude unsaturated acetate **10**. A pure sample of **10** was obtained by GLC using a 15% SE-30 column at 145°: ir ($CCl_4$) 5.70, 6.00, and 11.34 $\mu$; NMR ($CCl_4$) 1.02 (s, 3, $CH_3C$–), 1.92 (s, 3, $CH_3CO$–), 2.65 (m, 1), 4.03 (t, 2, -$CH_2O$–), and 4.45 and 4.68 ppm (s, 2, -C=$CH_2$).

Anal. Calcd for $C_{13}H_{20}O_2$: C, 74.96; H, 9.68. Found: C, 74.85; H, 9.92.

**10-Methylcamphene (7).** Lithium aluminum hydride reduction of 1.00 g of unsaturated acetate **10** gave 0.8 g of 10-hydroxymethylcamphene: ir 2.95, 6.02, and 11.40 $\mu$; NMR ($CDCl_3$) 1.02 (s, 3,

Chart IV



$CH_3C$–), 2.66 (m, 1), 3.68 (m, 2, $-CH_2O$), and 4.50 and 4.73 ppm (s, 2, $-C{=}CH_2$).

To an ice-cold solution of 0.8 g of 10-hydroxymethylcamphene in 20 ml of dry pyridine was added 1.6 g of mesyl chloride. The solution was kept at −20° for 24 hr and then poured onto ice and extracted with a mixture of ether and methylene chloride. The extracts were washed with 10% hydrochloric acid and water, dried ($MgSO_4$), and evaporated to yield an oil which could not be induced to crystallize. The crude mesylate was dissolved in 10 ml of ether and added to a slurry of 0.6 g of lithium aluminum hydride in ether. After stirring at ambient temperature for 18 hr, work-up in the usual manner yielded 0.70 g of an oil. An analytical sample of 10-methylcamphene (7) was obtained by GLC using a 15% SE-30 column at 90°: ir (neat) 6.05 and 11.31 μ; NMR ($CCl_4$) 0.97 (s, 3, $CH_3C$–), 2.65 (m, 1), and 4.42 and 4.66 (s, 2, $-C{=}CH_2$); mass spectrum *m/e* (rel intensity) 150 (14), 121 (100), 93 (95), 91 (30), 79 (53), 77 (30), 67 (35), 55 (28), 41 (51), and 39 (30).

Anal. Calcd for $C_{11}H_{18}$: C, 87.92; H, 12.08. Found: C, 87.95; H, 12.19.

**(±)-8-Cyanocamphor (12).** A stirred mixture of 20 g (0.087 mol) of (±)-8-bromocamphor (11)[11] and 13 g (0.20 mol) of potassium cyanide in 150 ml of dimethyl sulfoxide was heated at 100° overnight. The solution was diluted with water and extracted with ether. The organic solution was dried ($MgSO_4$) and evaporated to leave a white solid which yielded 6.0 g (39%) of (±)-8-cyanocamphor after two recrystallizations from hexane: mp 163.5–165° [lit.[11b] (+)-**12**, mp 168°]; NMR 0.95 and 1.05 ppm (s, 6, 2 $CH_3C$–); mass spectrum *m/e* (rel intensity) 177 (26), 133 (100), 109 (28), 108 (23), 95 (72), 93 (23), 81 (54), 67 (26), and 41 (23).

**(±)-Camphor-8-carboxylic Acid (13).** A mixture of 5.8 g of 8-cyanocamphor (12), 5.6 g of potassium hydroxide, and 150 ml of water was heated at reflux for 44 hr. The mixture was cooled and extracted with ether. The aqueous solution was acidified with dilute sulfuric acid and extracted with a mixture of ether and methylene chloride. The organic solution was washed with water, dried ($MgSO_4$), and evaporated to yield 6.3 g (100%) of crude (±)-camphor-8-carboxylic acid (13). An analytical sample was prepared by sublimation in vacuo and showed mp 140–141°; ir ($CHCl_3$) 3.0–4.0, 5.73, and 5.83 μ; NMR ($CDCl_3$) 0.94 and 1.02 (s, 6, 2 $CH_3C$–) and 11.10 ppm (s, 1, $-CO_2H$).

Anal. Calcd for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22. Found: C, 67.10; H, 8.25.

**(±)-8-Hydroxymethylisoborneol (14).** A mixture of 6.25 g of keto acid 13 and 2.60 g of lithium aluminum hydride in 50 ml of ether was refluxed for 24 hr. The usual work-up afforded 3.10 g of a mixture whose NMR spectrum indicated the presence of 80% of 8-hydroxymethylisoborneol (14) and 20% of 8-hydroxymethylborneol. Acidification of the residual salts obtained during reaction work-up gave a mixture of what appeared to be isoborneol and borneol-8-carboxylic acid which was not examined further. When the $LiAlH_4$ reduction was conducted in THF for 44 hr at reflux the yield of diols rose to 86%.

Pure diol 14 was obtained by recrystallization from ether–hexane and displayed mp 135–136°; NMR ($CDCl_3$) 0.90 and 1.02 (s, 6, 2 $CH_3C$–) and 3.3–3.9 ppm (m, 5, $CH_2OH$ and CHOH); mass spectrum *m/e* (rel intensity) 184 (1), 166 (15), 140 (42), 139 (36), 125 (47), 121 (29), 111 (22), 107 (24), 96 (28), 95 (100), 93 (33), 81 (29), 67 (34), 55 (36), 43 (36) and 41 (44).

Anal. Calcd for $C_{11}H_{20}O_2$: C, 71.70; H, 10.94. Found: C, 71.79; H, 11.21.

**(±)-8-Methylisoborneol (15).** To an ice-cold solution of 5.25 g (28.6 mmol) of diol 14 in 50 ml of pyridine was added 6.55 g (57 mmol) of methanesulfonyl chloride. The reaction mixture was kept at −20° for 36 hr and yielded 5.30 g of an oil after usual work-up.

Attempted reduction using lithium aluminum hydride in ether at ambient temperature for 18 hr gave back the monomesylate. The mesylate was then heated with $LiAlH_4$ in THF for 36 hr. The usual work-up afforded 3.0 g (62%) of 8-methylisoborneol (15). An analytical sample of 15 was obtained by two sublimations in vacuo and showed mp 81–84°; NMR ($CCl_4$) 0.86 (m, 6, $CH_3CH_2$ superimposed on $CH_3C$–), 0.96 (s, 3, $CH_3C$–), 3.10 (s, 1, –OH), and 3.55 ppm (t, 5, 1, –CHO); mass spectrum *m/e* (rel intensity) 168 (3), 150 (12), 139 (30), 121 (32), 96 (25), 95 (100), 93 (25), 55 (28), 43 (30), 41 (42), and 39 (17).

Anal. Calcd for $C_{11}H_{20}O$: C, 78.51; H, 11.98. Found: C, 78.48; H, 12.20.

**(±)-8-Methylcamphor.** To an ice-cold solution of 300 mg of diol 14 in acetone was added 3 ml of Jones reagent.[15] After standing for 30 min the excess oxidant was destroyed by adding isopropyl alcohol. Removal of the salts by filtration and evaporation of the solvent left 290 mg of a yellow oil. Sublimation in vacuo gave pure 8-methylcamphor: mp 61–62°; ir ($CCl_4$) 5.71 μ; NMR ($CCl_4$) 0.86 (m, 6, $CH_3CH_2$– superimposed on $CH_3C$–), 0.98 (s, 3, $CH_3C$–), and 2.0–2.2 ppm (m, 2, $-CH_2CO$); mass spectrum *m/e* (rel intensity) 166 (29), 122 (20), 109 (31), 95 (100), 81 (23), 67 (30), 55 (31) and 41 (35).

Anal. Calcd for $C_{11}H_{18}O$: C, 79.46; H, 10.91. Found: C, 79.46; H, 10.74.

**8-Methylisobornyl Trifluoroacetate (9b).** A solution of 1.85 g (11.0 mmol) of 8-methylisoborneol (14) in 6 ml of trifluoroacetic anhydride was kept at ambient temperature for 22 hr. Ice was added cautiously and after stirring for 10 min the mixture was extracted with ether. The ether was washed with aqueous sodium carbonate, dried, and evaporated to yield 2.76 g (95%) of trifluoroacetate **9b**: ir 5.59, 8.2, and 8.52–8.68 μ; NMR ($CCl_4$) 0.90 (s, 3, $CH_3C$–), 0.97 (s and t, 6, $CH_3C$– and $CH_3CH_2$–), and 4.86 ppm (m, 1, CHO–); mass spectrum *m/e* (rel intensity) 264 (2), 150 (39), 121 (100), 95 (45), 93 (50), 79 (22) and 69 (29).

Anal. Calcd for $C_{13}H_{19}O_2F_3$: C, 59.08; H, 7.36; F, 21.56. Found: C, 59.13; H, 7.36; F, 21.60.

**Attempted Preparation of 10-Methylisoborneol via 10-Hydroxymethylisoborneol.** To an ice-cold solution of 1.0 g (5.45 mmol) of 10-hydroxymethylisoborneol,[2] mp 91.5–92.5°, in 25 ml of dry pyridine was added 1.25 g (10.9 mmol) of methanesulfonyl chloride. The mixture was kept at −25° for 23 hr and worked up to afford an oil which showed an NMR signal at 2.86 ppm and ir bands at 8.4, 8.5, and 12.6 μ characteristic of a mesylate. The only product isolated when this mesylate was treated with lithium aluminum hydride was 10,10-dimethyltricyclo[4.3.1$^{1,7}$.0$^{1,5}$]-4-oxadecane (17): mp 136–137° (lit.[16] mp 129–130°); NMR ($CDCl_3$) 0.84 and 1.14 (s, 6, $CH_3CCH_3$) and 3.58–4.20 ppm (m, 3, $-CH_2OCH$–).

Attempts to react the mesylate with sodium methyl mercaptide or sodium iodide gave tricyclic ether 17. Acetylation of the mesylate using acetyl chloride and magnesium, followed by lithium aluminum hydride, also gave ether 17.

**Dehydration of 8-Methylisoborneol (15).** To an ice-cooled solution of 346 mg (2.06 mmol) of 8-methylisoborneol (15) (containing ca. 20% of 8-methylborneol) in 10 ml of pyridine was added 1.0 ml of phosphorus oxychloride. The solution was stirred at 25° for 6 hr and at 100° for 2 hr. The mixture was cooled, cautiously poured onto ice, and extracted with ether. The ether was removed, affording 260 mg of a clear oil which showed a single peak on GLC using a 150-ft UCON-P capillary column at 120°. The ir, NMR, and GLC retention time were identical with those of an authentic sample of 10-methylcamphene (7).

**Dehydration of 10-Methylisoborneol (19).** Dehydration of 256 mg of 10-methylisoborneol (19) by the procedure described above gave 189 mg (80.5%) of 8-methylcamphene (5 and a trace of 6).

**Dehydration of (−)-Isoborneol.** Dehydration of (−)-isoborneol, prepared by lithium aluminum hydride reduction of (+)-camphor ($[\alpha]^{24}D$ +44.6°) containing a small amount of borneol, gave 463 mg of camphene, mp 51–52°, $[\alpha]^{24}D$ .96.7° (*c* 1.23, EtOH).

Dehydration of borneol under the same conditions afforded 45% of camphene and 45% of recovered borneol.

**General Procedure for Reaction of 8-Methylcamphene with Trichloroacetic Acid.** A mixture of 1.0 g (6.67 mmol) of 8-methylcamphene (5 and 6) and 5.6 g (33.2 mmol) of trichloroacetic acid was heated at 40° for 4 days. The mixture was cooled, poured into water, and extracted with ether. The ether solution was washed with water and saturated sodium bicarbonate solution, dried ($MgSO_4$), and concentrated to give 1.4 g of a mixture of isobornyl trichloracetates.

The trichloracetate mixture was refluxed for 6 hr with 4 g of potassium hydroxide in ethanol. The solution was cooled, poured into water, and extracted with ether. The ether solution was washed with water, dried ($MgSO_4$), and evaporated to yield ca. 1.0 g of a semisolid mixture of isoborneols. This mixture was dehydrated using 2.0 g of phosphorus oxychloride in 10 ml of pyridine to afford a mixture of **5**, **6**, **7**, and **8** which was analyzed by NMR or GLC using a 150-ft UCON-P capillary column.

**Reaction of 9-Methylcamphene (8) with Trichloroacetic Acid.** A mixture of 600 mg (4 mmol) of 9-methylcamphene (8)[2] and 900 mg (5.5 mmol) of trichloroacetic acid was heated at 100° for 24 hr and worked up, hydrolyzed, and dehydrated as described above to yield a mixture of 55% of 9- and 10-methylcamphene (7 and 8) and 45% of 8-methylcamphene (5) as indicated by NMR analysis. Analysis using a 150-ft UCON-P capillary column indicated the presence of 40% of **5**, 30% of **7**, and 30% of **8**.

**8-Methylisobornyl Trifluoroacetate (9b) and Trifluoroacetic Acid.** A mixture of 831 mg (3.15 mmol) of trifluoroacetate **9b** and 75 mg (0.67 mmol) of trifluoroacetic acid was heated at 100° for 24 hr. The mixture was hydrolyzed and dehydrated in the usual manner to yield 321 mg of a mixture containing 74% of 8-methylcamphene (**5**) and 26% of 9- and 10-methylcamphenes (**7** and **8**).

**Registry No.**—**3**, 56906-70-8; **5**, 54382-52-4; **6**, 54382-53-5; **7**, 54345-89-0; **9b**, 56817-46-0; **10**, 56817-47-1; **11**, 3751-96-0; **12**, 56906-71-9; **13**, 56817-48-2; **14**, 56817-49-3; **15**, 56817-50-6; **16a**, 56817-51-7; **17**, 56906-72-0; **19**, 56817-52-8; 8-bromomethylcamphene, 6090-21-7; *exo,exo*-2,3-dimethyl-*endo*-3-(2-hydroxymethyl)-*endo*-2-norbornanol, 56817-53-9; 10-hydroxymethylcamphene, 56817-54-0; potassium cyanide, 151-50-8; 8-methylcamphor, 56817-55-1; trifluoroacetic anhydride, 407-25-0; (−)-isoborneol, 10334-13-1; (+)-camphene, 5794-03-6; trichloroacetic acid, 76-03-9; 10-hydroxymethylisoborneol, 56817-56-2; methanesulfonyl chloride, 124-63-0.

## References and Notes


(1) Abstracted from part of the thesis submitted by E. J. E. in partial fulfillment of the requirements for the Ph.D. degree, Purdue University, June 1972.
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(5) The configurations of **5** and **6** are tentatively assigned on the basis of the C-9 and C-10 methyl shifts which appear at 1.13 and 1.18 ppm for **6** and at 0.97 and 0.99 ppm for **5**. The syn C-8 methyl in **6** should reduce the anisotropic shielding of the C-9 and C-10 methyl groups by the carbon–carbon double bond and result in a downfield shift from the corresponding methyl signals of *anti*-**5** and camphene (1.02 and 1.05 ppm).
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(7) The proportion of **6** in the recovered olefin rose to 14%.
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(14) All melting and boiling points are uncorrected. Infrared spectra were recorded on a Perkin-Elmer Infracord. NMR spectra were measured with a Varian Associates A-60 spectrometer. Optical rotations were measured with a Zeiss polarimeter. Mass spectra were determined by the Purdue University Spectral Service employing a Hitachi RMU-6A spectrometer. Microanalyses were performed by Dr. C. S. Yeh and associates.
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# Bicyclic Amino Alcohols. The Isomeric 2-Dimethylaminomethyl-3-hydroxymethylbicyclo[2.2.1]hept-5-enes


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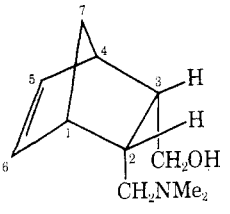
*Received May 1, 1975*

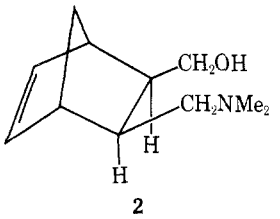

Preparation of the four isomeric 2-dimethylaminomethyl-3-hydroxymethylbicyclo[2.2.1]hept-5-enes is reported and characterization of the stereochemistry of each by NMR techniques is discussed. The cis isomers (**1** and **2**) were prepared from the cyclopentadiene–maleic anhydride Diels–Alder adduct, by reaction with dimethylamine, followed by reduction with $LiAlH_4$. The trans compounds (**3** and **4**) were prepared from appropriate adducts of cyclopentadiene and fumaric acid derivatives. Stereochemistry was assigned by NMR spin–spin decoupling techniques and use made of the anisotropic effects of the 5,6 unsaturation on the C-2 or C-3 methylene protons and on H-2, H-3.


Derivatives of amino alcohols in bicyclic systems have provided a number of interesting structures useful for the study of conformational and steric aspects of the action of drugs related to neurotransmitters, especially acetylcholine and its congeners. Previously, derivatives of the 2-alkylamino-3-hydroxybicyclo[2.2.2]octanes[1-3] and of boranes[4,5] have been reported. More recently, analogs of cholinergic drugs have been studied in semirigid butane systems, e.g., from *cis*- and *trans*-1-dimethylaminomethyl-2-hydroxymethylcyclopropane[6] and certain *cis*- and *trans*-2-butenes.[7]

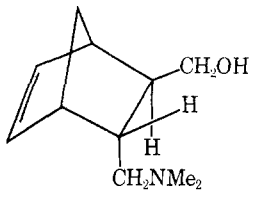
We have prepared isomeric 2-dimethylaminomethyl-3-hydroxymethylbicyclo[2.2.1]hept-5-enes (**1**–**4**) to provide



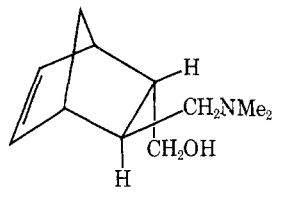

**1**




**2**




**3**




**4**

precursors for preparation of analogs of a muscarinic ganglionic stimulant, McN-A-343.[7,8] In this paper the synthesis of these amino alcohols is reported and facile characterization of the stereochemistry of each is demonstrated by use of NMR spectroscopic techniques.

Our initial efforts were concerned with the preparation of the three isomeric 2,3-di(hydroxymethyl)bicyclo[2.2.1]hept-5-enes (**8**, **11**, and **14**), available from the Diels–Alder adducts of cyclopentadiene with maleic anhydride or with dimethyl fumarate. Endo anhydride **5**, the kinetic product of the former addition,[9] was readily converted at 190° to a mixture of anhydrides from which exo anhydride **6** was obtained by crystallization.[10] 2-*endo*-3-*exo*-Dicarbomethoxybicyclo[2.2.1]hept-5-ene (**7**) was prepared by the