excess of water and extracted with methylene chloride. Evaporation of the extract *in vacuo*, and crystallization of the residue from methanol gave Il, mp 122–130°. The analytical sample (dried over benzene) had mp 122.5–126°; λ_{max} 229 mμ (ϵ 14,200) 273 (930), and 280 (810); $[\alpha]^{25}{}_{D}$ −34° (chloroform).

Anal. Calcd for $C_{28}H_{37}N_3O_3$ (463.60): C, 72.54; H, 8.04; N, 9.06. Found: C, 72.53; H, 8.13; N, 9.11.

16β-Azidopregn-5-ene-3β,20β-diol 3-*p*-Toluenesulfonate 20-Benzoate (Im).—A solution of the benzoate Il (6.4 g) and *p*-toluenesulfonyl chloride (6 g) in pyridine (46 ml) was allowed to stand at room temperature 20 hr and then poured into ice-water. The resultant precipitate was collected and crystallized from methylene chloride to give Im, mp 179.5–180.5°. The analytical sample, crystallized from methylene chloride–hexane, had the same melting point; $\lambda_{max}^{MeOH-CHCl_3}$ 227 mμ (ϵ 28,500); $[\alpha]^{25}{}_{D}$ −26° (chloroform).

Anal. Calcd for $C_{35}H_{43}N_3O_5S$ (617.72): C, 68.05; H, 7.02; N, 6.80; S, 5.19. Found: C, 67.82; H, 6.76; N, 6.79; S, 5.27.

16β-Azido-6β-methoxy-3α,5α-cyclopregnan-20β-ol Benzoate (IX).—A mixture of the tosylate benzoate Im (6.29 g) and potassium acetate (12.5 g, oven dried at 105°) in methylene chloride (100 ml) and methanol (1 l.) was refluxed 22 hr, whereupon complete solution resulted. Most of the solvent was distilled *in vacuo*, and the remainder was added to ice water. An amorphous solid resulted which could not be crystallized. It contained three components (one major and two minor) as revealed by thin layer chromatography. Chromatography on Florisil (500 g) gave IX as a noncrystallizable oil (4.5 g) from the petroleum ether–acetone (9:1) eluates, ν_{max} 2100, 1710, 1250, and 1020 cm^{-1}. A minor contaminant was present as shown by thin layer chromatography.

3β,16β-Diazidopregn-5-en-20β-ol Benzoate (X).—A solution of the cyclopregnane benzoate IX (4.50 g) in benzene (100 ml) containing hydrazoic acid[22] and freshly distilled boron trifluoride etherate (3.1 ml) was allowed to stand 3.5 hr at room temperature. Ammonium hydroxide (6 *N*, 100 ml) and then ether (200 ml) were added to the reaction mixture. The organic layer was collected, washed with 6 *N* ammonium hydroxide and water, and dried. Evaporation gave an oil which solidified on standing. Crystallization from acetone–hexane afforded X (3.65 g), mp 146–148°. The analytical sample had mp 155.5–156.5°; $[\alpha]^{25}{}_{D}$ −14° (chloroform); ν_{max} 2100, 1718, and 1270 cm^{-1}; nmr peaks appeared at 0.82 (18 H, singlet), 0.95 (19 H, singlet), 1.40 (J = 5.5 cps) (21 H, doublet), 3.19 (3 H, multiplet), 5.35 (6 H, multiplet), 4.18 (16 H, multiplet), 7.50 and 8.05 (phenyl, multiplets) ppm ($CDCl_3$).

Anal. Calcd for $C_{28}H_{36}N_6O_2$ (488.62): C, 68.82; H, 7.43; N, 17.20. Found: C, 69.04; H, 7.46; N, 17.24.

3β,16β-Diaminopregn-5-en-20β-ol (XI).—A mixture of the diazido benzoate X (2.77 g) and lithium aluminum hydride (4.0 g) in tetrahydrofuran (250 ml) was refluxed 17 hr and worked up as in the preparation of Ic. The residue obtained was dissolved in methanol and concentrated with heating to give a precipitate of an unknown material (0.25 g), mp 234–236°. Addition of ethyl acetate to the filtrate and concentration by heating gave XI (750 mg), mp 214–219°. Further crystallization gave an analytical sample: mp 224–225°; $[\alpha]^{25}{}_{D}$ −36° (methanol); ν_{max} 3360 cm^{-1}; nmr peaks appeared at 0.90 and 0.94 (18 H and 19 H, singlet), 1.12 (J = 5 cps) (21 H, doublet), and 5.28 (6 H, multiplet) ppm (DMSO-d_6), (the nmr spectral signals were very weak due to poor solubility).

Anal. Calcd for $C_{21}H_{36}N_2O$ (332.51): C, 75.85; H, 10.91; N, 8.43. Found: C, 75.80; H, 11.15; N, 8.45.

3′,6′(*R*)-Dimethyl-2′,3′,4′,5′-tetrahydro-1′,3′-oxazino[4′,5′:16β,17β]-3β-dimethylaminoandrost-5-ene (XII).—A solution of the 3β,16β-diamino-20β-ol XI (590 mg) in formaldehyde (10 ml) and formic acid (10 ml) was refluxed 7 hr. The reaction mixture was poured into ice water and made basic with dilute potassium hydroxide, and the resultant precipitate was collected. Crystallization from acetone–water gave XII (310 mg), mp 126.5–127°. The analytical sample had mp 127.5–128.5°; $[\alpha]^{25}{}_{D}$ −29° (chloroform); nmr peaks appeared at 1.01 (19 H, singlet), 1.19 (18 H, singlet), 1.39 (J = 7 cps) (21 H, doublet), 2.03 (N-methyl, singlet), 2.30 (N-dimethyl, singlet), 3.51 and 4.38 (J = 8 cps), (2′2′ H, pair of doublets), 3.91 (20 H, multiplet), and 5.33 (6 H, multiplet) ppm ($CDCl_3$).

Anal. Calcd for $C_{25}H_{42}N_2O$ (388.60): C, 77.66; H, 10.95; N, 7.25. Found: C, 77.45; H, 11.01; N, 7.05.

Registry No.—Ia, 14570-69-5; Ib, 14570-70-8; Ic, 14570-71-9; Id, 14570-72-0; Ie, 14570-73-1; If, 14570-74-2; Ig, 14570-75-3; Ih, 14734-05-5; Ii, 14570-76-4; Ik, 14570-77-5; Il, 14570-78-6; Im, 14734-06-6; IIIa, 14754-81-5; IIIb, 14570-79-7; IIIc, 14735-83-2; IIId, 14570-80-0; IV, 14570-81-1; Va, 14570-82-2; Vb, 14734-07-7; Vc, 14734-08-8; Vd, 14570-83-3; Ve, 14570-84-4; VI, 14570-85-5; VIIa, 14570-86-6; VIIb, 14570-87-7; VIII, 14570-88-8; IX, 14570-89-9; X, 14570-90-2; XI, 14570-91-3; XII, 14570-92-4.

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[22] P. A. S. Smith, *Org. Reactions*, **3**, 327 (1946).

Terpene–Formaldehyde Reactions. I. α-Terpinene[1]

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Reaction of α-terpinene with formaldehyde is best effected in solvent acetic acid at 110–115° in the absence of added catalyst. The reaction product (70% yield) comprises mainly (75%) a 2:1 mixture of *p*-mentha-2,4(8)-diene-1-methanol acetate and *p*-mentha-2,4-diene-1-methanol acetate. The stannic chloride catalyzed reaction, in solvent methylene chloride, gives a mixture of products (75% yield) whose principal component (80%) is the 1,3-dioxane, 6-methyl-9-isopropyl-2,4-dioxabicyclo[4.4.0]dec-9-ene. *p*-Menthane-1-methanol is obtained easily by hydrogenation of mixtures of the aforementioned acetates followed by hydrolysis.

Especial interest attaches to a study of the terpenes of gum turpentine as basic raw materials for the synthesis of primary alcohols and related compounds, in good yield and reasonable purity. To this end, a careful examination of terpene–formaldehyde reactions seems to merit specific consideration, giving attention to the more available terpenes. The conjugated diene α-terpinene, which is now conveniently available *via* isomerization of the pinenes,[3] is of particular interest. Up to the present time there is no report on its reactions with formaldehyde.

The most useful of the α-terpinene–formaldehyde reactions studied is the "noncatalyzed" thermal condensation in glacial acetic acid. Upon heating the

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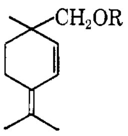
[1] For the preceding report from this laboratory on olefin-formaldehyde reactions, see A. T. Blomquist and J. Wolinsky, *J. Am. Chem. Soc.*, **79**, 6025 (1957).

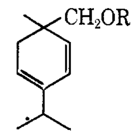
[2] Abstracted from part of the Ph.D. dissertation presented by J. D. Meador to the Graduate School of Cornell University, June 1967.

[3] H. Kroeper, W. Rau, and F. Wirth, U. S. Patent 2,792,436; *Chem. Abstr.*, **51**, 16550 (1957).

reactants for 72 hr at *ca.* 110–115° there is obtained, in 70% yield, a mixture of products that comprises the two acetates (75%, glpc analysis),[4a] *p*-mentha-2,4(8)-diene-1-methanol acetate (Ia), n^{18}D 1.5026, $\lambda_{\max}^{\text{MeOH}}$ 243 mμ (ε 23,000), and *p*-mentha-2,4-diene-1-methanol acetate (IIa), n^{19}D 1.4722; $\lambda_{\max}^{\text{MeOH}}$ 259 mμ (ε 3,800) in a 2:1 ratio. The yield and ratio of acetates vary with reaction conditions; *e.g.*, reaction at *ca.* 80° for 44 hr affords a 50% yield of products, 63% of which comprises the acetates Ia and IIa in a 1.0:1.6 ratio. The corresponding alcohols Ib ($n^{21.5}$D 1.5276) and IIb (n^{20}D 1.4924) show ultraviolet absorption maxima at λ 243 mμ (ε 22,000) and λ 258 ± 1 mμ (broad) (ε 3500).[5,6] The ultraviolet absorption maxima of model compounds, the dienes III, IV, and V, are respectively, 244,[7] 260,[8] and 263 mμ.[9]



Ia, R = Ac
b, R = H



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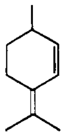
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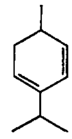
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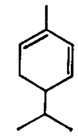
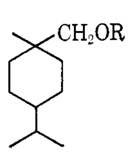

V

The infrared spectrum of the alcohol Ib shows characteristic bands at 3.00, 6.10, and 6.22 μ. Significant nmr absorptions are a pair of doublets centered at τ 3.58 and 4.59 (J = 10.5 cps) (2 H, vinylic), a singlet at 6.25 (1 H, -O*H*), a singlet at 6.67 (2 H, -C*H*₂OH), a singlet at 8.28 (6 H, =C(C*H*₃)₂), and a sharp singlet at 9.01 (3 H, >C(C*H*₃)CH₂OH). The infrared and nmr spectra of the acetate Ia, prepared from the alcohol Ib, support the structure proposed. It is interesting that in the nmr spectrum of Ia the geminal protons in $-CH_2OAc$ appear as a quartet (AB pattern) whose two outer peaks are very weak satellites.[10] The nmr spectrum of the acetate IIa shows a multiplet between τ *ca.* 4.08 and 4.73 (3 H, vinylic), a singlet at 6.22 (2 H, -C*H*₂OAc), a sharp singlet at 8.33 (3 H, -O₂C-C*H*₃), and also sharp singlets at 8.94, 9.03, and 9.05 (9 H, (C*H*₃)₂CH, C*H*₃).

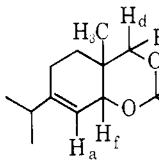
The reaction of α-terpinene with formaldehyde in acetic acid (72 hr at *ca.* 110–115°) with formic acid added as a catalyst gives 68% of a mixture of acetates and formates. Alkaline hydrolysis of this mixture affords (83%) a product mixture 71% of which comprises the alcohol Ib.

Pertinent to the relative stability of the isomeric acetates Ia and IIa, as well as the corresponding alcohols, is the observation that a sulfuric acid catalyzed methanolysis of a 1:1 mixture (74% pure) of the acetates gives a mixture of products that is almost entirely Ib (85%, by glpc analysis).[4a]

A mixture of the *cis,trans* isomers of *p*-menthane-1-methanol acetate (VIa, n^{20}D 1.4534) is obtained upon catalytic hydrogenation of a mixture of acetates Ia and IIa. Alkaline hydrolysis of the acetate VIa gives a mixture of the *cis* and *trans* isomers of the neopentyl-type alcohol *p*-menthane-1-methanol (VIb, n^{25}D 1.4671). The infrared spectrum of the alcohol VIb shows characteristic bands at 2.98 (OH) and at 7.22 as well as at 7.31 μ (CMe₂). Its nmr spectrum shows peaks at τ 6.15 (-CH₂O*H*), 6.53, and 6.83 (2 H, -C*H*₂OH), as well as at 9.08, 9.14, and 9.18 (9 H, (CH₃)₂CH and CH₃). The infrared spectrum of the saturated acetate VIa shows characteristic absorption bands for the carbonyl group at 5.77 μ and for the *gem*-dimethyl group at 7.23 and 7.30 μ. Its nmr spectrum shows peaks at τ 6.05 and 6.27 (2 H, -C*H*₂OAc), a singlet at 7.98 (C*H*₃CO-), and singlets at 9.09 and 9.18 (9 H), three protons (C*H*₃-).



VIa, R = Ac
b, R = H



VII

Interesting but perhaps less useful α-terpinene–formaldehyde condensations are those catalyzed by Lewis acids. Reaction of α-terpinene with formaldehyde for 24 hr at room temperature in methylene chloride containing stannic chloride gives *ca.* 75% of a product mixture whose principal component (*ca.* 80%) is 6-methyl-9-isopropyl-2,4-dioxabicyclo[4.4.0]-dec-9-ene (VII), n^{22}D 1.4820. Physical and chemical properties of the 1,3-dioxane agree with the structure VII. In the infrared spectrum the dioxane has characteristic absorption bands at 6.01 (unsaturation), 7.22, as well as at 7.34 (*gem*-dimethyl) and 9.62 μ. The nmr spectrum shows the following significant peaks which, on integration, support the structure VII: a symmetrical doublet centered at τ 4.55 (J = 5.5 cps) (H_a), a pair of unsymmetrical doublets (AB pattern) centered at 5.03 and 5.37 (H_b and H_c), a pair of unsymmetrical doublets (AB pattern) centered at 6.35 and 6.63 (J = 11 cps) (H_d and H_e), a symmetrical doublet centered at 6.35 (J = 5.5 cps) (H_f), and three sharp singlets at 8.98, 9.03, and 9.26 (9 H, (C*H*₃)₂CH, C*H*₃). Acid-catalyzed methanolysis of the 1,3-dioxane VII gives the alcohol Ib (77%) of purity *ca.* 90% (glpc analysis).[4c]

Reaction of α-terpinene with formaldehyde in methylene chloride–acetic anhydride containing boron trifluoride etherate as the catalyst gives, after 2.5 hr at room temperature, a 62% yield of products that comprises the two acetates Ia and IIa (77%, glpc analysis).[4a]

Reactions of formaldehyde with α-terpinene (a) in the absence of solvent and added catalyst, (b) in glacial acetic acid with sulfuric acid added as catalyst, and (c) in aqueous formic acid all give relatively low yields of rather complex mixtures of products.

Observations on the α-terpinene–formaldehyde condensation suggest that the reaction path, in simplified form, involves initial reaction of a conjugate acid of formaldehyde at site 1 of α-terpinene to form the

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(4) Glpc spectra were recorded on either an F & M Model 770 preparative gas chromatograph or an Aerograph manual temperature programmer gas chromatograph. The solid support in all glpc columns (analytical and preparatory) was 60–80 mesh, nonacid-washed Chromosorb W. Analytical columns were 0.25 in. in diameter and either 4 or 6 ft in length. The columns used for most of the analytical work were: (a) 15% diethylene glycol sebacate plus 5% Bentone 34 as liquid substrate; (b) 20% polyphenylether (five ring) as liquid substrate.

(5) Using Woodward's rules[6] the calculated maximum for the alcohol Ib is 242 mμ.

(6) L. Fieser and M. Fieser, "Advanced Organic Chemistry," Reinhold Publishing Corp., New York, N. Y., 1961, p 204.

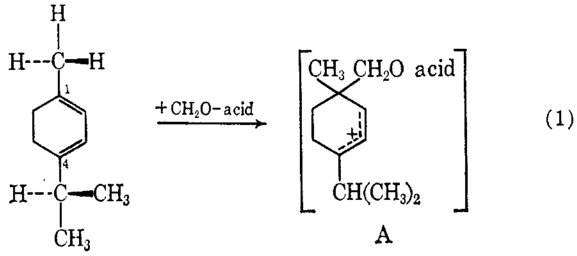
(7) H. Komae, *J. Sci. Hiroshima Univ.*, **A24**, 699 (1960); *Chem. Abstr.*, **56**, 6005 (1962).

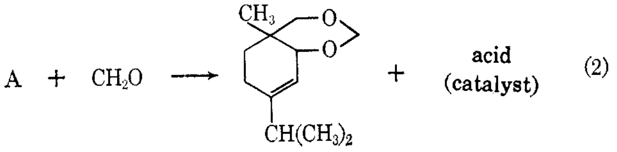
(8) G. Hunter and W. Brogden, Jr., *J. Org. Chem.*, **29**, 498 (1964).

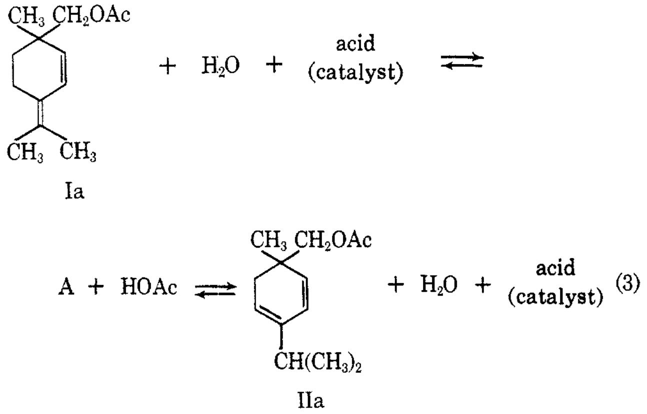
(9) H. Booker, L. K. Evans, and A. E. Gillam, *J. Chem. Soc.*, 1483 (1940).

(10) P. Nair and J. Roberts, *J. Am. Chem. Soc.*, **79**, 4565 (1957).

carbonium ion intermediate A (eq 1); reaction at position 1 rather than at position 4 is favored sterically. Reaction of A with another molecule of formaldehyde, in the inert solvent methylene chloride to give the 1,3-dioxane (eq 2), is to be expected. Formation of the unsaturated acetates Ia and IIa occurs *via* loss of β hydrogen from A. Expectedly, the transoid acetate Ia is formed at a slower rate than IIa (eq 3) but is the more stable of the two acetates.







Experimental Section[11]

Materials.—The α-terpinene used (90% pure) was a commercial product provided by the U. S. Department of Agriculture; the formaldehyde source was Fisher "trioxymethylene" (USP).

The Stannic Chloride Catalyzed Reaction of α-Terpinene with Formaldehyde.—Under a nitrogen atmosphere, a solution of 1.2 ml of fuming stannic chloride in 25 ml of methylene chloride was added dropwise over 45 min to a stirred mixture of 66.3 g (0.488 mole) of α-terpinene, 11.7 g (0.390 mole) of paraformaldehyde, and 100 ml of methylene chloride at room temperature. The reaction mixture was stirred for 23.2 hr after addition of the catalyst; a solution of dilute sodium hydroxide was then added, with stirring, to destroy the catalyst. This mixture was extracted with ether; the ether extracts were washed with water and dried ($MgSO_4$). Distillation of this dried ether extract gave 32 g of α-terpinene and 28 g of a principal product fraction: bp 96–110° (6.0–5.5 mm); $n^{20.5}\mathrm{D}$ 1.4878. Glpc analysis[4a] of this fraction at 165° indicated that it comprised *ca.* 80% of the 1,3-dioxane VII. Infrared analysis of the fraction showed that it contained an hydroxylic impurity.

The crude 1,3-dioxane VII (27.3 g) was added to 10.5 g of α-naphthyl isocyanate and the mixture was kept at room temperature for 24 hr in a sealed flask. Vacuum distillation then gave 20.7 g of the alcohol-free 1,3-dioxane VII. Traces of α-naphthyl isocyanate were removed by treatment of the dioxane VII (19.8 g) with 10 ml of methanol, followed by distillation *in vacuo*. There was obtained 17.6 g of the dioxane VII, bp 99–103° (4.5 mm). An analytical sample of VII was obtained by redistillation through a Vigreaux column, bp 75–76° (0.5 mm), $n^{22}\mathrm{D}$ 1.4820.

Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.66, 73.64; H, 10.20, 10.29.

Methanolysis of the 1,3-Dioxane VII. *p*-Mentha-2,4(8)-diene-1-methanol (Ib).—A mixture of 17.2 g (0.88 mole) of the dioxane VII, 20 ml of anhydrous methanol, and seven drops of concentrated sulfuric acid was refluxed 20 hr. Then, during a 7.2-hr period, portions of distillate were removed intermittently and fresh methanol was added. Finally, the mixture was refluxed for an additional 5 hr. The reaction mixture was diluted with water and extracted with ether, and the ether extracts were washed and dried. Distillation of the residue, after evaporation of ether, gave two principal product fractions: (1) 10.3 g, bp 87–100° (1.6 mm) and $n^{23}\mathrm{D}$ 1.5198; (2) 0.98 g, bp 100–110° (1.6 mm) and $n^{23}\mathrm{D}$ 1.5115. Alcohol Ib comprised 93% of fraction 1 and 67% of fraction 2.[4a] Three redistillations of the impure (93%) alcohol through a short Vigreaux column gave an analytical sample of Ib: bp 97.5–98° (2.1 mm); $n^{21.5}\mathrm{D}$ 1.5276; $\lambda_{\max}^{\mathrm{CH_3OH}}$ 243 mμ (ϵ 2.2 × 10^4).

Anal. Calcd for $C_{11}H_{18}O$: C, 79.46; H, 10.92. Found: C, 79.44; H, 11.06.

The 3,5-dinitrobenzoate derivative of the alcohol, prepared in the conventional way, has mp 103.5–104° after several recrystallizations from methanol.

Anal. Calcd for $C_{18}H_{20}N_2O_6$: C, 59.99; H, 5.59; N, 7.77. Found: C, 59.94, 59.85; H, 5.63, 5.70; N, 7.90, 7.99.

A mixture of 5.47 g of the impure (93%) alcohol Ib, 20 ml of acetic anhydride, and 1.0 g of sodium acetate was heated with stirring, at 58–67° for 12 hr. Conventional work-up of this reaction mixture gave, after vacuum distillation through a short Vigreaux column, 5 g of *p*-mentha-2,4(8)-diene-1-methanol acetate (Ia): bp 87–101° (1.9 mm); $n^{25}\mathrm{D}$ 1.4966. Careful redistillation of this acetate through a spinning band column gave the pure acetate Ia (glpc analysis[4a]): bp 102–105° (3.8 mm); $n^{18}\mathrm{D}$ 1.5026; $\lambda_{\max}^{\mathrm{CH_3OH}}$ 243 mμ (ϵ 2.3 × 10^4).

Anal. Calcd for $C_{13}H_{20}O_2$: C, 74.96; H, 9.68. Found: C, 75.08; H, 9.63.

Saponification of the acetate Ia regenerated the alcohol Ib described above (identical infrared and nmr spectra).

The Reaction of α-Terpinene with Formaldehyde in Acetic Acid. A. Mild Conditions.—A mixture of 49.8 g (0.366 mole) of α-terpinene and 6.00 g (0.200 mole) of paraformaldehyde in 75 ml of glacial acetic acid was stirred at 79–82° for 44 hr. The cooled mixture was then diluted with water and extracted with ether. From the washed and dried ether extracts, distillation *in vacuo* afforded 24.9 g of α-terpinene together with three principal-product fractions: (1) 18.1 g, bp 74–100° (1.3 mm), and $n^{20}\mathrm{D}$ 1.4849; (2) 2.19 g, bp 100–110° (1.3 mm), and $n^{20}\mathrm{D}$ 1.4905; (3) 7.23 g, bp 110–128° (1.3 mm), and $n^{20}\mathrm{D}$ 1.4775. Glpc analysis[4a] of the fractions 1 and 2 combined indicated that it was a complex mixture, 63% of which comprised the acetates Ia and IIb in a 1.0:1.6 ratio.

Saponification of 14.7 g of the combined fractions 1 and 2 gave 10.3 g of a mixture of products, bp 59–83° (0.2 mm), and $n^{20}\mathrm{D}$ 1.5008, that contained the alcohols Ib and IIb in a 1.0:2.0 ratio (glpc analysis[4a]) together with the 1,3-dioxane VII as major components. This product mixture (10.0 g) was chromatographed over 215 g of neutral alumina (Woelm, activity grade 1) and gave the following fractions (eluent in parentheses): (1′) 1.5 g (50:50 benzene-petroleum ether (30–60°)); (2′) 0.4 g (benzene); (3′) 0.8 g (60:40 benzene-ether; (4′) 1.9 g (ether); (5′) 2.8 g (acetone). Fraction 1′ contained the 1,3-dioxane VII (infrared analysis). Fraction 5′ was distilled *in vacuo* (to remove a low-boiling carbonyl contaminant) and combined with fraction 4′. The combined fractions were distilled through a spinning band column and then through a short Vigreaux column to give the pure alcohol IIb: bp 88–88.5° (3.3 mm); $n^{20}\mathrm{D}$ 1.4924; $\lambda_{\max}^{\mathrm{CH_3OH}}$ 258 ± 1 mμ (broad, ϵ 3.5 × 10^3).

Anal. Calcd for $C_{11}H_{18}O$: C, 79.46; H, 10.92. Found: C, 79.20; H, 10.88.

The acetate IIa, prepared in a conventional way by acetylation of the alcohol IIb (95% pure) with acetic anhydride and pyridine, has bp 103–106° (6.3 mm), $n^{19}\mathrm{D}$ 1.4722, and $\lambda_{\max}^{\mathrm{CH_3OH}}$ 259 mμ (ϵ 3.8 × 10^3).

Anal. Calcd for $C_{13}H_{20}O_2$: C, 74.96; H, 9.68. Found: C, 74.99, 74.98; H, 9.74, 9.69.

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[11] Infrared spectra were recorded on a Perkin-Elmer Infracord spectrophotometer; ultraviolet absorption spectra were obtained with a Cary 14 recording spectrophotometer; nmr spectra were observed on a Varian A-60 using either chloroform or carbon tetrachloride as solvents. Melting points are uncorrected.

B. **Vigorous Conditions.**—A mixture of 105.4 g (0.775 mole) of α-terpinene, 10.45 g (0.349 mole) of paraformaldehyde, and 200 ml of glacial acetic acid was stirred at 111–115° for 72 hr. The usual work-up of the reaction mixture (*supra vide*) gave 59 g of impure α-terpinene (*ca.* 68% pure by glpc analysis) and 50 g of a principal-product fraction, bp 60–108° (0.3–0.4 mm), $n^{24}\mathrm{D}$ 1.4882. Glpc analysis[4a] of this fraction showed that it comprised 96% α-terpinene–formaldehyde condensation products, 25% of which was the acetate IIb and 50% the acetate Ib; the remainder consisted of at least four minor products.

Catalytic hydrogenation, in a Parr apparatus, of 25 g of the above mixture of acetates in 75 ml of glacial acetic acid over 1.1 g of Adams catalyst for 70.5 hr at 47–48 psi gave 22 g of the stereoisomeric-saturated acetates VIa, bp 54–87° (1.1 mm), $n^{25}\mathrm{D}$ 1.4536. Glpc analysis indicated a purity of 95%.[4a] Saponification of 21 g of the acetates VIa, after a conventional work-up and distillation through a Vigreaux column, afforded two principal-product fractions: (1) 3.5 g, bp 64–72° (0.25 mm), $n^{25}\mathrm{D}$ 1.4685; (2) 12 g, bp 72–78° (0.25 mm), $n^{25}\mathrm{D}$ 1.4683. Redistillation of fraction 2 gave a center cut which had bp 73–77° (0.3 mm) and $n^{26}\mathrm{D}$ 1.4674. Glpc analysis of the latter sample of the isomeric saturated alcohols VIb at 165° on a column containing 15% diethylene glycol sebacate and 5% "Bentone 34" did not resolve the mixture cleanly and gave an unsymmetrical major peak. However, analysis at 165° on a column containing 20% polyphenyl ether (5 ring) partially resolved two major components and indicated the presence of a minor component (slight shoulder in peak with longer retention time).

Anal. Calcd for $C_{11}H_{22}O$: C, 77.58; H, 13.02; mol wt, 170. Found: C, 77.47; H, 12.98; mol wt, 166 (benzene).

The Reaction of α-Terpinene and Formaldehyde in Acetic Acid with Formic Acid as the Added Catalyst.—A mixture of 83.4 g (0.613 mole) of α-terpinene, 8.28 g (0.276 mole) of paraformaldehyde, 174 ml of glacial acetic acid, and 21.0 g of 98–100% formic acid was stirred at 111–114° for 72 hr. A normal work-up of the reaction mixture gave 37.1 g of crude α-terpinene (*ca.* 55% pure by glpc analysis) and 38.8 g of a principal-product fraction containing acetates and formates, bp 61–106° (0.55 mm), $n^{25}\mathrm{D}$ 1.4952.

A portion (22.5 g) of the above mixture of esters was added to a solution containing 10.0 g of potassium hydroxide in 100 ml of 95% ethanol and the resulting solution was refluxed for 22.5 hr. After the usual work-up of the reaction mixture the product was distilled to give 15.0 g of impure alcohol Ib, bp 68–80° (0.35 mm), $n^{25}\mathrm{D}$ 1.5177. Glpc analysis of the reaction product indicated that compound Ib comprised *ca.* 71%.

Methanolysis of the 1:1 Mixture of the Unsaturated Acetates Ia and IIa.—A mixture of 13 g of a 1:1 mixture of the acetates Ia and IIa (purity 74%), 16 ml of anhydrous methanol, and four drops of concentrated sulfuric acid was refluxed gently for 6.2 hr. Intermittently, 1-ml portions of distillate were removed and 1-ml portions of fresh methanol were added. Following a conventional work-up of the mixture there was obtained 7.5 g of a principal-product fraction that had bp 75–87° (0.7–0.9 mm) and $n^{20}\mathrm{D}$ 1.5218. Glpc analysis[4a] of this product showed that it comprised 85% of the single alcohol Ia.

The Boron Trifluoride Etherate Catalyzed Reaction of α-Terpinene with Formaldehyde.—Under a nitrogen atmosphere, a solution of 2 ml of boron trifluoride etherate in 40 ml of methylene chloride was added dropwise over a 1.5-hr period to a stirred mixture of 69.5 g (0.511 mole) of α-terpinene, 7.65 g (0.255 mole) of paraformaldehyde, 100 ml of methylene chloride, and 45 ml of acetic anhydride. This mixture was then stirred at room temperature for 1 more hour, poured into a solution of sodium carbonate, and extracted with ether. Distillation of the washed and dried ($MgSO_4$) ether extract gave 30 g of impure α-terpinene and two principal-product fractions: (1) 30.3 g, bp 67–97° (0.2 mm), $n^{20}\mathrm{D}$ 1.4877; (2) 2.2 g, bp 97–110° (0.2 mm), $n^{20}\mathrm{D}$ 1.5007. Glpc analysis[4a] showed that (a) the recovered α-terpinene is *ca.* 80% pure, (b) the unsaturated acetates Ia and IIa make up 77% of fraction 1 and fraction 2 is 92% acetate Ia. Presence of the two unsaturated acetates in the two fractions was confirmed by infrared analysis.

Catalytic hydrogenation of the combined fractions 1 and 2 (32 g) in 50 ml of glacial acetic acid over 1 g of Adams catalyst at *ca.* 40 psi for 24 hr at room temperature gave, after a conventional work-up, 21 g of the saturated acetates VIa (93% pure) together with some free alcohols (glpc analysis[4a]), bp 62–70° (0.1 mm), $n^{23}\mathrm{D}$ 1.4534. This product (20 g) was heated at 85–86° with 20 ml of acetic anhydride and 20 ml of pyridine for 6.5 hr and then, after a normal work-up, distilled *in vacuo*. Three product fractions were collected: (1) 8.82 g, bp 61–62° (0.2 mm), and $n^{17}\mathrm{D}$ 1.4550; (2) 5.92 g, bp 62° (0.15–0.20 mm), and $n^{17}\mathrm{D}$ 1.4547; (3) 3.20 g, bp 62° (0.15 mm), and $n^{17}\mathrm{D}$ 1.4548. Redistillation of fraction 2 gave a pure sample of the saturated acetates VIa, bp 79–86° (0.60 mm), and $n^{20}\mathrm{D}$ 1.4534.

Anal. Calcd for $C_{13}H_{24}O_2$: C, 73.53; H, 11.39. Found: C, 73.75; H, 11.45.

A conventional saponification of 3.86 g of the analytically pure acetates VIa gave, after two careful distillations *in vacuo*, 2.5 g (80%) of the saturated alcohols VIb, bp 83–85° (0.8 mm), $n^{25}\mathrm{D}$ 1.4671. Glpc analysis[4a] showed that the product contains only the two stereoisomeric saturated alcohols VIb.

Anal. Calcd for $C_{11}H_{22}O$: C, 77.58; H, 13.02. Found: C, 77.51, 77.39; H, 12.94, 12.75.

The α-Terpinene–Formaldehyde Reaction in Aqueous Formic Acid.—A solution of 15.6 g of 98–100% formic acid in 18 ml of water was added rapidly at room temperature to a mixture of 46.3 g (0.340 mole) of α-terpinene and 10.2 g (0.340 mole) of formaldehyde. This mixture was stirred at 60–61° for 24 hr, cooled, diluted with water, and extracted with ether. From the washed and dried ($MgSO_4$) ether extracts there was obtained, after distillation through a Vigreaux column, 22.8 g of α-terpinene and 19.6 g of a principal-product fraction, bp 90–101° (2.7 mm) and $n^{20}\mathrm{D}$ 1.4842, that comprised the 1,3-dioxane VII (74%) together with free alcohols and formates (glpc, infrared, and nmr analysis).

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O-Acylation of *dl*-Carnitine Chloride

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Excellent yields of very pure esters of *dl*-carnitine chloride with fatty acids having 2–18 carbon atoms are obtained by means of a special O-acylation method. Three different experimental procedures are described.

The known biochemical role of O-palmitylcarnitine chloride and the fact that the methods of preparation so far described lead to unsatisfactory yields[1–3] prompted us to study the synthesis of this substance and of its homologs. Previous experiments had shown that acetic acid, as well as acetyl chloride in which carnitine chloride is only slightly soluble, gave unsatisfactory results. The yield was 42% and the end product had to be recrystallized.[4]

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