The Synthesis of 5a,8,8-Trimethyl-3,10a-ethanoperhydrophenanthrene. Terpenes. VII[1]

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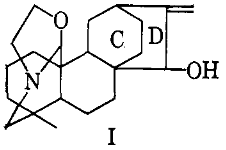
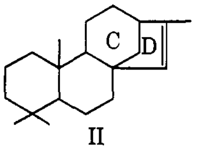
The synthesis of 5a,8,8-trimethyl-3,10a-ethanoperhydrophenanthrene (III, $C_{19}H_{32}$), which contains the same structure and relative stereochemistry as found in the diterpenoid skeleton of the atisine alkaloids is described.

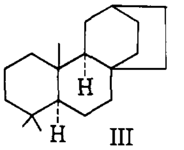
Atisine (I) and related diterpenoid alkaloids contain a bicyclo[2.2.2]octane C,D ring system, whereas the closely related Garrya alkaloids and the diterpenes of the phyllocladene group possess a bicyclo[3.2.1]-octane C,D ring structure.[2-5] A synthesis of phyllocladene (II) was reported recently by Turner and Ganshirt.[6] We wish now to report the synthesis of the hydrocarbon III, which contains nineteen of the twenty carbon atoms of the diterpenoid skeleton of atisine, and in addition contains a *trans–anti* ring fusion as found in the naturally occurring alkaloids.



I

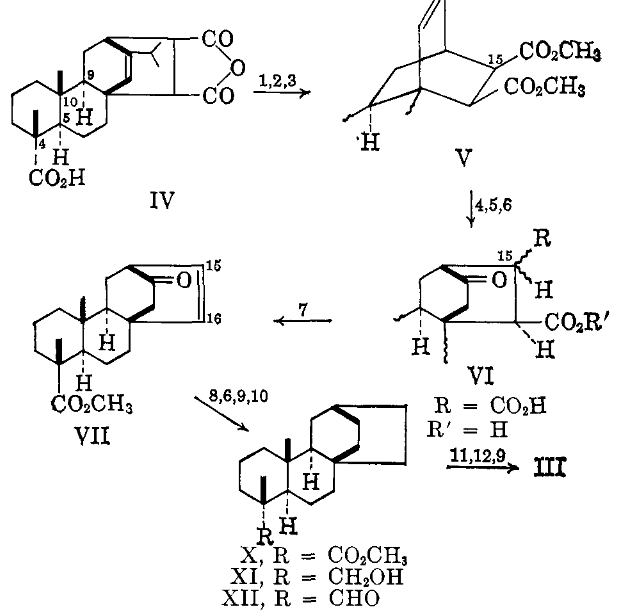


II



III

Maleopimaric acid (IV) was the starting material for the synthesis of III. It is readily prepared from maleic anhydride and abietic acid, and the latter compound has been totally synthesized.[7,8] The stereochemistry shown for maleopimaric acid (IV) is now well established.[9-14] The conversion of IV into III involves three phases: first, the removal of the isopropyl group of ring C; second, removal of the anhydride moiety of ring D; and finally, conversion of the C-4 carboxyl group to a methyl.[15]



1. PCl_3
2. CH_3OH
3. O_3
4. CF_3CO_3H
5. H^+
6. OH^-
7. $Pb[OAc]_4$
8. H_2, Pd/C
9. Wolff–Kishner
10. CH_2N_2
11. $LiAlH_4$
12. CrO_3, Pyridine

Diagram 1

The ozonolysis of the trimethyl ester of IV has been found to proceed in an unusual manner, leading to attack on the isopropyl group rather than the hindered double bond, to give as the major product the methyl ketone V.[14,16] The Baeyer–Villiger reaction on V followed by hydrolysis led directly to the ketone VI.[14] Again, the hindered double bond in V was not affected; peroxytrifluoroacetic acid converted V into an enol acetate which on hydrolysis gave the desired ketone.[14] Thus, the isopropyl group of the starting material could be removed readily.

The most obvious method of removing 1,2-dicarboxyl groups is that of oxidative bisdecarboxylation. However, this method has been known to be quite unreliable.[17-19] A recent modification[20] of the oxidative bisdecarboxylation procedure which utilizes lead tetraacetate in pyridine was found to give VII in good yield. The n.m.r. spectrum of VII showed the protons of the C-10 methyl group at δ 0.93, no noticeable shielding effect being exerted by the carbonyl group. In contrast, the C-10 methyl protons in IV and V appear at δ 0.59 and 0.50, a much larger shielding effect resulting from the C-13–C-14 double bond. Thus the n.m.r. spectrum of VII provides additional support for the assignment of the double bond at C-15–C-16. The C-15 proton in VII appeared as a doublet at δ 6.07 (J = 3) and the C-16 proton as a sharp singlet at δ 6.13, while the protons of the C-4 methyl group appeared at δ 1.12 and the protons of the carbomethoxy group at δ 3.62.

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[1] This work was supported generously by the National Science Foundation through grant GP-233.

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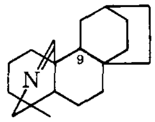
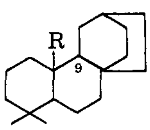
The further conversion of VII to III was accomplished as follows. The double bond of VII was reduced smoothly using palladium-on-charcoal catalyst to give VIII. Under identical conditions the double bond of IV was unaffected. The C-10 methyl protons of the saturated ketone VIII appeared slightly upfield (δ 0.82) from the corresponding protons in VII, while C-4 methyl protons in VIII (δ 1.10) were in almost the identical position to the corresponding protons in VII. The carbonyl group showed an absorption band at exactly the same wave length (1724 cm.$^{-1}$) in both VII and VIII. Compound VIII was saponified to give the keto acid IX in order to prevent reaction of the ester grouping with hydrazine during the Wolff–Kishner reaction. The carbonyl group of the keto acid IX was removed smoothly by the Huang-Minlon procedure to give an acid which was converted directly into the ester X with diazomethane. The n.m.r. spectrum of X showed the C-10 methyl protons at δ 0.95, while C-4 methyl protons appeared at δ 1.10. Reduction of X with lithium aluminum hydride gave the alcohol XI, which showed two sharp, three proton singlets at δ 0.73 (C-4 methyl) and 0.97 (C-10 methyl), and a pair of doublets (J = 10 c.p.s.) at δ 2.98 and 3.36 corresponding to the two protons attached to the carbon bearing the hydroxyl group; the hydroxyl proton appeared at δ 2.18 and this signal disappeared on the addition of deuterium oxide. Oxidation of alcohol XI with chromic anhydride in pyridine gave aldehyde XII which was characterized by infrared only ($\nu_{\max}^{\text{KBr}}$ 2680, 1724 cm.$^{-1}$) because of its rapid oxidation. Huang-Minlon reduction of XII gave hydrocarbon III (87%) as white needles, m.p. 86–87°, $[\alpha]_D + 38.7°$. The n.m.r. spectrum of III showed three sharp, three proton singlets at δ 0.82, 0.85, and 0.93 corresponding to the two methyl groups at C-4 and the one at C-10, respectively.

Hydrocarbon III, of absolute configuration shown, is potentially a useful intermediate for correlation with the atisine alkaloids. Atisine and ajaconine have both been degraded to the oxygen-free azomethine base, XIII, which in turn has been converted to XIV.[4]



XIII



XIV

R = CH_2OH, CHO, or CO_2H

The atisine alkaloids recently have been reported to possess a configuration at C-5, C-9, and C-10 which is the mirror image of that found in the resin acids and steroids.[21] Therefore, conversion of the carbonyl group of XIV (R = CHO) to a methyl group should give a hydrocarbon which is the enantiomer of III.

Experimental

Melting points were taken on a Fisher-Johns apparatus and are uncorrected. Analyses were performed by Midwest Microlab, Inc., Indianapolis, Ind. Infrared spectra were recorded using the Beckman IR-5 spectrophotometer. Nuclear magnetic resonance spectra were recorded with the Varian A-60 n.m.r. spectrometer, using tetramethylsilane as an internal standard (δ 0) and carbon tetrachloride as solvent (except where indicated).

Preparation of VII.—A mixture of ketone VI[14] (R = β CO_2CH_3, R′ = CH_3) (11.1 g.), methanol (55 cc.), sodium hydroxide (2.1 g.), and water (66 cc.) was refluxed for 45 min. After cooling, the reaction mixture was diluted with water (250 cc.), acidified with 6 N hydrochloric acid, and finally extracted with ether. The ether extract was washed with water, dried over anhydrous magnesium sulfate, and evaporated to give 10.9 g. of glassy solid which solidified on the addition of ethyl acetate. The solid (VI, R = α CO_2H, R′ = H) had m.p. 260–268° after recrystallization from ethyl acetate–acetone; $\nu_{\max}^{\text{KBr}}$ 3279 broad, 1730–1695 broad; n.m.r., δ 0.95 (3 protons), 1.22 (3), and 3.89 (3) (run in CF_3CO_2H).

The noncrystalline residue was converted to the previously described trimethyl ester VI (R = α CO_2CH_3, R = CH_3), with ethereal diazomethane; this latter ester could be partially saponified as described earlier to give VI (R = α CO_2H, R = H).

The diacid ester VI (R = α CO_2H, R = H), 8.1 g., was dissolved in 150 cc. of pyridine maintained at 70° and 8.8 g. of lead tetraacetate was added to the stirred solution under an atmosphere of nitrogen. After 10 min., when the initial reaction had subsided, an additional 4.4 g. of lead tetraacetate was added and the reaction mixture allowed to reflux for 1.5 hr. The pyridine was removed on the steam bath with a water aspirator and the dark brown residue was acidified with 6 N hyrdochloric acid and extracted with ether. The ether extract was washed with water, dried over anhydrous magnesium sulfate, and evaporated to give 6.3 g. of a brown solid. This solid was chromatographed on 100 g. of neutral alumina. Elution with 750 cc. of benzene and 9:1 benzene–ether (200 cc.) gave 3.46 g. of VII, m.p. 166–168°; positive tetranitromethane test; $\nu_{\max}^{\text{KBr}}$ 1724, 1616, 1248 cm.$^{-1}$; n.m.r., δ 0.93 (3), 1.12 (3), 3.62 (3), 6.06 (doublet J = 3 c.p.s., 1 proton), and 6.13 (1).

Anal. Calcd. for $C_{20}H_{28}O_3$: C, 75.91; H, 8.92. Found: C, 75.90; H, 8.92.

Hydrogenation of VII. Preparation of VIII.—The unsaturated ketone VII (3.46 g.) was hydrogenated with 0.37 g. of 10% palladium-on-charcoal catalyst in 130 cc. of ethyl acetate at atmospheric pressure. The theoretical volume of hydrogen was absorbed in 45 min. Filtration of the catalyst followed by evaporation of the ethyl acetate gave a quantitative yield of VIII, m.p. 128–130°. The analytical sample, prepared by recrystallization from hexane, had m.p. 129–130°, and gave a negative tetranitromethane test; $\nu_{\max}^{\text{KBr}}$ 1724, 1248 cm.$^{-1}$; n.m.r., δ 0.82 (3), 1.10 (3), and 3.60 (3).

Anal. Calcd. for $C_{20}H_{30}O_3$: C, 75.43; H, 9.49. Found: C, 75.36; H, 9.49.

Preparation of X.—A suspension of 3.5 g. of the saturated keto ester VIII in a mixture of 100 cc. of 5% sodium hydroxide and 100 cc. of methanol was refluxed for 10 hr. The clear, cooled solution was diluted with 500 cc. of water and extracted with ether to remove unchanged VIII. The remaining aqueous alkaline solution was made acidic with 6 N hydrochloric acid and then extracted with ether. After washing with water and drying over anhydrous magnesium sulfate, the ether was evaporated to give 2.68 g. of keto acid IX, m.p. 238–240°.

Keto acid IX (2.63 g.) was added to a solution of 5 g. of potassium hydroxide in 30 cc. of diethylene glycol and 5 cc. of 95% hydrazine. The reaction solution was refluxed for 4 hr., after which the temperature of the mixture was raised to 240° by distilling water and hydrazine. Hydrazine (5 cc.) was again added to the residue and refluxing was continued an additional 12 hr. After the addition of 250 cc. of water, the reaction mixture was made acidic with 6 N hydrochloric acid and extracted with ether. After washing with water and drying over anhydrous magnesium sulfate, the ether extract was evaporated to give a solid which was immediately treated with an excess of an ethereal solution of diazomethane. Removal of the solid gave crude X, which on recrystallization from methanol gave 2.5 g. (95%) of pure X, m.p. 97–98°; $\nu_{\max}^{\text{KBr}}$ 1724, 1253 cm.$^{-1}$; n.m.r., δ 0.95 (3), 1.10 (3), and 3.59 (3).

Anal. Calcd. for $C_{20}H_{32}O_2$: C, 78.89; H, 10.59. Found: C, 78.54; H, 10.28.

Ester X (2.18 g.) in 75 cc. of anhydrous ether was added dropwise to a well stirred suspension of 600 mg. of lithium aluminum hydride in 100 cc. of anhydrous ether. After refluxing the reaction mixture for 3 hr., the excess hydride was decomposed by the addition of ethyl acetate and then water. The solution was acidified with cold 6 N hydrochloric acid and extracted with ether. The ether layer, after washing with water and drying over anhydrous magnesium sulfate, was evaporated to give 1.9 g. of residue which on crystallization from methanol gave 1.8 g. (91%) of XI (m.p. 129–130°). The analytical sample was ob-

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tained by further recrystallization from *n*-hexane and gave m.p. 129–130°; ν_{max}^{KBr} 3311, 1038 cm.$^{-1}$; n.m.r., δ 0.73 (3), 0.97 (3), 2.18 (disappears on the addition of deuterium oxide), 2.98 (doublet, 1 proton), 3.36 (doublet, 1 proton).

Anal. Calcd. for $C_{19}H_{32}O$: C, 82.54; H, 11.66. Found: C, 82.93; H, 11.57.

A solution of 0.79 g. of XI in 10 cc. of anhydrous pyridine was added to a stirred mixture of 1 g. of chromic anhydride in 10 cc. of pyridine, and the entire mixture was then stirred at room temperature for 2 hr. After pouring into ice–water the solution was extracted with ether; the ether extract was washed successively with 5% hydrochloric acid and 5% sodium hydroxide, and then dried over anhydrous magnesium sulfate. The solvent was removed by evaporation and 0.7 g. of crude product was obtained. Crystallization from methanol gave the air-sensitive aldehyde (0.5 g.), m.p. 85–92°; ν_{max}^{KBr} 2680, 1724 cm.$^{-1}$. The aldehyde was reduced to III without further purification.

Potassium hydroxide (1.5 g.) was heated with 1.5 cc. of 95% hydrazine and 10 cc. of diethylene glycol until it dissolved. The aldehyde XII (400 mg.) was added to this solution and the reaction mixture was refluxed for 3 hr. Some of the product sublimed into the condenser during this period. Excess hydrazine and water were distilled until the temperature of the residue reached 240°. The distillate was saved and the sublimed material was washed out of the condenser with ether. Hydrazine (1.5 cc.) was again added to the residue and refluxing continued for an additional 12 hr. The reaction mixture, distillate, and ether washings were combined, added to water (150 cc.), and the entire mixture was extracted with ether. The ether extract was thoroughly washed with water and then dried over anhydrous magnesium sulfate. Evaporation of the ether gave 350 mg. of hydrocarbon III, m.p. 75–79°. Recrystallization from acetone gave 320 mg., m.p. 84–86°. The analytical sample was obtained by two recrystallizations from acetone and had m.p. 86–87°; $[\alpha]_D$ +38.7° (*c* 0.036 in CCl_4); ν_{max}^{KBr} 2941, 1460, 1390, 1370 cm.$^{-1}$; n.m.r., δ 0.82 (3), 0.85 (3), and 0.93 (3).

Anal. Calcd. for $C_{19}H_{32}$: C, 87.61; H, 12.38. Found: C, 87.96; H, 12.41.

Pyrolysis of Trityl Esters Possessing β-Hydrogen. II[1,2]

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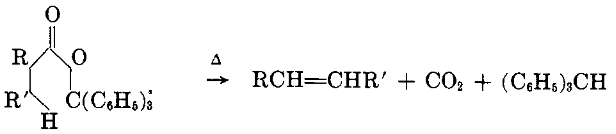
Pyrolysis of trityl propionate, trityl hydrocinnamate, and trityl pivalate has been examined over a temperature range of 225–430°. Nearly complete decomposition was observed in all examples whose reaction mixtures were analyzed meticulously by gas chromatography. Except in the case of trityl pivalate, the pyrolysates of the trityl esters were complex. The presence of tritan, tritanol, and benzophenone in the mixtures testified to the occurrence of both alkyl–oxygen and acyl–oxygen fission. Only with trityl pivalate was a degree of specificity observed, since isobutylene, carbon dioxide, and tritan were produced in high yields. Rather copious quantities of the respective acids were found in the other two pyrolysates, and only minor amounts of olefins were obtained. Mechanistic considerations involving radicals are proposed to explain the degradation results.

Trityl esters have been made readily accessible by a method described recently.[2] We now wish to report the pyrolysis studies of three trityl esters all of which possess at least one β-hydrogen atom in the acid portion of the molecule. Examination of the pyrolysate of trityl triphenylmethylacetate[5] appears to be the first recorded example in the area of trityl-substituted carbonyl compounds.[6] Tritan and carbon dioxide were the only components identified unequivocally in the reaction mixture.[5] Although stable at room temperature, trityl formate decomposed rapidly near 49° to give tritan and carbon dioxide.[7] Similarly, trityl fluoromethylacetate melted at 106° with decomposition but no details of a product analysis were presented.[8] In a study of the pyrolysis of several benzyl esters, Jones and Ritchie followed the thermal degradation of trityl benzoate.[9] The ester decomposed at 225° and 500° to give pyrolysates of nearly identical composition. The major pathway of cleavage involved aryl–acyl and alkyl–oxygen bond severance to give carbon dioxide and tetraphenylmethane. Minor products included benzoic acid, benzene, and triphenylmethane.[10]

Pyrolysis of acetates and xanthates has become a preferred method for preparation of olefins.[11] A decomposition process similar to that described in the acetate elimination reaction could be envisioned for the thermal collapse of a trityl ester whose structure is shown. Moreover, the absence of acidic products was an attractive possibility since a neutral medium at elevated temperatures would provide for minimum rearrangements.



Thermal decomposition of trityl propionate (1) was examined in a static system over the range 220–310°, which was above the boiling point of the ester. Contents of the pyrolysate were virtually unaltered at temperatures studied within the preceding range. Neither a bromine trap nor direct infrared analysis of the gaseous products from 1 indicated more than a trace of ethylene formed.

Clearly a concerted, intramolecular decomposition is not operative here as is known in acetate pyrolysis.[11] Table I contains pertinent data of a typical run on the type and weight of components in the pyrolysate from

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[1] (a) We gratefully acknowledge the support of the National Science Foundation, grant G-19733. Partial support by the Oklahoma State University Research Foundation is acknowledged. (b) Presented at the Southwest Regional Meeting of the American Chemical Society, Dallas, Tex., December 6–8, 1962.

[2] For paper I in the series, see *J. Org. Chem.*, **27**, 3595 (1962).

[3] To whom inquiries should be addressed.

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