The Total Synthesis of (±)-Perhydro-1,1,12-trimethylphenanthrene-6,14-dicarboxylic Acid

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WE report the stereoselective synthesis of the (±)-tricyclic dicarboxylic acid (I), a synthetic model for the *N*-acetyl-dicarboxylic acid (III) which served as the key intermediate in the correlation of atisine and the Garrya alkaloids[1] and also in the partial synthesis of atisine.[2]

Podocarpanone hydroxymethylene derivative (V),† prepared from the Cornforth–Robinson ketone (IV) in seven steps by the procedure of Ireland and his co workers,[3] was etherified with butanethiol[4] to afford the keto-thioether (VI) in 76% yield, m.p. 72—73°, ν_{max} (Nujol) 1660 (conj. >C=O), 1550 cm.$^{-1}$ (s) (>C=CHS-R), λ_{max} (EtOH) 314 mμ (ε 18,000). Reaction of the thioether (VI) as a sodio-enolate in benzene with allyl bromide[5] gave a product which consisted of the enol allyl ether (VIII), ν_{max} (film) 1635 (>C=C<), 1575 (conj. >C=C<), 920 (-CH=CH_2), 1120 cm.$^{-1}$ (C–O–C) [readily hydrolyzed by acid to the thioether (VI)] and the desired allyl ketone (VII), ν_{max}(film) 1660 (conj. >C=O), 1550 (conj. >C=C<), 1635 and 910 cm.$^{-1}$ (-CH=CH_2). Since the enol allyl ether (VIII) was found to rearrange at 200° to the allyl ketone (VII), the mixture obtained by the alkylation was directly heated at 200° to afford the homogeneous allyl ketone (VII) in 90% yield. Alkylation with ethyl bromoacetate or bromoacetonitrile proved unsatisfactory. A *cis*-B–C-ring juncture in compound (VII) is indicated, since the axial C-12 methyl group provides considerable hindrance to β-allylation at C-14.[6]

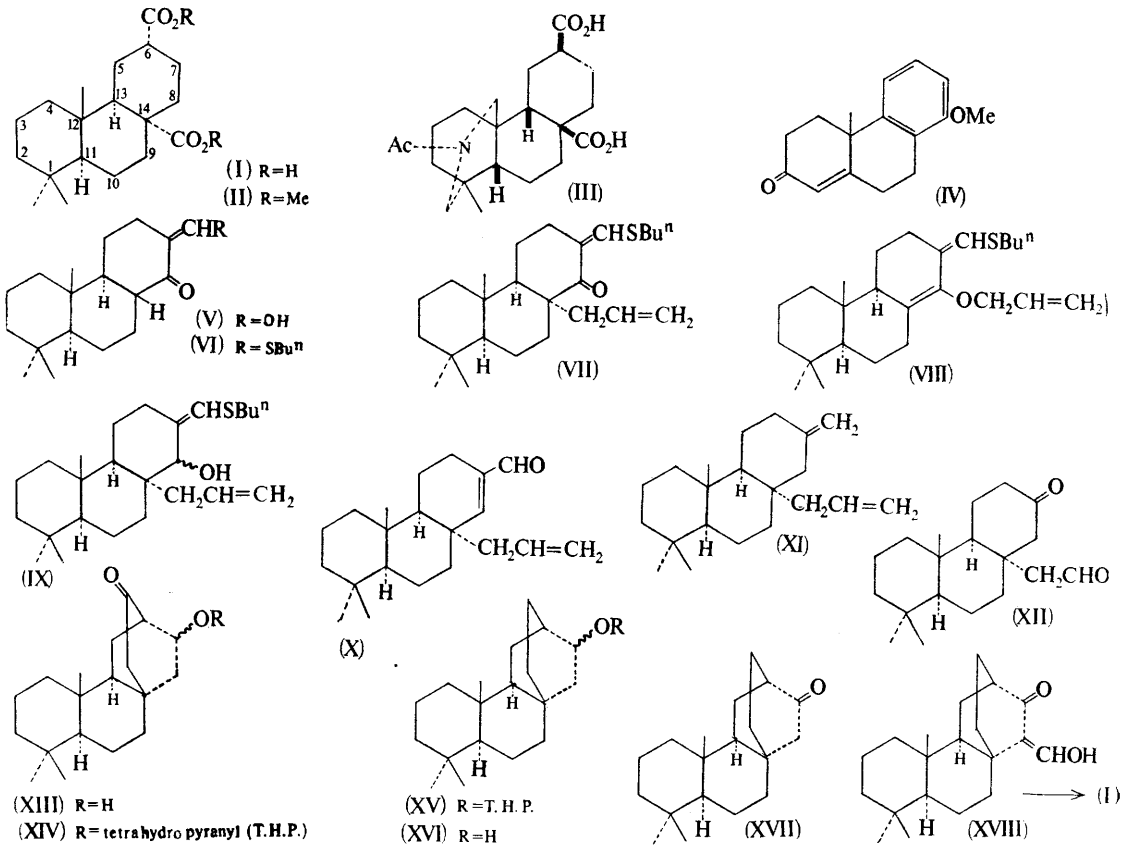
Contrary to expectations,[6a] sodium borohydride reduction of the allyl ketone (VII) proceeded smoothly to give (IX) which upon acid treatment, afforded the αβ-unsaturated aldehyde (X) in 38% yield, m.p. 111—112°, ν_{max} (Nujol) 2750, 1685 (-CHO), 1630 (>C=C<), 915 cm.$^{-1}$ (-CH=CH_2), λ_{max} (EtOH), 243 mμ (ε 10,300).

Wolff–Kishner reduction[7] of (X) gave the diene (XI), ν_{max} (film) 1590, 910 cm.$^{-1}$ (>C=CH_2), which upon ozonolysis afforded a product whose spectra, [ν_{max} (film) 3500, 2780 and sh 1710 cm.$^{-1}$ τ 0·12 (aldehyde proton)] indicated that it was a mixture of the keto-aldehyde (XII) and the tetracyclic ketol (XIII), formed from (XII) by aldol-type cyclization. Since (XII) could be easily converted into (XIII) by acid treatment, the mixture obtained from ozonolysis of (XI) was directly treated with acid to give exclusively the ketol (XIII), m.p. 209—211°, ν_{max} (Nujol) 3500 (OH), 1710 cm.$^{-1}$ (>C=O), previously described by Ireland.[8]

Removal of carbonyl group of (XIII) and oxidation to (XVII) was effected essentially by the method of Ireland *et al.*[8] Treatment of the tetrahydropyranyl ether (XIV), m.p. 125—127°, ν_{max} (CCl_4) 1720 (>C=O), 1125, 1080 cm.$^{-1}$ (C–O–C), under forcing Wolff–Kishner conditions[9] gave the norketone (XV), m.p. 85—87°, ν_{max} (CCl_4), 1125, 1080 cm.$^{-1}$ (C–O–C), which was hydrolyzed with acid to give the alcohol (XVI),[8] m.p. 142—144°, ν_{max} (Nujol) 3350 cm.$^{-1}$ (OH). The conversion of (XIII) to (XIV) was effected in an overall yield of 83%. Jones oxidation of the alcohol[8,10] (XIV) afforded the ketone (XVII), m.p. 128—130°, ν_{max} (CCl_4) 1720 cm.$^{-1}$, which was condensed with ethyl formate in the presence of sodium hydride to give the formyl derivative (XVIII), m.p. 109—111°, λ_{max} (EtOH) 278 mμ (ε 6,400), ν_{max} (KBr) 1665 (conj. >C=O), 1590 cm.$^{-1}$ (conj. >C=C<). Oxidative ozonolysis[11] of (XVIII) gave the diacid (I),‡ m.p. 295—298°, ν_{max} (KBr) 3400 (OH), 1690

† Although formulae of only one enantiomer of compounds (I) (II) (IV)—(XVIII) are drawn, they represent racemates. All new compounds gave satisfactory analytical data.

‡ In addition to the diacid (I), a small amount of the anhydride of (I) was obtained, ν_{max} (KBr) 1800, 1750 cm.$^{-1}$.



(-CO_2H), 1382, 1364 (C-1 *gem*-dimethyl). The yield from (XVI) to (I) was 57%. Treatment of the acid (I) with diazomethane afforded the dimethyl ester (II), ν_{max} (film) 1725 cm.$^{-1}$ (>C=O), τ 8·92 (3H), 9·17 (6H), 6·32 (3H), 6·35 (3H), which confirms the authenticity of the desired diacid (I).

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