# Synthesis and Conformation of Tricyclic 20-Norditerpenes* with Ring-C Aromatic†

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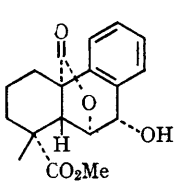
DURING our investigation on the chemical conversion of (−)-abietic acid into natural diterpene alkaloids,[1] we synthesised the *trans*- and *cis*-20-norditerpenes (III and IV). Alkaline hydrolysis of the hydroxy-lactone (I) obtained from (−)-abietic acid gave an oily acidic component in addition to the diacid (II) as previously reported. The oily component, which consisted of (III) and (IV), was methylated and then carefully chromatographed on alumina to give two isomeric keto-esters, $C_{17}H_{20}O_3$; (V), m.p. 77—79°, $\tau$ 8·72 (4-Me), 6·30 ($CO_2Me$); and (VI), m.p. 75—77°, $\tau$ 8·58 (4-Me), 6·29 ($CO_2Me$) in equal amounts. Since the same procedure (alkaline hydrolysis and methylation) of the diacid (II) yielded the same isomers (V and VI) in a ratio of **3 : 1**, it is evident that the decarboxylated compounds (V and VI) are stereoisomers only with respect to the configuration at C-10.

The 4-methyl groups of the ester (VII), $C_{17}H_{22}O_2$, m.p. 43—45°, $\tau$ 8·73 (4-Me), [obtained by hydrogenolysis of (V)], and of the corresponding alcohol (VIII), $C_{16}H_{22}O$, m.p. 81—83°, $\tau$ 8·96 (4-Me), show similar chemical shifts to the respective derivatives of podocarpic acid (IX), $\tau$ 8·73 and (X), $\tau$ 8·96.[2] This indicates that (V) has *trans*-A/B-ring fusion.

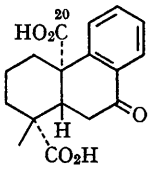
The other isomer (VI) was reduced by $NaBH_4$ to the hydroxy-ester (XI), $C_{17}H_{22}O_3$, m.p. 104—106°, $\nu_{max}(CCl_4)$ 3590 (free OH), 1738 (free C=O) cm.$^{-1}$, $\tau$ 6·27 ($CO_2Me$), and then hydrolysed to an oily hydroxy-acid (XII), which gave the original ester (XI) on methylation. A solution of (XII)

* The carbon atom C-20 is the one in the angular position, attached to C-10. If steroid numbering were followed this would be numbered C-19; see: R. McCrindle and K. H. Overton, *Adv. Org. Chem.*, 1965, **5**, 47.

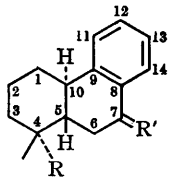
† Presented at the 23rd National Meeting of the Pharmaceutical Society of Japan at Sendai, October 1966 (Meeting Abstracts, p. 111). New compounds indicated by m.p. and b.p. gave satisfactory analytical values and were homogeneous on gas–liquid or thin-layer chromatography.



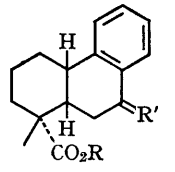
(I)



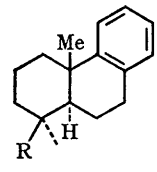
(II)



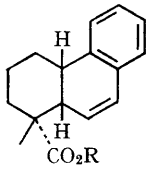
(III) R=$CO_2H$, R'=O
(V) R=$CO_2Me$, R'=O
(VII) R=$CO_2Me$, R'=$H_2$
(VIII) R=$CH_2OH$, R'=$H_2$



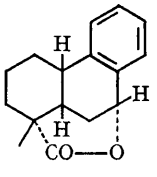
(IV) R=H, R'=O
(VI) R=Me, R'=O
(XI) R=Me, R'=α-OH, β-H
(XII) R=H, R'=α-OH, β-H
(XIII) R=Me, R'=$H_2$



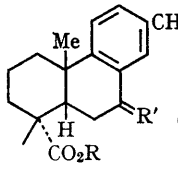
(IX) R=$CO_2Me$
(X) R=$CH_2OH$



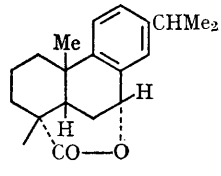
(XIV) R=Me
(XV) R=H



(XVI)



(XVII) R=H, R'=$H_2$
(XVIII) R=Me, R'=$H_2$
(XIX) R=Me, R'=O
(XX) R=Me, R=α-OH, β-H



(XXI)

kept at room temperature for a few days with aqueous-methanolic HCl, yielded the δ-lactone $C_{16}H_{18}O_2$ (XVI), m.p. 119—121°, $\nu_{max}$($CCl_4$) 1740 cm.$^{-1}$, τ 8·59 (4-Me), together with the oily acid (XV). Lactone formation by (XII) shows that derivatives of (VI) have a *cis*-A/B-fused ring-junction (10β-H), and that (XI) and (XII) have an α-hydroxy-group whose assignment is also consistent with attack by $NaBH_4$ from the less hindered side of (VI). Methylation of (XV) gave an unsaturated ester (XIV), $C_{17}H_{20}O_2$, b.p. 175—177°/2 mm., $\lambda_{max}$(EtOH) 263 mμ (ε 6890), τ 6·32 ($CO_2Me$). This was hydrogenated catalytically to the saturated ester (XIII), $C_{17}H_{22}O_2$, b.p. 168—171°/1 mm., τ 6·32 ($CO_2Me$), which was identical with the hydrogenolysis product from the keto-ester (VI). Thus no structural inversion had occurred in the sequence of reactions.

Recently there has been an interesting discussion on whether the preferred conformation of a *cis*-ring-fused system is of the steroid or nonsteroid type. For instance, the conformation assigned to *cis*-10-methyl-2-decalone was revised twice in only a few years,[3] and a subtle relationship between preferred conformation and the substituent in a *cis*-ring-fused system is now being discussed.[3c,4]

The conformation of the *cis*-isomer will be discussed in comparison with that of the *cis*-10-methyl-diterpene (XVII) and its derivatives‡ obtained from dehydroabietic acid by Wenkert's method.

Oxidation of the *cis*-10-methyl compound (XVIII), τ 6·63 ($CO_2Me$) afforded the 7-keto-ester (XIX), $C_{21}H_{28}O_3$, m.p. 100—102°, τ 7·06 ($CO_2Me$), and reduction of (XIX) with $NaBH_4$ yielded the hydroxy-ester (XX), $\nu_{max}$($CCl_4$) 3590, 1735 (free OH and C=O), 3520, 1705 (intramolecularly hydrogen-bonded OH and C=O) cm.$^{-1}$, τ 6·82 ($CO_2Me$), which after chromatography on alumina gave the δ-lactone (XXI), m.p. 166—167°, $\nu_{max}$(KBr) 1715 cm.$^{-1}$, τ 8·58 (4-Me) in quantitative yield.

Distinct differences were observed in the properties of the 20-nor and the corresponding 10-methyl series: (i) The i.r. spectrum of (XX) shows intramolecular hydrogen bonding between the 4-methoxycarbonyl and the 7-hydroxy-groups, while (XI) shows only the free groups. (ii) In contrast to the ready lactonisation of (XX) by alumina chromatography, (XI) was unaltered on alumina, and only a poor yield of the lactone (XVI) was obtained on treatment of (XII) with acid. These differences indicate that the 4-methoxycarbonyl group of (XX) is located near to the 7-hydroxy-group, while this is not the case in

‡ Wenkert and his co-workers first assigned *trans*-A/B ring-fusion to this compound (*J. Amer. Chem. Soc.*, 1961, **83**, 4440) but later revised the structure to (XVII) (*J. Org. Chem.*, 1965, **30**, 713; *cf.* S. N. Mahapatra and R. M. Dodson, *Chem. and Ind.*, 1963, 253). Their conformational study by n.m.r. led to the conclusion that (XVII) appears to be a more drastically reoriented form of a steroid-type conformer.

(XI). (iii) The methyl chemical shift of the methoxycarbonyl group of the 20-nor series appears in the usual region ($\tau$ 6·27—6·32), but the corresponding absorption of the 10-methyl compounds is shifted to a considerably higher magnetic field ($\tau$ 6·63—7·06). Thus, the methoxycarbonyl group at C-4 in the 10-methyl compound is oriented in a positive-shielding region above the benzene ring. We conclude from these observations that the steroid-type A/B-ring-fused conformation of the 10-methyl series is preferred to the nonsteroid-type conformation having a 1,3-diaxial nonbonding interaction between the C-10- and C-4-methyls and, conversely, a nonsteroid-type conformation is preferred in the 20-nor-compound where the C-10 proton is present.

The conformational assignments of ring-B in the hydroxy-esters (XI and XX) and the corresponding lactones (XVI and XXI) were settled by studying the n.m.r. spectra. The absorption due to their C-7 proton [hydroxy-esters: (XX) $\tau$ 5·34 (t, $J$ 6·8, 7·5 c./sec.); (XI) $\tau$ 5·24 (t, $J$ 7·5, 9·0 c./sec.); lactones: (XXI) $\tau$ 4·82 (half band width 9·0 c./sec.); (XVI) $\tau$ 4·75 (half band width 5·3 c./sec.)] indicates that in (XI) and (XX) the C-7 proton is axial, whereas in (XVI) and (XXI) the C-7 proton is equatorial. Accordingly, it is assumed that (XI) (nonsteroid type) should have a half-boat (or skew half-boat) B-ring, whereas (XX) (steroid type) should have a half-chair B-ring. Structural models of the lactones show that (XVI) and (XXI) should have a 7$\alpha$-hydroxy-group and a half-chair B-ring, and this assignment is also consistent with the n.m.r. analysis of the C-7 proton (equatorial). Thus conformational inversion (nonsteroid- → steroid-type) of the A/B-rings occurs in the lactonisation of the (XII) which has the same conformation as (XI).

These observations provide an interesting example of the preferred conformation of *cis*-A/B-fused rings being dependent on the presence of an angular methyl group.

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