Tetranortriterpenoids from *Melia azadirachta* L.

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IN order to explain the biogenesis of the ring-D epoxy-lactone in limonin, an attractive sequence of reactions and compounds has been assumed.[1] It was suggested that the epoxy-lactone could be formed by a Baeyer–Villiger oxidative cleavage of a 14,15-epoxy-16-ketone formed from a Δ^{14}-16-ketone in ring-D; such a system should originate from a compound of the apoeuphol type having a double bond at C-14 (methyl group at C-8).[1] We report the isolation of three compounds with the appropriate systems in ring-D from the seed oil of *Melia azadirachta* L. (Nim oil), namely epoxyazadiradione (I; 1%), azadiradione (II; 0·8%), and azadirone (III; 0·0025%) along with the corresponding epoxy-lactones gedunin and 7-deacetylgedunin. The occurrence of all these compounds

TABLE

Nuclear magnetic resonance signals of the compounds (given in δ-values)

Compound	H-1	H-2	H-7	H-15	H-17	Furan α-H	Furan β-H	Ac	Methyl groups
(I)	7·10d $J=10$ c./sec.	5·76d	4·68t	3·33t	3·83	7·52 7·35	6·18	1·98	1·00, 1·02(2), 1·19, 1·20
(II)	7·17d	5·83d	5·32	5·85	3·43	7·45	6·28	1·95	1·03, 1·08(2), 1·27, 1·35
(III)	7·18d	5·83d	5·35	5·24		7·25 7·35	6·30	1·97	0·81, 1·10(2), 1·20, 1·23
(IV)			4·70t	3·38	3·86	7·52 7·35	6·18	2·02	1·02(3), 1·06, 1·18
(V)			5·30	5·85	3·40	7·42	6·26	1·95	1·02(2), 1·03(1), 1·10, 1·3
(VI)			3·05m	3·55	3·87	7·50 7·38	6·2		1·0, 1·02, 1·05(3)
(VII)				3·58	3·76	7·5 7·38	6·2		0·86, 1·08, 1·20, 1·22(2)

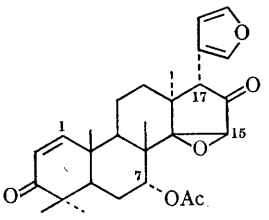
d = doublet t = triplet m = multiplet

in the same plant supports the suggested biogenetic scheme.[1]

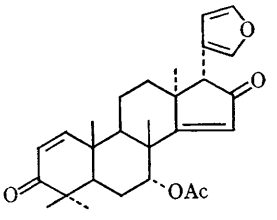
Epoxyazadiradione (I) $C_{28}H_{34}O_6$ (M^+ 466), m.p. 199—200°, $[\alpha]_D$ −75° ($CHCl_3$), λ_{max} (hexane) 225 mμ (ε 10,800), ν_{max} ($CHCl_3$) 1751 (αβ-epoxycyclopentanone), 1736 (acetate), 1678 (cyclohexenone), and 886 (furan) cm.$^{-1}$; the n.m.r. spectrum (see Table) showed all the appropriate peaks for the suggested structure. Hydrogenation of (I) over palladium on $CaCO_3$ in the presence of 0·1% NaOH yielded quantitatively 1,2-dihydroepoxyazadiradione (IV) $C_{28}H_{36}O_6$ (M^+ 468), m.p. 202—203°, $[\alpha]_D$ −4° ($CHCl_3$), λ_{max} (ethanol) 217 mμ (ε 5400), ν_{max} (KBr) 1751, 1730 (acetate), 1710 (cyclohexanone), and 886 cm.$^{-1}$. Treatment of (IV) with chromous chloride in acetic acid induced the elimination of the 14β,15β-epoxide affording the expected 1,2-dihydroazadiradione (V), $C_{28}H_{36}O_5$ (M^+ 452), m.p. 178—179° (acetone–pentane), $[\alpha]$ −30° ($CHCl_3$), λ_{max} (hexane) 217 (ε 8500) and 224 mμ (infl.), ν_{max} ($CHCl_3$), 1735 and 1710 cm.$^{-1}$ (C-3 and C-16 carbonyls). Hydrolysis of (IV) gave the 7-hydroxy-derivative (VI) which upon oxidation (CrO_3–pyridine) afforded the corresponding 7-ketone (VII). The positions of the 7H and 15-H signals in the n.m.r. spectra of the compounds were in accordance with the positions observed for the derivatives of meliacin,[2] cedrelone,[2] and grandifolione.[3]

Additional support for the suggested structure of epoxyazadiradione (I) was obtained from its mass spectrum in which the base peak is *m/e* 108, corresponding to a fragment (VIII). This peak was also observed for (IV), (VI), and (VII).

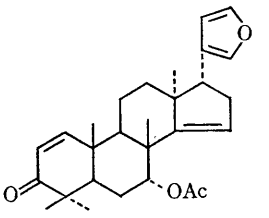
Azadiradione (II) $C_{28}H_{34}O_5$ (M^+ 450), $[\alpha]_D$ −24°



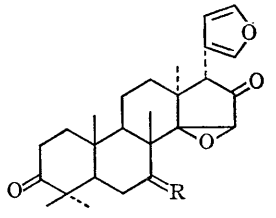
(I)



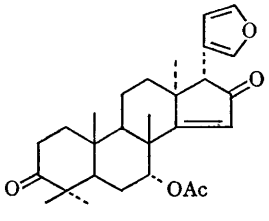
(II)



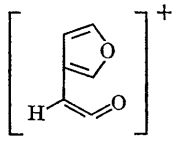
(III)



(IV) R = α-OAc, β-H
(VI) R = α-OH, β-H
(VII) R = O



(V)



(VIII)

($CHCl_3$), λ_{max} (hexane) 225 mμ (ε 14,800), ν_{max} ($CHCl_3$) 1738, 1710 (cyclopentenone), 1680 (cyclohexenone), and 885 cm.$^{-1}$ could not be induced to

crystallise; however, upon partial hydrogenation the crystalline 1,2-dihydroazadiradione (V) was obtained. Azadirone (III) $C_{28}H_{36}O_4$ (M^+ 436), $[\alpha]_D$ +26° ($CHCl_3$), λ_{max} (hexane) 225 mμ (ϵ 10,000), ν_{max} (KBr) 1740 (acetate), 1680 (cyclohexenone), and 876 cm.$^{-1}$ could not be crystallised. Selenium dioxide oxidation in aqueous dioxan at room temperature afforded azadiradione [identical with the natural (II)] which upon hydrogenation provided the crystalline 1,2-dihydroazadiradione (V).

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[2] J. W. Powell, *J. Chem. Soc.* (*C*), 1966, 1794.
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