Studies in the Chemical Constituents of *Azadirachta indica* A. Juss (Meliaceae). Part 10.[1] Isolation and Structure Elucidation of Isonimolicinolide, the First 17-Acetoxy Tetranortriterpenoid and Nimolicinoic Acid, the First Hexanortriterpenoid with an Apoeuphane (Apotirucallane) Skeleton

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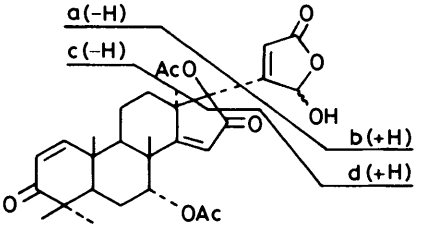
Isonimolicinolide (**1**) and nimolicinoic acid (**3**), two new triterpenoids have been isolated from the neutral fraction of the fresh, undried, unruptured, ripe fruits of *Azadirachta indica* (neem) and their structures elucidated through chemical and spectral studies. The mother fraction of the two triterpenoids showed insect growth regulating properties against the pulse beetle (*Callasobruchus analis*). Isonimolicinolide (**1**) is the first example of a tetranortriterpenoid with an acetoxy function at C-17, and nimolicinoic acid (**3**) is the first instance of a hexanortriterpenoid with an apoeuphane (apotirucallane) skeleton as well as the first hexanortriterpenoidal acid, isolated from any source.

The results of investigations into the terpenoidal constituents of neem, and the isolation and structure elucidation of various triterpenoids from fresh fruits[2-5] and leaves[1,4,6,7] have been communicated earlier. Work on the neutral fraction of fresh, undried, unruptured, ripe fruits resulted in the isolation of two new triterpenoids, isonimolicinolide and nimolicinoic acid, the structures of which have been established as (**1**) and (**3**) respectively, through chemical and spectral studies. Compounds (**1**) and (**3**) are of potential biological importance since preliminary experiments carried out on the neutral fraction-B have shown that it possesses insect growth regulating properties against the pulse beetle (*Callasobruchus analis*). Moreover, as already noted, other γ-hydroxy butenolides possess insect growth regulating[4] and insect antifeeding[8] properties.

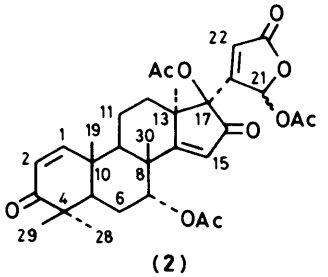
Results and Discussion

Ethanolic extracts of the fruits of neem were divided into acidic and neutral fractions. The residue obtained on work-up of the latter, was subjected to solvent fractionation followed by column chromatography. Subsequent purification of benzene–ethyl acetate (90:10 and 85:15 v/v) eluates through preparative t.l.c. on silica gel, yielded isonimolicinolide (**1**) and nimolicinoic acid (**3**) respectively.

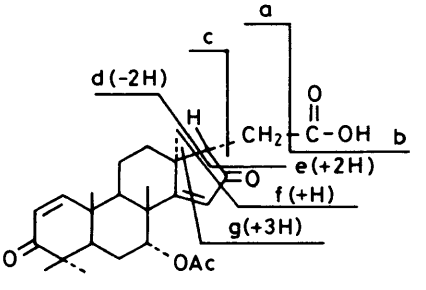
Isonimolicinolide (**1**) has molecular formula $C_{30}H_{36}O_9$ (high resolution mass spectroscopy). Its u.v. spectrum showed absorption at 230 nm, while the i.r. spectrum displayed peaks at 3 400 (OH), 1 765 (α,β-unsaturated-γ-lactone), 1 740br (ester carbonyl), 1 710 (cyclopentenone), 1 660 (cyclohexenone), 1 650, and 820 cm^{-1} (trisubstituted double bonds). The molecular formula, and the functionalities indicated by the i.r. spectrum were corroborated by the ^1H and ^{13}C n.m.r. spectra (Tables 1 and 2 respectively). The ^{13}C n.m.r. spectrum (broad band and GASPE) showed that (**1**) has two ketonic and three ester carbonyls, four tertiary and two quaternary olefinic carbons, one tertiary and one quaternary carbinylic carbon, a hemiacetal carbon, seven methyls, three methylenes, two methines, and four quaternary carbons. The ^1H n.m.r. spectrum (Table 1) showed a pair of doublets at δ 7.14 and 5.90 (J 10.1 Hz) related to 1-H and 2-H respectively, a 1 H singlet at δ 5.85 (15-H), a 1 H multiplet ($W_{\frac{1}{2}}$ = 7.5 Hz) at δ 5.33 (7-H), a 3 H singlet at δ 1.96 (OAc), and five singlets at δ 1.05, 1.07, 1.20, 1.26, and 1.35 (5 × Me). These values are in agreement with those reported for the same protons in azadiradione.[9] However, the signals for the furan ring were missing in the i.r. as well as ^1H and ^{13}C n.m.r. spectra (Tables 1 and 2) and instead a 21-hydroxybut-20(22)-ene-21,23-γ-lactone was indicated by the presence of two 1 H



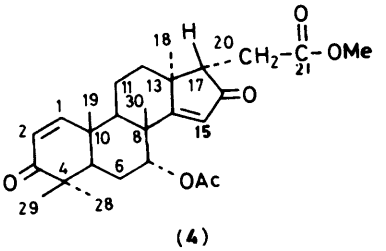
Isonimolicinolide (**1**)



(**2**)



Nimolicinoic acid (**3**)



(**4**)

Table 1. ^{1}H N.m.r. spectral data (δ_H and J/Hz)

Assignment	Azadoradione*	(1)	(2)	(3)	(4)
1-H	7.12 (d)	7.14 (d)	7.13 (d)	7.12 (d)	7.11 (d)
	$J_{1,2}$ 10.2	$J_{1,2}$ 10.1	$J_{1,2}$ 10.3	$J_{1,2}$ 10.1	$J_{1,2}$ 10.1
2-H	5.88 (d)	5.90 (d)	5.92 (d)	5.90 (d)	5.88 (d)
	$J_{2,1}$ 10.2	$J_{2,1}$ 10.1	$J_{2,1}$ 10.3	$J_{2,1}$ 10.1	$J_{2,1}$ 10.1
5-H	2.21 (dd)	2.20 (dd)	2.17 (dd)	2.21 (dd)	2.20 (dd)
	$J_{5,6\alpha}$ 3.5	$J_{5,6\alpha}$ 2.8	$J_{5,6\alpha}$ 3.0	$J_{5,6\alpha}$ 3.0	$J_{5,6\alpha}$ 3.1
	$J_{5,6\beta}$ 12.3	$J_{5,6\beta}$ 12.0	$J_{5,6\beta}$ 12.0	$J_{5,6\beta}$ 12.0	$J_{5,6\beta}$ 12.0
6α-H	2.07 (ddd)	2.04 (m)	2.09 (m)	2.02 (ddd)	2.04 (ddd)
	J_{gem} 15.0			J_{gem} 13.7	J_{gem} 13.7
	$J_{6\alpha,5}$ 3.5			$J_{6\alpha,5}$ 3.0	$J_{6\alpha,5}$ 3.0
	$J_{6\alpha,7}$ 3.5			$J_{6\alpha,7}$ 2.0	$J_{6\alpha,7}$ 3.0
6β-H	1.99 (m)	2.01 (m)	2.05 (m)	1.95 (m)	1.93 (m)
7-H	5.31 (m)	5.33 (m)	5.33 (m)	5.31 (dd)	5.27 (t)
	$W_{\frac{1}{2}}$ 7.0	$W_{\frac{1}{2}}$ 7.5	$W_{\frac{1}{2}}$ 7.2	$J_{7,6\alpha}$ 2.0	$J_{7,6\alpha}$ 3.0
				$J_{7,6\beta}$ 2.3	$J_{7,6\beta}$ 3.0
9-H	2.50 (dd)	2.48 (dd)	2.42 (m)	2.54 (dd)	2.50 (dd)
	$J_{9,11\alpha}$ 4.0	$J_{9,11\alpha}$ 5.0		$J_{9,11\alpha}$ 5.6	$J_{9,11\alpha}$ 5.3
	$J_{9,11\beta}$ 11.0	$J_{9,11\beta}$ 11.2		$J_{9,11\beta}$ 11.0	$J_{9,11\beta}$ 10.0
11α-H	2.11 (m)	2.09 (m)	2.12 (m)	2.10 (m)	2.15 (m)
11β-H	1.88 (m)	1.89 (m)	1.98 (m)	1.80 (m)	1.85 (m)
12α-H	1.80 (m)	2.34 (ddd)	2.30 (ddd)	2.30 (m)	2.28 (m)
		J_{gem} 14.7	J_{gem} 14.0		
		$J_{12\alpha,11\alpha}$ 3.0	$J_{12\alpha,11\alpha}$ 3.0		
		$J_{12\alpha,11\beta}$ 7.0	$J_{12\alpha,11\beta}$ 7.0		
12β-H	2.35 (m)	1.63 (m)	1.59 (m)	1.78 (m)	1.76 (m)
15-H	5.86 (s)	5.85 (s)	5.85 (s)	5.86 (s)	5.79 (s)
17-H	3.41 (s)			2.68 (t)	2.71 (dd)
				$J_{17,20a}$ 7.0	$J_{17,20a}$ 5.2
				$J_{17,20b}$ 7.0	$J_{17,20b}$ 8.5
20-H_a				2.84 (dd)	2.84 (dd)
				J_{gem} 15.0	J_{gem} 16.0
				$J_{20a,17}$ 7.0	$J_{20a,17}$ 5.2
20-H_b				2.41 (dd)	2.31 (dd)
				J_{gem} 15.0	J_{gem} 16.0
				$J_{20b,17}$ 7.0	$J_{20b,17}$ 8.5
21-H	7.46 (m)	6.24 (m)	6.99 (m)		
22-H	6.26 (m)	6.07 (m)	6.35 (m)		
23-H	7.42 (m)				
OH		2.50—2.80 (br m)			
OAc	1.94 (s)	1.95 (s)	1.95 (s)	1.93 (s)	1.90 (s)
		1.96 (s)	2.04 (s)		
			2.04 (s)		
OMe					3.34 (s)
13-Me	1.02 (s)	1.20 (s)	1.23 (s)	1.19 (s)	1.20 (s)
10-Me	1.24 (s)	1.35 (s)	1.26 (s)	1.24 (s)	1.29 (s)
4α-Me	1.09 (s)	1.05 (s)	1.10 (s)	1.09 (s)	1.07 (s)
4β-Me	1.09 (s)	1.07 (s)	1.10 (s)	1.09 (s)	1.07 (s)
8-Me	1.35 (s)	1.26 (s)	1.28 (s)	1.31 (s)	1.38 (s)

* Assignments based on the spectrum recorded on 300 MHz instrument and NOESY (see Experimental section).

Table 2. ^{13}C N.m.r. spectral data (δ_C/p.p.m.)

Carbon	Azadiradione[11]	(1)	(3)	Carbon	Azadiradione[11]	(1)	(3)
1	156.7	156.8	156.4	17	60.6	79.0	58.7
2	125.8	126.0	126.0			79.2	
3	203.8	204.4	203.5	18	26.3	31.9[b]	25.1
4	44.0[a]	44.1[a]	44.1[a]	19	18.9	19.1	19.0
5	38.1	38.3	38.1	20	118.4	160.2	30.2
6	23.4	23.6	23.5			160.5	
7	73.8	74.1	74.0	21	142.7	98.7	174.4
8	44.5[a]	45.3[a]	44.9[a]			99.0	
9	46.0	46.2	46.3	22	111.1	120.9	
10	39.9	40.1	40.0			121.2	
11	15.7	15.7	15.7	23	141.6	169.5	
12	30.2	24.8	30.5			170.0	
13	47.9	51.2	47.2	28	21.2	21.3[c]	21.2[b]
14	192.3	189.7	194.5	29	26.9	27.0	26.3
15	123.2	123.0	122.8	30	26.2	33.5[b]	27.0
				O ‖ O–C–CH_3	169.5	171.5	169.5
		123.2					
16	204.9	206.6	207.2			171.5	
				O ‖ O–C–CH_3	20.8	21.0[c]	20.9[b]
		206.8				25.6	

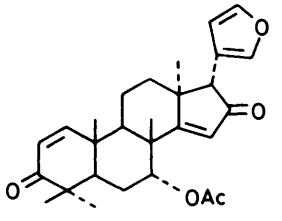
[a–c] Assignments in a vertical column may be interchanged.

signals at δ 6.24 (21-H) and 6.07 (22-H) in the ^{1}H n.m.r. spectrum.[4] This was supported by the presence of signals at δ 160.5 (C-20), 98.7 (C-21), 120.9 (C-22), and 170.0 (C-23) in the ^{13}C n.m.r. spectrum (Table 2), and a diagnostic fragment at *m/z* 440.2146 ($C_{26}H_{32}O_6$, fragment a) in the mass spectrum of (**1**), resulting from the loss of a side chain. The n.m.r. spectra showed the presence of a further acetoxy function, apart from one located at C-7, which could be placed at C-17 since the signal for 17-H (δ 3.41, s, in the case of azadiradione)[9] was missing in the ^{1}H n.m.r., and a quaternary carbon which appeared at δ 79.2 in the ^{13}C n.m.r. spectrum. This was supported by the appearance of a significant fragment at *m/z* 369.2042 ($C_{23}H_{29}O_4$, fragment c) in the mass spectrum, resulting from the loss of $C_7H_7O_5$. Acetylation of (**1**) yielded the acetyl derivative (**2**), the ^{1}H n.m.r. spectrum of which showed the signals of 21-H and 22-H shifted to δ 6.99 and 6.35 respectively along with the appearance of a total of three singlets for the methyl groups of acetoxy functions. The presence of double signals for C-15 to C-17 and C-20 to C-23 (Table 2) indicated that (**1**) epimerises at C-21, *via* opening and reclosing of the lactone ring in $CDCl_3$ containing trace acidic impurities. This phenomenon has also been noted earlier for other γ-hydroxybutenolides.[4,8]

The stereochemistry of various centres of isonimolicinolide (**1**) has been established through NOESY spectral analysis which showed the spatial connectivities of 13-Me with 22-H, 9-H, and 7-OAc; 4α-Me with 7-OAc, 6α-H, and 5-H; 4β-Me with 7-H, 6β-H, and 1-H; 10-Me with 12β-H, 11β-H, 7-H, 6β-H, 2-H, 1-H, 17-OAc, and 4β-Me; and 8-Me with 15-H, 11β-H, 7-H, 6β-H, and 17-OAc. The spatial proximity of 13-Me with 22-H showed that the side chain at C-17 has α orientation.

It may be noted that C-17 substituted tetranortriterpenoids are very rare in nature[2,10,12] and isonimolicinolide (**1**) which is the first example of a tetranortriterpenoid with an acetoxy function at C-17 may be regarded as the possible intermediate[13] in the biosyntheses of 17β-hydroxy-azadiradione[10,11] and nimolicinol[2] reported earlier from neem.

Nimolicinoic acid (**3**), the first hexanortriterpenoid with an apo-euphane (apo-tirucallane) skeleton and the first terpenoidal acid from the neem tree, has the molecular formula $C_{26}H_{34}O_6$ (high resolution mass spectroscopy). Its u.v. spectrum showed absorption at 235 nm, while the i.r. spectrum exhibited peaks at 3 350 (OH), 1 740 (ester carbonyl), 1 710 and 1 705 (acid carbonyl and cyclopentenone), 1 665 (cyclohexenone), 1 655, and 825 cm^{-1} (trisubstituted double bond).



Azadiradione

The ^1H and ^{13}C n.m.r. (broad band and GASPE) spectral data of (**3**) (Tables 1 and 2 respectively) indicated that it has the same carbocyclic nucleus as that of azadiradione (*loc. cit.*). Thus, a set of two doublets at δ 7.12 and 5.90 (*J* 10.1 Hz) were assigned to 1-H and 2-H respectively, a sharp singlet at δ 5.86 and a double doublet (*J* 2.0 and 2.3 Hz) at δ 5.31 were due to 15-H and 7-H respectively, while a 3 H singlet at δ 1.93 and four singlets at δ 1.31, 1.24, 1.19, and 1.09 (6 H) were assigned to an acetoxy methyl and five quaternary methyls respectively. The structural features recorded so far and a fragment at *m/z* 383.2198 ($C_{24}H_{31}O_4$, fragment c) in the mass spectrum of (**3**) indicated the composition of the C-17 side chain as $C_2H_3O_2$. Further, the signal of 17-H which appeared as a singlet at δ 3.41 in azadiradione, resonated as a triplet (*J* 7.0 Hz) at δ 2.68 in the case of (**3**). Moreover, a set of two double doublets at δ 2.41 and 2.84 (*J* 15.0 and 7.0 Hz) were also observed and the ^1H–^1H homonuclear decoupling experiments showed that these protons and 17-H are interrelated. Thus, irradiation at δ 2.84 collapsed the triplet at δ 2.68 into a doublet (*J* 7.0 Hz) and the double doublet at δ 2.41 to a doublet (*J* 7.0 Hz). Irradiation at δ 2.68 collapsed the double doublets at δ 2.84 and 2.41 to two doublets, each with a coupling constant of 15.0 Hz, while irradiation at δ 2.41 caused collapse of the double doublet at δ 2.84 to a doublet (*J* 7.0 Hz) and the triplet at δ 2.68 also to a doublet (*J* 7.0 Hz). These observations led to the assignment of the chemical shifts at δ 2.84 and 2.41 to 20-H_a and 20-H_b respectively, and showed that the carbons adjacent to C-17 and C-20 are quaternary since no other couplings of these protons were observed. These assignments were corroborated by COSY spectrum, which showed through-bond connectivities of 17-H with 20-H_a and 20-H_b. These findings suggested the presence of a carbonyl group at C-20 in the side chain. Finally, the structure of (**3**) was confirmed through high resolution mass spectroscopy, which showed the diagnostic fragments at *m/z* 397.2363 ($C_{25}H_{33}O_4$, fragment a), 45.0000 (CO_2H, fragment b), 383.2198 ($C_{24}H_{31}O_4$, fragment c), 368.1979 ($C_{23}H_{28}O_4$, fragment d), 74.0336 ($C_3H_6O_2$, fragment e), 101.0214 ($C_4H_5O_3$, fragment f), 116.0525 ($C_5H_8O_3$, fragment g), and 338.2204 ($C_{23}H_{30}O_2$, $M - C_2H_4O_2 - CO_2$). Methylation of compound (**3**) with diazomethane gave (**4**), the ^1H n.m.r. spectrum of which showed a 3 H singlet at δ 3.34 for OMe while the mass spectrum showed the molecular ion peak at *m/z* 456.2536 corresponding to the molecular formula $C_{27}H_{36}O_6$.

The stereochemistry of various centres of nimolicinoic acid (**3**) has been established through NOESY spectral analysis, which exhibited spatial connectivities of 13-Me with 20-H_b, 9-H, 5-H, and OAc; 10-Me with 12β-H, 11β-H, 7-H, 6β-H, 2-H, and 1-H; 8-Me with 15-H, 11β-H, 7-H, 6β-H, and 4β-Me; and also of 6β-H with 7-H and 15-H; 5-H with 9-H; 7-H with 15-H; and 1-H with 2-H. The spatial connectivity of 13-Me with 20-H_b showed that the side chain at C-17 is α oriented.

It is noteworthy in this context that nimolicinoic acid (**3**) is the first instance of isolation of a naturally occurring hexanortriterpene having the apoeuphane (apotirucallane) skeleton. Furthermore, only a few naturally occurring hexanortriterpenoids have been reported in the literature possessing the cucurbitacin,[14,15] dammarane, [16] and lanostane [17] skeleton but there is no record of such a triterpenoid with an euphane or tirucallane skeleton. Nimolicinoic acid is also the first example of a hexanortriterpenoidal acid isolated from any source.

Toxicity of neutral fraction-B was determined against the pulse beetle (*Callasobruchus analis*) by contact methods in which various dilutions (0.031 25—0.5%) of this fraction in acetone–water (1:1 v/v) were applied to filter paper (Whatman No. 1). The insects exposed to this filter paper showed mortality and the LD_{50} value was found to be 40 μg/cm^2 as compared to the LD_{50} value of diflubenzuron (dimilin) 20 μg/cm^2 by the same method. The residual effect of this fraction at 0.5% concentration was noted for 5 days, as against 7 days in the case of diflubenzuron. Further work on the insect growth pattern is in progress.

Experimental

M.p.s were recorded in glass capillary tubes and are uncorrected. I.r. (in $CHCl_3$) and u.v. (in MeOH) spectra were measured on JASCO IRA-I and Pye-Unicam SP-800 spectrometers respectively; mass spectra were recorded on Finnigan MAT 112 and 312 double focussing mass spectrometers. N.m.r. spectra were recorded in $CDCl_3$ on a Bruker AM 300 spectrometer operating at 300 MHz for ^1H and 75 MHz for ^{13}C nuclei, and chemical shifts are reported as δ values. Optical rotations were measured at 22 °C in $CHCl_3$, on a Polartronic-D polarimeter. Merck Kieselgel 60 PF_{254} coated on glass plates was used for analytical (thin layer) and preparative (thick layer) chromatography.

Isolation of Isonimolicinolide (**1**) *and Nimolicinoic acid* (**3**).—An ethanolic extract of fresh, undried, unruptured, ripe fruits of neem (nimoli, 20 kg) was divided into acidic and neutral fractions (pH 8—8.5). The residue (130 g, 2.16% on dry wt. basis), obtained on work-up of the neutral fraction, was repeatedly extracted with 50% ethanol, which was partitioned with a mixture of benzene and light petroleum (2:1, v/v). The residue obtained from the benzene–light petroleum phase was subjected to the classical procedures of separation, resulting in the isolation of three triterpenoids, nimolicinol,[2] azadirachtol,[3] and azadirachnol.[18] The mother liquors of these triterpenoids were combined and the residue was divided into light petroleum soluble (A) and insoluble (B) fractions. The powdery light petroleum insoluble fraction was chromatographed on a column (silica gel 40, 70—230 mesh), with benzene and benzene–ethyl acetate mixtures as eluants. The benzene eluate afforded a new tetranortriterpenoid nimocin, along with several known triterpenoids, communicated earlier,[4] while the benzene–ethyl acetate (90:10 and 85:15, v/v) eluates afforded isonimolicinolide (**1**) and nimolicinoic acid (**3**) respectively with some trace impurities. These were purified through preparative t.l.c. (silica gel, chloroform–methanol, 95:5).

Isonimolicinolide (**1**). Rods (0.02 g, 0.013% on the dry wt. basis), m.p. 100—102 °C (from ethyl acetate), $[\alpha]_D$ 20° (*c* 0.2 in $CHCl_3$) (Found: M^+, 540.2399. $C_{30}H_{36}O_9$ requires *M*, 540.2358); $\lambda_{max.}$ 230 nm (ε 5 981); $\nu_{max.}$ 3 400, 1 765, 1 740br, 1 710, 1 660, 1 650, and 820 cm^{-1}; *m/z* 540.2399 (M^+, 2%), 498.2272 (6, $M - C_2H_2O$), 480.2152 (4, $M - C_2H_4O_2$), 440.2146 (8, fragment a), 438.2050 (7, $M - C_2H_4O_2 - C_2H_2O$), 420.1926 (6, $M - 2 \times C_2H_4O_2$), 369.2042 (10, fragment c), 171 (30, fragment d), 137.0962 (70, ring A + H), 100 (40, fragment b), and 57 (100).

Nimolicinoic acid (**3**). Needles (8 mg, 0.005% on the dry wt. basis), m.p. 92—94 °C (from chloroform), $[\alpha]_D$ −14.28° (*c* 0.07 in $CHCl_3$) (Found: M^+, 442.2312, $C_{26}H_{34}O_6$ requires *M*, 442.2354); $\lambda_{max.}$ 235 nm (ε 7 160); $\nu_{max.}$ 3 350, 1 740, 1 710, 1 705, 1 665, 1 655, and 825 cm^{-1}; *m/z* 442.2312 (M^+, 10%), 424.2284 (2, $M - H_2O$), 400.2234 (3, $M - C_2H_2O$), 398.2423 (2, $M - CO_2$), 397.2363 (4, fragment a), 383.2198 (10, fragment c), 382.2187 (25, $M - C_2H_4O_2$), 368.1979 (6, fragment d), 365.2087 (3, $M - C_2H_3O_2 - H_2O$), 364.2062 (2, $M - C_2H_4O_2 - H_2O$), 338.2204 (10, $M - C_2H_4O_2 - CO_2$), 137.0938 (20, ring A + H), 121.0659 (100, C_8H_9O), 116.0525 (22, fragment g), 101.0214 (10, fragment f), 74.0336 (20, fragment e), and 45.0000 (22, fragment b).

Acetylation of Isonimolicinolide (**1**).—To a solution of (**1**) (7 mg) in pyridine (1 ml), acetic anhydride (2 ml) was added and the reaction mixture was kept over night at room temperature.

Work-up gave the acetylated product (**2**) as plates (5 mg, 71%), m.p. 110 °C (from $CHCl_3$) $[\alpha]_D$ 15.5° (*c* 0.04 in $CHCl_3$); $\lambda_{max.}$ 225 nm (ε 5 986); $\nu_{max.}$ 1 760 (α,β-unsaturated-γ-lactone), 1 740br (ester carbonyls), 1 710 (cyclopentenone), 1 665 (cyclohexenone), 1 660, and 820 cm^{-1} (trisubstituted double bonds); *m/z* 582.2459 (M^+, 2%), 522.2252 (3, $M - C_2H_4O_2$), 462.2039 (6, $M - 2 \times C_2H_4O_2$), 440.2186 (10, M − side chain − H), 369 (12, M − side chain − $C_3H_4O_2$), 213 (10), 142 (20, side chain + H), and 137 (30, ring A + H).

Methylation of Nimolicinoic acid (**3**).—Freshly prepared diazomethane was added to a solution of (**3**) (4 mg) in ether (1 ml) and the reaction mixture was kept for 1 h at room temperature. Work-up gave compound (**4**) which on recrystallization formed fine needles (3 mg, 75%), m.p. 104—106 °C (from chloroform), $[\alpha]_D$ −10° (*c* 0.03 in $CHCl_3$); $\lambda_{max.}$ 205 (ε 6 840) and 230 nm (ε 6 931); $\nu_{max.}$ 1 740, 1 710, and 1 700 (ester carbonyls and cyclopentenone), 1 660 (cyclohexenone), 1 650 and 820 cm^{-1} (trisubstituted double bond); *m/z* 456.2536 (M^+, 18), 441.2287 (6, M − Me), 425.2330 (10, M − OMe), 397.2355 (13, $M - C_2H_3O_2$), 396.2306 (15, $M - C_2H_4O_2$), and 383.2181 (8, M − side chain).

NOESY Analysis of Azadiradione.—The stereochemistry of various centres of azadiradione was established through its NOESY spectrum which exhibited the spatial connectivities of 13-Me with 22-H, 21-H, 9-H, and OAc; 4α-Me with 6α-H, 5-H, and OAc; 4β-Me with 10-Me, 6β-H, and 1-H; 10-Me with 12β-H, 11β-H, 7-H, 6β-H, 2-H, and 1-H; and 8-Me with 17-H, 15-H, 11β-H, 7-H, and 6β-H.

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