Pergamon

Tetrahedron 57 (2001) 10281–10286

TETRAHEDRON

Three novel tetracyclic triterpenoids of biogenetic interest from the leaves of *Azadirachta indica*

Bina S. Siddiqui,* Farhana Afshan and Shaheen Faizi

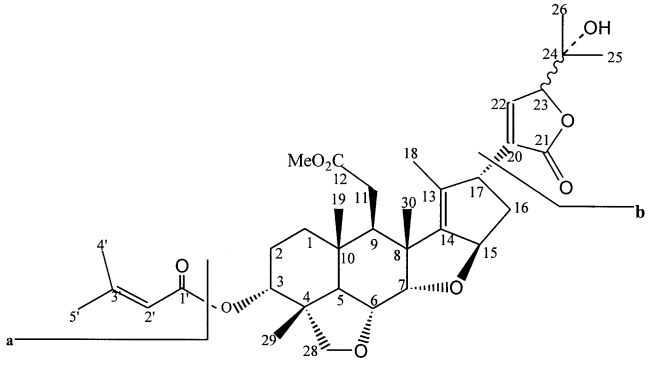
H.E.J. Research Institute of Chemistry, University of Karachi, Karachi 75270, Pakistan

Received 7 December 2000; revised 18 September 2001; accepted 11 October 2001

Abstract—From the methanolic extract of *Azadirachta indica* leaves, we have isolated three new tetracyclic triterpenoids of biogenetic interest, namely, melianol **1**, desfurano-desacetylnimbin-17-one **2** and meliatetraone **3**. The structure elucidation is based on extensive spectral studies including $^{1}H-^{1}H$-COSY, NOESY, HMQC, and HMBC experiments.

1. Introduction

The neem tree (*Azadirachta indica* A. Juss.; family: Meliaceae), is an important source of biologically active compounds and has been the focus of increasingly intense research in the past three decades since the isolation of the natural insecticide azadirachtin from its seeds.[1] A host of new terpenoidal constituents has so far been isolated by various groups of workers from its different parts.[2–6] A continuing search towards obtaining new compounds with potential significance has resulted in the isolation and structure elucidation of three new triterpenoides of biogenetic interest, namely, melianol (**1**), desfurano-desacetylnimbin-17-one (**2**) and meliatetraone (**3**) from the leaves. It is noteworthy that **2** is the first octanortriterpenoid bearing the cleaved ring C of nimbin[7] while **1** has the previously unknown seven carbon side chain (mono-nor) in the nimbin skeleton. Hence, **1** and **2** represent interesting biogenetic relationship with nimbin which has a four carbon furan ring at C-17 (i.e. a tetranortriterpenoid). The biosynthesis of **2** may be rationalized to proceed from **1**, a postulated biosynthetic precursor of deacetyl nimbin (or nimbin) as depicted in Scheme 1. Compound **3** on the other hand represents a tetranortriterpenoid lacking C-21, which is unprecedented.



1

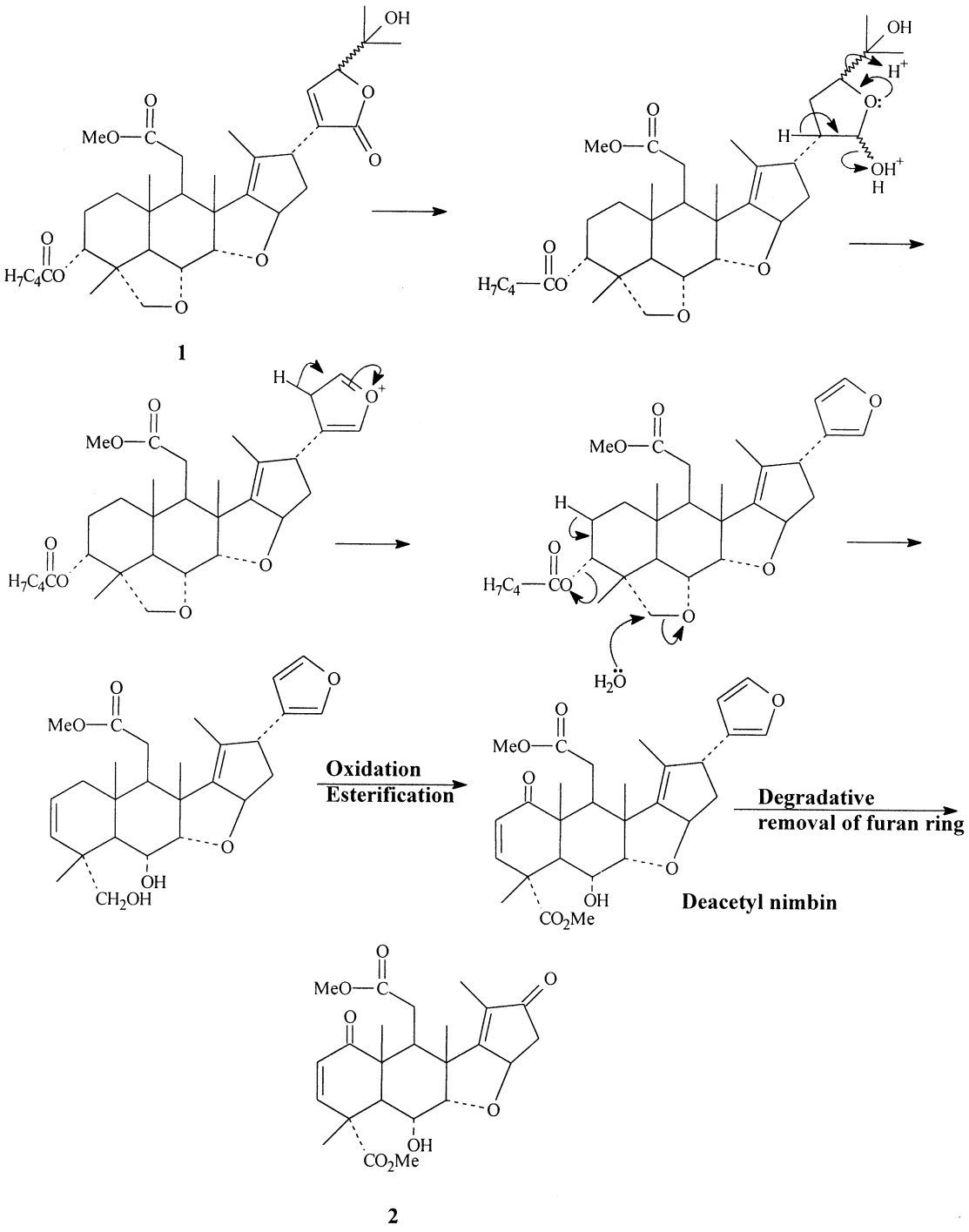
2. Results and discussion

Compound **1** showed the molecular ion peak at *m/z* 612.3269 in the HREIMS corresponding to the molecular formula $C_{35}H_{48}O_9$. Its UV spectrum exhibited maxima at 230 nm, while the IR spectrum showed peaks at 3600 (OH), 1762 (α,β-unsaturated γ-lactone), 1722 (α,β-unsaturated ester), 1740 (carbomethoxy), 1605, 847 (C=C), and 1375 (geminal methyls) cm^{-1}. The ^{1}H and ^{13}C NMR spectral data (Tables 1 and 2) of compound **1** displayed that it has the ring C-*seco* tetracyclic skeleton of nimbin[7] but instead of the 2-en-1-one moiety in ring A, a senecioyl substituent is present at C-3 ($\delta_{H\text{-}3}$ 4.93, t, J=3.0 Hz; $\delta_{H\text{-}2'}$ 5.68, br.s; $\delta_{H\text{-}4'}$ 1.92, br.s; $\delta_{H\text{-}5'}$ 2.14, s; $\delta_{C\text{-}3}$ 72.3, $\delta_{C\text{-}1'}$ 171.0, $\delta_{C\text{-}2'}$ 113.0, $\delta_{C\text{-}3'}$ 158.8, $\delta_{C\text{-}4'}$ 21.0, $\delta_{C\text{-}5'}$ 27.1), and the oxygen at C-6 now forms an ether linkage between C-6 and C-28 ($\delta_{H\text{-}6}$ 3.98, dd, J=12.5, 3.0 Hz; $\delta_{H\text{-}28a}$ 4.08, $\delta_{H\text{-}28b}$ 3.60, each 1H, d, J=8.0 Hz; $\delta_{C\text{-}6}$ 71.3, $\delta_{C\text{-}28}$ 78.0). The senecioyl group was also evident from the mass fragment at *m/z* 83.0513 (fragment **a** vide structure). A particular differentiating feature of **1** from nimbin was the presence of a side chain consisting of seven carbons which is unprecedented. This was evident from the mass fragment at *m/z* 141.0557 (fragment **b** vide structure), signals in the ^{1}H NMR spectrum at δ 6.80 (br.s, H-22), 5.19 (m, H-23), 1.24 and 1.39 (each 3H, s, H-25/H-26 and ^{13}C NMR shifts at

Keywords: *Azadirachta indica*; triterpenoid; nimbin.

* Corresponding author. Tel.: +92-21-9243199; fax: +92-21-9243190; e-mail: bina@khi.comsats.net.pk

0040–4020/01/$ - see front matter
PII: S0040-4020(01)01027-4



Scheme 1. Suggested biosynthetic pathway to **2** from **1**.

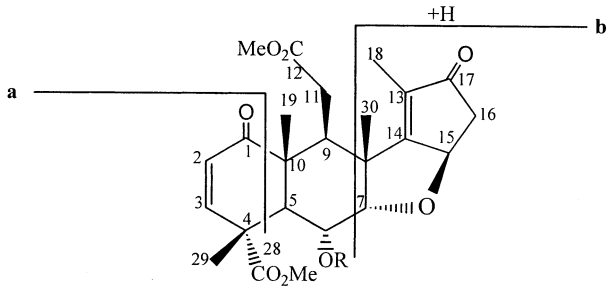
δ 137.1 (C-20), 170.1 (C-21), 145.3 (C-22), 77.0 (C-23), 79.8 (C-24), 23.0 (C-25) and 24.1 (C-26). The last two signals (C-25 and C-26) were unambiguously assigned from their interaction with H-23 in the HMBC plot. The chemical shifts and singlet nature of H-25 and H-26 supported the presence of a hydroxyl function at C-24. Further, the HMBC (Table 2) showed important interactions between C-3 and H-28a, H-28b; C-28 with H-3, H-5 and H-29; C-6 and C-7 with H-5 as well as C-6 with H-7 and C-7 with H-6 (Table 2) in support of the proposed structure. The interactions of C-1′ with H-3 in the HMBC plot displayed the senecioyl moiety at C-3. The sterochemistry of various centres was achieved from the coupling constants of clearly distinguished protons (Table 1) as well as interactions in the NOESY plot. Thus, H-3 showed spatial connectivity with H-6, H-19 and H-30; H-5 with H-9; and H-17 with H-30. An interaction between H-17 and H-23 was also observed but a decisive conclusion in favour of 23*R* or 23*S* could not be made, since this interaction was possible in both cases as revealed by the Dreiding model. The foregoing account of the spectral data led to elucidate the structure of melianol as **1**. The NMR assignments are based on 1D and 2D NMR data

Table 1. ^{1}H NMR chemical shifts (δ_H for **1–3** in $CDCl_3$ (300 MHz)

No.	1	2	3
1	2.00 (m)	–	–
2	–	5.89 (d, 10.1)	5.87 (d, 10.0)
2α	2.20 (m)	–	–
2β	2.05 (dddd, 15.5, 8.5, 3.0, 3.0)	–	–
3	4.93 (t, 3.0)	6.45 (d, 10.1)	6.39 (d, 10.0)
5	2.62 (d, 12.5)	3.44 (d, 11.4)	3.26 (d, 12.0)
6	3.98 (dd, 12.5, 3.0)	4.22 (dd, 11.4, 3.3)	4.28 (d, 12.0, 3.5)
7	4.16 (d, 3.0)	3.94 (d, 3.3)	5.38 (d, 3.5)
9	2.57 (dd, 8.5, 3.5)	2.90 (t, 5.4)	2.45 (dd, 8.0, 4.5)
11a	2.30 (dd, 15.5, 8.5)	2.20 (dd, 16.4, 5.4)	2.85 (dd, 16.0, 4.5)
11b	2.22 (m)	3.10 (dd, 16.4, 5.4)	2.35 (dd, 16.0, 8.0)
15	5.30 (m)	5.25 (m)	5.75 (s)
16	2.30 (m)	2.81–2.92 (m)	–
17	3.81 (dd, 3.0, 4.5)	–	3.40 (br.s)
18	1.68 (s)	1.81 (s)	1.03 (s)
19	1.13 (s)	1.24 (s)	1.20 (s)
20	–	–	6.50 (br.d, 13.0)
22	6.80 (br.s)	–	5.80 d (13.0)
23	5.19 m	–	–
24	–	–	2.10 (s)
25	1.24 s	–	–
26	1.39 s	–	–
28a	4.08 d (8.0)	–	1.24 (s)
28b	3.60 d (8.0)	–	–
29	1.24 (s)	1.35 (s)	1.26 (s)
30	1.29 (s)	1.36 (s)	1.29 (s)
2′	5.68 (br.s)	–	–
4′	1.92 (br.s)	–	–
5′	2.14 (s)	–	–
OCH_3	3.41 (s)	3.48 (s), 3.73 (s)	3.57 (s)
$OCOCH_3$	–	–	2.10 (s)

Multiplicities and coupling constant (Hz) given in parentheses.

including HMQC and HMBC as well as on comparison with the data of compounds having similar partial structures.[5,7–10]

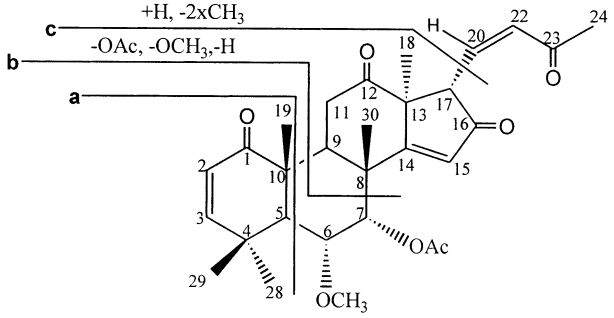


2 R=H
2a R=Ac

Compound **2** possessed the molecular formula $C_{24}H_{30}O_8$ as shown by HREIMS. Its IR spectrum showed peaks at 3300 (OH), 1735 (carbomethoxyl groups), 1665 (cyclohexenone), 1735 (cyclopentenone) cm^{-1}, while the UV spectrum exhibited a maximum at 230 nm. The molecular formula showed that **2** has 10° of unsaturation, six of which were accounted for by the cyclohexenone and cyclopentenone rings, and two by two carbomethoxy groups. The remaining two were taken for two rings as no further sp^2 carbon was observed in the ^{13}C NMR spectrum. In the ^{1}H NMR spectrum (Table 1), a pair of AB doublets of olefinic protons of enone system appeared at δ 5.89 (J=10.1 Hz; H-2) and 6.45 (J=10.1 Hz; H-3) and the carbons (Table 2) were observed at δ 202.0 (C-1), 127.2 (C-2) and 148.0 (C-3) similar to those of ring A of nimbin and other compounds possessing 2-en-1 one system in ring A.[4,7,8] This was further confirmed by the mass fragment at m/z 140.0462 ($C_7H_8O_3$; fragment **a**). Two doublets at δ 3.44 (J=11.4 Hz) and 3.94 (J=3.3 Hz) were attributable to H-5 and H-7, respectively, and a double doublet at δ 4.22 (J=11.4, 3.3 Hz) was ascribable to H-6. The coupling constants of H-6 and H-7 revealed that the substituents at C-6 and C-7 have α disposition. These data and the absence of an acetoxy signal clearly indicated that **1** has the same carbocyclic nucleus as that of nimbin but has a hydroxy group at C-6 instead of an acetoxy function as in desacetylnimbinolide.[4] This was supported by a downfield shift of the H-6 signal from δ 4.22–5.30 on acetylation. The molecular formula and ^{13}C NMR spectrum of **2** demonstrated that it is an octanortriterpenoid and has 24 carbons, 22 of which form the skeleton, while two were accounted for by the two methoxy groups (δ_H 3.48, 3.73; δ_C 52.2, 53.2). The ^{13}C NMR spectrum further showed two signals at δ 32.9 and 42.1, each a CH_2 carbon (DEPT), which were assigned to C-11 and C-16, respectively, and had their connectivity with H-11a/b and H-16a/b in the HMQC spectrum. The data described so far left a carbonyl function (δ_C 207.0) to be accounted for. A mass fragment at m/z 151.0757 ($C_9H_{11}O_2$; fragment **b** vide structure), suggested that it is in ring D. Further, the chemical shift of C-14 (δ 192.0, Table 2) and HMBC correlation of C-17 with H-16a/b and with H-18 led to place this carbon at C-17. In the light of these spectral data the structure of **2** has been deduced as desfurano-desacetylnimbin-17-one.

Table 2. ^{13}C NMR chemical shifts (δ_C) and HMBC data of **1–3** in $CDCl_3$ at 125 MHz

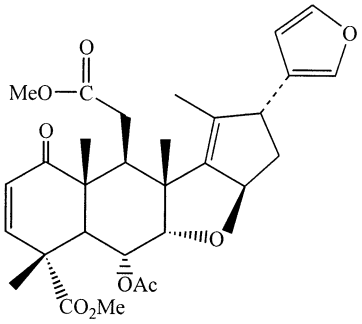
C No.	1		2		3	
	δ_C	HMBC correlated protons	δ_C	HMBC correlated proton	δ_C	HMBC correlate proton
1	37.6	H-3, H-19	202.0	H-2, H-3, H-5, H-9	203.1	H-2, H-3, H-5, H-19
2	28.5	H-3	127.2	H-3	126.0	H-3
3	72.3	H-2, H-28a/b, H-29	148.0	H-2, H-5, H-29	147.6	H-2, H-5, H-28, H-29
4	42.5	H-3, H-28a/b, H-29	38.7	H-2, H-3, H-6, H-29	40.0	H-2, H-3, H-5, H-28, H-29
5	40.3	H-28a/b, H-29	50.3	H-3, H-6, H-7, H-19, H-29	49.2	H-3, H-6, H-7, H-19, H-28, H-29
6	71.3	H-5, H-7, H-28a/b	65.1	H-5, H-7	68.0	H-5, H-7, OCH_3
7	86.1	H-5, H-6	89.1	H-5, H-6, H-9, H-30	79.0	H-5, H-6
8	47.0	H-7, H-15	47.9	H-6, H-7, H-9, H-11a/b, H-15	45.4	H-7, H-9, H-15
9	39.5	H-11a/b, H-19, H-30	38.7	H-5, H-7, H-11a/b, H-19, H-30	42.1	H-5, H-7, H-11a/b
10	41.8	H-11a/b, H-19	48.5	H-2, H-5, H-6, H-9, H-11a/b	47.9	H-2, H-5, H-6, H-11a/b
11	34.4	–	32.9	H-9	33.4	H-9
12	173.9	H-11a/b, OCH_3	172.3	H-9, H-11a/b	208.1	H-9, H-11a/b, H-18
13	135.3	H-15, H-17, H-18	143.5	H-15, H-16a/b, H-18	59.5	H-15, H-18
14	145.8	H-15, H-17, H-18	192.0	H-7, H-9, H-15, H-16a/b, H-18	192.2	H-7, H-15, H-17, H-18
15	87.1	–	85.0	H-16a/b	126.0	H-17
16	39.7	–	42.1	H-15	206.0	H-15, H-17
17	50.1	H-15, H-18, H-22	207.0	H-16a/b, H-18	57.8	H-15, H-18, H-20, H-22
18	14.0	H-17	16.0	–	25.0	H-17
19	17.5	H-5	19.5	H-5, H-9	18.9	H-5, H-9
20	137.0	H-17, H-22	–	–	142.9	H-17, H-22
21	170.1	H-17, H-22	–	–	–	–
22	145.3	H-17, H-23	–	–	131.3	H-17, H-20, H-24
23	77.0	H-22, H-25/H-26		–	197.1	H-20, H-24
24	79.8	H-22, H-25/H-26	–	–	23.0	H-20, H-22
25	23.0	H-23	–	–	–	–
26	24.1	H-23	–	–	–	–
28	78.0	H-3, H-5, H-29	172.0	H-3, H-5, H-29	24.9	H-2, H-3, H-5
29	19.5	H-3, H-5, H-28a/b	21.2	H-3, H-5	21.0	H-2, H-3, H-5
30	20.9	H-7	16.0	H-7, H-9	26.0	H-7, H-9
1′	171.0	H-2′, H-3	–	–		–
2′	113.0	H-4′/H-5′	–	–	–	–
3′	158.8	H-2′, H-4′/H-5′	–	–	–	–
4′	21.0	H-2′	–	–	–	–
5′	27.1	H-2′	–	–	–	–
OMe	52.0	–	52.2, 53.2	–	53.1	H-6
$COCH_3$	–	–	–	–	169.2	H-7
$COCH_3$	–	–	–	–	20.1	–



3

The HREIMS of compound **3** showed its molecular formula as $C_{29}H_{36}O_7$. The IR spectrum indicated the presence of an α,β-unsaturated ketone (1685 cm^{-1}), six-membered saturated ketone (1725 cm^{-1}) and α,β-unsaturated cyclopentenone (1740 cm^{-1}). The presence of five methyl signals at quaternary carbons in the ^1H NMR spectrum (Table 1) at δ 1.03, 1.20, 1.24, 1.26, and 1.29 indicated its triterpenoidal nature. A pair of AB doublets at δ 5.87 and 6.39 (J=10.0 Hz; H-2 and H-3; $\delta_{C\text{-}1}$ 203.1, $\delta_{C\text{-}2}$ 126.0, $\delta_{C\text{-}3}$ 147.6; Table 2) could be assigned to the olefinic protons of 2-en-1-one system (loc.cit). Two doublets at δ 3.26 (J=12.0 Hz) and 5.38 (J=3.5 Hz) were attributed to H-5 and H-7, respectively, while a double doublet at δ 4.28 (J=12.0, 3.5 Hz) was ascribed to H-6. These signals were suggestive of an α-oriented acetoxy group at C-7 (δ_C 79.0) and an oxygen substitutent also with α disposition at C-6 (δ_C 68.0). This could possibly be a methoxy group because a three-proton singlet was present at δ 3.57 in the ^1H NMR spectrum which had a connected carbon at δ 53.1 in the HMQC spectrum. A six-membered saturated ketone (ν_{max} 1725 cm^{-1}; δ_C 208.1) could be placed at C-12 since H-11a and H-11b showed up as two double doublets at δ 2.85 (J=16.0, 4.5 Hz) and 2.35 (J=16.0, 8.0 Hz) and their connected carbon appeared downfield (δ 33.4) than normally observed in similar compounds.[2] Further, C-13 also suffered a downfield shift due to adjacent carbonyl group. Two singlets at δ 5.75, and 3.40 (broad) were assignable to H-15 and H-17, respectively, in analogy with those of azadiradione.[2] Their respective carbons had shifts at δ 126.0 and 57.8 in the HMQC spectrum. In this case, however, instead of a furan ring at C-17, an α,β-unsaturated carbonyl system was indicated by the mass fragment (vide structure) and NMR data (Tables 1 and 2). Thus a set of two doublets at δ 6.50 and 5.80 (each J=13.0 Hz) due to H-20 ($\delta_{C\text{-}20}$ 142.9) and H-22 ($\delta_{C\text{-}22}$ 131.3), respectively, along with a three-proton singlet

at δ 2.10 (H-24, $\delta_{C\text{-}24}$ 23.0) manifested a *cis*-20 (22)-en-23-one system. It may be noted that H-17 appeared as a broad singlet showing its negligible coupling with H-20. Dreiding model suggests that the hydrogen bonding between carbonyl oxygen at C-16 and H-20 may hold the side chain in such a position which results in a dihedral angle of about 90° between H-17 and H-20. The α orientation of the side chain could be deduced from the spatial interaction of H-18 with H-20 and H-22 and that of H-17 with H-30 in the NOESY spectrum. In the HMBC plot, C-15 had a connectivity with H-17 while C-22 showed connectivity with H-17 as well as with H-20 and H-24 (Table 2). In the light of these observations, the structure of meliatetraone has been elucidated as 21,25,26,27-tetranorapotirucalla-(apoeupha)-6α-methoxy-7α-acetoxy-2,14,20 (22)-trien-1, 12,16,23-tetraone (**3**). The mass spectral fragments (**a**–**c**; vide structure) are also consistent with this structure. This is the first instance of isolation of a tetranortriterpenoid which lacks C-21.



Nimbin

3. Experimental

3.1. General

IR ($CHCl_3$) and UV (MeOH) spectra were measured on JASCO-A302 and Hitachi-3200 spectrophotometers, respectively. The ^1H NMR spectra were recorded in $CDCl_3$ on a Bruker Aspect AM 300 operating at 300 MHz, while the ^{13}C NMR spectra (BB, DEPT, HMQC and HMBC) were recorded in $CDCl_3$ on a Bruker Aspect AM-500 spectrometer operating at 125 MHz. The chemical shifts are recorded in ppm (δ) and coupling constants (J) are in Hz. Mass spectra were recorded on double focussing Finnigan MAT-112 spectrometer with E_i energy 70 eV and ion source temperature 250°C. TLC was performed on precoated alumina (Riedel-de Haen Dc-cards ALF) cards. Plates were visualized under UV light (254 and 366 nm).

Leaves were collected in the spring from the Karachi region and identified by Professor Dr S. I. Ali, Department of Botany, University of Karachi and a voucher specimen (No. NM-1) has been deposited in the Herbarium of the Department of Botany, University of Karachi.

The fresh, uncrushed leaves (20 kg) were repeatedly (5×) extracted with MeOH at room temperature. The combined extract, after removal of the solvent under reduced pressure, was partitioned between EtOAc and H_2O. The EtOAc layer was washed, dried (anhydrous Na_2SO_4), treated with charcoal and filtered. The charcoal bed was successively eluted with EtOAc and C_6H_6–MeOH (1:1; v/v). The EtOAc and C_6H_6–MeOH filtrates were combined and the solvent removed at reduced pressure. The residue, thereby obtained, was divided into petrol-soluble and petrol-insoluble fractions. The latter fraction was treated with 4% Na_2CO_3 to separate the acidic and neutral fractions. The EtOAc layer containing the neutral fraction was washed with H_2O, dried (anhydrous Na_2SO_4) and evaporated under vacuum. The neutral fraction thereby obtained was divided into petrol-soluble and petrol-insoluble fractions and the latter was successively treated with different percentages of aqueous MeOH [10, 20, …, 100%]. As a result, several fractions were obtained and combined on the basis of their TLC analysis. The 40, 50 and 60% aq. MeOH fractions were combined together and subjected to VLC (silica gel-60 GF_{254}; $CHCl_3$, $CHCl_3$–MeOH, MeOH in order of increasing polarity). The $CHCl_3$–MeOH (9.8:02) eluate furnished a fraction 'A' which resolved into one major component with three minor spots when subjected to thick layer chromatography (silica gel-60 GF_{254}, $CHCl_3$–MeOH, 9.5:0.5) and afforded melianol (**1**) (8 mg) while the $CHCl_3$–MeOH (9.9:0.1 and 9.85:0.15) eluates were combined together and freed of solvent to give fraction 'B' (3.9 gm) which was further subjected to VLC (silica gel-60, GF_{-254}, petrol, petrol–EtOAc, $CHCl_3$, $CHCl_3$–MeOH, MeOH in order of increasing polarity) The petrol–EtOAc (1:1) and $CHCl_3$ eluates were also combined together on the basis of TLC and after removal of solvent furnished fraction 'C' which resolved into three major (bands a–c) and two minor components showing single spots on TLC (silica gel 60 GF_{254}, $CHCl_3$–MeOH, 9.5:0.5). However, their ^1H NMR revealed that they all were still mixture of several constituents with one or two major bands. Thus band 'b' after a number of trials, could ultimately be purified on precoated alumina cards (petrol–EtOAc, 7.0:3) to afford desfurano-desacetylnimbin-17-one **2** (24 mg) and band 'c' afforded meliatetraone **3** (7 mg) in the same system. The other components did not afford any workable quantities.

3.1.1. Melianol (1). Fine colourless needles (MeOH); mp 95–98°C; $[\alpha]^{27}_D = +10.7$ (c, 0.14, $CHCl_3$); UV: 230 nm; IR: 3600, 1762, 1743, 1722, 1605, 1375, 1080 and 847 cm^{-1}. HR-EI-MS m/z (%) Found: 612.3269 (17.4) $C_{35}H_{48}O_9$: requires M^+ 612.3305, 289.1459 [$C_{17}H_{21}O_4$] (6.8), 141.0557 [$C_7H_9O_3$, fragment **b**]$^+$ (6.2), 83.0513 [C_5H_7O, fragment **a**]$^+$ (35.1); δ_H (Table 1); δ_C (Table 2).

3.1.2. Desfurano-desacetylnimbin-17-one (2). Compound **2** formed fine colourless needles (MeOH); mp 60–62°C; $[\alpha]^{27}_D = -25$ (c, 0.024, $CHCl_3$); UV: 230 nm; IR: 3300 (OH), 1735 (carbomethoxy), 1665 (cyclohexenone), 1155 and 820 cm^{-1}. HR-EI-MS m/z (%) Found: 446.1898 (57.99) $C_{24}H_{30}O_8$: requires M^+ 446.1940, 415.1725 [$C_{23}H_{27}O_7$]$^+$ (7.5), 207.1002 [$C_{12}H_{15}O_3$]$^+$ (6.5), 151.0757 [$C_9H_{11}O_2$, fragment **b**]$^+$ (7.8), 140.0462 [$C_7H_8O_3$, fragment **a**]$^+$ (26.0); δ_H (Table 1); δ_C (Table 2).

3.1.3. Acetylation of 2. A solution of **2** (10 mg) in pyridine

(1 ml) was added to acetic anhydride (1 ml) and the reaction mixture kept at room temperature overnight. On usual workup, the mono-acetylated product **2a** was obtained showing a single spot on TLC; UV λ_{max} (nm): 225; IR ν_{max} (cm^{-1}): 1720–1735 (ester carbonyls); EIMS: *m/z* 488; ^1H NMR δ: 5.30 (1H, dd, *J*=11.4, 3.4 Hz; H-6), 2.03 (3H, s, $OCOCH_3$).

3.1.4. Meliatetraone (3). Fine colourless needles (MeOH); mp 130–135°C; $[\alpha]^{27}_D=-35$ (*c*, 0.014, $CHCl_3$); UV: 232 nm; IR: 1685, 1725, 1740, 1600, 1375 and 850 cm^{-1}. HR-EI-MS *m/z* (%) Found: 496.2439 (46.20) $C_{29}H_{36}O_7$: requires M^+, 496.2460, 464.2139 $[C_{28}H_{32}O_6]^+$ (52.6), 398.1745 $[C_{23}H_{26}O_6$, fragment **c**$]^+$ (15.2), 259.1324 $[C_{16}H_{18}O_3]^+$ (77.5), 227.1170 $[C_{15}H_{17}O_2]^+$ (16.9), 161.0959 $[C_{11}H_{13}O$, fragment **b**$]^+$ (18.2), 136.0868 $[C_9H_{12}O$, fragment **a**$]^+$ (12.7); δ_H (Table 1); δ_C (Table 2).

References

1. Zanano, P. R.; Miura, I.; Nakanishi, K.; Elder, D. L. *J. Am. Chem. Soc.* **1975**, *97*, 1975–1977.
2. Lavie, D.; Levy, E. C.; Jain, M. K. *Tetrahedron* **1971**, *27*, 3927–3939.
3. Kraus, W.; Cramer, R.; Sawitzki, G. *Phytochemistry* **1981**, *20*, 117–120.
4. Siddiqui, S.; Siddiqui, B. S.; Mahmood, T.; Faizi, S. *J. Nat. Prod.* **1986**, *49*, 1068–1073.
5. Siddiqui, B. S.; Afshan, F.; Ghiasuddin; Faizi, S.; Naqvi, S. N. H.; Tariq, R. M. *J. Chem. Soc., Perkin Trans. 1* **1999**, *16*, 2367–2370.
6. Akhila, A.; Rani, K. Progress in the Chemistry of Organic Natural Products. In *Chemistry of the Neem Tree (Azadirachta indica* A. Juss.), Herz, W., Falk, H., Kirby, G. W., Moore, R. E., Tamm, Ch., Eds.; Springer: Wein, 1999; pp 47–132.
7. Harris, M.; Henderson, R.; McCrindle, R.; Overton, K. H.; Turner, D. W. *Tetrahedron* **1968**, *24*, 1517–1523.
8. Siddiqui, S.; Faizi, S.; Mahmood, T.; Siddiqui, B. S. *Tetrahedron* **1986**, *42*, 4849–4856.
9. Ara, I.; Siddiqui, B. S.; Faizi, S.; Siddiqui, S. *Heterocycles* **1989**, *29*, 729–735.
10. Ara, I.; Siddiqui, B. S.; Faizi, S.; Siddiqui, S. *J. Nat. Prod.* **1989**, *52*, 1209–1213.