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TETRANORTRITERPENOIDS FROM THE SEEDS OF *AZADIRACHTA INDICA*

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Key Word Index—*Azadirachta indica*; Meliaceae; Neem tree; tetranortriterpenoids; 1α-methoxy-1,2-dihydroepoxyazadiradione; 1β,2β-diepoxyazadiradione; 7-acetylneotrichilenone; 7-desacetyl-7-benzoylazadiradione; 7-desacetyl-7-benzoylepoxyazadiradione; 7-desacetyl-7-benzoyl-gedunin.

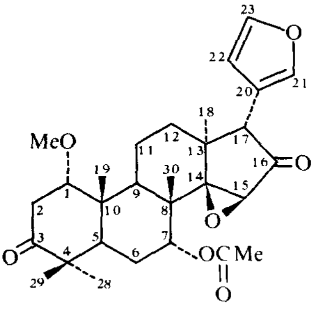
Abstract—Six new tetranortriterpenoids have been isolated from the extract of neem seeds. The C-7 benzoates of tetranortriterpenoids occurring in *Azadirachta indica* are described for the first time. The structures of all new compounds were determined by spectroscopical methods.

INTRODUCTION

Recently we reported on the isolation of 17-*epi*-azadiradione and 17β-hydroxyazadiradione from dried neem seeds [1]. Further chromatography of the petrol extract gave three new tetranortriterpenoids: 1α-methoxy-1,2-dihydroepoxyazadiradione (**1**), 1β,2β-diepoxyazadiradione (**2**) and 7-acetylneotrichilenone (**3**). In addition we isolated three C-7 benzoates **4**, **5** and **6**, which are closely related to azadiradione, epoxyazadiradione and gedunin, respectively. Compounds **4**, **5** and **6** are the first C-7 benzoates of tetranortriterpenoids to have been isolated from *Azadirachta indica*. The structure elucidation of **1**–**6** has been carried out by ^{1}H NMR spectroscopy using the double resonance technique, by measuring nuclear Overhauser effects (NOE) in the Fourier transform (FT) difference spectra [2], and by selective proton decoupling of the ^{13}C NMR signals.

RESULTS AND DISCUSSION

1α-Methoxy-1,2-dihydroepoxyazadiradione (**1**), mp 235–236°, $[\alpha]_D^{20}-1.4°$ ($CHCl_3$, $c = 1$), was found in



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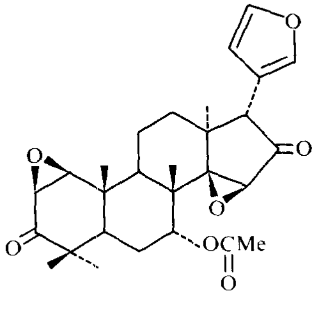

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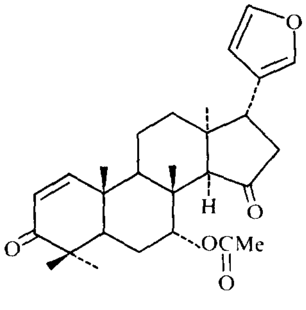

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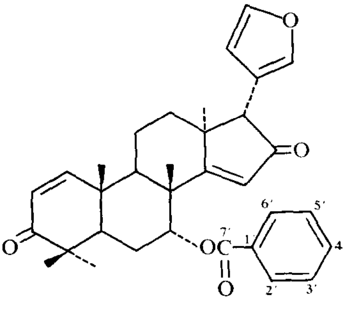

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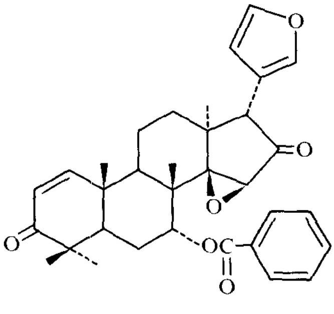

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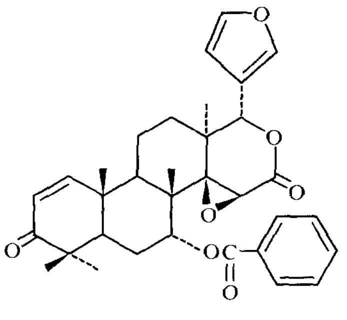

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addition to **3** in the mother liquor of the gedunin fraction, and was isolated by reversed-phase chromatography. The ^{1}H and ^{13}CNMR spectra of **1** and epoxyazadiradione [3, 4] were very similar. It was therefore possible to assign the proton and ^{13}C signals of rings B, C and D, and the signals of the methyl groups, C-7 acetyl and furan ring by comparison of the spectra. The presence of the methoxy group followed from a sharp proton signal at δ 3.32 (*s*) and from a ^{13}C signal at 56.81 (*q*). The connection of the methoxy group to a tertiary carbon atom was indicated by a ^{13}C signal at 82.65 (*d*) and a proton signal at 3.39 [*t*, J = 3.7 Hz, 1-H, X-part of an AMX spin system; part A appears at 2.90 (*dd*, J = 3.7 and 16.5 Hz), part M at 2.64 (*dd*, J = 3.7 and 16.5 Hz)]. The large coupling constant (16.5 Hz) corresponded to geminal coupling of a methylene group in a cyclohexane system, and the smaller coupling constant (3.7 Hz) indicated the equatorial position of the X-proton (1-H). Connection to C-1 of the methoxy group was deduced from a triplet at 3.39 (J = 3.7 Hz, 1-Hβ), and the α-configuration of the methoxy group was determined by NOE measurements from the FT difference spectrum. Irradiation at 1.60 (11-H) only influenced the signal of 1-Hβ (3.39), whereas irradiation at 2.24 (5-H) only affected the 9-H signal (3.24) but not the 1-H signal at 3.39. Similarly, the signal of 2-Hβ (2.90) increased by irradiation at 1.11 (19-H) or 1.02 (29-H). The α-configuration of the acetoxy group at C-7 followed from the triplet at 4.66 (J = 3.0 Hz).

1β,2β-Diepoxyazadiradione (**2**), mp 110–112°, $[\alpha]_D^{20}$ −3.5° (CHCl$_3$, c = 1) was isolated together with **5** and **6** by chromatography of the mother liquor of the epoxyazadiradione fraction. The NMR spectra of **2** and epoxyazadiradione [3] were very similar. The presence of an epoxy group in ring A was indicated by proton signals at 3.62 (*d*, J = 4.5 Hz, broadened by long range coupling) and 3.42 (*d*, J = 4.5 Hz) and ^{13}C NMR signals at 63.15 (*d*) and 56.68 (*d*) for C-1 and C-2, respectively. There was no further coupling in the NMR spectrum for 1-H and 2-H, and therefore the oxirane ring was connected to quarternary carbon atoms at both sides. The β-orientation of the oxirane ring followed from the upfield shift of the 19-H signal (δ 1.06), the C-19 signal (15.93) caused by the anisotropic effect of the oxygen atom, and from NOE experiments. Irradiation at 1.06 (19-H) only gave a small effect on 1-H, whereas irradiation at 0.96 (29-H) did not affect the signal of 2-H. There should be a large effect, however, if the oxirane ring were in an α-orientation. Compound **2** did not seem to be identical to diepoxyazadiradione prepared by Lavie [3] by epoxidation of epoxyazadiradione and it was claimed to be the 1α,2α-epimer.

The proton signals of 7-acetylneotrichilenone (**3**), mp 208°, $[\alpha]_D^{20}$ −21° (CHCl$_3$, c = 1) were assigned by correlation of the chemical shifts with the spectrum of epoxyazadiradione [3], by double resonance, and NOE experiments. The position of the ring D carbonyl group at C-15 followed from the 17-H signal at δ 3.50 (*t*, J = 10 Hz). The position of the acetoxy group at C-7 (axial) was indicated by a triplet at 4.94 (J = 3.0 Hz) and a nuclear Overhauser effect on 7-H during irradiation at 1.16 (30-H). The stereochemistry of the ring fusion was also determined by NOE experiments. Irradiation at 1.14 (19-H) showed an increase in the 29-H signal (1.08) but there was no effect on 5-H (2.08–2.12). Irradiation at 1.08 (29-H) gave the signal of 6-H (1.90–1.94) in addition to the signal of 19-H (1.14). The multiplet of 5-H would only be seen by irradiation of 28-H, and therefore 5-H was not in the same plane as 19-H and 29-H. Therefore, rings A and B were *trans*-fused. Irradiation at δ 1.16 (30-H) gave the signals of 7-H (4.96), 6-Hβ (1.90–1.94), and 17-H (3.50) but there was no effect on 9-H and 14-H. There was also no influence on 9-H during irradiation at 19-H. Therefore 9-H and the methyl groups were on different sides and rings B and C were *trans*-fused. Irradiation on 18-H gave the signals of 22-H (δ 6.30), 14-H (2.44), and 16-H (2.51). These experiments showed that 14-H, 18-H and the furan ring were on the same side in the α-position, and further, that rings C and D were *cis*-fused. The structure derived from the NMR spectra was fully confirmed by X-ray structure analysis (Fig. 1).

The ^{1}H NMR spectra of 7-desacetyl-7-benzoylazadiradione (**4**), $[\alpha]_D^{20}$ + 38.8° (CHCl$_3$, c = 1) and azadiradione [3, 5, 6] differed only slightly from each other. The singlet for the acetoxy group was missing but there were additional signals corresponding to a benzoyl group. The signals of the methyl groups (18-H and 28-H) were shifted upfield and the signals for 19-H and 30-H appeared downfield due to the anisotropic effect of the phenyl group. The ^{1}H NMR spectra of 7-desacetyl-7-benzoylepoxyazadiradione (**5**), $[\alpha]_D^{20}$ + 81.4° (CHCl$_3$, c = 1) and 7-desacetyl-7-benzoylgedunin (**6**), mp 278°, $[\alpha]_D^{20}$ + 105° (CHCl$_3$, c = 1) were also very similar to the spectra of the parent compounds epoxyazadiradione and gedunin [3], respectively, apart from the differences caused

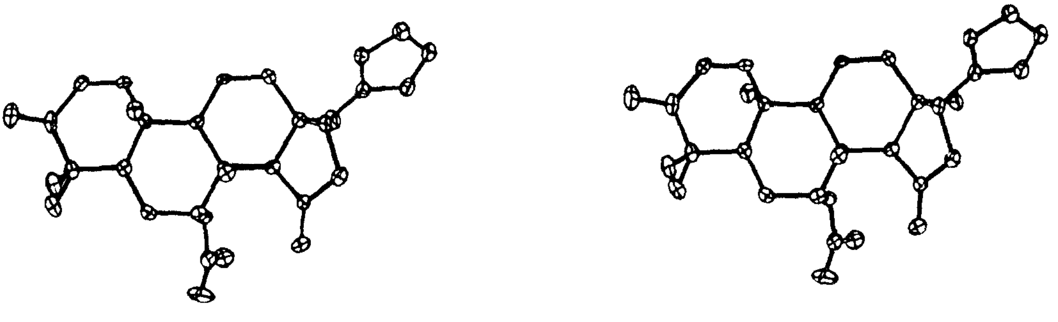

Fig. 1. Crystal structure of 7-acetylneotrichilenone (**3**) (ORTEP diagram). Compound **3** crystallized orthorhombically from methanol, space group P2$_1$2$_1$2$_1$, a = 11.412 (5) Å, b = 13.757 (6) Å, c = 15.730 (5) Å, Z = 4. The intensities of 3188 independent reflexes were collected on a SYNTEX-P2$_1$ four circle diffractometer (MoK$_\alpha$, ω-scan, $2\theta \leq 55°$, $T \approx -100°$). On refinement (all H atoms included) the conventional R value converged to R = 0.044 for 2729 reflections with $I > 2\sigma(I)$ (B. Neukäter, unpublished results; [7–9]). The positions of the substituents are 3-oxo, 4α-Me, 4β-Me, 7α-OAc, 8β-Me, 10β-Me, 13α-Me, 14α-H, 15-oxo, 17α-C$_4$H$_3$O (furan ring). Rings A, B and C have a chair conformation, ring D has an envelope conformation.

by the benzoyloxy groups at C-7. The structures of **5** and **6** could be assigned by comparing the spectra. There were similar upfield shifts of 18-H and 28-H and downfield shifts of 19-H and 30-H in the ^{1}H NMR spectra of **5** and **4** but only a downfield shift of 28-H and an upfield shift of 30-H in the spectrum of **6**.

EXPERIMENTAL

Elemental analyses. Mikronalytisches Laboratorium der Universität Stuttgart. The neem seeds were collected in Maiduguri, Nigeria. Air-dried, finely powdered neem seeds (10 kg) were extracted with petrol in a Soxhlet apparatus for 12 hr. Removal of the solvent gave 1.8 kg of a yellow-brown viscous oil. Separation of lipophilic impurities was accomplished by repeated distribution between 2 l. petrol and 2 l. MeOH–H_2O (95:5) until the methanolic layer remained colourless. The combined methanolic layers were dried (Na_2SO_4) and distilled at 40° under red. pres. The residue (450 g) gave, after chromatography on 4.5 kg Sil gel 60 (63–230 μm, Merck) with C_6H_6–EtOAc (9:1→2:3), 8 fractions. The separation was monitored by TLC (Kieselgel 60 F_{254}, Merck) with C_6H_6–EtOAc (9:1).

Fraction 1 (92 g), $R_f = 0.65$, mainly oily components which were not further investigated.

Fraction 2 (83.3 g), $R_f = 0.5$, gave, after crystallization from MeOH, 40 g gazadirone, mp 134°. Chromatography over 0.9 kg Sil gel of the mother liquor with petrol–EtOAc (4:1) yielded 21 g oily products, 5 g azadiron and 1.5 g 7-desacetyl-7-benzoylgedunin (**6**), mp 278° (from MeOH), $[\alpha]_D^{20} + 105°$ ($CHCl_3$, $c = 1$). (Found: C, 72.58, H, 6.57. $C_{33}H_{36}O_7$ (544) requires: C, 72.77; H, 6.65%). IR ν_{max}^{KBr} cm^{-1}: 3140 (furane), 3030 (C_6H_5), 1745 (lactone), 1715 (ester carbonyl), 1670 (α,β-unsat. 6-ring ketone), 1275, 1105, (C–O), 1200, 1100 (lactone), 1030, 720 (C_6H_5). MS *m/e*: 544 (M^+). UV λ_{max}^{EtOH} nm: 230, $\varepsilon = 24000$. ^{1}H NMR (360 MHz) [2]: δ 7.98 (2 H, *m*, 2′-H, 6′-H), 7.58 (1 H, *m*, 4′-H), 7.45 (2 H, *m*, 5′-H, 3′-H), 7.39 (1 H, *m*, 21-H), 7.38 (1 H, *m*, 23-H), 7.17 (1 H, *d*, $J = 10$ Hz, 1-H), 6.79 (1 H, *m*, 22-H), 5.89 (1 H, *d*, $J = 10$ Hz, 2-H), 5.58 (1 H, *s*, 17-H), 4.91 (1 H, *m*, 7-H), 3.70 (1 H, *s*, 15-H), 2.66 (1 H, *m*, 9-H), 2.34 (1 H, *m*, 5-H), 2.00–1.56 (6 H, *m*, 6-H, 11-H, 12-H), 1.27 (3 H, *s*, 30-H), 1.23 (3 H, *s*, 19-H), 1.21 (3 H, *s*, 29-H), 1.07 (3 H, *s*, 28-H), 0.96 (3 H, *s*, 18-H). ^{13}C NMR spectrum see Table 1.

Fraction 3 (106.8 g). $R_f = 0.36$, gave 67 g epoxyazadiradione by crystallization from MeOH. Chromatography over 1.2 kg Sil gel of the mother liquor (41 g) with petrol–EtOAc (4:1) yielded 5 g epoxyazadiradione and 3 g of a mixture of **2** and **5** which could be separated by prep. HPLC [LiChroprep SI 60 (15–25 μm) with petrol–EtOAc, 4:1] into 300 mg 1β,2β-diepoxyazadiradione (**2**) and 1.2 g 7-desacetyl-7-benzoylepoxyazadiradione (**5**).

1β,2β-Diepoxyazadiradione (**2**). Mp 110–111°, $[\alpha]_D^{20} - 3.5°$, $CHCl_3$, $c = 1$. (Found: C, 69.65; H, 7.22. $C_{28}H_{34}O_7$ (482.6) requires: C, 69.69; H, 7.10%). IR ν_{max}^{KBr} cm^{-1}: 3140 (furane), 1755

Table 1. ^{13}C NMR spectra of 1α-methoxy-1,2-dihydroepoxyazadiradione (**1**), 1β,2β-diepoxyazadiradione (**2**), 7-acetylneotrichilenone (**3**), 7-desacetyl-7-benzoylazadiradione (**4**), 7-desacetyl-7-benzoylepoxyazadiradione (**5**) and 7-desacetyl-7-benzoylgedunin (**6**) (22.63 MHz, $CDCl_3$ δ referring to TMS = 0)

C atom	**1**	**2**	**3**	**4**	**5**	**6**
1	82.65 *d*	63.15 *d*	157.83 *d*	156.66 *d*	157.60 *d*	157.05 *d*
2	37.22 *t*	56.68 *d*	125.98 *d*	125.78 *d*	125.91 *d*	126.04 *d*
3	213.86 *s*	211.17 *s*	204.41 *s*	203.63 *s*	204.15 *s*	203.85 *s*
4	47.03 *s*	44.30 *s*	44.11 *s*	43.91 *s**	44.36 *s**	44.07 *s*
5	41.50 *d*	38.54 *d*	45.15 *d*	46.51 *d*	47.45 *d*	46.58 *d*
6	24.18 *t*	23.89 *t*	22.26 *t*	23.56 *t*	24.96 *t*	23.66 *t*
7	74.04 *d*	73.58 *d*	73.36 *d*	74.04 *d*	73.58 *d*	73.20 *d*
8	42.90 *s*	42.74 *s*	41.08 *s*	44.56 *s**	43.52 *s**	43.00 *s*
9	35.33 *d*	38.87 *d*	47.10 *d*	38.52 *d*	40.10 *d*	39.85 *d*
10	41.83 *s*	38.74 *s*	39.59 *s*	40.01 *s*	39.95 *s*	40.24 *s*
11	15.76 *t*	16.54 *t*	17.68 *t*	15.76 *t*	16.25 *t*	15.11 *t*
12	28.76 *t*	28.54 *t*	34.45 *t*	30.00 *t*	28.83 *t*	25.87 *t*
13	42.25 *s*	42.74 *s*	42.16 *s*	48.04 *s*	42.74 *s*	38.84 *s*
14	72.94 *s*	72.74 *s*	61.33 *d*	191.70 *s*	72.54 *s*	69.55 *s*
15	57.50 *d*	57.75 *d*	218.61 *s*	123.28 *d*	57.76 *d*	57.07 *d*
16	208.83 *s*	208.47 *s*	43.23 *dd*	204.60 *s*	207.88 *s*	166.70 *s*
17	50.87 *d*	50.87 *d*	38.00 *d*	60.45 *d*	50.74 *d*	78.04 *d*
18	24.83 *q*	27.37 *q*	27.89 *q*	26.47 *q*	27.27 *q*	19.79 *q*
19	16.35 *q*	15.93 *q*	19.31 *q*	18.85 *q*	19.89 *q*	18.72 *q*
20	116.88 *s*	116.65 *s*	122.89 *s*	118.31 *s*	116.52 *s*	120.45 *s*
21	141.61 *d*	141.71 *d*	140.28 *d*	141.48 *d*	141.58 *d*	141.22 *d*
22	111.13 *d*	111.03 *d*	110.83 *d*	111.06 *d*	110.96 *d*	109.89 *d*
23	142.33 *d*	142.55 *d*	143.01 *d*	142.49 *d*	142.36 *d*	143.01 *d*
28	23.63 *q*	24.25 *q*	27.37 *q*	26.91 *q*	24.96 *q*	27.27 *q*
29	20.90 *q*	20.61 *q*	21.13 *q*	21.12 *q*	21.03 *q*	21.16 *q*
30	19.44 *q*	19.47 *q*	18.20 *q*	26.46 *q*	19.89 *q*	18.01 *q*
$\mathrm{Me\underline{C}O}$	170.02 *s*	169.97 *s*	169.30 *s*	—	—	—
$\mathrm{\underline{C}H_3CO}$	21.32 *q*	21.35 *q*	21.13 *q*	—	—	—
Me-O-	56.81 *q*	—	—	—	—	—
1′	—	—	—	129.62 *s*	129.98 *s*	129.68 *s*
2′,6′	—	—	—	129.23 *d*	129.46 *d*	129.29 *d*
3′,5′	—	—	—	128.38 *d*	128.71 *d*	128.74 *d*
4′	—	—	—	133.13 *d*	133.45 *d*	133.55 *d*
7′	—	—	—	164.95 *s*	165.70 *s*	165.66 *s*

* Assignment uncertain.

(5-ring epoxyketone), 1745 (ester carbonyl), 1700 (6-ring epoxyketone), 1245, 1030 (C-0), 1260, 830 (epoxide), 875 (furane). MS *m/e*: 482 (M^+). ^{1}H NMR (360 MHz, $CDCl_3$) [2]: δ 7.56 (1 H, *m*, 21-H), 7.40 (1 H, *m*, 23-H), 6.23 (1 H, *m*, 22-H), 4.66 (1 H, *m*, 7-H), 3.88 (1 H, *s*, 17-H), 3.62 (1 H, *d*, J = 4.5 Hz, 1-H), 3.42 (1 H, *d*, J = 4.5 Hz, 2-H), 3.40 (1 H, *s*, 15-H), 2.92 (1 H, *m*, 9-H), 2.45 (1 H, *m*, 5-H), 2.20–1.80 (6 H, *m*, 6-H, 11-H, 12-H), 2.07 (3 H, *s*, Me—CO), 1.19 (3 H, *s*, 30-H), 1.09 (3 H, *s*, 18-H), 1.06 (3 H, *s*, 19-H), 1.03 (3 H, *s*, 28-H), 0.97 (3 H, *s*, 29-H). ^{13}C NMR spectrum see Table 1.

7-Desacetyl-7-benzoylepoxyazadiradione (**5**). Amorphous, $[\alpha]_D^{20}$ +81.4° ($CHCl_3$, $c = 1$). (Found *m/e* 528.2528. $C_{33}H_{36}O_6$, MS: Calc. *m/e* 528.2512). IR ν_{max}^{KBr} cm^{-1}: 3140 (furane), 3030 (C_6H_5), 1755 (5-ring-epoxyketone), 1670 (α,β-unsat. 6-ring ketone), 1275 and 1105 (C-O), 1030, 718 (C_6H_5). UV λ_{max}^{EtOH} nm: 228, ε = 26 000. ^{1}H NMR (360 MHz, $CDCl_3$) [2]: δ 7.93 (2 H, *m*, 2′-H, 6′-H), 7.57 (1 H, *m*, 4′-H), 7.42 (2 H, *m*, 3′-H, 5′-H), 7.40 (1 H, *m*, 21-H), 7.33 (1 H, *m*, 23-H), 7.23 (1 H, *d*, J = 10 Hz, 1-H), 6.11 (1 H, *m*, 22-H), 5.92 (1 H, *d*, J = 10 Hz, 2-H), 5.13 (1 H, *m*, 7-H), 3.83 (1 H, *s*, 17-H), 3.56 (1 H, *s*, 15-H), 2.81 (1 H, *s*, 9-H), 2.41 (1 H, *m*, 5-H), 2.20–1.75 (6 H, *m*, 6-H, 11-H, 12-H), 1.31 (3 H, *s*, 30-H), 1.29 (3 H, *s*, 19-H), 1.09 (3 H, *s*, 29-H), 1.01 (3 H, *s*, 28-H), 0.92 (3 H, *s*, 18-H). ^{13}C NMR spectrum see Table 1.

Fraction 4 (32.3 g), R_f = 0.28. Chromatography on 800 g silica gel with petrol–EtOAc (3:1) gave 6.7 g gedunin and 1.7 g of a mixture of **1** and **3**, separated by prep. HPLC over LiChroprep RP-18 (30 μm, Merck) with MeOH–H_2O (4:1) into 300 mg **1** and 700 mg **3**. 1α-Methoxy-1,2-dihydroepoxyazadiradione (**1**): mp 235–236° (from MeOH), $[\alpha]_D^{20}$ − 1.4° ($CHCl_3$, $c = 1$). (Found: C, 69.63; H, 7.65. $C_{29}H_{38}O_7$ (498.6) requires: C, 69.86; H, 7.68%). IR ν_{max}^{KBr} cm^{-1}: 3150 (furane), 1753 (5-ring-epoxyketone), 1735 (ester carbonyl), 1700 (6-ring ketone), 1245, 1030 (C—O), 1095 (Me—O), 875 (furane), 835 (epoxide). MS *m/e*: 498 (M^+). ^{1}H NMR (360 MHz, $CDCl_3$) [2]: δ 7.53 (1 H, *m*, 21-H), 7.20 (1 H, *m*, 23-H), 6.24 (1 H, *m*, 22-H), 4.66 (1 H, *m*, 7-H), 3.88 (1 H, *s*, 17-H), 3.39 (1 H, *t*, J = 3.7 Hz, 1-H), 3.37 (1 H, *s*, 15-H), 3.32 (3 H, *s*, —OMe), 3.24 (1 H, *m*, 9-H), 2.90 (1 H, *dd*, $J_{1,2\beta} = 3.7$, $J_{gem.} = 16.5$ Hz, 2-Hβ), 2.64 (1 H, *dd*, $J_{1,2\alpha} = 3.7$, $J_{gem.} = 16.5$ Hz, 2-Hα), 2.24 (1 H, *m*, 5-H), 2.04 (3 H, *s*, Me—C = O), 2.13–1.50 (6 H, *m*, 6-H, 11-H, 12-H), 1.17 (3 H, *s*, 30-H), 1.11 (3 H, *s*, 19-H), 1.05 (3 H, *s*, 18-H), 1.02 and 0.99 (3 H, *s* each, 28-H, 29-H). ^{13}C NMR see Table 1. 7-Acetylneotrichilenone (**3**): mp 208° (from MeOH), $[\alpha]_D^{20}$ − 21° ($CHCl_3$, $c = 1$). (Found: *m/e* 452.2548. $C_{28}H_{36}O_5$, MS: Calc. *m/e* 452.2553 (M^+)). IR ν_{max}^{KBr} cm^{-1}: 3140 (furane), 1735 (ester carbonyl), 1745 (5-ring ketone), 1675 (α,β-unsat. 6-ringketone), 1250, 1030 (C-O), 875 (furane). ^{1}H NMR (360 MHz, $CDCl_3$) [2]: δ 7.40 (1 H, *m*, 21-H), 7.31 (1 H, *m*, 23-H), 7.17 (1 H, *d*, $J_{1,2} = 10.4$ Hz, 1-H), 6.30 (1 H, *m*, 22-H), 5.89 (1 H, *m*, $J_{2,1} = 10.4$ Hz, 2-H), 4.96 (1 H, *t*, $J_{7,6\alpha} = J_{7,6\beta} = 3$ Hz, 7-H), 3.50 (1 H, *t*, $J_{17,16} = 10$ Hz, 17-H), 2.51 (1 H, *d*, $J_{16,17} = 10$ Hz, 16-H), 2.44 (1 H, *s*, 14-H), 2.10 (3 H, *s*, MeCO), 2.13–2.0 (1 H, *m*, 5-H), 1.95–1.84 (2 H, *m*, 6-H), 1.83–1.78 (2 H, *m*, 11-H), 1.43–1.36 (1 H, *m*, 9-H), 1.35–1.20 and 2.07–2.0 (2 H, *m*, 12-H), 1.16 (3 H, *s*, 30-H), 1.14 (3 H, *s*, 19-H), 1.08 (3 H, *s*, 29-H), 1.06 (3 H, *s*, 28-H), 0.78 (3 H, *s*, 18-H). ^{13}C NMR see Table 1.

Fraction 5 (92.6 g), R_f = 0.14. Chromatography over Si gel with CH_2Cl_2–EtOAc (4:1) gave a main fraction (61 g). Addition of MeOH gave 39 g azadiradione. Prep. HPLC of the mother liquor [LiChroprep RP-18 (30 μm, Merck) with MeOH–H_2O, 3:1] afforded 8 g azadiradione, 480 mg 17-*epi*-azadiradione [1], 3.5 g 17β-hydroxyazadiradione [1], and 700 mg 7-desacetyl-7-benzoylazadiradione (**4**) (amorphous), $[\alpha]_D^{20}$ +38.8° ($CHCl_3$, c = 1). (Found: *m/e* 512.2536. $C_{13}H_{36}O_5$, MS: Calc. *m/e* 512.2522). IR ν_{max}^{KBr} cm^{-1}: 3130 (furane), 3030 (C_6H_5), 1710 (ester carbonyl), 1700 (α,β-unsat. 5-ring ketone), 1670 (α,β-unsat. 6-ring ketone), 1275 and 1110 (C—O), 1030, 710 (C_6H_5). UV λ_{max}^{EtOH} nm: 232, ε = 30 210. ^{1}H NMR (90 MHz, $CDCl_3$): δ 8.0–7.54 (2 H, *m*, 2′-H, 6′-H), 7.51–7.28 (5 H, *m*, 3′-H, 4′-H, 5′-H, 21-H, 23-H), 7.18 (1 H, *d*, J = 10 Hz, 1-H), 6.19 (1 H, *m*, 22-H), 5.90 (1 H, *d*, J = 10 Hz, 2-H), 5.93 (1 H, *s*, 15-H), 5.62 (1 H, *m*, 7-H), 3.40 (1 H, *s*, 17-H), 2.84–1.55 (8 H, *m*, 5-H, 6-H, 9-H, 11-H, 12-H), 1.42 (3 H, *s*, 30-H), 1.31 (3 H, *s*, 19-H), 1.11 (3 H, *s*, 29-H), 1.04 (3 H, *s*, 28-H), 1.00 (3 H, *s*, 18-H). ^{13}C NMR see Table 1.

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