Tetranortriterpenoids and Related Compounds. Part 26.[1] Tecleanin, a Possible Precursor of Limonin, and Other New Tetranortriterpenoids from *Teclea grandifolia* Engl. (Rutaceae)

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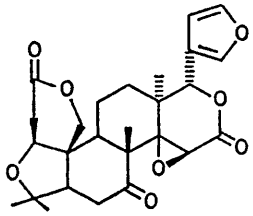
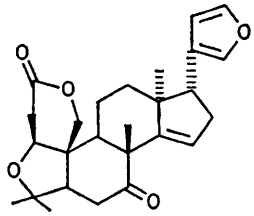
Tecleanin and 7-deacetylproceranone, two new tetranortriterpenoids from *Teclea grandifolia* Engl. (Rutaceae), have been assigned structures (2) and (4) respectively. Tecleanin has the same highly oxidised ring A as limonin but a carbocyclic ring D. A third new limonoid was identified as 7-deacetylazadirone (13).

LIMONIN (1), a bitter principle of citrus species, is the best known member of the tetranortriterpenoids. Its structural elucidation in 1960 by the formidable team of Arigoni, Barton, Corey, and Jeger, and their collaborators [2] provided the impetus for subsequent work in this field. We now report the isolation from *Teclea grandifolia* Engl. (Rutaceae) [3] of three new tetranortriterpenoids, tecleanin (2), 7-deacetylproceranone (4), and 7-deacetylazadirone (13). Tecleanin (2), the most interesting of these, is a possible precursor of limonin (1) and has not been isolated previously, while the other two have already been obtained as their acetates from plants of the Meliaceae family.

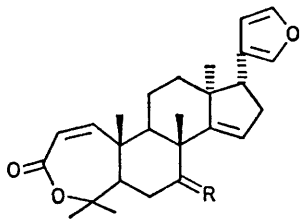
Tecleanin (2), $C_{26}H_{32}O_5$, {*m/e* 424; $[\alpha]_D$ −143°, $\nu_{max.}$



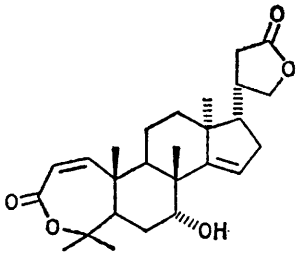
(1)



(2)



(3) R=O
(4) R=H, α-OH
(5) R=H, α-OAc



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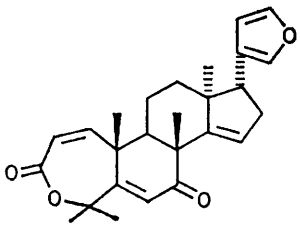

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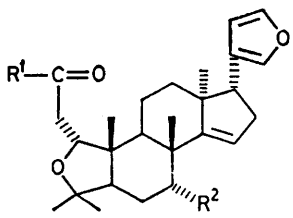
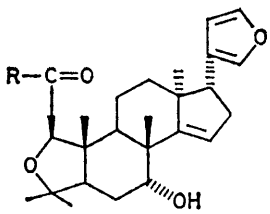
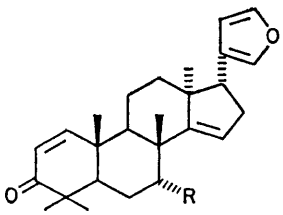


(8) R^1 = OH, R^2 = OH
(9) R^1 = OMe, R^2 = OH
(10) R^1 = OMe, R^2 = OAc



(11) R = OH
(12) R = OMe



(13) R = OH
(14) R = OAc

(CCl_4) 1 770 (δ-lactone) and 1 718 (cyclohexanone) cm^{-1}} has resonances in its ^1H n.m.r. spectrum for four tertiary methyl groups (δ 0.78, 1.04, 1.19, and 1.23), a secondary ether proton (δ 4.07br s, H-1), an AB quartet (δ 4.53 and 4.72, J 13 Hz, H_2-19), a vinyl proton (δ 6.24, m, H-15), and the characteristic β-substituted furan (δ 7.33, 7.22, and 6.25). Four of the five oxygens are accounted for by the furan, ketone, and δ-lactone and the fifth must therefore be present as an ether in view of the lack of hydroxy-absorption in the i.r. spectrum. The ^{13}C n.m.r. spectrum (see Table 1) confirmed the presence of a

TABLE 1

^{13}C N.m.r. data of tecleanin, limonin, and 7-deacetylproceranone and derivatives [a]

Carbon no.	(2)	(1)	(4)	(5)	(3)
1	79.2	79.2	155.8	155.7	153.9
2	36.1 †	36.4 †	119.8	119.8	120.7
3	169.7	169.7	167.8	167.6	166.9
4	80.4	80.3	85.2	84.8	83.8
5	58.9	60.6	47.8	49.2	55.3
6	35.6 †	35.7 †	26.4	27.4	39.3
7	207.6	206.1	71.6	74.3	208.9
8	45.4	46.0	44.2	42.2	52.3
9	45.6	48.1	39.5	41.2	47.9
10	50.8	51.4	44.2	44.1	44.0
11	19.1	18.9	17.7	18.2	19.4
12	32.5	30.8	32.7	33.4	34.9
13	47.8	38.0	47.1	47.0	47.6
14	151.7	65.8	160.6	158.3	152.2
15	127.2	53.9	120.4	119.6	126.6
16	34.6	166.6	34.4	34.4	34.4
17	51.7	77.8	51.7	51.7	51.7
19	65.1	65.4			
20	124.3	120.1	124.2	124.4	124.4
21	142.7	143.3	142.7	142.6	142.7
22	111.0	110.7	111.0	111.0	111.0
23	139.8	141.2	139.7	139.7	139.8
CMe	30.3	30.2	32.1	32.0	31.7
	28.3	20.7	28.0	27.0	27.4
	21.4	21.4	27.1	26.2	25.8
	21.4	17.7	20.7	21.1	22.3
			15.7	16.0	16.0
OAc				21.2	
				170.1	

[a] Pulsed Fourier-transform spectra were obtained at 25.2 MHz for solutions in $CDCl_3$ at room temperature (*ca.* 25 °C). Shifts are given as positive downfield from internal Me_4Si. Assignments are based on chemical-shift rules, multiplicities in off-resonance-decoupled spectra, correlation with ^1H chemical shifts using two off-resonance-decoupled spectra, and comparison with published data for similar compounds (B. Sabata, J. D. Connolly, C. Labbé, and D. S. Rycroft, *J. Chem. Soc., Perkin Trans. 1*, 1977, 1875; J. D. Connolly, C. Labbé, D. S. Rycroft, and D. A. H. Taylor, *ibid.*, 1979, 2959).

† These assignments may be interchanged.

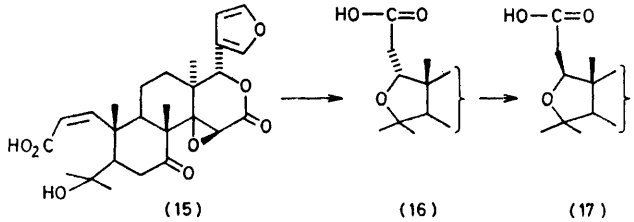
ketone, lactone, trisubstituted double bond, and secondary tertiary ether. These functional groups can be satisfactorily accommodated in structure (2) with the same modified ring A as limonin (1) and a trisubstituted double bond in ring D. Convincing support for the proposed structure (2) can be obtained by examination of the ^{13}C n.m.r. data in Table 1. The chemical shifts of the carbons of the modified ring A are virtually identical with those of limonin (1). Likewise, the shifts of the ring-D and furan carbons compare favourably with those of 7-deacetyl-7-oxoproceranone (3).

7-Deacetylproceranone (4), $C_{26}H_{34}O_4$, m.p. 168—170 °C, $[\alpha]_D$ +31°, has $\nu_{max.}$ (KBr) 1 690 (αβ-unsaturated ε-lactone), 3 140, 875 (β-substituted furan), and 3 560 cm^{-1} (OH). The ^1H n.m.r. spectrum (Table 2) proved to be most informative. This was particularly so when it was compared with the ^1H n.m.r. spectrum of tricoccin S_{13} (6) recently reported [4] from *Cneoraceae tricoccon* L. Thus 7-deacetylproceranone (4) and tricoccin S_{13} (6) both showed resonances of the expected intensity and multiplicity for protons at C-1, -2, -7, and -15, the chemical-shift differences being not greater than 0.04 p.p.m. This similarity also extended to the C-methyl region. At the same time the expected differences between (4) and (6) were clearly discernible, the characteristic β-substituted furan resonances of (4) replacing the signals associated with the γ-lactone of (6). The ^{13}C n.m.r. spectrum of 7-deacetylproceranone (4) (Table 1) and tricoccin S_{13} (6) [4] also show marked similarities with very little difference in the chemical shifts of C-1, C-2, C-3, and C-15. The above data suggested that 7-deacetylproceranone (4) and tricoccin S_{13} have the same overall structure with the exception of the furan ring, which is unmodified in (4).

Oxidation of 7-deacetylproceranone (4) afforded the 7-oxo-derivative (3), [$\nu_{max.}$ (KBr) 1 710 (cyclohexanone) and 1 690 (αβ-unsaturated ε-lactone) cm^{-1}] and acetylation gave the monoacetate (5), which was found to be identical with proceranone, a tetranortriterpenoid recently isolated from *Carapa procera*.[5]

Selenium dioxide oxidation of the 7-ketone (3) gave a dehydro-compound (7), M^+ 406, m.p. 211—212 °C with an intense u.v. maximum ($CHCl_3$) at 247 nm (ε 12 500) and a new i.r. band at 1 700 cm^{-1} appropriate to an αβ-unsaturated ketone. In the ^1H n.m.r. spectrum (Table 2) of the oxidation product (7) an extra one-proton singlet attributable to the H-6 vinyl proton appeared at δ 5.88. These data readily led to structure (7) for the dehydro-compound.

On brief treatment with boiling methanolic sodium hydroxide, 7-deacetylproceranone (4) was converted into a 1 : 1 mixture of two isomeric acids (8) and (11) which were characterised as their methyl esters (9) and (12), prepared by esterification with ethereal diazomethane. Compound (9), a white solid, has m.p. 149—152 °C while (12) is an oil. On prolonged heating with



the same alkaline solution, followed by methylation only the non-crystalline methyl ester (12) was obtained. The structures of these esters were assigned by analogy with similar transformations of obacunone.[6,7,8] Obacunone is first converted by base into obacunoic acid (15)

TABLE 2

^{1}H N.m.r. spectra † of 7-deacetylproceranone and related compounds

Compound	H-1	H-2	H-7	H-15	H-α-furan	H-β-furan	Methyls	Others
7-Deacetylproceranone (4)	6.44 (d) (*J* 10)	5.82 (d) (*J* 10)	3.94 (m)	5.50 (t) (*J* 3)	7.35 (m) 7.24	6.26	0.78, 1.13, 1.25, 1.42 (6 H)	2.77br (s) (7-OH)
Tricoccin S_{13} [a] (6)	6.42 (d) (*J* 10)	5.81 (d) (*J* 10)	3.90 (m)	5.48 (t) (*J* 3)			5 s between 1.00 and 1.43	
7-Deacetyl-7-oxoproceranone (3)	6.42 (d) (*J* 10)	5.90 (d) (*J* 10)		5.96 (m)	7.34 7.25	6.25	0.71, 1.38, 1.40 (6 H), 1.44	
Proceranone (5)	6.52 (d) (*J* 10)	5.87 (d) (*J* 10)	5.40 (t) (*J* 3)	5.25 (t) (*J* 3)	7.30 7.25	6.28	0.80, 1.24, 1.32, 1.38, 1.47	2.0 (7-OAc)
$\Delta^{5,6}$-7-Deacetyl-7-oxoproceranone (7)	6.40 (d) (*J* 10)	5.90 (d) (*J* 10)		5.87 (m)	7.35 7.24	6.30	0.70, 1.30, 1.58, 1.68 (6 H)	5.87 (H-6)
7-Deacetylazadirone (13)	7.08 (d) (*J* 10)	5.80 (d) (*J* 10)	4.00 (m)	5.06 (m)	7.32 7.20	6.25	0.75, 1.05, 1.12 (9 H)	2.10 (7-OH)
Azadirone [b] (14)	7.15 (d) (*J* 10)	5.83 (d) (*J* 10)	5.33 (m)	5.27 (m)	7.32 7.20	6.27	0.78, 1.05 (6 H), 1.18, 1.20	1.93 (7-OAc)

† Spectra determined with tetramethylsilane as internal standard; unless otherwise indicated, all signals are singlets; coupling constants (*J*) are given in Hz.

[a] Spectrum kindly provided by Professor Dr. A. Mondon, Institute of Chemistry, Kiel, West Germany. [b] Agrees with values reported in ref. 9.

which on mild treatment with alkali gives *epi*-iso-obacunoic acid (16) which is transformed under more vigorous conditions to iso-obacunoic acid (17). The *epi*-iso-isomer is thus the less stable. It follows that brief but vigorous treatment of 7-deacetylproceranone (4) with alkali gives directly a mixture of the *epi*-iso- and iso-acids (8) and (11), respectively, and that on prolonged treatment the less stable *epi*-iso-acid (8) is totally transformed into the iso-acid (11). The ^{1}H n.m.r. spectra (see Experimental section) of the two methyl esters (9) and (12) are in accord with their proposed structures.

The third new limonoid (13), $C_{26}H_{34}O_3$, $[\alpha]_D$ +10°, $\nu_{max.}$ 3 560 (OH) and 1 676 cm^{-1} (cyclohexenone), was shown by its ^{1}H n.m.r. spectrum (Table 1) to be deacetylazadirone (13), and its structure was confirmed by acetylation to azadirone (14).[9]

EXPERIMENTAL

M.p.s were measured with a Kofler hot-stage apparatus. Optical rotations were recorded with an automatic Perkin-Elmer 141 polarimeter. N.m.r. spectra were run (^{1}H) on Perkin-Elmer R12 and R32 spectrometers and (^{1}H and ^{13}C) on a Varian XL-100 spectrometer with VFT-100 accessory. Microanalyses were determined by M. Hemmert of the Institute of Chemistry, Strasbourg, France.

Isolation.—The powdered stem bark (10 kg) of *Teclea grandifolia* obtained from a forest near the Nachtigal Fall in the Sanaga River, about 100 miles from Yaoundé, was extracted (Soxhlet) with chloroform (15 l). The extract was concentrated to 1.5 l and washed several times with hydrochloric acid (2M) to remove alkaloids. The solvent was removed *in vacuo* and the residual green syrup (150 g) was chromatographed over silica gel (700 g) in hexane. Elution with hexane–ether afforded a crude solid (56 g) in the early fractions which was crystallised from ethyl acetate–hexane to give lupeol [10] (50 g), m.p. 214—216 °C. Later fractions afforded 7-*deacetylazadirone* (13) as granular crystals from methanol–hexane (480 mg), m.p. 203—205 C°, $[\alpha]_D^{21}$ +10° (*c*, 0.3 in $CHCl_3$), $\lambda_{max.}$ ($CHCl_3$) 240 nm (ε 8 000), $\nu_{max.}$ (KBr) 3 560 (OH), 1 676 (cyclohexenone), and 870 cm^{-1} (β-substituted furan) (Found: C, 79.0; H, 8.5. $C_{26}H_{34}O_3$ requires C, 79.15; H, 8.7%). The fractions eluted with hexane–ether (3 : 7 v/v) were combined and recrystallised from methylene chloride–hexane to give 7-*deacetylproceranone* (4) (4 g), m.p. 168—170 °C, $[\alpha]_D^{21}$ +31° (*c*, 0.5 in $CHCl_3$), $\nu_{max.}$ (KBr) 3 560, 3 140, and 870 cm^{-1}; *m/e* 410 (M^+, 30%), 377 (10), 315 (35), 270 (10), 257 (25), 138 (100), 131 (20), and 119 (15) (Found: C, 76.1; H, 8.3. $C_{26}H_{34}O_4$ requires C, 76.05; H, 8.35%). Ether eluted a mixture which was separated (preparative t.l.c.) into an unidentified gum and *tecleanin* (2) (80 mg), needles from methylene chloride–hexane, m.p. 254—256 °C, $[\alpha]_D^{21}$ −143° (*c*, 0.3 in $CHCl_3$), *m/e* 424 (M^+, 100%), 409 (20), 391 (15), 381 (50), 352 (6), 214 (18), and 199 (18) (Found: C, 73.5; H, 7.4. $C_{26}H_{32}O_5$ requires C, 73.5; H, 7.4%).

7-*Deacetyl-7-oxoproceranone* (3).—7-Deacetylproceranone (4) (100 mg) was dissolved in acetone (20 ml) and the solution cooled to 0 °C. Jones reagent (3 ml) was added; after 10 min the reaction mixture was diluted with water (40 ml) and extracted with chloroform. The chloroform solution was further washed successively with a saturated solution of sodium chloride and water. The product, after recrystallisation from hexane–ethyl acetate, gave 7-*deacetyl-7-oxoproceranone* (3) (78 mg), m.p. 212—214 °C, $[\alpha]_D^{21}$ −26° (*c*, 0.33 in $CHCl_3$), *m/e* 408 (M^+, 100%), 393 (40), 375 (42), 241 (26), and 159 (20) (Found: C, 76.45; H, 7.85. $C_{26}H_{32}O_4$ requires C, 76.45; H, 7.9%).

Acetylation of 7-Deacetylproceranone (4).—7-Deacetylproceranone (4) (100 mg) in a mixture of acetic acid (10 ml), acetic anhydride (2.5 ml), and toluene-*p*-sulphonic acid (100 mg) was stirred at room temperature for 1 h and the mixture worked up. The acetate (95 mg), purified by preparative t.l.c., had m.p. 180—181 °C (from hexane–ether), alone or when mixed with an authentic sample of proceranone (5),[5] $[\alpha]_D^{21}$ +28° (*c*, 0.8 in $CHCl_3$) (^{1}H n.m.r. and i.r. spectra identical).

$\Delta^{5,6}$-7-*Deacetyl-7-oxoproceranone* (7).—A solution of 7-deacetyl-7-oxoproceranone (3) (80 mg) in dioxan (2 ml) was added to selenium dioxide (100 mg) dissolved in dioxan (6 ml) and water (2 ml), and the mixture was heated under reflux for 5 h. The hot solution was filtered, diluted with water (100 ml), and extracted with chloroform (3 × 20 ml). The chloroform solution was washed with water, dried (Na_2SO_4), and evaporated to dryness. The resulting residue was taken up into chloroform (50 ml), treated with activated nickel (1 g) and barium sulphate (0.5 g), and refluxed for 30 min. Filtration followed by evaporation gave a

residue which was chromatographed on a short silica gel column. Elution with hexane–ethyl acetate (2 : 1 v/v) afforded $\Delta^{5,6}$-7-*deacetyl*-7-*oxoproceranone* (7) as plates, m.p. 211—212 °C (from hexane), $\lambda_{max.}$ ($CHCl_3$) 247 nm (ε 12 000), *m/e* 406 (M^+, 100%), 391 (30), 375 (15), 312 (24), 241 (32), and 191 (30) (Found: C, 76.6; H, 7.0. $C_{26}H_{30}O_4$ requires C, 76.85; H, 7.35%).

Alkaline Hydrolysis of 7-Deacetylproceranone (4).—7-Deacetylproceranone (4) (500 mg) was heated under reflux with methanolic sodium hydroxide (10%; 100 ml) for 30 min. Acidification with concentrated hydrochloric acid, and extraction of the solution yielded a crude product (400 mg) composed of a mixture of two acids (t.l.c.). Methylation of the mixture (200 mg) in dry methanol (20 ml) with an excess of ethereal diazomethane for 30 min at room temperature (destruction of the excess of diazomethane with 2 drops of formic acid) yielded a mixture of the crude methyl esters (202 mg). Crystallisation from hexane–ether afforded the epi-*iso-ester* (9) (72 mg) as needles, m.p. 149—152 °C, $[\alpha]_D$ +18° (*c*, 0.1 in $CHCl_3$), $\nu_{max.}$ 3 570 (OH), 1 740 (ester carbonyl), and 870 cm^{-1} (β-substituted furan), δ ($CDCl_3$) 0.78 (3 H, s) 1.11 (9 H, s) 1.25 (3 H, s), 4.05 (1 H, dd, *J* 4 and 10 Hz, H-1), 3.63 (3 H, s, OMe), 3.96 (1 H, t, *J* 3 Hz, H-7), 5.55 (1 H, m, H-15), 6.21 (1 H, β-furan), and 7.23 and 7.30 (each 1 H, α-furan), *m/e* 442 (M^+, 100%) (Found: C, 73.6; H, 8.6. $C_{27}H_{38}O_5$ requires C, 74.0; H, 8.45%).

Analytical t.l c. of the mother-liquors indicated the presence of the second methyl ester which was isolated by preparative t.l.c. to yield the non-crystalline *iso-ester* (12) (85 mg), $\nu_{max.}$ 3 570 (OH), 1 740 (ester C=O), and 875 cm^{-1} (β-furan), δ ($CDCl_3$) 0.80 (3 H, s), 0.92 (3 H, s), 1.10 (6 H, s), 1.20 (3 H, s), 3.65 (3 H, s, OMe), 3.85 (1 H, dd, *J* 4 and 8 Hz, H-1), 3.98 (1 H, t, *J* 3 Hz, H-7), 5.55 (1 H, m, H-15), 6.20 (1 H, β-furan), and 7.20 and 7.30 (1 H, each, α-furan), M^+, 442.

When the hydrolysis with methanolic sodium hydroxide was carried out for 2 h only the non-crystalline iso-ester (12) was obtained after methylation.

The epi-*Iso-ester Acetate* (10).—The *epi*-iso-ester (9) (50 mg) was acetylated as above to give the *acetate* (10) (60 mg), m.p. 172 °C (from hexane–methylene chloride), δ ($COCl_3$) 0.78 (3 H, s), 1.10 (3 H, s) 1.14 (6 H, s), 1.94 (3 H, s, OAc), 3.65 (3 H, s, OMe), 4.06 (1 H, dd, *J* 4 and 10 Hz, H-1), 5.20 (1 H, s, H-15), 5.32 (1 H, t, *J* 3 Hz, H-7), and 6.20 and 7.30 (furan), M^+, 484.

Azadirone (14).—7-Deacetylazadirone (13) (100 mg) was treated in pyridine (3 ml) with acetic anhydride (3 ml) on a steam-bath for 1 h. After the usual work-up, the product was purified by preparative t.l.c. to give azadirone (14) as a gum (78 mg). Its ^1H n.m.r. data were identical with those reported [9] for azadirone.

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