Apotirucallane Triterpenes from Dysoxylum roseum

S. A. Adesanya, M. Païs, T. Sévenet, and J. P. Cosson

J. Nat. Prod., **1991**, 54 (6), 1588-1594• DOI:
10.1021/np50078a015 • Publication Date (Web): 01 July 2004

Journal of Natural Products
Vol. 54, No. 6, pp. 1588-1594, Nov-Dec 1991

APOTIRUCALLANE TRITERPENES FROM *DYSOXYLUM ROSEUM*[1]

S.A. ADESANYA,[2] M. PAÏS,* T. SÉVENET,

Institut de Chimie des Substances Naturelles, CNRS, 91198 Gif-sur-Yvette, France

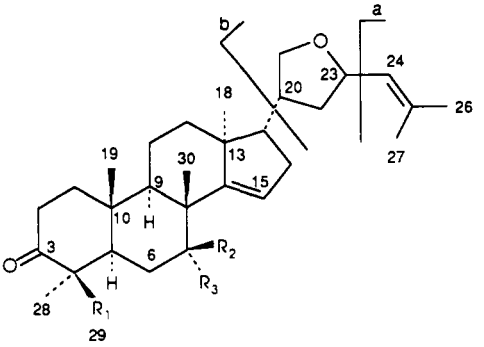
and J.P. COSSON

Laboratoire des Plantes Médicinales du CNRS, BP 643, Nouméa, Nouvelle Calédonie

ABSTRACT.—Chemical investigation of the biologically active compounds in *Dysoxylum roseum* leaves has led to the isolation and characterization of five new apotirucallane-derived triterpenes, dysorones A [**1**], B [**2**], C [**3**], D [**4**], and E [**5**], and β-sitosterol. The major compound, dysorone E [**5**], exhibits moderate cytotoxic activity in vitro against the growth of KB human buccal carcinoma cells (ED_{50} 3.5 μg/ml).

Dysoxylum roseum C. DC. (Meliaceae) belongs to a genus with wide traditional uses which include fish poisoning (1) and alleviating aches (2) and pains in Polynesia and the Indo-Malaysia regions of the world. Members have been shown to possess antibacterial (2), CNS depressant and anti-inflammatory (3), immunomodulatory (4), and cardioactive (5) activities. Chemical investigations have led to the isolation of alkaloids in *Dysoxylum lenticellare* (5) and *Dysoxylum binectariferum* (4), and a polysulfide dysoxysulfone and dammarane triterpenoids in *Dysoxylum richii* (2,6). Terpenes were also found in *Dysoxylum acutangulum* and *Dysoxylum alliaceum* (1). An apotirucallane-derived nortriterpene, dysobinin, with significant CNS depressant action was isolated from *D. binectariferum* (3).

In a systematic study of plants from New Caledonia, the EtOH extract of *D. roseum* leaves demonstrated cytotoxic activity against KB human buccal carcinoma cells (7). The MeOH extract was fractionated by solvent partitioning, and the activity was located in the CH_2Cl_2 fraction. Tlc of this fraction showed several spots which were separated by cc and preparative tlc on Si gel to give compounds **1–5** and β-sitosterol. These



1 $R_1 = CH_2OH$, $R_2, R_3 = O$
2 $R_1 = CH_2OH$, $R_2 = H$, $R_3 = OH$
3 $R_1 = Me$, $R_2, R_3 = O$, Δ^1
4 $R_1 = Me$, $R_2 = H$, $R_3 = OH$, Δ^1
5 $R_1 = CH_2OH$, $R_2, R_3 = O$, Δ^1
6 $R_1 = CH_2OAc$, $R_2, R_3 = O$
7 $R_1 = CH_2OAc$, $R_2, R_3 = O$, Δ^1

[1]Plants of New Caledonia, 138. For Part 137 see R. Benkrief, A.L. Skaltsounis, F. Tillequin, M. Koch, and J. Pusset, *J. Nat. Prod.*, **54**, 532 (1991).

[2]Present address: Department of Pharmacognosy, Faculty of Pharmacy, Obafemi Awolowo University, Ile-Ife, Nigeria.

compounds were identified by spectroscopic methods which established **1–5** as meliacins with new apotirucallane structures (3,8).

Compound **1** had a molecular formula $C_{32}H_{44}O_4$ (hreims, *m/z* 468 $[M]^+$) with ir (1705, 3475 cm^{-1}) and ^{13}C-nmr (δ 218, 210) data indicating the presence of two keto groups on cyclohexane ring(s) and an alcohol function. Acetylation gave a monoacetate **6** (*m/z* 510 $[M]^+$) with a ^1H-nmr signal at δ 4.14 indicating a collapse and shift of the AB spin system (centered at δ 3.58 and 3.88) of **1**, showing the presence of a CH_2OH group. The remaining oxygen is therefore an ether. Other signals in the ^{13}C nmr are those of six Me groups located on quarternary carbons with two on a double bond as a gem dimethyl group; nine CH_2, two as oxymethylenes; seven CH, two on double bonds and an oxymethine; and five quarternary carbons, two trisubstituted (Table 1). These data together with the (−) optical rotation indicated a triterpenoid belonging to the tirucallane rather than euphane series (9,10). $^1H/^1H$ COSY and $^1H/^{13}C$ HETCOSY 2D shift correlated experiments allowed the assignment of each signal. Thus, apparent are the existence of C-5–C-6, C-1–C-2, C-23–C-24, C-20–C-21 bonds and CH_2OH-29 (Table 1).

TABLE 1. Nmr Data for Compound **1**.

Carbon	δC	Carbon-correlated proton[a]		Proton-correlated proton[b]	
		δH (*J* Hz)[c]	Long range	^1H-^1H COSY	NOESY
C-1 . . .	37.8 t	H-1β[d] 2.01 m	H_a-2, H_b-2[e]	H-1α, H_a-2 H_b-2	H-1α, H_a-2 Me-19β
		H-1α 1.40 m		H-1β, H_b-2 H_a-2	H-1β
C-2 . . .	34.1 t	H_a-2 2.58 m H_b-2 2.58 m	H-1β, H-1α	H-1α, H-1β	H-1β, Me-19β
C-3 . . .	218.0 s		H-1β, H_b-2, H_a-2 H_a-29β, H_b-29β		
C-4 . . .	51.9 s		H-5α, H-6β, H-6α H_a-29β, Me-28α		
C-5 . . .	55.6 d	H-5α 2.01 m	H_a-29, H-6β, H-6α H-1α, H-1β, Me-28α, Me-19β	H-6α, H-6β	
C-6 . . .	36.6 t	H-6β 2.89 t (14, 14) 2.68 t[f]	H-5α	H-5α, H-6α	H-6α, Me-19β, Me-30β
		H-6α 2.38 m		H-5α	Me-28α, H-6β
C-7 . . .	210.0 s		H-6α, H-6β, Me-30β		
C-8 . . .	52.0 s		H-9α, Me-30β		
C-9 . . .	48.8 d	H-9α 1.89 dd (12, 7)	Me-19β, Me-30β	H-1α, H-1β	Me-18α
C-10 . . .	36.7 s		H-6α, H-6β, H-5α H-9α		
C-11 . . .	17.8 t	H_a-11 1.73 m H_b-11 1.73 m	H-9α		
C-12 . . .	34.4 t	H_a-12 1.60 m H_b-12 1.60 m			
C-13 . . .	47.1 s		H_a-12, H_b-12, H-17β, Me-18α		
C-14 . . .	152.4 s		H_a-16, H_b-16 Me-18α, Me-30β		
C-15 . . .	126.4 d	H-15β 5.83 dd (2, 3) 6.20 dd[f]	H_a-16, H_b-16	H_a-16, H_b-16	Me-30β
C-16 . . .	35.7 t	H_a-16 2.65 dd (10, 3) H_b-16 2.40 d (10)	H-15β	H-17β	
C-17 . . .	58.3 t	H-17β 1.50 m	H-15β, H-21β, Me-18α		

TABLE 1. Continued.

Carbon	δC	Carbon-correlated proton[a]		Proton-correlated proton[b]	
		δH (*J* Hz)[c]	Long range	^{1}H-^{1}H COSY	NOESY
C-18 . . .	20.9 q	Me-18α 0.98 s	H-17β		H-9α
C-19 . . .	15.3 q	Me-19β 1.23 s	H-1α, H-1β, H-9α		H-1β, H-2β, H-6β
C-20 . . .	40.4 d	H-20 2.38 m		H_a-22, H_b-22	
C-21 . . .	72.1 t	H_a-21 4.05 t (8, 8) 4.16 t[f]		H_b-21, H-20	H_b-21
		H_b-21 3.26 t (8, 8) 3.32 t[f]			H_a-21
C-22 . . .	38.2 t	H_a-22 1.50 m H_b-22 1.50 m	H_a-21, H_b-21		
C-23 . . .	74.7 d	H-23 4.62 m 4.75 m[f]	H_a-21	Me-26 Me-27	
C-24 . . .	126.7 d	H-24 5.23 dd (9, 1.2) 5.49 dd[f]	Me-26, Me-27	H-23	
C-25 . . .	135.1 s		Me-26, Me-27		
C-26[g] . .	25.7 q	Me-26 1.74 s	H-24, Me-27		
C-27[g] . .	18.7 q	Me-27 1.73 s	H-24, Me-26		
C-28 . . .	21.4 q	Me-28α 1.24 s	H_a-29, H_b-29, H-5α		H-6α, H_a-29 H_b-29
C-29 . . .	64.9 t	H_a-29 3.88 d (11) 3.62 d[f]	H-5α, Me-28α	H_b-29	Me-28α, H_b-29
		H_b-29 3.58 d (11) 3.45 d[f]		H_a-29	Me-28α, H_a-29
C-30 . . .	37.2 q	Me-30β 1.37 s	H-9α		H-6β, H-15β

[a]These data were obtained by 2D ^{1}H/^{13}C COSY spectrum.

[b]These data were obtained from ^{1}H/^{1}H 2D COSY spectrum and NOESY 2D spatial proton correlated spectrum.

[c]*J* values in Hz obtained from 1D ^{1}H nmr spectrum (400 MHz) in $CDCl_3$ with TMS as internal standard.

[d]α,β: established stereochemistry as well as those apparent from NOESY 2D spatial connectivities.

[e]a,b: Protons of unassigned stereochemistry.

[f]Chemical shift of protons from 1D ^{1}H nmr spectrum (400 MHz) in C_6D_6 with TMS as internal standard.

[g]Assignments exchangeable.

Analysis of the hreims showed peaks at *m/z* 55 (fragment a), *m/z* 125 ($C_8H_{13}O$, fragment b) both attributed to the side chain (9,11), and *m/z* 343 ($C_{22}H_{31}O_3$, [M − side chain]$^+$). Compound **6** also had a peak at *m/z* 125, locating the CH_2OH on the fused ring. Therefore the side chain must be a tetrahydrofuran ring bearing a dimethylallyl group. The ^{1}H/^{13}C heteronuclear inverse detected long range spectrum (12) confirmed the structure (Table 1). It was found to be identical (^{1}H nmr, ^{13}C nmr, ms fragments) with the side chain of 21,23-epoxytirucalla-7,24-dien-3-one (9) and prieurone (11). This long range spectrum also showed strong connectivities of H-1, H-2, H-28, and H-29 with C-3 carbonyl and H-5, H-6, and H-30 with the C-7 carbonyl. Other connectivities (Table 1) established the fused rings. The fragment peaks at *m/z* 147 ($C_{11}H_{13}$) and *m/z* 197 ($C_{11}H_{18}O_3$) in hreims can be assumed to represent fused rings C/D and A/B, respectively. The remaining double bond was located at Δ^{11} based on the long range connectivities between H-15 and C-16 and nOe between H-15 and Me-30 (Table 1). The shift of the H-15 signal at δ 5.82 ($CDCl_3$) to δ 6.20 in C_6D_6 (13) (Table 1), as was observed with the synthesized 3,7-dione derivatives of grandifolione

TABLE 2. ^{13}C-nmr Data for Compounds **2–5** in $CDCl_3$.

Carbon	Compound			
	2	**3**	**4**	**5**
C-1	38.5[a] t	156.5 d	161.2 d	156.5 d
C-2	34.3 t	126.0[a] d	126.5[a] d	126.4[a] d
C-3	219.8 s	203.5 s	204.7 s	203.5 s
C-4	50.9 s	47.4 s	44.0[b] s	49.5 s
C-5	40.6[b] d	52.9 d	36.6 d	52.3 d
C-6	24.7 t	36.0[b] t	24.0 t	36.4 t
C-7	71.9 d	210.0 s	71.3 d	210.0 s
C-8	44.0 s	47.4 s	44.3[b] s	49.5 s
C-9	47.4 d	45.0 d	43.9[b] d	44.7 d
C-10	37.8 s	39.9 s	40.2 s	39.7 s
C-11	16.7 t	17.5 t	16.0 t	17.4 t
C-12	33.1 t	34.2 t	32.7 t	34.2 t
C-13	47.0 s	45.0 s	46.2 s	47.2 s
C-14	161.4 s	152.3 s	158.1 s	152.2 s
C-15	120.2 d	126.7 d	119.8 d	126.7 d
C-16	35.4 t	35.9[b] t	35.1 t	35.9 t
C-17	58.7 d	58.9 d	58.3 d	58.4 d
C-18	21.6[c] q	21.0[c] q	19.3 q	20.8 q
C-19	15.5 q	18.3 q	18.7 q	18.3 q
C-20	40.9[b] d	40.6 d	40.2 d	40.2 d
C-21	72.3 t	72.1 t	71.8 t	72.0 t
C-22	38.3[a] t	38.5 t	38.3 t	38.3 t
C-23	74.7 d	74.5 d	74.3 d	74.4 d
C-24	126.9 d	126.6[a] d	125.2[a] d	126.5[a] d
C-25	135.2 s	135.3 s	134.7 s	135.2 s
C-26[a]	25.5 q	25.9 q	26.9 q	25.7 q
C-27[a]	18.3 q	18.0 q	19.2 q	18.0 q
C-28	21.6[c] q	21.1[c] q	21.3 q	21.5 q
C-29	65.8 t	27.0 q	27.4 q	64.7 t
C-30	26.8 q	28.0 q	26.0 q	27.9 q

[a,b,c]Assignments with the same superscript in a column are exchangeable.

(14) and sapelin C (15), confirmed this assignment. These data are consistent with dysorone A [**1**] as 29-hydroxy-3,7-dioxo-apotirucalla-14,24-dien-21,23-oxide.

Compounds **2–5** had spectral data indicating a similar apotirucallane nucleus. All four compounds had fragment peaks at *m/z* 55 and *m/z* 125 in their hreims, together with ^{1}H-nmr and ^{13}C-nmr signals (Tables 2 and 3) confirming a side chain identical to that of **1**.

Compound **2** had an $[M]^+$ peak at *m/z* 470 ($C_{30}H_{46}O_4$), indicating two extra protons on the fused rings, and a ^{13}C-nmr signal at δ 219.8 showing the presence of the C-3 carbonyl when compared to **1** (Table 2). In addition, it had peaks at δ 5.47 (H-15), an upfield shift of 0.38 ppm, and δ 1.30 (Me-30), a shift of 0.07 ppm in the ^{1}H nmr (Table 3), consistent with the expected shielding of a 7α-hydroxy substituent in place of the 7-keto group when compared to **1** (15). The coupling of the H-7 at δ 3.94 (J = 3.0, 3.0 Hz) confirms a β position. The ^{1}H-nmr signals were also identical with those of the fused ring protons of the synthesized 7α-hydroxy-14-ene derivative of sapelin B (15); these establish dysorone B [**2**] as 7,29-dihydroxy-3-oxo-apotirucalla-14,24-dien-21,23-oxide.

Compound **3**, with an eims peak at *m/z* 470 $[M]^+$ formulated as $C_{30}H_{42}O_3$, differs from **1** by the presence of a pair of coupled doublets centered at δ 5.98 and 7.19

TABLE 3. ^{1}H-nmr Data for Compounds **2–5** in $CDCl_3$.

Proton[a]	Compound[b]			
	2	**3**	**4**	**5**
H-1		7.17 d (10)	7.14 d (10)	7.33 d (10) 6.50[c] d
H-2		5.91 d (10)	5.82 d (10)	6.05 d (10) 6.28[c] d
H-6α				2.48 dd (14, 3) 2.32[c] d
H-6β		2.89 t (14, 14)		2.96 t (14, 14) 2.59[c] t
H-7β	3.94 t (3, 3)		3.97 t (3, 3)	
H-15β	5.48 m (8)[d]	5.97 m (8)[d]	5.49 m (8)[d]	6.08 m (8)[d] 6.28 m[c]
Me-18α	0.95 s	0.98 s	1.02 s	0.98 s
Me-19β	1.04 s	1.10 s	1.09 s	1.48 s
H-20				2.35 m
H_a-21	4.09 t (8, 8)	4.06 t (8, 8)	4.09 t (8, 8)	4.07 t (8,8) 4.14[c] t
H_b-21	3.50 t (8, 8)	3.28 t (8, 8)	3.25 t (8, 8)	3.28 t (8, 8) 3.28[c] t
H-23	4.62 m	4.63 m	4.61 m	4.64 m 4.61[c] m
H-24	5.22 d (10)	5.23 d (10)	5.22 d (10)	5.23 d (10) 5.47[c] d
Me-26[e]	1.72 s	1.72 s	1.71 s	1.72 s
Me-27[e]	1.69 s	1.69 s	1.69 s	1.69 s
Me-28α	1.08 s	1.14 s	1.16 s	1.29 s
Me-29β		1.35 s	1.13 s	
CH_a-29β	3.94 d (12)			3.85 d (12) 3.49[c] d
CH_b-29β	3.50 d (12)			3.62 d (12) 3.40[c] d
Me-30β	1.30 s	1.38 s	1.09 s	1.48 s

[a]Protons with chemical shifts overlapping between δ 1.50 and 2.50 are not indicated.
[b]*J* values, in parentheses, in Hz.
[c]Chemical shift in C_6D_6 (400 MHz).
[d]$W_{1/2}$.
[e]Exchangeable assignments.

($J = 10.0$ Hz) in the ^{1}H-nmr spectrum (Tables 1 and 3), assigned to H-2 and H-1 respectively, since such coupling excludes the alternative Δ^2-1-ketone (3,15). Comparison of the ^{13}C nmr with that of **1** (Tables 1 and 2) showed a shift of only the C-3 carbonyl signal, confirming a keto-diene system, as well as the appearance of an Me peak (δ 27.0) in place of the CH_2OH (δ 64.9) at C-29. The similarity of the chemical shifts of the Me group assigned to the C-28 position with that of **1** (Tables 1–3) indicates an identical stereochemistry at C-4 for both compounds. This identifies dysorone C [**3**] as 3,7-dioxo-apotirucall-1,14,24-trien-21,23-oxide.

Compound **4** had an $[M]^+$ peak at *m/z* 452 ($C_{30}H_{44}O_3$) indicating two extra protons when compared to that of **3**. The signals in the ^{1}H nmr and ^{13}C nmr (Tables 2 and 3) are similar to those of **3** except for the C-6 and C-7 protons and carbons. The chemical shifts of H-6α, H-6β, and H-7β were similar to those of **2**. The fused ring proton signals were similar to those of sapelin C (15) and 7-deacetylazadirone (17). Thus **4** is a 7α-hydroxy derivative of dysorone C [**3**] and was assigned the name dysorone D.

Compound **5** (*m/z* 466 $[M]^+$, $C_{30}H_{42}O_4$) had the CH_2OH AB spin system located at C-29 as in **1** and **2** (Table 3) and formed a monoacetate **7** (*m/z* 508 $[M]^+$) but was otherwise similar to **3** (Table 2). It is a 29-hydroxy derivative of **3** named dysorone E. Compound **5** was the major and the only compound that exhibited moderate toxicity in vitro (ED_{50} 3.5 μg/ml) against the growth of KB human buccal carcinoma cells (7).

The similarity of the spectral data of compounds **1–5** and of the fused rings of those of **2** and **4** to known products (15, 17) indicates similar tirucallane stereochemistry at C-21 (16). The observed spatial interactions in the NOESY spectrum of **1** (Table 1) confirm the stereochemistry of the fused rings (except that of H-17).

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Melting points (uncorrected) were determined on a micro hot-stage apparatus. Optical rotations at 20° were taken on a Perkin-Elmer 241 polarimeter in $CHCl_3$. Uv spectra were recorded on a Shimidzu UV-161 uv-visible spectrophotometer; ir on a Nicolet 205 FT-IR spectrometer; eims (70 eV) on a Kratos MS 50; hreims and cims on a Kratos MS 80 spectrometer; and nmr on Bruker AC 200 (normal ^1H and ^{13}C spectra), AC 250 ($^1H/^{13}C$ HETCOR spectrum), and AC 400 ($^1H/^{13}C$ inverse detected long range HETCOR, $^1H/^1H$ COSY, and NOESY spectra) (12). All nmr spectra were recorded in $CDCl_3$ with TMS as internal standard unless otherwise stated. Vacuum liquid chromatography (vlc) and cc were performed using Si gel Merck H60, and tlc with Si gel 60 F_{254}. Visualization was by viewing under uv light and spraying with Dragendorff's reagent followed by 50% H_2SO_4.

PLANT MATERIAL.—The leaves of *D. roseum* were collected at Riviere Bleue forest reserve, New Caledonia, and authenticated by Dr. J.M. Veillon, ORSTOM, Nouméa. A voucher specimen was deposited at the Herbarium of ORSTOM, Nouméa, New Caledonia.

EXTRACTION AND ISOLATION.—The powdered, air-dried leaves (1.5 kg) were percolated with MeOH (5 liters for 24 h) twice at room temperature. The pooled MeOH extract was concentrated in vacuo to give 250 g of a greenish extract. This was dissolved in H_2O and extracted successively with C_7H_{16}, CH_2Cl_2, and EtOAc to afford 16, 70, and 14 g of extract, respectively. Cytotoxicity assay located 90% of the activity in the CH_2Cl_2 extract. Vlc of 35 g of the extract using CH_2Cl_2-MeOH (49:1) followed by CH_2Cl_2-MeOH (9:1) gave two bulked fractions. Cc of the polar fraction (20 g) eluted with CH_2Cl_2, followed by increasing concentration of MeOH in CH_2Cl_2 (fraction collected was 30 ml) gave fractions 1–68 (4.5 g), fractions 69–125 (4.7 g), fractions 126–161 (4.0 g), and fractions 162–250 (1.0 g). Repeated cc of fractions 69–125 and purification by preparative tlc [CH_2Cl_2-MeOH (19:1)] gave β-sitosterol (23 mg), **4** (250 mg), **3** (100 mg), **5** (700 mg), and **1** (200 mg). Similar purification of fractions 126–161 gave **5** (400 mg), **1** (300 mg), and **2** (20 mg). β-sitosterol was identified by comparing its spectral data (uv, ^1H nmr, ^{13}C nmr, ms) with an authentic sample.

Dysorone A [**1**].—White powder (MeOH): mp 75–76°; uv λ max (MeOH) 223.5 nm; $[\alpha]_D$ −59°; ir ν max (film) cm^{-1} 1377, 1463, 1709, 2360, 2951, 3462; ^1H nmr and ^{13}C nmr see Table 1; hreims (% rel. int.) *m/z* $[M]^+$ 468 (10), (468.3231, $C_{30}H_{44}O_4$ requires 468.3483), $[M-Me]^+$ 453 (5), $[M-H_2O]^+$ 450 (6), $[M-2\times Me]^+$ 438 (11), $[M-3\times Me]^+$ 423 (7), $[M-2\times Me-H_2O]^+$ 420 (7), $[M-2\times Me-CH_2OH]^+$ 407 (4), 386 (3), 368 (2), 356 (4), [M − side chain]$^+$ 343 (10), (343.2235, $C_{22}H_{31}O_3$ requires 343.2453), [M − side chain − CH_2OH]$^+$ 313 (12), 269 (3), 263 (4), 250 (2), 233 (5), 220 (4), 197 (7) ($C_{11}H_{18}O_3$), 175 (7) ($C_{12}H_{15}O$), 151 (3), 147 (4) ($C_{11}H_{15}$), 145 (4), ($C_{11}H_{13}$), 133 (8), ($C_{10}H_{13}$), 131 (8) ($C_{10}H_{11}$), 125 (64), (125.0942, $C_8H_{13}O$ requires 125.1830, side chain), 123 (100) ($C_8H_{11}O$), 109 (40), 107 (20), 105 (20), 95 (19), 83 (20), 69 (40), 55 (40).

Dysorone B [**2**].—White amorphous solid: uv λ max (MeOH) 219, 227 sh nm; $[\alpha]_D$ −53°; ir ν max (film) cm^{-1} 1333, 1449, 1707, 2368, 2926, 3385; ^1H nmr see Table 3; ^{13}C nmr see Table 2; eims *m/z* (% rel. int.) $[M]^+$ 470 (7) ($C_{30}H_{46}O_4$), 441 (9), $[M-3\times Me]^+$ 425 (7), 409 (3), 388 (3), 358 (5), [M − side chain]$^+$ 345 (6), 315 (10), 297 (5), 159 (10), 157 (6), 149 (3), 147 (8), 135 (5), 133 (7), 131 (6), 125 (70) (side chain), 123 (100), 109 (45), 107 (40), 105 (35), 95 (40), 83 (40), 69 (45), 55 (50).

Dysorone C [**3**].—White solid: mp 149–151°; uv λ max (MeOH) 226.5 nm; $[\alpha]_D$ −44°; iv ν max (film) cm^{-1} 1370, 1449, 1707, 2368, 2926, 3385; ^1H nmr see Table 3; ^{13}C nmr see Table 2; eims *m/z* (% rel. int.) $[M]^+$ 450 (30) ($C_{30}H_{42}O_3$), 435 (35), 432 (15), 419 (10), 395 (12), 368 (13), 351 (5), [M − side chain]$^+$ 325 (25), 310 (10), 257 (10), 245 (10), 232 (10), 177 (12), 165 (10), 147 (12), 145 (15), 125 (100) (side chain), 123 (90), 109 (60), 107 (40), 95 (30), 83 (50), 69 (60), 55 (65).

Dysorone D [**4**].—Amorphous gum: uv λ max (MeOH) 214.5, 225 sh; $[\alpha]_D$ −34°; ir ν max (film) cm^{-1} 1333, 1449, 1707, 2368, 2926, 3385; ^1H nmr see Table 3; ^{13}C nmr see Table 2; eims *m/z* (% rel.

int.) $[M]^+$ 452 (24) ($C_{30}H_{44}O_3$), 443 (7), 439 (15), 437 (15), 421 (7), 400 (7), 399 (29), 381 (5), 370 (7), 329 (20), 328 (15), 327 (30), 311 (5), 309 (5), 159 (5), 143 (40), 125 (98), 123 (100), 109 (30), 107 (30), 95 ([25), 93 (25), 85 (10), 69 (50), 67 (40), 55 (70).

Dysorone E [**5**].—White amorphous solid: mp 98–100°; uv λ max (MeOH) 226.5; $[\alpha]_D$ −58.3°; ir ν max (film) cm^{-1} 1376, 1458, 1669, 1709, 2364, 2930, 3450; ^1H nmr see Table 3; ^{13}C nmr see Table 2; hreims *m/z* (% rel. int.) $[M]^+$ 466 (9) (466.3095, $C_{30}H_{42}O_4$ requires 466.3323), 451 (7) ($C_{29}H_{39}O_4$), 448 (6), 436 (8), 421 (8), 405 (4), 384 (6), 366 (4), 354 (8), 342 (4), $[M-$ side chain$]^+$ 341 (9) (341.2100, $C_{22}H_{30}O_3$ requires 341.2293), 311 (9) ($C_{21}H_{27}O_2$), 175 (7) ($C_{12}H_{15}O$), 173 (6), 159 (6), 157 (6), 151 (4), 147 (7) ($C_{11}H_{15}$), 135 (19) ($C_9H_{11}O$), 133 (9) ($C_{10}H_{13}$), 131 (10), ($C_{10}H_{11}$), 125 (94) ($C_8H_{13}O$, side chain), 123 (100), 109 (40), 93 (40), 83 (50), 69 (70), 55 (50).

PREPARATION OF ACETYL DERIVATIVES.—Compounds **1** and **5** (20 mg each) were acetylated by the addition of 2 ml Ac_2O-pyridine (1:1) for 24 h. Usual workup gave the respective monoacetates **6** (10 mg) and **7** (15 mg).

Dysorone A acetate [**6**].—Eims (% rel. int.) $[M]^+$ 510 (7), 468 (3), 455 (11), 442 (11), 400 (12), $[M-$ side chain$]^+$ 385 (12), 313 (2), 125 (36) (side chain), 123 (100), 109 (25), 55 (20); ^1H nmr δ 1.29 (3H, s, Me-28α), 2.06 (3H, s, Ac), 4.14 (2H, m, CH_2O-29β).

Dysorone E acetate [**7**].—Eims (% rel. int.) $[M]^+$ 508 (35), 490 (30), 477 (15), 383 (12), 339 (8), 303 (15), 287 (10), 175 (8), 125 (100), 55 (30); ^1H nmr δ 1.32 (3H, s, Me-28α), 2.05 (3H, s, Ac), 4.20 (2H, m, CH_2O-29β).

ACKNOWLEDGMENTS

S.A.A. acknowledges fellowship support from the OAU/STRC, Lagos, Nigeria, and CNRS, France.

LITERATURE CITED

1. M. Nishizawa, A. Inoue, S. Sastrapradja, and Y. Hayashi, *Phytochemistry*, **22**, 2083 (1983).
2. M.K. Jogia, R.J. Anderson, E.K. Mantus, and J. Clardy, *Tetrahedron Lett.*, **30**, 4919 (1989).
3. S. Singh, H.S. Garg, and N.M. Khanna, *Phytochemistry*, **15**, 2001 (1976).
4. R.G. Naik, S.L. Kattige, S.V. Bhat, B. Alreja, N.J. de Souza, and R.H. Rupp, *Tetrahedron*, **44**, 20881 (1988).
5. A.J. Aladesanmi and O.R. Ilesanmi, *J. Nat. Prod.*, **50**, 1041 (1987).
6. W. Aalbersberg and Y. Singh, *Phytochemistry*, **30**, 921 (1991).
7. G.M. Williams, V.C. Dunkel, and V.A. Ray, Eds., "Annals of New York Academy of Sciences, Vol. 407, Cellular Systems for Toxicity Testing," New York Academy of Sciences, New York, 1983.
8. J.D. Connolly and R.A. Hill, *Nat. Prod. Rep.*, **6**, 475 (1989).
9. R.S. Bhakuni, Y.N. Shukla, and R.S. Thakur, *Phytochemistry*, **26**, 2607 (1987).
10. T. Itoh, T. Tamura, and T. Matsumoto, *Lipids*, **11**, 434 (1976).
11. T.A. Olugbade, *Phytochemistry*, **30**, 698 (1991).
12. A.F. Barrero, E.A. Manzaneda, R.S. Arseniyadis, and E. Guittet, *Tetrahedron*, **46**, 8161 (1990).
13. J.D. Connolly and R. McCrindle, *J. Chem. Soc., Chem. Commun.*, 1193 (1967).
14. W.R. Chan, D.R. Taylor, and T.H. Yee, *J. Chem. Soc. C*, 2662 (1971).
15. D.H. Williams and N.S. Bhacca, *Tetrahedron*, **21**, 1641 (1965).
16. G.P. Cotterell, T.G. Halsall, and M.J. Wriglesworth, *J. Chem. Soc. C*, 1503 (1970).
17. J.F. Ayafor, B.L. Sondengam, J.D. Connolly, D.S. Rycroft, and J.I. Okogun, *J. Chem. Soc., Perkin Trans. 1*, 1750 (1981).

Received 15 April 1991