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Limonoids from *Carapa grandiflora* (Meliaceae)

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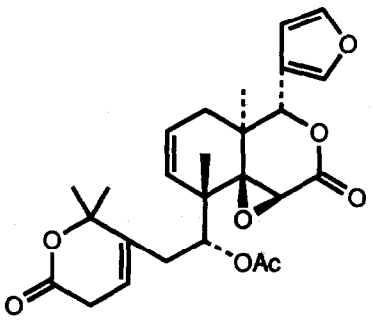
Abstract: Eight limonoids, carapolides C **1**, D **3**, E **4**, F **5**, G **6**, H **7** and I **8** and evodoulone **13** have been isolated from the extracts of the seeds of *Carapa grandiflora* (Meliaceae). Compounds **2**, **3**, and **4** are new C-9, C-10 cleaved tetranortriterpenoids while **5** and **6** are novel tetranortriterpenoid spirolactones. Finally, carapolides H **7** and I **8** are new ring A cleaved derivatives with an intact ring D. All their structures were determined from spectroscopic data and chemical correlations.

The seeds of *Carapa grandiflora* sprague (Meliaceae), popularly known in Cameroon as "engang", are used in traditional medicine as a febrifuge and for the treatment of arthritis, general fatigue and skin diseases[1]. As part of our continuing search for plant filaricides related to carapolide A **1**, which had shown strong *in vitro* activity against *Onchocerca volvulus* microfilariae[2,3], we have investigated the extract of the seeds of *C. grandiflora* and obtained eight tetranortriterpenoids, some of which are related to carapolide A **1**, but not compound **1** itself. A preliminary communication[4] reported the structural elucidation of three of them, carapolide D **3**, E **4**, and F **5**. The present paper reports the isolation and structure determination of four additional limonoids from the seeds and presents full experimental details concerning **3**-**5** and **13**.

An acetone extract of the defatted seeds was subjected to repeated column chromatography, affording compounds **2**, **3**, **4**, **5**, **6**, **7**, **8**, and **13** in yields of 0.002, 0.001, 0.23, 0.01, 0.02, 0.018, 0.002, and 0.3%, respectively. Evodoulone **13**, previously obtained from *C. procera*[5], was characterised by direct comparison (mmp, $[\alpha]_D$, IR and NMR) with an authentic sample.

The structures of carapolides C **2**[6], D **3**, and E **4** have already been reported[4]. They constitute further members of the rare group of tetranortriterpenoids with a C-9, C-10 cleaved carbon skeleton. Attempts were made to correlate chemically these three compounds. Thus treatment of carapolide E **4** with p-toluene sulfonic acid yielded carapolide C **2**, identical in all respects with the natural sample. Efforts to convert carapolide E **4** into carapolide D **3** through dehydration with thionyl chloride in dry pyridine at 0°C were, however, unsuccessful and led to the formation of the chloride **9**. The IR spectrum of **9** lacked a hydroxyl absorption band and, though its ^{1}H NMR spectrum was very similar to that of **4**, the hydroxyl proton resonance at δ 2.41 ppm in the spectrum of **4** was absent. As expected, reaction of carapolide E **4** with acidic methanol yielded the methyl acetal **10**. The ^{1}H NMR spectral data of the acetal (experimental section) were consistent with structure **10**. Paucity of material precluded attempts to transform **3** into **4** by hydration.



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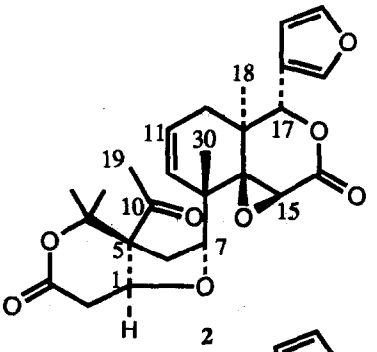

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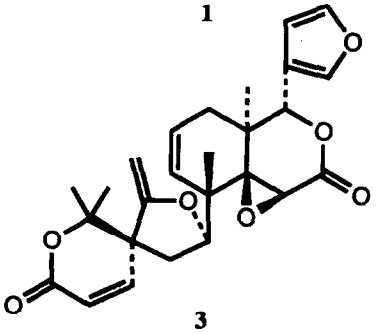

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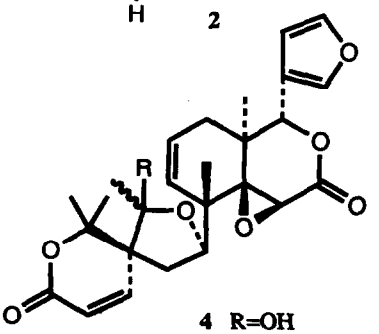
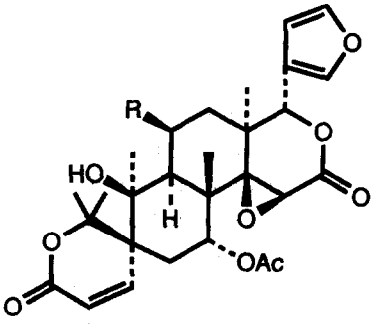


4 R=OH
9 R=Cl
10 R=OMe



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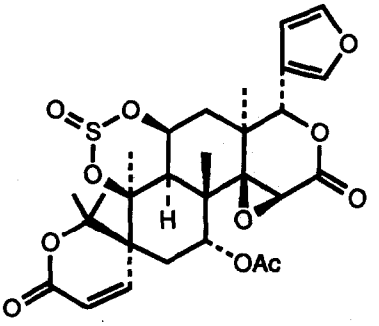
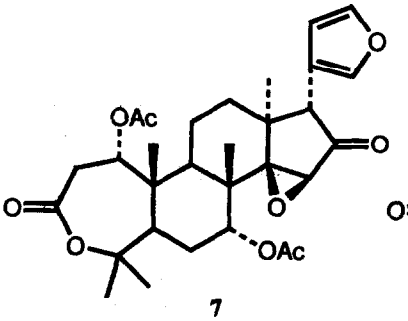
6 R=H



11
12



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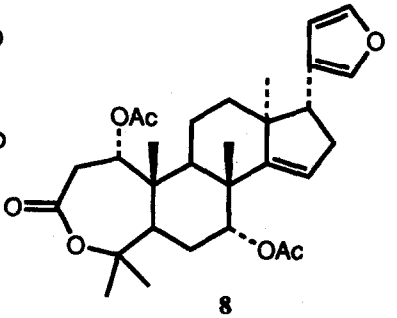


8

For carapolide F **5**, EI-LRMS and elemental analysis established the molecular formula $C_{28}H_{34}O_{10}$. Its spectroscopic properties clearly indicate that it has an intact ring B and are consistent with the spirostructure **5**. Thus it has in addition to a β-substituted furan and a ring D epoxylactone, resonances (^{1}H and ^{13}C NMR spectra Tables 1 and 3) for five tertiary methyl groups, a ring A αβ-unsaturated δ-lactone and a secondary acetate {δ_H 2.01 (3H, s), 4.55 (dd, J 2.3, 3.7 Hz, H-7); δ_C 170.2 (s) and 74.3 (d, C-7)}. H-7 is coupled to an isolated methylene group 2H-6 {δ_H 2.63 (dd, J 15.2 and 2.3 Hz) and 2.13 (dd, J 15.2 and 3.7 Hz)} showing that C-5 is fully substituted. There are two additional oxygenated carbons, δ_C 78.6 (s, C-10) and δ_C 65.4 (d, C-11), both bearing hydroxyl groups. H-11 appears as a multiplet (δ_H 4.85) and is coupled to H-9 {δ_H 2.50 (d, J 5.0 Hz)} and to the C-12 methylene group {δ_H 1.79 (dd, J 13.5 and 9.4 Hz, H-12α) and 2.21 (dd, J 13.5 and 7.4 Hz, H-12β)}. The coupling data suggest that the 11-hydroxyl group is pseudoequatorial (β) with ring C adopting a boat conformation and the C-7 acetoxyl group is axial in a chair ring B. The relative stereochemistry of the methyl group at C-10 was defined as equatorial by strong nOe interactions between Me-19 and H-1 (4.6%), Me-19 and H-11 (7.3%), and Me-19 and H-9 (1.8%). All other nOe enhancements, particularly those observed between H-9 and H-1 (9.6%), H-9 and H-11 (5.2%) and H-9 and Me-18 (9.4%) are fully consistent with structure **5**.

Treatment of carapolide F **5** with $SOCl_2$ in pyridine afforded two diastereoisomeric cyclic sulphites **11** and **12**, differing in the configuration at sulphur, which were separated by preparative TLC. The ^{1}H NMR spectra of these derivatives (Experimental) are similar in chemical shifts and coupling constants to that of **5**, apart from showing downfield shifts of H-11 and the C-10 methyl. The major differences between the spectra of the sulphites **11** and **12** involve the shifts of H-11 (δ_H 5.49 and 5.78), H-9 (2.46 and 2.59), and the C-10 methyl group (δ_H 1.99 and 2.20). The formation of these cyclic esters supports the assigned structure **5** for carapolide F.

Carapolide G **6**, $C_{28}H_{34}O_9$ by elemental analysis, has IR bands at 3500, 1760, 1740, 1715, and 1700 cm^{-1}, indicative of hydroxyl and carbonyl functionality. All the spectroscopic data are appropriate for an intact ring B skeleton and are consistent with the spirolactone structure **6**. The ^{1}H NMR spectrum of **6** is almost superimposable on that of carapolide F **5**, except for the appearance in the up-field region of the spectrum of a multiplet of four protons at δ 1.50-1.95 and the absence of the oxymethine proton signal at δ 4.80. These data suggest that the C-11 hydroxyl of **5** is absent in carapolide G **6**. This was confirmed by the ^{13}C NMR spectrum of **6**. Thus the methine resonance at δ 65.7 (C-11) in the ^{13}C spectrum of **5** is replaced by a methylene signal at δ 14.5 in that of carapolide G **6**. The ^{1}H and ^{13}C NMR assignments, made using ^{1}H-^{1}H COSY and ^{1}H-^{13}C correlations, are fully consistent with structure **6**. The α (equatorial) orientation of the C-10 methyl group (Me-19) was established by nOe experiments, key nOe interactions being observed between Me-19 and H-1 and Me-19 and H-9. All other nOe enhancements, including those between Me-18 and H-9, H-9 and H-1, and H-9 and Me-18 support the relative stereochemistry as in **6**. The stereochemistry of carapolide F **5** and G **6** at C-10 is identical with that of pedonin **14** whose structure was established by X-ray crystallography[7].

The tetranortriterpenoid nature of carapolide H **7** and its close relationship to 7α-acetoxydihydronomilin **15**[8] is apparent from its spectroscopic data. It analysed for $C_{30}H_{38}O_9$ and showed three strong carbonyl absorptions, ν_{max} 1740, 1720, and 1700 cm^{-1} in its IR spectrum. Its ^{1}H NMR spectrum (Table 4) revealed resonances for five tertiary methyl groups, two acetoxy groups, and a secondary epoxide proton (δ_H 3.39, H-15). In addition to the characteristic β-substituted furan signals, two oxymethine resonances are clearly discernable at δ 4.95 (d, J 7.0 Hz, H-1) and 4.65 (bt, J 3.0 Hz, H-7), respectively. A proton resonating as

Table 1. 50.32 MHz ^{13}C NMR Data for Compounds 2-5.

Carbon #	2[a]	3[a]	4[a]	5[b]
1	75.8d	148.7d	149.7d	154.4d
2	35.7t	118.3d	120.5d	117.0d
3	169.7s	163.1s	163.3s	165.2s
4	81.7s	84.0s	85.1s	90.8s
5	66.8s	52.1s	55.4s	47.4s
6	33.2t	35.7t	36.6t	31.3t
7	81.5d	81.2d	80.3d	74.4d
8	42.0s	41.6s	42.2s	41.0s
9	131.3d	131.0d	131.7d	39.9s
10	206.3s	159.8s	105.2s	78.6s
11	122.7d	123.0d	122.4d	65.4d
12	32.2t	32.1t	32.1t	38.2t
13	38.1s	38.1s	38.1s	38.4s
14	65.2s	66.7s	67.7s	70.1s
15	52.5d	52.5d	52.7d	57.1d
16	167.0s	166.9s	167.3s	168.8s
17	77.8d	77.8d	77.8d	78.8d
20	120.1s	120.0s	120.3s	120.6s
21	141.0d	141.0d	141.0d	141.8d
22	109.9d	109.9d	109.9d	110.2d
23	143.2d	143.2d	143.2d	143.7d
28	27.0*q	25.0*q	26.7*q	27.6q
29	26.5*q	23.3*q	24.9*q	27.6q
30	16.7q	16.8q	18.2q	19.8
18	16.1q	16.1q	16.1q	16.3
19	28.6q	86.3t	24.9q	26.1q
OAc	-	-	-	170.2s
	-	-	-	21.1q
OAc	-	-	-	-

*Assignments are interchangeable
[a] $CDCl_3$, [b] $CDCl_3 + CD_3OD$

Table 2. 50.32 MHz ^{13}C NMR Data for Compounds 6-8.

Carbon #	6[a]	7[a]	8[b]	8[c]
1	153.7d	72.0d	70.9d	71d
2	116.4d	35.6t	34.9t	34.9t
3	164.1s	172.6s	170.3s	170.2s
4	89.7s	87.2s	85.5s	85.5s
5	48.1s	45.4d	44.1d	44.1d
6	30.4t	27.5t	26.3t	26.4t
7	72.8d	74.8d	74.2d	74.3d
8	40.8s	43.5s	41.8s	41.8s
9	37.4d	37.9d	36.0d	36.0d
10	76.0s	43.4s	44.2s	44.3s
11	14.5t	16.7t	16.3t	16.3t
12	25.1t	30.2t	32.8t	32.9t
13	38.5s	45.3s	47.0s	47.1s
14	67.7s	73.2s	158.6s	158.1s
15	56.8d	57.7d	119.1d	119.1d
16	168.0s	209.9s	34.3t	34.4t
17	78.1d	51.8d	51.2d	51.3d
20	120.0s	117.6s	124.4s	124.5s
21	140.9d	142.4d	139.6d	139.6d
22	109.8d	111.8d	110.9d	111.0d
23	143.0d	143.4d	142.6d	142.6d
C-Me	27.1q	34.7q	34.4q	34.4q
C-Me	26.7q	25.4q	27.2q	27.2q
C-Me	25.3q	23.4q	23.6q	23.6q
C-Me	17.5q	19.7q	19.8q	19.8q
C-Me	16.4q	16.3q	15.2q	15.2q
OAc	169.5s	171.1s	170.0s	170.0s
	20.9q	21.5*q	21.1*q	21.2*q
OAc	-	170.7s	169.8s	169.7s
	-	21.0*q	20.7*q	20.7*q

[a] $CDCl_3 + CD_3OD$, [b] $CDCl_3$, [c] Values from ref. 10; * Assignments are interchangeable

Table 3. ^{1}H NMR Data for Compounds 2-5

Carbons	2*a	3[a]	4[a]	5[b]
1	4.83 (dd, 7.3, 2.2)	6.58 (d, 9.7)	6.78 (d, 10.0)	6.78 (d, 10.0)
2	3.03 (dd, 18.3, 7.3) 2.68 (dd, 18.3, 2.2)	5.98 (d, 9.7)	6.11 (d, 10.0)	5.91 (d, 10.0)
6	2.25 (d, 8.2)	1.85 (d, 8.0)	1.80 (d, 8.0)	2.13 (dd, 15.2, 3.7) 2.63 (dd, 15.2, 2.3)
7	4.17 (t, 8.2)	4.34 (dd, 7.6, 8.7)	4.13 (dd, 8.0, 8.7)	4.55 (dd, 2.2, 3.7)
9	5.52 (m)	5.84 (dd, 10.3, 2.5)	5.85 (m)	2.15 (d, 5.0)
11	5.57 (m)	5.76 (m)	5.77 (m)	4.85 (m)
12	1.80 (dd, 18.1, 2.2) 2.15 (d, 18.1)	-	-	1.79 (dd, 13.5, 9.4) 2.21 (dd, 13.5, 7.4)
15	3.72 (s)	3.88 (s)	3.77 (s)	3.50 (s)
17	5.57 (s)	5.59 (s)	5.60 (s)	5.62 (s)
19	2.30 (s)	4.17 (d, 2.0) 4.49 (d, 2.0)	-	-
21	7.40 (m)	7.40 (m)	7.40 (m)	7.43 (m)
22	6.35 (m)	6.35 (m)	6.35 (m)	6.35 (m)
23	7.40 (m)	7.40 (m)	7.40 (m)	7.40 (m)
OAc	-			2.01
OH	-		2.41 (s)	
C-Me	0.85		0.81	1.16
C-Me	1.00	0.88	1.08	1.55
C-Me	1.40	1.11	1.50	1.59
C-Me	1.55	1.48	1.52	1.64
C-Me		1.50	1.63	1.65

*500 MHz; [a] $CDCl_3$; [b] $CDCl_3$ + CD_3OD
Multiplicities and values of coupling constants (Hz) are given in parentheses.

Table 4. ^{1}H NMR Data for Compounds 6-8.

Carbons	6[b]	7[b]	8[a]	8[c]
1	6.85 (d, 10.0)	4.91 (dd, 6.5,1.5)	4.80 (brt)	4.82 (d, 7.0)
2	5.80 (d, 10.0)	3.05 (d, 7.0) 2.95 (dd, 7.0, 2.0)	3.10 (m)	3.12 (d, 15.0) 3.17 (dd, 15.0, 7.0)
5		2.46(dd,13.2,2.6)	2.50 (m)	2.52 (m)
6	2.51 (dd, 15.0, 4.0) 2.05 (dd, 15.0, 3.0)	1.80-2.15 (m)	1.94 (m)	1.95 (m)
7	4.45 (t, 3.0)	4.65 (t, 3.0)	5.17 (t, 3.0)	5.19 (brs)
9	2.46 (t.9.5)	2.92 (dd, 11.7,3.2)	2.53 (m)	2.56 (m)
11	1.50-1.90 (m)	1.90-2.15 (m)	1.40-1.60 (m)	1.42 (m) 1.57 (m)
12	1.50-1.90 (m)	1.55-1.75 (m)	1.40-1.60 (m)	1.57 (m)
15	3.38 (s)	3.39 (s)	5.34 (dd, 3.0, 2.0)	5.36 (brs)
17	5.52 (bs)	3.86 (s)	2.77 (t, 7.8)	2.73 (t, 7.5)
21	7.32 (bs)	7.50 (t, 2.0)	7.20 (m)	7.23 (m)
22	6.23 (bs)	6.22 (dd, 2.0, 1.0)	6.20 (dd, 2.0, 1.0)	6.26 (s)
23	7.32 (m)	7.40 (m)	7.35 (t, 2.0)	7.37 (brs)
OAc	1.93 (s)	2.03 (s)	1.98 (s)	2.01(s)
OAc		2.05 (s)	2.06 (s)	2.11 (s)
C-Me	1.10 (s)	0.98 (s)	1.15 (s)	1.17 (s)
C-Me	1.23 (s)	1.14 (s)	1.19 (s)	1.21(s)
C-Me	1.26 (s)	1.16 (s)	1.38 (s)	1.40 (s)
C-Me	1.50 (s)	1.36 (s)	1.49 (s)	1.51 (s)
C-Me	1.55 (s)	1.47 (s)	0.72 (s)	0.75 (s)

[a] $CDCl_3$; [b] $CDCl_3$ + CD_3OD
Multiplicities and values of coupling constants (Hz) are given in parentheses
[c] values from ref. 10

a singlet at δ_H 3.86 was assigned to H-17, in view of its nOe to the furan H-22. The up-field nature of the chemical shift of this proton in **7** relative to that (δ_H 5.60) observed for the same proton in 7α-acetoxy dihydronomilin[8] suggested that carapolide H **7** has an intact ring D. Structure **7** was thus attributed to carapolide H. Its ^{13}C and ^{1}H NMR spectral data were assigned using ^{1}H-^{1}H COSY and ^{1}H-^{13}C correlation experiments (Tables 2 and 4). NOe experiments support the relative stereochemistry of **7** as shown. In particular, nOes from Me-19 to H-1β (3.0%) and from Me-30 to H-7β (6.0%) establish the configurations of the acetate groups.

Carapolide I **8**, $C_{30}H_{40}O_7$, ν_{max} 1730, 1725, and 875 cm^{-1}, has the same carbon skeleton as **7** but lacks the 14, 15-epoxide and the 16-keto group. All its spectroscopic data including ^{1}H and ^{13}C NMR (Tables 2 and 4) are consistent with structure **8**. {Compound **8** was presented at the 4th NAPRECA International Symposium on Natural Product Development held in Addis Ababa, Ethiopia, in September 1991[9]. However, at the time of submission of this manuscript, we came across a reference in which the same compound has been communicated from a different source as kihadalactone A[10]}.

A possible biogenetic pathway leading to the formation of the carapolides of *Carapa grandiflora* can now be proposed (scheme 1). The spirolactone carapolide G **6** appears to be the biogenetic progenitor. Hydroxylation of **6** yields carapolide F **5**. A retro-Prins reaction of **5** results in cleavage of the C-9, C-10, bond with formation of the ring C double bond and a methyl ketone as in **16**. Subsequent hydrolysis of the C-7 acetoxyl group followed by internal hemiacetal formation involving the methyl ketone and the C-7 hydroxyl group then leads directly to carapolide E **4** and indirectly to D **3** by dehydration. Carapolide C **2** can arise from the 7-deacetyl derivative of **16**, by addition of the C-7 hydroxyl group to the ring A unsaturated lactone to form the cyclic ether.

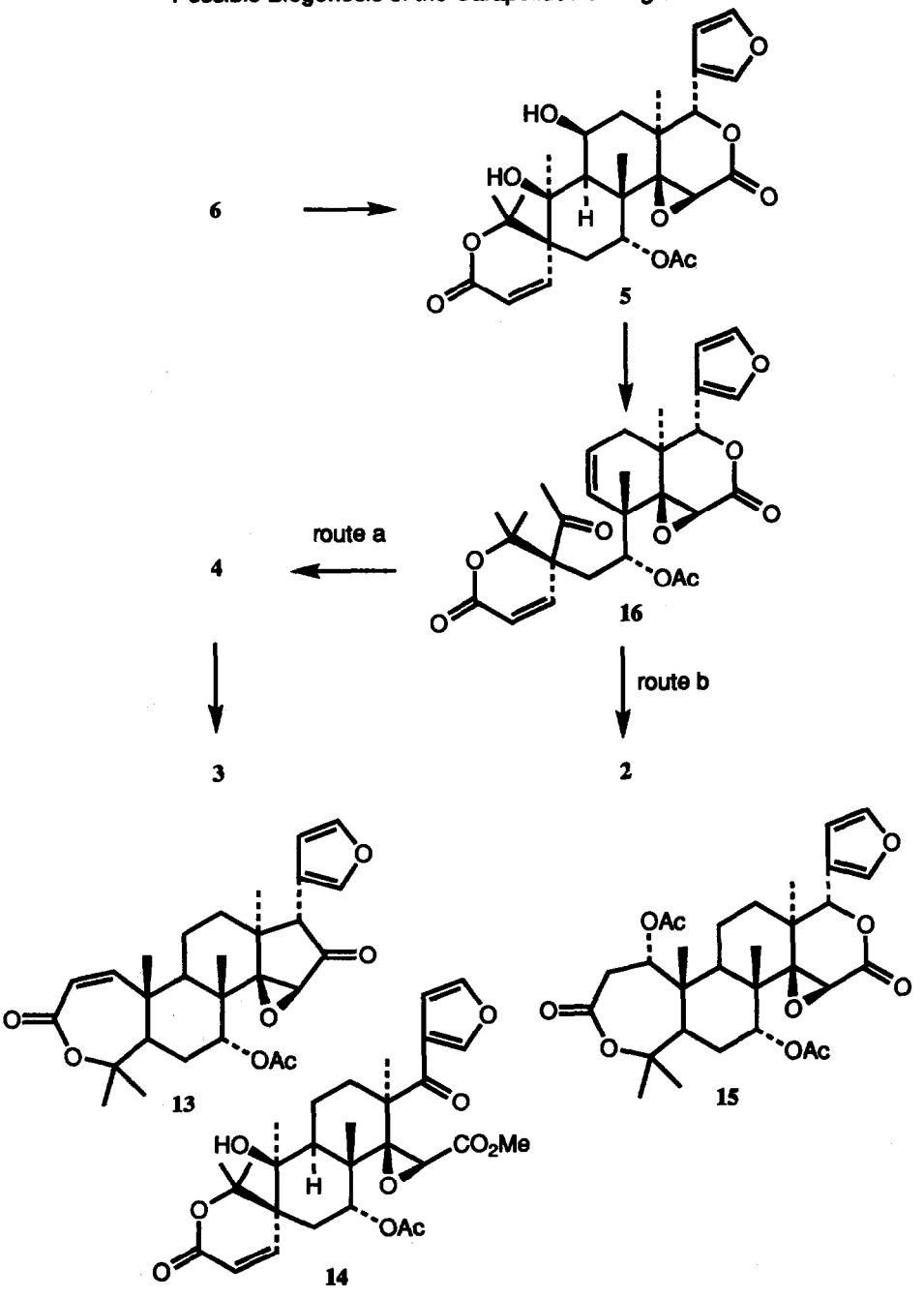
EXPERIMENTAL

Melting points were measured on a Kofler hot stage apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer 727B spectrophotometer. NMR spectra in $CDCl_3$ solutions were run at 25°C in pulsed Fourier transform mode either on a Varian XL-100 spectrometer (25.16 MHz for ^{13}C, shifts relative to Me_4Si at δ 0.00) or on a Bruker WP 200SY spectrometer (200.13 MHz for ^{1}H, shifts relative to $CHCl_3$ at δ 7.25; 50.32 MHz for ^{13}C, shifts relative to $CDCl_3$ at δ 77.00). Mass spectra were determined using an MS 902S instrument. Kieselgel 60 (0.063-0.200 mm, Merck) was used for column chromatography, and (0.0400-0.063 mm, Merck) for Medium Pressure liquid chromatography (Baeckström Separo AB Apparatus). TLC was run on Merck GF_{254} silica gel precoated plates (0.2 mm thickness).

Isolation of Limonoids from Carapa grandiflora

The powdered sun-dried seeds (3 kg), obtained from the fruits of *C. grandiflora* collected in August 1983 from Yaoundé, Cameroon, were extracted successively with n-hexane (10 l) and acetone (10 l) in a Soxhlet apparatus. The hexane extract was concentrated *in vacuo* to leave an oil (1100 g) while evaporation of the solvent under reduced pressure from the acetone extract yielded a brown gum (330 g). A sample of the acetone extract (110 g) was dissolved in $CHCl_3$ (60 ml) and chromatographed on a column of Si gel (1.5 kg). Elution started with *n*-hexane and continued stepwise through n-hexane/EtOAc mixtures, EtOAc, and EtOAc/MeOH mixtures. The eluate was collected in 250 ml fractions which were combined using TLC comparisons in appropriate solvent systems. From this chromatographic separation evodoulone[5] **13** (1.8 g),

Scheme 1
Possible Biogenesis of the Carapolides of *C. grandifolia*



carapolide D **3** (120 mg), carapolide I **8** (600 mg), carapolide E **4** (1.5 g), a mixture of 2.5 g of carapolides - C **3**, E **4**, and G **6**, and a mixture of 2.7 g of carapolides F **5** and H **7** were obtained. Further purification of the various mixtures by MPLC using the recently developed Baeckström AB Separo Columns (15 and 25 mm diameter) with a continuous gradient hexane-EtOAc-MeOH afforded pure carapolides C **2** (85 mg), F **5** (300 mg), G **6** (480 mg), and H **7** (380 mg). Evodoulone **13** was identified by direct comparison with an authentic specimen previously available in our laboratory from *Carapa procera* while the new limonoids were characterised as follows.

Carapolide C **2**. Colourless glass; $[\alpha]_D^{25}$ + 102° (c, in $CHCl_3$); IR (KBr) ν_{max} 1752, 1710, 1600, 878 cm^{-1}: EI-HRMS *m/z* 470.1948, $C_{26}H_{30}O_8$ requires *m/z* 470.1931. ^1H and ^{13}C NMR see Tables 1 and 3.

Carapolide D **3**. Prisms from EtOAc/ hexane, mp 234-236°; $[\alpha]_D^{20}$ -362° (c = 1.8, acetone); EI-HRMS: *m/z* 452.1844, $C_{26}H_{28}O_7$ requires 452.1833; IR (KBr) ν_{max} 3150, 3070, 1750, 1710, 1650, 1630, 1462, 1400, 1380, 1300, 1260, 1220, 1160, 1120, 1100, 1060, 1025, 990, 940, 905, 880, 810 cm^{-1}. ^1H and ^{13}C NMR see Tables 1 and 3.

Carapolide E **4**. Mp 178-180° (*ex* EtOAc/ hexane); $[\alpha]_D^{20}$ + 106° (c, 4.3 in acetone): IR (KBr) ν_{max} 3370, 3140, 3080, 1735, 1720, 1450, 1380, 1280, 1165, 1135, 1080, 1040, 980, 878, 825, 810, 740 cm^{-1}. EI-HRMS: *m/z* 470.1950, $C_{26}H_{30}O_8$ requires *m/z* 470.1939. Found: C, 66.29; H, 6.52. $C_{26}H_{30}O_8$ requires: C, 66.37; H, 6.43. ^1H and ^{13}C NMR see Tables 1 and 3.

Conversion of Carapolide E **4** *to Carapolide C* **2**

Carapolide E **4** (150 mg) and *p*-toluene sulfonic acid (500 mg) were dissolved in dry benzene and the solution refluxed in a Dean and Stark apparatus for 15 min. The reaction mixture was then cooled, washed with aqueous Na_2CO_3 solution (5%), dried with anhydrous Na_2SO_4 and evaporated *in vacuo*. Purification by MPLC gave *carapolide C* **2** (132 mg) identical in all respects with the natural sample.

Attempted conversion of Carapolide E **4** *into Carapolide D* **3**

Carapolide E chloride **9**. To a solution of *carapolide E* **4** (30 mg) in dry pyridine (2 ml) at 0°C was added $SOCl_2$ (8 drops). After 2h, the reaction mixture was warmed up to r.t., diluted with water (50 ml) and extracted with $CHCl_3$. Preparative TLC of the product afforded the *chloride* **9** (25 mg) as a colourless glass; IR (KBr) ν_{max} 3140, 1750, 1730, 880 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) 6.8 (d, 10.0 Hz, H-1), 5.95 (d, J 10.0 Hz, H-2), 1.90 (d, J 9.0 Hz, 2H-6), 4.10 (t, J 9.0 Hz, H-7), 5.85 (dd, J 10.3, 2.5 Hz, H-9), 5.80 (ddd, J 10.3, 6.1, 1.7 Hz, H-11), 3.76 (s, H-15), 5.65 (s, H-17), 0.81, 1.10, 1.48 (6H), 1.50 (Me), 7.40 (bs, 2Hα-furan), 6.37 (bs Hβ-furan).

Methanolic HCl treatment of Carapolide E **4**

Methyl acetal **10**. Carapolide E **4** (50 mg) was dissolved in a mixture of CH_3OH and HCl (8 M) (15 ml) and the solution refluxed for 1h. The reaction mixture was diluted with water and extracted with $CHCl_3$. Column chromatography afforded a single non-crystalline product, the *methyl acetal* **10** (43 mg). IR ($CHCl_3$) ν_{max} 1738, 1720, 1600, 878 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) 6.75 (d, J 10 Hz, H-1), 6.08 (d, J 10 Hz, H-2),

4.13 (dd, J 11.0, 6.0 Hz, H-7), 5.85 (dd, J 10.3, 2.5 Hz, H-9), 5.77 (m, H-11), 3.69 (s, H-15), 5.60 (s, H-17), 3.50 (s, OMe), 0.75, 1.12, 1.40, 1.43, 1.58 (Me), 7.35 (m, H-21), 6.35 (m, H-22), 7.35 (m, H-23).

Carapolide F **5**. Mp 252-255° (*ex* $CHCl_3$/MeOH); $[\alpha]_D^{20}$ + 105° (c, 3.0 in MeOH) and +128° (c, 0.4 in $CHCl_3$); IR (KBr) ν_{max} 3490, 3400, 3140, 1760, 1750, 1700, 1650, 1610, 1230, 1070, 1010, 875, 830, 800 cm^{-1}. MS *m/z* (%) 530 (M^+, 10), 514 (5), 470 (20), 452 (30), 412 (28), 396 (28), 376 (100), 365 (80), 343 (60), 329 (75), 303 (50). Found: C, 63.29; H, 6.55. $C_{28}H_{34}O_{10}$ requires C, 63.38; H, 6.46. ^1H and ^{13}C NMR see Tables 1 and 2.

Carapolide F Sulphites **11** *and* **12**. To a solution of carapolide F **5** (10 mg) in dry pyridine (5 drops) was added redistilled $SOCl_2$ (5 drops). After 15 min, the reaction mixture was warmed to r.t., diluted with water, and extracted with $CHCl_3$. Preparative TLC of the crude product afforded two isomeric sulphites **11** (4 mg) and **12** (5 mg). **11** Brown gum: IR (KBr) ν_{max} 3142, 1750, 1720, 875 cm^{-1}. ^1H NMR (200 MHz, $CHCl_3$) 6.71 (d, J 10.0 Hz, H-1), 5.89 (d, J 10.0 Hz, H-2), 2.13 (dd, J 15.5, 3.9 Hα-6), 2.59 (dd, J 15.5, 2.0 Hz, H-6β), 4.58 (dd, J 3.9, 2.0 Hz, H-7), 2.59 (d, J 3.4 Hz, H-9), 5.78 (m, H-11), 1.89 (dd, J 14.6, 5.0 Hz, H-12α), 2.38 (dd, J 14.6, 10.3 Hz, H-12β), 3.59 (s, H-15), 5.72 (s, H-17), 7.45 (m, H-21), 6.32 (m, H-22), 7.45 (m, H-23), 1.22, 1.49, 1.64, 1.67, 2.20 (Me), 2.05 (s, OAc).

The second sulphite **12** was also obtained as a brown gum, IR (KBr) ν_{max} 3140, 1752, 1733, 1720, 875 cm^{-1}. ^1H NMR (200 MHz, $CHCl_3$) 6.73 (d, J 10.0 Hz, H-1), 5.93 (d, J 10 Hz, H-2), 2.21 (dd, J 15.5, 4.0 Hz, H-6α), 2.69 (dd, J 15.5, 2.2, H-6β), 4.58 (dd, J 4.0, 2.2 Hz, H-7), 2.46 (d, J 3.4 Hz, H-9), 5.49 (m, H-11), 1.90 (dd, J 14.4, 5.0 Hz, H-12α), 2.38 (dd, J 14.4, 10.2 Hz, H-12β), 3.50 (s, H-15), 5.70 (s, H-17), 7.45 (m, H-21), 6.32 (m, H-22), 7.45 (m, H-23), 1.18, 1.55, 1.67 (z), 1.99 (Me), 2.05 (s, OAc).

Carapolide G **6**. Mp 280° (*ex* $CHCl_3$/MeOH); $[\alpha]_D^{20}$ + 142° (c, 0.6 in $CHCl_3$); IR (KBr) ν_{max} 3500, 3140, 1760, 1740, 1715, 1700, 1400, 1080, 880, 845, 805 cm^{-1}. MS *m/z* (%) 514 (M^+, 8), 496 (10), 454 (25), 436 (85), 413 (20), 413 (20), 391 (20), 360 (100), 345 (40), 331 (95), 313 (90), 313 (90), 301 (20). Found: C, 65.28; H, 6.75. $C_{28}H_{34}O_9$ requires C, 65.35; H, 6.66. ^1H and ^{13}C NMR see Tables 2 and 4.

Carapolide H **7**. Mp 188-190° (*ex* MeOH); $[\alpha]_D^{20}$ -58° (c = 0.8 in $CHCl_3$); IR (KBr) ν_{max} 3140, 1770, 1740, 1720, 1700, 1370, 1225, 1030, 950, 910, 880, 860, 830, 800, 740 cm^{-1}. MS *m/z* (%) 543 (M^+ + 1, 3), 542 (M^+, 9), 482 (6), 422 (5), 364 (6), 351 (5), 190 (15), 174 (12), 161 (10), 108 (42), 43 (100). Found: C, 66.32; H, 7.14. $C_{30}H_{38}O_9$ requires C, 66.40; H, 7.06. ^1H and ^{13}C NMR see Tables 2 and 4.

Carapolide I **8**. Mp 208-210° (*ex* EtOAc/ hexane); $[\alpha]_D^{20}$ -46° (c = 1.2 in $CHCl_3$). IR ν_{max} 1730, 1725, 1370, 1250, 1120, 1025, 875, 805, 780 cm^{-1}. MS *m/z* (%) 512 (M^+, 3), 452 (10), 392 (10), 377 (8), 334 (10), 319 (15), 225 (15), 209 (11), 171 (10), 145 (15), 105 (20), 91 (25), 81 (30), 43 (100). Found: C, 70.38; H, 7.78. $C_{30}H_{40}O_7$ requires C, 70.29; H, 7.87. ^1H and ^{13}C NMR see Tables 2 and 4.

Evodoulone **9**. Mp 198-200° (lit.[5] 199-200°). IR ν_{max} 1745, 1730, 1715, 1680, 1390, 1370, 1240, 1030, 915, 880, 835, 780 cm^{-1}.

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