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DAMMARANE TRITERPENES FROM THE STEM BARK OF *COMMIPHORA DALZIELII**

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Key Word Index—*Commiphora dalzielii*; Burseraceae; dammaranes; cabraleadiol; cabraleadiol 3-acetate; cabraleone; isofouquierone; chemical taxonomy.

Abstract—From the stem bark of *Commiphora dalzielii* the isolation and identification of the 20,24-epoxydammarane triterpenes cabraleadiol 3-acetate, cabraleadiol and cabraleone and isofouquierone are reported. Both the acetate and isofouquierone appear to be novel. The chemotaxonomic implications of finding this type of triterpene in the Burseraceae are discussed.

INTRODUCTION

Commiphora dalzielii Hutch. is a shrub or small tree indigenous to Ghana where it is found growing in thickets in drier parts of the coastal area [2]. An examination of the stem bark of this previously unworked species [3] has led to the isolation of a number of dammarane triterpenes. This is only the second record of dammaranes in the Burseraceae [3], and follows their recent discovery in the resin of *Boswellia frereana* [4]. These finds are of particular note for two reasons. Firstly, they demonstrate interesting chemotaxonomic affinities between Burseraceae and the allied family Meliaceae. Secondly, the isolation of isofouquierone (this study) and other dammaranes oxygenated at C-16 and C-20 [4] suggest possible precursors for the guggulsterols from *C. mukul* [5] and the tanaane series of octanortriterpenes that occur in the resin of *C. incisa* [6].

RESULTS AND DISCUSSION

Extraction of the stem bark of *C. dalzielii* with petroleum (bp 40–60°) gave seven triterpenes, five of which were separated by column chromatography over silica gel and circular preparative thin layer chromatography. The remaining two compounds were identified as the common triterpenes lupeol and β-amyrin by direct comparison with authentic material.

Of the five purified compounds one was identified as epilupeol by its conversion to lupeonone which was in turn reduced to give a mixture of lupeol (major product) and epilupeol. Three of the remaining triterpenes were characterized by a base peak at *m/z* 143 in the mass spectrum which is attributable to fragment **1**. Their relationship as the 3-oxo-, and the corresponding 3α-hydroxy and 3α-acetoxy compounds was established by simple chemical interconversions. The ^{1}H and ^{13}C NMR spectra were typical of the dammarane group of triterpenes [7–10]. Comparison with literature data revealed that the ketone and alcohol were cabraleone (**2**) and cabraleadiol (**3**), previously isolated from two species of Meliaceae, *Cabralea polytricha* [9] and *Cabralea eichleriana* [10]. The corresponding acetate (**4**) had been synthesized but not previously recorded as a natural product. The ^{13}C NMR spectra of **2** and **3** were recorded (Table 1) and confirm the C-20 and C-24 configurations of all three compounds as *S* [7, 8, 11–13].

The other triterpene also had the spectral characteristics of a 3-oxodammarane. However, whilst an ion *m/z* 143 was still present in the mass spectrum it was no longer the base peak. In the ^{1}H NMR spectrum notable features were the occurrence of singlets at δ1.32 (6H) and δ1.12 (3H) for C-25 and C-20 methyl substituents and a multiplet at δ5.62 for two olefinic protons. These data suggested an uncyclized C-17 side-chain with hydroxy functions at C-20 and C-25 and a double bond between either C-22 and C-23 or C-23 and C-24. This hypothesis was sustained by the ^{13}C NMR spectrum (Table 1) which revealed two tertiary olefinic carbons and two quaternary carbinol resonances. Placement of the double bond between C-23 and C-24 was indicated by the mass spectrum which showed a major fragment at *m/z* 359 (**5**) due to fission of the side-chain between C-20 and C-22, β to the double bond. ^{1}H and ^{13}C NMR chemical shifts for the side-chain agreed closely with published data for isofouquierol (**6**) [14] and chikusetsusaponin-L_{9a} (**7**) [15], respectively. The identification of this compound as the previously unrecorded isofouquierone (**8**) was confirmed by its reduction to the corresponding 3β-hydroxy derivative which showed close agreement with **6**, which has been reported from *Fouquieria splendens* [14].

The isolation of these dammarane triterpenes, together with the octonordammaranes of *C. incisa* [6], represents a significant departure from the patterns of triterpene production previously noted [3] in the Burseraceae. Their occurrence is also notable in highlighting the chemotaxo-

* Part 2 in the series "Chemistry of the Burseraceae". For Part 1 see ref. [1].

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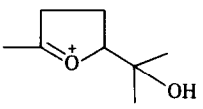

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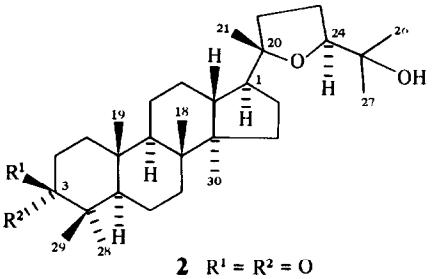
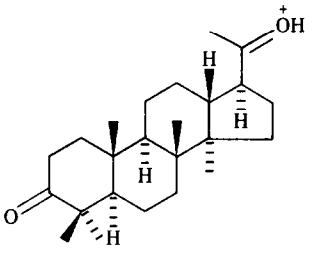


2 $R^1 = R^2 = O$
3 $R^1 = H$; $R^2 = OH$
4 $R^1 = H$; $R^2 = OAc$



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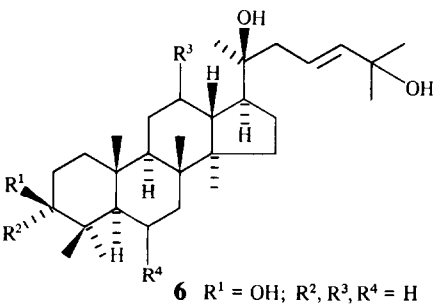
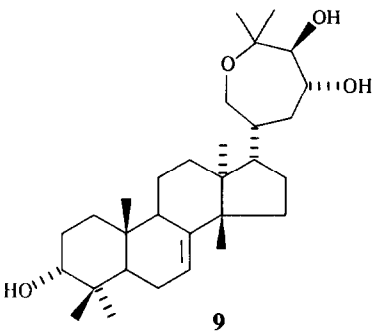


6 $R^1 = OH$; $R^2, R^3, R^4 = H$
7 $R^1, R^3, R^4 = OH$; $R^2 = H$
8 $R^1 = R^2 = O$; $R^3, R^4 = H$



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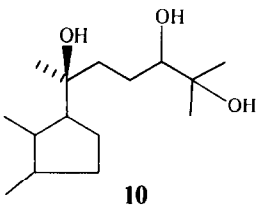

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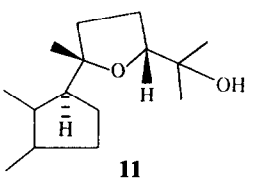

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nomic relationship of Burseraceae to Meliaceae, or more specifically to the meliaccous genus *Cabralea*. Indeed, the very similar triterpenes of *Cabralea* and of *C. dalzielii* and *B. frereana* appear to be at odds with normal triterpene metabolism within both families, in which the euphane skeleton and epoxy cyclizations involving the C-21 methyl, as typified by sapelin-B (**9**), are normal [3, 16], rather than those involving C-20 oxidation.

Isofouquierone (**8**) can be considered to represent an alternate pathway to that leading to **2–4** if the 20,24,25-triol (**10**) is viewed as a precursor of both groups. It is interesting that *Fouquieria splendens*, which yields the corresponding isofouquierol (**6**) [17], also produces the 20,24-epoxydammarane derivative ocotillol (**11**) which has the alternate 20*S*,24*R* stereochemistry. Triterpenes like **6** would also appear to be possible precursors of the guggulsterones, in which the C-17 side-chain is fragmented between C-20 and C-22 [4], and possibly the tanaanes, in which there is fission between C-17 and C-20.

EXPERIMENTAL

IR: KBr disc. ^1H and ^{13}C NMR run in $CDCl_3$ using TMS as int. standard. Electron impact MS at 70 eV using direct probe insertion at 130–150°. Petrol refers to the bp 40–60° fraction. R_f values quoted are for silica gel with toluene–EtOAc–AcOH (49:9:1) as solvent.

Plant material. Stem bark was collected in Ghana, from trees growing beside the Accra–Winneba road. A voucher specimen, FE-2330, has been deposited at the Herbarium of the Royal Botanic Garden, Edinburgh.

Isolation of compounds. Ground stem bark (600 g) was extracted with petrol and then with EtOAc. TLC of the two concd extracts revealed the same spectrum compounds so they were

Table 1. ^{13}C NMR chemical shifts for **2**, **3** and **8** isolated in this study and for the C-17 side-chain of chikusetsusaponin-L_{9a} (**7**) [15]

C	2	3	8	7
1	39.96	33.74	39.81	
2	34.12	25.84	34.00	
3	217.96	76.31	217.73	
4	47.42	37.66	47.31	
5	55.41	50.70	55.31	
6	19.71	18.30	19.59	
7	34.66	34.96	34.49	
8	40.35	40.68	40.24	
9	50.23	49.88	49.93	
10	36.91	37.34	36.77	
11	23.36	21.70	21.94	
12	25.84	25.46	27.44	
13	43.35	42.88	43.32	
14	50.04	50.19	50.18	
15	31.46	31.44	31.02	
16	27.80	28.34	27.44	
17	49.84	49.60	49.83	
18	16.08	16.08	15.90	
19	15.23	15.56	15.14	
20	86.40	86.55	74.86	73.3
21	24.11	24.11	25.76	27.6
22	34.91	35.27	43.32	40.8
23	27.05	27.83	122.22	123.5
24	86.50	86.31	141.92	141.5
25	70.27	70.27	70.62	69.8
26	26.40	26.42	29.83	31.2
27	26.78	27.05	29.88	31.2
28	27.15	27.05	26.65	
29	21.02	22.15	20.92	
30	16.34	16.55	16.25	

Spectra run at 90.56 MHz in $CDCl_3$.

bulked. After filtration through active charcoal to remove chlorophylls the concd extract was subjected to CC over silica gel, eluting with petrol and then with petrol containing increasing amounts of EtOAc. Elution with 5% EtOAc gave crude epilupeol which was subsequently purified by circular prep. TLC (silica gel; solvent, petrol–EtOAc, 95:5) to give pure epilupeol (53 mg, R_f 0.64). Elution with 6% gave a mixture of lupeol and β-amyrin which was not further treated. 8% EtOAc gave a mixture which on further purification by prep. TLC using the same eluting solvent yielded **4** (153 mg, R_f 0.44). Similar treatment of the 10% EtOAc and 15% EtOAc eluates gave **2** (450 mg, R_f 0.36) and **3** (300 mg, R_f 0.29), respectively. A final washing of the column with 50% EtOAc followed by the same purification procedure gave **8** (22 mg, R_f 0.10).

Epilupeol. Needles from MeOH, mp 200° (lit. [18] 197°). $[\alpha]_D$ +15° (*c* 0.1, $CHCl_3$) (lit. [19] +16°). Found: $[M]^+$ 426.3808; $C_{30}H_{50}O$ requires 426.3861. ^1H NMR (90 MHz): δ0.76–1.20 (6 × *s*, 6 × Me), 1.67 (3H, *br s*, =C–Me), 4.67, 4.55 (1H each, 2 × *br s*, $=CH_2$). Oxidation of epilupeol (26 mg) with Jones reagent followed by normal work-up yielded lupeonone (20 mg), identical in all respects (mp, TLC, IR, ^1H NMR) with an authentic sample. Reduction of the lupeonone with $NaBH_4$ gave a mixture of the isomeric hydroxy compounds from which lupeol was obtained by prep. TLC and identified by direct comparison (mixed mp, OR, IR) with an authentic sample.

Cabraleadiol 3-*acetate* (**4**). Small plates from petrol, mp 155° (lit. [9] 148°]. $[\alpha]_D$ +10° (*c* 0.1, $CHCl_3$) (lit. [9] +12°). IR ν_{max} cm^{-1}: 3450, 1740, 1460. ^1H NMR (250 MHz): δ0.77, 0.90, 0.90, 0.94, 1.02 (5 × 3H, 5 × *s*, 18-, 19-, 28-, 29-, 30-Me), 1.11, 1.15, 1.18 (3 × 3H, 3 × *s*, 21-, 26-, 27-Me), 2.05 (3H, *s*, OAc), 3.65 (1H, *m*, H-24), 4.65 (1H, *t*, *J* = 3 Hz, H-3β). EIMS *m/z* (rel. int.): 487 $[M-Me]^+$ (8), 443 $[M-C_3H_7O]^+$ (24), 427 (9), 383 (67), 143 (100), 125 (54). Compound **4** (10 mg) was left to stand overnight in alcoholic KOH (7 ml). After acidification of the reaction mixture and normal workup a product identical to **3** was obtained.

Cabraleone (**2**). Needles from petrol, mp 160° (lit. [9] 160°). $[\alpha]_D$ +60° (*c* 0.1, $CHCl_3$) (lit. [9] +60°). IR ν_{max} cm^{-1}: 3450, 1692, 1460. ^1H NMR (250 MHz): δ0.89, 0.95, 1.01, 1.04, 1.08 (5 × 3H, 5 × *s*, 18-, 19-, 28-, 29-, 30-Me), 1.11, 1.15, 1.18 (3 × 3H, 3 × *s*, 21-, 26-, 27-Me), 3.64 (1H, *dd*, *J* = 7, 6 Hz, H-24). ^{13}C NMR: see Table 1. EIMS *m/z* (rel. int.): 443 $[M-Me]^+$ (1), 399 $[M-C_3H_7O]^+$ (8), 381 (11), 143 (100), 125 (13). *Reduction of* **2**. Addition of $NaBH_4$ to **2** (20 mg) in EtOH (10 ml) gave a mixture of two products (R_f 0.29 and 0.25) in a ratio of about 1:9. The minor component was separated by prep. TLC and was found to be identical (^1H NMR, TLC) with **3**. *Oxidation of* **2**. A soln of **2** (20 mg) in Me_2CO (5 ml) was oxidized with Jones reagent to give the 24-oxo derivative cabralealactone, recrystallized from Et_2O as an amorphous solid, $[M]^+$ 414.3108; $C_{27}H_{42}O_3$ requires 414.3134. ^1H NMR (250 MHz): δ0.89, 0.93, 0.99, 1.02, 1.08 (5 × 3H, 5 × *s*, 18-, 19-, 28-, 29-, 30-Me), 1.37 (3H, *s*, 21-Me).

Cabraleadiol (**3**). Needles from petrol–EtOAc mixtures, mp 175° (lit. [9] 175°). $[\alpha]_D$ +19° (*c* 0.1, $CHCl_3$) (lit. [9] +18°). Found: $[M]^+$ 460.3952; $C_{30}H_{52}O_3$ requires 460.3916. IR ν_{max} cm^{-1}: 3450, 2950, 1460. ^1H NMR (250 MHz): δ0.84, 0.86, 0.88, 0.94, 0.97 (5 × 3H, 5 × *s*, 18-, 19-, 28-, 29-, 30-Me), 1.11, 1.14, 1.19 (3 × 3H, 3 × *s*, 21-, 26-, 27-Me), 3.39 (1H, *t*, *J* = 3 Hz, H-3β), 3.64 (1H, *dd*, *J* = 7, 6 Hz, H-24). ^{13}C NMR: see Table 1. EIMS *m/z* (rel. int.): 460 $[M]^+$ (1), 445 (7), 401 (36), 383 (84), 143 (100), 125 (62). *Acetylation of* **3**. Compound **3** (20 mg) was left in a soln of C_5H_5N and Ac_2O for 24 hr at room temp. Normal work-up of the reaction mixture gave a product identical in all respects to **4**. *Oxidation of* **3** with Jones reagent following the same procedure indicated above gave cabralealactone, identical in all respects with the product obtained by comparable oxidation of **2**.

Isofouquierone (**8**). A gum, $[\alpha]_D$ +34° (*c* 0.1, $CHCl_3$). IR ν_{max} cm^{-1}: 3450, 2950, 1700, 1460. ^1H NMR (250 MHz): δ0.89, 0.94, 1.00, 1.03, 1.07 (5 × 3H, 5 × *s*, 18-, 19-, 28-, 29-, 30-Me), 1.12 (3H, *s*, 21-Me), 1.31 (6H, *s*, 26-, 27-Me), 2.20 (2H, *m*, CH_2-22), 2.45 (2H, *m*, CH_2-2), 5.69 (2H, *m*, H-23, H-24). ^{13}C NMR: see Table 1. EIMS *m/z* (rel. int.): 359 $[M-C_6H_{11}O]^+$ (43), 315 (9), 205 (12), 143 (2), 125 (13), 82 $[C_6H_{10}]^+$ (100). *Isofouquierol* (**6**). Compound **8** (8 mg) was reduced with $NaBH_4$ as described under **2** to give, on pptn from Et_2O, **6** as a gum (5 mg), $[\alpha]_D$ +22° (*c* 0.1, $CHCl_3$) (lit. [14] +24°). IR ν_{max} cm^{-1}: 3450, 2950, 1460. ^1H NMR (250 MHz): δ0.78, 0.86, 0.87, 0.98, 0.98 (5 × 3H, 5 × *s*, 18-, 19-, 28-, 29-, 30-Me), 1.12 (3H, *s*, 21-Me), 1.32 (6H, *s*, 26-, 27-Me), 2.20 (2H, *m*, CH_2-22), 3.20 (1H, *dd*, *J* = 10, 6 Hz, H-3α), 5.70 (2H, *m*, H-23, H-24); identical to data previously reported for **6** [13]. EIMS *m/z* (rel. int.): 361 $[M-C_6H_{11}O]^+$ (33), 343 (11), 317 (3), 207 (13), 143 (3), 125 (15), 82 (100).

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