Phytochemistry, Vol. 25, No. 4, pp. 851–853, 1986.
Printed in Great Britain.

0031–9422/86 \$3.00 + 0.00

ALKALOIDS OF *ERYTHROXYLUM MACROCARPUM* AND *E. SIDEROXYLOIDES**

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(*Received* 1 *August* 1985)

Key Word Index—*Erythroxylum macrocarpum*; *E. sideroxyloides*; Erythroxylaceae; tropane alkaloids; 3α-benzoyloxytropan-6β-ol, 3α-benzoyloxynortropane; 3α-benzoyloxynortropan-6β-ol; chemotaxonomy.

Abstract—*Erythroxylum macrocarpum* and *E. sideroxyloides*, two closely related species indigenous to Mauritius, contain a similar range of alkaloids consisting mainly of benzoyl esters of tropan-3α-ol, tropan-3β-ol, and tropan-3α,6β-diol together with their nor-derivatives. 3α-Benzoyloxytropan-6β-ol (*E. sideroxyloides*), and 3α-benzoyloxynortropane and 3β-benzoyloxynortropan-6β-ol (both species) are reported for the first time.

INTRODUCTION

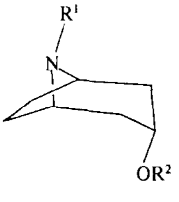
Erythroxylum macrocarpum O. E. Schulz and *E. sideroxyloides* Lam. are two of nine species placed by O. E. Schulz [1] in section *Packylobus* of the genus; they are members of the *E. laurifolium sensu lato* complex and are indigenous to Mauritius, Rèunion and the Seychelles. In Mauritius these small trees are known as 'bois de ronde' and find use as a popular treatment for kidney disorders as well as furnishing a hard timber. No phytochemical work appears to have reported specifically on the above two species but in 1888 [2] and 1889 [3] the leaves of *E. laurifolium s.l.* were stated to contain 0.16 % and 0.05 % of alkaloids, respectively. Lincoln [4] considered the species *sensu stricto* as devoid of cocaine and Benzanger-Beauquesne *et al.* [5] while observing a trace of alkaloid were unable to characterize any specific base, but reported on the presence of rutin and quercetin, as well as tannin, in both bark and roots. We report here out findings on the alkaloid composition of *E. macrocarpum* and *E. sideroxyloides* collected in Mauritius.

RESULTS AND DISCUSSION

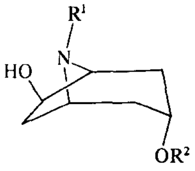
The alkaloids obtained by ether extraction of the plant materials were purified by chromatography and characterized by standard methods; structures of new alkaloids were elucidated by the application of those spectroscopic principles relevant to tropane alkaloids which have been previously elaborated in a previous paper of this series [6]. The alkaloids isolated from the various morphological parts and collections of *Erythroxylum macrocarpum* and *E. sideroxyloides* are recorded in Table 1.

The new alkaloid 3α-benzoyloxynortropane (**1a**) which was also prepared by partial synthesis constituted the principal base of all the examined morphological parts of *E. macrocarpum* irrespective of site of collection. Impure fractions of this alkaloid, on mass spectroscopy evidence, appeared to contain the corresponding cinnamoyl ester but lack of material prevented its isolation in a pure form. A second new alkaloid, 3α-benzoyloxynortropan-6β-ol (**2a**), was isolated as a major component of the alkaloid fraction of leaves collected in the wet forest of the Perrier Nature Reserve. *Erythroxylum sideroxyloides* also contained 3α-benzoyloxynortropane in all parts of the plant examined but the principal alkaloid of the leaves was the new ester 3α-benzoyloxytropan-6β-ol (**2b**). Otherwise the alkaloid content of the two species was very similar and reflected their close taxonomic relationship.

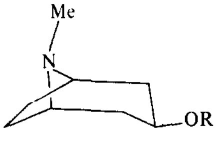
The overall rather simple spectrum of the principal alkaloids of the two species, based on esters of benzoic acid, is similar to that of a number of South American species [7] in which the same acid, and particularly tropacocaine (**3b**), is predominant. It is of interest that with the Mauritius species, including the aerial parts of *E. hypericifolium* Lam. section *Venelia* [8], 3α-benzoyloxy-



1a $R^1 = H$, $R^2 = PhCO$ (Bz)
1b $R^1 = Me$, $R^2 = Bz$



2a $R^1 = H$, $R^2 = Bz$
2b $R^1 = Me$, $R^2 = Bz$



3a $R = H$
3b $R = Bz$

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*Part 6 in the series "Alkaloids of the Genus *Erythroxylum*". For part 5 see ref. [6].

Table 1. Alkaloids of *Erythroxylum macrocarpum* and *E. sideroxyloides* collected in Mauritius

	Total alkaloid (% dry weight)	Alkaloids characterized
Erythroxylum macrocarpum		
Leaves		
Macchabée Forest Reserve, mixed collection from wet and dry areas	0.05	3α-Benzoyloxynortropane (**1a**) (new alkaloid); tropan-3β-ol (**3a**), tropacocaine (**3b**)
Perrier Nature Reserve	0.06	3α-Benzoyloxynortropane (principal alkaloid); 3α-benzoyloxynortropan-6β-ol (**2a**) (new alkaloid); tropacocaine; unidentified tropan-3-ol ester
Stem-bark		
Macchabée Forest Reserve, high, dry area	0.003	3α-Benzoyloxynortropane
Perrier Nature Reserve	0.02	3α-Benzoyloxynortropane
Root-bark		
Macchabée Forest Reserve, high, dry area	0.01	3α-Benzoyloxynortropane
E. sideroxyloides		
Vocoas Ridges, high, dry forest		
Leaves	0.06	3α-Benzoyloxynortropan-6β-ol (minor alkaloid); 3α-benzoyloxytropan-6β-ol (**2b**) (new alkaloid, principal base 0.03 %); 3α-benzoyloxynortropane (0.014 %); 3α-benzoyloxytropane (**1b**) (0.01 %); tropacocaine; unidentified base
Stem-bark	0.01	3α-Benzoyloxynortropane
Root-bark	0.06	3α-Benzoyloxynortropane (minor alkaloid, TLC characterization); unresolved mixture of diol esters involving butyric and other acids (principal component)

nortropane is common, but in *E. mamacoca* Mart. from Peru it is the corresponding 3β-compound (nortropacocaine) that is found [7]. The alkaloid pattern is in contrast to the higher yield of a more complex mixture of esters involving a number of acids and tropanols found in several African species [9] and in *E. hypericifolium* [6]. In accord with the earlier reports (*loc. cit.*) on the *E. laurifolium* complex none of the fractions examined in this work contained bases with the properties of cocaine, but in view of the local medicinal reputation of these plants a pharmacological study of the relevant alkaloids would be of interest.

EXPERIMENTAL

Prep. TLC for the fractionation of alkaloids involved the following systems: A, Al_2O_3 0.5 mm layer with Et_2O–EtOH (1 : 1); B, silica gel 0.5 mm layer with $CHCl_3$–Et_2NH (9 : 1).

Plant material. Collected Mauritius, December 1978 as below: *E. macrocarpum*, Macchabée Forest Reserve *ca* 15 km SW of Curepipe, wet and dry areas, and Perrier Nature Reserve *ca* 4 km W of Curepipe, *Erythroxylon sideroxyloides*: Vacaos Ridges *ca* 7 km SW of Curepipe. Material air-dried at 25°. Voucher specimens were examined by M. Friedmann, Muséum National d'Histoire Naturelle, Paris and designated in accordance with the current taxonomic revision of the genus for the Flora of Mauritius, now in preparation. Voucher specimens originally deposited in the University of Bradford (reference F316A) are now lodged at the Kew Herbarium, Richmond, Surrey.

Isolation of alkaloids. Alkaloids were extracted from the powdered plant materials by standard methods [7] and their total equivalent obtained by titration. Fractionation of bases was achieved by prep. TLC as indicated.

E. macrocarpum *leaves, Macchabée Forest collection.* Prep. TLC (system A) of the alkaloids from 203 g gave four bases: (i) 3α-benzoyloxynortropane (**1a**), R_f 0.27 (system A), 0.40 (system B); IR ν_{max}^{KBr} cm^{-1} 3400 (NH), 1723 (ester C=O); EIMS (probe) 70 eV, *m/z* (rel. int.): 231.1259 $[M]^+$ ($C_{14}H_{17}NO_2$ requires *m/z* 231.1259), 126 $[M-PhCO]^+$, 110 $[C_7H_{12}N]^+$ (100), 105.0340 (calc. for C_7H_5O 105.0340), 91, 82, 81, 80, 77; CIMS (CH_4, probe) *m/z* 232 $[M+1]^+$; ^1H NMR ($CDCl_3$): δ 1.7–2.3 (8H, *m*, CH_2-2, CH_2-4, CH_2-6, CH_2-7), 3.49 (2H, *m*, H-1, H-5), 5.28 (1H, *t*, *J* = 5 Hz, H-3) 7.50 (3H, *m*, ArH_3), 7.95 (2H, *m*, ArH_2). Authentic base (**1a**) was prepared by oxidative demethylation of 3α-benzoyloxytropane by the method used for the 3β-isomer [7]; after purification by prep. TLC (system B) it formed a picrate, mp 232° (from EtOH–H_2O) (Found: C, 52.4; H, 4.55; N, 11.8. $C_{14}H_{17}NO_2 \cdot C_6H_3N_3O_7$ requires: C, 52.2; H, 4.35; N, 12.2 %). Mmp with picrate of natural base (mp 234°) 233–234°, mmp with picrate of corresponding 3β-ester (mp 232°) 196°. Some samples of this alkaloid gave an EIMS containing *m/z* 257.1416 $[M]^+$ (calc. for $C_{16}H_{19}NO_2$: 257.1416, 3-cinnamoyloxytropane?), 131 (C_9H_7O, PhCH=CHCO?); (ii) tropan-3β-ol (**3a**) (R_f, mp and mmp of picrates, as authentic sample), tigloyl chloride afforded tigloidine (R_f, mp and mmp of picrates, IR identical with authentic alkaloid); (iii) tropacocaine (R_f, mp and mmp of picrates, IR as authentic alkaloid), EIMS 70 eV *m/z* 245.1415 $[M]^+$ (calc. for $C_{15}H_{19}NO_2$ 245.1416); (iv) unidentified base.

E. macrocarpum *leaves, Perrier Nature Reserve collection.* Prep. TLC (system B) of the bases from 194 g indicated six alkaloid bands; three bases were identified on further fractionation (systems A and B): (i) 3α-benzoyloxynortropan-6-β-ol, R_f 0.48, 0.28 (systems A and B respectively), ^1H NMR (100 MHz, $CDCl_3$): δ 2.8 (1H, *m*, NH), 3.4 (2H, *m*, H-1, H-5), 3.75 (1H, *s*, OH-6), 4.84 (1H, *dd*, H-6), 5.33 (1H, *t*, *J* = 5 Hz, H-3), 7.53 3H, *m*, Ar H_3), 7.99 (2H, *m*, ArH_2); picrate, mp 225° (nodules from EtOH–H_2O) ($C_{14}H_{17}NO_3$ requires M_r, 247.1208; Found M_r (MS), 247.1184); IR ν_{max}^{KBr} cm^{-1} 3480, 1710 (ester C=O); EIMS *m*/*z* (rel. int): 247 $[M]^+$ (2), 229 [picric acid]$^+$ (31), 203 $[M-44]^+$ (4), 126.0925 (calc. for $C_7H_{12}NO$, 126.0919) (18), 125 (19), 122.0339 (calc. for $C_7H_6O_2$, 122.0368) (3), 108, 105.0352 (calc. for C_7H_5O, 105.0368) (21), 81.0527 (calc. for C_5H_7N, 81.0578) (100), 80 (45), 77(21); (ii) 3α-benzoyloxynortropane (see above); (iii) tropacocaine (R_f, IR, MS as authentic compound; mp and mmp of picrates); and (iv) several unidentified bases.

E. macrocarpum *barks*, *stem bark*, *Perrier collection* (39 g). Two chromatographic bands (system B) yielded 3α-benzoyloxynortropane (MS, R_f as above) and unidentified minor bases.

Root bark, *Macchabée Forest collection* (160 g). Three chromatographic bands (system B); R_f 0.4, 3α-benzoyloxynortropane (MS, R_f as above); R_f 0.2 and 0.9 unidentified minor bases.

E. sideroxyloides *leaves*. From 140 g six bases were isolated (system B): (i) 3α-benzoyloxynortropan-6β-ol (R_f values in three systems; MS, see above); (ii) 3α-benzoyloxytropan-6β-ol (**2b**), R_f 0.31 (system B); picrate, mp 110° (amorphous masses from EtOH–H_2O); IR $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 3440, 1722 (ester C=O); EIMS (probe) 70 eV, *m*/*z* (rel. int.): 261.1374 $[M]^+$ ($C_{15}H_{19}NO_3$ requires *m*/*z* 261.1365) (14), 229 (picric acid)$^+$ (52), 217.1135 $[M-(C(6)HOH\text{–}C(7)H_2)]^+$ (6), 156 ($C_8H_{14}NO_2$) (5), 140.1064 (calc. for $C_8H_{14}NO$: 140.1075) (32), 122.0359 (calc. for $C_7H_6O_2$: 122.0367) (12), 105.0307 (calc. for C_7H_5O 105.0340) (35), 95, 94; ^{1}H NMR (250 MHz, $CDCl_3$) diagnostic signals: δ3.10 (3H, *s*, NMe). 4.17 (1H, *s*, HO-6), 5.05 (1H, *dd*, J = 5.2 and 1.5 Hz, H-6), 5.33 (1H, *t*, J = 4.95 Hz, H-3); (iii) 3α-benzoyloxynortropane (R_f of base, mp and mmp of picrate, IR as above); (iv) a base which gave picrate, mp 250° and MS similar to that of 3-benzoyloxytropane but R_f values inconsistent with either the 3α- or 3β-yl ester (picrates, mp 252–255° and 240–242°, respectively), (v) 3-benzoyloxytropane (R_f, mp and mmp of picrates, MS as those of authentic compound).

Stem-bark. Powdered bark (105 g) gave three bases (system A): 3α-benzoyloxynortropane [R_f (system B) and MS as above], and two bases which were not identified.

Root-bark. Fractionation of alkaloids from root-bark (19 g) by system A gave (i) 3α-benzoyloxynortropane [R_f (system B) and MS as above], and (ii) unresolved mixture of diol esters R_f 0.33 (system B); IR $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 3400 (OH), 1730 (C=O); EIMS (probe) 70 eV, *m*/*z* (rel. int.): 305 $[M]_a^+$(9), 227 $[M]_b^+$, 261 $[M_a-44]^+$ (3), 183 $[M_b-44]^+$ (4), 156 (4), 140 $[M_a-165, M_b-87]^+$ (30), 141 (4), 122 (9), 110 (9), 105 [C_7H_5O] (13), 96 (19) 95 (80), 94 (100), 93 (19), 82 (14).

Acknowledgements—We thank the University of Mauritius and the Sugar Industry Research Institute, Mauritius for providing facilities for the collection of plant materials. We are indebted to Mr. J. Guého and Mr. A. W. Owadally for invaluable assistance with the field-work and to Mr. J. Bosser and Mr. Friedmann for the botanical examination of the specimens. One of us (M.S.A.S) acknowledges the King Saud University, Riyadh for financial assistance.

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