Phytochemistry, 1973, Vol. 12, pp. 693 to 698. Pergamon Press. Printed in England.

PEPTIDE AND TETRAHYDROISOQUINOLINE ALKALOIDS FROM *EUONYMUS EUROPAEUS**

D. W. BISHAY and Z. KOWALEWSKI

Department of Pharmacognosy, Medical Academy, Poznań, Poland

and

J. D. PHILLIPSON

Pharmacognosy Research Laboratories, Department of Pharmacy, Chelsea College, University of London, Manresa Road, London SW3

(*Received* 13 *July* 1972. *Accepted* 5 *October* 1972)

Key Word Index—*Euonymus europeaus*; Celastraceae; *p*-aryloxy macrocyclic peptide; 1-benzyltetrahydroisoquinoline alkaloids; frangulanine; franganine; frangufoline; armepavine; chemotaxonomy.

Abstract—Three *p*-aryloxy macrocyclic peptide alkaloids frangulanine, franganine and frangufoline together with the 1-benzyltetrahydroisoquinoline alkaloid armepavine have been isolated from *Euonymus europaeus* native to Poland. These types of alkaloids are new to the Celastraceae and are of chemotaxonomic interest.

INTRODUCTION

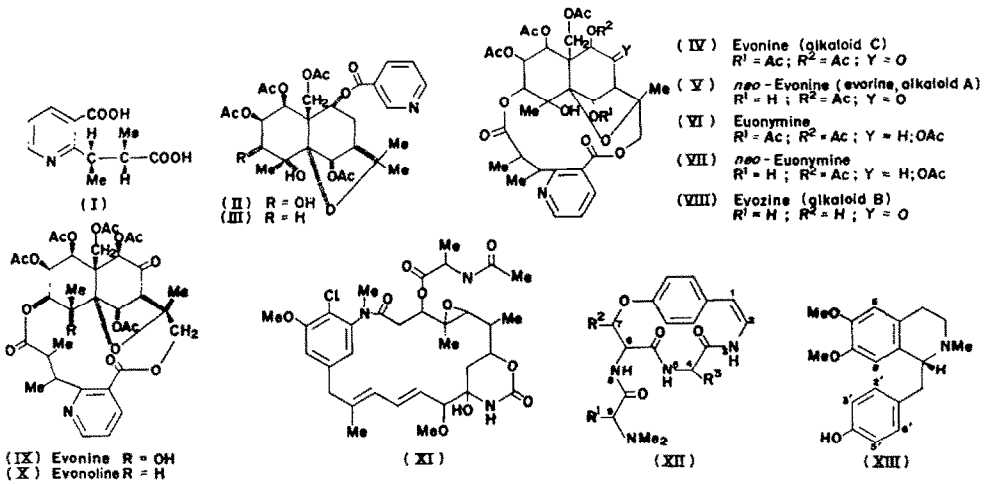
THE PRESENT chemical investigation of *Euonymus europaeus* L. was undertaken since it is said to be used as a cardiotonic, emetic and purgative and also against insects and vermin. The cardiac activity of the plant is accounted for by the presence of cardenolide glycosides and these substances may also be responsible for its reputed emetic properties. *Euonymus* is an unusual genus since some of its species contain cardiac glycoside and alkaloids. The presence of alkaloids in the seeds of *E. europaeus* was noted during the isolation of cardenolides[1] and subsequently three crystalline alkaloids A, B and C were isolated.[2] One mol of the alkaloid C, which has been named evonine,[3] on hydrolysis yielded 5 mol HOAc, a decahydroxy $C_{15}H_{26}O_{10}$ portion and 1 mol of evoninic acid (I).[4,5]

The determination of the structure of the two alkaloids maytoline (II) and maytine (III)[6] from *Maytenus ovatus* Loes., another member of the Celastraceae, has contributed towards establishing the structure of the *Euonymus* alkaloids. The two *Maytenus* alkaloids are nicotinoyl esters of a highly oxygenated sesquiterpene nucleus and they have characteristics similar to those of the *Euonymus* alkaloids.[6] Evonine (IV) has also been isolated as

* Part III in the series "Investigations of Alkaloids of *Euonymus europaeus* L. growing in Poland". For part II see D. W. BISHAY and Z. KOWALEWSKI, *Herba Polonica* **17**, 97 (1971). The identification of armepavine was reported at the Glasgow Conference of the Pharmaceutical Society of Great Britain in September 1971 and appears as an abstract, *J. Pharm. Pharmac.* **23**, 244 S (1971). This work forms part of a thesis to be submitted by D. W. Bishay for a doctor's degree in phytochemistry at the Medical Academy, Poznań, Poland.

[1] F. SANTAVÝ and T. REICHSTEIN, *Helv. Chim. Acta* **31**, 1655 (1948).
[2] K. DOEBEL and T. REICHSTEIN, *Helv. Chim. Acta* **32**, 592 (1949).
[3] M. PAILER and R. LIBISELLER, *Montsch. Chem.* **93**, 403 (1962).
[4] M. PAILER and R. LIBISELLER, *Montsch. Chem.* **93**, 511 (1962).
[5] R. LIBISELLER and A. PREISINGER, *Montsch. Chem.* **93**, 417 (1962).
[6] S. M. KUPCHAN, R. M. SMITH and R. F. BRYAN, *J. Am. Chem. Soc.* **92**, 6667 (1970).

the major alkaloid from the dried fruits of *E. sieboldiana* Bl. and its structure determined[7,8] together with the structures of three new alkaloids named neo-evonine (V), euonymine (VI) and neo-euonymine (VII).[9] Alkaloids A and B from *E. europaeus* have been named evorine and evozine, respectively, and it has been shown that the NMR spectrum of evorine is identical with that of neo-evonine so that the two are considered to be identical. On the basis of NMR arguments the structure of evozine (alkaloid B) (VIII) has been proposed.[10,11] The constitution and configuration of evonine (IX) and the related alkaloid evonoline (X), also isolated from the seeds of *E. europaeus*, have been determined independently and it is claimed that at least 12 alkaloids are present in the seeds.[12]



Alkaloids from *Tripterygium wilfordii* Hook f. (Celastraceae) have insecticidal activity, as do those of *Euonymus*, and although their structures have not been fully determined it is apparent that they are similar in structure, having a polyhydroxy $C_{15}H_{26}O_{10}$ nucleus esterified with acetic acid and either benzoic or 3-furoic acid together with a nicotinoyl dicarboxylic acid unit similar to evoninic acid.[13,14]

Similar alkaloids have also been reported from *Catha edulis* Forsk. (Celastraceae), since cathidine on hydrolysis yields 2 mol of acetic acid, 1 mol of benzoic acid, 1 mol of nictotinic acid and a C-15 alcohol.[15]

The structure of the novel alkaloid maytansine (XI), isolated from the fruits of *Maytenus ovatus* Loes., has recently been reported.[16] This anti-leukaemic ansa-macrolide has structural similarities to the rifamycins, streptovaricins, tolypomycins and geldamycins, compounds which are of interest as antiviral and antimicrobial agents.[16]

[7] H. WADA, Y. SHIZURI, K. YAMADA and Y. HIRATA, *Tetrahedron Letters* 2655 (1971).
[8] Y. SHIZURI, H. WADA, K. SUGIURA, K. YAMADA and Y. HIRATA, *Tetrahedron Letters* 2659 (1971).
[9] K. SUGIURA, Y. SHIZURI, H. WADA, K. YAMADA and Y. HIRATA, *Tetrahedron Letters* 2733 (1971).
[10] A. KLÁSEK, F. ŠANTAVÝ, A. M. DUFFIELD and T. REICHSTEIN, *Helv. Chim. Acta* **54**, 2144 (1971).
[11] A. KLÁSEK, Z. SAMEK and F. ŠANTAVÝ, *Tetrahedron Letters* 941 (1972).
[12] M. PAILER, W. STREICHER and J. LEITICH, *Montsch. Chem.* **102**, 1873 (1971).
[13] F. ACREE, JR. and H. L. HALLER, *J. Am. Chem. Soc.* **72**, 1608 (1950).
[14] M. BEROZA, *J. Org. Chem.* **28**, 3562 (1963); and references cited therein.
[15] M. CAIS, D. GINSBURG and A. MANDELBAUM, *I.U.P.A.C. Symposium, The Chemistry of Natural Products*, Abstracts of Papers, Kyoto, Japan, p. 95 (1964).
[16] S. M. KUPCHAN, Y. KOMODA, W. A. COURT, G. J. THOMAS, R. M. SMITH, A. KARIM, C. J. GILMORE, R. C. HALTIWANGER and R. F. BRYAN, *J. Am. Chem. Soc.* **94**, 1354 (1972).

The present publication deals with the identification of four alkaloids A, B, C and D isolated from *E. europaeus* native to Poland[17] and shows that they are alkaloids of the *p*-aryloxy macrocyclic peptide and tetrahydroisoquinoline types hitherto unknown in *Euonymus* species and in the Celastraceae.

RESULTS AND DISCUSSION

Identification of Alkaloid A as Frangulanine

The UV and IR spectra of alkaloid A clearly indicate that it is not a sesquiterpene ester alkaloid of the evonine type (IV–X). Moreover, the strong amide carbonyl absorption in the IR spectrum suggests that alkaloid A is a peptide alkaloid. The MS is consistent with a *p*-aryloxy macrocyclic peptide-type structure (XII)[18] having a weak molecular-ion peak at *m/e* 500, a base peak at *m/e* 114, a peak at *m/e* 115 (10%) and the absence of any other peaks above 5% relative abundance. This spectrum points to one or other of the following two structures:[19] (1) the known alkaloid, frangulanine[20] (= ceanothamine A)[21] (XII, R^1 = *sec*-butyl, R^2 = *iso*-propyl, R^3 = *iso*-butyl) or (2) a new alkaloid (XII, R^1 = *sec*-butyl, R^2 = *iso*-propyl, R^3 = *sec*-butyl).

Confirmatory evidence for the structure of alkaloid A is obtained from the NMR spectrum. Signals for 4 *C*-methyl groups between δ 0·83 and 1·0 are interpreted as a triplet at δ 1·0 overlapping with a doublet for the 2 *C*-methyl groups of the *N,N*-dimethyl-isoleucine portion, leaving 2 overlapping doublets at δ 0·83 and 0·90 and suggesting that R^3 is *iso*-butyl. This is further confirmed by hydrolysis of alkaloid A which yields leucine and not isoleucine. Alkaloid A is identified therefore as frangulanine (XII, R^1 = *sec*-butyl, R^2 = *iso*-propyl, R^3 = *iso*-butyl). Authentic frangulanine is not available at present for comparison.

Identification of Alkaloid B as Franganine

The UV, IR and MS of alkaloid B are very similar to those of alkaloid A, suggesting that the two compounds are closely related. The MS is consistent with either of the two structures: (1) franganine[22,23] (XII, R^1 = *iso*-butyl, R^2 = *iso*-propyl, R^3 = *iso*-butyl) and (2) adouetine X[24,25] (= ceanothamine B)[21,26] (XII, R^1 = *iso*-butyl, R^2 = *iso*-propyl, R^3 = *sec*-butyl). Authentic franganine and adouetine X are not available for comparison and sufficient alkaloid B is not available for hydrolysis. Since the m.p. of franganine is reported to be 248° and that of adouetine X is 277–279° it is suggested that alkaloid B, m.p. 240–242·5°, is franganine.

Identification of Alkaloid C as Frangufoline

The UV spectrum of alkaloid C differs slightly from those of alkaloids A and B but the IR spectra are all very similar. The MS also shows close similarities to the spectra of alkaloids A and B but the molecular ion appears at *m/e* 534, the base peak at *m/e* 148 and,

[17] D. W. Bishay and Z. Kowalewski, *Herba Polonica* **17**, 97, 233 (1971).
[18] E. W. Warnhoff, *Forts. Chem. Organ. Naturstoffe* **28**, 163 (1970).
[19] R. Tschesche, J. Rheingans, H.-W. Fehlhaber and G. Legler, *Chem. Ber.* **100**, 3924 (1967).
[20] R. Tschesche, H. Last and H.-W. Fehlhaber, *Chem. Ber.* **100**, 3937 (1967).
[21] E. W. Warnhoff, S. K. Pradhan and J. C. N. Ma, *Can. J. Chem.* **43**, 2594 (1965).
[22] R. Tschesche and H. Last, *Tetrahedron Letters* 2993 (1968).
[23] R. Tschesche and I. Reutel, *Tetrahedron Letters* 3817 (1968).
[24] M. Pais, J. Mainil and R. Goutarel, *Ann. Pharm. Franc.* **21**, 139 (1963).
[25] M. Pais, J. Marchand, F.-X. Jarreau and R. Goutarel, *Bull. Soc. Chim. Fr.* 1145 (1968).
[26] R. E. Servis, A. I. Kosak, R. Tschesche, E. Frohberg and H.-W. Fehlhaber, *J. Am. Chem. Soc.* **91**, 5619 (1969).

apart from the peak at *m/e* 149, no other peak is above 10% relative abundance. This spectrum is consistent with either of the two structures: (1) frangufoline[22] (XII, R^1 = benzyl, R^2 = *iso*-propyl, R^3 = *iso*-butyl) or (2) adouetine Y'[23–25] (= myrianthine B)[27] (XII, R^1 = benzyl, R^2 = *iso*-propyl, R^3 = *sec*-butyl). The 60 MHz NMR spectrum confirms this type of structure but does not permit the resolution of the 4 *C*-methyl group signals. TLC comparison of alkaloid C with authentic alkaloids shows that it has R_f identical with that of frangufoline and that it is not adouetine Y'. Alkaloid C is therefore frangufoline.

Identification of Alkaloid D as R-(−)-armepavine

Although the MS of alkaloid D shows some similarities to the MS of the sesquiterpene ester alkaloids evonine, desacetylevonine, evozine, evorine and isoevorine in having prominent peaks at *m/e* 107 and 206,[10] the UV, IR, NMR and MS confirm the identity of this alkaloid as armepavine (XIII). The m.p. of alkaloid D oxalate is not depressed by admixture with authentic armepavine oxalate and alkaloid D has R_f in 3 TLC systems identical with those of authentic armepavine. The ORD curve of alkaloid D is consistent with *R*-(−)-armepavine (XIII).

TABLE 1. ORDERS AND FAMILIES CONTAINING *p*-ARYLOXY MACROCYCLIC PEPTIDE ALKALOIDS

Cronquist classification[28]			Hutchinson classification[29]
Subclass	Order	Family	Order
Hamamelidae	Urticales	Moraceae	Urticales
Dilleniidae	Malvales	Sterculiaceae	Tiliales
	Violales	Flacourtiaceae	Bixales
Rosidae	Euphorbiales	Euphorbiaceae	Euphorbiales
		Pandaceae	Celastrales
	Rhamnales	Rhamnaceae	Rhamnales

Chemotaxonomic Considerations

The yields of frangulanine, franganine, frangufoline and armepavine obtained from the leaves, stems and roots of the Polish *E. europaeus* investigated are very low. TLC of the total crude alkaloids indicates that a further eight alkaloids are present and further studies would be of interest to see whether any of these alkaloids are of the sesquiterpene ester type (IV–IX) previously found in *Euonymus* species. It is interesting to find *p*-aryloxy macrocyclic peptide alkaloids and a 1-benzyl tetrahydroisoquinoline alkaloid occurring in the same plant and this may indicate that a biosynthetic relationship exists between these two types of alkaloids. These alkaloids have not previously been reported in *Euonymus* or in the Celastraceae which elaborates the unique sesquiterpene nicotinyl ester alkaloids. According to Warnhoff[18] *p*-aryloxy macrocyclic peptide alkaloids are found in genera of the Euphorbiaceae, Flacourtiaceae, Moraceae, Pandaceae, Rhamnaceae and Sterculiaceae (Table 1). Following Cronquist's classification,[28] five of the six families are in the two subclasses Dilleniidae and Rosidae which are considered as two parallel groups not well distinguished morphologically. According to Cronquist, the orders Rhamnales and Euphorbiales within the subclass Rosidae are closely linked through the Rosales and the Celastrales; it is therefore of particular interest to be able to report the presence of *p*-aryloxy macro-

[27] J. MARCHAND, X. MONSEUR and M. PAIS, *Ann. Pharm. Franc.* **26**, 771 (1968).
[28] A. CRONQUIST, *The Evolution and Classification of Flowering Plants*, Thomas Nelson, London (1968).

cyclic peptide alkaloids within the family Celastraceae, order Celastrales. Within the Dilleniidae the orders containing this type of peptide alkaloid are the Violales and Malvales which also are considered to be closely linked.

In the phylogenetic scheme of Hutchinson,[29] the six families containing *p*-aryloxy macrocyclic peptide alkaloids represent six different orders (Table 1), five of which are considered to be related to each other in the sequence: Bixales → Tiliales → Celastrales → Euphorbiales → Rhamnales. Although Pandaceae are now considered to be in the order Euphorbiales rather than the Celastrales, the latter order can still be represented in this scheme since this type of peptide alkaloid is now known to be in a member of the Celastraceae.

1-Benzyltetrahydroisoquinoline alkaloids together with the closely related aporphine and proaporphine alkaloids[30] are reported to be more widely distributed in the plant kingdom than the *p*-aryloxy macrocyclic peptide alkaloids, but this may only be due to the more recent discovery of the latter type of alkaloid. Since 1-benzyltetrahydroisoquinoline-type alkaloids have been found in the orders Euphorbiales (Euphorbiaceae) and in the Rhamnales (Rhamnaceae) it is not too surprising from the chemotaxonomic view point to find this type of alkaloid and *p*-aryloxy macrocyclic peptide alkaloids in the order Celastrales. Although this is the first time that both these types of alkaloids have been reported in the same genus it can be envisaged that they may occur together in other genera. Furthermore, peptide-type alkaloids are known to be present in a member of the Urticales so that they may be more widely distributed than our present knowledge indicates.

EXPERIMENTAL

M.ps were determined on a hot-stage microscope (Petius) and are uncorrected; IR spectra in KBr; NMR spectra with TMS as internal reference; MS were determined in a high-resolution AEI MS 902 mass spectrometer at 70 eV, inlet temp. between 230 and 250°; ORD curves, Bellingham and Stanley Polarimatic 62, in $CHCl_3$.

Plant material. Wild plants were collected 10 km east of Poznań, Poland. A sample, which is held at the museum of the Pharmacognosy Department, Chelsea College, University of London, was found to correspond with material identified as *Euonymus europaeus* L. kept in the herbarium of the Royal Botanical Gardens at Kew.

Isolation of alkaloids A, B, C and D. The isolation of these alkaloids has previously been described.[17] Alkaloid A was isolated from stem (0·00038%), whole root (0·0018%), root bark (0·015%) and leaves (0·00015%); alkaloid B from whole root (0·00006%) and root bark (0·0005%); alkaloids C (0·0007%) and D (0·003%) from leaves.

Identification of alkaloid A as frangulanine. Alkaloid A, colourless needles from $CHCl_3$–light petrol., m.p. 276–279° (m.p. frangulanine 276–279°);[21] UV (EtOH) λ_{max} 255 nm (log ϵ, 4·19) sh, only end absorption 200–235 nm; IR ν 3250 cm^{-1} (NH), 1630 cm^{-1} (CONH), 1240 cm^{-1} (C–O–C); NMR ($CDCl_3$) 100 MHz δ 7·1 (4 H, broad *s*, aromatic protons), 6·4–6·7 (2 H, *dd*, C-1 and C-2 protons), 5·0 (1 H, *dd*, J_{6H-7H} 7·5 Hz $J_{7H\text{-}iso\text{-}propyl}$ 2 Hz, C-7 proton), 4·5 (1 H, *dd*, J_{6H-7H} 7·5 Hz. J_{6H-NH} 10 Hz C-6 proton), 4·05 (1 H, *m*, C-4 proton), 2·7 (1 H, *d*, $J_{9H\text{-}isobutyl}$ 3·5 Hz C-9 proton), 2·2 (6 H, *s*, 2 × NMe), 1·32 and 1·08 (2 × 3H, *d*, *J* 6·5 Hz *iso*propyl of R^2), 0·83, 0·90 (6 H, overlapping *dd*, *J* 6Hz, *iso*propyl of R^2), 1·0 (6 H, overlapping *t*, *d*, CH_3CH_2– and CH_3CH– of R^1). MS, *m/e* 500 (M^+ 0·03%), 499 (0·05%), 485 (M_-^+ – Me, 0·15%), 471 ($\overline{M^+}$ – Et, 0·02%), 457 (M^+ – Pr, 0·035%), 443 (0·35%), 387 (0·015%), 344 (0·03%), 303 (0·05%), 274 (0·03), 210 (0·1%), 190 (0·45%), 182 (0·35%), 135 (1·7%), 115 (10%), 114 (100%), 97 (3·0%), 85 (3·5%); *m/e* 114 → 85, $m^*_{obs.}$ 63·4 ($m^*_{calc.}$ 63·4) hence R^1 = *sec*-butyl.[19] Accurate mass measurements. Found 115·1314. $C_7H_{17}N$ requires: 115·1360. Found 135·0673. C_8H_9NO requires: 190·1231. Found 444·2691. $C_{24}H_{36}N_4O_4$ requires: 444·2736.

[29] J. HUTCHINSON, *The Families of Flowering Plants*, Vol. 1, Clarendon Press, Oxford (1959).
[30] R. F. RAFFAUF, *A Handbook of Alkaloids and Alkaloids Containing Plants*, Wiley–Interscience, New York (1970).

Hydrolysis of alkaloid A. Alkaloid A (10 mg) was refluxed at 110° for 12 hr in HOAc–HCl–H_2O (1:2:1, 1 ml). The residue, after evaporation to dryness over KOH, was dissolved in MeOH and examined by: (a) PC, Whatman No. 1, *n*-BuOH–HOAc–H_2O (4:1:5), ninhydrin, R_f leucine 0·68, *iso*leucine 0·65, hydrolysis product 0·68; (b) TLC, Cellulose (purified MN 300), *iso*PrOH–H_2O (3:1), ninhydrin, R_f leucine 0·71, *iso*leucine 0·64, hydrolysis product 0·71.

Identification of alkaloid B as franganine. Alkaloid B, colourless needles from ether, m.p. 240–242·5°(m.p. franganine 248°[22]); UV (EtOH), only end absorption 200–325 nm; IR ν 3280 cm^{-1} (NH), 1640 cm^{-1} (CONH), 1250 cm^{-1} (C–O–C); MS, *m/e* 500 (M^+, 0·07%), 499 (0·1%), 485 (M^+–Me, 0·3%), 471 (M^+–Et, 0·03%), 457 (M^+–Pr, 0·1%), 443 (0·2%), 387 (0·03%), 344, (0·15%), 303 (0·05%), 274 (0·1%), 210 (0·1%), 190 (0·3%), 182 (0·5%), 135 (3%), 115 (12%), 114 (100%), 97 (3·5%), 72 (7%); *m/e* 114 → 72, $m^*_{obs.}$ 45·5 ($m^*_{calc.}$ 45·5) hence R^1 = *iso*-butyl.[19] Accurate mass measurements. Found 115·1312. $C_7H_{17}N$ requires: 115·1360. Found 135·0673. C_8H_9NO requires: 135·0684. Found 190·1222. $C_{12}H_{16}NO$ requires: 190·1231. Found 444·2691. $C_{24}H_{36}N_4O_4$ requires: 444·2736.

Identification of alkaloid C as frangufoline. Alkaloid C, colourless needles from Et_2O, m.p. 235–245° (m.p. frangufoline 244°); UV (EtOH) λ_{max} 225 nm (log ϵ, 4·09) sh; IR ν 3260 cm^{-1} (NH), 1625 cm^{-1} (CONH), 1240 cm^{-1} (C – O – C); NMR (TFA) 60 MHz δ 7·4 (4H, *m*, aromatic protons), 7·05 (5H, *m*, aromatic protons), 6·10 (1H, *d J* 7 Hz C-2-proton), 6·6 (1H, obscured by aromatic protons, C-1-proton), 3·22 and 3·28 (6H, 2 *s*, 2 × NMe), 0·90–1·23 (12H, *m*, 4 × C-Me). MS, *m/e* 534 (M^+, 0·1%), 533 (0·15%), 519 (M^+–Me, 0·3%), 491 (M^+–Pr), 489 (M^+–HNMe, 1·5%), 443 (7%), 387 (0·1%), 344 (0·2%), 303 (1%), 274 (0·3%), 210 (0·25%), 190 (2%), 182 (0·55%), 149 (15%), 148 (100%), 135 (7%), 97 (3%), 91 (3%), 86 (7·5%). Accurate mass measurements. Found 534·317. $C_{31}H_{42}N_4O_4$requires: 534·3206. Found 444·2687. $C_{24}H_{36}N_4O_4$ requires: 444·2736. Found 190·1221. $C_{12}H_{16}NO$ requires: 190·1231. TLC on Silicagel G + Silica gel GF (90–10) identical with frangufoline and different from adouetine *Y'*; R_fs (a) $CHCl_3$–MeOH (97:3) frangufoline 0·85, adouetine *Y'* 0·81; (b) $CHCl_3$–Et_2O–MeOH (45:15:1) frangufoline 0·66, adouetine *Y'* 0·58; (c) $CHCl_3$ frangufoline 0·25, adouetine *Y'* 0·19.

Identification of alkaloid D as R-(−)-armepavine (XIII). Alkaloid D, colourless needles from MeOH–light petrol. m.p. 138–140°, (m.p. armepavine 143–145°[31]) oxalate m.p. 199–200° undepressed by admixture with an authentic sample of armepavine oxalate; UV (EtOH) λ_{max} 232 nm (log ϵ, 4·62), 285 nm (log ϵ, 4·22), λ_{min} 255 nm (log ϵ, 3·35), λ_{max} (NaOH) 292 nm; IR ν 3450 cm^{-1} (OH), 1610 cm^{-1} (C = C); NMR ($CDCl_3$) 60 MHz δ 6·59–7·0 (4H, *dd*, *J* 8·5 Hz C-2′, C-3′, C-5′, C-6′ protons), 6·59 (1H, *s*, C-5 proton), 6·02 (1H, *s*, C-8 proton), 3·86 (3H, *s*, OMe), 3·57 (3H, *s*, OMe), 2·55 (3H, *s*, NMe). MS *m/e* 313 (M^+, 1%), 312 (3%), 207 (96%), 206 (100%), 190 (34%), 191 (95%), 162 (38%), 107 (41%). TLC on Silica gel G identical with armepavine, R_fs (a) $CHCl_3$–C_6H_6–MeOH (5:4:1) 0·33; (b) EtOAc–*iso*PrOH–5·5% NH_4OH (9:7:4) 0·88; (c) EtOAc–*iso*PrOH–conc. NH_4OH (100:2:1) 0·25. ORD curve of alkaloid D ($CHCl_3$) consistent with *R*-(−)-armepavine.

Acknowledgements—We thank Mr. D. Carter and Dr. B. J. Millard of the School of Pharmacy, University of London, and Dr. M. Holub, Czechoslovak Academy of Science, Prague, for the determination of the mass spectra. We also thank Mr. P. Jenkins of Imperial College and Mr. G. McDonough of Chelsea College for determination of NMR spectra and Mr. R. Brown, Chelsea College for the formulae in this publication. We gratefully acknowledge generous gifts of alkaloid reference samples from Professors J. L. Beal and R. W. Doskotch (*R*-(−)-armepavine oxalate), Ohio State University, Dr. R. Goutarel (adouetine *Y'*), Gif-sur-Yvette, and Professor Tschesche (frangufoline), Bonn University. Professor E. J. Shellard is thanked for his continued interest in the work. One of us (D.W.B.) thanks the Ministry of Higher Education, Mission Department, Cairo, for financial support. We acknowledge the many helpful comments of Dr. N. G. Bisset during the preparation of the manuscript.

[31] S. R. JOHNS, J. A. LAMBERTON and H. J. TWEEDDALE, *Austral. J. Chem.* **22**, 1313 (1969).