BISBENZYLISOQUINOLINE ALKALOIDS

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The first comprehensive tabular review of the bisbenzylisoquinoline alkaloids was published by Guha *et al.* in this journal in early 1979 (110) and reported on the literature through 1977. This was followed by a second review, also published in this journal, which described the literature from 1978 through 1981 and was published in early 1983 (111).

This present review is concerned with the literature from 1982 through 1985 (*Chemical Abstracts* volumes **96** through **103**) and is presented principally in a tabular form as before (110,111). The numbers of the alkaloids and the structural-type nomenclature have been retained according to the previous reviews (110,111) in order to preserve a sense of literary consistency. Since the publication of the last tabular review of 1983 (111), approximately 32 new bisbenzylisoquinoline alkaloids have been isolated and characterized, and the structures of several alkaloids have been revised. The acquisition of additional physicochemical and spectral data for numerous alkaloids has likewise continued. An additional feature of this review is the inclusion of the secobisbenzylisoquinoline alkaloids. These alkaloids, which have been assigned numbers **257** through **271**, are presumed to be in vivo catabolic products of bisbenzylisoquinolines.

Each alkaloid in the tabular section is described according to its name, molecular formula, molecular weight, melting point, specific rotation, and available spectral data, the last of which may include ir, uv, ^{1}H-nmr, ^{13}C-nmr, cd, and ms spectra. The numbering of the skeleton and the systematic numerical classification describing the oxygenation and dimerization patterns of the alkaloids follow the convention established by Shamma and Moniot (226) as exemplified by:
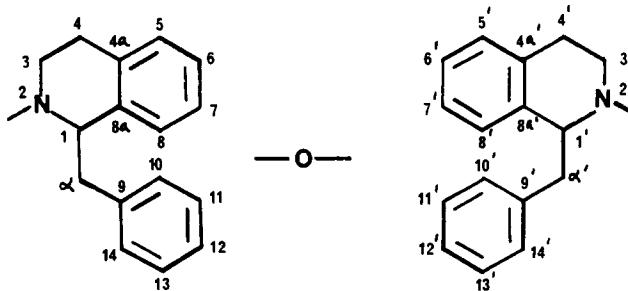

Unless otherwise stated, the uv spectra (nm, log ϵ) the cd spectra, and the ord spectra were obtained in MeOH, the ir spectra (cm^{-1}) in CHCl$_3$, and both the ^{1}H-nmr and ^{13}C-nmr spectra in CDCl$_3$. Chemical shifts are in δ units and coupling constants in Hz.

TABLE 1.   Revised Structures of Previously Reported Bisbenzylisoquinoline Alkaloids

52   THALRUGOSAMINE (Homoaromoline)   C$_{37}$H$_{40}$O$_6$N$_2$: 608.2886
Type VI (*R,S*) 6,7*,11^{+},12-6,7,8*,12^{+}

A reevaluation of the assignment of structure as published in 1972 (182) demonstrated an inconsistency in the structural representation (but not the actual work) of the alkaloid (110,111) with the revelation that (+)-thalrugosamine was in reality (+)-homoaromoline {**42**} (180).

42
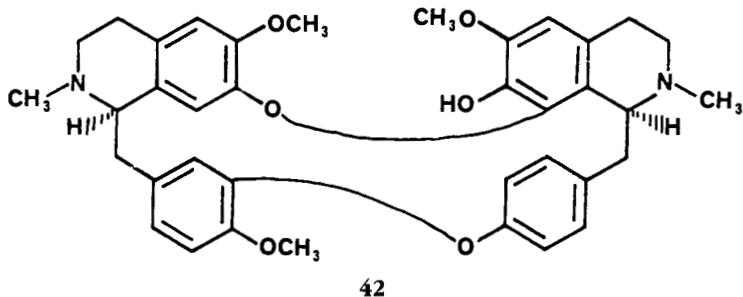
73 PHAEANTHARINE　　　　　　　　　　　　　　$C_{39}H_{40}O_6N_2^{++}$: 632.2886
Type I 6,7,11*,12-6,7,12*
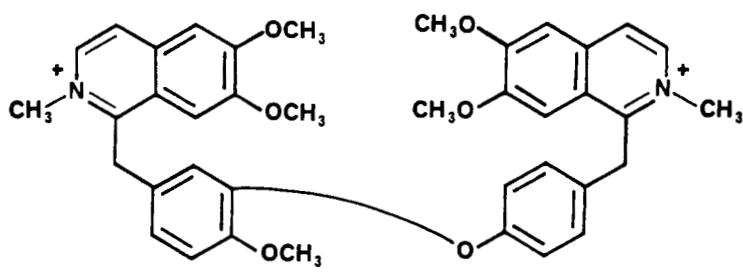
73

MP:　None reported (100)
TLC:　0.37 (Si60 F_{254}; MeOH-4M NH_4OH-1M NH_4NO_3 [7:2:1]); 0.00 (Si60 F_{254}; MeOH-H_2O-conc NH_4OH [8:1:1]) (100)
UV:　228,256,282,316,340 (sh) (100)
^1H nmr (CD$_3$OD):　NCH$_3$ 4.33 (6H); OCH$_3$ 3.70 (C-12), 3.89 (C-7 or C-7'), 3.99 (C-7' or C-7), 4.12 (C-6 or C-6'), 4.13 (C-6' or C-6); ArH 6.76 (H-11' and H-13'), (2H) (d) (J=8.5 Hz), 6.85 (H-10) (d) (J=1.8 Hz), 6.89 (H-14) (dd) (J=1.8, 8.5 Hz), 7.02 (H-10' and H-14') (2H) (d) (J=8.5 Hz), 7.05 (H-13), 7.65 (H-5 or H-5'), 7.67 (H-5' or H-4'), 7.69 (H-8 or H-8'), 7.74 (H-8' or H-8), 8.13 (H-4 or H-4') (d) (J=6.7 Hz), 8.16 (H-4' or H-4) (d) (J=6.7 Hz), 8.38 (H-3 or H-3') (d) (J=6.7 Hz), 8.41 (H-3' or H-3) (d) (J=6.7 Hz); H-α, H-α, H-α', H-α' were not observable {In D_2O at 62° two singlets at 4.80 (2H) and 4.85 (2H) were observed while in DMSO-d_6 two singlets at 5.01 and 5.04 were seen} (100)
^{13}C nmr (D_2O):　33.9 (t) (CH$_2$), 34.1 (t) (CH$_2$), 46.6 (q) (NCH$_3$), 46.6 (q) (NCH$_3$), 56.4 (q) (OCH$_3$), 56.8 (q) (OCH$_3$), 57.5 (q) (OCH$_3$), 57.5 (q) (OCH$_3$), 105.8 (d), 107.0 (d), 107.0 (d), 114.8 (d), 118.0 (d), 118.0 (d), 120.8 (d), 123.5 (d), 123.5 (d), 124.7 (s), 126.6 (d), 128.0 (s), 129.7 (s), 129.7, (s), 130.1 (d), 136.5 (d), 136.5 (d), 136.9 (s), 136.9 (s), 144.8 (s), 150.8 (s), 153.0 (s), 155.5 (s), 155.6 (s), 157.0 (s), 157.0 (s), 157.3 (s) (Due to the relative large symmetry of the isoquinoline rings, much signal overlap occurs, and a separate signal for every carbon atom was not observed) (100)
MS(FD):　633 (14), M$^+$ 632 (48), 631 (100)
SOURCES:　*Phaeanthus ebracteolatus* (Presl) Merill. (Menispermaceae) (100)
DERIVATIVES:　RR, RS, SR, SS O-Methyldauricine Mixture (Phaeantharine+NaBH$_4$) (uv, ^1H nmr, eims, fdms) (100)

84　THALISAMINE (*N'*-Norhernandezine)　　　　　　　　$C_{38}H_{42}O_7N_2$: 638.2992
Type IX (*S,S*) 5,6,7,8*,11$^+$,12-6,7*,12$^+$

212
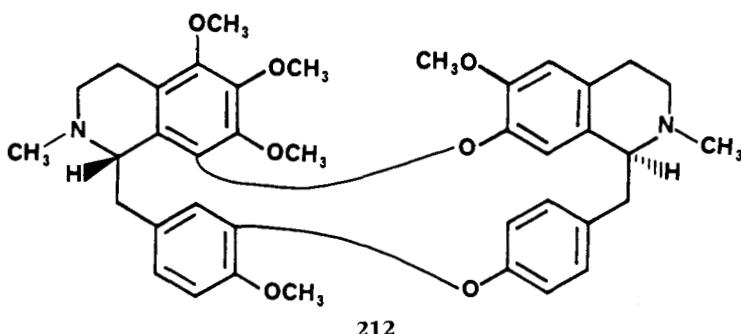
Thalisamine is in reality N'-norhernandizine (N-2′-norhernandezine) [**212**] and not N-2-norhernandezine as reported earlier (110,111,180,183).

116   NORTILIACORININE A $C_{35}H_{34}O_5N_2$: 562.2468
Type XVIII (S,S) 6,7*,8$^+$,12-6*,7$^+$,12(11-11)

116
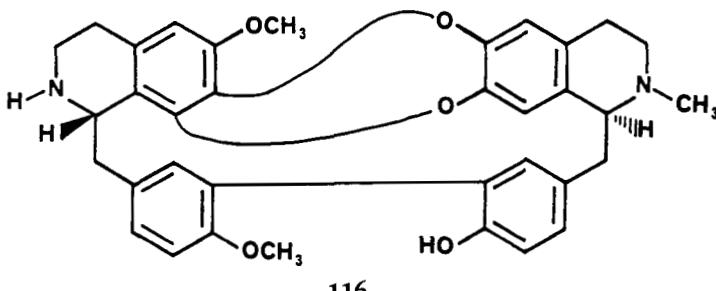
Assigned as a result of feedings of labelled precursors to intact plants (8).

TABLE 2.   Additional Physical and Spectral Data on Previously Reported
Bisbenzylisoquinoline Alkaloids

31   AROMOLINE(N-Methyldaphnoline)   ($C_{36}H_{38}O_6N_2$: 594.2730)
^{13}C nmr: 64.3 (C-1), 43.6 (C-3), 28.4 (C-4), 128.7 (C-4a), 111.2 (C-5), 148.2 (C-6), 143.3 (C-7), 117.3 (C-8), 124.3 (C-8a), 38.3 (C-α), 138.6 (C-9), 116.8 (C-10), 143.7 (C-11), 146.0 (C-12), 114.2 (C-13), 124.5 (C-14), 60.9 (C-1′), 45.0 (C-3′), 24.4 (C-4′), 122.9 (C-4a′), 104.7 (C-5′), 146.7 (C-6′), 133.4 (C-7′), 141.3 (C-8′), 122.7 (C-8a′), 40.0 (C-α′), 130.6 (C-9′), 128.6 (C-10′), 121.4 (C-11′), 152.6 (C-12′), 120.5 (C-13′), 131.3 (C-14′), 41.8 (NCH$_3$), 41.8 (NCH$_3$), 55.3 (OCH$_3$), 56.1 (OCH$_3$), 56.1 (OCH$_3$) (52)

37   DAPHNANDRINE   ($C_{36}H_{38}O_6N_2$: 594.2730)
^{13}C nmr: 55.0 (C-1), 39.3 (C-3), 29.9 (C-4), 129.1 (C-4a), 112.2 (C-5), 148.5 (C-6), 144.1 (C-7), 116.4 (C-8), 127.9 (C-8a), 42.6 (C-α), 139.3 (C-9), 116.2 (C-10), 146.2 (C-11), 149.5 (C-12), 110.9 (C-13), 123.0 (C-14), 61.3 (C-1′), 45.3 (C-3′), 24.8 (C-4′), 122.9 (C-4a′), 104.7 (C-5′), 147.0 (C-6′), 133.6 (C-7′), 141.7 (C-8′), 123.4 (C-8a′), 39.8 (C-α′), 130.9 (C-9′), 127.9 (C-10′), 121.9 (C-11′), 151.9 (C-2′), 120.8 (C-13′), 131.0 (C-14′), 41.9 (NCH$_3$), 55.2 (OCH$_3$), 56.1 (OCH$_3$) (52)

37 derivative   0-METHYLDAPHNANDRINE (N-2-Norobaberine)   ($C_{37}H_{40}O_6N_2$: 608.2886)

^{13}C nmr: 54.8 (C-1), 38.9 (C-3), 29.6 (C-4), 128.2 (C-4a), 111.7 (C-5), 148.3 (C-6), 144.7 (C-7), 115.7 (C-8 or C-10), 127.9 (C-8a), 42.3 (C-α), 139.3 (C-9), 115.9 (C-10 or C-8), 147.0 (C-11), 149.5 (C-12), 110.8 (C-13), 123.0 (C-14), 61.5 (C-1′), 45.3 (C-3′), 25.2 (C-4′), 127.5 (C-4a′), 105.7 (C-5′), 151.3 (C-6′), 137.5 (C-7′), 147.9 (C-8′), 122.7 (C-8a′ or C-11′), 39.8

(C-α'), 130.7 (C-9'), 127.6 (C-10'), 122.1 (C-11' or C-8a'), 151.6 (C-12'), 120.8 (C-13'), 131.1 (C-14'), 41.3 (NCH$_3$), 54.8 (OCH$_3$), 55.9 (OCH$_3$), 60.3 (C-7' OCH$_3$) (52)

38 DAPHNOLINE   (C$_{35}$H$_{36}$O$_6$N$_2$: 580.2574)
^{13}C nmr: 54.7 (C-1), 38.5 (C-3), 29.0 (C-4), 128 (C-4a), 111.8 (C-5), 148.3 (C-6), 144.0 (C-7), 116.3
        (C-8), 127.2 (C-8a), 42.0 (C-α), 138.7 (C-9), 115.8 (C-10), 144.0 (C-11), 145.9 (C-12), 114.7
        (C-13), 123.2 (C-14), 60.8 (C-1'), 44.6 (C-3'), 23.6 (C-4), 121.9 (C-4a'), 104.5 (C-5'), 147.9
        (C-6'), 133.6 (C-7'), 141.2 (C-8'), 121.9 (C-8a'), 39.9 (C-α'), 130.2 (C-9'), 127.7 (C-10'),
        121.7 (C-11'), 151.6 (C-12'), 120.4 (C-13'), 130.9 (C-14'), 41.8 (NCH$_3$), 55.0 (OCH$_3$), 55.9
        (OCH$_3$) (52)
[α]^{25}D: +273° (c=0.15, CHCl$_3$) (175)
MS: M+1 581 (10), 579 (100), 473 (3), 368 (20), 367 (32), 353 (19), 335 (3), 192 (16), 184 (17), 162
        (5) (175)

40 or 41   (+)-EPISTEPHANINE or (−)-EPISTEPHANINE (stereochemistry not specified)
                                                                        (C$_{37}$H$_{38}$O$_6$N$_2$: 606.2730)

^{13}C nmr: 63.3 (C-1), 46.4 (C-3), 26.9 (C-4 or C-4'), 130.2 (C-4a), 111.1 (C-5), 147.1 (C-6), 149.1
        (C-7), 113.7 (C-8), 37.7 (C-α or C-α'), 130.8 (C-9), 116.8 (C-10), 144.3 (C-11), 145.7 (C-
        12), 110.3 (C-13), 122.8 (C-14), 164.2 (C-1), 49.8 (C-3'), 22.8 (C-4' or C-4), 135.1 (C-4a'),
        105.9 (C-5'), 154.9 (C-6'), 138.2 (C-7'), 147·4 (C-8'), 44.4 (C-α' or C-α), 134.8 (C-9'),
        127.8 (C-10'), 121.5 (C-11' or C-13'), 152.2 (C-12'), 122.0 (C-13' or C-11'), 131.4 (C-14'),
        43.1 (NCH$_3$) (96)

43 HYPOEPISTEPHANINE   (C$_{36}$H$_{36}$O$_6$N$_2$: 592.2573)
^{13}C nmr: 63.1 (C-1), 46.0 (C-3), 27.0 (C-4 or C-4'), 130.3 (C-4a), 111.1 (C-5), 147.1 (C-6), 149.1
        (C-7), 113.7 (C-8), 37.9 (C-α or C-α'), 128.8 (C-9), 116.8 (C-10), 144.3 (C-11), 145.7 (C-
        12), 114.6 (C-13), 123.2 (C-14), 164.6 (C-1'), 49.2 (C-3'), 27.3 (C-4' or C-4), 135.6 (C-4a'),
        105.7 (C-5'), 155.1 (C-6'), 138.1 (C-7'), 147.7 (C-8'), 44.0 (C-α' or C-α), 134.7 (C-9'),
        127.3 (C-10'), 121.4 (C-11'), 152.3 (C-12'), 131.5 (C-13'), 134.7 (C-14'), 43.0 (NCH$_3$) (96)

45 0-METHYLREPANDINE   (C$_{38}$H$_{42}$O$_6$N$_2$: 622.3043)
^{13}C nmr: 65.5 (C-1), 46.6 (C-3), 23.2 C-4), 131.1 (C-4a), 112.5 (C-5), 149.0 (C-6), 144.5 (C-7),
        120.3 (C-8), 127.6 (C-8a), 43.6 (C-α), 137.9 (C-9), 120.3 (C-10), 148.5 (C-11 or C-12),
        148.6 (C-12 or C-11), 113.3 (C-13), 123.4 (C-14), 60.5 (C-1'), 44.4 (C-3'), 26.4 (C-4'),
        127.6 (C-4a'), 106.8 (C-5'), 151.9 (C-6'), 136.0 (C-7'), 148.5 (C-8'), 121.9 (C-8a'), 40.6 (C-
        α'), 133.9 (C-9'), 129.9 (C-10'), 120.3 (C-11'), 155.4 (C-12'), 121.7 (C-13'), 131.4 (C-14'),
        41.6 (2'-NCH$_3$), 42.2 (2-NCH$_3$), 56.3 (OCH$_3$), 55.7 (OCH$_3$), 59.7 (C-7' OCH$_3$) (52)

49 REPANDINE   (C$_{37}$H$_{40}$O$_6$N$_2$: 608.2886)
^{13}C nmr: 65.4 (C-1), 46.1 (C-3), 22.5 (C-4), 130.9 (C-4a), 112.1 (C-5), 148.9 (C-6), 144.2 (C-7),
        119.8 (C-8), 127.2 (C-8a), 43.8 (C-α), 137.5 (C-9), 119.4 (C-10), 146.5 (C-11), 145.9 (C-12),
        116.7 (C-13), 123.7 (C-14), 59.7 (C-1'), 43.8 (C-3'), 25.9 (C-4'), 127.0 (C-4a'), 106.5 (C-
        5'), 151.2 (C-6'), 136.0 (C-7'), 148.3 (C-8'), 121.1 (C-8a'), 40.7 (C-α'), 132.3 (C-9'), 129.9
        (C-10'), 120.1 (C-11'), 155.0 (C-12'), 121.6 (C-13'), 131.4 (C-14'), 41.1 (2-NCH$_3$), 41.8
        (2'-NCH$_3$), 54.9 (OCH$_3$), 55.4 (OCH$_3$), 59.4 (C-7' OCH$_3$) (52)

64 LIMACINE   (C$_{37}$H$_{40}$O$_6$N$_2$: 608.2886)
^{13}C nmr: 61.2 (C-1), 44.0 (C-3), 21.8 (C-4), 122.8 (C-4a), 104.7 (C-5), 145.7 (C-6), 134.5 (C-7),
        141.8 (C-8), 123.2 (C-8a), 37.9 (C-α or C-α'), 134.7 (C-9), 115.9 (C-10), 143.4 (C-11), 146.7
        (C-12), 111.2 (C-13), 122.5 (C-14), 63.5 (C-1'), 44.0 (C-3'), 25.0 (C-4'), 27.6 (C-4a'), 112.0
        (C-5'), 148.4 (C-6'), 149.0 (C-7'), 128.1 (C-8a'), 41.7 (C-α' or C-α), 134.8 (C-9'), 129.8 (C-
        10'), 121.6 (C-11'), 153.4 (C-12'), 121.6 (C-13'), 132.2 (C-14'), 42.1 (N-2 or N-2' NCH$_3$),
        42.2 (N-2' or N-2 NCH$_3$), OCH$_3$ signals not reported (96)

68 NORBERBAMINE   (C$_{36}$H$_{38}$O$_6$N$_2$: 594.2730)
MS: M$^+$594 (41), 593 (42), 382 (21), 381 (100), 367 (14), 192 (17), 191 (68), 190 (21), 174 (22), 168
        (18) (175)
CD: Positive tail, −5 (215), 0 (220), +27 (238), 0 (240), −14 (246), −1.5 (sh) (258), 0 (275), +4
        (284), 0 (302) (175)

71   OBAMEGINE $(C_{36}H_{38}O_6N_2: 594.2730)$

^{1}H nmr: NCH$_3$ 2.33 (N-2), 2.50 (N-2'), OCH$_3$ 3.79 (C-6), 3.94 (C-6'), ArH 6.07 (H-8'), 6.24 (d, J=2.2 Hz) (H-10), 6.37 (H-5), 6.44 (dd, J=2.9 and 8.6 Hz) (H-10'), 6.62 (dd, J=2.2 and 8.6 Hz) (H-14), 6.75 (d, J=8.6 Hz) (H-5'), 6.77 (H-13), 6.84 (dd, J=2.9 and 8.6 Hz) (H-11'), 7.11 (dd, J=2.9 and 8.6 Hz) (H-13'), 7.33 (dd, J=2.9 and 8.6 Hz) (H-14') (16)

72   PENDULINE $(C_{37}H_{40}O_6N_2: 608.2886)$

MS: M$^+$ 608 (100), 607 (76), 416 (11), 396 (29), 395 (96), 381 (49), 364 (10), 349 (6), 198 (92), 175 (26), 174 (52) (175)

CD: Negative tail, 0 (209), +54 (225), 0 (242), −4 (246), 0 (251), +5 (285), 0 (310) (175), +58.47 (225), −6.40 (247), +5.40 (287) (122)

76   TETRANDRINE $(C_{38}H_{42}O_6N_2: 622.3043)$

^{13}C nmr: 61.2 (C-1), 44.0 (C-3), 21.9 (C-4), 127.7 (C-4a), 105.5 (C-5), 151.1 (C-6), 137.6 (C-7), 148.1 (C-8), 127.7 (C-8a), 38.2 (C-α or C-α'), 134.9 (C-9), 116.0 (C-10), 143.5 (C-11), 146.7 (C-12), 111.3 (C-13), 122.4 (C-14), 63.8 (C-1'), 45.2 (C-3'), 25.2 (C-4'), 127.9 (C-4a'), 112.5 (C-5'), 148.2 (C-6'), 149.1 (C-7'), 119.1 (C-8'), 127.9 (C-8a'), 41.8 (C-α' or C-α), 134.7 (C-9'), 129.8 (C-10'), 121.6 (C-11'), 153.4 (C-12'), 121.6 (C-13'), 132.4 (C-14'), 42.1 (N-2 or N-2' NCH$_3$), 42.5 (N-2' or N-2 NCH$_3$), OCH$_3$ signals not reported (96)

CD: 0 (210), +70 (223), 0 (242), −5 (245), 0 (253), +5.7 (280), 0 (310) (175)

81   HERNANDEZINE $(C_{39}H_{44}O_7N_2: 652.3149)$

^{13}C nmr: 61.3 (C-1 or C-1'), 43.5 (C-3), 16.4 (C-4), 121.6 (C-4a), 145.3 (C-5), 142.2 (C-6), 149.1 (C-7), 144.2 (C-8), 125.5 (C-8a), 37.8 (C-α), 134.7 (C-9), 116.0 (C-10), 143.5 (C-11), 146.8 (C-12), 111.4 (C-13), 122.6 (C-14), 63.7 (C-1' or C-1), 45.2 (C-3'), 25.4 (C-4'), 127.9 (C-4a'), 112.5 (C-5'), 148.1 (C-6'), 149.1 (C-7'), 120.0 (C-8'), 128.3 (C-8a'), 41.7 (C-α'), 134.9 (C-9'), 129.9 (C-10'), 121.7 (C-11'), 153.5 (C-12'), 121.7 (C-13'), 132.4 (C-14'), 42.3 (N-2 or N-2' NCH$_3$), 42.6 (N-2 or N-2' NCH$_3$), OCH$_3$ signals not reported (96)

110   PANURENSINE $(C_{37}H_{40}O_6N_2: 608.2886)$

^{13}C nmr: 64.8 (C-1 or C-1'), 44.0 (C-3), 18.5 (C-4), 119.4 (C-4a), 138.6 (C-5), 136.6 (C-6), 144.0 (C-7), 108.6 (C-8), 39.4 (C-α or C-α'), 131.5 (C-9), 118.6 (C-10), 145.0 (C-11), 146.7 (C-12), 113.3 (C-13), 121.5 (C-14), 66.2 (C-1' or C-1), 46.8 (C-3'), 26.1 (C-4'), 125.5 (C-4a'), 111.3 (C-5'), 146.8 (C-6'), 148.5 (C-7'), 112.7 (C-8'), 40.5 (C-α' or C-α), 137.2 (C-9'), 130.2 (C-10'), 121.5 (C-11'), 152.5 (C-12'), 121.5 (C-13'), 130.2 (C-14'), 41.5 (N-2 or N-2' NCH$_3$), 41.8 (N-2' or N-2 NCH$_3$) (96)

112   THALIBRUNIMINE $(C_{38}H_{40}O_8N_2: 652.2785)$

^{13}C nmr: 61.5 (C-1), 42.9 (C-3), 16.5 (C-4), 121.0 (C-4a), 146.0 (C-5), 143.0 (C-6 or C-7), 142.9 (C-7 or C-6), 144.7 (C-8), 38.8 (C-α or C-α'), 118.3 (C-9), 44.3 (C-10), 142.9 (C-11), 151.6 (C-12), 102.3 (C-13), 122.9 (C-14), 167.0 (C-1'), 47.0 (C-3'), 25.8 (C-4'), 133.9 (C-4a'), 110.9 (C-5'), 147.8 (C-6'), 147.8 (C-7'), 124.0 (C-8'), 43.8 (C-α' or C-α), 134.9 (C-9'), 129.5 (C-10'), 118.3 (C-11'), 154.3 (C-12'), 117.9 (C-13'), 130.2 (C-14'), 40.7 (NCH$_3$), OCH$_3$ signals not reported (96) [Note: These assignments were based on the original structure proposed for thalibrunimine (110) and not the revised structure (111)]

113   THALIBRUNINE $(C_{39}H_{44}O_8N_2: 668.3098)$

^{13}C nmr: 61.2 (C-1), 42.3 (C-3), 14.9 (C-4), 120.4 (C-4a), 144.8 (C-5), 142.3 (C-6), 144.8 (C-7), 145.1 (C-8), 122.2 (C-8a), 38.0 (C-α), 119.9 (C-9), 143.5 (C-10), 141.5 (C-11), 152.3 (C-12), 101.5 (C-13), 121.7 (C-14), 64.1 (C-1'), 44.9 (C-3'), 24.9 (C-4'), 128.1 (C-4a'), 112.0 (C-5'), 148.1 (C-6'), 149.1 (C-7'), 126.4 (C-8'), 128.1 (C-8a'), 42.3 (C-α'), 133.1 (C-9'), 129.6 (C-10'), 157.2 (C-11'), 120.6 (C-12'), 132.5 (C-13'), 133.1 (C-14'), 39.4 (N-2 NCH$_3$), 40.1 (N-2' NCH$_3$), OCH$_3$ signals not reported (96) [Note: These assignments were based on the original structure proposed for thalibrunine (110) and not the revised structure (111)]

120   TILIAMOSINE $(C_{36}H_{36}O_6N_2: 592.2573)$

MP: 167-170° (CHCl$_3$/MeOH) (amorph.) (120)

$[\alpha]^{25}$D: +267° (c=0.48, CHCl$_3$) (120)

UV: 235 (sh) (4.70), 290 (3.98) (120)

IR (KBr):   2940, 2840, 2800, 1590, 1505, 1480, 1460, 1435, 1415, 1365, 1330, 1305, 1280, 1240,

1205, 1180, 1140, 1120, 1110, 1090, 1055, 1030, 1020, 990, 970, 955, 940, 925, 900, 865, 835, 820, 755 (120)

^{1}H nmr: NCH$_3$ 2.32, OCH$_3$ 3.83, 3.94, 3.98, ArH 6.66, 6.97 (d) (1H) (J=8.5 Hz), 7.00 (d) (1H) (J=8.5 Hz), 7.32 (dd) (1H) (J=2.2, 8.1 Hz), 7.35 (dd) (1H) (J=2.2, 8.5 Hz), 7.62 (d) (1H) (1.8 Hz), 7.69 (d) (1H) (J=2.2 Hz), 8.13 (120)

MS: M$^+$ 592, 591, 366, 365, 351, 211, 183 (100) (120)

DERIVATIVES: N,O-Diacetyltiliamosine (Tiliamosine+Ac$_2$O+pyridine) (120)

MP: 182-184° (CHCl$_3$) (120)

$[\alpha]^{25}$D: +423° (c=0.35, CHCl$_3$) (120)

UV: 236 (sh) (4.59), 291 (3.79) (120)

IR (KBr):   1765, 1645 (120)

^{1}H nmr: OCOCH$_3$ 2.13, NCH$_3$ 2.24, NCOCH$_3$ 2.24, OCH$_3$ 3.81 (s) (6H), 3.84, ArH 6.61, 6.79-7.95 (m) (6H), 8.05 (120)

MS: M$^+$676, 634, 408, 393, 366, 365, 211, 183 (100) (120)

130 derivative   (*R,S*)-DIMETHYLCHONDROCURINE   (C$_{38}$H$_{42}$O$_6$N$_2$: 622.3043)
           (Prepared via treatment of (*R,S*)-chondrocurine with CH$_2$N$_2$) (198)

^{13}C nmr: 61.1 (C-1), 43.3 (C-3), 21.7 (C-4), 129.8 (C-4a), 109.1 (C-5), 152.0 (C-6), 140.2 (C-7), 145.2 (C-8), 124.4 (C-8a), 39.5 (C-α), 132.3 (C-9), 122.7 (C-10), 144.6 (C-11), 149.3 (C-12), 112.5 (C-13 or C-5'), 125.7 (C-14), 65.2 (C-1'), 45.3 (C-3'), 24.4 (C-4'), 126.2 (C-4a'), 112.1 (C-5' or C-13), 148.5 (C-6'), 143.2 (C-7'), 116.3 (C-8'), 129.8 (C-8a'), 39.5 (C-α'), 132.3 (C-9'), 134.7 (C-10' or C-14'), 115.2 (C-11'), 155.8 (C-12'), 113.2 (C-14'), 134.2 (C-14' or C-10'), 41.5 (NCH$_3$), 41.6 (NCH$_3$), 55.9 (OCH$_3$), 56.0 (OCH$_3$), 60.6 (C-7 OCH$_3$) (198)

131   (−)-CHONDROFOLINE   (C$_{37}$H$_{40}$O$_6$N$_2$: 608.2886)
^{1}H nmr: ArH 5.84 (H-8'), 6.36 (dd) (1H) (J=2.0, 8.2 Hz) (H-10'), 6.61 (H-5), 6.67 (m) (2H) (H-11' and H-13'), 6.73 (d) (1H) (J=1.8 Hz) (H-10), 6.79 (H-5'), 6.87 (d) (1H) (J=8.2 Hz) (H-13), 7.04 (dd) (1H) (J=1.8, 8.2 Hz) (H-14), 7.29 (dd) (1H) (J=2.0, 8.1 Hz) (H-14') (193)

133   (−)CURINE   (C$_{36}$H$_{38}$O$_5$N$_2$: 594.2730)
^{1}H nmr: ArH 5.97 (H-8'), 6.46 (dd) (1H) (J=1.9, 8.2 Hz) (H-10'), 6.55 (H-5), 6.61 (d) (1H) (J=1.8 Hz) (H-10), 6.69 (H-5'), 6.66-6.73 (m) (2H) (H-11' and H-13'), 6.82 (d) (1H) (J=8.3 Hz) (H-13), 6.96 (dd) (1H) (J=1.8, 8.3 Hz) (H-14), 7.11 (dd) (1H) (J=1.9, 8.2 Hz) (H-14') (193)

152   COCSOLINE   (C$_{34}$H$_{32}$O$_5$N$_2$: 548.2311)
MS: M$^+$548 (57), 547 (57), 349 (4), 335 (100), 334 (27), 321 (26), 305 (13), 168 (6), 107 (4) (175)
CD: Negative tail 0 (215), +32 (229), 0 (251), +1 (252), +9 (290), 0 (315) (175)

153   COCSULINE   (C$_{35}$H$_{34}$O$_5$N$_2$: 562.2468)
CD: +44 (239), +11 (292) (122)
        Negative tail, 0 (214), +27 (232), +2 (250), +7.3 (292), 0 (320) (175)

157   ISOTRILOBINE   (C$_{36}$H$_{36}$O$_5$N$_2$: 576.2624)
UV: 234 (4.56), 287 (3.65) (175)
MS: M$^+$576 (22), 575 (15), 349 (100), 335 (44), 319 (7), 175 (59) (175)
CD: Negative tail, 0 (213), +31 (234), +2 (251), +8 (290), 0 (320) (175)

161   TRICORDATINE   (C$_{34}$H$_{32}$O$_5$N$_2$: 548.2311)
CD: Negative tail, 0 (218), +9 (234), 0 (255), +2.3 (sh) (270), +2.5 (290), 0 (310) (175)

168   REPANDULINE   (C$_{37}$H$_{36}$O$_7$N$_2$: 620.2523)
^{1}H nmr: NCH$_3$ 2.40 (N-2), 2.65 (N-2'), OCH$_3$ 3.62, CH$_2$O$_2$ 5.92 +5.97, AlH 2.9-3.0 (H-1), 2.9-3.05 (H-3eq), 2.4-2.6 (H-3ax), 1.95-2.15 (H-4eq), 2.3-2.5 (H-4ax), 4.15 (H$_A$), 3.88 (H$_B$), 2.95-3.10 (H-α), 2.90-3.05 (H-α), 3.30-3.38 (H-α'), 2.63-2.73 (H-α'), ArH 5.11 (H-8'), 5.54 (H-5), 6.08 (H-14), 6.49 (H-5'), 6.73 (H-14'), 6.77 (H-10), 6.92 (H-13'), 7.12 (H-11'), 7.37 (H-10') (112) [NOE difference experiments in both CDCl$_3$ and C$_6$D$_6$ (20%) in CDCl$_3$ allowed the establishment of regioisomerism, relative stereochemistry, and solution conformation of the alkaloid (112)]

190   CALAFATINE   (C$_{39}$H$_{44}$O$_7$N$_2$: 652.3149)

TLC: 0.34 (Si gel F$_{254}$, CHCl$_3$-MeOH-NH$_4$OH [95.5:0.5]) (146)
[α]D: −154° (c=0.28, CHCl$_3$) (146)
^{1}H nmr: NCH$_3$ 2.35 (N-2'), 2.59 (N-2), OCH$_3$ 3.29 (C-7), 3.68 (C-6), 3.73 (C-10), 3.75 (C-6'),
            3.84 (C-12), ArH 5.39 (H-8'), 5.90 (1H), 6.35 (1H) (dd) (J=2.1, 8.5 Hz) (H-11') (dd)
            (J=2.1, 8.5 Hz) (H-10'), 6.36 (H-5'), 6.51 (H-5), 6.72 (1H) (d) (J=8.5 Hz) (H-13), 6.92
            (1H) (d) (J=8.5 Hz) (H-14), 6.92 (1H) (dd) (J=2.1, 8.5 Hz) (H-13'), 7.11 (1H) (dd) (J=2.1,
            8.5 Hz) (H-14') (146)
MS: M$^+$ 652 (41), 651 (34), 637 (10), 396 (36), 395 (88), 381 (100), 198 (69), 192 (4), 174 (72) (162)
CD: 0 (212), +10 (219), 0 (225), −18 (234), 0 (242), +9 (247), 0 (300) (146)
SOURCE: *Berberis buxifolia* Lam. (Berberidaceae) (146)
DERIVATIVES: Birch reduction (Na/NH$_3$) afforded S-(+)-2-methyl-6,7,2',4'-tetramethoxy-1-ben-
            zyl-1,2,3,4-tetrahydroisoquinoline + R-(−)-N-methylcoclaurine (146).
NOTE: The specific rotation is negative (146) and not positive as reported earlier (148). In addition, the
            cleavage products allow the assignment of absolute configuration as S,R (146).

193   1,2-DEHYDROAPATELINE   (C$_{34}$H$_{30}$N$_2$O$_5$: 560.3211)
MS: M$^+$ 546 (70), 545 (100), 349 (1.6), 335 (2), 333 (8), 273 (9) (175)
CD: Negative tail, 0 (217), +38 (225), 0 (255), −2 (260), 0 (263), +7 (272), +1.6 (290), +4 (305), 0
            (350) (175)

207   *N*-METHYLAPATELINE   (C$_{35}$H$_{34}$O$_5$N$_2$: 562.2468)
CD: Negative tail, 0 (210), +51 (228), 0 (243), −2 (245), 0 (250), +9 (272), 0 (320) (175)

218   BERBACOLORFLAMMINE (1,2,3,4-Tetradehydrolimacine)   (C$_{37}$H$_{37}$O$_6$N$_2$: 605.2652)
TLC: 0.44 (Si gel, CHCl$_3$-MeOH-NH$_4$OH [14:5:1]) and stained with iodoplatinate reagent (15). Ex-
            tinction at 254nm and orange fluorescence at 366nm (15)
[α]D: +1000° (c=0.004, CHCl$_3$) (15)
UV: 234, 294, 338, 445 (15); 228, 268, 275, 323, 372 (acidic MeOH) (15)
^{1}H nmr: NCH$_3$ 2.57 (N-2'), 3.53 (N-2), OCH$_3$ 3.85, 3.90 (6H), OH 4.08 (br), AlH 5.65 (1H), ArH
            6.10-7.52 (15)
^{13}C nmr: 25.6 (t, C-4'), 35.4 (t), 35.8 (t), 42.3 (q, N-2' CH$_3$), 45.6 (t, C-3'), 46.2 (q, N-2 CH$_3$),
            55.9 (q, OCH$_3$), 56.2 (q, OCH$_3$), 56.2 (q, OCH$_3$), 63.9 (d, C-1'), 100.8 (d), 112.1 (d), 112.2
            (d), 119.4 (d), 119.4 (s), 121.4 (d), 121.5 (d), 123.0 (s), 123.1 (d), 127.0 (s), 127.4 (s), 128.3
            (s), 129.7 (d), 129.8 (s), 132.0 (d), 135.0 (s), 138.5 (s), 143.4 (s), 148.3 (s), 148.6 (s), 149.0
            (s), 150.0 (s), 155.5 (s), 162.5 (s) (15)
MS(FD):   M$^+$ 605 (15)
DERIVATIVES: Limacine (S,S) (Berbacolorflammine + NaBH$_4$) (15)
            Trideuterioberbacolorflammine (Berbacolorflammine + NaBD$_4$ in C$_2$H$_5$OD + D$_2$O) (15)

219   COLORFLAMMINE (1,2,3,4-Tetradehydrolimacusine)   (C$_{37}$H$_{37}$O$_6$N$_2$: 605.2652)
TLC: 0.48 (Si gel, CHCl$_3$-MeOH-NH$_4$OH [14:5:1]) and stained with iodoplatinate reagent (15)
            Extinction at 254nm and orange fluorescence at 366nm (15)
[α]^{20}D: +1050° (c=0.06, CHCl$_3$) (15)
UV: 233, 292, 333, 439 (15); 244, 267, 326, 374 (acidic Me$_3$OH) (15)
IR: (KBr) 3410, 2910, 1492 (15)
^{1}H nmr: NCH$_3$ 2.45 (N-2), 3.86 (N-2'), OCH$_3$ 3.86, 4.01, 4.08, OH 4.34 (br), AlH 4.74 (1H), 5.92
            (1H), ArH 6.04-7.71 (15)
^{13}C nmr: 25.1 (t, C-4), 35.9 (t), 37.6 (t), 42.0 (q, N-2 CH$_3$), 46.2 (q, N-2' CH$_3$), 47.5 (t, C-4), 55.5
            (q, OCH$_3$), 55.8 (q, OCH$_3$), 56.0 (q, OCH$_3$), 62.6 (d, C-1), 102.3 (d), 110.7 (d), 111.1 (d),
            112.0 (d), 116.1 (d), 120.0 (d), 122.2 (d), 122.9 (d), 123.6 (d), 123.6 (d), 124.1 (d), 126.2 (d),
            126.2 (s), 129.4 (s), 129.6 (s), 130.6 (d), 131.2 (d), 132.6 (s), 134.5 (s), 143.4 (s), 146.5 (s),
            147.3 (s), 148.7 (s), 149.1 (s), 153.3 (s), 153.7 (s), 161.6 (s, C-1') (15)
MS (FD):   M$^+$ 605 (15)
DERIVATIVES: Limacusine (S,S) (Colorflammine + NaBH$_4$) (15)
            Trideuteriocolorflammine (Colorflammine + NaBD$_4$ in C$_2$H$_5$O + D$_2$O) (15)

TABLE 3.   Known Natural Bisbenzylisoquinoline Alkaloids Reisolated from New Sources

3   DAURICINE   (C$_{38}$H$_{44}$O$_6$N$_2$: 624.3199)
            Menispermum dauricum DC. (Menispermaceae) (113)

Polyalthia nitidissima Benth. (Annonaceae) (128)

10 GRISABINE   ($C_{37}H_{42}O_6N_2$: 610.3043)
   Sciadotenia eichleriana Moldenke (Menispermaceae) (197)

11 LINDOLDHAMINE   ($C_{34}H_{36}O_6N_2$: 568.2573)
   Albertisia papuana Becc. (Menispermaceae) (125)
   Polyalthia nitidissima Benth. (Annonaceae) (128)

12 MAGNOLINE   ($C_{36}H_{40}O_6N_2$: 596.2886)
   Michelia fuscata Blume (Magnoliaceae) (9)

14b THALIRUGINE   ($C_{38}H_{44}O_7N_2$: 640.3149)
   Thalictrum minus L. var. *microphyllum* Boiss. (Ranunculaceae) (180)

15 MAGNOLAMINE   ($C_{37}H_{42}O_7N_2$: 626.2992)
   Berberis empetrifolia Lam. (Berberidaceae) (24)
   Michelia fuscata Blume (Magnoliaceae) (9)

16 N-DESMETHYLTHALISTYLINE   ($C_{40}H_{46}O_8N_2$: 682.3254)
   Thalictrum baicalense Turcz. (Ranunculaceae) (174)

17a THALIRABINE (5-O-Demethylthalistyline)   ($C_{40}H_{47}O_8N_2^{+}X^{-}$: 683.3332)
   Thalictrum baicalense Turcz. (Ranunculaceae) (174)

31 AROMOLINE   ($C_{36}H_{38}O_6N_2$: 594.2730)
   Albertisia papuana Becc. (Menispermaceae) (125)
   Berberis aristata DC. (Berberidaceae) (156)
   Thalictrum minus L. var. *microphyllum* Boiss. (Ranunculaceae) (180)

34 CEPHARANTHINE   ($C_{37}H_{38}O_6N_2$: 606.2730)
   Stephania erecta Craib. (Menispermaceae) (47)

38 DAPHNOLINE   ($C_{35}H_{36}O_6N_2$: 580.2573)
   Albertisia papuana Becc. (Menispermaceae) (125)
   Cocculus pendulus (Forsk) Diels (Menispermaceae) (175)

42 HOMOAROMOLINE   ($C_{37}H_{40}O_6N_2$: 608.2886)
   Albertisia papuana Becc. (Menispermaceae) (125)
   Arcangelisia flava (L.) Merr. (Menispermaceae) (60)
   Stephania erecta Craib. (Menispermaceae) (47)
   Thalictrum minus L. var. *microphyllum* Boiss. (Ranunculaceae) (180)

46 OBABERINE   ($C_{38}H_{42}O_6N_2$: 622.3043)
   Albertisia papuana Becc. (Menispermaceae) (125)
   Laurelia sempervirens R. et P. (Monimiaceae) (210)
   Mahonia repens (Lindl.) G. Don (Berberidaceae) (16)
   Pseudoxandra aff. *lucida* Fries (Annonaceae) (196)
   Stephania sasakii Hayata (Menispermaceae) (192)
   Thalictrum minus L. var. *microphyllum* Boiss. (Ranunculaceae) (14)

48 OXYACANTHINE   ($C_{37}H_{40}O_6N_2$: 608.2886)
   Albertisia papuana Becc. (Menispermaceae) (125)
   Berberis aristata DC. (Berberidaceae) (156)
   Berberis chitria D. Don (Berberidaceae) (203)
   Berberis lycium Royle (Berberidaceae) (221)
   Laurelia sempervirens R. et P. (Monimiaceae) (210)
   Mahonia repens (Lindl.) G. Don (Berberidaceae) (16)

51 STEBISIMINE   ($C_{36}H_{34}O_6N_2$: 590.2417)
   Stephania japonica Miers (Menispermaceae) (50)

54 THALISOPINE (Thaligosine) $(C_{37}H_{42}O_7N_2: 638.2992)$
  Thalictrum faberi Ulbr. (Ranunculaceae) (166)
  Thalictrum javanicum Bl. (Ranunculaceae) (216)
  Thalictrum minus L. var. *microphyllum* Boiss. (Ranunculaceae) (14,180)

55 THALRUGOSAMININE $(C_{39}H_{44}O_7N_2: 652.3149)$
  Thalictrum javanicum Bl. (Ranunculaceae) (216)

57 BERBAMINE $(C_{37}H_{40}O_6N_2: 608.2886)$
  Berberis aristata DC. (Berberidaceae) (156)
  Berberis lycium Royle (Berberidaceae) (221)
  Stephania cepharantha Hayata (Menispermaceae) (7)
  Stephania tetrandra S. Moore (Menispermaceae) (194) (alkaloid detected but not isolated)

61 FANGCHINOLINE $(C_{37}H_{40}O_6N_2: 608.2886)$
  Stephania tetrandra S. Moore (Menispermaceae) (194) (alkaloid detected but not identified)

62 ISOTETRANDRINE $(C_{38}H_{42}O_6N_2: 622.3043)$
  Stephania cepharantha Hayata (Menispermaceae) (7)
  Mahonia siamensis Takeda (Berberidaceae) (184)

64 LIMACINE $(C_{37}H_{40}O_6N_2: 608.2886)$
  Arcangelisia flava (L.) Merr. (Menispermaceae) (60)

68 NORBERBAMINE $(C_{36}H_{38}O_6N_2: 594.2730)$
  Cocculus pendulus (Forsk) Diels (Menispermaceae) (175)

71 OBAMEGINE $(C_{36}H_{38}O_6N_2: 594.2730)$
  Mahonia repens (Lindl.) G. Don (Berberidaceae) (16)
  Thalictrum minus L. var. *microphyllum* Boiss. (Ranunculaceae) (180)

72 PENDULINE $(C_{37}H_{40}O_6N_2: 608.2886)$
  Andrachne cordifolia Muell (Euphorbiaceae) (122)[a]
  Cocculus leabe DC. (Menispermaceae) (59)
  Cocculus pendulus (Forsk) Diels (Menispermaceae) (175)

76 TETRANDRINE $(C_{38}H_{42}O_6N_2: 622.3043)$
  Aristolochia debilis Sieb. and Zucch. (Aristolochiaceae) (215)
  Cocculus pendulus (Forsk) Diels (Menispermaceae) (175)
  Stephania tetrandra S. Moore (Menispermaceae) (194) (alkaloid detected but not isolated)

79 THALRUGOSINE $(C_{37}H_{40}O_6N_2: 608.2886)$
  Laurelia sempervirens R. et P. (Monimiaceae) (210)
  Mahonia repens (Lindl.) G. Don (Berberidaceae) (16)
  Stephania sasakii Hayata (Menispermaceae) (192)
  Thalictrum minus L. var. *microphyllum* Boiss. (Ranunculaceae) (14)

81 HERNANDEZINE $(C_{39}H_{44}O_7N_2: 652.3149)$
  Thalictrum sultanabadense Stapf. (Ranunculaceae) (211)

95 0-METHYLTHALICBERINE (Thalmidine) $(C_{38}H_{42}O_6N_2: 622.3043)$
  Berberis chilensis Gill. ex Hook. (Berberidaceae) (36)
  Thalictrum faberi Ulbr. (Ranunculaceae) (166)
  Thalictrum kuhistanicum Ovcz. and Koczk. (Ranunculaceae) (145)
  Thalictrum longipedunculatum E. Nikit. (Ranunculaceae) (165)
  Thalictrum minus L. (Ranunculaceae) (103)
  Thalictrum minus L. var. *microphyllum* Boiss. (Ranunculaceae) (14,180)

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[a]A recent communication from Professor Maurice Shamma, Department of Chemistry, The Pennsylvania State University, indicates that Dr. Fazal Hussain has determined that the plant identified as *Andrachne cordifolia* is really *Cocculus pendulus* (Forsk) Diels.

97   THALICBERINE $(C_{37}H_{40}O_6N_2: 608.2886)$
   Thalictrum longipedunculatum E. Nikit. (Ranunculaceae) (165)
   Thalictrum minus L. var. *microphyllum* Boiss. (Ranunculaceae) (180)

98   THALMETHINE $(C_{36}H_{36}O_6N_2: 592.2573)$
   Thalictrum minus L. (Ranunculaceae) (103)

99   THALFOETIDINE $(C_{38}H_{42}O_7N_2: 638.2992)$
   Thalictrum longipedunculatum E. Nikit. (Ranunculaceae) (165)

100 THALIDASINE $(C_{39}H_{44}O_7N_2: 652.3149)$
   Thalictrum longipedunculatum E. Nikit. (Ranunculaceae) (165)
   Thalictrum foliolosum DC. (Ranunculaceae) (35)

101 THALRUGOSIDINE $(C_{38}H_{42}O_7N_2: 638.2992)$
   Thalictrum faberi Ulbr. (Ranunculaceae) (166)
   Thalictrum foliolosum DC. (Ranunculaceae) (35)

102 THALFINE $(C_{38}H_{36}O_8N_2: 648.2472)$
   Thalictrum foetidum L. (Ranunculaceae) (104)

103 THALFININE $(C_{39}H_{42}O_8N_2: 666.2941)$
   Thalictrum foetidum L. (Ranunculaceae) (104)

106a THALABADENSINE $(C_{36}H_{38}O_6N_2: 594.2724)$
   Thalictrum minus L. (Ranunculaceae) (103)
   Thalictrum sultanabadense Stapf. (Ranunculaceae) (211)

107 THALICTINE $(C_{37}H_{40}O_6N_2: 608.2886)$
   Thalictrum sultanabadense Stapf. (Ranunculaceae) (188,211)

108 THALMINE $(C_{37}H_{40}O_6N_2: 608.2886)$
   Thalictrum kuhistanicum Ovcz. and Koczk. (Ranunculaceae) (145)
   Thalictrum minus L. (Ranunculaceae) (103)

116 NORTILIACORININE A $(C_{35}H_{34}O_5N_2: 562.2468)$
   Tiliacora racemosa Colebr. (Menispermaceae) (8)
   Tiliacora triandra Diels (Menispermaceae) (2)

118 TILIACORINE $(C_{36}H_{36}O_5N_2: 576.2624)$
   Tiliacora triandra Diels (Menispermaceae) (2)

119 TILIACORININE $(C_{36}H_{36}O_5N_2: 576.2624)$
   Tiliacora triandra Diels (Menispermaceae) (2)

120 TILIAMOSINE $(C_{36}H_{36}O_6N_2: 592.2574)$
   Pachygone ovata (Poir.) Miers ex Hook. (Menispermaceae) (120,200)

121 CYCLEANINE $(C_{38}H_{42}O_6N_2: 622.3043)$
   Cleistopholis staudtii Engl and Diels (Annonaceae) (193)
   Cyclea hypoglauca Diels (Menispermaceae) (37)
   (identified by preparation of the metho–quaternary salt)
   Isolona hexaloba Engl. (Annonaceae) (170)
   Stephania glabra (Roxb.) Miers (Menispermaceae) (65)
   Synclisia scabrida Miers (Menispermaceae) (86)

122 ISOCHONDODENDRINE $(C_{36}H_{38}O_6N_2: 594.2730)$
   Isolona hexaloba Engl. (Annonaceae) (170)
   Isolona pilosa Diels (Annonaceae) (170)
   Cleistopholis staudtii Engl. et Diels (Annonaceae) (192)

124 (+)-NORCYCLEANINE $(C_{37}H_{40}O_6N_2: 608.2886)$

Synclisia scabrida Miers (Menispermaceae) (86)

125 (−)-NORCYCLEANINE $(C_{37}H_{40}O_6N_2: 608.2886)$
        Isolona hexaloba Engl. (Annonaceae) (170)

130 (+)-CHONDROCURINE $(C_{36}H_{38}O_6N_2: 594.2730)$
        Peruvian Curare (198)

131 (−)-CHONDROFOLINE $(C_{37}H_{40}O_6N_2: 608.2886)$
        Cleistopholis staudtii Engl. et Diels (Annonaceae) (193) (*R,R* not *S,S* as in ref 110)

133 (−)-CURINE $(C_{36}H_{38}O_6N_2: 594.2730)$
        Cleistopholis staudtii Engl. et Diels (Annonaceae) (192)
        Isolona pilosa Diels (Annonaceae) (170)
        Peruvian Curare (198)

135 *O,O,*-DIMETHYLCURINE $(C_{37}H_{40}O_6N_2: 608.2886)$
        Cyclea hypoglauca Diels (Menispermaceae) (37)
        (identified by preparation of the metho-quaternary salt)

142 (+)-TUBOCURARINE CHLORIDE $(C_{37}H_{41}O_6N_2{}^{+2}2Cl^-: 609.3042)$
        Peruvian Curare (198)

152 COCSOLINE $(C_{34}H_{32}O_5N_2: 548.2311)$
        Albertisia papuana Becc. (Menispermaceae) (125)
        Cocculus leaebe DC. (Menispermaceae) (59)
        Cocculus pendulus (Forsk) Diels (Menispermaceae) (175)
        Synclisia scabrida Miers (Menispermaceae) (86)

153 COCSULINE $(C_{35}H_{34}O_5N_2: 562.2468)$
        Albertisia papuana Becc. (Menispermaceae) (125)
        Andrachne cordifolia Muell., O.F. (Euphorbiaceae) (122)[a]
        Cocculus leaebe (*C. pendulus*) (Menispermaceae) (59)
        Cocculus pendulus (Forsk) Diels (Menispermaceae) (175)
        Synclisia scabrida Miers (Menispermaceae) (86)

157 ISOTRILOBINE $(C_{36}H_{36}O_5N_2: 576.2624)$
        Albertisia papuana Becc. (Menispermaceae) (125)
        Cocculus pendulus (Forsk) Diels (Menispermaceae) (175)
        Cocculus trilobus Thunb. (Menispermaceae) (1)

161 TRICORDATINE $(C_{34}H_{32}O_5N_2: 548.2311$
        Cocculus pendulus (Forsk) Diels (Menispermaceae) (175)

163 TRILOBINE $(C_{35}H_{34}O_5N_2: 562.2468)$
        Cocculus trilobus Thunb. (Menispermaceae) (1)

190 CALAFATINE $(C_{39}H_{44}O_7N_2: 652.3149)$
        Berberis buxifolia Lam. (Berberidaceae) (146)

192 DAURISOLINE $(C_{37}H_{42}O_6N_2: 610.3043)$
        Polyalthia nitidissima Benth. (Annonaceae) (128)

193 1,2-DEHYDROAPATELINE $(C_{34}H_{30}O_5N_2: 560.2311)$
        Cocculus pendulus (Forsk) Diels (Menispermaceae) (175)

194 1,2-DEHYDROTELOBINE $(C_{35}H_{32}O_5N_2: 560.2311)$
        Albertisia papuana Becc. (Menispermaceae) (125)

195 7-*O*-DEMETHYLISOTHALICBERINE $(C_{36}H_{38}O_6N_2: 594.2724)$
        Berberis chilensis Gill. ex Hook. (Berberidaceae) (36)

205 ISOTHALICBERINE $(C_{37}H_{40}O_6N_2: 608.2886)$
         Berberis chilensis Gill. ex Hook. (Berberidaceae) (36)

207 N-METHYLAPATELINE $(C_{35}H_{34}O_5N_2: 562.2468)$
         Cocculus pendulus (Forsk) Diels (Menispermaceae) (175)

209 *0*-METHYLTHALIBRINE $(C_{39}H_{46}O_6N_2: 638.3356)$
         Thalictrum faberi Ulbr. (Ranuinculaceae) (166)

218 BERBACOLORFLAMMINE $(C_{37}H_{37}O_6N_2: 605.2652)$
         Pycnarrhena longifolia (Decne. ex Miq.) Becc. (Menispermaceae) (15)

219 COLORFLAMMINE $(C_{37}H_{37}O_6N_2: 605.2652)$
         Pycnarrhena longifolia (Decne. ex Miq.) Becc. (Menispermaceae) (15)

<center>TABLE 4.   New Bisbenzylisoquinoline Alkaloids[1]</center>

225 ANTIOQUINE $C_{37}H_{40}O_6N_2: 608.2886$

<center>Type IV (S,R) 6,7,8*,12-6,7*,12(11-11)</center>

<center>**225**</center>
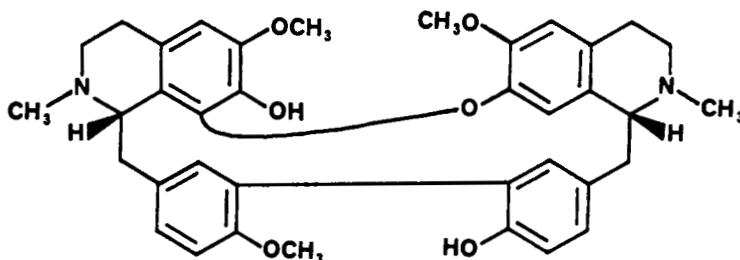
MP: 197°(MeOH) (196)

$[\alpha]_D$:   +214°(c=0.9, CHCl$_3$) (196)

UV(EtOH):   212 (4.28), 236 (sh) (3.84), 290 (3.38) (196)

IR(film):   3300, 2900, 2810, 2750, 1615, 1585, 1500, 1455, 1410, 1325, 1295, 1275, 1230, 1110, 1055, 1015, 940, 860, 815, 800 (196)

^{1}H nmr: NCH$_3$ 2.34 (N-2), 2.63 (N-2'), OCH$_3$ 3.49 (C-6'), 3.83 (C-6), 3.87 (C-12), AlH 2.43 (1H) (H-4), 2.60 (2H (H-4'), 2.75 (1H) (H-α), 2.93 (4H) (H-3, H-3', H-3', H-4), 3.04 (3H) (H-α, H-α', H-α'), 3.46 (1H) (H-3), 3.71 (H-1'), 3.97 (H-1), ArH 6.34 (H-5), 6.46 (H-5'), 6.65 (d) (1H) (J=2 Hz) (H-10'), 6.85 (d) (1H) (J=8.2 Hz) (H-13), 6.85 (d) (1H) (J58.2 Hz) (H-13'), 6.96 (H-8'), 7.09 (d) (1H) (J=2 Hz) (H-10), 7.19 (dd) (1H) (J=2,8.2 Hz) (H-14'), 7.26 (dd) (1H) (J= 2, 8.2 Hz) (H-14) (196)

NOE: (196)

^{13}C nmr: 62.6 (C-1), 44.2 (C-3), 22.3 (C-4), 121.9 (C-4a), 104.5 (C-5), 145.7 (C-6), 134.7 (C-7), 141.7 (C-8), 123.7 (C-8a), 39.5 (C-α), 130.3 (C-9), 135.1 (C-10), 130.3 (C-11), 152.7 (C-12), 116.6 (C-13), 129.2 (C-14), 42.2 (N-2 NCH$_3$), 56.0 (C-6 OCH$_3$) (C-11), 152.7 (C-12), 116.6 (C-13), 129.2 (C-14), 42.2 (N-2 NCH$_3$), 56.0 (C-6 OCH$_3$), 56.2 (C-12 OCH$_3$), 64.7 (C-1'), 48.9 (C-3'), 27.1 (C-4'), 127.8 (C-4a'), 112.4 (C-5'), 148.0 (C-6'), 142.5 (C-7'), 119.0 (C-8'), 125.3 (C-8a'), 38.0 (C-α'), 137.8 (C-9'), 135.1 (C-10'), 119.0 (C-8'), 125.3 (C-8a'), 38.0 (C-α'), 137.8 (C-9'), 135.1 (C-10'), 129.5 (C-11'), 151.7 (C-12'), 110.5 (C-13'), 131.0 (C-14'), 43.3 (N-2' NCH$_3$), 55.6 (C-6' OCH$_3$) (196)

MS: M$^+$608 (100), 607 (67), 416 (4), 391 (98), 367 (31), 191.5 (19), 191 (59), 175.5 (2), 175 (6), 174 (11) (196)

SOURCE: *Pseudoxandra* aff. *lucida* Fries (Annonaceae) (196)

DERIVATIVES: *0,0*-Diacetylantioquine (Antioquine + Ac$_2$O + pyridine) (196)

MP: 164-166° (196)

$[\alpha]_D$:   +150°(c=0.2, CHCl$_3$) (196)

UV(EtOH):   210 (4.82), 287 (3.91) (196)

IR(film):   1770 (196)

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[1]Not previously reported in the review by Schiff (111)

[^1]H nmr: OCOCH$_3$ 1.51 (C-7), 2.04 (C-12'), NCH$_3$ 2.34 (N-2), 2.57 (N-2'), OCH$_3$ 3.47 (C-6'), 3.70
            (C-6), 3.76 (C-12), ArH 6.20-7.60 (m) (9H) (196)
MS: M$^+$692 (87), 691 (49), 650 (9), 649 (12), 633 (5), 424 (26), 423 (83), 381 (11), 349 (9), 212 (49),
            191 (100), 175 (13), 174 (31), 145 (15) (196)
            7-O-Methylantioquine (Antioquine + CH$_2$N$_2$) (196)
MP: Amorphous (196)
[α]D: +168°(c=0.3, CHCl$_3$) (196)
UV(EtOH):   210 (4.86), 282 (4.04((196)
IR(film):   1605, 1500 (196)
[^1]H nmr: NCH$_3$ 2.34 (N-2), 2.64 (N-2'), OCH$_3$ 3.38 (C-7), 3.49 (C-6'), 3.80 (C-6), 3.87 (C-12), ArH
            6.15-7.66 (m) (9H) (196)
MS: M$^+$622, 396, 395, 334, 229, 198, 194, 175, 174 (196)
            0,0-Dimethylantioquine (Antioquine + CH$_2$N$_2$) (196)
MP: Not reported (196)
[α]D: +78°(c=0.9, CHCl$_3$) (196)
UV(EtOH):   210 (4.79), 286 (3.88) (196)
[^1]H nmr: NCH$_3$ 2.43 (N-2), 2.68 (N-2'), OCH$_3$ 3.29 (C-7), 3.51 (C-6'), 3.76 (C-6), 3.80 (6H) (C-12
            and C-12'), ArH 6.18-7.72 (m) (9H) (196)
MS: M$^+$636 (20), 395 (69), 381 (20), 379 (10), 364 (4), 198 (100), 175 (32), 174 (23) (196)
            Ceric ammonium nitrate oxidation of 0,0-dimethylantioquine followed by appropriate
            workup afforded 2,2'-dimethoxy-5,5'-dicarboxybiphenyl + following diamine (196):
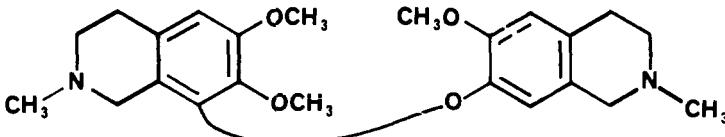
Birch reduction (Na/NH$_3$) afforded the following biphenyl derivative (196):
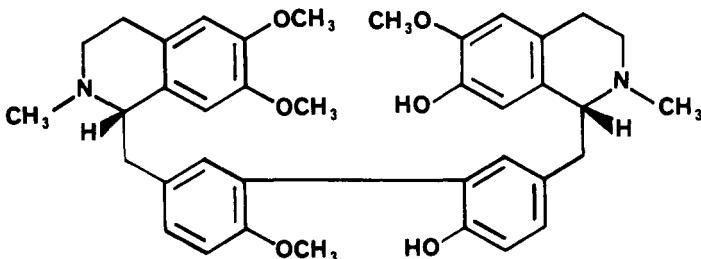
MP: Amorphous (196)
[α]D: +60°(c=0.07, CHCl$_3$) (196)
UV(EtOH):   209 (4.69), 230 (sh) (4.38), 286 (3.97); (EtOH+OH$^-$) 220 (4.70), 294 (4.24) (196)
IR(film):   3310, 1610, 1510 (196)
[^1]H nmr: NCH$_3$ 2.56, 2.57, OCH$_3$ 3.52, 3.80, 3.84 (3s) (12H), ArH 6.02 (H-8 or H-8'), 6.28 (H-8'
            or H-8), 6.55 (H-5 or H-5'), 6.57 (H-5' or H-5), 6.82-7.17 (m) (6H) (196)
MS: M$^+$ 624 (0.6), 432 (3), 418 (0.4), 312 (1), 226 (1), 206 (100), 194 (7), 193 (58), 192 (100), 190
            (31) (196)
            Diacetylsecoantioquine (0,0-Diacetylantioquine + KMnO$_4$) (196)
MP: Amorphous (196)
[α]D: −4°(c=0.6, CHCl$_3$) (196)
UV(EtOH):   210 (4.66), 220 (4.68), 270 (4.06), 290 (3.90); (EtOH+OH$^-$) 222 (5.29), 300 (4.27),
            346 (4.33) (196)
IR(film):   1760, 1690, 1640 (196)
[^1]H nmr: OCOCH$_3$ 1.98 (C-7), 2.01 (C-12'), NCH$_3$ 2.24 (N-2), NCOCH$_3$ 3.06 (N-2'), OCH$_3$ 3.70
            (C-6'), 3.71 (C-12), 3.79 (C-6), ArH 6.56 (H-5), 6.60 (H-5'), 6.81 (d) (1H) (J=8.5 Hz) (H-
            13), 6.96 (d) (1H) (J=2 Hz) (H-10), 7.20 (dd) (1H) (J=2,8.5 Hz) (H-14), 7.33 (H-8'), 7.32 (d)
            (1H) (J=8.5 Hz) (H-13'), 7.75 (d) (1H) (J=2 Hz) (H-10'), 7.88 (dd) (1H) (J=2,8.5 Hz) (H-
            14'), 9.96 (C-9' CHO) (196)
MS(CI)(CH$_4$):   M$^+$+1 723 (18), 681 (8), 665 (7) (196)
MS: 439 (100), 397 (44), 351 (6), 241 (4), 234 (8), 192 (8), 191 (9) (196)

226 CALAFATINE-2α-N-OXIDE $C_{39}H_{44}O_8N_2$: 668.3098
Type Xa (S,R) 6,7,8*,10,11$^+$,12-6,7*,12$^+$

226
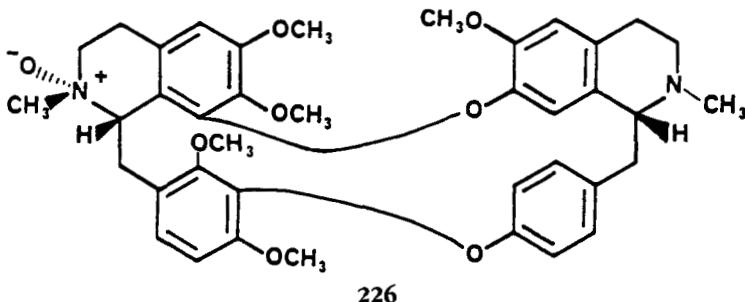
MP: Amorphous (162)
TLC: 0.26 (Si gel F_{254}; CHCl$_3$-MeOH-NH$_4$OH [90:10:1]) (162)
$[\alpha]^{25}$D: −48° (c=0.17, MeOH) (162)
UV: 210 (4.95), 237 (sh) (4.67), 281 (3.91) (162)
^{1}H nmr: NCH$_3$ 2.33 (N-2), 3.40 (N-2'), OCH$_3$ 3.36 (C-7), 3.74 (C-10), 3.75 (C-6), 3.77 (C-6'),
      3.86 (C-12), AlH 2.41 (m) (H-4), 2.53 (m) (H-α'), 2.55 (m) (H-α), 2.78 (m) (H-3), 2.83 (m)
      (H-3'), 2.89 (H-4'), 2.92 (m) (H-4), 3.32 (m) (H-3), 3.38 (m) (H-α), 3.45 (m) (H-4'), 3.66
      (m) (H-α'), 3.90 (m) (H-3'), 4.10 (m) (H-1), 4.36 (m) (H-1'), ArH 5.47 (H-8'), 5.97 (dd) (1H)
      (J=2.2, 8.2 Hz) (H-10'), 6.36 (H-5), 6.51 (dd) (1H) (J=2.2, 8.2 Hz) (H-11'), 6.61 (H-5'),
      6.75 (d) (1H) (J=8.5 Hz) (H-13), 6.94 (d) (1H) (J=8.5 Hz) (H-14), 6.94 (dd) (1H) (J=2.2, 8.2
      Hz) (H-13'), 7.11 (dd) (1H) (J=2.2, 8.2 Hz) (H-14') (163)
MS: M$^+$668 (3), 667 (6), 652 (54), 396 (26), 395 (76), 387 (73), 222 (5), 207 (2), 206 (8), 198 (100),
      191 (28), 174 (42) (162)
CD: 0 (211), +27 (217), 0 (225), − 42 (233), 0 (242), +12 (247), 0 (300) (162)
SOURCE: *Berberis buxifolia* Lam. (Berberidaceae) (162)
DERIVATIVES: Calafatine (Calafatine-2α-N-Oxide+Zn/HCl) (162)

227 CALAFATINE-2β-N-OXIDE $C_{39}H_{44}O_8N_2$: 668.3098
Type Xa (S,R) 6,7,8*,10,11$^+$,12-6,7*,12$^+$

227
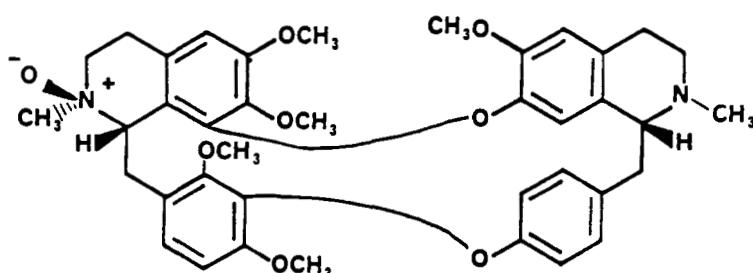
MP: Amorphous (162)
TLC: 0.17 (Si gel F_{254}; CHCl$_3$-MeOH-NH$_4$OH [90:10:1]) (162)
$[\alpha]^{25}$D: −19° (c=0.14, MeOH) (162)
UV: 206 (4.91), 229 (sh) (4.63), 280 (3.85) (162)
^{1}H nmr: NCH$_3$ 2.32 (N-2), 3.26 (N-2'); OCH$_3$ 3.42 (C-7), 3.74 (C-6'), 3.74 (C-10), 3.76 (C-6), 3.86
      (C-12); Alh 2.46 (m) (H-4), 2.57 (m) (H-α), 2.70 (m) (H-α'), 2.85 (m) (H-3), 2.94 (m) (H-4),
      3.08 (m) (H-3'), 3.15 (m) (H-4'), 3.32 (m) (H-α), 3.40 (m) (H-3), 3.57 (m) (H-4'), 3.98 (m)
      (H-α'), 4.09 (m) (H-3'), 4.11 (m) (H-1), 4.19 (m) (H-1'); ArH 5.39 (H-8'), 5.89 (dd) (1H)
      (J=2.2, 8.2 Hz) (H-10'), 6.40 (H-5), 6.42 (dd) (1H) (J=2.2, 8.2 Hz) (H-11'), 6.59 (H-5'),
      6.75 (d) (1H) (J=8.5 Hz) (H-13), 6.91 (dd) (1H) (J=2.2, 8.2 Hz) (H-13'), 6.93 (d) (1H)
      (J=8.5 Hz) (H-14), 7.17 (dd) (1H) (J=2.2, 8.2 Hz) (H-14') (163)
MS: M$^+$668 (2), 668 (1), 652 (44), 396 (28), 395 (80), 387 (76), 222 (3), 206 (6), 198 (100), 191 (8),
      174 (65) (162)

CD: 0 (210), +25 (217), 0 (224), −38 (232), 0 (240), +15 (245), 0 (300) (162)
SOURCE: *Berberis buxifolia* Lam. (Berberidaceae) (162)
DERIVATIVES: Calafatine (Calafatine-2β-*N*-Oxide+Zn/HCl) (162)

228 CHERATAMINE $C_{36}H_{34}O_7N_2$: 606.2366

Type VIII (-,*S*) 6,7,8*,11$^+$,12-6,7*,12$^+$

228
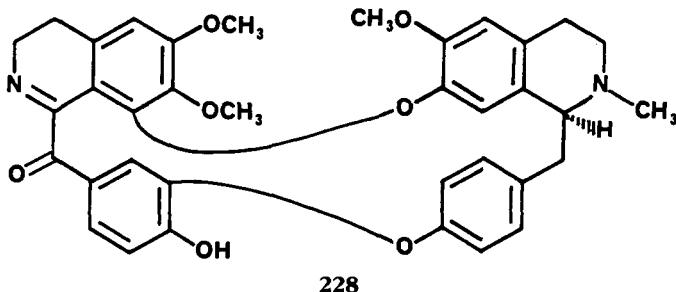
MP: None reported (175)
$[\alpha]^{25}$D: +190°(*c*=0.33, MeOH) (175)
UV: 227 (4.28), 289 (3.99); (MeOH+OH$^-$) 288 (3.95), 349 (3.91); (MeOH+H$^+$) 287 (3.87), 337 (3.95) (175)
IR: 1675, 1600 (175)
^{1}H nmr: NCH$_3$ 2.48; OCH$_3$ 3.00 (C-7), 3.66 (C-6′), 3.80 (C-6); AlH 3.71 (t) (1H) (H-1′); ArH 5.50 (H-8′), 6.35 (dd) (1H) (*J*=2, 8.2 Hz) (H-10′), 6.44 (H-5), 6.55 (dd) (1H) (*J*=2, 8.2 Hz) (H-11′), 6.56 (H-5′), 6.88 (d) (1H) (*J*=8.4 Hz) (H-13), 6.92 (d) (1H) (*J*=2 Hz) (H-10), 7.15 (dd) (1H) (*J*=2, 8.2 Hz) (H-13′), 7.26 (dd) (1H) (*J*=2, 8.2 Hz) (H-14′), 7.43 (dd) (1H) (*J*=2, 8.4 Hz) (H-14) (175)
NOE: (175)
MS: M$^+$606 (73), 605 (100), 589 (4), 379 (8), 363 (2), 347 (3.5), 333 (2), 190 (9), 174 (7) (175)
CD: Positive tail, −13 (216), 0 (223), +20 (232), +2 (260), +1 (284), 0 (290), −2 (303), 0 (317), +2 (335), 0 (365) (175)
SOURCE: *Cocculus pendulus* (Forsk) Diels (Menispermaceae) (175)

229 CHILLANAMINE $C_{37}H_{42}O_7N_2$: 626.2992

Type Ib^2 (*S,R,*) 6,7,10,11*,12-6,7,12*
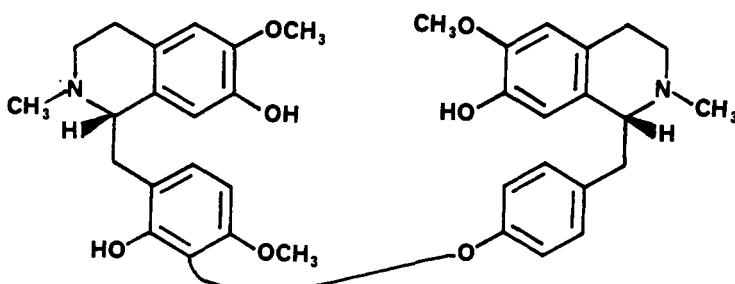
229

MP: None reported (146)
TLC: 0.06 (Si gel F$_{254}$; CHCl$_3$-MeOH-NH$_4$OH [95:5:0.5]) (146)
$[\alpha]$D: None reported (146)
UV: 209 (4.81), 226 (sh) (4.54), 283 (4.02) (146)
^{1}H nmr: NCH$_3$ 2.43 (N-2 or N-2′), 2.58 (N-2′ or N-2); OCH$_3$ 3.79 (C-6′ or C-6), 3.84 (C-6 or C-6′), 3.91 (C-12); ArH 5.96 (H-8 or H-8′), 6.09 (H-8′ or H-8), 6.53 (H-5 or H-5′), 6.54 (H-5′ or

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^{2}This is a new class that supplements Class I as presented in the review of Guha *et al.* (110)

H-5), 6.58 (d) (1H) (J=8.5 Hz) (H-14), 6.69 (d) (1H) (J=8.5 Hz) (H-13), 6.78 (d) (2H)
(J=8.5 Hz) (H-11' and H-13'), 6.98 (d) (2H) (J=8.5 Hz) (H-10' and H-14') (146)
NOE: (146)
MS: M$^+$626 (0.1), 625 (0.1), 192 (100), 177 (18) (146)
CD: +8.3 (212), 0 (220), −6 (230), 0 (265), +0.5 (271), 0 (300) (146)
SOURCE: *Berberis buxifolia* Lam. (Berberidaceae) (146)

230 NOR-N_b-CHONDROCURINE $C_{35}H_{36}O_6N_2$: 580.2573
Type XXI (R,S,) 6,7,8*,11$^+$,12-6,7$^+$,12*

230
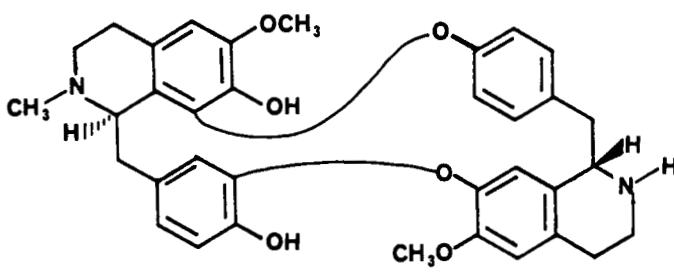
MP: 159-161°(EtOAc) (198)
[α]^{20}D: −242°(c=0.5, CHCl$_3$) (198)
UV: 230 (4.39), 285 (4.02) (198)
^{1}H nmr: NCH$_3$ 2.22, OCH$_3$ 3.84 (6H), ArH 6.12 (H-8'), 6.5-6.9 (9H) (198)
^{13}C nmr: 60.2 (C-1), 43.6 (C-3), 21.7 (C-4), 124.2 (C-4a), 107.8 (C-5), 147.0 (C-6), 137.8 (C-7),
138.8 (C-8), 124.2 (C-8a), 39.7 (C-α), 133.3 (C-9), 120.4 (C-10), 143.4 (C-11 or C-7'), 146.1
(C-12), 115.4 (C-13), 126.4 (C-14), 41.5 (2-NCH$_3$), 55.8 (C-6 OCH$_3$ and C-6' OCH$_3$), 56.5
(C-1'), 42.1 (C-3'), 28.1 (C-4'), 124.1 (C-4a'), 112.3 (C-5'), 148.3 (C-6'), 143.8 (C-7' or C-
11), 118.7 (C-8'), 130.2 (C-8a'), 38.9 (C-α'), 131.4 (C-9'), 133.3 (C-10'), 114.5 (C-11'),
155.4 (C-12'), 113.5 (C-13'), 129.8 (C-14') (198)
MS: M$^+$580 (74), 579 (87), 298 (56), 297 (100), 296 (94), 284 (34), 283 (24) (198)
ORD: −79,000 (235), +9,700 (276), −16,600 (288) (198)
SOURCE: Only specified as a "Peruvian curare", thus, it is likely a species of the genus *Chondodendron*
(198)
DERIVATIVES: (R,S)-Chondrocurine [**130**] (Nor-N_b-Chondrocurine+CH$_2$O+HCOOH) (198)

231 COCSULINE-N-2-OXIDE $C_{35}H_{34}O_6N_2$: 578.2417
Type XXIII (S,S) 6*,7$^+$,11‡,12-6,7*,8$^+$,12‡

231
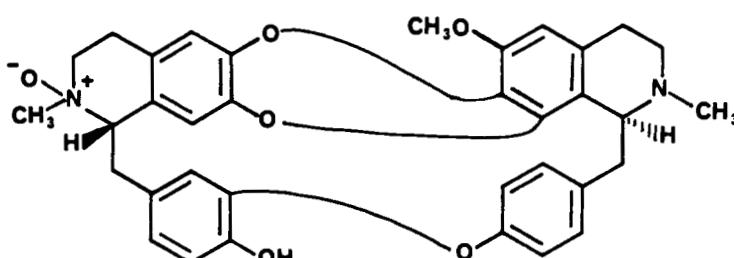
MP: 182-187°(MeOH) (amorph) (161)
TLC: 0.42 (Si gel G; CHCl$_3$-MeOH-NH$_4$OH [85:15:0.2]) (161)
[α]^{25}D: +125°(c=0.5, MeOH) (161)
UV: 285 (3.48) and 300 (3.45) (161)
IR(KBr): 3400 (br), 1590, 1508, 1450, 1440, 1385, 1280, 1220, 1115 (161)
^{1}H nmr (CDCl$_3$+CD$_3$OD): NCH$_3$ 2.60, N$^+$O$^-$CH$_3$ 2.85, OCH$_3$ 3.87, ArH 6.25-7.70 (m, 10H)
(161)

MS: M$^+$578 (2%), 557 (3), 562 (7), 561 (8), 350 (21), 349 (19), 336 (15), 335 (2), 334 (7), 175 (100) (161)
SOURCE: *Cocculus hirsutus* DC. (Menispermaceae) (161)
DERIVATIVES: Cocsuline (Cocsuline-*N*-2-Oxide+H$_2$SO$_3$) (uv, ir, ^{1}H nmr, ms, [α]D) (161)

232   CYCLEANINE *N*-OXIDE   C$_{38}$H$_{42}$O$_7$N$_2$: 636.2836
Type XX (*R,R*) 6,7,8*,12$^+$-6,7,8$^+$,12*
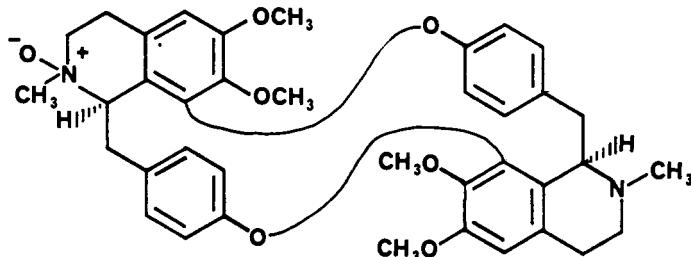
232

MP: None reported (86)
TLC: 0.37 (Si gel 60 PF$_{254}$; EtOAc-iPrOH-NH$_4$OH ([9:7:2]) (86)
[α]^{25}D: −7.6°(*c*=0.38, MeOH) (86)
UV: 275, 285 (86)
^{1}H nmr: NCH$_3$ 2.60, N$^+$O$^-$CH$_3$ 3.32, OCH$_3$ 3.42 (2), 3.84 (2), ArH 4.31 (2H) (d) (*J*= 10 Hz), 5.81 (2H) (dd) (*J*=2.7, 8.5 Hz), 6.27 (2H) (dd) (*J*=2.0, 8.5 Hz), 6.58 (2H) (dd) (*J*=2.7, 8.5 Hz), 7.10 (2H) (dd) (*J*=2.0, 8.5 Hz) (86)
MS(EI):   M$^+$638 (3), 622 (55), 607 (8), 313 (23), 312 (100), 311 (35), 204 (25), 190 (15), 174 (9) (86)
MS(FD):   M$^+$638 (100), 622 (40) (86)
SOURCES: *Synclisia scabrida* Miers (Menispermaceae) (86)
DERIVATIVES: Cycleanine (Cycleanine *N*-Oxide+H$_2$SO$_3$) (tlc, color reactions) (86)
PREPARATION: Via oxidation (3% H$_2$O$_2$) of cycleanine tlc (86)

233   N-DESMETHYLCYCLEANINE   C$_{37}$H$_{40}$O$_6$N$_2$: 608.2886
Type XX (*R,R*) 6,7,8*,12$^+$-6,7,8$^+$,12*
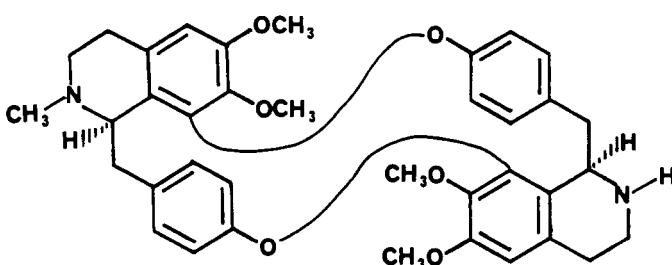
233

MP: 102-103° (MeOH) (65)
[α]^{32}D: −165°(*c*=0.29, CHCl$_3$) (65)
UV: 237 (4.03), 281 (3.26) (65)
IR(KBr):   3350, 2900, 1570, 1480, 1400, 1340, 1290, 1210, 1110, 1070 and 840 (65)
^{1}H nmr: NCH$_3$ 2.51, OCH$_3$ 3.40, 3.45, 3.80, 3.85, AlH 2.65-3.40 (m, 12H), 4.23 (m) (H-1), 4.62 (m) (H-1'), ArH 5.77 (dd) (1H) (*J*=2, 8 Hz) (H-13 or H-13'), 5.81 (dd) (1H) (*J*=2, 8 Hz) (H-13' or H-13), 6.25 (dd) (1H) (*J*=2, 8 Hz) (H-14 or H-14'), 6.30 (dd) (1H) (*J*=2, 8 Hz) (H-14' or H-14), 6.54 (dd) (1H) (*J*=2, 8 Hz) (H-11 or H-11'), 6.55 (s) (2H) H-5 and H-5'), 6.57 (dd) (1H) (*J*=2, 8 Hz) (H-11' or H-11), 7.03 (dd) (1H) (*J*=2, 8 Hz) (H-10 or H-10'), 7.23 (dd) (1H) (*J*=2, 8 Hz) (H-10' or H-10) (65)
^{13}C nmr: 56.71 (C-1 or C-1'), 60.9 (C-1' or C-1), 42.66 (C-3 or C-3'), 44.84 (C-3' or C-3), 24.93 (C-4 or C-4'), 26.64 (C-4' or C-4), 128.73 (C-4a or C-4a'), 128.98 (C-4a' or C-4a), 108.98 (C-5 or

C-5'), 109.56 (C-5' or C-5), 152.04 (C-6 or C-6'), 153.46 (C-6' or C-6), 139.14 (C-7 or C-7'), 140.26 (C-7' or C-7), 143.76 (C-8 or C-8'), 143.97 (C-8' or C-8), 125.36 (C-8a or C-8a'), 125.66 (C-8a' or C-8a), 129.91 (C-9 or C-9'), 131.42 (C-9' or C-9), 128.41 (C-10 or C-10'), 128.64 (C-10' or C-10), 113.91 (C-11 or C-11'), 114.16 (C-11' or C-11), 153.69 (C-12 or C-12'), 154.64 (C-12' or C-12), 117.54 (C-13 or C-13'), 117.85 (C-13' or C-13), 128.64 (C-14 or C-14'), 128.73 (C-14' or C-14), 37.52 (C-α or C-α'), 38.09 (C-α' or C-α), 42.48 (NCH$_3$), 56.17 (2×OCH$_3$), 59.52 (2×OCH$_3$ (65)

MS: M$^+$608, 312 (100%), 311, 298, 204, 190, 176, 174, 160, 146, 145, 132, 131 (65)

SOURCES: *Stephania glabra* (Roxb.) Miers. (Menispermaceae) (65)

DERIVATIVES: Cycleanine [**121**] (*N*-Desmethylcycleanine+CH$_2$O+HCOOH) (uv, ir, ^{1}H nmr, ms, mp, sp. rotation) (65)

234   *N,N'*-DIMETHYLLINDOLDHAMINE (128) or GUATTEGAUMERINE (129)

C$_{36}$H$_{40}$O$_6$N$_2$: 596.2886

Type I (*R,R*) 6,7,11*,12-6,7,12*
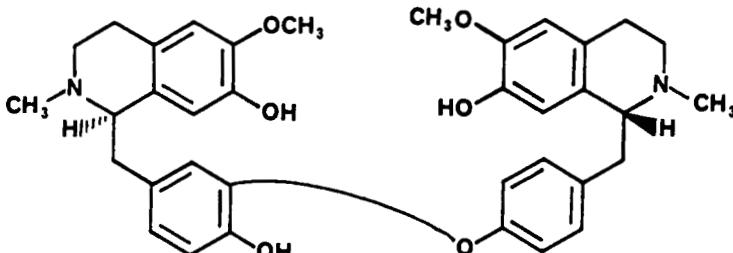
234

MP: Gum (128); yellowish-white powder (129)

TLC: 0.28 (Si gel; toluene-Me$_2$CO-EtOH-conc NH$_4$OH [45:45:7:3]) (129)

[α]D: −90°(*c*=0.7, CHCl$_3$) (128)

UV(EtOH):   208 (4.83), 224 (sh) (4.49), 286 (4.02) (128); (EtOH+NaOH) 226, 244 (sh), 303 (128)

UV: 212 (4.62), 227 (4.49), 286 (3.97) (129); (MeOH+NaOH) 245, 305 (129)

IR(KBr):   3400, 1600, 1505, 1370, 1260, 1100, 1020, 870, 825, 760 (129)

^{1}H nmr: NCH$_3$ 2.45, 2.48, OCH$_3$ 3.80 (6H), ArH 6.18 (H-8 or H-8'), 6.23 (H-8' or H-8), 6.46 (H-5 or H-5'), 6.53 (H-5' or H-5), 6.55-7.00 (m) (7H) (128), NCH$_3$ 2.42, 2.46, OCH$_3$ 3.81, 3.82, ArH 6.23 (H-8 or H-8'), 6.29 (H-8' or H-8), 6.47 (H-5 or H-5'), 6.53 (H-5' or H-5), 6.61 (d) (1H) (*J*=2 Hz) (H-10), 6.74-7.04 (m) (6H) (129)

MS: M$^+$596 (0.2), 192 (100), 177 (10) (128); M$^+$596 (0.1) (C$_{36}$H$_{40}$O$_6$N$_2$; measured 596.2807 and calculated 596.2886), 404 (0.3) (C$_{25}$H$_{26}$O$_4$N; measured 404.1878 and calculated 404.1862), 192 (100) (measured 192.1040 and calculated 192.1025), 177 (19) (129)

CD: [θ]$_{235}$ −48,000, [θ]$_{251}$ +2,500, [θ]$_{287}$ −18,500 (129)

SOURCES: *Guatteria gaumeri* Greenman (Annonaceae) (Guattegaumerine) (129)
            Polyalthia nitidissima Benth. (Annonaceae) (*N,N'*-Dimethyllindoldhamine) (128)

235   ISODAURISOLINE

C$_{37}$H$_{42}$O$_6$N$_2$: 610.3043

Type I (*R,R*) 6,7,11*,12-6,7,12*
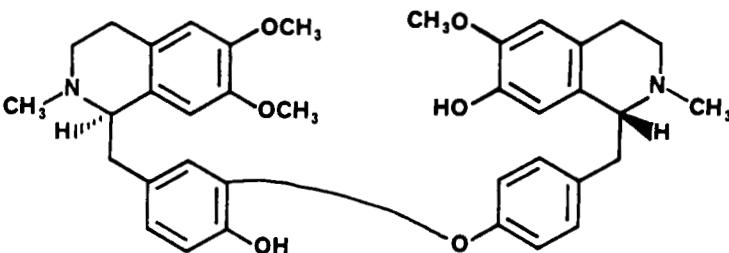
235

MP: 105-115° (Et$_2$O) (Precipitates as an amorphous powder) (128)
[α]D: −150°(c=0.6, MeOH) (128)
UV(EtOH):   208 (4.80), 228 (sh) (4.50), 284 (4.01) (128); (EtOH+NaOH) 230, 244 (sh), 303 (128)
^{1}H nmr: NCH$_3$ 2.42, 2.45; OCH$_3$ 3.56 (C-7), 3.80 (C-6 or C-6'), 3.81 (C-6' or C-6), ArH 6.05 (H-8 or H-8'), 6.15 (H-8' or H-8), 6.47 (s) (2H) (H-5 and H-5'), 6.50-7.20 (m) (7H) (128)
MS: M$^+$610 (0.5), 206 (100), 192 (85), 191 (4), 177 (6) (128)
SOURCES: *Polyalthia nitidissima* Benth. (Annonaceae) (128); *Guatteria gaumeri* Greenman (Annonaceae) (129)
PREPARATION: Via methylation (CH$_2$O+NaBH$_4$) of lindoldhamine (128,129)

236   KOHATINE   C$_{34}$H$_{32}$O$_6$N$_2$: 564.2260
Type XXIIIa^3 (S,S) 5,6,7*,8$^+$12‡-6*,7$^+$,11‡,12

236
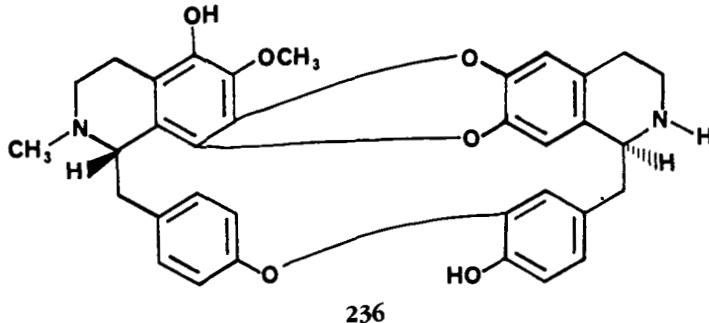
MP: None reported (175)
[α]^{25}D: +183°(c=0.2, MeOH) (175)
UV: 233 (4.59), 288 (3.77) (175)
^{1}H nmr: NCH$_3$ 2.59; OCH$_3$ 3.96; AlH 3.67 (brd) (1H) (H-1'), 4.00 (brd) (1H) (H-1), ArH 6.23 (H-8'), 6.59 (d) (1H), (J=2.2 Hz) (H-10'), 6.61 (H-5'), 6.81 (dd) (1H) (J=1.8, 8.2 Hz) (H-11), 6.89 (dd) (1H), (J=2.2, 8.2 Hz) (H-14'), 6.93 (d) (1H) (J=8.2 Hz) (H-13'), 7.11 (dd) (1H) (J=1.8, 8.2 Hz) (H-10), 7.20 (dd) (1H) (J=1.8, 8.2 Hz) (H-13), 7.54 (dd) (1H) (J=1.8, 8.2 Hz) (H-14) (175)
NOE: (175)
MS: M$^+$564 (49), 365 (30), 352 (39), 351 (100), 337 (32), 321 (15), 214 (8), 176 (39), 168 (29), 107 (7) (175)
CD: Negative tail, 0 (215), +30 (234), 0 (251), +8 (284), 0 (323) (175)
SOURCE: *Cocculus pendulus* (Forsk) Diels (Menispermaceae) (175)

237   KURRAMINE   C$_{33}$H$_{28}$O$_5$N$_2$: 532.1998
Type XXIII (-,S) 6*,7$^+$,11‡,12-6,7*,8$^+$,12‡

237
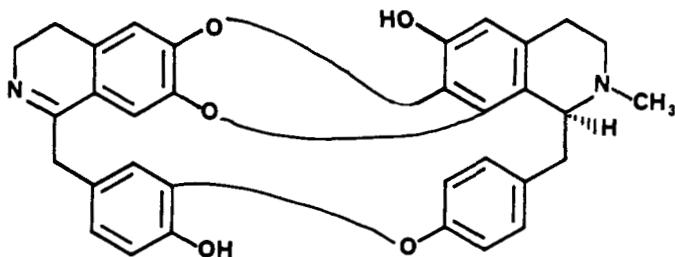
MP: None reported (175)
[α]^{25}D: +83°(c=0.13, MeOH) (175)

^{3}This is a new class that supplements Class XXIII as presented in the review of Guha *et al.* (110)

UV: 224 (sh) (4.71), 261 (sh) (4.25), 290 (3.86), 338 (3.77); (MeOH $+H^+$) 222 (sh) (4.67), 263 (sh)
        (4.26), 329 (3.80), 389 (3.85) (175)

^{1}H nmr: NCH$_3$ 2.57, ArH 6.44 (H-5' or H-5 or H-8), 6.55 (H-8 or H-5 or H-5'), 6.55 (d) (1H)
        (J=1.8 Hz) (H-10), 6.71 (dd) (1H) (J=2, 8.2 Hz) (H-11'), 6.85 (d) (1H) (J=8.2 Hz) (H-13),
        6.87 (H-5 or H-8 or H-5'), 6.90 (dd) (1H) (J=1.8, 8.2 Hz) (H-14), 6.93 (dd) (1H) (J=2, 8.2
        Hz) (H-10'), 7.21 (dd) (1H) (J=2, 8.2 Hz) (H-13'), 7.41 (dd) (1H) (J=2, 8.2 Hz) (H-14')
        (175)

MS: M$^+$532 (64), 531 (100), 327 (5), 326 (7), 319 (13), 107 (16) (175)

CD: Negative tail, 0 (215), +47 (226), 0 (255), −2.4 (258), 0 (265), +9 (212), +2 (291), +6 (305), 0
        (325) (175)

SOURCE: *Cocculus pendulus* (Forsk) Diels (Menispermaceae) (175)

238   MALEKULATINE $C_{39}H_{46}O_8N_2$: 670.3254

Type Va^4 (S,S) 6,7,10*,12,13-6,7*,11,12
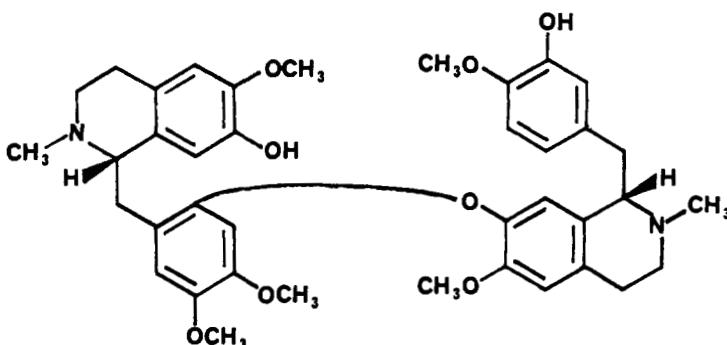
238

MP: None reported (115)

[α]^{25}D: +156°(*c*=0.14, MeOH) (115)

UV: 211 (4.79), 230 (sh) (4.50), 284 (4.18) (115)

^{1}H nmr: NCH$_3$ 2.39 (N-2'), 2.48 (N-2), OCH$_3$ 3.71 (C-13), 3.77 (C-6), 3.78 (C-12'), 3.83 (C-6'),
        3.87 (C-12), AlH 3.59 (H-1), 3.75 (H-1'), ArH 6.14 (H-8), 6.31 (H-8'), 6.37 (H-14), 6.49
        (dd) (1H) (J=2.1, 8.2 Hz) (H-14'), 6.50 (d) (1H) (J=2.1 Hz) (H-10'), 6.53 (H-5), 6.53 (H-
        5'), 6.61 (d) (1H) (J=8.2 Hz) (H-13'), 6.67 (H-11) (115)

NOE: (115)

MS: M$^+$670 (0.1), 669 (0.2), 533 (8.4), 478 (0.1), 192 (100) (115)

CD: +26.5 (232), +5.8 (282)(115)

SOURCES: *Hernandia peltata* Meissn. (Hernandiaceae) (115)

DERIVATIVES: 0,0-Dimethylmalekulatine (Malekulatine $+CH_2N_2$) (115); ^{1}H nmr: NCH$_3$ 2.46 (N-
        2 or N-2'), 2.49 (N-2 or N-2'); OCH$_3$ 3.50 (C-7), 3.72, 3.74 (6H), 3.81, 3.83, 3.84; ArH
        6.04 (H-8 or H-8'), 6.23 (H-8' or H-8), 6.44 H-5 or H-5'), 6.48 (H-5' or H-5), 6.52 (dd) (1H)
        (J=1.83, 8.24 Hz) (H-14'), 6.56 (d) (1H) (J=2.44 Hz) (J=2.44 Hz) (H-10'), 6.56 (H-14),
        6.64 (d) (1H) (J=8.24 Hz) (H-13'), 6.66 (H-11) (115)

MS: M$^+$698 (0.4), 547 (38), 492 (0.2), 206 (100) (115)

CD: +14.9 (236), +3.05 (283) (115)

      Birch reduction (Na/NH$_3$) afforded S-(−)-2-methyl-6,7,4',5'-tetramethoxy-2'-hydroxy-1,2,3,4-
tetrahydroisoquinoline (positive cd maximum near 233 nm indicates the S configuration while the nega-
tive specific rotation indicates that ring C is turned toward the N-methyl group) and S-(+)-2-methyl-
6,3',4'-trimethoxy-1,2,3,4-tetrahydroisoquinoline (115)

239   0-METHYLCOCSOLINE $C_{35}H_{34}O_5N_2$: 562.2468

Type XXIII (S,S) 6*,7$^+$,11‡,12-6,7*,8$^+$,12‡

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^{4}This is a new class that supplements Class V as presented in the review of Guha *et al.* (110)

239
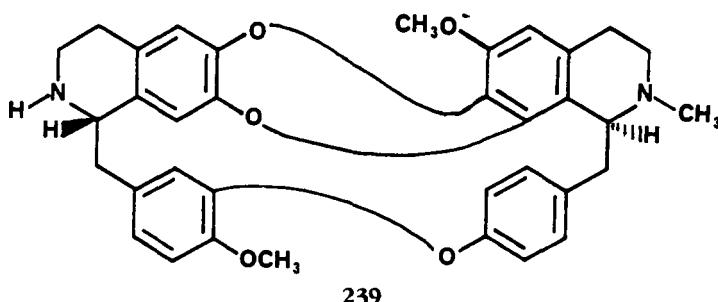
MP: None reported (125)
[α]D: None reported (125)
UV: None reported (125)
IR: None reported (125)
^{1}H nmr: NCH$_3$ 2.61, OCH$_3$ 3.86, 3.98 (125)
MS: M$^+$562, 336, 335, 321, 168 (125)
SOURCES: *Albertisia papuana* Becc. (Menispermaceae) (125)
PREPARATION: Cocsoline [152] +CH$_2$N$_2$ afforded O-Methylcocsoline (125)

240   7'-O-METHYLCUSPIDALINE   C$_{38}$H$_{44}$O$_6$N$_2$: 624.3199
Type I (R,R) 6,7,11*,12-6,7,12*

240
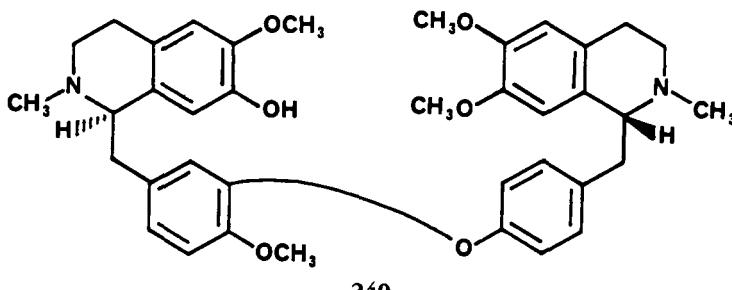
MP: Amorphous (190)
[α]D: − 105°(c=0.001, CHCl$_3$) (190)
UV: 285 (3.98) (190); (MeOH+NaOH) 285, 305 (190)
^{1}H nmr: NCH$_3$ 2.46 (N-2), 2.54 (N-2'); OCH$_3$ 3.59 (C-7'), 3.80, 3.81, 3.84; ArH 6.05 (H-8), 6.36
          (H-8'), 6.47 (H-5 or H-5'), 6.56 (H-5' or H-5), 6.62 (d) (1H) (J=1.7 Hz) (H-10), 6.78 (d)
          (2H) (J=8 Hz) (H-10' and H-11' or H-13' and H-14'), 6.86 (dd) (1H) (J=1.7, 8.2 Hz) (H-14),
          6.91 (d) (1H) (J=8.2 Hz) (H-13), 7.00 (d) (2H) (J=8 Hz) (H-13' and H-14' or H-10' and H-
          11') (190)
MS: M$^+$624 (1) (found 624.3188 and calculated 624.3199), 417 (2), 326 (2), 211 (2), 206 (99), 192
          (100), 191 (26), 177 (34) (190)
SOURCE: *Aristolochia elegans* (Aristolochiaceae) (190)

241   7-O-METHYLLINDOLDHAMINE   C$_{35}$H$_{38}$O$_6$N$_2$: 582.2730
Type I (R,R) 6,7,11*,12-6,7,12*
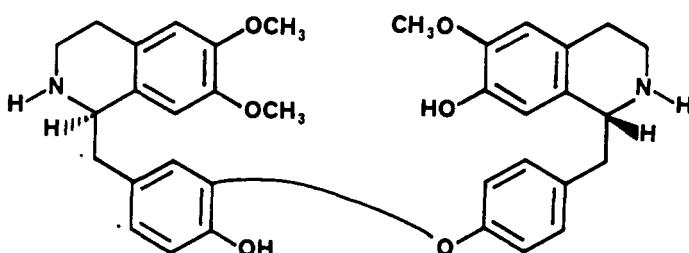
241

MP: None reported (128)
[α]D: +21°(c=0.2, MeOH) (128)
UV(EtOH):   208 (4.70), 228 (sh) (4.42), 286 (4.00) (128); (EtOH+NaOH) 226, 244 (sh), 303 (128)
^{1}H nmr: NCH$_3$ None; OCH$_3$ 3.73 (C-7 or C-7') 3.80 (s) (6H) (c-6 and C-6'); ArH 6.54-7.10 (m)
          (11H) (128)
MS: M$^+$582 (0.5), 404 (12), 390 (10), 192 (100), 178 (89) (128)
SOURCE: *Polyalthia nitidissima* Benth. (Annonaceae) (128)
DERIVATIVES: Isodaurisoline (7-0-Methyllindoldhamine+CH$_2$O+NaBH$_4$) (128)
NOTE: 7-0-Methyllindoldhamine and 7'-0-methyllindoldhamine [242] were isolated as a nonsepara-
          ble mixture which on N-methylation furnished isodaurisoline and daurisoline, respectively
          (128).

242   7'-0-METHYLLINDOLDHAMINE   C$_{35}$H$_{38}$O$_6$N$_2$: 582.2730
                     Type I (R,R) 6,7,11*,12-6,7,12*
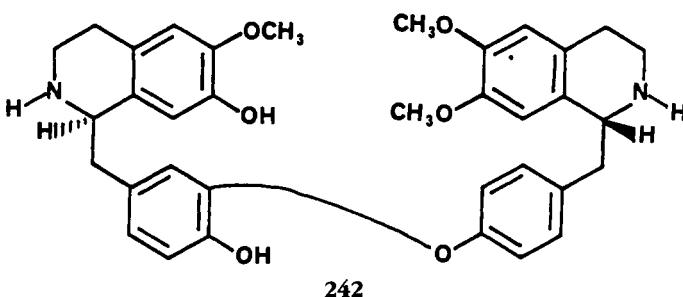
242

MP: None reported (128)
[α]D: +21°(c=0.2, MeOH) (128)
UV(EtOH):   208 (4.70), 228 (sh) (4.42), 286 (4.00) (128); (EtOH+NaOH) 226, 244 (sh), 303 (128)
^{1}H nmr: NCH$_3$ None; OCH$_3$ 3.73 (C-7 or C-7') 3.80 (s) (6H) (C-6 and C-6'); ArH 6.54-7.10 (m)
          (11H) (128)
MS: M$^+$582 (0.5), 404 (12), 390 (10), 192 (100), 178 (89) (128)
SOURCE: *Polyalthia nitidissima* Benth. (Annonaceae) (128)
DERIVATIVES: Daurisoline (7'-0-Methyllindoldhamine+CH$_2$O+NaBH$_4$) (128)
NOTE: 7'-0-Methyllindoldhamine and 7-0-methyllindoldhamine [241] were isolated as a nonsepara-
          ble mixture which on N-methylation furnished daurisoline and isodaurisoline, respectively
          (128).

243   N-METHYLPACHYGONAMINE   C$_{35}$H$_{34}$O$_6$N$_2$: 578.2417
                     Type XIX 5,6,7*,8$^+$,12-6*,7$^+$,12(11-11)
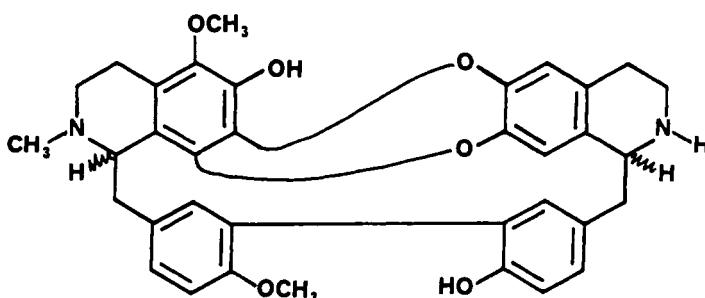
243

MP: 183-185° dec. (CHCl$_3$/MeOH) (120)
[α]^{27}D: +287°(c=0.23, MeOH) (120)
UV: 235 (sh) (4.19), 291 (3.59) (120)
IR(KBr):   3400, 2940, 1590, 1505, 1465, 1435, 1375, 1330, 1275, 1235, 1200, 1137, 1100, 1040,
          1020, 1008, 980, 860, 810, 750 (120)

^{1}H nmr (CDCl$_3$+CH$_3$OD):   NCH$_3$ 2.31; OCH$_3$ 3.92, 3.99; ArH 6.60, 6.90-7.65 (m) (6H), 8.10
      (120)
MS: M$^+$578, 352 (100), 337, 211, 176 (120)
SOURCES: *Pachygone ovata* (Poir.) Miers ex Hook. (Menispermaceae) (120,200)

244   O-METHYLTHALMINE   C$_{38}$H$_{42}$O$_6$N$_2$: 622.3043

Type XIV (*S,S*) 6,7*,11$^+$,12-5*,6,7,12$^+$
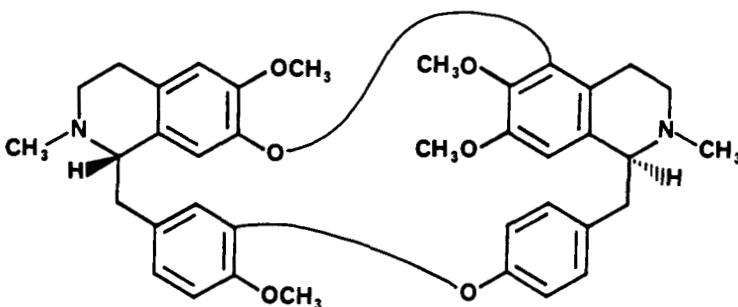
244

MP: Amorphous (188)
[α]D: −43°(MeOH) (188)
UV: 285 (188)
^{1}H nmr: NCH$_3$ 2.10, 2.58; OCH$_3$ 3.60, 3.78, 3.81 (6H); ArH 5.76 (H-8), 5.98 (H-8'), 6.49-6.85
      (m) (8H) (188)
MS: M+622, 621, 396, 395, 381, 198, 175, 174 (188)
CD: Demonstrated *S,S* configuration (188)
SOURCE: *Thalictrum sultanabadense* Stapf. (Ranunculaceae) (188)

245   2-NORLIMACUSINE   C$_{36}$H$_{38}$O$_6$N$_2$: 594.2730

Type VI (*R,R*) 6,7*,11$^+$,12-6,7,8*,12$^+$
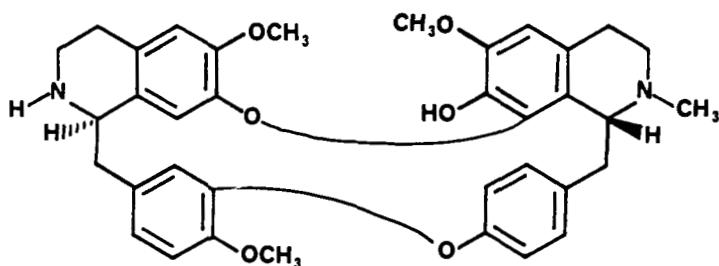
245

MP: 172°(MeOH) (197)
[α]D: +167°(*c*=0.7, CHCl$_3$) (197)
UV: 210 (4.70), 224 (sh) (4.52), 279 (3.72), 291 (sh) (3.71) (197)
^{1}H nmr: NCH$_3$ 2.69; OCH$_3$ 3.50 (C-6), 3.80 (C-6'), 3.92 (C-12); AlH 4.14 (q) (H-1'), 4.69 (q) (H-
      1); ArH 6.42 (s) (3H) (H-6, H-6', H-8), 6.65 (brs) (1H) (H-10), 6.87 (brs) (1H) (H-14), 6.87
      (dd) (1H) (*J*=1.5, 8.0 Hz) (H-10'), 6.88 (d) (1H) (*J*=8.4 Hz) (H-13), 6.95 (dd) (1H) (*J*=1.5,
      8.0 Hz) (H-11'), 7.01 (dd) (1H) (*J*=1.5, 8.0 Hz) (H-13'), 7.44 (dd) (1H) (*J*=1.5, 8.0 Hz) (H-
      14') (197)
MS: M$^+$594 (88), 593 (100), 487 (14), 367 (82), 353 (20), 351 (21), 192 (52), 184 (88), 161 (27) (197)
SOURCE: *Sciadotenia eichleriana* Moldenke (Menispermaceae) (197)
DERIVATIVES: Limacusine [**44**] (2-Norlimacusine+CH$_2$O+HCOOH) (ir, ^{1}H nmr, [α]D, tlc) (197)

246   NORPENDULINE   C$_{36}$H$_{38}$O$_6$N$_2$: 594.2730

Type VIII (*S,S*) 6,7,8*,11$^+$,12-6,7*,12$^+$

246
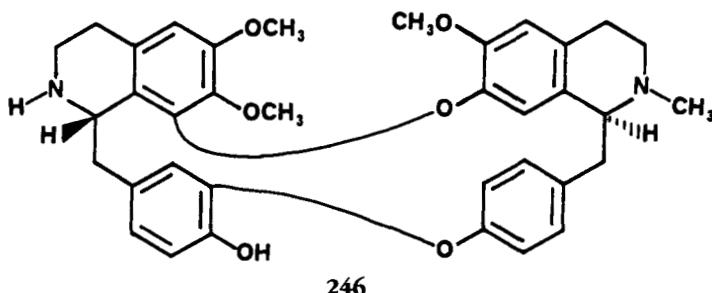
MP: None reported (175)
$[\alpha]^{25}$D: +260°(c=0.09, MeOH) (175)
UV: 239 (sh) (4.36), 283 (3.95), 293 (sh) (3.83), 311 (3.44) (175)
^{1}H nmr: NCH$_3$ 2.63; OCH$_3$ 3.11 (C-7), 3.21 (C-6'), 3.73 (C-6); ArH 5.88 (dd) (1H) (J=2, 8.2 Hz)
      (H-10'), 5.97 (H-8'), 6.25 (d) (1H) (J=1.5 Hz) (H-10), 6.27 (H-5), 6.46 (H-5'), 6.58 (dd)
      (1H) (J=2, 8.2 Hz) (H-11'), 6.67 (dd) (1H) (J=1.5, 8 Hz) (H-14), 6.74 (d) (1H) (J=8 Hz) (H-
      13), 6.98 (dd) (1H) (J=2, 8.2 Hz) (H-13'), 7.30 (dd) (1H) (J=2, 8.2 Hz) (H-14') (175)
MS: M$^+$594 (35), 381 (100), 367 (11), 351 (13), 335 (7), 191 (57), 174 (15) (175)
CD: −24 (212), 0 (222), +20 (229), 0 (238), −11 (244), 0 (257), +3 (282) (175)
SOURCE: *Cocculus pendulus* (Forsk) Diels (Menispermaceae) (175)

247   NORTRILOBINE   C$_{34}$H$_{32}$O$_5$N$_2$: 548.2311
                Type XXIII (S,S) 6*,7$^+$,11‡,12-6,7*,8$^+$,12‡

247
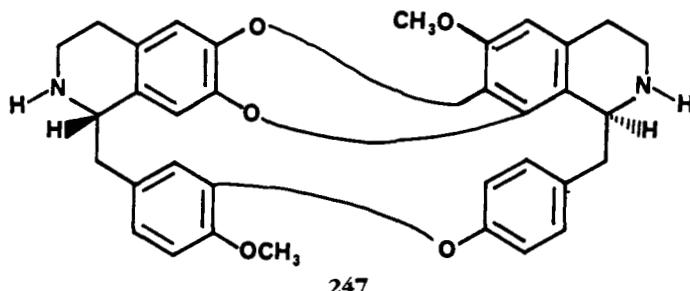
MP: 177-180°(MeOH) (169)
TLC: 0.21 (double development) (Si gel G; C$_6$H$_6$-Me$_2$CO-NH$_4$OH [4:8:0.1]) (169)
$[\alpha]^{25}$D: +216°(c=0.44, CHCl$_3$) (169)
UV: 218 (4.60), 237 (4.62), 275 (3.66), 287 (3.68), 300 (sh) (3.53) (169)
IR(KBr):   1625, 1590, 1505, 1450, 1440, 1365, 1295, 1275, 1230, 1170, 1125, 1025, 825 (169)
^{1}H nmr: OCH$_3$ 3.78, 3.92; ArH 6.21-7.4 (m) (10H) (169)
MS: M$^+$548 (6) (measured 548.2299), 335 (3), 322 (15), 321 (100), 307 (7), 211 (5), and 161 (53)
      (169)
SOURCE: *Pachygone ovata* Miers ex Hook. f. and Thoms. (Menispermaceae) (169)
DERIVATIVES: Isotrilobine [157] (Nortrilobine+CH$_2$O+HCOOH) (uv, ir, ^{1}H nmr, ms, cd) (169)

248   OSORNINE   C$_{38}$H$_{42}$O$_7$N$_2$: 638.2992
                Type VIa^5 (S,R) 6,7*,10,11$^+$,12-6,7,8*,12$^+$

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^{5}This is a new class that supplements Class VI as mentioned in the review of Guha *et al.* (110)

248
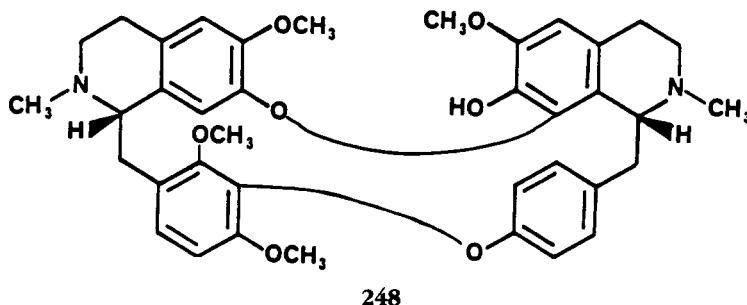
MP: 244-245°(MeOH) (146)
TLC: 0.19 (Si gel F-$_{254}$; CHCl$_3$-MeOH-NH$_4$OH [95:5:0.5]) (146)
[α]^{25}D: −151°(c=0.36, CHCl$_3$) (146)
UV: 207 (4.80), 230 (sh) (4.53), 282 (3.75) (146)
^{1}H nmr: NCH$_3$ 2.31 (N-2'), 2.46 (N-2); OCH$_3$ 3.71, 3.82, 3.83, 3.88; ArH 4.60 (H-8), 6.46 (H-5
    or H-5'), 6.48 (H-5' or H-5), 6.65 (2H) (brs), 6.74 (1H) (d) (J=8.8 Hz) (H-13), 6.90 (1H) (dd)
    (J=1.8, 8.2 Hz), 7.16 (1H) (d) (J=8.5 Hz) (H-14), 7.29 (1H) (dd) (J=2.1, 8.2 Hz) (146)
MS: M$^+$638 (47), 381 (100), 191 (79), 174 (22) (146)
CD: −60 (209), 0 (219), +41 (232), 0 (250), −2 (270), 0 (276), +0.6 (282), 0 (300) (146)
SOURCE: *Berberis buxifolia* Lam. (Berberidacee) (146)
DERIVATIVES: 0-Methylosornine (Osornine+CH$_2$N$_2$) (146)
^{1}H nmr: NCH$_3$ 2.33 (N-2'), 2.57 (N-2); OCH$_3$ 2.97 (C-7'), 3.72 (C-6' or C-6), 3.78 (C-6 or C-6'),
    3.81 (C-10), 3.87 (C-12); AlH 4.02 (H-1'), 4.48 (H-1); ArH 4.79 (H-8), 6.37 (1H) (dd)
    (J=2.1, 8.2 Hz) (H-10'), 6.42 (H-5 or H-5'), 6.46 (1H) (dd) (J=2.1, 8.2 Hz) (H-11'), 6.48
    (H-5' or H-5), 6.74 (1H) (d) (J=8.5 Hz) (H-13), 7.00 (1H) (dd) (J=2.1, 8.2 Hz) (H-11'), 7.09
    (1H) (d) (J=8.5 Hz) (H-14), 7.29 (1H) (dd) (J=2.1, 8.2 Hz) (146)
MS: M$^+$652 (42), 395 (68), 198 (100), 174 (36) (146)
NOE: (146)
    Birch reduction (Na/NH$_3$) afforded *S*-(+)-2-methyl-6,2',4'-trimethoxy-7-hydroxy-1-benzyl-
1,2,3,4-tetrahydroisoquinoline and *R*-(−)-armepavine (146)

249   PACHYGONAMINE   C$_{34}$H$_{32}$O$_6$N$_2$: 564.2260
                      Type XIX 5,6,7*,8$^+$,12-6*,7$^+$,12(11-11)

249
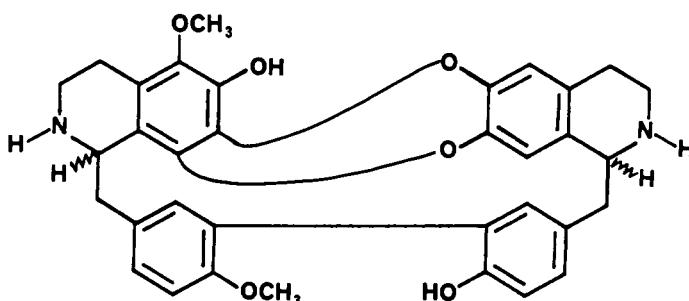
MP: 225-227°dec. (CHCl$_3$) (120)
[α]^{25}D: +257°(c=0.28, MeOH) (120)
UV: 234 (sh) (4.71), 291 (4.05) (120)
IR(KBr):   3400, 2930, 1595, 1505, 1462, 1435, 1370, 1335, 1305, 1285, 1240, 1200, 1140, 1110,
    1040, 995, 970, 945, 885, 860, 810, 750 (120)
^{1}H nmr: NCH$_3$ none; OCH$_3$ 3.89, 3.95; ArH 6.58, 6.90-7.65 (m) (6H), 8.12 (120)
MS: M$^+$564, 338, 337 (100), 323, 211, 169 (120)
SOURCES: *Pachygone ovata* (Poir.) Miers ex Hook. (Menispermaceae) (120,200)
DERIVATIVES: *N,N*-Dimethylpachygonamine (Pachygonamine+CH$_2$O+HCOOH) (120)
MP: 199-202°dec (CHCl$_3$/MeOH) (120)
[α]^{25}D: +327° (c=0.43, CHCl$_3$) (120)
UV: 235 (sh) (3.95), 290 (3.26) (120)

IR(KBr): 3400, 2930, 1600, 1505, 1465, 1370, 1270, 1235, 1040, 1005, 985, 870, 810 (120)
[1]H nmr: NCH$_3$ 2.28, 2.63; OCH$_3$ 3.97, 4.01; ArH 6.62, 6.6-7.75 (m) (6H), 8.90 (120)
MS: M$^+$592, 577, 366, 365, 351, 211, 183, 175 (100) (120)

N,N,O-Trimethylpachygonamine (*N*-Methyltiliamosine) (*N,N*-Dimethylpachygonamine
+CH$_2$N$_2$) (120)
MP: 142-145°(CHCl$_3$) (120)
[α]^{26}D: +264° (c=0.44, CHCl$_3$) (120)
UV: 235 (sh) (4.06), 288 (3.61) (120)
[1]H nmr: NCH$_3$ 2.30, 266; OCH$_3$ 3.85, 3.95, 3.99; ArH 6.63, 6.88-7.78 (m) (6H), 8.08 (120)
MS: M$^+$606, 605, 591, 380, 379 (100), 365, 211, 190 (120)

250   PACHYOVATAMINE   C$_{34}$H$_{32}$O$_5$N$_2$: 548.2311
Type XVII (*S,S*) 6,7*,8$^+$,12-6*,7$^+$,12(11-11)
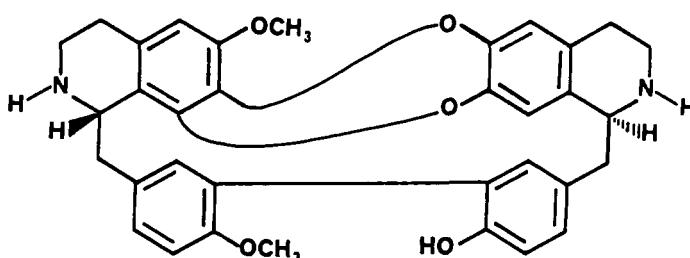
250

MP: 182-185°(Amorphous) (200)
TLC: 0.30 (Si gel HF$_{254}$; CHCl$_3$-MeOH-NH$_4$OH [9:1:0.1]) (200)
[α]^{25}D: +259° (c=0.29, CHCl$_3$) (200)
UV: 230 (4.34), 291 (3.68) (200)
IR(KBr): 2930, 2840, 1625, 1590, 1505, 1450, 1435, 1415, 1360, 1290, 1277, 1240, 1225, 1130,
895, 865, 825 (200)
[1]H nmr: OCH$_3$ 3.83, 3.96; ArH 6.25, 6.60, 6.8-7.6 (m) (6H), 8.07 (200)
MS: M$^+$548 (3), 335 (15), 322 (16), 321 (100), 211 (6), 161 (30) (200)
CD: [θ]$_{238}$ +134,900, [θ]$_{271}$ +13,700, [θ]$_{309}$ +6,300
SOURCE: *Pachygone ovata* Miers ex Hook. f. and Thoms. (Menispermaceae) (200)
DERIVATIVES: *N,N*-Dimethylpachyovatamine (Pachyovatamine+CH$_2$O+HCOOH) (200)
MP: 135-138°(Me$_2$CO) (Amorphous)
TLC: 0.78 (Si gel HF$_{254}$; CHCl$_3$-MeOH-NH$_4$OH [8.5:1.5:0.1]) (200)
[α]^{25}D: +287° (c=0.37, CHCl$_3$) (200)
UV: 234 (sh) (4.75), 290 (3.95) (200)
IR(KBr): 2940, 2850, 2800, 1630, 1595, 1590, 1508, 1468, 1460, 1450, 1430, 1420, 1362, 1280,
1275, 1240, 1205, 1130, 1120, 1070, 1015, 990, 970, 952, 895, 875, 850, 825, 815, 780,
755
[1]H nmr: NCH$_3$ 2.29, 2.63; OCH$_3$ 3.85, 3.98; ArH 6.29, 6.63, 6.88-7.70 (m) (6H), 8.08 (200)
MS: M$^+$576 (10), 349 (100), 335 (30), 211 (1), 175 (50) (200)

N,N-Dimethyl-*O*-Acetylpachyovatamine (*O*-Acetyltiliacorinine) (200)
MP: 170-174°(Amorphous) (200)
TLC: 0.70 (Si gel HF$_{254}$); CHCl$_3$-MeOH-NH$_4$OH [9:1:0.1]) (200)
[α]^{27}D: +269°(c=0.42, pyridine) (200)
UV: 232 (sh) (4.72), 288 (3.90) (200)
IR(KBr): 2940, 2860, 2800, 1770, 1630, 1590, 1510, 1470, 1450, 1440, 1430, 1420, 1380, 1365,
1300, 1282, 1270, 1240, 1220, 1210, 1200, 1120, 1070, 1045, 1030, 1010, 955, 915, 895,
880, 832, 810, 750
[1]H nmr: OCOCH$_3$ 2.13; NCH$_3$ 2.32, 2.61; OCH$_3$ 3.82, 3.86; ArH 6.30, 6.64, 6.83-7.68 (m) (6H),
8.00 (200)
MS: M$^+$618 (1), 617 (6), 350 (10), 349 (34), 335 (14), 175 (100) (200)

251 TEMUCONINE $C_{37}H_{42}O_6N_2$: 610.3043

Type I (R,S) 6,7,11*,12-6,7,12*
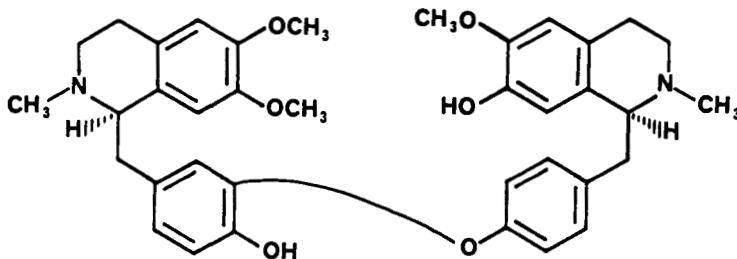
251

MP: Not reported (40)

$[\alpha]^{25}D$:   +77°(c=0.24, MeOH) (40)

UV: 211 (4.74), 227 (4.57), 282 (4.09) (40)

¹H nmr: NCH₃ 2.47, 2.56; OCH₃ 3.60 (C-6), 3.81, 3.85; ArH 6.12 (H-8'), 6.31 (H-8), 6.46 (br) (H-10), 6.46 (H-5 or H-5'), 6.58 (H-5' or H-5), 6.84 (H-14, H-11', H-13') (3H) (d) (J=8.3 and 8.85 Hz), 6.89 (H-13) (d) (J=8.3 Hz), 7.06 (H-10' and H-14') (d) (J=8.85 Hz) (NOE used) (40)

MS: 609 (M-1) (0.2), 417 (0.6), 386 (0.5), 355 (0.2), 206 (94), 192 (100), 177 (23) (40)

CD: +18.3 (210), +5.3 (221), +9.8 (234), +0.34 (255), +3.4 (278) (40)

SOURCES: *Berberis valdiviana* Phil. (Berberidaceae) (40)

252 THALIGRISINE $C_{37}H_{42}O_6N_2$: 610.3043

Type I (R,S) 6,7,11*,12-6,7,12*
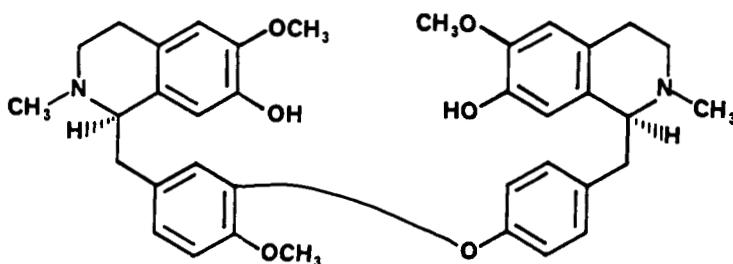
252

MP: None reported (180)

$[\alpha]^{25}D$:   +57°(c=0.13, MeOH) (180)

UV: 226 (sh) (4.48), 284 (3.98) (180)

¹H nmr: NCH₃ 2.44 (N-2 or N-2'), 2.51 (N-2' or N-2); OCH₃ 3.83 (C-6 or C-6' or C-12), 3.83 (C-6 or C-6' or C-12), 3.84 (C-6 or C-6' or C-12); ArH 6.26 (H-8 or H-8' or H-5 or H-5'), 6.35 (H-8' or H-8 or H-5 or H-5'), 6.45 (H-5 or H-5' or H-8 or H-8'), 6.54 (H-5' or H-5 or H-8 or H-8'), 6.58 (brs) (1H) (H-10), 6.81 (d) (2H) (J=8.5 Hz) (H-11' and H-13'), 6.85 (d) (1H) (H-13) (J=8.2 Hz), 6.86 (d) (1H) (J=8.2 Hz) (H-14), 7.03 (d) (2H) (J=8.5 Hz) (H-10' and H-14') (180)

MS: M⁺-1 609 (0.2), 608 (0.6), 418 (0.1), 381 (0.4), 364 (0.1), 206 (1), 192 (100), 175 (2.3) (180)

CD: 215 (positive tail), +2 (228), +15 (244), +2.5 (sh) (254), 0 (300) (180)

SOURCE: *Thalictrum minus* L. var. *microphyllum* Boiss. (Ranunculaceae) (180)

253 THALIPHYLLINE $C_{37}H_{40}O_6N_2$: 608.2886

Type XI (S,S) 6,7,8*,11⁺,12-6*,7,12⁺
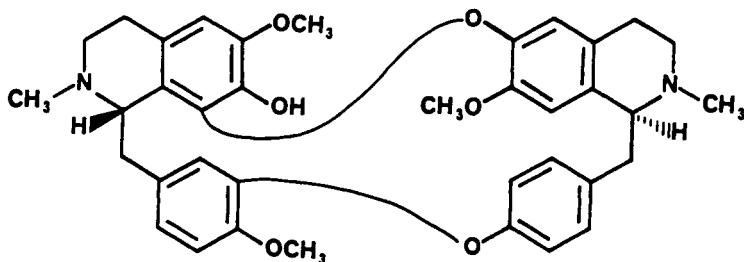
253

MP: Not reported (180)
[α]^{25}D: +198°(c=0.12, MeOH) (180)
UV: 222 (4.71), 279 (3.89), 290 (sh) (3.75) (180)
^{1}H nmr: NCH$_3$ 2.10 (N-2), 2.57 (N-2'); OCH$_3$ 3.65 (C-7'), 3.90 (6H) (C-6 and C-12); ArH 6.07 (H-
    8'), 6.12 (H-5'), 6.34 (d) (1H) (J=2.2 Hz), 6.55 (H-5), 6.71 (dd) (1H) (J=2.2, 8.2 Hz) (H-
    14), 6.74 (dd) (1H) (J=2, 8.2 Hz) (H-10'), 6.78 (dd) (1H) (J=2, 8.2 Hz) (H-11'), 6.82 (d)
    (1H) (J=8.2 Hz) (H-13'), 7.01 (dd) (1H) (J=2, 8.2 Hz) (H-13'), 7.23 (dd) (1H) (J=2, 8.2 Hz)
    (H-14') (180)
MS: M$^+$608 (38), 607 (24), 593 (4.5), 577 (1.7), 381 (100), 367 (16), 204 (2.6), 192 (21), 191 (89),
    190 (22), 176 (33), 174 (48) (180)
CD: +61 (214), 0 (246), −4.2 (250), 0 (270), +21 (286), 0 (300) (180)
SOURCE: *Thalictrum minus* L. var. *microphyllum* Boiss. (Ranunculaceae) (180)
DERIVATIVES: 0-Methylthalicberine (Thaliphylline+CH$_2$N$_2$) (180)

   Birch reduction (Na/NH$_3$) of 0-methylthaliphylline afforded S-(+)-0-methylarmepavine, S-(+)-N-
methylisococlaurine, and S-(+)-1-(4-hydroxybenzyl)-2-methyl-7-methoxy-1,2,3,4-tetrahydroisoquino-
line (180)

254   TILIACORININE-2'-N-OXIDE   C$_{36}$H$_{36}$O$_6$N$_2$: 592.2573
              Type XVIII (S,S) 6,7*,8$^+$,12-6*,7$^+$,12(11-11)

254
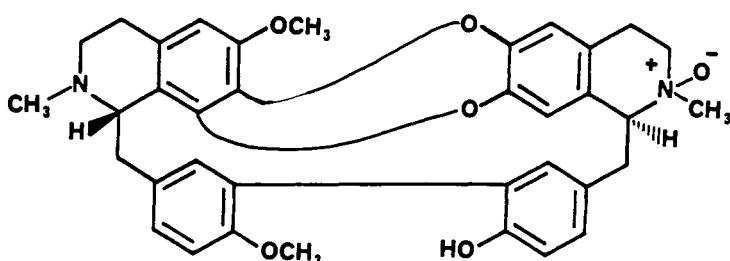
MP: 215-217°dec. (2)
[α]^{19}D: +238.2°(c=1.1, CHCl$_3$) (2)
UV: None reported (2)
IR: None reported (2)
^{1}H nmr: NCH$_3$ 2.32 (N-2), 2.99 (N-2'); OCH$_3$ 3.87, 3.97; AlH 2.55-4.90 (m, 14H); ArH 6.33,
    6.73, 6.90-7.90 (m, 6H), 8.27 (2)
MS: M$^+$592 (20%) (found 592.2563), 591 (20), 576 (46), 575 (46), 574 (46), 561 (17), 560 (23), 559
    (14), 558 (24), 557 (11), 556 (14), 544 (20), 543 (20), 542 (11), 350 (38), 349 (100), 348 (19),
    347 (22), 336 (22), 335 (11), 333 (20), 308 (22), 250 (22), 241 (11), 240 (38), 239 (23), 236
    (11), 220 (26), 208 (26), 207 (13), 190 (14), 187 (20), 180 (28), 179 (200) (2)
SOURCES: *Tiliacora triandra* Diels (Menispermaceae)
DERIVATIVES: Tiliacorinine (Tiliacorinine-2'-N-Oxide+PCl$_3$) (mp, ^{1}H nmr) (2)

255 VANUATINE $C_{39}H_{46}O_8N_2$: 670.3254

Type IIa[6] (S,S) 6,7,10*,12,13-6,7,11*,12
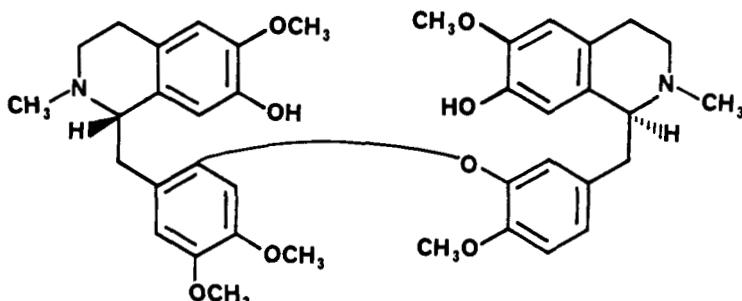
255

MP: None reported (115)

$[\alpha]^{25}$D: +138°(c=0.12, MeOH) (115)

UV: 210 (4.83), 230 (sh) (4.48), 286 (4.11) (115)

¹H nmr: NCH₃ 2.38 (N-2), 2.41 (N-2'); OCH₃ 3.72 (C-12), 3.75 (C-6 or C-6'), 3.76 (C-6' or C-6), 3.84 (C-13), 3.88 (C-12'); AlH 3.41 (C-1'), 3.65 (C-1); ArH 5.48 (H-8), 6.01 (H-8'), 6.34 (H-11), 6.42 (H-5' or H-5), 6.42 (dd) (1H) (J=2.1, 8.2 Hz) (H-14'), 6.47 (H-5 or H-5'), 6.71 (H-14), 6.72 (d) (1H) (J=2.1 Hz) (H-10'), 6.77 (d) (1H) (J=8.2 Hz) (H-13') (115)

NOE: (115)

MS: M⁺ 670 (0.2), 669 (1), 655 (0.4), 535 (0.1), 478 (0.8), 477 (1), 341 (0.1), 192 (100) (115)

CD: +23.2 (232), +6.2 (289) (115)

SOURCES: *Hernandia peltata* Meissn. (Hernandiaceae) (115)

DERIVATIVES: O,O,-Dimethylvanuatine (Vanuatine+CH₂N₂) (115)

$[\alpha]^{25}$D: +78°(c=0.12, MeOH) (115)

¹H nmr: NCH₃ 2.43 (N-2 or N-2'), 2.44 (N-2' or N-2); OCH₃ 3.55 (C-7 or C-7'), 3.61 (C-7' or C-7), 3.73, 3.77, 3.79, 3.82, 3.86; ArH 6.13 (H-8 or H-8'), 6.14 (H-8' or H-8), 6.46 (d) (1H) (J=2.44 Hz) (H-10'), 6.48 (H-5 or H-5'), 6.48 (H-11), 6.54 (H-5' or H-5), 6.58 (H-14), 6.76 (dd) (1H) (J=1.83 and 8.24 Hz) (H-14'), 6.87 (d) (1H) (J=8.24 Hz) (H-13') (115)

MS: M⁺ 698 (0.2), 492 (0.5), 206 (100) (115)

CD: +28.4 (235), +5.2 (287) (115)

Birch reduction (Na/NH₃) afforded S-(-)-2-methyl-6,7,4',5'-tetramethoxy-2'-hydroxy-1,2,3,4-tetrahydroisoquinoline (positive cd maximum near 233 nm indicates the S configuration, while the negative specific rotation indicates that ring C is turned toward the N-methyl group) and S-(+)-O-methylarmepavine (115)

256 VATEAMINE $C_{38}H_{44}O_8N_2$: 656.3097

Type IIb[7] (S,S) 6,7,10*,11,12-6,7,11*,12
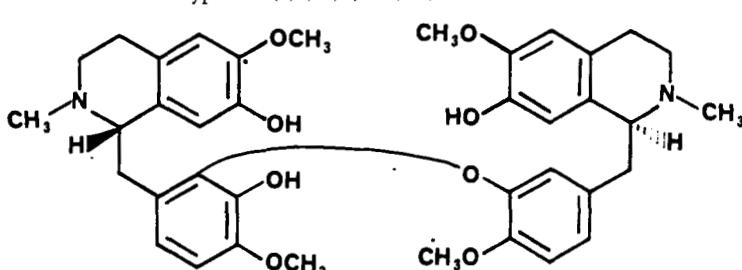
256

MP: None reported (115)

$[\alpha]^{25}$D: +204°(c=0.14, MeOH) (115)

UV: 212 (4.72), 230 (sh) (4.48), 283 (4.07) (115)

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[6]This is a new class that supplements Class II as presented in the review of Guha *et al.* (110)

[7]This is a new class that supplements Class II as presented in the review of Guha *et al.* (110)

^{1}H nmr: NCH$_3$ 2.39 (N-2), 2.52 (N-2'); OCH$_3$ 3.72 (C-6 or C-6'), 3.75 (C-6' or C-6), 3.87 (C-12'),
            3.91 (C-12); AlH 3.58 (H-1), 3.81 (H-1'); ArH 5.15 (H-8), 5.71 (H-8'), 6.17 (d) (1H) (J=8.5
            Hz) (H-14), 6.22 (dd) (1H) (J=2.1, 8.2 Hz) (H-14'), 6.40 (H-5' or H-5), 6.42 (H-5 or H-5'),
            6.65 (d) (1H) (J=8.5 Hz) (H-13), 6.72 (d) (1H) (J=8.2 Hz) (H-13), 6.92 (d) (1H) (J=2.1 Hz)
            (H-10') (115)

NOE: (115)
MS: M$^+$656 (0.1), 655 (0.2), 519 (0.1), 464 (0.3), 327 (0.2), 192 (100) (115)
CD: +14.6 (233), +7.5 (286) (115)
SOURCES: *Hernandia peltata* Meissn. (Hernandiaceae) (115)
DERIVATIVES: 0,0,0,-Trimethylvateamine (Vateamine+CH$_2$N$_2$) (115)
$[\alpha]^{25}$D: +118° (c=0.2, MeOH) (115)
^{1}H nmr: NCH$_3$ 2.38 (N-2 or N-2'), 2.39 (N-2 or N-2'); OCH$_3$ 3.55 (C-7 or C-7'), 3.56 (C-7' or C-7);
            ArH 6.05 (H-8 or H-8'), 6.06 (H-8' or H-8), 6.40 (d) (1H) (J=2.44 Hz) (H-10'), 6.45 (H-5 or
            H-5'), 6.53 (H-5' or H-5), 6.59 (dd) (1H) (J=1.3 and 8.24 Hz) (H-14'), 6.70 (H-13), 6.77
            (H-14), 6.82 (d) (1H) (J=8.24 Hz) (H-13') (115)

MS: M$^+$698 (0.1), 492 (0.4), 206 (100) (115)
CD: +11.3 (235), +3.2 (284) (115)

Birch reduction (Na/NH$_3$) afforded S-(+)-laudanosine and S-(+)-laudanidine (115)

SECOBISBENZYLISOQUINOLINE ALKALOIDS

257   BALUCHISTANAMINE   C$_{37}$H$_{38}$O$_8$N$_2$: 638.2628

Type VI (-, S)
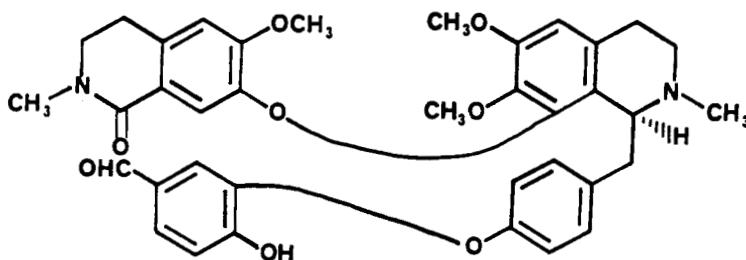
257

MP: 122-124° (C$_6$H$_{12}$/C$_6$H$_6$) (222)
$[\alpha]$D: Not reported (222)
UV(EtOH):   224 (4.57), 260 (4.05), 270 (4.06), 282 (sh) (3.97), 294 (sh) (3.90), 305 (3.80) with a
            bathochromic shift in OH$^-$ (222)
IR: 1720 (ArCHO), 1640 (ArCONR$_2$) (222)
^{1}H nmr: NCH$_3$ 2.35; ArCONCH$_3$ 3.10; OCH$_3$ 3.62, 3.85, 3.90; ArH 10H at 6.55, 6.73, 6.90,
            7.05, 7.20, 7.36, 7.48, 7.61 as a complex pattern; ArCHO 9.76 (222)
MS: M$^+$638 (small), 411 (100), 365, 227, 206, 204, 120 (222)
CD: [θ]$_{220}$ O, [θ]$_{231}$−14,000, [θ]$_{253}$ O, [θ]$_{263}$+2,560 (222)
SOURCE: *Berberis baluchistanica* Ahrendt (Berberidaceae) (222)
PREPARATION: Via oxidation (KMnO$_4$/Me$_2$CO) of oxyacanthine [48] (110) (uv, ms, tlc) (224)
NOTE: Stirring an EtOH solution (4 ml) of oxyacanthine [48] (1 mg) for 3 days failed to produce any
        baluchistanamine, as determined by tlc, thus suggesting the latter alkaloid is not of artifactual
        origin (222).
APPARENT BIOGENETIC PRECURSOR: Oxyacanthine [48] (110)

258   CHENABINE   C$_{37}$H$_{40}$O$_7$N$_2$: 624.2836

Type VIII (-, S)

258
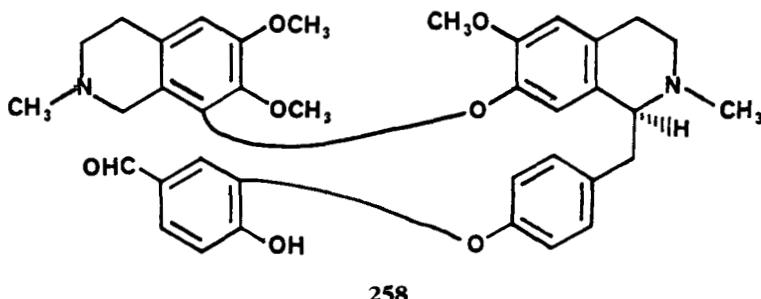
MP: Amorphous (224)
TLC: 0.46 (Si gel GF$_{254}$; CHCl$_3$-MeOH-NH$_4$OH [90:10:1]) (224)
[α]D: None reported (224)
UV: 209 (4.72), 227 (sh) (4.49), 281 (4.08), 326 (3.87) (224); (MeOH+OH$^-$) 211 (4.83), 283 (3.91),
342 (4.28) (224)
IR: 1680 (ArCHO) (224)
^{1}H nmr: NCH$_3$ 2.50 (N-2' or N-2), 2.55 (N-2 or N-2'); OCH$_3$ 3.25 (C-7), 3.77 (C-6'), 3.90 (C-6);
ArH 5.23 (H-8'), 6.44 (H-5'), 6.68 (H-5), 6.77 (brs) (4H) (H-10', H-11', H-13', H-14'),
7.04 (d) (1H) (J=8.2 Hz) (H-13), 7.42 (d) (1H) (J=2.1 Hz) (H-10), 7.59 (dd) (1H) (J=1.8, 8.2
Hz) (H-14) (224)
NOE: (224)
MS: M$^+$ 624 (0.2), 397 (100), 365 (17), 227 (4), 222 (2), 206 (4) (224)
CD: +10 (210), 0 (217), +8.3 (236), 0 (270), +4 (287), 0 (310) (224)
SOURCE: *Berberis lycium* Royle (Berberidaceae) (224)
DERIVATIVES: O-Acetylchenabine (Ac$_2$O+ pyridine) (224)
^{1}H nmr: ArOCOCH$_3$ 2.26; NCH$_3$ 2.42, 2.46; OCH$_3$ 3.68 (C-7), 3.81 (C-6'), 3.92 (C-6); ArH 6.21
(H-8'), 6.54 (H-5'), 6.66 (H-5), 6.82 (dd) (2H) (J=8.5 Hz) (H-11' and H-13'), 7.02 (dd) (2H)
(J=8.5 Hz) (H-10' and H-14'), 7.30 (d) (1H) (J=8.2 Hz) (H-13), 7.33 (d) (1H) (J=2.0 Hz)
(H-10), 7.60 (dd) (1H) (J=2.0, 8.2 Hz) (H-14); ArCHO 9.87 (224)
MS: M$^+$ 666 (0.3), 624 (0.2), 623 (0.4), 397 (100), 269 (0.2) (224)
APPARENT BIOGENETIC PRECURSOR: Berbamine [57] (110)

259 CURACAUTINE   C$_{39}$H$_{42}$O$_9$N$_2$: 682.2891

Type Xa (S,-)

259
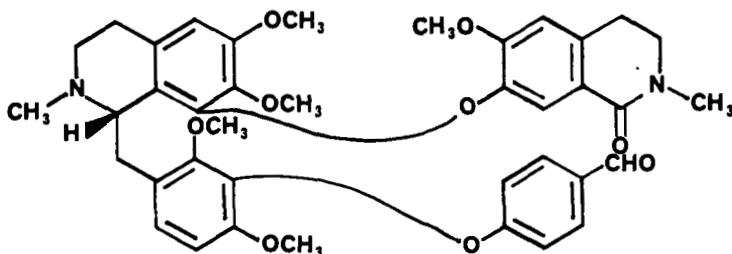
MP: Amorphous (146)
TLC: 0.54 (Si gel GF$_{254}$; CHCl$_3$-MeOH-NH$_4$OH [95:5:0.5]) (146)
[α]^{25}D: −5°(c=0.18, MeOH) (146)
UV: 207 (4.85), 223 (sh) (4.74), 271 (4.35), 282 (4.29) (146)
IR: 1690 (ArCHO), 1640 (ArCONR$_2$), 1610 (146)
^{1}H nmr: NCH$_3$ 2.20; ArCONCH$_3$ 3.04; OCH$_3$ 3.53 (C-7), 3.61 (C-6), 3.79 (C-6' or C-10), 3.84 (C-
10 or C-6'), 3.92 (C-12); ArH 6.46 (H-5), 6.65 (H-5'), 6.73 (d) (1H) (J=8.5 Hz) (H-13), 6.85
(d) (2H) (J=8.8 Hz) (H-11' and H-13'), 6.96 (d) (1H) (J=8.5 Hz) (H-14), 7.16 (s) (H-8'), 7.59
(d) (2H) (J=8.8 Hz) (H-10' and H-14'); ArCHO 9.80 (146)
MS: M$^+$ 682 (0.1), 681 (0.1), 411 (100), 365 (11), 271 (0.3), 206 (2.2), 204 (6) (146)
CD: +4.3 (214), 0 (218), −16 (230), 0 (249), +3 (263), +1.7 (285), 0 (290), −1.5 (300), 0 (320)
(146)
SOURCE: *Berberis buxifolia* Lam. (Berberidaceae) (146)

PREPARATION: Via oxidation ($KMnO_4$/Me_2CO) of calafatine [190] (111) (146)
APPARENT BIOGENETIC PRECURSOR: Calafatine [190] (111)

260 DIHYDROSECOCEPHARANTHINE $C_{37}H_{38}O_8N_2$: 638.2628
Type VI (-,*S*)
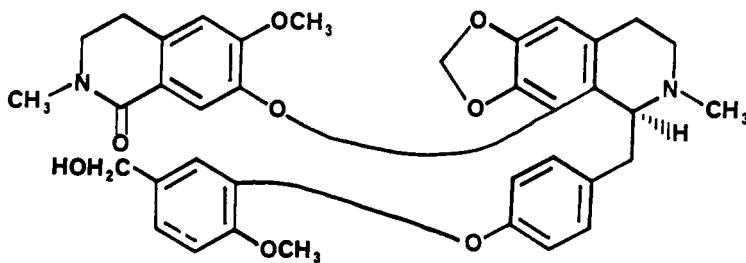
260

MP: 192-194°(MeOH) (192)
[α]D: −1.67°(*c*=0.12, $CHCl_3$) (192)
UV(EtOH): 224 (4.65), 263 (4.03), 273 (4.03), 286 (3.95), 294 (sh) (3.87), 306 (sh) (3.62) (192)
IR: 1640 ($ArCONR_2$) (192)
^1H nmr: NCH_3 2.28; $CONCH_3$ 3.07; OCH_3 3.84, 3.95; AlH 2.35-2.45 (m) (1H) (H-4'A), 2.75-
    3.00 (m) (6H), 3.27-3.38 (m) (1H) (H-3'), 3.53 (t) (2H) (*J*=6.8 Hz) (H-3), 3.87 (dd) (1H)
    (*J*=2.6, 8.9 Hz) (H-1'); $ArCH_2O$ 4.55; $ArCH_2O_2$ 5.84 (q) (2H) (*J*=1.5 Hz); ArH 6.47, 6.72,
    6.81 (d) (2H) (*J*=8.6 Hz) (H-11' and H-13'), 6.92 (d) (1H) (*J*=2.0 Hz) (H-10), 6.95 (d) (1H)
    (*J*=8.2 Hz), (H-13), 7.07 (dd) (1H) (*J*=2.0, 8.2 Hz) (H-14), 7.12 (d) (2H) (*J*=8.6 Hz) (H-10'
    and H-14'), 7.44 (H-8) (192)
MS(EI): 395 (100), 244 (53.5) (192)
MS(CI): $M+H^+$639 (100), 395 (30) (192)
ORD: (*c*=4.2×10^{-4}) +24,920 (216) (trough), +29,080 (222) (peak), 0 (232), −27,690 (241)
    (trough), 0 (287), +3,785 (297) (peak), 0 (311), −600 (316) (trough), −338 (350), −249
    (400) (192)
CD: (7.5×10^{-5}) [θ]$_{230}$ −42,390, [θ]$_{261}$ +5,030, [θ]$_{270}$ +5,652, [θ]$_{285}$ +5,596, [θ]$_{307}$ −1,187
   (192)
SOURCE: *Stephania sasakii* Hayata (Menispermaceae) (192)
PREPARATION: Reduction ($NaBH_4$/MeOH) of secocepharanthine (192)
APPARENT BIOGENETIC PRECURSOR: Cepharanthine [34] (110)

261 GILGITINE $C_{36}H_{34}O_8N_2$: 622.2316
Type XXIII (-,*S*)
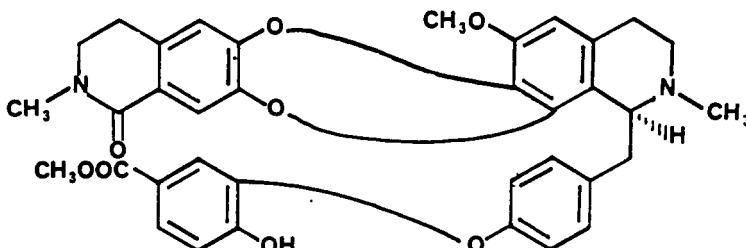
261

MP: Amorphous (221)
TLC: 0.34 (Si gel GF$_{254}$; C_6H_6-EtOAc-MeCN-MeOH-NH_4OH [30:20:40:5:5]) (221)
[α]D: Not recorded due to paucity of sample (221)
UV: 224 (4.32), 250 (sh) (3.96), 285 (3.57), 325 (3.22) (221); (MeOH+OH$^-$) 208 (4.66), 252 (sh)
    (3.99), 297 (3.82) (221)
IR: 1710 ($ArCOOCH_3$), 1645 ($ArCONR_2$), 1620 (221)

^{1}H nmr: NCH$_3$ 2.53; ArCONCH$_3$ 3.17; ArCOOCH$_3$ 3.81; OCH$_3$ 3.87; ArH 6.36 (H-5'), 6.65 (H-
    5), 6.92 (d) (2H) (J=8.5 Hz) (H-11' and H-13'), 7.16, 7.04 (d) (1H (J=8.5 Hz) (H-13), 7.16
    (d) (2H) (J=8.5 Hz) (H-10' and H-14'), 7.29 (H-8), 7.56 (d) (1H) (J=2.1 Hz) (H-10'), 7.73
    (dd) (1H (J=2.1, 8.5 Hz) (H-14) (221)

MS: M$^+$622 (0.1), 621 (0.3), 365 (100), 257 (2) (221)

CD: +2 (220), 0 (232), −4 (249), 0 (285) (221)

SOURCE: *Berberis lycium* Royle (Berberidaceae) (221)

APPARENT BIOGENETIC PRECURSOR: *N*-Methylapateline [**207**] (111)

262   JHELUMINE   C$_{36}$H$_{38}$O$_7$N$_2$: 610.2679

Type VIII (-,*S*)
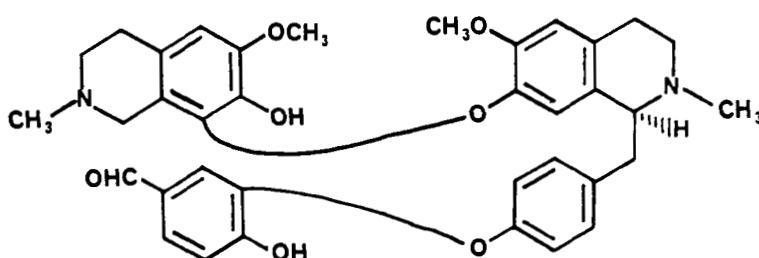
262

MP: Amorphous (224)

TLC: 0.29 (Si gel GF$_{254}$; CHCl$_3$-MeOH-NH$_4$OH {90:10:1}) (224)

[α]^{25}D: +28°(c=0.6, MeOH) (224)

UV: 211 (4.72), 227 (sh) (4.56), 281 (4.17), 326 (3.89) (224); (MeOH+OH$^-$) 214 (4.78), 233 (sh)
    (4.47), 287 (4.07), 341 (4.31) (224)

IR: 1680 (ArCHO) (224)

^{1}H nmr: NCH$_3$ 2.50 (N-2 or N-2'), 2.53 (N-2' or N-2); OCH$_3$ 3.80 (C-6'), 3.92 (C-6); ArH 5.33 (H-
    8'), 6.44 (H-5'), 6.68 (H-5), 6.75 (d) (2H) (J=8.8 Hz) (H-11' and H-13'), 6.78 (d) (2H)
    (J=8.8 Hz) (H-10' and H-14'), 7.04 (d) (1H) (J=8.2 Hz) (H-13), 7.41 (d) (1H) (J=2.1 Hz)
    (H-10), 7.58 (dd) (1H) (J=2.1, 8.2 Hz) (H-14), ArCHO 9.72 (224)

MS: M$^+$610 (0.1), 609 (0.4), 608 (0.5), 383 (100), 227 (4), 192 (26) (224)

CD: +7 (210), 0 (217), +5.3 (235), 0 (270), +2.3 (286), 0 (310) (224)

SOURCE: *Berberis lycium* Royle (Berberidaceae) (224)

APPARENT BIOGENETIC PRECURSOR: Atherospermoline [**56**] (110)

263   *0*-METHYLDEOXOPUNJABINE   C$_{36}$H$_{36}$O$_6$N$_2$: 592.2573

Type XXIII (-,*S*)
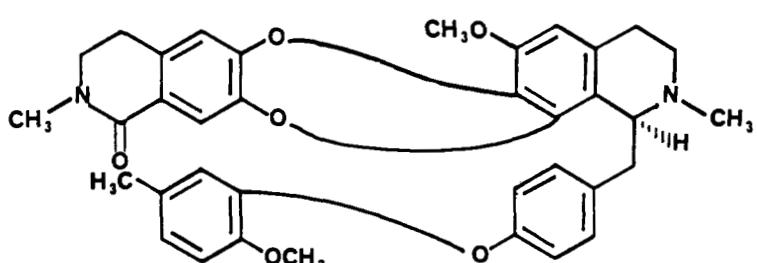
263

MP: 182-185°(MeOH or Me$_2$CO) (192)

[α]D: None reported (192)

UV(EtOH):   226 (4.71), 277 (3.93), 287 (sh) (3.91), 325 (3.69) (192)

IR: 1640 (ArCONR$_2$) (192)

^{1}H nmr: ArCH$_3$ 2.24; NCH$_3$ 2.37; CONCH$_3$ 3.12; OCH$_3$ 3.81, 3.86; AlH 2.28-2.45 (m) (1H) (H-
    4'A), 2.68-3.00 (m) (6H), 3.17-3.35 (m) (1H) (H-3'A), 3.52 (t) (2H) (J=6.6 Hz) (H-3), 3.92-

4.00 (m) (1H) (H-1'); ArH 6.29, 6.75 (brs) (2H) (H-10+one other ArH), 6.86 (d) (2H) (J=8.6 Hz) (H-11' and H-13'), 6.87 (s) (2H) (H-13 and H-14), 7.18 (d) (2H) (J=8.6 Hz) (H-10' and H-14'), 7.59 (H-8) (192)

MS(EI): 365 (100), 228 (14.2) (192)

MS(CI): M+H$^+$539 (100), 365 (100) (192)

ORD: (c=8.2×10^{-5}) +7,802 (218) (trough), +66,710 (232) (peak), 0 (251), −27,110 (262) (trough), −1,990 (297) (peak), 2,575 (306) (trough), −1,443 (323) (peak), −3550 (348) (trough), −1209 (400) (192)

CD: (c=8.2×10^{-6}) [θ]$_{224}$ +34,330, [θ]$_{246}$ −53,840, [θ]$_{284}$ +1,701, [θ]$_{301}$ −2,169, [θ]$_{330}$ −2,419 (192)

SOURCE: *Stephania sasakii* Hayata (Menispermaceae) (192)

PREPARATION: Via Wolff-Kishner reduction (NH$_2$NH$_2$/KOH) of O-methylpunjabine [264] (192)

APPARENT BIOGENETIC PRECURSOR: Isotrilobine [157] (110)

264 0-METHYLPUNJABINE C$_{36}$H$_{34}$O$_7$N$_2$: 606.2366

Type XXIII (-,S)
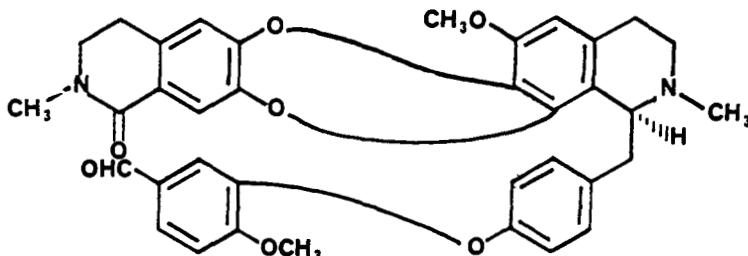
264

MP: 144-146°(Me$_2$CO/MeOH) (192)

[α]D: −4.12° (c=0.19, CHCl$_3$) (192)

UV(EtOH): 228 (4.74), 252 (sh) (4.45), 274 (sh) (4.22), 314 (sh) (3.91) (192)

IR: 1690 (ArCHO), 1650 (ArCONR$_2$) (192)

^{1}H nmr: NCH$_3$ 2.39; CONCH$_3$ 3.12; OCH$_3$ 3.86, 3.96; AlH 2.28-2.42 (m) (1H) (H-4'A), 2.68-2.82 (m) (2H) (H-3'$_A$ and H-4'$_B$), 2.85-3.00 (m) (4H) (H-4 and H-α'), 3.18-3.32 (m) (1H) (H-3$_B$), 3.53 (t) (2H) (J=6.8 Hz) (H-3), 3.92-3.98 (m) (1H) (H-1'); ArH 6.31, 6.76, 6.90 (d) (2H) (J=8.6 Hz) (H-11' and H-13'), 7.09 (d) (1H) (J=8.5 Hz) (H-13), 7.22 (d) (2H) (J=8.6 Hz) (H-10' and H-14'), 7.39 (d) (1H) (J=2.1 Hz) (H-10), 7.58 (H-8), 7.64 (dd) (1H) (J=2.1, 8.5 Hz) (H-14); ArCHO 9.80 (192)

MS(EI): 365 (100), 242 (5.9) (192)

MS(CI): M+H$^+$607 (100), 365 (100) (192)

ORD: (c=7.0×10^{-5}) 0 (216), +41,570 (235) (peak), 0 (257), −8,313 (272) (trough), −7,023 (281) (peak), −8,934 (293) (trough), −4,300 (319) (peak), −6,641 (343) (trough), −2628 (400) (192)

CD: (c=1.8×10^{-5}) +23,280 (221), −32,100 (248), −3,803 (325) (192)

SOURCE: *Stephania sasakii* Hayata (Menispermaceae) (192)

PREPARATION: Via oxidation (KMnO$_4$/Me$_2$CO) of isotrilobine [157] (110) (192)

APPARENT BIOGENETIC PRECURSOR: Isotrilobine [157] (110)

265 PUNJABINE C$_{35}$H$_{32}$O$_7$N$_2$: 592.2210

Type XXIII (-,S)
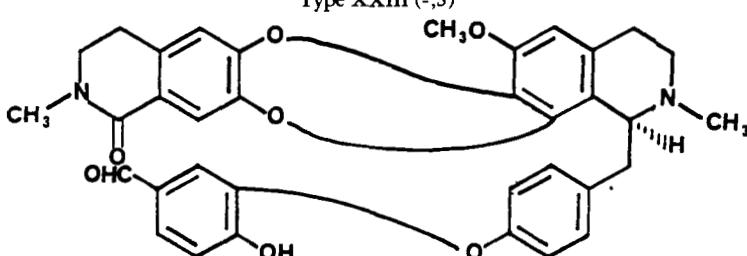
265

MP: Amorphous (221)
TLC: 0.16 (Si gel GF$_{254}$: C$_6$H$_6$-EtOAc-MeCN-MeOH-NH$_4$OH [30:30:40:5:5]) (221)
[α]^{25}D: −40°(c=0.48, MeOH) (221)
UV: 231 (4.81), 274 (4.32), 325 (3.98) (221); (MeOH+OH$^-$) 228 (4.78), 253 (sh) (4.57), 295 (4.11), 339 (4.50) (221)
IR: 1690 (ArCHO), 1645 (ArCONR$_2$), 1620 (221)
^{1}H nmr: NCH$_3$ 2.54; ArCONCH$_3$ 3.17; OCH$_3$ 3.87; ArH 6.36 (H-5′), 6.67 (H-5), 6.94 (d) (2H) (J=8.5 Hz) (H-11′ and H-13′), 7.11 (d) (1H) (J=8.2 Hz) (H-13), 7.18 (d) (2H) (J=8.5 Hz) (H-10′ and H-14′), 7.26 (H-8), 7.37 (d) (1H) (J=1.8 Hz) (H-10), 7.54 (dd) (1H) (J=1.8, 8.2 Hz) (H-14) ArCHO 9.74 (221)
MS: M$^+$592 (0.3), 365 (100), 227 (12) (221)
CD: +10.4 (222), 0 (232), −12.6 (247), −3.6 (280), 0 (300) (221)
SOURCE: *Berberis lycium* Royle (Berberidaceae) (221)
APPARENT BIOGENETIC PRECURSOR: *N*-Methylapateline [207] (111)

266   REVOLUTINONE   C$_{38}$H$_{40}$O$_8$N$_2$: 652.2785

Type XI (S,-)
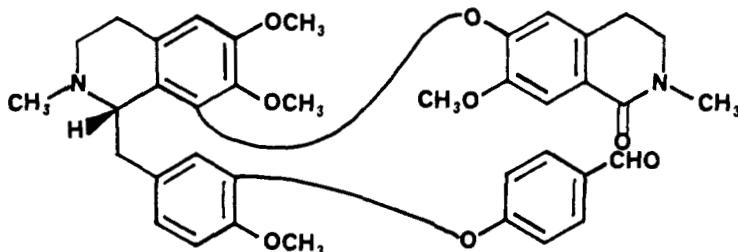
266

MP: Amorphous solid (223)
[α]^{28}D: −10°(c=0.5, MeOH) (223)
UV: 205 (sh) (5.13), 250 (4.78), 258 (4.76), 272 (4.69), 280 (sh) (4.66), 301 (sh) (4.31) (223)
IR: 2720, 1694, 1644 (223)
^{1}H nmr: NCH$_3$ 2.27; ArCONCH$_3$ 3.09; OCH$_3$ 3.67, 3.73, 3.85, 3.86; ArH 6.27 (H-5 or H-5′), 6.56 (H-5′ or H-5), 6.79-7.04 (m) (3H) (ABC pattern), 6.92 and 7.77 (q) (4H) (J=8.9 Hz), 7.63 (H-8′); ArCHO 9.89 (223)
MS: M$^+$652 (0.15), 411 (100), 241 (4), 221 (3), 205 (2), 203 (2), 190 (3) (223)
CD: [θ]$_{230}$ +26,000, [θ]$_{260}$ −14,000, [θ]$_{396}$ −2,600 (223)
SOURCE: *Thalictrum revolutum* DC. (Ranunculaceae) (223)
PREPARATION: Via oxidation (KMnO$_4$/Me$_2$CO) of O-methylthalicberine [95] (223)
NOTE: Stirring an EtOH solution of O-methylthalicberine [95] (110) for 24 h followed by refluxing for 2.5 h failed to produce any revolutinone, thus suggesting the latter alkaloid is not of artifactual origin (223).
APPARENT BIOGENETIC PRECURSOR: O-Methylthalicberine [95] (110)

267   SECANTIOQUINE   C$_{37}$H$_{38}$O$_8$N$_2$: 638.2628

Type IV (S,-)
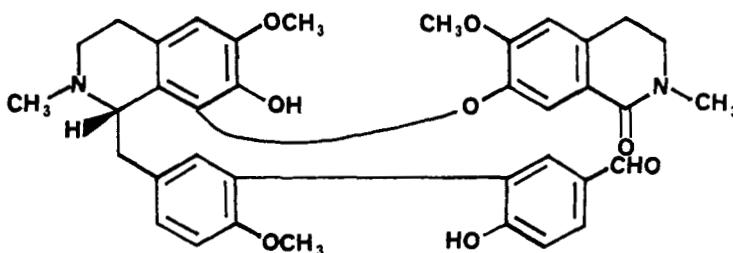
267

MP: Amorphous (196,225)

$[\alpha]_D$: $-15°(c=1, CHCl_3)$ (225)

UV(EtOH):   206 (4.77), 225 (4.84), 272 (4.32), 288 (4.36) (225); (EtOH+OH$^-$) 226 (5.28), 299
         (4.50), 346 (4.56) (225)

IR(film):   3250, 2970, 2910, 2810, 1680, 1640, 1600, 1500, 1450, 1340, 1280, 1240, 1200, 1115,
         1030, 810 (196)

^{1}H nmr: NCH$_3$ 2.34; ArCONCH$_3$ 3.03; OCH$_3$ 3.73 (C-6'), 3.79 (C-12), 3.86 (C-6); ArH 6.52 (H-
         5), 6.60 (H-5'), 6.89 (d) (1H) (J=8.5 Hz) (H-13), 7.02 (d) (1H) (J=2.5 Hz) (H-10), 7.08 (d)
         (1H) (J=8.5 Hz) (H-13'), 7.22 (dd) (1H) (J=2.5, 8.5 Hz) (H-14), 7.24 (H-8'), 7.66 (d) (1H)
         (J=2.5 Hz) (H-10'), 7.80 (dd) (1H) (J=2.5, 8.5 Hz) (H-14'); ArCHO 9.84 (225)

NOE: (225)

MS: M$^+$638, 397 (100), 351, 241, 225, 192, 190 (225)

CD: 0 (214), -9.3 (230), 0 (240), $+3.9$ (285), $+1.6$ (sh) (300), 0 (307) (225)

SOURCE: *Pseudoxandra* aff. *lucida* Fries (Annonaceae) (196,225)

DERIVATIVES: *0,0*-Diacetylsecantioquine (Secantioquine+Ac$_2$O/pyridine) (196,225)

MP: Amorphous (196)

$[\alpha]_D$: $-4°$ (c=0.6, CHCl$_3$) (196)

UV(EtOH):   210 (4.66), 220 (4.68), 270 (4.06), 290 (3.90) (196); (EtOH+OH$^-$) 222 (5.29), 300
         (4.27), 346 (4.33) (196)

IR(film):   1760 (ArOCOCH$_3$), 1690 (ArCHO), 1640 (ARCONR$_2$) (196)

^{1}H nmr: ArOCOCH$_3$ 1.98 (C-7), 2.01 (C-12'); NCH$_3$ 2.24; ArCONCH$_3$ 3.06; OCH$_3$ 3.70, 3.71,
         3.79 (C-6, C-6', C-12 with assignments interchangeable), ArH 6.56 (H-5), 6.60 (H-5'), 6.81
         (d) (1H) (J=8.5 Hz) (H-13), 6.96 (d) (1H) (J=2.5 Hz) (H-10), 7.20 (dd) (1H) (J=2.5, 8.5 Hz)
         (H-14), 7.32 (d) (1H) (J=8.5 Hz) (H-13'), 7.33 (H-8'), 7.75 (d) (1H) (J=2.5 Hz) (H-10'),
         7.88 (dd) (1H) (J=2.5, 8.5 Hz) (H-14'); ArCHO 9.96 (196,225)

MS(EI):   439 (100), 397 (44), 351 (6), 241 (4), 234 (8), 192 (8), 191 (9) (196)

MS(CI) (CH$_4$):   M+1 723 (18), 681 (8), 665 (7) (196)

         0,0-Dimethylsecantioquine (Secantioquine+CH$_2$N$_2$) (196)

MP: Amorphous (196)

$[\alpha]_D$: $+32°$(c=0.4, CHCl$_3$) (196)

UV(EtOH):   210 (4.64), 224 (4.70), 272 (4.20), 282 (4.18) (196)

IR(film):   1685 (ArCHO), 1640 (ArCONR$_2$), 1600 (196)

^{1}H nmr: NCH$_3$ 2.35; ArCONCH$_3$ 3.03; OCH$_3$ 3.63 (C-7), 3.70 (s) (6H), 3.76, 3.80; ArH 6.55 (H-
         5), 6.60 (H-5'), 6.81 (d) (1H) (J=8.5 Hz) (H-13), 6.96 (d) (1H) (J=2 Hz) (H-10), 7.06 (d)
         (1H) (J=8.5 Hz) (H-13'), 7.20 (dd) (1H) (J=2, 8.5 Hz) (H-14), 7.23 (H-8'), 7.63 (d) (1H)
         (J=2 Hz) (H-10'), 7.86 (dd) (1H) (J=2, 8.5 Hz) (H-14'); ArCHO 9.90 (196,225)

^{13}C nmr: 60.6 (C-1), 44.2 (C-3), 22.8 (C-4), 125.5 (C-4a), 109.4 (C-5), 151.3 (C-6), 140.0 (C-7),
         145.2 (C-8), 123.7 (C-8a), 39.8 (C-α), 129.3 (C-9), 133.3 (C-10), 129.8 (C-11), 152.0 (C-12),
         113.2 (C-13), 130.0 (C-14); 164.2 (C-1'), 48.1 (C-3'), 27.4 (C-4'), 132.5 (C-4a'), 110.6 (C-
         5'), 155.0 (C-6'), 146.5 (C-7'), 110.0 (C-8'), 121.8 (C-8a'), 132.9 (C-9'), 131.7 (C-10'),
         129.8 (C-11'), 162.2 (C-12'), 110.4 (C-13'), 130.9 (C-14'); 42.1 (N-2 NCH$_3$), 34.8 (N-2'
         NCH$_3$), 55.5 (C-6 and C-6' OCH$_3$), 55.8 (C-12 and C-12' OCH$_3$), 190.9 (C-9') (196)

MS:M$^+$666 (1), 411 (100), 397 (1), 395 (1), 365 (2), 256 (7), 178 (2) (196)

APPARENT BIOGENETIC PRECURSOR: Antioquine [**225**] (196)

268   SECOCEPHARANTHINE   C$_{37}$H$_{36}$O$_8$N$_2$: 636.2472

                    Type VI (-,S)

                    268
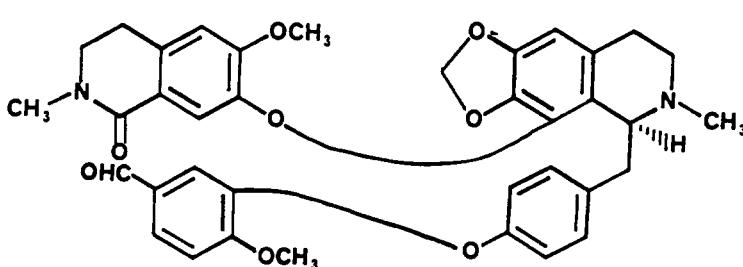
MP: Amorphous (192)
[α]D: Not reported (192)
UV(EtOH):   226 (4.75), 270 (4.34), 290 (sh) (4.21), 302 (sh) (4.07) (192)
IR: 1690 (ArCHO), 1645 (ArCONR$_2$), 930 (CH$_2$O$_2$) (192)
^{1}H nmr: NCH$_3$ 2.29; ArCONCH$_3$ 3.08; OCH$_3$ 3.95 (6H); AlH 2.33-2.45 (m) (1H) (H-4'$_A$), 2.75-
      3.00 (m) (4H) (H-3'$_A$, H-α, H-4'$_B$), 2.95 (m) (2H) (H-4), 3.27-3.37 (m) (1H) (H-3'$_B$), 3.53 (t)
      (2H) (J=6.8 Hz) (H-3), 3.86 (dd) (1H) (J=2.8, 9.0 Hz) (H-1'), OCH$_3$ 3.95 (6H); CH$_2$O$_2$ 5.84
      (q) (2H) (J=1.5 Hz); ArH 6.47, 6.73, 6.83 (d) (2H) (J=8.6 Hz) (H-11' and H-13'), 7.08 (d)
      (1H) (J=8.6 Hz) (H-13), 7.17 (d) (2H) (J=8.6 Hz) (H-10' and H-14'), 7.39 (d) (1H) (J=2.1
      Hz) (H-10), 7.45 (H-8), 7.62 (dd) (1H) (J=2.1, 8.6 Hz) (H-14); ArCHO 9.79 (192)
MS(EI):   395 (100), 242 (7.1) (192)
MS(CI):   M+H 637 (100), 395 (27) (192)
ORD: (c=2.2×10^{-3}) +11,740 (216) (trough), +22,000 (226) (peak), 0 (233), −24,210 (241)
      (trough), 0 (288), −3374 (298) (peak), 0 (308), −1,467 (320) (trough), −748 (350), −440
      (400) (192)
CD: c=1.8×10^{-5} [θ]$_{231}$ −37,720, [θ]$_{261}$ +1,932, [θ]$_{271}$ +2,429, [θ]$_{286}$ +2,760, [θ]$_{305}$ −1,509
   (192)
SOURCE: *Stephania sasakii* Hayata (Menispermaceae) (192)
DERIVATIVES: Dihydrosecocepharanthine (Secocepharanthine+NaBH$_4$/MeOH) (192)
PREPARATION: Via oxidation (KMnO$_4$/Me$_2$CO) of cepharanthine [34] (110) (192)
APPARENT BIOGENETIC PRECURSOR: Cepharanthine [34] (110)

269   SECO-OBABERINE   C$_{38}$H$_{40}$O$_8$N$_2$: 652.2785

Type VI (-,*S*)
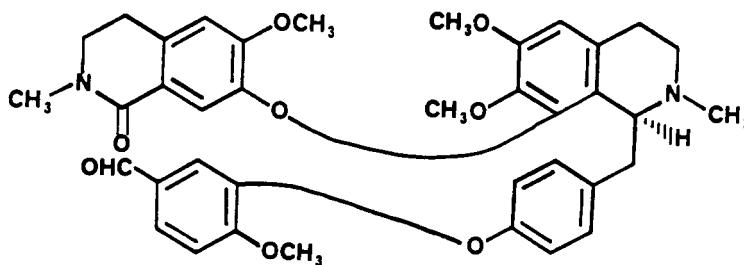
269

MP: Amorphous (196)
[α]D: −5° (c=0.2, CHCl$_3$) (196)
UV(EtOH):   204 (4.62), 224 (4.57), 262 (sh) (4.11), 272 (4.13), 298 (sh) (4.06) (196)
IR(film):   1685 (ArCHO), 1640 (ArCONR$_2$), 1600 (196)
^{1}H nmr: NCH$_3$ 2.32; CONCH$_3$ 3.07; OCH$_3$ 3.68 (C-7'), 3.86, 3.96, 3.97; ArH 6.51 (H-5'), 6.69
      (H-5), 6.80 (d) (2H) (J=8.5 Hz) (H-11' and H-13'), 7.04 (d) (1H) (J=8.5 Hz) (H-13), 7.11 (d)
      (2H) (J=8.5 Hz) (H-10' and H-14'), 7.34 (d) (1H) (J=2 Hz) (H-10), 7.58 (dd) (1H) (J=2, 8.5
      Hz) (H-14); ArCHO 9.76 (196)
MS(EI):   411 (100), 365 (21), 241 (6), 206 (6), 204 (13), 192 (6), 191 (3), 190 (7) (196)
MS(CI):   M$^+$ 652 (196)
SOURCE: *Pseudoxandra* aff. *lucida* Fries (Annonaceae) (196)
PREPARATION: Via oxidation (KMnO$_4$/Me$_2$CO) of obaberine [46] (110) (tlc, uv, ir, ^{1}H nmr, ms)
      (196)
APPARENT BIOGENETIC PRECURSOR: Obaberine [46] (110)

270   SINDAMINE   C$_{37}$H$_{38}$O$_8$N$_2$: 638.2628

Type VIII (*S*, -)
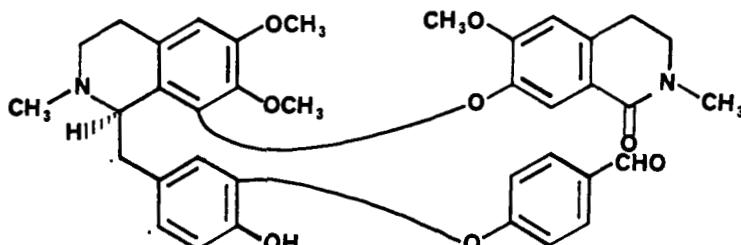
270

MP: Amorphous (221)
TLC: 0.55 (Si gel GF$_{254}$; C$_6$H$_6$-EtOAc-MeCN-MeOH-NH$_4$OH [30:20:40:5:5]) (221)
[α]D: Not reported (221)
UV: 208 (4.62), 259 (4.09), 270 (4.07), 283 (4.04) (221); (MeOH+OH$^-$) 212 (4.86), 272 (4.05), 294 (4.08) (221)
IR: 1695 (ArCHO), 1645 (ArCONR$_2$), 1605 (221)
^{1}H nmr: NCH$_3$ 2.31; ArCONCH$_3$ 3.04; OCH$_3$ 3.61 (C-7), 3.81 (C-6 or C-6'), 3.82 (C-6' or C-6); ArH 6.52 (H-5), 6.59 (H-5'), 6.70-7.01 (m) (3H) (H-10, H-13, H-14), 7.03 (d) (2H) (J=8.8 Hz) (H-11' and H-13'), 7.81 (d) (2H) (J=8.8 Hz) (H-10' and H-14'); ArCHO 9.91 (221)
MS: M$^+$638 (1.2), 411 (100), 365 (24), 227 (9), 206 (13), 204 (31) (221)
CD: 0 (220), +5 (232), 0 (245), −1.7 (255), 0 (300) (221)
SOURCE: *Berberis lycium* Royle (Berberidaceae) (221)
DERIVATIVES: 0-Acetylsindamine (Secoberbamine acetate aldehydolactam) (0-Acetylberbamine + KMnO$_4$/Me$_2$CO) (221)
MP: Amorphous (221)
[α]^{25}D: +38°(c=0.04, MeOH) (221)
UV: 221 (sh) (4.48), 259 (4.11), 270 (4.10) (221)
^{1}H nmr: NCH$_3$ 2.26; CONCH$_3$ 3.05; OCOCH$_3$ 2.08; OCH$_3$ 3.64 (C-7), 3.82 (C-6 or C-6'), 3.84 (C-6' or C-6); ArH 6.53 (H-5), 6.59 (H-5'), 6.90-7.18 (m) (3H) (H-10, H-13, H-14), 6.98 (d) (2H) (J=8.8 Hz) (H-11' and H-13'), 7.23 (H-8'), 7.80 (d) (2H) (J=8.8 Hz) (H-10' and H-14') (221)
MS: M$^+$680 (0.1), 411 (100), 365 (17), 269 (0.4), 227 (2.4), 206 (4), 204 (9) (221)
CD: 0 (220), +3 (233), 0 (245), −1 (258), 0 (300) (221)
APPARENT BIOGENETIC PRECURSOR: Berbamine [57] (110)

271   TALCAMINE   C$_{40}$H$_{44}$O$_{10}$N$_2$: 712.2996
Type Xa (S,-)
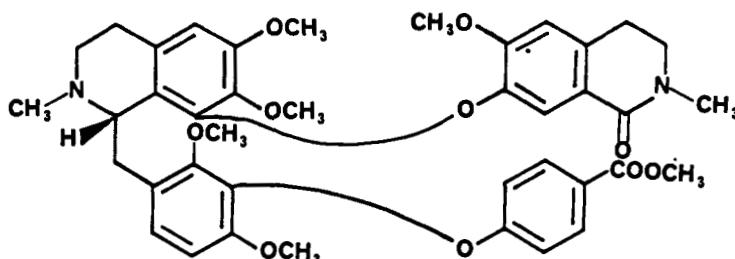
271

MP: Amorphous (146)
TLC: 0.55 (Si gel GF$_{254}$: CHCl$_3$-MeOH-NH$_4$OH [95:5:0.5]) (146)
[α]^{25}D: −2°(c=0.29, MeOH) (146)
UV: 208 (4.93), 225 (sh) (4.79), 260 (4.41), 272 (sh) (4.27), 305 (3.67) (146)
IR: 1710 (ArCOOR), 1640 (ArCONR$_2$), 1605 (146)
^{1}H nmr: NCH$_3$ 2.24; ArCONCH$_3$ 3.04; ArCOOCH$_3$ 3.86; OCH$_3$ 3.54 (C-7), 3.59 (C-6), 3.79 (C-6' or C-10), 3.84 (C-10 or C-6'), 3.91 (C-12); ArH 6.46 (H-5), 6.64 (H-5'), 6.72 (d) (1H) (J=8.5 Hz) (H-13), 6.75 (d) (2H) (J=8.8 Hz) (H-11' and H-13'), 6.96 (d) (1H) (J=8.5 Hz) (H-14), 7.17 (H-8'), 7.77 (d) (2H) (J=8.8 Hz) (H-10' and H-14') (146)

MS: M$^+$712 (0.1), 681 (0.4), 653 (0.1), 411 (100), 365 (9), 301 (0.4), 206 (2) (146)
CD: +14 (214), 0 (221), −23 (230), 0 (245), +4 (252), 0 (266), −3 (295), 0 (320) (146)
SOURCE: *Berberis buxifolia* Lam. (Berberidaceae) (146)
APPARENT BIOGENETIC PRECURSOR: Calafatine [190] (111)

TABLE 5.   Calculated Molecular Weights of New Bisbenzylisoquinoline Alkaloids

532.1998: $C_{33}H_{28}O_5N_2$
            Kurramine [237] (175)
548.2311: $C_{34}H_{32}O_5N_2$
            Nortrilobine [247] (169)
            Pachyovatamine [250] (200)
562.2468: $C_{35}H_{34}O_5N_2$
            O-Methylcocsoline [239] (125)
564.2260: $C_{34}H_{32}O_6N_2$
            Kohatine [236] (175)
            Pachygonamine [249] (120)
578.2417: $C_{35}H_{34}O_6N_2$
            Cocsuline-N-2-Oxide [231] (161)
            N-Methylpacygonamine [243]
            (120)
580.2573: $C_{35}H_{36}O_6N_2$
            Nor-N_b-Chondrocurine [230]
            (198)
582.2730: $C_{35}H_{38}O_6N_2$
            7-O-Methyllindoldhamine [241]
            (128)
            7'-O-Methyllindoldhamine [242]
            (128)
592.2210: $C_{35}H_{32}O_7N_2$
            Punjabine [265] (221)
592.2573: $C_{36}H_{36}O_6N_2$
            O-Methyldeoxopunjabine [263]
            (192)
            Tiliacorinine-2'-N-Oxide [254] (2)
594.2730: $C_{36}H_{38}O_6N_2$
            2-Norlimacusine [245] (197)
            Norpenduline [246] (175)
596.2886: $C_{36}H_{40}O_6N_2$
            Guattegaumerine [234] (129)
            N,N-Dimethyllindoldhamine
            [234] (128)
606.2366: $C_{36}H_{34}O_7N_2$
            Cheratamine [228] (175)
            O-Methylpunjabine [264] (192)
608.2886: $C_{37}H_{40}O_6N_2$
            Antioquine [225] (196)
            N-Desmethylcycleanine [233] (65)
            Thaliphylline [253] (180)
610.2679: $C_{36}H_{38}O_7N_2$
            Jhelumine [262] (224)

610.3043: $C_{37}H_{42}O_6N_2$
            Isodaurisoline [235] (128)
            Temuconine [251] (40)
            Thaligrisine [252] (180)
622.2316: $C_{36}H_{34}O_8N_2$
            Gilgitine [261] (221)
622.3043: $C_{38}H_{42}O_6N_2$
            O-Methylthalmine [244] (188)
624.2836: $C_{37}H_{40}O_7N_2$
            Chenabine [258] (224)
624.3199: $C_{38}H_{44}O_6N_2$
            7'-O-Methylcuspidaline [240]
            (190)
626.2992: $C_{37}H_{42}O_7N_2$
            Chillanamine [229] (146)
636.2472: $C_{37}H_{36}O_8N_2$
            Secocepharanthine [268] (192)
636.2836: $C_{38}H_{42}O_7N_2$
            Cycleanine N-Oxide [232] (86)
638.2628: $C_{37}H_{38}O_8N_2$
            Baluchistanamine [257] (222)
            Dihydrosecocepharanthine [260]
            (192)
            Secantioquine [267] (196,225)
            Sindamine [270] (221)
638.2992: $C_{38}H_{42}O_7N_2$
            Osornine [248] (146)
652.2785: $C_{38}H_{40}O_8N_2$
            Revolutinone [266] (223)
            Seco-obaberine [269] (196)
656.3097: $C_{38}H_{44}O_8N_2$
            Vateamine [256] (115)
668.3098: $C_{39}H_{44}O_8N_2$
            Calafatine-2α-N-Oxide [226]
            (162,163)
            Calafatine-2β-N-Oxide [227]
            (162,163)
670.3254: $C_{39}H_{46}O_8N_2$
            Malekulatine [238] (115)
            Vanuatine [255] (115)
682.2891: $C_{39}H_{42}O_9N_2$
            Curacautine [259] (146)
712.2996: $C_{40}H_{44}O_{10}N_2$
            Talcamine [271] (146)

TABLE 6. Distribution of the Different Types of New Bisbenzylisoquinoline Alkaloids in Different Genera and Families

Family	Annonaceae			Aristolo-chiaceae	Berberi-daceae	Hernand-iaceae	Menispermaceae								Ranuncu-laceae
Genus	*Guatteria*	*Polyalthia*	*Pseudoxandra*	*Aristolochia*	*Berberis*	*Hernandia*	*Albertisia*	*Chondodendron*	*Cocculus*	*Pachygone*	*Sciadotenia*	*Stephania*	*Synclisia*	*Tiliacora*	*Thalictrum*
Type															
I	1	4		1	1										1
Ia															
Ib[a]					1										
II															
IIa[b]						1									
IIb[c]						1									
III															
IV			1												
V															
Va[d]						1									
VI															
VIa[e]					1							1			
VII															
VIII									2						
IX															
X															
Xa					2										
Xb															
XI															1
XII															
XIII															
XIV															1
XV															
XVI															
XVII										1					
XVIII														1	
XIX										2					
XX												1	1		
XXI								1							
XXII															
XXIII							1			2	1				
XXIIIa[f]										1					
XXIV															
XXV															
XXVI															
Seco-Compounds			2		8							4			1

[a]Type Ib is a new type which follows the numbering system 6,7,10,11*,12-6,7,12* according to the precedent of Shamma and Moniot (226).

[b]Type IIa is a new type which follows the numbering system 6,7,10*,12,13-6,7,11*,12 according to the precedent of Shamma and Moniot (226).

[c]Type IIb is a new type which follows the numbering system 6,7,10*,11,12-6,7,11*,12 according to the precedent of Shamma and Moniot (226).

[d]Type Va is a new type which follows the numbering system 6,7,10*,12,13-6,7*,11,12 according to the precedent of Shamma and Moniot (226).

[e]Type VIa is a new type which follows the numbering system 6,7*,10,11$^+$,12-6,7,8*,12$^+$ according to the precedent of Shamma and Moniot (226).

[f]Type XXIIIa is a new type which follows the numbering system 5,6,7*,8$^+$,12‡-6*,7$^+$,11‡,12 according to the precedent of Shamma and Moniot (226).

TABLE 7. Incompletely Characterized Alkaloids

A fangchinoline [61] or limacine [64] enantiomer (215)
$C_{37}H_{40}O_6N_2$: 608.2886
MS: M$^+$608
No other data reported

TABLE 8.   Botanical Sources of Bisbenzylisoquinoline Alkaloids by Family

ANNONACEAE

Cleistopholis
(-)-Chondrofoline [**131**] (193)
(-)-Curine [**133**] (193)
(-)-Cycleanine [**121**] (193)
(-)-Isochondodendrine [**122**] (193)

Guatteria
Guattegaumerine [**234**] (129)

Isolona
(-)-Curine [**133**] (170)
Cycleanine [**121**] (170)
Isochondodendrine [**122**] (170)
(-)-Norcycleanine [**125**] (170)

Polyalthia
Dauricine [**3**] (128)
Daurisoline [**192**] (128)
N,N'-Dimethyllindoldhamine [**234**] (128)
Isodaurisoline [**235**] (128)
Lindoldhamine [**11**] (128)
7-O-Methyllindholdhamine [**241**] (128)
7'-O-Methyllindoldhamine [**242**] (128)

Pseudoxandra
Antioquine [**225**] (196)
Obaberine [**46**] (196)
Secantioquine [**267**] (196,225)
Seco-obaberine [**269**] (196)

ARISTOLOCHIACEAE

Aristolochia
7'-O-Methylcuspidaline [**240**] (190)
Tetrandrine [**76**] (215)

BERBERIDACEAE

Berberis
Aromoline [**31**] (156)
Baluchistanamine [**257**] (222)
Berbamine [**57**] (156,221)
Calafatine [**190**] (146)
Calafatine-2α-N-Oxide [**226**] (162,163)
Calafatine-2β-N-Oxide [**227**] (162,163)
Chenabine [**258**] (224)
Chillanamine [**229**] (146)
Curacautine [**259**] (146)
7-O-Demethylisothalicberine [**195**] (36)
Gilgitine [**261**] (221)
Jhelumine [**262**] (224)
Isotetrandrine [**62**] (24)
Isothalicberine [**205**] (36)
O-Methylthalicberine [**95**] (36)
Osornine [**248**] (146)
Oxyacanthine [**48**] (156,200,221)
Punjabine [**265**] (221)
Sindamine [**270**] (221)
Talcamine [**271**] (146)
Temuconine [**251**] (40)

Mahonia
Isotetrandrine [**62**] (184)
Obaberine [**46**] (16)
Obamegine [**71**] (16)

Oxyacanthine [**48**] (16)
Thalrugosine [**79**] (16)

EUPHORBIACEAE

Andrachne
Cocsuline [**153**] (122)
Penduline [**72**] (122)

HERNANDIACEAE

Hernandia
Malekulatine [**238**] (115)
Vanuatine [**255**] (115)
Vateamine [**256**] (115)

MAGNOLIACEAE

Michelia
Magnolamine [**15**] (9)
Magnoline [**12**] (9)

MENISPERMACEAE

Albertisia
Aromoline [**31**] (125)
Cocsoline [**152**] (125)
Cocsuline [**153**] (125)
Daphnoline [**38**] (125)
Dehydroteloline [**194**] (125)
Homoaromoline [**42**] (125)
Isotrilobine [**157**] (125)
Lindoldhamine [**11**] (125)
O-Methylcocsoline [**239**] (125)
Obaberine [**46**] (125)
Oxyacanthine [**48**] (125)

Arcangelisia
Homoaromoline [**42**] (60)
Limacine [**64**] (60)

Chondodendron (Peruvian Curare)
(R,S)-Chondrocurine [**130**] (198)
(R,S)-Nor-N_b-Chondrocurine [**230**] (198)
(R,R)-Curine [**133**] (198)
(+)-Tubocurarine Chloride [**142**] (198)

Cocculus
Cheratamine [**228**] (175)
Cocsoline [**152**] (59,175)
Cocsuline [**153**] (59,175)
Cocsuline-N-2-Oxide [**231**] (161)
Daphnoline [**38**] (175)
1,2-Dehydroapateline [**193**] (175)
Isotrilobine [**157**] (1,175)
Kohatine [**236**] (175)
Kurramine [**237**] (175)
N-Methylapateline [**207**] (175)
Norberbamine [**68**] (175)
Norpenduline [**246**] (175)
Penduline [**72**] (59,175)
Tetrandrine [**76**] (175)
Tricordatine [**161**] (175)
Trilobine [**163**] (1)

Cyclea
Cycleanine [**121**] (37)
O,O-Dimethylcurine [**135**] (37)

Menispermum
  Dauricine [3] (113)
Phaeanthus
  Phaeantharine [73] (100)
Pachygone
  N-Methylpachygonamine [243] (120,200)
  Nortrilobine [247] (169)
  Pachygonamine [249] (120,200)
  Pachyovatamine [250] (200)
  Tiliamosine [120] (120)
  Trilobine [163] (169)
Pycnarrhena
  Berbacolorflammine [218] (15)
  Colorflammine [219] (15)
Sciadotenia
  Grisabine [10] (197)
  2-Norlimacusine [245] (197)
Stephania
  Berbamine [57] (7,194 [alkaloid detected
    but not isolated])
  Cepharanthine [34] (47)
  Cycleanine [121] (65)
  N-Desmethylcycleanine [233] (65)
  Dihydrosecocepharanthine [260] (192)
  Fangchinoline [61] (194 [alkaloid detected
    but not isolated])
  Homoaromoline [42] (47)
  Isotetrandrine [62] (7)
  O-Methyldeoxopunjabine [263] (192)
  O-Methylpunjabine [264] (192)
  Obaberine [46] (192)
  Secocepharanthine [268] (192)
  Stebisimine [51] (50)
  Tetrandrine [76] (194 [alkaloid detected
    but not isolated])
  Thalrugosine [79] (192)
Synclisia
  Cycleanine [121] (86)
  Cycleanine N-Oxide [232] (86)
  Cocsoline [152] (86)
  Cocsuline [153] (86)
  (+)-Norcycleanine [124] (86)

Tiliacora
  Nortiliacorinine A [116] (2,8)
  Tiliacorine [118] (2)
  Tiliacorinine [119] (2)
  Tiliacorinine-2'-N-Oxide [254] (2)
MONIMIACEAE
  Laurelia
    Obaberine [46] (210)
    Oxyacanthine [48] (210)
    Thalrugosine [79] (210)
RANUNCULACEAE
  Thalictrum
    Aromoline [31] (180)
    N-Desmethylthalistyline [16] (174)
    Hernandezine [81] (21)
    Homoaromoline (Thalrugosamine)
      [42] (180)
    O-Methylthalicberine (Thalmidine) [95]
      (14, 103, 145, 165, 166, 180, 205)
    O-Methylthalibrine [209] (166)
    O-Methylthalmine [244] (188)
    Obaberine [46] (14)
    Obamegine [71] (180)
    Revolutinone [266] (223)
    Thalabadensine [106a] (103,211)
    Thalfine [102] (104)
    Thalfinine [103] (104)
    Thalfoetidine [99] (165)
    Thalicberine [97] (165, 180, 205)
    Thalictine [107] (188,211)
    Thalidasine [100] (35,165)
    Thaligrisine [252] (180)
    Thaliphylline [253] (180)
    Thalirabine (5-O-Demethylthalistyline)
      [17a] (174)
    Thalirugine [14b] (180)
    Thalisopine (Thaligosine) [54]
      (14, 166, 180, 216)
    Thalmethine [98] (103,204)
    Thalmine [108] (103, 145, 204)
    Thalrugosaminine [55] (216)
    Thalrugosidine [101] (35,166)
    Thalrugosine [79] (14)

TABLE 9.   Botanical Sources of Bisbenzylisoquinoline Alkaloids[a]

Name of Plant	Plant Part	Alkaloid	Structural Type of Alkaloid
Albertisia papuana Becc.	St	Aromoline [31] (125)	VI
		Cocsoline [152] (125)	XXIII
		Cocsuline [153] (125)	XXIII
		Daphnoline [38] (125)	VI
		Dehydrotelobine [194] (125)	XXIII
		Homoaromoline [42] (125)	VI
		Isotrilobine [157] (125)	XXIII
		Lindoldhamine [11] (125)	I

		O-Methylcocsoline [239] (125)	XXIII
		Obaberine [46] (125)	VI
		Oxyancanthine [48] (125)	VI
Andrachne cordifolia Muell., O.F.	R	Cocsuline [153] (122)	XXIII
		Penduline [72] (122)	VIII
Arcangelisia flava (L.) Merr.	R, St	Homoaromoline [42] (60)	VI
		Limacine [64] (60)	VIII
Aristolochia debilis Sieb. & Zucch.	R	Tetrandrine [76] (215)	VIII
Aristolochia elegans	L	7'-O-Methylcuspidaline [240] (190)	I
Berberis aristata DC.	RB	Aromoline [31] (156)	VI
		Berbamine [57] (156)	VIII
		Oxyacanthine [48] (156)	VI
Berberis baluchistanica Ahrendt		Baluchistanamine [257] (222)	
Berberis buxifolia Lam.	Unknown	Calafatine [190] (146)	Xa
		Chillanamine [229] (146)	Ib
		Curacautine [259] (146)	
		Osornine [248] (146)	VIa
		Talcamine [271] (146)	
Berberis buxifolia Lam.	WP (minus L)	Calafatine-2α-N-Oxide [226] (162, 163)	Xa
		Calafatine-2β-N-Oxide [227] (162, 163)	Xa
Berberis chilensis Gill. ex Hook.	L, St	7-O-Demethylisothalicberine [195] (36)	XI
		Isothalicberine [205] (36)	XI
		O-Methylthalicberine [95] (36)	XI
Berberis chitria D. Don	WP	Oxyacanthine [48] (203)	VI
Berberis empetrifolia	R	Isotetrandrine [62] (24)	VIII
Berberis lycium (Royle)	R	Berbamine [57] (221)	VIII
		Gilgitine [261] (221)	
		Oxyacanthine [48] (221)	VI
		Punjabine [265] (221)	
		Sindamine [270] (221)	
		Chenabine [258] (224)	
		Jhelumine [262] (224)	
Berberis valdiviana Phil.	WP	Temuconine [251] (40)	I
Cleistopholis staudtii Engl. et Diels	StB	(−)-Chondrofoline [131] (193)	XXI
		(−)-Curine [133] (193)	XXI
		(−)-Cycleanine [121] (193)	XX
		(−)-Isochondodendrine [122] (193)	XX
Cocculus leaebe DC.	R	Cocsoline [152] (59)	XXIII
		Cocsuline [153] (59)	XXIII
		Penduline [72] (59)	VIII
Cocculus hirsutus DC.	R, St	Cocsuline-N-2-Oxide [231] (161)	XXIII
Cocculus pendulus (Forsk) Diels	St	Cheratamine [228] (175)	VIII
		Cocsoline [152] (175)	XXIII
		Cocsuline [153] (175)	XXIII
		Daphnoline [38] (175)	VI
		1,2-Dehydroapateline [193] (175)	XXIII
		Isotrilobine [157] (175)	XXIII
		Kohatine [236] (175)	XXIIIa
		Kurramine [237] (175)	XXIII
		N-Methylapateline [207] (175)	XXIII
		Norberbamine [68] (175)	VIII
		Norpenduline [246] (175)	VIII
		Penduline [72] (175)	VIII
		Tetrandrine [76] (175)	VIII
		Tricordatine [161] (175)	XXIII
Cocculus trilobus Thunb.		Isotrilobine [157] (1)	XXIII
		Trilobine [163] (1)	XXIII
Cyclea hypoglauca Diels	R, Bb	Cycleanine [121] (37)	XX

		O,O-Dimethylcurine [135] (37)	XXI
Guatteria gaumeri Greenman	Trunk B	Guattegaumerine [234] (129)	I
Hernandia peltata Meissn.	B	Malekulatine [238] (115)	Va
		Vanuatine [255] (115)	IIa
		Vateamine [256] (115)	IIb
Isolona hexaloba Engl.	RB	Cycleanine [121] (170)	XX
		Isochondodendrine [122] (170)	XX
		Norcycleanine [125] (170)	XX
Isolona pilosa Diels	StB	‒(-)-Curine [133] (170)	XXI
		Isochondodendrine [122] (170)	XX
Laurelia sempervirens R. et P.	StB	Obaberine [46] (210)	VI
		Oxyacanthine [48] (210)	VI
		Thalrugosine [79] (210)	VIII
Mahonia repens (Lindl.) G. Don	St, R	Obaberine [46] (16)	VI
		Obamegine [71] (16)	VIII
		Oxyacanthine [48] (16)	VI
		Thalrugosine [79] (16)	VIII
Mahonia siamensis Takeda	StB	Isotetrandrine [62] (184)	VIII
Menispermum dauricum DC.	Rh	Dauricine [3] (113)	I
Michelia fuscata Blume	L	Magnolamine [15] (9)	II
		Magnoline [12] (9)	I
Pachygone ovata (Poir.) Miers ex Hook	L, St	N-Methylpachygonamine [243] (120,200)	XIX
		Pachygonamine [249] (120, 200)	XIX
		Pachyovatamine [250] (200)	XVIII
		Tiliamosine [120] (120, 200)	XIX
	R	Nortrilobine [247] (169)	XXIII
		Trilobine [163] (169)	XXIII
Peruvian curare		(R,S)-Chondrocurine [130] (198)	XXI
		(R,R)-Curine [133] (198)	XXI
		(R,S)-Nor-N_b-Chondrocurine [230] (198)	XXI
		(+)-Tubocurarine chloride [142] (198)	XXI
Phaenthus ebracteolatus (Presl) Merill.	L	Phaentharine [73] (100)	I
Polyalthia nitidissima Benth.	StB	Daurisoline [192] (128)	I
		N,N'-Dimethyllindoldhamine [234] (128)	I
		Isodaurisoline [235] (128)	I
		Lindoldhamine [11] (128)	I
		7-O-Methyllindoldhamine [241] (128)	I
		7'-O-Methyllindoldhamine [242] (128)	I
Pseudoxandra aff. *lucida* Fries	StB	Antioquine [225] (196)	IV
		Obaberine [46] (196)	VI
		Secantioquine [267] (196, 225)	
		Seco-obaberine [269] (196)	
Pycnarrhena longifolia (Decne. ex Miq.) Becc.	St, R	Berbacolorflammine [218] (15)	VIII
		Colorflammine [219] (15)	VI
Sciadotenia eichleriana Moldenke	St, R	Grisabine [10] (197)	I
		2-Norlimacusine [245] (197)	VI
Stephania cepharantha Hayata	Sd	Berbamine [57] (7)	VIII
		Isotetrandrine [62] (7)	VIII
Stephania erecta Craib.	Tb	Cepharanthine [34] (47)	VI
		Homoaromoline [42] (47)	VI
Stephania glabra (Roxb.) Miers	Rh	Cycleanine [121] (65)	XX
		N-Desmethylcycleanine [233] (65)	XX
Stephania japonica Miers	L	Stebisimine [51] (50)	VI
Stephania sasakii Hayata		Dihydrosecocepharanthine [260] (192)	
		O-Methyldeoxopunjabine [263] (192)	
		O-Methylpunjabine [264] (192)	

		Obaberine [46] (192)	VI
		Secocepharanthine [268] (192)	
		Thalrugosine [79] (192)	VIII
Stephania tetrandra S. Moore		Berbamine [57] (194 [alkaloid detected but *not isolated*])	VIII
		Fangchinoline [61] (194 [alkaloid detected but not isolated])	VIII
		Tetrandrine [76] (194 [alkaloid detected but not isolated])	VIII
Synclisia scabrida Miers	St	Cocsoline [152] (86)	XXIII
		Cocsuline [153] (86)	XXIII
		Cycleanine [121] (86)	XX
		Cycleanine N-Oxide [232] (86)	XX
		(+)-Norcycleanine [124] (86)	XX
Thalictrum baicalense Turcz.	R	N-Desmethylthalistyline [16] (174)	III
		Thalirabine (5-O-Demethylthalistyline) [17a] (174)	
Thalictrum faberi Ulbr.	R	O-Methylthalibrine [209] (166)	I
		O-Methylthalicberine [95] (166)	XI
		Thalisopine (Thaligosine) [54] (166)	VII
		Thalrugosidine [101] (166)	XII
Thalictrum foetidum L	R	Thalfine [102] (104)	XIII
		Thalfinine [103] (104)	XIII
Thalictrum foliolosum DC	WP?	Thalidasine [100] (35)	XII
		Thalrugosidine [101] (35)	XII
Thalictrum javanicum Bl.	R	Thalisopine [54] (216)	VII
		Thalrugosaminine [55] (216)	VII
Thalictrum kuhistanicum Ovcz. A, and Koczk.	WP	O-Methylthalicberine (Thalmidine) [95] (145)	XI
		Thalmine [108] (145)	XIV
Thalictrum longipedunculatum E. Nikit.	T	O-Methylthalicberine [95] (165)	XI
		Thalfoetidine [99] (165)	XII
		Thalicberine [97] (165)	XI
		Thalidasine [100] (165)	XII
Thalictrum minus L.	R	Thalmethine [98] (204)	XI
		Thalmine [108] (204)	XIV
	T	O-Methylthalicberine [95] (103, 205)	XI
		Thalabadensine [106a] (103)	XIV
		Thalicberine [97] (205)	XI
		Thalmethine [98] (103)	XI
		Thalmine [108] (103)	XIV
	St	O-Methylthalicberine [95] (103)	XI
		Thalmethine [98] (103)	XI
Thalictrum minus L. var. *microphyllum* Boiss	WP	O-Methylthalicberine [95] (14)	XI
		Obaberine [46] (14)	VI
		Thalisopine (Thaligosine) [54] (14)	VII
		Thalrugosine [79] (14)	VIII
	Rh, R	Aromoline [31] (180)	VI
		Homoaromoline [42] (180)	VI
		O-Methylthalicberine [95] (180)	XI
		Obamegine [71] (180)	VIII
		Thalicberine [97] (180)	XI
		Thaligrisine [252] (180)	I
		Thaliphylline [253] (180)	XI
		Thalirugine [14b] (180)	I
		Thalisopine (Thaligosine) [54] (180)	VII
Thalictrum revolutum DC.	Fr	Revolutinone [266] (223)	
Thalictrum sultanabadense Stapf.	T	O-Methylthalmine [244] (188)	XIV

		Thalictine [107] (188)	XIV
	R+T	Hernandezine [81] (211)	IX
		Thalabadensine [106a] (211)	XIV
		Thalictine [107] (211)	XIV
Tiliacora racemosa Colebr.	WP	Nortiliacorinine A [116] (8)	XVIII
Tiliacora triandra Diels	R	Nortiliacorinine A [116] (2)	XVIII
		Tiliacorine [118] (2)	XVIII
		Tiliacorinine [119] (2)	XVIII
		Tiliacorinine 2′-N-Oxide [254] (2)	XVIII

ᵃB=Bark, Bb=Bulb, Fr=Fruits, L=Leaves, R=Roots, RB=Root Bark, Rh=Rhizomes, Sd=Seeds, St=Stems, StB=Stembark, T=Tops, Tb=Tubers, W=Wood, WP=Whole Plant.

TABLE 10.   Biosynthesis of Bisbenzylisoquinoline Alkaloids
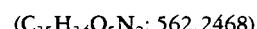
116   NORTILIACORININE A $(C_{35}H_{34}O_5N_2: 562.2468)$
The biosynthesis of nortiliacorinine A in *Tiliacora racemosa* Colebr. (Menispermaceae) was studied utilizing ^3H and ^{14}C labelled N-methylcoclaurine, (+)-(S)-N-methylcoclaurine, (−)-(R)-N-methylcoclaurine, (−)-(S)-coclaurine, and (+)-(R)-coclaurine. The study supported the following sequence for the biosynthesis of nortiliacorinine A: tyrosine↦→norcoclaurine↦→(S)-coclaurine↦→dimerization↦→nortiliacrorinine A (8).

118   TILIACORINE $(C_{36}H_{36}O_5N_2: 576.2624)$
It has been postulated that the biosynthesis of tiliacorine may proceed through a 1,2,-dehydroderivative via nucleophilic displacement of a methoxy group (18).

145   CISSAMPAREINE $(C_{37}H_{38}O_6N_2: 606.2730)$
A dihydroisoquinolinium intermediate is postulated to arise via oxidation of a cycleanine [121] analogue. Deprotonation of the intermediate could generate an eneamine conjugated with an aromatic nucleus. Finally, oxidation of an appropriate methoxyl group might furnish an oxonium ion which, in turn, may enter into an electrophilic substitution reaction with the above eneamine to furnish an intermediate with a 1,4-dioxene ring. Subsequent ring opening and reduction would produce cissampareine (18).

157   ISOTRILOBINE $(C_{36}H_{36}O_5N_2: 576.2624)$
It has been postulated that the biosynthesis isotrilobine may proceed through a 1,2,-dehydroderivative via nucleophilic displacement of a methoxyl group (18).

159   MICRANTHINE $(C_{34}H_{32}O_5N_2: 548.2311)$
It has been postulated that the biosynthesis of micranthine may proceed from daphnoline [38] through their 1,2,-dehydroderivatives via nucleophilic displacement of a methoxyl group (18).

168   REPANDULINE $(C_{37}H_{36}O_7N_2: 620.2523)$
A dihydroisoquinolinium intermediate is postulated to arise via oxidation of a cycleanine [121] analogue. Deprotonation of the intermediate could generate an eneamine conjugated with an aromatic nucleus. Finally, oxidation of an appropriate methoxyl group might furnish an oxonium ion which, in turn, may enter into an electrophilic substitution reaction with the above eneamine to furnish an intermediate with a 1,4-dioxene ring. A similar ring bearing a spiro-carbon occurs in the alkaloid repanduline (18).

187   APATELINE $(C_{34}H_{32}O_5N_2: 548.3211)$
It has been postulated that apateline may be biosynthesized from daphnoline [38] through their 1,2-dehydro-derivatives via nucleophilic displacement of the methoxyl group at C-6 by a phenoxide anion at C-7′ (18).

TABLE 11.   Pharmacological Activities of Bisbenzylisoquinoline Alkaloids

BERBAMINE
Found to inhibit platelet aggregation induced by collagen (90%) or APP 65% (3).

Found to inhibit (67%) K^+ release from lysolecithin treated erythrocytes (3).

A review was made of the pharmacology, toxicology, and clinical applications (treatment of radiation-induced of chemical-induced leukopenia, tuberculosis, and silicosis) (animals, human) (94).

A review was made citing the pharmacological activities, including hypotensive, antileukopenic, antimicrobial (acid-fast organisms), antisilicotic, and immunostimulant (94).

The acute intraperitoneal and oral LD_{50} values of a fraction of *Berberis vulgaris* roots containing 80% berbamine and three unidentified isoquinoline alkaloids were 72.5 and 520 mg/kg, respectively, in mice and 347 and 1280 mg/kg, respectively, in rats. Intravenous administration of this fraction in dosages of 1,2, and 5 mg/kg, respectively, to cats lowered the blood pressure by 25-30% for 1-2 h, 40% for 3 h and 50% for greater than 4 h, respectively. The highest dose tended to prolong and stabilize hypotension by alleviation of the depressor effect of acetylcholine without affecting the pressor effect of norepinephrine. It was postulated that the extract acts on the M-cholinergic receptors. At 5 and 10 mg/kg, the extract induced a positive and a negative inotropic effect, respectively, in the in situ feline heart. The extract also produced a spasmolytic effect on smooth muscles while an intrapertoneal injection (5 mg/kg) stimulated bile secretion in rats by 72%. The divergence between the hypotensive and spasmolytic effects of the extract and the established cardiac depressant and toxic activities of berbamine alone suggest a pharmacological effect of the unidentified alkaloids (218)

No significant changes on monoamine metabolism in the brain were produced by intraperitoneal administration (60 mg/kg) as measured 30 min after dosing (rat) (220).

CEPHARANTHINE

Found to inhibit platelet aggregation induced by collagen (83%) or ADP (33%). An inhibitor (88%) of K^+ release from lysolecithin treated erythrocytes (3).

Oral administration (5 mg/kg) enhanced the activity of antibody-dependent cellular toxicity in the spleen in rodents with MH-134 hepatic tumors (mouse) (19).

An effective inhibitor of T cell transformation at a concentration of 20-200 µg in in vitro cultured human peripheral lymphocytes stimulated with mitogens. Doses $\geq$ 20 µg in mixed lymphocyte culture produced a dose-dependent reduction of lymphocyte stimulation. Helper T-cell activity was inhibited while suppressor T-cell function was accelerated by a dose of 100 µg (20).

Collagen or thrombin-induced platelet aggregation was inhibited in a concentration dependent manner by cepharanthine. The inhibition of thrombin-induced aggregation was correlated with membrane phospholipid arachidonate release. Apparently, the alkaloid disturbs the plasma membrane via its incorporation which subsequently results in a change in membrane morphology and inhibition of aggregation (human platelets) (33).

The alkaloid possesses an in vitro antisickling activity of the same magnitude as chlorpromazine but lacking neuroleptic activity. The alkaloid was capable of desickling sickled cells when added anaerobically to a suspension that had been previously deoxygenated. The lack of effect on both oxygen affinity and hemoglobin and the delay time of gelation of sickle hemoglobin suggests the effect on sickle cells may be mediated through some kind of membrane-linked reaction (Human heparinized blood from a patient with homozygous sickle-cell hemoglobin [HbS]) (58).

Spleen cells of mice (CBF_1) subjected to unilateral femur amputation were mixed with spleen cells of BALB/c mice and injected subcutaneously into untreated CBF_1 mice to measure graft versus host reactions as estimated by change in lymph node weight. Pretreatment with the alkaloid (10 mg/kg/day) significantly prevented the inhibition of graft versus host reaction by the spleen cells of the operated animals whereas smaller doses (2.5-5 mg/kg) of the alkaloid increased the graft versus host-inhibiting activity of the spleen cells of operated as well as untreated mice. It is likely that suppressor T lymphocytes may be involved in the mechanism of graft versus host reaction (mouse) (68).

Collagen-induced blood platelet aggregation was slightly inhibited (30 mg) and almost completely inhibited (60 mg) 1 h after oral administration. Secondary aggregation induced by ADP was also inhibited 1-2 h after administration. The inhibitory effect disappeared in 2-4 h. Arachidonic acid-induced aggregation was not inhibited nor was platelet membrane morphology affected by 60 mg dosage. The alkaloid apparently inhibits the collagen-induced and ADP-induced release of arachidonic acid from membrane phospholipids and, thus, inhibits platelet aggregation (human) (87).

Antitumor-induced leukopenia was improved by the simultaneous administration of the alkaloid with cytotoxic drugs (mouse) (92).

A review was made citing the pharmacological activities of the alkaloid including antitumor, antimicrobial (acid-fast organisms), and anti-leukopenic (94).

A method was developed to prepare irreversibly sickled cells in vitro under physiological conditions. Repeated deoxygenation-reoxygenation cycles for 15 h at 37° resulted in the formation of 20-30% irreversibly sickled cells that were separated from biconcave-shaped cells by a gradient density centrifugation. The precentage of irreversibly sickled cells was subsequently determined spectrophotometrically to alter

hemolysis. The alkaloid inhibited the in vitro formation of irreversibly sickled human cells by 50% at 15 μM. This concentration inhibiting irreversibly sickled cells was much lower than that required to inhibit the in vitro sickling cells (human) (136).

In the presence of the alkaloid, collagen-induced stimulated platelets became spherical but did not form pseudopodia nor aggregate. The alkaloid inhibited accelerated oxygen consumption, release of membrane-bound Ca^{+2}, release of Ca^{+2} into the extracellular medium and depolarization of the membrane potential. The alkaloid inhibited phospholipase A_2 activity using D,L-dipalmitoyl phosphatidyl choline liposome as substrate. Apparently, changes in the membrane following interaction of collagen with its receptor are important for platelet activation, and the alkaloid may inhibit these membrane state changes (human) (158).

The enhancement of antibody production (plaque-forming cell method in vitro and graft versus host reaction in vivo) and helper cell activity by pain stress (tail quenching) was dose-dependently suppressed by pretreatment or simultaneous treatment with the alkaloid (25-100 mg/kg). There was no anesthetic effect due to the alkaloid at comparable doses (mouse) (177).

The alkaloid (0.1 mM) protected Na^+, K^+ activated ATPase of synaptosomal plasma membrane from inhibition by ascorbate alone in the presence of Fe^{+3} but failed to protect against the inhibitory action of EtOH, Pb^{+2}, Hg^{+2}, or ouabain. The alkaloid alone did not affect peroxidation but stopped peroxidation increase induced by ascorbate, ATP plus Fe^{+3}. Thus, the alkaloid prevents both membrane lipid peroxidation (which in turn inhibits the ATPase integrated in the lipid bilayer) and the deleterious effects of ascorbate, whose effective form is apparently its radical (181).

The alkaloid incorporated into platelets dose-dependently inhibited Ca influx as well as aggregation in response to collagen and also inhibited arachidonate release in response to collagen. The latter action was demonstrated not to be due to the direct action on phospholipase A_2 molecules but to the depression of susceptibility of substrate phospholipids to enzymatic hydrolysis. By removing the bound alkaloid from platelets these depressed functions and the inhibition of aggregation were almost restored. Arachidonate-induced aggregation and prostaglandin synthesis from externally added arachidonate were not suppressed by addition of the alkaloid. Apparently, the alkaloid alters the lipid properties of platelets and, thus, inhibits the function of the Ca channel or the susceptibility of substrate phospholipids to enzymatic hydrolysis by phospholipase A_2 (rabbit) (199).

CURINE

A review citing the pharmacological activities of the alkaloid including antitumor and antimalarial (94).

CURINE DIMETHIODIDE (N,N'-Dimethylcurine iodide)

The effects of the alkaloid as a muscle relaxant were cited (94).

CYCLEANINE

Found to inhibit platelet aggregation induced by collagen (2%) or ADP (19%). An inhibitor (72%) of K^+ release from lysolecithin treated erythrocytes (3).

A review was made citing the pharmacological activities of the alkaloid including analgesic, muscle relaxant, antisilicotic, and antiinflammatory (94).

The α-phase of intravenously administered ^{14}C-labelled cycleanine dimethiodide was 4 min. Radioactivity was higher in the kidneys (where it remained the longest), lungs, and liver than in the heart, intestines, spleen, and muscle. Twenty-four hours after administration of an interperitonel dose, 58% had been renally excreted (mainly as unchanged alkaloid) and 6% in the feces. The alkaloid bound extensively to plasma protein and hepatic plus renal homogenates in vitro (rat) (141).

CYCLEANINE DIMETHOBROMIDE

Blocked the transmission of impulses through the supracervical, sympathic ganglion with an EC_{50} of 58 μg/ml (rabbit). Blocked neuromuscular transmission in the phrenic nerve-diaphragm preparation at an EC_{50} 46 μg/ml (rat). These effects are much weaker than those of (+)-tubocurarine (13).

A review was given of the pharmacology as it pertains to its hypotensive properties (209).

DAURICINE

Found to inhibit platelet aggregation induced by collagen (69%) or ADP (63%). An inhibitor (33%) of K^+ release from lysolecithin treated erythrocytes (3).

Intravenous and intraperitoneal (3,5, and 8.33 mg/kg) injections in anesthetized cats produced a dose-dependent hypotensive response (19-57%). Vertebrarterial injection (0.5 mg/kg) also decreased

blood pressure for a short period ($<$ 10 min), while intravenous injection at this dosage did not. There was no decrease in epinephrine- or carotid-induced hypertension, suggesting that the alkaloid is neither an α-receptor blocker nor a ganglionic blocker. The epinephrine-enhanced tension of thoracic aorta strips (rat and rabbit) was decreased (17-59%) in the presence of a solution (1-6×10^{-5}M) suggesting that the hypotensive response may be related to direct relaxation (dilitation) of vascular, smooth muscle (cat, rat, rabbit) (26).

Inhibited the epinephrine- or hyperkalemic-induced contractions in thoracic aortic strips (rabbit) and norepinephrine-induced contractions in aortic strips (hypertensive rat). The dose-response curves for norepinephrine, KCl, and CaCl$_2$ were shifted to the right with depressed maximal responses. No α-adrenoceptor blockade nor β-adrenoceptor stimulation was observed. Inhibition of the fast/transitory (Ca^{++} dependent) contractile responses evoked by norepinephrine in a Ca^{++}-free medium and the slow/sustained (Ca^{++}-dependent) contractile responses after CaCl$_2$ administration was noted (rabbit, rat) (55).

Intravenous administration at 3-8 mg/kg dosages produced a concentration-dependent acute hypotension without affecting the heart rate in anesthetized cats. Continuous infusion (0.3 mg/0.01 ml/kg) produced an immediate reduction in infusion pressure which was similar to that produced by administration of an identical dosage of papaverine, suggesting that the hypotensive effect involved direct vasodilation and decrease in peripheral resistance. Intravenous administration (5 mg/kg) to rats also produced hypotension, the maximal effect being noted within 1 min. The alkaloid-induced hypotension was not affected by vagotomy or intravenous administration of epinephrine (5 μg/kg), thus precluding the participation of vagal stimulation of α-receptor blockade. Administration via the vertebral artery (0.5 mg/kg) also produced a hypotensive effect, indicating the involvement of a central factor in induced hypotension (cat, rat) (74).

The description of a method for the isolation of the alkaloid from biological specimens is presented. Quantitation was via alumina G tlc and CS-910 densitometry. The logarithm of drug concentration in plasma versus time curve after intravenous administration was fitted to a two-compartment open model with first order elimination. Pharmacokinetic parameters were observed as $t_{1/2} \alpha$ 0.1078h, $t_{1/2} \beta$ 6.506h, V_c 8.56 liter/kg, V_d 46.09 liter/kg, K_{21} 0.9257/h, K_{10} 0.5834/h, and TBCl 81.92 ml/min (rabbit) (76).

A review was made citing the pharmacological activities of the alkaloid including hypotensive, uterine relaxant, and central nervous system depressant (94).

Oral administration (150 mg/kg) resulted in 52.5% disappearance from the gastrointestinal tract and rapid appearance in the liver, lungs, kidneys, brain, and spleen suggesting that the blood-brain barrier had been crossed. Peak levels were observed 1 h after administration in the liver, lung, and brain but 12 h afterward in the spleen. The distribution of the alkaloid in the liver, spleen, and kidney was relatively high but low in the brain. Combined fecal and urinary excretion of the alkaloid accounted for only 22.27% of the orally administered drug 48 h after administration with the balance being unaccounted for (rat) (97).

The alkaloid produced electrocardiographic changes similar to quinidine by prolongation of the PR and QT$_c$ intervals, widening the QRS complex, and inducing a bradycardia (cat). The alkaloid also possessed a local anesthetic activity (guinea pig) (131).

The disappearance of intravenously administered ^{3}H-labelled alkaloid (120 Ci/kg) from circulation fit a two-compartmental model with $t_{102\alpha}$=0.265h and $t_{102\beta}$=2.888h. The urinary and fecal [^{3}H] activity accounted for only 9.24 and 9.80%, respectively, of the total administered ^{3}H-dauricine after 72 h with the fate of the remaining ^{3}H-alkaloid unknown (rat) (139).

The alkaloid (32 μM) decreased contractility, shifted the duration-intensity curve to the right, increased the concentration of epinephrine necessary to induce automaticity, and prolonged the functional refractory period when added to papillary muscle preparations. The role of the alkaloid as a possible Ca^{+2} antagonist is suggested (cat) (151).

Intravenous administration (5 mg/kg) of the alkaloid produced a lowered arterial blood pressure (presumably due to dilation) that was not accompanied by any depression of sinus node automaticity or left-ventricular contractibility, as measured by systolic time intervals (173).

A solution of the alkaloid (0.1 mM) decreased the contractile force (73.6%), the amplitude (24.5%), and the dv/dI$_{max}$ of action potential of isolated auricle and papillary muscle. The alkaloid (1-300 μM) also dose-dependently increased the action potential, repolarization, and functional refractory period. The dV/dT$_{max}$ of the action potential and force of contraction were dose-dependently decreased by the alkaloid. The alkaloid antagonized the effects of acetylcholine on the action potential and may act by nonspecific inhibition of Na$^+$, Ca^{+2} currents in myocardial tissue (rabbit) (195).

DIMETHYL-(-)-CURINE DIMETHOCHLORIDE

A study was made of the distribution, excretion, metabolism, and pharmacokinetics of ^{3}H-dimethyl-(-)-curine dimethochloride. Intravenous administration (375 μg/kg) via bolus resulted in the disappearance from the blood in a triexponential model form. These results imply a wide distribution with the drug passing quickly into peripheral components and being eliminated at a slower rate. Levels of radioactivity

were highest in the kidney; moderate in the liver, lung, and skeletal muscle; and trace in the fat and brain. Renal excretion predominated with biliary-fecal excretion being minor. No metabolite was found in the bile or urine (rat) (41).

The pharmacokinetics of ^{3}H-labelled alkaloid administered intravenously fit a three compartment open model with the half-lives of the π-, α- and β-phases being 1.73, 31.94, and 346.50 min, respectively. The alkaloid was rapidly cleared from the plasma and distributed into various organs, but its elimination was relatively slow. No metabolites were detected in the urine or feces, but 2 min after administration the radioactivity was highest in the kidney with varying amounts in other organs. The brain accumulated the least radioactivity. About 28 and 37% of injected radiolabel appeared in the urine and feces, respectively, 96 h after administration (mouse) (168).

No detectable change was observed in the stability of injections containing this alkaloid over a 2-year period as measured by the head-drop method (rabbit) (53).

($\pm$)-DIMETHYLCURINE DIMETHOCHLORIDE

Studies using the rat phrenic nerve-diaphragm and the chick nerve-muscle preparations demonstrate the alkaloid to be a nondepolarizing, neuromuscular blocking agent which acts by blocking cholinergic receptors (rat, chick) (45).

No detectable change in the stability of injections containing this alkaloid over a 2-year period as measured by the head-drop method (rabbit) (53).

^{3}H-labelled alkaloid was intravenously administered with rapid distribution into the peripheral compartment from the central compartment and elimination at a slower rate. Highest levels were in the liver and kidney, with moderate amounts in spleen, lung, muscle, and heart whereas trace amounts were detected in the brain and lipid. Small amounts of radioactivity were detected in the fetus after intravenous administration to pregnant mice. After intravenous administration to rats, the radioactivity excreted in the urine in 12 h was 65% of the dose, while in bile it was 20%. In mice the radioactivity excreted in 72 h in urine and feces was 66% and 27% of the dose, respectively. The drug-plasma binding rate was found to be 13-21% (rat, mouse) (140).

DIMETHYLCURINE METHOCHLORIDE

Reported to be skeletal muscle relaxant (human) (4).

DIMETHYLTRILOBINE IODIDE (Trilobine Dimethiodide)

An intravenous injection (1 mg/kg) of the alkaloid delayed the onset of aconitine-induced arrhythmias (anesthetized rats). Similarly, an intraperitoneal injection (1.5 mg/kg) also delayed the onset of ouabain-induced arrhythmias (anesthetized guinea pigs) and prevented (0.25 mg/kg intraperitoneally) $CHCl_3$-epinephrine-induced arrhythmias (rabbits). The mean duration of the action potential of ventricular myocardial cells (guinea pigs) was prolonged by an intraperitoneal injection (1.5 mg/kg) of the alkaloid. The functional refractory period was prolonged by the alkaloid in isolated rabbit atrial muscle (3.0×10^{-6}M) (167).

Intravenous injection (0.5 mg/kg) of the alkaloid to acute renal hypertensive rats produced a hypotensive response (148.8 mm Hg lowered to 123.6 mm Hg) that persisted for longer than 40 min. The alkaloid also produced a decrease in blood pressure when given in feed (3-10 mg/kg) daily for 28 days (rat) (185).

Intravenous injection of the alkaloid at a dosage of 0.05-0.1 mg/kg reduced the blood pressure in anesthetized dogs by 42.3-61.5% for about 1 h. In anesthetized cats the reduction in blood pressure was 26.5-43.5% for 2 to 4 h when the alkaloid was intravenously administered at a dosage of 0.625×10^{-2}-1.25×10^{-2} mg/kg. A similar administration to rabbits (0.005-0.01 mg/kg) produced a hypotensive effect which lasted 5 h. The alkaloid also produced a hypotensive response in rats. The mechanism of action of this effect is probably related to ganglionic blockade. The acute oral and intravenous LD_{50} in mice was 522.0 and 2.23 mg/kg, respectively (201).

Intravenous administration (0.16 mg/kg) of the alkaloid produced head drop (rabbit) and was 1.4 times greater than that of (+)-tubocurarine. Combined use of the two alkaloids produced an additive muscle relaxant effect. The action of the alkaloid is like (+)-tubocurarine with the acetylcholine receptor on the postsynaptolemma of the neuromuscular junction as the site of action. An injection (4 mg/kg) lowered blood pressure and blocked the fast twitch fiber contraction of the carotid sympathetic ganglia. The ED_{50} and LD_{50} values of the alkaloid on intravenous injection (mice) were 0.8 mg/kg and 1.68 mg/kg, respectively, with a therapeutic index of 2.1. Treatment (0.2 mg/kg) (rabbits) for 14 days produced no apparent changes in morphology and cytochemical indices (178).

DIMETHYLTUBOCURARINE

The resistance to paralysis in induced unilateral gastrocnemius disuse atrophy afforded by the alkaloid

was measured. The 50% paralyzing dose (tetanus) for control versus casted gastrocnemius muscle was 64 versus 813 mg/kg, with corresponding plasma concentrations being 0.12 versus 2.0 g/ml. Hence, in vivo simultaneous tension measurements of one casted and one uncasted gastrocnemius muscle demonstrated resistance to paralysis by the alkaloid in muscle with disease atrophy (dog) (179).

FANGCHINOLINE

An inhibition of platelet aggregation was induced by collagen (41%) or ADP (60%). An inhibitor (88%) of K^+ released from lysolecithin treated erythrocytes (3).

A review was made citing the pharmacological activities of the alkaloid including analgesic, antitumor, antisilicotic, and antimicrobial (acid-fast) (94).

HAYATINE

A review was made citing the pharmacological activities of the alkaloid including antitumor and antisilicotic (94).

HAYATINE DIMETHO SALTS (N,N'-Dimethylhayatine Salt)

A review was made citing the pharmacological activities of the alkaloid including muscle relaxation (94).

HOMOAROMOLINE

Produced an inhibition of platelet aggregation induced by collagen (45%) or ADP (13%). Produced an inhibition (78%) of K^+ release from lysolecithin treated erythrocytes (3).

ISOTRILOBINE

Produced an inhibition of platelet aggregation induced by collagen (97%) or ADP (22%). Failed to inhibit K^+ release from lysolecithin treated erythrocytes (3).

(+)-ISOCHONDODENDRINE HYDROCHLORIDE

Intraperitoneal administration produced analgesia but not muscle relaxation (mouse). Pentetrazole- and strychnine-induced convulsions were delayed but not inhibited by pretreatment with the alkaloid (mouse) (6).

ISOTETRANDRINE

A review was made citing the pharmacological activities of the alkaloid including analgesic, antitumor, antisilicotic, and antimicrobial (acid-fast) (94).

METOCURINE

The alkaloid failed to act as an antagonist of dopamine-induced inhibition of adrenergic neurotransmission in the isolated, perfused ear artery (rabbit) (191).

Tissue distribution and urinary excretion were investigated and the pharmacokinetic parameters compared with those of (+)-tubocurarine. Serum concentrations were correlated with neuromuscular transmission as measured by twitch tension and evoked compd. electromyog. (ECEMG) of the adductor muscle of the thumb. Administration of equipotent doses of the two alkaloids resulted in no significant difference in the time required for 50% recovery of ECEMG. Metocurine appeared to be stored in body tissue and released slowly over a period of days. Pharmacokinetic parameters differ for the two alkaloids and suggest a decreased free tissue fraction for metocurine (humans) (63).

In vitro and in vivo experiments both demonstrate that there is no interaction between the alkaloid and pancuronium relative to plasma and tissue binding, thus failing to explain the potentiation that exists between these two drugs (85).

N-METHYLTUBOCURARINE

The alkaloid failed to act as an antagonist of dopamine-induced inhibition of adrenergic neurotransmission in the isolated, perfused ear artery (rabbit) (191).

OBAMEGINE

Intravenous administration (0.5-4 mg/kg) produced hypotension with tachyphlaxis (dog). Inconsistent results were produced when administered as a hypertensive-blocking agent prior to the administration

of dopamine and norepinephrine. The alkaloid antagonized the phenylephrine-induced contractions of aortic strips (rabbit) and, thus, possessed α-adrenoreceptor blocking activity. There was no effect on canine respiration, nor was there inhibition of neuromuscular transmission ($1-30 \times 10^{-6}$M) (27).

PHAEANTHARINE

The antimicrobial (*Bacillus subtilis, Staphylococcus aureus*) effects were cited (100).

TETRANDRINE

Produced an inhibition of platelet aggregation induced by collagen (64%) or ADP (26%). Produced an inhibition (88%) of K^+ release from lysolecithin treated erythrocytes (3).

Intravenous administration significantly decreased cardenolide glycoside toxicity (guinea pig). Administration of Ca^{+2} totally eliminated this protective effect (5).

Decreased the contractility and automaticity but prolonged the refractory period of the isolated atrium (guinea pig). There was no influence on myocardial excitability. The alkaloid has antiarrhythmic and negative inotropic effects and may be a Ca^{+2} antagonist (11).

Intravenous administration (9 mg/kg) prevented $BaCl_2$ induced arrhythmias or induced reversion to sinus rhythm immediately (anesthetized rat). Similar administration (6-9 mg/kg) delayed aconitine-induced arrhythmias and prevented $CaCl_2$ induced ventricular fibrillation and death (anesthetized rat). Ouabain-induced arrhythmias were shortened by similar administration (6 mg/kg) (anesthetized guinea pig). Ventricular fibrilation threshold was not elevated in another animal (anesthetized rabbit) (12).

Antagonized isoproterenol and calcium in a noncompetitive manner and shifted calcium dose response curves to the right in isolated papillary muscles. Produced excitation-contraction uncoupling and, thus, inhibited the inward displacement of calcium through the voltage dependent channel (cat) (46).

An increased inotropic effect with a decreased ouabain and divaricoside toxicity was observed in isolated left atrial preparations. The response was antagonized by Ca^{+2}. Increased extracellular Ca^{+2} increased the inotropic effect and toxicity of ouabain but had no effect on divaricoside. Apparently tetrandrine is a Ca^{+2} antagonist, and ouabain is more dependent on extracellular Ca^{+2} than divaricoside (rabbit) (54).

Intravenous administration (10 mg/kg and 15 mg/kg) to anesthetized open-chest dogs lowered systemic blood pressure and decreased left ventricular pressure and dp/dt max. There was also a bradycardia and a prolongation of the P-R interval. Recovery of decreased left ventricular pressure and dp/dt max was more rapid than systemic blood pressure. There was a marked reduction in peripheral resistance consistent with the hypotensive effect. Pulse pressure increased due to a decrease in diastolic pressure which was larger than systolic blood pressure. The hypotensive effect is mainly due to vasodilation of resistance blood vessels (dog) (64).

Exerted a protective effect on experimental myocardial infarction (dog) (67).

Administration of the antisilicosis alkaloid to humans (orally) and rats (intragastrically) resulted in recovery of predominantly unchanged alkaloid in human and rat urine and in rat hepatic and lung tissue. Small amounts of tetrandrine-2'-N-oxide and N-2'-nortetrandrine were detected in human and rat urine and in rat hepatic and lung tissue (human, rat) (70).

Intravenous administration to pentobarbitone-anesthetized and conscious normotensive and hypotensive rats produced an acute, long-lasting, and dose dependent decrease in mean arterial pressure with no significant alteration in heart rate. Intraarterial administration of the alkaloid to pithed rats (15 min previously) impaired the increase in diastolic pressure induced by intravenous administration of the highly selective alpha-adrenoceptor-stimulant B-HT 920, in a dose-dependent manner. The alkaloid displayed only minor affinities for specific binding sites in rat membranes for ^{3}H-prazosin (α_1-adrenoceptors) and for ^{3}H-clonidine (α_2-adrenoceptors). These results suggest that the hypotensive effect of tetrandrine may be related to an impairment of vasoconstrictor tone mediated by vascular postsynaptic α_2-adrenoceptors (rat) (71).

Oral administration of the alkaloid at dosages of 3 mg/kg and 10 mg/kg failed to produce toxic effects. However, similar administration at a dosage of 40 mg/kg for 2 months induced focal hepatic cell necrosis, abnormal hepatic function, and acceleration of erythrocyte sedimentation rate. Continuous administration for six months produced hepatic necrosis. The alkaloid accumulated in hepatic, renal, lung, and adrenal tissue on continued administration in a dose-dependent fashion (dog) (72).

Intraperitoneal administration (100 mg/kg) increased myocardial blood flow but did not counteract isoprenaline-induced increased blood flow. The alkaloid antagonized the increase in blood flow induced by $CaCl_2$ (as did verapamil) and, thus, may be a calcium antagonist (mouse) (77).

The alkaloid inhibited isoprenaline-induced tachycardia and antagonized the positive chronotropic responses to calcium ion in isolated, spontaneously beating atria. Hence, the alkaloid may be a calcium antagonist similar to verapamil (rabbit) (78).

The alkaloid did not antagonize isoprenaline-induced increase in cAMP nor the increase in contractile force of isolated atrial strips, suggesting that the alkaloid may be a Ca^{+2} antagonist but not a β-receptor blocker (90).

A review was made citing the pharmacological activities of the alkaloid including analgesic, antitumor, antisilicotic, antimicrobial (acid-fast organisms), and antiarrhythmic (94).

The alkaloid inhibited Ca^{+2} induced contractions of the isolated uterus and, thus, may be a Ca^{+2} antagonist similar to verapamil (rat) (102).

Oral administration (200 mg/kg) resulted in O-demethylation and N-oxidation as demonstrated by the appearance of O-demethyltetrandrine and tetrandrine N-2'-oxide in the liver and excreta. A possible relationship between the antisilicotic activity of the alkaloid and its metabolites is discussed (rat) (107).

The alkaloid blocked the ouabain (0.85 μM) contractions of the coronary artery. The alkaloid also antagonized the contractile-synergistic effect of ouabain (85 nm) and Ca^{+2} (2-16 mM) and depressed the contractile response to electrical stimuli in the presence of ouabain. All of these effects were reversed by excess Ca^{+2} and were similar to but less potent than verapamil (pig) (117).

Perfusion of isolated myocardium with a Tyrode's buffer (pH 7.25-7.4) containing tetrandrine (20 μg/ml) markedly increased the ventricular action potential duration and effective refractory period by 36-39% and 50%, respectively, but did not significantly alter the V_{max} and action potential height. These tetrandrine-induced increases in ventricular action potential duration and effective refractory period were partially antagonized by perfusion with a high Ca^{+2} (4.4 mM) Tyrode's buffer. In contrast, perfusion with verapamil (1 mg/ml) solution did not cause marked changes in action potential duration and effective refractory period (pig) (130).

The alkaloid produced concentration-dependent negative inotropic effects on isolated papillary muscle without affecting resting potential or the amplitude of action potential, indicating excitation-contraction uncoupling. The alkaloid also decreased the amplitude of the Ca^{+2} mediated slow potential induced by high K^+ and, in contrast to quinidine, is apparently a slow-channel blocker (guinea pig) (132).

The increase in the ST segment of the electrocardiogram and the release of myocardial creatine kinase in animals with acute experimental myocardial infarction (induced by ligation of the left anterior descending coronary artery) were both markedly decreased by intravenous (5 mg/kg) pretreatment 5 min prior to ligation. The alkaloid caused only a slight hypotension and bradycardia (dog) (135).

The alkaloid relaxed contractions in coronary artery strips which were reversed by increasing the Ca^{+2} concentration from 2.7-14.4 μM. The alkaloid inhibited norepinephrine-induced release of intracellular Ca^{+2} but failed to inhibit norepinephrine-induced contractions nor to block isoproterenol-induced relaxation (pig) (147).

Various cardiac indices, including contractability, automaticity, excitability, electrical activity, cardiac circulation, cAMP content, and Ca^{+2} induced changes in these indices were all markedly affected by the alkaloid. The effects of the alkaloid on these indices were antagonized by high Ca^{+2} concentrations lending support to the theory that the alkaloid is a Ca^{+2} antagonist (150).

The alkaloid diminished the Ca^{+2}-dependent contractile force and the oxygen consumption in isolated left atrial strips (guinea pig) and papillary muscles (cat). These effects were antagonized by increasing the extracellular Ca^{+2} concentration. A linear reduction of isometric tension and oxygen consumption due to mechanical activity were seen with increasing concentrations (5-210 μM) of the alkaloid (at 0.21 mM, the tension development and contraction-dependent oxygen consumption were greatly decreased). The alkaloid is an effective Ca^{+2} antagonist very similar to verapamil (guinea pig, cat) (160).

Subcutaneous administration of the alkaloid in a dose of 100 mg/kg inhibited the isoproterenol-induced (3 mg/kg once or 5 mg/kg twice-both subcutaneous) alterations of the electrocardiogram. This suggests protection against myocardial hypoxia and necrosis and may relate to the Ca^{+2} antagonistic properties of the alkaloid (rat) (172).

The effects of the alkaloid on isolated vascular strips were compared with those of verapamil and phentolamine. All three of the drugs antagonized norepinephrine-induced contractions of the vascular strips with the antagonism being competitive for phentolamine but noncompetitive for verapamil and the alkaloid. K^+ (60mM)-induced contraction of thoracic aorta strips was inhibited by the alkaloid, and Ca^{+2} related vascular effects were antagonized by both the alkaloid and verapamil. Thus, vascular relaxation due to the alkaloid is probably because of Ca^{+2} antagonism (rabbit) (186).

TETRADRINE DIMETHIODIDE (*N,N'*-Dimethyltetrandrine Diiodide)

The effect of the alkaloid as a striated muscle relaxant and smooth muscle contractant is discussed (94).

THALIDASINE

Failed to inhibit the in vitro growth of *Streptococcus faecalis, Klebsiella pneumoniae, Escherichia coli,*

Pseudomonas aeruginosa, Staphylococcus aureus, Candida albicans, Cryptococcus neoformans, Sporotrichium schenckii, Trichophyton mentagrophytes, and *Aspergillus fumigatus* (35).

Polyphase liposomes containing the alkaloid possessed immunosuppressant, antitumor activity. Preparation #76 produced a 40% inhibition of the growth of S-180 tumor cells when injected intraperitoneally in a dose of 200 mg/kg day (mouse) (62).

Properties of polyphase liposomes containing the alkaloid were discussed. Liposome preparations #76 and #139 possessed antineoplastic properties with the former having a LD_{50} of 90 mg/kg and the latter a LD_{50} of 16 mg/kg following intravenous administration (mouse).

Subacute toxicity tests of #139 (rabbit) revealed no pathological changes while neither preparation had adverse effects on leukocytes (rabbit) (66).

THALISTYLINE CHLORIDE

Intravenous administration produced transient hypotension (0.1-0.4 mg/kg), tachyphylaxis, respiratory depression, and death (>0.4 mg/kg) (dogs). The alkaloid was about one-fourth as potent as (+)-tubocurarine as a neuromuscular blocker (rat hemidiaphragm) with a similar pharmacological mechanism. Phenylephrine-induced contractions of the aorta (rabbit) were antagonized with increasing concentrations of the alkaloid, producing parallel shifts to the right in phenylephrine dose-response curves. An α-adrenergic blockade in the vascular preparation is evident, but the hypotensive mechanism remains to be established (27).

THALRUGOSIDINE

Failed to inhibit the in vitro growth of *Streptococcus faecalis, Klebsiella pneumoniae, Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus, Candida albicans, Cryptococcus neoformans, Sporotrichium schenckii, Tricophyton mentagrophytes,* and *Aspergillus fumigatus* (35).

(+)-TUBOCURARINE (chloride)

Quantitative hplc used in the analysis of the alkaloid in human plasma (10).

The interactions of the alkaloid with the ionic channel of the nicotinic acetylcholine receptor were studied biochemically in *Torpedo* elec. organ membranes and electrophysiologically in frog sciatic nerve-sartorius muscle preparations. Interaction with both the acetylcholine receptor sites and its ionic channel sites in closed and open conformations occurs (17).

Accelerated reactivation (decarbamylation) of dimethylcarbamyl-bovine erythrocyte acetylcholinesterase at physiological pH and ionic strength by the alkaloid was noted. The alkaloid also enhanced the effect of the nucleophile, 3,3-dimethylbutanol, on decarbamylation and retarded aging (dealkylation) of isopropylmethylphosphonyl bovine erythrocyte acetylcholinesterase. The allosteric effect of the alkaloid at low ionic strength apparently persisted at physiological ionic strength (bovine erythrocyte) (28).

Isolated atria responded to the alkaloid with a delayed stimulation that showed tachyphylaxis and cross-tachyphylaxis indicating a common indirect mechanism (frog) (32).

Single intravenous injections and infusions into anesthetized rhesus macaque, bonnett macaque, and mangabey monkeys were administered. The relative potencies varied markedly with those obtained in humans. The elimination rates indicate that the duration of action, maintenance dosage, and ED_{50} varied for each type of monkey with the rhesus macaque appearing to be the closest to humans with respect to duration of action (monkey) (34).

A decrease of ATP levels was noted in hepatic cells within 5 min of intravenous administration. This decrease was due to either increased energy demands during cellular metabolism or a decrease in ATP production in the respiratory chain. There was a subsequent activation of glycolysis as demonstrated by a decrease of cytoplasmic glycogen and an increase in glucose-6-phosphate. Cytoplasmic lactate levels simultaneously increased and redox potentials shifted, the latter being due to an alteration in the lactate/pyruvate ratio (rat) (38).

Measurement was made of the influence of renal function on the neuromuscular blocking effect of a large single dose via observation of the duration of action as measured by single-twitch response using sciatic nerve-gastrocnemius muscle preparations. In the absence of renal function, (+)-tubocurarine was observed to produce a prolonged neuromuscular blockade (cat) (39).

The effect of a bolus intravenous injection (0.1-0.13 mg/kg) was followed by registration of the rectified smoothed electromyogram (rs EMG) from the soleus muscle (71% slow twitch muscle fibers) and from the (mixed) gastrocnemius muscle (54% slow twitch muscle fibers). Tubocurarine apparently affects human muscles in proportion to their slow twitch muscle fiber content (human males) (44).

The effect of low K^+ diets with and without deoxycorticosterone, furosemide, chlorothiazide, or ethacrynic acid on the sensitivity of isolated lumbrical nerve-muscle preparations to the alkaloid was examined. The ED_{50} of the alkaloid decreased as the K^+ level was lowered via dietary restriction. Addition

of desoxycorticosterone was without effect, while chlorothiazide reduced and ethacrynic acid enhanced the effect of diet alone. Acute restoration of K^+ levels partially reversed the effects of chronic depletion. Hence, a patient with chronic hypokalemia would be expected to require a decreased dose of tubocurarine with acute presurgical replacement of K^+ being partially helpful (guinea pig) (48).

Extracellular and intracellular recordings of the CA3 region of in vitro hippocampal slices produced results consistent with the fact that the alkaloid interferes with the function of the inhibitory neurotransmitter GABA, and this action is implicated in the observed epileptiform effects produced by the alkaloid (guinea pig) (56).

The effects of hippocampal EEG on intraventricular injections in gallamine-immobilized and methane-anesthetized rats were studied. The alkaloid provoked a 3.5-5 Hz θ rhythm in both hippocampi. Higher doses elicited rhythmic spike and wave complexes that appeared at a preferred phase of θ rhythm. Atropine and median septal lesions blocked θ rhythm and disrupted the rhythmicity of epileptiform activity. Hence, different neural subsystems sustain the θ rhythm and epileptiform spikes (rat) (73).

The action on extracellular excitatory postsynaptic current (EPSC) and on the L-glutamate-induced current relaxation after voltage pumps was studied at the neuromuscular junction where L-glutamate is a candidate transmitter. In the presence of the alkaloid, the glutamate-induced current relaxed in the direction of decreasing conductance during hyperpolarizing voltage steps, in contrast to the normal situation. The rate constant for this outward relaxation was increased by hyperpolarization. The alkaloid also produced a negative slope in the membrane potential-glutamate current relation with hyperpolarization. The alkaloid greatly shortened the decay of extracellular EPSC in a voltage-dependent fashion with hyperpolarization strongly facilitating the decay (mealworm) (81).

A study was made of the twitch and fade in a train of 10 stimuli of variable stimulus intervals to the sciatic nerve. The amplitudes of evoked compound electromyograph and mechanical contraction of the gastrocnemius muscle were measured simultaneously during the recovery phase from alkaloid-induced neuromuscular block. There was no significant difference between the evoked compound electromyograph and mechanical contraction. The alkaloid may occlude open ion end plate channels. Tests utilizing mechanical contraction rather than evoked compound electromyography may be preferable in residual neuromuscular block in clinical anesthesia due to ease of technical measurement (rabbit) (82).

In vitro experiments using the hypogastric nerve-vas deferens preparation and the phrenic nerve-hemidiaphragm preparation were used to determine the separation between the neuromuscular and ganglionic blocking effects of the alkaloid and atracurium debresylate. The equipotent molar ratio (based on EC_{50} values) for ganglionic/neuromuscular blockade was 48 h for atracurium and 9.4 h for the alkaloid (guinea pig) (83).

The amplitude of spontaneous subthreshold activity was reduced by treatment of the sartoris muscle preparation with solution of the alkaloid. A greater reduction was observed in a more concentrated solution indicating a stronger postjunctional effect. Similar studies also indicated a prejunctional effect of the drug also (frog) (84).

In vitro and in vivo experiments both demonstrate that there is no interaction between the alkaloid and pancuronium relative to plasma and tissue binding, thus failing to explain the potentiation that exists between these two drugs (85).

The alkaloid produced a close correlation between degrees of twitch strength depression and train-of-four response for in vivo soleus (ED_{50} 150 μg/kg) and gastrocnemius (ED_{50} 105 μg/kg) muscles. Prior to drug administration, the train-of-four response was 0.87 for the soleus and 1.0 for the gastrocnemius muscles. The results demonstrated major differences between the alkaloid and other competitive neuromuscular-blocking agents and suggest multiple sites of action (cat) (88).

Muscle fibers in the presence of curare (5-100 μM) that were held at hyperpolarized potentials displayed excitatory junctional currents with an initial fast component followed by a slow tail. Hyperpolarization beyond -50 mV decreased the amplitude of the peak synaptic current with the decay time constant of the fast component being decreased by hyperpolarization and the slow component being increased. Ionophoretic application of brief pulses of glutamate also produced two-component glutamate currents, thus suggesting that the alkaloid may produce a transient block of glutamate-activated synaptic channels (locust) (89).

The alkaloid (0.015 mg/200 g) failed to affect blood coagulation in plasmin-and thrombin-treated animals, suggesting that the alkaloid may be used in physiological studies dealing with blood coagulation (rat) (93).

The effect of the alkaloid and local anesthetics on the dose-response relation between ionophoretically applied L-glutamate and synaptic current suggested that both acted as voltage dependent noncompetitive inhibitors. The neurally evoked excitatory postsynaptic current was depressed in the presence of these drugs and was voltage dependent (crayfish) (95).

The pharmacological response, as defined by the indirectly stimulated anterior muscle, was found to correlate with administered dose (bolus) according to Hill's equation. The equation was also applicable to

the biophase concentration-response relation with the time course of the relative byphase concentration indicating linear kinetics with dose levels ≤0.15 mg/kg and the occurrence of dose-dependent disposition with 0.30 mg/kg after bolus dosing (intravenous) with [3H]-(+)-tubocurarine. The plasma concentration obeyed a dose-independent two-compartment model with doses=0.15 mg/kg but not with 0.30 mg/kg. The active metabolite was not found in the plasma and urine. Plasma levels and response intensity were well correlated by Hill's equation and a three-compartment muscle (rat) (98).

Intravenous administration of ketamine (5 mg/kg) did not affect the degree of the time of occurrence of maximal muscle relaxation by an intravenous dose (1 mg/kg) of the alkaloid, as measured by the single twitch response to nerve stimulation of the exposed tibial muscle in situ. The time required for recovery of full muscle contraction in response to stimulation was prolonged 53% by ketamine (rabbit) (99).

A measurement was made of the erythema and induration of intradermal injections in healthy, male volunteers (human) (101).

The alkaloid antagonized the inhibitory effect of dopamine and apomorphine in a competitive manner in the isolated perfused artery of the ear. The calculated dissociation constants for the alkaloid against dopamine and apomorphine were 1.9 μM and 1.7 μM, respectively. The alkaloid (1-100 μM) did not affect the response of the artery to sympathetic nerve stimulation. Apparently, (+)-tubocurarine could attenuate the therapeutic benefit of dopamine, if both were administered concomitantly (rabbit) (108).

Administration of the alkaloid to anesthetized, optionally ventilated cats in dosages of 400, 800, and 1600 μg/kg resulted in hypotension and a decrease in ascending aortic blood flow. Blood flow to the stomach increased but was decreased to the kidneys, liver, skin, spleen, intestine, and adrenal glands. These effects are quite similar to those produced by histamine infusion. Blood flow to the nerve-stimulated tibalis anterior muscle (which was about six times that of the unstimulated muscle) was decreased significantly by the alkaloid (cat) (109).

The alkaloid did not affect the surface area of human serum albumin monolayers but produced an increase in the surface area of phosphatidylcholine monolayer (114).

Administration of a bolus of 0.6 mg/kg of the alkaloid produced an increase in heart rate and an initial decrease in mean arterial pressure of up to 50% of control values. In the fourth minute after injection, arterial pressure was still significantly different from control (anesthetized humans) (118).

The alkaloid is capable of opening myotube cholinergic channels as measured by the single-channel recording technique. Another molecule can then block the tubocurarine-activated open channel. Partial agonist activity can also be demonstrated in adult muscle and the conductance of the tubocurarine-activated channel is 50-60 pS higher than in the myotubes (35 pS) (rat) (119).

A study on acetylcholinesterase suggested the possible binding sites of verapamil and tubocurarine to be identical via a comparison of Hill coefficients (rabbit skeletal muscle sarcolemma) (121).

Mixtures of the alkaloid plus pancuronium and the alkaloid plus alcuronium produced synergistic effects in the isolated phrenic nerve-hemidiaphragm neuromuscular preparation (rat) (123).

An investigation was made of the effect of the alkaloid on the metabolism of exogenous ^{14}C-labeled arachidonic acid in isolated perfused lungs. Infusion of the alkaloid (4 or 40 μg/ml) into the pulmonary circulation produced no increase in perfusion pressure nor were the amounts of arachidonate metabolites changed dose-dependently (hamster) (124).

A self-tuning algorithm is presented for the online control of muscle relaxation. Simulations show that a twitch depression of 80% can be achieved in less than 20 min using the alkaloid without excessive overdosage (134).

The effect of an intravenous bolus injection of the alkaloid (0.1 mg/kg) was followed in six young subjects by registration of static, slow, fast, and dynamic maximal voluntary leg extensions. It was found that static as well as dynamic human muscle contractions can be divided into two parts with a different sensitivity for the alkaloid, one of which seems to have a sensitivity which depends on the contraction velocity (human) (137).

Rat fetuses were paralyzed by daily transuterine injections of the alkaloid from day 18 of gestation until term (day 21). The following anomalies were noted at the time of delivery: multiple joint contractures, pulmonary hypoplasia, micrognathia, fetal growth retardation, short umbilical cords, and polyhydramnios. The anomalies are presumed to result from the paralytic effect of the alkaloid. This phenotype bears a striking resemblance to the syndrome of ankyloses facial anomalies and pulmonary hypoplasia presumably inherited in an autosomal recessive manner. Perhaps this phenotype is not specific but represents a deformation sequence which results from fetal immobilization or akinesia (rat) (138).

Six healthy young male subjects performed repeated brisk maximal voluntary muscle contractions with the knee and hip extensors. On separate days, decamethonium bromide (0.03 mg/kg) and tubocurarine chloride (0.01 mg/kg) were intravenously administered during repeated maximal voluntary muscle contractions. The results suggest that the isometric mechanogram is composed of a phasically active component with a high innervation threshold primarily sensitive to decamethonium and a tonically active component with a lower innervation threshold and primarily sensitive to tubocurarine (human) (142).

The agonist-like action of the alkaloid at the neuromuscular junction of myotubes did not result from any contaminant, because the same action was observed with purified alkaloid. Apparently, binding of the alkaloid to the classical acetylcholine receptor site acts not only as an antagonist but also as an agonist, resulting in opening of the channel. The alkaloid binds to at least one other site of the receptor-ionophore complex, giving rise to its channel blocking activity (rat) (144).

The effects of the alkaloid were examined at voltage-lamped diaphragm neuromuscular junctions during single and repetitive stimulation of the phrenic nerve in cut muscles and repetitive iontophoretic application of acetylcholine. The alkaloid produced a concentration-dependent reduction in amplitude of neurially evoked end-plate currents and reduced the time constant delay in a manner independent of membrane potential and not markedly dependent on concentration. The alkaloid apparently reduced end-plate current amplitude by blocking the acetylcholine receptor and produced tetanic run-down of same by a prejunctional mechanism (rat) (152).

In omohyoid muscle preparations, hexamethonium dibromide (50-200 μM) caused an increase in the amplitude of nerve-evoked end plate currents recorded in the presence of the alkaloid (0.6 μM). The effect decreased with hyperpolarization of the muscle fiber (rat) (153).

A computer analysis of neuronal activity in the caudate nucleus following intramuscular administration (1.9, 17.0, 25.0 mg/kg) showed that the alkaloid produced changes in the discharge patterns of unit activity and appeared to promote firing at high frequency (rat) (155).

A review was made of the use of this alkaloid and other neuromuscular blocking agents in anesthesia to facilitate intubation, decrease anesthesia requirements, and provide relaxation plus immobility during surgery (human) (159).

The alkaloid (10-100 μM) reduced the duration of after-hyperpolarization, which was induced by the activation of Ca^{+2} dependent K^+-conductance following an action potential in the sympathetic ganglion cell but did not affect the maximum rates of rise and fall of Na^+-and Ca^{+2} dependent action potentials. The amplitudes of slow, rhythmic, membrane hyperpolarizations produced by rhythmic rises in Ca^{+2}-dependent K^+ conductance were also decreased without a change in their intervals. The alkaloid appeared to block the Ca^{+2}-dependent K^+ channel of the sympathetic ganglion cell (bullfrog) (164).

Anesthetized, healthy pediatric patients that had been administered the alkaloid and/or dantrolene prior to anesthesia had mean serum myoglobin levels of 336 ng/ml. None of these patients showed fasiculation (human) (176).

The in vivo effects of the alkaloid (0.20 mg/kg) on the responses of the indirectly stimulated gastrocnemius muscle (fast) and soleus muscle (slow) to single twitch and to a train-of-four and tetanic stimulation were studied. The soleus muscle demonstrated a greater degree of fade than the gastrocnemius in response to tetanic stimuli (50 Hz). There was no difference between the responses of the two muscles to twitch or train-of-four stimuli with the alkaloid (cat) (187).

The alkaloid acted as an antagonist of dopamine-induced inhibition of adrenergic neurotransmission in the isolated, perfused ear artery (rabbit) (191).

The alkaloid inhibited the binding of the muscarinic antagonist ^{3}H-labelled quinuclidinyl benzilate to myocardial atria and to ileal longitudinal muscles with $IC5_0$ values of 6.2-8.5 μmol/liter. The alkaloid did not antagonize the effects of the muscarinic antagonist methylfurmethide at concentration of up to 100 μmol/liter. Apparently, at lower concentrations the alkaloid binds to muscarinic receptors in these target organs in such a way that it interferes with the binding of ^{3}H-quinuclidinyl benzilate but not with methylfurmethide (rat) (202).

Injection of the alkaloid in a dosage of 1 μg directly into the hippocampus produced selective damage to dentate granule cells. Larger doses (5-10 μg) induced limbic and motor seizures with damage to hippocampal pyramidal cells. Studies suggest a nicotinic mechanism for both actions. These neurotoxic reactions were not elicited on systemic administration of the alkaloid even when the blood-brain barrier was disrupted (rat) (214).

The antagonism to the (+)-tubocurarine-induced neuromuscular blockade by neostigmine and 3,4-diaminopyridine was examined quantitatively in the isolated phrenic nerve-diaphragm preparation in vitro and in lethality of animals in vivo by assaying concentrations of the alkaloid necessary to produce a 70% block of indirect muscle contraction and LD_{50}, respectively. The synergism between neostigmine and 3,4-diaminopyridine, as evidenced from the marked increase of antagonistic efficacy in vitro, is more than expected from the possible interaction of the major pharmacological actions of these agents (mouse) (219).

The use of a chambered, respiratory apparatus based on an "iron-lung" for the study of acute and chronic toxicity of curariform drugs in small animals is described. Blood serum biochemical indices were unchanged after intravenous administration of 120 μg/kg/day and artificial respiration until spontaneous recovery (rat) (21).

A selective action on the slow, ionic channels (association rate constant of 2.8×10^6/M/s) as measured by its effects on the synaptic currents of rat submandibular ganglion cells (rat) (22).

An examination was made of the rates at which the alkaloid associates with and dissociates from the

nicotinic receptor while exerting its classical competitive effect. Apparently, the drug equilibrates very rapidly with the nicotinic receptor (frog) (23).

A measurement was made of the serum protein binding in normal and cirrhotic patients. The fraction bound to serum in the former is 56% with the latter being very similar (human) (25).

TABLE 12.   Names and Synonyms of Bisbenzylisoquinoline Alkaloids Cited In This Review[a]

Antioquine [225] n.a.
Apateline [187] b.s.
Aromoline [31] a.d., r.i.
Atherospermoline [56] syn.

Baluchistanamine [257] n.a.
Berbamine [57] p.c., r.i., tlc
^{3}H-Berbamine [57] syn.
Berbacolorflammine [218] a.d.
6',7-Bis-(O-demethyl)-tetrandrine [76 dvt] (57)

Calafatine [190] a.d.
Calafatine-2α-N-oxide [226] n.a.
Calafatine-2β-N-oxide [227] n.a.
Cepharanthine [34] p.c., r.i., syn., tlc
Cepharanthine (^{14}C-methylenedioxy) [34] syn.
Chenabine [258] n.a.
Cheratamine [228] n.a.
Chillanamine [229] n.a.
Chondrocurine [130] r.i.
(-)-Chondrofoline [131] r.i., a.d.
Cissampareine [145] b.s.
Cocsoline [152] r.i.
Cocsuline [153] r.i., a.d.
Cocsuline-N-2-oxide [231] n.a.
Colorflammine [219] a.d.
Curacautine [259] n.a.
Curine [133] p.c., tlc, r.i., a.d.
Curine dimethiodide [133 dvt] p.c.
Cycleanine [121] p.c., r.i., tlc
Cycleanine dimethobromide [121 dvt] p.c.
Cycleanine N-oxide [232] n.a.
Cycleanorine [60] tlc

Daphanandrine [37] a.d.
Daphnoline [38] a.d., r.i.
Dauricine [3] p.c., r.i., tlc, hplc
Dauricinoline [4] tlc, hplc
Daurisoline [192] r.i.
1,2-Dehydroapateline [193] r.i.
Dehydrotelobine [194] r.i.
7-O-Demethylisothalicberine [195] r.i.
6',7-Bis-(O-demethyl)-tetrandrine [76 dvt] syn.
6,7,12-Tris-(O-demethyl)-tetrandrine [76 dvt] syn.
Tetrakis-O-demethyl-tetrandrine [76 dvt] syn.
5-O-Demethylthalistyline [17a] r.i.
N-Desmethylcycleanine [233] n.a.
N-Desmethylthalistyline [16] r.i.
Dihydrosecocepharanthine [260] n.a.
0,0-Dimethylcurine [135] r.i.
N,N'-Dimethylcurine diiodide [133 dvt] p.c.
Dimethylcurine Methochloride [135 dvt] p.c.

N,N'-Dimethylhayatine salts [137 dvt] p.c.
N,N'-Dimethyllindoldhamine [234] n.a.
N,N'-Dimethyltetrandrine diiodide [76 dvt] p.c.
Dimethyltrilobine iodide [163 dvt] p.c.
Dimethyltubocurarine (Metocurine) [142] p.c., anal.

Epistephanine [40 or 41] a.d.
0-Ethyldauricine [3 dvt] (212)

Fangchinoline [61] p.c., syn., tlc, r.i.

Gilgitine [261] n.a.
Grisabine [10] r.i.
Guattegaumerine [234] n.a.

Hayatine [137] p.c.
Hayatine dimetho salts [137 dvt] p.c.
Hernandezine [81] a.d., r.i.
Homoaromoline (Thalrugosamine) [42] p.c., r.i., tlc
Hypoepistephanine [43] a.d.

(+)-Isochondodendrine [122] tlc
(-)-Isochondodendrine [122] r.i.
(+)-Isochondodendrine Hydrochloride [122 dvt] p.c.
Isotetrandrine [62] r.i., syn., p.c., tlc
Isothalicberine [205] r.i.
Isotrilobine [157] r.i., p.c., b.s.

Jhelumine [262] n.a.

Kohatine [236] n.a.
Kurramine [237] n.a.

Limacine [64] r.i., a.d.
Lindoldhamine [11] r.i.

Magnolamine [15] r.i., a.d., syn.
Magnoline [12] r.i.
Malekulatine [238] n.a.
N-Methylapateline [207] r.i.
0-Methylcocsoline [239] n.a.
7'-0-Methylcuspidaline [240] n.a.
0-Methyldaphnandrine [37 dvt] a.d.
0-Methyldauricine [12a] syn.
0-Methyldeoxopunjabine [263] n.a.
0-Methylthalicberine [95] r.i.
7-0-Methyllindoldhamine [241] n.a.
7'-0-Methyllindoldhamine [242] n.a.
N-Methylpachygonamine [243] n.a.
0-Methylpunjabine [264] n.a.
0-Methylrepandine [45] a.d.
2-N-Methyltetrandrine [76 dvt] syn.
2'-N-Methyltetrandrine [76 dvt] syn.

O-Methylthalibrine [**209**] r.i.
O-Methylthalicberine [**95**] r.i.
O-Methylthalmine [**244**] (188)
N-Methyltubocurarine [**142** dvt] p.c.
Micranthine [**159**] b.s.

Norberbamine [**68**] r.i.
Nor-N_b-Chondrocurine [**230**] n.a.
(+)-Norcycleanine [**124**] r.i.
(-)-Norcycleanine [**125**] r.i.
2-Norlimacusine [**245**] n.a.
N-2-Norobaberine [**46** dvt] a.d.
Norpenduline [**246**] n.a.
Nortiliacorinine A [**116**] r.i., b.s.
Nortrilobine [**247**] n.a.

Obaberine [**46**] r.i., syn.
Obamegine [**71**] r.i., a.d., p.c.
Osornine [**248**] n.a.
Oxyacanthine [**48**] r.i.

Pachygonamine [**249**] n.a.
Pachyovatamine [**250**] n.a.
Panurensine [**110**] a.d.
Penduline [**72**] syn., r.i., a.d.
Phaeantharine [**73**] r.s., p.c., syn.
Punjabine [**265**] n.a.

Repanduline [**168**] b.s., a.d.
Revolutinone [**266**] n.a.

Secantioquine [**267**] n.a.
Secocepharanthine [**268**] n.a.
Seco-obaberine [**269**] n.a.
Sindamine [**270**] n.a.
Stebisimine [**51**] syn., r.i.

Talcamine [**271**] n.a.
Temuconine [**251**] n.a.
Tetrandrine [**76**] p.c., tlc, a.d., r.i.
Tetrandrine dimethiodide [**76** dvt] p.c.
Tetrakis-O-demethyltetrandrine [**76** dvt] syn.
Tetrandrine-2'-N-α-oxide [**76** dvt] syn.

Tetrandrine-2'-N-β-oxide [**76** dvt] syn.
Tetrandrine-2-N-β-oxide-2'-N-α-oxide
    [**76** dvt] syn.
Tetrandrine-2-N-β-oxide-2'-N-β-oxide
    [**76** dvt] syn.
Thalabadensine [**106a**] r.i.
Thalfine [**102**] r.i.
Thalfinine [**103**] r.i.
Thalfoetidine [**99**] r.i.
Thalibrunimine [**112**] a.d.
Thalibrunine [**113**] a.d.
Thalicberine [**97**] r.i.
Thalictine [**107**] r.i.
Thalidasine [**100**] r.i., p.c.
Thaligrisine [**252**] n.a.
Thaliphylline [**253**] n.a.
Thalirabine (5-O-demethylthalistyline)
    [**17a**] r.i.
Thalirugine [**14b**] r.i.
Thalisopine (Thaligosine) [**54**] r.i.
Thalistyline [**18**] p.c.
Thalmethine [**98**] r.i.
Thalmine [**108**] r.i.
Thalrugosaminine [**55**] r.i.
Thalrugosidine [**101**] r.i., p.c.
Thalrugosine [**79**] r.i.
Tiliacorine [**118**] r.i., b.s.
Tiliacorinine [**119**] r.i.
Tiliacorinine-2'-N-oxide [**254**] n.a.
Tiliamosine [**120**] r.i., a.d.
Tricordatine [**161**] r.i.
Trilobine [**163**] r.i.
Trilobine dimethiodide [**163** dvt] p.c.
6',7,12-Tris-(O-demethyl)-tetrandrine
    [**76** dvt] syn.
(+)-Tubocurarine chloride
    [**142**] p.c., tlc, r.i., anal.
(+)-Tubocurine [**130**] p.c.

Vanuatine [**255**] n.a.
Vateamine [**256**] n.a.

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[a]a.d.=additional work; b.s.=biosynthesis; n.a.=new alkaloid; p.c.=pharmacology; r.i.=reiso-lated; r.s.=revised structure; s.s.=semisynthetic; dvt.=derivative (meaning a derivative of an alkaloid with the preceding number).

TABLE 13.   Alkaloids Synthesized

Atherospermoline [**56**] (57)
[3]H-Berbamine [**57**] (106)
6',7-Bis-(O-demethyl)-tetrandrine [**76** dvt] (57)
Cepharanthine [**34**] (79)
Cepharanthine (^{14}C-methylenedioxy) [**34**] (61)
O-Ethyldauricine [**3** dvt] (212)
Fangchinoline [**61**] (57)
Isotetrandrine [**62**] (42, 51, 206, 207)
Magnolamine [**15**] (9)
O-Methyldauricine [**12a**] (49)
2-N-Methyltetrandrine [**76** dvt] (154)
2'-N-Methyltetrandrine [**76** dvt] (154)
Obaberine [**46**] (42, 51, 206, 207)

Phaeantharine [**73**] (105,143)
Penduline [**72**] (57)
Stebisimine [**51**] (42, 51, 206, 207)
Tetrakis-O-demethyl-tetrandrine [**76** dvt] (57)
Tetrandrine-2'-N-α-oxide [**76** dvt] (157)
Tetrandrine-2'-N-β-oxide [**76** dvt] (157)
Tetrandrine-2-N-β-oxide-2'-N-α-oxide
    [**76** dvt] (157)
Tetrandrine-2-N-β-oxide-2'-N-β-oxide
    [**76** dvt] (157)
6,7,12-Tris-(O-demethyl)-tetrandrine
    [**76** dvt] (57)

ENZYMIC CONTROL OF STEREOCHEMISTRY AMONG THE THALICTRUM AL-
KALOIDS.—It has long been known that bisbenzylisoquinoline alkaloids are biosyn-
thesized via an in vivo condensation of two tetrahydrobenzylisoquinoline monomers
through phenolic oxidative coupling. This coupling may initially occur in a tail-to-tail
fashion (benzyl group linking to benzyl group) or a head-to-tail fashion (isoquinoline
group linking to a benzyl group) and be subsequently followed by a second and/or third
oxidative coupling, thus producing numerous alkaloids with different permutations in
oxidative linkage. Guinaudeau *et al.* have recently considered the general pathway for
the biogenesis of the bisbenzylisoquinolines of *Thalictrum minus* L. *microphyllum* Boiss.
and, perhaps more importantly, proposed four rules that appear to govern the forma-
tion of these alkaloids in *Thalictrum* species (180). In *T. minus* L. var. *microphyllum*
Boiss., thaligrisine [252] is the obvious precursor to obamegine [71], aromoline [31],
and homoaromoline [42] while thalirugine [14b] is the likely precursor of thalisopine
(thaligosine) [54]. Phenolic analogs of thalirugine [14b] lacking the C-5' hydroxyl
group are the possible precursors of thaliphylline [253], O-methylthalicberine [95],
and thalicberine [97]. In considering the *Thalictrum* bisbenzylisoquinolines as a group,
these alkaloids were first uniformly drawn with their two lower aromatic rings (tail por-
tions) in a position such that the phenolic hydroxyl or methoxy group in ring C at C-12
would be in the lower left ring, which then fixed the termini of the diphenyl ether
bridge at C-11 and C-12'. The following four rules were proposed to govern the forma-
tion of the *Thalictrum* bisbenzylisoquinolines:

1. The dimers may belong to any of seven different structural subgroups repre-
    sented by general formulas A to G (Table 14).
2. When a benzylisoquinoline moiety is oxygenated at C-5 or C-5', it has the S
    configuration.
3. The right hand benzylisoquinoline moiety incorporates the S configuration at
    C-1'.
4. The left hand benzylisoquinoline moiety has the S configuration at C-1, except
   in subgroups A, B, and C, where it may be R.

As an extension of rules 3 and 4, bisbenzylisoquinolines whose occurrence is re-
stricted to the genus *Thalictrum* or to its chemotaxonomically close relative, the *Hernan-
dia* genus (Hernandiaceae), possess the *1S, 1'S* configuration. However, *Thalictrum* bis-
benzylisoquinolines of *1R, 1'S* configuration are also found in other botanical families
and include some fairly common alkaloids (e.g., isotetrandrine [62], obaberine [46],
oxyacanthine [48]) of this type. It was also noted that when an imine function (either as
a single -C=N-bond or as part of an isoquinoline system) was present in a *Thalictrum*
bisbenzylisoquinoline, the imine was found on the right side of the dimer while the left
side was of the S configuration.

The following alkaloids are those with imine functions: subgroup B: (+)-thal-
simine [86], (+)-thalsimidine [85], (+)-thalibrunimine [112], (−)-dihydrothalic-
trinine [198], (−)-thalictrinine [99], (−)-oxothalibrunimine [215], and (−)-O-
methylthalibrunimine [210]; subgroup D: (+)-thalmethine [98] and (+)-O-methyl-
thalmethine [96]; and subgroup G: (+)-thalfine (thalphine) [102]. It was via a consid-
eration of these proposed rules that the structures of thalrugosamine [52] and (+)-
thalisamine [84] were revised (180). (−)-Isothalidezine [82] was cited out of 58 al-
kaloids as the sole exception to the rule that the right hand benzylisoquinoline moiety
of the dimer is characterized by the S configuration at C-1'. It was postulated that
isothalidezine [82] might be formed from thalidezine [83] via oxidation at C-1 to form
an iminium cation, followed by enzymatic reduction of the iminium bond from the
beta side of the dimer. The postulation may have credence because of the relative

amounts of (+)-thalidezine [83] (1.79 g) and (−)-isothalidezine [82] (92 mg) from 7 kg of powdered *Thalictrum podocarpum* Humb. roots (180).

TABLE 14.   Bisbenzylisoquinoline Alkaloidal Subgroups (180)
(R Substituents May Be H, OH, or OCH₃)

Subgroup A
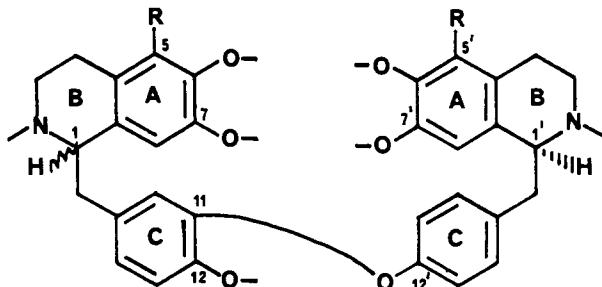
1R, 1′S: (+)-Thaligrisine [252]

1S, 1′S: (+)-*O*-Methylthalibrine [209], (+)-*N*-Methylthalistyline [17],
(+)-Neothalibrine [211], (+)-Northalibrine [13],
(+)-Thalibrine [14], (+)-Thalirabine [17a],
(+)-Thaliracebine [14a], (+)-Thalirugidine [17b],
(+)-Thalirugine [14b], (+)-Thaliruginine [14c],
(+)-Thalistine [221], (+)-Thalistyline [18]

Subgroup B
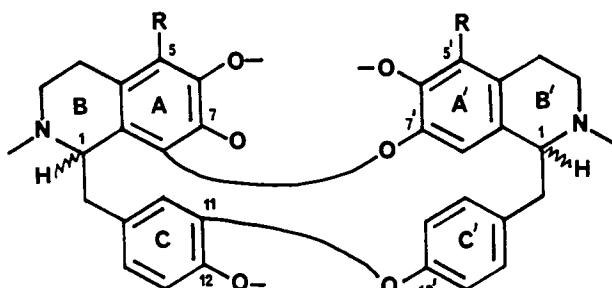
1R, 1′S: (+)-Berbamine [57], (+)-Isotetrandrine [62], (+)-Obamegine [71],
(+)-Thalrugosine [79]

1S, 1′S: (+)-*N*-Desmethylthalidezine [80], (+)-Hernandezine [81],
(+)-Hernandezine-*N*-oxide [203], (+)-*N*′-Norhernandezine [212],
(+)-*N*′-Northalibrunine [214], (+)-Thalibrunine [113],
(+)-Thalidezine [83]

1S, 1′R: (−)-Isothalidezine [82]

Subgroup C
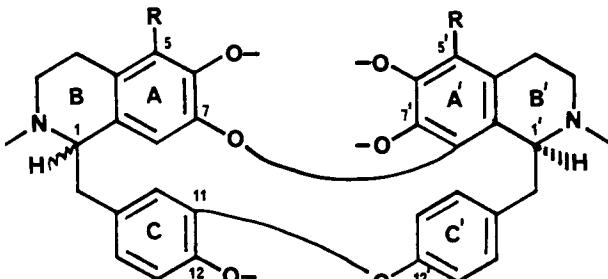
1R, 1'S: (+)-Aromoline [31], (+)-Homoaromoline [42], (+)-Obaberine [46],
           (+)-Oxyacanthine [48]

1S, 1'S: (−)-Thalisopidine [53], (−)-Thalisopine (54),
           (−)-Thaligosine [52a], (−)-Thalrugosaminine [55]

Subgroup D
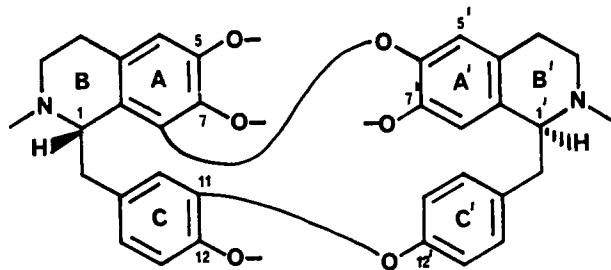
1S, 1'S: (+)-O-Methylthalicberine [95], (+)-Thalicberine [97],
   (+)-Thaliphylline [253]

Subgroup E
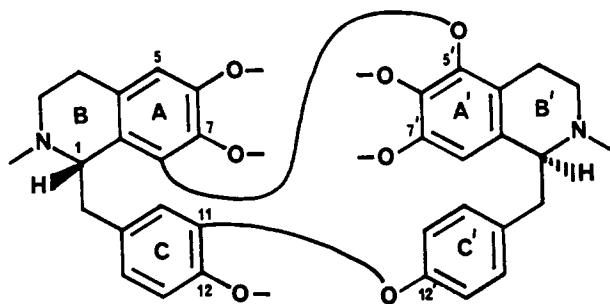
1S, 1'S: (−)-N-Desmethylthalidasine [196], (−)-N-Desmethylthalrugosidine [197],
           (−)-Thalfoetidine [99], (−)-Thalidasine [100],
           (−)-Thaligosidine [100a],, (−)-Thalpindione [223],
           (−)-Thalrugosidine [101], (−)-Thalrugosinone [224]

Subgroup F
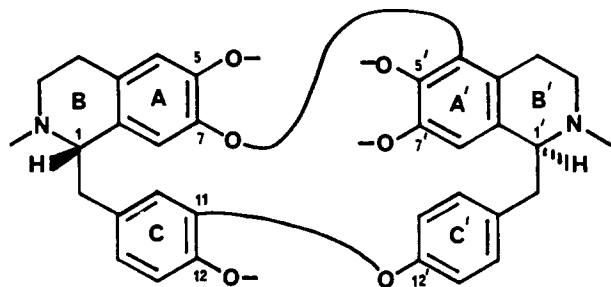
1S, 1'S: (−)-Thalabadensine [106a], (−)-Thalictine [107], (−)-Thalmine [108]

Subgroup G
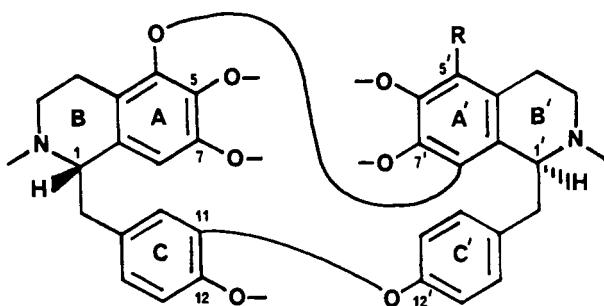
1*S*, 1'*S*:   (+)-Thalfinine [**103**], (+)-Thalmirabine [**222**]

THIN-LAYER CHROMATOGRAPHY.—Tubocurarine chloride [**142**] and other components of curare resin (found as impurities in purified tubocurarine) were evaluated by tlc on precoated Si gel 60F-254 plates in an unlined tank at ambient temperature. The developing solvent was the lower phase of a mixture of equal volumes of $CHCl_3$, MeOH, and 12.5% (w/v) aqueous Cl_3CCOOH while detection was via spraying with either 0.1M $K_3Fe(CN)_6$ + 0.1M $FeCl_3$ (1:1) or Dragendorff's reagent (43).

Fangchinoline [**61**] was detected in both oral and parenteral dosage forms of tetrandrine [**76**] by chromatography over Si gel G using cyclohexane-$CHCl_3$-Et_2NH (5:4:1) as a developing solvent and iodoplatinic acid as a spray reagent. The range of contamination was from about 4-8% (75).

Isochondodendrine [**122**], curine [**133**], berbamine [**57**], fangchinoline [**61**], homoaromoline [**42**], cycleanine [**121**], isotetrandrine [**62**], tetrandrine [**76**], and cepharanthine [**34**] were chromatographed on Si gel G using xylene-isopropyl ether-Me_2CO-MeOH (2:7:0.5) [note that only three members are presented] and visualized with modified Dragendorff's reagent + Wagner's reagent (1:1). Densitometry was subsequently used in quantitation (116).

Homoaromoline [**42**], isotetrandrine [**62**], berbamine [**57**], tetrandrine [**76**], fangchinoline [**61**], isochondodendrine [**122**], curine [**133**], cycleanine [**121**], and cycleanorine [**60**] were detected in the roots or stems of *Cyclea densiflora, C. hypoglauca, C. migoana, C. racemosa, C. polypetala,* and *C. hainanensis* by tlc (126).

Extraction of the powdered root of *Stephania tetrandra* with Et_2O-$CHCl_3$-EtOH-NH_4OH (10%) (25:8:2.5:1) afforded an extract which was dissolved, diluted with EtOH, and spectrophotometrically analyzed at 280 nm for the determination of total alkaloids. Tetrandrine [**76**] was determined by chromatography on a Si gel GF_{254} plate, elution with MeOH or EtOH, and spectrophotometric determination at 282 nm. The root of this plant from different locations in China contained 2.45-4.80% of total alkaloids and 0.70-1.54% tetrandrine [**76**] (189).

Extracts of the rhizome of *Menispermum dauricum* DC. were prepared and formulated into injections. Chromatography of an injection sample on a Si gel G plate using $CHCl_3$-EtOH-NH_4OH (80:1:5) as eluent was followed by dual-wavelength densitometry. The amounts of dauricine [**3**] and dauricinoline [**4**] in the injections were close to those in the total alkaloids of the extract (208). Of the 18 spots that were detected, 8 were alkaloids (213).

The content of tetrandrine [**76**] in the dried root of *Stephania tetrandra* was measured. A $CHCl_3$ extract of the dried, powdered root was evaporated, redissolved in anhydrous EtOH, and placed on a Si gel G tlc plate. The plate was developed with $CHCl_3$-Me_2CO-MeOH-NH_4OH (25%) (80:12:8:0.4) and the alkaloid eluted from

the plate with MeOH. The eluate was evaporated, dissolved in 0.1N HCl, and spectrophotometrically analyzed at 280 nm. The content ranged from 0.66%-1.25% with a relative standard deviation of 1.16% (217).

MISCELLANEOUS.—A review was made of the history of curare research discussing geobotanical and ethnographical aspects, the chemistry of the alkaloids of the Menispermaceae, the physiological effects of the alkaloids, and recent results of the chemistry of Yanoa curare plus Ticuna curare (69).

Tubocurarine chloride [142] was analyzed spectrophotometrically via a color reaction with O-hydroxyhydroquinonephthalein+Zr^{+4}+F^- and measurement of absorbance at 515 nm. The same results were obtained when Hf^{+4}, Fe^{+3}, Mo^{+6}, Cu^{+2}, Sb^{+3}, and Sn^{+4} were used instead of Zr^{+4}, but oxalate interfered. The absorbance was maximum and constant at pH2-2.7, with a maximum value noted after 15 min and constant for 2 h. The method could be applied for analysis of the drug at concentrations of 0.150 g/10 ml (133).

Cepharanthine [34], tetrandrine [76], isotetrandrine [62], cycleanine [121], homoaromoline [42], berbamine [57], and (-)-curine [133] were quantitatively determined in extracts of the roots or bulbs of Stephania delavayi, S. japonica, S. longa, S. tetrandra, S. excentrica, S. cepharantha, S. epigaea, S. brackyandra, S. sinica, S. dielsiana, S. yunnanensis, S. succifera, S. hainanensis, S. mashanica, S. micrantha, S. dicentrinifera, S. kwangsiensis, and S. viridiflavens (127).

An hplc method for the determination of (+)-tubocurarine chloride [142] or metocurine iodide (dimethyltubocurarine) in human plasma using MeCN-H_2O-dibutylamine phosphate as the mobile phase was developed. The alkaloids were extracted from plasma using Bond-Elut 100 mg C_{18} solid phase extraction columns and eluted with mobile phase. The samples were allowed to dry, reconstituted with mobile phase, and injected into the hplc (uv detection at 204 nm). This method was used to study the pharmacokinetics of these drugs in two patients (149).

A review of the bisbenzylisoquinoline alkaloids of Cyclea barbata (Menispermaceae) appeared in 1984. The use of the plant as a folk medicine and the biological effects were also discussed (171).

Hplc analysis was performed on an injection prepared from an extract of the rhizomes of Menispermum dauricum DC. A 6.0μl sample was analyzed for dauricine [3] and dauricinoline [4] by reversed-phase ion-pair hplc using Si gel G as a stationary phase and $CHCl_3$-MeOH-NH_4OH (100:5:0.35) as mobile phase (208). Eight fractions were separated, but these two alkaloids were predominant (213).

An improved method was reported for the estimation of the zwitterion constants of phenolic amines, including (+)-tubocurarine [142], which involves the exploratory least-squares fit of absorbance to pH, starting with estimates of pK and pK_2 obtained electrometrically. In 0.1M NaCl, estimates of pK_1, pK_2, and pK_3 were 7.6, 8.65, and 9.65, respectively, at 25° and 7.4, 8.6, and 9.7, respectively, at 37°. Ionization of the C-13 phenolic group probably occurs first with the phenolate form stabilized by hydration and by the protonated nitrogen atom (31).

There are two papers eloquently addressing the evolutionary pattern and chemosystematics of the Thalictrum alkaloids (29,30). The first paper discusses the chemosystematics of the Thalictrum minus L. complex (29) that is widely distributed in Europe, the Caucasus, Siberia, and southwestern Asia and is characterized by cytologic as well as morphologic variability. This paper lists the alkaloids found in Thalictrum species via their chemical nuclei and also cross-references particular alkaloids and alkaloid-types via section and subsection. Finally, it lists the alkaloids of the Thalictrum minus complex and their habitat and presents some correlations between the alkaloid pattern of the T. minus complex and the genus as a whole. The evolutionary pattern of the complex is evi-

dently connected with adaptive irradiation, hybridization, and polyploidy. Hexaploids are of the most frequent occurrence with decaploids also being quite common. Diploids and dodecaploids occur far less frequently. The biogenesis of alkaloids in hexaploids frequently extends to the bisbenzylisoquinolines while in decaploids the aporphine-benzylisoquinoline dimers prevail. These differences may be due to different genomes and to the involvement of different putative parents in the process of hybridization and polyploidization (29). The second paper contains a table showing the chromosome numbers and alkaloid content in 17 species of *Thalictrum* (30). In all of these species, quaternary protoberberine salts (primarily berberine) and/or aporphines were isolated. Furthermore, aporphine-benzylisoquinoline and bisbenzylisoquinoline dimeric alkaloids are common to most of these species. On the other hand, benzylisoquinoline monomeric alkaloids occur only infrequently, lending credence to the propensity of these bases to dimerization. Aporphines that are present are postulated to be so because of certain structural features that are not conducive to dimerization. Isoquinolones are believed to result from oxidation of a parent monomer or dimer. Polyploid species of *Thalictrum* are generally richer in both monomeric and dimer alkaloids than diploid species, while within the diploids, protoberberines prevail (30).

ACKNOWLEDGMENTS

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