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J. Nat. Prod., **1991**, 54 (3), 645-749• DOI:
10.1021/np50075a001 • Publication Date (Web): 01 July 2004

Journal of Natural Products
Vol. 54, No. 3, pp. 645-749, May-Jun 1991

BISBENZYLISOQUINOLINE ALKALOIDS

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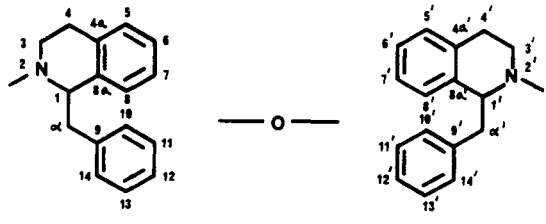
ABSTRACT.—The bisbenzylisoquinoline alkaloids constitute a series of almost 400 phenylalanine-derived metabolites with a rich and varied chemistry and pharmacology. This tabular review encompasses the literature from 1986 through 1989 and describes the botanical sources, physicochemical and spectral data, and pharmacological activities for the approximately 122 new alkaloids that have been isolated in this time period. Furthermore, additional physicochemical and spectral data for previously isolated bisbenzylisoquinoline alkaloids, as well as their botanical sources and pharmacological activities, are presented. Finally, various procedures useful in the isolation, separation, and quantitation of these alkaloids, as well as their biosynthesis and synthesis, are also cited.

The first comprehensive tabular review of the bisbenzylisoquinoline alkaloids was published by Guha *et al.* in this journal in early 1979 (1). This was followed by second review published in 1983 (2) and then a third review published in 1987 (3). These reviews described the literature from 1978 through 1981, and from 1982 through 1985, respectively.

The present review is concerned with the literature from 1986 through 1989 (*Chemical Abstracts* volumes 104 through 111) and is presented principally in a tabular form as before (1–3). The numbers of the alkaloids and the structural-type nomenclature have been retained according to the previous reviews (1–3) in order to preserve a sense of literary consistency. Since the publication of the last tabular review of 1987 (3), approximately 122 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, as well as the inclusion of secobisbenzylisoquinoline alkaloids, has likewise continued. This number of 122 new alkaloids is almost one and one-half times the amount of alkaloids isolated and characterized (approximately 85) in a time period that was twice as long (1978 through 1985). One can attribute this intensified activity to one or more of the following: first, the routine utilization of high resolution ^{1}H nmr, ^{13}C nmr, and ms, with particular emphasis on magnetic resonance nOe enhancement techniques; second, the routine characterization of extremely small amounts of alkaloids which are frequently isolated as pure, amorphous residues; third, the increasing emphasis and subsequent discovery of unique and interesting pharmacological properties of these alkaloids; and fourth, the cumulative knowledge amassed through one or more decades of experience by highly motivated and productive scientists from a handful of laboratories around the world.

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 mass spectra. The numbering of the skeleton and the systematic numerical classification describing oxygenation and dimerization patterns of the alkaloids follow (almost without exception) the convention established by Shamma and Moniot (4) as exemplified by:

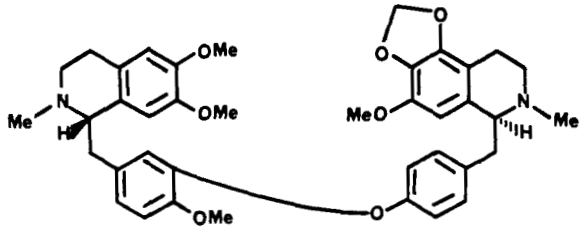


Unless otherwise stated, the uv spectra (nm, log ϵ), and the cd spectra were obtained in MeOH, the ir spectra (cm^{-1}) in $CHCl_3$, and both the ^{1}H-nmr and ^{13}C-nmr spectra in $CDCl_3$. Chemical shifts are in δ units and coupling constants in Hz.

TABLE 1. *Revised Structures of Previously Reported Bisbenzylisoquinoline Alkaloids.*

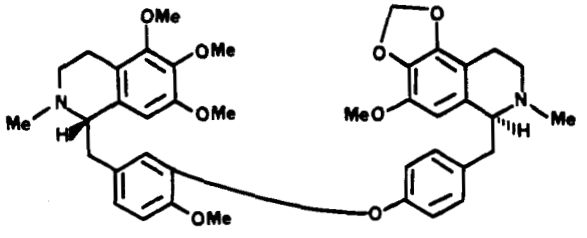
14a THALIRACEBINE[a] $C_{39}H_{44}O_7N_2$: 652.3149

Type Ia (*S,S*) 6,7,11*,12-5,6,7,12*



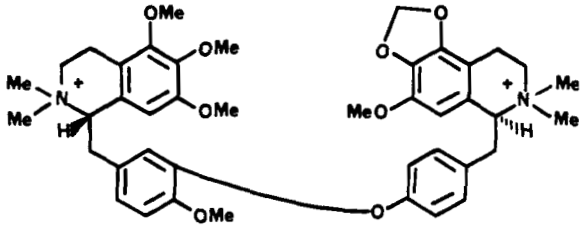
16 *N*-DESMETHYLTHALISTYLINE[a] $C_{40}H_{46}O_8N_2$: 682.3254

Type III (*S,S*) 5,6,7,11*,12-5,6,7,12*



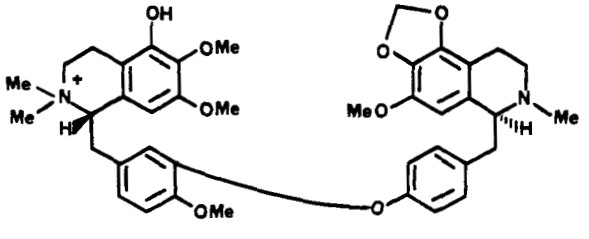
17 *N*-METHYLTHALISTYLINE[a] $C_{42}H_{52}O_8N_2$: 712.3724

Type III (*S,S*) 5,6,7,11*,12-5,6,7,12*



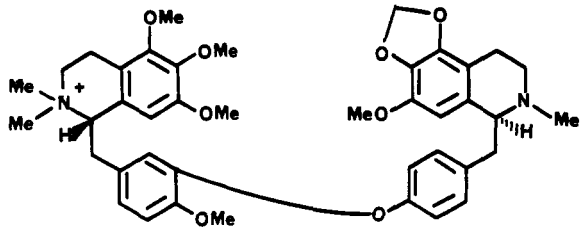
17a THALIRABINE[a] $C_{40}H_{47}O_8N_2$: 683.3332

Type III (*S,S*) 5,6,7,11*,12-5,6,7,12*



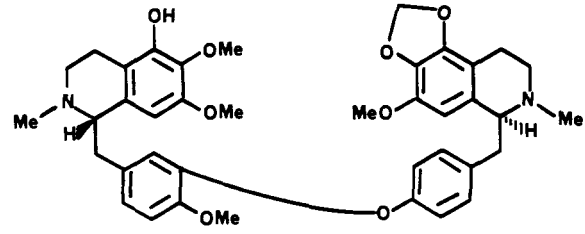
18 THALISTYLINE[a] $C_{41}H_{49}O_8N_2$: 697.3489

Type III (*S,S*) 5,6,7,11*,12-5,6,7,12*



221 THALISTINE[a] $C_{39}H_{44}O_8N_2$: 668.3098

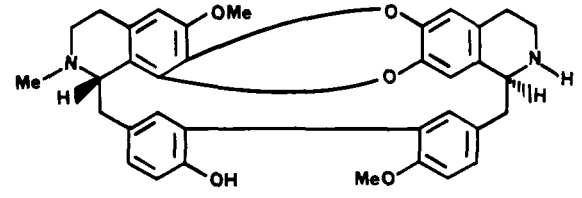
Type III (*S,S*) 5,6,7,11*,12-5,6,7,12*



[a]The structure of the isoquinolone alkaloid thalflavine, originally proposed as 1-oxo-2-methyl-5-methoxy-6,7-methylenedioxy-1,2,3,4-tetrahydroisoquinoline (isoquinolone A), was revised to 1-oxo-2-methyl-5,6-methylenedioxy-7-methoxy-1,2,3,4-tetrahydroisoquinoline (isoquinolone B), on the basis of synthesis (481). Because the structures of compounds **14a**, **16**, **17**, **17a**, **18**, and **221** were assigned (1) principally on the basis of the identification of their oxidation product, which was then identified as isoquinolone A (5-methoxy-6,7-methylenedioxy substitution) but has now been identified as isoquinolone B (5,6-methylenedioxy-7-methoxy substitution), the structures of these compounds must be revised accordingly.

185 TILIARINE $C_{35}H_{34}O_5N_2$: 562.2468

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



UV: 235 sh (4.77), 289 (4.15) (66)

^{1}H NMR: NMe 2.36; OMe 3.88 (C-6), 3.93 (C-12'); AlH 2.81 (m, 2H, C-α), 3.76 (m, 1H; H-1), 3.97 (m, 1H, H-1'); ArH 6.33 (H-5), 6.70 (H-5'), 6.98 (d, 1H, J = 8 Hz, H-13), 7.02 (d, 1H, J = 8 Hz, H-13'), 7.33 (dd, 1H, J = 2, 8 Hz, H-14), 7.49 (dd, 1H, J = 2, 8 Hz, H-14'), 7.54 (d, 1H, J = 2 Hz, H-10), 7.74 (d, 1H, J = 2 Hz, H-10') (nOe used) (66)

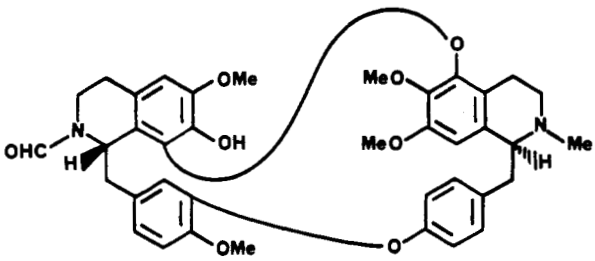
MS: $[M]^+$ 562 (74), 561 (81), 349 (27), 336 (30), 335 (100), 321 (27), 168 (18) (66)

CD: 0 (262), −8.2 (248), 0 (244), +10.4 (237), 0 (233), negative tail (66)

Sources: *Tiliacora racemosa* Colebr. (Menispermaceae) (66)

223 THALPINDIONE $C_{37}H_{36}O_9N_2$: 652.2421

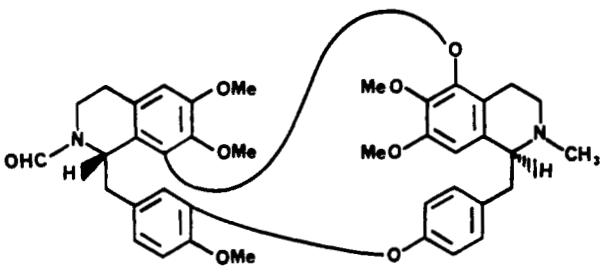
Type XII (*S,S*) 6,7,8*,11$^+$,12-5*,6,7,12$^+$



Inasmuch as *O*-methylation (CH_2N_2) of (−)-thalpindione afforded (−)-thalrugosinone, and (−)-thalrugosinone has been reassigned as **224** (12), it follows that (−)-thalpindione must be reassigned as **223** (12).

224 THALRUGOSINONE $C_{39}H_{42}O_8N_2$: 666.2941

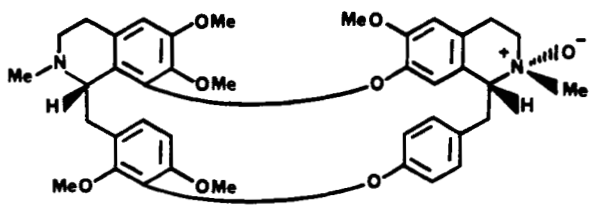
Type XII (*S,S*) 6,7,8*,11$^+$,12-5*,6,7,12$^+$



TLC: 0.43 [Si gel; C_6H_6-MeOH-NH_4OH (95:5:trace)] (12)
$[\alpha]^{22}D$: −42° (c = 0.30, MeOH) (12)
UV: 241 sh (4.34), 280 (3.62) (12)
IR: 1660(12)
^1H NMR: NMe 2.65; NCHO 7.50; OMe 3.34 (C-7), 3.47 (C-6′), 3.78 (C-6), 3.88 (C-7′), 3.90 (C-12); AlH 2.62 (m, 1H, H-α), 2.72 (m, 1H, H-α′), 3.20 (m, 1H, H-α), 3.24 (m, 1H, H-3), 3.28 (m, 1H, H-β), 3.88 (m, 1H, H-1′), 4.48 (m, 1H, H-1), 4.61 (m, 1H, H-3); ArH 6.12 (d, 1H, J = 1.9 Hz, H-10), 6.36 (H-5), 6.42 (dd, 1H, J = 2.2, 8.3 Hz, H-10′), 6.47 (H-8′), 6.52 (dd, 1H, J = 1.9, 8.2 Hz, H-14), 6.58 (dd, 1H, J = 2.2, 8.3 Hz, H-11′), 6.78 (d, 1H, J = 8.2 Hz, H-13), 6.99 (dd, 1H, J = 2.2, 8.3 Hz, H-13′), 7.62 (dd, 1H, J = 2.2, 8.3 Hz, H-14′) (nOe used) (12)
^{13}C NMR: 161.4 (amidic carbonyl) (12)
MS: $[M]^+$ 666.2882 (74), 665.2821, 651 (54), 635 (100), 439.1862 (72), 425.1704 (18), 411.1896 (32), 409 (36), 211.0762, 204 (49), 190 (30) (12)
CD: 0 (300), −3.9 (282), 0 (270), −0.2 (255), 0 (252), +11.8 (239), negative tail below 230 (12)
Sources: *Thalictrum cultratum* Wall. (Ranunculaceae) (12)
Derivatives: Thalidasine [**100**] (thalrugosinone + $LiAlH_4/Et_2O$) (tlc, ^1H nmr) (12)
2-Northalidasine (thalrugosinone + HCl + Heat) (tlc, ^1H nmr) (12)

226 CALAFATINE-2′α-*N*-OXIDE $C_{39}H_{44}O_8N_2$: 668.3098

Type Xa (*S,R*) 6,7,8*,10,11$^+$,12-6,7*,12



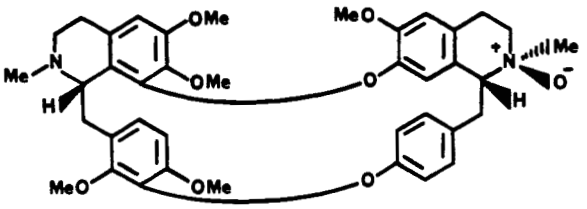
^1H NMR: NMe 2.33 (N-2), 3.40 (N-2′); OMe 3.36 (C-7), 3.75 (C-6), 3.77 (C-6′), 3.74 (C-10), 3.86 (C-12); AlH 2.41 (m, 1H, H-4), 2.53 (m, 1H, H-α′), 2.55 (m, 1H, H-α), 2.78 (m, 1H, H-3), 2.83 (m, 1H, H-3′), 2.89 (m, 1H, H-4′), 2.92 (m, 1H, H-4), 3.32 (m, 1H, H-3), 3.38 (m, 1H, H-α), 3.45 (m, 1H, H-4′),

3.66 (m, 1H, H-α'), 3.90 (m, 1H, H-3'), 4.10 (m, 1H, H-1), 4.36 (m, 1H, H-1'); ArH 5.47 (H-8'), 5.97 (dd, 1H, J = 2.2, 8.2 Hz, H-14'), 6.36 (H-5), 6.51 (dd, 1H, J = 2.2, 8.2 Hz, H-13'), 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-11'), 7.11 (dd, 1H, J = 2.2, 8.2 Hz, H-10') (nOe used) (482)

The alkaloid described as calafatine-2α-*N*-oxide in the previous review (3) is thus assigned as calafatine-2'α-*N*-oxide on the basis of NOEDS studies (482).

227 CALAFATINE-2'β-*N*-OXIDE $C_{39}H_{44}O_8N_2$: 668.3098

Type Xa (*S*,*R*) 6,7,8*,10,11$^+$,12-6,7*,12



^{1}H NMR: NMe 2.32 (N-2), 3.26 (N-2'); OMe 3.42 (C-7), 3.74 (C-6'), 3.76 (C-6), 3.74 (C-10), 3.86 (C-12); AlH 2.46 (m, 1H, H-4), 2.57 (m, 1H, H-α), 2.70 (m, 1H, H-α'), 2.85 (m, 1H, H-3), 2.94 (m, 1H, H-4), 3.08 (m, 1H, H-3'), 3.15 (m, 1H, H-4'), 3.32 (m, 1H, H-α), 3.40 (m, 1H, H-3), 3.57 (m, 1H, H-4'), 3.98 (m, 1H, H-α'), 4.09 (m, 1H, H-3'), 4.11 (m, 1H, H-1), 4.19 (m, 1H, H-1'); ArH 5.39 (H-8'), 5.89 (dd, 1H, J = 2.2, 8.2 Hz, H-14'), 6.40 (H-5), 6.42 (dd, 1H, J = 2.2, 8.2 Hz, H-13'), 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-11'), 6.93 (d, 1H, J = 8.5 Hz, H-14), 7.17 (dd, 1H, J = 2.2, 8.2 Hz, H-10') (nOe used) (482)

The alkaloid described as calafatine-2β-*N*-oxide in the previous review (3) is thus assigned as calafatine-2'β-*N*-oxide on the basis of NOEDS studies (482).

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

11 LINDOLDHAMINE $C_{34}H_{36}O_6N_2$: 568.2573

^{1}H NMR: OMe 3.85 (C-6 or C-6'), 3.86 (C-6' or C-6); AlH 4.05 (dd, 1H, H-1), 4.15 (dd, 1H, H-1'); ArH 6.51 (s, H-5), 6.58 (s, H-5'), 6.66 (d, 1H, H-10), 6.69 (s, 2H, H-8 and H-8'), 6.87 (d, 2H, H-11' and H-13'), 6.89 (d, 1H, H-13), 6.91 (dd, 1H, H-14), 7.17 (d, 2H, H-10' and H-14') (36)

12a *O*-METHYLDAURICINE $C_{39}H_{46}O_6N_2$: 638.3356

^{13}C NMR: 64.1 (C-1 or C-1'), 46.2 (C-3), 24.9 (C-4), 125.6 (C-4a), 110.7 (C-5), 146.7 (C-6), 146.7 (C-7), 110.7 (C-8), 128.4 (C-8a), 39.5 (C-α or C-α'), 132.3 (C-9), 116.0 (C-10), 143.8 (C-11), 149.1 (C-12), 116.0 (C-13), 125.6 (C-14), 64.2 (C-1' or C-1), 46.4 (C-3'), 24.9 (C-4'), 125.2 (C-4'a), 110.4 (C-5'), 145.8 (C-6'), 145.8 (C-7'), 110.4 (C-8'), 128.5 (C-8'a), 39.7 (C-α' or C-α), 133.1 (C-9'), 130.2 (C-10'), 112.0 (C-11'), 155.8 (C-12'), 122.0 (C-13'), 130.2 (C-14'), 42.0 (2-NMe and 2'-NMe), 55.0 (2 × OMe), 55.1 (2 × OMe), 55.4 (1 × OMe) (30)

20 FUNIFERINE $C_{38}H_{42}O_6N_2$: 622.3043

$[\alpha]_D$: +104° (c = 0.15, $CHCl_3$) (51)

UV: 228 (sh) (4.39), 285 (3.85) (51)

^{1}H NMR: NMe 2.41 (N-2), 2.68 (N-2'); OMe 3.40 (C-7), 3.51 (C-6'), 3.82 (C-6), 3.91 (C-12'); AlH 3.75 (H-1'), 4.06 (H-1); ArH 6.37 (H-5), 6.48 (H-5'), 6.68 (H-10'), 6.86 (H-13'), 6.88 (H-13), 6.89 (H-10), 7.09 (H-8'), 7.22 (H-14'), 7.33 (H-14) (51)

MS: $[M]^+$ 622 (87), 621 (73), 396 (30), 395 (100), 381 (41), 198 (87), 174 (50) (51)

CD: 0 (310), +1.02 (280), +2.9 (245), 0 (233), −2.9 (221) (51)

27 TILIAGEINE $C_{37}H_{40}O_6N_2$: 608.2886

MP: 270° (61)

TLC: 0.43 [Si gel 60 F_{254}; CH_2Cl_2-MeOH-NH_4OH (90:9:1)] (61)

$[\alpha]^{20}_D$: +179° (c = 1.2, $CHCl_3$) (61)

UV: 209 (4.88), 284 (4.18) (61)

IR: 3400, 2940, 2830, 1630, 1590, 1500, 1440, 1380, 1275, 1240, 1120, 1020, 880, 815 (61)

^{1}H NMR: ArH 6.35 (H-5), 6.39 (H-5'), 6.75 (d, 1H, J = 2.25 Hz, H-10), 6.80 (d, 1H, J = 8.25 Hz, H-13'), 6.81 (d, 1H, J = 8.3 Hz, H-13), 6.88 (d, 1H, J = 2.25 Hz, H-10'), 7.04 (H-8'), 7.16 (dd, 1H, J = 2.25, 8.25 Hz, H-14'), 7.22 (dd, 1H, J = 2.25, 8.25 Hz, H-14) (61); NMe 2.41 (N-2), 2.69 (N-2'); OMe 3.52 (C-6'), 3.86 (C-6), 3.91 (C-12'); AlH 3.79 (H-1'), 4.09 (H-1); ArH 6.37 (H-5), 6.47 (H-5'), 6.72 (H-10'), 6.88 (H-13'), 6.87 (H-13), 6.96 (H-10), 7.00 (H-8'), 7.20 (H-14'), 7.30 (H-14) (51)

MS: $[M]^+$ 608 (97), 607 (71), 593 (10), 577 (10), 382 (31), 381 (100), 367 (26), 365 (28), 351 (14), 205 (10), 192 (33), 191 (49), 175 (5), 174 (20) (61)

35 COCLOBINE $C_{37}H_{38}O_6N_2$: 606.2730

$[\alpha]^{20}D$: +130° (c = 1.5, $CHCl_3$) (59)
UV: 230 (4.40), 275 (4.20), 300 (3.80) (59)
^1H NMR: NMe 2.62 (N-2'); OMe 3.17 (C-7'), 3.53 (C-6), 3.80 (C-6'), 3.95 (C-12); ArH 6.43 (H-5'), 6.51 (H-5), 6.71 (dd, 1H, J = 2.2, 8.5 Hz, H-11'), 6.82 (dd, 1H, J = 2.2, 8.1 Hz, H-10'), 6.91 (d, 1H, J = 2.2 Hz, H-13), 7.00 (d, 1H, J = 2.2 Hz, H-10), 7.08 (dd, 1H, J = 2.2, 8 Hz, H-14), 7.11 (dd, 1H, J = 2.2, 8.3 Hz, H-13'), 7.19 (H-8), 7.34 (dd, 1H, J = 2.2, 8.5 Hz, H-14') (59)
MS: $[M]^+$ 606 (70), 605 (100), 591 (11), 575 (8), 499 (23), 379 (4), 303 (12), 280 (4) (59)

39 DEMERARINE $C_{36}H_{38}O_6N_2$: 594.2730

$[\alpha]^{20}D$: −80° (c = 0.25, $CHCl_3$) (59)
^1H NMR: NMe 2.55 (N-2'); OMe 3.04 (C-7'), 3.45 (C-6), 3.77 (C-6'); AlH 3.83 (m, 1H, H-1), 4.20 (m, 1H, H-1'); ArH 6.40 (H-5 or H-5'), 6.41 (H-5' or H-5), 6.56 (H-8), 6.58 (d, 1H, J = 2 Hz, H-10), 6.83 (dd, 2H, J = 1.4, 8 Hz, H-10' and H-11'), 7.02 (d, 1H, J = 2 Hz, H-13), 7.05 (dd, 1H, J = 2, 8 Hz, H-14), 7.22 (d, 1H, H-13'), 7.39 (dd, 1H, J = 1.4, 8 Hz, H-14') (59)
MS: $[M]^+$ 594 (28), 593 (100), 587 (10), 381 (30), 191 (25) (59)

40 (+)-EPISTEPHANINE $C_{37}H_{38}O_6N_2$: 606.2730

MP: Amorphous (49)
$[\alpha]^{25}D$: +220° ($CHCl_3$) (49)
UV(EtOH): 214, 282 (49); (EtOH + OH^-) 218, 281 (49); (EtOH + H^+) 212, 288, 335 (49)
IR: 1462 (49)
^1H NMR: NMe 2.52 (N-2); OMe 3.36 (C-7'), 3.86 (6H, C-6 and C-6'), 3.90 (C-12); AlH 4.02 (d, 1H, J = 13.8 Hz, H-α'), 4.42 (d, 1H, J = 13.8 Hz, H-α'); ArH 4.92 (br s, 1H, H-10), 6.11 (H-8), 6.46 (m, 2H, H-5 and H-11'), 6.57 (H-5'), 6.72 (d, 1H, J = 8.1 Hz, H-13), 6.76 (dd, 1H, J = 2.3, 8.3 Hz, H-13'), 6.86 (dd, 1H, J = 1.2, 8.1 Hz, H-14), 7.33 (dd, 1H, J = 2.0, 8.2 Hz, H-10'), 7.40 (dd, 1H, J = 2.0, 8.3 Hz, H-14') (49)

42 HOMOAROMOLINE $C_{37}H_{40}O_6N_2$: 608.2886

^{13}C NMR: 64.2 (C-1), 44.9 (C-3), 28.2 (C-4), 130.4 (C-4a or C-9'), 111.1 (C-5 or C-13), 148.5 (C-6), 143.9 (C-7), 117.0 (C-8), 127.0 (C-8a), 38.2 (C-α), 137.8 (C-9), 117.0 (C-10), 146.7 (C-11), 148.7 (C-12), 110.9 (C-13 or C-5), 123.7 (C-14); 60.7 (C-1'), 50.9 (C-3'), 24.6 (C-4'), 122.7 (C-4'a), 104.6 (C-5'), 147.2 (C-6'), 133.5 (C-7'), 142.0 (C-8'), 122.9 (C-8'a), 38.8 (C-α'), 130.9 (C-9' or C-4a), 128.4 (C-10'), 121.8 (C-11'), 152.9 (C-12'), 121.0 (C-13'), 131.4 (C-14'); 43.5 (2-NMe or 2'-NMe), 4.15 (2'-NMe or 2-NMe), 55.8 (6-OMe and 12-OMe), 55.2 (6'-OMe) (29)
CD: 0 (350), +11 (293), +46 (240), +90 (221) (29)

50 SEPEERINE $C_{36}H_{38}O_6N_2$: 594.2730

$[\alpha]^{20}D$: +200° (c = 0.5, $CHCl_3$) (59)
^1H NMR: NMe 2.68 (N-2'); OMe 3.23 (C-7'), 3.64 (C-6), 3.80 (C-6'); AlH 3.97 (m, 1H, H-1), 4.37 (m, 1H, H-1'); ArH 5.58 (d, 1H, J = 2 Hz, H-10), 6.32 (dd, 1H, J = 2, 8.2 Hz, H-11'), 6.39 (H-5 or H-5'), 6.41 (H-5' or H-5), 6.70 (H-8), 6.77 (d, 1H, J = 8 Hz, H-13), 6.89 (dd, 1H, J = 2, 8 Hz, H-14), 6.95 (dd, 1H, J = 2, 8.2 Hz, H-10'), 6.99 (d, H-13'), 7.50 (dd, 1H, J = 2, 8.2 Hz, H-14') (59)
MS: $[M]^+$ 594 (30), 593 (100), 587 (9), 381 (30), 191 (25) (59)

52a THALIGOSINE $C_{37}H_{42}O_7N_2$: 638.2992

^1H NMR: NMe 2.52 (N-2'), 2.58 (N-2); OMe 3.07 (C-7), 3.41 (C-6'), 3.80 (C-6), 3.96 (C-12'); AlH 3.50 (m, 1H, H-1'), 4.23 (m, 1H, H-1); ArH 6.40 (H-5'), 6.47 (H-8'), 6.65 (d, 1H, J = 1.8 Hz, H-10'), 6.85 (br s, 2H, H-10 and H-11), 6.90 (dd, 1H, J = 1.8, 8.3 Hz, H-14'), 6.97 (d, 1H, J = 8.3 Hz, H-13'), 7.13 (dd, 1H, J = 1.8, 8.2 Hz) H-13), 7.33 (dd, 1H, J = 1.8, 8.2 Hz, H-14) (41)

55 THALRUGOSAMININE $C_{39}H_{44}O_7N_2$: 652.3149

^1H NMR: NMe 2.52 (N-2'), 2.57 (N-2); OMe 3.07 (C-7), 3.46 (C-6'), 3.81 (C-5), 3.85 (C-6), 3.96 (C-12'); AlH 3.49 (H-1'), 4.24 (H-1); ArH 6.41 (H-5'), 6.48 (H-8'), 6.64 (d, 1H, J = 1.9 Hz, H-10'), 6.85 (br s, 2H, H-10 and H-11), 6.91 (dd, 1H, J = 1.9, 8.3 Hz, H-14'), 6.98 (d, 1H, J = 8.3 Hz, H-13'), 7.13 (dd, 1H, J = 2.0, 8.2 Hz, H-13), 7.32 (dd, 1H, J = 2.0, 8.2 Hz, H-14) (41)

101 THALRUGOSIDINE $C_{38}H_{42}O_7N_2$: 638.2992

CD: 0 (300), −4.6 (281), 0 (270), 0 (253), +11.5 (240), negative tail below 228 nm (24)

107 THALICTINE $C_{37}H_{40}O_6N_2$: 608.2886

CD: 0 (300), +5 (291), −2 (275), 0 (251), +3.5 (240), negative tail below 230 nm (24)

114 DINKLACORINE $C_{36}H_{36}O_5N_2$: 576.2624

MP: Amorphous, 230–236° (27)
TLC: 0.37 [Si gel 60 F_{254}; $CHCl_3$-MeOH (9:1)] (27); 0.32 [Si gel 60 F_{254}; cyclohexane-$CHCl_3$-Et_2NH (4:5:1)] (27)
$[\alpha]^{20}D$: +39° ($c = 0.44$, $CHCl_3$) (27)
UV: 203 (3.42), 235 (4.11), 290 (3.41) (27)
IR(KBr): 3440, 2960, 2880, 2820, 1640, 1605, 1510, 1460, 1400, 1385, 1375, 1290, 1250, 1130, 1075, 1040, 970, 895, 845, 830 (27)
^1H NMR: NMe 2.36 (N-2), 2.69 (N-2'); OMe 3.87 (C-6), 4.03 (C-12'); ArH 6.31 (H-5), 6.71 (H-5'), 6.92 (d, 1H, $J = 8.4$ Hz, H-13), 7.00 (H-8'), 7.13 (d, 1H, $J = 9.3$ Hz, H-13'), 7.19 (dd, 1H, $J = 2.2$, 8.4 Hz, H-14), 7.38 (dd, 1H, $J = 2.2$, 9.3 Hz, H-14'), 7.40 (d, 1H, $J = 2.2$ Hz, H-10'), 7.88 (d, 1H, $J = 2.2$ Hz, H-10) (27)
MS: $[M]^+$ 576 (50), 575 (28), 559 (4), 546 (2), 350 (32), 349 (100), 335 (32), 333 (17), 319 (6), 175 (50) (27)

115 NORTILIACORINE A $C_{35}H_{34}O_5N_2$: 562.2468

MP: 262–265°
TLC: 0.53 [Si gel 60 F_{254}; CH_2Cl_2-MeOH-25% NH_4OH (90:9:1)] (56)
$[\alpha]^{20}D$: +157° ($c = 0.6$, $CHCl_3$) (56)
UV: 210 (4.65), 234 (4.52), 288 (3.89) (56)
IR(KBr): 3400, 2900, 2850, 1600, 1475, 1360, 1275, 1120 (56)
^1H NMR: NMe 2.33 (N-2); 3.86 (C-6), 3.96 (C-12'); ArH 6.29 (H-5), 6.70 (H-5'), 6.92 (d, 1H, $J = 8.1$ Hz, H-13), 7.00 (dd, 1H, $J = 2.2$, 9.0 Hz, H-14'), 7.05 (d, 1H, $J = 9.0$ Hz, H-13'), 7.20 (H-8'), 7.26 (dd, 1H, $J = 2.2$, 8.1 Hz, H-14), 7.35 (d, 1H, $J = 2.2$ Hz, H-10'), 7.93 (d, 1H, $J = 2.2$ Hz, H-10) (56)
MS: $[M]^+$ 562 (100), 561 (95), 549 (10), 547 (10), 336 (48), 335 (100), 321 (30), 305 (15), 168 (30) (56)

116 NORTILIACORININE A (2'-Nortiliacorinine) $C_{35}H_{34}O_5N_2$: 562.2468

^1H NMR: NMe 2.39 (N-2); OMe 3.88 (C-6), 4.00 (C-12); AlH 2.43 (m, 1H, H-4a), 2.69 (m, 1H, H-4'a), 2.84 (m, 2H, H-α), 2.92 (m, 1H, H-3a), 3.05 (m, 1H, H-4b), 3.09 (m, 1H, H-3'a), 3.19 (m, 1H, H-4'b), 3.23 (m, 1H, H-α'a), 3.35 (m, 1H, H-α'b), 3.43 (m, 1H, H-3b), 3.52 (m, 1H, H-3'b), 3.79 (m, 1H, H-1), 4.14 (m, 1H, H-1'); ArH 6.34 (H-5), 6.71 (H-5'), 6.99 (dd, 1H, $J = 2$, 8 Hz, H-13), 7.02 (d, 1H, $J = 8$ Hz, H-13'), 7.39 (dd, 1H, $J = 2$, 8 Hz, H-14), 7.42 (dd, 1H, $J = 2$, 8 Hz, H-14'), 7.61 (d, 1H, $J = 2$ Hz, H-10'), 7.65 (d, 1H, $J = 2$ Hz, H-10), 8.18 (H-8') (nOe used) (66)

118 TILIACORINE $C_{36}H_{36}O_5N_2$: 576.2624

^1H NMR: ArH 6.29 (H-5), 6.71 (H-5'), 6.92 (d, 1H, $J = 8.4$ Hz, H-13), 7.02 (H-8'), 7.09 (d, 1H, $J = 9.3$ Hz, H-13'), 7.15–7.45 (m, H-14, -14', -10'), 7.92 (d, 1H, $J = 2.2$ Hz) (H-10) (27)
^{13}C NMR: 60.90 (C-1), 44.82 (C-3), 24.64 (C-4), 127.94 (C-4a), 106.37 (C-5), 146.11 (C-6), 129.53 (C-7), 139.43 (C-8), 120.55 (C-8a), 40.26 (C-α), 137.04 (C-9), 134.92 (C-10), 127.86 (C-11), 153.17 (C-12), 111.26 (C-13), 129.74 (C-14); 67.01 (C-1'), 49.99 (C-3'), 28.22 (C-4'), 133.63 (C-4'a), 115.68 (C-5'), 138.56 (C-6'), 138.39 (C-7'), 114.35 (C-8'), 129.66 (C-8'a), 41.10 (C-α'), 135.39 (C-9'), 134.48 (C-10'), 126.08 (C-11'), 152.48 (C-12'), 118.83 (C-13'), 129.95 (C-14'); 43.15 (2-NMe), 43.43 (2'-NMe), 56.28 (6-OMe), 59.29 (12-OMe) (27)

121 CYCLEANINE $C_{38}H_{42}O_6N_2$: 622.3043

The crystal structure of cycleanine, isolated from *Cissampelos pareira* L. (Menispermaceae), was determined (73).

192 DAURISOLINE $C_{37}H_{42}O_6N_2$: 610.3043

^1H NMR: NMe 2.47 (N-2), 2.53 (N-2'); OMe 3.62 (C-7), 380 (C-6 or C-6'), 3.83 (C-6' or C-6); AlH 3.62 (dd, 1H, H-1), 3.77 (dd, 1H, H-1'); ArH 6.14 (s, H-8'), 6.34 (s, H-8), 6.46 (s, H-5), 6.53 (d, 1H, H-10), 6.57 (s, H-5'), 6.81 (d, 2H, H-11' and H-13), 6.84 (dd, 1H, H-14), 6.90 (d, 1H, H-13), 7.03 (d, 2H, H-10' and H-14') (36)

211 NEOTHALIBRINE $C_{38}H_{44}O_6N_2$: 624.3199

^1H NMR: NMe 2.47 (N-2), 2.55 (N-2'); OMe 3.60 (C-7'), 3.81 (C-6 or C-6'), 3.82 (C-6' or C-6); ArH 6.08 (H-8'), 6.38 (H-8), 6.47 (H-5), 6.57 (H-5'), 6.62 (d, 1H, $J = 1.8$ Hz, H-10), 6.80 (d, 2H, $J = 8.5$ Hz, H-11' and H-13'), 6.86 (d, 1H, $J = 8.2$ Hz, H-13), 6.91 (dd, 1H, $J = 1.8$, 8.2 Hz, H-14), 7.02 (d, 2H, $J = 8.5$ Hz, H-10' and H-14') (41)

225 ANTIOQUINE (*N*-2'-METHYLTILITRIANDRINE) $C_{37}H_{40}O_6N_2$: 608.2886

^1H NMR: ArH 6.35 (H-5), 6.49 (H-5'), 6.60 (d, 1H, $J = 2.25$ Hz, H-10), 6.84 (d, 1H, $J = 8.25$ Hz, H-13'), 6.88 (d, 1H, $J = 8.25$ Hz, H-13'), 6.91 (H-8'), 7.16 (d, 1H, $J = 2.25$ Hz, H-10'), 7.22 (dd, 1H, $J = 2.25$, 8.25 Hz, H-14'), 7.33 (dd, 1H, $J = 2.25$, 8.25 Hz, H-14) (2D nmr used) (61)
The chemical shifts of the protons at H-10 and H-10' are reversed in comparison to those originally assigned (3).

234 *N,N'*-DIMETHYLLINDOLDHAMINE (Guattegaumerine) $C_{36}H_{40}O_6N_2$: 596.2886

^{1}H NMR: NMe 2.45 (N-2'), 2.50 (N-2); OMe 3.84 (C-6 or C-6'), 3.85 (C-6 or C-6'); AlH 3.62 (dd, 1H, H-1), 3.72 (dd, 1H, H-1'); 6.24 (s, H-8), 6.32 (s, H-8'), 6.48 (s, H-5), 6.54 (s, H-5'), 6.61 (d, 1H, H-10), 6.76 (dd, 1H, H-14), 6.82 (d, 2H, H-11' and H-13'), 6.87 (d, 1H, H-13), 7.02 (d, 2H, H-10' and H-14') (36)

236 KOHATINE $C_{34}H_{32}O_6N_2$: 564.2260

^{1}H NMR: NMe 2.59 (N-2); OMe 3.96 (C-6); AlH 3.67 (H-1'), 4.00 (H-1); ArH 6.23 (H-8'), 6.59 (d, 1H, J = 1.8 Hz, H-10'), 6.61 (H-5'), 6.81 (dd, 1H, J = 2.2, 8.2 Hz, H-11), 6.89 (dd, 1H, J = 1.8, 8.2 Hz, H-14'), 6.93 (d, 1H, J = 8.2 Hz, H-13'), 7.11 (dd, 1H, J = 2.2, 8.2 Hz, H-10), 7.20 (dd, 1H, J = 2.2, 8.2 Hz, H-12), 7.54 (dd, 1H, J = 2.2, 8.2 Hz, H-14) (33)

254 TILIACORININE-2'-*N*-OXIDE $C_{36}H_{36}O_6N_2$: 592.2573

MP: 215° (56)
$[\alpha]^{20}D$: +255° (c = 1.1, $CHCl_3$) (56)
UV: 209 (4.60), 230 (sh) (4.48), 287 (3.88) (56)
IR(KBr): 3400, 2930, 2830, 2820, 1630, 1600, 1500, 1440, 1360, 1280, 1240, 1120, 1035, 850 (56)
^{1}H NMR: NMe 2.37 (N-2), 3.03 (N-2'); OMe 3.87 (C-6), 3.98 (C-12); 6.34 (H-5), 6.74 (H-5'), 6.98 (d, 1H, J = 8.4 Hz, H-13), 7.22 (d, 1H, J = 8.4 Hz, H-13'), 7.35 (dd, 1H, J = 2.2, 8.4 Hz, H-14), 7.54 (d, 1H, J = 2.2 Hz, H-10), 7.60 (dd, 1H, J = 2.2, 8.4 Hz, H-14'), 7.64 (d, 1H, J = 2.2 Hz, H-10'), 8.29 (H-8') (56)
MS: $[M]^+$ 592 (71), 591 (69), 576 (42), 575 (37), 350 (31), 349 (100), 335 (31), 175 (55) (56)

2-NOROBABERINE[a] (**46** dvt) $C_{37}H_{40}O_6N_2$: 608.2886

^{1}H NMR: NMe 2.69 (N-2'); OMe 3.23 (C-7'), 3.64 (C-6), 3.79 (C-6'), 3.92 (C-12); AlH 4.23 (m) (2H) (H-1 and H-1'); ArH 5.61 (br s) (H-10), 6.31 (dd, 1H, J = 2.2, 8.2 Hz, H-11'), 6.36 (H-5 or H-5'), 6.37 (H-5' or H-5), 6.69 (H-8), 6.81 (br s), 2H, H-13 and H-14), 6.87 (dd, 1H, J = 2.2, 8.2 Hz, H-10'), 6.99 (dd, 1H, J = 2.2, 8.2 Hz, H-13'), 7.47 (dd, 1H, J = 2.2, 8.2 Hz, H-14') (64)

[a]This alkaloid has no number because it was not included in the first review (*1*).

TABLE 3. Known Natural Bisbenzylisoquinoline Alkaloids Reisolated from New Sources.

1	Berbamunine *Berberis boliviana* Lechl. (Berberidaceae) (62) *Berberis cretica* L. (Berberidaceae) (13) *Berberis stolonifera* (Berberidaceae) (32,54) *Pseudoxandra sclerocarpa* Maas (Annonaceae) (29) *Stephania pierrii* Diels (Menispermaceae) (64)	$C_{36}H_{40}O_6N_2$: 596.2886
3	Dauricine *Popowia pisocarpa* (Bl.) Endl. (Annonaceae) (30)	$C_{38}H_{44}O_6N_2$: 624.3199
5	Dauricoline *Popowia pisocarpa* (Bl.) Endl. (Annonaceae) (30)	$C_{36}H_{40}O_6N_2$: 596.2886
9	Espinine *Berberis chilensis* Gill. ex Hook (Berberidaceae) (65)	$C_{36}H_{40}O_6N_2$: 596.2886
10	Grisabine *Gyrocarpus americanus* Jacq. (Hernandiaceae) (15)	$C_{37}H_{42}O_6N_2$: 610.3043
11	Lindoldhamine *Abuta pahni* (Martius) Krukoff and Barneby (Menispermaceae) (36) *Albertisia papuana* Becc. (Menispermaceae) (35)	$C_{34}H_{36}O_6N_2$: 568.2573
12a	*O*-Methyldauricine *Popowia pisocarpa* (Bl.) Endl. (Annonaceae) (30)	$C_{39}H_{46}O_6N_2$: 638.3356
14b	Thalirugine *Thalictrum cultratum* Wall. (Ranunculaceae) (41)	$C_{38}H_{44}O_7N_2$: 640.3149
20	Funiferine *Guatteria guianensis* (Aublet) R.E. Fries (Annonaceae) (51)	$C_{38}H_{42}O_6N_2$: 622.3043
27	Tiliageine *Guatteria guianensis* (Aublet) R.E. Fries (Annonaceae) (51) *Tiliacora triandra* Diels (Menispermaceae) (61)	$C_{37}H_{40}O_6N_2$: 608.2886
28	Isoliensinine *Nelumbo nucifera* Gaertn. (Nymphaeaceae) (463)	$C_{37}H_{42}O_6N_2$: 610.3043

30 Neferine — $C_{38}H_{44}O_6N_2$: 624.3199
Nelumbo nucifera Gaertn. (Nymphaeaceae) (463)

31 Aromoline — $C_{36}H_{38}O_6N_2$: 594.2730
Albertisia laurifolia (Menispermaceae) (8)
Berberis boliviana Lechl. (Berberidaceae) (62)
Berberis bumeliaefolia Schneid. (Berberidaceae) (62)
Berberis cretica L. (Berberidaceae) (13)
Berberis koreana Palib. (Berberidaceae) (44)
Berberis laurina Billbg. (Berberidaceae) (62)
Berberis stolonifera (Berberidaceae) (32)
Guatteria guianensis (Aublet) R.E. Fried (Annonaceae) (59)
Mahonia aquifolium (Pursh) Nutt. (Berberidaceae) (20)
Stephania cepharantha Hayata (Menispermaceae) (46,58)
Stephania pierrii Diels (Menispermaceae) (64)
Thalictrum cultratum Wall. (Ranunculaceae) (41)

32 *N,N'*-Bisnoraromoline — $C_{34}H_{34}O_6N_2$: 566.2417
Albertisia papuana Becc. (Menispermaceae) (35)
Pachygone loyaltiensis Diels (Menispermaceae) (39)

34 Cepharanthine — $C_{37}H_{38}O_{6N2}$: 606.2730
Stephania epigeae (Menispermaceae) (7,40)
Stephania pierrii Diels (Menispermaceae) (64)
Stephania sinica Diels (Menispermaceae) (9)
Stephania suberosa Forman (Menispermaceae) (21)

35 Coclobine — $C_{37}H_{38}O_6N_2$: 606.2730
Guatteria guianensis (Aublet) R.E. Fries (Annonaceae) (59)

37 Daphnandrine — $C_{36}H_{38}O_6N_2$: 594.2730
Albertisia papuana Becc. (Menispermaceae) (35)
Guatteria guianensis (Aublet) R.E. Fries (Annonaceae) (59)
Pachygone loyaltiensis Diels (Menispermaceae) (39)
Stephania pierrii Diels (Menispermaceae) (64)

38 Daphnoline — $C_{35}H_{36}O_6N_2$: 580.2573
Albertisia laurifolia (Menispermaceae) (8)
Albertisia papuana Becc. (Menispermaceae) (35)
Guatteria guianensis (Aublet) R.E. Fries (Annonaceae) (59)
Pachygone loyaltiensis Diels (Menispermaceae) (39)
Pycnarrhena ozantha Diels (Menispermaceae) (38)

40 (+)-Epistephanine — $C_{37}H_{38}O_6N_2$: 606.2730
Stephania hernandifolia Walp. (Menispermaceae) (49)

42 Homoaromoline (Thalrugosamine) — $C_{37}H_{40}O_6N_2$: 608.2886
Berberis boliviana Lechl. (Berberidaceae) (62)
Berberis laurina Billbg. (Berberidaceae) (62)
Pseudoxandra sclerocarpa Maas (Annonaceae) (29)
Stephania cepharantha Hayata (Menispermaceae) (46)
Stephania pierrii Diels (Menispermaceae) (64)
Stephania venosa Spreng. (Menispermaceae) (43)

44 Limacusine — $C_{37}H_{40}O_6N_2$: 608.2886
Curarea candicans (L.C. Rich) Barneby and Krukoff (Menispermaceae) (83,84)

46 Obaberine — $C_{38}H_{42}O_6N_2$: 622.3043
Berberis boliviana Lechl. (Berberidaceae) (62)
Berberis cretica L. (Berberidaceae) (13)
Berberis paucidenta Rusby. (Berberidaceae) (62)
Berberis pseudambalata (Berberidaceae) (36)
Dehaasia triandra Merr. (Lauraceae) (63)
Stephania pierrii Diels (Menispermaceae) (64)
Thalictrum cultratum Wall. (Ranunculaceae) (41)

46 dvt 2-Norobaberine — $C_{37}H_{40}O_6N_2$: 608.2886
Stephania pierrii Diels (Menispermaceae) (64)

48 Oxyacanthine — $C_{37}H_{40}O_6N_2$: 608.2886
Berberis boliviana Lechl. (Berberidaceae) (62)
Berberis bumeliaefolia Schneid. (Berberidaceae) (62)
Berberis cretica L. (Berberidaceae) (13)
Berberis koreana Palib. (Berberidaceae) (44)

Berberis oblonga (Berberidaceae) (23)
Berberis paucidentata Rusby. (Berberidaceae) (62)
Berberis pseudambalata (Berberidaceae) (37)
Mahonia aquifolium (Pursh) Nutt. (Berberidaceae) (20,22)
Thalictrum cultratum Wall. (Ranunculaceae) (41)
Thalictrum minus L. (Ranunculaceae) (452)

52a Thaligosine — $C_{37}H_{42}O_7N_2$: 638.2992
Thalictrum cultratum Wall. (Ranunculaceae) (41)

52b Thaligosinine — $C_{38}H_{42}O_7N_2$: 638.2992
Thalictrum isopyroides C.A.M. (Ranunculaceae) (14)

53 Thalisopidine — $C_{37}H_{40}O_7N_2$: 624.2836
Thalictrum isopyroides C.A.M. (Ranunculaceae) (14)

54 Thalisopine — $C_{38}H_{42}O_7N_2$: 638.2992
Thalictrum cultratum Wall. (Ranunculaceae) (24)

55 Thalrugosaminine — $C_{39}H_{44}O_7N_2$: 652.3149
Thalictrum cultratum Wall. (Ranunculaceae) (24)

57 Berbamine — $C_{37}H_{40}O_6N_2$: 608.2886
Berberis boliviana Lechl. (Berberidaceae) (62)
Berberis brandisiana Ahrendt (Berberidaceae) (25)
Berberis bumeliaefolia Schneid. (Berberidaceae) (62)
Berberis cretica L. (Berberidaceae) (13)
Berberis koreana Palib. (Berberidaceae) (44)
Berberis oblonga (Regl.) (Berberidaceae) (23)
Berberis paucidentata Rusby. (Berberidaceae) (62)
Berberis regeliana (Berberidaceae) (18)
Berberis stolonifera (Berberidaceae) (32,54)
Berberis wilsoniae Hemsl. et Wils. (Berberidaceae) (6)
Isopyrum thalictroides (Ranunculaceae) (60)
Mahonia aquifolium (Pursh) Nutt. (Berberidaceae) (5,20,22)
Pycnarrhena manillensis Vidal (Menispermaceae) (48)
Stephania cepharantha Hayata (Menispermaceae) (46)

61 Fangchinoline — $C_{37}H_{40}O_6N_2$: 608.2886
Stephania tetrandra S. Moore (Menispermaceae) (16,52)

62 Isotetrandrine — $C_{38}H_{42}O_6N_2$: 622.3043
Berberis boliviana Lechl. (Berberidaceae) (62)
Berberis brandisiana Ahrendt (Berberidaceae) (25)
Berberis bumeliaefolia Schneid. (Berberidaceae) (62)
Berberis cretica L. (Berberidaceae) (13)
Berberis paucidentata Rusby. (Berberidaceae) (62)
Berberis stolonifera (Berberidaceae) (32)
Berberis wilsoniae Hemsl. et Wils. (Berberidaceae) (6)
Gyrocarpus americanus Jacq. (Hernandiaceae) (15)
Isopyrum thalictroides (Ranunculaceae) (60)
Mahonia aquifolium (Pursh) Nutt. (Berberidaceae) (20,22)
Pycnarrhena manillensis Vidal (Menispermaceae) (48)
Stephania cepharantha Hayata (Menispermaceae) (46)
Stephania pierrii Diels (Menispermaceae) (64)
Stephania tetrandra S. Moore (Menispermaceae) (16)

63 Krukovine — $C_{36}H_{38}O_6N_2$: 594.2730
Curarea candicans (L.C. Rich) Barneby and Krukoff (Menispermaceae) (83,84)

64 Limacine — $C_{37}H_{40}O_6N_2$: 608.2886
Curarea candicans (L.C. Rich) Barneby and Krukoff (Menispermaceae) (83,84)
Gyrocarpus americanus Jacq. (Hernandiaceae) (15,50)

68 2-Norberbamine — $C_{36}H_{38}O_6N_2$: 594.2730
Pycnarrhena ozantha Diels (Menispermaceae) (38)
Stephania pierrii Diels (Menispermaceae) (64)

69 2-Norobamegine — $C_{35}H_{36}O_6N_2$: 580.2573
Pycnarrhena ozantha Diels (Menispermaceae) (38)

71 Obamegine — $C_{36}H_{38}O_6N_2$: 594.2730
Berberis boliviana Lechl. (Berberidaceae) (62)
Berberis cretica L. (Berberidaceae) (13)

Berberis koreana Palib. (Berberidaceae) (44)
Mahonia aquifolium (Pursh) Nutt. (Berberidaceae) (20)

72 Penduline — $C_{37}H_{40}O_6N_2$: 608.2886
Berberis brandisiana Ahrendt (Berberidaceae) (25)

74 Phaeanthine (*O*-Methyllimacine) — $C_{38}H_{42}O_6N_2$: 622.3043
Gyrocarpus americanus Jacq. (Hernandiaceae) (15,50)
Pycnarrhena manillensis Vidal (Menispermaceae) (48)

75 Pycnamine — $C_{37}H_{40}O_6N_2$: 608.2886
Pycnarrhena manillensis Vidal (Menispermaceae) (48)

76 Tetrandrine — $C_{38}H_{42}O_6N_2$: 622.3043
Stephania tetrandra S. Moore (Menispermaceae) (16,45,52)

79 Thalrugosine — $C_{37}H_{40}O_6N_2$: 608.2886
Berberis boliviana Lechl. (Berberidaceae) (62)
Berberis cretica L. (Berberidaceae) (13)
Berberis laurina Billbg. (Berberidaceae) (62)
Berberis polymorpha (Berberidaceae) (57)

81 Hernandezine — $C_{39}H_{44}O_7N_2$: 652.3149
Thalictrum delavayi (Ranunculaceae) (34)
Thalictrum lankesteri Standl. (Ranunculaceae) (55)

82 Isothalidezine — $C_{38}H_{42}O_7N_2$: 638.2992
Thalictrum delavayi (Ranunculaceae) (34)

84 Thalidezine — $C_{38}H_{42}O_7N_2$: 638.2992
Thalictrum delavayi (Ranunculaceae) (34)

93 Belarine — $C_{37}H_{40}O_6N_2$: 608.2886
Berberis laurina Billbg. (Berberidaceae) (62)

95 *O*-Methylthalicberine — $C_{38}H_{42}O_6N_2$: 622.3043
Thalictrum collinum Wallr. (Ranunculaceae) (42)
Thalictrum cultratum Wall. (Ranunculaceae) (24)
Thalictrum minus var. *hypoleucum* L. (Ranunculaceae) (53)
Thalictrum minus var. *minus* L. (Ranunculaceae) (10)

96 *O*-Methylthalmethine — $C_{37}H_{38}O_6N_2$: 606.2730
Thalictrum minus L. (Ranunculaceae) (452)
Thalictrum minus var. *minus* L. (Ranunculaceae) (10)

97 Thalicberine — $C_{37}H_{40}O_6N_2$: 608.2886
Thalictrum minus var. *minus* L. (Ranunculaceae) (10)

98 Thalmethine — $C_{36}H_{36}O_6N_2$: 592.2573
Thalictrum minus L. (Ranunculaceae) (452)
Thalictrum minus var. *minus* L. (Ranunculaceae) (10)

100 Thalidasine — $C_{39}H_{44}O_7N_2$: 652.3149
Thalictrum cultratum Wall. (Ranunculaceae) (12)
Thalictrum squarrosum Steph. ex Willd. (Ranunculaceae) (47)

101 Thalrugosidine — $C_{38}H_{42}O_7N_2$: 638.2992
Thalictrum cultratum Wall. (Ranunculaceae) (24)

106 Lauberine — $C_{37}H_{40}O_6N_2$: 608.2886
Berberis laurina Billbg. (Berberidaceae) (62)

107 Thalictine — $C_{37}H_{40}O_6N_2$: 608.2886
Thalictrum cultratum Wall. (Ranunculaceae) (24)

108 Thalmine — $C_{37}H_{40}O_6N_2$: 608.2886
Thalictrum collinum Wallr. (Ranunculaceae) (42)
Thalictrum cultratum Wall. (Ranunculaceae) (12)

114 Dinklacorine — $C_{36}H_{36}O_5N_2$: 576.2624
Tiliacora triandra Diels (Menispermaceae) (26,27)

115 Nortiliacorine A — $C_{35}H_{34}O_5N_2$: 562.2468
Tiliacora triandra Diels (Menispermaceae) (56)

116 Nortiliacorinine A — $C_{35}H_{34}O_5N_2$: 562.2468
Tiliacora triandra Diels (Menispermaceae) (17,26)

118 Tiliacorine — $C_{36}H_{36}O_5N_2$: 576.2624
Tiliacora triandra Diels (Menispermaceae) (17,26)

119 Tiliacorinine — $C_{36}H_{36}O_6N_2$: 576.2624
Tiliacora triandra Diels (Menispermaceae) (17)

121 Cycleanine — $C_{38}H_{42}O_6N_2$: 622.3043
Stephania cepharantha (Menispermaceae) (46)
Stephania epigeae Diburong (Menispermaceae) (7)
Stephania pierrii Diels (Menispermaceae) (64)
Stephania tetrandra S. Moore (Menispermaceae) (52)

152 Cocsoline — $C_{34}H_{32}O_5N_2$: 548.2311
Albertisia laurifolia (Menispermaceae) (8)
Albertisia papuana Becc. (Menispermaceae) (35)
Anisocycla cymosa Troupin (Menispermaceae) (82)

153 Cocsuline — $C_{35}H_{34}O_5N_2$: 562.2468
Albertisia laurifolia (Menispermaceae) (8)
Albertisia papuana Becc. (Menispermaceae) (35)

157 Isotrilobine — $C_{36}H_{36}O_5N_2$: 576.262
Cocculus hirsutus (Menispermaceae) (28)
Pachygone loyaltiensis Diels (Menispermaceae) (39)

160 Telobine — $C_{35}H_{34}O_5N_2$: 562.2468
Guatteria guianensis (Aublet) R.E. Fries (Annonaceae) (59)

163 Trilobine — $C_{35}H_{34}O_5N_2$: 562.2468
Anisocycla cymosa Troupin (Menispermaceae) (82)
Cocculus hirsutus (Menispermaceae) (28)

169 Insulanoline — $C_{37}H_{38}O_6N_2$: 606.2730
Cyclea hypoglauca (Menispermaceae) (11)

170 Insularine — $C_{38}H_{40}O_6N_2$: 620.2886
Cyclea hypoglauca (Menispermaceae) (11)

187 Apateline — $C_{34}H_{32}O_5N_2$: 548.2311
Albertisia laurifolia (Menispermaceae) (8)
Albertisia papuana Becc. (Menispermaceae) (35)
Guatteria guianensis (Aublet) R.E. Fries (Annonaceae) (59)
Pachygone loyaltiensis Diels (Menispermaceae) (39)

188 Baluchistine — $C_{36}H_{38}O_6N_2$: 594.2724
Mahonia aquifolium (Pursh) Nutt. (Berberidaceae) (31)

192 Daurisoline — $C_{37}H_{42}O_6N_2$: 610.3043
Abuta pahni (Martius) Krukoff and Barneby (Menispermaceae) (36)

193 1,2-Dehydroapateline — $C_{35}H_{32}O_5N_2$: 560.2311
Anisocycla cymosa Troupin (Menispermaceae) (82)
Guatteria guianensis (Aublet) R.E. Fries (Annonaceae) (59)
Pachygone loyaltiensis Diels (Menispermaceae) (39)
Stephania pierrii Diels (Menispermaceae) (64)

194 1,2-Dehydrotelobine — $C_{35}H_{32}O_5N_2$: 560.2311
Anisocycla cymosa Troupin (Menispermaceae) (82)
Guatteria guianensis (Aublet) R.E. Fries (Annonaceae) (59)
Pachygone loyaltiensis Diels (Menispermaceae) (39)

195 7-*O*-Demethylisothalicberine — $C_{36}H_{38}O_6N_2$: 594.2724
Berberis laurina Billbg. (Berberidaceae) (62)

196 *N*-Desmethylthalidasine — $C_{38}H_{42}O_7N_2$: 638.2992
Thalictrum cultratum Wall. (Ranunculaceae) (12)

207 *N*-Methylapateline — $C_{35}H_{34}O_5N_2$: 562.2468
Albertisia laurifolia (Menispermaceae) (8)

211 Neothalibrine — $C_{38}H_{44}O_6N_2$: 624.3199
Thalictrum cultratum Wall. (Ranunculaceae) (41)

213 2′-Norisotetrandrine — $C_{37}H_{40}O_6N_2$: 608.2886
Stephania pierrii Diels (Menispermaceae) (64)

222 Thalmirabine — $C_{39}H_{44}O_8N_2$: 668.3098
Thalictrum delavayi (Ranunculaceae) (34)

223 *N*-Desmethylcycleanine — $C_{37}H_{40}O_6N_2$: 608.2886
Stephania pierrii Diels (Menispermaceae) (64)

234 *N,N'*-Dimethyllindoldhamine (Guattegaumerine) — $C_{36}H_{40}O_6N_2$: 596.2886
Abuta pahni (Martius) Krukoff and Barneby (Menispermaceae) (36)
Caryomene olivascens Barneby et Krukoff (Menispermaceae) (19)

236 Kohatine — $C_{34}H_{32}O_6N_2$: 564.2260
Cocculus pendulus (Forsk.) Diels (Menispermaceae) (33)

239 *O*-Methylcocsoline — $C_{35}H_{34}O_5N_2$: 562.2468
Albertisia papuana Becc. (Menispermaceae) (35)
Pachygone loyaltiensis Diels (Menispermaceae) (39)

244 *O*-Methylthalmine — $C_{38}H_{42}O_6N_2$: 622.3043
Thalictrum cultratum Wall. (Ranunculaceae) (24)

245 2-Norlimacusine — $C_{36}H_{38}O_6N_2$: 594.2730
Caryomene olivascens Barneby et Krukoff (Menispermaceae) (19)

252 Thaligrisine — $C_{37}H_{42}O_6N_2$: 610.3043
Pseudoxandra sclerocarpa Maas (Annonaceae) (29)

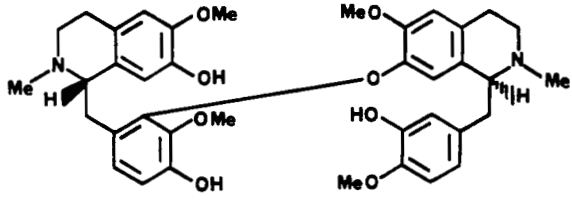
253 Thaliphylline — $C_{37}H_{40}O_6N_2$: 608.2886
Thalictrum cultratum Wall. (Ranunculaceae) (24)
Thalictrum minus var. *minus* L. (Ranunculaceae) (10)

254 Tiliacorinine-2'-*N*-oxide — $C_{36}H_{36}O_6N_2$: 592.2573
Tiliacora triandra Diels (Menispermaceae) (56)

TABLE 4. New Bisbenzylisoquinoline Alkaloids.[a]

272 AMBRIMINE — $C_{38}H_{44}O_8N_2$: 656.3097

Type Vb[b] (*S,S*) 6,7,10*,11,12-6,7*,11,12

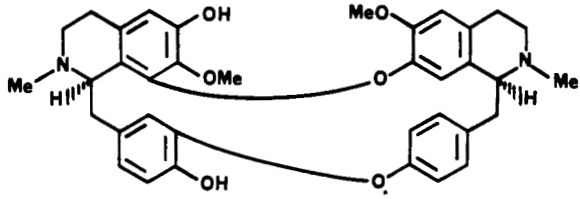


MP: Amorphous (68)
[α]D: +128° (*c* = 0.78, $CHCl_3$) (68)
UV: 227, 282 (68), with a bathochromic shift in alkali (68)
^{1}H NMR: NMe 2.39 (N-2'), 2.46 (N-2); ArH 5.93 (H-8), 6.05 (H-8'), 6.42 (H-10'), 6.47 (H-13), 6.51 (H-14'), 6.53 (H-5), 6.60 (H-13'), 6.63 (H-5'), 6.66 (H-14) (nOe used) (68)
MS: $[M]^+$ 656 (0.1), 519 (8), 192 (100) (68)
Sources: *Hernandia peltata* Meissner (Hernandiaceae) (68)
Derivatives: *O,O,O*-Trimethylambrimine (ambrimine + CH_2N_2) (68)
^{1}H NMR: NMe 2.40, 2.43; OMe 3.59 (C-7), 3.71 (C-6), 3.73 (C-6'), 3.80 (C-11), 3.83 (C-12), 3.90 (6H) (C-11' and C-12'); ArH 5.96 (s, 1H, H-8), 6.10 (s, 1H, H-8'), 6.51 (s, 1H, H-5), 6.53 (s, 1H, H-5'), 6.58 (d, 1H, *J* = 8.2 Hz), 6.60 (d, 1H, *J* = 8.2 Hz) (68)
MS: $[M]^+$ 698 (0.1), 548 (18), 206 (100) (68)
Triacetylambrimine (68)

[a]Not previously reported in the reviews by Schiff (2,3).
[b]This new class, bearing a bisreticuline base, supplements the head-to-tail-linked Class V as presented in the review of Guha *et al.* (1).

273 AQUIFOLINE $C_{36}H_{38}O_6N_2$: 594.2730

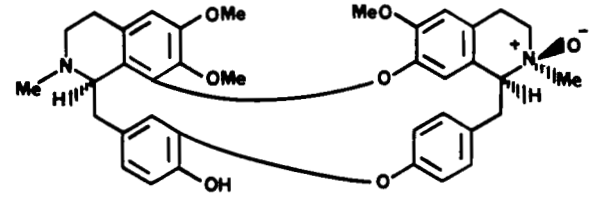
Type VIII (*R,S*) 6,7,8*,11$^+$,12-6,7*,12$^+$



MP: 168° (C_6H_6/$CHCl_3$) (31)
$[\alpha]_{578}^{25}$: +80° (*c* = 0.1, MeOH) (31)
UV: 229 (sh) (4.6), 282 (3.9) (31)
IR(KBr): 3460, 2940, 2840, 1570, 1495, 1475, 1370, 1230, 1080, 1020, 930, 752 (31)
^{1}H NMR: NMe 2.24 (N-2), 2.59 (N-2′); OMe 3.16 (C-7), 3.52 (C-6′); ArH 6.06–7.33 (1OH) (31)
MS: $[M]^+$ 594.2726, 593, 471, 385, 381, 367, 192, 174, 168 (31)
CD: +2.87 (288), −1.13 (269), −0.62 (260), −10.57 (247), +19.27 (229), 0 (218), +16.51 (27), −26.39 (193) (31)
Sources: *Mahonia aquifolium* (Pursh) Nutt. (Berberidaceae) (31)

274 BERBAMINE-2′β-*N*-OXIDE $C_{37}H_{40}O_7N_2$: 624.2836

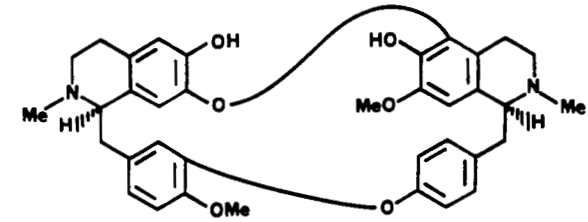
Type VIII (*R,S*) 6,7,8*,11,12$^+$-6,7*,12$^+$



MP: Amorphous (25)
$[\alpha]_D$: +14° (*c* = 0.08, MeOH) (25)
UV: 234 (sh) (4.55), 282 (4.04) (25)
^{1}H NMR: NMe 2.25 (N-2), 3.27 (N-2′); OMe 3.10 (C-7), 3.59 (C-6′), 3.76 (C-6); AlH 2.80 (m, 1H, H-α′6), 3.86 (m, 1H, H-1), 4.15 (m, 2H, H-α′a, and H-3′), 4.46 (m, 1H, H-1′); ArH 6.03 (H-8′), 6.31 (br s, 2H, H-5 and H-10), 6.55 (dd, 1H, *J* = 2.1, 8.2 Hz, H-10′), 6.57 (H-5′), 6.64 (dd, 1H, *J* = 2.1, 8.2 Hz, H-11′), 6.77 (dd, 1H, *J* = 1.7, 8 Hz, H-14), 6.88 (d, 1H, *J* = 8 Hz, H-13), 7.16 (dd, 1H, *J* = 2.1, 8.2 Hz, H-13′), 7.37 (dd, 1H, *J* = 2.1, 8.2 Hz, H-14′) (nOe used) (25)
MS: $[M]^+$ 624 (38), 608 (100), 594 (29), 396 (80), 382 (61), 206 (12), 198 (97), 175 (52) (25)
Sources: *Berberis brandisiana* Ahrendt (Berberidaceae) (25)
Derivatives: Berbamine [**57**] (berbamine-2′β-*N*-oxide + Zn/HCl) (25)

275 BERBILAURINE $C_{36}H_{38}O_6N_2$: 594.2730

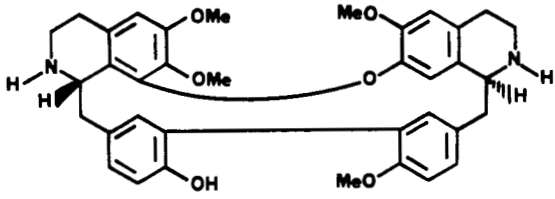
Type XIV (*R,S*) 6,7*,11$^+$,12-5*,6,7,12$^+$



$[\alpha]_D$: Negative (*c* = 0.1, EtOH) (62)
UV(EtOH): 213, 229 (sh), 290 (62); (EtOH + OH^-) 217, 236 (sh), 292 (62)
^{1}H NMR: NMe 2.24 (N-2), 2.65 (N-2′); OMe 3.91 (C-12), 3.95 (C-7′); AlH 3.45 (H-1), 3.73 (H-1′); ArH 5.99 (H-8), 6.21 (d, 1H, *J* = 1.4 Hz, H-10), 6.67 (H-5), 6.79 (H-8′), 6.81 (d, 1H, *J* = 8.5 Hz, H-13), 6.87 (dd, 1H, *J* = 1.4, 8.5 Hz, H-14), 6.92 (d, 2H, *J* = 8 Hz, H-11′ and H-13′), 7.10 (d, 2H, *J* = 8 Hz, H-10′ and H-14′) (2D nmr used) (62)
MS: $[M]^+$ 594 (28), 593 (17), 368 (18), 367 (65), 353 (8), 192 (47), 190 (53), 184 (100), 176 (54), 168 (28), 162 (25) (62)
Sources: *Berberis laurina* Billbg. (Berberidaceae) (62)

276 2,2′-BISNORGUATTAGUIANINE $C_{36}H_{38}O_6N_2$: 594.2730

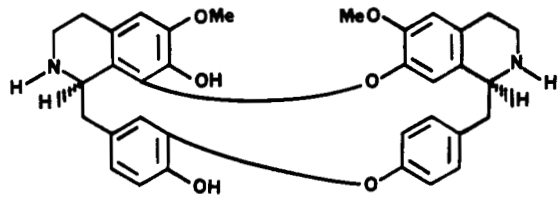
Type IV (*S,S*) 6,7,8*,12-6,7*,12(11-11)



[α]D: +40° (*c* = 0.8, $CHCl_3$) (51)
UV: 230 (sh) (3.86), 283 (3.42) (51)
^{1}H NMR: OMe 3.36 (C-6′), 3.57 (C-7), 3.83 (C-6), 3.90 (C-12′); AlH 4.44 (H-1), 4.50 (H-1′); ArH 6.41 (H-5), 6.43 (H-5′), 6.88 (H-13), 6.90 (H-13′), 7.18 (H-14), 7.22 (H-10′), 7.20 (H-8′), 7.38 (H-14′), 7.55 (H-10) (51)
MS: $[M]^+$ 594 (2), 593 (5), 592 (10< 367 (100), 365 (17), 184 (19) (51)
CD: 0 (310), +2.7 (295), 0 (289), −5.5 (275), 0 (261), +4.6 (255), 0 (250), −5.5 (245), 0 (242), +73 (224), 0 (215) (51)
Sources: *Guatteria guianensis* (Aublet) R.E. Fries (Annonaceae) (51)
Derivatives: Guattaguianine (2,2′-bisnorguattaguianine + $CH_2O/NaBH_4$) (51)

277 BISNOROBAMEGINE $C_{34}H_{34}O_6N_2$: 566.2417

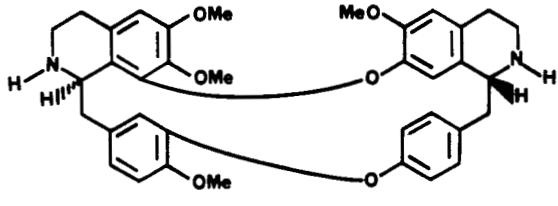
Type VIII (*R,S*) 6,7,8*,11$^+$,12-6,7*,12$^+$



[α]D: +260° (*c* = 0.65, $CHCl_3$) (38)
UV: 232 (3.80), 284 (3.37) (38); (MeOH + OH^-) 246, 288 (38)
^{1}H NMR: OMe 3.75 (C-6), 3.87 (C-6′); AlH 4.01 (m, 1H, H-′), 4.21 (m, 1H, H-1); ArH 6.12 (H-8′), 6.19 (d, 1H, *J* = 1.5 Hz, H-10), 6.35 (h-5), 6.49 (dd, 1H, *J* = 2.0, 8.5 Hz, H-10′), 6.64 (dd, 1H, *J* = 2.0, 8.5 Hz, H-11′), 6.70 (H-5′), 6.78 (dd, 1H, *J* = 1.5, 8.0 Hz, H-14), 6.79 (d, 1H, *J* = 8.0 Hz, H-13), 6.94 (dd, 1H, *J* = 2.0, 8.5 Hz, H-13′), 7.25 (dd, 1H, *J* = 2.0, 8.5 Hz, H-14′) (38)
MS: $[M]^+$ 566 (7), 565 (13), 389 (7), 354 (23), 353 (100), 184 (5), 178 (14), 177 (46), 175 (12) (38)
Sources: *Pycnarrhena ozantha* Diels (Menispermaceae) (38)
Derivatives: Obamegine [**71**] (bisnorobamegine + $CH_2O/NaBH_4$) (38)

278 2,2′-BISNORPHAEANTHINE $C_{36}H_{38}O_6N_2$: 594.2730

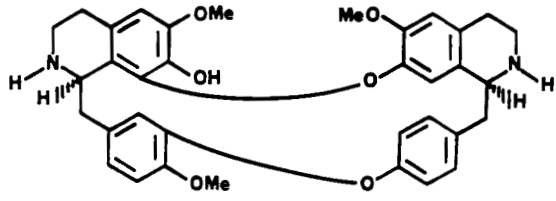
Type VIII (*R,R*) 6,7,8*,11$^+$,12-6,7*,12$^+$



MP: Amorphous (35)
[α]D: −272° (*c* = 0.1, $CHCl_3$) (35)
UV(EtOH): 213 (4.29), 232 (4.58), 283 (3.86) (35)
^{1}H NMR: OMe 3.25 (C-7), 3.41 (C-6′), 3.78 (C-6), 3.95 (C-12); AlH 4.06 (H-1), 4.35 (H-1′); ArH 6.03 (H-8′), 6.33 (H-5′), 6.40 (H-10′), 6.42 (H-10), 6.53 (H-5′), 6.79 (H-14), 6.87 (H-11′), 6.89 (H-13), 7.16 (H-13′), 7.44 (H-14′) (35)
MS: $[M]^+$ 594 (6), 593 (8), 367 (100), 184 (28), 161 (10) (35)
Sources: *Albertisia papuana* Becc. (Menispermaceae) (35)
Derivatives: Phaeanthine [**74**] (2,2′-bisnorphaeanthine + $CH_2O/NaBH_4$) (35)

279 BISNORTHALRUGOSINE $C_{35}H_{36}O_6N_2$: 580.2573

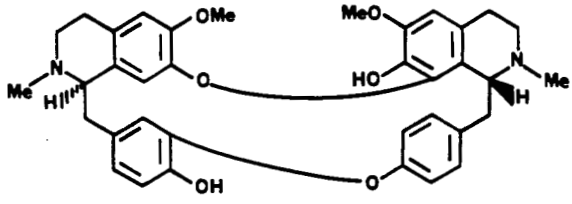
Type VIII (*R,S*) 6,7,8*,11$^+$,12-6,7*,12$^+$



[α]D: +142° (*c* = 0.13, $CHCl_3$) (38)
UV: 240 (4.40), 285 (3.80) (38); (MeOH + OH^-) 242, 288 (38)
^{1}H NMR: OMe 3.78 (C-6), 3.92 (C-6′ or C-12), 3.95 (C-12 or C-6′); AlH 3.98 (m, 1H, H-1′), 4.20 (m, 1H, H-1); ArH 6.13 (H-8′), 6.38 (H-5), 6.21 (d, 1H, *J* = 1.8 Hz, H-10), 6.50 (dd, 1H, *J* = 2.2, 8.3 Hz, H-10′), 6.71 (dd, 1H, *J* = 2.2, 8.3 Hz, H-11′), 6.73 (H-5′), 6.83 (d, 1H, *J* = 8.2 Hz, H-13), 6.85 (dd, 1H, *J* = 1.8, 8.2 Hz, H-14), 6.97 (dd, 1H, *J* = 2.2, 8.3 Hz, H-13′), 7.26 (dd, 1H, *J* = 2.2, 8.3 Hz, H-14′) (38)
MS: [M]$^+$ 580 (4), 579 (7), 565 (4), 547 (5), 532 (2), 389 (3), 367 (5), 354 (16), 353 (100), 192 (36) 178 (28), 177 (27), 160 (17) (38)
Sources: *Pycnarrhena ozantha* Diels (Menispermaceae) (38)
Derivatives: Thalrugosine [**79**] (bisnorthalrugosine + CH_2O/$NaBH_4$) (38)

280 CANDICUSINE $C_{36}H_{38}O_6N_2$: 594.2730

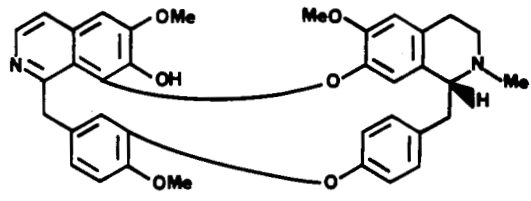
Type VI (*R,R*) 6,7*,11$^+$,12-6,7,8*,12$^+$



[α]D: +75° (*c* = 0.07, MeOH) (83,84)
UV: 232 (sh) (4.33), 282 (4.01) (84)
^{1}H NMR: NMe 2.54 (N-2′), 2.55 (N-2); OMe 3.41 (C-6), 3.78 (C-6′); AlH 3.47 (H-1), 4.29 (H-1′); ArH 6.38 (H-5), 6.49 (H-5′), 6.45 (H-8), 6.56 (d, 1H, *J* = 1.2 Hz, H-10), 6.83 (br s, H-10′), 6.83 (br s, H-11′), 6.88 (dd, 1H, *J* = 1.2, 8.4 Hz, H-14), 7.00 (d, 1H, *J* = 8.4 Hz, H-13), 7.13 (dd, 1H, *J* = 1.2, 8.2 Hz, H-13′), 7.37 (dd, 1H, *J* = 1.2, 8.2 Hz, H-14′) (nOe used) (83–85)
MS: [M]$^+$ 594 (45) (found 594.2790), 593 (41), 488 (2), 487 (5), 381 (100), 367 (67), 192 (48), 191 (90), 174 (47) (84)
CD: 0 (300), −1 (280), −3 (255), 0 (342), −39 (22), negative tail (84)
Sources: *Curarea candicans* (L.C. Rich) Barneby and Krukoff (Menispermaceae) (84)

281 CARYOLIVINE $C_{36}H_{34}O_6N_2$: 590.2417

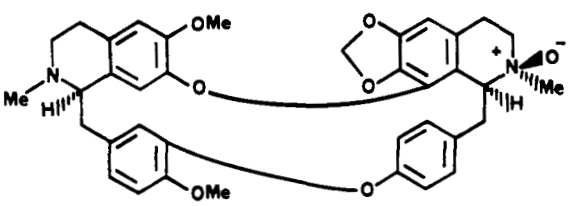
Type VIII (−,*R*) 6,7,8*,11$^+$,12-6,7*,12$^+$



MP: Amorphous (19)
[α]D: −46° (*c* = 0.08, MeOH) (19)
UV: 212 (4.67), 254 (4.53), 286 (3.88), 336 (3.51) (19)
^{1}H NMR: NMe 2.65 (N-2′); OMe 3.38 (C-6′), 3.90 (C-6), 3.91 (C-12); AlH 4.02 (H-1′), 4.13 (d, 1H, *J* = 12.8 Hz, H-α), 4.99 (d, 1H, *J* = 12.8 Hz, H-α); ArH 6.05 (1H, H-8′), 6.55 (1H, H-5′), 6.74 (dd, 1H, *J* = 2, 8.2 Hz, H-10′), 6.75 (1H, H-5), 6.85 (d, 2H, *J* = 2 Hz, H-10, *J* = 8.4 Hz, H-13), 7.02 (dd, 1H, *J* = 2, 8.2 Hz, H-11′), 7.23 (dd, 1H, *J* = 2, 8.4 Hz, H-14), 7.25 (dd, 1H, *J* = 2, 8.2, Hz, H-13′), 7.32 (d, 1H, *J* = 5.6 Hz, H-4), 7.52 (dd, 1H, *J* = 2, 8.3, H-14′), 8.33 (d, 1H, *J* = 5.6 Hz, H-3) (19)
MS: [M]$^+$ 590 (80), 589 (100), 588 (16), 484 (20), 483 (6), 295 (12), 174 (17) (19)
Sources: *Caryomene olivascens* Barneby et Krukoff (Menispermaceae) (19)

282 CEPHARANTHINE-2′β-*N*-OXIDE $C_{37}H_{38}O_7N_2$: 622.2679

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



MP: Amorphous (21)

[α]D: +152° (*c* = 0.22, MEOH) (21)

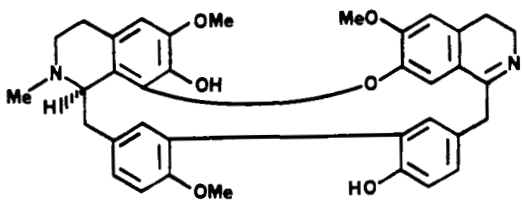
^{1}H NMR: NMe 2.58 (N-2), 3.31 (N-2′); OMe 3.71 (C-6), 3.89 (C-12); CH_2O_2 5.66 (1H, *J* = 1 Hz), 5.71 (1H, *J* = 1 Hz); AlH 3.64 (m, 1H, H-1), 4.63 (m, 1H, H-1′); ArH 5.42 (br s, H-10), 6.34 (dd, 1H, *J* = 2, 8, 2 Hz, H-11′), 6.37 (H-5), 6.39 (H-5′), 6.70 (H-8), 6.76 (br s, 2H, H-13 and H-14), 6.98 (dd, 2H, *J* = 2, 8.2 Hz, H-10′ and H-13′), 7.85 (dd, 1H, *J* = 2, 8.2 Hz, H-14′) (nOe used) (21)

MS: [M]$^+$ 622 (8), 621 (17), 620 (31), 606 (95), 605 (98), 592 (19), 591 (29), 516 (4), 380 (25), 379 (97), 366 (24), 365 (98), 190 (100), 183 (23), 174 (67) (21)

Sources: *Stephania suberosa* Forman (Menispermaceae) (21)

283 CORDOBIMINE $C_{36}H_{36}O_6N_2$: 592.2573

Type IV (*R*,−) 6,7,8*,12-6,7*,12(11-11)



MP: Amorphous (79)

[α]D: −185° (*c* = 0.5, $CHCl_3$) (79)

UV: 218 (4.64), 284 (4.07), 308 (3.85); MeOH + NaOH) 230, 302 (79); (MeOH + HCl) 218, 245 (sh), 288, 346 (79)

IR(KBr): 1620 (79)

^{1}H NMR: NMe 2.28 (N-2); OMe 3.46 (C-6′), 3.42 (C-6′), 3.82 (C-6), 3.94 (C-12); AlH 4.09 (m, 1H, H-1); ArH 6.37 (H-5), 6.43 (H-5′), 6.79 (d, 1H, *J* = 8.5 Hz, H-13′), 6.88 (d, 1H, *J* = 8.5 Hz, H-13), 7.15 (dd, 1H, *J* = 2.2, 8.5 Hz, H-14′), 7.26 (dd, 1H, *J* = 2.2, 8.5 Hz, H-14), 7.41 (d, 1H, *J* = 2.2 Hz, H-10′), 7.64 (d, 1H, *J* = 2.2 Hz, H-10), 7.77 (H-8′) (nOe used) (79)

MS: [M]$^+$ 592 (100), 591 (89), 577 (18), 561 (22), 367 (2), 296 (15), 192 (7), 191 (12), 190 (13) (79)

CD: 0 (337), −36.0 (301), 0 (279), +10.4 (269), 0 (260), −35.2 (250), −35.5 (226), 20 (215) (79)

Sources: *Crematosperma* sp. (Annonaceae) (79)

Derivatives: Reduction ($NaBH_4$/MeOH) afforded *S*-dihydrocordobimine and *R*-dihydrocordobimine in a ratio of 1:2 (79)

S-Dihydrocordobimine

MP: 205–209° (MeOH) (79)

$[\alpha]^{20}$D: −215° (*c* = 1, $CHCl_3$) (79)

UV: 215 (4.44), 238 (sh) (4.16), 286 (3.83) (79)

^{1}H NMR: NMe 2.38 (N-2); OMe 3.49 (C-6′), 3.83 (C-6), 3.88 (C-12); AlH 3.97 (m, 1H, H-1), 4.45 (m, 1H, H-1′); ArH 6.37 (H-5), 6.48 (H-5′), 6.85 (d, 1H, *J* = 2.2 Hz, H-10′), 6.86 (d, 1H, *J* = 8.5 Hz, H-13′), 6.88 (d, 1H, *J* = 8.5 Hz, H-13), 6.91 (d, 1H, *J* = 2.2 Hz, H-10), 7.15 (H-8′), 7.20 (dd, 1H, *J* = 2.2, 8.5 Hz, H-14′), 7.42 (dd, 1H, *J* = 2.2, 8.5 Hz, H-14) (nOe used) (79)

MS: 594 (40), 593 (42), 580 (4), 579 (9), 559 (7), 368 (36), 353 (43), 208 (16), 192 (62), 191 (36), 190 (25), 184 (100) (79)

CD: 0 (315), −8.9 (284), −26.3 (244), 0 (225), +18.4 (217) (79)

R-Dihydrocordobimine

MP: 185–190° (MeOH) (79)

$[\alpha]^{20}$D: −9° (*c* = 1, $CHCl_3$) (79)

UV: 220 (4.60), 238 (sh) (4.40), 286 (4.05) (79)

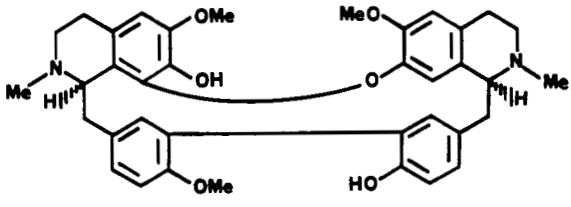
^{1}H-NMR: NMe 2.34 (N-2); OMe 3.33 (C-6′), 3.83 (C-6), 3.88 (C-12); AlH 4.13 (m, 1H, H-1), 4.37 (m, 1H, H-1′); ArH 6.38 (H-5), 6.40 (H-5′), 6.84 (d, 1H, *J* = 8.5 Hz, H-13′), 6.86 (d, 1H, *J* = 8.5 Hz, H-13), 7.09 (d, 1H, *J* = 2.2 Hz, H-10′), 7.21 (dd, 1H, *J* = 2.2, 8.5 Hz, H-14′), 7.27 (dd, 1H, *J* = 2.2, 8.5 Hz, H-14), 7.28 (H-8′), 7.62 (d, 1H, *J* = 2.2 Hz, H-10) (nOe used) (79)

MS: 594 (42), 593 (44), 580 (5), 579 (9), 563 (3), 368 (36), 367 (64), 353 (40), 208 (13), 192 (43), 191 (22), 190 (15), 184 (100) (79)
CD: CD: 0 (320), −5.1 (296), 0 (273), −13.3 (254), 0 (246), +3.5 (243), 0 (238), −38.0 (226) (79)
N-Methyldihydrocordobimine (1′*S*-cordobine) [**284**] (*S*-dihydrocordobimine + $CH_2O/NaBH_4$) (ms, ^1H nmr, tlc, sp rotation, cd) (79)

284 CORDOBINE

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

Type IV (*R*,*S*) 6,7,8*,12-6,7*,12(11-11)

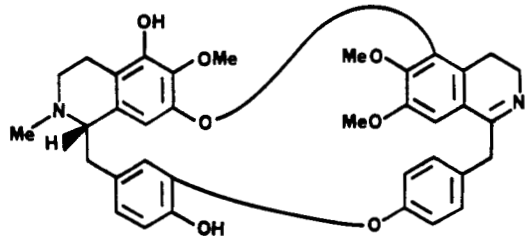


MP: Amorphous (79)
$[\alpha]^{20}D$: −140° (*c* = 0.7, $CHCl_3$) (79)
UV: 213 (4.60), 238 (sh) (4.32), 285 (3.99) (79)
^1H NMR: NMe 2.42 (N-2), 2.64 (N-2′); OMe 3.52 (C-6′), 3.82 (C-6), 3.89 (C-12); AlH 3.80 (m, 1H, H-1′), 4.16 (m, 1H, H-1); ArH 6.36 (H-5), 6.50 (H-5′), 6.53 (d, 1H, *J* = 2.2 Hz, H-10′), 6.84 (H-8′), 6.87 (d, 1H, *J* = 8.5 Hz, H-13), 6.89 (d, 1H, *J* = 8.5 Hz, H-13′), 7.17 (d, 1H, *J* = 2.2 Hz, H-10), 7.23 (dd, 1H, *J* = 2.2, 8.5 Hz, H-14′), 7.44 (dd, 1H, *J* = 2.2, 8.5 Hz, H-14) (nOe used) (79)
MS: $[M]^+$ 608 (21), 607 (21), 593 (3), 577 (2), 382 (20), 381 (70), 367 (21), 353 (13), 192 (47), 191 (100), 174 (26) (79)
CD: 0 (335), 320 (0.9), 0 (305), −4.9 (285), 0 (260), −12.8 (246), 0 (231), +31.6 (218) (79)
Sources: *Crematosperma* sp. (Annonaceae) (79)
Derivatives: *O,O*-Dimethylcordobine (granjine) [**302**] (cordobine + CH_2N_2) (tlc, ms, ^1H nmr, sp rotation, cd) (79)

285 CULTITHALMININE

$C_{36}H_{36}O_7N_2$: 608.2522

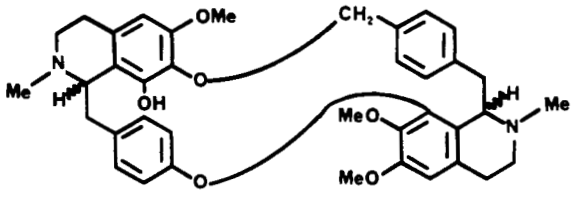
Type XIVa^c (*S*,−) 5,6,7*,11$^+$,12-5*,6,7,12$^+$



MP: Amorphous (41)
$[\alpha]D$: +7° (*c* = 0.17, MeOH) (41)
^1H NMR: NMe 2.22 (N-2); OMe 3.69 (C-6′), 3.91 (C-7′), 4.07 (C-6); ArH 5.18 (H-8), 5.79 (d, 1H, *J* = 1.8 Hz, H-10), 6.80 (dd, 1H, *J* = 1.8, 8.1 Hz, H-14), 6.85 (d, 1H, *J* = 8.1 Hz, H-13), 7.00 (br d), 2H, *J* = 7.8 Hz, H-11′ and H-13′), 7.05 (H-8′), 7.40 (br d, 2H, *J* = 7.8 Hz, H-10′ and H-14′) (41)
MS: $[M]^+$ 608 (100), 607 (94), 593 (10), 304 (9), 192 (20), 191 (10), 190 (18), 164 (11) (41)
Sources: *Thalictrum cultratum* Wall. (Ranunculaceae) (41)
Derivatives: 2′-Norcultithalmine (41) (cultithalminine + $NaBH_4$/MeOH (41)
$[\alpha]D$: −39° (*c* = 0.17, MeOH) (41)
^1H NMR: NMe 2.23 (N-2); OMe 3.67 (C-6′), 3.94 (C-7′), 4.05 (C-6); ArH 5.46 (H-8), 6.06 (d, 1H, *J* = 1.8 Hz, H-10), 6.85 (br s, 2H, H-13 and H-14), 6.87 (H-8′), 7.04 (br d, 2H, *J* = 7.7 Hz, H-11′ and H-13′), 7.41 (br d, 2H, *J* = 7.7 Hz, H-10′ and H-14′) (41)
MS: $[M]^+$ 610 (65), 609 (47), 411 (15), 397 (100), 383 (26), 199 (72), 192 (31), 191 (39), 190 (44), 176 (21) (41)

286 CYCLEANEONINE $C_{38}H_{42}O_6N_2$: 622.3043

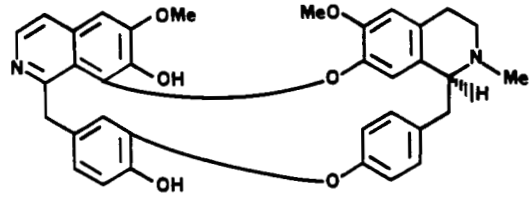
Type XXII 6,7,8,12*-6,7,8*,12[7-12]



MP: 96–97° (pentane) (81)
TLC: 0.48 [Basic Si gel G (C_6H_6-EtOAc-Et_2NH (7:2:0.5)] (81); 0.77 [High efficiency Si gel (cyclohexane-EtOAc-Et_2NH) (6:3:1)] (81)
$[\alpha]^{16}D$: +377° (c = 0.5, $CHCl_3$) (81)
UV(EtOH): 204 (4.92), 225 (sh) (4.62), 275 (3.62), 282 (sh) (3.54) (81)
IR(KBr): 3496, 2927, 2846, 2780, 1608, 1590, 1463, 1446, 1434, 1265, 1212, 1108, 1069, 1015, 835, 810 (81)
^{1}H NMR: NMe 2.22 (N-2), 2.38 (N-2'); OMe 3.71 (C-7'), 3.88 (6H, C-6 and C-6'); AlH 2.84 (m, 12H, ring CH_2), 4.02 (d, 2H, H-1 and H-1'), 4.99 (d, 1H, J = 13.6 Hz, 1 $ArCH_2$ proton), 5.19 (d, 1H, J = 13.6 Hz, 1 $ArCH_2$ proton), 6.17 (H-5), 6.57 (H-5'), 6.67 (d, 2H, J = 8.8 Hz, H-11 and H-13), 6.87 (d, 2H, J = 8.8 Hz, H-10 and H-14), 7.05 (d, 2H, J = 8.0 Hz, H-11' and H-13'), 7.21 (d, 2H, J = 8.0 Hz, H-10' and H-14') (81)
^{13}C NMR: 58.0 (d, C-1), 49.0 (t, C-3), 27.8 (t, C-4), 129.5 (s, C-4a), 103.0 (d, C-5), 151.8 (s, C-6), 141.7 (s, C-7), 144.8 (s, C-8), 116.8 (s, C-8a), 35.1 (t, C-α), 130.9 (s, C-9), 129.6 (d, C-10), 114.3 (d, C-11), 154.5 (s, C-12), 114.3 (d, C-13), 29.6 (d, C-14); 59.7 (d, C-1'), 44.3 (t, C-3'), 24.6 (t, C-4'), 129.5 (s, C-4'a), 108.6 (d, C-5'), 150.5 (s, C-6'), 140.4 (s, C-7'), 146.8 (s, C-8'), 125.9 (s, C-8'a), 39.4 (t, C-α), 132.6 (s, C-9'), 128.4 (d, C-10'), 128.4 (d, C-11'), 134.0 (s, C-12'), 128.4 (d, C-13'), 128.4 (d, C-14'); 42.3 (q, 2'-NMe), 43.6 (q, 2-NMe); 55.4 (q, 6-OMe), 55.9 (q, 6'-OMe), 60.7 (q, 7'-OMe) (81)
MS: $[M]^+$ 622, 519, 518, 312, 311, 208, 207, 206, 204, 190 (81)
CD: $[\theta]_{246}$ +33,588, $[\theta]_{277}$ −7,464 (81)
Sources: *Cyclea racemosa* Oliv. (Menispermaceae) (81)

287 DEHATRIDINE $C_{35}H_{32}O_6N_2$: 576.2260

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



MP: 274–276° (MeOH) (63)
$[\alpha]^{23}D$: +98° (c = 0.1, MeOH) (63)
UV(EtOH): 202 (4.4), 243 (4.2), 282 (3.4), 335 (3.2) (63); (EtOH + KOH) 207 (5.0), 263 (4.1), 293 (sh) (3.6), 373 (3.3) (63)
^{1}H NMR(DMSO-d_6): NMe 2.56 (N-2'); OMe 3.38 (C-6 or C-6'), 3.82 (C-6' or C-6); AlH 3.85 (d, 1H, J = 12.5 Hz, H-α), 4.66 (d, 1H, J = 12.5 Hz, H-α); ArH 5.92 (H-8'), 6.60 (d, 1H, J = 2 Hz, H-10), 6.62 (H-5'), 6.69 (d, 1H, J = 8.2 Hz, H-13), 6.82 (dd, 1H, J = 2, 8.2 Hz, H-10'), 6.84 (dd, 1H, J = 2, 8.2 Hz, H-14), 6.94 (dd, 1H, J = 2, 8.2 Hz, H-11'), 7.02 (H-5), 7.19 (dd, 1H, J = 8.2 Hz, H-13'), 7.43 (d, 1H, J = 5.48 Hz, H-4), 7.66 (dd, 1H, J = 2, 8.2 Hz, H-14'), 8.20 (d, 1H, J = 5.48 Hz, H-3); ArOH 8.65 (1H, D_2O exchangeable), 9.03 (1H, D_2O exchangeable) (63)
MS: $[M]^+$ 576 (100), 575 (92), 190 (30), 174 (60) (63)
Sources: *Dehaasia triandra* Merr. (Lauraceae) (63)
Derivatives: *O,O*-Dimethyldehatridine (dehatridine + CH_2N_2) (63)
$[\alpha]^{23}D$: +73° (c = 0.1, MeOH) (63)
^{1}H NMR: NMe 2.60 (N-2'); OMe 3.10 (C-7), 3.40 (C-6'), 3.83 (C-6), 3.87 (C-12); AlH 4.10 (d, 1H, J = 12 Hz, H-α), 5.00 (d, 1H, J = 12 Hz, H-α); ArH 5.97 (H-8'), 6.53 (H-5'), 6.64 (d, 1H, J = 8 Hz, H-13), 6.67 (d, 1H, J = 2 Hz, H-10), 6.80 (dd, 1H, J = 2, 8 Hz, H-10'), 6.86 (H-5), 6.87 (dd, 1H, J = 2, 8 Hz, H-14), 7.00 (dd, 1H, J = 2, 8 Hz, H-11'),

[c]This is a new class that supplements Class XIV as presented in the review of Guha *et al.* (1).

7.13 (dd, 1H, J = 2, 8 Hz, H-13'), 7.27 (d, 1H, J = 5 Hz, H-4), 7.50 (dd, 1H, J = 2, 8 Hz, H-14'), 8.30 (d, 1H, J = 5 Hz, H-3) (63)

MS: $[M]^+$ 604 (94), 603 (100), 302 (23) (63)

O,O-Diethyldehatridine (dehatridine + CH_3CHN_2) (63)

MP: 196–197° (Me_2CO) (63)

$[\alpha]^{22}D$: +106° (c = 0.1, MeOH) (63)

^1H NMR: NMe 2.60 (N-2'); OMe 3.37 (C-6'), 3.83 (C-6); OEt 0.97 (t, 3H, J = 8 Hz, C-7OCH$_2$*Me*), 1.47 (t, 3H, J = 8 Hz, C-12OCH$_2$*Me*), 3.60 (q, 2H, J = 8 Hz, C-7OC*H*$_2$Me), 4.13 (q, 2H, J = 8 Hz, C-12OC*H*$_2$Me); AlH 4.07 (d, 1H, J = 12 Hz, H-α), 4.97 (d, 1H, J = 12 Hz, H-α); ArH 5.97 (H-8'), 6.53 (H-5'), 6.63 (d, 1H, J = 8 Hz, H-13), 6.70 (d, 1H, J = 2 Hz, H-10), 6.77 (dd, 1H, J = 2, 8 Hz, H-10'), 6.90 (H-5), 6.93 (dd, 1H, J = 2, 8 Hz, H-14), 7.03 (dd, 1H, J = 2, 8 Hz, H-11'), 7.13 (dd, 1H, J = 2, 8 Hz, H-13'), 7.27 (d, 1H, J = 5.6 Hz, H-4), 7.53 (dd, 1H, J = 2, 8 Hz, H-14'), 8.33 (d, 1H, J = 5.6 Hz, H-3) (63)

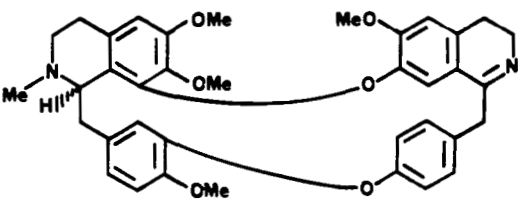
MS: $[M]^+$ 632 (100), 631 (98), 316 (30) (63)

Derivatives: Birch reduction (Na/NH_3) afforded racemic *O,O*-diethylcoclaurine + (+)-*N*-methylcoclaurine (63)

Attempted reduction of dehatridine with Na, Na/Hg, Zn + HOAc, Zn + H_2SO_4, Zn/Hg, $NaBH_4$, and Pd/C + H_2 all failed (63).

288 DEHATRINE $C_{37}H_{38}O_6N_2$: 606.2730

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



MP: 158–160° (EtOH) (63)

$[\alpha]^{27}D$: +27° (c = 1.0, $CHCl_3$) (63)

UV: 223 (4.5), 281 (3.8), 310 (3.5) (63)

IR(KBr): 1620 (63)

^1H NMR: NMe 2.46 (N-2'); OMe 3.51 (3H, 3.70 (3H, 3.91 (6H); AlH 4.12 (d, 1H, J = 2 Hz, H-α), 5.32 (d, 1H, J = 2 Hz, H-α); ArH 6.05 (H-8'), 6.63 (H-5), 6.66–6.88 (m, 3H), 7.01 (d, 2H, J = 8 Hz, H-11' and H-13'), 7.35 (d, 2H, J = 8 Hz, H-10' and H-14') (63)

MS: $[M]^+$ 606 (100), 605 (70), 591 (35), 303 (68), 280 (15), 204 (20), 155 (15), 141 (45) (63)

Sources: *Dehaasia triandra* Merr. (Lauraceae) (63)

Derviatives: Racemic 1',2'-Dihydrodehatrine (dehatrine + $NaBH_4$/MeOH) (63)

$[\alpha]^{23}D$: −23° (c = 0.1, MeOH) (63)

UV: 228 (4.6), 280 (3.6) (63)

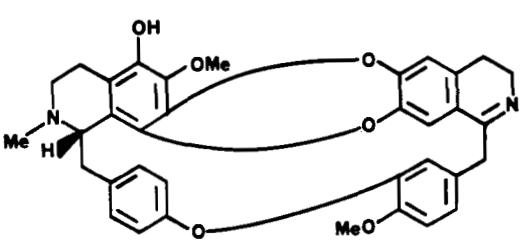
^1H NMR: NMe 2.30 (N-2); OMe 3.20, 3.63, 3.73, 3.90; ArH 6.00 (H-8'), 6.27 (H-5'), 6.50((H-5), 6.63–7.25 (m, 7H) (63)

Isotetrandrine [**62**] + phaeanthine [**74**] (racemic 1',2'-dihydrodehatrine + CH_2O/$NaBH_4$)

Birch reduction (Na/NH_3) of dehatrine afforded (−)-*O*-methylarmepavine + racemic coclaurine (63).

289 1',2'-DEHYDROKOHATAMINE $C_{35}H_{32}O_6N_2$: 576.2260

Type XXIIIa (S,−) 5,6,7*,8$^+$,12*-6*,7$^+$,11*,12

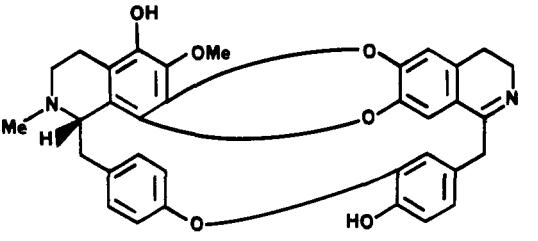


$[\alpha]^{25}D$: +100° (c = 0.09, $CHCl_3$) (33)

UV: 236 (4.55), 274 (4.14), 283 (4.13), 305 (4.08) (33)

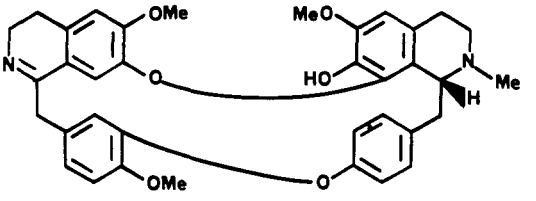
^{1}H NMR: NMe 2.56 (N-2); OMe 3.90 (C-12'), 3.94 (C-6); AlH 4.02 (H-1); ArH 6.57 (H-8'), 6.59 (H-5'), 6.61 (d, 1H, J = 1.8 Hz, H-10'), 6.74 (dd, 1H, J = 2.2, 8.2 Hz, H-11), 6.84 (d, 1H, J = 8.2 Hz, H-13'), 6.92 (d, 1H, J = 2.2, 8.2 Hz, H-10), 6.97 (dd, 1H, J = 1.8, 8.2 Hz, H-14'), 7.20 (dd, 1H, J = 2.2, 8.2 Hz, H-13), 7.38 (dd, 1H, J = 2.2, 8.2 Hz, H-14) (33)
MS: $[M]^+$ 576 (85), 575 (100), 561 (7), 559 (7), 288 (5) (33)
Sources: *Cocculus pendulus* (Forsk.) Diels (Menispermaceae) (33)
Derivatives: (+)-5-Hydroxytelobine [**310**] (1',2'-dehydrokohatamine + $NaBH_4$/MeOH) (33)

290 1',2'-DEHYDROKOHATINE $C_{34}H_{30}O_6N_2$: 562.2104
Type XXIIIa (S,−) 5,6,7*,8$^+$,12$^\#$-6*,7$^+$,11$^\#$,12



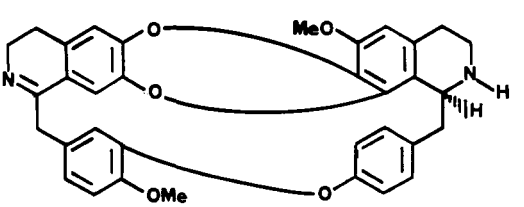
$[\alpha]^{25}$D: +53° (c = 0.08, $CHCl_3$) (33)
UV: 235 (sh) (4.45), 259 (4.29), 287 (sh) (3.85), 347 (3.47) (33)
^{1}H NMR: NMe 2.56 (N-2); OMe 3.95 (C-6); AlH 4.02 (H-1); ArH 6.53 (H-8'), 6.55 (d, 1H, J = 1.8 Hz, H-10'), 6.59 (H-5'), 6.72 (dd, 1H, J = 2.2, 8.2 Hz, H-11), 6.84 (d, 1H, J = 8.2 Hz, H-13'), 6.91 (dd, 1H, J = 1.8, 8.2 Hz, H-14'), 6.94 (dd, 1H, J = 2.2, 8.2 Hz, H-10), 7.21 (dd, 1H, J = 2.2, 8.2 Hz, H-13), 7.41 (dd, 1H, J = 2.2, 8.2 Hz, H-14) (33)
MS: $[M]^+$ 562 (75), 561 (100), 547 (6), 545 (6), 281 (11) (33)
Sources: *Cocculus pendulus* (Forsk.) Diels (Menispermaceae) (33)
Derivatives: (+)-5-Hydroxyapateline [**309**] (1',2'-dehydrokohatine + $NaBH_4$/MeOH) (33)

291 1,2-DEHYDRO-2-NORLIMACUSINE $C_{36}H_{36}O_6N_2$: 592.2573
Type VI (−,R) 6,7*,11$^+$,12-6,7,8*,12$^+$



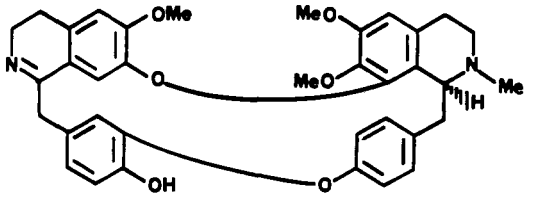
[α]D: +94° (c = 0.16, MeOH) (19)
^{1}H NMR: NMe 2.56 (N-2'); OMe 3.49 (C-6), 3.79 (C-6'), 3.92 (C-12); AlH 4.01 (m, 1H, H-1'), 4.52 (d); ArH 6.36 (br s, 1H, H-10), 6.38 (H-5'), 6.39 (H-5), 6.74 (H-8), 6.86 (m, H-13, H-14, H-11', H-13'), 6.94 (dd, 1H, J = 2.2, 8 Hz, H-10'), 7.34 (dd, 1H, J = 2.2, 8 Hz, H-14') (19)
MS: $[M]^+$ 592 (100), 591 (50), 590 (45), 560 (45), 486 (20), 296 (16), 204 (16), 202 (20), 190 (23), 189 (31), 160 (14) (19)
Sources: *Caryomene olivascens* Barneby et Krukoff (Menispermaceae) (19)
Derivatives: (−)-2-Norlimacusine [**245**] (1,2-dehydro-2-norlimacusine + $NaBH_4$) (19)

292 1,2-DEHYDRO-2'-NORTELOBINE $C_{34}H_{30}O_5N_2$: 546.2155
Type XXIII (−,S) 6*,7$^+$,11$^\#$,12-6,7*,8$^+$,12$^\#$



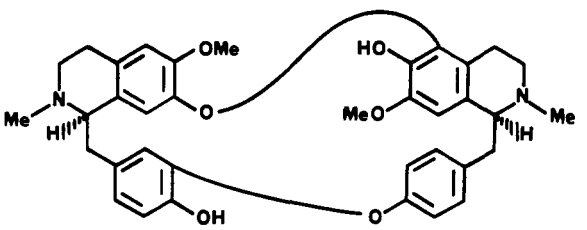
$[\alpha]^{25}D$: +100° (c = 0.15, $CHCl_3$) (33)
UV: 229 (4.45), 265 (sh) (4.06), 294 (sh) (3.73), 335 (3.51) (33)
^1H NMR: OMe 3.89 (C-6'), 3.91 (C-12); AlH 4.43 (H-1'); ArH 6.41 (H-5'), 6.56 (H-8), 6.57 (d, 1H, J = 1.8 Hz, H-10), 6.64 (H-5), 6.77 (dd, 1H, J = 2.2, 8.2 Hz, H-11'), 6.85 (d, 1H, J = 8.2 Hz, H-13), 6.88 (dd, 1H, J = 2.2, 8.2 Hz, H-10'), 6.98 (dd, 1H, J = 1.8, 8.2 Hz, H-14), 7.19 (dd, 1H, J = 2.2, 8.2 Hz, H-13'), 7.47 (dd, 1H, J = 2.2, 8.2 Hz, H-14') (33)
MS: $[M]^+$ 546 (73), 545 (100), 332 (2), 273 (16) (33)
Sources: *Cocculus pendulus* (Forsk.) Diels (Menispermaceae) (33)

293 12-*O*-DEMETHYLCOCLOBINE $C_{36}H_{36}O_6N_2$: 592.2573
Type VI (−,*S*) 6,7*,11$^+$,12-6,7,8*,12$^+$



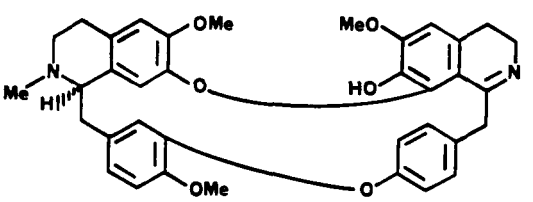
$[\alpha]^{20}D$: +220° (c = 0.25, $CHCl_3$) (59)
UV: 228 (3.22), 274 (4.20), 281 (3.80); (MeOH + H^+) 305 (3.60), 344 (3.58); (MeOH + NaOH) 234, 305, 381 (59)
^1H NMR: NMe 2.60 (N-2'); OMe 3.17 (C-7'), 3.51 (C-6), 3.80 (C-6'); AlH 2.85 (1H, H-4), 3.70 (m, 3H, H-1' and H-3 and H-4), 4.70 (1H, H-3); ArH 6.42 (H-5'), 6.48 (H-5), 6.69 (dd, 1H, J = 1.7, 8.4 Hz, H-13'), 6.84 (dd, 1H, J = 1.7, 8.4 Hz, H-10'), 6.92 (d, 1H, J = 8 Hz, H-13), 6.97 (d, 1H, J = 1.8 Hz, H-13), 7.06 (dd, 1H, J = 1.8, 8 Hz, H-14), 7.08 (dd, 1H, J = 1.7, 8.4 Hz), 7.17 (H-8), 7.35 (dd, 1H, J = 1.7, 8.4 Hz, H-14') (59)
MS: $[M]^+$ 592 (62), 591 (100), 577 (9), 561 (4), 545 (9), 485 (16), 439 (4), 408 (2), 377 (7) (59)
Sources: *Guatteria guianensis* (Aublet) R.E. Fries (Annonaceae) (59)
Derivatives: Coclobine [**35**] (12-*O*-demethylcoclobine + CH_2N_2) (59)
(−)-Demerarine [**39**] and (+)-Sepeerine [**50**] (12-*O*-demethylcoclobine + $NaBH_4$/MeOH) (59)

294 12-*O*-DESMETHYLLAUBERINE $C_{36}H_{38}O_6N_2$: 594.2730
Type XIV (*R*,*S*) 6,7*,11$^+$,12-5*,6,7,12$^+$



MP: Amorphous (65)
$[\alpha]^{20}D$: −334° (c = 0.5, MeOH) (65)
UV: 283 (3.82) (65)
^1H NMR: NMe 2.38 (N-2'), 2.66 (N-2); OMe 3.93 (C-6), 3.96 (C-7'); ArH 6.07 (H-8), 6.10 (s, 1H, H-10), 6.13 (H-8'), 6.64 (H-5), 6.83 (s, 2H, H-13 and H-14), 6.86 (d, 2H, J = 8 Hz, H-11' and H-13'), 7.17 (d, 2H, H-10' and H-14') (65)
MS: $[M]^+$ 594 (60), 382 (25), 381 (84) (65)
Sources: *Berberis chilensis* Gill. ex Hook (Berberidaceae) (65)

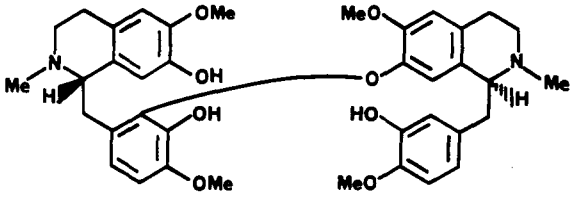
295 3',4'-DIHYDROSTEPHASUBINE $C_{36}H_{36}O_6N_2$: 592.2573
Type VI (*R*,−) 6,7*,11$^+$,12-6,7,8*,12$^+$



MP: Amorphous (49)
$[\alpha]^{25}D$: +286° (MeOH) (49)
UV(EtOH): 216, 223, 283 (49); (EtOH + OH^-) 223; (EtOH + H^+) 216, 284, 338 (49)
IR: 3675, 3610, 3525, 1605, 1510, 1460 (49)
^1H NMR: NMe 2.51 (N-2); OMe 3.88, 3.91, 3.95; AlH 3.59 (br s, 1H, H-1), 4.08 (1H, J = 14.0 Hz, H-α'), 4.52 (1H, J = 14.0 Hz, H-α'); ArH 4.91 (br s, 1H, H-10), 6.08 (H-8), 6.48 (dd, 1H, J = 2.0, 8.2 Hz, H-11'), 6.51 (H-5), 6.60 (H-5'), 6.73 (d, 1H, J = 8.3 Hz, H-13), 6.77 (dd, 1H, J = 2.0, 8.2 Hz, H-13'), 6.84 (dd, 1H, J = 1.0, 8.3 Hz, H-14), 7.36 (dd, 1H, J = 2.0, 8.2 Hz, H-10'), 7.40 (dd, 1H, J = 2.0, 8.2 Hz, H-14') (decoupling used) (49)
MS: $[M]^+$ 592 (38), 591 (100) (49)
Sources: *Stephania hernandifolia* Walp. (Menispermaceae) (49)
Derivatives: Epistephanine [**40**] (3',4'-dihydrostephasubine + CH_2N_2) (^1H nmr, tlc) (49)

296 EFATINE $C_{38}H_{44}O_8N_2$: 656.3097

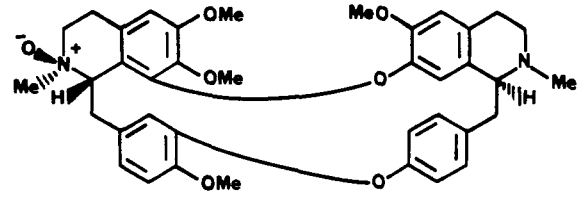
Type Vb[d] (*S,S*) 6,7,10*,11,12-6,7*,11,12



MP: Amorphous (68)
$[\alpha]D$: +70° (*c* = °0.86, $CHCl_3$) (68)
UV: 227, 282 (68), with a bathochromic shift in alkali (68)
^1H NMR: NMe 2.38 (N-2'), 2.46 (N-2); ArH 5.98 (H-8), 6.13 (H-8'), 6.42 (H-10'), 6.49 (H-14'), 6.52 (H-13), 6.53 (H-5), 6.57 (H-14), 6.62 (H-13'), 6.68 (H-5') (nOe used) (68)
MS: $[M]^+$ 656 (0.1), 519 (8), 192 (100) (68)
Sources: *Hernandia peltata* Meissner (Hernandiaceae) (68)
Derivatives: *O,O,O*-Trimethylefatine (efatine + CH_2N_2) (68)
^1H NMR: NMe 2.40, 2.43; OMe 3.59 (C-7), 3.71 (C-6), 3.73 (C-6'), 3.80 (C-11), 3.83 (C-12), 3.90 (6H, C-11' and C-12'); ArH 5.96 (s, 1H, H-8), 6.10 (s, 1H, H-8'), 6.51 (s, 1H, H-5), 6.53 (s, 1H, H-5'), 6.58 (d, 1H, J = 8.2 Hz), 6.60 (d, 1H, J = 8.2 Hz) (68)
MS: $[M]^+$ 698 (0.1), 548 (18), 206 (100) (68)
Triacetylefatine (68)

297 FENFANGJINE A (Tetrandrine-2β-*N*-oxide) $C_{38}H_{42}O_7N_2$: 638.2992

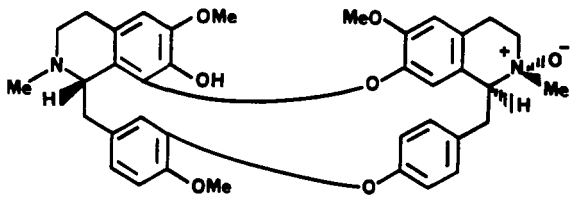
Type VIII (*S,S*) 6,7,8*,11^+,12-6,7*,12^+



MP: 174–176° (Me_2CO) (52)
$[\alpha]^{21}D$: +328° (*c* = 1.043, $CHCl_3$) (52)
^1H NMR: NMe 2.62 (N-2'), 3.08 (N-2); OMe 3.14 (C-7), 3.43 (C-6'), 3.76 (C-6), 3.95 (C-12); AlH 4.91 (d, 1H, J = 9.8 Hz, H-1); ArH 5.92 (H-8'), 6.39 (H-5), 6.43 (dd, 1H, J = 2.0, 8.3 Hz, H-10'), 6.50 (H-5'), 6.68 (dd, 1H, J = 2.0, 8.1 Hz, H-14), 6.78 (d, 1H, J = 2.0 Hz, H-10), 6.84 (d, 1H, J = 8.1 Hz, H-13), 6.92 (dd, 1H, J = 2.4, 8.3 Hz, H-11'), 6.99 (dd, 1H, J = 2.4, 8.3 Hz, H-13'), 7.34 (dd, 1H, J = 2.0, 8.3 Hz, H-14') (52)
MS: $[M]^+$ 638, 622, 395, 381, 198 (52)
Sources: *Stephania tetrandra* S. Moore (Menispermaceae) (52)

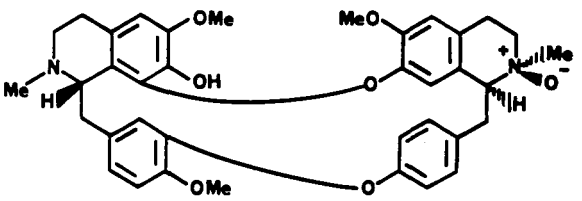
[d]This is a new class that supplements Class V as presented in the review of Guha *et al.* (1).

298 FENFANGJINE B (Fangchinoline-2′α-*N*-oxide) $C_{37}H_{40}O_7N_2$: 624.2836
Type VIII (*S,S*) 6,7,8*,11$^+$,12-6,7*,12$^+$



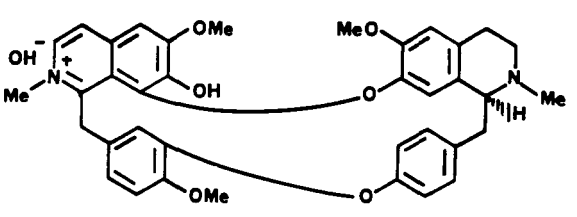
MP: 211–213° (EtOH) (52)
[α]D: +243° (*c* = 0.640, $CHCl_3$) (52)
^{1}H NMR($CDCl_3 + CD_3OD$): NMe 2.32 (N-2), 3.34 (N-2′); OMe 3.34 (C-6′), 3.71 (C-6), 3.92 (C-12); AlH 4.44 (dd, 1H, *J* = 11.5 Hz, H-1′); ArH 6.08 (H-8′), 6.24 (dd, 1H, *J* = 2.0, 8.3 Hz, H-10′), 6.26 (H-5), 6.56 (d, 1H, H-10), 6.81 (dd, 1H, *J* = 2.4, 8.3 Hz, H-11′), 6.87 (m, 2H, H-13 and H-14), 7.15 (dd, 1H, *J* = 2.4, 8.3 Hz, H-13′), 7.30 (dd, 1H, *J* = 2.0, 8.3 Hz, H-14′) (52)
MS: [M]$^+$ 624, 608, 381, 191 (52)
Sources: *Stephania tetrandra* S. Moore (Menispermaceae) (52)
Derivatives: Tetrandrine-2′α-*N*-oxide (via methylation of fenfangjine B) (52)

299 FENFANGJINE C (Fangchinoline-2′β-*N*-oxide) $C_{37}H_{40}O_7N_2$: 624.2836
Type VIII (*S,S*) 6,7,8*,11$^+$,12-6,7*,12$^+$



MP: 165–166° (EtOH) (52)
[α]D: +239° (*c* = 0.630, MeOH) (52)
^{1}H NMR: NMe 2.39 (N-2), 2.94 (N-2′); OMe 3.37 (C-6′), 3.78 (C-6), 3.88 (C-12); AlH 4.72 (dd, 1H, *J* = 11.5 Hz, H-1′); ArH 6.18 (H-8′), 6.22 (dd, 1H, *J* = 2.0, 8.3 Hz, H-10′), 6.32 (H-5), 6.56 (H-5′), 6.77 (d, 1H, *J* = 2.0 Hz, H-10), 6.77 (dd, 1H, *J* = 2.4, 8.3 Hz, H-11′), 6.85 (d, 1H, *J* = 8.3 Hz, H-13), 6.92 (dd, 1H, *J* = 2.0, 8.3 Hz, H-14), 6.96 (dd, 1H, *J* = 2.4, 8.3 Hz, H-13′), 7.43 (dd, 1H, *J* = 2.0, 8.3 Hz, H-14′) (52)
MS: [M]$^+$ 624, 608, 381, 191 (52)
Sources: *Stephania tetrandra* S. Moore (Menispermaceae) (52)
Derivatives: Tetrandrine-2′β-*N*-oxide (via methylation of fenfangjine C) (52)

300 FENFANGJINE D (1,3,4-Tridehydrofangchinolinium hydroxide) $C_{37}H_{37}O_6N_2$: 605.2652
Type VIII (−,*S*) 6,7,8*,11$^+$,12-6,7*,12$^+$

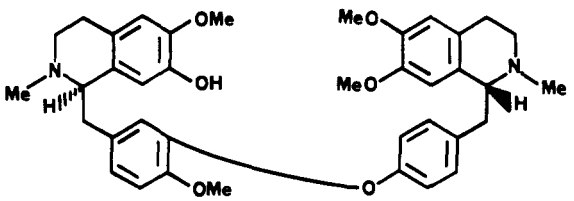


MP: Orange amorphous powder (52); HCl salt, >300° (MeOH) (Me_2CO) (52)
[α]D: (HCl salt) +68° (*c* = 0.116, MeOH) (52)
^{1}H NMR: NMe 2.52 (N-2′), 4.31 (N-2); OMe 3.24 (C-6′), 3.84 (C-6), 3.88 (C-12); AlH 4.32 (d, 1H, *J* = 16 Hz, H-α), 5.53 (d, 1H, *J* = 16 Hz, H-α); ArH 6.05 (H-8′), 6.51 (d-like, 1H, H-10′), 6.53 (H-5), 6.61 (d, 1H, *J* = 2.0 Hz, H-10), 6.70 (d-like, 1H, H-14), 6.85 (d-like, 1H, H-11), 6.86 (d, 1H, *J* = 8.3 Hz, H-13), 7.03 (d-like, 1H, H-13′), 7.05 (H-5′), 7.49 (d-like, 1H, H-14′), 7.75 (d, 1H, *J* = 6.6 Hz, H-4), 7.86 (d, 1H, *J* = 6.6 Hz, H-3) (52)
^{13}C NMR: 121.0 (d, C-4), 127.0 (d, C-3), 150.1 (s, C-1) (52)

FDMS: $[M]^+$ 605 (52)
Sources: *Stephania tetrandra* S. Moore (Menispermaceae) (52)
Preparation: Via the oxidation (MnO_2/EtOH) of fangchinoline [**61**] (52)

301 GERALDOAMINE $C_{37}H_{42}O_6N_2$: 610.3043

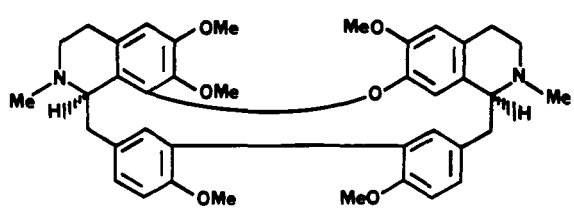
Type I (*R,R*) 6,7,11*,12-6,7,12*



MP: Amorphous (71)
$[\alpha]_D$: $-65°$ ($c = 0.1$, MeOH) (71)
UV: 227 (4.24), 285 (3.80); (MeOH + OH^-) 227 (4.24), 285 (3.83), 303 (3.28) (71)
^{1}H NMR: NMe 2.47 (N-2); OMe 3.78 (C-12 or C-6 or C-6′ or C-7′), 3.80 (C-7′ or C-6′ or C-6 or C-12), 3.83 (s, 6H, C-6 + C-12 or C-6 + C-6′ or C-6 + C-7′ or C-6′ + C-7′ or C-6′ + C-12 or C-7′ + C-12); ArH 6.30 (H-8′), 6.48 (H-8), 6.59 (H-5), 6.62 (H-5′), [6.49 (H-10) + 6.87 (H-13 + H-14) − ABX system], [6.86 (H-11 + H-13) + 7.27 (H-10 + H-14) − A_2B_2 system] (71)
EIMS: 419 (0.1), 192 (100) (71)
CIMS: $[M + 1]^+$ 611 (9), 419 (13), 192 (100), 178 (12) (71)
CD: 0 (310), −4.7 (288), 0 (276), 0.6 (251), 0 (247), −23 (228) (71)
Sources: *Aristolochia gigantea* Mart. (Aristolochiaceae) (71)

302 GRANJINE $C_{39}H_{44}O_6N_2$: 636.3199

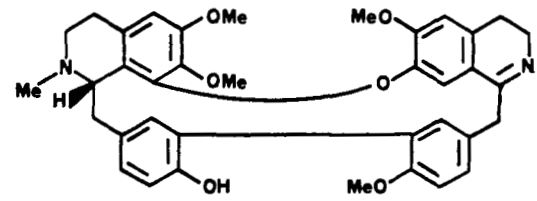
Type IV (*R,S*) 6,7,8*,12-6,7*,12(11-11)



MP: Amorphous (79)
$[\alpha]^{20}_D$: $-63°$ ($c = 0.6$, $CHCl_3$) (79)
UV: 211 (4.61), 238 (sh) (4.28), 284 (3.92) (79)
^{1}H NMR: Stable Conformer "a": NMe 2.31 (N-2), 2.60 (N-2′); OMe 3.50 (C-6′), 3.74 (C-12), 3.78 (C-6), 3.81 (C-12′); AlH 3.55 (m, 1H, H-1′), 4.26 (m, 1H, H-1); ArH 6.16 (d, 1H, $J = 2.2$ Hz, H-10′), 6.33 (H-5), 6.33 (H-8′), 6.57 (H-5′), 6.72 (d, 1H, $J = 8.5$ Hz, H-13), 6.90 (d, 1H, $J = 8.5$ Hz, H-13′), 7.10 (dd, 1H, $J = 2.2$, 8.5 Hz, H-14), 7.21 (dd, 1H, $J = 2.2$, 8.5 Hz, H-14′), 7.66 (d, 1H, $J = 2.2$ Hz, H-10), (nOe used) (79)
Stable Conformer "b": NMe 2.42 (N-2), 2.67 (N-2′); OMe 3.45 (C-6′), 3.71 (C-12′), 3.76 (C-12), 3.80 (C-6); AlH 3.90 (m, 1H, H-1); ArH 6.26 (H-5), 6.33 (H-5′), 6.60 (d, 1H, $J = 2.2$ Hz, H-10), 6.68 (d, 1H, $J = 8.5$ Hz, H-13′), 6.78 (d, 1H, $J = 8.5$ Hz, H-13), 6.75 (d, 1H, $J = 2.2$ Hz, H-10′), 7.08 (H-8′), 7.19 (dd, 1H, $J = 2.2$, 8.5 Hz, H-14′), 7.27 (dd, 1H, $J = 2.2$, 8.5 Hz, H-14) (nOe used) (79)
^{1}H NMR(pyridine-d_5): 21°C: NMe 2.28 (N-2) and 2.45 (N-2); 2.58 (N-2′) and 2.60 (N-2′); 3.32 (C-7) and 3.43 (C-7) and 3.48 (C-6′) and 3.54 (C-6′), 3.57 (C-12), 3.72 (C-6), 3.74 (C-12′); ArH 6.35–7.67 (9H) (79)
90°C: NMe 2.49 (N-2), 2.64 (N-2′); OMe 3.44 (C-7), 3.55 (C-6′), 3.66 (C-12), 3.76 (C-6), 3.78 (C-12′); ArH 6.30–7.45 (9H) (79)
MS: $[M]^+$ 636 (27), 635 (16), 621 (3), 396 (21), 395 (54), 381 (17), 199 (30), 198 (100), 175 (34), 174 (30) (79)
CD: 0 (310), −10.4 (282), −30.0 (246), 0 (235), +22 (227) (79)
Sources: *Crematosperma* sp. (Annonaceae) (79)

303 GUATTAMINE $C_{37}H_{40}O_6N_2$: 608.2886

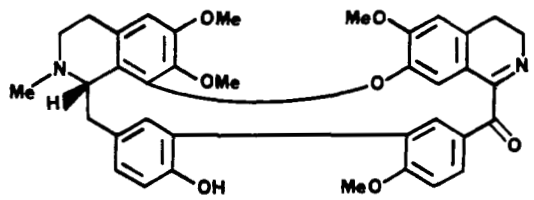
Type IV (*S*,−) 6,7,8*,12-6,7*,12(11-11)



[α]D: +142° (*c* = 0.67, $CHCl_3$) (51)
UV: 213 (4.58), 282 (3.76), 296 (3.70) (51); (MeOH + H^+) 213 (4.55), 298 (3.71), 346 (3.70) (51)
^{1}H NMR: NMe 2.32 (N-2); OMe 3.48 (C-7), 3.56 (C-6'), 3.84 (C-6), 3.92 (C-12'); AlH 4.21 (H-1); ArH 6.43 (H-5), 6.53 (H-5'), 6.86 (H-13'), 6.87 (H-13), 7.19 (H-14), 7.33 (H-14'), 7.58 (H-10), 7.60 (H-10'), 7.77 (H-8') (nOe used) (51)
MS: $[M]^+$ 606 (94), 605 (100), 379 (2), 303 (13), 190 (7) (51)
Sources: *Guatteria guianensis* (Aublet) R.E. Fries (Annonaceae) (51)
Derivatives: (+)-2'-Norguattaguianine [**332**] + (+)-2'-norfuniferine [**331**] in a 70:30 ratio (guattamine + $NaBH_4$/MeOH) (51)

304 GUATTAMINONE $C_{37}H_{36}O_7N_2$: 620.2523

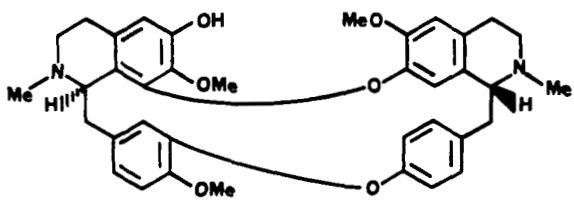
Type IV (*S*,−) 6,7,8*,12-6,7*,12(11-11)



[α]D: +78° (*c* = 0.26, $CHCl_3$) (51)
UV: 235 (sh) (4.20), 290 (3.80) (51); (MeOH + H^+) 235 (4.20), 290 (3.80), 360 (3.70) (51)
IR: 1660 (51)
^{1}H NMR: NMe 2.25 (N-2); OMe 3.51 (C-7), 3.55 (C-6'), 3.83 (C-6), 4.05 (C-12'); AlH 4.28 (H-1); ArH 6.42 (H-5), 6.66 (H-5'), 6.84 (H-13), 7.09 (H-14), 7.16 (H-13'), 7.31 (H-8'), 7.35 (H-10), 7.66 (H-10'), 8.36 (H-14') (nOe used) (51)
MS: $[M]^+$ 620 (67), 619 (92), 618 (100), 617 (81), 604 (22), 603 (41), 381 (26), 189 (27) (51)
Sources: *Guatteria guianensis* (Aublet) R.E. Fries (Annonaceae) (51)

305 GYROAMERICINE $C_{37}H_{40}O_6N_2$: 608.2886

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

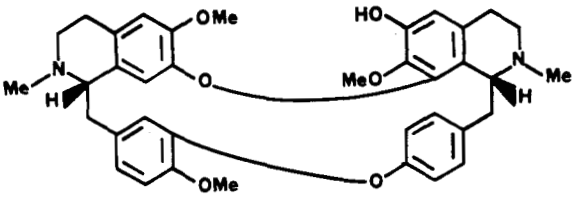


MP: 210° (MeOH) (15)
[α]D: −238° (*c* = 1, $CHCl_3$) (15)
UV: 241 (4.30), 282 (3.84) (15)
^{1}H NMR: NMe 2.30 (N-2), 2.64 (N-2'); OMe 3.32 (C-7), 3.37 (C-6'), 3.94 (C-12); ArH 5.99 (H-8'), 6.35 (H-10'), 6.39 (H-5), 6.53 (H-10), 6.56 (H-5'), 6.84 (H-11'), 6.87 (H-13, H-14), 7.17 (H-13'), 7.37 (H-14') (15)
MS: $[M]^+$ 608 (28), 607 (18), 593 (4), 382 (28), 381 (100), 380 (31), 367 (18), 191 (17), 190.5 (68), 190 (5), 189.5 (31), 175 (8), 174 (10), 169 (23) (15)
Sources: *Gyrocarpus americanus* Jacq. (Hernandiaceae) (15)
Derivatives: Phaeanthine [**74**] (gyroamericine + CH_2N_2) (15)

306 GYROCARPINE

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

Type VI 6,7*,11$^+$,12-6,7,8*,12$^+$

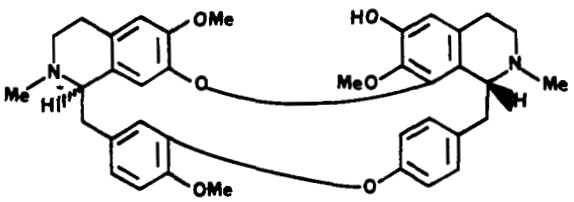


MP: 192° (Et_2O/MeOH) (15)
$[\alpha]_D$: −239° ($c = 1$, $CHCl_3$) (15)
UV: 239 (sh) (4.34), 284 (3.87) (15)
^{1}H NMR: NMe 2.56 (N-2), 2.66 (N-2'); OMe 3.25 (C-7'), 3.59 (C-6), 3.89 (C-12); ArH 5.48 (H-10), 6.35 (H-5, H-5'), 6.44 (H-11'), 6.71 (H-8), 6.77 (H-13, H-14), 6.90 (H-10'), 6.95 (H-13'), 7.39 (H-14') (15)
MS: $[M]^+$ 608 (47), 607 (30), 593 (5), 502 (1), 501 (4), 382 (26), 381 (100), 367 (21), 191 (21), 190 (82), 175 (11), 174 (36) (15)
Sources: *Gyrocarpus americanus* Jacq. (Hernandiaceae) (15)
Derivatives: Gyrolidine [**308**] (gyrocarpine + CH_2N_2) (15)

307 GYROCARPUSINE

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

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

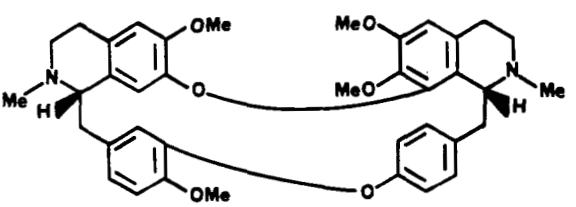


MP: Amorphous (15)
$[\alpha]_D$: +66° ($c = 1$, $CHCl_3$) (15)
UV: 234 (4.42), 283 (3.85) (15)
^{1}H NMR: NMe 2.52 (N-2), 2.58 (N-2'); OMe 3.25 (C-7'), 3.38 (C-6), 3.96 (C-12); ArH 6.46 (H-5), 6.47 (H-5'), 6.48 (H-8), 6.72 (H-10), 6.85 (H-10', H-11'), 6.92 (H-14), 6.97 (H-13), 7.16 (H-13'), 7.38 (H-14') (15)
MS: $[M]^+$ 608 (43), 607 (10), 593 (6), 502 (2), 501 (4), 382 (28), 381 (100), 379 (26), 367 (23), 192 (16), 191 (69), 190 (26), 174 (32), 168 (24) (15)
Sources: *Gyrocarpus americanus* Jacq. (Hernandiaceae) (15)
Derivatives: *O*-Methyllimacusine [**320**] (gyrocarpusine + CH_2N_2) (15)

308 GYROLIDINE

$C_{38}H_{42}O_6N_2$: 622.3043

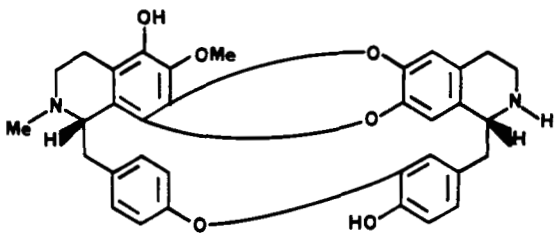
Type VI (*S,R*) 6,7*,11$^+$,12-6,7,8*,12$^+$



MP: Amorphous (15)
$[\alpha]_D$: −115° ($c = 1.1$, $CHCl_3$) (15)
UV: 261 (4.23), 282 (4.12) (15)
^{1}H NMR: NMe 2.57 (N-2), 2.66 (N-2'); OMe 3.19 (C-7'), 3.63 (C-6), 3.79 (C-6'), 3.89 (C-12); ArH 5.47 (H-10), 6.32 (H-5'), 6.36 (H-5), 6.37 (H-11'), 6.65 (H-8), 6.78 (H-13, H-14), 6.95 (H-13'), 7.42 (H-14') (15)
MS: $[M]^+$ 622 (86), 621 (72), 607 (14), 606 (14), 605 (20), 592 (4), 396 (28), 395 (100), 381 (55), 349 (22), 198 (71), 175 (25), 174 (64) (15)
Sources: *Gyrocarpus americanus* Jacq. (Hernandiaceae) (15)

309 5-HYDROXYAPATELINE $C_{34}H_{32}O_6N_2$: 564.2260

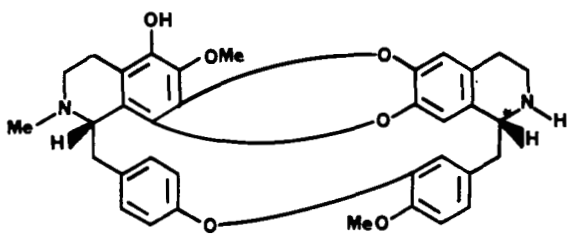
Type XXIIIa (*S,R*) 5,6,7*,8$^+$,12$^{\#}$-6*,7$^+$,11$^{\#}$,12



$[\alpha]^{25}D$: +185° (c = 0.07, MeOH) (33)
UV: Same as (+)-kohatine [**236**] (33)
^{1}H NMR: NMe 2.57 (N-2); OMe 3.96 (C-6); AlH 4.03 (H-1), 4.04 (H-1′); ArH 6.32 (H-8′), 6.33 (d, 1H, J = 1.8 Hz, H-10′), 6.44 (H-5′), 6.70 (dd, 1H, J = 2.2, 8.2 Hz, H-11), 6.76 (dd, 1H, J = 1.8, 8.2 Hz, H-14′), 6.80 (dd, 1H, J = 2.2, 8.2 Hz, H-10), 6.84 (d, 1H, J = 8.2 Hz, H-13′), 7.05 (dd, 1H, J = 2.2, 8.2 Hz, H-13), 7.36 (dd, 1H, J = 2.2, 8.2 Hz, H-14) (33)
MS: Same as (+)-kohatine [**236**] (33)
Sources: *Cocculus pendulus* (Forsk.) Diels (Menispermaceae) (33)

310 5-HYDROXYTELOBINE $C_{35}H_{34}O_6N_2$: 578.2417

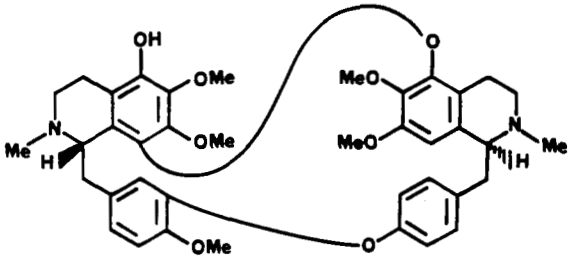
Type XXIIIa (*S,R*) 5,6,7*,8$^+$,12$^{\#}$-6*,7$^+$,11$^{\#}$,12



$[\alpha]^{25}D$: +154° (c = 0.11, $CHCl_3$) (33)
UV: Same as kohatamine [**314**] (33)
^{1}H NMR: NMe 2.60 (N-2); OMe 3.90 (C-12′), 3.96 (C-6); AlH 4.02 (H-1 and H-1′); ArH 6.34 (d, 1H, J = 1.8 Hz, H-10′), 6.37 (H-8′), 6.44 (H-5′), 6.64 (d, 1H, J = 2.2, 8.2 Hz, H-11), 6.80 (d, 1H, J = 2.2, 8.2 Hz, H-10), 6.82 (d, 1H, J = 8.2 Hz, H-13′), 6.82 (dd, 1H, J = 1.8, 8.2 Hz, H-14′), 7.03 (dd, 1H, J = 2.2, 8.2 Hz, H-13), 7.36 (dd, 1H, J = 2.2, 8.2 Hz, H-14) (33)
MS: Same as kohatamine [**314**] (33)
Sources: *Cocculus pendulus* (Forsk.) Diels (Menispermaceae) (33)

311 5-HYDROXYTHALIDASINE $C_{39}H_{44}O_8N_2$: 668.3098

Type XIIa[c] (*S,S*) 5,6,7,8*,11$^+$,12-5*,6,7,12$^+$



MP: Amorphous (24)
$[\alpha]D$: −51° (c = 0.1, MeOH) (24)
UV: 237 (sh) (4.20), 282 (3.54) (24)

[c]This is a new class that supplements Class XII as mentioned in the review of Guha *et al.* (1).

^{1}H NMR: NMe 2.25 (N-2), 2.62 (N-2′); OMe 3.35 (C-7), 3.52 (C-6′), 3.79 (C-6), 3.89 (C-7′), 3.90 (C-12); AlH 2.13 (m, 1H, H-4′), 2.32 (m, 1H, H-4′), 2.51 (m, 1H, H-4), 2.66 (m, 1H, H-α), 2.72 (m, 1H, H-α′), 2.74 (m, 1H, H-4), 3.04 (m, 1H, H-α), 3.22 (m, 1H, H-α′), 3.81 (m, 1H, H-1), 3.88 (m, 1H, H-1′); ArH 6.30 (br s, 1H, H-10), 6.36 (dd, 1H, J = 2.1, 8.3 Hz, H-10′), 6.46 (H-8′), 6.56 (dd, 1H, J = 2.1, 8.3 Hz, H-11′), 6.81 (br s, 2H, H-13 and H-14), 6.98 (dd, 1H, J = 2.1, 8.3 Hz, H-13′), 7.53 (dd, 1H, J = 2.1, 8.3 Hz, H-14′) (nOe used) (24)

MS: $[M]^+$ 668 (8), 667 (31), 666 (75), 651 (21), 441 (65), 427 (60), 411 (36), 221 (100), 206 (28), 204 (30), 190 (23) (24)

CD: 0 (300), −6.8 (282), 0 (269), 0 (255), +12.0 (242), negative tail below 230 nm (24)

Sources: *Thalictrum cultratum* Wall. (Ranunculaceae) (24)

Derivatives: 5-Methoxythalidasine (5-hydroxythalidasine + CH_2N_2) (24)

MP: Amorphous (24)

UV: 237 (sh) (4.40), 281 (3.67) (24)

^{1}H NMR: NMe 2.24 (N-2), 2.62 (N-2′); OMe 3.35 (C-7), 3.49 (C-6′), 3.80 (6H) (C-5 and C-6), 3.89 (C-7′), 3.90 (C-12); ArH 6.31 (br s) (H-10), 6.35 (dd, 1H, J = 2, 8.3 Hz, H-10′), 6.46 (H-8′), 6.54 (dd, 1H, J = 2.5, 8.3 Hz, H-11′), 6.81 (br s, 2H, H-13 and H-14), 6.99 (dd, 1H, J = 2.5, 8.3 Hz, H-13′), 7.52 (dd, 1H, J = 2, 8.3 Hz, H-14′) (24)

MS: $[M]^+$ 682 (70), 681 (30), 455 (41), 441 (42), 424 (14), 228 (100), 205 (23) (24)

CD: 0 (300), −6.8 (282), 0 (269), 0 (255), +12 (242), negative tail below 230 nm (24)

5-Acetoxythalidasine (24)

MP: Amorphous (24)

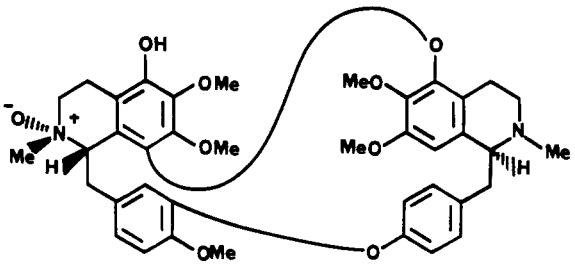
IR: 1710 cm^{-1} (24)

^{1}H NMR: NMe 2.22 (N-2), 2.62 (N-2′); OAc 2.32; OMe 3.36 (C-7), 3.49 (C-6′), 3.71 (C-6), 3.88 (C-7′), 3.90 (C-12); ArH 6.27 (br s, H-10), 6.35 (dd, 1H, J = 2.5, 8.2 Hz, H-10′), 6.46 (H-8′), 6.52 (dd, 1H, J = 2.5, 8.2 Hz, H-11′), 6.80 (br s, 2H, H-13 and H-14), 6.98 (dd, 1H, J = 2.5, 8.5 Hz, H-13′), 7.53 (dd, 1H, J = 2.5, 8.5 Hz, H-14′) (24)

MS: $[M]^+$ 710 (100), 709 (23), 695 (23), 484 (20), 483 (62), 469 (49), 242 (57) (24)

312 5-HYDROXYTHALIDASINE-2′α-*N*-OXIDE $C_{39}H_{44}O_9N_2$: 684.3046

Type XIIa[f] (*S*,*S*) 5,6,7,8*,11$^+$,12-5*,6,7,12$^+$



MP: Amorphous (41)

[α]D: −11° (c = 0.4, MeOH) (41)

^{1}H NMR: NMe 2.62 (N-2′), 3.04 (N-2); OMe 3.28 (C-7), 3.42 (C-6′), 3.77 (C-6), 3.87 (C-7′), 3.89 (C-12); AlH 3.89 (m, 1H, H-1′), 4.91 (m, 1H, H-1); ArH 6.22 (dd, 1H, J = 2.1, 8.2 Hz, H-10′), 6.27 (dd, 1H, J = 2.1, 8.2 Hz, H-11′), 6.48 (H-8′), 6.58 (d, 1H, J = 1.8 Hz, H-10), 6.69 (dd, 1H, J = 1.8, 8.1 Hz, H-14), 6.81 (d, 1H, J = 8.1 Hz, H-13), 7.06 (dd, 1H, J = 2.1, 8.2 Hz, H-13′), 7.47 (dd, 1H, J = 2.1, 8.2 Hz, H-14′) (41)

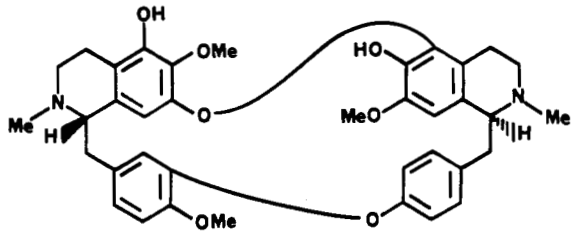
MS: $[M]^+$ 684 (0.4), 683 (0.6), 682 (2), 668 (68), 667 (27), 653 (23), 457 (2), 411 (86), 227 (58), 222 (57), 221 (100), 206 (22), 204 (34), 198 (35), 190 (35), 176 (15) (41)

Sources: *Thalictrum cultratum* Wall. (Ranunculaceae) (41)

[f]This is a new class that supplements Class XII as mentioned in the review of Guha *et al.* (1).

313 5-HYDROXYTHALMINE $C_{37}H_{40}O_7N_2$: 624.2836

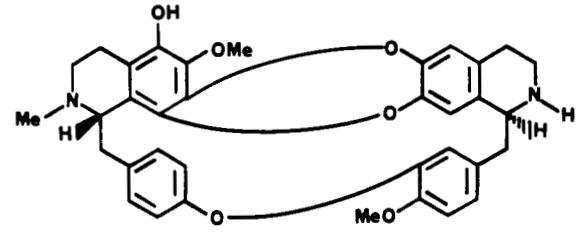
Type XIVa[g] (*S,S*) 5,6,7•,11$^+$,12-5•,6,7,12$^+$



MP: Amorphous (24)
[α]D: −69° (*c* = 0.08, MeOH) (24)
UV: 236 (sh) (4.43), 281 (3.78) (24)
^{1}H NMR: NMe 2.19 (N-2), 2.66 (N-2′); OMe 3.93 (6H, C-7′ and C-12), 4.04 (C-6); AlH 3.23 (m, 1H, H-1), 3.63 (m, 1H, H-1′); ArH 5.54 (H-8), 6.11 (d, 1H, *J* = 2 Hz, H-10), 6.75 (dd, 1H, *J* = 2, 8.2 Hz, H-14), 6.79 (H-8′), 6.80 (d, 1H, *J* = 8.2 Hz, H-13), 6.95 (2H, H-11′ and H-13′), 7.35 (2H, H-10′ and H-14′) (24)
MS: [M]$^+$ 624 (50), 623 (41), 397 (100), 383 (37), 199 (57), 190 (57), 176 (23) (24)
CD: 0 (300), −3.5 (280), 0 (272), +1.6 (262), +1.1 (258), +12.1 (238), negative tail below 235 nm (24)
Sources: *Thalictrum cultratum* Wall. (Ranunculaceae) (24)
Derivatives: *O*-Methylthalmiculine (5-hydroxythalmine + CH_2N_2)

314 KOHATAMINE $C_{35}H_{34}O_6N_2$: 578.2417

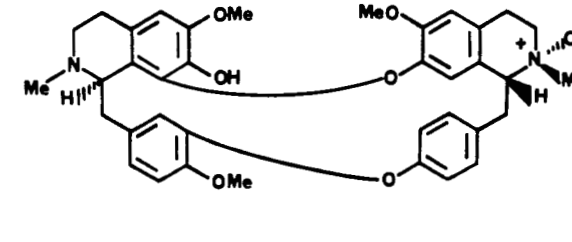
Type XXIIIa (*S,S*) 5,6,7•,8$^+$,12$^{\#}$-6•,7$^+$,11$^{\#}$,12



[α]^{25}D: +99° (*c* = 0.26, $CHCl_3$) (33)
UV: 237 (sh) (4.30), 267 (sh) (3.98) (33)
^{1}H NMR: NMe 2.60 (N-2); OMe 3.91 (C-12′), 3.96 (C-6); AlH 3.63 (H-1′), 4.02 (H-1); ArH 6.22 (H-8′), 6.60 (H-5′), 6.62 (d, 1H, *J* = 1.8 Hz, H-10′), 6.87 (dd, 1H, *J* = 2.2, 8.2 Hz, H-11), 6.91 (d, 1H, *J* = 8.2 Hz, H-13′), 6.91 (dd, 1H, *J* = 1.8, 8.2 Hz, H-14′), 7.12 (dd, 1H, *J* = 2.2, 8.2 Hz, H-10), 7.23 (dd, 1H, *J* = 2.2, 8.2 Hz, H-13), 7.53 (dd, 1H, *J* = 2.2, 8.2 Hz, H-14) (33)
MS: [M]$^+$ 578 (58), 577 (48), 365 (17), 351 (100), 350 (22), 335 (24), 321 (13), 176 (24), 168 (11) (33)
Sources: *Cocculus pendulus* (Forsk.) Diels (Menispermaceae) (33)

315 LIMACINE-2′α-*N*-OXIDE $C_{37}H_{40}O_7N_2$: 624.2836

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

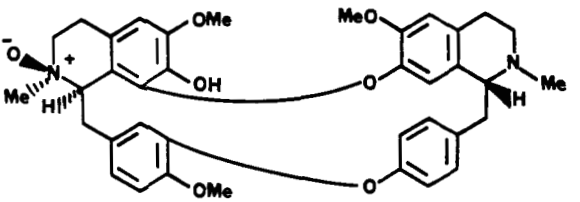


[g]This is a new class that supplements Class XIV as mentioned in the review of Guha *et al.* (1).

[α]D: −170° (*c* = 0.16, $CHCl_3$) (83,84)
^{1}H NMR: NMe 2.34 (N-2), 3.45 (N-2′); OMe 3.36 (C-6′), 3.72 (C-6), 3.93 (C-12); AlH 3.75 (H-1), 4.52 (H-1′); ArH 6.10 (H-8′), 6.24 (dd, 1H, *J* = 2.4, 8.2 Hz, H-10′), 6.27 (H-5), 6.54 (d, 1H, *J* = 1.5 Hz, H-10), 6.58 (H-5′), 6.82 (dd, 1H, *J* = 2.4, 8.2 Hz, H-11′), 6.85 (d, 1H, *J* = 8.5 Hz, H-13), 6.89 (dd, 1H, *J* = 1.5, 8.5 Hz, H-14), 7.14 (dd, 1H, *J* = 2.4, 8.2 Hz, H-13′), 7.31 (dd, 1H, *J* = 2.4, 8.2 Hz, H-14′) (nOe used) (83–85)
MS: $[M]^+$ 624 (14) (found 624.2880), 623 (17), 622 (15), 608 (46), 607 (52), 594 (20), 593 (33), 381 (87), 367 (63), 192 (70), 191 (100), 174 (41) (84)
Sources: *Curarea candicans* (L.C. Rich) Barneby and Krukoff (Menispermaceae) (84)

316 LIMACINE-2β-*N*-OXIDE $C_{37}H_{40}O_7N_2$: 624.2836

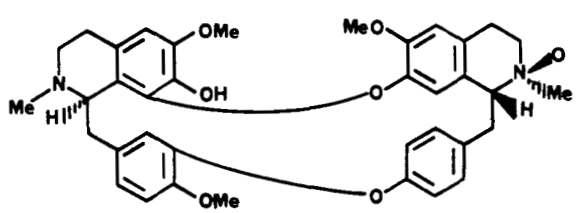
Type VIII (*R*,*R*) 6,7,8*,11$^+$,12-6,7*,12$^+$



[α]D: −191° (*c* = 0.09, $CHCl_3$) (83,84)
^{1}H NMR: NMe 2.62 (N-2′), 2.98 (N-2); OMe 3.41 (C-6′), 3.77 (C-6), 3.95 (C-12); AlH 3.89 (H-1′), 4.90 (H-1); ArH 5.94 (H-8′), 6.36 (H-5), 6.45 (dd, 1H, *J* = 2.4, 8.2 Hz, H-10′), 6.50 (H-5′), 6.66 (dd, 1H, *J* = 1.5, 8.5 Hz, H-14), 6.75 (d, 1H, *J* = 1.5 Hz, H-10), 6.83 (d, 1H, *J* = 8.5 Hz, H-13), 6.93 (dd, 1H, *J* = 2.4, 8.2 Hz, H-11′), 6.99 (dd, 1H, *J* = 2.4, 8.2 Hz, H-13′), 7.33 (dd, 1H, *J* = 2.4, 8.2 Hz, H-14′) (nOe used) (83–85)
MS: $[M]^+$ 624 (5) (found 624.2875), 623 (7), 622 (7), 608 (73), 607 (55), 594 (14), 381 (93), 367 (59), 192 (73), 191 (100), 174 (43) (84)
Sources: *Curarea candicans* (L.C. Rich) Barneby and Krukoff (Menispermaceae) (84)

317 LIMACINE-2′β-*N*-OXIDE $C_{37}H_{40}O_7N_2$: 624.2836

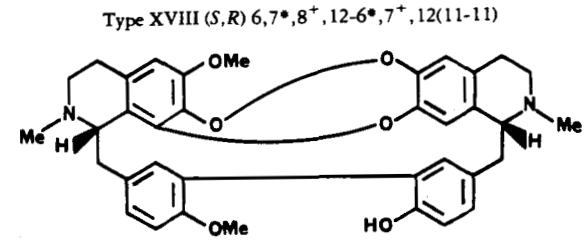
Type VIII (*R*,*R*) 6,7,8*,11$^+$,12-6,7*,12$^+$



[α]D: −154° (*c* = 0.1, $CHCl_3$) (83,84)
^{1}H NMR: NMe 2.39 (N-2), 2.97 (N-2′); OMe 3.38 (C-6′), 3.79 (C-6), 3.88 (C-12); AlH 3.89 (H-1), 4.70 (H-1′); ArH 6.17 (H-8′), 6.23 (dd, 1H, *J* = 2.4, 8.2 Hz, H-10′), 6.32 (H-5), 6.56 (H-5′), 6.74 (d, 1H, *J* = 1.5 Hz, H-10), 6.79 (dd, 1H, *J* = 2.4, 8.2 Hz, H-11′), 6.85 (d, 1H, *J* = 8.5 Hz, H-13), 6.91 (dd, 1H, *J* = 1.5, 8.5 Hz, H-14), 6.95 (dd, 1H, *J* = 2.4, 8.2 Hz, H-13′), 7.42 (dd, 1H, *J* = 2.4, 8.2 Hz, H-14′) (nOe used) (83–85)
MS: $[M]^+$ 624 (5) (found 624.2832), 623 (10), 622 (21), 608 (80), 607 (79), 594 (22), 593 (40), 381 (100), 367 (72), 192 (71), 191 (99), 174 (40) (84)
Sources: *Curarea candicans* (L.C. Rich) Barneby and Krukoff (Menispermaceae) (84)

318 MEDELLINE $C_{37}H_{38}O_6N_2$: 606.2730

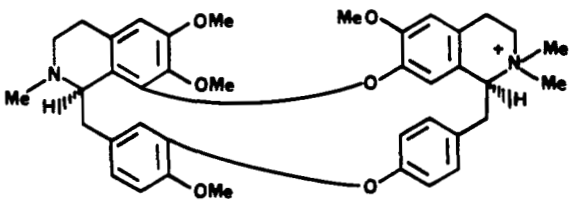
Type XVIII (*S*,*R*) 6,7*,8$^+$,12-6*,7$^+$,12(11-11)



MP: Amorphous (67)
[α]D: −38° (*c* = 0.16, MeOH) (67)
UV(EtOH): 220 (4.38), 250 (sh) (3.98), 282 (3.82); (EtOH + OH^-) 222 (4.58), 300 (3.95) (67)
IR(film): 3325, 2930, 2840, 1610, 1580, 1500, 1120, 1070, 1020, 990, 910 (67)
^{1}H NMR: NMe 2.27 (N-2), 2.61 (N-2′); OMe 3.83 (C-5), 3.91 (C-12); AlH 3.62 (H-1′), 4.14 (H-1), 4.89 (d, 1H, *J* = 4 Hz, H_A), 4.96 (d, 1H, *J* = 4 Hz, H_B); ArH 6.41 (H-5), 6.78 (d, 1H, *J* = 2 Hz, H-10′), 6.84 (H-8′), 6.88 (d, 1H, *J* = 8 Hz), 6.90 (H-5′), 7.00 (d, 1H, *J* = 8 Hz), 7.21 (dd, 1H, *J* = 2, 8 Hz, H-14), 7.26 (dd, 1H, *J* = 2, 8 Hz, H-14′), 7.51 (d, 1H, *J* = 2 Hz, H-10) (nOe used) (67)
^{13}C NMR: 62.1 (C-1), 44.8 (C-3), 24.5 (C-4), 105.9 (C-5), 134.2 (C-10), 120.0 (C-13), 128.7 (C-14); 66.1 (C-1′), 44.8 (C-3′), 25.3 (C-4′), 110.8 (C-5′), 124.5 (C-8′), 133.1 (C-10′), 112.3 (C-13′), 129.1 (C-14′); 42.5 (N-2, N-Me), 43.5 (N-2′, N-Me); 56.0 (6-OMe), 56.2 (12-OMe), 56.4 (12′-OMe); 94.8 (OCH_2O)' (67)
MS: $[M]^+$ 606.270 (11), 380 (20), 379.145 (29), 349 (1), 190 (67), 174 (100) (67)
CD: 0 (300), +12.5 (288), +68 (249), 0 (232), −109 (218) (67)
Sources: *Pseudoxandra* aff. *lucida* (Annonaceae) (67)
Derivatives: 12′-Acetylmedelline (medelline + Ac_2O/pyridine) (67)
[α]D: −42° (*c* = 0.60, $CHCl_3$) (67)
UV(EtOH): 222 (4.60), 283 (3.90) (67)
IR(film): 1765, 1605, 1580, 1500 (67)
^{1}H NMR: NMe 2.34 (N-2), 2.60 (N-2′); OAc 2.10; OMe 3.72 (C-12), 3.83 (C-6); AlH 3.60 (m, 1H, H-1′), 4.37 (m, 1H, H-1), 4.88 and 4.94 (*J* = 4 Hz, H_A, H_B); ArH 6.41 (H-5), 6.66 (H-8′), 6.73 (d, 1H, *J* = 2 Hz, H-10′), 6.77 (d, 1H, *J* = 8 Hz, H-13), 6.94 (H-5′, 7.15 (d, 1H, *J* = 8 Hz, H-13′), 7.21 (dd, 1H, *J* = 2, 8 Hz, H-14), 7.34 (dd, 1H, *J* = 2, 8 Hz, H-14′), 7.49 (d, 1H, *J* = 2 Hz, H-10) (67)
MS: $[M]^+$ 648 (84), 380 (22), 379 (68), 307 (11), 235 (24), 190 (97), 170 (100) (67)

319 *N*-2′-METHYLISOTETRANDRINE $C_{39}H_{45}O_6N_2$: 637.3278

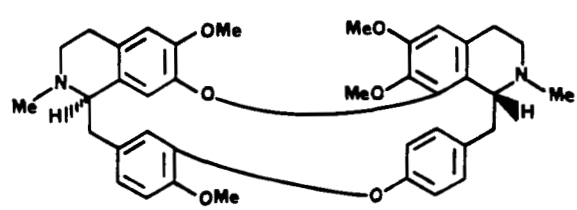
Type VIII (*R,S*) 6,7,8*,11,12$^+$-6,7*,12$^+$



MP: Iodide: 221–222° (THF) (23)
[α]D: Iodide: +29.5° (*c* = 0.1, $CHCl_3$) (23)
UV(EtOH): Iodide: 284 (3.91) (23)
^{1}H NMR: Iodide: NMe 2.15 (N-2), 3.06 (N-2′) and 3.55 (N-2′); ArH 6.20–6.90 (10H) (23)
MS: Iodide: 636 (M-HI), 6.22 (M-MeI), 607, 431, 395, 381, 198, 175, 142, 127, 58 (100) (23)
Sources: *Berberis oblonga* (Regl.) (Berberidaceae) (23)

320 *O*-METHYLLIMACUSINE $C_{38}H_{42}O_6N_2$: 622.3043

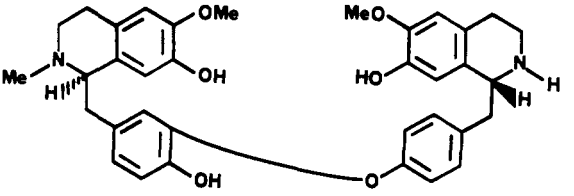
Type VI (*R,R*) 6,7*,11,12$^+$-6,7,8*,12$^+$



^{1}H NMR: NMe 2.55 (N-2), 2.57 (N-2′); OMe 3.02 (C-7′), 3.43 (C-6), 3.77 (C-6′), 3.96 (C-12); ArH 6.40 (H-5, H-5′), 6.45 (H-8), 6.65 (H-10), 6.81 (H-10′, H-11′), 6.96 (H-14), 6.99 (H-13), 7.13 (H-13′), 7.36 (H-14′) (15)
Sources: *Gyrocarpus americanus* Jacq. (Hernandiaceae) (15)

321 2-*N*-METHYLLINDOLDHAMINE $C_{35}H_{38}O_6N_2$: 582.2730

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



$[\alpha]_D$: $-185°$ ($c = 0.10$, MeOH) (36)

UV(EtOH): 213 (4.97), 225 (sh) (4.83), 285 (4.36) (36)

^{1}H NMR: NMe 2.46 (N-2); OMe 3.81 (C-6 or C-6'), 3.85 (C-6' or C-6); AlH 3.61 (dd, 1H, H-1), 4.11 (dd, 1H, H-1'); ArH 6.30 (s, H-8), 6.45 (s, H-5), 6.48 (d, 1H, H-10), 6.57 (s, H-5'), 6.77 (s, H-7'), 6.82 (d, 2H, H-11' and H-13'), 6.84 (dd, 1H, H-14), 6.87 (d, 1H, H-13), 7.14 (d, 2H, H-10' and H-14') (nOe used) (36)

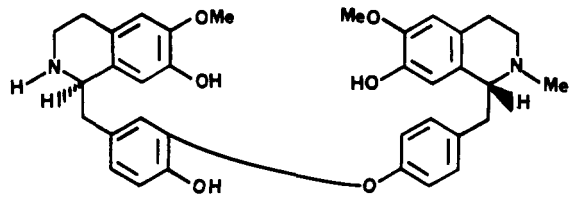
MS: $[M]^+$ 582 (<1), 192 (100), 178 (20) (36)

Sources: *Abuta pahni* (Martius) Krukoff and Barneby (Menispermaceae) (36)

Derivatives: *N,N'*-Dimethyllindoldhamine **[234]** (2-*N*-methyllindoldhamine + $CH_2O/NaBH_4$) (36)

322 2'-*N*-METHYLLINDOLDHAMINE $C_{35}H_{38}O_6N_2$: 582.2730

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



$[\alpha]_D$: $-47°$ ($c = 0.17$, MeOH) (36)

^{1}H NMR: NMe 2.47 (N-2'); OMe 3.81 (C-6 or C-6'), 3.85 (C-6' or C-6); AlH 3.61 (dd, 1H, H-1'), 4.16 (dd, 1H, H-1); 6.35 (s, H-8'), 6.45 (s, H-5), 6.48 (d, 1H, H-10), 6.62 (s, H-5'), 6.66 (s, H-8), 6.84 (d, 2H, H-11' and H-13'), 6.85 (dd, 1H, H-14), 6.90 (d, 1H, H-13), 7.17 (d, 2H, H-10' and H-14') (nOe used) (36)

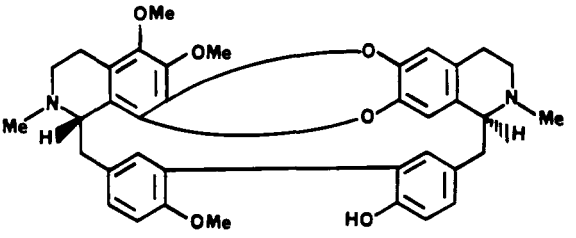
MS: $[M]^+$ 582 (<1), 192 (47), 178 (100) (36)

Sources: *Abuta pahni* (Martius) Krukoff and Barneby (Menispermaceae) (36)

Derivatives: *N,N'*-Dimethyllindoldhamine **[234]** (2'-*N*-methyllindoldhamine + $CH_2O/NaBH_4$) (36)

323 *N*-METHYLTILIAMOSINE $C_{37}H_{38}O_6N_2$: 606.2730

Type XIX (S,S) 5,6,7,8$^+$,12-6*,7$^+$,12(11-11)*



$[\alpha]^{25}_D$: $+510°$ ($c = 1.5$, $CHCl_3$) (78)

UV(EtOH): 240 (sh) (4.65), 291 (4.0) (78); (EtOH + OH^-) 304 (3.84) (78)

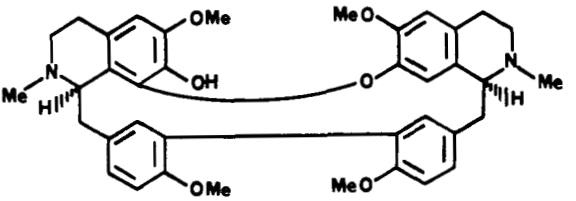
^{1}H NMR($CDCl_3 + CD_3OD$): NMe 2.20 (N-2), 2.51 (N-2'); OMe 3.72 (C-5), 3.82 (C-6), 3.89 (C-12); AlH 2.37 (dd, 1H, $J = .5$, 17.5 Hz, H_a-α), 2.47 (br dd, 1H, $J = 4$, 5.17, 6 Hz) (H_b-4'), 2.60 (dd, 1H, $J = 7$, 12 Hz, H_b-3), 2.63 (dd, 1H, $J = 12$, 17.5 Hz, H_b-α), 2.66 (dd, 1H, $J = 6$, 12 Hz, H_a-3), 2.72–2.74 (m, 2H, H_a-4 and H_b-4), 2.83–2.91 (m, 3H, H_a-4', H_b-3', H_a-α), 3.0 (octet, 1H, H_a-3'), 3.20 (dd, 1H, $J = 5$, 13 Hz, H-1), 3.25 (m, 1H, H_b-α'), 3.35 (dd, 1H, $J = 6.5$, 7.5 Hz, H-1'); ArH 6.54 (H-5'), 6.88 (d, 1H, $J = 8.3$ Hz, H-13), 6.91 (d, 1H, $J = 8.1$ Hz, H-13'), 7.17 (dd, 1H, $J = 2.2$, 8.3 Hz, H-14'), 7.27 (dd, 1H, $J = 2.2$, 8.3 Hz, H-14), 7.50 (d, 1H, $J = 1.96$ Hz, H-10'), 7.59 (d, 1H, $J = 2.2$ Hz, H-10), 7.99 (H-8') (78)

MS: $[M]^+$ 606, 605, 591, 380, 379, 366, 365, 349, 303, 190 (78)
Sources: *Tiliacora racemosa* Colebr. (Menispermaceae) (78)
Preparation: Via the methylation ($CH_2O/NaBH_4$) of tiliamosine (78)

324 MONTERINE

$C_{38}H_{42}O_6N_2$: 622.3043

Type IV (*R,S*) 6,7,8*,12-6,7*,12(11-11)

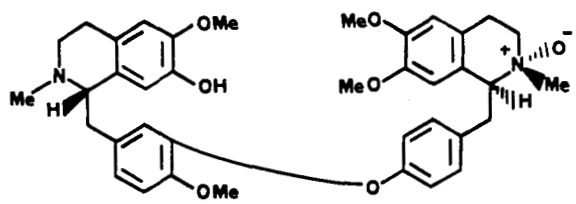


MP: Amorphous (79)
$[\alpha]^{20}D$: −135° (c = 0.4, $CHCl_3$) (79)
UV: 213 (4.53), 238 (sh) (4.16), 285 (3.75) (79)
^1H NMR: Stable Conformer "a": NMe 2.37 (N-2), 2.56 (N-2'); OMe 3.46 (C-6'), 3.73 (C-12), 3.79 (C-6), 3.80 (C-12'); AlH 3.52 (m, 1H, H-1'), 4.26 (m, 1H, H-1); ArH 6.15 (d, 1H, J = 2.2 Hz, H-10'), 6.31 (H-5), 6.36 (H-8'), 6.57 (H-5'), 6.70 (d, 1H, J = 8.5 Hz, H-13), 6.90 (d, 1H, J = 8.5 Hz, H-13'), 7.10 (dd, 1H, J = 2.2, 8.5 Hz, H-14), 7.20 (dd, 1H, J = 2.2, 8.5 Hz, H-14'), 7.67 (d, 1H, J = 2.2 Hz, H-10), (nOe used) (79)
Stable Conformer "b": NMe 2.38 (N-2), 2.62 (N-2'); OMe 3.44 (C-6'), 3.70 (C-12'), 3.76 (C-12), 3.77 (C-6); AlH 3.75 (m, 1H, H-1'), 3.92 (m, 1H, H-1); ArH 6.30 (H-5), 6.30 (H-5'), 6.60 (d, 1H, J = 2.2 Hz, H-10), 6.68 (d, 1H, J = 8.5 Hz, H-13'), 6.78 (d, 1H, J = 8.5 Hz, H-13), 6.80 (d, 1H, J = 2.2 Hz, H-10'), 7.15 (H-8'), 7.18 (dd, 1H, J = 2.2, 8.5 Hz, H-14'), 7.25 (dd, 1H, J = 2.2, 8.5 Hz, H-14) (nOe used) (79)
^1H NMR(pyridine-d_5): 21°: NMe 2.28 (N-2) and 2.48 (N-2); 2.53 (N-2'), and 2.56 (N-2'); 3.34 (C-6') and 3.43 (C-6'), 3.55 (C-12), 3.68 (C-6), 3.72 (C-12'); ArH 6.33–7.70 (9H) (79)
90°: NMe 2.46 (N-2), 2.63 (N-2'); OMe 3.49 (C-6'), 3.56 (C-12), 3.75 (C-6), 3.78 (C-12'); ArH 6.30–7.60 (9H) (79)
MS: $[M]^+$ 622 (47), 621 (34), 607 (7), 591 (4), 382 (37), 381 (100), 367 (30), 192 (14), 191 (53), 175 (5), 174 (10) (79)
CD: 0 (305), −14.5 (283), 0 (264), −44.2 (246), 0 (233), +37.1 (225) (79)
Sources: *Crematosperma* sp. (Annonaceae) (79)
Derivatives: *O*-Methylmonterine (granjine) [**302**] (monterine + CH_2N_2) (tlc, ms, ^1H nmr, sp rotation, cd) (79)

325 NEOTHALIBRINE-2'α-*N*-OXIDE

$C_{38}H_{44}O_7N_2$: 640.3149

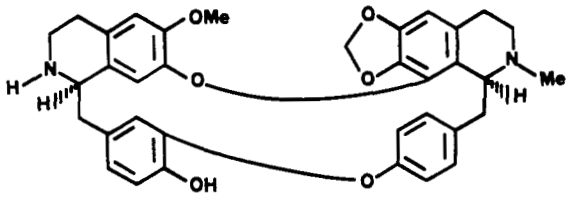
Type I (*S,S*) 6,7,11*,12-6,7,12*



MP: Amorphous (41)
$[\alpha]D$: +74° (c = 0.2, MeOH) (41)
^1H NMR: NMe 2.51 (N-2), 3.24 (N-2'); OMe 3.82 (C-12), 3.85 (C-6), 3.86 (C-6'); AlH 3.67 (m, 1H, H-1), 4.75 (m, 1H, H-1'); ArH 6.33 (H-8), 6.48 (s, 2H, H-5 and H-8'), 6.51 (d, 1H, J = 1.8 Hz, H-10), 6.63 (H-8'), 6.81 (d, 2H, J = 8.5 Hz, H-11' and H-13'), 6.88 (d, 1H, J = 8.3 Hz, H-13), 6.99 (dd, 1H, J = 1.8, 8.3 Hz, H-14), 7.25 (d, 2H, J = 8.5 Hz, H-10' and H-14') (nOe used) (41)
MS: 222 (0.5), 208 (0.7), 206 (52), 192 (100), 190 (5), 177 (6) (41)
Sources: *Thalictrum cultratum* Wall. (Ranunculaceae) (41)

326 2-NORCEPHARANOLINE $C_{35}H_{34}O_6N_2$: 578.2417

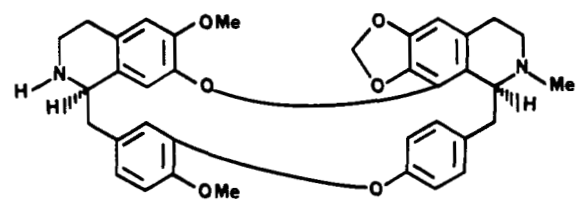
Type VI (*R,S*) 6,7*,11$^+$,12-6,7,8*,12$^+$



[α]D: +257° (*c* = 0.17, $CHCl_3$) (64)
UV: 209 (4.69), 242 (sh) (4.16), 283 (3.81) (64)
^{1}H NMR: NMe 2.68 (N-2'); OMe 3.71 (C-6) CH_2O_2 5.60 (d, 1H, *J* = 1.2 Hz, 5.64 (d, 1H, *J* = 1.2 Hz, C-6' and C-7'); AlH 4.20 (m, 1H, H-1'), 4.27 (m, 1H, H-1); ArH 5.56 (d, 1H, *J* = 1.8 Hz, H-10), 6.30 (dd, 1H, *J* = 2.2, 8.3 Hz, H-11'), 6.35 (H-5), 6.42 (H-5'), 6.72 (H-8), 6.73 (dd, 1H, *J* = 1.8, 8.2 Hz, H-14), 6.83 (d, 1H, *J* = 8.2 Hz, H-13), 6.99 (dd, 2H, *J* = 2.2, 8.3 Hz, H-10' and H-13'), 7.51 (dd, 1H, *J* = 2.2, 8.3 Hz, H-14') (64)
MS: [M]$^+$ 578 (72), 577 (96), 576 (47), 575 (65), 366 (57), 365 (57), 351 (68), 349 (50), 206 (25), 192 (73), 183 (100) (64)
Sources: *Stephania pierrii* Diels (Menispermaceae) (64)

327 2-NORCEPHARANTHINE $C_{36}H_{36}O_6N_2$: 592.2573

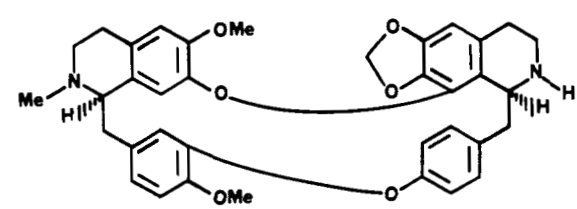
Type VI (*R,S*) 6,7*,11$^+$,12-6,7,8*,12$^+$



MP: Amorphous (21)
[α]D: +318° (*c* = 0.25, MeOH) (21)
^{1}H NMR: NMe 2.68 (N-2'); OMe 3.71 (C-6), 3.91 (C-12); CH_2O_2 5.60 (d, 1H, *J* = 1 Hz), 5.63 (d, 1H, *J* = 1 Hz, C-6', C-7'); AlH 4.19 (m, 1H, H-1'), 4.32 (m, 1H, H-1); ArH 5.58 (d, 1H, *J* = 1.5 Hz, H-10), 6.32 (dd, 1H, *J* = 2, 8.2 Hz, H-11'), 6.34 (H-5), 6.41 (H-5'), 6.71 (H-8), 6.82 (d, 1H, *J* = 8.2 Hz, H-13), 6.84 (dd, 1H, *J* = 1.5, 8.2 Hz, H-14), 6.97 (dd, 1H, *J* = 2, 8.2 Hz, H-10'), 6.98 (dd, 1H, *J* = 2, 8.2 Hz, H-13'), 7.46 (dd, 1H, *J* = 2, 8.2 Hz, H-14') (21)
MS: [M]$^+$ 592 (78), 591 (100), 486 (4), 485 (10), 365 (59), 351 (39), 349 (40), 206 (20), 192 (18), 183 (32), 160 (31) (21)
Sources: *Stephania suberosa* Forman (Menispermaceae) (21)
Derivatives: Cepharanthine [**34**] (2-norcepharanthine + CH_2O/HCOOH) (21)

328 2'-NORCEPHARANTHINE $C_{36}H_{36}O_6N_2$: 592.2573

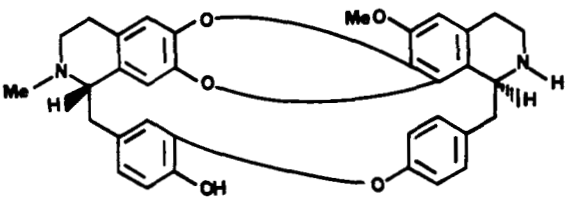
Type VI (*R,S*) 6,7*,11$^+$,12-6,7,8*,12$^+$



[α]D: +206° (*c* = 0.24, $CHCl_3$) (64)
UV: 210 (4.61), 241 (sh) (4.17), 282 (3.71) (64)
^{1}H NMR: NMe 2.58 (N-2); OMe 3.70 (C-6), 3.89 (C-12); CH_2O_2 5.56 (d, 1H, *J* = 1.3 Hz), 5.61 (d, 1H, *J* = 1.3 Hz, C-6' and C-7'); AlH 3.61 (m, 1H, H-1), 4.56 (m, 1H, H-1'); ArH 5.56 (br s, 1H, H-10), 6.33 (H-5), 6.37 (H-5'), 6.39 (m, 1H, H-11'), 6.63 (H-8), 6.79 (br s, 2H, H-13 and H-14), 6.92 (m, 1H, H-10'), 6.94 (dd, 1H, *J* = 2.1, 8.3 Hz, H-13'), 7.48 (dd, 1H, *J* = 2.1, 8.3 Hz, H-14') (64)
MS: [M]$^+$ 592 (22), 591 (23), 577 (4), 366 (24), 365 (100), 363 (14), 351 (14), 190 (10), 183 (49), 174 (19) (64)
Sources: *Stephania pierrii* Diels (Menispermaceae) (64)

329 2′-NORCOCSULINE $C_{34}H_{32}O_5N_2$: 548.2311

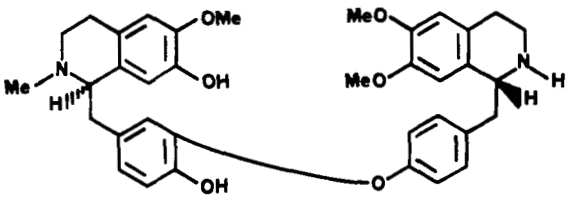
Type XXIII (*S,S*) 6*,7$^+$,11$^\#$,12-6,7*,8$^+$,12$^\#$



[α]D: +238° (*c* = 0.15, $CHCl_3$) (35)
UV(EtOH): 212 (4.53), 225 (4.43), 287 (3.60) (35)
^{1}H NMR: NMe 2.44 (N-2); OMe 3.86 (C-6′); AlH 3.32 (H-1), 4.35 (H-1′); ArH 6.12 (H-8), 6.31 (H-5′), 6.50 (H-10), 6.60 (H-5), 6.79 (H-14), 6.90 (H-13), 6.96 (H-11′), 7.13 (H-10′), 7.17 (H-13′), 7.63 (H-14′) (35)
MS: [M]$^+$ 548 (27), 547 (27), 335 (100), 321 (27), 319 (24), 168 (32), 167 (7) (35)
Sources: *Albertisia papuana* Becc. (Menispermaceae) (35)
Derivatives: Cocsuline [**153**] (2′-norcocsuline + $CH_2O/NaBH_4$) (35)

330 2′-NORDAURISOLINE $C_{36}H_{40}O_6N_2$: 596.2886

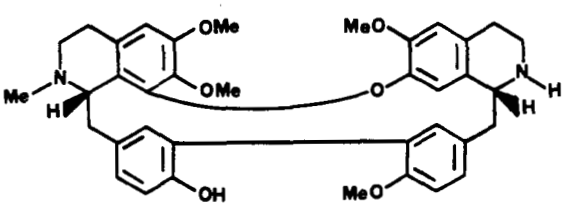
Type I (*R,R*) 6,7,11*,12-6,7,12*



[α]D: Negative (36)
^{1}H NMR: NMe 2.43 (N-2); OMe 3.81 (C-6 or C-6′), 3.84 (C-7), 3.86 (C-6′ or C-6); AlH 3.61 (dd, 1H, H-1), 4.15 (dd, 1H, H-1′); ArH 6.32 (s, H-8), 6.45 (s, H-5), 6.49 (d, H-10), 6.60 (s, H-5′), 6.69 (s, H-8′), 6.83 (d, 2H, H-11′ and H-13′), 6.84 (dd, H-14), 6.90 (d, H-13), 7.16 (d, 2H, H-10′ and H-14′) (nOe used) (36)
MS: [M]$^+$ 596 (<1), 192 (100) (36)
Sources: *Abuta pahni* (Martius) Krukoff and Barneby (Menispermaceae) (36)
Derivatives: Daurisoline [**192**] (2′-*N*-nordaurisoline + $CH_2O/NaBH_4$) (36)

331 2′-NORFUNIFERINE $C_{37}H_{40}O_6N_2$: 608.2886

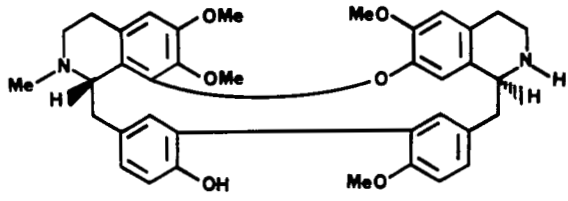
Type IV (*S,R*) 6,7,8*,12-6,7*,12(11-11)



[α]D: +196° (*c* = 0.17, $CHCl_3$) (51)
UV: 218 (4.42), 290 (3.38) (51)
^{1}H NMR: NMe 2.40 (N-2); OMe 3.48 (C-7), 3.50 (C-6′), 3.83 (C-6), 3.90 (C-12′); AlH 3.90 (H-1), 4.34 (H-1′); ArH 6.39 (H-5), 6.45 (H-5′), 6.77 (H-10), 6.88 (H-13′), 6.89 (H-13), 7.09 (H-10′), 7.21 (H-8′), 7.24 (H-14′), 7.32 (H-14) (nOe used) (51)
MS: [M]$^+$ 608 (76), 607 (100), 381 (49), 365 (30), 191 (54) (51)
CD: 0 (300), +13.2 (277), 0 (255), +37 (240), 0 (218), −4.80 (215) (51)
Sources: *Guatteria guianensis* (Aublet) R.E. Fries (Annonaceae) (51)
Derivatives: Funiferine [**20**] (2′-norfuniferine + $CH_2O/NaBH_4$) (51)

332 2′-NORGUATTAGUIANINE $C_{37}H_{40}O_6N_2$: 608.2886

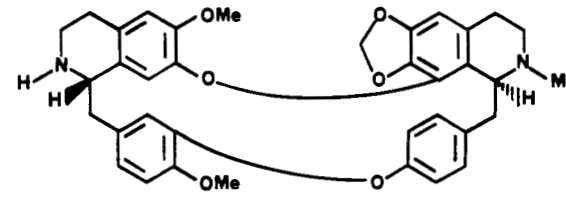
Type IV (*S,S*) 6,7,8*,12-6,7*,12(11-11)



[α]D: +18° (*c* = 0.12, $CHCl_3$) (51)
UV: 220 (4.64), 290 (3.70) (51)
^{1}H NMR: NMe 2.39 (N-2); OMe 3.37 (C-6′), 3.56 (C-7), 3.83 (C-6), 3.93 (C-12′); AlH 4.21 (H-1), 4.40 (H-1′); ArH 6.41 (H-5), 6.42 (H-5′), 6.86 (d, *J* = 8.1 Hz, H-13), 6.88 (d, *J* = 8.33 Hz, H-13′), 7.20 (dd, *J* = 2.1, 8.1 Hz, H-14), 7.24 (d, *J* = 2.1 Hz, H-10′), 7.28 (H-8′), 7.31 (dd, *J* = 2.1, 8.3 Hz, H-14′), 7.55 (H-10, d, *J* = 2.1 Hz) (nOe used) (51)
MS: $[M]^+$ 608 (73), 607 (100), 380 (51), 191 (48) (51)
CD: 0 (320), +5.9 (296), 0 (285), −2.3 (276), 0 (265), +12.9 (254), 0 (243), +45.9 (227) (51)
Sources: *Guatteria guianensis* (Aublet) R.E. Fries (Annonaceae) (51)
Derivatives: Guattaguianine (2′-norguattaguianine + $CH_2O/NaBH_4$) (51)
[α]D: +40° (*c* = 0.09, $CHCl_3$) (51)
UV: 228 (sh) (3.96), 281 (3.38) (51)
^{1}H NMR: NMe 2.40 (N-2), 2.67 (N-2′); OMe 3.35 (C-6′), 3.50 (C-7), 3.83 (C-6), 3.90 (C-12′); AlH 3.49 (H-1), 4.09 (H-1′); ArH 6.41 (H-5), 6.45 (H-5′), 6.87 (H-13), 6.88 (H-13′), 6.98 (H-10′), 7.06 (H-8′), 7.20 (H-14), 7.34 (H-14′), 7.54 (H-10) (51)
MS: $[M]^+$ 622 (68), 396 (29), 395 (100), 381 (39), 198 (94), 174 (53) (51)
CD: 0 (310), +1 (300), 0 (292), −1.3 (277), 0 (262), +0.9 (255), 0 (250), −2.9 (245), 0 (240), +24.8 (225) (51)

333 2′-NORISOCEPHARANTHINE $C_{36}H_{36}O_6N_2$: 592.2573

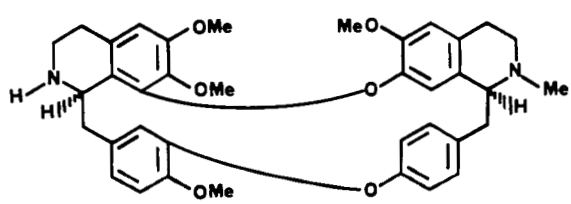
Type VI (*R,S*) 6,7*,11$^+$,12-6,7,8*,12$^+$



[α]D: −84° (*c* = 0.25, $CHCl_3$) (64)
UV: 236 (sh) (4.08), 280 (3.67) (64)
^{1}H NMR: NMe 2.63 (N-2′); OMe 3.59 (C-6), 3.93 (C-12), CH_2O_2 5.56 (d, 1H, *J* = 1.3 Hz) and 5.67 (d, 1H, *J* = 1.3 Hz) (C-6′ and C-7′); AlH 4.07 (m, 1H, H-1′), 4.57 (m, 1H, H-1); ArH 6.38 (H-5 or H-5′), 6.39 (d, 1H, *J* = 1.8 Hz, H-10), 6.44 (H-5′ or H-5), 6.55 (H-8), 6.84 (dd, 1H, *J* = 2.0, 8.3 Hz, H-11′), 6.89 (d, 1H, *J* = 8.2 Hz, H-13), 6.92 (m, 1H, H-10′ and H-13′), 6.95 (dd, 1H, *J* = 1.8, 8.2 Hz, H-14), 7.39 (dd, 1H, *J* = 2.0, 8.3 Hz, H-14′) (64)
MS: $[M]^+$ 592 (100), 591 (88), 365 (45), 351 (22), 349 (32), 206 (12), 192 (12), 183 (72), 160 (19) (64)
Sources: *Stephania pierrii* Diels (Menispermaceae) (64)

334 2-NORISOTETRANDRINE $C_{37}H_{40}O_6N_2$: 608.2886

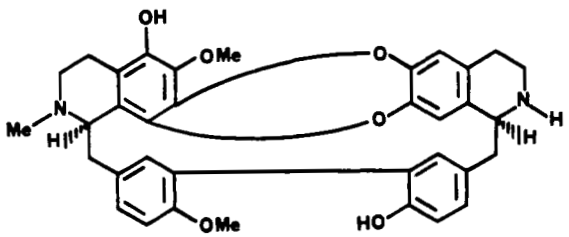
Type VIII (*R,S*) 6,7,8*,11$^+$,12-6,7*,12$^+$



[α]D: +100° (c = 0.16, $CHCl_3$) (64)
UV: 208 (4.82), 239 (sh) (4.34), 282 (3.86) (64)
^{1}H NMR: NMe 2.57 (N-2′); OMe 3.08 (C-7), 3.63 (C-6′), 3.75 (C-7), 3.93 (C-12); AlH 3.88 (M, 1H, H-1′), 4.06 (M, 1H, H-1); ArH 6.05 (H-8′), 6.30 (H-5), 6.42 (d, 1H, J = 1.8 Hz, H-10), 6.45 (dd, 1H, J = 2.2, 8.3 Hz, H-10′), 6.55 (H-5′), 6.71 (dd, 1H, J = 2.2, 8.3 Hz, H-11′), 6.75 (dd, 1H, J = 1.8, 8.0 Hz, H-14), 6.83 (d, 1H, J = 8.0 Hz, H-13), 7.09 (dd, 1H, J = 2.2, 8.3 Hz, H-13′), 7.29 (dd, 1H, J = 2.2, 8.3 Hz, H-14′) (64)
MS: $[M]^+$ 608 (48) (hrms, found 608.2893), 607 (41), 606 (10), 381 (100), 367 (13), 191 (71), 190 (10), 174 (17), 168 (15) (64)
Sources: *Stephania pierrii* Diels (Menispermaceae) (64)

335 NORISOYANANGINE $C_{35}H_{34}O_6N_2$: 578.2417

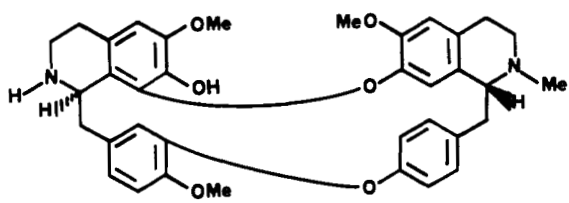
Type XIX (*R,S*) 5,6,7*,8$^+$,12-6*,7$^+$,12(11-11)



TLC: 0.25 [Si gel 60 F_{254}, CH_2Cl_2-MeOH-25% NH_4OH (90:9:1)] (56)
$[\alpha]^{20}$D: +139° (c = 1.2, $CHCl_3$) (56)
UV: 203 (4.70), 230 (sh) (4.44), 288 (3.74) (56)
IR(KBr): 3400, 2950, 2800, 1620, 1500, 1450, 1370, 1320, 1270, 1230, 1100, 1020, 800, 700 (56)
^{1}H NMR: NMe 2.29 (N-2); OMe 3.92 (C-6), 3.97 (C-12); ArH 6.66 (H-5′), 6.88 (d, 1H, J = 8.2 Hz, H-13), 7.04 (d, 1H, J = 8.2 Hz, H-13′), 7.18 (H-8′), 7.23 (dd, 1H, J = 2.2, 8.2 Hz, H-14), 7.32 (d, 1H, J = 2.2 Hz, H-10′), 7.35 (dd, 1H, J = 2.2, 8.2 Hz, H-14′), 7.93 (d, 1H, J = 2.2 Hz, H-10) (56)
^{13}C NMR: 61.54 (C-1), 43.83 (C-3), 18.25 (C-4), 114.55 (C-4a), 141.70 (C-5), 132.77 (C-6), 132.81 (C-7), 131.56 (C-8), 122.78 (C-8a), 39.88 (C-α), 137.32 (C-9), 135.38 (C-10), 126.32 (C-11), 153.21 (C-12), 111.19 (C-13), 129.80 (C-14), 58.42 (C-1′), 45.15 (C-3′), 29.53 (C-4′), 133.00 (C-4′a), 116.15 (C-5′), 138.85 (C-6′), 136.20 (C-7′), 114.29 (C-8′), 129.30 (C-8′a), 42.62 (C-α′), 138.85 (C-9′), 134.56 (C-10′), 128.03 (C-11′), 152.80 (C-12′), 118.80 (C-13′), 130.40 (C-14′), 42.96 (2-NMe), 56.61 (12-OMe), 61.51 (6-OMe) (56)
MS: $[M]^+$ 578 (64), 577 (56), 561 (8), 381 (10), 365 (60), 352 (46), 351 (100), 337 (34), 335 (34), 321 (15), 183 (22), 176 (28), 175 (26) (56)
Sources: *Tiliacora triandra* Diels (Menispermaceae) (56)

336 2-NORLIMACINE $C_{36}H_{38}O_6N_2$: 594.2730

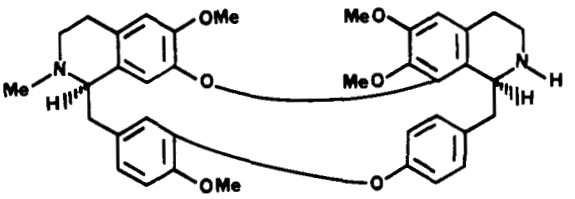
Type VIII (*R,R*) 6,7,8*,11$^+$,12-6,7*,12$^+$



[α]D: −193° (c = 0.13, $CHCl_3$) (19)
UV: 211 (4.91), 238 (4.46), 282 (3.96) (19)
^{1}H NMR: NMe 2.63 (N-2′); OMe 3.37 (C-6′), 3.78 (C-6), 3.95 (C-12); AlH 3.87 (m, H-1′), 4.01 (d, 1H, H-1); ArH 6.04 (H-8′), 6.30 (H-5), 6.38 (dd, 1H, J = 1.8, 8.2 Hz, H-10′), 6.45 (d, 1H, J = 1.8 Hz, H-10), 6.54 (H-5′), 6.74 (dd, 1H, J = 1.8, 8.2 Hz, H-11′), 6.83 (dd, 1H, J = 1.8, 8 Hz, H-14), 6.87 (d, 1H, J = 8 Hz, H-13), 7.14 (dd, 1H, J = 1.8, 8.2 Hz, H-13′), 7.37 (dd, 1H, J = 1.8, 8.2 Hz, H-14′) (19)
MS: $[M]^+$ 594 (47), 593 (39), 369 (25), 367 (100), 366 (16), 365 (49), 353 (13), 190 (12), 184 (39), 183 (14), 174 (32) (19)
Sources: *Caryomene olivascens* Barneby et Krukoff (Menispermaceae) (19)
Derivatives: Limacine [**64**] (2-norlimacine + CH_2O + $NaBH_4$) (^{1}H nmr) (19)

337 2′-NOROBABERINE $C_{37}H_{40}O_6N_2$: 608.2886

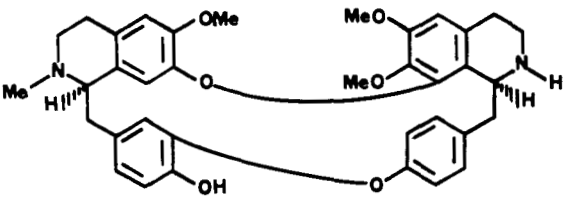
Type VI (*R,S*) 6,7*,11$^+$,12-6,7,8*,12$^+$



^{1}H NMR: NMe 2.60 (N-2′); OMe 3.20 (C-7′), 3.67 (C-6), 3.80 (C-6′), 3.90 (C-12); AlH 3.65 (m, 1H, H-1), 4.70 (m, 1H, H-1′); ArH 5.44 (br s, 1H, H-10), 6.34 (H-5 or H-5′), 6.36 (H-5′ or H-5), 6.36 (m, 1H, H-11′), 6.96 (m, 1H, H-10′), 6.97 (m, 1H, H-13′), 7.62 (dd, 1H, J = 2.2, 8.2 Hz, H-14′) (64)
MS: [M]$^+$ 608 (42), 607 (42), 593 (9), 381 (100), 367 (20), 192 (7), 191 (54), 190 (10), 174 (19), 168 (17) (64)
Sources: *Stephania pierrii* Diels (Menispermaceae) (64)

338 2′-NOROXYACANTHINE $C_{36}H_{38}O_6N_2$: 594.2730

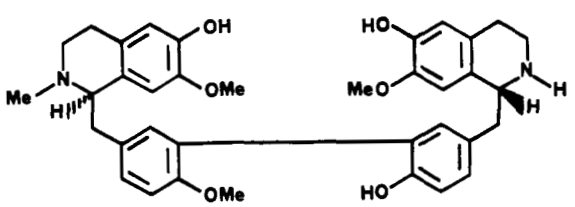
Type VI (*R,S*) 6,7*,11$^+$,12-6,7,8*,12$^+$



MP: Amorphous (41)
[α]D: +125° (c = 0.1, MeOH) (41)
^{1}H NMR: NMe 2.57 (N-2); OMe 3.19 (C-7′), 3.66 (C-6), 3.80 (C-6′); AlH 3.62 (m, 1H, H-1), 4.56 (m, 1H, H-1′); ArH 5.42 (br s, 1H, H-10), 6.30 (dd, 1H, J = 2.4, 8.4 Hz, H-11′), 6.34 (H-5′), 6.35 (H-5), 6.61 (H-8), 6.78 (br s, 2H, H-13 and H-14), 6.92 (m, 1H, H-13′), 6.97 (m, 1H, H-14′), 7.55 (dd, 1H, J = 2.4, 8.4 Hz, H-14′) (41)
MS: [M]$^+$ 594 (67), 593 (55), 382 (26), 381 (100), 367 (21), 192 (30), 191 (76), 174 (27) (41)
Sources: *Thalictrum cultratum* Wall. (Ranunculaceae) (41)

339 2′-NORPISOPOWIARIDINE $C_{36}H_{40}O_6N_2$: 596.2886

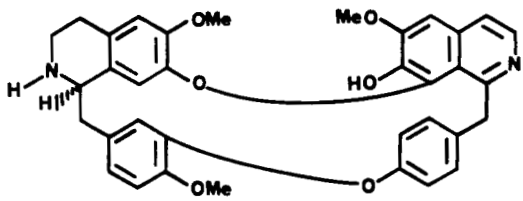
Type XXVII (*R,R*) 6,7,12-6,7,12(11-11)



MP: Amorphous (30)
[α]D: −46° (c = 0.33, MeOH) (30)
UV(EtOH): 209 (4.30), 230 (sh) (4.18), 289 (3.73) (30)
^{1}H NRM: NMe 2.64 (N-2); OMe 3.25 (C-7 or C-7′), 3.73 (C-7′ or C-7), 3.92 (C-12′); AlH 4.14 (m, 1H, H-1′); ArH 5.41 (s, H-8 or H-8′), 6.28 (d, 1H, J = 2 Hz, H-10′), 6.37 (d, 1H, J = 2 Hz, H-10), 6.57 (s, 2H, H-8′ or H-8 and H-5 or H-5′), 6.67 (s, H-5′ or H-5), 6.98 (d, 1H, J = 8 Hz, H-13), 6.99 (d, 1H, J = 8 Hz, H-13′), 7.19 (dd, 1H, J = 2, 8 Hz, H-14′), 7.23 (dd, 1H, J = 2, 8 Hz, H-14) (nOe used) (30)
CIMS: [M + 1]$^+$ 597 (100), 596 (4), 420 (4), 406 (4), 192 (96), 178 (65) (30)
CD: −3.2 (296), 0 (288), +1.8 (280), 0 (264), +1.8 (253), 0 (247), −12.9 (226) (30)
Sources: *Popowia pisocarpa* (Bl.) Endl. (Annonaceae) (30)
Derivatives: Pisopowiaridine [**359**] (nor-2-pisopowiaridine + $CH_2O/NaBH_4$) (30)

340 NORSTEPHASUBINE $C_{35}H_{32}O_6N_2$: 576.2260

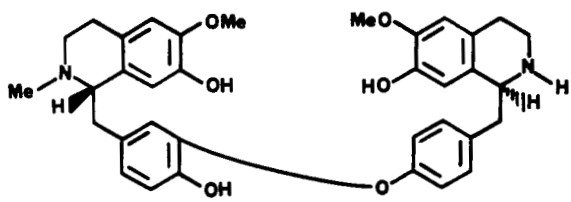
Type VI (*R*,−) 6,7*,11$^+$,12-6,7,8*,12$^+$



MP: Amorphous (21)
[α]D: +309° (*c* = 0.09, MeOH) (21)
UV: 240 (4.53), 286 (3.62), 338 (3.42) (21); (MeOH + H^+) 235 (4.30), 264 (4.36), 321 (3.32), 368 (3.40), 374 (3.39) (21)
^{1}H NMR: OMe 3.88 (C-12), 4.02 (C-6), 4.03 (C-6′); AlH 4.02 (m, 1H, H-1), 4.50 (d, 1H, *J* = 13.7 Hz, H-α′), 5.35 (d, 1H, *J* = 13.7 Hz, H-α′); ArH 4.87 (d, 1H, *J* = 1.5 Hz, H-10), 6.02 (H-8), 6.43 (dd, 1H, *J* = 2, 8.4 Hz, H-13′), 6.53 (H-5), 6.66 (dd, 1H, *J* = 2, 8.4 Hz, H-11′), 6.71 (dd, 1H, *J* = 1.5, 8.1 Hz, H-14), 6.73 (d, 1H, *J* = 8.1 Hz, H-13), 6.93 (H-5′), 7.09 (dd, 1H, *J* = 2, 8.4 Hz, H-10′), 7.37 (dd, 1H, *J* = 2, 8.4 Hz, H-14′), 7.46 (d, 1H, *J* = 5.6 Hz, H-4′), 8.41 (d, 1H, *J* = 5.6 Hz, H-3′) (21)
MS: [M]$^+$ 576 (72), 575 (100), 561 (20), 549 (29), 288 (15), 190 (8), 174 (25), 146 (16), 145 (18) (21)
Sources: *Stephania suberosa* Forman (Menispermaceae) (21)
Derivatives: Stephasubine [**374**] (norstephasubine + CH_2O + HCOOH) (21)

341 NORTHALIBROLINE $C_{35}H_{38}O_6N_2$: 582.2730

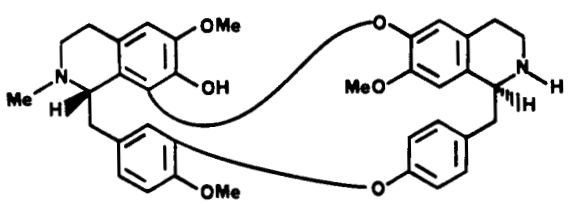
Type I (*S*,*S*) 6,7,11*,12-6,7,12*



UV: 282 (76)
IR(KBr): 3400, 2924, 1620, 1508, 1450, 1369, 1259, 1220, 1125, 1021 (76)
^{1}H NMR($CDCl_3$ + CD_3OD): NMe 2.49 (N-2); AlH 3.67 (dd, 1H, H-1), 4.10 (dd, 1H, H-1′); OMe 3.81 (C-6 or C-6′), 3.85 (C-6′ or C-6); ArH 6.13 (H-8), 6.49 (H-8′), 6.51 (H-10[?]), 6.58 (H-5′), 6.71 (H-5), 6.82 (d, 2H, *J* = 8.6 Hz) (H-11′ and H-13′), 6.85 (d, 1H, *J* = 7.1 Hz, H-14), 6.87 (d, 1H, *J* = 7.1 Hz, H-13), 7.12 (d, 2H, *J* = 8.6 Hz, H-10′ and H-14′) (76)
MS: 192 (63), 191 (14), 190 (90), 179 (12), 178 (100), 177 (13) (76)
Sources: *Thalictrum minus* L. var. *minus* (Ranunculaceae) (76)

342 2-′-NORTHALIPHYLLINE $C_{36}H_{38}O_6N_2$: 594.2730

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

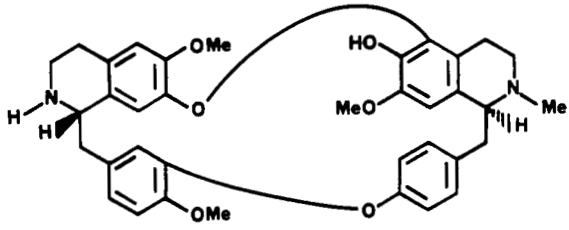


UV: 237 (sh) (4.16), 2.85 (3.83) (24,41)
^{1}H NMR: NMe 2.09 (*N*-2); OMe 3.64 (C-7′), 3.90 (6H) (C-6 and C-12); AlH 4.46 (m, 1H, H-1′); ArH 6.11 (2H, H-5′ and H-8′), 6.23 (d, 1H, *J* = 2.2 Hz, H-10), 6.55 (H-5), 6.68 (dd, 1H, *J* = 2.2, 8.2 Hz, H-14), 6.69 (dd, 1H, *J* = 2.1, 8.1 Hz, H-10′), 6.82 (d, 1H, *J* = 8.2 Hz, H-13), 6.94 (dd, 1H, *J* = 2.1, 8.1 Hz, H-11′), 7.08 (dd, 1H, *J* = 2.1, 8.1 Hz, H-13′), 7.26 (dd, 1H, *J* = 2.1, 8.1 Hz, H-14′) (24,41)
MS: [M]$^+$ 594 (89), 593 (84), 592 (25), 367 (100), 353 (10), 208 (31), 192 (22), 191 (39), 190 (20), 184 (84) (24,41)
CD: 0 (300), −7 (285), 0 (270), −1 (250), positive tail below 220 nm (24,41)
Sources: *Thalictrum cultratum* Wall. (Ranunculaceae) (41)

343 2-NORTHALMINE

$C_{36}H_{38}O_6N_2$: 594.2730

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

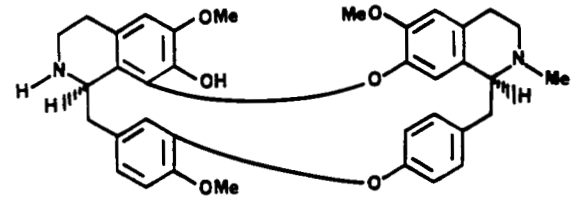


TLC: 0.18 (Si gel) [C_6H_6-MeCO-NH_4OH (95:5:trace)] (12)
$[\alpha]^{25}D$: −31.8° (*c* = 0.43, MeOH) (12)
UV: 234 (sh) (4.45), 283 (3.97) (12)
^1H NMR: NMe 2.62 (N-2′); OMe 3.90 (C-6), 3.93 (C-12), 3.94 (C-7′); AlH 3.51 (m, 1H, H-1), 3.62 (m, 1H, H-1′); ArH 5.93 (d, 1H, *J* = 1.9 Hz, H-10), 5.97 (H-8), 6.68 (dd, 1H, *J* = 1.9, 8.0 Hz, H-14), 6.77 (H-8′), 6.80 (d, 1H, *J* = 8.0 Hz, H-13), 6.91 (br s, 2H, H-11′, H-13′), 7.07 (br s, 1H, H-10′), 7.63 (br s, 1H, H-14′) (nOe used) (12)
MS: $[M]^+$ 594 (22), 367 (100) (12)
CD: 0 (300), +7.6 (289), 0 (276), −2.1 (260), 0 (257), +6.3 (238), negative tail below 230 (12)
Sources: *Thalictrum cultratum* Wall. (Ranunculaceae) (12)
Preparation: Via *N*-methylation (CH_2O + $NaBH_4$) of thalmine **[108]** (tlc, ^1H nmr) (12)

344 2-NORTHALRUGOSINE

$C_{36}H_{38}O_6N_2$: 594.2730

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

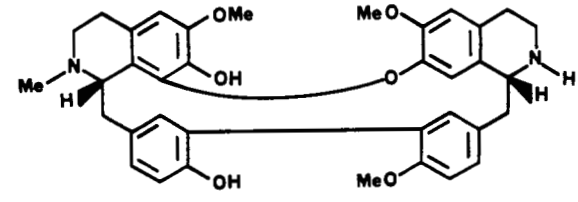


[α]D: +209° (*c* = 0.16, $CHCl_3$) (38)
UV: 234 (4.60), 282 (4.06) (38); (MeOH + OH^-) 244, 298 (38)
^1H NMR: NMe 2.49 (N-2′); OMe 3.76 (C-6), 3.94 (C-6′ or C-12), 3.96 (C-12 or C-6′); AlH 3.74 (m, 1H, H-1′), 4.23 (m, 1H, H-1); ArH 6.14 (H-8′), 6.25 (d, 1H, *J* = 1.5 Hz, H-10), 6.39 (H-5), 6.46 (dd, 1H, *J* = 2.0, 8.2 Hz, H-10′), 6.72 (dd, 1H, *J* = 2.0, 8.2 Hz, H-11′), 6.76 (H-5′), 6.83 (d, 1H, *J* = 8.0 Hz, H-13), 6.88 (dd, 1H, *J* = 1.5, 8.0 Hz, H-14), 6.99 (dd, 1H, *J* = 2.0, 8.2 Hz, H-13′), 7.31 (dd, 1H, *J* = 2.0, 8.2 Hz, H-14′) (38)
MS: $[M]^+$ 594 (12), 593 (7), 368 (22), 367 (91), 353 (10), 314 (38), 301 (10), 192 (33), 190 (20), 184 (100), 178 (22), 174 (25), 161 (24) (38)
Sources: *Pycnarrhena ozantha* Diels (Menispermaceae) (38)
Derivatives: Thalrugosine **[79]** (2-northalrugosine + $CH_2O/NaBH_4$) (38)

345 2′-NORTILIAGEINE

$C_{36}H_{38}O_6N_2$: 594.2730

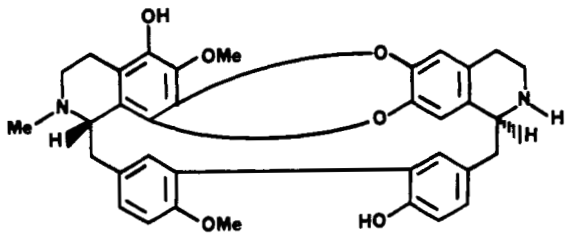
Type IV (*S,R*) 6,7,8*,12-6,7*,12(11-11)



[α]D: +203° (*c* = 0.18, $CHCl_3$) (51)
UV: 230 (4.60), 285 (3.86) (51)
^1H NMR: NMe 2.39 (N-2); OMe 3.51 (C-6′), 3.86 (C-6), 3.90 (C-12′); AlH 3.90 (H-1), 4.44 (H-1′); ArH 6.38 (H-5), 6.48 (H-5′), 6.74 (H-10), 6.86 (H-13′), 6.89 (H-13), 7.14 (H-10′), 7.23 (H-14′), 7.29 (H-8′), 7.34 (H-14) (51)
MS: $[M]^+$ 594 (58), 593 (88), 367 (100), 353 (17), 184 (56) (51)
Sources: *Guatteria guianensis* (Aublet) R.E. Fries (Annonaceae) (51)
Derivatives: Tiliageine **[27]** (2′-nortiliageine + $CH_2O/NaBH_4$) (51)

346 NORYANANGINE $C_{35}H_{34}O_6N_2$: 578.2417

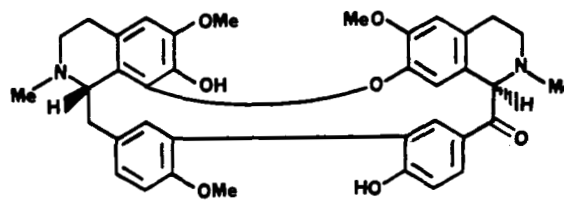
Type XIX (*S,S*) 5,6,7*,8$^+$,12-6*,7$^+$,12(11-11)



MP: 196–198° (56)
TLC: 0.35 (Si gel 60 F_{254}) [CH_2Cl_2-MeOH-25% NH_4OH (90:9:1)] (56)
$[\alpha]^{20}D$: +295° (c = 0.5, $CHCl_3$) (56)
UV: 211 (5.17), 230 (sh) (5.01), 289 (4.32) (56)
IR(KBr): 3400, 2920, 2830, 1660, 1630, 1590, 1500, 1446, 1370, 1330, 1275, 1230, 1100, 1000, 890, 860 (56)
^{1}H NMR: NMe 2.29 (N-2); OMe 3.96 (C-6), 3.99 (C-12); 6.63 (H-5'), 6.95 (d, 1H, J = 8.25 Hz, H-13), 6.98 (d, 1H, J = 8.25 Hz, H-13'), 7.31 (dd, 1H, J = 2.1, 8.25 Hz, H-14'), 7.35 (dd, 1H, J = 2.1, 8.25 Hz, H-14), 7.60 (d, 1H, J = 2.1 Hz, H-10'), 7.69 (d, 1H, J = 2.1 Hz, H-10), 8.11 (H-8') (56)
^{13}C NMR: 62.73 (C-1), 44.19 (C-3), 16.00 (C-4), 115.52 (C-4a), 141.79 (C-5), 133.00 (C-6), 133.36 (C-7), 133.06 (C-8), 121.18 (C-8a), 40.43 (C-α), 137.71 (C-9), 135.83 (C-10), 126.46 (C-11), 153.33 (C-12), 111.11 (C-13), 129.59 (C-14), 59.51 (C-1'), 44.26 (C-3'), 28.59 (C-4'), 133.64 (C-4'a), 115.79 (C-5'), 139.47 (C-6'), 139.90 (C-7'), 113.81 (C-8'), 130.45 (C-8'a), 43.21 (C-α'), 137.15 (C-9'), 134.09 (C-10'), 126.46 (C-11'), 152.69 (C-12'), 118.35 (C-13'), 130.64 (C-14'); 42.06 (2-NMe), 56.52 (12-OMe), 61.53 (6-OMe) (56)
MS: $[M]^+$ 578 (50), 577 (41), 365 (22), 352 (24), 351 (47), 337 (22), 176 (10), 149 (42), 38 (100) (56)
Sources: *Tiliacora triandra* Diels (Menispermaceae) (56)

347 OXANDRINE $C_{37}H_{38}O_7N_2$: 622.2679

Type IV (*S,S*) 6,7,8*,12-6,7*,12(11-11)

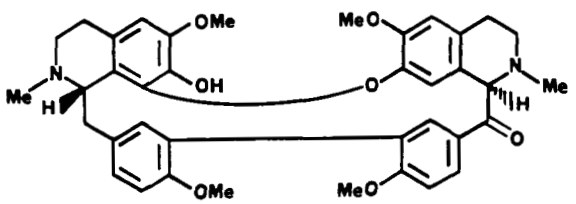


MP: Amorphous (80)
[α]D: −11° (c = 0.9, $CHCl_3$) (80); +9° (c = 0.96, MeOH) (80)
UV(EtOH): 209 (4.73), 282 (4.02) (80); (EtOH + NaOH) 224 (4.92), 296 (4.30) (80)
IR(film): 3320, 1670, 1605 (80)
^{1}H NMR: NMe 2.32 (N-2'), 2.33 (N-2); OMe 3.66 (C-6'), 3.82 (C-6), 3.85 (C-12); AlH 3.80 (d, H-1), 4.21 (s, H-1'); ArH 6.37 (H-5), 6.65 (H-5'), 6.70 (d, 1H, J = 2 Hz, H-10), 6.85 (d, 1H, J = 8.5 Hz, H-13), 6.91 (d, 1H, J = 8.5 Hz, H-13'), 6.93 (d, 1H, J = 2 Hz, H-10'), 7.12 (H-8'), 7.25 (dd, 1H, J = 2, 8.5 Hz, H-14'), 7.27 (dd, 1H, J = 2, 8.5 Hz, H-14) (nOe used) (80)
^{13}C NMR: 63.8 (C-1), 45.5 (C-3), 22.6 (C-4), 124.4 (C-4a), 107.3 (C-5), 146.4 (C-6), 133.6 (C-7), 137.0 (C-8), 126.8 (C-8a or C-8'a), 38.1 (C-α), 131.2 (C-9 or C-11 or C-11'), 134.8 (C-10), 133.3 (C-11 or C-9 or C-11'), 154.0 (C-12), 117.7 (C-13 or C-8'), 131.4 (C-14 or C-10' or C-14'), 84.0 (C-1'), 53.0 (C-3'), 35.0 (C-4'), 131.2 (C-4'a or C-11 or C-11'), 113.2 (C-5'), 150.9 (C-6'), 139.8 (C-7'), 117.8 (C-8' or C-13), 126.9 (C-8'a or C-8a), 205.5 (C-α'), 143.2 (C-9'), 131.5 (C-10' or C-14 or C-14'), 131.9 (C-11'), 153.1 (C-12'), 111.2 (C-13'), 129.6 (C-14' or C-10' or C-14), 41.7 (2-NMe and 2'-NMe), 42.8 (2'-NMe or 2-NMe), 55.8 (12-OMe or 6'-OMe), 55.9 (6-OMe), 56.4 (6'-OMe or 12-OMe) (80)
EIMS: $[M]^+$ 622 (16), 381 (3), 367 (1), 192 (100), 191 (30), 175 (5) (80)
CIMS: $[M+1]^+$ 623 (80)
CD: 0 (310), −4.6 (sh) (293), −25 (250), 0 (233), +80 (221) (80)
Sources: *Pseudoxandra* aff. *lucida* (Annonaceae) (80)
Derivatives: *O,O*-Diacetyloxandrine (oxandrine + Ac_2O/pyridine) (80)
[α]D: +88° (c = 0.9, $CHCl_3$) (80)
UV(EtOH): 224 (4.62), 282 (3.69) (80)
IR(film): 1765, 1680, 1605 (80)

^{1}H NMR: NMe 2.25 (N-2'), 2.29 (N-2); OAc 2.01 (C-12'), 2.07 (C-7); OMe 3.43 (C-6'), 3.65 (C-12), 3.81 (C-6); AlH 3.48 (d, H-1), 4.16 (s, H-1'); ArH 6.50 (H-5), 6.59 (H-5'), 6.77 (d, 1H, J = 8.5 Hz, H-13), 6.83 (d, 1H, J = 2 Hz, H-10), 7.02 (d, 1H, J = 2 Hz, H-10'), 7.11 (d, 1H, J = 8.5 Hz, H-13'), 7.13 (H-8'), 7.29 (dd, 2H, J = 2, 8.5 Hz, H-14 and H-14') (80)
EIMS: $[M]^+$ 706 (100), 664 (50), 663 (58), 649 (19), 437 (5), 381 (5), 368 (4), 353 (9), 191 (30) (80)
CIMS: $[M+1]^+$ 707 (80)
O,O-Dimethyloxandrine (oxandrine + CH_2N_2) (80)
^{1}H NMR: NMe 2.26 (N-2'), 2.27 (N-2); OMe 3.41 (C-7), 3.69 (C-6'), 3.74 (C-12 or C-12'), 3.76 (C-12' or C-12), 3.83 (C-6); AlH 3.45 (m, H-1), 4.13 (s, H-1'); ArH 6.44 (H-5), 6.58 (H-5'), 6.77 d, 1H, J = 8.5 Hz, H-13), 6.81 (d, 1H, J = 8.5 Hz, H-13 or H-13'), 6.85 (d, 1H, J = Δ8.5 Hz, H-13' or H-13), 7.02 (d, 1H, J = 2 Hz, H-10'), 7.12 (H-8'), 7.26 (dd, 1H, J = 2, 8.5 Hz, H-14'), 7.28 (dd, 1H, J = 2, 8.5 Hz, H-14) (80)
EIMS: $[M]^+$ 650 (100), 396 (1), 381 (12), 198 (60), 175 (39) (80)
Dihydrooxandrine (oxandrine + $NaBH_4$/MeOH) (80)
$[\alpha]_D$: +140° (c = 0.38, $CHCl_3$) (80)
UV(EtOH): 210 (4.99), 285 (4.02) (80)
IR(film): 3350, 1610 (80)
^{1}H NMR: NMe 2.08 (N-2'), 2.35 (N-2); OMe 3.42 (C-6'), 3.70 (C-6), 3.82 (C-12), AlH 3.67 (d, J = 4 Hz, H-1'), 5.30 (d, 1H, J = 4 Hz, H-α'); ArH 6.32 (H-5), 6.57 (H-5'), 6.88 (d, H-13), 6.90–7.41 (6H, 80)
EIMS: $[M[^+$ 624 (100), 623 (60), 609 (34), 381 (3), 206 (14), 191 (27) (80)
Reduction (Zn/HCl) afforded two isomeric products, one of which was antioquine [**225**] (80)

348 OXANDRININE $C_{38}H_{40}O_7N_2$: 636.2836

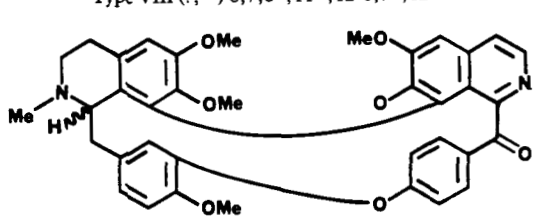
Type IV (*S,S*) 6,7,8*,12-6,7*,12(11-11)



MP: Amorphous (80)
$[\alpha]_D$: +60° (c = 0.5, $CHCl_3$) (80)
UV(EtOH): 208 (4.50), 282 (3.64) (80); (EtOH + NaOH) 216 (4.78), 290 (4.00) (80)
IR(film): 3340, 1675, 1600, 1500 (80)
^{1}H NMR: NMe 2.27 (s, 6H, N-2 and N-2'); OMe 3.74 (C-6'), 3.80 (C-6), 3.84 (s, 6H, C-12 and C-12'); AlH 4.18 (s, H-1'); ArH 6.43 (H-5), 6.65 (H-5'), 6.81–7.32 (m, 7H) (80)
EIMS: $[M]^+$ 636, 635, 621, 607, 417, 411, 381, 368, 191, 190, 175, 174 (80)
CIMS: $[M+1]^+$ 637 (80)
CD: 0 (355), +1 (330), 0 (281), −2.5 (252), 0 (236), +8.5 (223), 0 (210) (80)
Sources: *Pseudoxandra* aff. *lucida* (Annonaceae) (80)
Derivatives: *O*-Methyloxandrinine (*O,O*-dimethyloxandrine) (oxandrinine + CH_2N_2) (80)
^{1}H NMR: NMe 2.26 (N-2'), 2.27 (N-2); OMe 3.41 (C-7), 3.69 (C-6'), 3.74 (C-12 or C-12'), 3.76 (C-12' or C-12), 3.83 (C-6); AlH 3.45 (m, H-1), 4.13 (s, H-1'); ArH 6.44 (H-5), 6.58 (H-5'), 6.77 (d, 1H, J = 8.5 Hz, H-13), 6.81 (d, 1H, J = 8.5 Hz, H-13 or H-13'), 6.85 (d, 1H, J = 8.5 Hz, H-13' or H-13), 7.02 (d, 1H, J = 2 Hz, H-10'), 7.12 (H-8'), 7.26 (dd, 1H, J = 2, 8.5 Hz, H-14'), 7.28 (dd, 1H, J = 2, 8.5 Hz, H-14) (80)
EIMS: $[M]^+$ 650 (100), 396 (1), 381 (12), 198 (60), 175 (39) (80)

349 OXOFANGCHIRINE $C_{37}H_{34}O_7N_2$: 618.2366

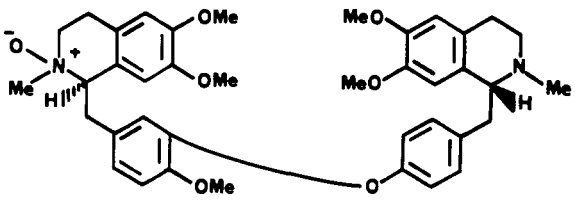
Type VIII (?,−) 6,7,8*,11$^+$,12-6,7*,12$^+$



MP: 184–186° (Me_2CO) (327)
[α]D: +47° (c = 0.42, $CHCl_3$) (327)
UV: 235 (4.68), 280 (sh), (4.10), 325 (3.77) (327)
IR(KBr): 1680, 1600, 1580, 1220, 1060 (327)
^{1}H NMR: NMe 2.42 (N-2); OMe 3.29 (C-7), 3.69 (C-6'), 3.79 (C-6), 3.94 (C-12); AlH 2.3–3.05 (m, 6H); ArH 5.87 (d, 1H, H-10), 6.38 (H-5), 6.74 (H-8'), 6.8 + 6.9 (AB, H-13' + H-14'), 7.02 (H-5'), 7.38 (dd, 1H, H-11'), 7.64 (d, 1H, J = 5.5 Hz, H-4'), 8.34 (dd, 1H, H-10'), 8.6 (d, 1H, J = 5.5 Hz, H-3') (327)
^{13}C NMR: 77.0 (d, C-1), 44.9 (t, C-3), 23.2 (t, C-4), 41.2 (C-α); 141.7 (d, C-3'), 160.1 (s, C-1'), 194.3 (s, C-α'); others include 137.8 (s), 146.2 (s) 146.8 (s), 147.1 (s), 149.4 (s), 151.0 (s), 153.7 (s), 155.6 (s); 42.5 (q, 2-NMe), 55.7 (q, OMe), 56.1 (q, OMe), 56.4 (q, OMe), 60.4 (q, OMe) (327)
MS: $[M]^+$ 618 (100) (found 618.2326), 603 (99), 587 (9), 557 (10), 481 (2), 379 (7), 309 (19), 206 (6), 105 (2), 58 (70) (327)
Sources: *Stephania tetrandra* S. Moore (Menispermaceae) (327)

350 *N*-2-OXY-*O*-METHYLDAURICINE $C_{39}H_{46}O_7N_2$: 654.3305

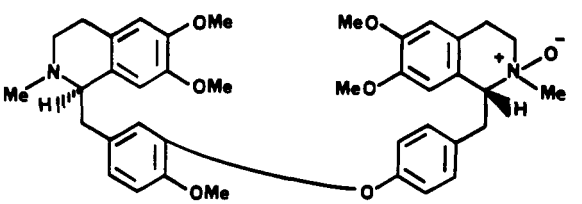
Type I (*R*,*R*) 6,7,11*,12-6,7,12*



This was isolated as a nonseparable mixture with *N*-2'-oxy-*O*-methyldauricine [**351**] in a ratio of 10:7 or 7:10 (30). The data that is reported for each alkaloid is the data obtained for the 10:7 or 7:10 mixture (30).
MP: Amorphous (30)
[α]D: −138° (c = 0.5, MeOH) (30)
UV(EtOH): 209 (4.41), 230 (sh) (4.20), 285 (4.13) (30)
^{1}H NMR: NMe 2.50 and 2.53; N^+O^-Me 3.27 and 3.32; OMe 3.51 and 3.51 and 3.58 and 3.59 (all for C-7 or C-7'); 3.76–3.82 (C-6 and C-6' and C-12); ArH 6.47 and 6.53 and 6.55 and 6.57 (all for H-5 and H-5'); 6.04 and 6.09 and 6.26 and 6.30 (all for H-8 and H-8'); 6.6–7.2 (7H, H-10 and H-13 and H-14 and H-10' and H-11' and H-13' and H-14') (30)
CIMS: $[M + 1]^+$ 665 (1), $[M]^+$ 654 (2), 653 (5), 640 (12), 639 (28), 448 (4), 434 (5), 206 (100), 204 (12), 192 (15), 190 (14) (30)
Sources: *Popowia pisocarpa* (Bl.) Endl. (Annonaceae) (30)
Derivatives: *O*-Methyldauricine [**12a**] (*N*-2-oxy-*O*-methyldauricine + Zn/HCl) (^{1}H nmr, tlc, sp rotation) (30)

351 *N*-2'-OXY-*O*-METHYLDAURICINE $C_{39}H_{46}O_7N_2$: 654.3305

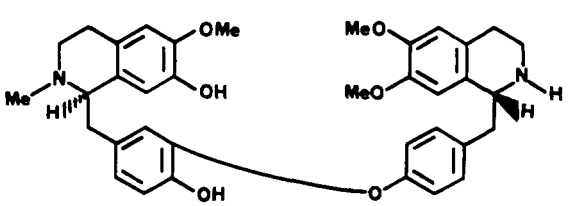
Type I (*R*,*R*) 6,7,11*,12-6,7,12*



This was isolated as a nonseparable mixture with *N*-2-oxy-*O*-methyldauricine [**350**] in a ratio of 7:10 or 10:7 (30). The data that is reported for each alkaloid is the data obtained for the 7:10 or 10:7 mixture (30). See data listed for *N*-2-oxy-*O*-methyldauricine [**350**].

352 PAMPULHAMINE $C_{36}H_{40}O_6N_2$: 596.2886

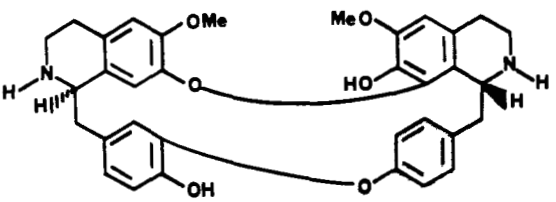
Type I (*R*,*R*) 6,7,11*,12-6,7,12*



MP: Amorphous (71)
$[\alpha]_D$: $-58°$ ($c = 0.18$, MeOH) (71)
UV: 233 (4.18), 290 (3.75) (71); (MeOH + OH^-) 236 (4.08), 296 (3.51), 312 (sh) (3.42) (71)
^{1}H NMR: NMe 2.49 (N-2); OMe 3.81 (C-7′ or C-6′ or C-6), 3.85 (C-6′ or C-7′ or C-6), 3.87 (C-6 and C-6′ or C-7′); ArH 6.30 (H-8′ and H-8), 6.46 (H-8′ or H-8′), 6.47 (d, 1H, $J = 1.7$ Hz, H-10), 6.61 (H-5), 6.69 (H-5′), 6.83 (d, 2H, $J = 8.45$ Hz, H-11′ and H-13′), 6.85 (dd, 1H, $J = 1.7$, 8.2 Hz, H-14), 6.91 (d, 1H, $J = 8.2$ Hz, H-13), 7.16 (d, 1H, $J = 8.45$ Hz, H-10′ and H-14′) (71)
EIMS: 192 (100) (71)
CIMS: $[M + 1]^+$ 597, 405 (12), 192 (100) (71)
CD: −3.1 (289), 0 (256), 0 (248), −11.6 (226) (71)
Sources: *Aristolochia gigantea* Mart. (Aristolochiaceae) (71)
Derivatives: *O,O*-Dimethylpampulhamine (pampulhamine + CH_2N_2) (71)
^{1}H NMR: NMe 2.47 (N-2); OMe 3.61 (s, 3H), 3.80 (s, 3H), 3.83 (s, 6H), 3.86 (s, 3H); ArH 6.2–7.2 (m, 11H) (71)
EIMS: $[M]^+$ 624 (0.1), 433 (1.5), 419 (0.5), 206 (100), 192 (23) (71)
Daurisoline [**192**] (pampulhamine + $CH_2O/NaBH_4$) (71)

353 PANGKORAMINE $C_{34}H_{34}O_6N_2$: 566.2417

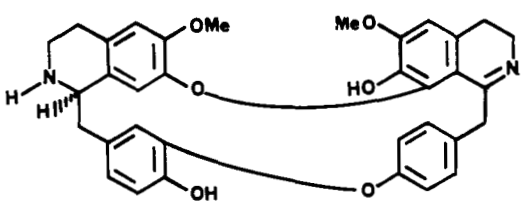
Type VI (*R,R*) 6,7*,11$^+$,12-6,7,8*,12$^+$



MP: Amorphous (35)
$[\alpha]_D$: $+126°$ ($c = 0.05$, MeOH) (35)
UV(EtOH): 214 (4.72), 230 (4.39), 280 (4.58) (35); (EtOH + OH^-) 212, 290 (35)
^{1}H NMR: OMe 3.57 (C-6), 3.81 (C-6′); AlH 4.07 (H-1), 4.99 (H-1′); ArH 6.25 (H-8), 6.41 (H-5 and H-5′), 6.71 (H-10), 6.76 (H-14), 6.82 (H-10′ and H-13′), 6.84 (H-13), 6.89 (H-11′), 7.40 (H-14′) (35)
MS: $[M]^+$ 564 (24), 563 (36), 353 (100), 339 (9), 192 (22), 177 (35) (35)
Sources: *Albertisia papuana* Becc. (Menispermaceae) (35)
Derivatives: Candicusine [**280**] (pangkoramine + $CH_2O/NaBH_4$) (35)

354 PANGKORIMINE $C_{34}H_{32}O_6N_2$: 564.2260

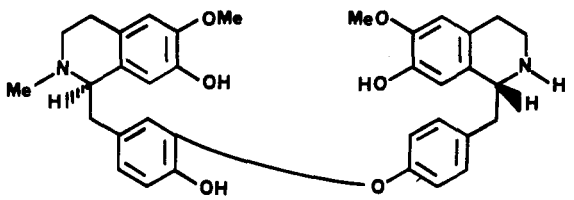
Type VI (*R*,−) 6,7*,11$^+$,12-6,7,8,12$^+$



$[\alpha]_D$: $+65°$ ($c = 0.05$, MeOH) (35)
UV(EtOH): 213 (4.64), 228 (4.48), 283 (4.26), 314 (3.80) (35); (EtOH + H^+) 213 (4.63), 279 (4.13), 333 (4.09 (35)
^{1}H NMR: OMe 3.92 (C-6′), 3.97 (C-6); AlH 4.04 (d, 1H, $J = 13.6$ Hz, H-α'_2), 4.13 (H-1), 4.63 (d, 1H, $J = 13.6$ Hz, H-α'_1); ArH 5.02 (H-10), 6.22 (H-8), 6.41 (H-11′), 6.53 (H-5), 6.57 (H-5′), 6.67 (H-14), 6.78 (H-13′), 6.79 (H-13), 7.25 (H-10′), 7.41 (H-14′) (nOe used) (35)
MS: $[M]^+$ 564 (100), 563 (94), 562 (46), 549 (8), 534 (20), 533 (53), 283 (16) (35)
Sources: *Albertisia papuana* Becc. (Menispermaceae) (35)
Derivatives: Pangkoramine [**354**] (pangkorimine + $NaBH_4$/MeOH) (35)

355 PEDROAMINE $C_{35}H_{38}O_6N_2$: 582.2730

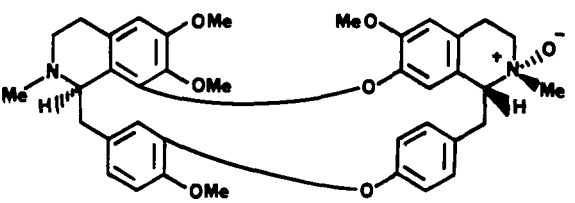
Type I (*R,R*) 6,7,11*,12-6,7,12*



MP: Amorphous (71)
[α]D: −74° (*c* = 0.1, MeOH) (71)
UV: 232 (4.32), 287 (3.95) (71); (MeOH + OH^-) 232 (4.37), 295 (3.92) (71)
^{1}H NMR($CD_3OD + CD_3CN$): NMe 2.53 (N-2); OMe 3.83 (C-6 or C-6′), 3.90 (C-6′ or C-6); ArH 6.30 (H-8), 6.48 (H-8′), 6.50 (m, 1H, H-10), 6.55 (H-5 or H-5′), 6.57 (H-5′ or H-5), 6.62 (d, 2H, *J* = 8.5 Hz, H-11′ and H-13′), 6.64 (m, 2H, H-13 + H-14), 6.82 (d, 2H, *J* = 8.5 Hz, H-10′ and H-14′) (71)
EIMS: 405 (1.7), 192 (100), 178 (75) (71)
CIMS: $[M + 1]^+$ 583 (72), 192 (100), 178 (69) (71)
CD: 0 (338), −2.6 (289), 0 (254), 0.5 (249), 0 (245), −10.5 (228) (71)
Sources: *Aristolochia gigantea* Mart. (Aristolochiaceae) (71)
Derivatives: *O,O,O*-Trimethylpedroamine [*O,O*-dimethylpampulhamine] (pedroamine + CH_2N_2) (co-tlc, ms, ^{1}H nmr) (71)
N-Methylpedroamine (pedroamine + $CH_2O/NaBH_4$) (71)
^{1}H NMR: NMe 2.47 (N-2), 2.53 (N-2′); 3.83 (C-6 or C-6′), 3.85 (C-6′ or C-6); ArH 6.10–7.20 (m, 11H) (71)
CIMS: $[M + 1]^+$ 597 (11), 406 (6), 192 (100), 178 (7), 176 (28) (71)

356 PHAEANTHINE-2′α-*N*-OXIDE $C_{38}H_{42}O_7N_2$: 638.2992

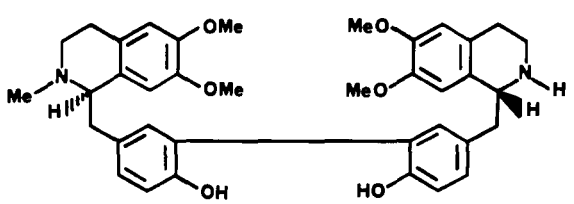
Type VIII (*R,R*) 6,7,8*,11$^+$,12-6,7*,12$^+$



MP: 193–195° (Me_2CO) (48)
$[\alpha]^{22}$D: −253° (*c* = 0.17, $CHCl_3$) (48)
UV: 282 (3.95) (48)
IR(KBr): 2930, 2850, 1603, 1580, 1503, 1460, 1445, 1435, 1410, 1350, 1340, 1322, 1310, 1265, 1231, 1215, 1185, 1162, 1120, 1101, 1060, 1020, 995, 962, 912, 860, 852, 835, 819, 745 (48)
^{1}H NMR: NMe 2.36 (N-2), 3.42 (N-2′); OMe 3.21 (C-7), 3.42 (C-6′), 3.76 (C-6), 3.93 (C-12) (48)
MS: $[M]^+$ 638, 622, 396, 395, 381, 198 (48)
Sources: *Pycnarrhena manillensis* Vidal (Menispermaceae) (48)
Derivatives: Phaeanthine [**74**] (phaeanthine-2′α-*N*-oxide + H_2SO_3) (48)

357 PISOPOWAMINE $C_{37}H_{42}O_6N_2$: 610.3043

Type XXVII (*R,R*) 6,7,12-6,7,12(11-11)



MP: Amorphous (30)
[α]D: −68° (*c* = 0.15, MeOH) (30)
UV: 208 (4.69), 228 (sh), (4.38), 288 (3.92) (30)

^{1}H NMR($CDCl_3/CD_3OD$ 10%): NMe 2.64 (N-2'); OMe 3.46 (C-7 or C-7'), 3.66 (C-7' or C-7), 3.81 (C-6 or C-6'), 3.85 (C-6' or C-6); AlH 4.14 (m, H-1'); ArH 5.88 (s, H-8 or H-8'), 6.53 (s, H-8' or H-8), 6.59 (s, H-5 or H-5'), 6.63 (s, H-5' or H-5), 6.79 (d, 1H, J = 2 Hz, H-10 or H-10'), 6.86 (d, 1H, J = 8 Hz, H-13' or H-13), 6.88 (d, 1H, J = 8 Hz, H-13 or H-13'), 6.88 (d, 1H, J = 2 Hz, H-10' or H-10), 6.98 (dd, 1H, J = 2, 8 Hz, H-14 or H-14'), 7.04 (dd, 1H, J = 2, 8 Hz, H-14' or H-14) (30)

CIMS: $[M+1]^+$ 611 (20), 420 (18), 406 (24), 206 (100), 192 (64) (30)

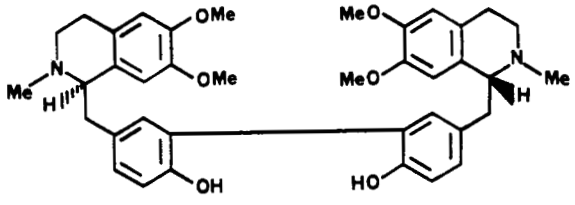
Sources: *Popowia pisocarpa* (Bl.) Endl. (Annonaceae) (30)

Derivatives: Pisopowetine [**358**] (pisopowamine + $CH_2O/NaBH_4$) (30)

358 PISOPOWETINE

$C_{38}H_{44}O_6N_2$: 624.3199

Type XXVII (*R,R*) 6,7,12-6,7,12(11-11)



MP: Amorphous (30)

$[\alpha]_D$: −80° (c = 0.2, MeOH) (30)

UV(EtOH): 210 (4.74), 232 (sh) (4.54), 284 (4.19) (30)

^{1}H NMR: NMe 2.45 (s, 6H, N-2 and N-2'); OMe 3.43 (s, 6H, C-7 and C-7'), 3.74 (s, 6H, C-6 and C-6'); ArH 5.98 (s, 2H, H-8 and H-8'), 6.50 (s, 2H, H-5 and H-5'), 6.69 (d, 2H, J = 8 Hz, H-13 and H-13'), 6.86 (dd, 2H, J = 2, 8 Hz, H-14 and H-14'), 6.93 (d, 2H, J = 2 Hz, H-10 and H-10') (30)

CIMS: $[M+1]^+$ 625 (4), 420 (10), 206 (100), 192 (18) (30)

Sources: *Popowia pisocarpa* (Bl.) Endl. (Annonaceae) (30)

Derivatives: *O,O*-Diacetylpisopowetine (pisopowetine + Ac_2O/pyridine) (30)

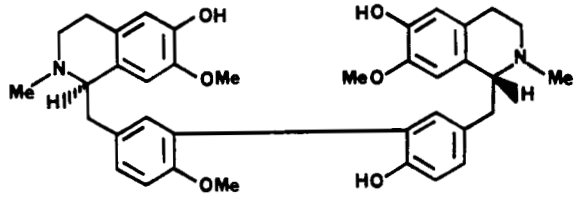
^{1}H NMR: OAc 2.01 (s), (6H), (C-12 and C-12') (30)

CIMS: $[M+1]^+$ 709 (22), 667 (5), 504 (9), 462 (4), 206 (100) (30)

359 PISOPOWIARIDINE

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

Type XXVII (*R,R*) 6,7,12-6,7,12(11-11)



MP: 184–185° (MeOH) (30)

$[\alpha]_D$: −78° (c = 1, MeOH) (30)

UV: 209 (4.75), 226 (sh) (4.55), 288 (4.15) (30)

^{1}H NMR($CDCl_3/CD_3OD$ 5%): NMe 2.70, 2.73; OMe 3.39 (C-7 or C-7'), 3.47 (C-7' or C-7), 3.90 (C-12); ArH 5.47 (H-8 or H-8'), 5.52 (H-8' or H-8), 6.27 (d, 1H, J = 2 Hz, H-10 or H-10'), 6.37 (d, 1H, J = 2 Hz, H-10' or H-10), 6.62 (s, 2H, H-5 and H-5'), 6.91 (d, 1H, J = 8 Hz, H-13 or H-13'), 6.95 (d, 1H, J = 8 Hz, H-13' or H-13), 7.04 (dd, 1H, J = 2, 8 Hz, H-14 or H-14'), 7.10 (dd, 1H, J = 2, 8 Hz, H-14' or H-14) (30)

^{13}C NMR($CDCl_3$ + CD_3OD 5%): 64.5 (C-1 or C-1'), 44.8 (C-3), 23.3 (C-4), 124.4 (C-4a), 111.2 (C-5), 144.3 (C-6), 144.4 (C-7), 111.0 (C-8), 126.8 (C-8a), 39.6 (C-α or C-α'), 131.8 (C-9), 133.2 (C-10), 125.3 (C-11), 154.0 (C-12), 114.8 (C-13), 129.7 (C-14); 64.5 (C-1' or C-1), 44.8 (C-3'), 23.1 (C-4'), 124.3 (C-4'a), 114.8 (C-5'), 144.1 (C-6'), 144.3 (C-7'), 111.0 (C-8'), 126.8 (C-8'a), 39.3 (C-α' or C-α), 130.2 (C-9'), 134.0 (C-10'), 125.5 (C-11'), 152.0 (C-12'), 116.4 (C-13'), 129.7 (C-14'), 40.7 (2-NMe and 2'-NMe), 54.6 (OMe), 54.7 (OMe), 55.7 (OMe) (30)

CIMS: $[M+1]^+$ 611 (12), 420 (21), 192 (100) (30)

CD: −3.5 (289), 0 (279), +1.5 (275), +1.3 (253), 0 (258), −18.3 (229), −20.9 (213) (30)

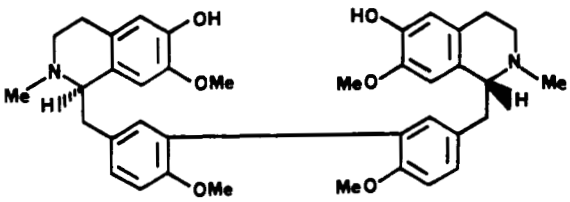
Sources: *Popowia pisocarpa* (Bl.) Endl. (Annonaceae) (30)

Derivatives: *O,O,O*-Triacetylpisopowiaridine (30)

^{1}H NMR: OAc 2.03 (s, 3H), 2.22 (s, 3H), 2.23 (s, 3H) (30)

360 PISOPOWIARINE $C_{38}H_{44}O_6N_2$: 624.3199

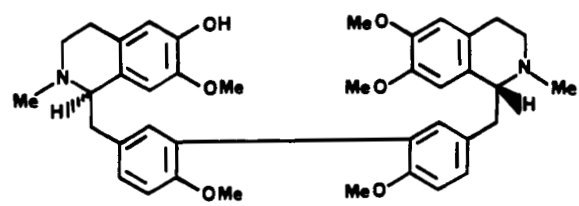
Type XXVII (*R,R*) 6,7,12-6,7,12(11)



MP: 187–188° (Me_2CO) (30)
$[\alpha]_D$: −112° (*c* = 1, MeOH) (30)
UV: 209 (4.58), 226 (sh) (4.36), 288 (3.91) (30)
^1H NMR: NMe 2.62 (6H, N-2 and N-2′); OMe 3.42 (6H, C-7 and C-7′), 3.71 (6H, C-12 and C-12′); ArH 5.71 (s, 2H, H-8 and H-8′), 6.52 (d, 2H, *J* = 2 Hz, H-10 and H-10′), 6.62 (s, 2H, H-5 and H-5′), 6.78 (d, 2H, *J* = 8 Hz, H-13 and H-13′), 6.98 (dd, 2H, *J* = 2, 8 Hz, H-14 and H-14′) (30)
^{13}C NMR: 65.0 (C-1), 45.7 (C-3), 23.9 (C-4), 125.5 (C-4a), 111.1 (C-5), 144.2 (C-6), 144.4 (C-7), 110.7 (C-8), 127.9 (C-8a), 40.6 (C-α), 131.4 (C-9), 133.5 (C-10), 126.9 (C-11), 155.6 (C-12), 115.0 (C-13), 129.6 (C-14), 65.0 (C-1′), 45.7 (C-3′), 23.9 (C-4′), 125.5 (C-4′a), 111.1 (C-5′), 144.2 (C-6′), 144.4 (C-7′), 110.7 (C-8′), 127.9 (C-8′a), 40.6 (C-α′), 131.4 (C-9′), 133.5 (C-10′), 126.9 (NC-11′), 155.6 (C-12′), 115.0 (C-13′), 129.6 (C-14′), 41.5 (2-NMe and 2′-NMe), 55.2, 55.8 (30)
CIMS: $[M + 1]^+$ 625 (0.9), 434 (19), 192 (100) (30)
CD: −5.7 (296), 0 (288), +4.7 (280), +1.2 (255), 0 (252), −33.2 (220) (30)
Sources: *Popowia pisocarpa* (Bl.) Endl. (Annonaceae) (30)
Derivatives: *O,O*-Diacetylpisopowiarine (pisopowiarine + Ac_2O/pyridine (30)
^1H NMR: OAc 2.23 (s, 6H) (30
CIMS: $[M + 1]^+$ 709 (32), 667 (25), 476 (4), 434 (2), 234 (87), 192 (100) (30)

361 PISOPOWIDINE $C_{39}H_{46}O_6N_2$: 638.3359

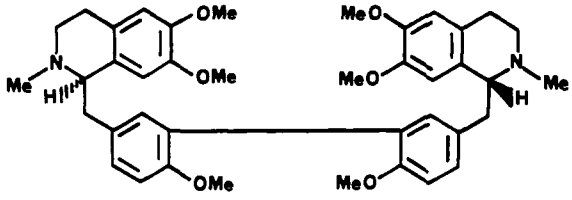
Type XXVII (*R,R*) 6,7,12-6,7,12,-(11-11)



MP: Amorphous (30)
$[\alpha]_D$: −137° (*c* = 1.2, MeOH) (30)
UV(EtOH): 208 (4.49), 228 (sh) (4.19), 287 (3.73) (30)
^1H NMR: NMe 2.57 (N-2 and N-2′); OMe 3.39 (C-7 or C-7′), 3.52 (C-7′ or C-7), 3.71 (C-12 or C-12′), 3.74 (C-12′ or C-12), 3.82 (C-6′); ArH 5.69 (H-8 or H-8′), 6.00 (H-8′ or H-8), 6.54 (d, 1H, *J* = 2 Hz, H-10), 6.58 (H-5 or H-5′), 6.65 (H-5′ or H-5), 6.75 (d, 1H, *J* = 8 Hz, H-13′), 6.81 (d, 1H, *J* = 2 Hz, H-10′), 6.85 (dd, 1H, *J* = 2, 8 Hz, H-14′), 6.90 (d, 1H, *J* = 8 Hz, H-13), 7.14 (dd, 1H, *J* = 2, 8 Hz, H-14) (nOe used) (30)
^{13}C NMR: 65.2 (C-1 or C-1′), 46.0 (C-3), 24.2 (C-4), 126.5 (C-4a), 111.5 (C-5), 144.4 (C-6), 144.7 (C-7), 110.8 (C-8), 128.4 (C-8a), 41.4 (C-α or C-α′), 131.6 (C-9), 133.7 (C-10), 127.5 (C-11), 155.8 (C-12), 115.2 (C-13), 129.8 (C-14), 64.9 (C-1′ or C-1), 46.6 (C-3′), 25.3 (C-4′), 124.7 (C-4′a), 111.2 (C-5′), 146.7 (C-6′), 147.8 (C-7′), 111.4 (C-8′), 128.5 (C-8′a), 39.9 (C-α′ or C-α), 131.5 (C-9′), 132.9 (C-10′), 127.7 (C-11′), 155.7 (C-12′), 111.6 (C-13′), 129.9 (C-14′), 42.6 (2-NMe and 2′-NMe), 55.2 (1 × OMe), 55.6 (1 × OMe), 55.9 (2 × OMe), 56.0 (1 × OMe) (30)
CIMS: $[M + 1]^+$ 639 (27), 206 (60), 192 (100) (30)
CD: −4.0 (294), 0 (285), +2.0 (277), 0 (248), −23.5 (218) (30)
Sources: *Popowia pisocarpa* (Bl.) Endl. (Annonaceae) (30)
Derivatives: *O*-Acetylpisopowidine (pisopowidine + Ac_2O/pyridine) (30)
^1H NMR: OAc 2.23 (30)
CIMS: $[M + 1]^+$ 681 (80), 639 (20), 476 (4), 234 (47), 206 (100), 192 (63) (30)

362 PISOPOWINE $C_{40}H_{48}O_6N_2$: 652.3512

Type XXVII (*R,R*) 6,7,12-6,7,12(11-11)



MP: Amorphous (30)

$[\alpha]_D$: $-152°$ ($c = 0.4$, MeOH) (30)

UV(EtOH): 209 (4.68), 228 (sh) (4.49), 288 (4.03) (30)

^{1}H NMR: NMe 2.61 (6H, N-2 and N-2′); OMe 3.51 (6H, C-7 and C-7′), 3.73 (6H, C-12 and C-12′); 3.83 (6H, C-6 and C-6′); ArH 5.94 (2H, H-8 and H-8′), 6.56 (2H, H-5 and H-5′), 6.82 (d, 2H, $J = 8$ Hz, H-13 and H-13′), 6.96 (dd, 2H, $J = 2$, 8 Hz, H-14 and H-14′), 6.98 (d, 2H, $J = 2$ Hz, H-10 and H-10′) (nOe used) (30)

^{13}C NMR: 64.6 (C-1), 46.2 (C-3), 24.8 (C-4), 124.8 (C-4a), 111.0 (C-5), 146.1 (C-6), 147.3 (C-7), 111.0 (C-8), 128.1 (C-8a), 39.9 (C-α), 130.9 (C-9), 132.4 (C-10), 127.5 (C-11), 155.4 (C-12), 111.0 (C-13), 129.7 (C-14); 64.6 (C-1′), 46.2 (C-3′), 24.8 (C-4′), 124.8 (C-4′a), 111.0 (C-5′), 146.1 (C-6′), 147.3 (C-7′), 111.0 (C-8′), 128.1 (C-8′a), 39.9 (C-α′), 130.9 (C-9′), 132.4 (C-10′), 127.5 (C-11′), 155.4 (C-12′), 111.0 (C-13′), 129.7 (C-14′); 42.0 (2-NMe and 2′-NMe), 55.2 (2 × OMe), 55.5 (4 × OMe) (30)

MS: $[M]^+$ 652 (0.1), 651 (0.2) (observed for $[M-1]^+$, 651.3450; calculated for $[M-1]^+$, 651.3434), 446 (0.2), 445 (0.3), 206 (100), 192 (3) (30)

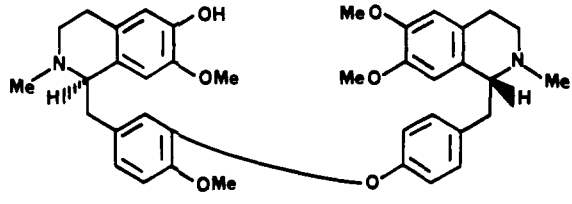
CD: −5.0 (292), 0 (280), +0.9 (275), 0 (254), −27.0 (217) (30)

Sources: *Popowia pisocarpa* (Bl.) Endl. (Annonaceae) (30)

Derivatives: Ceric ammonium nitrate oxidation of pisopowine followed by appropriate workup afforded 2,2′-dimethoxy-5,5′-diphenyldicarboxaldehyde and 6,7-dimethoxy-2-methyl-1,2,3,4-tetrahydroisoquinoline (30).

363 POPIDINE $C_{38}H_{44}O_6N_2$: 624.3199

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



This was isolated as a nonseparable mixture with popisidine [**364**] in a ratio of 2:1 (popidine to popisidine) (30). The data that is reported is the data obtained for the 2:1 mixture (30).

MP: Amorphous (30)

$[\alpha]_D$: $-128°$ ($c = 1$, MeOH) (30)

UV(EtOH): 208, 228 (sh), 282 (30)

^{1}H NMR: NMe 2.43 (N-2′), 2.49 (N-2); OMe 3.56 (C-7 or C-7′), 3.57 (C-7′ or C-7), 3.74 (6H) and 3.76 (6H) (C-6, C-6′, C-12′); ArH 5.88, 6.00, 6.03, 6.08 (H-5 and H-5′); 6.4–7.1 (H-8, H-8′, H-10, H-13, H-14, H-10′, H-11′, H-13′, H-14′) (30)

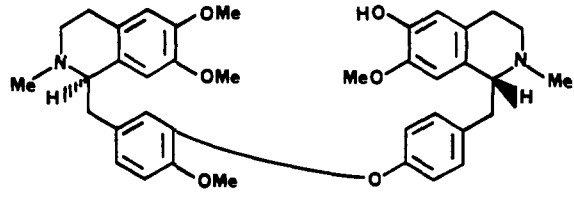
CIMS: $[M+1]^+$ 625 (61), 434 (4), 420 (3), 206 (100), 192 (88) (30)

Sources: *Popowia pisocarpa* (Bl.) Endl. (Annonaceae) (30)

Derivatives: Birch reduction (Na/NH_3) afforded (*R*)-(−)-*O*-methylarmepavine + (*R*)-(−)-6-*O*-ethyl-4′-*O*-methyl-*N*-methylisococlaurine + (*R*)-(−)-armepavine + (*R*)-(−)-6-*O*-ethyl-*N*-methylisococlaurine (30).

364 POPISIDINE $C_{38}H_{44}O_6N_2$: 624.3199

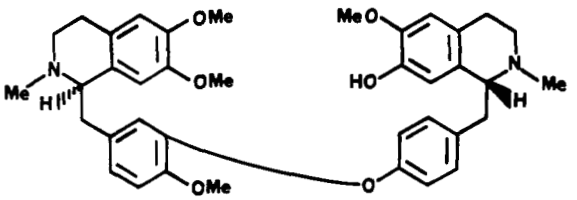
Type I (*R,R*) 6,7,11*,12-6,7,12*



This was isolated as a nonseparable mixture with popidine [**363**] in a ratio of 1:2 (popisidine to popidine) (30). See data listed for popidine [**363**].

365 POPISINE $C_{38}H_{44}O_6N_2$: 624.3199

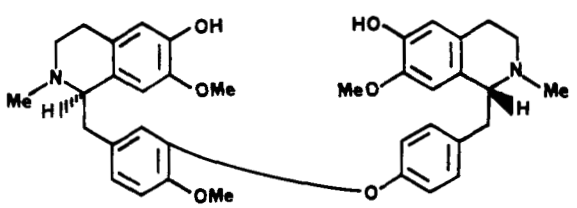
Type I (*R,R*) 6,7,11*,12-6,7,12*



MP: Amorphous (30)
$[\alpha]_D$: $-148°$ ($c = 1$, MeOH) (30)
UV(EtOH): 208 (4.64), 228 (sh) (4.36), 285 (3.91) (30)
^{1}H NMR: NMe 2.44 (N-2'), 2.48 (N-2); OMe 3.57 (C-7), 3.80 (9H, C-6, C-6', C-12); ArH 5.98 (H-8 or H-8'), 6.08 (H-8' or H-8), 6.48 (H-5 or H-5'), 6.52 (H-5' or H-5), 6.67 (dd, 1H, $J = 2$, 8 Hz, H-14), 6.79 (d, 1H, $J = 2$ Hz, H-10), 6.80 (d, 1H, $J = 8$ Hz, H-13), 6.80 (d, 2H, H-11' and H-13'), 6.98 (d, 2H, H-10' and H-14') (30)
CIMS: $[M + 1]^+$ 625 (51), 434 (21), 420 (25), 206 (100), 192 (77) (30)
CD: −6.2 (290), 0 (275), +0.6 (252), 0 (248), −24.2 (226), −33.2 (212) (30)
Sources: *Popowia pisocarpa* (Bl.) Endl. (Annonaceae) (30)
Derivatives: *O*-Acetylpopisine (30)
CIMS: $[M + 1]^+$ 667 (51), 625 (7), 476 (7), 234 (57), 206 (100), 192 (24) (30)
O-Ethylpopisine (30) (popisine + $MeCHN_2$) (30)
^{1}H NMR: OEt 1.33 (t, Me) and 3.85 (q, CH_2) (30)
Birch reduction (Na/NH_3) afforded (*R*)-(−)-*O*-methylarmepavine and (*R*)-(−)-7-*O*-ethylarmepavine (30).

366 POPISONINE $C_{37}H_{42}O_6N_2$: 610.3043

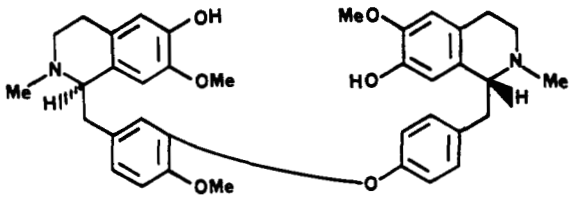
Type I (*R,R*) 6,7,11*,12-6,7,12*



MP: Amorphous (30)
$[\alpha]_D$: $-118°$ ($c = 1$, MeOH) (30)
UV(EtOH): 208 (4.66), 229 (sh) (4.44), 286 (3.93) (30)
^{1}H NMR: NMe 2.48 (N-2'), 2.54 (N-2); OMe 3.58 (6H) (C-7 and C-7'), 3.82 (C-12); ArH 5.98 (H-8 or H-8'), 6.00 (H-8' or H-8), 6.47 (H-5 or H-5'), 6.53 (d, 1H, $J = 2$ Hz, H-10), 6.56 (H-5' or H-5), 6.56 (d, 2H, H-11' and H-13'), 6.77 (dd, 1H, $J = 2$, 8 Hz, H-14), 6.85 (d, 1H, $J = 8$ Hz, H-13), 6.97 (d, 2H, H-10' and H-14') (30)
^{13}C NMR: 64.4 (C-1), 46.0 (C-3), 24.4 (C-4), 125.8 (C-4a), 114.6 (C-5), 144.1 (C-6), 144.4 (C-7), 110.6 (C-8), 127.2 (C-8a), 39.9 (C-α), 132.5 (C-9), 116.6 (C-10), 144.3 (C-11), 149.3 (C-12), 116.6 (C-13), 125.6 (C-14), 64.4 (C-1'), 46.2 (C-3'), 24.4 (C-4'), 125.6 (C-4'a), 114.6 (C-5'), 144.1 (C-6'), 144.4 (C-7'), 110.6 (C-8'), 127.2 (C-8'a), 39.9 (C-α'), 133.4 (C-9'), 130.5 (C-10'), 112.3 (C-11'), 155.8 (C-12'), 121.9 (C-13'), 130.5 (C-14'), 41.8 (2-NMe and 2'-NMe), 55.2 (2 × OMe), 55.8 (1 × OMe) (30)
CIMS: $[M + 1]^+$ 611 (54), 420 (12), 192 (100), 177 (5) (30)
CD: −1.5 (298), 0 (292), +3.7 (282), +2.7 (254), 0 (247), −13.2 (230), −12.5 (222) (30)
Sources: *Popowia pisocarpa* (Bl.) Endl. (Annonaceae) (30)
Derivatives: Birch reduction (Na/NH_3) of *O,O*-diethylpopisonine afforded (*R*)-(−)-6-*O*-ethyl-4'-*O*-methyl-*N*-methylisococlaurine + (*R*)-(−)-6-*O*-ethyl-*N*-methylisococlaurine (30).

367 POPISOPINE $C_{37}H_{42}O_6N_2$: 610.3043

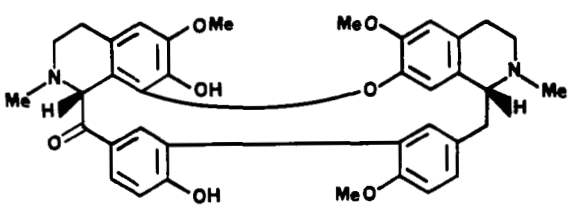
Type I (*R,R*) 6,7,11*,12-6,7,12*



MP: Amorphous (30)
[α]D: −119° (*c* = 1, MeOH)
UV(EtOH): 208 (4.65), 228 (sh) (4.37), 286 (3.92) (30)
^{1}H NMR: NMe 2.44 (N-2'), 2.48 (N-2); OMe 3.56 (C-7), 3.80 (6H, C-6' and C-12); ArH 6.05 (H-8 or H-8'), 6.28 (H-8' or H-8), 6.42 (H-5 or H-5'), 6.50 (H-5' or H-5), 6.56 (d, 1H, *J* = 2 Hz, H-10), 6.74 (d, 2H, H-11' and H-13'), 6.76 (dd, 1H, *J* = 2, 8 Hz, H-14), 6.83 (d, 1H, *J* = 8 Hz, H-13), 7.01 (d, 2H, H-10' and H-14') (30)
CIMS: $[M+1]^+$ 611 (71), 420 (19), 192 (100) (30)
CD: −4.4 (290), 0 (277), +1.7 (251), 0 (246), −19.7 (227), −25.4 (213) (30)
Sources: *Popowia pisocarpa* (Bl.) Endl. (Annonaceae) (30)
Derivatives: Birch reduction (Na/NH_3) of *0,0*-diethylpopisopine afforded (*R*)-(−)-6-*O*-ethyl-4'-*O*-methyl-*N*-methylisococlaurine + (*R*)-(−)-7-*O*-ethyl-*N*-methylcoclaurine (30).

368 PSEUDOXANDRINE $C_{37}H_{38}O_7N_2$: 622.2679

Type IV (*S,S*) 6,7,8*,12-6,7*,12(11-11)

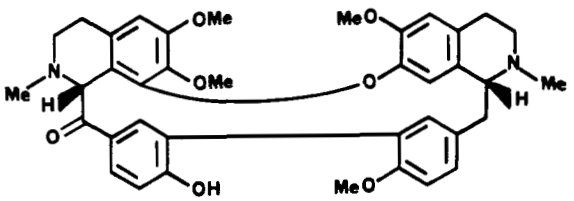


MP: Amorphous (80)
[α]D: +23° (*c* = 1.13, $CHCl_3$) (80)
UV(EtOH): 208 (4.78), 282 (3.94) (80); (EtOH + NaOH) 222 (4.96), 300 (4.24) (80)
IR(film): 3340, 1680, 1605, 1510, 1460, 1305, 1270, 1240, 1120 (80)
^{1}H NMR: NMe 2.27 (N-2'), 2.39 (N-2); OMe 3.63 (C-6'), 3.85 (C-6), 3.86 (C-12'); AlH 4.05 (d, H-1'), 4.25 (s, H-1); ArH 6.42 (H-5), 6.66 (H-5'), 6.73 (d, 1H, *J* = 2 Hz, H-10), 6.85 (d, 1H, *J* = 8.5 Hz, H-13'), 6.95 (d, 1H, *J* = 8.5 Hz, H-13), 6.96 (d, 1H, *J* = 2 Hz, H-10'), 7.14 (H-8'), 7.20 (dd, 1H, *J* = 2, 8.5 Hz, H-14'), 7.36 (dd, 1H, *J* = 2, 8.5 Hz, H-14) (nOe used) (80)
^{13}C NMR: 84.4 (C-1), 52.0 (C-3), 35.2 (C-4), 121.9 (C-4a), 106.1 (C-5), 145.8 (C-6), 134.3 (C-7), 141.5 (C-8), 124.0 (C-8a), 205.1 (C-α), 136.4 (C-9), 131.4 (C-10 or C-14 or C-14'), 131.6 (C-11 or C-11'), 153.1 (C-12), 110.9 (C-13), 129.5 (C-14 or C-10'), or C-14'), 63.0 (C-1'), 45.2 (C-3'), 22.6 (C-4'), 127.6 (C-4'a), 114.1 (C-5'), 151.2 (C-6'), 143.3 (C-7'), 120.8 (C-8'), 126.7 (C-8'a), 39.5 (C-α'), 135.8 (C-9'), 133.6 (C-10'), 130.4 (C-11' or C-11), 153.9 (C-12'), 117.5 (C-13'), 130.9 (C-14' or C-10 or C-14), 42.6 (2-NMe and 2'-NMe), 43.1 (2'-NMe or 2-NMe), 55.9 (6-OMe), 56.2 (6-OMe or 12'-OMe), 56.2 (12'-OMe or 6-OMe) (80)
EIMS: $[M]^+$ 622 (100), 621 (80), 607 (18), 593 (14), 382 (3), 381 (8), 367 (4), 311 (11), 192 (8), 191.5 (8), 191 (30), 190 (9), 175 (4), 174 (3) (80)
CIMS: $[M+1]^+$ 623 (80)
CD: 0 (295), +5 (sh) (277), +35.6 (242), 0 (228), −47 (218) (80)
Sources: *Pseudoxandra* aff. *lucida* (Annonaceae) (80)
Derivatives: *0,0*-Diacetylpseudoxandrine (pseudoxandrine + Ac_2O/pyridine (80)
[α]D: +47° (*c* = 0.53, $CHCl_3$) (80)
UV(EtOH): 212 (4.75), 281 (3.92) (80)
IR(film): 1760, 1685, 1610, 1500 (80)
^{1}H NMR: NMe 2.28 (N-2'), 2.72 (N-2); OAc 1.75 (C-7), 2.12 (C-12); OMe 3.62 (C-6'), 3.68 (C-12'), 3.83 (C-6); AlH 4.29 (s, H-1); ArH 6.50 (H-5), 6.71 (H-5'), 6.59–7.30 (7H) (80)
EIMS: $[M]^+$ 706 (100), 705 (55), 691 (13), 664 (28), 663 (34), 649 (19), 622 (3), 621 (8), 423 (2), 381 (4), 368 (2), 206 (3), 204 (2), 191 (34), 175 (4) (80)
CIMS: $[M+1]^+$ 707 (80)
0,0-Dimethylpseudoxandrine (pseudoxandrine + CH_2N_2) (80)
[α]D: +6° (*c* = 0.66, $CHCl_3$) (80)
UV(EtOH): 210 (4.70), 286 (3.95) (80)

IR(film): 1680, 1605 (80)
^{1}H NMR: NMe 2.29 (N-2'), 2.39 (N-2); OMe 3.52 (C-7), 3.56 (C-6'), 3.73 (C-6 or C-12 or C-12'), 3.79 (C-12' or C-12 or C-6), 3.84 (C-12 or C-12' or C-6); AlH 4.25 (1H, H-1); ArH 6.02–7.96 (9H) (80)
EIMS: $[M]^+$ 650 (100), 649 (89), 635 (61), 621 (21), 607 (10), 395 (10), 382 (12), 381 (17), 368 (5), 354 (7), 325 (26), 311 (15), 206 (98), 198.5 (17), 198 (67), 192 (14), 191 (15), 190 (27), 175 (27), 174 (21) (80)
Dihydrodimethylpseudoxandrine (*O,O*-dimethylpseudoxandrine + $NaBH_4$MeOH) (80)
IR(film): 1605, 1585, 1500 (80)
CIMS: $[M+1]^+$ 653, 652, 639, 621, 395, 369, 206 (80)
Reduction (Zn/HCl) afforded two isomeric products, one of which was tiliageine [27] (80).

369 PSEUDOXANDRININE $C_{38}H_{40}O_7N_2$: 636.2836

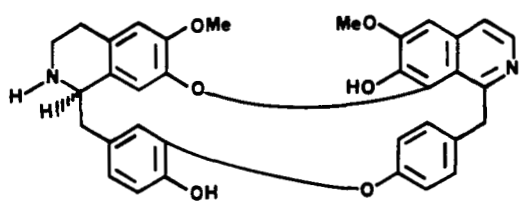
Type IV (*S,S*) 6,7,8*,12-6,7*,12(11-11)



MP: Amorphous (80)
[α]D: +7° (*c* = 0.7, $CHCl_3$) (80)
UV(EtOH): 208 (4.4), 224 (sh) (4.34), 280 (3.80); (EtOH + NaOH) 220 (4.90), 296 (4.33) (80)
IR(film): 3340, 1675, 1600, 1500, 1270, 1230, 1120, 1070, 1020 (80)
^{1}H NMR: NMe 2.26 (N-2'), 2.37 (N-2); OMe 3.55 (C-7), 3.56 (C-6'), 3.82 (C-6), 3.85 (C-12'); AlH 4.16 (H-1'), 4.24 (H-1); ArH 6.42 (H-5), 6.65 (H-5'), 6.66 (d, 1H, *J* = 2 Hz, H-10), 6.86 (d, 1H, *J* = 8.5 Hz, H-13'), 6.93 (d, 1H, *J* = 8.5 Hz, H-13), 6.98 (d, 1H, *J* = 2 Hz, H-10'), 7.20 (H-8'), 7.26 (dd, 1H, *J* = 2, 8.5 Hz, H-14'), 7.36 (dd, 1H, *J* = 2, 8.5 Hz, H-14) (nOe used) (80)
EIMS: $[M]^+$ 636 (100), 635 (85), 621 (28), 607 (12), 593 (6), 411 (2), 396 (1), 395 (2), 381 (5), 367 (1), 365 (9), 198.5 (5), 198 (19), 191 (3), 175 (6), 174 (6) (80)
CD: 0 (362), −2.9 (341), 0 (313), +2.9 (296), +19 (249), 0 (232), 21.7 (219) (80)
Sources: *Pseudoxandra* aff. *lucida* (Annonaceae) (80)
Derivatives: *O*-Methylpseudoxandrinine (*O,O*-dimethylpseudoxandrine) (pseudoxandrinine + CH_2N_2) (80)
[α]D: +6° (*c* = 0.66, $CHCl_3$) (80)
UV(EtOH): 210 (4.70), 286 (3.95) (80)
IR(film): 1680, 1605 (80)
^{1}H NMR: NMe 2.29 (N-2'), 2.39 (N-2); OMe 3.52 (C-7), 3.56 (C-6'), 3.73 (C-6 or C-12 or C-12'), 3.79 (C-12' or C-12 or C-6), 3.84 (C-12 or C-12' or C-6); AlH 4.25 (1H, H-1); ArH 6.02–7.96 (9H) (80)
EIMS: $[M]^+$ 650 (100), 649 (89), 635 (61), 621 (21), 607 (10), 395 (10), 382 (12), 381 (17), 368 (5), 354 (7), 325 (26), 311 (15), 206 (98), 198.5 (17), 198 (67), 192 (14), 191 (15), 190 (27), 175 (27), 174 (21) (80)

370 PYCNAZANTHINE[h] $C_{34}H_{30}O_6N_2$: 562.2104

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



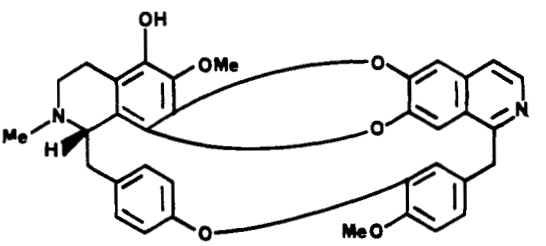
[α]D: +186° (*c* = 0.29, MeOH) (38)
UV: 230 (4.80), 284 (sh) (4.12), 318 (sh) (3.80) (38); (MeOH + OH^-) 267, 290, 364 (38); (MeOH + H^+) 265, 320, 372 (38)
^{1}H NMR(CD_3OD): OMe 4.03, 4.08; ArH 7.70 (d, 1H, *J* = 6 Hz), 8.26 (d, 1H, *J* = 6 Hz) (38)

[h]A possible, but less likely structure, could be one with a 6-hydroxy, 12-methoxy arrangement (38).

^{1}H NMR(pyridine-d_6): OMe 3.73, 3.87; AlH 4.80 (d, 1H, J = 13.4 Hz, H-α), 5.75 (d, 1H, J = 13.4 Hz, H-α) (38)
MS: [M]$^+$ 562 (100), 561 (37), 543 (23), 528 (39), 281 (9), 178 (19), 174 (13) (38)
Sources: *Pycnarrhena ozantha* Diels (Menispermaceae) (38)
Derivatives: *N,O,O*-Trimethylpycnazanthine (pycnazanthine + CH_2N_2 followed by CH_2O/$NaBH_4$) (38)
[α]D: +125° (c = 0.15, $CHCl_3$) (38)
UV: 238 (sh) (4.60), 289 (3.78), 317 (3.72) (38); (MeOH + OH^-) unchanged (38); (MeOH + H^+) 258, 300, 365 (38)
^{1}H NMR: NMe 2.53 (N-2); OMe 3.51 (C-7), 3.85 (C-12), 3.98 (C-6 or C-6′), 4.01 (C-6′ or C-6); AlH 3.58 (br s, 1H, H-1), 4.52 (d, 1H, J = 14 Hz, H-α), 5.29 (d, 1H, J = 14 Hz, H-α); ArH 5.98 (H-8), 6.53 (H-5), 6.98 (H-5′), 6.4–7.4 (m, 6H), 7.46 (d, 1H, J = 6 Hz, H-4′), 8.48 (d, 1H, J = 6 Hz, H-3′) (38)
MS: [M]$^+$ 604 (100), 603 (75), 590 (11), 589 (32), 302 (11), 206 (4), 190 (5), 189 (3), 188 (3), 174 (23) (38)

371 SIDDIQUAMINE $C_{35}H_{30}O_6N_2$: 574.2104

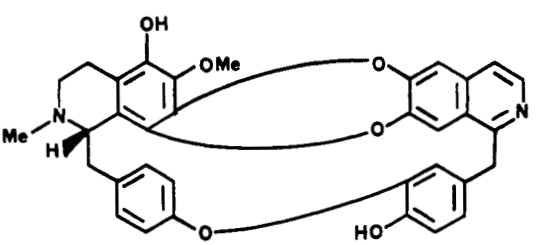
Type XXIIIa (S,−) 5,6,7*,8$^+$,12#-6*,7$^+$,11#,12



[α]^{25}D: +113° (c = 0.08, $CHCl_3$) (33)
UV: 233 (4.63), 267 (sh) (4.32), 355 (3.63) (33)
^{1}H NMR: NMe 2.61 (N-2); OMe 3.90 (C-12′), 4.05 (C-6); AlH 4.10 (H-1), 4.10 (d, 1H, J = 13 Hz, H-α′$_2$), 4.39 (d, 1H, J = 13 Hz, H-α′$_1$); ArH 6.68 (dd, 1H, J = 2.2, 8.2 Hz, H-11), 6.74 (d, 1H, J = 1.8 Hz, H-10′), 6.85 (d, 1H, J = 8.2 Hz, H-13′), 6.97 (dd, 1H, J = 2.2, 8.2 Hz, H-10), 7.11 (H-8′), 7.12 (dd, 1H, J = 1.8, 8.2 Hz, H-14′), 7.17 (H-5′), 7.24 (dd, 1H, J = 2.2, 8.2 Hz, H-13), 7.24 (d, 1H, J = 5.5 Hz, H-4′), 7.46 (dd, 1H, J = 2.2, 8.2 Hz, H-14), 8.24 (d, 1H, J = 5.5 Hz, H-3′) (nOe used) (33)
MS: [M]$^+$ 574 (86), 573 (100), 559 (10), 544 (5), 287 (17), 279 (10) (33)
Sources: *Cocculus pendulus* (Forsk.) Diels (Menispermaceae) (33)

372 SIDDIQUINE $C_{34}H_{28}O_6N_2$: 560.1947

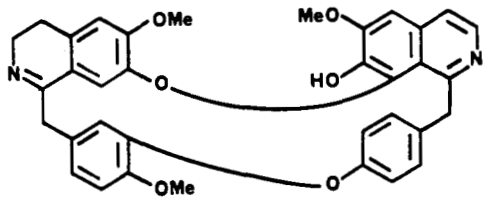
Type XXIIIa (S,−) 5,6,7*,8$^+$,12#-6*,7$^+$,11#,12



[α]^{25}D: +172° (c = 0.12, $CHCl_3$) (33)
UV: 232 (4.70), 267 (sh) (4.39), 355 (3.68) (33)
^{1}H NMR: NMe 2.61 (N-2); OMe 4.02 (C-6); AlH 4.10 (H-1), 4.11 (d, 1H, J = 13 Hz, H-α′$_2$), 4.35 (d, 1H, J = 13 Hz, H-α′$_1$); ArH 6.65 (dd, 1H, J = 2.2, 8.2 Hz, H-11), 6.70 (d, 1H, J = 1.8 Hz, H-10′), 6.86 (d, 1H, J = 8.2 Hz, H-13′), 7.00 (dd, 1H, J = 2.2, 8.2 Hz, H-10), 7.05 (dd, 1H, J = 1.8, 8.2 Hz, H-14′), 7.06 (H-8′), 7.14 (H-5′), 7.22 (d, 1H, J = 5.6 Hz, H-4′), 7.24 (dd, 1H, J = 2.2, 8.2 Hz, H-13), 7.46 (dd, 1H, J = 2.2, 8.2 Hz, H-14), 8.23 (d, 1H, J = 5.6 Hz, H-3′) (nOe used) (33)
MS: [M]$^+$ 560 (79), 559 (100), 545 (10), 530 (18), 280 (13) (33)
Sources: *Cocculus pendulus* (Forsk.) Diels (Menispermaceae) (33)

373 STEPHASUBIMINE $C_{35}H_{30}O_6N_2$: 574.2104

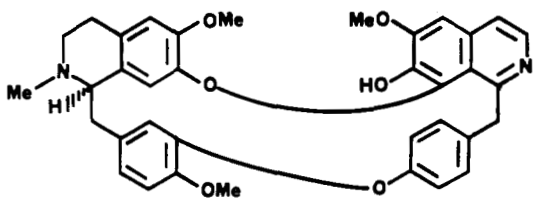
Type VI (−,−) 6,7*,11$^+$,12-6,7,8*,12$^+$



MP: Amorphous (21)
UV: 242 (4.64), 281 (3.91), 323 (3.70) (21); (MeOH + H^+) 264 (4.57), 307 (4.02), 362 (3.92), 368 (3.91) (21)
^{1}H NMR: OMe 3.87 (C-12), 4.02 (C-6), 4.11 (C-6′); AlH 2.47 (m, 2H, H-4), 3.11 (m, 1H, H-3), 3.33 (d, 1H, J = 12 Hz, H-α), 3.63 (d, 1H, J = 12 Hz, H-α), 3.81 (m, 1H, H-3), 4.54 (d, 1H, J = 14.1 Hz, H-α′), 4.54 (d, 1H, J = 14.1 Hz, H-α′); ArH 5.37 (d, 1H, J = 1.8 Hz, H-10), 6.42 (dd, 1H, J = 2, 8.4 Hz, H-13′), 6.50 (H-5), 6.74 (d, 1H, J = 8.2 Hz, H-13), 6.75 (dd, 1H, J = 2, 8.4 Hz, H-11′), 6.81 (H-8), 6.82 (dd, 1H, J = 1.8, 8.2 Hz, H-14), 6.96 (H-5′), 6.97 (dd, 1H, J = 2, 8.4 Hz, H-10′), 7.10 (dd, 1H, J = 2, 8.4 Hz) (21)
MS: [M]$^+$ 574 (100), 559 (24), 206 (43), 192 (10) (21)
Sources: *Stephania suberosa* Forman (Menispermaceae) (21)
Derivatives: Norstephasubine [**340**] (stephasubine + $NaBH_4$) (tlc, ^{1}H nmr, ms) (21)

374 STEPHASUBINE $C_{36}H_{34}O_6N_2$: 590.2417

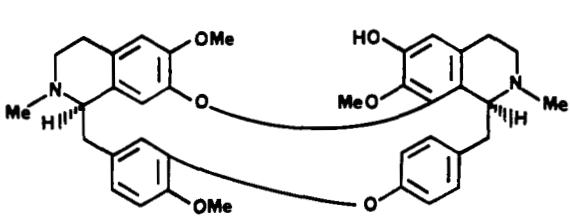
Type VI (*R*,−) 6,7*,11$^+$,12-6,7,8*,12$^+$



MP: Amorphous (21)
[α]D: +339° (c = 0.09, MeOH) (21)
UV: 240 (4.56), 287 (3.61), 337 (3.43); (MeOH + H^+) 235 (4.35), 264 (4.41), 290 (sh) (3.69), 321 (3.39), 368 (3.48), 374 (3.48) (21)
^{1}H NMR: NMe 2.51 (N-2); OMe 3.88 (C-12), 4.07 (s, 6H, C-6 and C-6′); AlH 2.18 (m, 1H, H-4), 2.25 (m, 1H, H-α), 2.27 (m, 1H, H-4), 2.35 (m, 1H, H-3), 2.72 (m, 1H, H-3), 2.97 (m, 1H, H-α), 3.56 (m, 1H, H-1), 4.52 (d, 1H, J = 13.8 Hz, H-α′), 5.37 (d, 1H, J = 13.8 Hz, H-α′); ArH 4.79 (br s, H-10), 5.99 (H-8), 6.49 (dd, 1H, J = 2, 8.4 Hz, H-13′), 6.56 (H-5), 6.65 (dd, 1H, J = 2, 8.4 Hz, H-11′), 6.71 (br s, 2H, H-13 and H-14), 7.01 (H-5′), 7.03 (dd, 1H, J = 2, 8.4 Hz, H-10′), 7.43 (dd, 1H, J = 2, 8.4 Hz, H-14′), 7.48 (d, 1H, J = 5.6 Hz, H-4′), 8.45 (d, 1H, J = 5.6 Hz, H-3′) (nOe used) (21)
MS: [M]$^+$ 590 (76), 589 (100), 575 (26), 295 (18), 190 (5), 174 (24), 145 (13), 144 (13) (21)
CD: 0 (270), +64 (245), +4sh (218), negative tail (21)
Sources: *Stephania suberosa* Forman (Menispermaceae) (21)

375 STEPHIBABERINE $C_{37}H_{40}O_6N_2$: 608.2886

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

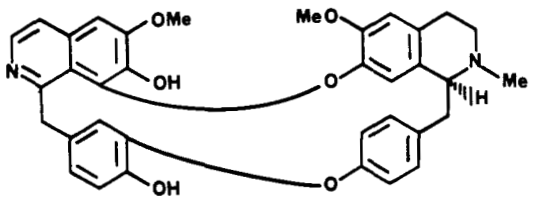


[α]D: +207° (c = 0.17, $CHCl_3$) (64)
UV: 241 (sh) (4.36), 283 (4.00) (64); (MeOH + OH^-) 243 (sh), 285 (64)
^{1}H NMR: NMe 2.59 (N-2), 2.67 (N-2′); OMe 3.26 (C-7′), 3.61 (C-6), 3.90 (C-12); AlH 3.75 (m, 1H, H-1), 4.26 (m, 1H, H-1′); ArH 5.46 (br s, 1H, H-10), 6.37 (H-5), 6.46 (H-5′), 6.45 (dd, 1H, J = 2.1, 8.4 Hz, H-11′), 6.71 (H-8), 6.79 (br s, 2H, H-13 and H-14), 6.87 (dd, 1H, J = 2.1, 8.4 Hz, H-13′), 6.91 (dd, 1H, J = 2.1, 8.4 Hz, H-10′), 7.44 (dd, 1H, J = 2.1, 8.4 Hz, H-14′) (64)

MS: $[M]^+$ 608 (45), 607 (27), 594 (1), 593 (4), 501 (6), 382 (26), 381 (100), 367 (25), 191 (54), 190 (13), 175 (11), 174 (36), 168 (31) (64)
Sources: *Stephania pierrii* Diels (Menispermaceae) (64)

376 STEPIERRINE $C_{35}H_{32}O_6N_2$: 576.2260

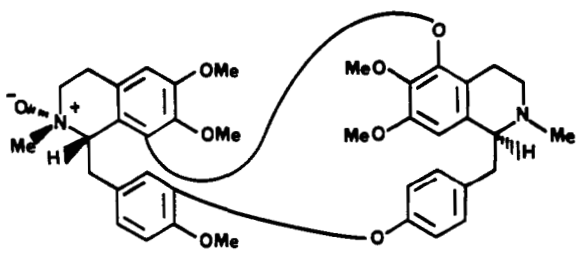
Type VIII (−,*S*) 6,7,8*,11$^+$,12-6,7*,12$^+$



$[\alpha]_D$: +55° (*c* = 0.10, $CHCl_3$) (64)
UV: 239 (sh) (4.49), 278 (3.97), 331 (3.69) (64); (MeOH + OH^-) 264, 290 (sh) (64); (MeOH + H^+) 230 (sh), 263, 287 (sh), 321, 371 (64)
^{1}H NMR: NMe 2.66 (N-2′); OMe 3.38 (C-7′), 3.90 (C-7); AlH 4.14 (d, 1H, *J* = 12.8 Hz, H-α_1), 4.96 (d, 1H, *J* = 12.8 Hz, H-α_1); ArH 6.00 (H-8′), 6.55 (H-5′), 6.75 (H-5), 6.77 (d, 1H, *J* = 1.7 Hz, H-10), 6.78 (dd, 1H, *J* = 1.7, 8.3 Hz, H-14), 6.85 (d, 1H, *J* = 8.3 Hz, H-13), 7.04 (dd, 1H, *J* = 2.3, 8.1 Hz, H-11′), 7.13 (dd, 1H, *J* = 2.3, 8.1 Hz, H-10′), 7.21 (dd, 1H, *J* = 2.3, 8.1 Hz, H-13′), 7.32 (d, 1H, *J* = 5.6 Hz, H-4), 7.53 (dd, 1H, *J* = 2.3, 8.1 Hz, H-14′), 8.33 (d, 1H, *J* = 5.6 Hz, H-3) (64)
MS: $[M]^+$ 576 (21) (hrms, found 576.2266), 575 (100), 288 (13), 192 (21), 191 (8), 190 (13), 177 (14), 174 (32) (64)
Sources: *Stephania pierrii* Diels (Menispermaceae) (64)

377 THALIDASINE-2α-*N*-OXIDE $C_{39}H_{44}O_8N_2$: 668.3098

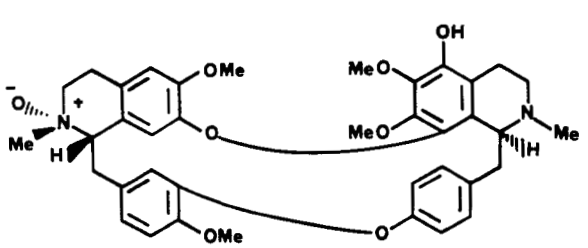
Type XII (*S*,*S*) 6,7,8*,11$^+$,12-5*,6,7,12$^+$



MP: Amorphous (41)
$[\alpha]_D$: +6° (*c* = 0.15, MeOH) (41)
^{1}H NMR: NMe 2.62 (N-2′), 3.05 (N-2′); OMe 3.20 (C-7), 3.41 (C-6′), 3.76 (C-6), 3.85 (C-7′), 3.90 (C-12); AlH 2.62 (m, 2H, H-α and H-α′), 3.18 (m, 1H, H-α′), 3.85 (m, 1H, H-α), 3.89 (m, 1H, H-1′), 4.88 (m, 1H, H-1); ArH 6.39 (H-5), 6.44 (H-8′), 6.20 (dd, 1H, *J* = 2.0, 8.2 Hz, H-10′), 6.27 (dd, 1H, *J* = 2.0, 8.2 Hz, H-11′), 6.62 (d, 1H, *J* = 1.8 Hz, H-10), 6.68 (dd, 1H, *J* = 1.8, 8.0 Hz, H-14), 6.81 (d, 1H, *J* = 8.0 Hz, H-13), 7.04 (dd, 1H, *J* = 2.0, 8.2 Hz, H-13′), 7.44 (dd, 1H, *J* = 2.0, 8.2 Hz, H-14′) (nOe used) (41)
MS: $[M]^+$ 668 (3), 667 (6), 666 (12), 652 (70), 637 (25), 425 (69), 411 (86), 213 (100), 206 (58), 204 (59), 190 (89), 176 (18), 174 (21) (41)
Sources: *Thalictrum cultratum* Wall. (Ranunculaceae) (41)

378 THALIGOSINE-2β-*N*-OXIDE (Thalisopine-2β-*N*-oxide) $C_{38}H_{42}O_8N_2$: 654.2941

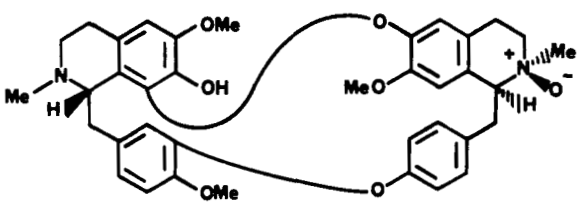
Type VII (*S*,*S*) 5,6,7,8*,12$^+$-6,7*,11$^+$,12



MP: Amorphous (41)
$[\alpha]_D$: $-59°$ ($c = 0.13$, MeOH) (41)
^{1}H NMR: NMe 2.61 (N-2), 3.46 (N-2'); OMe 3.06 (C-7), 3.45 (C-6'), 3.83 (C-6), 3.96 (C-12'); AlH 4.42 (m, 1H, H-1), 4.81 (m, 1H, H-1'); ArH 6.36 (H-8'), 6.51 (H-5'), 6.57 (d, 1H, $J = 1.8$ Hz, H-10'), 6.83 (br s, 2H, H-10 and H-11), 6.98 (d, 1H, $J = 8.2$ Hz, H-13'), 7.05 (dd, 1H, $J = 1.8$, 8.2 Hz, H-14'), 7.11 (dd, 1H, $J = 2.1$, 8.1 Hz, H-13), 7.50 (dd, 1H, $J = 2.1$, 8.1 Hz, H-14) (nOe used) (41)
MS: $[M]^+$ 654 (2), 653 (8), 652 (18), 651 (21), 638 (47), 637 (39), 624 (13), 623 (21), 425 (5), 411 (100), 397 (79), 206 (57), 192 (54), 191 (15), 190 (21), 176 (20) (41)
Sources: *Thalictrum cultratum* Wall. (Ranunculaceae) (41)

379 THALIPHYLLINE-2'β-*N*-OXIDE $C_{37}H_{40}O_7N_2$: 624.2836

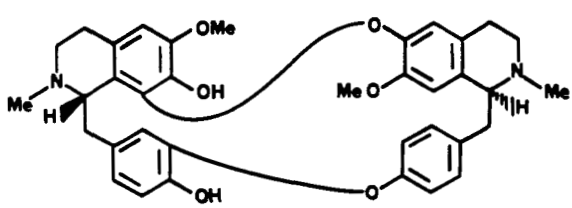
Type XI (*S,S*) 6,7,8•,11$^+$,12-6•,7,12$^+$



MP: Amorphous (41)
$[\alpha]_D$: $+257°$ ($c = 0.7$, MeOH) (41)
^{1}H NMR: NMe 2.07 (N-2), 3.26 (N-2'); OMe 3.60 (C-7'), 3.90 (C-6), 3.93 (C-12); AlH 2.61 (m, 1H, H-α), 2.95 (m, 1H, H-α'), 3.20 (m, 2H, H-α and H-1), 4.02 (m, 1H, H-α'), 4.63 (m, 1H, H-1'); ArH 5.83 (H-8'), 6.21 (H-5'), 6.26 (dd, 1H, $J = 2.1$, 8.0 Hz, H-10'), 6.58 (H-5), 6.58 (d, 1H, $J = 1$, 8 Hz, H-10), 6.64 (dd, 1H, $J = 2.1$, 8.0 Hz, H-11'), 6.77 (dd, 1H, $J = 1.8$, 8.2 Hz, H-14), 6.86 (d, 1H, $J = 8.2$ Hz, H-13), 7.22 (dd, 1H, $J = 2.1$, 8.0 Hz, H-13'), 7.33 (dd, 1H, $J = 2.1$, 8.0 Hz, H-14') (nOe used) (41)
MS: $[M]^+$ 624 (3), 623 (9), 622 (22), 608 (43), 607 (31), 594 (6), 381 (87), 367 (20), 192 (24), 191 (100), 190 (33), 176 (28), 174 (39) (41)
Sources: *Thalictrum cultratum* Wall. (Ranunculaceae) (41)

380 THALIVARMINE $C_{36}H_{38}O_6N_2$: 594.2730

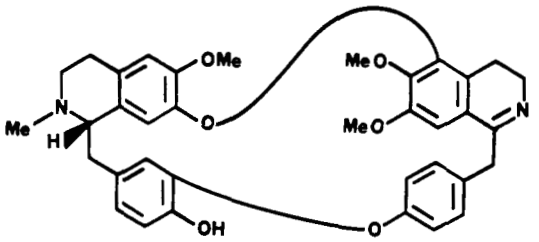
Type XI (*S,S*) 6,7,8•,11$^+$,12-6•,7,12$^+$



TLC: (Si gel) 0.23 [toluene-Me_2CO-NH_4OH (10:10:0.5)]; 0.12 [$CHCl_3$-MeOH (9:1)]; 0.26 [$CHCl_3$-MeOH-NH_4OH (90:10:0.2)]; 0.26 [EtOAc-iPrOH-NH_4OH (80:15:5)] (10)
UV(EtOH): 277 (10); (EtOH + NaOH) 292 (10)
^{1}H NMR: NMe 2.09 (N-2), 2.55 (N-2'); OMe 3.63 (C-7'), 3.89 (C-6); ArH 6.03 (H-8'), 6.11 (H-5'), 6.27 (d, 1H, $J = 1.8$ Hz, H-10); 6.53 (H-5), 6.63 (dd, 1H, $J = 1.8$, 8.0 Hz, H-14), 6.68 (dd, 1H, $J = 2.0$, 8.0 Hz, H-10'), 6.74 (dd, 1H, $J = 2.0$, 8.0 Hz, H-11'), 6.80 (d, 1H, $J = 8.0$ Hz, H-13), 7.02 (dd, 1H, $J = 2.0$, 8.2 Hz, H-13'), 7.22 (dd, 1H, $J = 2.0$, 8.2 Hz, H-14') (10)
MS: $[M]^+$ 594 (15), 593 (41), 592 (23), 382 (23), 381 (87), 191.5 (20), 191 (100), 176 (18), 174 (24), 168 (13) (10)
Sources: *Thalictrum minus* L. var. *minus* (Ranunculaceae) (10)
Derivatives: *O*-Methylthalicberine [**95**] (thalivarmine + CH_2N_2) (tlc) (10)

381 THALMICULATIMINE $C_{36}H_{36}O_6N_2$: 592.2573

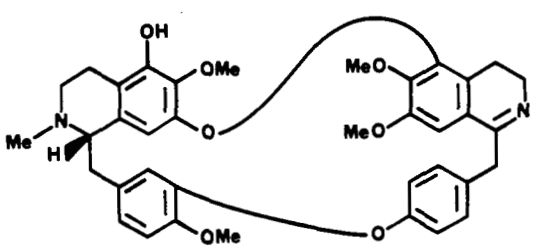
Type XIV (*S*,−) 6,7*,11$^+$,12-5*,6,7,12$^+$



MP: Amorphous (24)
[α]D: +7.5° (*c* = 0.093, MeOH) (24)
UV: 280 (4.02); (MeOH + H$^+$) 237 (sh) (4.38), 285 (4.01) (24)
^{1}H NMR: NMe 2.17 (N-2); OMe 3.76 (C-6′), 3.90 (C-7′), 3.94 (C-6); AlH 3.09 (m, 1H, H-1); ArH 5.58 (H-8), 5.81 (d, 1H, *J* = 2 Hz, H-10), 6.73 (dd, 1H, *J* = 2, 8.2 Hz, H-14), 6.79 (d, 1H, *J* = 8.2 Hz), 7.02 (d, 2H, *J* = 8 Hz, H-11′ and H-13′), 7.40 (d, 2H, *J* = 8 Hz, H-10′ and H-14′) (24)
MS: [M]$^+$ 592 (72), 591 (100), 397 (5), 296 (11), 273 (4) (24)
CD: 0 (330), −6.5 (302), 0 (294), +7.5 (278), 0 (267), −10.5 (245), positive tail below 238 nm (24)
Sources: *Thalictrum cultratum* Wall. (Ranunculaceae) (24)
Derivatives: 2′-Northalictine (thalmiculatimine + $NaBH_4$) (24)
[α]D: −54° (*c* = 0.1, MeOH) (24)
UV: 237 (sh) (4.33), 284 (3.90) (24)
^{1}H NMR: NMe 2.19 (N-2); OMe 3.73 (C-6′), 3.91 (C-6 or C-7′), 3.92 (C-7′ or C-6); AlH 4.46 (m, 1H, H-1′); ArH 5.85 (H-8), 6.04 (d, 1H, *J* = 2 Hz, H-10), 6.63 (H-5), 6.74 (d, 1H, *J* = 2 Hz, H-14), 6.84 (dd, 2H, *J* = 2, 8.2 Hz, H-8′ and H-13), 6.95 (d, 2H, *J* = 8 Hz, H-11′ and H-13′), 7.37 (d, 2H, *J* = 8 Hz, H-10′ and H-14′) (24)
MS: [M]$^+$ 594 (52), 593 (77), 592 (78), 591 (100), 395 (17), 381 (47), 365 (24), 191 (38) (24)
CD: 0 (300), +2.4 (291), 0 (288), −3.3 (281), 0 (268), 0 (258), +14.5 (240), negative tail below 230 nm (24)
Thalictine [**107**] (thalmiculatimine + $NaBH_4$ followed by CH_2O + $NaBH_4$) (24)

382 THALMICULIMINE $C_{37}H_{38}O_7N_2$: 622.2679

Type XIVa[1] (*S*,−) 5,6,7*,11$^+$,12-5*,6,7,12$^+$



MP: Amorphous (24)
[α]D: −5° (*c* = 0.09, MeOH) (24)
UV: 274 (3.97); (MeOH + H$^+$) 237 (sh) (4.40), 284 (3.93) (24)
^{1}H NMR: NMe 2.16 (N-2); OMe 3.69 (C-6′), 3.92 (6H, C-7′ and C-12), 4.07 (C-6); AlH 3.04 (m, 1H, H-1); ArH 5.17 (H-8), 5.84 (d, 1H, *J* = 2 Hz, H-10), 6.75 (dd, 1H, *J* = 2, 8.2 Hz, H-14), 6.81 (dd, 1H, *J* = 8.2 Hz, H-13), 7.04 (d, 2H, *J* = 8 Hz, H-11′ and H-13′), 7.06 (H-8′), 7.38 (d, 2H, *J* = 8 Hz, H-10′ and H-14′) (24)
MS: [M]$^+$ 622 (86), 621 (100), 607 (44), 591 (16), 561 (18), 311 (18), 288 (10) (24)
CD: 0 (330), −5.4 (302), 0 (289), +7.4 (278), 0 (269), −12 (245), positive tail below 235 nm (24)
Sources: *Thalictrum cultratum* Wall. (Ranunculaceae) (24)
Derivatives: 2′-Northalmiculine (thalmiculimine + $NaBH_4$) (24)
MP: Amorphous (24)
(α)D: −44° (*c* = 0.1, MeOH) (24)
UV: 236 (sh) (4.33), 281 (3.63) (24)
^{1}H NMR: NMe 2.26 (N-2); OMe 3.69 (C-6′), 3.93 (C-7′), 3.95 (C-12), 4.05 (C-6); AlH 3.30 (m,

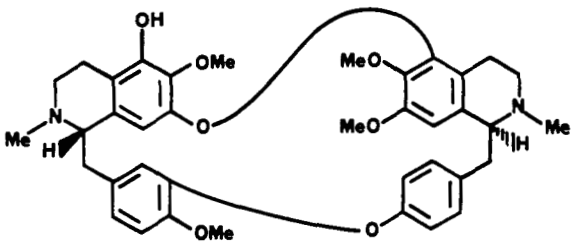
[1]This is a new class that supplements Class XIV as presented in the review of Guha *et al.* (1).

1H, H-1), 4.50 (m, 1H, H-1′); ArH 5.46 (H-8), 6.12 (d, 1H, J = 2 Hz, H-10), 6.81 (dd, 1H, J = 2, 8.2 Hz, H-14), 6.85 (d, 1H, J = 8.2 Hz, H-13), 6.99 (H-11′ and H-13′), 7.35 (H-10′ and H-14′) (24)

MS: $[M]^+$ 624 (72), 623 (100), 397 (57), 383 (49), 199 (71), 176 (64) (24)

CD: 0 (300), −7 (281), 0 (268), 0 (255), +23.5 (238), negative tail below 225 nm (24)

Thalmiculine [**383**] (thalmiculimine + $NaBH_4$ followed by CH_2O + $NaBH_4$) (24)



383 THALMICULINE $C_{38}H_{42}O_7N_2$: 638.2992

Type XIVa[1] (*S*,*S*) 5,6,7*,11$^+$,12-5*,6,7,12$^+$

MP: Amorphous (24)

$[\alpha]_D$: −35° (c = 2.2, MeOH) (24)

UV: 235 (sh) (4.28), 281 (3.58) (24)

^{1}H NMR: NMe 2.18 (N-2), 2.67 (N-2′); OMe 3.63 (C-6′), 3.90 (C-7′), 3.93 (C-12), 4.05 (C-6); AlH 3.22 (m, 1H, H-1), 3.64 (m, 1H, H-1′); ArH 5.45 (H-8), 6.09 (d, 1H, J = 2 Hz, H-10), 6.75 (dd, 1H, J = 2, 8.2 Hz, H-14), 6.80 (d, 1H, J = 8.2 Hz, H-13), 6.81 (H-8′), 6.95 (br s, 1H, H-11′ and H-13′), 7.30 (br hump, 2H, H-10′ and H-14′) (24)

MS: $[M]^+$ 638 (100), 637 (62), 411 (67), 397 (41), 206 (73), 183 (38) (24)

CD: 0 (300), −3.2 (280), −0.8 sh (268), 0 (260), +11.2 (238), negative tail below 225 nm (24)

Sources: *Thalictrum cultratum* Wall. (Ranunculaceae) (24)

Derivatives: *O*-Methylthalmiculine (thalmiculine + CH_2N_2) (24)

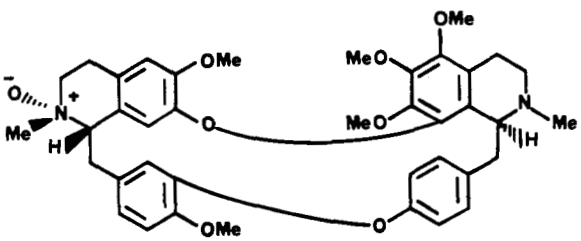
$[\alpha]_D$: −38° (c = 0.2, MeOH) (24)

^{1}H NMR: NMe 2.18 (N-2), 2.66 (N-2′); OMe 3.65 (C-6′), 3.88 (C-7′), 3.93 (C-12), 4.00 (C-6); AlH 3.27 (m, 1H, H-1), 3.63 (m, 1H, H-1′); ArH 5.70 (H-8), 6.12 (d, 1H, J = 2 Hz, H-10), 6.76 (d, 1H, J = 2 Hz, H-14), 6.79 (dd, 1H, J = 2, 8.2 Hz, H-13), 6.93 (2H, H-11′ and H-13′), 7.37 (2H, H-10′ and H-14′) (nOe used) (24)

MS: $[M]^+$ 652 (91), 651 (12), 638 (18), 622 (19), 426 (82), 412 (79), 410 (31), 213.5 (100), 206.5 (16), 204 (41), 190.5 (73) (24)

384 THALRUGOSAMININE-2α-*N*-OXIDE $C_{39}H_{44}O_8N_2$: 668.3098

Type VII (*S*,*S*) 5,6,7,8*,12$^+$-6,7*,11$^+$,12



MP: Amorphous (41)

$[\alpha]_D$: −33° (c = 0.2, MeOH) (41)

^{1}H NMR: NMe 2.58 (N-2), 3.45 (N-2′); OMe 3.05 (C-7), 3.45 (C-6′), 3.81 (C-5), 3.89 (C-6), 3.96 (C-12′); AlH 2.55 (m, 2H, H-α_b and H-α'_b), 3.13 (m, 1H, H-α_a), 3.55 (m, 1H, H-α'_a), 4.47 (m, 1H, H-1), 4.83 (m, 1H, H-1′); ArH 6.37 (H-8′), 6.50 (H-5′), 6.59 (br s, 1H, H-10′), 6.82 (br s, 2H, H-10 and H-11), 6.99 (br s, 2H, H-13′ and H-14′), 7.16 (dd, 1H, J = 2.2, 8.1 Hz, H-13), 7.51 (dd, 1H, J = 2.2, 8.1 Hz, H-14) (nOe used) (41)

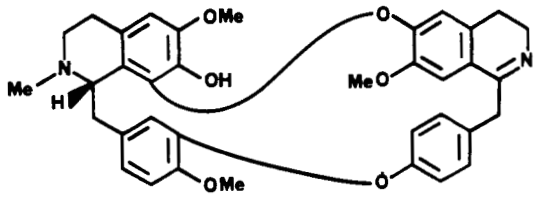
MS: $[M]^+$ 668 (6), 667 (10), 666 (22), 652 (81), 651 (60), 637 (35), 608 (18), 607 (19), 441 (1), 425 (63), 412 (26), 411 (92), 397 (15), 213 (100), 206 (51), 174 (42) (41)

Sources: *Thalictrum cultratum* Wall. (Ranunculaceae) (41)

[1]This is a new class that supplements Class XIV as mentioned in the review of Guha *et al.* (1).

385 THALSIVASINE $C_{36}H_{36}O_6N_2$: 592.2573

Type XI (*S*,−) 6,7,8•,11$^+$-12,6•,7,12$^+$



TLC: (Si gel) 0.36 [toluene-Me_2CO-NH_4OH (10:10:0.5)], 0.33 [$CHCl_3$-MeOH (9:1)], 0.55 [$CHCl_3$-MeOH-NH_4OH (90:10:0.2)], 0.50 [EtOAc-iPrOH-NH_4OH (80:15:5)] (10)

$[\alpha]_D$: +196° (c = 0.2, MeOH) (24)

UV: 283, 324 (10); 234 (sh) (4.39), 281 (4.05), 313 (3.78); (MeOH + H^+) 239 (4.36, 285 (3.99), 308 (3.69), 354 (3.82) (24)

^{1}H NMR: NMe 1.95 (N-2); OMe 3.71 (C-7'), 3.90 (C-6), 3.92 (C-12); AlH 4.20 (br s, 1H, H-1); ArH 5.80 (d, 1H, J = 1.7, H-10), 6.27 (H-8'), 6.56 (H-5), 6.63 (dd, 1H, J = 1.7, 8.0, H-14), 6.68 (H-5'), 6.78 (s, 2H, H-10', H-11'), 6.79 (d, 1H, J = 8.0, H-13), 7.16 (d, 1H, J = 8.0, H-13'), 7.47 (d, 1H, J = 8.0, H-14') (10)

NMe 1.96 (N-2); OMe 3.71 (C-7'), 3.92 (C-12), 3.93 (C-6); ArH 5.80 (d, 1H, J = 1.8 Hz, H-10), 6.28 (H-8'), 6.56 (H-5), 6.63 (dd, 1H, J = 1.8, 8 Hz, H-14), 6.67 (H-5'), 6.78 (dd, 1H, J = 2, 8.2 Hz, H-10'), 6.79 (d, 1H, J = 1.8 Hz, H-13), 6.81 (dd, 1H, J = 2, 8.2 Hz, H-11'), 7.16 (dd, 1H, J = 2, 8.2 Hz, H-13'), 7.48 (dd, 1H, J = 2, 8.2 Hz, H-14') (24)

MS: $[M]^+$ 592 (39), 591 (100), 590 (50), 576 (15), 561 (12), 560 (26), 368 (17), 236 (14), 204 (8), 183 (7) (10)
$[M]^+$ 592 (94), 591 (100), 578 (25), 577 (62), 561 (38), 296 (28), 204 (13), 191 (17), 190 (12) (24)

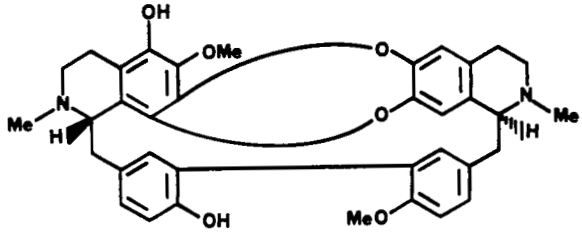
Cd: 0 (320), +14 (280), 0 (271), −9.6 (265), −11.0 (255), −14.4 (245), negative tail below 225 nm (24)

Sources: *Thalictrum minus* L. var. *minus* (Ranunculaceae) (10), *Thalictrum cultratum* Wall. (Ranunculaceae) (24)

Derivatives: *O*-Methylthalmethine [**96**] (thalsivasine + CH_2N_2) (tlc) (10)
2'-Northaliphylline (thalsivasine + $NaBH_4$) (24)
(See data recorded for new alkaloid 2'-northaliphylline [**342**] in this review.)
Thaliphylline [**253**] (thalsivasine + $NaBH_4$ followed by CH_2O + $NaBH_4$) (24)

386 TILIANANGINE $C_{36}H_{36}O_6N_2$: 592.2573

Type XIX (*S*,*S*) 5,6,7•,8$^+$,12-6•,7$^+$,12(11-11)



MP: Amorphous, 143–149° (26)

TLC: (Si gel F_{254}) 0.25 [$CHCl_3$-MeOH (9:1)], 0.17 [cyclohexane-$CHCl_3$-Et_2NH (4:5:1)] (26)

$[\alpha]^{20}_D$: +259° (c = 0.6, $CHCl_3$) (26)

UV: 205 (4.28), 233 (4.05), 290 (3.42) (26)

IR(KBr): 3370, 2940, 2860, 2800, 1635, 1600, 1505, 1470, 1440, 1385, 1375, 1280, 1240, 1205, 1120, 1045, 1030, 1015, 990, 950, 875, 820, 760 (26)

^{1}H NMR: NMe 2.33 (N-2), 2.67 (N-2'); OMe 3.93 (C-6), 3.96 (C-12'); AlH 2.43 (dd, 1H, J = 18.2, 4.8 Hz, H-4a), 2.67 (1H, H-4'a), 2.70 (1H, H-4b), 2.82 (2H, H-α and H-β), 3.00 (1H, H-3'a), 3.02 (1H, H-α'b), 3.04 (2H, H-3a and H-4'b), 3.26 (dd, 1H, J = 12.5, 4.4, H-3'b), 3.36 (ddd, 1H, J = 13.5, 13.5, 4.8 Hz, H-3b), 3.58 (d, 1H, J = 14.4, H-α'a), 3.72 (br s, 1H, H-1'), 3.77 (d, 1H, J = 6.8 Hz, H-1); ArH 6.65 (H-5'), 6.97 (d, 1H, J = 8.4 Hz, H-13), 7.03 (d, 1H, J = 8.6 Hz, H-13'), 7.33 (dd, 1H, J = 1.8, 8.4 Hz, H-14), 7.49 (dd, 1H, J = 1.8, 8.6 Hz, H-14'), 7.57 (d, 1H, J = 2.1, Hz, H-10), 7.71 (d, 1H, J = 1.8 Hz, H-10'), 8.09 (H-8') (2D nmr used) (26)

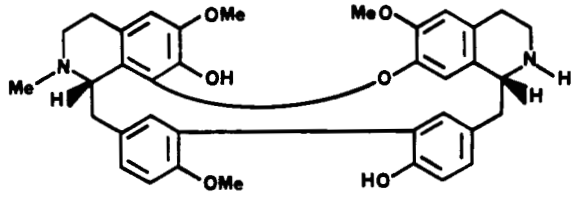
^{13}C NMR: 62.89 (C-1), 43.15 (C-3), 15.89 (C-4), 115.36 (C-4a), 141.67 (C-5), 132.74 (C-6), 133.39 (C-7), 132.94 (C-8), 121.41 (C-8a), 40.78 (C-α), 136.17 (C-9), 135.88 (C-10), 127.76 (C-11), 152.16 (C-12), 112.12 (C-13), 130.54 (C-14); 66.81 (C-1'), 52.70 (C-3'), 26.22 (C-4'), 134.65 (C-4'a), 115.29 (C-5'), 139.83 (C-6'), 140.57 (C-7'), 114.55 (C-8'), 128.95 (C-8'a), 42.37 (C-α'), 134.30 (C-9'), 134.65 (C-10'), 126.72 (C-11'), 154.10 (C-12'), 117.30 (C-13'), 130.31 (C-14'); 40.40 (2'-NMe), 42.05 (2-NMe), 56.42 (12'-OMe), 62.89 (6-OMe) (26,56)

MS: $[M]^+$ 592 (45), 591 (25), 575 (7), 560 (7), 366 (24), 365 (100), 351 (27), 349 (17), 335 (14), 183 (31), 182 (5), 175 (22) (26)

Sources: *Tiliacora triandra* Diels (Menispermaceae) (26)

387 TILITRIANDRINE $C_{36}H_{38}O_6N_2$: 594.2730

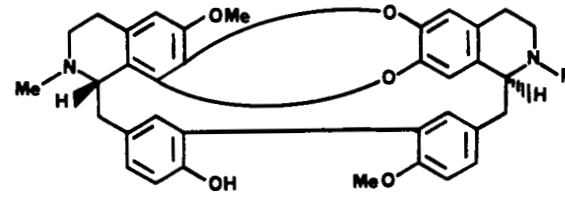
Type IV (*S,R*) 6,7,8*,12-6,7*,12(11-11)



MP: 192° (CH_2Cl_2/MeOH) (61)
TLC: (Si gel 60 F_{254}) 0.22 [CH_2Cl_2-MeOH-NH_4OH (90:9:1)] (61)
$[\alpha]^{20}D$: +198° (c = 1.1, $CHCl_3$) (61)
UV: 212 (4.38), 285 (3.57) (61)
IR(KBr): 3380, 2920, 2840, 1620, 1580, 1500, 1460, 1450, 1410, 1300, 1280, 1240, 1110, 1060, 1040, 880, 810 (61)
^{1}H NMR: NMe (2.36 (N-2); OMe 3.48 (C-6'), 3.84 (C-6), 3.88 (C-12); ArH 6.36 (H-5), 6.49 (H-5'), 6.86 (d, 1H, J = 2.0 Hz, H-10), 6.88 (d, 1H, J = 8.4 Hz, H-13'), 6.90 (d, 1H, J = 8.4 Hz, H-13), 7.04 (d, 1H, J = 2.0 Hz, H-10'), 7.13 (dd, 1H, J = 2.0, 8.4 Hz, H-14'), 7.37 (dd, 1H, J = 2.0, 8.4 Hz, H-14) (2D nmr used) (61). The signals for the H-10 and H-10' protons are reversed in comparison to those assigned for antioquine (196).
^{13}C NMR: 62.61 (C-1), 44.18 (C-3), 21.52 (C-4), 122.02 (C-4a), 104.93 (C-5), 145.62 (C-6), 134.69 (C-7), 142.00 (C-8), 124.14 (C-8a), 40.39 (C-α), 130.94 (C-9), 135.09 (C-10), 129.09 (C-11), 152.96 (C-12), 111.36 (C-13), 129.54 (C-14), 56.50 (C-1'), 42.40 (C-3'), 29.50 (C-4'), 127.69 (C-4'a), 113.72 (C-5'), 148.05 (C-6'), 143.03 (C-7'), 118.16 (C-8'), 126.34 (C-8'a), 39.61 (C-α'), 138.03 (C-9'), 136.13 (C-10'), 129.95 (C-11'), 152.45 (C-12'), 117.38 (C-13'), 130.51 (C-14'); 42.18 (2-NMe), 55.95 (6'-OMe), 56.37 (6-OMe), 56.68 (12-OMe) (61)
MS: $[M]^+$ 594 (100), 593 (100), 579 (19), 381 (26), 368 (75), 367 (76), 353 (28), 351 (15), 192 (30), 191 (25), 184 (40), 161 (12) (61)
Sources: *Tiliacora triandra* Diels (Menispermaceae) (61)
Derivatives: Antioquine [**225**] (tilitriandrine + CH_2O/$NaBH_4$) (61)

388 YANANGCORININE $C_{36}H_{36}O_5N_2$: 576.2624

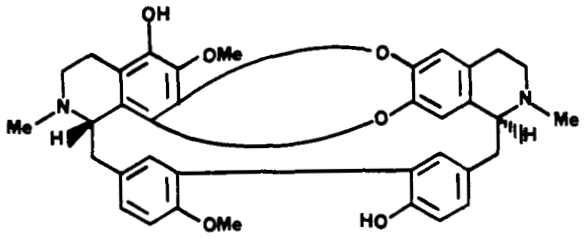
Type XVIII (*S,S*) 6,7*,8$^+$,12-6*,7$^+$,12(11-11)



MP: Amorphous; 174–180° (17)
$[\alpha]^{19}D$: +368° (c = 0.6, $CHCl_3$) (17)
UV: 205 (4.57), 235 (4.27), 290 (3.62) (17)
IR(KBr): 3400, 2940, 2840 2800, 1630, 1600, 1505, 1450, 1365, 1280, 1240, 1125, 1030, 960, 880, 820 (17)
^{1}H NMR: NMe 2.33 (N-2), 2.66 (N-2'); OMe 3.83 (C-6), 3.93 (C-12'); AlH 3.71 (H-1), 3.00 and 3.38 (H-3), 2.84 and 2.88 (H-4), 2.80 (H-α), 3.47 (H-1'), 2.75 and 3.16 (H-3'), 2.58 and 3.00 (H-4'), 3.00 and 3.47 (H-α'); ArH 6.32 (H-5), 6.68 (H-5'), 6.98 (H-13), 7.03 (H-13'), 7.32 (H-14), 7.41 (H-14'), 7.55 (H-10), 7.72 (H-10'), 8.07 (H-8') (2D nmr COSY used) (17)
^{13}C NMR: 62.96 (C-1), 43.79 (C-3), 21.33 (C-4), 130.02 (C-4a), 106.36 (C-5), 146.30 (C-6), 130.18 (C-7), 140.06 (C-8), 118.96 (C-8a), 40.65 (C-α), 135.69 (C-9), 134.72 (C-10), 126.75 (C-11), 152.10 (C-12), 112.03 (C-13), 130.31 (C-14), 67.55 (C-1'), 53.15 (C-3'), 27.16 (C-4'), 135.59 (C-4a'), 115.33 (C-5'), 139.99 (C-6' and C-7'), 114.23 (C-8'), 128.95 (C-8a'), 41.46 (C-α'), 136.37 (C-9'), 135.88 (C-10'), 127.79 (C-11'), 153.91 (C-12'), 117.24 (C-13'), 130.02 (C-14'), 42.18 (2-NMe), 42.01 (2'-NMe), 56.29 (6-OMe), 56.35 (12'-OMe) (17)
MS: $[M]^+$ 576 (55), 561 (3), 350 (30), 349 (100), 335 (30), 319 (7), 175 (50) (17)
Sources: *Tiliacora triandra* Diels (Menispermaceae) (17)
Derivatives: *O*-Methyltiliacorinine (yanangcorinine + CH_2N_2) (ir, ms, ^{1}H nmr, $[\alpha]D$) (17)
MP: Amorphous; 166–174° (17)
$[\alpha]^{20}D$: +240.3° (c = 0.4, $CHCl_3$) (17)
IR(KBr): 2940, 2840, 2800, 1630, 1595, 1505, 1440, 1415, 1360, 1270, 1120, 1030, 960, 880, 820, 740 (17)
^{1}H NMR: NMe 2.31 (N-2), 2.60 (N-2'); OMe 3.79 (C-6), 3.85 (C-12), 3.88 (C-12') (17)
MS: $[M]^+$ 590 (32), 589 (19), 350 (28), 349 (100), 335 (30), 319 (6), 175 (25), 174 (20) (17)

389 YANANGINE $C_{36}H_{36}O_6N_2$: 592.2573

Type XIX (*S,S*) 5,6,7*,8$^+$,12-6*,7$^+$,12(11-11)



MP: 237–240° (CH_2Cl_2) (27)
TLC: (Si gel 60 F_{254}) 0.37 [$CHCl_3$-MeOH (9:1)]; 0.19 [cyclohexane-$CHCl_3$-Et_2NH (4:5:1)] (27)
$[\alpha]^{19}D$: +356° (c = 0.6, $CHCl_3$) (27)
UV: 205 (4.50), 233 (4.27), 290 (3.62) (27)
IR(KBr): 3370, 2910, 2840, 2800, 1630, 1595, 1500, 1460, 1435, 1370, 1270, 1235, 1200, 1100, 1095, 1040, 1010, 985, 970, 945, 870, 820, 765 (27)
^1H NMR: NMe 2.29 (N-2), 2.67 (N-2'); OMe 3.96 (C-6), 4.00 (C-12); AlH 2.42 (dd, 1H, H-4), 2.57 (d, 1H, H-4'), 2.68 (1H, H-4), 2.76 (d, 1H, H-3'), 2.80 (2H, H-α), 2.94 (1H, H-α'), 3.00 (1H, H-4'), 3.04 (1H, H-3), 3.15 (dd, 1H, H-3'), 3.34 (1H, H-3), 3.47 (d, 1H, H-α'), 3.53 (1H, H-1'), 3.72 (d, 1H, H-1); ArH 6.53 (H-5'), 6.98 (H-13), 7.03 (H-13'), 7.33 (H-14'), 7.36 (H-14), 7.59 (H-10'), 7.69 (H-10), 8.11 (H-8') (2D nmr used, nOe used) (27)
NMe 2.29 (N-2), 2.67 (N-2'); OMe 3.96 (C-6), 4.00 (C-12); ArH 6.64 (H-5'), 6.98 (d, 1H, J = 8.3 Hz, H-13), 7.03 (d, 1H, J = 8.3 Hz, H-14'), 7.33 (dd, 1H, J = 1.9, 8.3 Hz, H-14'), 7.36 (dd, 1H, J = 2.1, 8.3 Hz, H-14), 7.59 (d, 1H, J = 1.9 Hz, H-10'), 7.69 (d, 1H, J = 2.1 Hz, H-10), 8.11 (H-8') (56)
^{13}C NMR: 62.96 (C-1), 43.11 (C-3), 15.83 (C-4), 115.52 (C-4a), 141.77 (C-5), 133.03 (C-6), 133.61 (C-7), 133.10 (C-8), 120.99 (C-8a), 40.33 (C-α), 137.82 (C-9), 135.82 (C-10), 127.92 (C-11), 153.26 (C-12), 111.18 (C-13), 129.96 (C-14), 67.42 (C-1'), 53.12 (C-2'), 27.29 (C-3'), 134.20 (C-4'), 115.04 (C-4'a), 139.34 (C-5'), 140.25 (C-6'), 114.32 (C-7'), 129.63 (C-8'), 41.53 (C-α'), 136.27 (C-9'), 134.46 (C-10'), 126.49 (C-11'), 152.65 (C-12'), 118.53 (C-13'), 130.25 (C-14'), 42.30 (2-NMe), 41.95 (2'-NMe), 56.55 (12-OMe), 61.53 (6-OMe) (27)
62.96 (C-1), 43.23 (C-3), 15.93 (C-4), 115.43 (C-4a), 141.75 (C-5), 132.99 (C-6), 133.51 (C-7), 133.02 (C-8), 120.97 (C-8a), 40.39 (C-α), 137.73 (C-9), 135.79 (C-10), 127.94 (C-11), 153.34 (C-12), 111.32 (C-13), 130.02 (C-14), 67.10 (C-1'), 52.92 (C-2'), 26.83 (C-3'), 26.83 (C-4'), 133.70 (C-4'a), 115.09 (C-5'), 139.55 (C-6'), 140.36 (C-7'), 114.43 (C-8'), 129.30 (C-8'a), 41.20 (C-α'), 136.27 (C-9'), 134.39 (C-10'), 126.50 (C-11'), 152.73 (C-12'), 118.57 (C-13'), 130.31 (C-14'), 42.04 (2-NMe), 41.95 (2'-NMe), 56.61 (12-OMe), 61.53 (6-OMe) (56)
MS: $[M]^+$ 592 (37), 591 (21), 366 (30), 365 (100), 351 (29), 349 (12), 335 (8), 183 (74), 182 (8), 175 (47) (27)
Sources: *Tiliacora triandra* Diels (Menispermaceae) (27)
Derivatives: *O,O*-Dimethylyanangine (yanangine + CH_2N_2) (27)
MP: Amorphous, 150–155° (27)
TLC: (Si gel 60 F_{254}) 0.53 [cyclohexane-$CHCl_3$-Et_2NH (4:5:1)] (27)
$[\alpha]^{20}D$: +257° (c = 0.6, $CHCl_3$) (27)
IR: 2930, 2840, 2800, 1605, 1590, 1500, 1460, 1430, 1410, 1360, 1275, 1245, 1130, 1070, 1050, 1030, 875, 870 (27)
^1H NMR: NMe 2.30 (N-2), 2.61 (N-2'); OMe 3.79 (C-12 OMe), 3.81 (C-12'), 3.87 (C-5), 3.92 (C-6) (27)
^{13}C NMR: 62.66 (C-1), 43.21 (C-3), 16.05 (C-4), 122.12 (C-4a), 145.98 (C-5), 134.29 (C-6), 136.17 (C-7), 135.52 (C-8), 121.44 (C-8a), 40.59 (C-α), 139.54 (C-9), 135.36 (C-10), 128.76 (C-11), 155.66 (C-12), 110.89 (C-13), 129.12 (C-14); 67.45 (C-1'), 53.15 (C-3'), 26.64 (C-4'), 134.29 (C-4'a), 115.23 (C-5'), 139.44 (C-6'), 139.96 (C-7'), 114.52 (C-8'), 130.09 (C-8'a), 40.95 (C-α'), 135.88 (C-9'), 135.10 (C-10'), 128.44 (C-11'), 155.59 (C-12'), 112.12 (C-13'), 129.31 (C-14'), 41.95 (2-NMe), 41.20 (2'-NMe), 60.56 (5-OMe), 61.34 (6-OMe), 56.06 (12-OMe), 56.93 (12'-OMe) (27)
MS: $[M]^+$ 620 (55), 619 (28), 380 (32), 379 (100), 365 (29), 363 (13), 349 (5), 333 (4), 190 (47), 189 (14) (27)
5-*O*-Methylyanangine (yanangine + CH_2N_2) (27)
MP: Amorphous, 108–112° (27)
TLC: (Si gel 60 F_{254}) 0.37 [cyclohexane-$CHCl_3$-Et_2NH (4:5:1)] (27)
$[\alpha]D$: +294° (c = 0.6, $CHCl_3$) (27)
IR(KBr): 3400, 2940, 2840, 2800, 1595, 1505, 1465, 1435, 1420, 1470, 1280, 1240, 1070, 1055, 1020, 880, 830, 735 (27)
^1H NMR: NMe 2.29 (N-2), 2.64 (N-2'); OMe 3.81 (C-5), 3.92 (C-6), 3.97 (C-12) (27)
^{13}C NMR: 62.92 (C-1), 43.37 (C-3), 16.05 (C-4), 122.35 (C-4a), 146.11 (C-5), 134.42 (C-6), 136.14 (C-7), 135.46 (C-8), 120.96 (C-8a), 40.33 (C-α), 137.66 (C-9), 135.78 (C-10), 127.92 (C-11), 153.33 (C-12), 111.22 (C-13), 130.02 (C-14); 67.23 (C-1'), 52.99 (C-

3'), 26.96 (C-4'), 134.42 (C-4'a), 115.23 (C-5'), 139.70 (C-6'), 140.15 (C-7'), 114.32 (C-8'), 129.57 (C-8'a), 41.24 (C-α'), 136.14 (C-9'), 134.42 (C-10'), 126.49 (C-11'), 152.74 (C-12'), 118.63 (C-13'), 130.35 (C-14'), 42.01 (2-NMe), 41.75 (2'-NMe), 60.63 (5-OMe), 61.37 (6-OMe), 56.55 (12-OMe) (27)

MS: $[M]^+$ 606 (53), 605 (25), 380 (35), 379 (100), 365 (31), 363 (12), 349 (5), 333 (4), 190 (46), 189 (13) (27)

12'-*O*-Methylyanangine (yanangine + CH_2N_2) (27)

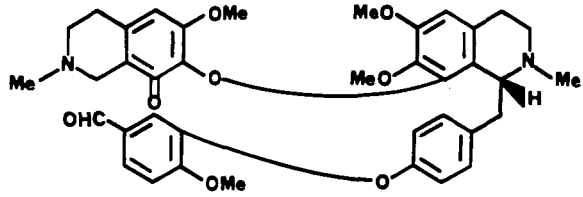
TLC: (Si gel 60 F_{254}) 0.38 [cyclohexane-$CHCl_3$-Et_2NH (4:5:1)] (27)

^{1}H NMR: NMe 2.36 (N-2), 2.70 (N-2'); OMe 3.77 (C-12), 3.87 (C-12'), 3.93 (C-6) (27)

SECOBISBENZYLISOQUINOLINE ALKALOIDS

390 AURORAMINE $C_{38}H_{40}O_8N_2$: 652.2785

Type VI (−,*R*)



[α]D: Positive (50)

UV(EtOH): 220, 260, 270, 305 (50)

IR(KBr): 2940, 2840, 1690, 1640, 1600, 1500, 1280, 1120 (50)

^{1}H NMR: NMe 2.29 (N-2'), 3.05 (N-2); OMe 3.67 (C-7'), 3.85 (C-6'), 3.95 (C-6 or C-12), 3.96 (C-12 or C-6); ArH 6.54 (H-5'), 6.72 (H-5), 6.83 (H-11' and H-13'), 7.14 (H-10' and H-14'), 7.26 (H-8), 7.38 (H-10), 7.62 (H-14), 7.68 (H-13); ArCHO 9.79 (50)

MS: $[M[^+$ 652 (0.2), 651 (0.3), 411 (100), 365 (8.4), 241 (3), 206 (2.1), 204 (4.8) (50)

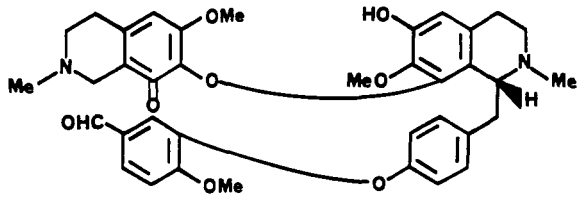
Sources: *Gyrocarpus americanus* Jacq. (Hernandiaceae) (50)

Preparation: Via oxidation ($KMnO_4$/Me_2CO) of *O*-methyllimacusine (50)

Apparent biogenetic precursor: *O*-Methyllimacusine (50)

391 MAROUMINE $C_{37}H_{38}O_8N_2$: 638.2628

Type VI (−,*R*)



[α]D: Positive (50)

UV(EtOH): 220, 270, 305 (50)

IR: 2840, 1690, 1650, 1600 (50)

^{1}H NMR: NMe 2.31 (N-2'), 3.06 (N-2'); OMe 3.75 (C-7), 3.95 (C-6 or C-12), 3.96 (C-12 or C-6); ArH 6.59 (H-5'), 6.74 (H-5), 6.83 (H-11' and H-13'), 7.08 (H-13), 7.13 (H-10' and H-14'), 7.28 (H-8), 7.38 (H-10), 7.62 (H-14); ArCHO 9.79 (50)

MS: $[M]^+$ 638 (0.6), 637 (0.6), 397 (100), 351 (14), 242 (8.3), 207 (23), 164 (30) (50)

Sources: *Gyrocarpus americanus* Jacq. (Hernandiaceae) (50)

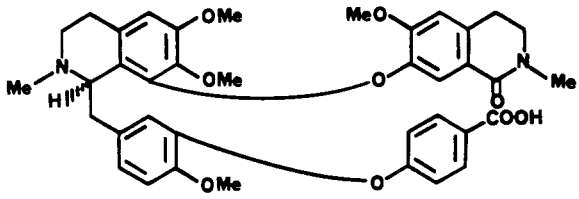
Derivatives: *O*-Acetylmaroumine (maroumine + Ac_2O/pyridine) (50)

Preparation: Oxidation of *O*-acetylgyrocarpine with $KMnO_4$/Me_2CO afforded seco-acetylgyrocarpine which was identical to *O*-acetylmaroumine (50)

Apparent biogenetic precursor: Gyrocarpine [**306**] (15,50)

392 PYCMANILLINE $C_{38}H_{40}O_9N_2$: 668.2734

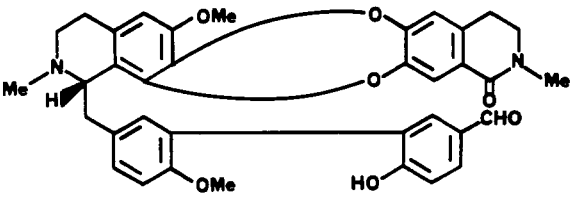
Type VIII (*R*, −)



MP: Amorphous (48); 254–255° (48)
TLC: (Si gel 60 F_{254}) 0.05 [$CHCl_3$-MeOH-NH_4OH (9:1:0.05)] (48)
$[\alpha]^{22}D$: +50° ($c = 0.1$, $CHCl_3$) (48); +33° ($c = 0.61$, $CHCl_3$) (48)
UV: 225 (sh) (4.79), 250 (sh) (4.52), 261 (sh) (4.41), 272 (sh) (4.25), 285 (sh) (4.08), 295 (sh) (3.92), 306 (sh) (3.77) (48)
IR(KBr): 2930, 1710, 1650, 1605, 1505 (48)
^{1}H NMR: NMe 2.52 (N-2), 3.03 (N-2′); OMe 3.62 (C-7), 3.69 (C-6), 3.79 (C-6′), 3.86 (C-12); ArH 6.50 (H-5), 6.62 (H-5′), 6.75–7.05 (m, 3H, ring C), 6.83 (d, 2H, $J = 8.1$ Hz, H-11′ and H-13′), 7.16 (H-8′), 7.83 (d, 2H, $J = 8.1$ Hz, H-10′ and H-14′) (48)
CIMS(i-butane): $[M + 1]^+$ 669 (100), 668 (16) 623 (10), 411 (81) (48)
CIMS(NH_3): $[M + 1]^+$ 669 (100), 668 (24), 411 (35) (48)
Sources: *Pycnarrbena manillensis* Vidal (Menispermaceae) (48)
Preparation: Via oxidation of phaeanthine [**74**] with $KMnO_4/Me_2CO$ (48)
Apparent biogenetic precursor: Isotetrandrine [**62**] (1) or phaeanthine [**74**] (1)

393 SECOLUCIDINE $C_{36}H_{34}O_7N_2$: 606.2366

Type XVIII (*S*, −)



$[\alpha]D$: +82° ($c = 0.5$, $CHCl_3$) (29)
UV(EtOH): 222 (4.63), 254 (sh) (4.32), 284 (4.12); (EtOH + OH^-) 220 (4.66), 292 (3.98), 346 (4.10) (29)
IR(film): 1680, 1640, 1620, 1580, 1500 (29)
^{1}H NMR: NMe 2.37 (N-2), 3.11 (N-2′); OMe 3.80 (C-6), 3.86 (C-12); ArH 6.30 (H-5), 6.70 (H-5′), 7.23 (H-8′), 6.94–7.87 (m, 6H, H-10, H-13, H-14, H-10′, H-13′, H-14′); ArCHO 9.90 (29)
EIMS: 365 (100), 242, 2431, 225 (29)
CIMS: $[M]^+$ 607, $[M + 1]^+$ (29)
CD: 0 (331), + (298), 0 (284), −8 (243), 0 (228), +5 (219) (29)
Sources: *Pseudoxandra sclerocarpa* Maas (Annonaceae) (29)
Derivatives: *O*-Acetylsecolucidine (secolucidine + Ac_2O/pyridine) (29)
$[\alpha]D$: −35° ($c = 0.6$, $CHCl_3$) (29)
IR(film): 1765, 1695, 1645, 1620, 1585 (29)
^{1}H NMR: NMe 2.61 (N-2), 3.11 (N-2′); OAc 2.03; OMe 3.68 (C-12), 3.88 (C-6); ArH 6.36 (H-5), 6.68 (H-5′), 7.27 (H-8′), 6.95–7.86 (m, 6H, H-10, H-13, H-14, H-10′, H-13′, H-14′); ArCHO 9.98 (29)
MS: $[M]^+$ 648 (6), 606 (11), 365 (100), 242 (7), 225 (2) (29)
Apparent biogenetic precursor: Tiliacorinine [**119**] (1)

TABLE 5. Calculated Molecular Weights of New Bisbenzylisoquinoline Alkaloids.

546.2155	$C_{34}H_{30}O_5N_2$	1,2-Dehydro-2′-nortelobine [**292**] (33)
548.2311	$C_{34}H_{32}O_5N_2$	2′-Norcocsuline [**329**] (35)
560.1947	$C_{34}H_{28}O_6N_2$	Siddiquine [**372**] (33)
562.2104	$C_{34}H_{30}O_6N_2$	1′,2′-Dehydrokohatine [**290**] (33) Pycnazanthine [**370**] (38)
564.2260	$C_{34}H_{32}O_6N_2$	5-Hydroxyapateline [**309**] (33) Pangkorimine [**354**] (35)
566.2417	$C_{34}H_{34}O_6N_2$	Bisnorobamegine [**277**] (38) Pangkoramine [**353**] (35)
574.2104	$C_{35}H_{30}O_6N_2$	Siddiquamine [**371**] (33) Stephasubimine [**373**] (21)
576.2260	$C_{35}H_{32}O_6N_2$	Dehatridine [**287**] (63) 1′,2′-Dehydrokohatamine [**289**] (33) Norstephasubine [**340**] (21) Stepierrine [**376**] (64)
576.2624	$C_{36}H_{36}O_5N_2$	Yanangcorinine [**388**] (17)
578.2417	$C_{35}H_{34}O_6N_2$	5-Hydroxytelobine [**310**] (33) Kohatamine [**314**] (33) 2-Norcepharanoline [**326**] (64) Norisoyanangine [**335**] (56) Noryanangine [**346**] (56)
580.2573	$C_{35}H_{36}O_6N_2$	Bisnorthalrugosine [**279**] (38)
582.2730	$C_{35}H_{38}O_6N_2$	2-*N*-Methyllindoldhamine [**321**] (36) 2′-*N*-Methyllindoldhamine [**322**] (36) Northalibroline [**341**] (76) Pedroamine [**355**] (71)
590.2417	$C_{36}H_{34}O_6N_2$	Caryolivine [**281**] (19) Stephasubine [**374**] (21)
592.2573	$C_{36}H_{36}O_6N_2$	Cordobimine [**283**] (79) 1,2-Dehydro-2-norlimacusine [**291**] (19) 12-*O*-Demethylcoclobine [**293**] (59) 3′,4′-Dihydrostephasubine [**295**] (49) 2-Norcepharanthine [**327**] (21) 2′-Norcepharanthine [**328**] (64) 2-Norisocepharanthine [**333**] (64) Thalmiculatimine [**381**] (24) Thalsivasine [**385**] (10,24) Tilianangine [**386**] (26) Yanangine [**389**] (27)
594.2730	$C_{36}H_{38}O_6N_2$	Aquifoline [**273**] (31) Berbilaurine [**275**] (62) 2,2′-Bisnorguattaguianine [**276**] (51) 2,2′-Bisnorphaeanthine [**278**] (35) Candicusine [**280**] (83–85) 12-*O*-Desmethyllauberine [**294**] (65) 2-Norlimacine [**336**] (19) 2′-Noroxyacanthine [**338**] (41) 2′-Northaliphylline [**342**] (24,41) 2-Northalmine [**343**] (12) 2-Northalrugosine [**344**] (38) 2′-Nortiliageine [**345**] (51) Thalivarmine [**380**] (10) Tilitriandrine [**387**] (61)
596.2886	$C_{36}H_{40}O_6N_2$	2′-Nordaurisoline [**330**] (36) 2′-Norpisopowiaridine [**339**] (30) Pampulhamine [**352**] (71)
605.2652	$C_{37}H_{37}O_6N_2$	Fenfangjine D (1,3,4-tridehydrofangchinolinium hydroxide) [**300**] (52)
606.2366	$C_{36}H_{34}O_7N_2$	Secolucidine [**393**] (29)
606.2730	$C_{37}H_{38}O_6N_2$	Dehatrine [**288**] (63) Medelline [**318**] (67) *N*-Methyltiliamosine [**323**] (78)
608.2522	$C_{36}H_{36}O_7N_2$	Cultithalminine [**285**] (41)
608.2886	$C_{37}H_{40}O_6N_2$	Cordobine [**284**] (79) Guattamine [**303**] (51) Gyroamericine [**305**] (15) Gyrocarpine [**306**] (15) Gyrocarpusine [**307**] (15) 2′-Norfuniferine [**331**] (51) 2′-Norguattaguianine [**332**] (51) 2-Norisotetrandrine [**334**] (64) 2′-Norobaberine [**337**] (64) Stephibaberine [**375**] (64)
610.3043	$C_{37}H_{42}O_6N_2$	Geraldoamine [**301**] (71) Pisopowamine [**357**] (30) Pisopowiaridine [**359**] (30) Popisonine [**366**] (30) Popisopine [**367**] (30)
618.2366	$C_{37}H_{34}O_7N_2$	Oxofangchirine [**349**] (327)
620.2523	$C_{37}H_{36}O_7N_2$	Guattaminone [**304**] (51)
622.2679	$C_{37}H_{38}O_7N_2$	Cepharanthine-2′β-*N*-oxide [**282**] (21) Oxandrine [**347**] (80) Pseudoxandrine [**368**] (80) Thalmiculimine [**382**] (24)
622.3043	$C_{38}H_{42}O_6N_2$	Cycleaneonine [**286**] (81) Gyrolidine [**308**] (15) *O*-Methyllimacusine [**320**] (15) Monterine [**324**] (79)
624.2836	$C_{37}H_{40}O_7N_2$	Berbamine 2′β-*N*-oxide [**274**] (25) Fenfangjine B (fangchinoline-2′α-*N*-oxide) [**298**] (52) Fenfangjine C (fangchinoline-2′β-*N*-oxide) [**299**] (52) 5-Hydroxythalmine [**313**] (24) Limacine-2′α-*N*-oxide [**315**] (83–85) Limacine-2β-*N*-oxide [**316**] (83–85) Limacine-2′β-*N*-oxide [**317**] (83–85 Thaliphylline-2′β-*N*-oxide [**379**] (41)
624.3199	$C_{38}H_{44}O_6N_2$	Pisopowetine [**358**] (30) Pisopowiarine [**360**] (30) Popidine [**363**] (30) Popisidine [**364**] (30) Popisine [**365**] (30)
636.2836	$C_{38}H_{40}O_7N_2$	

	Oxandrinine [**348**] (80)
	Pseudoxandrinine [**369**] (80)
636.3199	$C_{39}H_{44}O_6N_2$
	Granjine [**302**] (79)
637.3278	$C_{39}H_{45}O_6N_2$
	N-2′-Methylisotetrandrine [**319**] (23)
638.2628	$C_{37}H_{38}O_8N_2$
	Maroumine [**391**] (50)
638.2992	$C_{38}H_{42}O_7N_2$
	Fenfangjine A (tetrandrine-2β-*N*-oxide) [**297**] (52)
	Phaeanthine-2′α-*N*-oxide [**356**] (48)
	Thalmiculine [**383**] (24)
638.3359	$C_{39}H_{46}O_6N_2$
	Pisopowidine [**361**] (30)
640.3149	$C_{38}H_{44}O_7N_2$
	Neothalibrine-2′-*N*-oxide [**325**] (41)
652.2785	$C_{38}H_{40}O_8N_2$
	Auroramine [**390**] (50)
652.3512	$C_{40}H_{48}O_6N_2$
	Pisopowine [**362**] (30)
654.2941	$C_{38}H_{42}O_8N_2$
	Thaligosine-2β-*N*-oxide (thalisopine-2β-*N*-oxide) [**378**] (41)
654.3305	$C_{39}H_{46}O_7N_2$
	N-2-Oxy-*O*-methyldauricine [**350**] (30)
	N-2′-Oxy-*O*-methyldauricine [**351**] (30)
656.3097	$C_{38}H_{44}N_2$
	Ambrimine [**272**] (68)
	Efatine [**296**] (68)
668.2734	$C_{38}H_{40}O_9N_2$
	Pycmanilline [**392**] (48)
668.3098	$C_{39}H_{44}O_8N_2$
	5-Hydroxythalidasine [**311**] (24)
	Thalidasine-2α-*N*-oxide [**377**] (41)
	Thalrugosaminine-2α-*N*-oxide [**384**] (41)
684.3046	$C_{39}H_{44}O_9N_2$
	5-Hydroxythalidasine-2α-*N*-oxide [**312**] (41)

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

Family and Genus	Structure Type																
	I	IV	Vb[a]	VI	VII	VIII	XI	XII	XIIa[b]	XIV	XIVa[c]	XVIII	XIX	XXII	XXIII	XXIIIa	XXVII	Seco-Compounds
Annonaceae																		
Crematosperma		4																
Guatteria		6		1														
Popowia	7																7	
Pseudoxandra		4										1						1
Aristolochiaceae																		
Aristolochia	3																	
Berberidaceae																		
Berberis						2				2								
Mahonia						1												
Hernandiaceae																		
Gyrocarpus				4		1												2
Hernandia			2															
Lauraceae																		
Dehaasia						2												
Menispermaceae																		
Abuta	3																	
Albertisia				2		1									1			
Caryomene				2		1												
Cocculus															1	7		
Curarea				1		3												
Cyclea														1				
Pycnarrhena				1		4												1
Stephania				11		7												
Tiliacora		1										1	5					
Ranunculaceae																		
Thalictrum	2			1	2		4	1	2	2	4							

TABLE 7. Botanical Sources of Bisbenzylisoquinoline Alkaloids by Family.

Annonaceae
Crematosperma
Cordobimine [**283**] (79)
Cordobine [**284**] (79)
Granjine [**302**] (79)
Monterine [**324**] (79)
Guatteria
Apateline [**187**] (59)
Aromoline [**31**] (59)
2,2′-Bisnorguattaguianine [**276**] (51)
Coclobine [**35**] (59)
Daphnandrine [**37**] (59)
Daphnoline [**38**] (59)
1,2-Dehydroapateline [**193**] (59)
1,2-Dehydrotelobine [**194**] (59)
12-*O*-Demethylcoclobine [**293**] (59)
Funiferine [**20**] (51)
Guattamine [**303**] (51)
Guattaminone [**304**] (51)
2′-Norfuniferine [**331**] (51)
2′-Norguattaguianine [**332**] (51)
2′-Nortiliageine [**345**] (51)
Telobine [**160**] (59)
Tiliageine [**27**] (51)
Popowia
Dauricine [**3**] (30)
Dauricoline [**5**] (30)
O-Methyldauricine [**12a**] (30)
N-2-Oxy-*O*-methyldauricine [**350**] (30)
N-2′-Oxy-*O*-methyldauricine [**351**] (30)
2′-Norpisopowiaridine [**339**] (30)
Pisopowamine [**357**] (30)
Pisopowetine [**358**] (30)
Pisopowiaridine [**359**] (30)
Pisopowiarine [**360**] (30)
Pisopowidine [**361**] (30)
Pisopowine [**362**] (30)
Popidine [**363**] (30)
Popisidine [**364**] (30)
Popisine [**365**] (30)
Popisonine [**366**] (30)
Popisopine [**367**] (30)
Pseudoxandra
Berbamunine [**1** (29)
Homoaromoline [**42**] (29)
Medelline [**318**] (67)
Oxandrine [**347**] (80)
Oxandrinine [**348**] (80)
Pseudoxandrine [**368**] (80)
Pseudoxandrinine [**369**] (80)
Secolucidine [**393**] (29)
Thaligrisine [**252**] (29)
Aristolochiaceae
Aristolochia
Geraldoamine [**301**] (71)
Pampulhamine [**352**] (71)
Pedroamine [**355**] (71)
Berberidaceae
Berberis
Aromoline [**31**] (13,32,44,62)
Belarine [**93**] (62)
Berbamine [**57**] (6,13,18,23,25,32,44,54,62)
Berbamine 2′β-*N*-oxide [**274**] (25)
Berbamunine [**1**] (13,32,54,62)
Berbilaurine [**275**] (62)
7-*O*-Demethylisothalicberine [**195**] (62)
12-*O*-Desmethyllauberine [**294**] (65)
Espinine [**9**] (65)
Homoaromoline [**42**] (62)
Isotetrandrine [**62**] (6,13,25,32,62)
Lauberine [**106**] (62)
N-2′-Methylisotetrandrine [**319**] (23)
Obaberine [**46**] (13,36,62)
Obamegine [**71**] (13,44,62)
Oxyacanthine [**48**] (13,23,37,44,62)
Penduline [**72**] (25)
Thalrugosine [**79**] (13,57,62)
Mahonia
Aquifoline [**273**] (31)
Aromoline [**31**] (20)
Baluchistine [**188**] (31)
Berbamine [**57**] (5,20,22)
Isotetrandrine [**62**] (20,22)
Obamegine [**71**] (20)
Oxyacanthine [**48**] (20,22)
Hernandiaceae
Gyrocarpus
Auroramine [**390**] (5)
Grisabine [**10**] (15)
Gyroamericine [**305**] (15)
Gyrocarpine [**306**] (15,50)
Gyrocarpusine [**307**] (15)
Gyrolidine [**308**] (15)
Isotetrandrine [**62**] (15)
Limacine [**64**] (15,50)
Maroumine [**391**] (50)
O-Methyllimacusine [**320**] (15)
Phaeanthine (*O*-methyllimacine) [**74**] (15,50)
Hernandia
Ambrimine [**272**] (68)
Efatine [**296**] (68)
Lauraceae
Dehaasia
Dehatridine [**287**] (63)
Dehatrine [**288**] (63)
Obaberine [**46**] (63)
Menispermaceae
Abuta
Daurisoline [**192**] (36)
N,N′-Dimethyllindoldhamine (Guattegaumerine) [**234**] (36)
Lindoldhamine [**11**] (36)
2-*N*-Methyllindoldhamine [**321**] (36)
2′-*N*-Methyllindoldhamine [**322**] (36)
2′-Nordaurisoline [**330**] (36)
Albertisia
Apateline [**187**] (8,35)
Aromoline [**31**] (8)
N,N′-Bisnoraromoline [**32**] (35)
2,2′-Bisnorphaeanthine [**278**] (35)
Cocsoline [**152**] (8,35)
Cocsuline [**153**] (8,35)
Daphnandrine [**37**] (35)
Daphnoline [**38**] (8,35)
Lindoldhamine [**11**] (35)
N-Methylapateline [**207**] (8)
O-Methylcocsoline [**239**] (35)
2′-Norcocsuline [**329**] (35)
Pangkoramine [**353**] (35)
Pangkorimine [**354**] (35)
Anisocycla
Cocsoline [**152**] (82)

Neothalibrine-2′α-*N*-oxide [**325**] (41)
2′-Noroxyacanthine [**338**] (41)
Northalibroline [**341**] (76)
2′-*Northaliphylline* [**342**] (24,41)
2-Northalmine [**343**] (12)
Obaberine [**46**] (41)
Oxyacanthine [**48**] (41,452)
Thalicberine [**97**] (10)
Thalictine [**107**] (24)
Thalidasine [**100**] (12,47)
Thalidasine-2α-*N*-oxide [**377**] (41)
Thalidezine [[**83**] (34)
Thaligosine (thalisopine) [**52a**] (41)
Thaligosine-2β-*N*-oxide (thalisopine-2β-*N*-oxide) [**378**] (41)
Thaligosinine [**52b**] (14)
Thaliphylline [**253**] (10,24)
Thaliphylline-2′β-*N*-oxide [**379**] (41)
Thalirugine [**14b**] (41)
Thalisopidine [**53**] (14)
Thalisopine [**54**] (24)
Thalivarmine [**380**] (10)
Thalmethine [**98**] (10,452)
Thalmiculatimine [**381**] (24)
Thalmiculimine [**382**] (24)
Thalmiculine [**383**] (24)
Thalmine [**108**] (12,42)
Thalmirabine [**222**] (34)
Thalrugosaminine [**55**] (24)
Thalrugosaminine-2α-*N*-oxide [**384**] (41)
Thalrugosidine [**101**] (24)
Thalrugosinine [**224**] (12)
Thalsivasine [**385**] (10)

TABLE 8. Botanical Sources of Bisbenzylisoquinoline Alkaloids.

Name of Plant	Plant Part[a]	Alkaloid	Structural Type of Alkaloid
Abuta pahni	St	Daurisoline [**192**] (36)	I
(Martius) Krukoff and Barneby		*N,N′*-Dimethyllindoldhamine [**234**] (36)	I
(Menispermaceae)		Lindoldhamine [**11**] (36)	I
		2-*N*-Methyllindoldhamine [**321**] (36)	I
		2′-*N*-Methyllindoldhamine [**322**] (36)	I
		2′-Nordaurisoline [**330**] (36)	I
Albertisia laurifolia	Rh	Apateline [**187**] (8)	XXIII
(Menispermaceae)		Aromoline [**31**] (8)	VI
		Cocsoline [**152**] (8)	XXIII
		Cocsuline [**153**] (8)	XXIII
		Daphnoline [**38**] (8)	VI
		N-Methylapateline [**207**] (8)	XXIII
Albertisia papuana Becc.	St	Apateline [**187**] (35)	XXIII
(Menispermaceae)		*N,N′*-Bisnoraromoline [**32**] (35)	VI
		2,2′-Bisnorphaeanthine [**278**] (35)	VIII
		Cocsoline [**152**] (35)	XXIII
		Cocsuline [**153**] (35)	XXIII
		Daphnandrine [**37**] (35)	VI
		Daphnoline [**38**] (35)	VI
		Lindoldhamine [**11**] (35)	I
		O-Methylcocsoline [**239**] (35)	XXIII
		2′-Norcocsuline [**329**] (35)	XXIII
		Pangkoramine [**353**] (35)	VI
		Pangkorimine [**354**] (35)	VI
Anisocycla cymosa	R	Cocsoline [**152**] (82)	XXIII
Troupin (Menispermaceae)		1,2-Dehydroapateline [**193**] (82)	XXIII
		1,2-Dehydrotelobine [**194**] (82)	XXIII
		Trilobine [**163**] (82)	XXIII
Aristolochia gigantea	L	Geraldoamine [**301**] (71)	I
Mart. (Aristolochiaceae)		Pampulhamine [**352**] (71)	I
		Pedroamine [**355**] (71)	I
Berberis boliviana	R	Aromoline [**31**] (62)	VI
Lechl. (Berberidaceae)		Berbamine [**57**] (62)	VIII
		Homoaromoline [**42**] (62)	VI
		Isotetrandrine [**62**] (62)	VIII
		Obaberine [**46**] (62)	VI
		Obamegine [**71**] (62)	VIII
		Oxyacanthine [**48**] (62)	VI
		Thalrugosine [**79**] (62)	VIII

TABLE 8. Continued.

Name of Plant	Plant Part[a]	Alkaloid	Structural Type of Alkaloid
	St	Aromoline [**31**] (62)	VI
		Berbamine [**57**] (62)	VIII
		Berbamunine [**1**] (62)	I
		Isotetrandrine [**62**] (62)	VIII
		Obaberine [**46**] (62)	VI
		Obamegine [**71**] (62)	VIII
		Oxyacanthine [**48**] (62)	VI
Berberis brandisiana	T	Berbamine [**57**] (25)	VIII
Ahrendt (Berberidaceae)		Berbamine-2′β-*N*-oxide [**274**] (25)	VIII
		Isotetrandrine [**62**] (25)	VIII
		Penduline [**72**] (25)	VIII
Berberis bumeliaefolia	R	Aromoline [**31**] (62)	VI
Schneid. (Berberidaceae)		Berbamine [**57**] (62)	VIII
		Isotetrandrine [**62**] (62)	VIII
		Oxyacanthine [**48**] (62)	VI
Berberis chilensis	L	12-*O*-Desmethyllauberine [**294**] (65)	XIV
Gill. ex Hook (Berberidaceae)		Espinine [**9**] (65)	I
Berberis cretica L.	WP	Aromoline [**31**] (13)	VI
(Berberidaceae)		Berbamine [**57**] (13)	VIII
		Berbamunine [**1**] (13)	I
		Isotetrandrine [**62**] (13)	VIII
		Obaberine [**46**] (13)	VI
		Obamegine [**71**] (13)	VIII
		Oxyacanthine [**48**] (13)	VI
		Thalrugosine [**79**] (13)	VIII
Berberis koreana Palib.	T	Aromoline [**31**] (44)	VI
(Berberidaceae)		Berbamine [**57**] (44)	VIII
		Obamegine [**71**] (44)	VIII
		Oxyacanthine [**48**] (44)	VI
Berberis laurina Billbg.	R	Aromoline [**31**] (62)	VI
(Berberidaceae)		Belarine [**93**] (62)	XI
		Berbilaurine [**275**] (62)	XIV
		7-*O*-Demethylisothalicberine [**195**] (62)	XI
		Homoaromoline [**42**] (62)	VI
		Lauberine [**106**] (62)	XIV
		Thalrugosine [**79**] (62)	VIII
Berberis oblonga (Regl.)	Sh	Berbamine [**57**] (23)	VIII
(Berberidaceae)		*N*-2′-Methylisotetrandrine [**319**] (23)	VIII
		Oxyacanthine [**48**] (23)	VI
Berberis paucidentata	R	Berbamine [**57**] (62)	VIII
Rusby. (Berberidaceae)		Isotetrandrine [**62**] (62)	VIII
		Obaberine [**46**] (62)	VI
		Oxyacanthine [**48**] (62)	VI
	St	Berbamine [**57**] (62)	VIII
		Isotetrandrine [**62**] (62)	VIII
		Obaberine [**46**] (62)	VI
		Oxyacanthine [**48**] (62)	VI
Berberis polymorpha (Berberidaceae)	St	Thalrugosine [**79**] (57)	VIII
Berberis pseudambalata	T	Obaberine [**46**] (36)	VI
(Berberidaceae)		Oxyacanthine [**48**] (37)	VI
Berberis regeliana (Berberidaceae)	Fr	Berbamine [**57**] (18)	VIII
Berberis stolonifera	Culture	Aromoline [**31**] (32)	VI
(Berberidaceae)		Berbamine [**57**] (32,54)	VIII
		Berbamunine [**1**] (32,54)	I
		N,*N*′-Dimethyllindoldhamine (guattegaumerine) [**234**] (54)	I
		Isotetrandrine [**62**] (32)	VIII
		2-Norberbamunine [**1** dvt] (32,54)	I
Berberis wilsoniae	T	Berbamine [**57**] (6)	VIII
Hemsl. et Wils. (Berberidaceae)		Isotetrandrine [**62**] (6)	VIII
Caryomene olivascens	St	Caryolivine [**281**] (19)	VIII
Barneby et Krukoff		1,2-Dehydro-2-norlimacusine [**291**] (19)	VI

TABLE 8. Continued.

Name of Plant	Plant Part[a]	Alkaloid	Structural Type of Alkaloid
(Menispermaceae)		*N,N'*-Dimethyllindoldhamine (guattegaumerine) [**234**] (19)	I
		2-Norlimacine [**336**] (19)	VIII
		2-Norlimacusine [**245**] (19)	VI
Cocculus hirsutus	L	Isotrilobine [**157**] (28)	XXIII
(Menispermaceae)		Trilobine [**163**] (28)	XXIII
Cocculus pendulus	L	1',2'-Dehydrokohatamine [**289**] (33)	XXIIIa
(Forsk.) Diels (Menispermaceae)		1',2'-Dehydrokohatine [**290**] (33)	XXIIIa
		1,2-Dehydro-2'-*nortelobine* [**292**] (33)	XXIII
		5-Hydroxyapateline [**309**] (33)	XXIIIa
		5-Hydroxytelobine [**310**] (33)	XXIIIa
		Kohatamine [**314**] (33)	XXIIIa
		Kohatine [**236**] (33)	XXIIIa
		Siddiquamine [**371**] (33)	XXIIIa
		Siddiquine [**372**] (33)	XXIIIa
Crematosperma sp.	StB	Cordobimine [**283**] (79)	IV
(Annonaceae)		Cordobine [**284**] (79)	IV
		Granjine [**302**] (79)	IV
		Monterine [**324**] (79)	IV
Curarea candicans	R	Candicusine [**280**] (83–85)	VI
(L.C. Rich) Barneby and		Krukovine [**63**] (83,84)	VIII
Krukoff (Menispermaceae)		Limacine [**64**] (83,84)	VIII
		Limacine-2'α-*N*-oxide [**315**] (83–85)	VIII
		Limacine-2β-*N*-oxide [**316**] (83–85)	VIII
		Limacine-2'β-*N*-oxide [**317**] (83–85)	VIII
		Limacusine [**44**] (83,84)	VI
Cyclea hypoglauca		Insulanoline [**169**] (11)	XXVI
(Menispermaceae)		Insularine [**170**] (11)	XXVI
Cyclea racemosa Oliv.	R	Cycleaneonine [**286**] (81)	XXII
(Menispermaceae)			
Debaasia triandra Merr.	L	Dehatridine [**287**] (63)	VIII
(Lauraceae)	W	Dehatrine [**288**] (63)	VIII
		Obaberine [**46**] (63)	VI
Guatteria guianensis (Aublet)	StB	Apateline [**187**] (59)	XXIII
R.E. Fries (Annonaceae)		Aromoline [**31**] (59)	VI
		2,2'-*Bisnorguattaguianine* [**276**] (51)	IV
		Coclobine [**35**] (59)	VI
		Daphnandrine [**37**] (59)	VI
		Daphnoline [**38**] (59)	VI
		1,2-Dehydroapateline [**193**] (59)	XXIII
		1,2-Dehydrotelobine [**194**] (59)	XXIII
		12-*O*-Demethylcoclobine [**293**] (59)	VI
		Funiferine [**20**] (51)	IV
		Guattamine [**303**] (51)	IV
		Guattaminone [**304**] (51)	IV
		2'-Norfuniferine [**331**] (51)	IV
		2'-Norguattaguianine [**332**] (51)	IV
		2'-Nortiliageine [**345**] (51)	IV
		Telobine [**160**] (59)	XXIII
		Tiliageine [**27**] (51)	IV
Gyrocarpus americanus Jacq.	L	Auroramine [**390**] (50)	Seco VI
(Hernandiaceae)		Gyrocarpine [**306**] (50)	VI
		Limacine [**64**] (50)	VIII
		Maroumine [**391**] (50)	Seco VI
		Phaeanthine [**74**] (50)	VIII
	StB	Grisabine [**10**] (15)	I
		Gyroamericine [**305**] (15)	VIII
		Gyrocarpine [**306**] (15)	VI
		Gyrocarpusine [**307**] (15)	VI
		Gyrolidine [**308**] (15)	VI
		Isotetrandrine [**62**] (15)	VIII
		Limacine [**64**] (15)	VIII

TABLE 8. Continued.

Name of Plant	Plant Part[a]	Alkaloid	Structural Type of Alkaloid
		O-Methyllimacusine [**320**] (15)	VI
		Phaeanthine (*O*-methyllimacine) [**74**] (15)	VIII
Hernandia peltata	StB	Ambrimine [**272**] (68)	Vb
Meissner (Hernandiaceae)		Efatine [**296**] (68)	Vb
Isopyrum thalictroides		Berbamine [**57**] (60)	VIII
(Ranunculaceae)		Isotetrandrine [**62**] (60)	VIII
Mahonia aquifolium	B,L	Aquifoline [**273**] (31)	VIII
(Pursh) Nutt. (Berberidaceae)		Aromoline [**31**] (20)	VI
		Berbamine [**57**] (5,20)	VIII
		Isotetrandrine [**62**] (20)	VIII
		Obamegine [**71**] (20)	VIII
		Oxyacanthine [**48**] (20)	VI
	L,St,Fr	Berbamine [**57**] (22)	VIII
		Isotetrandrine [**62**] (22)	VIII
		Oxyacanthine [**48**] (22)	VI
	R	Baluchistine [**188**] (31)	VI
Nelumbo nucifera	Sd	Isoliensinine [**28**] (463)	V
Gaertn. (Nymphaeaceae)		Neferine [**30**] (463)	V
Pachygone loyaltiensis	St	Apateline [**187**] (39)	XXIII
Diels (Menispermaceae)		*N,N'*-Bisnoraromoline [**32**] (39)	VI
		Daphnandrine [**37**] (39)	VI
		Daphnoline [**38**] (39)	VI
		1,2-Dehydroapateline [**193**] (39)	XXIII
		1,2-Dehydrotelobine [**194**] (39)	XXIII
		Isotrilobine [**157**] (39)	XXIII
		O-Methylcocsoline [**239**] (39)	XXIII
Popowia pisocarpa	B and/or L	Dauricine [**3**] (30)	I
(Bl.) Endl. (Annonaceae)		Dauricoline [**5**] (30)	I
		O-Methyldauricine [**12a**] (30)	I
		N-2-Oxy-*O*-methyldauricine [**350**] (30)	I
		N-2'-Oxy-*O*-methyldauricine [**351**] (30)	I
		2'-Norpisopowiaridine [**339**] (30)	XXVII
		Pisopowamine [**357**] (30)	XXVII
		Pisopowetine [**358**] (30)	XXVII
		Pisopowiaridine [**359**] (30)	XXVII
		Pisopowiarine [**360**] (30)	XXVII
		Pisopowidine [**361**] (30)	XXVII
		Pisopowine [**362**] (30)	XXVII
		Popidine [**363**] (30)	I
		Popisidine [**364**] (30)	I
		Popisine [**365**] (30)	I
		Popisonine [**366**] (30)	I
		Popisopine [**367**] (30)	I
Pseudoxandra aff. *lucida*	B	Medelline [**318**] (67)	XVIII
(Annonaceae)		Oxandrine [**347**] (80)	IV
		Oxandrinine [**348**] (80)	IV
		Pseudoxandrine [**368**] (80)	IV
		Pseudoxandrinine [**369**] (80)	IV
Pseudoxandra sclerocarpa Maas	StB	Berbamunine [**1**] (29)	I
(Annonaceae)		Homoaromoline [**42**] (29)	VI
		Secolucidine [**393**] (29)	Seco XVIII
		Thaligrisine [**252**] (29)	I
Pycnarrhena manillensis Vidal	R,S	Berbamine [**57**] (48)	VIII
(Menispermaceae)		Isotetrandrine [**62**] (48)	VIII
		Phaeanthine [**74**] (48)	VIII
		Phaeanthine-2'α-*N*-oxide [**356**] (48)	VIII
		Pycmanilline [**392**] (48)	Seco VIII
		Pycnamine [**75**] (48)	VIII
Pycnarrhena ozantha Diels	St	Bisnorobamegine [**277**] (38)	VIII
(Menispermaceae)		Bisnorthalrugosine [**279**] (38)	VIII
		Daphnoline [**38**] (38)	VI
		2-Norberbamine [**68**] (38)	VIII

TABLE 8. Continued.

Name of Plant	Plant Part[a]	Alkaloid	Structural Type of Alkaloid
		2-Norobamegine [**69**] (38)	VIII
		2-Northalrugosine [**344**] (38)	VIII
		Pycnazanthine [**370**] (38)	VI
Stephania cepharantha Hayata (Menispermaceae)	R (Culture)	Aromoline [**31**] (46,58)	VI
		Berbamine [**57**] (46)	VIII
		Cycleanine [**121**] (46)	XX
		Homoaromoline [**42**] (46)	VI
		Isotetrandrine [**62**] (46)	VIII
Stephania epigeae Diburong (Menispermaceae)		Cepharanthine [**34**] (7,40)	VI
		Cycleanine [**121**] (7)	XX
Stephania bernandifolia Walp. (Menispermaceae)	St	3′,4′-Dihydrostephasubine [**295**] (49)	VI
		(+)-Epistephanine [**40**] (49)	VI
		Stephasubine [**374**] (49)	VI
Stephania pierrii Diels (Menispermaceae)	Tb	Aromoline [**31**] (64)	VI
		Berbamunine [**1**] (64)	I
		Cepharanthine [**34**] (64)	VI
		Cycleanine [**121**] (64)	XX
		Daphnandrine [**37**] (64)	VI
		1,2-Dehydroapateline [**193**] (64)	XXIII
		N-Desmethylcycleanine [**233**] (64)	XXIII
		Homoaromoline [**42**] (64)	VI
		Isotetrandrine [**62**] (64)	VIII
		2-Norberbamine [**68**] (64)	VIII
		2-Norcepharanoline [**326**] (64)	VI
		2′-Norcepharanthine [**328**] (64)	VI
		2-Norisocepharanthine [**333**] (64)	VI
		2-Norisotetrandrine [**334**] (64)	VIII
		2′-Norisotetrandrine [**213**] (64)	VIII
		2-Norobaberine [**46** dvt] (64)	VI
		2′-Norobaberine [**337**] (64)	VI
		Obaberine [**46**] (64)	VI
		Stephibaberine [**375**] (64)	VI
		Stepierrine [**376**] (64)	VIII
		Thalrugosamine [**55**]	VI
Stephania sinica Diels (Menispermaceae)	R	Cepharanthine [**34**] (9)	VI
Stephania suberosa Forman (Menispermaceae)	R	Cepharanthine [**34**] (21)	VI
		Cepharanthine-2′β-*N*-oxide [**282**] (21)	VI
		2-Norcepharanthine [**327**] (21)	VI
		Norstephasubine [**340**] (21)	VI
		Stephasubimine [**373**] (21)	VI
		Stephasubine [**374**] (21)	VI
Stephania tetrandra S. Moore (Menispermaceae)	R	Cycleanine [**121**] (52)	XX
		Fangchinoline [**61**] (16,52)	VIII
		Fenfangjine A (tetrandrine-2β-*N*-oxide) [**297**] (52,75)	VIII
		Fenfangjine B (fangchinoline-2′α-*N*-oxide) [**298**] (52,75)	VIII
		Fenfangjine C (fangchinoline-2′β-*N*-oxide) [**299**] (52,75)	VIII
		Fenfangjine D (1,3,4-tridehydrofangchinolium hydroxide) [**300**] (52,74)	VIII
		Isotetrandrine [**62**] (16)	
		Oxofangchirine [**349**] (327)	VIII
		Tetrandrine [**76**] (16,45,52)	VIII
Stephania venosa Spreng. (Menispermaceae)	Rh	Homoaromoline (thalrugosamine) [**42**] (43)	VI
Thalictrum collinum Wall. (Ranunculaceae)	T	*O*-Methylthalicberine [**95**] (42)	XI
		Thalmine [**108**] (42)	XIV
	R	*O*-Methylthalicberine [**95**] (42)	XI
Thalictrum cultratum Wall. (Ranunculaceae)	WP	Aromoline [**31**] (41)	VI
		Cultithalminine [**285**] (41)	XIVa

TABLE 8. Continued.

Name of Plant	Plant Part[a]	Alkaloid	Structural Type of Alkaloid
		N-Desmethylthalidasine (2-northalidasine) [**196**] (12)	XII
		5-Hydroxythalidasine [**311**] (24)	XIIa
		5-Hydroxythalidasine-2′α-*N*-oxide [**312**] (41)	XIIa
		5-Hydroxythalmine [**313**] (24)	XIVa
		O-Methylthalicberine [**95**] (24)	XI
		O-Methylthalmine [**244**] (24)	XIV
		Neothalibrine [**211**] (41)	I
		Neothalibrine-2′α-*N*-oxide [**325**] (41)	I
		2′-Noroxyacanthine [**338**] (41)	VI
		2′-Northaliphylline [**342**] (24,41)	XI
		2-Northalmine [**343**] (12)	XIV
		Obaberine [**46**] (41)	VI
		Oxyacanthine [**48**] (41)	VI
		Thalictine [**107**] (24)	XIV
		Thalidasine [**100**] (12)	XII
		Thalidasine-2α-*N*-oxide [**377**] (41)	XII
		Thaligosine (thalisopine) [**52a**] (41)	VII
		Thaligosine-2β-*N*-oxide (thalisopine-2β-*N*-oxide) [**378**] (41)	VII
		Thaliphylline [**253**] (24)	XI
		Thaliphylline-2′β-*N*-oxide [**379**] (41)	XI
		Thalirugine [**14b**] (41)	Ia
		Thalisopine [**54**] (24)	VII
		Thalmiculatimine [**381**] (24)	XIV
		Thalmiculimine [**382**] (24)	XIVa
		Thalmiculine [**383**] (24)	XIVa
		Thalmine [**108**] (12)	XIV
		Thalrugosaminine [**55**] (24)	VII
		Thalrugosaminine-2α-*N*-oxide [**384**] (41)	VII
		Thalrugosidine [**101**] (24)	XII
		Thalrugosinone [**224**] (12)	XII
		Thalsivasine [**385**] (24)	XI
Thalictrum delavayi (Ranunculaceae)	R	Hernandezine [**81**] (34)	IX
		Isothalidezine [**82**] (34)	IX
		Thalidezine [**83**] (34)	IX
		Thalmirabine [**222**] (34)	XIII
Thalictrum isopyroides C.A.M. (Ranunculaceae)	R	Thaligosinine [**52b**] (14)	VII
		Thalisopidine [**53**] (14)	VII
Thalictrum lankesteri Standl. (Ranunculaceae)	T	Hernandezine [**81**] (55)	IX
Thalictrum minus L. (Ranunculaceae)	T	*O*-Methylthalmethine [**96**] (452)	XI
		Oxyacanthine [**48**] (452)	VI
		Thalmethine [**98**] (452)	XI
Thalictrum minus var. *hypoleucum* L. (Ranunculaceae)		*O*-Methylthalicberine [**95**] (53)	XI
Thalictrum minus var. *minus* L. (Ranunculaceae)	L	*O*-Methylthalicberine [**95**] (10)	XI
		O-Methylthalmethine [**96**] (10)	XI
		Thalicberine [**97**] (10)	XI
		Thaliphylline [**253**] (10)	XI
		Thalivarmine [**380**] (10)	XI
		Thalmethine [**98**] (10)	XI
		Thalsivasine [**385**] (10)	XI
	R,Rh	Northalibroline [**341**] (76)	I
Thalictrum squarrosum Steph. ex Willd. (Ranunculaceae)	R	Thalidasine [**100**] (47)	XII
Tiliacora racemosa Colebr. (Menispermaceae)	R	*N*-Methyltiliamosine [**323**] (78)	XIX
		Nortiliacorinine A [**115**] (66)	XVIII
		Tiliarine [**185**] (66)	XVIII
Tiliacora triandra Diels (Menispermaceae)	L,St	Dinklacorine [**114**] (26,27)	XVIII
		Nortiliacorinine A [**116**] (17,26)	XVIII
		Nortiliacorine A [**115**] (56)	XVIII

TABLE 8. Continued.

Name of Plant	Plant Part[a]	Alkaloid	Structural Type of Alkaloid
		Norisoyanangine [**335**] (56)	XIX
		Noryanangine [**346**] (56)	XIX
		Tiliacorine [**118**] (17,26)	XVIII
		Tiliacorinine [**119**] (17)	XVIII
		Tiliacorinine-2′-*N*-oxide [**254**] (56)	XVIII
		Tiliageine [**27**] (61)	IV
		Tilianangine [**386**] (26)	XIX
		Tilitriandrine [**387**] (61)	IV
		Yanangcorinine [**388**] (17)	XVIII
		Yanangine [**389**] (27)	XIX

[a]B = Bark, Bb = Bulb, Fr = Fruits, L = Leaves, R = Roots, RB = Root bark, Rh = Rhizomes, Sd = Seeds, Sh = Shoots, St = Stems, StB = Stem bark, T = Tops, Tb = Tubers, W = Wood, WP = Whole Plant.

TABLE 9. Biosynthesis of Bisbenzylisoquinoline Alkaloids.

1 BERBAMUNINE $C_{36}H_{40}O_6N_2$: 596.2886

Feeding experiments with (1-^{13}C)-(*R*)- and (*S*)-coclaurine in *Berberis stolonifera* cell cultures, followed by nmr studies of the resulting alkaloids, confirmed the biosynthetic route to berbamunine (*R,S*) (54).

A specific cythochrome P-450-linked microsome-bound plant enzyme from *Berberis stolonifera* is involved in C-C and C-O bond formation in berbamunine (480).

122 ISOCHONDRODENDRINE $C_{36}H_{38}O_6N_2$: 594.2730

Tracer experiments demonstrated that (*R,R*)-isochondrodendrine is stereospecifically biosynthesized in young *Cissampelos pareira* L. (Menispermaceae) plants by oxidative dimerization of (*R*)-*N*-methylcoclaurine (72).

133 CURINE (BEBEERINE) $C_{36}H_{38}O_6N_2$: 594.2730

Tracer experiments demonstrated that (*R,R*)-curine (bebeerine) is stereospecifically biosynthesized in young *Cissampelos pareira* L. (Menispermaceae) plants by oxidative dimerization of (*R*)-*N*-methylcoclaurine (72).

136 HAYATIDINE $C_{37}H_{40}O_6N_2$: 608.2886

Tracer experiments demonstrated that (*S,R*)-hayatidine is stereospecifically biosynthesized in young *Cissampelos pareira* L. (Menispermaceae) plants by intermolecular oxidative coupling of (*S*)-*N*-methylcoclaurine and (*R*)-*N*-methylcoclaurine (72).

137 HAYATINE $C_{36}H_{38}O_6N_2$: 594.2730

Tracer experiments demonstrated that hayatine [a racemic mixture of (+,+) and (−,−) forms] is stereospecifically biosynthesized in young *Cissampelos pareira* L. (Menispermaceae) plants by oxidative dimerization of *N*-methylcoclaurine. Results support the following sequence: Tyrosine→Coclaurine→(*S*)-*N*-methylcoclaurine⇌1,2-Didehydro-*N*-methylcoclaurine⇌(*R*)-*N*-methylcoclaurine→Hayatine (470).

234 *N,N′*-DIMETHYLLINDOLDHAMINE (Guattegaumerine) $C_{36}H_{40}O_6N_2$: 596.2886

Feeding experiments with (1-^{13}C)-(*R*)- and (*S*)-coclaurine in *Berberis stolonifera* cell cultures, followed by nmr studies of the resulting alkaloids, confirmed the biosynthetic route to berbamunine (*R,S*) (54), and also showed that the (*R*) isomer is incorporated in similar excess into both halves of the (*R,R*) dimer guattegaumerine (54).

TABLE 10. Pharmacological Activities of Bisbenzylisoquinoline Alkaloids.

O-Acetyldauricine [**3** dvt]

O-Acetyldauricine showed antiarrhythmic activity in guinea pigs (310) but did not as strongly inhibit calmodulin-dependent phosphodiesterase as did the *O*-propionyl ester (323).

Antioquine [**225**]

Antioquine demonstrated in vitro activity against the flagellated protozoa *Leishmania brasiliensis, Leishmania amazonensis,* and *Leishmania donovani* (378). In addition, the alkaloid was investigated for in vitro activity against the eipmastigotes of three genetically typed strains of the flagellated protozoa *Trypanosoma cruzi* (Chagas disease) and found to lack sufficient activity to warrant in vivo analysis (379). Antioquine produced a relaxation of Ca^{++}-induced sustained contractions in the rat uterus in a K-depolarizing solution, as well as the spontaneous activity of the rat uterus. The alkaloid induced a displacement to the right of the dose-response curves to Ca^{++}. This antagonism was noncompetitive. These and other experiments suggest that the relaxant effects of the alkaloid may be due to the blockade of Ca^{++} movements across the cell membrane, mainly through voltage-operated channels (390).

Aromoline [31]

Aromoline exhibited in vitro antimalarial activity (IC_{50} 0.67 μg/ml) (chloroquine phosphate; IC_{50} 0.14 μg/ml) against *Plasmodium falciparum* (464).

Berbamine [57]

Antimicrobial effects.—Berbamine demonstrated in vitro activity against the flagellated protozoa *L. brasiliensis, L. amazonensis,* and *L. donovani* (378).

Berbamine was investigated for in vitro activity against the epimastigotes of three genetically typed strains of the flagellated protozoa *T. cruzi* (Chagas disease) and found to lack sufficient activity to warrant in vivo analysis (379).

Cardiovascular effects.—Berbamine markedly inhibited the force of contraction, prolonged the effective refractory period, and attenuated adrenaline-induced automaticity in the isolated atria of guinea pigs. In addition, the alkaloid antagonized the effect of isoproterenol in a noncompetitive manner, shifted the concentration-response curve of Ca^{++} to the right in a noncompetitive manner, and noncompetitively antagonized the effect of histamine on the atria (124). Berbamine inhibited contractility and automaticity of isolated guinea pig papillary muscles and human pectinate muscles and prolonged the functional refractory period of these muscles, but failed to effect excitability. The alkaloid antagonized the positive inotropic action of isoproterenol and histamine on guinea pig papillary muscle but with kinetics different from those of propranolol and cimetidine, respectively, suggesting that the antagonistic action of the alkaloid was not through a competitive blockade of beta- or histaminic H_2 receptors. Finally, the alkaloid antagonized the positive inotropic action of Ca^{++}, with kinetics similar to those of verapamil, suggesting that berbamine is a Ca^{++} channel blocker (132).

Berbamine (5 mg/kg) decreased the size of ligated coronary-artery-induced myocardial infarction in rabbits and rats, with a corresponding increase in serum-free fatty acids and a decrease in the number of Q waves and the levels of serum creatine kinase in rabbits, thus exerting a myocardial protective effect (133). The alkaloid was effective against experimental cardiac arrhythmias induced by ouabain, aconitine, $CaCl_2$, and ligation of the coronary artery in guinea pigs, rats, and mice. The alkaloid was still effective post bilateral vagotomy; however, it inhibited neither the arrhythmia induced by direct injection of picrotoxin or aconitine into the lateral ventricle of rats nor isoprenaline-induced cAMP increases in mouse plasma (268). Berbamine and its various derivatives inhibited Ca^{++}-Mg^{++}-ATPase stimulated by calmodulin, by partial proteolysis, or by oleic acid in erythrocyte membranes. The capability of these derivatives to inhibit trypsin-activated Ca^{++}-Mg^{++}-ATPase compared favorably with their ability to inhibit the calmodulin-stimulated enzyme. *O*-4-(Ethoxybutyl)-berbamine inhibition of Ca^{++}-Mg^{++}-ATPase was competitive with respect to ATP (277).

Berbamine was found to inhibit calmodulin-dependent phosphodiesterase (IC_{50} 22 μmol/liter).

O-Acylated and *O*-alkylated derivatives were prepared from berbamine and found to possess high anti calmodulin-dependent Ca^{++}-Mg^{++}-ATPase activities. Those derivatives with a long alkyl side chain had very high activities. The IC_{50} of *O*-(4-ethoxylbutyl)berbamine was about 0.35 μM, which implies that this compound is one of the most potent of these type of antagonists (333).

Iv administration of berbamine inhibited ouabain-induced arrhythmia in guinea pigs, with the alkaloid inhibiting the inotropic effect of ouabain in a concentration-dependent manner in the isolated guinea pig left atrium. Calcium channel blockade is implicated as a likely mechanism (395).

Berbamine (100 μM) relaxed the high K^+-induced contractions of pig coronary artery. This effect was reversed by raising the concentration of Ca^{++} in the medium. The alkaloid shifted the dose-contraction curve of $CaCl_2$ on pig coronary artery strips to the right and inhibited (30 μM) norepinephrine-induced contractions of the coronary artery in Ca^{++}-free medium. Berbamine had no significant effect on the inhibition of coronary artery contraction induced by Ca^{++} influx through norepinephrine-opened receptor-operated Ca^{++} channels (458).

Central effects.—(+)-Berbamine has a relatively high affinity (K_i 1.9×10^{-7} M) for the muscarinic receptors of rat brain, as determined by its effect on the binding of [^{3}H]QNB (quinuclidinyl benzilate) in an in vitro receptor binding assay (394).

The effects of berbamine on focal cerebral ischemia in rats was evaluated via the measurement of $PGF_{2\alpha}$ in the right cortex 15 min after the onset of ischemia and the activity of creatine phosphokinase in the venous blood 24h after. $PGF_{2\alpha}$ was less in the berbamine (15 mg/kg) group, and berbamine decreased the infarct size. It was concluded that the alkaloid had some protective effect on acute focal cerebral ischemia in the rat (448).

Immunomodulatory effects.—Administration (ip) of berbamine to mice inoculated with influenza virus (A/FM_1) produced an immunostimulant effect as observed via enhanced phagocytic activity of the alveolar macrophages, as well as increased intracellular bactericidal activity and phagosome-lysosome fusion in the lung. The alkaloid did not affect the hemagglutinating titer in bronchoalveolar spaces, the production of anti-influenza antibodies, or the pathological profile of this viral pneumonia (158).

Berbamine partially overcame the resistance of a multidrug-resistant subline (Ch^R-24, derived from human KB carcinoma cells) to vincristine, actinomycin D, daunomycin, and adriamycin (216).

Berbamine produced a 56.4% inhibition of formylmethionyl-leucyl-phenylalanine-induced superoxide (O_2^-) generation by polymorphonuclear leukocytes, suggesting that the alkaloid possesses membrane-modifying activity (226).

Berbamine has lesser in vitro suppressive effects on adherence, locomotion, and ^{3}H-deoxyglucose uptake of neutrophils, as well as mitogen-induced lymphocyte responses and mixed lymphocyte reactions, than does tetrandrine. Tetrandrine displays anti-oxidant activity, while berbamine does not. Berbamine, however, has a significantly greater capacity for inhibition of natural killer cell cytotoxicity (435).

Miscellaneous effects.—A hair tonic formulation of berbamine + poly(oxyethylene) hydrogenated castor oil + per-

fume + H_2O applied to male patients for 3 months resulted in dandruff control (90%) and prevention of alopecia (80%) (433).

Cepharanoline [33]

Cepharanoline produced a 56.0% inhibition of formylmethionyl-leucyl-phenylalanine-induced superoxide (O_2^-) generation by polymorphonuclear leukocytes, suggesting that the alkaloid possesses membrane-modifying activity (226).

Cepharanthine [34]

Anti-inflammatory effects.—Cepharanthine was found to suppress the release of arachidonic acid from rat peritoneal exudate cells in vitro. The alkaloid may be able to inhibit inflammation via blocking the metabolism of arachidonic acid (399).

Cepharanthine inhibited, in a dose-dependent fashion, the Ca ionophore A23187-stimulated LTB_4 formation in rat periotenal exudate cells, while PGE_2 formation was enhanced. The 5-lipoxygenase system and LTB_4 formation were likewise inhibited by the alkaloid. These results suggest that the anti-inflammatory effects of the alkaloid may be related to its effects on arachidonate metabolism (421).

Cepharanthine inhibited the inflammatory activity induced by local application of 12-*O*-tetradecanoylphorbol-13-acetate to the mouse ear. The alkaloid also markedly suppressed the tumor-promoting effect of the acetate ester on skin tumor formation in mice initiated with 7,12-dimethylbenz[*a*]anthracene. The anti-tumor-promoting activity of the alkaloid is apparently due to the presence of its anti-inflammatory activity (454).

Blood coagulation effects.—Cepharanthine markedly prolonged both the prothrombin time and the activated partial thromboplastin time. The alkaloid further prolonged the kaolin-activated clotting time but had no effect on the recalcification clotting time nor on the activity of individual coagulation factors. The alkaloid inhibited the release of platelet factor 4. The use of the alkaloid in the therapy of hypercoagulation state or in disseminated intravascular coagulation was discussed (255).

The prothrombin time, activated partial thromboplastin time, and kaolin-activated clotting time were markedly prolonged in the presence of cepharanthine in rats with experimental disseminated intravascular coagulation, while the recalcification clotting time remained unaffected. The alkaloid inhibited both platelet aggregation and release of platelet factor 4, as well as preventing both the decrease of platelet count and antithrombin III activity. Potential use of the alkaloid in the therapy of human-disseminated intravascular coagulation was discussed (356).

Carcinogenic inhibitory effects.—Superoxide anion production by phorbol myristate acetate-induced mouse peritoneal exudate cells was inhibited by cepharanthine (34% at 5 μg/ml and 85% at 50 μg/ml). No inhibition of the superoxide anion by a xanthine-xanthine oxidase system was observed, indicating that the alkaloid is not a scavenger of superoxide anion. No significant inhibition of carrageenan-induced rat paw edema was observed (350).

Cepharanthine (locally, 2 mg) was shown to be an inhibitor (78%) of the carcinogen promoter (locally, 1 μg) 12-*O*-tetradecanoylphorbol-13-acetate at the same area when tested on mice ears (351).

Central effects.—Although one study suggested that cepharanthine demonstrated an affinity for dopaminergic receptors by inhibiting [^{3}H] spiperone binding to rat striatal membranes (99), a second study reported that the alkaloid failed to effectively displace ^{3}H-spiperone binding from rat striatal membranes (128), thus suggesting that the alkaloid lacks potent dopamine receptor blocking activity (antidopaminergic effects) (128).

Cepharanthine increased corticosterone levels in rat plasma and increased plasma ACTH and corticosterone in propranolol-pretreated rats. Pretreatment with dexamethasone as a pituitary-adrenocortical suppressant blocked increased plasma corticosterone levels in rats treated with the alkaloid. The alkaloid increased corticosterone levels when beta blockade (*Bordetella pertussis*-induced) occurred but did not affect corticosterone metabolism in adrenal cell suspensions. Hence, the alkaloid appears to stimulate the pituitary-adrenocortical system (113).

Cytotoxic effects.—Cepharanthine potentiated the cytotoxicities of adriamycin and vincristine in cultured L1210 cells at a noncytotoxic dose. This potentiating activity was stronger when the cells were preincubated with the alkaloid prior to treatment of the cells with the alkaloid and vincristine, suggesting that a long-term contact with cells is required for enhancement. Cepharanthine induced the increase of the cellular level of vincristine in L1210 cultured cells, with this accumulation of vincristine probably being due to inhibition of a vincristine efflux function of the cells. The alkaloid (5 mg/kg per day for 10 days) enhanced the antitumor activity of vincristine in mice in the P388 leukemia and L1210 leukemia systems (266).

The intracellular uptake, retention, and cytotoxicity of adriamycin combined with cepharanthine were investigated by flow cytometry in NIH 3T3 cells. Cepharanthine suppressed the efflux of adriamycin in a similar fashion to verapamil. The alkaloid increased adriamycin intracellular uptake, and the cytotoxicity of adriamycin was enhanced 5-fold in cells pre- and co-incubated with the alkaloid. When the alkaloid was present in the medium before, during, and after colony formation (10 days), after incubation with adriamycin, the cytotoxicity increased about 300-fold. A possible novel use of this alkaloid to improve drug sensitivity to adriamycin-resistant tumors is discussed (267).

Cepharanthine inhibited cell growth and cell cycle traversal by a human colon cancer cell line in vitro. Flow cytometry studies suggest that the alkaloid exerts its growth-inhibiting effect on tumor cells by blocking the traversal of cells through the S phase. The alkaloid may be clinically useful when administered directly into tumors or into cavities containing malignant fluids (287). Cepharanthine enhanced the cytotoxicity of peplomycin in cultured Chinese hamster V-79 cells. The alkaloid alone was almost without toxicity to these cells and did not appear to affect the mechanism of action of peplomycin (290).

Cepharanthine produced an 8-fold enhancement of the cytotoxic effect of a conjugate of epidermal growth factor

coupled with *Pseudomonas* exotoxin in HeLa cells. The alkaloid appears to accumulate in lysosomes and to delay degradation of *Pseudomonas* exotoxin in the cells (295).

Cepharanthine suppresses the multidrug-resistant human KB carcinoma cell membrane P-glycoprotein phenotype via inhibition of the photolabeling of this protein in doses comparable to those that reverse multidrug resistance (298).

The antitumor activity of 5-fluorouracil in mice with sarcoma-180 tumors was enhanced by co-administration of cepharanthine (303). Cepharanthine was found to potentiate harringtonine cytotoxicity in adriamycin-resistant P388 murine leukemia and K562 human leukemia cells (419). The mechanism of this potentiation was probably inhibition of the active efflux of harringtonine in these cells (419).

The cytocidal effect of adriamycin was enhanced by hyperthermia and cepharanthine. The alkaloid decreased adriamycin efflux (429). The sensitivity of Ehrlich ascites tumor cells to adriamycin was enhanced by treatment with cepharanthine. Complete inhibition of adriamycin efflux occurred in the presence of 50 μg/ml of the alkaloid, but little inhibition occurred when the concentration was 1 μg/ml (430).

Immunomodulatory effects.—Cepharanthine-treated mice showed an increase in the number of T cells in the parathymic lymph nodes, with these node cells exhibiting augmented proliferative responses to T cell mitogens and exogenous interleukin 2. These and other results suggest that the migration of mature T cells from the thymus to the parathymic lymph nodes is increased by cepharanthine and that the alkaloid is able to regulate their traffic by a prostaglandin-mediated system (110). Cepharanthine demonstrated maximum colony-stimulating activity at 0.2 μg/ml in a mononucleocyte-conditioned medium, while the alkaloid totally inhibited the colony formation at 20 and 200 μg/ml. This colony-stimulating activity was not observed in alkaloid nonadherent conditioned medium. Application of the alkaloid directly into bone marrow mononucleocytes did not affect colony-forming activity during 14 days, suggesting that cepharanthine has no colony-stimulating activity (119).

The administration of cepharanthine (ip, 10 mg/kg) for 10 days prior to the injection of anti-basic liver protein antibody into mice previously immunized with normal rabbit IgG and complete Freund's adjuvant suppressed the development of hepatic injury. Hence, the experimental model of hepatic injury in mice is useful for immunopharmacological research on liver diseases (339). Oral administration of cepharanthine (25 or 50 mg/kg) to whole-body irradiated mice decreased the radiation-induced hemopoietic suppression and increased spleen weight (426).

Lipid peroxidation inhibitory effects.—Cepharanthine markedly suppressed increased lipid peroxides and serum GOT and GPT activities in a homogenate of regenerating rat liver after partial hepatectomy. There was no effect on serum lipid peroxide concentration or on serum lipid concentration. These results suggest that the alkaloid may lessen partial-hepatectomy-induced hepatic damage but may have little effect on serum lipid metabolism (111).

Cepharanthine exhibited a weak inhibition of radiation-induced peroxidation of lipids dissolved in $CHCl_3$-MeOH-H_2O (1:2:0.8). By contrast, α-tocopherol strongly inhibited this peroxidation and seemed to be oxidized at a high rate by free radicals (117).

Cepharanthine (≥ 50 μM) inhibited radiation-induced lipid peroxidation in egg lecithin liposomes and also Fe^{++}-induced lipid peroxidation in mitochondria, with a proposed mechanism of action that involves lipid membrane structure (118).

Membrane modulatory effects.—Cepharanthine inhibited concanavalin-A-induced platelet activation in a dose-dependent fashion, as estimated by the release of serotonin. The alkaloid is a membrane-interacting amphiphile which may inhibit the concanavalin-A-induced assembly of the cytoskeletal proteins and their association with surface membrane glycoproteins, probably via the alteration of membrane properties (130).

The membrane modulator cepharanthine inhibited the superoxide generation produced by the chemotactic peptide formyl-Met-Leu-Phe and/or digitonin in neutrophile. Further studies using inhibitory profiles of the activation parameters suggested that receptor-mediated membrane depolarization is not a necessary event for the activation of superoxide generation by digitonin (136). Treatment of mitochondria with the membrane stabilizer cepharanthine prior to exposure to anoxic conditions improved mitochondrial energy functons and was helpful in the study of anoxia-induced mitochondrial injury (157).

Of 55 pups born to rats treated with excess vitamin A (a teratogen), 54 had external malformations, although only 23 of 55 pups born to rats treated with vitamin A plus cepharanthine (which possesses membrane-stabilizing activity) were malformed, suggesting the teratogenic effect of vitamin A is apparently caused by damage to cell membranes (166).

Cepharanthine was found to overcome completely the resistance of a multidrug-resistant subline (Ch^R-24, derived from human KB carcinoma cells) to vincristine, actinomycin D, and daunomycin, and overcome partially resistance to adriamycin. Further studies with phospholipids suggest that the alkaloid may overcome drug resistance by binding to phosphatidylserine in the plasma membrane and perturbing membrane function (216).

Cepharanthine and chlorpromazine (both amphiphiles) inhibited aggregation and morphologic changes of platelets previously stimulated with arachidonic acid. When treated with these amphiphiles, extended platelet pseudopodia (arachidonic-acid-stimulated) were completely extinguished, with these results indicating that this action was due to the dissociation of previously assembled cytoskeletons (218).

Cepharanthine inhibited various metabolic responses of polymorphomuclear leukocytes, particularly the inhibition of O_2^- generation of polymorphonuclear leukocytes, with this activity probably being attributed to its membrane modifying action. Inhibition of O_2^- generation of polymorphonuclear leukocytes by the alkaloid was stronger than any other inhibition of metabolic responses. This inhibitory effect was observed in other biscoclaurine alkaloids, with the number of diphenylether oxygen atoms dictating level of activity (3>2>1) (226).

Cepharanthine inhibited formylmethionyl-leucyl-phenylalanine-induced guinea pig polymorphonuclear leukocyte metabolic response and superoxide formation, with this inhibition being promoted via the membrane modulating effect of the alkaloid. In addition, other biscoclaurine alkaloids had the effect, which was structurally related to the number of ether bridges in these bases (3>2>1) (230).

The structure-activity relationships of 4′-*O*-substituted 1-benzyltetrahydroisoquinolines were studied with respect to their actions on the cell membrane of blood platelets and erythrocytes. The effects of these compounds are comparable to those of cepharanthine and appear to be due to a perturbing action of the membrane lipid bilayer (294).

Cepharanthine protected myocardial membrane phospholipid from peroxidative injury. The alkaloid acted to prevent, in a concentration-dependent manner, the cardiac phospholipid peroxidation that resulted from lipid exposure to superoxide-dependent, Fe-promoted *O*-radical chemistry of the type thought to be a causative factor in ischemic-reperfusion tissue damage. The alkaloid (at an effective antiperoxidant concentration) did not inhibit the enzymic superoxide source (xanthine oxidase), scavenge superoxide radical, or act like a chain-breaking antioxidant. The alkaloid is a membrane-active compound which acts as a lipophilic anesthetic and may exert its antiperoxidant effects by inducing structural changes in the lipid-rich membrane or liposome target of free radical attack (374).

Pharmacokinetics.—^{14}C-labelled (methylenedioxy group) cepharanthine was administered (po and iv) to Wistar rats in a dosage of 5 mg/kg. Almost 70% of the dose was absorbed from the digestive tract, with radioactivity being mainly found in the feces as polar metabolites (83–85% of the dose), via the bile, and only slight enterohepatic recycling. High radioactivity was found in the liver, spleen, adrenals, thyroid, hypophysis, kidneys, and lungs, with low radioactivity in the eyeballs and CNS after po administration. Serum protein binding was 74–93%. Slight radioactivity was found in fetuses, with radioactivity in maternal milk being 1.3–1.8 times that of maternal blood. The radioactivity disappeared slowly from most tissues with $t_{1/2}$ being 8–24 days, except in the testis where the value was 36 days. A biphasic decrease in blood radioactivity ($t_{1/2}$ 0.3 h and 44 h) occurred after iv administration. Radioactivity was high in the feces (71% of the dose), lungs, and thyroid (137).

Miscellaneous effects.—Cosmetics containing the alkaloid stimulate the metabolic activity of the skin (102).

Colchicine administered in combination with cepharanthine (1.25 μg/25 g, 10 times) more effectively inhibited *Mycobacterium*-induced amyloidosis in mice than did colchicine alone. In addition, the combination of these two drugs significantly decreased the death rate associated with secondary reactions in experimental amyloidosis, when compared with sole therapy with colchicine (107).

In both actively and passively sensitized rhinitis models, cepharanthine (0.025–25 mg/kg) suppressed the leakage of pontamine sky blue dye in the perfusate of the nasal cavity, suggesting that the alkaloid may be clinically useful in the therapy of nasal allergy (150).

Cepharanthine (ip, 2 mg/kg) was used in the therapy of otitis media with infusion [induced by intrabullar injection of a keyhole limpet hemocyanin (KLH)-anti-KLH immune complex] in chinchillas. No correlation of histamine and PGE_2 levels in the middle ear effusion and otitis media was noted. The alkaloid did not produce these effects at a dosage of 5 mg/kg (241). In the kanamycin-treatment guinea pig model for cochlear hair cell damage, cepharanthine prevented the induction of damage to the outer and inner hair cells but failed to prevent damage to the outer hair cells in the first row of the spiral organ and the first turn of the cochlea (276).

The effect of cepharanthine on the teratogenicity of vitamin A was studied using maternal-induced hypervitaminosis ear malformations in mice. There was a decrease in internal malformations in the ear region in the vitamin A + cepharanthine group as compared with the vitamin A group alone (280).

Administration of cepharanthine (0.1 mg/ml) to rats via local nasal perfusion inhibited antigen-stimulated dye leakage and increase in liposomal enzyme activity. This antiallergic action was weaker when the rat model was pretreated with metyrapone (sc, 20 mg/kg/day for 5 days). Membrane stimulation or pituitary-adrenotropic stimulation were advanced as potential antiallergic mechanisms for the alkaloid (346).

After administration of cepharanthine (iv, 1 and 3 mg/kg) in rabbits with transparent round chambers implanted in their ears, an enhancement of rhythmic perfusion of microvascular blood due to vasomotion occurred for a period of 1 h or longer. This activity was not observed at a dosage of 10 mg/kg. This microvascular dilator effect did not appear to have a direct association with systemic hemodynamics (348).

Administration of cepharanthine (po, 5 and 10 mg/kg per day) to hamsters minimized the ototoxicity (slight cochlear damage) induced by kanamycin (im, 300–700 mg/kg per day). However, administration of the alkaloid (intratympanically unilaterally, 0.15 mg/animal) facilitated the ototoxicity of the aminoglycoside (349). The decrease in the survival fractions of thermotolerant V-79 cells was examined with cepharanthine. The alkaloid did not enhance hyperthermic cell killing (single heating) nor decrease the survival fraction of sublethally heated cells. Administration of the alkaloid during the second heating decreased the survival fraction (363).

Cepharanthine inhibited the opsonized zymosan-induced increase of reactive oxygen production by leukocytes in a concentration-dependent manner, with total inhibition at 30 μM. The alkaloid also inhibited formyl-Met-Leu-Phe-induced leukocyte aggregation and in combination with heparin prevented the decrease in leukocytes in endotoxin-treated rats (406).

Formulation of cepharanthine in an oral oleaginous ointment containing Plastibase is effective in the topical therapy of leukoplakia and lichen planus (409). No significant antitoxic effects on the venom of the mamushi snake (*Agkistrodon blomhoffii*) were produced by cepharanthine in a study involving injections of the venom into the thighs of mice (417). Cepharanthine was observed to inhibit [^{3}H]azidopine photolabeling of P-glycoprotein in a human cell line (418).

Chondodendrine [132]

Chondodendrine demonstrated in vitro activity against the flagellated protozoa *Leishmania brasiliensis*, *Leishmania amazonensis*, and *Leishmania donovani* (378). In addition, the alkaloid was investigated for in vitro activity against the epimastigotes of three genetically typed strains of the flagellated protozoa *Trypanosoma cruzi* (Chagas disease) but was found to lack sufficient activity to warrant in vivo analysis (379).

Cocculus trilobus Alkaloids

The total alkaloids of Mufangi (*Cocculus trilobus*) roots and stems competitively inhibited the noradrenaline-in-

duced contraction of isolated rabbit aortic strips. This inhibition was likened to that produced by the α-adrenergic blocker phentolamine. The alkaloids had little or no antagonistic action on contractions induced by KCl, $CaCl_2$, acetylcholine, or histamine (245).

Cocsuline [**153**]

Cocsuline demonstrated in vitro activity against the flagellated protozoa *Leishmania brasiliensis, Leishmania amazonensis,* and *Leishmania donovani* (378). In addition, the alkaloid was investigated for in vitro activity against the epimastigotes of three genetically typed strains of the flagellated protozoa *Trypanosoma cruzi* (Chagas disease) but was found to lack sufficient activity to warrant in vivo analysis (379). Cocsuline exhibited weak in vitro anti-malarial activity (IC_{50} 15.56 μg/ml) (chloroquine phosphate: IC_{50} 0.14 μg/ml) against *Plasmodium falciparum* (464). A subsequent test (465) afforded results (IC_{50} 12.02 μg/ml) consistent with the first test.

Cycleaneonine [**286**]

Cycleaneonine demonstrated significant inhibitory activity against stomach carcinoma cells in cell culture (81).

Cycleanine [**121**]

Antimicrobial effects.—Cycleanine demonstrated in vitro activity against the flagellated protozoa *Leishmania brasiliensis, Leishmania amazonensis,* and *Leishmania donovani* (378). In addition, the alkaloid was investigated for in vitro activity against the epimastigotes of three genetically typed strains of the flagellated protozoa *Trypanosoma cruzi* (Chagas disease) but was found to lack sufficient activity to warrant in vivo analysis (379).

Carcinogenic inhibitory effects.—Cycleanine formulated in tablets was found to produce a 91% inhibition of 12-*O*-tetradecanoylphorbol-13-acetate-promoted tumor formation in the rat ear, at a dosage of 2 mg (405).

Cardiovascular effects.—Administration of the dimethobromide salt (1 mg/kg iv) of cycleanine to rabbits improved sinoatrial node conduction. However, at an increased dosage (2 mg/kg iv) the alkaloid transiently inhibited sinoatrial (SA) node automaticity without affecting the atrioventricular (AV) node. In dogs, the alkaloid did not affect the SA node but inhibited the AV node (103).

Central effects.—Although one study reported that cycleanine demonstrated an affinity for dopaminergic receptors by producing an inhibitory effect of [^{3}H] spiperone binding to rat striatal membranes (99), a second report stated that the alkaloid failed to effectively displace ^{3}H-spiperone binding from rat striatal membranes (128). In addition, the alkaloid failed to antagonize apomorhine-induced rotation in mice with unilateral striatal 6-hydroxydopamine lesions, suggesting that the alkaloid lacks potent dopamine receptor blocking activity (antidopaminergic effects) (128).

Membrane modulatory effects.—Cycleanine produced a 36.2% inhibition of formylmethionyl-leucyl-phenylalanine-induced superoxide (O_2^-) generation by polymorphonuclear leukocytes, suggesting that the alkaloid possesses membrane-modifying activity (226).

Miscellaneous effects.—A hair tonic formulation of cycleanine + poly(oxyethylene) hydrogenated castor oil + perfume + H_2O applied to male patients for 3 months resulted in dandruff control (90%) and prevention of alopecia (80%) (433).

Daphnandrine [**37**]

Daphnandrine demonstrated in vitro activity against the flagellated protozoa *Leishmania brasiliensis, Leishmania amazonensis,* and *Leishmania donovani* (378). In addition, the alkaloid was investigated for in vitro activity against the epimastigotes of three genetically typed strains of the flagellated protozoa *Trypanosoma cruzi* (Chagas disease) and was found to possess sufficient activity to warrant in vivo analysis (379).

Daphnoline [**38**]

Daphnoline demonstrated in vitro activity against the flagellated protozoa *Leishmania brasiliensis, Leishmania amazonensis,* and *Leishmania donovani* (378). In addition, the alkaloid was investigated for in vitro activity against the epimastigotes of three genetically typed strains of the flagellated protozoa *Trypanosoma cruzi* (Chagas disease) but was found to lack sufficient activity to warrant in vivo analysis (379).

Dauricine [**3**]

Anti-inflammatory effects.—Injection (ip) of dauricine (LD_{50} 205 mg/kg) markedly inhibited croton oil-induced mouse ear edema and carrageenin-induced rat paw swelling. This inhibition in rats was slightly reduced via bilateral adrenalectomy. The alkaloid decreased the adrenal ascorbic acid levels, suggesting that its anti-inflammatory action was mediated via the adrenal cortex. Finally, the alkaloid also inhibited croton oil-induced exudate and granuloma formation and CMC-induced leukocyte migration in rats, with an analgesic effect on mice (writhing test) (154).

Cardiovascular effects.—Administration of dauricine in isolated rat hearts produced a concentration-dependent increase in coronary arterial flow and a decrease in myocardial contractile force. Administration of the alkaloid to mice (ip, 50 mg/kg) antagonized the increased myocardial blood flow induced by $CaCl_2$, as did verapamil (7.5 mg/kg), while increases in isoproterenol-induced myocardial blood flow were not inhibited by dauricine but were antagonized by propranolol (30 mg/kg). These results suggest that the myocardial effects of the alkaloid are due to Ca^{++} antagonism (168).

Administration of dauricine (iv) or verapamil to dogs dose-dependently decreased blood pressure and inhibited the function of the SA node and left ventricle (dauricine less than verapamil). In addition, total peripheral resistance, heart rate, stroke volume, and cardiac output were decreased and the preventricular ejection period/left ventricular ejection time was increased (183). The subacute toxicity of different doses of dauricine to the heart, kidney, and suprarenal

glands was evaluated. Hepatic and renal damage was slight after doses of 150 or 300 mg/kg (po) for 3 months, while myocardial damage was insignificant after doses of 4.8–300 mg/kg per day (po) for 2 or 3 months or after 600 mg/kg for 18 days. The alkaloid has hypotensive and anti-arrhythmic effects with little toxicity and a large safety range (232).

Dauricine (iv, 1.2–10 mg/kg) increased the threshold of electrical stimulation-induced ventricular fibrillation in a dose-dependent fashion. This effect was potentiated by lidocaine, additive with amiodarone or propranolol, and not affected by phenytoin (283).

Dauricine (1.0–10 mM) decreased in a concentration-dependent manner the amplitude and V_{max} while prolonging the duration of the action potential of in vitro toad sciatic nerve preparation. Its action was more potent than lidocaine but less potent than dicaine and quinidine in these systems. These results were similar to those in guinea pig heart and indicate that the alkaloid inhibits Na^+ influx (357).

Dauricine and a number of its derivatives were studied via Q-model information cluster analysis. Results indicated that derivatives of different clusters have more varied calmodulin-antagonistic activities, with derivatives of the same cluster having less varied activities (434).

Dauricine was used successfully in the therapy of human patients with frequent ectopic activity at rest. Impedence cardiogram and systolic time interval showed no significant changes in cardiac output, stroke volume, total peripheral resistance, PEP, PEP/LVET, and mean arterial pressure. Prolongation in LVET and decrease in heart rate were observed after treatment with the alkaloid for 4 weeks (459).

Central effects.—Although one study reported that dauricine has an affinity for dopaminergic receptors by producing an inhibitory effect of [^{3}H] spiperone binding to rat striatal membranes (99), a second study reported that the alkaloid demonstrated an ability to displace ^{3}H-spiperone binding from rat striatal membranes and to antagonize apomorhine-induced rotation in mice with unilateral striatal 6-hydroxydopamine lesions (128). The results of the second study suggest that the alkaloid has potent dopamine receptor blocking activity (antidopaminergic effects) (128).

Membrane modulating effects.—Dauricine produced a 50.8% inhibition of formylmethionyl-leucyl-phenylalanine-induced superoxide (O_2^-) generation by polymorphonuclear leukocytes, suggesting that the alkaloid possesses membrane-modifying activity (226).

Platelet aggregation inhibitory effects.—Dauricine inhibited (in vivo and in vitro) rabbit platelet aggregation induced by ADP, arachidonic acid, or collagen, but with no selective inhibition of this aggregation, suggesting that Ca^{++} antagonism may be involved (147).

Dauricine was observed to inhibit in a dose-dependent manner the formation of 5-lipoxygenase products and cyclooxygenase products of arachidonic acid metabolism in rat pleural neutrophils (403). In addition, the alkaloid inhibited, in a concentration-dependent fashion, the ADP-, arachidonic acid-, or epinephrine-induced in vitro rat and human platelet aggregation. Various arachidonic acid congeners were inhibited by dauricine in washed rat platelets (407).

Miscellaneous effects.—The effects of dauricine on human erythrocytic membrane calmodulin-dependent Ca^{++}-Mg^{++}-ATPase were examined, but results were not stated in this abstract (224).

Dauricine did not induce sex-linked recessive lethal effects in male fruit flies (*Drosophila melanogaster*) and thus is probably not a mutagen (228).

7-*O*-Demethylisothalicberine [**195**]

7-*O*-Demethylisothalicberine blocked the action potential of transitional pacemaker cells in spontaneously beating preparations of sinus venosus of the Chilean frog *Caudiverbera caudiverbera*. This blockade was preceded by subthreshold oscillations and membrane potential depolarization. Transitional cells completely blocked by the alkaloid were depolarized to about 40 mV. These results suggest a similarity between the alkaloid and verapamil on these cells (455).

N,N-Dimethylcurine [**133** dvt]

Dimethylcurine methylchloride administered to dogs exhibited hypotensive activity characterized by a rapid onset and offset of action. These effects were well controlled and unaccompanied by depression of cardiovascular function (313).

O,O-Dimethylliensinine [**29** dvt]

O,O-Dimethylliensinine formulated in tablets was found to inhibit 12-*O*-tetradecanoylphorbol-13-acetate-promoted tumor formation in the ear of rats (405).

N,N-Dimethyltetrandrine iodide (Tetrandrine dimethiodide) [**76** dvt]

The hemodynamic and respiratory effects of *N,N*-dimethyltetrandrine iodide (tetrandrine dimethiodide, "hanjisong") were studied in pentobarbital-anesthetized dogs at an intravenous dosage of 1.3–1.5 mg/kg. Rapid responses were evoked which peaked within 5 minutes and dissipated in 15 min. The most obvious effect noted was that of a transient drop in arterial blood pressure without subsequent compensation reactions. The alkaloid appears to affect arteriolar and pulmonary vessel resistance (272). Tetrandrine dimethiodide administered to dogs exhibited hypotensive activity characterized by a rapid onset and offset of action. These effects were well controlled and unaccompanied by depression of cardiovascular function (313).

Dimethyltrilobine [**163** dvt]

Dimethyltrilobine blocked neuromuscular transmission in isolated rat phrenic-nerve diaphragm and chick biventer cervicis preparations without affecting the conditions of the nerve or the contractile response of the muscle to direct stimuli. The sensitivity of the chick muscle to acetylcholine was reduced and high Ca^{++} levels antagonized its

neuromuscular blockade, presumably by increasing acetylcholine release from the presynaptic membranes. The alkaloid apparently acts on nicotinic receptors, and with an action lesser than that of curare (176).

Dimethyltrilobine iodide was observed to competitively inhibit acetylcholine-induced contraction of isolated toad rectus abdominis, suggesting that the alkaloid is a competitive antagonist of the N_2 receptors, with this antagonism and N_2-receptor affinity comparable to those of (+)-tubocurarine (235, 246). Dimethyltrilobine iodide produced a direct positive inotropic effect on isolaterd guinea pig papillary muscle, with prolongation of the duration of the action potential APD_{50} and APD_{90} and effective refractory period. The alkaloid decreased blood pressure, heart rate, and left ventricular systolic pressure, but did not affect left ventricular diastolic pressure and cardiac output in dogs (243).

Dimethyltrilobine iodide was found to inhibit the action potentials of isolated rabbit superior cervical ganglion. This inhibition was weaker than that induced by (+)-tubocurarine; it was antagonized by neostigmine, enhanced in a Ca^{++}-free or ½ Ca^{++} medium, and decreased in a 2[Ca^{++}] medium. The alkaloid inhibited ganglionic N, P, and LN waves (248).

Dimethyltubocurarine (Metocurine) [**14** dvt]

Raised concentrations of DMT apparently block open receptor channels of clonal BC3H-1 muscle cells in a voltage-dependent fashion, with both brief and long-duration openings arising from receptors bound with 2 mol of DMP (88). Addition of metocurine to primary cultures of rat hepatic cells did not produce a leakage of lactic dehydrogenase into the culture medium, which implies that this compound does not produce the same membrane damage as other related compounds such as atracurium or its metabolites (165).

The administration of metocurine (0.3 mg/kg) and other nondepolarizing muscle relaxants to dogs did not alter intraocular pressure (236). Metocurine was employed in the study of the influence of respiratory-induced acid-base changes on the action of various non-depolarizing muscle relaxants in rats. With an increase in CO_2 from 2.5% to 7.5%, the partial neuromuscular blockade produced by metocurine was augmented (292).

Trimetaphan in combination with metocurine produced a dose-dependent potentiation of neuromuscular blocking effects in the rat phrenic nerve diaphragm preparation (347). Chronic muscle disuse is known to decrease the sensitivity of skeletal muscle to nondepolarizing relaxants, such as metocurine. In a study with dogs that were exercised daily by running over a period of 5 weeks, it was demonstrated that exercise increases the sensitivity to metocurine (413).

Increasing CO_2 concentration (respiratory) and decreasing HCO_3^- concentration (metabolic) inhibited the effects of metocurine in rats, while reversing these parameters augmented the effects of the alkaloid (444).

A comparison of parametric with semiparametric analysis of the concentration-vs.-effect relationship of metocurine was performed in dogs and pigs (453).

O-(4-Ethoxybutyl)berbamine

A new semisynthetic derivative of berbamine [*O*-(4-ethoxybutyl)berbamine (EBB)] is a powerful and specific inhibitor of calmodulin. The alkaloid inhibited calmodulin-stimulated Ca^{++}-Mg^{++}-ATPase in human erythrocyte membranes (IC_{50} 0.35 μM) in comparison to berbamine (IC_{50} 60 μM). Calmodulin-independent basal Ca^{++}-Mg^{++}-ATPase, Na^+-K^+-ATPase, and Mg^{++}-ATPase were not affected at 1.0 μM EBB at which calmodulin-dependent Ca^{++}-Mg^{++}-ATPase was already potently inhibited (competitive with respect to calmodulin). Higher concentrations of calmodulin reversed the inhibition induced by higher concentrations of EBB. It was demonstrated that EBB binds directly to dansyl-calmodulin, causing a conformational change of the calmodulin polypeptide chain. Data obtained from fluorescence titration curves obtained in the presence of Ca^{++} suggested the presence of two specific binding sites for EBB and additional nonspecific binding sites (174).

O-Ethylfangchinoline

Administration of *O*-ethylfangchinoline (prepared via the ethylation of fangchinoline with $PhEt_3N^+ I^-$ in EtOH) (po, 50 mg/kg) produced a hypotensive response (147–169 mm Hg) in rats (200 mm Hg original blood pressure) (355).

Fangchinoline [**61**]

Fangchinoline produced an 82.4% inhibition of formylmethionyl-leucyl-phenylalanine-induced superoxide (O_2^-) generation by polymorphonuclear leukocytes, suggesting that the alkaloid possesses membrane-modifying activity (226). Fangchinoline antagonized the Ca^{++} channel blocker ^{3}H-diltiazem in receptor binding studies (IC_{50} 1.0 μM) (460).

Fenfangjine A [**297**]

Fenfangjine A exhibited inhibitory activity against angiotensin converting enzyme I (ACE) (52,311) and is thus a potentially useful antihypertensive (52,75,311).

Fenfangjine B [**298**]

Fenfangjine B exhibited inhibitory activity against angiotensin converting enzyme I (ACE) (52,311) and is thus a potentially useful antihypertensive (52,75,311).

Fenfangjine C [**299**]

Fenfangjine C exhibited inhibitory activity against angiotensin converting enzyme I (ACE) (52) and is thus a potentially useful antihypertensive (52,75,311).

Fenfangjine D [**300**]

Fenfangjine D exhibited inhibitory activity against angiotensin converting enzyme I (ACE) (52,311) and is thus a potentially useful antihypertensive (52,74,75,311).

Gilletine [**202**]

Gilletine exhibited in vitro anti-malarial activity (IC_{50} 1.10 μg/ml) (chloroquine phosphate: IC_{50} 0.14 μg/ml) against *Plasmodium falciparum* (465).

N,N'-Dimethyllindoldhamine (Guattegaumerine) [**234**]

Guattegaumerine exerted a strong antimitotic and cytotoxic effect on L1210 and B16 melanoma cells in culture, with a lower activity on HeLa cells and Flow 2002 cells (normal human cells). The alkaloid exerts some activity at concentrations below 5 μg/ml on B16 melanoma but is more than two times less toxic on normal human cells (195).

Gyrocarpine [**306**]

Gyrocarpine demonstrated in vitro activity against the flagellated protozoa *Leishmania brasiliensis*, *Leishmania amazonensis*, and *Leishmania donovani* (378). In addition, the alkaloid was investigated for in vitro activity against the epimastigotes of three genetically typed strains of the flagellated protozoa *Trypanosoma cruzi* (Chagas disease) and found to possess sufficient activity to warrant in vivo analysis (379).

Homoaromoline [**42**]

Homoaromoline produced a 67.0% inhibition of formylmethionyl-leucyl-phenylalanine-induced superoxide (O_2^-) generation by polymorphonuclear leukocytes, suggesting that the alkaloid possesses membrane-modifying activity (226).

Hypoepistephanine [**43**]

Hypoepistephanine produced a 34.1% inhibition of formylmethionyl-leucyl-phenylalanine-induced superoxide (O_2^-) generation by polymorphonuclear leukocytes, suggesting that the alkaloid possesses membrane-modifying activity (226).

Isochondodendrine [**122**]

Isochondodendrine demonstrated in vitro activity against the flagellated protozoa *Leishmania brasiliensis*, *Leishmania amazonensis*, and *Leishmania donovani* (378). In addition, the alkaloid was investigated for in vitro activity against the epimastigotes of three genetically typed strains of the flagellated protozoa *Trypanosoma cruzi* (Chagas disease) but found to lack sufficient activity to warrant in vivo analysis (379).

Isoliensinine [**28**]

Isoliensinine produced a 59.6% inhibition of formylmethionyl-leucyl-phenylalanine-induced superoxide (O_2^-) generation by polymorphonuclear leukocytes, suggesting that the alkaloid possesses membrane-modifying activity (226). Isoliensinine, formulated in tablets, was found to inhibit 12-*O*-tetradecanoylphorbol-13-acetate-promoted tumor formation in the ear of rats (405).

Isotetrandrine [**62**]

A hair tonic formulation of isotetrandrine + poly(oxyethylene) hydrogenated castor oil + perfume + H_2O applied to male patients for 3 months resulted in dandruff control (90%) and prevention of alopecia (80%) (433). Isotetrandrine exhibited strong in vitro anti-malarial activity (IC_{50} 0.07 μg/ml) (chloroquine phosphate; IC_{50} 0.14 μg/ml) against *Plasmodium falciparum* (465).

Krukovine [**63**]

Krukovine demonstrated in vitro activity against the flagellated protozoa *Leishmania brasiliensis*, *Leishmania amazonensis*, and *Leishmania donovani* (378). In addition, the alkaloid was investigated for in vitro activity against the epimastigotes of three genetically typed strains of the flagellated protozoa *Trypanosoma cruzi* (Chagas disease) but found to lack sufficient activity to warrant in vivo analysis (379).

Limacine [**64**]

Limacine was found to have little effect on the kinetics of soybean lipoxygenase type I using linoleic acid as a substrate in vitro (261). Limacine was found to be inactive as an antitrypanocidal agent in tests involving mice infected with *Trypanosoma brucei brucei* (286) and failed (sc, 100 mg/kg) to demonstrate antimalarial activity in mice as measured with the sporozoan parasite *Plasmodium berghei berghei* (305). Limacine demonstrated in vitro activity against the flagellated protozoa *Leishmania brasiliensis*, *Leishmania amazonensis*, and *Leishmania donovani* (378). In addition, the alkaloid was investigated for in vitro activity against the epimastigotes of three genetically typed strains of the flagellated protozoa *Trypanosoma cruzi* (Chagas disease) but found to lack sufficient activity to warrant in vivo analysis (379).

Limacusine [**44**]

Limacusine was found to have little effect on the kinetics of soybean lipoxygenase type I using linoleic acid as a substrate in vitro (261). Limacusine was found to be inactive as an antitrypanocidal agent in tests involving mice infected with *Trypanosoma brucei brucei* (286) and failed (sc, 200 mg/kg) to demonstrate antimalarial activity in mice as measured with the sporozoan parasite *Plasmodium berghei berghei* (305).

Malekulatine [**238**]

Malekulatine demonstrated in vitro activity against the flagellated protozoa *Leishmania brasiliensis*, *Leishmania amazonensis*, and *Leishmania donovani* (378). In addition, the alkaloid was investigated for in vitro activity against the

epimastigotes of three genetically typed strains of the flagellated protozoa *Trypanosoma cruzi* (Chagas disease) but found to lack sufficient activity to warrant in vivo analysis (379).

O-(4-Methoxyphenyl)-dauricine [**3** dvt]

O-(4-Methoxyphenyl)-dauricine was prepared from dauricine and showed antihypertensive activity in rats (310).

N-Methylcurine chloride (Curine methylchloride) [**132** dvt]

Enflurane, via inhalation (3%), increased the neuromuscular blocking of *N*-methylcurine chloride in a dose-dependent manner in patients during endotracheal intubation, with this blockade increasing from 25 to >90% (324).

Neferine [**30**]

Neferine produced a 63.6% inhibition of formylmethionyl-leucyl-phenylalanine-induced superoxide (O_2^-) generation by polymorphonuclear leukocytes, suggesting that the alkaloid possesses membrane-modifying activity (226). Neferine (iv, 6 mg/kg) reduced both blood pressure and cardiac contractility in normotensive and hypertensive rats. At 2 mg/kg, only the hypotensive effects were noted. The alkaloid reduced peripheral resistance in the perfused hindlimbs of cats at 0.6 mg/kg. The alkaloid decreased diastolic pressure more than systolic pressure (389). Neferine, formulated in tablets, was found to inhibit 12-*O*-tetradecanoylphorbol-13-acetate-promoted tumor formation in the ear of rats (405). Neferine suppressed the amplitude of action potential and the maximal upstroke velocity in rabbit sinoatrial nodes and clusters of cultured cardiac myocytes from neonatal rats. The alkaloid apparently has an inhibitory effect on the slow transmembrane Na^+ and/or Ca^{++} current of the myocardium (431). The effects of neferine on the action potential duration and V_{max} in guinea pig heart papillary muscles were related to the stimulation frequency, and the antiarrhythmic action (ouabain-induced arrhythmias) was due to inhibition of Na^+, K^+, and Ca^{++} myocardial currents (447).

Nortiliacorinine A [**116**]

The antifungal effects of nortiliacorinine A were studied, with results suggesting that the alkaloid was probably not a promising antifungal agent (445).

Obaberine [**46**]

Obaberine demonstrated in vitro activity against the flagellated protozoa *Leishmania brasiliensis, Leishmania amazonensis,* and *Leishmania donovani* (378). In addition, the alkaloid was investigated for in vitro activity against the epimastigotes of three genetically typed strains of the flagellated protozoa *Trypanosoma cruzi* (Chagas disease) and found to possess sufficient activity to warrant in vivo analysis (379).

Obamegine [**71**]

Obamegine exhibited in vitro anti-malarial activity (IC_{50} 0.51 μg/ml) (chloroquine phosphate; IC_{50} 0.14 μg/ml) against *Plasmodium falciparum* (465).

Oxyacanthine [**48**]

Oxyacanthine produced a 63.1% inhibition of formylmethionyl-leucyl-phenylalanine-induced superoxide (O_2^-) generation by polymorphonuclear leukocytes, suggesting that the alkaloid possesses membrane-modifying activity (226).

Phaeantharine [**73**]

Phaeantharine chloride was found to inhibit the growth of some Gram positive bacteria, as measured by the plate diffusion test. Several synthetic intermediates were found to lack cytostatic activity, while one showed spasmolytic activity (344).

Phaeanthine [**74**]

Phaeanthine was found to be inactive as an antitrypanocidal agent in tests involving mice infected with *Trypanosoma brucei brucei* (286). Furthermore, the alkaloid (sc, 200 mg/kg) failed to demonstrate activity antimalarial activity in mice as measured with the sporozoan parasite *Plasmodium berghei berghei* (305). Phaeanthine demonstrated in vitro activity against the flagellated protozoa *Leishmania brasiliensis, Leishmania amazonensis,* and *Leishmania donovani* (378). In addition, the alkaloid was investigated for in vitro activity against the epimastigotes of three genetically typed strains of the flagellated protozoa *Trypanosoma cruzi* (Chagas disease) but found to lack sufficient activity to warrant in vivo analysis (379). Phaeanthine exhibited in vitro anti-malarial activity (IC_{50} 1.43 μg/ml) (chloroquine phosphate; IC_{50} 0.14 μg/ml) against *Plasmodium falciparum* (464). A subsequent test (465) afforded results (IC_{50} 1.41 μg/ml) consistent with the first test.

O-Propionyldauricine [**3** dvt]

O-Propionyldauricine, prepared from dauricine, was found to strongly inhibit calmodulin-dependent phosphodiesterase (IC_{50} 2.8 μmol/liter) (323) and to be one of the most potent calmodulin antagonists (IC_{50} 1.2 μM) among this series of compounds (383).

Pycnamine [**75**]

Pycnamine exhibited in vitro anti-malarial activity (IC_{50} 0.15 μg/ml) (chloroquine phosphate; IC_{50} 0.14 μg/ml) against *Plasmodium falciparum* (464).

Tetrandrine [76]

Anti-allergic effects.—Tetrandrine inhibited histamine-stimulated $^{45}Ca^{++}$ influx partially and high-K^+-stimulated and/or potential-operated channel-opened $^{45}Ca^{++}$ influx completely in guinea pig and dog tracheal muscle preparations. Blockade of potential-operated and receptor-operated Ca^{++} channels via the alkaloid and its resultant anti-allergic action are discussed (242). Tetrandrine prevented experimentally induced mast cell degranulation and histamine release, as well as inhibiting $^{45}Ca^{++}$ inward currents (253).

Anti-inflammatory effects.—Tetrandrine produced significant inhibition of random movement, chemotaxis, superoxide anion generation, and interleukin-1 production in human monocytes. Degranulation and hexose-monophosphate shunt activity were unaffected, however. The alkaloid may be useful in the therapy of chronic inflammatory diseases where interleukin-1 plays a major role as an inflammatory mediator (373). The effects of tetrandrine on vascular permeability and neutrophil functions in carrageenin-induced air-pouch inflammation in rats (sc) were studied. Vascular permeability, neutrophil migration, beta-glucuronidase release, and superoxide anion generation were suppressed by the alkaloid (20, 40, 100 mg/kg), but the intracellular superoxide dismutase and cAMP levels in neutrophils were increased by the same dose of the alkaloid. The alkaloid apparently inhibits prostaglandin synthesis and scavenges free radicals (402).

Antimicrobial effects.—Tetrandrine was found to possess potent in vitro antimalarial effects on both chloroquine-sensitive and chloroquine-resistant strains of *Plasmodium falciparum*. The alkaloid was about 3 times more potent against the chloroquine-resistant strain than it was against the chloroquine-sensitive strain, as determined by their IC_{50} values. The alkaloid did not reverse chloroquine resistance but did possess calcium channel blocking activity, similar to verapamil (393).

Antisilicotic effects.—Tetrandrine (0.1–1.0 μg/ml) produced dose-dependent inhibition of human neutrophil and monocyte adherence, with monocytes being more sensitive than neutrophils. Dye-exclusion experiments indicated that the alkaloid is non-toxic to these cells at 10 μg/ml concentrations. Adherence was suppressed via washing, and enhancement of adherence by the tumor promoter, phorbol myristate acetate, was abolished by the alkaloid. Deoxyglucose uptake by neutrophils and monocytes was suppressed. It is suggested that the alkaloid may act in human silicosis by interfering with the recruitment of neutrophils and monocytes into silicotic lesions (145).

Tetrandrine markedly suppressed random movement, chemotaxis, and phagocytosis of human neutrophils, with a minimum inhibition of lyosomal enzyme secretion from specific (secondary) but not azurophil (primary) granules. There was a marked depression of hexose-monophosphate shunt activity and H_2O_2 production at 10 μg/ml, but inhibition of superoxide anion generation was observed at 0.1 μg/ml. This difference was attributed to the capacity of the alkaloid to act as a scavenger of oxygen radicals, as demonstrated via experiments with hypoxanthine-xanthine oxidase. The use of the alkaloid in the therapy of silicosis may be explained by its potent antiphagocytic and antioxidant properties (299).

Low concentrations (1 μg/tube) of tetrandrine did not depolymerize microtubules as examined via immunofluorescence microscopy in 3T3 cells. Colchicine and high concentrations (>5 mg/tube) of tetrandrine were toxic to microtubules, while P_{204} did not affect the microtubules. Combinations of tetrandrine and P_{204} may be of use in the therapy of silicosis (308). Tetrandrine only slightly inhibited the polymerization process in guinea pig brain tubulin, with only slight depolymerizing actions on microtubules (309).

Tetrandrine was found to inhibit experimental pulmonary fibrosis and reduce immunologic alterations in rats as determined by light and electon microscopic histological evaluation of the lungs, plus hydroxyproline content and wet wt of the lungs. Combined therapy with the alkaloid and with polyvinylpyridine *N*-oxide could offer significant advantages in the treatment of silicotic patients leading to long-lasting recovery periods (331).

Blood coagulation effects.—Tetrandrine was compounded in the form of granules with the aid of silicic acid, cornstarch, and hydroxypropylcellulose for administration to patients in order to decrease blood viscosity (45).

Cardiovascular effects.—Tetrandrine exhibited effectiveness in the therapy of hypertension in clinical testing (52). Repeated determinations of cardiac output, pulmonary capillary wedge pressure, and EKG parameters in anesthetized dogs demonstrated the alkaloid to be a potent arteriolar vasodilator with slight effects on atrioventricular conduction, but lacking significant negative inotropic effects (100). Tetrandrine inhibited both KCl- and $CaCl_2$-induced contraction in isolated rabbit pulmonary arteries, being similar to verapamil and different from papaverine in its effects. The alkaloid appears to be a Ca^{++}-channel blocker (114).

Tetrandrine (3 or 5 mg/kg, iv) decreased the area of myocardial ischemia and necrosis and lowered the ST segment of epicardial ECG in open-chest dogs with experimental ischemia and infarction induced by ligation of the left descending coronary artery (126). Tetrandrine, like verapamil, produced excitation-contraction decoupling in the cardiac muscle and inhibited the slow action potential evoked in partially depolarized papillary muscle by electrostimulation. The alkaloid possessed negative inotropic and chronotropic effects in myocardial preparations and inhibited Ca^{++}-induced contractions in the isolated coronary artery and uterus. These inhibitory effects were reduced by increasing the external Ca^{++} concentration, and there was no competitive antagonism between tetrandrine and isoprenaline Hence, the alkaloid is a Ca^{++} antagonist in both cardiac and smooth muscle, though less potent than verapamil (178).

Pretreatment of anesthetized guinea pigs with tetrandrine (iv, 5 mg/kg) increased the doses of ouabain required to induce and reach the peak of inotropic effect as well as toxic reactions, without altering the peak inotropic effect, peak blood pressure, toxicity, and safety margin. The alkaloid prevented and controlled ouabain-induced arrhythmia, probably via prevention of Ca^{++} influx (203).

Tetrandrine was found to exhibit antihypertensive, anti-arrhythmogenic, anti-anginal (anti-angina pectoris), and antitumor effects, with evidence that the alkaloid antagonizes calmodulin, and it is a new and natural inhibitor of calmodulin-stimulated Ca^{++}-Mg^{++}-ATPase of erythrocytic membranes (224). The hypotensive action of tetrandrine in conscious rats (iv, 15 mg/kg) is mainly attributed to its inhibition of myocardial contraction at the early stage followed

by vasodilation at a later stage. At higher doses (40 mg/kg), the alkaloid induced cardiac arrest, with the occurrence of an excitation-contraction decoupling, as that observed with verapamil (231). Tetrandrine and verapamil (but not propranolol) reversed positive staircase phenomena of left atrial contraction in the guinea pig. Partial depolarization of the preparation with K^+ increased this effect. The alkaloid also produced a depressed post-rest potentiation of left atrial contraction. The negative inotropism of the alkaloid related not only to the inhibition of Ca^{++} into cells, but also to the decrease of intracellular Ca^{++} release (269). Large doses of either tetrandrine or verapamil inhibited the acetylcholine-induced release of Ca-dependent endothelium-derived relaxant factor in isolated rabbit aortic rings. This release was also inhibited in a Ca-free medium. These results suggest that the characteristics of endothelial Ca channel cells are not identical with those in smooth muscle cells (270).

Tetrandrine exhibited both negative inotropic (frequency dependent) and chronotropic effects on isolated myocardial preparations, as well as the heart in situ. The alkaloid induced excitation-contraction decoupling, a decrease in the amplitude of slow action potential, and a diminution of inward Ca^{++} current T_{si} peak values. The alkaloid protected the guinea pig from isoprenaline-induced myocardial ischemia. Ca^{++}-, high K^+-, norepinephrine-, and ouabain-induced contractions of aortic and coronary artery strips were counteracted by the alkaloid, with similar inhibition of Ca^{++}-induced or ouabain-induced rat uterine musculature contractions. Addition of extra Ca^{++} neutralized these inhibitory effects. The alkaloid is a Ca^{++} channel blocker but much less potent than verapamil (271).

The amount of ouabain required to induce the onset and peaking of inotropic effect, as well as toxocity, of tetrandrine was increased after pretreatment of guinea pigs with the alkaloid. The peak value of the positive inotropic effect was unaffected and neither the toxicity of ouabain nor its margin of safety was changed (120,288).

The effects of tetrandrine on the binding of 3 chemical classes of Ca^{++} entry blockers in porcine cardiac sarcolemmal membrane vesicles were studied. The alkaloid, which appears to be a structurally unique natural product Ca^{++}-entry blocker, may interact directly at the benzothiazepine-binding site of the Ca^{++} entry blocker receptor complex and allosterically modulate ligand binding at other receptors in this complex (291). Tetrandrine produced an in vitro inhibition of angiotensin I converting enzyme (311).

Reductive cleavage of tetrandrine afforded *O*-methylarmepavine and *N*-methylcoclaurine. These monomeric products exhibited Ca^{++}-antagonistic effects only at higher doses, but did produce positive inotropic effects on isolated rat atria and α_2-adrenoceptor antagonistic effects on isolated vas deferens, respectively (332). The anti-arrhythmic effect of tetrandrine (iv, 3 mg/kg) plus propranolol (iv, 0.2 mg/kg) in rabbits with epinephrine-induced heart arrhythmias was greater than that of either drug alone, with the pharmacokinetic parameters of propranolol not being altered by the alkaloid (336).

The effects of tetrandrine on the slow-inward currents in canine cardiac Purkinje fibers were studied via the 2-microelectrode voltage clamp technique. The alkaloid inhibited the peak value of the slow-inward current in concentration-dependent and time-dependent manners. The slow-inward current induced by Sr^{++} instead of Ca^{++} was also reduced after exposure to solutions of the alkaloid. The alkaloid is considered to be a slow channel blocker (366).

Tetrandrine (0.32 mM) and verapamil (30 μM), but not propranolol, reversed the positive staircase phenomenon of contraction in the left atrium of guinea pigs. Partial depolarization of the preparation with K^+ (20 mM) resulted in a more pronounced effect. These and other results suggest that the negative inotropism of the alkaloid is not only related to the inhibition of Ca^{++} into cells but also to a decrease of intracellular Ca^{++} release (408).

The hypotensive action of tetrandrine in rats (iv, 15 mg/kg) is principally due to inhibition of cardiac contractility and to vasodilation (442).

Tetrandrine antagonized the Ca^{++} channel blocker ^{3}H-diltiazem in receptor binding studies (IC_{50} 0.63 μM) (460).

Central effects.—(−)-Tetrandrine has a very high affinity (K_i 7.3×10^{-8} M) for the muscarinic receptors of rat brain, as determined by its effect on the binding of [^{3}H]QNB (quinuclidinyl benzilate) in an in vitro receptor binding assay (394).

Cytotoxic effects.—The inhibiting effect of tetrandrine on unscheduled DNA synthesis of human lung adenocarcinoma cells was measured by direct scintillation counting of [^{3}H]thymidine incorporated into the uv-irradiation-damaged DNA (285).

Immunomodulatory effects.—Tetrandrine was shown to have potent immunosuppressive properties, as mitogen-induced lymphoproliferative responses were markedly reduced even when the alkaloid was added after the initiation of cultures. The alkaloid suppressed in vitro antibody synthesis by B cells, as well as natural killer-cell-mediated lysis of K562 cells. Tetrandrine does not interfere with receptor-ligand binding, but does affect the inositol triphosphate second messenger system (296).

Tetrandrine was shown to possess significant inhibitory effects on receptor-ligand-mediated histamine release from rat mast cells at concentrations similar to or lower than those observed with theophylline and sodium cromoglycate. The alakloid does not bind tightly to these cell membrane nor cytoplasmic components, since inhibition of ovalbumin-IgE and concanavalin-A-mediated histamine release was reversible by washing the cells. These results, combined with the anti-phagocytic, anti-oxidant, and immunosuppressive properties of the alkaloid, suggest that tetrandrine may have a broad-spectrum non-steroidal properties useful in the therapy of allergic diseases (307).

Tetrandrine has greater in vitro suppressive effects than berbamine on adherence, locomotion, and ^{3}H-deoxyglucose uptake of neutrophils, as well as mitogen-induced lymphocyte responses and mixed lymphocyte reactions. In addition, tetrandrine displays anti-oxidant activity, while berbamine does not. Berbamine, however, has a significantly greater capacity for inhibition of natural killer cell cytotoxicity (435).

There was a consistent suppression of phosphoinositide turnover in concanavalin-A-stimulated human lymphocytes in the presence of tetrandrine. In addition, concanavalin-A-stimulated calcium flux was inhibited, as well as protein kinase C activity. The immunosuppressive properties of the alkaloid may be mediated by the capacity of the alkaloid to interfere with transmembrane signalling (439).

Membrane modulatory effects.—Tetrandrine (a calmodulin antagonist) specifically inhibited calmodulin-stimulated Ca^{++}-Mg^{++}-activated ATPase in human erythrocyte membrane (in vitro). The alkaloid also inhibited Na^{+}-K^{+}-Mg^{++} ATPase, as well as basal Ca^{++}-Mg^{++}-activated ATPase. Tetrandrine also inhibits the osmotic lysis of erythrocytes. The results suggest that the alkaloid may bind to membrane Ca^{++}-Mg^{++}-ATPase and that the calmodulin antagonistic effect of the alkaloid is related to its membrane-stabilizing activity (170). Tetrandrine produced a 92.2% inhibition of formylmethionyl-leucyl-phenylalanine-induced superoxide (O_2^-) generation by polymorphonuclear leukocytes, suggesting that the alkaloid possesses membrane-modifying activity (226).

Mutagenic effects.—The potential genotoxic and carcinogenic hazards of tetrandrine were studied using the *Salmonella*/histidine reversion assay and the SOS/Umu test. The results indicated that the alkaloid was a weak promutagen inducing frameshift mutations and was a potent genotoxic enhancer. Experimental details suggest that the enhancement of genotoxicity may result from an increase in error-prone DNA repair (388).

The genotoxicity of tetrandrine was studied utilizing the micronucleus and sister chromatid exchange assay systems. The alkaloid elevated sister chromatid exchange levels in cultured Chinese hamster lung cells and in spleen cells but failed to induce micronuclei. These and other results suggest that the alkaloid is a weak indirect-acting genotoxicant (443).

The enhancement of tetrandrine on the genotoxic activity of two known mutagens, mitomycin C and cigaret-smoke condensate, was studied utilizing cultured Chinese hamster lung cells, with the sister chromatid exchange being used as the genetic endpoint to measure genotoxicity. The frequencies of sister chromatid exchange induced by the two mutagens were enhanced by tetrandrine in an alkaloid concentration-dependent fashion (451).

Platelet aggregation effects.—Tetrandrine markedly inhibited ADP-, collagen-, and arachidonic-acid-induced rabbit platelet aggregation in a concentration-dependent manner (201,365,384). These effects are likely due to the inhibition of calmodulin-dependent phosphodiesterase activity by the alkaloid (384). Platelets pretreated with the alkaloid were not activated by collagen, nor were there morphologic changes or granule release. Dipyridamole enhanced the inhibition of alkaloid-induced platelet aggregation, but increased extracellular Ca^{++} weakened this inhibition (365).

Tetrandrine was found to exhibit inhibitory effects on platelet-activating factor-induced platelet aggregation in a dose-dependent manner, with preferential inhibition of platelet aggregation induced by collagen, thrombin, epinephrine, and ADP. Arachidonic acid- and Ca ionophore A23187-induced platelet aggregation was unaffected by the alkaloid. The results support a possible interference with the phosphatidylinositol second-messenger system as a mechanism of action and further suggest a clinical role for the alkaloid as a nonsteroidal broad-spectrum anti-allergy medication (397).

Tetrandrine inhibited platelet aggregation induced by arachidonic acid, platelet activating factor, or ADP in a concentration-dependent manner in rabbits and pigs in vitro (2–10 times greater than verapamil) and rabbits in vivo. Calcium antagonism may be responsible for the inhibitory effect of the alkaloid on platelet aggregation (400).

Miscellaneous effects.—Tetrandrine failed to influence the yield of DNA single strand breaks in cultured mouse cells. In addition, the alkaloid inhibited the rejoining of DNA single strand breaks, irrespective of when irradiation was applied. Finally, the inhibition of undetermined synthesis and DNA synthesis by tetrandrine was observed (129).

A review, in Japanese, of the pharmacological and biological effects of tetrandrine from the Fang Ji preparation *Stephania tetrandra* was presented (186).

Administration of tetrandrine (ip, 20, 50, and 100 mg/kg) to mice once daily for 7 days increased the formation of micronuclei in blood lymphocytes in a dose-dependent manner. The mechanism of action was proposed to be one of interference with the incorporation of deoxythymidine into DNA leading to chromosome fragmentation (202). Tetrandrine inhibited phenylephrine-induced contractions and spontaneous contractions in isolated rabbit oviductal isthmus. The alkaloid (iv) suppressed the increase in intraluminal pressure in response to phenylephrine and, at 48 h post-ovulation, delayed the transport of the ovum through the oviduct. The alkaloid also suppressed the activity of ova accelerated by estradiol cyclopenylpropionate (273).

A hair tonic formulation of tetrandrine + poly(oxyethylene) hydrogenated castor oil + perfume + H_2O applied to male patients for 3 months resulted in dandruff control (90%) and prevention of alopecia (80%) (433).

Tetrandrine-*N*-oxides

Tetrandrine-*N*-oxides exhibited inhibitory activity against angiotensin converting enzyme I in an in vitro study (75,311).

Thalrugosine [**79**]

Thalrugosine produced a 77.6% inhibition of formylmethionyl-leucyl-phenylalanine-induced superoxide (O_2^-) generation by polymorphonuclear leukocytes, suggesting that the alkaloid possesses membrane-modifying activity (226).

Tiliacorinine [**119**]

The antifungal activity of tiliacorinine was studied, with the results demonstrating that concentrations of tiliacorinine equal to/greater than 500 ppm inhibited fungal growth. The alkaloid may thus be a promising antifungal agent (445).

Trigilletimine [**162**]

Trigilletimine exhibited weak in vitro anti-malarial activity (IC_{50} 21.57 μg/ml) (chloroquine phosphate; IC_{50} 0.14 μg/ml) against *Plasmodium falciparum* (464). A subsequent test (465) afforded results (IC_{50} 23.44 μg/ml) consistent with the first test.

Trilobine [163]

Administration of trilobine HCl (po or ip) produced an anti-inflammatory effect in rats which was not decreased by bilateral adrenalectomy. The alkaloid failed to prolong post-adrenalectomy survival time but did decrease prostaglandin E levels in the inflammatory tissue. In addition, the alkaloid produced marked involution of the thymus, increased weight of the adrenal glands, and increased plasma cortisol levels (155). A review, in Japanese, of the pharmacological and biological effects of trilobine from the Fang Ji preparation *Cocculus trilobus* was presented (186).

Trilobine produced a 98.8% inhibition of formylmethionyl-leucyl-phenylalanine-induced superoxide (O_2^-) generation by polymorphonuclear leukocytes, suggesting that the alkaloid possesses membrane-modifying activity (226). Administration of trilobine HCl (ip, 5 mg/kg) to mice decreased ventricular fibrillation and (ip, 10 mg/kg) decreased the occurrence of $CaCl_2$-acetylcholine-induced atrial fibrillation. When given intravenously (5 mg/kg), the alkaloid increased the dose of ouabain needed to produce ventricular extrasystole, ventricular fibrillation, and cardiac arrest in guinea pigs. Administration to rats (iv, 5 mg/kg) converted $BaCl_2$-induced arrhythmias into sinus rhythm for >10 min, while in rabbits the alkaloid delayed the onset and shortened the duration of epinephrine-$CHCl_3$-induced arrhythmias. The picrotoxin-induced arrhythmias produced by intracerebroventricular injection were antagonized by the alkaloid (intracerebral injection, 0.5 mg/kg; iv, 5 mg/kg) (314).

Trilobine HCl (5 and 10 mg/kg) was injected into the sublingual vein of female rats whose left efferent vagal trunk had been sectioned at the distal end. Pre-drug spontaneous firing of the central trunk was recorded, and the action potentials were recorded at the time of injection and every 30 min thereafter for 2 h. There was no statistically significant change in vagal firing post alkaloid administration (462).

(+)-Tubocurarine [142]

The widespread use of this alkaloid in medicine is well known. The literature abounds with references to its basic and clinical pharmacology and the following numbered references have appeared in only a three-year time period, 1986–1989: 87, 89, 90, 92–97, 101, 105, 106, 108, 109, 112, 115, 116, 121–123, 125, 127, 131, 135, 138–144, 146, 148, 149, 151–153, 156, 159–164, 169, 171, 172, 175, 177, 179–182, 184, 185, 187–193, 197–200, 204–215, 219–223, 227, 229, 233, 234, 237, 238, 247, 249, 251, 252, 256, 259, 260, 262–264, 274, 275, 278, 279, 281, 282, 284, 289, 292, 297, 300, 302, 304, 315–322, 325, 326, 329, 330, 334, 335, 337, 340–343, 345, 347, 352, 358–362, 367, 368, 371, 375–377, 380, 382, 385–387, 391, 392, 396, 398, 401, 404, 410–412, 415, 416, 423–425, 432, 436–438, 440, 444, 449, 450, 456, 457, 466–469.

TABLE 11. Names and Synonyms of Bisbenzylisoquinoline Alkaloids Cited in This Review.[a]

O-Acteyldauricine [3 dvt] p.c., syn.
Ambrimine [272] n.a.
Antioquine (*N*-2′-Methyltilitriandrine) [225] a.d., p.c.
Apateline [187] r.i.
Aquifoline [273] n.a.
Aromoline [31] c.c., r.i., p.c.
Auroramine [390] n.a.
Baluchistine [188] r.i.
Belarine [93] r.i.
Berbamine [57] c.c, c.s., p.c., r.i.
Berbamine-2′β-*N*-oxide [274] n.a.
Berbamunine [1] b.s., c.c., r.i.
Berbilaurine [275] n.a.
N,N′-Bisnoraromoline [32] r.i.
2,2′-Bisnorguattaguianine [276] n.a.
Bisnorobamegine [277] n.a.
2,2′-Bisnorphaeanthine [278] n.a.
Bisnorthalrugosine [279] n.a.
Calafatine-2′α-*N*-oxide [226] r.s.
Calafatine-2′β-*N*-oxide [227] r.s.
Candicusine [280] n.a.
Caryolivine [281] n.a.
Cepharanoline [33] p.c.
Cepharanthine [34] c.s., p.c., r.i.
Cepharanthine-2′β-*N*-oxide [282] n.a.
Chondodendrine [132] p.c.
Coclobine [35] a.d., r.i.
Cocsoline [152] r.i.
Cocsuline [153] p.c., r.i.
Cordobimine [283] n.a.
Cordobine [284] n.a.
Cultithalminine [285] n.a.
Curine (bebeerine) [133] b.s.
Cycleaneonine [286] n.a., p.c.
Cycleanine [121] a.d., c.s., p.c., r.i.
Daphnandrine [37] p.c., r.i.
Daphnoline [38] p.c., r.i.
Dauricine [3] c.s., p.c., r.i.
Dauricoline [5] r.i.
Daurisoline [192] a.d., r.i., syn.
Dehatridine [287] n.a.
Dehatrine [288] n.a.
1,2-Dehydroapateline [193] r.i.
1′,2′-Dehydrokohatamine [289] n.a.
1′,2′-Dehydrokohatine [290] n.a.
1,2-Dehydro-2-norlimacusine [291] n.a.
1,2-Dehydro-2′-nortelobine [292] n.a.
1,2-Dehydrotelobine [194] r.i.
Demerarine [39] a.d.
12-*O*-Demethylcoclobine [293] n.a.
7-*O*-Demethylisothalicberine [195] p.c., r.i.
N-Desmethylcycleanine [233] r.i.
12-*O*-Desmethyllauberine [294] n.a.
N-Desmethylthalidasine (2-Northalidasine) [196] r.i.
N-Desmethylthalistyline [16] r.s.
3′,4′-Dihydrostephasubine [295] n.a.
N,N-Dimethylcurine [133 dvt] p.c.
O,O-Dimethylliensinine [29 dvt] p.c.
N,N′-Dimethyllindoldhamine (Guattegaumerine) [234] a.d., b.s., c.c., r.i., p.c.
N,N-Dimethyltetrandrine [76 dvt] p.c.
Dimethyltrilobine [163 dvt] p.c.
Dimethyltubocurarine (Metocurine) [142] p.c.
Dinklacorine [114] a.d., r.i.
Efatine [296] n.a.
(+)-Epistephanine [40] a.d., r.i.

Espinine [**9**] r.i.
Fangchinoline [**61**] c.s., r.i., syn., p.c.
Fenfangjine A (Tetrandrine-2β-*N*-oxide) [**297**] n.a., p.c.
Fenfangjine B (Fangchinoline-2′α-*N*-oxide) [**298**] n.a., p.c.
Fenfangjine C (Fangchinoline-2′β-*N*-oxide) [**299**] n.a., p.c.
Fenfangjine D (1,3,4-tridehydrofangchinolinium hydroxide) [**300**] n.a., p.c.
Funiferine [**20**] a.d., r.i.
Geraldoamine [**301**] n.a.
Gilletine [**202**] p.c.
Granjine [**302**] n.a.
Grisabine [**10**] r.i.
Guattaguianine [**276** dvt] s.s.
Guattamine [**303**] n.a.
Guattaminone [**304**] n.a.
Gyroamericine [**305**] n.a.
Gyrocarpine [**306**] n.a., p.c.
Gyrocarpusine [**307**] n.a.
Gyrolidine [**308**] n.a.
Hayatidine [**136**] b.s., c.s.
Hayatine [**137**] b.s., c.s.
Hayatinine [**138**] c.s.
Hernandezine [**81**] c.s., r.i.
Homoaromoline [**42**] a.d., r.i., p.c.
5-Hydroxyapateline [**309**] n.a.
5-Hydroxytelobine [**310**] n.a.
5-Hydroxythalidasine [**311**] n.a.
5-Hydroxythalidasine-2′α-*N*-oxide [**312**] n.a.
5-Hydroxythalmine [**313**] n.a.
Insulanoline [**169**] r.i.
Insularine [**170**] r.i.
Isochondrodendrine [**122**] b.s., c.s., p.c.
Isoliensinine [**28**] p.c., r.i.
Isotetrandrine [**62**] c.c., c.s., r.i., p.c.
Isothalidezine [**82**] r.i.
Isotrilobine [**157**] c.s., r.i.
Kohatamine [**314**] n.a.
Kohatine [**236**] a.d., r.i.
Krukovine [**63**] p.c., r.i.
Lauberine [**106**] r.i.
Limacine [**64**] p.c., r.i.
Limacine-2′α-*N*-oxide [**315**] n.a.
Limacine-2β-*N*-oxide [**316**] n.a.
Limacine-2′β-*N*-oxide [**317**] n.a.
Limacusine [**44**] r.i., p.c.
Lindoldhamine [**11**] a.d., r.i.
Malekulatine [**238**] p.c.
Maroumine [**391**] n.a.
Medelline [**318**] n.a.
O-(4-Methoxyphenyl)-dauricine [**3** dvt] p.c., syn.
N-Methylapateline [**207**] r.i.
O-Methylcocsoline [**239**] r.i.
N-Methylcurine [**133** dvt] p.c.
O-Methyldauricine [**12a**] a.d., r.i.
N-2′-Methylisotetrandrine [**319**] n.a.
O-Methyllimacusine [**320**] n.a.
2-*N*-Methyllindoldhamine [**321**] n.a.
2′-*N*-Methyllindoldhamine [**322**] n.a.
O-Methylthalicberine [**95**] r.i.
N-Methylthalistyline [**17**] r.s.
O-Methylthalmethine [**96**] c.s., r.i.
O-Methylthalmine [**244**] r.i.
N-Methyltiliamosine [**323**] n.a.
Monterine [**324**] n.a.
Neferine [**30**] p.c., r.i.
Neothalibrine [**211**] a.d., r.i.
Neothalibrine-2′α-*N*-oxide [**325**] n.a.
2-Norberbamine [**68**] r.i.
2-Norberbamunine [**1** dvt] c.c.
2-Norcepharanoline [**326**] n.a.
2-Norcepharanthine [**327**] n.a.
2′-Norcepharanthine [**328**] n.a.
2′-Norcocsuline [**329**] n.a.
2′-Nordaurisoline [**330**] n.a.
2′-Norfuniferine [**331**] n.a.
2′-Norguattaguianine [**332**] n.a.
2′-Norisocepharanthine [**333**] n.a.
2-Norisotetrandrine [**334**] n.a.
2′-Norisotetrandrine [**213**] r.i.
Norisoyanangine [**335**] n.a.
2-Norlimacine [**336**] n.a.
2-Norlimacusine [**245**] r.i.
2-Norobaberine [**46** dvt] a.d., r.i.
2′-Norobaberine [**337**] n.a.
2-Norobamegine [**69**] r.i.
2′-Noroxyacanthine [**338**] n.a.
2′-Norpisopowiaridine [**339**] n.a.
Norstephasubine [**340**] n.a.
Northalibroline [**341**] n.a.
2′-Northaliphylline [**342**] n.a.
2-Northalmine [**343**] n.a.
2-Northalrugosine [**344**] n.a.
Nortiliacorine A [**115**] a.d., *r.i.*
Nortiliacorinine A (2′-Nortiliacorine) [**116**] a.d., p.c., r.i.
2′-Nortiliageine [**345**] n.a.
Noryanangine [**346**] n.a.
Obaberine [**46**] p.c., r.i.
Obamegine [**71**] r.i., p.c.
Oxandrine [**347**] n.a.
Oxandrinine [**348**] n.a.
Oxofangchirine [**349**] n.a.
Oxyacanthine [**48**] r.i., p.c.
N-2-Oxy-*O*-methyldauricine [**350**] n.a.
N-2′-Oxy-*O*-Methyldauricine [**351**] n.a.
Pampulhamine [**352**] n.a.
Pangkoramine [**353**] n.a.
Pangkorimine [**354**] n.a.
Pedroamine [**355**] n.a.
Penduline [**72**] r.i.
Phaeantharine [**73**] syn., p.c.
Phaeanthine (*O*-Methyllimacine) [**74**] c.s., p.c., r.i.
Phaeanthine-2′α-*N*-oxide [**356**] n.a.
Pisopowamine [**357**] n.a.
Pisopowetine [**358**] n.a.
Pisopowiaridine [**359**] n.a.
Pisopowiarine [**360**] n.a.
Pisopowidine [**361**] n.a.
Pisopowine [**362**] n.a.
Popidine [**363**] n.a.
Popisidine [**364**] n.a.
Popisine [**365**] n.a.
Popisonine [**366**] n.a.
Popisopine [**367**] n.a.
O-Propionyldauricine [**3** dvt] p.c.
Pseudoxandrine [**368**] n.a.
Pseudoxandrinine [**369**] n.a.
Pycmanilline [**392**] n.a.
Pycnamine [**75**] r.i., p.c.
Pycnazanthine [**370**] n.a.
Secolucidine [**393**] n.a.
Seeperine [**50**] a.d.
Siddiquamine [**371**] n.a.
Siddiquine [**372**] n.a.

Stephasubimine [**373**] n.a.
Stephasubine [**374**] n.a.
Stephibaberine [**375**] n.a.
Stepierrine [**376**] n.a.
Telobine [**160**] r.i.
Tetrandrine [**76**] c.s., p.c., r.i.
Thalicberine [**97**] r.i.
Thalictine [**107**] a.d., r.i.
Thalidasine [**100**] c.s., r.i.
Thalidasine-2α-*N*-oxide [**377**] n.a.
Thalidezine [**83**] c.s., r.i.
Thaligosine (Thalisopine) [**52a**] a.d., r.i.
Thaligosine-2β-*N*-oxide (Thalisopine-2β-*N*-oxide) [**378**] n.a.
Thaligosinine [**52b**] r.i.
Thaligrisine [**252**] r.i.
Thaliphylline [**253**] r.i.
Thaliphylline-2′β-*N*-oxide [**379**] n.a.
Thalirabine (5-*O*-Desmethylthalistyline) [**17a**] r.s.
Thaliracebine [**14a**] r.s.
Thalirugine [**14b**] r.i.
Thalisopidine [**53**] r.i.
Thalisopine [**54**] r.i.
Thalistine [**221**] r.s.
Thalistyline [**18**] r.s.
Thalivarmine [**380**] n.a.
Thalmethine [**98**] r.i.
Thalmiculatimine [**381**] n.a.
Thalmiculimine [**382**] n.a.
Thalmiculine [**383**] n.a.
Thalmine [**108**] r.i.
Thalmirabine [**222**] r.i.
Thalpindione [**223**] r.s.
Thalrugosaminine [**55**] a.d., r.i.
Thalrugosaminine-2α-*N*-oxide [**384**] n.a.
Thalrugosidine [**101**] a.d., r.i.
Thalrugosine [**79**] r.i., p.c.
Thalrugosinone [**224**] r.s.
Thalsivasine [**385**] n.a.
Tiliacorine [**118**] a.d., r.i.
Tiliacorinine [**119**] p.c., r.i.
Tiliacorinine-2′-*N*-oxide [**254**] a.d., r.i.
Tiliageine [**27**] a.d., r.i.
Tilianangine [**386**] n.a.
Tiliarine [**185**] r.s., a.d.
Tilitriandrine [**387**] n.a.
Trilobine [**163**] c.s., r.i.
(+(-Tubocurarine chloride [**142**] p.c.
Yanangcorinine [**388**] n.a.
Yanangine [**389**] n.a.

[a]a.d. = additional work; b.s. = biosynthesis; c.c. = cell culture; c.s. = chromatographic separation; n.a. = new alkaloid; p.c. = pharmacology; r.i. = reisolated; r.s. = revised structure; s.s = semisynthetic; syn. = synthesized; dvt = derivative (meaning a derivative of an alkaloid with the preceding number).

TABLE 12. Alkaloids Synthesized.

O-Acetyldauricine [[**3** dvt] (310)
Daurisoline [**192**] (177)
Fangchinoline [**61**] (69)
O-(4-Methoxyphenyl)-dauricine [**3** dvt] (310)

TABLE 13. Alkaloids Produced In Cell Culture.

Berberis stolonifera (Berberidaceae) (54)
Aromoline [**31**]
Berbamine [**57**]
Berbamunine [**1**]
N,N′-Dimethyllindoldhamine (Guattegaumerine) [**234**]
Isotetrandrine [**62**]
2-Norberbamunine [**1** dvt]
Stephania cepharantha (Menispermaceae)
Aromoline [**31**]
Berbamine [**57**]

PUBLISHED REVIEWS

A massive review (English, 649 references) on the literature of the bisbenzylisoquinoline alkaloids from 1974 to 1986 was published by Buck in 1987 (312).

A comprehensive review (German, 42 references) of the chemistry and pharmacology of the bisbenzylisoquinoline alkaloids reported in the literature from 1986 through 1988 was presented by Pachaly in 1990 (471). In a separate work (English, 21 references) published in 1988, the same author described his research on the bisbenzylisoquinoline alkaloids (and other related compounds) from four Menispermaceous plants: *Cyclea barbata* Miers, *Tiliacora triandra* Diels, *Tinospora (cordifolia) baenzigeri* Forman, and *Tinospora crispa* (L.) Hook f. + Thoms (472).

A small review (Chinese, 10 references) describing the methods for determining the structure of bisbenzylisoquinoline alkaloids was published by Lu in 1989 (414).

A small review (Spanish, 21 references) describing the benzylisoquinoline-derived alkaloids (including bisbenzylisoquinoline alkaloids) of the genus *Berberis* was published by Fajardo *et al.* in 1986 (473).

A review (Spanish, 42 references) describing the 1-benzyltetrahydroisoquinoline alkaloids (including bisbenzylisoquinoline alkaloids) isolated from some Chilean species of the genus *Berberis* was published by Gaona in 1988 (381).

Reviews describing the alkaloids of the genus *Thalictrum* (including bisbenzylisoquinoline alkaloids) were published by Baser in 1986 (English, 37 references) (173), Lin *et al.* in 1988 (Chinese, 88 references) (301), and Schiff in 1987 (English, 669 references) (474).

A review (English, 120 references) describing the alkaloids (including bisbenzylisoquinoline alkaloids) of the genus *Guatteria* was published by Cavé *et al.* in 1989 (475).

A review (English, 37 references) describing the alkaloids (including bisbenzylisoquinoline alkaloids) of *Cocculus pendulus*, as well as 7 other medicinal plants of Pakistani origin, was published by Atta-ur-Rahman in 1987 (354).

A review (English, 174 references) describing the methods of isolation and determination of isoquinoline alkaloids (including bisbenzylisoquinoline alkaloids) from various sources was published by Valka in 1989 (420).

An incisive and key review (English, 27 references) of the ^{1}H-nmr and mass spectral characteristics of bisbenzylisoquinoline alkaloids was published by Guinaudeau, Freyer, and Shamma in 1986 (476). These alkaloids were divided into 12 subgroups (A to L), according to the nature of the linkage(s) between the two monomeric coclaurine parts, and over 100 ^{1}H-nmr spectra are presented in a tabular form. A thorough discussion of each group is presented. This landmark paper is required reading for anyone utilizing these techniques in the identification of bisbenzylisoquinoline alkaloids.

THIN-LAYER CHROMATOGRAPHY.—A new tlc method is described which afford excellent resolution of 12 alkaloids present in curare resin (91).

The quantitative determination of trilobine [**163**] in rabbit plasma was accomplished via extraction (Et_2O) of the alkalinized plasma, back extraction (first with H_2SO_4, followed by alkalinization and then extraction with CH_2Cl_2), and tlc using cyclohexane-iPrOH-Et_2NH (7.5:1.5:1) as the developing agent and scanning at 265 nm. The recovery was 101.5% and the minimum detectable concentration was 0.005 mcg/ml plasma (217).

A discussion of some commonly used systems in the separation of bisbenzylisoquinoline alkaloids was presented as one part of a larger review of classical tlc of alkaloids (258). The R_f values of berbamine [**57**], cepharanthine [**34**], cycleanine [**121**], dauricine [**3**], hayatidine [**136**], hayatine [**137**], hayatinine [**138**], hernandezine [**81**], isochondrodendrine [**122**], isotetrandrine [**62**], isotrilobine [**157**], *O*-methylthalmethine [**96**], phaeanthine [**74**], thalidasine [**100**], and thalidezine [**83**] were recorded, as observed in the development of Si gel G and alumina plates in 9 solvent systems (258).

Extraction of *Stephania tetrandra* preparations with EtOH and appropriate workup afforded tetrandrine [**76**], which was separated by tlc using $CHCl_3$-MeOH (8:2) and quantitated via scanning (369). In a separate study, tetrandrine [**76**] and fangchinoline [**61**] were extracted from the roots of *S. tetrandra* with $CHCl_3/NH_4OH$ and determined by tlc densitometry using $CHCl_3$-MeOH (10:1.1) (370).

A review of recent developments in the tlc of alkaloids, including those of the bisbenzylisoquinoline type, was presented. Subjects discussed included high performance tlc, sandwich chamber tlc, overpressure tlc, high pressure circular chromatography, centrifugal layer chromatography, and sequential centrifugal layer chromatography (427).

MISCELLANEOUS.—Fangchinoline [**61**] was separated from tetrandrine [**76**] by low-pressure cc [Si gel G column at 0.5–0.6 kg pressure with cyclohexane-EtOAc-Et_2NH (6:2:1)] and pH gradient extraction ($CHCl_3$ solution extracted with McIlvaine buffer solutions at pH 5.4, 5.0, and 3.8) (98).

Tetrandrine [**76**] and fangchinoline [**61**], extracted from *S. tetrandra* roots, were isolated and purified by tlc and cc and then determined by differential scanning calorimetry of hplc (446).

A review was made of the products and mechanisms of action of microbial transformations of 14 compounds with antitumor activity, including tetrandrine [**76**], isolated from higher plants (104).

A rapid, simple, and sensitive method for the qualitative analysis and quantitative determination of tetrandrine [**76**] in rat bile or urine was developed; it consisted of extraction of alkalinized bile/urine with Et_2O and hplc analysis (428).

(+)-Tubocurarine forms a colored ionic complex with methyl orange, which can be extracted with $CHCl_3$ and pH 7.8 measured by its uv absorbance at 419–424 nm. The detection limit was 25 μg/10 ml of alkaloid, with Beer's Law being obeyed in the range of 25–100 μg (relative standard deviation = 1.4%) (167). A separate study (194) reported measurement of this complex at 490 nm, with Beer's Law being followed in the range of 6–130 μg of alkaloid (detection limit = 6 μg/15 ml; relative standard devia-

tion = 1.11%). This method is not suitable for determination of the alkaloid in biological fluids because proteins can react with methyl orange (194).

A photo-oxidative cleavage reaction, modelled after that developed for the benzylisoquinoline alkaloid laudanosine, was applied to the dimeric benzylisoquinoline alkaloids berbamine [**57**], phaeanthine [**74**], nortenuipine [**89**], tenuipine [**92**], obaberine [**46**], aromoline [**31**] diacetate, nemuarine [**111**], micranthine [**159**], apateline [**187**], *N*-methyltelobine [**160** dvt], and cycleanine [**121**] (or derivatives of some of these bases). In general, this reaction results in the cleavage of the isoquinoline-portion ("top portion;" rings A, B, C, and D) from the benzyl-portion ("bottom portion;" rings E and F), with the former being characterized as a tetrahydroisoquinoline-*O*-tetrahydroisoquinolone dimer (after reduction with $NaBH_4$ and thermal dehydration) and the latter as a dialdehydediaryl ether. By way of example, photolysis of isotetrandrine [**62**] afforded 3-(4′-formylphenoxy)-4-methoxybenzaldehyde ("bottom portion") and after further reaction ($NaBH_4$ reduction and thermal dehydration) the amino-lactam 3′,4′-dihydro-6′-methoxy-7′-[1,2,3,4-tetrahydro-6,7-dimethoxy-2-methyl-(isoquinolin-8-yl)oxy]-2′-methyl-1′(2*H*)-isoquinolone ("top portion"). The utility of this reaction sequence as an alternative degradative procedure for use in structure determination/confirmation of these type of alkaloids is discussed (225).

A small-interfacial voltaic cell (Sb scratch) was found to be satisfactory for end-point detection in titration of berbamine [**57**] (0.4–4 mg) and other alkaloids and their salts in EtOH, $CHCl_3$, or dibutylether media with picric acid in the same medium. Advantages include its simplicity and sharp end-points, with recoveries being 96.5–100.8% for determinations of 19 drugs and their salts. The relative error was ±5% for 5 pharmaceutical tablets and injections (250). Crude berbamine, obtained from the waste solutions of coptisine extracts, was extracted with $CHCl_3$ and determined by potentiometric titration with picric acid (0.06 N) in $CHCl_3$ (306).

The pharmacokinetic data obtained after rabbits were administered trilobine [**163**] (iv, 40 mg) fit a 2-compartment open model. The alkaloid was extracted from rabbit plasma with *n*-hexane (containing 2% *n*-BuOH) and determined by hplc using MeOH-NH_4OH (100:0.02) as mobile phase, with detection at 236 nm. The detection limit was 7.2 ng or 20 ng/ml of plasma (265).

High-speed countercurrent chromatography was used to separate a mixture of tetrandrine [**76**], fangchinoline [**61**], and cyclanoline originally extracted from *S. tetrandra*. The separations were performed using a two-phase solvent system composed of *n*-hexane/EtOAc/MeOH/H_2O in two different elution modes over a period of 100 min, with the peak fraction of each component being analyzed via ms (338).

Polyphase-liposome injections containing thalidasine [**100**] were diluted with EtOH-0.01 N HCl (4:1) and the alkaloid quantitated by spectrofluorometry at 235 nm (for excitation) and 318 nm (for emission). The recovery was >96% with a coefficient of variation of <3.1%. The polyphase-liposome encapsulation rate was determined with this method after separation via Sephadex gel cc (364). The pharmacokinetics of intravenously administered thalidasine in polyphase liposome and aqueous solutions in mice were studied by hplc. The blood alkaloid concentration curve fit a 2-compartment open model, with the distribution and elimination half-lives being 3.52 and 23.58 min, respectively, for the liposome form, and 1.293 and 11.12 min, respectively, for the aqueous solution (372).

Fabms was utilized in the study of 12 known tail-to-tail linked benzylisoquinoline-aporphine dimeric alkaloids and 5 known tail-to-tail linked bisbenzylisoquinoline alkaloids (northalibrine [**13**], thalibrine [**14**], thaliracebine [**14a**], thaliruginine [**14c**], and thalirugidine [**17b**]). This method, while retaining almost the same fragmentation pattern as that by conventional ei analysis, provides relatively intense molecular ions (10–35%), which would be barely discernible via ei analysis (441).

A correlation was made between the level of ploidy and the type of dimeric isoquinoline alkaloids present in *Thalictrum minus* populations of southern Bulgaria. Up to the present time, 27 populations of this plant in Bulgaria have been studied for their chromosome number, with dimeric alkaloids being detected in 13 of them. The hexaploid cytotype is more common in the lowlands while the decaploids are found more frequently in the high mountains (above 1500 m). The bisbenzylisoquinoline alkaloids (oxyacanthine [**48**], thalmethine [**98**], and *O*-methylthalmethine [**96**]) are found only in the hexaploids while the aporphine-benzylisoquinoline alkaloids (thalicarpine, thalmelatine, thalipine) are found only in the decaploids. The assumption can be made that two cytotypes and two chemotypes have been found in Bulgaria up to this time (452).

A review by Gottlieb *et al.* (477) discussed the chemical dichotomies in the Magnolialean complex. The most characteristic chemosystematic feature of the Magnolialean families is the rich diversification of two groups of secondary metabolites, the neolignans and the benzylisoquinolines. Biogenetic considerations and correlation with morphological advancement suggest the evolutionary primacy of neolignans over benzylisoquinolines.

A review by Hegnauer (478) discussed the biochemistry, distribution, and taxonomic revelance of higher plant alkaloids, with all of the major classes of alkaloids being classified according to their biosynthetic origin.

Waterman and Gray (479) provided a major review on chemical systematics, including alkaloids.

This particularly incisive paper discussed the development of chemical systematics and the handling and interpretation of chemical data, while citing numerous examples of the successful taxonomic use of phytochemistry. This work is highly recommended for botanists, chemists, pharmacognosists, taxonomists, and all others utilizing chemistry characters in the study of systematics.

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Received 17 September 1990