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O-Methyldeoxopunjabine, a Secobisbenzylisoquinoline Alkaloid Bearing an Aryl Methyl Group, and Three Other Secobisbenzylisoquinoline Alkaloids, *O*-Methylpunjabine, Secocepharanthine, and Dihydrosecocepharanthine, from *Stephania Sasakii*[1)]

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Two new secobisbenzylisoquinoline alkaloids, secocepharanthine (base J) (**3**) and *O*-methylpunjabine (base K) (**4**), were isolated from *Stephania sasakii* HAYATA (Menispermaceae). Their structures were established and the structures of two other alkaloids [base B (**1**) and base C (**2**)] were also established as dihydrosecocepharanthine (**1**) and *O*-methyldeoxopunjabine (**2**).

In addition, two known bisbenzylisoquinoline alkaloids, obaberine (**5**) and thalrugosine (**6**), were newly isolated from the same plant.

Keywords——*Stephania sasakii*; Menispermaceae; secobisbenzylisoquinoline alkaloid; structural establishment; secocepharanthine; *O*-methylpunjabine; dihydrosecocepharanthine; *O*-methyldeoxopunjabine; obaberine; thalrugosine

We[2)] have reported the natural occurrence of a number of alkaloids including seven structurally unestablished ones [base B[2a)] (**1**), base C[2a)] (**2**), and base E[2b)] through base I[2b)]] in *Stephania sasakii* HAYATA (Menispermaceae). Recently, minute amounts of two new alkaloids [base J (**3**) and base K (**4**)] were also isolated from the same plant. Further, two known bisbenzylisoquinoline alkaloids,[3)] obaberine[4)] (**5**) and thalrugosine[5)] (**6**), have been newly isolated. The structures of four of the above alkaloids [base B (**1**), base C (**2**), base J (**3**), and base K (**4**)] are reported here.

Secocepharanthine (Base J) (3) and Dihydrosecocepharanthine (Base B) (1)

Base J (**3**) and base B[2a)] (**1**) have been obtained as a colorless amorphous mass and colorless plates, mp 192—194 °C,[2a)] respectively. A clue for the structural elucidation of these alkaloids came from a diagnostic inspection of the mass spectrum (MS) of base J (**3**). In the electron impact mass spectrum (EIMS), base J (**3**) shows a base peak at *m/z* 395 with a minor peak at *m/z* 242, but no peak could be observed in the higher mass region. On the other hand, in the desorption/chemical ionization[6)] mass spectrum (D/CIMS) using isobutane as a reagent gas, the protonated molecule (MH^+) could be clearly observed at *m/z* 637, corresponding to $C_{37}H_{36}N_2O_8$ as a base peak, along with a minor peak at *m/z* 395 (Table I). In the proton magnetic resonance (^{1}H-NMR) spectrum, base J (**3**) shows a 3H singlet due to an *N*-methyl

TABLE I. Physicochemical Properties of Secobisbenzylisoquinoline Alkaloids

	Base J (3)	Base B (1)	Base K (4)	Base C (2)
Appearance	Colorless amorphous	Colorless plates	Colorless needles	Colorless prisms
mp (°C)	—	192—194	144—146	183—185
Molecular Formula	$C_{37}H_{36}N_2O_8$	$C_{37}H_{38}N_2O_8$	$C_{36}H_{34}N_2O_7$	$C_{36}H_{36}N_2O_6$
IR ($CHCl_3$): cm^{-1}				
Amide	1645	1640	1650	1640
Aldehyde	1690	—	1690	—
D/CIMS: *m/z* (r.i., %)[a]				
MH^+	637 (100)	639 (100)	607 (100)	539 (100)
Fragment ion A or B	395 (27) Fragment A	395 (30) Fragment A	365 (100) Fragment B	365 (100) Fragment B
EIMS[b]: *m/z* (r.i., %)[a]				
Fragment ion A or B	395 (100) Fragment A	395 (100) Fragment A	365 (100) Fragment B	365 (100) Fragment B
Fragment ion I—IV+H	242 (7.1) Fragment I	244 (53.5) Fragment II	242 (5.9) Fragment III	228 (14.2) Fragment IV

a) r.i.: relative intensity. *b*) Neither M^+ nor doubly charged ions were observed.

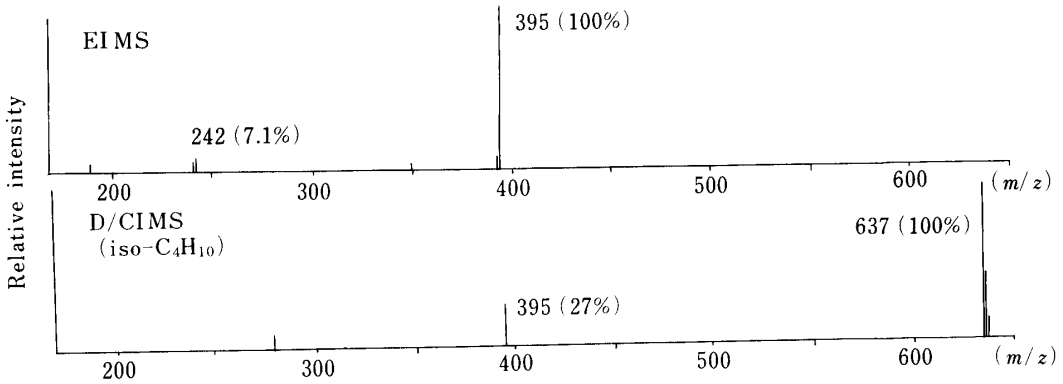


Fig. 1. Mass Spectra of Secocepharanthine (Base J) (3)

group at δ 2.29 and a 6H singlet due to two methoxy groups at δ 3.95 together with an additional methyl signal at δ 3.08. Taking into account the appearance of an amide band at 1645 cm^{-1} in the infrared (IR) spectrum of base J (**3**), the methyl signal was ascribable to a lactam *N*-methyl group. Moreover, in the ^{1}H-NMR spectrum, base J (**3**) shows a 2H diffused AB-quartet (J=1.5 Hz) due to a methylenedioxy group at δ 5.84 and an aldehydic signal at δ 9.79 as a 1H singlet. These assignments were supported by the appearance of an additional carbonyl band at 1690 cm^{-1} and a methylenedioxy band at 930 cm^{-1} in the IR spectrum. These spectral data could be reasonably interpreted by supposing that base J (**3**) is a secobisbenzylisoquinoline alkaloid[7] derived from cepharanthine[3] (**7**) which co-occurs naturally in *S. sasakii* as one of the major alkaloids. This speculation was supported by the observation that doubly charged ions, which are evident in the cases of normal bisbenzylisoquinoline alkaloids,[8] were not detected in the EIMS of base J (**3**). Further, the base peak at *m/z* 395 was assignable to fragment A and the minor peak at *m/z* 242 to fragment I, respectively (Chart 1).

In order to confirm our speculation, controlled oxidation[7c] of cepharanthine[3] (**7**) was carried out. Treatment of cepharanthine (**7**) with potassium permanganate in the presence of

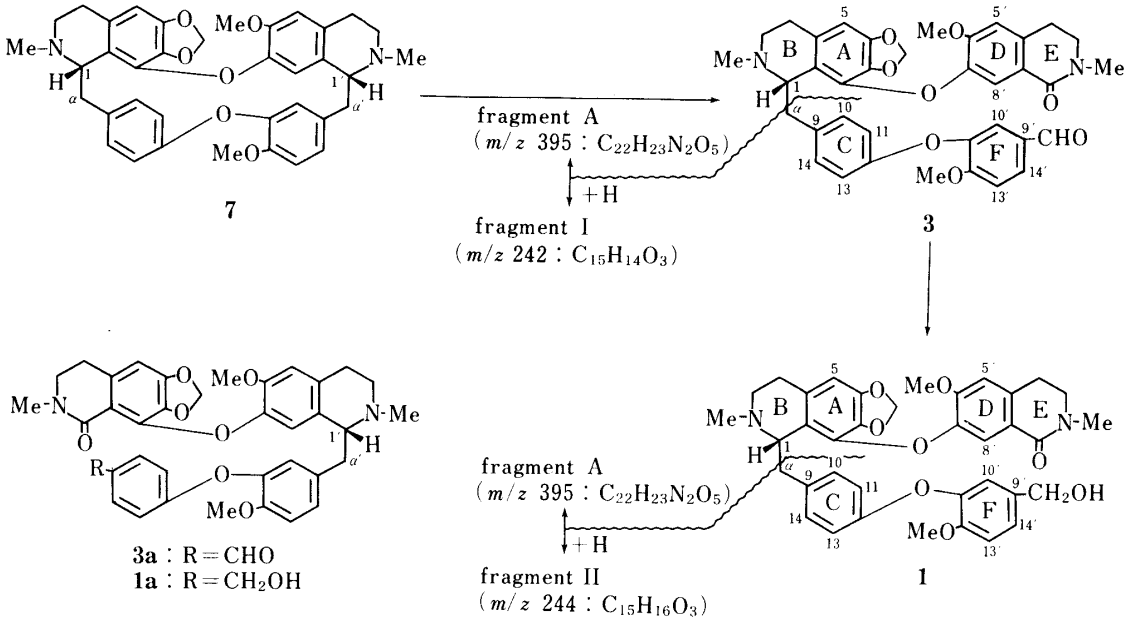
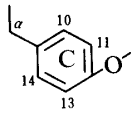
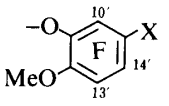


Chart 1

TABLE II. Chemical Shifts (δ) of Proton Nuclear Magnetic Resonance Signals of Rings C and F of the Secobisbenzylisoquinoline Alkaloids

Numbering	Compound			
	Base J (3) X=CHO	Base B (1) X=CH_2OH	Base K (4) X=CHO	Base C (2) X=Me
	6.83 (2H, d, J=8.6 Hz, C_{11}-H and C_{13}-H)	6.81 (2H, d, J=8.6 Hz, C_{11}-H and C_{13}-H)	6.90 (2H, d, J=8.6 Hz, C_{11}-H and C_{13}-H)	6.86 (2H, d, J=8.6 Hz, C_{11}-H and C_{13}-H)
	7.17 (2H, d, J=8.6 Hz, C_{10}-H and C_{14}-H)	7.12 (2H, d, J=8.6 Hz, C_{10}-H and C_{14}-H)	7.22 (2H, d, J=8.6 Hz, C_{10}-H and C_{14}-H)	7.18 (2H, d, J=8.6 Hz, C_{10}-H and C_{14}-H)
	7.39 (1H, d, J=2.1 Hz, $C_{10'}$-H)	6.92 (1H, d, J=2.0 Hz, $C_{10'}$-H)	7.39 (1H, d, J=2.1 Hz, $C_{10'}$-H)	6.75 (1H, brs, $C_{10'}$-H)
	7.08 (1H, d, J=8.6 Hz, $C_{13'}$-H)	6.95 (1H, d, J=8.2 Hz, $C_{13'}$-H)	7.09 (1H, d, J=8.5 Hz, $C_{13'}$-H)	6.87 (2H, s, $C_{13'}$-H and $C_{14'}$-H)
	7.62 (1H, dd, J=8.6, 2.1 Hz, $C_{14'}$-H)	7.07 (1H, dd, J=8.2, 2.0 Hz, $C_{14'}$-H)	7.64 (1H, dd, J=8.5, 2.1 Hz, $C_{14'}$-H)	

magnesium sulfate in acetone gave base J (**3**) in moderate yield. The synthetic specimen was identical with naturally occurring base J (**3**) even in the signs of the Cotton effects. Thus, we concluded that base J (**3**) is secocepharanthine.

On the other hand, in various kinds of spectra, base B[2a] (**1**) shows common features with base J (**3**), as shown in Table I. In the EIMS, base B (**1**) shows a base peak at the same m/z 395 as that of base J (**3**). However, a minor peak appears at m/z 244, while the corresponding ion of base J (**3**) is observed at m/z 242. Moreover, in the D/CIMS (NH_3), base B (**1**) shows the protonated molecule (MH^+) at m/z 639, instead of the ion at m/z 637 corresponding to that of base J (**3**), indicating that both alkaloids (**3** and **1**) have a common moiety (fragment A) and a different one (fragment I or II). Base B (**1**) has two additional hydrogen atoms in fragment II, as compared with base J (**3**). In the ^{1}H-NMR spectrum, base B (**1**) exhibits a 2H singlet due to an $ArCH_2O$ group at δ4.55 in place of an aldehydic signal of base J (**3**). These observations allowed us to conclude that base B (**1**) was a dihydro derivative of secocepharanthine (**3**). In

fact, treatment of secocepharanthine (**3**) with sodium borohydride gave base B (**1**) in which the sign of the Cotton effect coincided with that of the natural specimen, demonstrating that base B is dihydrosecocepharanthine (**1**) itself.

Although the synthetic transformation of cepharanthine (**7**) into secocepharanthine (**3**) and dihydrosecocepharanthine (**1**) demonstrates that these alkaloids belong to a group of secobisbenzylisoquinoline alkaloids,[7] the cleaved position in the molecule of cepharanthine (**7**) remained to be established because cepharanthine (**7**) has two positions susceptible to oxidative cleavage (the C_1–C_α and the $C_{1'}$–$C_{\alpha'}$ bonds) in its molecule. Evidence in favor of formula (**3**) rather than the isomeric one (**3a**) for base J came from comparative studies of the ^{1}H-NMR spectral data of both alkaloids (**3** and **1**). In the ^{1}H-NMR spectra, both alkaloids commonly showed signals due to 1,4-disubstituted (ring C) and 1,2,4-trisubstituted (ring F) benzene ring systems. The signals due to the former system were observed as two 2H doublets having similar chemical shifts of δ 6.83 and 7.17 (J=8.6 Hz). However, as regards the signals due to the latter system, base B (**1**) shows two signals due to the C_3- and C_5-protons (the $C_{10'}$- and the $C_{14'}$-protons of the ring F) at δ 6.92 and 7.07 as a doublet (J=2.0 Hz) and double doublets (J=2.0 and 8.2 Hz), while base J (**3**) shows the corresponding signals at δ 7.39 and 7.62 as a doublet (J=2.1 Hz) and double doublets (J=2.1 and 8.6 Hz). The downfield shift of these signals in base J (**3**) in contrast with those of base B (**1**) could be reasonably explained only by supposing that base J (**3**) has an aldehyde group at the C_4-position of the 1,2,4-trisubstituted benzene ring system and that the aldehyde group is replaced by a CH_2OH group in base B (**1**), indicating that the aldehyde and the CH_2OH groups are located at the $C_{9'}$-position (the C_4-position of the 1,2,4-trisubstituted benzene ring system) of both alkaloids (**3** and **1**). In other words, secocepharanthine was formed by cleavage of the $C_{1'}$–$C_{\alpha'}$ bond of cepharanthine (**7**). Such a deduction establishes the structures of base J and base B as **3** and **1**, respectively.

O-Methylpunjabine (Base K) (4) and *O*-Methyldeoxopunjabine (Base C) (2)

Next, we established the structures of base K (**4**) and base C[2a] (**2**). Base K (**4**) and base C[2a] (**2**) were isoalted as colorless needles, mp 144—146 °C, and colorless prisms, mp 183—

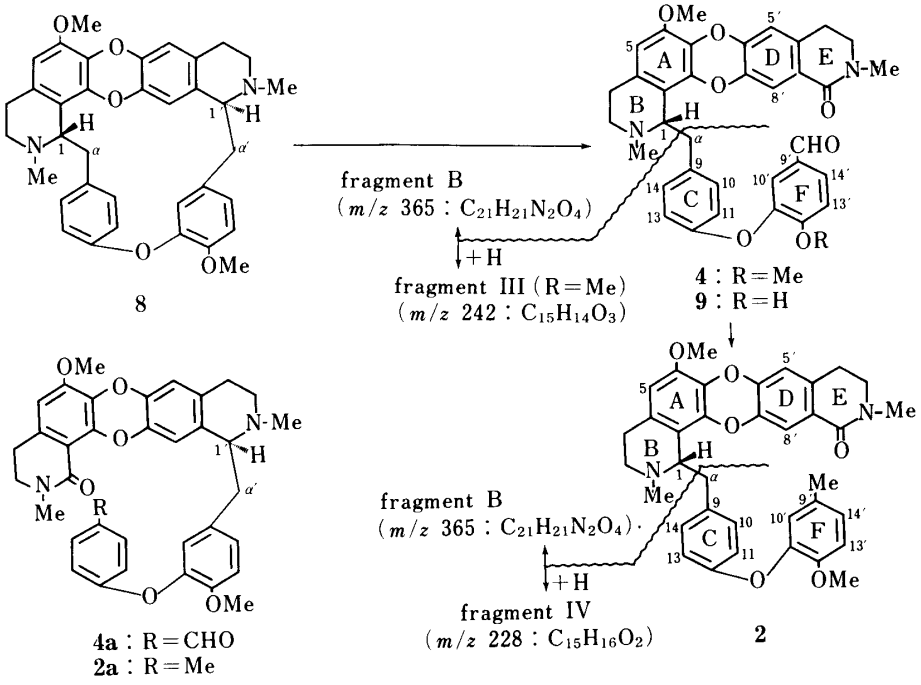


Chart 2

185 °C,[2a] respectively. In the EIMS, base K (**4**) and base C (**2**) also did not show molecular ion peaks, but their base peaks were commonly observed at *m/z* 365. On the other hand, in the D/CIMS (NH_3), the protonated molecules of base K (**4**) and base C (**2**) could be clearly observed at *m/z* 607 and at *m/z* 593, respectively. Moreover, in the IR spectra, base K (**4**) and base C (**2**) show amide bands at 1650 cm^{-1} and at 1640 cm^{-1}, respectively. Further, base K (**4**) shows an additional carbonyl band at 1690 cm^{-1}. In the ^{1}H-NMR spectrum, these alkaloids (**4** and **2**) also show two methoxy, one *N*-methyl, and one lactam *N*-methyl signals, suggesting that these alkaloids also belong to a group of secobisbenzylisoquinoline alkaloids.[7] Base K (**4**) shows an aldehydic proton at δ 9.80 as a 1H singlet and base C (**2**) shows an additional methyl singlet ascribable to an aryl methyl group at δ 2.24, instead of an aldehydic signal. Although these spectral data characterized four oxygen atoms in the former (**4**) and three in the latter (**2**), the other three oxygen atoms of these alkaloids remained uncharacterized. At this point, we imagined that these alkaloids (**4** and **2**) might have three diaryl ethers in their molecules. Treating these two alkaloids (**4** and **2**) with potassium nitrate in sulfuric acid[9] gave a blue coloration, indicating the presence of a dibenzo-*p*-dioxin skeleton in the molecule. In addition, in the ^{1}H-NMR spectrum, both alkaloids (**4** and **2**) showed signals due to the protons of 1,4-disubstituted and 1,2,4-trisubstituted benzene ring systems, and, in the EIMS, they exhibited a common fragment ion at *m/z* 365 assignable to fragment B (Chart 2). These observations led us to speculate that isotrilobine[3] (**8**) might be the parent alkaloid of these compounds (**4** and **2**). Therefore, we carried out controlled oxidation of isotrilobine[7c] (**8**). Although, the yield of the secobase was extemely poor, as reported by Shamma and Foy,[10] the resulting product was identical with the naturally occurring base K (**4**).

Wolff–Kishner reduction of the synthetic base K (**4**) provided base C (**2**). These results allowed us to conclude that base K (**4**) and base C (**2**) are secobases. The cleaved position of isotrilobine (**8**), the $C_{1'}$–$C_{\alpha'}$ bond, in these secobases (**4** and **2**) was established from a consideration of the downfield shift of the signals due to $C_{10'}$-H and $C_{14'}$-H of base K (**4**), compared with the corresponding signals of base C (**2**), as in the case of base J (**3**) and base B (**1**). This deduction allowed us to exclude the formulae **4a** and **2a**. In the circular dichroism (CD) spectrum, the signs of the synthetic specimens agreed with those of the natural products (**4** and **2**), indicating that base K (**4**) and base C (**2**) have the same absolute configuration at the C_1-position (ring B) of isotrilobine (**8**).

Shamma and co-workers[7b–d] described the natural occurrence of various types of secobisbenzylisoquinoline alkaloids, other than alkaloids having an aldehyde group. They reported alkaloids having a primary alcohol, an ester, or a carboxylic acid, instead of an aldehyde group, but not one having a methyl group. Base C (**2**) is the first such alkaloid. On the other hand, they[7d] isolated a phenolic secobisbenzylisoquinoline alkaloid having a dibenzo-*p*-dioxin skeleton from *Berberis lycium* ROYLE, and designated it as punjabine (**9**). This alkaloid corresponds to the *O*-demethyl derivative of our base K (**4**), including the absolute configuration. Therefore, we can designate base K and base C as *O*-methylpunjabine (**4**) and *O*-methyldeoxopunjabine (**2**), respectively.

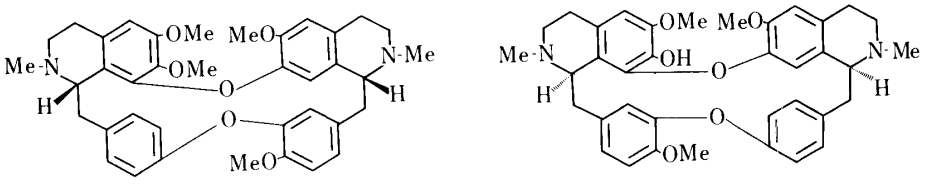
It should be noted here that the four newly isolated alkaloids have a chiral center, but the values of specific rotation of the synthetic specimens were abnormally low, as described in the experimental section. Therefore, we confirmed their optical activities by measurement of the CD and the optical rotatory dispersion (ORD) spectra in this work. This investigation is continuing, and the results will be reported in due course.

According to the biogenetic scheme tentatively proposed by Shamma,[7b] isotrilobine (**8**) should be the precursor of these alkaloids (**4** and **2**), but there has been no report on the isolation of isotrilobine (**8**) itself from *S. sasakii*, even though many researchers[11] have done detailed isolation studies. Finally, it is also of interest that the natural occurrence of *O*-methyldeoxopunjabine (**2**) indicates that the aldehyde group of secobisbenzylisoquinoline

alkaloids can be biogenetically reduced to a methyl group in a plant.

Total Bases Isolated From *S. sasakii* HAYATA

Recently, we have also newly isolated two alkaloids which were identical with authentic samples of obaberine (**5**) and thalrugosine (**6**) by direct comparison. Since the structures of thirty-two alkaloids[2a,b,12] isolated from *S. sasakii* have been established so far, the total number of structurally established alkaloids is now thirty-eight, including the six alkaloids reported in this paper.



5 6

Chart 3

However, the structures of five alkaloids, tentatively named bases E-I,[2b] isolated from this plant still remain to be established.

Experimental

All melting points were measured on a micro melting point hot stage apparatus (Yanagimoto) and are uncorrected. IR and ultraviolet (UV) spectra were recorded on a Hitachi EPI-G3 spectrometer (in Nujol) and on a Hitachi 340 spectrophotometer (as solutions in 95% EtOH), respectively. ^{1}H-NMR spectra were recorded on a JEOL FX-270 spectrometer in deuteriochloroform, with tetramethylsilane as an internal reference. EIMS were measured on a Hitachi RMU-6E spectrometer at 70 eV chamber voltage with a direct inlet system. D/CIMS were measured on a Shimadzu LKB 9000A mass spectrometer equipped with a chemical ionization (CI) source, which was modified to accommodate a field desorption (FD) emitter holder. CD and ORD spectra (as solutions in MeOH) were measured on a JASCO J-500A spectropolarimeter and a JASCO J-20 spectropolarimeter, respectively. $[\alpha]_D$ was measured on a JASCO DIP-140 digital polarimeter. For chromatography (column), silicic acid (100 mesh), Mallinckrodt Chemical Works, Silica gel 60 (70—230 mesh ASTM), Merck, and aluminum oxide (neutral, grade I), Woelm, and for preparative thin layer chromatography (TLC), Silica gel GF_{254}, Merck, were used. All identification of products was done by IR and TLC comparisons, and by mixed melting point determination. The abbreviations used are as follows: s, singlet; d, doublet; dd, double doublets; t, triplet; m, multiplet; br, broad; dif, diffused; sh, shoulder. The assignment of OH signals was confirmed by the disappearance of the signals after addition of deuterium oxide.

Dihydrosecocepharanthine (Base B[2a]) (1)——Colorless plates, mp 192—194 °C (MeOH). *Anal.* Calcd for $C_{37}H_{38}N_2O_8$: C, 69.58; H, 6.00; N, 4.39. Found: C, 69.31; H, 6.08; N, 4.37. D/CIMS *m/z*: 639 (MH^+). IR ($CHCl_3$) cm^{-1}: 1640 (amide). UV λ_{max}^{EtOH} nm (log ε): 224 (4.65), 263 (4.03), 273 (4.03), 286 (3.95), 294 (3.87) sh, 306 (3.62) sh. ^{1}H-NMR ($CDCl_3$) δ: 2.28 (3H, s, NMe), 2.35—2.45 (1H, m, C_4-H_A), 2.75—3.00 (6H, m, aliph. H×6), 3.07 (3H, s, CONMe), 3.27—3.38 (1H, m, C_3-H_A), 3.53 (2H, t, J=6.8 Hz, $C_{3'}$-H_2), 3.84 (3H, s, OMe), 3.87 (1H, dd, J=2.6 and 8.9 Hz, C_1-H), 3.95 (3H, s, OMe), 4.55 (2H, s, $ArCH_2O$), 5.84 (2H, dif. AB-q, J=1.5 Hz, OCH_2O), 6.47 (1H, s, arom. H), 6.72 (1H, s, arom. H), 6.81 (2H, d, J=8.6 Hz, C_{11}-H and C_{13}-H), 6.92 (1H, d, J=2.0 Hz, $C_{10'}$-H), 6.95 (1H, d, J=8.2 Hz, $C_{13'}$-H), 7.07 (1H, dd, J=2.0 and 8.2 Hz, $C_{14'}$-H), 7.12 (2H, d, J=8.6 Hz, C_{10}-H and C_{14}-H), 7.44 (1H, s, $C_{8'}$-H). CD ($c=7.5\times10^{-5}$) $[\theta]^{27}$ (nm): −1187 (307) (negative maximum), +5596 (285) (positive maximum); +5652 (270) (positive maximum), +5030 (261) (positive maximum), −42390 (230) (negative maximum). ORD ($c=4.2\times10^{-4}$) $[M]^{23}$ (nm): −249° (400), −338° (350), −600° (316) (trough), 0° (311), +3785° (297) (peak), 0° (287), −27690° (241) (trough), 0° (232), +29080° (222) (peak), +24920° (216) (trough).

***O*-Methyldeoxopunjabine (Base C[2a]) (2)**——Colorless prisms, mp 183—185 °C [MeOH (or acetone)]. *Anal.* Calcd for $C_{36}H_{36}N_2O_6\cdot3/2CH_3OH$; C, 70.29; H, 6.61; N, 4.37. Found: C, 70.16; H, 6.88; N, 4.48.[13] D/CIMS *m/z*: 593 (MH^+), 365 (13%). IR ($CHCl_3$) cm^{-1}: 1640 (amide). UV λ_{max}^{EtOH} nm (log ε): 226 (4.71), 277 (3.93), 287 (3.91) sh, 325 (3.69). ^{1}H-NMR ($CDCl_3$) δ: 2.24 (3H, s, ArMe), 2.28—2.45 (1H, m, C_4-H_A), 2.37 (3H, s, NMe), 2.68—3.00 (6H, m, aliph. H×6), 3.12 (3H, s, CONMe), 3.17—3.35 (1H, m, C_3-H_A), 3.52 (2H, t, J=6.6 Hz, $C_{3'}$-H_2), 3.81 (3H, s, OMe), 3.86 (3H, s, OMe), 3.92—4.00 (1H, m, C_1-H), 6.29 (1H, s, arom. H), 6.75 (2H, br s, $C_{10'}$-H and arom. H), 6.86 (2H, d, J=8.6 Hz, C_{11}-H and C_{13}-H), 6.87 (2H, s, $C_{13'}$-H and $C_{14'}$-H), 7.18 (2H, d, J=8.6 Hz, C_{10}-H and C_{14}-H), 7.59 (1H, s, $C_{8'}$-H). CD ($c=8.2\times10^{-6}$) $[\theta]^{23}$ (nm): −2419 (330) (negative maximum), −2169 (301) (negative maximum), +1701 (284) (positive maximum), −53840 (246) (negative maximum), +34330 (224) (positive maxi-

mum). ORD ($c=8.2\times10^{-5}$) $[M]^{23}$ (nm): −1209° (400), −3550° (348) (trough), −1443° (323) (peak), −2575° (306) (trough); −1990° (297) (peak), −27110° (262) (trough), 0° (251), +66710° (232) (peak), +7802° (218) (trough).

Secocepharanthine (Base J) (3)——Colorless amorphous mass. IR ($CHCl_3$) cm^{-1}: 1690 (C=O), 1645 (amide), 930 (OCH_2O). D/CIMS *m/z*: 637 (MH^+). UV λ_{max}^{EtOH} nm (log ε): 226 (4.75), 270 (4.34), 290 (4.21) sh, 302 (4.07) sh. ^{1}H-NMR ($CDCl_3$) δ: 2.29 (3H, s, NMe), 2.33—2.45 (1H, m, C_4-H_A), 2.75—3.00 (4H, m, C_3-H_A, C_α-H_2, and C_4-H_B), 2.95 (2H, m, $C_{\alpha'}$-H_2), 3.08 (3H, s, CONMe), 3.27—3.37 (1H, m, C_3-H_B), 3.53 (2H, t, J=6.8 Hz, $C_{3'}$-H_2), 3.86 (1H, dd, J=2.8 and 9.0 Hz, C_1-H), 3.95 (6H, s, OMe×2), 5.84 (2H, dif. AB-q, J=1.5 Hz, OCH_2O), 6.47 (1H, s, arom. H), 6.73 (1H, s, arom. H), 6.83 (2H, d, J=8.6 Hz, C_{11}-H and C_{13}-H), 7.08 (1H, d, J=8.6 Hz, $C_{13'}$-H), 7.17 (2H, d, J=8.6 Hz, C_{10}-H and C_{14}-H), 7.39 (1H, d, J=2.1 Hz, $C_{10'}$-H), 7.45 (1H, s, $C_{8'}$-H), 7.62 (1H, dd, J=2.1 and 8.6 Hz, $C_{14'}$-H), 9.79 (1H, s, CHO). CD ($c=6.9\times10^{-5}$) $[\theta]^{27}$ (nm): −1509 (305) (negative maximum), +2760 (286) (positive maximum), +2429 (271) (positive maximum), +1932 (261) (positive maximum), −37720 (231) (negative maximum). ORD ($c=2.2\times10^{-3}$) $[M]^{24}$ (nm): −440° (400), −748° (350), −1467° (320) (trough), 0° (308), −3374° (298) (peak), 0° (288), −24210° (241) (trough), 0° (233), +22000° (226) (peak), +11740° (216) (trough).

***O*-Methylpunjabine (Base K) (4)**——Colorless needles,[14] mp 144—146 °C (acetone–MeOH). D/CIMS *m/z*: 607 (MH^+). IR ($CHCl_3$) cm^{-1}: 1690, (C=O), 1650 (amide). UV λ_{max}^{EtOH} nm (log ε): 228 (4.74), 252 (4.45) sh, 274 (4.22) sh, 314 (3.91) sh. ^{1}H-NMR ($CDCl_3$) δ: 2.28—2.42 (1H, m, C_4-H_A), 2.39 (3H, s, NMe), 2.68—2.82 (2H, m, C_3-H_A and C_4-H_B), 2.85—3.00 (4H, m, $C_{4'}$-H_2 and C_α-H_2), 3.12 (3H, s, CONMe), 3.18—3.32 (1H, m, C_3-H_B), 3.53 (2H, t, J=6.8 Hz, $C_{3'}$-H_2), 3.86 (3H, s, OMe), 3.96 (3H, s, OMe), 3.92—3.98 (1H, m, C_1-H), 6.31 (1H, s, arom. H), 6.76 (1H, s, arom. H), 6.90 (2H, d, J=8.6 Hz, C_{11}-H and C_{13}-H), 7.09 (1H, d, J=8.5 Hz, $C_{13'}$-H), 7.22 (2H, d, J=8.6 Hz, C_{10}-H and C_{14}-H), 7.39 (1H, d, J=2.1 Hz, $C_{10'}$-H), 7.58 (1H, s, $C_{8'}$-H), 7.64 (1H, dd, J=2.1 and 8.5 Hz, $C_{14'}$-H), 9.80 (1H, s, CHO). CD ($c=1.8\times10^{-5}$) $[\theta]^{28}$ (nm): −3803 (325) (negative maximum), −32100 (248) (negative maximum), +23280 (221) (positive maximum). ORD ($c=7.0\times10^{-5}$) $[M]^{23}$ (nm): −2628 (400), −6641 (343) (trough), −4300 (319) (peak), −8934 (293) (trough), −7023 (281) (peak), −8313 (272) (trough), 0 (257), +41570 (235) (peak), 0 (216).

Oxidation of Cepharanthine (7) [Synthetic Secocepharanthine (3)]——A solution of $KMnO_4$ (0.250 g) in acetone (270 ml) was added dropwise to a stirred solution of a benzene adduct (0.302 g) of cepharanthine (**7**) in acetone (30 ml) in the presence of $MgSO_4$ (0.200 g) at room temperature for 2 h with stirring. The reaction mixture was left to stand at room temperature for 24 h, and the resulting precipitates were filtered off. The filtrate was evaporated to dryness *in vacuo*. The residue was extracted with CH_2Cl_2. The methylene chloride solution was washed with H_2O, dried over $MgSO_4$, and evaporated to dryness *in vacuo*. Column chromatography of the residue on SiO_2 with $CHCl_3$–acetone [3 : 1 (v/v)] gave a colorless amorphous mass (0.158 g). IR ($CHCl_3$) cm^{-1}: 1690 (C=O), 1645 (amide), 930 (OCH_2O). $[\alpha]_D$ −7.2° (c=2.08, $CHCl_3$).

This material was identical with a sample of the naturally occurring base J (**3**).

Reduction of Secocepharanthine (3) [Synthetic Dihydrosecocepharanthine (1)]——Sodium borohydride (0.500 g) was added to a solution of secocepharanthine (0.10 g) (**3**) in MeOH (20 ml) under ice-cooling. The mixture was stirred for 30 min. After addition of 10% HCl aq. (30 ml), the methanol was distilled off under reduced pressure. The mixture was made alkaline with conc. NH_4OH aq. and extracted with Et_2O. The ethereal solution was washed with H_2O, dried over Na_2SO_4, and evaporated to dryness *in vacuo*. Recrystallization of the residue from MeOH–acetone gave colorless plates, mp 194—196 °C (0.095 g). *Anal.* Calcd for $C_{37}H_{38}N_2O_8$: C, 69.58; H, 6.00; N, 4.39. Found: C, 69.28; H, 5.95; N, 4.28. IR ($CHCl_3$) cm^{-1}: 1640 (amide). $[\alpha]_D$ −1.67° (c=0.12, $CHCl_3$).

This material was identical with a sample of the naturally occurring base B (**1**).

Oxidation of Isotrilobine (8) [Synthetic *O*-Methylpunjabine (4)]——A solution of $KMnO_4$ (0.050 g) in acetone (100 ml) was added dropwise to a solution of isotrilobine (**8**) (0.20 g) in acetone (100 ml) at room temperature for 2 h with stirring. The reaction mixture was stirred at room temperature for 6 h. The precipitates were filtered off and the filtrate was evaporated to dryness *in vacuo*. The same treatment was repeated three times on the residue with a solution of $KMnO_4$ (0.050 g) in acetone (100 ml). The final residue was chromatographed on SiO_2 with acetone–$CHCl_3$ to give colorless needles (0.078 g), mp 137—139 °C, which were recrystallized from MeOH–acetone. IR ($CHCl_3$) cm^{-1}: 1690 (C=O), 1650 (amide). *Anal.* Calcd for $C_{36}H_{34}N_2O_7\cdot1/2CHCl_3$: C, 65.79; H, 5.22; N, 4.20. Found: C, 65.43; H, 5.21; N, 4.17. $[\alpha]_D$ −4.12° (c=0.19, $CHCl_3$).

This material was identical with a sample of the naturally occurring base K (**4**).

Wolff–Kishner Reduction of *O*-Methylpunjabine (4) [Synthetic *O*-Methyldeoxopunjabine (2)]——A solution of *O*-methylpunjabine (**4**) (0.040 g) and $NH_2NH_2\cdot H_2O$ (0.2 ml) in ethylene glycol (5 ml) containing KOH (0.20 g) was heated at 150—180 °C for 3 h. After addition of H_2O (5 ml), the resulting precipitates were collected by filtration. Column chromatography of the precipitates on SiO_2 with acetone–$CHCl_3$ [15 : 1—9 : 1 (v/v)] gave colorless prisms, mp 197—198 °C, which were recrystallized from $CHCl_3$–acetone (or $CHCl_3$–MeOH). *Anal.* Calcd for $C_{36}H_{36}N_2O_6\cdot1/2CHCl_3$: C, 67.20; H, 5.64; N, 4.29. Found: C, 67.80; H, 5.78; N, 4.24. IR ($CHCl_3$) cm^{-1}: 1640 (amide).

This material was identical with a sample of the naturally occurring Base C (**2**).

Obaberine (5)——Colorless fine needles, mp 134—139 °C (Et_2O–hexane) (lit.[4] mp 139—140 °C). ^{1}H-NMR

($CDCl_3$) δ: 2.57 and 2.66 (each 3H, NMe), 3.19, 3.63, 3.78, and 3.89 (each 3H, s, OMe), 5.46 (1H, s, arom. H), 6.31—7.44 (9H, m, arom. H×9). EIMS *m/z*: 623 ($M^+ + 1$, 38.5%), 622 (M^+, 82.0%), 396 (28.7%), 395 (85.2%), 381 (47.5%), 379 (26.2%), 198.5 (29.5%), 198 (100%), 175 (44.3%), 174 (39.3%). $[\alpha]_D$ +312° (c=0.31, $CHCl_3$) [lit.[4]) $[\alpha]_D$ +302° (c=0.21, $CHCl_3$)].

This material was identified by direct comparison with an authentic sample of obaberine (**5**).

Thalrugosine (6)——Colorless fine needles, mp 211—213 °C (acetone) [lit.[5a]) mp 212—214 °C (dec.)]. IR ($CHCl_3$) cm^{-1}: 3330 (OH). ^{1}H-NMR ($CDCl_3$) δ: 2.31 and 2.50 (each 3H, s, NMe), 3.78 (3H, s, OMe), 3.93 (6H, s, OMe×2), 6.07—7.34 (10H, m, arom. H×10). EIMS *m/z*: 609 ($M^+ + 1$, 22.9%), 608 (M^+, 51.3%), 382 (23.2%), 381 (74.3%), 367 (40.5%), 192 (41.0%), 191.5 (25.1%), 191 (100%), 174 (24.4%), 168 (20.3%). $[\alpha]_D^{15}$ +177.5° (c=0.25, MeOH) [lit.[5a]) $[\alpha]_D^{30}$ +128° (MeOH)].

This material was identified by direct comparison with an authentic sample of thalrugosine (**6**).

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stesakine,[2a] *d*-isocorydine,[2a] *N*-acetylstepharine,[2b] 7-oxocrebanine,[2b] dehydrophanostenine,[2b] *N*-methyl-6,7-dimethoxy-1-isoquinolone,[2b] dehydroroemerine,[2b] cepharadione-A,[2b] lysicamine,[2b] cepharamine,[2b] 4-hydroxycrebanine,[2c] and (*R*)-roemeroline.[2c]

13) Elemental analyses were carried out on a sample recrystallized from MeOH.

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