JOC Article
pubs.acs.org/joc

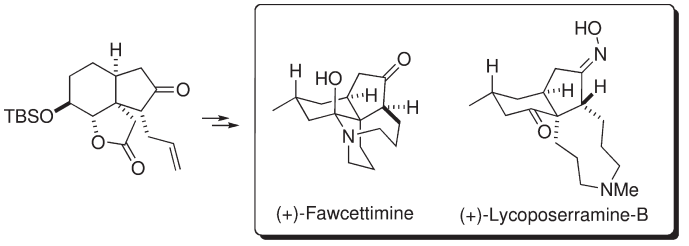
Total Syntheses of (+)-Fawcettimine and (+)-Lycoposerramine-B

Yasunari Otsuka, Fuyuhiko Inagaki, and Chisato Mukai*

Division of Pharmaceutical Sciences, Graduate School of Natural Science and Technology, Kanazawa University, Kakuma-machi, Kanazawa 920-1192, Japan

cmukai@kenroku.kanazawa-u.ac.jp

Received March 19, 2010

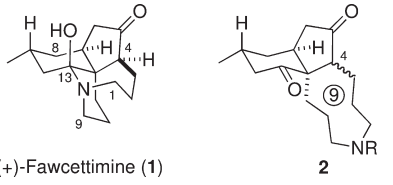


The total synthesis of (+)-fawcettimine was completed in a highly stereoselective manner starting from the oxatricyclo[7.3.0.0^{1,5}]dodecanedione derivative. The crucial step in this total synthesis involves the efficient construction of the azonane framework by the intramolecular Mitsunobu reaction. Furthermore, the first total synthesis of (+)-lycoposerramine-B was also accomplished via the common synthetic intermediate.

Introduction

Fawcettimine (**1**, Scheme 1),[1,2] one of the representative compounds of many *Lycopodium* alkaloids,[3] was first isolated by Burnell from *Lycopodium fawcetti* Lloyd et Underwood in 1959.[1] Because of an intriguing fused-tetracyclic structural feature involving four stereogenic centers and the carbinol amine moiety,[4] three total syntheses of fawcettimine (**1**) have so far been reported.[5−8] In 1979, Inubushi[5] and co-workers completed the first total synthesis of (±)-**1** via the Diels−Alder reaction and aldol reaction as crucial steps.

SCHEME 1. Fawcettimine (1) and Its Precursor 2



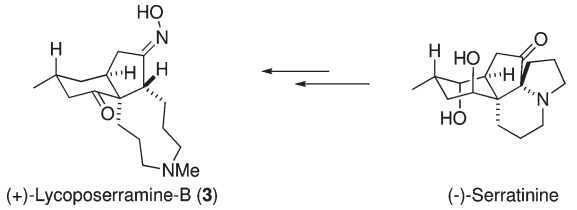
A more efficient and fewer step synthesis of (±)-**1** was achieved by Heathcock[6] and co-workers. They also revealed the details[6b] of an equilibrium between the two precursor C_4-*trans*- and C_4-*cis*-bicyclo[4.3.0] skeletons **2** (R = H), keto-amine isomers of **1** possessing an azonane ring (a nine-membered azacyclic skeleton), in which the former could spontaneously be transformed into fawcettimine (**1**) whereas the latter could not. Very recently, Toste[7] and co-workers accomplished the first asymmetric total synthesis of (+)-**1** by taking advantage of the organocatalytic asymmetric annulation as a key step; therefore, the absolute stereochemistry of the natural (+)-**1** was unambiguously established.

On the other hand, fawcettimine-related *Lycopodium* alkaloid, (+)-lycoposerramine-B (**3**) was recently isolated from the club moss *Lycopodium serratum* Thunb by Takayama,[9] and its structure was unambiguously established by chemical

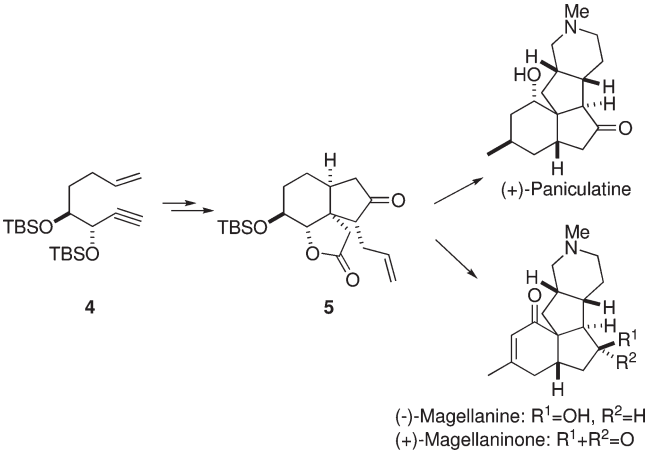
(1) Burnell, R. H. *J. Chem Soc*. **1959**, 3091–3093.
(2) (a) Burnell, R. H.; Mootoo, B. S. *Can. J. Chem*. **1961**, *39*, 1090–1093. (b) Burnell, R. H.; Chin, C. G.; Mootoo, B. S.; Taylor, D. R. *Can. J. Chem*. **1963**, *41*, 3091–3094.
(3) Ma, X.; Gang, D. R. *Nat. Prod. Rep*. **2004**, *21*, 752–772.
(4) (a) Inubushi, Y.; Ishii, H.; Harayama, T.; Burnell, R. H.; Ayer, W. A.; Altenkirk, B. *Tetrahedron Lett*. **1967**, 1069–1072. (b) Nishio, K.; Fujiwara, T.; Tomita, K.; Ishii, H.; Inubushi, Y.; Harayama, T. *Tetrahedron Lett*. **1969**, 861–864. (c) Inubushi, Y.; Harayama, T.; Yamaguchi, K.; Ishii, H. *Chem. Pharm. Bull*. **1981**, *29*, 3418–3420.
(5) (a) Harayama, T.; Takatani, M.; Inubushi, Y. *Tetrahedron Lett*. **1979**, *20*, 4307–4310. (b) Harayama, T; Takatani, M.; Inubushi, Y. *Chem. Pharm. Bull*. **1980**, *28*, 2394–2402.
(6) (a) Heathcock, C. H.; Smith, K. M.; Blumenkopf, T. A. *J. Am. Chem. Soc*. **1986**, *108*, 5022–5024. (b) Heathcock, C. H.; Blumenkopf, T. A.; Smith, K. M. *J. Org. Chem*. **1989**, *54*, 1548–1562.
(7) Linghu, X.; Kennedy-Smith, J. J.; Toste, F. D. *Angew. Chem., Int. Ed*. **2007**, *46*, 7671–7673.
(8) For the synthetic studies of fawcettimine, see: (a) Mehta, G.; Reddy, M. S.; Radhakrishnan, R.; Manjula, M. V.; Viswamitra, M. A. *Tetrahedron Lett*. **1991**, *32*, 6219–6222. (b) Liu, K.-M.; Chau, C.-M.; Sha, C.-K. *Chem. Commun*. **2008**, 91–93.
(9) Katakawa, K.; Kitajima, M.; Aimi, N.; Seki, H.; Yamaguchi, K.; Furihata, K.; Harayama, T.; Takayama, H. *J. Org. Chem*. **2005**, *70*, 658–663.

Published on Web 04/26/2010 DOI: 10.1021/jo100499h

SCHEME 2. Transformation of (−)-Serratinine into (+)-Lycoposerramine-B



SCHEME 3. Syntheses of (−)-Magellanine, (+)-Magellaninone, and (+)-Paniculatine from Common Intermediate 5

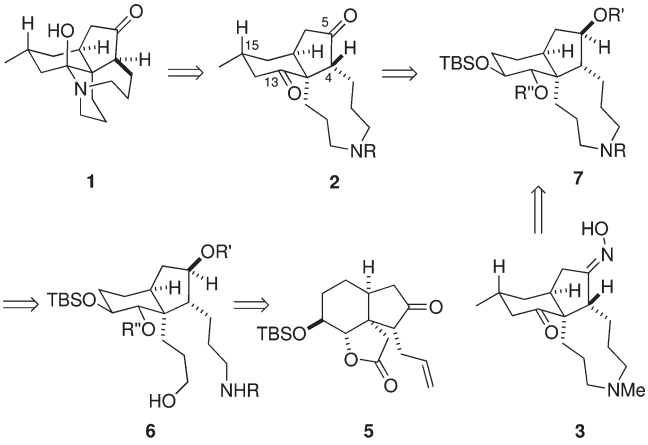


transformation from the known (−)-serratinine,[10] via consecutive dehydroxylation, oxidation, C−N bond cleavage, and oxime formation (Scheme 2). Takayama[9] proposed the hypothetical biogenetic route of **3**, in which fawcettimine (**1**) was regarded as a biogenetic precursor.

We have recently developed a highly stereoselective method[11] for the preparation of the bicyclo[4.3.0]nonenone derivative **5** starting from diethyl L-tartrate through the Pauson−Khand reaction of the corresponding enyne derivative **4**. The oxatricyclo[7.3.0.0^{1,5}]dodecanedione derivative **5** was then successfully transformed into three *Lycopodium* alkaloids, (−)-magellanine, (+)-magellaninone, and (+)-paniculatine, in a stereoselective manner (Scheme 3).

We now envisaged our retrosynthetic analysis of the total syntheses of two *Lycopodium* alkaloids, (+)-fawcettimine (**1**) and (+)-lycoposerramine-B (**3**) from the common starting material **5** as outlined in Scheme 4. The appropriate chemical modification of the functional groups of **5** would lead to **6**, the intramolecular Mitsunobu reaction of which should produce the azonane derivative **7**. The transformation of **7** into **2** would be realized via the construction of the α,β-unsaturated carbonyl functionality and introduction of a methyl group at the C_{15}-position by the Michael reaction. Removal of the protecting group on the nitrogen atom of **2**

SCHEME 4. Retrosynthetic Analysis of 1 and 3



should be accompanied by not only the epimerization at the C_4-position but also the ring-closing reaction resulting in the completion of the total synthesis of (+)-fawcettimine (**1**). In addition, some chemical modifications of the synthetic intermediate **7** involving oxidation of the C_{13}-hydroxyl group and oxime formation of the C_5-carbonyl functionality would lead to the first total synthesis of (+)-lycoposerramine-B (**3**).

Results and Discussion

At the beginning of this program, the carbonyl group of **5**[11] was converted into a benzyloxy group by the selective reduction and benzylation to afford **8** in 76% yield. Upon treatment with LAH, **8** furnished a mixture of the expected diol derivative and its TBS-migrated isomers. Acid treatment of these products converged into the triol derivative **9** as a sole product. The two hydroxyl groups of **9** were selectively protected with a TBS group, and the MOM group was introduced on the remaining secondary hydroxyl group. The allyl moiety was then transformed into a hydroxypropyl residue by hydroboration and oxidation to yield **10** in a 45% overall yield from **8**. The Mitsunobu reaction of **10** with *o*-nitrobenzenesulfonamide ($NsNH_2$) followed by selective desilylation on a primary hydroxyl group led to **11** in 86% yield. The one-carbon homologation of **11** that occurred under conventional conditions produced **12** in 43% yield (Scheme 5).

The efficient construction of the azonane framework must be one of the critical steps for this synthesis.[12] With the Ns-hydroxyl derivative **12** in hand, our endeavor focused on the ring-closing reaction using the intramolecular Mitsunobu reaction.[13] After screening several conditions, we found that the azonane derivative **13** was obtained in a highly efficient manner (96%) under the typical Mitsunobu conditions using diethyl azodicarboxylate and triphenylphosphine in toluene at room temperature (Scheme 6).

The next task was the introduction of a methyl group at the C_{15}-position. Thus, the production of the double bond on the cyclohexane ring of **13** was achieved by removal of the

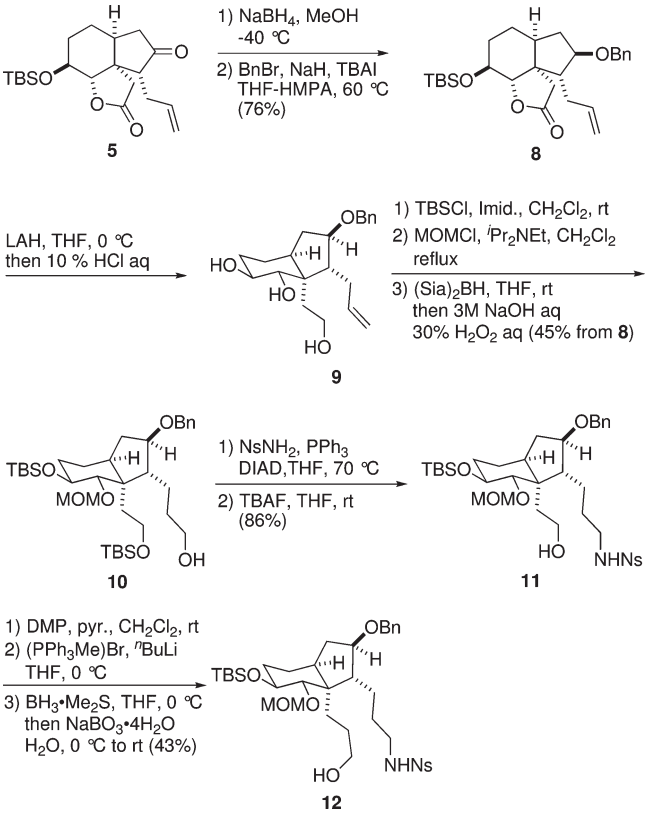
(10) (a) Inubushi, Y.; Ishii, H.; Yasui, B.; Hashimoto, M. *Tetrahedron Lett*. **1966**, *7*, 1537–1549. (b) Inubushi, Y.; Ishii, H.; Harayama, T. *Tetrahedron Lett*. **1966**, *7*, 1551–1559. (c) Inubushi, Y.; Ishii, H.; Yasui, B.; Hashimoto, M.; Harayama, T. *Chem. Pharm. Bull*. **1968**, *16*, 82–91. (d) Inubushi, Y.; Ishii, H.; Yasui, B.; Hashimoto, M.; Harayama, T. *Chem. Pharm. Bull*. **1968**, *16*, 92–100. (e) Inubushi, Y.; Ishii, H.; Yasui, B.; Harayama, T. *Chem. Pharm. Bull*. **1968**, *16*, 101–112.

(11) Kozaka, T.; Miyakoshi, N.; Mukai, C. *J. Org. Chem*. **2007**, *72*, 10147–10154.

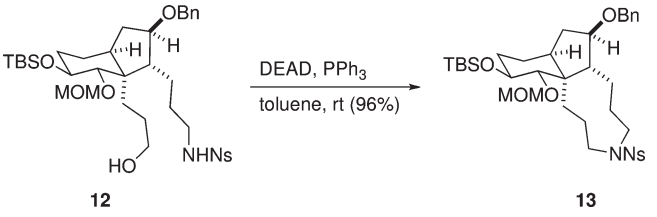
(12) In the previous three total syntheses,[5−7] construction of the azonane ring was attained in moderate yields.

(13) During this program ongoing, Takayama reported the similar Mitsunobu reaction for the formation of the azonane framework in the total synthesis of lycoposerramine-C and phlegmariurine-A; see: Nakayama, A.; Kogure, N.; Kitajima, M.; Takayama, H. *Org. Lett*. **2009**, *11*, 5554–5557.

SCHEME 5. Conversion of 5 into 12

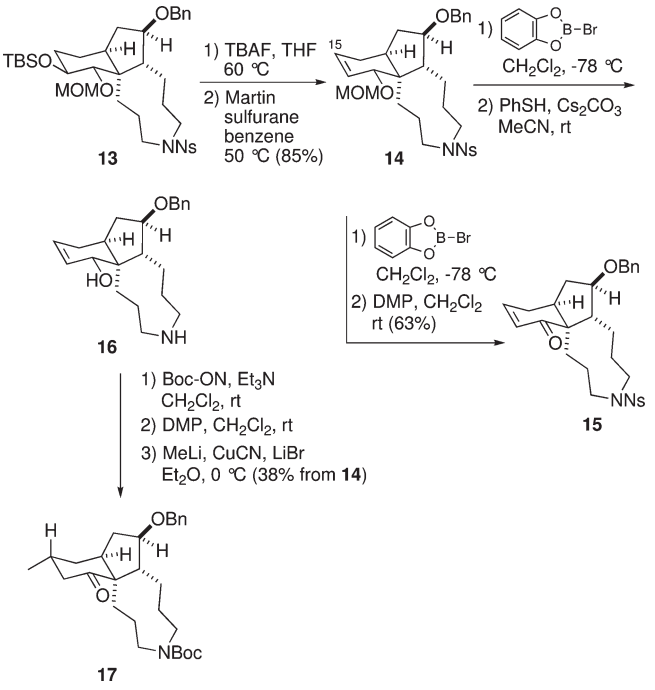


SCHEME 6. Formation of Perhydroazonine Framework 13



TBS group, followed by treatment with Martin sulfurane[14] to give **14** in 85% yield. Compound **14** was then exposed to *B*-bromocatecholborane[15] at −78 °C and Dess−Martin periodinane (DMP) to produce **15** in 63% yield. Although the 1,4-conjugation addition of $Me_2Cu(CN)Li_2$ to **15** occurred as expected under the standard conditions, the Ns group seemed to concomitantly react with the reagents that produced an intractable mixture.[16] In order to change the Ns group to a suitable protecting group, **15** was exposed to cesium thiophenoxide.[17] Although the desired NH analogue of **15** could be detected in the reaction mixture, considerable amounts of the 1,4-conjugated adducts of thiophenoxide at the C_{15}-position were formed as well. Therefore, an

SCHEME 7. Preparation of Compound 17



alternative route was devised. The removal of the MOM group of **14** with *B*-bromocatecholborane was followed by treatment with cesium thiophenoxide to afford the allyl alcohol−secondary amine derivative **16**, which was subsequently protected with a Boc group, oxidized, and reacted with $Me_2Cu(CN)Li_2$ to produce the desired C_{15}-methylated **17** in a 38% overall yield from **14** in a highly stereoselective manner (Scheme 7).

The benzyloxy functionality of **17** was then converted into a keto group under standard conditions to give **18** in 74% yield. Finally, according to the literature precedents,[5−7] the acid-catalyzed conversion of **18** into the target natural product was executed. Compound **18** was treated with formic acid in methylene chloride at room temperature that involved the following three-step transformation: (i) removal of the Boc group, (ii) isomerization at the C_4-position forming **19**, and (iii) the carbinol−amine formation resulting in the efficient production of (+)-fawcettimine (**1**)[18] in 81% yield (Scheme 8).

In connection with the total synthesis of (+)-fawcettimine (**1**), we were very much interested in the first total synthesis of the fawcettimine-related alkaloid, lycoposerramine-B (**3**). Thus, debenzylation of the synthetic intermediate **17** under a hydrogen atmosphere was followed by removal of the Boc group to afford the corresponding secondary amine derivative, which was subsequently exposed to the reductive methylation conditions producing **20**. PCC oxidation of **20** furnished **21**[19] in a 50% overall yield from **17**. Takayama[9] had regio- and stereoselectively transformed **21** into (+)-lycoposerramine-B under the devised oxime formation conditions. By referring to Takayama's procedure, we independently converted **21** into (+)-**3**. The treatment of **21** with

(14) (a) Arhart, R. J.; Martin, J. C. *J. Am. Chem. Soc.* **1972**, *94*, 5003–5010. (b) Kuramochi, A.; Usuda, H.; Yamatsugu, K.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2005**, *127*, 14200–14201. (c) Tokumaru, K.; Arai, S.; Nishida, A. *Org. Lett.* **2006**, *8*, 27–30.

(15) Boeckman, R. K., Jr.; Potenza, J. C. *Tetrahedron Lett.* **1985**, *26*, 1411–1414.

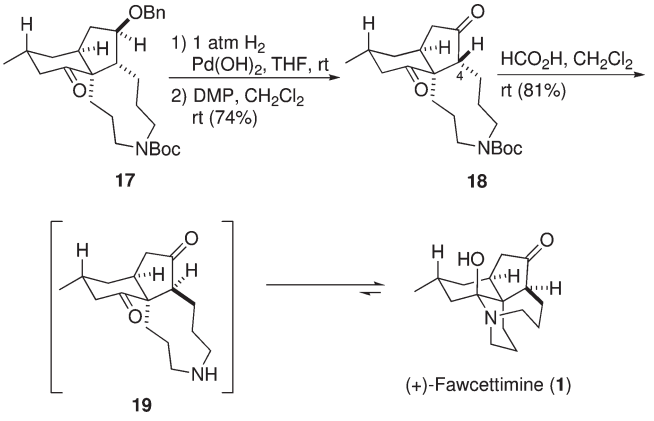
(16) Spectral analysis of the isolated products tentatively indicated that the Ns group was converted into some functionality, although their structures are uncertain yet.

(17) Kan, T.; Fukuyama, T. *Chem. Commun.* **2004**, 353–359.

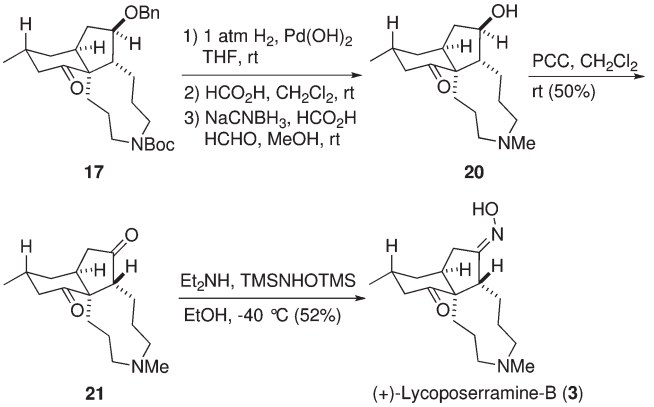
(18) The synthetic (+)-fawcettimine (**1**) was identical with the natural compound by comparison with their spectral data.

(19) The synthetic **21** was identical with the compound[9] derived from (−)-serratinine, by comparison of their spectral data.

SCHEME 8. Completion of Total Synthesis of (+)-Fawcettimine (1)



SCHEME 9. Completion of Total Synthesis of (+)-Lycoposerramine-B (3)



diethyamine and *N*,*O*-bis(trimethylsilyl)hydroxylamine in ethanol at −40 °C produced, after purification using amino silica gel, (+)-lycoposerramine-B (**3**)[20,21] in 52% yield along with the (*Z*)-isomer (33%). Thus, we have accomplished the first total synthesis of (+)-lycoposerramine-B (**3**) in a stereoselective manner (Scheme 9).

In conclusion, we have completed the total syntheses of two *Lycopodium* alkaloids, (+)-fawcettimine (**1**) and (+)-lycoposerramine-B (**3**), in a stereoselective manner from the lactone derivative **5**, which was derived from the Pauson−Khand product of the enyne compound **4**. In combination with the previous total syntheses of three *Lycopodium* alkaloids, (−)-magellanine, (+)-magenallinone, and (+)-paniculatine, the present total syntheses of additional two *Lycopodium* alkaloids, (+)-fawcettimine and (+)-lycoposerramine-B, strongly indicate that the lactone derivative **5** is a useful synthetic intermediate for the total syntheses of *Lycopodium* alkaloids.

Experimental Section

General Methods. Melting points are uncorrected. IR spectra were measured in $CHCl_3$. ^1H NMR spectra were taken in $CDCl_3$. $CHCl_3$ (7.26 ppm) for silyl compounds and tetramethylsilane (0.00 ppm) for compounds without a silyl group were used as internal standards unless otherwise stated. ^{13}C NMR spectra were recorded in $CDCl_3$ with $CDCl_3$ (77.00 ppm) as an internal standard unless otherwise stated. All reactions were carried out under a nitrogen atmosphere. Silica gel (silica gel 60, 230−400 mesh), Al_2O_3, and amino silica gel were used for chromatography. Organic extracts were dried over anhydrous Na_2SO_4.

(1*S*,5*S*,6*S*,9*S*,11*R*,12*R*)-11-Benzyloxy-6-*tert*-butyldimethylsilyloxy-12-(2-propenyl)-4-oxatricyclo[7.3.0.0^{1,5}]dodecan-3-one ((−)-8). To a solution of (−)-**5**[11] (1.09 g, 2.99 mmol) in MeOH (30 mL) was added $NaBH_4$ (226 mg, 5.98 mmol) at −40 °C. The reaction mixture was stirred for 5 h at the same temperature, quenched by addition of acetone, extracted with AcOEt, washed with water and brine, dried, and concentrated to dryness. The residue was passed through a short pad of silica gel with hexane−AcOEt (4:1) to afford the crude alcohol. To a solution of the crude alcohol in THF (3 mL) was added NaH (60% in oil; 180 mg, 4.50 mmol) at 0 °C. The reaction mixture was stirred for 30 min at the same temperature, and then BnBr (1.0 mL, 8.4 mmol), TBAI (554 mg, 1.50 mmol), and HMPA (0.6 mL, 3 mmol) were added to the reaction mixture at 0 °C. The reaction mixture was stirred for 24 h at 60 °C, quenched by addition of saturated aqueous $Na_2S_2O_3$, extracted with AcOEt, washed with water and brine, dried, and concentrated to dryness. The residue was chromatographed on silica gel with hexane−AcOEt (10:1) to give (−)-**8** (1.04 g, 76% from (−)-**5**) as a colorless oil: $[\alpha]^{26}_D$ −22.6 (*c* 0.44, $CHCl_3$); IR 1782, 1765, 1639 cm^{-1}; ^1H NMR δ 7.34−7.30 (m, 4H), 7.27−7.25 (m, 1H), 5.90−5.81 (m, 1H), 5.08 (d, 1H, *J* = 17.1 Hz), 5.00 (d, 1H, *J* = 10.4 Hz), 4.49, 4.37 (ABq, 2H, *J* = 12.2 Hz), 4.32 (d, 1H, *J* = 3.1 Hz), 4.15 (d, 1H, *J* = 3.1 Hz), 3.59−3.56 (m, 1H), 2.80−2.76 (m, 1H), 2.55, 2.04 (ABq, 2H, *J* = 17.1 Hz), 2.27−2.21 (m, 1H), 2.15−2.06 (m, 2H), 2.01 (ddd, 1H, *J* = 25.0, 12.8, 4.9 Hz), 1.77−1.72 (m, 1H), 1.62−1.55 (m, 3H), 1.40−1.35 (m, 1H), 0.90 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H); ^{13}C NMR δ 175.6, 138.8, 137.1, 128.2, 127.24, 127.22, 115.9, 84.5, 81.7, 71.1, 66.9, 50.6, 46.2, 41.3, 37.6, 35.0, 34.8, 27.3, 25.7, 22.6, 17.9, −5.0, −5.1; FAB MS *m*/*z* 457 (M^+ + 1, 7.0); FAB HRMS calcd for $C_{27}H_{41}O_4Si$ 457.2774, found 457.2779.

(1*S*,2*S*,3*S*,6*S*,8*R*,9*R*)-8-Benzyloxy-3-*tert*-butyldimethylsilyloxy-1-(2-*tert*-butyldimethylsilyloxyethyl)-9-(3-hydroxypropyl)-2-methoxymethoxybicyclo[4.3.0]nonane ((−)-10). To a suspension of $LiAlH_4$ (962 mg, 25.4 mmol) in THF (37 mL) was added lactone (−)-**8** (3.86 g, 8.45 mmol) in THF (19 mL) at 0 °C. The reaction mixture was stirred for 1 h at room temperature, 10% aqueous HCl was added at 0 °C, and the mixture was stirred for 1 h at room temperature, extracted with AcOEt, washed with water, saturated aqueous $NaHCO_3$, and brine, dried, and concentrated to dryness. The residue was passed through a short pad of silica gel with hexane−AcOEt (1:1) to afford the crude triol. To a solution of crude triol in CH_2Cl_2 (4 mL) were added TBSCl (3.17 g, 21.1 mmol) and imidazole (2.88 g, 42.3 mmol) at room temperature. The reaction mixture was stirred for 24 h at the same temperature, quenched by addition of water, extracted with AcOEt, washed with water and brine, dried, and concentrated to dryness. The residue was passed through a short pad of silica gel with hexane−AcOEt (20:1) to afford the crude alcohol. To a solution of the crude alcohol in CH_2Cl_2 (17 mL) were added $^i Pr_2NEt$ (5.9 mL, 34 mmol) and MOMCl (1.9 mL, 25 mmol) at room temperature. The reaction mixture was refluxed for 12 h, quenched by addition of saturated aqueous $NaHCO_3$, extracted with CH_2Cl_2, washed with water and brine, dried, and concentrated to dryness. The residue was passed through a short pad of silica gel with hexane−AcOEt (20:1) to give crude MOM ether. To a solution of crude MOM ether in THF (28 mL) was added $(Sia)_2BH$ (1.0 M in THF; 8.5 mL, 8.5 mmol) at 0 °C. The reaction mixture was warmed to room temperature and stirred

(20) The synthetic (+)-lycoposerramine-B (**3**) was identical with the natural compound[9] by comparison of their spectral data.

(21) The synthetic (+)-lycoposerramine-B shows $[\alpha]^{24}_D$ +149 (*c* 0.20, $CHCl_3$). No description on the $[\alpha]_D$ value of the natural lycoposerramine-B is available, although its CD spectral data were recorded.[9]

for 1 h. The reaction mixture was then cooled to 0 °C, and 30% aqueous H_2O_2 (8 mL) and aqueous 3 M NaOH (8 mL) were slowly added. The reaction mixture was warmed to room temperature, stirred for 1 h, extracted with AcOEt, washed with water and brine, dried, and concentrated to dryness. The residue was chlomatographed on silica gel with hexane−AcOEt (4:1) to give (−)-**10** (2.19 g, 45% from (−)-**8**) as a colorless oil: $[\alpha]^{28}_D$ −27.5 (*c* 0.94, $CHCl_3$); IR 3448 cm^{-1}; ^1H NMR δ 7.41−7.36 (m, 4H), 7.32−7.29 (m, 1H), 4.79, 4.73 (ABq, 2H, *J* = 6.4 Hz), 4.57, 4.47 (ABq, 2H, *J* = 12.0 Hz), 4.05−3.99 (m, 1H), 3.85−3.80 (m, 1H), 3.79−3.77 (m, 1H), 3.74−3.68 (m, 3H), 3.64 (d, 1H, *J* = 8.8 Hz), 3.43 (s, 3H), 2.52 (d, 1H, *J* = 12.5 Hz), 2.17 (dt, 1H, *J* = 13.7, 8.1 Hz), 2.00−1.89 (m, 2H), 1.83−1.74 (m, 3H), 1.67−1.59 (m, 6H), 1.52 (ddd, 1H, *J* = 14.5, 10.5, 3.7 Hz), 0.96 (s, 9H), 0.94 (s, 9H), 0.13−0.12 (m, 12H); ^{13}C NMR δ 139.0, 128.2, 127.5, 127.2, 99.5, 85.6, 85.0, 72.5, 70.9, 63.0, 61.3, 55.7, 50.4, 49.2, 42.1, 36.4, 35.5, 31.3, 29.8, 26.1, 25.9, 25.2, 22.3, 18.5, 18.0, −4.6, −4.7, −5.1, −5.2; FAB MS *m*/*z* 659 ($M^+ + 23$, 9.2); FAB HRMS calcd for $C_{35}H_{65}O_6Si_2$ 637.4320, found 637.4322.

(1*S*,2*S*,3*S*,6*S*,8*R*,9*R*)-8-Benzyloxy-3-*tert*-butyldimethylsilyloxy-1-(2-hydroxyethyl)-2-methoxymethoxy-9-[3-(2-nitrobenzenesulfonylamino)propyl]bicyclo[4.3.0]nonane ((−)-11). To a mixture of the alcohol (−)-**10** (307 mg, 0.482 mmol), 2-nitrobenzenesulfonamide (292 mg, 1.45 mmol), and PPh_3 (164 mg, 0.626 mmol) in THF (5 mL) was added DIAD (127 mg, 0.626 mmol) at room temperature. The reaction mixture was heated at 70 °C and stirred for 6 h. The reaction mixture was filtered through a pad of Celite, and the filtrate was concentrated to dryness. The residue was passed through a short pad of silica gel with hexane−AcOEt (4:1) to afford the crude sulfonamide. To a solution of the crude sulfonamide in THF (5 mL) was added dropwise TBAF (1.0 M in THF; 0.5 mL, 0.5 mmol) at room temperature. The reaction mixture was stirred for 12 h at the same temperature, quenched by addition of saturated aqueous NH_4Cl, extracted with AcOEt, washed with water and brine, dried, and concentrated to dryness. The residue was chromatographed on silica gel with hexane−AcOEt (2:1) to give (−)-**11** (291 mg, 86% from (−)-**10**) as a colorless oil: $[\alpha]^{30}_D$ −2.53 (*c* 0.96, $CHCl_3$); IR 3454, 3390, 1543 cm^{-1}; ^1H NMR δ 8.11−8.07 (m, 1H), 7.82−7.78 (m, 1H), 7.69−7.66 (m, 2H), 7.36−7.31 (m, 4H), 7.29−7.26 (m, 1H), 5.45 (t, 1H, *J* = 5.9 Hz), 4.79, 4.77 (ABq, 2H, *J* = 6.1 Hz), 4.46, 4.35 (ABq, 2H, *J* = 11.7 Hz), 3.88−3.83 (m, 1H), 3.80−3.78 (m, 1H), 3.72 (d, 1H, *J* = 9.3 Hz), 3.68−3.61 (m, 3H), 3.37 (s, 3H), 3.20−3.14 (m, 1H), 3.10−3.03 (m, 1H), 2.45 (d, 1H, *J* = 12.5 Hz), 2.13−2.05 (m, 1H), 1.89 (ddd, 1H, *J* = 15.9, 7.1, 4.2 Hz), 1.80−1.74 (m, 4H), 1.67−1.56 (m, 3H), 1.53−1.45 (m, 3H), 1.41−1.35 (m, 1H), 0.88 (s, 9H), 0.06 (s, 3H), 0.05 (s, 3H); ^{13}C NMR δ 148.0, 138.8, 133.9, 133.4, 132.6, 130.9, 128.3, 127.5, 127.4, 125.2, 99.9, 85.4, 84.3, 72.0, 70.8, 60.4, 56.2, 51.0, 48.7, 43.8, 43.6, 36.0, 35.4, 30.1, 28.0, 25.83, 25.81, 21.8, 17.9, −4.6, −4.7; FAB MS *m*/*z* 729 ($M^+ + 23$, 2.7); FAB HRMS calcd for $C_{35}H_{55}N_2O_9SSi$ 707.3397, found 707.3394.

(1*S*,2*S*,3*S*,6*S*,8*R*,9*R*)-8-Benzyloxy-3-*tert*-butyldimethylsilyloxy-1-(3-hydroxypropyl)-2-methoxymethoxy-9-[3-(2-nitrobenzenesulfonylamino)propyl]bicyclo[4.3.0]nonane ((−)-12). To a solution of (−)-**11** (688 mg, 0.976 mmol) in CH_2Cl_2 (10 mL) and pyridine (1 mL) was added Dess−Martin periodinane (434 mg, 1.02 mmol) at room temperature. The reaction mixture was stirred for 30 min at the same temperature, quenched by saturated aqueous $Na_2S_2O_3$, extracted with AcOEt, washed with 1 N HCl, saturated aqueous $NaHCO_3$, water, and brine, dried, and concentrated to dryness. The residue was passed through a short pad of silica gel with hexane−AcOEt (4:1) to afford the crude aldehyde. To a suspension of (PPh_3Me)Br (1.05 g, 2.44 mmol) in THF (9 mL) was added *n*-BuLi (1.46 M in hexane; 1.7 mL, 2.4 mmol) at 0 °C. The reaction mixture was stirred for 30 min at the same temperature, and then a solution of crude aldehyde in THF (2 mL) was added via cannula. The reaction mixture was stirred for 30 min at the same temperature, quenched by addition of saturated aqueous NH_4Cl, extracted with AcOEt, washed with water and brine, dried, and concentrated to dryness. The residue was passed through a short pad of silica gel with hexane−AcOEt (4:1) to afford the crude olefin compound. To a solution of the crude olefin compound in THF (10 mL) was added $BH_3 \cdot Me_2S$ (1 M in THF; 1.0 mL, 1.0 mmol) at 0 °C, and the mixture was stirred for 30 min at the same temperature. To the reaction mixture were added H_2O (3 mL) and $NaBO_3 \cdot 4H_2O$[22] (150 mg, 1.46 mmol) at the same temperature, and the reaction mixture was warmed to room temperature, stirred for 1 h, extracted with AcOEt, washed with water and brine, dried, and concentrated to dryness. The residue was chromatographed on silica gel with hexane−AcOEt (2:1) to give (−)-**12** (304 mg, 43% from (−)-**11**) as a colorless oil: $[\alpha]^{28}_D$ −13.5 (*c* 0.51, $CHCl_3$); IR 3602, 3381, 1543 cm^{-1}; ^1H NMR δ 8.10−8.08 (m, 1H), 7.79−7.77 (m, 1H), 7.69−7.66 (m, 2H), 7.34−7.26 (m, 5H), 5.51 (t, 1H, *J* = 5.6 Hz), 4.73, 4.68 (ABq, 2H, *J* = 6.3 Hz), 4.40 (s, 2H), 3.80−3.57 (m, 1H), 3.63−3.76 (m, 4H), 3.54 (d, 1H, *J* = 8.0 Hz), 3.34 (s, 3H), 3.12−3.10 (m, 2H), 2.44 (d, 1H, *J* = 11.8 Hz), 2.04−1.98 (m, 1H), 1.91−1.87 (m, 1H), 1.74−1.49 (m, 11H), 1.31−1.26 (m, 1H), 1.11−1.04 (m, 1H), 0.88 (s, 9H), 0.06 (s, 3H), 0.05 (s, 3H); ^{13}C NMR δ 148.0, 138.9, 133.9, 133.3, 132.6, 131.0, 128.2, 127.4, 127.3, 125.2, 99.5, 86.4, 85.2, 72.4, 70.8, 63.8, 55.7, 50.0, 49.9, 44.0, 40.7, 35.2, 29.5, 29.3, 28.3, 28.2, 26.4, 25.9, 22.4, 18.0, −4.6, −4.7; FAB MS *m*/*z* 743 ($M^+ + 23$, 3.2); FAB HRMS calcd for $C_{36}H_{57}N_2O_9SSi$ 721.3554, found 721.3550.

(1*S*,2*S*,3*S*,6*S*,8*R*,9*R*)-8-Benzyloxy-3-*tert*-butyldimethylsilyloxy-2-methoxymethoxy-13-(2-nitrobenzenesulfonyl)-13-azatricyclo[7.7.0.0^{1,6}]hexadecane ((+)-13). To a mixture of (−)-**12** (86.1 mg, 0.119 mmol) and PPh_3 (93.5 mg, 0.355 mmol) in toluene (8 mL) was added DEAD (40% in toluene; 0.16 mL, 0.35 mmol) at room temperature. The mixture was stirred for 30 min at the same temperature. The reaction mixture was filtered through a pad of Celite and concentrated under reduced pressure. The residue was chromatographed on silica gel with hexane−AcOEt (2:1) to give (+)-**13** (81.0 mg, 96%) as a colorless oil: $[\alpha]^{26}_D$ +1.39 (*c* 0.42, $CHCl_3$); IR 1547 cm^{-1}; ^1H NMR δ 7.91−7.89 (m, 1H), 7.68−7.63 (m, 2H), 7.58−7.56 (m, 1H), 7.36−7.31 (m, 4H), 7.27−7.24 (m, 1H) 4.76, 4.72 (ABq, 2H, *J* = 6.1 Hz), 4.58, 4.43 (ABq, 2H, *J* = 4.4 Hz), 3.78−3.66 (m, 3H), 3.57−3.53 (m, 2H), 3.38 (s, 3H), 3.13−3.03 (m, 2H), 2.40 (d, 1H, *J* = 8.0 Hz), 2.22−2.16 (m, 1H), 2.05−1.93 (m, 4H), 1.89−1.85 (m, 1H), 1.79−1.71 (m, 4H), 1.69−1.65 (m, 2H), 1.62−1.55 (m, 2H), 1.51−1.47 (m, 1H), 0.89 (s, 9H), 0.07 (s, 3H), 0.06 (s, 3H); ^{13}C NMR δ 148.4, 139.0, 133.2, 132.6, 131.3, 130.5, 128.3, 127.6, 127.3, 123.9, 100.2, 88.5, 86.3, 73.0, 71.1, 56.2, 51.8, 50.5, 50.2, 47.9, 42.6, 34.5, 30.4, 28.3, 25.91, 25.86, 25.3, 24.5, 21.8, 18.0, −4.5, −4.6; FAB MS *m*/*z* 725 ($M^+ + 23$, 5.6). FAB HRMS calcd for $C_{36}H_{55}N_2O_8SSi$ 703.3448, found 703.3447.

(1*S*,2*S*,6*S*,8*R*,9*R*)-8-Benzyloxy-2-methoxymethoxy-13-(2-nitrobenzenesulfonyl)-13-azatricyclo[7.7.0.0^{1,6}]hexadecan-3-ene ((−)-14). To a solution of (+)-**13** (698 mg, 0.933 mmol) in THF (9 mL) was added TBAF (1.0 M in THF; 1.4 mL, 1.4 mmol) at room temperature. The reaction mixture was stirred for 6 h at 60 °C, quenched by addition of saturated aqueous NH_4Cl, extracted with AcOEt, washed with water and brine, dried, and concentrated to dryness. The residue was passed through a short pad of silica gel with hexane−AcOEt (1:2) to afford the crude alcohol. To a solution of the crude alcohol in benzene (1 mL) was added Martin sulfurane (1.00 g, 1.49 mmol) at room temperature. The reaction mixture was stirred for 6 h at 50 °C, quenched by

(22) Only a trace amount of the desired **12** was obtained when the resulting organoborane was exposed to 30% aqueous H_2O_2 and aqueous 3 M NaOH; see: Kabalka, G. W.; Shoup, T. M.; Goudgaon, N. M. *J. Org. Chem.* **1989**, *54*, 5930–5933.

addition of saturated aqueous $NaHCO_3$, extracted with AcOEt, washed with water and brine, dried, and concentrated to dryness. The residue was chromatographed on silica gel with hexane−AcOEt (4:1) to give (−)-**14** (429 mg, 85% from (+)-**13**) as a colorless oil: $[\alpha]^{19}_D$ −28.1 (*c* 0.54, $CHCl_3$); IR 1547 cm^{-1}; ^1H NMR δ 7.91−7.89 (m, 1H), 7.68−7.63 (m, 2H), 7.58−7.56 (m, 1H), 7.33 (d, 4H, *J*=4.2 Hz), 7.28−7.25 (m, 1H), 5.67−5.64 (m, 1H), 5.62−5.59 (m, 1H), 4.73, 4.68 (ABq, 2H, *J* = 6.4 Hz), 4.48 (s, 2H), 4.43 (brs, 1H), 3.75−3.72 (m, 1H), 3.61−3.51 (m, 2H), 3.38 (s, 3H), 3.09 (dt, 1H, *J*= 14.2, 5.4 Hz), 2.92 (dt, 1H, *J* = 13.9, 3.9 Hz), 2.18−1.86 (m, 9H), 1.82−1.72 (m, 2H), 1.61 (dt, 1H, *J*=15.4, 5.6 Hz), 1.51 (td, 1H, *J*= 13.2, 6.1 Hz), 1.42−1.36 (m, 1H); ^{13}C NMR δ 148.1, 138.7, 133.2, 132.6, 131.3, 130.5, 128.3, 127.7, 127.5, 127.4, 125.2, 123.9, 97.3, 88.5, 79.0, 71.2, 55.6, 50.9, 50.4, 48.3, 47.5, 39.8, 36.7, 28.5, 25.6, 25.3, 24.8, 24.7; FAB MS *m*/*z* 593 (M^++23, 5.7); FAB HRMS calcd for $C_{30}H_{38}N_2NaO_7S$ 593.2297, found 593.2304.

(1*S*,6*S*,8*R*,9*R*)-8-Benzyloxy-13-(2-nitrobenzenesulfonyl)-13-azatricyclo[7.7.0.0^{1,6}]hexadecan-3-en-2-one ((+)-15). To a solution of (−)-**14** (75.7 mg, 0.132 mmol) in CH_2Cl_2 (7 mL) at −78 °C was added *B*-bromocatecholborane (78.9 mg, 0.397 mmol) in CH_2Cl_2 (1 mL). The reaction mixture was stirred for 30 min at the same temperature, quenched by addition of 2 M aqueous NaOH (3 mL), and stirred for 30 min at room temperature. The mixture was extracted with CH_2Cl_2, washed with water and brine, dried, and concentrated to dryness. The residue was passed through a short pad of silica gel with hexane−AcOEt (1:1) to afford the crude alcohol. To a solution of the crude alcohol in CH_2Cl_2 (2 mL) was added Dess−Martin periodinane (67.2 mg, 0.158 mmol) at room temperature. The reaction mixture was stirred for 30 min at the same temperature, quenched by addition of saturated aqueous $Na_2S_2O_3$, extracted with AcOEt, washed with water and brine, dried, and concentrated to dryness. The residue was chromatographed on silica gel with hexane−AcOEt (1:1) to give (+)-**15** (43.9 mg, 63% from (−)-**14**) as a colorless oil: $[\alpha]^{23}_D$ +107 (*c* 0.24, $CHCl_3$); IR 1659, 1549 cm^{-1}; ^1H NMR δ 7.91 (dd, 1H, *J*=7.6, 1.7 Hz), 7.72−7.66 (m, 2H), 7.59 (dd, 1H, *J* = 7.6, 1.7 Hz), 7.32−7.22 (m, 5H), 6.71−6.68 (m, 1H), 5.98 (dd, 1H, *J* = 10.0, 2.0 Hz), 4.45, 4.20 (ABq, 2H, *J*=11.7 Hz), 3.60−3.52 (m, 3H), 3.17−3.11 (m, 1H), 2.91 (dt, 1H, *J*=12.9, 4.0 Hz), 2.74 (brs, 1H), 2.59 (ddt, 1H, *J*= 20.0, 5.4, 2.5 Hz), 2.39−2.17 (m, 4H), 2.07−2.00 (m, 1H), 1.93−1.79 (m, 3H), 1.58−1.47 (m, 3H), 0.99−0.93 (m, 1H); ^{13}C NMR δ 200.5, 148.8, 144.8, 138.4, 133.5, 131.2, 130.9, 130.6, 128.8, 128.2, 127.7, 127.2, 123.9, 86.1, 69.6, 55.9, 50.3, 45.02, 44.98, 39.8, 37.0, 28.8., 26.0, 25.2, 21.6, 21.5; FAB MS *m*/*z* 547 (M^+ + 23, 12.7); FAB HRMS calcd for $C_{28}H_{33}N_2O_6S$ 525.2059, found 525.2054.

(1*S*,4*R*,6*S*,8*R*,9*R*)-8-Benzyloxy-13-(*tert*-butoxycarbonyl)-4-methyl-13-azatricyclo[7.7.0.0^{1,6}]hexadecan-3-en-2-one ((+)-17). To a solution of (−)-**14** (101 mg, 0.177 mmol) in CH_2Cl_2 (9 mL) at −78 °C was added *B*-bromocatecholborane (106 mg, 0.531 mmol) in CH_2Cl_2 (1 mL). The reaction mixture was stirred for 3 h at the same temperature, quenched by addition of 2 M aqueous NaOH (5 mL), and stirred for 30 min at room temperature. The mixture was extracted with CH_2Cl_2, washed with water and brine, dried, and concentrated to dryness. The residue was passed through a short pad of silica gel with hexane−AcOEt (1:1) to afford the crude alcohol. To a solution of the crude alcohol in MeCN (4 mL) were added Cs_2CO_3 (173 mg, 0.531 mmol) and PhSH (0.5 M in MeCN; 0.7 mL, 0.4 mmol) at room temperature. The reaction mixture was stirred for 12 h at the same temperature, the resulting suspension was diluted with CH_2Cl_2, cooled in an ice bath, and filtered through a pad of Celite, and the filtrate was concentrated to afford the crude amine. To the mixture of the crude amine and Et_3N (0.5 mL) in CH_2Cl_2 (3.5 mL) was added Boc-ON (89.2 mg, 0.354 mmol) at room temperature. The reaction mixture was stirred for 12 h at the same temperature, quenched by addition of water, extracted with AcOEt, washed with water and brine, dried, and concentrated to dryness. The residue was passed through a short pad of silica gel with hexane−AcOEt (2:1) to afford the crude alcohol. To a solution of the crude alcohol in CH_2Cl_2 (4 mL) was added Dess−Martin periodinane (90.1 mg, 0.212 mmol) at room temperature. The reaction mixture was stirred for 30 min at the same temperature, quenched by addition of saturated aqueous $Na_2S_2O_3$, extracted with AcOEt, washed with water and brine, dried, and concentrated to dryness. The residue was passed through a short pad of silica gel with hexane−AcOEt (2:1) to afford the crude ketone. To a suspension of CuCN (47.6 mg, 0.531 mmol) and LiBr (76.9 mg, 0.885 mmol) in Et_2O (5 mL) was added MeLi (1 M in Et_2O; 1.0 mL, 1.0 mmol) at 0 °C. The reaction mixture was stirred for 20 min at the same temperature. To the reaction mixture was added a solution of crude ketone in Et_2O (1 mL) at the same temperature. The reaction mixture was stirred for 30 min at the same temperature, quenched by addition of saturated aqueous NH_4Cl, and passed through a short pad of Celite with Et_2O. The filtrate was extracted with Et_2O, washed with water and brine, dried, and concentrated to dryness. The residue was chromatographed on silica gel with hexane−AcOEt (4:1) to give (+)-**17** (30.6 mg, 38% from (−)-**14**) as a colorless oil: $[\alpha]^{22}_D$ +99.7 (*c* 0.55, $CHCl_3$); IR 1684 cm^{-1}; ^1H NMR some peaks doubled and/or broadened due to amide conformational isomers δ 7.33−7.24 (m, 5H), 4.46, 4.14 (ABq, 2H, *J* = 12.0 Hz), 3.78−3.71 (m, 1H), 3.58−3.44 (m, 2H), 3.13−3.01 (m, 1H), 2.88−2.83 (m, 1H), 2.26−2.14 (m, 5H), 1.94−1.77 (m, 2H), 1.68−1.41 (m, 19H), 0.93 (d, 3H, *J* = 6.0 Hz), ^{13}C NMR some peaks doubled due to amide conformational isomers δ 212.1, 157.1, 138.7, 128.2, 127.5, 127.1, 85.9, 79.2, 68.8, 57.9, 49.0, 47.7, 44.0, 42.7, 36.0, 34.0, 28.5, 27.6, 26.5, 23.4, 22.2, 21.7, 21.4, 20.7; FAB MS *m*/*z* 478 (M^+ + 23, 6.2); FAB HRMS calcd for $C_{28}H_{42}NO_4$ 456.3114, found 456.3112.

(1*S*,4*R*,6*S*,9*R*)-13-(*tert*-Butoxycarbonyl)-4-methyl-13-azatricyclo[7.7.0.0^{1,6}]hexadecane-2,8-dione ((+)-18). A mixture of (+)-**17** (15.9 mg, 3.49×10^{-2} mmol) and $Pd(OH)_2$ (20 wt % on carbon; 4 mg) in THF (1 mL) was stirred under hydrogen atmosphere (1 atm) for 24 h at room temperature. The reaction mixture was passed through a short pad of Celite, and the filtrate was concentrated to dryness. The residue was passed through a short pad of silica gel with hexane−AcOEt (4:1) to afford the crude alcohol. To a solution of the crude alcohol in CH_2Cl_2 (1 mL) was added Dess−Martin periodinane (17.8 mg, 4.70×10^{-2} mmol) at room temperature. The reaction mixture was stirred for 30 min at the same temperature, quenched by addition of saturated aqueous $Na_2S_2O_3$ and saturated aqueous $NaHCO_3$, extracted with CH_2Cl_2, washed with water and brine, dried, and concentrated to dryness. The residue was chromatographed on silica gel with hexane−AcOEt (2:1) to give (+)-**18** (9.4 mg, 74% from (+)-**17**) as a colorless amorphous solid: $[\alpha]^{13}_D$ +143 (*c* 0.20, $CHCl_3$); IR 1736, 1701, 1686 cm^{-1}; ^1H NMR some peaks doubled and/or broadened due to amide conformational isomers δ 3.70−3.41 (m, 2H), 3.02−2.75 (m, 3H), 2.54−2.52 (m, 1H), 2.38−2.08 (m, 5H), 1.97−1.11 (m, 10H), 1.46 (s, 9H), 1.07 (d, 3H, *J* = 6.4 Hz); ^{13}C NMR some peaks doubled due to amide conformational isomers δ 219.0, 213.7, 156.8, 79.6, 59.9, 49.5, 47.4, 46.6, 44.7, 42.2, 38.9, 30.9, 30.1, 28.5, 27.9, 25.5, 22.3, 22.1, 21.0; EI MS *m*/*z* 363 (M^+, 5.1); EI HRMS calcd for $C_{21}H_{33}NO_4$ 363.2410, found 363.2404.

Fawcettimine (1). To a solution of (+)-**18** (11.1 mg, 3.05×10^{-2} mmol) in CH_2Cl_2 (1 mL) was added HCO_2H (1.0 mL, 30 mmol) at 0 °C. The reaction mixture was then warmed to room temperature and stirred for 12 h at the same temperature, quenched by addition of saturated aqueous $NaHCO_3$, extracted with $CHCl_3$, washed with water and brine, dried, and concentrated to dryness. The residue was chromatographed on Al_2O_3 with hexane−AcOEt (1:1) to give (+)-**1** (6.5 mg, 81%) as a white foam: $[\alpha]^{19}_D$ +71.0 (*c* 0.19, MeOH) [lit.[1] $[\alpha]^{rt}_D$ +89

(*c* 0.55, MeOH)]; IR 3329, 1728 cm^{-1}; ^1H NMR δ 3.49 (ddd, 1H, J = 13.8, 9.6, 4.1 Hz), 3.29 (td, 1H, J = 15.1, 4.1 Hz), 2.92 (dd, 1H, J = 15.1, 5.5 Hz), 2.76 (ddd, 1H, J = 14.6, 5.5, 4.6 Hz), 2.66 (dd, 1H, J = 17.8, 13,7 Hz), 2.28−2.05 (m, 6H), 1.97−1.85 (m, 4H), 1.64 (d, 1H, J = 14.2 Hz), 1.50−1.22 (m, 6H), 0.96 (d, 3H, J = 6.4 Hz); ^{13}C NMR δ 220.3, 60.1, 53.5, 50.0, 48.2, 44.3, 43.2, 41.9, 35.7, 31.9, 28.5, 28.1, 23.7, 22.4, 21.8; EI MS m/z 263 (M^+, 47.9); EI HRMS calcd for $C_{16}H_{25}NO_2$ 263.1885, found 263.1887. The synthetic fawcettimine (**1**) was identical with the natural compound by comparison with their spectral data.[6b,7]

(1*S*,4*R*,6*S*,9*R*)-4,13-Dimethyl-13-azatricyclo[7.7.0.0^{1,6}]hexadecane-2,8-dione ((+)-21). A mixture of (+)-**17** (49.8 mg, 0.109 mmol) and $Pd(OH)_2$ (20 wt % on carbon; 9 mg) in THF (5 mL) was stirred under hydrogen atmosphere (1 atm) for 12 h at room temperature. The reaction mixture was passed through a short pad of Celite, and the filtrate was concentrated to dryness. The residue was passed through a short pad of silica gel with hexane−AcOEt (4:1) to afford the crude alcohol. To a solution of the crude alcohol in CH_2Cl_2 (1 mL) was added HCO_2H (1.0 mL, 30 mmol) at room temperature. The reaction mixture was stirred for 12 h at the same temperature, quenched by addition of saturated aqueous $NaHCO_3$, extracted with $CHCl_3$, washed with water and brine, dried, and concentrated to dryness. To a solution of residue in MeOH (2 mL) were added aqueous formaldehyde (37% in H_2O; 0.2 mL, 3 mmol) and $NaCNBH_3$ (13.7 mg, 0.218 mmol) at room temperature. The mixture was stirred for 1 h and then acidified by HCO_2H (0.2 mL, 5 mmol). The reaction mixture was stirred for 1 h at the same temperature, quenched by addition of saturated aqueous $NaHCO_3$, extracted with $CHCl_3$, washed with water and brine, dried, and concentrated to dryness. The residue was passed through a short pad of Al_2O_3 with hexane−AcOEt (1:1) to afford the crude alcohol. To a solution of the crude alcohol in CH_2Cl_2 (1 mL) was added PCC (35.2 mg, 0.164 mmol) at room temperature. The reaction mixture was stirred for 1 h at the same temperature, diluted with $CHCl_3$, washed with aqueous 1 M NaOH, water, and brine, dried, and concentrated to dryness. The residue was chromatographed on silica gel with $CHCl_3$−MeOH (10:1) to give (+)-**21** (12.4 mg, 50% from (+)-**17**) as colorless prisms: mp 113−114 °C (hexane); $[\alpha]^{24}_D$ +204 (*c* 0.15, $CHCl_3$); IR 1734, 1701 cm^{-1}; ^1H NMR δ 2.88−2.87 (m, 1H), 2.60−2.50 (m, 2H), 2.42−1.25 (m, 18H), 2.25 (s, 3H), 1.07 (d, 3H, J = 6.4 Hz); ^{13}C NMR δ 220.2, 214.2, 60.7, 54.7, 50.2, 48.6, 46.6, 44.3, 42.5, 39.4, 31.1, 30.2, 28.0, 25.3, 22.4, 22.3, 21.6; FAB MS m/z 278 (M^+ + 1, 100); FAB HRMS calcd for $C_{17}H_{28}NO_2$ 278.2120, found 278.2112. The synthetic (+)-**21** was identical with the compound[9] derived from (−)-serratinine, by comparison of their spectral data.

Lycoposerramine B (3). To a solution of (+)-**21** (4.0 mg, 1.4×10^{-2} mmol) in EtOH (0.2 mL) were added Et_2NH (30 μL, 0.29 mmol) and TMSNHOTMS (10.1 mg, 5.69×10^{-2} mmol) in EtOH (0.1 mL) via cannula at −40 °C. The reaction mixture was stirred for 12 h at the same temperature and concentrated to dryness. The residue was passed through a short pad of silica gel with $CHCl_3$−MeOH (10:1) to afford the crude oxime. The crude oxime was chromatographed on amino silica gel with hexane−AcOEt (2:1) to give (+)-**3** (2.2 mg, 52% from (+)-**21**) as a colorless amorphous powder: $[\alpha]^{24}_D$ +149 (*c* 0.20, $CHCl_3$); IR 3281, 1699 cm^{-1}; ^1H NMR δ3.17 (d, 1H, J = 3.4 Hz), 2.68 (td, 1H, J = 13.1, 3.4 Hz), 2.56 (dd, 1H, J = 17.9, 10.3 Hz), 2.43−2.39 (m, 1H), 2.30−2.17 (m, 7H), 2.26 (s, 3H), 2.13−2.00 (m, 4H), 1.74−1.62 (m, 3H), 1.47−1.42 (m, 1H), 1.37−1.16 (m, 3H), 1.03 (d, 3H, J = 6.8 Hz); ^{13}C NMR δ 213.9, 169.6, 61.6, 55.0, 48.4, 46.7, 44.3, 42.80, 42.77, 31.5, 29.9, 28.6, 27.4, 25.43, 25.37, 22.4, 21.3; MS m/z 293 (M^+ + 1, 100); FAB HRMS calcd for $C_{17}H_{29}N_2O_2$ 293.2229, found 293.2231. The synthetic lycoposerramine-B (**3**) was identical with the natural compound by comparison with their spectral data.[9] Specific rotation was not reported.

Acknowledgment. This work was supported in part by a Grant-in Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science, and Technology, Japan, for which we are thankful.

Supporting Information Available: ^1H and ^{13}C NMR spectra for compounds **1**, **3**, **8**, **10**−**15**, **17**, **18**, and **21**. This material is available free of charge via the Internet at http://pubs.acs.org.