Synthesis of Vinca Alkaloids and Related Compounds. 90.[1] New Results in the Synthesis of Alkaloids with the Aspidospermane Skeleton. First Total Synthesis of (±)-3-Oxominovincine

György Kalaus,[†] Imre Juhász,[†,§] István Greiner,[§] Mária Kajtár-Peredy,[⊥] János Brlik,[§] Lajos Szabó,[†] and Csaba Szántay*[,†,⊥]

Department for Organic Chemistry, Technical University of Budapest, Gellért tér 4, H-1521, Budapest, Hungary, Chemical Works of Gedeon Richter Ltd., Gyömrôi út 19-21, H-1103 Budapest, Hungary, and Central Research Institute for Chemistry, Hungarian Academy of Sciences, Pusztaszeri út 59-67, H-1525 Budapest, Hungary

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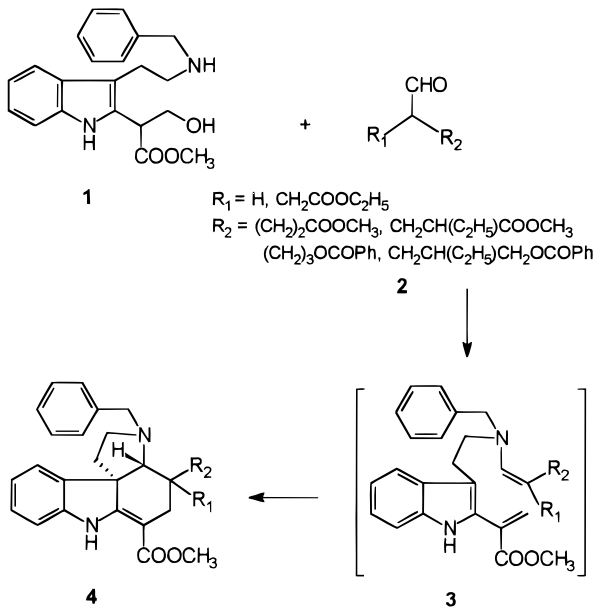
The tryptamine derivative **1** readily reacted with methyl 4-acetyl-5-bromopent-4-enoate (**9**) that had been built up from 2,4-pentanedione. On intramolecular dehydration and subsequent [4 + 2] cycloaddition, the reaction product **10** gave the epimers **12** and **13** having the D-secoaspidospermane skeleton. Compound **12** directly and **13** after epimerization yielded (±)-3-oxominovincine (**14**). Regioselective reduction of **14** furnished (±)-minovincine (**17**).

In the early 1990s we developed a convergent synthetic strategy to build up alkaloids with the aspidospermane[2] and pseudoaspidospermane[3] skeleton and some related compounds.[4,5] The key step of our method was to allow the secondary amine **1** to react with a suitable aldehyde (**2**) in boiling toluene or xylene, and the nonisolable primary intermediate (**3**) directly gave the molecule having the D-secoaspidospermane skeleton (**4**) (Scheme 1). The target compounds were then prepared by debenzylation followed by intramolecular acylation or alkylation, occasionally involving epimerization.[6]

We also reported our attempts directed toward the synthesis of (±)-3-oxominovincine (**14**).[1] However, when using the method described above, the reaction of the tryptamine derivative **1** and the aldehyde **2** (R_1 = $C(OCH_2CH_2O)CH_3$; R_2 = $CH_2CH_2COOCH_3$) did not give the expected compound, because cleavage of the carbon−carbon bond occurred, and the product was molecule **4** (R_1 = H; R_2 = $CH_2CH_2COOCH_3$) with the D-secoaspidospermane skeleton. In an independent way we succeeded in preparing the tetracyclic ester containing the acetyl group (**4**, where R_1 = $COCH_3$, R_2 = H), but our alkylation and acylation experiments aimed at forming the fifth ring, i.e., the aspidospermane skeleton, gave products of unexpected structures,[1] thus a new synthetic approach had to be found.

This paper is an account of the successful continuation of the above research. (+)-3-Oxominovincine (**14**), isolated from *Tabernaemontana riedelii*, has only been prepared up to now by the oxidation of (+)-minovincine

Scheme 1



(**17**).[7] Several total syntheses of the latter alkaloid are known, and the corresponding papers mentioned that the β-acetyl group of the enamines used in those experiments (e.g., **3**, where R_1 = H; R_2 = $COCH_3$) did not split off even at high temperatures, i.e., in boiling toluene or xylene.[8] This implied important information for us, since it could be concluded that the cleavage of the carbon−carbon bond, observed in our earlier work, had occurred before the formation of the enamine; hence the problem could be avoided by preparing the suitable enamine. Accordingly, we substituted the key compound aldehyde by the equivalent of its enol derivative. Formerly, activated vinyl halide derivatives had also been successfully used as the reaction partners of secondary amines in syntheses of the aspidospermane skeleton,[9] consequently we selected methyl 4-acetyl-5-bromopent-4-enoate (**9**), an equiva-

† Technical University of Budapest.
§ Chemical Works of Gedeon Richter Ltd.
⊥ Hungarian Academy of Sciences.
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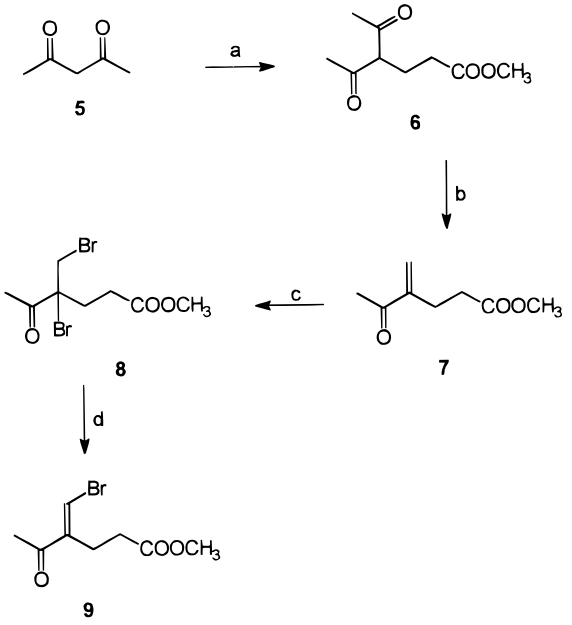
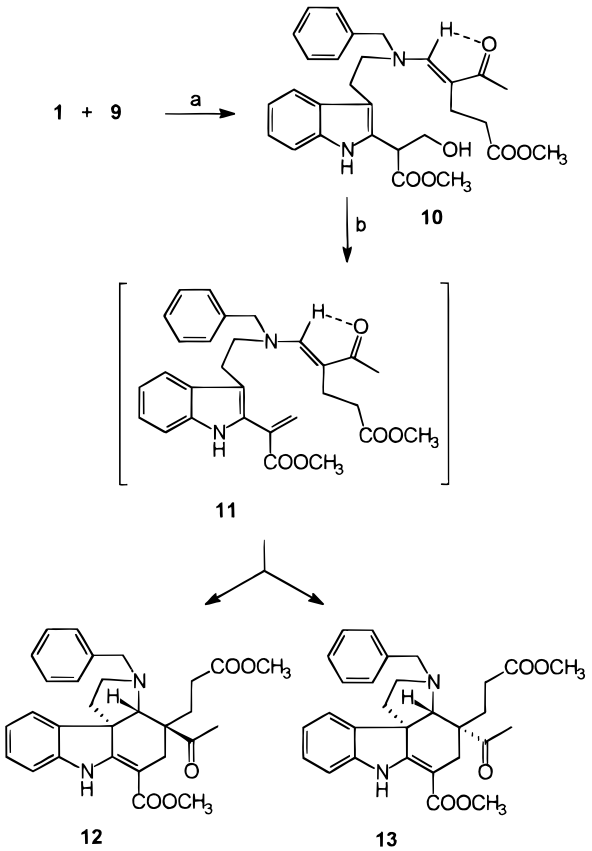
Scheme 2[a]



[a] Conditions: (a) CH_3OH, Na, $CH_2{=}CHCOOCH_3$, rt; (b) HCHO, K_2CO_3, H_2O, rt; (c) Br_2, CH_2Cl_2, rt; (d) $(nC_4H_9)_4NCl$, HMPA, rt.

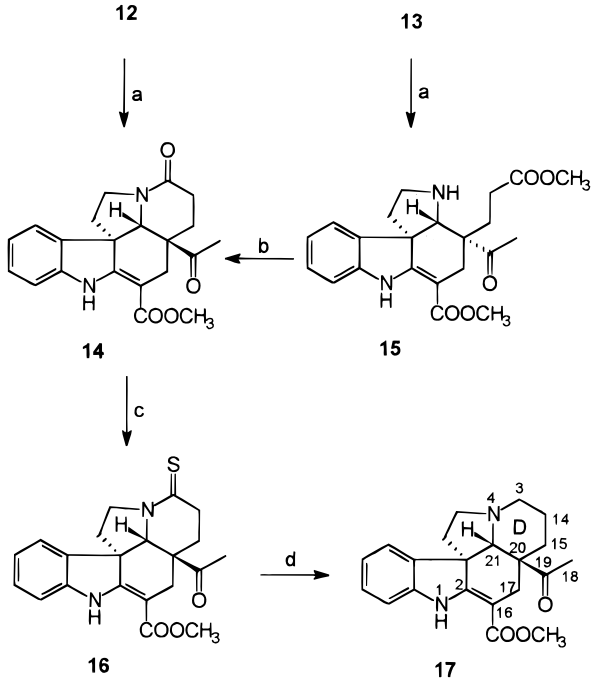
Scheme 3[a]



[a] Conditions: (a) NEt_3, CH_3OH, rt; (b) TsOH, xylene, Δ.

lent of the appropriate aldehyde. A simple reaction pathway was devised for preparing this compound. 2,4-Pentanedione (**5**) was alkylated with methyl acrylate, and the resulting diketoester[10] (**6**) was made to react with aqueous formaldehyde in the presence of potassium carbonate[11a] to give the unsaturated compound **7**; addition of bromine[11b] (**8**) and the elimination of hydrogen bromide[11b] yielded the desired compound **9** (Scheme 2).

Scheme 4[a]



[a] Conditions: (a) $Pd/C/H_2$, CH_3COOH, rt; (b) TsOH, toluene, Δ; (c) P_4S_{10}, THF, rt; (d) Raney Ni, THF, rt.

The secondary amine **1** and the halide **9** interacted in methanol in the presence of triethylamine even at room temperature as expected, and the stable enamine **10** was isolated from the reaction mixture in about 70% yield. It was then boiled in xylene in the presence of *p*-toluenesulfonic acid to give—via the nonisolable intermediate **11**—the tetracyclic ketones **12** and **13** having the D-secoaspidospermane ring system. The starting enamine (**10**) disappeared from the reaction mixture on boiling for about 24 h, and a 1:1 mixture of the resulting epimers was isolated in a total yield of 38% (Scheme 3).

The epimers **12** and **13** were separated by chromatography, and the benzyl group was removed by catalytic hydrogenation at ambient temperature. In the case of compound **12** the product was (±)-3-oxominovincine (**14**), directly resulting from spontaneous intramolecular N-acylation. The epimer **13** gave first the secondary amine **15**. Boiling of the latter in toluene in the presence of *p*-toluenesulfonic acid furnished, with epimerization, the same alkaloid, **14**.

The lactam **14** was reduced regioselectively in two steps, using the method reported earlier.[2] The compound was allowed to react with phosphorus pentasulfide, and the thioxo derivative **16** was treated with Raney nickel to give (±)-minovincine (**17**) (Scheme 4).

Experimental Section[12]

Methyl 4-Acetylpent-4-enoate (7). To a mixture of **6** (10.00 g, 53.7 mmol) and 30% aqueous formaldehyde (11 mL) was added a solution of K_2CO_3 (15.00 g, 108 mmol) in water (11 mL) at rt. The heterogeneous reaction mixture was stirred

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(12) For general experimental information, see ref 4.

for 12 h and then was diluted with water (110 mL), and the solution was extracted with ether three times (50 mL each). The combined organic layers were dried with $MgSO_4$, filtered, and concentrated in vacuo. The residue was distilled to yield **7** (3.60 g, 43%): bp 105−115 °C (15 Torr); IR (neat) ν_{max} 1738, 1684, 1608 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.35 (s, 3H, $COCH_3$), 2.47 (m, 2H, 2-H_2), 2.60 (m, 2H, 3-H_2), 3.67 (s, 3H, OCH_3), 5.86 + 6.06 (2 × 1H, 5-H_2); ^{13}C NMR ($CDCl_3$) δ 25.7, 26.2, 32.8, 51.5, 126.1, 147.2, 173.2, 199.1.

Methyl 4-Bromo-4-(bromomethyl)-5-oxohexanoate (8). To a solution of **7** (10.00 g, 64 mmol) in CH_2Cl_2 (50 mL) was added a solution of 3.5 mL (68 mmol) of bromine in 10 mL of CH_2Cl_2 dropwise at rt. After the solution was stirred for 1 h, the excess bromine was removed by washing with aqueous sodium thiosulfate until the solution was discolored. The organic layer was separated and washed with water (20 mL), dried with $MgSO_4$, and concentrated in vacuo. The residue was crystallized from methanol to yield **8** (15.60 g, 78%); mp 55−56 °C; IR (KBr) ν_{max} 1730, 1727 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.36−2.69 (m, 4H, 2-H_2 + 3-H_2), 2.46 (s, 3H, $COCH_3$), 3.72 (s, 3H, OCH_3), 3.76 + 4.09 (2 × d, J_{gem} = 10.6 Hz, 2 × 1H, 4-CH_2-Br); ^{13}C NMR ($CDCl_3$) δ 24.4, 30.0, 31.0, 34.1, 52.0, 66.8, 172.5, 199.0.

Methyl 4-Acetyl-5-bromopent-4-enoate (9). To a homogeneous solution of tetrabutylammonium chloride (11.10 g, 40 mmol) in 25 mL of HMPA was added **8** (10.00 g, 31 mmol) over a 30 min period at rt. After being stirred for 12 h at rt, the brown mixture was cooled (0 °C) and quenched with an aqueous solution of sulfuric acid (1 M, 65 mL) and then extracted with hexane five times (20 mL each). The combined organic extracts were washed with water until neutrality of the aqueous layer. The organic layer was dried with $MgSO_4$ and concentrated in vacuo. The main component was separated by column chromatography (eluent: CH_2Cl_2) to yield **9** (1.19 g, 16%) as an yellow oil (R_f = 0.47): IR (neat) ν_{max} 1730, 1675, 1582 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.34 (s, 3H, $COCH_3$), 2.43 (t, J = 7.5 Hz, 2H, 2-H_2), 2.77 (t, 2H, 3-H_2), 3.67 (s, 3H, OCH_3), 7.32 (s, 1H, 5-H); ^{13}C NMR ($CDCl_3$) δ 21.9, 26.0, 31.7, 51.7, 134.8, 142.8, 172.8, 195.1.

Enamine 10. To a mixture of 1.00 g (2.48 mmol) of **1**,[2] 0.40 g (4 mmol) of triethylamine, and 100 mL of methanol was added 0.70 g (3 mmol) of **9**. After being stirred for 24 h at rt, the mixture was concentrated in vacuo. The residue was purified by column chromatography (eluent: hexane/acetone 1:1) to yield **10** (1.00 g, 70%) as an amorphous solid (R_f = 0.76): IR (KBr) ν_{max} 3390, 1740, 1730, 1608, 1574 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.99 (s, 3H, $COCH_3$), 2.29 + 2.34 (2 × ddd, J_{gem} = 15.5, J_{vic} = 6.0 + 9.8 and 6.0 + 9.3 Hz, respectively, 2 × 1H, CH_2COOCH_3), 2.64 + 2.70 (2 × ddd, J_{gem} = 14.0, J_{vic} = 6.0 + 9.3 and 6.0 + 9.8 Hz, respectively, 2 × 1H, CH_2C═), 3.02 + 3.07 (2 × dt, J_{gem} = 14.2, J_{vic} = 7.0 Hz, 2 × 1H, 3-CH_2), 3.44 (br, 1H, OH), 3.55 (t, J = 7.0 Hz, 2H, CH_2CN), 3.58 + 3.68 (2 × s, 2 × 3H, 2 × OCH_3), 4.00−4.12 (m, 3H, 2-CHCH_2), 4.46 (s, 2H, NC$H_2C_6H_5$), 7.09 (ddd, $J_{4,5}$ = 7.8, $J_{5,6}$ = 7.1, $J_{5,7}$ = 1.1 Hz, 1H, 5-H), 7.16 (m, 2H, 2′-H + 6′-H), 7.17 (ddd, $J_{6,7}$ = 8,0, $J_{4,6}$ = 1.3 Hz, 1H, 6-H), 7.22 (s, 1H, −CH═), 7.29 (m, 1H, 4′-H), 7.33 (br d, 1H, 7-H), 7.35 (m, 2H, 3′-H + 5′-H), 7.41 (br d, 1H, 4-H), 9.04 (br s, 1H, NH); ^{13}C NMR ($CDCl_3$) δ 20.1, 23.9, 24.9, 34.5, 44.8, 51.5, 52.6, 53.6, 57.4, 63.9, 109.3, 109.7, 111.3, 118.0, 119.7, 122.4 126.9, 127.2, 127.8, 128.9, 129.9, 135.7, 137.0, 150.5, 172.6, 174.0, 196.6; MS m/z 507 (4.0, M^+), 467 (8.0), 445 (10.0), 332 (17), 274 (80), 91 (100).

(±)-2,16-Didehydro-14,16-bis(methoxycarbonyl)-3-phenyl-3,14-secoaspidospermidin-19-one (12) and (±)-2,16-Didehydro-14,16-bis(methoxycarbonyl)-3-phenyl-3,14-seco-20-epiaspidospermidin-19-one (13). A solution of 1.00 g (1.97 mmol) of **10** and 0.01 g (0.06 mmol) of *p*-toluenesulfonic acid monohydrate in 100 mL of xylene was refluxed under argon for 24 h. The reaction mixture was extracted twice with brine (40 mL), and the combined brine washes were extracted twice with CH_2Cl_2 (40 mL each). The combined organic layers were dried with $MgSO_4$ and evaporated in vacuo. The two main components were separated by column chromatography (eluent: CH_2Cl_2/ether 30:1). The more polar compound (**12**, R_f = 0.48) was obtained as white crystals after crystallization from methanol (0.18 g, 19%): mp 187−188 °C; IR (KBr) ν_{max} 3417, 1741, 1703, 1674, 1639, 1622 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.75 + 2.04 (2 × ddd, J_{gem} = 12.2, $J_{5,6}$ = 5.6 + 1.5 and 11.6 + 6.6 Hz, respectively, 2 × 1H, 6-H_2), 1.97 (s, 3H, 18-H_3), 2.12−2.23m + 2.36m + 2.63m (4H, 14-H_2 + 15-H_2), 2.62 + 2.93 (2 × d, J_{gem} = 15.5 Hz, 2 × 1H, 17-H_2), 2.69 + 3.01 (2 × ddd, J_{gem} = 9.5 Hz, 2 × 1H, 5-H_2), 3.55 + 3.79 (2 × s, 2 × 3H, 2 × OCH_3), 3.76 + 4.17 (2 × d, J_{gem} = 13.2 Hz, 2 × 1H, NC$H_2C_6H_5$), 4.00 (d, J_{lr} = 2.0 Hz, 1H, 21-H), 6.80 (d, 1H, 12-H), 6.95 (dd, 1H, 10-H), 7.16 (dd, 1H, 11-H), 7.19 (d, 1H, 9-H), 7.25−7.50 (m, 5H, C_6H_5), 8.75 (br s, 1H, NH); ^{13}C NMR ($CDCl_3$) δ 25.9, 27.9, 28.7, 30.5, 42.4, 51.1, 51.8, 53.0, 58.5, 59.1, 61.7, 68.3, 89.7, 109.5, 121.2, 122.1, 127.1, 127.8, 128.4, 128.6, 137.2, 139.2, 142.5, 166.8, 167.8, 172.9, 211.5; MS m/z 488 (3.0, M^+), 455 (8.0), 332 (15.0), 274 (100). Anal. Calcd for $C_{29}H_{32}N_2O_5$: C, 71.29; H, 6.60; N, 5.73. Found: C, 71.32; H, 6.61; N, 6.04.

The less polar compound (**13**, R_f = 0.54) was obtained as white crystals after crystallization from methanol (0.18 g, 19%): mp 131−132 °C; IR (KBr) ν_{max} 3365, 1738, 1690, 1615 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.14m + 1.92m + 2.00−2.12m (4H, 14-H_2 + 15-H_2), 1.69 + 2.21 (2 × ddd, J = 12.2, $J_{5,6}$ = 5.5 + ∼1 and 6.8 + 12.2 Hz, respectively, 2 × 1H, 6-H_2), 2.45 (s, 3H, 18-H_3), 2.68 + 2.97 (2 × ddd, J_{gem} = 9.6 Hz, 2 × 1H, 5-H_2), 2.88 + 2.93 (2 × d, J_{gem} = 15.0 Hz, 2 × 1H, 17-H_2), 3.28 (d, J_{lr} = 1.4 Hz, 1H, 21-H), 3.57 + 3.80 (2 × s, 2 × 3H, 2 × OCH_3), 3.63 + 4.06 (2 × d, J_{gem} = 13.0 Hz, 2 × 1H, NC$H_2C_6H_5$), 6.80 (br d, $J_{9,10}$ = 7.4 Hz, 1H, 9-H), 6.85 (br d, $J_{11,12}$ = 7.6 Hz, 1H, 12-H), 6.86 (ddd, $J_{10,11}$ = 7.4, $J_{10,12}$ = 1.2 Hz, 1H, 10-H), 7.17 (ddd, $J_{11,12}$ = 7.8, $J_{9,11}$ = 1.3 Hz, 1H, 11-H), 7.25−7.37 (m, 5H, C_6H_5), 8.97 (br s, 1H, NH); ^{13}C NMR ($CDCl_3$) δ 23.9, 28.6, 28.9, 31.3, 40.4, 51.2, 51.6, 56.3, 57.7, 60.9, 76.4, 88.6, 109.5, 121.0, 122.8, 127.1, 128.2, 128.3, 129.2, 136.6, 138.2, 142.7, 164.6, 168.2, 173.4, 213.3; MS m/z 488 (10.0, M^+), 457 (15.0), 445 (17.0), 332 (10.0), 274 (83.0), 91 (100). Anal. Calcd for $C_{29}H_{32}N_2O_5$: C, 71.29; H, 6.60; N, 5.73. Found: C, 71.08; H, 6.66; N, 5.52.

(±)-3-Oxominovincine (14). Method a. A mixture of 1.00 g of **12** (2.00 mmol) and 0.50 g of 10% palladium/charcoal in 20 mL of glacial acetic acid was hydrogenated for 1 h at rt and then filtered. The filtrate was poured into 50 mL of ice−water and neutralized with saturated Na_2CO_3 solution. The solution was extracted three times with CH_2Cl_2 (30 mL each), and the combined organic layers were dried with $MgSO_4$ and evaporated in vacuo. The main component was separated by preparative TLC (eluting with hexane/acetone 2:1) to yield a yellow oil (R_f = 0.28), which was crystallized from methanol to afford **14** (0.48 g, 64%) as white crystals: mp 245−246 °C; IR (KBr) ν_{max} 3345, 1702, 1671, 1602 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.77 + 2.17 (2 × ddd, J_{gem} = 14.0, $J_{14,15}$ = 4.8 + 11.2 and 4.8 + 5.6 Hz, respectively, 2 × 1H, 15-H_2), 1.88 + 1.97 (2 × ddd, J_{gem} = 12.2, $J_{5,6}$ = 5.8 + ∼1 and 12.4 + 7.5 Hz, respectively, 2 × 1H, 6-H_2), 2.08 (s, 3H, 18-H_3), 2.28 + 3.19 (2 × d, J_{gem} = 15.5 Hz, 2 × 1H, 17-H_2), 2.34 + 2.43 (2 × ddd, J_{gem} = 15.6 Hz, 2 × 1H, 14-H_2), 3.48 + 4.24 (2 × ddd, J_{gem} = 11.6 Hz, 2 × 1H, 5-H_2), 3.80 (s, 3H, OCH_3), 4.71 (d, J_{lr} = 2.0 Hz, 1H, 21-H), 6.86 (d, 1H, 12-H), 6.97 (dd, 1H, 10-H), 7.21 (dd, 1H, 11-H), 7.28 (d, 1H, 9-H), 8.82 (br s, 1H, NH); ^{13}C NMR ($CDCl_3$) δ 25.0, 28.6, 28.9, 30.7, 40.3, 43.4, 51.3, 53.7, 57.1, 62.3, 89.7, 109.9, 121.4, 121.7, 128.5, 135.4, 142.4, 165.3, 167.4, 169.8, 209.0; MS m/z 366 (40.0, M^+), 227 (85.0), 214 (100). Anal. Calcd for $C_{21}H_{22}N_2O_4$: C, 68.84; H, 6.05; N, 7.65. Found: C, 68.67; H, 6.35; N, 7.25. **Method b.** The solution of 1.00 g of **15** in 100 mL of anhydrous toluene and 0.01 g (0.06 mmol) of *p*-toluenesulfonic acid monohydrate was refluxed under argon for 1 h. The reaction mixture was extracted twice with brine (40 mL each), and the combined aqueous layers were extracted twice with CH_2Cl_2 (40 mL each), dried with $MgSO_4$, and evaporated in vacuo. The main component was separated as described above to yield **14** (0.39 g, 43%) which was identical spectroscopically to the material prepared by method a.

Secondary Amine 15. A mixture of 1.00 g of **13** (2.0 mmol) and 0.50 g of 10% palladium/charcoal in 20 mL of glacial acetic acid was hydrogenated for 1 h at rt. The filtrate was worked up as in the case of compound **14** to yield **15** (0.59 g, 73%, R_f = 0.77, eluent: hexane/acetone 2:1): mp 186−187 °C (crystallized from methanol); IR (KBr) ν_{max} 3400, 3368, 1731, 1710, 1673, 1646, 1619 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.37 + 1.71 (2 ×

ddd, J_{gem} = 14.2, $J_{14,15}$ = 5.5 + 11.6 and 4.5 + 11.5 Hz, respectively, 2 × 1H, 15-H_2), 1.78 + 1.97 (2 × ddd, J_{gem} = 11.8, $J_{5,6}$ = 4.6 + 1.5 and 11.3 + 7.0 Hz, 2 × 1H, 6-H_2), 1.85 + 2.11 (2 × ddd, J_{gem} = 16.0 Hz, 2 × 1H, 14-H_2), 1.90 (br, 1H, N(4)−H), 2.28 (s, 3H, 18-H_3), 2.56 + 2.84 (2 × d, J_{gem} = 15.6 Hz, 2 × 1H, 17-H_2), 3.04−3.14 (m, 2H, 5-H_2), 3.56 + 3.79 (2 × s, 2 × 3H, 2 × OCH_3), 3.76 (d, J_{lr} = 2.0 Hz, 1H, 21-H), 6.85 (d, 1H, 12-H), 6.91 (dd, 1H, 10-H), 7.18 (d, 1H, 9-H), 7.19 (dd, 1H, 11-H), 9.00 (br s, 1H, N(1)−H); ^{13}C NMR ($CDCl_3$) δ 22.0, 27.9, 28.6, 28.8, 44.0, 45.1, 51.1, 51.6, 56.8, 57.6, 68.4, 89.2, 109.6, 120.9, 121.7, 128.2, 137.1, 142.9, 165.4, 168.4, 173.1, 211.9; MS *m*/*z* 398 (35.0, M^+), 367 (10.0), 325 (5.0), 214 (64), 42 (100). Anal. Calcd for $C_{22}H_{26}N_2O_5$: C, 66.32; H, 6.58; N, 7.03. Found: C, 66.12; H, 6.66; N, 6.79.

(±)-3-Thioxominovincine (16). To the solution of 0.10 g (0.27 mmol) of **14** in 30 mL of anhydrous THF was added 0.13 g (0.30 mmol) of P_4S_{10}. The reaction mixture was stirred for 1 h at rt and was diluted with 30 mL of CH_2Cl_2. The solution was extracted with 20 mL of brine, and the brine was extracted with 10 mL of CH_2Cl_2. The combined organic layers were dried with $MgSO_4$ and evaporated in vacuo. The residue was purified by column chromatography (eluent: hexane/acetone 2:1) to yield a yellow oil (R_f = 0.38), which was crystallized from methanol to afford **16** (0.95 g, 91%) as white crystals: mp 253−254 °C; IR (KBr) ν_{max} 3410, 3381, 1700, 1674, 1610 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.59 + 2.21 (2 × ddd, J_{gem} = 14.2, $J_{14,15}$ = 13.5 + 3.5 and 4.8 + 3.0 Hz, respectively, 2 × 1H, 15-H_2), 2.01 + 2.12 (2 × ddd, J_{gem} = 12.5, $J_{5,6}$ = 6.4 + ∼1 and 12.5 + 7.7 Hz, 2 × 1H, 6-H_2), 2.12 (s, 3H, 18-H_3), 2.18 + 3.29 (2 × d, J_{gem} = 15.8 Hz, 2 × 1H, 17-H_2), 2.53 + 3.12 (2 × ddd, J_{gem} = 15.3 Hz, 2 × 1H, 14-H_2), 3.80 (s, 3H, OCH_3), 3.82 + 4.67 (2 × ddd, J_{gem} = 13.0 Hz, 2 × 1H, 5-H_2), 4.72 (br s, 1H, 21-H), 6.87 (d, 1H, 12-H), 6.99 (dd, 1H, 10-H), 7.23 (dd, 1H, 11-H), 7.30 (d, 1H, 9-H), 8.84 (br s, 1H, NH); ^{13}C NMR ($CDCl_3$) δ 24.8, 28.9, 30.2, 39.1, 41.0, 49.9, 51.4, 54.6, 57.0, 64.7, 89.9, 110.0, 121.5, 121.9, 128.9, 134.7, 142.4, 164.5, 167.3, 198.9, 208.1; MS *m*/*z* 382 (40.0, M^+), 349 (8.0), 238 (100.0), 227 (76). Anal. Calcd for $C_{21}H_{22}N_2O_3S$: C, 65.95; H, 5.80; N, 7.32; S,8.38. Found: C, 65.84; H, 5.83; N, 6.91; S, 8.25.

(±)-Minovincine (17). To a solution of 0.10 g (0.26 mmol) of **16** in 10 mL of anhydrous THF were added ∼1 g of water, methanol, and anhydrous THF-washed Raney Ni. The suspension was stirred for 2 h at rt and filtered. The Raney Ni was washed with 10 mL of anhydrous THF, and the combined filtrate was evaporated in vacuo. The residue was purified by column chromatography (eluent: hexane/acetone 2:1) to yield a yellow oil (R_f = 0.51), which was crystallized from methanol to afford **17** (0.85 g, 93%) as white crystals; mp 140−141 °C (lit.[8a] mp 141−142 °C); ^{13}C NMR ($CDCl_3$) δ 22.4, 25.1, 25.9, 45.3, 49.8, 51.1, 51.5, 53.9, 56.2, 67.7, 91.4, 109.4, 120.7, 121.1, 127.2, 138.2, 142.4, 168.2, 168.3, 212.1. Its ^{1}H NMR, IR, and MS spectral data were identical with those previously described in the literature.[8a]

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