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Regular Article

Conversion of Vindoline into 11-Mesyloxytabersonine

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Conversion of readily available vindoline to 11-mesyloxytabersonine, a versatile synthetic intermediate for indole alkaloids, has been achieved by a 9-step sequence in 39% overall yield.

Key words alkaloid; indole; natural product; vindoline; tabersonine

The *aspidosperma*-type indole alkaloids comprise one of the largest groups of indole alkaloids, with more than 250 compounds isolated from a variety of biological sources.[1,2] The intriguing structures of the *aspidosperma*-type indole alkaloids have attracted much attention as the challenging targets for total synthesis. The *aspidosperma*-skeletons have also been found as subunits in biologically active dimeric indole alkaloids (Fig. 1), such as conophylline (**1**)[3–7] and vinblastine (**2**).[8,9] Therefore, an efficient preparation of the *aspidosperma*-skeleton is important for the synthesis of novel analogs of these indole alkaloids.

In our synthetic studies of dimeric indole alkaloids and their analogs,[10–12] 11-mesyloxytabersonine (**3**) was used as the key intermediate. Our reported synthetic route toward **3** features synthesis of the indole unit *via* a radical cyclization and facile deprotection of a secondary amine by employing a 2,4-dinitrobenzenesulfonyl group as a protective group.[13,14] While this route supplied **3** in sufficient quantities to enable total syntheses of natural dimeric indole alkaloids, a gram-scale preparation of **3** needed for synthesis of a variety of analogs led to some difficulties. We therefore continued to investigate alternative methods for the efficient preparation of **3**.[15–31] Herein we disclose an efficient synthesis of 11-mesyloxytabersonine (**3**) starting from the readily available natural product vindoline (**4**).[32]

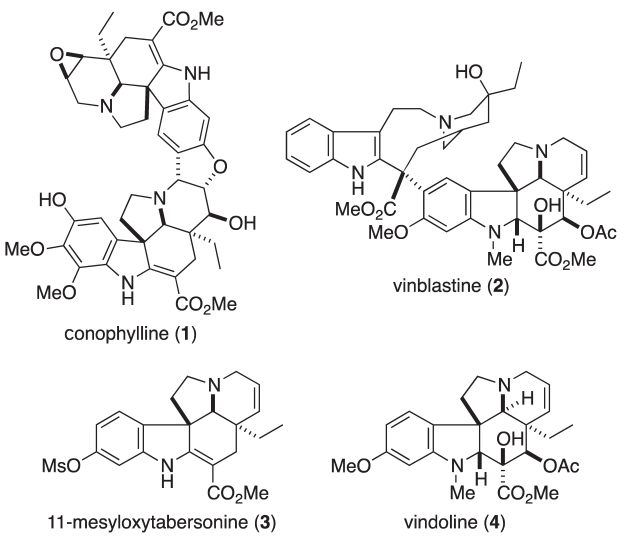

Fig. 1. Structures of Molecules with the *Aspidosperma*-Skeleton

Transformation of vindoline (**4**) into 11-mesyloxytabersonine (**3**) requires removal of the 1,2-diol moiety and cleavage of the *N*- and *O*-methyl groups. Removal of the 1,2-diol moiety was achieved *via* the Corey–Winter olefination. Thus, diol **5**, prepared by methanolysis of **4**, was treated with 1,1′-thiocarbonyldiimidazole (TCDI) in acetonitrile to afford thionocarbonate **6** in 86% yield (Chart 1). While heating with trimethyl or triethyl phosphite resulted in no reaction, treatment of **6** with 1,3-dimethyl-2-phenyl-1,3,2-diazaphospholidine (**7**)[33] in *o*-dichlorobenzene at 160°C afforded the desired olefin **8** in 91% yield.

We next focused on the cleavage of the *N*-methyl group.[34] Attempted oxidation of the *N*-methyl group of **8** with sodium dichromate by following the reported procedure[35] did not give the desired *N*-formyl product. The electron-rich nature of the aromatic ring might have complicated the oxidation. We therefore decided to replace the *O*-methyl group with a mesyl group to lower the electron density of the aromatic ring prior to *N*-demethylation.

Upon exposure to BBr_3 in dichloromethane, **8** underwent cleavage of the methyl ether to give **9**, which was converted into the mesylate **10** in a quantitative yield. Oxidation of the *N*-methyl group in **10** was then achieved by treatment with potassium permanganate to afford *N*-formyl compound **11**,[36] which was hydrolyzed under acidic conditions to furnish **12** in 90% yield over 2 steps.

The double bond in **12** was next isomerized by using an oxidation-reduction sequence. Oxidation of **12** with benzeneseleninic anhydride (**13**) followed by aqueous workup afforded allyl alcohol **15** in 84% yield. This reaction presumably proceeded *via* a 1,4-addition of water to unsaturated imine **14**.[37]

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Finally, reduction of **15** with sodium cyanoborohydride under acidic conditions afforded 11-mesyloxytabersonine (**3**) in 69% yield.[38]

In conclusion, we have established an efficient route for conversion of vindoline into 11-mesyloxytabersonine in 9 steps and 39% overall yield. A gram-scale preparation of this valuable intermediate has also been achieved. Application of this synthetic route to the synthesis of novel analogs of indole alkaloids will be reported in due course.

Experimental

General Procedures All reactions were carried out in oven-dried glassware under a positive pressure of argon unless otherwise noted. Air- and moisture-sensitive liquids and solution were transferred *via* syringe or stainless cannula. Concentration under reduced pressure was performed by rotary evaporation (*ca.* 30 mmHg) at 20–40°C. Flash column chromatography was performed as described by Still *et al.* [*J. Org. Chem.*, **43**, 2923 (1978)] employing KANTO CHEMICAL Silica Gel 60 (spherical) 40–100 μm or Silica Gel 60 N (spherical, neutral) 40–100 μm. Analytical TLC was performed on Merck analytical plates pre-coated with silica gel 60 F_{254} (0.25 mm thick). TLC plates were visualized by exposure to UV light and/or exposure to phosphomolybdic acid or ceric ammonium molybdate solution followed by brief heating on a hot plate. Preparative TLC separation was performed on Merck analytical plates pre-coated with silica gel 60 F_{254} (0.25 or 0.50 mm thick).

Materials Commercial reagents and solvents were used as received unless otherwise noted. Dehydrated acetonitrile, dichloromethane, methanol, tetrahydrofuran and benzene were dried over molecular sieves 3A (acetonitrile and methanol) or 4A (the other solvents).

Instrumentation Optical rotations were measured on a JASCO DIP-1000 digital polarimeter with a sodium lamp and reported as followed: $[\alpha]_D^T$ (concentration g/100 mL, solvent). IR spectra were recorded on a JASCO FT/R-410 Fourier transform infrared (FT-IR) spectrophotometer and are reported in wavenumbers (cm^{-1}). Where noted "neat," the sample was loaded as a thin film on zinc-selenium plate. ^{1}H- and ^{13}C-NMR spectra were determined on a JEOL-LA400 (^{1}H-NMR: 400 MHz, ^{13}C-NMR: 100 MHz) instrument. Chemical shifts for ^{1}H-NMR were reported in parts per million (δ scale) downfield from tetramethylsilane (TMS) as the internal standard and coupling constants were in hertz (Hz). The following abbreviations were used for spin multiplicity: s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet, br=broad. Chemical shifts for ^{13}C-NMR were reported in parts per million (δ scale) relative to the central line of the triplet at 77.0 ppm for deuteriochloroform. High resolution (HR)-MS were obtained on a JEOL JMS-GCmate MS-DIP20 quadruple using direct probe insertion. FAB-MS were obtained with poly(ethylene glycol) as a matrix.

(3a*R*,3a1*R*,4*R*,5*S*,5a*R*,10b*R*)-Methyl 3a-Ethyl-4,5-dihydroxy-8-methoxy-6-methyl-3a,3a^1,4,5,5a,6,11,12-octahydro-1*H*-indolizino-[8,1-*cd*]carbazole-5-carboxylate (5) To a stirred solution of vindoline (**4**, 10.0 g, 21.9 mmol) in 220 mL of methanol was added 15.1 g (110 mmol) of potassium carbonate and the resulting mixture was stirred for 3 h at 60°C. The reaction mixture was partitioned between saturated aqueous sodium bicarbonate and dichloromethane and the aqueous layer was extracted with dichloromethane 4 times. The combined organic extracts were washed with brine. The organic layer was dried over anhydrous sodium

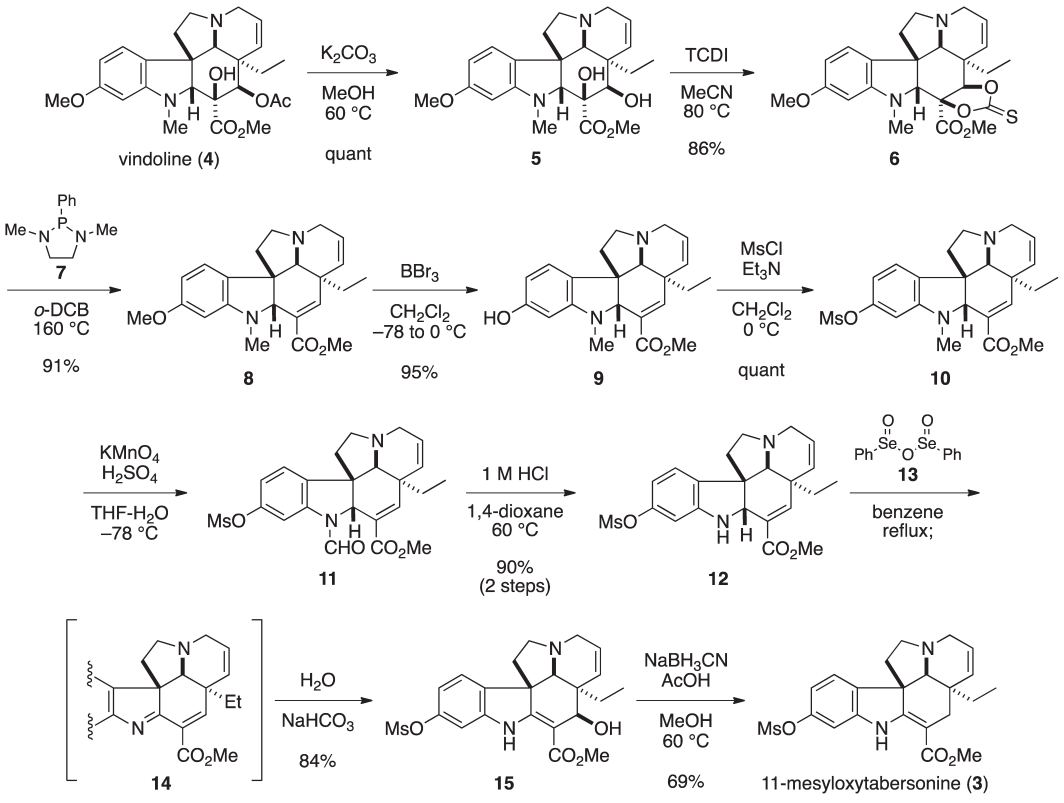

Chart 1. Synthetic Conversion of Vindoline into 11-Mesyloxytabersonine

sulfate, filtered and concentrated *in vacuo*. The residue was purified with flash column chromatography on silica gel (2–5% methanol in dichloromethane) to give 9.08 g (21.9 mmol, quant.) of **5** as a white foam. $[\alpha]_D^{22}$: −3.8° (c=1.55, $CHCl_3$). IR (neat): 3548, 2960, 1738, 1616, 1503, 1456, 1245, 1168, 1085, 1041, 822, 752 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 9.37 (br, 1H), 6.87 (d, J=8.2 Hz, 1H), 6.28 (dd, J=8.2, 2.3 Hz, 1H), 6.07 (d, J=2.3 Hz, 1H), 5.87 (dd, J=10.3, 4.8 Hz, 1H), 5.73 (d, J=10.3 Hz, 1H), 4.08 (d, J=6.6 Hz, 1H), 3.84 (s, 3H), 3.78 (s, 3H), 3.72 (s, 1H), 3.47–3.38 (m, 2H), 2.85 (d, J=15.8 Hz, 1H), 2.73 (s, 3H), 2.66 (s, 1H), 2.60–2.50 (m, 2H), 2.29–2.19 (m, 2H), 1.45 (dq, J=14.9, 7.3 Hz, 1H), 1.01 (dq, J=14.9, 7.3 Hz, 1H), 0.67 (t, J=7.3 Hz, 3H). ^{13}C-NMR ($CDCl_3$) δ: 173.3, 161.0, 153.6, 130.6, 125.0, 123.7, 122.7, 104.2, 95.7, 82.9, 80.7, 73.8, 67.8, 55.3, 52.8, 52.3, 51.2, 51.0, 44.4, 42.6, 38.6, 32.4, 7.7. HR-MS (FAB): Calcd for $C_{23}H_{30}N_2O_5$ (M^+) 414.2155. Found 414.2138.

(3a*R*,3a^1*R*,3b*R*,6a*S*,6b*R*,11b*R*)-Methyl 3a-Ethyl-9-methoxy-7-methyl-5-thioxo-3a,3a^1,3b,6a,6b,7,12,13-octahydro-1*H*-[1,3]dioxolo[4,5-*a*]indolizino[8,1-*cd*]carbazole-6a-carboxylate (6) To a stirred solution of **5** (1.54 g, 3.71 mmol) in 37 mL of acetonitrile was added 2.72 g (13.7 mmol) of thiocarbonyldiimidazole (90% purity) and the resulting mixture was stirred for 2 h at 80°C. The reaction mixture was partitioned between saturated aqueous sodium bicarbonate and ethyl acetate and the aqueous layer was extracted with ethyl acetate 3 times. The combined organic extracts were washed with brine. The organic layer was dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo*. The residue was purified with flash column chromatography on silica gel (10–100% ethyl acetate in hexane) to give 1.46 g (3.20 mmol, 86%) of **6** as a slightly yellow foam. $[\alpha]_D^{22}$: +49° (c=0.93, $CHCl_3$). IR (neat): 2958, 1746, 1617, 1501, 1456, 1355, 1306, 1265, 1221, 1087, 1041, 977, 831, 753 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 6.99 (d, J=8.2 Hz, 1H), 6.40 (dd, J=8.2, 2.3 Hz, 1H), 6.12 (d, J=2.3 Hz, 1H), 5.98 (ddd, J=9.8, 4.1, 1.8 Hz, 1H), 5.32 (dt, J=9.8, 2.3 Hz, 1H), 3.95 (s, 3H), 3.85 (s, 1H), 3.77 (s, 3H), 3.53 (ddd, J=16.7, 4.1, 2.3 Hz, 1H), 3.32 (s, 1H), 2.71 (dt, J=16.7, 1.8 Hz, 1H), 2.64 (s, 3H), 2.40–2.30 (m, 5H), 1.80 (dq, J=14.7, 7.4 Hz, 1H), 1.17 (dq, J=14.7, 7.4 Hz, 1H), 0.28 (t, J=7.4 Hz, 3H). ^{13}C-NMR ($CDCl_3$) δ: 190.2, 169.6, 160.7, 152.9, 129.8, 128.8, 127.3, 123.5, 105.9, 97.1, 87.7, 84.8, 76.2, 70.6, 55.4, 54.4, 53.7, 53.0, 51.5, 43.7, 42.2, 39.2, 27.9, 7.8. HR-MS (FAB): Calcd for $C_{24}H_{28}N_2O_5S$ (M^+) 456.1719. Found 456.1728.

(3a*S*,3a^1*S*,5a*R*,10b*R*)-Methyl 3a-Ethyl-8-methoxy-6-methyl-3a,3a^1,5a,6,11,12-hexahydro-1*H*-indolizino[8,1-*cd*]-carbazole-5-carboxylate (8) To a stirred solution of **6** (4.77 g, 10.4 mmol) in 104 mL of *o*-dichlorobenzene was added 8.12 g (41.8 mmol) of 1,3-dimethyl-2-phenyl-1,3,2-diazaphospholidine (**7**) and the resulting mixture was heated at 160°C for 2.5 h. The reaction mixture was purified with flash column chromatography on silica gel (100% hexane; 10–100% ethyl acetate in hexane) to give 3.61 g (9.49 mmol, 91%) of **8** as a white foam. $[\alpha]_D^{25}$: −105° (c=1.86, $CHCl_3$). IR (neat): 2958, 1711, 1618, 1498, 1436, 1253, 1147, 1085, 1001, 819, 767, 638 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 7.24 (s, 1H), 6.99 (d, J=8.0 Hz, 1H), 6.24 (dd, J=8.0, 2.3 Hz, 1H), 5.97 (d, J=2.3 Hz, 1H), 5.86 (ddd, J=9.8, 4.8, 1.4 Hz, 1H), 5.70 (d, J=9.8 Hz, 1H), 4.22 (s, 1H), 3.78 (s, 3H), 3.77 (s, 3H), 3.46 (dd, J=16.0, 4.8 Hz, 1H), 3.18 (t, J=8.0 Hz, 1H), 2.78 (d, J=16.0 Hz, 1H), 2.72 (s, 3H), 2.43–2.39 (m, 1H), 2.37 (s, 1H), 2.30 (dd, J=12.8, 6.4 Hz, 1H), 1.93–1.85 (m, 1H), 1.48–1.33 (m, 2H), 0.60 (t, J=7.6 Hz, 3H). ^{13}C-NMR ($CDCl_3$) δ: 167.8, 160.5, 152.2, 151.4, 132.2, 130.0, 126.8, 126.1, 123.0, 102.5, 93.8, 75.0, 68.3, 55.2, 54.2, 52.3, 52.0, 51.8, 44.2, 43.6, 34.1, 30.1, 8.1. HR-MS (FAB): Calcd for $C_{23}H_{28}N_2O_3$ (M^+) 380.2100. Found 380.2104.

(3a*S*,3a^1*S*,5a*R*,10b*R*)-Methyl 3a-Ethyl-8-hydroxy-6-methyl-3a,3a^1,5a,6,11,12-hexahydro-1*H*-indolizino[8,1-*cd*]-carbazole-5-carboxylate (9) To a stirred solution of **8** (77 mg, 0.20 mmol) in 2.0 mL of dichloromethane was added 2.0 mL (2.0 mmol) of boron tribromide (1.0 M solution in dichloromethane) at −78°C and the resulting mixture was stirred for 30 min. The reaction mixture was warm up to 0°C and stirred. After 3 h, the reaction mixture was added 2 mL of methanol, then partitioned between saturated aqueous sodium bicarbonate and ethyl acetate, and the aqueous layer was extracted with ethyl acetate 3 times. The combined organic extracts were washed with brine. The organic layer was dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo* to give a crude product. In the same manner, 123 mg (0.323 mmol) of **8** in 3.2 mL of dichloromethane was reacted with 3.2 mL (3.2 mmol) of boron tribromide (1.0 M solution of dichloromethane) to give another crude product. These crude products were purified with flash column chromatography on silica gel (50–80% ethyl acetate in hexane) to give 181 mg (0.494 mmol, 95%) of **9** as a slightly yellow foam. $[\alpha]_D^{24}$: −98° (c=1.14, $CHCl_3$). IR (neat): 2962, 2360, 1710, 1614, 1500, 1383, 1250, 1219, 1083, 1002, 824, 751 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 7.23 (s, 1H), 6.91 (d, J=7.8 Hz, 1H), 6.14 (dd, J=7.8, 2.3 Hz, 1H), 5.89 (d, J=2.3 Hz, 1H), 5.86 (ddd, J=9.8, 4.8, 1.4 Hz, 1H), 5.71 (d, J=9.8 Hz, 1H), 4.22 (s, 1H), 3.74 (s, 3H), 3.47 (dd, J=14.7, 4.8 Hz, 1H), 3.18 (t, J=8.0 Hz, 1H), 2.78 (d, J=14.7 Hz, 1H), 2.69 (s, 3H), 2.43–2.37 (m, 1H), 2.37 (s, 1H), 2.29 (dd, J=12.8, 6.4 Hz, 1H), 1.95–1.86 (m, 1H), 1.47–1.33 (m, 2H), 0.60 (t, J=7.3 Hz, 3H). ^{13}C-NMR ($CDCl_3$) δ: 167.8, 156.6, 152.3, 151.3, 132.3, 129.5, 126.9, 126.1, 123.2, 104.4, 94.9, 74.9, 68.3, 54.2, 52.3, 52.1, 51.8, 44.2, 43.6, 34.1, 30.1, 8.1. HR-MS (FAB): Calcd for $C_{22}H_{26}N_2O_3$ (M^+) 366.1943. Found 366.1932.

(3a*S*,3a^1*S*,5a*R*,10b*R*)-Methyl 3a-Ethyl-6-methyl-8-((methylsulfonyl)oxy)-3a,3a^1,5a,6,11,12-hexahydro-1*H*-indolizino[8,1-*cd*]carbazole-5-carboxylate (10) To a stirred solution of **9** (563 mg, 1.54 mmol) and 0.43 mL (3.1 mmol) of triethylamine in 15.4 mL of dichloromethane was added 0.18 mL (2.3 mmol) of methanesulfonyl chloride. After 5 min, the reaction mixture was partitioned between dichloromethane and saturated sodium bicarbonate. The aqueous layer was extracted with dichloromethane twice. The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (3% methanol in dichloromethane) to give 685 mg (1.54 mmol, quant.) of **10** as a slightly yellow foam. $[\alpha]_D^{18}$: −112° (c=0.58, $CHCl_3$). IR (neat): 2961, 1710, 1611, 1496, 1438, 1367, 1255, 1185, 1140, 1084, 961, 908, 816, 753 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 7.26 (s, 1H), 7.07 (d, J=8.0 Hz, 1H), 6.56 (dd, J=8.0, 2.1 Hz, 1H), 6.26 (d, J=2.1 Hz, 1H), 5.87 (ddd, J=9.9, 5.1, 1.4 Hz, 1H), 5.69 (d, J=9.9 Hz, 1H), 4.31 (s, 1H), 3.78 (s, 3H), 3.47 (dd, J=16.2, 4.3 Hz, 1H), 3.20 (t, J=8.0 Hz, 1H), 3.13 (s, 3H), 2.79 (d, J=16.2 Hz, 1H), 2.73 (s, 3H), 2.45–2.42 (m, 1H), 2.37 (s, 1H), 2.32 (dd, J=12.8, 6.4 Hz, 1H), 1.95–1.87 (m, 1H), 1.45–1.29 (m, 2H), 0.60 (t, J=7.6 Hz, 3H). ^{13}C-NMR ($CDCl_3$) δ: 167.6, 152.2, 151.6, 150.1, 136.5, 132.0, 126.3, 126.1, 123.4,

110.4, 100.3, 74.9, 68.0, 67.9, 54.2, 52.2, 51.9, 44.2, 43.6, 37.1, 33.7, 30.2, 8.0. HR-MS (FAB): Calcd for $C_{23}H_{28}N_2O_5S$ (M^+) 444.1719. Found 444.1715.

(3a*S*,3a^1*S*,5a*R*,10b*S*)-Methyl 3a-Ethyl-8-((methylsulfonyl)-oxy)-3a,3a^1,5a,6,11,12-hexahydro-1*H*-indolizino[8,1-*cd*]-carbazole-5-carboxylate (12) To a stirred solution of **10** (440 mg, 0.990 mmol) in 99 mL of tetrahydrofuran was added 4.4 mL of the aqueous solution which was containing 313 mg (1.98 mmol) of potassium permanganate and 0.67 mL of concentrated sulfuric acid at −78°C. The resulting mixture was stirred for 5 min at −78°C. After 30 mL of methanol was added at −78°C, the reaction mixture was partitioned between saturated aqueous sodium bicarbonate and dichloromethane and the aqueous layer was extracted with dichloromethane 3 times. The combined organic extracts were washed with brine. The organic layer was dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo* to give a crude product. In the same manner, 390 mg (0.877 mmol) of **10** in 88 mL of tetrahydrofuran was reacted with 3.9 mL of the aqueous solution which was containing 277 mg (1.75 mmol) of potassium permanganate and 0.60 mL of conc. sulfuric acid to give another crude product. These crude products were used for the next step without further purification. The crude products were dissolved in 12 mL of 1,4-dioxane and added 12 mL (12 mmol) of 1 M aqueous hydrochloric acid. The resulting solution was heated up to 60°C, and stirred for 40 min. Then, the mixture was cooled to room temperature, and partitioned between saturated aqueous sodium bicarbonate and dichloromethane. The aqueous layer was extracted with dichloromethane 3 times. The combined organic extracts were dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (2% methanol in dichloromethane) to give 727 mg (1.69 mmol, 90%) of **12** as a slightly yellow foam. $[\alpha]_D^{19}$: −135° (c=0.30, $CHCl_3$). IR (neat): 3405, 2964, 1771, 1704, 1612, 1490, 1456, 1364, 1325, 1254, 1181, 1119, 1037, 952, 863, 756 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 7.03 (d, J=8.0 Hz, 1H), 6.86 (s, 1H), 6.54 (dd, J=8.0, 2.1 Hz, 1H), 6.41 (d, J=2.1 Hz, 1H), 5.91 (ddd, J=11.0, 4.8, 1.1 Hz, 1H), 5.51 (d, J=11.0 Hz, 1H), 4.86 (s, 1H), 3.76 (s, 3H), 3.45 (dd, J=16.5, 5.0 Hz, 1H), 3.38–3.32 (m, 1H), 3.11 (s, 3H), 2.87 (d, J=16.5 Hz, 1H), 2.79 (s, 1H), 2.52–2.47 (m, 1H), 2.39–2.23 (m, 1H), 2.00–1.92 (m, 1H), 1.26–1.21 (m, 1H), 1.11–1.06 (m, 1H), 0.77 (t, J=7.3 Hz, 3H). ^{13}C-NMR ($CDCl_3$) δ: 167.5, 150.4, 149.7, 145.3, 132.1, 130.4, 126.9, 125.6, 123.3, 110.7, 102.1, 65.7, 62.7, 62.6, 52.4, 52.2, 51.8, 42.9, 40.8, 37.1, 31.3, 8.0. HR-MS (FAB): Calcd for $C_{22}H_{27}N_2O_5S$ ($M+H^+$) 431.1641. Found 431.1639.

(3a*R*,3a^1*R*,4*R*,10b*R*)-Methyl 3a-Ethyl-4-hydroxy-8-((methylsulfonyl)oxy)-3a,3a^1,4,6,11,12-hexahydro-1*H*-indolizino[8,1-*cd*]-carbazole-5-carboxylate (15) To a stirred solution of **12** (2.00 g, 4.65 mmol) in 47 mL of benzene was added 2.39 g (4.65 mmol) of benzeneseleninic anhydride (**13**, 70% purity) and the resulting mixture was stirred for 5 min at 90°C. The reaction mixture was partitioned between saturated aqueous sodium bicarbonate and dichloromethane and the aqueous layer was extracted with dichloromethane 3 times. The combined organic extracts were washed with brine. The organic layer was dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo*. In the same manner, 2.73 g (6.35 mmol) of **12** was reacted with 3.27 g (6.35 mmol) of benzeneseleninic anhydride (**13**, 70% purity) to give another crude product. These crude products were purified with flash column chromatography on silica gel (50–100% ethyl acetate in hexane) to give 4.11 g (9.20 mmol, 84%) of **15** as a slightly yellow foam. $[\alpha]_D^{20}$: −140° (c=0.31, $CHCl_3$). IR (neat): 3354, 2964, 1682, 1609, 1483, 1437, 1365, 1244, 1181, 1102, 952, 753 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 9.23 (br s, 1H), 7.18 (d, J=7.8 Hz, 1H), 6.80 (d, J=7.8 Hz, 1H), 6.80 (s, 1H), 6.61 (br s, 1H), 6.05 (dd, J=9.8, 4.1 Hz, 1H), 5.83 (d, J=9.8 Hz, 1H), 4.68 (d, J=2.1 Hz, 1H), 3.80 (s, 3H), 3.57 (dd, J=15.8, 4.8 Hz, 1H), 3.21–3.18 (m, 1H), 3.18 (s, 3H), 3.11 (d, J=15.8 Hz, 1H), 2.90 (s, 1H), 2.68–2.57 (m, 1H), 2.51–2.44 (m, 1H), 1.83 (dd, J=11.9, 4.4 Hz, 1H), 1.03–0.90 (m, 2H), 0.66 (t, J=7.6 Hz, 3H). ^{13}C-NMR ($CDCl_3$) δ: 168.5, 166.7, 149.0, 144.0, 136.3, 130.7, 127.0, 121.3, 114.0, 104.4, 98.6, 69.7, 68.9, 53.5, 51.4, 51.3, 51.0, 45.1, 44.4, 37.5, 28.7, 7.4. HR-MS (FAB): Calcd for $C_{22}H_{26}N_2O_6S$ (M^+) 446.1512. Found 446.1518.

11-Mesyloxytabersonine (3) To a stirred solution of **15** (826 mg, 1.85 mmol) in 18.5 mL of methanol was added 0.12 mL (2.0 mmol) of acetic acid and 151 mg (2.40 mmol) of sodium cyanoborohydride and the resulting mixture was stirred for 40 min at 60°C. The reaction mixture was partitioned between saturated aqueous sodium bicarbonate and dichloromethane and the aqueous layer was extracted with dichloromethane 3 times. The combined organic extracts were washed with brine. The organic layer was dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo*. In the same manner, 906 mg (2.03 mmol) of **15** was reacted with 0.13 mL (2.2 mmol) of acetic acid and 166 mg (2.64 mmol) of sodium cyanoborohydride to give another crude product. These crude products were purified with flash column chromatography on silica gel (20–60% ethyl acetate in hexane) to give 1.15 g (2.67 mmol, 69%) of **3** as a slightly yellow foam. $[\alpha]_D^{20}$: −153° (c=0.38, $CHCl_3$). IR (neat): 3363, 2963, 1682, 1610, 1483, 1437, 1363, 1182, 1102, 953, 865, 757 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 9.04 (br s, 1H), 7.22 (d, J=7.8 Hz, 1H), 6.76 (d, J=7.8 Hz, 1H), 6.75 (s, 1H), 5.79 (dd, J=10.1, 3.4 Hz, 1H), 5.71 (d, J=10.1 Hz, 1H), 3.78 (s, 3H), 3.46 (dd, J=16.0, 3.4 Hz, 1H), 3.18 (d, J=16.0 Hz, 1H), 3.17 (s, 3H), 3.06 (t, J=7.3 Hz, 1H), 2.71–2.63 (m, 1H), 2.65 (s, 1H), 2.55 (d, J=15.6 Hz, 1H), 2.41 (d, J=15.6 Hz, 1H), 2.15–2.02 (m, 1H), 1.81 (dd, J=11.4, 4.1 Hz, 1H), 1.04–0.95 (m, 1H), 0.91–0.82 (m, 1H), 0.65 (t, J=7.4 Hz, 3H). ^{13}C-NMR ($CDCl_3$) δ: 168.7, 165.7, 148.9, 144.5, 137.2, 132.8, 124.8, 122.1, 113.5, 103.7, 93.7, 70.0, 54.5, 51.2, 50.9, 50.4, 44.4, 41.1, 37.3, 28.4, 27.0, 7.5. HR-MS (FAB): Calcd for $C_{22}H_{26}N_2O_5S$ (M^+) 430.1562. Found 430.1552.

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Supplementary Materials The online version of this article contains supplementary materials.

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