Supporting Information for *Angew. Chem. Int. Ed.* Z18786

A short synthesis of (±)-13-deoxyserratine.

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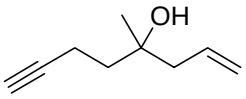
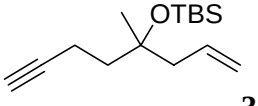
Experimental Section



2'

4-Methyl-oct-1-en-7-yn-4-ol (2'). To a solution of 5-hexyn-2-one (2.28 g, 23.7 mmol) in dry ether under argon was added allylmagnesium bromide (1.0M in ether, 26 ml, 26 mmol) and the reaction mixture was stirred at room temperature for 15 min. Saturated aqueous ammonium chloride was added and the mixture was extracted with ether. The combined organic layer was dried over magnesium sulfate, filtered and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, heptane-AcOEt, 90:10) to give **2'** (5.73 g, 96%) as a colorless oil. ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.19 (s, 3H), 1.74 (t, *J* = 7.3 Hz, 2H), 1.86 (s, 1H), 1.98 (t, *J* = 2.5 Hz, 1H), 2.24 (d, *J* = 8.1 Hz, 2H), 2.32 (td, *J* = 7.3, 2.5 Hz, 2H), 5.14 (m, 2H), 5.85 (m, 1H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 13.2, 26.4, 40.0, 46.5, 68.6, 71.9, 84.9, 119.1, 133.6. IR (neat) 3405, 3304, 3076, 2976, 2929, 2117, 1639, 1438, 1376, 1115 cm^{-1}. MS (CI+ NH_3) m/z 156 (MNH_4^+), 138 (M-OH+NH_3^+), 121 (M-OH^+).

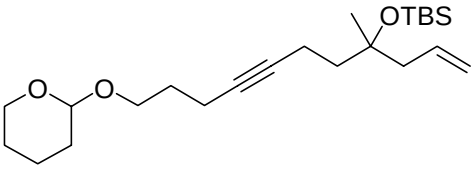


3

(1-Allyl-1-methyl-pent-4-ynyloxy)- *tert*-butyl-dimethyl-silane (3). To a solution of **2'** (1.55 g, 11.2 mmol) in dry dichloromethane under argon at 0°C were added 2,6-lutidine (3.26 ml, 28.0 mmol) and *tert*-butyldimethylsilyl trifluoromethanesulfonate (2.82 ml, 12.3 mmol) and the reaction mixture was stirred for 30 min. Aqueous 1.0M HCl was added and the mixture was extracted with ether. The combined organic layer was dried over magnesium sulfate, filtered, and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, heptane) to give **3** (2.81 g, 100%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.09 (s, 6H), 0.87 (s, 9H), 1.20 (s,3H), 1.71 (m, 2H), 1.92 (t, *J* = 2.3 Hz, 1H), 2.22 (d, *J* = 7.6 Hz, 2H),

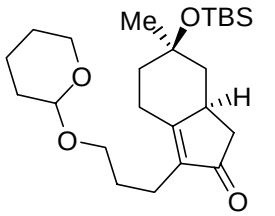
2.26 (td, *J* = 8.2, 2.3 Hz, 2H), 5.05 (m, 2H), 5.80 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ -1.9, 13.3, 18.4, 26.0, 27.3, 41.2, 47.2, 67.8, 74.8, 85.3, 117.7, 134.7.

IR (CCl_4) 3313, 2955, 2929, 2856, 2120, 1640, 1472, 1375, 1254, 1125, 1081, 1042 cm^{-1}. MS (CI+ NH_3) m/z 253 (MH^+), 211, 138, 121. Anal. calcd. for $C_{15}H_{28}OSi$: C, 71.36; H, 11.18, found: C, 71.32; H, 11.22.



4

[1-Allyl-1-methyl-8-(tetrahydro-pyran-2-yloxy) -oct-4-ynyloxy]-*tert*-butyl-dimethyl-silane (4). To a solution of **3** (1.0 g, 3.96 mmol) in dry tetrahydrofuran under argon at -78°C was added n-BuLi (1.53M in hexanes, 2.84 ml, 4.35 mmol) and the reaction mixture was stirred for 30 min. HMPT (3.5 ml) was added and the mixture was slowly cooled to O°C. 2-(3-Bromo-propoxy)-tetrahydro-pyran was then added and the mixture was stirred for 1 h at 0°C and 3 h at room temperature. Saturated aqueous ammonium chloride was added and the mixture was extracted with ether. The combined organic layer was dried over magnesium sulfate, filtered, and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, heptane-AcOEt, 95:5) to give **4** (1.29 g, 83%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.08(s, 6H), 0.86 (s, 9H), 1.18 (s, 3H), 1.50-1.85 (m, 8H), 1.77 (t, *J* = 6.4 Hz, 2H), 2.18-2.28 (m, 4H), 2.20 (d, *J* = 7.6 Hz, 2H), 3.44-3.53 (m, 2H), 3.74-3.90 (m, 2H), 4.60 (dd, J = 2.9, 2.9 Hz, 1H), 5.03 (m, 2H), 5.80 (m, 1H). ^{13}C NMR (250 MHz, $CDCl_3$) δ -1.9, 13.5, 15.8, 18.3, 19.6, 25.6, 25.9, 27.3, 29.3, 30.8, 41.8, 47.1,62.1, 66.1, 74.9, 79.0, 80.9, 98.8, 117.4, 134.8. IR (neat) 3076,2930, 2856, 1640, 1472, 1441, 1374, 1359, 1254, 1159, 1137, 1121, 1077, 1036 cm^{-1}. MS (CI+ NH_3) m/z 412 (MNH_4^+). Anal. calcd. for $C_{23}H_{42}O_3Si$: C, 70.00; H, 10.73, found: C, 70.29 ; H, 10.87.

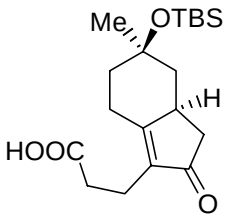


5

6-(*tert*-Butyl-dimethyl-silanyloxy)-6-methyl-3-[3-(tetrahydro-pyran-2-yloxy)-propyl]-1,4,5,6,7,7a-hexahydro-inden-2-one (5). To a solution of **4** (560 mg, 1.42 mmol) in dichloromethane (7 ml) was added dicobalt octacarbonyl (533 mg, 1.56 mmol) and the black reaction mixture was stirred at room temperature for 1 h. The mixture was diluted with dichloromethane (7 ml) and tetrahydrofuran (14 ml) and 4-Methylmorpholine *N*-oxide monohydrate (1.9 g, 14.2 mmol) was added. The solution was stirred at room temperature for 1h, at which time the mixture has turned purple and no cobalt complex was visible by TLC. The mixture was filtered through celite (washing solvent ether) and the solvents were

removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, heptane-AcOEt, 90:10) to give major isomer **5** (497 mg, 83%) as a colorless oil.

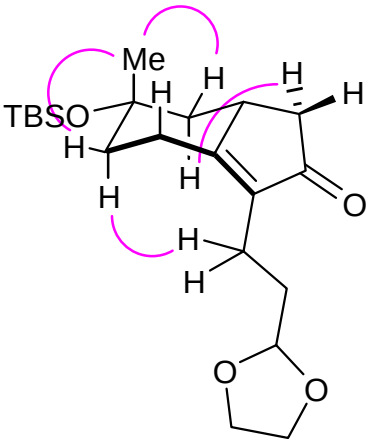
5 (mixture of THP isomers) : ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.05 (s, 6H), 0.85 (s, 9H), 0.98 (dd, *J* = 12.6, 12.6 Hz, 1H), 1.19 (s, 3H), 1.21-1.88 (m, 11H), 2.01 (ddd, *J* = 12.6, 5.2, 2.5 Hz, 1H), 2.16 (bt, *J* = 7.5 Hz, 2H), 2.44 (dd, *J* = 18.5, 6.5 Hz, 1H), 2.42-2.68 (m, 2H), 2.91 (dddd, *J* = 12.6, 6.5, 5.2, 2.5 Hz, 1H), 3.17-3.28 (m, 1H), 3.34-3.42 (m, 1H), 3.54-3.64 (m, 1H), 3.70-3.80 (m, 1H), 4.44 (m, 1H). ^{13}C NMR (50 MHz, $CDCl_3$) δ -2.0, 18.3, 19.2, (19.6, 19.7), 24.1, 25.4, 25.9, 28.5, 30.2, 30.7, 35.6, 39.8, 40.9, 48.0, (62.2, 62.3), 66.7, 72.3, 98.7, 136.5, 176.2, 208.3. IR (neat) 2930, 2856, 1699, 1651, 1440, 1373, 1255, 1137, 1035 cm^{-1}. MS (CI+ NH_3) m/z 339 ($M\text{-}THP+2H^+$).



6

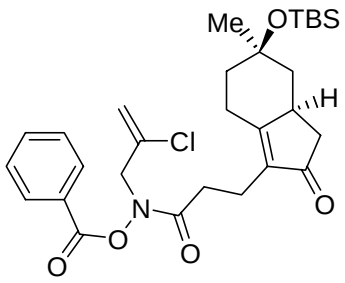
3-[5-(*tert*-Butyl-dimethyl-silanyloxy)-5-methyl-2-oxo-3,3a,4,5,6,7 -hexahydro-2*H*-inden-1-yl]-propionic acid (6). To a solution of **5** in acetone (25 ml) at 0°C was added a Jones solution (2.6 [Cr] M, 1.31 ml, 3.42 mmol) and the solution was stirred for 2h. Water was added and the mixture extracted with dichloromethane. The organic layer was basified with 1.0M NaOH until pH 9 and the aqueous layer was separated, acidified with 1.0M HCl until pH 1 and extracted with ether. The organic layer was dried over magnesium sulfate, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, heptane-AcOEt, 50:50) to give **6** (390 mg, 97%) as a colorless oil which crystallize with time as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.11 (s, 3H), 0.12 (s, 3H), 0.88 (s, 9H), 1.06 (dd, *J* = 12.9, 12.9 Hz, 1H), 1.26 (s, 3H), 1.33 (ddd, *J* = 13.5, 13.5, 4.7 Hz, 1H), 1.87 (dd, *J* = 18.8, 2.3 Hz, 1H), 1.91 (m, 1H), 2.08 (ddd, *J* = 12.9, 5.3, 2.3 Hz, 1H), 2.45-2.55 (m, 5H), 2.54 (dd, *J* = 18.8, 6.5 Hz, 1H), 2.71 (ddd, *J* = 14.0, 4.7, 2.3 Hz, 1H), 3.01 (dddd, *J* = 12.9, 6.5, 5.3, 2.3 Hz, 1H), 10.50 (bs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ -2.0, -1.9, 18.1, 18.4, 24.4, 26.1, 30.2, 32.4, 36.1, 39.9, 41.0, 48.1, 72.4, 135.0, 178.3, 178.7, 209.1. IR (CCl_4) 2955, 2929, 2856, 1708, 1652, 1255, 1098, 1050, 1036 cm^{-1}. MS (CI+ NH_3) m/z 353 (MH^+). MP (heptane) 88-90°C. Anal. calcd. for $C_{19}H_{32}O_4Si$: C, 64.73; H, 9.15, found: C, 64.57; H, 9.13.

Compound **6** can also be obtained by Jones oxidation of compound **6'** on which ^{1}H/^{1}H NOESY (400 MHz, CDCl3) experiments have been performed : the observed correlations are in good agreement with results recently reported by Saito and coworkers for similar molecules (Ishikawa, T.; Shimizu, K.; Ishii, H.; Ikeda, S.; Saito, S. *J. Org. Chem.* **2001**, *66*, 3834-3847.).



NOESY correlation

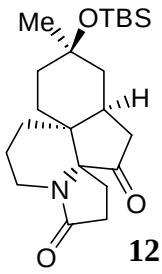
6'



10

***N*-Benzoyloxy-3-[5-(*tert*-butyl-dimethyl-silanyloxy) -5-methyl-2-oxo-3,3a,4,5,6,7-hexahydro-2*H*-inden-1-yl]-*N*-(2-chloro-allyl)-propionamide (10).** To a solution of **6** (200 mg, 0.567 mmol) in tetrahydrofuran under argon at 0°C were added triethylamine (87 µl, 0.624 mmol) and isobutylchloroformate (81 µl, 0.624 mmol) and the reaction mixture was stirred for 10 min. Excess of triethylamine was added (2 ml) and a solution of *N*-(2-Chloro-allyl)-hydroxylamine (610 mg, 5.68 mmol) in tetrahydrofuran was added. The reaction mixture was stirred for 10 min at 0°C and 30 min at room temperature. Aqueous 1.0M HCl was added and the mixture was extracted with ether. The separated organic layer was dried over magnesium sulfate, filtered and the solvents were remover under reduced pressure. The residue was taken up in dichloromethane and triethylamine (210 µl, 1.50 mmol) and benzoyl chloride (131 µl, 1.13 mmol) were added. The mixture was stirred for 1 h at room temperature. Water was then added and the mixture was extracted with ether. The separated organic layer was dried over magnesium sulfate, filtered and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, heptane-AcOEt, 85:15) to give **10** (250 mg, 81%) as a colorless oil.^{1}H NMR (300 MHz, $CDCl_3$) δ 0.11 (s, 3H), 0.12 (s, 3H), 0.88 (s, 9H), 1.09 (dd, *J* = 12.9, 12.9 Hz, 1H), 1.25 (s, 3H), 1.36 (ddd, *J* = 13.4, 13.4, 4.6 Hz, 1H), 1.85 (d, *J* = 18.0 Hz, 1H), 1.90 (m, 1H), 2.07 (ddd, *J* = 12.9, 5.5, 2.3 Hz, 1H), 2.50 (dd, *J* = 18.0, 6.5 Hz, 1H), 2.45-2.65 (m, 5H), 2.79 (ddd, *J* = 13.8, 4.6, 2.1 Hz, 1H), 2.99 (ddd, *J* = 12.9, 6.5, 5.5 Hz, 1H), 4.57 (bs, 1H), 5.38 (d, *J* = 9.2 Hz, 2H), 7.50 (t, *J* = 7.9 Hz, 2H), 7.65 (t, *J* = 7.9 Hz, 1H), 8.05 (d, *J* = 7.9 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ -2.0, -1.9, 18.1, 18.4, 24.4, 26.0, 30.1, 30.2, 35.9, 39.8, 41.0, 47.9, 53.5, 72.4, 115.9, 126.5, 128.9, 130.1, 134.5, 134.9, 135.6, 164.2, 172.9, 178.0, 208.0. IR (neat)

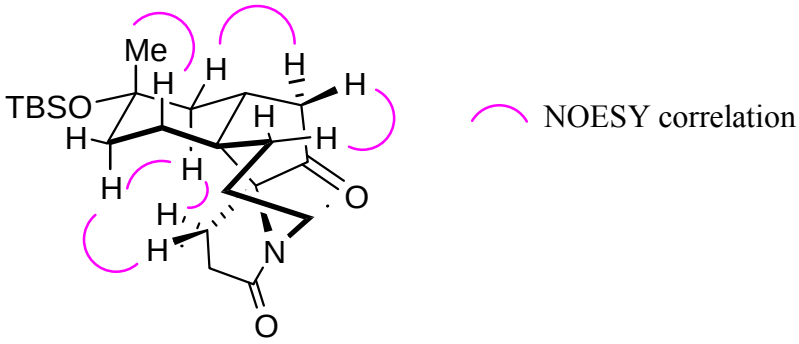
2929, 2855, 1766, 1694, 1650, 1452, 1254, 1099, 1038, 1006 cm^{-1}. MS (CI+ NH_3) m/z 546 (MH^+), 426 (M-BzO+$2H^+$), 390, 322. Anal. calcd. for $C_{29}H_{40}ClNO_5Si$: C, 63.77; H, 7.38, found: C, 63.78; H, 7.45.

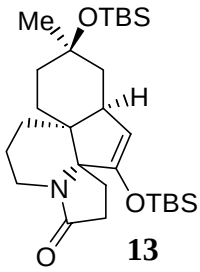


12

2-(*tert*-Butyl-dimethyl-silanyloxy)-2-methyl-decahydro-indeno[7a,1-*h*] indolizine-9,12-dione (12). To a degassed solution of **10** (100 mg, 0.183 mmol) and 1,1'-azobis(cyclohexanecarbonitrile) (2 mg, 0.009 mmol) in refluxing α,α,α-trifluorotoluene (1.5 ml) was added a degassed solution of Bu_3SnH (103 µl, 0.384 mmol) and 1,1'-azobis(cyclohexanecarbonitrile) (9 mg, 0.037 mmol) in α,α,α-trifluorotoluene (3 ml) over 8h. The reaction mixture was then cooled to room temperature and concentrated. The residue was purified by flash column chromatography (silicagel, heptane to heptane-AcOEt 70:30) to give **12** (37 mg, 52 %) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.10 (s, 3H), 0.11 (s, 3H), 0.90 (s, 9H), 1.26 (dd, J = 13.5, 13.5 Hz, 1H), 1.28-1.32 (m, 1H), 1.29 (s, 3H), 1.39 (m, 1H), 1.43-1.54 (m, 2H), 1.62 (m, 1H), 1.67-1.75 (m, 2H), 1.82-1.94 (m, 3H), 2.09 (dd, J = 20.5, 3.9 Hz, 1H), 2.13 (m, 1H), 2.26 (m, 1H), 2.33-2.44 (m, 3H), 2.66 (dd, J = 20.5, 10.0 Hz, 1H), 3.98 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ -1.9, -1.8, 18.5, 19.3, 25.8, 26.2, 27.2, 28.7, 31.0, 34.4, 37.8, 38.0, 38.6, 38.8, 38.9, 45.9, 71.8, 74.1, 175.5, 216.7. IR (CCl_4) 2933, 2856, 1748, 1703, 1393, 1253, 1153, 1122, 1106, 1020. MP 136-139°C. MS (CI+ NH_3) m/z 392 (MH^+), 260 (M-$OTBS^+$). HRMS (CI+ CH_4) Calcd. for $C_{22}H_{38}NO_3Si$ 392.2621, found 392.2626.

^{1}H/^{1}H NOESY (400 MHz, CDCl3):

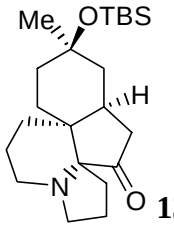




13

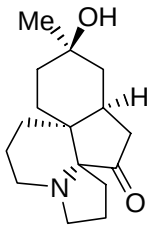
2,12-Bis-(*tert*-butyl-dimethyl-silanyloxy)-2-methyl-1,3,4,6,7,10,11,13a-octahydro-2*H*,5*H*-indeno[7a,1-*h*]indolizin-9-one (13). To a solution of **11** (28 mg, 0.071 mmol) in dry dichloromethane (0.8 ml) were added triethylamine (50 µl, 0.357 mmol) and *tert*-butyldimethylsilyl trifluoromethanesulfonate (65 µl, 0.286 mmol) and the reaction mixture was

stirred at room temperature for 3h. The mixture was diluted with dichloromethane and saturated aqueous sodium hydrogenocarbonate was added. The organic layer was separated dried over sodium sulfate, filtered and concentrated. The residue was purified by flash column chromatography (silica gel, heptane-AcOEt, 80:20) to give **13** (29 mg, 83%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.09 (s, 6H), 0.17 (s, 3H), 0.18 (s, 3H), 0.89 (s, 18H), 1.01 (dd, J = 12.3, 12.3 Hz, 1H), 1.25 (s, 3H), 1.23-1.48 (m, 4H), 1.57-1.85 (m, 6H), 2.15-2.25 (m, 2H), 2.31-2.53 (m, 3H), 4.05 (m, 1H), 4.63 (d, J = 3.5 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ -5.1, -4.6, -1.8, 17.8, 20.5, 25.6, 26.2, 26.6, 30.5, 31.1, 31.4, 38.2, 39.1, 39.2, 40.9, 43.2, 44.9, 72.1, 73.6, 104.4, 155.7, 175.6. IR (CCl_4) 2930, 2857, 1695, 1644, 1402, 1252, 1100. MS (CI+ NH_3) m/z 507 (MH^+).



13'

2-(*tert*-Butyl-dimethyl-silanyloxy)-2-methyl-decahydro-indeno[7a,1-*h*] indolizin-12-one (13'). To a solution of **13** (26 mg, 0.051 mmol) in dry tetrahydrofuran (4 ml) was added $LiAlH_4$ (19 mg, 0.514 mmol) and the reaction mixture was refluxed for 45 min. The mixture was cooled to 0°C, diluted with ether and carefully quenched with water. The organic layer was separated, dried over magnesium sulfate, filtered and concentrated. The residue was purified by flash column chromatography (silica gel, heptane-AcOEt, 70:30) to give **13'** (11mg, 58%) as a white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.09 (s, 6H), 0.89 (s, 9H), 1.25 (s,3H), 1.30-1.89 (m, 14H), 1.92 (dd, J = 19.8, 3.0 Hz, 1H), 2.33 (dddd, J = 10.9, 9.7, 5.5, 3.0 Hz, 1H), 2.51 (dd, J = 19.8, 9.7 Hz, 1H), 2.52 (dd, J = 11.0, 11.0 Hz, 1H), 2.72 (td, J = 11.0, 4.3 Hz, 1H), 2.97 (m, 1H), 3.18 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ -1.8, -1.7, 18.5, 19.9, 21.9, 26.2, 26.5, 30.2, 31.0, 34.2, 37.2, 37.9, 38.9, 40.0, 44.8, 47.2, 50.4, 72.2, 75.2, 216.2. IR (neat) 2930, 2854, 1734, 1471, 1252, 1106, 1058, 1022 cm^{-1}. MS (CI+ NH_3) m/z 378 (MH^+), 246 (M-$OTBS^+$). MP 65-67°C. HRMS (CI+ CH_4) Calcd. for $C_{22}H_{40}NO_2Si$ 378.2828, found 392.2825.



1

2-Hydroxy-2-methyl-decahydro-indeno[7a,1-*h*]indolizin-12-one. 13-deoxyserratine (1). To a solution of **13'** (11 mg, 0.029 mmol) in dry tetrahydrofuran (0.8 ml) was added tetrabutyl ammonium fluoride (1.0 M. in tetrahydrofuran, 87 µl, 0.087 mmol) and the reaction mixture was refluxed for 6h. Aqueous 1.0 M. NaOH was added and the mixture was extracted with ether. The separated organic layer was dried over sodium sulfate, filtered and concentrated to give pure **13** (7.2 mg, 96%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ

1.27 (s,3H), 1.25-1.89 (m, 14H), 2.01 (dd, J = 19.4, 4.1 Hz, 1H), 2.48 (m, 1H), 2.58 (dd, J = 19.4, 9.9 Hz, 1H), 2.58-2.64 (m, 2H), 2.90 (m, 1H), 3.10 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.0, 21.5, 27.1, 28.3, 29.8, 30.8, 33.7, 34.4, 36.3, 39.4, 42.1, 47.8, 50.9, 69.7, 76.1. IR (CCl_4) 3612 (OH), 2975, 2930, 2855, 1734 (C=O), 1117 . MS (CI+ NH_3) m/z 264 (MH^+), 246 (M-OH^+). MS (EI) m/z 263 (M^+, 9), 235 (M^+-28, 38), 136 (100) (fragmentations in good agreement with results reported in "Mass Spectra of serratinine and its derivatives", Inubushi, Y.; Ibuka, T.; Harayama, T. *Tetrahedron*, **1968**, *24*, 3541-3556). HRMS (CI+ CH_4) Calcd. for $C_{16}H_{26}NO_2$ 264.1964, found 264.1965.