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속보 (Communications)

SUPPORTING INFORMATION

The First Synthesis of 3-epi-Xestoaminol C

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Experiments

General; Chiral aziridines are available from Aldrich. All commercially available compounds were used as received unless stated otherwise. All reactions were carried out under an atmosphere of nitrogen in oven-dried glassware with magnetic stirring. Reactions were monitored by thin layer chromatography (TLC) with 0.25 mm E. Merck precoated silica gel plates (60 F254). Visualization was accomplished with either UV light, or by immersion in solutions of ninhydrin, p-anisaldehyde, or phosphomolybdic acid (PMA) followed by heating on a hot plate for about 10 sec. Purification of reaction products was carried out by flash chromatography using Kieselgel 60 Art 9385 (230-400 mesh). ¹H NMR and ¹³C NMR spectra were obtained using a Bruker 400 (400 MHz for ¹H, and 100 MHz for ¹³C) spectrometer. Chemical shifts are reported relative to chloroform ($\delta = 7.26$) for ¹H NMR and chloroform ($\delta = 77.2$) for ${}^{13}C$ NMR. Data are reported as (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet.) Coupling constants are given in Hz. Ambiguous assignments were resolved on the basis of standard one dimensional proton decoupling experiments. Optical rotations were obtained using a Rudolph Autopol III digital polarimeter and a JASCO P-2000 polarimeter. Optical rotation data was reported as follows: $[\alpha]^{20}$ (concentration c = g/100 mL, solvent).



1-((S)-1-((R)-1-phenylethyl)aziridin-2-yl)dodecan-1-one (3)

Magenesium (25 mg, 1.023 mmol) was added in cat. iodine dissolved THF (2.73 mL). The mixture was warmed to reflux. After 30 min, 1-bromoundecane (0.183 mL, 0.818 mmol) was dropping at the reaction mixture. After magenisium was dissolved, (S)-N-methoxy-N-methyl-1-

((R)-1-phenylethyl)aziridine-2-carboxamide (0.2 g, 0.854) mmol) dissolved THF (3.4 mL) was dropping at the mixture at 0 °C. After 1 h, the progress of the reaction was monitored by TLC. After completion of the reaction, the resulting mixture was quenched by ammonium chloride at 0 °C and extracted with ethyl acetate and washed with water. The organic extracts were dried over anhydrous MgSO₄, filtered and concentrated under vacuo. The residue was purified by flash column chromatography on silica gel (EtOAc/Hexane = 9:91) to give (0.13 g, 96%) as a transparent oil; $[\alpha]^{20}$ -63.9 (c2.07, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.26–7.12 (m, 5H), 2.45 (q, J = 6.6 Hz, 1H), 2.33-2.23 (m, 1H), 2.18-2.08 (m, 1H)2H), 2.02 (dd, J = 6.7, 3.1 Hz, 1H), 1.68 (dd, J = 6.7, 1.0 Hz, 1H), 1.36 (d, J = 6.6 Hz, 3H), 1.25–1.05 (m, 18H), 0.80 (t, J = 6.9 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 208.49, 143.95, 128.43, 127.26, 126.56, 77.48, 77.16, 76.84, 70.00, 43.98, 38.55, 35.32, 31.93, 29.63, 29.46, 29.37, 29.35, 29.15, 23.44, 23.38, 22.70, 14.12.



(S)-1-((S)-1-((R)-1-phenylethyl)aziridin-2-yl)dodecan-1-ol (4)

1-((*S*)-1-((*R*)-1-phenylethyl)aziridin-2-yl)dodecan-1-one (0.198 g, 0.601 mmol) was dissolved in THF (3.34 mL). L-selectride (1.803 mL, 1.803 mmol) was added at –78 °C. After 1 h, the progress of the reaction was monitored by TLC. After completion of the reaction, the resulting mixture was quenched by water at 0 °C and extracted with dichloromethane and washed with water. The organic extracts were dried over anhydrous MgSO₄, filtered and concentrated under *vacuo*. The residue was purified by flash column chromatography on silica gel (EtOAc/Hexane = 25:75) to give (0.165 g, 83%) as a transparent oil; [α]²⁰ 43.721 (*c* 4.28, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.28–7.15 (m, 5H), 3.12–3.05 (m, 1H), 2.39 (q, J = 6.5 Hz, 1H), 1.82 (d, J = 3.4 Hz, 1H), 1.69 (d, J = 5.1 Hz, 1H), 1.46–1.39 (m, 2H), 1.37 (d, J = 6.6 Hz, 3H), 1.24–1.01 (m, 20H), 0.81 (t, J = 6.9 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 144.62, 128.69, 127.60, 127.02, 77.48, 77.16, 76.84, 71.45, 69.86, 43.00, 35.55, 32.02, 31.79, 29.74, 29.72, 29.67, 29.65, 29.57, 29.44, 25.48, 22.78, 22.60, 14.20.



(*R*)-1-((*S*)-1-((*R*)-1-phenylethyl)aziridin-2-yl)dodecan-1-ol (5)

1-((S)-1-((R)-1-phenylethyl)aziridin-2-yl)dodecan-1one (0.13 g, 0.395 mmol) was dissolved in MeOH (3.95 mL). Zinc chloride (80 mg, 0.592 mmol) was added at -78 °C. After 30 min, sodium borohydride (44 mg, 1.184 mmol) was added. After 2 h, the progress of the reaction was monitored by TLC. After completion of the reaction, the resulting mixture was quenched by water at 0 °C and extracted with dichloromethane and washed with water. The organic extracts were dried over anhydrous MgSO₄, filtered and concentrated under vacuo. The residue was purified by flash column chromatography on silica gel (EtOAc/Hexane = 25:75) to give (85 mg, 65%) as a transparent oil; $[\alpha]^{20}$ 9.4 (c 2.84, CHCl₃) ¹H NMR (400 MHz, CDCl₃) δ 7.35–7.23 (m, 5H), 3.53 (dd, J=9.2, 5.5 Hz, 1H), 2.58 (q, J=6.5 Hz, 1H), 1.95 (d, J=6.5 Hz, 1H)J = 3.6 Hz, 1H), 1.57 (dt, J = 7.1, 3.6 Hz, 1H), 1.42 (d, J =6.6 Hz, 3H), 1.37 (d, J = 3.4 Hz, 1H), 1.36–1.15 (m, 20H), 0.88 (t, J = 6.9 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 144.54, 128.50, 127.21, 126.70, 77.48, 77.16, 76.84, 69.43, 68.53, 42.12, 34.80, 32.02, 29.84, 29.76, 29.73, 29.69, 29.63, 29.45, 25.33, 23.26, 22.79, 14.22.



tert-Butyl ((2*S*,3*S*)-3-hydroxytetradecan-2-yl)carbamate (6)

(*S*)-1-((*S*)-1-((*R*)-1-phenylethyl)aziridin-2-yl)dodecan-1-ol (0.424 g, 1.279 mmol) was dissolved in MeOH (12.79 mL). Di-*tert*-butyl dicarbonate (0.306 g, 1.406 mmol) and palladium hydroxide (0.272 g, 0.256 mmol) was added. The mixture was stirred at roomtemperature under hydrogen gas. After 6 h, the progress of the reaction was monitored by TLC. After completion of the reaction, the resulting mixture was filtered and concentrated under *vacuo*. The residue was purified by flash column chromatography on silica gel (EtOAc/Hexane = 11:89) to give (0.362 g, 86%) as a white solid; $[\alpha]^{20}$ -14.7 (*c* 4.28, CH₃OH); ¹H NMR (400 MHz, CDCl₃) δ 4.62 (s, 1H), 3.56 (s, 1H), 3.44–3.37 (m, 1H), 1.98 (s, 1H), 1.37 (s, 9H), 1.21 (d, *J* = 16.8 Hz, 20H), 1.10 (d, *J* = 6.8 Hz, 3H), 0.81 (t, *J* = 6.9 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 156.35, 79.45, 77.48, 77.16, 76.84, 75.20, 50.47, 34.39, 32.06, 29.80, 29.78, 29.77, 29.75, 29.71, 29.49, 28.54, 25.74, 22.82, 18.52, 14.24.



tert-butyl ((2*S*,3*R*)-3-hydroxytetradecan-2-yl)carbamate (7)

a white solid; $[\alpha]^{20}$ -4.7 (*c* 0.74, CH₃OH); ¹H NMR (400 MHz, CDCl₃) δ 4.91 (d, *J* = 7.9 Hz, 1H), 3.68 (s, 1H), 3.64 (s, 1H), 2.54 (s, 1H), 1.44 (s, *J* = 6.2 Hz, 9H), 1.27 (d, *J* = 9.5 Hz, 20H), 1.08 (d, *J* = 6.8 Hz, 3H), 0.88 (t, *J* = 6.8 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 155.99, 79.50, 77.48, 77.16, 76.84, 74.54, 50.66, 33.62, 32.03, 29.80, 29.77, 29.74, 29.71, 29.69, 29.46, 28.53, 26.18, 22.80, 14.40, 14.23.



(+)-Xestoaminol C (2)

tert-butyl ((2S,3R)-3-hydroxytetradecan-2-yl)carbamate (52 mg, 0.175 mmol) was dissolved in MeOH (1.75 mL). Hydrochloric acid (81 uL, 2.627 mmol) was added. The reaction mixture warmed to reflux. After 3 h, The progress of the reaction was monitored by TLC. After completion of the reaction, the mixture was concentrated under *vacuo*. The residue was purified by Amberlite IRA-410 chloride form anion exchange chromatography to give the expected product (33 mg, 82%) as white solid; $[\alpha]^{20}$ +5.0 (*c* 4.06, CH₃OH); ¹H NMR (400 MHz, CD₃OD) δ 3.43 (dt, *J*=7.4, 3.7 Hz, 1H), 2.81 (qd, *J*= 6.6, 4.2 Hz, 1H), 1.41–1.26 (m, 20H), 1.06 (d, *J*= 6.6 Hz, 3H), 0.92 (t, *J*= 6.9 Hz, 3H).¹³C NMR (101 MHz, CD₃OD) δ 76.35, 52.13, 49.64, 49.43, 49.21, 49.00, 48.79, 48.57, 48.36, 33.98, 33.09, 30.84, 30.81, 30.78, 30.49, 27.28, 23.75, 17.08, 14.47.



a white solid; $[\alpha]^{20}$ -6.1 (*c* 0.23, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 3.54 (t, *J* = 7.3 Hz, 1H), 3.21–3.17 (m, 1H), 1.56–1.38 (m, 3H), 1.29 (d, *J* = 6.3 Hz, 3H), 1.25–1.15 (m, 17H), 0.81 (t, *J* = 6.8 Hz, 3H).¹³C NMR (101 MHz, CDCl₃) δ 77.48, 77.16, 76.84, 73.28, 53.13, 33.71, 32.08, 29.86, 29.83, 29.81, 29.77, 29.53, 25.51, 22.84, 16.20, 14.25.











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