Asymmetric Iodolactamization Induced by Chiral Oxazolidine Auxiliary

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NMR spectra were recorded in CDCl₃ (¹H at 300 MHz and ¹³C at 75.47 MHz) using TMS as the internal standard. All products were isolated by column chromatography on silica gel with hexane - ethyl acetate in an appropriate ratio as the eluent. THF was refluxed with Na and distilled prior to use. The conditions for ordinary HPLC analysis: Diamonsil-C18 column, size: 4.6×150 mm, UV detector (220 nm), mobile phase: acetonitrile/water, 60/40 to 100/0. The conditions for chiral HPLC experiments: AD column, UV detector (205 nm), mobile phase: hexane/isopropanol = 80/20, speed: 0.7 mL/min.

1a: Colorless oil. [α]_D²⁵ = +4.5 (c 1.14, CH₃COCH₃); ¹H NMR (300 MHz, CDCl₃) δ 0.86 (3H, s), 0.88 (3H, s), 1.18 (6H, s), 1.52 (3H, s), 1.62 (3H, s), 1.89-2.00 (1H, m), 2.22-2.36 (2H, m), 3.63-3.68 (1H, m), 3.81-3.84 (1H, m), 3.92-3.97 (1H, m), 5.04-5.10 (2H, m), 5.65-5.79 (1H, m), 8.33 (1H, br); ¹³C NMR (CDCl₃) δ 18.4, 19.3, 23.0, 24.6, 24.7, 26.3, 30.7, 42.9, 44.3, 63.2, 65.3, 95.3, 118.6, 133.6, 151.3, 176.1; EIMS: *m/z* (rel intensity) 281 (M⁺-CH₃, 8), 238 (30), 210 (5), 155 (8), 128 (100), 100 (49), 83 (88), 70 (18); Anal. calcd for C₁₆H₂₈N₂O₃: C, 64.83; H, 9.52; N, 9.45. Found: C, 64.66; H, 9.52; N, 9.45.

1b: Colorless oil. [α]_D²⁵ = -10.4 (c 1.05, CH₃COCH₃); ¹H NMR (300 MHz, CDCl₃) δ 0.91 (9H, s), 1.19 (6H, s), 1.51 (3H, s), 1.68 (3H, s), 2.22-2.38 (2H, m), 3.68 (1H, br), 3.91-4.01 (2H, m), 5.06-5.11 (2H, m), 5.66-5.80 (1H, m), 8.33 (1H, br); ¹³C NMR (CDCl₃) δ 23.0, 24.4, 24.8, 26.6, 27.4, 35.3, 43.0, 44.3, 64.9, 65.8, 96.2, 118.7, 133.6, 153.4, 176.2; EIMS: *m/z* (rel intensity) 295 (M⁺-CH₃, 3), 253 (54), 210 (13), 171 (12), 142 (36), 112 (47), 100 (78), 83 (100); HRMS calcd for C₁₆H₂₇N₂O₃ (M⁺-CH₃): 295.2085. Found: 295.2054.

1c: Colorless oil. [α]_D²⁵ = -36.7 (c 1.03, CH₃COCH₃); ¹H NMR (300 MHz, CDCl₃) δ 1.15 (3H, s), 1.16 (3H, s), 1.55 (3H, s), 1.75 (3H, s), 2.20-2.34 (2H, m), 2.75-2.82 (1H, m), 2.97-3.03 (1H, m), 3.78-3.81 (1H, m), 3.91-3.96 (1H, m), 4.15-4.21 (1H, m), 5.05-5.11 (2H, m), 5.66-5.80 (1H, m), 7.11-7.31 (5H, m), 8.04 (1H, br); ¹³C NMR (CDCl₃) δ 23.1, 24.5, 24.7, 26.9, 29.9, 43.0, 44.2, 59.1, 66.8, 95.6, 118.6, 126.7, 128.6, 129.2, 133.6, 137.4, 150.5, 176.4; EIMS: *m/z* (rel intensity) 329 (M⁺-CH₃, 2), 286 (22), 253 (100), 210 (10), 176 (36), 117 (26), 100 (56), 83 (38); Anal. calcd for C₂₀H₂₈N₂O₃: C, 69.74; H, 8.19; N, 8.13. Found: C, 69.84; H, 8.15; N, 8.10.

1d: Colorless oil. [α]_D²⁵ = +25.2 (c 0.78, CH₃COCH₃); ¹H NMR (300 MHz, CDCl₃) δ 0.82 (3H, d, *J* = 6.6 Hz), 0.86 (3H, d, *J* = 6.3 Hz), 1.14 (3H, s), 1.16 (3H, s), 1.26-1.34 (1H, m), 1.40-1.58 (2H, m), 1.49 (3H, s), 1.61 (3H, s), 2.26 (2H, d, *J* = 7.4 Hz), 3.73-3.75 (1H, m), 3.97 (2H, d, *J* = 8.4 Hz), 5.02-5.04 (2H, m), 5.64-5.78 (1H, m), 8.18 (1H, br); ¹³C NMR (CDCl₃) δ 21.6, 23.1, 23.6, 24.5, 24.6, 25.6, 26.7, 42.6, 43.0, 44.2, 56.4, 67.1, 95.0, 118.6, 133.5, 150.1, 176.3; EIMS: *m/z* (rel intensity) 295 (M⁺-CH₃, 4), 252 (7), 237 (6), 210 (21), 169 (10), 142 (100), 100 (24), 83 (65); Anal. calcd for C₁₇H₃₀N₂O₃: C, 65.77; H, 9.74; N, 9.02. Found: C, 65.64; H, 9.70; N, 8.97.

1-(2,2-Dimethylpent-4-enoyl)-3,3-dimethylurea (4). To a suspension of hexane-washed NaH (60% □ 3.28 g □ 82 mmol) in dry THF (150 mL) was added *N, N*-dimethylurea (3.52 g □ 40 mmol) at room temperature under nitrogen atmosphere. The mixture was stirred for 15

min at rt and brought to reflux for 2 h. The solution was then cooled down to 0 °C and 2,2-dimethyl-4-pentenoic acid chloride was added dropwise. The resulting mixture was stirred at rt for 2 h and then refluxed for 15 h. After removal of the solvent, the residue was suspended in ethyl acetate / water and acidified with dilute HCl. The two layers were separated and the aqueous phase was extracted with EtOAc (3 × 100 mL). The combined organic layer was washed with brine (2 × 100 mL) and then dried over anhydrous MgSO₄. After removal of the solvent, the crude product was purified by column chromatography on silica gel using hexane-acetone (2:1) as the eluent to give pure **4** as a yellowish oil. Yield: 6.18 g (78 %). IR (film): ν (cm⁻¹) 3242, 3079, 1663; ¹H NMR (300 MHz, CDCl₃) δ 1.22 (6H, s), 2.32 (2H, d, J = 7.5 Hz), 2.96 (6H, s), 5.07 (1H, s), 5.10-5.13 (1H, m), 5.69-5.83 (1H, m), 8.23 (1H, br); ¹³C NMR (CDCl₃) δ 24.8, 43.1, 44.5, 118.5, 133.7, 155.1, 176.0; EIMS: m/z (rel intensity) 198 (M⁺, 34), 183 (6), 157 (4), 115 (34), 83 (44), 72 (100), 55 (58), 44 (52); HRMS calcd for C₁₀H₁₈N₂O₂: 198.1378. Found: 198.1373.

Synthesis of 5. General procedure for the iodolactamization reactions with BuLi. To a solution of **4** (99 mg, 0.5 mmol) in dry THF (12 mL) was added BuLi (2 M in cyclohexane, 0.25 mL, 0.5 mmol) at 0 °C under nitrogen atmosphere. The mixture was stirred at 0 °C for 30 min. Iodine (381 mg, 1.5 mmol) was added and the resulting mixture was stirred at rt for 15 h. Aqueous NaHSO₃ (12 mL) was then added slowly. The two layers were separated and the aqueous phase was extracted with ethyl acetate (3 × 10 mL). The combined organic layer was washed with brine (2 × 10 mL) and then dried over anhydrous MgSO₄. After removal of the solvent, the crude product was purified by column chromatography on silica gel using hexane-acetone (4:1) as the eluent to give **5** as a white solid. Yield: 123 mg (76 %). ¹H NMR (300 MHz, CDCl₃) δ 1.19 (3H, s), 1.25 (3H, s), 1.68-1.78 (1H, m), 1.96-2.03 (1H, m), 3.03 (3H, s), 3.05 (3H, s), 3.34-3.38 (1H, m), 3.57-3.63 (1H, m), 3.83-3.91 (1H, m); ¹³C NMR (CDCl₃) δ 12.2, 25.0, 36.5, 39.9, 41.2, 53.1, 153.6, 178.8; EIMS: m/z (rel intensity) 324 (M⁺, 1), 254 (3), 209 (1), 197 (55), 170 (2), 115 (6), 72 (100), 44 (34); HRMS calcd for C₁₀H₁₇N₂O₂ (M⁺-I): 197.1299. Found: 197.1295.

6a: White solid. The major isomer: ¹H NMR (300 MHz, CDCl₃) δ 0.86 (3H, d, J = 6.9 Hz), 0.90 (3H, d, J = 6.9 Hz), 1.17 (3H, s), 1.22 (3H, s), 1.48-1.56 (1H, m), 1.52 (3H, s), 1.69 (3H, s), 1.96-2.07 (1H, m), 2.33-2.39 (1H, m), 2.88-2.95 (1H, m), 3.58 (1H, dd, J = 3.3, 9.0 Hz), 3.86-3.90 (1H, m), 3.96-4.01 (1H, m), 4.05-4.09 (1H, m), 4.25-4.35 (1H, m); ¹³C NMR (CDCl₃) δ 6.7, 17.4, 20.0, 23.2, 24.2, 25.7, 26.0, 30.4, 41.5, 41.8, 55.3, 62.4, 64.6, 96.0, 150.8, 180.2. The minor isomer: ¹H NMR (300 MHz, CDCl₃) δ 0.82-0.92 (6H, m), 1.19 (3H, s), 1.20 (3H, s), 1.52 (3H, s), 1.68 (3H, s), 1.83-2.16 (3H, m), 3.24-3.31 (1H, m), 3.62-3.67 (1H, m), 3.83-4.09 (3H, m), 4.14-4.18 (1H, m); ¹³C NMR (CDCl₃) δ 6.7, 18.1, 19.8, 23.2, 24.2, 25.7, 26.0, 29.7, 41.5, 41.8, 55.6, 63.1, 64.7, 96.0, 153.8, 177.3. EIMS: m/z (rel intensity) 407 (M⁺-CH₃, 37), 379 (25), 364 (100), 297 (38), 254 (70), 209 (20), 111 (40), 83 (79); HRMS calcd for C₁₅H₂₄N₂O₃ (M⁺-CH₃): 407.0859. Found: 407.0846.

6b: White solid. The major isomer: ¹H NMR (300 MHz, CDCl₃) δ 0.84 (9H, s), 1.10 (3H, s), 1.16 (3H, s), 1.36-1.44 (1H, m), 1.42 (3H, s), 1.69 (3H, s), 2.34-2.40 (1H, m), 2.80-2.87 (1H, m), 3.58 (1H, dd, J = 3.8, 13.0 Hz), 3.83-4.00 (3H, m), 4.25-4.35 (1H, m); ¹³C NMR (CDCl₃)

δ 6.2, 23.2, 24.0, 25.6, 26.7, 27.9, 35.0, 41.4, 41.6, 56.2, 65.3, 65.9, 96.9, 153.0, 180.7. The minor isomer: ^1H NMR (300 MHz, CDCl_3) δ 0.84 (9H, s), 1.18 (3H, s), 1.23 (3H, s), 1.47 (3H, s), 1.68 (3H, s), 2.06-2.12 (2H, m), 3.18-3.25 (1H, m), 3.48-3.53 (1H, m), 3.83-4.00 (3H, m), 4.39-4.43 (1H, m); ^{13}C NMR(CDCl_3) δ 6.2, 22.7, 24.0, 26.1, 26.7, 27.9, 34.8, 41.4, 41.6, 57.2, 64.9, 65.8, 96.9, 156.0, 179.5. EIMS: m/z (rel intensity) 421 (M^+-CH_3 , 10), 379 (100), 297 (83), 280 (23), 254 (23), 209 (16), 170 (11), 83 (34); HRMS calcd for $\text{C}_{16}\text{H}_{26}\text{IN}_2\text{O}_3$ (M^+-CH_3): 421.0912. Found: 421.0950.

6c: White solid. ^1H NMR (300 MHz, CDCl_3) δ 1.14 (3H, d, $J = 1.5$ Hz), 1.24 (3H, d, $J = 1.5$ Hz), 1.47 (3H, s), 1.47-1.56 (1H, m), 1.72 (3H, s), 2.17-2.24 (1H, m), 2.69-2.81 (2H, m), 2.99 (1H, dd, $J = 3.9, 13.2$ Hz), 3.34-3.39 (1H, m), 3.69-3.72 (1H, m), 3.82-3.86 (1H, m), 4.06-4.16 (1H, m), 4.35-4.41 (1H, m), 7.02-7.26 (5H, m); ^{13}C NMR (CDCl_3) δ 7.8, 23.1, 24.4, 25.6, 27.2, 40.4, 41.4, 41.6, 54.6, 59.2, 66.9, 96.0, 126.8, 128.8, 129.1, 137.5, 149.8, 180.3; EIMS: m/z (rel intensity) 455 (M^+-CH_3 , 6), 412 (11), 379 (100), 297 (64), 280 (36), 254 (21), 159 (20), 83 (52); Anal. calcd for $\text{C}_{20}\text{H}_{27}\text{IN}_2\text{O}_3$: C, 51.07; H, 5.79; N 5.96. Found: C, 51.39 H, 5.49; N, 5.70. The structure was further confirmed by its X-ray diffraction analysis.

6d: White solid. ^1H NMR (300 MHz, CDCl_3) δ 0.79 (3H, d, $J = 6.6$ Hz), 0.86 (3H, d, $J = 6.6$ Hz), 1.12 (3H, s), 1.16 (3H, s), 1.14-1.23 (1H, m), 1.36-1.52 (3H, m), 1.46 (3H, s), 1.62 (3H, s), 2.22-2.29 (1H, m), 2.90-2.97 (1H, m), 3.47 (1H, dd, $J = 3.6, 9.3$ Hz), 3.69-3.72 (1H, m), 3.93-3.97 (1H, m), 4.14-4.20 (2H, m); ^{13}C NMR (CDCl_3) δ 7.4, 21.3, 23.0, 23.7, 24.4, 25.4, 25.7, 26.9, 41.6, 41.8, 43.6, 54.9, 56.2, 67.6, 95.3, 149.5, 180.2; EIMS: m/z (rel intensity) 421 (M^+-CH_3 , 32), 363 (4), 336 (100), 280 (34), 252 (29), 209 (46), 156 (20), 98 (45); HRMS calcd for $\text{C}_{16}\text{H}_{26}\text{IN}_2\text{O}_3$ (M^+-CH_3): 421.1056. Found: 421.1022.

Synthesis of 7. To a solution of **6a** (84 mg, 0.2 mmol) and K_2CO_3 (83 mg, 0.6 mmol) in DMF (4 mL) was added PhSH (61 μL , 0.6 mmol) at rt under nitrogen atmosphere. The resulting mixture was stirred at rt for 12 h. Ethyl acetate (8 mL) and water (8 mL) were added, and the two layers were separated. The aqueous phase was extracted with ethyl acetate (2×8 mL). The combined organic layer was washed with brine (2×10 mL) and dried over anhydrous MgSO_4 . Excess PhSH was removed by flash chromatography using hexane as the eluent. The resulting crude product was analyzed by HPLC and further brought to hydrolysis.

A solution of the above crude product in 30 % KOH (8 mL) was refluxed for 10 h. Ethyl acetate (8 mL) was added and the two layers were separated. The aqueous phase was extracted with ethyl acetate (3×8 mL). The combined organic layer was washed with brine (2×8 mL) and then dried over anhydrous MgSO_4 . After removal of the solvent, the crude product was purified by column chromatography on silica gel using hexane-acetone (2:1) as the eluent to give **7** as a white solid. Yield: 47 mg (100%). ^1H NMR (300 MHz, CDCl_3) δ 1.07 (3H, s), 1.13 (3H, s), 1.55-1.62 (1H, m), 2.03-2.10 (1H, m), 2.79-2.86 (1H, m), 2.98-3.04 (1H, m), 3.59-3.68 (1H, m), 6.26 (1H, br), 7.15-7.33 (5H, m); ^{13}C NMR (CDCl_3) δ 24.9, 25.3, 40.7, 40.8, 42.6, 49.9, 126.9, 129.1, 130.5, 134.5, 182.0; EIMS: m/z (rel intensity) 235 (M^+ , 4), 149 (1), 135 (2), 124 (100), 112 (86), 109 (10), 84 (39), 57 (7); Anal. calcd for

C₁₃H₁₇NOS: C, 66.34; H, 7.28; N, 5.95. Found: C, 66.17; H, 7.18; N, 5.80.

8: Colorless oil. $[\alpha]_D^{25} = -5.6$ (c 1.00, CH₃COCH₃); ¹H NMR (300 MHz, CDCl₃) δ 0.84-0.89 (6H, m), 0.97-1.10 (1H, m), 1.26-1.37 (1H, m), 1.47 (3H, s), 1.61 (3H, s), 1.63-1.71 (1H, m), 2.32 (2H, q, $J = 6.9$ Hz), 2.74-2.94 (2H, m), 3.82-3.92 (3H, m), 4.90-5.03 (2H, m), 5.71-5.85 (1H, m), 8.07 (1H, br); ¹³C NMR (CDCl₃) δ 12.1, 13.8, 23.2, 26.17, 26.24, 28.3, 35.6, 37.0, 61.0, 64.4, 95.3, 115.3, 137.0, 149.7, 175.6; EIMS: m/z (rel intensity) 282 (M⁺-CH₃, 1), 267 (21), 225 (20), 196 (19), 169 (12), 142 (80), 100 (100), 83 (58); Anal. calcd for C₁₅H₂₆N₂O₃: C, 63.80; H, 9.28; N, 9.92. Found: C, 63.70; H, 9.38; N, 9.58.

9: Colorless oil. $[\alpha]_D^{25} = +21.8$ (c 1.04, CH₃COCH₃); ¹H NMR (300 MHz, CDCl₃) δ 0.86-0.97 (6H, m), 1.08-1.17 (1H, m), 1.16 (3H, s), 1.17 (3H, s), 1.31-1.44 (1H, m), 1.54 (3H, s), 1.68 (3H, s), 1.75-1.80 (1H, m), 2.72-2.86 (2H, m), 3.83-3.98 (3H, m), 4.94-5.03 (2H, m), 5.93-6.02 (1H, m), 7.68 (1H, br); ¹³C NMR (CDCl₃) δ 12.1, 12.9, 23.2, 26.1, 26.4, 26.9, 27.2, 36.6, 37.1, 47.6, 61.2, 64.3, 95.3, 111.0, 146.9, 149.8, 173.1; EIMS m/z (rel intensity) 310 (M⁺, 3), 295 (21), 253 (20), 224 (23), 171 (8), 142 (91), 100 (100), 83 (52); HRMS calcd for C₁₇H₃₁N₂O₃ (M⁺+1): 311.2329. Found: 311.2343.

10: Colorless oil. $[\alpha]_D^{25} = -21.4$ (c 0.88, CH₃COCH₃); ¹H NMR (300 MHz, CDCl₃) δ 0.88-0.97 (6H, m), 1.05-1.17 (1H, m), 1.33-1.44 (1H, m), 1.54 (3H, s), 1.69 (3H, s), 1.72-1.80 (3H, m), 2.08-2.15 (2H, m), 2.71-2.91 (2H, m), 3.89-3.99 (3H, m), 4.97-5.07 (2H, m), 5.74-5.88 (1H, m), 8.02 (1H, br); ¹³C NMR (CDCl₃) δ 12.1, 13.8, 23.2, 23.5, 26.19, 26.25, 33.0, 35.7, 37.1, 61.0, 64.4, 95.3, 115.0, 137.9, 149.7, 176.2; EIMS: m/z (rel intensity) 296 (M⁺, 1), 281 (20), 239 (18), 210 (15), 197 (6), 142 (71), 100 (72), 84 (100); HRMS calcd for C₁₆H₂₉N₂O₃ (M⁺+1): 297.2173. Found 297.2189.

11: Colorless oil. $[\alpha]_D^{25} = -3.4$ (c 1.08, CH₃COCH₃); ¹H NMR (300 MHz, CDCl₃) δ 0.82-0.90 (6H, m), 0.96-1.07 (1H, m), 1.17 (6H, s), 1.22-1.31 (1H, m), 1.51 (3H, s), 1.58-1.71 (3H, m), 1.62 (3H, s), 1.95-2.02 (2H, m), 3.78-3.82 (2H, m), 3.92-3.98 (1H, m), 4.88-4.99 (2H, m), 5.66-5.80 (1H, m), 8.43 (1H, br); ¹³C NMR (CDCl₃) δ 12.1, 14.5, 23.1, 24.8, 25.0, 25.9, 26.1, 28.9, 37.2, 39.4, 42.9, 62.0, 65.0, 95.4, 114.6, 137.9, 151.4, 176.3; EIMS: m/z (rel intensity) 309 (M⁺-CH₃, 4), 267 (7), 238 (14), 212 (5), 169 (8), 142 (87), 113 (71), 100 (100); HRMS calcd for C₁₈H₃₂N₂O₃Na (M⁺+Na): 347.2305. Found 347.2316.

12: Colorless oil. $[\alpha]_D^{25} = +14.9$ (c 1.01, CH₃COCH₃); ¹H NMR (300 MHz, CDCl₃) δ 0.86-0.94 (6H, m), 0.98-1.14 (1H, m), 1.26-1.81 (12H, m), 1.57 (3H, s), 1.69 (3H, m), 1.94-2.07 (4H, m), 3.84-3.90 (2H, m), 3.98-4.04 (1H, m), 4.94-5.05 (2H, m), 5.70-5.83 (1H, m), 7.61 (1H, br); ¹³C NMR (CDCl₃) δ 12.1, 14.3, 22.8, 22.9, 23.1, 25.7, 26.0, 26.2, 28.0, 33.6, 34.0, 37.7, 38.9, 47.4, 62.3, 65.0, 95.4, 114.7, 137.9, 150.9, 175.2; EIMS: m/z (rel intensity) 349 (M⁺-CH₃, 3), 306 (8), 278 (15), 252 (8), 208 (4), 182 (9), 153 (99), 100 (100); Anal. calcd for C₂₁H₃₆N₂O₃: C, 69.19; H, 9.95; N, 7.68. Found: C, 69.03; H, 10.06; N, 7.60.

13: Colorless oil. $[\alpha]_D^{25} = +14.2$ (c 1.14, CH₃COCH₃); ¹H NMR (300 MHz, CDCl₃) δ 0.89-0.94 (6H, m), 1.01-1.13 (1H, m), 1.31-1.42 (1H, m), 1.51-1.81 (9H, m), 1.56 (3H, s),

1.68 (3H, s), 1.96-2.18 (4H, m), 3.81-3.89 (2H, m), 3.97-4.02 (1H, m), 4.94-5.05 (2H, m), 5.71-5.85 (1H, m), 7.46 (1H, br); ^{13}C NMR (CDCl_3) δ 12.2, 14.4, 23.2, 24.7, 24.8, 26.1, 26.4, 29.8, 35.5, 35.8, 37.5, 38.7, 55.3, 62.1, 64.9, 95.5, 114.9, 137.7, 150.3, 175.5; EIMS: m/z (rel intensity) 335 (M^+-CH_3 , 2), 264 (10), 238 (5), 169 (8), 142 (78), 139 (100), 123 (38), 100 (100); HRMS calcd for $\text{C}_{20}\text{H}_{34}\text{N}_2\text{O}_3\text{Na}$ (M^++Na): 373.2462. Found: 373.2465.

14: White solid. The major isomer: ^1H NMR (300 MHz, CDCl_3) δ 0.87-0.92 (6H, m), 1.06-1.33 (3H, m), 1.53 (3H, s), 1.65-1.85 (2H, m), 1.70 (3H, s), 2.43-2.59 (2H, m), 2.96-3.02 (1H, m), 3.54 (1H, dd, $J = 3.3, 12.3$ Hz), 3.84-3.89 (1H, m), 3.94-4.03 (1H, m), 4.25-4.30 (1H, m), 4.33-4.42 (1H, m); ^{13}C NMR (CDCl_3) δ 7.3, 12.1, 14.4, 23.4, 25.7, 26.4, 26.8, 31.7, 37.1, 58.2, 60.5, 64.4, 96.0, 150.6, 175.2. The minor isomer: ^1H NMR (300 MHz, CDCl_3) δ 0.87-0.92 (6H, m), 1.06-1.33 (3H, m), 1.55 (3H, s), 1.65-1.85 (2H, m), 1.68 (3H, s), 2.18-2.24 (2H, m), 3.37-3.43 (1H, m), 3.83-4.13 (5H, m); ^{13}C NMR (CDCl_3) δ 9.3, 12.2, 14.7, 23.3, 25.5, 25.9, 26.8, 29.6, 36.8, 58.2, 60.4, 61.1, 95.8, 151.1, 170.3. EIMS: m/z (rel intensity) 393 (M^+-CH_3 , 38), 351 (37), 322 (100), 269 (83), 252 (46), 226 (75), 142 (98), 83 (90); Anal. calcd for $\text{C}_{14}\text{H}_{22}\text{IN}_2\text{O}_3$: C, 44.13; H, 6.17; N, 6.86. Found: C, 43.94; H, 6.13; N, 6.76.

15: White solid. The major isomer: ^1H NMR (300 MHz, CDCl_3) δ 0.86-0.93 (6H, m), 1.06-1.34 (2H, m), 1.19 (3H, s), 1.42 (3H, s), 1.52 (3H, s), 1.72 (3H, s), 1.75-1.82 (1H, m), 2.37 (2H, d, $J = 1.8$ Hz), 3.04-3.11 (1H, m), 3.38 (1H, dd, $J = 3.9, 11.7$ Hz), 3.87 (1H, dd, $J = 2.4, 6.0$ Hz), 3.98-4.03 (1H, m), 4.25-4.30 (2H, m); ^{13}C NMR (CDCl_3) δ -1.9, 12.3, 14.2, 22.2, 23.2, 25.6, 26.8, 28.5, 36.0, 37.5, 47.9, 60.9, 64.2, 65.6, 96.0, 150.8, 173.1. The minor isomer: ^1H NMR (300 MHz, CDCl_3) δ 0.86-0.93 (6H, m), 1.06-1.34 (2H, m), 1.20 (3H, s), 1.27 (3H, s), 1.58 (3H, s), 1.75-1.82 (1H, m), 1.80 (3H, s), 2.05-2.15 (1H, m), 2.43 (2H, s), 2.69-2.75 (1H, m), 3.58-3.66 (2H, m), 3.94-4.03 (2H, m); ^{13}C NMR (CDCl_3) δ -1.9, 12.3, 14.4, 21.8, 22.8, 25.9, 27.1, 29.4, 36.0, 37.5, 45.3, 61.6, 64.5, 68.2, 96.0, 153.2, 171.8. EIMS: m/z (rel intensity) 421 (M^+-CH_3 , 39), 379 (38), 350 (100), 297 (88), 280 (47), 254 (64), 142 (62), 83 (76); HRMS calcd for $\text{C}_{17}\text{H}_{29}\text{IN}_2\text{O}_3\text{Na}$ (M^++Na): 459.1115. Found: 459.1121.

16: White solid. The major isomer: ^1H NMR (300 MHz, CDCl_3) δ 0.87-0.96 (6H, m), 1.12-1.36 (2H, m), 1.57 (3H, s), 1.64-1.99 (4H, m), 1.73 (3H, s), 2.33-2.53 (3H, m), 2.48-2.53 (2H, m), 2.93-3.00 (1H, m), 3.37-3.40 (1H, m), 3.81-3.97 (3H, m), 4.15-4.21 (1H, m); ^{13}C NMR (CDCl_3) δ 6.2, 12.4, 14.2, 19.3, 21.8, 25.4, 27.0, 28.8, 33.4, 38.4, 57.7, 59.8, 63.2, 96.3, 153.6, 171.8. The minor isomer: ^1H NMR (300 MHz, CDCl_3) δ 0.87-0.96 (6H, m), 1.10-1.36 (2H, m), 1.62 (3H, s), 1.64-1.99 (4H, m), 1.76 (3H, s), 2.33-2.53 (3H, m), 2.48-2.53 (2H, m), 3.20-3.27 (1H, m), 3.55-3.58 (1H, m), 3.81-3.97 (3H, m), 4.35-4.41 (1H, m); ^{13}C NMR (CDCl_3) δ 6.6, 12.4, 16.0, 19.3, 22.0, 25.1, 26.7, 29.7, 32.0, 38.3, 57.7, 59.8, 62.7, 96.0, 155.8, 170.1. EIMS: m/z (rel intensity) 407 (M^+-CH_3 , 7), 365 (10), 336 (17), 307 (5), 240 (14), 142 (25), 100 (20), 84 (100); HRMS calcd for $\text{C}_{16}\text{H}_{27}\text{IN}_2\text{O}_3\text{Na}$ (M^++Na): 445.0959. Found: 445.0963.

17: White solid. The major isomer: ^1H NMR (300 MHz, CDCl_3) δ 0.86-0.96 (6H, m), 1.00-1.22 (2H, m), 1.18 (3H, s), 1.20 (3H, s), 1.55 (3H, s), 1.66-1.82 (4H, m), 1.70 (3H, s),

2.32-2.41 (1H, m), 2.90-2.96 (1H, m), 3.34-3.37 (1H, m), 3.69-3.95 (3H, m), 4.05-4.20 (1H, m); ^{13}C NMR (CDCl_3) δ 6.6, 12.4, 13.1, 21.7, 25.3, 25.6, 26.2, 26.6, 27.0, 34.0, 38.1, 38.8, 58.3, 61.1, 63.3, 96.3, 154.3, 178.3. The minor isomer: ^1H NMR (300 MHz, CDCl_3) δ 0.86-0.96 (6H, m), 1.00-1.22 (2H, m), 1.18 (3H, s), 1.20 (3H, s), 1.55 (3H, s), 1.66-1.82 (4H, m), 1.70 (3H, s), 1.95-2.04 (1H, m), 3.15-3.21 (1H, m), 3.69-3.95 (4H, m), 4.40-4.49 (1H, m); ^{13}C NMR (CDCl_3) δ 6.8, 12.4, 13.6, 22.2, 25.4, 25.7, 26.3, 26.8, 27.6, 34.0, 38.2, 38.8, 58.4, 62.2, 64.1, 96.0, 154.1, 176.3. EIMS: m/z (rel intensity) 435 (M^+-CH_3 , 20), 393 (32), 364 (52), 294 (53), 266 (100), 224 (14), 140 (20), 95 (51); Anal. calcd for $\text{C}_{18}\text{H}_{31}\text{IN}_2\text{O}_3$: C, 48.00; H, 6.94; N, 6.22. Found: C, 47.92; H, 6.94; N, 5.96.

18: White solid. The major isomer: ^1H NMR (300 MHz, CDCl_3) δ 0.83-0.97 (6H, m), 1.04-1.82 (14H, m), 1.59 (3H, s), 1.73 (3H, s), 2.00-2.07 (2H, m), 2.30-2.35 (1H, m), 2.92-2.98 (1H, m), 3.35 (1H, dd, $J = 2.8, 9.2$ Hz), 3.70-3.73 (1H, m), 3.83-3.98 (2H, m), 4.13-4.20 (1H, m); ^{13}C NMR (CDCl_3) δ 6.7, 12.4, 13.0, 20.9, 21.1, 21.7, 24.7, 25.3, 25.5, 27.0, 27.8, 33.1, 33.6, 38.1, 42.2, 57.5, 61.2, 63.3, 96.3, 154.5, 178.6. The minor isomer: ^1H NMR (300 MHz, CDCl_3) δ 0.83-0.97 (6H, m), 1.04-1.82 (20H, m), 2.00-2.07 (2H, m), 2.30-2.35 (1H, m), 2.92-2.98 (1H, m), 3.15-3.21 (1H, m), 3.41-3.46 (1H, m), 3.70-3.98 (2H, m), 4.42-4.49 (1H, m); ^{13}C NMR (CDCl_3) δ 7.0, 12.4, 13.7, 20.6, 20.9, 22.0, 24.1, 25.2, 25.4, 26.6, 27.7, 32.6, 33.5, 38.2, 42.2, 57.5, 61.2, 64.0, 96.0, 154.3, 176.4. EIMS: m/z (rel intensity) 475 (M^+-CH_3 , 6), 433 (12), 404 (21), 308 (27), 306 (100), 180 (13), 156 (15), 135 (16); HRMS calcd for $\text{C}_{21}\text{H}_{36}\text{IN}_2\text{O}_3$ (M^++1): 491.1765. Found: 491.1764.

19: White solid. The major isomer: ^1H NMR (300 MHz, CDCl_3) δ 0.87-0.97 (6H, m), 1.12-1.37 (2H, m), 1.57 (3H, s), 1.62-1.82 (11H, m), 1.71 (3H, s), 2.35-2.41 (2H, m), 2.88-2.95 (1H, m), 3.36 (1H, dd, $J = 2.7, 9.3$ Hz), 3.69-3.72 (1H, m), 3.81-3.85 (1H, m), 3.91-3.96 (1H, m), 4.12-4.18 (1H, m); ^{13}C NMR (CDCl_3) δ 6.7, 12.4, 13.1, 21.8, 25.4, 25.6, 26.7, 27.1, 32.9, 36.6, 38.1, 39.0, 49.9, 58.0, 61.2, 63.4, 96.4, 154.4, 178.4. The minor isomer: ^1H NMR (300 MHz, CDCl_3) δ 0.87-0.97 (6H, m), 1.12-1.37 (2H, m), 1.57 (3H, s), 1.62-1.82 (11H, m), 1.72 (3H, s), 2.35-2.41 (2H, m), 3.28-3.35 (1H, m), 3.42-3.46 (1H, m), 3.69-3.96 (3H, m), 4.38-4.45 (1H, m); ^{13}C NMR (CDCl_3) δ 7.1, 11.8, 12.7, 22.1, 24.5, 25.7, 26.7, 27.1, 31.7, 36.5, 38.0, 38.4, 49.6, 57.9, 62.1, 64.3, 95.6, 154.3, 176.4. EIMS: m/z (rel intensity) 461 (M^+-CH_3 , 9), 419 (18), 390 (33), 320 (22), 292 (100), 184 (10), 156 (76), 142 (12); Anal. calcd for $\text{C}_{20}\text{H}_{33}\text{IN}_2\text{O}_3$: C, 50.42; H, 6.98; N, 5.88. Found: C, 50.43; H, 6.81; N, 5.76.

Figure 1. X-ray Crystal Structure of **6c**.