Pushing Radical Cyclization from Regioselective to Regiospecific: Cyclization of Amidyl Radicals Controlled by Vinylic Halogen Substitution

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Pb(OAc)₄ (96 %) was purchased from Aldrich. CH₂Cl₂ was refluxed with CaH₂ and distilled prior to use. All products were isolated by column chromatography on silica gel with hexane - acetone in an appropriate ratio as the eluent. ¹H NMR and ¹³C NMR spectra were recorded on a 300 MHz NMR spectrometer with TMS as the internal standard. 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.

Table S1. The results of iodolactonization

This compound was isolated from the dark reaction of **6a** with $\text{Pb}(\text{OAc})_4/\text{I}_2$ at rt (see manuscript) as a yellowish oil. Yield: 37%. ^1H NMR (300MHz, CDCl_3) δ 1.62-1.71 (1H, m), 1.83-1.96 (2H, m), 2.36-2.48 (2H, m), 2.53-2.62 (1H, m), 3.85 (1H, dt, $J = 10.5, 3.6$ Hz), 5.21 (1H, d, $J = 3.6$ Hz). ^{13}C NMR (CDCl_3) δ -23.4, 17.8, 27.5, 29.3, 82.7, 176.8. EIMS: m/z (rel intensity) 366 (M^+ , 21), 239 (32), 211 (100), 169 (37), 141 (12), 127 (9), 99 (16), 55 (31). HRMS calcd for $\text{C}_6\text{H}_8\text{I}_2\text{O}_2$ (M^+): 365.8614. Found: 365.8617.

This compound was isolated in 37% yield from the reaction of **8c** with $\text{NaHCO}_3/\text{I}_2$ in acetonitrile at rt for 16 h (see manuscript). Yellowish oil. ^1H NMR (300 MHz, CDCl_3) δ 1.94-2.04 (2H, m), 2.45 (2H, t, $J = 6.9$ Hz), 2.95 (2H, t, $J = 6.8$ Hz), 3.84 (2H, d, $J = 0.9$ Hz); ^{13}C NMR (CDCl_3) δ 5.6, 16.1, 19.6, 36.8, 119.0, 201.4; EIMS m/z (rel intensity) 237 (M^+ , 12), 209 (4), 195 (3), 169 (17), 141 (11), 110 (16), 96 (100), 68 (48); Anal. calcd for $\text{C}_6\text{H}_8\text{INO}$: C, 30.40; H, 3.40; N, 5.91. Found: C, 30.42; H, 3.52; N, 5.83.

Colorless oil. Yield: 25%. ^1H NMR (300MHz, CDCl_3) δ 1.62-1.73 (2H, m), 1.94-2.02 (2H, m), 2.13-2.23 (2H, m), 2.53-2.63 (1H, m), 2.68-2.76 (1H, m), 3.25-3.39 (2H, m), 4.30-4.37 (1H, m).

Known compound: Simonot, B.; Rousseau, G. *J. Org. Chem.* **1994**, 59, 5912.

Typical Procedure for Bu_3SnH -Initiated Amidyl Radical Cyclization: *N*-(Phenylthio)hept-5-enamide (**1**) (235 mg, 1.0 mmol) was dissolved in 80 mL of anhydrous benzene, and the solution was brought to reflux. Into this refluxing solution was added with the aid of a syringe pump over a period of 4 h Bu_3SnH (0.54 mL, 2 mmol) and AIBN (49 mg, 0.3 mmol) in benzene solution (20 mL) under nitrogen atmosphere. The mixture was cooled down to room temperature and checked by HPLC. After removal of the solvent, the residue was chromatographed on silica gel with hexane-acetone (100:1 to 5:1) as the eluent to give lactam **2** (85.1 mg, 67% yield), lactam **3** (10.2 mg, 8% yield) and hept-5-enamide (19.1 mg, 15%).

Typical Procedures for $\text{Pb}(\text{OAc})_4/\text{I}_2$ –Initiated Amidyl Radical Cyclization.

Method A: To the solution of $\text{Pb}(\text{OAc})_4$ (466 mg, 1.05 mmol) in dry CH_2Cl_2 (10 mL) was added iodine (190 mg, 0.75 mmol) at rt under nitrogen atmosphere. The mixture was stirred for 3 min, then a haloenamide (0.3 mmol) was added and the resulting mixture was irradiated at rt with a 125 W high pressure mercury lamp for 4 h. Aqueous $\text{Na}_2\text{S}_2\text{O}_3$ (10 mL) was then added. The two layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3×10 mL). The combined organic layer was washed with aqueous Na_2CO_3 and brine, dried over anhydrous Na_2SO_4 . 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 the products.

Method B: The same procedure in Method A was followed except that the reaction temperature was set at 0 °C.

Method C: The same procedure in Method A was followed except that the reaction temperature was set at 0 °C and that the amount of iodine was 1.3 equiv. rather than 2.5 equiv.

White solid. Yield: 48%. Mp 44-45 °C. Two isomers (2:1). ¹H NMR (300MHz, CDCl₃) δ 1.56-1.76 (5H, m), 2.01-2.16 (2H, m), 2.35-2.53 (2H, m), 5.36-5.46 (2H, m), 6.49 and 6.87 (1H, br), 7.20-7.26 (5H, m). ¹³C NMR (CDCl₃) δ 12.8/17.8, 24.4/25.3, 26.1/30.3, 31.9/35.9, 117.9/123.3, 125.1/125.6, 126.1/126.8, 129.0/129.2, 130.0, 138.8, 174.9/180.0. EIMS: *m/z* (rel intensity) 236 (M⁺+1, 5), 202 (2), 167 (3), 150 (10), 125 (100), 109 (28), 93 (23), 55 (75). Anal. calcd for C₁₃H₁₇NOS: C, 66.34; H, 7.28; N, 5.95. Found: C, 66.45; H, 7.25; N, 5.69.

Colorless oil. Yield: 51%. Two isomers (2.3:1). ¹H NMR (300 MHz, CDCl₃) δ 1.69 (3H, s), 1.74-1.88 (2H, m), 2.01-2.06 (2H, m), 2.35/2.53 (2H, m), 4.66-4.73 (2H, m), 6.59/7.11 (1H, br), 7.18-7.35 (5H, m). ¹³C NMR (CDCl₃) δ 22.0/22.3, 23.2, 30.2, 35.6/36.8, 110.5, 123.8, 124.6, 126.5, 128.7, 129.1, 138.8, 144.6, 175.7. EIMS: *m/z* (rel intensity) 235 (M⁺, 4), 218 (1), 150 (2), 150 (3), 125 (100), 109 (15), 93 (18), 55 (66). Anal. calcd for C₁₃H₁₇NOS: C, 66.34; H, 7.28; N, 5.95. Found: C, 66.27; H, 7.45; N, 5.81.

White solid. Yield: 70%. *Z* : *E* = 55:45 (HPLC). ^1H NMR (300 MHz, CDCl_3) δ 1.71-1.84 (2H, m), 2.09-2.31 (4H, m), 5.61 (1H, br), 5.95 (1H, br), 6.04-6.23 (2H, m). ^{13}C NMR (CDCl_3) δ 23.7/24.0, 29.0/32.1, 34.6/34.9, 105.1/108.7, 133.7/136.9, 175.5. EIMS m/z (rel intensity) 191 (M^+ , 2), 155 (2), 119 (8), 112 (93), 98 (8), 85 (6), 59 (100), 44 (41). Anal. calcd for $\text{C}_6\text{H}_{10}\text{BrNO}$: C, 37.52; H, 5.25; N, 7.29. Found: C, 37.27; H, 5.18; N, 7.08.

White solid. Yield: 65%. *Z* : *E* = 14:86 (HPLC). ^1H NMR (300 MHz, CDCl_3) δ 1.70-1.80 (2H, m), 2.10-2.33 (2H, m), 5.54 (1H, br), 5.75-6.08 (3H, m). ^{13}C NMR (CDCl_3) δ 24.0/24.3, 26.2/30.1, 34.6/34.9, 117.7/117.9, 130.5/132.8, 174.9. EIMS m/z (rel intensity) 148 (M^+ , 21), 112 (11), 100 (1), 95 (2), 75 (9), 67 (8), 59 (100), 44 (49). Anal. calcd for $\text{C}_6\text{H}_{10}\text{ClNO}$: C, 48.82; H, 6.83; N, 9.49. Found: C, 49.00; H, 6.81; N, 9.59.

Yellowish solid. Yield: 60%. Mp 74-76 °C. ^1H NMR (300MHz, CDCl_3) δ 1.25 (6H, s), 1.61-1.66 (2H, m), 2.11-2.19 (2H, m), 5.64 (2H, br), 6.16-6.19 (2H, m). ^{13}C NMR (CDCl_3) δ 25.5, 30.6, 38.9, 41.9, 82.7, 140.6, 179.9. EIMS: m/z (rel intensity) 268 (M^+ , 1), 181 (2), 167 (8), 140 (3), 127 (1), 87 (100), 72 (19), 41 (15). Anal. calcd for $\text{C}_8\text{H}_{14}\text{INO}$: C, 35.97; H, 5.28; N, 5.24. Found: C, 36.13; H, 5.08; N, 5.31.

Yellowish solid. Yield: 72%. Mp 46-48 °C. *Z* : *E* = 30:70. ^1H NMR (300MHz, CDCl_3) δ 1.21 (6H, s), 1.88-1.92 (2H, m), 2.12-2.24 (2H, m), 5.48 (2H, br), 5.55-5.58 (1H, m), 5.96-5.99 (1H, m), ^{13}C NMR (CDCl_3) δ 26.7/27.7, 31.3/31.7, 36.3, 37.5/37.7, 116.1/116.9, 138.2/142.3, 175.7. EIMS: m/z (rel intensity) 176 (M^+ , 24), 140 (68), 123 (15), 103 (31), 95 (43), 81 (35), 67 (66), 44 (100). HRMS calcd for $\text{C}_8\text{H}_{14}\text{NO}$ (M^+ -Cl): 140.1075. Found: 140.1071.

Yellowish oil. Yield: 66%. *Z* : *E* = 40:60. ^1H NMR (300MHz, CDCl_3) δ 3.94-3.97 (2H, m), 4.06 (1H, dd, J = 6.6, 1.5 Hz), 4.29 (1H, dd, J = 6.6, 1.5 Hz), 5.92-6.07 (1H, m), 6.24-6.33 (1H, m), 6.56 (2H, br). ^{13}C NMR (CDCl_3) δ 66.3, 69.1/69.3, 121.7/122.4, 127.1/128.7, 172.4/172.6. EIMS: m/z (rel intensity) 150 (M^+ , 17), 132 (1), 114 (37), 89 (3), 105 (2), 75 (79), 59 (100), 44 (70). Anal. calcd for $\text{C}_5\text{H}_8\text{ClNO}_2$: C, 40.15; H, 5.39; N, 9.36. Found: C, 40.18; H, 5.38; N, 9.30.

Method A: White solid. Yield: 85%. Mp 160-161 °C. ^1H NMR (300 MHz, CDCl_3) δ 1.39-1.53 (1H, m), 1.72-1.87 (1H, m), 1.91-2.00 (1H, m), 2.17-2.48 (3H, m), 3.19-3.24 (1H, m), 5.16 (1H, d, $J = 3.8$ Hz), 6.44 (1H, br). ^{13}C NMR (CDCl_3) δ -14.9, 18.8, 28.9, 31.1, 60.5, 172.8. EIMS m/z (rel intensity) 366 ($\text{M}^+ + 1$, 1), 365 (M^+ , 2), 238 (2), 167 (3), 127 (5), 111 (6), 98 (100), 82 (9), 55 (25). HRMS calcd for $\text{C}_6\text{H}_9\text{I}_2\text{NO}$ ($\text{M}^+ + \text{H}$) 365.8846. Found 365.8862.

Method A: White solid. Two stereoisomers in ~1:1 ratio. Yield: 79%. ^1H NMR (300 MHz, CDCl_3) 1.43-1.58 (1H, m), 1.61-1.79 (1H, m), 1.81-1.96 (1H, m), 2.03-2.41 (3H, m), 3.34-3.48 (1H, m), 5.49 (1H, m), 6.64/6.78 (1H, br). ^{13}C NMR (CDCl_3) δ 18.8/18.9, 19.2/19.3, 27.6/27.7, 31.1/31.2, 60.2/60.5, 172.7. EIMS m/z (rel intensity) 318 ($\text{M}^+ + 1$, 3), 190 (1), 127 (2), 121 (1), 98 (100), 82 (4), 55 (36). Anal. calcd. for $\text{C}_6\text{H}_9\text{BrINO}$: C, 22.67; H, 2.85; N, 4.41. Found: C, 22.70; H, 2.85; N, 4.38.

Method A: White solid. Two stereoisomers in ~1:1 ratio. Yield: 81%. ^1H NMR (300 MHz, CDCl_3) δ 1.53-1.87 (2H, m), 1.92-2.03 (1H, m), 2.07-2.50 (3H, m), 3.39-3.45/3.61-3.67 (1H, m), 5.68/5.72 (1H, d, $J = 4.2$ Hz), 6.44/6.58 (1H, br). ^{13}C NMR (CDCl_3) δ 18.8/18.9, 26.4/26.9, 31.1/31.2, 35.7/35.9, 60.3/60.6, 172.7. EIMS m/z (rel intensity) 274 ($\text{M}^+ + 1$, 1), 175 (1), 146 (1), 127 (5), 98 (100), 82 (4), 70 (7), 55 (76). Anal. calcd. for $\text{C}_6\text{H}_9\text{ClINO}$: C, 26.35; H, 3.32; N, 5.12. Found: C, 26.69; H, 3.39; N, 5.18.

Method C: White solid. Yield: 81%. Mp 145-147 °C. ^1H NMR (300MHz, CDCl_3) δ 1.23 (3H, s), 1.29 (3H, s), 1.60-1.85 (4H, m), 3.13-3.19 (2H, m), 5.17 (1H, d, $J = 3.3$ Hz), 6.30 (1H, br). ^{13}C NMR (CDCl_3) δ -15.8, 26.2, 26.6, 27.0, 33.7, 37.3, 61.3, 178.4. EIMS: m/z (rel intensity) 393 (M^+ , 9), 254 (1), 167 (4), 139 (3), 126 (100), 111 (5), 96 (21), 81 (41). HRMS calcd for $\text{C}_8\text{H}_{14}\text{I}_2\text{NO}$ ($\text{M}^+ + 1$): 393.9165. Found: 393.9155.

Method B: White solid. Yield: 89%. Mp 96-98 °C. Two stereoisomers in ~5:1 ratio. ^1H NMR (300MHz, CDCl_3) δ 1.14 (6H, s), 1.42-1.51 (1H, m), 1.98-2.08 (1H, m), 2.36-2.48 (2H, m), 3.12/3.78 (1H, 2d, $J =$

2.7 Hz), 6.01/6.27 (1H, 2d, $J = 1.5$ Hz) 6.24 (1H, br). ^{13}C NMR (CDCl_3) δ 23.7/24.3, 27.9/28.1, 29.3/31.2, 32.2/32.4, 34.3, 68.6/70.5, 172.0. EIMS: m/z (rel intensity) 301 (M^+ , 1), 204 (1), 174 (15), 126 (100), 104 (9), 84 (6), 69 (34), 55 (57). Anal. calcd for $\text{C}_8\text{H}_{13}\text{ClINO}$: C, 31.86; H, 4.35; N, 4.64. Found: C, 32.09; H, 4.32; N, 4.47.

Method B: White solid. Yield: 81%. Mp 131-133 °C. Two stereoisomers in ~1:1 ratio. ^1H NMR (300MHz, CDCl_3) δ 3.73-3.92 (2H, m), 4.08 (1H, d, $J = 4.2$ Hz), 4.11-4.18 (2H, m), 5.74/5.77 (1H, 2d, $J = 1.8$ Hz), 7.18 (1H, br). ^{13}C NMR (CDCl_3) δ 29.9/30.7, 59.4/59.6, 64.5/66.6, 68.1/68.2, 168.3/168.4. EIMS: m/z (rel intensity) 275 (M^+ , 1), 183 (6), 164 (4), 148 (5), 127 (5), 100 (100), 86 (31), 55 (10). Anal. calcd for $\text{C}_5\text{H}_7\text{ClINO}_2$: C, 21.80; H, 2.56; N, 5.08. Found: C, 21.94; H, 2.98; N, 5.01.

White solid. Yield: 76%. Mp 70-72 °C. ^1H NMR (300 MHz, CDCl_3) δ 1.85-1.94 (2H, m), 2.20-2.25 (2H, m), 2.48 (2H, t, $J = 7.0$ Hz), 5.42 (1H, s), 5.60 (1H, s), 5.68 (1H, br), 6.17 (1H, br); ^{13}C NMR (CDCl_3) δ 23.3, 33.9, 40.3, 117.5, 133.4, 175.0; EIMS m/z (rel intensity) 192 ($\text{M}^+ + 1$, 17), 175 (1), 119 (1), 113 (8), 112 (100), 95 (6), 69 (34). Anal. calcd. for $\text{C}_6\text{H}_{10}\text{BrNO}$: C, 37.52; H, 5.25; N, 7.29. Found: C, 37.44; H, 5.31; N, 7.24.

White solid. Yield: 69%. Mp 72-74 °C. ^1H NMR (300 MHz, CDCl_3) δ 1.80-1.89 (2H, m), 2.16-2.21 (2H, m), 2.34 (2H, t, $J = 7.2$ Hz), 5.11-5.13 (2H, m), 5.93 (1H, br), 6.48 (1H, br). ^{13}C NMR (CDCl_3) δ 22.6, 34.0, 38.1, 112.8, 141.6, 175.4. EIMS m/z (rel intensity) 148 ($\text{M}^+ + 1$, 1), 113 (7), 112 (100), 95 (2), 69 (16), 67 (10), 59 (95), 44 (41); Anal. calcd. for $\text{C}_6\text{H}_{10}\text{ClNO}$: C, 48.82; H, 6.83; N, 9.49. Found: C, 48.70; H, 6.81; N, 9.34.

Reddish solid. Yield: 55%. Mp 76-78 °C. ^1H NMR (300MHz, CDCl_3) δ 1.26 (6H, s), 1.72-1.79 (2H, m), 2.38-2.43 (2H, m), 5.45 (1H, br), 5.63 (1H, br), 5.68-5.70 (1H, m), 6.04-6.05 (1H, m). ^{13}C NMR (CDCl_3) δ 25.6, 40.8, 41.1, 41.5, 111.4, 125.5, 179.6. EIMS: m/z (rel intensity) 268 ($\text{M}^+ + 1$, 4), 181 (2), 167 (5), 140 (100), 127 (4), 112 (5), 87 (38), 55 (72). Anal. calcd for $\text{C}_8\text{H}_{14}\text{INO}$: C, 35.97; H, 5.28; N, 5.24. Found: C, 36.24; H, 5.21; N, 5.23.

Yellowish solid. Yield: 66%. Mp 71-73 °C. ^1H NMR (300MHz, CDCl_3) δ 1.19 (6H, s), 1.80-1.86 (2H, m), 2.08-2.17 (2H, m), 5.17 (1H, t, $J = 1.8$ Hz), 5.24 (1H, t, $J = 1.8$ Hz), 5.46 (1H, br), 5.63 (1H, br). ^{13}C NMR (CDCl_3) δ 26.6, 31.3, 35.6, 41.4, 111.9, 150.4, 175.4. EIMS: m/z (rel intensity) 176 ($\text{M}^+ + 1$, 1), 140 (74), 123 (10), 114 (11), 95 (20), 81 (21), 67 (46), 44 (100). HRMS calcd for $\text{C}_8\text{H}_{14}\text{NO}$ ($\text{M}^+ - \text{Cl}$): 140.1075. Found: 140.1075.

Yellowish solid. Yield: 67%. Mp 68-70 °C. ^1H NMR (300MHz, CDCl_3) δ 4.00 (2H, s), 4.15 (1H, s), 5.45 (1H, d, $J = 1.8$ Hz), 5.48 (1H, d, $J = 1.2$ Hz), 5.77 (1H, br), 6.57 (1H, br). ^{13}C NMR (CDCl_3) δ 69.2, 73.9, 115.3, 137.1, 171.8. EIMS: m/z (rel intensity) 149 (M^+ , 1), 114 (6), 105 (2), 92 (1), 75 (24), 59 (100), 49 (8), 44 (62). Anal. calcd for $\text{C}_5\text{H}_8\text{ClNO}_2$: C, 40.15; H, 5.39; N, 9.36. Found: C, 40.17; H, 5.31; N, 9.29.

Method A: White solid. Yield: 72%. Mp 136-138 °C. ^1H NMR (300 MHz, CDCl_3) δ 1.61 (2H, br), 2.47-2.51 (2H, m), 2.77 (2H, br), 3.54 (2H, d, $J = 5.7$ Hz), 6.57 (1H, br). ^{13}C NMR (CDCl_3) δ 14.8, 24.3, 35.4, 58.2, 61.0, 177.3. EIMS m/z (rel intensity) 365 (M^+ , 3), 280 (1), 238 (39), 181 (8), 167 (7), 127 (12), 111 (100), 82 (35). HRMS calcd for $\text{C}_6\text{H}_9\text{I}_2\text{NO}$ ($\text{M}^+ + \text{H}$) 365.8846. Found 365.8862.

Method A: White solid. Yield: 89%. Mp 123-125 °C. ^1H NMR (300 MHz, CDCl_3) δ 1.68-1.88 (2H, m), 2.47-2.55 (2H, m), 2.59-2.67 (1H, m), 2.83-2.92 (1H, m), 3.56-3.59 (1H, m), 3.74-3.81 (1H, m), 6.70 (1H, br). ^{13}C NMR (CDCl_3) δ 23.1, 35.4, 55.8, 59.2, 177.2. EIMS m/z (rel intensity) 318 ($\text{M}^+ + 1$, 4), 289 (1), 190 (52), 133 (15), 110 (62), 82 (52), 67 (100). Anal. calcd. for $\text{C}_6\text{H}_9\text{BrINO}$: C, 22.67; H, 2.85; N, 4.41. Found: C, 22.94; H, 2.81; N, 4.24.

Method A: White solid. Yield: 70%. Mp 139-141 °C. ^1H NMR (300 MHz, CDCl_3) δ 1.66-1.69 (1H, m), 1.87-1.95 (1H, m), 2.43-2.54 (3H, m), 2.78-2.87 (1H, m), 3.53-3.56 (1H, m), 3.78-3.83 (1H, m), 6.80

(1H, br). ^{13}C NMR (CDCl_3) δ 22.2, 35.4, 54.7, 58.6, 177.3. EIMS m/z (rel intensity) 273 (M^+ , 2), 245 (2), 188 (4), 148 (33), 146 (100), 127 (7), 110 (28), 82 (28). Anal. calcd. for $\text{C}_6\text{H}_9\text{ClINO}$: C, 26.35; H, 3.32; N, 5.12. Found: C, 26.36; H, 3.48; N, 5.04.

Method C: White solid. Yield: 72%. Mp 135-137 °C. ^1H NMR (300MHz, CDCl_3) δ 1.16 (6H, br), 1.62 (2H, br), 2.75 (2H, br), 3.58 (2H, br), 6.13 (1H, br). ^{13}C NMR (CDCl_3) δ 14.1, 22.7, 29.4, 29.6, 30.2, 31.9, 61.5, 179.8. EIMS: m/z (rel intensity) 394 ($\text{M}^+ + 1$, 32), 266 (30), 238 (13), 167 (6), 139 (28), 127 (13), 111 (100), 96 (69). HRMS calcd for $\text{C}_8\text{H}_{13}\text{I}_2\text{NO}$ (M^+): 392.9087. Found: 392.9095.

Method B: White solid. Mp 167-170 °C. Yield: 77%. ^1H NMR (300MHz, CDCl_3) δ 1.37 (6H, s), 1.68-1.87 (2H, m), 2.41-2.44 (2H, m), 3.68-3.80 (2H, m), 6.41 (1H, br). ^{13}C NMR (CDCl_3) δ 22.3, 31.1, 31.9, 32.7, 33.1, 46.9, 55.1, 176.6. EIMS: m/z (rel intensity) 301 (M^+ , 3), 253 (2), 210 (1), 174 (36), 145 (33), 127 (19), 98 (100), 67 (79). Anal. calcd for $\text{C}_8\text{H}_{13}\text{ClINO}$: C, 31.86; H, 4.35; N, 4.64. Found: C, 31.98; H, 4.27; N, 4.42.

Method B: White solid. Mp 108-110 °C. Yield: 52%. ^1H NMR (300MHz, CDCl_3) δ 3.74-3.81 (1H, m), 3.92-3.99 (1H, m), 4.10-4.14 (1H, m), 4.27-4.33 (3H, m), 6.68 (1H, br). ^{13}C NMR (CDCl_3) δ 52.4, 57.1, 73.6, 85.8, 173.6. EIMS: m/z (rel intensity) 275 (M^+ , 1), 256 (1), 217 (1), 188 (13), 148 (10), 120 (25), 90 (100), 75 (20). HRMS calcd for $\text{C}_5\text{H}_8\text{ClINO}_2$ ($\text{M}^+ + 1$): 275.9288. Found: 275.9278. Anal. calcd for $\text{C}_5\text{H}_7\text{ClINO}_2$: C, 21.80; H, 2.56; N, 5.08. Found: C, 21.97; H, 2.60; N, 4.93.

White solid. Mp 47-48 °C. Yield: 61%. Two isomers (2:1). ^1H NMR (300MHz, CDCl_3) δ 1.69-1.83 (2H, m), 2.05-2.08 (1H, m), 2.24-2.26 (1H, m), 2.33-2.40 (1H, m), 2.55-2.58 (1H, m), 5.67-6.05 (1H, m), 6.64 (1H, m), 7.21-7.35 (5H, m). ^{13}C NMR (CDCl_3) δ 24.1/24.6, 26.3/30.1, 35.4/35.7, 117.9/119.1, 123.4, 125.5/126.8, 129.0/129.3, 130.5/132.6, 138.7, 174.5/179.5. EIMS: m/z (rel intensity) 255 (M^+ , 2), 220 (2), 167 (2), 150 (4), 125 (100), 109 (23), 93 (24), 67 (31). Anal. calcd for $\text{C}_{12}\text{H}_{14}\text{ClINOS}$: C, 56.35; H, 5.52; N, 5.48. Found: C, 56.44; H, 5.52; N, 5.12.

White solid. Mp 50-52 °C. Yield: 52%. Two isomers (2:1). ^1H NMR (300MHz, CDCl_3) δ 1.88-2.01 (2H, m), 2.39 and 2.59 (4H, m), 5.09-5.18 (2H, m), 6.52 and 6.93 (1H, br), 7.22-7.30 (5H, m). ^{13}C NMR (CDCl_3) δ 22.0/22.8, 29.5, 34.8/38.1, 112.7/113.1, 123.4, 125.9, 126.8/127.1, 129.1/129.3, 138.6/141.6, 174.2. EIMS: m/z (rel intensity) 255 (M^+ , 1), 220 (10), 159 (1), 125 (100), 109 (27), 93 (22), 67 (30), 55 (47). Anal. calcd for $\text{C}_{12}\text{H}_{14}\text{ClNOS}$: C, 56.35; H, 5.52; N, 5.48. Found: C, 56.34; H, 5.43; N, 5.12.

White solid. Mp 127-129 °C. Yield: 61%. ^1H NMR (300MHz, CDCl_3) δ 1.43-1.56 (1H, m), 1.68-1.83 (1H, m), 1.88-2.01 (2H, m), 2.26-2.47 (2H, m), 3.40 and 3.57 (1H, m), 3.61-3.65 (1H, m), 6.12 (1H, br). ^{13}C NMR (CDCl_3) δ 19.2, 26.2, 31.3, 47.8 (t, $J = 18$ Hz), 53.9, 172.1. EIMS: m/z (rel intensity) 148 (M^+ , 2), 131 (1), 98 (100), 79 (4), 70 (14), 55 (99), 44 (57). Anal. calcd for $\text{C}_6\text{H}_9\text{DCINO}$: C, 48.49; H, 6.78; N, 9.43. Found: C, 48.76; H, 6.86; N, 8.97.

White solid. $Z:E = 50:50$. Mp 54-56 °C. Yield: 18%. ^1H NMR (300MHz, CDCl_3) δ 1.66-1.84 (2H, m), 2.09-2.33 (4H, m), 5.43 (1H, br), 5.72-6.08 (2H, m). ^{13}C NMR (CDCl_3) δ 24.0/24.3, 26.4/30.2, 34.6/34.9, 117.8/119.0, 130.6/132.8, 174.6/174.9. EIMS: m/z (rel intensity) 149 ($\text{M}^+ + 1$, 1), 129 (1), 113 (45), 95 (8), 83 (6), 67 (26), 60 (100), 55 (39). Anal. calcd for $\text{C}_6\text{H}_9\text{DCINO}$: C, 48.49; H, 6.78; N, 9.43. Found: C, 48.56; H, 6.66; N, 9.42.

White solid. Mp 90-92 °C. Yield: 52%. ^1H NMR (300MHz, CDCl_3) δ 1.65-1.75 (1H, m), 1.91-2.06 (2H, m), 2.25-2.33 (1H, m), 2.41-2.56 (2H, m), 3.38-3.57 (2H, m), 6.47 (1H, br). ^{13}C NMR (CDCl_3) δ 20.6, 35.9, 39.6, 48.5, 57.4 (t, $J = 17$ Hz), 178.1. EIMS: m/z (rel intensity) 148 (M^+ , 1), 98 (100), 83 (2), 70 (14), 55 (95), 42 (38). Anal. calcd for $\text{C}_6\text{H}_9\text{DCINO}$: C, 48.49; H, 6.78; N, 9.43. Found: C, 48.83; H, 6.88; N, 9.12.

White solid. Mp 66-68 °C. Yield: 31%. ^1H NMR (300MHz, CDCl_3) δ 1.91-1.95 (2H, m), 2.25 (2H, t, $J = 7.5$ Hz), 2.42 (2H, t, $J = 7.5$ Hz), 5.18 (2H, d, $J = 7.2$ Hz), 5.49 (1H, br). ^{13}C NMR (CDCl_3) δ 22.7, 34.0, 38.2, 112.9, 141.8, 174.5. EIMS: m/z (rel intensity) 149 ($\text{M}^+ + 1$, 3), 113 (44), 95 (5), 83 (5), 69 (24), 60 (100), 55 (33), 41 (68). Anal. calcd for $\text{C}_6\text{H}_9\text{DClNO}$: C, 48.49; H, 6.78; N, 9.43. Found: C, 48.79; H, 6.91; N, 9.44.

Yellowish oil. Yield: 56%. $Z : E = 23:77$. ^1H NMR (300MHz, CDCl_3) δ 1.01 (1H, s), 1.16 (5H, s), 1.49-1.62 (4H, m), 2.14-2.21 (2H, m), 5.57-5.59 (1H, m), 5.62 (1H, br), 5.85-5.93 (1H, m), 5.97 (1H, br). ^{13}C NMR (CDCl_3) δ 20.6/20.9, 26.7/27.7, 36.2/36.3, 36.4/37.0, 41.7/42.2, 115.5/116.4, 138.9/142.9, 175.6/175.8. EIMS: m/z (rel intensity) 190 ($\text{M}^+ + 1$, 15), 154 (19), 137 (7), 109 (17), 95 (28), 86 (35), 67 (53), 59 (100). HRMS calcd for $\text{C}_9\text{H}_{16}\text{ClNO}$ (M^+): 189.0920. Found: 189.0912.

Yellowish oil. Yield: 53%. $Z : E = 33:67$. ^1H NMR (300MHz, CDCl_3) δ 1.02 (1H, s), 1.19 (5H, s), 1.53-1.66 (4H, m), 2.16-2.24 (2H, m), 5.55 (1H, br), 5.89 (1H, br), 5.94-6.16 (2H, m). ^{13}C NMR (CDCl_3) δ 20.6/20.9, 26.5/27.6, 36.2/36.4, 37.0/38.5, 41.5/42.0, 102.9/104.5, 141.8/147.0, 175.3/175.5. EIMS: m/z (rel intensity) 234 ($\text{M}^+ + 1$, 32), 154 (81), 147 (13), 137 (33), 109 (33), 95 (77), 86 (64), 59 (100). Anal. calcd for $\text{C}_9\text{H}_{16}\text{BrNO}$: C, 46.17; H, 6.89; N, 5.98. Found: C, 46.21; H, 6.64; N, 5.79.

Yellowish oil. Yield: 58%. ^1H NMR (300MHz, CDCl_3) δ 1.25 (6H, s), 1.57-1.62 (4H, m), 2.17-2.24 (2H, m), 5.54 (1H, br), 5.87 (1H, br), 6.13-6.16 (1H, m), 6.44-6.47 (1H, m). ^{13}C NMR (CDCl_3) δ 20.8, 27.6, 36.4, 37.5, 41.2, 75.3, 147.7, 175.6. EIMS: m/z (rel intensity) 282 ($\text{M}^+ + 1$, 4), 217 (2), 195 (13), 154 (50), 137 (20), 109 (25), 95 (75), 59 (100). HRMS calcd for $\text{C}_9\text{H}_{16}\text{INNaO}$ ($\text{M}^+ + \text{Na}$): 304.0174. Found: 304.0160.

Method A: Colorless oil. Yield: 64%. Two stereoisomers in $\sim 80:20$ ratio. ^1H NMR (300MHz, CDCl_3) δ 1.03-1.14 (6H, m), 1.46-1.56 (2H, m), 1.70-1.79 (2H, m), 2.42-2.54 (2H, m), 3.28/3.93 (1H, 2dd, $J = 7.5, 1.5$ Hz), 6.01 (1H, br), 6.07/6.36 (1H, 2d, $J = 2.1$ Hz). ^{13}C NMR (CDCl_3) δ 19.6, 20.6, 27.0, 27.3, 35.6, 38.1, 47.0, 69.6, 176.1. EIMS: m/z (rel intensity) 316 ($\text{M}^+ + 1$, 3), 254 (1), 188 (52), 140 (6), 111 (20), 83 (49), 69 (96), 41 (100). HRMS calcd for $\text{C}_9\text{H}_{15}\text{ClINO}$ (M^+): 314.9887. Found: 314.9896.

Method A: Yellowish oil. Yield: 70%. Two stereoisomers in ~82:18 ratio. ^1H NMR (300MHz, CDCl_3) δ 1.04-1.14 (6H, m), 1.43-1.52 (2H, m), 1.70-1.80 (2H, m), 2.39-2.55 (2H, m), 3.48/3.96 (1H, 2dd, $J = 7.5$ 1.5 Hz), 5.93 (1H, br), 5.96/6.12 (1H, 2d, $J = 1.8$ Hz). ^{13}C NMR (CDCl_3) δ 8.8, 19.6/20.2, 27.0, 35.8, 38.5, 47.5, 69.3, 176.1. EIMS: m/z (rel intensity) 360 ($\text{M}^+ + 1$, 3), 280 (3), 232 (22), 190 (2), 149 (12), 111 (29), 83 (43), 41 (100). HRMS calcd for $\text{C}_9\text{H}_{15}\text{INO}$ ($\text{M}^+ - \text{Br}$): 280.0198. Found: 280.0209.

Method A: Yellowish oil. Yield: 60%. ^1H NMR (300MHz, CDCl_3) δ 1.00-1.03 (3H, m), 1.11-1.14 (3H, m), 1.21-1.41 (2H, m), 1.69-1.75 (2H, m), 2.41-2.54 (2H, m), 3.56-3.61 (1H, m), 5.62-5.66 (1H, m), 5.81 (1H, br). ^{13}C NMR (CDCl_3) δ -30.6, 19.6, 26.4, 29.7, 36.2, 48.3, 68.8, 176.4. EIMS: m/z (rel intensity) 407 (M^+ , 20), 315 (1), 279 (48), 237 (2), 169 (30), 127 (11), 111 (26), 69 (83). HRMS calcd for $\text{C}_9\text{H}_{15}\text{I}_2\text{NO}$ (M^+): 406.9243. Found: 406.9237.

Yellowish solid. Yield: 61%. Mp 52-54 °C. ^1H NMR (300MHz, CDCl_3) δ 1.17 (6H, s), 1.50-1.53 (4H, m), 2.15-2.32 (2H, m), 5.15-5.16 (1H, m), 5.20-5.21 (1H, m), 5.50 (1H, br), 5.72 (1H, br). ^{13}C NMR (CDCl_3) δ 20.6, 26.7, 36.2, 39.7, 41.7, 111.5, 151.0, 175.3. EIMS: m/z (rel intensity) 190 ($\text{M}^+ + 1$, 5), 154 (69), 128 (7), 111 (4), 95 (16), 86 (52), 67 (35), 59 (100). HRMS calcd for $\text{C}_9\text{H}_{16}\text{NO}$ ($\text{M}^+ - \text{Cl}$): 154.1232. Found: 154.1230.

Yellowish solid. Yield: 63%. Mp 62-64 °C. ^1H NMR (300MHz, CDCl_3) δ 1.16 (6H, s), 1.44-1.55 (4H, m), 2.18-2.22 (2H, m), 5.46 (1H, s), 5.56 (1H, s), 5.58 (1H, br), 5.93 (1H, br). ^{13}C NMR (CDCl_3) δ 20.5, 27.0, 36.1, 40.5, 42.5, 116.1, 145.1, 175.4. EIMS: m/z (rel intensity) 154 ($\text{M}^+ - \text{Br}$, 20), 137 (6), 121 (2), 109 (8), 86 (27), 67 (32), 59 (100), 44 (57). HRMS calcd for $\text{C}_9\text{H}_{16}\text{NO}$ ($\text{M}^+ - \text{Br}$): 154.1232. Found: 154.1231.

Yellowish oil. Yield: 53%. ^1H NMR (300MHz, CDCl_3) δ 1.17 (6H, s), 1.26-1.34 (2H, m), 1.39-1.52 (2H, m), 2.20-2.25 (2H, m), 5.48 (2H, br), 5.83 (1H, d, $J = 2.4$ Hz), 6.08 (1H, d, $J = 2.1$ Hz). ^{13}C NMR

(CDCl₃) δ 20.5, 27.1, 36.1, 42.0, 43.4, 125.2, 127.4, 175.1. EIMS: m/z (rel intensity) 282 ($M^+ + 1$, 1), 196 (1), 154 (63), 137 (15), 109 (24), 95 (48), 67 (70), 44 (100). HRMS calcd for C₉H₁₆NO ($M^+ - I$): 154.1232. Found: 154.1234.

White solid. Yield: 75%. Mp 97-99 °C. ¹H NMR (300MHz, CDCl₃) δ 1.61-1.69 (4H, m), 2.26 (2H, t, J = 6.9 Hz), 2.38 (2H, J = 6.9 Hz), 5.14-5.17 (2H, m), 5.48 (1H, br), 5.60 (1H, br). ¹³C NMR (CDCl₃) δ 24.2, 26.6, 35.5, 38.8, 112.3, 142.3, 175.3. EIMS: m/z (rel intensity) 162 ($M^+ + 1$, 2), 145 (1), 126 (17), 102 (1), 81 (12), 72 (16), 59 (100), 44 (58). Anal. calcd for C₇H₁₂ClNO: C, 52.02; H, 7.48; N, 8.67. Found: C, 51.97; H, 7.65; N, 8.65.

White solid. Yield: 77%. Mp 90-92 °C. ¹H NMR (300MHz, CDCl₃) δ 1.57-1.68 (4H, m), 2.21-2.27 (2H, m), 2.45-2.47 (2H, m), 5.40 (1H, s), 5.59 (1H, s), 5.98 (1H, br), 6.48 (1H, br). ¹³C NMR (CDCl₃) δ 24.0, 27.2, 35.4, 40.9, 116.7, 133.9, 175.8. EIMS: m/z (rel intensity) 206 ($M^+ + 1$, 0.7), 126 (100), 119 (2), 109 (13), 93 (1), 84 (20), 67 (12), 59 (40). Anal. calcd for C₇H₁₂BrNO: C, 40.80; H, 5.87; N, 6.80. Found: C, 40.77; H, 5.81; N, 6.79.

Method C: White solid. Yield: 80%. Mp 139-141 °C. ¹H NMR (300MHz, CDCl₃) δ 1.36 (6H, br), 1.64-1.71 (2H, m), 2.42 (2H, br), 4.09 (2H, br), 6.41 (1H, br). ¹³C NMR (CDCl₃) δ 23.3, 29.7, 31.9, 32.2, 38.9, 46.7, 58.9, 175.2. EIMS: m/z (rel intensity) 315 (M^+ , 2), 253 (1), 188 (18), 159 (52), 123 (50), 95 (100), 67 (59), 55 (97). HRMS calcd for C₉H₁₅ClNO ($M^+ - I$): 188.0842. Found: 188.0847.

Method C: White solid. Yield: 72%. Mp 156-157 °C. ¹H NMR (300MHz, CDCl₃) δ 1.38 (6H, br), 1.91 (2H, br), 2.44 (2H, br), 4.16 (2H, br), 6.40 (1H, br). ¹³C NMR (CDCl₃) δ 23.4, 29.7, 31.6, 31.9, 38.9, 46.3, 62.1, 175.2. EIMS: m/z (rel intensity) 359 (M^+ , 2), 253 (1), 232 (8), 203 (21), 152 (33), 123 (60), 95 (100), 67 (69). HRMS calcd for C₉H₁₅BrNO ($M^+ - I$): 232.0337. Found: 232.0340.

Method C: Yellowish solid. Yield: 45%. Mp 150-152 °C. ^1H NMR (300MHz, CDCl_3) δ 1.27 (6H, br), 1.99 (2H, br), 2.44 (2H, br), 4.15 (2H, br), 6.41 (1H, br). ^{13}C NMR (CDCl_3) δ 20.2, 29.7, 31.3, 31.7, 38.6, 46.1, 60.2, 175.5. EIMS: m/z (rel intensity) 407 (M^+ , 2), 377 (12), 280 (20), 251 (29), 152 (26), 124 (86), 105 (48), 41 (100). HRMS calcd for $\text{C}_9\text{H}_{15}\text{I}_2\text{NO}$ (M^+): 406.9243. Found: 406.6232.

Method A: White solid. Yield: 80%. Mp 113-115 °C. ^1H NMR (300MHz, CDCl_3) δ 1.21-1.48 (1H, m), 1.60-2.14 (4H, m), 2.32-2.48 (2H, m), 2.64-2.75 (1H, m), 3.59-4.22 (2H, m), 6.67 (1H, br). ^{13}C NMR (CDCl_3) δ 21.0, 25.0, 26.2/26.8, 33.5, 47.9/49.7, 58.4/60.5, 176.9. EIMS: m/z (rel intensity) 288 (M^+ +1, 13), 252 (1), 160 (100), 124 (15), 96 (33), 82 (12), 67 (36), 55(35). Anal. calcd for $\text{C}_7\text{H}_{11}\text{ClINO}$: C, 29.24; H, 3.86; N, 4.87. Found: C, 29.31; H, 3.95; N, 4.65.

Method A: White solid. Yield: 85%. Mp 136-138 °C. ^1H NMR (300MHz, CDCl_3) δ 1.29-1.45 (1H, m), 1.69-1.95 (4H, m), 2.33-2.36 (2H, m), 2.74-2.95 (1H, m), 3.80-4.26 (2H, m), 6.33 (1H, br). ^{13}C NMR (CDCl_3) δ 26.1/26.5, 26.7/27.2, 33.7, 46.3/47.3, 49.1/50.3, 58.8/59.1, 176.6. EIMS: m/z (rel intensity) 204 (M^+ -127, 74), 176 (4), 160 (5), 147 (4), 125 (23), 96 (42), 79 (54), 67 (73). Anal. calcd for $\text{C}_7\text{H}_{11}\text{BrINO}$: C, 25.33; H, 3.34; N, 4.22. Found: C, 25.50; H, 3.23; N, 3.81. The structure was further confirmed by its X-ray diffraction analysis.

Method A: White solid. Yield: 79%. Mp 175-178 °C. ^1H NMR (300MHz, CDCl_3) δ 1.15-1.26 (1H, m), 1.65-1.83 (2H, m), 1.90-1.95 (1H, m), 2.40-2.49 (2H, m), 2.53-2.64 (1H, m), 2.87-2.96 (1H, m). ^{13}C NMR (CDCl_3) δ 1.0, 26.2, 28.3, 34.1, 51.7, 60.5, 176.3. EIMS: m/z (rel intensity) 379 (M^+ , 0.7), 252 (100), 223 (2), 167 (3), 125 (37), 96 (23), 81 (40), 69 (36). HRMS calcd for $\text{C}_7\text{H}_{12}\text{I}_2\text{NO}$ (M^+ +1): 379.9008. Found: 379.9004. The structure was further confirmed by its X-ray diffraction analysis.

White solid. Yield: 75%. Mp 64-66 °C. $Z:E = 25:75$. ^1H NMR (300MHz, CDCl_3) δ 1.43-1.54 (2H, m), 1.64-1.74 (2H, m), 2.05-2.29 (4H, m), 5.48 (1H, br), 5.53 (1H, br), 5.73-6.06 (2H, m). ^{13}C NMR

(CDCl₃) δ 24.8, 26.6, 27.8, 35.5, 118.5, 131.2, 175.2. EIMS: m/z (rel intensity) 162 ($M^+ + 1$, 14), 126 (32), 109 (4), 99 (6), 81 (14), 72 (60), 59 (83), 44 (100). Anal. calcd for C₇H₁₂ClNO: C, 52.02; H, 7.48; N, 8.67. Found: C, 51.92; H, 7.68; N, 8.53.

White solid. Yield: 80%. Mp 63-65 °C. $Z : E = 20:80$. ¹H NMR (300MHz, CDCl₃) δ 1.43-1.49 (2H, m), 1.64-1.74 (2H, m), 2.20-2.28 (4H, m), 5.46 (1H, br), 5.65 (1H, br), 6.06-6.19 (2H, m). ¹³C NMR (CDCl₃) δ 24.7/24.8, 27.5/28.1, 29.3/32.6, 35.5, 108.2, 134.3, 175.3. EIMS: m/z (rel intensity) 206 ($M^+ + 1$, 2), 126 (37), 109 (5), 93 (2), 86 (5), 72 (48), 59 (98), 44 (100). Anal. calcd for C₇H₁₂BrNO: C, 40.80; H, 5.87; N, 6.80. Found: C, 40.77; H, 5.79; N, 6.81.

White solid. Yield: 70%. Mp 63-65 °C. $Z : E = 10:90$. ¹H NMR (300MHz, CDCl₃) δ 1.45-1.53 (2H, m), 1.63-1.72 (2H, m), 2.14-2.28 (4H, m), 5.45 (2H, br), 6.13-6.23 (2H, br). ¹³C NMR (CDCl₃) δ 24.8, 27.4, 34.3, 35.6, 82.8, 140.7, 175.2. EIMS: m/z (rel intensity) 254 ($M^+ + 1$, 5), 167 (6), 126 (58), 109 (13), 81 (23), 59 (53), 44 (100). Anal. calcd for C₇H₁₂INO: C, 33.22; H, 4.78; N, 5.53. Found: C, 33.67; H, 4.94; N, 5.40.

Method B: Colorless oil. Yield: 82%. $Z : E = 1:1$. ¹H NMR (300MHz, CDCl₃) δ 1.65-1.78 (1H, m), 1.88-2.13 (3H, m), 2.45-2.72 (2H, m), 4.83-4.94 (0.5H, m), 5.30-5.37 (0.5H, m), 5.92-6.11 (1H, m), 6.21-6.47 (1H, m). ¹³C NMR (CDCl₃) δ 18.2/18.4, 27.0/28.2, 29.4/29.5, 76.1/78.3, 120.7/122.3, 130.2/131.2, 170.5/171.1. ESI-MS: m/z (rel intensity) 161 ($M^+ + 1$), 183 ($M^+ + Na$). HRMS calcd for C₇H₉O₂ ($M^+ - Cl$): 125.0603. Found: 125.0607.

Method B: Colorless oil. Yield: 69%. $Z : E = 1:1$. ¹H NMR (300MHz, CDCl₃) δ 1.84-2.04 (4H, m), 2.41-2.58 (2H, m), 4.72-7.79 (0.5H, m), 5.12-5.20 (0.5H, m), 6.15-6.23 (1H, m), 6.29 (0.5H, dd, $J = 7.5, 0.6$ Hz), 6.43 (0.5H, dd, $J = 13.5, 0.6$ Hz). ¹³C NMR (CDCl₃) δ 18.0/18.3, 26.7/27.8, 29.3/29.4, 78.4/79.4, 109.7/109.9, 133.1/135.1, 170.3/170.7. ESI-MS: m/z (rel intensity) 205 ($M^+ + 1$), 227 ($M^+ + Na$). Anal. calcd for C₇H₉BrO₂: C, 41.00; H, 4.42. Found: C, 39.61; H, 4.73.

Method B: Yellowish oil. Yield: 37%. $Z : E = 1:1.8$. ¹H NMR (300MHz, CDCl₃) δ 1.61-1.74 (1H, m), 1.85-2.11 (3H, m), 2.44-2.71 (2H, m), 4.78 (0.36H, dt, $J = 9.9, 3.6$ Hz), 5.00-5.07 (0.64H, m), 6.37-6.58 (2H, m). ¹³C NMR (CDCl₃) δ 18.0/18.4, 26.6/27.6, 29.4/29.7, 79.9/81.1, 82.7/83.7, 139.1/143.1,

170.2/170.6. EIMS: m/z (rel intensity) 252 (M^+ , 2), 235 (1), 180 (13), 167 (1), 125 (33), 97 (100), 70 (20), 55 (77). HRMS calcd for $C_7H_9IO_2$ (M^+): 251.9647. Found: 251.9658.

References for known compounds

Compound	Reference
2	Shechter, H.; Kirk J. C. <i>J. Am. Chem. Soc.</i> 1951 , 73, 3087.
3	Matallana, A.; Kruger, A. W.; Kingsbury, C. A. <i>J. Org. Chem.</i> 1994 , 59, 3020.
4	Hodjat-Kachani, H.; Lattes, A.; Perie, J. J.; Roussel, J. <i>J. Organomet. Chem.</i> 1975 , 96, 175.
5	Curini, M.; Epifano, F.; Marcotullio, M. C.; Montanari, F. <i>Synlett.</i> 2004 , 368.
6a, 8a, 18f	Hu, T.; Li, C. <i>Org. Lett.</i> 2005 , 7, 2035.

All calculations were performed with the Gaussian 98 program¹ using the density functional theory method of B3LYP.² The geometries were fully optimized at 6-31G* level.

References:

1. Gaussian 98, Revision A.7, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, V. G. Zakrzewski, J. A. Montgomery, Jr., R. E. Stratmann, J. C. Burant, S. Dapprich, J. M. Millam, A. D. Daniels, K. N. Kudin, M. C. Strain, O. Farkas, J. Tomasi, V. Barone, M. Cossi, R. Cammi, B. Mennucci, C. Pomelli, C. Adamo, S. Clifford, J. Ochterski, G. A. Petersson, P. Y. Ayala, Q. Cui, K. Morokuma, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. Cioslowski, J. V. Ortiz, A. G. Baboul, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. Gomperts, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, C. Gonzalez, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, J. L. Andres, C. Gonzalez, M. Head-Gordon, E. S. Replogle, and J. A. Pople, Gaussian, Inc.: Pittsburgh PA, 1998.
2. (a) Becke, A. D. *Phys. Rev. A* **1988**, 38, 3098. (b) Becke, A. D. *J. Chem. Phys.* **1993**, 98, 1372, 5648. (v) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1988**, 37, 785.

22 (R = Cl) -radical

%chk=22 (R = Cl) -radical

ub3lyp/6-31g* opt freq=noraman

calculate for 22 (R = Cl) -radical HF = -824.149327

0 2
N

C	1	1.375627				
C	2	1.512661	1	116.967731		
O	2	1.237469	1	118.700777	3	173.025412
C	3	1.530193	2	113.561032	1	175.660368
C	5	1.539643	3	111.678654	2	178.539329
C	6	1.504320	5	113.967701	3	179.500590
C	7	1.331017	6	126.289079	5	112.294809
Cl	7	1.774089	6	114.377153	5	-67.645359
H	3	1.098321	2	107.581195	1	51.908520
H	1	1.028622	2	108.313064	4	-30.124611
H	3	1.100465	2	107.385247	1	-60.896329
H	5	1.096298	3	109.867967	2	56.836727
H	5	1.094518	3	109.375583	2	-59.443071
H	6	1.097688	5	109.729500	3	-59.860375
H	6	1.098664	5	109.443025	3	57.118040
H	8	1.084043	7	122.542056	6	-179.750152
H	8	1.086385	7	119.678973	6	0.340457

22 (R = Cl) TS (6-exo)

%chk=22-Cl-6-exo

ub3lyp/6-31g* opt=(ts,noeigen,readfc,nofreeze) freq=noraman

calculate for 22-Cl-6-exo HF = -824.137489

0 2

C						
C	1	1.535155				
C	2	1.513681	1	116.832138		
N	3	2.185454	2	96.199418	1	53.314529
C	4	1.374191	3	110.114177	2	-50.239032
C	5	1.516468	4	115.438492	3	53.035859
C	3	1.370359	2	123.376101	1	153.509399
O	5	1.231566	4	120.999646	3	-132.611271
Cl	3	1.780500	2	114.722479	1	-53.892176
H	2	1.096674	1	110.194794	6	55.413007
H	2	1.098606	1	108.670114	6	172.439485
H	1	1.096167	2	109.407961	3	56.626155
H	1	1.096306	2	107.943058	3	172.002611
H	6	1.098101	5	108.111210	4	62.777452
H	6	1.093421	5	107.964603	4	179.346109
H	4	1.024147	3	100.598182	2	-165.979637
H	7	1.083659	3	121.992607	2	164.313965
H	7	1.085009	3	119.217786	2	-22.822960

22 (R = Cl) TS (7-endo)

%chk=22-Cl-7-endo

ub3lyp/6-31g* opt=(ts,noeigen,readfc,nofreeze) freq=noraman

calculate for 22-Cl-7-endo HF = -824.142949

0 2

C					
C	1	1.508164			
N	1	2.846320	2	100.216065	
C	2	1.542444	1	112.966556	3 11.814137
C	3	1.375107	1	87.576629	2 48.577430
C	5	1.528649	3	118.824339	1 -59.235453
O	5	1.233835	3	120.857384	1 128.944106
C	1	1.355735	2	124.144952	4 -38.703439
Cl	1	1.754866	2	116.461523	4 136.379479
H	2	1.094813	1	109.338496	8 -161.051485
H	4	1.095400	2	110.402618	1 58.198074
H	2	1.100065	1	108.937812	8 83.248636
H	4	1.097040	2	107.564369	1 173.587929
H	6	1.098795	5	105.727747	3 -98.221410
H	6	1.096207	5	106.351211	3 149.771679
H	3	1.026040	1	107.822381	2 155.806459
H	8	1.083939	1	121.441635	2 -179.873713
H	8	1.081806	1	119.920893	2 -14.702466

22 (R = Cl) TS (1,5-H migration)

%chk=22-Cl-1,5-H

ub3lyp/6-31g* opt=(ts,noeigen,readfc,nofreeze) freq=noraman

calculate for 22-Cl-1,5-H HF = -824.134882

0 2

C					
C	1	2.517701			
C	2	1.524179	1	35.129900	
O	2	1.227043	1	137.865892	3 -83.063131
N	2	1.382481	1	92.258714	3 130.590023

C	1	1.531654	2	90.206348	4	148.838914
C	6	1.472473	1	120.406333	2	-127.524086
C	7	1.341345	6	125.133776	1	-136.765679
Cl	7	1.771185	6	116.187976	1	46.103987
H	3	1.092372	2	108.182378	1	-121.912682
H	3	1.098049	2	108.880708	1	120.766571
H	1	1.097585	2	144.909700	4	-84.386262
H	6	1.239759	1	101.423607	2	-6.436119
H	6	1.095975	1	112.175681	2	100.767527
H	1	1.094948	2	91.834852	4	39.063918
H	8	1.083788	7	122.351916	6	-178.017568
H	8	1.085949	7	119.706045	6	2.305999
H	5	1.024763	2	111.263934	1	122.478011

23 (R = Cl) -radical

%chk=23 (R = Cl) -radical

ub3lyp/6-31g* opt freq=noraman

calculate for 23 (R = Cl) -radical HF = -824.148182

0 2

N

C	1	1.375516				
C	2	1.512637	1	116.989071		
O	2	1.237507	1	118.691827	3	172.857748
C	3	1.530216	2	113.599970	1	177.711123
C	5	1.540001	3	112.196193	2	179.789391
C	6	1.505074	5	112.546281	3	178.058768
C	7	1.330387	6	123.296650	5	119.786314
Cl	8	1.753017	7	123.388319	6	-179.780530
H	3	1.098619	2	107.528858	1	54.017037
H	1	1.028578	2	108.383552	4	-30.447383
H	3	1.100088	2	107.560116	1	-58.805919
H	5	1.096467	3	109.793429	2	57.715034
H	5	1.096368	3	109.190048	2	-58.052235
H	6	1.097999	5	109.904507	3	-59.117442
H	6	1.100791	5	108.893907	3	57.045817
H	8	1.084791	7	124.078602	6	0.498589
H	7	1.088965	6	117.269673	5	-59.611283

23 (R = Cl), TS (6-exo)

%chk=23-Cl-6-exo

ub3lyp/6-31g* opt=(ts,noeigen,readfc,nofreeze) freq=noraman

calculate for 23-Cl-6-exo HF = -824.143349

```

0 2
C
C      1      1.538072
C      2      1.509735  1      114.442581
N      3      2.303896  2      97.002902  1      53.678922
C      4      1.372107  3      105.815523  2      -51.803755
C      5      1.517596  4      115.441437  3      54.894869
C      3      1.355956  2      122.324537  1      156.238979
O      5      1.234175  4      121.313249  3      -130.222944
Cl     7      1.737586  3      122.718944  2      171.093238
H      2      1.096915  1      110.352262  6      55.971539
H      2      1.100206  1      107.901792  6      172.041744
H      1      1.098980  2      109.162175  3      54.833075
H      1      1.096416  2      108.376374  3      170.047537
H      6      1.097560  5      108.468111  4      57.948062
H      6      1.093660  5      107.853646  4      174.865263
H      3      1.088359  2      117.086167  1      -41.501719
H      4      1.025610  3      100.066453  2      -165.618289
H      7      1.083957  3      123.687111  2      -14.010986

```

23 (R = Cl) TS (7-endo)

%chk=23-Cl-7-endo

ub3lyp/6-31g* opt=(ts,noeigen,readfc,nofreeze) freq=noraman

calculate for 23-Cl-7-endo HF = -824.138248

```

0 2
C
C      1      1.506365
N      1      2.752114  2      99.774560
C      2      1.541594  1      114.607501  3      12.259836
C      3      1.375964  1      90.693318  2      47.415845
C      5      1.527575  3      118.512176  1      -58.208744
O      5      1.232106  3      120.993650  1      129.294479
C      1      1.367671  2      121.875952  4      -36.500288
Cl     8      1.755868  1      120.356334  2      -174.525506
H      2      1.097099  1      108.808043  8      -159.276458
H      4      1.096094  2      110.372960  1      58.051155
H      2      1.101856  1      109.007811  8      85.930037
H      4      1.096824  2      108.052356  1      173.591183
H      6      1.098566  5      105.942042  3      -101.177170
H      6      1.096532  5      106.407703  3      146.715944
H      3      1.025257  1      107.411625  2      156.791347
H      1      1.086557  2      119.185689  4      138.320861
H      8      1.080320  1      123.584941  2      -18.929087

```

23 (R = Cl) TS (1,5-H migration)

%chk=23-Cl-1,5-H

ub3lyp/6-31g* opt=(ts,noeigen,readfc,nofreeze) freq=noraman

calculate for 23-Cl-1,5-H HF = -824.136224

```
0 2
C
C      1      2.517688
C      2      1.524017  1      35.108024
O      2      1.228707  1      137.213087  3      -83.590282
N      2      1.379759  1      92.629130  3      130.061703
C      1      1.533333  2      90.685845  4      147.960990
C      6      1.469614  1      117.220950  2      -127.355150
C      7      1.342115  6      123.274180  1      -144.292891
Cl     8      1.742250  7      123.134062  6      -178.416403
H      3      1.092522  2      108.246231  1      -122.043553
H      3      1.097883  2      108.939754  1      120.515128
H      1      1.097492  2      144.908445  4      -83.786407
H      6      1.225537  1      101.366129  2      -7.385064
H      6      1.096614  1      112.477155  2      99.195715
H      1      1.098257  2      91.676164  4      38.621991
H      7      1.088983  6      117.703712  1      37.230022
H      8      1.084687  7      123.821757  6      1.668099
H      5      1.025186  2      111.000939  1      123.962803
```

22 (R = Me) -radical

%chk=22 (R = Me) -radical

ub3lyp/6-31g* opt freq=noraman

calculate for 22 (R = Me) -radical HF = -403.869303

```
0 2
N
C      1      1.375959
C      2      1.512101  1      117.061020
O      2      1.237755  1      118.516664  3      172.829522
```

C	3	1.530316	2	113.734154	1	178.635214
C	5	1.541152	3	112.086488	2	-179.860666
C	6	1.515182	5	113.896786	3	-178.920314
C	7	1.337042	6	121.372825	5	113.235100
C	7	1.509973	6	116.848425	5	-67.110600
H	3	1.098868	2	107.464973	1	54.981940
H	1	1.028581	2	108.361816	4	-30.666063
H	3	1.100059	2	107.567637	1	-57.739908
H	5	1.096893	3	109.662108	2	58.409285
H	5	1.095310	3	108.806106	2	-57.218946
H	6	1.097599	5	109.116259	3	-56.531062
H	6	1.101458	5	108.576065	3	59.141236
H	8	1.087414	7	121.783367	6	-179.979546
H	8	1.087536	7	121.769310	6	0.093568
H	9	1.094171	7	111.534588	6	-177.492207
H	9	1.098933	7	110.971303	6	-56.913595
H	9	1.097665	7	111.711448	6	61.803426

22 (R = Me), TS (6-exo)

%chk=22-Me-6-exo

ub3lyp/6-31g* opt=(ts,noeigen,readfc,nofreeze) freq=noraman

calculate for 22-Me-6-exo HF = -403.861359

0 2

C						
C	1	1.536971				
C	2	1.520584	1	116.483870		
N	3	2.209391	2	96.816482	1	53.880559
C	4	1.373007	3	105.690826	2	-53.992769
C	5	1.518963	4	114.888837	3	59.447168
C	3	1.376888	2	119.138814	1	151.546228
O	5	1.234238	4	122.180338	3	-123.809173
C	3	1.515177	2	117.310551	1	-52.083616
H	2	1.096309	1	109.652011	6	59.183941
H	2	1.100868	1	108.067127	6	174.949148
H	1	1.097615	2	110.027529	3	58.321967
H	1	1.096652	2	108.359887	3	173.816306
H	6	1.097255	5	108.550819	4	55.613673
H	6	1.093507	5	108.190281	4	173.055760
H	4	1.024588	3	99.790381	2	-166.950295
H	7	1.086495	3	121.341127	2	169.277148
H	7	1.085481	3	121.255585	2	-16.506065
H	9	1.094215	3	111.272873	2	-177.581020
H	9	1.099030	3	109.656593	2	-58.427209
H	9	1.093546	3	112.732679	2	60.922461

22 (R = Me) TS (7-endo)

%chk=22-Me-7-endo

ub3lyp/6-31g* opt=(ts,noeigen,readfc,nofreeze) freq=noraman

calculate for 22-Me-7-endo HF = -403.865796

0 2

C						
C	1	1.515786				
N	1	2.810265	2	100.043644		
C	2	1.542408	1	113.648486	3	8.309000
C	3	1.377218	1	85.061291	2	53.585125
C	5	1.529647	3	117.835585	1	-64.339739
O	5	1.234075	3	121.830511	1	122.761350
C	1	1.364425	2	120.096331	4	-43.751230
C	1	1.501383	2	117.707522	4	130.485649
H	2	1.097820	1	109.414271	8	-166.196792
H	4	1.095329	2	110.069896	1	60.508186
H	2	1.100783	1	109.358483	8	78.207929
H	4	1.097355	2	108.315133	1	176.347954
H	6	1.099128	5	106.050142	3	-93.331005
H	6	1.096125	5	106.538051	3	154.215782
H	3	1.025991	1	106.198602	2	159.507801
H	8	1.086422	1	120.685899	2	-178.847995
H	8	1.082644	1	121.826316	2	-13.755225
H	9	1.094154	1	112.301014	2	177.516854
H	9	1.099844	1	110.657852	2	-61.503959
H	9	1.098826	1	110.765102	2	56.245044

23 (R = Me) -radical

%chk=23 (R = Me) -radical

ub3lyp/6-31g* opt freq=noraman

calculate for 23 (R = Me) -radical HF = -403.870276

0 2

N						
C	1	1.375864				
C	2	1.511670	1	117.167224		
O	2	1.237996	1	118.414771	3	-173.176869
C	3	1.530295	2	113.873060	1	-173.564696
C	5	1.540042	3	112.389074	2	-178.189707
C	6	1.504814	5	112.765872	3	178.572365
C	7	1.335596	6	125.256885	5	119.062481

C	8	1.502069	7	125.313550	6	-179.567830
H	3	1.100819	2	107.312292	1	63.229361
H	3	1.098196	2	107.645398	1	-49.448085
H	5	1.095912	3	109.465842	2	59.700898
H	5	1.097486	3	109.424507	2	-55.940034
H	6	1.098459	5	109.695941	3	-58.887145
H	6	1.101768	5	108.607549	3	56.948844
H	8	1.092125	7	118.645675	6	0.604446
H	7	1.092612	6	115.900179	5	-60.173411
H	9	1.098544	8	111.264237	7	120.877363
H	9	1.098603	8	111.307638	7	-120.463573
H	9	1.095331	8	111.552327	7	0.229366
H	1	1.028586	2	108.337089	4	30.725501

23 (R = Me), TS (6-exo)

%chk=23-Me-6-exo

ub3lyp/6-31g* opt=(ts,noeigen,readfc,nofreeze) freq=noraman

calculate for 23-Me-6-exo HF = -403.866641

0 2

C						
C	1	1.537233				
C	2	1.508398	1	114.759476		
N	3	2.280952	2	97.353862	1	53.559600
C	4	1.372899	3	105.628427	2	-52.101056
C	5	1.518710	4	115.208187	3	55.866996
C	3	1.364397	2	123.898434	1	156.091190
O	5	1.234417	4	121.831978	3	-128.566981
C	7	1.495171	3	124.868383	2	171.229581
H	2	1.097275	1	110.268429	6	56.613011
H	2	1.100968	1	107.858895	6	172.465951
H	1	1.099305	2	109.245155	3	55.280552
H	1	1.096744	2	108.705144	3	170.696502
H	6	1.097558	5	108.598918	4	56.881225
H	6	1.093716	5	107.880818	4	173.993483
H	3	1.091060	2	115.961157	1	-41.908575
H	7	1.090189	3	118.300699	2	-13.277277
H	9	1.095107	7	111.942531	3	-5.031290
H	9	1.099434	7	110.952785	3	115.980899
H	9	1.098811	7	111.101251	3	-126.025092
H	4	1.025349	3	100.728711	2	-165.249879

23 (R = Me), TS (7-endo)

%chk=23-Me-7-endo

ub3lyp/6-31g* opt=(ts,noeigen,readfc,nofreeze) freq=noraman

calculate for 23-Me-7-endo HF = -403.864116

0 2

C					
C	1	1.506471			
N	1	2.738465	2	100.693337	
C	2	1.543050	1	113.902231	3 11.648823
C	3	1.375520	1	89.899696	2 48.196609
C	5	1.528211	3	118.434286	1 -59.148213
O	5	1.233589	3	121.355212	1 127.887425
C	1	1.369308	2	123.311574	4 -40.962778
C	8	1.503829	1	123.373776	2 -174.849131
H	2	1.097240	1	109.413325	8 -163.597256
H	4	1.095825	2	110.144791	1 58.602436
H	2	1.101911	1	109.515693	8 80.966572
H	4	1.097327	2	108.275488	1 174.279559
H	6	1.098985	5	105.996948	3 -99.887572
H	6	1.096543	5	106.284376	3 148.047096
H	3	1.025700	1	107.672548	2 156.033613
H	1	1.089523	2	118.100734	4 133.756720
H	8	1.085854	1	118.670515	2 -13.381665
H	9	1.094843	8	111.213121	1 -145.506722
H	9	1.095154	8	111.765046	1 -23.688052
H	9	1.098383	8	110.052789	1 96.167561

[illegible]

Compound 7a:

Compound **7d**:

Compound 8e:

Compound 9a:

Compound **9d**:

Compound 16a:

Compound 16c:

Compound **17a**:

Compound **17b**:

Compound 17c:

Compound 18a:

Compound 18b:

Compound 18c:

Compound 19a:

Compound **19b**:

Compound 19c:

Compound **19f**:

Compound 21a:

Compound **21c**: