Supplementary Material (ESI)

Green chemistry: Solvent- and metal-free Prins cyclization. Application to sequential reactions.

Damien Clarisse,[a] Béatrice Pelotier,[a] Olivier Piva[a] and Fabienne Fache*[a]

Université de Lyon, Université Lyon 1, ICBMS, équipe SURCOOF, CNRS, UMR 5246, Bât. Raulin, 43 Bd du 11 Nov. 1918, 69622 Villeurbanne cedex France. Fax: 33 472448136; Tel: 33472448521; E-mail: fache@univ-lyon1.fr.

Supplementary informations

^{1}H and ^{13}C NMR spectra were measured in $CDCl_3$ on a Bruker AC 300 or 400 spectrometers. Mass spectra were recorded on a Finigan-MAT 95 XL instrument; IR spectra were recorded on a Nicolet IR100. Melting points were measured with a B-540 Büchi. Column chromatography was carried out with silica gel 60A 40-63 µm (SDS). All the commercially available products were used as received, without purification or distillation.

Table 1

Products **3a** and **3b**: P. O. Miranda, R. M. Carballo, M. A. Ramírez, V. S. Martín and J. I. Padrón, *Arkivoc*, 2007, **iv**, 331.

Product **3c**, **3e** and **3h *cis*,** : J. S. Yadav, B. V. S. Reddy, M. K. Gupta and S. K. Biswas, *Synthesis*, 2004, 2711.

Product **3d**: J. Li and C.-J. Li, *Tetrahedron Lett*., 2001, **42**, 793.

Product **3n *cis*** and **3o *cis***: J. S. Yadav, B. V. S. Reddy, M. D. Reddy, N. Niranjan and A. R. Prasad*, Eur. J. Org. Chem*., **2003**, 1779.

3f: 4-bromo-2-phenyltetrahydro-2H-pyran

85/15 *cis/trans* mixture. Yellow oil. **^{1}H NMR:** (300 MHz, $CDCl_3$) δ 7.54 – 7.19 (5H, m), 4.93 (0.15H, dd, *J* = 10.4, 2.4 Hz), 4.81 (0.15H, tt, *J* = 3.3, 3.0 Hz), 4.44 – 4.24 (1.7H, m), 4.23 – 4.11 (1H, m), 4.04 (0.15H, dd, *J* = 11.8, 4.9 Hz), 3.60 (0.85H, td, *J* = 11.7, 2.7 Hz), 2.56 – 2.47 (0.85H, m), 2.33 – 1.92 (3.15H, m). **^{13}C NMR:** (100 MHz, $CDCl_3$) δ 141.9, 141.3, 128.6, 128.5, 128.0, 127.7, 126.0, 125.9, 80.2, 74.4, 68.3, 63.5, 50.3, 46.6, 45.6, 41.8, 37.7, 34.0. **IR:** 3031, 3060, 2960, 2923, 2851, 1603, 1452, 1249, 1081, 849, 757, 699, 555 cm^{-1}.

3g: 4-iodo-2-phenyltetrahydro-2H-pyran

70/30 *cis/trans* mixture. Brown oil. **^{1}H NMR:** (300 MHz, $CDCl_3$) δ 7.45 – 7.19 (5H, m), 4.97 – 4.91 (0.3H, m), 4.85 (0.3H, dd, *J* = 10.5, 2.0 Hz), 4.51 – 4.27 (1.4H, m), 4.14 – 3.96 (1.3H, m), 3.69 – 3.50 (0.7H, m), 2.63 – 2.51 (0.7H, m), 2.41 – 2.16 (2.3H, m), 2.01 – 1.82 (1H, m). **^{13}C NMR:** (75 MHz, $CDCl_3$) δ 141.8, 141.2, 128.6, 128.5, 127.9, 127.7, 126.0, 125.8, 81.3, 75.7, 69.5, 64.8, 47.6, 42.8, 39.6, 35.2, 30.7, 22.2. **IR:** 3062, 2955, 2848 1602, 1452, 1247, 1079, 756 cm^{-1}. **HRMS:** (CI M^{+}) 288.0002 (calcd: 288.0006).

3h: *trans*-4-chloro-2-(4-nitrophenyl)tetrahydro-2H-pyran

Yellow solid. **^{1}H NMR:** (300 MHz, $CDCl_3$) δ 8.19 (2H, d, *J* = 8.7 Hz), 7.51 (2H, d, *J* = 8.7 Hz), 4.98 (1H, d, *J* = 9.9 Hz), 4.69 – 4.63 (1H, m), 4.15 (1H, td, *J* = 11.8, 1.8 Hz), 4.03 (1H, dd, *J* = 11.8, 5.0 Hz), 2.29 – 2.07 (2H, m), 2.04 – 1.83 (2H, m). **^{13}C NMR:** (75 MHz, $CDCl_3$) δ 149.5, 147.4, 126.6, 123.7, 72.8, 62.8, 55.9, 41.5, 33.2. **IR:** 3071, 3030, 2963, 2929, 2854, 1607, 1519, 1347, 1251, 1084, 852, 752, 698, 562 cm^{-1}. **mp:** 77-78 °C. **HRMS:** (CI M^+) 241.0500 (calcd: 241.0506).

3i: *cis*-4-chloro-2-(2-nitrophenyl)tetrahydro-2H-pyran

Yellow solid. **^{1}H NMR:** (300 MHz, $CDCl_3$) δ 7.94 (1H, d, *J* = 7.8 Hz), 7.80 (1H, d, *J* = 7.8 Hz), 7.65 (1H, t, *J* = 7.8 Hz), 7.43 (1H, t, *J* = 7.8 Hz), 4.92 (1H, dd, *J* = 11.5, 1.5 Hz), 4.29 – 4.11 (2H, m), 3.60 (1H, td, *J* = 12.4, 2.0 Hz), 2.69 – 2.60 (1H, m), 2.22 – 2.15 (1H, m), 1.99 (1H, qd, *J* = 12.4, 4.9 Hz), 1.75 (1H, q, *J* = 11.5 Hz). **^{13}C NMR:** (75 MHz, $CDCl_3$) δ 147.3, 136.9, 133.8, 128.5, 128.2, 124.5, 75.0, 67.5, 55.2, 44.1, 36.9. **IR:** 3111, 3077, 2964, 2923, 2855, 1611, 1526, 1347, 1249, 1081, 863, 745, 565 cm^{-1}. **mp:** 74-75 °C. **HRMS:** (ESI M+Na) 264.0391 (calcd: 264.0398).

3i: *trans*-4-chloro-2-(2-nitrophenyl)tetrahydro-2H-pyran

Yellow solid. **^{1}H NMR:** (300 MHz, $CDCl_3$) δ 7.89 (1H, dd, *J* = 7.8, 0.9 Hz), 7.77 (1H, d, *J* = 7.8 Hz), 7.62 (1H, td, *J* = 7.8, 0.9 Hz), 7.41 (1H, t, *J* = 7.8 Hz), 5.43 (1H, dd, *J* = 10.7, 1.8 Hz), 4.65 (1H, tt, *J* = 3.2, 3.0 Hz), 4.14 (1H, td, *J* = 11.9, 2.0 Hz), 3.99 (1H, dd, *J* = 11.9, 5.1 Hz), 2.40 (1H, ddd, *J* = 14.2, 3.0, 1.8 Hz), 2.21 (1H, m), 2.01 – 1.82 (2H, m). **^{13}C NMR:** (75 MHz, $CDCl_3$) δ 147.7, 137.4, 133.5, 128.3, 128.2, 124.3, 70.0, 63.1, 55.8, 40.6, 33.4. **IR:** 3099, 3060, 2961, 2917, 2866, 1611, 1525, 1355, 1244, 1070, 860, 743, 573 cm^{-1}. **mp:** 82-84 °C. **HRMS:** (ESI M+Na) 264.0391 (calcd: 264.0398).

3j: *cis*-4-chloro-2-(4-methoxyphenyl)tetrahydro-2H-pyran

Yellow oil. **^{1}H NMR:** (300 MHz, $CDCl_3$) δ 7.26 (2H, d, *J* = 8.6 Hz), 6.88 (2H, d, *J* = 8.6 Hz), 4.28 (1H, dd, *J* = 11.4, 2.0 Hz), 4.23 – 4.06 (2H, m), 3.80 (3H, s), 3.59 (1H, td, *J* = 12.2, 2.2 Hz), 2.39 – 2.29 (1H, m), 2.25 – 2.11 (1H, m), 2.06 – 1.82 (2H, m). **^{13}C NMR:** (100 MHz, $CDCl_3$) δ 159.3, 133.5, 127.2, 113.9, 113.8, 79.0, 67.4, 55.9, 55.3, 44.6, 36.9. **IR:** 3030, 2959, 2838, 1515, 1248, 1080, 1030, 829 cm^{-1}. **HRMS:** (ESI M+Na) 249.0652 (calcd: 249.0653).

3k: *cis*-5-(4-chlorotetrahydro-2H-pyran-2-yl)-6-nitrobenzo[d][1,3]dioxole

Yellow solid. **^{1}H NMR:** (300 MHz, $CDCl_3$) δ 7.47 (1H, s), 7.22 (1H, s), 6.09 (2H, s), 4.94 (1H, dd, *J* = 10.8, 1.8 Hz), 4.28 – 4.06 (2H, m), 3.59 (1H, td, *J* = 12.3, 2.2 Hz), 2.60 (1H, ddt, *J* = 12.3, 4.0, 1.8 Hz), 2.24 – 2.14 (1H, m), 1.97 (1H, qd, *J* = 12.3, 5.0 Hz), 1.67 (1H, dt, *J* = 12.3, 10.8 Hz). **^{13}C NMR:** (75 MHz, $CDCl_3$) δ 152.6, 147.3, 141.1, 134.8, 107.0, 105.2, 103.1, 75.3, 67.4, 55.1, 44.1, 36.9. **IR:** 3071, 2961, 2922, 2852, 1618, 1521, 1505, 1484, 1337, 1260, 1037, 761, 583 cm^{-1}. **mp:** 124-125°C. **HRMS:** (ESI M+H) 286.0480 (calcd: 286.0477).

3k: *trans*-5-(4-chlorotetrahydro-2H-pyran-2-yl)-6-nitrobenzo[d][1,3]dioxole

Yellow oil. **^{1}H NMR:** (300 MHz, $CDCl_3$) δ 7.46 (1H, s), 7.22 (1H, s), 6.09 (2H, s), 5.46 (1H, dd, *J* = 10.7, 1.3 Hz), 4.68 – 4.57 (1H, m), 4.14 (1H, td, *J* = 11.8, 2.2 Hz), 3.99 (1H, dd, *J* =

11.8, 4.9 Hz), 2.44 – 2.35 (1H, m), 2.27 – 2.11 (1H, m), 1.92 – 1.78 (2H, m). **^{13}C NMR:** (75 MHz, $CDCl_3$) δ 152.4, 147.1, 137.9, 135.4, 107.1, 105.2, 103.0, 70.2, 63.1, 55.8, 40.6, 33.5. **IR:** 3067, 2963, 2925, 2853, 1618, 1521, 1505, 1484, 1337, 1260, 1037, 761, 583 cm^{-1}. **HRMS:** (CI M^+) 285.0399 (calcd: 285.0399).

3l: *cis*-4-chloro-2-(4-methyl-3-nitrophenyl)tetrahydro-2H-pyran

White solid. **^{1}H NMR:** (300 MHz, $CDCl_3$) δ 7.97 (1H, d, *J* = 1.6 Hz), 7.47 (1H, dd, *J* = 8.0, 1.6 Hz), 7.32 (1H, d, *J* = 8.0 Hz), 4.39 (1H, dd, *J* = 11.5, 1.8 Hz), 4.28 – 4.06 (2H, m), 3.60 (1H, td, *J* = 12.2, 2.2 Hz), 2.59 (3H, s), 2.47 – 2.32 (1H, m), 2.24 – 2.09 (1H, m), 2.07 – 1.94 (1H, m), 1.83 (1H, dt, *J* = 12.0, 11.5 Hz). **^{13}C NMR:** (75 MHz, $CDCl_3$) δ 149.1, 140.8, 132.8, 132.9, 130.2, 121.9, 77.6, 67.3, 55.2, 44.3, 36.6, 20.1. **IR:** 3071, 2964, 2932, 2855, 1531, 1347, 1251, 1085, 840, 760, 579 cm^{-1}. **mp:** 77-78 °C. **HRMS:** (ESI M+Na) 278.0547 (calcd: 278.0554).

3l: *trans*-4-chloro-2-(4-methyl-3-nitrophenyl)tetrahydro-2H-pyran

Yellow oil. **^{1}H NMR:** (300 MHz, $CDCl_3$) δ 7.98 (1H, d, *J* = 1.6 Hz), 7.46 (1H, dd, *J* = 8.0, 1.6 Hz), 7.31 (1H, d, *J* = 8.0 Hz), 4.92 (1H, dd, *J* = 11.0, 2.0 Hz), 4.66 (1H, tt, *J* = 3.6, 2.9 Hz), 4.14 (1H, td, *J* = 11.9, 2.2 Hz), 4.02 (1H, dt, *J* = 11.9, 4.8 Hz), 2.58 (3H, s), 2.28 – 2.09 (2H, m), 2.08 – 1.84 (2H, m). **^{13}C NMR:** (100 MHz, $CDCl_3$) δ 149.4, 141.7, 132.9, 132.8, 130.4, 122.2, 72.4, 62.9, 56.0, 41.3, 33.3, 20.3. **IR**: 3073, 2961, 2867, 1531, 1347, 1266, 1074, 836, 757, 579 cm^{-1}. **HRMS:** (ESI M+Na) 278.0550 (calcd: 278.0554).

3m: *cis*-4-chloro-2-(2-chloro-6-nitrophenyl)tetrahydro-2H-pyran

White solid. **^{1}H NMR:** (300 MHz, $CDCl_3$) δ 7.52 (1H, dd, *J* = 7.8, 1.6 Hz), 7.43 – 7.30 (2H, m), 4.85 (1H, dd, *J* = 10.8, 3.0 Hz), 4.19 – 4.03 (2H, m), 3.49 (1H, td, *J* = 12.1, 2.4 Hz), 2.53 – 2.29 (2H, m), 2.14 – 1.86 (2H, m). **^{13}C NMR:** (100 MHz, $CDCl_3$) δ 151.2, 133.3, 132.4, 131.2, 129.2, 122.7, 75.9, 67.6, 54.9, 39.8, 36.0. **IR:** 3090, 2962, 2929, 2852, 1540, 1371, 1251, 1084, 799, 757, 568 cm^{-1}. **mp:** 97-99°C. **HRMS:** (ESI M+Na) 298.0004 (calcd: 298.0008).

3m: *trans*-4-chloro-2-(2-chloro-6-nitrophenyl)tetrahydro-2H-pyran

White oil. **^{1}H NMR:** (300 MHz, $CDCl_3$) δ 7.51 (1H, dd, *J* = 7.8, 0.9 Hz), 7.41 – 7.28 (2H, m), 5.44 (1H, dd, *J* = 11.3, 2.3 Hz), 4.67 (1H, m), 4.06 (1H, td, *J* = 12.0, 1.9 Hz), 3.91 (1H, dd, *J* = 12.0, 4.7 Hz), 2.58 (1H, ddd, *J* = 14.4, 11.3, 3.1 Hz), 2.25 – 2.11 (2H, m), 1.86 – 1.75 (1H, m). **^{13}C NMR:** (100 MHz, $CDCl_3$) δ 151.4, 133.5, 132.3, 132.2, 128.9, 122.6, 71.1, 62.9, 56.1, 36.8, 32.7. **IR:** 3086, 2967, 2870, 1541, 1372, 1245, 1071,798, 759, 731, 569 cm^{-1}. **HRMS:** (ESI M+H) 276.0189 (calcd: 276.0189).

3n: *trans*-4-chloro-2,6-diphenyltetrahydro-2H-pyran

White solid. **^{1}H NMR:** (400 MHz, $CDCl_3$) δ 7.43 (4H, d, *J* = 7.6 Hz), 7.34 (4H, t, *J* = 7.6 Hz), 7.29 – 7.22 (2H, m), 5.12 (2H, d, *J* = 11.1 Hz), 4.84 – 4.62 (1H, m), 2.24 – 2.16 (2H, m), 2.07 (2H, ddd, *J* = 14.4, 11.1, 3.1 Hz). **^{13}C NMR:** (100 MHz, $CDCl_3$) δ 142.2, 128.5, 127.7, 126.0, 74.1, 57.0, 41.2. **IR:** 3064, 2955, 2919, 2851, 1495, 1453, 1266, 1060, 755, 697 cm^{-1}. **mp:** 58-60°C. **HRMS:** (ESI MH^+) 273.1039 (calcd: 273.1041).

3o: 4-chloro-2,6-dicyclohexyltetrahydro-2H-pyran

80/20 *Cis/ trans* mixture. White oil. **^{1}H NMR:** (300 MHz, $CDCl_3$) δ 4.65 – 4.61 (0.2H, m), 3.99 (0.8H, tt, *J* = 11.8, 4.5 Hz), 3.47 (0.4H, dd, *J* = 10.2, 8.1 Hz), 2.93 (1.6H, ddd, *J* = 11.1, 6.9, 1.3 Hz), 2.14 (1.6H, dd, *J* = 12.3, 4.5 Hz), 2.05 – 1.87 (2.4H, m), 1.86 – 0.78 (22H, m). **^{13}C NMR:** (75 MHz, $CDCl_3$) δ 81.2, 75.9, 57.8, 43.0, 42.8, 40.1, 36.9, 29.2, 29.0, 26.7, 26.3, 26.1. **IR:** 2924, 2852, 1449, 1361, 1265, 1069, 840, 804, 763 cm^{-1}.

Table2

Sequential Prins-Bartoli reaction:

Homoallylic alcohol (0.5 mmol), aldehyde (0.5 mmol) and trimethylsilyl chloride (0.75 mmol, 100 µl) were stirred at room temperature for the required time (generally 2 h). THF (7 mL) and alkyl magnesium bromide derivative (2.5 mmol) were added to the reaction mixture at -40°C. After 30 min of stirring, the reaction was quenched with NH_4Cl and extracted with diethyl ether (3 x 10 mL). The combined organic layers were dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography on silica gel (EtOAc/ petroleum ether: 10/90).

5a: *cis*-7-(4-chlorotetrahydro-2H-pyran-2-yl)-1H-indole

Yellow oil. **^{1}H NMR:** (300 MHz, $CDCl_3$) δ 9.04 (1H, bs), 7.59 (1H, d, *J* = 7.8 Hz), 7.23 (1H, t, *J* = 2.9 Hz), 7.07 (1H, dd, *J* = 7.8, 7.3 Hz), 6.94 (1H, d, *J* = 7.3 Hz), 6.56 (1H, dd, *J* = 2.9, 2.2 Hz), 4.73 (1H, dd, *J* = 11.4, 2.1 Hz), 4.35 – 4.14 (2H, m), 3.67 (1H, td, *J* = 12.2, 2.2 Hz), 2.54 – 2.45 (1H, m), 2.30 – 1.98 (3H, m). **^{13}C NMR:** (75 MHz, $CDCl_3$) δ 133.4, 129.1, 124.4, 123.9, 120.3, 119.5, 118.6, 102.4, 80.3, 67.6, 55.4, 43.7, 37.2. **IR:** 3449, 3055, 2961, 2918, 2852, 1436, 1338, 1250, 1139, 1077, 795, 732 cm^{-1}. **HRMS:** (ESI M+H) 236.0837 (calcd: 236.0837).

5b: *cis*-6-chloro-7-(4-chlorotetrahydro-2H-pyran-2-yl)-1H-indole

Yellow oil. **^{1}H NMR:** (400 MHz, Acetone-d_6) δ 10.39 (1H, bs), 7.48 (1H, d, *J* = 8.4 Hz), 7.30 (1H, t, *J* = 3.0 Hz), 7.02 (1H, d, *J* = 8.4 Hz), 6.47 (1H, dd, *J* = 3.0, 2.2 Hz), 5.16 (1H, dd, *J* = 11.3, 2.2 Hz), 4.49 – 4.40 (1H, m), 4.26 (2H, ddd, *J* = 12.0, 4.8, 1.8 Hz), 3.76 (2H, td, *J* = 12.0, 2.4 Hz), 2.47 – 2.41 (1H, m), 2.25 – 2.10 (3H, m). **^{13}C NMR:** (100 MHz, Acetone-d_6) δ 134.8, 129.3, 126.8, 123.9, 122.9, 121.6, 121.2, 102.3, 78.3, 68.2, 56.2, 42.5, 37.7. **IR:** 3455, 2956, 2923, 2854, 1602, 1540, 1443, 1132, 1079, 805, 730 cm^{-1}. **HRMS:** (ESI M+H) 270.0046 (calcd: 270.0047).

5b*: trans*-6-chloro-7-(4-chlorotetrahydro-2H-pyran-2-yl)-1H-indole

Yellow oil. **^{1}H NMR:** (300 MHz, Acetone-d_6) δ 10.40 (1H, bs), 7.47 (1H, d, *J* = 8.4 Hz), 7.28 (1H, t, *J* = 2.9 Hz), 7.01 (1H, d, *J* = 8.4 Hz), 6.46 (1H, dd, *J* = 2.9, 2.2 Hz), 5.61 (1H, dd, *J* = 10.7, 2.6 Hz), 4.86 – 4.83 (1H, m), 4.18 – 4.08 (2H, m), 2.54 – 2.41 (1H, m), 2.34 – 1.85 (3H, m). **^{13}C NMR:** (75 MHz, Acetone-d_6) δ 135.0, 129.0, 126.5, 123.8, 123.3, 121.3, 121.1, 102.1, 73.3, 63.6, 57.7, 38.8, 33.9. **IR:** 3448, 2962, 2922, 2868, 1601, 1539, 1435, 1132, 1069, 920, 806, 731 cm^{-1}. **HRMS:** (ESI M+H) 270.0450 (calcd: 270.0447).

5c: 5-(4-chlorotetrahydro-2H-pyran-2-yl)-8H-[1,3]dioxolo[4,5-g]indole

60/*40 cis/trans* mixture. Yellow oil. **^{1}H NMR:** (300 MHz, Acetone-d_6) δ 10.17 (1H, bs), 7.29 – 7.20 (1H, m), 6.77 – 6.66 (1H, m), 6.35 – 6.27 (1H, m), 5.93 (2H, s), 5.11 (0.4H, d, *J* = 11.0 Hz,), 4.80 – 4.70 (1H, m), 4.39 – 4.26 (0.6H, m), 4.17 – 3.88 (1.4 H, m), 3.64 (0.6H, td, *J* =

12.1, 2.1 Hz), 2.45 – 1.75 (4H, m). **^{13}C NMR:** (100 MHz, Acetone-d_6) δ 140.3, 140.3, 138.4, 138.4, 133.1, 132.6, 127.2, 127.2, 118.3, 118.3, 115.0, 114.9, 102.5, 102.3, 101.4, 97.2, 97.1, 78.7, 73.6, 67.9, 63.3, 57.9, 56.8, 44.5, 40.3, 37.8, 34.1. **HRMS:** (ESI M+H) 280.0739 (calcd: 280.0735).

5d: 4-(4-chlorotetrahydro-2H-pyran-2-yl)-7-methyl-1H-indole

80/20 *cis/trans* mixture. Yellow oil. **^{1}H NMR:** (300 MHz, $CDCl_3$) δ 8.16 (1H, bs), 7.22 (1H, s), 7.12 – 6.95 (2H, m), 6.73 – 6.63 (1H, m), 5.36 – 5.26 (0.2H, m), 4.71 (1H, m), 4.45 – 4.17 (1.8H, m), 4.07 (0.2H, dd, *J* = 11.7, 4.3 Hz), 3.68 (0.8H, t, *J* = 12.1 Hz), 2.48 (3.8H, m), 2.39 – 1.80 (3.2H, m). **^{13}C NMR:** (75 MHz, $CDCl_3$) δ 135.7, 135.6, 131.5, 130.8, 124.9, 124.8, 124.0, 123.9, 122.5, 122.5, 120.1, 119.8, 116.9, 116.6, 101.4, 78.7, 72.9, 67.6, 63.0, 57.1, 56.3, 43.8, 40.6, 37.2, 33.8, 21.2, 16.6. **IR:** 3417, 3014, 2960, 2927, 2854, 1505, 1446, 1344, 1075, 733 cm^{-1}. **HRMS:** (ESI M+H) 250.0991 (calcd: 250.0993).

5e: 4-(4-chlorotetrahydro-2H-pyran-2-yl)-2,7-dimethyl-1H-indole

70/*30 cis/trans* mixture. Yellow oil. **^{1}H NMR:** (300 MHz, $CDCl_3$) δ 7.89 (1H, bs), 7.05 – 6.84 (2H, m), 6.32 (1H, m), 5.22 (0.3H, dd, *J* = 10.1, 2.9 Hz), 4.71 (0.3H, t, *J* = 2.9 Hz), 4.63 (0.7H, dd, *J* = 11.3, 1.8 Hz), 4.31 – 4.13 (1.7H, m), 4.05 (0.3H, dd, *J* = 11.8, 4.7 Hz), 3.66 (0.7H, td, *J* = 12.1, 2.2 Hz), 2.55 – 2.37 (6.7 H, m), 2.37 – 2.0 (3.3H, m). **^{13}C NMR:** (100 MHz, $CDCl_3$) δ 135.9, 135.8, 134.9, 134.8, 130.6, 129.8, 125.9, 121.7, 119.3, 119.0, 116.8, 116.5, 99.5, 79.0, 73.0, 67.6, 63.1, 57.2, 56.4, 43.6, 40.4, 37.3, 33.8, 22.8, 16.7, 14.3, 13.9. **HRMS:** (ESI M+H) 264.1150 (calcd: 264.1150).

Prins cyclisation-elimination procedure:

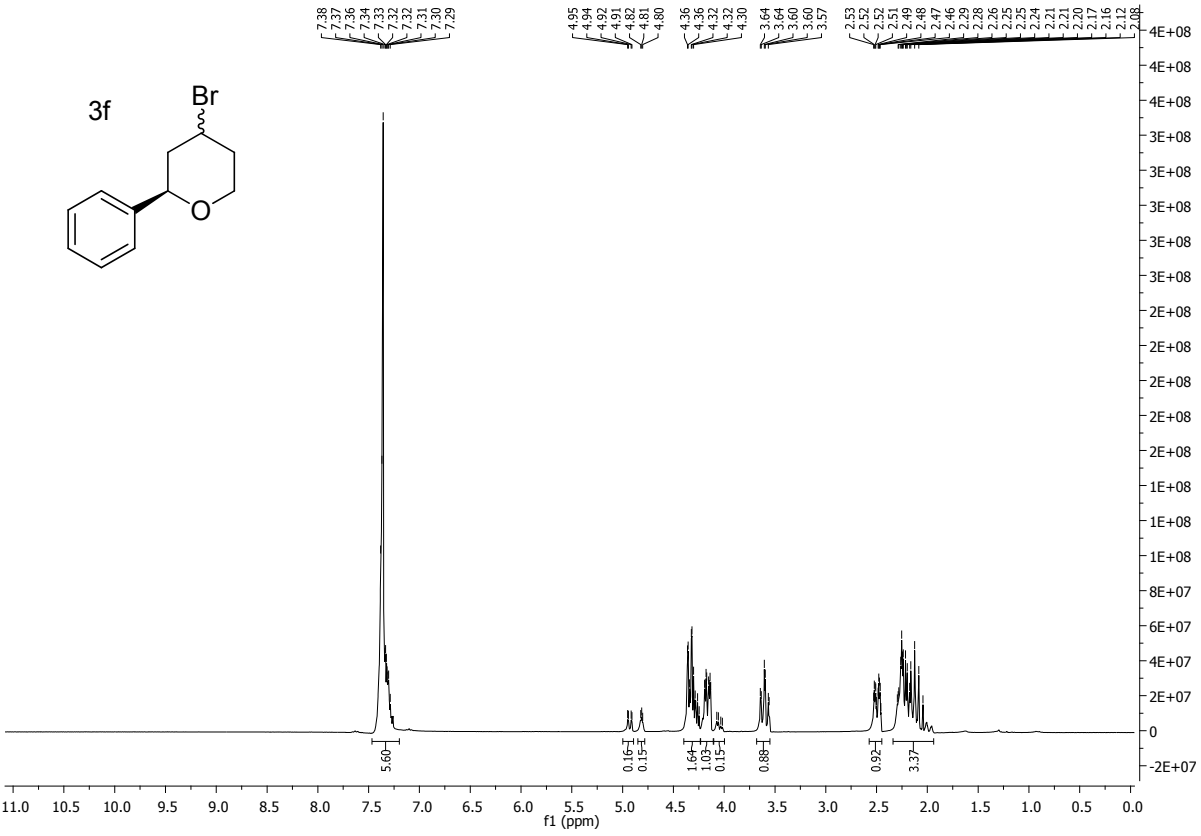
3-Buten-1-ol (0.5 mmol, 36 mg), benzaldehyde (0.5 mmol, 53 mg) and trimethylsilyl bromide (0.75 mmol 106 µL) were stirred at room temperature for 30 min. Then, DMF (1 mL), KI (0.25 mmol, 16.5 mg) and K_2CO_3 (1.25 mmol, 173 mg) were added and stirred under reflux for 4 hours. Water was added at room temperature and the aqueous phase was extracted with diethyl ether (3 x 10 mL). The combined organic layers were dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography on silica gel (EtOAc/ petroleum ether: 5/95).

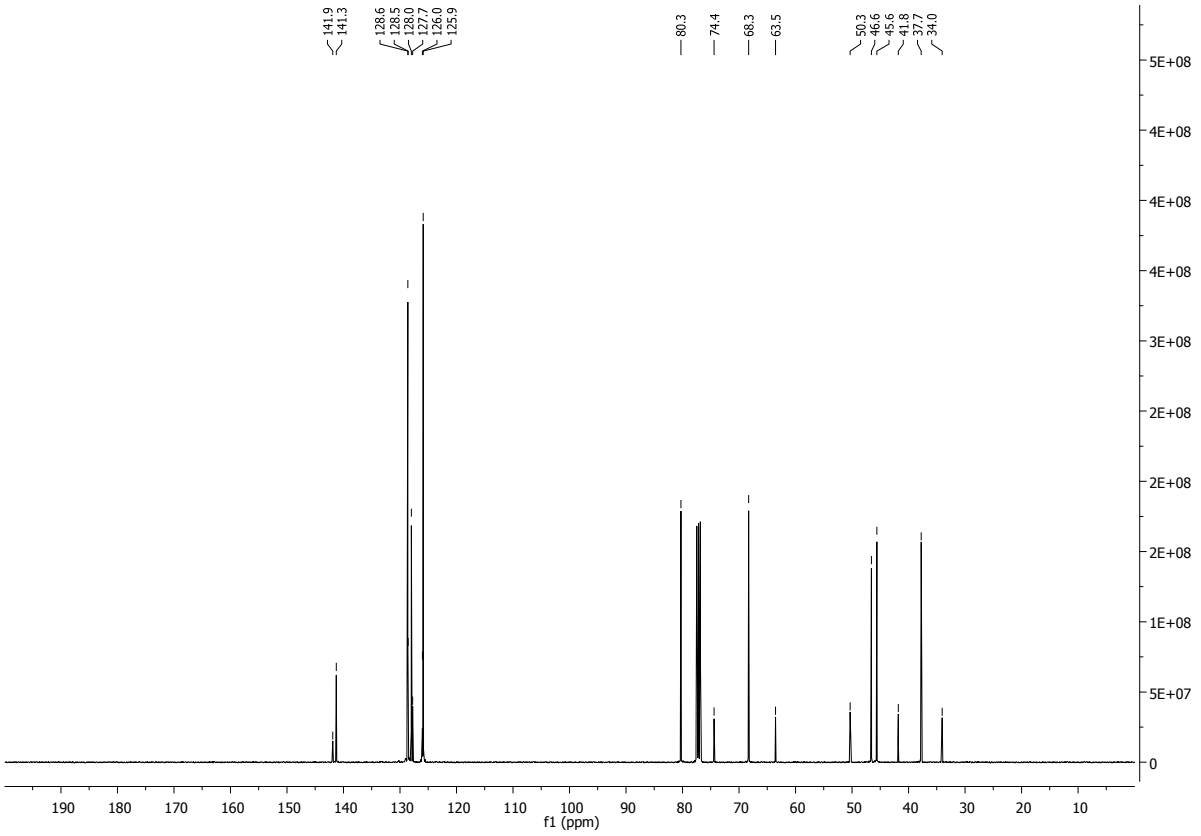
Products described in F. Michalek, D. Mädge, J. Rühe and W. Bannwarth, *J. Organomet. Chem*. 2006, **691**, 5172.

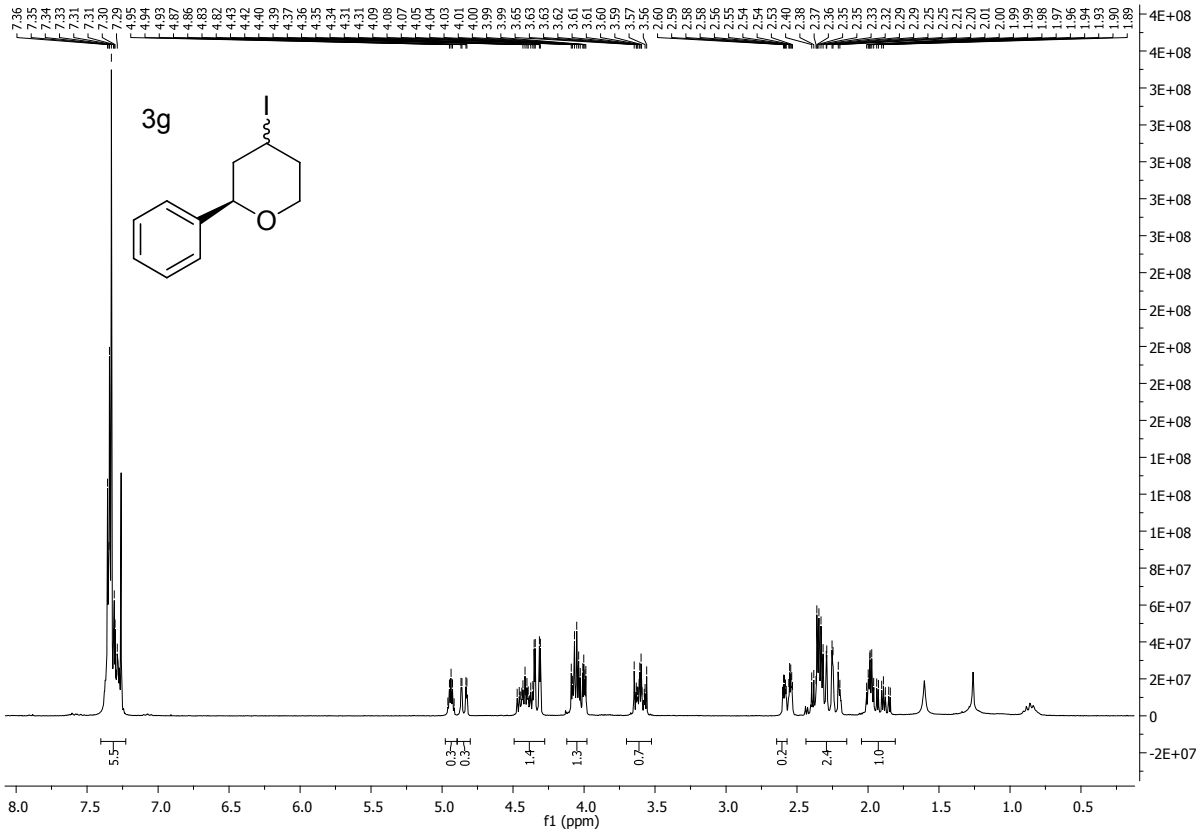
Prins cyclisation–dehalogenation procedure:

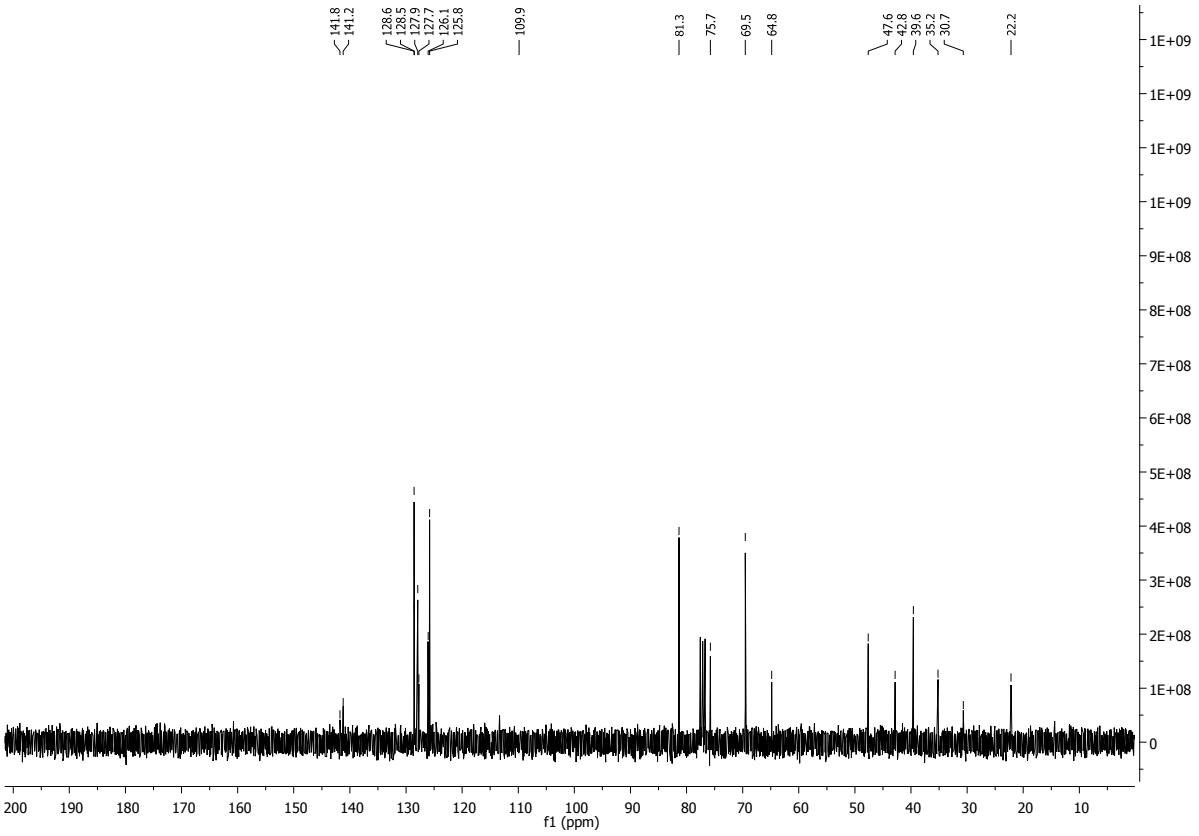
3-Buten-1-ol (0.5 mmol, 36 mg), benzaldehyde (0.5 mmol, 53 mg) and trimethylsilyl chloride (0.75 mmol 100 µL) were stirred at room temperature for 2 hours. Then, toluene (4 mL), Bu_3SnH (1.25 mmol, 364 mg) and AIBN (0.1 mmol, 17 mg) were added and stirred 5 hours under reflux. The reaction mixture was concentrated *in vacuo* and purified by column chromatography on silica gel (EtOAc/ petroleum ether: 5/95).

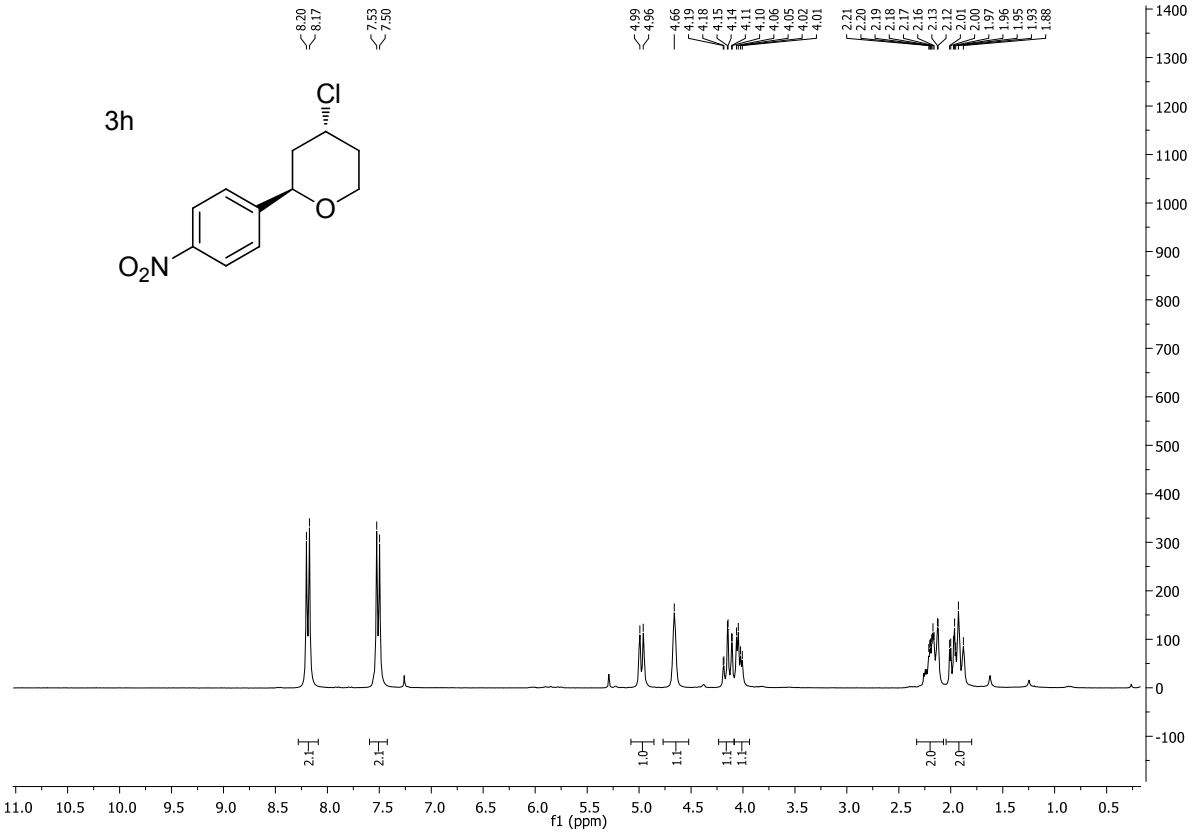
Product described in Y. Jeong, D.-Y. Kim, Y. Choi and J.-S. Ryu, *Org. Biomol. Chem.*, 2011, **9**, 374.

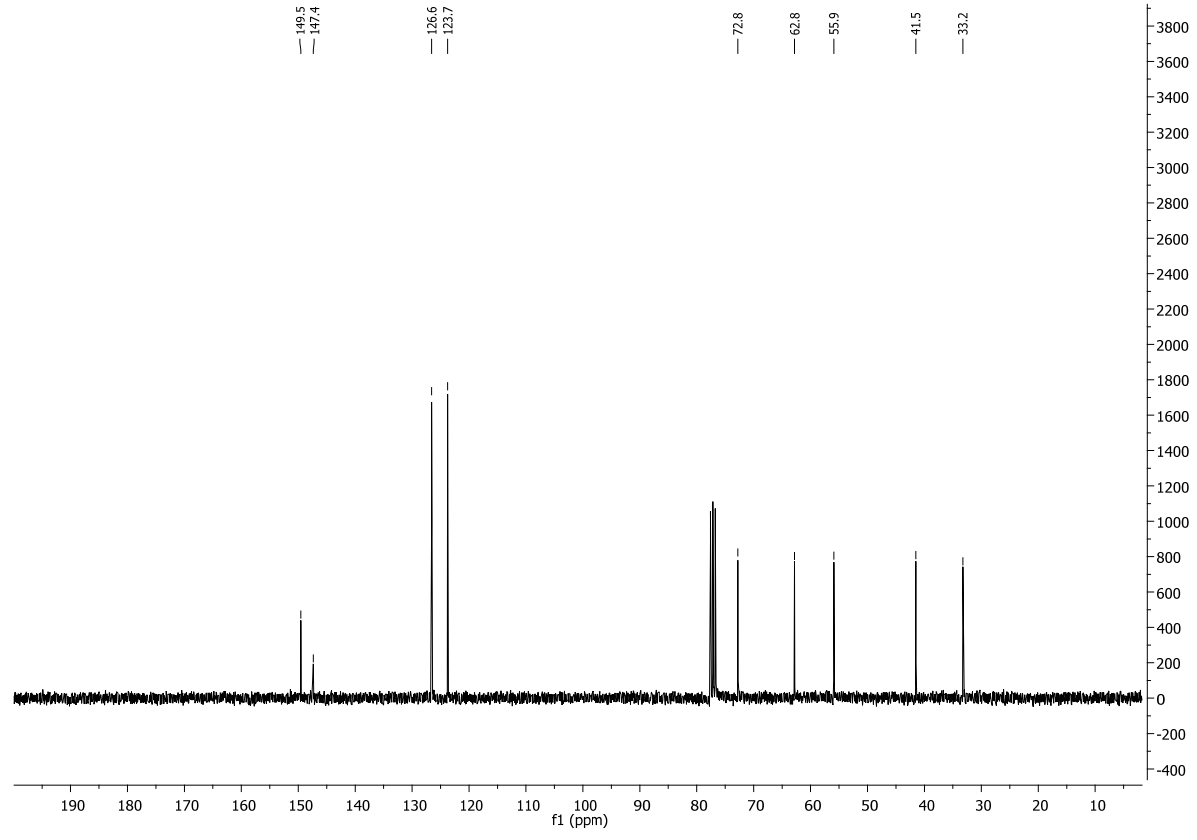

3f
Br
O
f1 (ppm)

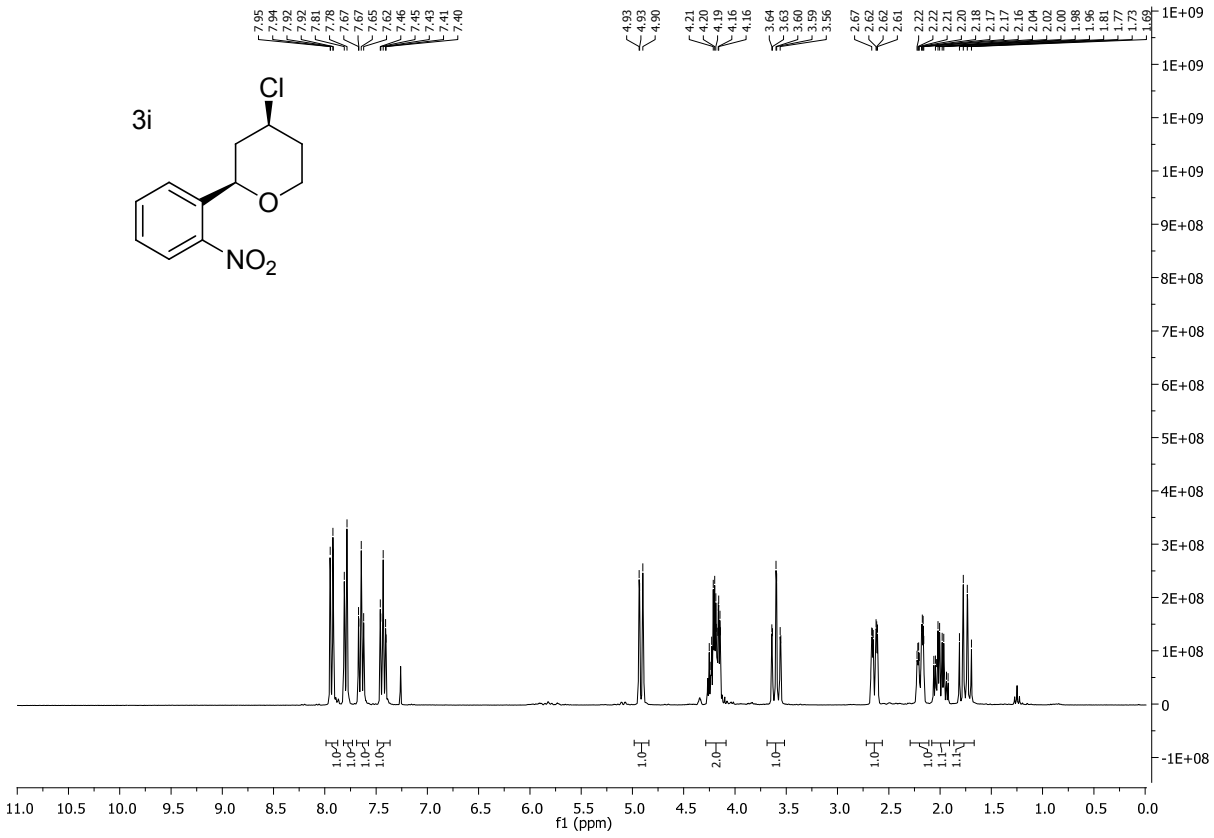

f1 (ppm)

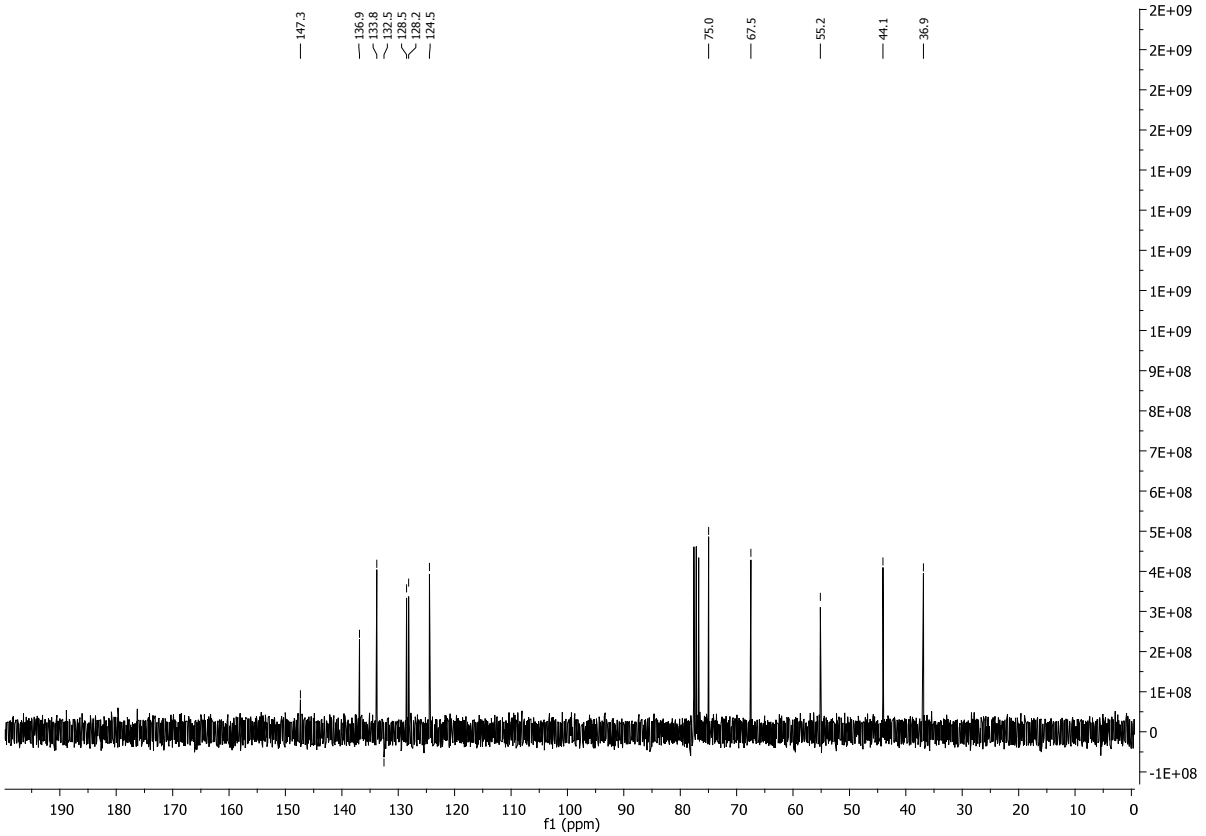


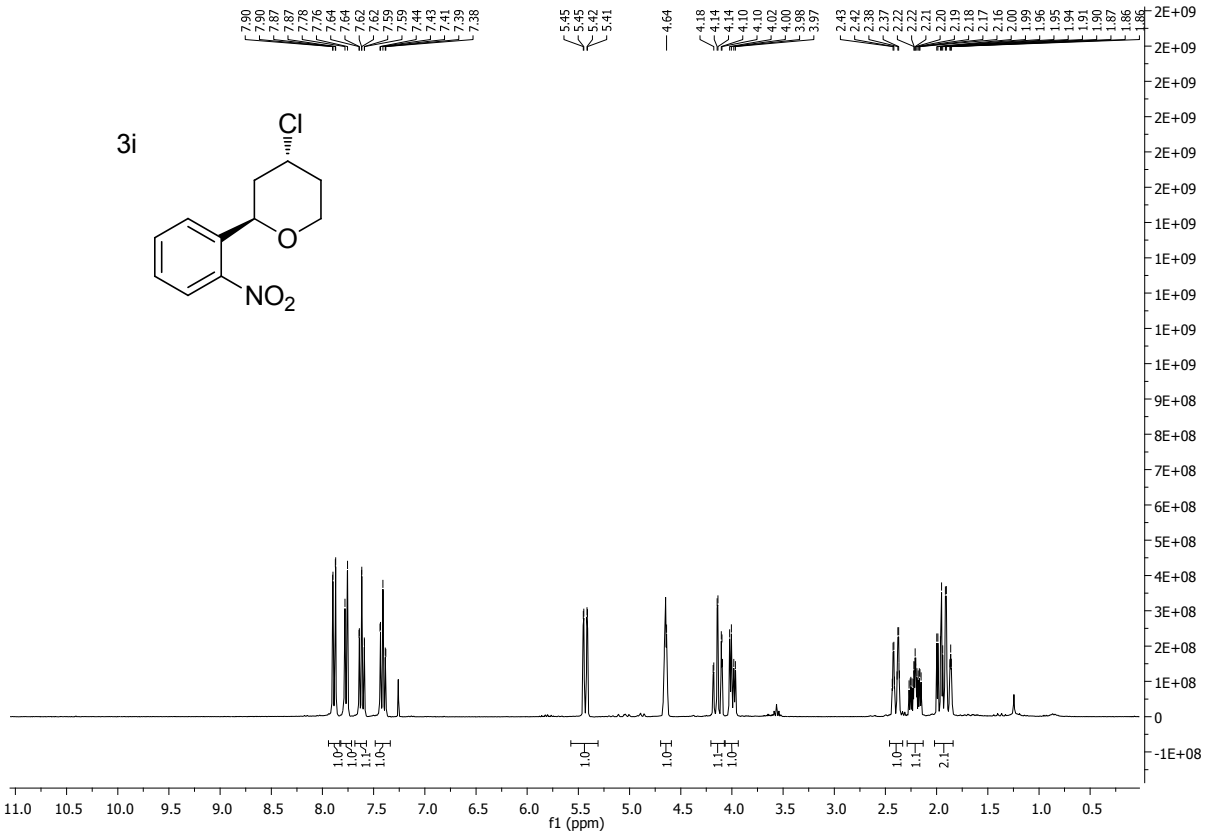


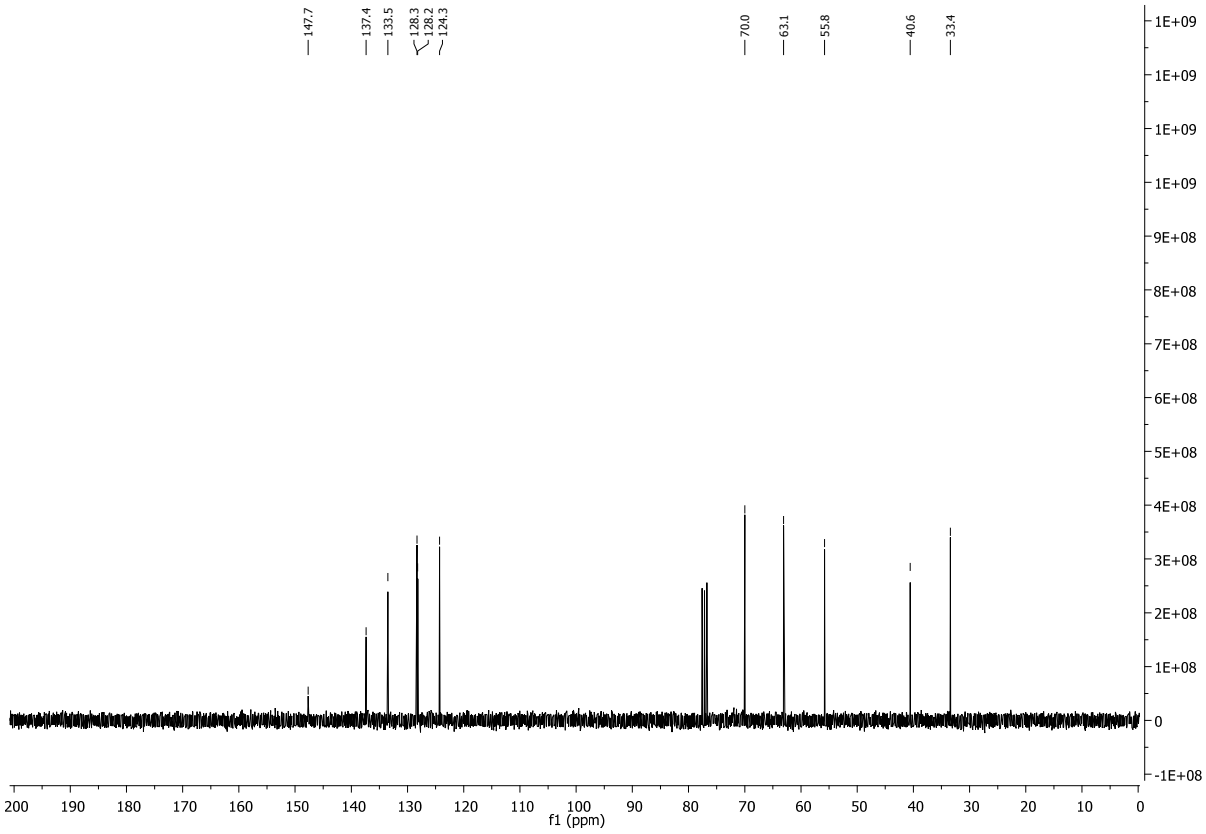

3h
Cl
O
O_2N
8.20
8.17
7.53
7.50
4.99
4.96
4.66
4.19
4.18
4.15
4.14
4.11
4.10
4.06
4.05
4.02
4.01
2.21
2.20
2.19
2.18
2.17
2.16
2.13
2.12
2.01
2.00
1.97
1.96
1.95
1.93
1.88
2.1
2.1
1.0
1.1
1.1
1.1
2.0
2.0
f1 (ppm)

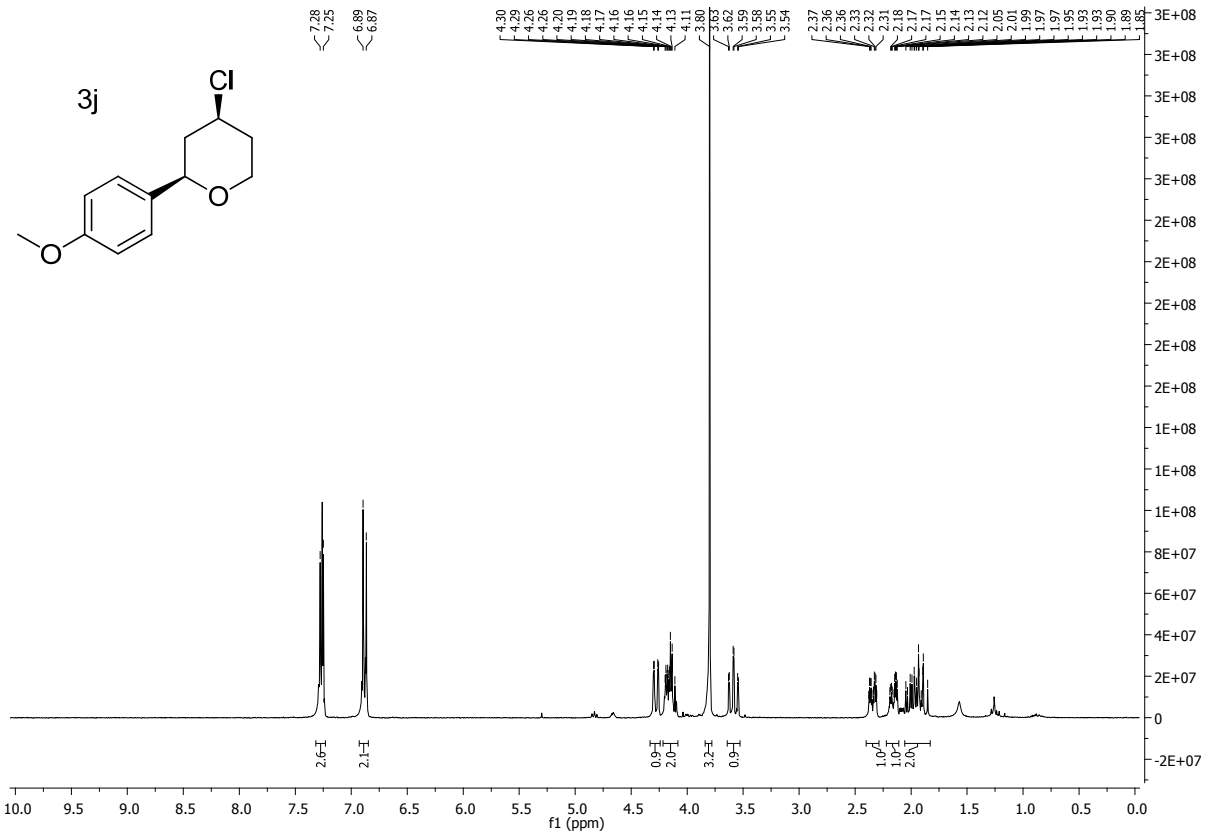

149.5
147.4
126.6
123.7
72.8
62.8
55.9
41.5
33.2
f1 (ppm)

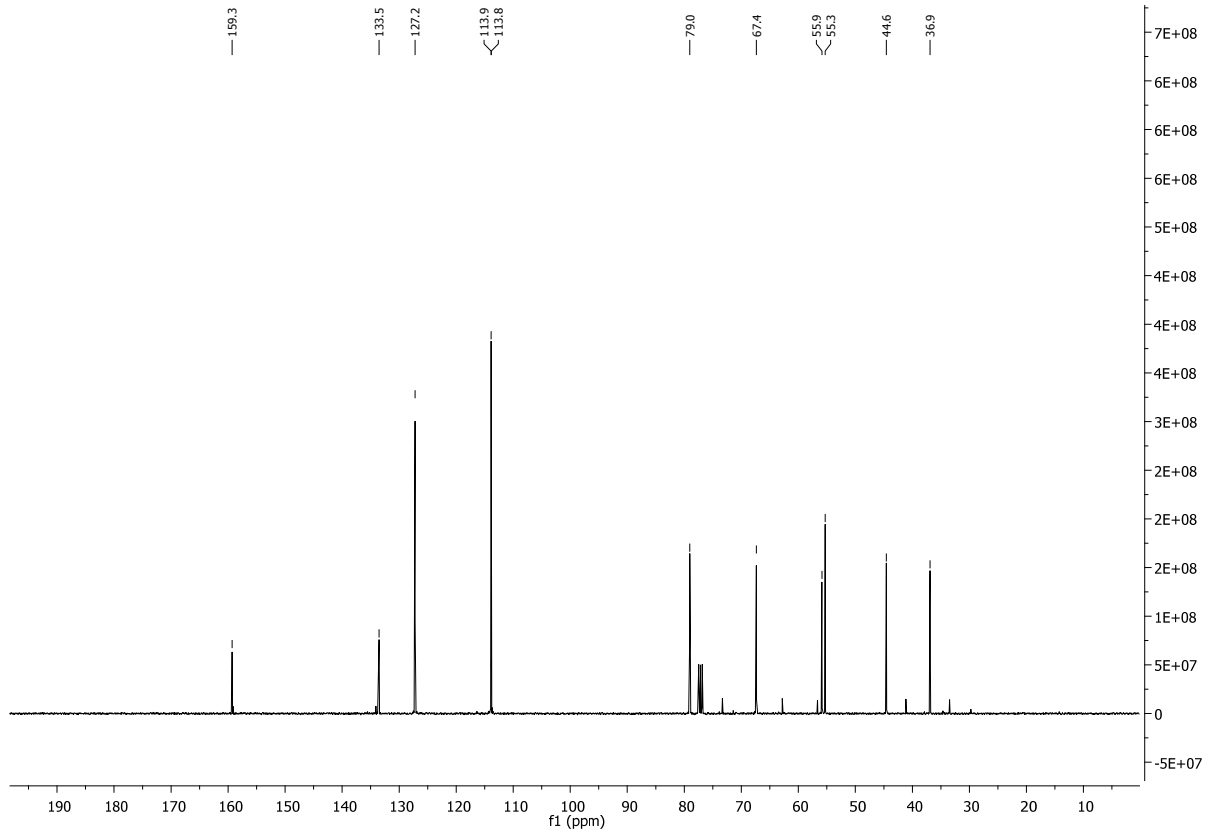

3i
Cl
O
NO2
f1 (ppm)

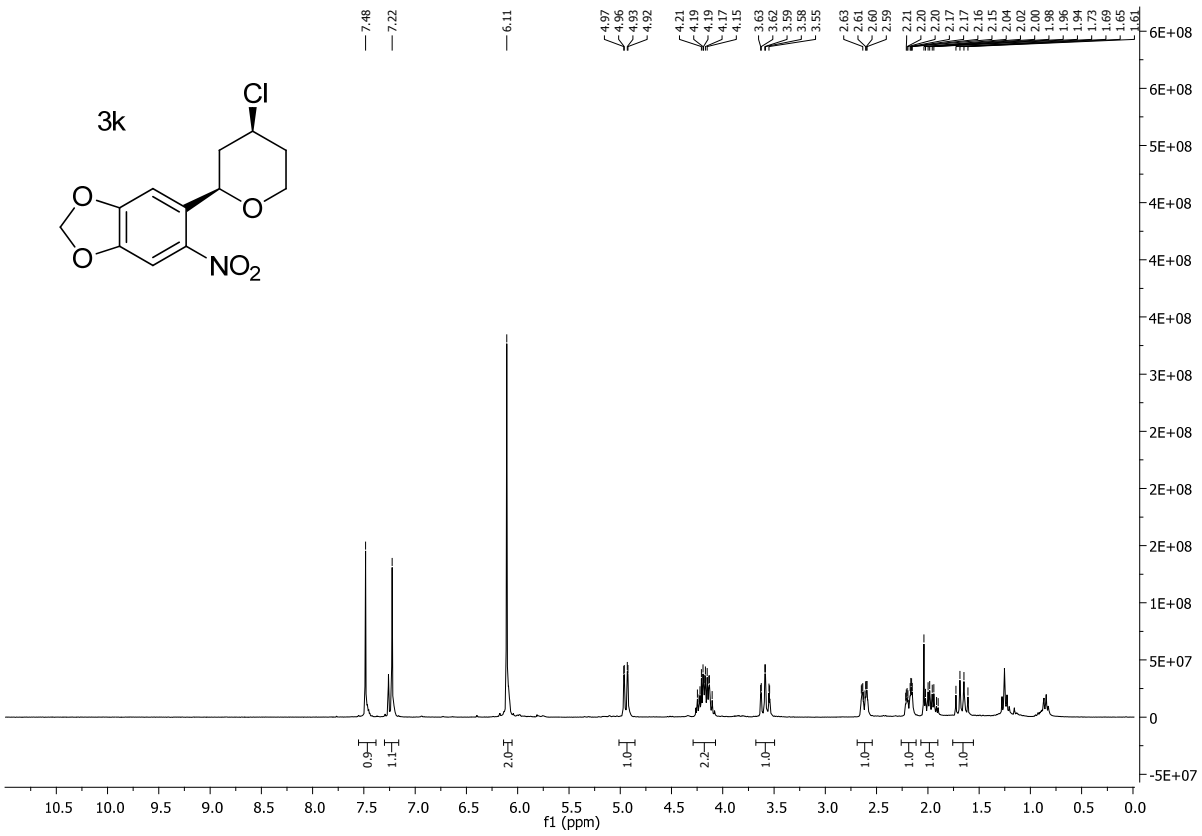

f1 (ppm)

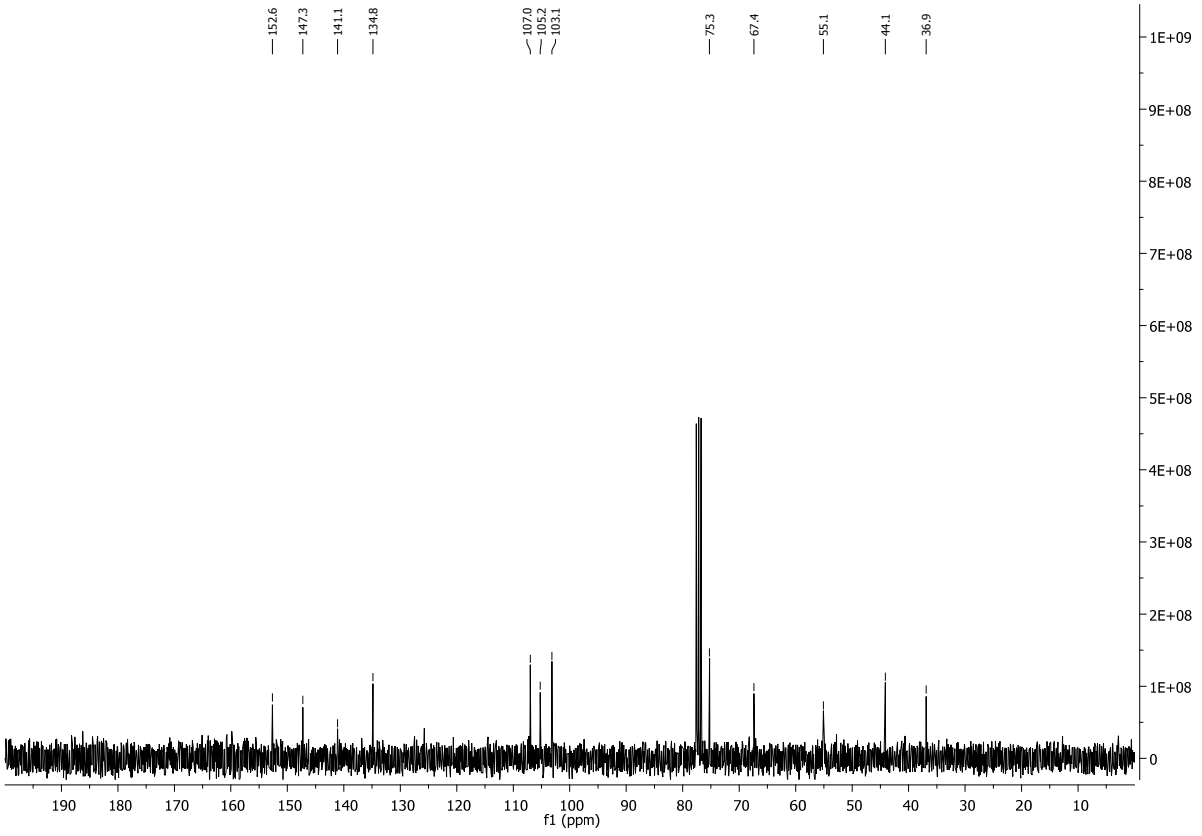


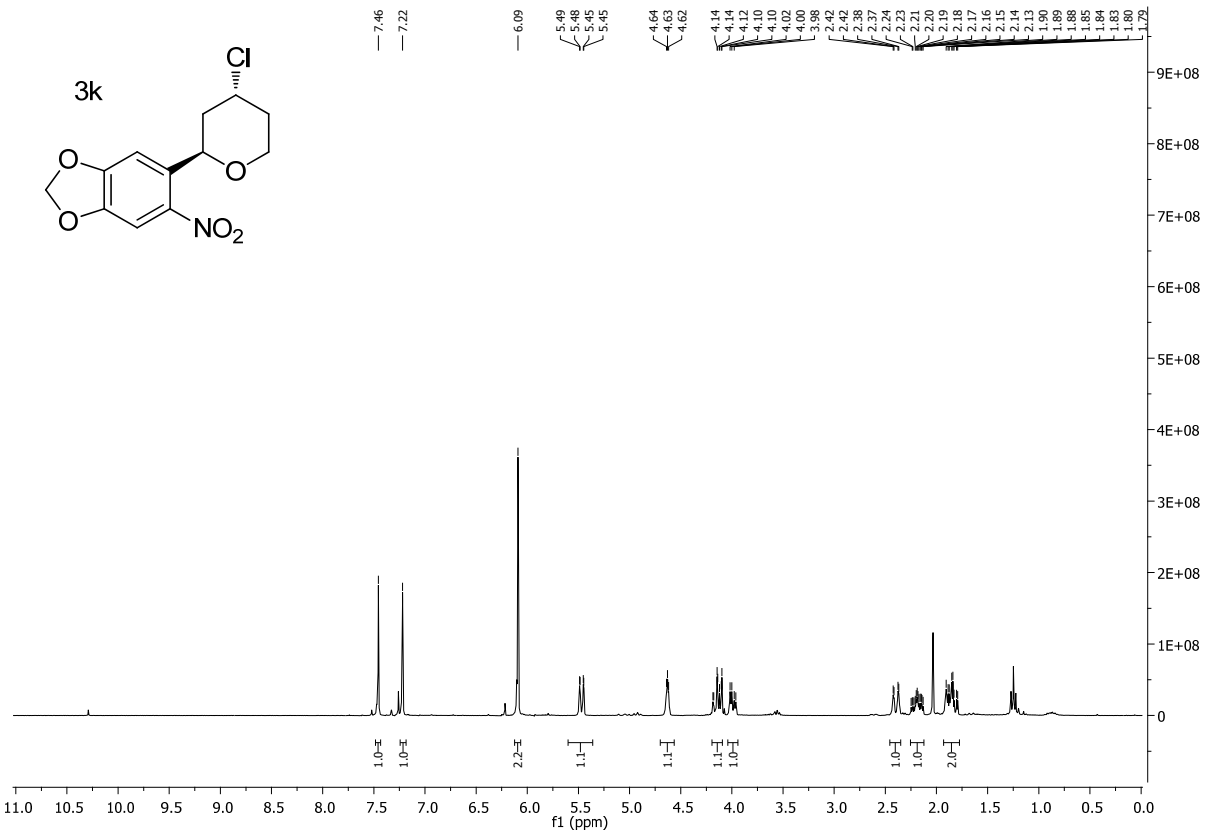


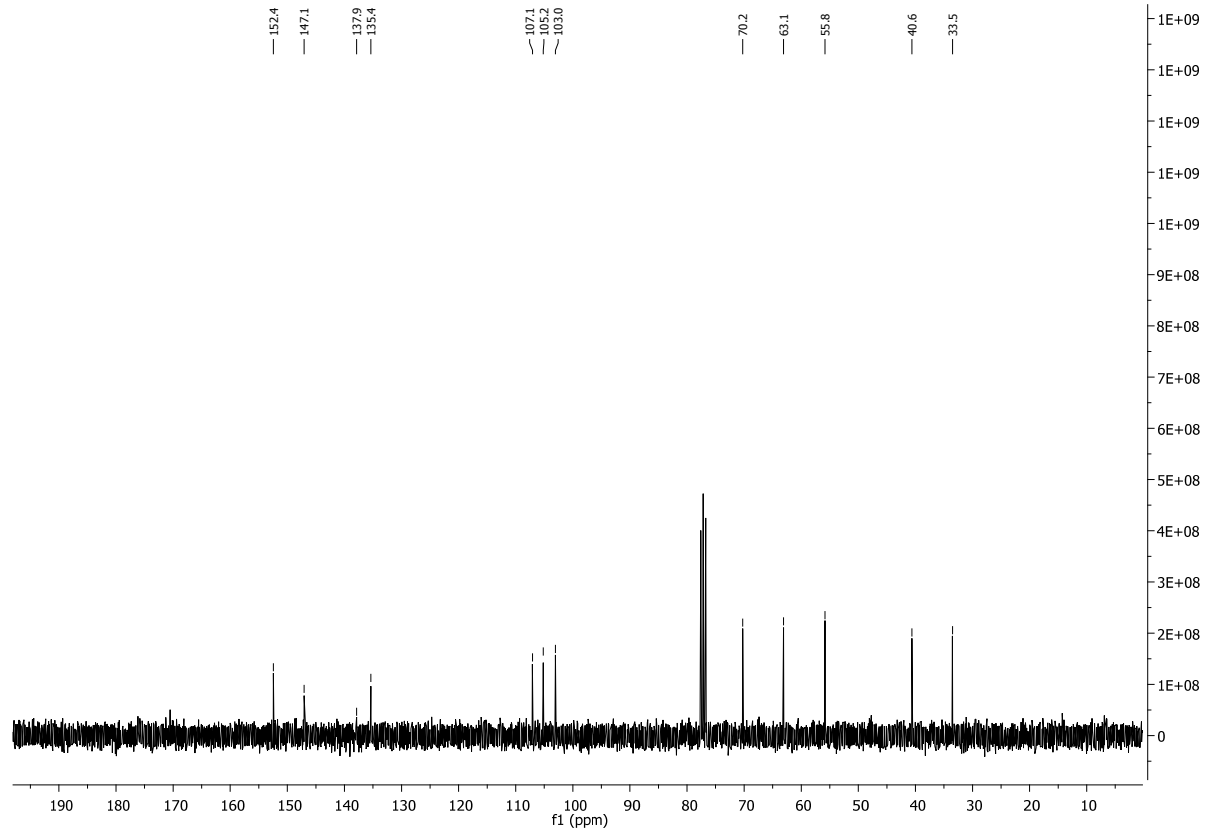

3j
Cl
O
O
f1 (ppm)

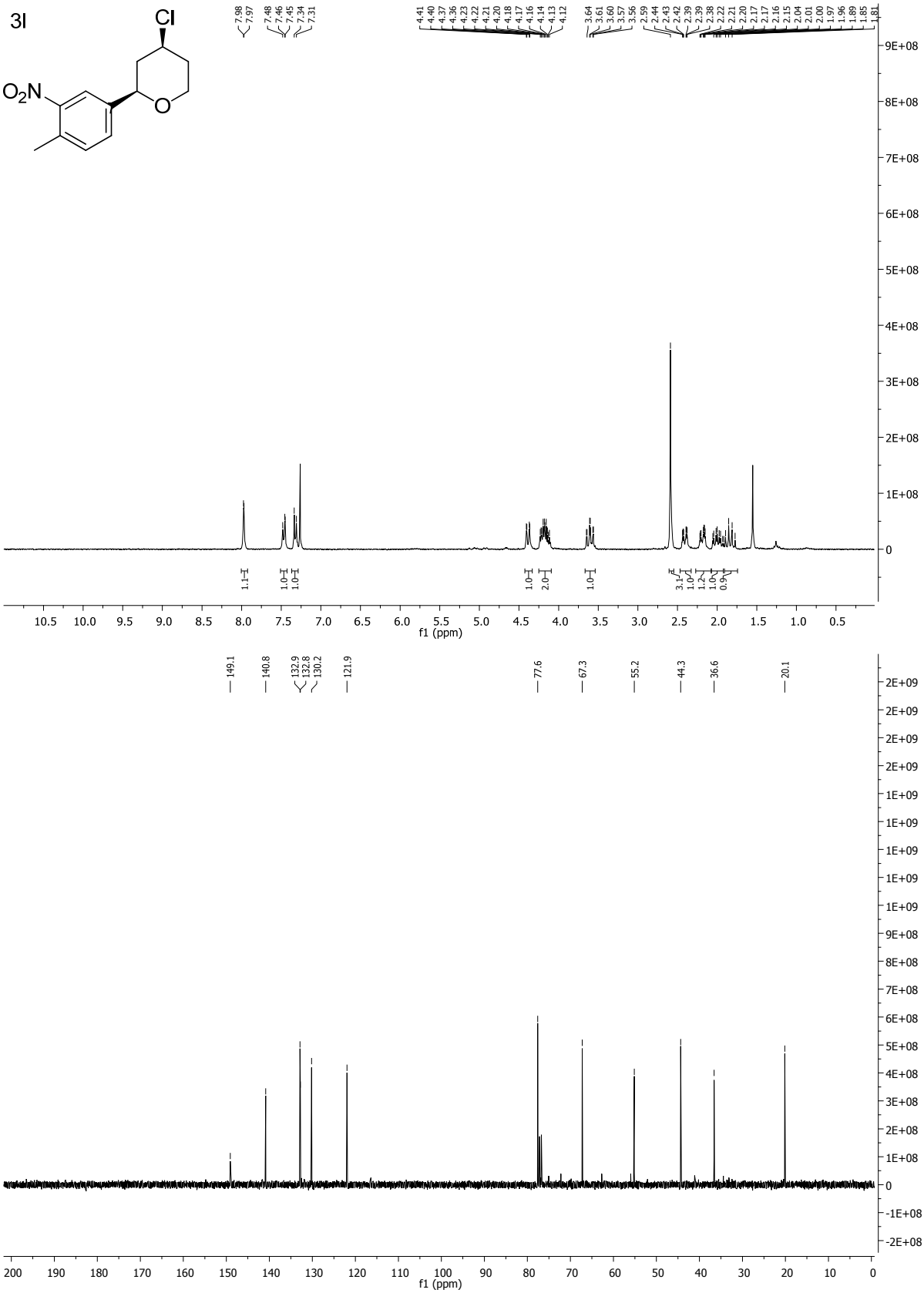

159.3
133.5
127.2
113.9
113.8
79.0
67.4
55.9
55.3
44.6
36.9
f1 (ppm)










3l
Cl
O2N
O
f1 (ppm)
f1 (ppm)