

Copper mediated synthesis of mono- and dichlorinated diaryl ethers

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(A) General remarks and apparatus

All chemicals were used either as purchased from commercial suppliers or purified by standard techniques. Flash column chromatography was performed on HPFC Biotage system with two parallel pre-packed Grace Resolv 40g silica cartridges (hexane). All melting points were taken on Stuart SMP10 apparatus and were uncorrected. ^1H NMR and ^{13}C NMR spectra were measured on a Varian Mercury VX 300 MHz spectrometer (^1H : 300 MHz, ^{13}C : 75 MHz) at room temperature. Chemical shifts were referenced to chloroform ($\delta = 7.26$ ppm for ^1H NMR and 77.00 ppm for ^{13}C NMR) using CDCl_3 as the solvent. GC data were measured on HP 5890 chromatograph. The yields were calculated using internal standard (pentadecane). For retention indices measuring a 30 m x 0.25 mm capillary column Thermo TR-5MS (0.25 μm film) was used in temperature programmed mode (8 $^\circ\text{C}/\text{min}$, $T_{\text{start}} = 100$ $^\circ\text{C}$, $T_{\text{end}} = 300$ $^\circ\text{C}$). The injector temperature was 250 $^\circ\text{C}$ and the detector temperature was 250 $^\circ\text{C}$. Nitrogen was used as a carrier gas. The retention indices were calculated by the van der Dool and Kratz equation:

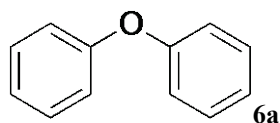
$$\text{RI}_{(X)} = 100n + 100[t_{(X)} - t_{(n+1)}] / [t_{(n+1)} - t_{(n)}]$$

where $t_{(X)}$ is a retention time of a compound in question, $t_{(n)}$ and $t_{(n+1)}$ are retention times of reference n -alkanes (Alkanes Mix 10, Dr. Ehrenstorfer) eluting immediately before and after compound. Electron impact (EI) mass spectra (Thermo Scientific Focus DSQ) were determined at an ionising voltage of 70 eV.

(B) Typical procedure

To a solution of phenol (**1a-j**) (1.0 mmol) and phenylboronic acid (**2-5**) (2 mmol) in dry CH_2Cl_2 (5 ml) were added powdered activated 4 \AA molecular sieves (1.0 g), catalyst $\text{Cu}(\text{OAc})_2$ (1.0 mmol) and Et_3N (5 mmol). The mixture was cooled to 0 $^\circ\text{C}$ and stirred for 6 hours under air atmosphere. The reaction was quenched with an excess of n -hexane and precipitated catalyst and molecular sieves were separated by filtration. The filtrate was evaporated under vacuum and the residue was purified by flash chromatography to afford pure product (**6a-p**).

(C) Analytical data for compound 6a-p



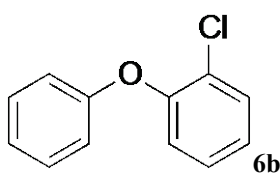
Diphenyl ether

Colourless oil.

$^1\text{H NMR}$ (CDCl_3 , 300 MHz): δ (ppm) 7.41 (dd, $J = 8.6, 7.4$ Hz, $4\text{H}^{3',5',5'}$), 7.18 (tt, $J = 7.4, 1.1$ Hz, $2\text{H}^{4',4'}$), 7.11 (dd, $J = 8.6, 1.1$ Hz, $4\text{H}^{2',2',6',6'}$).

$^{13}\text{C NMR}$ (CDCl_3 , 75 MHz): δ (ppm) 157.19, 129.68, 123.15, 118.83.

GC/MS (EI, 70 eV): m/z (%) 171 (13), 170 (M^+ , 100), 169 (35), 142 (28), 141 (44), 114 (8).



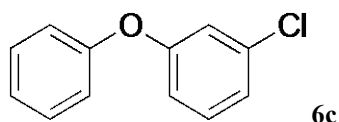
2-chlorodiphenyl ether

White solid, Mp: 46 - 47 °C.

$^1\text{H NMR}$ (CDCl_3 , 300 MHz): δ (ppm) 7.46 (dd, $J = 7.9, 1.7$ Hz, 1H^3), 7.34 (dd, $J = 8.6, 7.4$ Hz, $2\text{H}^{3',5'}$), 7.22 (ddd, $J = 8.0, 7.4, 1.7$ Hz, 1H^5), 7.14 - 7.06 (m, 2H), 7.01 - 6.94 (m, 3H)

$^{13}\text{C NMR}$ (CDCl_3 , 75 MHz): δ (ppm) 156.94, 152.46, 130.77, 129.75, 127.90, 125.87, 124.65, 123.30, 120.83, 117.91.

GC/MS (EI, 70 eV): m/z (%) 206 ($(\text{M} + 2)^+$, 19), 204 (M^+ , 66), 170 (10), 169 ($(\text{M} - \text{Cl})^+$, 100), 141 ($(\text{M} - \text{COCl})^+$, 26).



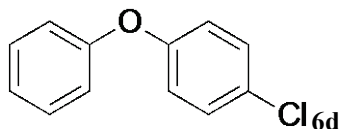
3-chlorodiphenyl ether

Colourless oil.

$^1\text{H NMR}$ (CDCl_3 , 300 MHz): δ (ppm) 7.37 (dd, $J = 8.6, 7.6$ Hz, $2\text{H}^{3',5'}$), 7.25 (dd, $J = 8.1, 8.1$ Hz, 1H^5), 7.16 (t, $J = 7.6$ Hz, $1\text{H}^{4'}$), 7.07 (ddd, $J = 8.1, 2.0, 1.0$ Hz, $1\text{H}^{4'}$), 7.05 - 6.98 (m, 3H), 6.90 (ddd, $J = 8.1, 2.4, 1.0$ Hz, 1H^6)

$^{13}\text{C NMR}$ (CDCl_3 , 75 MHz): δ (ppm) 158.32, 156.28, 135.01, 130.45, 129.91, 123.98, 123.15, 119.40, 118.75, 116.66.

GC/MS (EI, 70 eV): m/z (%) 206 ($(\text{M} + 2)^+$, 31), 204 (M^+ , 100), 169 ($(\text{M} - \text{Cl})^+$, 23), 141 ($(\text{M} - \text{COCl})^+$, 45).



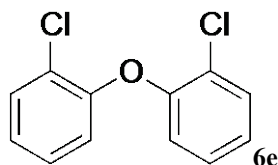
4-chlorodiphenyl ether

Colourless oil.

$^1\text{H NMR}$ (CDCl_3 , 300 MHz): δ (ppm) 7.35 (dd, $J = 8.5, 7.4$ Hz, $2\text{H}^{3',5'}$), 7.29 (dd, $J = 6.7, 2.3$ Hz, $2\text{H}^{3,5}$), 7.13 (tt, $J = 7.4, 1.1$ Hz, $1\text{H}^{4'}$), 7.01 (dd, $J = 8.5, 1.2$ Hz, $2\text{H}^{2',6'}$), 6.95 (dd, $J = 6.7, 2.3$ Hz, $2\text{H}^{2,6}$)

$^{13}\text{C NMR}$ (CDCl_3 , 75 MHz): δ (ppm) 156.84, 155.93, 129.84, 129.68, 128.17, 123.61, 120.01, 118.91.

GC/MS (EI, 70 eV): m/z (%) 206 ($(\text{M} + 2)^+$, 29), 205 (14), 204 (M^+ , 100), 169 ($(\text{M} - \text{Cl})^+$, 9), 141 ($(\text{M} - \text{COCl})^+$, 35).



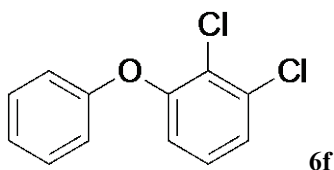
2,2'-dichlorodiphenyl ether

Colourless oil.

$^1\text{H NMR}$ (CDCl_3 , 300 MHz): δ (ppm) 7.47 (dd, $J = 7.9, 1.7$ Hz, $2\text{H}^{3',3'}$), 7.21 (ddd, $J = 8.1, 7.4, 1.7$ Hz, $2\text{H}^{5',5'}$), 7.09 (ddd, $J = 7.9, 7.4, 1.6$ Hz, $2\text{H}^{4',4'}$), 6.87 (dd, $J = 8.1, 1.6$ Hz, $2\text{H}^{6',6'}$)

$^{13}\text{C NMR}$ (CDCl_3 , 75 MHz): δ (ppm) 152.17, 130.83, 127.89, 125.11, 124.69, 119.53.

GC/MS (EI, 70 eV): m/z (%) 242 ($(\text{M} + 4)^+$, 7), 240 ($(\text{M} + 2)^+$, 45), 238 (M^+ , 72), 203 ($(\text{M} - \text{Cl})^+$, 40), 175 ($(\text{M} - \text{COCl})^+$, 8), 168 ($(\text{M} - 2\text{Cl})^+$, 100), 139 (14).



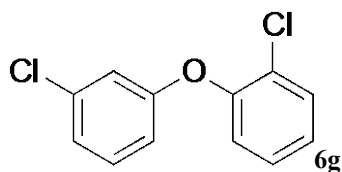
2,3-dichlorodiphenyl ether

Colourless oil.

$^1\text{H NMR}$ (CDCl_3 , 300 MHz): δ (ppm) 7.41 - 7.33 (m, $2\text{H}^{3',5'}$), 7.25 (dd, $J = 8.1, 1.4$ Hz, $1\text{H}^{4'}$), 7.19 - 7.11 (m, 2H), 6.99 (dd, $J = 7.6, 1.1$ Hz, $2\text{H}^{2',6'}$), 6.88 (dd, $J = 8.2, 1.4$ Hz, $1\text{H}^{6'}$)

$^{13}\text{C NMR}$ (CDCl_3 , 75 MHz): δ (ppm) 156.38, 154.16, 134.22, 129.88, 127.46, 125.17, 124.78, 123.85, 118.31, 118.21, 77.00.

GC/MS (EI, 70 eV): m/z (%) 242 ($(\text{M} + 4)^+$, 6), 240 ($(\text{M} + 2)^+$, 38), 238 (M^+ , 63), 205 (16), 203 ($(\text{M} - \text{Cl})^+$, 48), 175 ($(\text{M} - \text{COCl})^+$, 8), 168 ($(\text{M} - 2\text{Cl})^+$, 100), 139 (14).



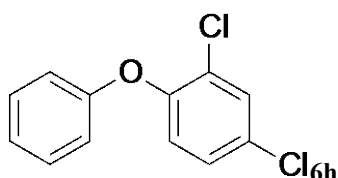
2,3'-dichlorodiphenyl ether

Colourless oil.

$^1\text{H NMR}$ (CDCl_3 , 300 MHz): δ (ppm) 7.43 (dd, $J = 7.9, 1.8$ Hz, 1H^3), 7.26 - 7.16 (m, 2H), 7.10 (ddd, $J = 7.9, 7.5, 1.6$ Hz, 1H^4), 7.05 - 6.98 (m, 2H), 6.88 (dd, $J = 2.4, 2.2$ Hz, 1H^2), 6.79 (ddd, $J = 8.2, 2.4, 1.0$ Hz, 1H^6)

$^{13}\text{C NMR}$ (CDCl_3 , 75 MHz): δ (ppm) 157.76, 151.27, 134.92, 130.81, 130.39, 128.04, 126.16, 125.45, 123.11, 121.53, 117.55, 115.45.

GC/MS (EI, 70 eV): m/z (%) 242 ($(\text{M} + 4)^+$, 6), 240 ($(\text{M} + 2)^+$, 35), 238 (M^+ , 61), 205 (16), 203 ($(\text{M} - \text{Cl})^+$, 54), 175 ($(\text{M} - \text{COCl})^+$, 10), 168 ($(\text{M} - 2\text{Cl})^+$, 100), 139 (14).



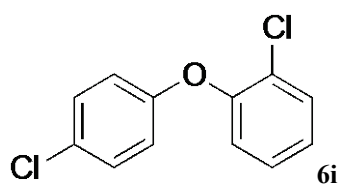
2,4-dichlorodiphenyl ether

Yellow oil.

$^1\text{H NMR}$ (CDCl_3 , 300 MHz): δ (ppm) 7.47 (d, $J = 2.5$ Hz, 1H^3), 7.35 (dd, $J = 8.7, 7.4$ Hz, $2\text{H}^{3',5'}$), 7.19 (dd, $J = 8.8, 2.5$ Hz, 1H^5), 7.13 (tt, $J = 7.4, 1.1$ Hz, 1H^4), 6.99 - 6.93 (m, $2\text{H}^{2',6'}$), 6.91 (d, $J = 8.8$ Hz, 1H^6)

$^{13}\text{C NMR}$ (CDCl_3 , 75 MHz): δ (ppm) 156.55, 151.38, 130.42, 129.86, 129.06, 127.98, 126.55, 123.67, 121.30, 117.97.

GC/MS (EI, 70 eV): m/z (%) 242 ($(\text{M} + 4)^+$, 9), 240 ($(\text{M} + 2)^+$, 58), 238 (M^+ , 98), 205 (17), 203 ($(\text{M} - \text{Cl})^+$, 50), 175 ($(\text{M} - \text{COCl})^+$, 18), 168 ($(\text{M} - 2\text{Cl})^+$, 100), 139 (13).



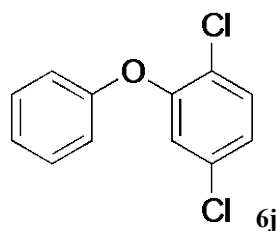
2,4'-dichlorodiphenyl ether

Yellow oil.

$^1\text{H NMR}$ (CDCl_3 , 300 MHz): δ (ppm) 7.47 (dd, $J = 8.0, 1.6$ Hz, 1H^3), 7.29 (dd, $J = 6.9, 2.3$ Hz, $2\text{H}^{3',5'}$), 7.25 (ddd, $J = 8.1, 7.4, 1.6$ Hz, 1H^5), 7.12 (ddd, $J = 8.0, 7.4, 1.6$ Hz, 1H^4), 7.00 (dd, $J = 8.1, 1.6$ Hz, 1H^6), 6.89 (dd, $J = 6.9, 2.3$ Hz, $2\text{H}^{2',6'}$)

$^{13}\text{C NMR}$ (CDCl_3 , 75 MHz): δ (ppm) 155.66, 151.98, 130.91, 129.71, 128.25, 128.05, 126.05, 125.17, 121.07, 118.92.

GC/MS (EI, 70 eV): m/z (%) 242 ($(\text{M} + 4)^+$, 9), 240 ($(\text{M} + 2)^+$, 58), 238 (M^+ , 94), 203 ($(\text{M} - \text{Cl})^+$, 36), 175 ($(\text{M} - \text{COCl})^+$, 13), 168 ($(\text{M} - 2\text{Cl})^+$, 100), 139 (15).



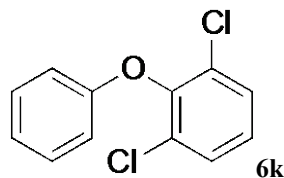
2,5-dichlorodiphenyl ether

Colourless oil.

$^1\text{H NMR}$ (CDCl_3 , 300 MHz): δ (ppm) 7.42 - 7.34 (m, 3H), 7.17 (tt, $J = 7.5, 1.1$ Hz, 1H^d), 7.05 (dd, $J = 8.6, 2.4$ Hz, 1H^f), 7.01 (dd, $J = 8.7, 1.1$ Hz, $2\text{H}^{2',5'}$), 6.93 (d, $J = 2.4$ Hz, 1H^g)

$^{13}\text{C NMR}$ (CDCl_3 , 75 MHz): δ (ppm) 155.98, 153.43, 133.09, 131.27, 130.00, 124.33, 124.18, 123.77, 120.08, 118.63.

GC/MS (EI, 70 eV): m/z (%) 242 ((M + 4) $^+$, 7), 240 ((M + 2) $^+$, 43), 238 (M $^+$, 70), 205 (18), 203 ((M - Cl) $^+$, 55), 175 ((M - COCl) $^+$, 8), 168 ((M - 2Cl) $^+$, 100), 139 (13).



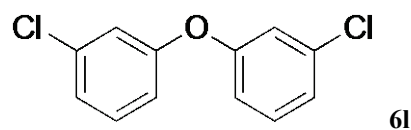
2,6-dichlorodiphenyl ether

White solid, Mp: 38 °C.

$^1\text{H NMR}$ (CDCl_3 , 300 MHz): δ (ppm) 7.43 (d, $J = 8.2$ Hz, $2\text{H}^{3,5}$), 7.35 (dd, $J = 8.6, 7.5$ Hz, $2\text{H}^{3',5'}$), 7.16 (t, $J = 8.2$ Hz, 1H^d), 7.10 (tt, $J = 7.5, 1.1$ Hz, 1H^f), 6.90 (dd, $J = 8.7, 1.1$ Hz, $2\text{H}^{2',6'}$)

$^{13}\text{C NMR}$ (CDCl_3 , 75 MHz): δ (ppm) 156.70, 147.12, 129.98, 129.58, 129.11, 126.28, 122.48, 114.90.

GC/MS (EI, 70 eV): m/z (%) 242 ((M + 4) $^+$, 8), 240 ((M + 2) $^+$, 46), 238 (M $^+$, 80), 205 (20), 203 ((M - Cl) $^+$, 61), 175 ((M - COCl) $^+$, 10), 168 ((M - 2Cl) $^+$, 100), 139 (12).

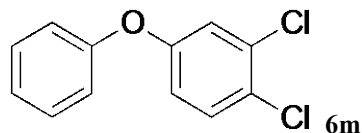


3,3'-dichlorodiphenyl ether

$^1\text{H NMR}$ (CDCl_3 , 300 MHz): δ (ppm) 7.28 (dd, $J = 8.1, 8.1$ Hz, $2\text{H}^{5,5'}$), 7.12 (ddd, $J = 8.1, 2.2, 1.0$ Hz, $2\text{H}^{4,4'}$), 7.01 (dd, $J = 2.2, 2.2$ Hz, $2\text{H}^{2,2'}$), 6.90 (ddd, $J = 8.1, 2.2, 1.0$ Hz, $2\text{H}^{6,6'}$)

$^{13}\text{C NMR}$ (CDCl_3): δ (ppm) 157.36, 135.20, 130.65, 123.98, 119.38, 117.18.

GC/MS (EI, 70 eV): m/z (%) 242 ((M + 4) $^+$, 10), 240 ((M + 2) $^+$, 58), 238 (M $^+$, 100), 221 (18), 203 ((M - Cl) $^+$, 7), 175 ((M - COCl) $^+$, 41), 168 ((M - 2Cl) $^+$, 25).



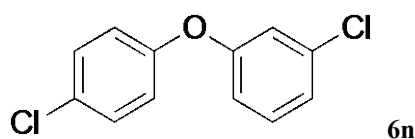
3,4-dichlorodiphenyl ether

Colourless oil.

$^1\text{H NMR}$ (CDCl_3 , 300 MHz): δ (ppm) 7.42 - 7.33 (m, 3H), 7.17 (tt, $J = 7.4, 1.1$ Hz, 1H^d), 7.08 (d, $J = 2.8$ Hz, 1H^2), 7.02 (dd, $J = 8.7, 1.1$ Hz, $2\text{H}^{2':6'}$), 6.85 (dd, $J = 8.8, 2.8$ Hz, 1H^6)

$^{13}\text{C NMR}$ (CDCl_3 , 75 MHz): δ (ppm) 156.63, 156.00, 133.12, 130.93, 130.00, 126.32, 124.27, 120.18, 119.36, 117.87.

GC/MS (EI, 70 eV): m/z (%) 242 ((M + 4)⁺, 9), 240 ((M + 2)⁺, 56), 238 (M⁺, 100), 175 ((M - COCl)⁺, 29), 168 ((M - 2Cl)⁺, 18), 139 (9).



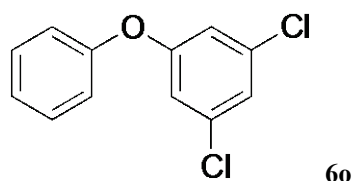
3,4'-dichlorodiphenyl ether

Yellow oil.

$^1\text{H NMR}$ (CDCl_3 , 300 MHz): δ (ppm) 7.32 (d, $J = 8.6$ Hz, $2\text{H}^{3':5'}$), 7.26 (dd, $J = 8.2, 8.1$ Hz, 1H^5), 7.09 (dddd, $J = 8.1, 2.1, 1.0, 0.4$ Hz, 1H^4), 7.00 - 6.93 (m, 3H), 6.88 (dddd, $J = 8.2, 2.4, 1.0, 0.4$ Hz, 1H^6)

$^{13}\text{C NMR}$ (CDCl_3 , 75 MHz): δ (ppm) 157.89, 154.97, 135.15, 130.57, 129.91, 129.05, 123.58, 120.56, 118.84, 116.69.

GC/MS (EI, 70 eV): m/z (%) 242 ((M + 4)⁺, 10), 240 ((M + 2)⁺, 60), 238 (M⁺, 100), 177 (12), 175 ((M - COCl)⁺, 41), 168 ((M - 2Cl)⁺, 17).



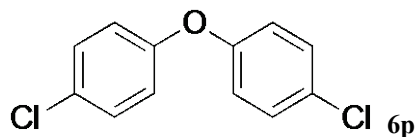
3,5-dichlorodiphenyl ether

Colourless oil.

$^1\text{H NMR}$ (CDCl_3 , 300 MHz): δ (ppm) 7.40 (dd, $J = 8.6, 7.5$ Hz, $2\text{H}^{3':5'}$), 7.21 (tt, $J = 7.5, 1.1$ Hz, 1H^d), 7.08 (t, $J = 1.8$ Hz, 1H^4), 7.05 (dd, $J = 8.6, 1.1$ Hz, $2\text{H}^{2':6'}$), 6.88 (d, $J = 1.8$ Hz, $2\text{H}^{2,6}$)

$^{13}\text{C NMR}$ (CDCl_3 , 75 MHz): δ (ppm) 158.96, 155.39, 135.55, 130.10, 124.70, 123.00, 119.85, 116.75.

GC/MS (EI, 70 eV): m/z (%) 242 ((M + 4)⁺, 11), 240 ((M + 2)⁺, 64), 238 (M⁺, 100), 203 ((M - Cl)⁺, 11), 175 ((M - COCl)⁺, 44), 168 ((M - 2Cl)⁺, 29), 139 (12).



4,4'-dichlorodiphenyl ether

Colourless oil.

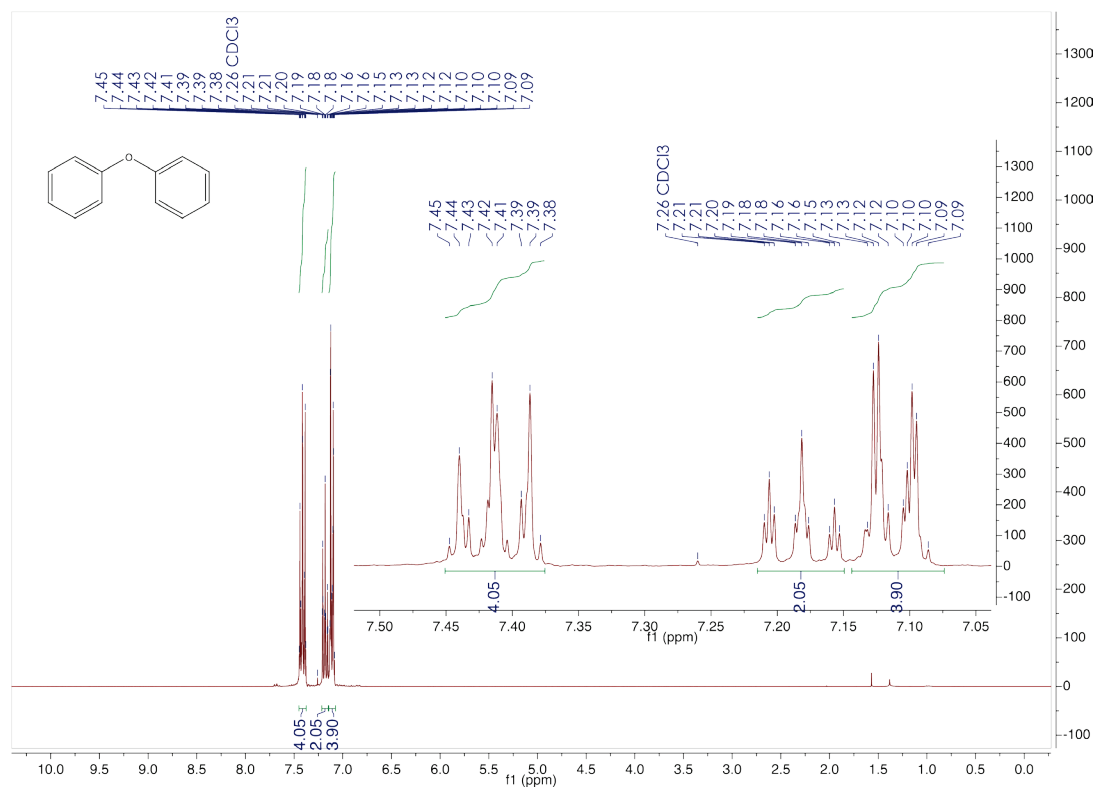
$^1\text{H NMR}$ (CDCl_3 , 300 MHz): δ (ppm) 7.30 (ddd, $J = 8.9, 3.3, 2.2$ Hz, $4\text{H}^{3,3';5,5'}$), 6.93 (ddd, $J = 8.9, 3.3, 2.2$ Hz, $4\text{H}^{2,2';6,6'}$)

$^{13}\text{C NMR}$ (CDCl_3 , 75 MHz): δ (ppm) 155.53, 129.82, 128.64, 120.06.

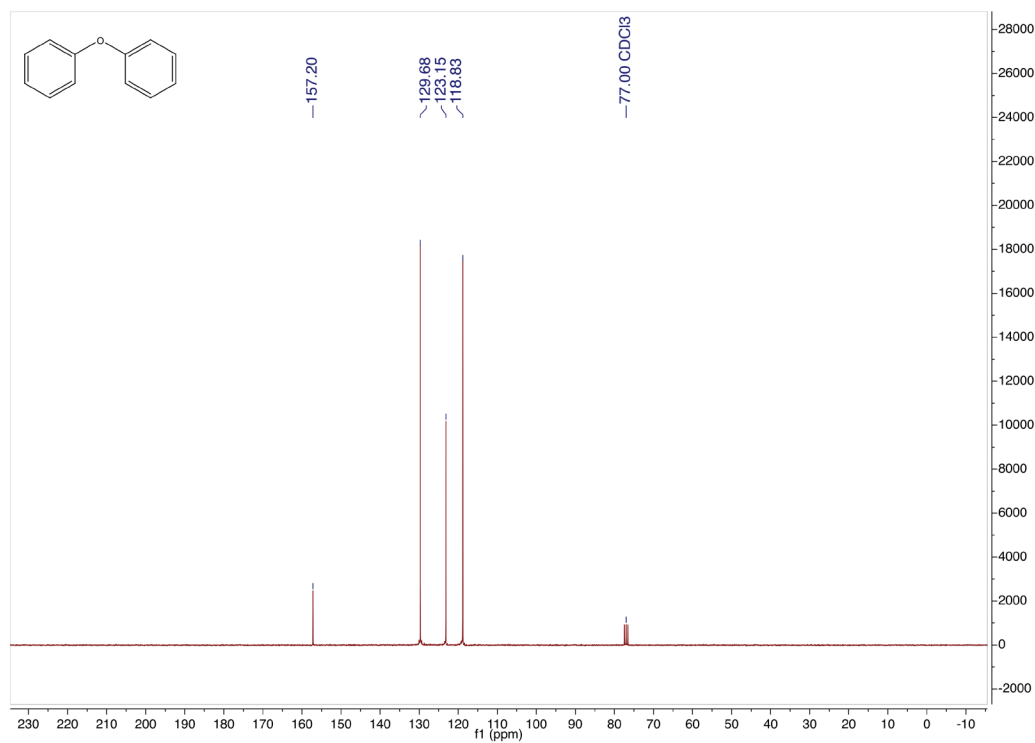
GC/MS (EI, 70 eV): m/z (%) 242 ($(\text{M} + 4)^+$, 9), 240 ($(\text{M} + 2)^+$, 59), 238 (M^+ , 100), 203 ($(\text{M} - \text{Cl})^+$, 2), 177 (9), 175 ($(\text{M} - \text{COCl})^+$, 30), 168 ($(\text{M} - 2\text{Cl})^+$, 13).

(D) NMR spectra

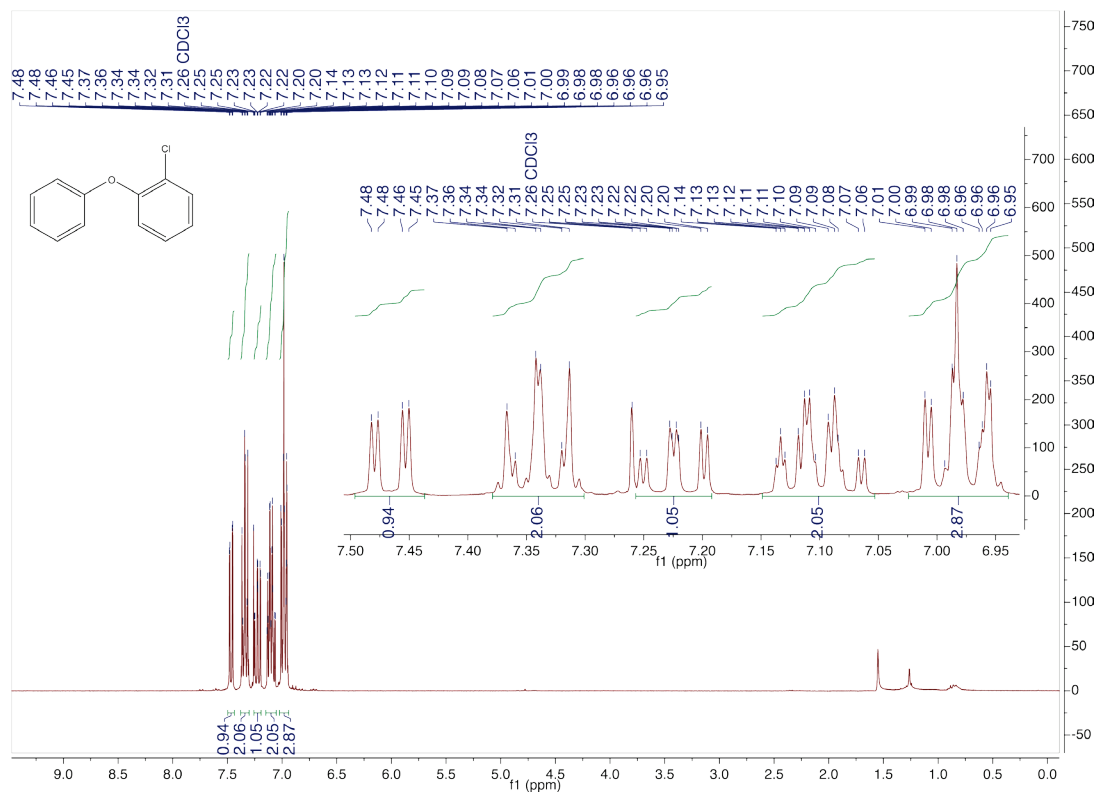
6a



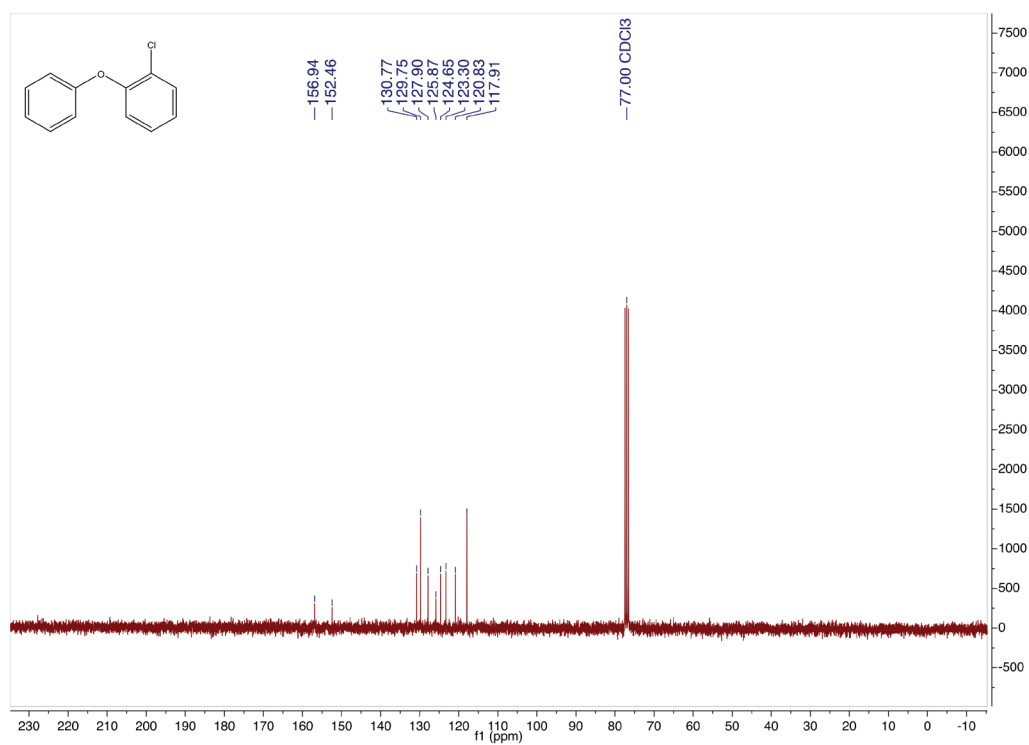
6a



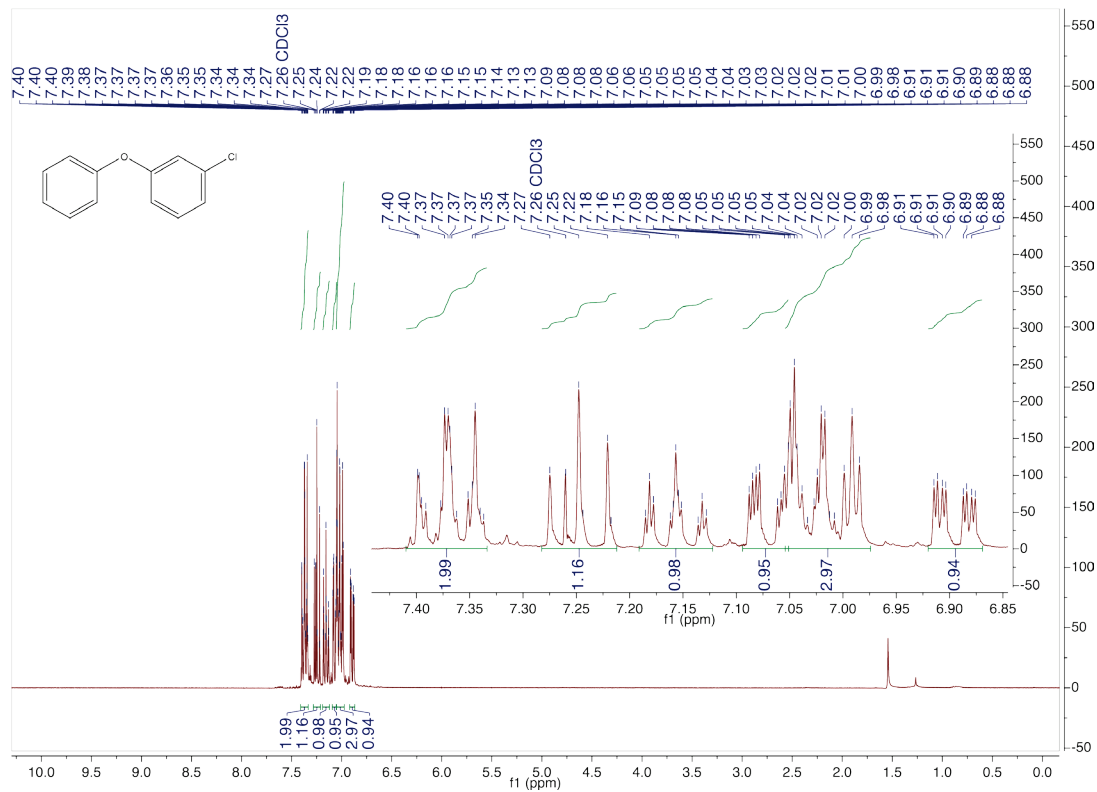
6b



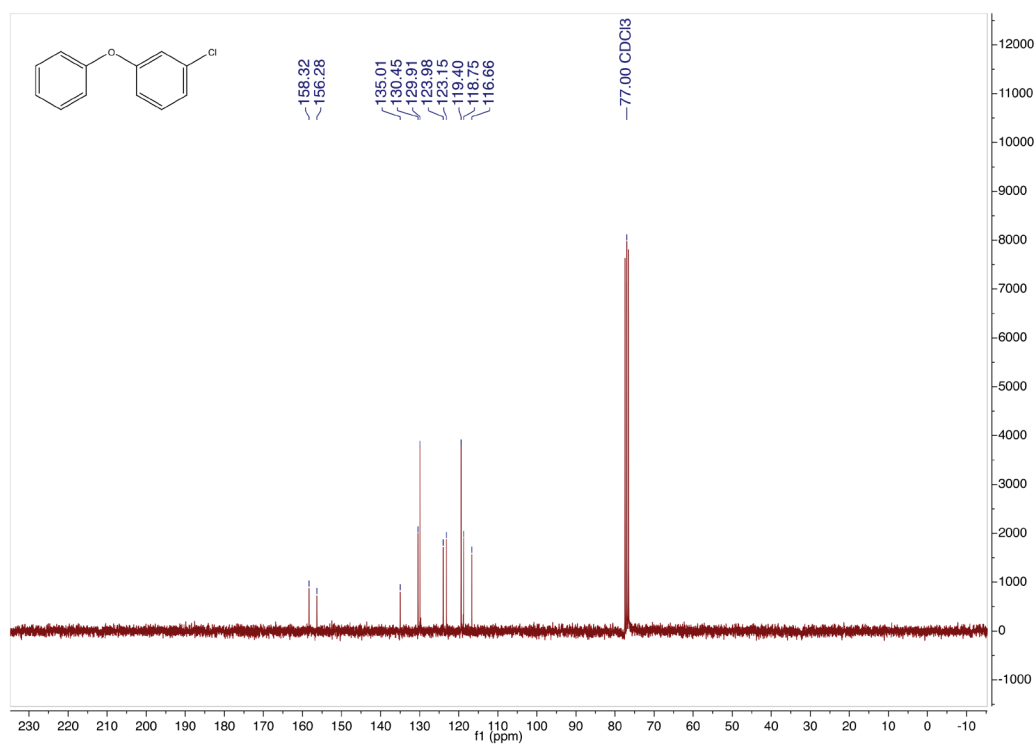
6b



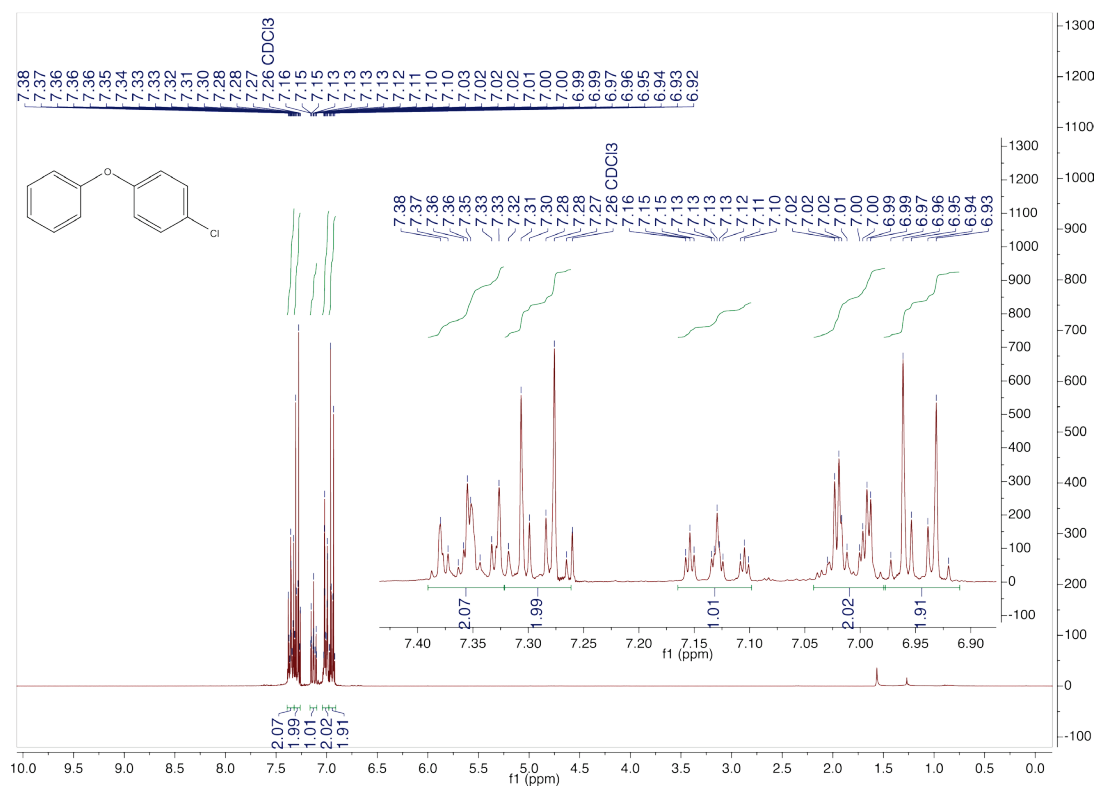
6c



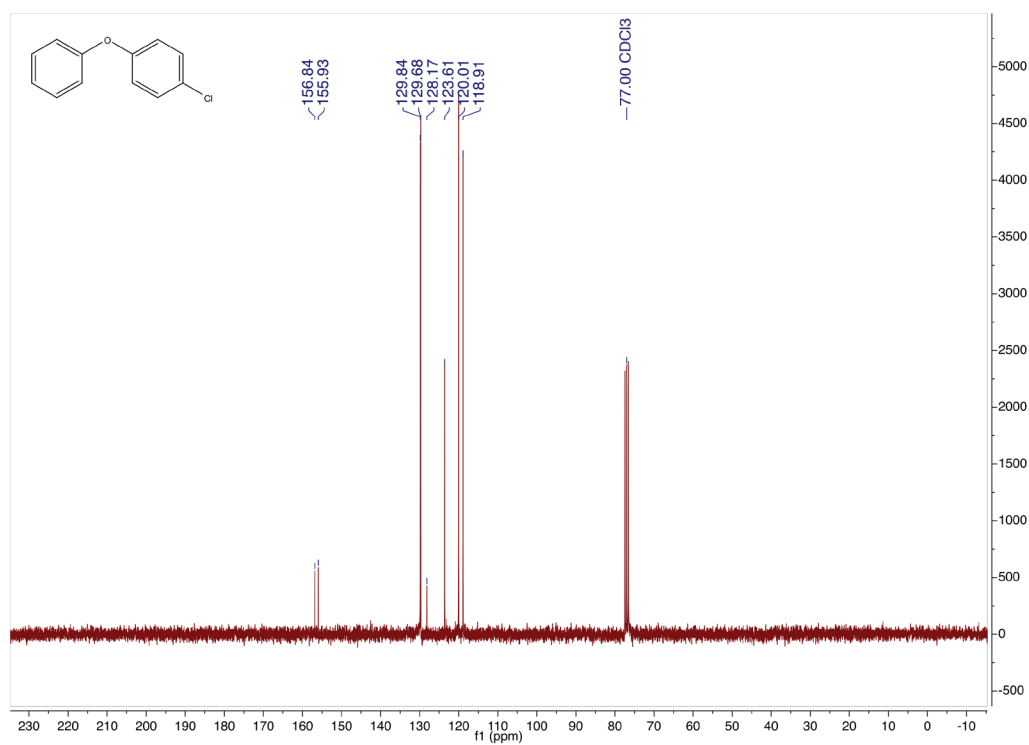
6c



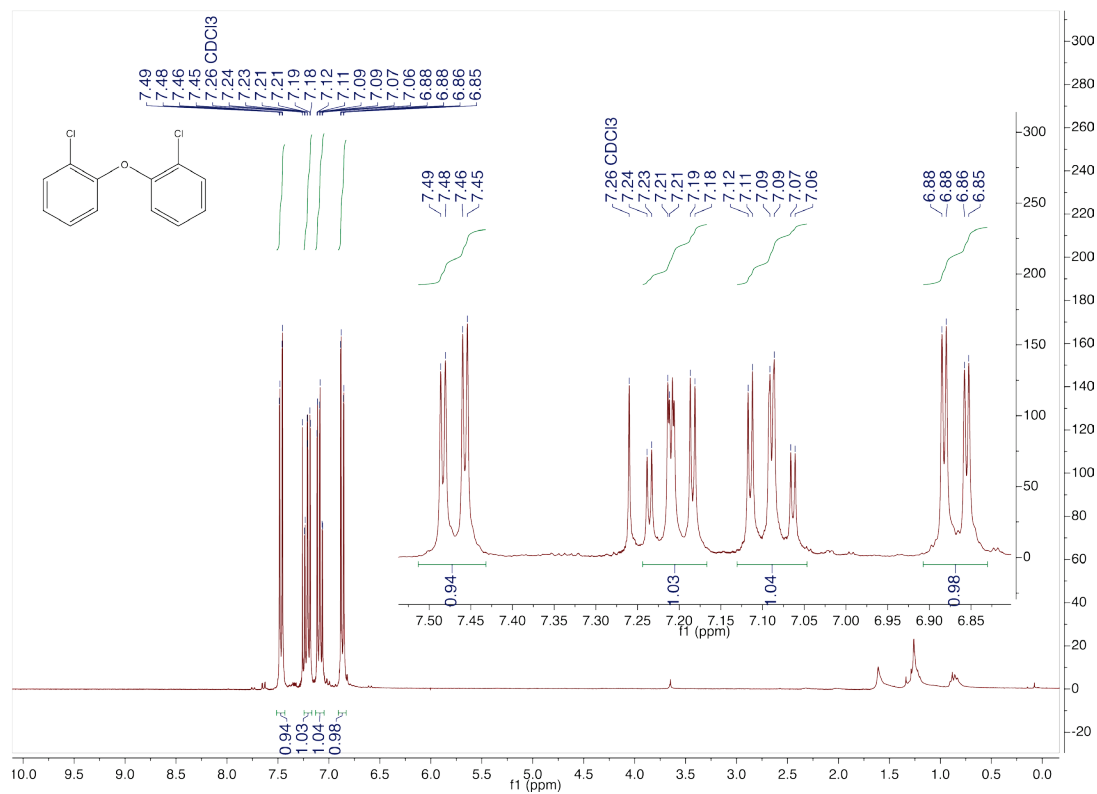
6d



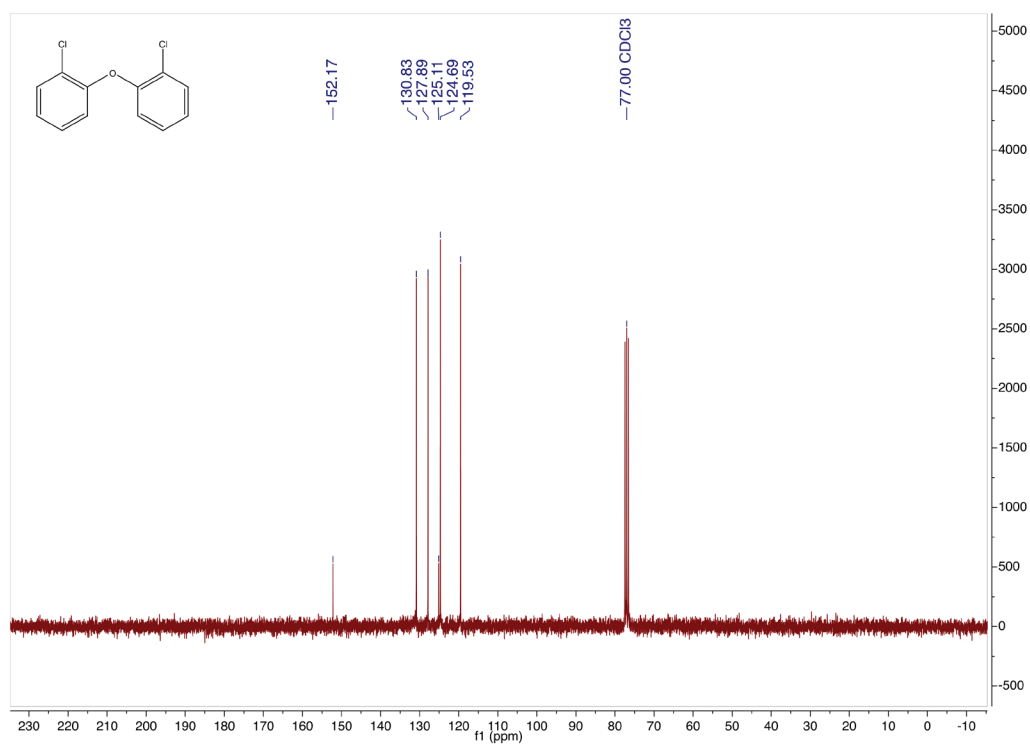
6d



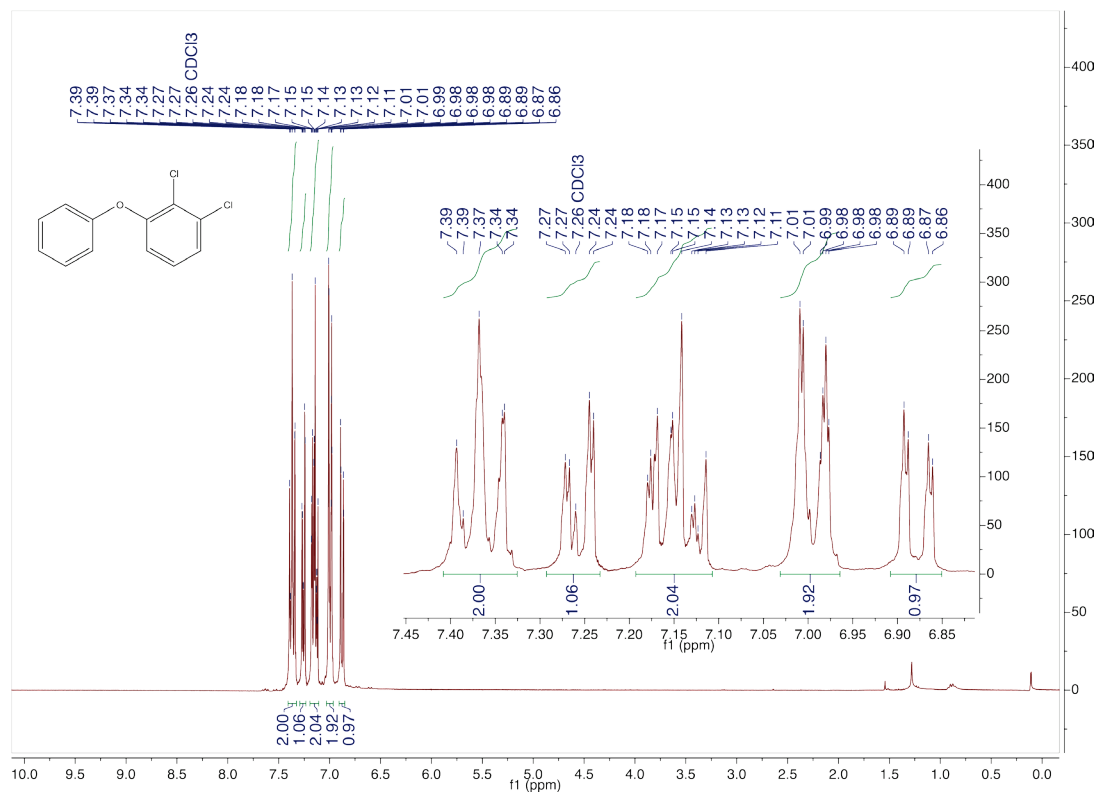
6e



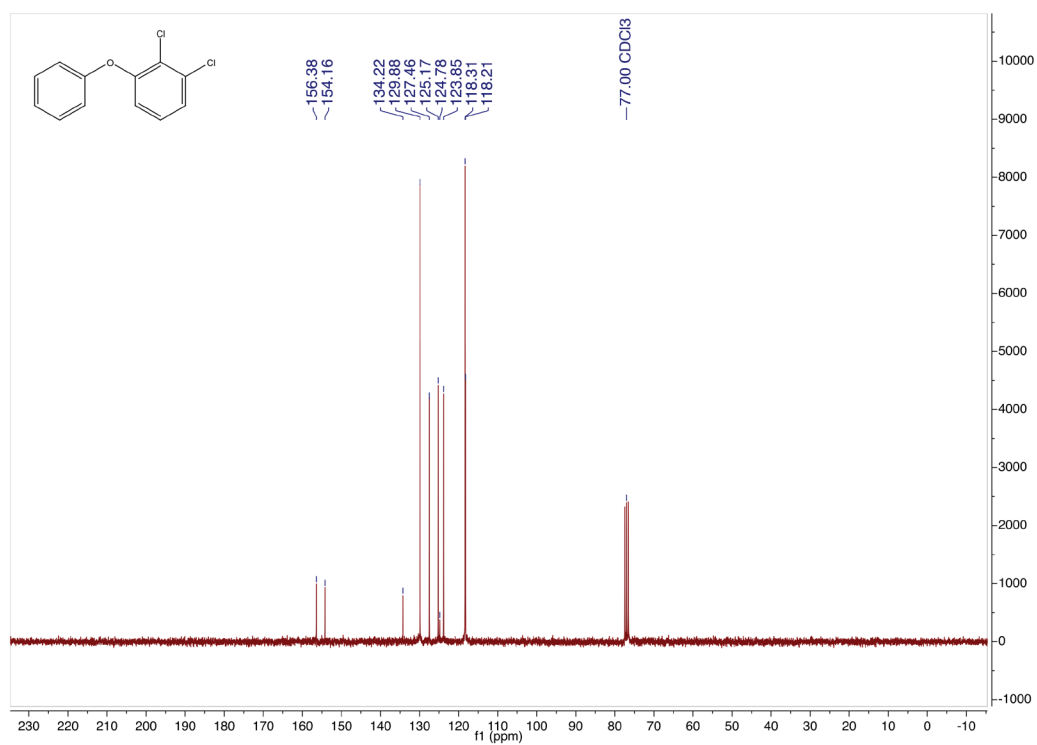
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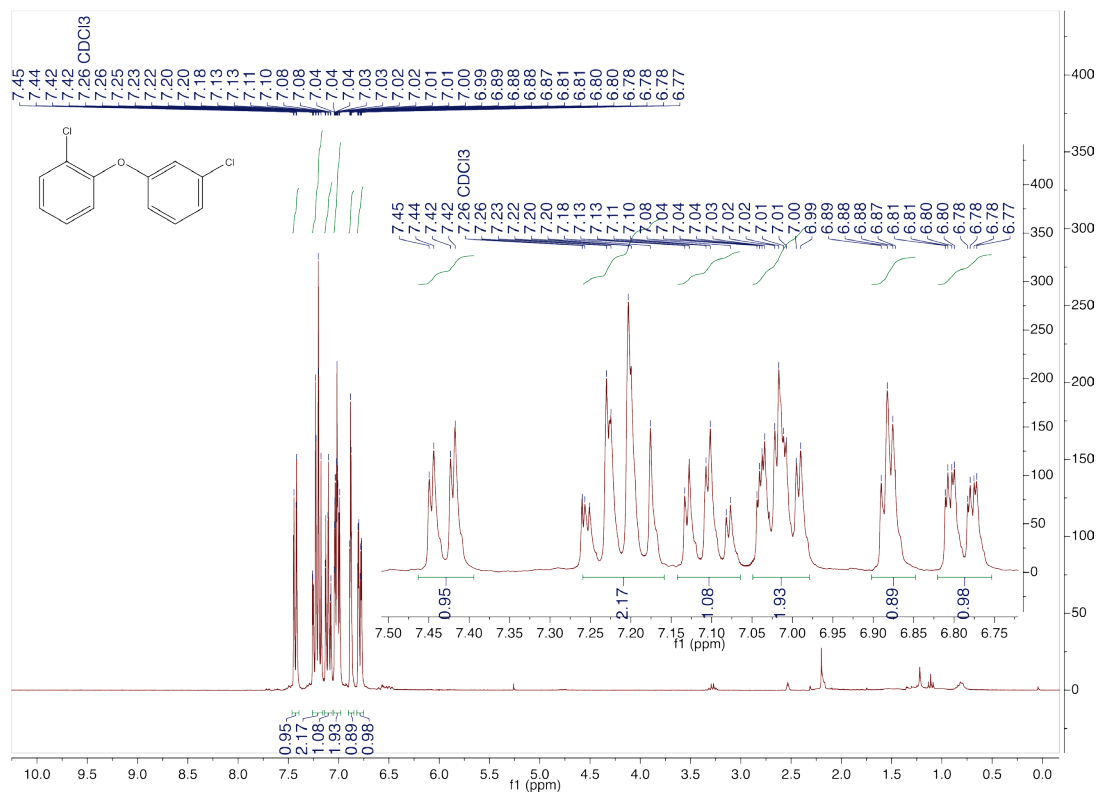
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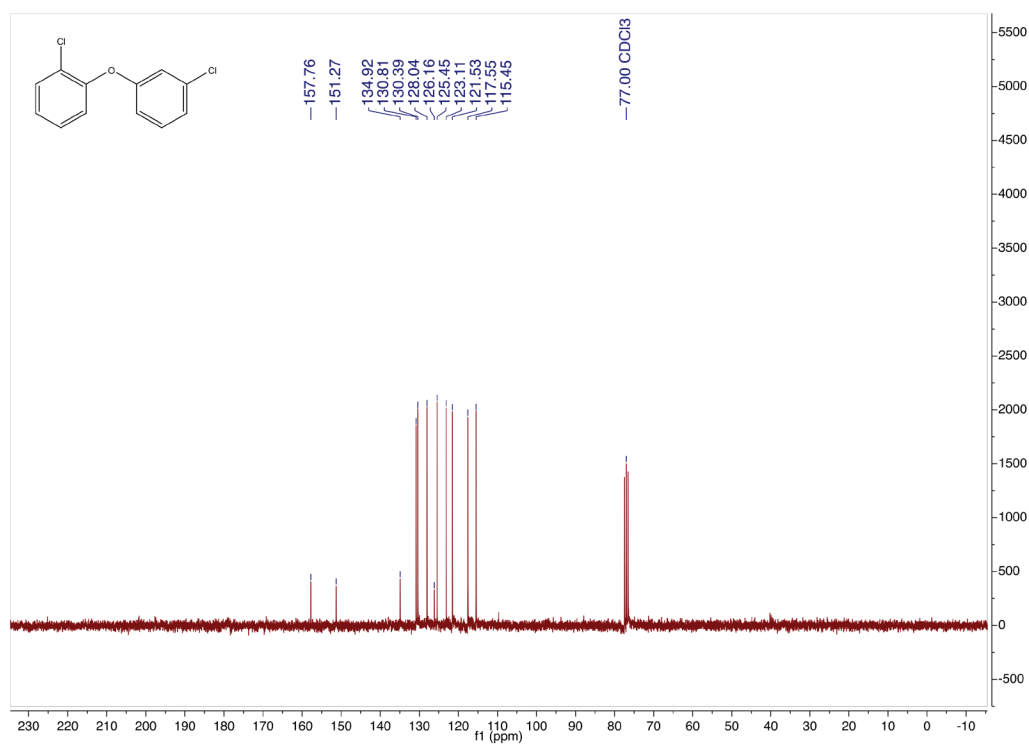
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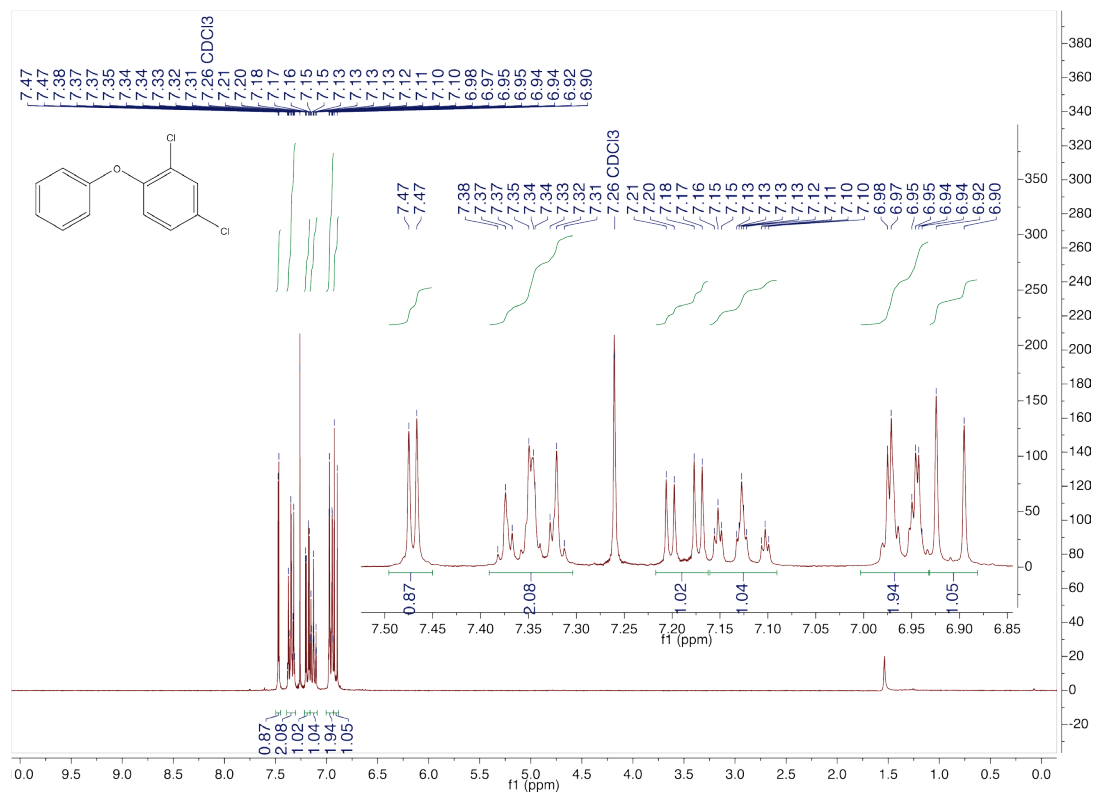
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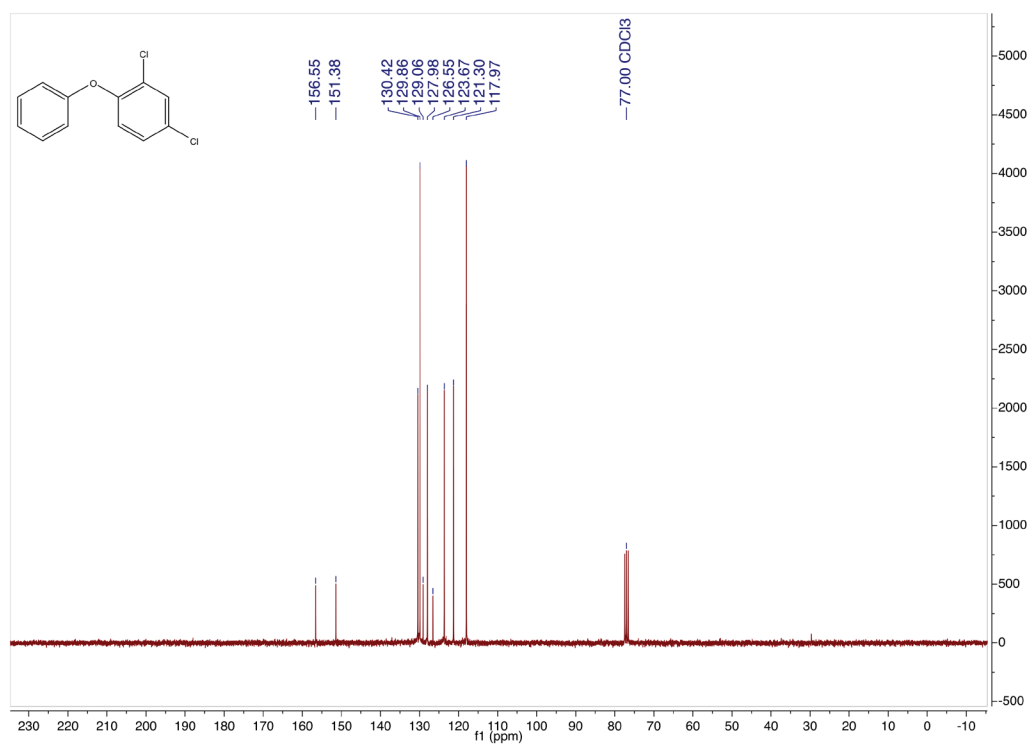
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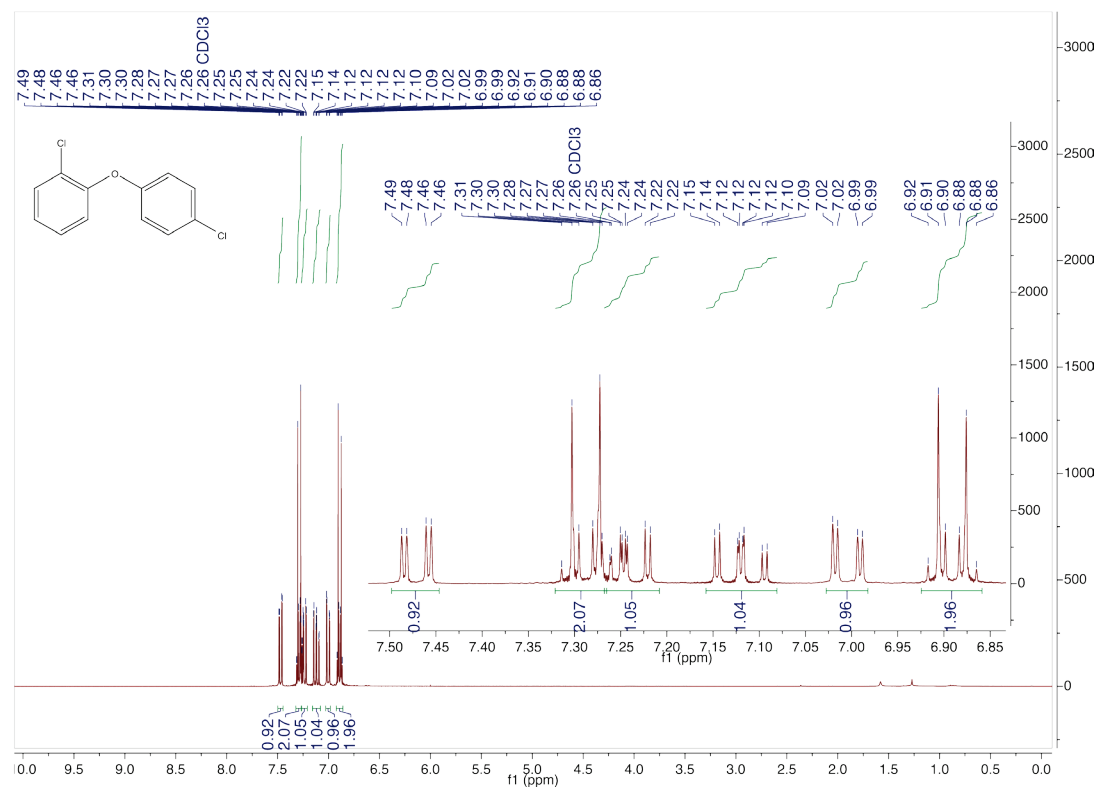
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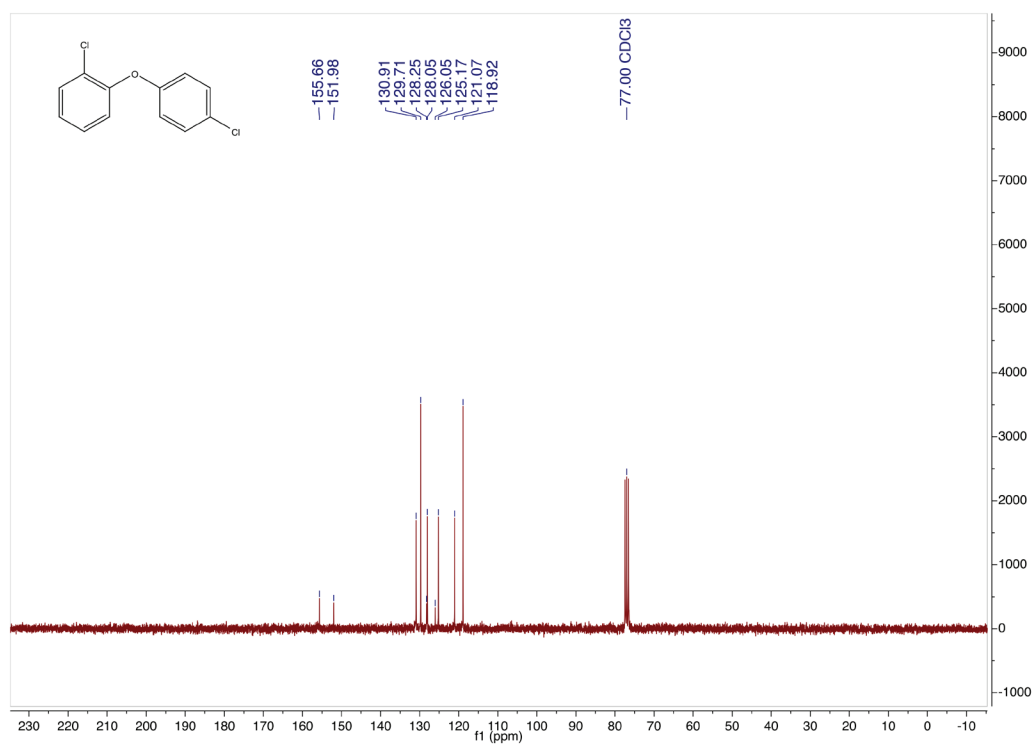
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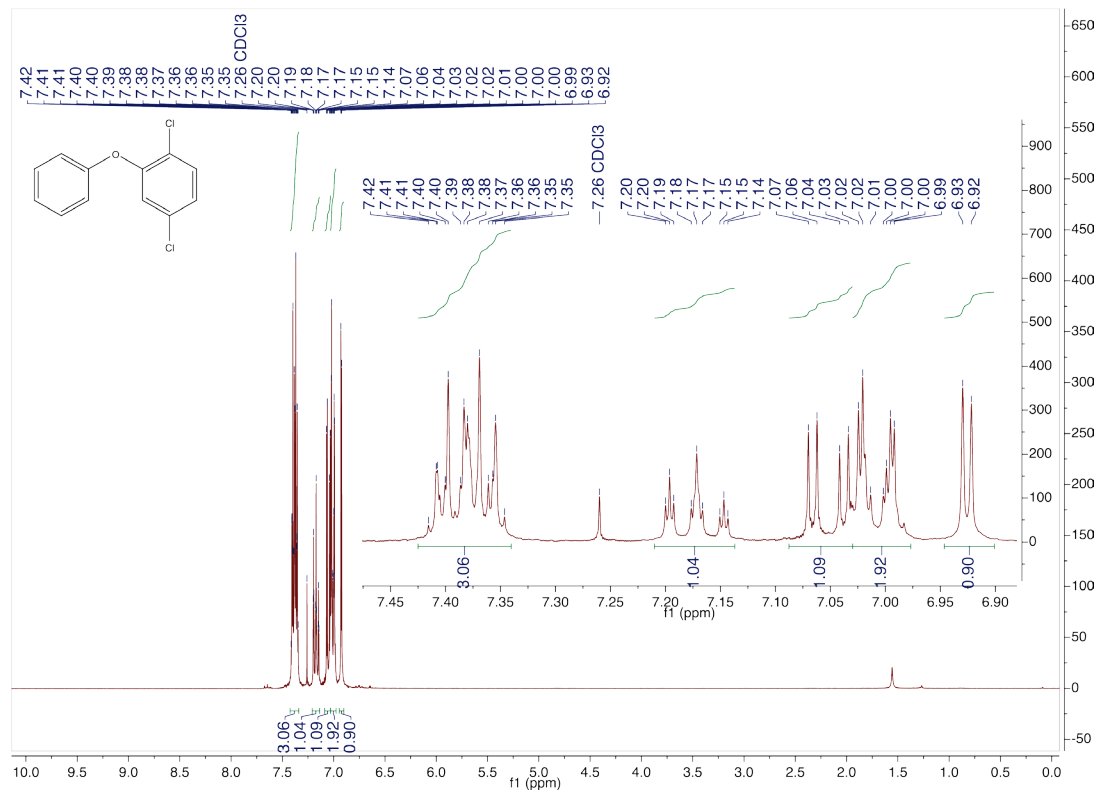
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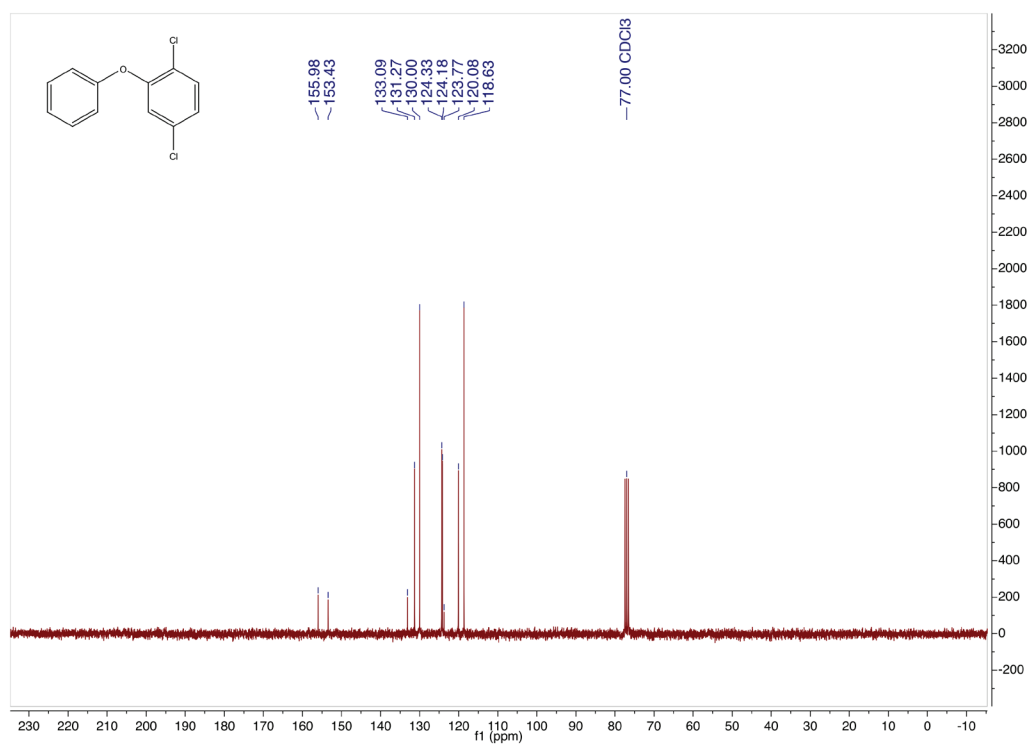
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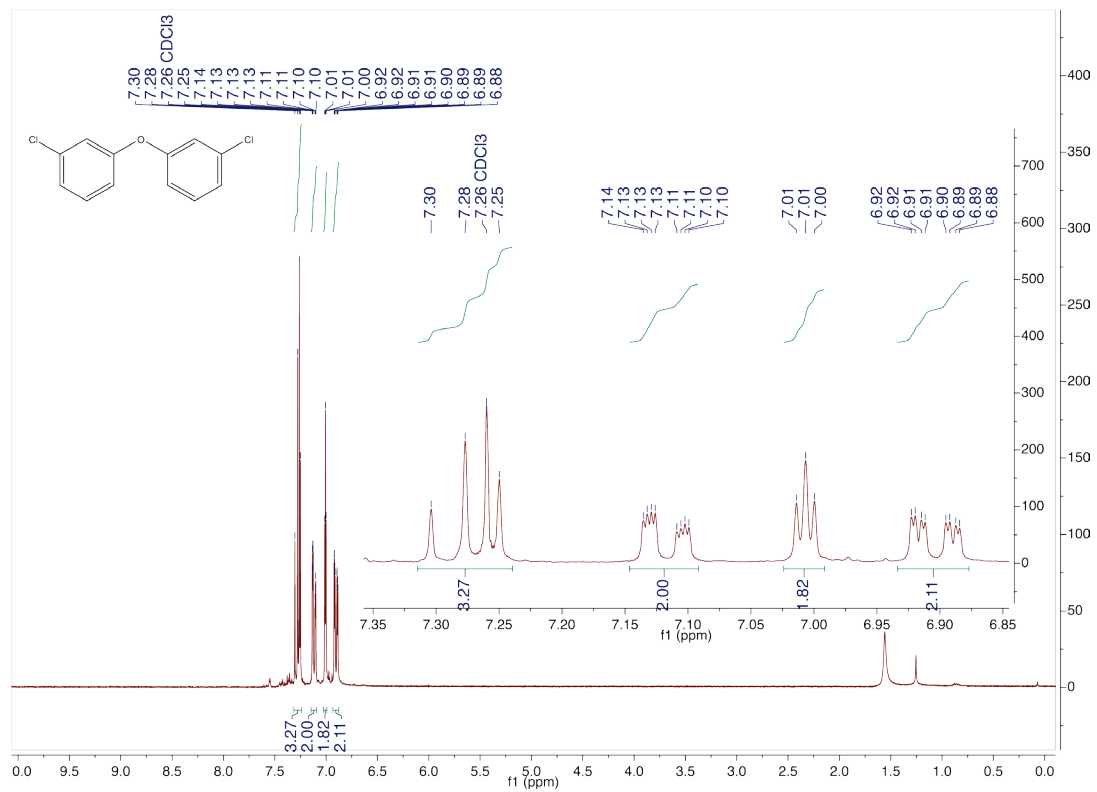
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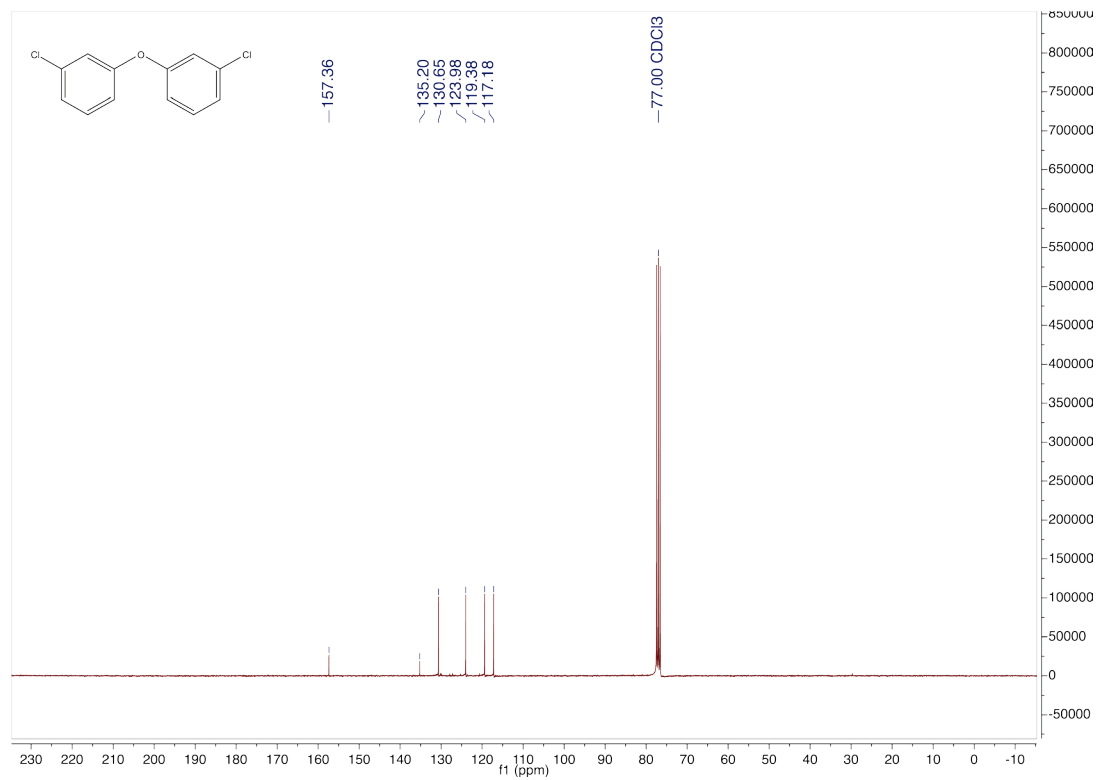
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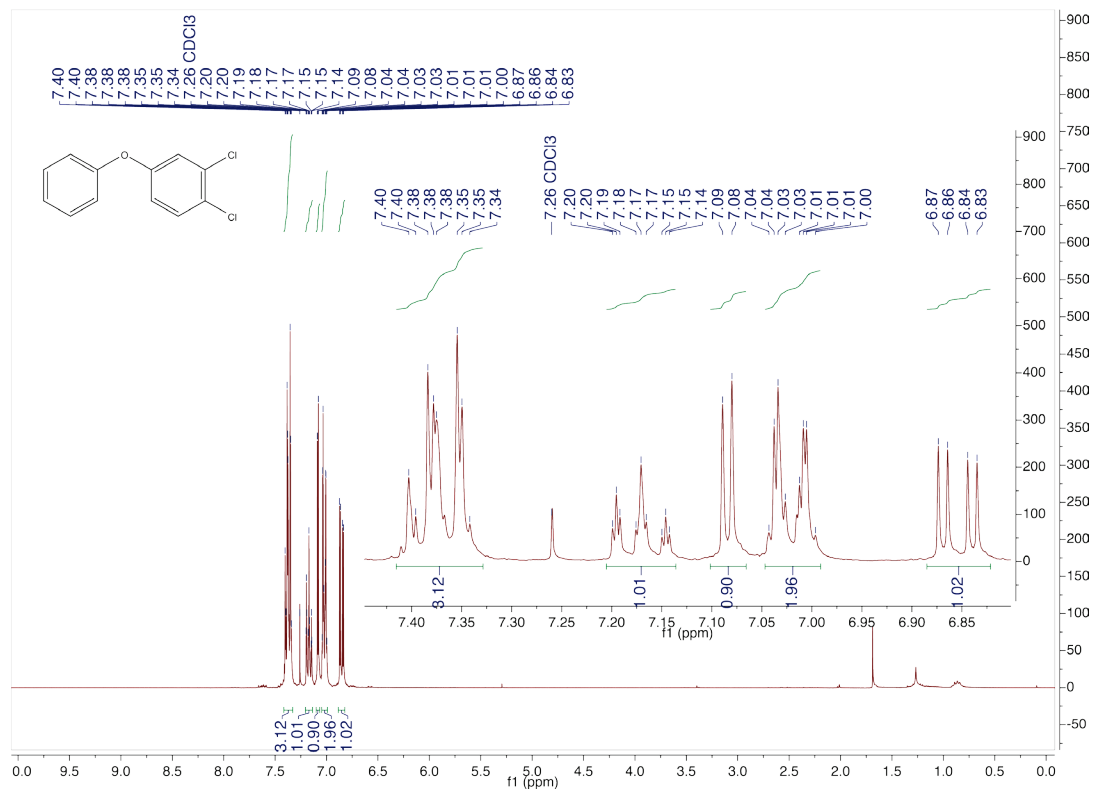
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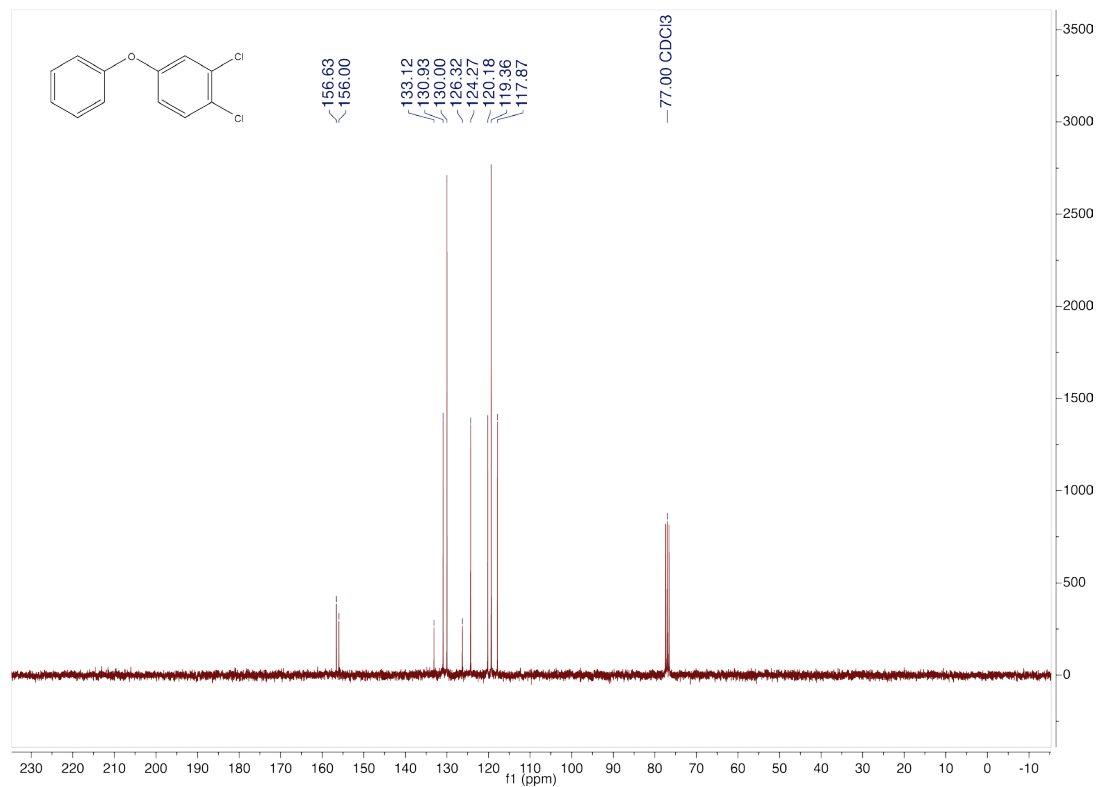
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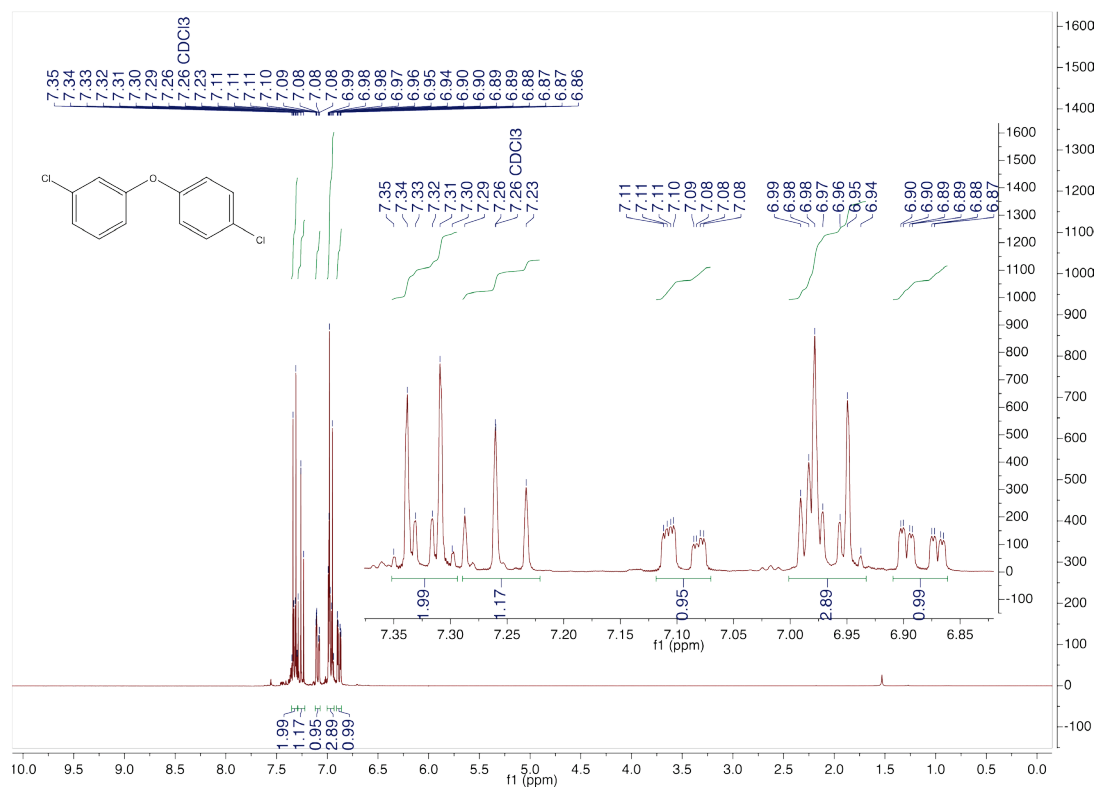
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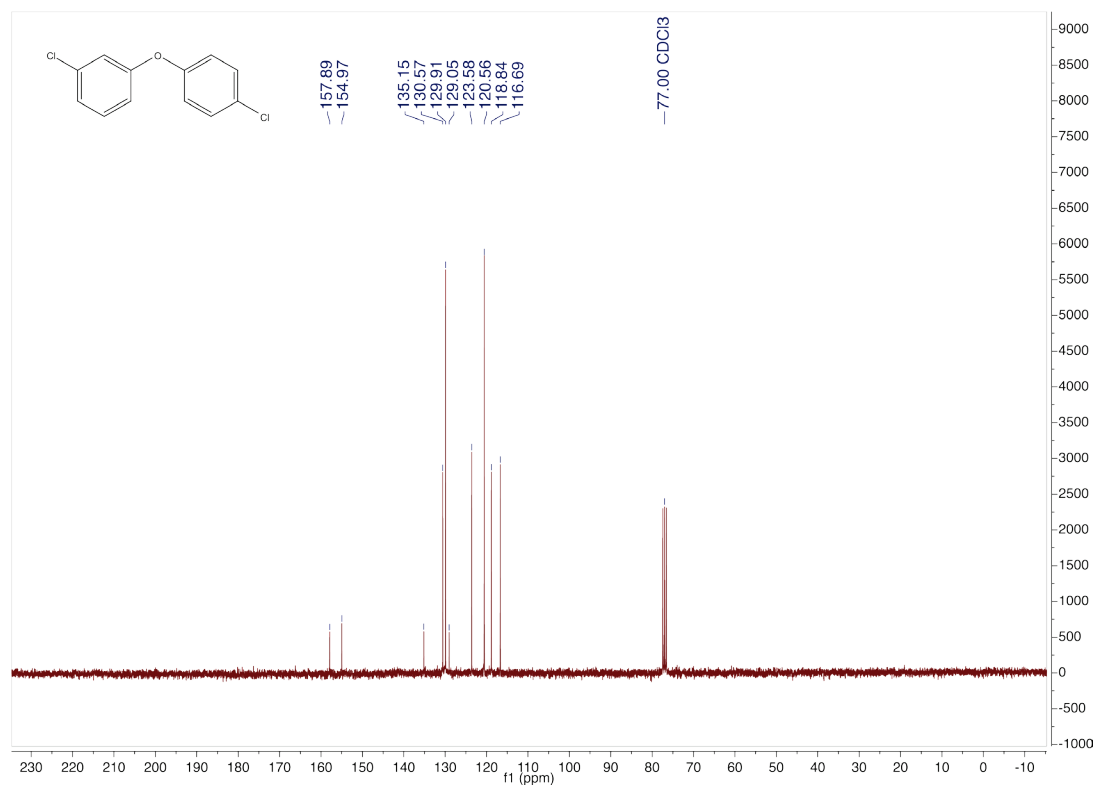
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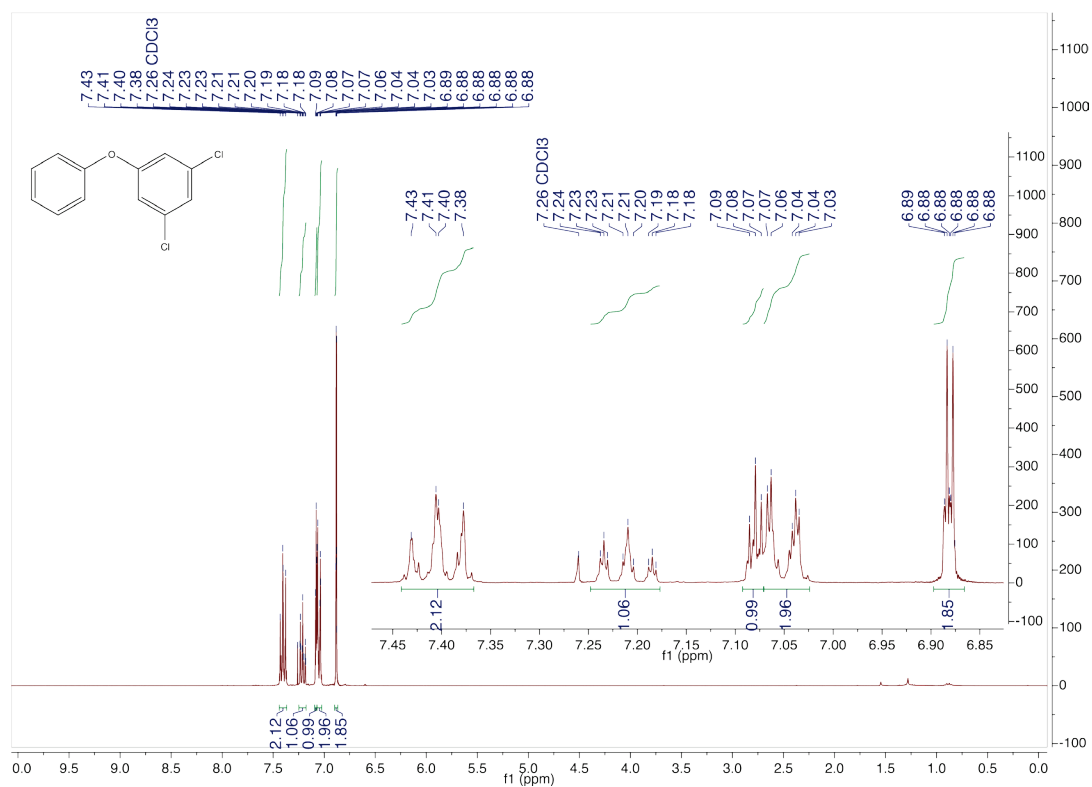
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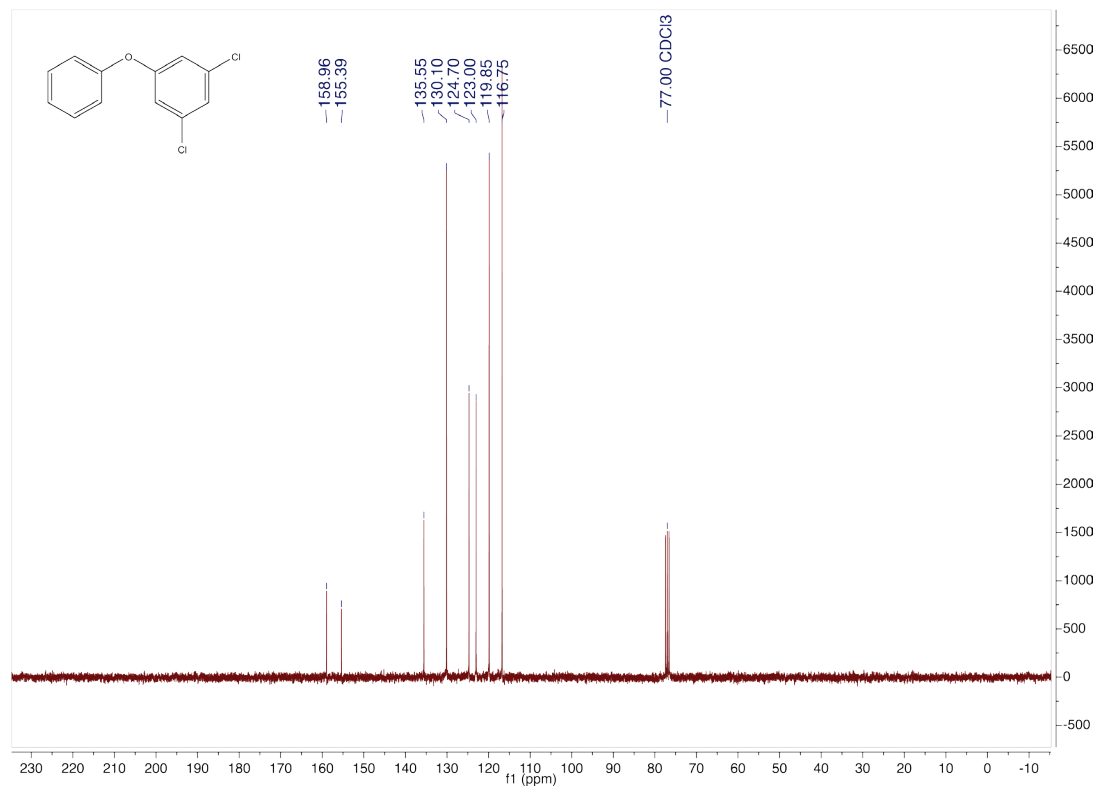
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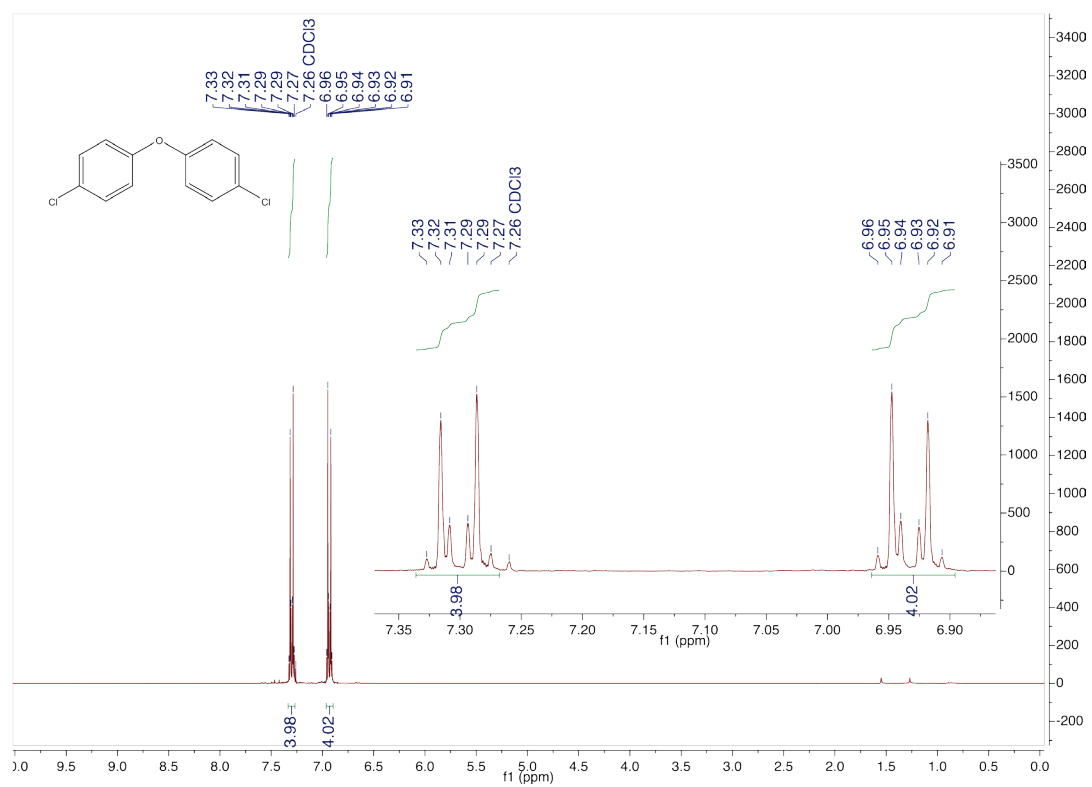
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60



6p



6p

