Chlorination Increases the Persistence of Semiquinone Free Radicals Derived from Polychlorinated Biphenyl Hydroquinones and Quinones

Supporting Information

Yang Song,[†,§] *Garry R. Buettner,*[§,||] *Sean Parkin,*[‡] *Brett A. Wagner,*[§] *Larry W. Robertson,*[†,||]

and Hans-Joachim Lehmler[*,†,||]

[†]The University of Iowa, Department of Occupational and Environmental Health, 100 Oakdale Campus, 124 IREH, Iowa City, IA 52242-5000, USA; [§]The University of Iowa, Free Radical and Radiation Biology Program & ESR Facility, Iowa City, IA 52242-1101, USA; [||]The University of Iowa, Interdisciplinary Graduate Program in Human Toxicology, Iowa City, IA 52242-5000, USA; and [‡]University of Kentucky, Department of Chemistry, Lexington, KY 40506-0055, USA

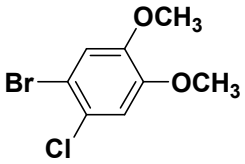
Table of Content

General Experimental Methods

All chemicals were purchased from commercial suppliers and used without further purification. Column chromatography was carried out on silica gel (100-200 mesh, FisherChemical). ^{1}H NMR spectra were recorded at 400 MHz at ambient temperature with $CDCl_3$ as solvents. ^{13}C NMR spectra were recorded at 100 MHz at ambient temperature with $CDCl_3$ as solvents. Chemical shifts are reported in parts per million relative to $CDCl_3$ (^{1}H, δ7.27; ^{13}C, δ 77.23). 4'-Chloro-biphenyl-2,5-diol (**28**), 2-(4-chloro-phenyl)-[1,4]benzoquinone (**29**) and 4'-chloro-biphenyl-3,4-diol (**30**) were synthesized as published before.[1,2] All dihydroxylated PCBs were silylated with BSTFA containing 1% TMCS for GC-MS analysis.[3]

Synthesis and Characterization

1-Bromo-2-chloro-4,5-dimethoxy-benzene (3): Hydrogen peroxide (30%, 30 mL, 290 mmol) was added over 1 h to a rapidly stirred solution of 1-bromo-3,4-dimethoxy-benzene **1** (15.2 g, 70 mmol) in $CHCl_3$ (50 mL) and concentrated HCl (47 mL, 560 mmol). After 16 h at room temperature, the mixture was extracted with $CHCl_3$ (3 × 60 mL). The organic extracts were combined, washed with 5% $NaHSO_3$ (50 mL), dried over Na_2SO_4, filtered, and the solvent was evaporated under reduced pressure. The product was purified by column chromatography on silica gel with *n*-hexanes : $CHCl_3$ = 1 : 1 (v/v), yield 12.5 g (71%) of **3** as white crystals. mp 75-77 °C (Lit.: 110-112 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.01(s, 1H), 6.90(s, 1H), 3.83(s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.9, 148.4, 125.6, 115.8, 112.9, 112.3, 56.4, 56.3; MS *m/z* (relative intensity): 250(70, $M^{\bullet+}$), 235(34), 128(70); Anal. Calcd for $C_8H_8BrClO_2$: C, 38.18; H, 3.21. Found: C, 38.31; H, 3.10.



1-Chloro-2-iodo-4,5-dimethoxy-benzene (4): Hydrogen peroxide (30%, 15 mL, 145 mmol) was added over 1 h to a rapidly stirred solution of 1-iodo-3,4-dimethoxy-benzen e **2** (8.8 g, 35 mmol) in $CHCl_3$ (30 mL) and concentrated HCl (24 mL, 280 mmol). After 16 h at room temperature, the mixture was extracted with $CHCl_3$ (3 × 30 mL). The organic extracts were combined, washed with 5% $NaHSO_3$ (25 mL), dried over Na_2SO_4, filtered, and the solvent was evaporated under reduced pressure. The product was purified by column chromatography on silica gel with *n*-hexanes : $CHCl_3$ = 1 : 1 (v/v), yield 2.34 g (24%) of **4** as white solid. mp 61-62°C (Lit.: 70-73 °C[4]); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.20(s, 1H), 6.94(s, 1H), 3.85(s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.0, 148.3, 130.2, 121.8, 112.3, 85.8, 56.5, 56.3; MS *m/z*(relative intensity): 298(100, $M^{\bullet+}$), 283(36), 335(13), 128(44), 113(31); Anal. Calcd for $C_8H_8ClIO_2$: C, 32.17; H, 2.70. Found: C, 32.36; H, 2.65.

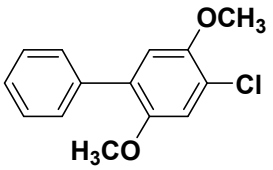
2-Chloro-4,5-dimethoxy-biphenyl (7): Sodium carbonate (10 mL, 2 M aq.) was added to a solution of 1-bromo-2-chloro-4,5-dimethoxy-benzene(**3**) (2.5 g, 10.0 mmol) and $Pd(PPh_3)_4$ (0.36 g, 3% molar ratio) in toluene(40 mL). A solution of a phenylboronic acid (1.8 g, 15.0 mmol) in ethanol : toluene : H_2O = 8 : 1 : 1 (20 mL total) was added slowly to the mixture under a nitrogen atmosphere. The reaction mixture was maintained at 80 °C for 12 h. Hydrogen peroxide (30%, 2.0 mL) was added slowly to the warm reaction mixture to destroy unreacted boronic acid. The mixture was stirred at room temperature for an additional 4 h and diluted with diethyl ether (60 mL). The reaction mixture was extracted once with NaOH (20 mL, 2 M aq.) and three times with water (20 mL). The organic phase was dried over $MgSO_4$ and the solvents were removed under reduced pressure. Column chromatography over silica gel with *n*-hexanes : $CHCl_3$

= 3 : 1 (v/v) as eluent, then recrystallized with *n*-hexanes : $CHCl_3$ = 3 : 1 (v/v), yield 1.65 g (66%) of **7** as white crystals. mp 111-113 °C (Lit.: 108 °C[5]); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47-7.36(m, 5H), 6.98(s, 1H), 6.86(s, 1H), 3.93(s, 3H), 3.89(s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.8, 147.8, 139.6, 132.6, 129.7, 128.2, 127.6, 123.6, 113.9, 112.9, 56.4, 56.3; MS *m/z*(relative intensity): 248(100, $M^{\bullet+}$), 233(18), 205(25), 170(21), 155(18), 127(18); Anal. Calcd for $C_{14}H_{13}ClO_2$: C, 67.59; H, 5.27. Found: C, 67.57; H, 5.24.

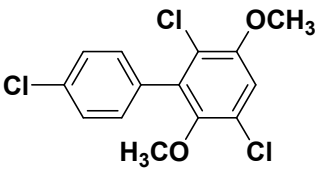
2,4'-Dichloro-4,5-dimethoxy-biphenyl (8): Sodium carbonate (17 mL, 2 M aq.) was added to a solution of 1-bromo-2-chloro-4,5-dimethoxy-benzene(**3**) (4.3 g, 17.0 mmol) and $Pd(PPh_3)_4$ (0.61 g, 3% molar ratio) in toluene(60 mL). A solution of a phenylboronic acid (3.0 g, 25.5 mmol) in ethanol : toluene : H_2O = 8 : 1 : 1 (30 mL total) was added slowly to the mixture under a nitrogen atmosphere. The reaction mixture was maintained at 80 °C for 12 h. Hydrogen peroxide (30%, 2.0 mL) was added slowly to the warm reaction mixture to destroy unreacted boronic acid. The mixture was stirred at room temperature for an additional 4 h and diluted with diethyl ether (100 mL). The reaction mixture was extracted once with NaOH (35 mL, 2 M aq.) and three times with water (35 mL). The organic phase was dried over $MgSO_4$ and the solvents were removed under reduced pressure. Column chromatography over silica gel with *n*-hexanes : $CHCl_3$ = 3 : 1 (v/v) as eluent, then recrystallized with *n*-hexanes : $CHCl_3$ = 3 : 1 (v/v), yield 4.6 g (98%) of **8** as white solid. mp 67-69 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42-7.36(m, 4H), 6.96(s, 1H), 6.80(s, 1H), 3.92(s, 3H), 3.88(s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.2, 148.1, 138.0, 133.7, 131.5, 131.1, 128.5, 123.7, 113.9, 113.2, 56.5,

56.4; MS *m/z*(relative intensity): 282(100, $M^{\bullet+}$), 267(25), 239(25), 204(30), 189(21), 168(18), 126(21); Anal. Calcd for $C_{14}H_{12}Cl_2O_2$: C, 59.36; H, 4.27. Found: C, 59.51; H, 4.31.

4-Chloro-2,5-dimethoxy-biphenyl (11): Sodium carbonate (10 mL, 2 M aq.) was added to a solution of 1-bromo-4-chloro-2,5-dimethoxy-benzene(**3**) (2.5 g, 10.0 mmol) and $Pd(PPh_3)_4$ (0.36 g, 3% molar ratio) in toluene(40 mL). A solution of a phenylboronic acid (1.8 g, 15.0 mmol) in ethanol : toluene : H_2O = 8 : 1 : 1 (20 mL total) was added slowly to the mixture under a nitrogen atmosphere. The reaction mixture was maintained at 80 °C for 12 h. Hydrogen peroxide (30%, 2.0 mL) was added slowly to the warm reaction mixture to destroy unreacted boronic acid. The mixture was stirred at room temperature for an additional 4 h and diluted with diethyl ether (60 mL). The reaction mixture was extracted once with NaOH (20 mL, 2 M aq.) and three times with water (20 mL). The organic phase was dried over $MgSO_4$ and the solvents were removed under reduced pressure. Column chromatography over silica gel with *n*-hexanes : $CHCl_3$ = 3 : 1 (v/v) as eluent, then recrystallized with *n*-hexanes : $CHCl_3$ = 3 : 1 (v/v), yield 1.8 g (71%) of **11** as white solid. mp 83-84 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56-7.36(m, 5H), 7.06(s, 1H), 6.96(s, 1H), 3.92(s, 3H), 3.78(s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.8, 149.5, 137.9, 130.2, 129.6, 128.4, 127.6, 121.8, 115.5, 114.4, 57.1, 56.7; MS *m/z*(relative intensity): 248(100, $M^{\bullet+}$), 233(47), 198(80), 183(23), 155(16), 127(20); Anal. Calcd for $C_{14}H_{13}ClO_2$: C, 67.59; H, 5.27. Found: C, 67.30; H, 5.23.

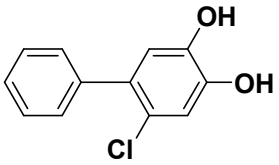


3,6,4'-Trichloro-2,5-dimethoxy-biphenyl (19): Sodium carbonate (14 mL, 2 M aq.) was added to a solution of 3-bromo-2,5-dichloro-1,4-dimethoxy-benzene (**18**) (4.0 g, 14.0 mmol) and



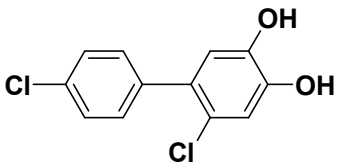
$Pd(PPh_3)_4$ (0.50 g, 3% molar ratio) in toluene(40 mL). A solution of a 4-chloro-phenylboronic acid (2.5 g, 21.0 mmol) in ethanol : toluene : H_2O = 8 : 1 : 1 (30 mL total) was added slowly to the mixture under a nitrogen atmosphere. The reaction mixture was maintained at 80 °C for 12 h. Hydrogen peroxide (30%, 2.0 mL) was added slowly to the warm reaction mixture to destroy unreacted boronic acid. The mixture was stirred at room temperature for an additional 4 h and diluted with diethyl ether (90 mL). The reaction mixture was extracted once with NaOH (30 mL, 2 M aq.) and three times with water (30 mL). The organic phase was dried over $MgSO_4$ and the solvents were removed under reduced pressure. Column chromatography over silica gel with *n*-hexanes : $CHCl_3$ = 3 : 1 (v/v) as eluent, then recrystallized with *n*-hexanes : $CHCl_3$ = 3 : 1 (v/v), yield 3.2 g (48%) of **19** as white solid. mp 85-87 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44-7.41(m, AA'XX' system, 2H), 7.28-7.25(m, AA'XX' system, 2H), 6.99(s, 1H), 3.91(s, 3H, 3.41(s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.2, 148.2, 136.4, 134.3, 133.3, 131.6, 128.6, 126.9, 112.9, 61.0, 56.9; MS *m/z*(relative intensity): 316(62, $M^{\bullet+}$), 266(100), 207(50), 160(30), 84(32); Anal. Calcd for $C_{14}H_{11}Cl_3O_2$: C, 52.92; H, 3.49. Found: C, 53.16; H, 3.44.

6-Chloro-biphenyl-3,4-diol (9):[6,7] Boron tribromide (7.0 mL, 1M in *n*-hexanes, 2.2 equiv) was added to a solution of the 2-chloro-4,5-dimethoxy-biphenyl **7** (0.85 g, 3.4 mmol) in anhydrous dichloromethane (20 mL) under a nitrogen atmosphere. The reaction mixture was stirred at room temperature for 14 hours, cooled with ice/salt and hydrolyzed with an equal volume of ice-cold water. The aqueous phase was extracted with dichloromethane (2 × 20 mL). The combined organic layers were washed with water (3 × 10 mL), dried over $MgSO_4$ and the solvent was removed under reduced pressure. The product was purified by column chromatography on silica gel with *n*-hexanes : ethyl

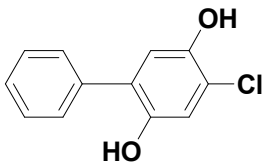


acetate = 1 : 1 (v/v) as eluent, followed by recrystallization using *n*-hexanes : $CHCl_3$ = 3 : 1 (v/v), yield 0.33 g (45%) of crude **9** as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43-7.35(m, 5H), 7.02(s, 1H), 6.88(s, 1H), 5.49(s, 1H), 5.34(s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.6, 142.4, 139.2, 133.4, 129.7, 128.2, 127.6, 123.8, 117.9, 116.9; MS *m/z*(relative intensity): 364(100, $[M+TMS_2]^{\bullet+}$), 73(80, $[Si(CH_3)_3]^+$); HRMS(EI) Calcd for $C_{12}H_9ClO_2$ *m/z*($[M]^{\bullet+}$) 220.0291. Found 220.0284.

6,4'-Dichloro-biphenyl-3,4-diol (10): Boron tribromide (19.0 mL, 1M in *n*-hexanes, 2.2 equiv) was added to a solution of the 2,4'-dichloro-4,5-dimethoxy-biphenyl **8** (2.5 g, 8.8 mmol) in anhydrous dichloromethane (50 mL) under a nitrogen atmosphere. The reaction mixture was stirred at room temperature for 14 hours, cooled with ice/salt and hydrolyzed with an equal volume of ice-cold water. The aqueous phase was extracted with dichloromethane (2 × 50 mL). The combined organic layers were washed with water (3 × 25 mL), dried over $MgSO_4$ and the solvent was removed under reduced pressure. The product was purified by column chromatography on silica gel with *n*-hexanes : ethyl acetate = 1 : 1 (v/v) as eluent, followed by recrystallization using *n*-hexanes : $CHCl_3$ = 3 : 1 (v/v), yield 1.2 g (53%) of **10** as white solid. mp 89-90 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40-7.32(m, 4H), 7.01(s, 1H), 6.84(s, 1H), 5.31(s, 1H), 5.17(s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.8, 142.5, 137.6, 133.7, 132.3, 131.0, 128.5, 123.9, 117.8, 117.1; MS *m/z*(relative intensity): 398(100, $[M+TMS_2]^{\bullet+}$), 276(12), 73(84, $[Si(CH_3)_3]^+$); Anal. Calcd for $C_{12}H_8Cl_2O_2$: C, 56.48; H, 3.16. Found: C, 56.39; H, 3.28.

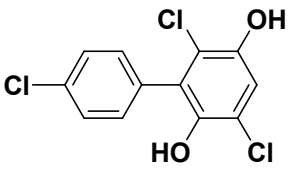


4-Chloro-biphenyl-2,5-diol (13): Boron tribromide (2.5 mL, 1M in *n*-hexanes, 2.2 equiv) was added to a solution of the 4-chloro-2,5-dimethoxy-biphenyl **11**



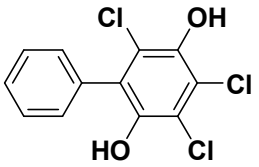
(0.3 g, 1.2 mmol) in anhydrous dichloromethane (10 mL) under a nitrogen atmosphere. The reaction mixture was stirred at room temperature for 14 hours, cooled with ice/salt and hydrolyzed with an equal volume of ice-cold water. The aqueous phase was extracted with dichloromethane (2 × 10 mL). The combined organic layers were washed with water (3 × 5 mL), dried over $MgSO_4$ and the solvent was removed under reduced pressure. The product was purified by column chromatography on silica gel with *n*-hexanes : ethyl acetate = 1 : 1 (v/v) as eluent, followed by recrystallization using *n*-hexanes : $CHCl_3$ = 3 : 1 (v/v), yield 0.18 g (67%) of **13** as white crystals. mp 96-97 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.52-7.40(m, 5H), 7.00(s, 1H), 6.94(s, 1H), 5.19(s, 1H), 4.93(s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.5, 145.6, 136.2, 129.6, 129.1, 128.6, 128.5, 119.6, 117.2, 116.3; MS *m/z*(relative intensity): 364(100, $[M+TMS_2]^{\bullet+}$), 349(13), 314(34), 73(35, $[Si(CH_3)_3]^+$); Anal. Calcd for $C_{12}H_9ClO_2$: C, 65.32; H, 4.11. Found: C, 65.35; H, 4.18.

3,6,4'-Trichloro-biphenyl-2,5-diol (20): Boron tribromide (8.0 mL, 1M in *n*-hexanes, 2.2 equiv) was added to a solution of the 3,6,4'-trichloro-2,5-dimethoxy-biphenyl **19** (1.15 g, 3.6 mmol) in anhydrous dichloromethane (20 mL) under a nitrogen atmosphere. The reaction mixture was stirred at room temperature for 14 hours, cooled with ice/salt and hydrolyzed with an equal volume of ice-cold water. The aqueous phase was extracted with dichloromethane (2 × 20 mL). The combined organic layers were washed with water (3 × 10 mL), dried over $MgSO_4$ and the solvent was removed under reduced pressure. The product was purified by column chromatography on silica gel with *n*-hexanes : ethyl acetate = 1 : 1 (v/v) as eluent, followed by recrystallization using *n*-hexanes : $CHCl_3$ = 3 : 1 (v/v), yield 0.81 g (77%) of **20** as white solid. mp 142-143 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48-7.45(m,

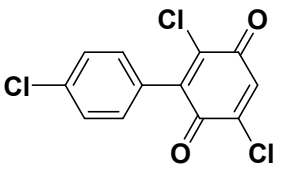


AA'XX' system, 2H), 7.28-7.25(m, AA'XX' system, 2H), 7.10(s, 1H), 5.34(s, 1H), 5.13(s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.7, 143.5, 134.9, 132.4, 131.6, 129.1, 127.3, 119.8, 119.0, 115.7; MS *m/z*(relative intensity): 432(81, $[M+TMS_2]^{\bullet+}$), 417(18), 382(100), 93(43), 73(100, $[Si(CH_3)_3]^+$); Anal. Calcd for $C_{12}H_7Cl_3O_2$: C, 49.76; H, 2.44. Found: C, 49.65; H, 2.37.

3,4,6-Trichloro-biphenyl-2,5-diol (25): Boron tribromide (2.5 mL, 1M in *n*-hexanes, 2.2 equiv) was added to a solution of the 3,4,6-trichloro-2,5-dimethoxy-biphenyl **24** (0.35 g, 1.1 mmol) in anhydrous dichloromethane (10 mL) under a nitrogen atmosphere. The reaction mixture was stirred at room temperature for 14 hours, cooled with ice/salt and hydrolyzed with an equal volume of ice-cold water. The aqueous phase was extracted with dichloromethane (2 × 10 mL). The combined organic layers were washed with water (3 × 5 mL), dried over $MgSO_4$ and the solvent was removed under reduced pressure. The product was purified by column chromatography on silica gel with *n*-hexanes : ethyl acetate = 1 : 1 (v/v) as eluent, followed by recrystallization using *n*-hexanes : $CHCl_3$ = 3 : 1 (v/v), yield 0.20 g (63%) of **25** as white solid. mp 124-125 °C (Lit.: 136-138 °C[8]); ^{1}H NMR (400 MHz, $CDCl_3$): δ7.55-7.46(m, AA'XX' system, 3H), 7.34-7.31(m, AA'XX' system, 2H), 5.69(s, 1H), 5.22(s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.1, 143.1, 133.3, 130.1, 129.16, 129.14, 127.2, 119.5, 119.3, 118.8; MS *m/z*(relative intensity): 432(82, $[M+TMS_2]^{\bullet+}$), 417(20), 382(63), 309(21), 93(43), 73(90, $[Si(CH_3)_3]^+$); Anal. Calcd for $C_{12}H_7Cl_3O_2$: C, 49.76; H, 2.44. Found: C, 49.87; H, 2.42.

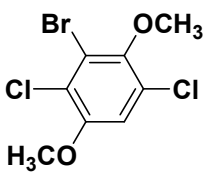


2,5-Dichloro-3-(4-chloro-phenyl)-[1,4]benzoquinone (21):[9] 3,6,4'-trichloro-2,5-dimethoxy-biphenyl **19** (0.80 g, 2.5 mmol) was dissolved in



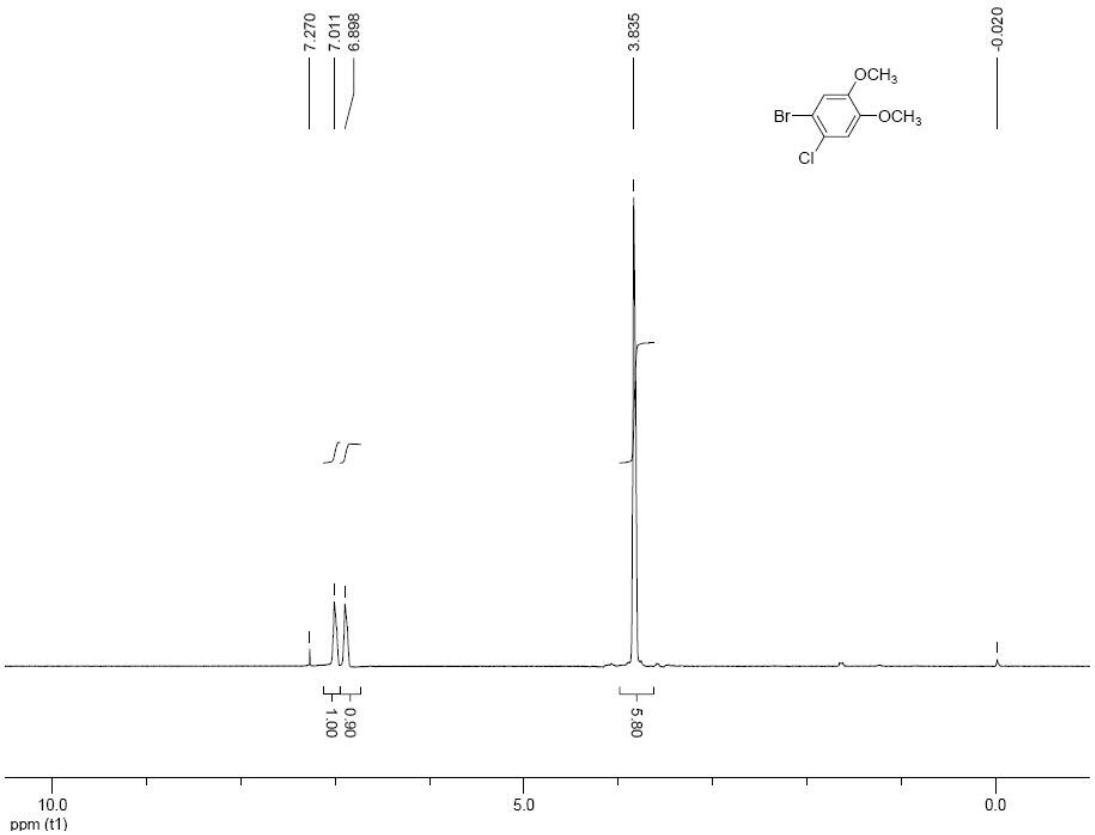
acetonitrile (15 mL) at 50 °C, a solution of cerium ammonium nitrate (5.8 g, 10.0 mmol) in water (15 mL) was added, and the reaction mixture was stirred at room temperature for 3 h. The solution was extracted with chloroform (2 × 30 mL) and washed with water (2 × 75 mL). The combined organic phase was and dried over $MgSO_4$ and the product was purified by column chromatography on silica gel with $CHCl_3$: *n*-hexanes = 2 : 1 (v/v) as eluent, yield 0.70 g (97%) of **21** as yellow solid. mp 143-144 °C (Lit.: 143-144 °C[10] and 144-145 °C[11]); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49-7.46(m, AA'XX' system, 2H), 7.27-7.24(m, AA'XX' system, 2H), 7.25(s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.5, 177.0, 144.8, 142.9, 141.5, 136.5, 133.3, 131.4, 129.1, 129.0; MS *m/z*(relative intensity): 288(30, $[M+2H]^{\bullet+}$), 251(100); Anal. Calcd for $C_{12}H_5Cl_3O_2$: C, 50.10; H, 1.75. Found: C, 50.24; H, 1.65.

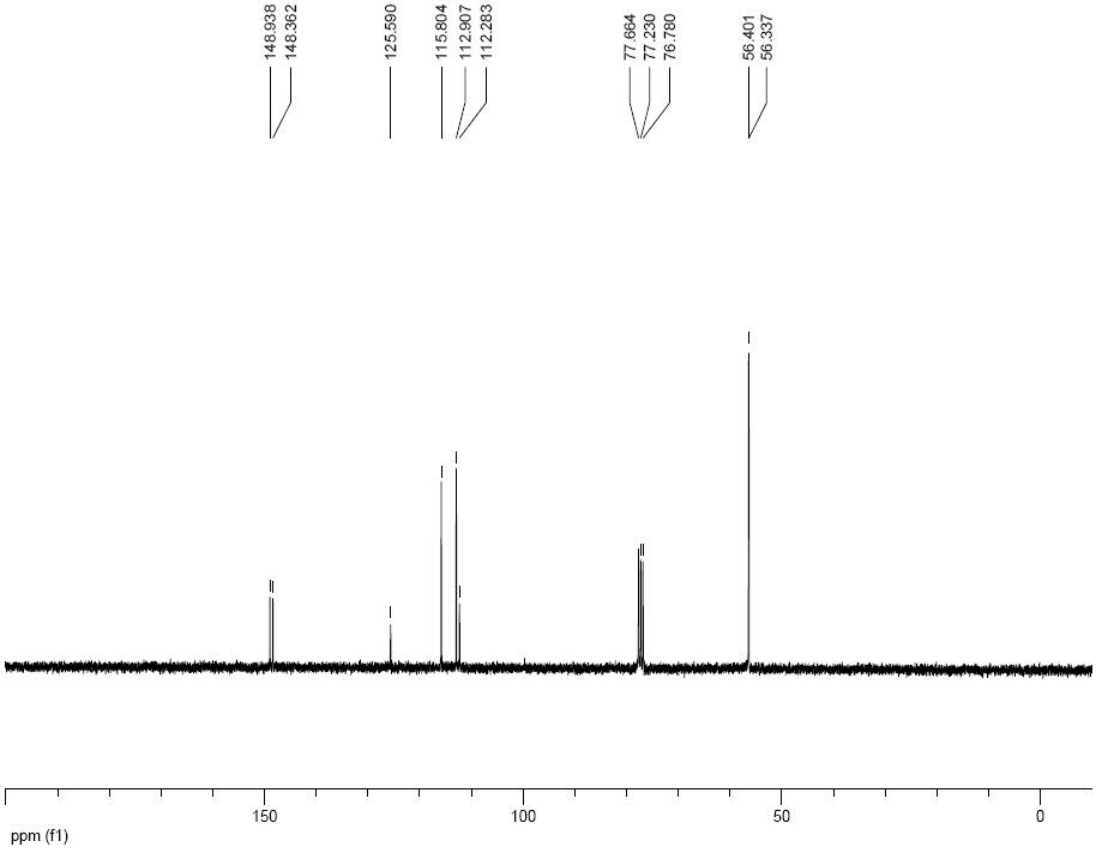
3-Bromo-2,5-dichloro-1,4-dimethoxy-benzene (18):[7] 2-Bromo-3,6-dichloro-4-methoxy-phenol **17** (2.0 g, 7.35 mmol) and dimethyl sulfate (0.94 mL, 10 mmol) were added slowly to an aqueous solution of NaOH (0.4 g, 10 mmol). The reaction mixture was heated under reflux for 30 min to destroy excess dimethyl sulfate, allowed to cool to ambient temperature and extracted with diethyl ether (3 × 20 mL). The combined organic layers were dried over sodium sulfate and the solvent was removed under reduced pressure. Recrystallization from *n*-hexanes yielded 1.8 g (85%) of **18** as white solid. mp 76-77 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.95(s, 1H), 3.89(s, 3H), 3.86(s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.8, 148.2, 127.2, 123.1, 121.2, 112.4, 60.9, 57.1; MS *m/z*(relative intensity): 284(57, $M^{\bullet+}$), 269(64); Anal. Calcd for $C_8H_7BrCl_2O_2$: C, 33.58; H, 2.47. Found: C, 33.77; H, 2.36.



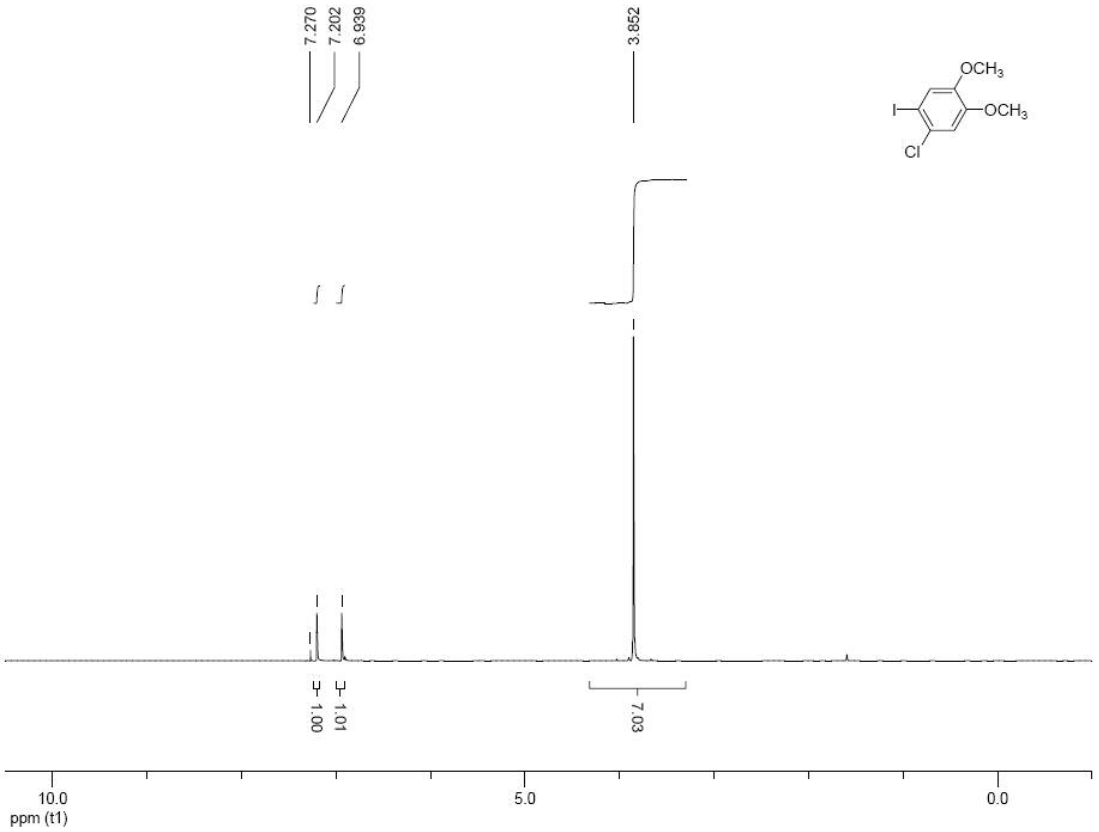
1,2,4,5-Tetrachloro-3,6-dimethoxy-benzene (23): 2,3,5,6-tetrachloro-benzene-1,4-diol **22** (12.4 g, 50.0 mmol) and dimethyl sulfate (10.3 mL, 110 mmol) were added slowly to an aqueous solution of NaOH (4.4 g, 110 mmol). The reaction mixture was heated under reflux for 30 min to destroy excess dimethyl sulfate, allowed to cool to ambient temperature and extracted with diethyl ether (3 × 200 mL). The combined organic layers were dried over sodium sulfate and the solvent was removed under reduced pressure. Recrystallization from *n*-hexanes yielded 7.5 g (57%) of **23** as white needles. mp 154-157 °C (Lit.: 98-99 °C[12] and 162-164 °C[13]); ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.90(s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.7, 127.8, 61.0; MS *m/z*(relative intensity):[14] 274(46, $M^{\bullet+}$), 259(86, M-CH_3), 209(41), 181(18), 87(45); Anal. Calcd for $C_8H_6Cl_4O_2$: C, 34.80; H, 2.19. Found: C, 34.90; H, 1.97.

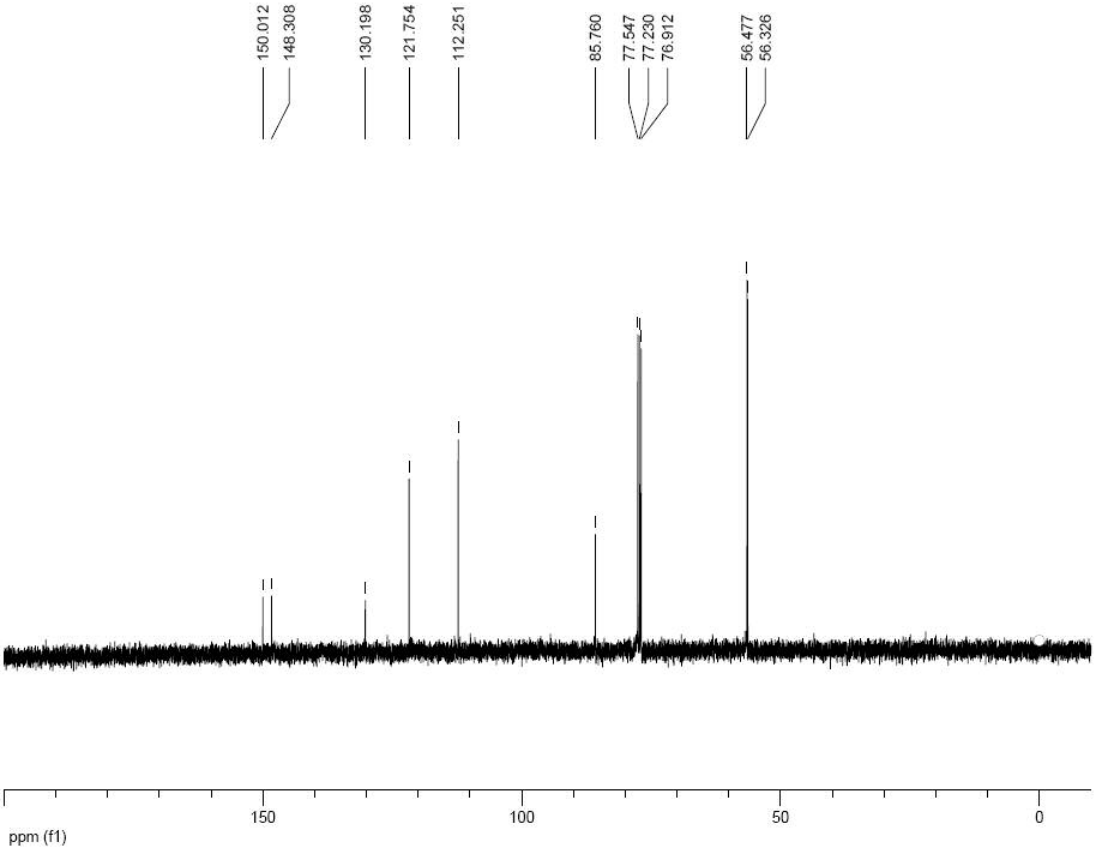
1-Bromo-2-chloro-4,5-dimethoxy-benzene (3)



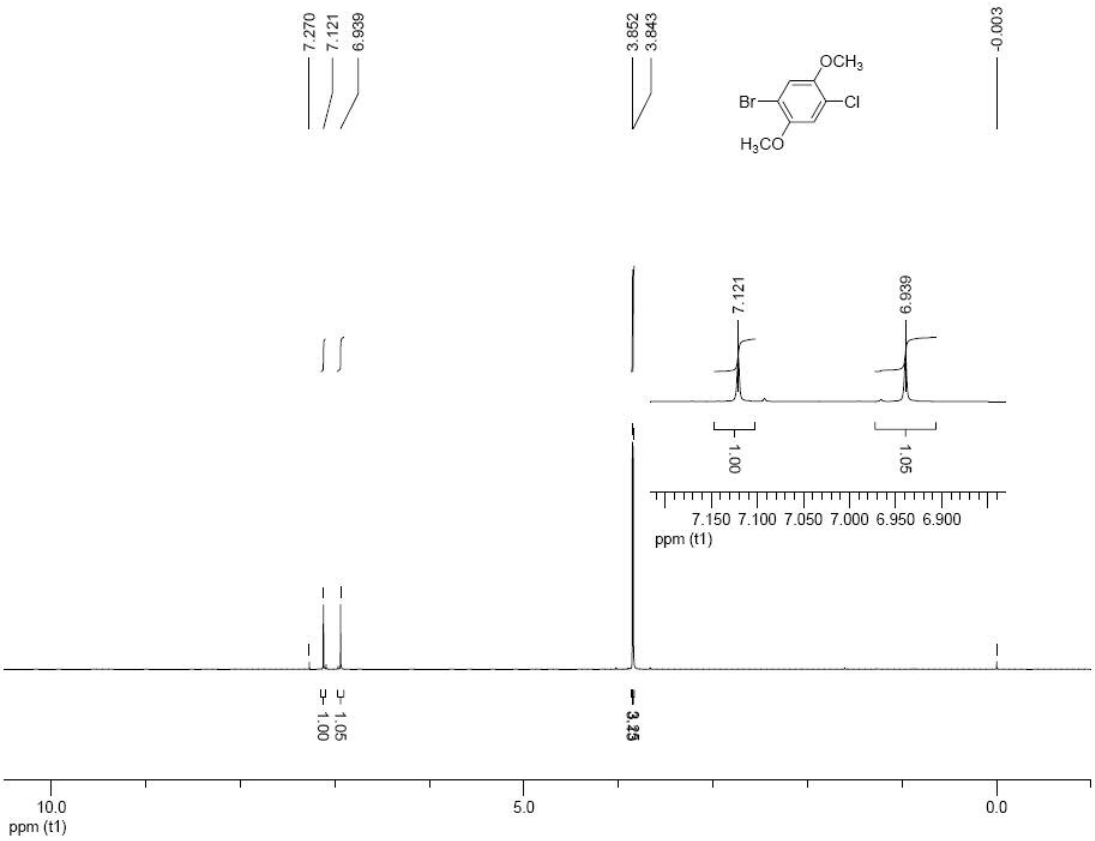


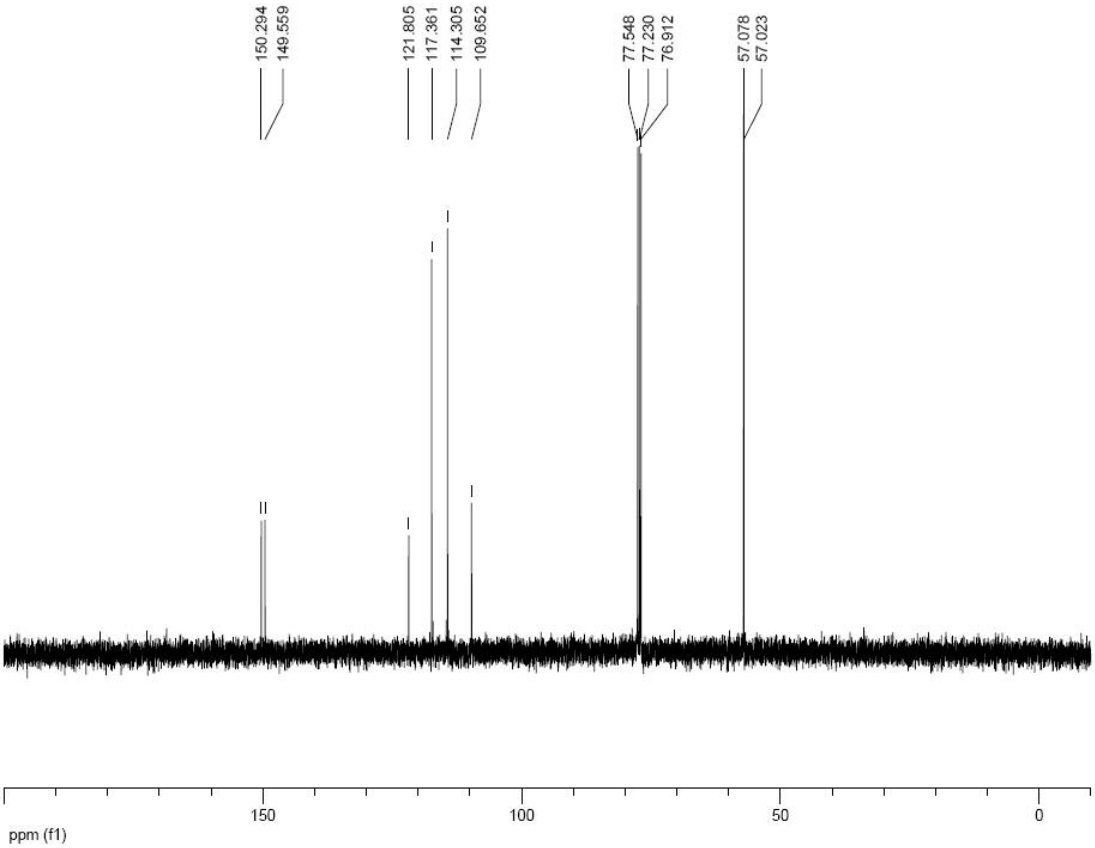
1-Chloro-2-iodo-4,5-dimethoxy-benzene (4)



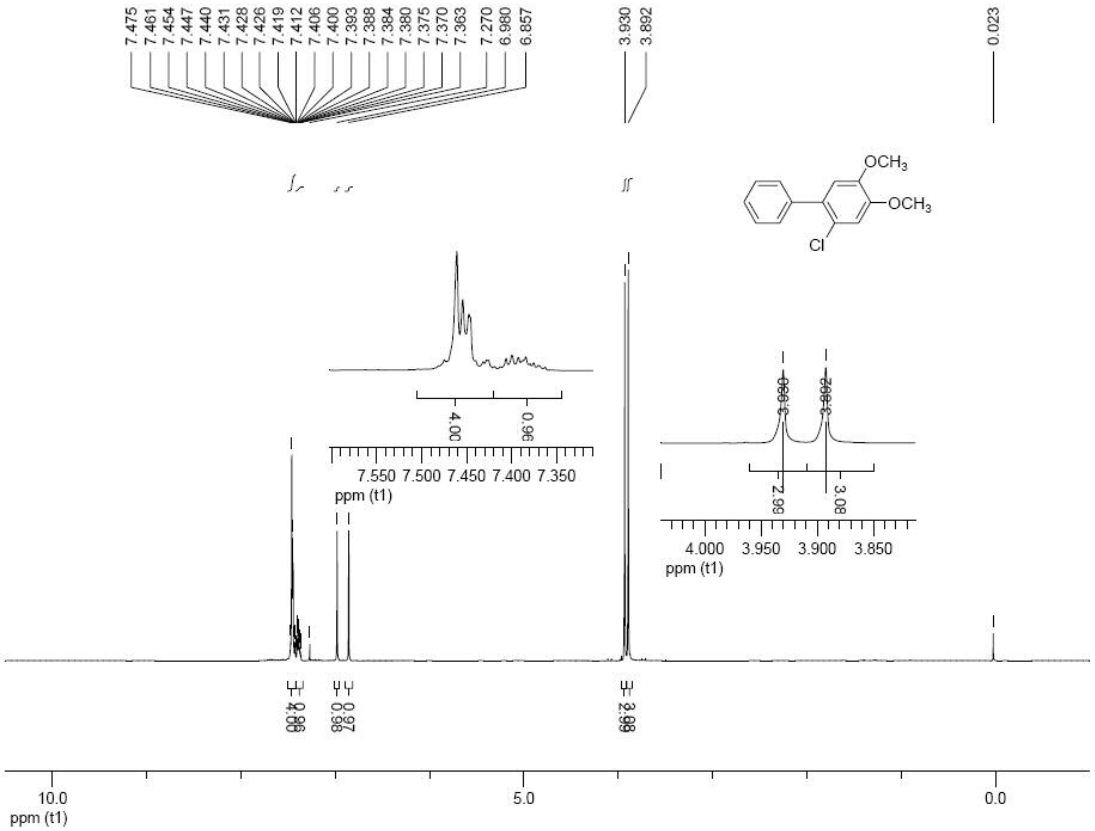


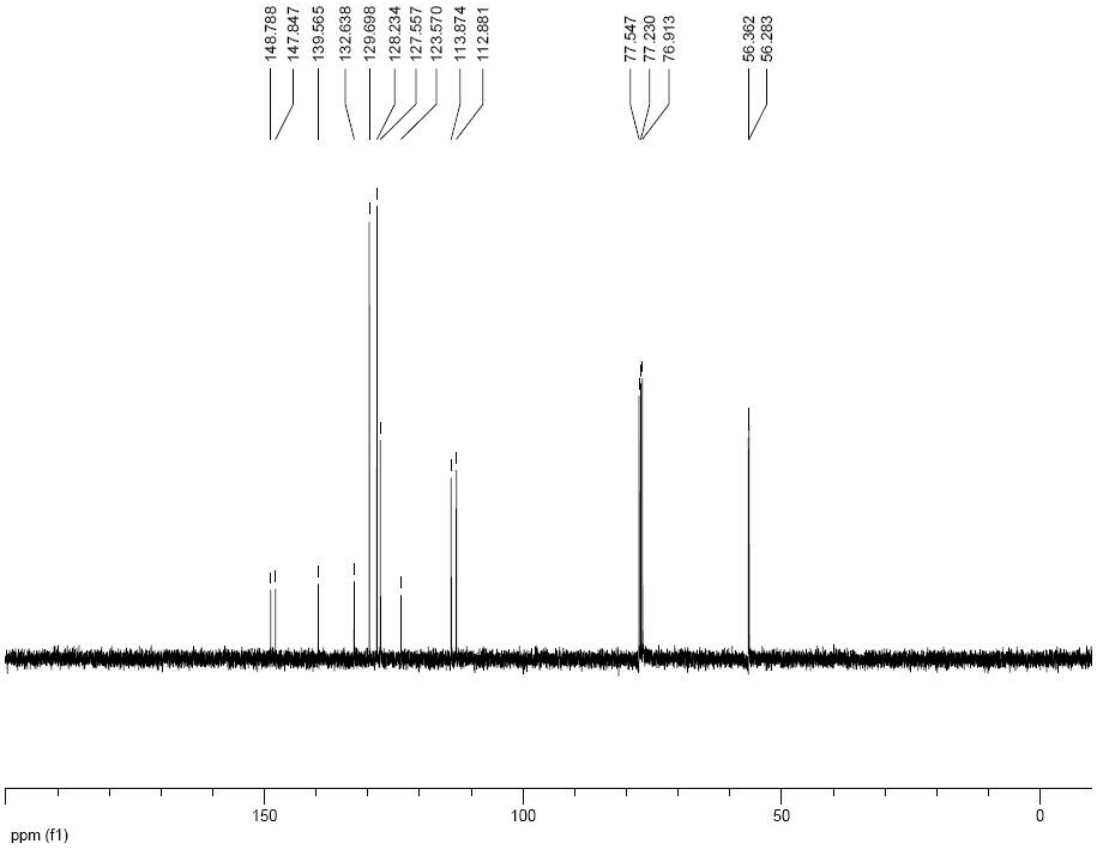
1-Bromo-4-chloro-2,5-dimethoxy-benzene (6)



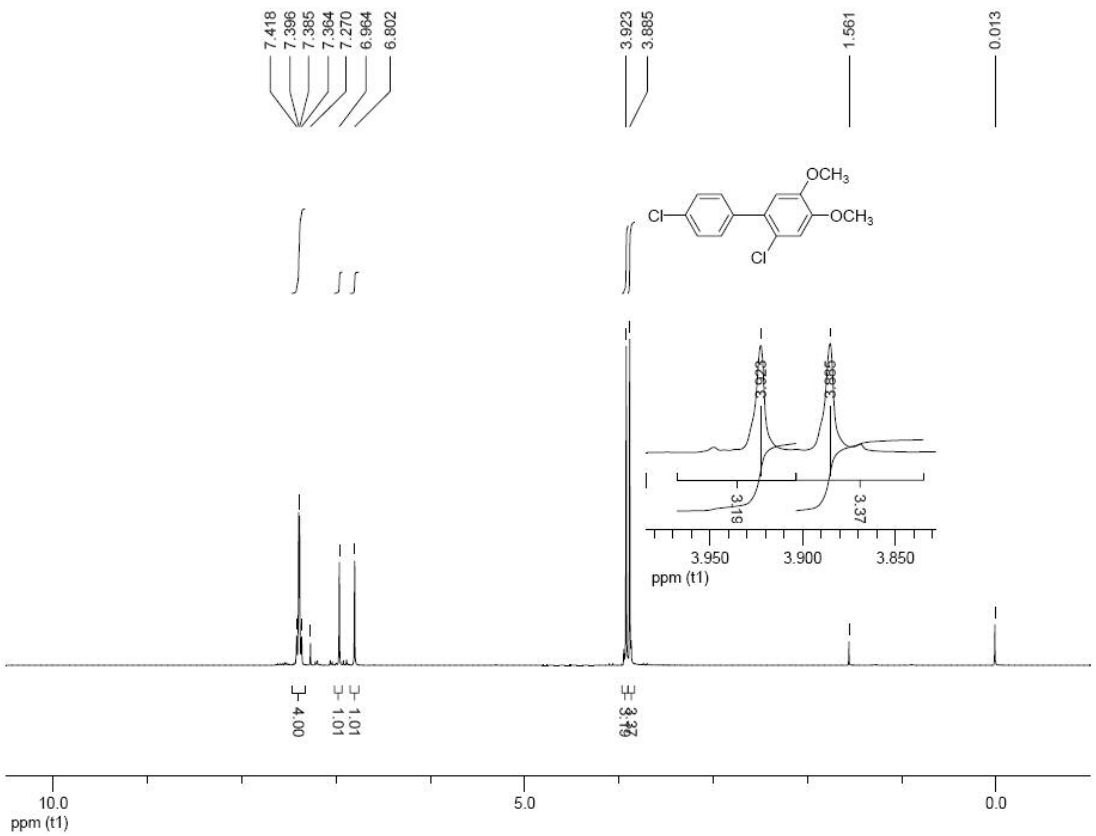


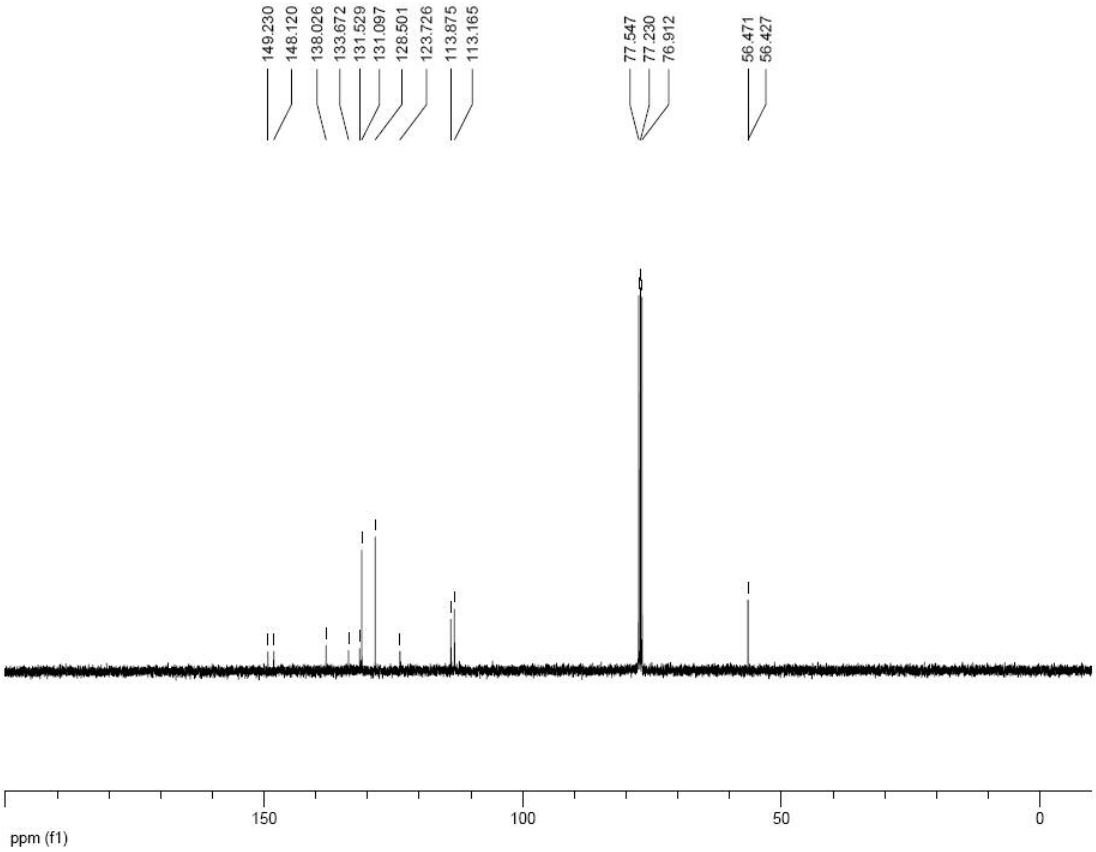
2-Chloro-4,5-dimethoxy-biphenyl (7)



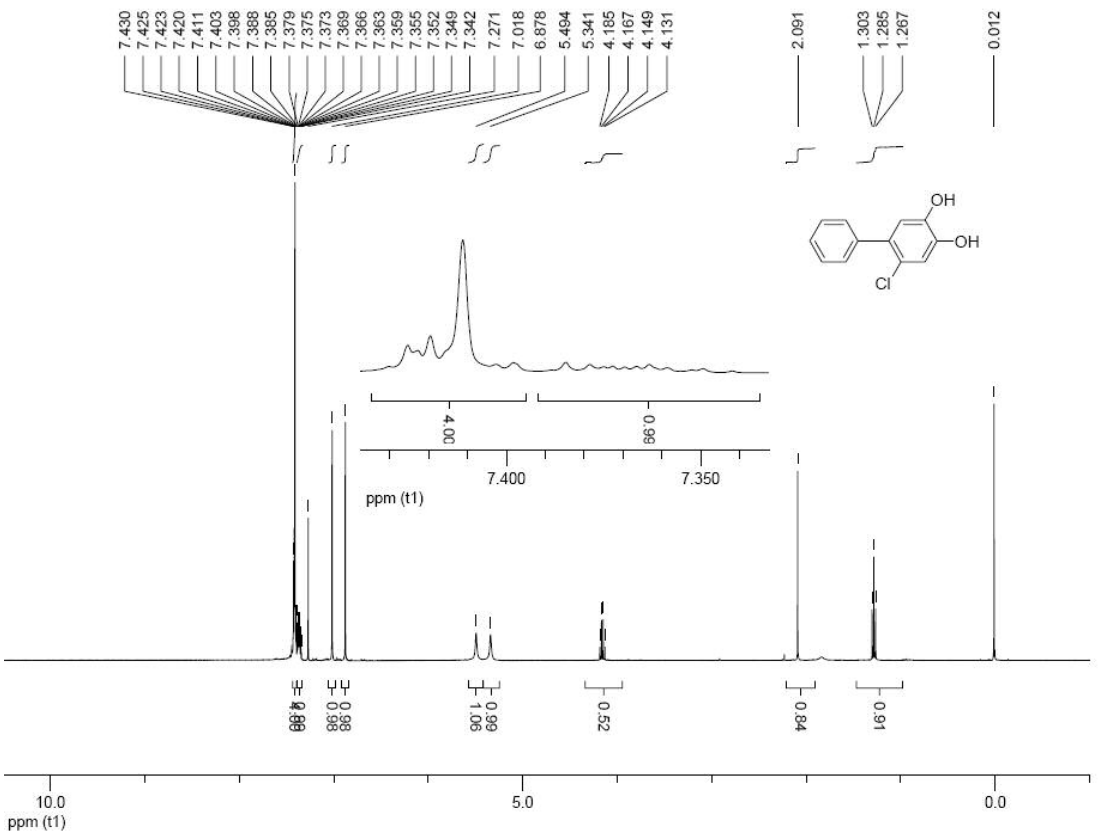


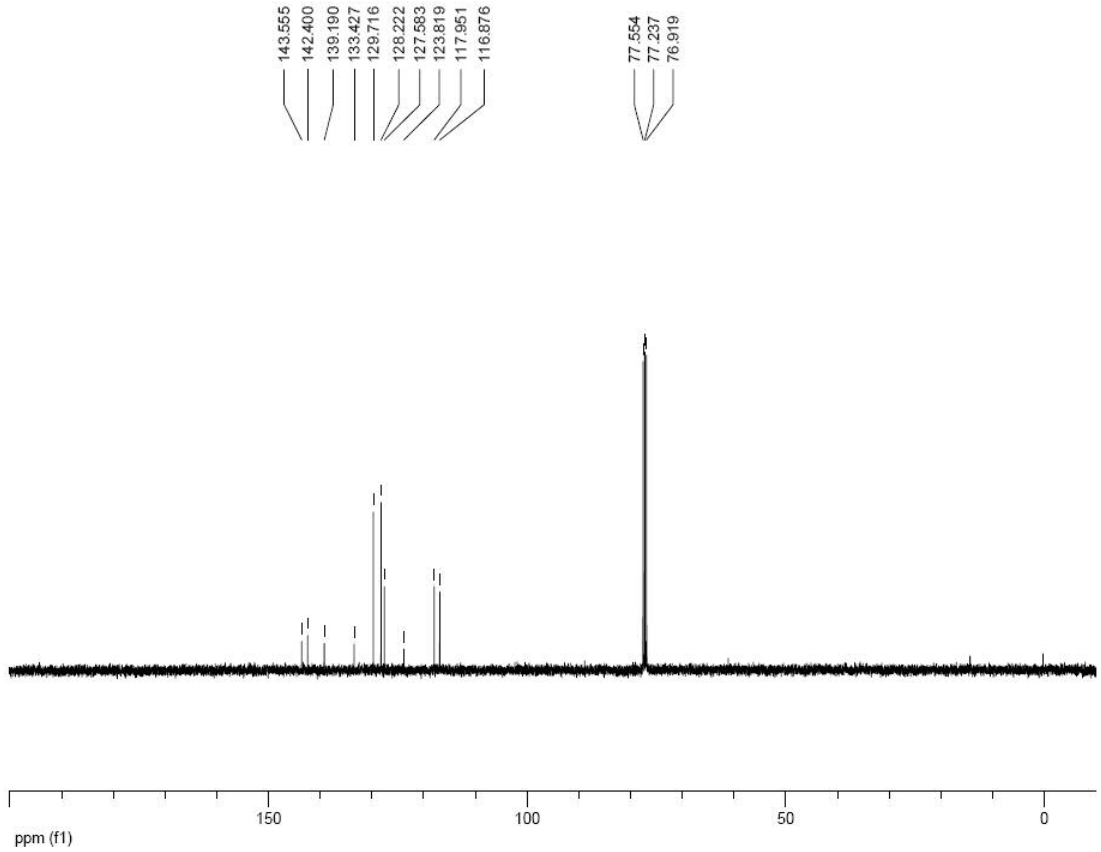
2,4'-Dichloro-4,5-dimethoxy-biphenyl (8)



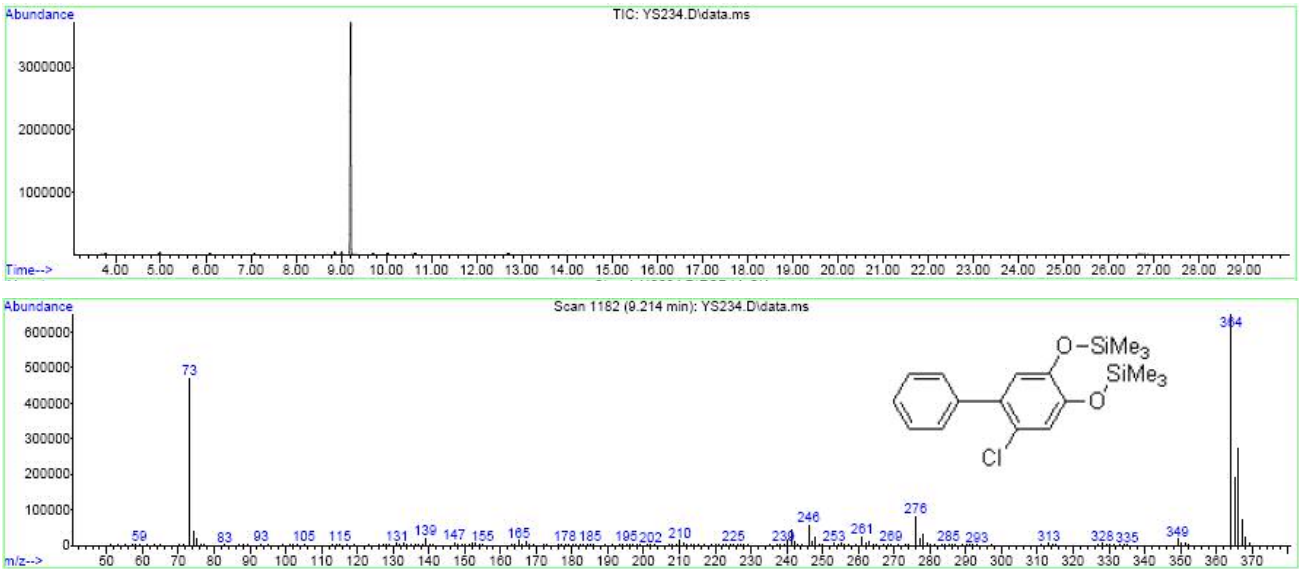


6-Chloro-biphenyl-3,4-diol (9)

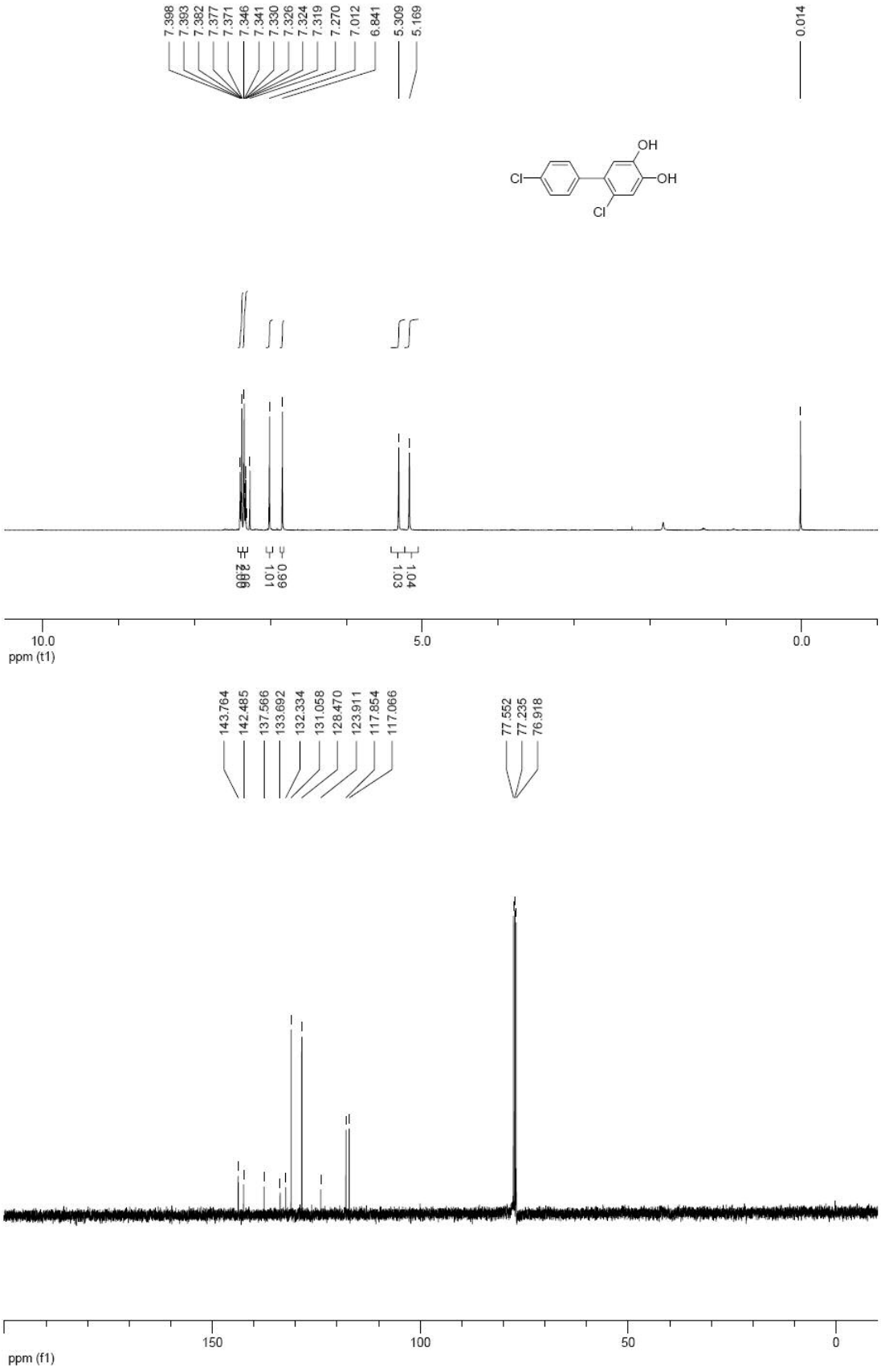




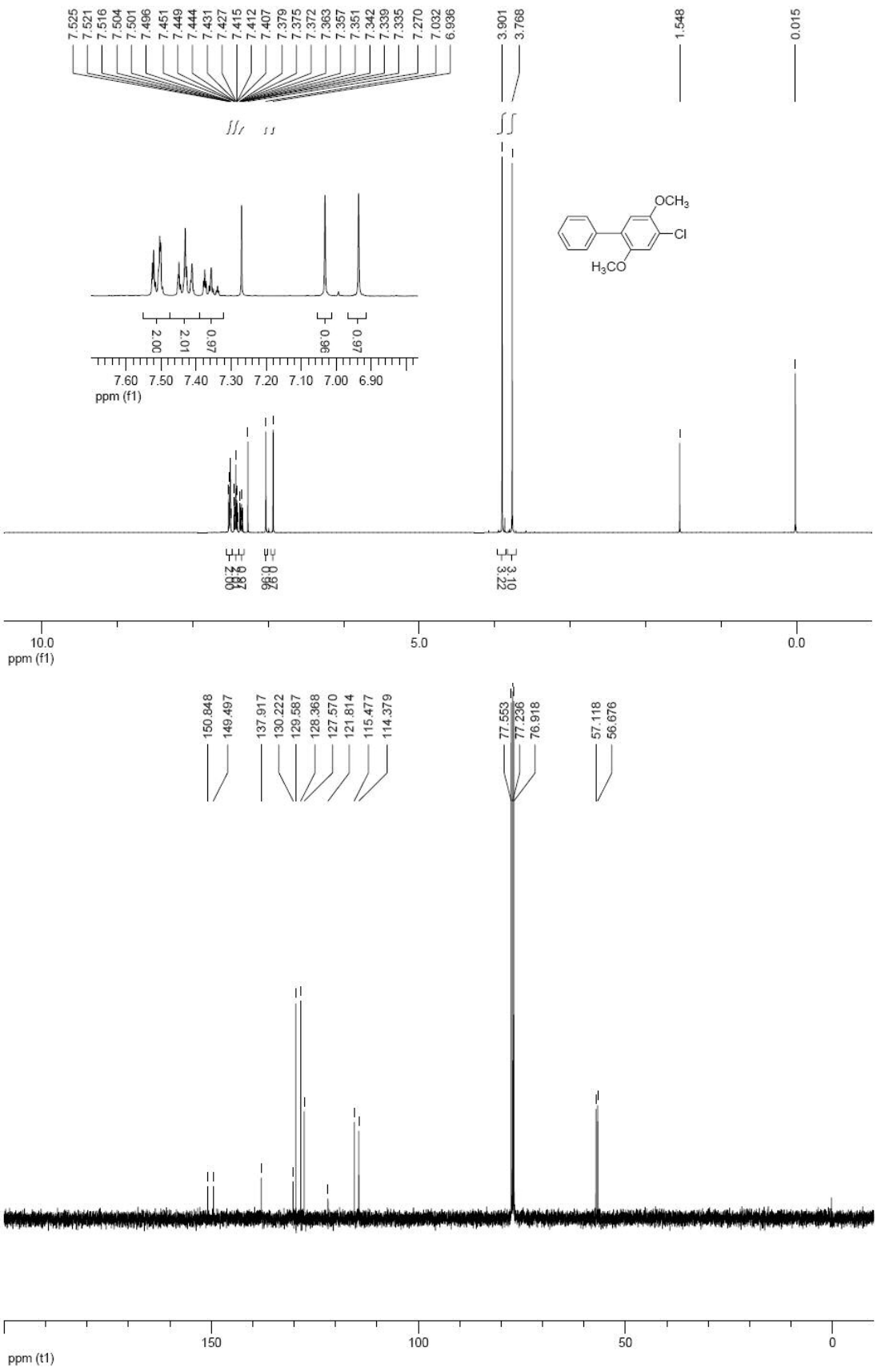
Gas chromatogram and mass spectrum of 6-chloro-biphenyl-3,4-diol (9)



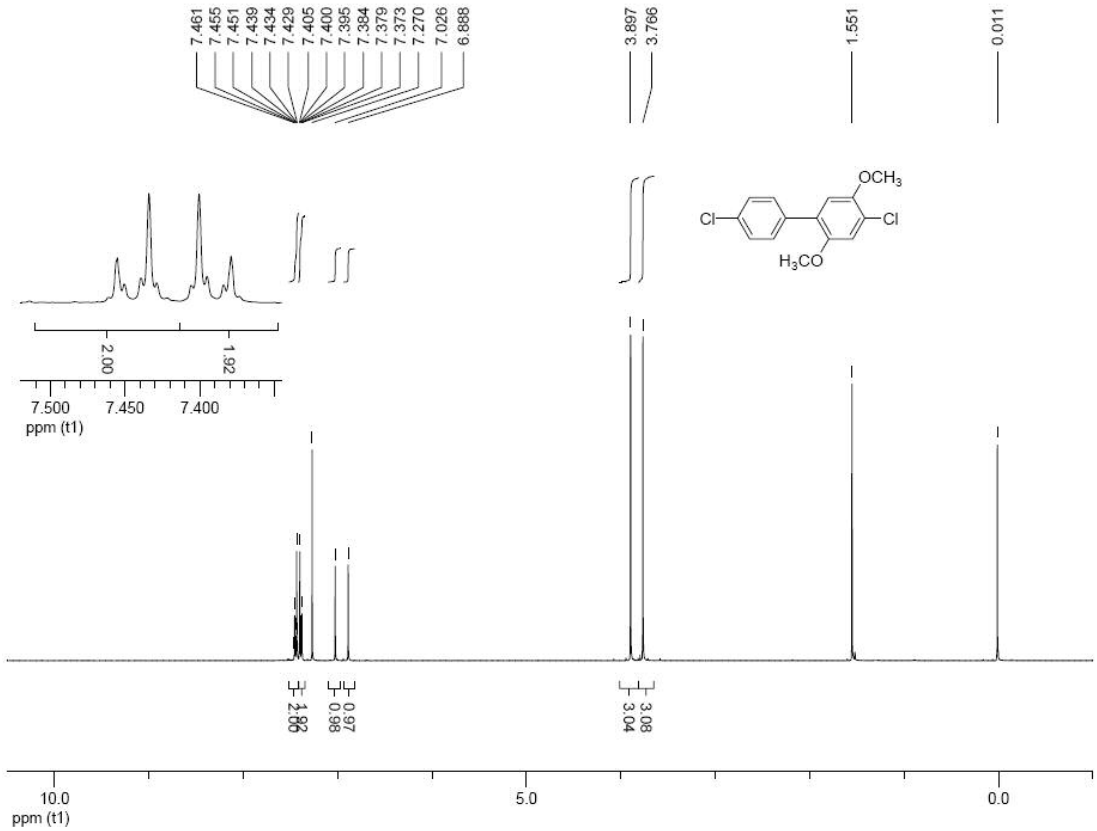
6,4'-Dichloro-biphenyl-3,4-diol (10)

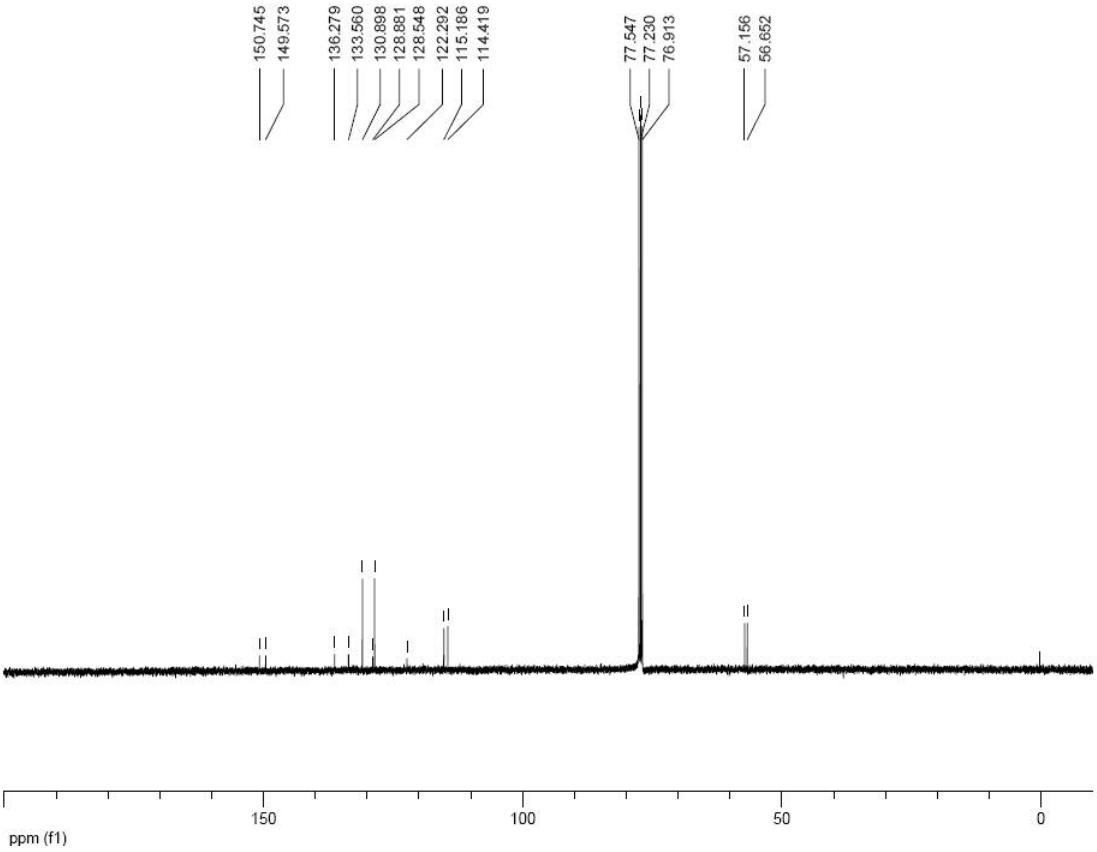


4-Chloro-2,5-dimethoxy-biphenyl (11)

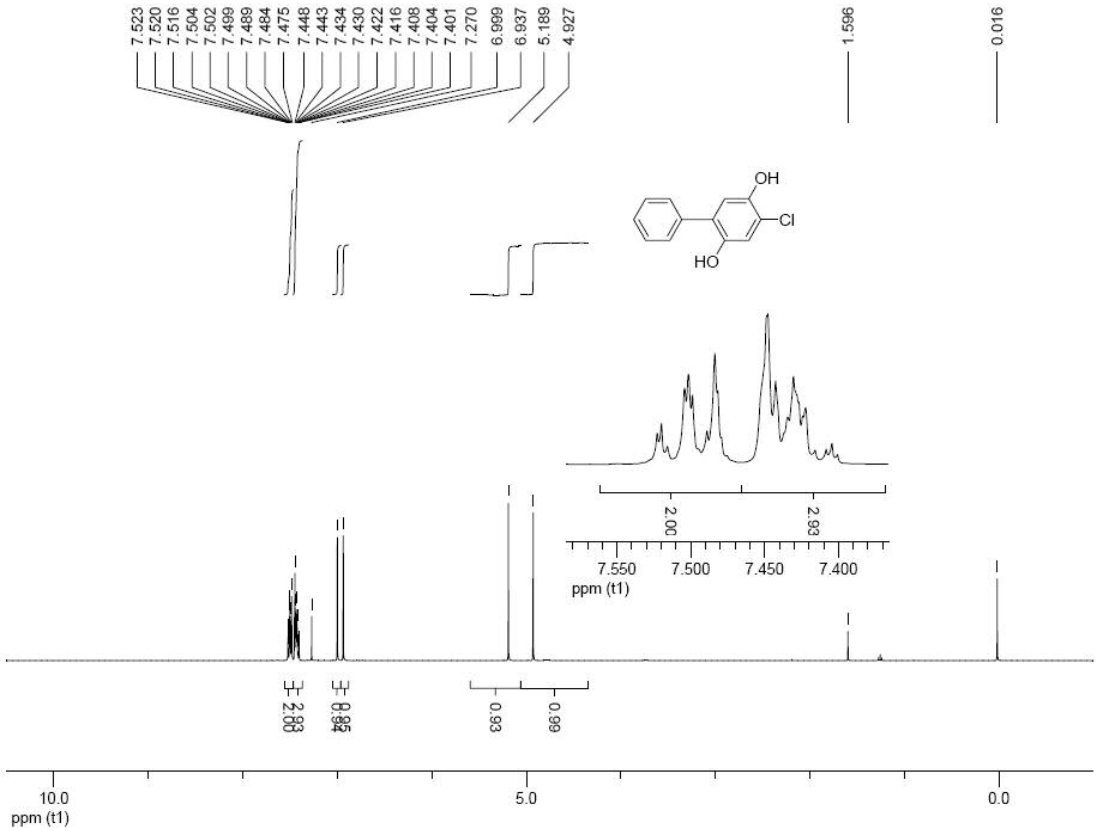


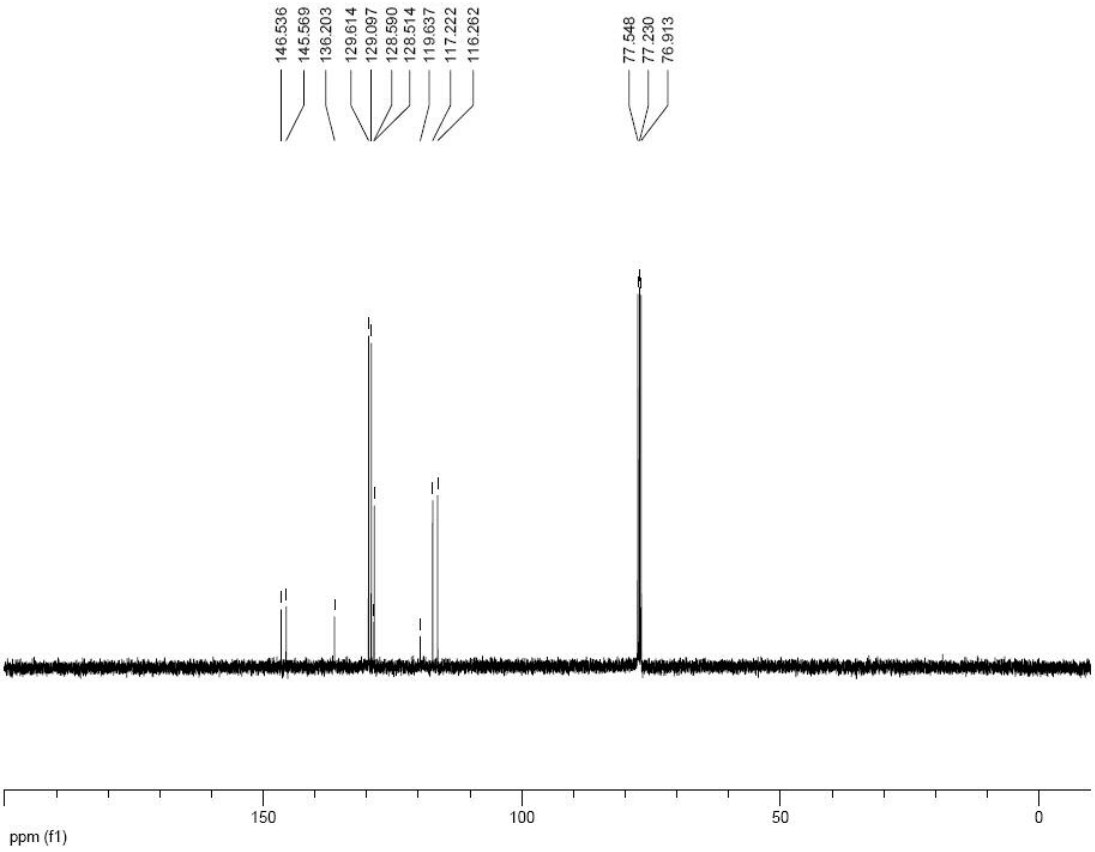
4,4’-Dichloro-2,5-dimethoxy-biphenyl (12)



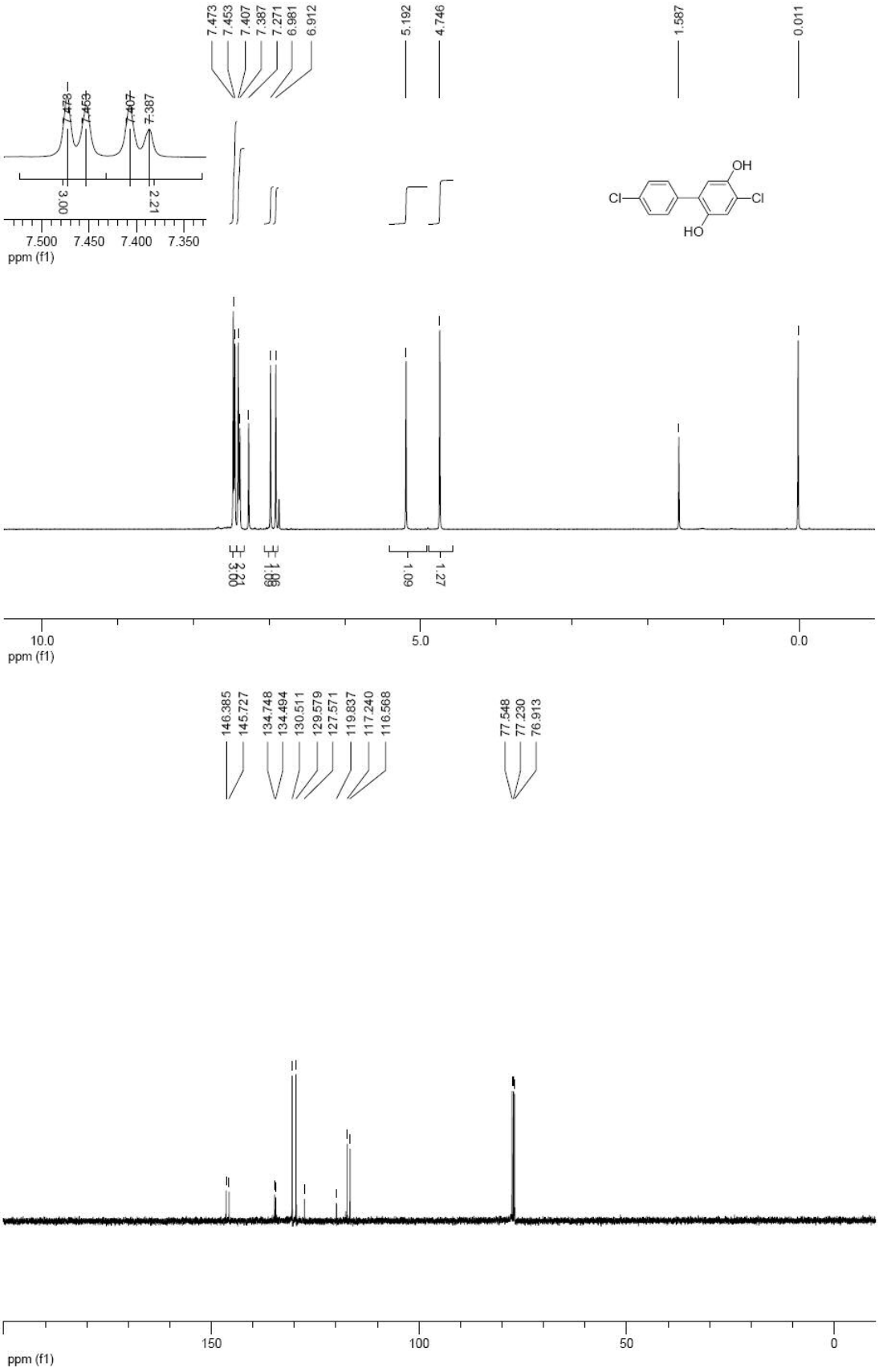


4-Chloro-biphenyl-2,5-diol (13)

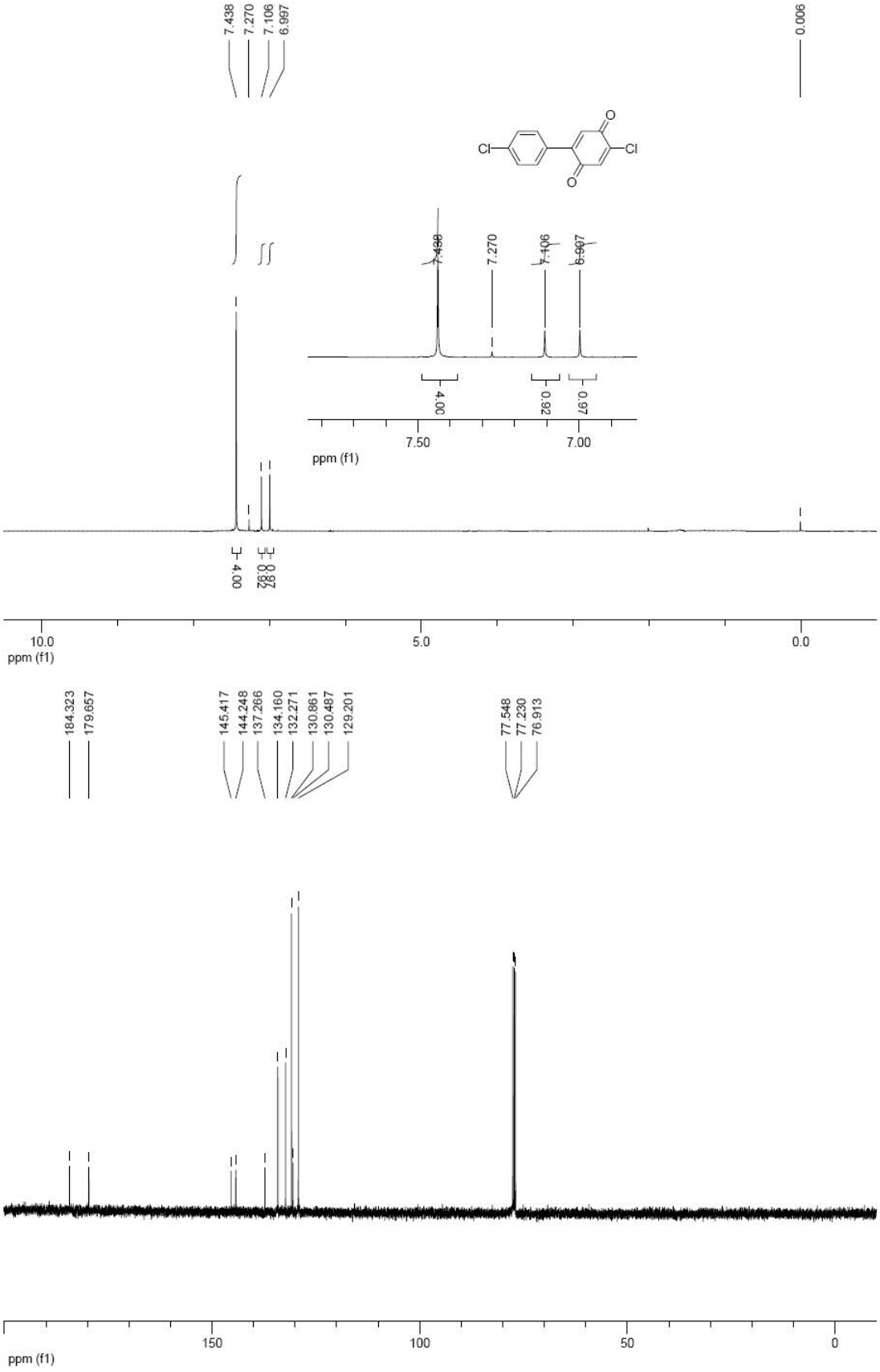




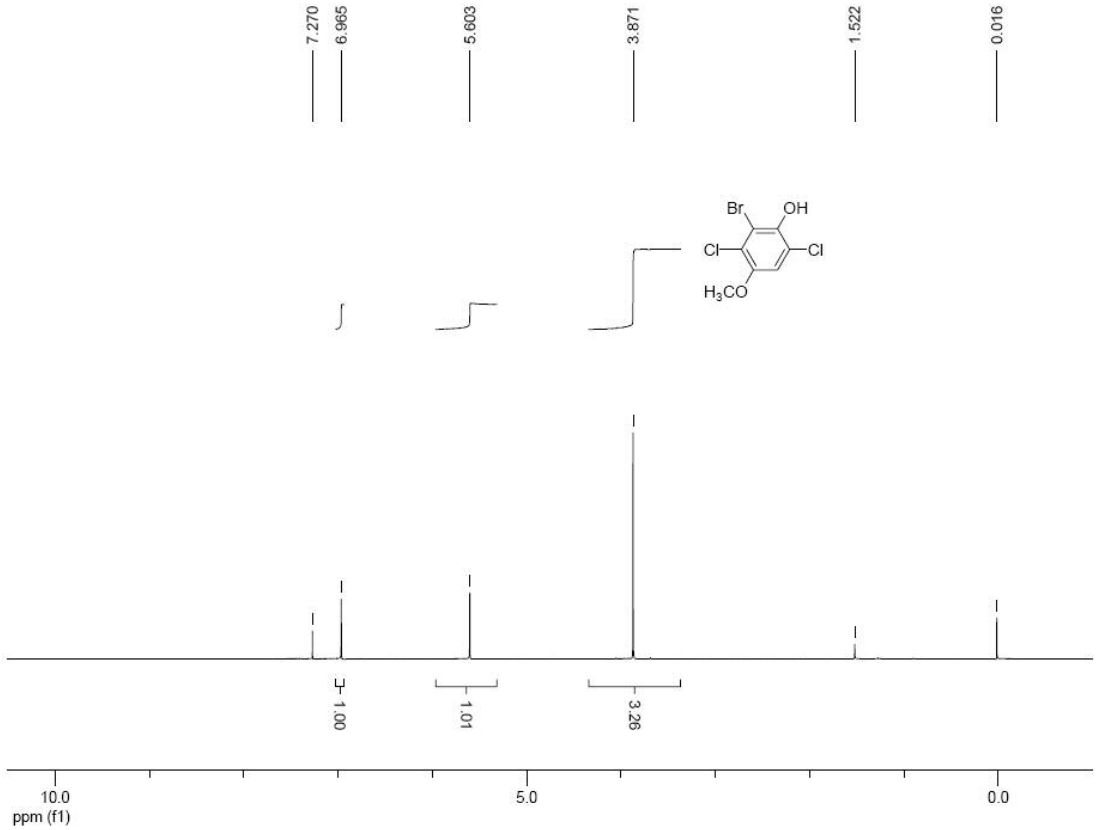
4,4’-Dichloro-biphenyl-2,5-diol (14)

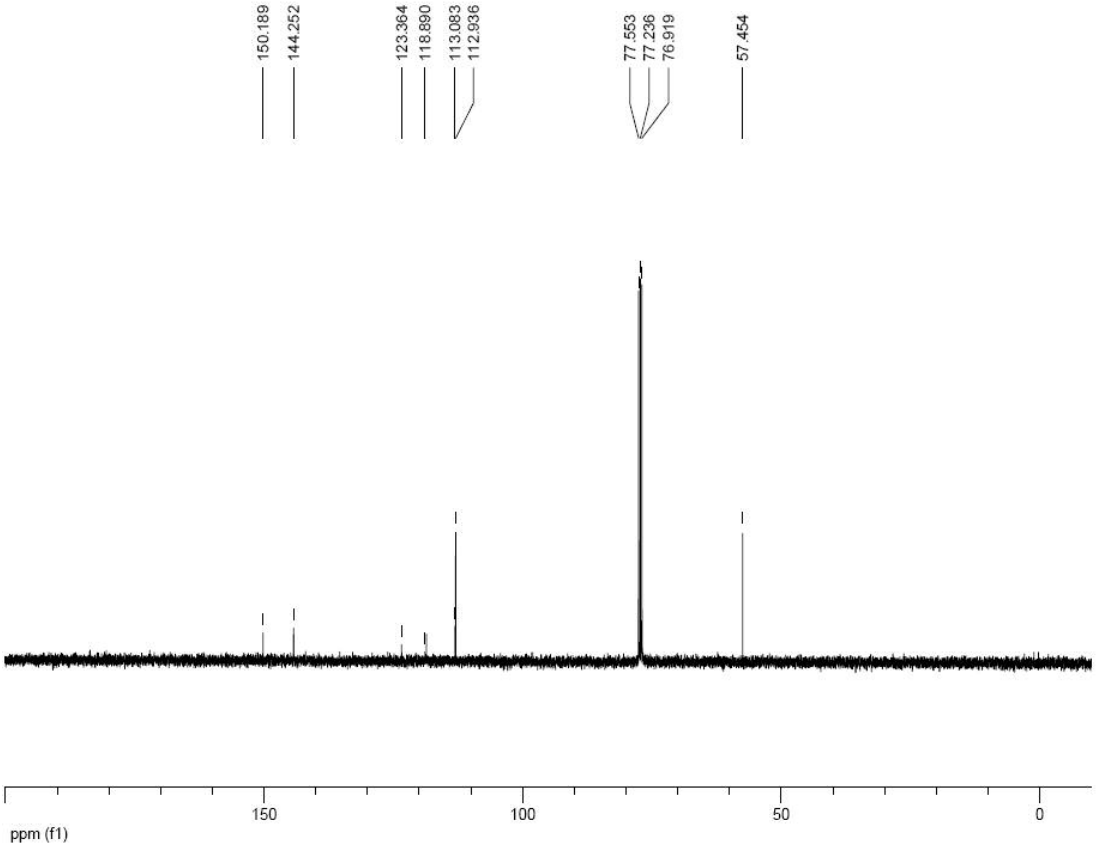


2-Chloro-5-(4-chloro-phenyl)-[1,4]benzoquinone (15)

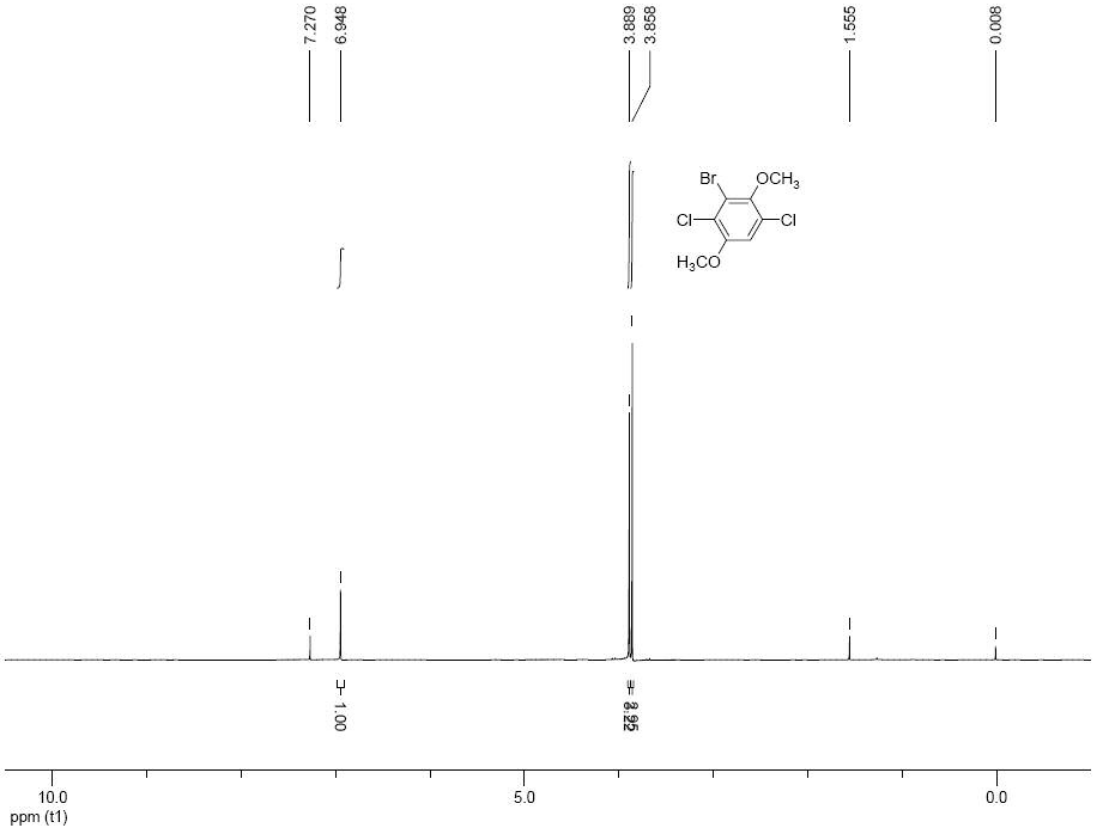


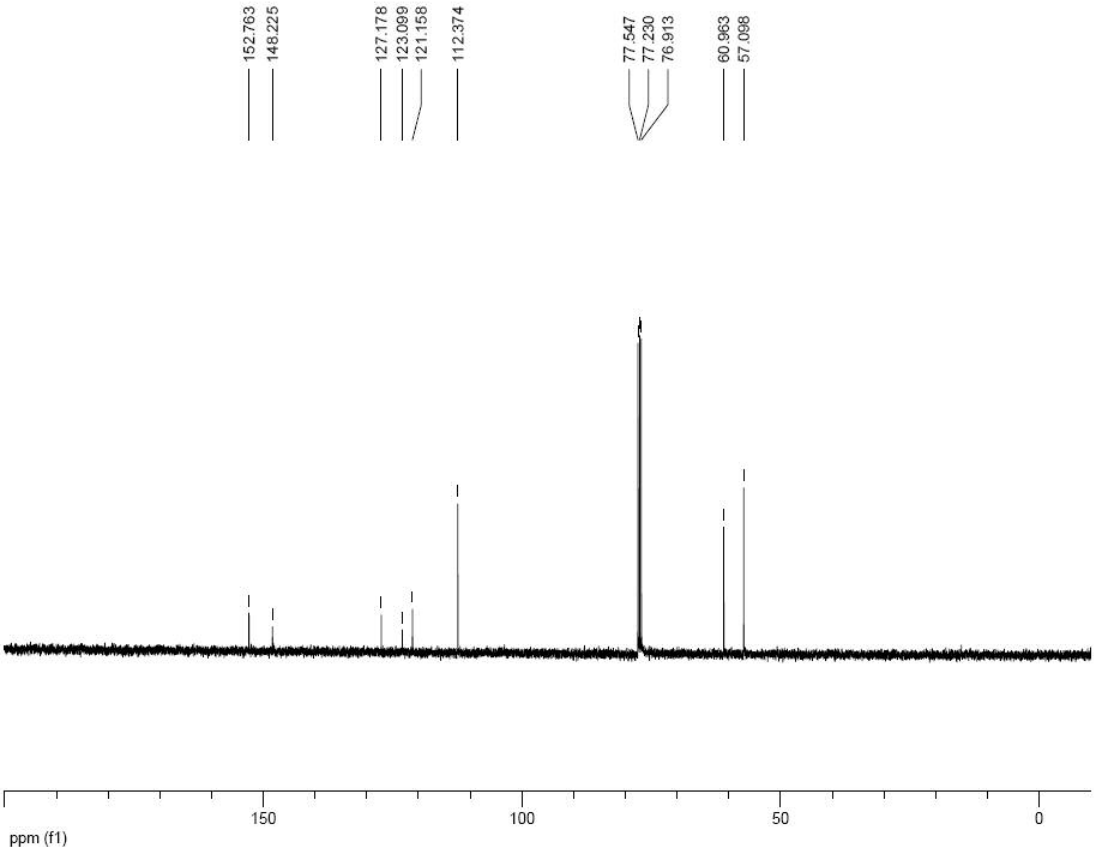
2-Bromo-3,6-dichloro-4-methoxy-phenol (17)



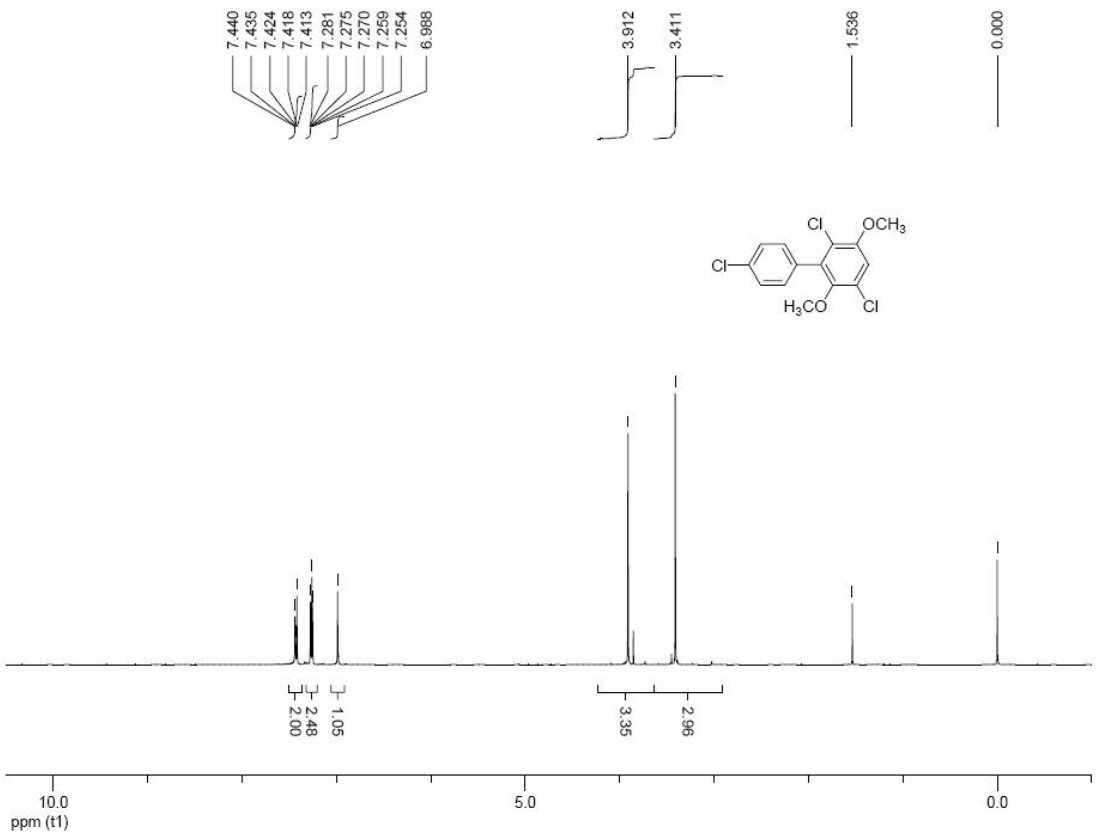


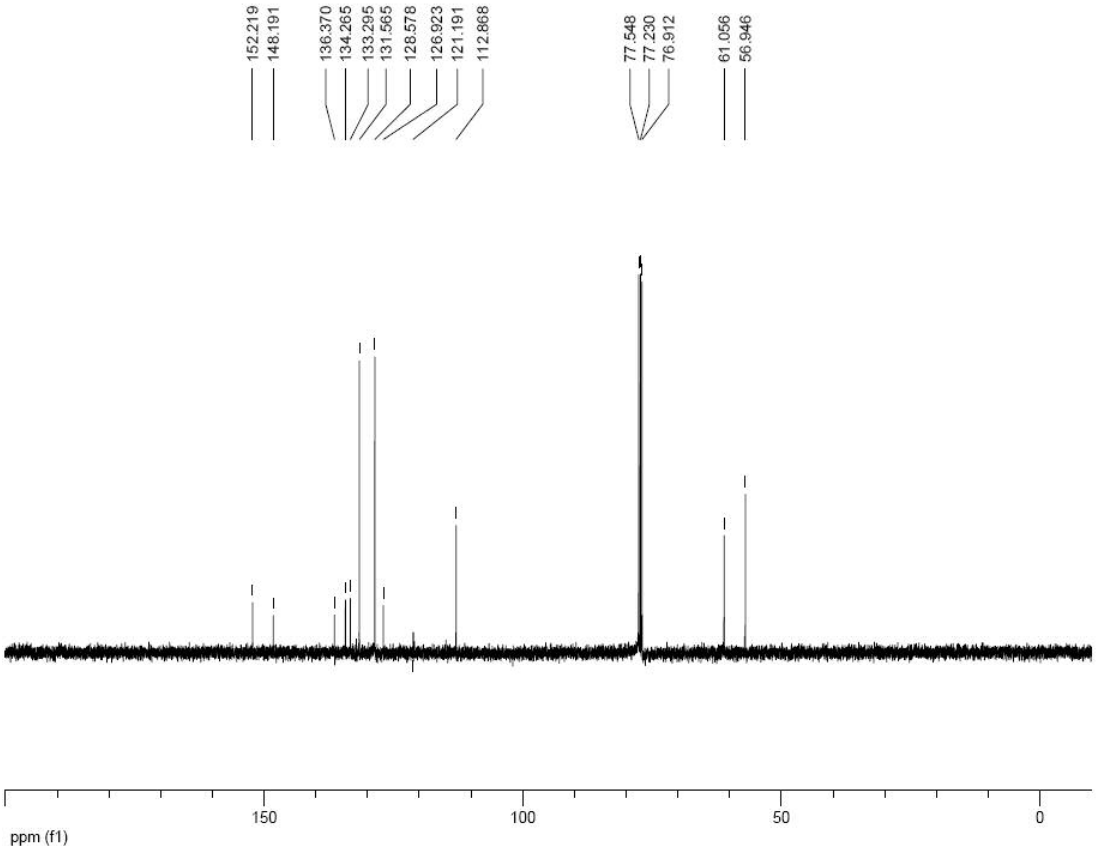
3-Bromo-2,5-dichloro-1,4-dimethoxy-benzene (18)



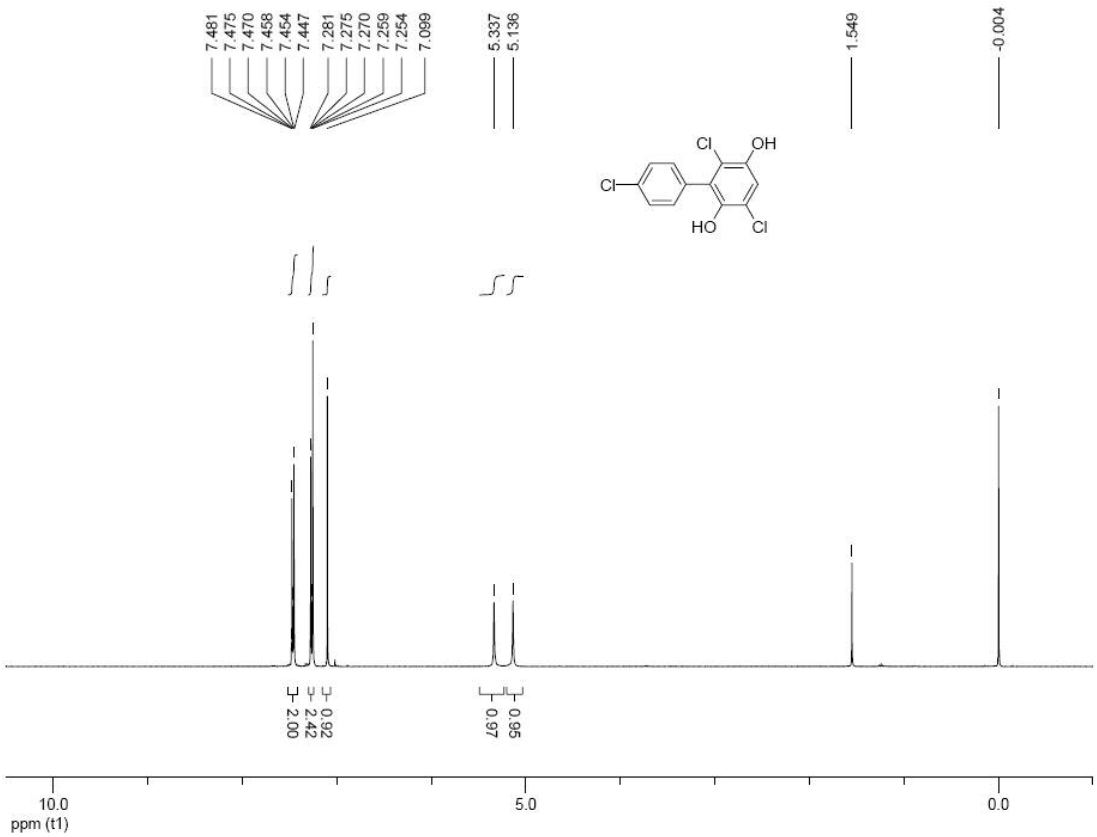


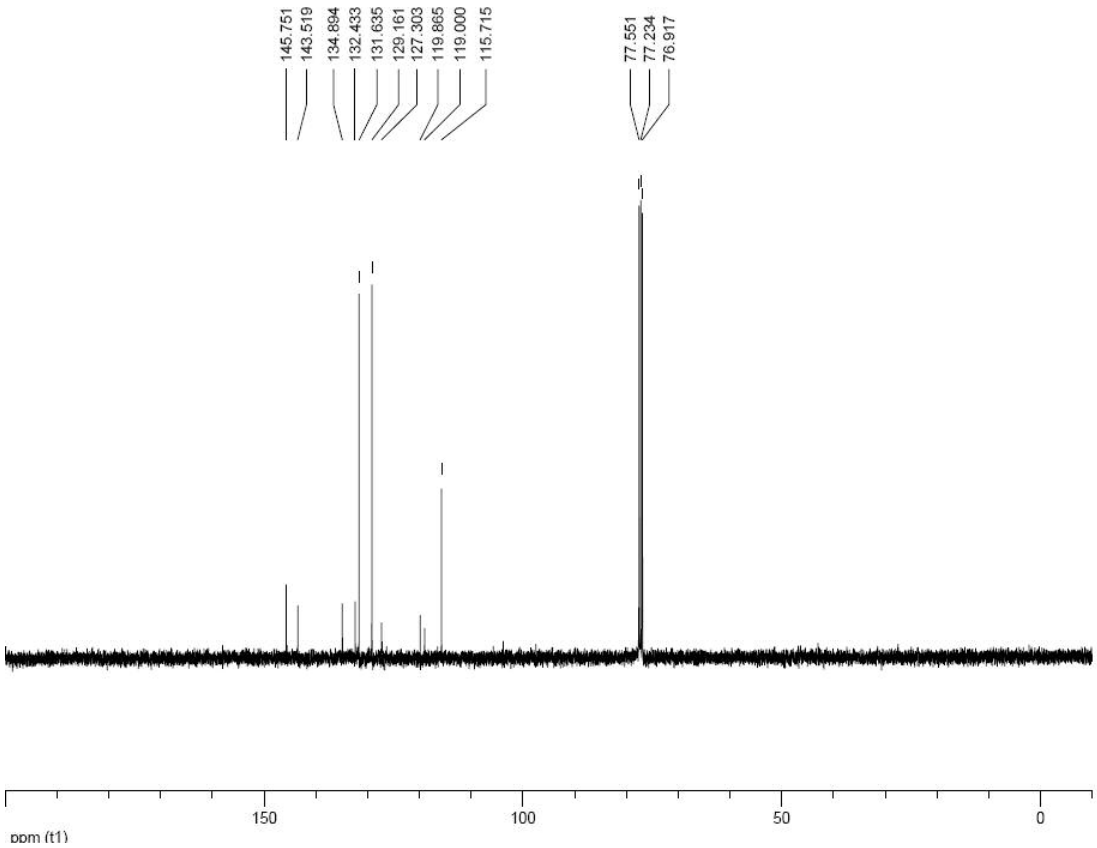
3,6,4'-Trichloro-2,5-dimethoxy-biphenyl (19)



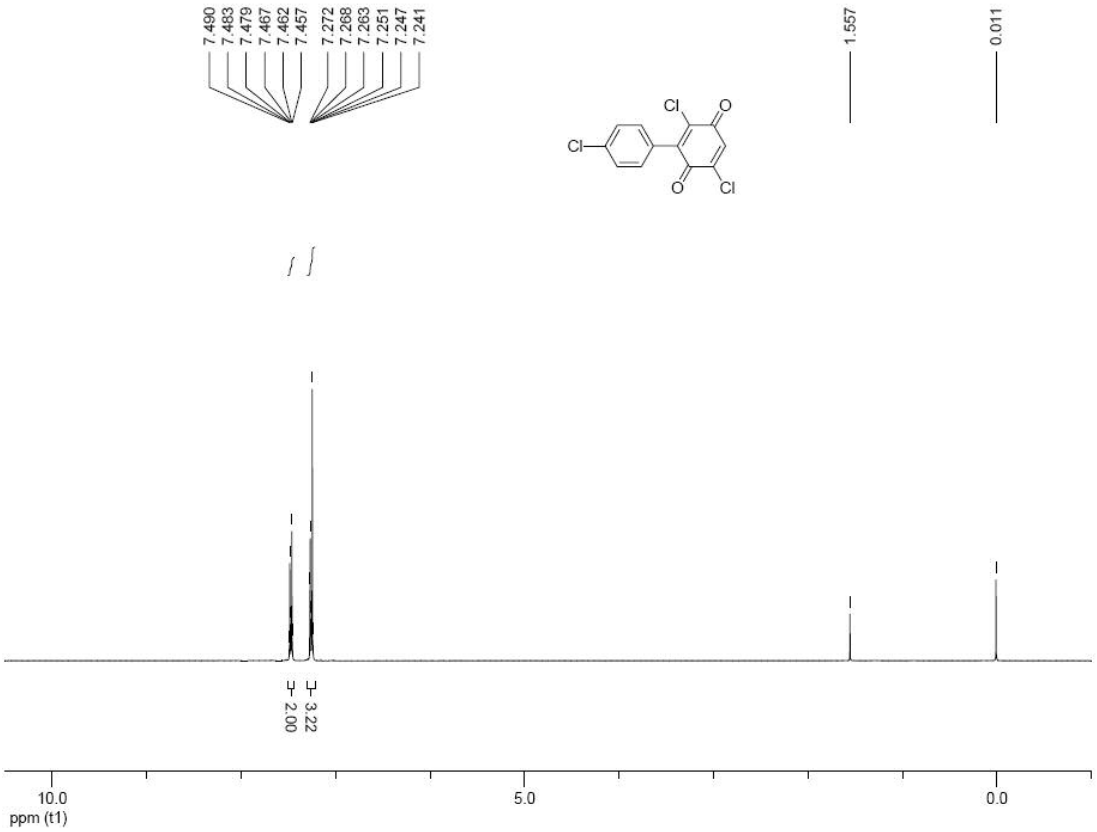


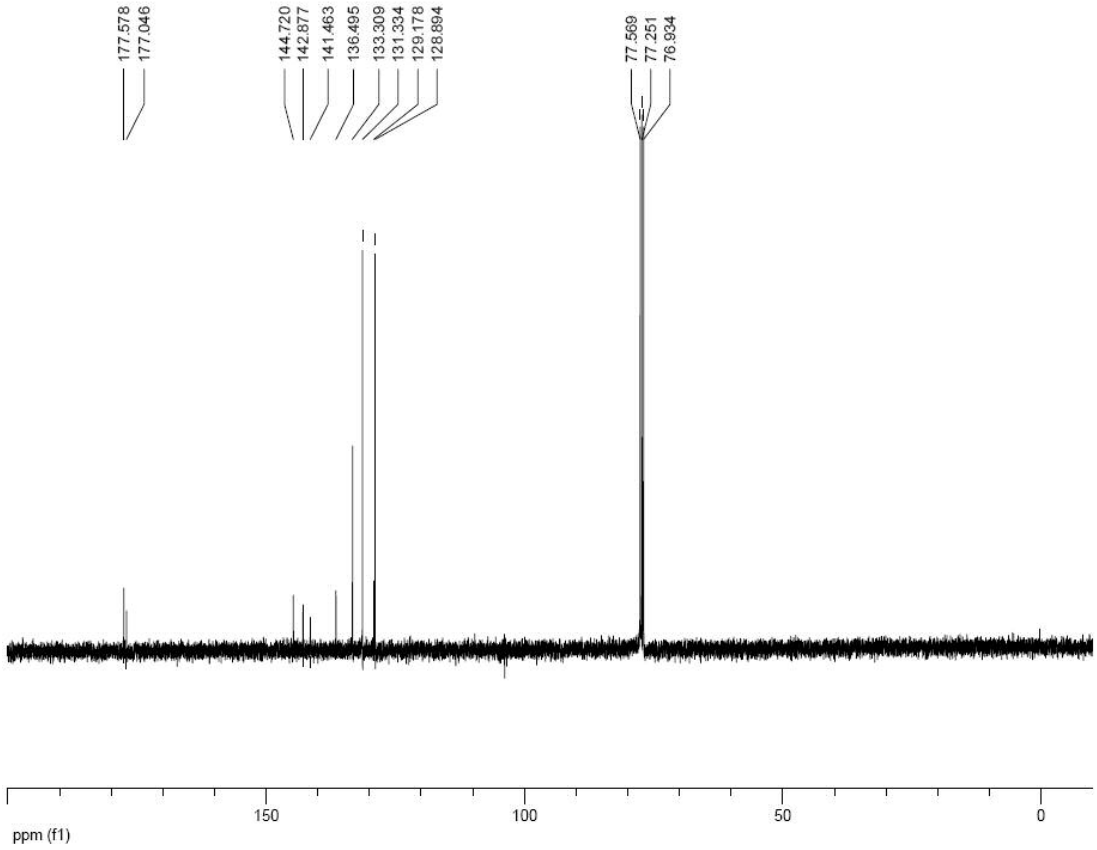
3,6,4'-Trichloro-biphenyl-2,5-diol (20)



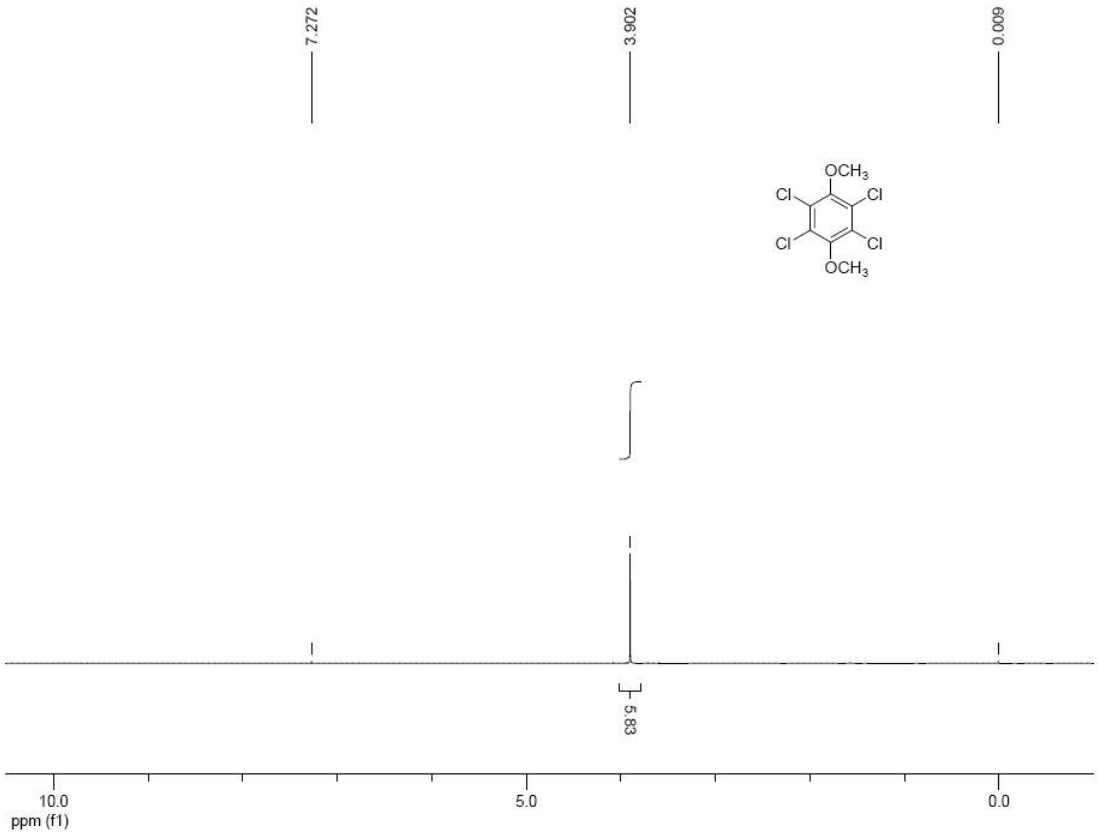


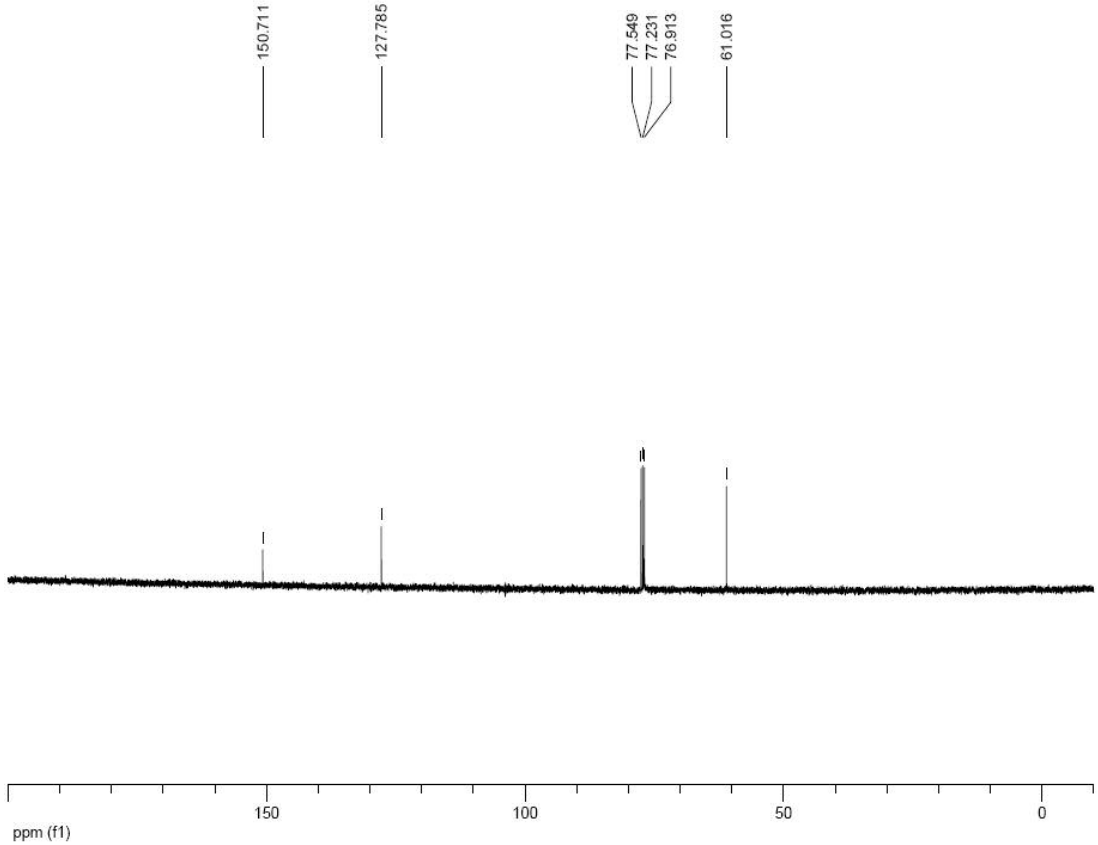
2,5-Dichloro-3-(4-chloro-phenyl)-[1,4]benzoquinone (21)



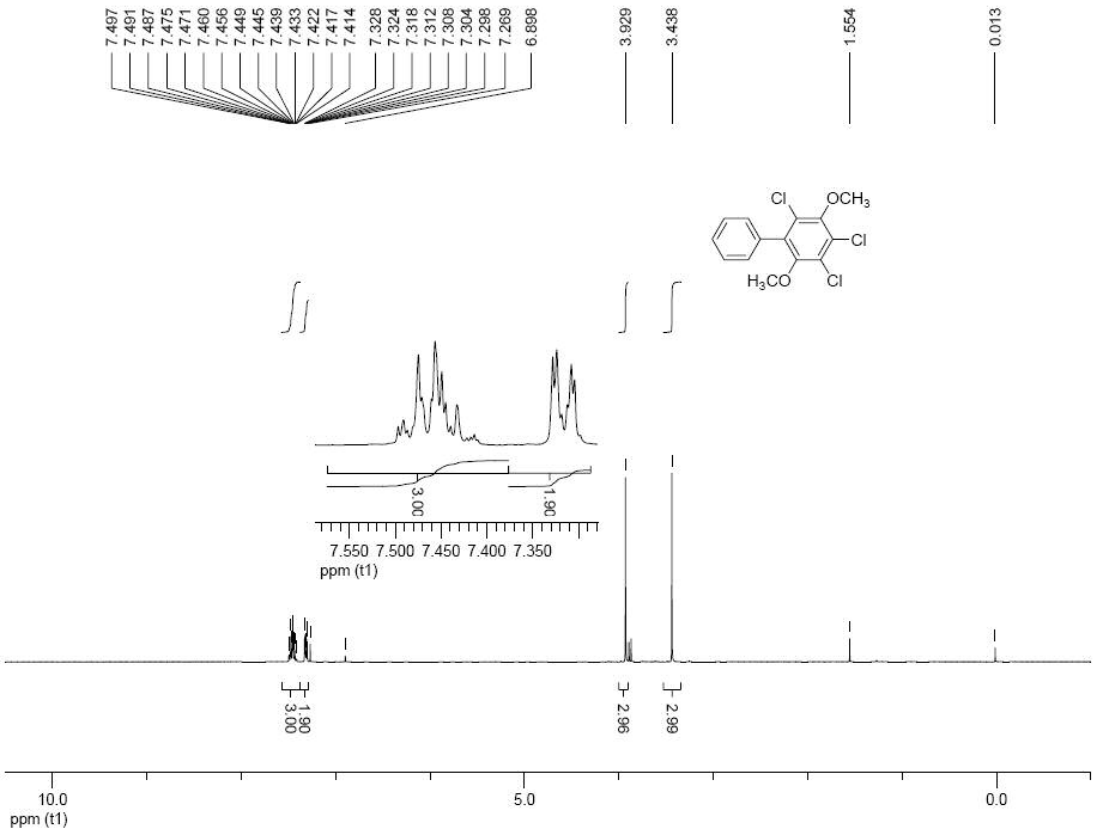


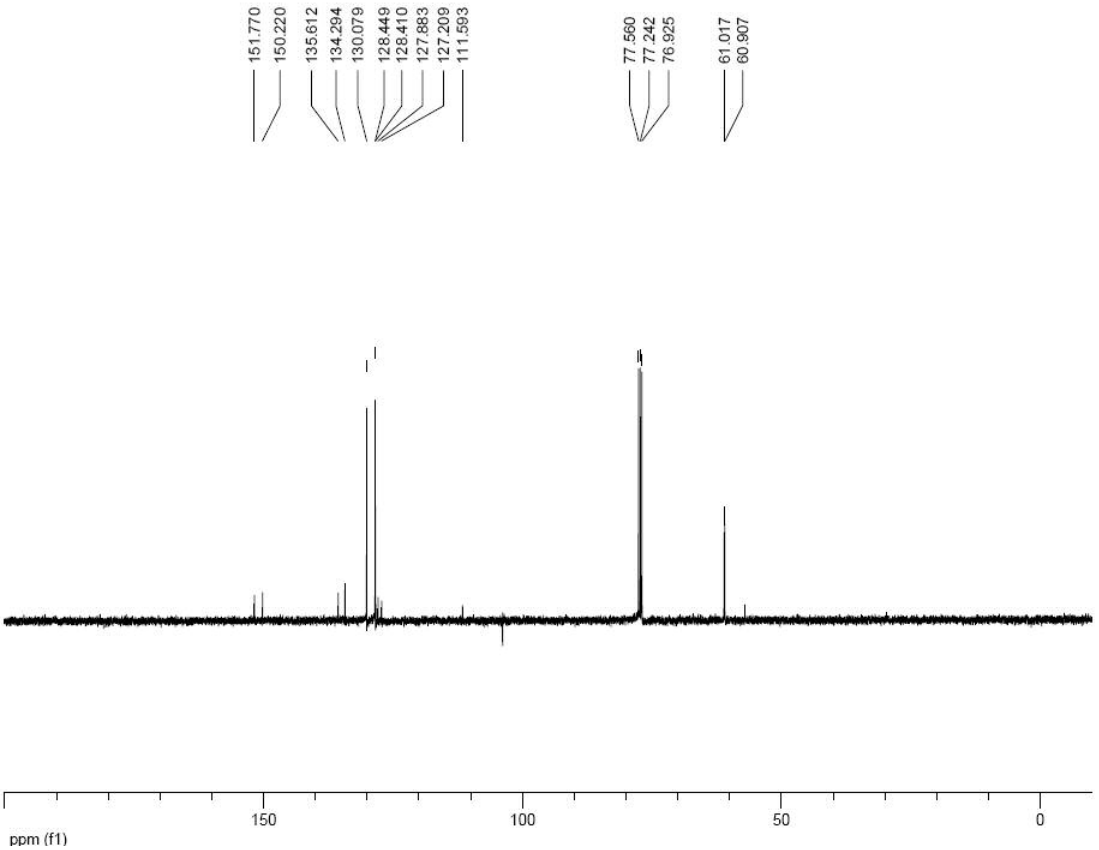
1,2,4,5-Tetrachloro-3,6-dimethoxy-benzene (23)



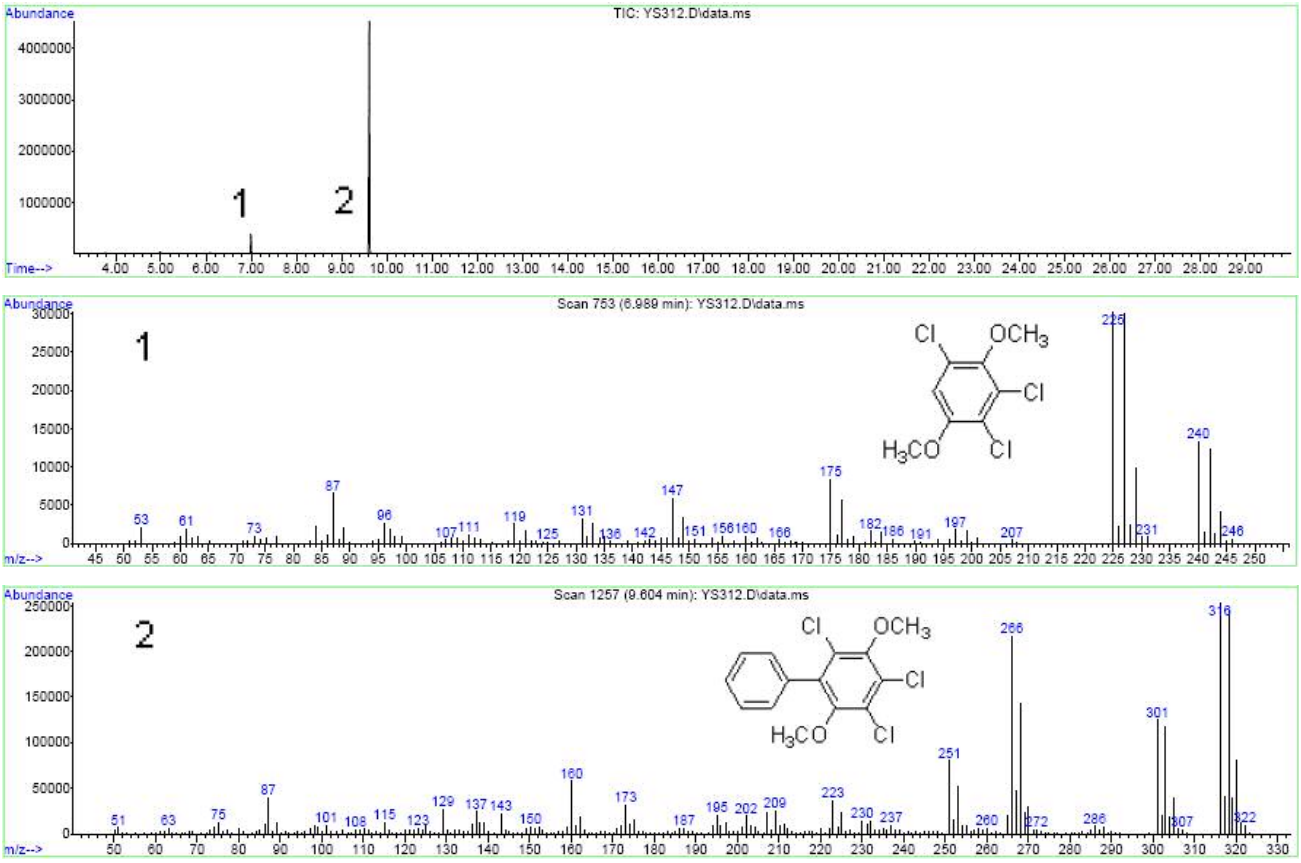


3,4,6-Trichloro-2,5-dimethoxy-biphenyl (24), crude (contains 12.5% of 2,3,6-trichloro-1,4-dimethoxy-benzene)

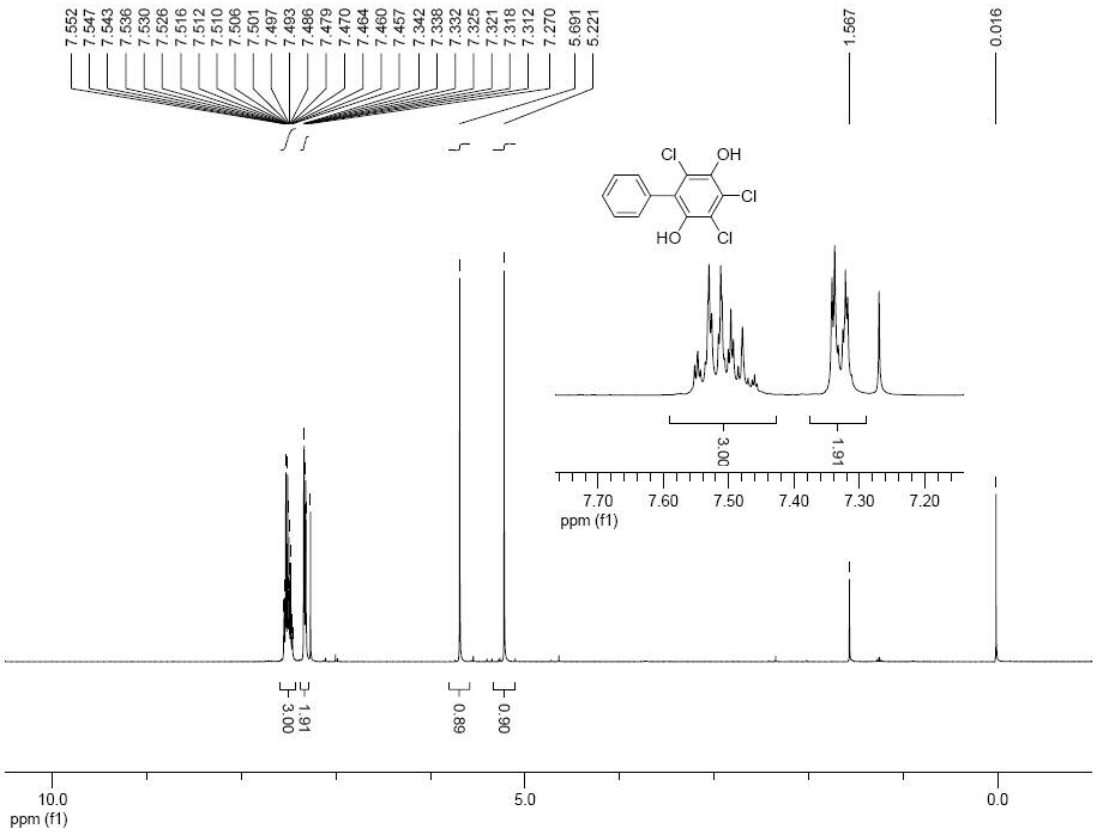


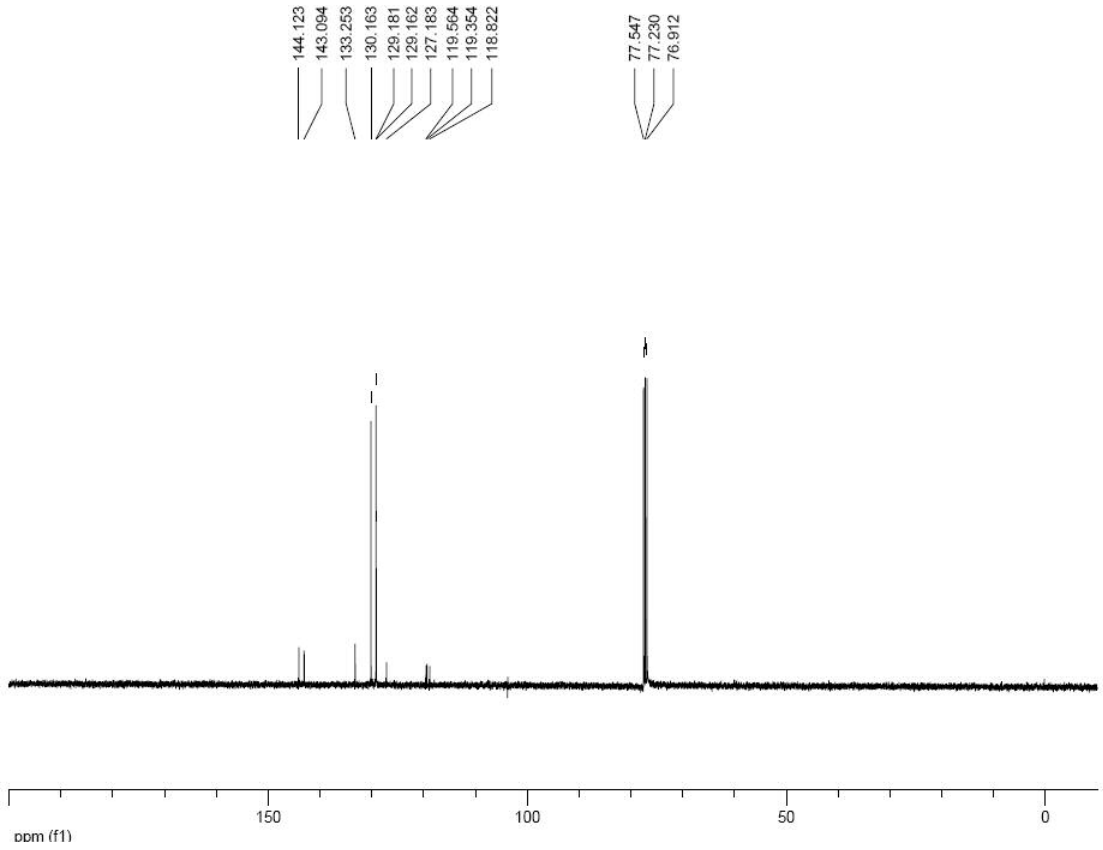


Gas chromatogram and mass spectrum of 3,4,6-trichloro-2,5-dimethoxy-biphenyl (24) (contains 12.5% of 2,3,6-trichloro-1,4-dimethoxy-benzene)

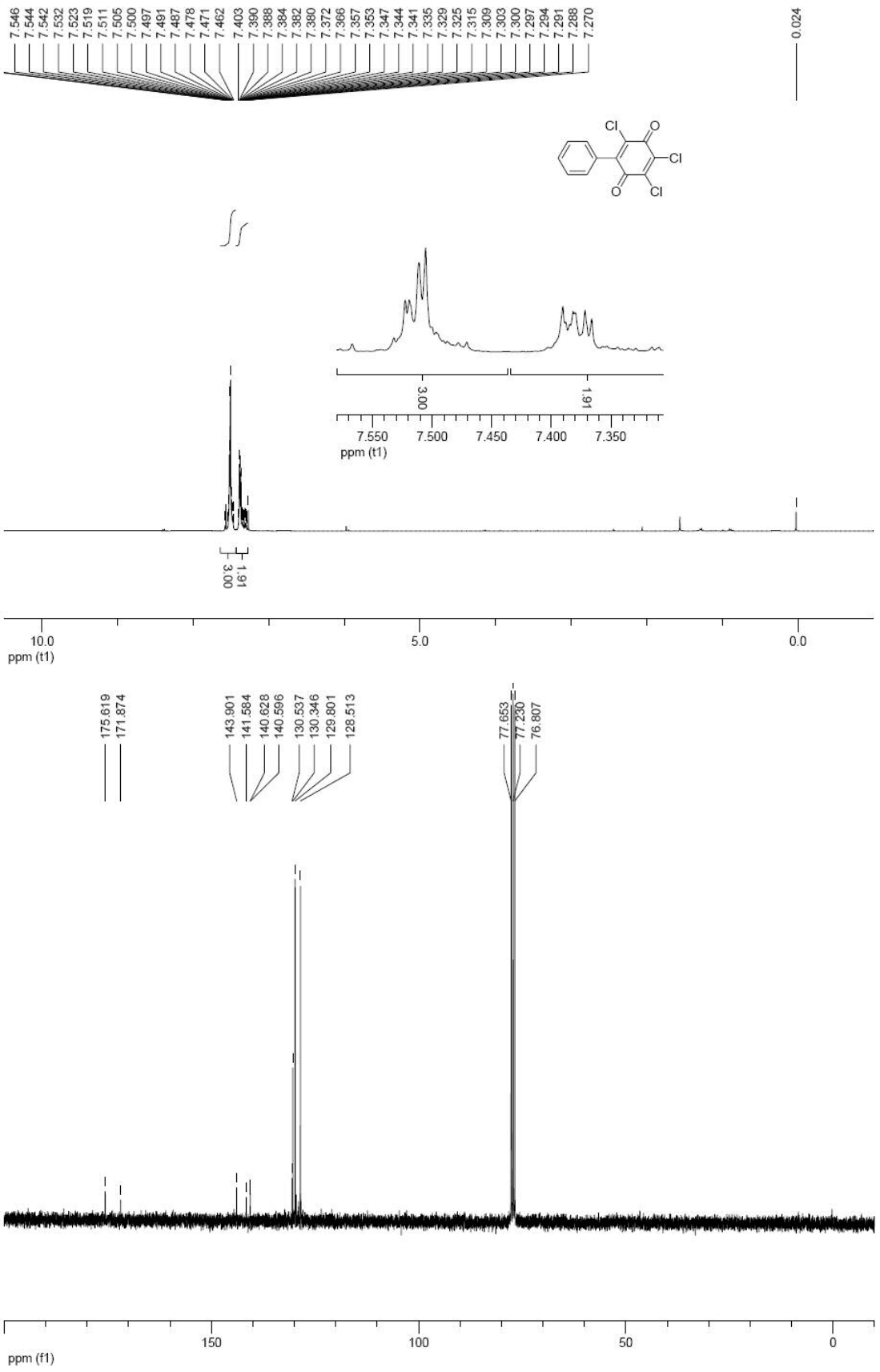


3,4,6-Trichloro-biphenyl-2,5-diol (25)

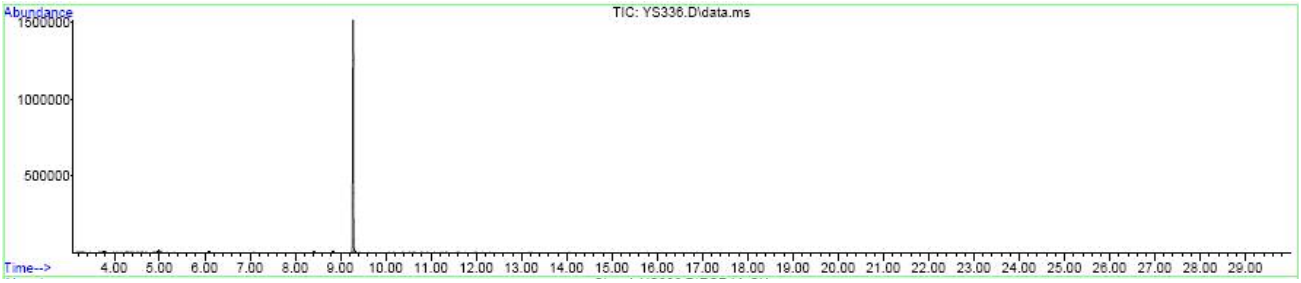




2,3,5-Trichloro-6-phenyl-[1,4]benzoquinone (26)



Gas chromatogram and mass spectrum of 2,3,5-trichloro-6-phenyl-[1,4]benzoquinone (26)



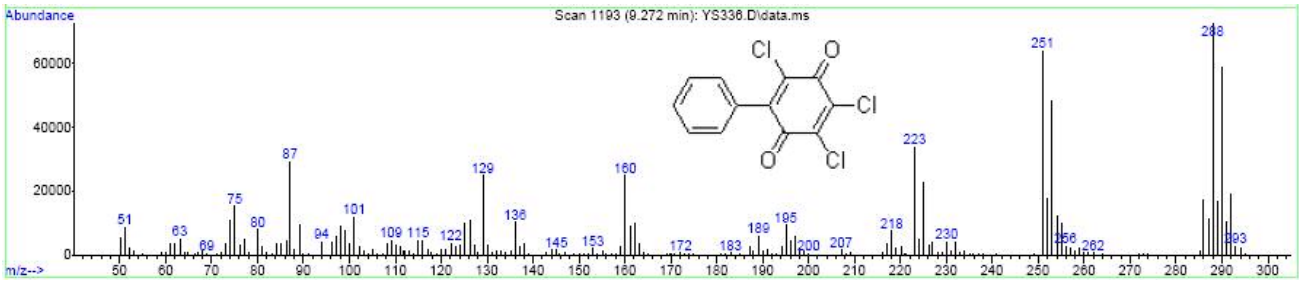


Table S1. Crystal data and structure refinement for compound 13

Crystal data

$C_{12}H_9ClO_2$	$Z = 4$
$M_r = 220.64$	$D_x = 1.486$ Mg m^{-3}
Monoclinic, P 21/n	Mo $K\alpha$ radiation
$a = 7.4814(2)$ Å	Cell parameters from 2374 reflections
$b = 11.3273(3)$ Å	$\theta = 1.0–27.5°$
$c = 11.7221(3)$ Å	$\mu = 0.36$ mm^{-1}
$\beta = 97.00°$	$T = 90.0(2)$ K
$V = 985.97(4)$ Å^3	Block, colourless

Data collection

Nonius KappaCCD diffractometer	1800 reflections with $I > 2\sigma(I)$
ω scans at fixed $\chi = 55°$	$R_{int} = 0.024$
Absorption correction: multi-scan (based on symmetry-related measurements)	$\theta_{max} = 27.5°$
$T_{min} = 0.925$, $T_{max} = 0.948$	$h = -9 \rightarrow 9$
4332 measured reflections	$k = -14 \rightarrow 14$
2257 independent reflections	$l = -15 \rightarrow 15$

Refinement

Refinement on F^2	138 parameters
	H atoms constrained to parent site
$wR(F^2) = 0.097$	$\Delta\rho_{max} = 0.29$ e Å^{-1}
$S = 1.055$	$\Delta\rho_{min} = -0.30$ e Å^{-1}
2257 reflections	Extinction correction: none

Table S2. Crystal data and structure refinement for compound 17

Crystal data

$C_7H_5BrCl_2O_2$	$Z = 4$
$M_r = 271.92$	$D_x = 2.081$ Mg m^{-3}
triclinic, P $\bar{1}$	Mo $K\alpha$ radiation
$a = 8.10327(10)$ Å	Cell parameters from 14313 reflections
$b = 9.2723(2)$ Å	$\theta = 1.00\text{-}27.48°$
$c = 12.0905(2)$ Å	$\mu = 5.303$ mm^{-1}
$\alpha = 85.87°$	$T = 90.0(2)$ K
$\beta = 75.37°$	Slab, colourless
$\gamma = 81.08º$	
$V = 867.85(3)$ Å^3	

Data collection

Nonius KappaCCD diffractometer	3440 reflections with $I > 2\sigma(I)$
ω scans at fixed $\chi = 55°$	$R_{int} = 0.0393$
Absorption correction: multi-scan (based on symmetry-related measurements)	$\theta_{max} = 27.5°$
$T_{min} = 0.16$, $T_{max} = 0.588$	$h = -10 \rightarrow 10$
19069 measured reflections	$k = -12 \rightarrow 12$
3978 independent reflections	$l = -15 \rightarrow 15$

Refinement

Refinement on F^2	222 parameters
	H atoms constrained to parent site
$wR(F^2) = 0.052$	$\Delta\rho_{max} = 0.57$ e Å^{-1}
$S = 1.045$	$\Delta\rho_{min} = -0.48$ e Å^{-1}
3978 reflections	Extinction correction: none

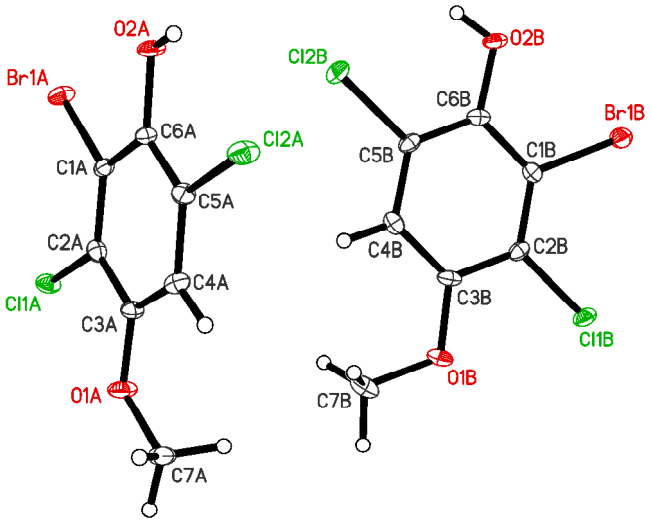


Figure S1. Molecular structure derived from the crystal structure of **17**.

Table S3. Crystal data and structure refinement for compound 20

Crystal data

$C_{12}H_7Cl_3O_2$	$Z = 4$
$M_r = 289.53$	$D_x = 1.676$ Mg m^{-3}
monoclinic, P 21/c	Cu $K\alpha$ radiation
$a = 9.2876(4)$ Å	Cell parameters from 15828 reflections
$b = 9.0426(4)$ Å	$\theta = 4.82\text{-}69.28°$
$c = 13.8328(7)$ Å	$\mu = 7.113$ mm^{-1}
$\beta = 98.89°$	$T = 90.0(2)$ K
$V = 1147.76(9)$ Å^3	Lath, colourless

Data collection

Nonius KappaCCD diffractometer	2022 reflections with $I > 2\sigma(I)$
ϕ and ω scans	$R_{int} = 0.0432$
Absorption correction: multi-scan (based on symmetry-related measurements)	$\theta_{max} = 69.3°$
$T_{min} = 0.553$, $T_{max} = 0.871$	$h = -11 \rightarrow 11$
15828 measured reflections	$k = -10 \rightarrow 10$
2126 independent reflections	$l = -16 \rightarrow 13$

Refinement

Refinement on F^2	156 parameters
	H atoms constrained to parent site
$wR(F^2) = 0.070$	$\Delta\rho_{max} = 0.28$ e Å^{-1}
$S = 1.050$	$\Delta\rho_{min} = -0.28$ e Å^{-1}
2126 reflections	Extinction correction: none

References

(1) McLean, M. R.; Bauer, U.; Amaro, A. R.; Robertson, L. W. *Chem. Res. Toxicol.* **1996**, *9*, 158-164.

(2) Amaro, A. R.; Oakley, G. G.; Bauer, U.; Spielmann, H. P.; Robertson, L. W. *Chem. Res. Toxicol.* **1996**, *9*, 623-629.

(3) Bauer, U.; Amaro, A. R.; Robertson, L. W. *Chem. Res. Toxicol.* **1995**, *8*, 92-95.

(4) Homer, L.; Weber, K. H. *Chemische Berichte* **1963**, *96*, 1568-1578.

(5) Blatchly, J. M.; McOmie, J. F. W.; Watts, M. L. *f. Chem. Soc.* **1962**, 5085-5090.

(6) Kania-Korwel, I.; Parkin, S.; Robertson, L. W.; Lehmler, H. J. *Chemosphere* **2004**, *56*, 735-744.

(7) Lehmler, H.-J.; Robertson, L. W. *Chemosphere* **2001**, *45*, 1119-1127.

(8) Wilson, J. G. *Aust. J. Chem.* **1972**, *25*, 2383-2391.

(9) Lopez-Alvarado, P.; Avendano, C.; Menendez, J. C. *Synthetic Communications* **2002**, *32*, 3233-3239.

(10) Cain, B. F. *J. Chem. Soc. C: Organic* **1966**, 1041-1045.

(11) Brassard, P.; L'Ecuyer, P. *Can. J. Chem.* **1958**, *36*, 814-819.

(12) Dunn, J. A.; Pezacki, J. P.; McGlinchey, M. J.; Warkentin, J. *J. Org. Chem.* **1999**, *64*, 4344-4352.

(13) Ramirez, F.; Dershowitz, S. *J. Am. Chem. Soc.* **1959**, *81*, 587-590.

(14) Reddy, G. V. B.; Gold, M. H. *Microbiology* **2000**, *146*, 405-413.