

Synthesis of Highly Substituted Furans by the Electrophile-Induced Coupling of 2-(1-Alkynyl)-2-alken-1-ones and Nucleophiles

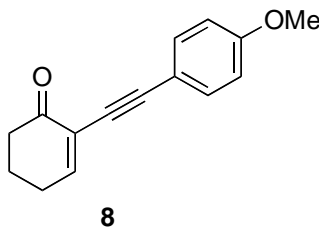
Tuanli Yao, Xiaoxia Zhang and Richard C. Larock*

Department of Chemistry, Iowa State University, Ames, Iowa 50011

larock@iastate.edu

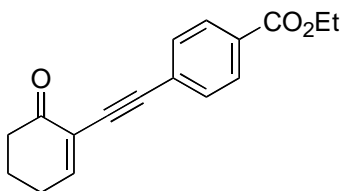
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General procedures. All ^1H and ^{13}C NMR spectra were recorded at 300 and 75.5 MHz. Thin-layer chromatography was performed using commercially prepared 60-mesh silica gel plates (Whatman K6F), and visualization was effected with short wavelength UV light (254 nm) and a basic KMnO_4 solution [3 g of KMnO_4 + 20 g of K_2CO_3 + 5 mL of NaOH (5%) + 300 mL of H_2O]. All melting points are uncorrected. High resolution mass spectra were recorded on a Kratos MS50TC double focusing magnetic sector mass spectrometer using EI at 70 eV. Compounds **1**, **2**, **16**, **17**, **29**, **30**, **36**, **38**, **40**, **47**, **49**, **54**, **56**, **60**, **62**, **63**, **65**, **66**, **69** and **70** have been previously reported.¹



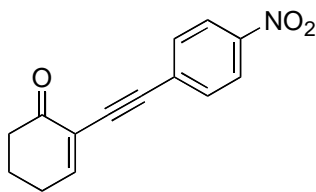
2-(4-Methoxyphenyl)ethynyl-2-cyclohexen-1-one (8). This 2-(1-alkynyl)-2-alken-1-one was prepared from 2-iodo-2-cyclohexen-1-one² by following a procedure from the literature.³ 2-Iodo-2-cyclohexen-1-one (444 mg, 2.0 mmol), $\text{PdCl}_2(\text{PPh}_3)_2$ (70.2 mg, 0.05 equiv), (4-methoxyphenyl)ethyne (529 mg, 2.0 equiv) and CuI (38 mg, 0.1 equiv) were taken up in THF (14 mL) at 0 °C. Diisopropylamine (0.84 mL, 3.0 equiv) was added, and the resulting mixture was stirred at 0 °C for 45 min. The mixture was diluted with Et_2O (100 mL) and washed with 1M HCl (50 mL) and brine (20 mL). The organic layer was dried over MgSO_4 , filtered and concentrated. The residue was purified by flash column chromatography (silica gel, 3:1 hexane/ EtOAc) to afford 301 mg (67%) of the indicated compound **8** as light yellow solid: mp 70-71 °C; ^1H NMR (CDCl_3) δ 2.03-2.10 (m, 2H), 2.46-2.55 (m, 4H), 3.80 (s, 3H), 6.83 (dt, J = 8.4, 2.1 Hz, 2H), 7.32 (t, J = 4.5

Hz, 1H), 7.43 (dt, $J = 9.0, 2.1$ Hz, 2H); ^{13}C NMR (CDCl_3) δ 22.7, 26.7, 38.4, 55.5, 82.7, 92.4, 114.1, 115.2, 125.7, 133.5, 153.8, 159.9, 196.0; IR (CH_2Cl_2) 2952, 1688, 1510, 1249 cm^{-1} ; HRMS m/z 226.0996 (calcd for $\text{C}_{15}\text{H}_{14}\text{O}_2$, 226.0994).



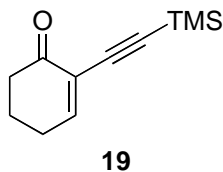
11

Ethyl 4-[(6-oxocyclohexenyl)ethynyl]benzoate (11). This 2-(1-alkynyl)-2-alken-1-one was prepared from 2-iodo-2-cyclohexen-1-one² by following the same procedure as that used for compound **8**. 2-Iodo-2-cyclohexen-1-one (222 mg, 1.0 mmol), ethyl 4-ethynylbenzoate (348 mg, 2.0 equiv), $\text{PdCl}_2(\text{PPh}_3)_2$ (35.6 mg, 0.05 equiv), CuI (20 mg, 0.1 equiv) and diisopropylamine (0.42 mL, 3.0 equiv) afforded, after purification by flash column chromatography (silica gel, 3:1 hexane/EtOAc), 160 mg (60%) of the indicated compound **11** as a yellow solid: mp 116-117 $^\circ\text{C}$; ^1H NMR (CDCl_3) δ 1.38 (t, $J = 6.9$ Hz, 3H), 2.05-2.10 (m, 2H), 2.48-2.57 (m, 4H), 4.36 (q, $J = 6.9$ Hz, 2H), 7.39 (t, $J = 4.5$ Hz, 1H), 7.54 (dt, $J = 8.4, 1.8$ Hz, 2H), 7.98 (dt, $J = 8.7, 1.8$ Hz, 2H); ^{13}C NMR (CDCl_3) δ 14.5, 22.6, 26.8, 38.3, 61.4, 86.8, 91.5, 125.3, 127.7, 129.6, 130.2, 131.9, 155.3, 166.3, 195.6; IR (CH_2Cl_2) 2981, 1714, 1682 cm^{-1} ; HRMS m/z 268.1103 (calcd for $\text{C}_{17}\text{H}_{16}\text{O}_3$, 268.1099).



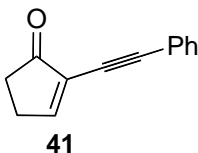
14

2-(4-Nitrophenyl)ethynyl-2-cyclohexen-1-one (14). This 2-(1-alkynyl)-2-alken-1-one was prepared from 2-iodo-2-cyclohexen-1-one² by following the same procedure as that used for compound **8**. 2-Iodo-2-cyclohexen-1-one (222 mg, 1.0 mmol), (4-nitrophenyl)ethyne (294 mg, 2.0 equiv), PdCl₂(PPh₃)₂ (35.6 mg, 0.05 equiv), CuI (20 mg, 0.1 equiv) and diisopropylamine (0.42 mL, 3.0 equiv) afforded, after purification by flash column chromatography (silica gel, 2:1 hexane/EtOAc), 168 mg (70%) of the indicated compound **14** as a yellow solid: mp 113-115 °C; ¹H NMR (CDCl₃) δ 2.06-2.11 (m, 2H), 2.51-2.58 (m, 4H), 4.36 (q, *J* = 6.9 Hz, 2H), 7.44 (t, *J* = 4.5 Hz, 1H), 7.62 (d, *J* = 9.0 Hz, 2H), 8.18 (d, *J* = 9.0 Hz, 2H); ¹³C NMR (CDCl₃) δ 22.5, 26.9, 38.3, 89.3, 90.3, 123.8, 125.0, 130.1, 132.7, 147.3, 156.2, 195.4; IR (CH₂Cl₂) 3055, 2952, 1682, 1592 cm⁻¹; HRMS *m/z* 241.0743 (calcd for C₁₄H₁₁NO₃, 241.0739).

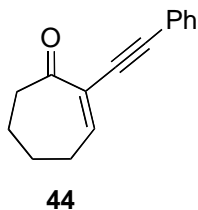


2-(Trimethylsilyl)ethynyl-2-cyclohexen-1-one (19). This 2-(1-alkynyl)-2-alken-1-one was prepared from 2-iodo-2-cyclohexen-1-one² by following the same procedure as that used for compound **8**. 2-Iodo-2-cyclohexen-1-one (222 mg, 1.0 mmol), (trimethylsilyl)ethyne (196 mg, 2.0 equiv), PdCl₂(PPh₃)₂ (35.6 mg, 0.05 equiv), CuI (20 mg, 0.1 equiv) and diisopropylamine (0.42 mL, 3.0 equiv) afforded, after purification by flash column chromatography (silica gel, 5:1 hexane/EtOAc), 159 mg (83%) of the indicated compound **19** as a white solid: mp 100-101 °C; ¹H NMR (CDCl₃) δ 0.20 (t, *J* = 3.5 Hz, 9H), 1.98-2.03 (m, 2H), 2.40-2.49 (m, 4H), 7.32 (t, *J* = 4.4 Hz, 1H); ¹³C NMR

(CDCl₃) δ 0.0, 22.4, 26.5, 38.1, 97.6, 99.3, 125.4, 155.5, 195.5; IR (CH₂Cl₂) 3042, 2960, 1682, 1349 cm⁻¹; HRMS m/z 192.0974 (calcd for C₁₁H₁₆OSi, 192.0970).

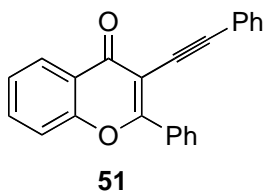


2-Phenylethynyl-2-cyclopenten-1-one (41). This 2-(1-alkynyl)-2-alken-1-one was prepared from 2-iodo-2-cyclopenten-1-one² by following the same procedure as that used for compound **8**. 2-Iodo-2-cyclopenten-1-one (208 mg, 1.0 mmol), phenylacetylene (204 mg, 2.0 equiv), PdCl₂(PPh₃)₂ (35.6 mg, 0.05 equiv), CuI (20 mg, 0.1 equiv) and diisopropylamine (0.42 mL, 3.0 equiv) afforded, after purification by flash column chromatography (silica gel, 3:1 hexane/EtOAc), 182 mg (100%) of the indicated compound **41** as a brown solid: mp 65-66 °C; ¹H NMR (CDCl₃) δ 2.49-2.53 (m, 2H), 2.74-2.78 (m, 2H), 7.31-7.33 (m, 3H), 7.49-7.53 (m, 2H), 7.84 (t, J = 3.2 Hz, 1H); ¹³C NMR (CDCl₃) δ 27.7, 34.3, 80.1, 96.0, 122.7, 128.5, 129.0, 130.3, 132.1, 165.4, 205.9; IR (CH₂Cl₂) 3061, 2923, 1716, 1488 cm⁻¹; HRMS m/z 182.0734 (calcd for C₁₃H₁₀O, 182.0732).

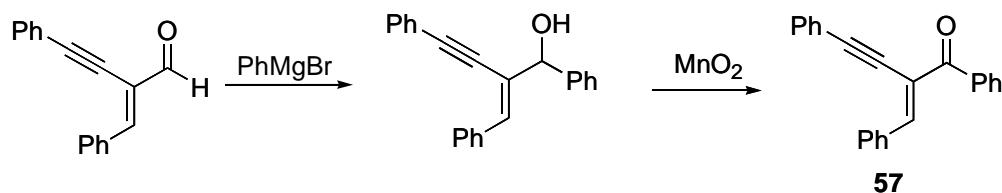


2-Phenylethynyl-2-cyclohepten-1-one (44). This 2-(1-alkynyl)-2-alken-1-one was prepared from 2-iodo-2-cyclohepten-1-one⁴ by following the same procedure as that used for compound **8**. 2-Iodo-2-cyclohepten-1-one (236 mg, 1.0 mmol), phenylacetylene (204

mg, 2.0 equiv), PdCl₂(PPh₃)₂ (35.6 mg, 0.05 equiv), CuI (20 mg, 0.1 equiv) and diisopropylamine (0.42 mL, 3.0 equiv) afforded, after purification by flash column chromatography (silica gel, 5:1 hexane/EtOAc), 90 mg (43%) of the indicated compound **44** as a yellow oil: ¹H NMR (CDCl₃) δ 1.77-1.86 (m, 4H), 2.47-2.54 (m, 2H), 2.68 (t, *J* = 6.5 Hz, 2H), 7.14 (t, *J* = 6.3 Hz, 1H), 7.25-7.31 (m, 3H), 7.44-7.48 (m, 2H); ¹³C NMR (CDCl₃) δ 21.7, 25.2, 28.7, 42.6, 86.6, 90.4, 123.3, 128.4, 128.5, 128.9, 131.9, 151.2, 201.2; IR (CH₂Cl₂) 3055, 2940, 1679, 1421 cm⁻¹; HRMS *m/z* 210.1047 (calcd for C₁₅H₁₄O, 210.1045).

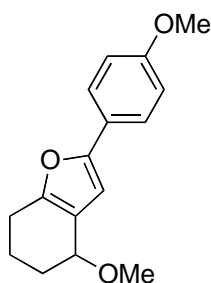


2-Phenyl-3-phenylethynyl-4H-benzopyran-4-one (51). This 2-(1-alkynyl)-2-alken-1-one was prepared from 3-iodo-2-phenyl-4H-benzopyran-4-one⁵ by the following procedure. To a solution of 3-iodo-2-phenyl-4H-benzopyran-4-one (696 mg, 2.0 mmol) and phenylacetylene (245 mg, 1.2 equiv) in Et₃N (20 mL) and DMF (1 mL) were added PdCl₂(PPh₃)₂ (14 mg, 1 mol %) and CuI (2.0 mg, 0.5 mol %). The resulting mixture was stirred at room temperature overnight. The mixture was diluted with CHCl₃ (100 mL) and washed with H₂O (30 mL). The organic layer was dried over MgSO₄ and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, 4:1 hexane/EtOAc) to afford 516 mg (80%) of the indicated compound **51** as a light yellow solid: mp 155-157 °C; ¹H NMR (CDCl₃) δ 7.31-7.35 (m, 3H), 7.42-7.59 (m, 7H), 7.68-7.74 (m, 1H), 8.23-8.32 (m, 3H); IR (CH₂Cl₂) 3071, 1644, 1614, 1463 cm⁻¹; HRMS *m/z* 322.0997 (calcd for C₂₃H₁₄O₂, 322.0994).



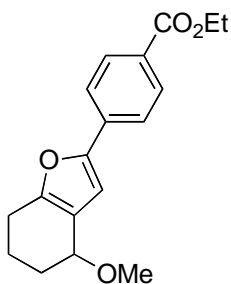
(*E*)-2-Benzylidene-1,4-diphenylbut-3-yn-1-one (57). This 2-(1-alkynyl)-2-alken-1-one was prepared from (*E*)-2-benzylidene-4-phenylbut-3-ynal⁶ by following a procedure from the literature.⁷ To a solution of (*E*)-2-benzylidene-4-phenylbut-3-ynal (531 mg, 2.3 mmol) in dry THF (5 mL) cooled to $-78\text{ }^{\circ}\text{C}$ was added PhMgBr (1 M in THF, 3.5 mL, 3.5 mmol). The reaction was stirred at the same temperature for 30 min and quenched with satd aq NH_4Cl (3 mL). The resulting mixture was extracted with Et_2O (20 mL). The organic layer was washed with brine (20 mL), dried over anhydrous MgSO_4 , filtered and concentrated under reduced pressure. The residue was dissolved in dry THF (30 mL). To this solution was added MnO_2 (4.0 g, 20 equiv), followed by stirring at room temperature for 12 h. The reaction mixture was filtered through a short pad of Celite, which was rinsed with EtOAc. The combined organic layer was concentrated under reduced pressure, and the residue was purified by flash column chromatography (silica gel, 7:1 hexane/EtOAc) to afford 470 mg (66%) of the indicated compound **57** as a light yellow oil: ^1H NMR (CDCl_3) δ 7.33-7.38 (m, 3H), 7.41-7.53 (m, 7H), 7.57-7.63 (m, 1H), 7.67 (s, 1H), 8.02-8.06 (m, 2H), 8.13-8.17 (m, 2H); ^{13}C NMR (CDCl_3) δ 87.5, 101.2, 121.2, 123.1, 128.4, 128.7, 128.9, 129.1, 130.0, 130.7, 130.9, 131.6, 132.8, 135.1, 137.4, 145.4, 193.6; IR (CH_2Cl_2) 3059, 1663, 1597, 1564, 1490, 1446, 1318, 1264 cm^{-1} ; HRMS m/z 308.1209 (calcd for $\text{C}_{23}\text{H}_{16}\text{O}$, 308.1201).

Representative procedure for the AuCl₃-catalyzed cyclizations. A solution of AuCl₃ (30.3 mg) in MeCN (970 mg) was prepared. To the appropriate 2-(1-alkynyl)-2-alken-1-one (0.2 mmol) and nucleophile (1.5 equiv) in CH₂Cl₂ (1.0 mL), was added a portion of the above AuCl₃ solution (20 mg, 1 mol %). The mixture was stirred at room temperature for 1 h unless otherwise specified. The solvent was removed under reduced pressure and the residue was purified by flash chromatography on silica gel.



9

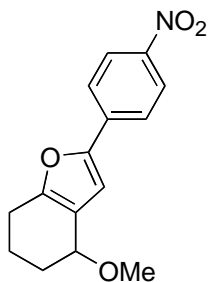
4-Methoxy-2-(4-methoxyphenyl)-4,5,6,7-tetrahydrobenzofuran (9). Compound **8** (45.2 mg, 0.2 mmol) was allowed to react with methanol (9.6 mg, 1.5 equiv) under our standard reaction conditions for 1 h. The reaction mixture was chromatographed (silica gel, 7:1 hexane/EtOAc) to afford 45.5 mg (88%) of the indicated compound **9** as a colorless oil: ¹H NMR (CDCl₃) δ 1.74-1.88 (m, 2H), 1.91-2.11 (m, 2H), 2.53-2.64 (m, 1H), 2.67-2.77 (m, 1H), 3.45 (s, 3H), 3.82 (s, 3H), 4.29 (t, *J* = 3.9 Hz, 1H), 6.51 (s, 1H), 6.90 (dt, *J* = 9.0, 3.0 Hz, 2H), 7.56 (dt, *J* = 9.0, 3.0 Hz, 2H); ¹³C NMR (CDCl₃) δ 19.2, 23.5, 28.7, 55.5, 56.4, 72.7, 104.0, 114.3, 120.0, 124.5, 125.1, 152.3, 152.5, 159.0; IR (CH₂Cl₂) 2943, 1613, 1503, 1463, 1411 cm⁻¹; HRMS *m/z* 258.1260 (calcd for C₁₆H₁₈O₃, 258.1256).



12

Ethyl 4-(4-methoxy-4,5,6,7-tetrahydro-1-benzofuran-2-yl)benzoate (12).

Compound **11** (53.6 mg, 0.2 mmol) was allowed to react with methanol (9.6 mg, 1.5 equiv) under our standard reaction conditions for 1 h. The reaction mixture was chromatographed (silica gel, 3:1 hexane/EtOAc) to afford 54.7 mg (91%) of the indicated compound **12** as a light yellow oil: ^1H NMR (CDCl_3) δ 1.39 (t, $J = 7.4$ Hz, 3H), 1.75-1.88 (m, 2H), 1.91-2.11 (m, 2H), 2.54-2.66 (m, 1H), 2.68-2.78 (m, 1H), 3.44 (s, 3H), 4.29 (t, $J = 3.9$ Hz, 1H), 4.37 (q, $J = 6.9$ Hz, 2H), 6.78 (s, 1H), 7.66 (dd, $J = 6.9, 1.8$ Hz, 2H), 8.03 (dd, $J = 6.9, 1.8$ Hz, 2H); ^{13}C NMR (CDCl_3) δ 14.6, 19.0, 23.5, 28.5, 56.4, 61.1, 72.5, 107.8, 120.7, 123.1, 128.6, 130.3, 135.2, 151.5, 154.4, 166.6; IR (CH_2Cl_2) 2942, 1713, 1607, 1574, 1423 cm^{-1} ; HRMS m/z 300.1365 (calcd for $\text{C}_{18}\text{H}_{20}\text{O}_4$, 300.1362).

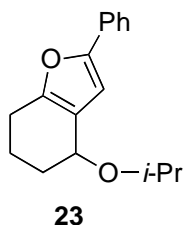


15

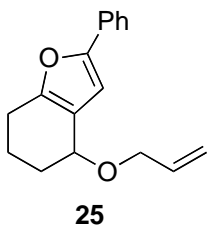
4-Methoxy-2-(4-nitrophenyl)-4,5,6,7-tetrahydrobenzofuran (15). Compound **14**

(48.3 mg, 0.2 mmol) was allowed to react with methanol (9.6 mg, 1.5 equiv) under our

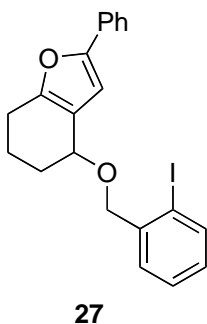
standard reaction conditions for 1 h. The reaction mixture was chromatographed (silica gel, 3:1 hexane/EtOAc) to afford 54.3 mg (99%) of the indicated compound **15** as a yellow oil: ^1H NMR (CDCl_3) δ 1.76-1.89 (m, 2H), 1.91-2.11 (m, 2H), 2.54-2.67 (m, 1H), 2.69-2.79 (m, 1H), 3.44 (s, 3H), 4.30 (t, $J = 3.6$ Hz, 1H), 6.87 (s, 1H), 7.70 (dt, $J = 9.0$, 2.4 Hz, 2H), 8.19 (dt, $J = 9.3$, 2.1 Hz, 2H); ^{13}C NMR (CDCl_3) δ 18.9, 23.5, 28.3, 56.5, 72.4, 109.7, 121.4, 123.6, 124.5, 136.9, 146.2, 150.3, 155.7; IR (CH_2Cl_2) 2943, 1595, 1514, 1453 cm^{-1} ; HRMS m/z 273.1004 (calcd for $\text{C}_{15}\text{H}_{15}\text{NO}_4$, 273.1001).



4-Isopropoxy-2-phenyl-4,5,6,7-tetrahydrobenzofuran (23). Compound **1** (39.2 mg, 0.2 mmol) was allowed to react with isopropanol (18 mg, 1.5 equiv) under our standard reaction conditions for 1 h. The reaction mixture was chromatographed (silica gel, 9:1 hexane/EtOAc) to afford 36.1 mg (71%) of the indicated compound **23** as a colorless oil: ^1H NMR (CDCl_3) δ 1.22-1.26 (m, 6H), 1.77-1.88 (m, 3H), 2.00-2.13 (m, 1H), 2.53-2.64 (m, 1H), 2.68-2.75 (m, 1H), 3.77-3.89 (m, 1H), 4.46 (t, $J = 3.8$ Hz, 1H), 6.60 (s, 1H), 7.18-7.24 (m, 1H), 7.32-7.38 (m, 2H), 7.61-7.65 (m, 2H); ^{13}C NMR (CDCl_3) δ 19.3, 22.9, 23.4, 23.5, 30.0, 68.7, 69.6, 105.3, 121.2, 123.7, 127.0, 128.8, 131.5, 152.5, 152.9; IR (CH_2Cl_2) 2968, 1604, 1487, 1449, 1122, 1066 cm^{-1} ; HRMS m/z 256.1467 (calcd for $\text{C}_{17}\text{H}_{20}\text{O}_2$, 256.1463).

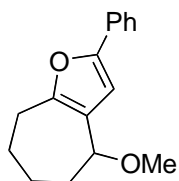


4-Allyloxy-2-phenyl-4,5,6,7-tetrahydrobenzofuran (25). Compound **1** (39.2 mg, 0.2 mmol) was allowed to react with allyl alcohol (17.4 mg, 1.5 equiv) under our standard reaction conditions for 1 h. The reaction mixture was chromatographed (Al₂O₃, 70:1 hexane/EtOAc) to afford 37.8 mg (75%) of the indicated compound **25** as a colorless oil: ¹H NMR (CDCl₃) δ 1.78-1.88 (m, 2H), 1.92-2.17 (m, 2H), 2.55-2.66 (m, 1H), 2.70-2.79 (m, 1H), 4.12-4.15 (m, 2H), 4.46 (t, *J* = 3.8 Hz, 1H), 5.22 (dd, *J* = 10.4, 1.4 Hz, 1H), 5.31-5.39 (m, 1H), 5.93-6.07 (m, 1H), 6.65 (s, 1H), 7.20-7.26 (m, 1H), 7.33-7.39 (m, 2H), 7.62-7.66 (m, 2H); ¹³C NMR (CDCl₃) δ 19.2, 23.5, 29.2, 69.7, 70.7, 105.5, 116.9, 120.4, 123.7, 127.1, 128.8, 131.4, 135.7, 152.5, 153.2; IR (CH₂Cl₂) 3079, 2943, 1633, 1553, 1449 cm⁻¹; HRMS *m/z* 254.1311 (calcd for C₁₇H₁₈O₂, 254.1307).



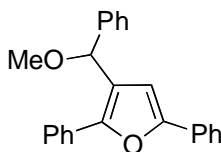
4-[(2-Iodobenzyl)oxy]-2-phenyl-4,5,6,7-tetrahydrobenzofuran (27). Compound **1** (39.2 mg, 0.2 mmol) was allowed to react with 2-iodobenzyl alcohol (70.2 mg, 1.5 equiv) under our standard reaction conditions for 1 h. The reaction mixture was chromatographed (Al₂O₃, 90:1 hexane/EtOAc) to afford 75.1 mg (87%) of the indicated compound **27** as a light yellow oil: ¹H NMR (CDCl₃) δ 1.82-1.95 (m, 2H), 2.04-2.22 (m,

2H), 2.58-2.69 (m, 1H), 2.73-2.80 (m, 1H), 4.59 (t, $J = 4.2$ Hz, 1H), 4.64 (d, $J = 3.9$ Hz, 2H), 6.71 (s, 1H), 6.98 (dt, $J = 7.8, 1.7$ Hz, 1H), 7.20-7.25 (m, 1H), 7.34-7.39 (m, 3H), 7.52 (dd, $J = 7.5, 1.5$ Hz, 1H), 7.63-7.67 (m, 2H), 7.84 (dd, $J = 7.8, 1.2$ Hz, 1H); ^{13}C NMR (CDCl_3) δ 19.3, 23.5, 29.1, 71.4, 74.6, 98.3, 105.6, 120.2, 123.7, 127.2, 128.5, 128.8, 129.3, 129.4, 131.4, 139.4, 141.3, 152.6, 153.3; IR (CH_2Cl_2) 3059, 2942, 1604, 1553, 1486 cm^{-1} ; HRMS m/z 430.0437 (calcd for $\text{C}_{21}\text{H}_{19}\text{IO}_2$, 430.0430).



46

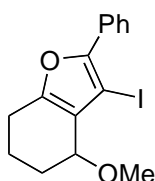
4-Methoxy-2-phenyl-5,6,7,8-tetrahydro-4H-cyclohepta[b]furan (46). Compound **44** (42 mg, 0.2 mmol) was allowed to react with methanol (9.6 mg, 1.5 equiv) under our standard reaction conditions for 1 h. The reaction mixture was chromatographed (silica gel, 9:1 hexane/EtOAc) to afford 39.7 mg (82%) of the indicated compound **9** as a light yellow oil: ^1H NMR (CDCl_3) δ 1.70-1.90 (m, 4H), 1.99-2.14 (m, 2H), 2.84-2.90 (m, 2H), 3.37 (s, 3H), 4.20 (dd, $J = 6.3, 2.4$ Hz, 1H), 6.59 (s, 1H), 7.17-7.24 (m, 1H), 7.32-7.38 (m, 2H), 7.59-7.63 (m, 2H); ^{13}C NMR (CDCl_3) δ 24.4, 26.6, 28.9, 33.3, 56.6, 75.6, 108.4, 123.48, 123.54, 126.9, 128.8, 131.3, 150.3, 154.0; IR (CH_2Cl_2) 2927, 2845, 1602, 1552, 1486, 1447, 1084 cm^{-1} ; HRMS m/z 242.1310 (calcd for $\text{C}_{16}\text{H}_{18}\text{O}_2$, 242.1307).



59

3-[Methoxy(phenyl)methyl]-2,5-diphenylfuran (59). Compound **57** (61.6 mg, 0.2 mmol) was allowed to react with methanol (9.6 mg, 1.5 equiv) under our standard reaction conditions for 4 h (2 mol % of AuCl₃ was used). The reaction mixture was chromatographed (silica gel, 12:1 hexane/EtOAc) to afford 60.4 mg (89%) of the indicated compound **59** as a colorless oil: ¹H NMR (CDCl₃) δ 3.44 (s, 3H), 5.57 (s, 1H), 6.75 (s, 1H), 7.25-7.54 (m, 11H), 7.72-7.76 (m, 4H); ¹³C NMR (CDCl₃) δ 57.0, 77.9, 107.3, 124.1, 124.2, 126.8, 127.4, 127.8, 128.1, 128.8, 128.9, 129.0, 130.8, 131.1, 141.1, 150.5, 153.1 (one sp² carbon missing due to overlap); IR (CH₂Cl₂) 3060, 2933, 1594, 1493, 1086 cm⁻¹; HRMS *m/z* 340.1469 (calcd for C₂₄H₂₀O₂, 340.1463).

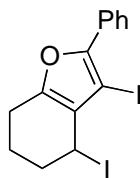
Representative procedure for the iodine-induced cyclizations. To the mixture of appropriate 2-(1-alkynyl)-2-alken-1-one (0.2 mmol), I₂ (3.0 equiv) and NaHCO₃ (3.0 equiv), was added a solution of nucleophile (8.0 equiv) in CH₃CN (2.0 mL). The resulting mixture was stirred at room temperature for 1 h unless otherwise specified. The mixture was diluted with ether (25 mL), washed with satd Na₂S₂O₃ (15 mL) and dried (MgSO₄). The solvent was removed under reduced pressure and the residue was purified by flash chromatography on silica gel.



3

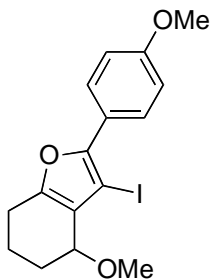
3-Iodo-4-methoxy-2-phenyl-4,5,6,7-tetrahydrobenzofuran (3). Compound **1** (39.2 mg, 0.2 mmol) was allowed to react with methanol (51.2 mg, 8.0 equiv) under our standard reaction conditions for 1 h. The reaction mixture was chromatographed (silica gel, 10:1 hexane/EtOAc) to afford 56.8 mg (80%) of the indicated compound **3** as a

colorless oil: ^1H NMR (CDCl_3) δ 1.52-1.65 (m, 1H), 1.83-2.10 (m, 2H), 2.14-2.23 (m, 1H), 2.51-2.63 (m, 1H), 2.69-2.79 (m, 1H), 3.52 (s, 3H), 4.13 (t, $J = 2.9$ Hz, 1H), 7.27-7.34 (m, 1H), 7.37-7.44 (m, 2H), 7.90-7.98 (m, 2H); ^{13}C NMR (CDCl_3) δ 18.5, 23.5, 27.1, 57.3, 65.3, 72.2, 123.7, 126.4, 128.1, 128.5, 130.8, 150.4, 154.1; IR (CH_2Cl_2) 2938, 2817, 1628, 1483, 1414, 1083 cm^{-1} ; HRMS m/z 354.0121 (calcd for $\text{C}_{15}\text{H}_{15}\text{IO}_2$, 354.0117).



7

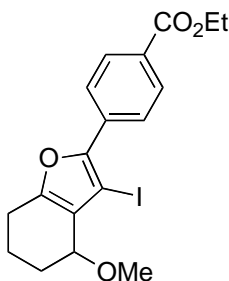
3,4-Diiodo-2-phenyl-4,5,6,7-tetrahydrobenzofuran (7). Compound **1** (39.2 mg, 0.2 mmol) was allowed to react under our standard reaction conditions, in the absence of any nucleophile for 1 h. The reaction mixture was chromatographed (silica gel, 40:1 hexane/EtOAc) to afford 55.0 mg (41%) of the indicated compound **7** as a white solid: mp 160-162 $^{\circ}\text{C}$; ^1H NMR (CDCl_3) δ 1.49-1.60 (m, 1H), 1.86-2.00 (m, 1H), 2.38-2.66 (m, 2H), 2.73-2.84 (m, 2H), 4.56 (s, 1H), 7.26-7.33 (m, 1H), 7.37-7.43 (m, 2H), 7.86-7.90 (m, 2H); ^{13}C NMR (CDCl_3) δ 19.1, 23.5, 27.3, 65.3, 67.9, 123.0, 126.7, 128.1, 128.5, 130.9, 150.4, 155.1; IR (CH_2Cl_2) 3060, 2984, 2941, 1620, 1603, 1483 cm^{-1} .



10

3-Iodo-4-methoxy-2-(4-methoxyphenyl)-4,5,6,7-tetrahydrobenzofuran (10).

Compound **8** (45.2 mg, 0.2 mmol) was allowed to react with methanol (51.2 mg, 8.0 equiv) under our standard reaction conditions for 1 h. The reaction mixture was chromatographed (silica gel, 6:1 hexane/EtOAc) to afford 63.9 mg (83%) of the indicated compound **10** as a colorless oil: ^1H NMR (CDCl_3) δ 1.58 (tt, $J = 3.5, 13.6$ Hz, 1H), 1.81-1.92 (m, 1H), 1.94-2.10 (m, 1H), 2.12-2.21 (m, 1H), 2.50-2.61 (m, 1H), 2.67-2.76 (m, 1H), 3.51 (s, 3H), 3.83 (s, 3H), 4.11 (t, $J = 3.0$ Hz, 1H), 6.94 (dt, $J = 9.0, 2.7$ Hz, 2H), 7.85 (dt, $J = 9.0, 2.7$ Hz, 2H); ^{13}C NMR (CDCl_3) δ 18.5, 23.5, 27.1, 55.5, 57.3, 63.8, 72.3, 114.0, 123.4, 123.6, 128.0, 150.6, 153.5, 159.5; IR (CH_2Cl_2) 2939, 2835, 1612, 1495 cm^{-1} ; HRMS m/z 384.0229 (calcd for $\text{C}_{16}\text{H}_{17}\text{IO}_3$, 384.0223).

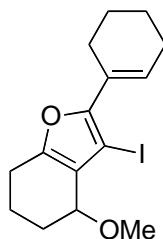


13

Ethyl 4-(3-iodo-4-methoxy-4,5,6,7-tetrahydrobenzofuran-2-yl)benzoate (13).

Compound **11** (53.6 mg, 0.2 mmol) was allowed to react with methanol (51.2 mg, 8.0 equiv) under our standard reaction conditions for 1 h. The reaction mixture was chromatographed (silica gel, 5:1 hexane/EtOAc) to afford 70.7 mg (83%) of the indicated compound **13** as a colorless oil: ^1H NMR (CDCl_3) δ 1.40 (t, $J = 7.2$ Hz, 3H), 1.62 (tt, $J = 3.3, 13.8$ Hz, 1H), 1.88-2.10 (m, 2H), 2.14-2.22 (m, 1H), 2.50-2.62 (m, 1H), 2.68-2.79 (m, 1H), 3.51 (s, 3H), 4.12 (t, $J = 3.0$ Hz, 1H), 4.38 (q, $J = 7.2$ Hz, 3H), 8.02-8.09 (m, 4H); ^{13}C NMR (CDCl_3) δ 14.6, 18.4, 23.5, 26.9, 57.3, 61.2, 67.6, 72.1, 124.4, 125.7,

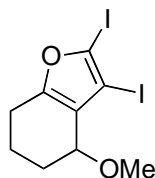
129.4, 129.9, 134.7, 149.2, 155.1, 166.5; IR (CH₂Cl₂) 2932, 2817, 1713, 1607, 1276 cm⁻¹; HRMS *m/z* 426.0336 (calcd for C₁₈H₁₉IO₄, 426.0328).



18

2-(Cyclohex-1-en-1-yl)-3-iodo-4-methoxy-4,5,6,7-tetrahydrobenzofuran (18).

Compound **16** (40.0 mg, 0.2 mmol) was allowed to react with methanol (51.2 mg, 8.0 equiv) under our standard reaction conditions for 1 h. The reaction mixture was chromatographed (silica gel, 11:1 hexane/EtOAc) to afford 33.0 mg (46%) of the indicated compound **18** as a colorless oil: ¹H NMR (CDCl₃) δ 1.43-1.75 (m, 5H), 1.77-1.85 (m, 1H), 1.92-2.06 (m, 1H), 2.08-2.22 (m, 3H), 2.40-2.52 (m, 3H), 2.58-2.66 (m, 1H), 3.47 (s, 3H), 4.04 (s, 1H), 6.42-6.46 (m, 1H); ¹³C NMR (CDCl₃) δ 18.5, 22.1, 22.8, 23.4, 25.6, 26.7, 27.1, 57.2, 63.0, 72.3, 122.8, 127.9, 128.2, 152.4, 152.5; IR (CH₂Cl₂) 2928, 2858, 1629, 1435, 1346 cm⁻¹; HRMS *m/z* 358.0435 (calcd for C₁₅H₁₉IO₂, 358.0430).

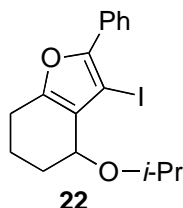


21

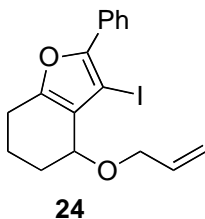
2,3-Diiodo-4-methoxy-4,5,6,7-tetrahydrobenzofuran (21). Compound **19** (38.4 mg, 0.2 mmol) was allowed to react with methanol (51.2 mg, 8.0 equiv) under our standard reaction conditions for 1 h. The reaction mixture was chromatographed (silica gel, 9:1

hexane/EtOAc) to afford 47.2 mg (60%) of the indicated compound **21** as a colorless oil:

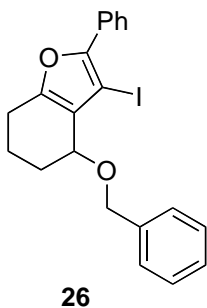
^1H NMR (CDCl_3) δ 1.47-1.60 (m, 1H), 1.72-1.84 (m, 1H), 1.89-2.13 (m, 2H), 2.48-2.59 (m, 1H), 2.64-2.73 (m, 1H), 3.46 (s, 3H), 4.04 (t, $J = 3.0$ Hz, 1H); ^{13}C NMR (CDCl_3) δ 18.3, 23.7, 27.2, 57.4, 72.0, 83.1, 96.4, 124.2, 159.8; IR (CH_2Cl_2) 2940, 2817, 1625, 1452, 1410 cm^{-1} ; HRMS m/z 403.8777 (calcd for $\text{C}_9\text{H}_{10}\text{I}_2\text{O}_2$, 403.8770).



3-Iodo-4-isopropoxy-2-phenyl-4,5,6,7-tetrahydrobenzofuran (22). Compound **1** (39.2 mg, 0.2 mmol) was allowed to react with isopropanol (96 mg, 8.0 equiv) under our standard reaction conditions for 1 h. The reaction mixture was chromatographed (silica gel, 12:1 hexane/EtOAc) to afford 55.5 mg (73%) of the indicated compound **22** as a light yellow oil: ^1H NMR (CDCl_3) δ 1.25 (d, $J = 6.3$ Hz, 3H), 1.36 (d, $J = 6.0$ Hz, 3H), 1.53-1.63 (m, 1H), 1.82-1.93 (m, 1H), 2.02-2.17 (m, 2H), 2.50-2.62 (m, 1H), 2.69-2.78 (m, 1H), 3.87-3.97 (m, 1H), 4.35 (s, 3H), 7.26-7.33 (m, 1H), 7.37-7.43 (m, 2H), 7.90-7.94 (m, 2H); ^{13}C NMR (CDCl_3) δ 18.3, 23.2, 23.6, 24.2, 28.6, 65.3, 68.7, 70.5, 123.7, 126.6, 128.0, 128.5, 130.9, 150.3, 154.2; IR (CH_2Cl_2) 3058, 2967, 2882, 1625, 1483, 1445 cm^{-1} ; HRMS m/z 382.0437 (calcd for $\text{C}_{17}\text{H}_{19}\text{IO}_2$, 382.0430).



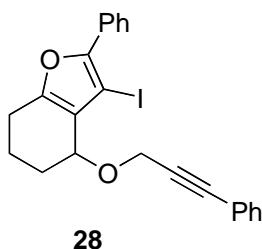
4-Allyloxy-3-iodo-2-phenyl-4,5,6,7-tetrahydrobenzofuran (24). Compound **1** (39.2 mg, 0.2 mmol) was allowed to react with allyl alcohol (139 mg, 8.0 equiv) under our standard reaction conditions for 1 h. The reaction mixture was chromatographed (Al₂O₃, 100:1 hexane/EtOAc) to afford 43.3 mg (57%) of the indicated compound **24** as a light yellow oil: ¹H NMR (CDCl₃) δ 1.61 (tt, *J* = 13.5, 3.2 Hz, 1H), 1.83-1.93 (m, 1H), 1.99-2.21 (m, 2H), 2.51-2.63 (m, 1H), 2.70-2.79 (m, 1H), 4.15-4.26 (m, 2H), 4.29-4.32 (m, 1H), 5.20 (dd, *J* = 10.4, 1.2 Hz, 1H), 5.35 (dd, *J* = 17.4, 1.4 Hz, 1H), 6.01-6.13 (m, 1H), 7.28-7.33 (m, 1H), 7.38-7.44 (m, 2H), 7.91-7.96 (m, 2H); ¹³C NMR (CDCl₃) δ 18.5, 23.5, 27.8, 65.3, 70.7, 70.9, 117.2, 123.7, 126.5, 128.0, 128.5, 130.8, 135.6, 150.3, 154.2; IR (CH₂Cl₂) 3079, 2940, 2860, 1627, 1603, 1483 cm⁻¹; HRMS *m/z* 380.0278 (calcd for C₁₇H₁₇IO₂, 380.0273).



4-Benzyloxy-3-iodo-2-phenyl-4,5,6,7-tetrahydrobenzofuran (26). Compound **1** (39.2 mg, 0.2 mmol) was allowed to react with benzyl alcohol (173 mg, 8.0 equiv) under our standard reaction conditions for 1 h. The reaction mixture was chromatographed (Al₂O₃, 100:1 hexane/EtOAc) to afford 51.5 mg (60%) of the indicated compound **26** as a light yellow oil: ¹H NMR (CDCl₃) δ 1.65 (tt, *J* = 13.5, 3.3 Hz, 1H), 1.85-1.97 (m, 1H), 2.05-2.20 (m, 1H), 2.21-2.29 (m, 1H), 2.53-2.65 (m, 1H), 2.71-2.80 (m, 1H), 4.43 (t, *J* = 2.9 Hz, 1H), 4.73 (s, 1H), 7.25-7.50 (m, 8H), 7.93-7.97 (m, 2H); ¹³C NMR (CDCl₃) δ 18.6, 23.5, 27.7, 65.4, 71.1, 72.1, 123.8, 126.5, 127.9, 128.1, 128.5, 128.56, 128.58,

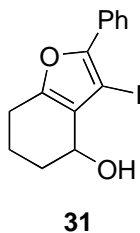
130.8, 138.8, 150.3, 154.3; IR (CH₂Cl₂) 3062, 3029, 2940, 1628, 1603, 1484 cm⁻¹;

HRMS *m/z* 419.9653 (calcd for C₂₁H₁₉IO₂, 419.9647).



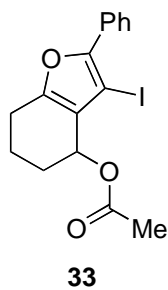
3-Iodo-2-phenyl-4-(3-phenyl-2-propynyl)oxy-4,5,6,7-tetrahydrobenzofuran (28).

Compound **1** (39.2 mg, 0.2 mmol) was allowed to react with 3-phenyl-2-propyn-1-ol (211 mg, 8.0 equiv) under our standard reaction conditions for 1 h. The reaction mixture was chromatographed (silica gel, 18:1 hexane/EtOAc) to afford 70.0 mg (77%) of the indicated compound **28** as a colorless oil: ¹H NMR (CDCl₃) δ 1.67 (tt, *J* = 13.8, 3.3 Hz, 1H), 1.86-1.97 (m, 1H), 2.05-2.20 (m, 1H), 2.28-2.37 (m, 1H), 2.53-2.66 (m, 1H), 2.72-2.82 (m, 1H), 4.56 (t, *J* = 3.2 Hz, 1H), 4.61 (d, *J* = 5.7 Hz, 2H), 7.29-7.36 (m, 4H), 7.38-7.45 (m, 2H), 7.47-7.52 (m, 2H), 7.93-7.98 (m, 2H); ¹³C NMR (CDCl₃) δ 18.5, 23.5, 27.8, 57.7, 65.1, 70.3, 86.3, 86.4, 123.2, 123.5, 126.5, 128.1, 128.55, 128.58, 128.60, 130.8, 132.0, 150.5, 154.6; IR (CH₂Cl₂) 3057, 2940, 1660, 1626, 1487 cm⁻¹; HRMS *m/z* 454.0437 (calcd for C₂₃H₁₉IO₂, 454.0430).

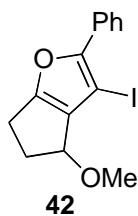


3-Iodo-2-phenyl-4,5,6,7-tetrahydrobenzofuran-4-ol (31). Compound **1** (39.2 mg, 0.2 mmol) was allowed to react with H₂O (28.8 mg, 8.0 equiv) under our standard reaction conditions for 1 h. The reaction mixture was chromatographed (silica gel, 4:1

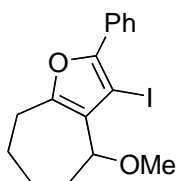
hexane/EtOAc) to afford 52.1 mg (77%) of the indicated compound **31** as a white solid: mp 83-84 °C; ^1H NMR (CDCl_3) δ 1.75-1.96 (m, 3H), 1.99-2.14 (m, 2H), 2.53-2.65 (m, 1H), 2.70-2.79 (m, 1H), 4.70 (q, $J = 3.9$ Hz, 1H), 7.29-7.35 (m, 1H), 7.38-7.45 (m, 2H), 7.92-7.97 (m, 2H); ^{13}C NMR (CDCl_3) δ 18.6, 23.5, 31.8, 63.7, 64.1, 125.0, 126.3, 128.2, 128.6, 130.6, 150.3, 153.8; IR (CH_2Cl_2) 3340, 2940, 1624, 1483, 1442, 1223 cm^{-1} ; HRMS m/z 339.9970 (calcd for $\text{C}_{14}\text{H}_{13}\text{IO}_2$, 339.9960).



3-Iodo-2-phenyl-4,5,6,7-tetrahydrobenzofuran-4-yl acetate (33). Compound **1** (39.2 mg, 0.2 mmol) was allowed to react with acetic acid (144 mg, 8.0 equiv) under our standard reaction conditions for 1 h. The reaction mixture was chromatographed (silica gel, 6:1 hexane/EtOAc) to afford 50.3 mg (66%) of the indicated compound **33** as a light yellow solid: mp 115-116 °C; ^1H NMR (CDCl_3) δ 1.82-1.97 (m, 3H), 2.00-2.14 (m, 4H), 2.57-2.65 (m, 1H), 2.76-2.87 (m, 1H), 5.79 (t, $J = 3.0$ Hz, 1H), 7.29-7.35 (m, 1H), 7.38-7.45 (m, 2H), 7.92-7.96 (m, 2H); ^{13}C NMR (CDCl_3) δ 19.1, 21.5, 23.3, 29.3, 63.9, 66.3, 121.6, 126.4, 128.3, 128.6, 130.5, 150.7, 155.3, 170.8; IR (CH_2Cl_2) 2951, 1731, 1628, 1483, 1370 cm^{-1} ; HRMS m/z 382.0071 (calcd for $\text{C}_{16}\text{H}_{15}\text{IO}_3$, 382.0066).



3-Iodo-4-methoxy-2-phenyl-5,6-dihydro-4H-cyclopentafuran (42). Compound **41** (36.4 mg, 0.2 mmol) was allowed to react with MeOH (51.2 mg, 8.0 equiv) under our standard reaction conditions for 4 h. The reaction mixture was chromatographed (silica gel, 6:1 hexane/EtOAc) to afford 50.3 mg (74%) of the indicated compound **42** as a light yellow solid: mp 70-71 °C; ^1H NMR (CDCl_3) δ 2.36-2.45 (m, 1H), 2.64-2.78 (m, 2H), 2.98-3.06 (m, 1H), 3.47 (s, 3H), 4.65-4.69 (m, 1H), 7.29-7.35 (m, 1H), 7.39-7.45 (m, 2H), 7.92-7.96 (m, 2H); ^{13}C NMR (CDCl_3) δ 24.2, 35.2, 56.6, 60.0, 77.7, 126.5, 128.2, 128.6, 131.1, 133.2, 155.7, 162.3; IR (CH_2Cl_2) 2974, 2931, 2819, 1619, 1601, 1479 cm^{-1} ; HRMS m/z 399.9968 (calcd for $\text{C}_{14}\text{H}_{13}\text{IO}_2$, 399.9960).

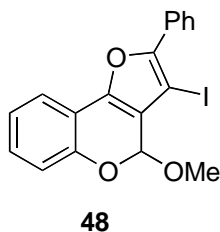


45

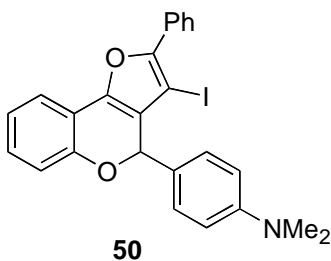
3-Iodo-4-methoxy-2-phenyl-5,6,7,8-tetrahydro-4H-cycloheptafuran (45).

Compound **44** (42.0 mg, 0.2 mmol) was allowed to react with MeOH (51.2 mg, 8.0 equiv) under our standard reaction conditions for 1 h. The reaction mixture was chromatographed (silica gel, 9:1 hexane/EtOAc) to afford 56.0 mg (76%) of the indicated compound **45** as a light yellow oil: ^1H NMR (CDCl_3) δ 1.50-1.68 (m, 2H), 1.78-1.87 (m, 1H), 1.96-2.11 (m, 2H), 2.35-2.42 (m, 1H), 2.87-2.94 (m, 2H), 3.40 (s, 3H), 4.28 (dd, J = 1.8, 5.1 Hz, 1H), 7.25-7.34 (m, 1H), 7.38-7.44 (m, 2H), 7.91-7.96 (m, 2H); ^{13}C NMR (CDCl_3) δ 23.2, 26.4, 28.8, 31.8, 56.6, 70.1, 74.5, 125.0, 126.4, 128.0, 128.5, 130.8,

149.0, 155.3; IR (CH₂Cl₂) 3055, 2926, 1602, 1485, 1445 cm⁻¹; HRMS *m/z* 368.0279 (calcd for C₁₆H₁₇IO₂, 368.0273).



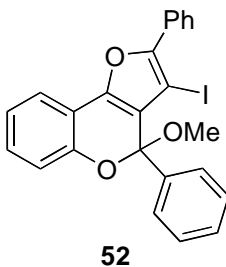
3-Iodo-4-methoxy-2-phenyl-4*H*-furo[3,2-*c*]chromene (48). Compound **47** (49.2 mg, 0.2 mmol) was allowed to react with MeOH (12.8 mg, 2.0 equiv) under our standard reaction conditions for 1 h. The reaction mixture was chromatographed (silica gel, 4:1 hexane/EtOAc) to afford 70.1 mg (87%) of the indicated compound **48** as a white solid: mp 74-75 °C; ¹H NMR (CDCl₃) δ 3.64 (s, 3H), 6.10 (s, 1H), 7.06-7.14 (m, 2H), 7.23-7.29 (m, 1H), 7.36-7.42 (m, 1H), 7.44-7.51 (m, 2H), 7.63 (dd, *J* = 7.5, 1.4 Hz, 1H), 8.03-8.08 (m, 2H); ¹³C NMR (CDCl₃) δ 55.8, 61.2, 98.9, 114.6, 117.4, 119.4, 120.2, 122.3, 126.7, 128.77, 128.81, 129.5, 130.1, 147.6, 151.6, 152.0; IR (CH₂Cl₂) 3059, 2927, 2828, 1642, 1497 cm⁻¹; HRMS *m/z* 403.9918 (calcd for C₁₈H₁₃IO₃, 403.9910).



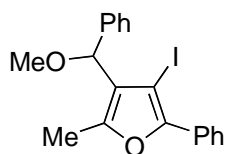
4-[4-(Dimethylamino)phenyl]-3-iodo-2-phenyl-4*H*-furo[3,2-*c*]chromene (50).

Compound **47** (49.2 mg, 0.2 mmol) was allowed to react with *N,N*-dimethylaniline (36.2 mg, 1.5 equiv) under our standard reaction conditions for 1 h. The reaction mixture was chromatographed (silica gel, 8:1 hexane/EtOAc) to afford 78.4 mg (80%) of the indicated

compound **50** as a white solid: mp 157-158 °C; ^1H NMR (CDCl_3) δ 2.94 (s, 6H), 6.31 (s, 1H), 6.67 (d, J = 8.7 Hz, 2H), 6.85 (d, J = 8.1 Hz, 1H), 6.96 (t, J = 7.5 Hz, 1H), 7.09 (t, J = 7.6 Hz, 1H), 7.27 (d, J = 8.4 Hz, 2H), 7.34-7.39 (m, 1H), 7.43-7.55 (m, 3H), 8.09 (d, J = 8.7 Hz, 2H); ^{13}C NMR (CDCl_3) δ 40.6, 62.7, 79.1, 112.3, 115.6, 117.2, 119.8, 121.4, 121.7, 126.5, 127.0, 128.5, 128.7, 129.35, 129.43, 130.3, 146.3, 151.1, 151.6, 152.7 (one sp^2 carbon missing due to overlap; IR (CH_2Cl_2) 2962, 2918, 1612, 1522 cm^{-1} ; HRMS m/z 493.0544 (calcd for $\text{C}_{25}\text{H}_{20}\text{INO}_2$, 493.0539).

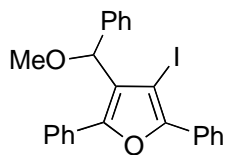


3-Iodo-4-methoxy-2,4-diphenyl-4H-furo[3,2-c]chromene (52). Compound **51** (64.4 mg, 0.2 mmol) was allowed to react with MeOH (32.0 mg, 5 equiv) under our standard reaction conditions for 1 h. The reaction mixture was chromatographed (silica gel, 3:1 hexane/EtOAc) to afford 58.7 mg (61%) of the indicated compound **52** as a yellow oil: ^1H NMR (CDCl_3) δ 3.39 (s, 3H), 7.02-7.09 (m, 2H), 7.23-7.28 (m, 1H), 7.36-7.51 (m, 6H), 7.61-7.70 (m, 3H), 8.11 (d, J = 7.5 Hz, 2H); ^{13}C NMR (CDCl_3) δ 51.6, 61.7, 105.5, 112.7, 116.1, 117.2, 120.1, 121.5, 127.0, 127.1, 128.2, 128.7, 129.0, 129.05, 129.9, 130.1, 141.4, 148.7, 152.5, 153.1; IR (CH_2Cl_2) 3061, 3031, 2934, 1636, 1491, 1448 cm^{-1} ; HRMS m/z 480.0229 (calcd for $\text{C}_{24}\text{H}_{17}\text{IO}_3$, 480.0223).



55

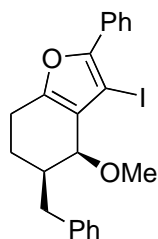
3-Iodo-4-[methoxy(phenyl)methyl]-5-methyl-2-phenylfuran (55). Compound **54** (49.2 mg, 0.2 mmol) was allowed to react with MeOH (51.2 mg, 8.0 equiv) under our standard reaction conditions for 50 h. The reaction mixture was chromatographed (silica gel, 12:1 hexane/EtOAc) to afford 58.2 mg (72%) of the indicated compound **55** as a colorless oil: ^1H NMR (CDCl_3) δ 2.25 (s, 3H), 3.46 (s, 3H), 5.34 (s, 1H), 7.26-7.47 (m, 8H), 7.94-7.98 (m, 2H); ^{13}C NMR (CDCl_3) δ 13.1, 57.2, 67.3, 79.6, 123.3, 126.5, 127.0, 127.7, 128.1, 128.5, 130.6, 140.8, 150.08, 150.13 (one sp^2 carbon missing due to overlap); IR (CH_2Cl_2) 3060, 3028, 2925, 1602, 1485 cm^{-1} ; HRMS m/z 404.0279 (calcd for $\text{C}_{19}\text{H}_{17}\text{IO}_2$, 404.0273).



58

3-Iodo-4-[methoxy(phenyl)methyl]-2,5-diphenylfuran (58). Compound **57** (61.6 mg, 0.2 mmol) was allowed to react with MeOH (51.2 mg, 8.0 equiv) under our standard reaction conditions for 50 h. The reaction mixture was chromatographed (silica gel, 12:1 hexane/EtOAc) to afford 66.1 mg (71%) of the indicated compound **58** as a white solid: mp 94-95 $^{\circ}\text{C}$; ^1H NMR (CDCl_3) δ 3.43 (s, 3H), 5.75 (s, 1H), 7.25-7.51 (m, 11H), 7.69-7.72 (m, 2H), 8.11-8.15 (m, 2H); ^{13}C NMR (CDCl_3) δ 57.1, 68.2, 123.3, 127.0, 127.1, 127.6, 128.4, 128.59, 128.63, 128.65, 128.67, 130.1, 130.4, 140.2, 151.5, 152.1 (one sp^2

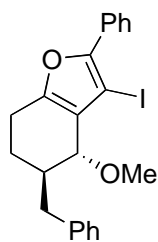
carbon missing due to overlap); IR (CH₂Cl₂) 3059, 3029, 2927, 1602, 1481 cm⁻¹; HRMS *m/z* 466.0437 (calcd for C₂₄H₁₉IO₂, 466.0430).



67

***cis*-5-Benzyl-3-iodo-4-methoxy-2-phenyl-4,5,6,7-tetrahydrobenzofuran (67).**

Compound **66** (57.2 mg, 0.2 mmol) was allowed to react with MeOH (51.2 mg, 8.0 equiv) under our standard reaction conditions for 1 h. The reaction mixture was chromatographed (silica gel, 12:1 hexane/EtOAc) to afford 19.8 mg (22%) of the indicated compound **67** as a light yellow oil: ¹H NMR (CDCl₃) δ 1.76-1.80 (m, 1H), 1.97-2.04 (m, 2H), 2.51-2.63 (m, 1H), 2.69-2.81 (m, 2H), 2.96-3.03 (m, 1H), 3.63 (s, 3H), 3.98 (s, 1H), 7.21-7.28 (m, 3H), 7.29-7.36 (m, 3H), 7.38-7.43 (m, 2H), 7.91-7.95 (m, 2H); ¹³C NMR (CDCl₃) δ 23.2, 23.6, 38.6, 43.1, 59.4, 66.1, 73.8, 124.9, 126.2, 126.6, 128.1, 128.5, 128.6, 129.5, 130.8, 140.9, 150.6, 154.3; IR (CH₂Cl₂) 3025, 2930, 2818, 1629, 1602, 1484, 1459 cm⁻¹; HRMS *m/z* 444.0593 (calcd for C₂₂H₂₁IO₂, 444.0586).



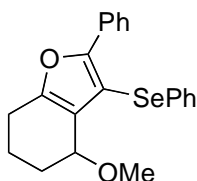
68

***trans*-5-Benzyl-3-iodo-4-methoxy-2-phenyl-4,5,6,7-tetrahydrobenzofuran (68).**

The reaction mixture was chromatographed (silica gel, 12:1 hexane/EtOAc) to afford,

together with **67**, 42.1 mg (47%) of the indicated compound **68** as a light yellow oil: ^1H NMR (CDCl_3) δ 1.71-1.78 (m, 1H), 2.13-2.21 (m, 1H), 2.44-2.59 (m, 3H), 2.67-2.72 (m, 2H), 3.43 (s, 3H), 3.90 (d, $J = 0.9$ Hz, 1H), 7.18-7.22 (m, 2H), 7.24-7.28 (m, 1H), 7.30-7.37 (m, 3H), 7.39-7.47 (m, 2H), 7.96-8.01 (m, 2H); ^{13}C NMR (CDCl_3) δ 19.9, 22.2, 36.2, 38.0, 57.2, 65.9, 76.1, 122.3, 126.4, 128.1, 128.6, 128.7, 129.1, 130.8, 140.5, 150.7, 153.2; IR (CH_2Cl_2) 3025, 2930, 2821, 1615, 1603, 1484, 1453 cm^{-1} ; HRMS m/z 444.0592 (calcd for $\text{C}_{22}\text{H}_{21}\text{IO}_2$, 444.0586).

Representative procedure for the PhSeCl-induced cyclizations. To the mixture of appropriate 2-(1-alkynyl)-2-alken-1-one (0.2 mmol), PhSeCl (3.0 equiv) and NaHCO_3 (3.0 equiv), was added a solution of nucleophile (10 equiv) in CH_3CN (2.0 mL). The resulting mixture was stirred at room temperature for 1 h unless otherwise specified. The mixture was diluted with ether (25 mL), washed with brine (15 mL) and dried (MgSO_4). The solvent was removed under reduced pressure and the residue was purified by flash chromatography on silica gel.

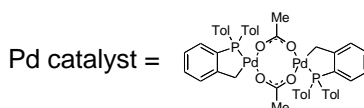
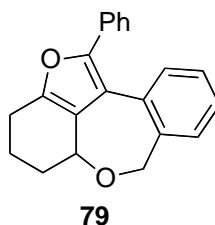


5

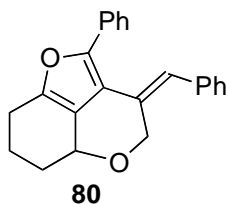
4-Methoxy-2-phenyl-3-phenylseleno-4,5,6,7-tetrahydrobenzofuran (5).

Compound **1** (39.2 mg, 0.2 mmol) was allowed to react with MeOH (64 mg, 10 equiv) under our standard reaction conditions for 1 h. The reaction mixture was chromatographed (silica gel, 9:1 hexane/EtOAc) to afford 34.2 mg (45%) of the indicated compound **5** as a light yellow oil: ^1H NMR (CDCl_3) δ 1.44-1.57 (m, 1H), 1.82-1.91 (m, 1H), 2.00-2.14 (m, 2H), 2.55-2.68 (m, 1H), 2.72-2.82 (m, 1H), 3.31 (s, 3H), 4.13 (t, $J =$

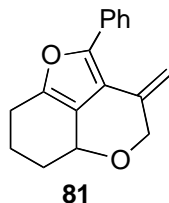
2.7 Hz, 1H), 7.11-7.24 (m, 3H), 7.26-7.38 (m, 5H), 7.93-7.98 (m, 2H); ^{13}C NMR (CDCl_3) δ 18.2, 23.4, 27.3, 57.1, 71.3, 103.6, 124.1, 126.1, 126.6, 128.1, 128.5, 129.2, 129.4, 130.9, 132.8, 153.6, 154.4; IR (CH_2Cl_2) 3056, 2938, 1603, 1577, 1478 cm^{-1} ; HRMS m/z 384.0636 (calcd for $\text{C}_{21}\text{H}_{20}\text{O}_2\text{Se}$, 384.0629).



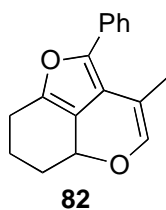
This compound was prepared by following a procedure from the literature.⁸ The Pd catalyst (11.8 mg, 5 mol %), Cs_2CO_3 (195 mg, 0.6 mmol), furan **27** (87.1 mg, 0.20 mmol) and DMA (2.5 mL), were placed in a vial. The resulting mixture was heated under a N_2 atmosphere at 100 $^\circ\text{C}$ for 17 h. The mixture was allowed to cool to room temperature, diluted with diethyl ether (30 mL), washed with satd aq NH_4Cl (15 mL), dried (MgSO_4), and filtered. The solvent was removed under reduced pressure and the residue was purified by column chromatography (9:1 hexane/EtOAc) on silica gel to afford 46.6 mg (76%) of the indicated compound **79** as a white solid: mp 156-157 $^\circ\text{C}$; ^1H NMR (CDCl_3) δ 1.81-2.05 (m, 4H), 2.55-2.64 (m, 1H), 2.73-2.80 (m, 1H), 4.49-4.56 (m, 2H), 4.76 (d, J = 9.0 Hz, 1H), 7.24-7.35 (m, 5H), 7.42-7.45 (m, 1H), 7.54-7.56 (m, 1H), 7.69-7.71 (m, 2H); ^{13}C NMR (CDCl_3) δ 20.7, 23.4, 30.8, 68.2, 68.8, 120.5, 121.0, 125.8, 127.6, 127.70, 127.73, 128.7, 128.8, 131.1, 131.5, 134.7, 137.5, 146.0, 152.1; IR (CH_2Cl_2) 3057, 2945, 2856, 1603, 1497 cm^{-1} ; HRMS m/z 302.1312 (calcd for $\text{C}_{21}\text{H}_{18}\text{O}_2$, 302.1307).



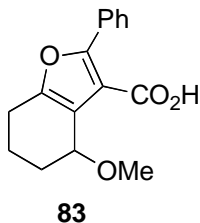
This compound was prepared by following a procedure from the literature.⁹ Pd(OAc)₂ (4.5 mg, 10 mol %), PPh₃ (10.5 mg, 20 mol %), *n*-Bu₄NCl (55.3 mg, 0.2 mmol), 88% HCO₂H (31.4 mg, 0.6 mmol), piperidine (68.2 mg, 0.8 mmol), furan **28** (90.7 mg, 0.20 mmol) and CH₃CN (5 mL), were placed in a vial. The resulting mixture was heated under a N₂ atmosphere at 60 °C for 14 h. The mixture was allowed to cool to room temperature, diluted with diethyl ether (30 mL), washed with satd aq NH₄Cl (15 mL), dried (MgSO₄), and filtered. The solvent was removed under reduced pressure and the residue was purified by column chromatography (9:1 hexane/EtOAc) on silica gel to afford 49.2 mg (75%) of the indicated compound **80** as a yellow oil: ¹H NMR (CDCl₃) δ 1.35-1.48 (m, 1H), 1.78-1.92 (m, 1H), 2.13-2.29 (m, 2H), 2.58-2.77 (m, 2H), 4.48 (dd, *J* = 2.1, 14.4 Hz, 1H), 4.52-4.59 (m, 1H), 5.03 (dd, *J* = 1.2, 14.1 Hz, 1H), 7.11-7.15 (m, 2H), 7.19-7.26 (m, 1H), 7.29-7.36 (m, 4H), 7.39-7.55 (m, 2H), 7.76-7.80 (m, 2H); ¹³C NMR (CDCl₃) δ 20.7, 22.9, 29.4, 67.5, 71.9, 114.8, 121.9, 123.4, 127.1, 127.7, 128.2, 128.5, 128.8, 129.4, 132.6, 136.8, 147.9, 148.4; IR (CH₂Cl₂) 3056, 3021, 2946, 2846, 1673, 1599, 1486 cm⁻¹; HRMS *m/z* 328.1471 (calcd for C₂₃H₂₀O₂, 328.1463).



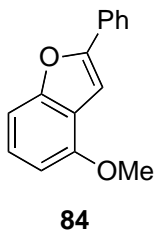
This compound was prepared by following a procedure from the literature.¹⁰ Pd(OAc)₂ (4.5 mg, 10 mol %), PPh₃ (10.5 mg, 20 mol %), Et₃N (81 mg, 0.8 mmol) and furan **24** (76.9 mg, 0.20 mmol) in CH₃CN (4.5 mL) were refluxed for 3 h. The mixture was allowed to cool to room temperature, diluted with diethyl ether (30 mL), washed with satd aq NH₄Cl (15 mL), dried (MgSO₄), and filtered. The solvent was removed under reduced pressure and the residue was purified by column chromatography (12:1 hexane/EtOAc) on silica gel to afford 23.3 mg (46%) of the indicated compound **81** as a light yellow solid: mp 68-70 °C; ¹H NMR (CDCl₃) δ 1.34-1.44 (m, 1H), 1.76-1.91 (m, 1H), 2.09-2.25 (m, 2H), 2.56-2.72 (m, 2H), 4.31-4.43 (m, 2H), 4.48-4.53 (m, 1H), 4.89 (s, 1H), 5.66 (s, 1H), 7.26-7.31 (m, 1H), 7.39 (t, *J* = 5.9 Hz, 2H), 7.68-7.71 (m, 2H); ¹³C NMR (CDCl₃) δ 20.6, 22.7, 29.2, 72.0, 72.2, 106.8, 113.6, 121.5, 127.3, 128.0, 128.5, 132.0, 135.2, 147.7, 149.0; IR (CH₂Cl₂) 3007, 2946, 2848, 1669, 1602, 1443 cm⁻¹; HRMS *m/z* 252.1154 (calcd for C₁₇H₁₆O₂, 252.1150).



The reaction mixture was chromatographed (silica gel, 12:1 hexane/EtOAc) to afford, together with **81**, 7.6 mg (15%) of the indicated compound **82** as a colorless oil: ¹H NMR (CDCl₃) δ 1.60-1.69 (m, 1H), 1.79-1.88 (m, 1H), 1.92 (d, *J* = 1.2 Hz, 3H), 2.14-2.21 (m, 1H), 2.29-2.35 (m, 1H), 2.63-2.68 (m, 2H), 4.87-4.92 (m, 1H), 6.29 (d, *J* = 1.2 Hz, 1H), 7.27-7.31 (m, 1H), 7.35-7.41 (m, 2H), 7.56-7.60 (m, 2H); IR (CH₂Cl₂) 3013, 2941, 2851, 1669, 1600, 1445 cm⁻¹; HRMS *m/z* 252.1154 (calcd for C₁₇H₁₆O₂, 252.1150).



Pd(PCy₃)₂ (8.4 mg, 10 mol %), CsO₂CCMe₃ (117 mg, 20 mol %), furan **3** (88.5 mg, 0.25 mmol), H₂O (9 mg, 0.5 mmol) and DMF (6 mL) were placed in a vial. The resulting mixture was heated under a CO atmosphere (1 atm) at 110 °C for 7 h. The mixture was allowed to cool to room temperature, diluted with diethyl ether (30 mL), washed with satd aq NH₄Cl (15 mL), dried (MgSO₄), and filtered. The solvent was removed under reduced pressure and the residue was purified by column chromatography (2:1 hexane/EtOAc) on silica gel to afford 36.2 mg (53%) of the indicated compound **83** as a white solid: mp 159-160 °C; ¹H NMR (CDCl₃) δ 1.78-1.90 (m, 2H), 1.97-2.10 (m, 2H), 2.51-2.66 (m, 1H), 2.69-2.80 (m, 1H), 3.50 (s, 3H), 4.64 (t, *J* = 3.7 Hz, 1H), 7.36-7.44 (m, 3H), 7.83-7.89 (m, 2H); ¹³C NMR (CDCl₃) δ 18.5, 23.2, 26.8, 56.5, 72.2, 112.8, 118.6, 128.3, 128.8, 129.5, 130.0, 153.5, 157.9, 166.8; IR (CH₂Cl₂) 3059, 2930, 1711, 1681, 1491 cm⁻¹; HRMS *m/z* 272.1052 (calcd for C₁₆H₁₆O₄, 272.1049).



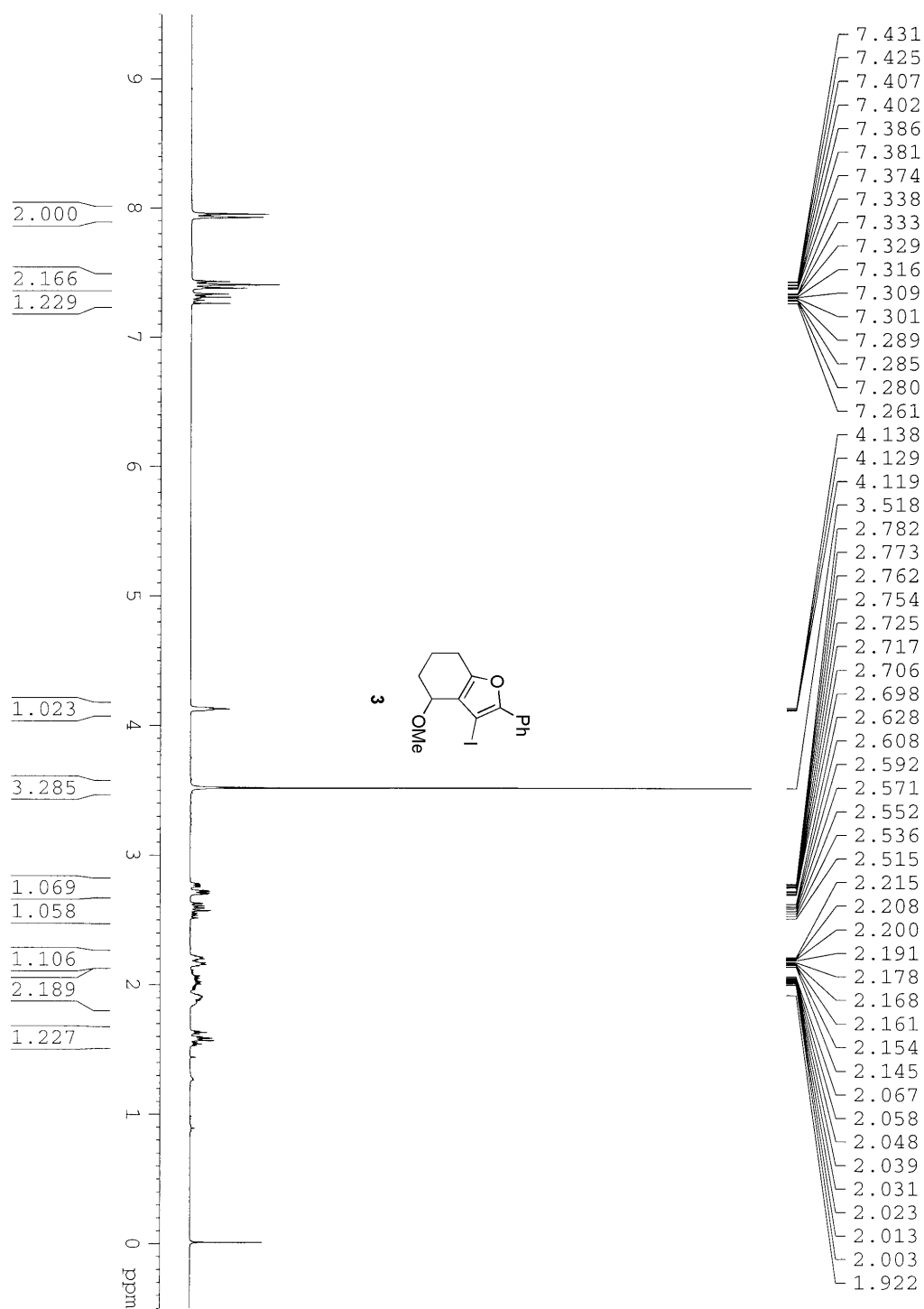
This compound was prepared by following a procedure from the literature.¹¹ Furan **2** (45.6 mg, 0.20 mmol) and DDQ (85 mg, 0.34 mmol) in benzene (6.5 mL) were refluxed for 6 h. The mixture was allowed to cool to room temperature, filtrated, washed with 10

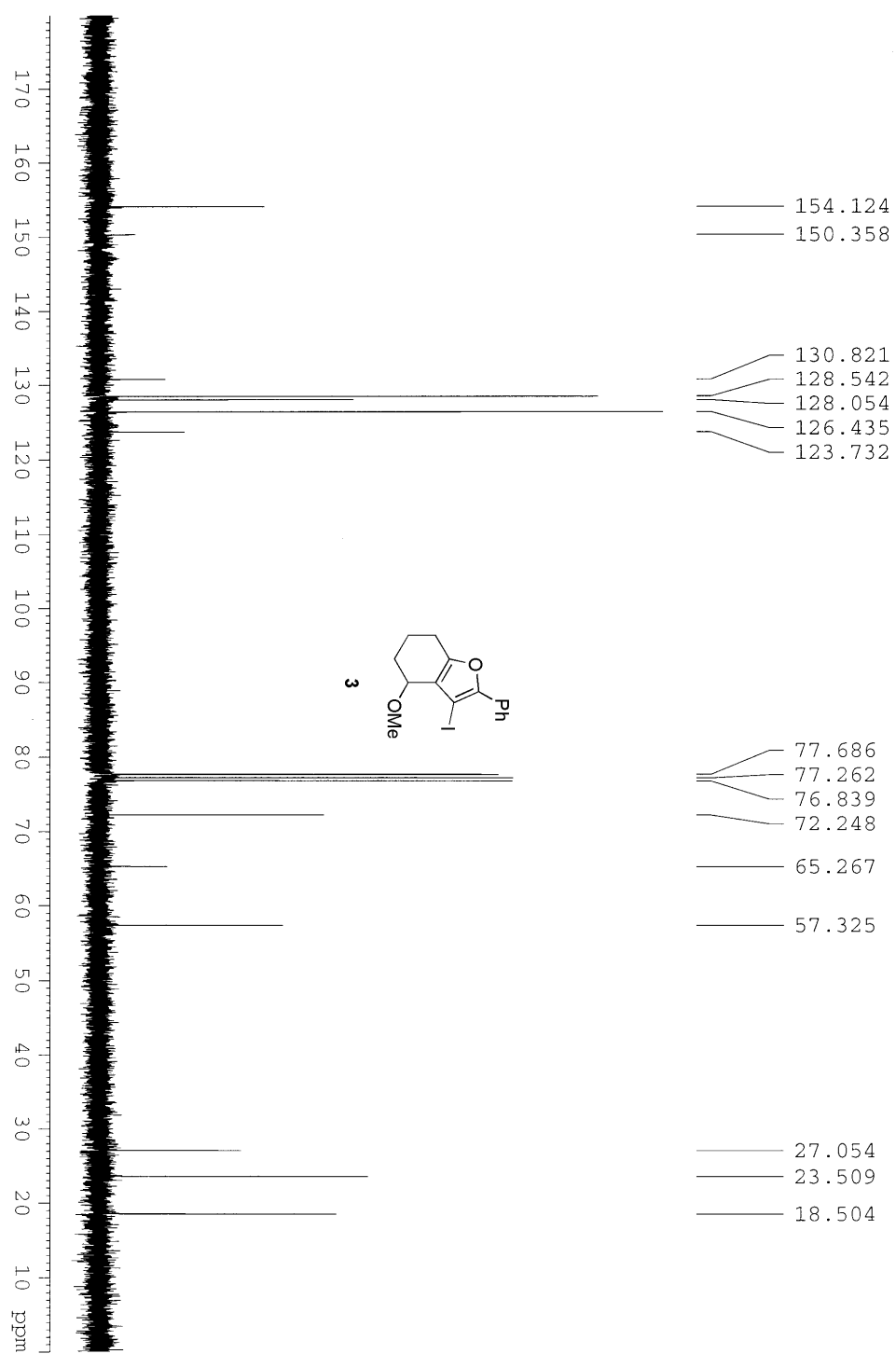
% Na₂CO₃ (6 mL), dried (MgSO₄), and filtered. The solvent was removed under reduced pressure and the residue was purified by column chromatography (12:1 hexane/EtOAc) on silica gel to afford 17.7 mg (40%) of the indicated compound **84** as a colorless oil: ¹H NMR (CDCl₃) δ 3.97 (s, 3H), 6.67 (dd, *J* = 0.9, 7.5 Hz, 1H), 7.13-7.26 (m, 3H), 7.31-7.36 (m, 1H), 7.41-7.48 (m, 2H), 7.83-7.87 (m, 2H); ¹³C NMR (CDCl₃) δ 55.8, 99.0, 103.5, 104.7, 119.8, 125.0, 125.2, 128.5, 129.0, 130.8, 153.7, 154.9, 156.3; IR (CH₂Cl₂) 2961, 1607, 1486, 1252 cm⁻¹; HRMS *m/z* 224.0841 (calcd for C₁₅H₁₂O₂, 224.0837).

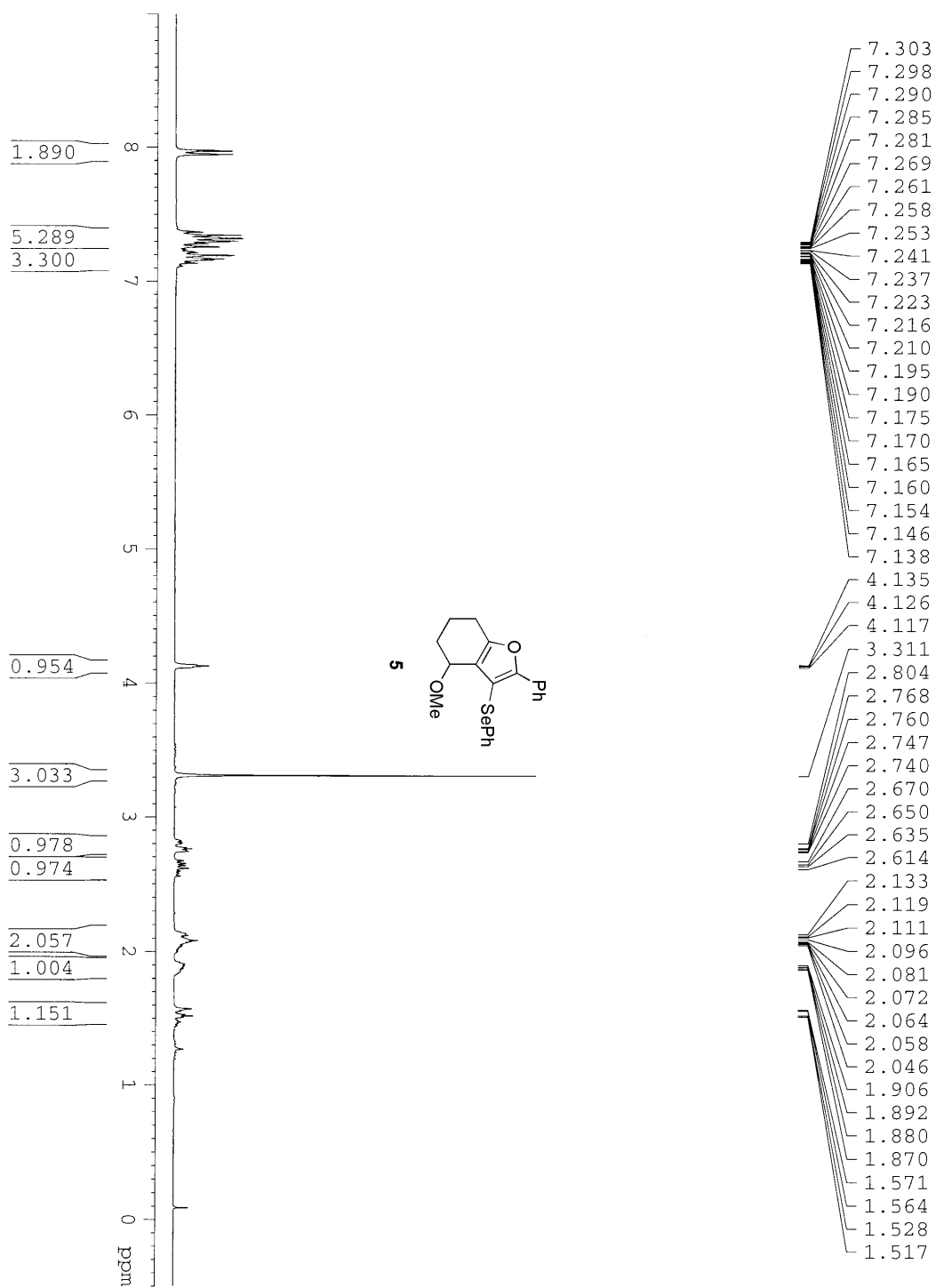
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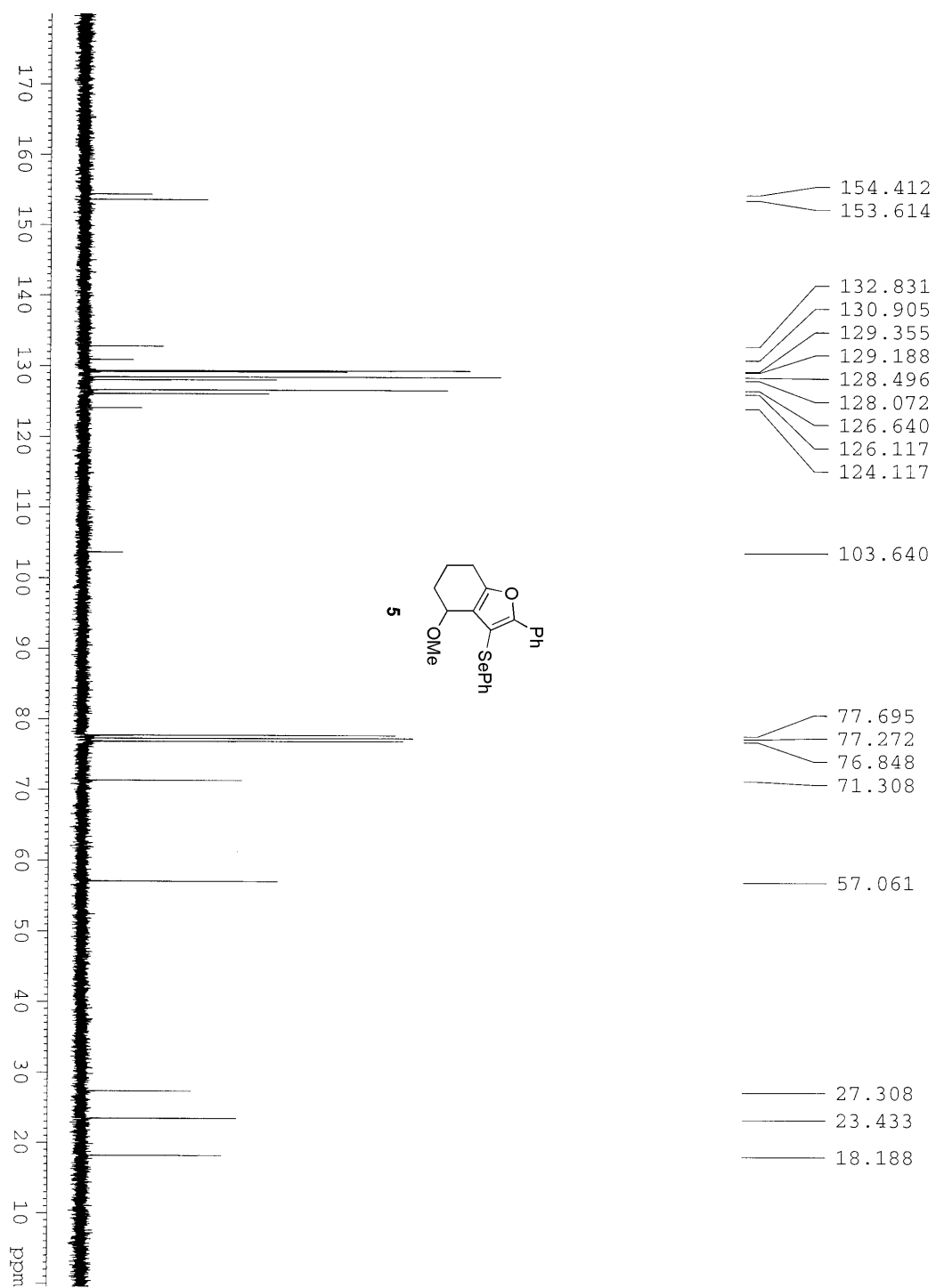
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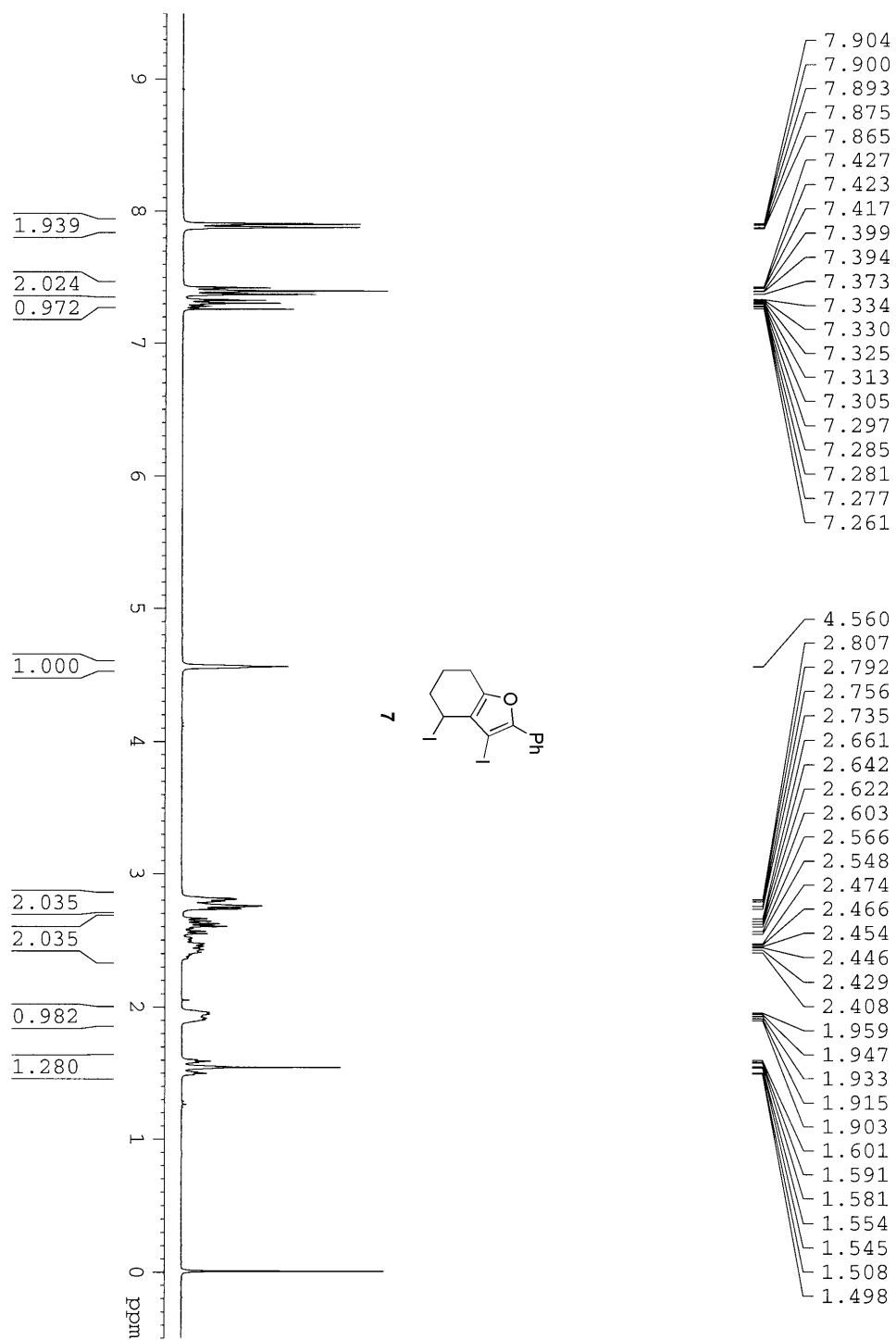
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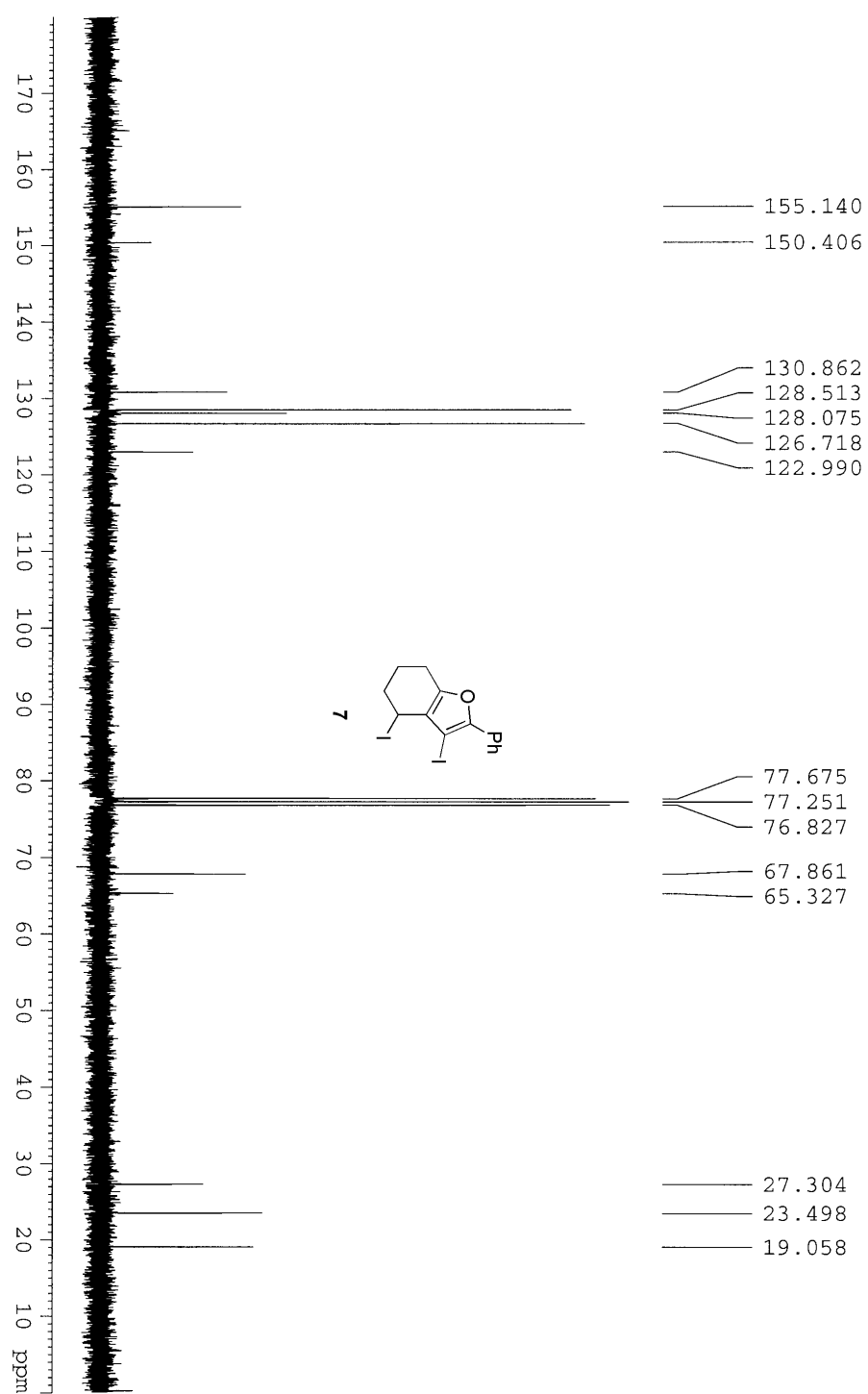


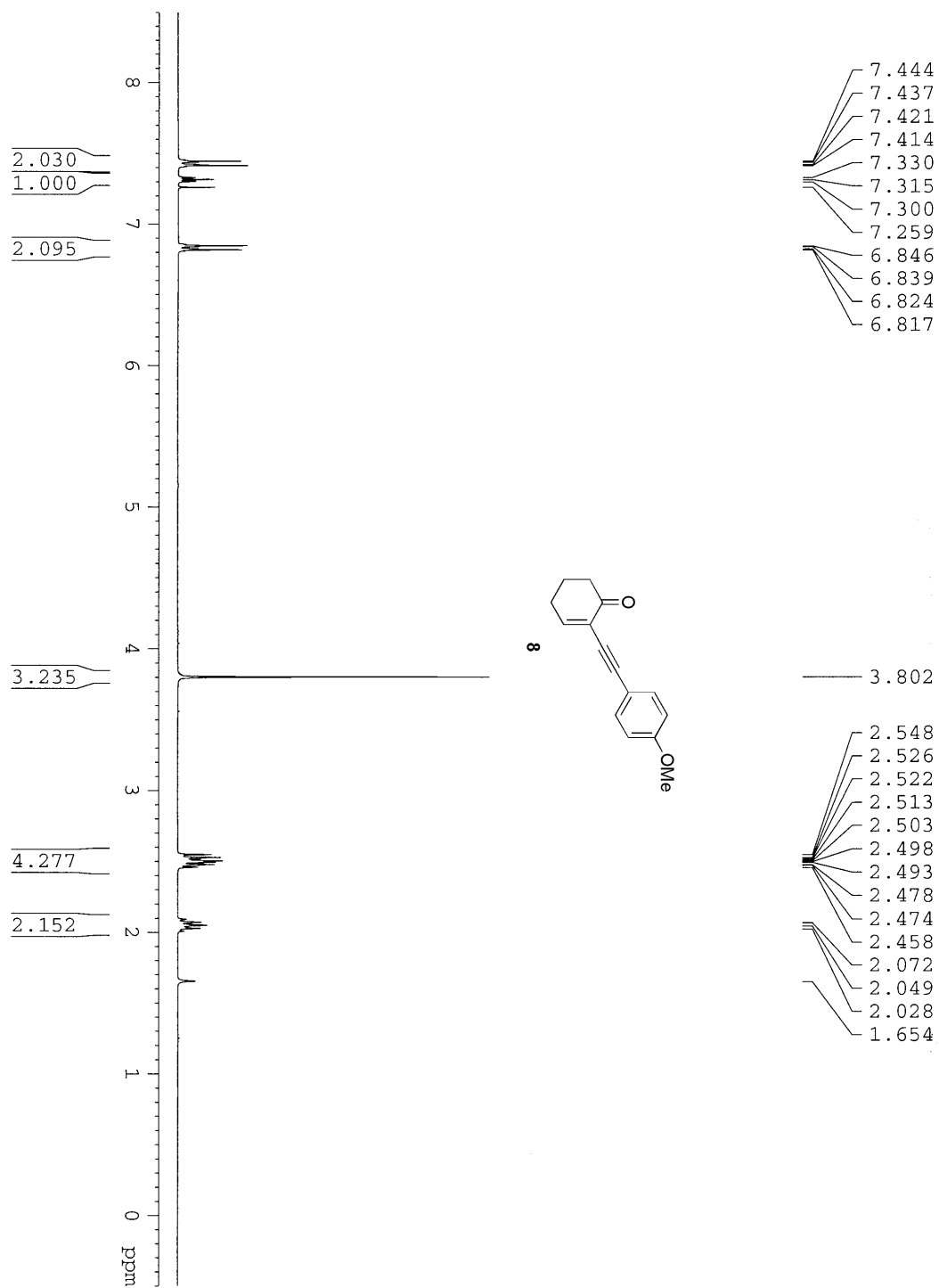


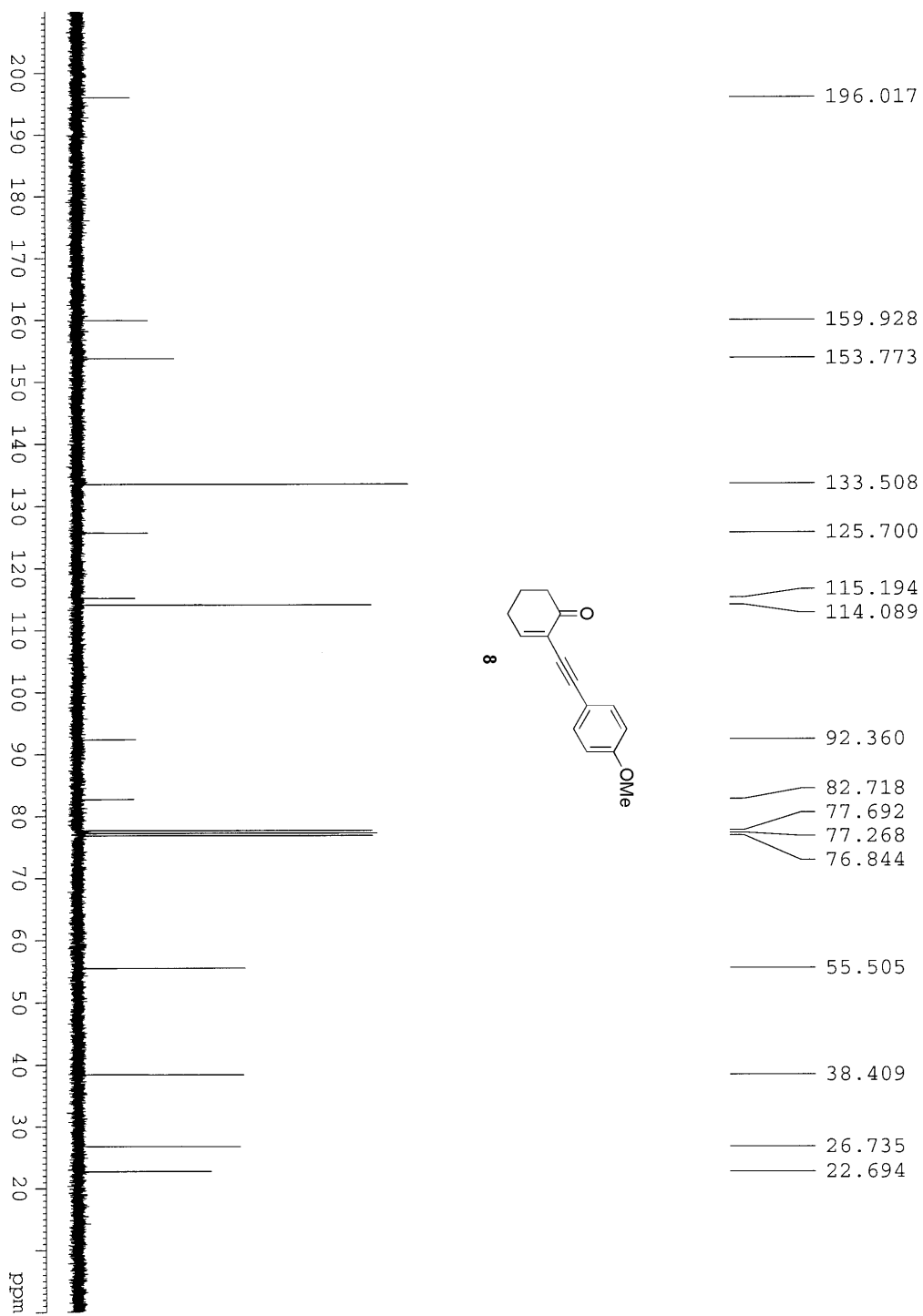


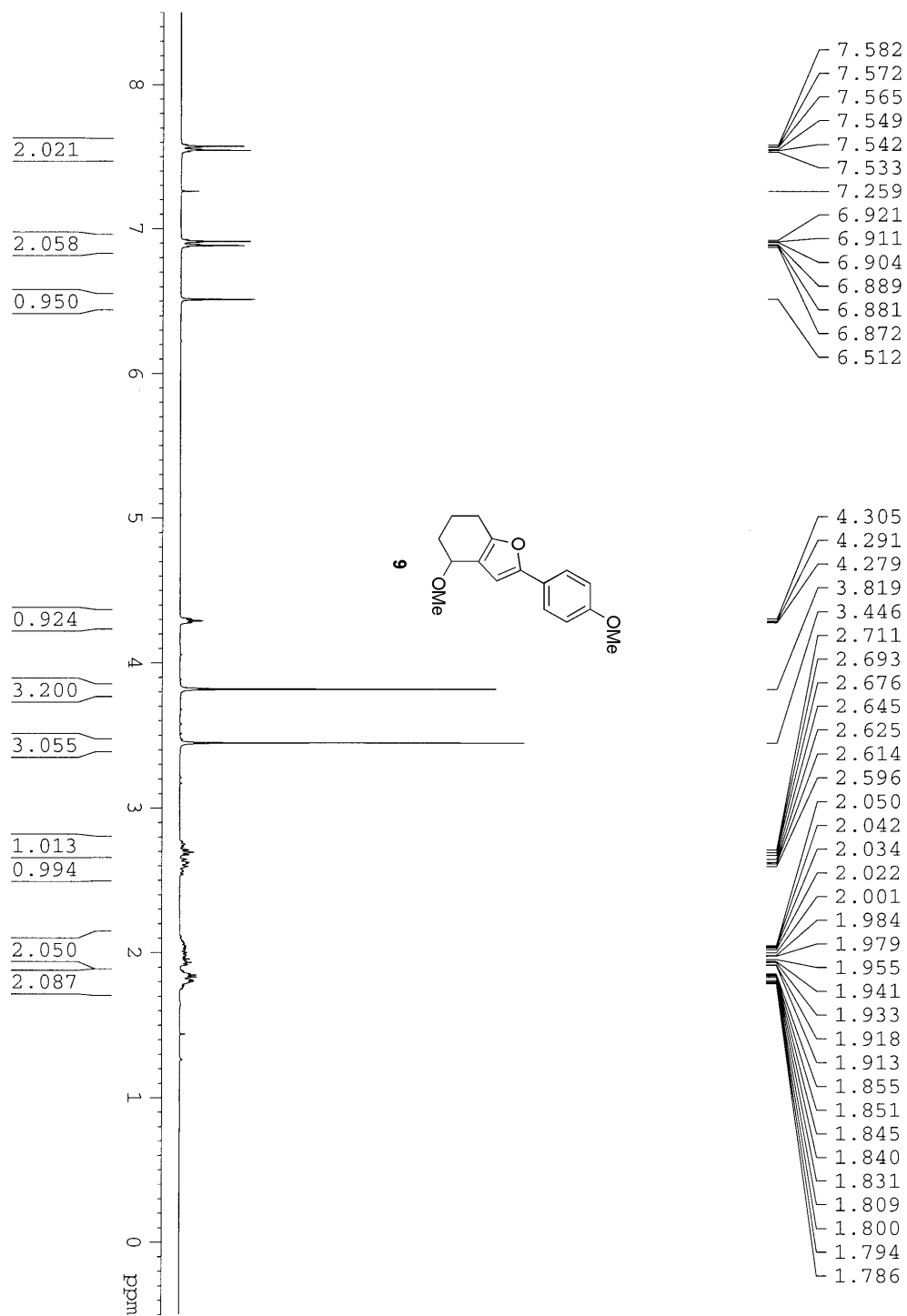


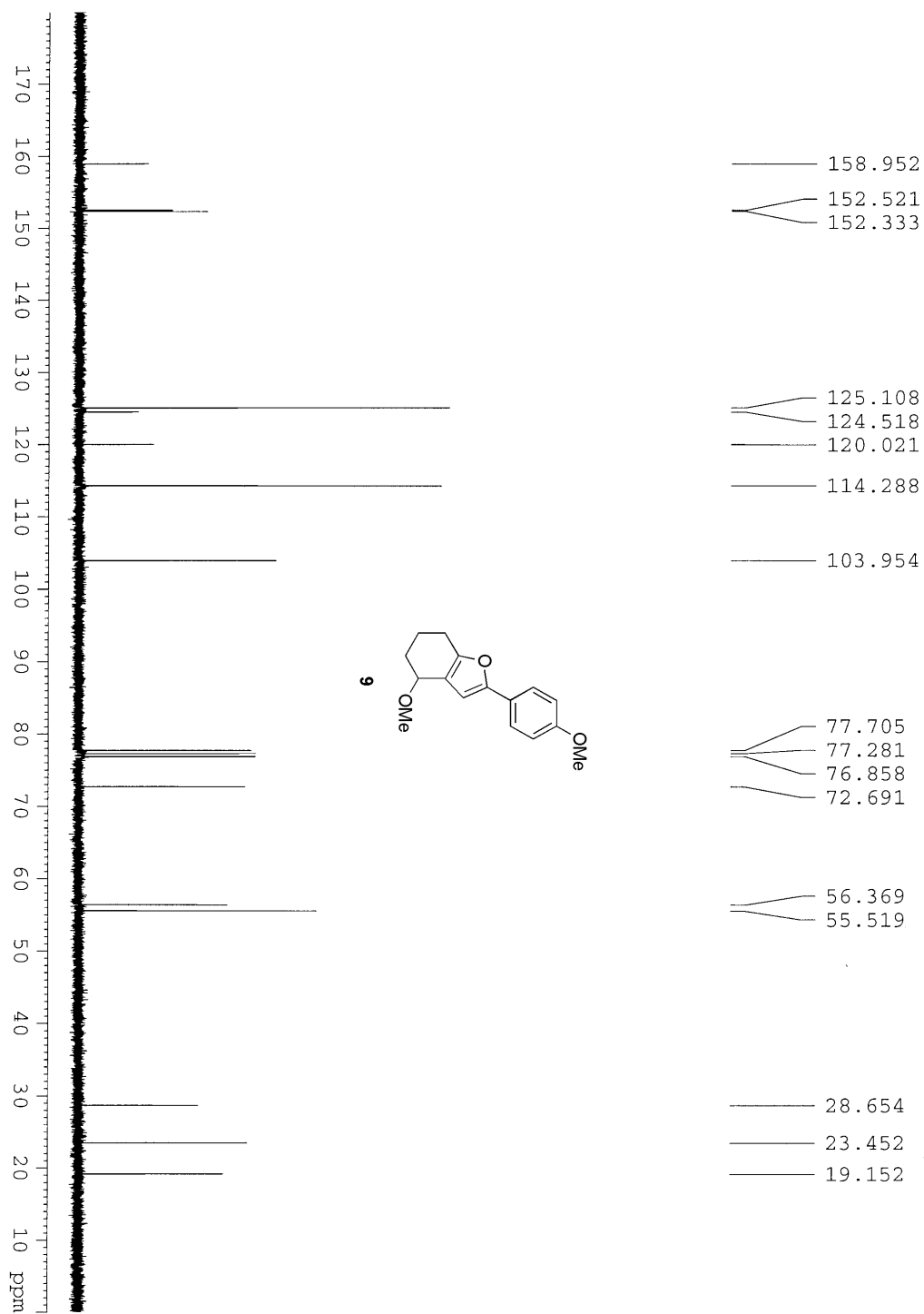


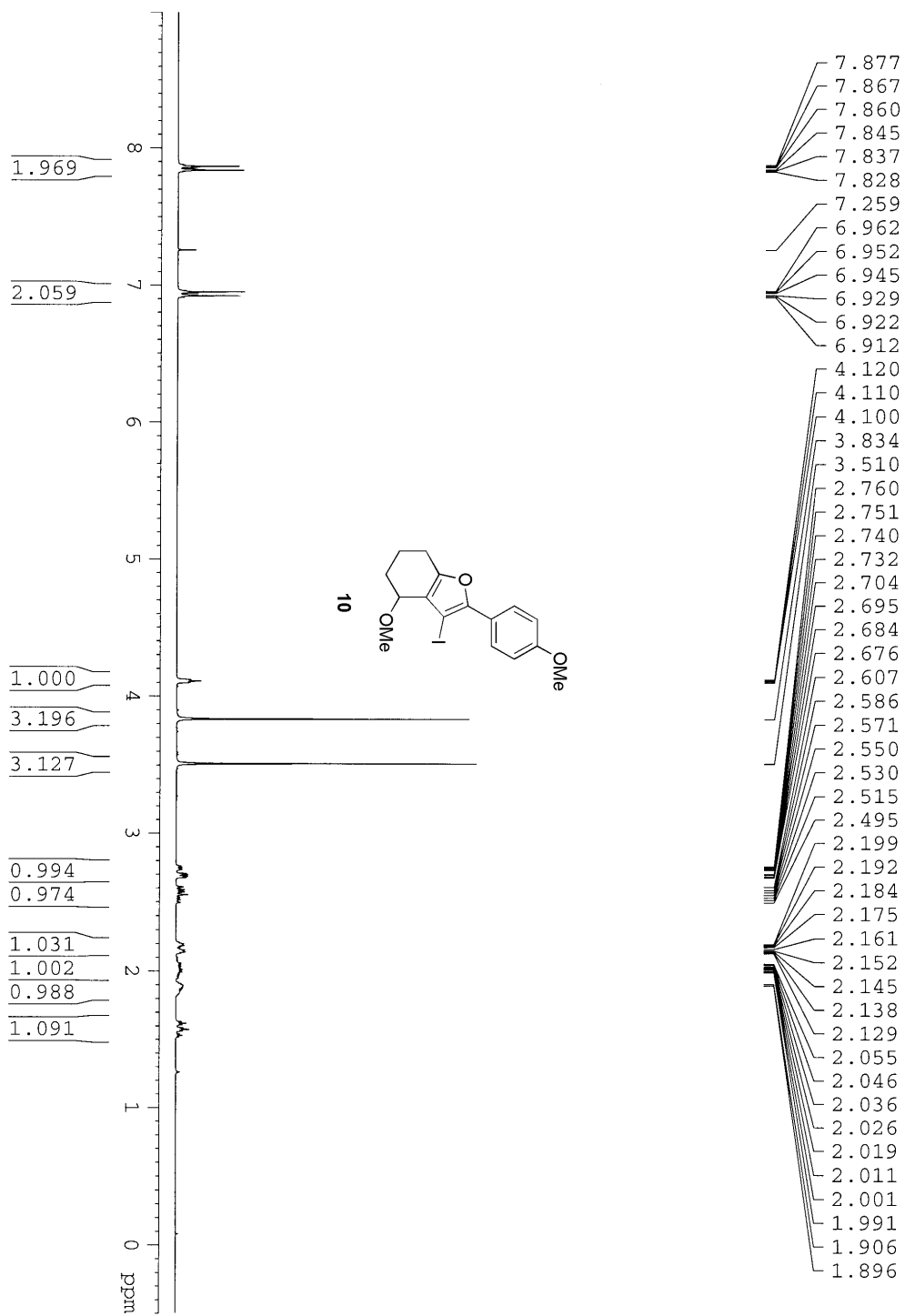


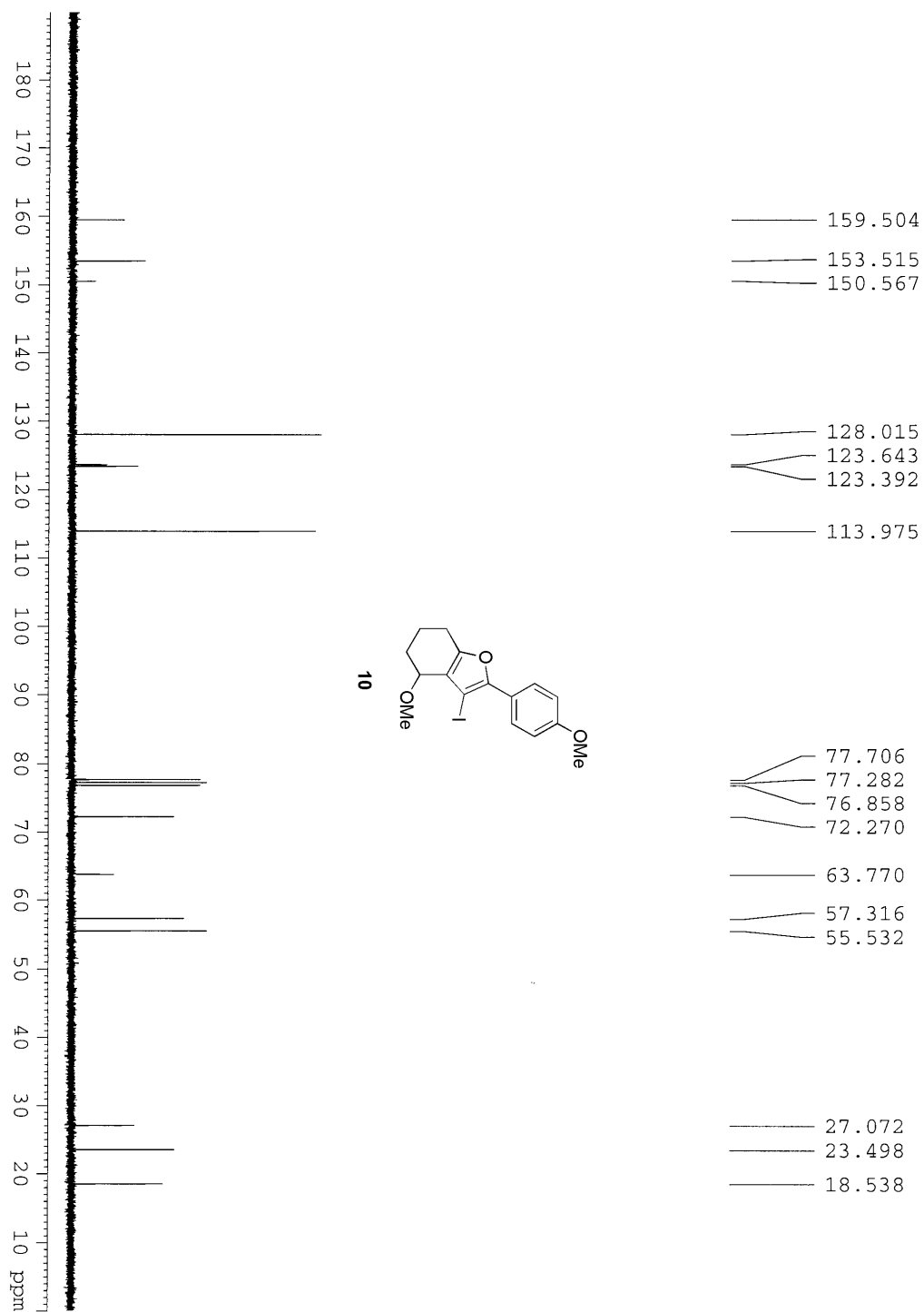


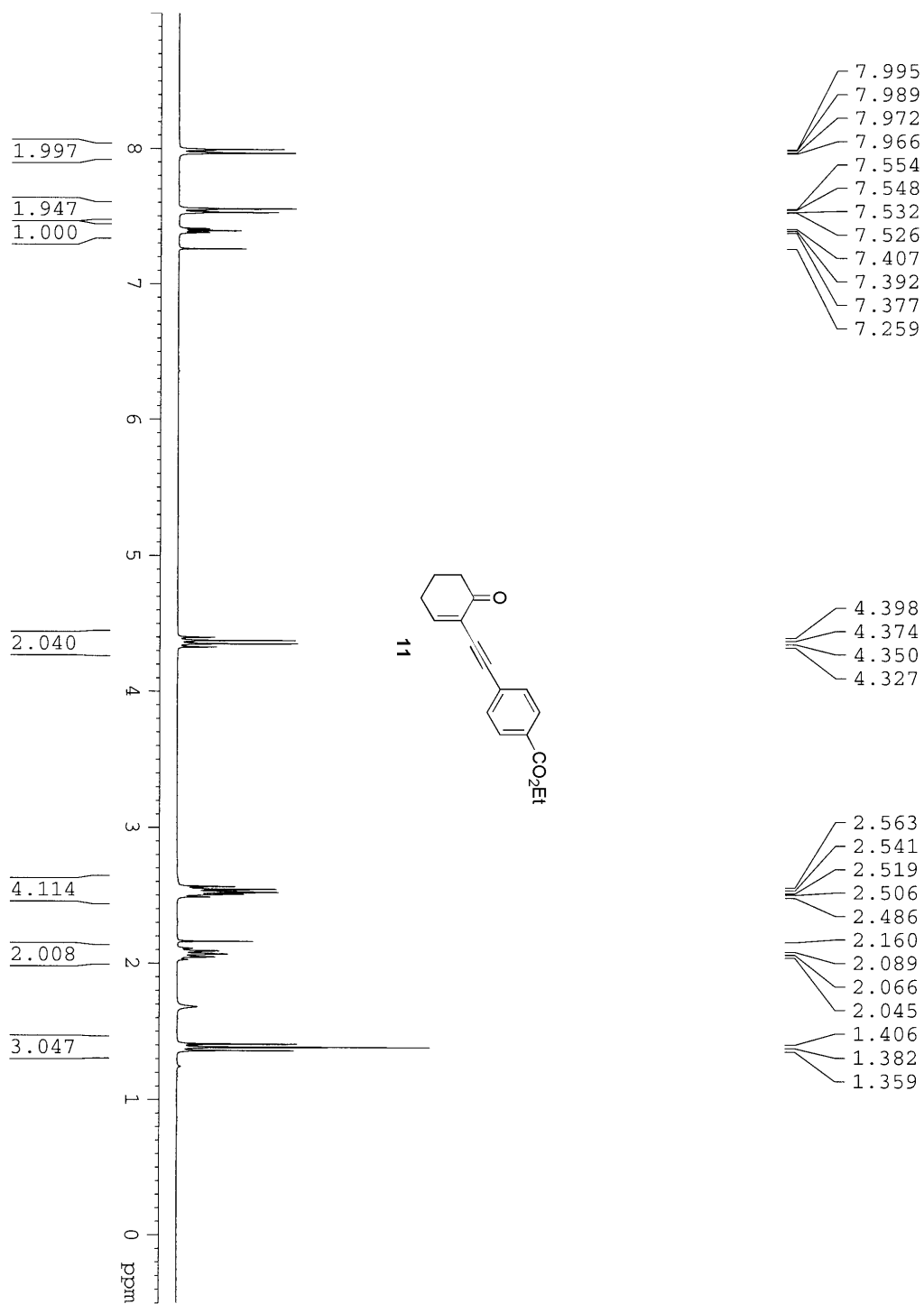


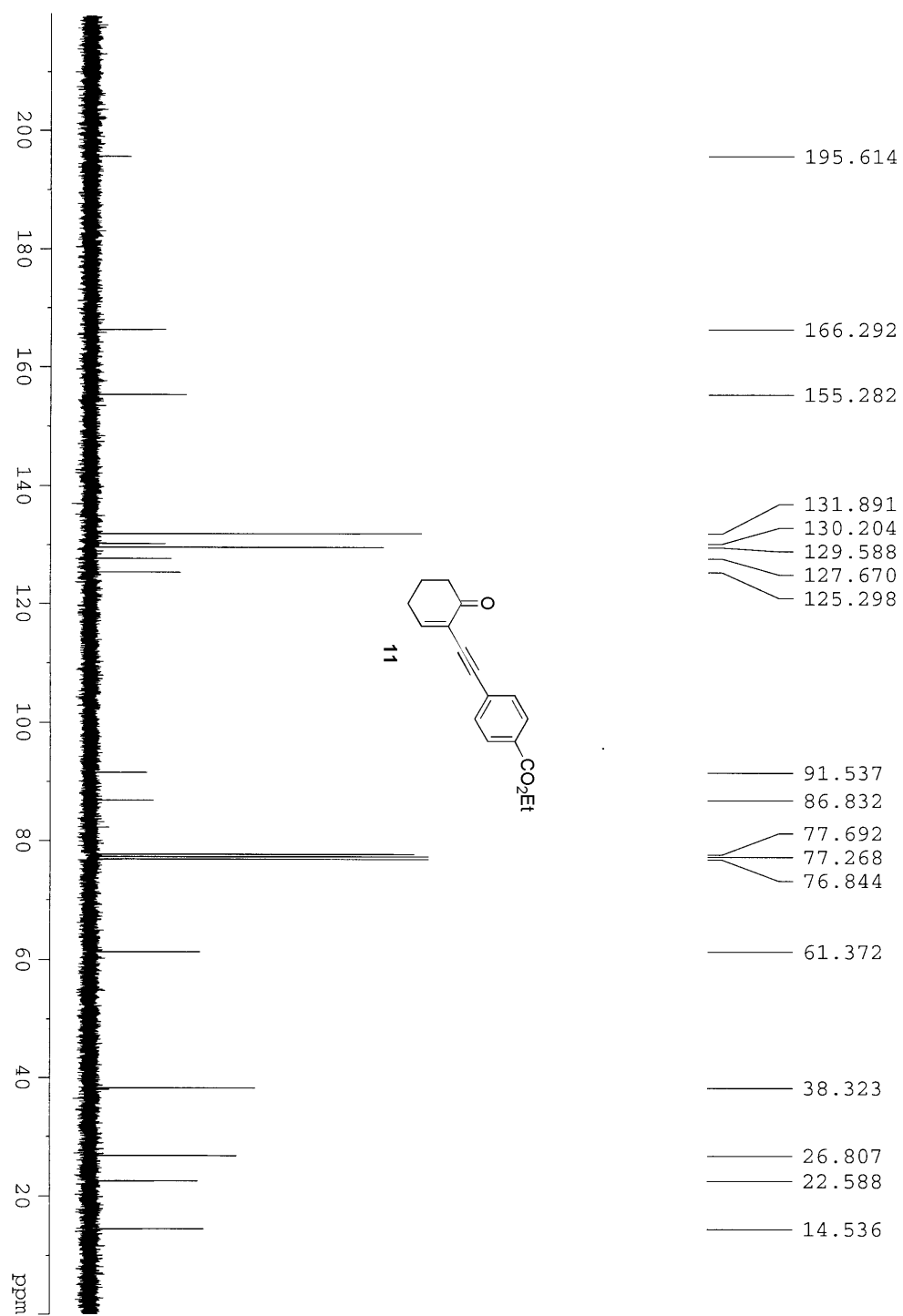


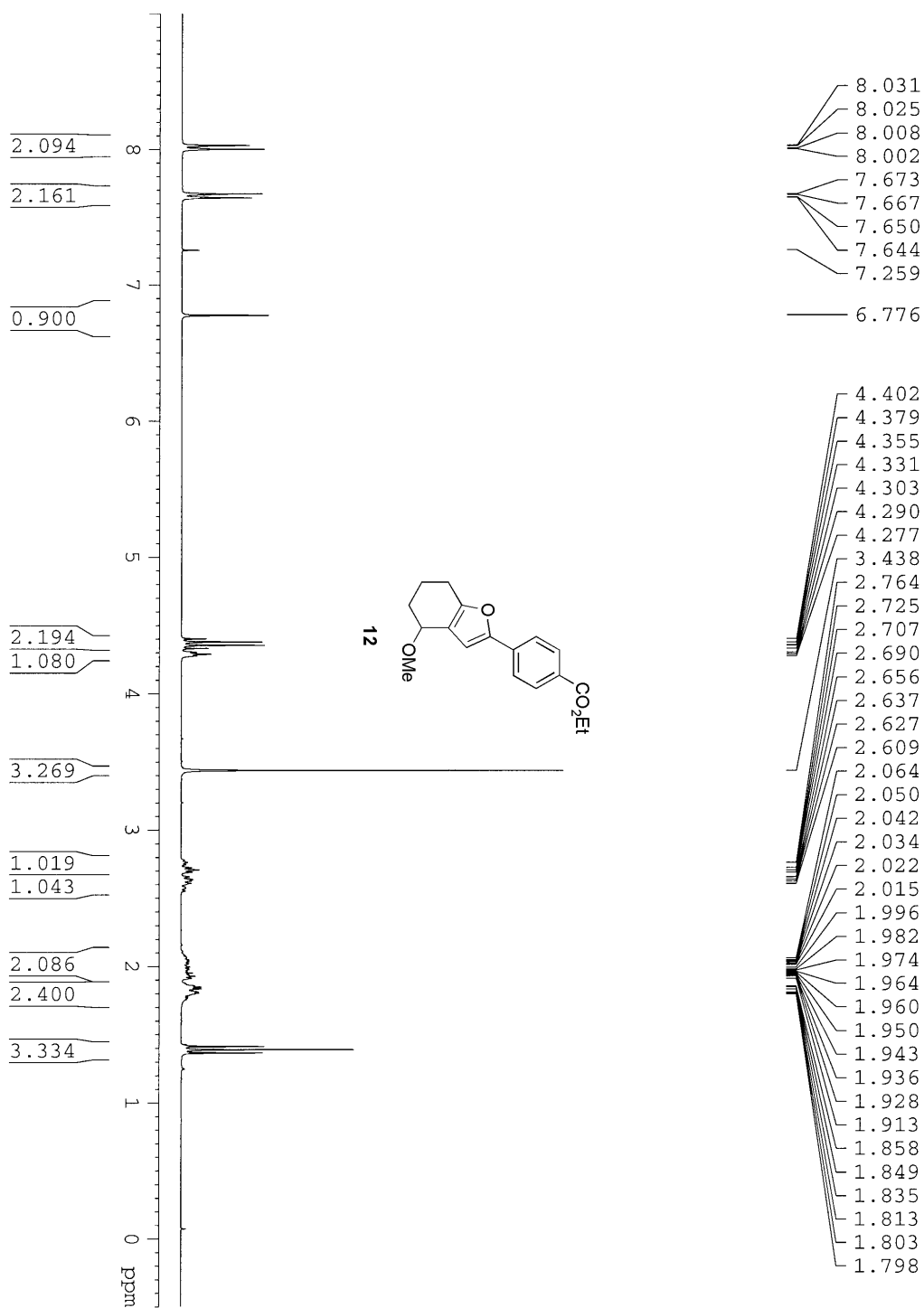


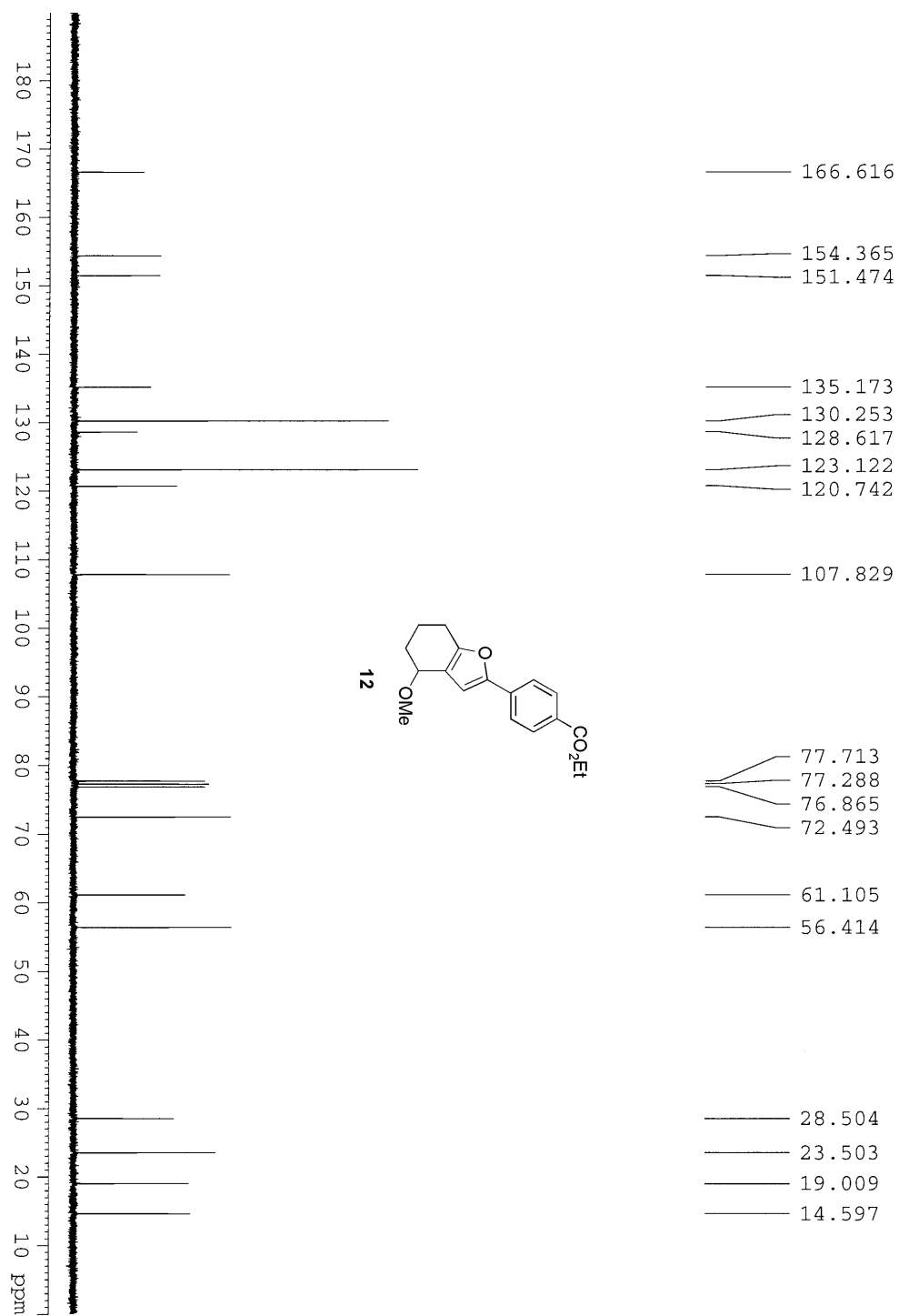


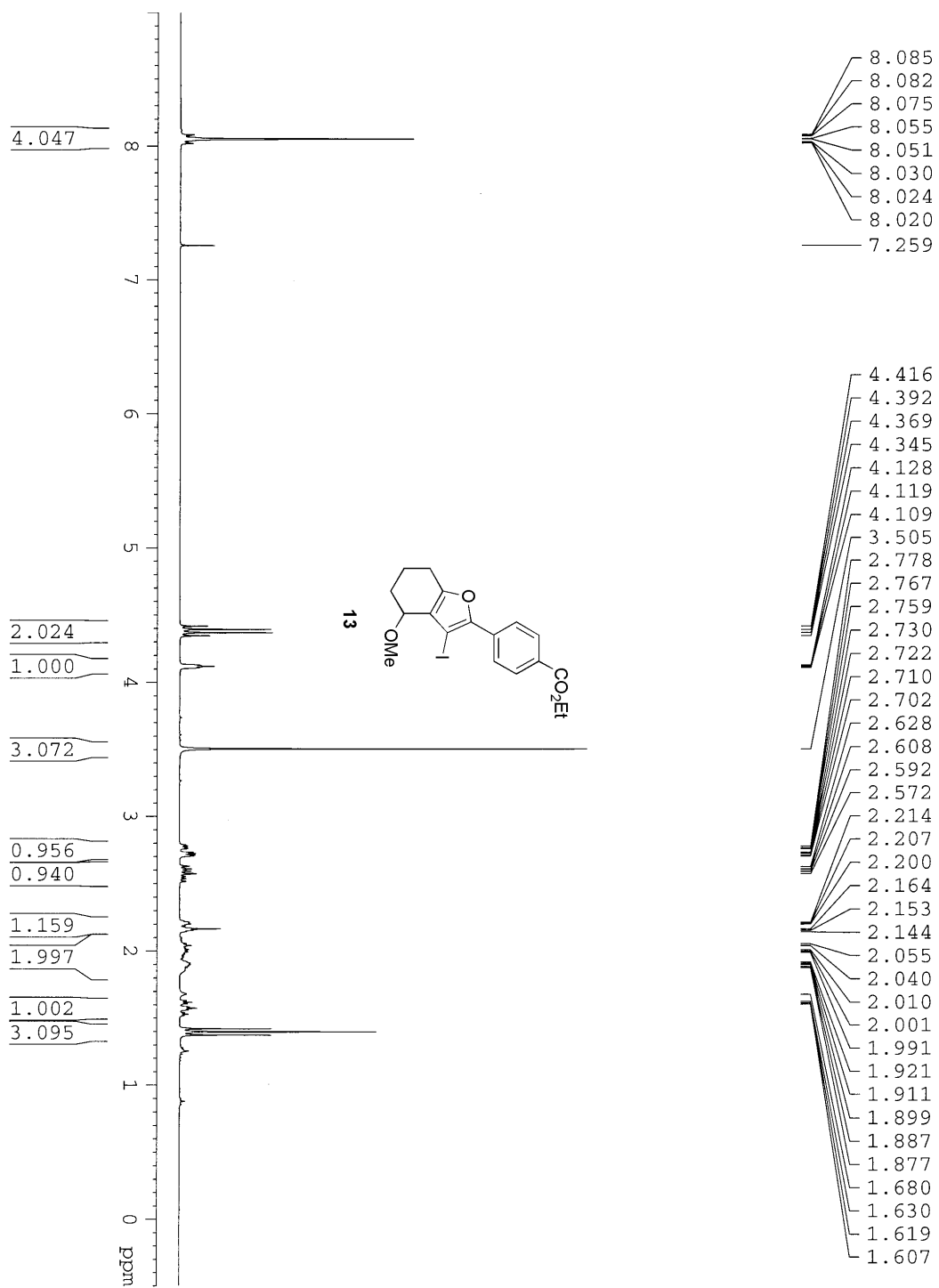


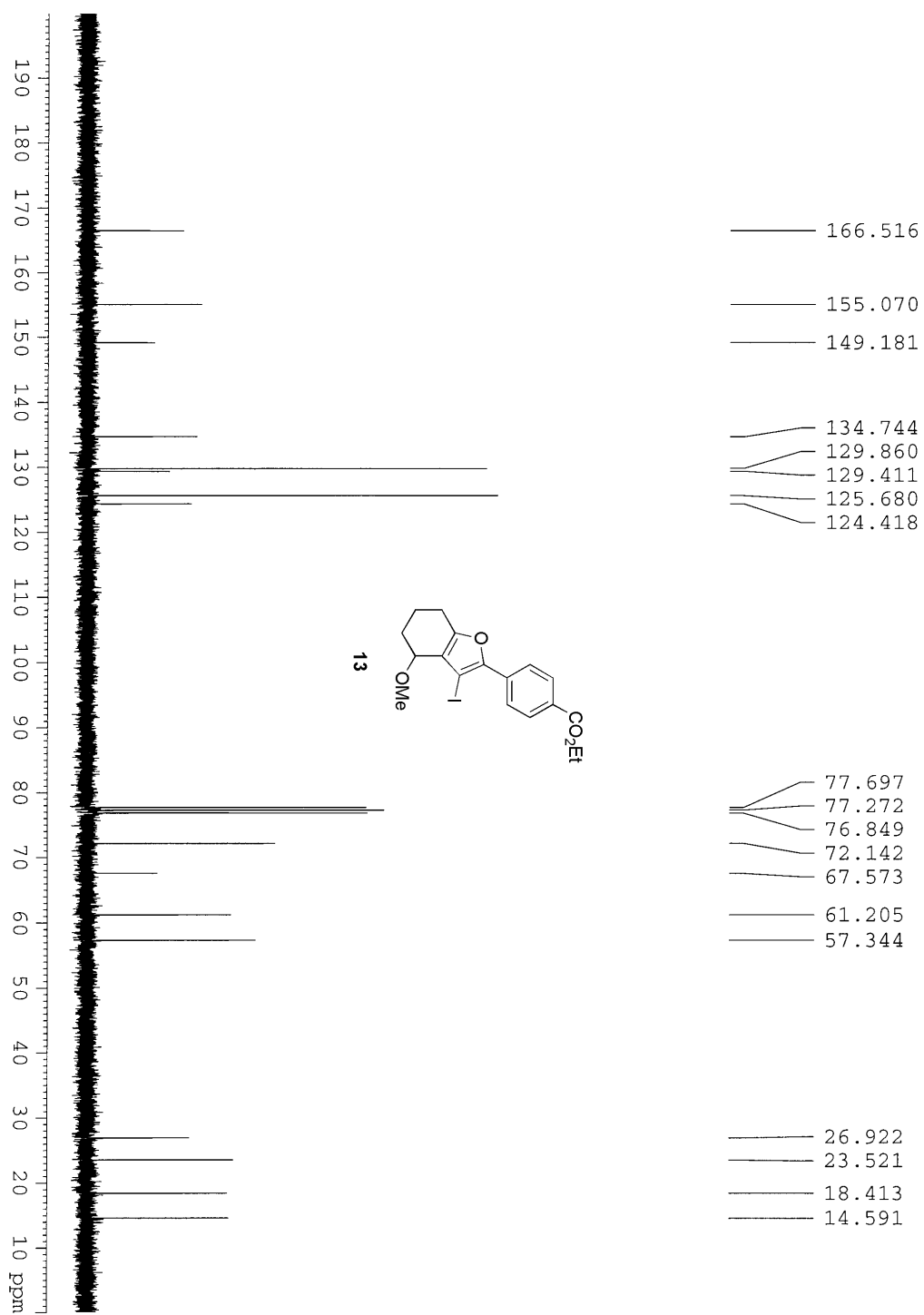


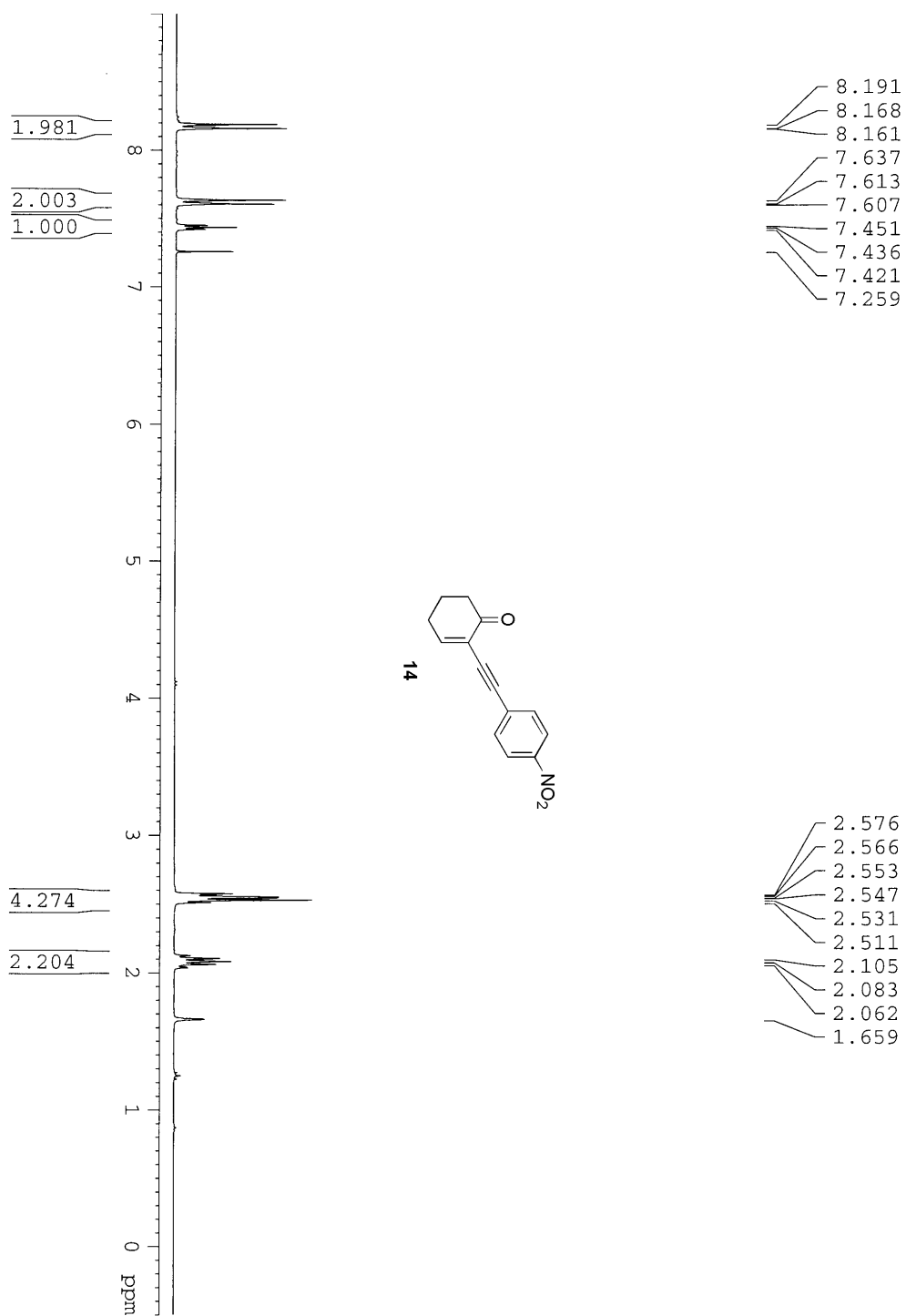


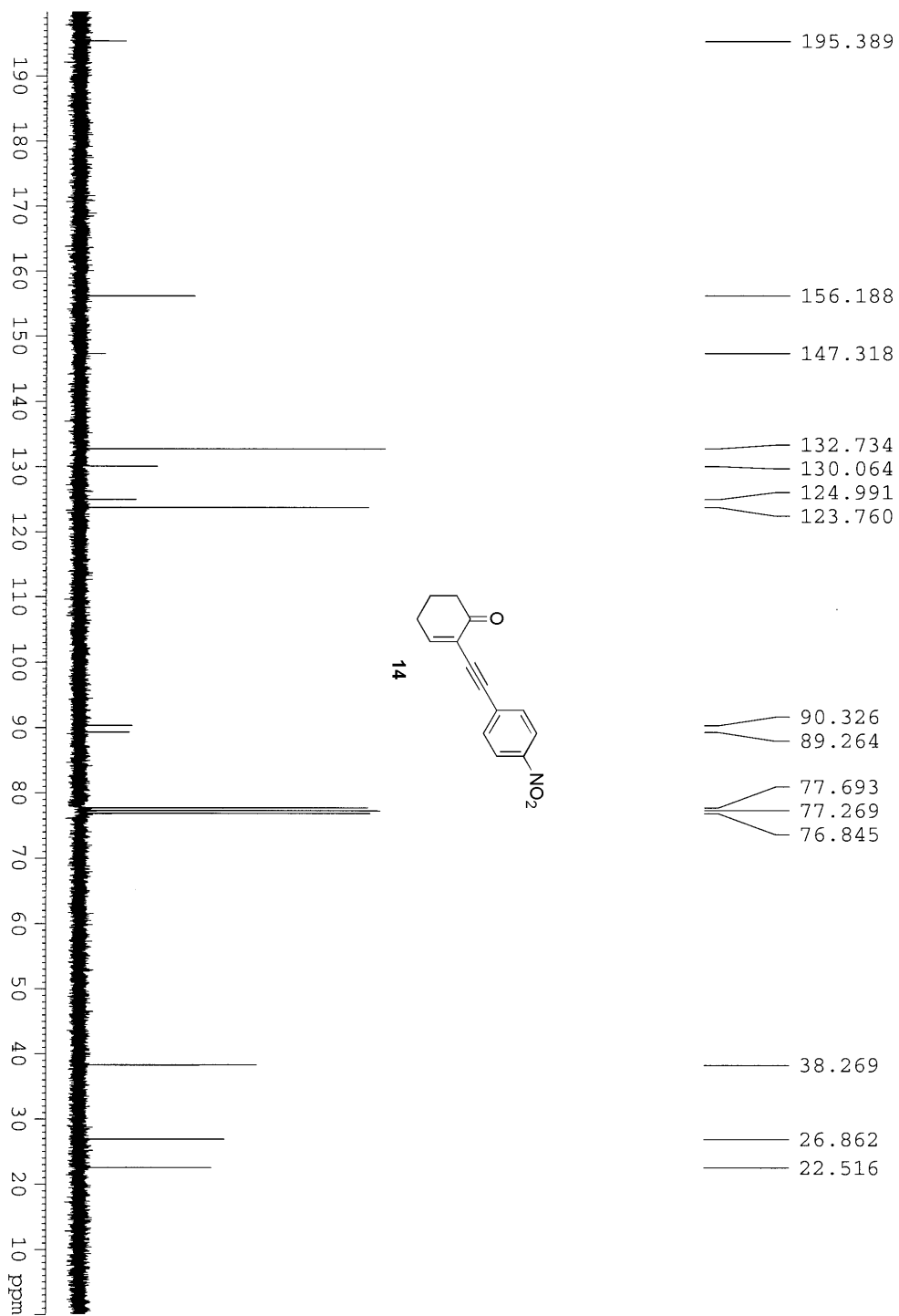


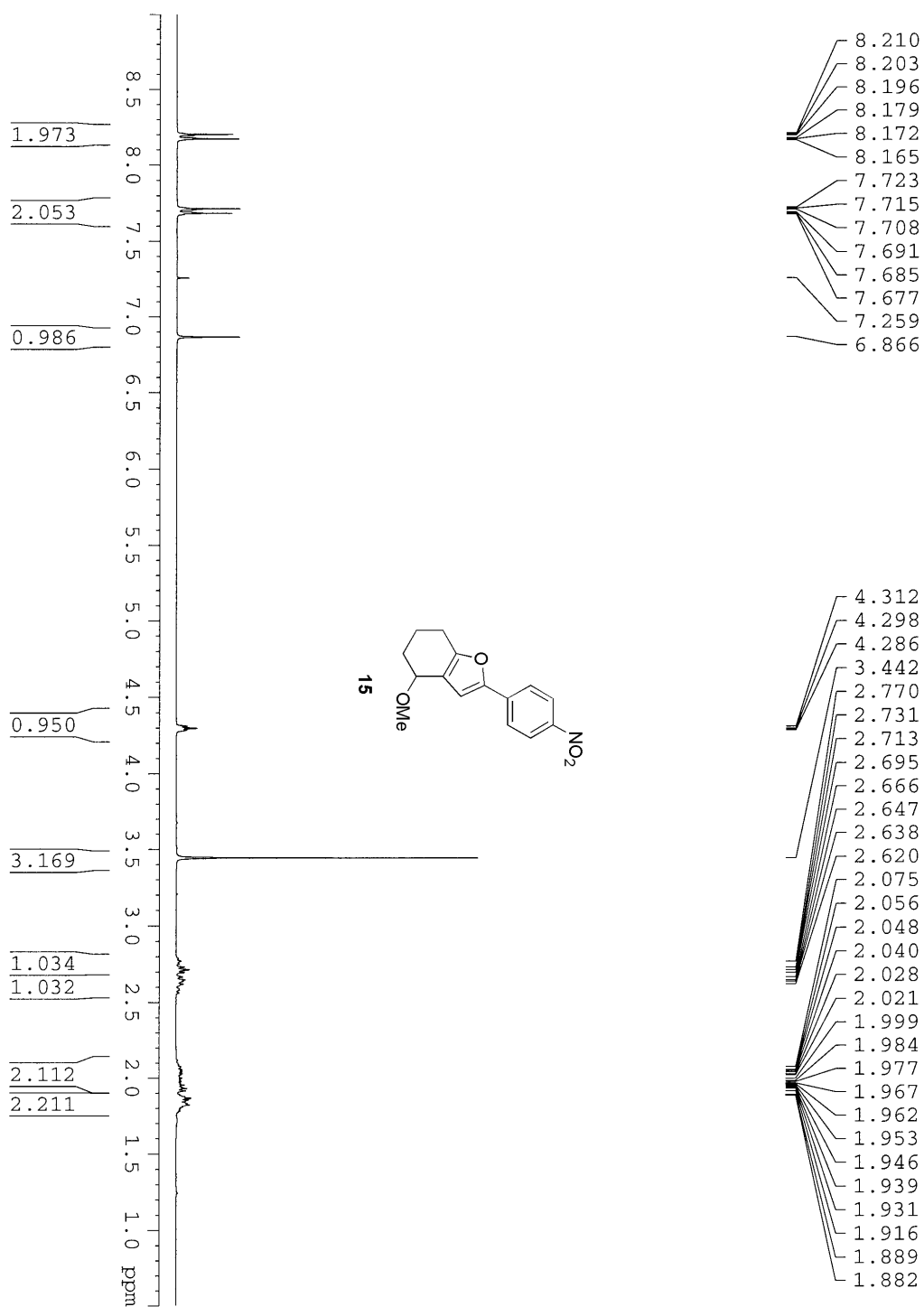


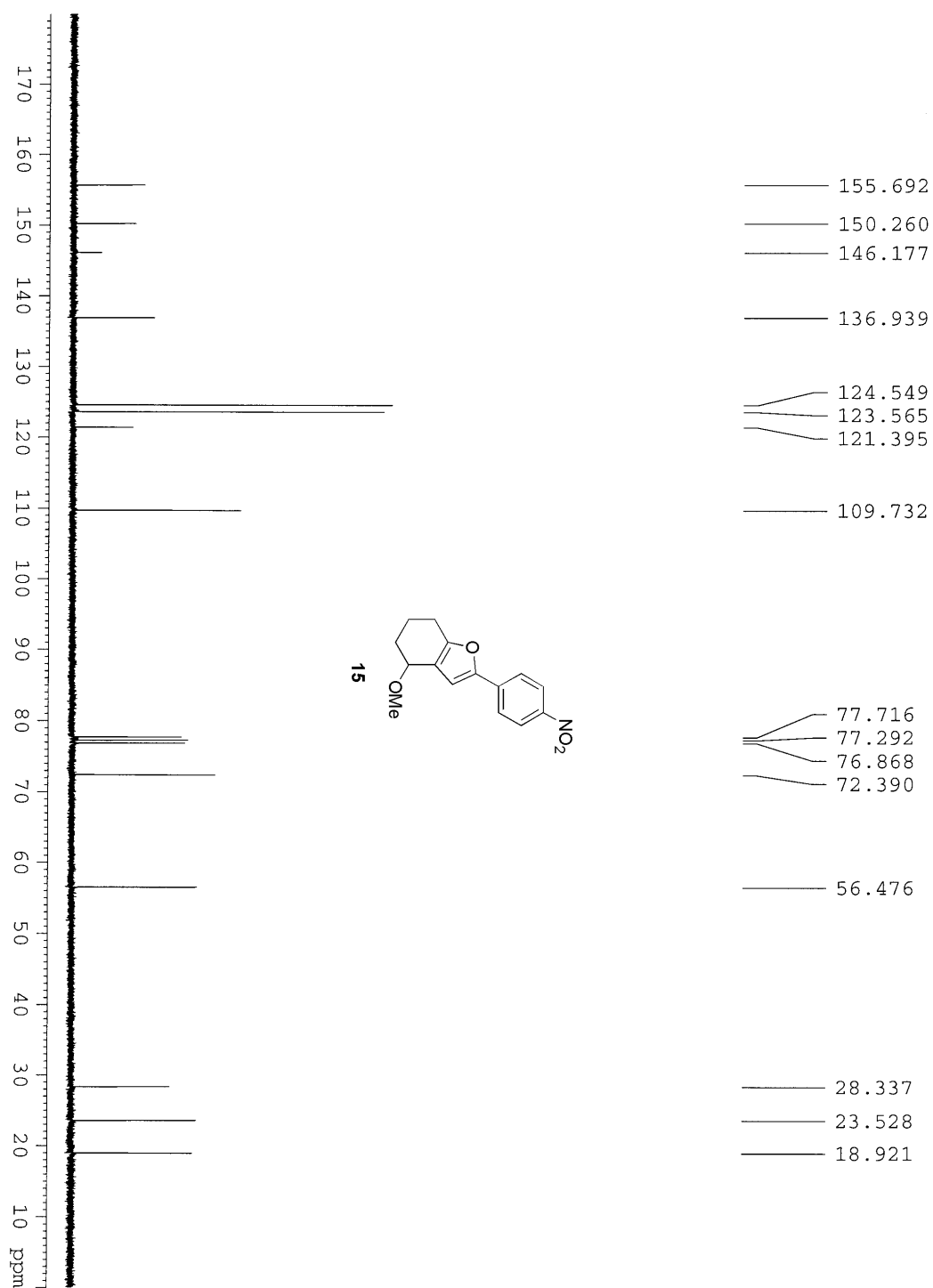


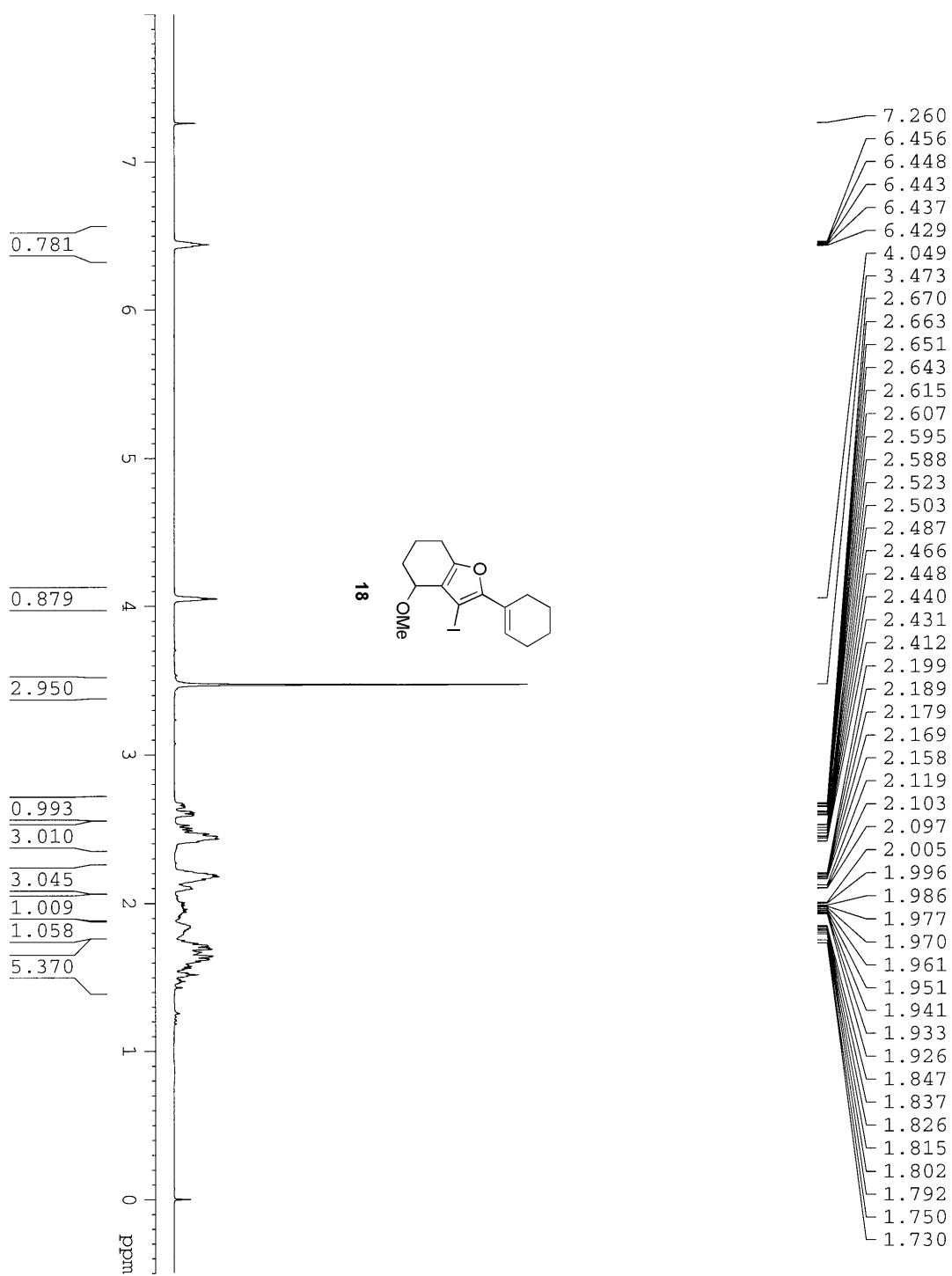


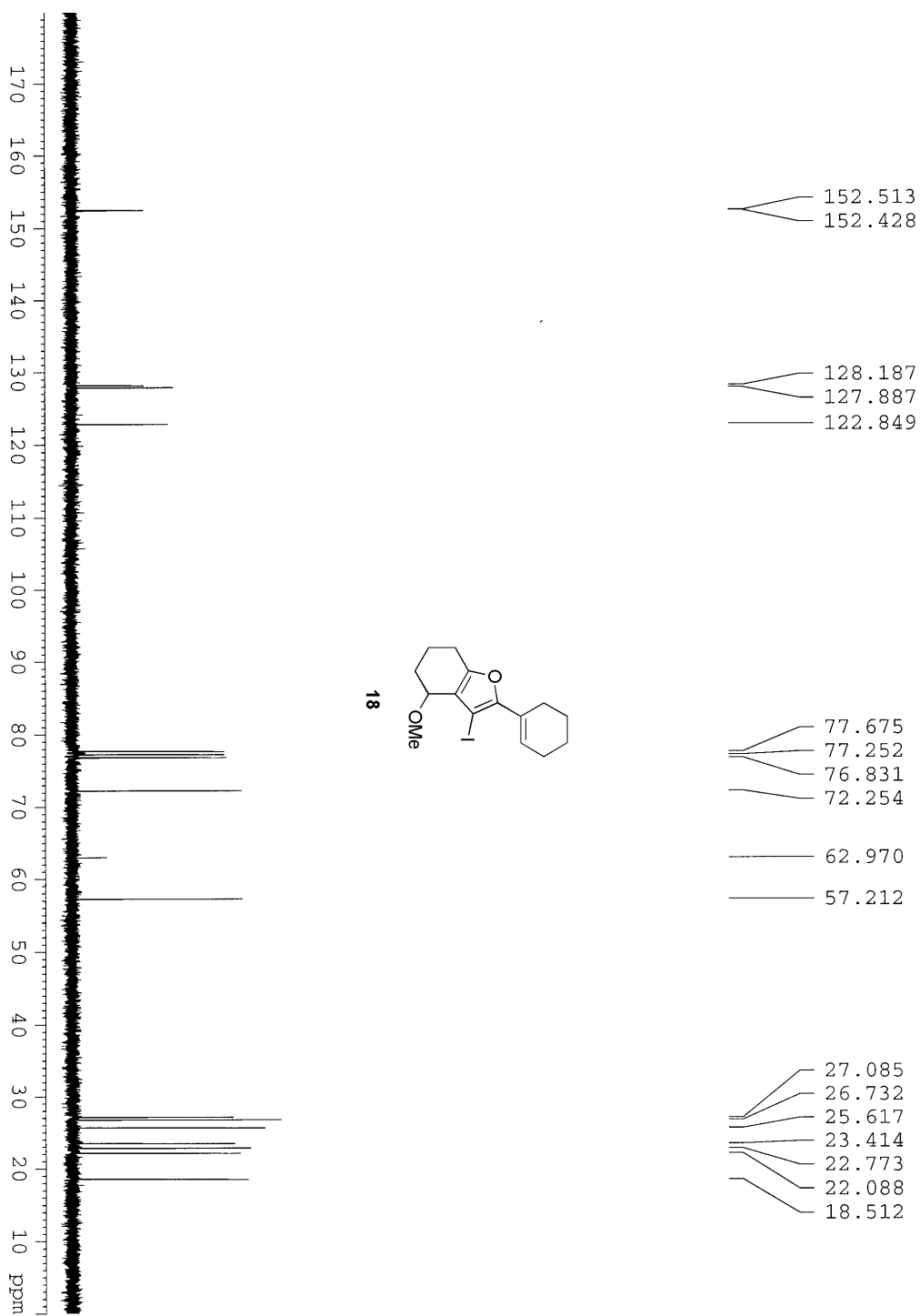


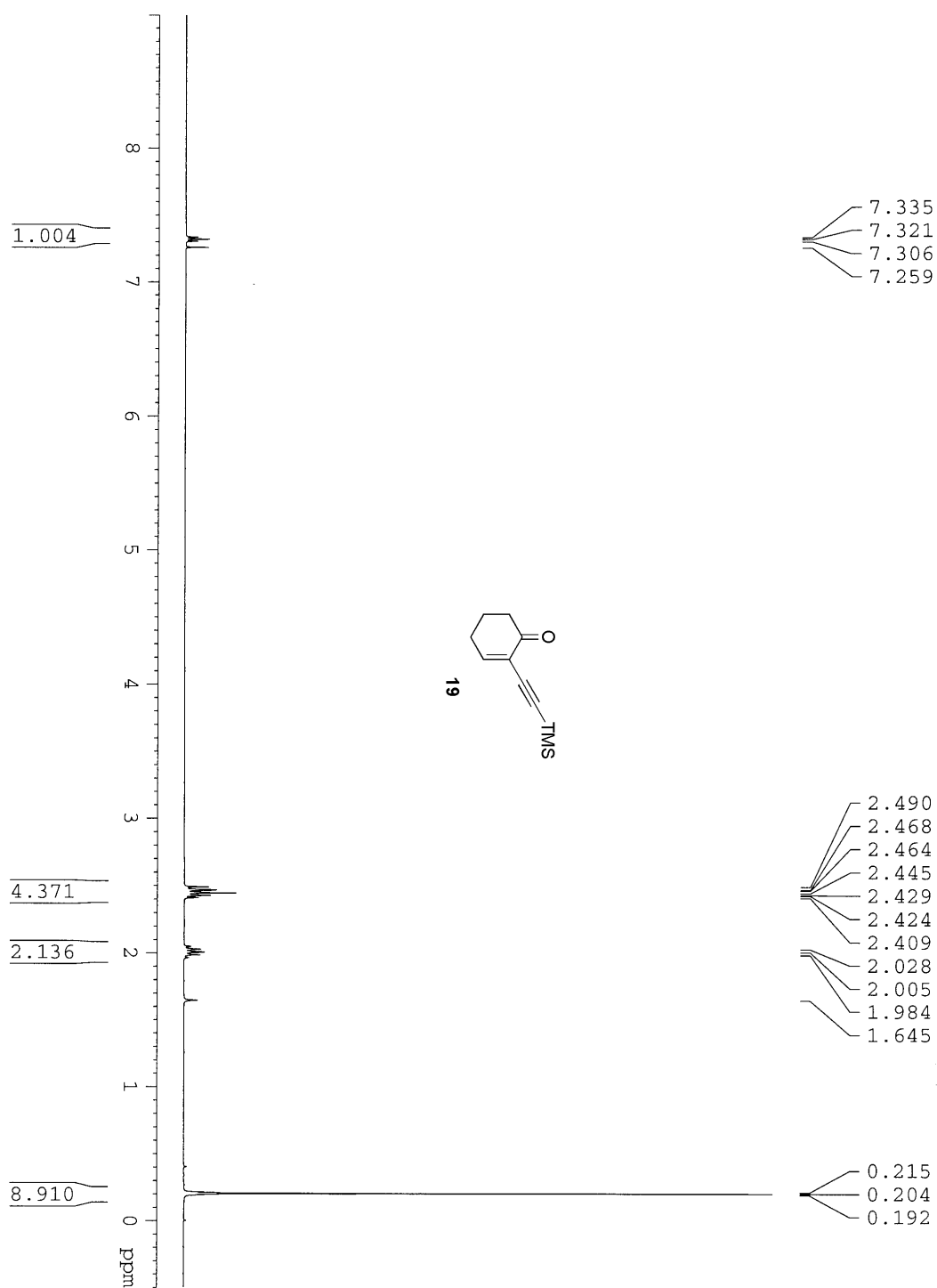


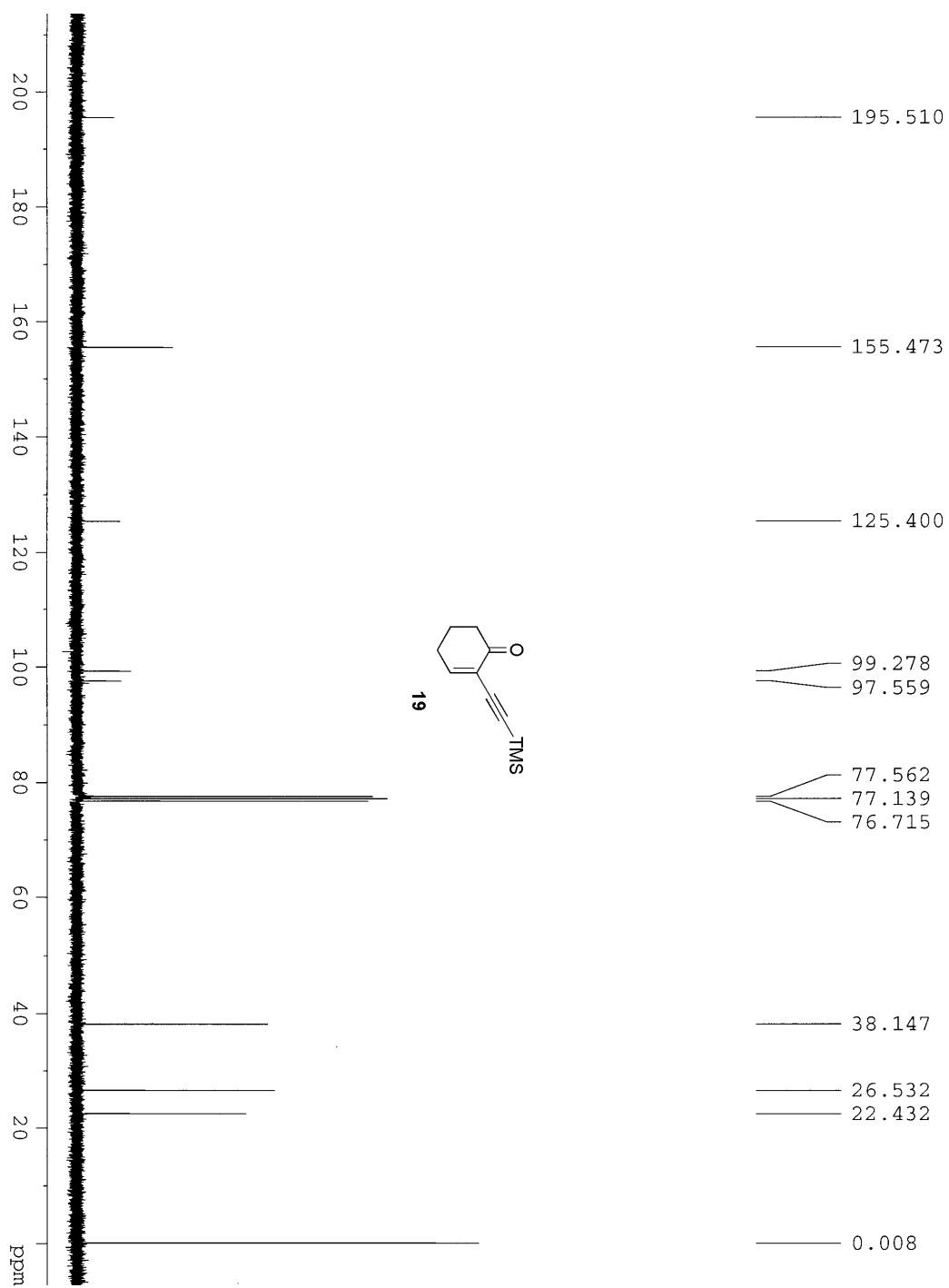


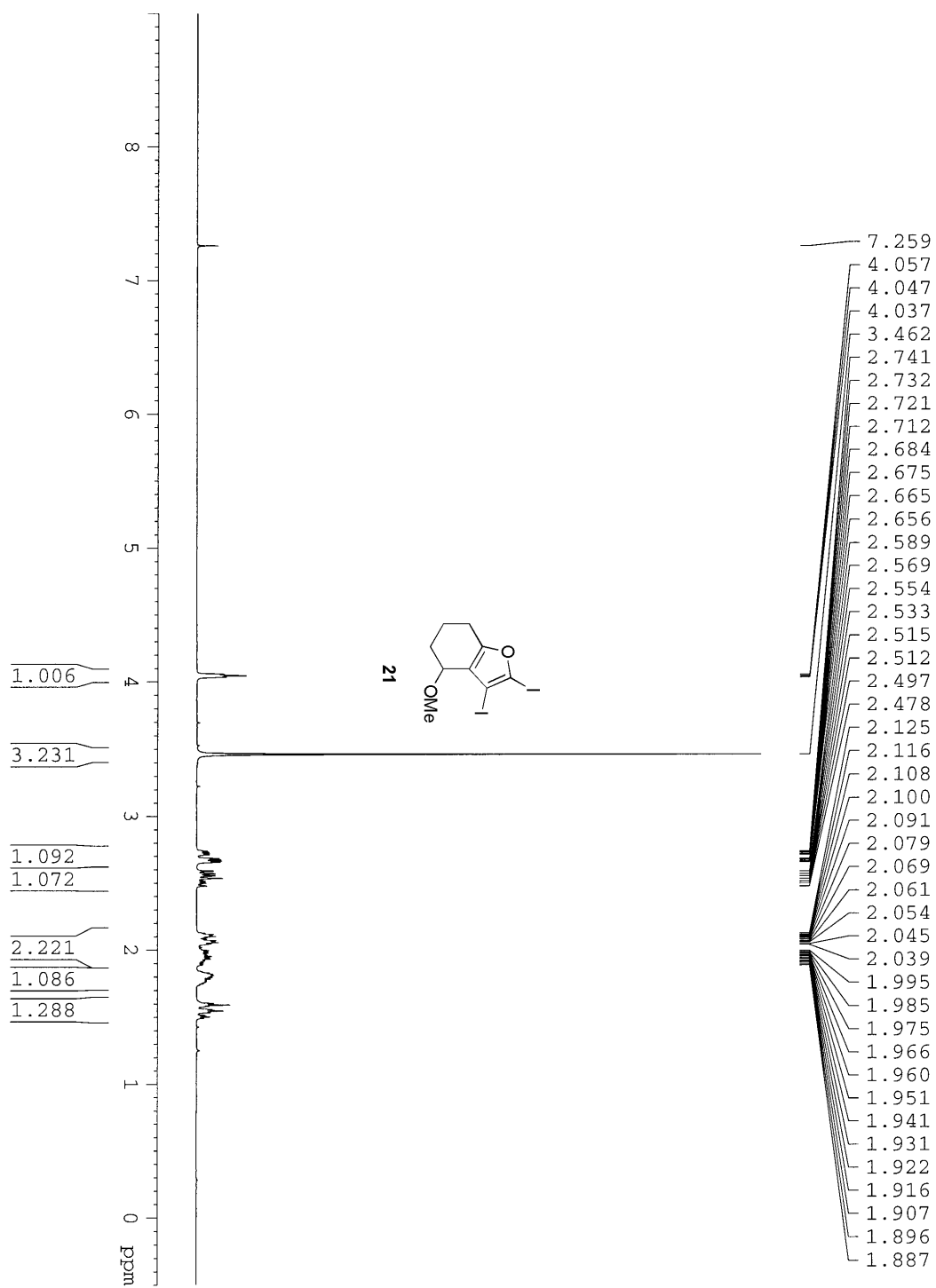


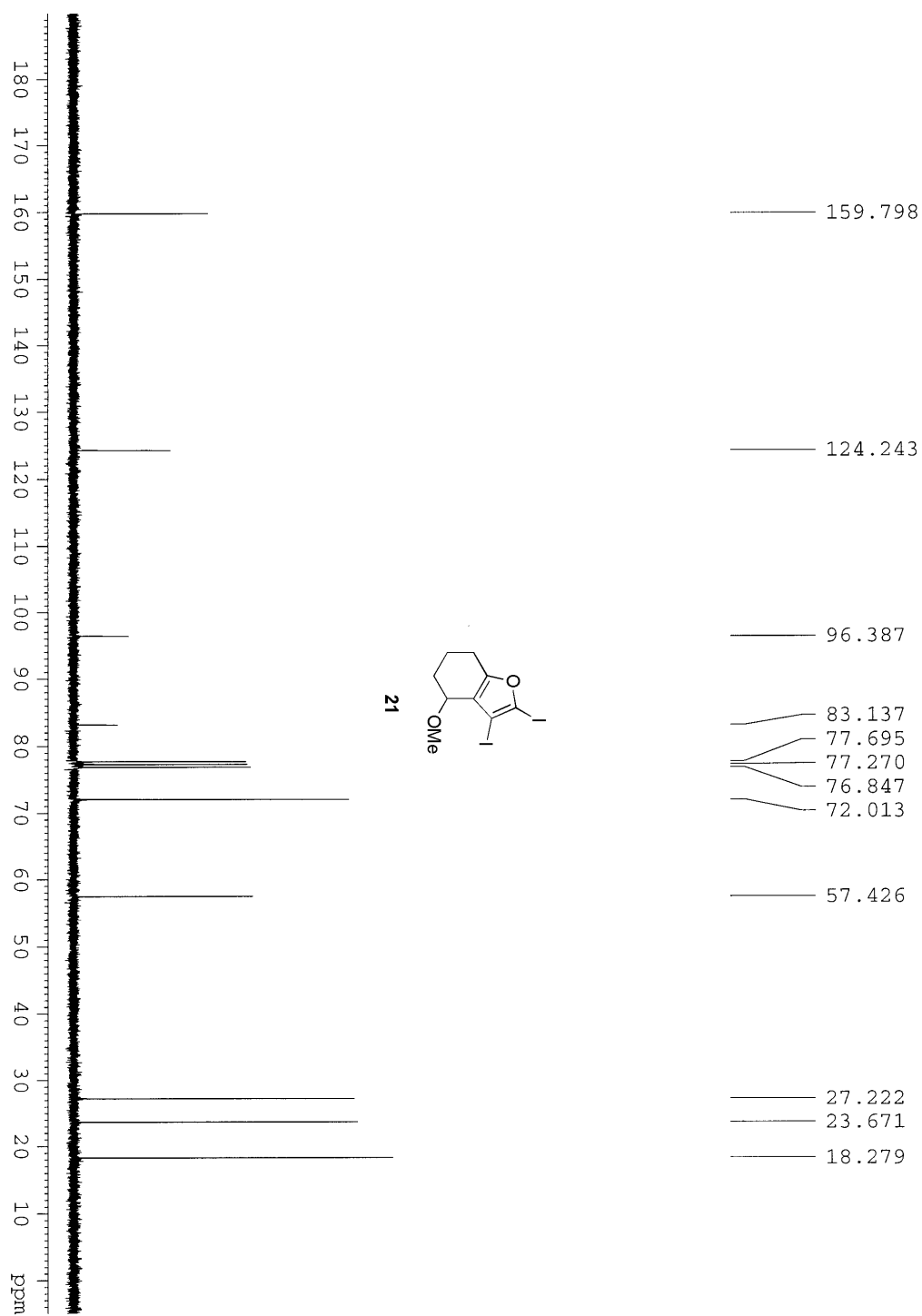


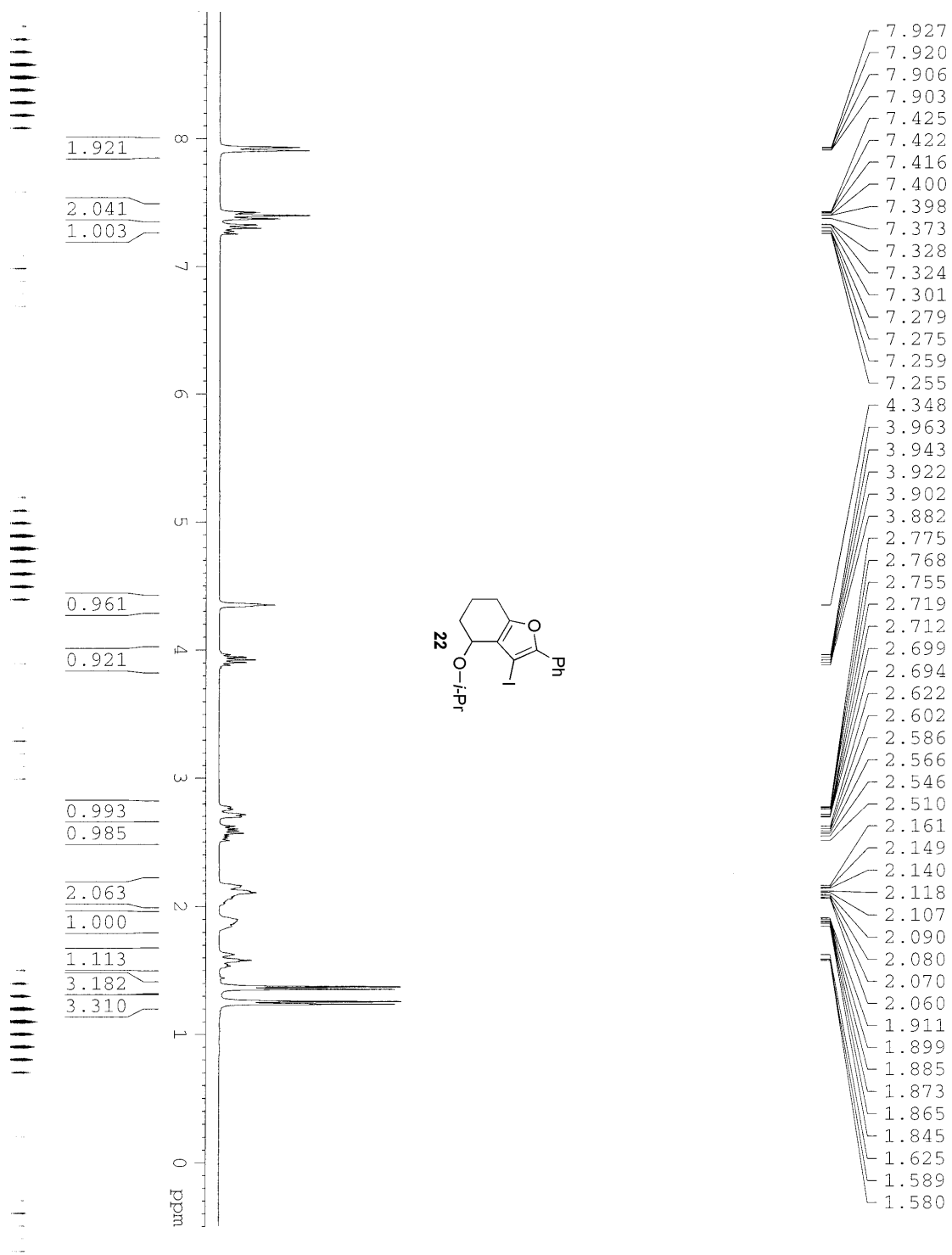


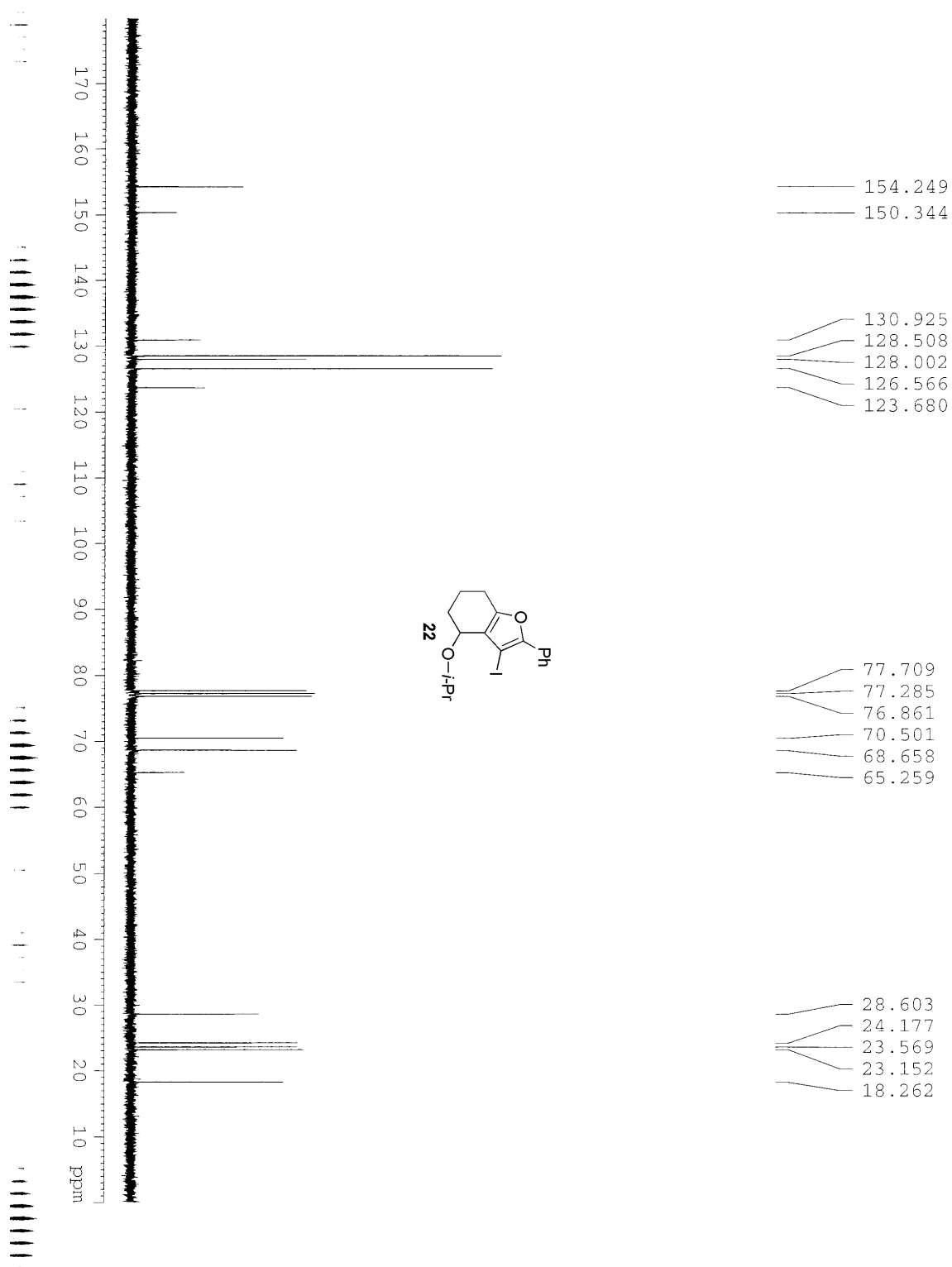


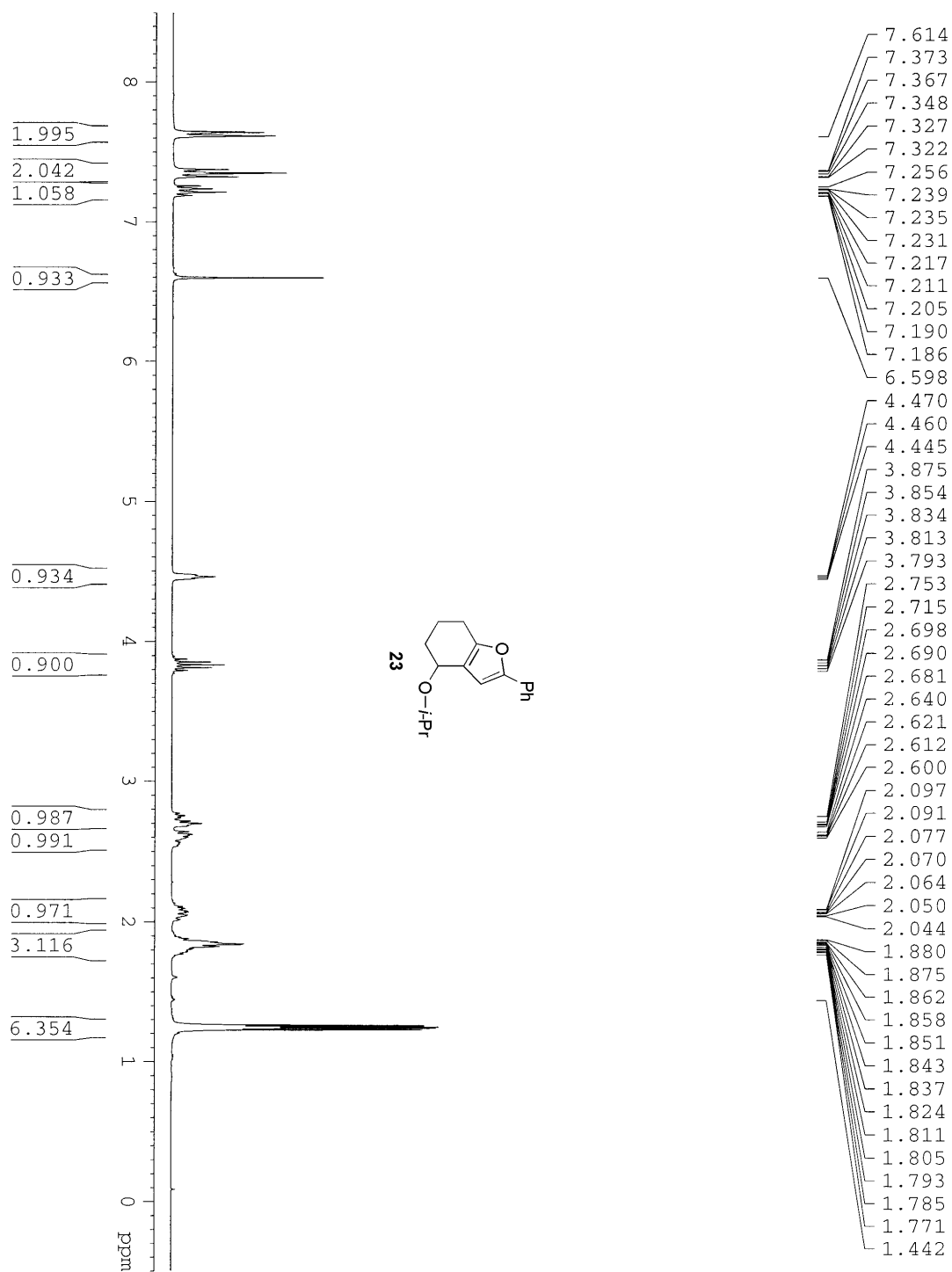


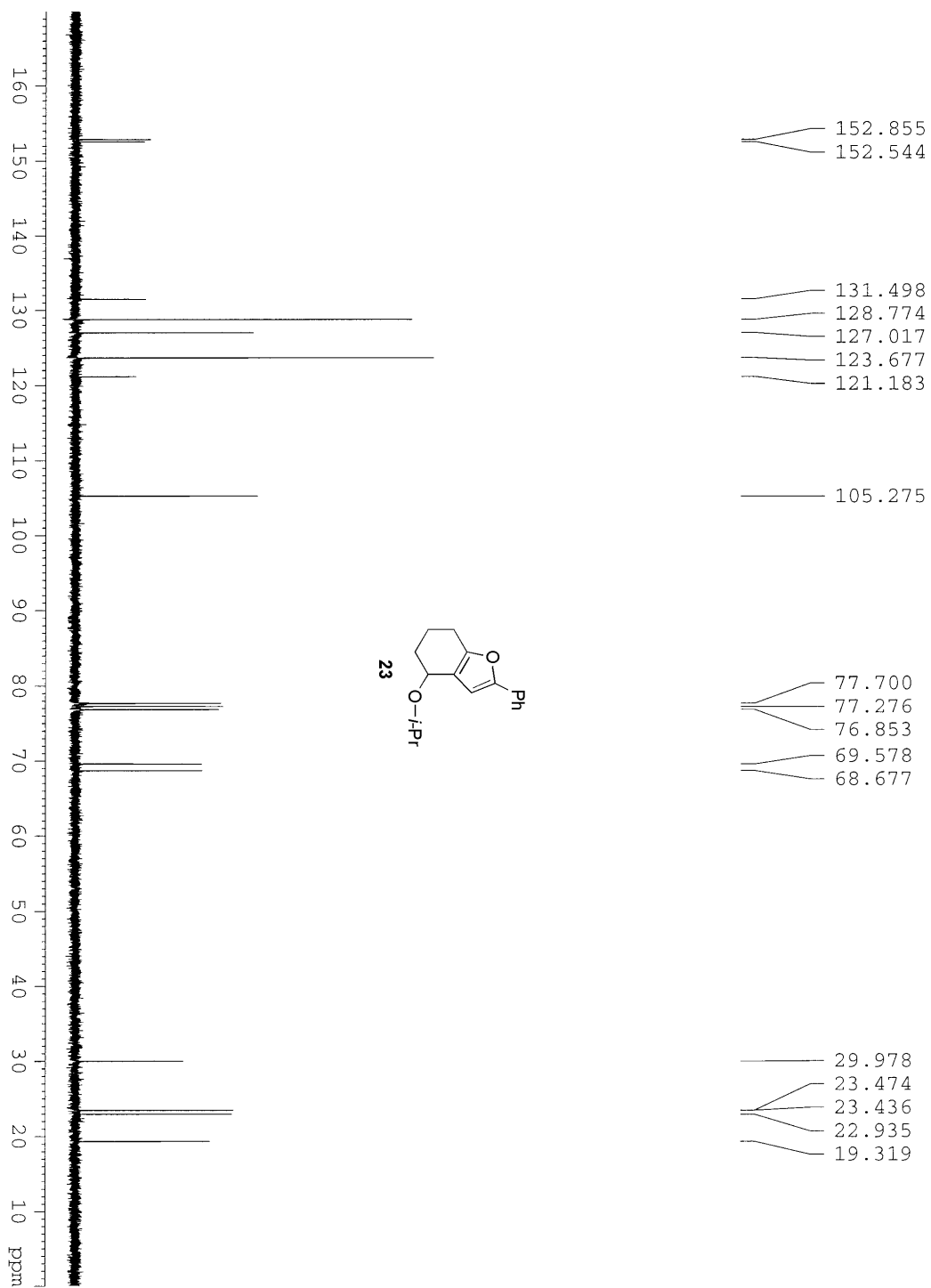


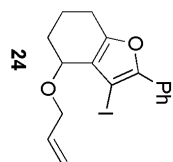
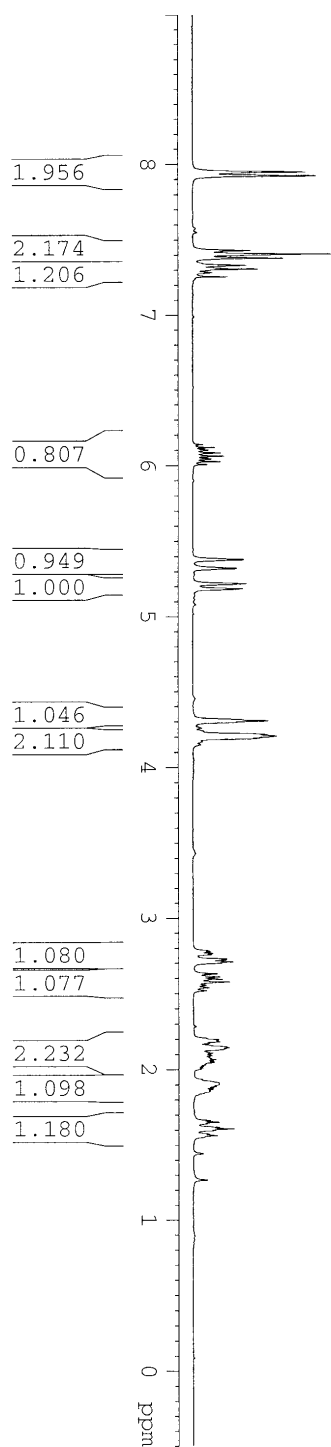


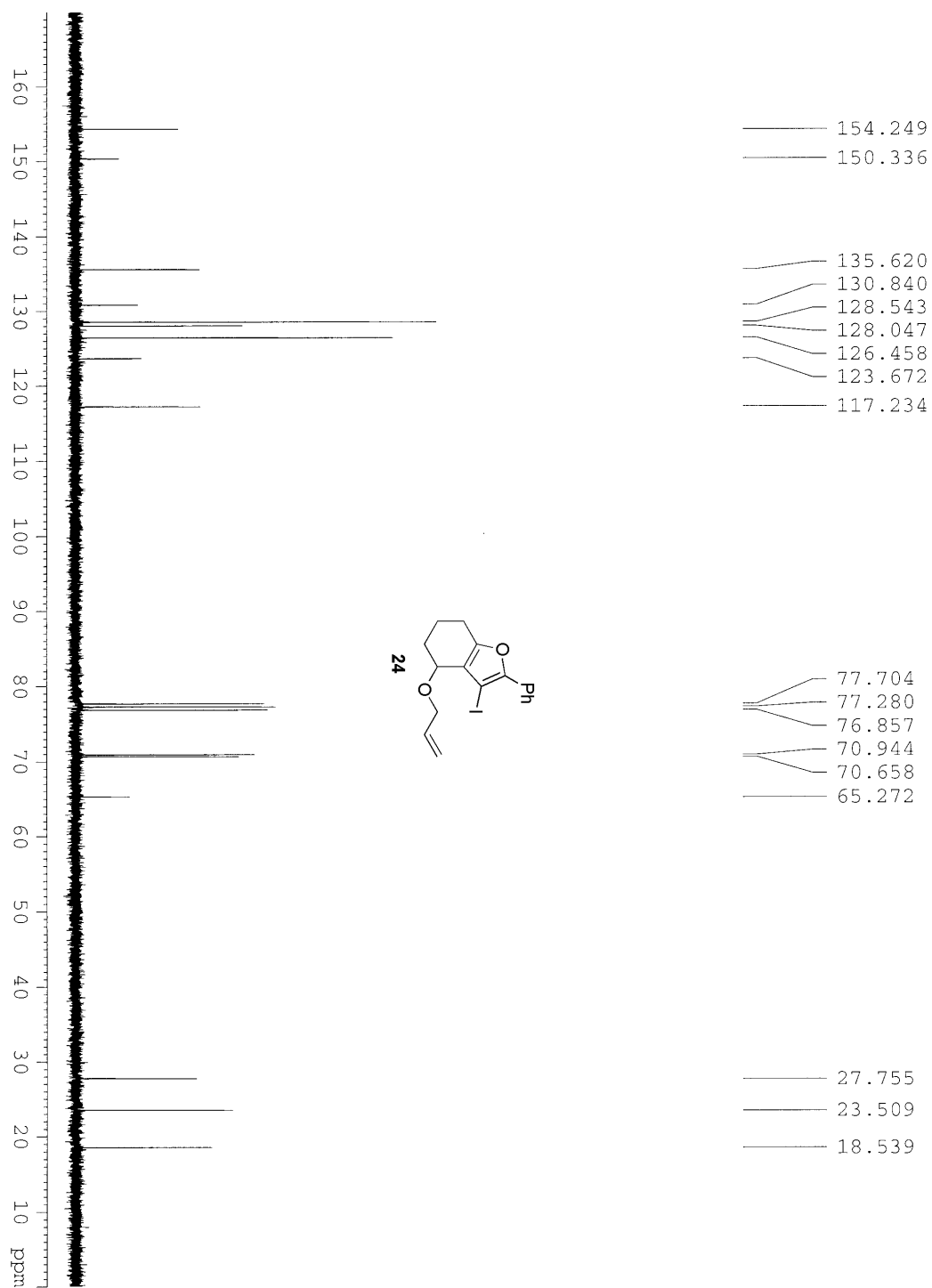


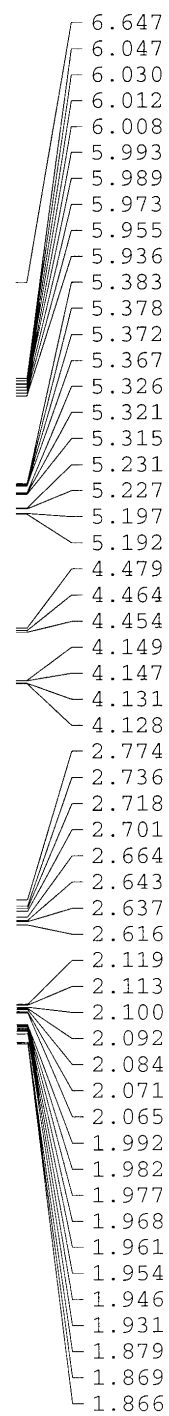
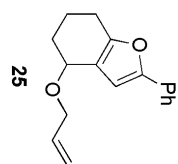
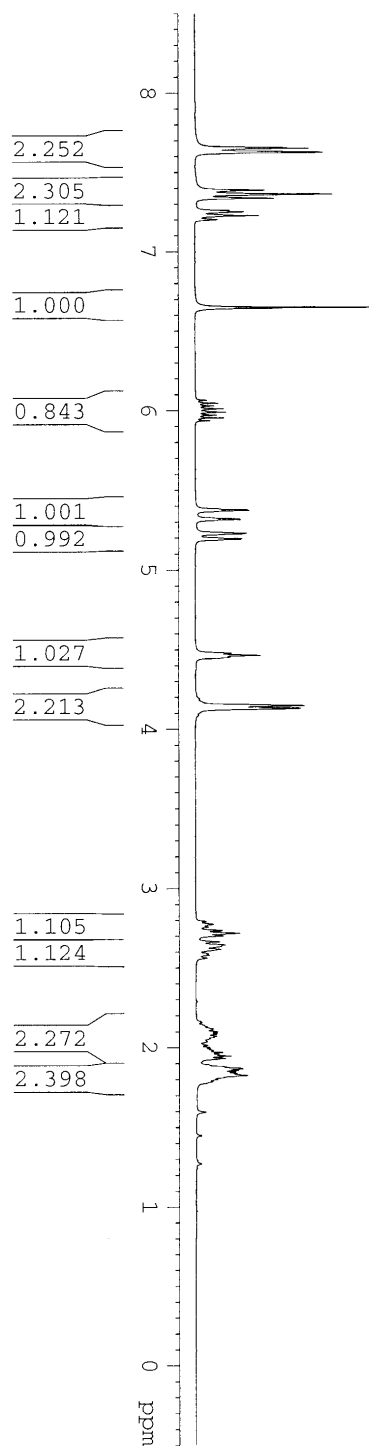


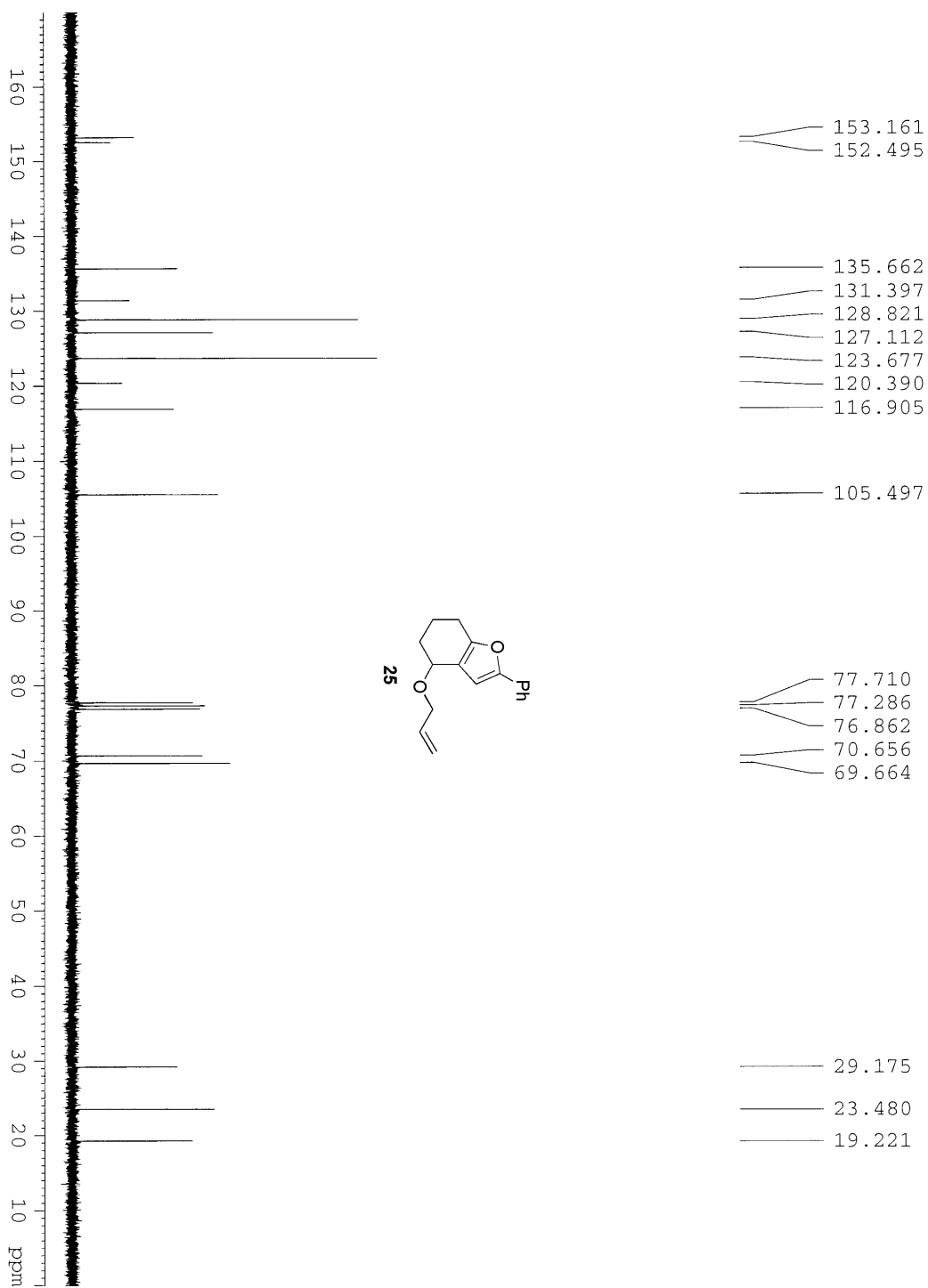


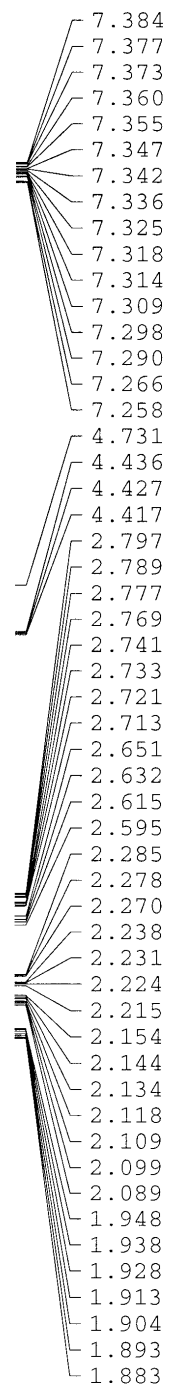
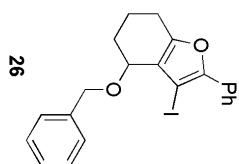
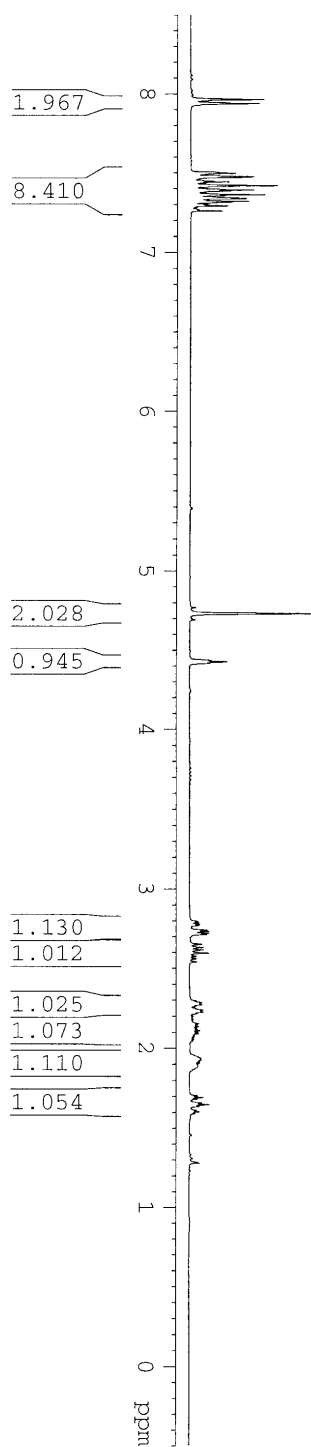


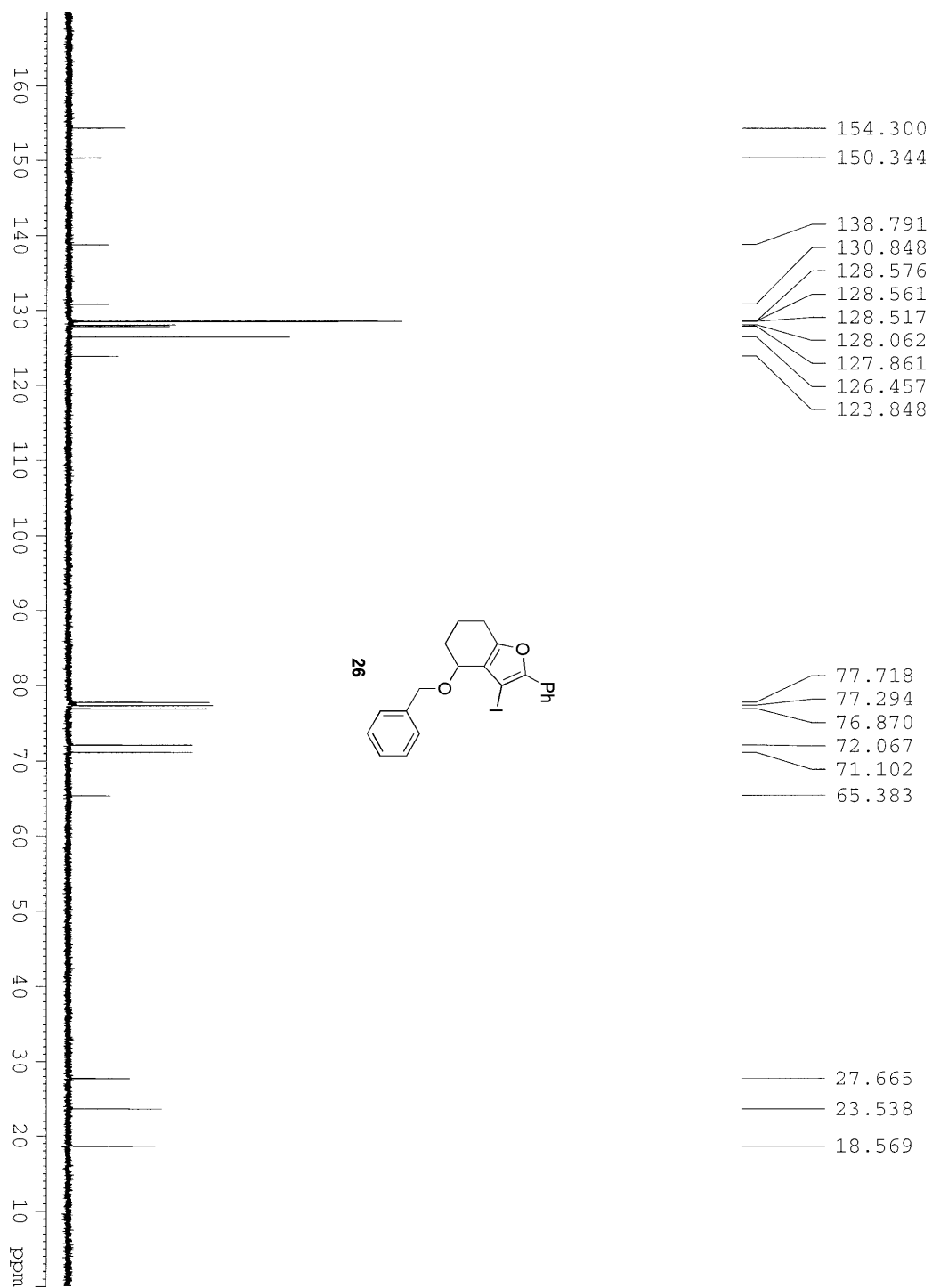


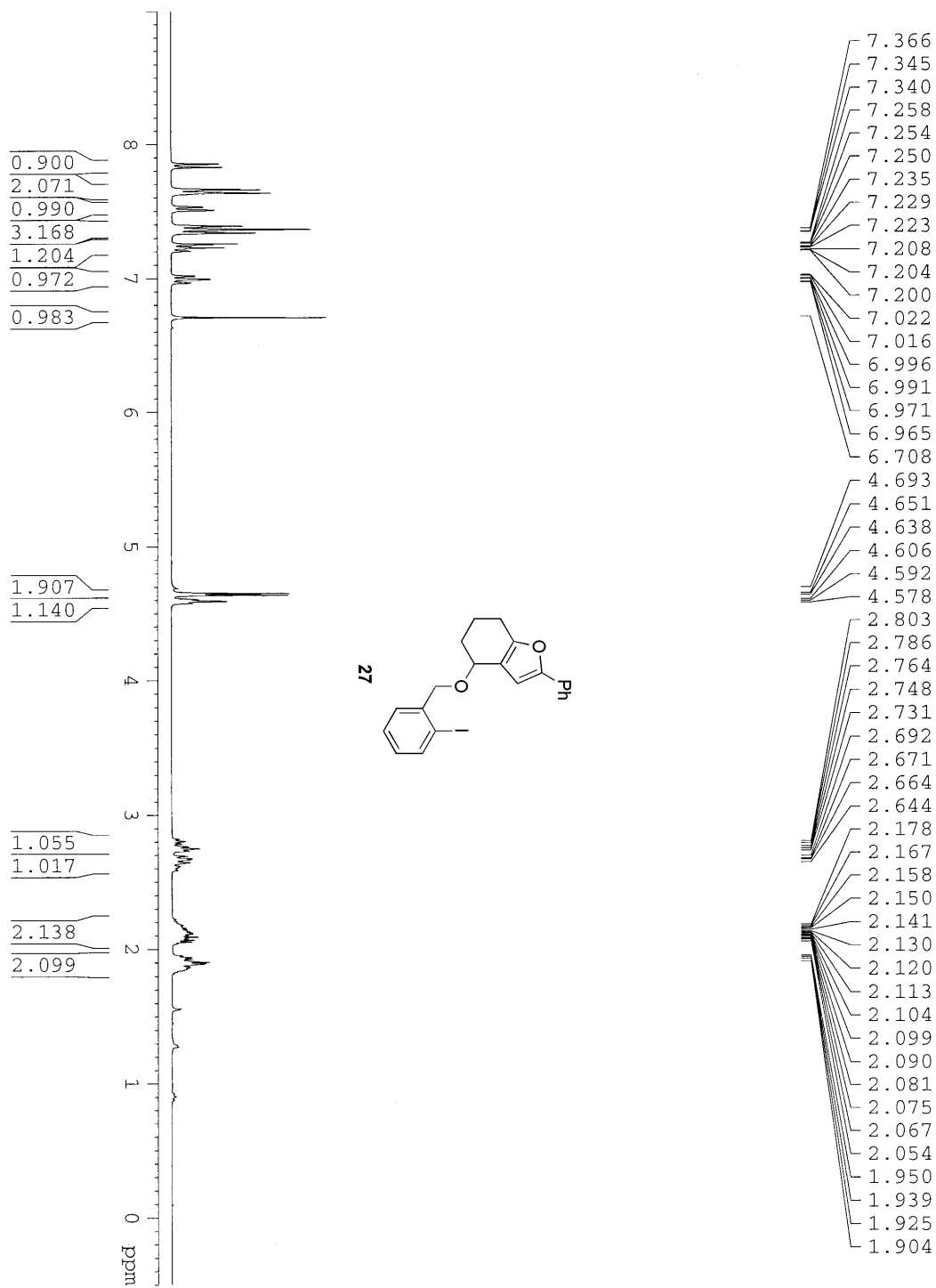


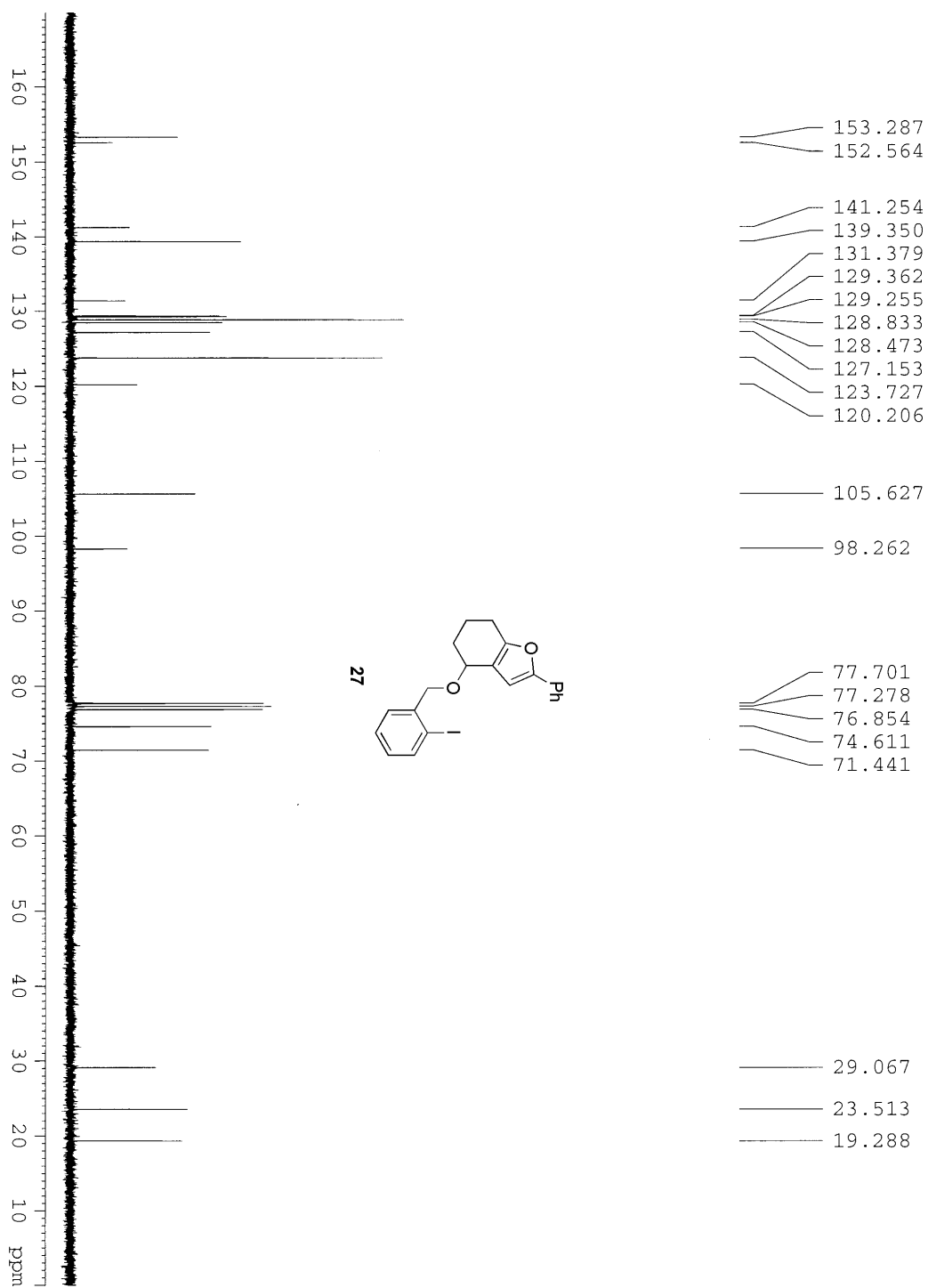


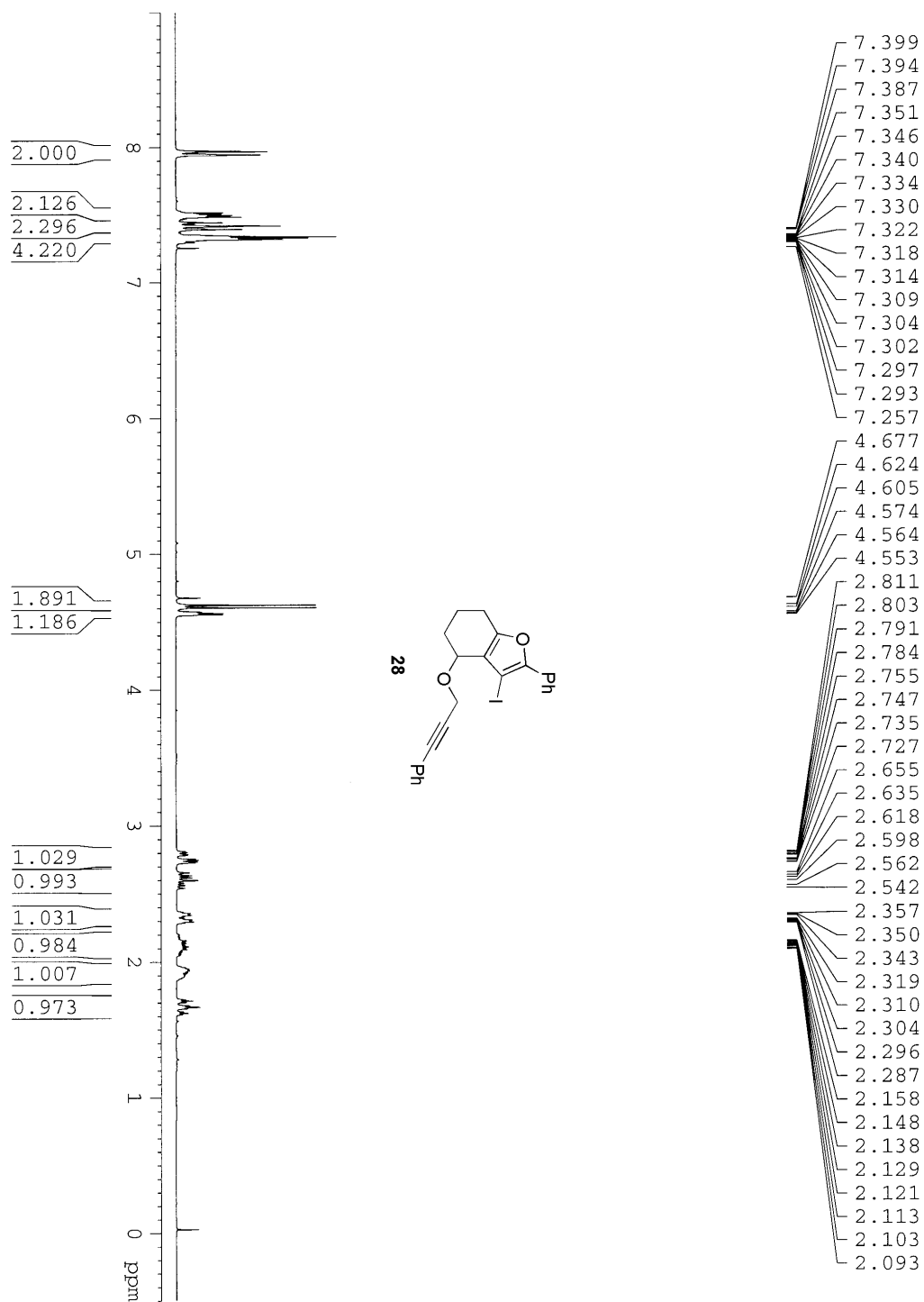


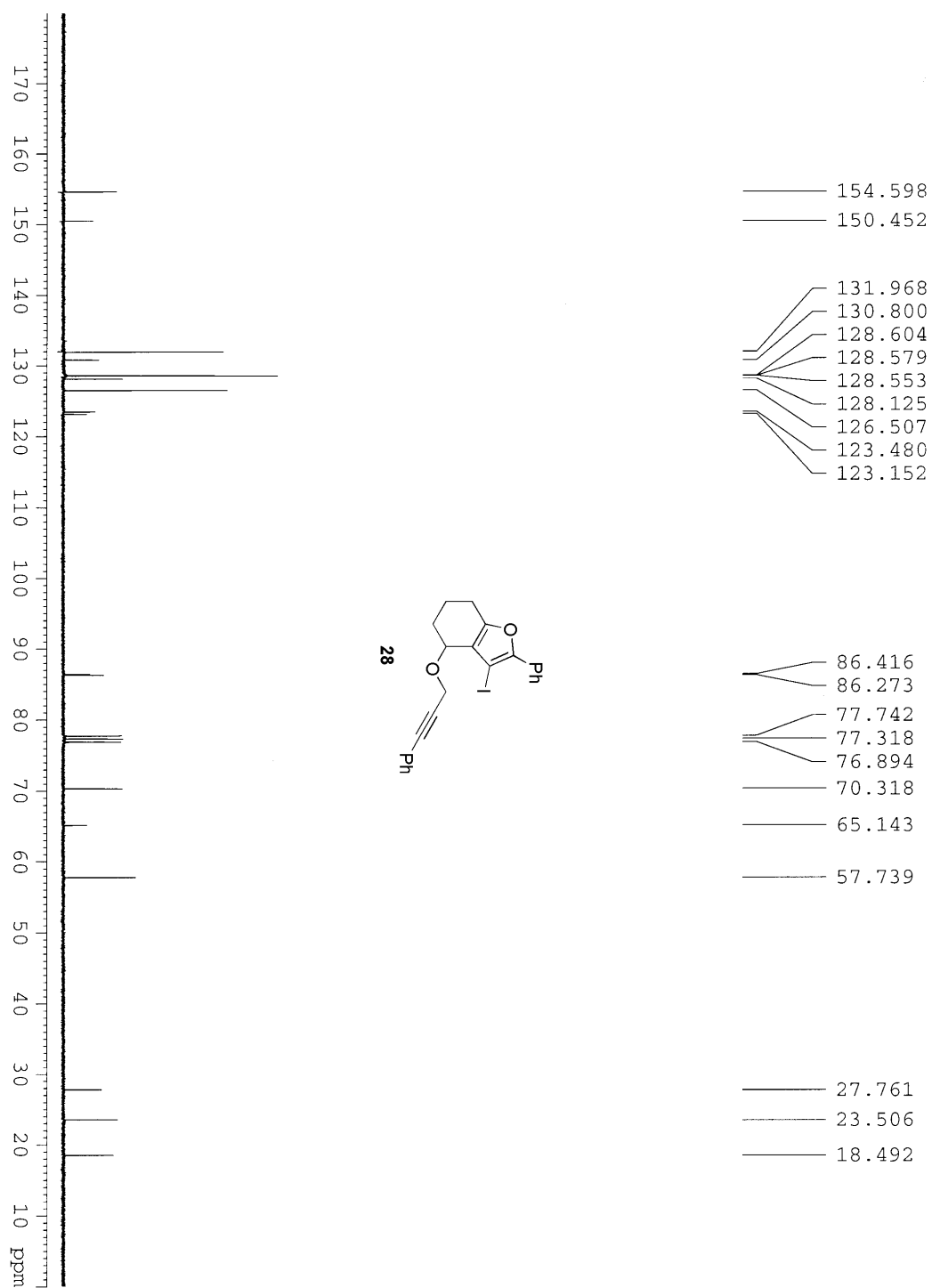


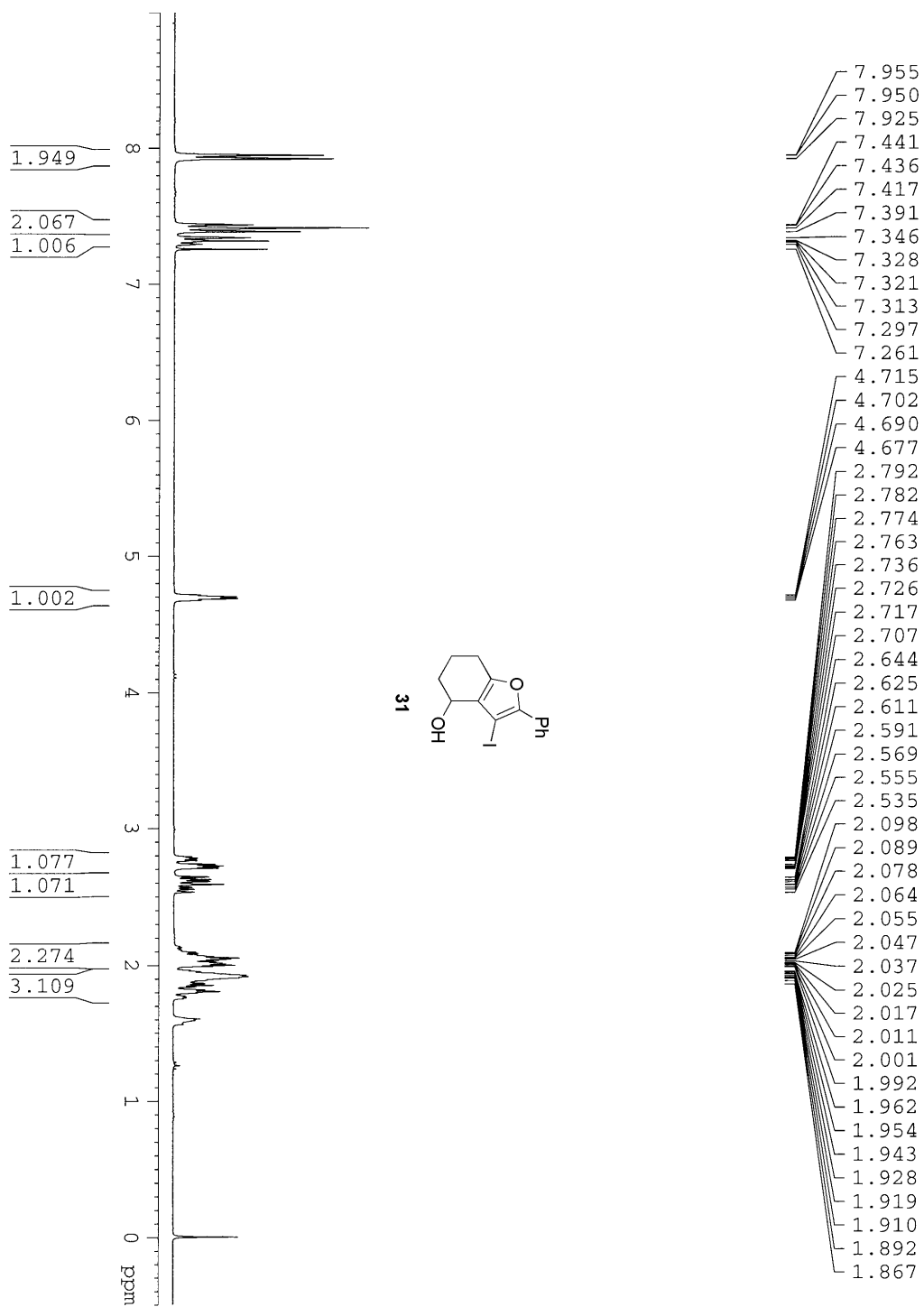


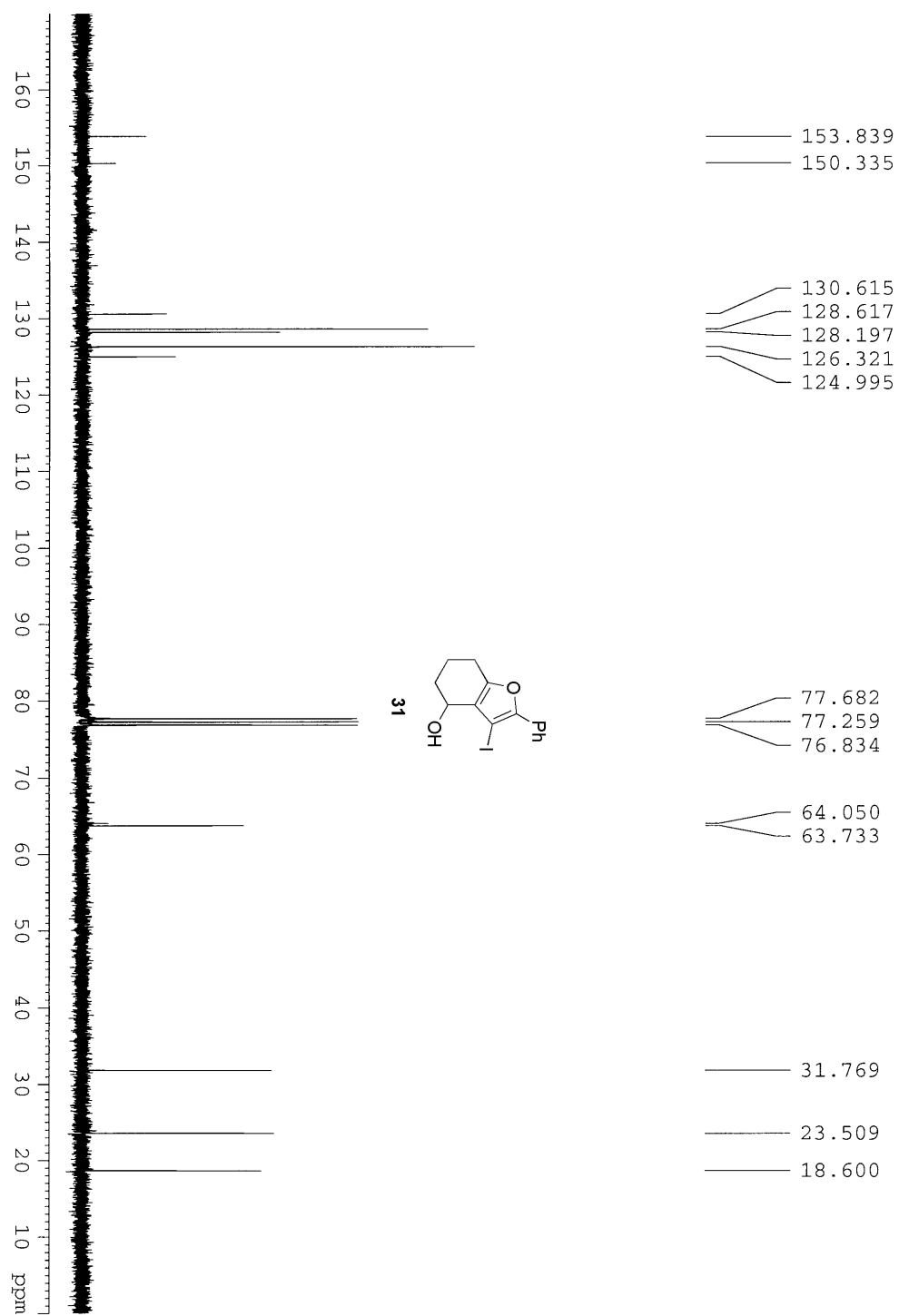


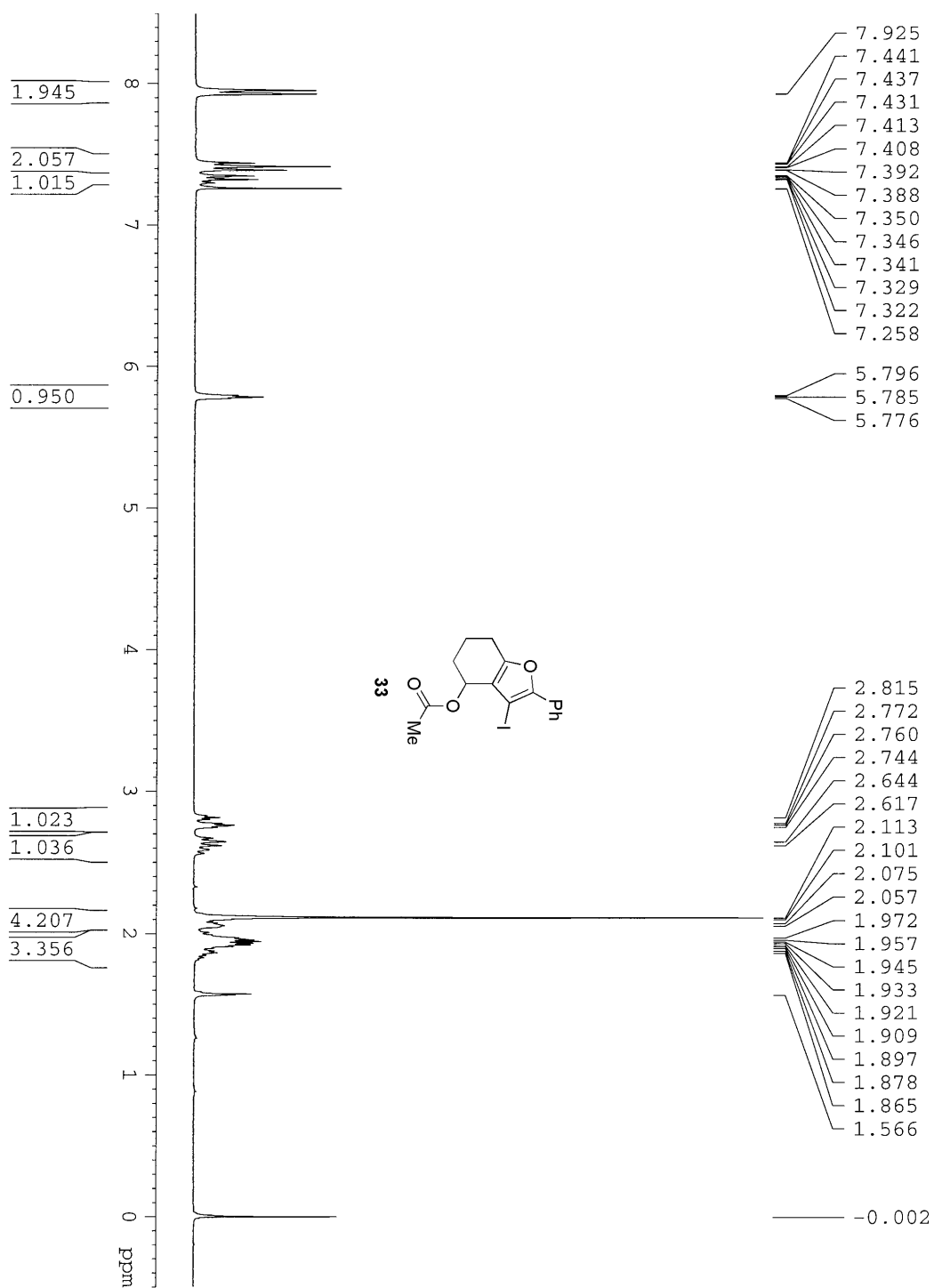


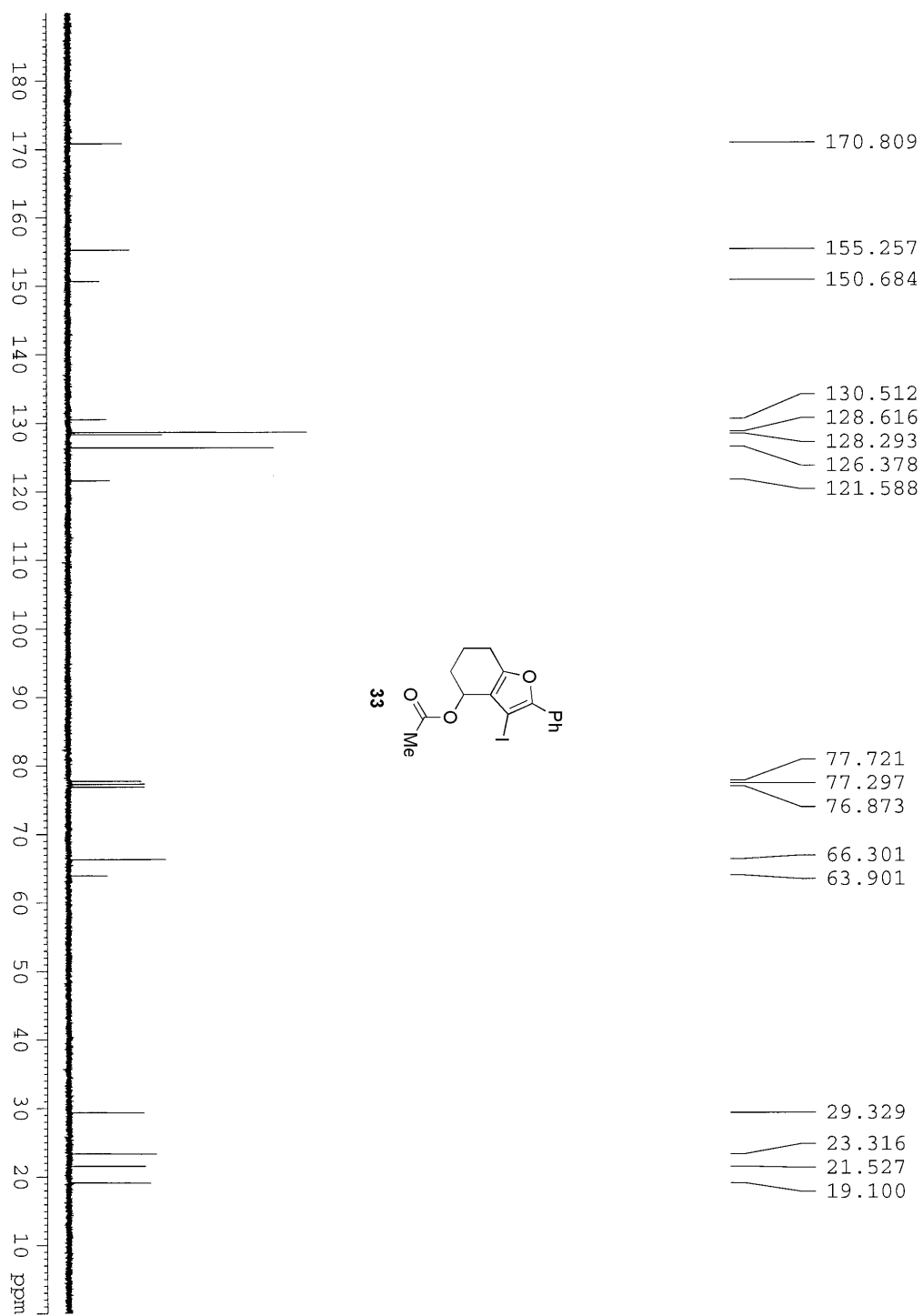


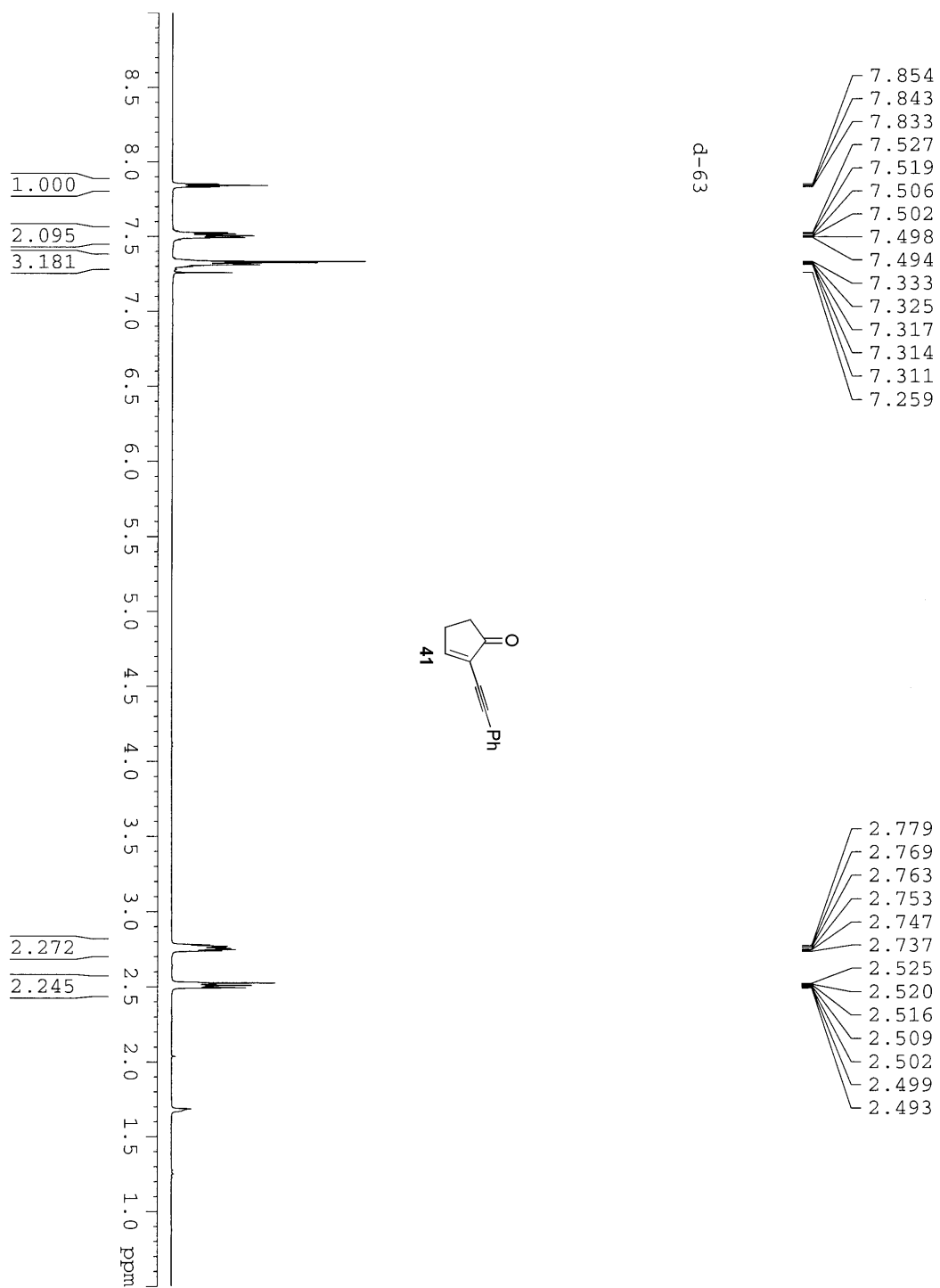


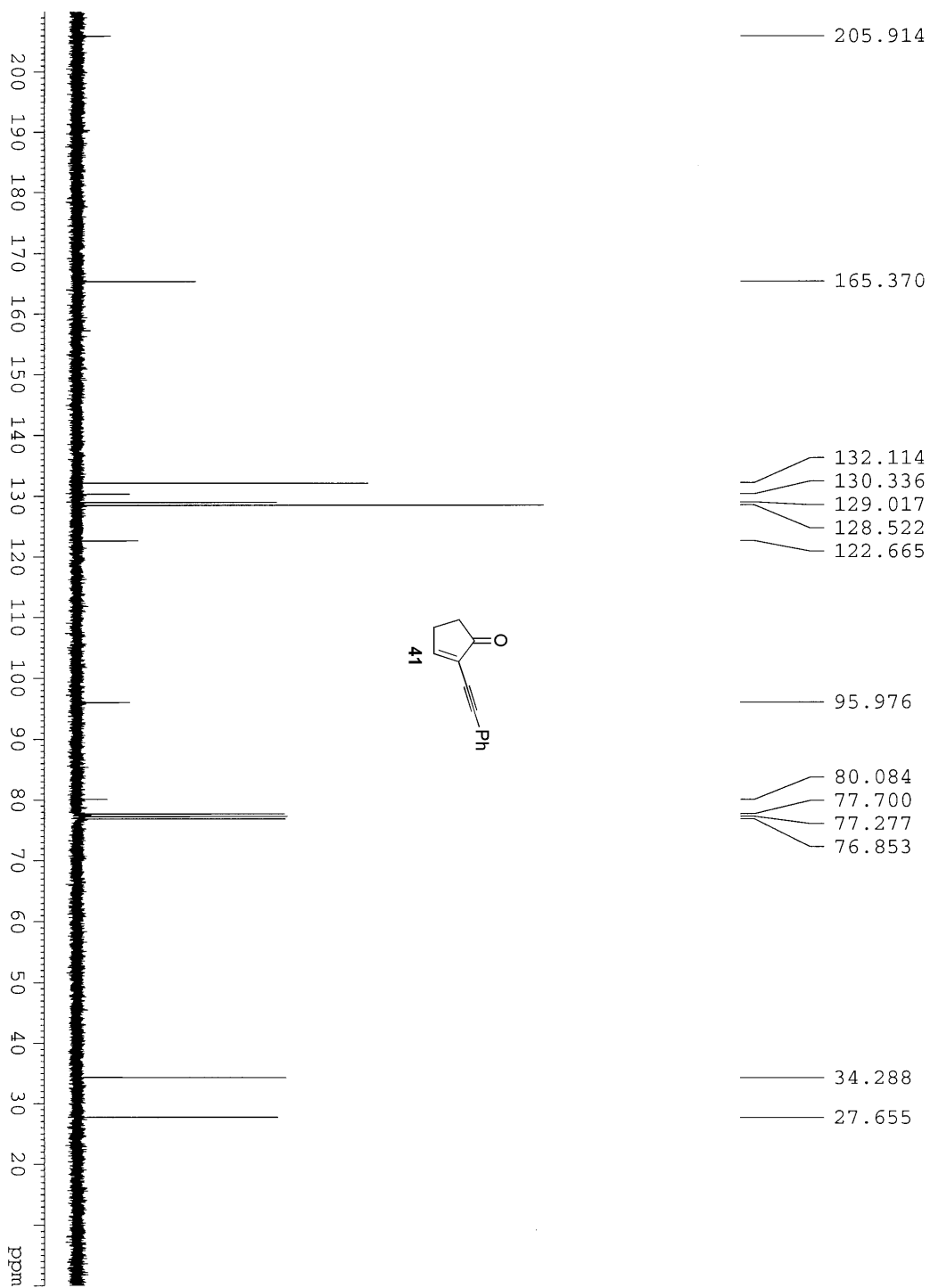


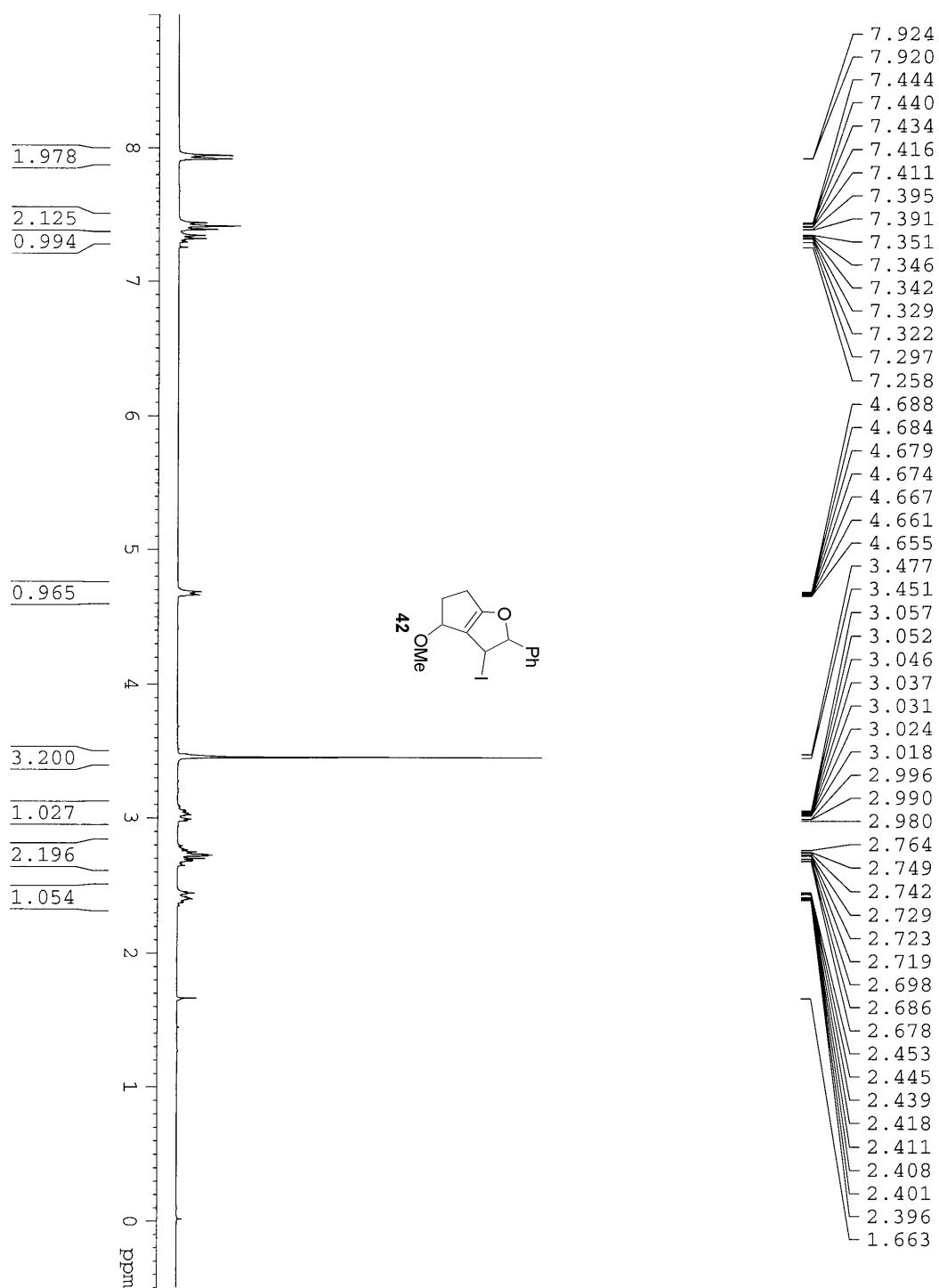


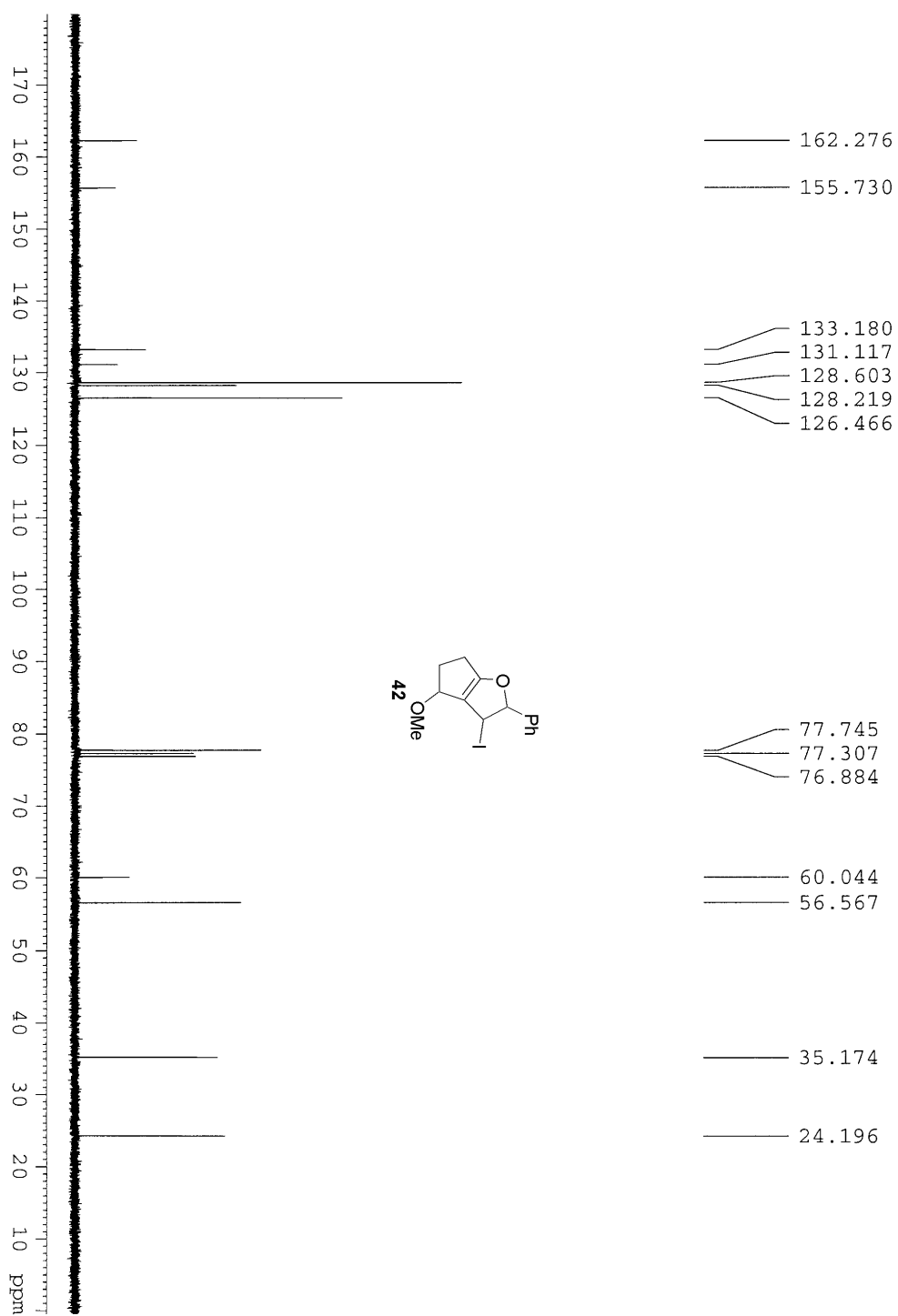




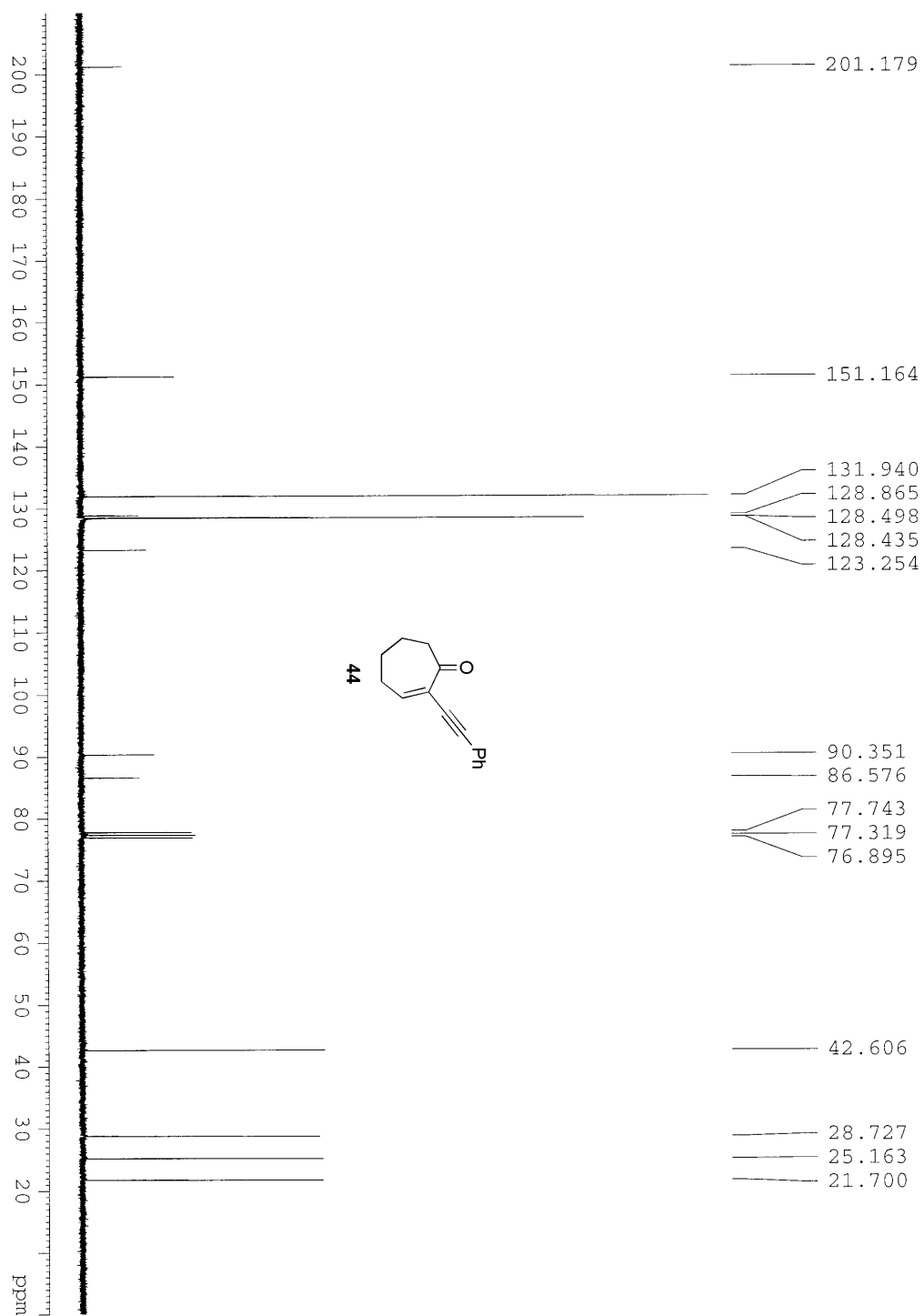


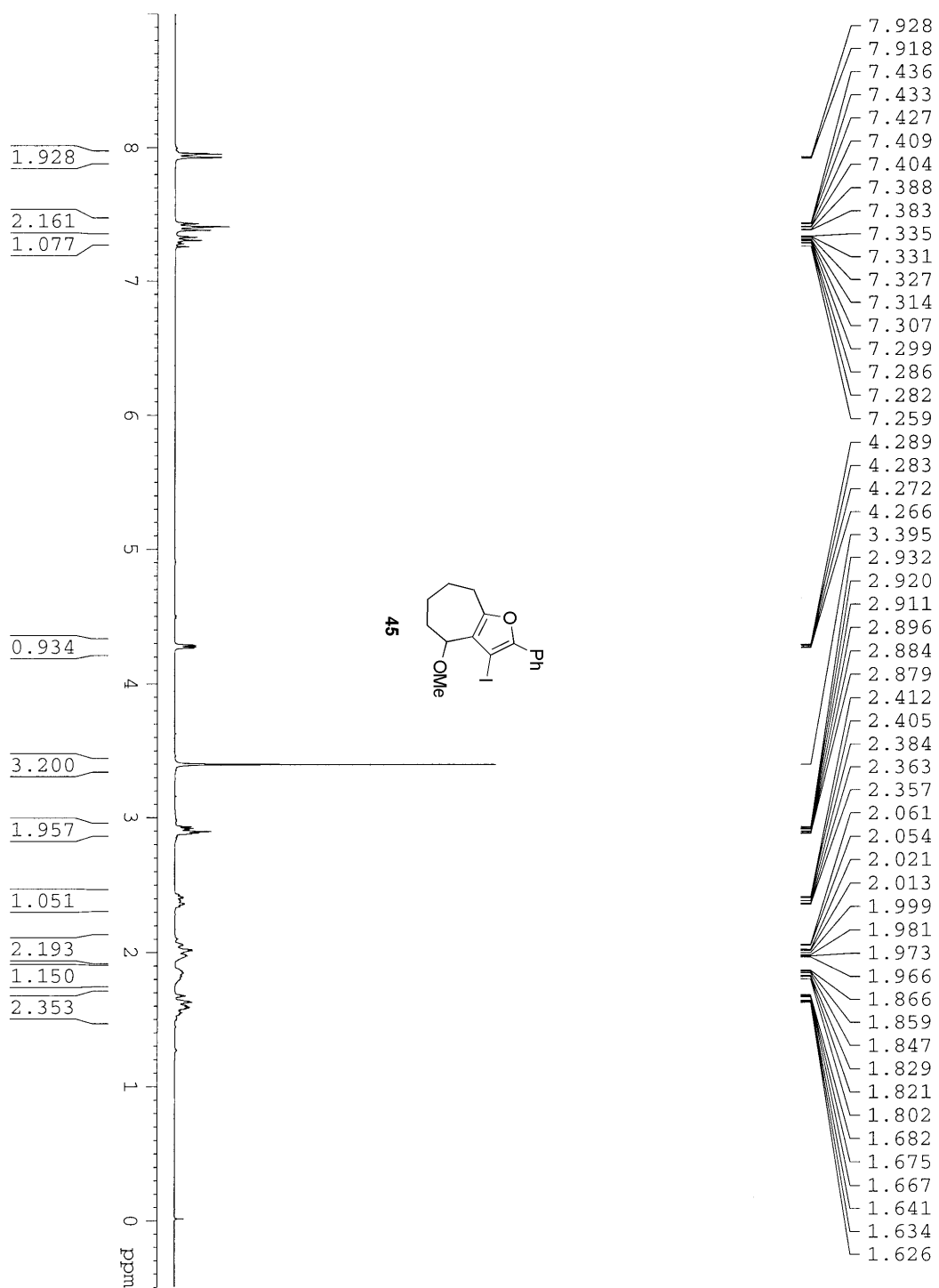


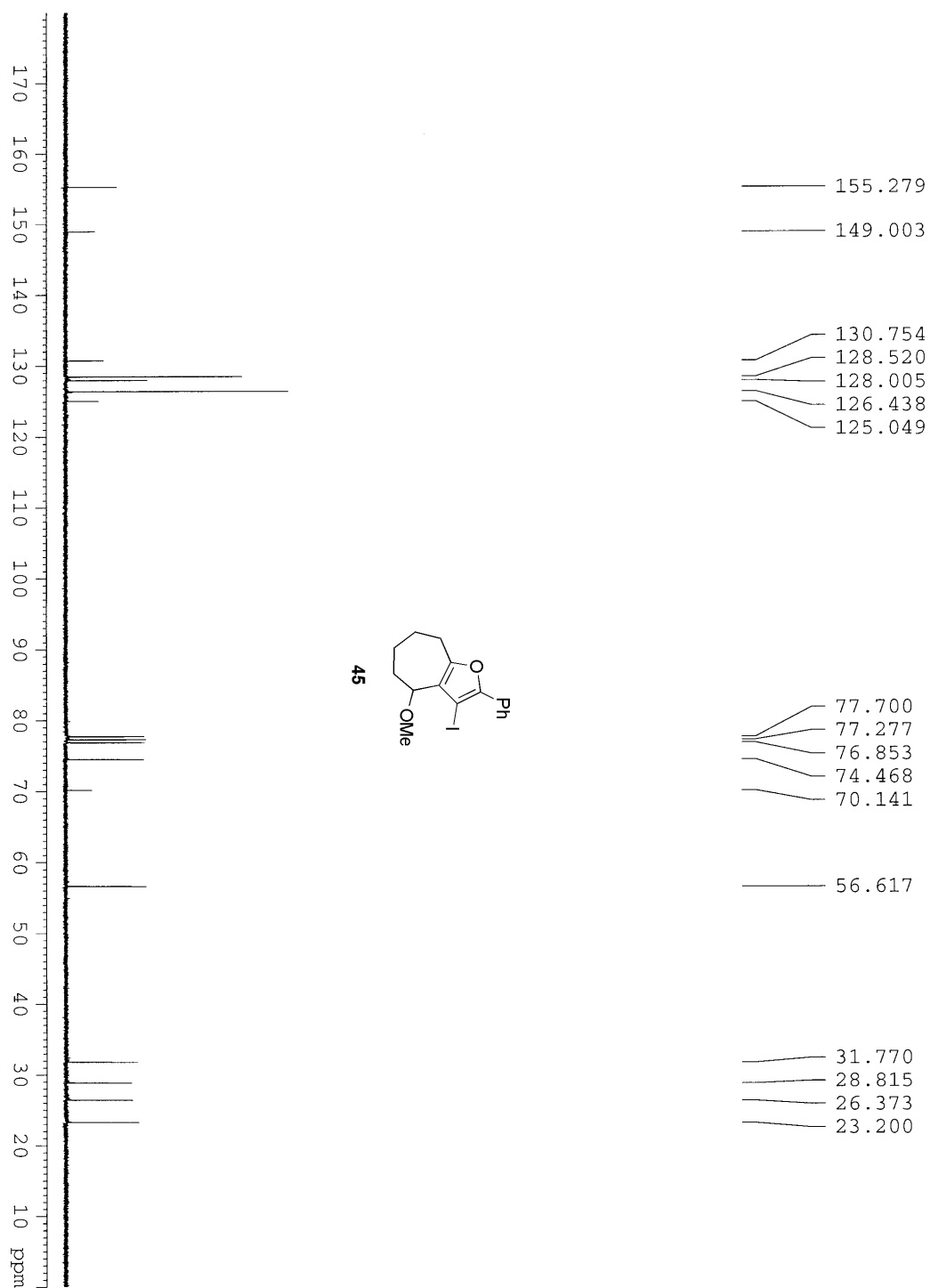


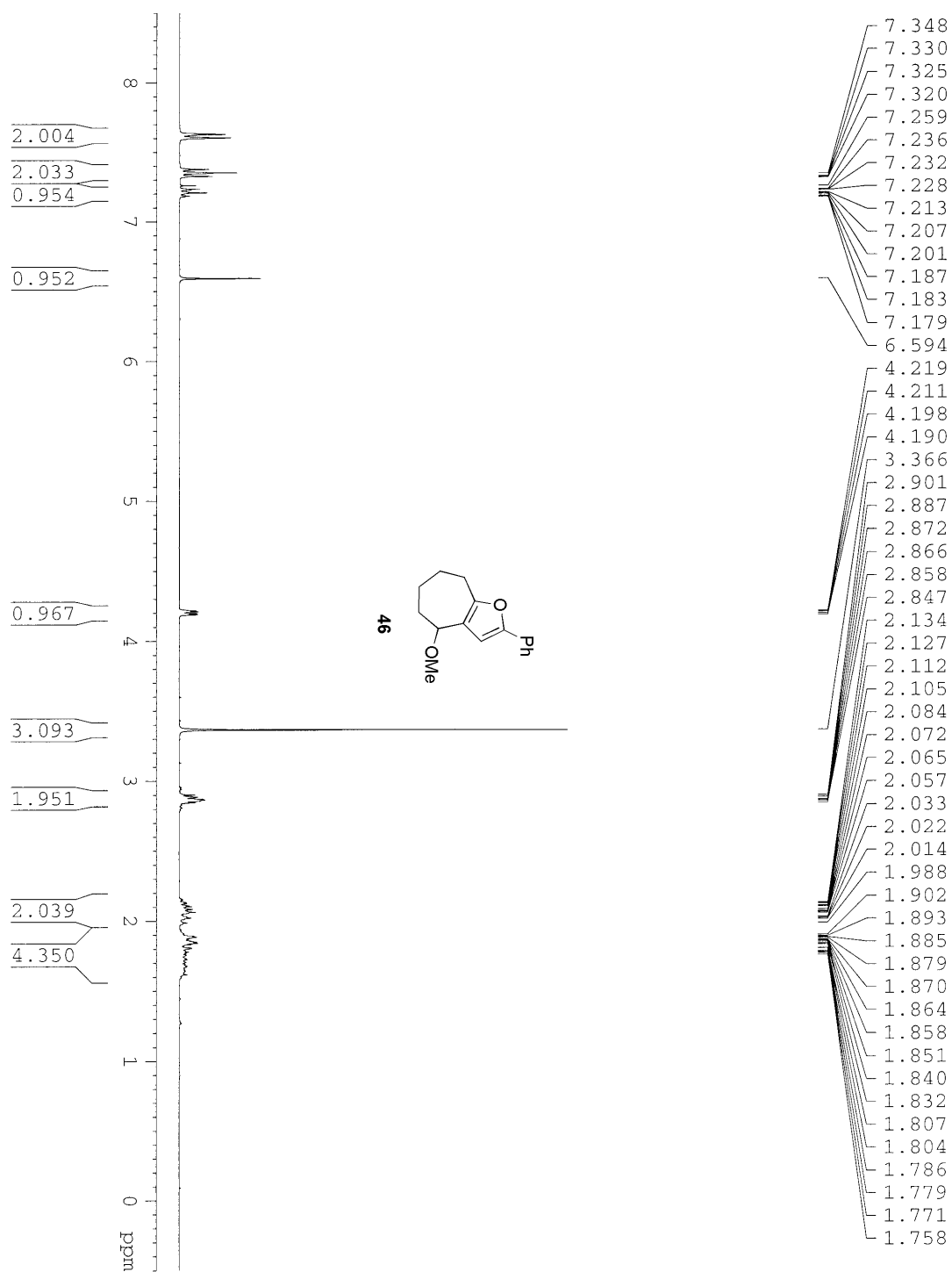


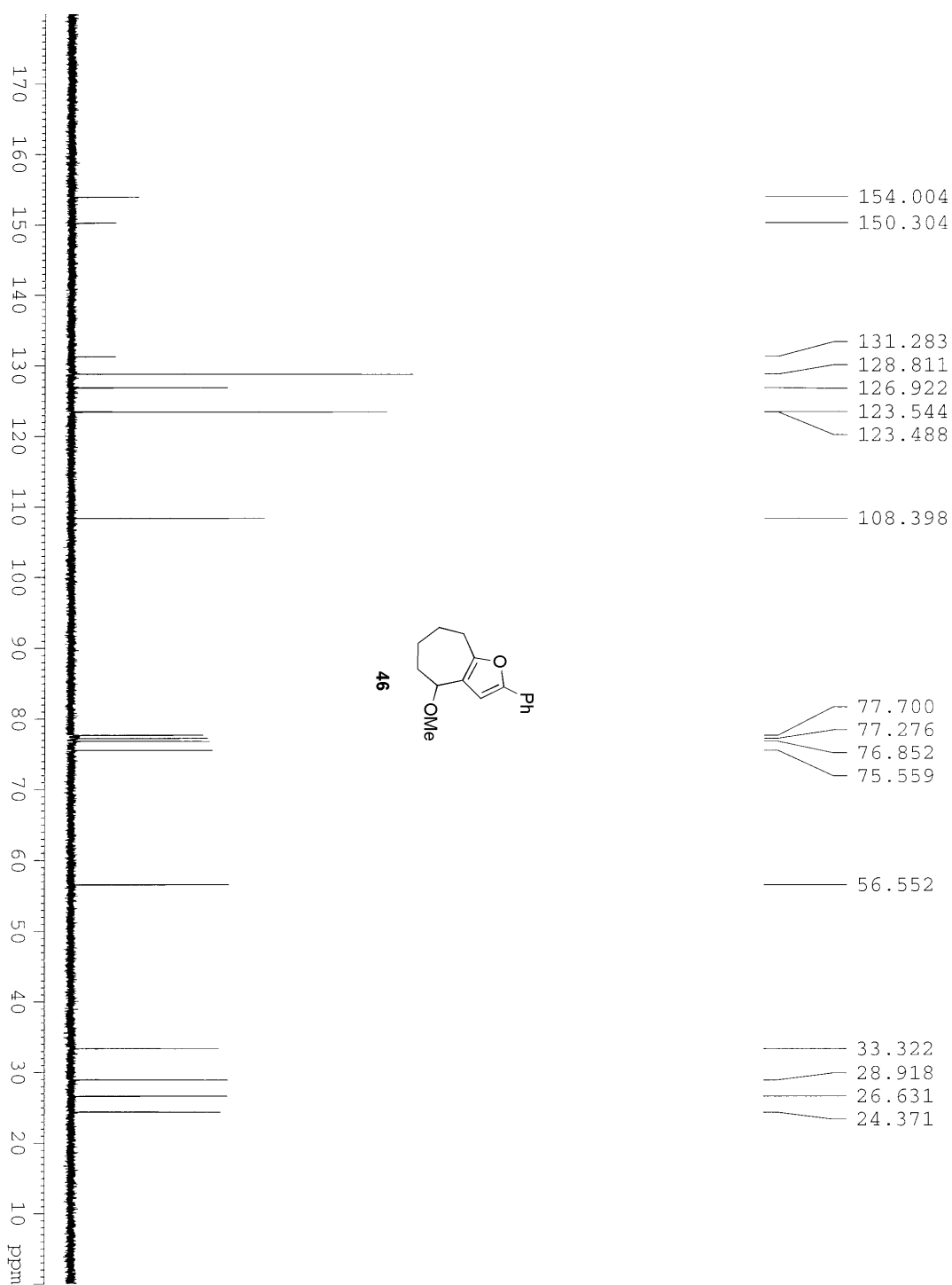


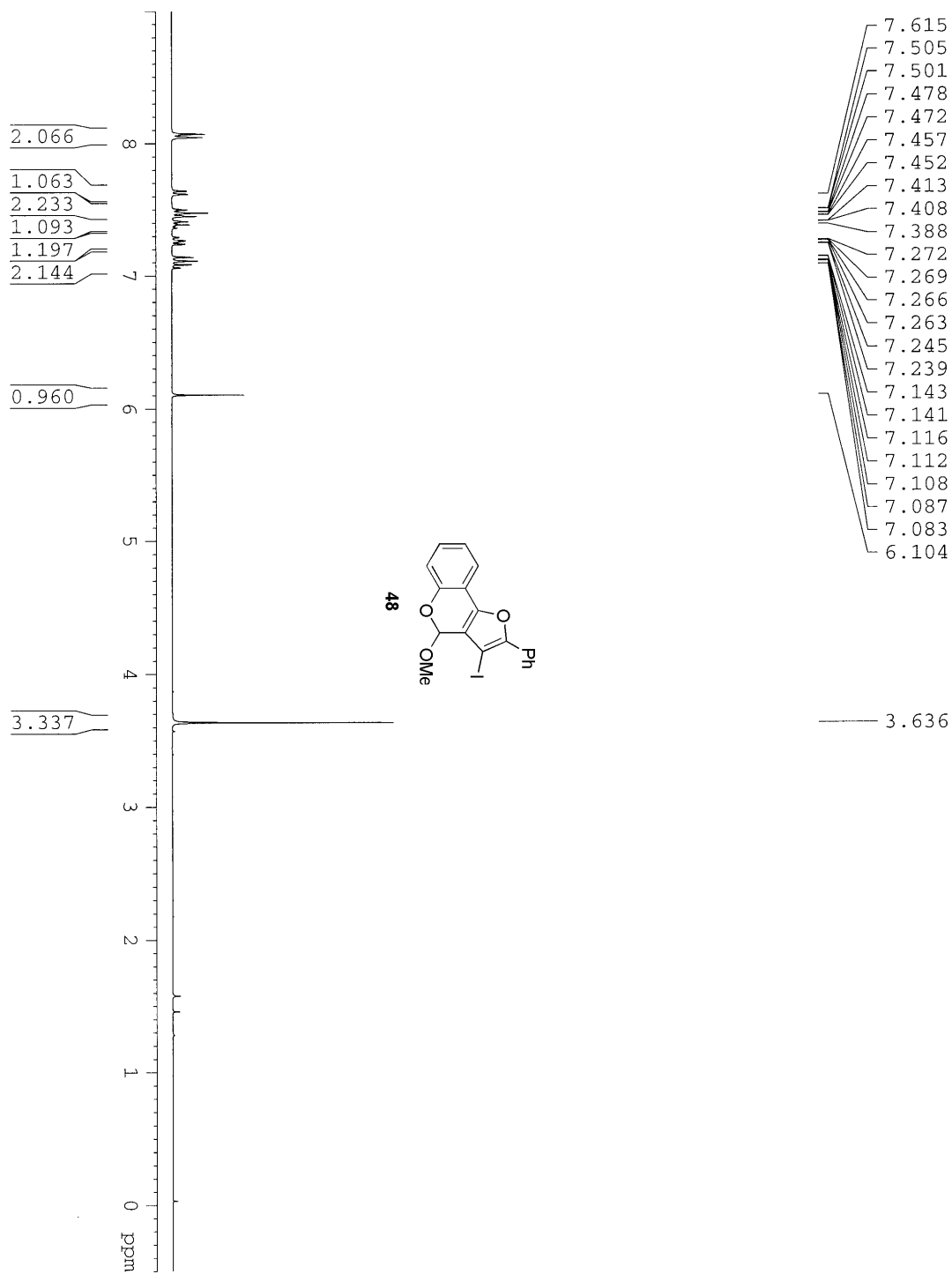


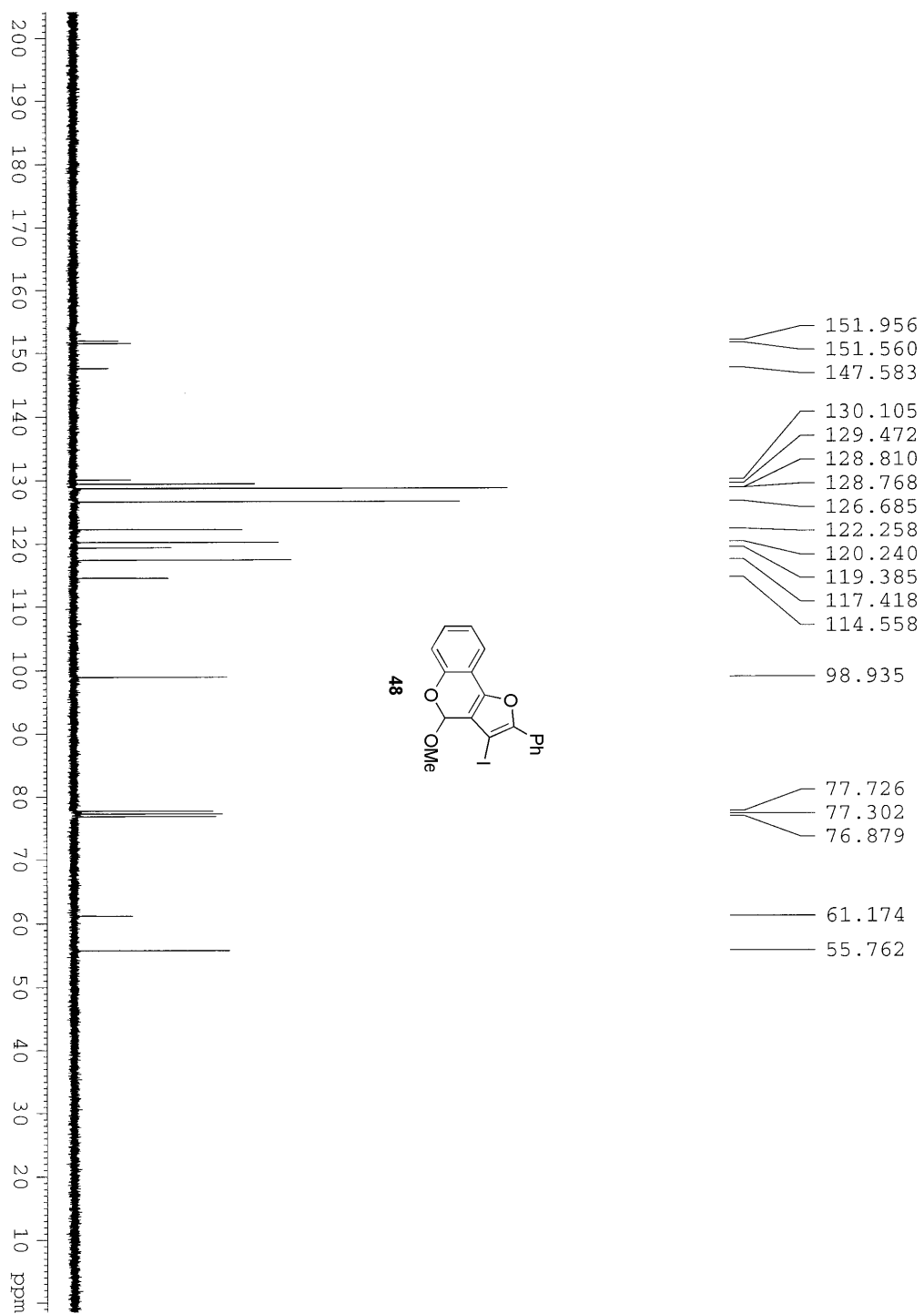


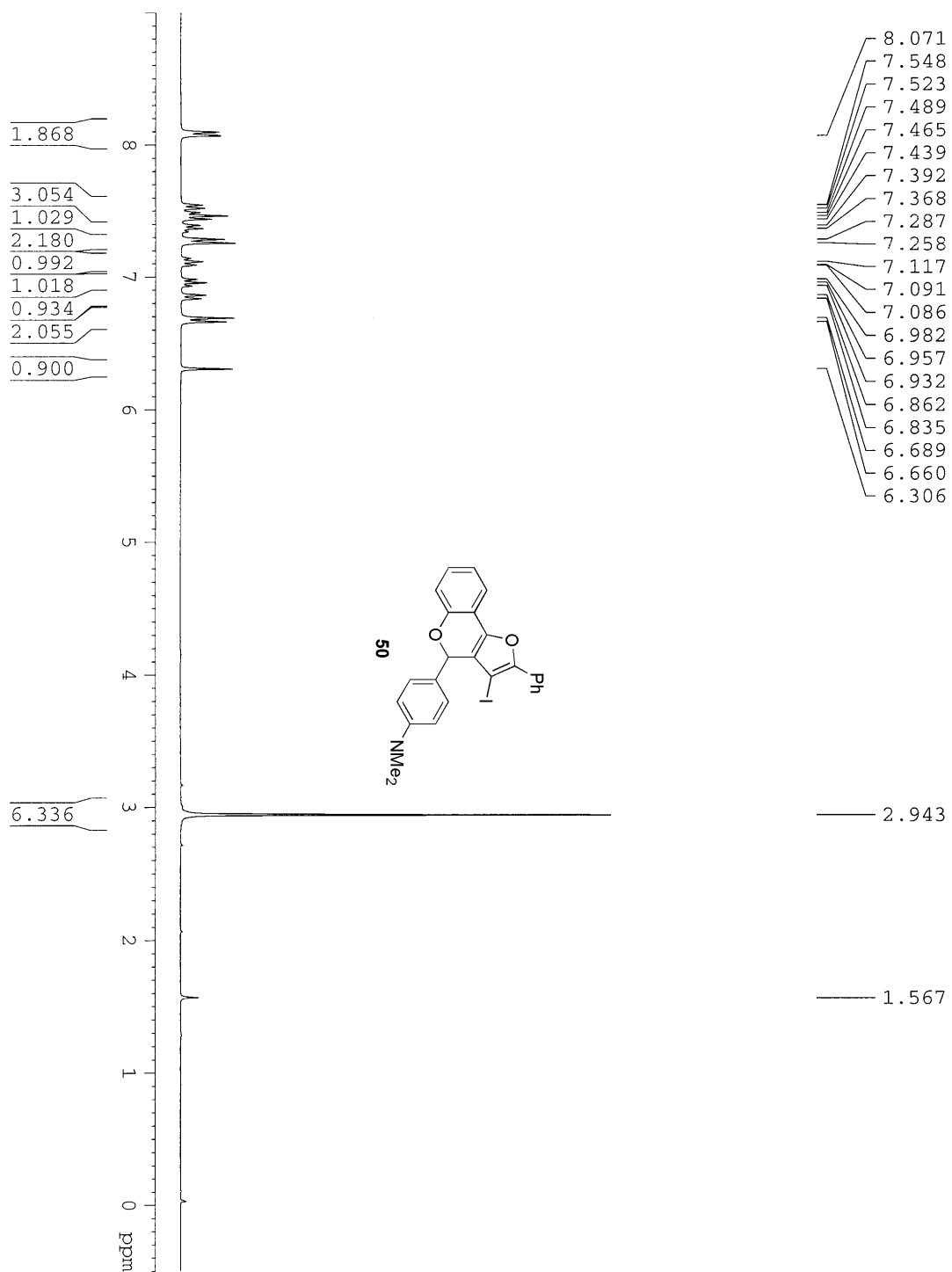


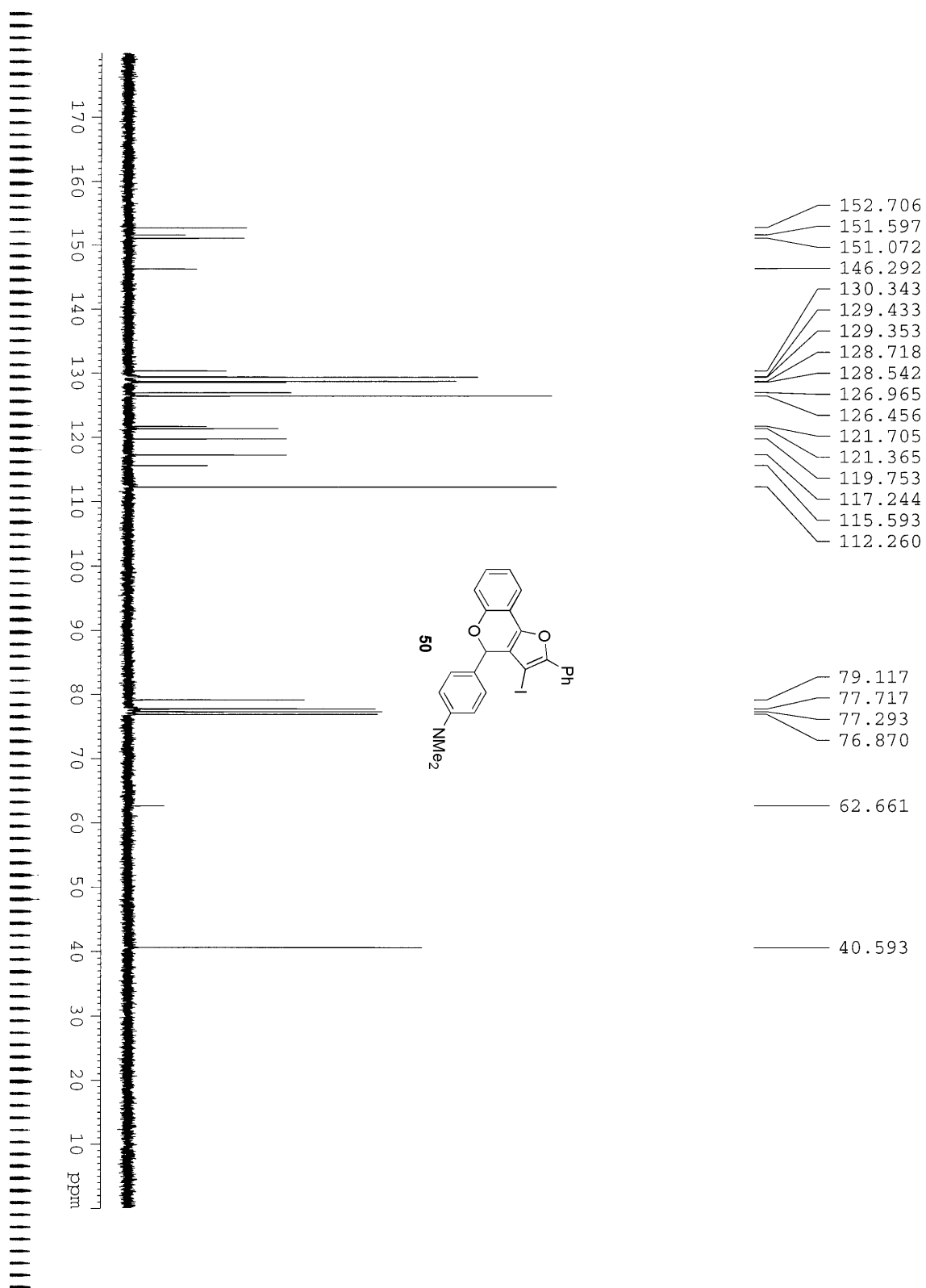


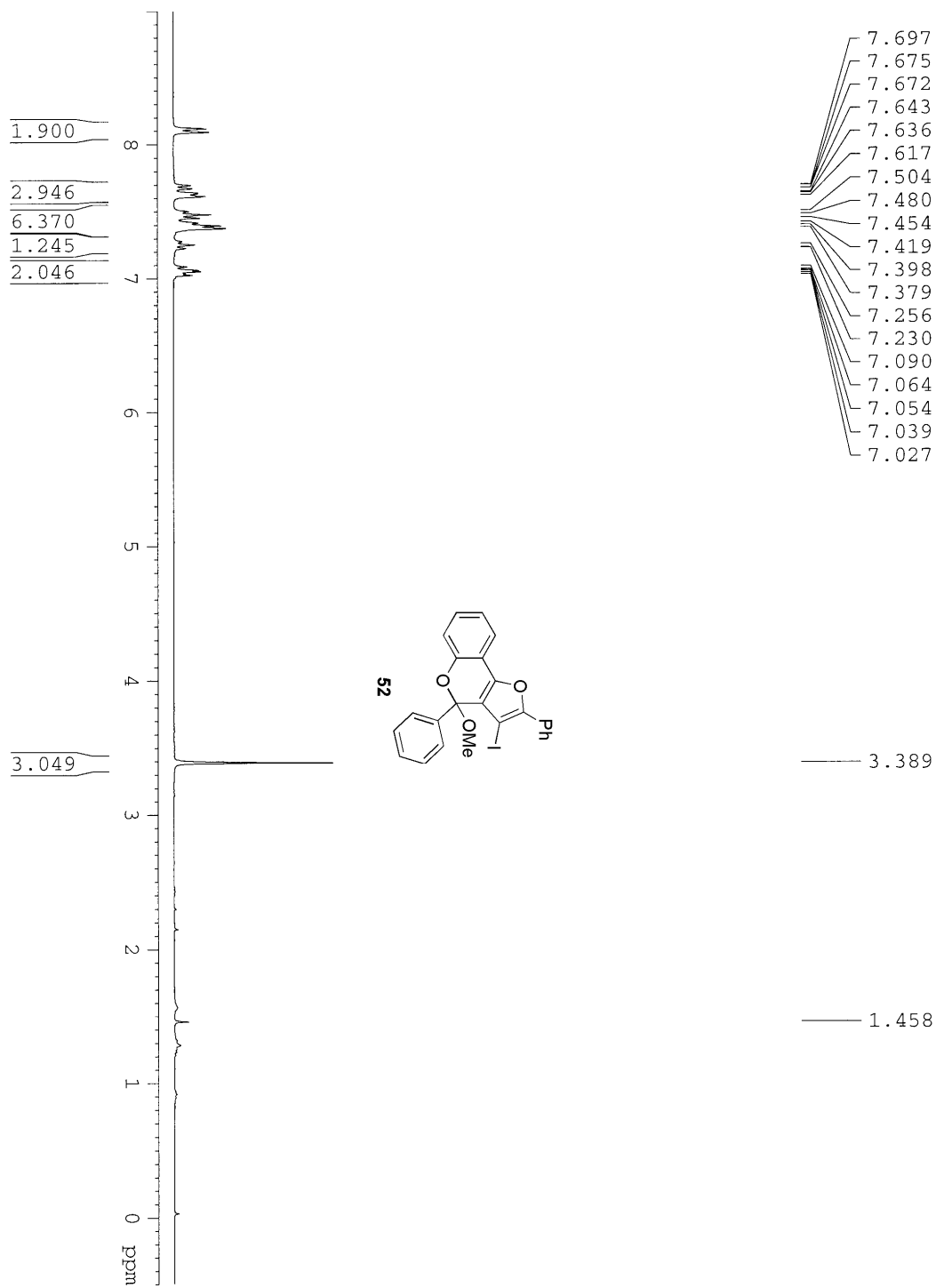


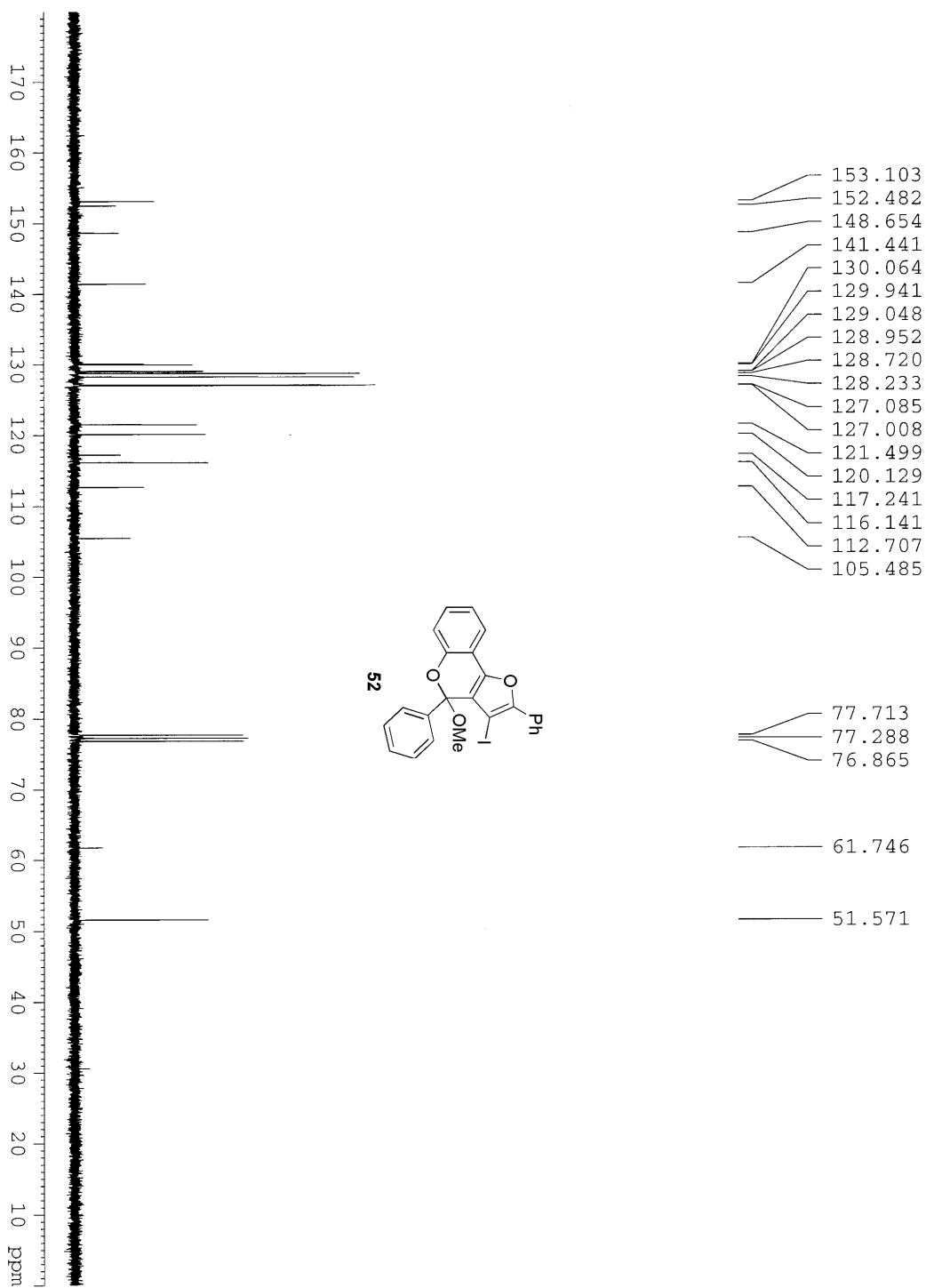


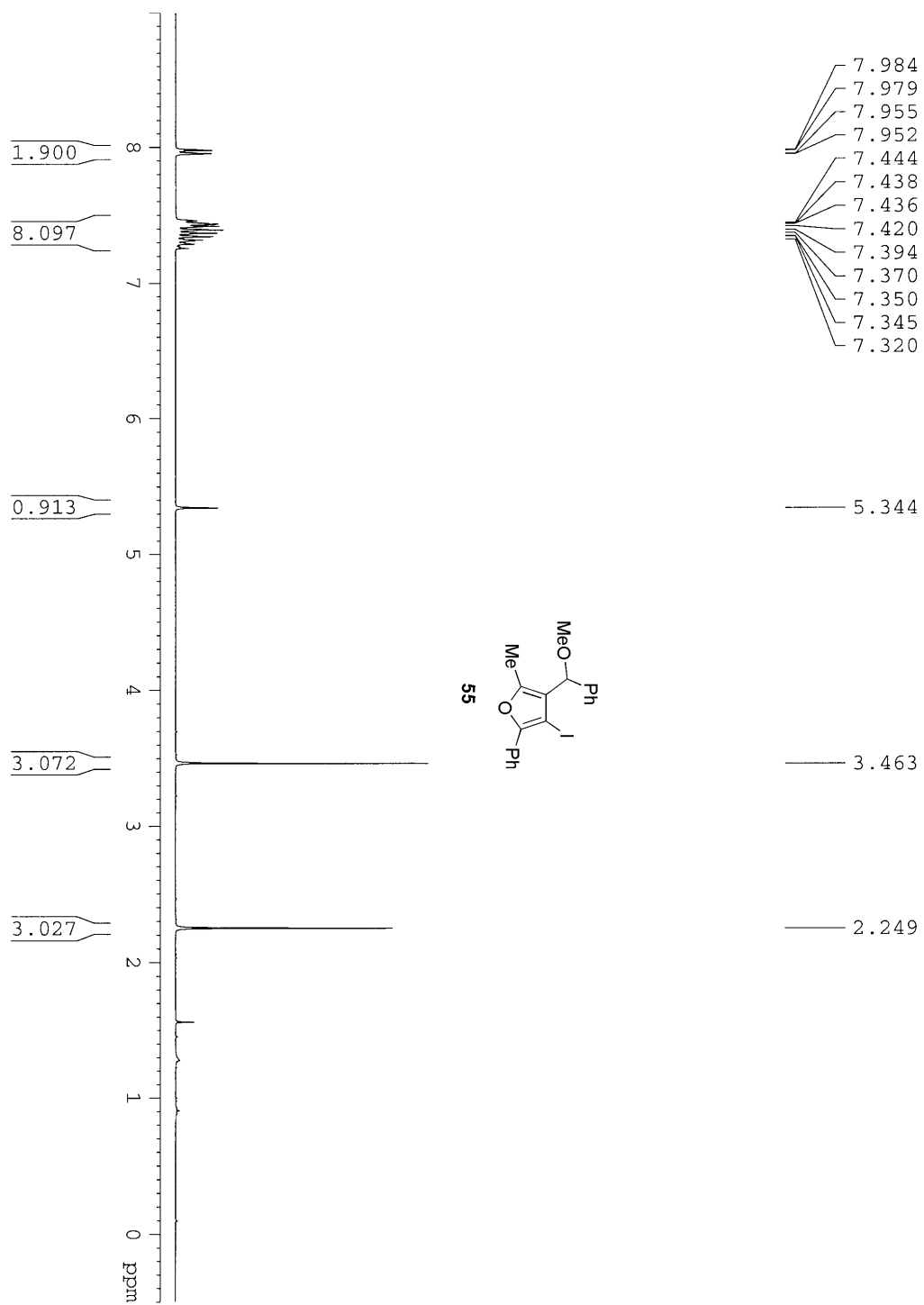


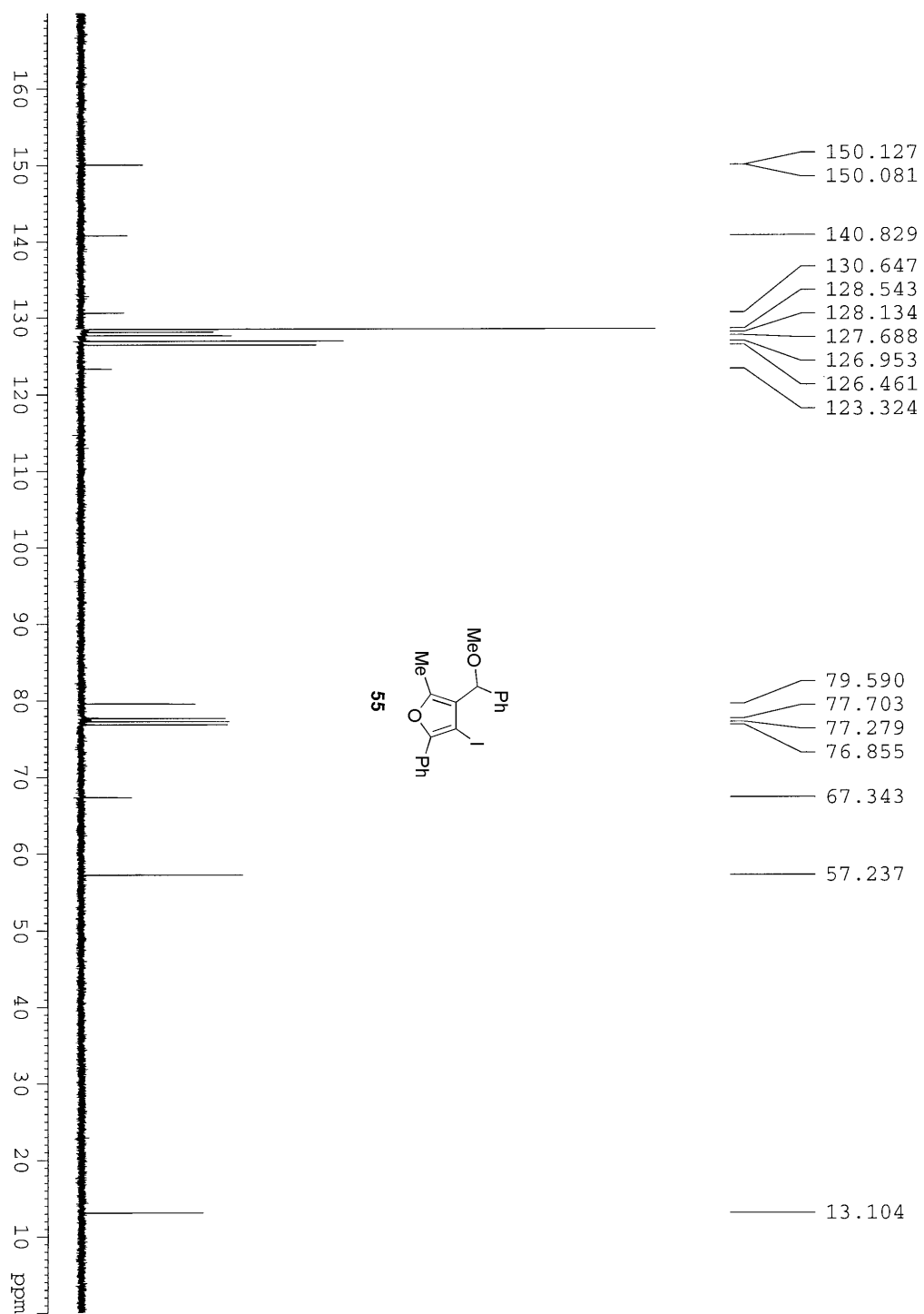


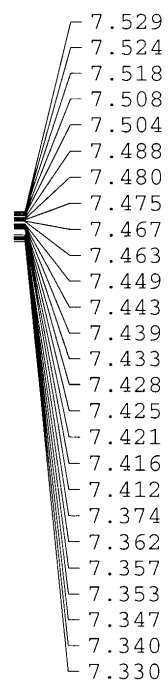
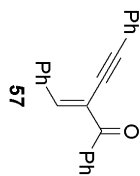
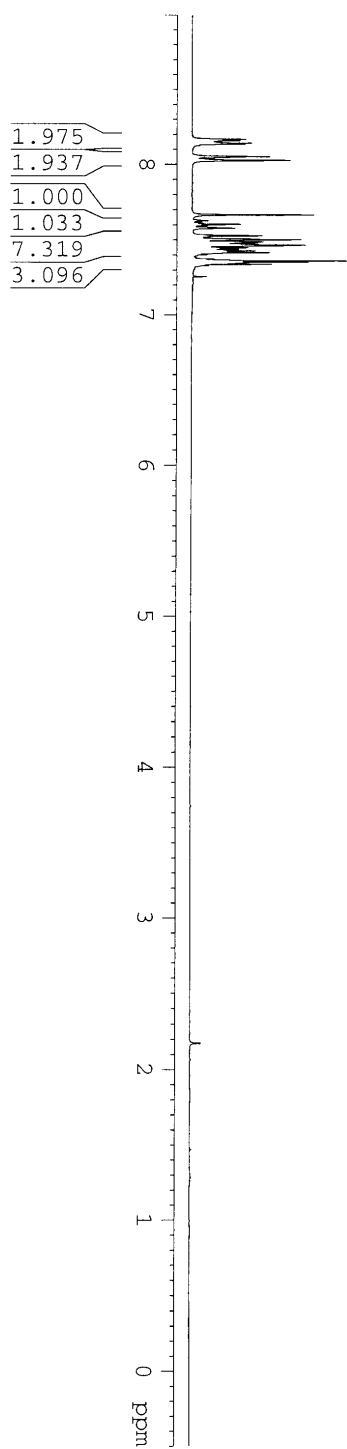


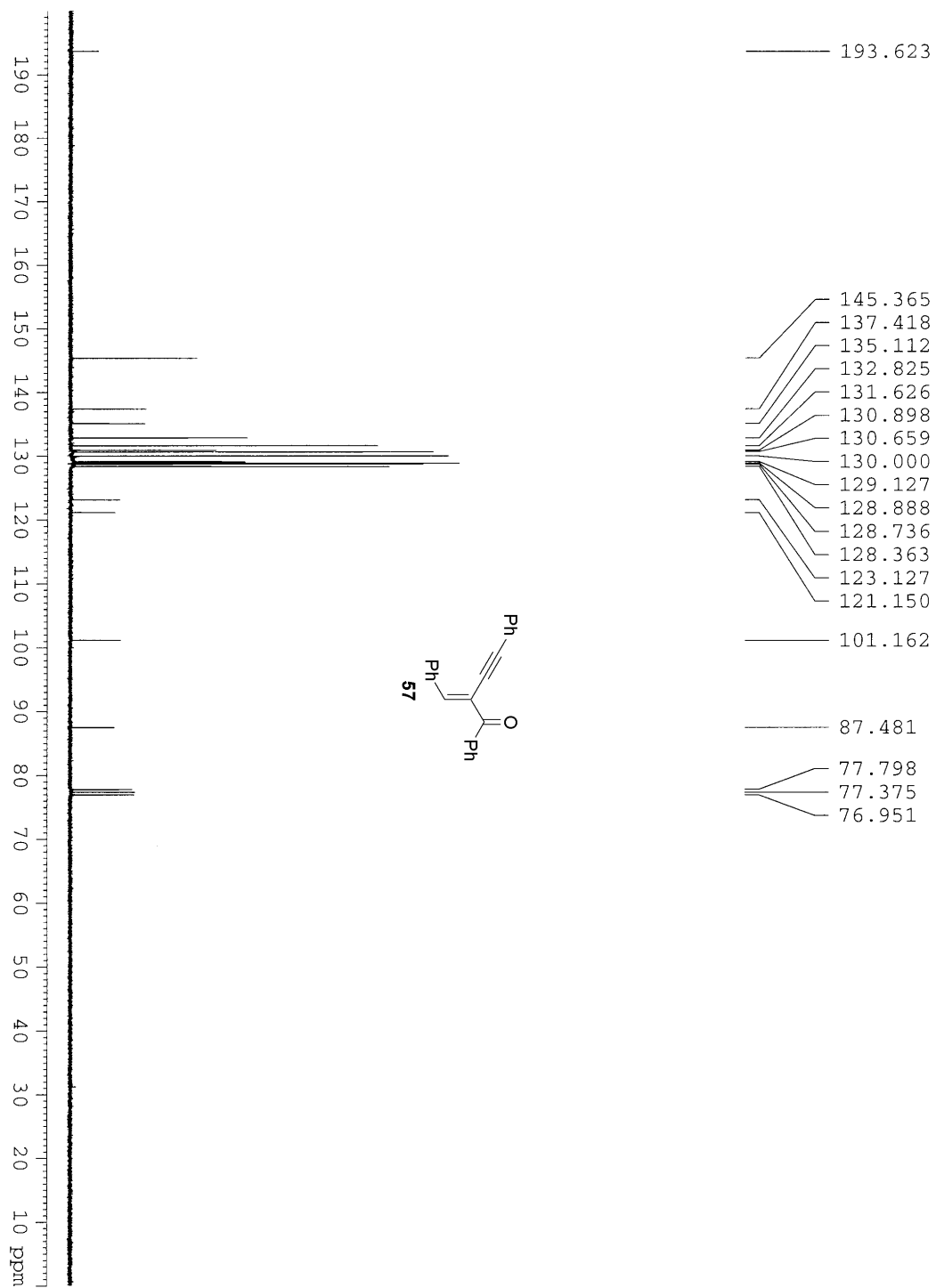


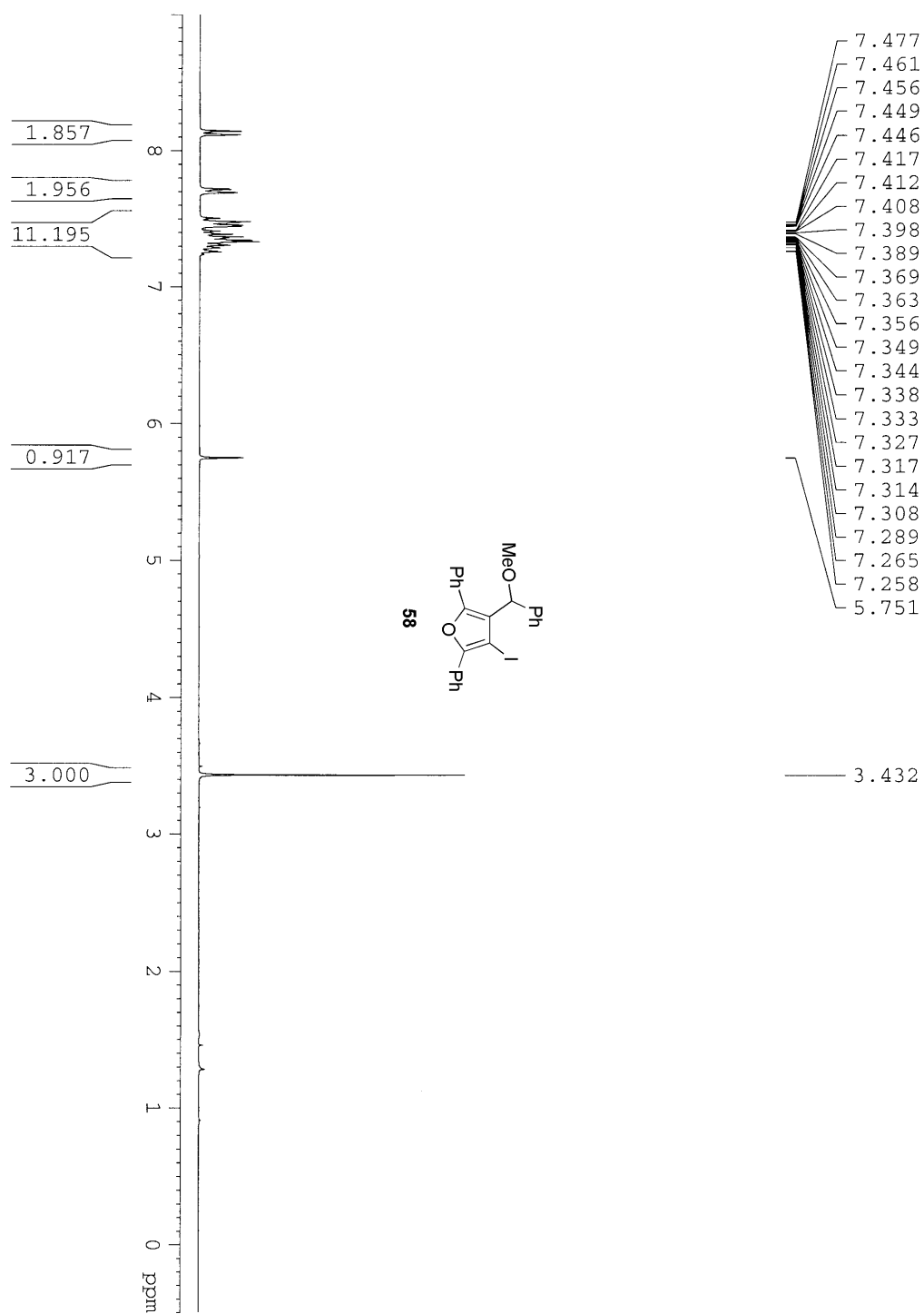


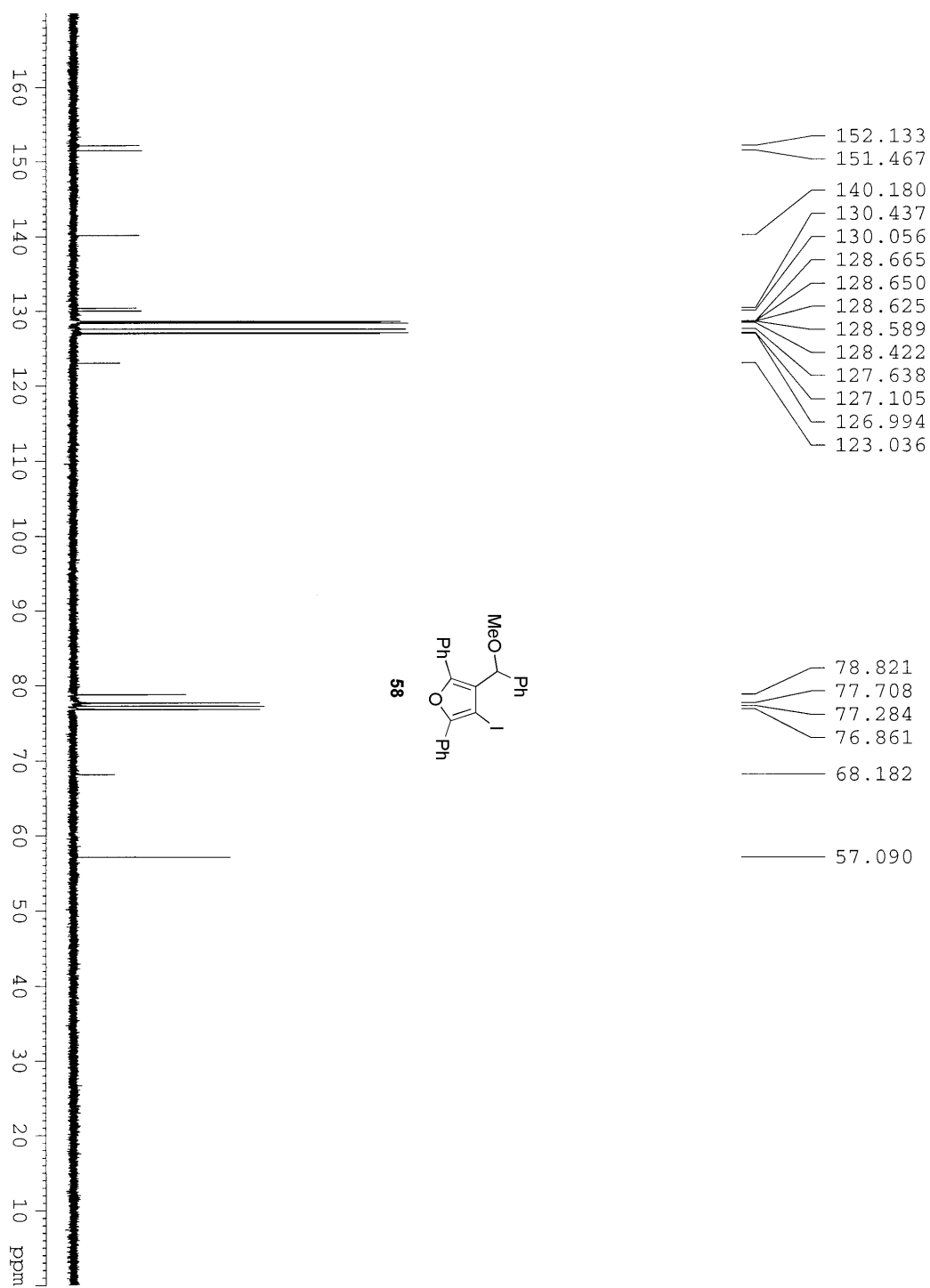


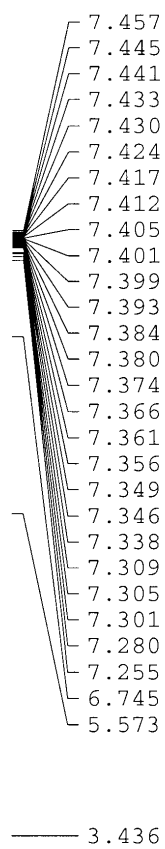
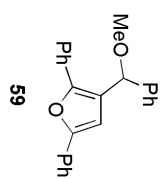
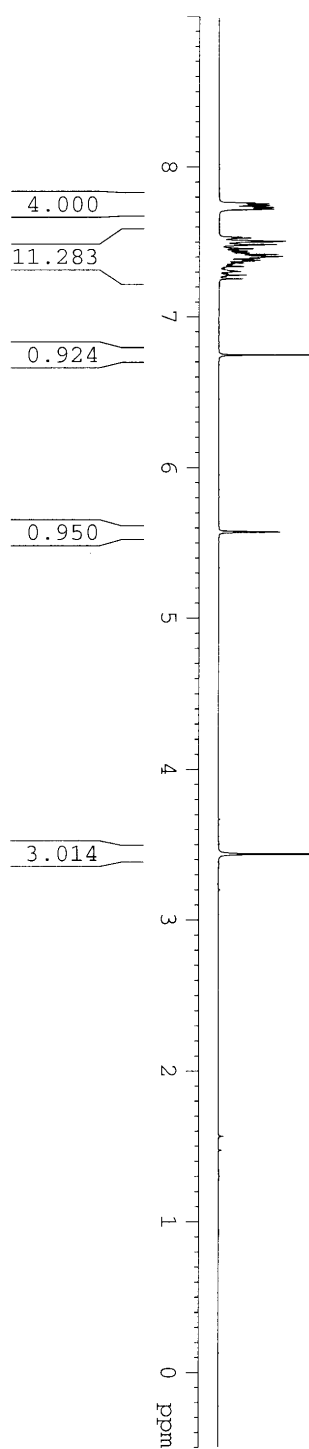


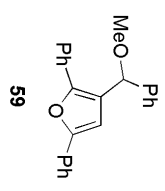
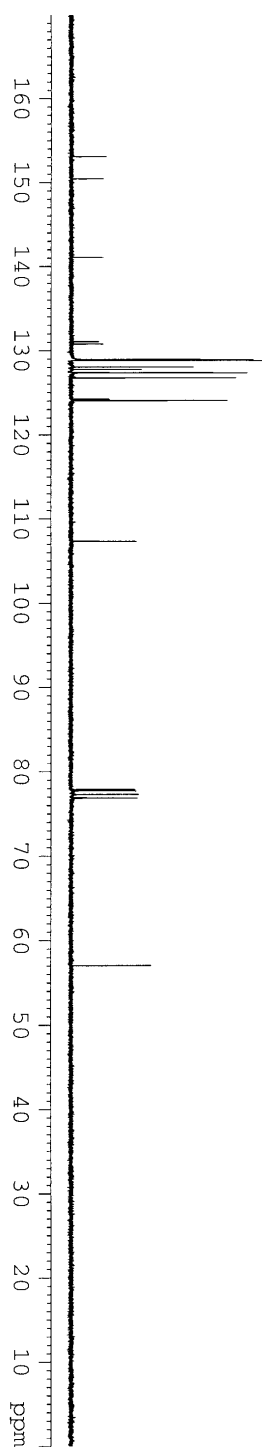












- 153.070
- 150.468
- 141.075
- 131.068
- 130.784
- 128.958
- 128.928
- 128.841
- 128.066
- 127.769
- 127.381
- 126.765
- 124.244
- 124.088
- 107.339

- 77.884
- 77.729
- 77.305
- 76.882

- 57.037

