Supporting Information

Total Synthesis of Diptoindonesin G and Its Analogues as Selective Modulators of Estrogen Receptors

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General remarks

All reactions in non-aqueous media were conducted under a positive pressure of dry argon in glassware that had been oven dried prior to use unless noted otherwise. Oxygen and moisture-sensitive reaction were carried out under argon atmosphere. Solvents were purified and dried by standard methods prior to use. All commercially available reagents were used without further purification unless otherwise noted. Thin layer chromatography was performed using precoated silica gel plates (EMD Chemical Inc. 60, F254). Flash column chromatography was performed with silica gel (Sillicycle, 40-63μm). Infrared spectra (IR) were obtained as neat oils on a Bruker Equinox 55 Spectrophotometer. ^{1}H and ^{13}C Nuclear magnetic resonance spectra (NMR) were obtained on a Varian Unity-Inova 400 MHz or 500 MHz recorded in ppm (δ) downfield of TMS (δ = 0) in $CDCl_3$ or $(CD_3)_2CO$ or $(CD_3)_2SO$. Signal splitting patterns were described as singlet (s), doublet (d), triplet (t), quartet (q), quintet (quint),or multiplet (m), with coupling constants (*J*) in Hertz. High resolution mass spectra (HRMS) were performed by Analytical Instrument Center at the School of Pharmacy or Department of Chemistry on an Electron Spray Injection (ESI) mass spectrometer.

Procedure for the preparation of 7:

To a mixture of phenol **5** (0.9 g, 4.95 mmol) and Cs_2CO_3 (3.3 g, 10 mmol) in 30 mL of MeCN was added 2-bromo-1,1-dimethoxyethane (0.9 mL, 7.5 mmol) at room temperature. The mixture was stirred at reflux for 40 h before the reaction was completed. After cooling down, water was added and extracted with ethyl acetate for three times. The combined organic phase was collected, concentrated and purified on flash column to give methoxybenzoate **7** (1.33 g, 4.9 mmol, 99%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ 3.46 (s, 6H), 3.81 (s, 3H), 3.89 (s, 3H), 4.02 (d, *J* = 5.2 Hz, 2H), 4.72 (t, *J* = 5.2 Hz, 1H), 6.68 (t, *J* = 2.4 Hz, 1H), 7.19 (d, *J* = 2.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 52.4, 54.3, 55.7, 68.0, 102.1, 106.4, 107.7, 107.9, 132.2, 159.7, 160.8, 166.8; IR: ν 3384, 2365, 1715, 1260, 1179, 736 cm^{-1}. HRMS (ESI) for $C_{13}H_{18}NaO_6$ (M+Na), (Calc.) 293.0995, found 293.0985.

Procedure for the preparation of 4:

To a solution of methoxybenzoate **7** (1.3 g, 4.8 mmol) in 40 mL of chlorobenzene was added Amberlyst-15 (130 mg, 10 wt%). The mixture was heated at 120 ^{o}C for 3 h. After cooling down to room temperature, the mixture was filtered and the valotile solvent was removed under reduced pressure to give a yellow residue. The residue was purified by flash column to give **4** (760 mg, 3.7 mmol, 77%) as a white solid. m.p. = 49-50 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ 3.84 (s, 3H), 3.94 (s, 3H), 7.18 (dd, *J* = 0.9, 2.3 Hz, 1H), 7.21 (dd, *J* = 0.9, 2.2 Hz, 1H), 7.55 (d, *J* = 2.3

Hz, 1H), 7.59 (d, *J* = 2.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 52.2, 56.1, 101.5, 107.7, 113.4, 121.7, 122.8, 145.7, 156.4, 157.4, 166.8; IR: ν 3406, 2340, 1600, 1348, 1196, 770cm^{-1}. HRMS (ESI) for $C_{11}H_{10}NaO_4$ (M+Na), (Calc.) 229.0471, found 229.0469.

Procedure for the preparation of 3:

To a solution of carboxylate **4** (100 mg, 0.49 mmol) in 5 mL of DMF was added NBS (360 mg, 1.5 mmol) in one portion. The mixture was heated at 70 ^{o}C for 4 h before the reaction was completed. Saturated $Na_2S_2O_3$ solution was added and extracted with ethyl acetate for three times. The combined organic phase was collected, concentrated and purified by flash column to give **3** (55 mg, 0.15 mmol, 31%) as a white solid. m.p. = 92-94 ^{o}C.^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ 3.87 (s, 3H), 3.98 (s, 3H), 7.11 (d, *J* = 2.4 Hz, 1H), 7.34 (d, *J* = 2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 52.4, 56.3, 99.0, 99.9, 114.4, 119.0, 124.8, 130.6, 156.4, 157.7, 166.4; IR: ν 3385, 1720, 1622, 1314, 1127, 734 cm^{-1}. HRMS (ESI) for $C_{11}H_8Br_2NaO_4$ (M+Na) 386.8667, (Calc.), found 386.8664.

Procedure for the preparation of 9:

To a solution of **4** (412 mg, 2 mmol) in 20 mL of 1, 2-dichloroethane was added NBS (540 mg, 3 mmol) and 0.1mL DMF. The mixture was stirred at 70 ^{o}C for 3 h before all the substrate was converted to the product. Sat. $Na_2S_2O_3$ solution was added to quench the reaction and extracted with ethyl acetate. The combined organic

phase was collected, concentrated and purified by flash column to give carboxylate **9** (545 mg, 1.91 mmol, 96%) as white solid. m.p. = 92-93 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ 3.87 (s, 3H), 3.97 (s, 3H), 7.16 (dd, *J* = 0.9, 2.3 Hz, 1H), 7.20 (d, *J* = 0.9 Hz, 1H), 7.56 (d, *J* = 2.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 52.4, 56.3, 101.3, 109.5, 113.5, 122.0, 122.9, 128.8, 157.0, 157.3, 166.4; IR: ν 3407, 2360, 1717, 1317, 1143, 736 cm^{-1}. HRMS (ESI) for $C_{11}H_9BrNaO_4$ (M+Na), (Calc.) 306.9576, found 306.9578.

Procedure for the preparation of 10:

To a 50 mL flask was added **9** (540 mg, 1.9 mmol), (4-methoxyphenyl)boronic acid (590 mg, 3.8 mmol), K_2CO_3 powder (1.3 mg, 10 mmol) and DMF (30 mL). The mixture was degassed three times for a total time of 30 min before $Pd(PPh_3)_4$ (60 mg, 0.05 mmol) was added. The flask was degassed again and refilled with argon. The mixture was heated at 70 ^{o}C overnight. Water was added and extracted with ethyl acetate three times. The organic phase was collected and washed with brine. The organic layer was dried with Na_2SO_4, concentrated and purified on silica gel to give **10** (5.5 mg, 1.76 mmol, 93%) as a white solid. m.p. = 101-103 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ 3.87 (s, 3H), 3.90 (s, 3H), 4.00 (s, 3H), 6.97 (d, *J* = 9.0 Hz, 2H), 7.25 (dd, *J* = 0.9, 2.3 Hz, 1H), 7.39 (d, *J* = 0.9 Hz, 1H), 7.56 (d, *J* = 2.3 Hz, 1H), 7.79 (d, *J* = 9.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 52.0, 55.3, 56.0, 100.6, 101.4, 112.5, 114.3, 121.7, 123.0, 124.0, 126.4, 156.0, 156.7, 157.0, 160.1, 166.8; IR: ν 3404, 2359, 1715, 1531, 1175, 766 cm^{-1}. HRMS (ESI) for $C_{18}H_{16}NaO_5$

(M+Na), (Calc.) 335.0890, found 335.0875.

Procedure for the preparation of 8:

To a solution of **10** (550 mg, 1.76 mmol) in 30 mL of 1, 2-dichloroethane was added NBS (470 mg, 2.64 mmol). The mixture was stirred at 70 ^{o}C for 10 min before the reaction was completed. Saturated $Na_2S_2O_3$ solution was added to quench the reaction and extracted with ethyl acetate for three times. The combined organic phase was collected, concentrated and purified by flash column chromatography to give bromide **8** (510 mg, 1.31 mmol, 77%) as a white solid. m.p. = 109-110 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ 3.85 (s, 3H), 3.86 (s, 3H), 3.99 (s, 3H), 6.97 (d, *J* = 9.0 Hz, 2H), 7.12 (d, *J* = 2.3 Hz, 1H), 7.23 (d, *J* = 2.3 Hz, 1H), 8.02 (d, *J* = 9.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 52.2, 55.4, 56.0, 90.8, 99.3, 113.1, 114.0, 120.0, 122.0, 125.4, 128.9, 152.0, 154.7, 157.4, 160.3, 167.0; IR: ν 3369, 1716, 1503, 1309, 1134, 735 cm^{-1}. HRMS (ESI) for $C_{18}H_{15}BrNaO_5$ (M+Na), (Calc.) 412.9995, found 412.9975.

Procedure for the preparation of 2:

To a 50 mL flask was added bromide **8** (390 mg, 1 mmol), (3,5-dimethoxyphenyl)boronic acid (570 mg, 3 mmol), K_2CO_3 power (700 mg, 5 mmol) and DMF (30 mL). The mixture was degassed three times for a total time of 30 min before $Pd(PPh_3)_4$ (55 mg, 0.05 mmol) was added. The flask was degassed again and refilled with argon. Then the mixture was heated at 110 ^{o}C for 4 h. Water was added

and the aqueous solution was extracted with ethyl acetate three times. The organic phases were combined and washed with brine. Then the organic layer was dried with Na_2SO_4, concentrated and purified by flash column chromatography with 10% acetone in hexane as fluent to give **2** (415 mg, 0.93 mmol, 93%) as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ 3.23 (s, 3H), 3.77 (s, 6H), 3.80 (s, 3H), 3.90 (s, 3H), 6.50 (s, 3H), 6.81 (d, *J* = 9.0 Hz, 2H), 7.21 (d, *J* = 2.3 Hz, 1H), 7.24 (d, *J* =2.3 Hz, 1H), 7.47 (d, *J* = 9.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 51.5, 55.3, 55.5, 56.1, 99.6, 100.1, 107.5, 112.3, 113.9, 115.7, 121.6, 123.0, 125.2, 128.2, 136.6, 151.7, 155.3, 157.1, 159.7, 161.1, 168.0; IR: ν 3377, 2360, 1720, 1620, 1203, 735 cm^{-1}. HRMS (ESI) for $C_{26}H_{24}NaO_7$ (M+Na), (Calc.) 471.1414, found 471.1413. All spectroscopic data are in accordance with literature.[5]

Procedure for the preparation of 11:

To a 25 mL flask was added **9** (100 mg, 0.35 mmol), phenyl boronic acid (122 mg, 1 mmol), K_2CO_3 powder (210 mg, 1.7 mmol) and DMF (10 mL). The mixture was degassed three times for a total time of 30 min before $Pd(PPh_3)_4$ (19 mg, 0.017 mmol) was added. The flask was degassed again and refilled with argon. The mixture was heated at 75 ^{o}C overnight. Water was added and the aqueous solution was extracted with ethyl acetate three times. The organic phases were combined and washed with brine. The organic layer was dried with Na_2SO_4, concentrated and purified on silica gel to give **11** (98 mg, 0.34 mmol, 97%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ 3.91 (s, 3H), 4.02 (s, 3H), 7.25 (dd, *J* = 0.8, 2.2 Hz, 1H), 7.38 (t, *J*

= 7.4 Hz, 1H), 7.46 (t, *J* = 7.2 Hz, 2H), 7.53 (d, *J* = 0.8 Hz, 1H), 7.59 (d, *J* = 2.3 Hz, 1H), 7.88 (d, *J* = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 52.1, 56.0, 101.4, 102.2, 112.9, 122.1, 123.6, 124.8, 128.6, 128.8, 130.2, 156.2, 156.7, 157.1, 166.8; IR: ν 2952, 2361, 1716, 1564, 1310, 1131, 735 cm^{-1}. HRMS (ESI) for $C_{17}H_{14}NaO_4$ (M+Na), (Calc.) 305.0784, found 305.0778.

Procedure for the preparation of 12:

To a solution of **11** (50 mg, 0.177 mmol) in 10 mL of 1, 2-dichloroethane was added NBS (62 mg, 0.35 mmol) and 2 mL of DMF. The mixture was stirred at 80 ^{o}C for 10 min before the reaction was completed. Saturated $Na_2S_2O_3$ solution was added to quench the reaction and extracted with ethyl acetate. The combined organic phases were collected, concentrated and purified by flash column chromatography to give bromide **12** (32 mg, 0.089 mmol, 50%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ 3.89 (s, 3H), 4.00 (s, 3H), 7.16 (d, J = 2.3 Hz, 1H), 7.25 (d, J = 2.3 Hz, 1H), 7.41 (td, J = 1.4, 8.4 Hz, 1H), 7.46-7.50 (m, 2H), 8.08 (td, J = 1.7, 7.1 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 52.2, 56.0, 92.3, 99.2, 113.5, 119.8, 125.8, 127.3, 128.5, 129.2, 129.4, 151.8, 155.0, 157.8, 167.0; IR: ν 3404, 2924, 2361, 1734, 1374, 1045, 737 cm-1. HRMS (ESI) for $C_{17}H_{13}BrNaO_4$ (M+Na), (Calc.) 382.9889, found 382.9877.

Procedure for the preparation of 13:

To a 10 mL flask was added bromide **12** (30 mg, 0.083 mmol), (3,5-

dimethoxyphenyl)boronic acid (48 mg, 0.25 mmol), K_2CO_3 powder (62 mg, 0.4 mmol) and DMF (5 mL). The mixture was degassed three times for a total time of 30 min before $Pd(PPh_3)_4$ (5 mg, 0.004 mmol) was added. The flask was degassed again and refilled with argon. Then the mixture was heated at 110 ^oC for 3 h. Water was added and extracted with ethyl acetate for three times. The combined organic phase was washed with brine. The organic layer was dried with Na_2SO_4, concentrated and purified on silica gel with 10% acetone in hexane as fluent to give **13** (31 mg, 0.074 mmol, 89%) as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$, TMS): δ 3.24 (s, 3H), 3.76 (s, 6H), 3.90 (s, 3H), 6.51 (s, 3H), 7.23 (d, *J* = 1.9 Hz, 1H), 7.25 (d, *J* = 2.4 Hz, 1H), 7.27-7.31 (m, 3H), 7.54-7.57 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 51.5, 55.5, 56.1, 99.5, 100.3, 107.4, 112.7, 117.3, 121.4, 125.7, 126.8, 128.3, 128.4, 130.3, 136.3, 151.4, 155.5, 157.5, 161.1, 167.9; IR: ν 3368, 2923, 2360, 1721, 1593, 1134, 693 cm^{-1}. HRMS (ESI) for $C_{25}H_{22}NaO_6$ (M+Na), (Calc.) 441.1309, found 441.1308.

Procedure for the preparation of 14:

To a solution of **13** (30mg, 0.071 mmol) in 5 mL of dry dichloromethane was added BBr_3 (1.4 mL, 1M in CH_2Cl_2) dropwise at -78 ^oC. The temperature was allowed warm to room temperature slowly and stirred overnight. After the reaction was completed, the flask was cooled down to -78 ^oC again and saturated $NaHCO_3$ solution was added slowly to quench the reaction. The mixture was filtered and washed with CH_2Cl_2 and water. The filtrate was collected and purified on silica gel

(dichloromethane : acetone : methanol = 60 : 10 : 1) to give compound **14** (21 mg, 0.061mmol, 86%) as a yellow solid. m.p. >260 ^{o}C.^{1}H NMR (500 MHz, DMSO-d6, TMS): δ 6.36 (d, *J* =1.8 Hz, 1H), 7.13 (d, *J* =1.8 Hz, 1H), 7.44 (dd, *J* = 1.3, 11.7 Hz, 2H), 7.69-7.74 (m, 3H), 7.96 (dd, *J* = 1.5, 6.3 Hz, 2H) 10.34 (s, 1H), 10.87 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d6): δ 102.5, 103.2, 104.2, 107.7, 109.0, 110.4, 123.0, 124.6, 128.8, 129.2, 129.9, 130.7, 133.7, 152.8, 155.0, 157.8, 164.1, 166.7, 186.3; IR: ν 3390, 2922, 2361, 1699, 1423, 1238, 1066 cm^{-1}. HRMS (ESI) for $C_{21}H_{12}NaO_5$ (M+Na), (Calc.) 367.0577, found 367.0574.

Procedure for the preparation of 15:

To a 10 mL flask was added bromide **8** (50 mg, 0.13 mmol), phenylboronic acid (47 mg, 0.39 mmol), K_2CO_3 powder (90 mg, 0.65 mmol) and DMF (10 mL). The mixture was degassed three times for a total time of 30 min before $Pd(PPh_3)_4$ (7 mg, 0.006 mmol) was added. The flask was degassed again and refilled with argon. The mixture was heated at 110 ^{o}C for 2 h. Water was added and extracted with ethyl acetate for three times. The organic phase was collected and washed with brine. The organic layer was dried with Na_2SO_4, concentrated to give crude product (48 mg, 0.124 mmol) as a colorless oil.

To a solution of crude product obtained in the last step (30 mg, 0.077) in 5 mL of dry dichloromethane was added BBr_3 (1.5 mL, 1M in CH_2Cl_2) dropwise at -78 ^{o}C. The temperature was allowed to warm to room temperature slowly and stirred overnight. After the reaction was completed, the flask was cooled down to -78 ^{o}C

again and saturated $NaHCO_3$ solution was added slowly to quench the reaction. The mixture was filtered and washed with CH_2Cl_2 and water. The filtrate was collected and dried under vacuum to give compound **15** (22 mg, 0.067mmol, 83% for two steps) as a yellow solid. m.p. >260 ^oC. ^1H NMR (400 MHz, DMSO-d6, TMS): δ 7.03 (d, *J* = 8.6 Hz, 2H), 7.39 (d, *J* = 12.6 Hz, 2H), 7.54 (t, *J* = 7.7 Hz, 1H), 7.67 (t, *J* = 7.0 Hz, 1H), 7.77 (d, *J* = 8.6 Hz, 2H), 8.09 (d, *J* = 8.0 Hz, 1H), 8.34 (d, *J* = 8.0 Hz, 1H), 10.21 (s, 1H), 10.27 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d6): δ 104.6, 107.6, 107.8, 116.5, 120.9, 124.3, 124.4, 125.4, 128.2, 129.0, 131.1, 131.6, 132.5, 133.3, 153.6, 155.8, 158.0, 160.1, 181.9; IR: νcm^{-1}. HRMS (ESI) for $C_{21}H_{12}NaO_4$ (M+Na), (Calc.) 351.0628, found 351.0618.

Procedure for the preparation of 16:

To a 10 mL flask was added bromide **8** (30 mg, 0.08 mmol), 3-methoxyphenylboronic acid (36mg, 0.24 mmol), K_2CO_3 powder (56 mg, 0.4 mmol) and DMF (3 mL). The mixture was degassed three times for a total time of 30 min before $Pd(PPh_3)_4$ (5 mg, 0.004 mmol) was added. The flask was degassed again and refilled with argon. The mixture was heated at 110 ^oC for 3 h. Water was added and extracted with ethyl acetate for three times. The organic phases were combined and washed with brine. The organic layer was dried with Na_2SO_4, concentrated and purified on silica gel with 10% acetone in hexane as fluent to give **16** (31 mg, 0.074 mmol, 93%) as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$, TMS): δ 3.16 (s, 3H), 3.78 (s, 3H), 3.79 (s, 3H), 3.90 (s, 3H), 6.79 (d, *J* = 9.2 Hz, 2H), 6.87 (dd, *J* = 1.5,

2.1 Hz, 1H), 6.92 (d, *J* = 2.0 Hz, 1H), 6.93-6.95 (m, 1H), 7.22 (d, *J* = 2.4 Hz, 1H), 7.25 (d, *J* = 2.4 Hz, 1H), 7.33 (td, *J* = 7.8, 0.3 Hz, 1H), 7.42 (d, *J* = 9.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 51.4, 55.26, 55.34, 56.1, 99.7, 112.5, 113.5, 113.9, 114.7, 115.8, 121.8, 122.3, 123.1, 125.1, 128.2, 129.7, 136.1, 151.8, 155.3, 157.1, 159.6, 160.0, 167.8; IR: ν 3368, 2922, 2852, 1717, 1247, 832 cm^{-1}. HRMS (ESI) for $C_{25}H_{22}NaO_6$ (M+Na), (Calc.) 441.1309, found 441.1308.

Procedure for the preparation of 17 and 18:

To a solution of **16** (65mg, 0.15 mmol) in 15 mL of dry dichloromethane was added BBr_3 (3.0 mL, 1M in CH_2Cl_2) dropwise at -78 ^{o}C. The temperature was allowed to warm to room temperature slowly and stirred overnight. After the reaction was completed, the flask was cooled down to -78 ^{o}C again and saturated $NaHCO_3$ solution was added slowly to quench the reaction. The mixture was filtered and washed with CH_2Cl_2 and water. The filtrate was collected and purified on silica gel (dichloromethane : acetone : methanol = 60 : 10 : 1) to give compound **17** (35 mg, 0.102 mmol, 68%) and compound **18** (14 mg, 0.04 mmol, 27%) as yellow solids.

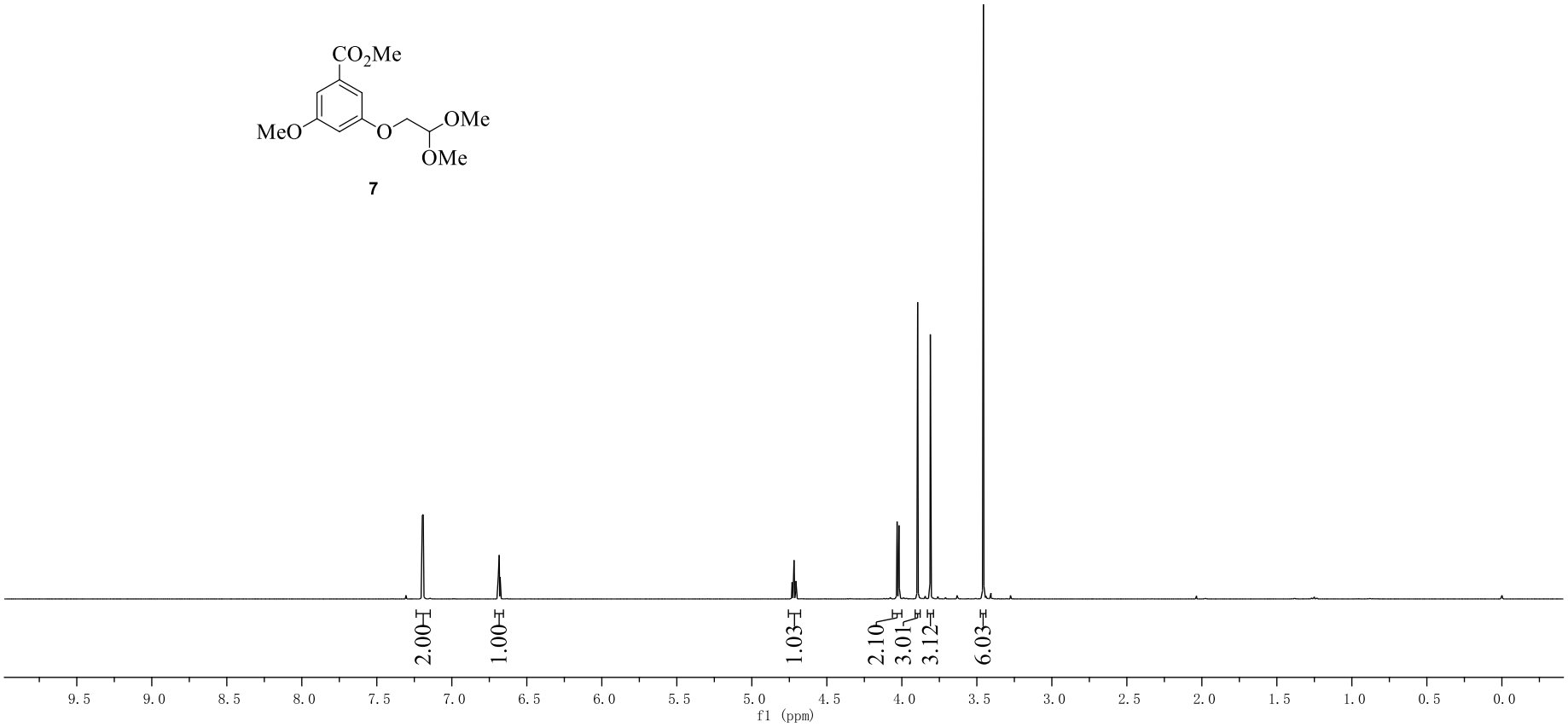
17, m.p. >260 ^{o}C. ^{1}H NMR (500 MHz, acetone-d6, TMS): δ 7.01 (dd, *J* = 1.9, 7.0 Hz, 1H), 7.12 (d, *J* = 7.0 Hz, 2H), 7.33 (d, *J* = 1.6 Hz, 1H), 7.53 (d, *J* = 1.3 Hz, 1H), 7.63 (d, *J* = 1.9 Hz, 1H), 7.83 (d, *J* = 7.0 Hz, 2H), 8.33 (d, *J* = 7.0 Hz, 1H); ^{13}C NMR (125 MHz, acetone-d6): δ 103.9, 108.3, 108.9, 110.3, 116.7, 116.9, 122.7, 125.6, 126.9, 127.0, 131.6, 132.2, 134.7, 154.5, 156.2, 158.3, 160.3, 162.2, 181.8; IR: ν 3365, 2925, 2360, 2125, 1641, 1370, 1238 cm^{-1}. HRMS (ESI) for $C_{21}H_{12}NaO_5$

(M+Na), (Calc.) 367.0577, found 367.0573.

18, m.p. >260 ^{o}C. ^{1}H NMR (500 MHz, DMSO-d6, TMS): δ 6.94 (dd, *J* = 1.2, 8.0 Hz, 1H), 7.02 (d, *J* = 9.1 Hz, 2H), 7.43 (q, *J* = 1.8 Hz, 2H), 7.58 (t, *J* = 8.0 Hz, 1H), 7.63 (dd, *J* = 1.2, 8.0 Hz, 1H), 7.78 (d, *J* = 9.1 Hz, 2H), 10.30 (s, 2H), 13.82 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d6): δ 105.0, 107.2, 107.5, 114.4, 116.0, 116.3, 116.5, 120.2, 123.8, 124.0, 130.6, 132.3, 135.8, 152.8, 156.7, 157.6, 159.9, 164.1, 188.0; IR: 3369, 2921, 2360, 1695, 1238, 1139, 669 cm^{-1}. HRMS (ESI) for $C_{21}H_{12}NaO_5$ (M+Na), (Calc.) 367.0577, found 367.0574.

Procedure for Western blot analyses:

MCF7 cells were treated with Dip G and analogues for 24 hours before harvesting. Hs578T-tet-on-ERβ cells were treated with Dox for 24 hours to induce ERβ expression. The cells were then treated with compounds for 5 days before harvesting. 15 μg of total cell lysates were resolved on SDS-PAGE and Western blot analyses were performed as previously described using ERα antibody (HC-20, Santa Cruz) and anti-FLAG antibody (F7425, Sigma) for ERβ. (Ref: Z. Zhao, L. Wang, T. James, Y. Jung, I. Kim, R. Tan, F. M. Hoffmann and W. Xu, *Chem. Biol.*, 2015, **22**, 1608.)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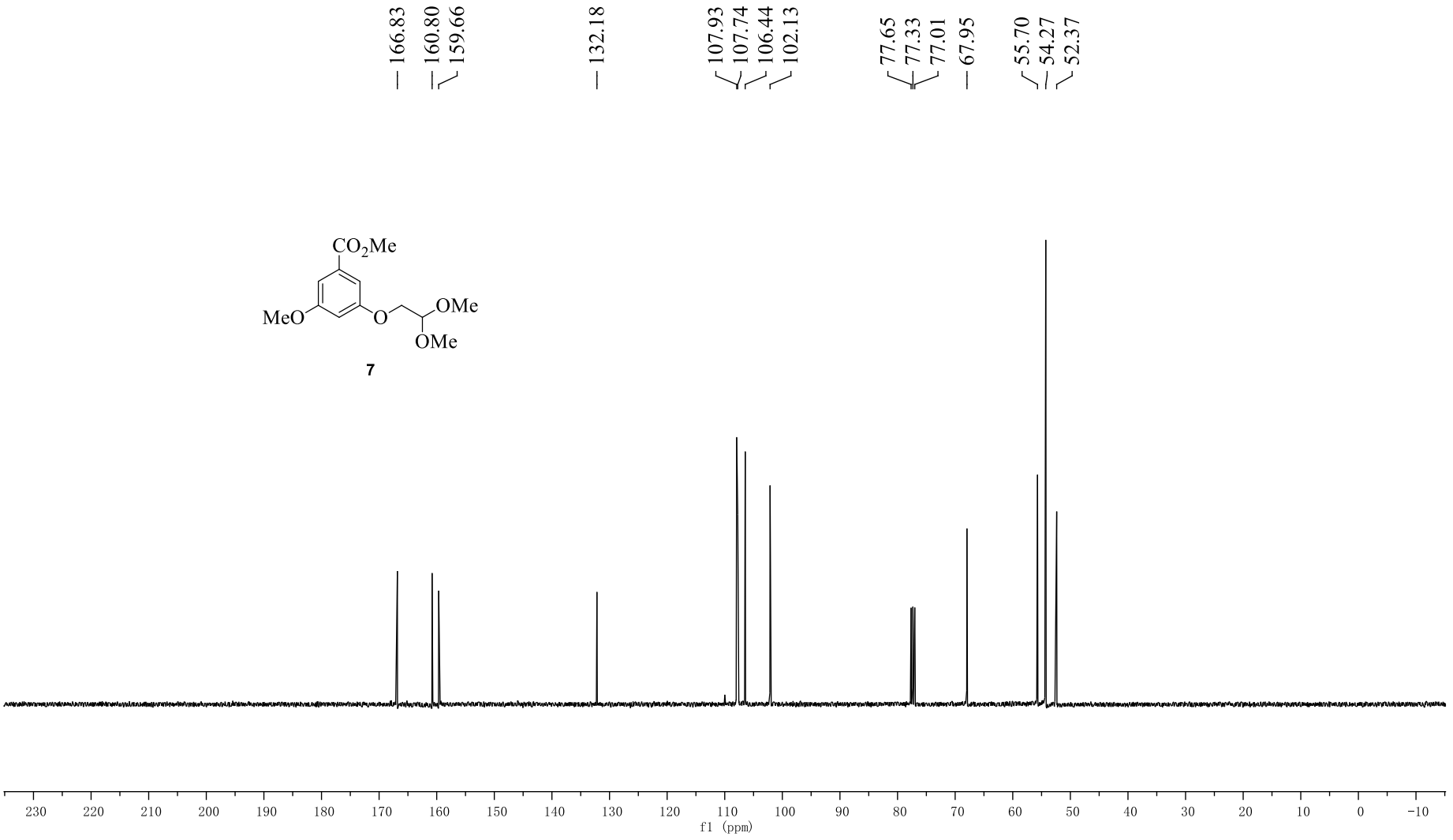
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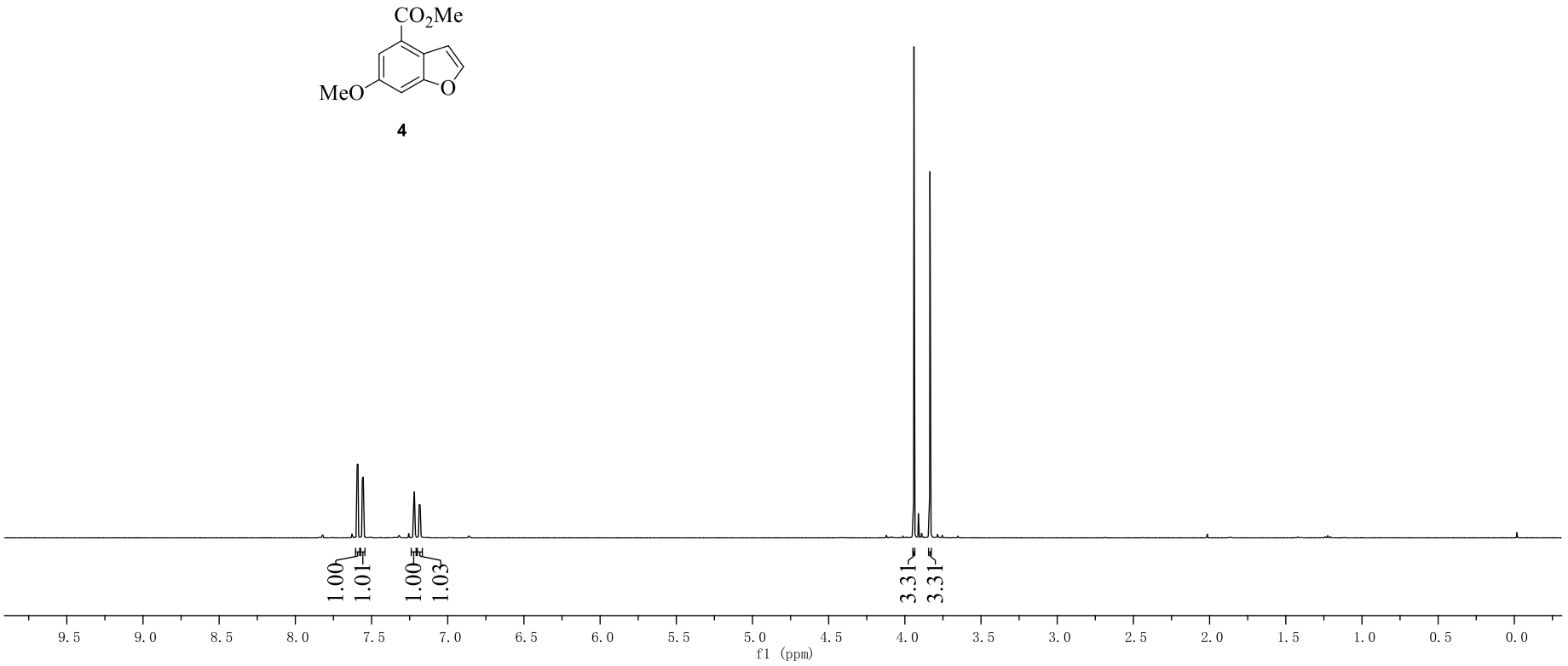
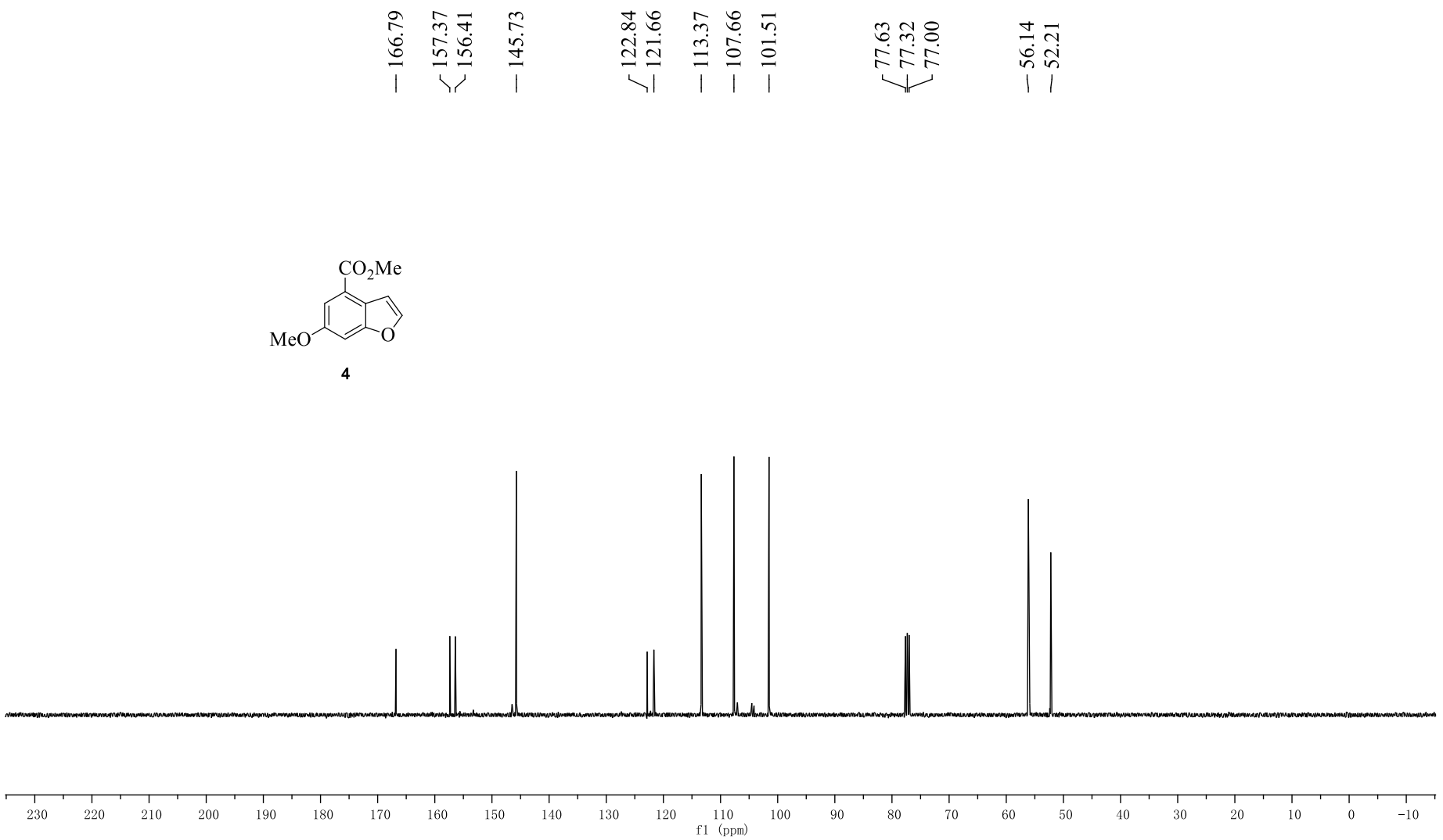
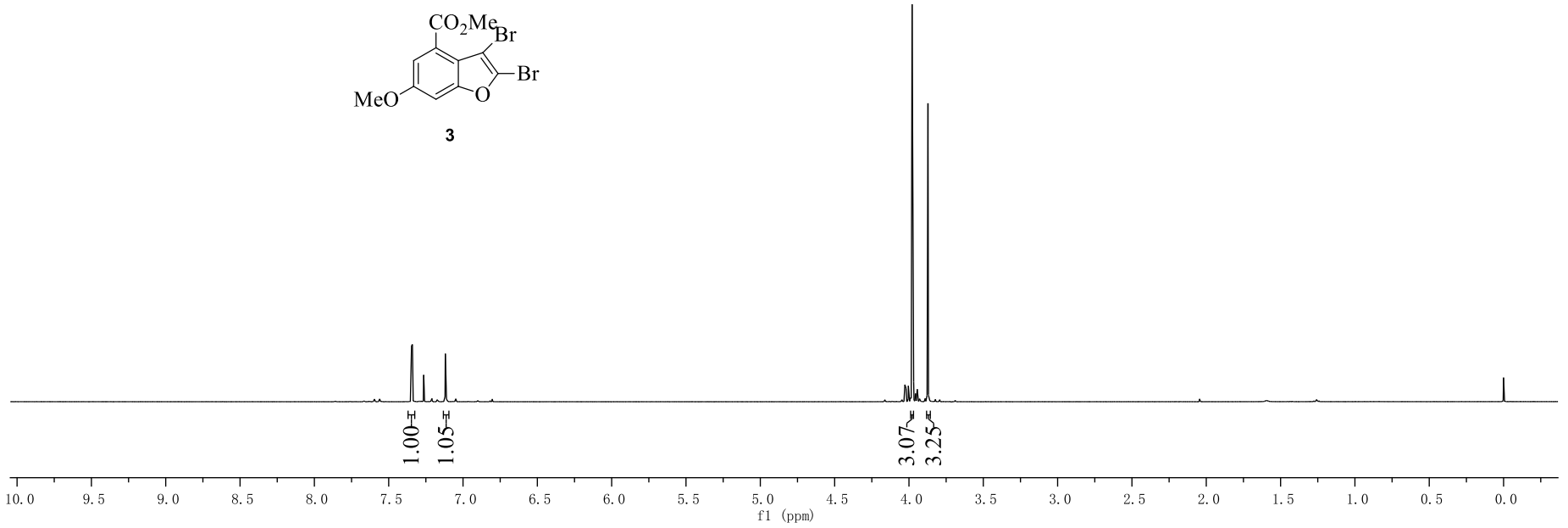
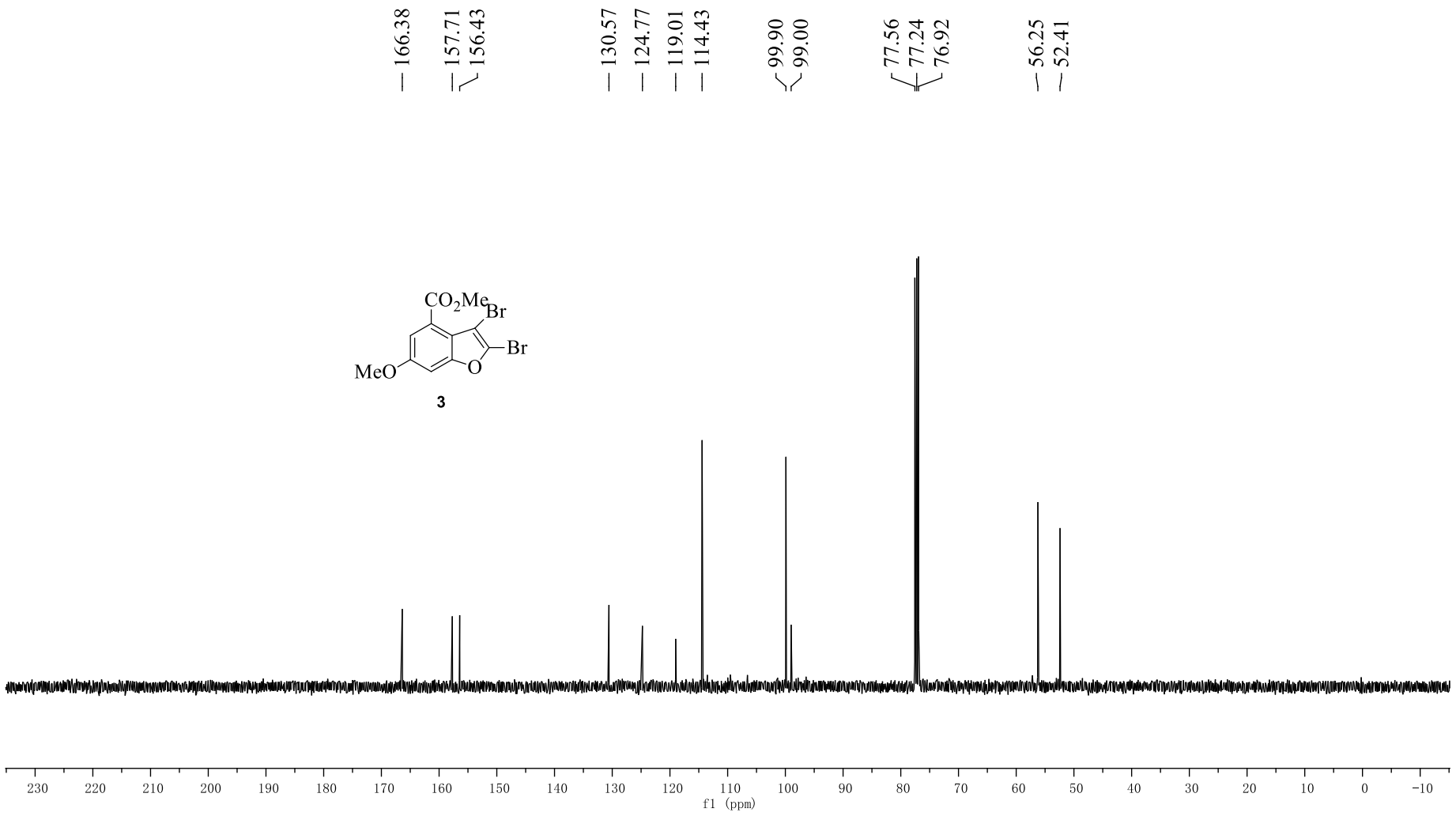
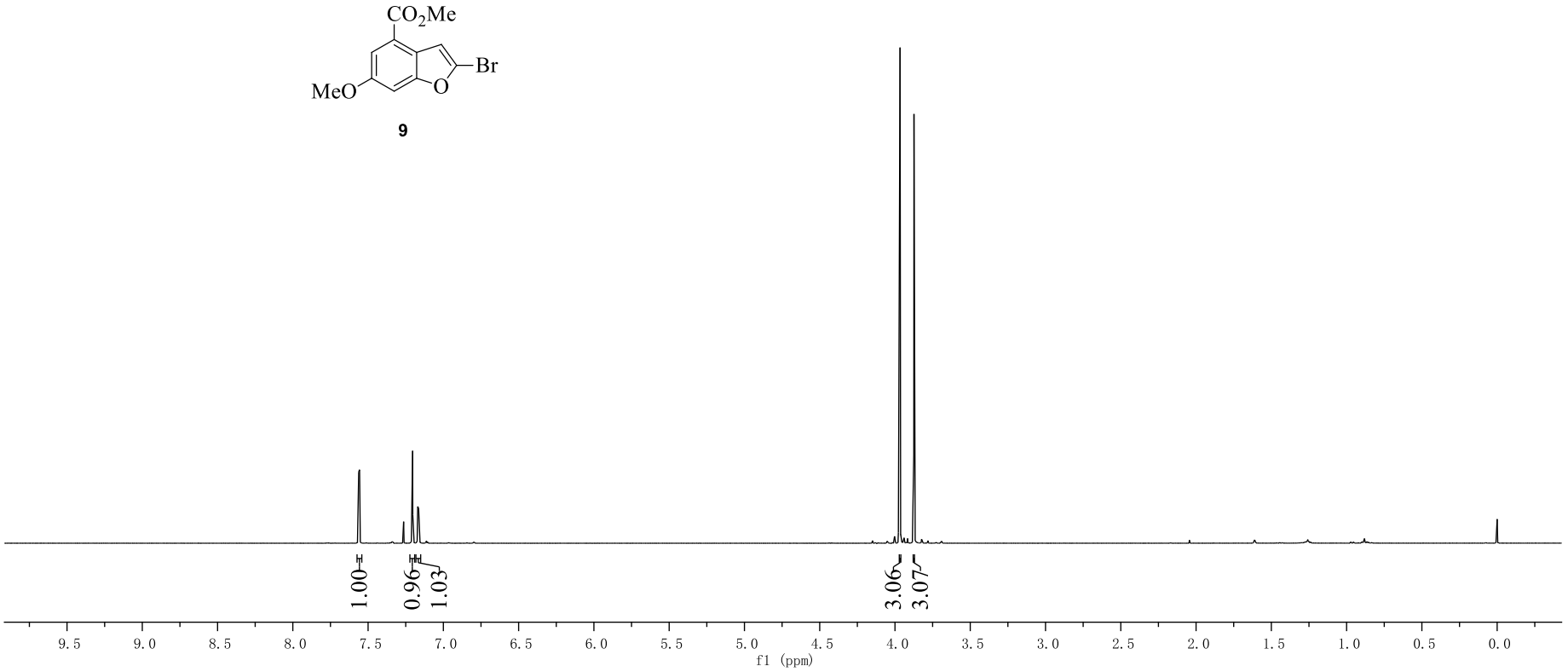
67.95
55.70
54.27
52.37
CO2Me
MeO
O
OMe
OMe
7
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)

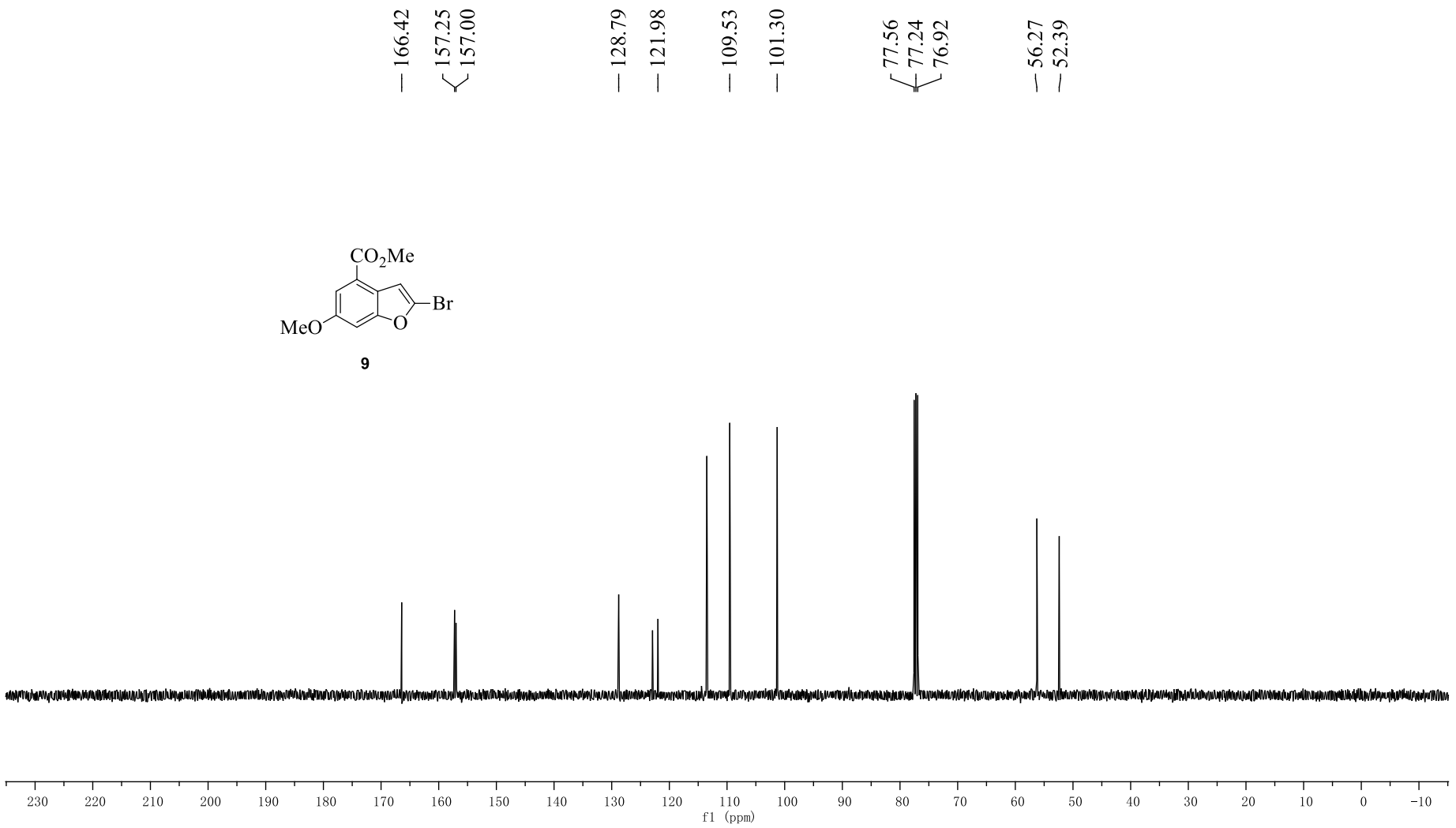

CO2Me
MeO
O
4
1.00
1.01
1.00
1.03
3.31
3.31
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

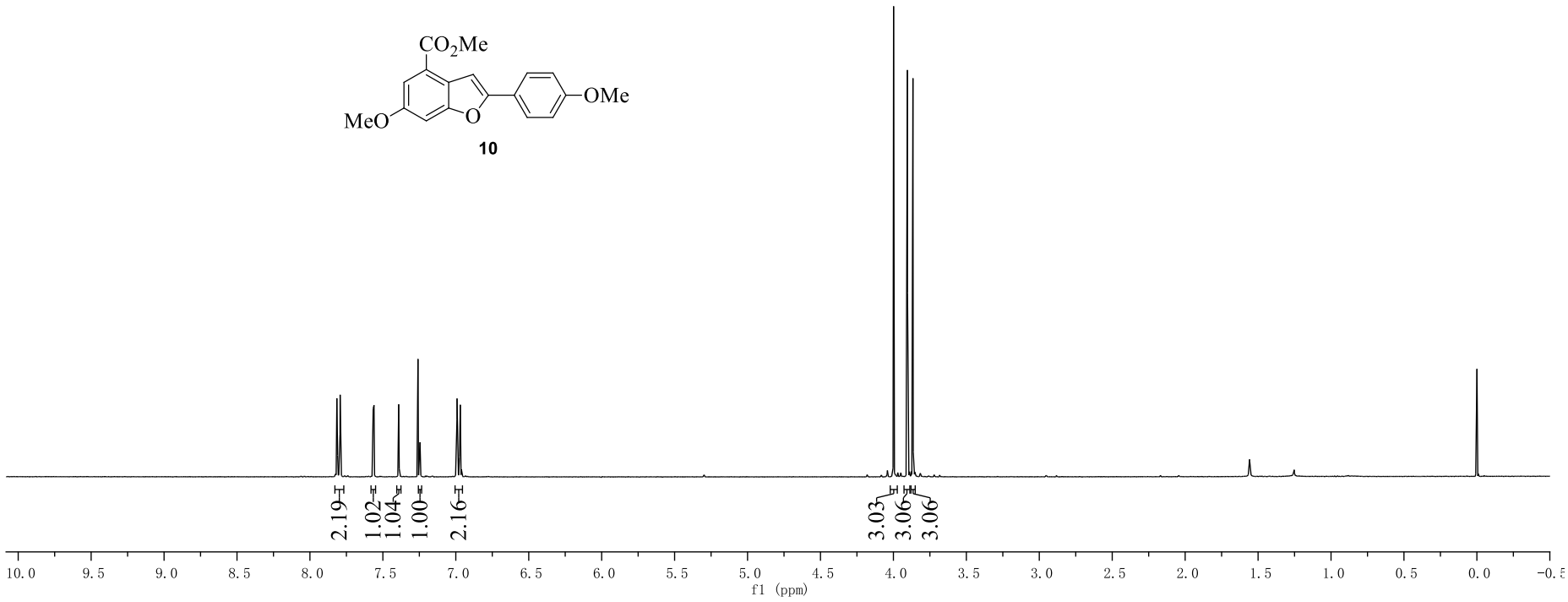

166.79
157.37
156.41
145.73
122.84
121.66
113.37
107.66
101.51
77.63
77.32
77.00
56.14
52.21
CO2Me
MeO
O
4
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

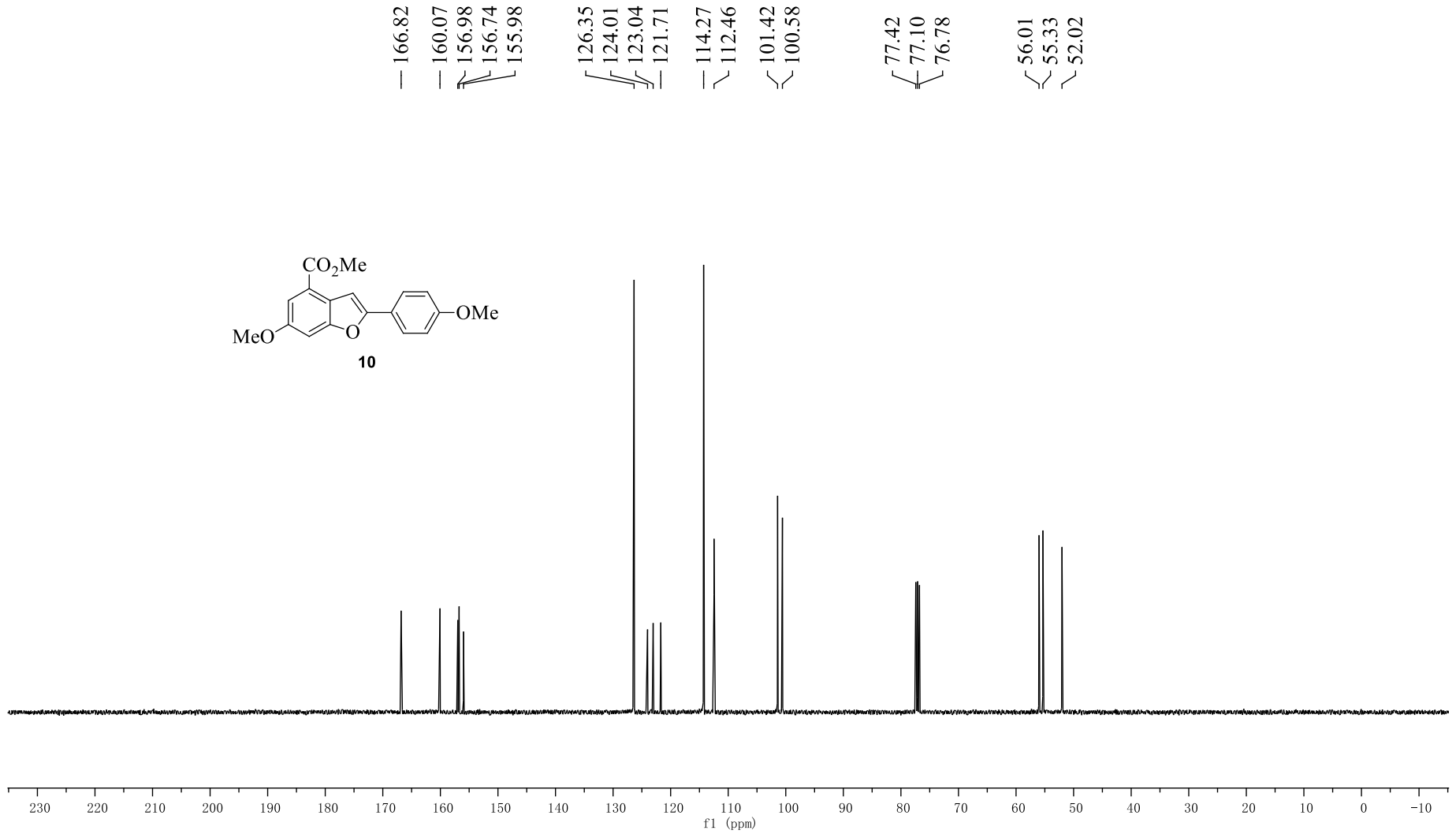

CO2Me
Br
Br
MeO
O
3
1.00
1.05
3.07
3.25
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

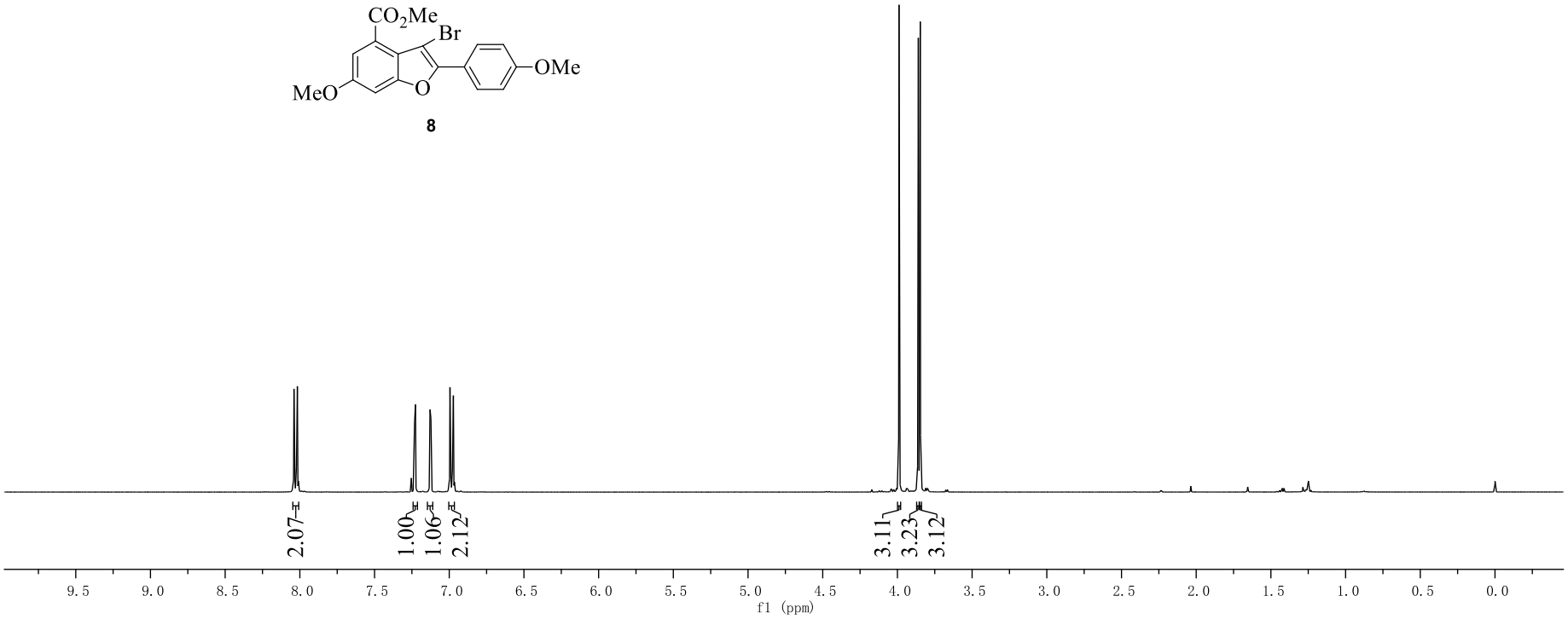

166.38
157.71
156.43
130.57
124.77
119.01
114.43
99.90
99.00
77.56
77.24
76.92
56.25
52.41
CO2Me
Br
Br
MeO
O
3
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)

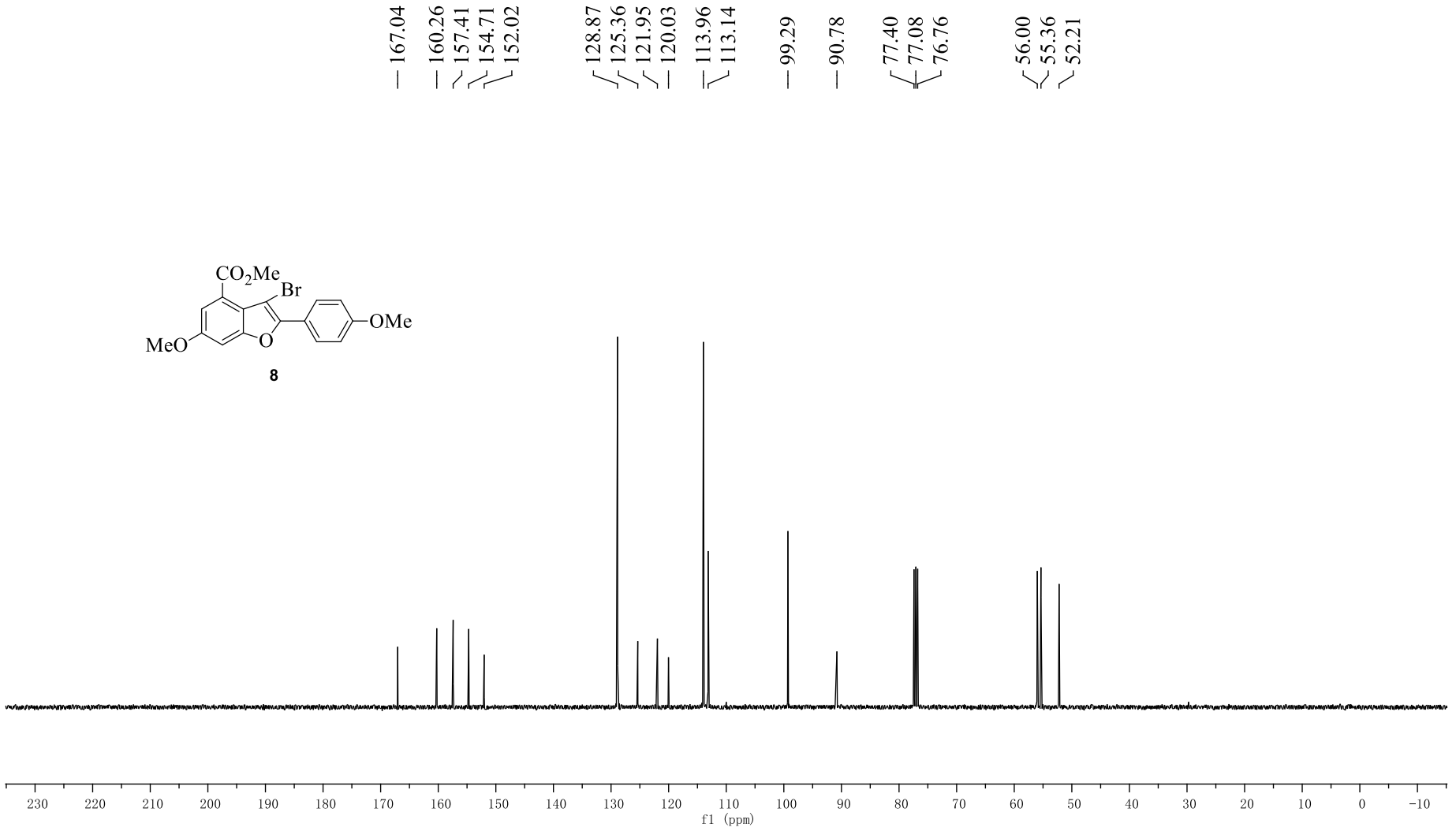

CO2Me
Br
MeO
O
9
1.00
0.96
1.03
3.06
3.07
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

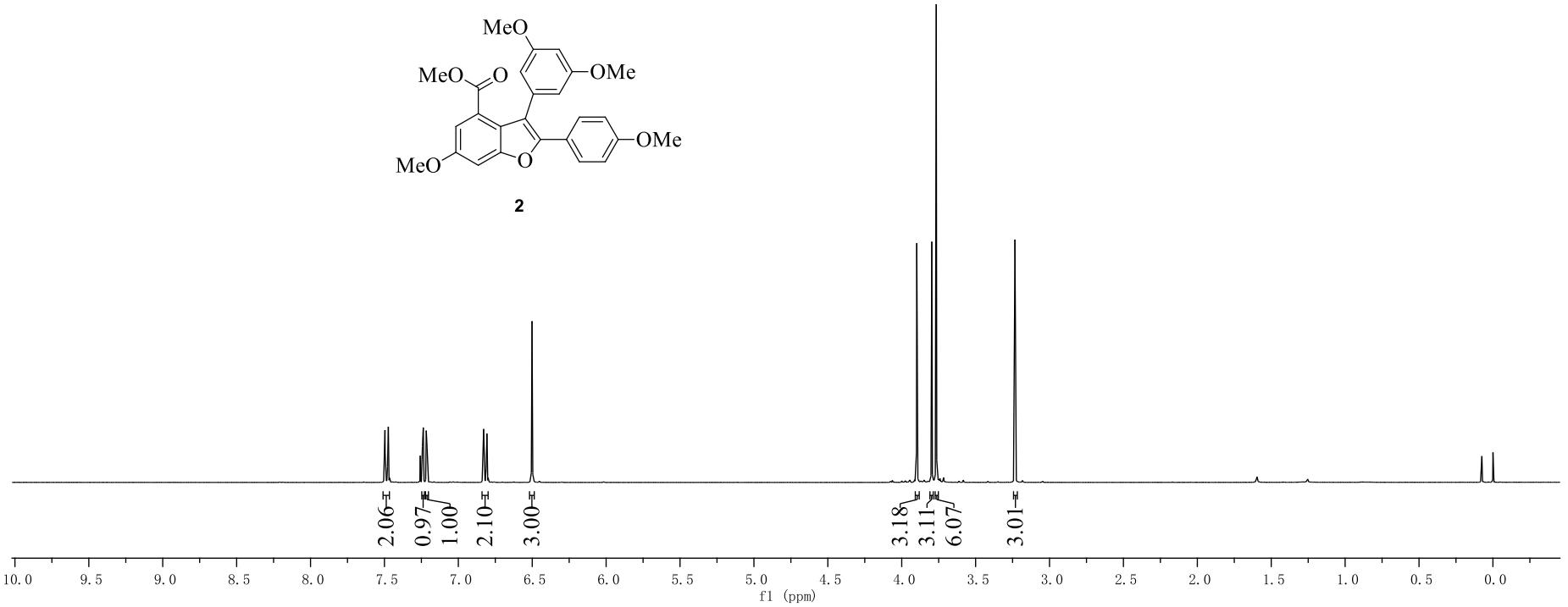

166.42
157.25
157.00
128.79
121.98
109.53
101.30
77.56
77.24
76.92
56.27
52.39
CO2Me
Br
MeO
O
9
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)

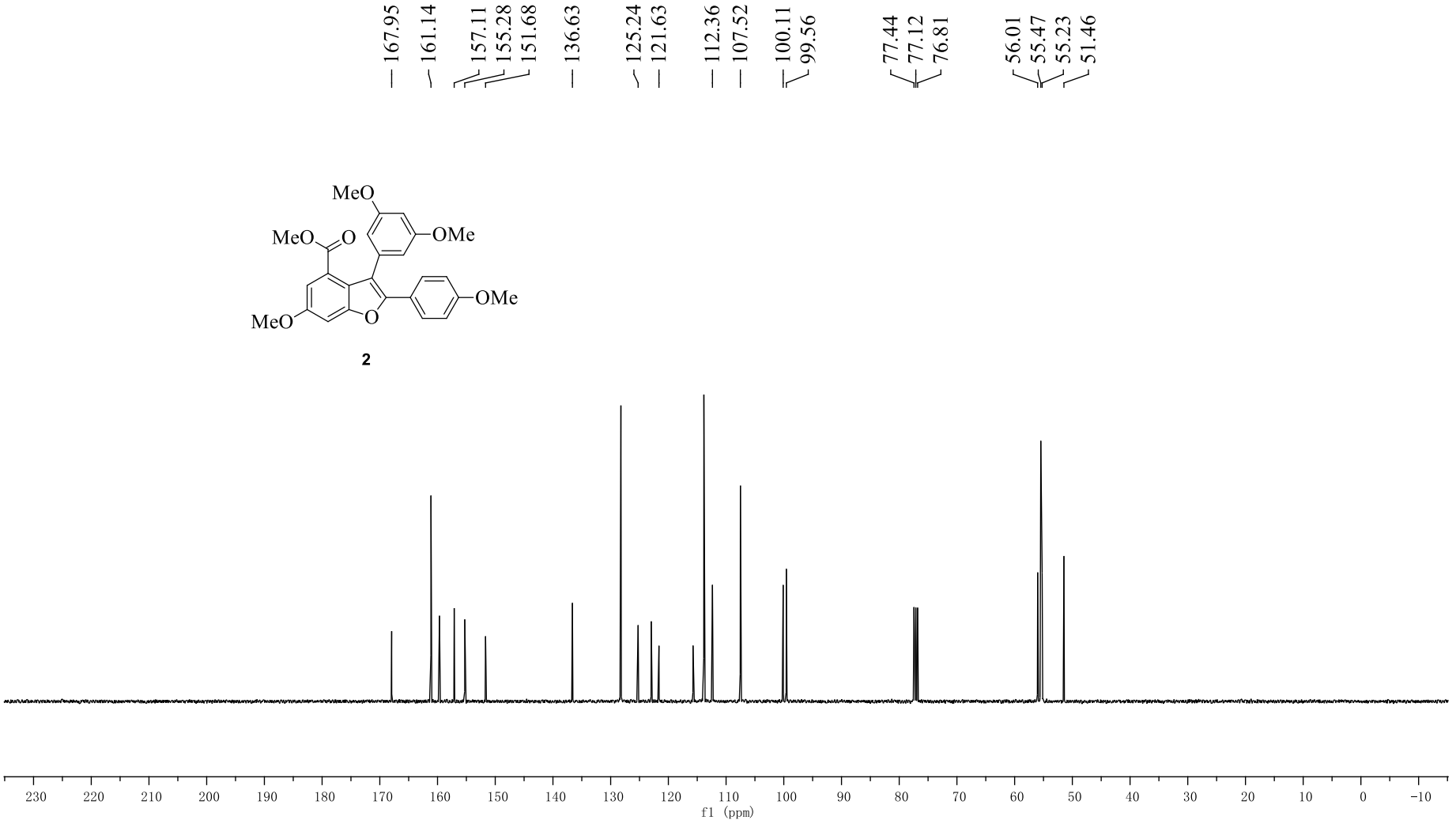

CO2Me
MeO
O
OMe
10
2.19
1.02
1.04
1.00
2.16
3.03
3.06
3.06
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

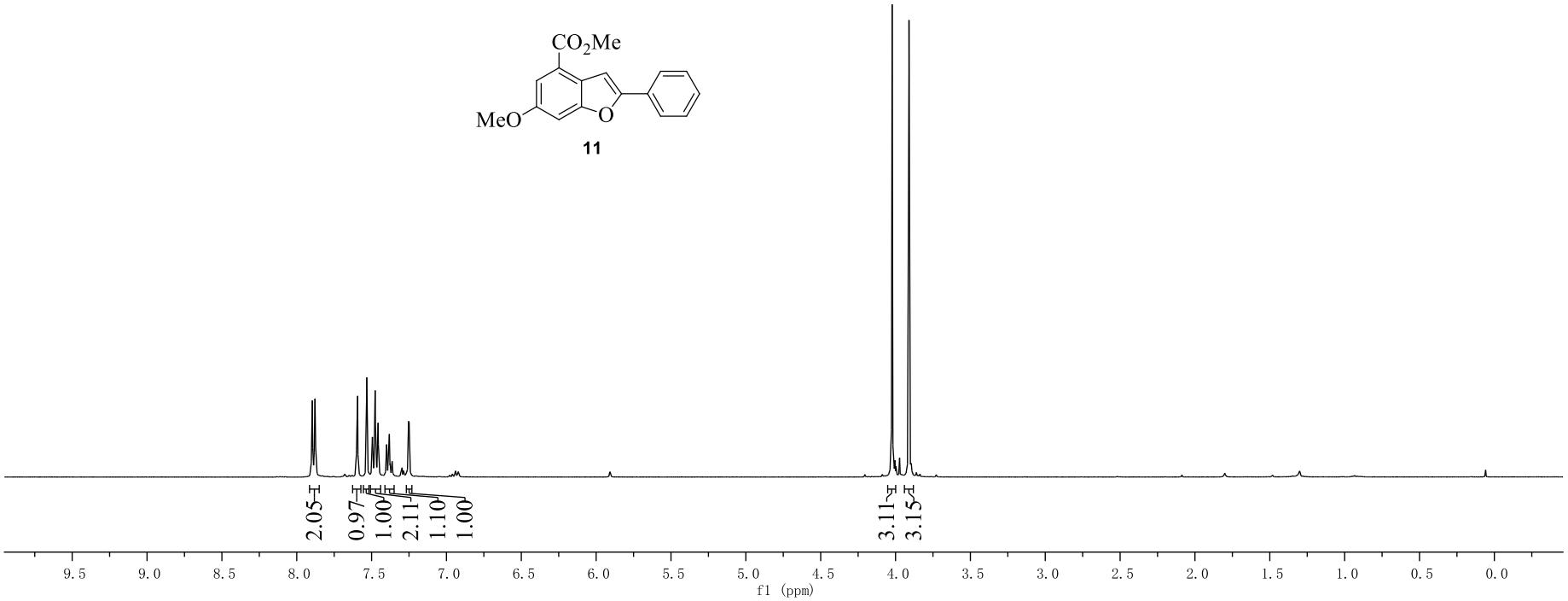

166.82
160.07
156.98
156.74
155.98
126.35
124.01
123.04
121.71
114.27
112.46
101.42
100.58
77.42
77.10
76.78
56.01
55.33
52.02
CO2Me
MeO
O
OMe
10
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)

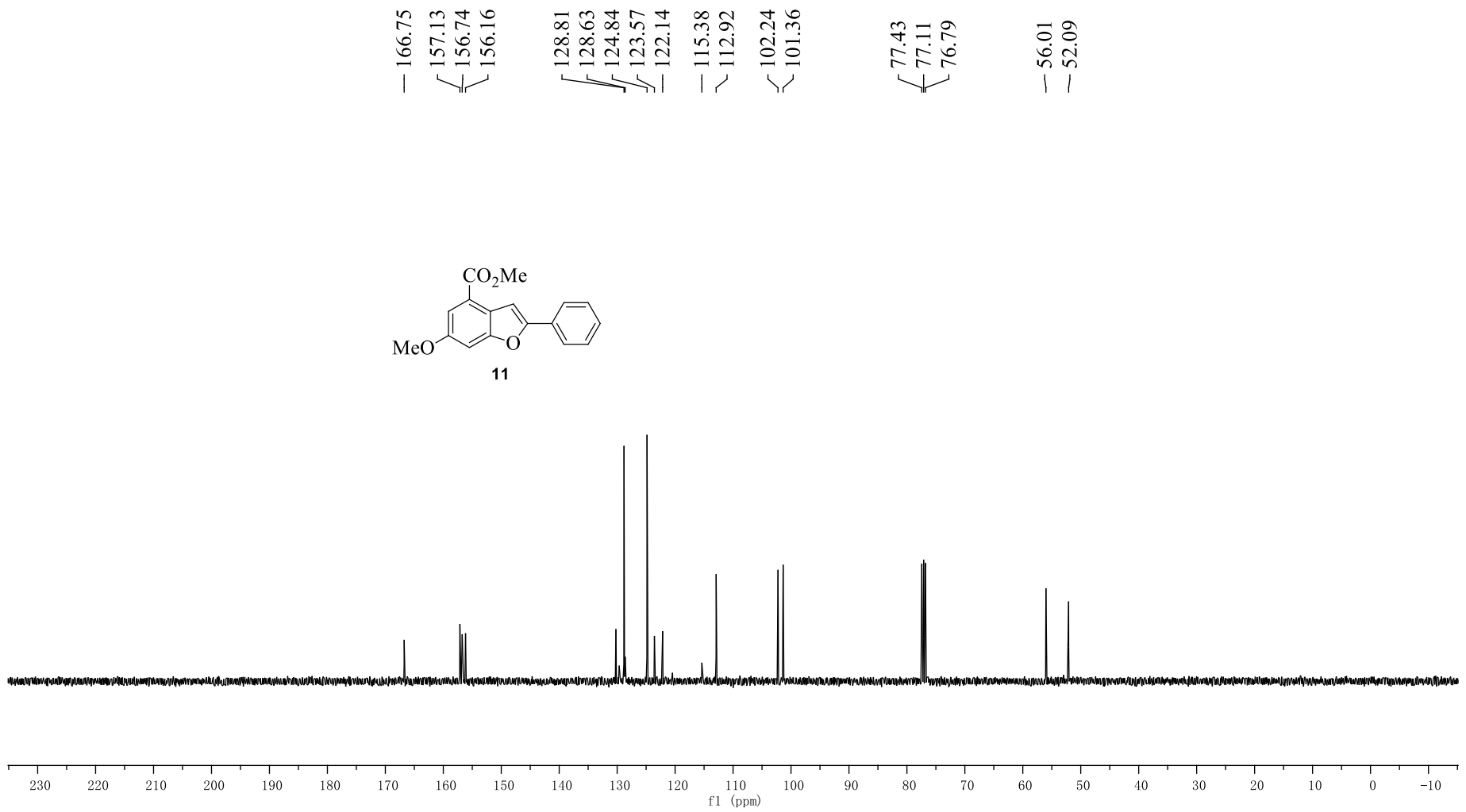

CO2Me
Br
MeO
O
OMe
8
2.07
1.00
1.06
2.12
3.11
3.23
3.12
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

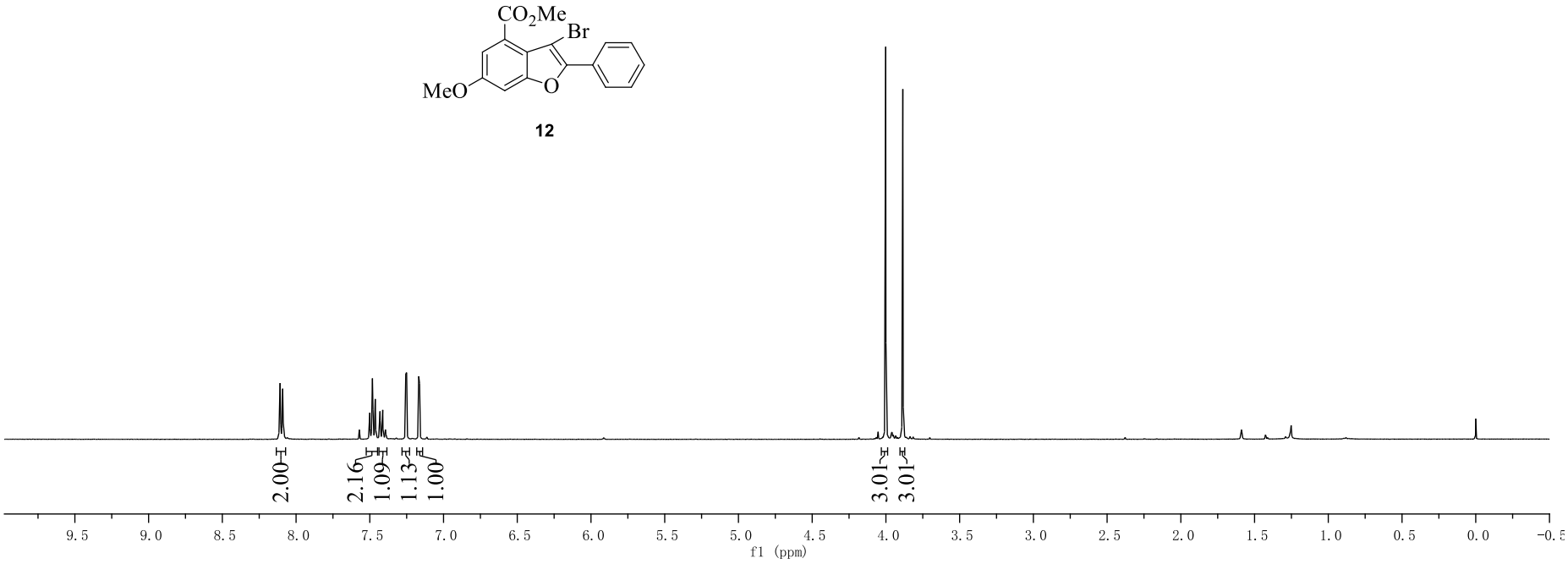

167.04
160.26
157.41
154.71
152.02
128.87
125.36
121.95
120.03
113.96
113.14
99.29
90.78
77.40
77.08
76.76
56.00
55.36
52.21
CO2Me
Br
OMe
MeO
O
8
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

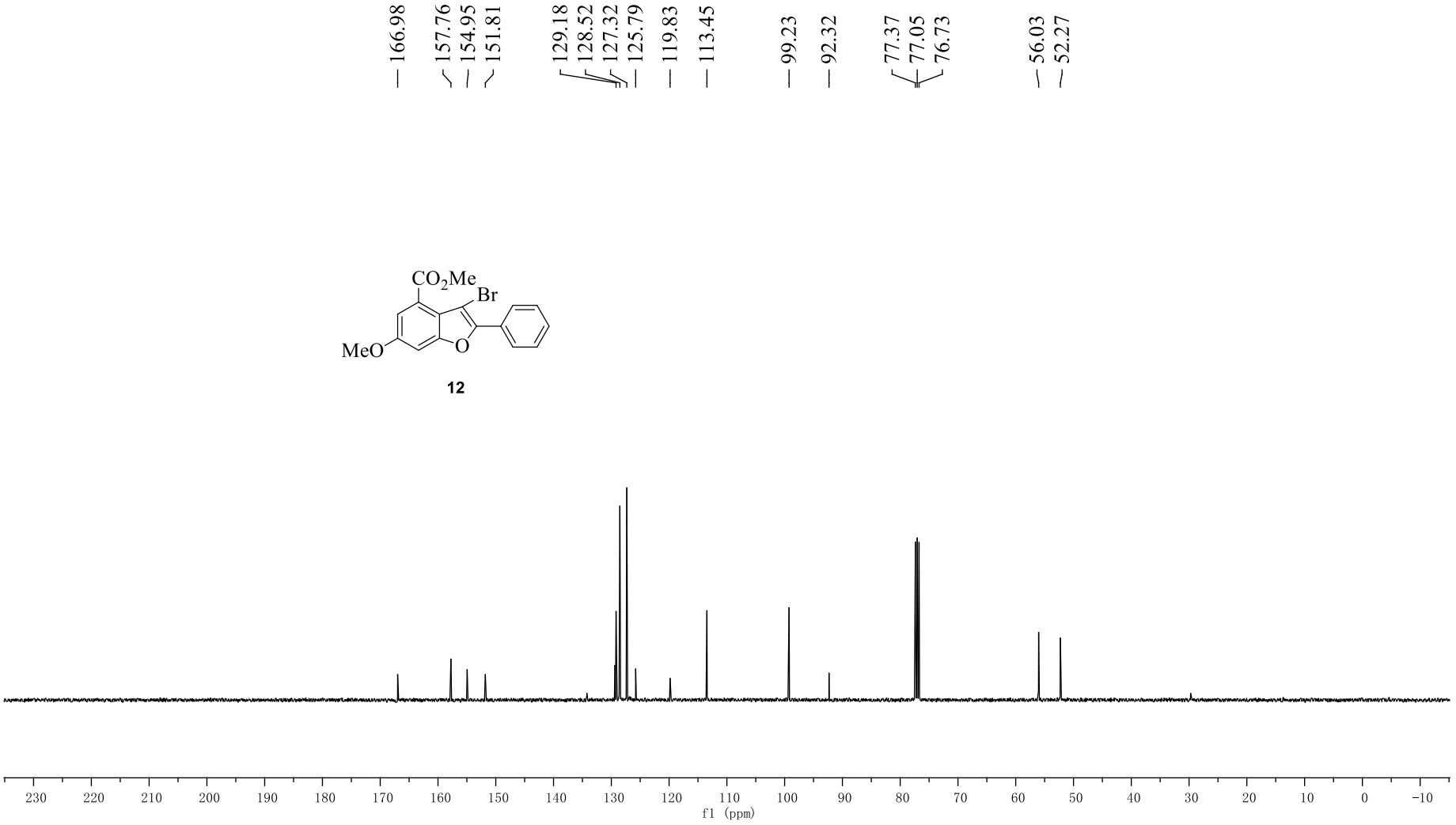

MeO
MeO
O
OMe
OMe
MeO
O
2
2.06
0.97
1.00
2.10
3.00
3.18
3.11
6.07
3.01
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

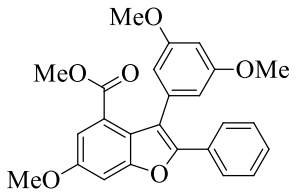

167.95
161.14
157.11
155.28
151.68
136.63
125.24
121.63
112.36
107.52
100.11
99.56
77.44
77.12
76.81
56.01
55.47
55.23
51.46
MeO
MeO
O
OMe
OMe
MeO
O
2
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)


CO2Me
MeO
O
11
2.05
0.97
1.00
2.11
1.10
1.00
3.11
3.15
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

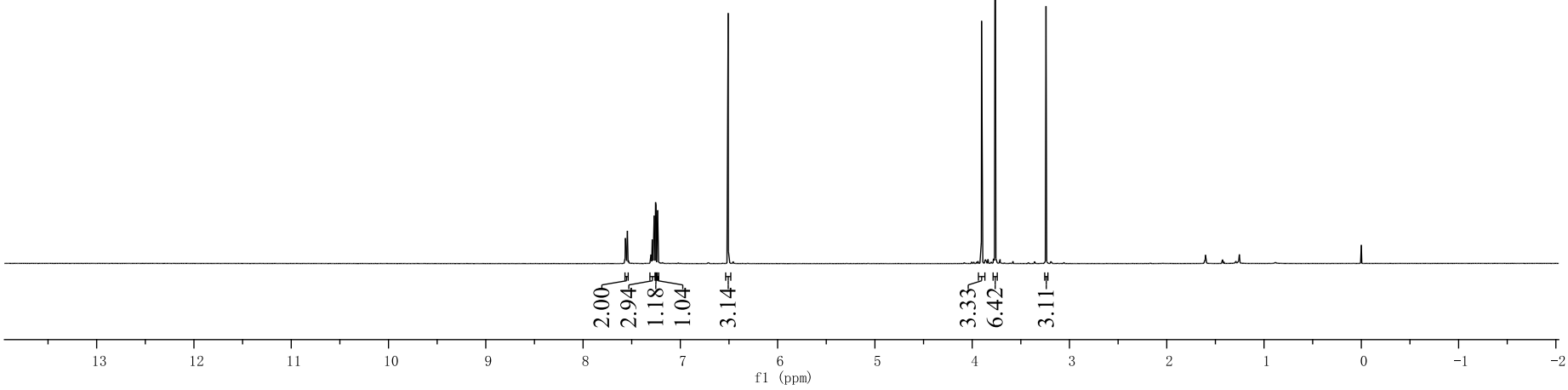

166.75
157.13
156.74
156.16
128.81
128.63
124.84
123.57
122.14
115.38
112.92
102.24
101.36
77.43
77.11
76.79
56.01
52.09
CO2Me
MeO
O
11
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

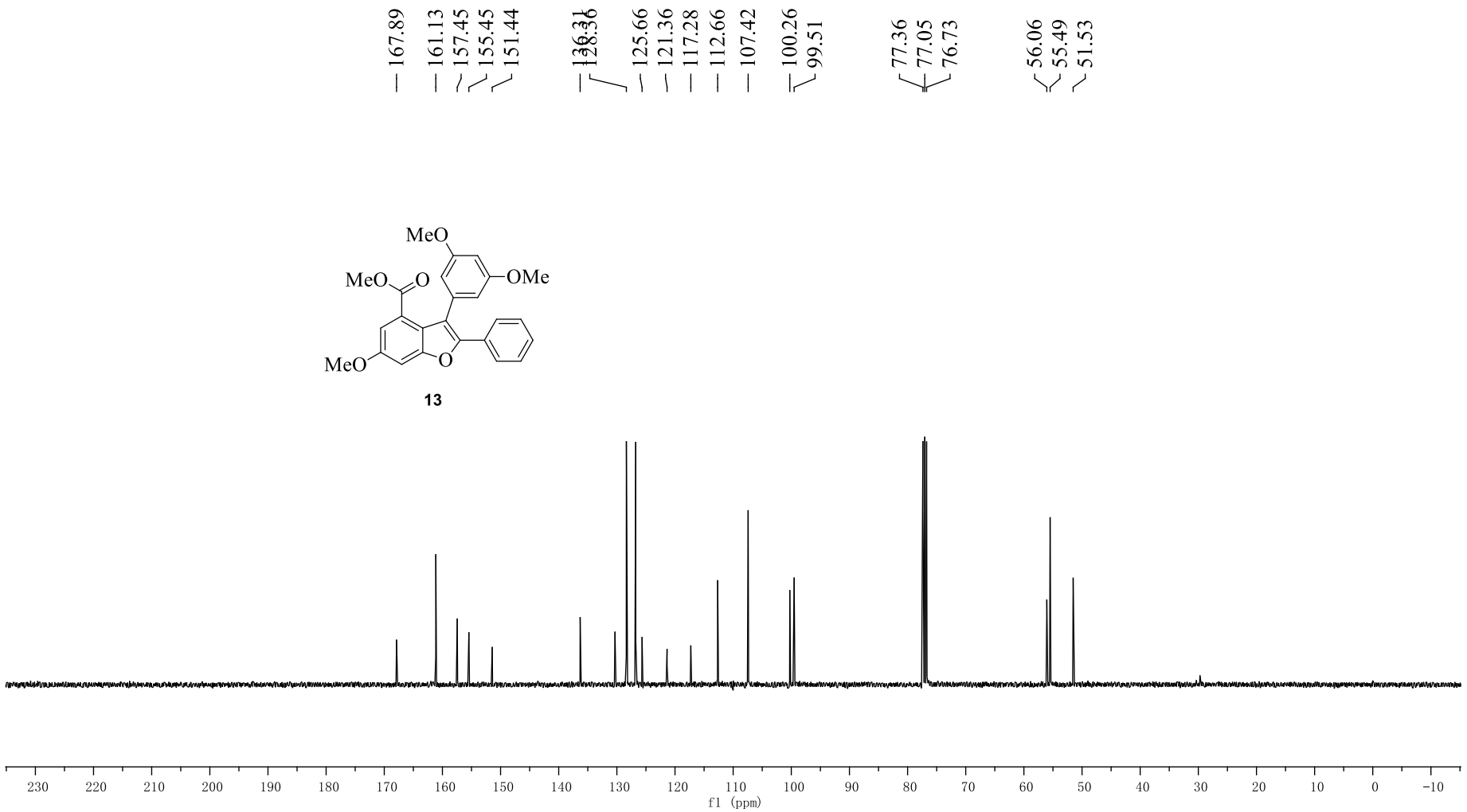

CO2Me
Br
MeO
O
12
2.00
2.16
1.09
1.13
1.00
3.01
3.01
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

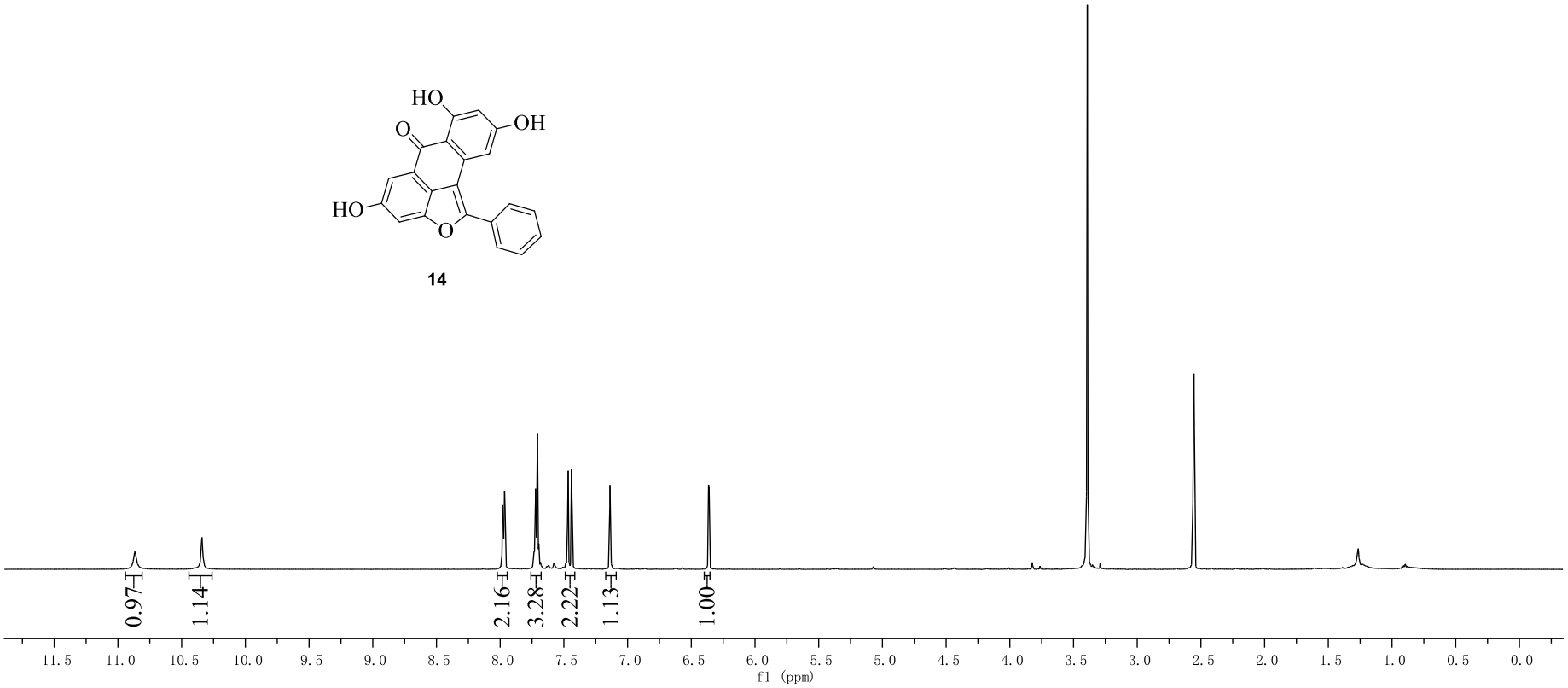

166.98
157.76
154.95
151.81
129.18
128.52
127.32
125.79
119.83
113.45
99.23
92.32
77.37
77.05
76.73
56.03
52.27
CO2Me
Br
MeO
O
12
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)

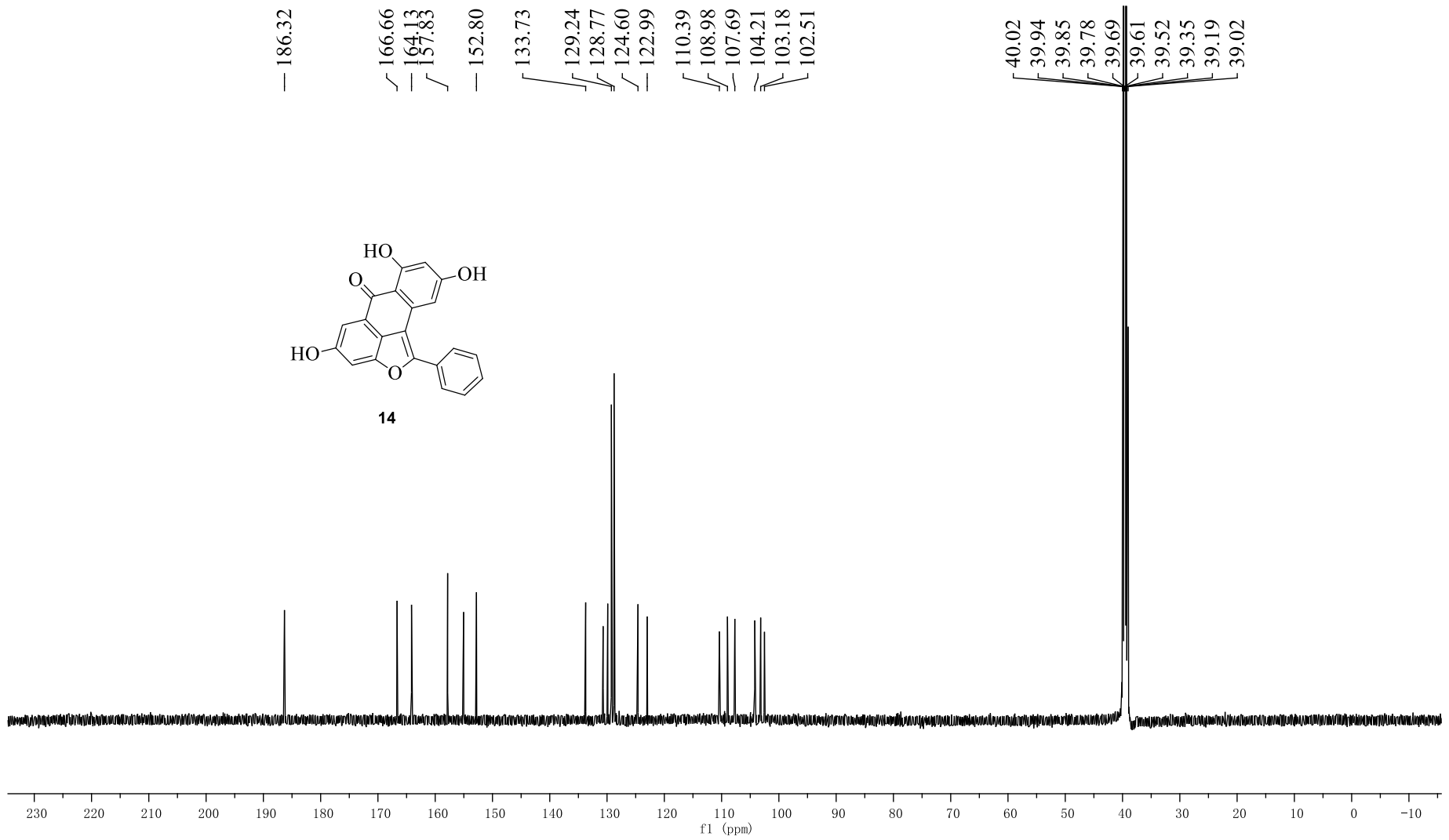

MeO
MeO
O
OMe
MeO
O

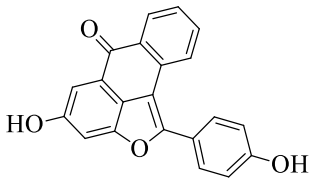
13


2.00
2.94
1.18
1.04
3.14
3.33
6.42
3.11
13
12
11
10
9
8
7
6
5
4
3
2
1
0
−1
−2
f1 (ppm)


167.89
161.13
157.45
155.45
151.44
136.31
128.36
125.66
121.36
117.28
112.66
107.42
100.26
99.51
77.36
77.05
76.73
56.06
55.49
51.53
MeO
MeO
O
OMe
MeO
O
13
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

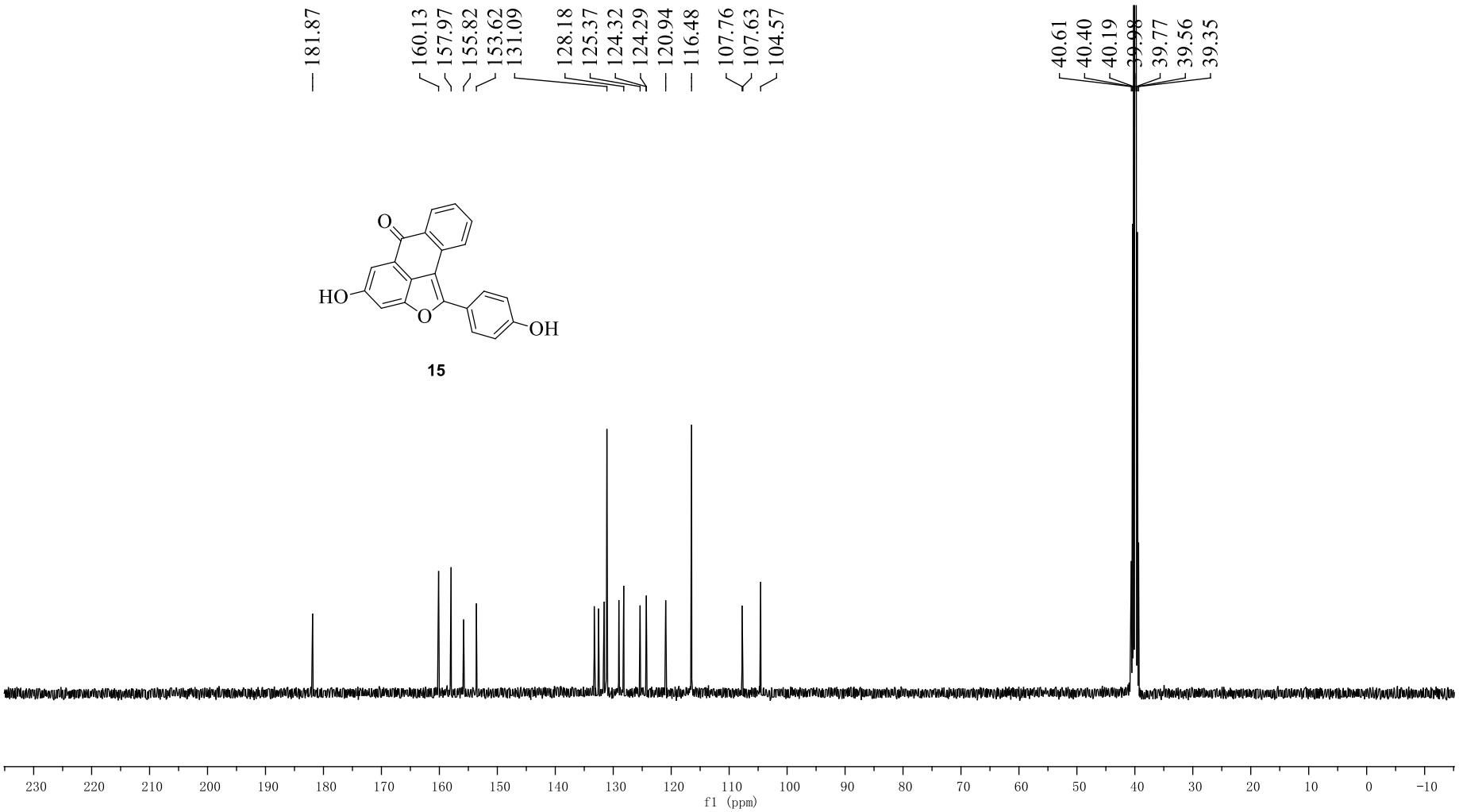

HO
O
OH
HO
O
14
0.97
1.14
2.16
3.28
2.22
1.13
1.00
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

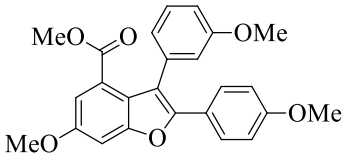

186.32
166.66
164.13
157.83
152.80
133.73
129.24
128.77
124.60
122.99
110.39
108.98
107.69
104.21
103.18
102.51
40.02
39.94
39.85
39.78
39.69
39.61
39.52
39.35
39.19
39.02
HO
O
OH
HO
O
14
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
HO
O
OH

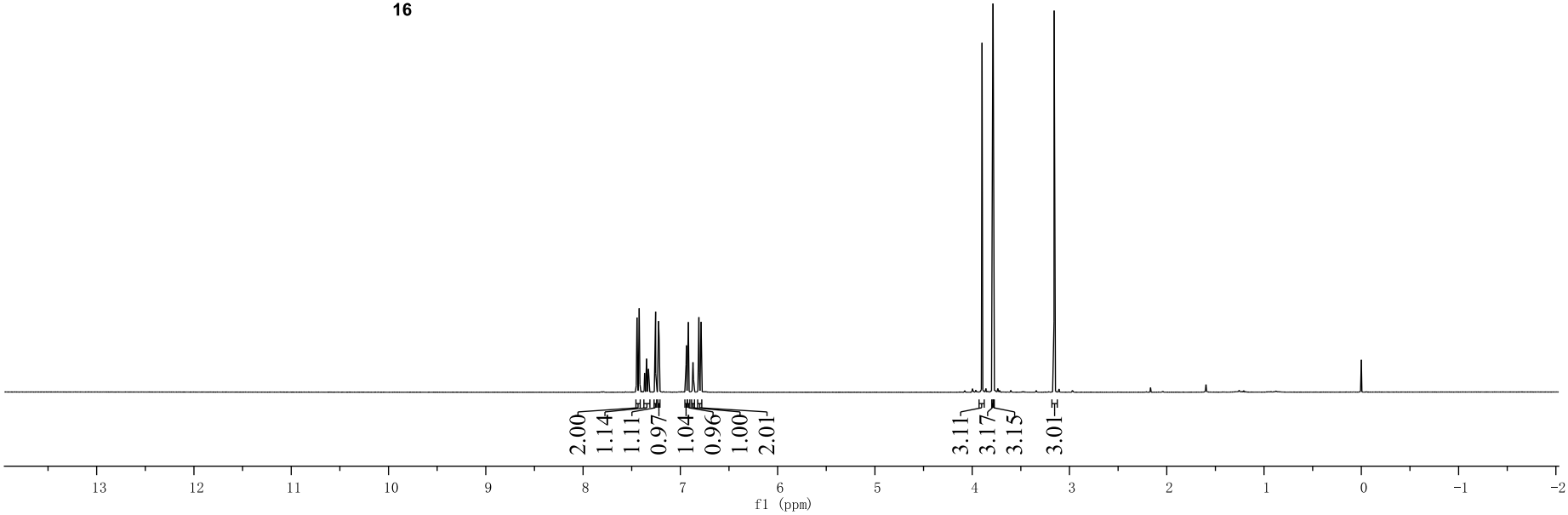
15

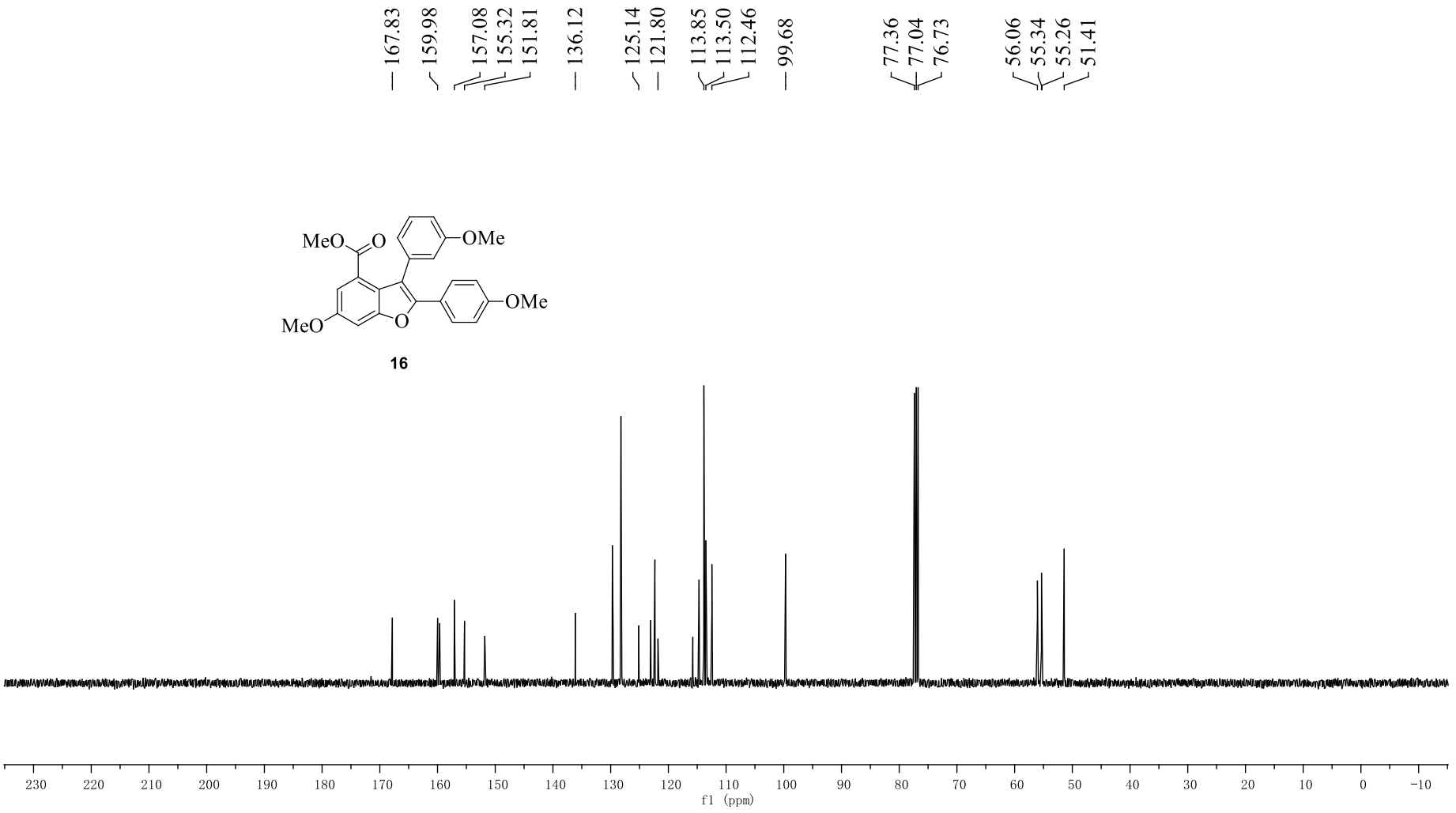
1.00
1.05
1.00
1.06
2.04
1.06
2.21
2.06
13
12
11
10
9
8
7
6
5
4
3
2
1
0
−1
f1 (ppm)

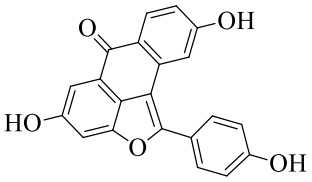

181.87
160.13
157.97
155.82
153.62
131.09
128.18
125.37
124.32
124.29
120.94
116.48
107.76
107.63
104.57
40.61
40.40
40.19
39.98
39.77
39.56
39.35
O
HO
O
OH
15
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)


MeO
O
OMe
MeO
O
OMe

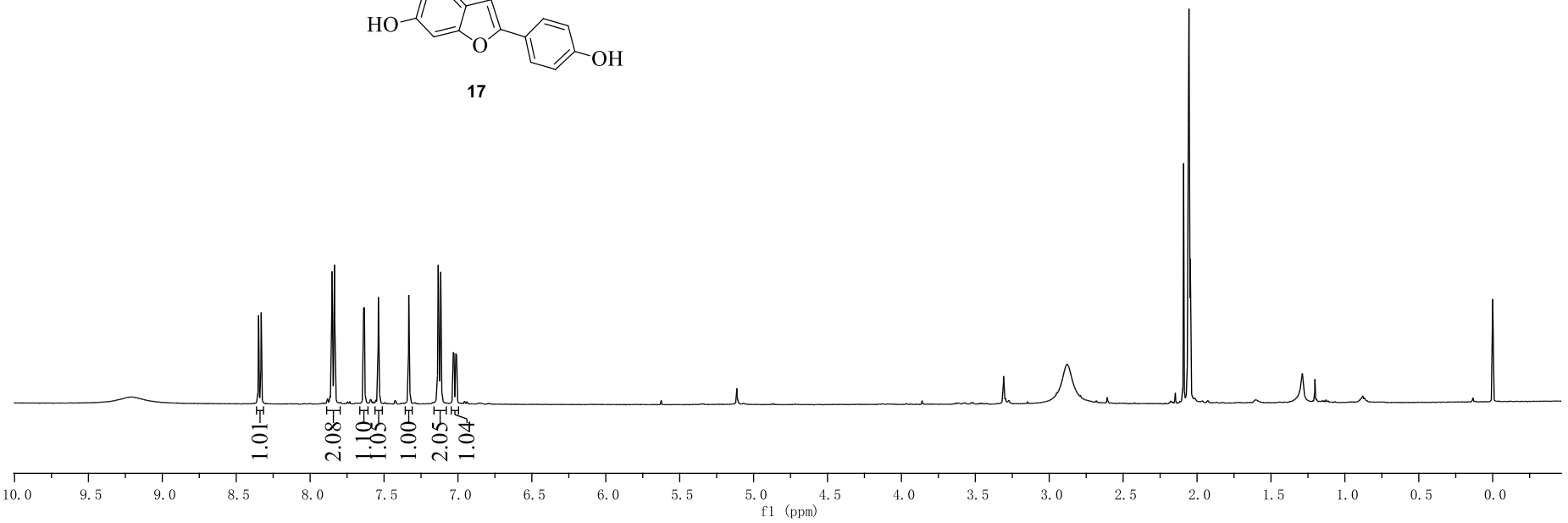
16

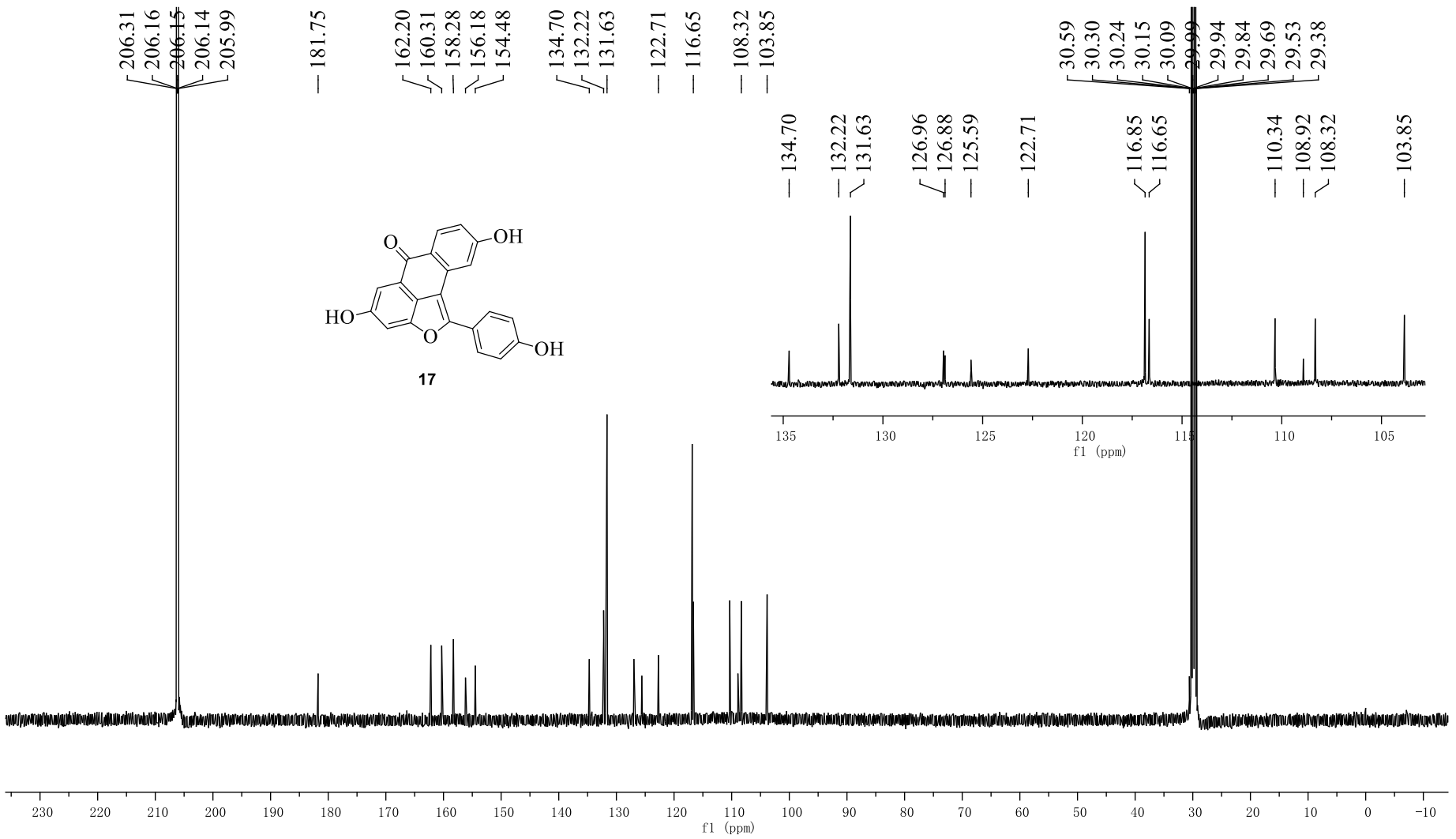

2.00
1.14
1.11
0.97
1.04
0.96
1.00
2.01
3.11
3.17
3.15
3.01
13
12
11
10
9
8
7
6
5
4
3
2
1
0
−1
−2
f1 (ppm)

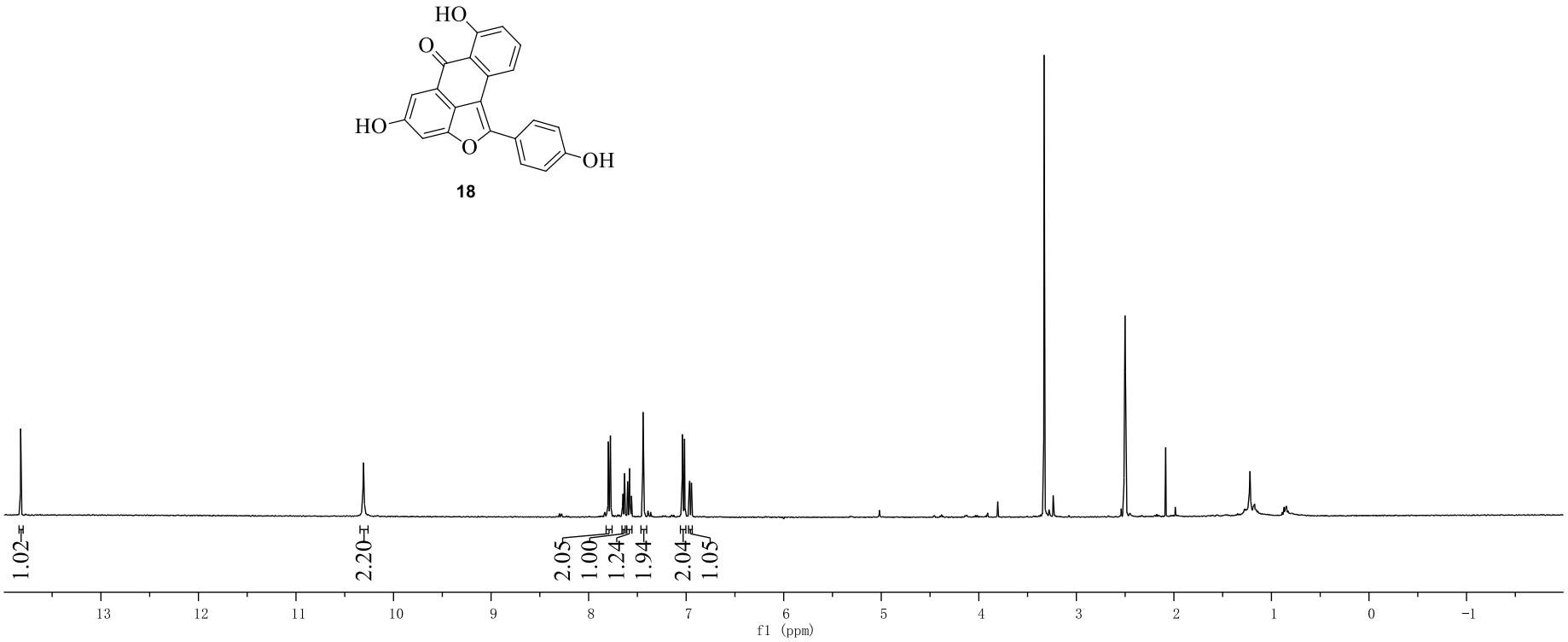

167.83
159.98
157.08
155.32
151.81
136.12
125.14
121.80
113.85
113.50
112.46
99.68
77.36
77.04
76.73
56.06
55.34
55.26
51.41
MeO
O
OMe
OMe
MeO
O
16
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

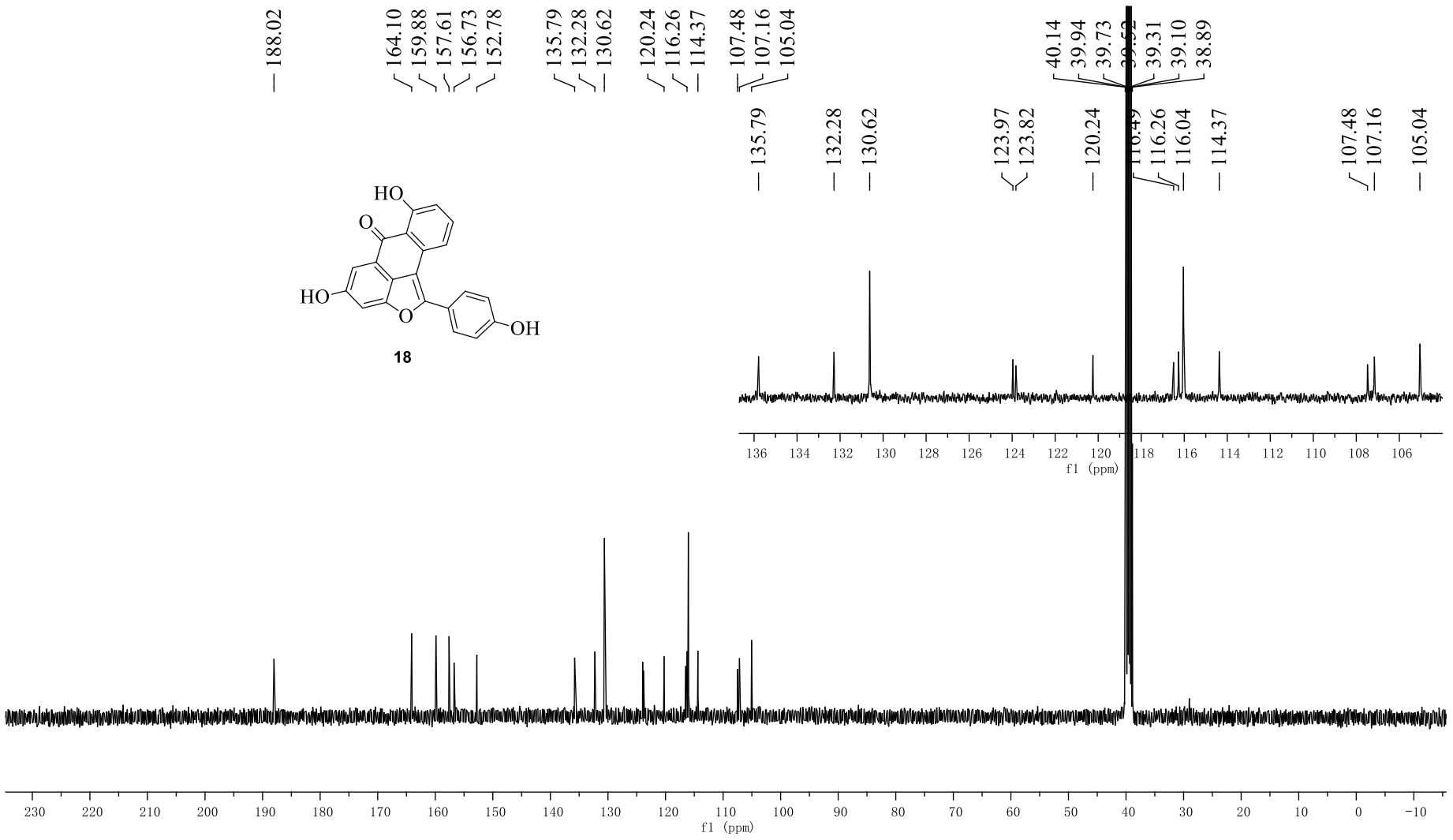

O
OH
HO
O
OH

17


1.01
2.08
1.10
1.05
1.00
2.05
1.04
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


206.31
206.16
206.15
206.14
205.99
181.75
162.20
160.31
158.28
156.18
154.48
134.70
132.22
131.63
122.71
116.65
108.32
103.85
30.59
30.30
30.24
30.15
30.09
29.99
29.94
29.84
29.69
29.53
29.38
O
OH
HO
O
OH
17
f1 (ppm)
f1 (ppm)


HO
O
HO
O
OH
18
1.02
2.20
2.05
1.00
1.24
1.94
2.04
1.05
13
12
11
10
9
8
7
6
5
4
3
2
1
0
−1
f1 (ppm)


188.02
164.10
159.88
157.61
156.73
152.78
135.79
132.28
130.62
120.24
116.26
114.37
107.48
107.16
105.04
40.14
39.94
39.73
39.52
39.31
39.10
38.89
HO
O
HO
O
OH
18
f1 (ppm)
f1 (ppm)