Cobalt(II)-Catalyzed Regioselective C–H Halogenation of Anilides

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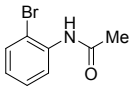
1.General information

All compounds are characterized by ^{1}H NMR, ^{13}C NMR and MS. Analytical thin-layer chromatography is performed on glass plates precoated with silica gel impregnated with a fluorescent indicator (254 nm), and the plates are visualized by exposure to ultraviolet light. ^{1}H NMR and ^{13}C NMR spectra are recorded on an AVANCE 500 Bruker spectrometer operating at 500 MHz and 125 MHz in $CDCl_3$, respectively, and chemical shifts are reported in ppm.GC analyses are performed on an Agilent 7890A instrument (Column: Agilent 19091J-413:30 m × 320 μm × 0.25 μm, H, FID detection). GC-MS data was recorded on a 5975C Mass Selective Detector,coupled with a 7890A Gas Chromatograph (Agilent Technologies).

2.General procedure

General procedure for the synthesis of ortho-bromination product : To a mixture of acetanilide (0.5 mmol) **1a**, $Co(acac)_2$ (10%mmol), additives Ag_2O (20% mmol), additives TFA (25% mmol), and solvent (DCE =1.5ml) in a reaction tube was added N-bromosuccinimide (NBS) (1.2 equiv.). The reaction mixture was stirred at 60°C for 16h in air. The reaction mixture was extracted with ethyl acetate (15 mL × 3). The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The residue was purified by column chromatography on silica gel to afford the desired products **3**.

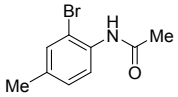
3.Characterization data



Formula: C_8H_8BrNO

Mass: 213

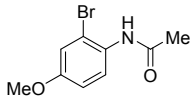
N-(2-bromophenyl)acetamide (3a): The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 4:1) to give **3a** as white solid (91.59mg, 86%). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.33 (d, *J* = 8.0 Hz, 1H), 7.61 (s, 1H), 7.53 (d, *J* = 7.8 Hz, 1H), 7.31 (t, *J* = 7.8 Hz, 1H), 6.97 (t, *J* = 7.5 Hz, 1H), 2.24 (s, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 167.3, 134.7, 131.2, 127.4, 124.2, 121.0, 112.2, 23.9. GC-MS (EI) *m/z*: 213.



Formula: $C_9H_{10}BrNO$

Mass: 227

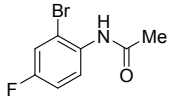
N-(2-bromo-4-methylphenyl)acetamide (3b): The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 4:1) to give **3b** as white solid (96.48mg, 85%). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.15 (d, *J* = 8.3 Hz, 1H), 7.52 (s, 1H), 7.35 (s, 1H), 7.10 (d, *J* = 8.3 Hz, 1H), 2.29 (s, 3H), 2.22 (s, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 167.2, 134.3, 132.2, 131.5, 128.0, 121.0, 112.3, 23.8, 19.6. GC-MS (EI) *m/z*: 227.



Formula: $C_9H_{10}BrNO_2$

Mass: 243

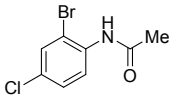
N-(2-bromo-4-methoxyphenyl)acetamide (3c): The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 4:1) to give **3c** as white solid (96.20mg, 80%). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.10 (d, *J* = 9.1 Hz, 1H), 7.38 (s, 1H), 7.08 (d, *J* = 2.7 Hz, 1H), 6.86 (dd, *J* = 9.0, 2.8 Hz, 1H), 3.77 (s, 3H), 2.21 (s, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 167.2, 155.5, 128.1, 122.6, 116.5, 113.6, 112.9, 54.8, 23.6. GC-MS (EI) *m/z*: 243.



Formula: C_8H_7BrFNO

Mass: 231

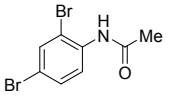
N-(2-bromo-4-fluorophenyl)acetamide (3d): The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 4:1) to give **3d** as white solid (64.68mg, 56%). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.27 (dd, *J* = 9.2, 5.6 Hz, 1H), 7.47 (s, 1H), 7.29 (dd, *J* = 7.8, 2.9 Hz, 1H), 7.05 (ddd, *J* = 9.1, 7.8, 2.9 Hz, 1H), 2.23 (s, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 167.2, 131.2, 122.1, 118.4, 118.2, 114.4, 114.2, 112.4, 23.7. GC-MS (EI) *m/z*: 231.



Formula: $C_8H_7BrClNO$

Mass: 247

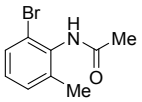
N-(2-bromo-4-chlorophenyl)acetamide (3e): The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 4:1) to give **3e** as white solid (97.57mg, 79%). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.30 (d, *J* = 8.8 Hz, 1H), 7.55 (s, 1H), 7.53 (d, *J* = 2.2 Hz, 1H), 7.28 (dd, *J* = 8.9, 2.3 Hz, 1H), 2.23 (s, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 167.2, 133.5, 130.7, 128.4, 127.5, 121.5, 112.3, 23.9. GC-MS (EI) *m/z*: 247.



Formula: $C_8H_7Br_2NO$

Mass: 293

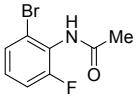
N-(2,4-dibromophenyl)acetamide (3f): The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 4:1) to give **3f** as white solid (109.88mg, 75%). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.25 (d, *J* = 8.8 Hz, 1H), 7.67 (d, *J* = 2.1 Hz, 1H), 7.56 (s, 1H), 7.42 (dd, *J* = 8.9, 2.1 Hz, 1H), 2.23 (s, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 167.2, 134.0, 133.4, 130.5, 121.8, 115.7, 112.5, 23.9. GC-MS (EI) *m/z*: 293.



Formula: $C_9H_{10}BrNO$

Mass: 227

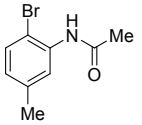
N-(2-bromo-6-methylphenyl)acetamide (3g): The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 4:1) to give **3g** as white solid (91.94mg, 81%). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.44 (d, *J* = 8.0 Hz, 1H), 7.19 (d, *J* = 7.6 Hz, 1H), 7.06 (t, *J* = 7.8 Hz, 1H), 6.96 (s, 1H), 2.30 (s, 3H), 2.24 (s, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 167.4, 137.5, 133.0, 129.2, 129.0, 127.5, 121.1, 22.4, 18.3. GC-MS (EI) *m/z*: 227.



Formula: C_8H_7BrFNO

Mass: 231

N-(2-bromo-6-fluorophenyl)acetamide (3h): The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 4:1) to give **3h** as white solid (84.68mg, 73%). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.39 (d, *J* = 6.4 Hz, 1H), 7.11 (q, *J* = 9.2, 8.4 Hz, 2H), 6.97 (s, 1H), 2.23 (s, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 167.2, 158.3,156.3, 127.8, 127.2, 123.4, 121.2, 114.7, 22.2. GC-MS (EI) *m/z*: 231.

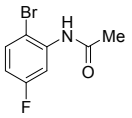


Formula: $C_9H_{10}BrNO$

Mass: 227

N-(2-bromo-5-methylphenyl)acetamide (3i): The crude product was purified by

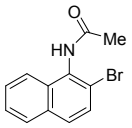
column chromatography on silica gel (petroleum ether/ethyl acetate = 4:1) to give **3i** as white solid (87.39mg, 77%). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.51 (s, 1H), 7.42 (dd, *J* = 5.6, 3.0 Hz, 2H), 7.19 (dd, *J* = 8.6, 2.6 Hz, 1H), 2.34 (s, 3H), 2.15 (s, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 167.5, 137.6, 136.1, 131.6, 121.2, 118.5, 117.9, 23.6, 22.1. GC-MS (EI) *m/z*: 227.



Formula: C_8H_7BrFNO

Mass: 231

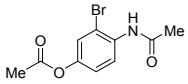
N-(2-bromo-5-methylphenyl)acetamide (3j): The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 4:1) to give **3j** as white solid (80.59mg, 71%). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.24 (dd, *J* = 11.2, 2.9 Hz, 1H), 7.64 (s, 1H), 7.46 (dd, *J* = 8.9, 5.8 Hz, 1H), 6.72 (ddd, *J* = 8.8, 7.5, 3.0 Hz, 1H), 2.24 (s, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 167.3, 162.2, 160.2, 135.9, 131.7, 111.1, 108.0, 105.8, 24.0. GC-MS (EI) *m/z*: 231.



Formula: $C_{12}H_{10}BrNO$

Mass: 263

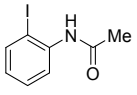
N-(2-bromonaphthalen-1-yl)acetamide (3k): The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 4:1) to give **3k** as white solid (52.60mg, 40%). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.89 – 7.80 (m, 2H), 7.66 (q, *J* = 8.8 Hz, 2H), 7.56 – 7.48 (m, 2H), 7.20 (s, 1H), 2.36 (s, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 168.3, 130.5, 128.9, 128.3, 128.2, 127.4, 127.2, 126.4, 126.1, 125.6, 122.8, 22.5. GC-MS (EI) *m/z*: 263.



Formula: $C_{10}H_{10}BrNO_3$

Mass: 271

4-acetamido-3-bromophenyl acetate (3m): The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 4:1) to give **3m** as white solid (104.34mg, 77%). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.38 (d, *J* = 9.0 Hz, 1H), 7.58 (s, 1H), 7.37 (d, *J* = 2.6 Hz, 1H), 7.09 (dd, *J* = 9.0, 2.6 Hz, 1H), 2.32 (s, 3H), 2.27 (s, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 168.1, 167.1, 145.5, 132.6, 124.4, 121.2, 120.6, 111.9, 23.8, 20.0. GC-MS (EI) *m/z*: 271.

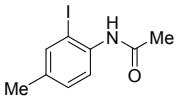


Formula: C_8H_8INO

Mass: 261

N-(2-iodophenyl)acetamide (4a): The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 4:1) to give **4a** as white solid (111.78mg, 85%). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.20 (d, *J* = 8.0 Hz, 1H), 7.77 (d, *J* = 7.8 Hz, 1H), 7.42 (s, 1H), 7.34 (t, *J* = 7.7 Hz, 1H), 6.84 (t, *J* = 7.4 Hz, 1H), 2.24 (s, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 167.3, 137.8, 137.3, 128.3, 125.0,

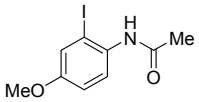
121.1, 89.0, 23.9. GC-MS (EI) *m/z*: 261.



Formula: $C_9H_{10}INO$

Mass: 275

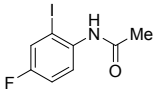
N-(2-iodo-4-methylphenyl)acetamide (4b): The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 4:1) to give **4b** as white solid (108.42mg, 79%). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.02 (d, *J* = 8.3 Hz, 1H), 7.60 (s, 1H), 7.33 (s, 1H), 7.14 (d, *J* = 8.1 Hz, 1H), 2.28 (s, 3H), 2.22 (s, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 167.2, 138.0, 135.1, 134.8, 129.0, 121.1, 89.2, 23.8, 19.4. GC-MS (EI) *m/z*: 275.



Formula: $C_9H_{10}INO_2$

Mass: 291

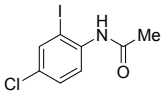
N-(2-iodo-4-methoxyphenyl)acetamide (4c): The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 4:1) to give **4c** as white solid (119.31mg, 82%). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.93 (d, *J* = 9.0 Hz, 1H), 7.31 (d, *J* = 2.7 Hz, 1H), 7.20 (s, 1H), 6.91 (dd, *J* = 9.0, 2.8 Hz, 1H), 3.77 (s, 3H), 2.21 (s, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 167.2, 155.8, 130.7, 122.8, 122.7, 113.8, 90.5, 54.7, 23.5. GC-MS (EI) *m/z*: 291.



Formula: C_8H_7FINO

Mass: 279

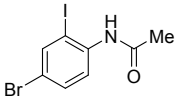
N-(4-fluoro-2-iodophenyl)acetamide (4d): The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 4:1) to give **4d** as white solid (71.28mg, 51%). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.11 (dd, *J* = 9.1, 5.5 Hz, 1H), 7.50 (dd, *J* = 7.6, 2.9 Hz, 1H), 7.29 (s, 1H), 7.09 (ddd, *J* = 9.1, 7.7, 2.9 Hz, 1H), 2.24 (s, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 167.2, 133.8, 124.5, 124.3, 122.2, 122.1, 115.2, 115.0, 23.7. GC-MS (EI) *m/z*: 279.



Formula: C_8H_7ClINO

Mass: 295

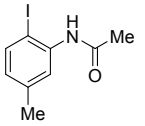
N-(4-chloro-2-iodophenyl)acetamide (4e): The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 4:1) to give **4e** as white solid (112.10mg, 76%). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.16 (d, *J* = 8.7 Hz, 1H), 7.79 – 7.71 (m, 1H), 7.39 (s, 1H), 7.32 (dd, *J* = 8.8, 2.2 Hz, 1H), 2.24 (s, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 167.2, 136.9, 136.1, 128.9, 128.3, 121.4, 88.6, 23.8. GC-MS (EI) *m/z*: 295.



Formula: C_8H_7BrINO

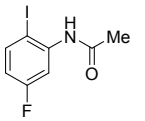
Mass: 339

N-(4-bromo-2-iodophenyl)acetamide (4f): The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 4:1) to give **4f** as white solid (115.26mg, 68%). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.12 (d, *J* = 8.8 Hz, 1H), 7.90 (d, *J* = 2.3 Hz, 1H), 7.45 (dd, *J* = 8.8, 2.3 Hz, 1H), 7.39 (s, 1H), 2.24 (s, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 167.2, 139.5, 136.5, 131.3, 121.7, 116.4, 89.0, 23.9. GC-MS (EI) *m/z*: 339.



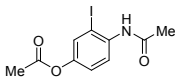
Formula: $C_9H_{10}INO$
Mass: 275

N-(2-iodo-5-methylphenyl)acetamide (4g): The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 4:1) to give **4g** as white solid (75.63mg, 55%). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.04 (s, 1H), 7.62 (d, *J* = 8.1 Hz, 1H), 7.36 (s, 1H), 6.68 (d, *J* = 8.2 Hz, 1H), 2.32 (s, 3H), 2.23 (s, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 167.2, 138.7, 137.3, 136.9, 126.1, 121.8, 85.0, 23.9, 20.3. GC-MS (EI) *m/z*: 275.



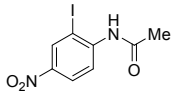
Formula: C_8H_7FINO
Mass: 279

N-(5-fluoro-2-iodophenyl)acetamide (4h): The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 4:1) to give **4h** as white solid (80.91mg, 58%). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.15 (dd, *J* = 11.4, 3.0 Hz, 1H), 7.70 (dd, *J* = 8.8, 6.0 Hz, 1H), 7.47 (s, 1H), 6.69 – 6.58 (m, 1H), 2.25 (s, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 167.3, 163.2, 161.3, 138.5, 138.1, 112.1, 108.1, 80.8, 24.0. GC-MS (EI) *m/z*: 279.



Formula: $C_{10}H_{10}INO_3$
Mass: 319

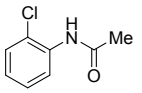
4-acetamido-3-iodophenyl acetate (4k): The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 4:1) to give **4k** as white solid (113.25mg, 71%). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.24 (d, *J* = 9.0 Hz, 1H), 7.58 (d, *J* = 2.5 Hz, 1H), 7.41 (s, 1H), 7.14 (dd, *J* = 9.0, 2.6 Hz, 1H), 2.31 (s, 3H), 2.27 (s, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 168.2, 167.2, 145.9, 135.2, 130.6, 121.4, 121.2, 99.0, 23.6, 20.0. GC-MS (EI) *m/z*: 319.



Formula: $C_8H_7IN_2O_3$
Mass: 306

N-(2-iodo-4-nitrophenyl)acetamide (4m): The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 4:1) to give **4m** as white solid (91.8mg, 60%). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.69 (d, *J* = 2.5 Hz, 1H), 8.58 (d, *J* = 9.1 Hz, 1H), 8.27 (dd, *J* = 9.2, 2.5 Hz, 1H), 7.77 (s, 1H), 2.35 (s, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 167.4, 142.8, 142.5, 133.2, 124.0, 118.7, 86.3, 24.2.

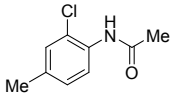
GC-MS (EI) *m/z*: 306.



Formula: C_8H_8ClNO

Mass: 169

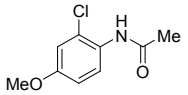
N-(2-chlorophenyl)acetamide (5a): The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 4:1) to give **5a** as white solid (60.84mg, 72%). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.33 (d, *J* = 8.1 Hz, 1H), 7.66 (s, 1H), 7.34 (d, *J* = 8.0 Hz, 1H), 7.25 (t, *J* = 7.6 Hz, 1H), 7.02 (t, *J* = 7.5 Hz, 1H), 2.22 (s, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 167.3, 133.6, 128.0, 126.7, 123.7, 121.7, 120.8, 23.9. GC-MS (EI) *m/z*: 169.



Formula: $C_9H_{10}ClNO$

Mass: 183

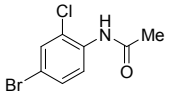
N-(2-chloro-4-methylphenyl)acetamide (5b): The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 4:1) to give **5b** as white solid (59.48mg, 65%).^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.19 (d, *J* = 8.4 Hz, 1H), 7.52 (s, 1H), 7.18 (s, 1H), 7.07 (d, *J* = 8.3 Hz, 1H), 2.29 (s, 3H), 2.22 (s, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 167.1, 133.8, 131.0, 128.3, 127.4, 121.5, 120.6, 23.8, 19.7. GC-MS (EI) *m/z*: 183.



Formula: $C_9H_{10}ClNO_2$

Mass: 199

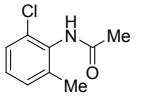
N-(2-chloro-4-methoxyphenyl)acetamide (5c): The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 4:1) to give **5c** as white solid (58.71mg, 59%). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.14 (d, *J* = 9.1 Hz, 1H), 7.40 (s, 1H), 6.92 (d, *J* = 2.8 Hz, 1H), 6.82 (dd, *J* = 9.1, 2.8 Hz, 1H), 3.78 (s, 3H), 2.21 (s, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 167.1, 155.3, 126.9, 123.1, 122.4, 113.5, 112.2, 54.7, 23.6. GC-MS (EI) *m/z*: 199.



Formula: $C_8H_7BrClNO$

Mass: 247

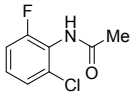
N-(4-bromo-2-chlorophenyl)acetamide (5d): The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 4:1) to give **5d** as white solid (79.04mg, 64%). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.29 (d, *J* = 8.8 Hz, 1H), 7.56 (s, 1H), 7.51 (d, *J* = 2.1 Hz, 1H), 7.38 (dd, *J* = 8.9, 2.1 Hz, 1H), 2.24 (s, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 167.2, 132.9, 130.4, 129.9, 122.2, 121.6, 115.2, 23.9. GC-MS (EI) *m/z*: 247.



Formula: $C_9H_{10}ClNO$

Mass: 183

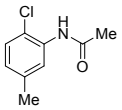
N-(2-chloro-6-methylphenyl)acetamide (5e): The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 4:1) to give **5e** as white solid (57.65mg, 66%). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.28 – 7.24 (m, 1H), 7.17 – 7.08 (m, 2H), 7.03 (s, 1H), 2.27 (s, 3H), 2.23 (s, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 167.6, 137.3, 131.7, 130.3, 128.3, 127.0, 126.0, 22.3, 18.0. GC-MS (EI) *m/z*: 183.



Formula: C_8H_7ClFNO

Mass: 187

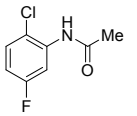
N-(2-chloro-6-fluorophenyl)acetamide (5f): The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 4:1) to give **5f** as white solid (66.39mg, 71%). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.40 (d, *J* = 6.3 Hz, 1H), 7.38 (s, 1H), 7.05 – 6.96 (m, 2H), 2.22 (s, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 167.2, 150.6, 148.6, 128.8, 126.3, 122.9, 120.5, 114.5, 23.7. GC-MS (EI) *m/z*: 187.



Formula: $C_9H_{10}ClNO$

Mass: 183

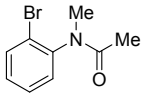
N-(2-chloro-5-methylphenyl)acetamide (5g): The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 4:1) to give **5g** as white solid (46.67mg, 51%). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.18 (s, 1H), 7.56 (s, 1H), 7.22 (d, *J* = 8.2 Hz, 1H), 6.84 (d, *J* = 7.9 Hz, 1H), 2.33 (s, 3H), 2.23 (s, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 167.2, 137.0, 133.2, 127.5, 124.5, 121.1, 118.5, 23.9, 20.4. GC-MS (EI) *m/z*: 183.



Formula: C_8H_7ClFNO

Mass: 187

N-(2-chloro-5-fluorophenyl)acetamide (5h): The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 4:1) to give **5h** as white solid (55.17mg, 59%). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.26 (dd, *J* = 11.2, 3.0 Hz, 1H), 7.65 (s, 1H), 7.31 (dd, *J* = 8.9, 5.5 Hz, 1H), 6.76 (ddd, *J* = 8.8, 7.4, 3.0 Hz, 1H), 2.25 (s, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 167.3, 161.6, 159.6, 134.6, 128.5, 115.9, 110.3, 107.7, 24.0. GC-MS (EI) *m/z*: 187.



Formula: $C_9H_{10}BrNO$

Mass: 227

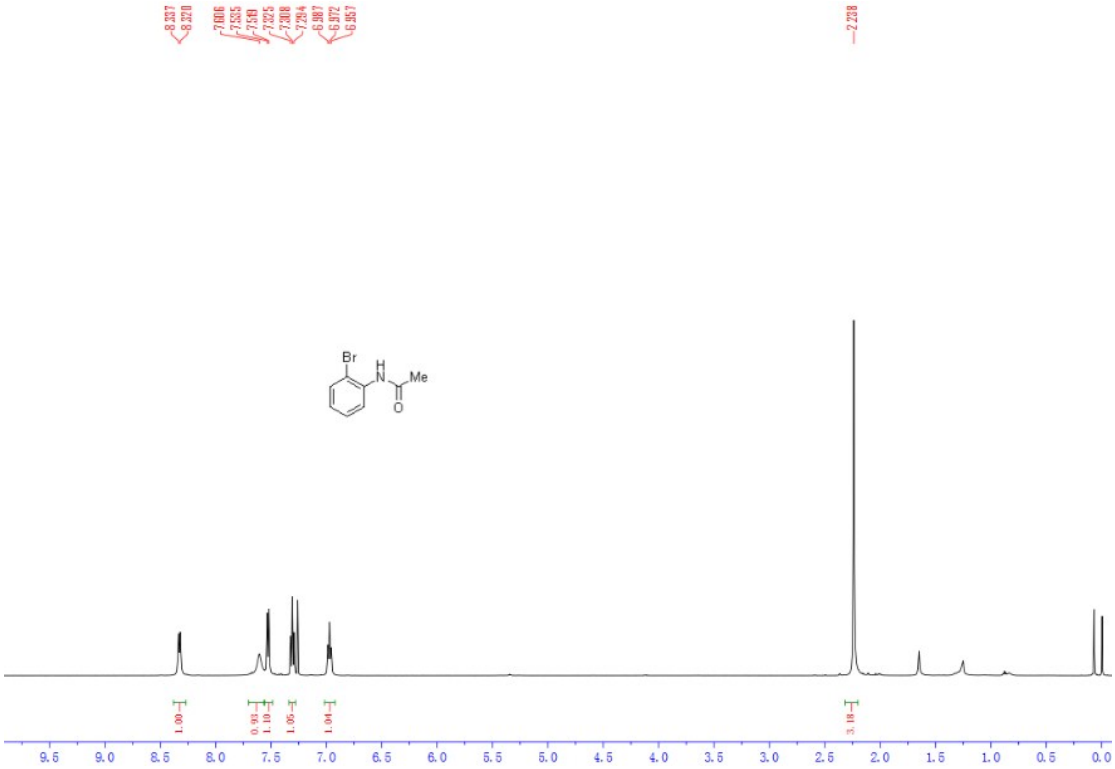
N-(2-bromophenyl)-N-methylacetamide (6a): The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 4:1) to give **6a** as white solid (81.72mg, 72%). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.97 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.46 (td, *J* = 7.6, 1.4 Hz, 1H), 7.34 – 7.30 (m, 1H), 7.11 (td, *J* = 7.7, 1.6

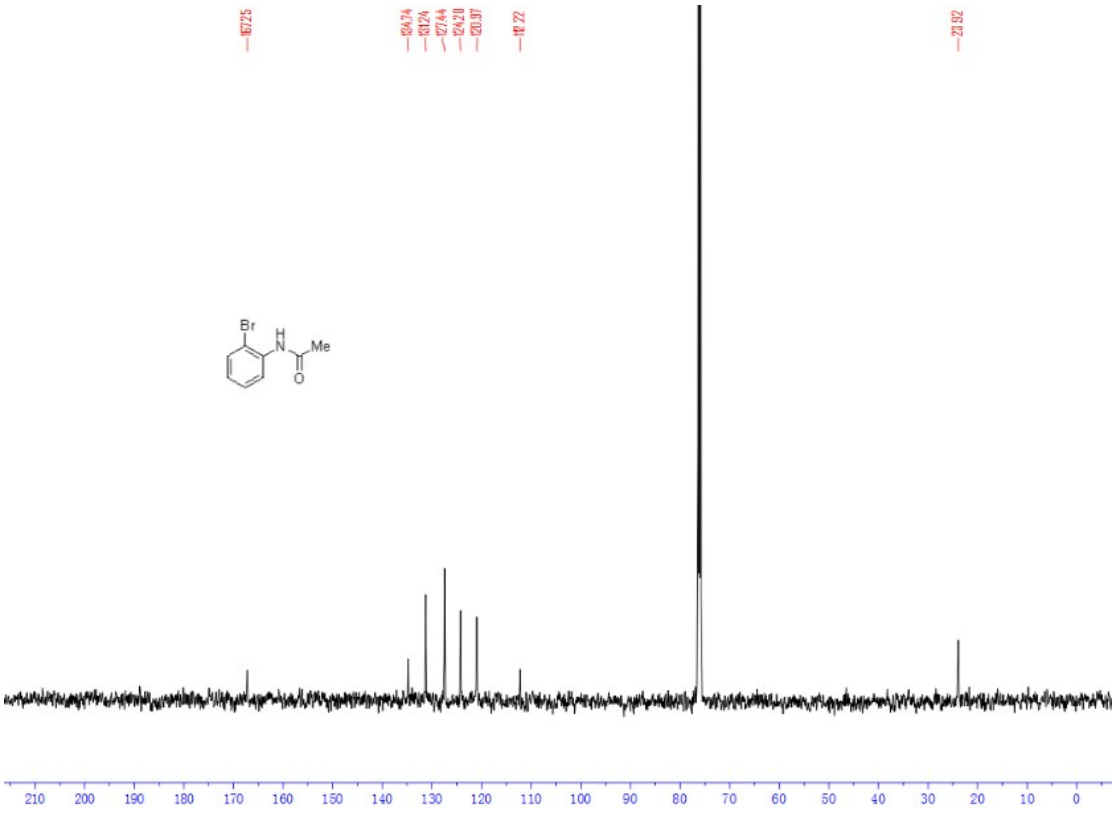
Hz, 1H), 3.21 (s, 3H), 1.83 (s, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 169.3, 145.7, 139.3, 129.0, 128.8, 127.9, 98.5, 34.9, 21.5. GC-MS (EI) *m/z*: 227.

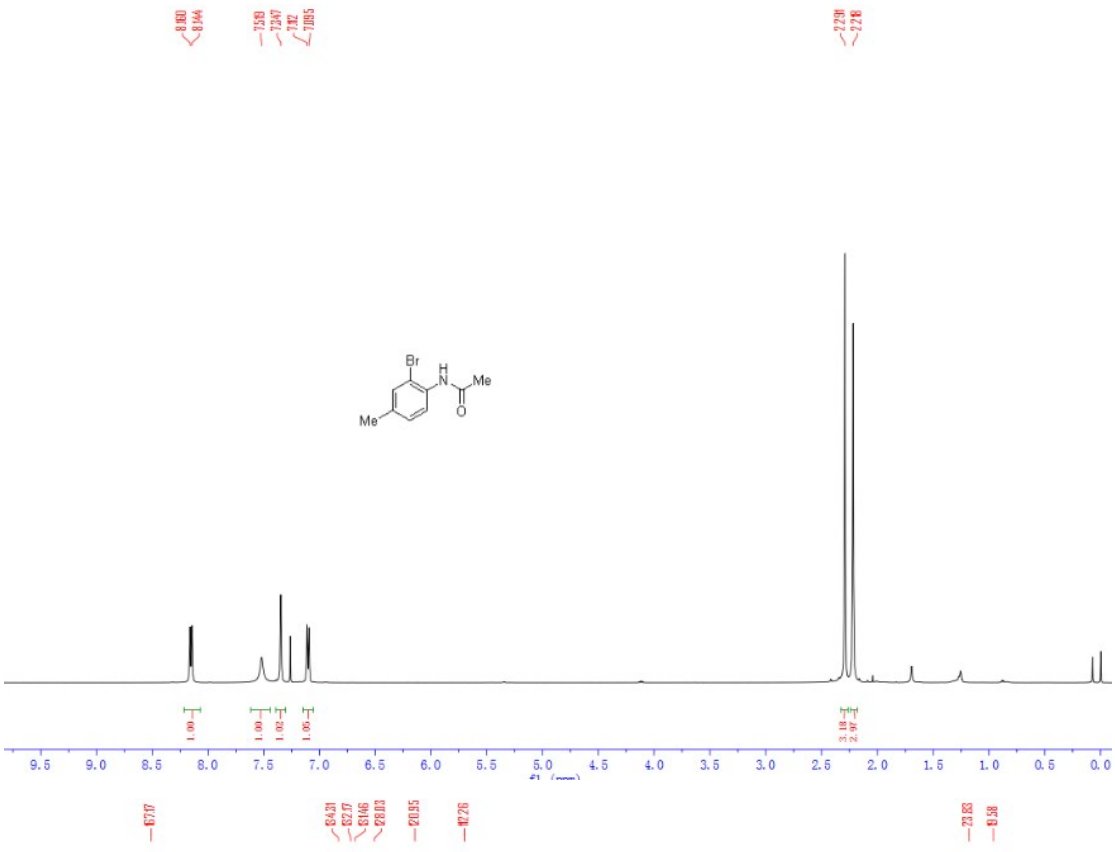
Reference

1. S. Kathiravan and I. A. Nicholls, *Chem. Eur. J.* 2017, **23**, 7031 – 7036.
   (Compounds 3a-3f, 3i, 3m, 4a-4f, 4g, 4k, 5b, 5d, 5f)
2. R. Das and M. Kapur, *J. Org. Chem.* 2017, **82**, 1114-1126.
   (Compounds 3h, 3j, 3k)
3. R. B. Bedford, M. F. Haddow, C. J. Mitchell, and R. L. Webster, *Angew. Chem. Int. Ed*. 2011, **50**, 5524 –5527.
   (Compounds 5a, 5e, 5g, 5h)
4. N. Zheng, K. W. Anderson, X. H. Huang, H. N. Nguyen, and S. L. Buchwald, *Angew. Chem. Int. Ed.* 2007, **46**, 7509 –7512.
   (Compounds 3g)
5. B. Michelet, C. Deldaele, S. Kajouj, C. Moucheron, and G. Evano, *Org. Lett.* 2017, **19**, 3576-3579.
   (Compounds 4h)
6. X. B. Wan, Z. X. Ma, B. J. Li, K. Y. Zhang, S. K;. Cao, S. W. Zhang, and Z. J. Shi, *J. AM. CHEM. SOC.* 2006, **128**, 7416-741.
   (Compounds 5c)
7. H. C. Cheng, W. J. Hou, Z. W. Li, M. Y. Liu and B. T. Guan, *Chem. Commun.,* 2015, **51**, 17596—17599.
   (Compounds 6a)
8. H. J. Shen, J. K. Fu, H. Yuan, J. X. Gong, and Z. Yang, *J. Org. Chem.* 2016, **81**, 10180-10192.
   (Compounds 4m)

4. NMR spectra



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Me
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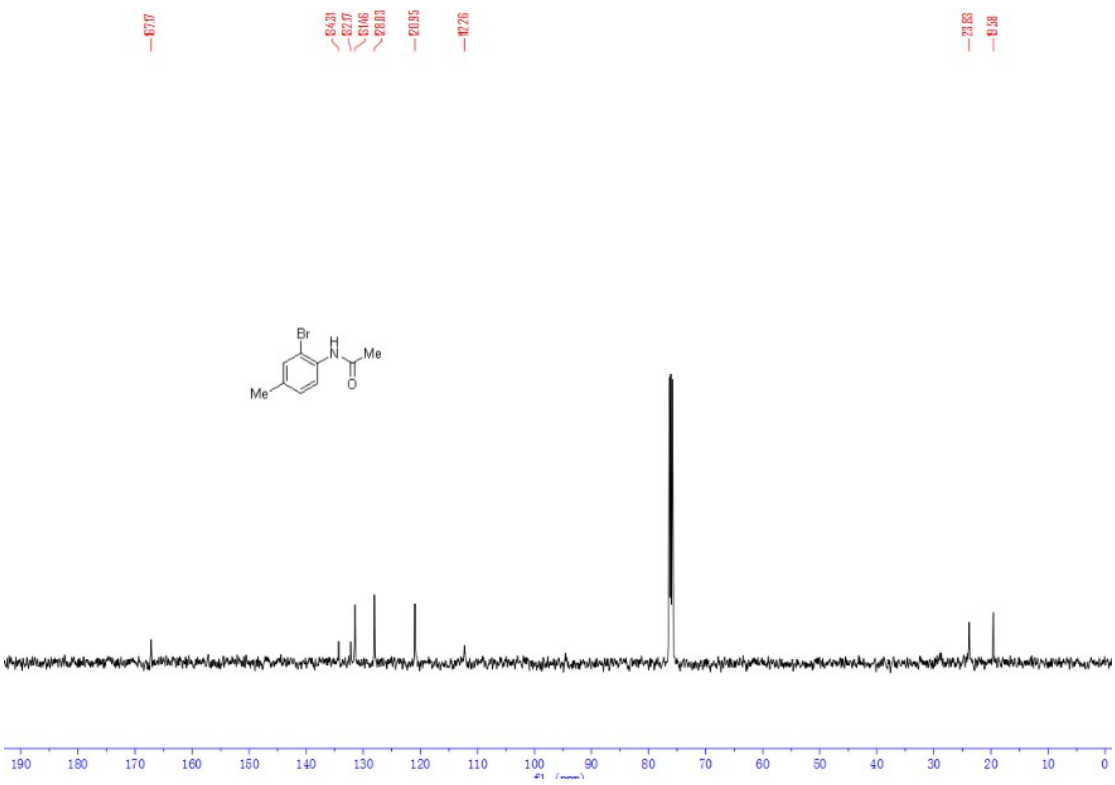
2.97
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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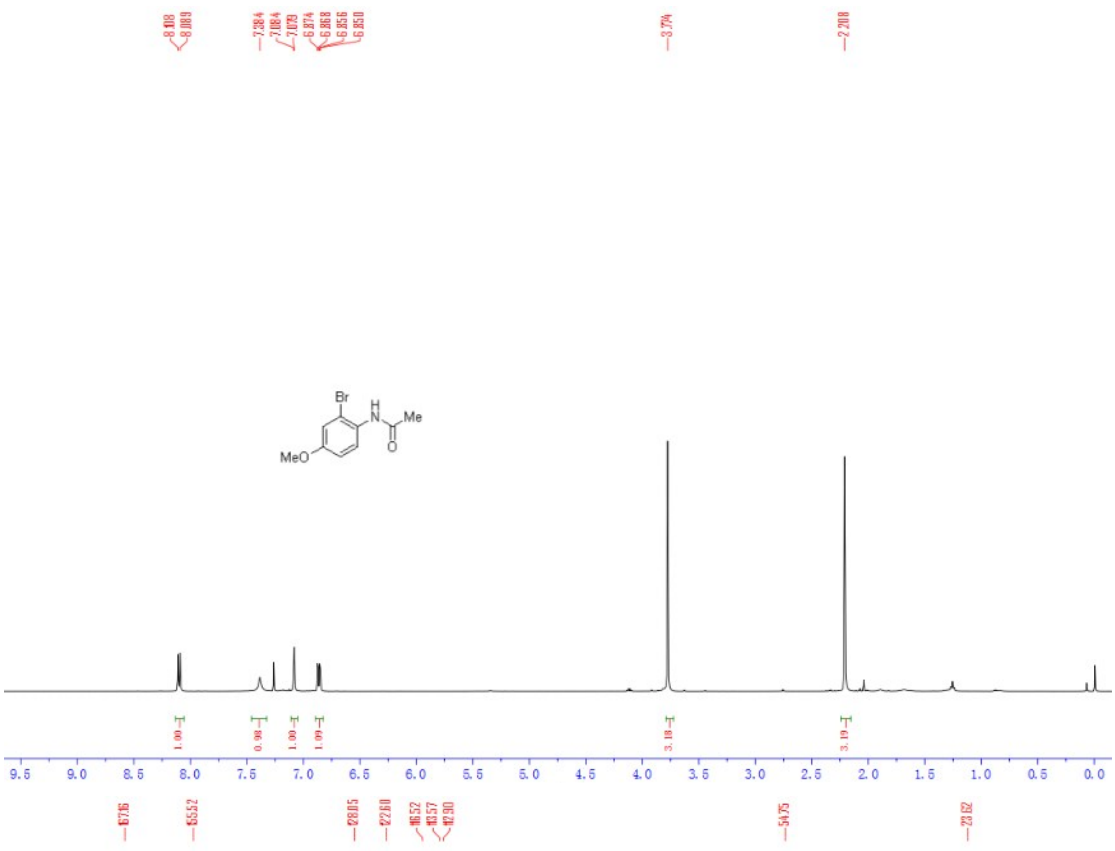
f1 (ppm)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1.00
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8.0
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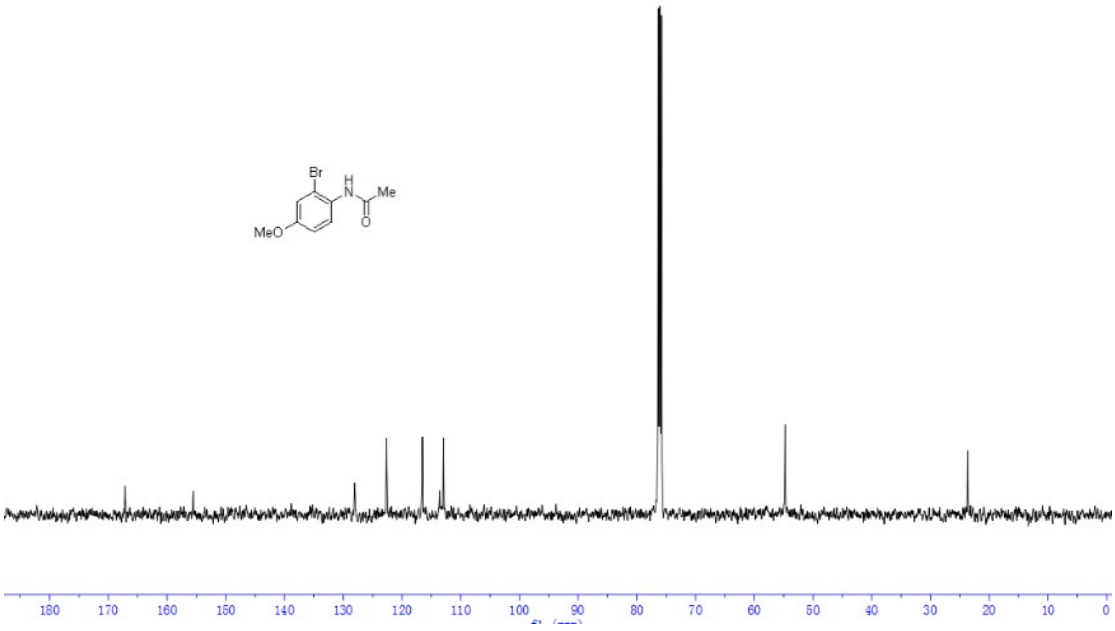
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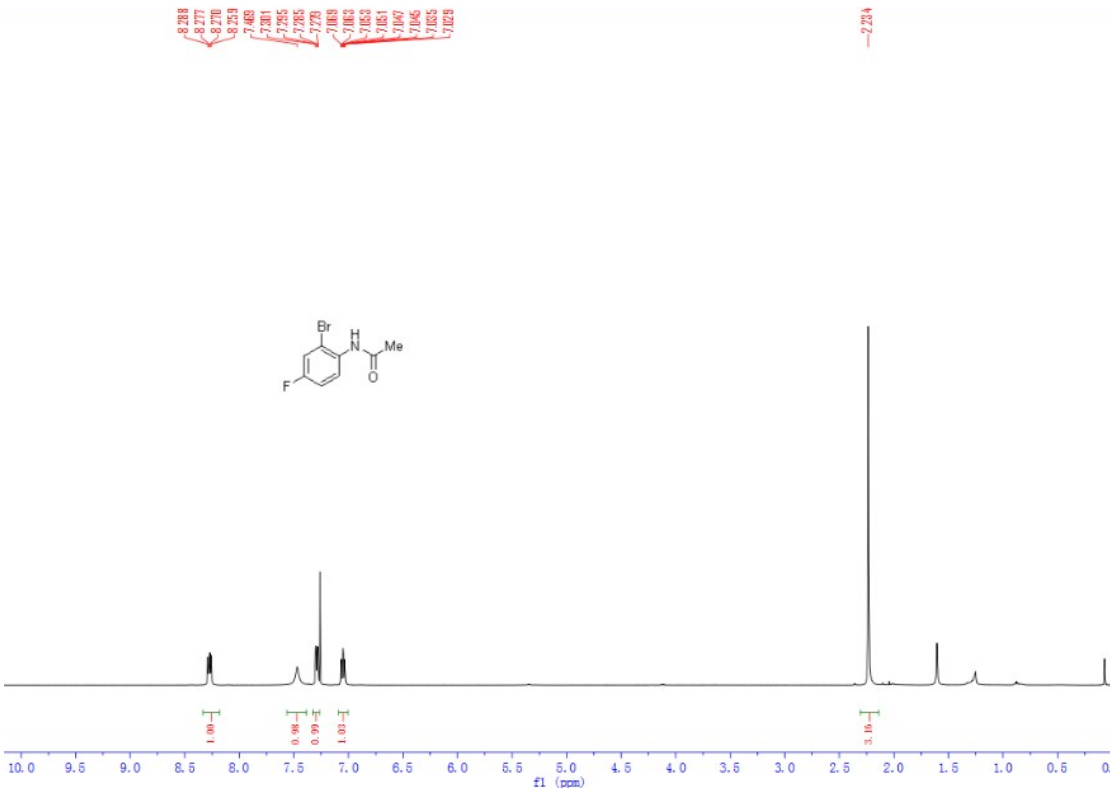
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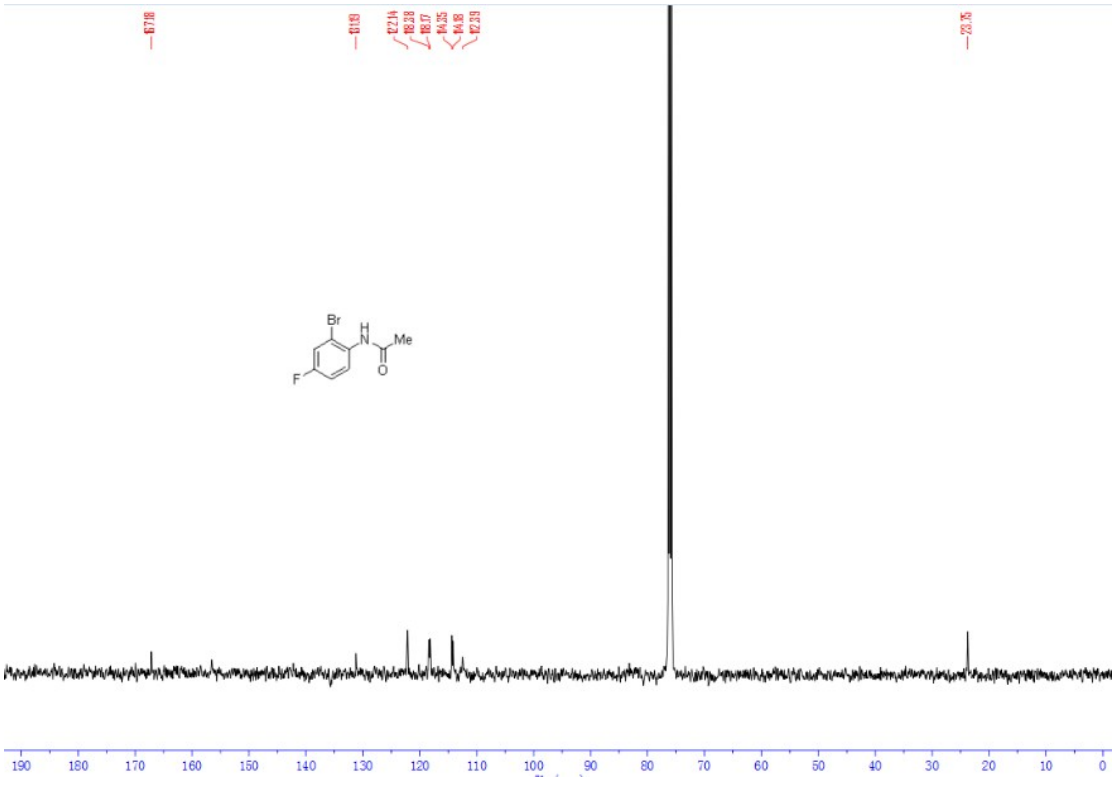
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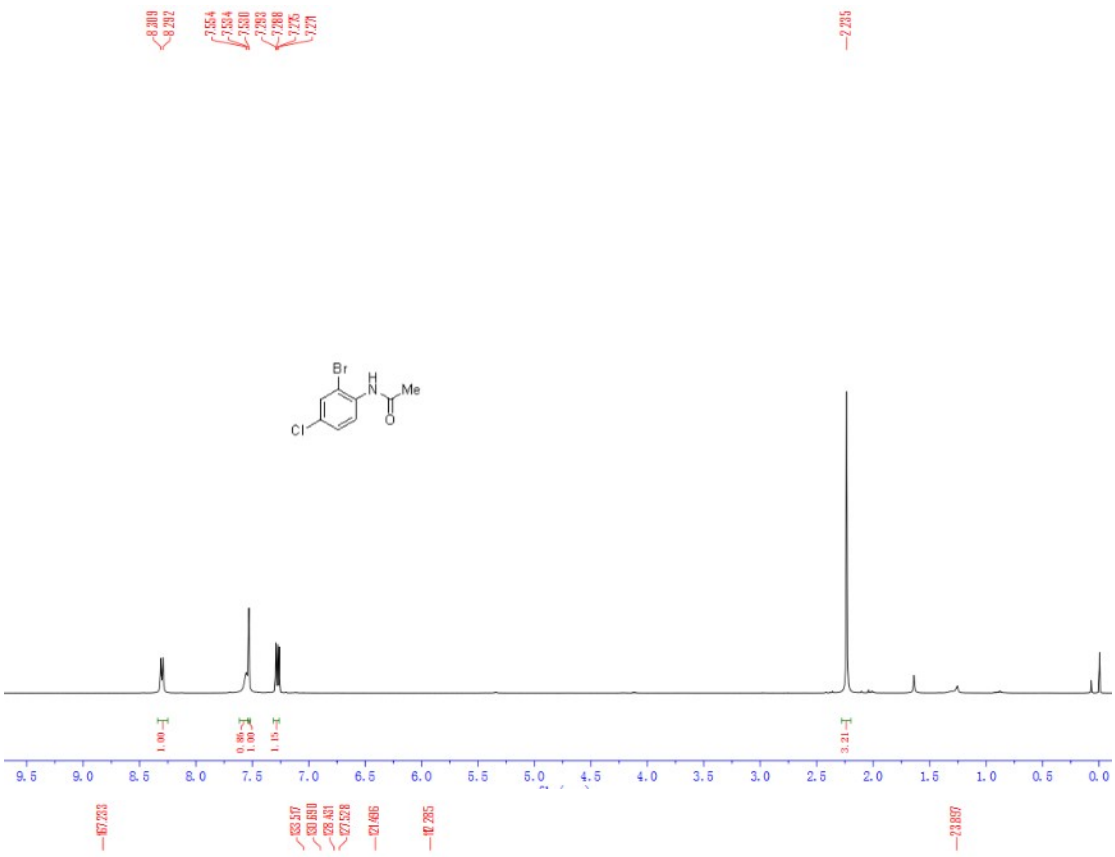
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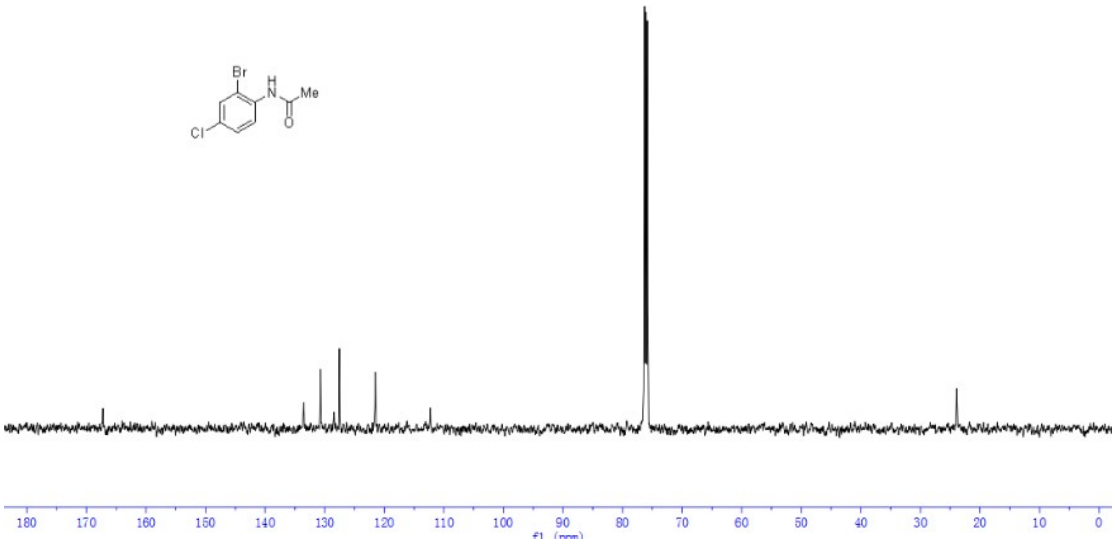
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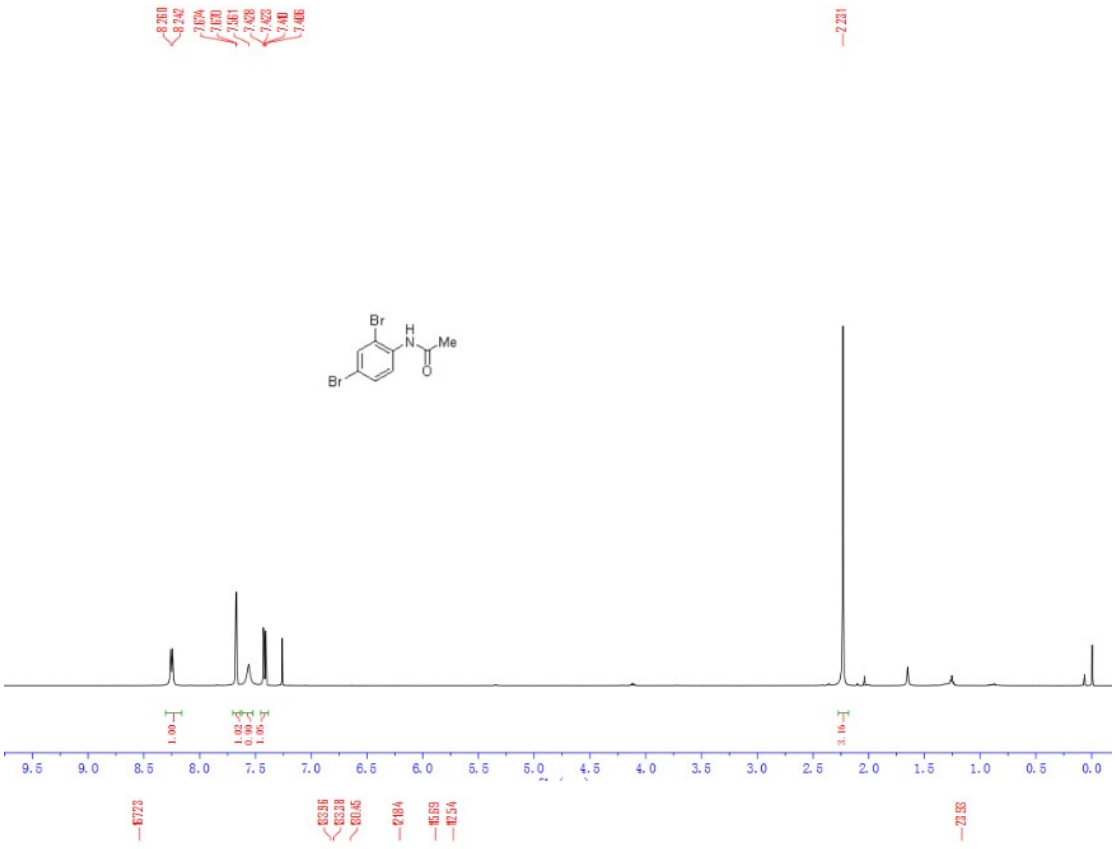
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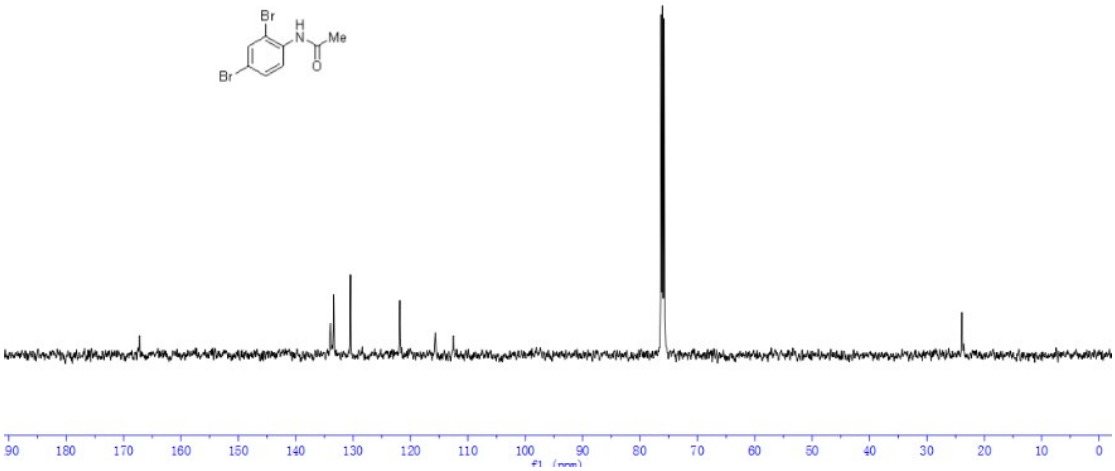
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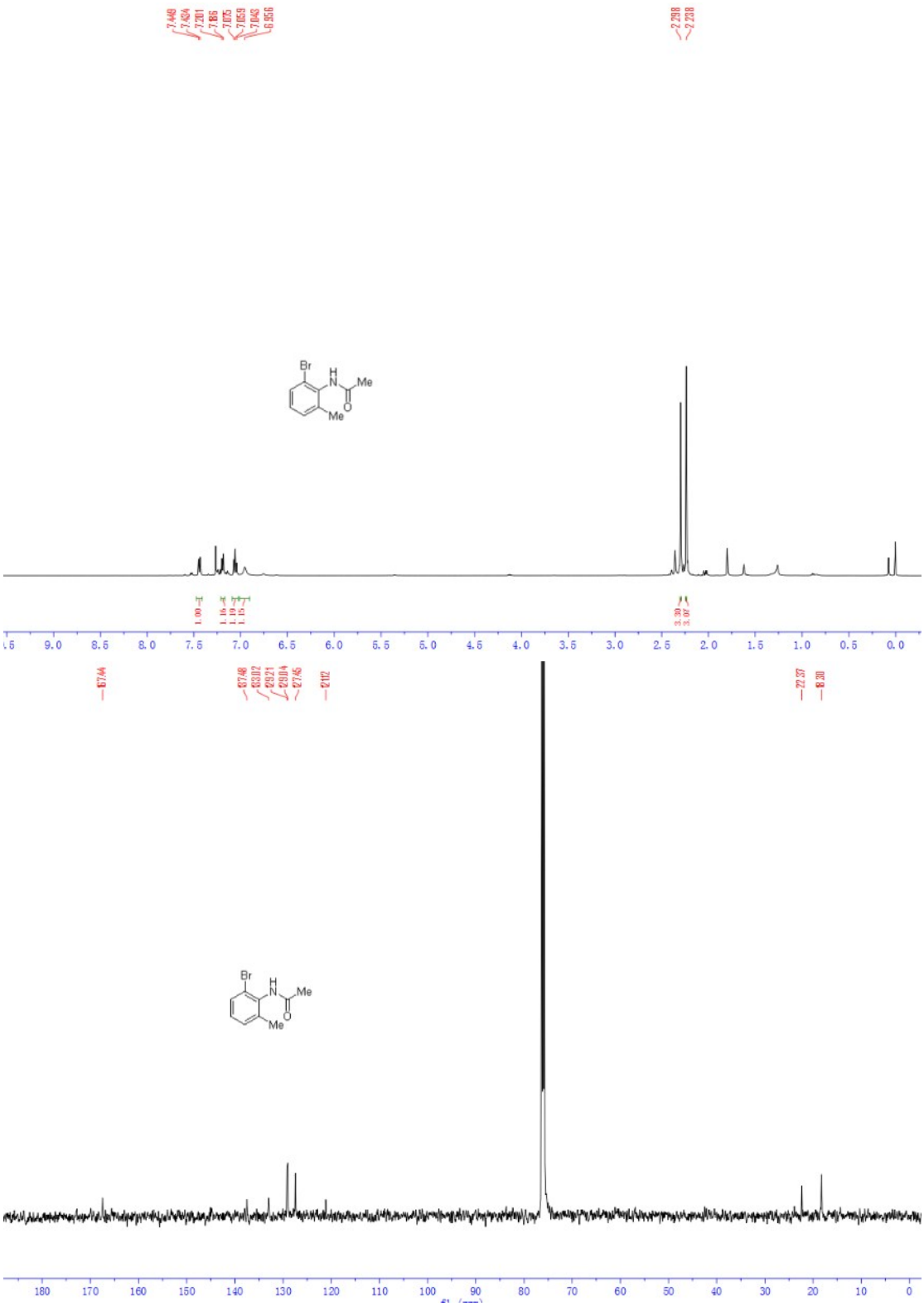
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20
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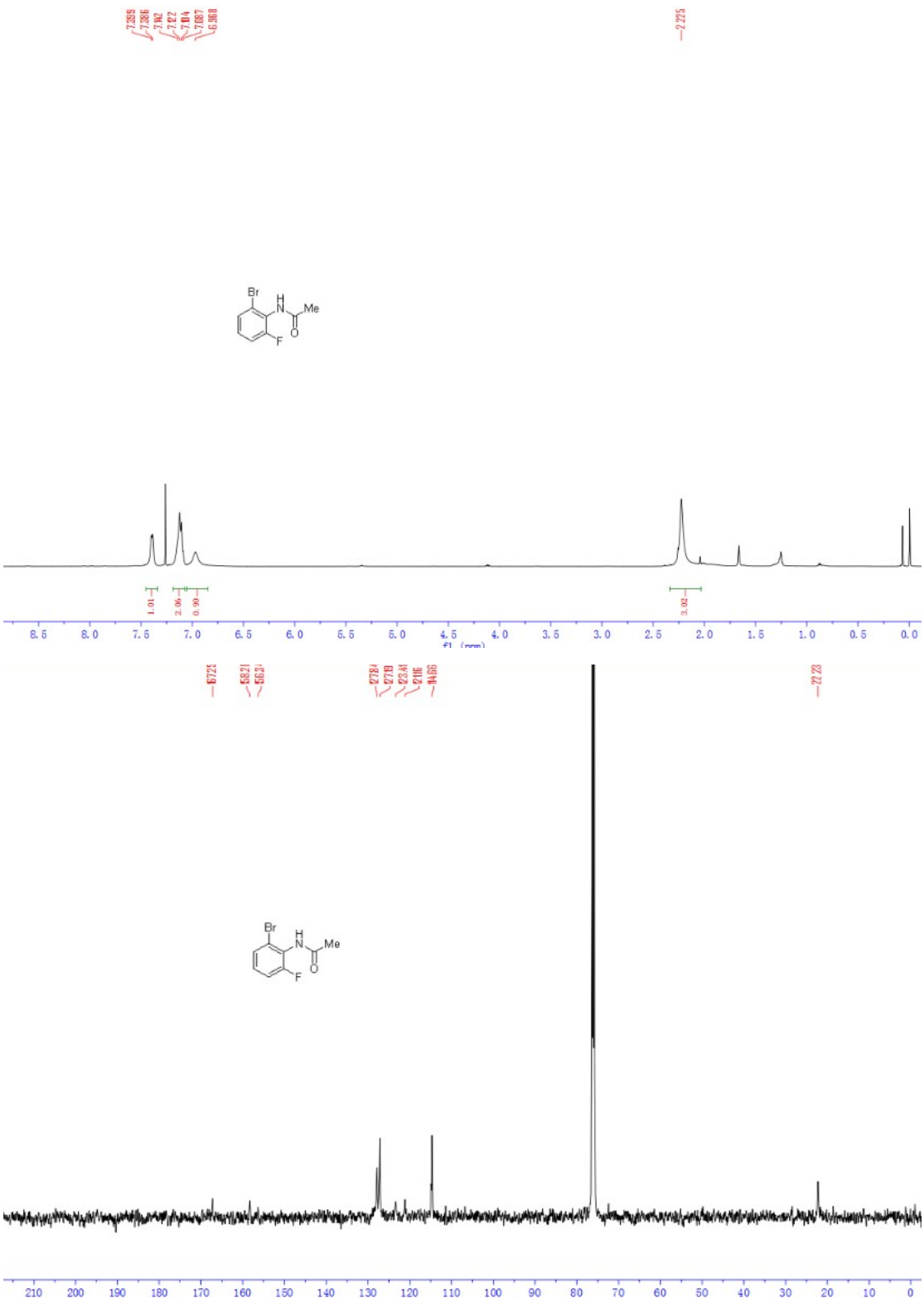
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H
N
Me
O
F
1.01
2.06
0.99
3.02
8.5
8.0
7.5
7.0
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6.0
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4.0
3.5
3.0
2.5
2.0
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1.0
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f1 (ppm)
167.24
158.21
156.31
127.84
127.19
126.41
121.16
114.06
22.23
Br
H
N
Me
O
F
210
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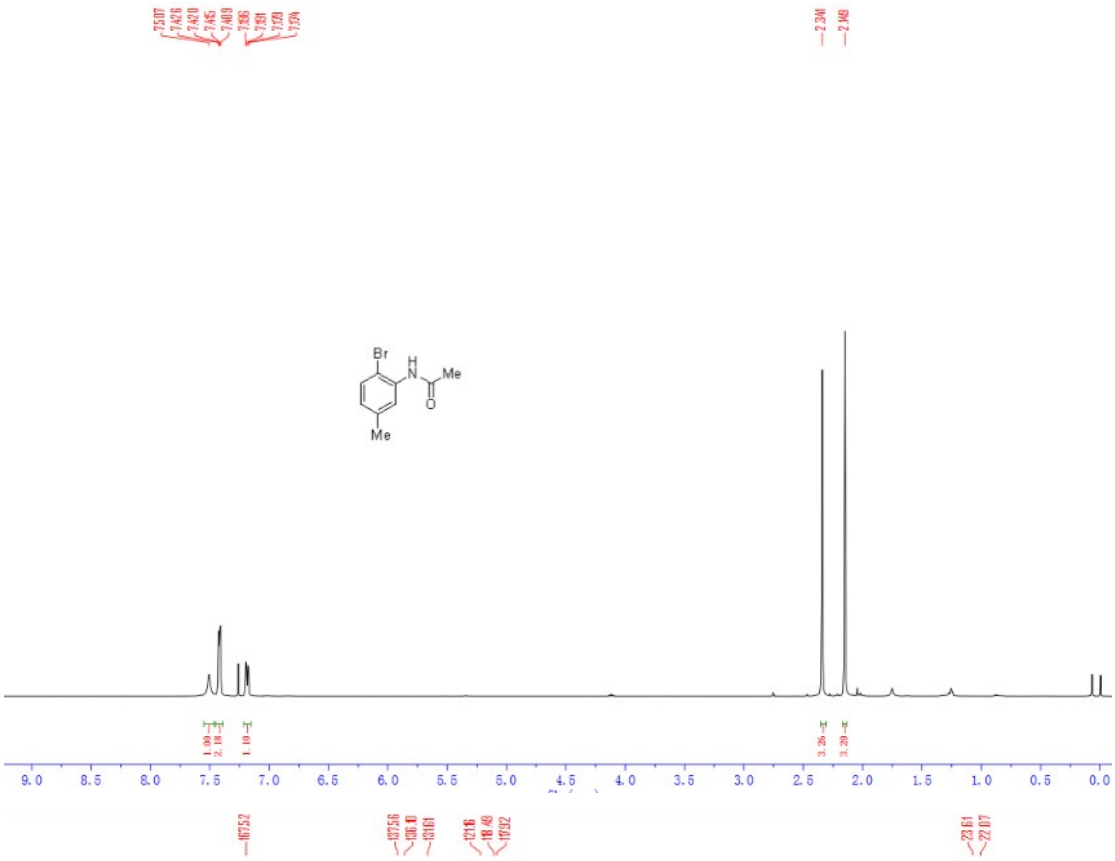
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7.3251
7.2929
7.2594
2.3341
2.1481
Br
H
N
Me
O
Me
1.00
2.18
1.10
3.26
3.20
9.0
8.5
8.0
7.5
7.0
6.5
6.0
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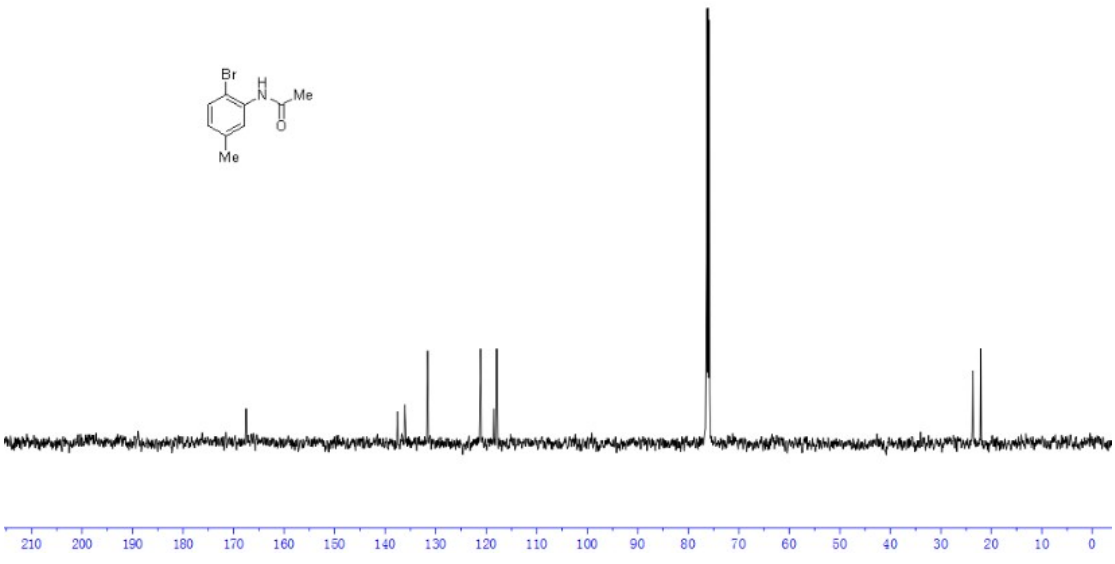
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Me
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Me
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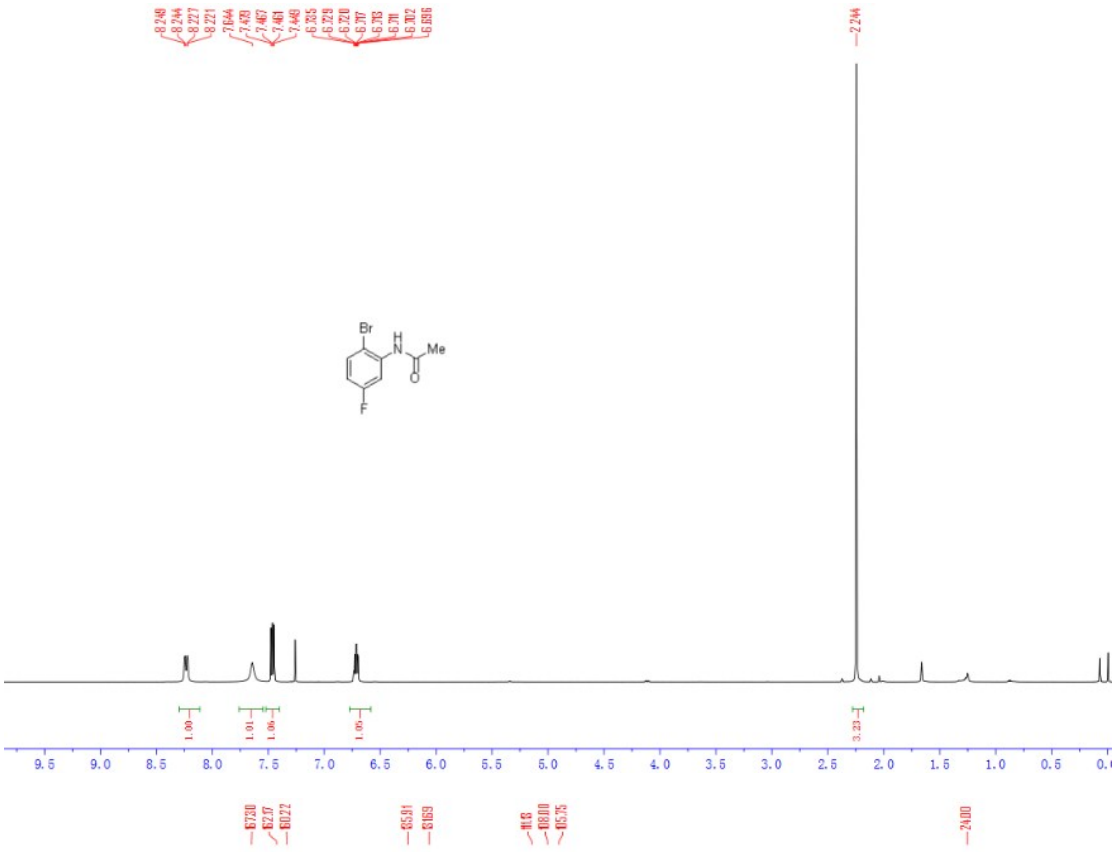
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7.461
7.446
6.735
6.729
6.720
6.707
6.703
6.701
6.702
6.696
2.244
Br
H
N
Me
O
F
1.00
1.01
1.00
1.00
3.23
9.5
9.0
8.5
8.0
7.5
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6.5
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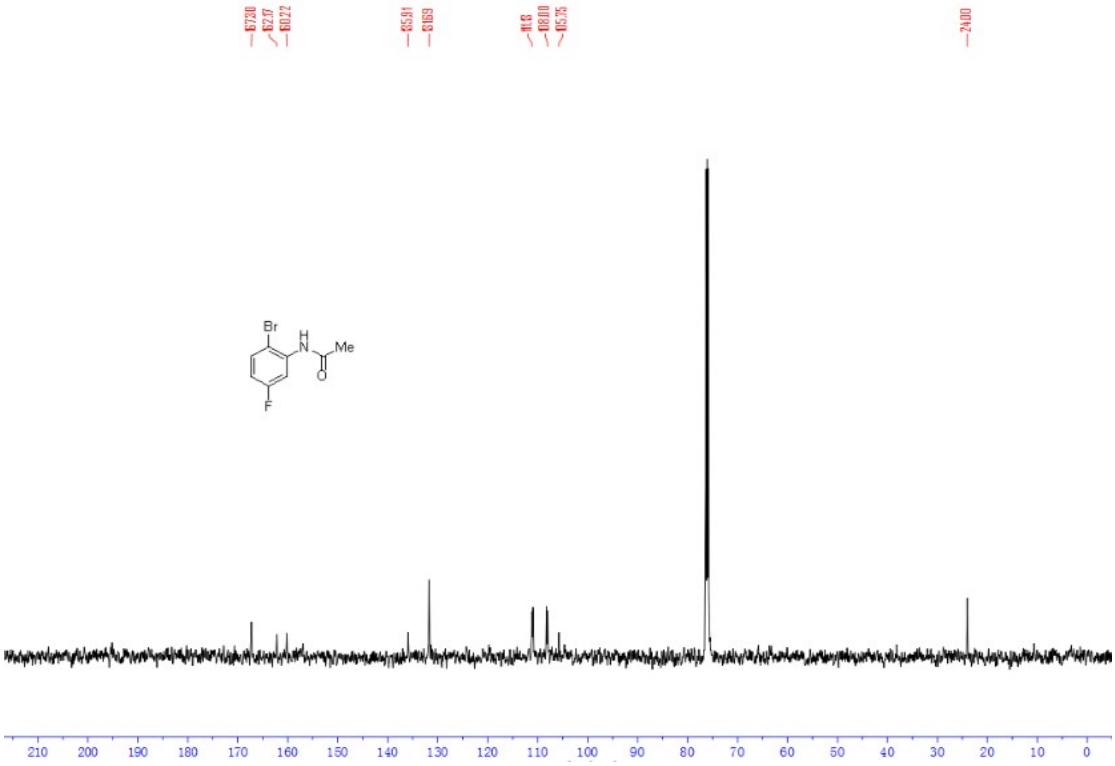
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160.22
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108.00
105.75
24.00
Br
H
N
Me
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F
210
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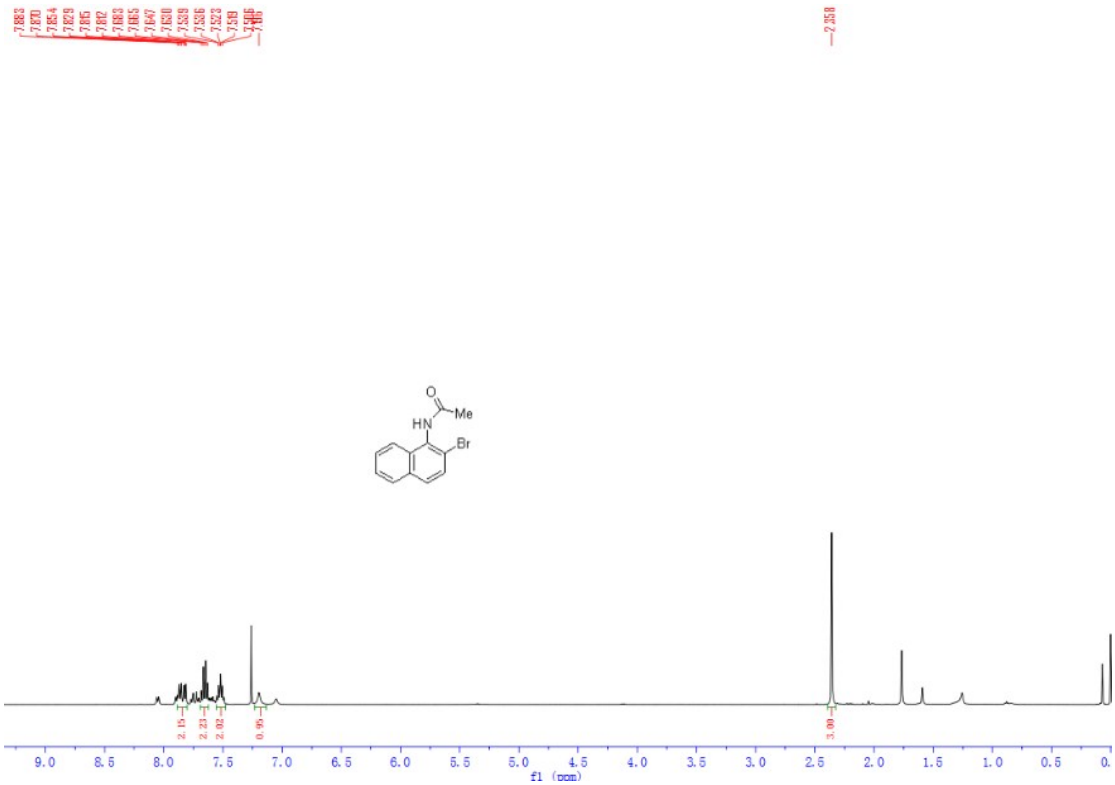
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7.7883
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7.7528
7.7526
7.7523
7.7519
7.7505
2.358
O
Me
HN
Br
2.15
2.23
2.02
0.95
3.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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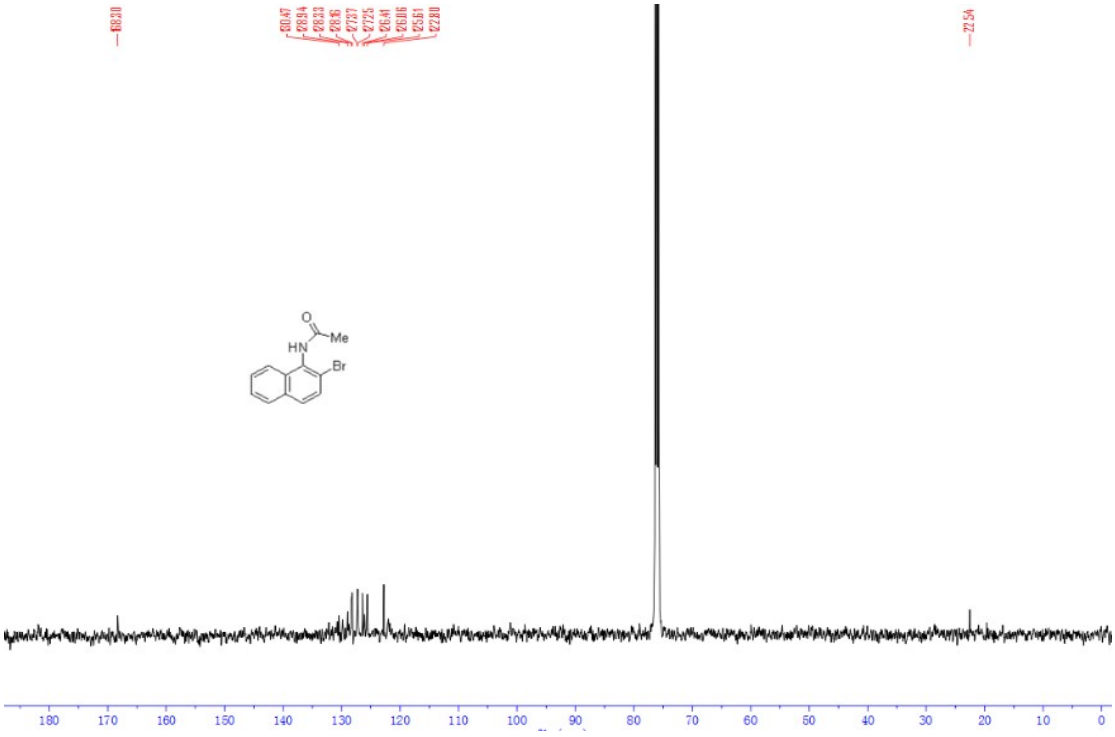
f1 (ppm)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126.48
126.06
125.61
122.80
22.54
O
Me
HN
Br
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150
140
130
120
110
100
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70
60
50
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30
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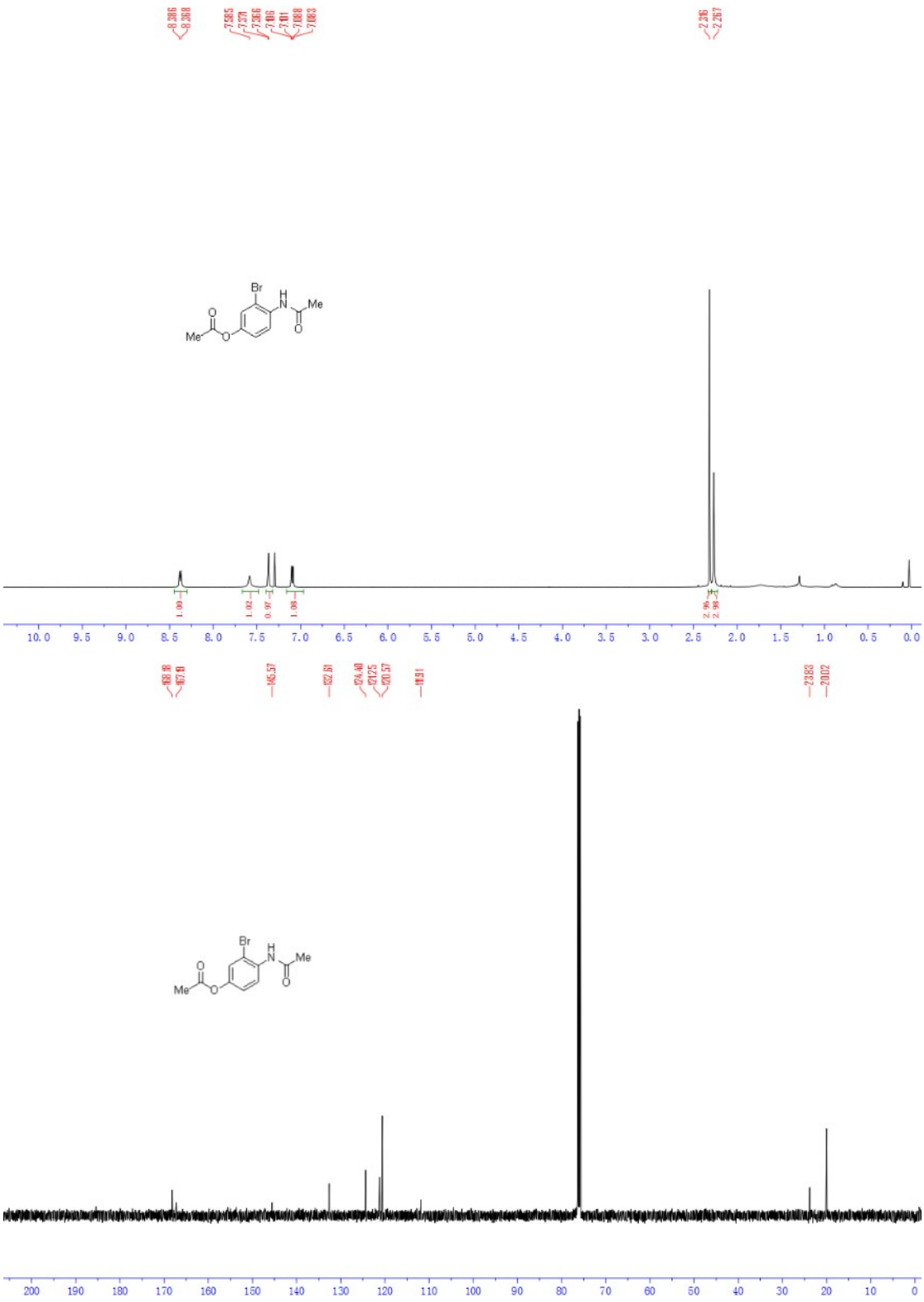
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7.305
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7.088
7.083
2.285
2.267
Br
N
H
Me
O
Me
O
1.00
1.02
0.98
1.00
2.99
2.98
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
168.18
167.91
145.57
132.51
124.40
121.25
120.57
114.91
23.83
23.02
Br
N
H
Me
O
Me
O
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150
140
130
120
110
100
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80
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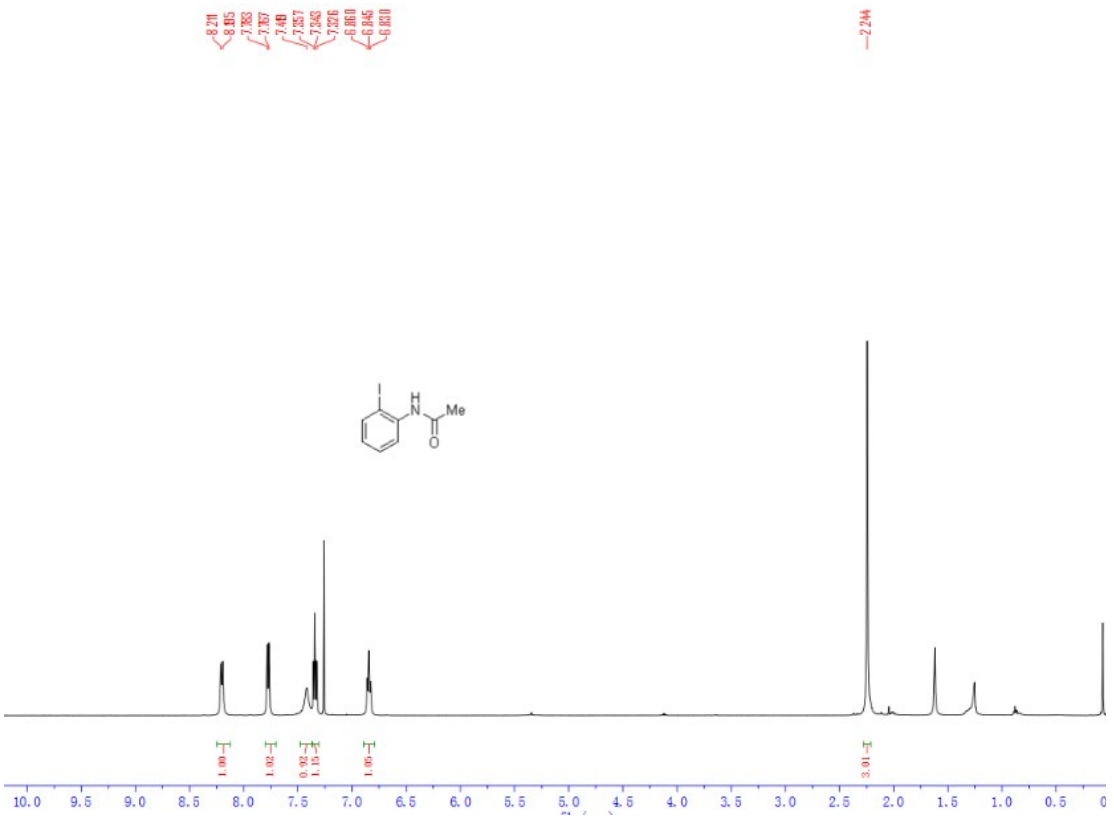
10
0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7.543
7.526
6.861
6.845
6.830
2.244
1.09
1.02
0.92
1.15
1.05
3.01
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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4.0
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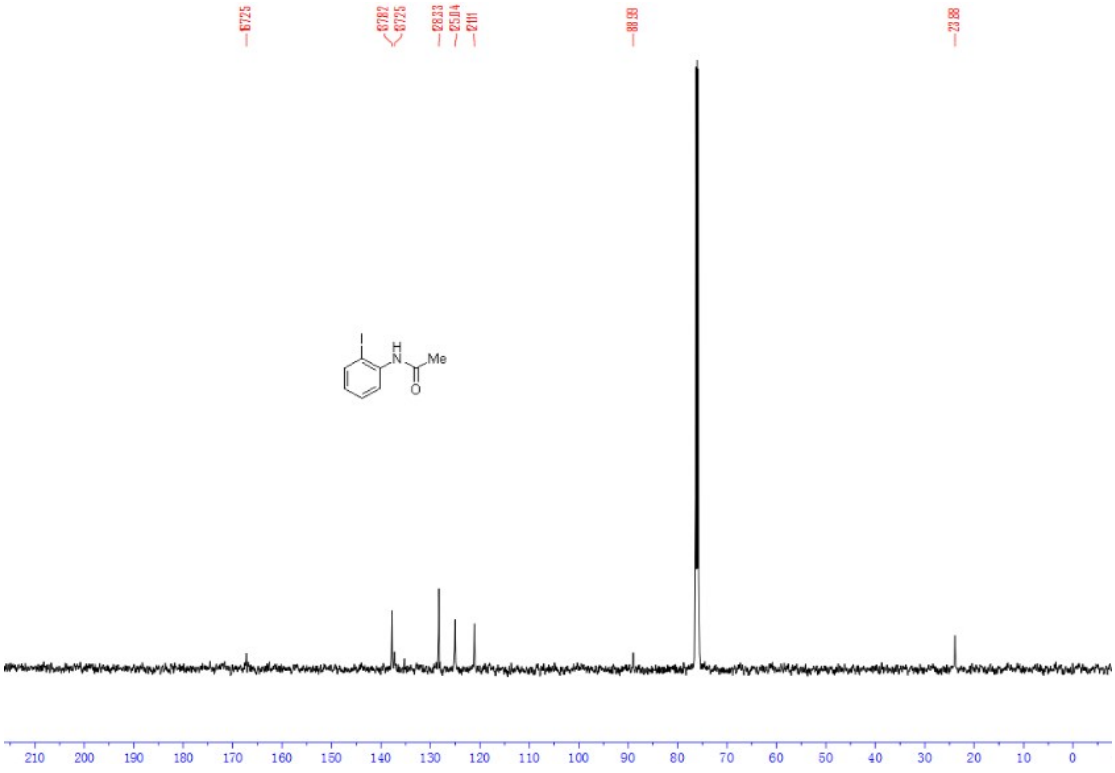
3.0
2.5
2.0
1.5
1.0
0.5
0
H
N
Me
O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137.25
129.33
125.04
121.11
89.33
23.88
210
200
190
180
170
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110
100
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80
70
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30
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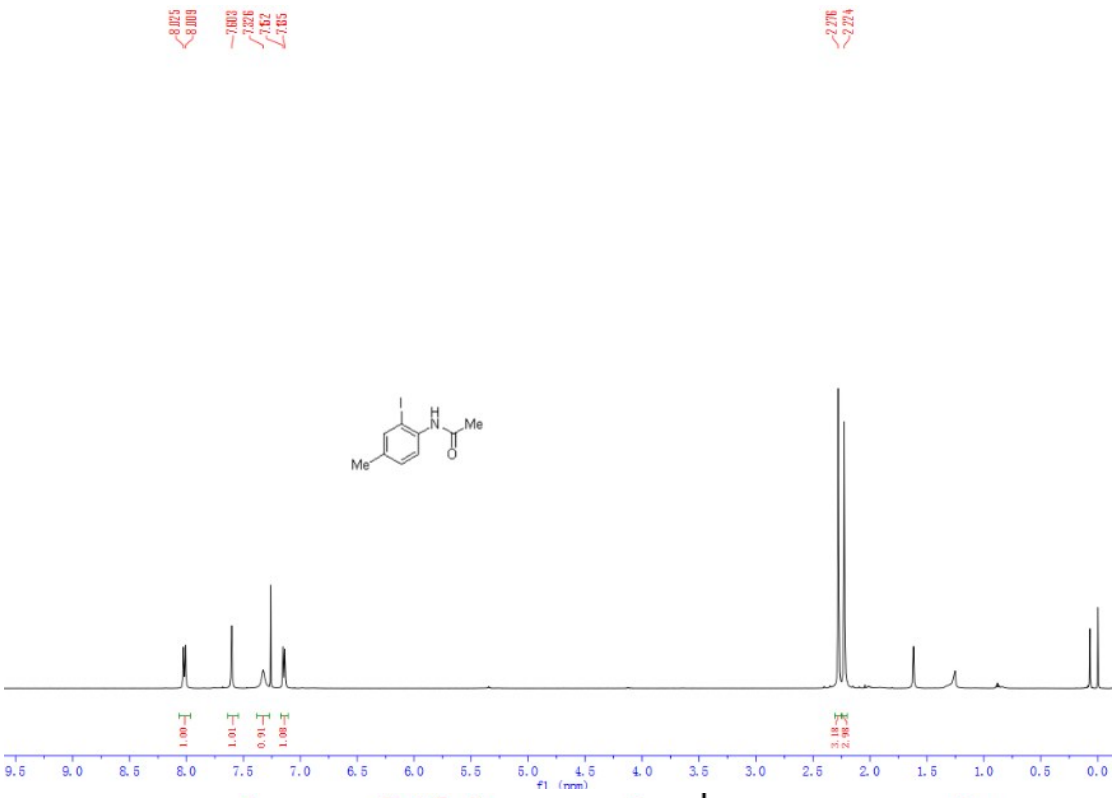
0
H
N
Me
O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7.326
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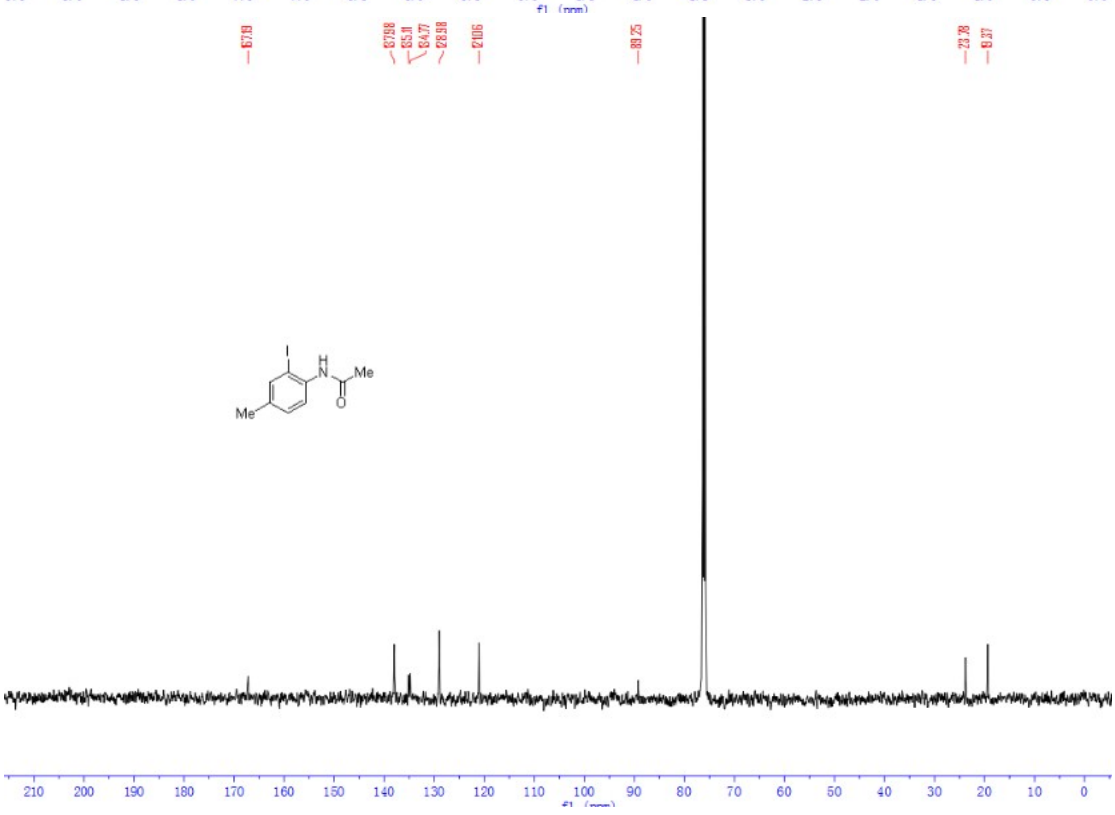
2.276
2.224
I
H
N
Me
O
Me
1.00
1.01
0.91
1.00
3.18
2.98
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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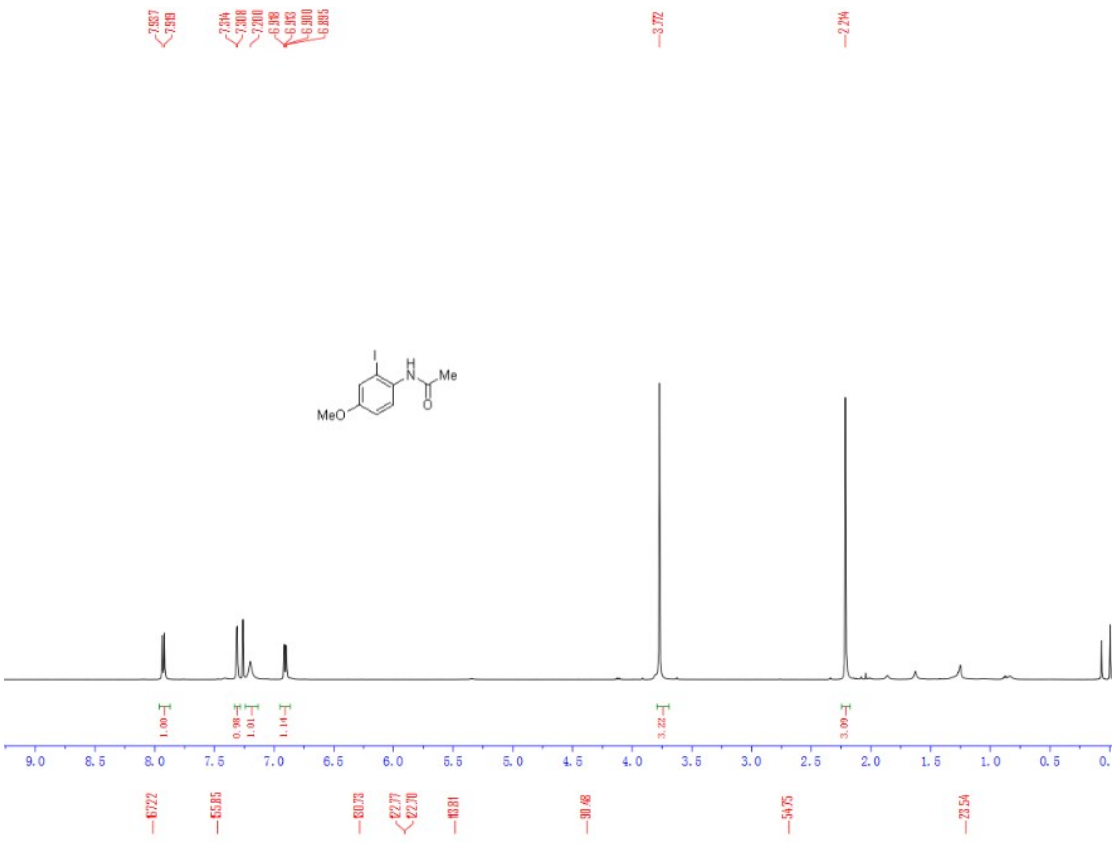
134.77
128.98
121.06
89.25
23.28
19.37
I
H
N
Me
O
Me
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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6.9310
6.8865
3.7722
2.2744
I
N
H
Me
O
MeO
1.00
0.98
1.01
1.14
3.22
3.09
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
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0.
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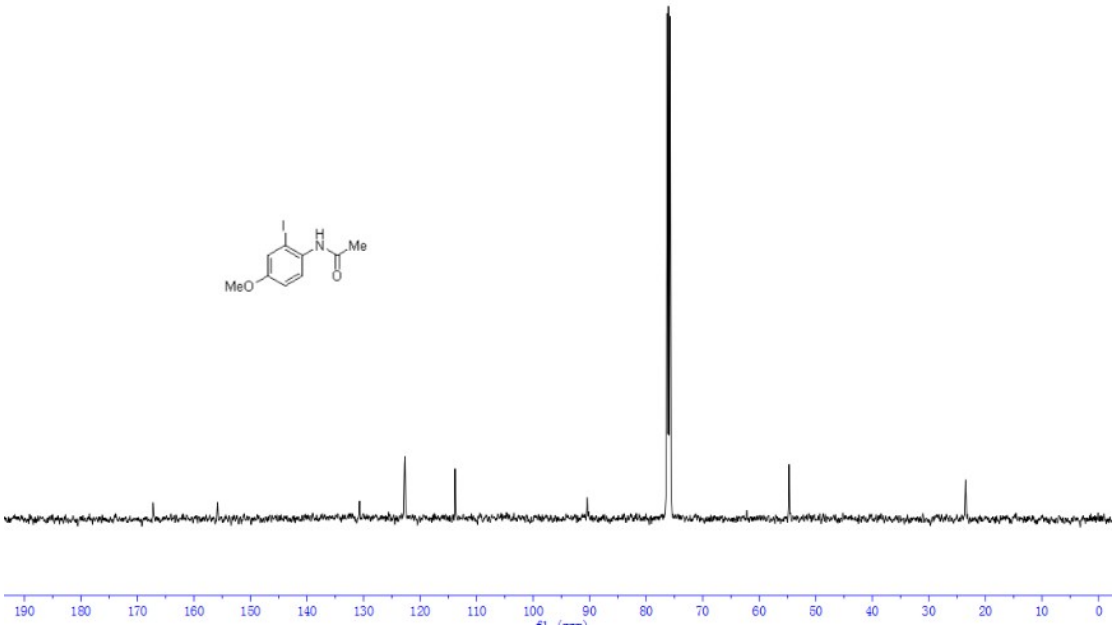
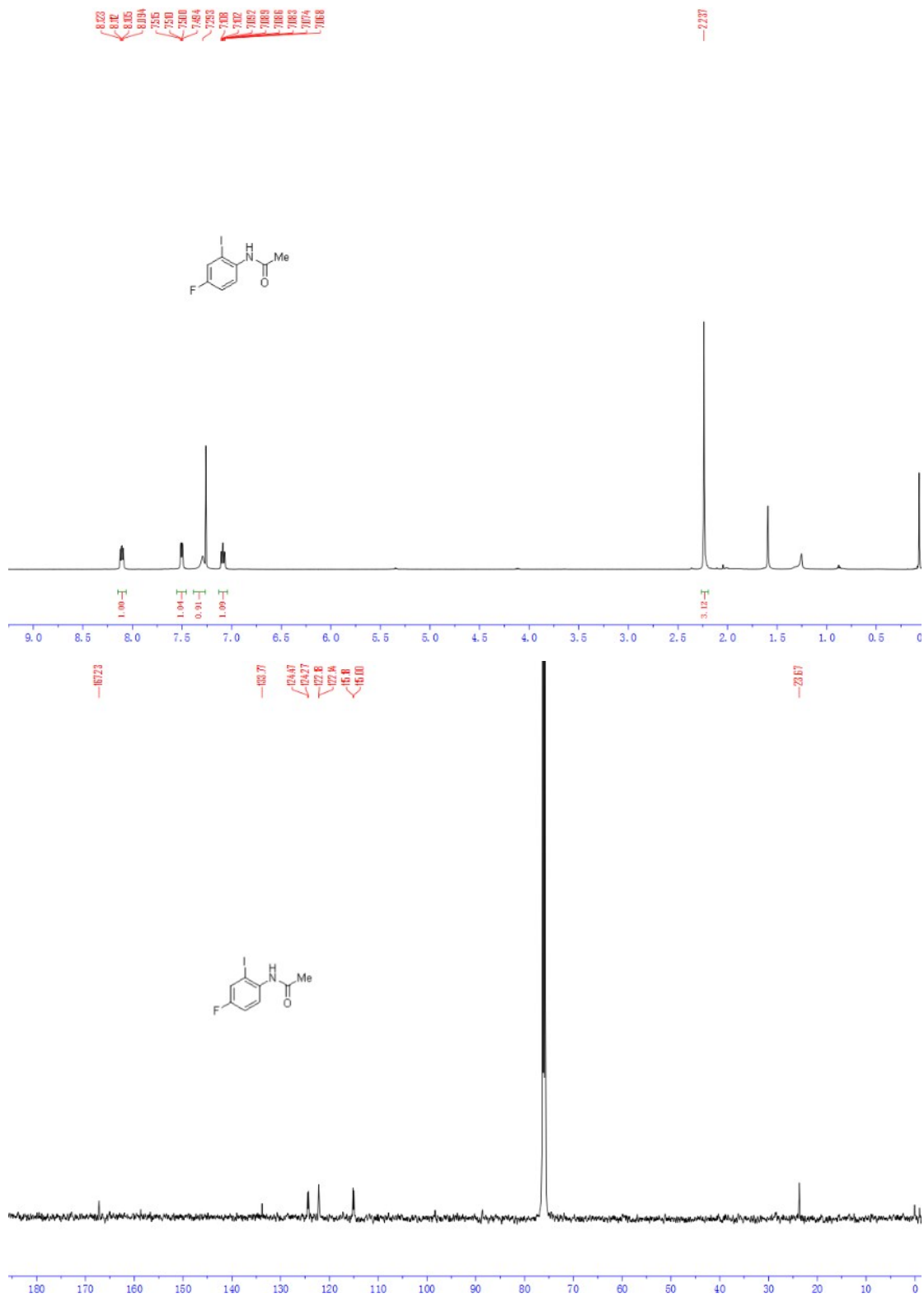
130.78
122.77
122.70
113.81
100.68
54.75
23.54


I
N
H
Me
O
MeO
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0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7.102
7.092
7.089
7.086
7.083
7.074
7.068
2.237
I
H
N
Me
O
F
1.00
1.04
0.91
1.09
3.12
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
167.23
133.77
124.67
124.27
122.18
122.04
115.81
115.60
23.67
I
H
N
Me
O
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110
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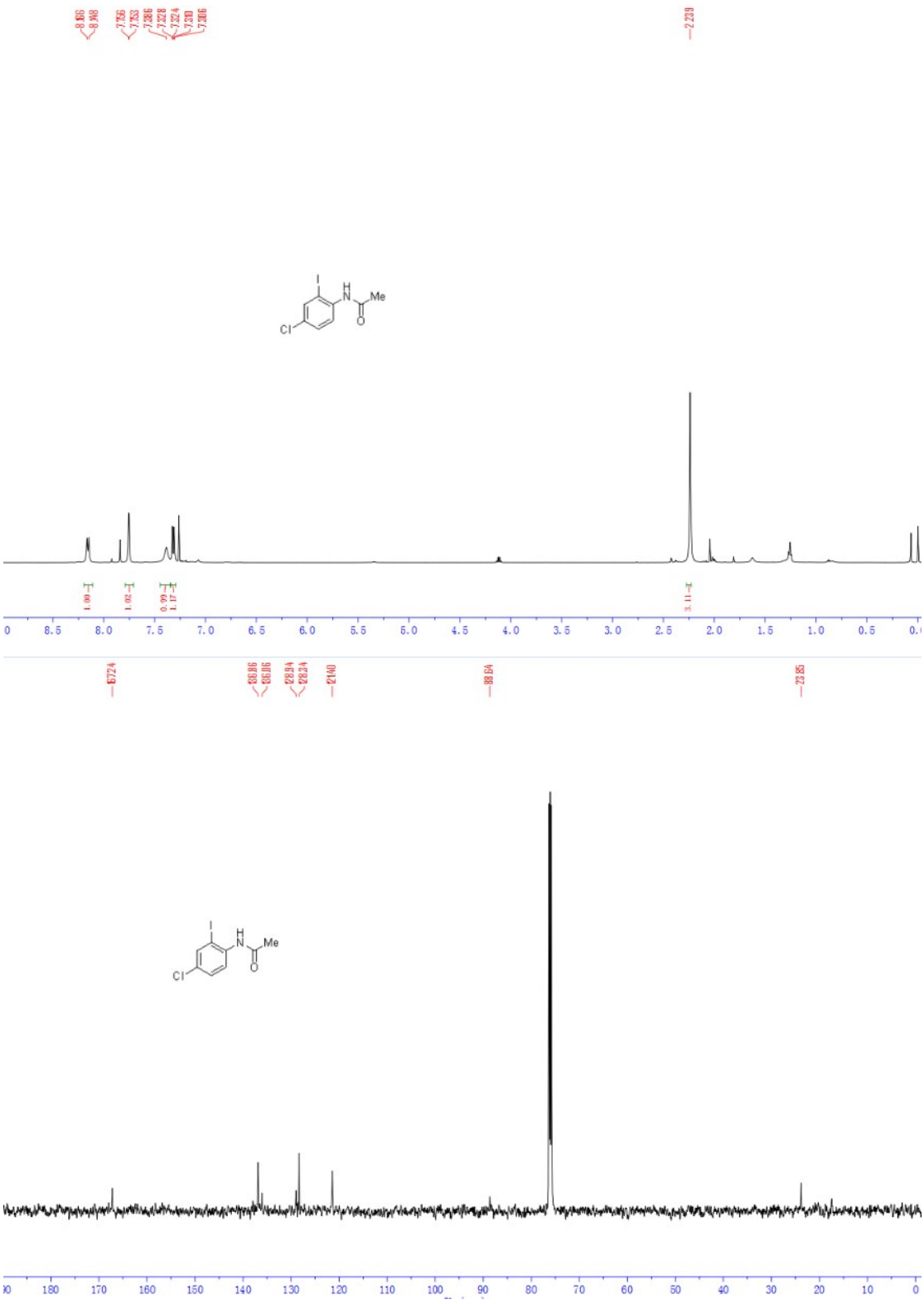
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7.210
7.206
2.239
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H
N
Me
O
Cl
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1.02
0.99
1.17
3.11
0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
167.24
136.86
136.06
128.94
128.34
121.40
88.64
23.85
I
H
N
Me
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Cl
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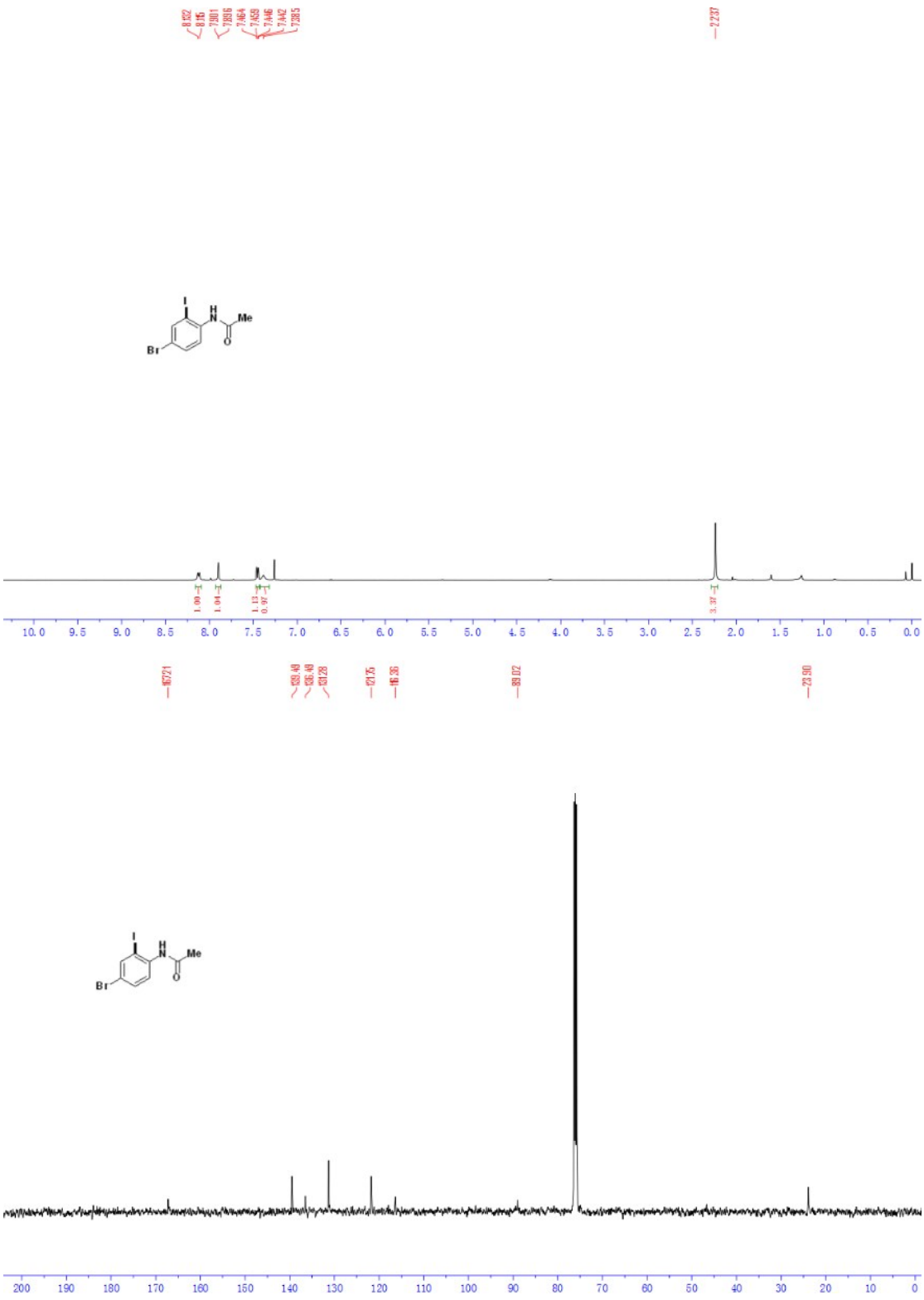
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7.7446
7.7442
7.7265
2.237
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H
N
Me
O
Br
1.00
1.04
1.13
0.97
3.37
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
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4.5
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3.5
3.0
2.5
2.0
1.5
1.0
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0.0
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139.49
136.49
131.28
121.75
116.36
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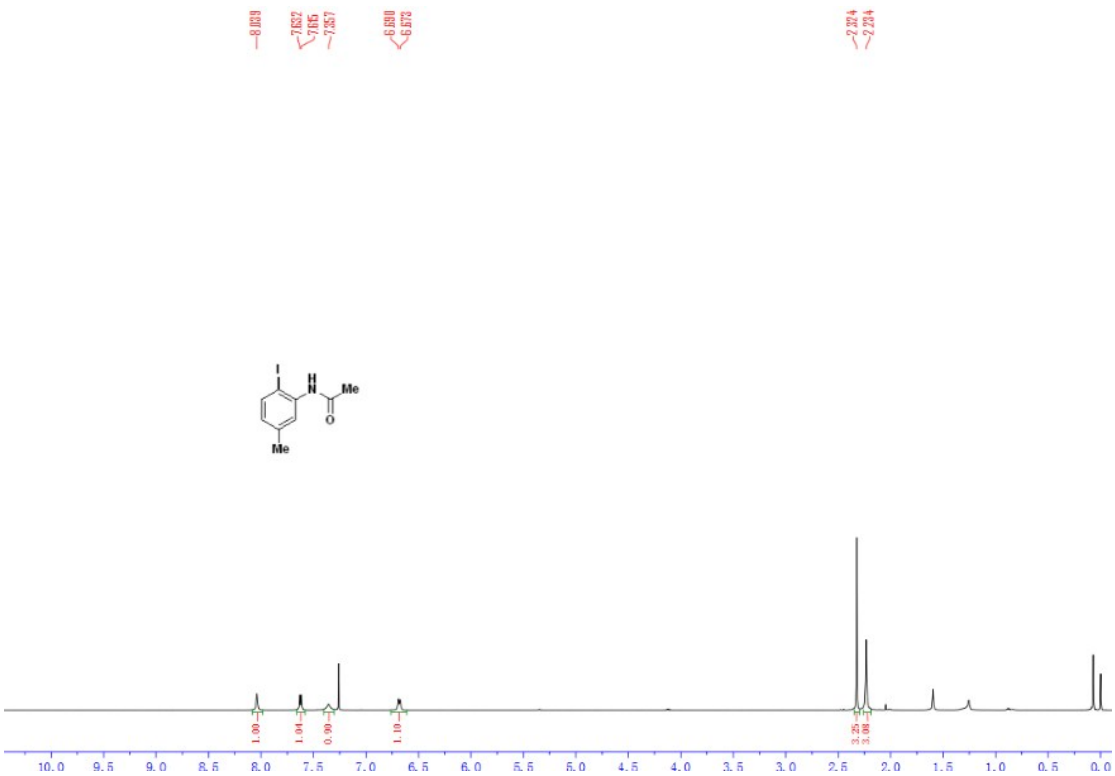
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6.878
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2.264
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N
Me
O
Me
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1.04
0.99
1.10
3.25
3.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
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6.0
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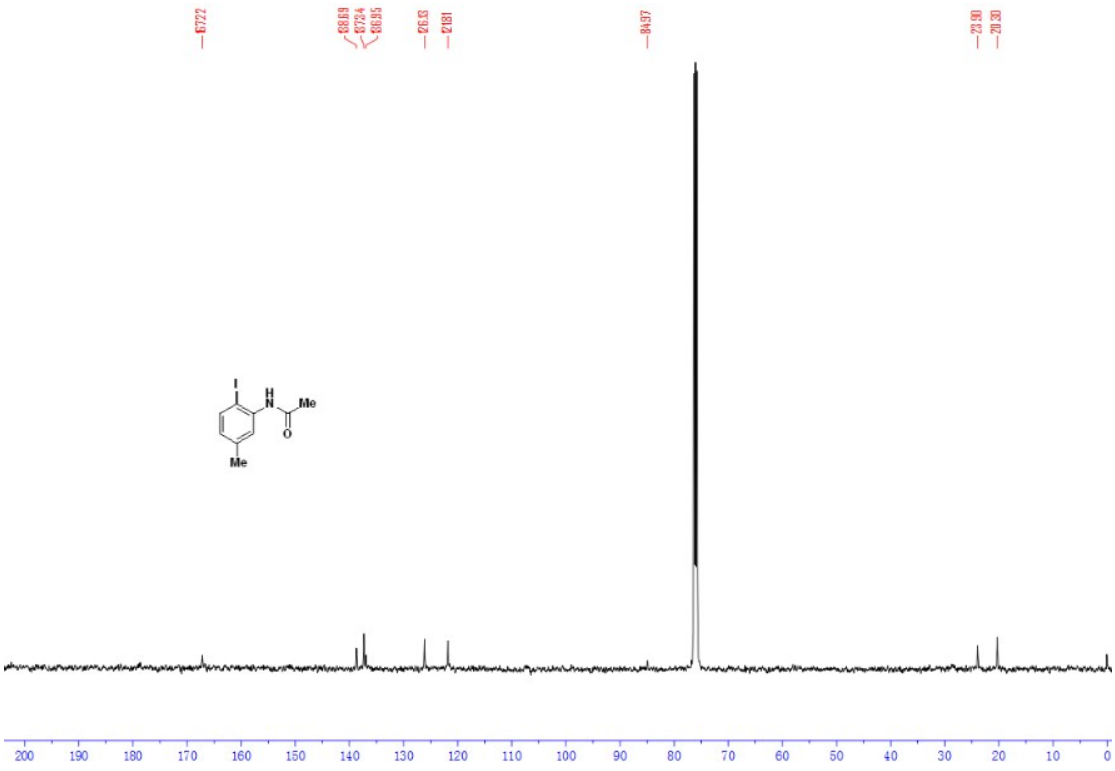
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29.90
29.30
I
H
N
Me
O
Me
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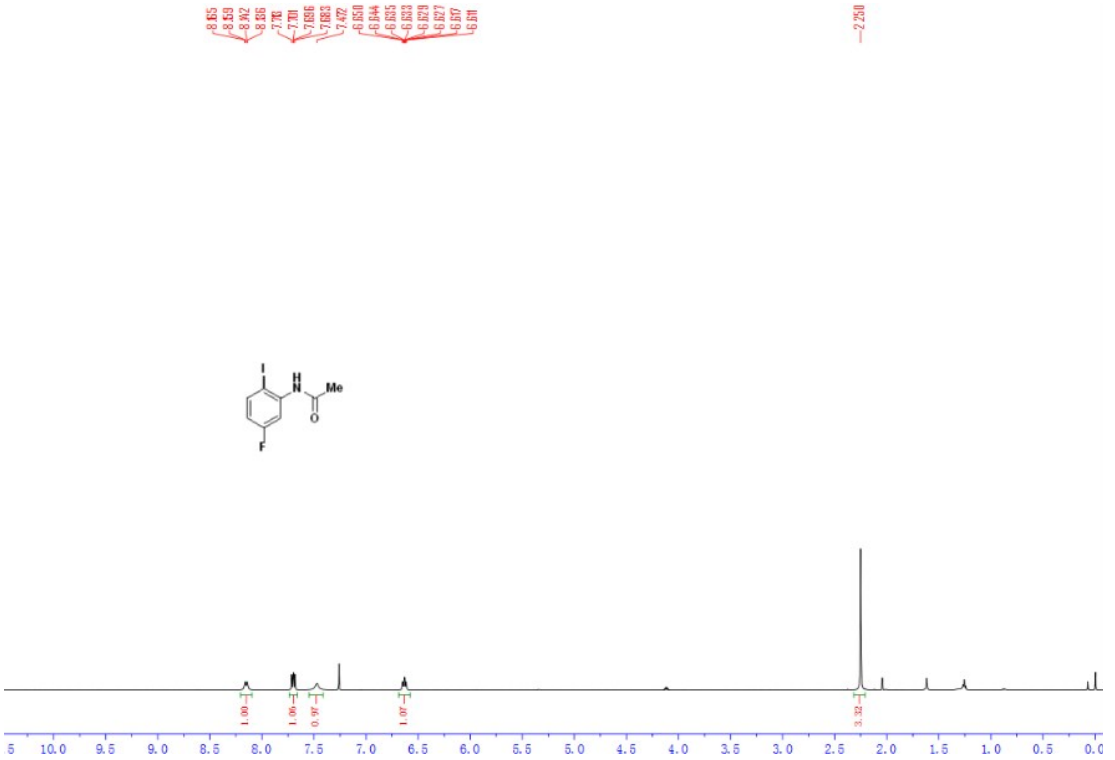
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6.644
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6.633
6.629
6.627
6.617
6.611
2.258
I
H
N
Me
O
F
1.09
1.09
0.97
1.07
3.32
5
10.0
9.5
9.0
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8.0
7.5
7.0
6.5
6.0
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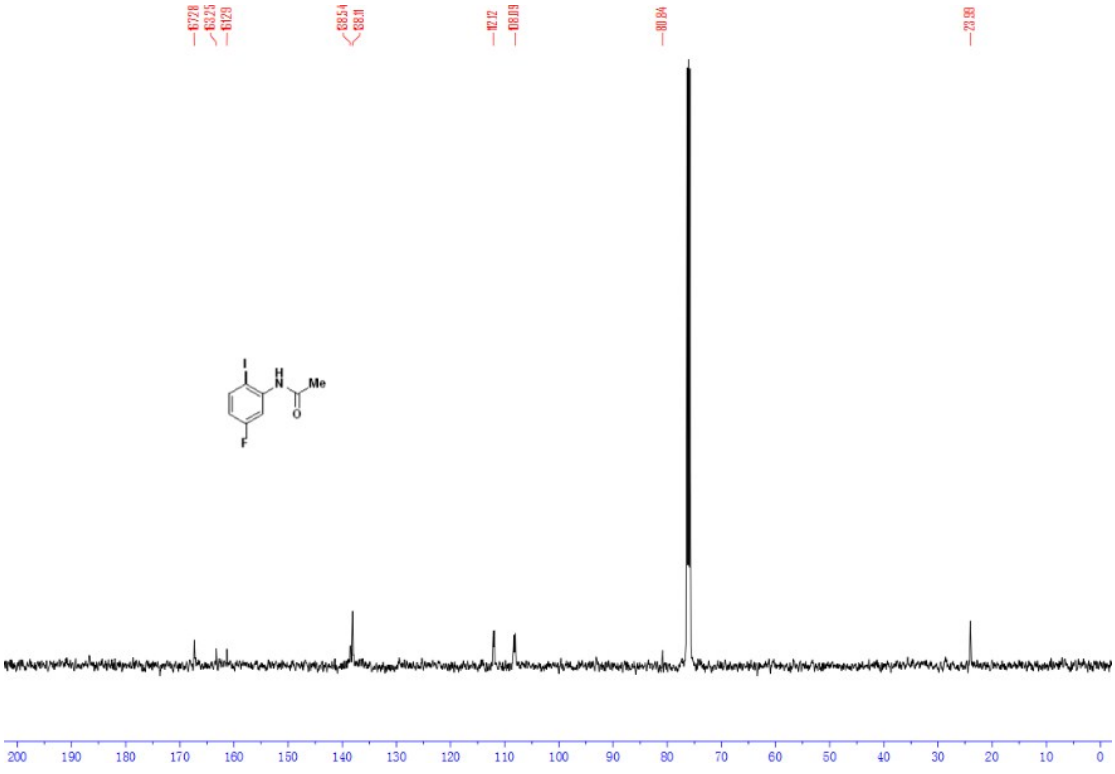
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H
N
Me
O
F
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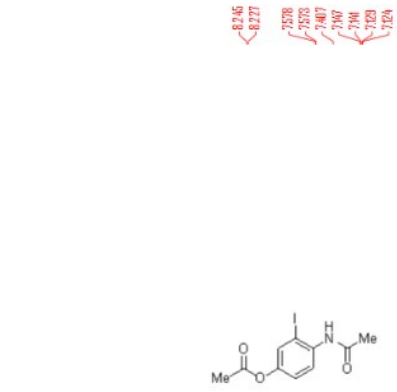
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7.183
7.124
2.316
2.271
I
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H
Me
O
Me
O
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1.02
1.03
1.10
3.00
2.96
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10.0
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9.0
8.5
8.0
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7.0
6.5
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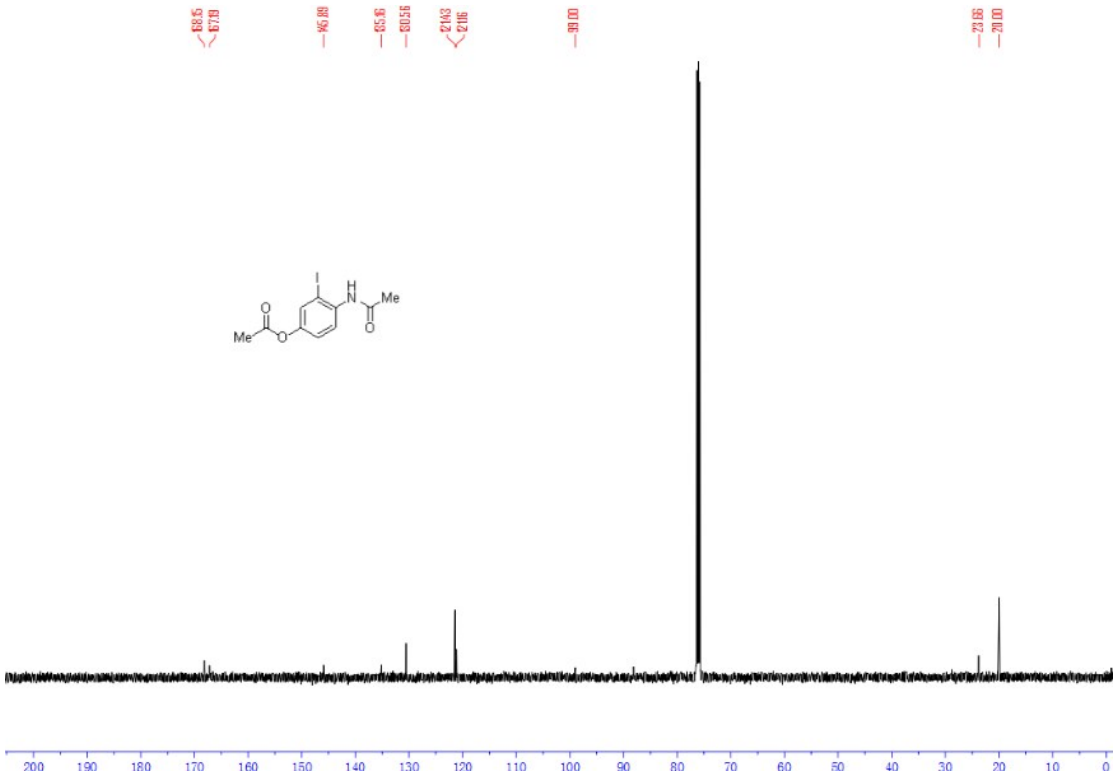
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20.00
I
N
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Me
O
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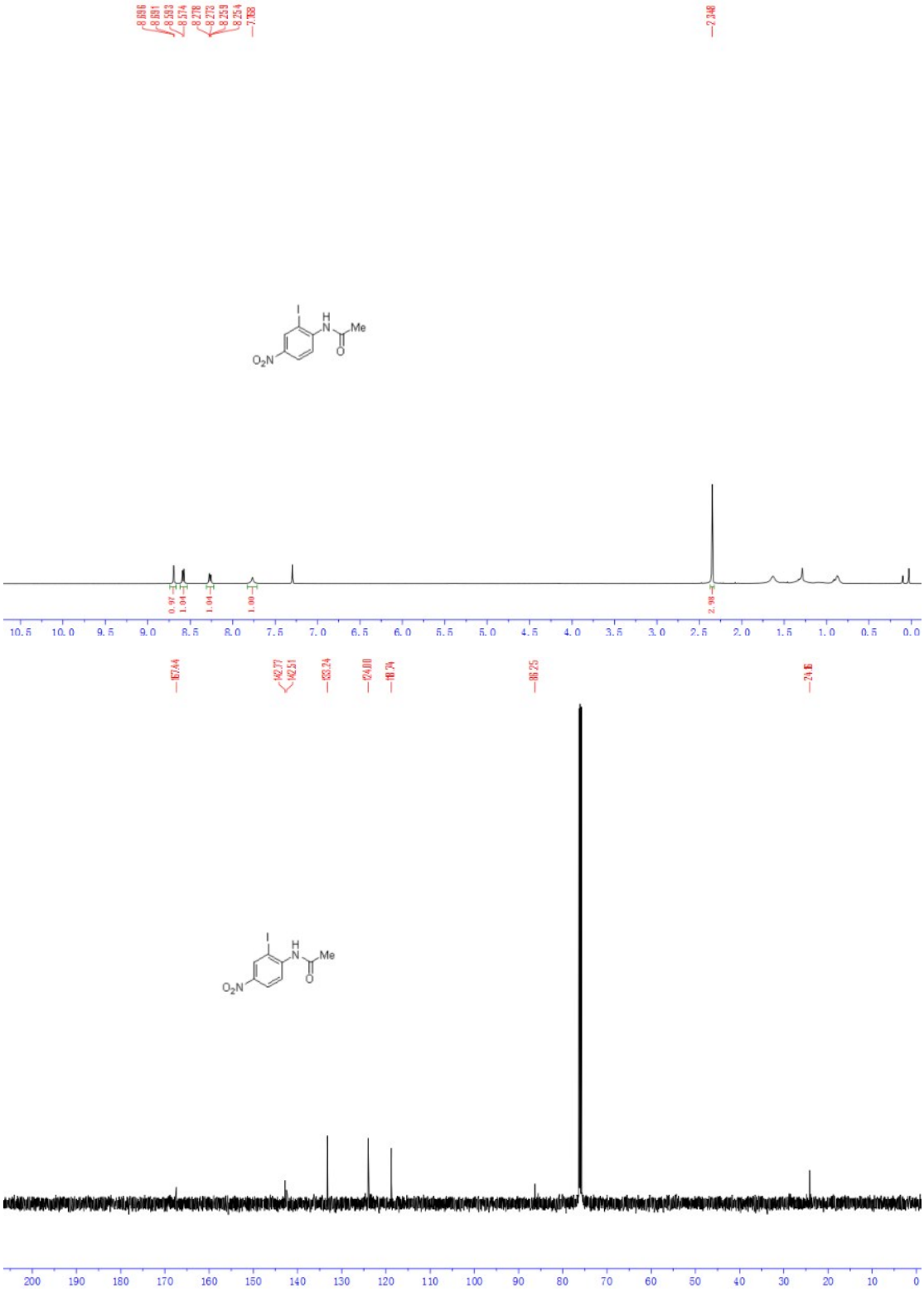
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H
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Me
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O_2N
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1.04
1.00
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2.5
2.0
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Me
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O_2N
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170
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150
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130
120
110
100
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80
70
60
50
40
30
20
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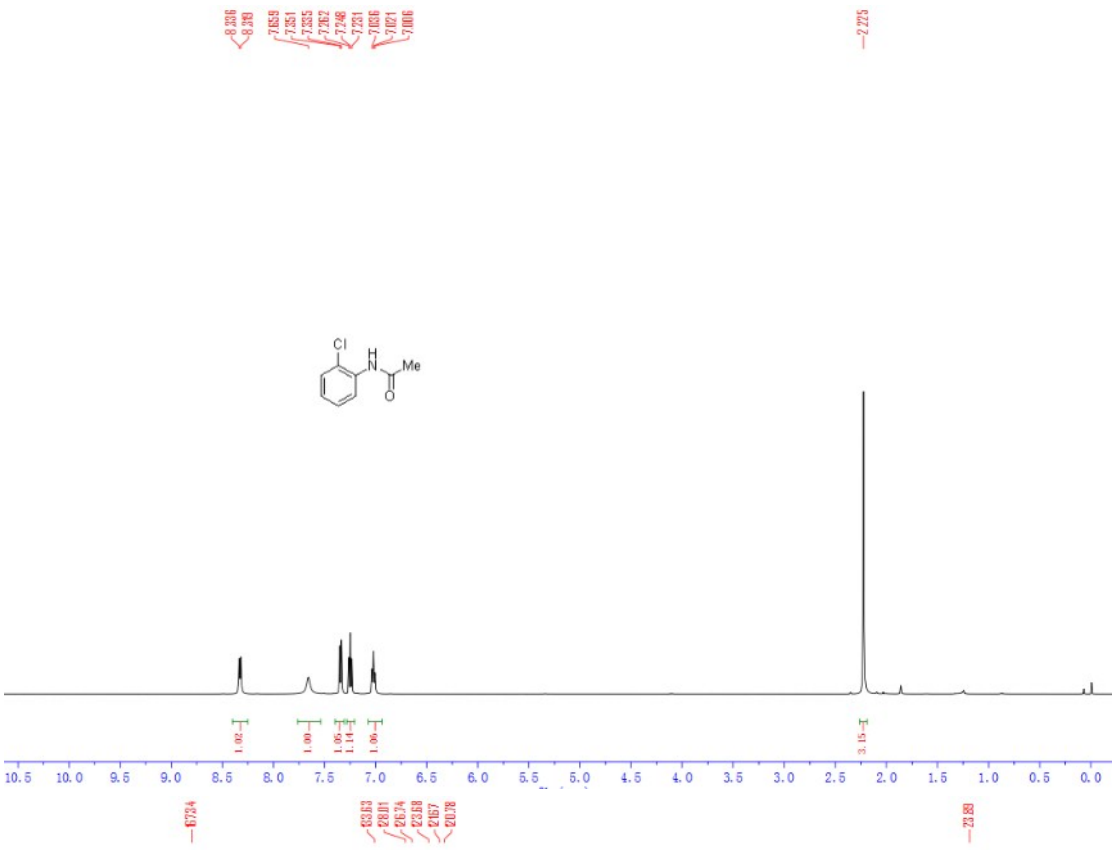
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7.335
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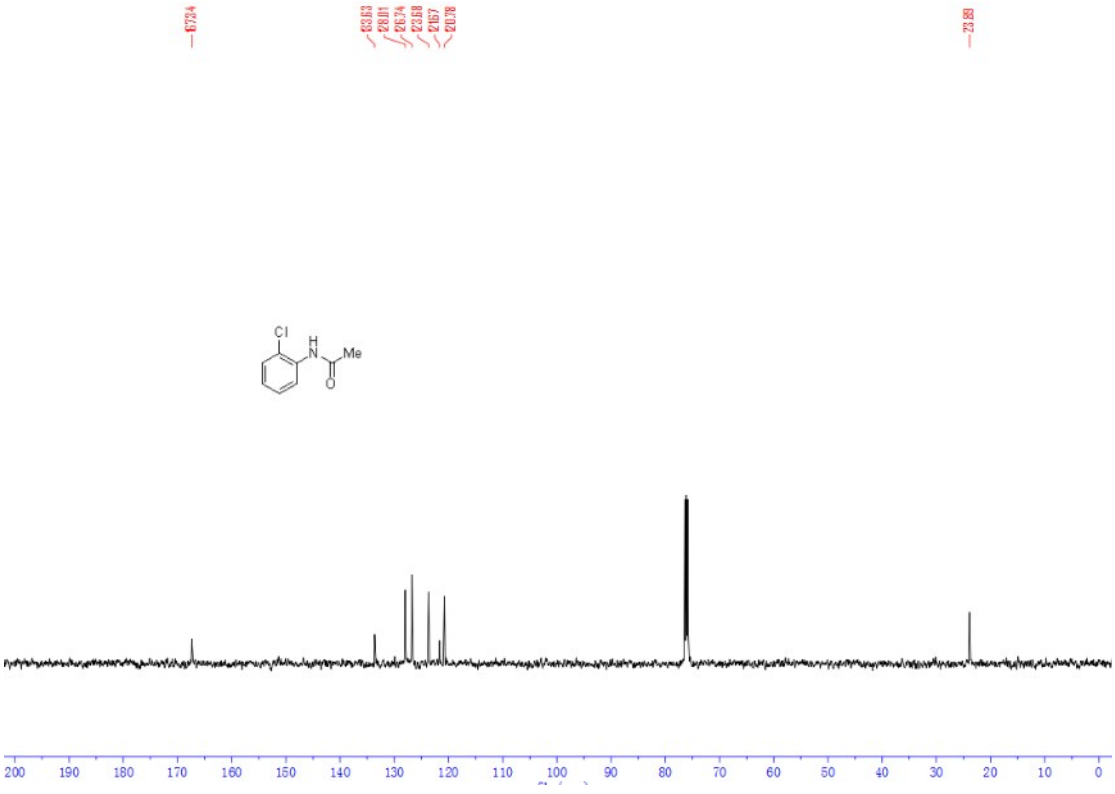
7.246
7.231
7.056
7.021
7.006
2.225
Cl
H
N
Me
O
1.02
1.00
1.06
1.14
1.06
3.15
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0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135.83
128.81
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123.68
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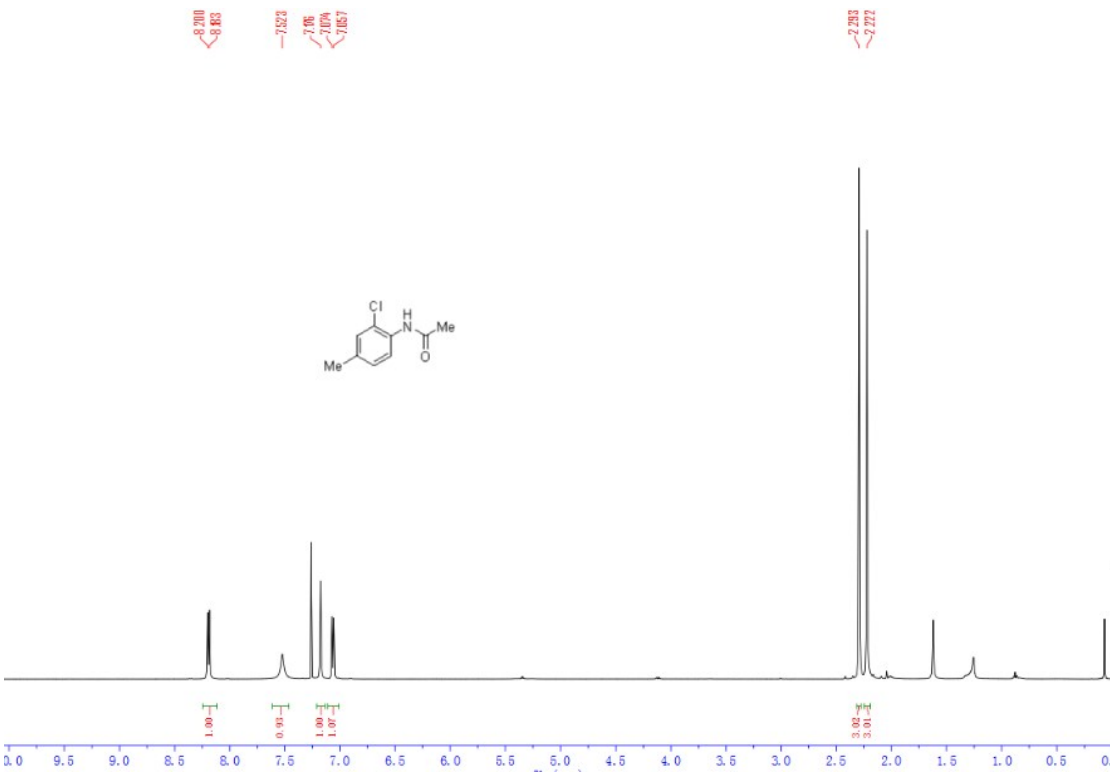
120.78
23.88
Cl
H
N
Me
O
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0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7.074
7.057
2.293
2.222
Cl
H
N
Me
O
Me
1.00
0.93
1.00
1.07
3.02
3.01
0.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
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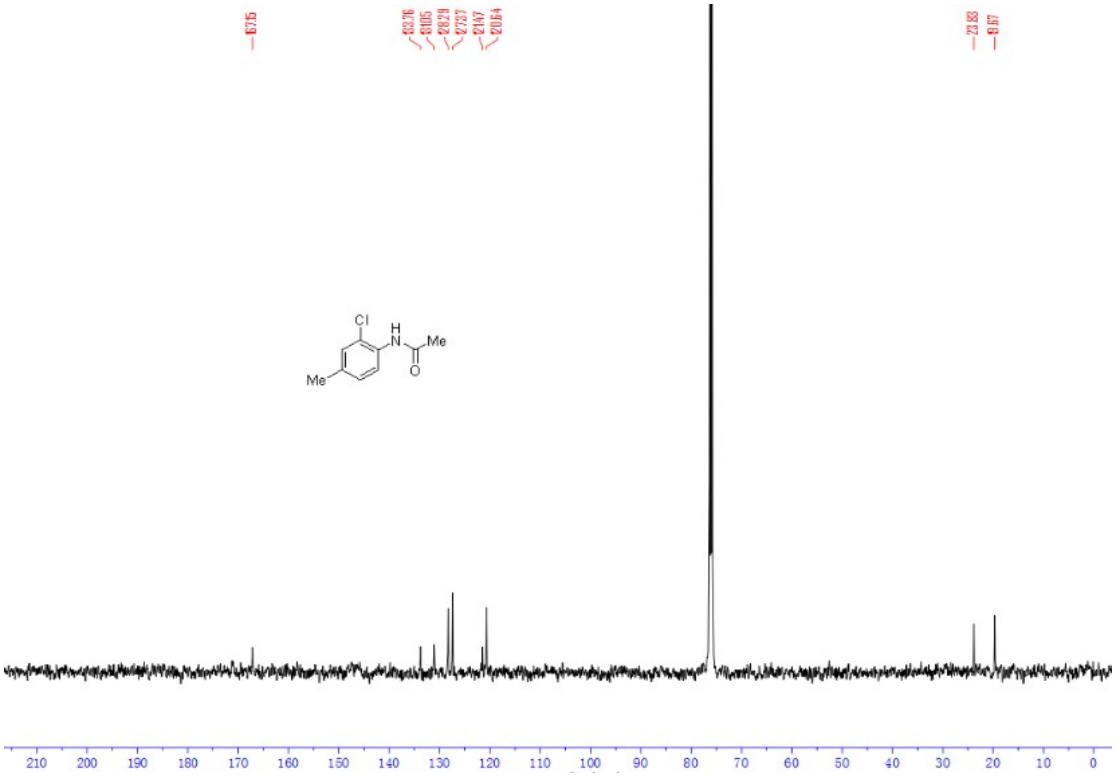
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5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131.05
128.29
127.37
121.47
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23.83
19.07
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N
Me
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Me
210
200
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150
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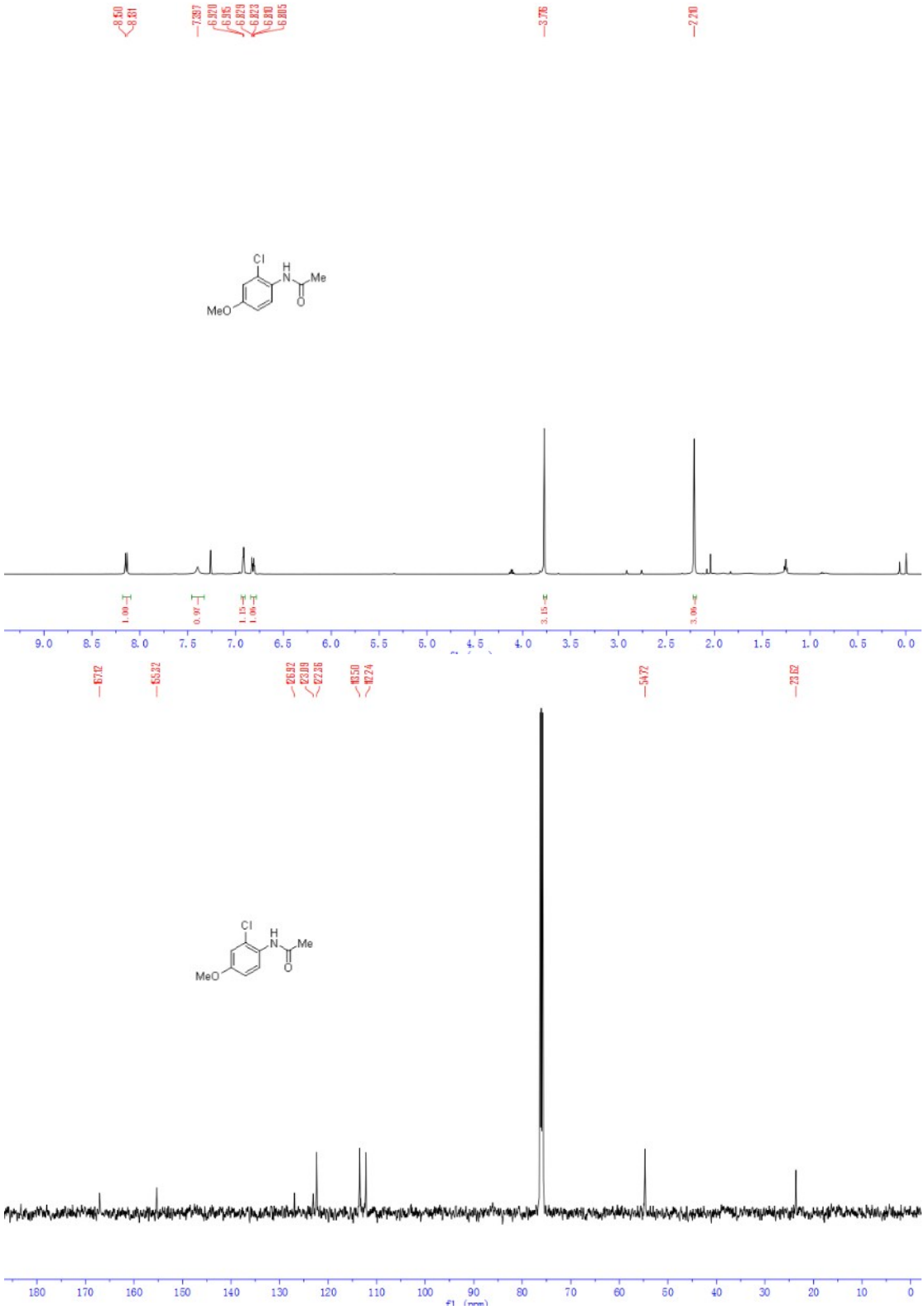
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6.9135
6.8979
6.8823
6.8680
6.8605
3.786
2.290
Cl
H
N
Me
O
MeO
1.00
0.97
1.15
1.06
3.15
3.06
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
167.12
155.32
126.82
123.89
122.36
113.50
112.24
54.72
23.62
180
170
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150
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120
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50
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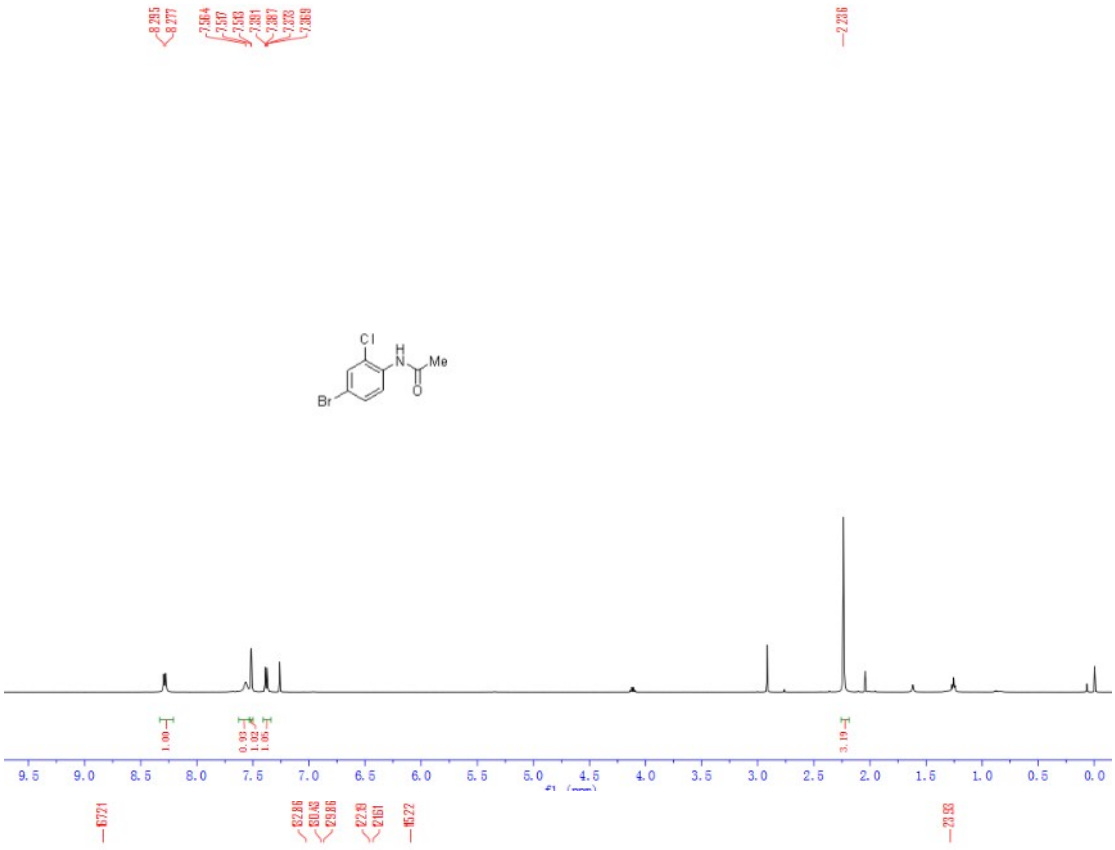
f1 (ppm)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7.333
7.319
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Cl
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N
Me
O
Br
1.00
0.93
1.04
1.05
3.19
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
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0.0
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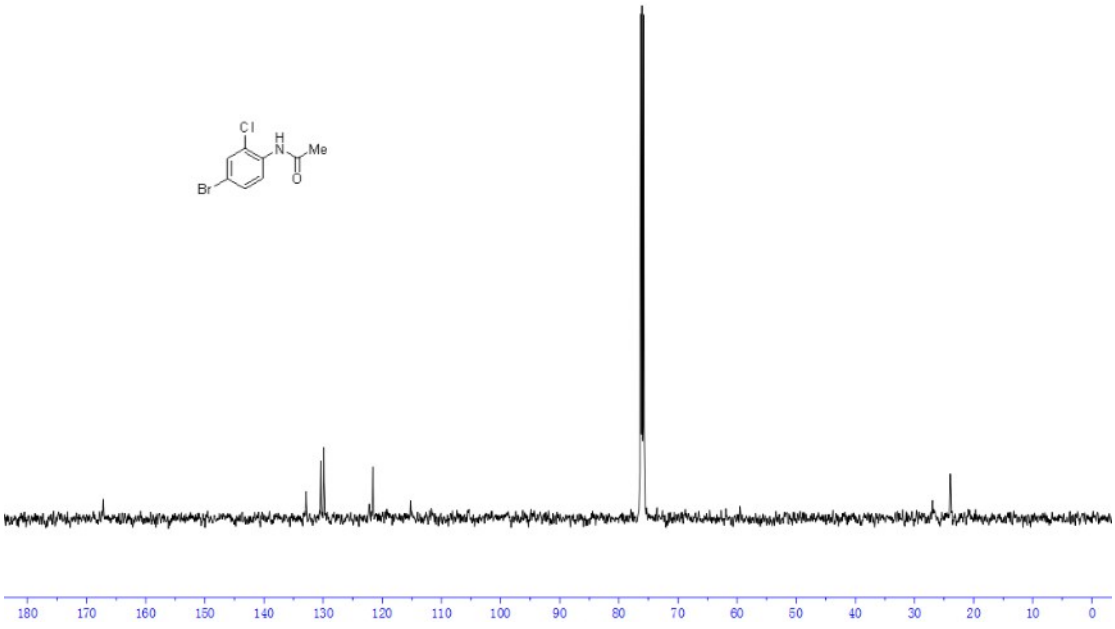
132.86
130.43
129.86
122.89
121.61
115.22
29.93


Cl
H
N
Me
O
Br
180
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150
140
130
120
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100
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70
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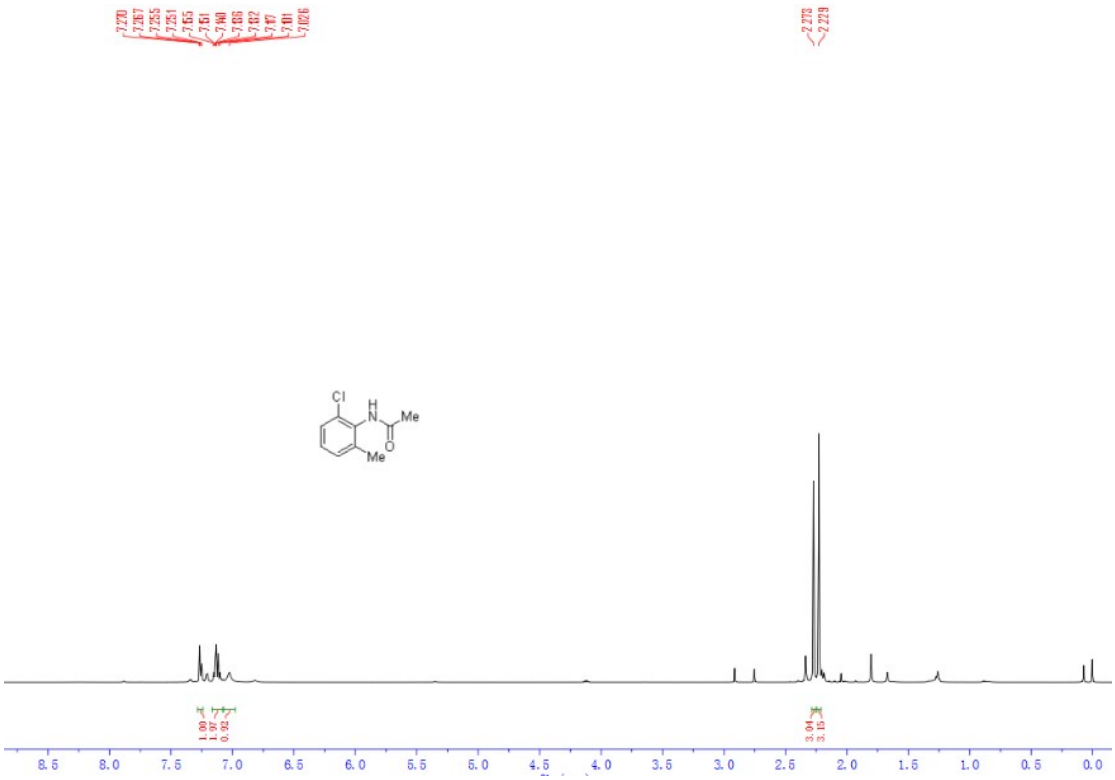
50
40
30
20
10
0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7.267
7.255
7.251
7.155
7.151
7.140
7.136
7.132
7.107
7.101
7.026
2.273
2.229
Cl
H
N
Me
O
Me
1.00
1.00
0.92
3.04
3.15
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
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3.0
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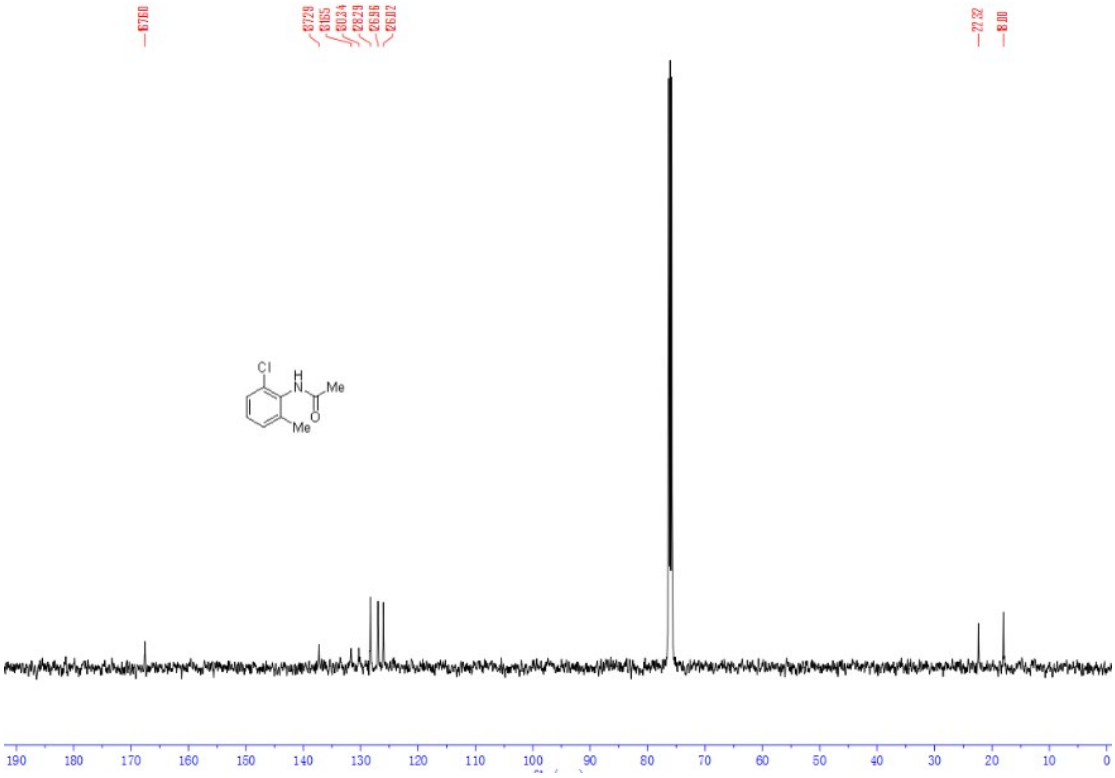
2.0
1.5
1.0
0.5
0.0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63.28
61.65
60.34
28.29
26.96
26.02
22.32
8.80
Cl
H
N
Me
O
Me
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180
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160
150
140
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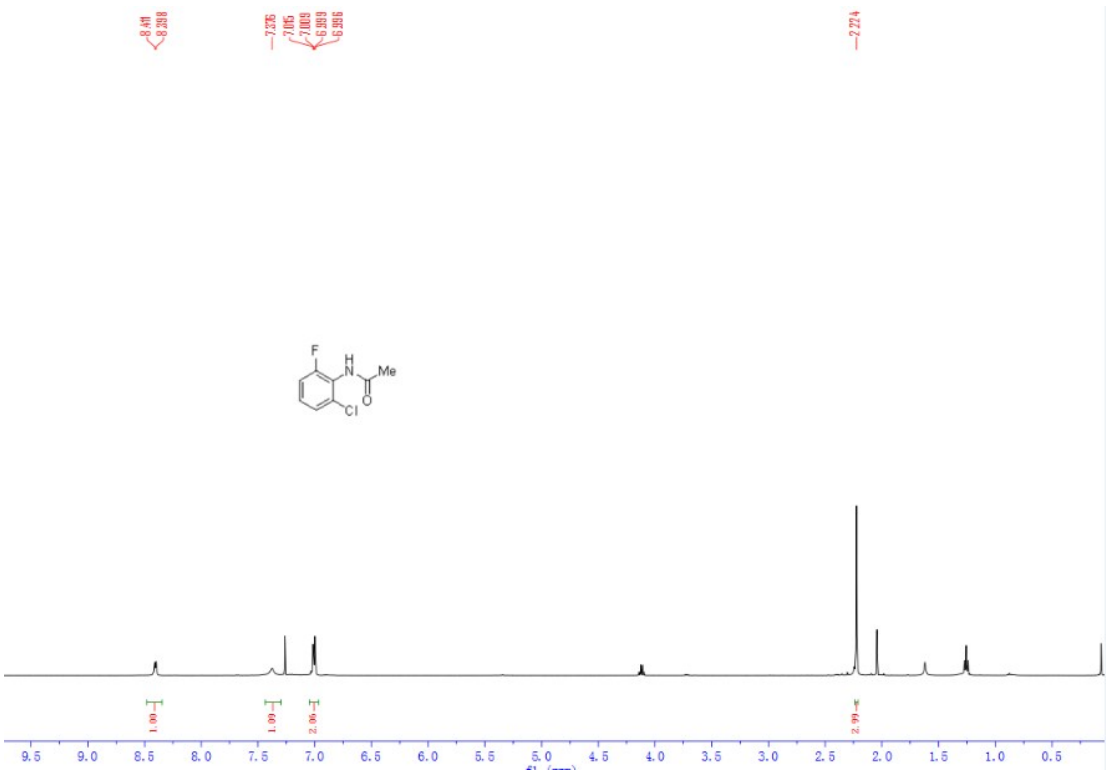
120
110
100
90
80
70
60
50
40
30
20
10
0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7.008
6.889
6.886
2.274
F
H
N
Me
O
Cl
1.00
1.09
2.06
2.99
9.5
9.0
8.5
8.0
7.5
7.0
6.5
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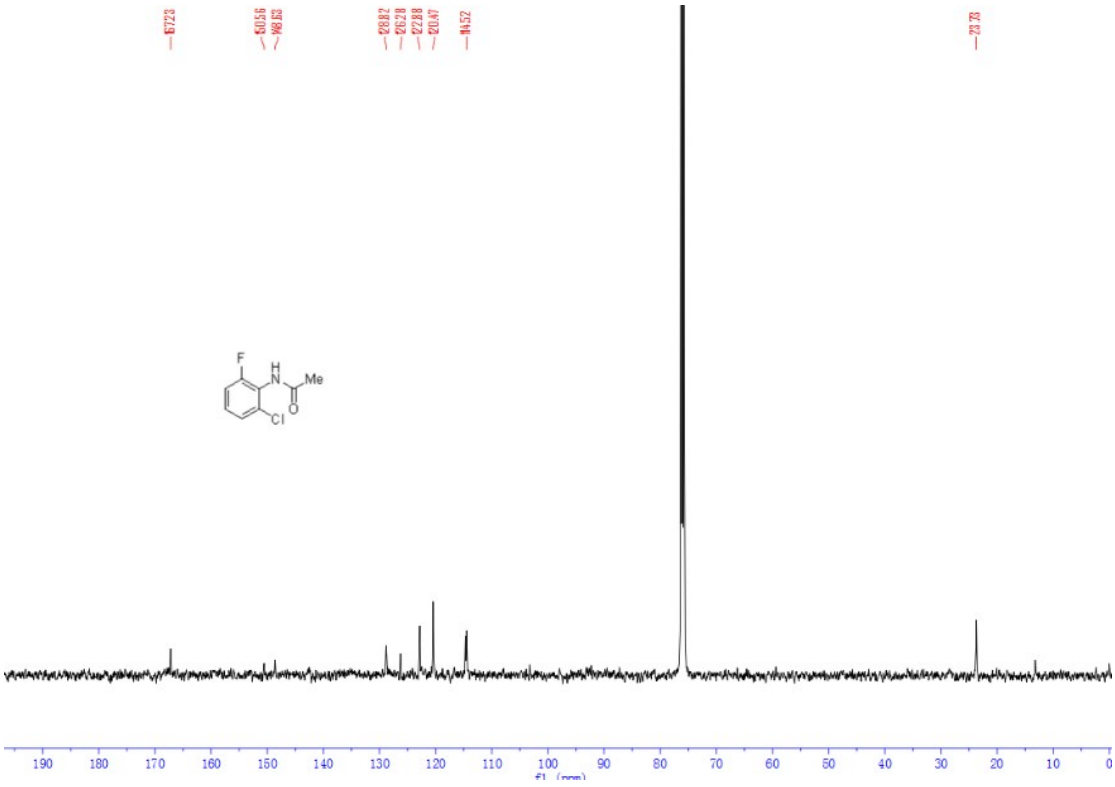
1.0
0.5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150.56
146.62
126.82
126.28
122.88
120.47
114.52
23.73
F
H
N
Me
O
Cl
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180
170
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150
140
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120
110
100
90
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50
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30
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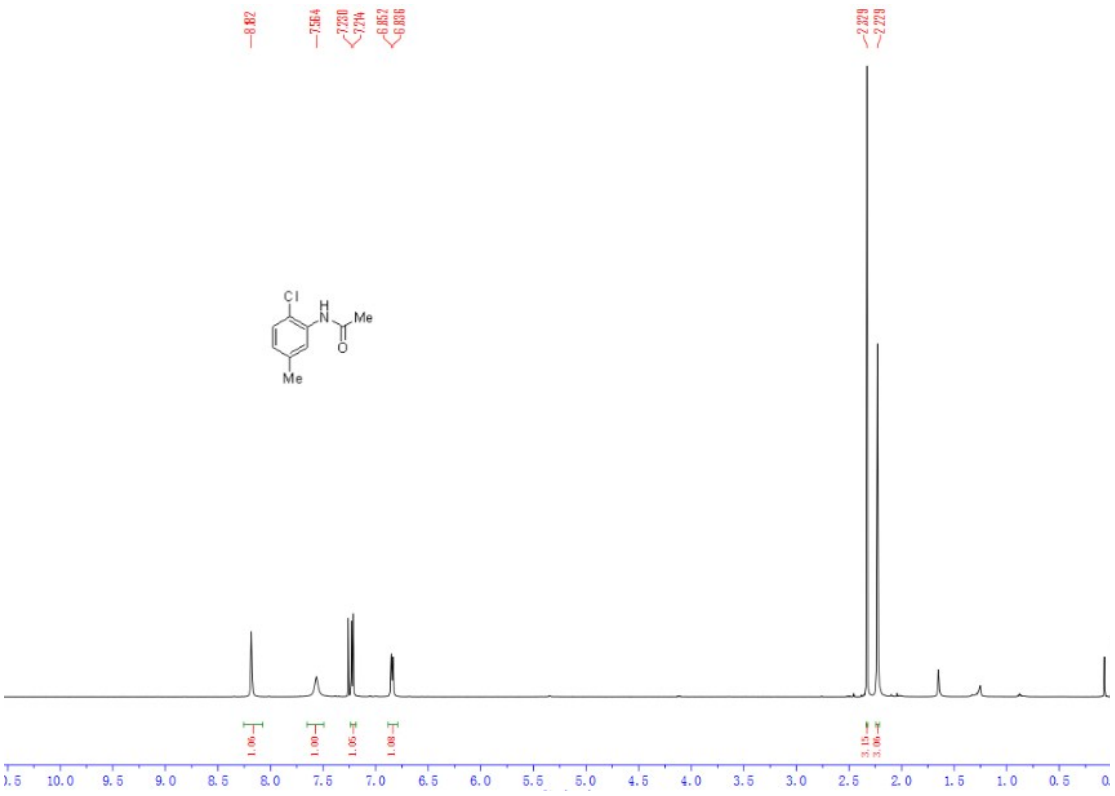
10
0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7.564
7.220
7.214
6.852
6.836
2.279
2.229
Cl
H
N
Me
O
Me
1.06
1.00
1.06
1.08
3.15
3.06
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
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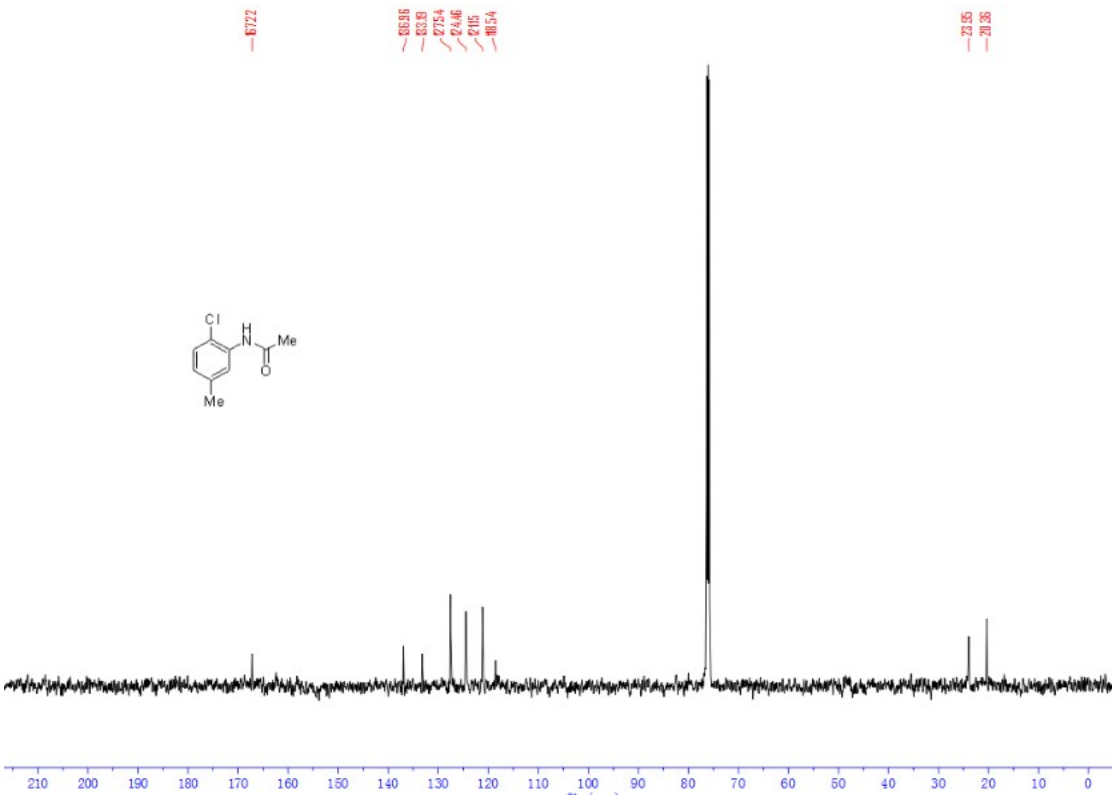
0.5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136.56
133.83
127.54
124.46
121.05
118.54
23.95
20.36
Cl
H
N
Me
O
Me
210
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110
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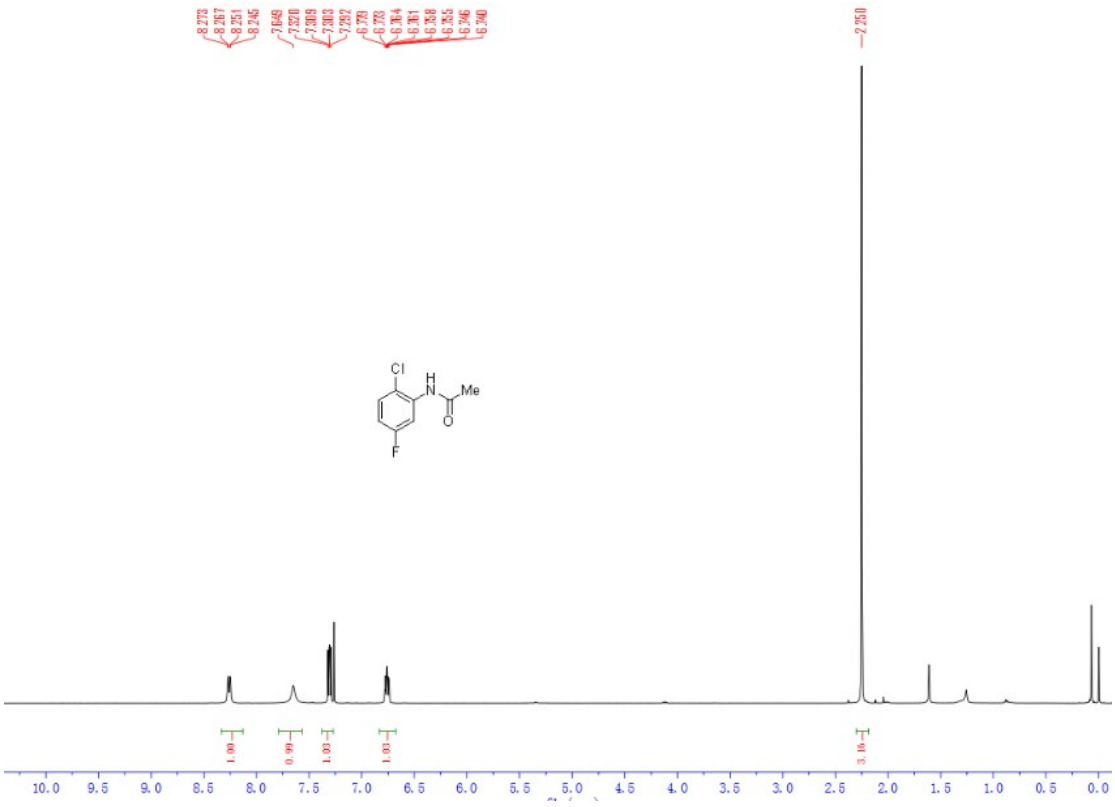
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8.267
8.251
8.245
7.648
7.320
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7.303
7.292
6.779
6.773
6.364
6.361
6.358
6.355
6.346
6.340
2.250
Cl
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N
Me
O
F
1.00
0.99
1.03
1.03
3.16
10.0
9.5
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8.0
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7.0
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6.0
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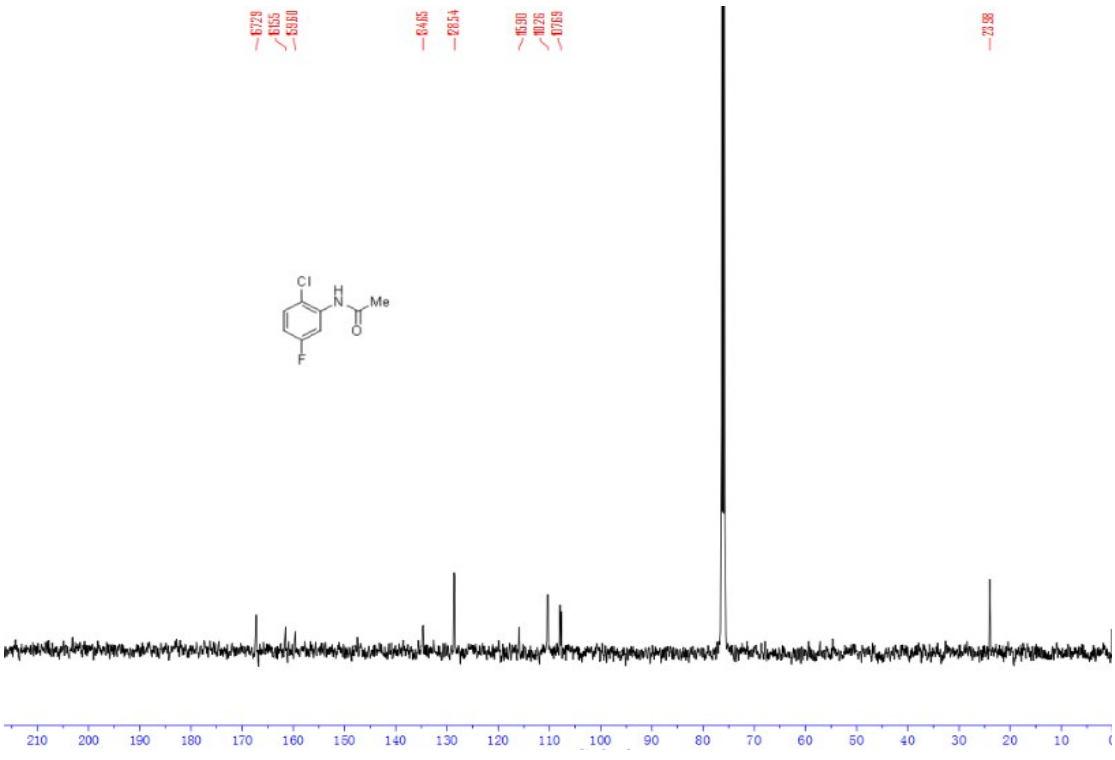
167.29
161.55
159.60
134.65
128.54
115.90
110.26
107.69
23.98
Cl
H
N
Me
O
F
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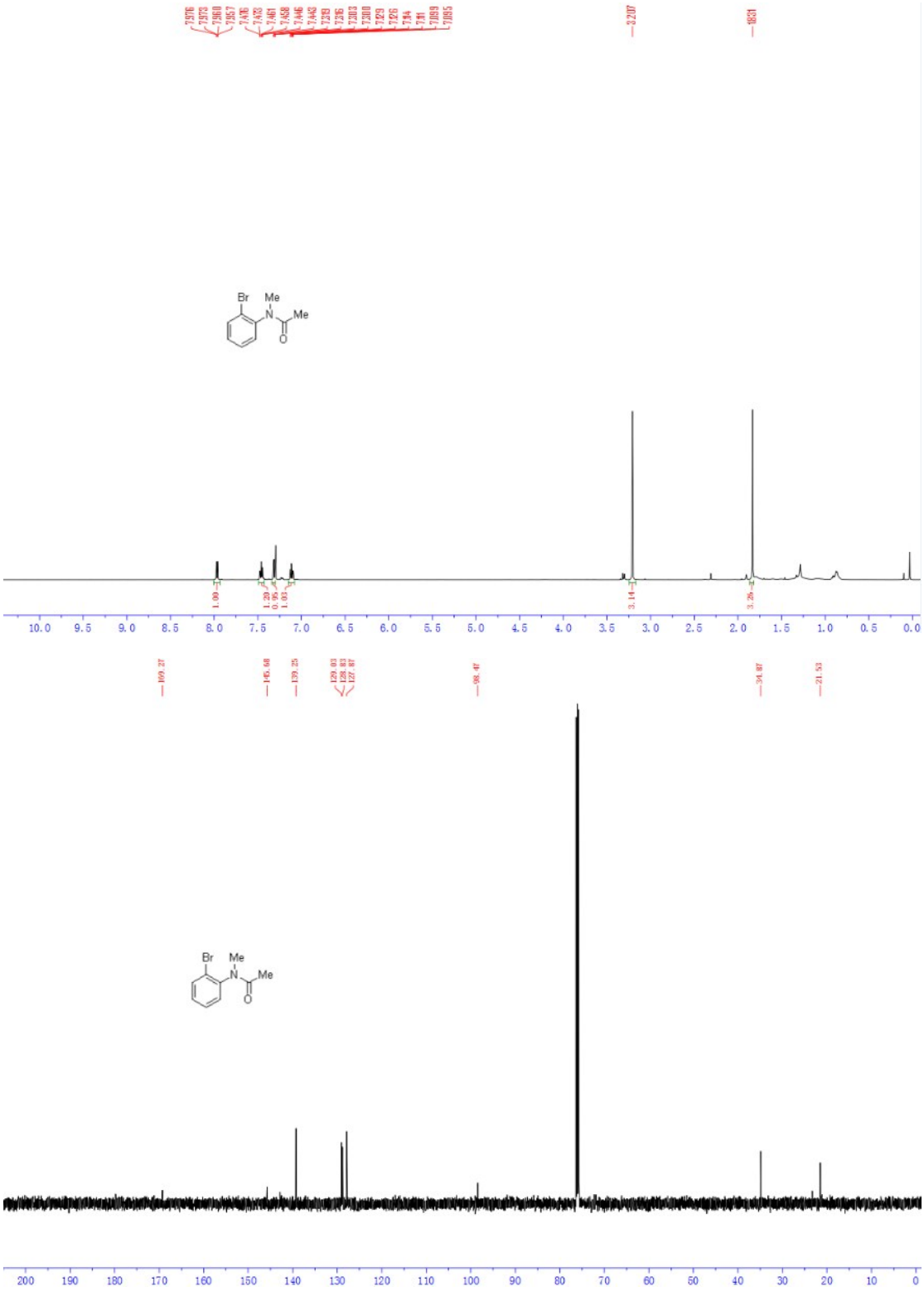
Br
Me
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Me
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8.0
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7.0
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6.0
5.5
5.0
4.5
4.0
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3.0
2.5
2.0
1.5
1.0
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200
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100
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0