Supporting information

Visible Light-Induced Intramolecular Dearomative Cyclization of α-Bromo-*N*-benzyl-alkylamide for the Synthesis of 2-Azaspiro[4.5]decanes

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Content

1. General Information

Unless otherwise noted, all reactions were carried out under an atmosphere of nitrogen using standard Schlenk techniques. Materials were purchased from commercial source and were used without further purification. Anhydrous DMF, DMA, NMP, DCE, CH_3CN, DCM were freshly distilled from calcium hydride, ^1H NMR and ^{13}C NMR spectra were recorded on a 400 MHz spectrometer. The chemical shifts for ^1H NMR were recorded in ppm downfield from tetramethylsilane (TMS) with the solvent resonance as the internal standard. The chemical shifts for ^{13}C NMR were recorded in ppm downfield using the central peak of deuterochloroform (77.00 ppm) as the internal standard. Coupling constants (*J*) are reported in Hz and refer to apparent peak multiplications. HRMS were performed under ESI ionization technique on a Q-TOF Premier Mass Spectrometer. Flash column chromatography was performed on silica gel (300-400 mesh).

2. Preparation of substrates

2.1 Representative procedure for the preparation of 2-bromo-*N*-(*tert*-butyl)- *N*-(4-methoxybenzyl)-2-methylpropanamide. (1a-1o, 1q-1s)[1]

To a solution of 4-methoxybenzaldehyde (10.0 mmol) in ethanol (20 mL), *tert*-butylamine (15 mmol) was added at room temperature. After 4 h, $NaBH_4$ (6 mmol) was added at 0 ºC and stirred for 2-3 h. After completion, the reaction was quenched with H_2O (5 mL) and the solvent was evaporated after filtered over a celite pad. The resulting residue was dissolved in EtOAc (25 mL) and washed with water (2 x 20 mL), dried over Na_2SO_4 and concentrated under reduced pressure to afford the corresponding secondary amine, which was used to the next reaction without further purification.

To a solution of the crude amine in dichloromethane (20 mL) and $^iPr_2NEt$ (12 mmol), 2-bromo-2-methylpropionyl bromide (12 mmol) was added dropwise slowly at 0 ^oC.

After completion, the reaction was quenched with H_2O (20 mL) and extracted with DCM (3 x 25 mL). The combined organic extracts were dried over Na_2SO_4 and the solvent was removed under reduced pressure. The crude product was purified by silica-gel column chromatography to give 2-bromo-*N*-(*tert*-butyl)-*N*-(4-methoxybenzyl)-2-methylpropanamide (**1a**) as a white solid (2.9 g, 86% yield, mp: 97 - 100 ºC).^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15 (d, *J* = 8.8, 2H), 6.89 – 6.86 (m, 2H), 4.97 (s, 2H), 3.80 (s, 3H), 1.93 (s, 6H), 1.37 (s, 9H) ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.4, 158.5, 131.8, 127.4, 113.8, 60.5, 59.7, 55.2, 50.1, 33.6, 28.4.

2.2 The preparation of 2-bromo-*N*-(*tert*-butyl)- *N*-(4-hydroxybenzyl)-2-methylpropanamide (1p)[2]

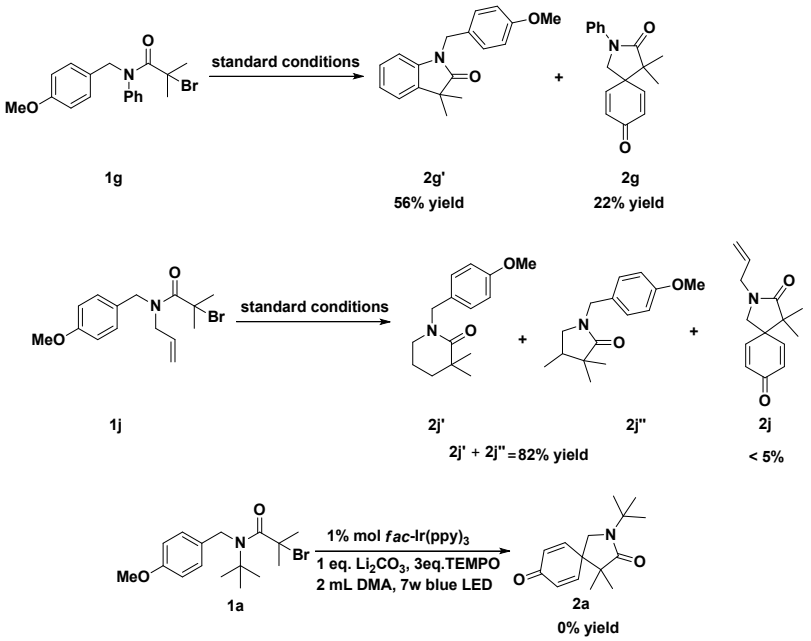
A mixture of TBS-protected 2-bromo-*N*-(*tert*-butyl)-*N*-(4-((*tert*-butyldimethylsilyl)oxy)benz-yl)-2-methylpropanamide **1o** (1 mmol) and K_3PO_4 (0.25 mmol) in DMF-H_2O (2 mL, 10:1,V/V) was stirred at room temperature until the substrate finished as indicated by TLC. Then, the reaction mixture was diluted with brine (10 mL), extracted with EtOAc (3 x 5 mL), and dried over anhydrous Na_2SO_4. The solvent was removed in a vacuum and was purified by flash column chromatography over silica gel using ethyl hexane:acetate (5:1) as eluent. Finally, the desired product **1p** was obtained with 70% yield.^{1}H NMR (400 MHz, DMSO) δ 9.29 (s, 1H), 7.04 (d, *J* = 8.4, 2H), 6.72 (d, *J* = 8.4, 2H), 4.87 (s, 2H), 1.84 (s, 6H), 1.27 (s, 9H). ^{13}C NMR (100 MHz, DMSO) δ 174.7, 160.5, 134.3, 131.8, 131.5, 119.6, 66.2, 63.4, 53.9, 37.8, 32.3.

3. A general procedure for *fac*-Ir(ppy)$_3$-catalyzed intramolecular dearomative cyclization under visible light

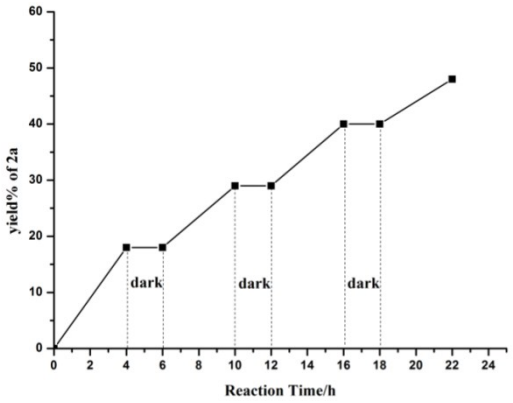
A dried Schlenk tube equipped with a stirrer bar which was evacuated and backfilled with nitrogen was added substrate **1** (0.5 mmol), *fac*-Ir(ppy)$_3$ (0.005 mmol) and Li_2CO_3 (0.5 mmol). Then 2 mL of DMA was added into the reaction tube via a syringe. The reaction mixture was

degassed by the freeze-pump-thaw method and then irradiated with a 7W blue LED in N_2 atmosphere (distance app. 5 cm) for 48 h. After the completion of the reaction, it was quenched by water and extracted with DCM (3 x 15 mL). The organic layers were combined and the pure product was obtained by flash column chromatography on silica gel.

4. The *fac*-Ir(ppy)$_3$-catalyzed intramolecular dearomative cyclization in 1g or 1j and control experiments of 1a



Intramolecular dearomative cyclization in **1g** or **1j** and radical inhibition experiments of **1a**

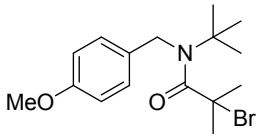


The experiment of turn on/off the light of **1a**

5. Spectral data for substrates and products

5.1 Spectral data for substrates.

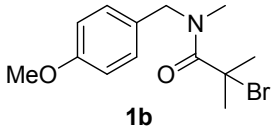
2-Bromo-*N*-(*tert*-butyl)-*N*-(4-methoxybenzyl)-2-methylpropanamide



1a

White solid, 86% yield, mp: 97 - 100 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15 (d, *J* = 8.8, 2H), 6.89 – 6.86 (m, 2H), 4.97 (s, 2H), 3.80 (s, 3H), 1.93 (s, 6H), 1.37 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.4, 158.5, 131.8, 127.4, 113.8, 60.5, 59.7, 55.2, 50.1, 33.6, 28.4. HRMS-ESI (m/z): Calculated for $C_{16}H_{25}{}^{79}BrNO_2$ $(M + H)^+$: 342.1069, Found: 342.1073.

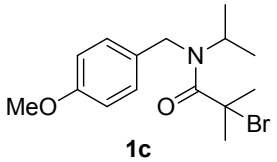
2-Bromo-*N*-methyl-*N*-(4-methoxybenzyl)-2-methylpropanamide



1b

Pale yellow liquid, 56% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 (d, *J* = 8.0, 2H), 6.87 (d, *J* = 8.4, 2H), 4.67 (s, 2H), 3.80 (s, 3H), 3.12 (s, 3H), 2.01 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 158.9, 128.6, 114.0, 57.0, 55.2, 53.2, 36.6, 32.6. HRMS-ESI (m/z): Calculated for $C_{13}H_{18}{}^{79}BrNO_2Na$ $(M + Na)^+$: 322.0419, Found: 322.0428.

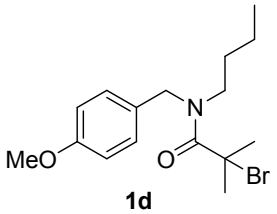
2-Bromo-*N*-isopropyl-*N*-(4-methoxybenzyl)-2-methylpropanamide



1c

Pale yellow liquid, 62% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.13 (d, *J* = 7.6, 2H), 6.83 (d, *J* = 8.4, 2H), 4.99 (s, 1H), 4.43 (s, 2H), 3.78 (s, 3H), 2.00 (s, 6H), 1.24 (d, *J* = 6.4, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.1, 158.2, 131.0, 127.4, 113.7, 57.6, 55.1, 49.7, 44.8, 32.9, 20.7. HRMS-ESI (m/z): Calculated for $C_{15}H_{23}{}^{79}BrNO_2$ $(M + H)^+$: 328.0912, Found: 328.0917.

2-Bromo-*N*-butyl-*N*-(4-methoxybenzyl)-2-methylpropanamide

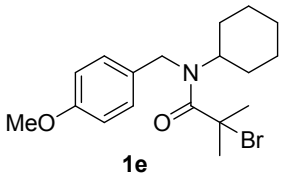


1d

Pale yellow liquid, 95% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15 – 7.12 (m, 2H), 6.87 – 6.85 (m, 2H), 4.91 – 4.57 (m, 2H), 3.78 (s, 3H), 3.59 – 3.22 (m, 2H), 1.97 (s, 6H), 1.52 (s, 2H), 1.27 – 1.26 (m, 2H), 0.89 (t, *J* = 6.4, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.2, 128.2, 114.0,

57.3, 55.1, 51.9, 48.2, 47.8, 46.7, 32.86, 29.6, 28.9, 28.4, 20.0, 13.8. HRMS-ESI (m/z): Calculated for $C_{16}H_{25}{}^{79}BrNO_2$ $(M + H)^+$: 342.1069, Found: 342.1070.

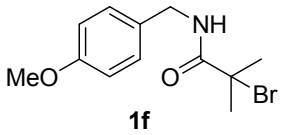
2-Bromo-*N*-cyclohexyl-*N*-(4-methoxybenzyl)-2-methylpropanamide



1e

Pale yellow liquid, 84% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.12 (d, *J* = 8.0, 2H), 6.82 (d, *J* = 8.4, 2H), 4.46 (s, 3H), 3.78 (s, 3H), 2.00 (s, 6H), 1.81 (t, *J* = 14.8, 4H), 1.68 – 1.64 (m, 2H), 1.54 – 1.45 (m, 2H), 1.37 – 1.33 (m, 1H), 1.12 – 1.05 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.2, 158.1, 131.1, 127.4, 113.6, 58.2, 57.7, 55.1, 45.9, 32.9, 31.4, 25.8, 25.2. HRMS-ESI (m/z): Calculated for $C_{18}H_{27}{}^{79}BrNO_2$ $(M + H)^+$: 368.1225, Found: 368.1230.

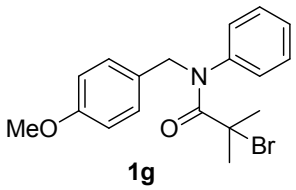
2-Bromo-*N*-(4-methoxybenzyl)-2-methylpropanamide



1f

White solid, 80% yield，mp: 47 - 49 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 – 7.20 (m, 2H), 6.89 (s, 1H), 6.90 – 6.86 (m, 2H), 4.39 (d, *J* = 5.6, 2H), 3.80 (s, 3H), 1.98 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.8, 159.1, 129.8, 128.9, 114.2, 62.9, 55.3, 43.9, 32.7. HRMS-ESI (m/z): Calculated for $C_{12}H_{16}{}^{79}BrNO_2Na$ $(M + Na)^+$: 308.0262, Found: 308.0266.

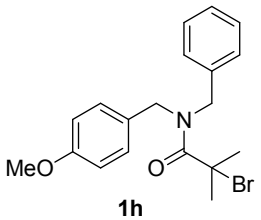
2-Bromo-*N*-(4-methoxybenzyl)-2-methyl-*N*-phenylpropanamide



1g

Pale yellow liquid, 77% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.26 (m, 3H), 7.18 – 7.06 (m, 4H), 6.82 – 6.75 (m, 2H), 4.83 (s, 2H), 3.78 (s, 3H), 1.71 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.8, 158.8, 142.0, 130.2, 129.9, 129.0, 128.6, 128.1, 113.5, 58.4, 56.2, 55.0, 33.3. HRMS-ESI (m/z): Calculated for $C_{18}H_{21}{}^{79}BrNO_2$ $(M + H)^+$: 362.0756, Found: 362.0750.

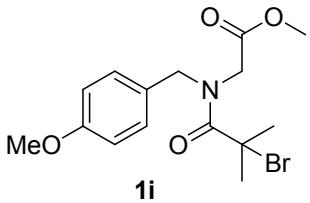
***N*-Benzyl-2-bromo-*N*-(4-methoxybenzyl)-2-methylpropanamide**



1h

Pale yellow liquid, 79% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.27 (m, 3H), 7.23 – 7.07 (m, 4H), 6.88 (s, 2H), 4.90 (s, 2H), 4.53 (s, 2H), 3.81 (s, 3H), 2.03 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 158.8, 136.3, 128.5, 127.2, 114.0, 57.1, 55.1, 51.2, 48.5, 32.9. HRMS-ESI (m/z): Calculated for $C_{19}H_{23}{}^{79}BrNO_2$ $(M + H)^+$: 376.0912, Found: 376.0913.

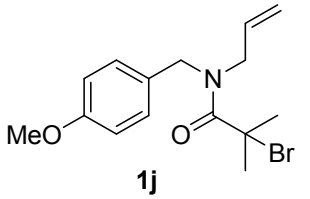
Methyl 2-(2-bromo-*N*-(4-methoxybenzyl)-2-methylpropanamido)acetate



1i

Colorless liquid, 88% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20 (s, 2H), 6.88 (d, *J* = 8.4, 2H), 5.04 (s, 2H), 3.87 (s, 2H), 3.80 (s, 3H), 3.71 (s, 3H), 2.03 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.5, 159.2, 129.0, 128.5, 127.4, 114.1, 56.1, 55.2, 53.2, 52.0, 47.8, 32.5. HRMS-ESI (m/z): Calculated for $C_{15}H_{20}{}^{79}BrNO_4$ Na $(M + Na)^+$: 380.0473, Found: 380.0474.

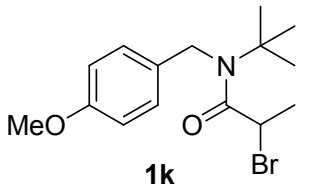
***N*-Allyl-2-bromo-*N*-(4-methoxybenzyl)-2-methylpropanamide**



1j

Colorless liquid, 80% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15 (d, *J* = 8.4, 2H), 6.87 (d, *J* = 8.4, 2H), 5.79 (s, 1H), 5.18 (s, 2H), 4.96 – 4.18 (m, 4H), 3.80 (s, 3H), 2.00 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.2, 158.6, 132.6, 128.5, 117.7, 113.8, 56.9, 54.9, 50.2, 47.9, 32.6, 30.5. HRMS-ESI (m/z): Calculated for $C_{15}H_{20}{}^{79}BrNO_2Na$ $(M + Na)^+$: 348.0575, Found: 348.0578.

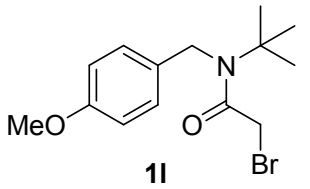
2-Bromo-*N*-(*tert*-butyl)-*N*-(4-methoxybenzyl)propanamide



1k

Pale yellow liquid, 73% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.07 (d, *J* = 8.4, 2H), 6.91 (d, *J* = 8.4, 2H), 4.71 (d, *J* = 18.8, 1H), 4.57 (d, *J* = 18.8, 1H), 4.31 (q, *J* = 6.4, 1H), 3.81 (s, 3H), 1.75 (d, *J* = 6.4, 3H), 1.45 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 158.7, 130.8, 126.2, 114.3, 58.4, 55.2, 48.0, 41.9, 28.2, 22.0. HRMS-ESI (m/z): Calculated for $C_{15}H_{22}{}^{79}BrNO_2Na$ $(M + Na)^+$: 350.0732, Found: 350.0731.

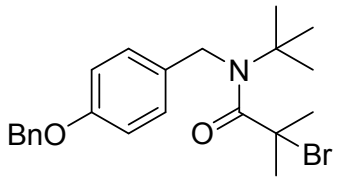
2-Bromo-*N*-(*tert*-butyl)-*N*-(4-methoxybenzyl)acetamide



1l

Pale yellow liquid, 89% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11 (d, *J* = 8.8, 2H), 6.94 – 6.86 (m, 2H), 4.61 (s, 2H), 3.81 (s, 3H), 3.75 (s, 2H), 1.44 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.8, 158.8, 130.4, 126.4, 114.4, 58.5, 55.3, 48.8, 30.0, 28.3. HRMS-ESI (m/z): Calculated for $C_{14}H_{20}{}^{79}BrNO_2Na$ $(M + Na)^+$: 336.0575, Found: 336.0561.

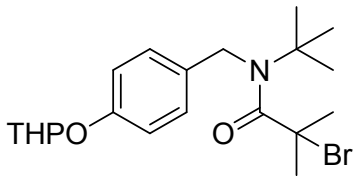
***N*-(4-(Benzyloxy)benzyl)-2-bromo-*N*-(*tert*-butyl)-2-methylpropanamide**



1m

Pale yellow liquid, 85% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 – 7.30 (m, 5H), 7.15 (d, *J* = 8.4, 2H), 6.99 – 6.92 (m, 2H), 5.05 (s, 2H), 1.93 (s, 6H), 1.38 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.4, 157.8, 136.8, 132.1, 128.5, 127.9, 127.4, 114.7, 70.0, 60.4, 59.6, 50.1, 33.6, 28.3. HRMS-ESI (m/z): Calculated for $C_{22}H_{28}{}^{79}BrNO_2Na$ $(M + Na)^+$: 440.1201, Found: 440.1212.

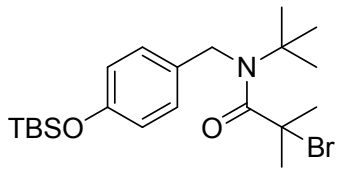
2-Bromo-*N*-(*tert*-butyl)-2-methyl-*N*-(4-((tetrahydro-2H-pyran-2-yl)oxy)benzyl)propanamide



1n

White solid, 70% yield, mp: 145 - 149 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.13 (d, *J* = 8.8, 2H), 7.05 – 6.97 (m, 2H), 5.38 (t, *J* = 3.6, 1H), 4.98 (s, 2H), 3.98 – 3.89 (m, 1H), 3.67 – 3.57 (m, 1H), 2.03 – 1.96 (m, 2H), 1.92 (s, 6H), 1.88 – 1.83 (m, 2H), 1.72 – 1.64 (m, 2H), 1.37 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.4, 156.0, 132.8, 127.3, 116.4, 96.6, 62.2, 60.6, 59.7, 50.2, 33.7, 30.4, 29.7, 28.4, 25.2, 18.9. HRMS-ESI (m/z): Calculated for $C_{20}H_{31}{}^{79}BrNO_3$ $(M + H)^+$: 412.1487, Found: 412.1486.

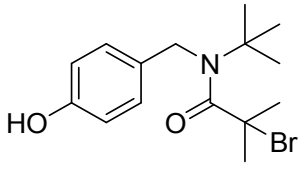
2-Bromo-*N*-(*tert*-butyl)-*N*-(4-((*tert*-butyldimethylsilyl)oxy)benzyl)-2-methylpropanamide



1o

White solid, 81% yield, mp: 79 - 82 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.08 (d, *J* = 8.4, 2H), 6.83 – 6.78 (m, 2H), 4.96 (s, 2H), 1.93 (s, 6H), 1.36 (s, 9H), 0.98 (s, 9H), 0.19 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, 154.5, 132.5, 127.4, 119.9, 60.6, 59.7, 50.2, 33.7, 28.4, 25.6, 18.2, -4.4. HRMS-ESI (m/z): Calculated for $C_{21}H_{37}{}^{79}BrNO_2Si$ $(M + H)^+$: 442.1777, Found: 442.1486.

2-Bromo-*N*-(*tert*-butyl)-*N*-(4-hydroxybenzyl)-2-methylpropanamide

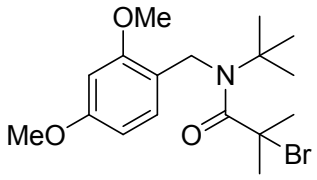


1p

White solid, 70% yield, mp: 149 - 150 ºC. ^{1}H NMR (400 MHz, DMSO) δ 9.29 (s, 1H), 7.04

(d, *J* = 8.4, 2H), 6.72 (d, *J* = 8.4, 2H), 4.87 (s, 2H), 1.84 (s, 6H), 1.27 (s, 9H). ^{13}C NMR (100 MHz, DMSO) δ 174.7, 160.5, 134.3, 131.8, 131.5, 119.6, 66.2, 63.4, 53.9, 37.8, 32.3. HRMS-ESI (m/z): Calculated for $C_{15}H_{23}{}^{79}BrNO_2$ $(M + H)^+$: 328.0912, Found: 328.0922.

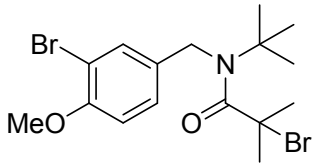
2-Bromo-*N*-(*tert*-butyl)-*N*-(2,4-dimethoxybenzyl)-2-methylpropanamide



1q

White solid, 65% yield，mp: 106 - 112 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.10 (d, *J* = 8.4, 1H), 6.52 – 6.38 (m, 2H), 4.91 (s, 2H), 3.83 (s, 3H), 3.80 (s, 3H), 1.89 (s, 6H), 1.38 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.6, 159.7, 156.7, 128.1, 120.6, 103.6, 98.2, 60.7, 59.6, 55.3, 45.0, 33.6, 28.1. HRMS-ESI (m/z): Calculated for $C_{17}H_{27}{}^{79}BrNO_3$ $(M + H)^+$: 372.1174, Found: 372,1165.

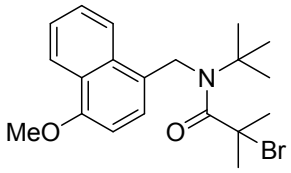
2-Bromo-*N*-(3-bromo-4-methoxybenzyl)-*N*-(*tert*-butyl)-2-methylpropanamide



1r

White solid, 82% yield, mp: 119 - 122 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, *J* = 1.6, 1H), 7.15 (dd, *J* = 8.4, 1.6, 1H), 6.87 (d, *J* = 8.4, 1H), 4.99 – 4.93 (m, 2H), 3.89 (s, 3H), 1.92 (s, 6H), 1.37 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 154.8, 133.5, 132.6, 131.1, 127.8, 126.4, 111.8, 60.21, 59.8, 56.2, 49.6, 43.2, 33.6, 32.5, 28.4. HRMS-ESI (m/z): Calculated for $C_{16}H_{24}Br_2NO_2$ $(M + H)^+$: 422.0153 (^{81}Br), 420.0174 (^{79}Br) Found: 420.0183 (^{79}Br), 422.0170 (^{81}Br).

2-Bromo-*N*-(*tert*-butyl)-*N*-((4-methoxynaphthalen-1-yl)methyl)-2-methylpropanamide

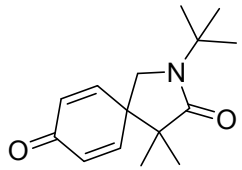


1s

Pale yellow solid, 82% yield, mp: 138 - 140 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (d, *J* = 8.4, 1H), 7.92 (d, *J* = 8.2, 1H), 7.62 – 7.51 (m, 2H), 7.34 (d, *J* = 8.0, 1H), 6.80 (d, *J* = 8.0, 1H), 4.01 (s, 3H), 1.82 (s, 6H), 1.47 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.4, 154.7, 130.5, 126.9, 125.8, 125.2, 124.1, 123.0, 121.6, 102.8, 61.1, 59.9, 55.4, 47.7, 28.1. HRMS-ESI (m/z): Calculated for $C_{20}H_{27}{}^{79}BrNO_2$ $(M + H)^+$: 392.1225, Found: 392.1227.

5.1 Spectral data for products

2-(*tert*-Butyl)-4,4-dimethyl-2-azaspiro[4.5]deca-6,9-diene-3,8-dione

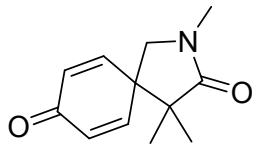


2a

.

White solid, 85% yield，mp: 108 - 112 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.91 – 6.87 (m, 2H), 6.40 – 6.36 (m, 2H), 3.39 (s, 2H), 1.42 (s, 9H), 1.05 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 185.0, 177.1, 148.9, 130.7, 54.2, 50.1, 49.5, 47.5, 27.5, 20.4. HRMS-ESI (m/z): Calculated for $C_{15}H_{22}NO_2$ $(M + H)^+$: 248.1651, Found: 248.1654.

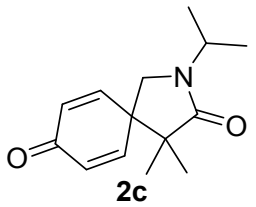
2,4,4-Trimethyl-2-azaspiro[4.5]deca-6,9-diene-3,8-dione



2b

Pale yellow liquid, 85% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.88 (d, J = 10.4, 2H), 6.39 (d, J = 10.4, 2H), 3.35 (s, 2H), 2.93 (s, 3H), 1.09 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 184.9, 177.0, 148.6, 130.6, 53.4, 49.4, 48.3, 30.0, 20.6. HRMS-ESI (m/z): Calculated for $C_{12}H_{16}NO_2$ $(M + H)^+$: 206.1181, Found: 206.1182.

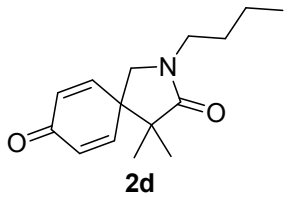
2-Isopropyl-4,4-dimethyl-2-azaspiro[4.5]deca-6,9-diene-3,8-dione



2c

Pale yellow solid, 91% yield，mp: 102 - 107 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.89 – 6.83 (m, 2H), 6.43 – 6.34 (m, 2H), 4.48 – 4.38 (m, 1H), 3.29 (s, 2H), 1.15 (d, J = 7.8, 6H), 1.08 (s, 6H).^{13}C NMR (100 MHz, $CDCl_3$) δ 184.8, 176.0, 148.6, 130.6, 49.7, 48.0, 46.2, 42.6, 20.3, 19.3. HRMS-ESI (m/z): Calculated for $C_{14}H_{20}NO_2$ $(M + H)^+$: 234.1494, Found: 234.1491.

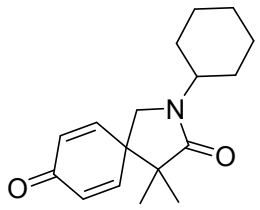
2-Butyl-4,4-dimethyl-2-azaspiro[4.5]deca-6,9-diene-3,8-dione



2d

Pale yellow liquid, 73% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.88 (d, J = 10.2, 2H), 6.39 (d, J = 10.2, 2H), 3.36 – 3.33 (m, 4H), 1.55 – 1.48 (m, 2H), 1.37 – 1.30 (m, 2H), 1.09 (s, 6H), 0.94 (t, J = 7.2, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 184.8, 176.6, 148.6, 130.5, 51.1, 49.5, 48.2, 42.3, 29.0, 20.5, 19.8, 13.5. HRMS-ESI (m/z): Calculated for $C_{15}H_{22}NO_2$ $(M + H)^+$: 248.1651, Found: 248.1646.

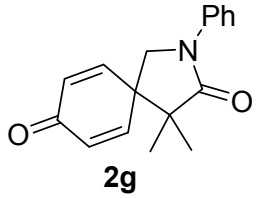
2-Cyclohexyl-4,4-dimethyl-2-azaspiro[4.5]deca-6,9-diene-3,8-dione



2e

Pale yellow solid, 78% yield，mp: 101 - 110 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.86 (d, *J* = 10.2, 2H), 6.37 (d, *J* = 10.2, 2H), 4.04 – 3.95 (m, 1H), 3.30 (s, 2H), 1.87 – 1.62 (m, 7H), 1.44 – 1.31 (m, 4H), 1.07 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 184.8, 176.0, 148.6, 130.6, 50.5, 49.6, 48.2, 47.3, 29.9, 25.1, 20.4. HRMS-ESI (m/z): Calculated for $C_{18}H_{24}NO_2$ $(M + H)^+$: 274.1807, Found: 274.1802.

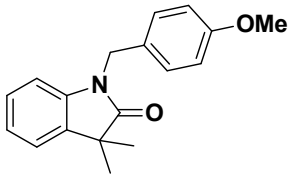
4,4-Dimethyl-2-phenyl-2-azaspiro[4.5]deca-6,9-diene-3,8-dione



2g

Pale yellow solid, 22% yield，mp: 105 - 110 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 – 7.60 (m, 2H), 7.44 – 7.36 (m, 2H), 7.22 – 7.18 (m, 1H), 7.02 – 6.94 (m, 2H), 6.51 – 6.37 (m, 2H), 3.84 (s, 2H), 1.21 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 184.7, 176.0, 148.0, 138.7, 131.0, 129.0, 125.0, 119.7, 52.4, 50.3, 47.7, 29.5, 20.8. HRMS-ESI (m/z): Calculated for $C_{17}H_{18}NO_2$ $(M + H)^+$: 268.1333, Found: 268.1337.

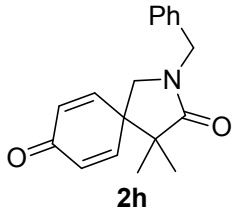
1-(4-Methoxybenzyl)-3,3-dimethylindolin-2-one



2g'

Pale yellow liquid, 56% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 – 7.19 (m, 3H), 7.16 – 7.12 (m, 1H), 7.02 (t, *J* = 7.2, 1H), 6.84 (d, *J* = 8.8, 2H), 6.74 (d, *J* = 7.6, 1H), 4.85 (s, 2H), 3.77 (s, 3H), 1.42 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 181.4, 159.0, 141.6, 135.8, 128.5, 128.2, 127.5, 122.4, 122.3, 114.12, 109, 55.2, 44.1, 43.0, 24.5. HRMS-ESI (m/z): Calculated for $C_{18}H_{19}NO_2Na$ $(M + Na)^+$: 304.1313, Found: 304.1313.

2-Benzyl-4,4-dimethyl-2-azaspiro[4.5]deca-6,9-diene-3,8-dione

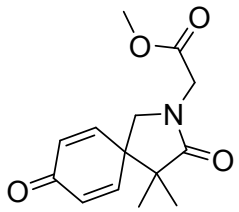


2h

Pale yellow liquid, 87% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.29 (m, 3H), 7.28 – 7.24 (m, 2H), 6.82 – 6.79 (m, 2H), 6.36 – 6.33 (m, 2H), 4.52 (s, 2H), 3.20 (s, 2H), 1.12 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 184.8, 176.8, 148.4, 135.5, 130.6, 128.8, 128.1, 127.9, 50.6, 49.4,

48.0, 46.8, 20.5. HRMS-ESI (m/z): Calculated for $C_{18}H_{19}NO_2Na$ $(M + Na)^+$: 304.1313, Found: 304.1310.

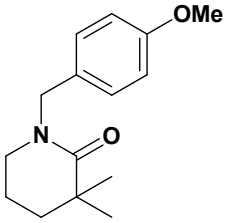
Methyl 2-(4,4-dimethyl-3,8-dioxo-2-azaspiro[4.5]deca-6,9-dien-2-yl)acetate



2i

Pale yellow liquid, 89% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.99 (d, *J* = 10.4, 2H), 6.40 (d, *J* = 10.4, 2H), 4.13 (s, 2H), 3.75 (s, 3H), 3.46 (s, 2H), 1.13 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 184.9, 177.6, 168.8, 148.4, 130.7, 52.3, 51.6, 49.0, 48.4, 43.6, 20.6. HRMS-ESI (m/z): Calculated for $C_{14}H_{18}NO_4$ $(M + H)^+$: 264.1236, Found: 264.1234.

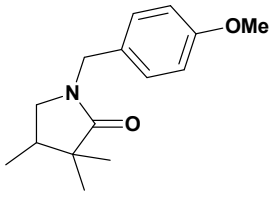
1-(4-Methoxybenzyl)-3,3-dimethylpiperidin-2-one



2j'

colorless liquid, **2j**'+**2j**"=82% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15 – 7.12 (m, 2H), 6.88 – 6.81 (m, 2H), 4.46 (d, *J* = 14.4, 1H), 4.29 (d, *J* = 14.4, 1H), 3.78 (s, 3H), 3.46 (dd, *J* = 10.0, 4.8, 1H), 3.35 (dd, *J* = 10.0, 7.6, 1H), 3.22 (t, *J* = 10.4, 1H), 2.86 (dd, *J* = 10.0, 8.4, 1H), 2.44 – 2.35 (m, 1H), 1.90 (s, 1H), 1.23 (s, 3H), 0.97 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.2, 159.1, 129.4, 128.3, 114.1, 55.2, 48.7, 46.0, 44.0, 31.4, 29.6, 24.2, 18.2. HRMS-ESI (m/z): Calculated for $C_{15}H_{21}NO_2Na$ $(M + Na)^+$: 270.1470, Found: 270.1457.

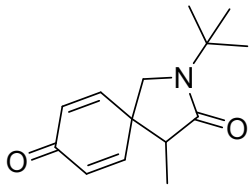
1-(4-Methoxybenzyl)-3,3,4-trimethylpyrrolidin-2-one



2j"

colorless liquid, **2j**'+**2j**"=82% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.13 (d, *J* = 8.4, 2H), 6.88 – 6.81 (m, 2H), 4.43 (d, *J* = 14.4, 1H), 4.30 (d, *J* = 14.4, 1H), 3.79 (s, 3H), 3.15 (dd, *J* = 9.6, 7.6, 1H), 2.70 (t, *J* = 9.2, 1H), 2.07 – 1.96 (m, 1H), 1.14 (s, 3H), 0.92 – 0.91 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.7, 159.0, 129.3, 128.9, 114.0, 55.2, 50.4, 45.9, 43.3, 38.3, 23.6, 18.2, 12.4. HRMS-ESI (m/z): Calculated for $C_{15}H_{21}NO_2Na$ $(M + Na)^+$: 270.1470, Found: 270.1465.

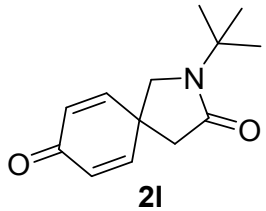
2-(*tert*-Butyl)-4-methyl-2-azaspiro[4.5]deca-6,9-diene-3,8-dione



2k

Pale yellow liquid, 80% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.88 – 6.85 (m, 1H), 6.82 – 6.78 (m, 1H), 6.39 (d, *J* = 10.0, 2H), 3.52 (d, *J* = 10.0, 1H), 3.31 (d, *J* = 10.0, 1H), 2.66 (q, *J* = 7.2, 14.4, 1H), 1.42 (s, 9H), 0.93 (d, *J* = 7.2, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 185.4, 174.0, 150.1, 148.0, 131.3, 130.4, 54.5, 51.1, 47.3, 46.3, 27.6, 9.7. HRMS-ESI (m/z): Calculated for $C_{14}H_{20}NO_2$ $(M + H)^+$: 234.1494, Found: 234.1491.

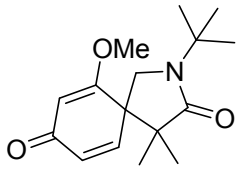
2-(*tert*-Butyl)-2-azaspiro[4.5]deca-6,9-diene-3,8-dione[2]



2l

Pale yellow liquid, 84% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.97 – 6.89 (m, 2H), 6.34 – 6.31 (m, 2H), 3.48 (s, 2H), 2.53 (s, 2H), 1.43 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 184.9, 171.6, 150.0, 129.3, 54.6, 53.0, 42.5, 40.8, 27.6.

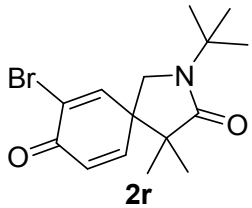
2-(*tert*-Butyl)-6-methoxy-4,4-dimethyl-2-azaspiro[4.5]deca-6,9-diene-3,8-dione



2q

Pale yellow solid, 66% yield，mp: 132 - 134 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.64 (d, *J* = 10.2, 1H), 6.32 – 6.29 (m, 1H), 5.56 (s, 1H), 3.69 (s, 3H), 3.56 – 3.49 (m, 2H), 1.41 (s, 9H), 1.18 (s, 3H), 0.90 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.8, 177.4, 176.4, 144.6, 130.2, 102.6, 55.2, 54.1, 50.6, 49.3, 49.2, 29.6, 27.3, 23.1, 19.0. HRMS-ESI (m/z): Calculated for $C_{16}H_{24}NO_3$ $(M + H)^+$: 278.1756, Found: 278.1759.

7-Bromo-2-(*tert*-butyl)-4,4-dimethyl-2-azaspiro[4.5]deca-6,9-diene-3,8-dione

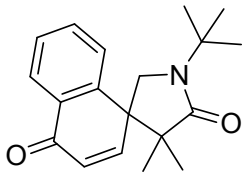


2r

Pale yellow solid, 45% yield，mp: 90 - 94 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (d, *J* = 2.8, 1H), 6.92 (dd, *J* = 10.0, 2.8, 1H), 6.47 (d, *J* = 10.0, 1H), 3.45 (d, *J* = 10.4, 1H), 3.41 (d, *J* = 10.4, 1H), 1.41 (s, 9H), 1.06 (d, *J* = 8.4, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.8, 176.6, 149.2, 149.0, 129.1, 126.1, 54.5, 51.1, 50.5, 49.0, 27.5, 20.6. HRMS-ESI (m/z): Calculated for $C_{15}H_{21}BrNO_2$ $(M + H)^+$: 326.0756 (^{79}Br), 328.0735 (^{81}Br), Found: 326.0752 (^{79}Br),

328.0749 (^{81}Br).

1'-(*tert*-Butyl)-4',4'-dimethyl-4H-spiro[naphthalene-1,3'-pyrrolidine]-4,5'-dione



2s

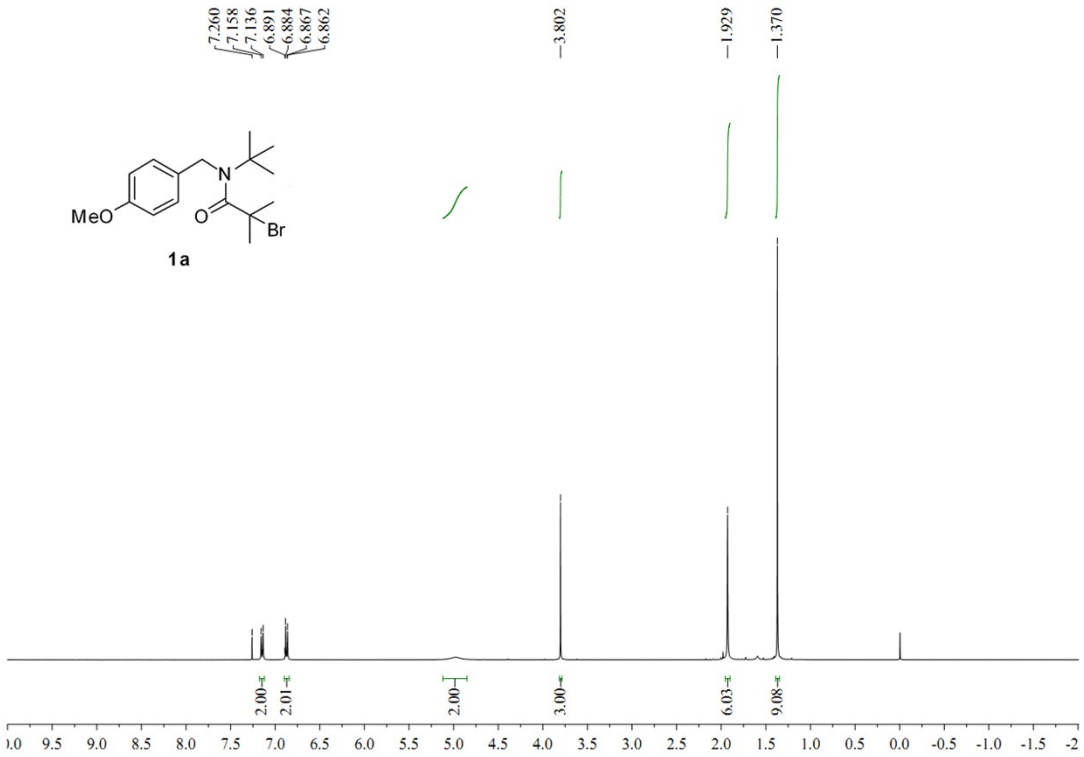
Pale yellow solid, 50% yield，mp: 110 - 114 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, *J* = 8.0, 1H), 7.66 (d, *J* = 8.0, 1H), 7.56 – 7.52 (m, 1H), 7.44 (t, *J* = 8.0, 1H), 7.02 (d, *J* = 10.4, 1H), 6.58 (d, *J* = 10.4, 1H), 3.85 (d, *J* = 10.4, 1H), 3.78 (d, *J* = 10.4, 1H), 1.52 (s, 9H), 1.17 (s, 3H), 0.64 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 184.0, 178.0, 150.4, 144.6, 132.6, 131.6, 130.1, 127.6, 127.0, 125.4, 54.4, 52.8, 52.2, 46.8, 27.4, 23.3, 20.3. HRMS-ESI (m/z): Calculated for $C_{16}H_{23}NO_3Na$ $(M + Na)^+$: 320.1626, Found: 320.1621.

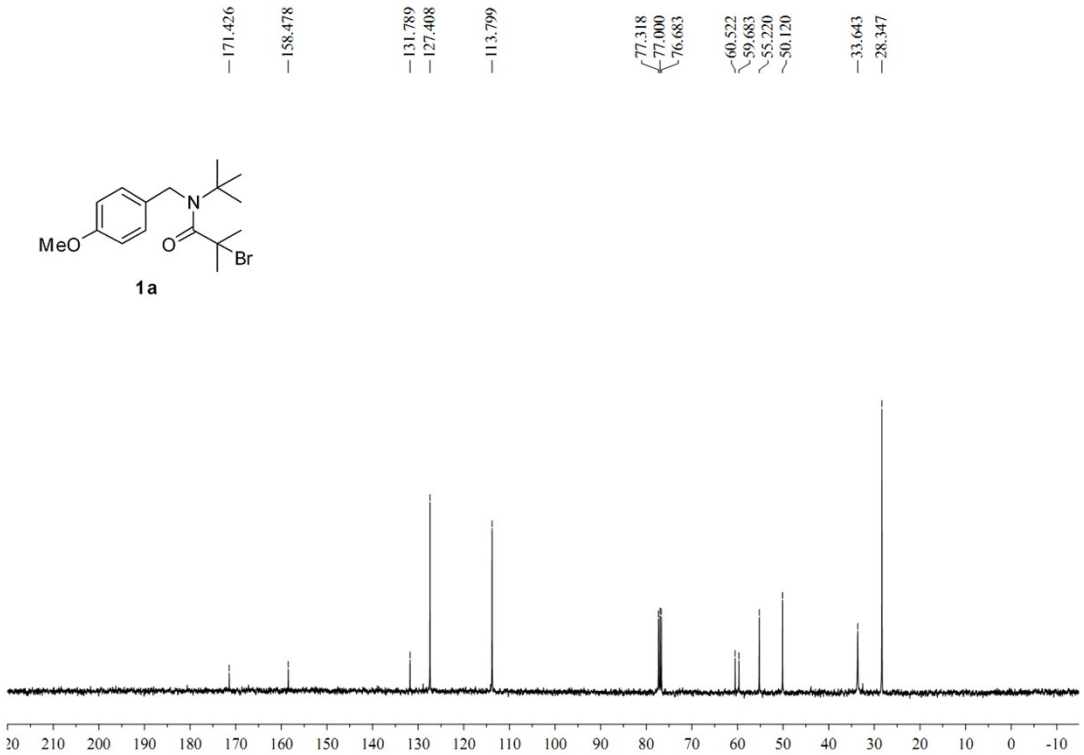
6. References:

1. S. D. Bull, S. G. Davies, G. Fenton, A. W. Mulvaney, R. S. Prasad and A. D. Smith, *J. Chem. Soc., Perkin Trans. 1*, 2000, 3765;
2. T. R. Ibarra-Rivera, R. Gamez-Montano and L. D. Miranda, *Chem. Commun.*, 2007, 3485.
3. L. Yan, F. Zhao, Y. Gan, J. Zhao and Z. Jiang, *Synth. Commun.*, 2011, **42**, 285.

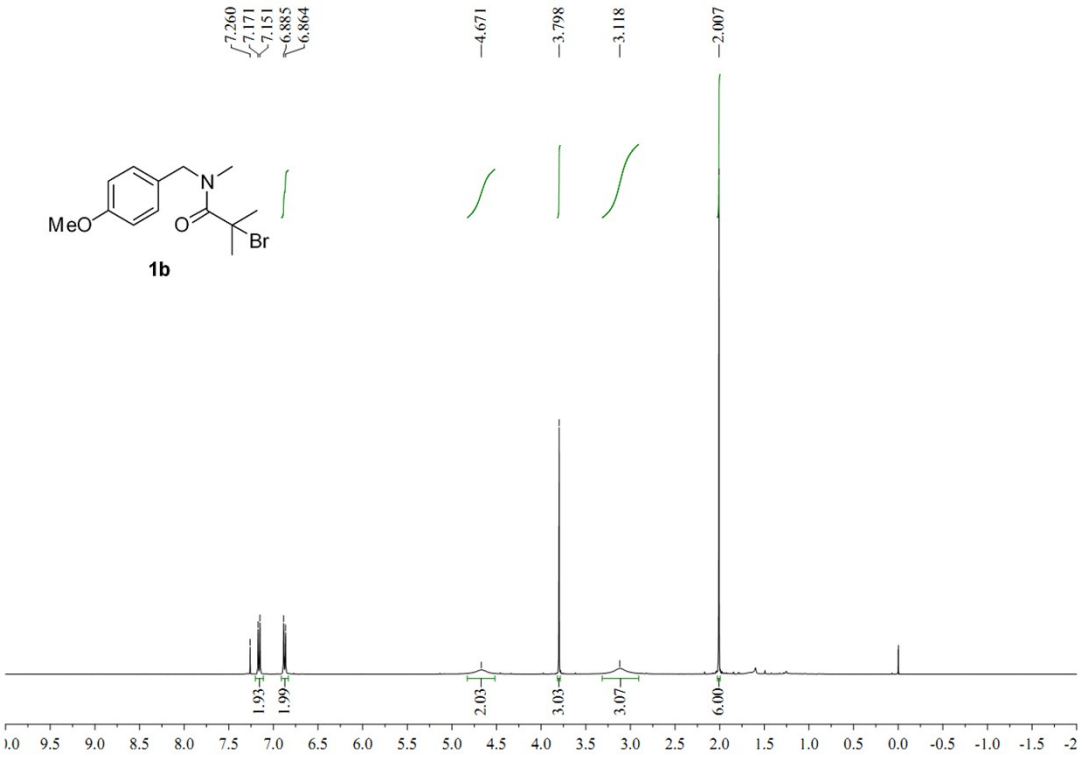
7. NMR spectra of the products

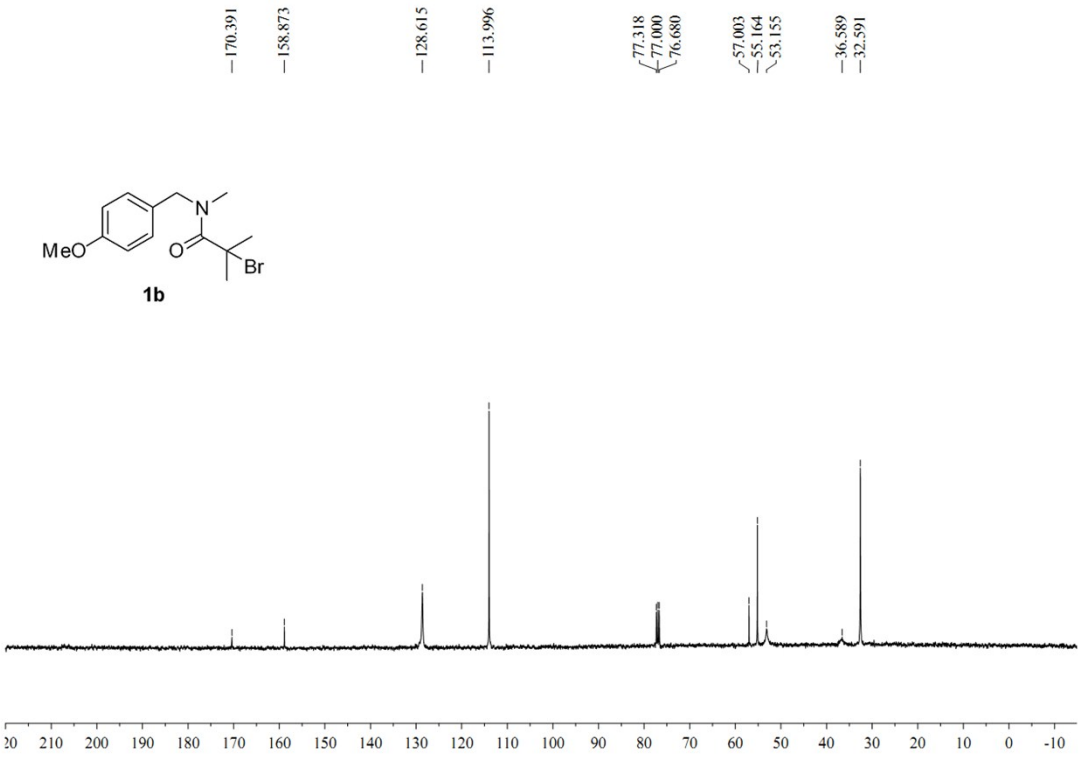
2-Bromo-*N*-(*tert*-butyl)-*N*-(4-methoxybenzyl)-2-methylpropanamide (1a)





2-Bromo-*N*-methyl-*N*-(4-methoxybenzyl)-2-methylpropanamide (1b)





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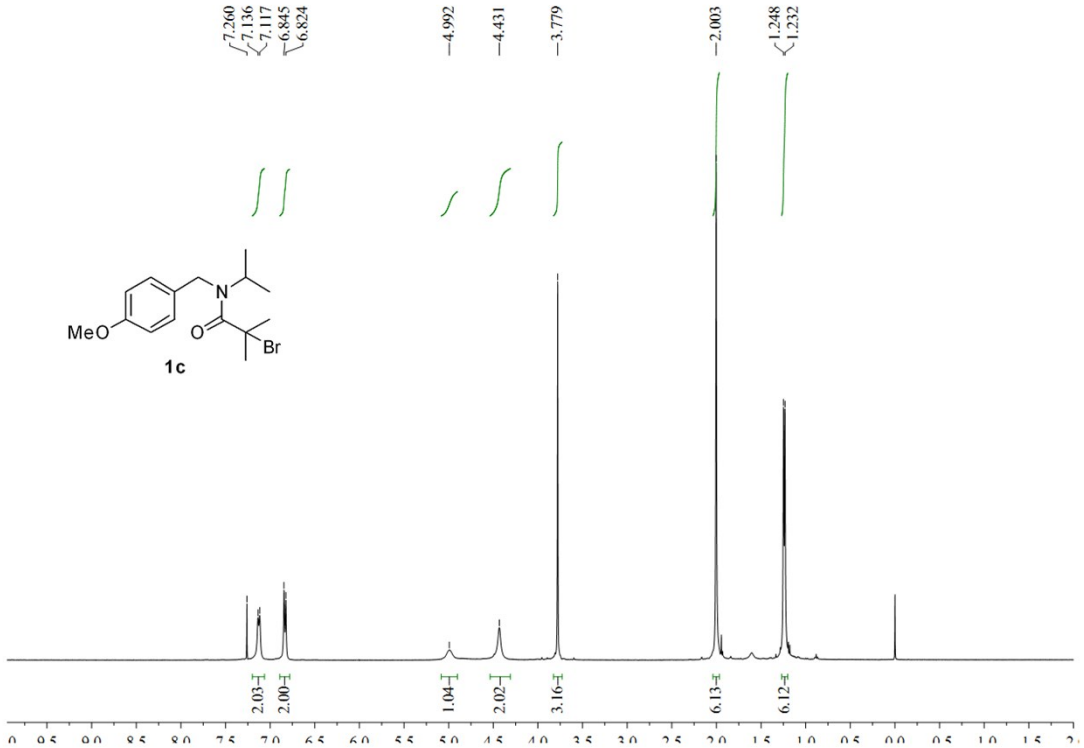

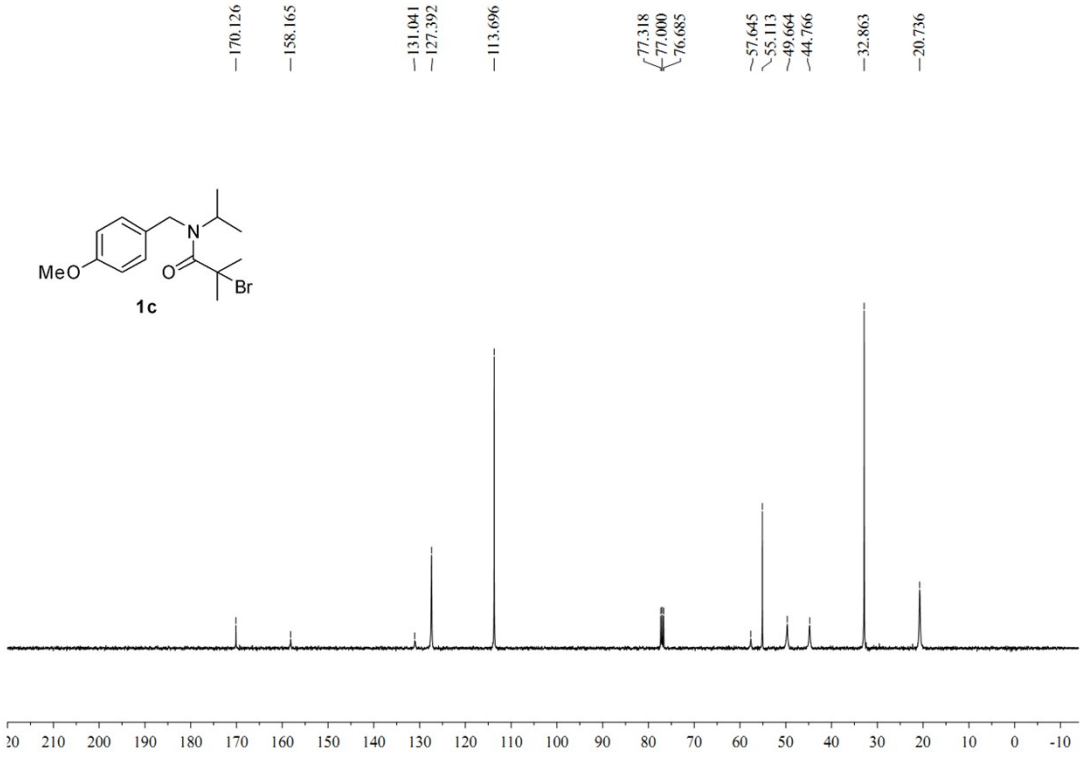

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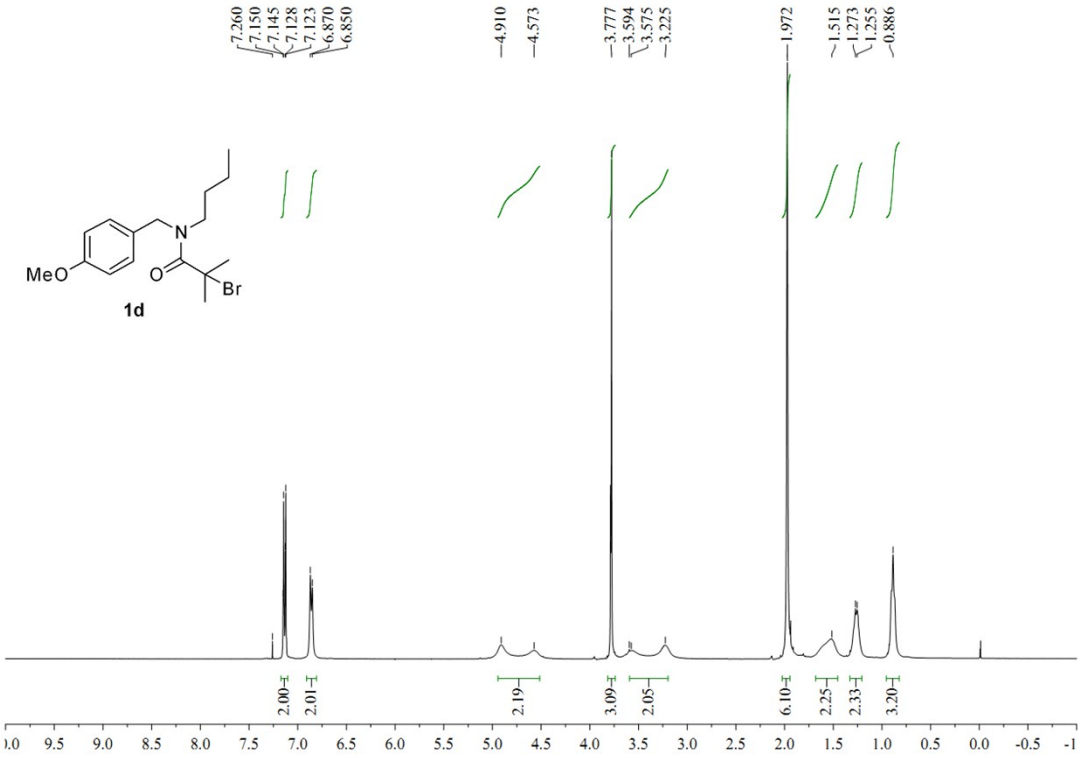

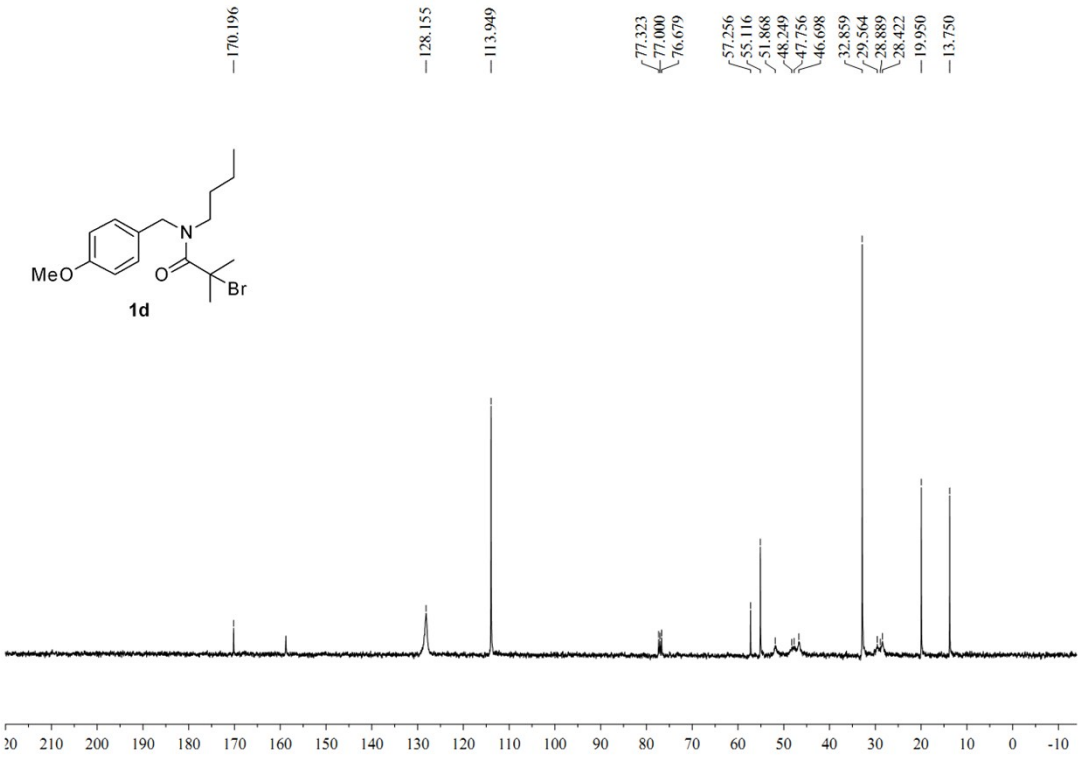

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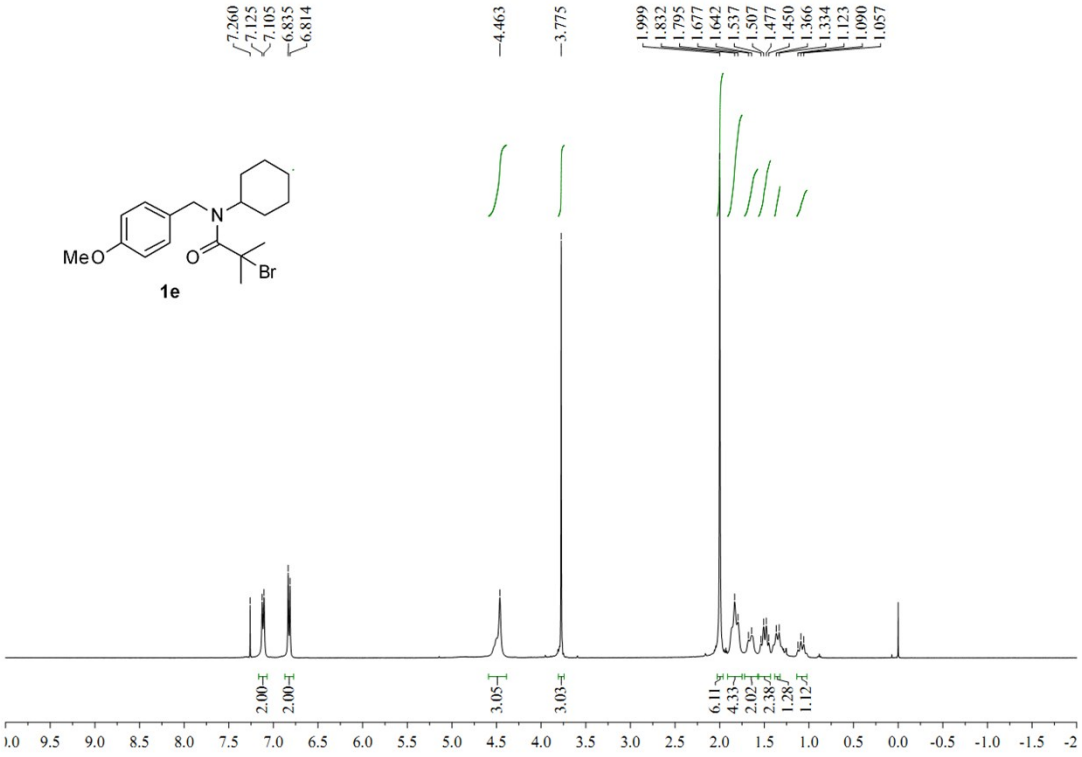

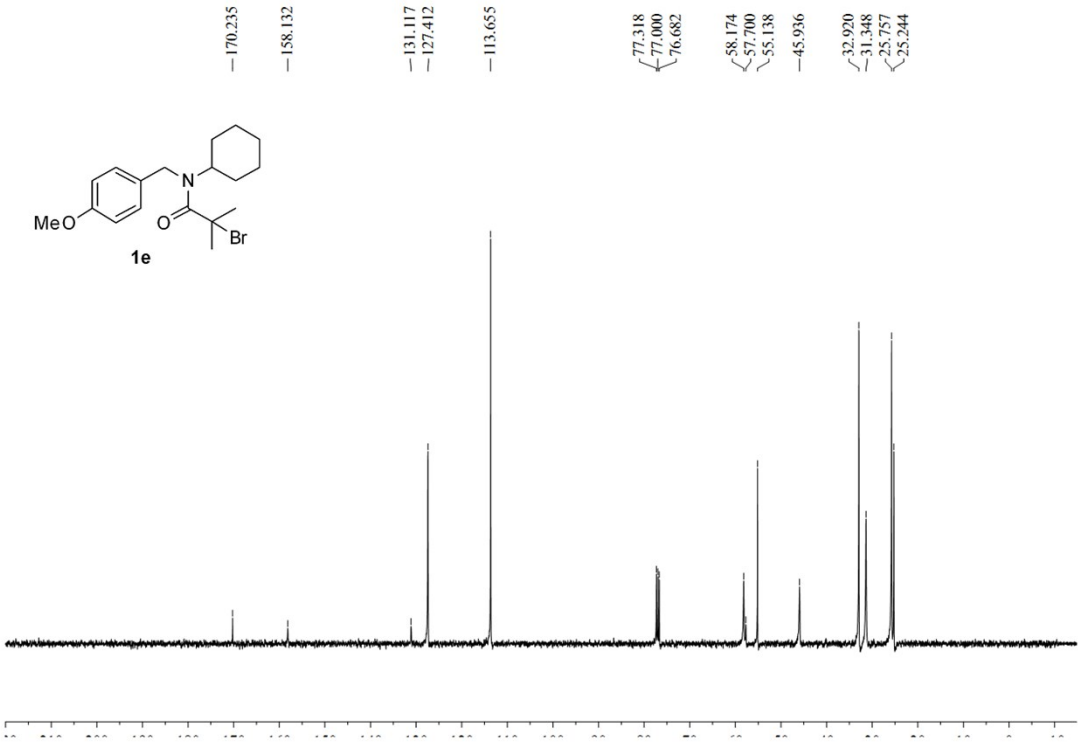

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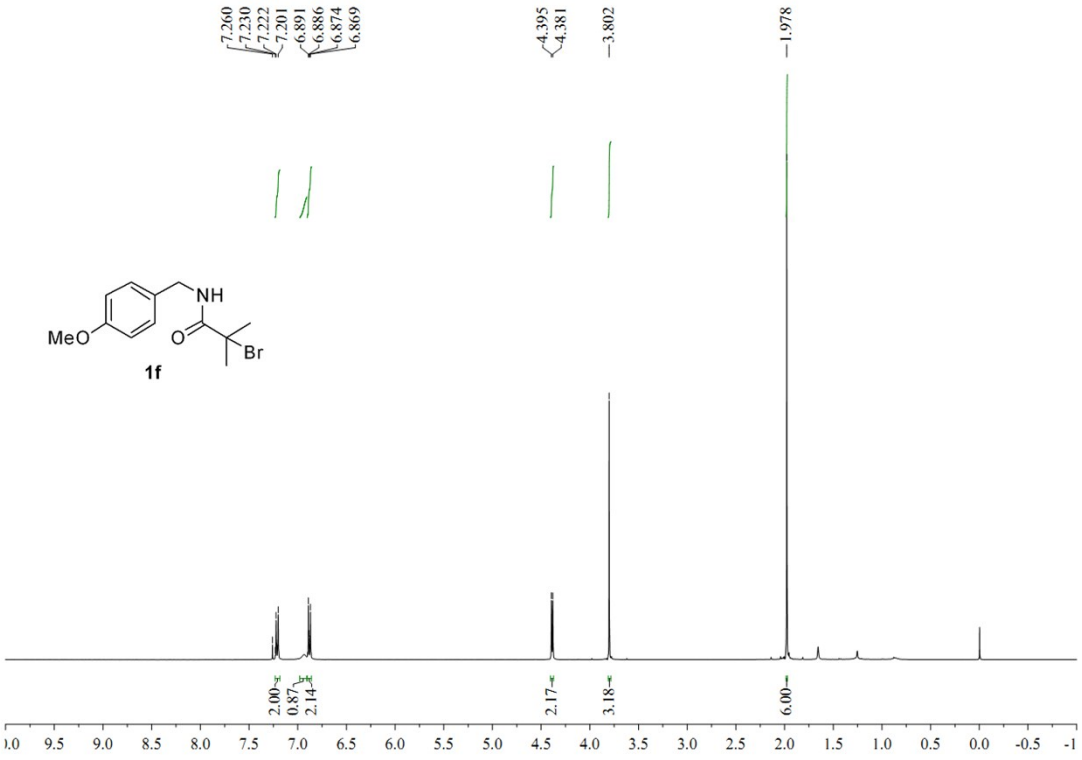

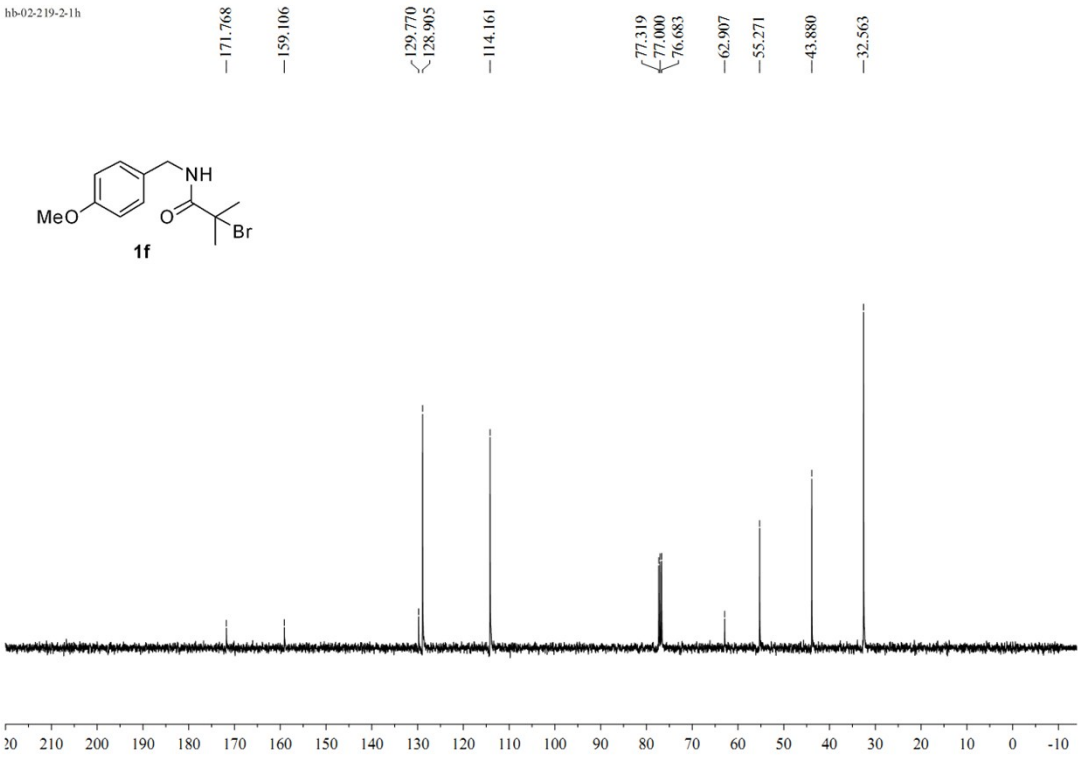

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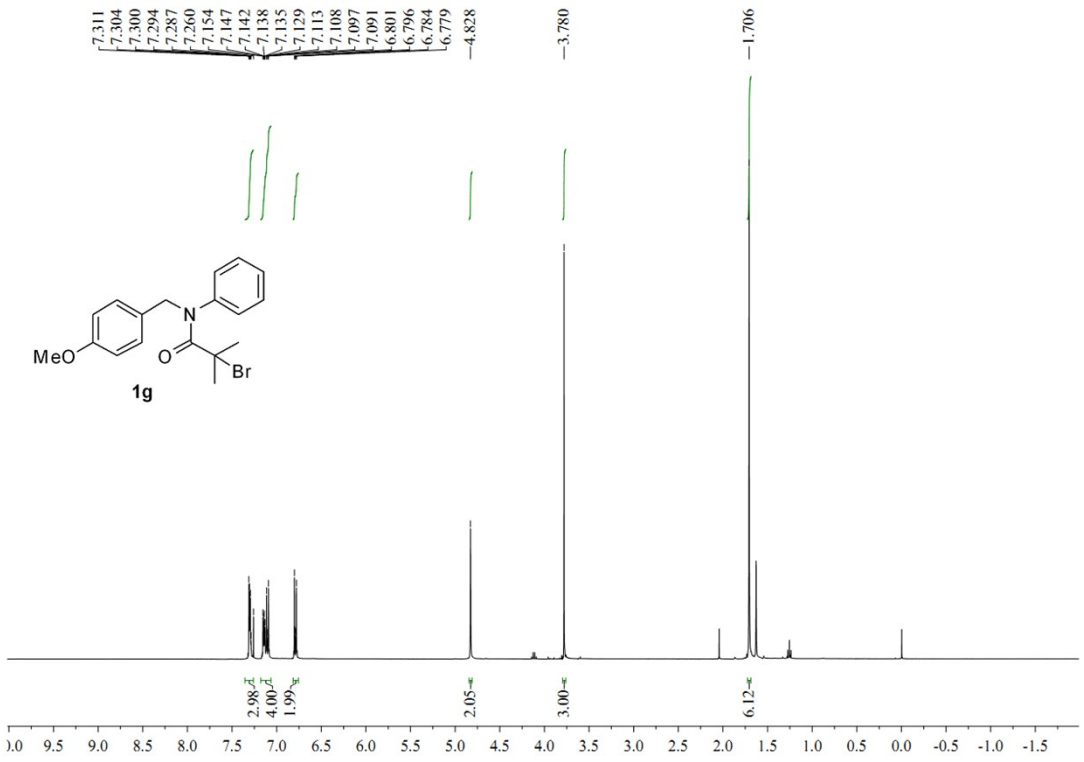
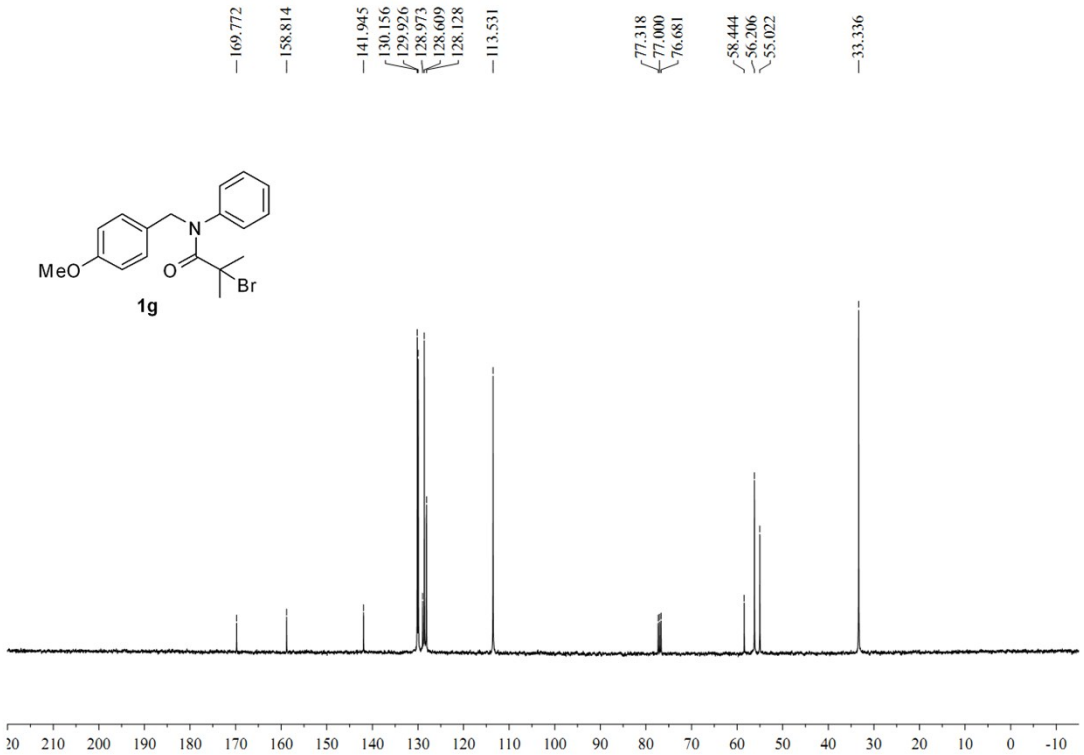
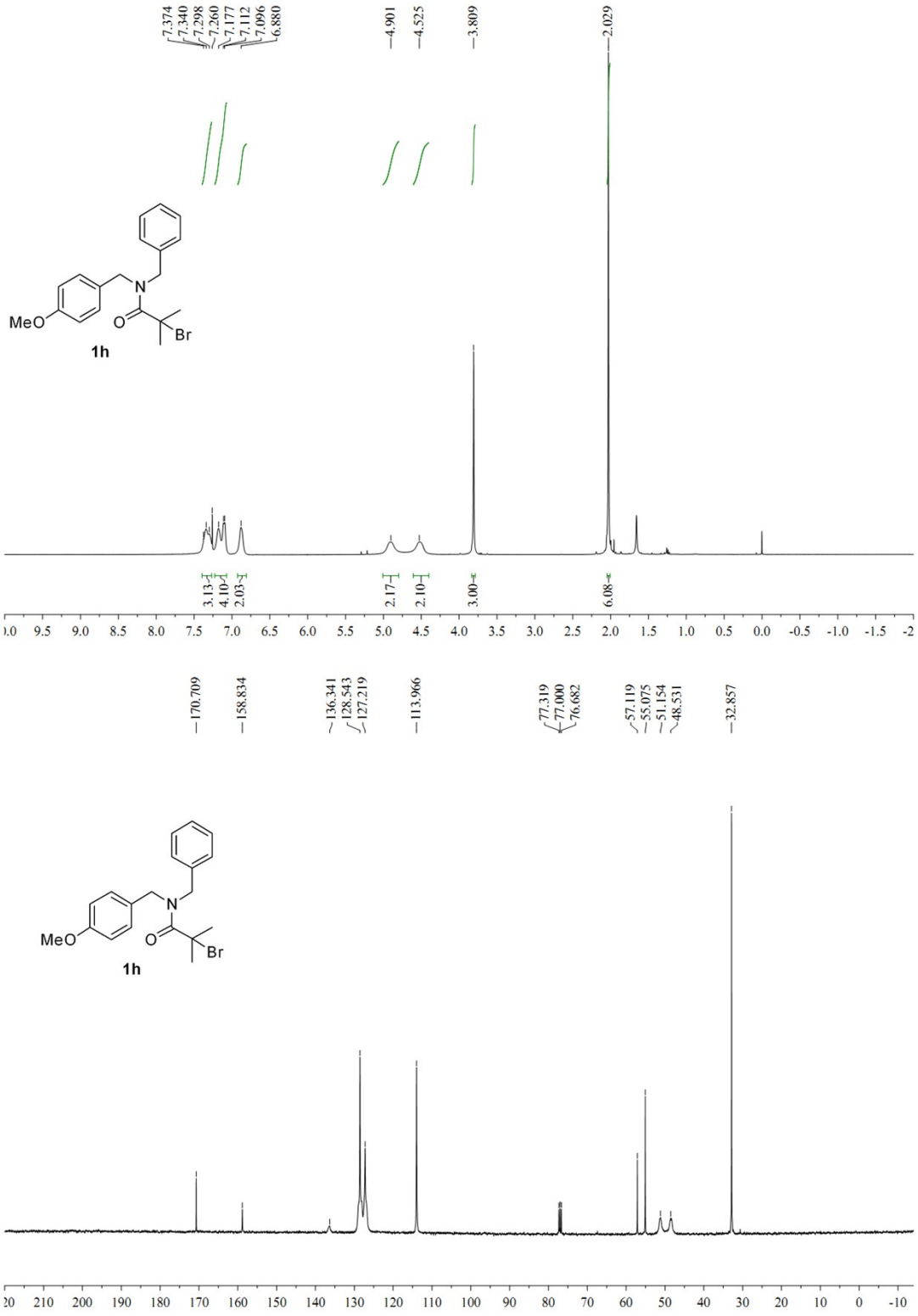
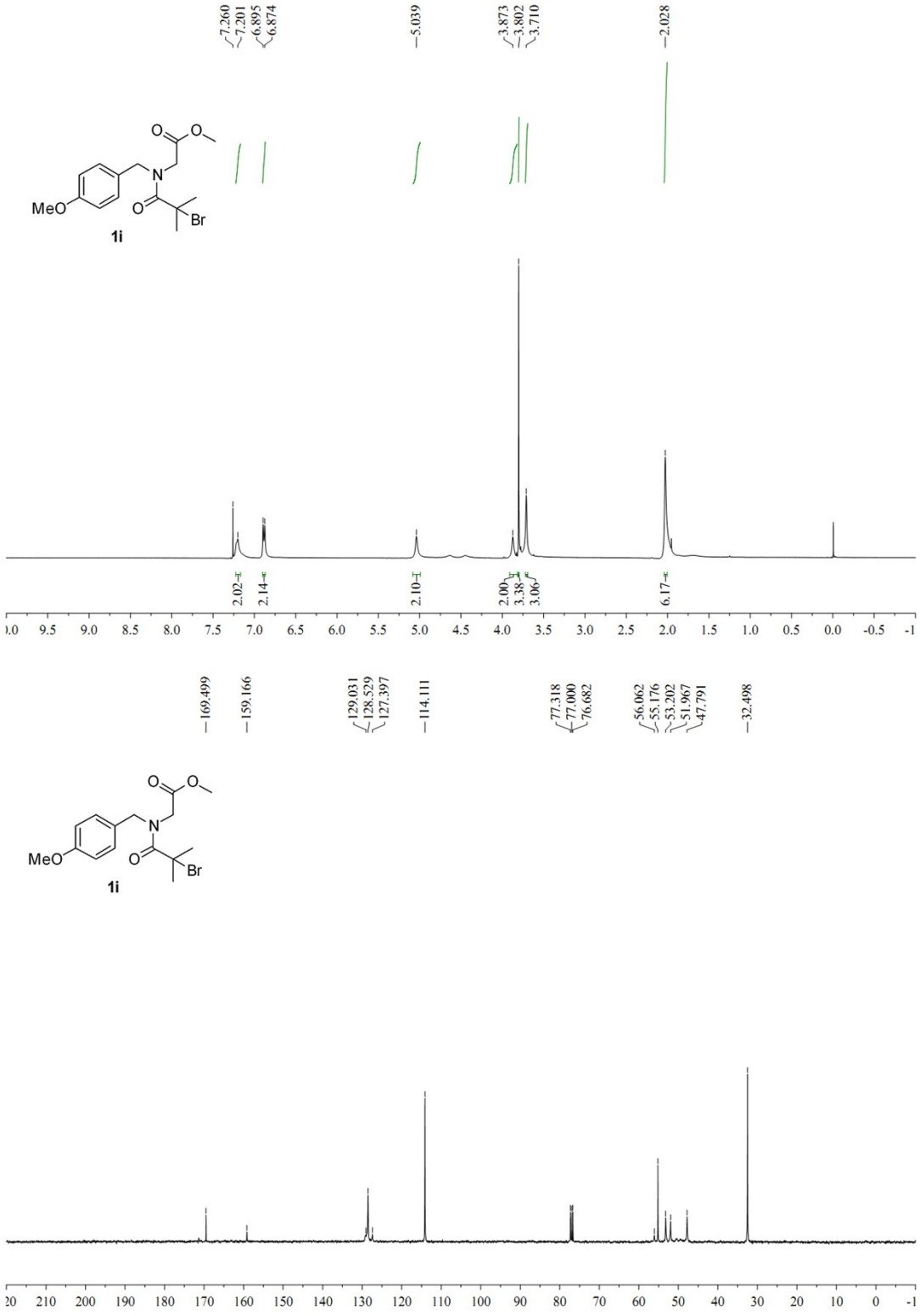




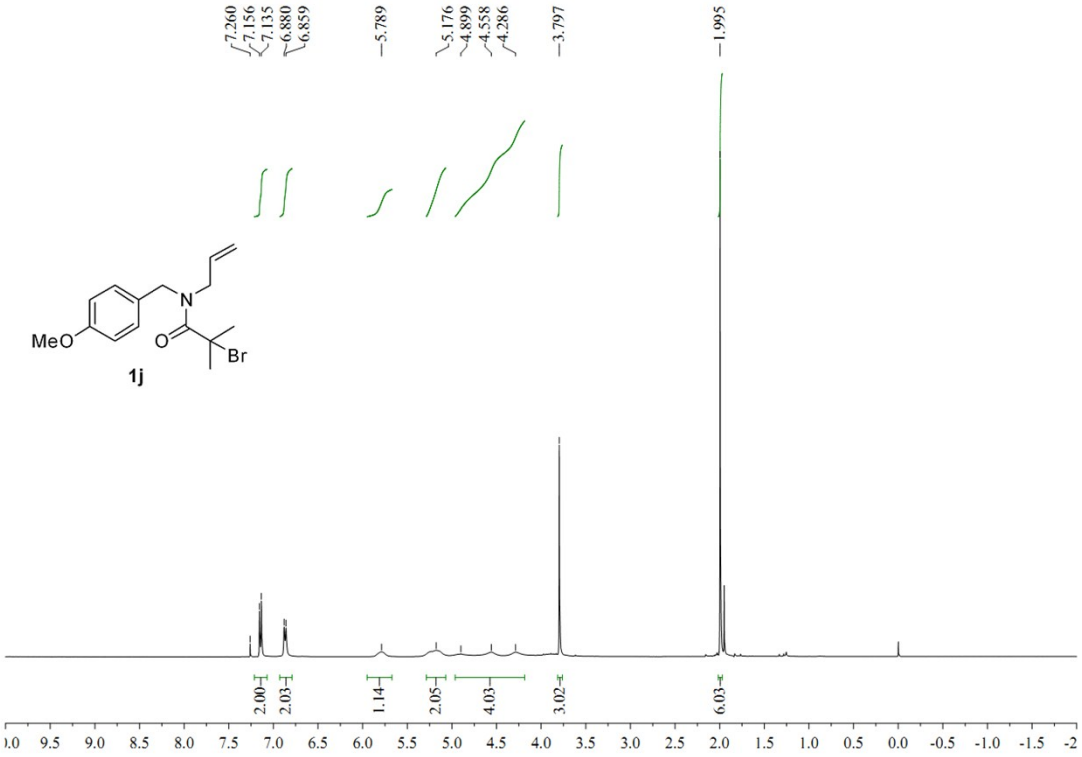
_N_-Benzyl-2-bromo-_N_-(4-methoxybenzyl)-2-methylpropanamide (1h)

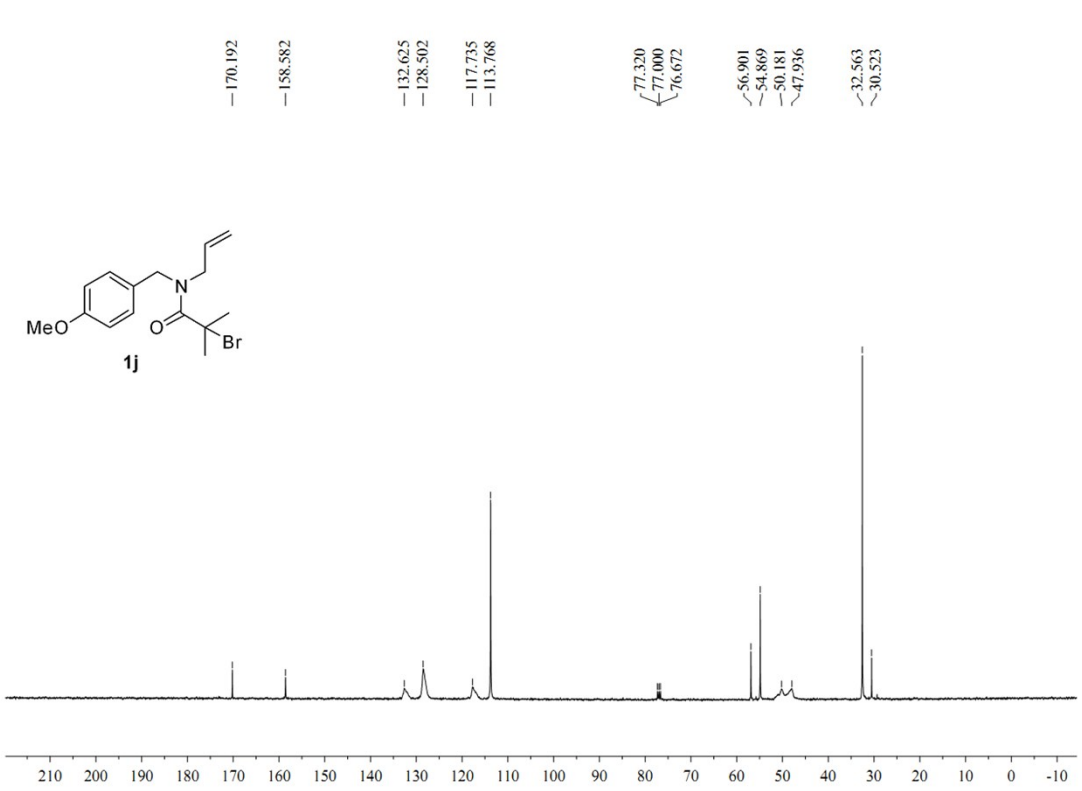


Methyl 2-(2-bromo-*N*-(4-methoxybenzyl)-2-methylpropanamido)acetate (1i)

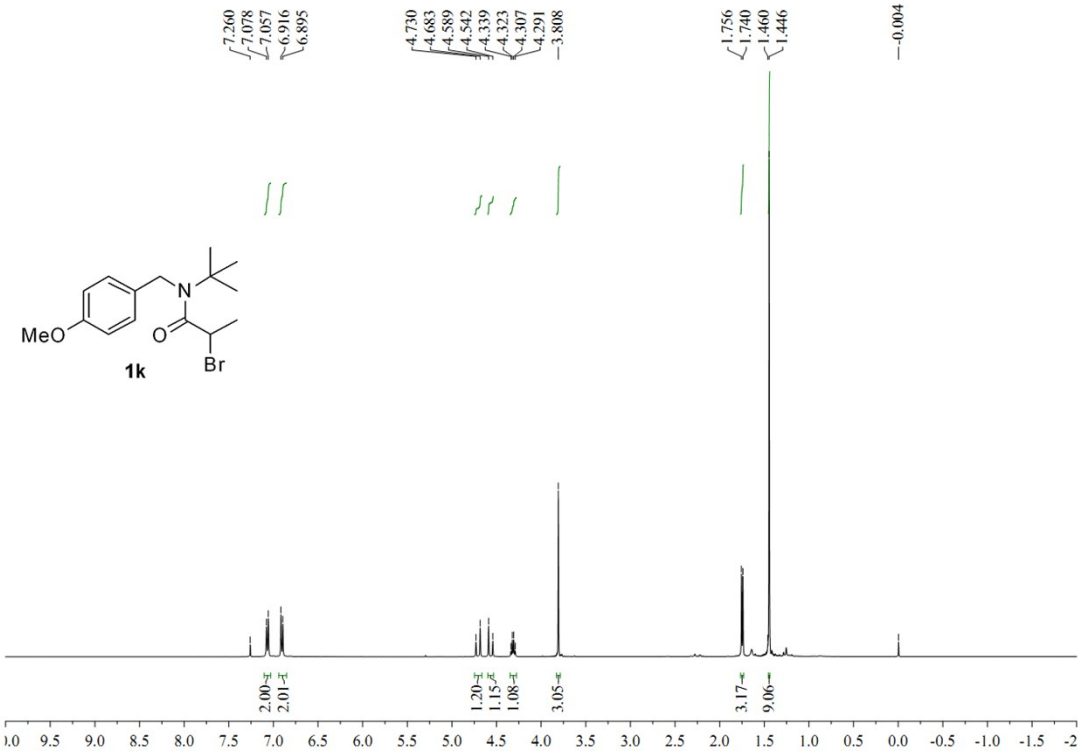


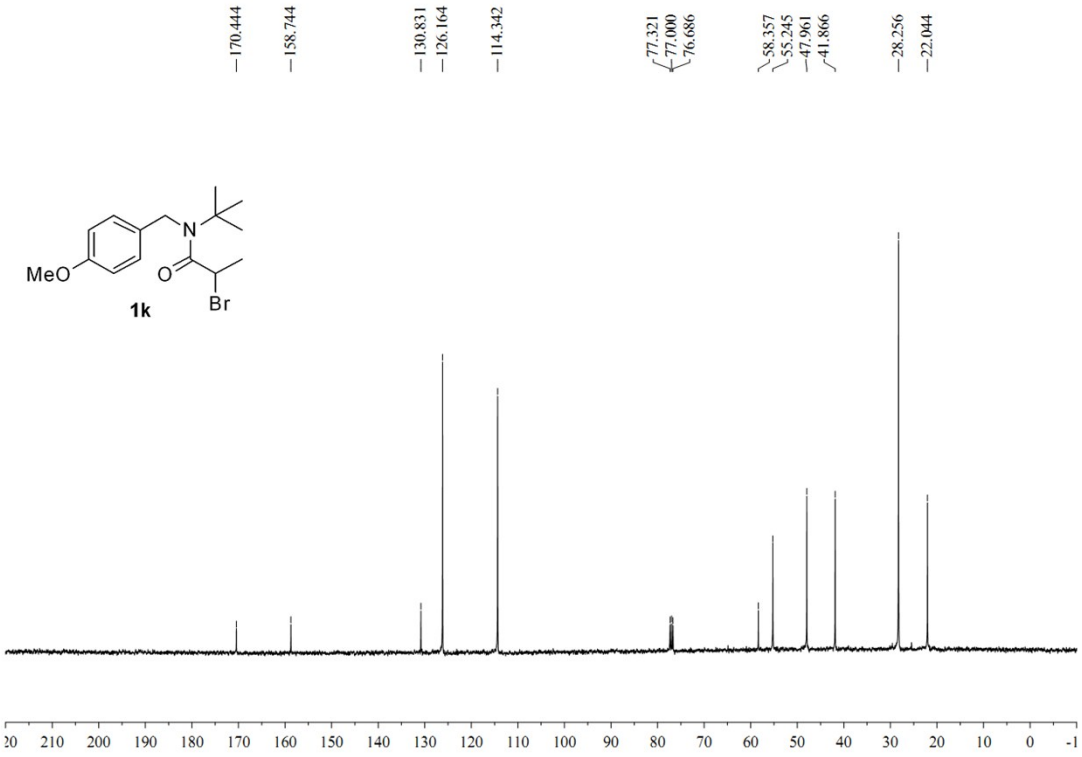
***N*-Allyl-2-bromo-*N*-(4-methoxybenzyl)-2-methylpropanamide (1j)**



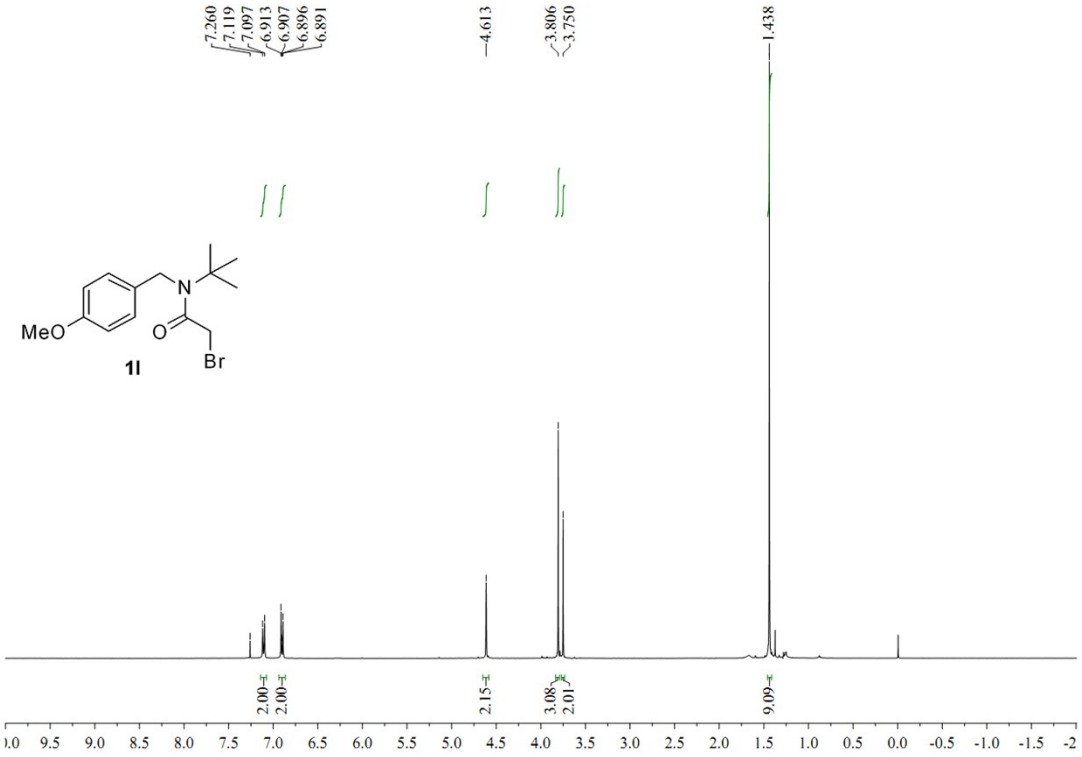


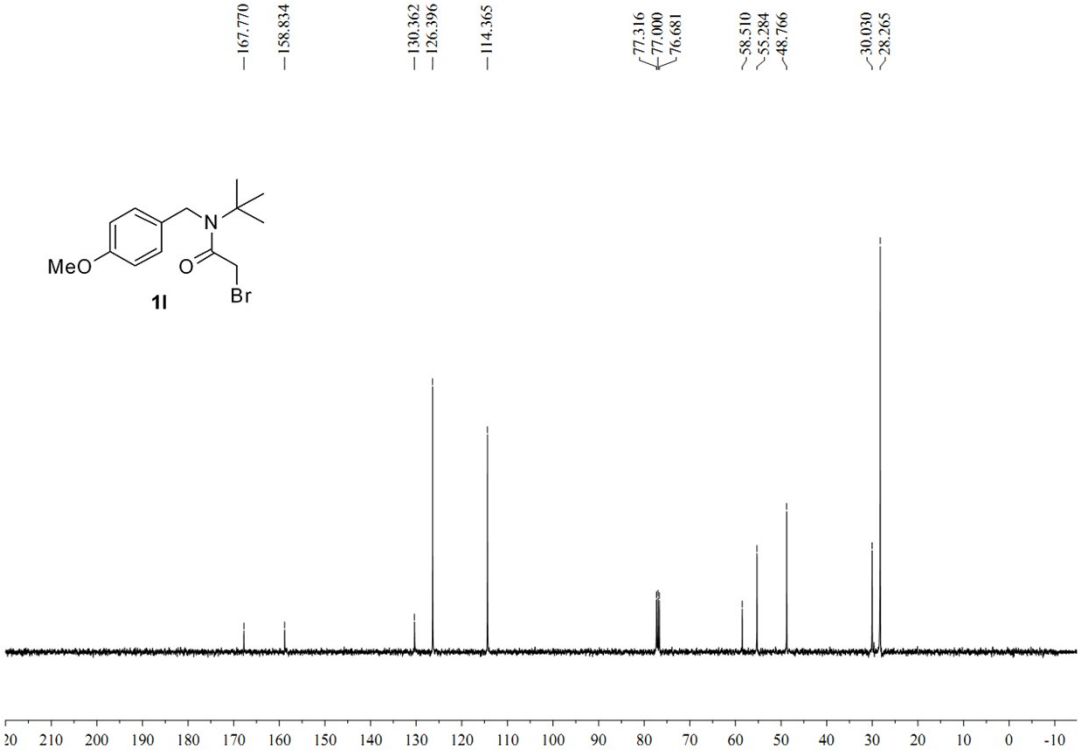
2-Bromo-*N*-(*tert*-butyl)-*N*-(4-methoxybenzyl)propanamide (1k)



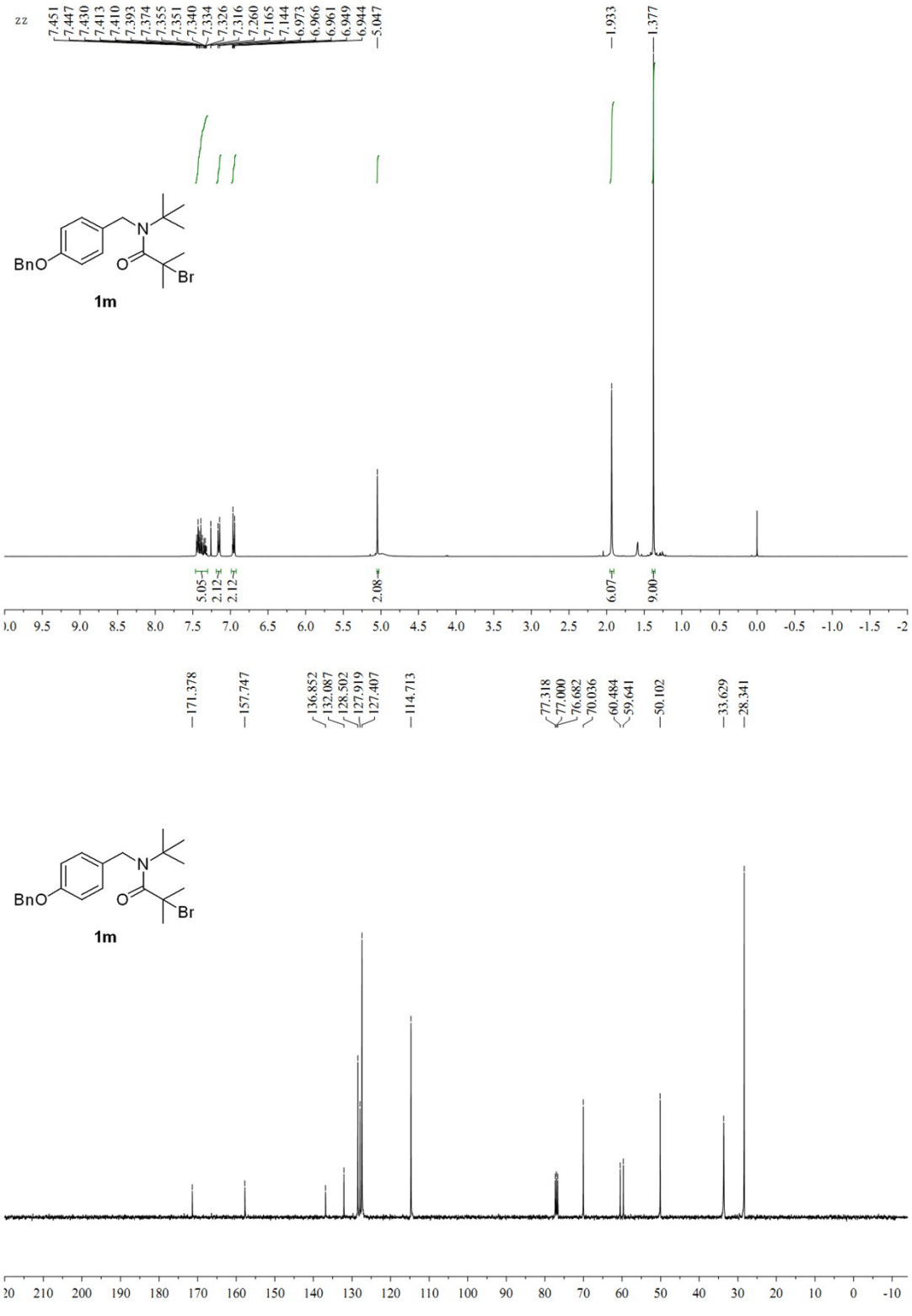


2-Bromo-*N*-(*tert*-butyl)-*N*-(4-methoxybenzyl)acetamide (1l)

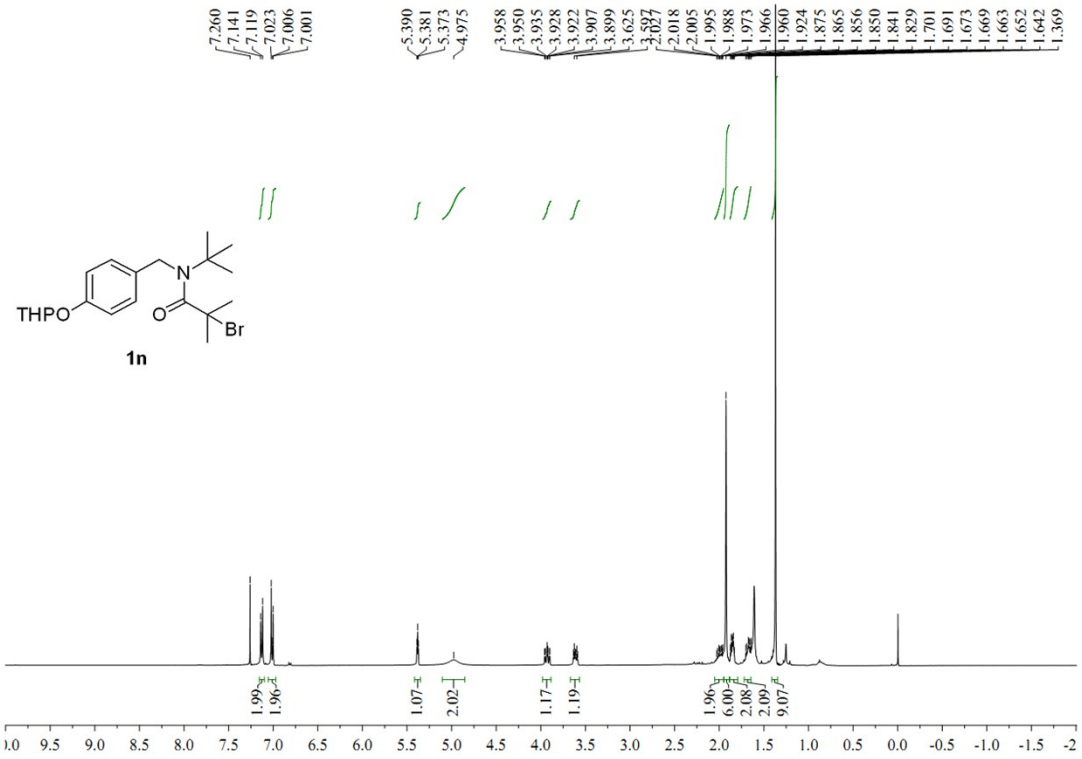


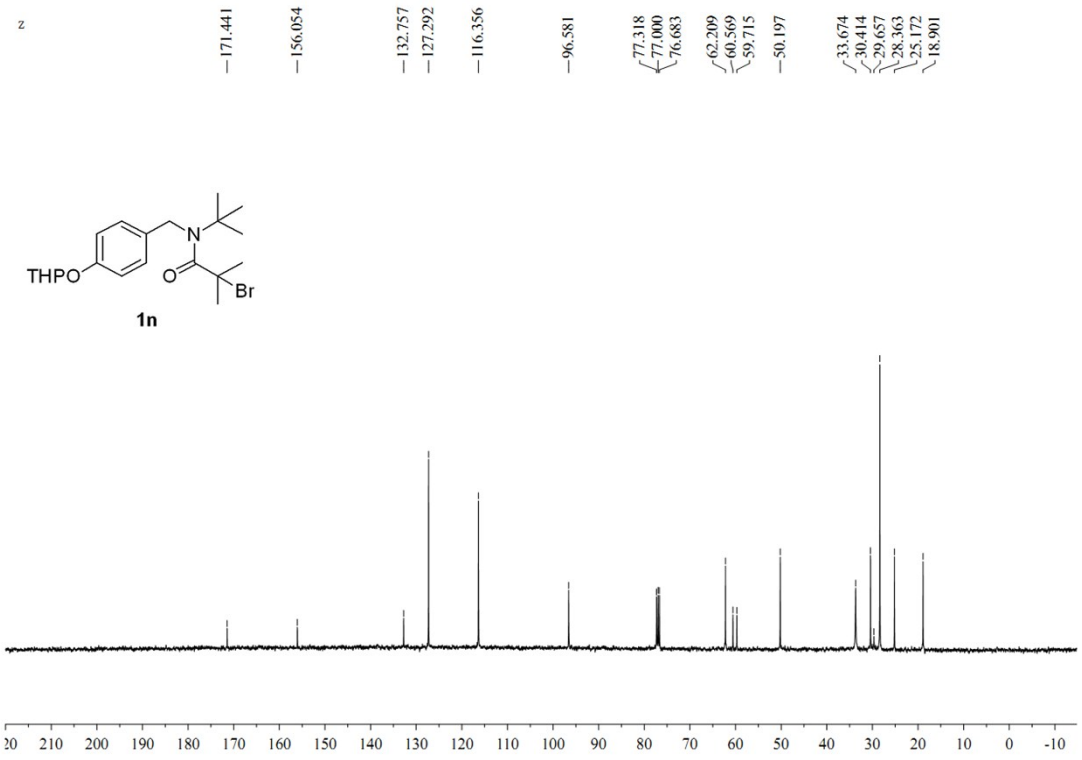


***N*-(4-(Benzyloxy)benzyl)-2-bromo-*N*-(*tert*-butyl)-2-methylpropanamide (1m)**

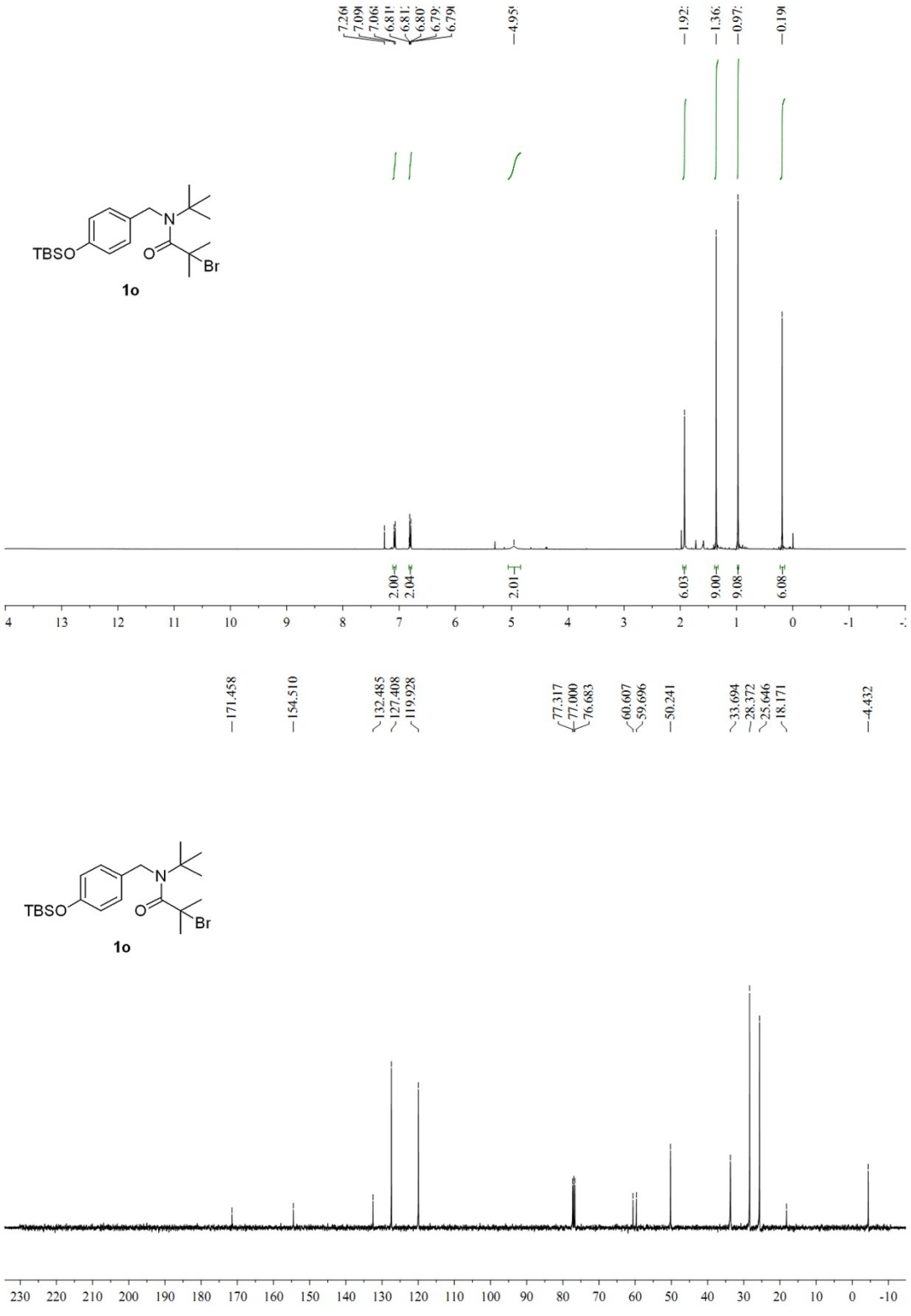


2-Bromo-*N*-(*tert*-butyl)-2-methyl-*N*-(4-((tetrahydro-2H-pyran-2-yl)oxy)benzyl)propanamide (1n)





2-Bromo-*N*-(*tert*-butyl)-*N*-(4-((*tert*-butyldimethylsilyl)oxy)benzyl)-2-methylpropanamide (1o)



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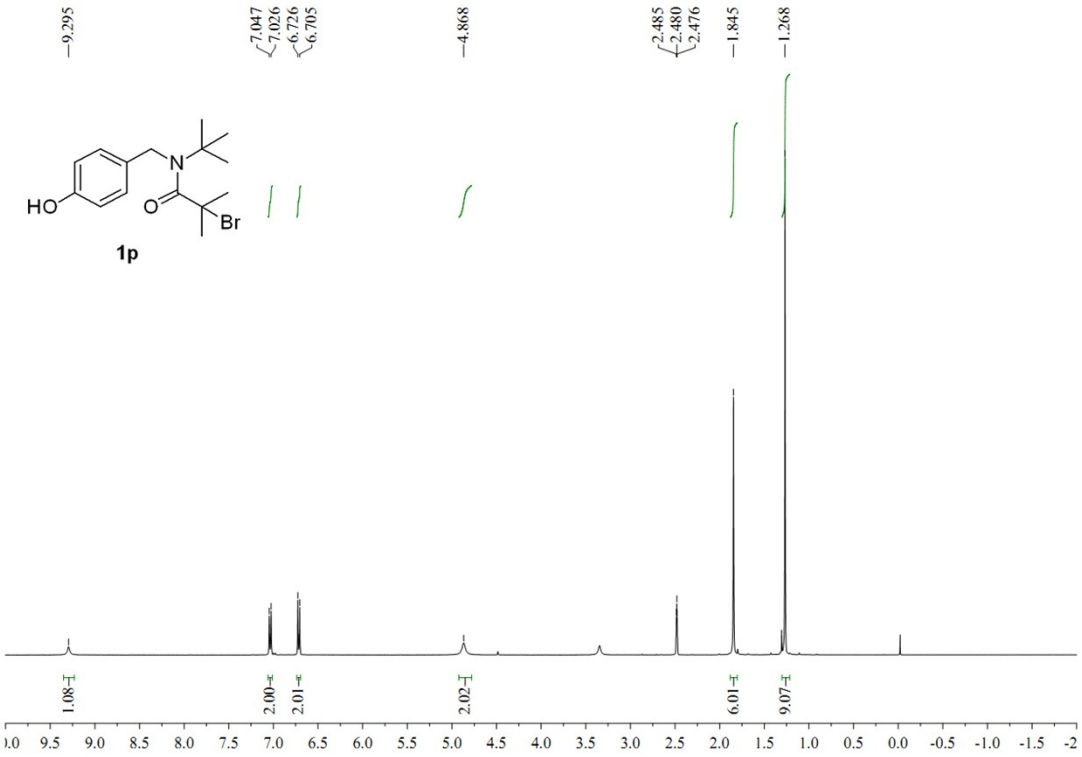

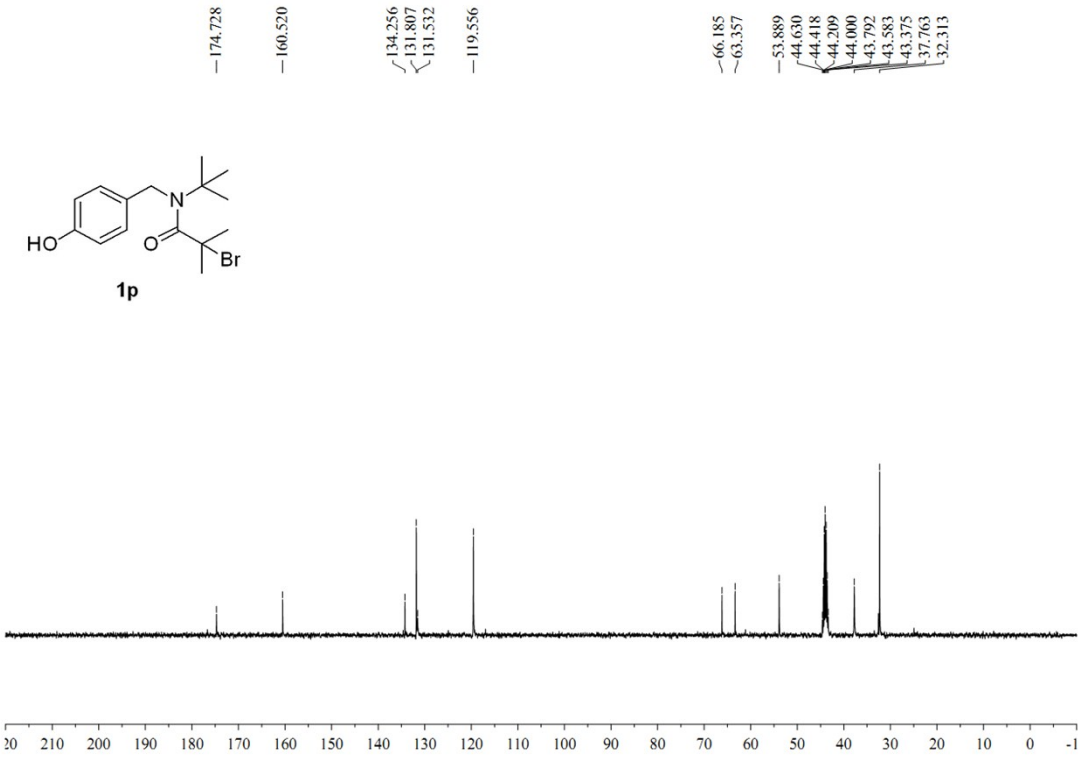

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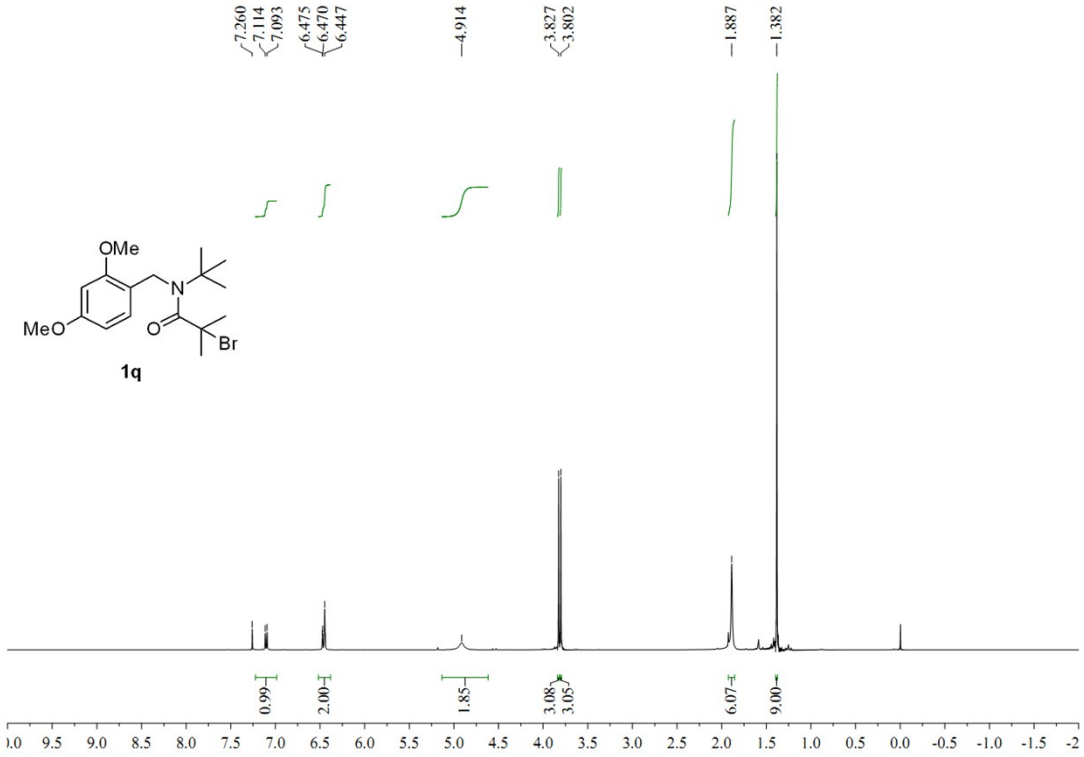
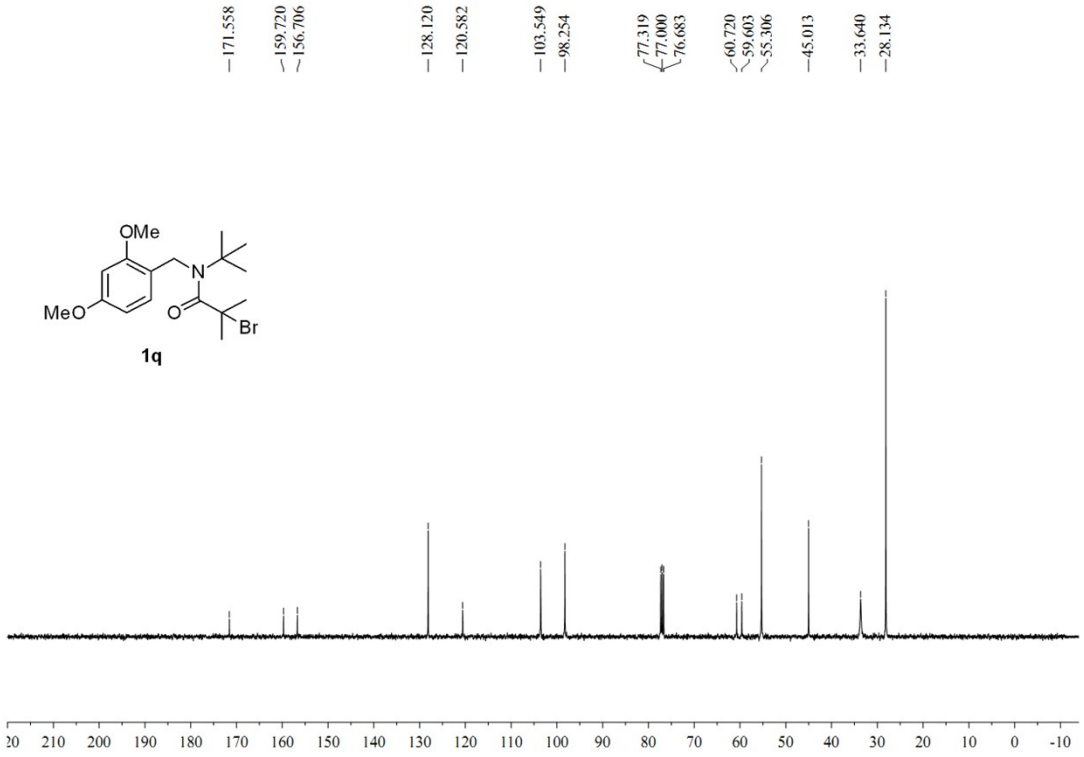
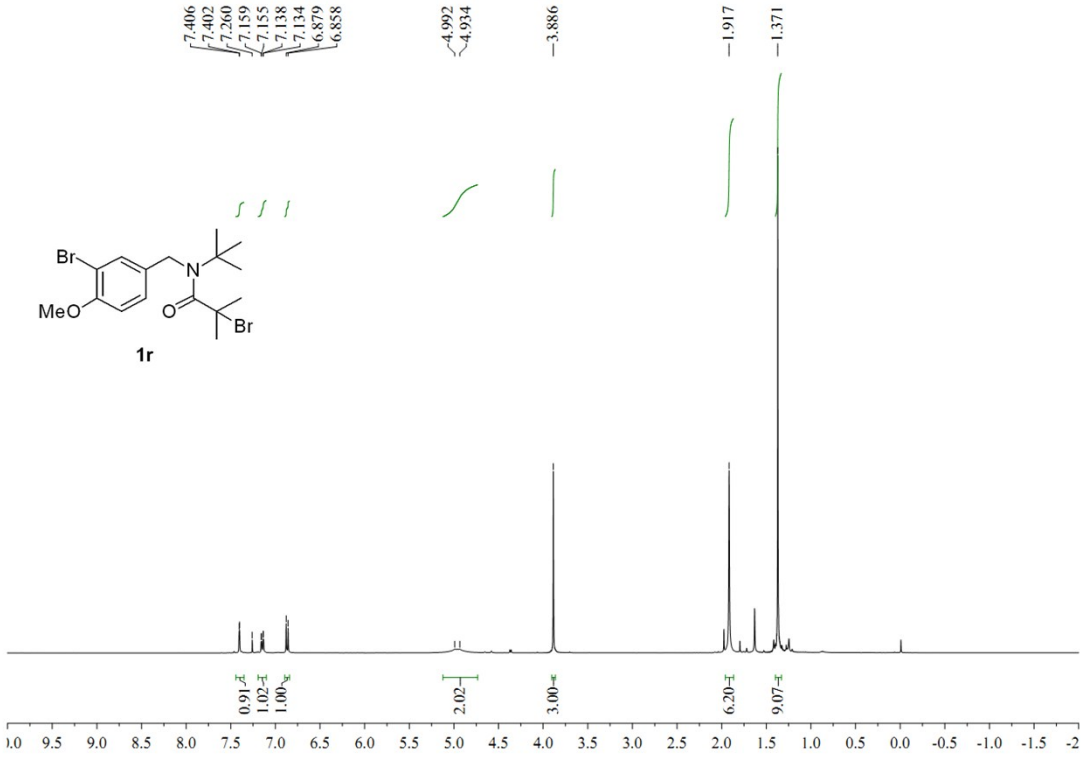
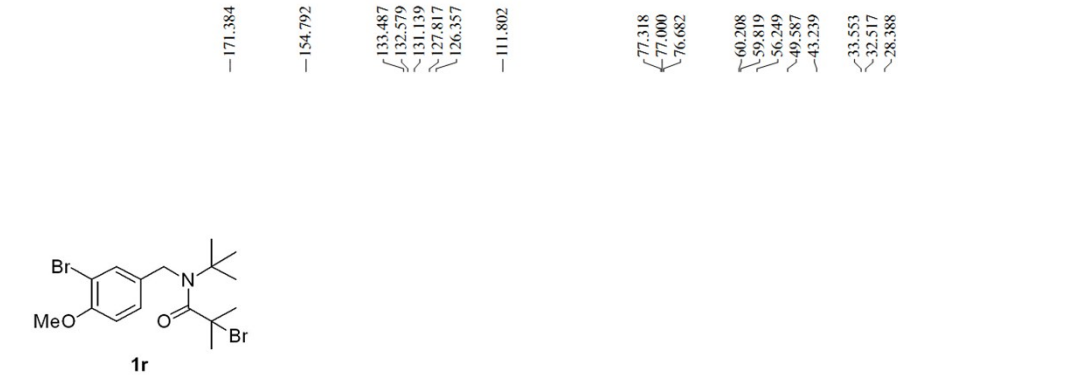
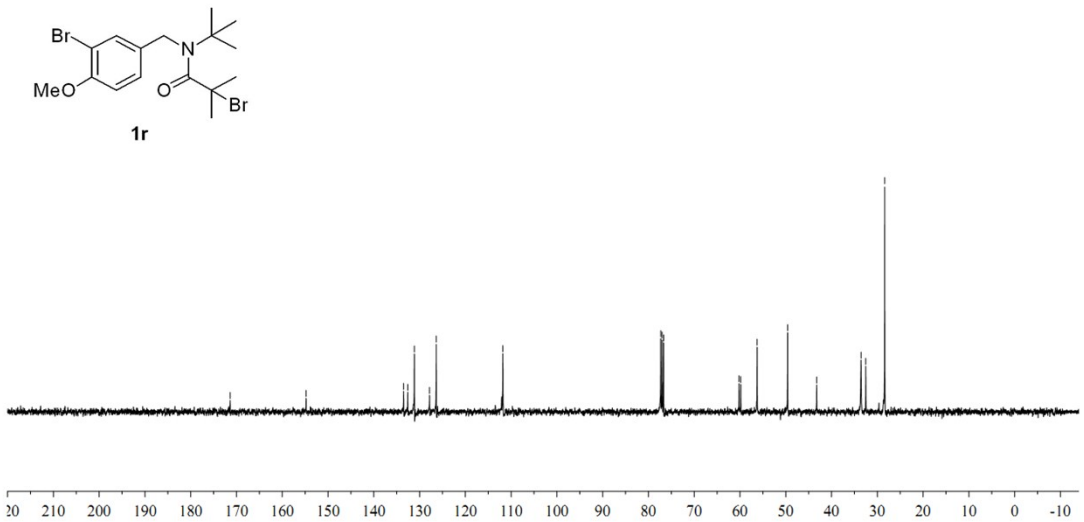




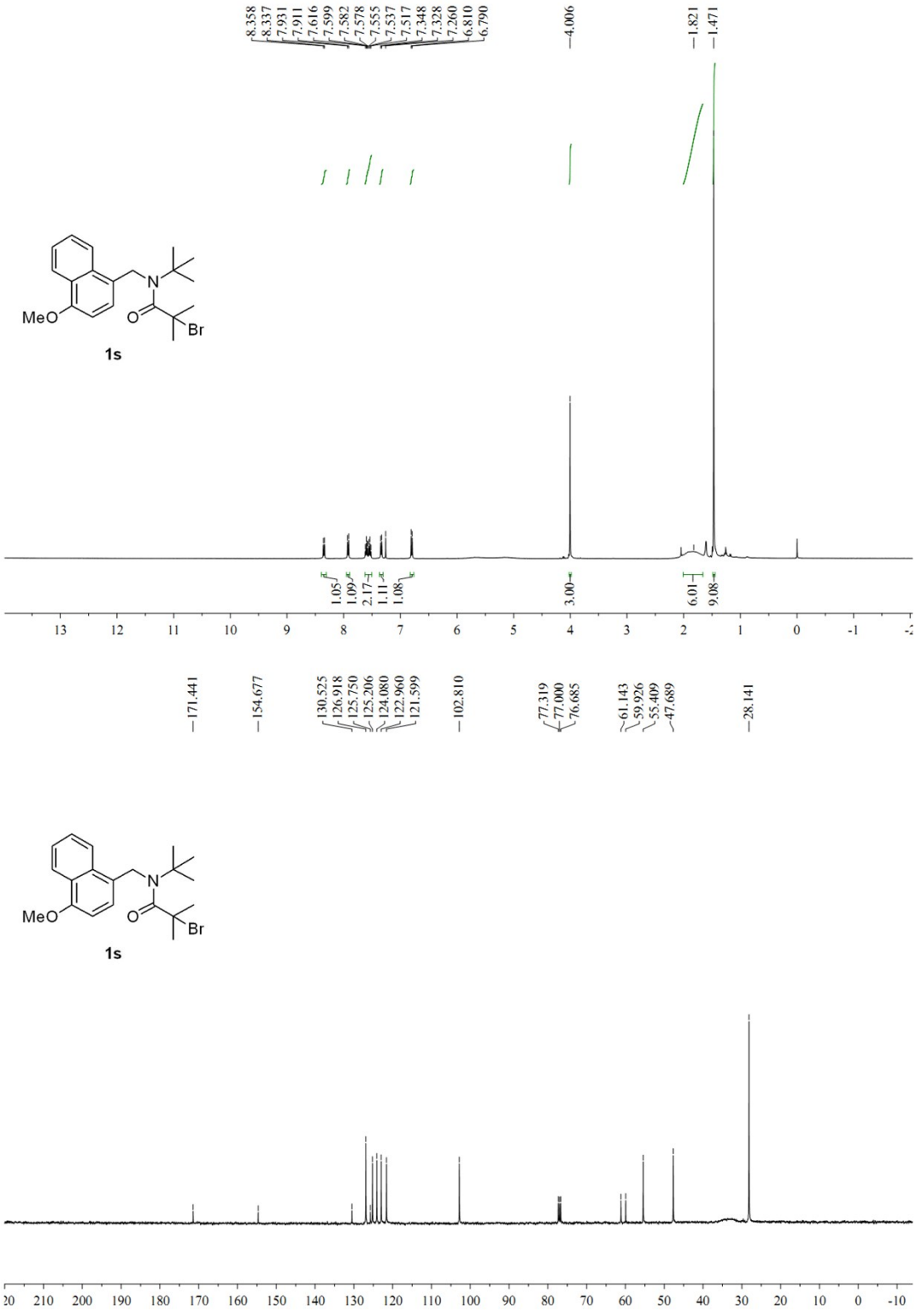
2-Bromo-*N*-(3-bromo-4-methoxybenzyl)-*N*-(*tert*-butyl)-2-methylpropanamide (1r)



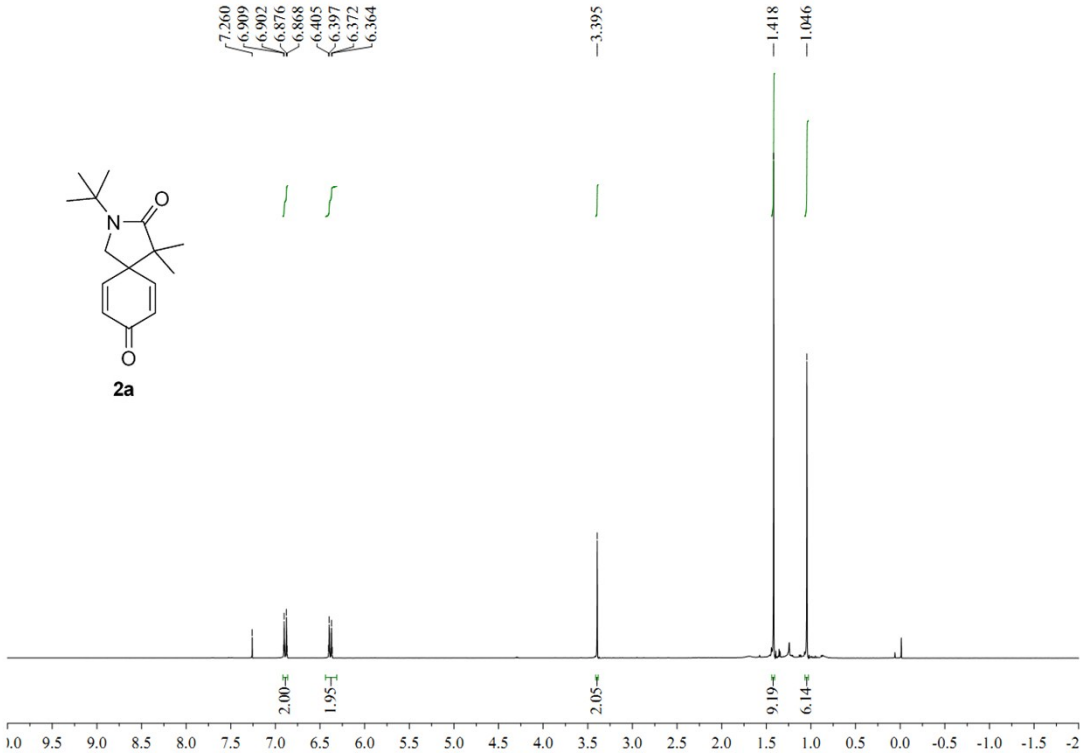


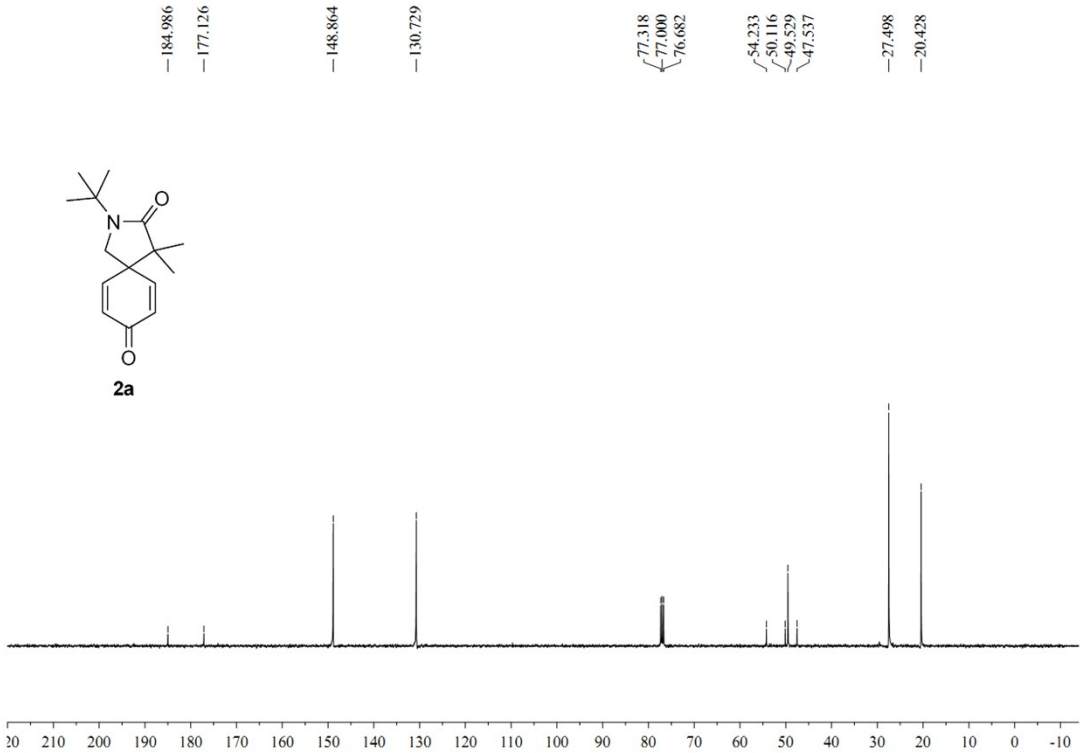


2-Bromo-*N*-(*tert*-butyl)-*N*-((4-methoxynaphthalen-1-yl)methyl)-2-methylpropanamide (1s)

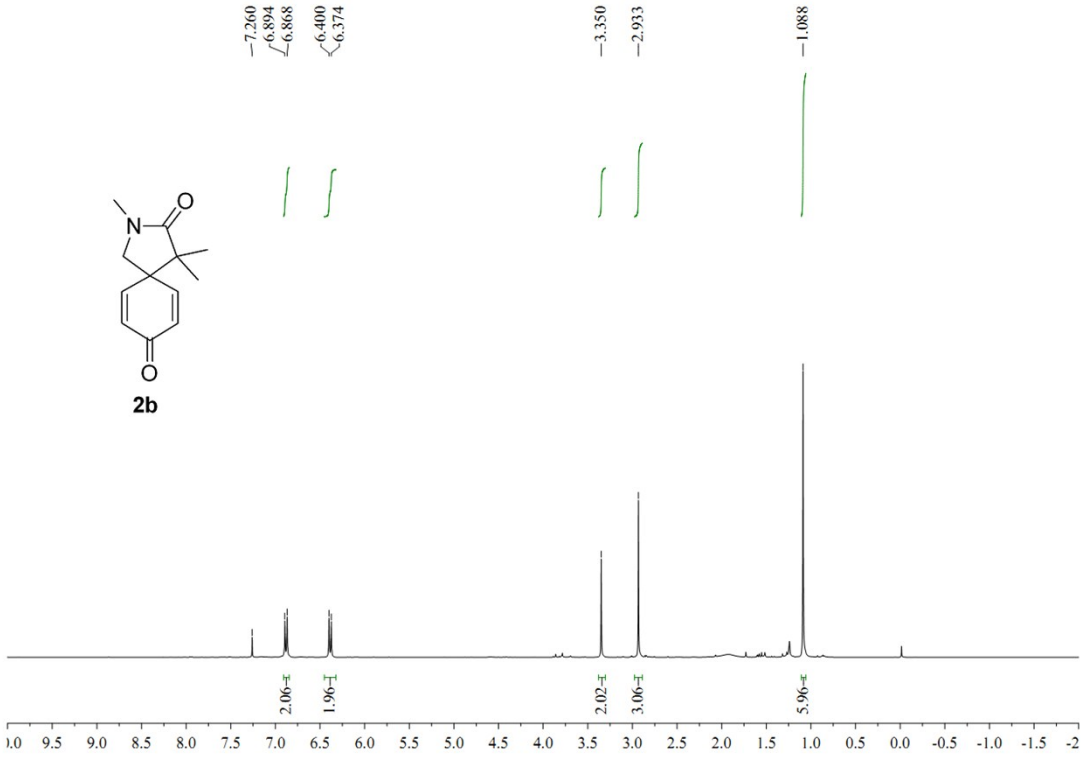


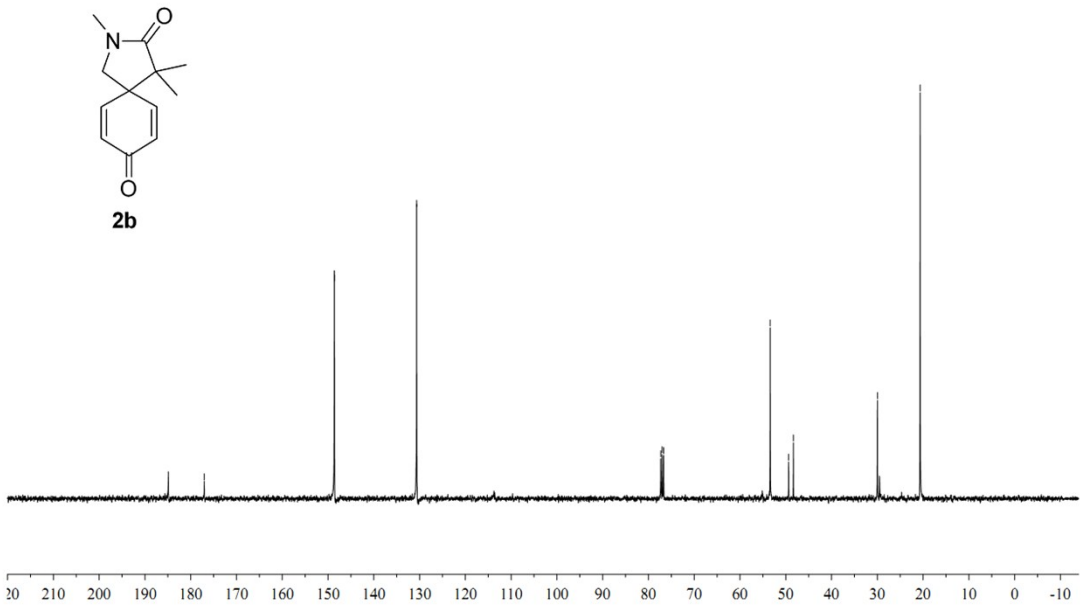
2-(*tert*-Butyl)-4,4-dimethyl-2-azaspiro[4.5]deca-6,9-diene-3,8-dione (2a)



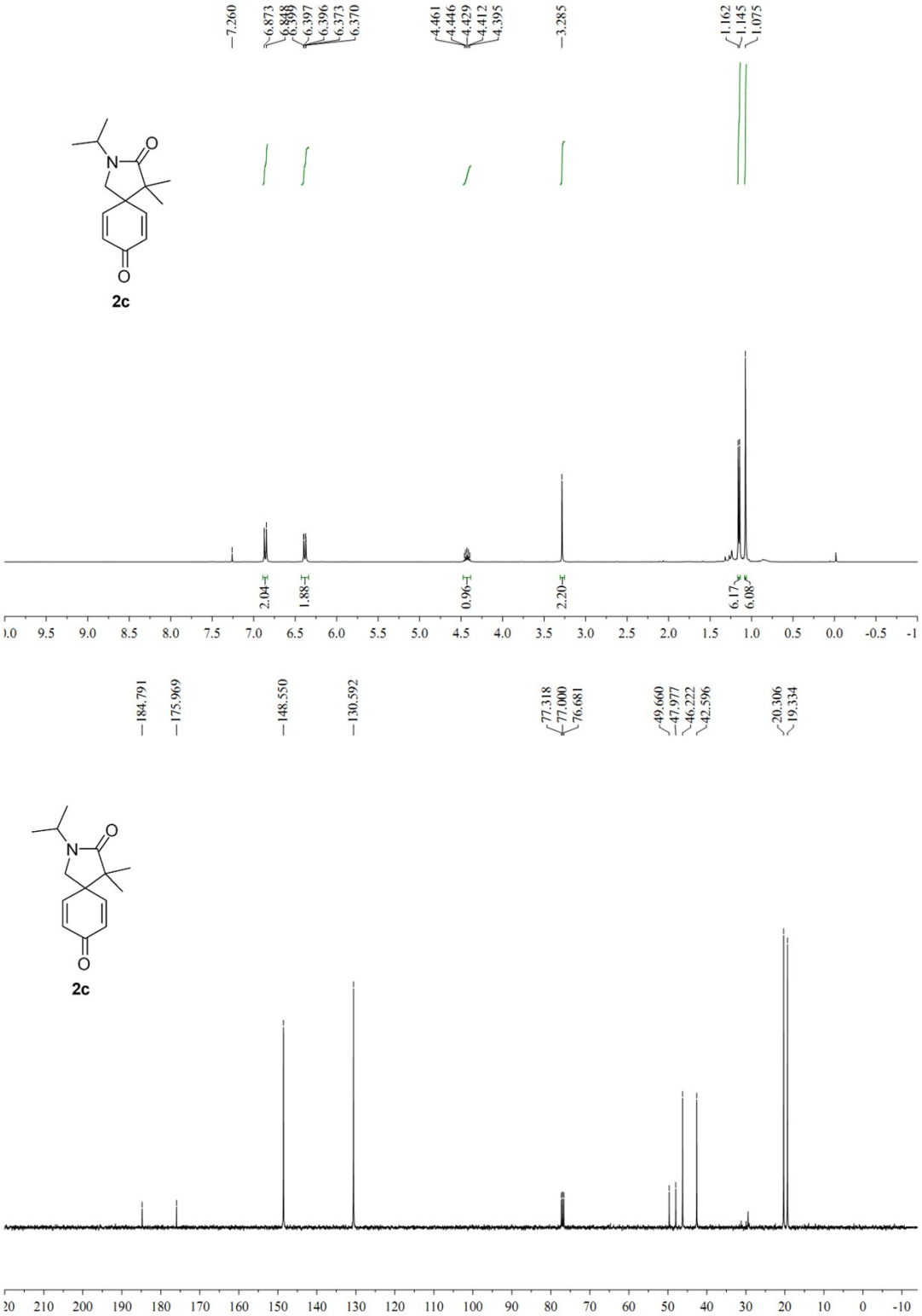


2,4,4-Trimethyl-2-azaspiro[4.5]deca-6,9-diene-3,8-dione (2b)

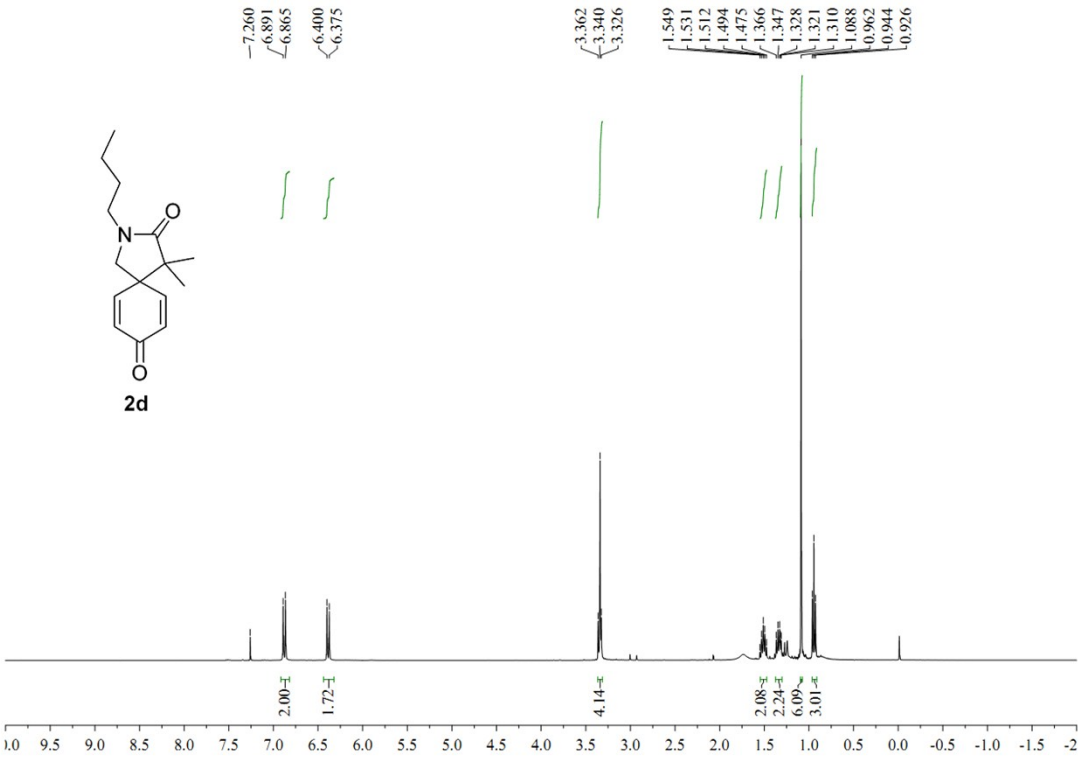


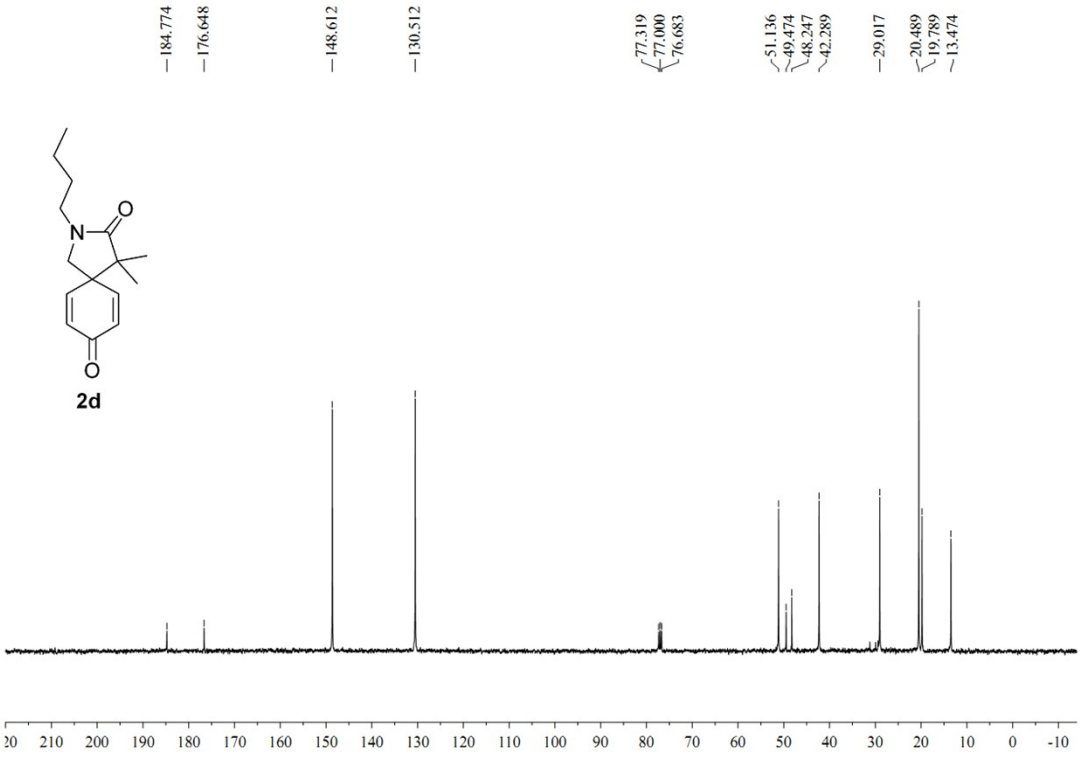


2-Isopropyl-4,4-dimethyl-2-azaspiro[4.5]deca-6,9-diene-3,8-dione (2c)

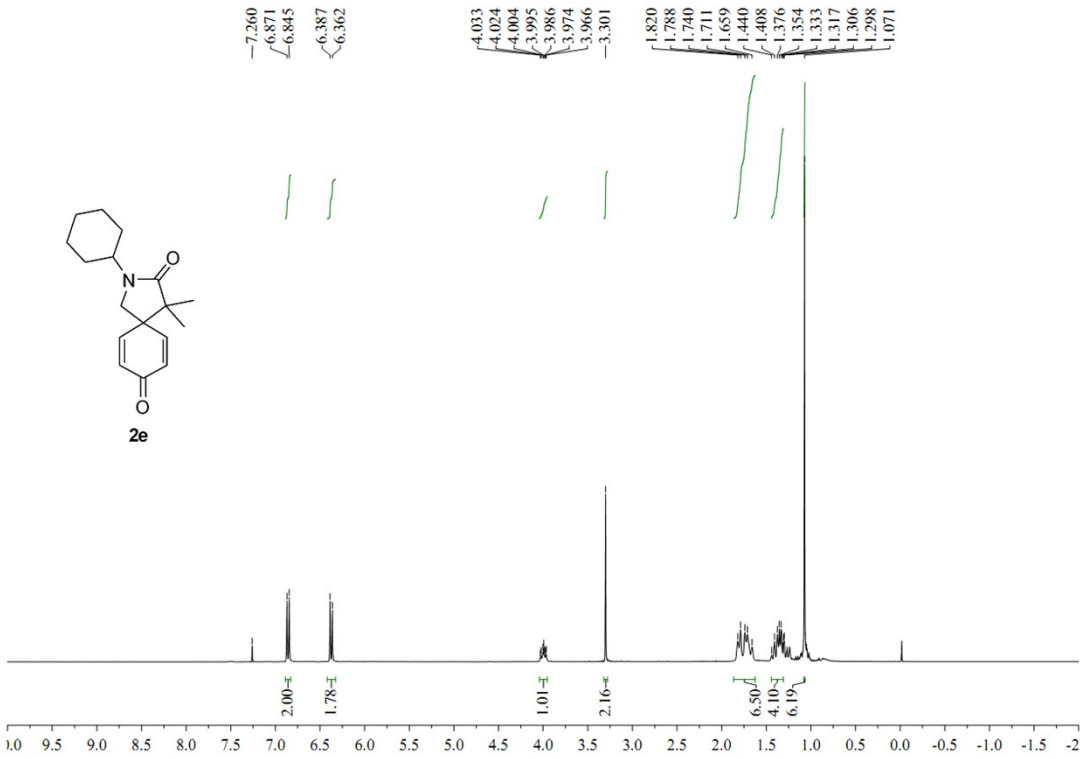


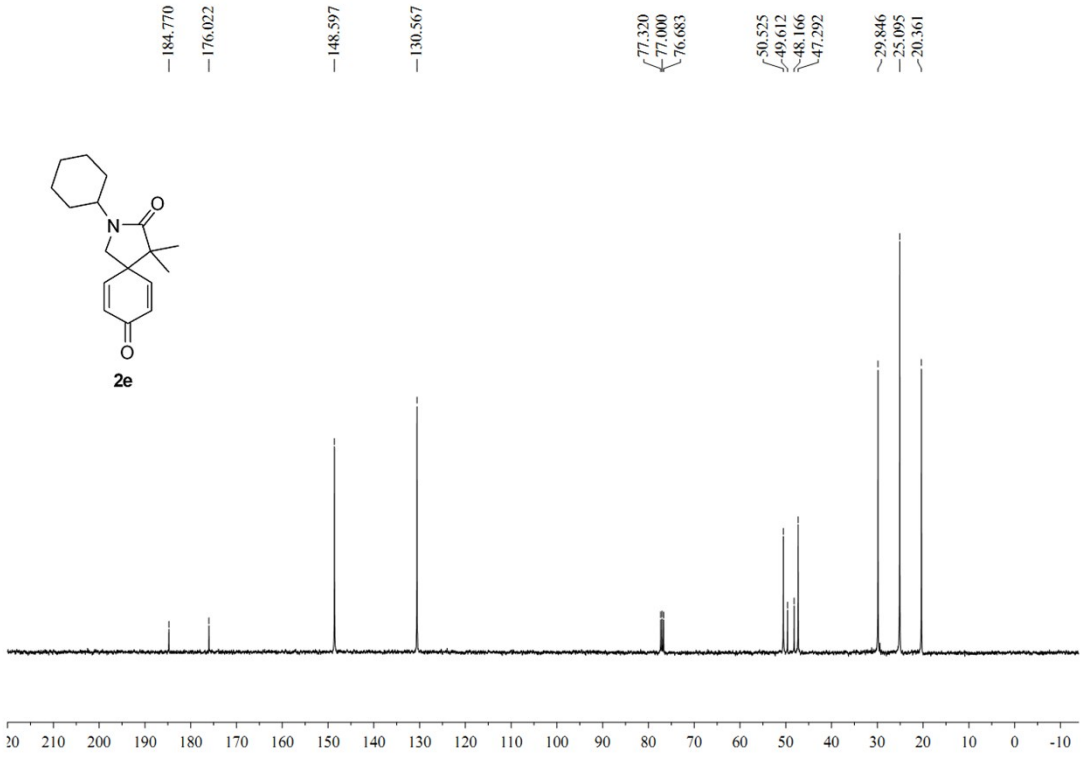
2-Butyl-4,4-dimethyl-2-azaspiro[4.5]deca-6,9-diene-3,8-dione (2d)



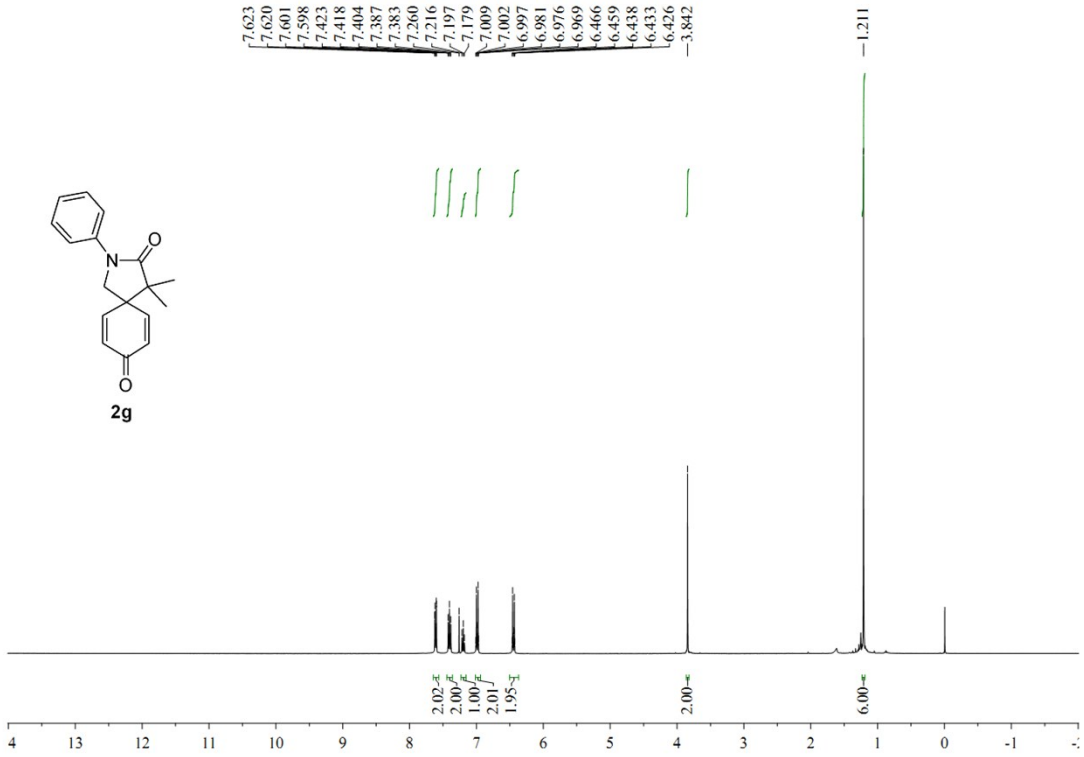


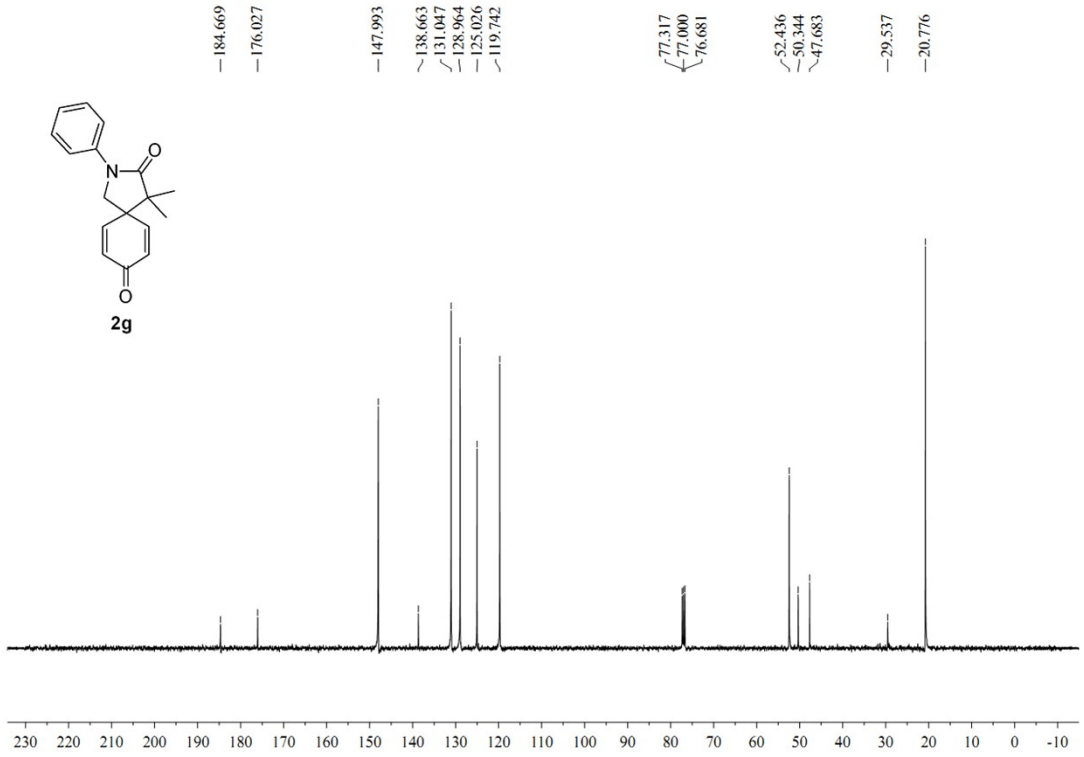
2-Cyclohexyl-4,4-dimethyl-2-azaspiro[4.5]deca-6,9-diene-3,8-dione (2e)



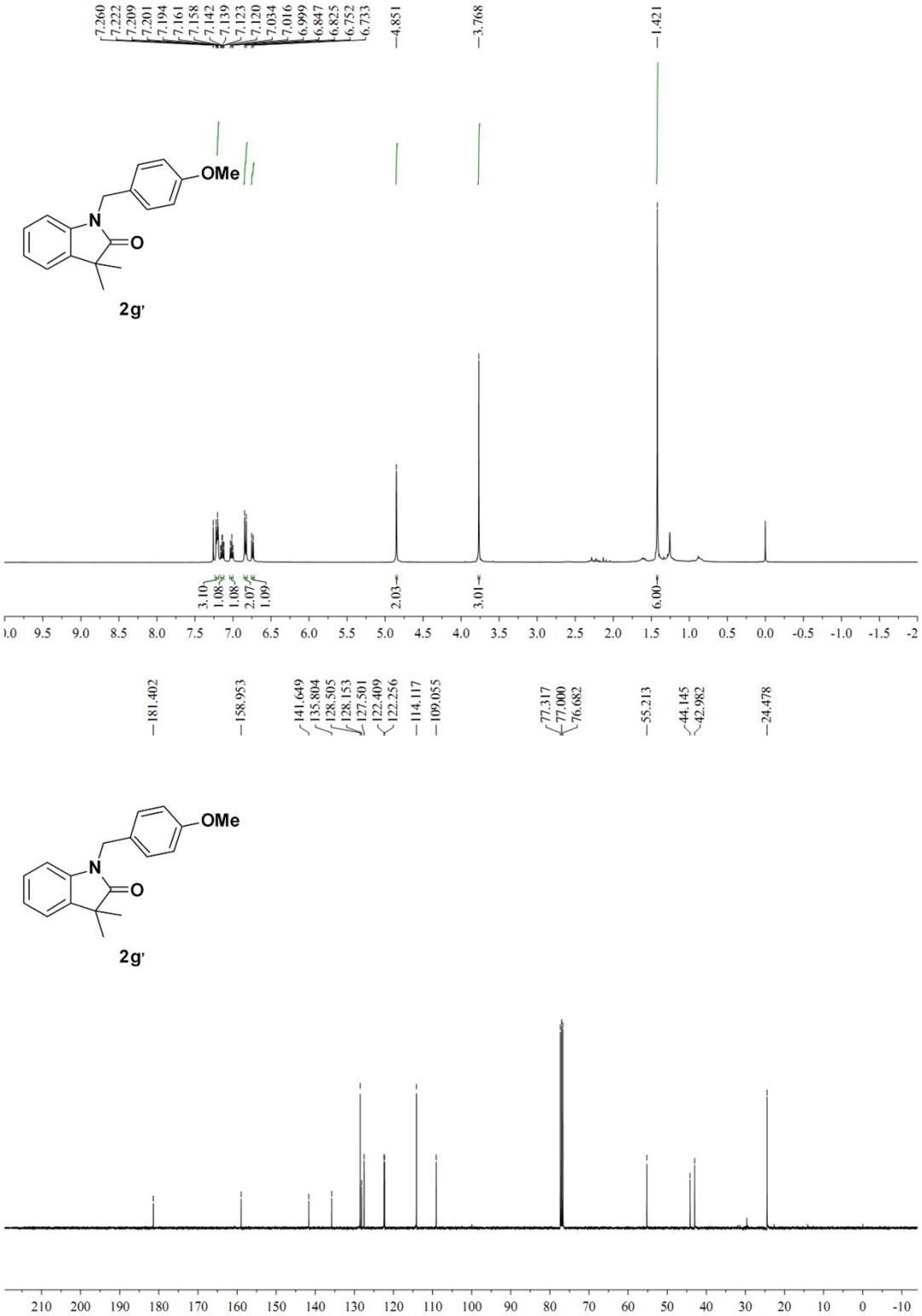


4,4-Dimethyl-2-phenyl-2-azaspiro[4.5]deca-6,9-diene-3,8-dione (2g)

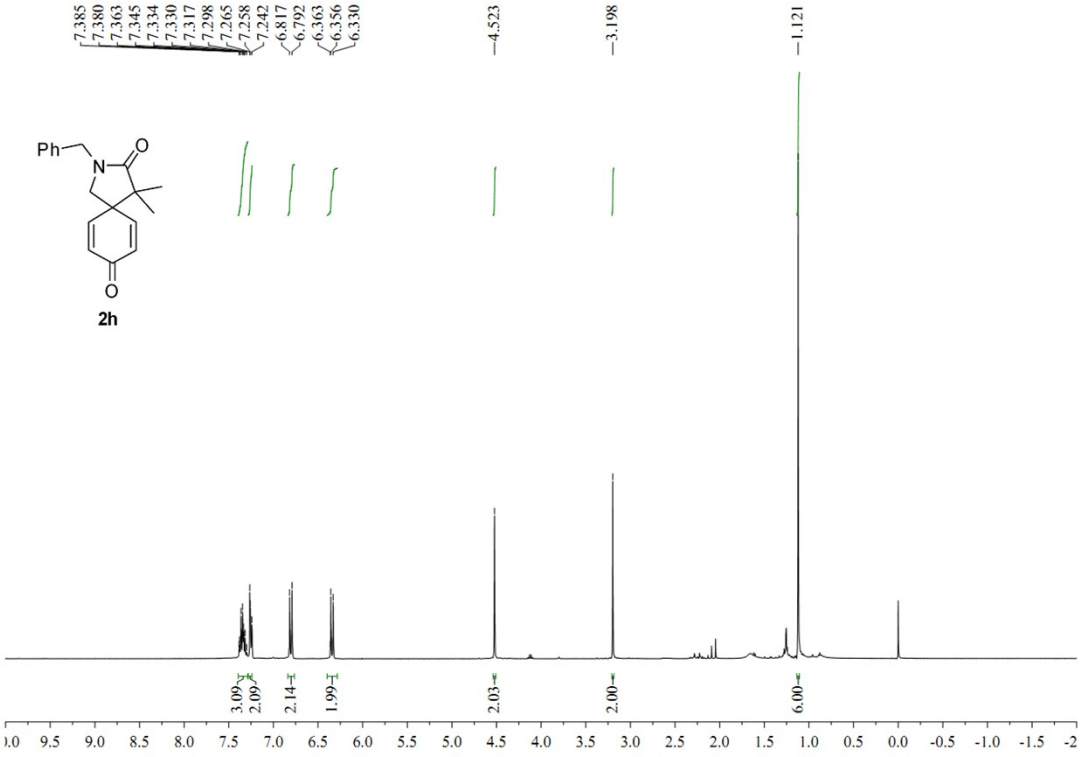


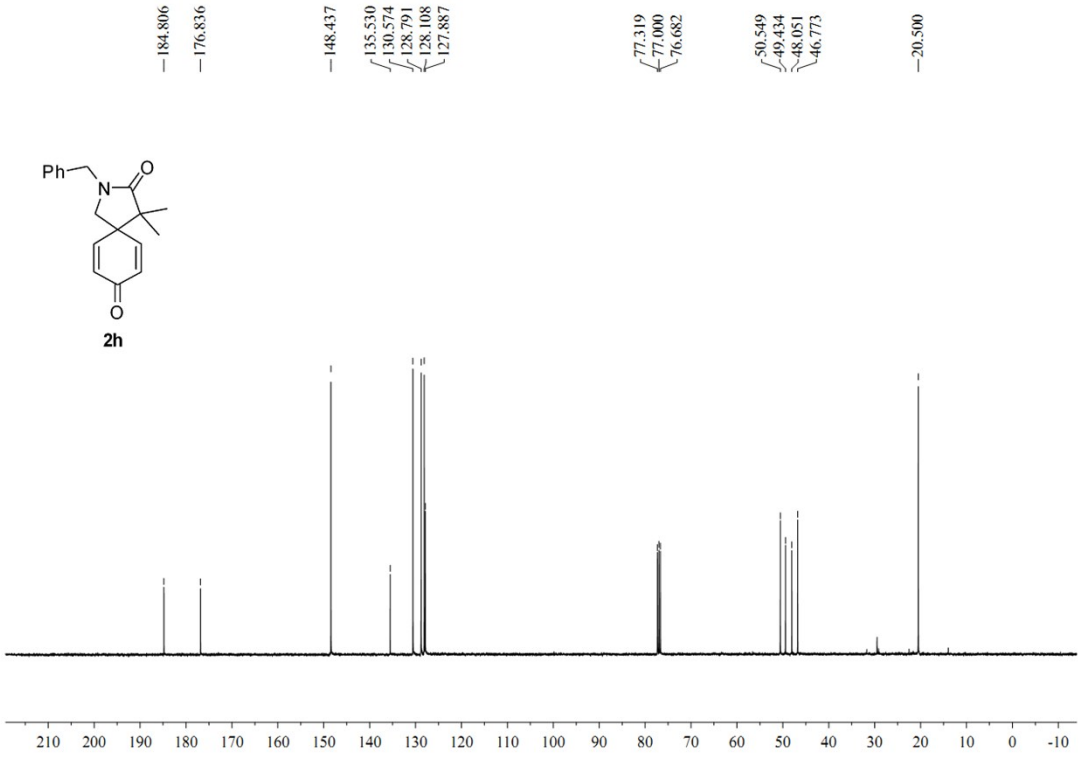


1-(4-Methoxybenzyl)-3,3-dimethylindolin-2-one (2g')

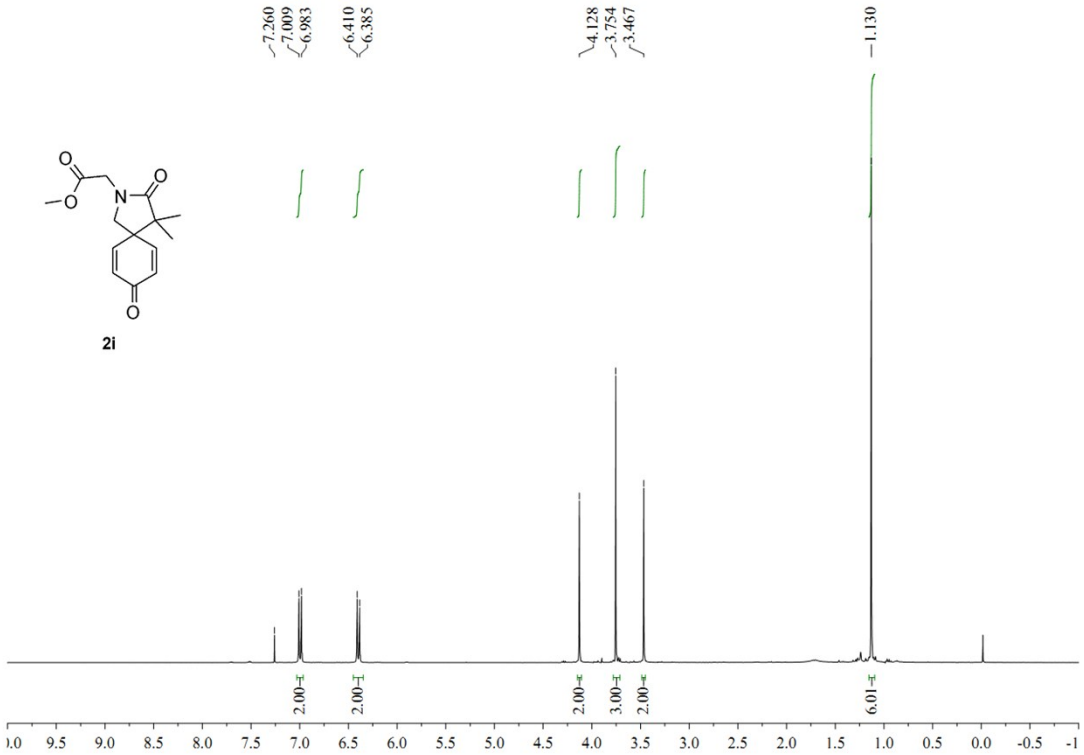


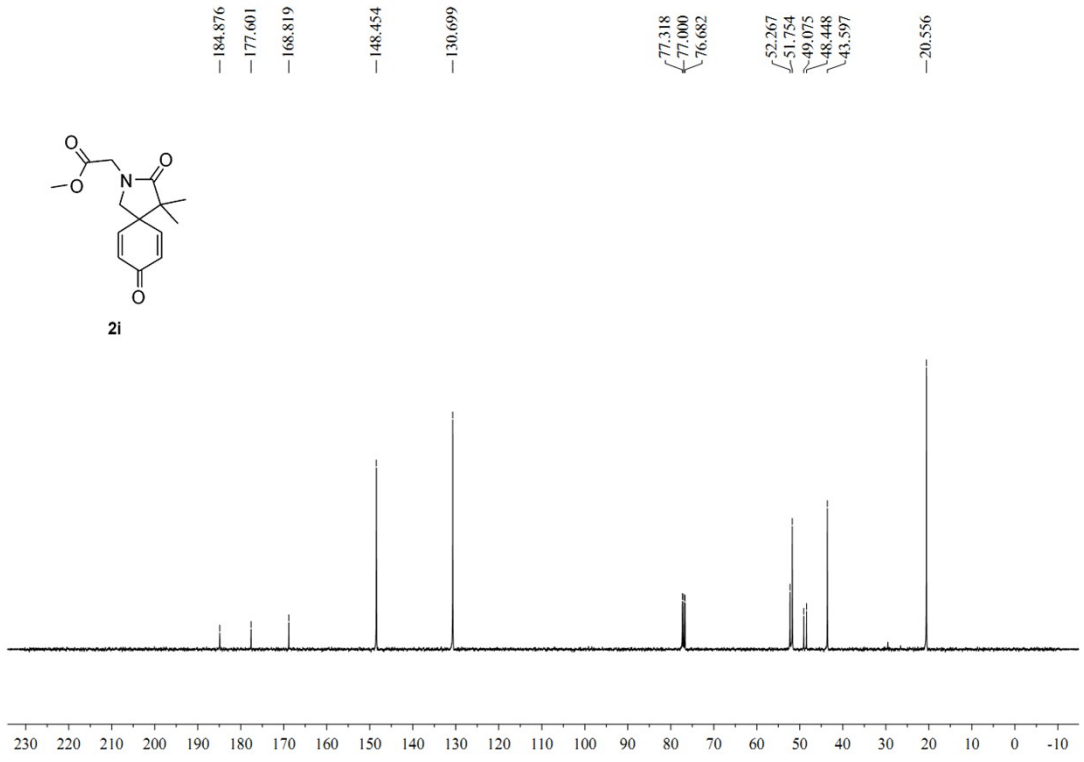
2-Benzyl-4,4-dimethyl-2-azaspiro[4.5]deca-6,9-diene-3,8-dione (2h)



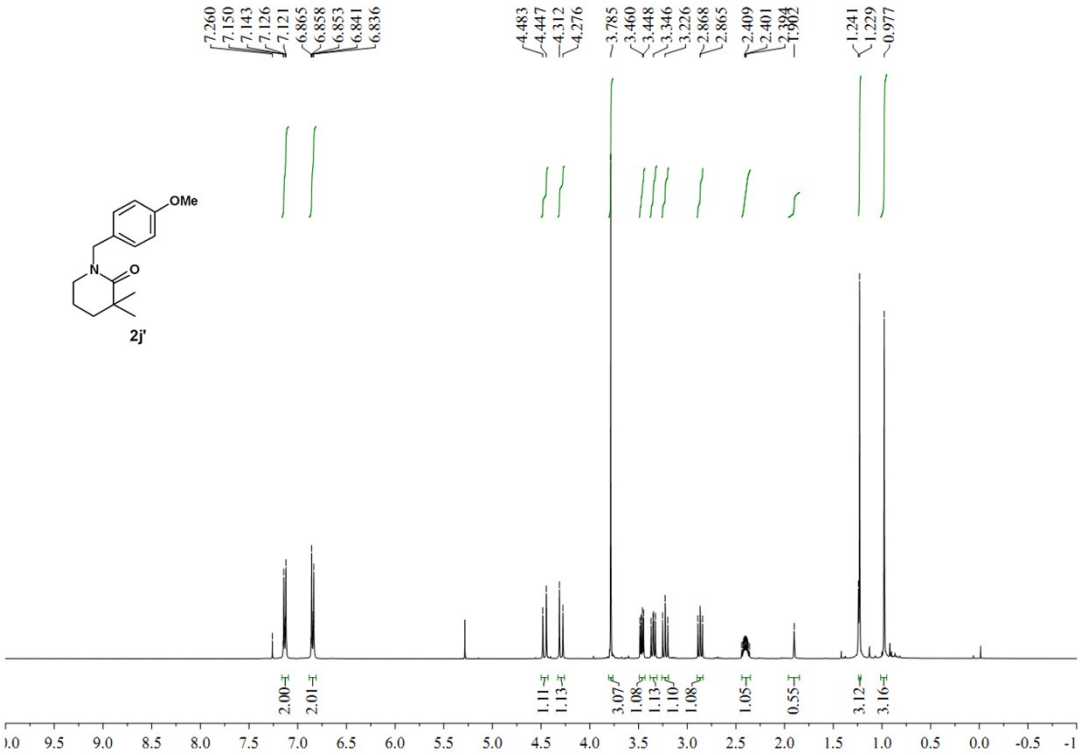


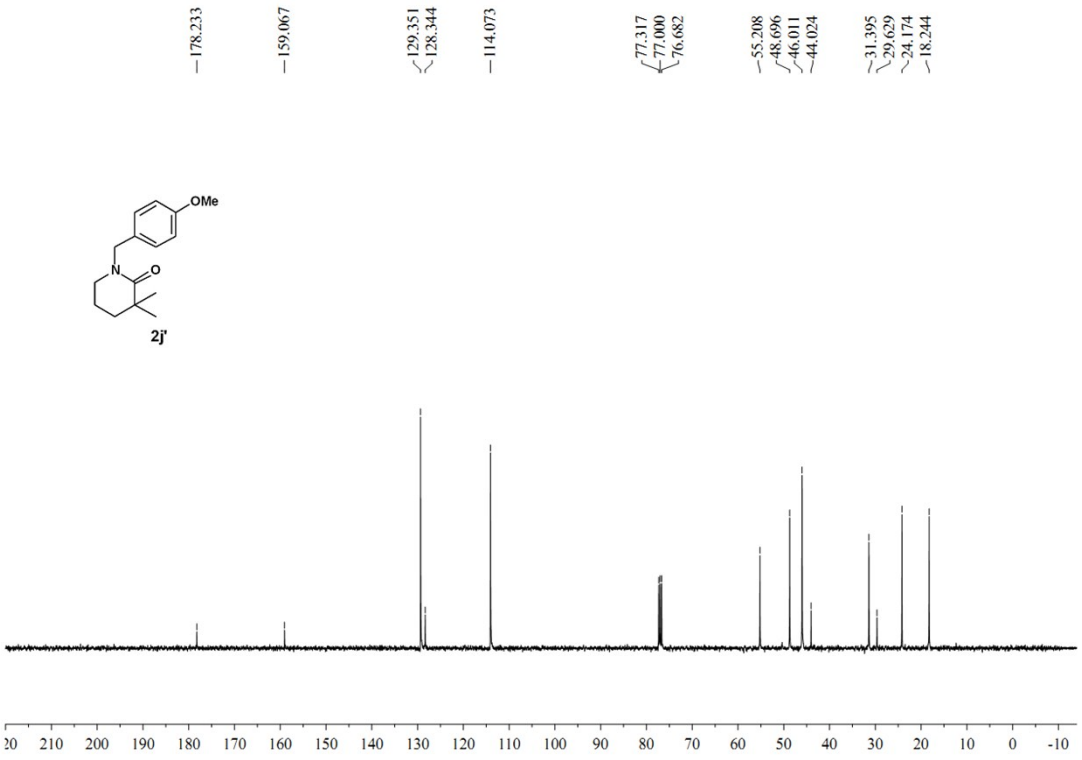
Methyl 2-(4,4-dimethyl-3,8-dioxo-2-azaspiro[4.5]deca-6,9-dien-2-yl)acetate (2i)



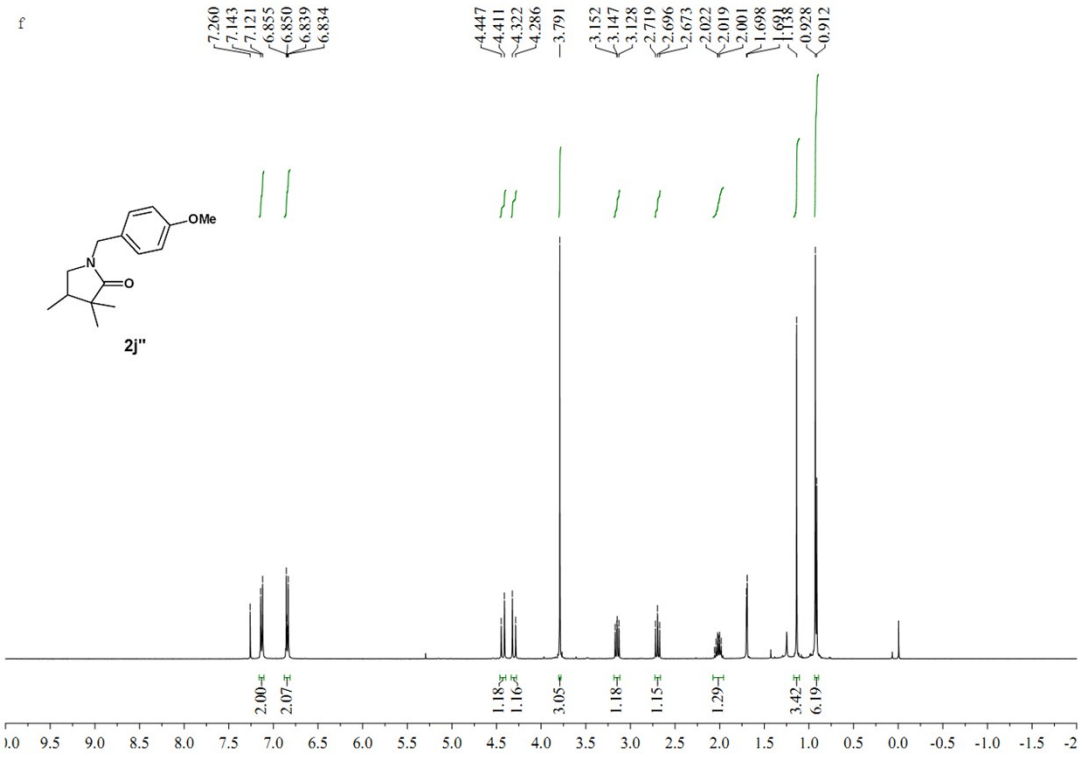


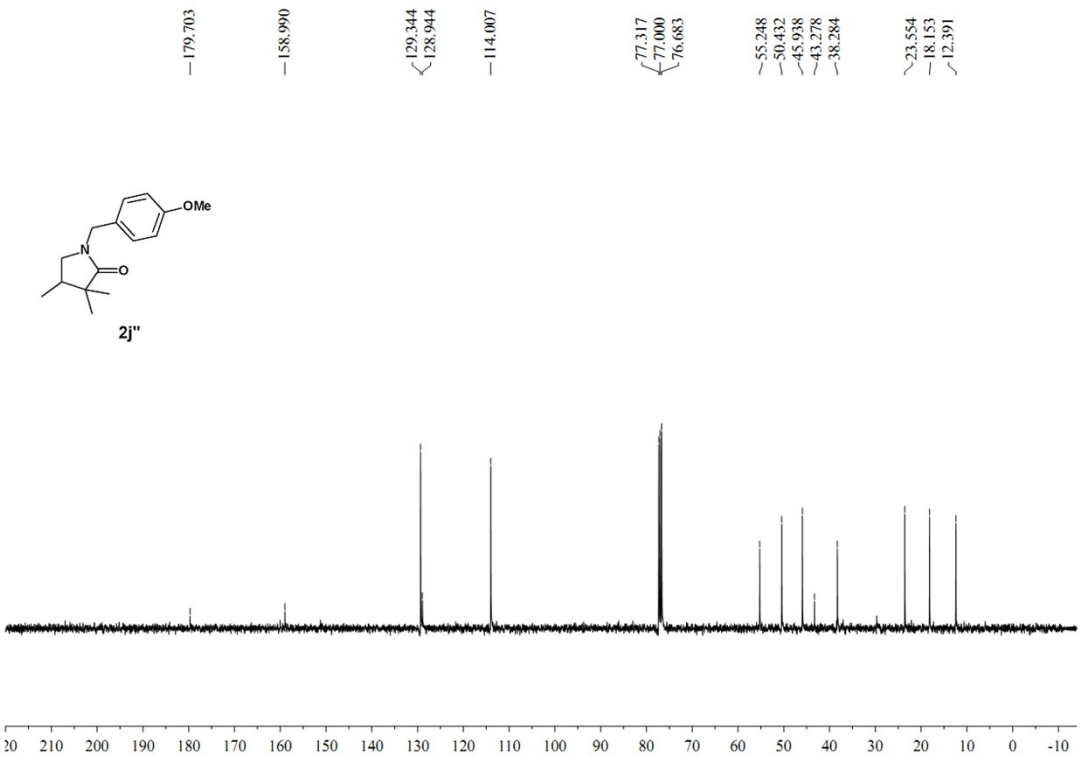
1-(4-Methoxybenzyl)-3,3-dimethylpiperidin-2-one (2j')



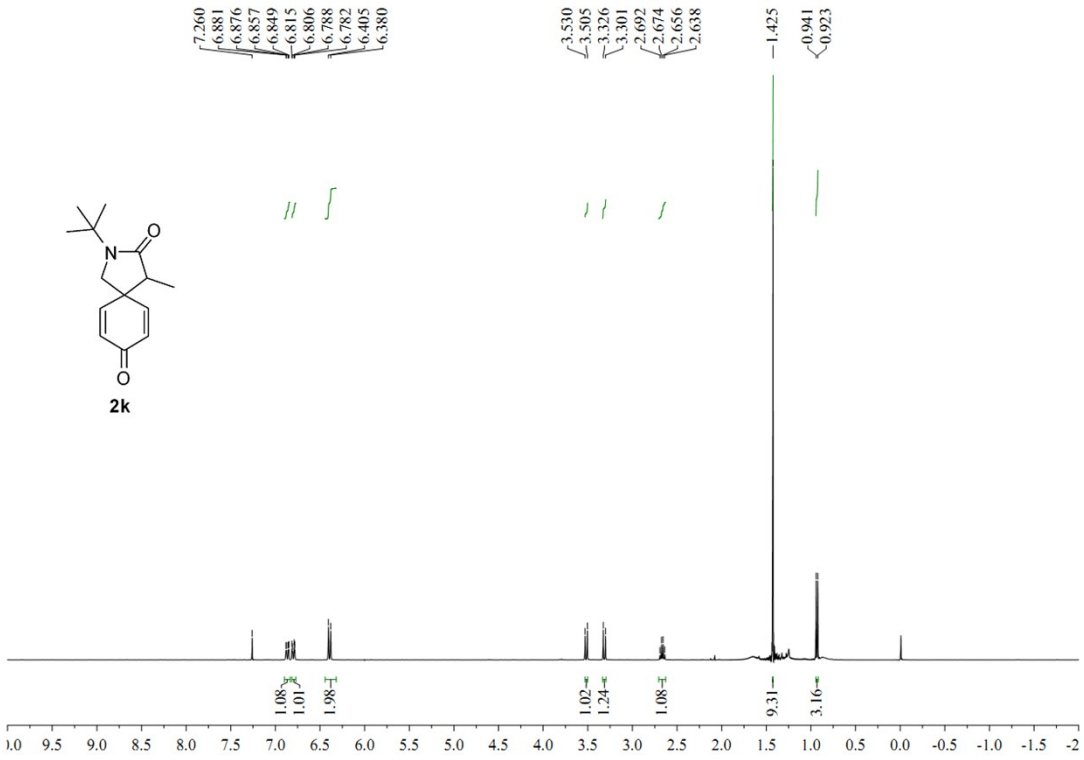


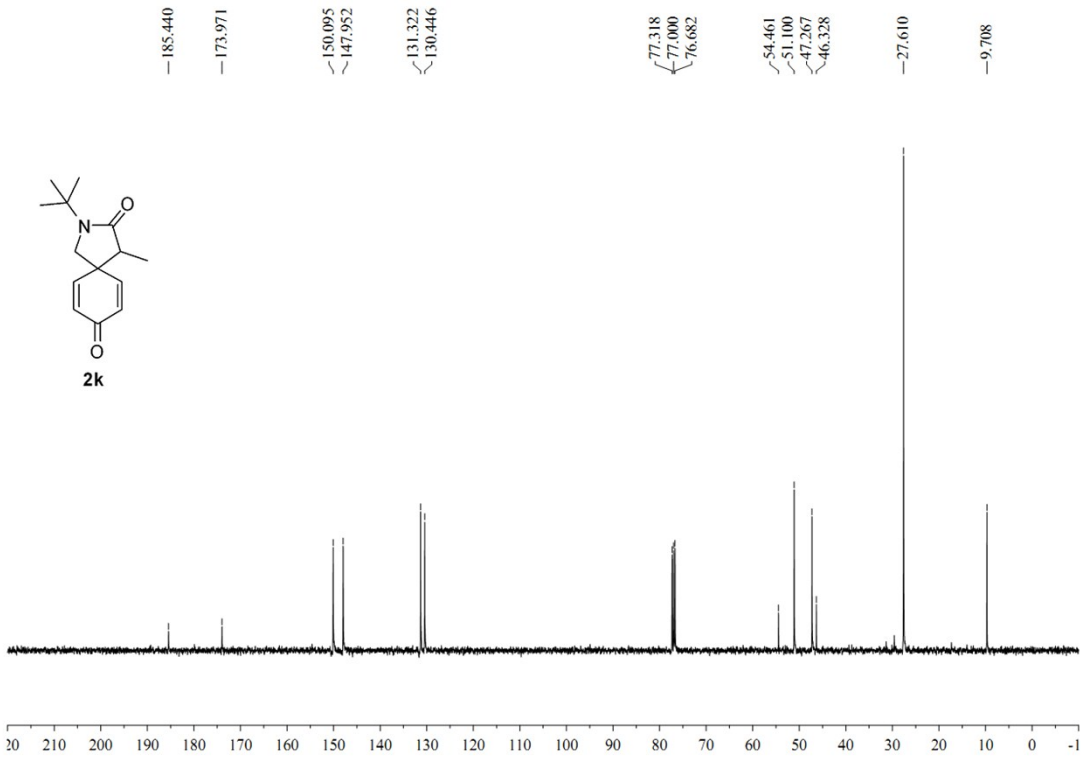
1-(4-Methoxybenzyl)-3,3,4-trimethylpyrrolidin-2-one (2j")





2-(*tert*-Butyl)-4-methyl-2-azaspiro[4.5]deca-6,9-diene-3,8-dione (2k)





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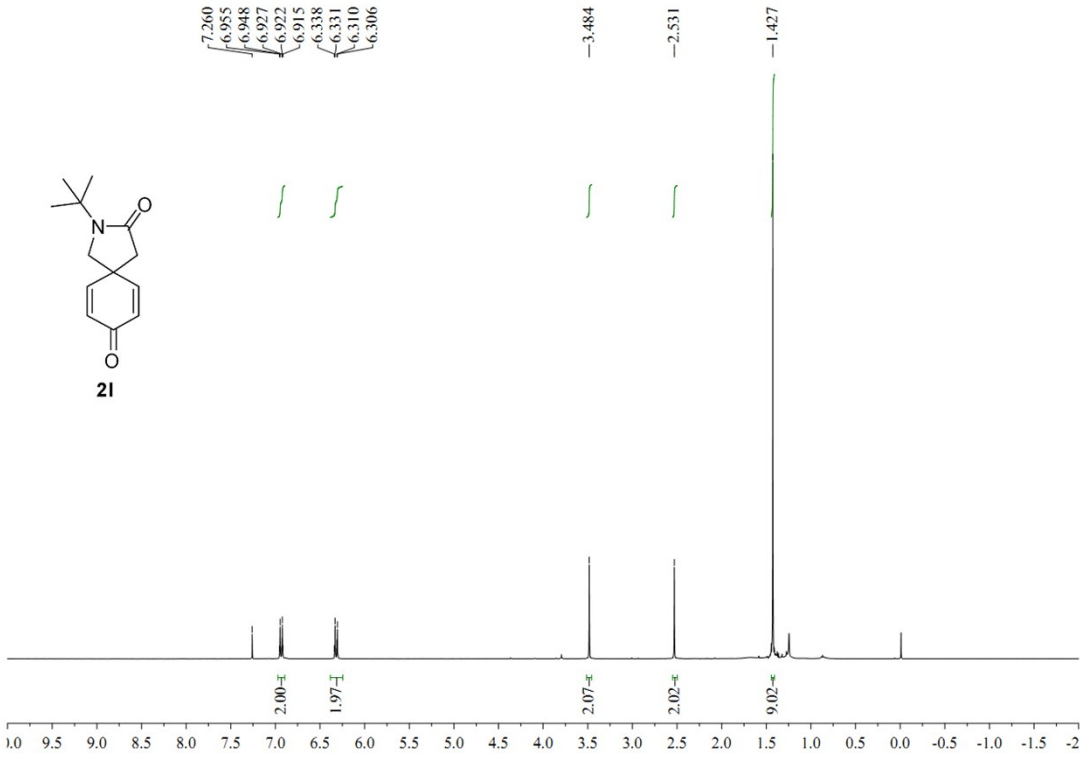
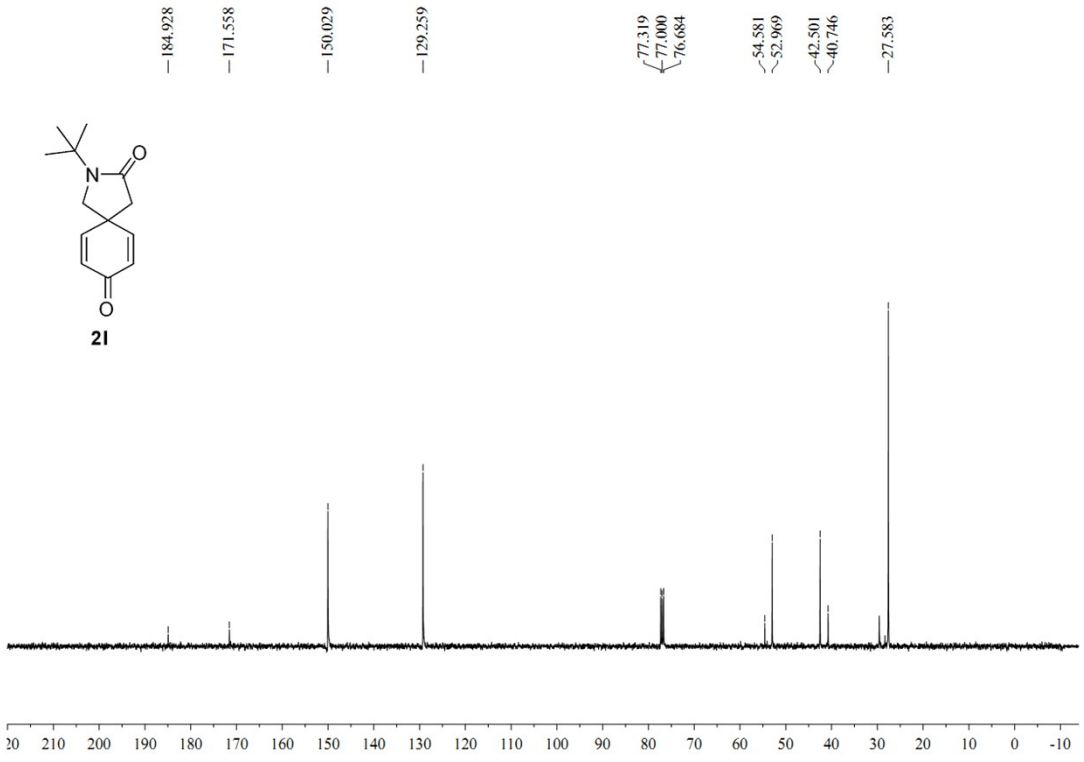
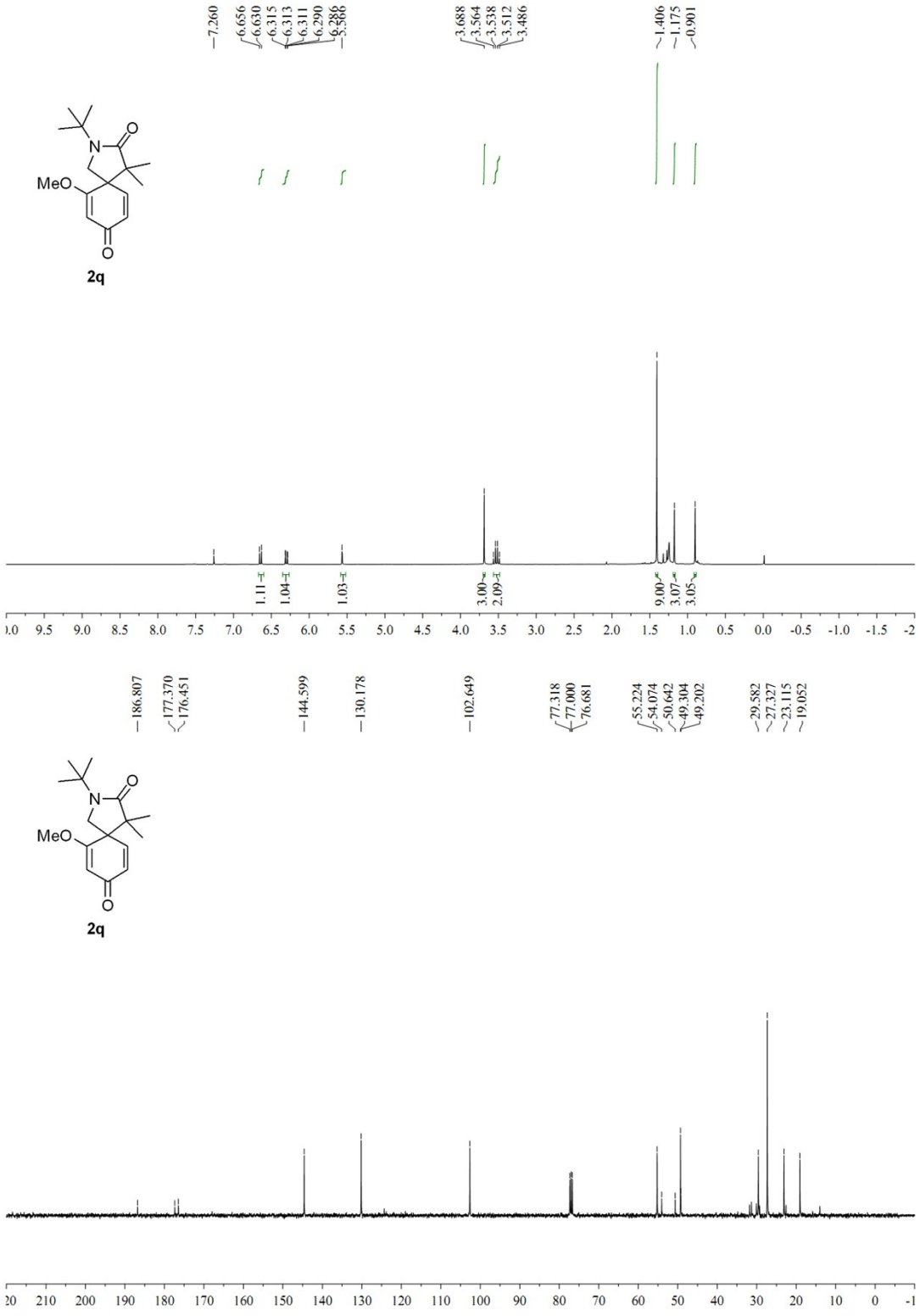
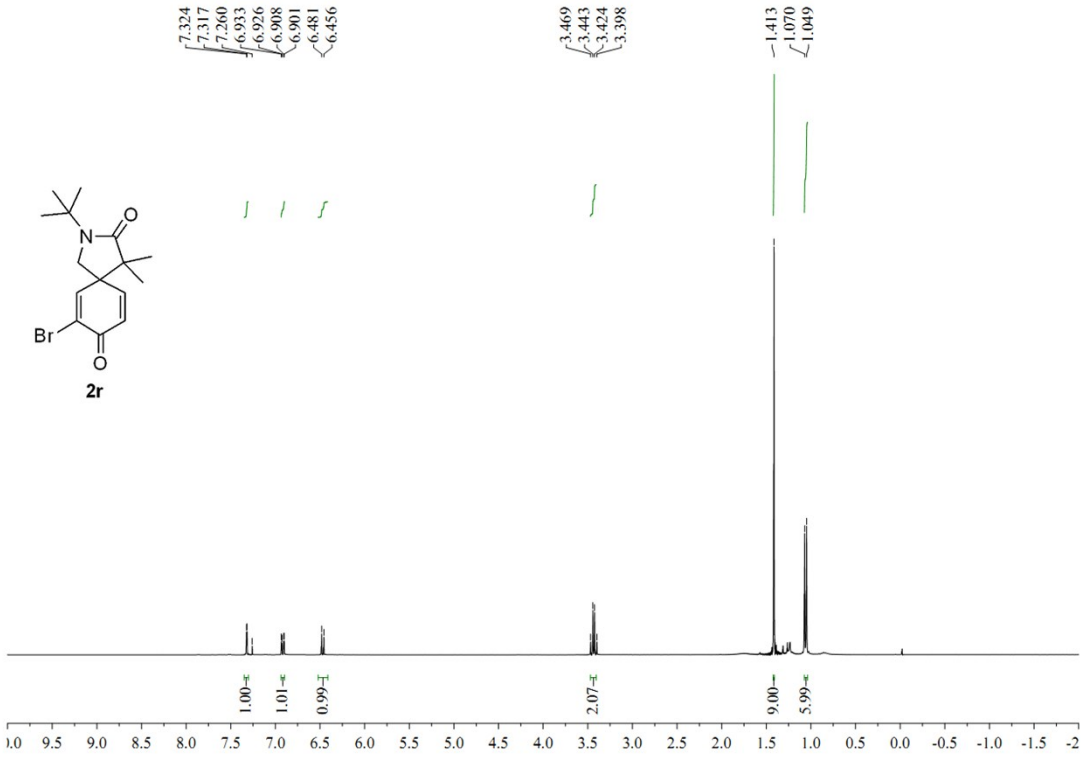


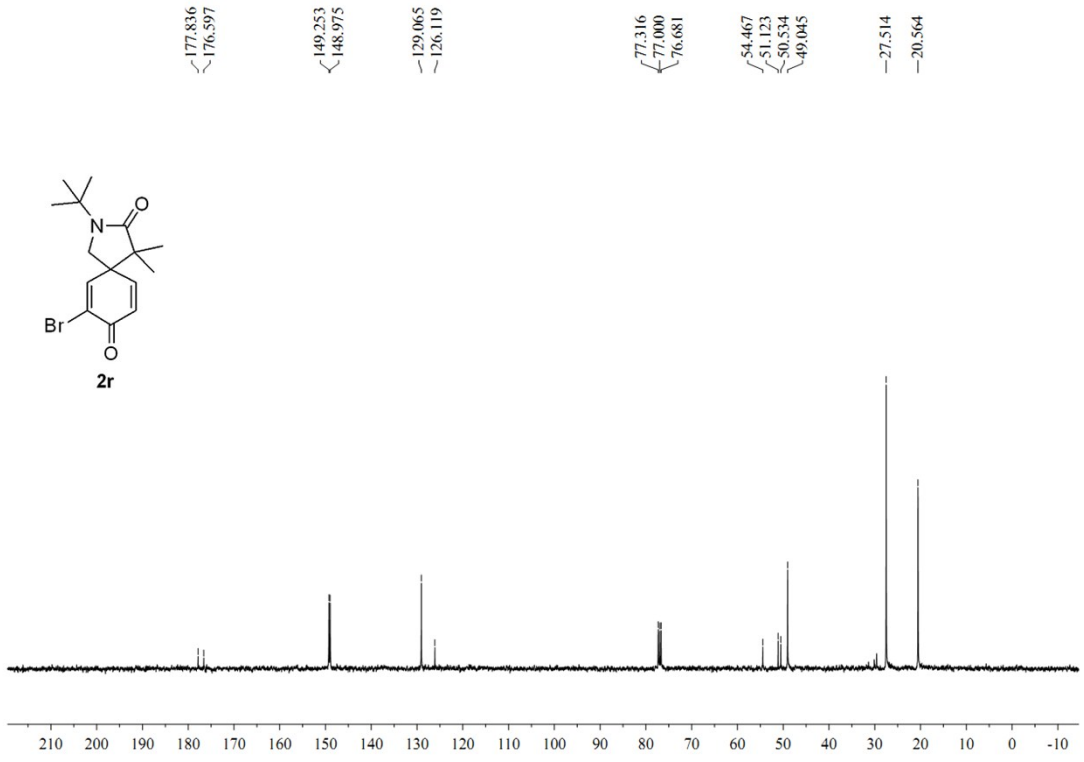


2-(*tert*-Butyl)-6-methoxy-4,4-dimethyl-2-azaspiro[4.5]deca-6,9-diene-3,8-dione (2q)



7-Bromo-2-(*tert*-butyl)-4,4-dimethyl-2-azaspiro[4.5]deca-6,9-diene-3,8-dione (2r)





1'-(*tert*-Butyl)-4',4'-dimethyl-4H-spiro[naphthalene-1,3'-pyrrolidine]-4,5'-dione (2s)