Efficient synthesis of tetrahydronaphthalene- or isochroman-fused spirooxindoles using tandem reactions

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Supporting Information

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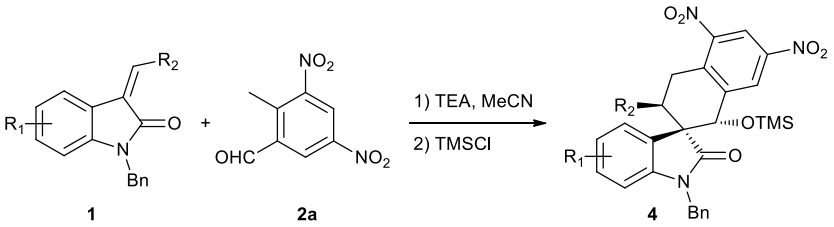
1. General methods

NMR data was obtained for ^{1}H at 400 MHz, and for ^{13}C at 100 MHz. Chemical shifts were reported in ppm from tetramethylsilane with the solvent resonance as the internal standard in $CDCl_3$ solution. ESI HRMS was performed on a Waters SYNAPT G2. Column chromatography was performed on silica gel (200-300 mesh) using an eluent of ethyl acetate and petroleum ether. TLC was performed on glass-backed silica plates; products were visualized using UV light and I_2. Melting points were determined on a Mel-Temp apparatus and were not corrected. All chemicals were used from Adamas-beta without purification unless otherwise noted.

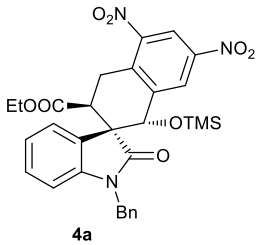
2. General procedure for the synthesis of tetrahydronaphthalene-fused spirooxindole 4



1 2a 4

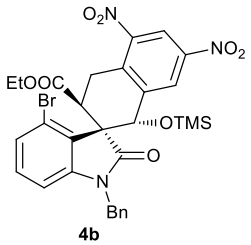
The reaction was carried out with 3-ylideneoxindole **1** (0.3 mmol), 2-methyl-3,5-dinitro-benzaldehyde **2a** (75.7 mg, 0.36 mmol) and TEA (8.4 μL, 0.06 mmol) in acetonitrile (4.0 mL) at 0 ^{o}C for 4h. Then the reaction mixture was concentrated and the residue was purified by flash chromatography on silica gel to afford the cycloaddition product **3**.

The protection of the hydroxyl group of the intermediate **3** gave the corresponding easily separable spirooxindole derivative **4**. To a solution of the intermediate **3** in methylene chloride (4 mL) was added TMSCl (25.9 μL, 0.3 mmol) and imidazole (40.8 mg, 0.6 mmol). The mixture was stirred at 0 ^{o}C for 30 min. The reaction was quenched with aqueous $NaHCO_3$, extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4 and concentrated. The residue was purified by chromategraphy on silica gel (petroleum ether/ethyl acetate = 15:1) to give the tetrahydronaphthalene-fused spirooxindole **4**.



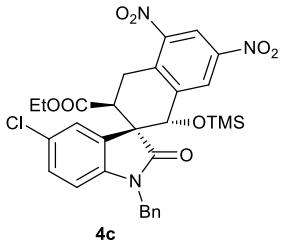
4a

4a was obtained as a white solid in 90% yield for two steps after flash chromatography. The dr value was calculated to be 90:10 by ^{1}H NMR analysis of the crude reaction mixture. m.p. 197-200 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.76 (s, 1H), 8.56 (s, 1H), 7.38-7.22 (m, 7H), 7.05 (t, *J* = 7.2 Hz, 1H), 6.77 (d, *J* = 8.0 Hz, 1H), 5.17 (s, 1H), 4.88 (s, 2H), 3.96 (dd, *J* = 16.0, 4.0 Hz, 1H), 3.68 (q, *J* = 7.2 Hz, 2H), 3.33-3.20 (m, 2H), 0.60 (t, *J* = 7.2 Hz, 3H), -0.21 (s, 9H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.5, 170.9, 148.4, 146.8, 144.7, 144.3, 137.5, 135.8, 129.6, 129.6, 128.9, 128.1, 127.9, 123.8, 123.6, 122.9, 118.8, 109.5, 74.6, 61.3, 54.8, 46.7, 44.4, 25.9, 13.5, -0.3 ppm; ESI HRMS: calcd. For $C_{30}H_{31}N_3O_8Si$+Na 612.1778, found 612.1773.



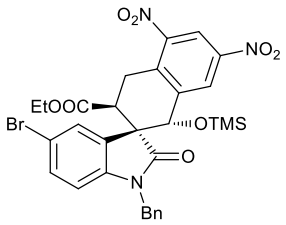
4b

4b was obtained as a white solid in 91% yield for two steps after flash chromatography. The dr value was calculated to be 92:8 by ^{1}H NMR analysis of the crude reaction mixture. m.p. 180-182 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.75 (s, 1H), 8.56 (s, 1H), 7.35-7.08 (m, 7H), 6.68 (d, *J* = 6.8 Hz, 1H), 5.80 (s, 1H), 5.12 (d, *J* = 15.6 Hz, 1H), 4.56 (d, *J* = 16.0 Hz, 1H), 4.32 (dd, *J* = 10.0, 6.4 Hz, 1H), 4.13-4.10 (m, 1H), 3.99-3.90 (m, 2H), 3.54 (dd, *J* = 18.0, 6.4 Hz, 1H), 0.97 (t, *J* = 7.2 Hz, 3H), -0.11 (s, 9H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.8, 170.4, 148.1, 146.8, 146.3, 143.0, 137.4, 135.1, 130.8, 128.7, 127.7, 127.4, 126.9, 126.8, 125.3, 118.7, 118.2, 108.5, 71.7, 61.3, 54.9, 43.9, 42.4, 26.2, 13.7, -0.3 ppm; ESI HRMS: calcd. For $C_{30}H_{30}N_3O_8BrSi$+Na 690.0883, found 690.0885.



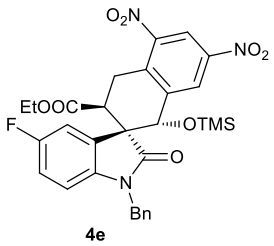
4c

4c was obtained as a white solid in 88% yield for two steps after flash chromatography. The dr value was calculated to be 90:10 by ^{1}H NMR analysis of the crude reaction mixture. m.p. 142-144 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.77 (s, 1H), 8.55 (s, 1H), 7.34-7.21 (m, 7H), 6.69 (d, *J* = 8.4 Hz, 1H), 5.18 (s, 1H), 4.86 (s, 2H), 3.98 (dd, *J* = 16.0, 4.0 Hz, 1H), 3.86-3.73 (m, 2H), 3.32-3.20 (m, 2H), 0.72 (t, *J* = 7.2 Hz, 3H), -0.16 (s, 9H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.9, 170.6, 148.3, 146.7, 143.7, 143.1, 137.2, 135.2, 131.3, 129.3, 129.0, 128.2, 128.2, 127.8, 124.1, 123.6, 119.0, 110.4, 74.3, 61.5, 54.8, 46.5, 44.5, 25.8, 13.6, -0.3 ppm; ESI HRMS: calcd. For $C_{30}H_{30}N_3O_8ClSi$+Na 646.1388, found 646.1391.



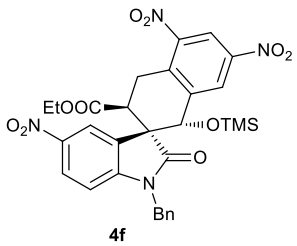
4d

4d was obtained as a white solid in 86% yield for two steps after flash chromatography. The dr value was calculated to be 85:15 by ^{1}H NMR analysis of the crude reaction mixture. m.p. 158-160 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.78 (s, 1H), 8.55 (s, 1H), 7.39-7.28 (m, 7H), 6.64 (d, *J* = 8.4 Hz, 1H), 5.18 (s, 1H), 4.86 (s, 2H), 3.98 (dd, *J* = 16.4, 4.0 Hz, 1H), 3.86-3.75 (m, 2H), 3.32-3.18 (m, 2H), 0.73 (t, *J* = 7.2 Hz, 3H), -0.16 (s, 9H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.8, 170.6, 148.3, 146.7, 143.7, 143.6, 137.2, 135.2, 132.3, 131.7, 129.0, 128.2, 127.7, 126.8, 123.8, 119.0, 115.2, 110.8, 74.3, 61.5, 54.7, 46.5, 44.4, 25.8, 13.6, -0.3 ppm; ESI HRMS: calcd. For $C_{30}H_{30}N_3O_8BrSi$+Na 690.0883, found 690.0880.



4e

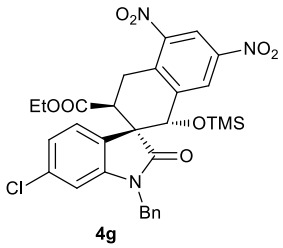
4e was obtained as a white solid in 92% yield for two steps after flash chromatography. The dr value was calculated to be 82:18 by ^{1}H NMR analysis of the crude reaction mixture. m.p. 165-168 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.77 (s, 1H), 8.55 (s, 1H), 7.34-7.28 (m, 5H), 7.04 (dd, *J* = 8.0, 2.8 Hz, 1H), 6.96 (td, *J* = 8.8, 2.4 Hz, 1H), 6.69 (q, *J* = 4.4 Hz, 1H), 5.17 (s, 1H), 4.87 (s, 2H), 3.98 (dd, *J* = 15.6, 3.2 Hz, 1H), 3.84-3.72 (m, 2H), 3.32-3.21 (m, 2H), 0.70 (t, *J* = 7.2 Hz, 3H), -0.16 (s, 9H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.10, 170.7, 159.2 (d, J_{CF} = 241.1 Hz), 148.4, 146.8, 143.8, 140.7, 137.2, 135.4, 131.1 (d, J_{CF} = 7.4 Hz), 129.0, 128.1, 127.8, 123.9, 118.9, 115.7 (d, J_{CF} = 23.2 Hz), 112.0 (d, J_{CF} = 24.3 Hz), 110.0 (d, J_{CF} = 7.6 Hz), 74.4, 61.4, 55.1, 46.5, 44.5, 25.8, 13.6, -0.3 ppm; ESI HRMS: calcd. For $C_{30}H_{30}N_3O_8FSi$ +Na 630.1684, found 630.1688.



4f

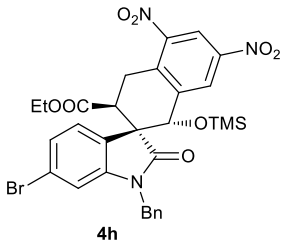
4f was obtained as a white solid in 85% yield for two steps after flash chromatography. The dr value was calculated to be 80:20 by ^{1}H NMR analysis of the crude reaction mixture. m.p. 185-188 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.89 (s, 1H), 8.44 (s, 1H), 8.10 (d, *J* = 8.8 Hz, 1H), 7.41-7.30 (m, 5H), 6.80 (d, *J* = 8.4 Hz, 1H), 6.69 (s, 1H), 5.42 (d, *J* = 15.6 Hz, 1H), 5.31 (s, 1H), 4.68 (d, *J* = 16.0 Hz, 1H), 3.99 (dd, *J* = 18.4, 7.6 Hz, 1H), 3.89 (t, *J* = 7.6 Hz, 1H), 3.82-3.72 (m, 2H), 3.61 (dd, *J* = 18.3, 7.6 Hz, 1H), 0.80 (t, *J* = 7.2 Hz, 3H), 0.17 (s, 9H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.4, 169.1, 149.7, 148.3, 146.2, 142.7, 142.5, 136.0, 133.7, 128.6, 127.8, 127.1, 126.8, 125.6, 124.2, 119.2, 118.9, 108.3, 73.9, 61.3, 54.5, 44.4, 44.3,

25.2, 13.2, -0.2 ppm; ESI HRMS: calcd. For $C_{30}H_{30}N_4O_{10}Si$ +Na 657.1629, found 657.1633.



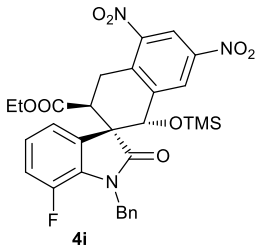
4g

4g was obtained as a white solid in 85% yield for two steps after flash chromatography. The dr value was calculated to be 88:12 by ^{1}H NMR analysis of the crude reaction mixture. m.p. 168-170 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.77 (s, 1H), 8.54 (s, 1H), 7.3-7.29 (m, 5H), 7.16 (d, *J* = 8.0 Hz, 1H), 7.04 (dd, *J* = 8.0, 2.0 Hz, 1H), 6.77 (d, *J* = 1.6 Hz, 1H), 5.13 (s, 1H), 4.85 (s, 2H), 3.96 (dd, *J* = 16.0, 3.6 Hz, 1H), 3.74 (q, *J* = 7.2 Hz, 2H), 3.31-3.19 (m, 2H), 0.70 (t, *J* = 7.2 Hz, 3H), -0.16 (s, 9H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.3, 170.6, 148.3, 146.7, 145.9, 143.8, 137.2, 135.4, 135.1, 129.0, 128.2, 127.9, 127.7, 124.4, 123.8, 122.4, 118.9, 109.9, 74.3, 61.4, 54.4, 46.5, 44.4, 25.7, 13.6, -0.3 ppm; ESI HRMS: calcd. For $C_{30}H_{30}N_3O_8ClSi$+Na 646.1388, found 646.1384.



4h

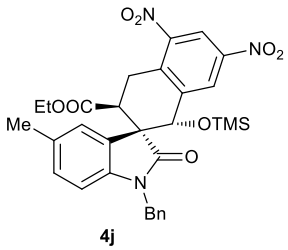
4h was obtained as a white solid in 81% yield for two steps after flash chromatography. The dr value was calculated to be 92:8 by ^{1}H NMR analysis of the crude reaction mixture. m.p. 176-178 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.77 (s, 1H), 8.53 (s, 1H), 7.35-7.28 (m, 5H), 7.20 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.10 (d, *J* = 8.0 Hz, 1H), 6.92 (s, 1H), 5.13 (s, 1H), 4.85 (s, 2H), 3.95 (dd, *J* = 16.0, 3.6 Hz, 1H), 3.74 (q, *J* = 7.2 Hz, 2H), 3.31-3.19 (m, 2H), 0.71 (t, *J* = 7.2 Hz, 3H), -0.16 (s, 9H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.2, 170.6, 146.7, 146.0, 143.7, 137.2, 135.1, 129.0, 128.5, 128.2, 127.7, 125.5, 124.7, 123.8, 123.1, 118.9, 112.6, 74.3, 61.4, 54.5, 46.4, 44.4, 25.7, 13.6, -0.3 ppm; ESI HRMS: calcd. For $C_{30}H_{30}N_3O_8BrSi$+Na 690.0883, found 690.0886.



4i

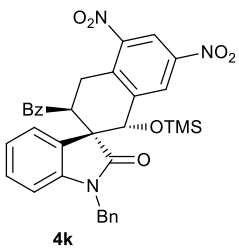
4i was obtained as a white solid in 84% yield for two steps after flash chromatography. The dr value was calculated to be 85:15 by ^{1}H NMR analysis of the crude reaction mixture. m.p. 96-98 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.77 (s, 1H), 8.54 (s, 1H), 7.41-7.28 (m, 5H), 7.0-7.01 (m, 3H), 5.13 (s, 1H), 5.02 (dd, *J* = 23.2, 15.2 Hz, 2H), 3.95 (dd, *J* = 15.6, 3.2 Hz, 1H), 3.72-3.62 (m, 2H), 3.30-3.18 (m, 2H), 0.61 (t, *J* = 7.2 Hz, 3H), -0.19 (s, 9H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.3, 170.6, 148.4, 147.6 (d, J_{CF} = 243.6 Hz), 146.8, 143.9, 137.3, 137.0,

132.8 (d, J_{CF} = 3.5 Hz), 131.4 (d, J_{CF} = 8.5 Hz), 128.7, 128.2 (d, J_{CF} = 1.5 Hz), 128.0, 123.8, 123.6, 123.6, 119.4 (d, J_{CF} = 3.2 Hz), 118.9, 117.8 (d, J_{CF} = 19.5 Hz), 74.8, 61.3, 46.9, 45.9 (d, J_{CF} = 4.5 Hz), 25.8, 13.5, -0.3 ppm; ESI HRMS: calcd. For $C_{30}H_{30}N_3O_8FSi$ +Na 630.1684, found 630.1682.



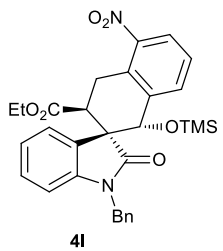
4j

4j was obtained as a light yellow solid in 78% yield for two steps after flash chromatography. The dr value was calculated to be 86:14 by ^{1}H NMR analysis of the crude reaction mixture. m.p. 154-156 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.76 (s, 1H), 8.56 (s, 1H), 7.36-7.25 (m, 5H), 7.08 (s, 1H), 7.33 (d, *J* = 8.0 Hz, 1H), 6.65 (d, *J* = 7.9 Hz, 1H), 5.16 (s, 1H), 4.86 (dd, *J* = 23.6, 15.6 Hz, 2H), 3.96 (dd, *J* = 16.0, 4.0 Hz, 1H), 3.75-3.66 (m, 2H), 3.32-3.18 (m, 2H), 2.31 (s, 3H), 0.62 (t, *J* = 7.2 Hz, 3H), -0.20 (s, 9H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.4, 170.9, 148.4, 146.7, 144.4, 142.2, 137.5, 135.9, 132.5, 129.7, 129.7, 129.0, 128.0, 128.0, 124.4, 123.8, 118.8, 109.3, 74.6, 61.2, 54.8, 46.7, 44.4, 25.9, 21.3, 13.5, -0.3 ppm; ESI HRMS: calcd. For $C_{31}H_{33}N_3O_8Si$ +Na 626.1935, found 626.1937.



4k

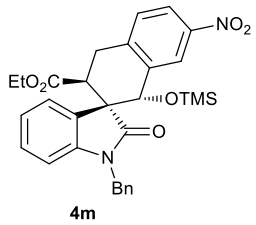
4k was obtained as a white solid in 75% yield for two steps after flash chromatography. The dr value was calculated to be 80:20 by ^{1}H NMR analysis of the crude reaction mixture. m.p. 185-187 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.81 (s, 1H), 8.59 (s, 1H), 7.38 (t, *J* = 7.2 Hz, 1H), 7.32-7.12 (m, 10H), 7.04-6.96 (m, 2H), 6.32 (d, *J* = 7.2 Hz, 1H), 5.17 (s, 1H), 5.03 (d, *J* = 15.2 Hz, 1H), 4.10-3.95 (m, 3H), 3.47 (dd, *J* = 16.8, 11.6 Hz, 1H), -0.27 (s, 9H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 199.3, 177.1, 148.7, 146.9, 144.6, 144.4, 138.4, 137.0, 135.7, 133.4, 129.5, 129.2, 128.7, 128.6, 128.3, 128.2, 128.1, 125.1, 123.9, 123.3, 119.1, 109.3, 75.2, 55.3, 49.2, 44.7, 26.0, -0.2 ppm; ESI HRMS: calcd. For $C_{34}H_{31}N_3O_7Si$ +Na 644.1829, found 644.1825.



4l

4l was obtained as a semisolid in 52% yield for two steps after flash chromatography. The dr value was calculated to be 88:12 by ^{1}H NMR analysis of the crude reaction mixture; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.16 (d, *J* = 8.4 Hz, 1H), 7.42 (d, *J* = 8.4 Hz, 1H), 7.36-7.25 (m, 6H), 7.19 (t, *J* = 8.0 Hz, 1H), 7.13 (d, *J* = 7.6 Hz, 1H), 6.98 (t, *J* = 7.6 Hz, 1H), 6.74 (d, *J* = 7.6 Hz, 1H), 4.95 (d, *J* = 15.6 Hz, 1H), 4.79 (d, *J* = 15.6 Hz, 1H), 4.70 (s, 1H), 3.99-3.91 (m, 1H), 3.86-3.78 (m, 2H),

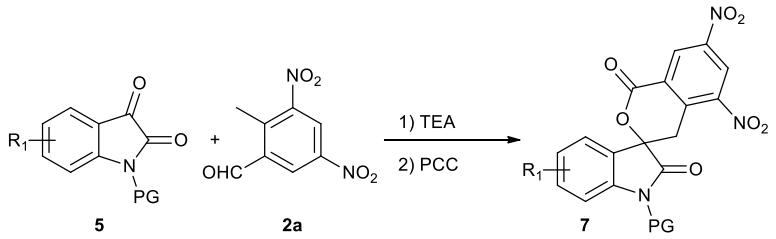
3.71 (dd, *J* = 17.2, 12.0 Hz, 1H), 3.35 (dd, *J* = 16.8, 6.0 Hz, 1H), 0.86 (t, *J* = 7.2 Hz, 3H), -0.03 (s, 9H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.9, 171.6, 145.9, 143.2, 142.5, 137.0, 135.4, 128.9, 128.8, 128.3, 128.2, 127.2, 127.0, 125.2, 123.9, 122.5, 121.5, 108.5, 72.2, 60.5, 52.4, 43.3, 41.9, 28.8, 13.2, -0.1 ppm; ESI HRMS: calcd. For $C_{30}H_{32}N_2O_6Si$+Na 567.1927, found 567.1929.



4m

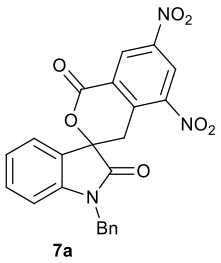
4m was obtained as a semisolid in 58% yield for two steps after flash chromatography. The dr value was calculated to be 85:15 by ^{1}H NMR analysis of the crude reaction mixture. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.21 (d, *J* = 8.4, 1H), 8.14 (s, 1H), 7.53 (d, *J* = 8.4 Hz, 1H), 7.43-7.41 (m, 2H), 7.35-7.27 (m, 3H), 7.06 (t, *J* = 8.0 Hz, 1H), 6.68 (d, *J* = 8.0 Hz, 1H), 6.61 (t, *J* = 7.6 Hz, 1H), 5.63 (d, *J* = 7.6 Hz, 1H), 5.25 (d, *J* = 4.8 Hz, 1H), 4.69 (d, *J* = 15.6 Hz, 1H), 3.88 (dd, *J* = 9.2, 5.6 Hz, 1H), 3.65-3.52 (m, 3H), 3.26 (dd, *J* = 17.2, 9.2 Hz, 1H), 0.52 (t, *J* = 7.2 Hz, 3H), 0.15 (s, 9H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 178.1, 170.1, 147.1, 144.5, 142.8, 140.5, 135.7, 128.6, 128.6, 128.3, 127.7, 127.6, 126.8, 124.1, 122.6, 122.0, 120.8, 108.7, 74.2, 60.9, 56.1, 44.9, 44.3, 28.1, 13.2, 0.2 ppm; ESI HRMS: calcd. For $C_{30}H_{32}N_2O_6Si$+Na 567.1927, found 567.1931.

3. General procedure for the synthesis of isochroman-fused spirooxindole 7



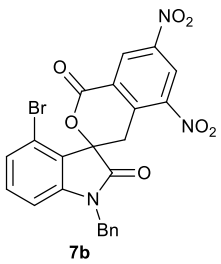
The reaction was carried out with isatin **5** (0.3 mmol), 2-methyl-3,5-dinitro-benzaldehyde **2a** (0.36 mmol) and TEA (0.06 mmol) in acetonitrile (4.0 mL) at room temperature for 1h. Then the reaction mixture was concentrated and the residue was purified by flash chromatography on silica gel to afford the hemiacetal **6**.

Hemiacetal **6** were oxidized to the corresponding stable isochroman-fused spirooxindole **7**. To a solution of **6** in toluene (4 mL) was added PCC (107.8 mg, 0.5 mmol). The mixture was stirred for 1 h at 60 ^{o}C. The solid was removed by filtration through celite. The filtrate was evaporated under reduced pressure and the residual was purified by column chromatography (petroleum ether/ethyl acetate = 10:1) to give the isochroman-fused spirooxindole **7**.



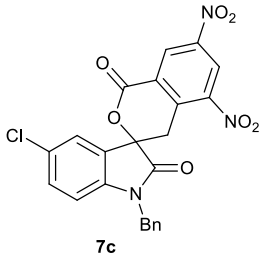
7a

7a was obtained as a white solid in 79% yield for two steps after flash chromatography. m.p. 171-172 ^{o}C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 9.28 (s, 1H), 9.12 (s, 1H), 7.47 (d, *J* = 7.8 Hz, 1H), 7.38-7.27 (m, 4H), 7.23-7.17 (m, 3H), 6.82 (d, *J* = 7.8 Hz, 1H), 4.79 (dd, *J* = 33.6, 15.6 Hz, 2H), 4.02 (d, *J* = 19.2 Hz, 1H), 3.81 (d, *J* = 19.2 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.4, 160.8, 147.9, 147.0, 142.5, 137.2, 134.3, 132.0, 129.8, 129.1, 128.7, 128.2, 127.2, 125.3, 124.7, 124.3, 124.2, 110.5, 79.3, 44.2, 32.4 ppm; ESI HRMS: calcd. For $C_{23}H_{15}N_3O_7$+Na 468.0808, found 468.0803.



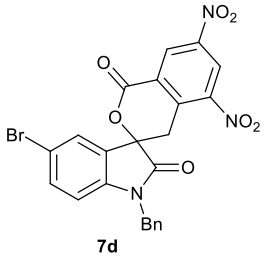
7b

7b was obtained as a white solid in 81% yield for two steps after flash chromatography. m.p. 212-214 ^{o}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.31 (s, 1H), 9.16 (s, 1H), 7.35-7.29 (m, 4H), 7.25-7.20 (m, 3H), 6.77 (d, *J* = 7.8 Hz, 1H),4.82-4.70 (m, 3H), 3.73 (d, *J* = 19.2 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.2, 160.4, 147.9, 147.0, 144.4, 137.3, 133.8, 133.1, 129.5, 129.2, 128.8, 128.4, 128.3, 127.2, 124.4, 123.1, 120.6, 109.5, 80.1, 44.3, 29.4 ppm; ESI HRMS: calcd. For $C_{23}H_{14}N_3O_7Br$+Na 545.9913, found 545.9916.



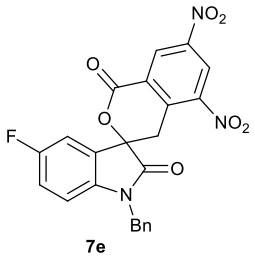
7c

7c was obtained as a white solid in 78% yield for two steps after flash chromatography. m.p. 160-162 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 9.28 (s, 1H), 9.13 (s, 1H), 7.48 (s, 1H), 7.34-7.28 (m, 4H), 7.20 (d, *J* = 7.2 Hz, 2H), 6.74 (d, *J* = 8.4 Hz, 1H), 4.77 (dd, *J* = 46.2, 15.2 Hz, 2H), 4.00 (d, *J* = 18.6 Hz, 1H), 3.81 (d, *J* = 19.2 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.1, 160.3, 147.9, 147.1, 140.9, 136.7, 133.8, 131.9, 129.7, 129.6, 129.2, 128.8, 128.4, 127.2, 126.8, 125.3, 124.4, 111.6, 79.0, 44.3, 32.2 ppm; ESI HRMS: calcd. For $C_{23}H_{14}N_3O_7Cl$+Na 502.0418, found 502.0421.



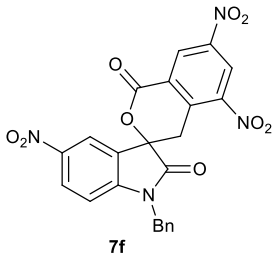
7d

7d was obtained as a white solid in 70% yield for two steps after flash chromatography. m.p. 162-163 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.29 (s, 1H), 9.15 (s, 1H), 7.63 (d, *J* = 1.6 Hz, 1H), 7.49 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.37-7.29 (m, 3H), 7.24-7.13 (m, 2H), 6.69 (d, *J* = 8.4 Hz, 1H), 4.77 (dd, *J* = 35.2, 15.6 Hz, 2H), 4.00 (d, *J* = 18.8 Hz, 1H), 3.81 (d, *J* = 19.2 Hz, 1H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 172.0, 160.3, 147.8, 147.1, 141.4, 136.7, 134.7, 133.7, 129.6, 129.2, 128.8, 128.4, 128.0, 127.2, 127.1, 124.4, 116.8, 112.0, 78.9, 44.3, 32.2 ppm; ESI HRMS: calcd. For $C_{23}H_{14}N_3O_7Br$+Na 545.9913, found 545.9911.



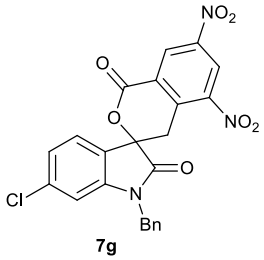
7e

7e was obtained as a white solid in 80% yield for two steps after flash chromatography. m.p. 185-186 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 9.30 (s, 1H), 9.15 (s, 1H), 7.35-7.27 (m, 3H), 7.23 (dd, *J* = 20.4, 7.2 Hz, 3H), 7.07 (t, *J* = 8.4 Hz, 1H), 6.75 (dd, *J* = 9.0, 4.2 Hz, 1H), 4.78 (dd, *J* = 45.6, 15.6 Hz, 2H), 3.99 (d, *J* = 18.6 Hz, 1H), 3.82 (d, *J* = 18.6 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.3, 160.4, 159.7 (d, J_{CF} = 253.5 Hz), 147.9, 147.2, 138.4, 136.8, 133.9, 129.7, 129.2, 128.8, 128.4, 127.2, 126.7 (d, J_{CF} = 7.8 Hz), 124.4, 118.5 (d, J_{CF} = 23.3 Hz), 113.0 (d, J_{CF} = 25.2 Hz), 111.5 (d, J_{CF} = 8.9 Hz), 79.2, 44.4, 32.3 ppm; ESI HRMS: calcd. For $C_{23}H_{14}N_3O_7F$+Na 486.0713, found 486.0715.



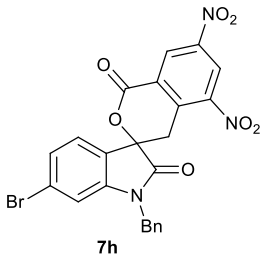
7f

7f was obtained as a white solid in 79% yield for two steps after flash chromatography. m.p. 183-185 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.93 (s, 1H), 8.75 (s, 1H), 8.32 (d, *J* = 2.0 Hz, 1H), 8.28 (dd, *J* = 8.8, 3.0 Hz, 1H), 7.39-7.31 (m, 3H), 7.23-7.21 (m, 2H), 6.90 (d, *J* = 8.8 Hz, 1H), 4.90 (s, 2H), 3.73 (d, *J* = 18.8 Hz, 1H), 3.50 (d, *J* = 18.4 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 178.1, 160.5, 148.3, 147.1, 146.9, 144.7, 140.2, 133.3, 131.8, 129.5, 129.4, 128.7, 127.6, 127.1, 127.0, 120.4, 120.4, 110.2, 92.0, 44.6, 33.0 ppm; ESI HRMS: calcd. For $C_{23}H_{14}N_4O_9$+Na 513.0658, found 513.0662.



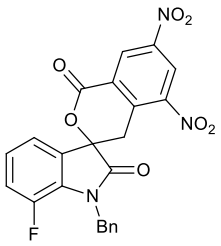
7g

7g was obtained as a white solid in 74% yield for two steps after flash chromatography. m.p. 143-145 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.27 (s, 1H), 9.13 (s, 1H), 7.42-7.29 (m, 4H), 7.22-7.15 (m, 3H), 6.82 (d, *J* = 1.6 Hz, 1H), 4.76 (dd, *J* = 27.2， 15.6 Hz, 2H), 3.99 (d, *J* = 18.8 Hz, 1H), 3.79 (d, *J* = 19.2 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 172.4, 160.5 147.9, 147.2, 143.7, 138.1, 136.8, 133.7, 129.7, 129.3, 128.8, 128.4, 127.2, 125.7, 124.4, 124.2, 123.6, 111.2, 78.8, 44.4, 32.2 ppm; ESI HRMS: calcd. For $C_{23}H_{14}N_3O_7Cl$+Na 502.0418, found 502.0415.



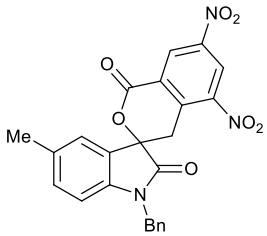
7h

7h was obtained as a white solid in 70% yield for two steps after flash chromatography. m.p. 192-194 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.26 (s, 1H), 9.12 (s, 1H), 7.37-7.28 (m, 5H), 7.22-7.20 (m, 2H), 6.97 (s, 1H), 4.75 (dd, *J* = 25.6, 15.6 Hz, 2H), 3.98 (d, *J* = 18.8 Hz, 1H), 3.79 (d, *J* = 18.8 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.3, 160.5, 147.9, 147.1, 143.8, 136.8, 133.7, 129.6, 129.2, 128.8, 128.4, 127.2, 127.2, 126.0, 125.9, 124.4, 124.2, 113.9, 78.9, 44.3, 32.1 ppm; ESI HRMS: calcd. For $C_{23}H_{14}N_3O_7Br$ +Na 545.9913, found 545.9915.



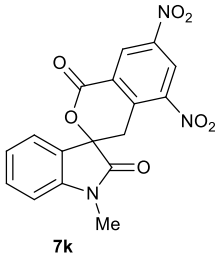
7i

7i was obtained as a white solid in 80% yield for two steps after flash chromatography. m.p. 175-177 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.27 (s, 1H), 9.13 (s, 1H), 7.33-7.14 (m, 8H), 4.92 (dd, *J* = 33.2, 15.6 Hz, 2H), 3.97 (d, *J* = 18.8 Hz, 1H), 3.79 (d, *J* = 18.8 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.3, 160.4, 147.9, 147.6 (d, J_{CF} = 245.6 Hz), 147.1, 136.7, 135.4, 129.7, 129.2 (d, J_{CF} = 9.4 Hz), 128.9, 128.7, 128.2, 128.0 (d, J_{CF} = 3.1 Hz), 127.5 (d, J_{CF} = 1.5 Hz), 125.2, 125.2, 124.4, 120.6 (d, J_{CF} = 3.4 Hz), 120.2 (d, J_{CF} = 19.5 Hz), 79.1 (d, J_{CF} = 2.6 Hz), 45.9 (d, J_{CF} = 4.7 Hz), 32.4 ppm; ESI HRMS: calcd. For $C_{23}H_{14}N_3O_7F$+Na 486.0713, found 486.0717.



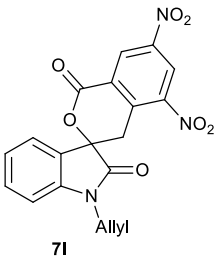
7j

7j was obtained as a white solid in 65% yield for two steps after flash chromatography. m.p. 181-183 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.28 (s, 1H), 9.13 (s, 1H), 7.34-7.15 (m, 7H), 6.70 (d, *J* = 8.0 Hz, 1H), 4.76 (dd, *J* = 28.8, 15.6 Hz, 2H), 4.01 (d, *J* = 19.2 Hz, 1H), 3.79 (d, *J* = 19.2 Hz, 1H), 2.36 (s, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 169.5, 157.9, 145.0, 144.1, 137.1, 134.4, 131.5, 131.2, 129.3, 127.0, 126.1, 125.8, 125.2, 124.3, 122.5, 122.4, 121.4, 109.6, 107.4, 76.6, 41.3, 29.5, 18.2 ppm; ESI HRMS: calcd. For $C_{24}H_{17}N_3O_7$+Na 482.0964, found 482.0965.



7k

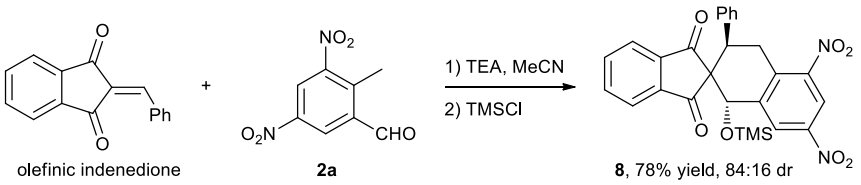
7k was obtained as a white solid in 72% yield for two steps after flash chromatography. m.p. 180-182 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.28 (s, 1H), 9.13 (s, 1H), 7.50 (t, *J* = 8.0 Hz, 2H), 7.23 (t, *J* = 7.6 Hz, 1H), 6.94 (d, *J* = 8.0 Hz, 1H), 3.99 (d, *J* = 18.8 Hz, 1H), 3.75 (d, *J* = 18.8 Hz, 1H), 3.15 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.3, 160.8, 147.9, 147.1, 143.3, 137.2, 132.1, 129.9, 128.7, 125.3, 124.6, 124.2, 124.2, 109.4, 79.3 , 32.3, 26.5 ppm; ESI HRMS: calcd. For $C_{17}H_{11}N_3O_7$+Na 392.0495, found 392.0497.



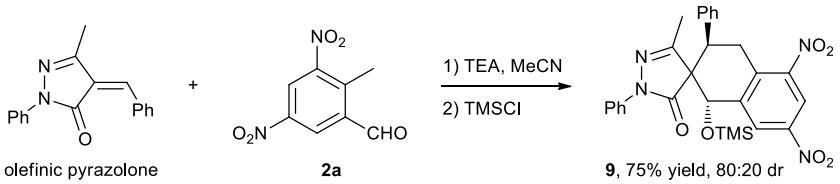
7l

7l was obtained as a white solid in 78% yield for two steps after flash chromatography. m.p. 160-162 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.23 (s, 1H), 9.11 (s, 1H), 7.47 (dd, *J* = 15.2, 7.6 Hz, 2H), 7.21 (t, *J* = 7.6 Hz, 1H), 6.94 (d, *J* = 8.0 Hz, 1H), 5.82-5.73 (m, 1H), 5.27-5.23 (m, 2H), 4.22 (d, *J* = 5.2 Hz, 2H), 4.01 (d, *J* = 18.8 Hz, 1H), 3.76 (d, *J* = 18.8 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.0, 160.7, 147.9, 147.1, 142.6, 137.2, 132.0, 130.1, 129.9, 128.7, 125.3, 124.7, 124.3, 124.1, 118.9, 110.3, 79.2, 42. 8, 32.4 ppm; ESI HRMS: calcd. For $C_{19}H_{13}N_3O_7$+Na 418.0651, found 418.0652.

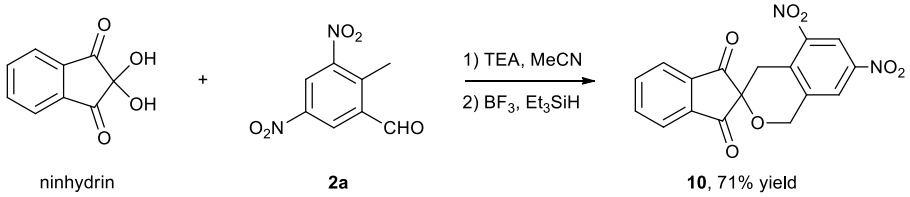
4. Procedure for the synthesis of drug-like spirocyclic products 8-12



The reaction was carried out with olefinic indenedione (70.3 mg, 0.3 mmol), 2-methyl-3,5-dinitro-benzaldehyde **2a** (75.7 mg, 0.36 mmol) and TEA (8.4 μL, 0.06 mmol) in acetonitrile (4.0 mL) at 0 °C for 4h. Then the reaction mixture was concentrated and the residue was purified by flash chromatography on silica gel to afford the cycloaddition product. To a solution of the intermediate in methylene chloride (4 mL) was added TMSCl (25.9 μL, 0.3 mmol) and imidazole (40.8 mg, 0.6 mmol). The mixture was stirred at 0 °C for 30 min. The reaction was quenched with aqueous $NaHCO_3$, extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4 and concentrated. The residue was purified by chromategraphy on silica gel (petroleum ether/ethyl acetate = 15:1) to give the tetrahydronaphthalene-fused spirocyclic indenedione **8** in 78% yield. The dr value was calculated to be 84:16 by ^{1}H NMR analysis of the crude reaction mixture. m.p. 174-176 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.88 (s, 1H), 8.68 (s, 1H), 7.99 (d, *J* = 7.6 Hz, 1H), 7.88-7.78 (m, 3H), 7.18 (br s, 5H), 5.58 (s, 1H), 4.13 (dd, *J* = 19.2, 12.0 Hz, 1H), 3.86 (dd, *J* = 12.4, 6.0 Hz, 1H), 3.70 (dd, *J* = 19.2, 5.6 Hz, 1H), 0.12 (s, 9H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 201.5, 200.4, 148.4, 146.2, 143.7, 143.3, 143.0, 138.1, 137.1, 135.9, 135.5, 128.7, 128.3, 128.0, 125.0, 122.8, 122.7, 118.9, 74.4, 61.2, 44.1, 31.2, -0.1 ppm; ESI HRMS: calcd. For $C_{27}H_{24}N_2O_7$-Si+Na 539.1250, found 539.1252.

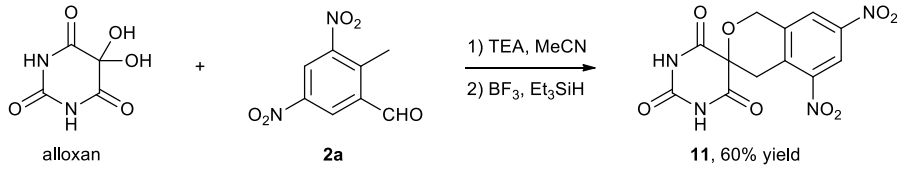


The reaction was carried out with olefinic pyrazolone (78.7 mg, 0.3 mmol), 2-methyl-3,5-dinitro-benzaldehyde **2a** (75.7 mg, 0.36 mmol) and TEA (8.4 μL, 0.06 mmol) in acetonitrile (4.0 mL) at 0 ^{o}C for 4h. Then the reaction mixture was concentrated and the residue was purified by flash chromatography on silica gel to afford the cycloaddition product. To a solution of the intermediate in methylene chloride (4 mL) was added TMSCl (25.9 μL, 0.3 mmol) and imidazole (40.8 mg, 0.6 mmol). The mixture was stirred at 0 ^{o}C for 30 min. The reaction was quenched with aqueous $NaHCO_3$, extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4 and concentrated. The residue was purified by chromategraphy on silica gel (petroleum ether/ethyl acetate = 15:1) to give the tetrahydronaphthalene-fused spirocyclic pyrazolone **9** in 75% yield. The dr value was calculated to be 80:20 by ^{1}H NMR analysis of the crude reaction mixture. m.p. 232-234 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.74 (s, 1H), 8.59 (s, 1H), 7.73 (d, *J* = 8.0 Hz, 2H), 7.36 (m, *J* = 7.8 Hz, 2H), 7.27 (d, *J* = 3.2 Hz, 3H), 7.20 (d, *J* = 6.8 Hz, 3H), 5.30 (s, 1H), 4.09 (dd, *J* = 20.4, 13.6 Hz, 1H), 3.53-3.41 (m, 2H), 2.11 (s, 3H), 0.28 (s, 9H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.9, 158.2, 147.8, 146.0, 141.3, 137.8, 137.4, 137.1, 129.0, 128.5, 128.2, 126.6, 125.6, 125.1, 118.8, 118.7, 73.1, 61.0, 43.1, 30.4, 14.0, 0.3 ppm; ESI HRMS: calcd. For $C_{28}H_{28}N_4O_6Si$+Na 567.1676, found 567.1673.



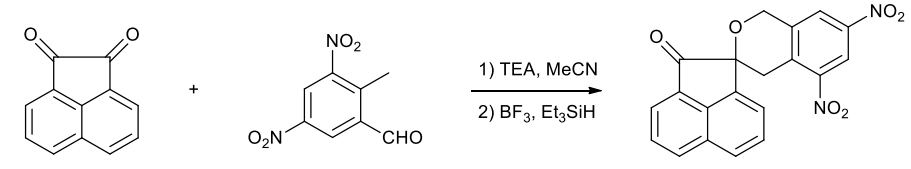
The reaction was carried out with ninhydrin (53.4 mg, 0.3 mmol), 2-methyl-3,5-dinitro-benzaldehyde **2a** (75.7 mg, 0.36 mmol) and TEA ((8.4 μL, 0.06 mmol) in acetonitrile (4.0 mL) at room temperature for 1h. Then the reaction mixture was concentrated and the residue was purified by flash chromatography on silica gel to afford the hemiacetal. To a solution of hemiacetal and triethyl silane (47.9 μL, 0.3 mmol) in DCM (5 mL) was added BF_3 Ɛt$_2$O (44.4 μL, 0.36 mmol). The mixture was stirred at 0 ^{o}C for 2 h. The reaction was quenched with aqueous $NaHCO_3$, extracted

with CH_2Cl_2. The organic layer was dried over Na_2SO_4 and concentrated. The residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 20:1). The isochroman-fused spirocyclic indenedione **10** was obtained in 71% yield after flash chromatography. m.p. 194-196 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.82 (s, 1H), 8.27 (s, 1H), 8.05 (dd, *J* = 5.6, 3.2 Hz, 2H), 7.97 (dd, *J* = 5.6, 3.2 Hz, 2H), 5.32 (s, 2H), 3.48 (s, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.2, 148.7, 146.0, 140.2, 138.9, 137.2, 132.9, 124.5, 124.3, 123.8, 123.4, 118.9, 65.4, 27.4 ppm; ESI HRMS: calcd. For $C_{17}H_{10}N_2O_7$+Na 377.0386, found 377.0388.



alloxan **2a** **11**, 60% yield

The reaction was carried out with alloxan (48.0 mg, 0.3 mmol), 2-methyl-3,5-dinitro-benzaldehyde **2a** (75.7 mg, 0.36 mmol) and TEA (8.4 μL, 0.06 mmol) in acetonitrile (4.0 mL) at room temperature for 1h. Then the reaction mixture was concentrated and the residue was purified by flash chromatography on silica gel to afford the hemiacetal. To a solution of hemiacetal and triethyl silane (47.9 μL, 0.3 mmol) in DCM (5 mL) was added BF_3·Et_2O (44.4 μL, 0.36 mmol). The mixture was stirred at 0 °C for 2 h. The reaction was quenched with aqueous $NaHCO_3$, extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4 and concentrated. The residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 20:1). The isochroman-fused spirocyclic pyrimidinetrione **11** was obtained in 60% yield after flash chromatography. m.p. 226-228 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.83 (s, 1H), 8.72 (s, 1H), 8.64 (s, 1H), 8.29 (s, 1H), 5.17 (d, *J* = 15.6 Hz, 1H), 5.00 (dd, *J* = 11.2, 2.8 Hz, 1H), 3.49 (d, *J* = 18.0 Hz, 1H), 3.26 (dd, *J* = 18.4, 10.8 Hz, 1H) ppm; ^{13}C NMR (100 MHz, DMSO): δ = 150.4, 148.2, 145.7, 145.2, 144.0, 138.9, 135.4, 135.1, 123.7, 70.9, 67.5, 31.6 ppm; ESI HRMS: calcd. For $C_{12}H_8N_4O_8$+Na 359.0240, found 359.0244.

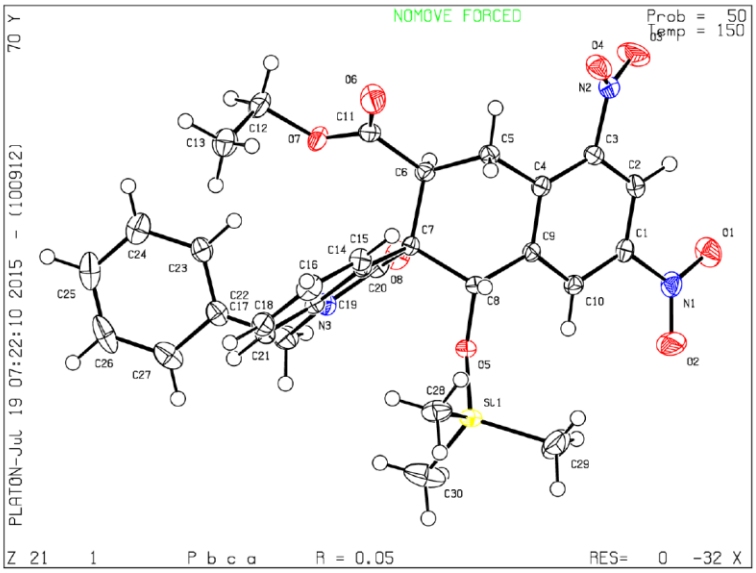


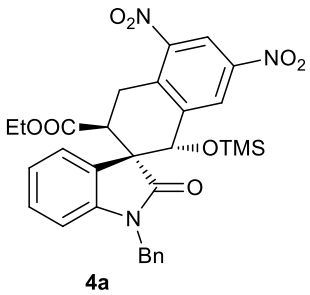
acenaphthenequinone **2a** **12**, 74% yield

The reaction was carried out with acenaphthenequinone (54.7 mg, 0.3 mmol), 2-methyl-3,5-

dinitro-benzaldehyde **2a** (75.7 mg, 0.36 mmol) and TEA (8.4 μL, 0.06 mmol) in acetonitrile (4.0 mL) at room temperature for 1h. Then the reaction mixture was concentrated and the residue was purified by flash chromatography on silica gel to afford the hemiacetal. To a solution of hemiacetal and triethyl silane (47.9 μL, 0.3 mmol) in DCM (5 mL) was added $BF_3 \cdot Et_2O$ (44.4 μL, 0.36 mmol). The mixture was stirred at 0 °C for 2 h. The reaction was quenched with aqueous $NaHCO_3$, extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4 and concentrated. The residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 20:1). The isochroman-fused spirocyclic acenaphthylenone **12** was obtained in 74% yield after flash chromatography. m.p. 224-226 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.83 (s, 1H), 8.31 (s, 1H), 8.19 (d, *J* = 8.4 Hz, 1H), 7.99 (t, *J* = 7.8 Hz, 2H), 7.80 (t, *J* = 7.8 Hz, 1H), 7.67 (t, *J* = 7.8 Hz, 1H), 7.44 (d, *J* = 7.2 Hz, 1H), 5.49 (d, *J* = 16.8 Hz, 1H), 5.25 (d, *J* = 16.2 Hz, 1H), 3.67 (d, *J* = 19.2 Hz, 1H), 3.60 (d, *J* = 18.6 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 200.2, 149.0, 146.0, 141.8, 139.5, 137.6, 134.3, 132.5, 130.9, 130.4, 128.8, 128.7, 126.5, 123.3, 122.9, 120.8, 118.7, 64.9, 31.1 ppm; ESI HRMS: calcd. For $C_{20}H_{12}N_2O_6$+Na 399.0593, found 399.0595.

5. Crystal data of 4a

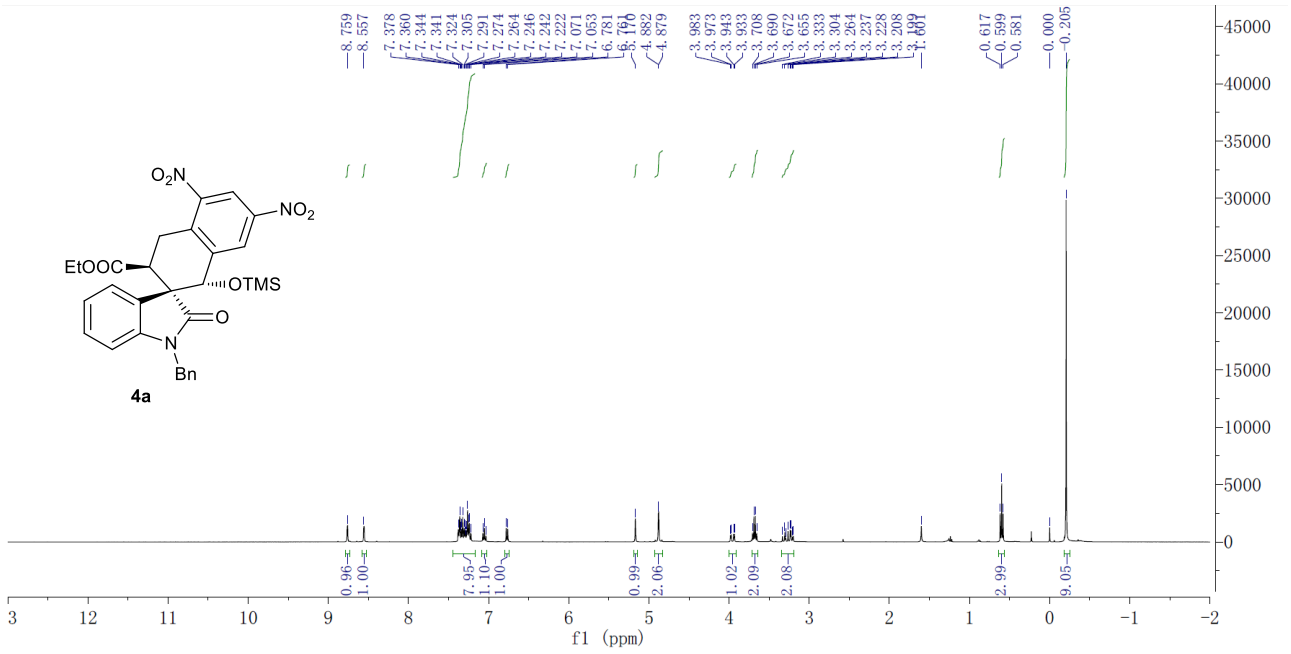


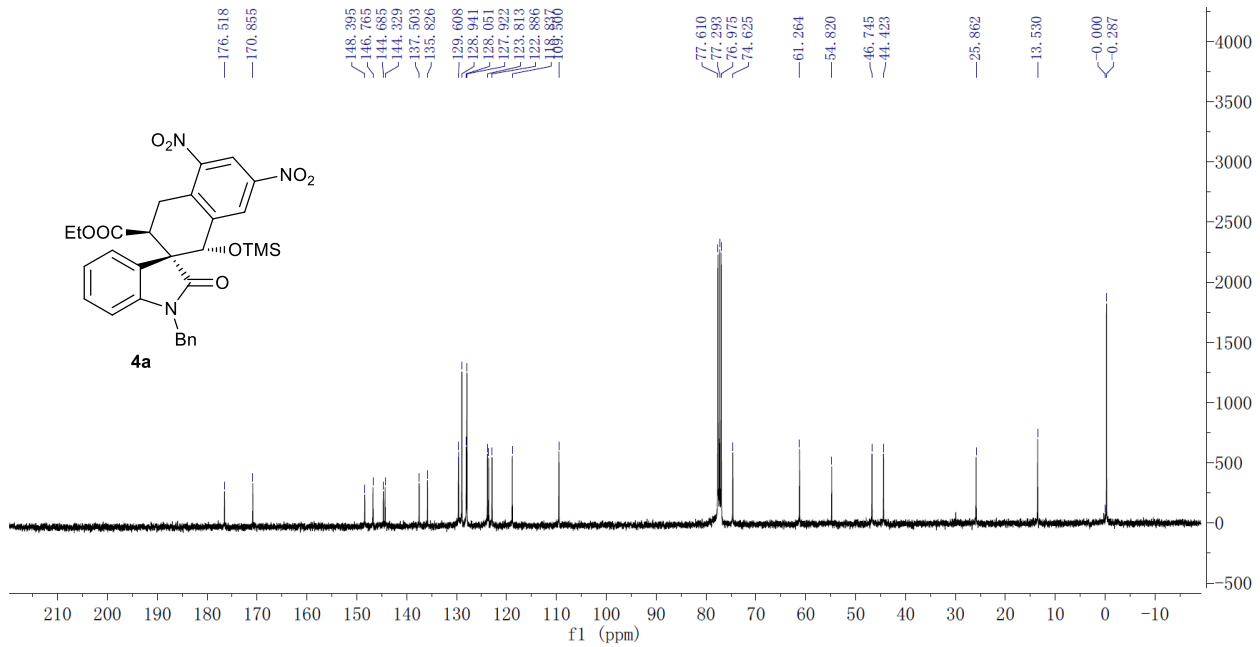


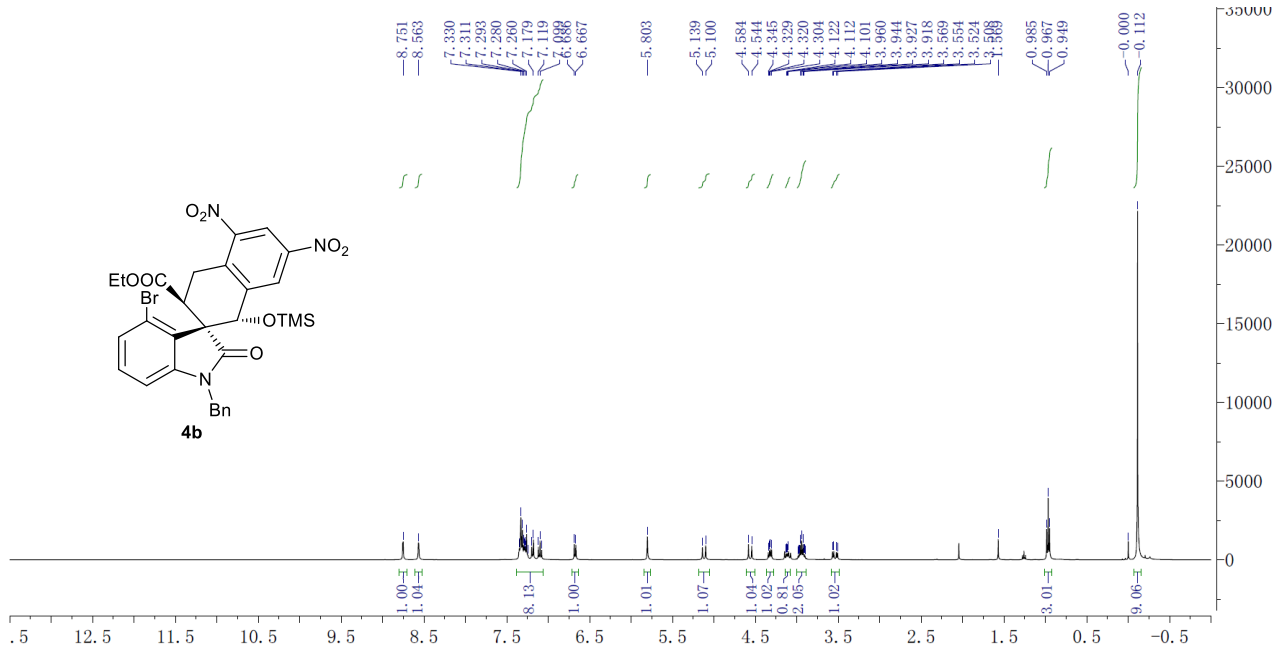
4a

Empirical formula	$C_{30}H_{31}N_3O_8Si$
Formula weight	589.67
Temperature/K	150(2)
Crystal system	orthorhombic
Space group	Pbca
a/Å	12.4185(4)
b/Å	19.1948(7)
c/Å	24.2024(9)
α/°	90
β/°	90
γ/ °	90
Volume/Å^3	5769.1(4)
Z	8
ρ_{calc}g/cm^3	1.358
μ/mm^{-1}	0.138
F(000)	2480.0
Crystal size/mm^3	0.491 ×0.148 ×0.139
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	6.334 to 55.04
Index ranges	-16 ≤ h ≤ 16, -24 ≤ k ≤ 24, -31 ≤ l ≤ 31
Reflections collected	85112
Independent reflections	6620 [R_{int} = 0.0933, R_{sigma} = 0.0446]
Data/restraints/parameters	6620/0/383
Goodness-of-fit on F^2	1.028
Final R indexes [I>=2σ (I)]	R_1 = 0.0519, wR_2 = 0.1343
Final R indexes [all data]	R_1 = 0.0902, wR_2 = 0.1567
Largest diff. peak/hole / e Å^{-3}	0.53/-0.24

6. NMR spectra



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4.584
4.544
4.345
4.329
4.320
4.304
4.122
4.112
4.101
3.960
3.944
3.927
3.918
3.569
3.554
3.524
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0.967
0.949
0.000
0.112
1.00
1.04
8.13
1.00
1.01
1.07
1.04
1.02
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1.02
3.01
9.06
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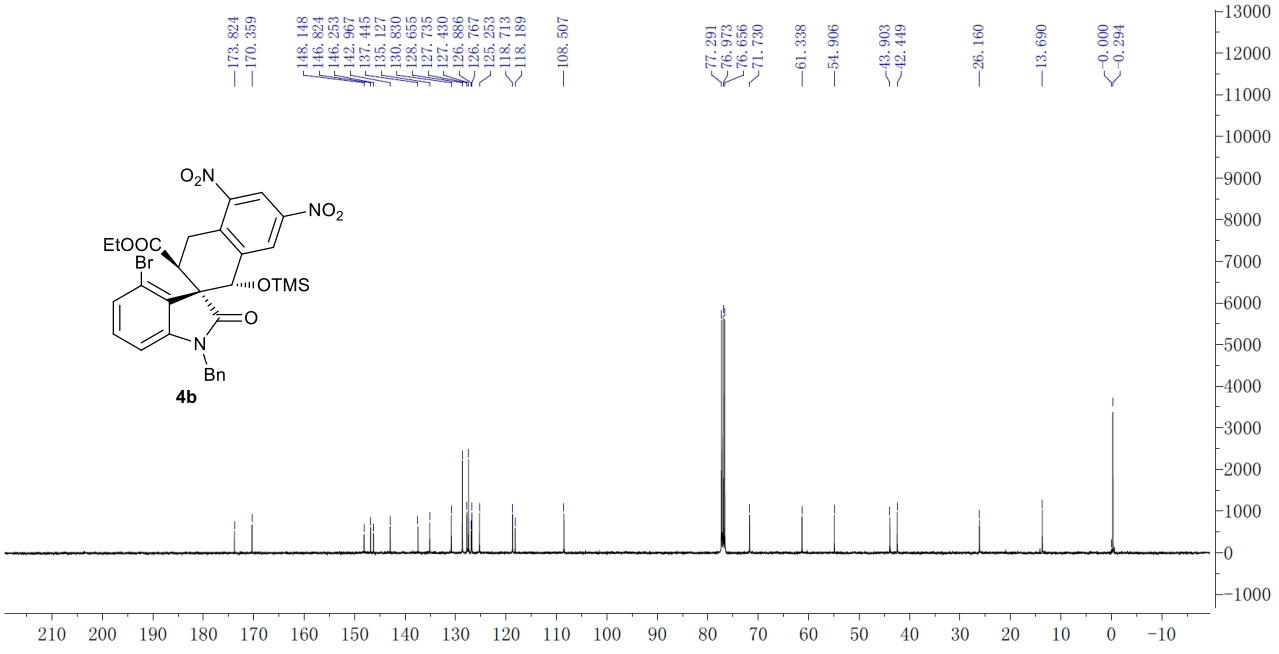
EtOOC
Br
OTMS
O
N
Bn
4b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125.253
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118.189
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76.973
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Br
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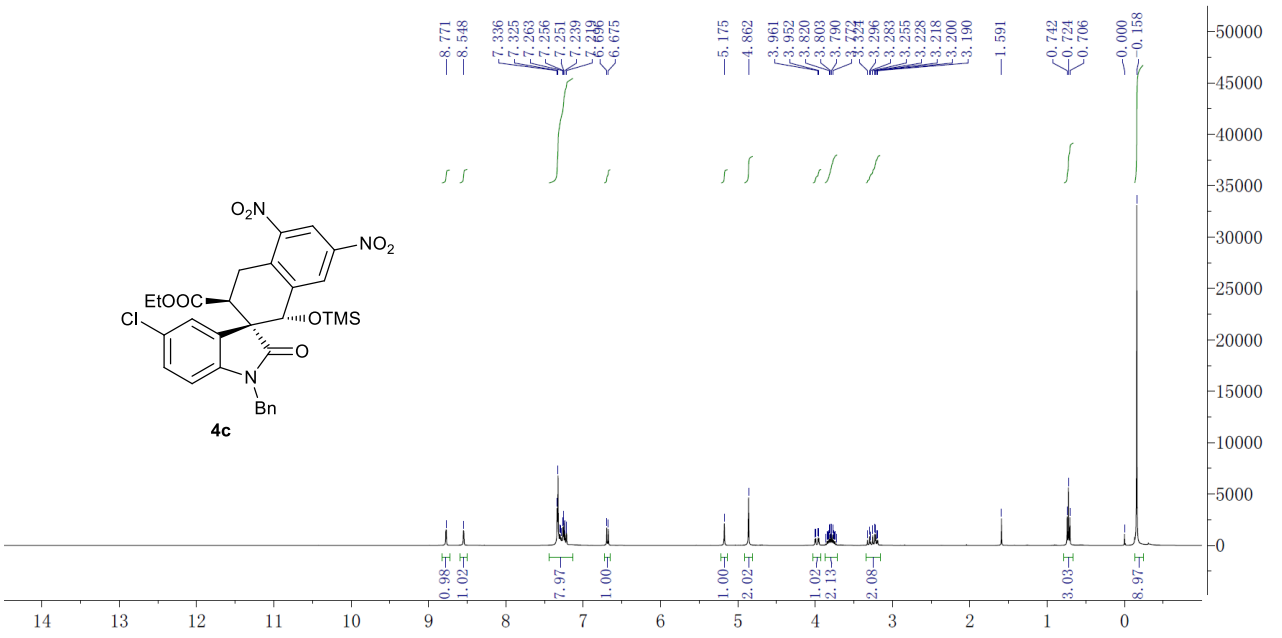
O
N
Bn
4b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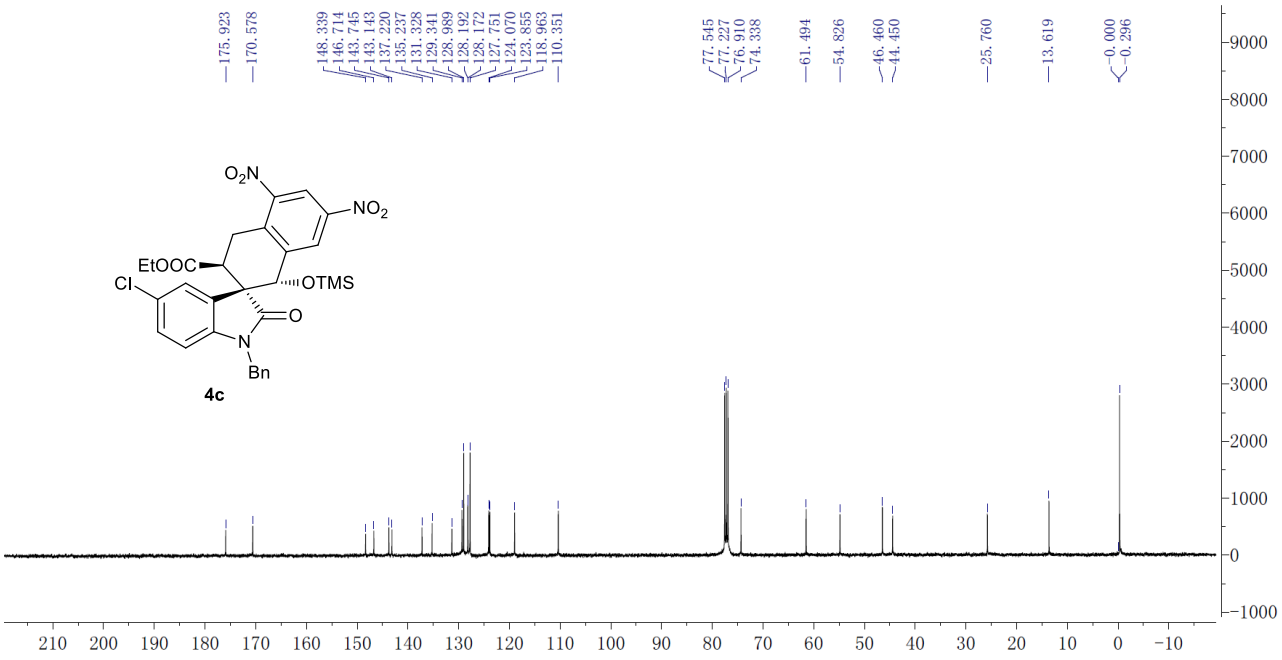
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54.826
46.460
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Cl
OTMS
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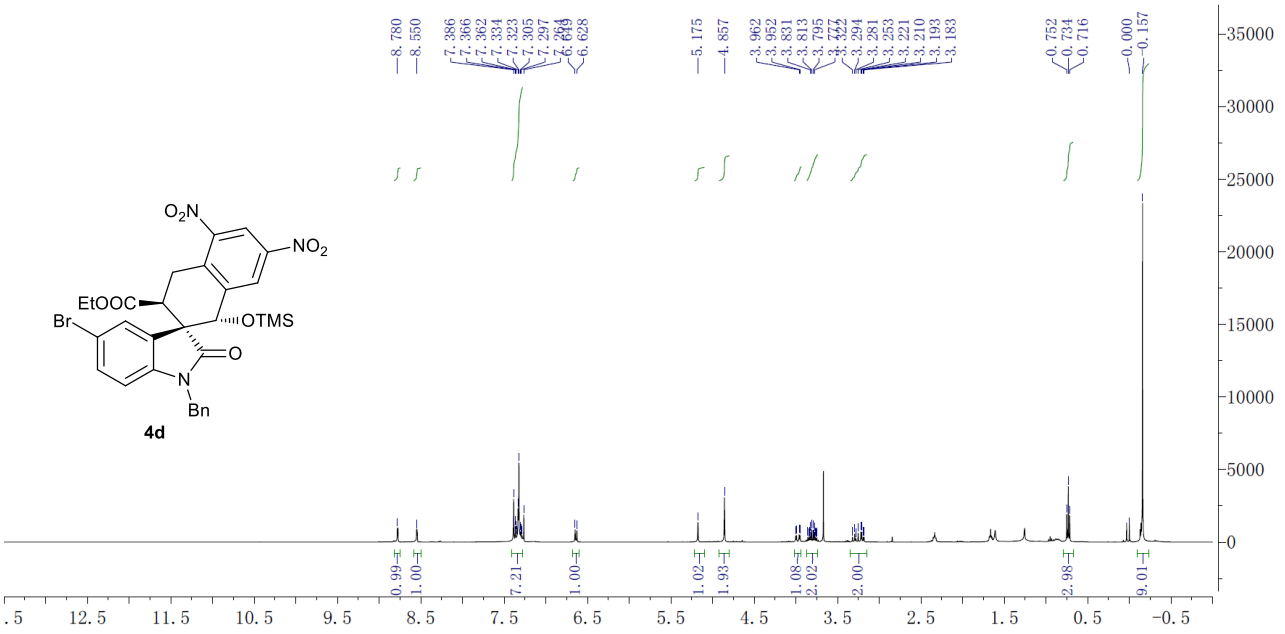
4c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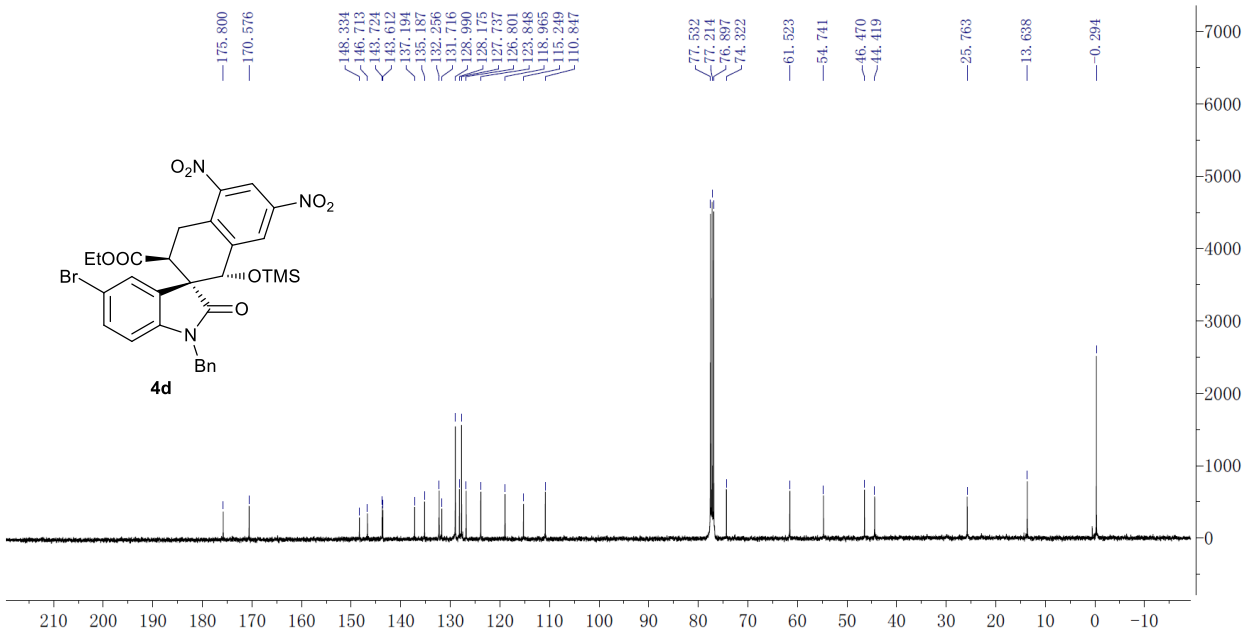
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76.897
74.322
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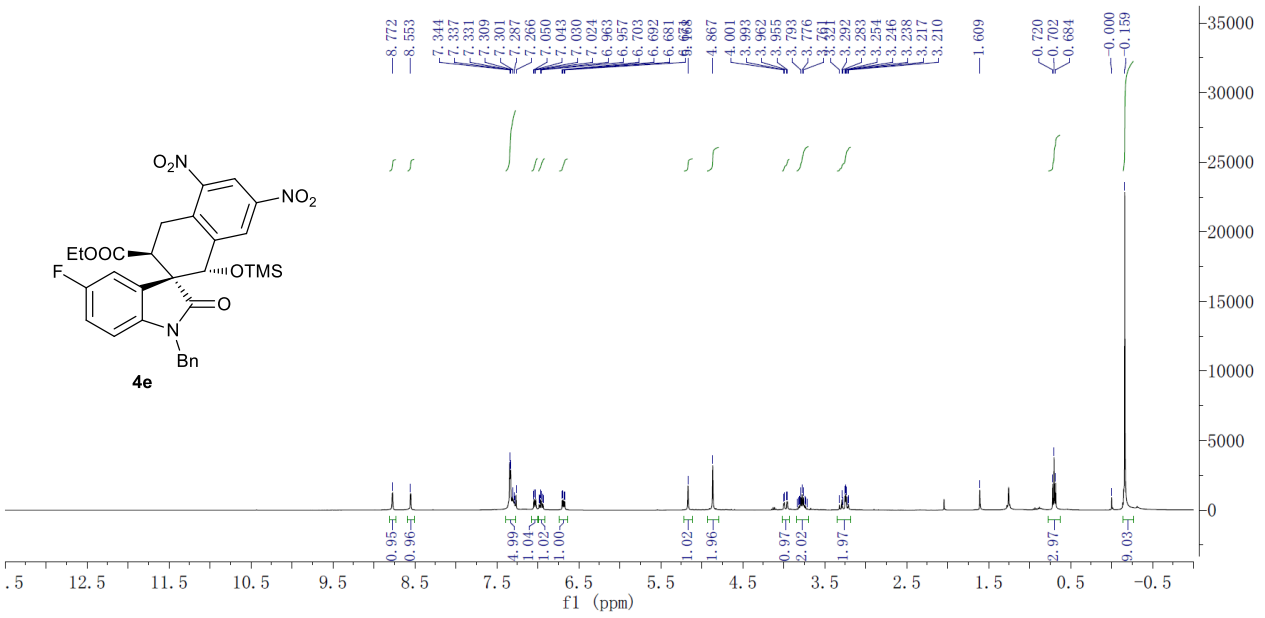
4d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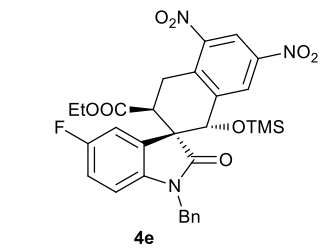
f1 (ppm)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F
OTMS
O
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4e

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f1 (ppm)

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EtOOC
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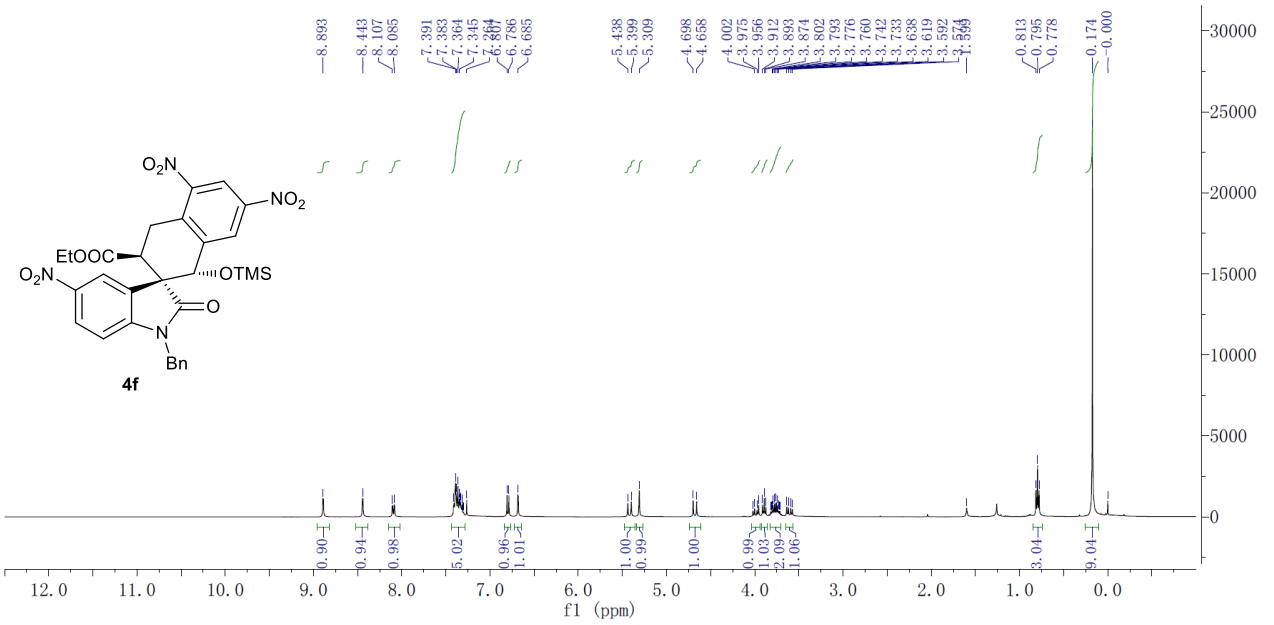
OTMS
O
N
Bn

4e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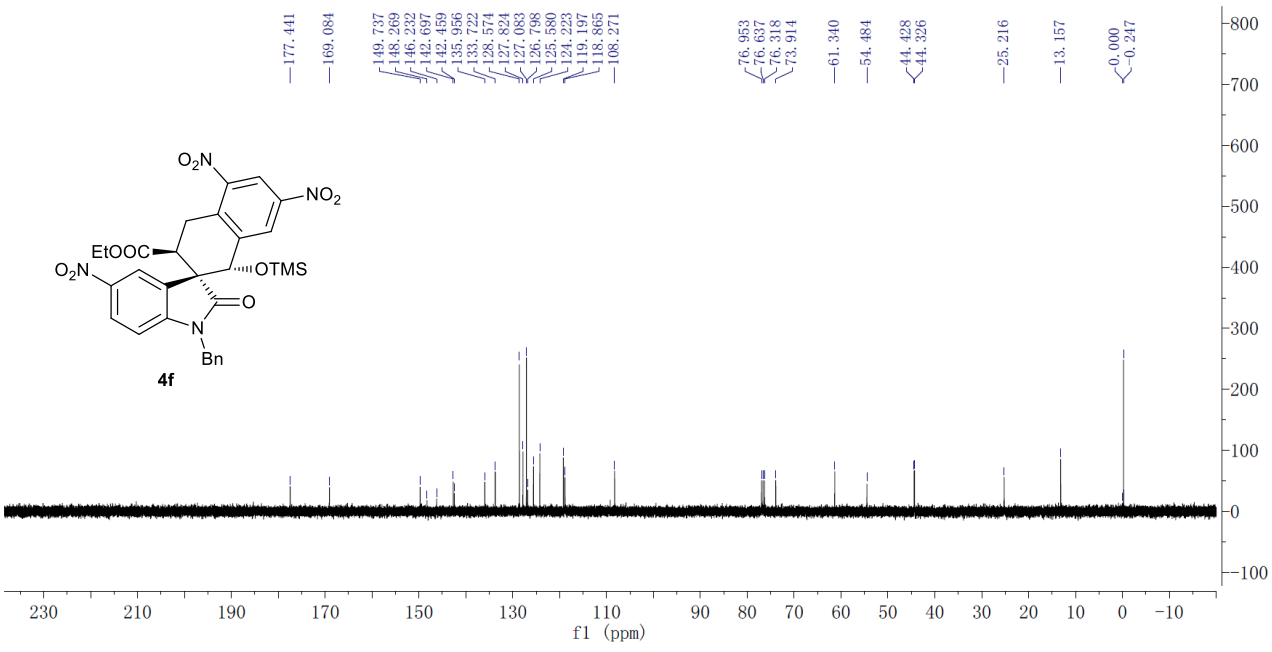
4f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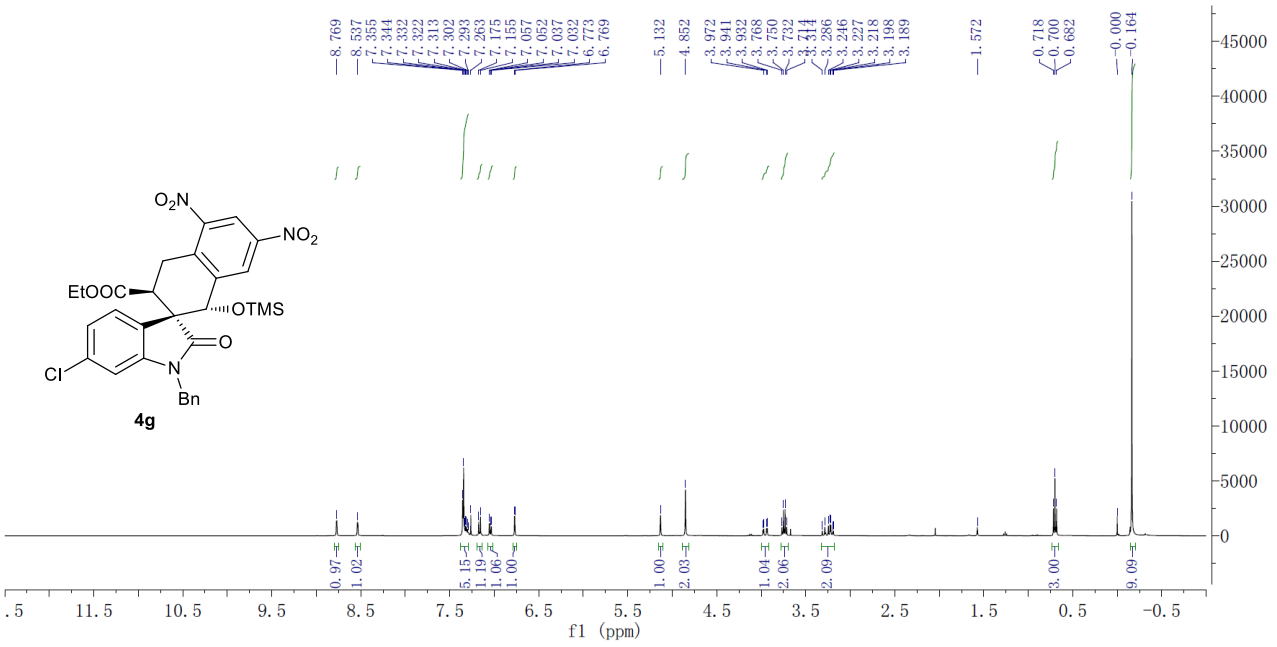
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NO2
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OTMS
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Cl
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Bn
4g
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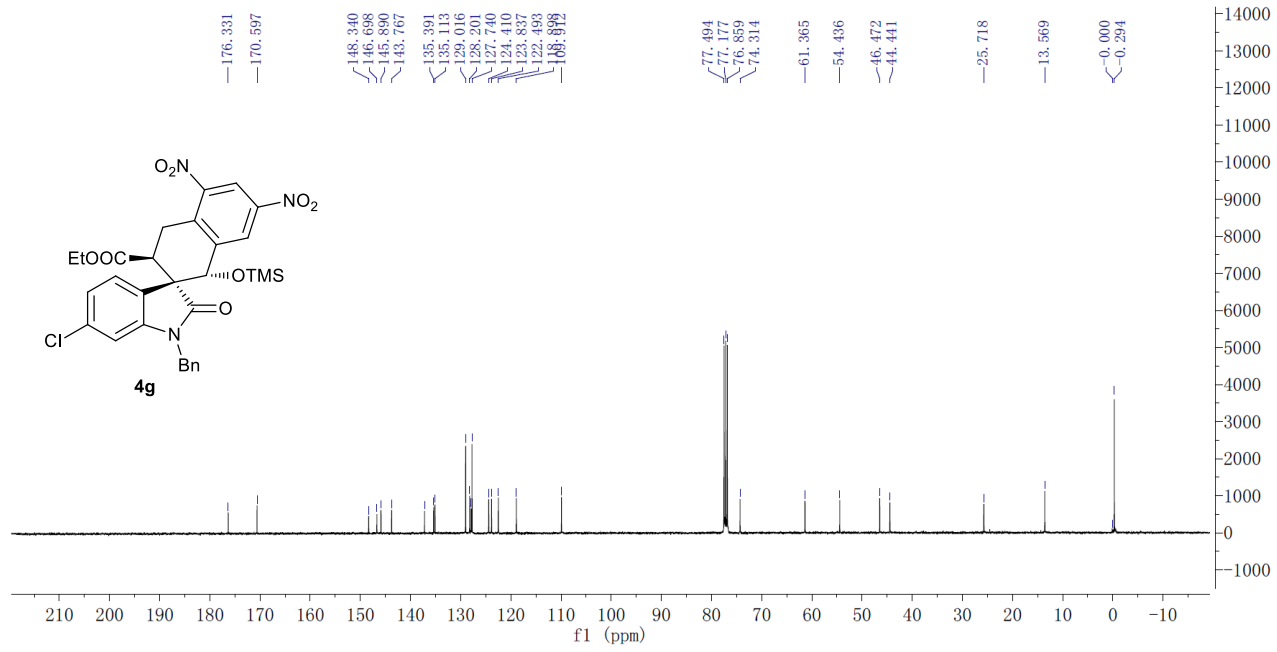
f1 (ppm)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Cl
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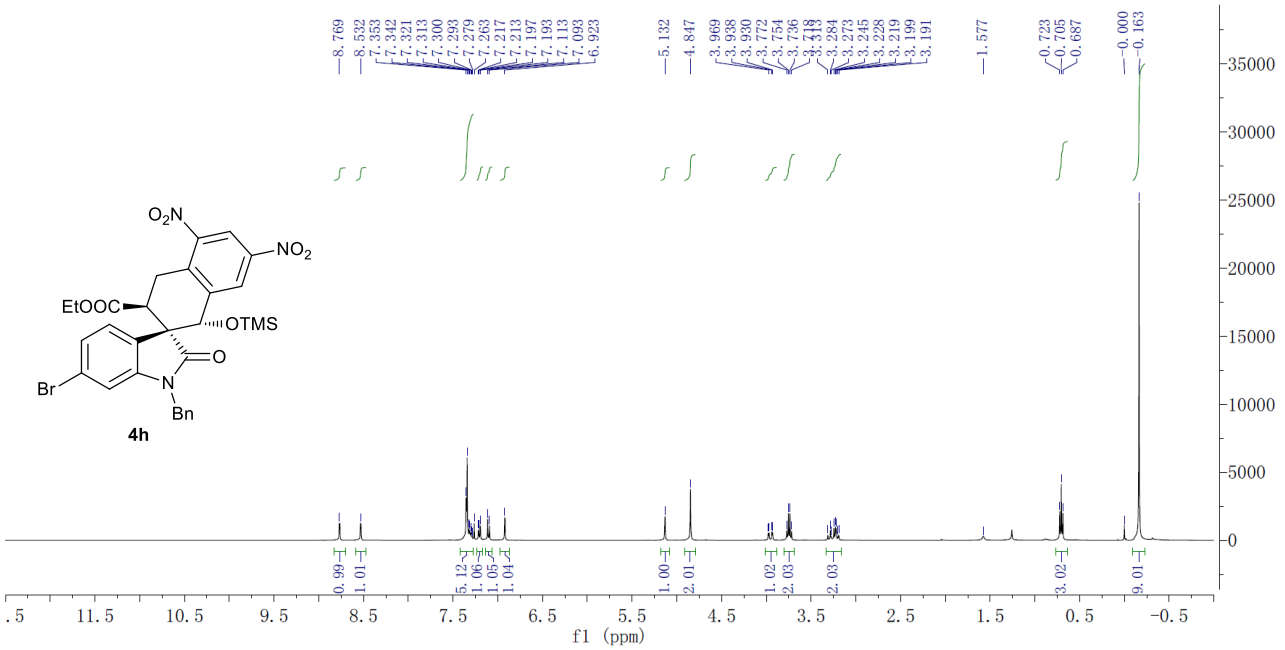
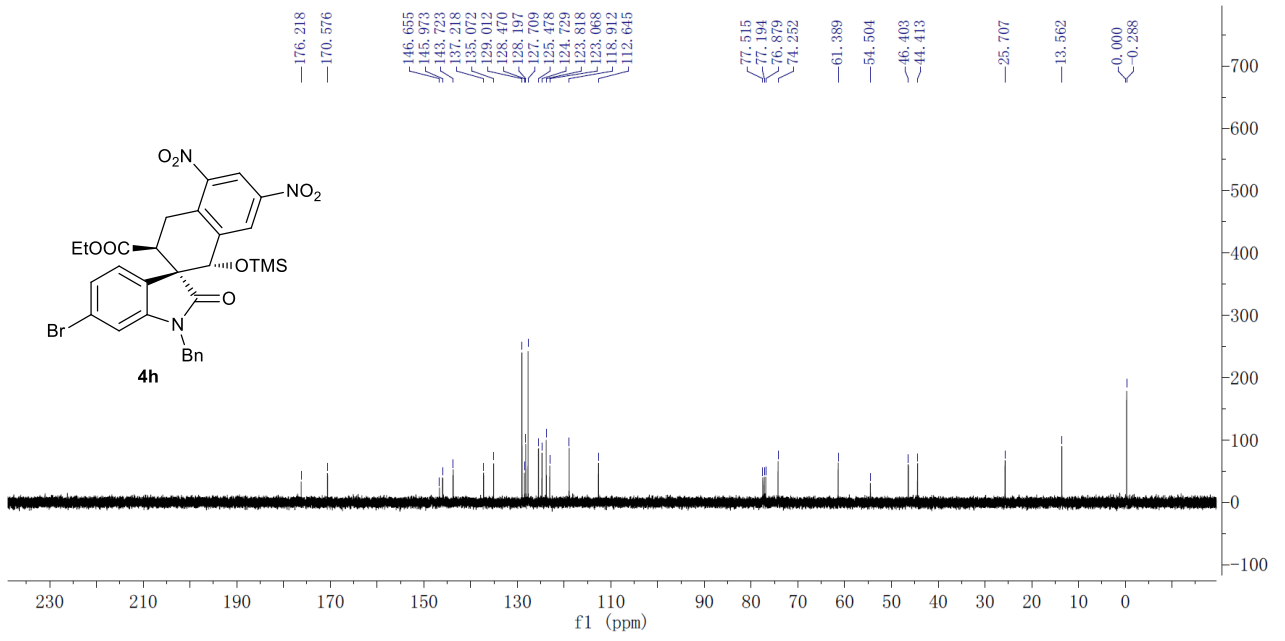
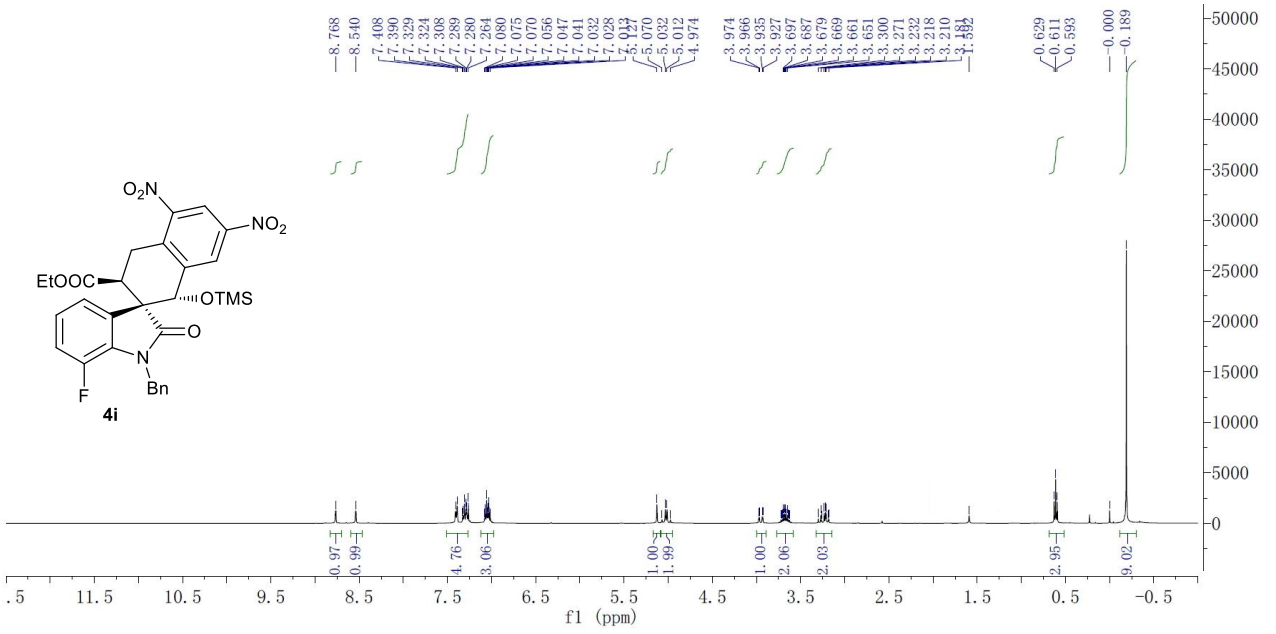
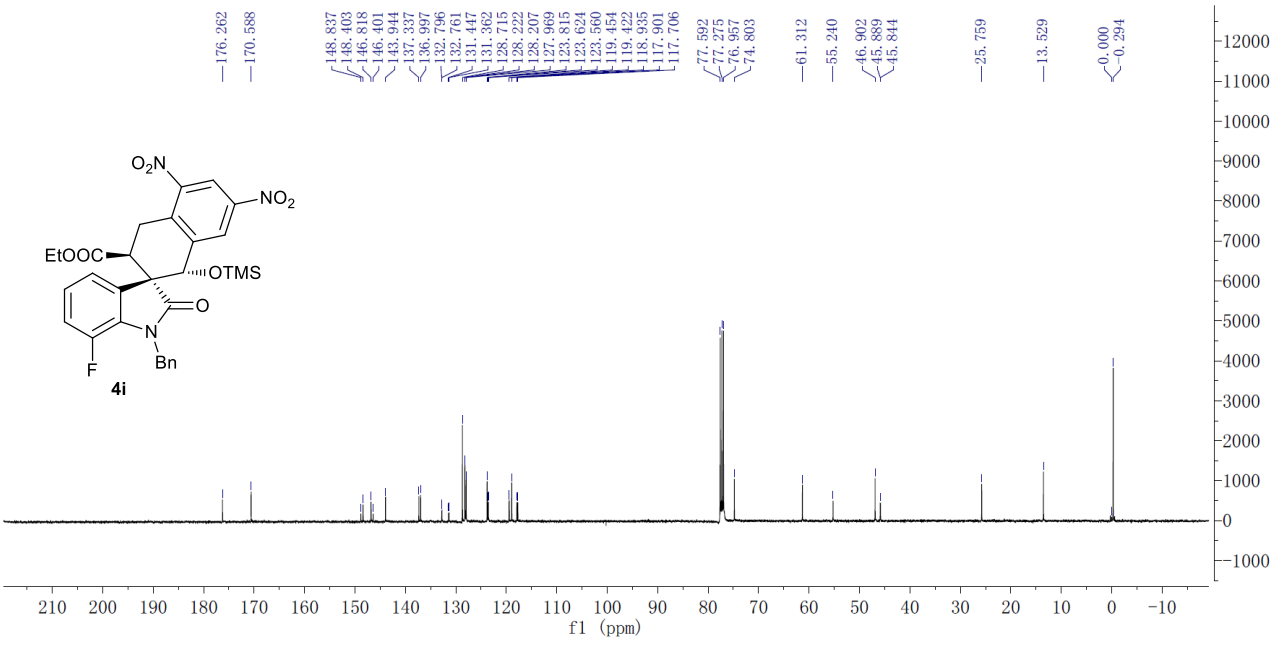
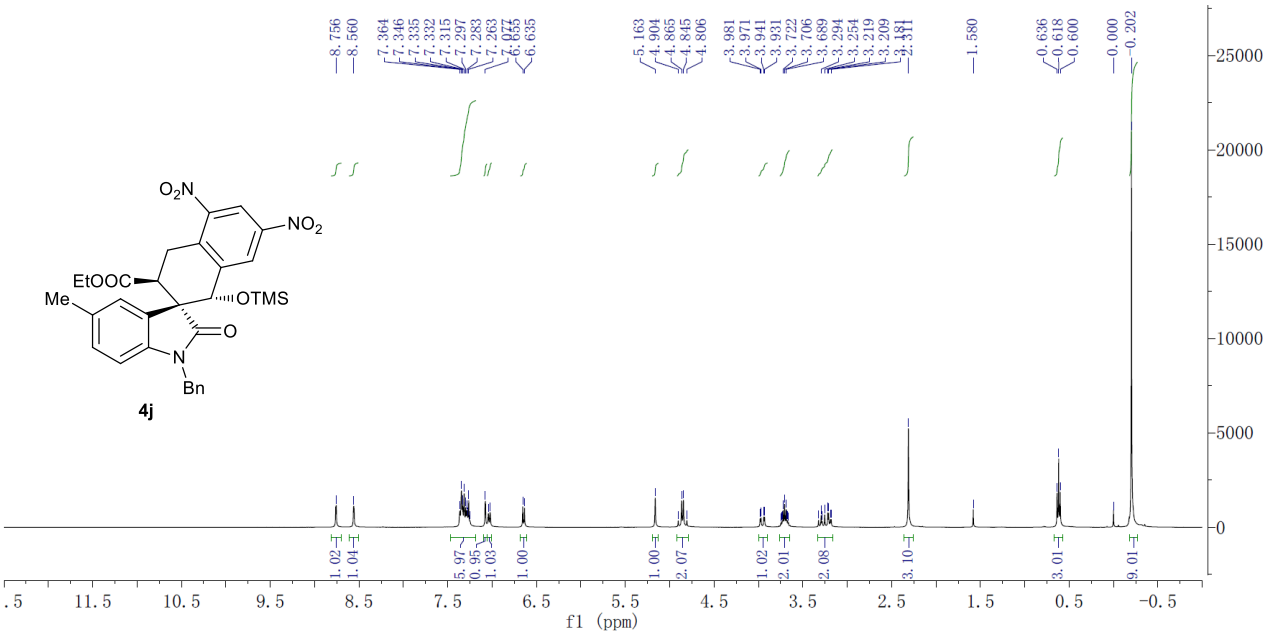
Bn
4g
f1 (ppm)

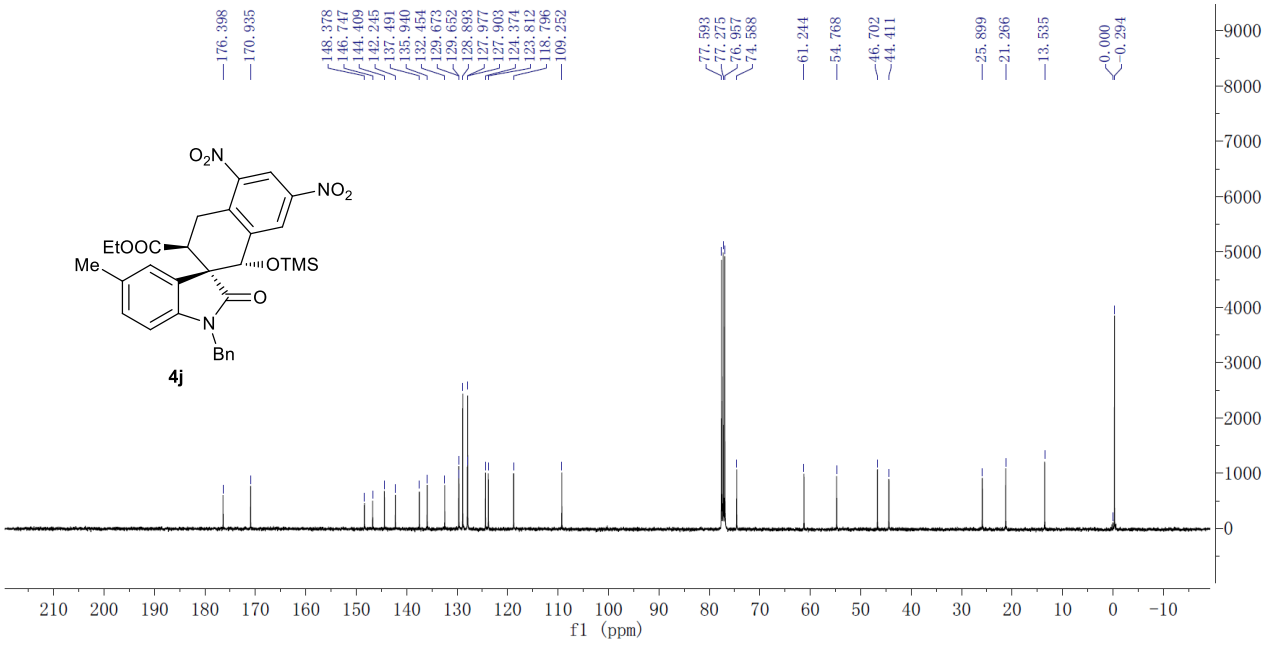

8.769
8.532
7.353
7.342
7.321
7.313
7.300
7.293
7.279
7.263
7.217
7.213
7.197
7.193
7.113
7.093
6.923
5.132
4.847
3.969
3.938
3.930
3.772
3.754
3.736
3.718
3.313
3.284
3.273
3.245
3.228
3.219
3.199
3.191
1.577
0.723
0.705
0.687
0.000
0.163
O2N
NO2
EtOOC
OTMS
O
Br
N
Bn
4h
0.99
1.01
5.12
1.06
1.05
1.04
1.00
2.01
1.02
2.03
2.03
3.02
9.01
f1 (ppm)

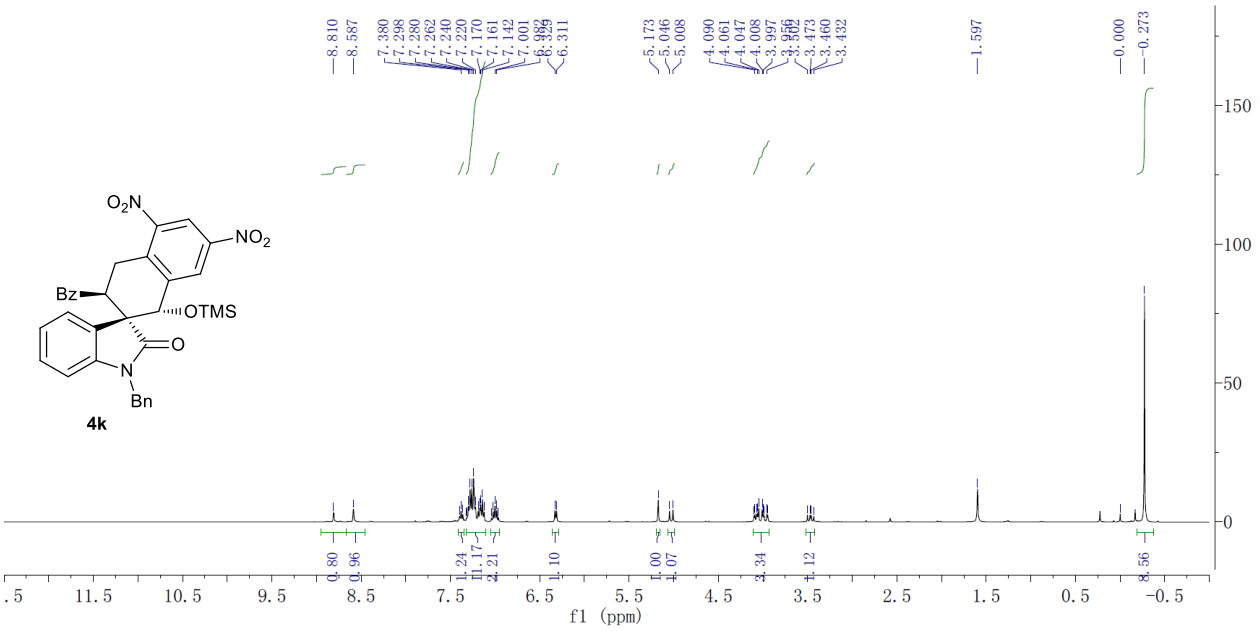

176.218
170.576
146.655
145.973
143.723
137.218
135.072
129.012
128.470
128.197
127.709
125.478
124.729
123.818
123.068
118.912
112.645
77.515
77.194
76.879
74.252
61.389
54.504
46.403
44.413
25.707
13.562
0.000
-0.288
O2N
NO2
EtOOC
OTMS
O
Br
N
Bn
4h
f1 (ppm)


8.768
8.540
7.408
7.390
7.329
7.324
7.308
7.289
7.280
7.264
7.080
7.075
7.070
7.056
7.047
7.041
7.032
7.028
5.070
5.032
5.012
4.974
3.974
3.966
3.935
3.927
3.697
3.687
3.679
3.669
3.661
3.651
3.300
3.271
3.232
3.218
3.210
0.629
0.611
0.593
0.000
0.189
0.97
0.99
4.76
3.06
1.00
1.99
1.00
2.06
2.03
2.95
9.02
f1 (ppm)
O2N
NO2
EtOOC
OTMS
O
N
Bn
F
4i


176.262
170.588
148.837
148.403
146.818
146.401
143.944
137.337
136.997
132.796
132.761
131.447
131.362
128.715
128.222
128.207
127.969
123.815
123.624
123.560
119.454
119.422
118.935
117.901
117.706
77.592
77.275
76.957
74.803
61.312
55.240
46.902
45.889
45.844
25.759
13.529
0.000
-0.294
f1 (ppm)
O2N
NO2
EtOOC
OTMS
O
N
Bn
F
4i

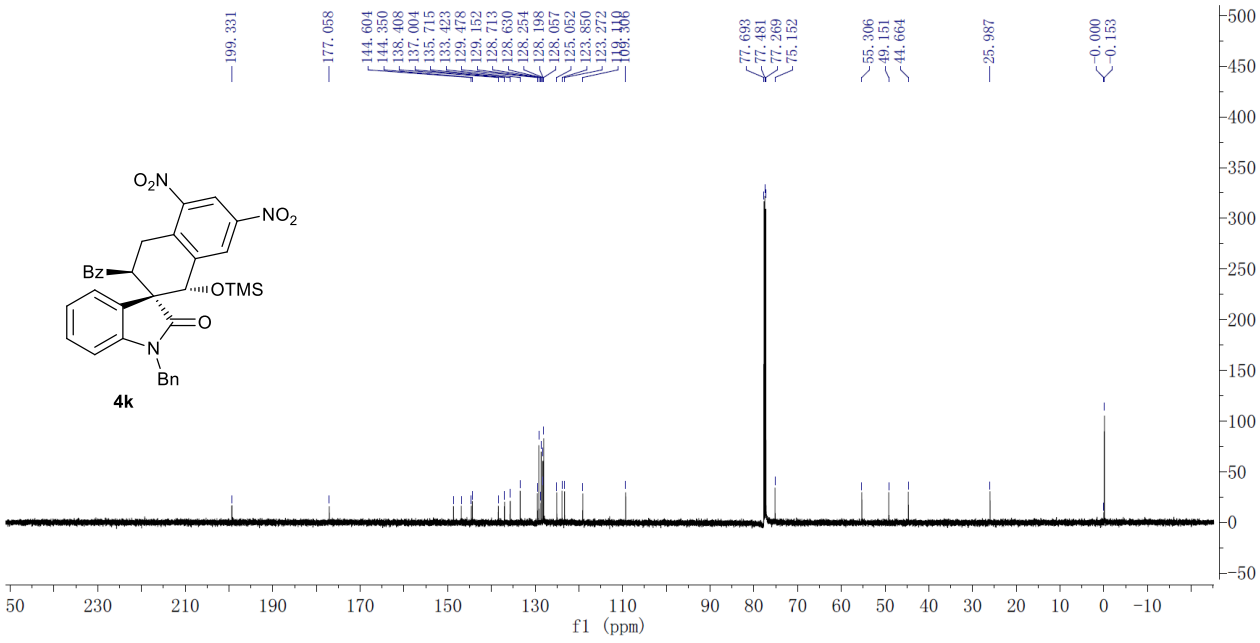

O2N
NO2
EtOOC
Me
OTMS
O
N
Bn
4j
f1 (ppm)


O2N
NO2
EtOOC
Me
OTMS
O
N
Bn
4j
f1 (ppm)


8.810
8.587
7.380
7.298
7.280
7.262
7.240
7.220
7.170
7.161
7.142
7.001
6.311
5.173
5.046
5.008
4.090
4.061
4.047
4.008
3.997
3.473
3.460
3.432
1.597
0.000
-0.273
0.80
0.96
1.24
11.17
2.21
1.10
1.00
4.07
3.34
1.12
8.56
f1 (ppm)

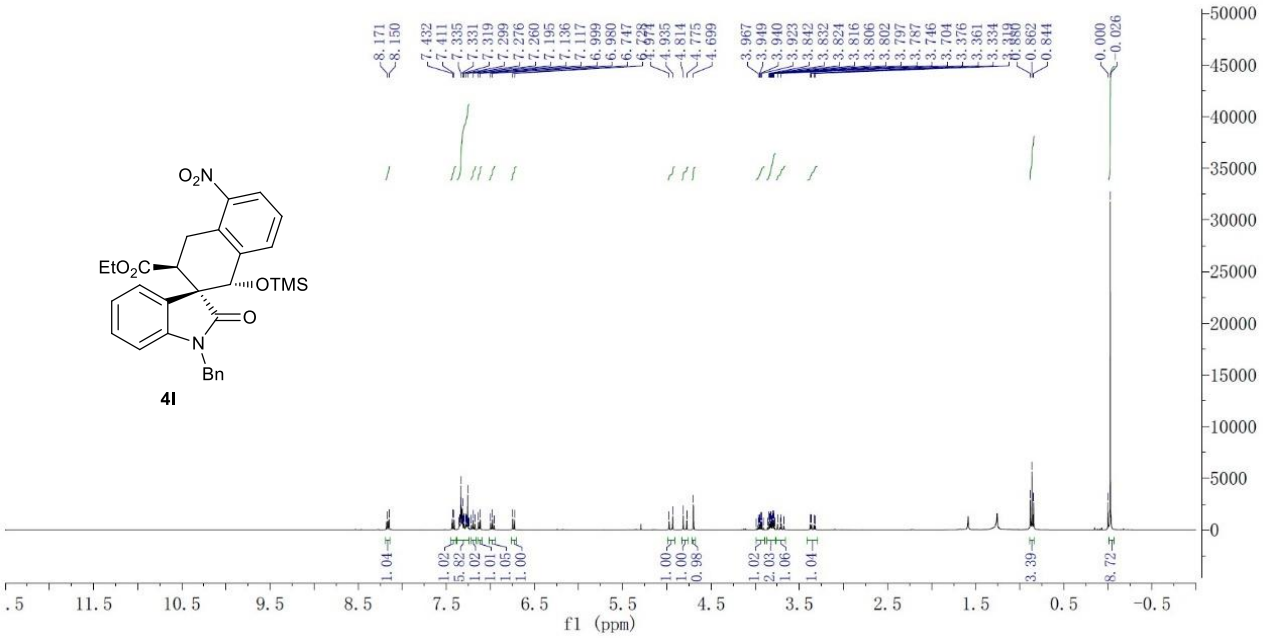
O2N
NO2
Bz
OTMS
O
N
Bn

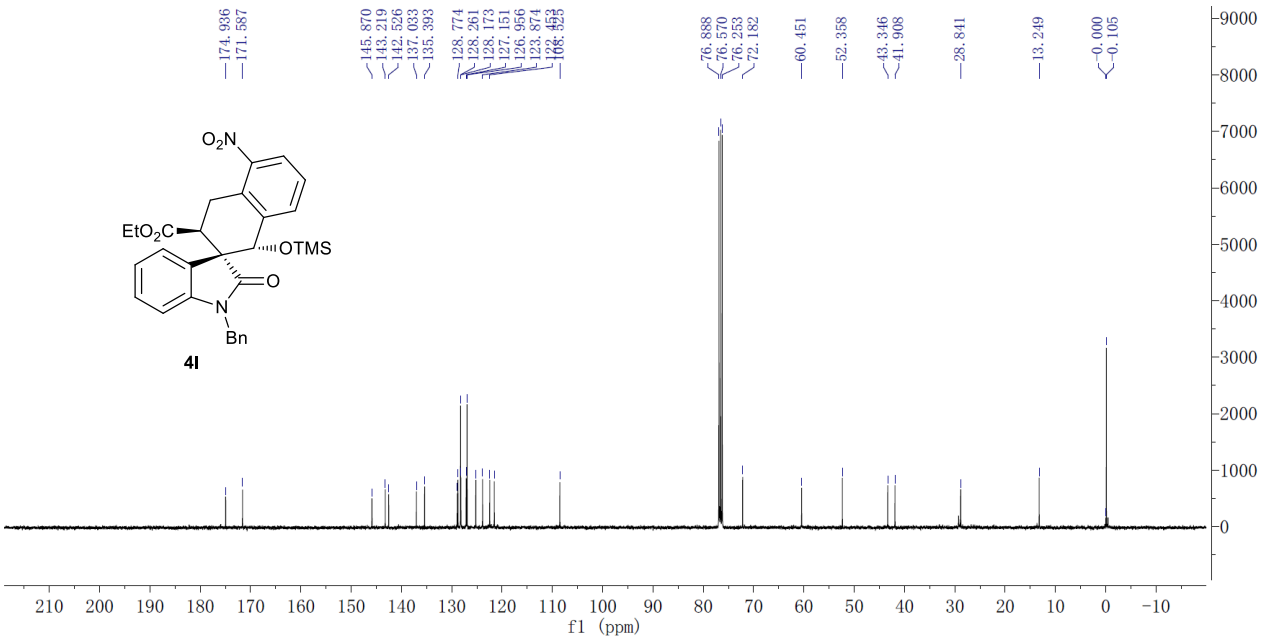
4k

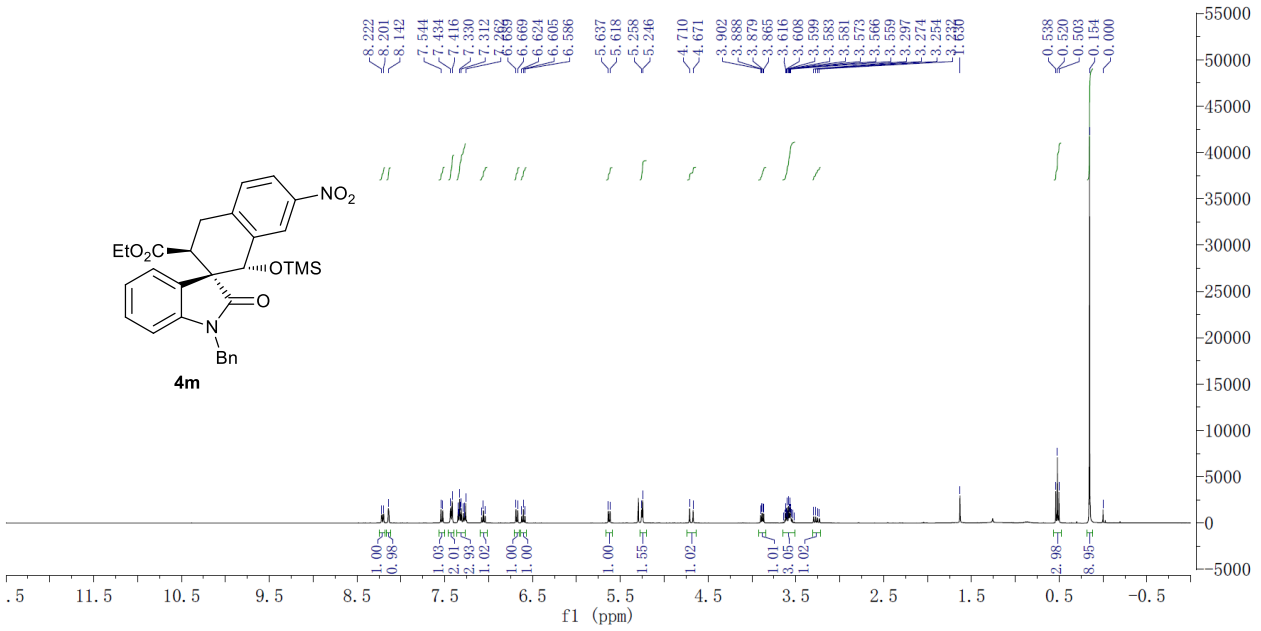

199.331
177.058
144.604
144.350
138.408
137.004
135.715
133.423
129.478
129.152
128.713
128.630
128.254
128.198
128.057
125.052
123.850
123.272
77.693
77.481
77.269
75.152
55.306
49.151
44.664
25.987
0.000
-0.153
f1 (ppm)

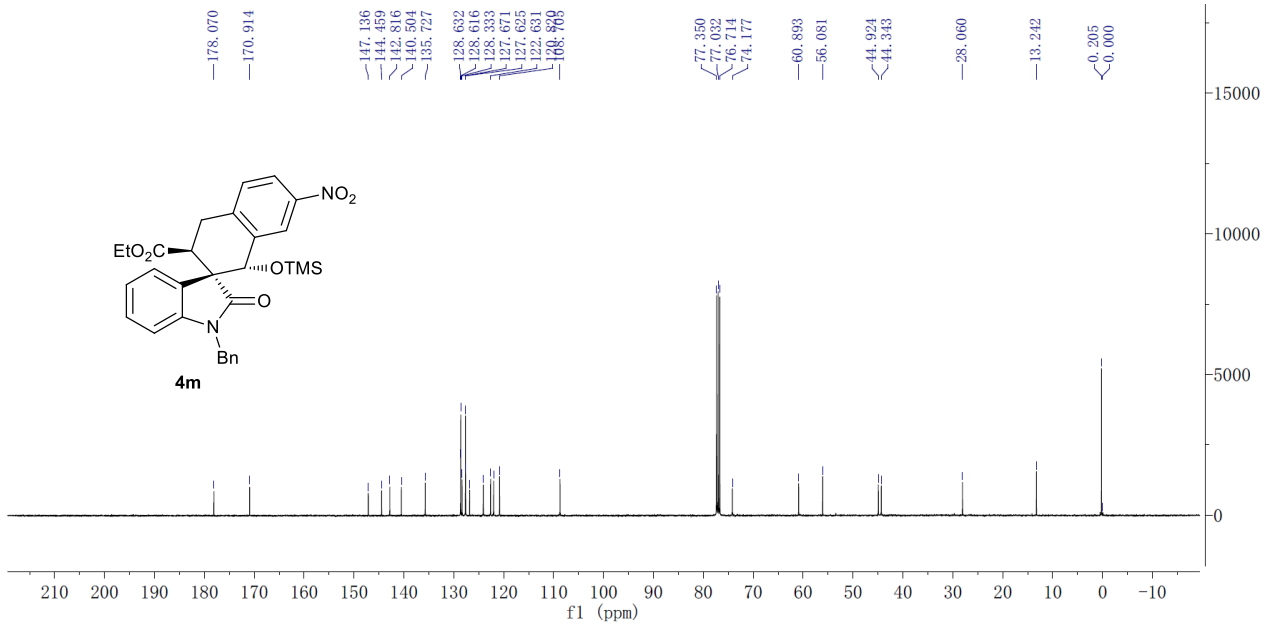
O2N
NO2
Bz
OTMS
O
N
Bn

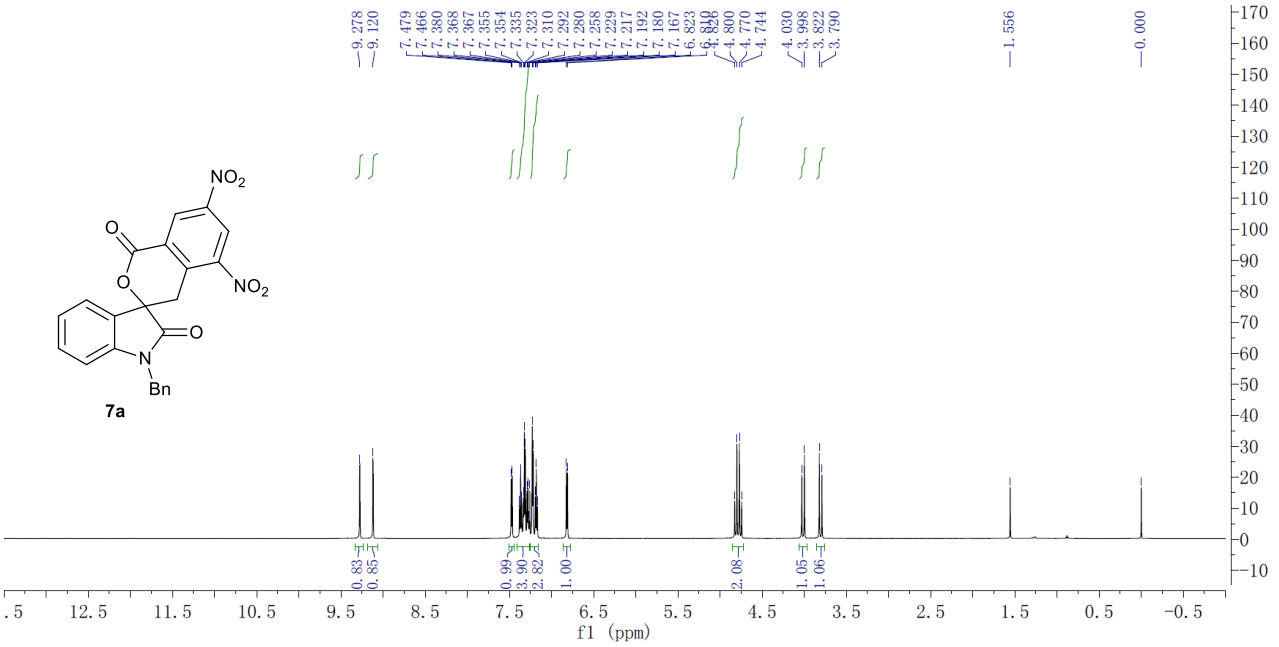
4k

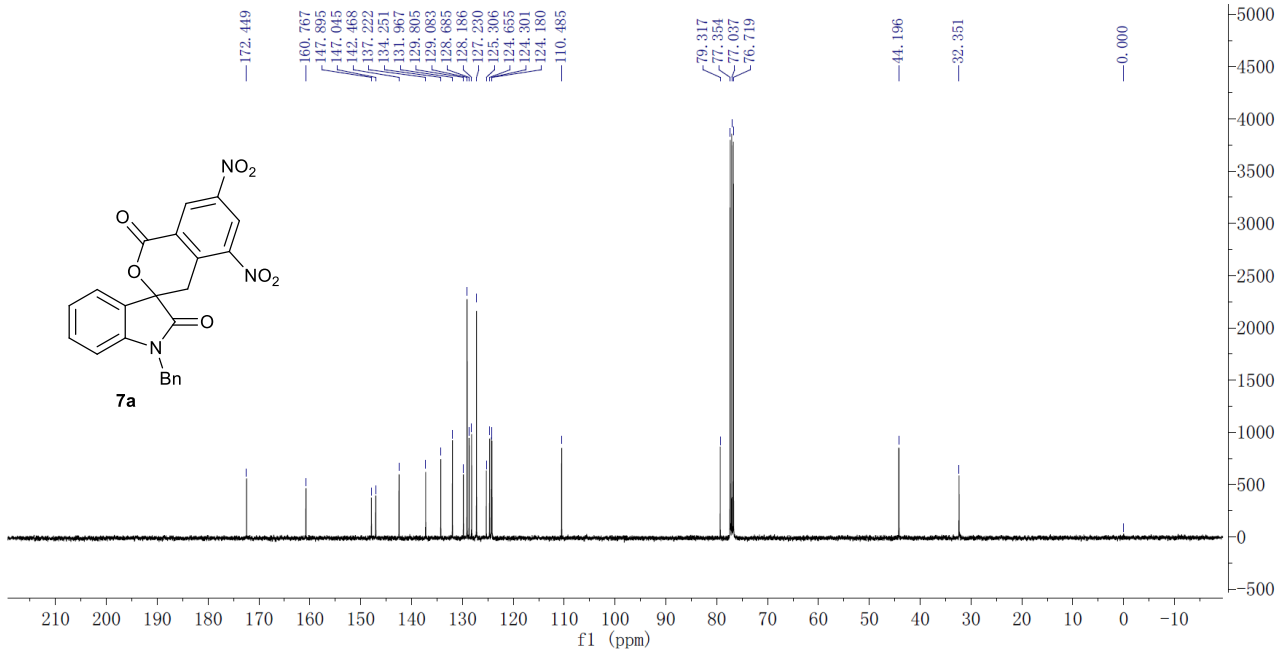

O2N
EtO2C
OTMS
O
N
Bn
4l
f1 (ppm)

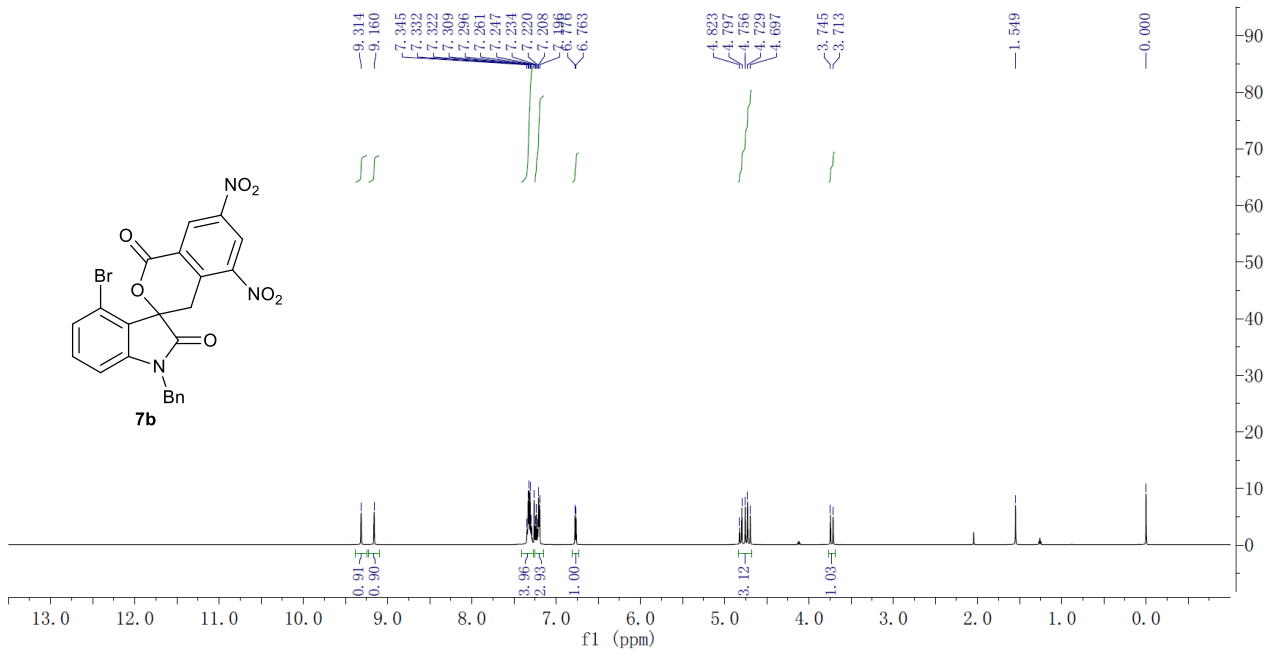

O2N
EtO2C
OTMS
O
N
Bn
4l
f1 (ppm)


NO2
EtO2C
OTMS
O
N
Bn
4m
f1 (ppm)


NO2
EtO2C
OTMS
O
N
Bn
4m
f1 (ppm)

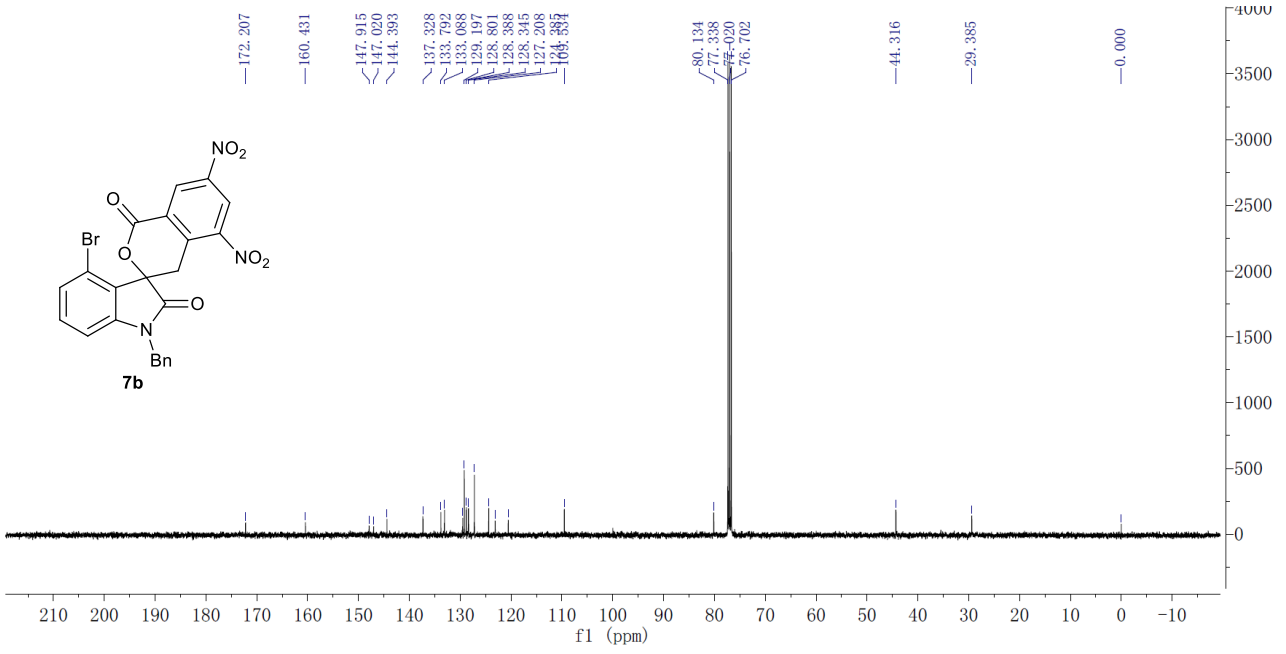

9.278
9.120
7.479
7.466
7.380
7.368
7.367
7.355
7.354
7.335
7.323
7.310
7.292
7.280
7.258
7.229
7.217
7.192
7.180
7.167
6.823
4.800
4.770
4.744
4.030
3.998
3.822
3.790
1.556
0.000
0.83
0.85
0.99
3.90
2.82
1.00
2.08
1.05
1.06
f1 (ppm)
NO2
NO2
O
O
O
N
Bn
7a


172.449
160.767
147.895
147.045
142.468
137.222
134.251
131.967
129.805
129.083
128.685
128.186
127.230
125.306
124.655
124.301
124.180
110.485
79.317
77.354
77.037
76.719
44.196
32.351
0.000
f1 (ppm)
NO2
NO2
O
O
O
N
Bn
7a


9.314
9.160
7.345
7.332
7.322
7.309
7.296
7.261
7.247
7.234
7.220
7.208
6.778
6.763
4.823
4.797
4.756
4.729
4.697
3.745
3.713
1.549
0.000
0.91
0.90
3.96
2.93
1.00
3.12
1.03
f1 (ppm)

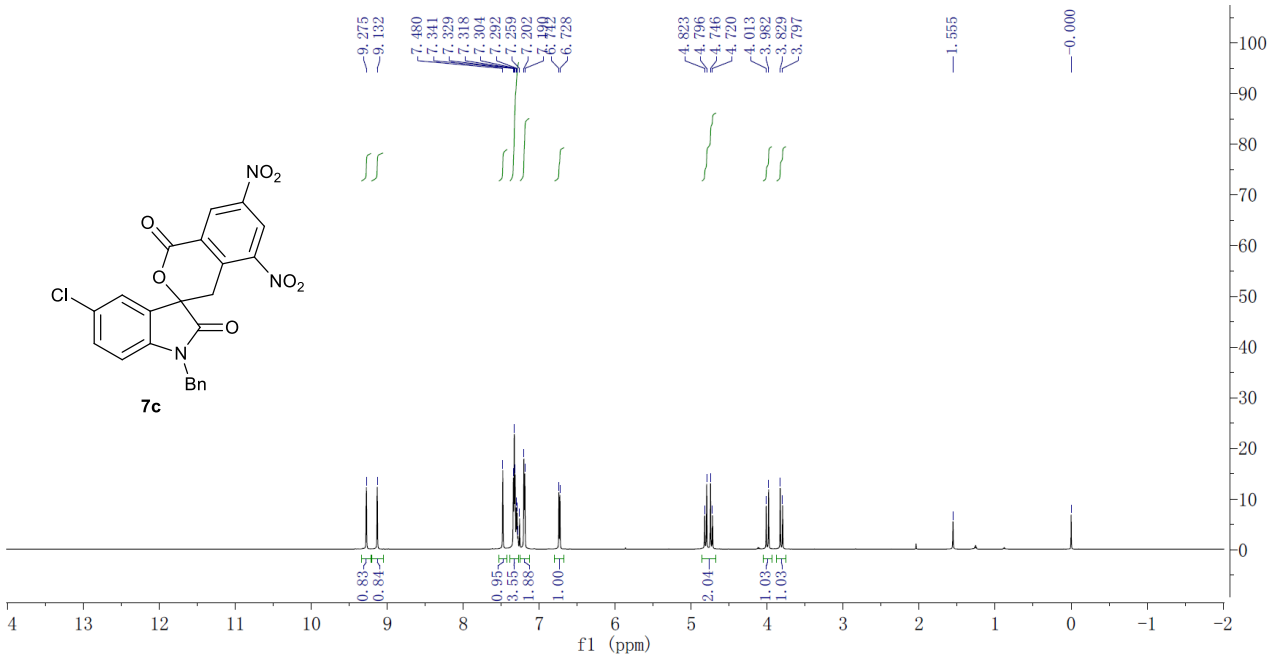
NO2
O
Br
O
NO2
O
N
Bn

7b


172.207
160.431
147.915
147.020
144.393
137.328
133.792
133.088
129.197
128.801
128.388
128.345
127.208
80.134
77.338
76.702
44.316
29.385
0.000
f1 (ppm)

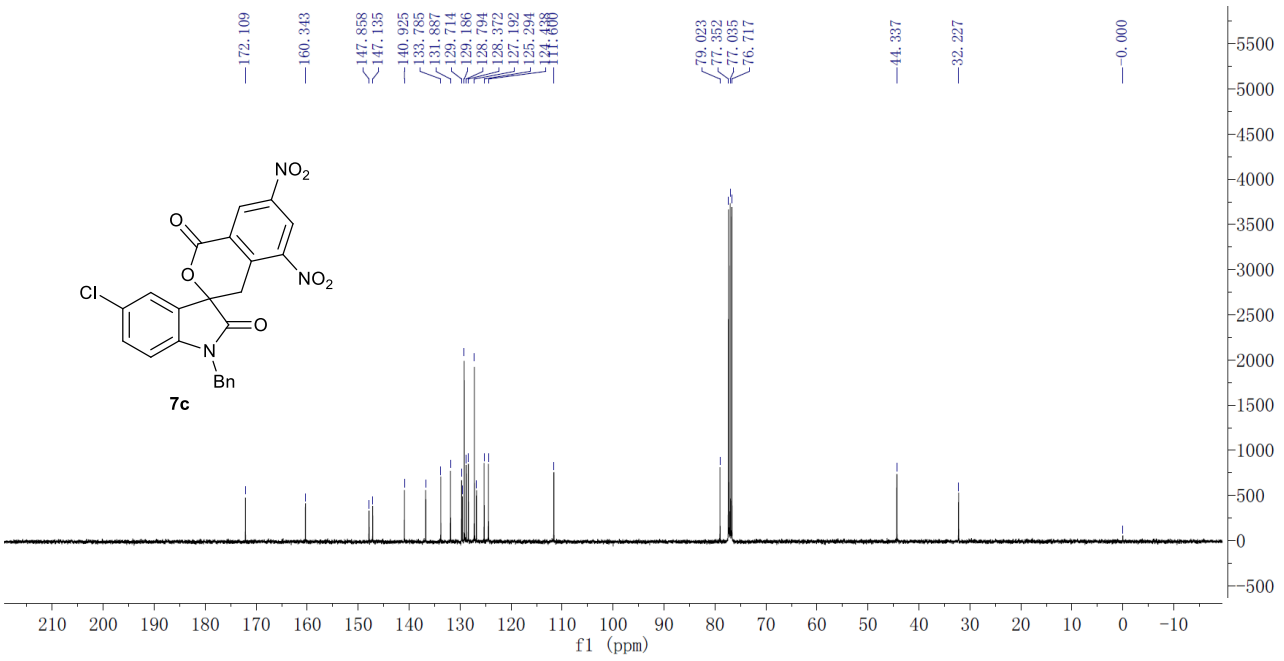
NO2
O
Br
O
NO2
O
N
Bn

7b


9.275
9.132
7.480
7.341
7.329
7.318
7.304
7.292
7.259
7.202
6.728
4.823
4.796
4.746
4.720
4.013
3.982
3.829
3.797
1.555
0.000
0.83
0.84
0.95
3.55
1.88
1.00
2.04
1.03
1.03
f1 (ppm)

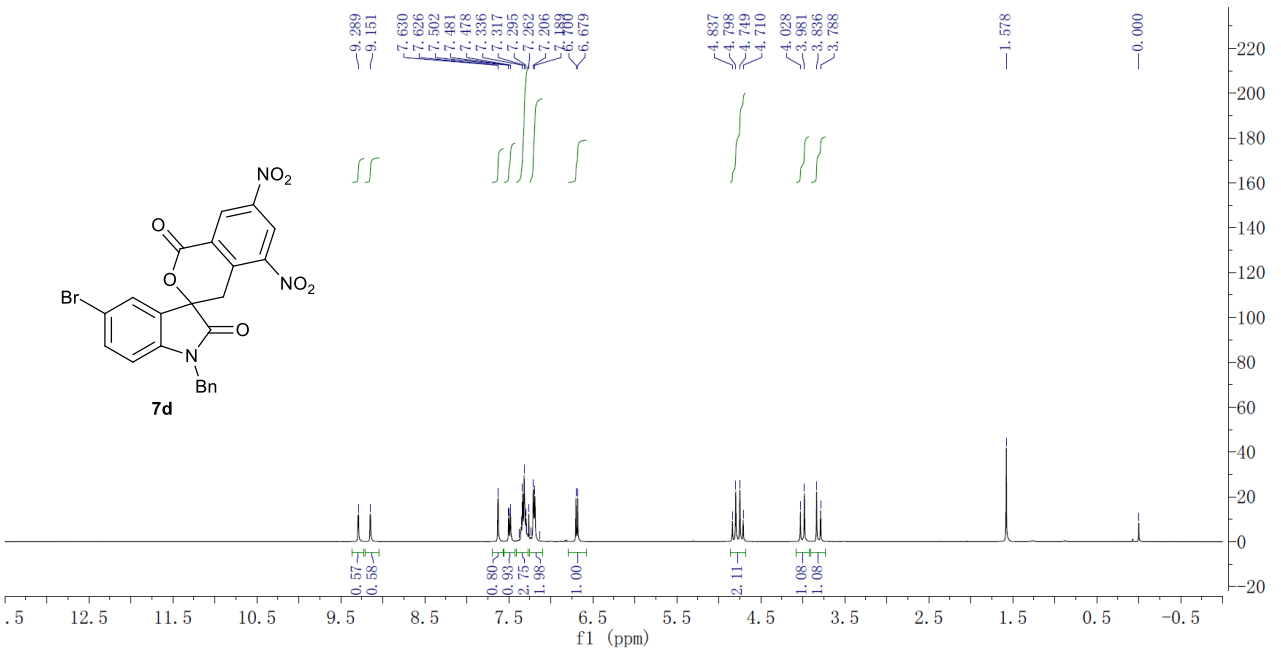
NO2
O
O
NO2
Cl
O
N
Bn

7c


172.109
160.343
147.858
147.135
140.925
133.785
131.887
129.714
129.186
128.794
128.372
127.192
125.294
79.023
77.352
77.035
76.717
44.337
32.227
0.000
f1 (ppm)

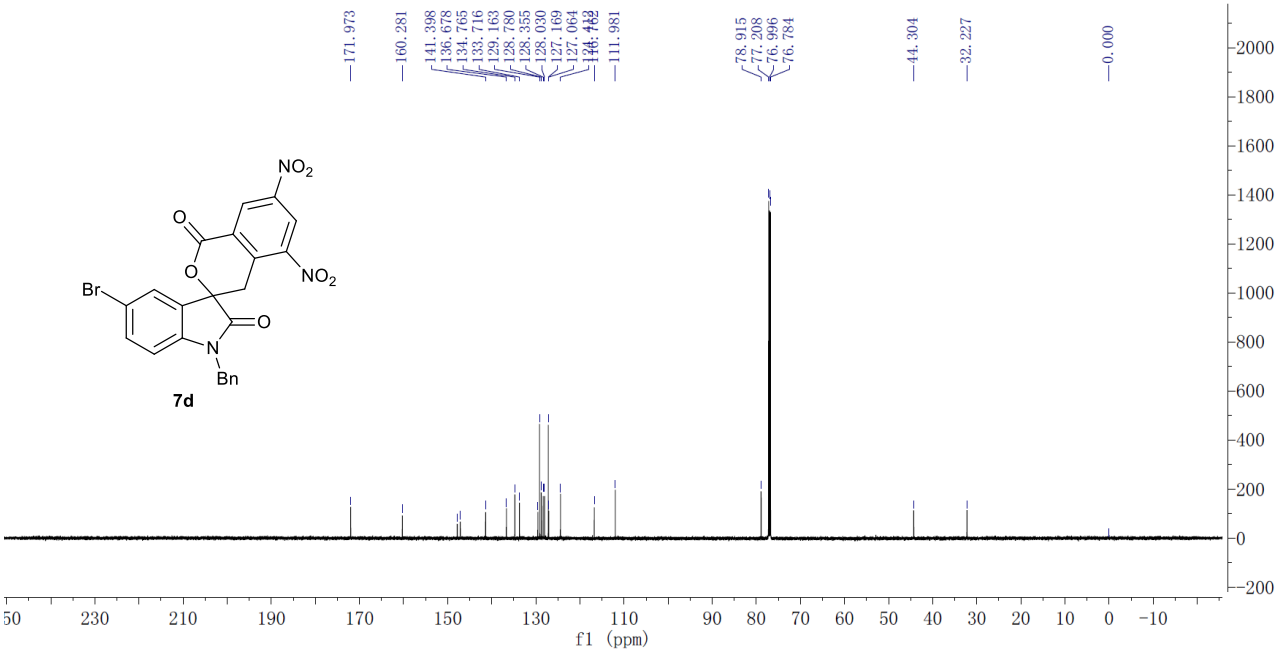
NO2
O
O
NO2
Cl
O
N
Bn

7c


9.289
9.151
7.630
7.626
7.502
7.481
7.478
7.336
7.317
7.295
7.262
7.206
6.679
4.837
4.798
4.749
4.710
4.028
3.981
3.836
3.788
1.578
0.000
0.57
0.58
0.80
0.93
2.75
1.98
1.00
2.11
1.08
1.08
f1 (ppm)

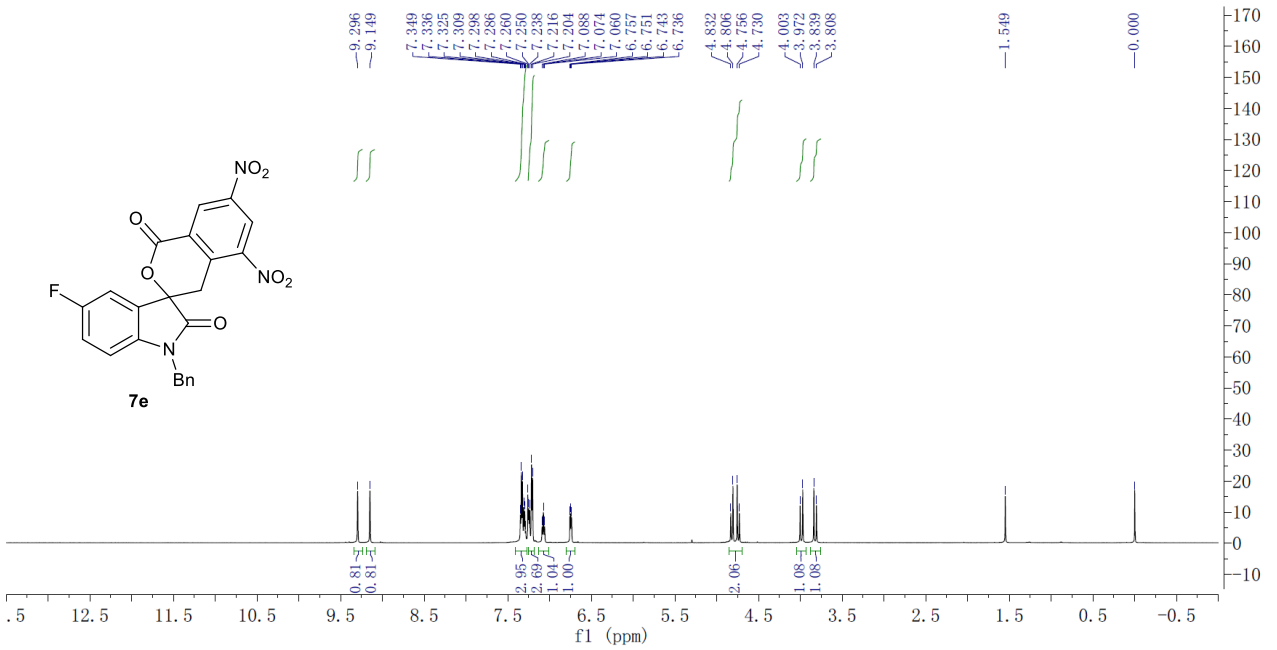
NO2
O
O
NO2
Br
O
N
Bn

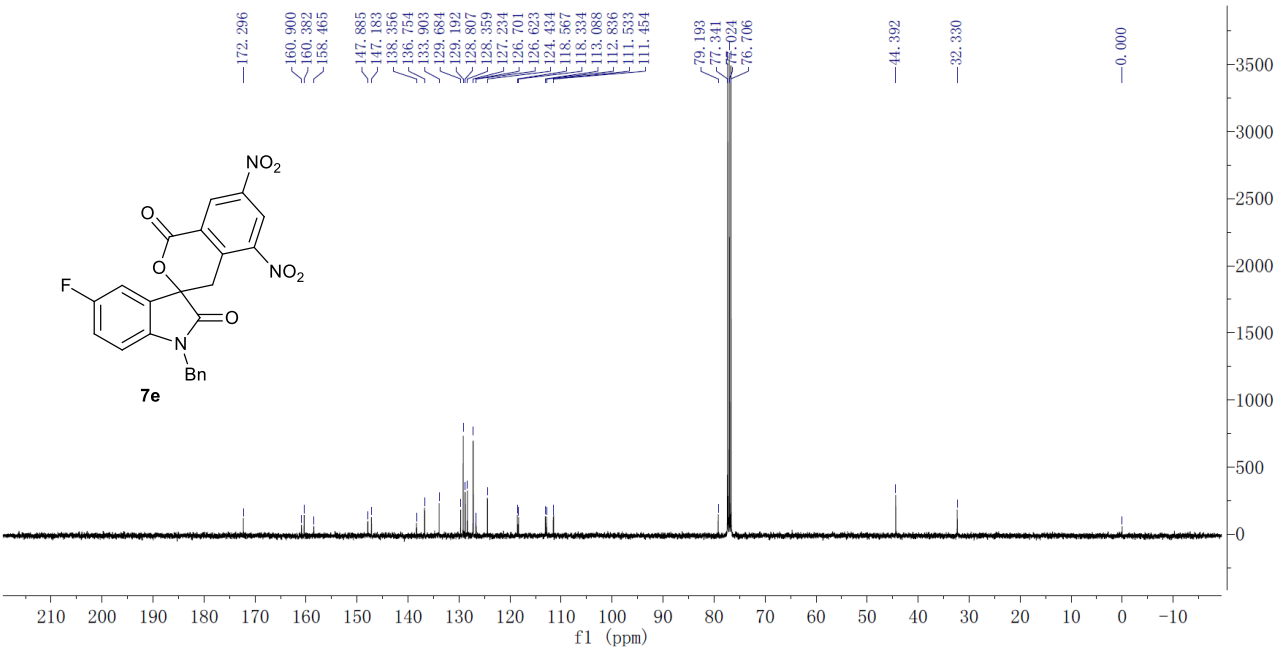
7d

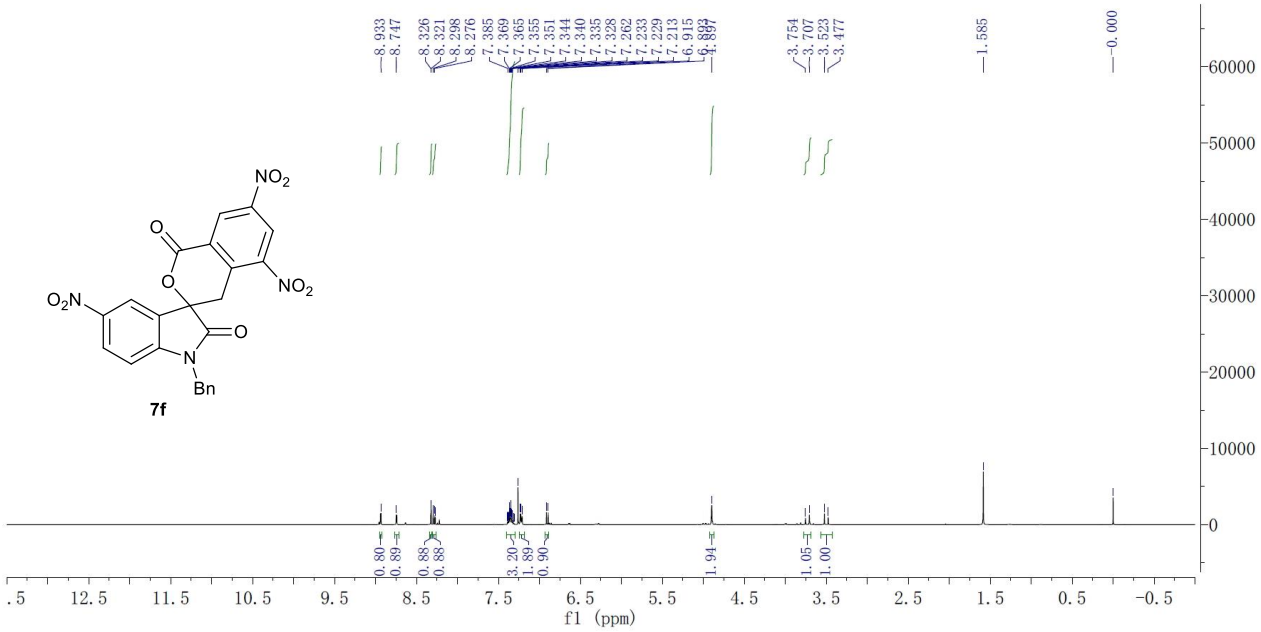

171.973
160.281
141.398
136.678
134.765
133.716
129.163
128.780
128.355
128.030
127.169
127.064
111.981
78.915
77.208
76.996
76.784
44.304
32.227
0.000
f1 (ppm)

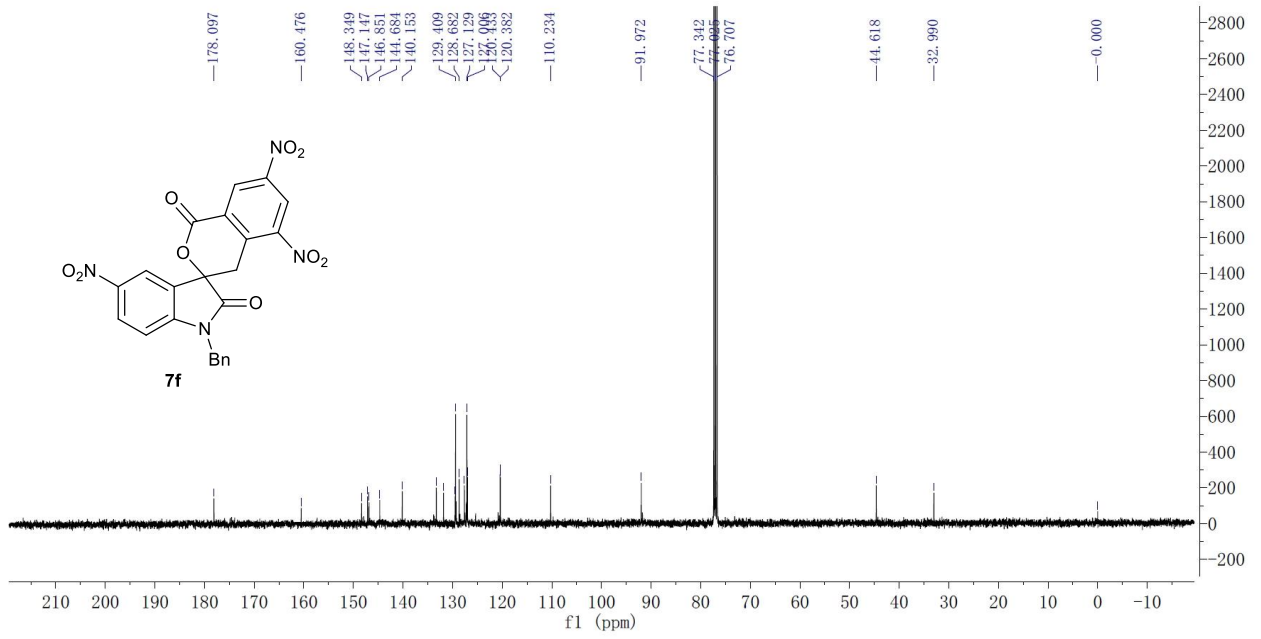
NO2
O
O
NO2
Br
O
N
Bn

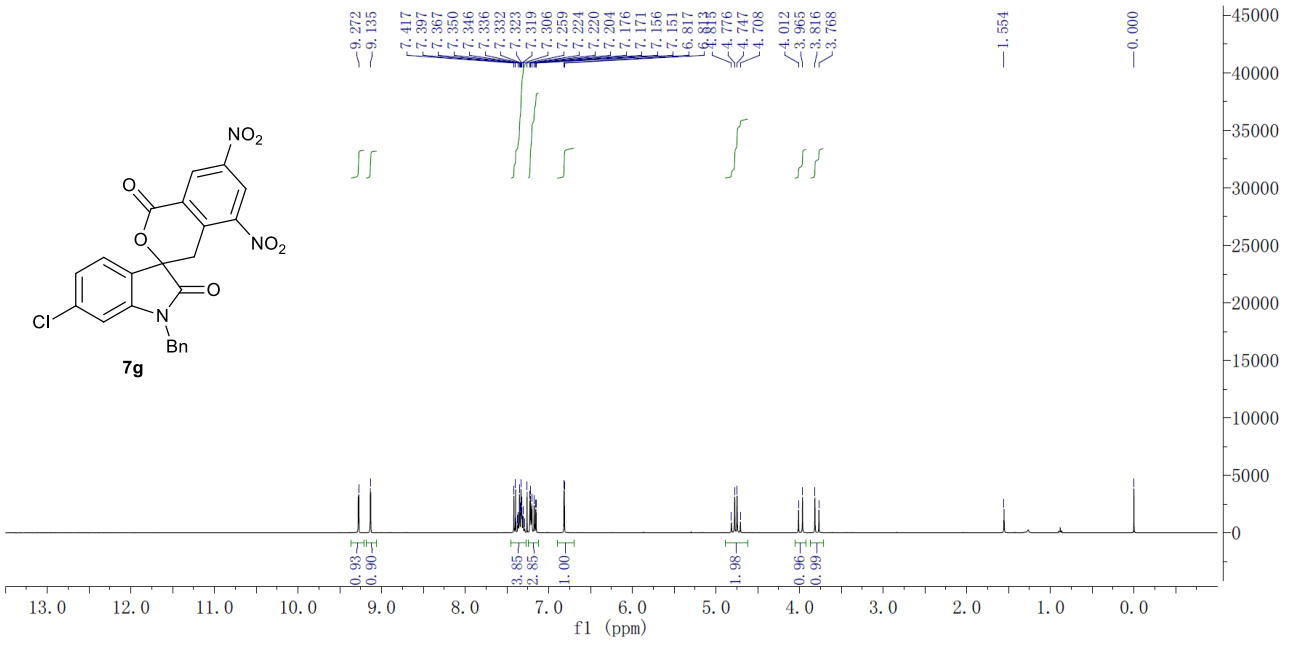
7d

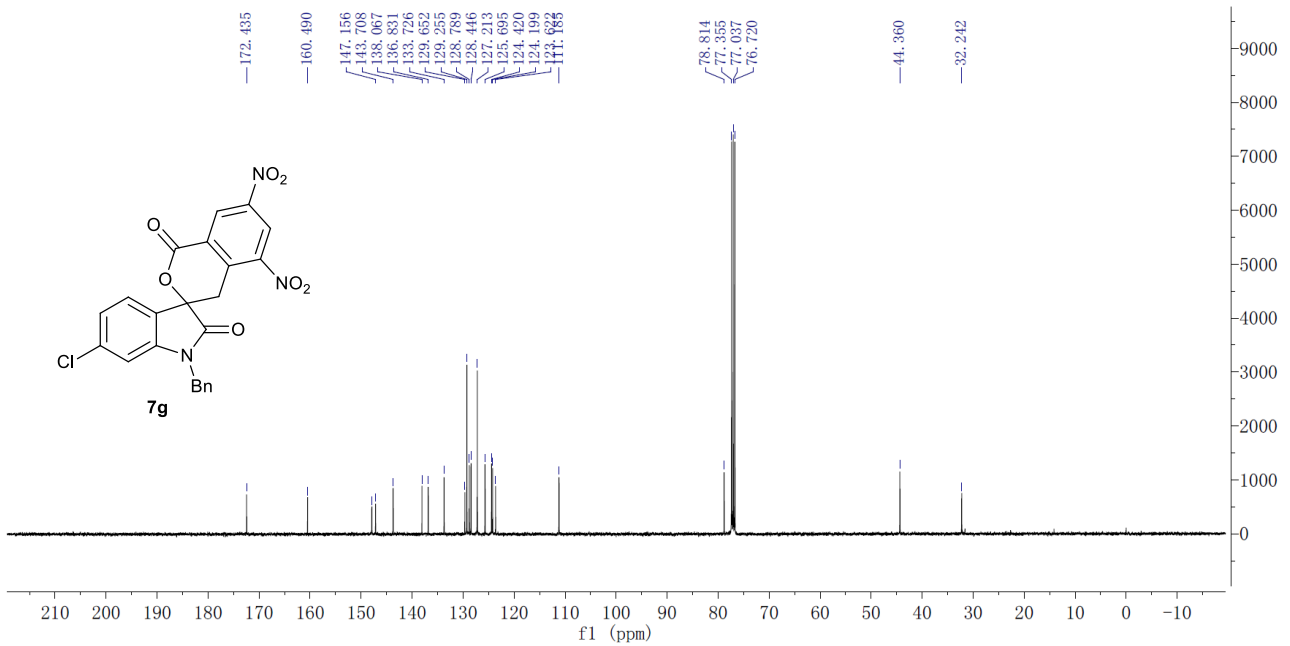

9.296
9.149
7.349
7.336
7.325
7.309
7.298
7.286
7.260
7.250
7.238
7.216
7.204
7.088
7.074
7.060
6.757
6.751
6.743
6.736
4.832
4.806
4.756
4.730
4.003
3.972
3.839
3.808
1.549
0.000
0.81
0.81
2.95
2.69
1.04
1.00
2.06
1.08
1.08
NO2
NO2
O
O
F
O
N
Bn
7e
f1 (ppm)

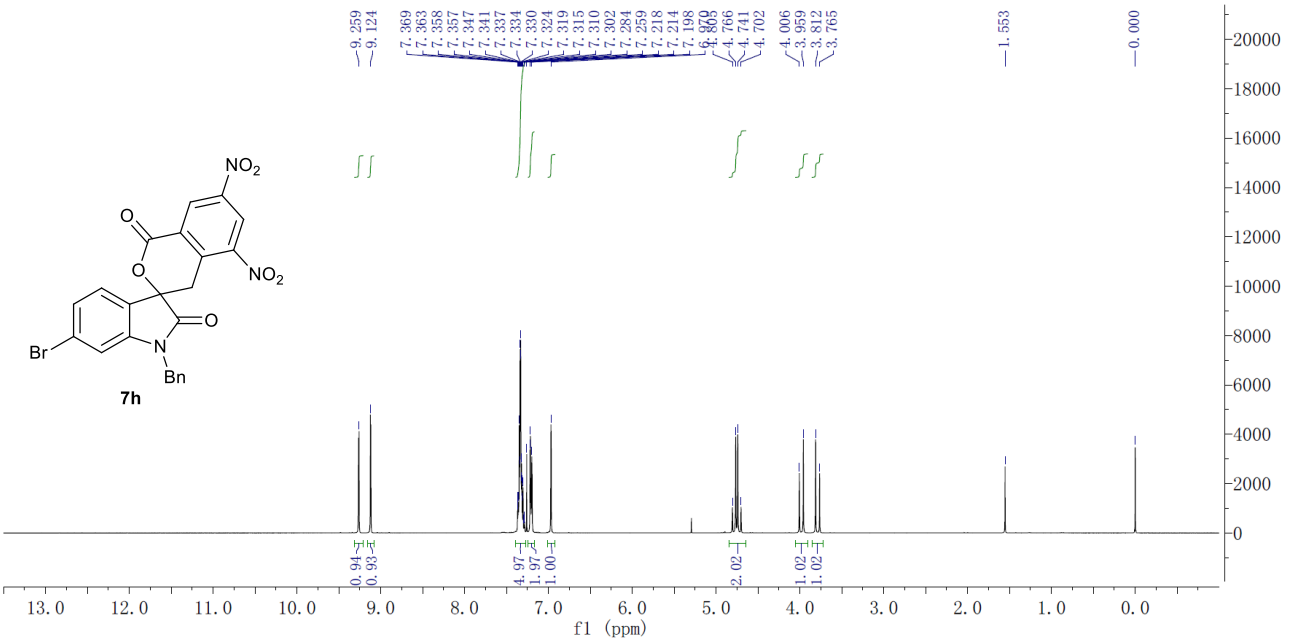

172.296
160.900
160.382
158.465
147.885
147.183
138.356
136.754
133.903
129.684
129.192
128.807
128.359
127.234
126.701
126.623
124.434
118.567
118.334
113.088
112.836
111.533
111.454
79.193
77.341
77.024
76.706
44.392
32.330
0.000
NO2
NO2
O
O
F
O
N
Bn
7e
f1 (ppm)

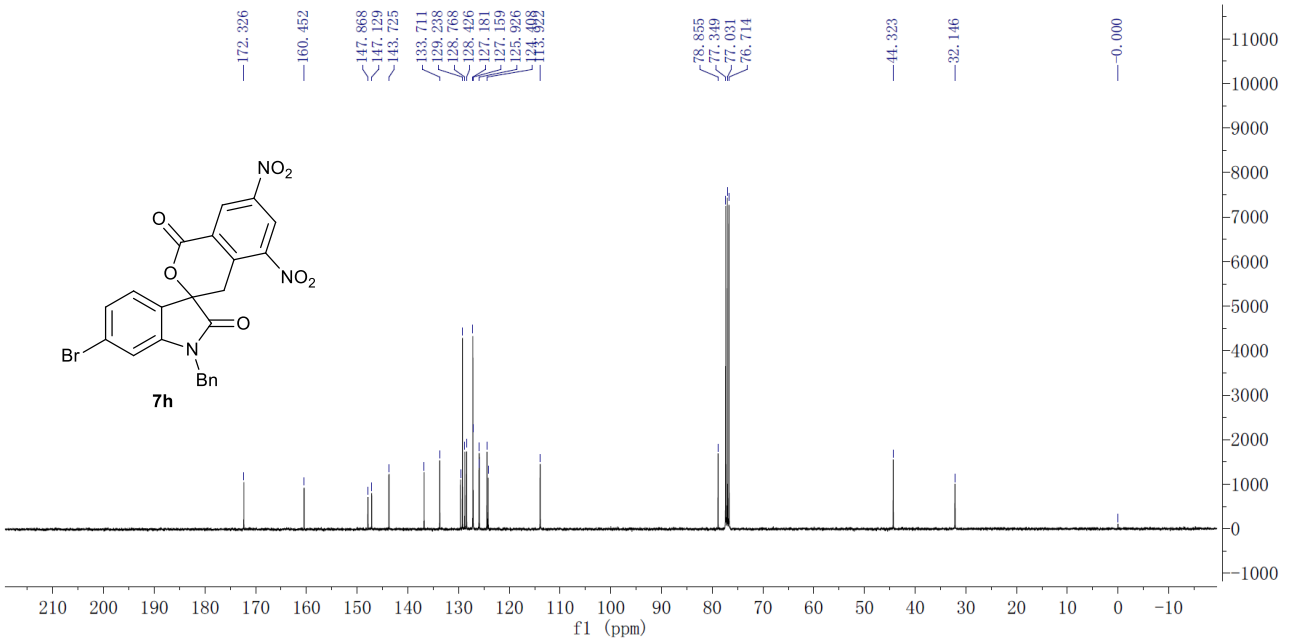

8.933
8.747
8.326
8.321
8.298
8.276
7.385
7.369
7.365
7.355
7.351
7.344
7.340
7.335
7.328
7.262
7.233
7.229
7.213
6.915
3.754
3.707
3.523
3.477
1.585
0.000
0.80
0.89
0.88
0.88
3.20
1.89
0.90
1.94
1.05
1.00
f1 (ppm)
7f

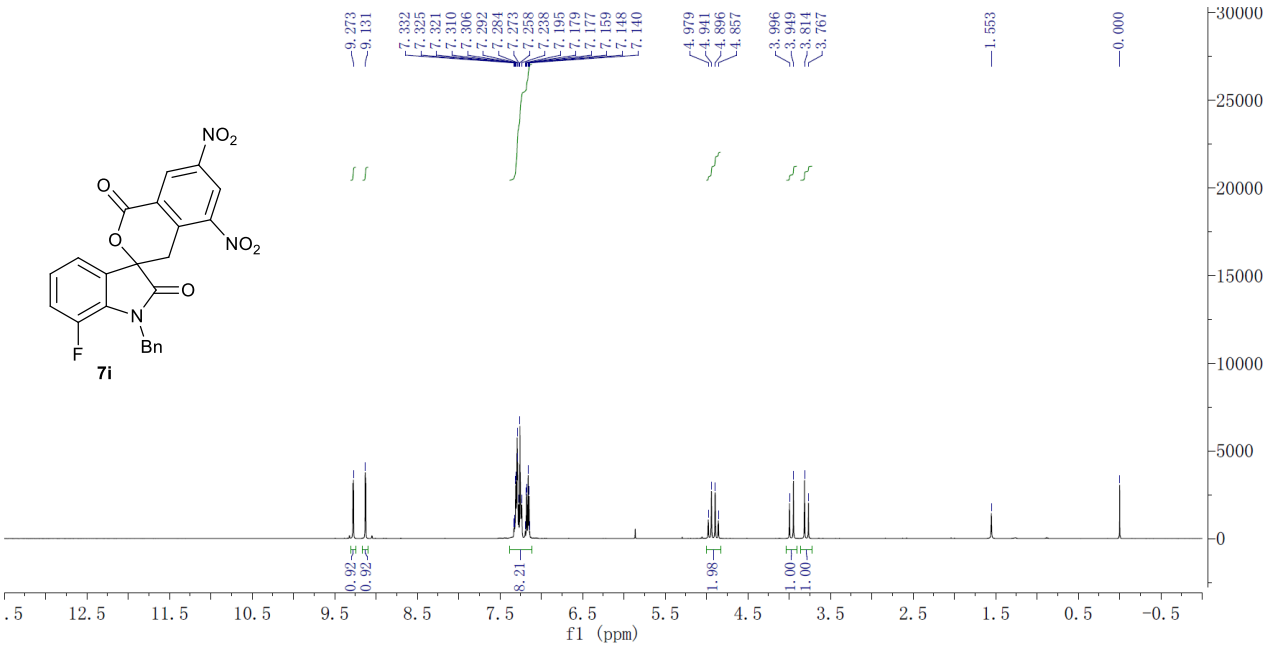

178.097
160.476
148.349
147.147
146.851
144.684
140.153
129.409
128.682
127.129
120.382
110.234
91.972
77.342
76.707
44.618
32.990
0.000
f1 (ppm)
7f

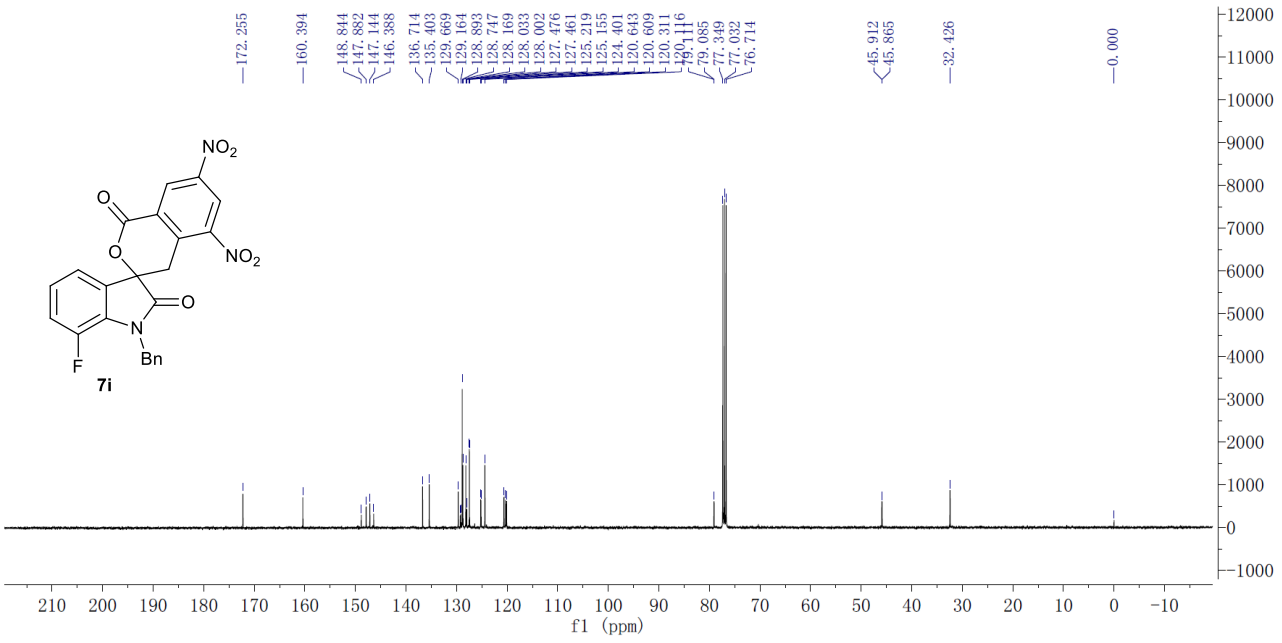

9.272
9.135
7.417
7.397
7.367
7.350
7.346
7.336
7.332
7.323
7.319
7.306
7.259
7.224
7.220
7.204
7.176
7.171
7.156
7.151
6.817
6.813
6.815
4.776
4.747
4.708
4.012
3.965
3.816
3.768
1.554
0.000
NO2
NO2
O
O
O
N
Cl
Bn
7g
0.93
0.90
3.85
2.85
1.00
1.98
0.96
0.99
f1 (ppm)

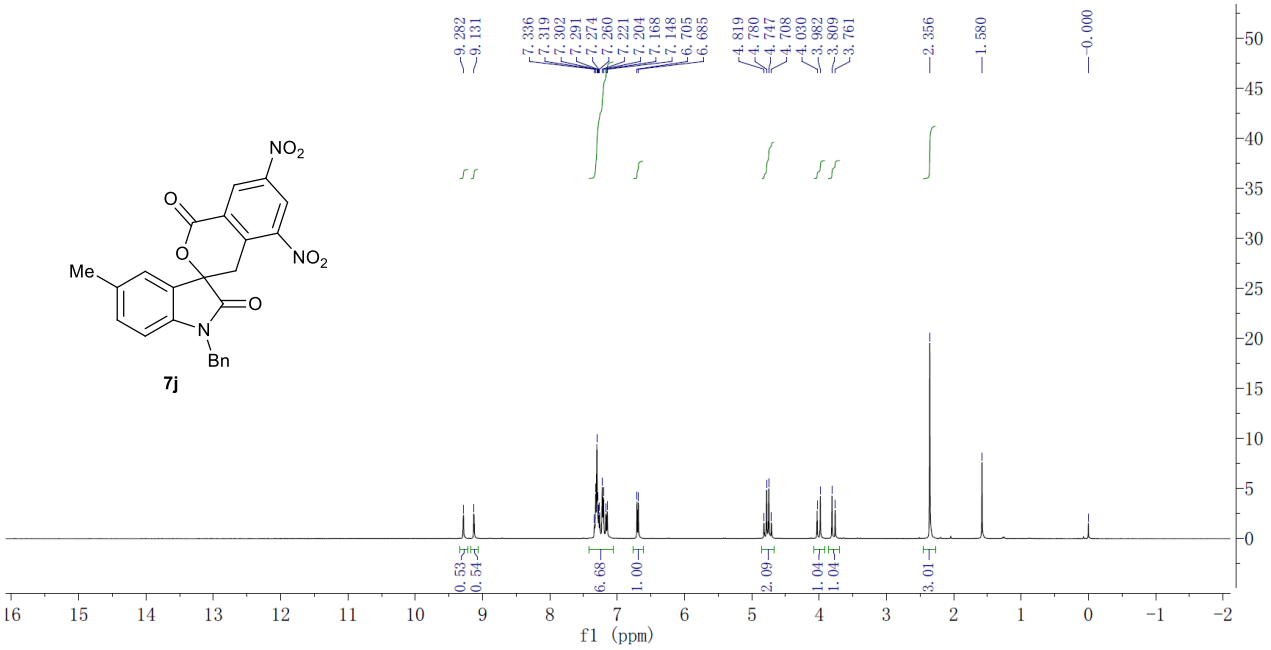

172.435
160.490
147.156
143.708
138.067
136.831
133.726
129.652
129.255
128.789
128.446
127.213
125.695
124.420
124.199
78.814
77.355
77.037
76.720
44.360
32.242
NO2
NO2
O
O
O
N
Cl
Bn
7g
f1 (ppm)

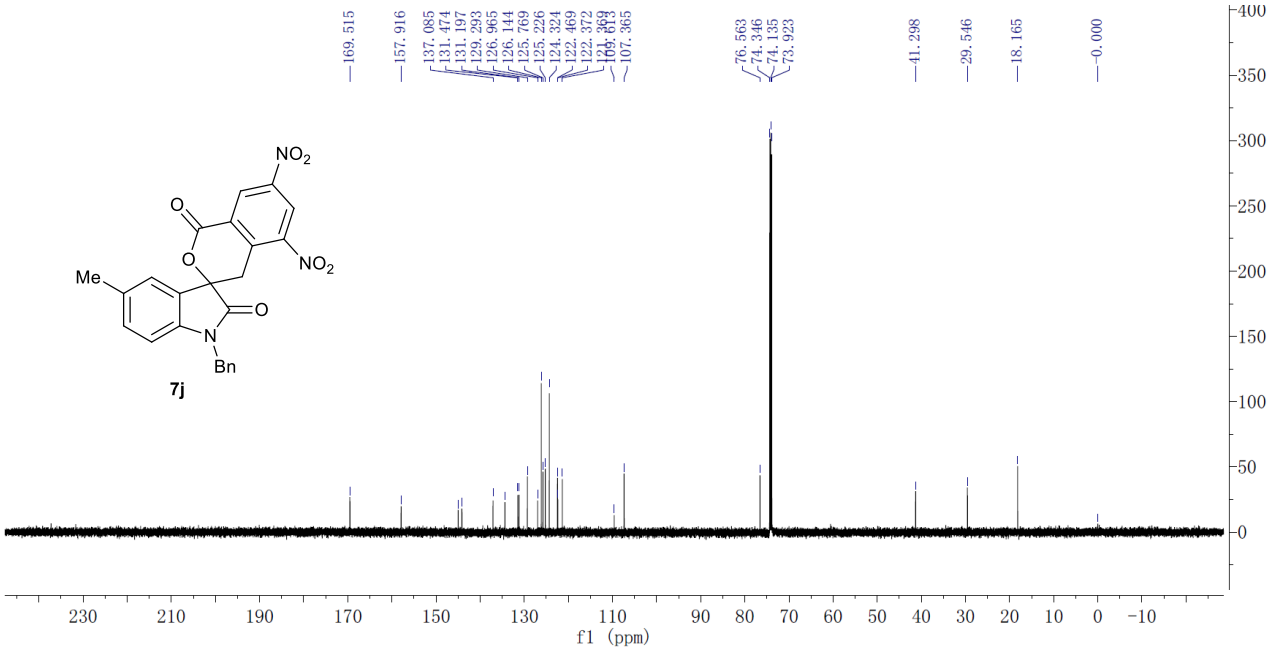

9.259
9.124
7.369
7.363
7.358
7.357
7.347
7.341
7.337
7.334
7.330
7.324
7.319
7.315
7.310
7.302
7.284
7.259
7.218
7.214
7.198
4.803
4.766
4.741
4.702
4.006
3.959
3.812
3.765
1.553
0.000
0.94
0.93
4.97
1.97
1.00
2.02
1.02
1.02
NO2
NO2
O
O
O
Br
N
Bn
7h
f1 (ppm)

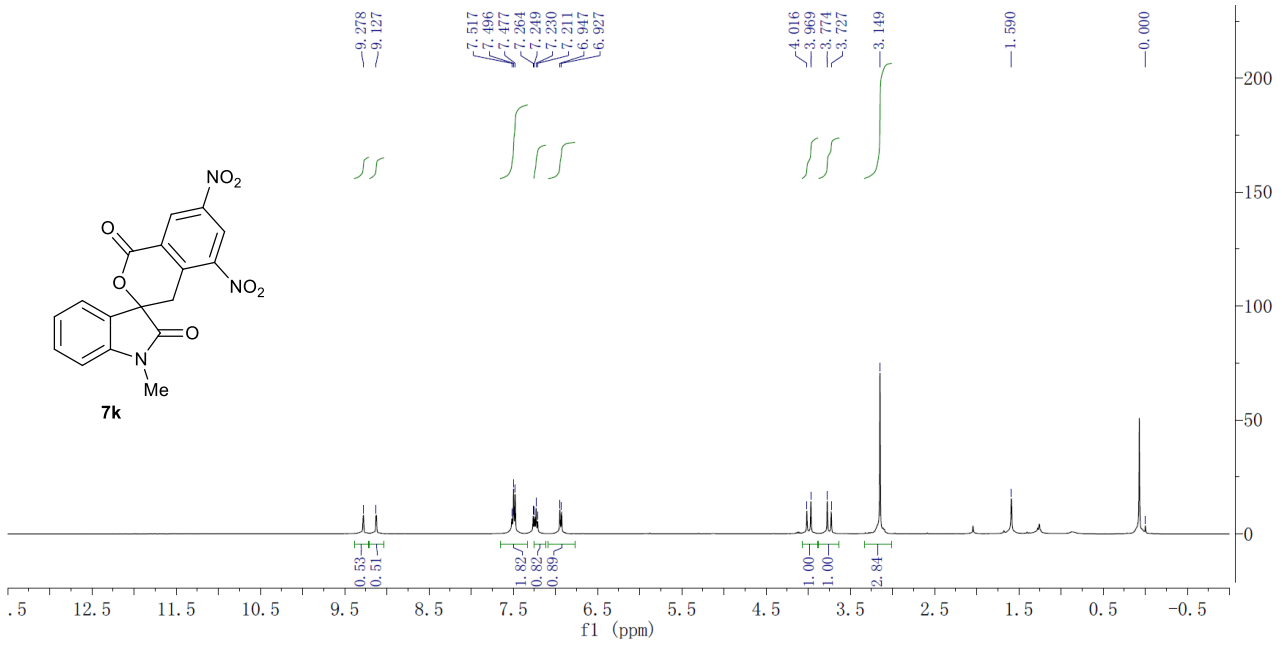

172.326
160.452
147.868
147.129
143.725
133.711
129.238
128.768
128.426
127.181
127.159
125.926
124.498
123.922
78.855
77.349
77.031
76.714
44.323
32.146
0.000
NO2
NO2
O
O
O
Br
N
Bn
7h
f1 (ppm)

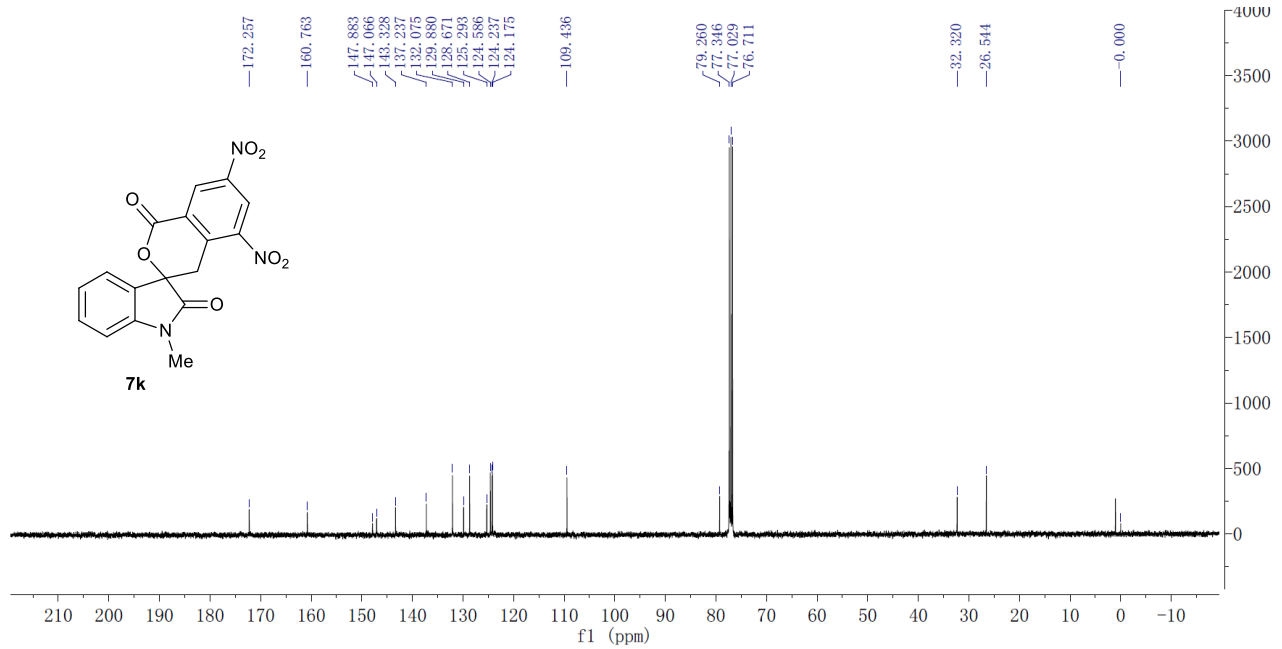

9.273
9.131
7.332
7.325
7.321
7.310
7.306
7.292
7.284
7.273
7.258
7.238
7.195
7.179
7.177
7.159
7.148
7.140
4.979
4.941
4.896
4.857
3.996
3.949
3.814
3.767
1.553
0.000
0.92
0.92
8.21
1.98
1.00
1.00
f1 (ppm)
7i

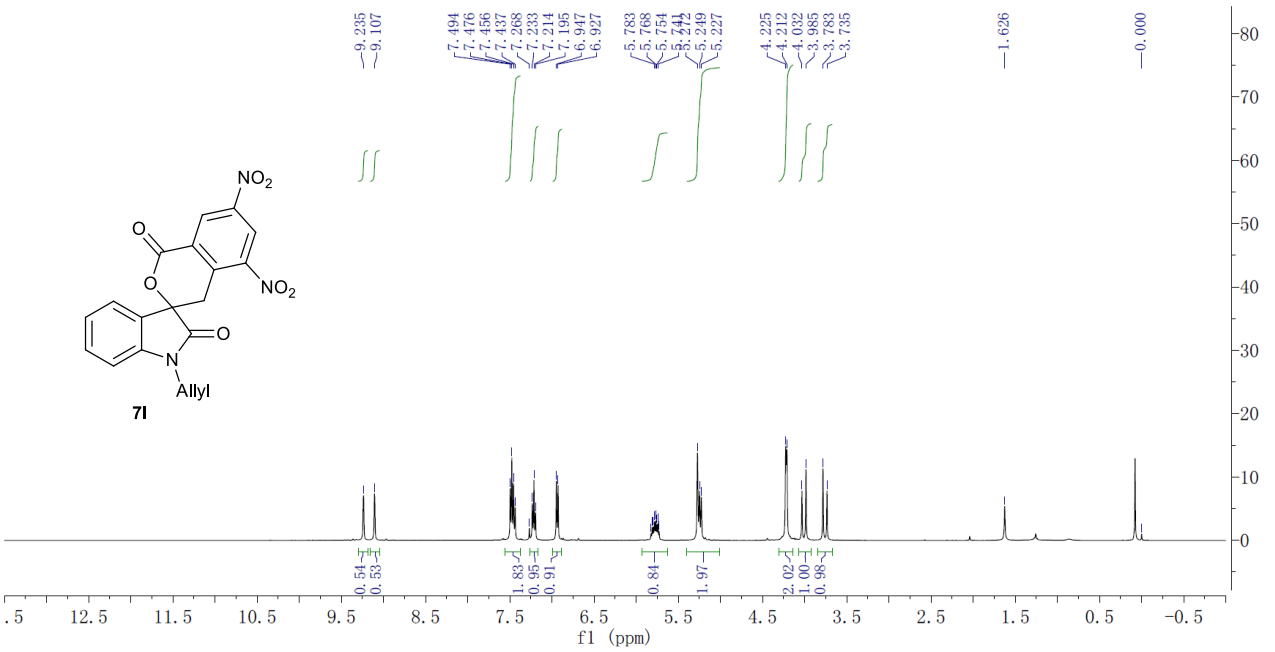

172.255
160.394
148.844
147.882
147.144
146.388
136.714
135.403
129.669
129.164
128.893
128.747
128.169
128.033
128.002
127.476
127.461
125.219
125.155
124.401
120.643
120.609
120.311
120.116
79.111
79.085
77.349
77.032
76.714
45.912
45.865
32.426
0.000
f1 (ppm)
7i

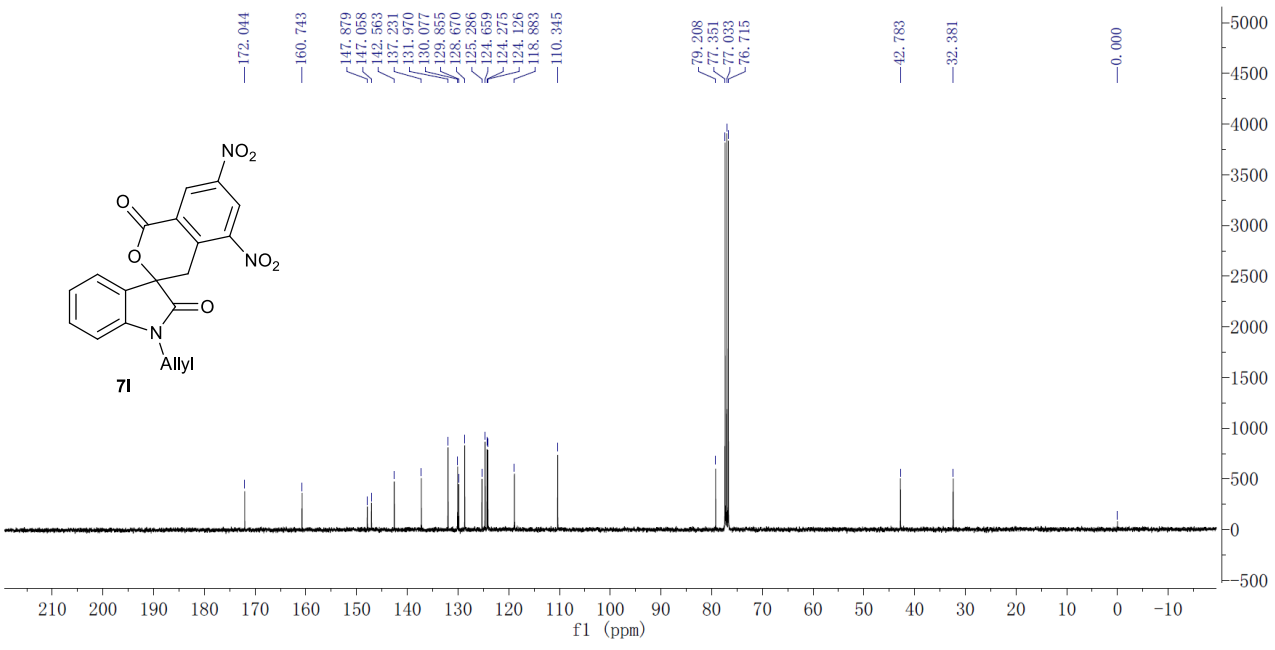

9.282
9.131
7.336
7.319
7.302
7.291
7.274
7.260
7.221
7.204
7.168
7.148
6.705
6.685
4.819
4.780
4.747
4.708
4.030
3.982
3.809
3.761
2.356
1.580
0.000
0.53
0.54
6.68
1.00
2.09
1.04
1.04
3.01
f1 (ppm)
NO2
NO2
O
O
Me
O
N
Bn
7j

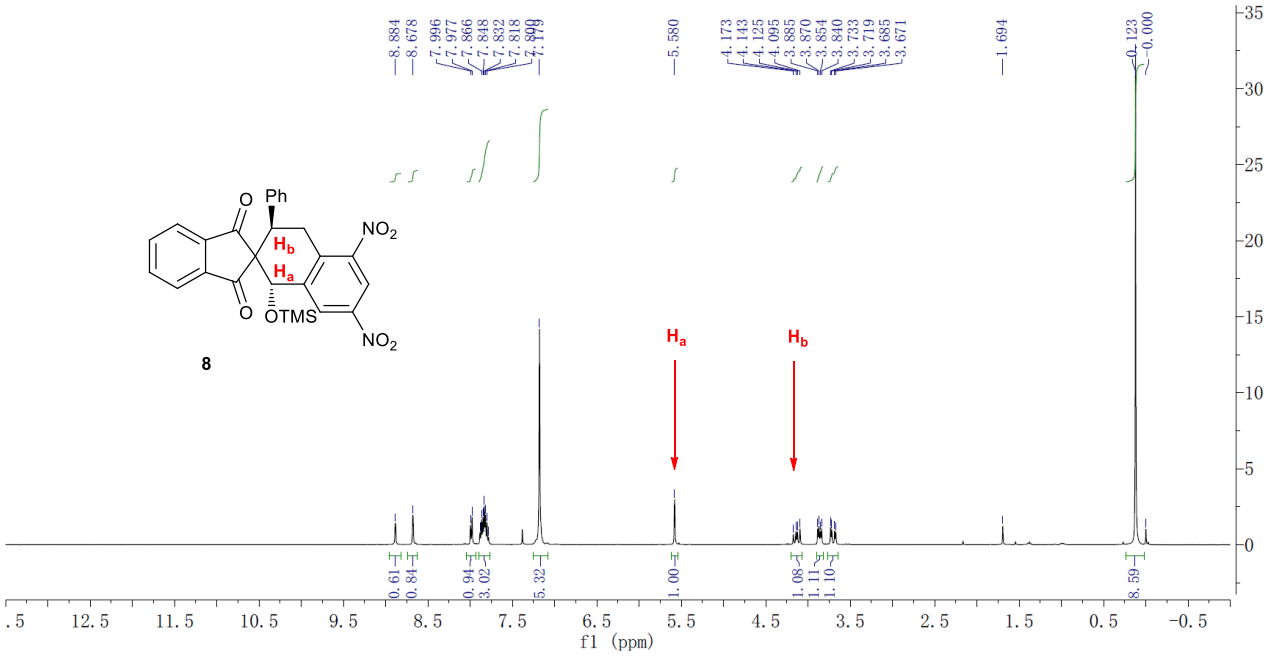

169.515
157.916
137.085
131.474
131.197
129.293
126.965
126.144
125.769
125.226
124.324
122.469
122.372
107.365
76.563
74.346
74.135
73.923
41.298
29.546
18.165
0.000
f1 (ppm)
NO2
NO2
O
O
Me
O
N
Bn
7j

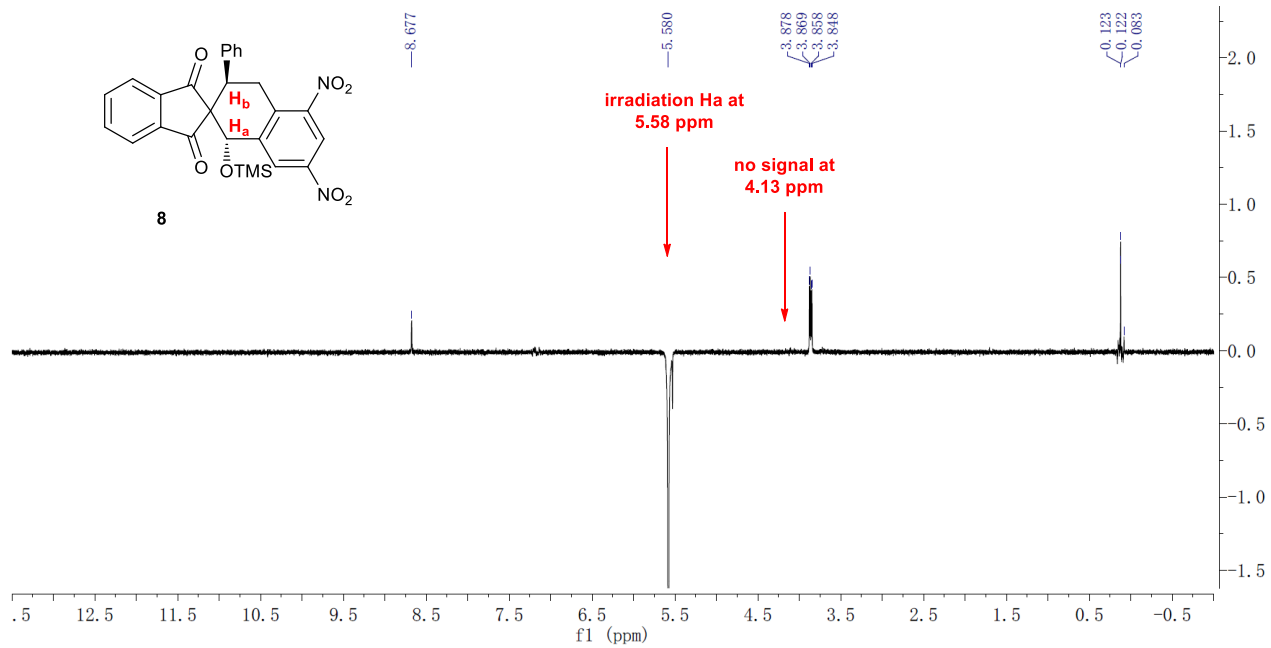

9.278
9.127
7.517
7.496
7.477
7.264
7.249
7.230
7.211
6.947
6.927
4.016
3.969
3.774
3.727
3.149
1.590
0.000
0.53
0.51
1.82
0.82
0.89
1.00
1.00
2.84
f1 (ppm)
7k

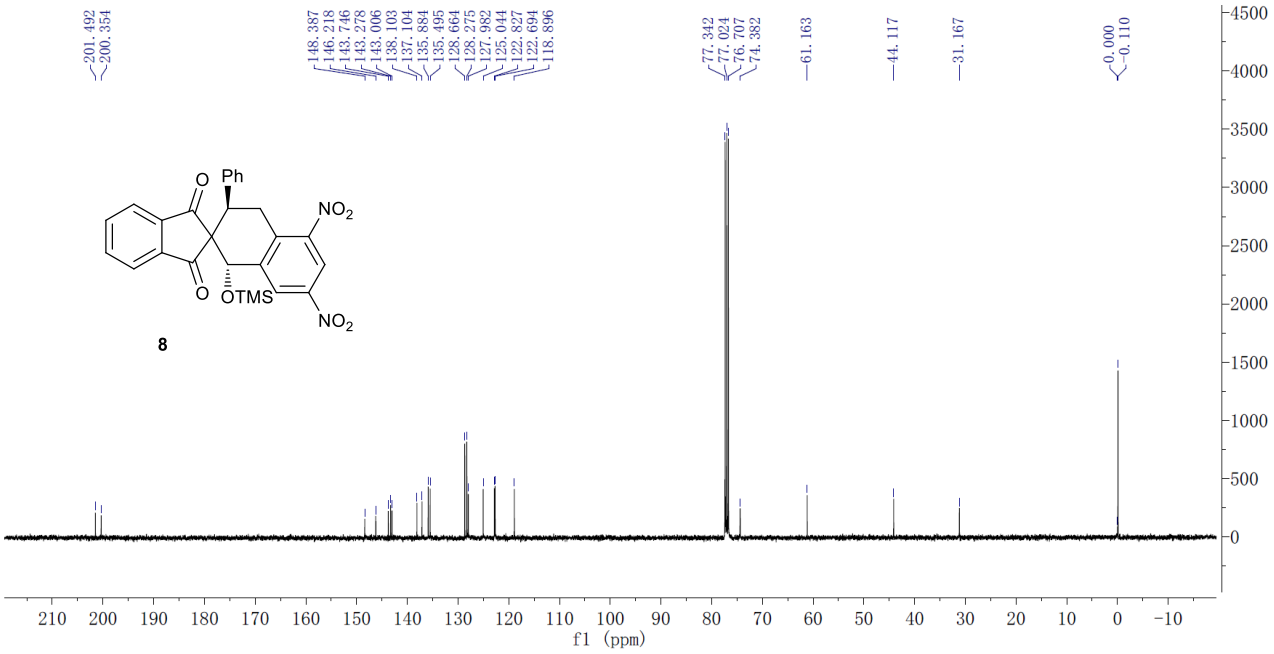

172.257
160.763
147.883
147.066
143.328
137.237
132.075
129.880
128.671
125.293
124.586
124.237
124.175
109.436
79.260
77.346
77.029
76.711
32.320
26.544
0.000
f1 (ppm)
7k

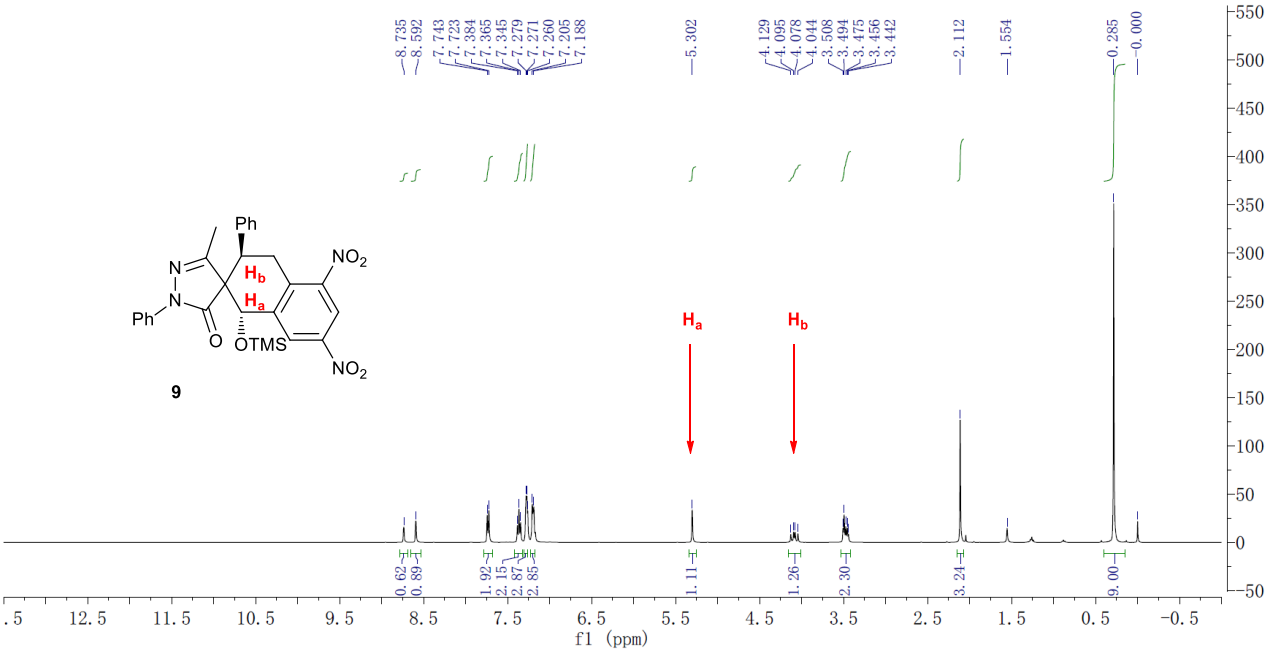

9.235
9.107
7.494
7.476
7.456
7.437
7.268
7.233
7.214
7.195
6.947
6.927
5.783
5.768
5.754
5.241
5.242
5.249
5.227
4.225
4.212
4.032
3.985
3.783
3.735
1.626
0.000
0.54
0.53
1.83
0.95
0.91
0.84
1.97
2.02
1.00
0.98
f1 (ppm)
NO2
NO2
O
O
O
N
Allyl
7l

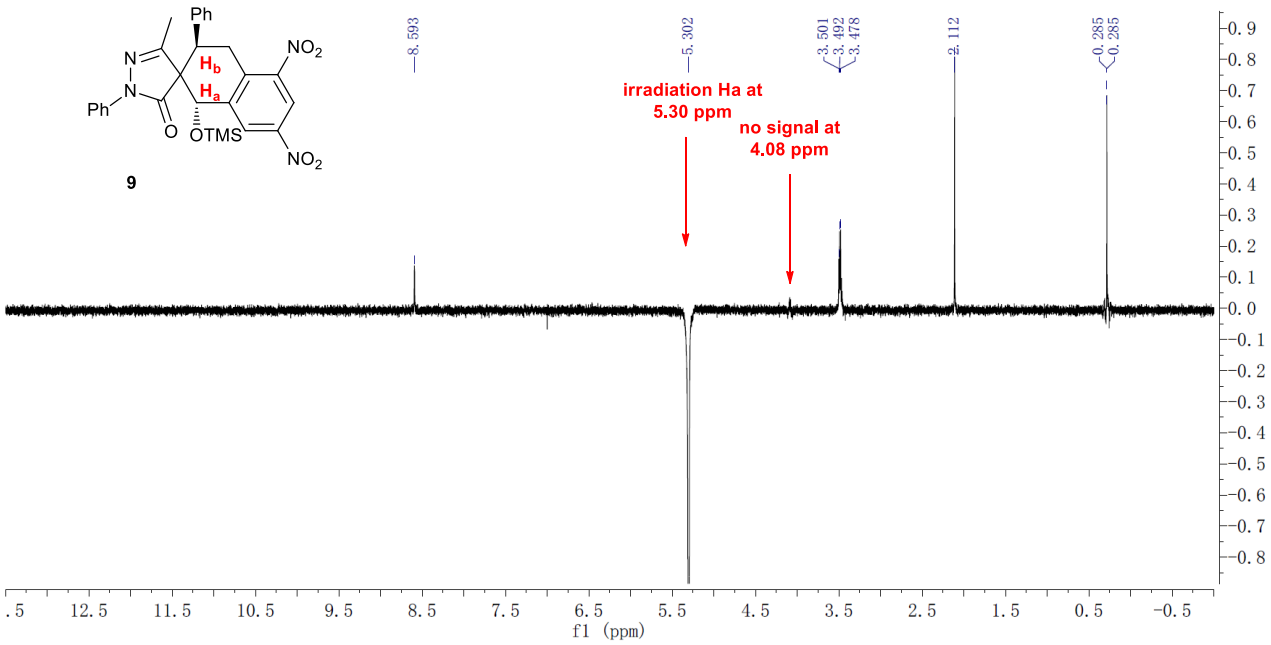

172.044
160.743
147.879
147.058
142.563
137.231
131.970
130.077
129.855
128.670
125.286
124.659
124.275
124.126
118.883
110.345
79.208
77.351
77.033
76.715
42.783
32.381
0.000
f1 (ppm)
NO2
NO2
O
O
O
N
Allyl
7l

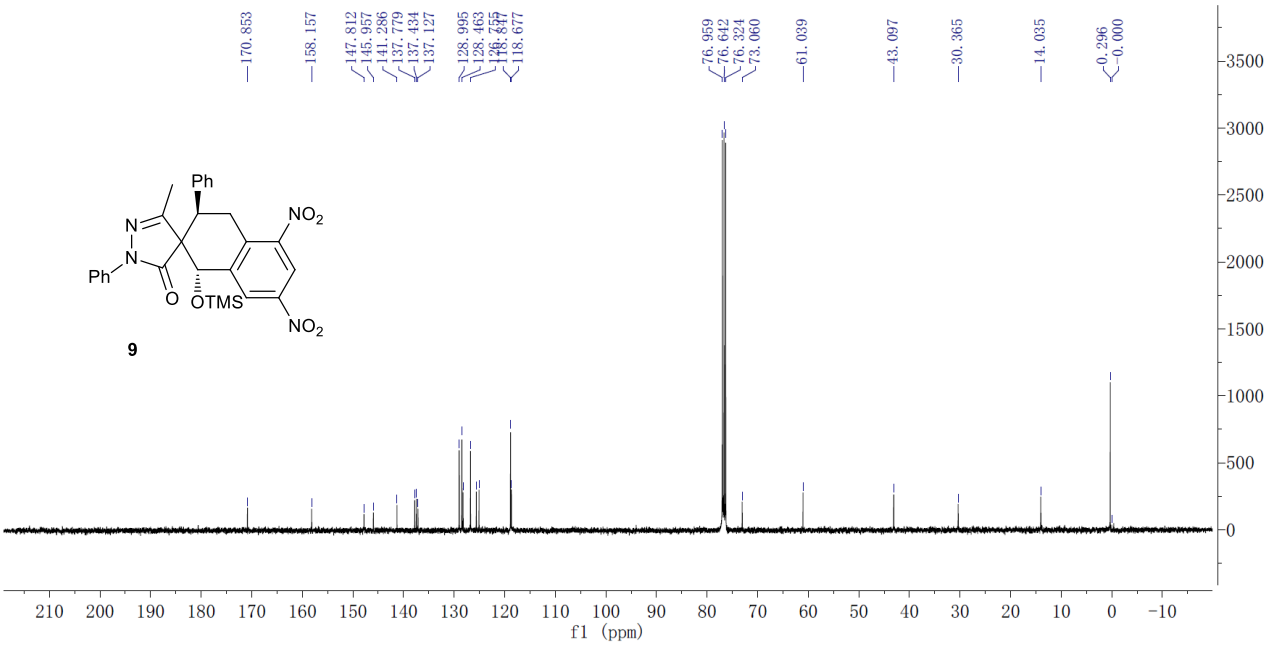

8.884
8.678
7.996
7.977
7.866
7.848
7.832
7.818
5.580
4.173
4.143
4.125
4.095
3.885
3.870
3.854
3.840
3.733
3.719
3.685
3.671
1.694
0.123
0.000
Ph
O
O
Hb
Ha
OTMS
NO2
NO2
8
Ha
Hb
0.61
0.84
0.94
3.02
5.32
1.00
1.08
1.11
1.10
8.59
f1 (ppm)

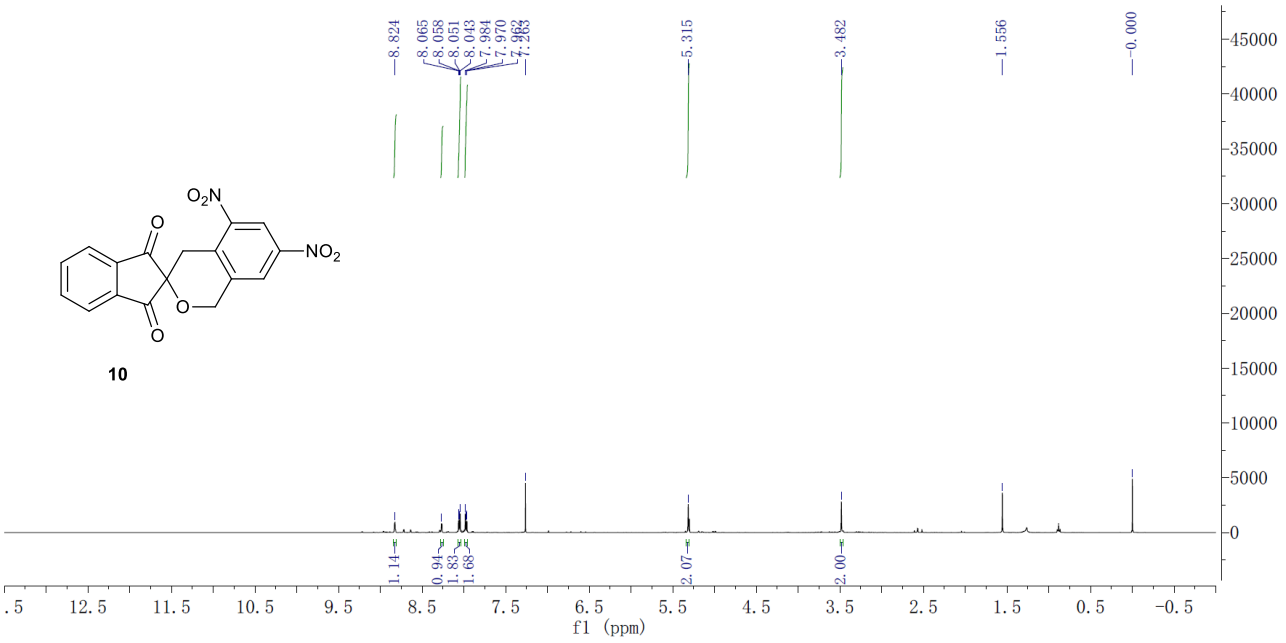

8.677
5.580
3.878
3.869
3.858
3.848
0.123
0.122
0.083
Ph
O
O
Hb
Ha
OTMS
NO2
NO2
8
irradiation Ha at
5.58 ppm
no signal at
4.13 ppm
f1 (ppm)


201.492
200.354
148.387
146.218
143.746
143.278
143.006
138.103
137.104
135.884
135.495
128.664
128.275
127.982
125.044
122.827
122.694
118.896
77.342
77.024
76.707
74.382
61.163
44.117
31.167
0.000
-0.110
Ph
O
O
OTMS
NO2
NO2
8
f1 (ppm)

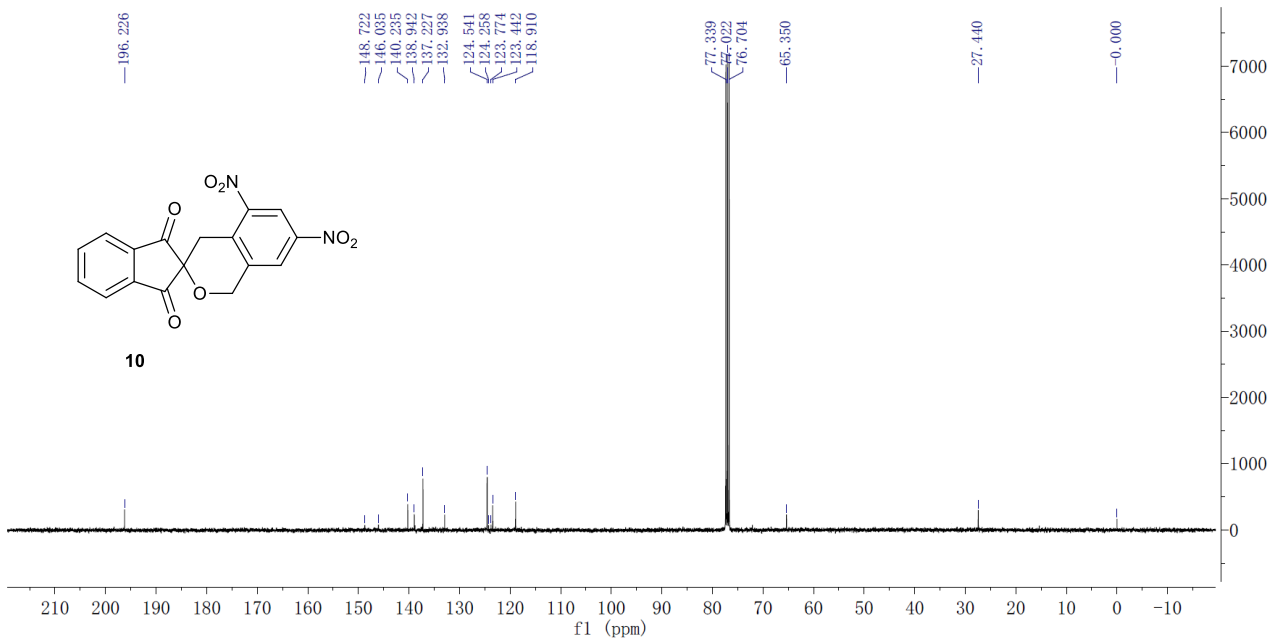

8.735
8.592
7.743
7.723
7.384
7.365
7.345
7.279
7.271
7.260
7.205
7.188
5.302
4.129
4.095
4.078
4.044
3.508
3.494
3.475
3.456
3.442
2.112
1.554
0.285
0.000
Ph
N
N
Ph
O
Hb
Ha
OTMS
NO2
NO2
9
Ha
Hb
0.62
0.89
1.92
2.15
2.87
2.85
1.11
1.26
2.30
3.24
9.00
f1 (ppm)


Ph
N
N
Ph
O
OTMS
H_b
H_a
NO_2
NO_2
9
irradiation Ha at
5.30 ppm
no signal at
4.08 ppm
8.593
5.302
3.501
3.492
3.478
2.112
0.285
0.285
f1 (ppm)

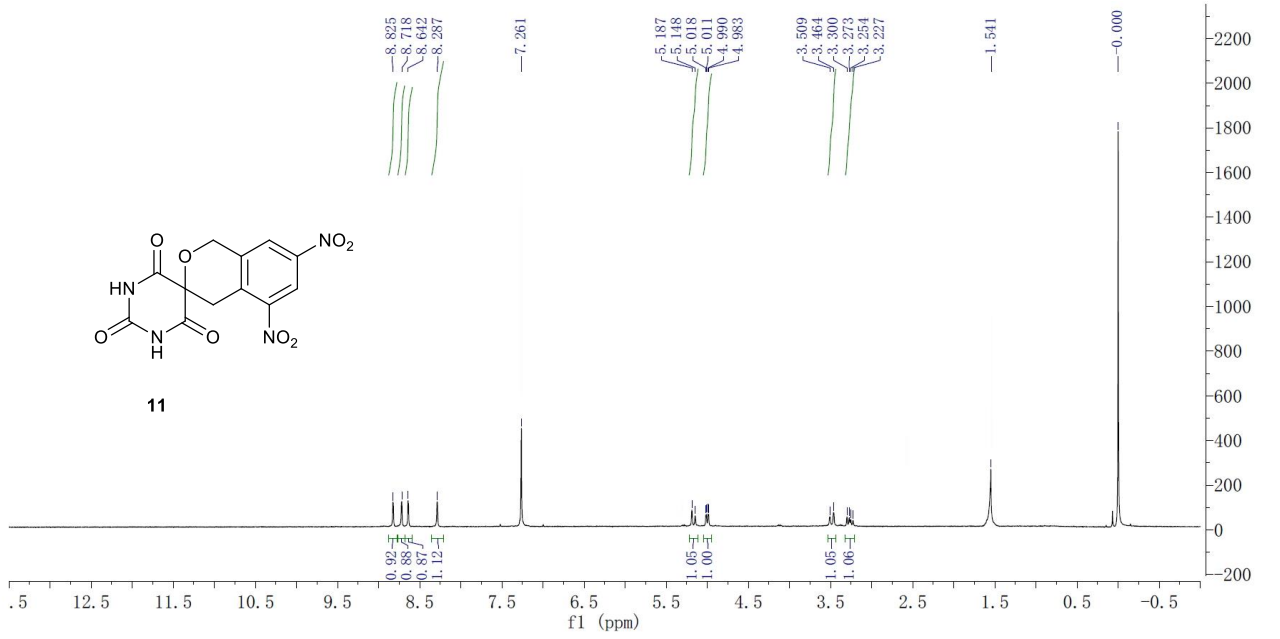

170.853
158.157
147.812
145.957
141.286
137.779
137.434
137.127
128.995
128.463
118.677
76.959
76.642
76.324
73.060
61.039
43.097
30.365
14.035
0.296
0.000
Ph
N
N
Ph
O
OTMS
NO_2
NO_2
9
f1 (ppm)


8.824
8.065
8.058
8.051
8.043
7.984
7.970
5.315
3.482
1.556
-0.000
1.14
0.94
1.83
1.68
2.07
2.00
f1 (ppm)

10

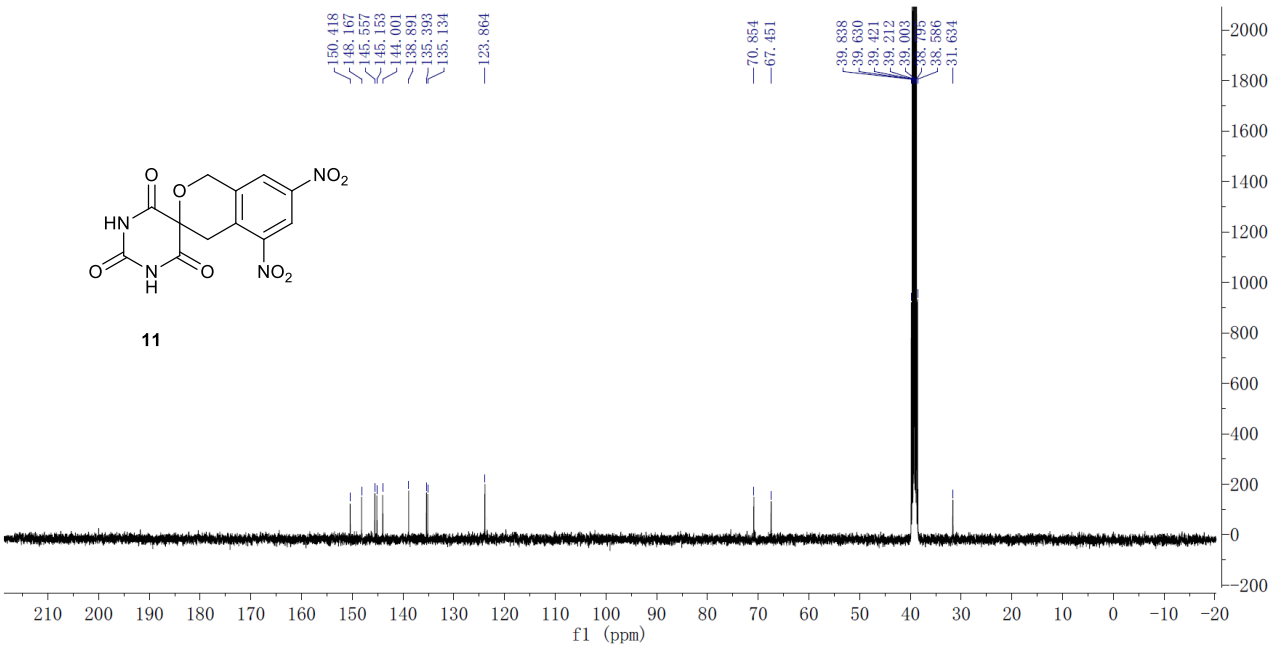

196.226
148.722
146.035
140.235
138.942
137.227
132.938
124.541
124.258
123.774
123.442
118.910
77.339
77.022
76.704
65.350
27.440
-0.000
f1 (ppm)

10


8.825
8.718
8.642
8.287
7.261
5.187
5.148
5.018
5.011
4.990
4.983
3.509
3.464
3.300
3.273
3.254
3.227
1.541
0.000
0.92
0.88
0.87
1.12
1.05
1.00
1.05
1.06
f1 (ppm)

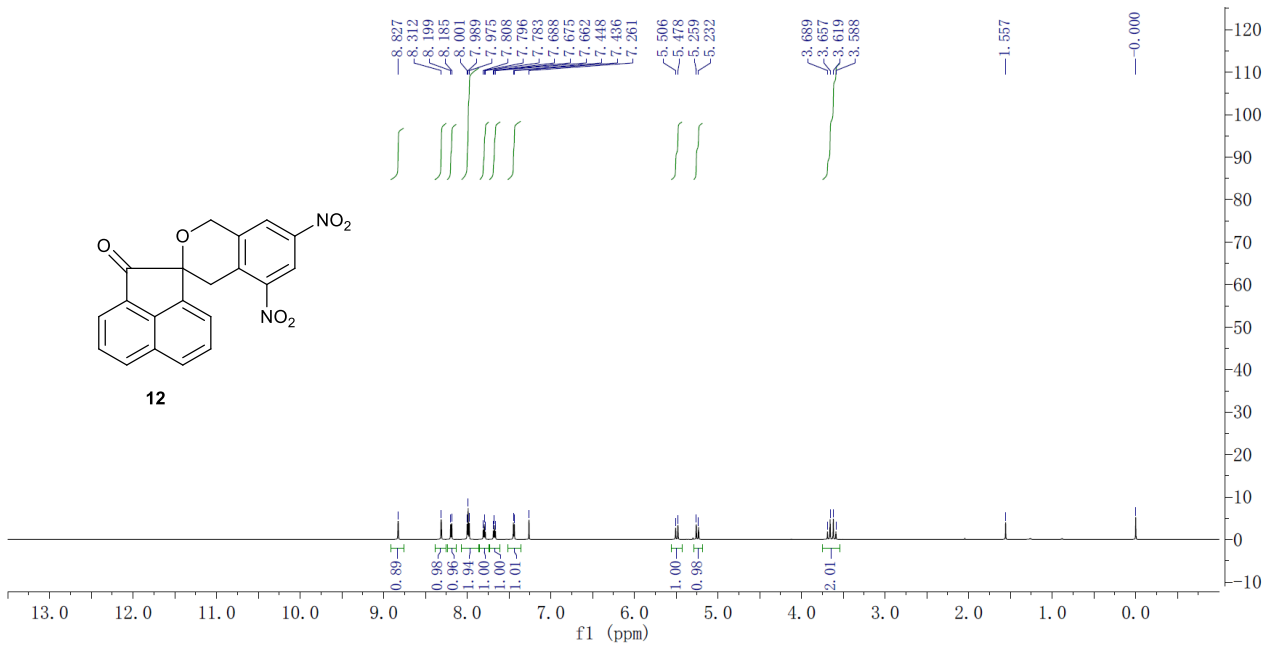
O
O
HN
O
N
H
O
O
NO2
NO2

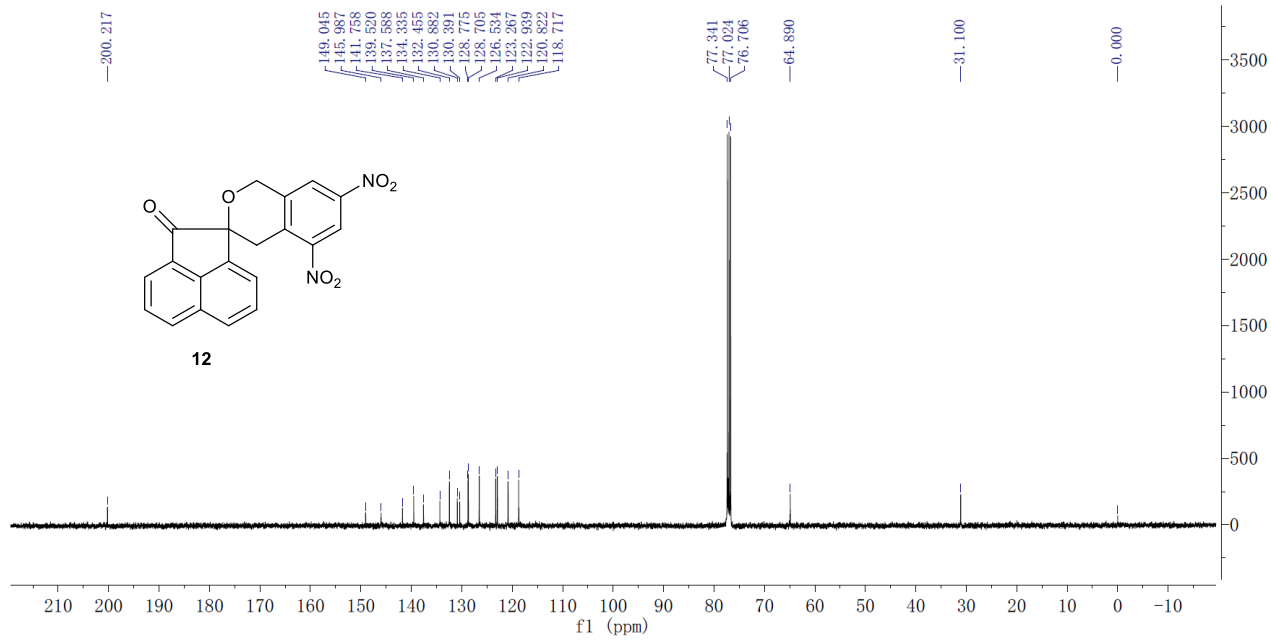
11


150.418
148.167
145.557
145.153
144.001
138.891
135.393
135.134
123.864
70.854
67.451
39.838
39.630
39.421
39.212
39.003
38.795
38.586
31.634
f1 (ppm)

O
O
HN
O
N
H
O
O
NO2
NO2

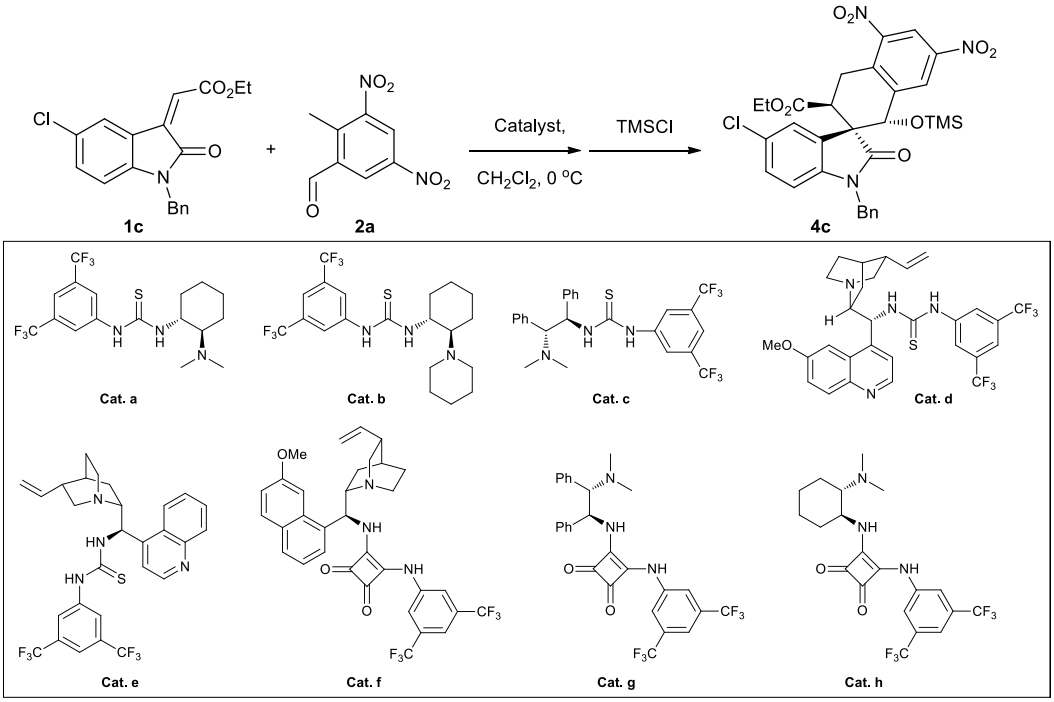
11


8.827
8.312
8.199
8.185
8.001
7.989
7.975
7.808
7.796
7.783
7.688
7.675
7.662
7.448
7.436
7.261
5.506
5.478
5.259
5.232
3.689
3.657
3.619
3.588
1.557
0.000
O
O
NO2
NO2
12
0.89
0.98
0.96
1.94
1.00
1.00
1.01
1.00
0.98
2.01
f1 (ppm)


200.217
149.045
145.987
141.758
139.520
137.588
134.335
132.455
130.882
130.391
128.775
128.705
126.534
123.267
122.939
120.822
118.717
77.341
77.024
76.706
64.890
31.100
0.000
O
O
NO2
NO2
12
f1 (ppm)

7. The preliminary investigation on the asymmetric versions of these tandem reactions

Table S1. Screening the optimal bifunctional organocatalyst for the asymmetric synthesis of chiral tetrahydronaphthalene-fused spirooxindoles[a]

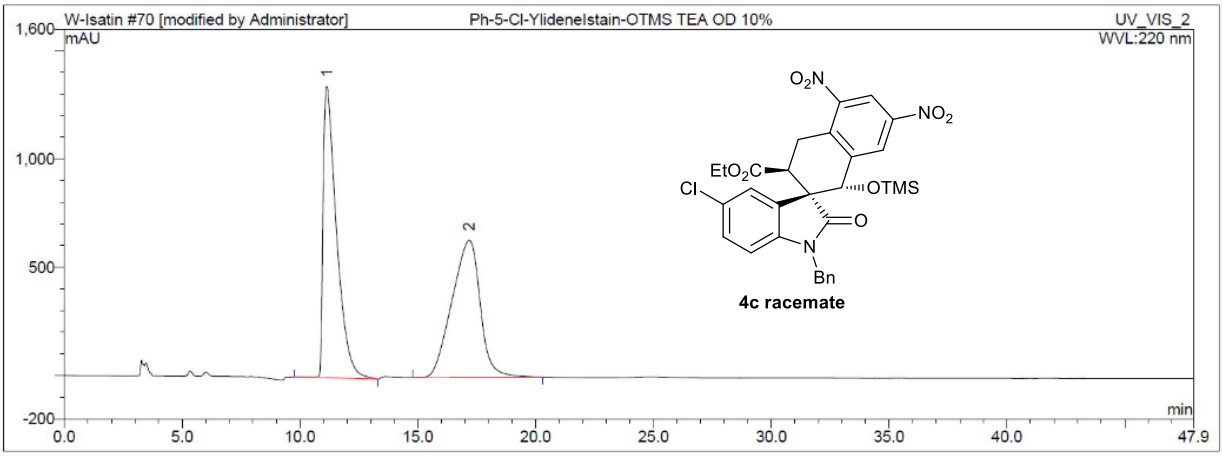


Entry	Catalyst	Time (h)	Yield (%)[b]	dr[c]	ee[d]
1	**a**	48	49	90:10	94
2	**b**	48	31	92:8	92
3	**c**	48	40	85:15	50
4	**d**	72	30	80:20	30
5	**e**	72	25	82:18	38
6	**f**	72	35	90:10	-46
7	**g**	48	43	88:12	-60
8	**h**	48	47	90:10	-85

[a] Unless noted otherwise, reactions were performed with **1c** (0.15 mmol), **2a** (0.3 mmol), catalyst (10 mol%) and 4Å MS (40 mg) in dichloromethane (0.5 mL) at 0 °C for the time shown in the Table. [b] Yield of isolated **4c**. [c] Calculated based on ^{1}HNMR analysis of the crude reaction mixture. [d] Determined by HPLC analysis on chiral column (Chiralpak OD-H column, hexane/2-propanol = 90/10, 1.0 mL/min, t_{major} = 11.14 min, t_{minor} = 17.12 min).

Peak Analysis Report

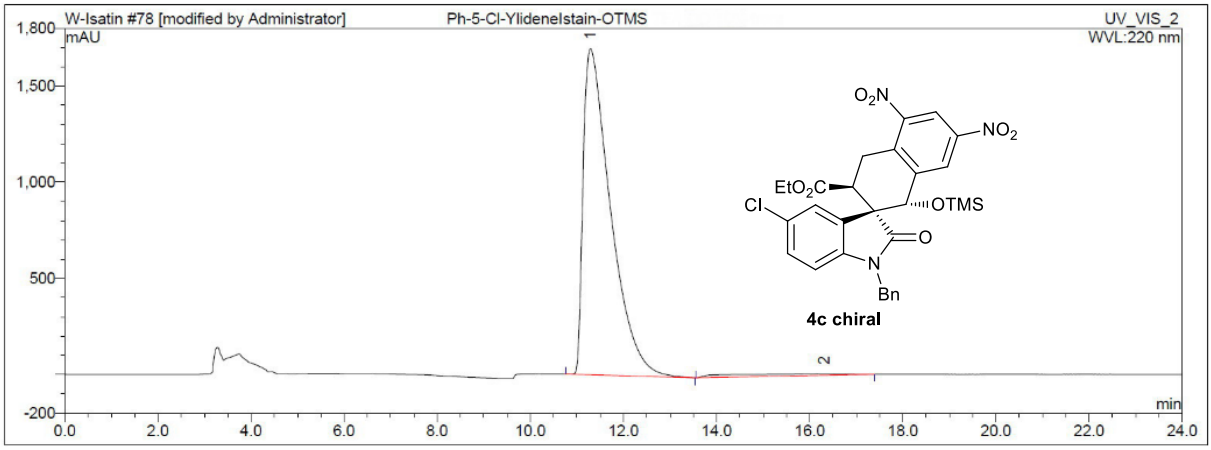
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	11.14	886.597	50.28	1345.902	n.a.
2	n.a.	17.18	876.726	49.72	633.108	n.a.



4c racemate

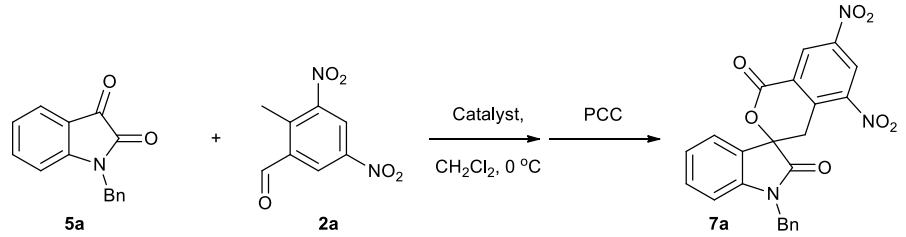
Peak Analysis Report

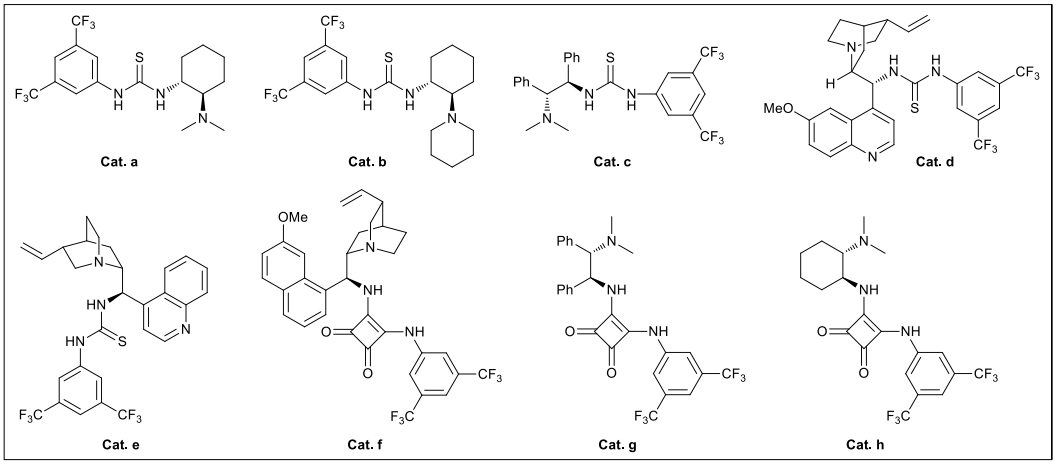
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	11.14	1154.785	97.22	1695.984	n.a.
2	n.a.	17.12	33.058	2.78	8.979	n.a.



4c chiral

Table S2. Screening the optimal bifunctional organocatalyst for the asymmetric synthesis of chiral isochroman-fused spirooxindoles



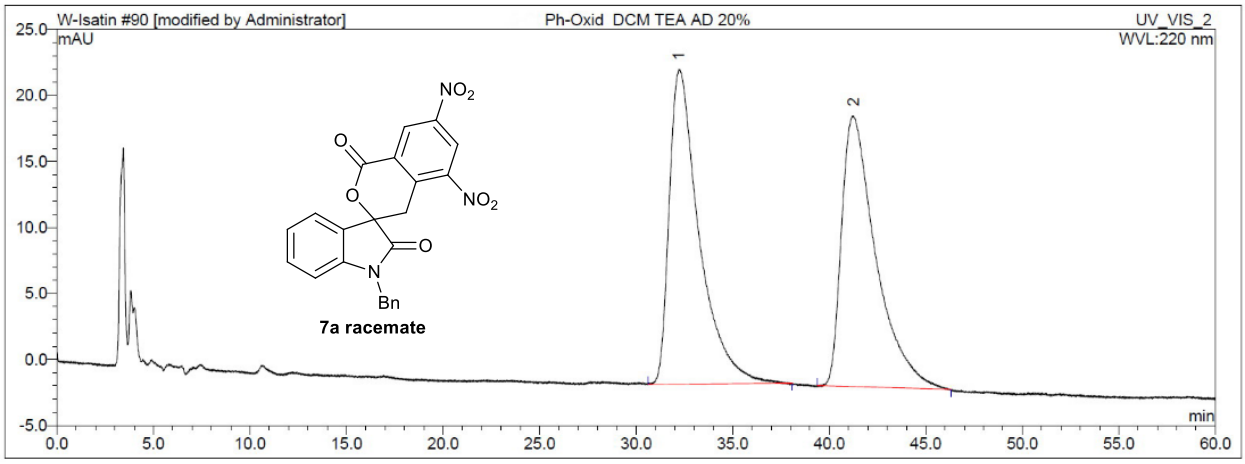


Entry	Catalyst	Time (h)	Yield (%)[b]	ee[c]
1	**a**	72	30	-30
2	**b**	72	25	-40
3	**c**	72	33	24
4	**d**	48	40	-80
5	**e**	48	35	-55
6	**f**	48	47	97
7	**g**	48	40	60
8	**h**	48	51	72

[a] Unless noted otherwise, reactions were performed with **5a** (0.15 mmol), **2a** (0.3 mmol), catalyst (10 mol%) and 4Å MS (40 mg) in dichloromethane (0.5 mL) at 0 °C for the time shown in the Table. [b] Yield of isolated **4c**. [c] Determined by HPLC analysis on chiral column (Chiralpak AD-H column, hexane/2-propanol = 80/20, 1.0 mL/min, t_{minor} = 32.04 min, t_{major} = 40.88 min).

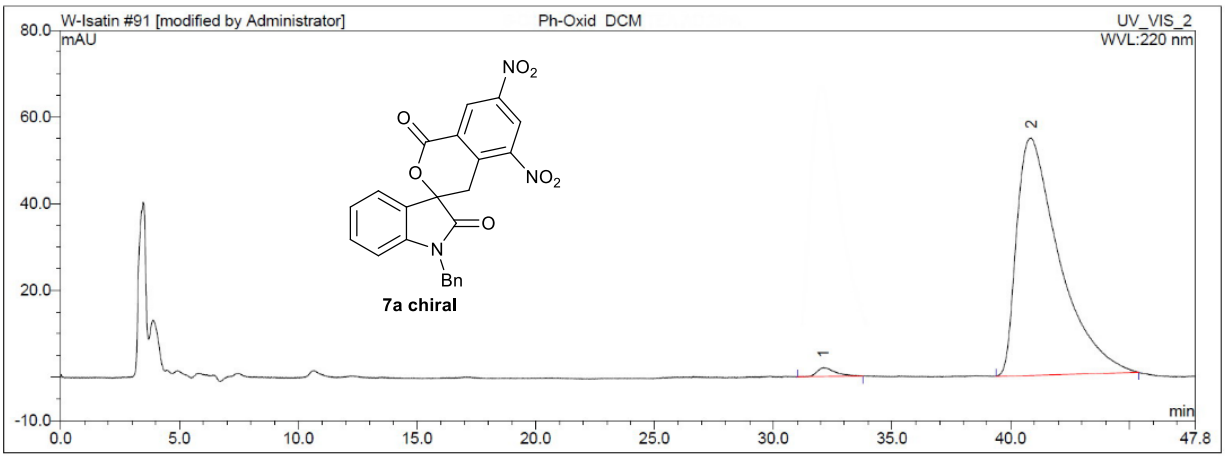
Peak Analysis Report

No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	32.21	42.812	50.39	23.849	n.a.
2	n.a.	41.27	42.149	49.61	20.526	n.a.



Peak Analysis Report

No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	32.04	1.874	1.62	2.093	n.a.
2	n.a.	40.88	113.996	98.38	54.787	n.a.



In the preliminary screening studies (Table S1 and S2), we examined a number of chiral bifunctional tertiary amine-hydrogen-bond donor catalysts (Cat. **a**-**h**). This led to the identification of thiourea-based bifunctional organocatalyst **a** as the optimal catalyst for the synthesis of chiral tetrahydronaphthalene-fused spirooxindole with high stereoselectivity and in moderate yields (Table S1, entry 1). Meanwhile, the squaramide-cinchona bifunctional catalyst **f** could provide chiral isochroman-fused spirooxindole with high enantioselectivity (Table S2, entry 6).