[*Supporting Information***]**

"On water" directly catalytic vinylogous Henry (nitroaldol) reactions of isatins for the efficient synthesis of isoxazole substituted 3-hydroxyindolin-2-ones

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1. General information

General methods

NMR spectra were recorded on a liquid NMR spectrometer (400 MHz for ^{1}H and 100 MHz for ^{13}C) using DMSO as the solvent. The residual proton in DMSO (δ = 2.51) served as an internal standard for ^{1}H NMR, and the ^{13}C-atom of DMSO was used as an internal standard (δ = 39.5 for ^{13}C NMR. Chemical shifts are reported in ppm and the coupling constants *J* are given in Hz. The following abbreviations were used to explain the multiplicities: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet). Infrared spectra were recorded on an FT-IR spectrometer, and only major peaks were reported in cm^{-1}. HRMS data were obtained by the ESI ionization sources.

Materials

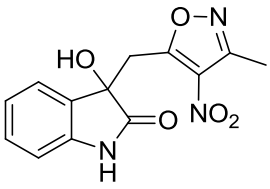
3,5-dimethyl-4-nitroisoxazole and isatins were commercially available. 3,5-diethyl-4-nitroisoxazole was prepared according to the literature procedures.[1]Unless otherwise noted, analytical grade solvents and commercially available reagents were used without further purification.

1. M. F. A. Adamo, S. Suresh, L. Piras, *Tetrahedron* **2009**, *65*, 5402.

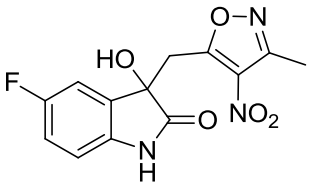
2. Experimental section

2.1 Representative procedure for "On water" direct vinylogous Henry (nitroaldol) additions of 3,5-dimethyl-4-nitroisoxazole with isatins

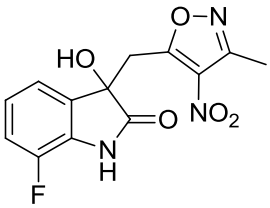
The mixture of 3,5-dimethyl-4-nitroisoxazole **2** (31.3 mg, 0.22 mmol), isatin **1a** (0.20 mmol) and catalyst (5 mol%, 0.01 mmol) in 0.5 mL H_2O were stirred at room temperature for the indicated time. After the reaction was completed (indicated by color change from red to white), the solid product was filtered, washed by water and then dried under vacuum to afford the product **3a** in high yield and purity.



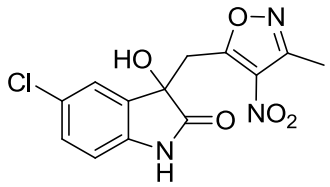
3-hydroxy-3-((3-methyl-4-nitroisoxazol-5-yl)methyl)indolin-2-one (3a): white solid; 57.3 mg, >99% yield; m.p. decomposed at 80 ^{o}C; **^{1}H NMR** (400 MHz, DMSO) δ (ppm) 10.45 (s, 1H), 7.23-7.18 (m, 2H), 6.95-6.81 (m, 2H), 6.49 (s, 1H), 3.78 (d, J = 14.1 Hz, 1H), 3.62 (d, J = 14.1 Hz, 1H), 2.44 (s, 3H); **^{13}C NMR** (100 MHz, DMSO) δ (ppm) 177.1, 169.5, 155.0, 141.3, 130.9, 130.4, 129.7, 123.9, 121.7, 109.8, 74.1, 34.7, 11.1. IR (KBr): v 3344 3245 1710 1619 1523 1471 1370 1183 1151 950 828 cm^{-1}; HRMS (ESI) calcd for $C_{13}H_{11}N_3O_5$+Na 312.0591, found 312.0584.



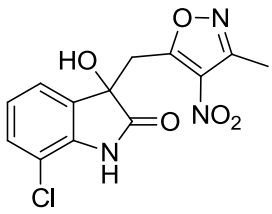
5-fluoro-3-hydroxy-3-((3-methyl-4-nitroisoxazol-5-yl)methyl)indolin-2-one (3b): pink solid; 59.6 mg, 97% yield; m.p. decomposed at 104.7 ^{o}C; **^{1}H NMR** (400 MHz, DMSO) δ (ppm) 10.49 (s, 1H), 7.12-7.05 (m, 2H), 6.83-6.81 (m, 1H), 6.65 (s, 1H), 3.78 (d, J = 14.5 Hz, 1H), 3.66 (d, J = 14.5 Hz, 1H), 2.44 (s, 3H); **^{13}C NMR** (100 MHz, DMSO) δ (ppm) 177.1, 169.2, 158.0 (d, $^{1}J_{CF}$ = 238 Hz), 155.2, 137.5, 132.2 (d, $^{3}J_{CF}$ = 7 Hz), 131.0, 116.5 (d, $^{2}J_{CF}$ = 23 Hz), 111.9 (d, $^{2}J_{CF}$ = 24 Hz), 110.8 (d, $^{3}J_{CF}$ = 8 Hz), 74.4, 34.6, 11.1. IR (KBr): v 3421 3245 3209 1719 1613 1522 1486 1416 1376 1270 1186 1139 1072 813 cm^{-1}; HRMS (ESI) calcd for $C_{13}H_{10}FN_3O_5$+Na 330.0497, found 330.0489.



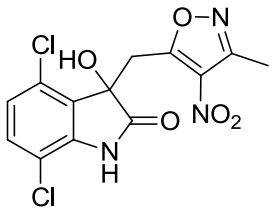
7-fluoro-3-hydroxy-3-((3-methyl-4-nitroisoxazol-5-yl)methyl)indolin-2-one (3c): pale yellow solid; 60.2 mg, 98% yield; m.p. decomposed at 110.1 ^{o}C; **^{1}H NMR** (400 MHz, DMSO) δ (ppm) 11.00 (s, 1H), 7.19-7.15 (m, 1H), 7.07-6.96 (m, 2H), 6.64 (s, 1H), 3.80 (d, J = 14.5 Hz, 1H), 3.66 (d, J = 14.5 Hz, 1H), 2.45 (s, 3H); **^{13}C NMR** (100 MHz, DMSO) δ (ppm) 176.9, 169.2, 155.1, 146.3 (d, $^{1}J_{CF}$ = 243 Hz), 133.3 (d, $^{3}J_{CF}$ = 3.3 Hz), 131.0, 128.3 (d, $^{2}J_{CF}$ = 13 Hz), 122.8 (d,$^{3}J_{CF}$ = 6 Hz), 120.0, 116.7 (d, $^{2}J_{CF}$ = 17 Hz), 74.2, 34.6, 11.1. IR (KBr): v 3375 3208 1716 1643 1607 1516 1417 1371 1151 824 cm^{-1}; HRMS (ESI) calcd for $C_{13}H_{10}FN_3O_5$+Na 330.0497, found 330.0490.



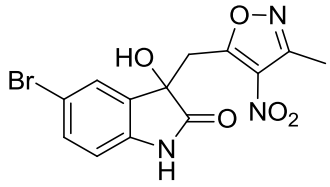
5-chloro-3-hydroxy-3-((3-methyl-4-nitroisoxazol-5-yl)methyl)indolin-2-one (3d): gray solid; 63.4 mg, 98% yield; m.p. decomposed at 99.2 °C; **^{1}H NMR** (400 MHz, DMSO) δ (ppm) 10.60 (s, 1H), 7.29 (s, 2H), 6.85 (s, 1H), 6.64 (s, 1H), 3.80 (d, J = 13.3 Hz, 1H), 3.68 (d, J = 13.1 Hz, 1H), 2.45 (s, 3H); **^{13}C NMR** (100 MHz, DMSO) δ (ppm) 176.7, 169.2, 155.1, 140.2, 132.5, 131.0, 129.5, 125.8, 124.3, 111.4, 74.1, 34.5, 11.1. IR (KBr): v 3399 3212 1714 1613 1518 1301 1214 1176 829 cm^{-1}; HRMS (ESI) calcd for $C_{13}H_{10}ClN_3O_5$+Na 346.0201, found 346.0195.



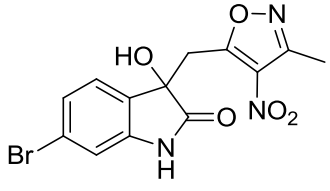
7-chloro-3-hydroxy-3-((3-methyl-4-nitroisoxazol-5-yl)methyl)indolin-2-one (3e): white solid; 63.4 mg, 98% yield; m.p. decomposed at 136.4 °C; **^{1}H NMR** (400 MHz, DMSO) δ (ppm) 10.94 (s, 1H), 7.32 (d, J = 8.1 Hz, 1H), 7.18 (d, J = 7.2 Hz, 1H), 7.00 (t, J = 7.7 Hz, 1H), 6.65 (s, 1H), 3.79 (d, J = 14.5 Hz, 1H), 3.67 (d, J = 14.5 Hz, 1H), 2.45 (s, 3H); **^{13}C NMR** (100 MHz, DMSO) δ (ppm) 177.0, 169.1, 155.1, 139.0, 132.3, 131.0, 129.6, 123.2, 122.6, 114.1, 74.6, 34.5, 11.0. IR (KBr): v 3428 3348 1731 1612 1522 1464 1370 1163 828 cm^{-1}; HRMS (ESI) calcd for $C_{13}H_{10}ClN_3O_5$+Na 346.0201, found 346.0195.



4,7-dichloro-3-hydroxy-3-((3-methyl-4-nitroisoxazol-5-yl)methyl)indolin-2-one (3f): gray solid; 70.6 mg, 99% yield; m.p. decomposed at 112.2 °C; **^{1}H NMR** (400 MHz, DMSO) δ (ppm) 11.17 (s, 1H), 7.37 (d, J = 8.7 Hz, 1H), 7.03 (d, J = 8.7 Hz, 1H), 6.78 (s, 1H), 3.98 (d, J = 14.9 Hz, 1H), 3.92 (d, J = 14.9 Hz, 1H), 2.43 (s, 3H); **^{13}C NMR** (100 MHz, DMSO) δ (ppm) 176.9, 169.0, 155.6, 141.6, 131.7, 131.4, 129.6, 128.3, 124.4, 113.7, 75.9, 32.8, 11.5. IR (KBr): v 3371 3261 1755 1612 1524 1469 1422 1372 1298 1160 1102 828 cm^{-1}; HRMS (ESI) calcd for $C_{13}H_9Cl_2N_3O_5$+Na 379.9811, found 379.9806.

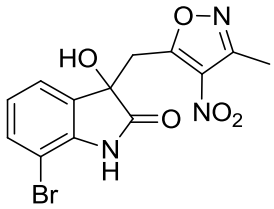


5-bromo-3-hydroxy-3-((3-methyl-4-nitroisoxazol-5-yl)methyl)indolin-2-one (3g): pale yellow solid; 72.1 mg, 98% yield; m.p. decomposed at 119.0 °C; **^{1}H NMR** (400 MHz, DMSO) δ (ppm) 10.61 (s, 1H), 7.40 (s, 2H), 6.80 (d, J = 6.5 Hz, 1H), 6.64 (s, 1H), 3.79 (d, J = 14.1 Hz, 1H), 3.68 (d, J = 14.0 Hz, 1H), 2.45 (s, 3H); **^{13}C NMR** (100 MHz, DMSO) δ (ppm) 176.5, 169.1, 155.1, 140.6, 132.8, 132.3, 131.0, 127.0, 113.4, 111.9, 74.1, 34.5, 11.0. IR (KBr): v 3387 3190 1724 1613 1519 1372 1221 1176 1076 826 cm^{-1}; HRMS (ESI) calcd for $C_{13}H_{10}BrN_3O_5$+Na 389.9696, found 389.9689.

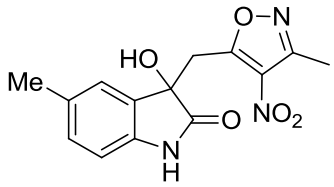


6-bromo-3-hydroxy-3-((3-methyl-4-nitroisoxazol-5-yl)methyl)indolin-2-one (3h): gray solid; 71.4 mg, 97% yield; m.p. decomposed at 169.7 °C; **^{1}H NMR** (400 MHz,

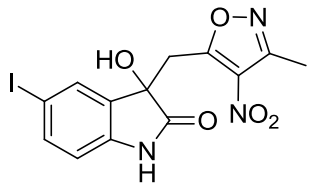
DMSO) δ (ppm) 10.62 (s, 1H), 7.18-7.13 (m, 2H), 6.98 (s, 1H), 6.59 (s, 1H), 3.78 (d, J = 14.5 Hz, 1H), 3.64 (d, J = 14.5 Hz, 1H), 2.45 (s, 3H); **^{13}C NMR** (100 MHz, DMSO) δ (ppm) 176.9, 169.2, 155.1, 143.0, 131.0, 129.7, 125.9, 124.5, 122.3, 112.7, 73.8, 34.4, 11.1. IR (KBr): v 3344 1721 1610 1519 1449 1371 1214 1144 1061 826 cm^{-1}; HRMS (ESI) calcd for $C_{13}H_{10}BrN_3O_5$+Na 389.9696, found 389.9689.



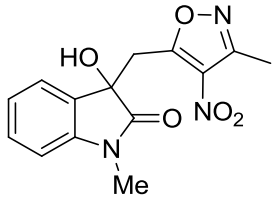
7-bromo-3-hydroxy-3-((3-methyl-4-nitroisoxazol-5-yl)methyl)indolin-2-one (3i): gray solid; 69.9 mg, 95% yield; m.p. decomposed at 149.1 ^{o}C; **^{1}H NMR** (400 MHz, DMSO) δ (ppm) 10.80 (s, 1H), 7.45 (d, J = 6.3 Hz, 1H), 7.21 (s, 1H), 6.94 (s, 1H), 3.78 (d, J = 13.8 Hz, 1H), 3.67 (d, J = 14.2 Hz, 1H), 2.46 (s, 3H); **^{13}C NMR** (100 MHz, DMSO) δ (ppm) 176.9, 169.2, 155.1, 140.7, 132.5, 132.4, 131.0, 123.6, 123.0, 102.2, 74.8, 34.6, 11.1. IR (KBr): v 3365 3266 1730 1611 1522 1462 1418 1371 1207 1162 829 cm^{-1}; HRMS (ESI) calcd for $C_{13}H_{10}BrN_3O_5$+Na 389.9696, found 389.9688.



3-hydroxy-5-methyl-3-((3-methyl-4-nitroisoxazol-5-yl)methyl)indolin-2-one (3j): gray solid; 58.2 mg, 96% yield; m.p. decomposed at 114.2 ^{o}C; **^{1}H NMR** (400 MHz, DMSO) δ (ppm) 10.35 (s, 1H), 7.04-7.01 (m, 2H), 6.70 (d, J = 7.8 Hz, 1H), 6.45 (s, 1H), 3.74 (d, J = 14.4 Hz, 1H), 3.61 (d, J = 14.4 Hz, 1H), 2.22 (s, 3H); **^{13}C NMR** (100 MHz, DMSO) δ (ppm) 177.1, 169.5, 155.0, 138.8, 131.0, 130.6, 130.5, 129.8, 124.5, 109.6, 74.2, 34.8, 20.6, 11.1. IR (KBr): v 3400 1711 1613 1520 1420 1370 1125 817 cm^{-1}; HRMS (ESI) calcd for $C_{14}H_{13}N_3O_5$+Na 326.0747, found 326.0740.

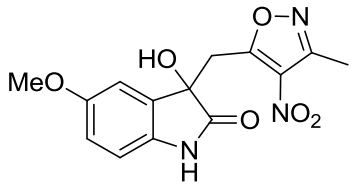


3-hydroxy-5-iodo-3-((3-methyl-4-nitroisoxazol-5-yl)methyl)indolin-2-one (3k): pink solid; 78.0 mg, 94% yield; m.p. decomposed at 128.1 ^{o}C; **^{1}H NMR** (400 MHz, DMSO) δ (ppm) 10.58 (s, 1H), 7.58 (dd, J = 8.1, 1.6 Hz, 1H), 7.51 (d, J = 1.3 Hz, 1H), 6.68 (d, J = 8.1 Hz, 1H), 6.60 (s, 1H), 3.77 (d, J = 14.6 Hz, 1H), 3.66 (d, J = 14.6 Hz, 1H), 2.45 (s, 3H); **^{13}C NMR** (100 MHz, DMSO) δ (ppm) 176.3, 169.2, 155.1, 141.1, 138.1, 133.0, 132.5, 131.0, 112.3, 84.5, 74.0, 34.5, 11.1. IR (KBr): v 3341 1710 1609 1518 1369 1280 1206 1165 1162 1026 820 cm^{-1}; HRMS (ESI) calcd for $C_{13}H_{10}IN_3O_5$+Na 437.9557, found 437.9547.

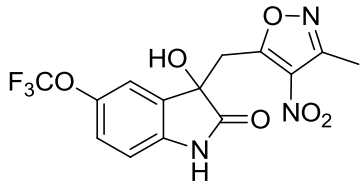


3-hydroxy-1-methyl-3-((3-methyl-4-nitroisoxazol-5-yl)methyl)indolin-2-one (3l): pale yellow solid; 58.2 mg, 96% yield; m.p. decomposed at 100.3 ^{o}C; **^{1}H NMR** (400 MHz, DMSO) δ (ppm) 7.34 (t, J = 7.7 Hz, 1H), 7.23 (d, J = 7.2 Hz, 1H), 7.06-7.01 (m, 2H), 6.57 (s, 1H), 3.78 (d, J = 14.4 Hz, 1H), 3.64 (d, J = 14.4 Hz, 1H), 3.10 (s, 3H), 2.44 (s, 3H); **^{13}C NMR** (100 MHz, DMSO) δ (ppm) 175.3, 169.4, 155.1, 142.7, 131.0, 129.8, 129.7, 123.5, 122.4, 108.8, 73.9, 34.9, 26.0, 11.1. IR (KBr): v 3365 1714 1610 1519 1470 1420 1377 1231 1149 830 cm^{-1};

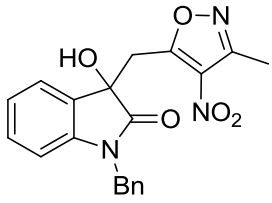
HRMS (ESI) calcd for $C_{14}H_{13}N_3O_5$+Na 326.0747, found 326.0742.



3-hydroxy-5-methoxy-3-((3-methyl-4-nitroisoxazol-5-yl)methyl)indolin-2-one (3m): gray solid; 61.9 mg, 97% yield; m.p. decomposed at 138.5 ^{o}C; **^{1}H NMR** (400 MHz, DMSO) δ (ppm) 10.27 (s, 1H), 6.83-6.72 (m, 3H), 6.52 (s, 1H), 3.77 (d, *J* = 14.2 Hz, 1H), 3.62 (d, *J* = 14.3 Hz, 1H), 3.68 (s, 3H), 2.43 (s, 3H); **^{13}C NMR** (100 MHz, DMSO) δ (ppm) 177.0, 169.5, 155.1, 154.9, 134.4, 131.5, 131.0, 114.7, 110.7, 110.4, 74.6, 55.5, 34.8, 11.1. IR (KBr): v 3341 1710 1609 1518 1369 1280 1206 1165 1026 827 cm^{-1}; HRMS (ESI) calcd for $C_{14}H_{13}N_3O_6$+Na 342.0697, found 342.0691.



3-hydroxy-3-((3-methyl-4-nitroisoxazol-5-yl)methyl)-5-(trifluoromethoxy)indolin-2-one (3n): yellow solid; 72.4 mg, 97% yield; m.p. decomposed at 117.9 ^{o}C; **^{1}H NMR** (400 MHz, DMSO) δ (ppm) 10.67 (s, 1H), 7.25 (d, *J* = 7.9 Hz, 1H), 7.18 (s, 1H), 6.91 (d, J = 8.4 Hz, 1H), 6.70 (s, 1H), 3.81 (d, *J* = 14.5 Hz, 1H), 3.68 (d, *J* = 14.5 Hz, 1H), 2.44 (s, 3H); **^{13}C NMR** (100 MHz, DMSO) δ (ppm) 177.1, 169.2, 155.1, 143.1, 140.5, 131.9, 131.0, 123.0, 117.8, 110.9, 74.3, 34.5, 11.1. IR (KBr): v 3325 1734 1610 1522 1420 1374 1272 1160 899 830 cm^{-1}; HRMS (ESI) calcd for $C_{14}H_{10}FN_3O_6$+Na 396.0414, found 396.0406.



1-benzyl-3-hydroxy-3-((9-methyl-4-nitroisoxazol-5-yl)methyl)indolin-2-one (3o): gray solid; 73.6 mg, 97% yield; m.p. decomposed at 98.1 ^{o}C; **^{1}H NMR** (400 MHz, DMSO) δ (ppm) 7.35-7.22 (m, 7H), 7.03 (t, *J* = 7.4 Hz, 1H), 6.85 (d, *J* = 7.8 Hz, 1H), 6.74 (s, 1H), 4.91 (d, *J* = 15.8 Hz, 1H), 4.81 (d, *J* = 15.8 Hz, 1H), 3.87 (d, *J* = 14.4 Hz, 1H), 3.76 (d, *J* = 14.4 Hz, 1H), 2.44 (s, 3H); **^{13}C NMR** (100 MHz, DMSO) δ (ppm) 175.5, 169.2, 155.1, 141.8, 135.9, 131.0, 129.8, 128.5, 127.4, 127.2, 123.8, 122.6, 109.4, 74.0, 42.7, 34.7, 11.1. IR (KBr): v 3327 1711 1608 1517 1418 1374 1234 1169 907 830 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{17}N_3O_5$+Na 402.1060, found 402.1052.

2.2 Large scale synthesis of 3a

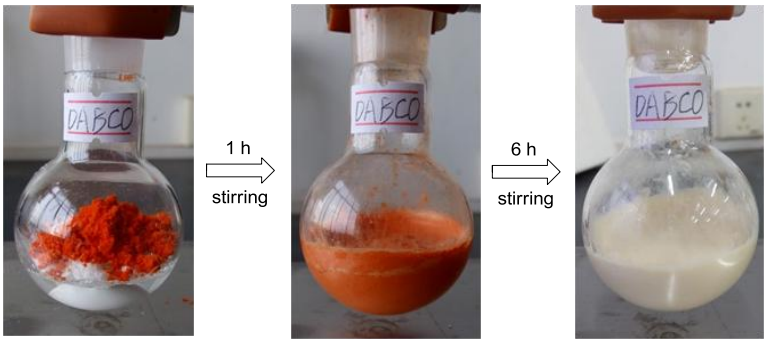


Fig. 1 The reaction was performed with 1.029 g of **1a**, 1.093 g of **2** and 5 mol% of DABCO in 5 mL water.

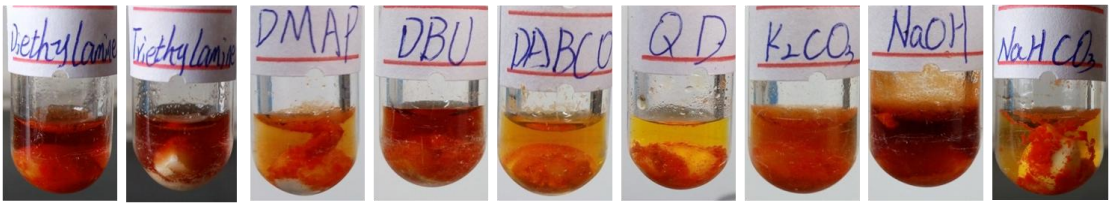
To a solution of DABCO in water were added 3,5-dimethyl-4-nitroisoxazole **2** (1.093 g, 7.69 mmol) and isatin **1a** (1.029 g, 7.00 mmol). After ten minutes of stirring, a slurry phase was formed for the mixture. The progress of the reaction can be monitored by visualization of the color change of the reaction mixture from red (at the start of the reaction) to white (at the end of the reaction). After 6 hours, the desired product **3aa** was collected by filtration. This material was washed with water and dried under high vacuum to afford 2.000 g (99%) of **3aa** as a white solid.

2.3 Conditions optimization for the vinylogous Henry (nitroaldol) addition of 3,5-diethyl-4-nitroisoxazole 4 with isatin 1a

entry	catalyst	time (h)	yield (%)[b]	dr
1	Diethylamine	24	trace	-
2	Triethylamine	1.5	93	97:3
3	DMAP	12	94	98:2
4	DBU	24	trace	-
5	DABCO	15	94	98:2
6	QD	20	92	93:7
7	K_2CO_3	24	nr[c]	-
8	NaOH	24	nr	-
9	$NaHCO_3$	24	nr	-
10[d]	Triethylamine	3.5	93	97:3

[a] Unless otherwise noted, the reaction was performed with 0.1 mmol of **1a**, 0.11 mmol of **4** and 10 mol% of catalyst in 0.5 mL solvent. [b] Isolated yield. [c] No reaction. [d] The mole ratio of **1a** and **4** was 1:1.

During stirring:



At the indicated time in table:

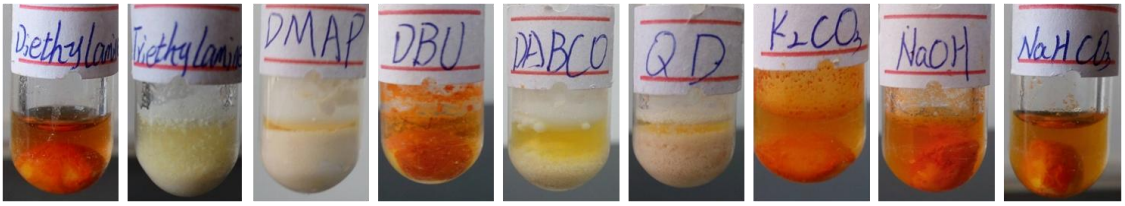


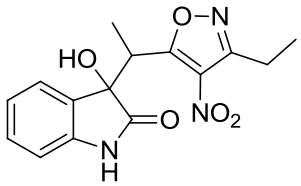
Fig. 2 The appearance of the reaction for different bases.

According to the Figure 2, we can see that: serious agglomeration phenomenon was observed for diethylamine, DBU and inorganic bases, leading to poor or no conversion of isatin; slurry phase separated from water were formed with DMAP,

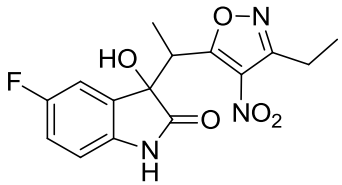
DABCO and QD as the catalysts; a suspension of solids in water was observed when using triethylamine as the catalyst.

2.4 Representative procedure for "On water" direct vinylogous Henry (nitroaldol) additions of 3,5-diethyl-4-nitroisoxazole with isatins

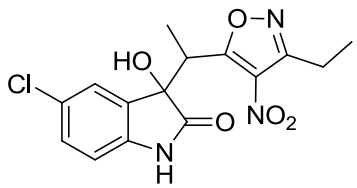
The mixture of 3,5-diethyl-4-nitroisoxazole **4** (34.1 mg, 0.20 mmol), isatin **1a** (0.20 mmol) and catalyst (5 mol%, 0.01 mmol) in 0.5 mL H_2O were stirred at room temperature for the indicated time. After the reaction was completed (indicated by color change from red to white), the solid product was filtered, washed by water and then dried under vacuum to afford the product **5a** in high yield and purity.



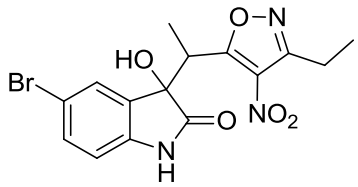
3-((3-ethyl-4-nitroisoxazol-5-yl)methyl)-3-hydroxyindolin-2-one (5a): white solid; 59.0 mg, 93% yield, 97:3 dr; m.p. decomposed at 98.7 °C; **^{1}H NMR** (400 MHz, DMSO) δ (ppm) 10.54 (s, 1H), 7.25 (s, 1H), 6.98 (s, 2H), 6.83 (d, J = 6.9 Hz, 1H), 6.40 (s, 1H), 4.35 (d, J = 6.5 Hz, 1H), 2.92 (d, J = 6.6 Hz, 2H), 1.23-1.14 (m, 6H); **^{13}C NMR** (100 MHz, DMSO) δ (ppm) 177.2, 173.2, 159.4, 142.0, 130.7, 129.8, 128.8, 124.9, 121.7, 109.9, 77.4, 38.5, 19.2, 11.1 10.9. IR (KBr): v 3464 3264 1714 1615 1518 1374 1192 1143 1052 830 770 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{15}N_3O_5$+Na 340.0909, found 340.0902.



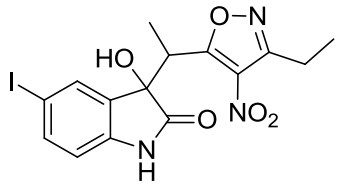
3-(1-(3-ethyl-4-nitroisoxazol-5-yl)ethyl)-5-fluoro-3-hydroxyindolin-2-one (5b): gray solid; 64.3 mg, 94% yield, 83:17 dr; m.p. decomposed at 115.5 °C; **^{1}H NMR** (400 MHz, DMSO) δ (ppm) 10.59 (s, 1H), 7.11 (s, 1H), 6.85 (s, 2H), 6.56 (s, 1H), 4.37 (d, J =6.7 Hz, 1H), 2.94 (d, J = 6.8 Hz, 2H), 1.24-1.16 (m, 6H); **^{13}C NMR** (100 MHz, DMSO) δ (ppm) 177.1, 173.0, 159.6, 157.9 (d, $^1J_{CF}$ = 257 Hz), 138.3, 130.7, 130.5 (d, $^3J_{CF}$ = 7 Hz), 116.1 (d, $^2J_{CF}$ = 23 Hz), 112.6 (d, $^2J_{CF}$ = 25 Hz), 110.8 (d, $^3J_{CF}$ = 8 Hz), 77.7, 38.5, 19.2, 11.2, 10.9. IR (KBr): v 3350 1728 1592 1481 1370 1258 1153 828 618 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{14}FN_3O_5$+Na 358.0815, found 358.0813.



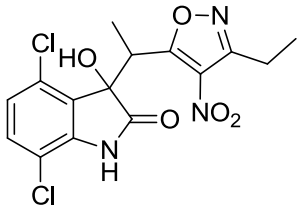
5-chloro-3-(1-(3-ethyl-4-nitroisoxazol-5-yl)ethyl)-3-hydroxyindolin-2-one (5c): gray solid; 66.7 mg, 95% yield, 92:8 dr; m.p. decomposed; **^{1}H NMR** (400 MHz, DMSO) δ (ppm) 10.54 (s, 1H), 7.32 (d, J = 7.8 Hz, 1H), 7.12 (s, 1H), 6.83 (d, J = 8.2 Hz, 1H), 6.64 (s, 1H), 4.31 (d, J = 7.1 Hz, 1H), 2.90 (dd, J = 14.5, 7.2 Hz, 2H), 1.38 (d, J = 6.9 Hz, 3H), 1.22 (t, J = 7.3 Hz, 3H),; **^{13}C NMR** (100 MHz, DMSO) δ (ppm) 176.9, 172.4, 159.2, 140.8, 131.9, 130.2, 129.6, 125.8, 124.3, 111.4, 76.8, 38.6, 19.1, 10.9, 10.8. IR (KBr): v 3327 1707 1593 1526 1448 1365 1263 1184 1138 828 615 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{14}ClN_3O_5$+Na 374.0520, found 374.0511.



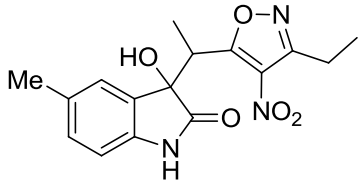
5-bromo-3-(1-(3-ethyl-4-nitroisoxazol-5-yl)ethyl)-3-hydroxyindolin-2-one (5d): pale yellow solid; 75.8 mg, 96% yield, 50:50 dr; m.p. decomposed at 103.2 ^{o}C; **^{1}H NMR** (400 MHz, DMSO) δ (ppm) 10.71 (s, 1H), 10.54 (s, 1H), 7.45 (dd, J = 8.3, 2.0 Hz, 2H), 7.20 (d, J = 1.8 Hz, 1H), 7.14 (d, J = 1.8 Hz, 1H), 6.83-6.78 (m, 2H), 6.63 (s, 1H), 6.58 (s, 1H), 4.39-4.27 (m, 2H), 2.95-2.88 (m, 4H) , 1.25-1.16 (m, 12H); **^{13}C NMR** (100 MHz, DMSO) δ (ppm) 176.8, 176.6, 172.9, 172.4, 159.5, 159.1, 141.3, 141.1, 132.4, 132.3, 132.2, 131.1, 130.7, 130.2, 127.8, 126.9, 113.3, 111.9, 111.8, 77.4, 76.6, 38.6, 38.4, 19.1, 19.0, 11.1, 10.9, 10.8, 10.7. IR (KBr): v 3329 1707 1523 1447 1366 1136 827 816 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{14}BrN_3O_5$+Na 418.0015, found 418.0014.



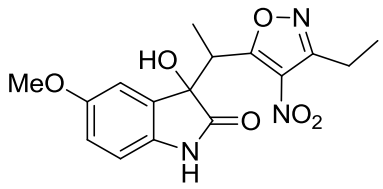
3-(1-(3-ethyl-4-nitroisoxazol-5-yl)ethyl)-3-hydroxy-5-iodoindolin-2-one (5e): pink solid; 85.1 mg, 96% yield, 98:2 dr; m.p. decomposed at 126.3 ^{o}C; **^{1}H NMR** (400 MHz, DMSO) δ (ppm) 10.53 (s, 1H), 7.60 (s, 1H), 7.29 (s, 1H), 6.63 (d, J = 34.5 Hz, 2H), 4.27 (s, 1H), 2.91 (s, 2H), 1.37 (s, 3H), 1.24 (s, 3H); **^{13}C NMR** (100 MHz, DMSO) δ (ppm) 176.6, 172.5, 159.2, 141.5, 138.2, 132.5, 132.4, 130.2, 112.3, 84.4, 76.5, 38.6, 19.2, 11.0, 10.6. IR (KBr): v 3335 1705 1593 1521 1364 1140 827 617 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{14}IN_3O_5$+Na 465.9876, found 465.9868.



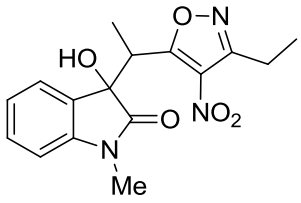
4,7-dichloro-3-(1-(3-ethyl-4-nitroisoxazol-5-yl)ethyl)-3-hydroxyindolin-2-one (5f): gray solid; 72.6 mg, 94% yield, 94:6 dr; m.p. decomposed; **^{1}H NMR** (400 MHz, DMSO) δ (ppm) 11.2 (s, 1H), 7.42 (d, J = 8.5 Hz, 1H), 7.08 (d, J = 8.5 Hz, 1H), 6.59 (s, 1H), 4.86 (d, J = 7.0 Hz, 1H), 2.94 (d, J = 6.5 Hz, 2H), 1.26 (t, J = 6.9 Hz, 3H), 1.10 (d, J = 6.7 Hz, 3H); **^{13}C NMR** (100 MHz, DMSO) δ (ppm) 175.5, 171.4, 159.0, 141.7, 131.3, 131.2, 128.8, 127.4, 124.2, 113.2, 79.2, 35.5, 19.0, 11.0, 10.2. IR (KBr): v 3398 3325 1737 1617 1589 1511 1468 1429 1371 1160 819 621 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{13}Cl_2N_3O_5$+Na 408.0130, found 408.0132.



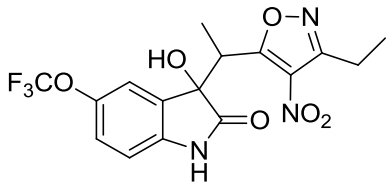
3-(1-(3-ethyl-4-nitroisoxazol-5-yl)ethyl)-3-hydroxy-5-methylindolin-2-one (5g): gray solid; 62.2 mg, 94% yield, 99:1 dr; m.p. decomposed; **^{1}H NMR** (400 MHz, DMSO) δ (ppm) 10.43 (s, 1H), 7.05 (s, 1H), 6.82 (s, 1H), 6.73 (s, 1H), 6.36 (s, 1H), 4.34 (s, 1H), 2.93 (s, 2H), 2.23 (s, 2H), 1.21 (d, J = 18.9 Hz, 6H); **^{13}C NMR** (100 MHz, DMSO) δ (ppm) 177.2, 173.3, 159.4, 139.5, 130.6, 130.4, 129.9, 129.0, 125.6, 109.6, 77.5, 38.6, 20.8, 19.2, 11.2, 11.0. IR (KBr): v 3396 3236 1716 1601 1517 1363 1211 1159 826 634 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{17}N_3O_5$+Na 354.1066, found 354.1067.



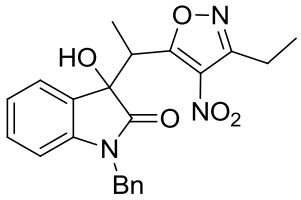
3-(1-(3-ethyl-4-nitroisoxazol-5-yl)ethyl)-3-hydroxy-5-methoxyindolin-2-one (5h): gray solid; 66.0 mg, 95% yield, 96:4 dr; m.p. decomposed at 116.5 ^{o}C; **^{1}H NMR** (400 MHz, DMSO) δ (ppm) 10.21 (s, 1H), 6.85-6.74 (m, 3H), 6.47 (s, 1H), 4.30 (d, J = 6.7 Hz, 1H), 3.71 (s, 3H), 2.90 (d, J = 6.9 Hz, 2H), 1.35 (d, J = 6.3 Hz, 3H), 1.22 (t, J = 6.6 Hz, 3H); **^{13}C NMR** (100 MHz, DMSO) δ (ppm) 177.0, 172.7, 159.1, 154.9, 135.0, 131.1, 130.3, 114.4, 111.0, 110.3, 77.1, 55.5, 38.8, 19.1, 10.9, 10.8. IR (KBr): v 3380 1699 1598 1523 1487 1367 1266 1208 1141 825 623 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{17}N_3O_6$+Na 370.1015, found 370.1020.



3-(1-(3-ethyl-4-nitroisoxazol-5-yl)ethyl)-3-hydroxy-1-methylindolin-2-one (5i): pale yellow solid; 64.2 mg, 97% yield, 97:3 dr; m.p. decomposed at 102.7 ^{o}C; **^{1}H NMR** (400 MHz, DMSO) δ (ppm) 7.36 (s, 1H), 7.08 (s, 3H), 6.48 (s, 1H), 4.39 (d, J = 6.0 Hz, 1H), 3.14 (s, 3H), 2.93 (d, J = 6.4 Hz, 2H), 1.23-1.15 (m, 6H); **^{13}C NMR** (100 MHz, DMSO) δ (ppm) 175.4, 173.1, 159.5, 143.4, 130.6, 129.9, 128.3, 124.5, 122.4, 108.7, 77.2, 38.8, 26.1, 19.2, 11.1, 10.9. IR (KBr): v 3363 1706 1600 1508 1368 1260 1134 1097 830 759 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{17}N_3O_5$+Na 354.1066, found 354.1060.

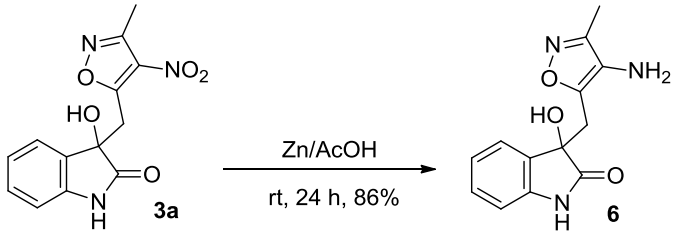


3-(1-(3-ethyl-4-nitroisoxazol-5-yl)ethyl)-3-hydroxy-5-(trifluoromethoxy)indolin-2-one (5j): yellow solid; 75.4 mg, 94% yield, 51:49 dr; m.p. decomposed at 108.1 ^{o}C; **^{1}H NMR** (400 MHz, DMSO) δ (ppm) 10.76 (s, 1H), 10.60 (s, 1H), 7.28 (d, J = 8.1 Hz, 2H), 7.00 (s, 2H), 6.92 (t, J = 8.9 Hz, 2H), 6.67 (d, J = 21.5 Hz, 2H), 4.40 (d, J = 7.0 Hz, 1H), 4.29 (d, J = 7.0 Hz, 1H), 2.91 (dd, J = 13.4, 7.1 Hz, 4H), 1.41 (d, J = 6.9 Hz, 3H),1.21 (dd, J = 14.8, 7.3 Hz, 9H); **^{13}C NMR** (100 MHz, DMSO) δ (ppm) 177.3, 177.1, 172.9, 172.5, 159.6, 159.2, 143.0, 141.2, 140.9, 131.5, 130.6, 130.5, 130.1, 123.2, 123.1, 118.9, 118.6, 117.8, 110.8, 77.4, 76.7, 38.6, 38.5, 19.1, 11.2, 10.9, 10.8, 10.7. IR (KBr): v 3512 3373 1729 1686 1597 1519 1371 1268 1157 832 621 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{14}F_3N_3O_6$+Na 424.0732, found 424.0726.



1-benzyl-3-(1-(3-ethyl-4-nitroisoxazol-5-yl)ethyl)-3-hydroxyindolin-2-one (5k): gray solid; 78.2 mg, 96% yield, 99:1 dr; m.p. decomposed at 138.1 ^{o}C; **^{1}H NMR** (400 MHz, DMSO) δ (ppm) 7.29-6.93 (m, 9H), 6.71 (s, 1H), 4.87 (d, J = 15.7 Hz, 1H), 4.75 (d, J = 15.5 Hz, 1H), 4.44 (d, J = 4.8 Hz, 1H), 2.88 (d, J = 5.6 Hz, 2H), 1.39 (d, J = 3.6 Hz, 3H), 1.21 (s, 3H); **^{13}C NMR** (100 MHz, DMSO) δ (ppm) 175.6, 172.4, 159.1, 142.4, 136.1, 130.2, 129.8, 129.3, 128.5, 127.4, 127.2, 124.2, 122.6, 109.4, 76.4, 42.7, 19.2, 11.1, 10.8. IR (KBr): v 3411 1716 1594 1511 1359 1283 1173 831 751 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{21}N_3O_5$+Na 430.1379, found 430.1386.

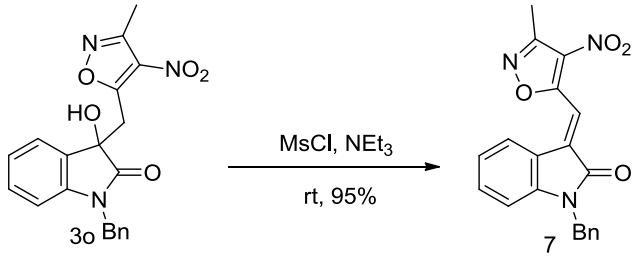
2.5 Synthesis of compound 6



To the solution of **3a** (87.6 mg, 0.3 mmol, 1.0 equiv.) in acetic acid (5 mL), zinc dust (0.7 g, 4.7 mmol, 15.6 equiv.) was added slowly. After 2 h at r.t., the mixture was filtered over celite, diluted with ethyl acetate (10 mL), and then washing with sodium bicarbonate solutiona (2×10 mL). The combined organic phase was dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by flash chromatography (EA/PE = 2:1) to give compound **6**.

3-((4-amino-3-methylisoxazol-5-yl)methyl)-3-hydroxyindolin-2-one (6): yellow solid; 66.9 mg, 86% yield; m.p. decomposed at 170.4 °C; **^{1}H NMR** (400 MHz, DMSO) δ (ppm) 10.27 (s, 1H), 7.19-7.11 (m, 2H), 6.91 (t, J = 7.4 Hz, 1H), 6.75 (d, J = 7.6 Hz, 1H), 6.27 (s, 1H) , 3.80 (s, 2H), 3.29 (d, J = 14.6 Hz, 1H), 3.04 (d, J = 14.6 Hz, 1H), 2.03 (s, 3H); **^{13}C NMR** (100 MHz, DMSO) δ (ppm) 178.6, 153.6, 148.0, 141.6, 130.9, 129.1, 124.8, 124.4, 121.5, 109.5, 75.0, 33.1, 9.1. IR (KBr): v 3336 3289 1722 1618 1473 1332 1206 1149 1088 868 759 cm^{-1}; HRMS (ESI) calcd for $C_{13}H_{13}N_3O_3^+$+Na 282.0849, found 282.0845.

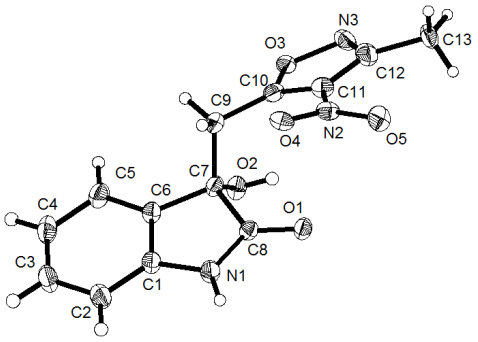
2.6 Synthesis of compound 7



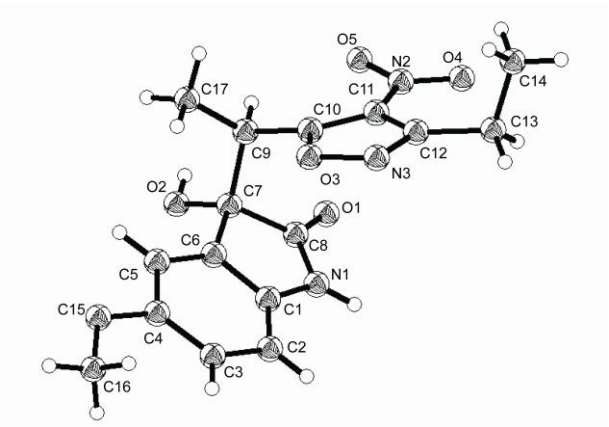
To the solution of **3a** (189.6 mg, 0.5 mmol, 1 equiv.) in CH_2Cl_2 (5 mL) was cooled to 0℃, followed by an addition of methanesulfonyl chloride (1.5 mmol, 1 equiv., 0.11 mL) and triethylamine (1.5 mmol, 1 equiv., 0.20 mL), then stirred at this temperature for the indicated time. The solvent was removed under reduced pressure and the residue was purified by column chromatography (silica gel, petroleumether/ethyl acetate = 6:1) to give compound **7**.

1-benzyl-3-((3-methyl-4-nitroisoxazol-5-yl)methylene)indolin-2-one (7): red solid; 171.4 mg, 95% yield; m.p. decomposed at 214.0 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 8.37 (d, J = 7.8 Hz, 1H), 8.17 (s, 1H), 7.35-7.29 (m, 6H), 7.07 (t, J = 7.7 Hz, 1H), 6.76 (d, J = 7.9 Hz, 1H), 4.90 (s, 2H), 2.69 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ (ppm) 167.3, 164.7, 156.5, 145.8, 135.9, 135.3, 133.5, 128.9, 127.9, 127.4, 123.0, 119.7, 109.7, 44.1, 29.7, 11.8. IR (KBr): v 3423 1714 1635 1598 1520 1467 1351 1141 826 700 623 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{15}N_3O_4$+H 362.1141, found 362.1134.

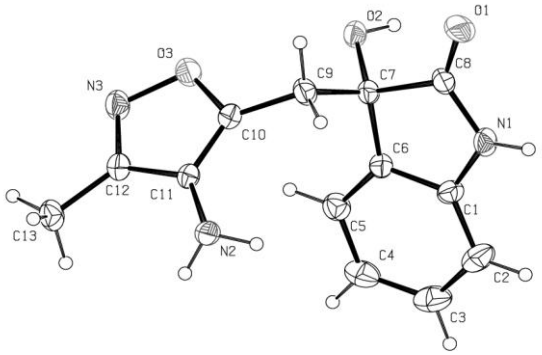
3. Crystal data and structure refinement for product 3a, 5h and 6



Identification code	3a
Empirical formula	C13H11N3O5
Formula weight	289.25
Temperature	296 (2) K
Wavelength	0.71073 A
Crystal system, space group	Monoclinic, P2(1)
Unit cell dimensions	a = 8.60650(10) A alpha = 90 deg. b = 7.18580(10) A beta =110.9850(10) deg. c = 11.1840(2) A gamma = 90 deg..
Volume	645.794 (16) A^3
Z, Calculated density	2, 1.487 Mg/m^3
Absorption coefficient	0.117 mm^-1
F(000)	300
Crystal size	0.15 x 0.15 x 0.10 mm
q for data collection	1.95 to 27.50 deg.
Limiting indices	-11<=h<=11, -9<=k<=9, -12<=l<=14
Reflections collected/unique	4451 / 2841 [R(int) = 0.0190]
Completeness to q = 27.49	99.3 %
Absorption correction	None
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	2841 / 1 / 191
Goodness-of-fit on F^2	0.992
Final R indices [I > 2sigma (I)]	R1 = 0.0308, wR2 = 0.0829
R indices (all data)	R1 = 0.0318, wR2 =0.0840
Absolute structure parameter	0.4(8)
Largest diff. peak and hole	0.169 and -0.139 e.A^-3

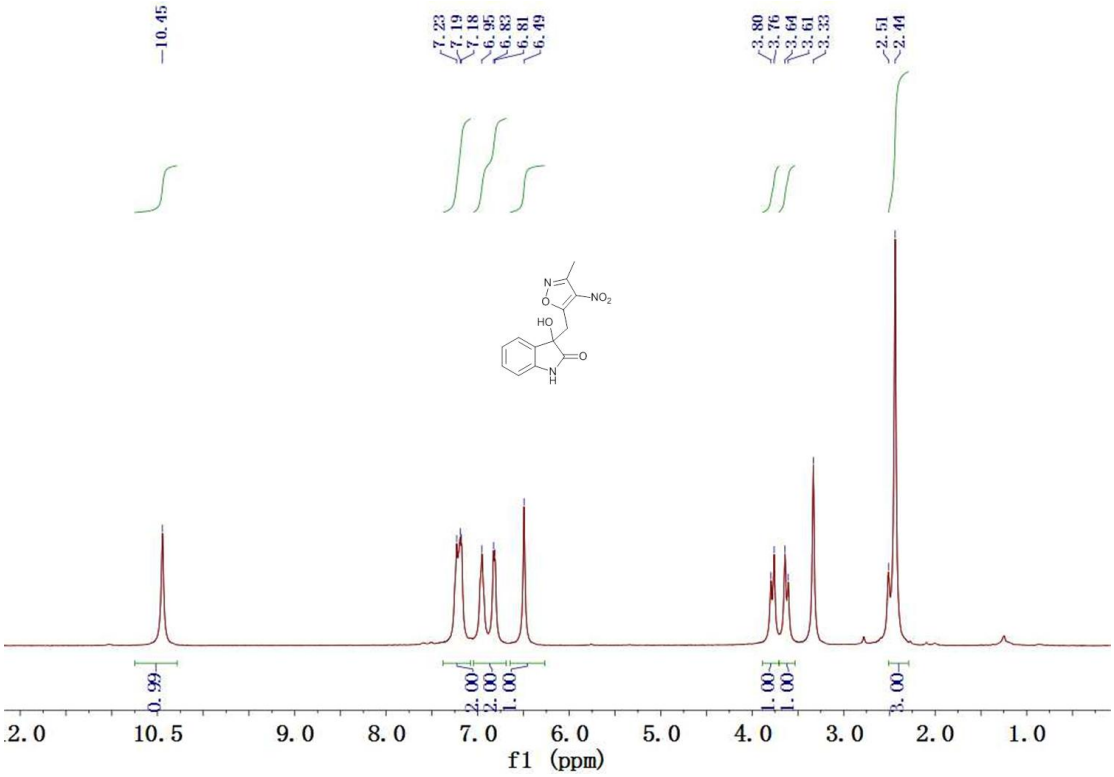


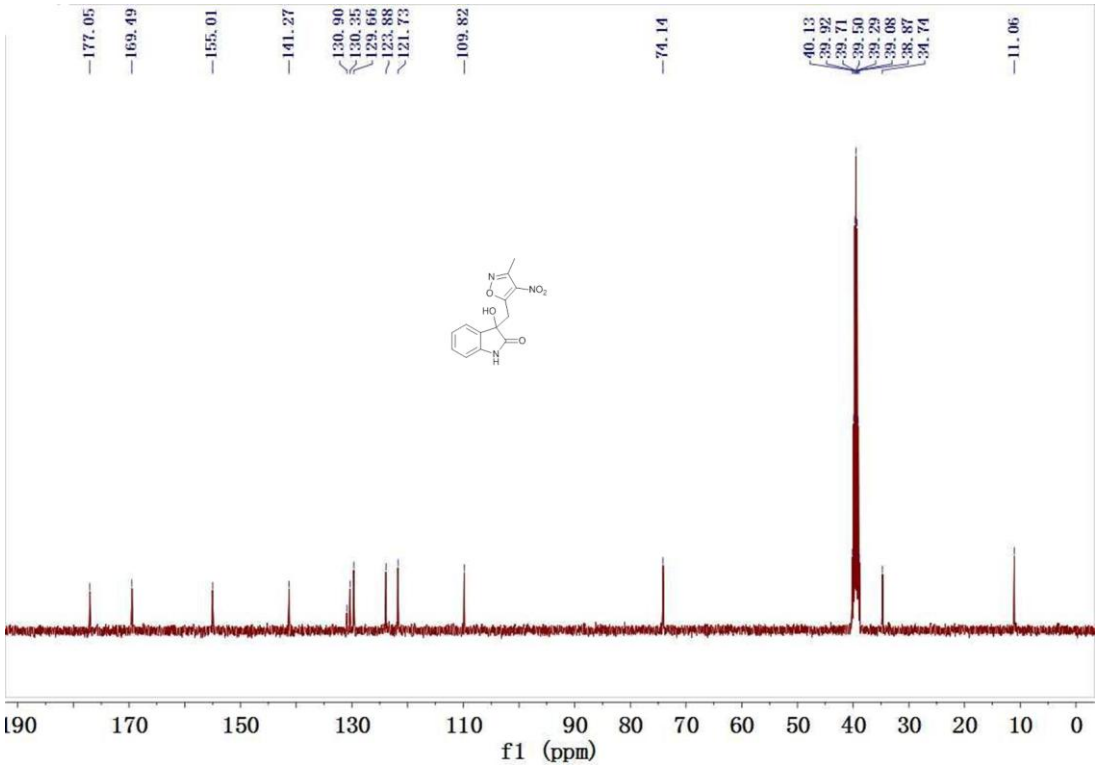
Identification code	5h
Empirical formula	C16H17 N3 O6
Formula weight	347.33
Temperature	296 (2) K
Wavelength	0.71073 A
Crystal system, space group	Monoclinic, P2(1)
Unit cell dimensions	a = 13.5271(6) A alpha = 90 deg. b = 7.4112(3) A beta = 94.7630(10) deg. c = 16.5010(8) A gamma = 90 deg..
Volume	1648.55 (13) A^3
Z, Calculated density	4, 1.399 Mg/m^3
Absorption coefficient	0.109 mm^-1
F (000)	728
Crystal size	0.20 x 0.15 x 0.10 mm
q for data collection	1.87to 27.44 deg.
Limiting indices	-17<=h<=17, -9<=k<=9, -21<=l<=12
Reflections collected/unique	10874 / 3768 [R(int) = 0.0428]
Completeness to = 27.44	99.9 %
Absorption correction	None
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	3768 / 0 / 227
Goodness-of-fit on F^2	1.020
Final R indices [I > 2sigma (I)]	R1 = 0.0601, wR2 = 0.1505
R indices (all data)	R1 = 0.1190, wR2 =0.1830
Absolute structure parameter	0.94(2)
Largest diff. peak and hole	0.423 and -0.266 e.A^-3

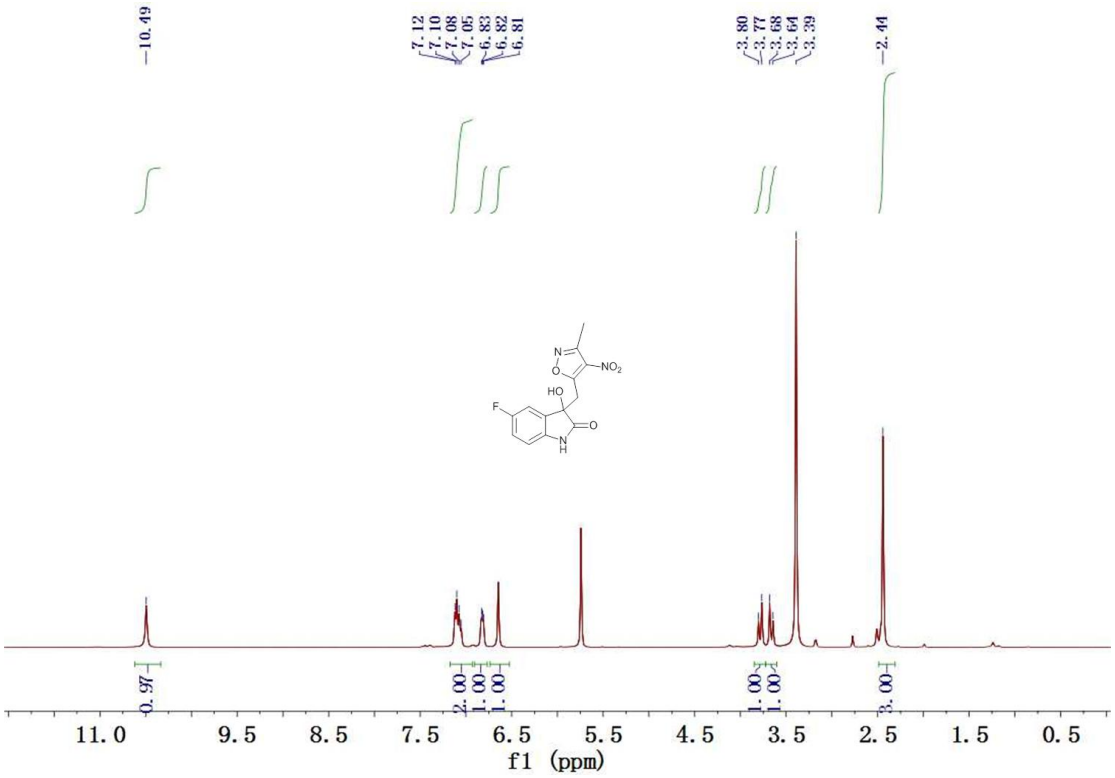


Identification code	6
Empirical formula	C13 H13 N3 O3
Formula weight	259.26
Temperature	295(10) K
Wavelength	0.71073 A
Crystal system, space group	Monoclinic, P2(1)
Unit cell dimensions	a = 6.3186(4) A alpha = 90 deg.
	b = 11.7574(8) A beta = 95.537(7) deg.
	c = 16.3886(12) A gamma = 90 deg..
Volume	1211.84 (14) A^3
Z, Calculated density	4, 1.421 Mg/m^3
F(000)	544
Crystal size	0.15 x 0.14 x 0.04 mm
for data collection	3.36 to 28.98 deg.
Limiting indices	-7<=h<=6, -13<=k<=14, -11<=l<=20
Completeness to = 26.32	99.8 %
Absorption correction	None
Final R indices [I > 2sigma(I)]	R1 = 0.0673, wR2 = 0.1623(2393)
R indices (all data)	R1 = 0.0366, wR2 =0.0865

4. NMR spectra



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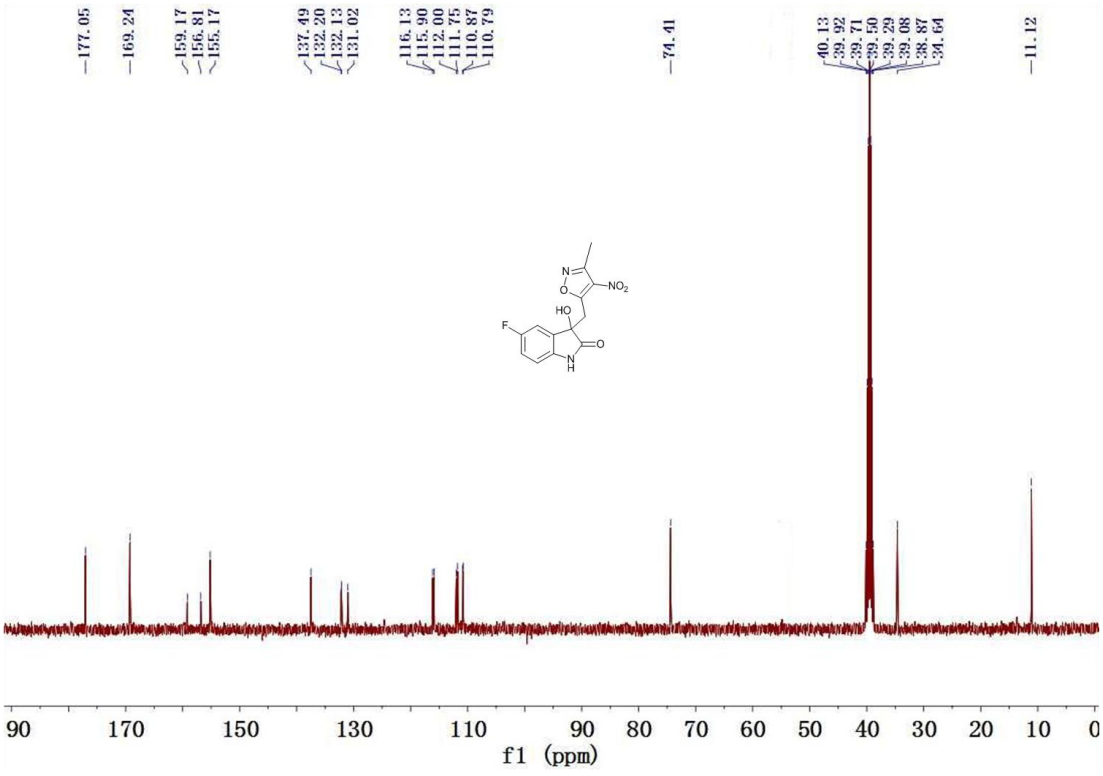
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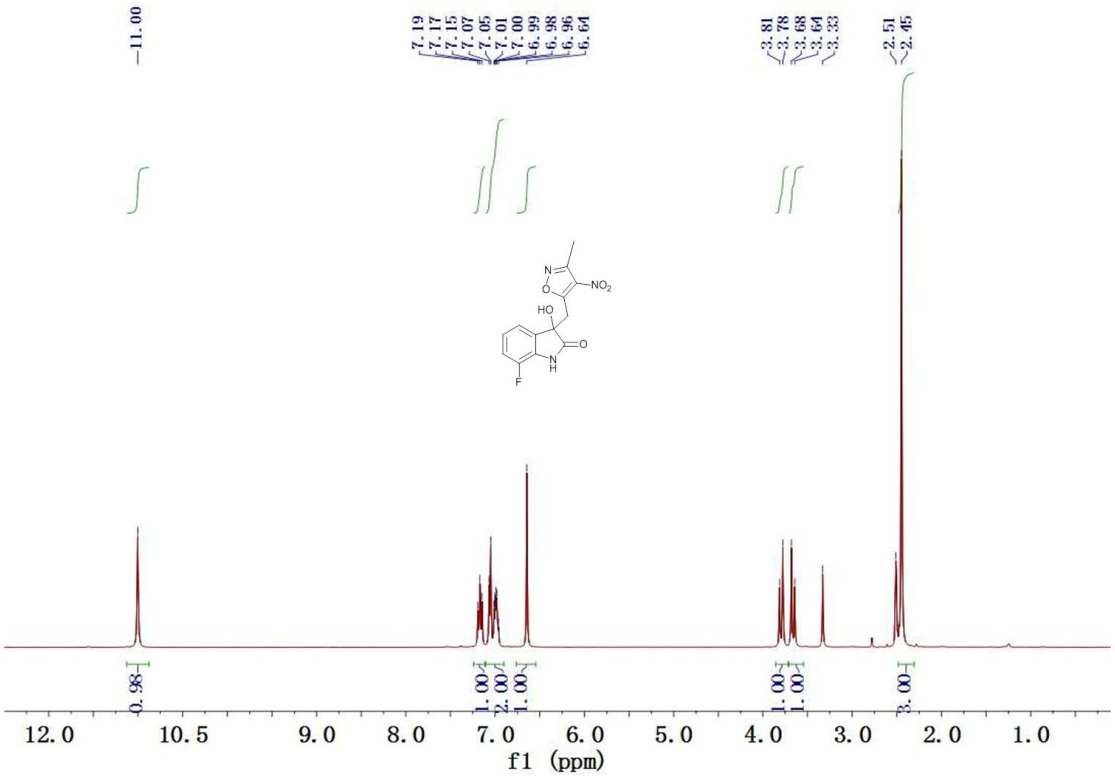
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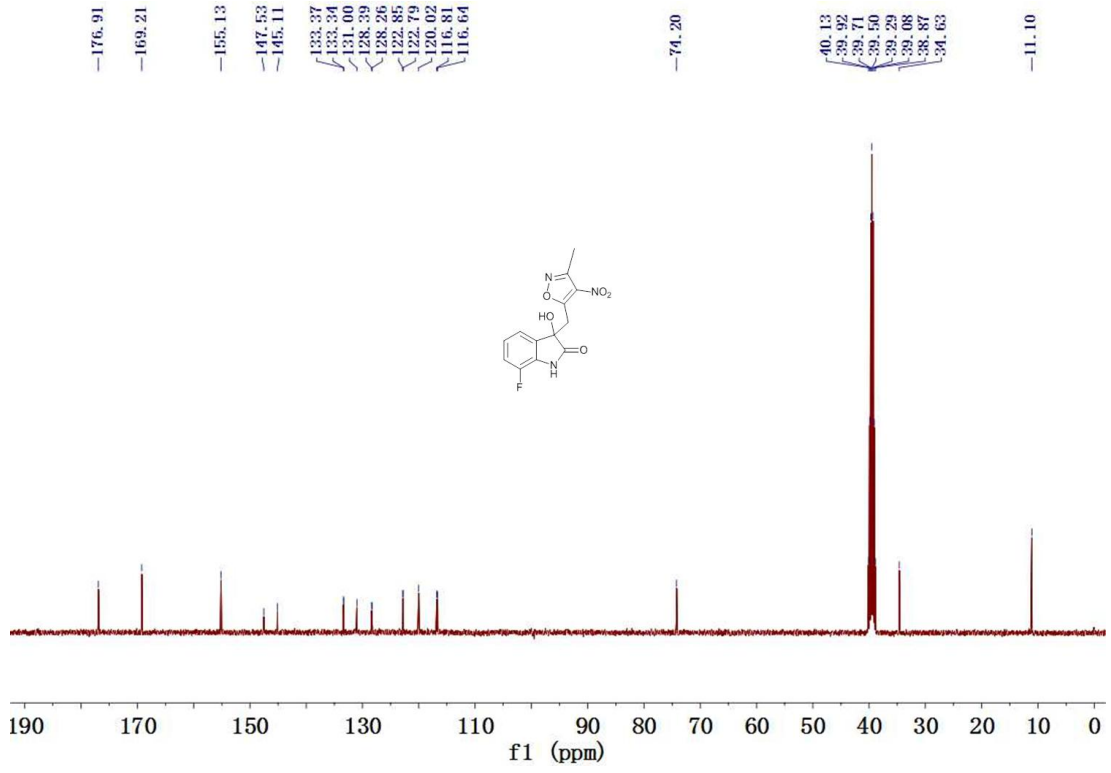
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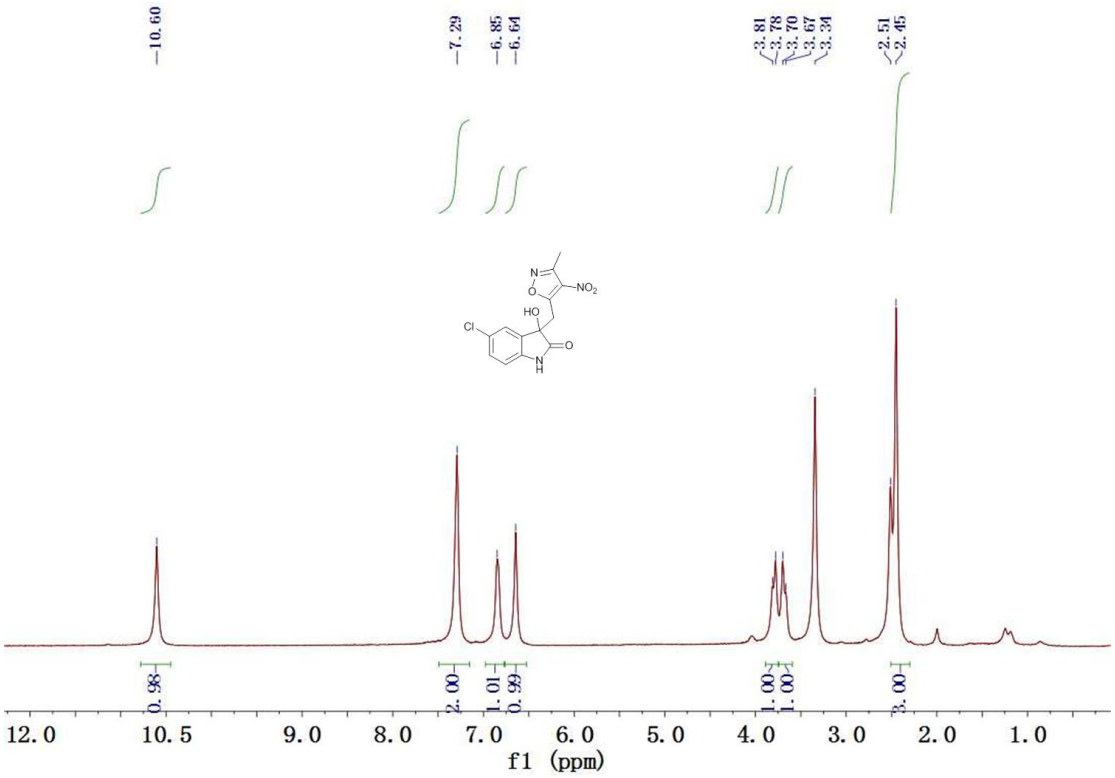
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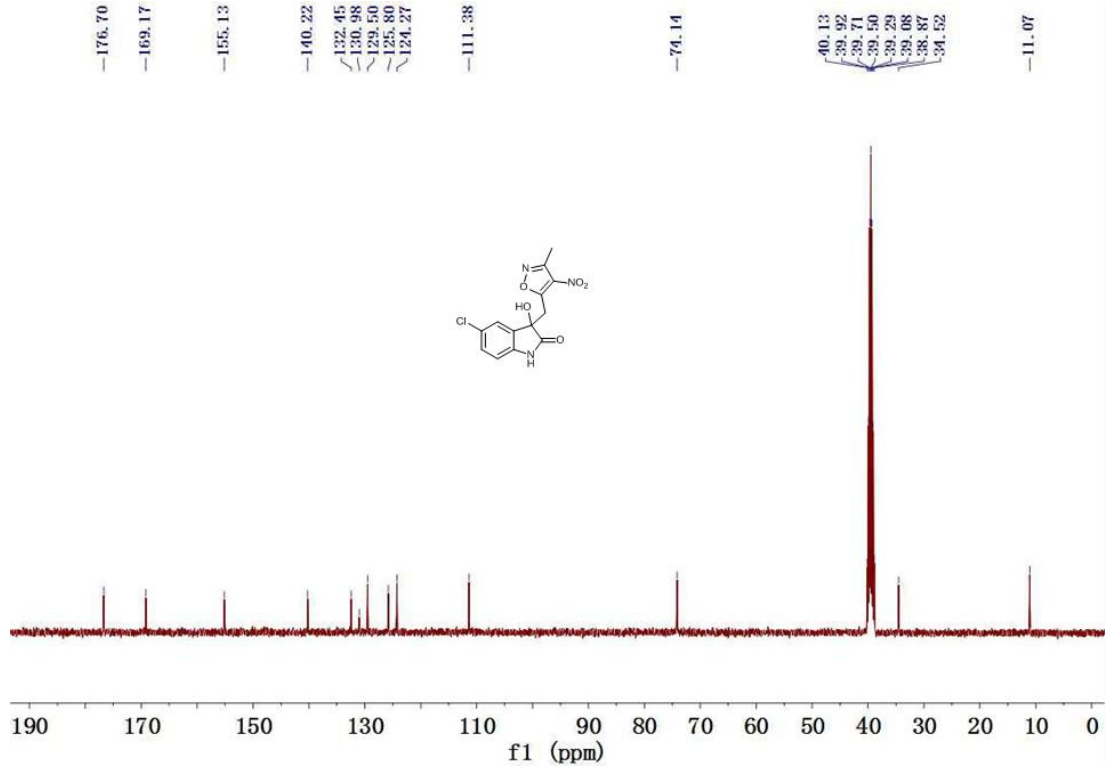
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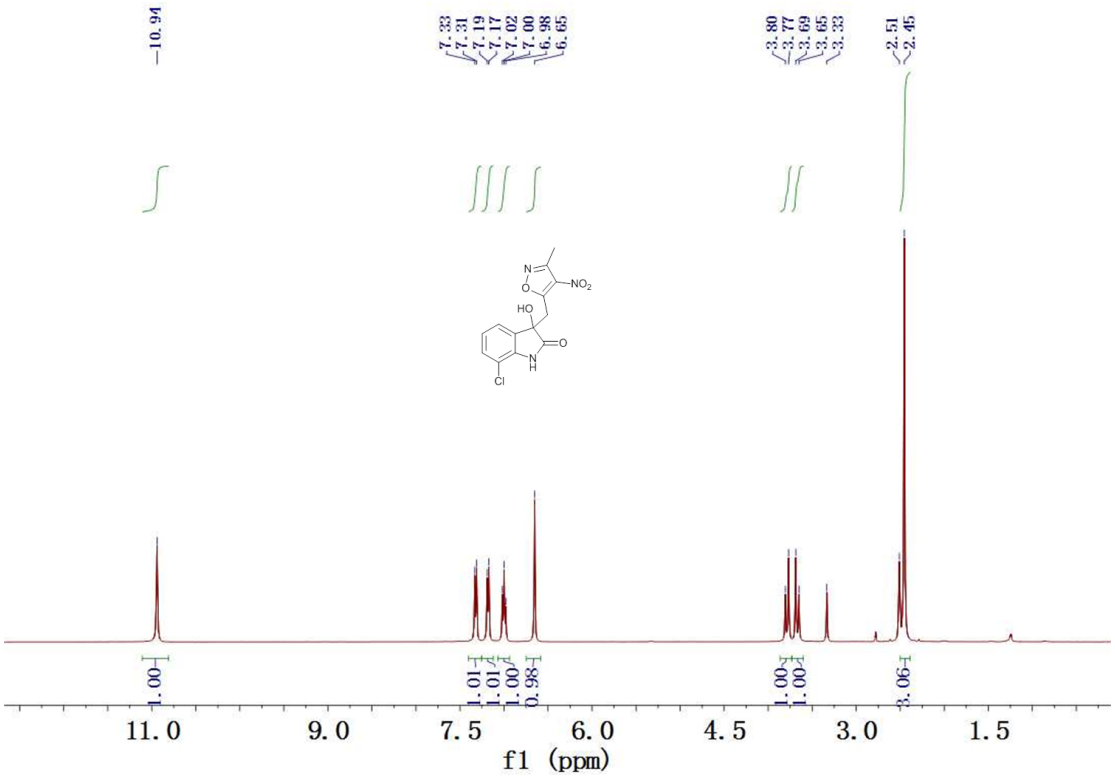
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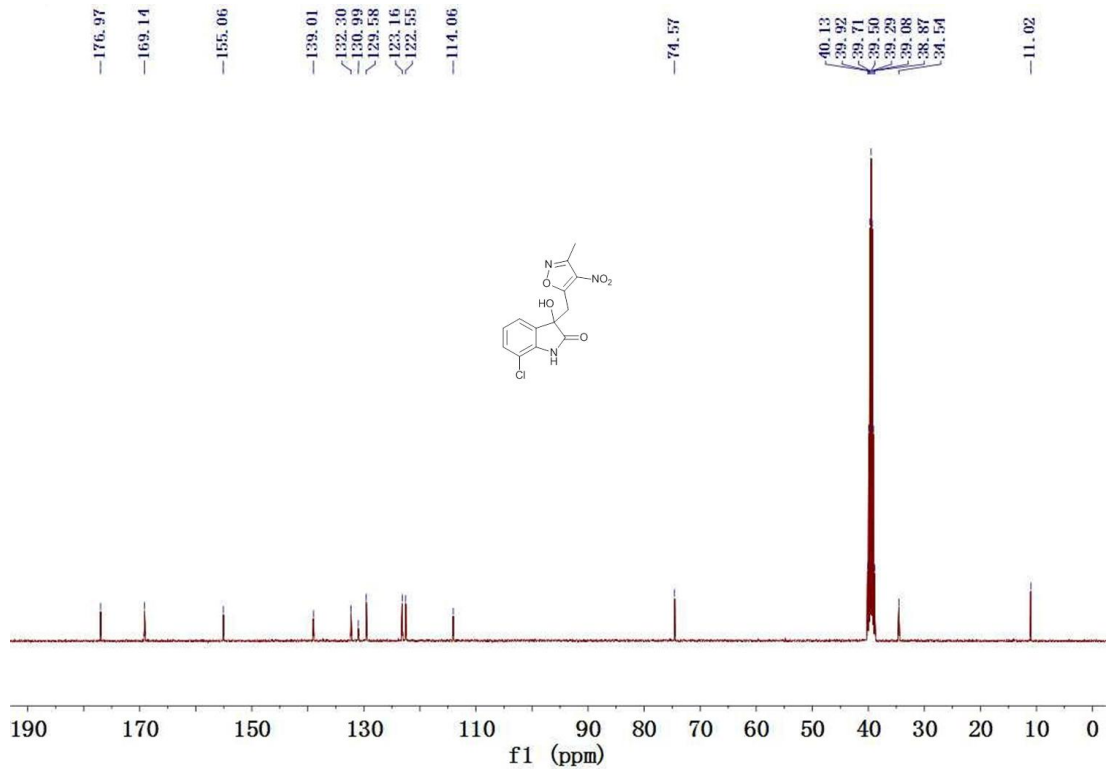
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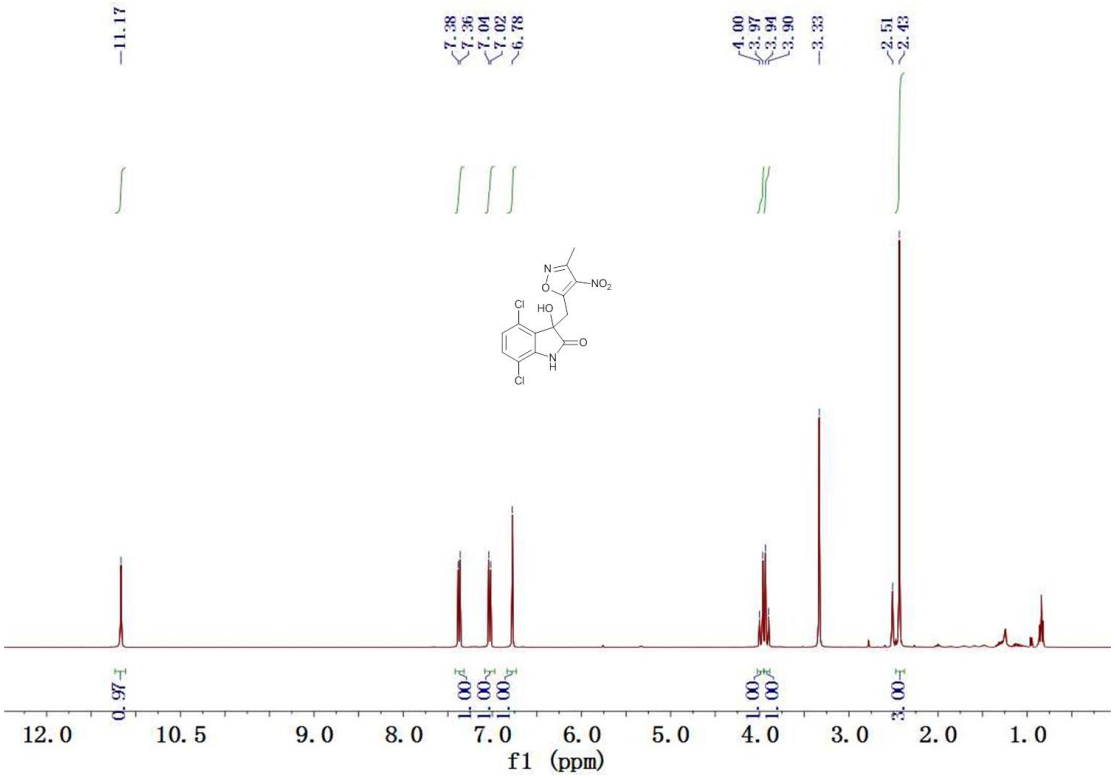
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1.00
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1.00
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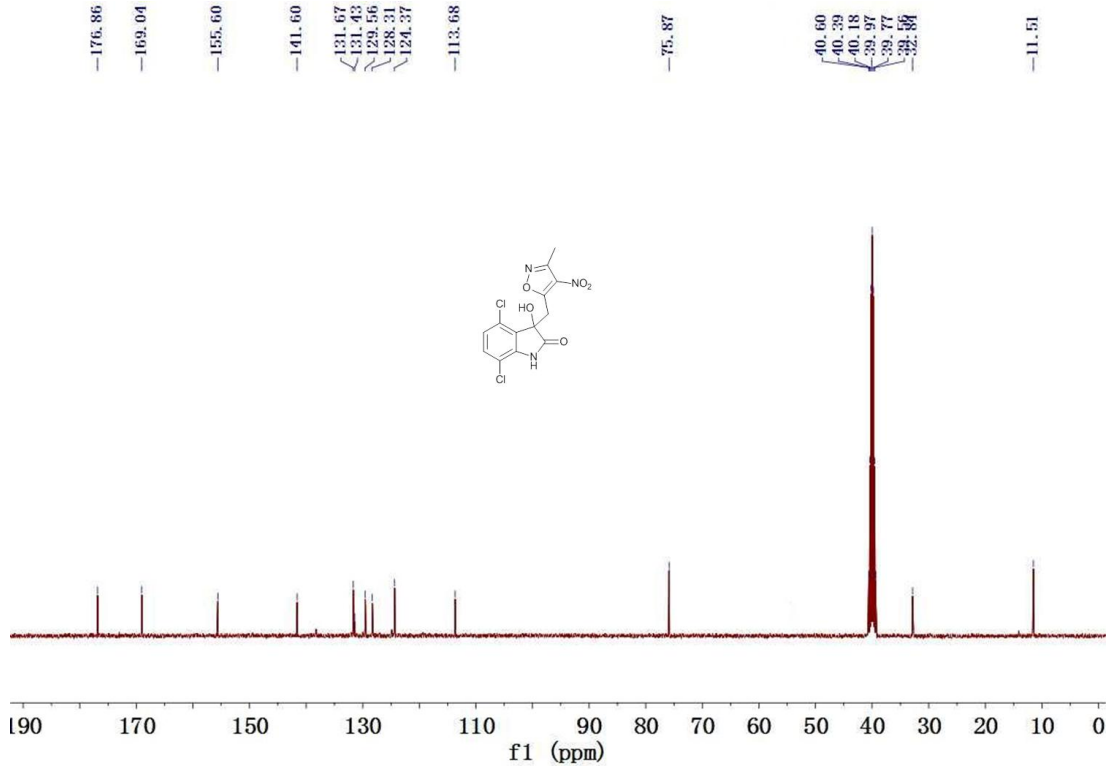
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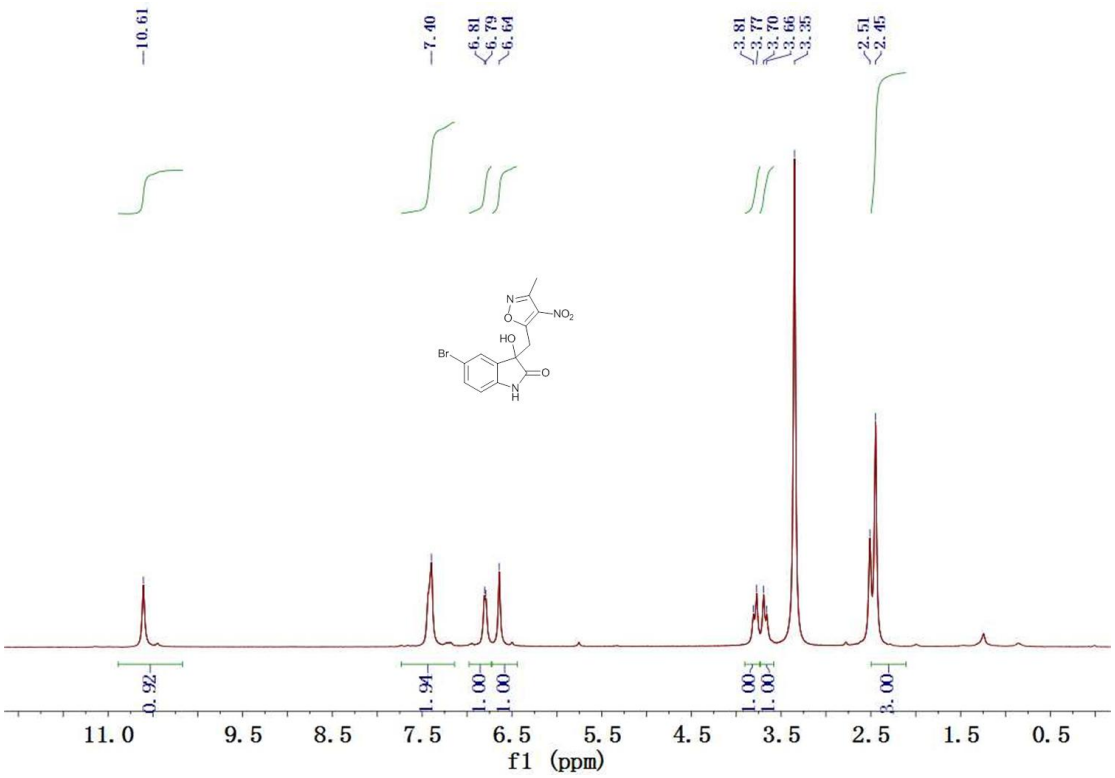
f1 (ppm)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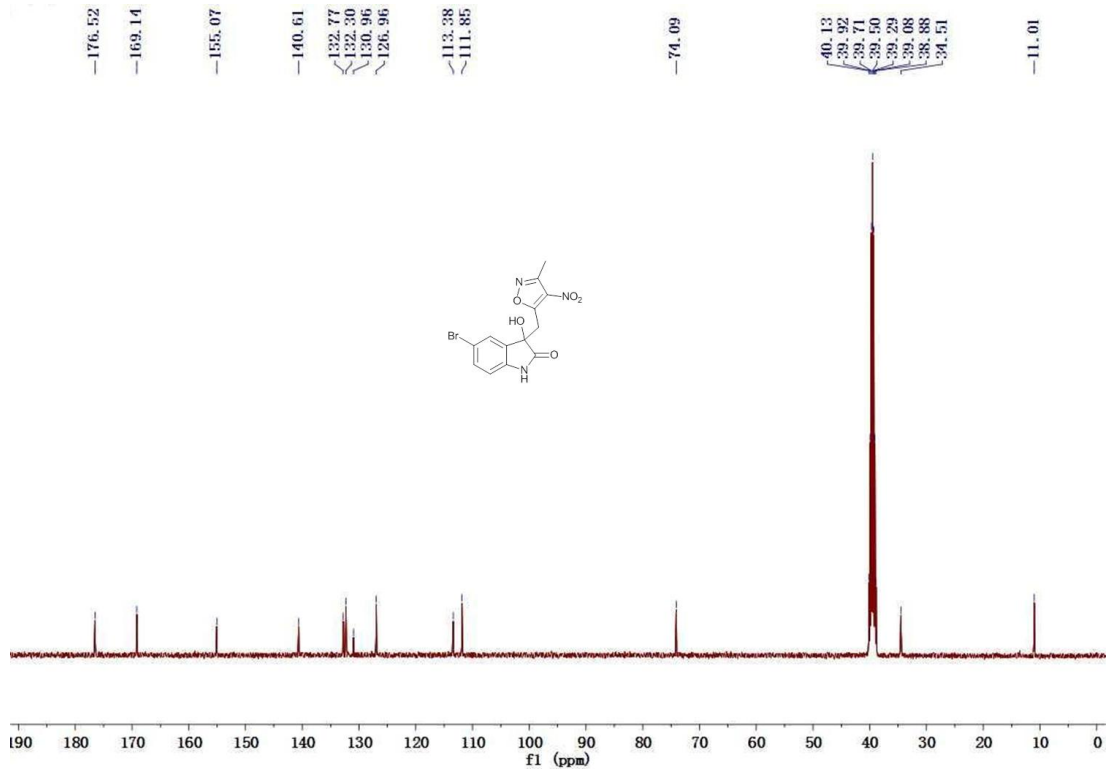
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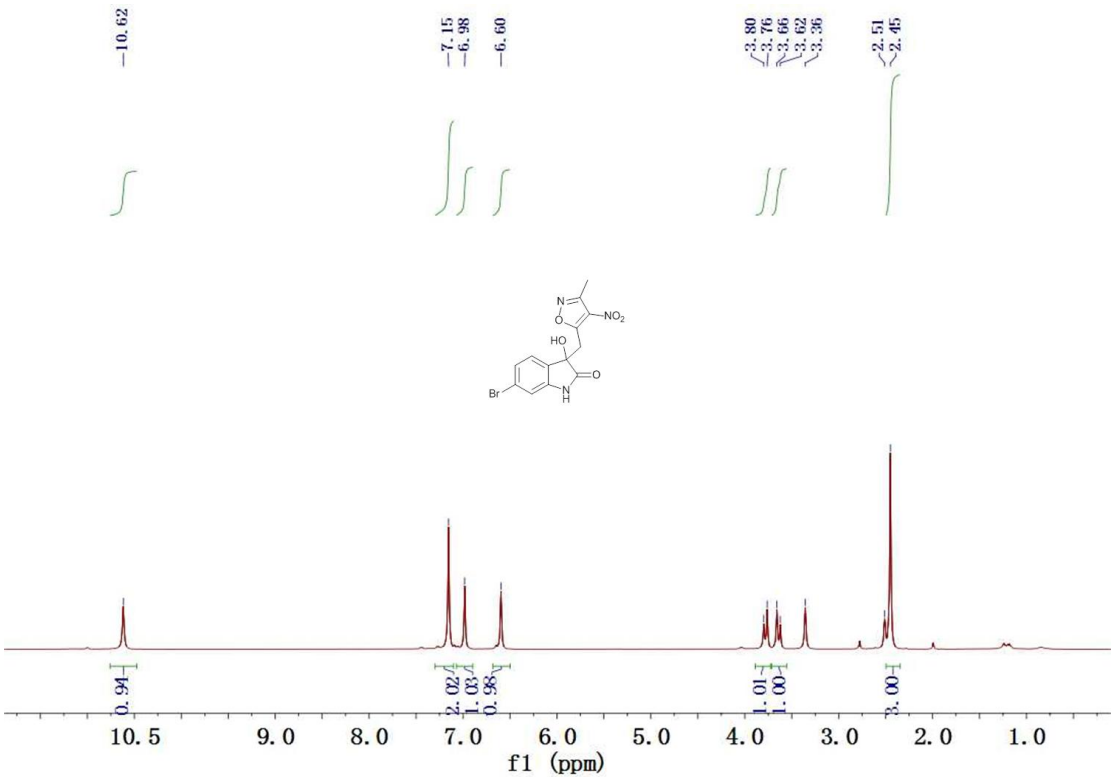
f1 (ppm)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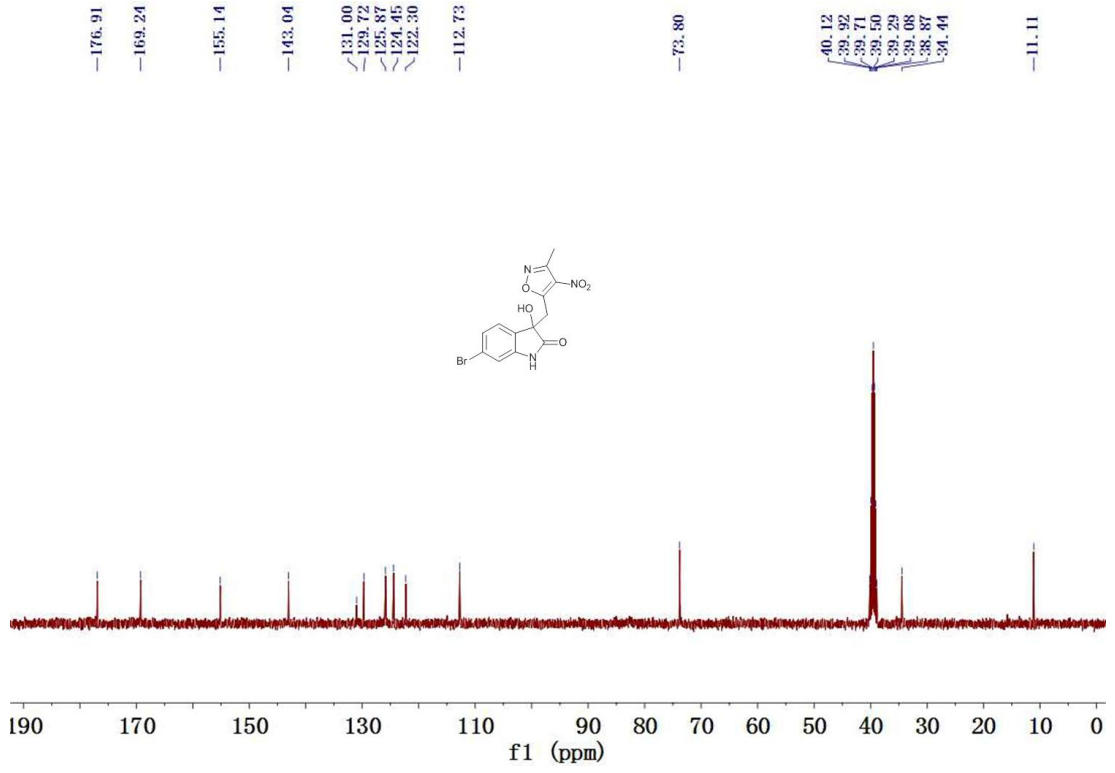
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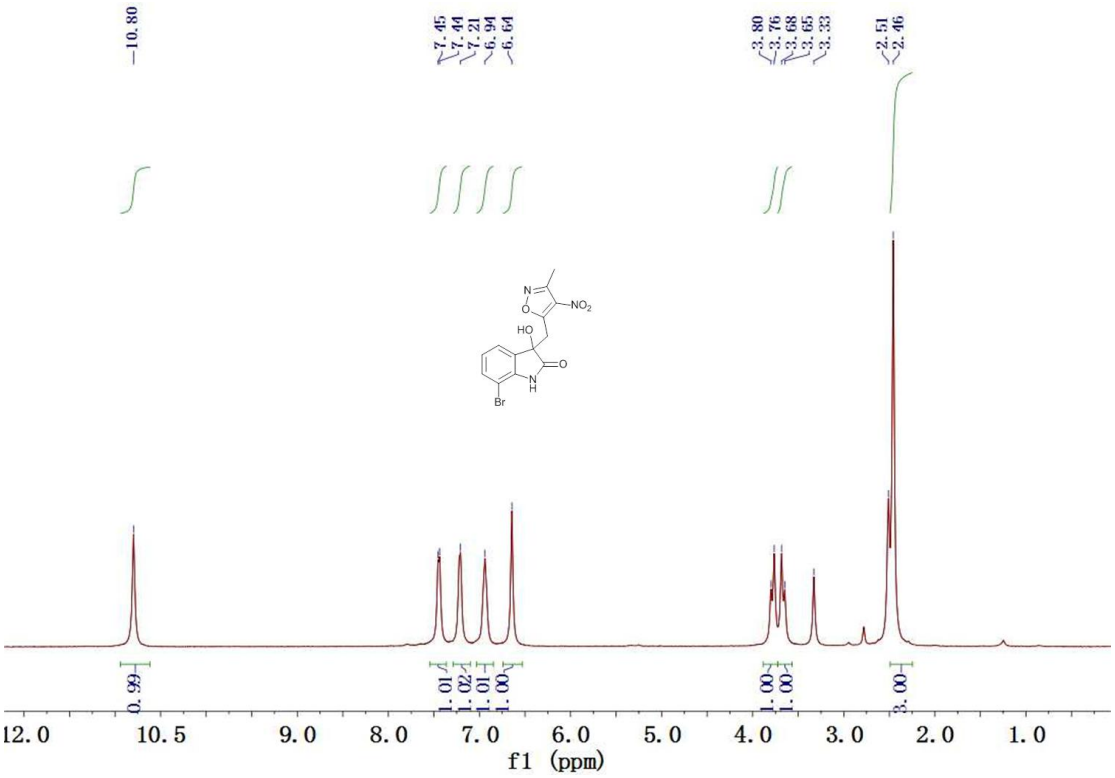
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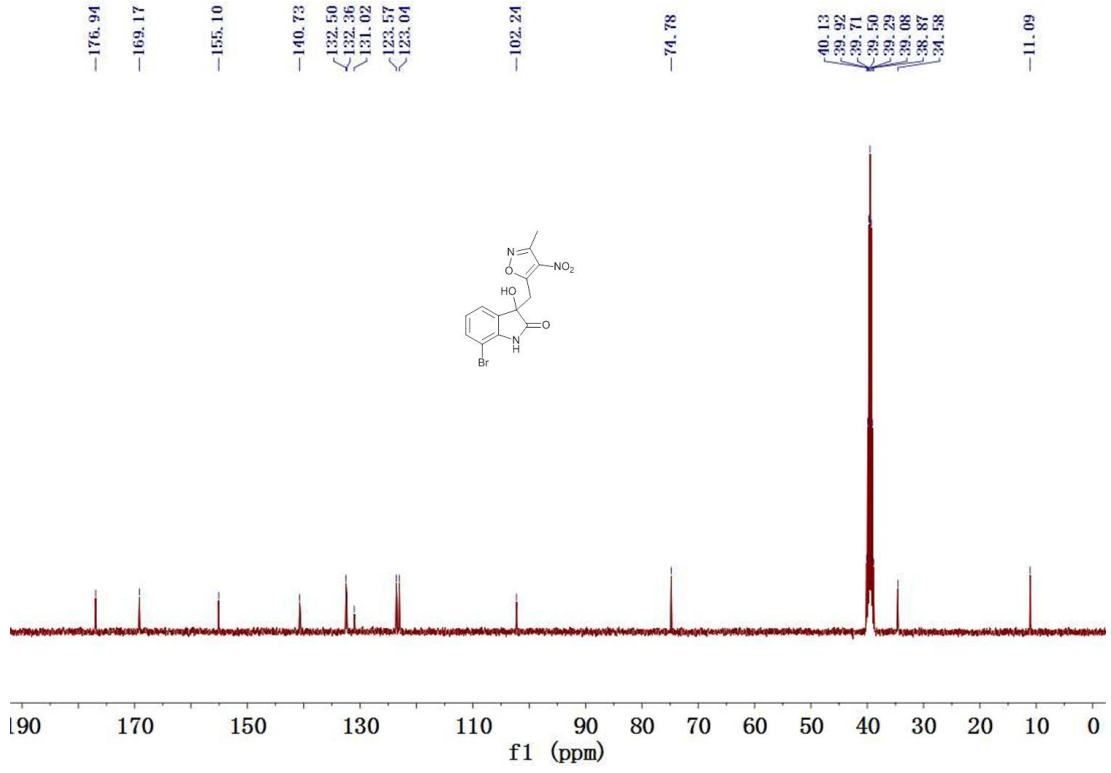
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39.50
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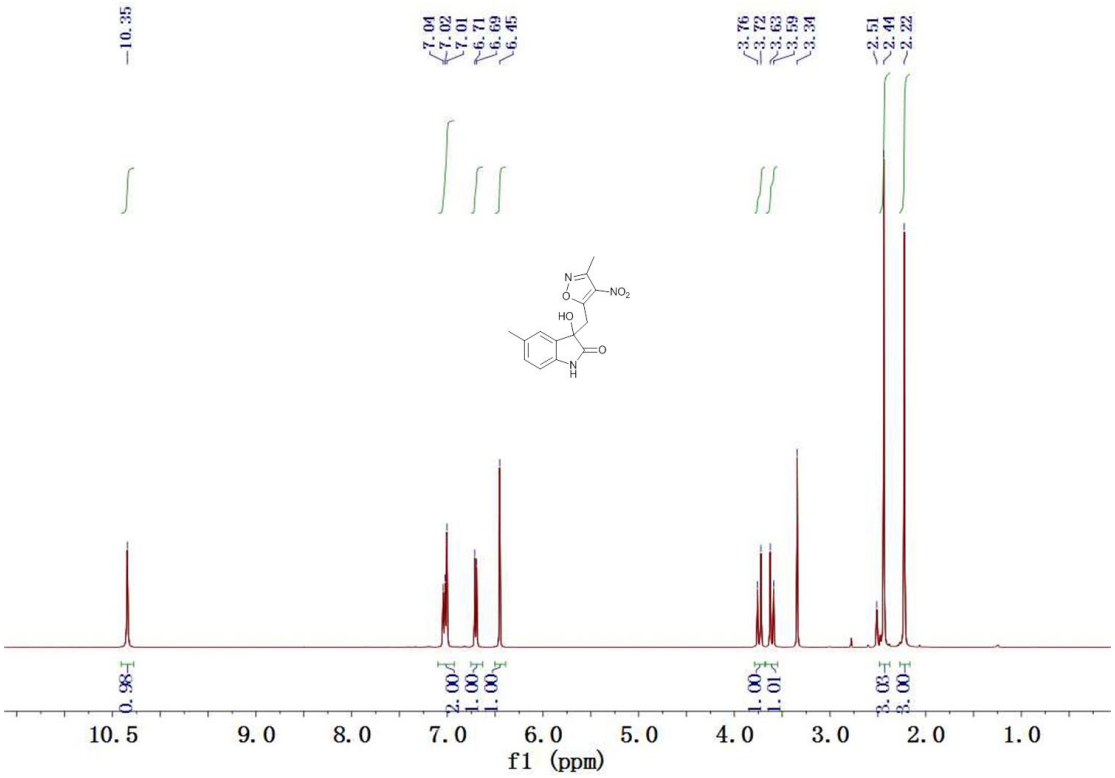
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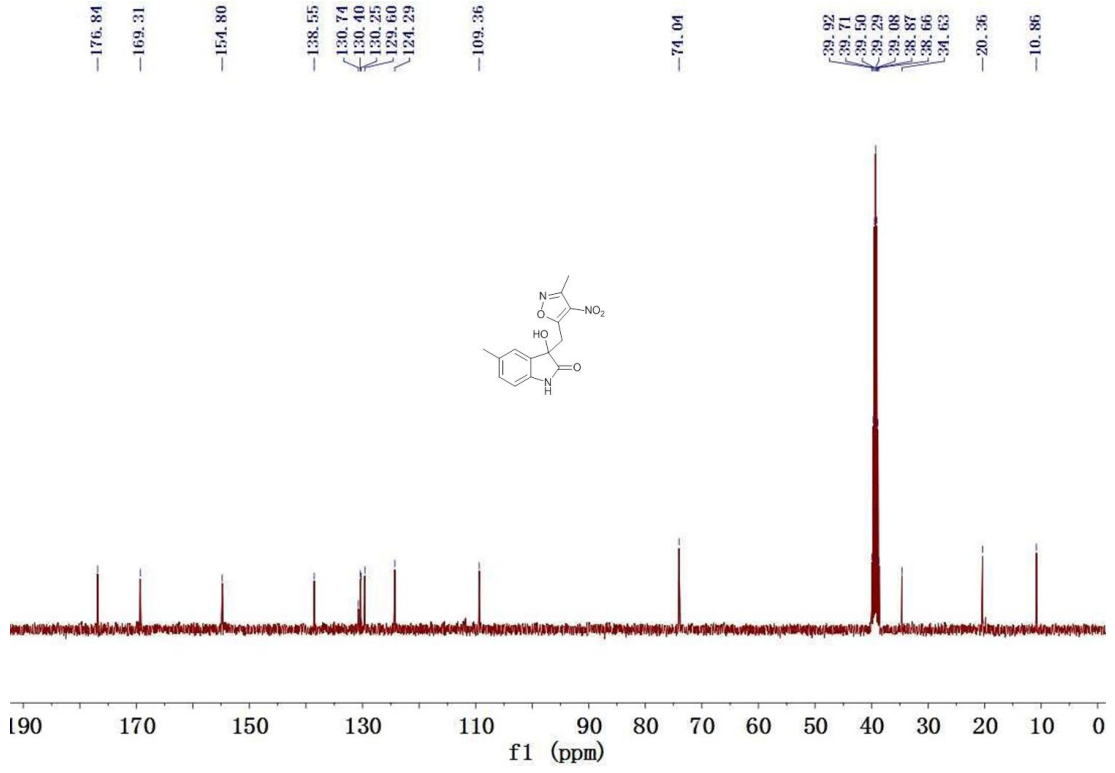
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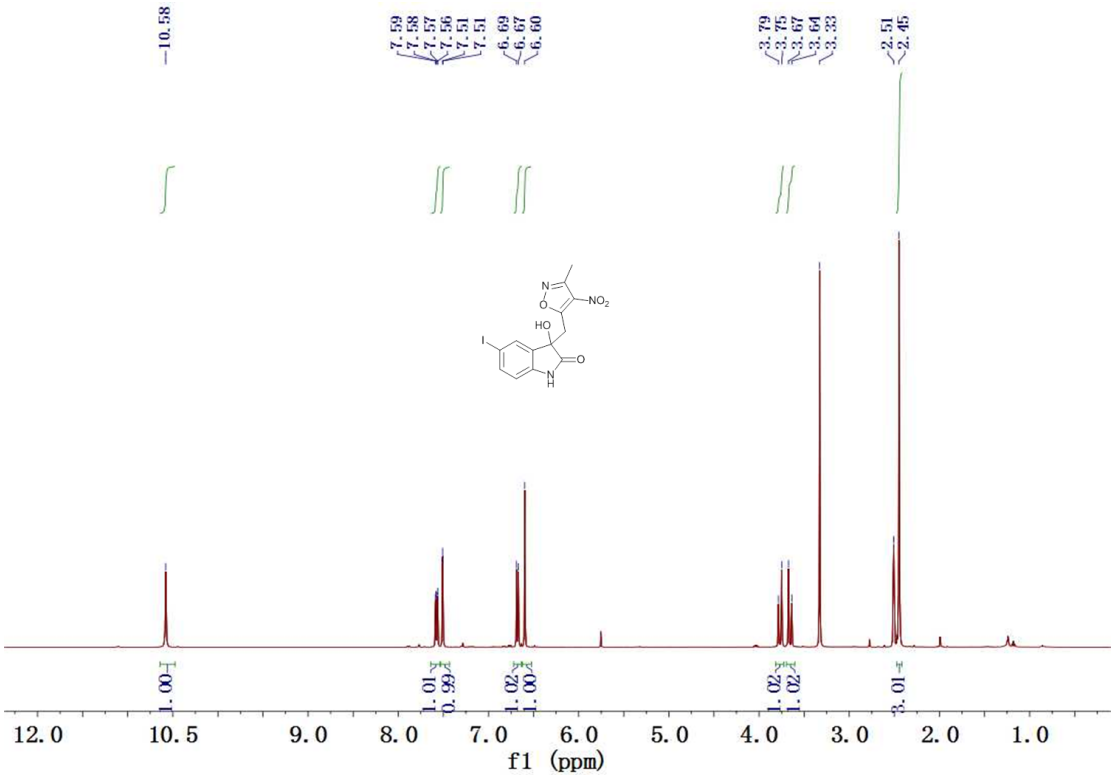
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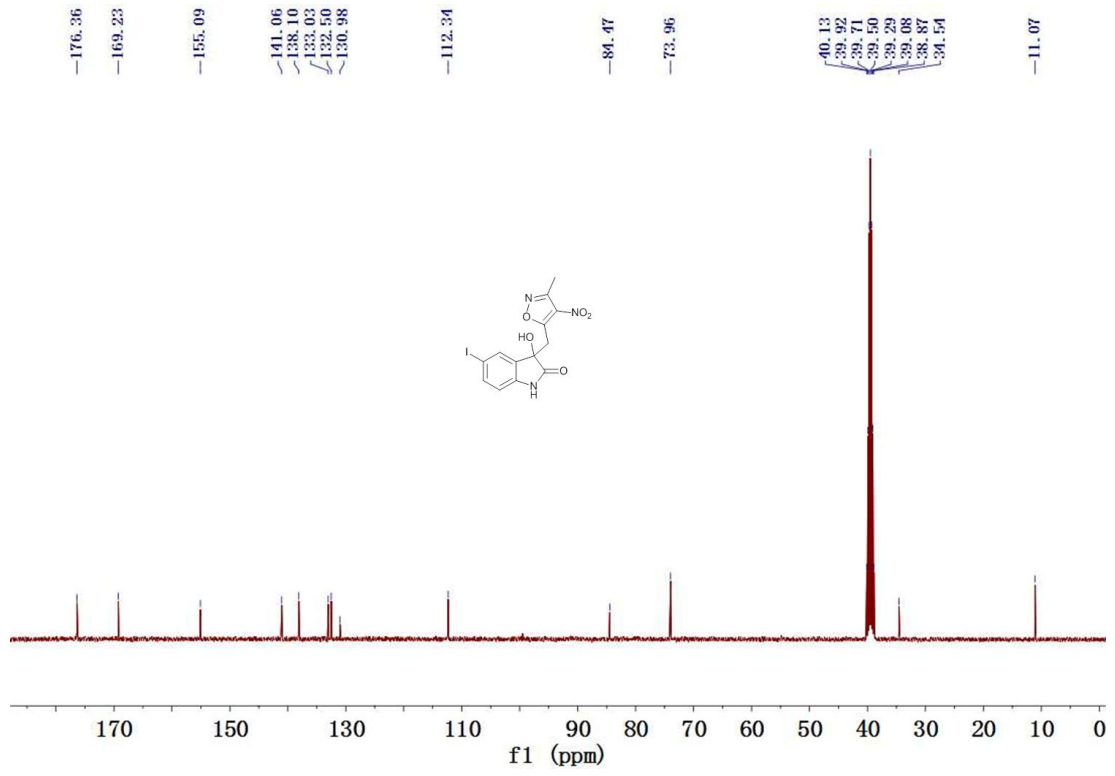
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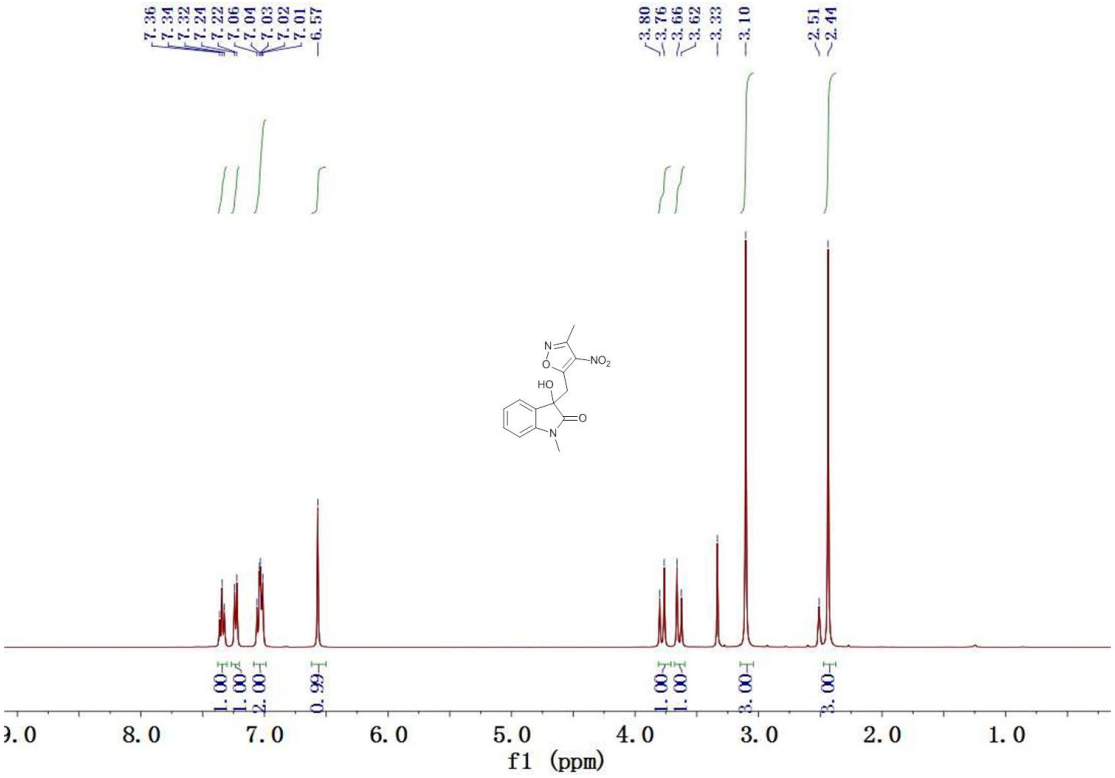
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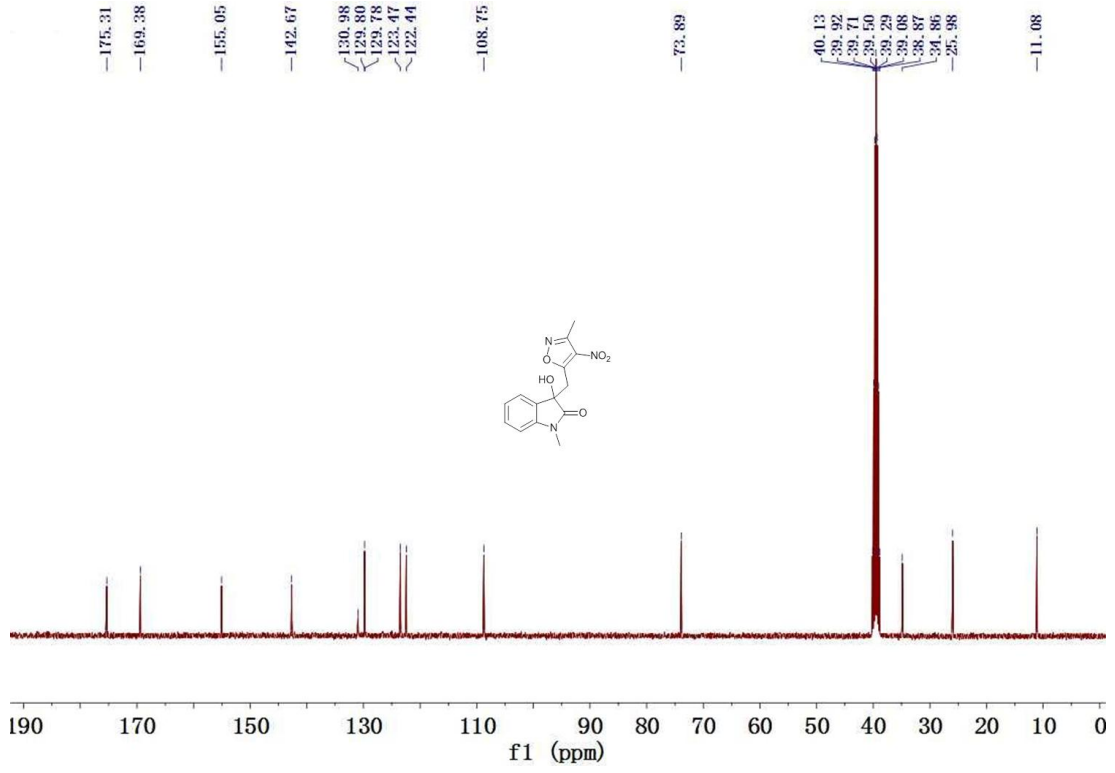
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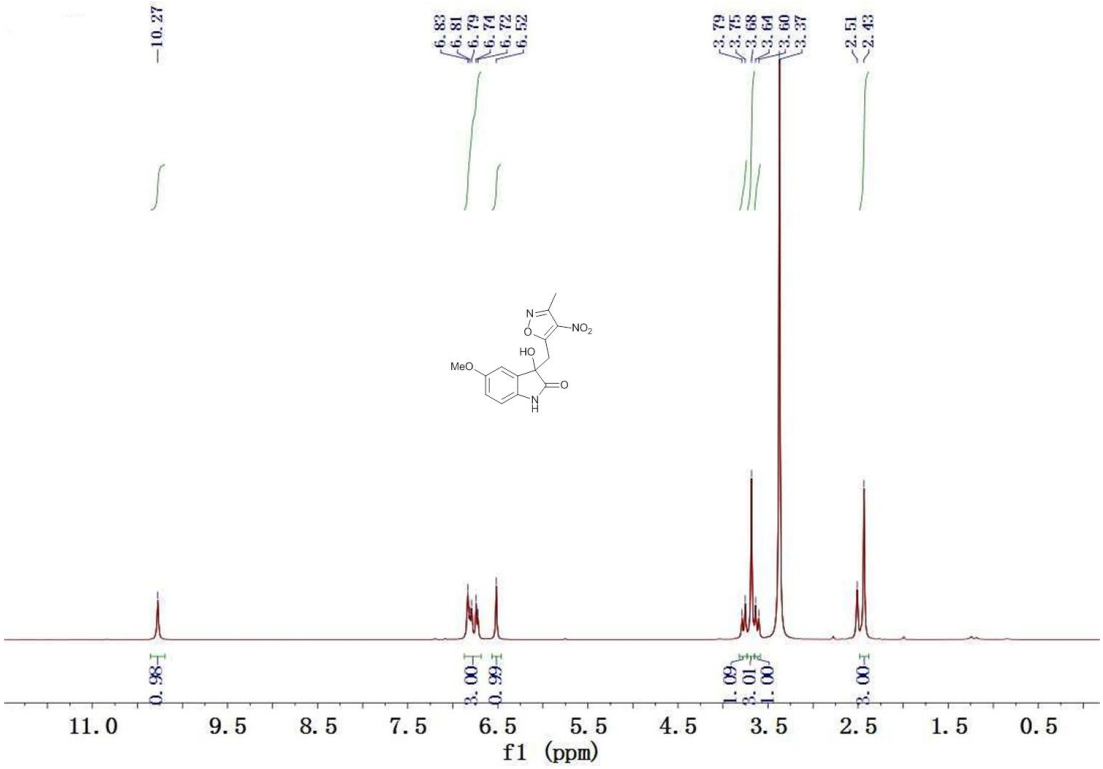
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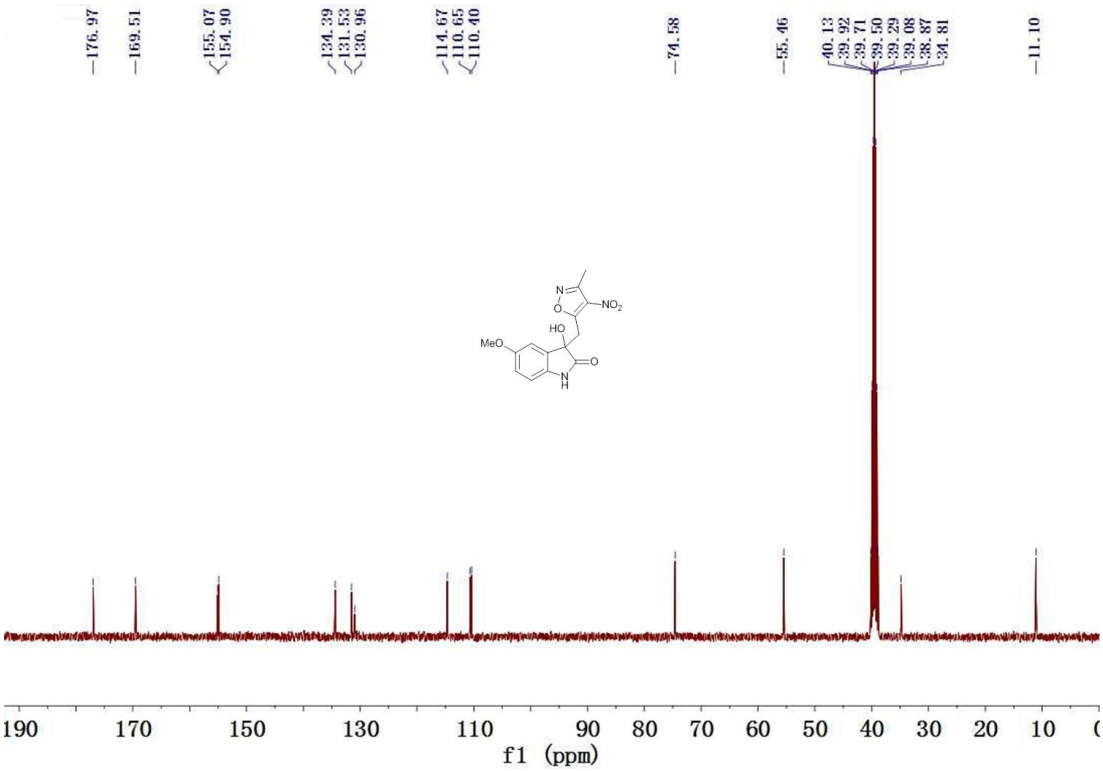
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39.08
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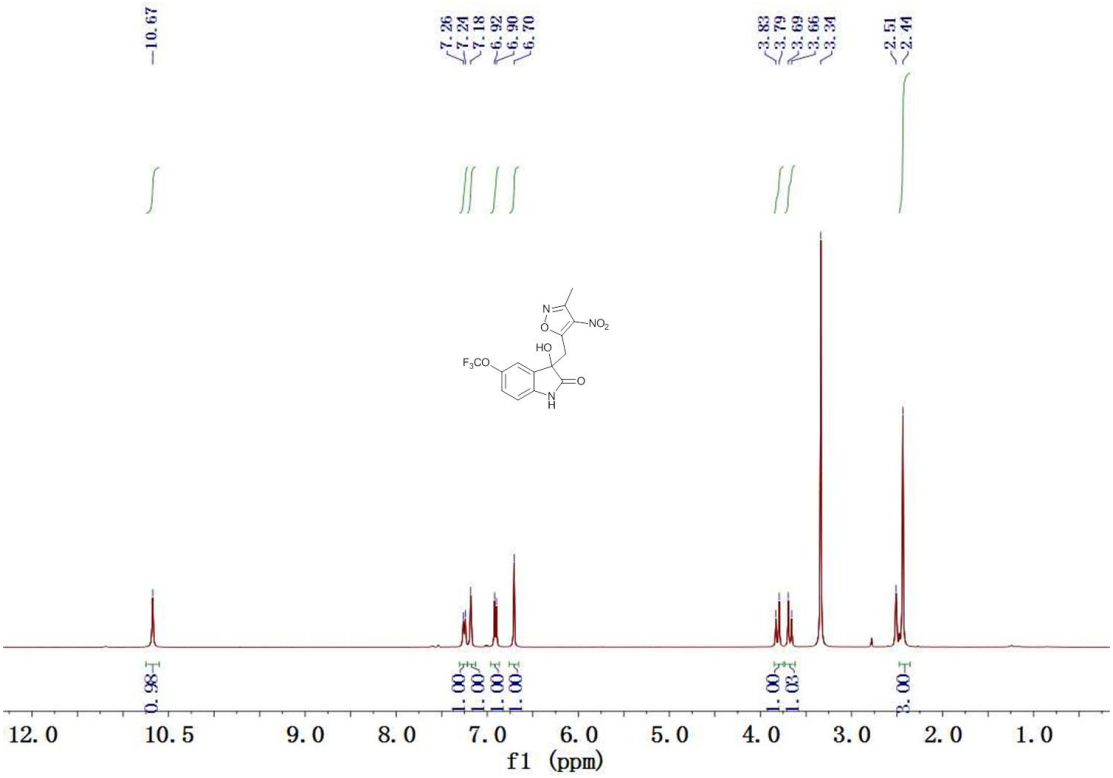
f1 (ppm)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1.00
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1.00
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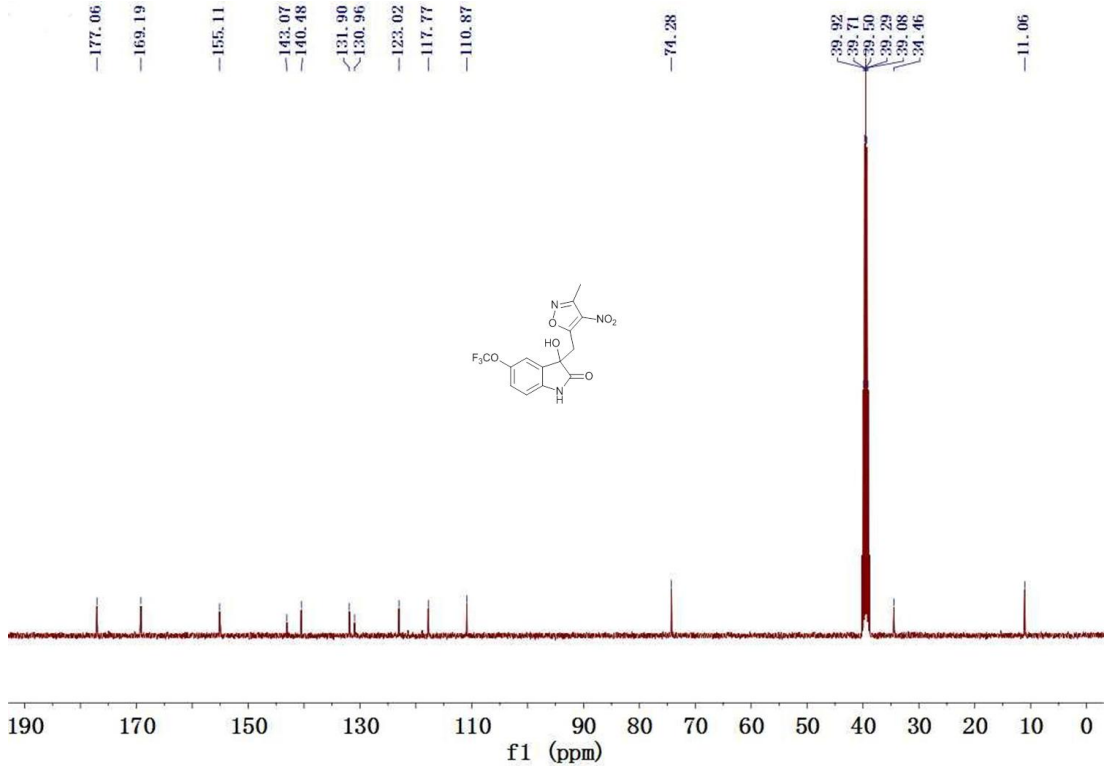
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39.29
39.08
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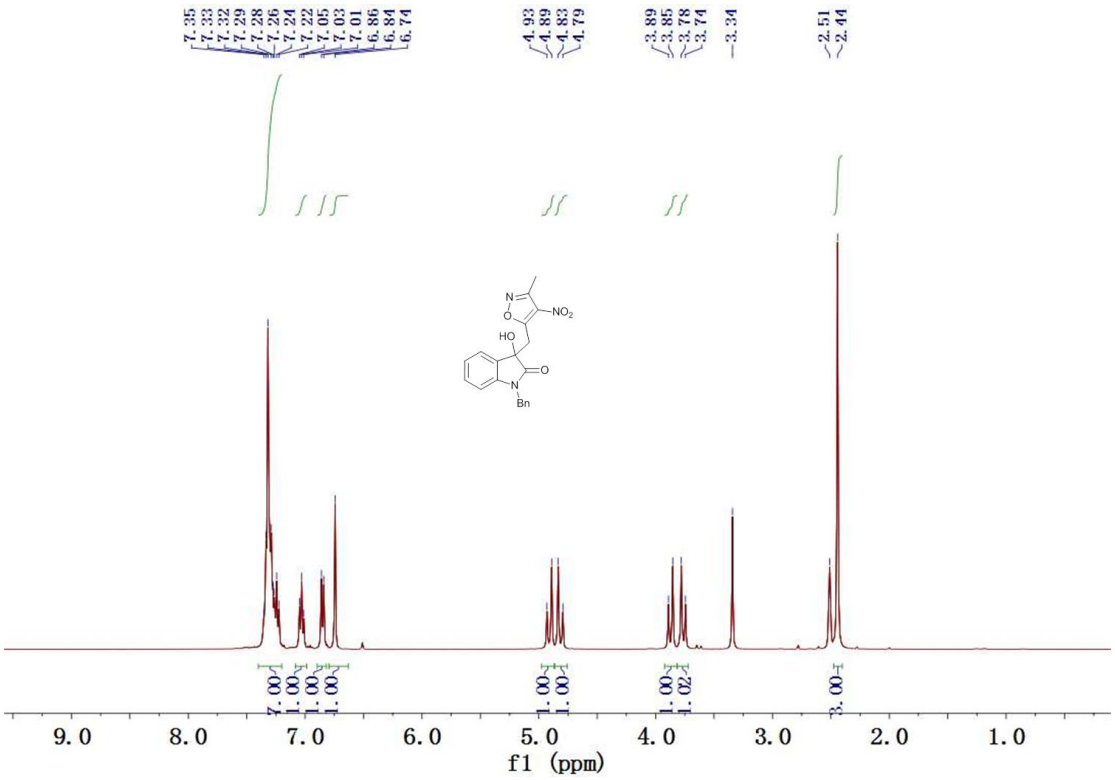
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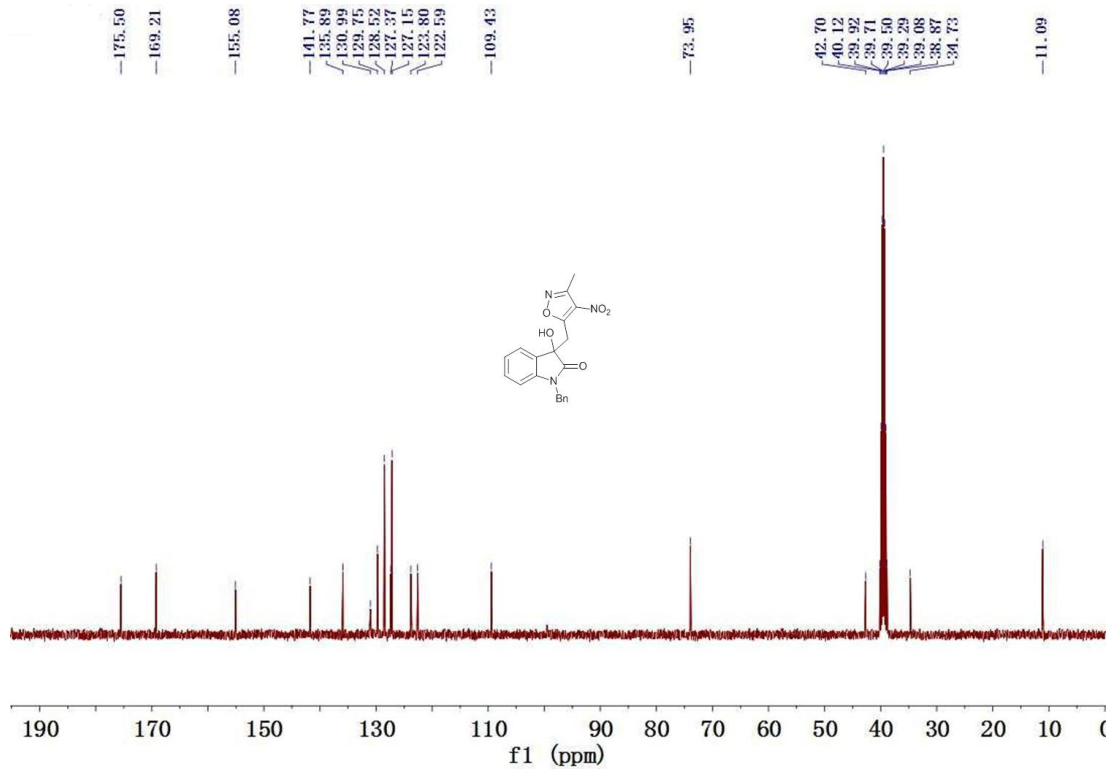
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39.71
39.50
39.29
39.08
38.87
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150
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110
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80
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60
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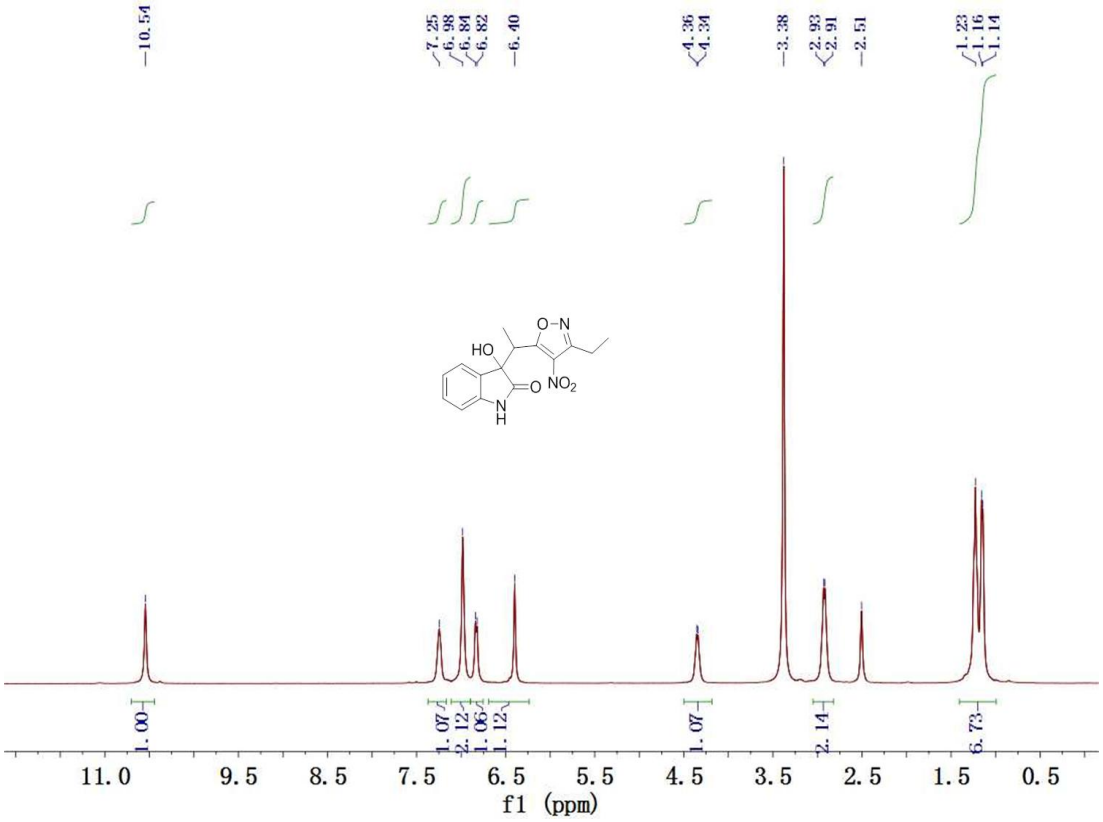
f1 (ppm)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4.34
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2.91
2.51
1.23
1.16
1.14
HO
O–N
O
NO2
N
H
1.00
1.07
2.12
1.06
1.12
1.07
2.14
6.73
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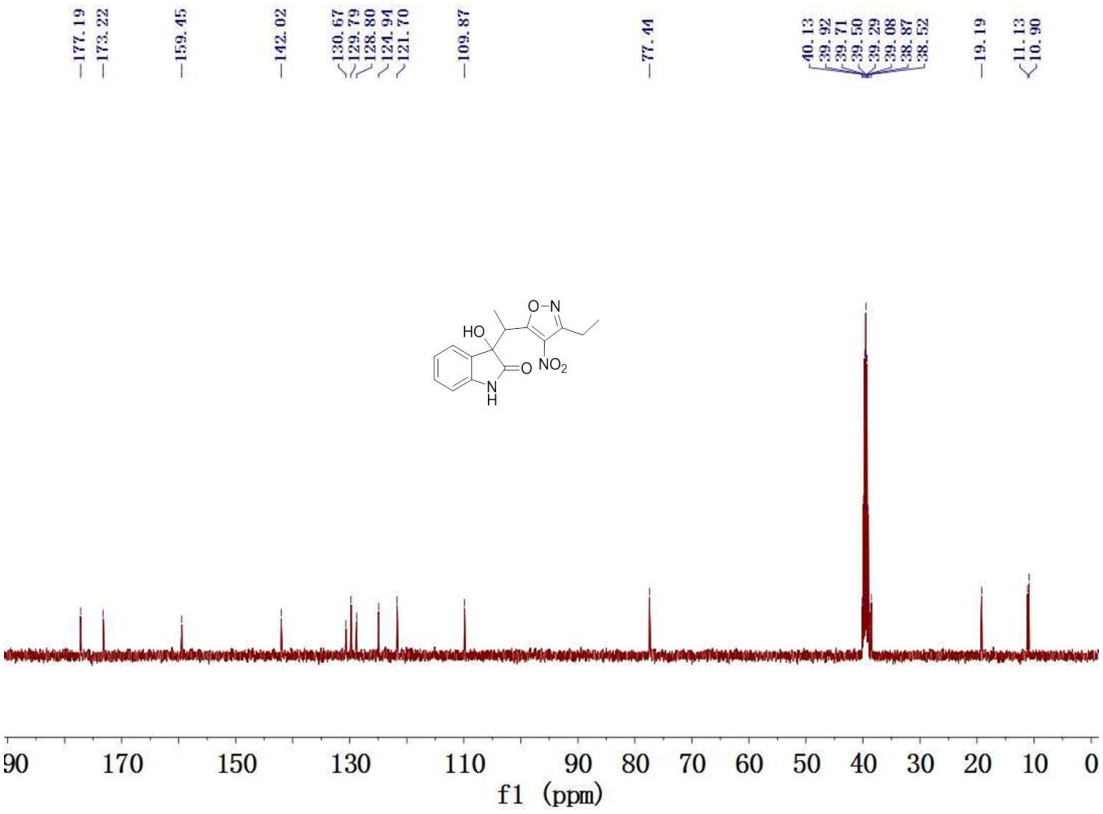
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39.29
39.08
38.87
38.52
19.19
11.13
10.90
HO
O–N
O
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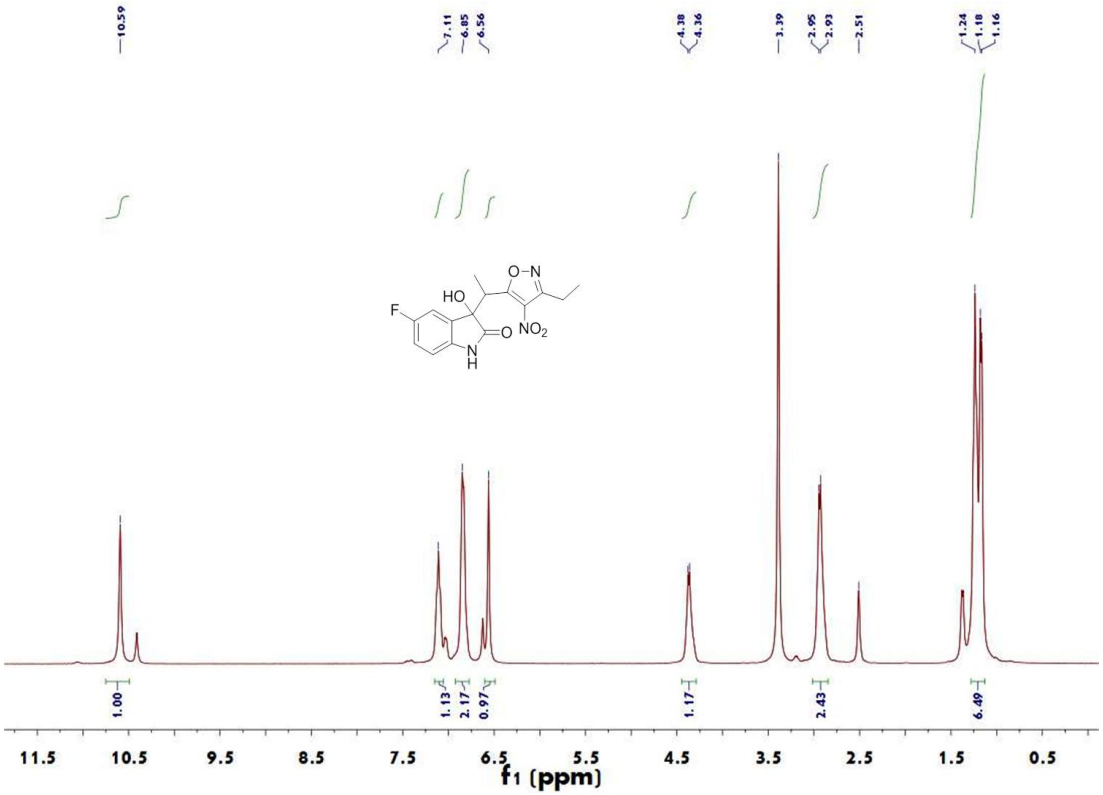
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O–N
F
O
NO2
N
H
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1.13
2.17
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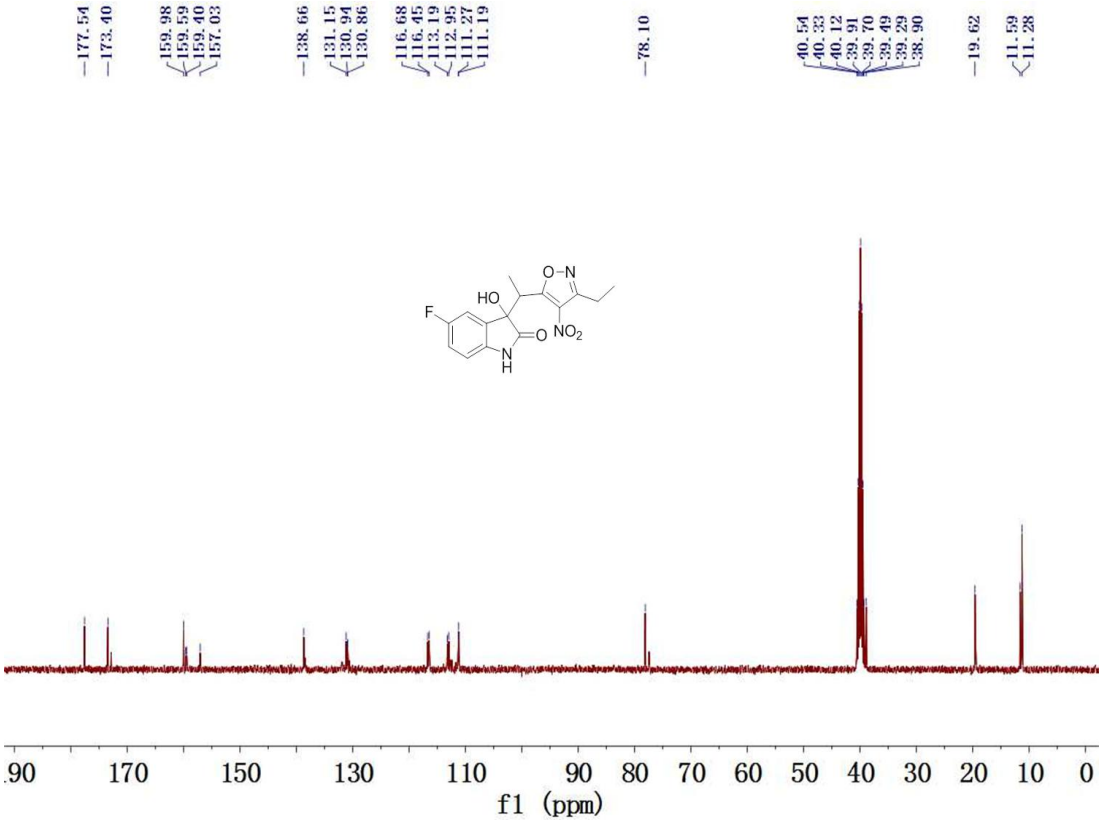
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111.19
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40.54
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39.70
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39.29
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19.62
11.59
11.28
HO
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F
O
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10
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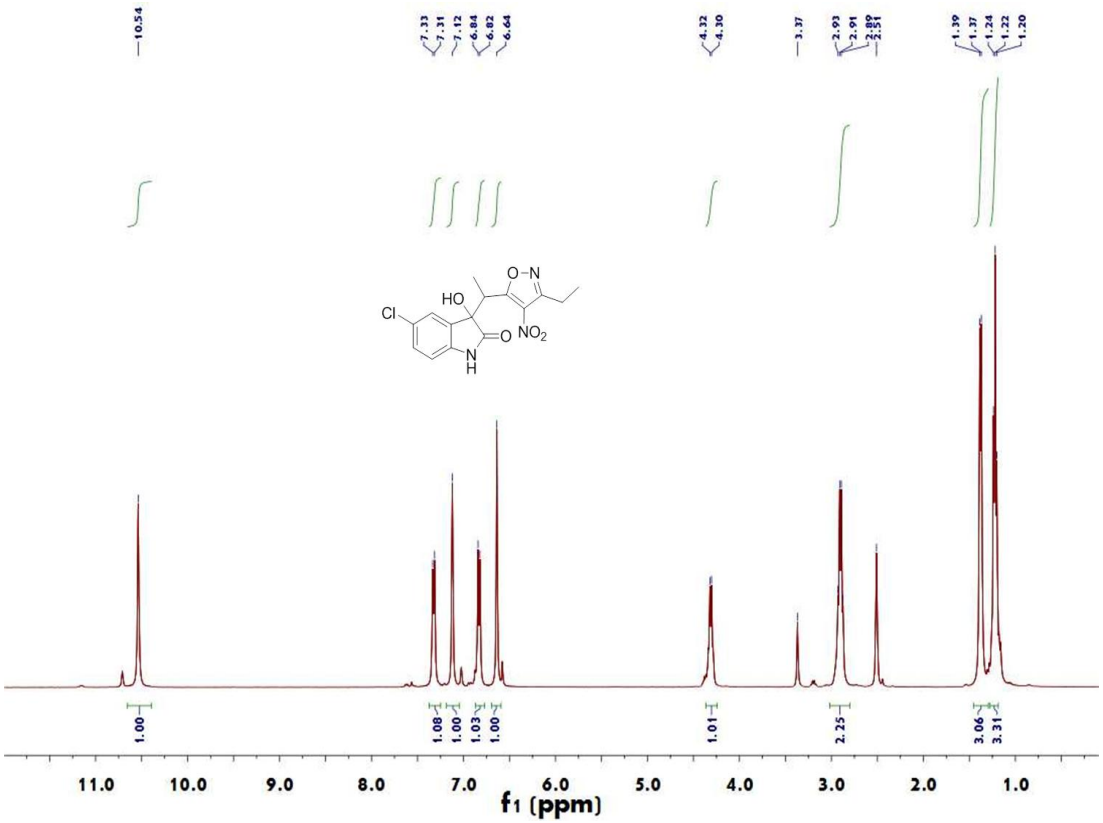
f1 (ppm)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3.37
2.93
2.91
2.89
2.51
1.39
1.37
1.24
1.22
1.20
HO
Cl
O
N
O
NO2
N
H
1.00
1.08
1.00
1.03
1.00
1.01
2.25
3.06
3.31
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10.0
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8.0
7.0
6.0
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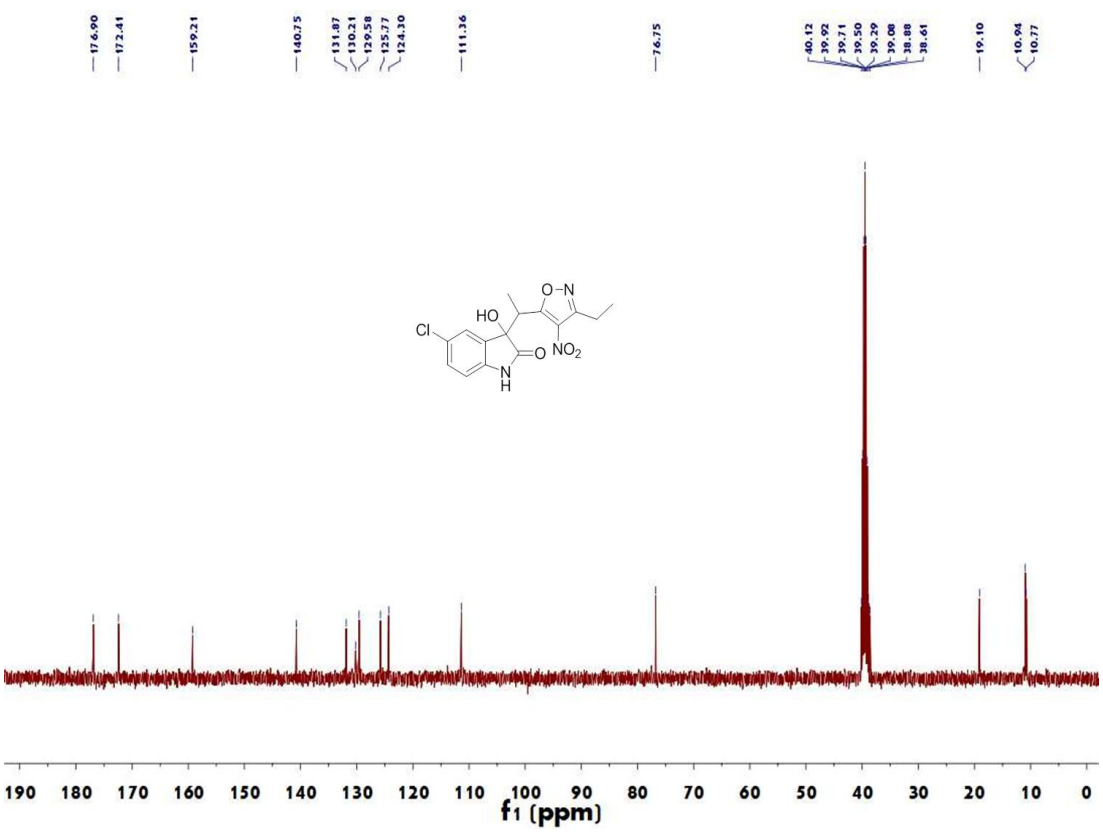
4.0
3.0
2.0
1.0
f1 (ppm)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39.71
39.50
39.29
39.08
38.88
38.61
19.10
10.94
10.77
HO
Cl
O
N
O
NO2
N
H
190
180
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120
110
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50
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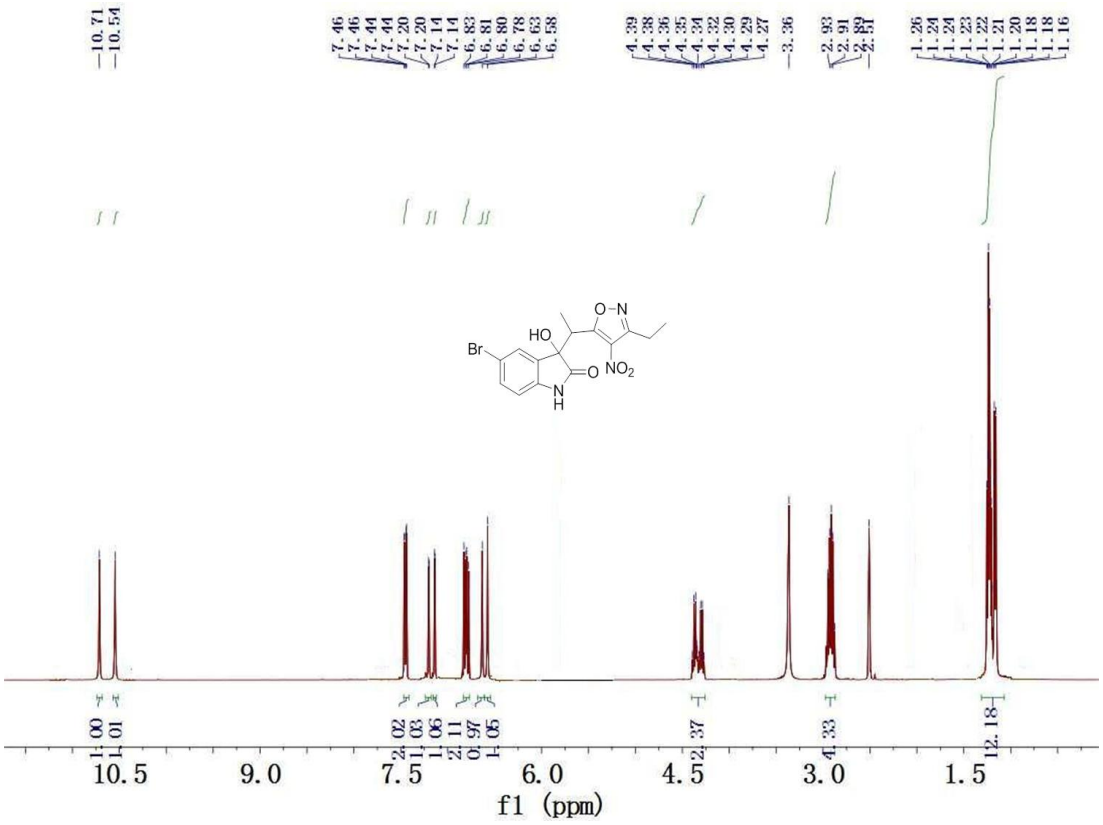
10
0
f1 (ppm)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7.14
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6.58
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4.29
4.27
3.36
2.93
2.91
2.89
2.87
1.26
1.24
1.24
1.23
1.22
1.21
1.20
1.18
1.18
1.16
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O-N
Br
O
NO2
N
H
1.00
1.01
2.02
1.03
1.06
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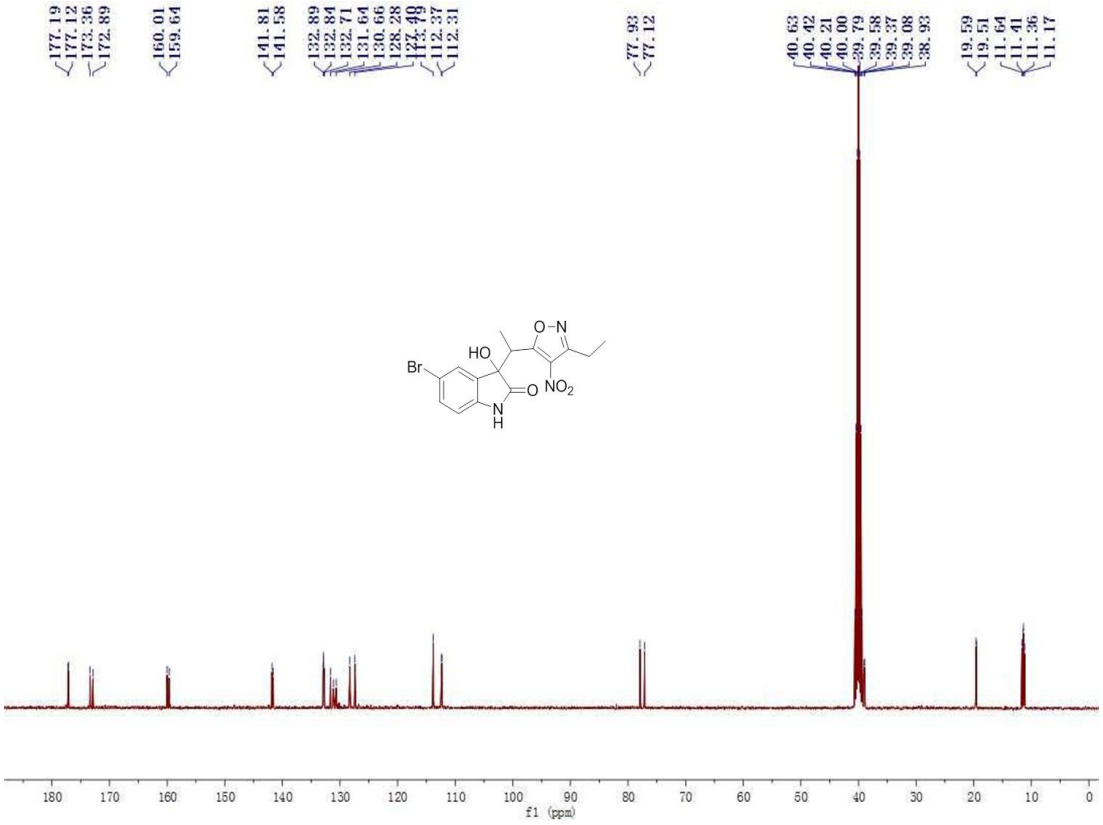
f1 (ppm)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77.93
77.12
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40.42
40.21
40.00
39.79
39.58
39.37
39.08
38.93
19.59
19.51
11.64
11.41
11.36
11.17
HO
O-N
Br
O
NO2
N
H
180
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130
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110
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90
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70
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50
40
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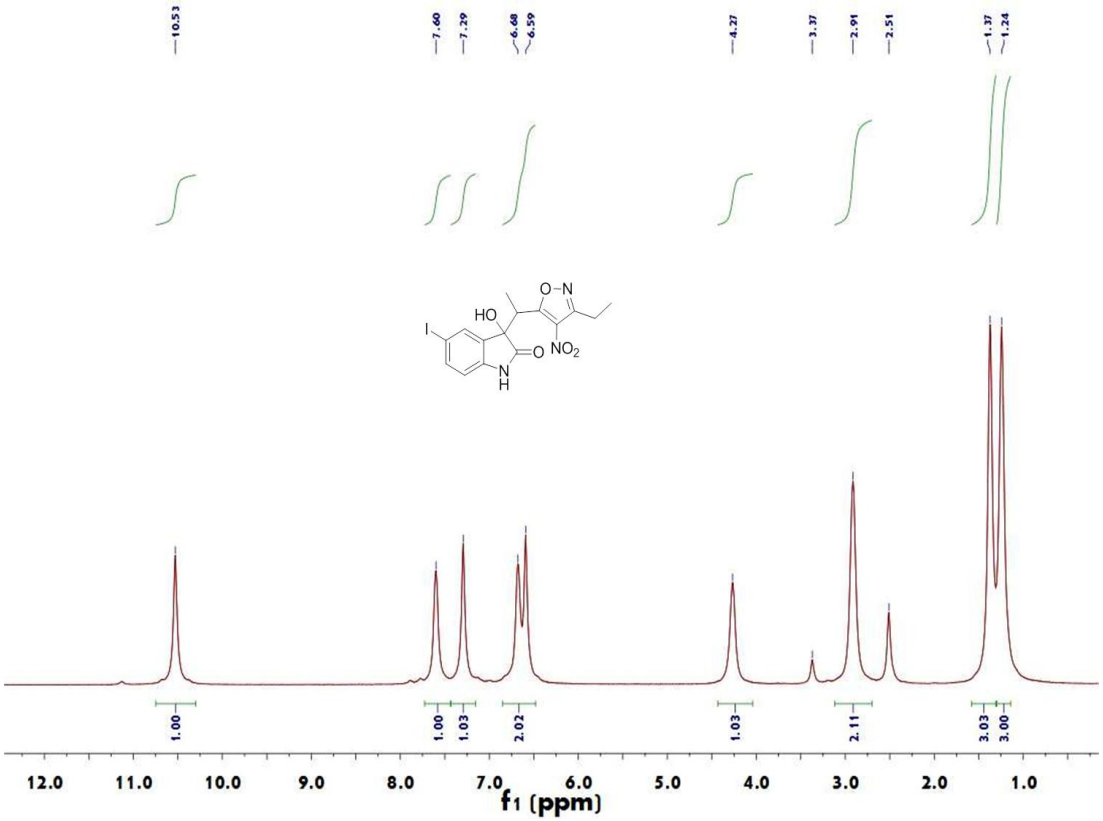
f1 (ppm)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1.37
1.24
HO
O–N
I
O
NO2
N
H
1.00
1.00
1.03
2.02
1.03
2.11
3.03
3.00
12.0
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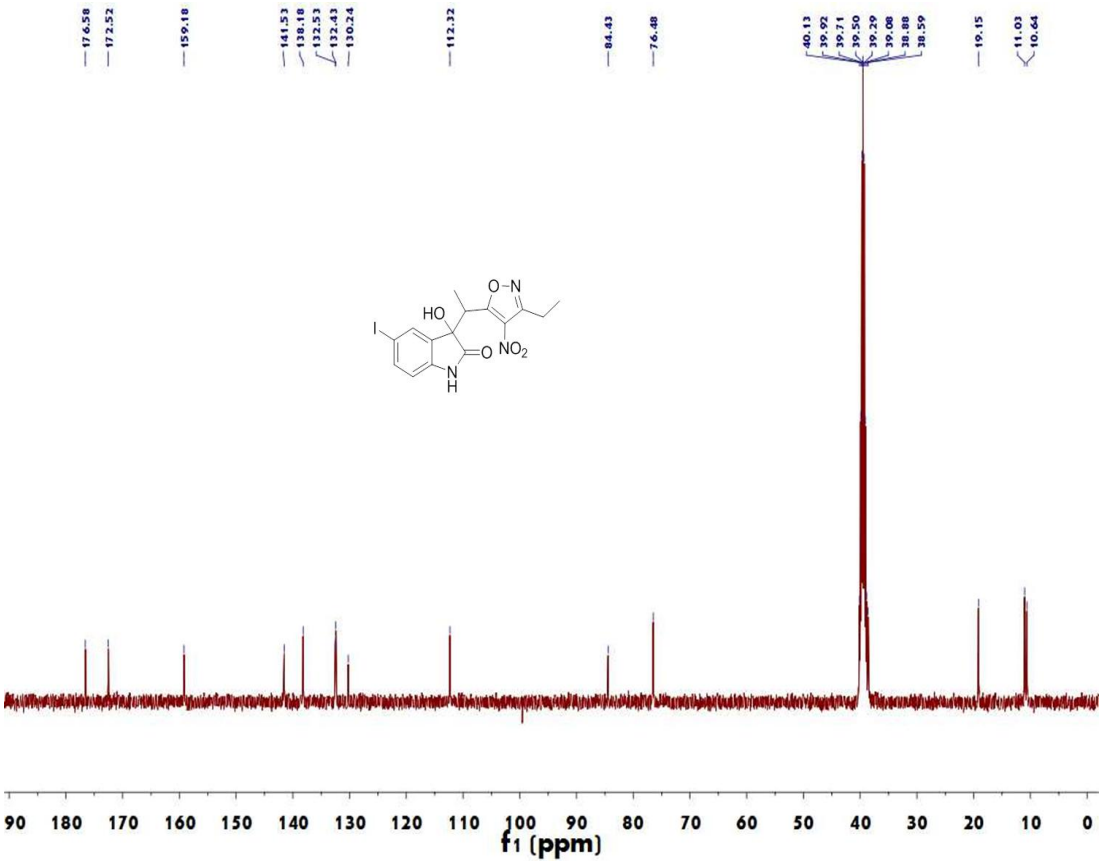
1.0
f1 (ppm)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39.50
39.29
39.08
38.88
38.59
19.15
11.03
10.64
HO
O–N
I
O
NO2
N
H
90
180
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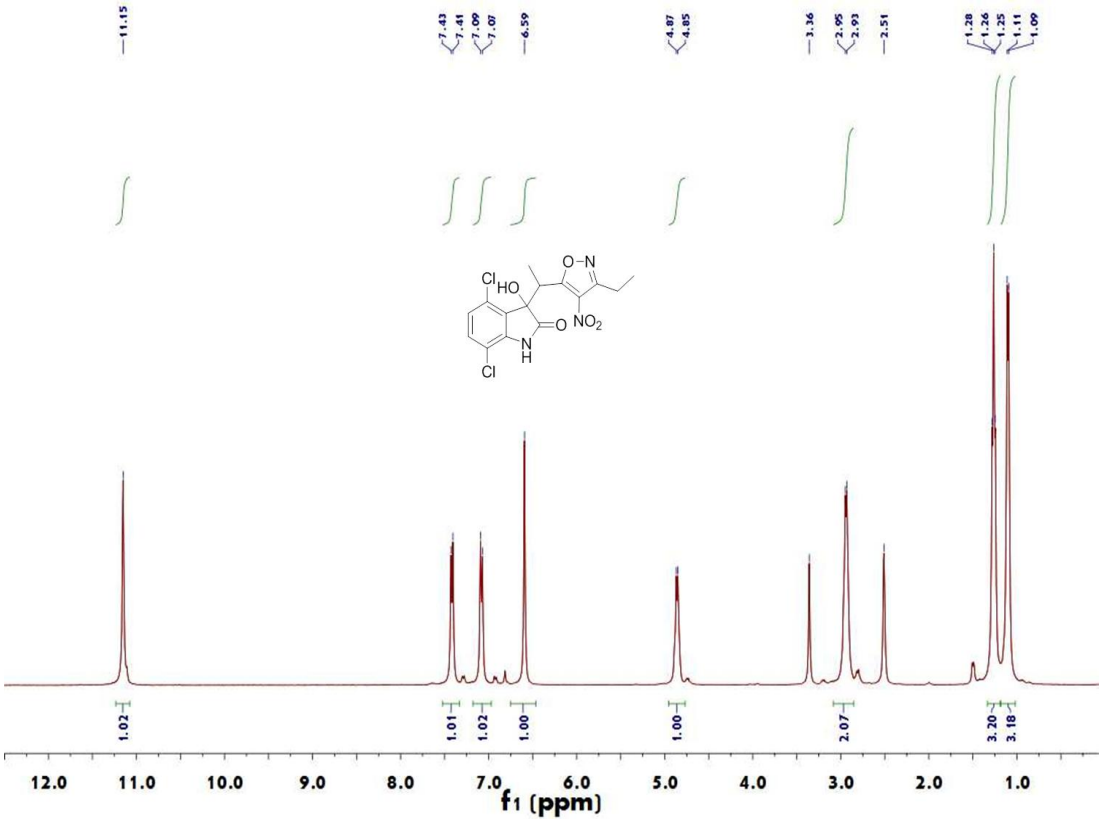
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4.85
3.36
2.95
2.93
2.51
1.28
1.26
1.25
1.11
1.09
Cl
HO
O-N
O
NO2
N
H
Cl
1.02
1.01
1.02
1.00
1.00
2.07
3.20
3.18
12.0
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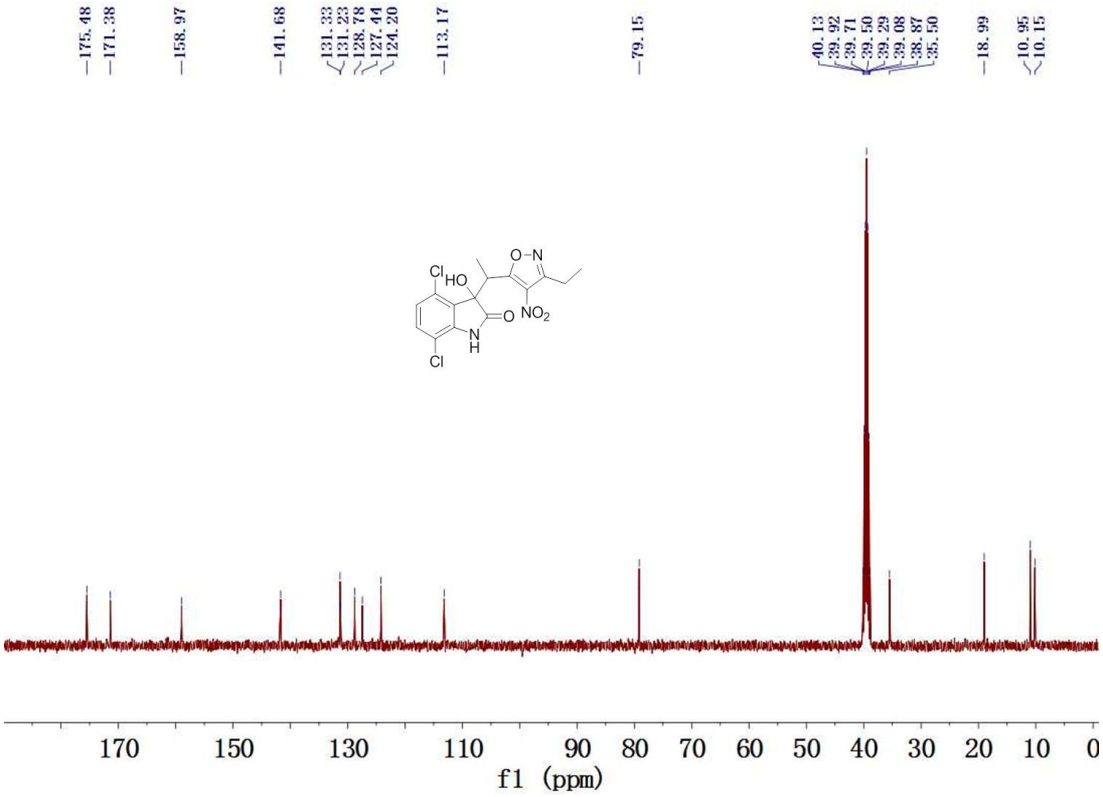
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39.71
39.50
39.29
39.08
38.87
35.50
18.99
10.95
10.15
Cl
HO
O-N
O
NO2
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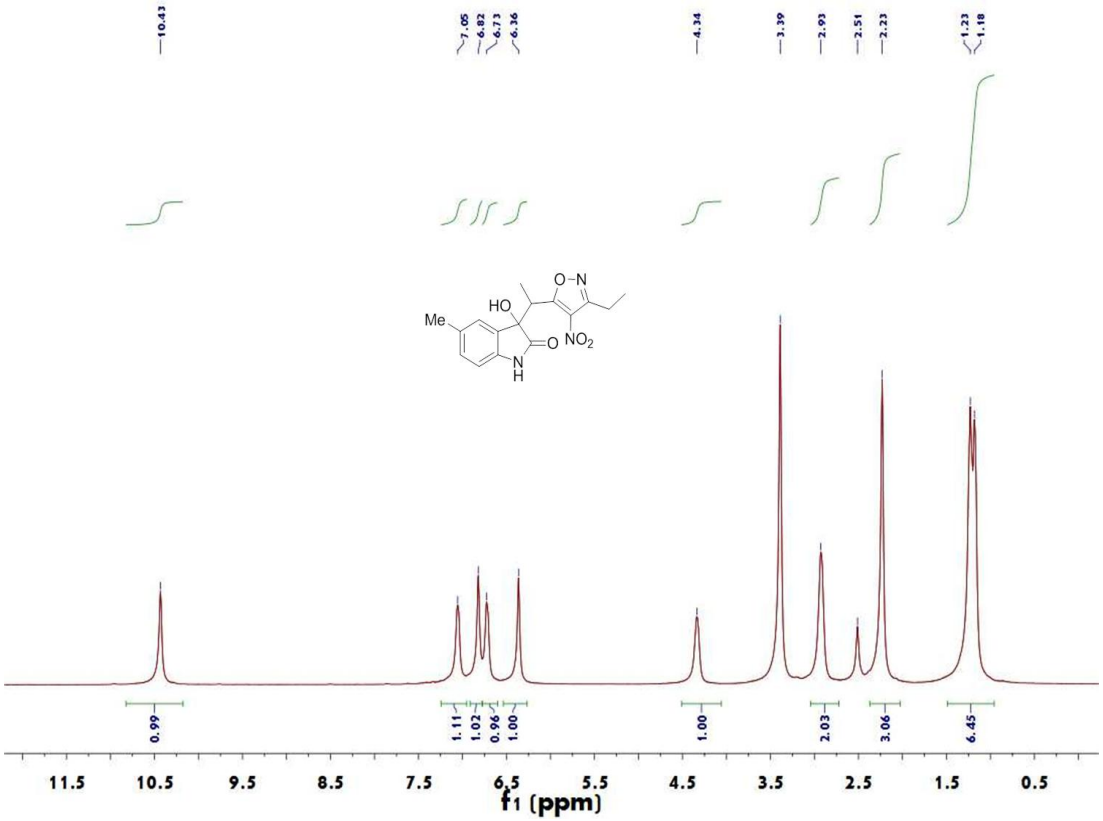
f1 (ppm)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2.23
1.23
1.18
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Me
O
N
H
O–N
NO2
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1.11
1.02
0.96
1.00
1.00
2.03
3.06
6.45
11.5
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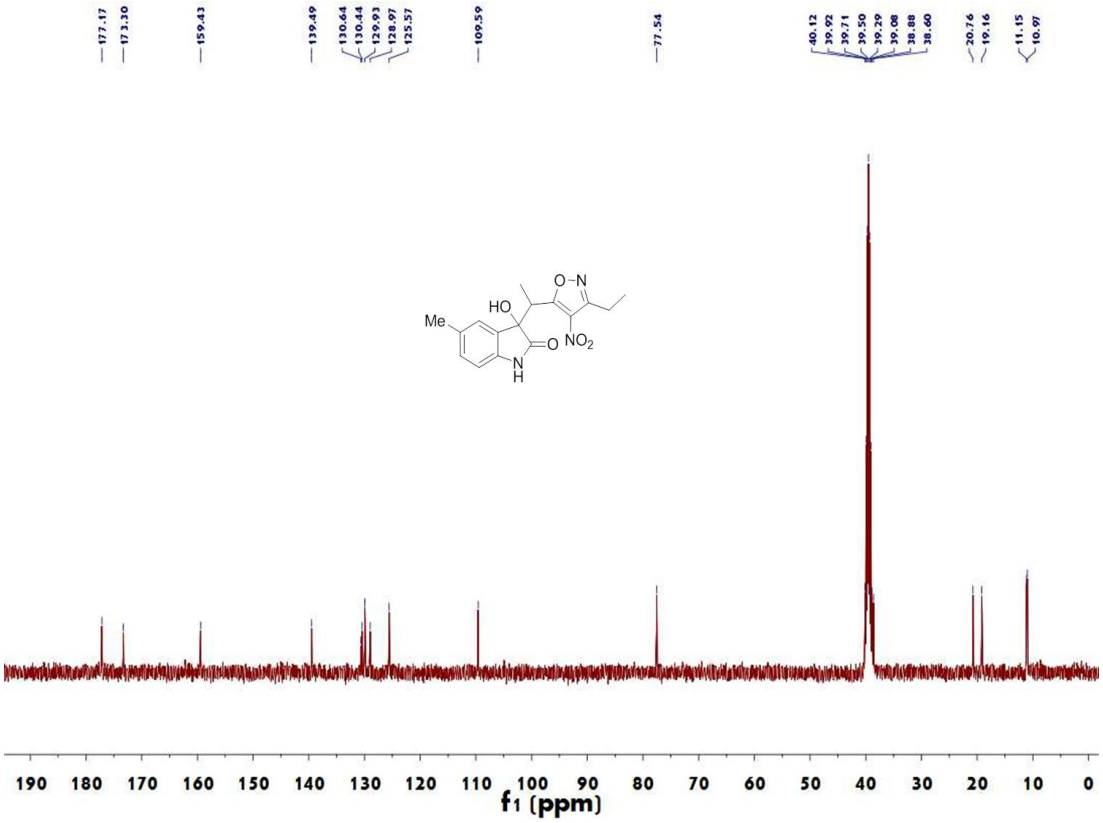
0.5
f1 (ppm)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39.50
39.29
39.08
38.88
38.60
20.76
19.16
11.15
10.97
HO
Me
O
N
H
O–N
NO2
190
180
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110
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90
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50
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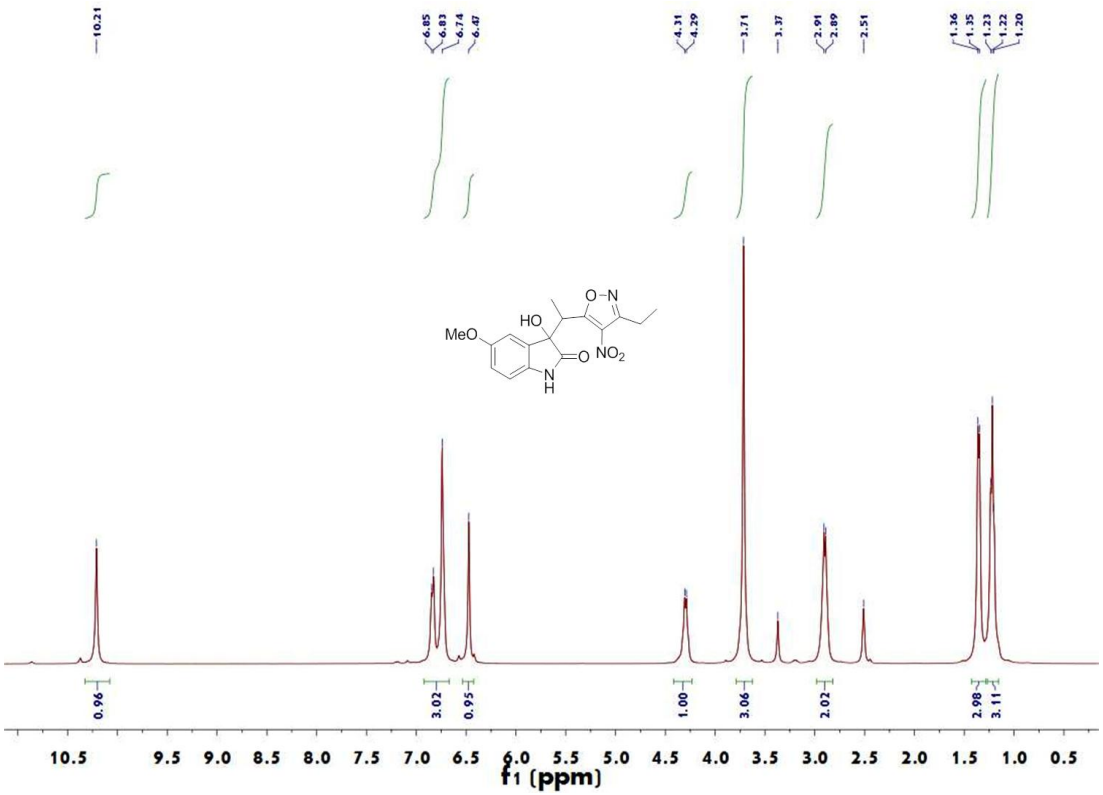
10
0
f1 (ppm)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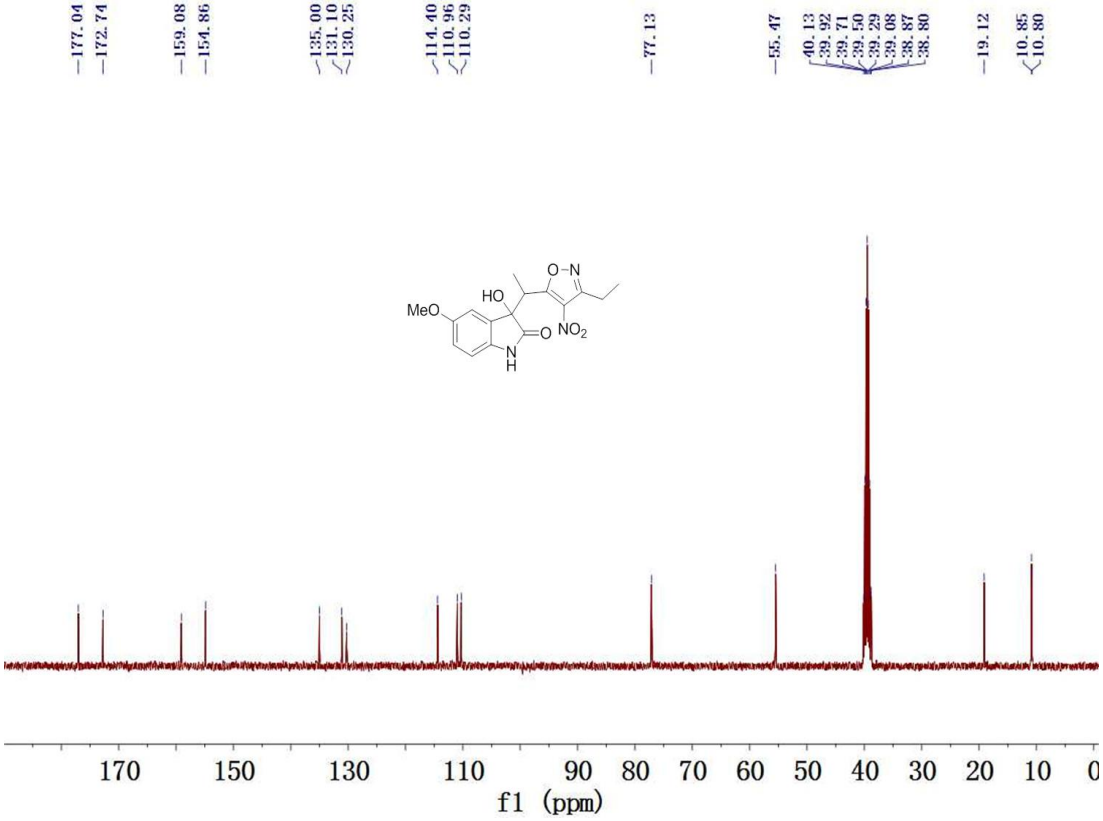
2.51
1.36
1.35
1.23
1.22
1.20
HO
MeO
O–N
O
NO2
N
H
0.96
3.02
0.95
1.00
3.06
2.02
2.98
3.11
10.5 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)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38.80
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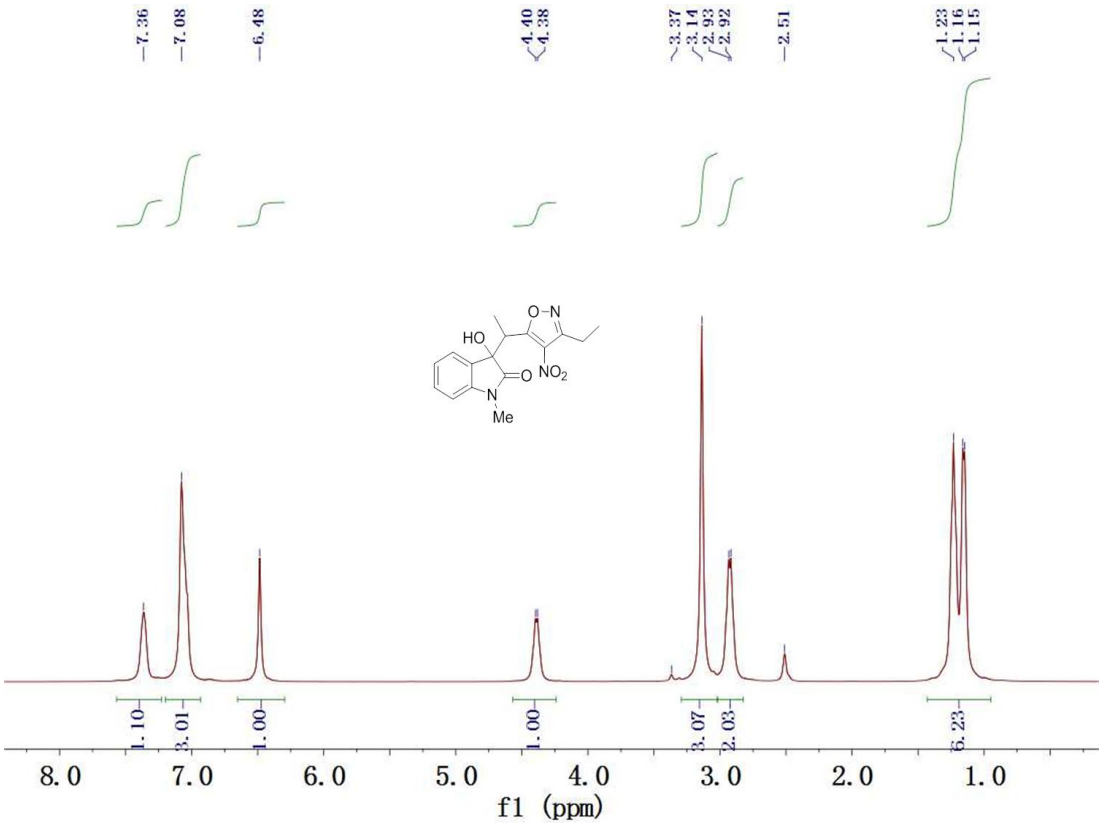
O
NO2
N
H
170 150 130 110 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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2.92
2.51
1.23
1.16
1.15
HO
O–N
NO2
O
N
Me
1.10
3.01
1.00
1.00
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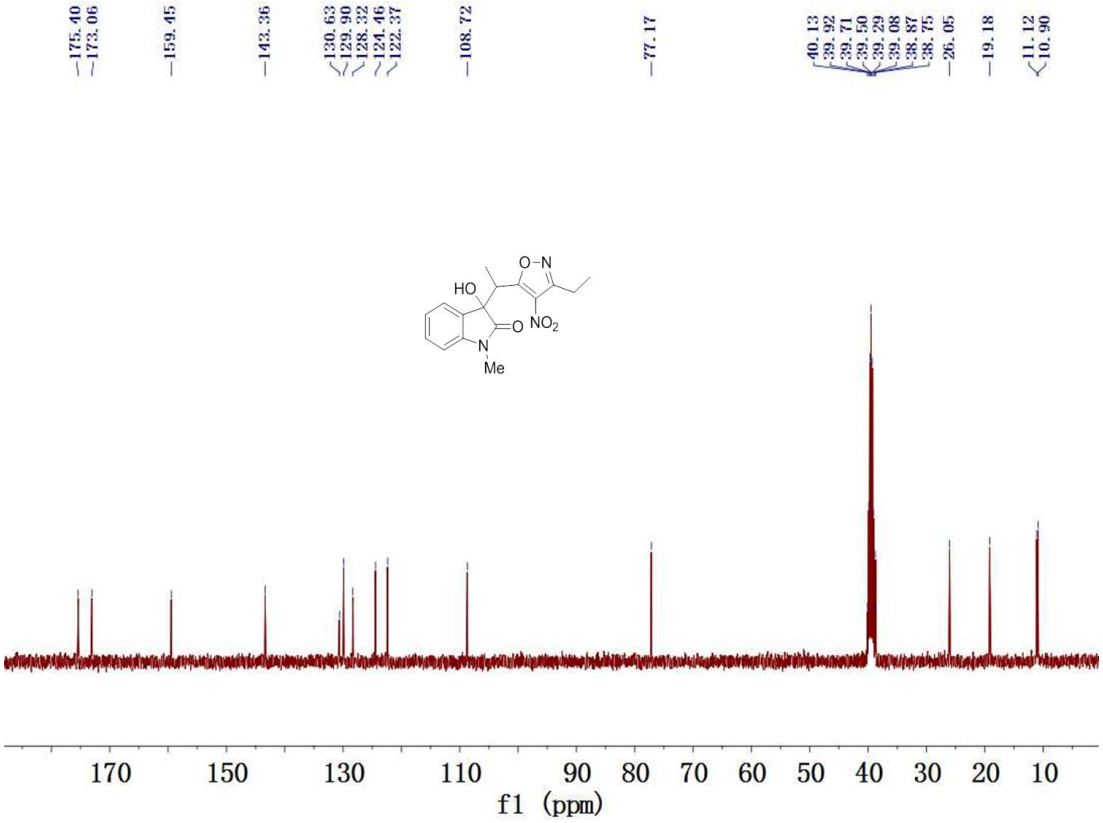
1.0
f1 (ppm)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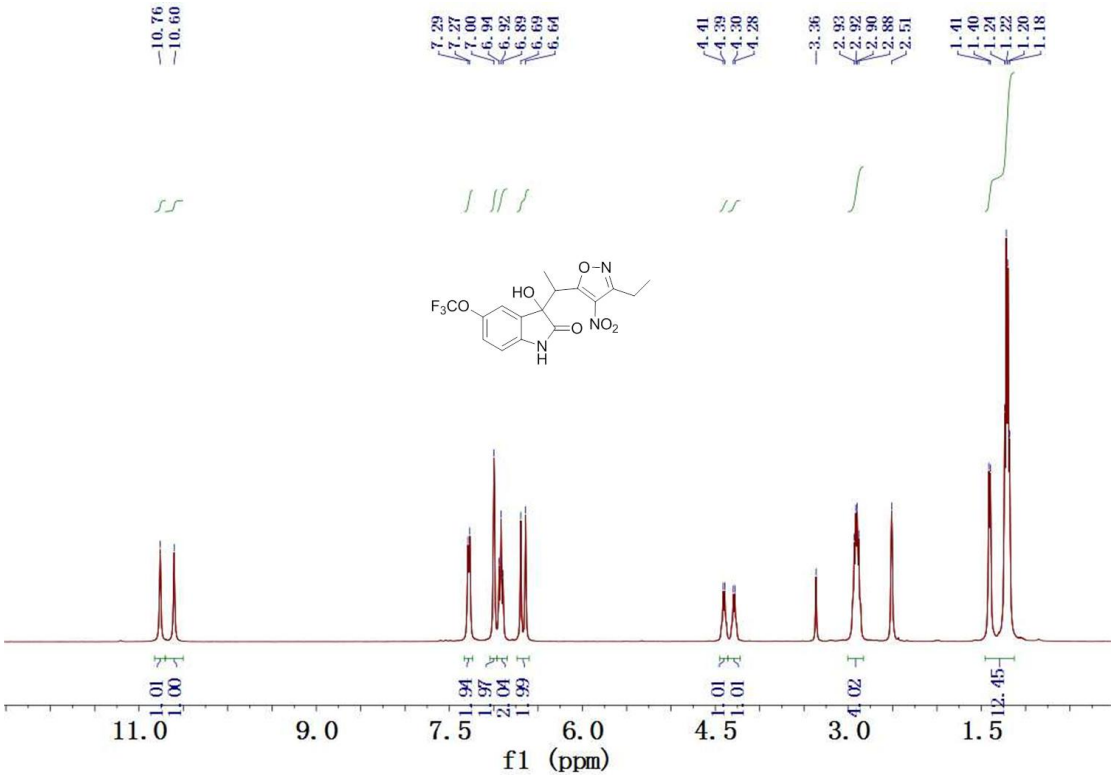
77.17
40.13
39.92
39.71
39.50
39.29
39.08
38.87
38.75
26.05
19.18
11.12
10.90
HO
O–N
NO2
O
N
Me
170
150
130
110
90
80
70
60
50
40
30
20
10
f1 (ppm)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4.30
4.28
3.36
2.93
2.92
2.90
2.88
2.51
1.41
1.40
1.24
1.22
1.20
1.18
HO
O-N
F3CO
O
NO2
N
H
1.01
1.00
1.94
1.97
2.04
1.99
1.01
1.01
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12.45
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4.5
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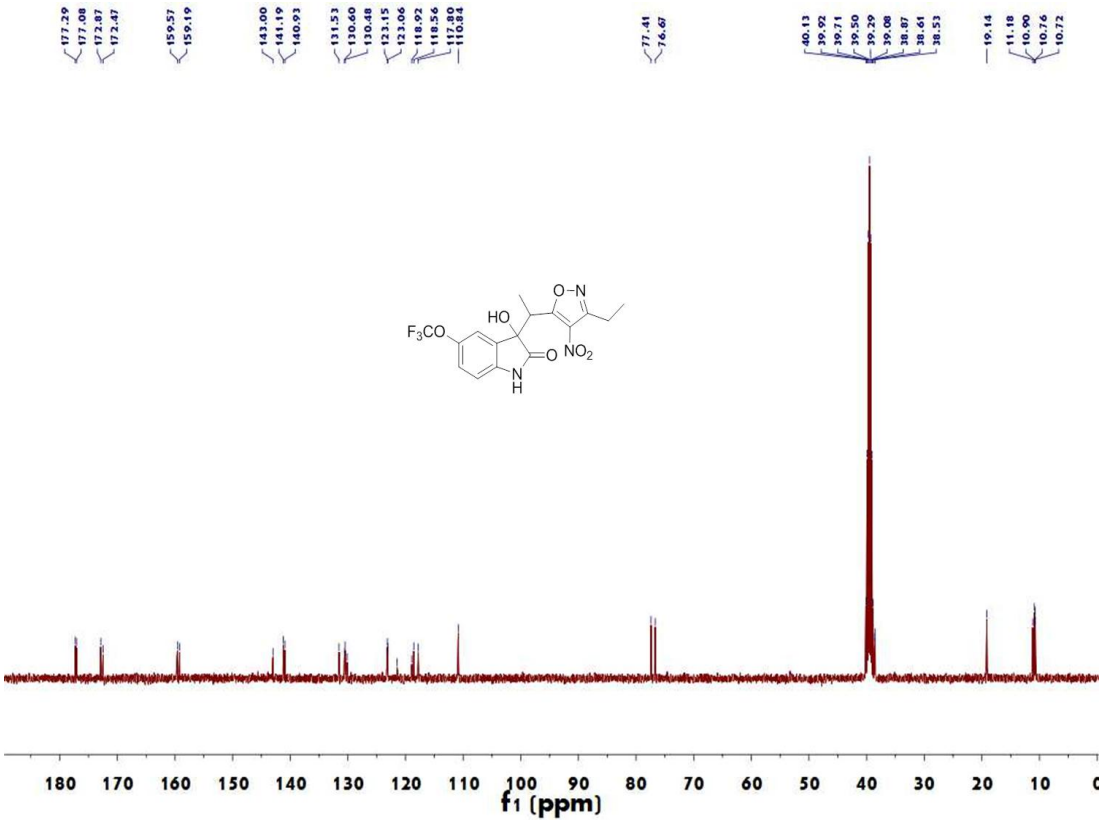
f1 (ppm)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172.47
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123.15
123.06
118.92
118.56
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39.92
39.71
39.50
39.29
39.08
38.87
38.61
38.53
19.14
11.18
10.90
10.76
10.72
HO
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F3CO
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NO2
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H
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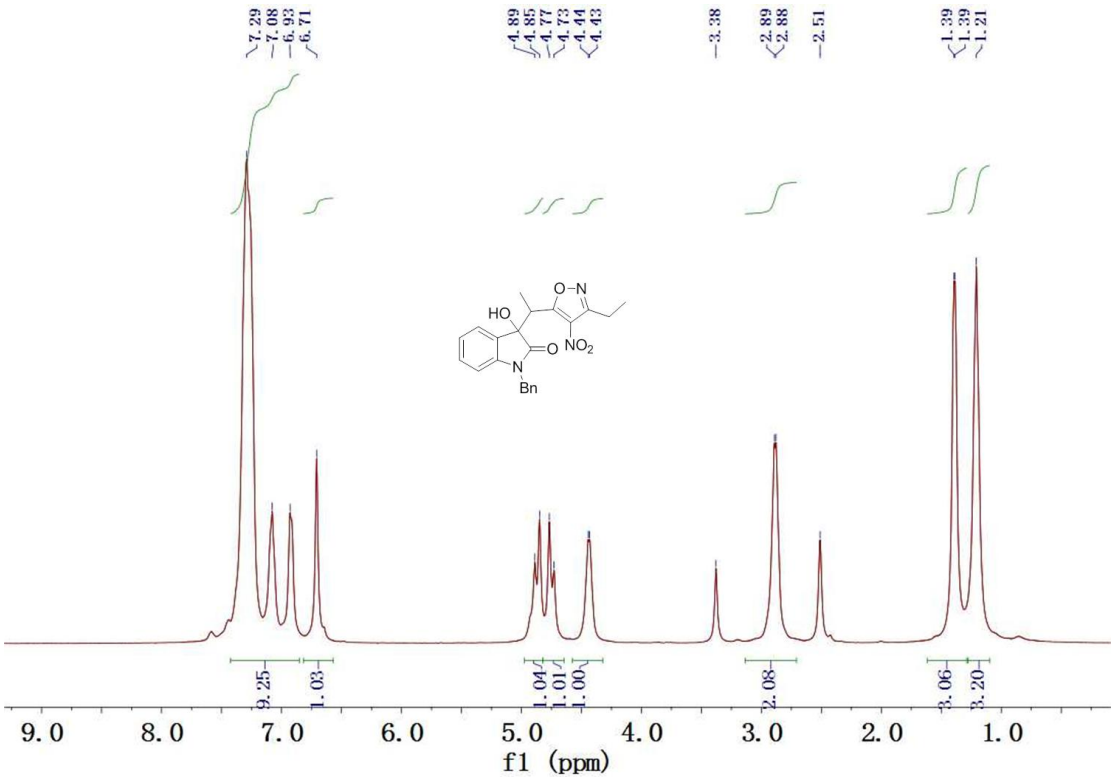
f1 (ppm)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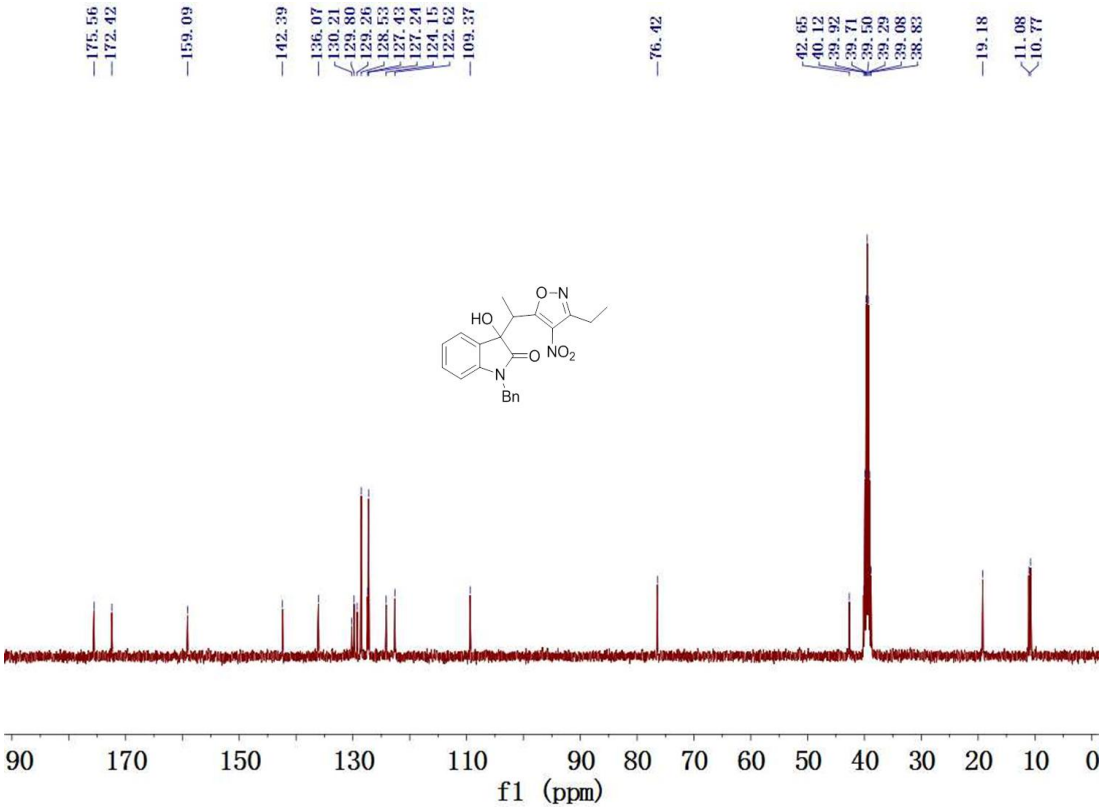
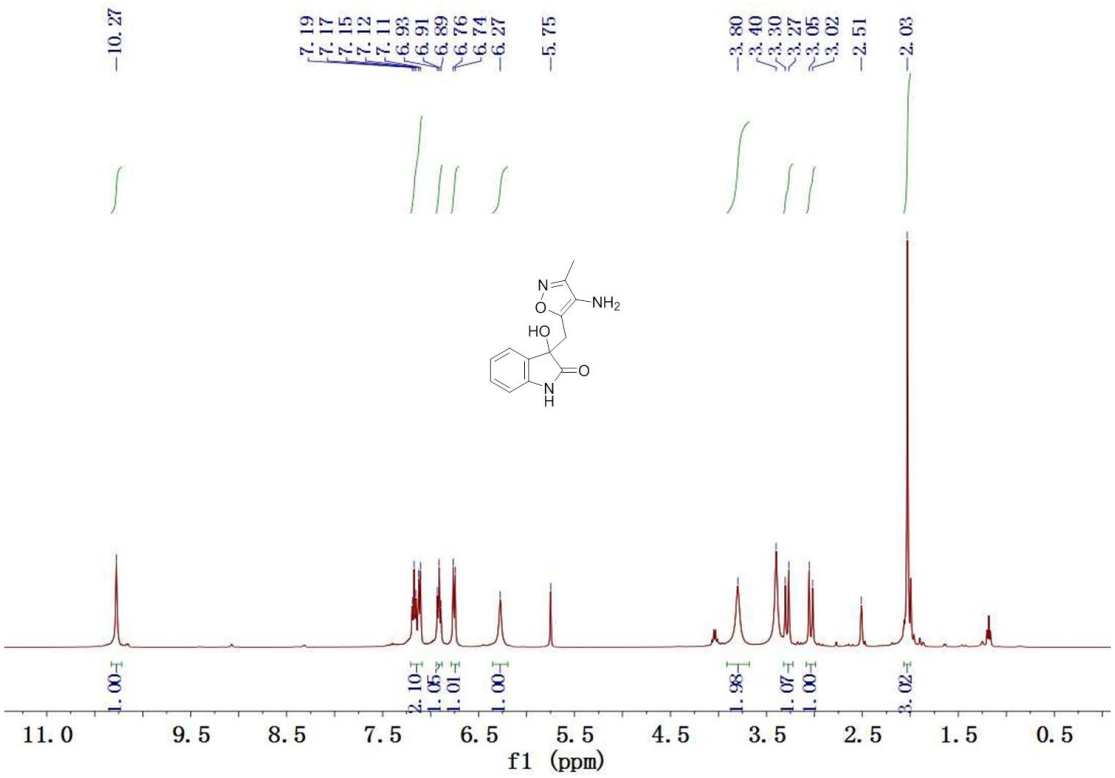
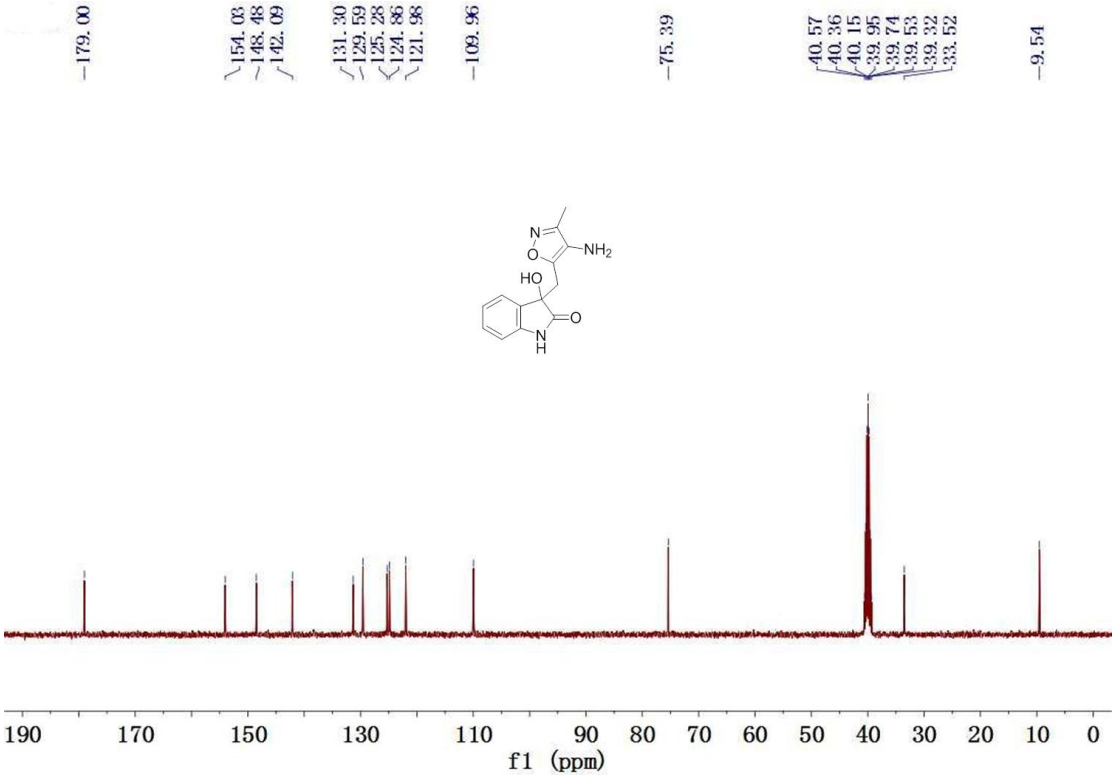
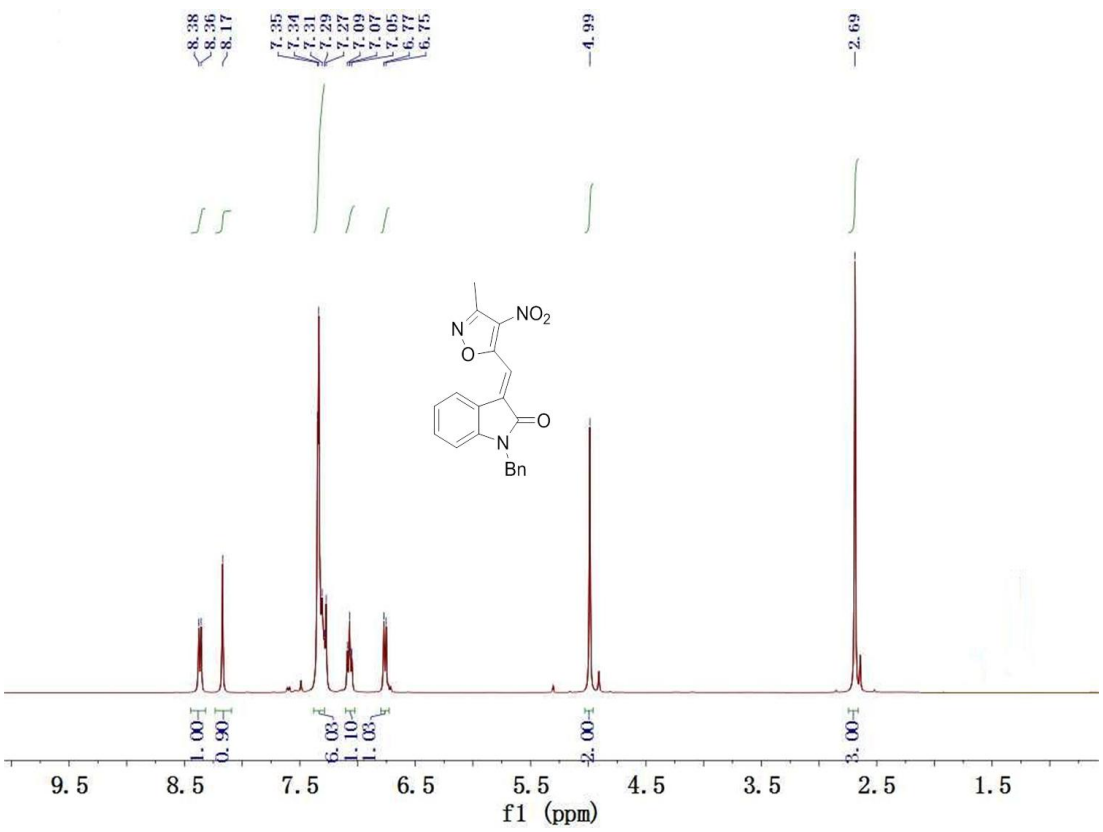
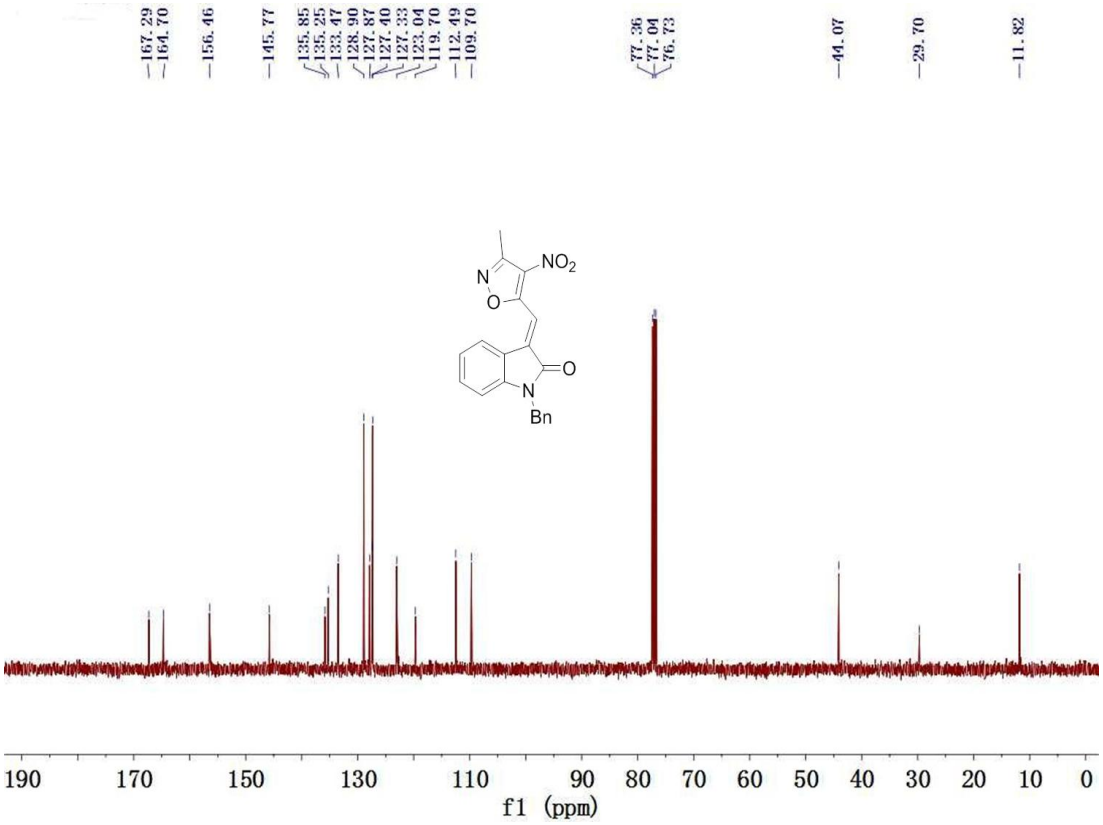
4.43
3.38
2.89
2.88
2.51
1.39
1.39
1.21
HO
O–N
O
NO2
N
Bn
9.25
1.03
1.04
1.01
1.00
2.08
3.06
3.20
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
f1 (ppm)


175.56
172.42
159.09
142.39
136.07
130.21
129.80
129.26
128.53
127.43
127.24
124.15
122.62
109.37
76.42
42.65
40.12
39.92
39.71
39.50
39.29
39.08
38.83
19.18
11.08
10.77
HO
O–N
O
NO2
N
Bn
90
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


10.27
7.19
7.17
7.15
7.12
7.11
6.93
6.91
6.89
6.76
6.74
6.27
5.75
3.80
3.40
3.30
3.27
3.05
3.02
2.51
2.03
N
O
NH2
HO
O
N
H
1.00
2.10
1.05
1.01
1.00
1.98
1.07
1.00
3.02
11.0
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
f1 (ppm)


179.00
154.03
148.48
142.09
131.30
129.59
125.28
124.86
121.98
109.96
75.39
40.57
40.36
40.15
39.95
39.74
39.53
39.32
33.52
9.54
N
O
NH2
HO
O
N
H
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


8.38
8.36
8.17
7.35
7.34
7.31
7.29
7.27
7.09
7.07
7.05
6.77
6.75
4.99
2.69
NO2
N
O
O
N
Bn
1.00
0.90
6.03
1.10
1.03
2.00
3.00
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
f1 (ppm)


167.29
164.70
156.46
145.77
135.85
135.25
133.47
128.90
127.87
127.40
127.33
123.04
119.70
112.49
109.70
77.36
77.04
76.73
44.07
29.70
11.82
NO2
N
O
O
N
Bn
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)