Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Metal-free Synthesis of Isatin Oximes *via* Radical Coupling Reactions of Oxindoles with *t*-BuONO in Water

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Supporting Information

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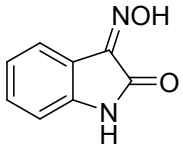
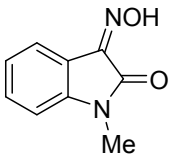
(A) Typical Experimental Procedure for the Radical Coupling Reaction:

To a Schlenk tube were added oxindole **1** (0.3 mmol), *t*-BuONO **2a** (1.2 mmol) and H_2O (2 mL). Then the tube was stirred at room temperature under air for the indicated time until complete consumption of starting material as monitored by TLC analysis. After the reaction was finished, the solution was diluted by ethyl acetate and washed with brine. The organic layer was extracted with ethyl acetate, and the combined organic layers were dried over anhydrous sodium sulfate. After removal of sodium sulfate through filtration, the solution was concentrated under reduced pressure, and the mixture was purified by flash column chromatography over silica gel (hexane/ethyl acetate) to afford the desired products **3**.

(B) Analytical data

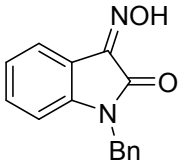


3-(Hydroxyimino)indolin-2-one (**3a**)[1], yellow solid （0.0467 g, 96% yield）; ^{1}H NMR (400 MHz, DMSO-*d6*) δ: 13.30 (s, 1H), 10.70 (s, 1H), 7.95 (d, *J* = 7.6 Hz, 1H), 7.36 (t, *J* = 7.2 Hz, 1H), 7.02 (t, *J* = 7.2 Hz, 1H), 6.89 (d, *J* = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-*d6*) δ: 164.9, 144.7, 143.1, 132.5, 127.5, 122.5, 116.4, 110.7; LRMS (EI, 70 eV) *m/z* (%): 162 (M^+, 1), 118 (100), 91 (43).

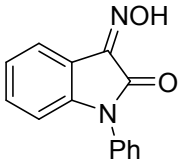


3-(Hydroxyimino)-1-methylindolin-2-one (**3b**)[2], yellow solid (0.0396 g, 75% yield); ^{1}H NMR (300 MHz, DMSO-*d6*) δ: 13.44 (s, 1H), 7.98 (t, *J* = 7.2 Hz, 1H), 7.45 (d, *J* = 8.1 Hz, 1H), 7.09 (d, *J* = 8.4 Hz, 2H), 3.18 (s, 3H); ^{13}C NMR (75 MHz, DMSO-*d6*) δ: 163.6, 144.2, 144.1, 132.5,

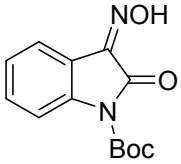
127.2, 123.1, 115.5, 109.4, 26.3; LRMS (EI, 70 eV) *m/z* (%): 176 (M^+, 1), 148 (68), 133 (100).



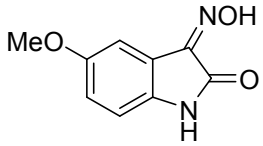
1-Benzyl-3-(hydroxyimino)indolin-2-one (**3c**)[3], yellow solid (0.0469 g, 62% yield); ^{1}H NMR (300 MHz, DMSO-*d6*) δ: 7.99 (d, *J* = 9.6 Hz, 1H), 7.39-7.12 (m, 6H), 7.08-6.95 (m, 2H), 4.93 (s, 2H); ^{13}C NMR (75 MHz, DMSO-*d6*) δ: 163.8, 144.0, 143.2, 136.6, 132.5, 129.2, 128.0, 127.7, 127.4, 123.3, 115.8, 110.0, 43.0; LRMS (EI, 70 eV) *m/z* (%):252 (M^+, 1), 161 (100), 118 (37).



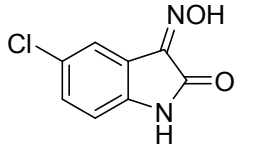
3-(Hydroxyimino)-1-phenylindolin-2-one (**3d**)[2], yellow solid (0.0636 g, 89% yield); ^{1}H NMR (300 MHz, DMSO-*d6*) δ: 8.13 (d, *J* = 7.5 Hz, 1H), 7.63-7.59 (m, 2H), 7.50 (d, *J* = 5.7 Hz, 2H), 7.44-7.39 (m, 2H), 7.17 (t, *J* = 7.5 Hz, 1H), 6.80 (d, *J* = 5.4 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-*d6*) δ: 163.0, 143.9, 143.8, 134.1, 132.5, 130.1, 128.8, 127.6, 127.3, 123.7, 115.8, 109.8; LRMS (EI, 70 eV) *m/z* (%): 238 (M^+, 1), 145 (61), 91 (100).



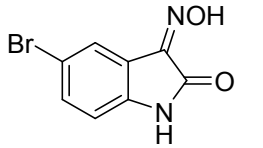
***tert*-Butyl 3-(hydroxyimino)-2-oxoindoline-1-carboxylate** (**3e**), light yellow solid (0.0354 g, 45% yield); ^{1}H NMR (400 MHz, DMSO-*d6*) δ: 13.75 (s, 1H), 8.16 (d, *J* = 8.4 Hz, 1H), 7.86 (d, *J* = 8.4 Hz, 1H), 7.52 (t, *J* = 8.0 Hz, 1H), 7.26 (t, *J* = 8.0 Hz, 1H), 1.59 (s, 9H); ^{13}C NMR (100 MHz, DMSO-*d6*) δ: 161.2, 148.8, 142.6, 139.9, 132.5, 127.1, 125.1, 116.8, 115.2, 84.4, 28.1; LRMS (EI, 70 eV) *m/z* (%): 262 (M^+, 1), 161 (100), 131 (93); HRMS *m/z* (ESI) calcd for $C_{13}H_{15}N_2O_4$ ($[M+H]^+$) 263.1026, found 263.1030.



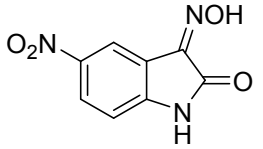
3-(Hydroxyimino)-5-methoxyindolin-2-one (**3f**)[4], saffron yellow solid (0.0364 g, 63% yield); ^{1}H NMR (300 MHz, DMSO-*d6*) δ: 13.38 (s, 1H), 10.54 (s, 1H), 7.54 (s, 1H), 6.96 (d, *J* = 8.1 Hz, 1H), 6.81 (d, *J* = 8.4 Hz, 1H), 3.74 (s, 3H); ^{13}C NMR (75 MHz, DMSO-*d6*) δ: 165.1, 155.2, 145.0, 136.6, 118.0, 116.8, 113.3, 111.4, 56.0; LRMS (EI, 70 eV) *m/z* (%): 192 (M^+, 2), 161 (27), 118 (100).



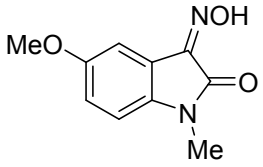
5-Chloro-3-(hydroxyimino)indolin-2-one (**3g**)[5], yellow solid (0.0525 g, 89% yield); ^{1}H NMR (300 MHz, DMSO-*d6*) δ: 13.71 (s, 1H), 10.88 (s, 1H), 7.93 (s, 1H), 7.44 (d, *J* = 7.5 Hz, 1H), 6.93 (d, *J* = 6.9 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-*d6*) δ: 164.7, 144.0, 141.7, 132.0, 126.7, 126.3, 117.5, 112.3; LRMS (EI, 70 eV) *m/z* (%): 198 (M+2, 3), 196 (M^+, 9), 161 (100), 118 (63).



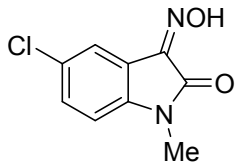
5-Bromo-3-(hydroxyimino)indolin-2-one (**3h**)[5], yellow solid (0.0702 g, 97% yield); ^{1}H NMR (300 MHz, DMSO-*d6*) δ: 13.67 (s, 1H), 10.87 (s, 1H), 8.04 (s, 1H), 7.54 (d, *J* = 8.1 Hz, 1H), 6.87 (d, *J* = 8.1 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-*d6*) δ: 164.6, 143.8, 142.1, 134.8, 129.5, 117.9, 113.9, 112.8; LRMS (EI, 70 eV) *m/z* (%): 242 (M+2, 2), 240 (M^+, 2), 118 (100), 91 (37).



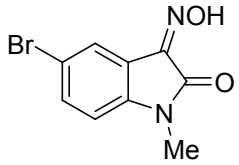
3-(Hydroxyimino)-5-nitroindolin-2-one (**3i**)[1], yellow solid (0.0398 g, 64% yield); ^{1}H NMR (300 MHz, DMSO-*d6*) δ: 14.02 (s, 1H), 11.43 (s, 1H), 8.65 (s, 1H), 8.30 (d, *J* = 8.7 Hz, 1H), 7.08 (d, *J* = 8.7 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 165.0, 148.4, 143.2, 142.4, 128.7, 122.1, 116.0, 110.8; LRMS (EI, 70 eV) *m/z* (%): 207 (M^+, 1), 118 (100), 91 (25).



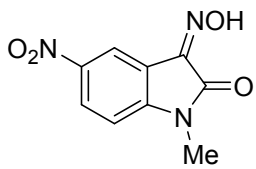
3-(Hydroxyimino)-5-methoxy-1-methylindolin-2-one (**3j**), red solid (0.0421 g, 68% yield); ^{1}H NMR (300 MHz, DMSO-*d6*) δ: 7.59 (s, 1H), 7.06-6.98 (m, 2H), 3.77 (s, 3H), 3.16 (s, 3H); ^{13}C NMR (75 MHz, DMSO-*d6*) δ: 163.4, 155.6, 144.3, 137.8, 117.2, 116.1, 113.4, 109.9, 56.0, 26.3; LRMS (EI, 70 eV) *m/z* (%): 206 (M^+, 2), 175 (27), 118 (100); HRMS *m/z* (ESI) calcd for $C_{10}H_{11}N_2O_3$ ($[M+H]^+$) 207.0764, found 207.0768.



5-Chloro-3-(hydroxyimino)-1-methylindolin-2-one (**3k**), yellow solid (0.0411 g, 65% yield); ^{1}H NMR (300 MHz, DMSO-*d6*) δ: 13.76 (s, 1H), 7.93 (s, 1H), 7.51 (d, *J* = 7.8 Hz, 1H), 7.11 (d, *J* = 8.4 Hz, 1H), 3.16 (s, 3H); ^{13}C NMR (75 MHz, DMSO-*d6*) δ: 163.2, 143.4, 143.0, 131.9, 126.9, 126.5, 116.6, 111.0, 26.4; LRMS (EI, 70 eV) *m/z* (%):212 (M+2, 1), 210 (M^+, 3), 179 (46), 118 (100); HRMS *m/z* (ESI) calcd for $C_9H_8ClN_2O_2$ ($[M+H]^+$) 211.0269, found 211.0272.

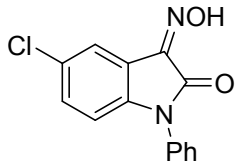


5-Bromo-3-(hydroxyimino)-1-methylindolin-2-one (**3l**)[6], yellow solid (0.0513 g, 67% yield); ^{1}H NMR (300 MHz, DMSO-*d6*) δ: 13.78 (s, 1H), 8.07 (s, 1H), 7.64 (d, *J* = 8.4 Hz, 1H), 7.07 (d, *J* = 8.4 Hz, 1H), 3.16 (s, 3H); ^{13}C NMR (75 MHz, DMSO-*d6*) δ: 163.1, 143.3, 143.2, 134.7, 129.1, 117.1, 114.5, 111.5, 26.4; LRMS (EI, 70 eV) *m/z* (%): 256 (M+2, 2), 254 (M^+, 2), 144 (100), 118 (35).



3-(Hydroxyimino)-1-methyl-5-nitroindolin-2-one (**3m**), yellow solid (0.0398 g, 60% yield); ^{1}H NMR (300 MHz, DMSO-*d6*) δ: 14.17 (s, 1H), 8.68 (s, 1H), 8.40 (d, *J* = 10.8 Hz,

1H), 7.31 (d, J = 8.7 Hz, 1H), 3.25 (s, 3H); ^{13}C NMR (75 MHz, DMSO-*d6*) δ: 163.9, 149.5, 142.9, 142.8, 128.9, 121.8, 115.4, 109.9, 26.9; LRMS (EI, 70 eV) *m/z* (%): 221 (M^+, 1), 190 (42), 91 (100); HRMS *m/z* (ESI) calcd for $C_9H_8N_3O_4$ ($[M+H]^+$) 222.0509, found 222.0513.



5-Chloro-3-(hydroxyimino)-1-phenylindolin-2-one (**3n**), yellow solid (0.0679 g, 83% yield); ^{1}H NMR (300 MHz, DMSO-*d6*) δ: 8.05 (s, 1H), 7.57 (d, J = 6.9 Hz, 2H), 7.50-7.33 (m, 4H), 6.77 (d, J = 8.4 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-*d6*) δ: 162.7, 143.1, 142.6, 133.9, 131.9, 130.2, 128.9, 127.9, 127.3, 126.8, 117.0, 111.4; LRMS (EI, 70 eV) *m/z* (%): 274 (M+2, 1), 272 (M^+, 3), 237 (52), 206 (100); HRMS *m/z* (ESI) calcd for $C_{14}H_{10}ClN_2O_2$ ($[M+H]^+$) 273.0425, found 273.0430.

(C) References

[1] Z. Wang, C. Wang, Y. Sun, N. Zhang, Z. Liu, J. Liu, *Tetrahedron* 2014, **70**, 906.

[2] N. Sin, B. L. Venables, X. Liu, S. Huang, Q. Gao, *J. Heterocyclic. Chem*. 2009, **46**, 432.

[3] J. Cao, H. Gao, G. Bemis, F. Salituro, M. Ledeboer, E. Harrington, S. Wilke, P. Taslimi, S. Pazhanisamy, X. Xie, M. Jacobs, J. Green, *Bioorg. Med. Chem. Lett.* 2009, **19**, 2891.

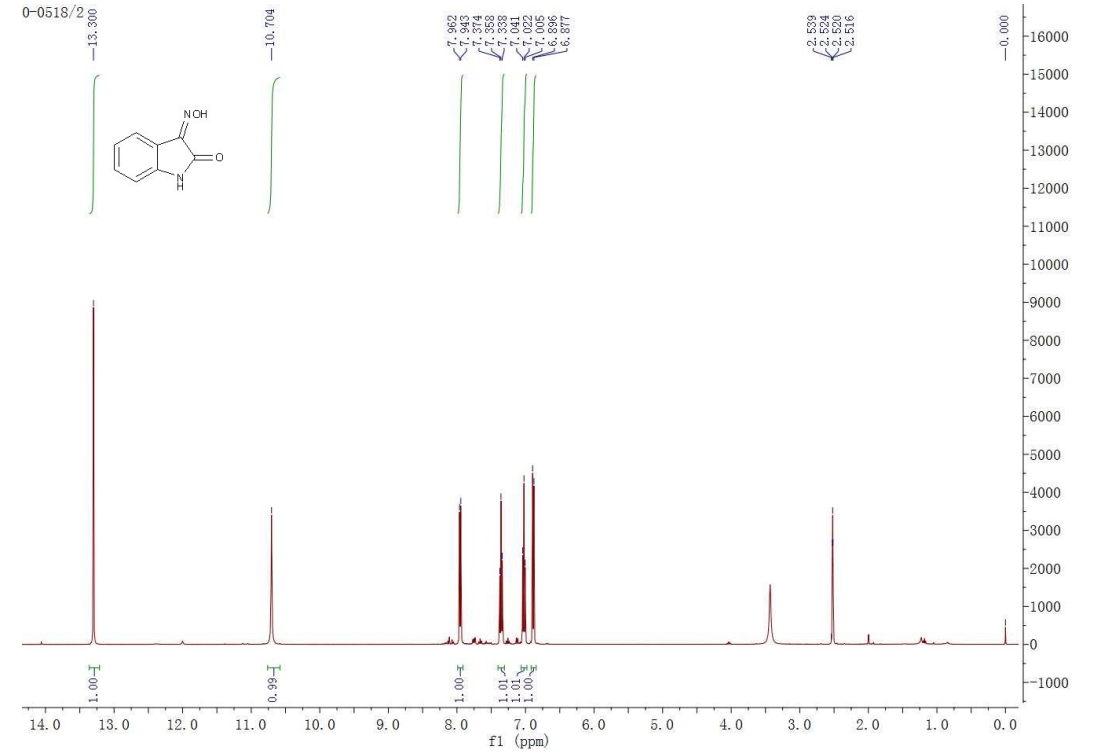
[4] A. C. Pinto, A. A. M. Lapis, B. V. Silva, R. S. Bastos, J. Dupont, B. A. D. Neto, *Tetrahedron Lett.* 2008, **49**, 5639.

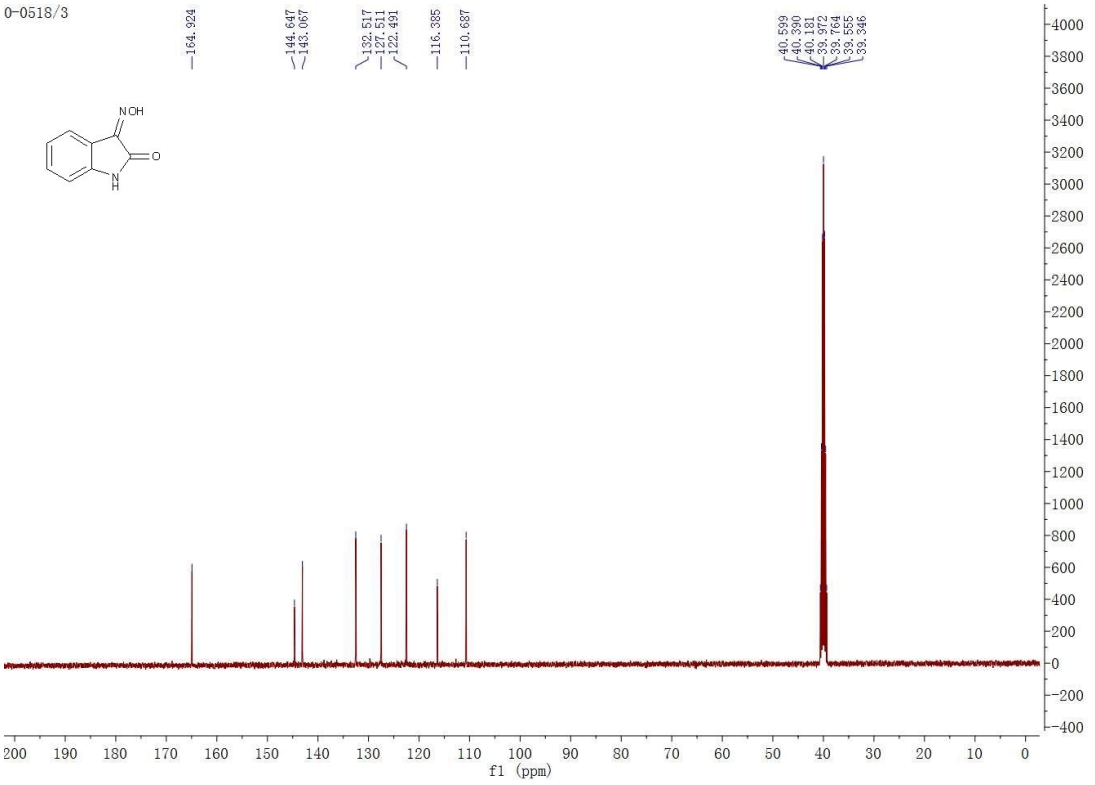
[5] T. Kearney, P. A. Harris, A. Jackson, J. A. Joule, *Synthesis* 1992, **8**,769.

[6] L.D. Pinkin, V. G. Dzyubenko, P. I. Abramenko, I. S. Shpileva. *Chem. Heterocycl. Com*. 1987, **23**, 345.

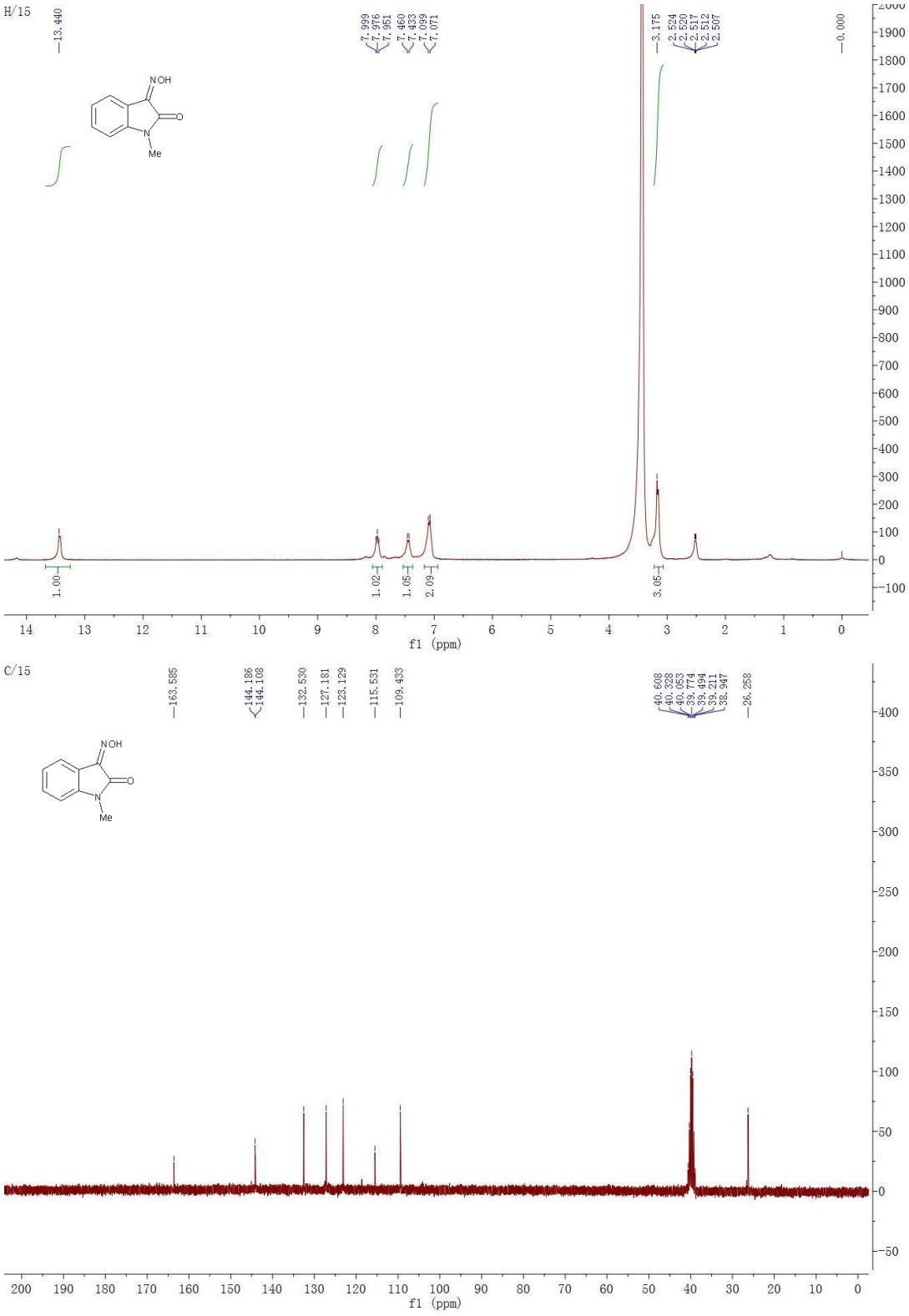
(D) Spectra

3-(Hydroxyimino)indolin-2-one (**3a**)

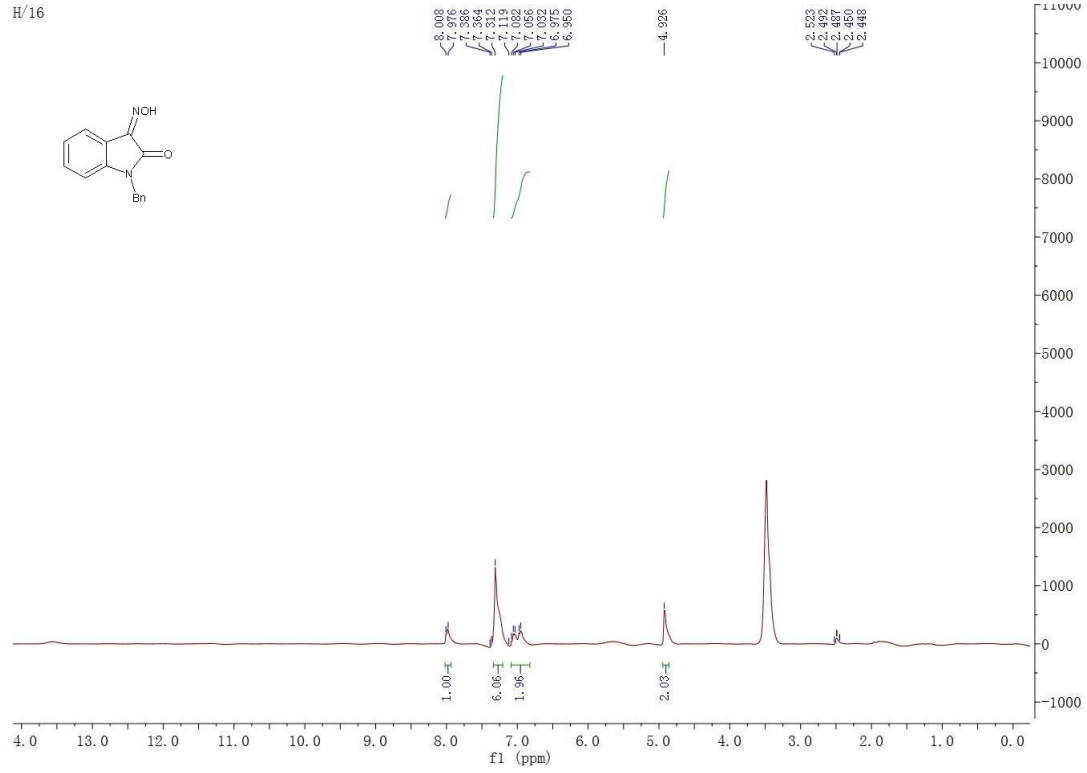


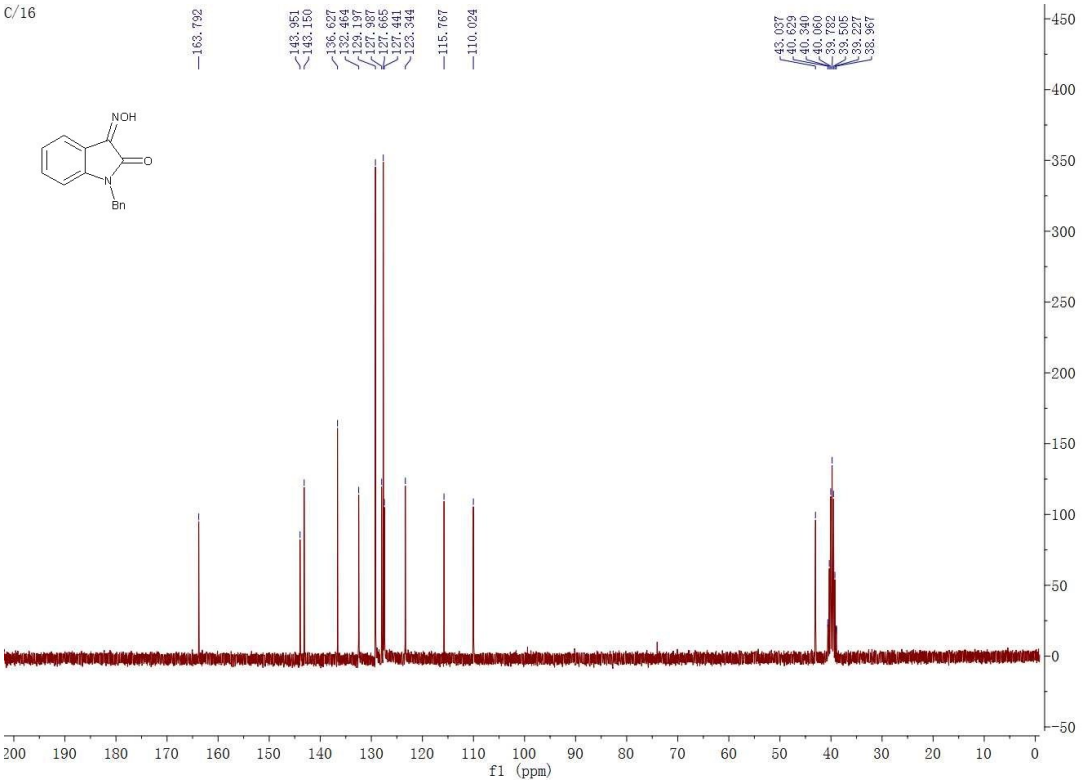


3-(Hydroxyimino)-1-methylindolin-2-one (**3b**)

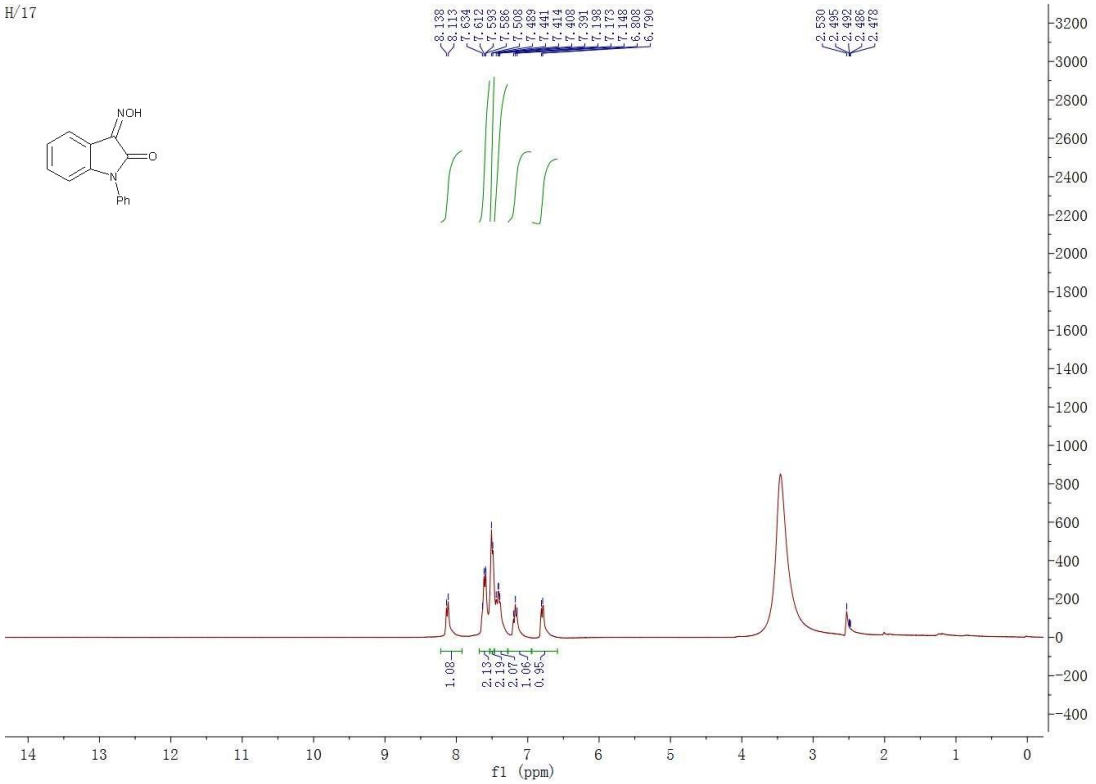


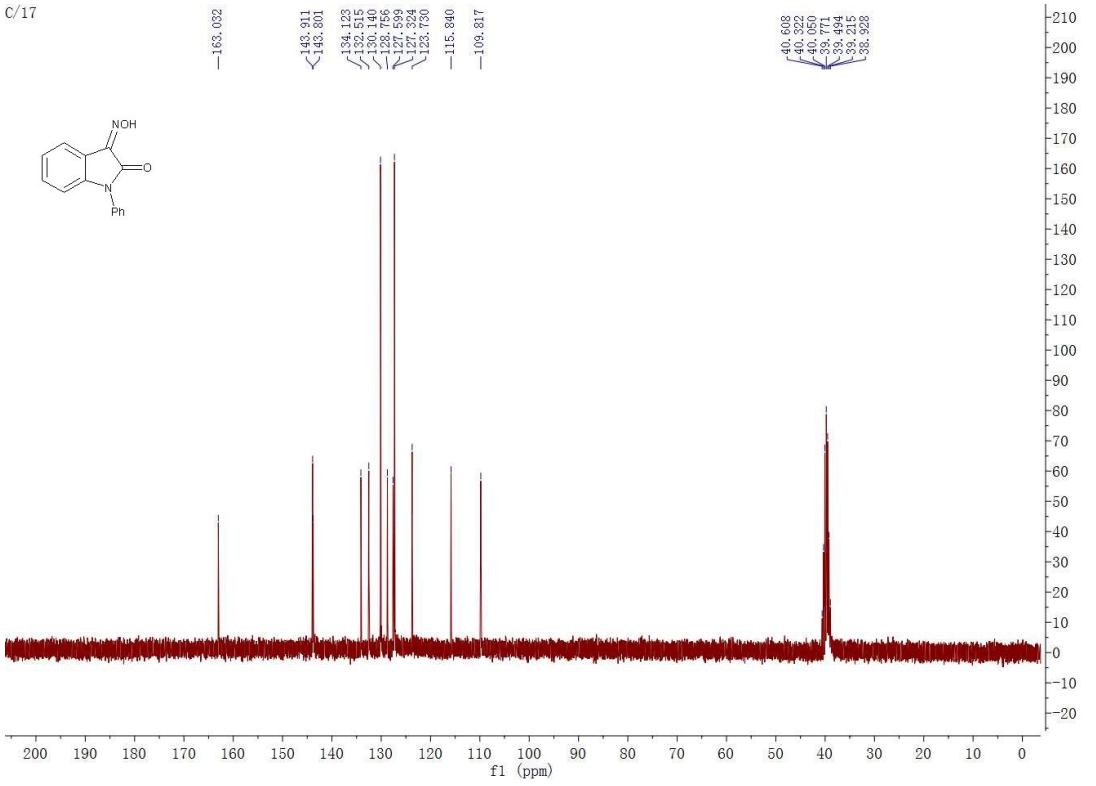
1-Benzyl-3-(hydroxyimino)indolin-2-one (**3c**)



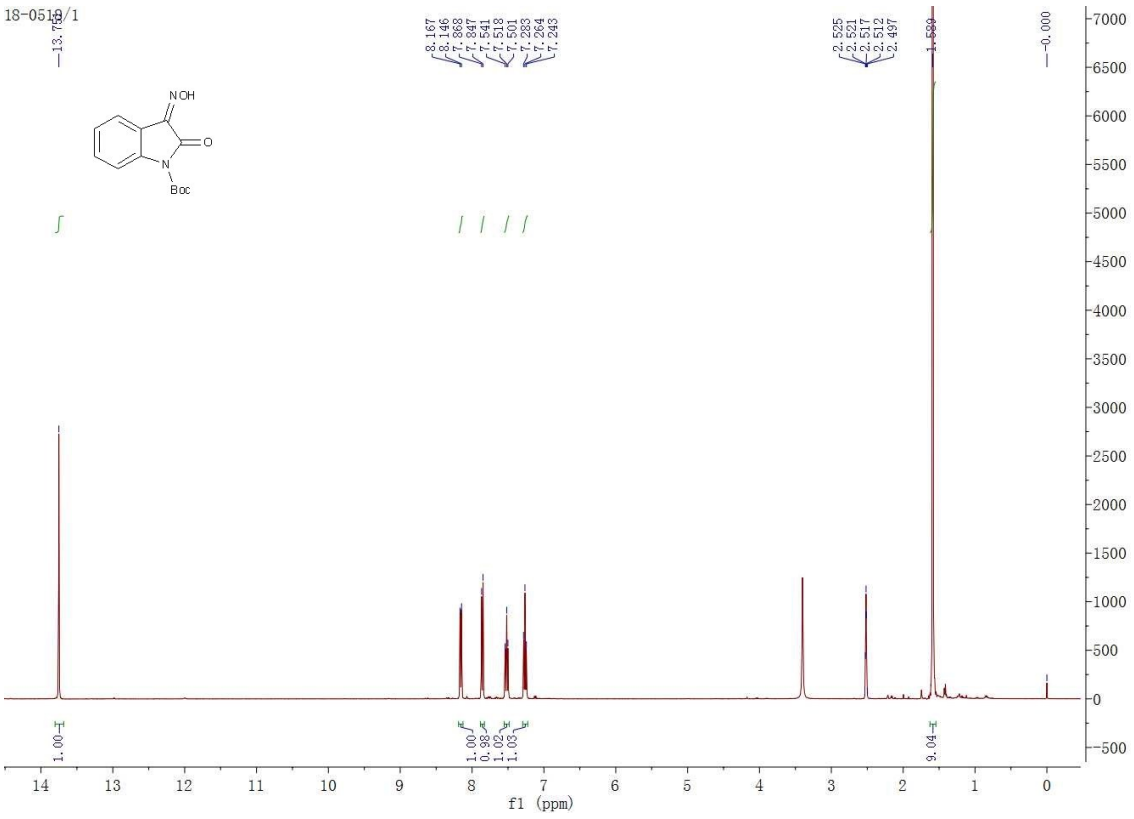


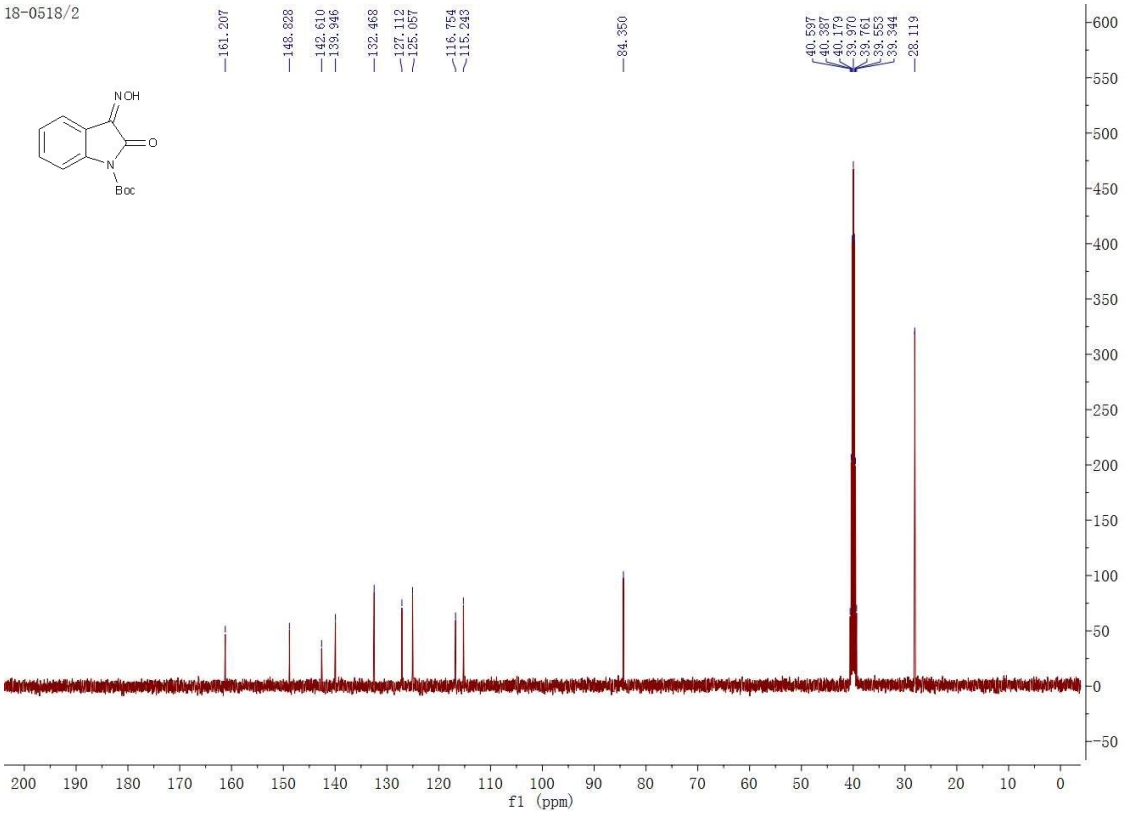
3-(Hydroxyimino)-1-phenylindolin-2-one (**3d**)



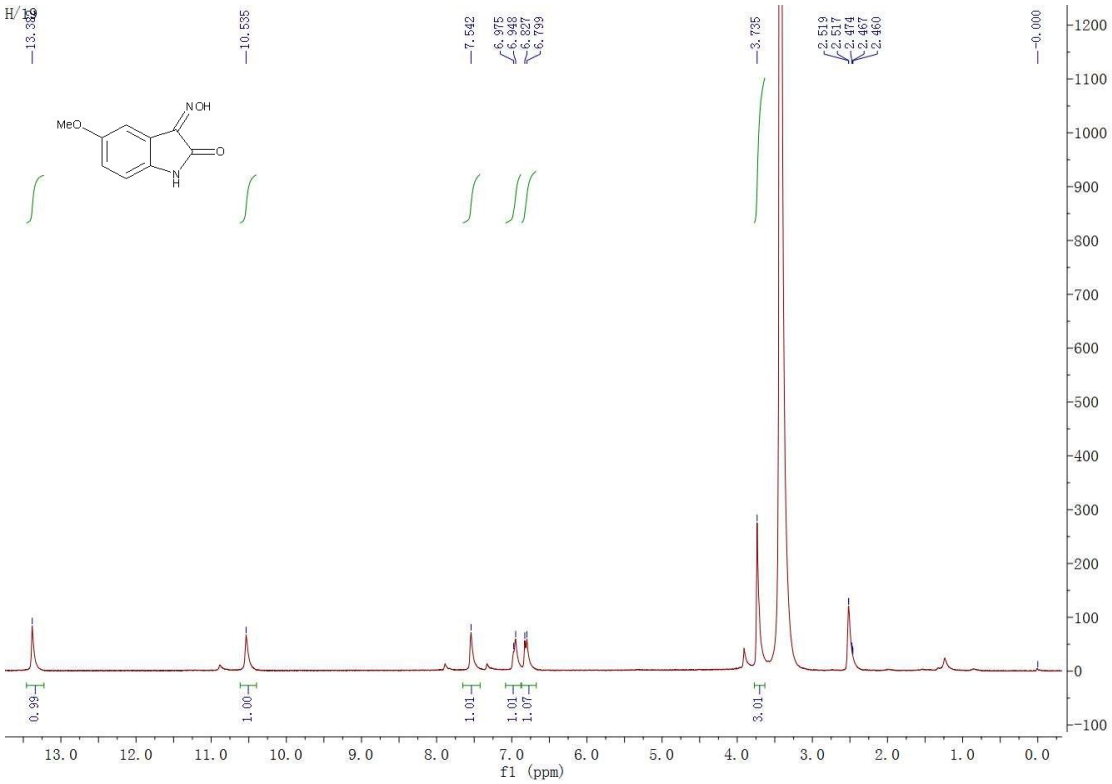


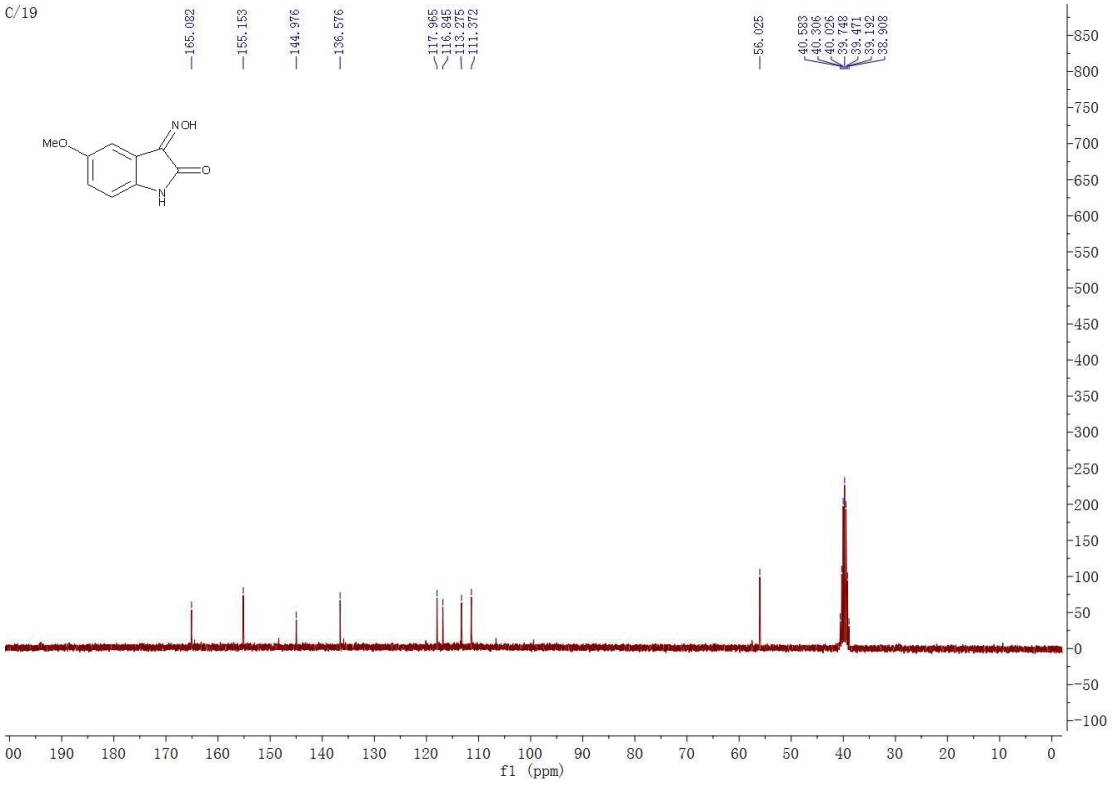
tert-Butyl-3-(hydroxyimino)-2-oxoindoline-1-carboxylate (**3e**)



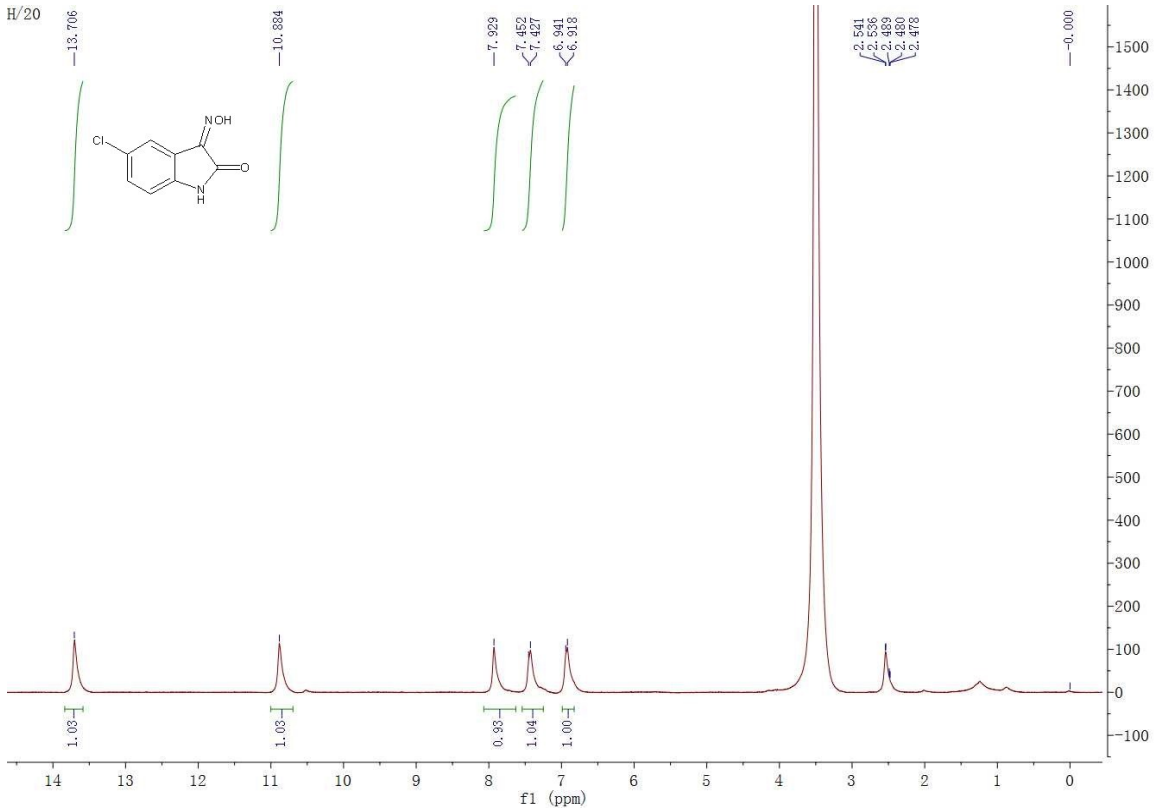


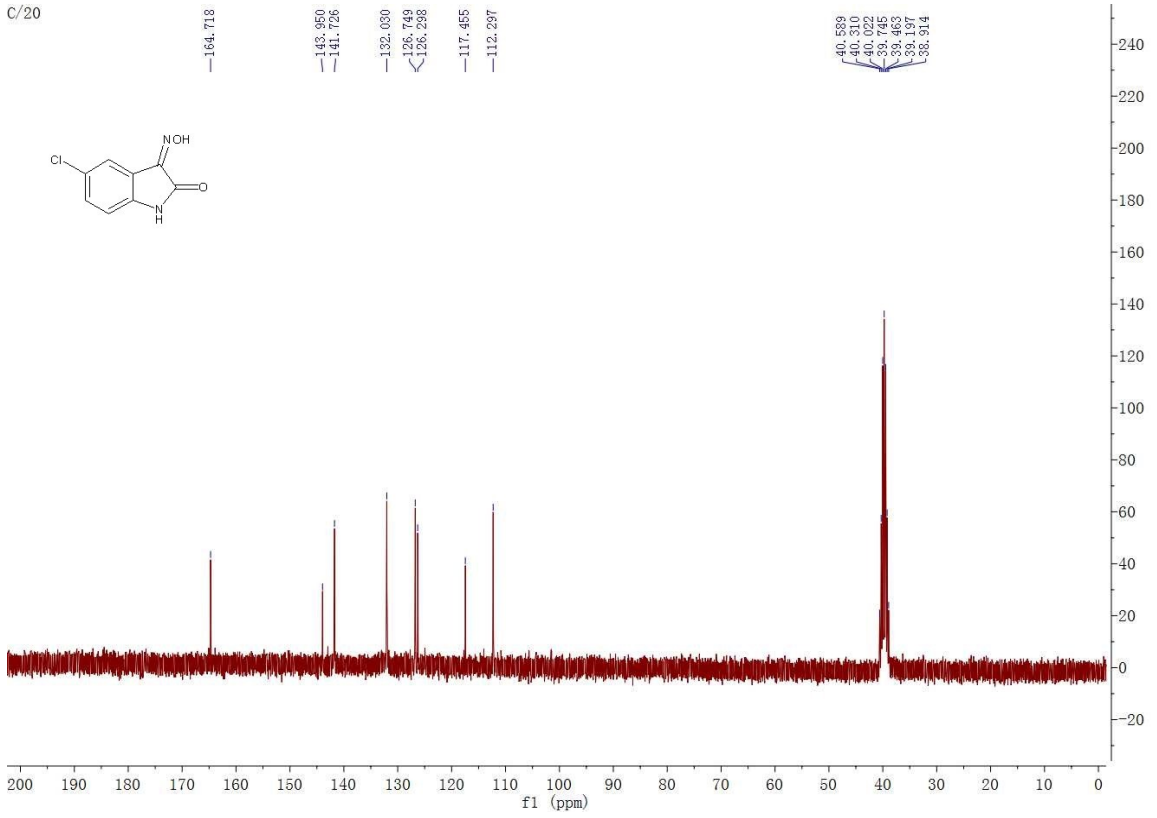
3-(Hydroxyimino)-5-methoxyindolin-2-one (**3f**)



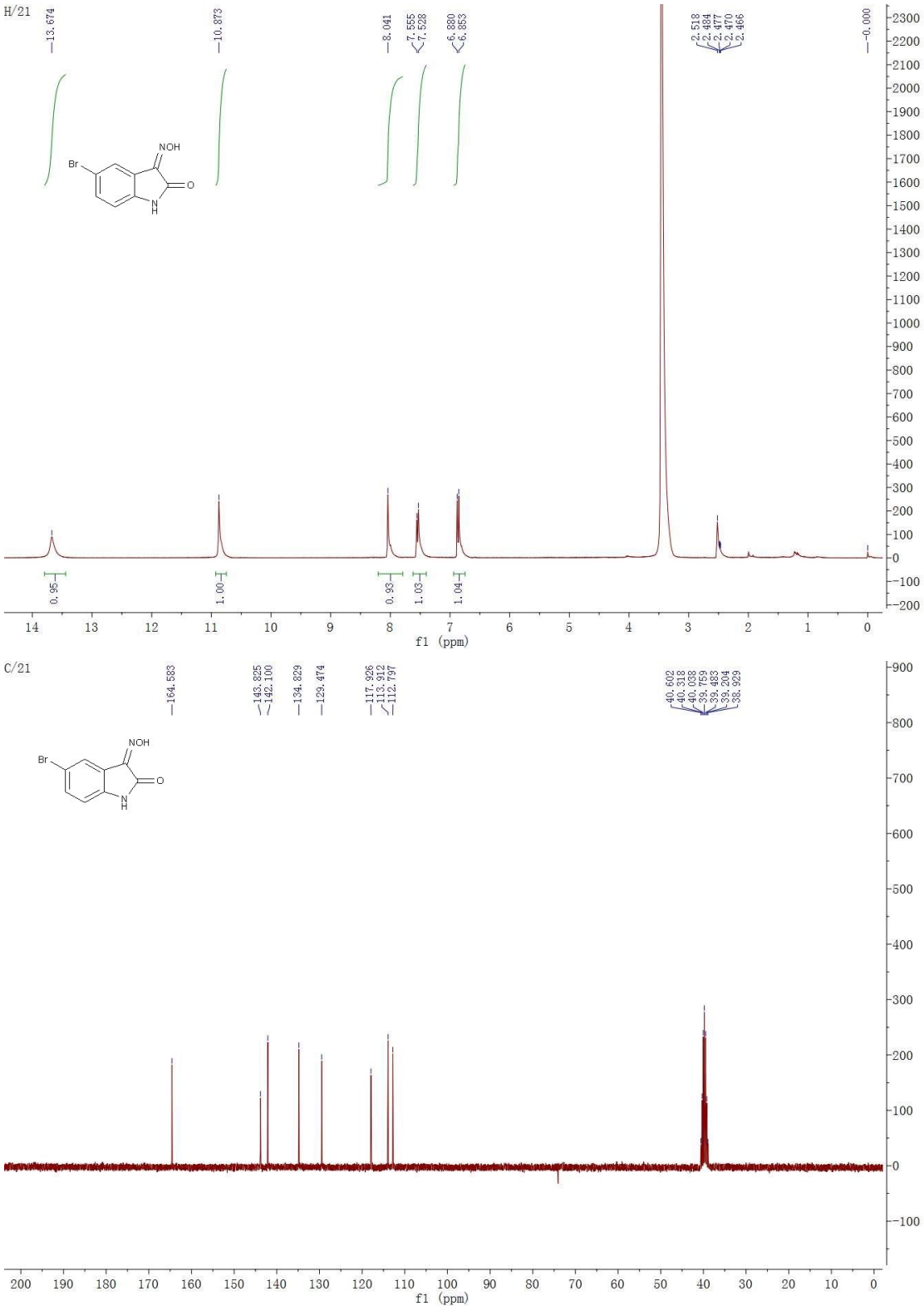


5-Chloro-3-(hydroxyimino)indolin-2-one (**3g**)

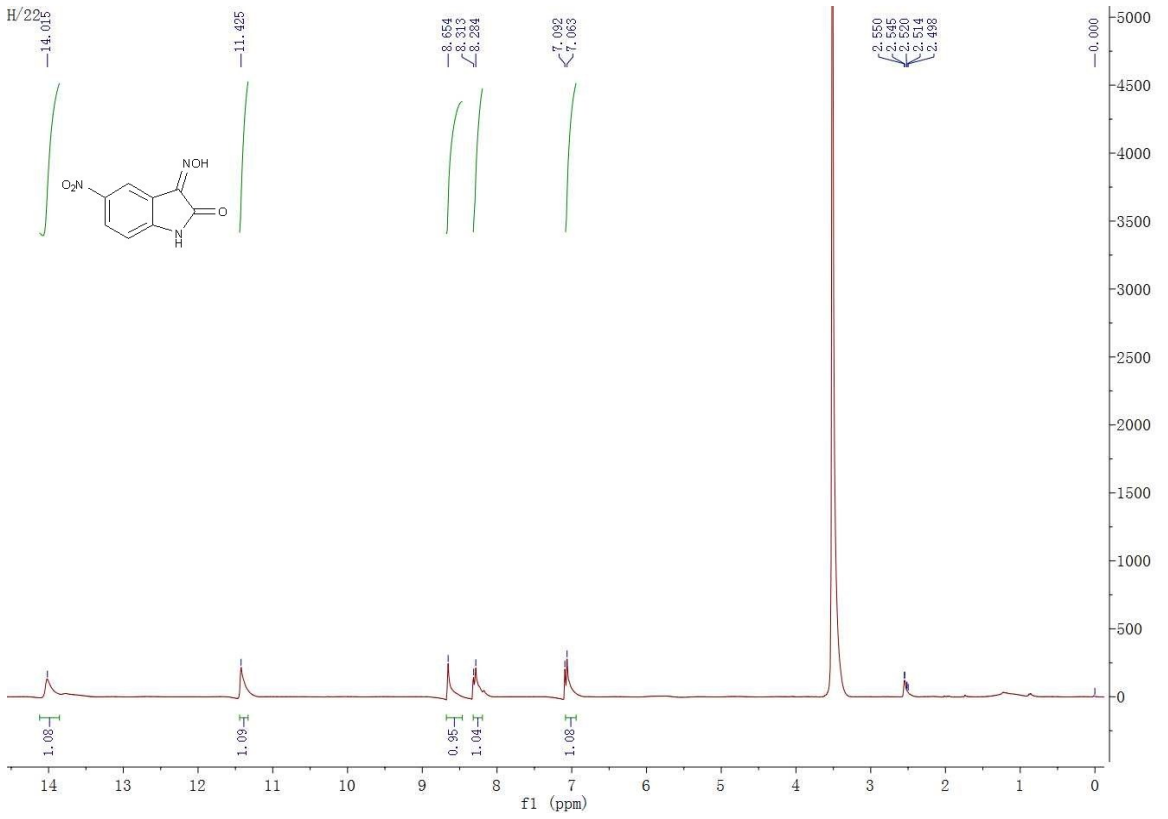


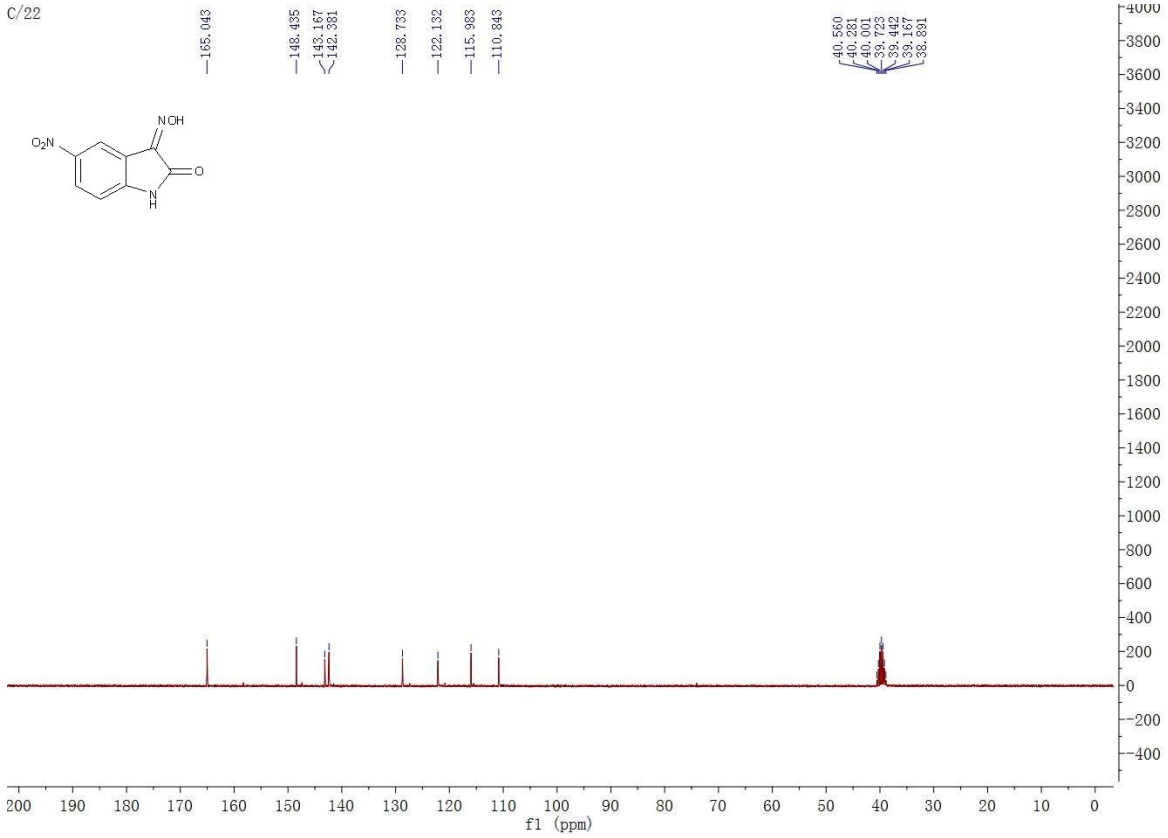


5-Bromo-3-(hydroxyimino)indolin-2-one (**3h**)

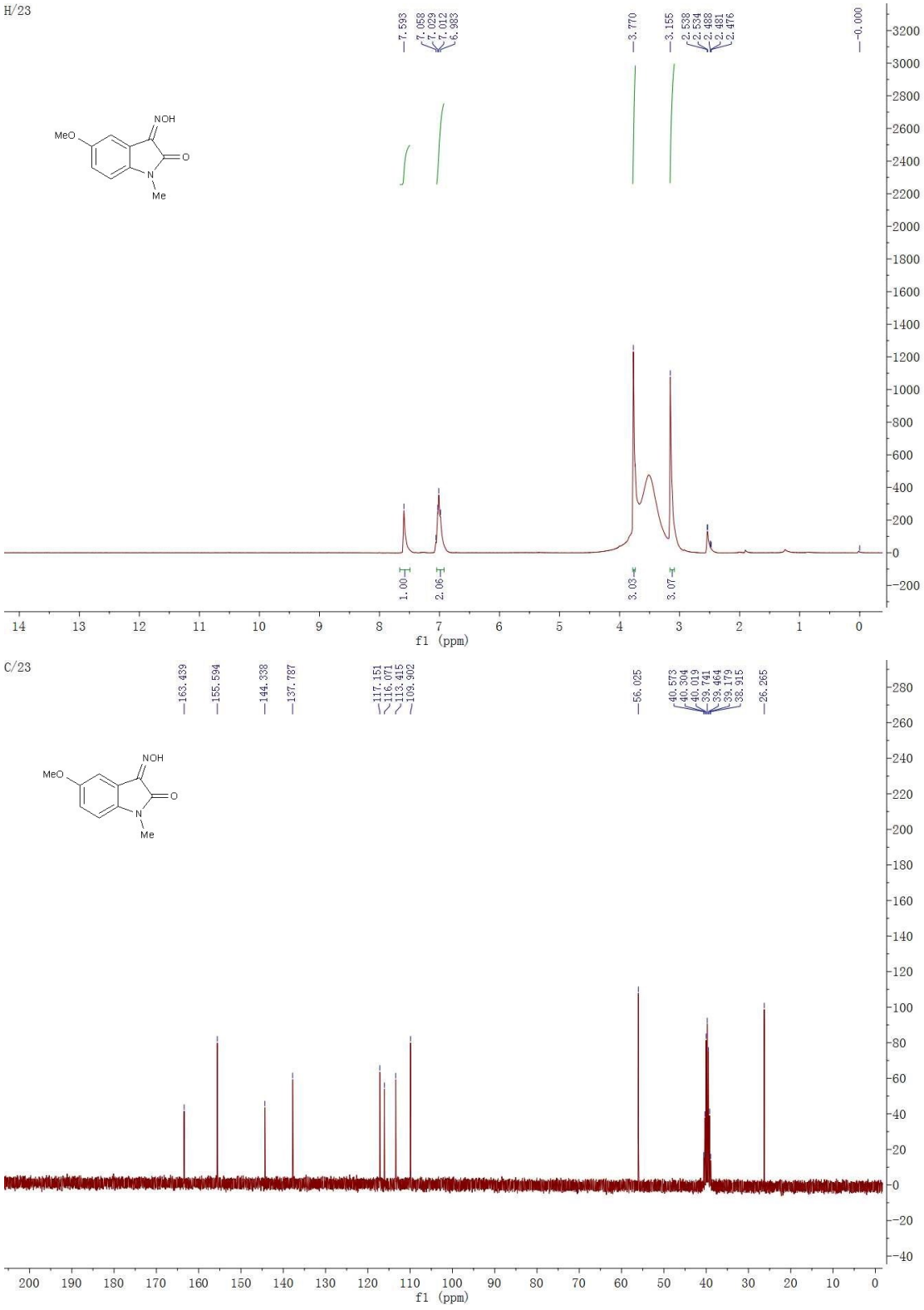


3-(Hydroxyimino)-5-nitroindolin-2-one (**3i**)

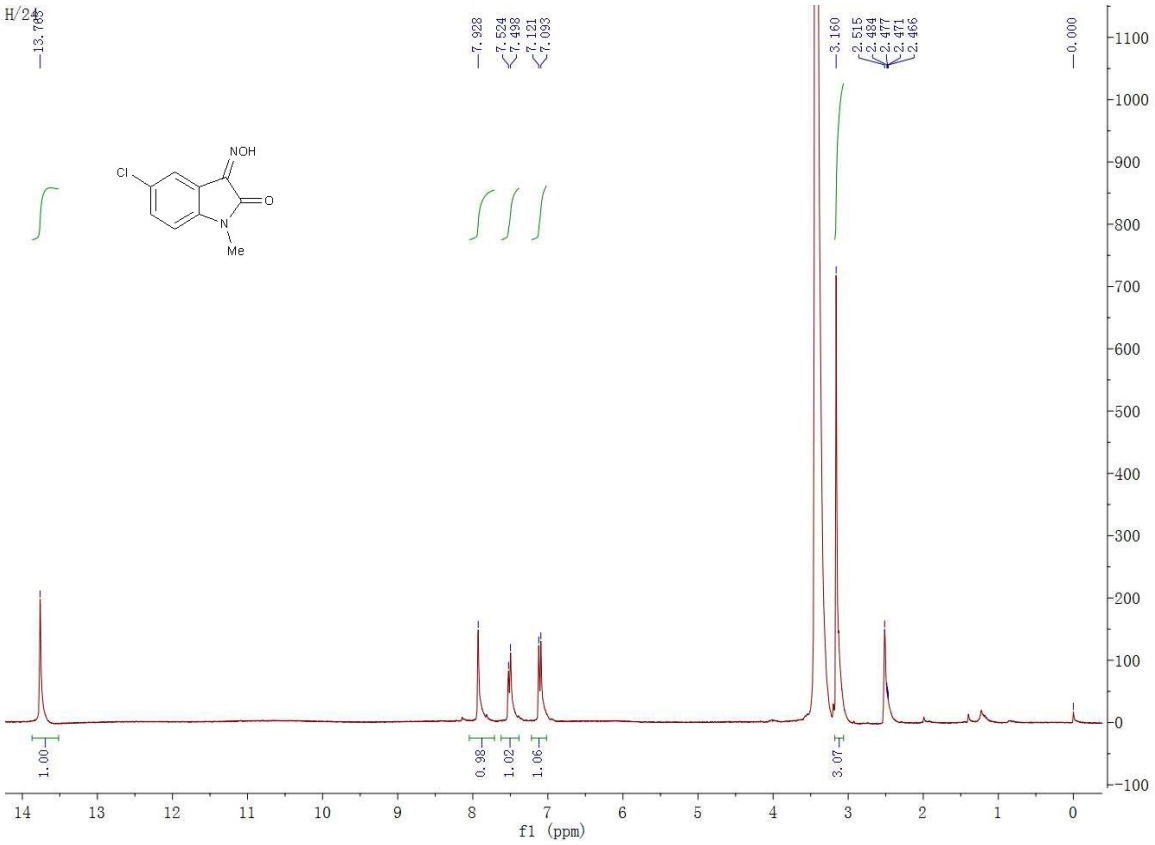


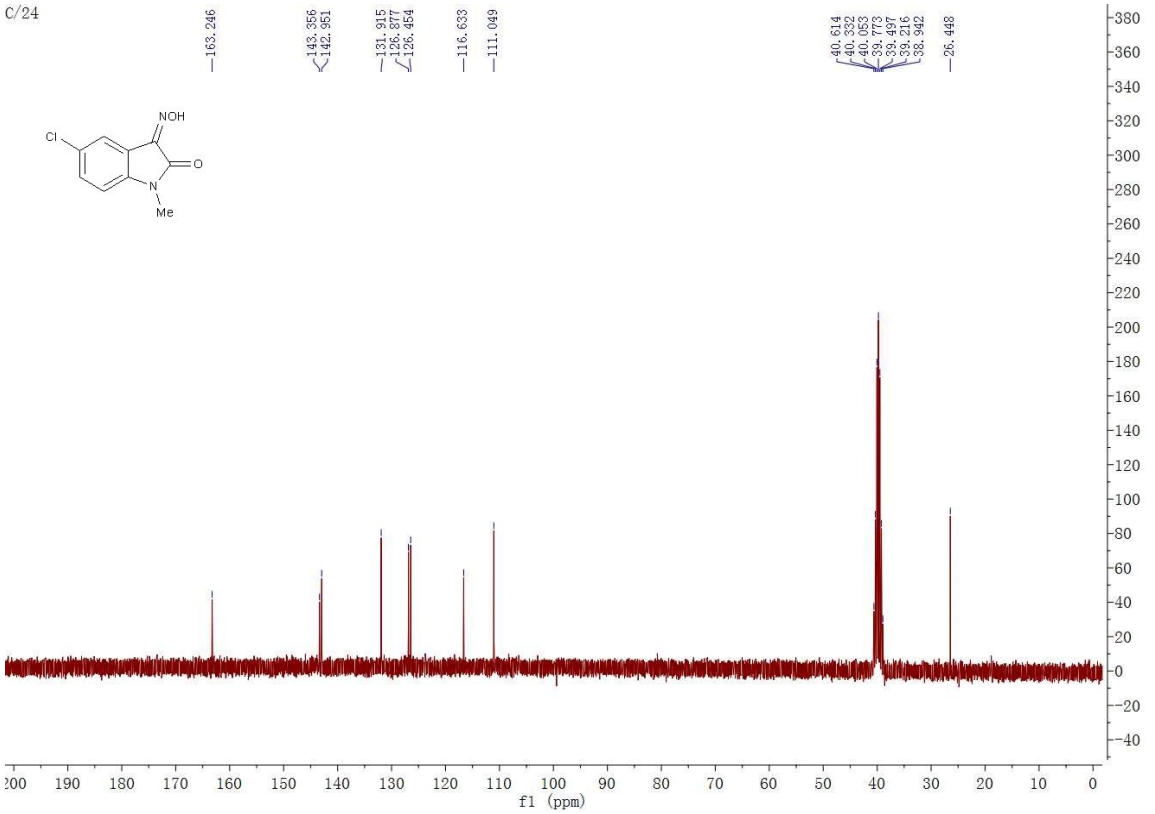


3-(Hydroxyimino)-5-methoxy-1-methylindolin-2-one (**3j**)

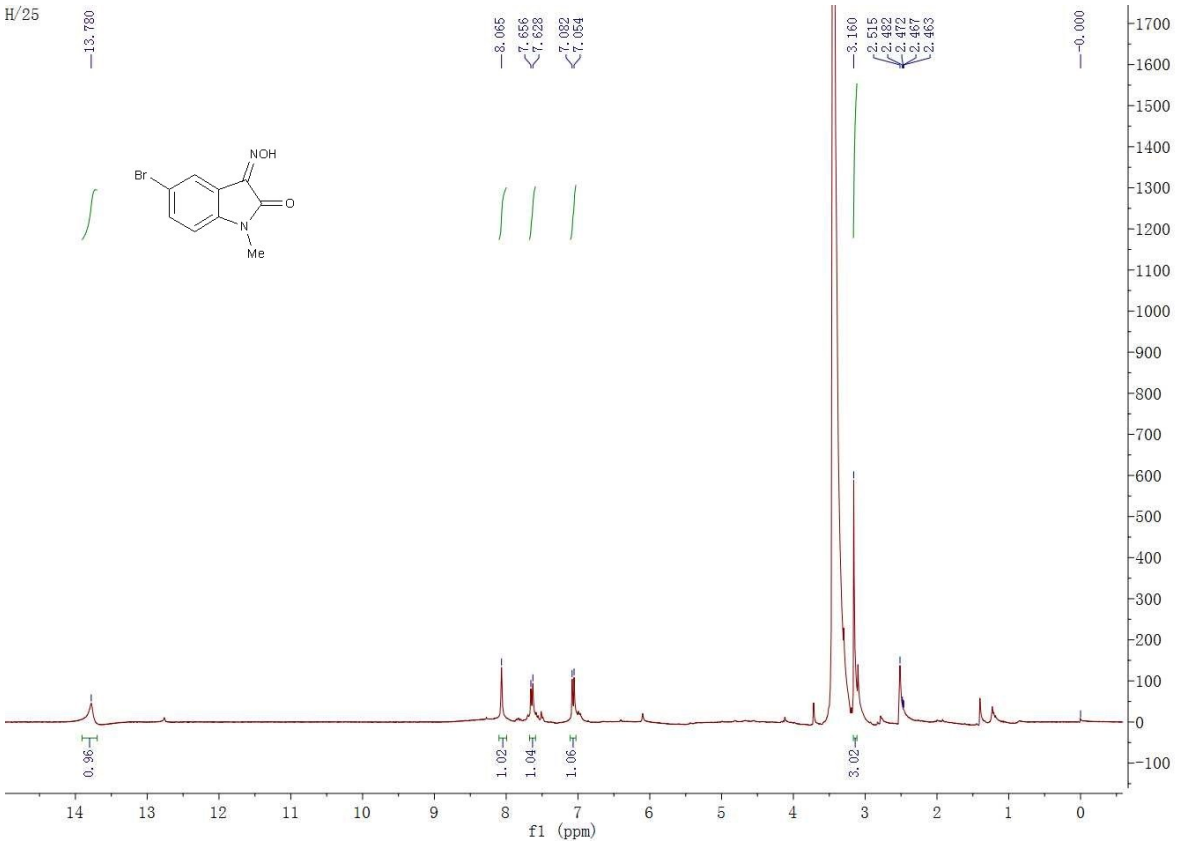


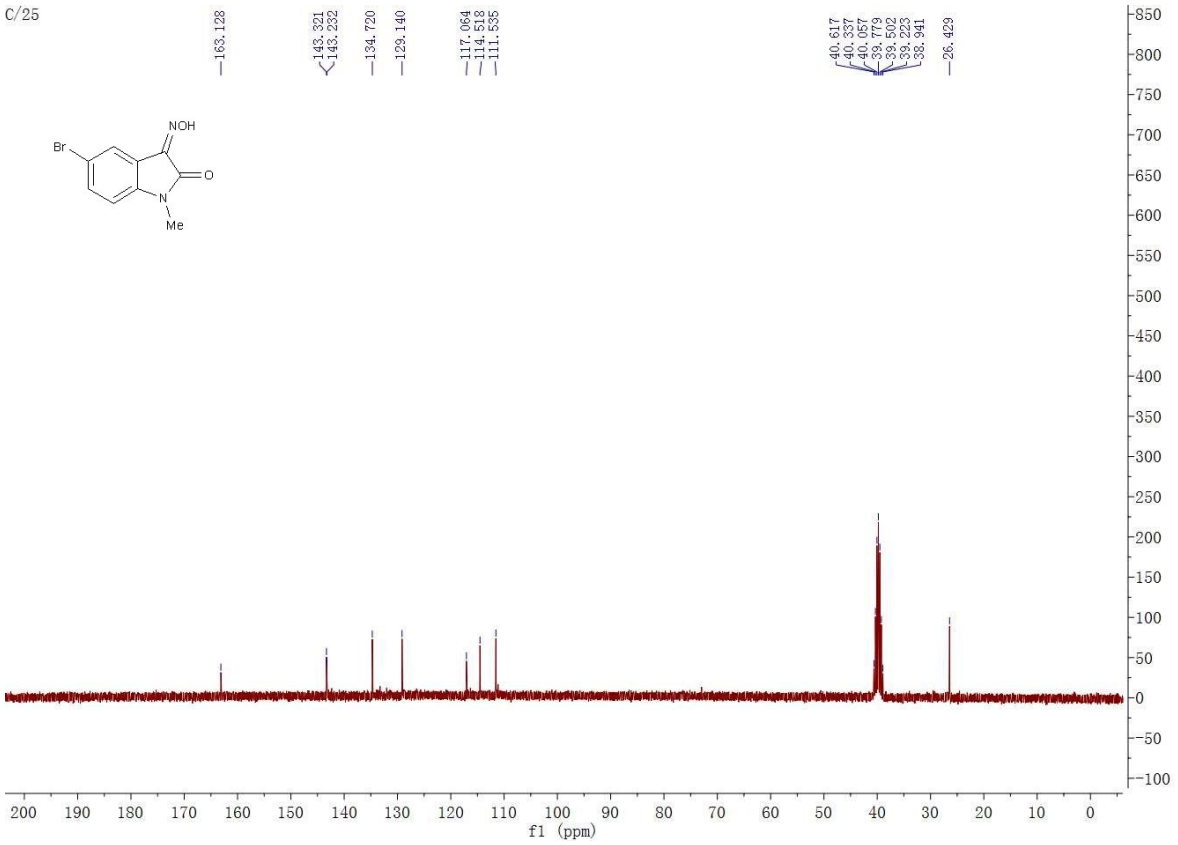
5-Chloro-3-(hydroxyimino)-1-methylindolin-2-one (**3k**)



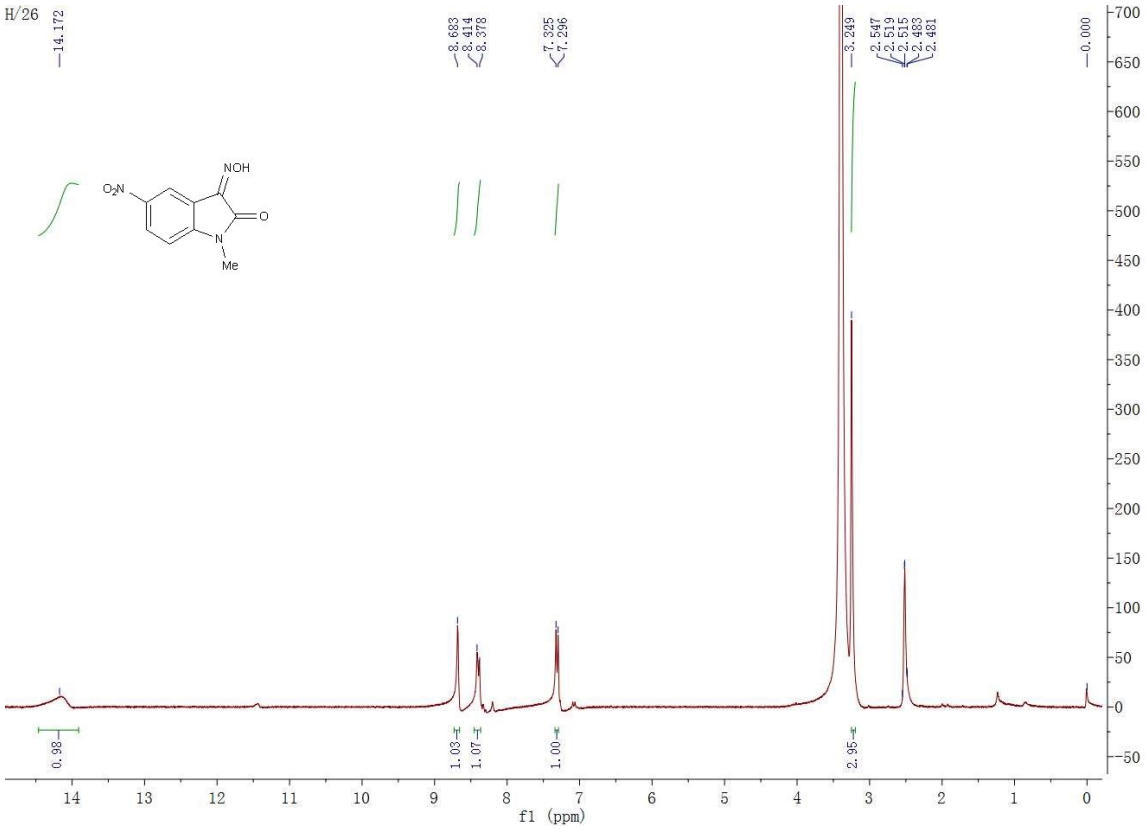


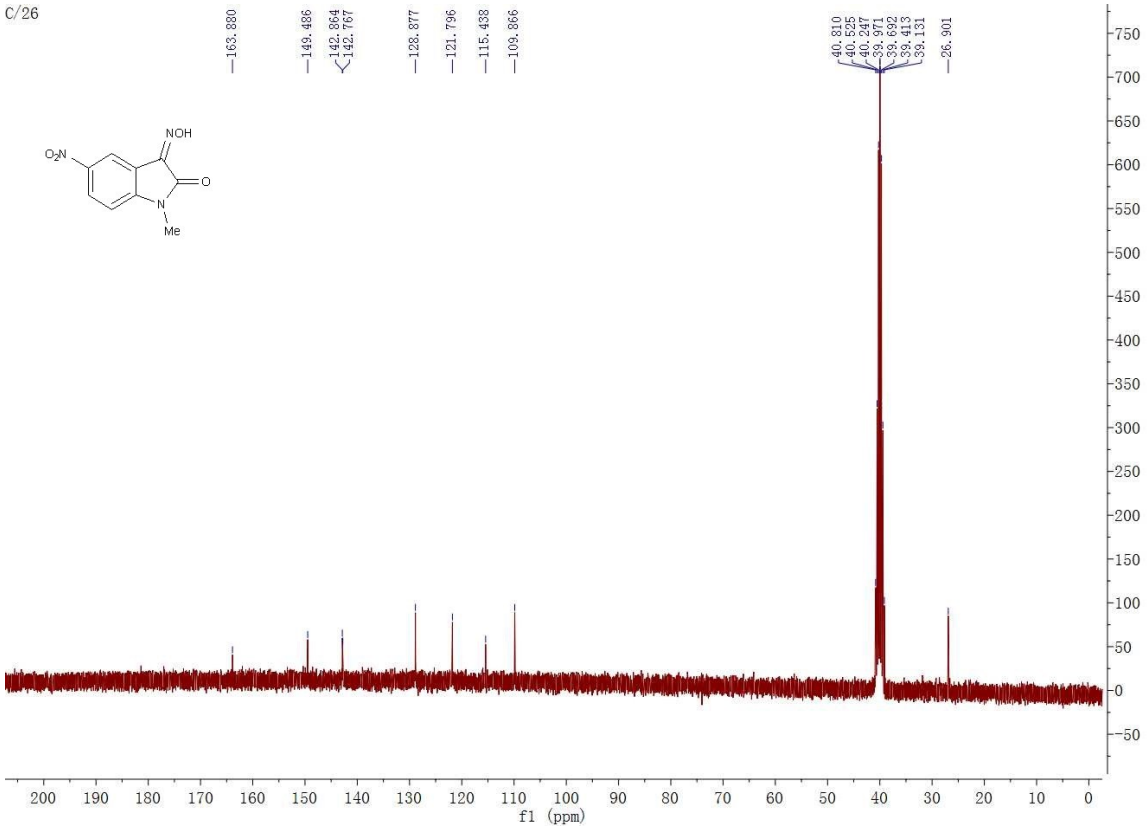
5-Bromo-3-(hydroxyimino)-1-methylindolin-2-one (**3l**)





3-(Hydroxyimino)-1-methyl-5-nitroindolin-2-one (**3m**)





5-Chloro-3-(hydroxyimino)-1-phenylindolin-2-one (**3n**)