Electronic Supplementary Material (ESI) for ChemComm.

Supporting Information

of

Iron Catalyzed Efficient Synthesis of Poly-functional Primary Amines via Direct Use of Ammonia

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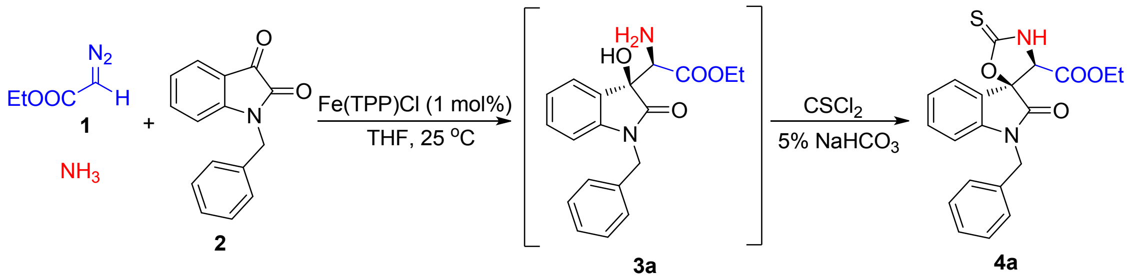
Table of Contents

1. General Information:

HRMS (ESI) Mass spectra were recorded on Bruker micrOTOF-Q 10198 mass spectrometer. NMR spectra were recorded on a Brucker Ascend-400 MHz spectrometer. All solvents and reagents were purchased from Sinopharm Chemical Reagent Co., Ltd, and directly used without any purification. Diazo compounds[1] and benzyl protected isatins[2] were prepared according to the literature procedure.

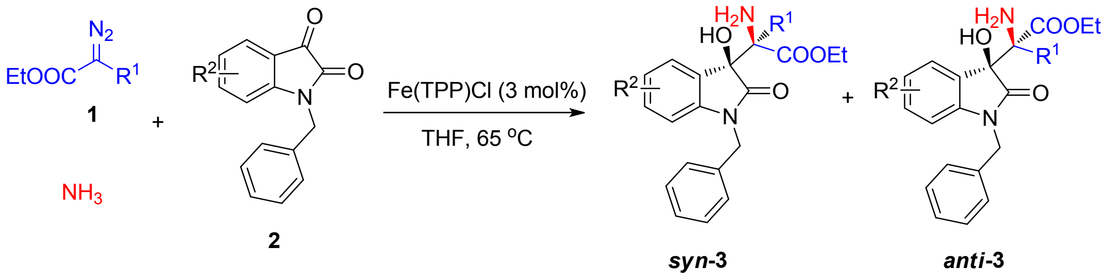
2. Experimental Procedures

2.1 General procedure for the three-component reaction of EDA, ammonia and *N*-benzyl isatin and cyclization with thiophosgen:



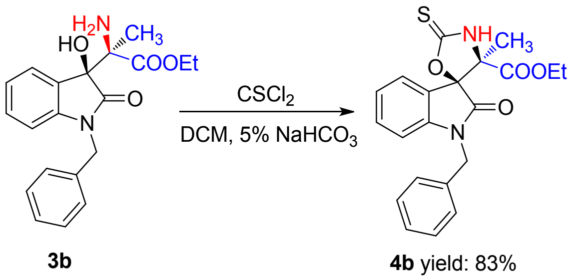
To a reaction tube equipped with a stir bar was added isatin (0.2 mmol), Fe(TPP)Cl (0.002 mmol) and THF (1.5 mL). This solution was purged with ammonia gas for 15 minutes at 25 °C. To this solution was added EDA (0.3 mmol) in one portion. Immediately nitrogen release was detected, the reaction was completed in 1 minute, then 5% $NaHCO_3$ (3mL) was added to the mixture, $CSCl_2$ (0.3 mmol) was added subsequently. After 30 minutes, the reaction was quenched with brine (2mL), extracted three times with EA (2mL*3). The organic phase was evaporated under vacuum and the crude products were passed through a short column of silica gel, which were subjected to ^{1}H NMR to detect the diastereoselectivity. The crude products were purified by flash chromatography on silica gel (eluent: ethyl acetate / petroleum ether: 1:2 to 2:1) to give corresponding products.

2.2 General procedure for the three-component reaction of alkyl diazoesters, ammonia and *N*-benzyl isatins:



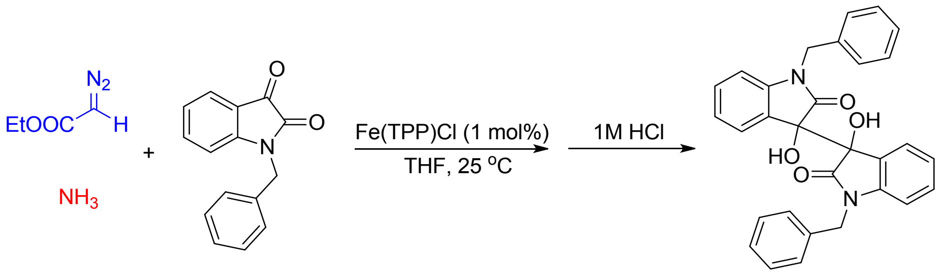
To a reaction tube equipped with a stir bar was added isatin (0.2 mmol), Fe(TPP)Cl (0.002 mmol) and THF (3 mL). This solution was purged with ammonia gas for 15 minutes at 65 °C. To this solution was added alkyl diazocompounds (0.3 mmol) in one portion. Immediately nitrogen release was detected, the reaction was completed in 1 minute, The solvent was removed under vacuum and the crude products were passed through a short column of silica gel, which were subjected to ^{1}H NMR to detect the diastereoselectivity. The crude products were purified by flash chromatography on silica gel (eluent: ethyl acetate / petroleum ether: 1:10 to 1:4) to give corresponding products.

2.3 Experimental procedure for the cyclization of 3c:



To a solution of **3c** (0.2 mmol) in DCM (2mL) was added 5% $NaHCO_3$ (3mL), $CSCl_2$ (0.3 mmol) was added subsequently. Afte 30 minutes, the reaction was quenched with brine (2mL), extracted three times with EA (2mL*3). The organic phase was removed under vacuum. The crude products were purified by flash chromatography on silica gel (eluent: ethyl acetate / petroleum ether: 1:2 to 2:1) to give corresponding products.

2.4 Transformation of intermediate a under basic conditions:

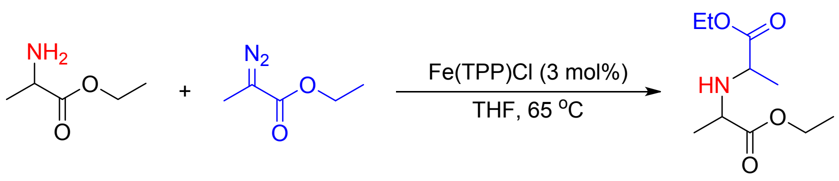


5a

To a reaction tube equipped with a stir bar was added isatin (0.2 mmol), Fe(TPP)Cl (0.002 mmol) and THF (3 mL). This solution was purged with ammonia gas for 15 minutes at 25 °C. To this solution was added EDA (0.3 mmol) in one portion. Immediately nitrogen release was detected, the reaction was completed in 1 minute, then 1M HCl (3mL) was added to the mixture, the reaction was quenched with brine (2mL), extracted three times with EA (2mL*3). The organic phase was removed under vacuum. The crude products were purified by flash chromatography on silica gel (eluent: ethyl acetate / petroleum ether: 1:10 to 1:4) to give **5a** in 85% yield.

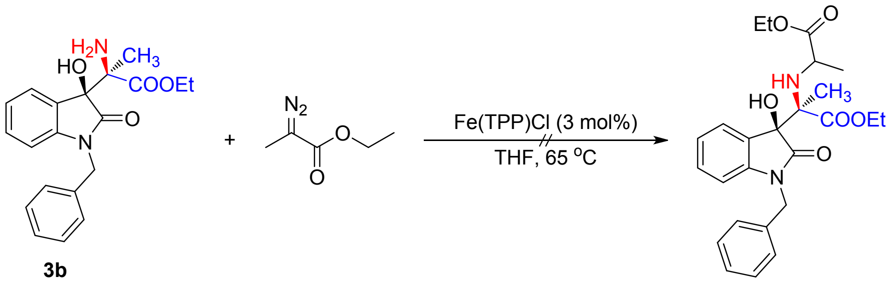
2.5 Control experiments for insights into excellent chemoselectivity of the three-component reaction:

2.5.1 N-H insertion with Ethyl 2-aminopropanoate



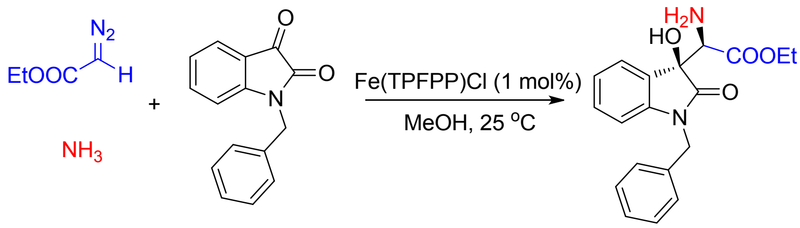
To a reaction tube equipped with a stir bar was added isatin (0.2 mmol), Fe(TPP)Cl (0.002 mmol) and THF (3 mL). This solution was purged with nitrogen gas for 20 minutes at 65 °C. To this solution was added diazocompounds (0.3 mmol) in one portion. Immediately nitrogen release was detected, the reaction was completed in 1 minute. The organic phase was removed under vacuum. The crude products were purified by flash chromatography on silica gel (eluent: ethyl acetate / petroleum ether: 1:8 to 1:4) to give corresponding product in 93% yield.

2.5.2 N-H insertion with three-component product



To a reaction tube equipped with a stir bar was added isatin (0.2 mmol), Fe(TPP)Cl (0.002 mmol) and THF (3 mL). This solution was purged with nitrogen gas for 20 minutes at 65 ºC. To this solution was added diazocompounds (0.3 mmol) in one portion. After the reaction, no desired product was detected.

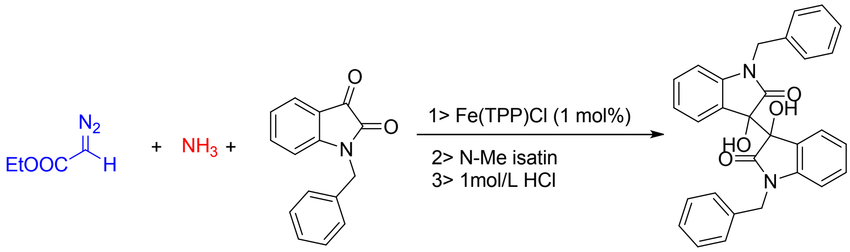
2.6 Experimental procedure for the synthesis of 3a:



3a
64% yield, 50:50 dr

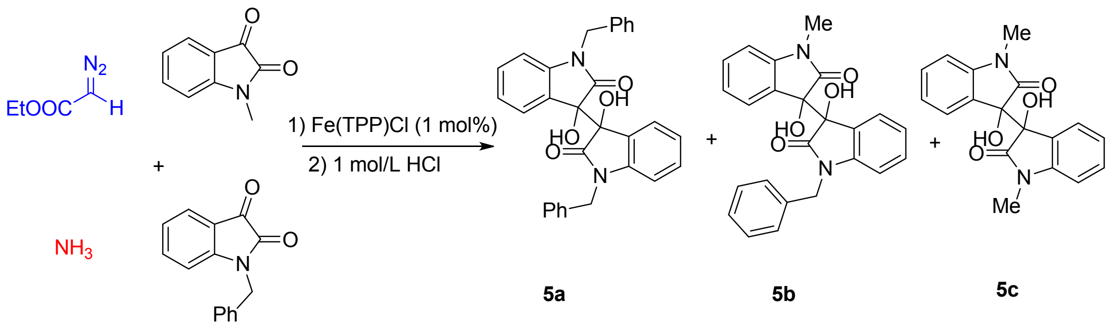
To a reaction tube equipped with a stir bar was added isatin (0.2 mmol), Fe(TPP)Cl (0.002 mmol) and Methanol (1.5 mL). This solution was purged with ammonia gas for 20 minutes at rt. To this solution was added EDA (0.3 mmol) in one portion. Immediately nitrogen release was detected, the reaction was completed in 1 minute, The solvent was removed under vacuum and the crude products were passed through a short column of silica gel, which were subjected to ^{1}H NMR to detect the diastereoselectivity. The crude products were purified by flash chromatography on silica gel (eluent: ethyl acetate / petroleum ether: 1:4 to 1:2) to give corresponding products in 64% yield and 50:50 dr value.

2.7 Control experiments of the formation of 5a and mechanism considerations



5a

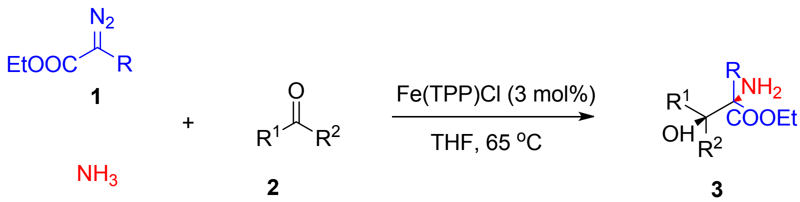
To a reaction tube equipped with a stir bar was added N-benzylisatin (0.2 mmol), Fe(TPP)Cl (0.002 mmol) and THF (3 mL). This solution was purged with ammonia gas for 15 minutes at 25 °C. To this solution was added EDA (0.3 mmol) in one portion. Immediately nitrogen release was detected, the reaction was completed in 1 minute, N-methylisatin (0.2mmol) was added subsequently, then 1M HCl (3mL) was added to the mixture, the reaction was quenched with brine (2mL), extracted three times with EA (2mL*3). The organic phase was removed under vacuum. The crude products were purified by flash chromatography on silica gel (eluent: ethyl acetate / petroleum ether: 1:10 to 1:4) to give corresponding products in 88% yield.

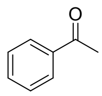
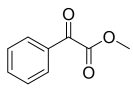
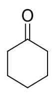
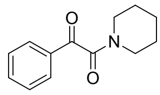
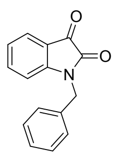


To a reaction tube equipped with a stir bar was added N-benzylisatin (0.2 mmol), N-methylisatin (0.2mmol), Fe(TPP)Cl (0.002 mmol) and THF (3 mL). This solution was purged with ammonia gas for 15 minutes at 25 °C. To this solution was added EDA (0.3 mmol) in one portion. Immediately nitrogen release was detected, the reaction was completed in 1 minute, then 1M HCl (3mL) was added to the mixture, the reaction was quenched with brine (2mL), extracted three times with EA (2mL*3). The organic phase was removed under vacuum. The crude products were passed through a short column of silica gel, which were subjected to ^{1}H NMR to detect the diastereoselectivity (**5a**:**5b**:**5c** = 1:2:1). The crude products were purified by flash chromatography on silica gel (eluent: ethyl acetate / petroleum ether: 1:10 to 1:4) to give corresponding products in 73% yield (**5a**, **5b** and **5c**).

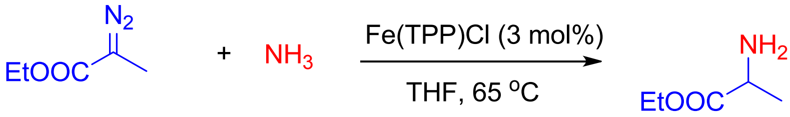
Mechanism considerations: After completion of the three-component reaction, N-methylisatin was added to the mixture, no cross-coupling isatide was detected after acidification of the mixture with 1M HCl, indicating isatin was not the reaction intermediate. The three-component reaction proceeded if equal mole of N-methyl and N-benzyl isatins were used as reaction substrates. Acidification of the mixture afforded 5a, 5b, and 5c with a ratio of 1:2:1. According to these facts, we reasoned that a bimolecular radical mechanism might be involved.

2.8 Examine of scope of diazocompounds and carbonyl substrates



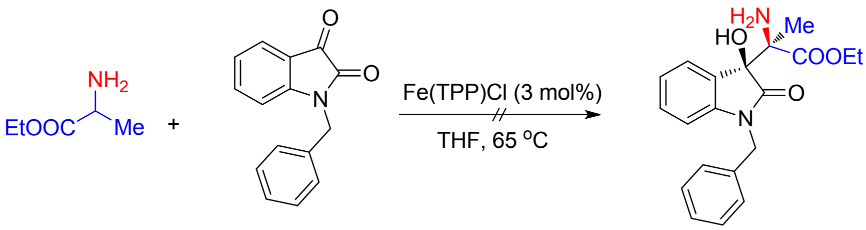
Entry	R	2	yield	dr
1	Me		NP	ND
2	Me		NP	ND
3	Me		NP	ND
4	Me		NP	ND
5	Ph		Diazocompound recovered	

2.9 control experiment of Fe(III)-catalyzed N-H insertion



To a reaction tube equipped with a stir bar was added, Fe(TPP)Cl (0.002 mmol) and THF (3 mL). This solution was purged with ammonia gas for 15 minutes at 65 °C. To this solution was added alkyl diazocompounds (0.3 mmol) in one portion. Immediately nitrogen release was detected, the reaction was completed in 1 minute. The crude product was purified by flash chromatography on silica gel (eluent: ethyl acetate / petroleum ether: 1:2 to 1:1) to give corresponding product in 94% yield.

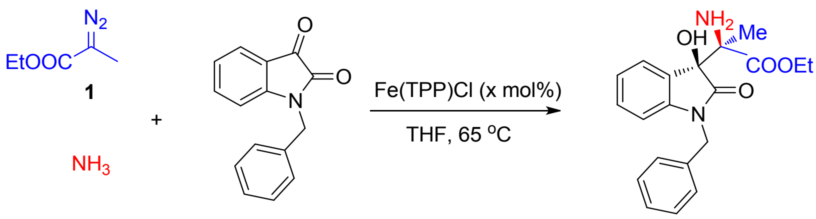
3.0 Control experiment of N-H insertion product and isatin



2

To a reaction tube equipped with a stir bar was added isatin (0.2 mmol), Fe(TPP)Cl (0.002 mmol) and THF (3 mL). This solution was purged with ammonia gas for 15 minutes at 65 °C. To this solution was added Ethyl 2-aminopropanoate (0.3 mmol) in one portion. No reaction was detected in 30 min.

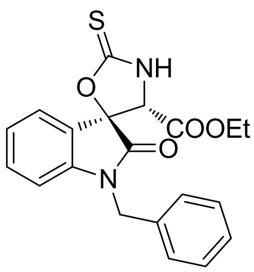
3.1 Screen of catalyst loading



entry	Catalyst loading (x mol%)	Yield(%)	dr
1	0.1	48	59:41
2	1	60	60:40
3	3	72	60:40
4	10	74	62:38

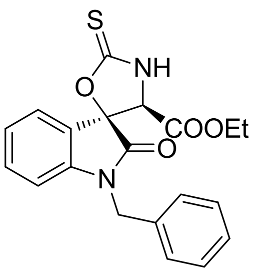
3. Characterization Data of the Products

(3S,4'R)-ethyl 1-benzyl-2-oxo-2'-thioxospiro[indoline-3,5'-oxazolidine]-4'-carboxylate (*anti*-4a)



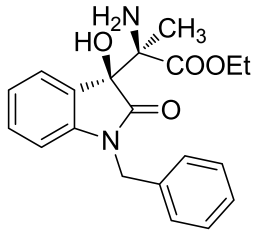
^{1}H NMR (400 MHz, DMSO) δ = 11.18 (s, 1H), 7.69 (d, *J* = 7.3, 1H), 7.44 (t, *J* = 7.3, 1H), 7.40 – 7.25 (m, 4H), 7.18 (t, *J* = 7.4, 1H), 7.06 (d, *J* = 7.9, 1H), 5.45 (s, 1H), 4.92 (s, 2H), 4.23 – 3.81 (m, 2H), 1.01 (t, *J* = 7.1, 3H). ^{13}C NMR (100 MHz, DMSO) δ = 186.68, 170.25, 166.23, 143.25, 135.39, 132.14, 128.71, 127.68, 127.25, 125.64, 124.27, 123.70, 110.26, 84.95, 63.45, 61.75, 42.95, 13.57. HRMS (ESI) m/z calcd for $C_{20}H_{18}N_2O_4NaS$ $(M+Na)^+$ 405.0885, found 405.0896.

(3S,4'R)-ethyl 1-benzyl-2-oxo-2'-thioxospiro[indoline-3,5'-oxazolidine]-4'-carboxylate (*syn*-4a)



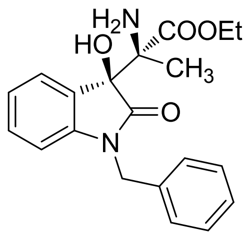
^{1}H NMR (400 MHz, DMSO) δ 11.17 (s, 1H), 7.41 (ddd, *J* = 5.6, 4.8, 1.2 Hz, 1H), 7.38 – 7.33 (m, 4H), 7.33 – 7.27 (m, 1H), 7.18 (dd, *J* = 7.5, 1.0 Hz, 1H), 7.11 (td, *J* = 7.5, 0.8 Hz, 1H), 7.07 (d, *J* = 7.9 Hz, 1H), 5.19 (s, 1H), 5.07 (d, *J* = 15.9 Hz, 1H), 4.92 (d, *J* = 15.9 Hz, 1H), 3.85 – 3.62 (m, 2H), 0.51 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, DMSO) δ 192.43, 175.92, 171.07, 148.10, 140.54, 137.41, 133.95, 132.96, 132.40, 129.69, 128.78, 127.58, 115.78, 89.53, 69.01, 68.08, 66.65, 48.45, 18.16. HRMS (ESI) m/z calcd for $C_{20}H_{18}N_2O_4NaS$ $(M+Na)^+$ 405.0885, found 405.0883.

(R)-ethyl 2-amino-2-((S)-1-benzyl-3-hydroxy-2-oxoindolin-3-yl)propanoate (*syn*-3b)



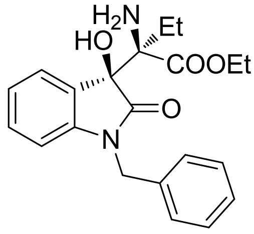
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, J = 7.5 Hz, 1H), 7.37 – 7.17 (m, 6H), 7.02 (t, J = 7.6 Hz, 1H), 6.69 (d, J = 7.9 Hz, 1H), 4.97 (d, J = 15.7 Hz, 1H), 4.79 (d, J = 15.7 Hz, 1H), 4.28 – 4.12 (m, 2H), 2.00 (s, 1H), 1.63 (s, 3H), 1.22 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.57, 174.64, 143.87, 135.50, 129.99, 128.75, 127.90, 127.62, 127.39, 124.86, 122.68, 109.40, 78.94, 62.19, 61.78, 43.87, 22.28, 13.92. HRMS (ESI) m/z calcd for $C_{20}H_{22}N_2O_4Na$ $(M+Na)^+$ 377.1477, found 377.1493.

(S)-ethyl 2-amino-2-((S)-1-benzyl-3-hydroxy-2-oxoindolin-3-yl)propanoate (*anti*-3b)



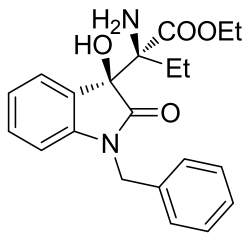
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (dd, J = 7.5, 0.6 Hz, 1H), 7.36 – 7.16 (m, 6H), 7.02 (td, J = 7.6, 0.8 Hz, 1H), 6.70 (d, J = 7.8 Hz, 1H), 4.95 (d, J = 15.6 Hz, 1H), 4.70 (d, J = 15.6 Hz, 1H), 4.04 – 3.84 (m, 2H), 1.48 (s, 3H), 0.97 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.08, 174.60, 143.87, 135.60, 129.79, 128.74, 127.83, 127.67, 127.57, 125.32, 122.69, 109.21, 62.48, 61.50, 43.86, 20.53, 13.63. HRMS (ESI) m/z calcd for $C_{20}H_{22}N_2O_4Na$ $(M+Na)^+$ 377.1477, found 377.1463.

(R)-ethyl 2-amino-2-((S)-1-benzyl-3-hydroxy-2-oxoindolin-3-yl)butanoate (*syn*-3c)



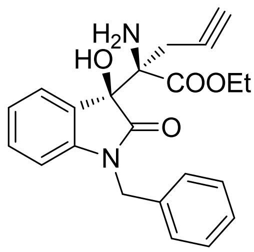
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (dd, J = 7.5, 0.8 Hz, 1H), 7.38 – 7.16 (m, 7H), 7.01 (td, J = 7.6, 1.0 Hz, 1H), 6.66 (d, J = 7.8 Hz, 1H), 5.00 (d, J = 15.8 Hz, 1H), 4.75 (d, J = 15.8 Hz, 1H), 4.27 (qd, J = 7.1, 0.8 Hz, 2H), 2.56 (dq, J = 14.9, 7.5 Hz, 1H), 1.82 (dq, J = 14.8, 7.4 Hz, 1H), 1.27 (t, J = 7.1 Hz, 3H), 0.90 (t, J = 7.5 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.17, 173.67, 144.16, 135.52, 129.94, 128.70, 127.67, 127.54, 127.32, 125.39, 122.50, 109.35, 79.87, 65.86, 62.16, 43.81, 27.27, 14.09, 7.63. HRMS (ESI) m/z calcd for $C_{21}H_{24}N_2O_4Na$ $(M+Na)^+$ 391.1634, found 391.1648.

(S)-ethyl 2-amino-2-((S)-1-benzyl-3-hydroxy-2-oxoindolin-3-yl)butanoate (*anti*-3c)



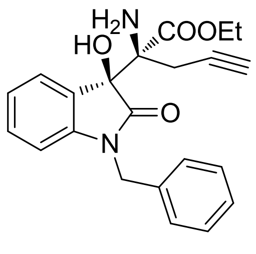
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.16 (m, 8H), 7.02 (t, J = 7.4 Hz, 1H), 6.70 (d, J = 7.8 Hz, 1H), 4.97 (d, J = 15.5 Hz, 1H), 4.62 (d, J = 15.5 Hz, 1H), 3.82 (m, 7.1 Hz, 2H), 2.28 – 2.04 (m, 2H), 0.87 (dt, J = 11.2, 7.3 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.97, 173.84, 143.87, 135.63, 129.61, 128.73, 128.13, 127.70, 127.32, 125.48, 122.57, 109.05, 66.67, 61.32, 43.85, 25.27, 13.59, 7.93. HRMS (ESI) m/z calcd for $C_{21}H_{24}N_2O_4Na$ $(M+Na)^+$ 391.1634, found 391.1814.

(R)-ethyl 2-amino-2-((S)-1-benzyl-3-hydroxy-2-oxoindolin-3-yl)pent-4-ynoate (*syn*-3d)



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.15 (m, 7H), 7.01 (t, J = 7.6 Hz, 1H), 6.69 (d, J = 7.8 Hz, 1H), 5.02 (s, 1H), 4.94 (d, J = 15.7 Hz, 1H), 4.80 (d, J = 15.7 Hz, 1H), 4.20 – 3.99 (m, 2H), 3.46 (dd, J = 16.9, 2.5 Hz, 1H), 2.90 (dd, J = 16.9, 2.5 Hz, 1H), 2.19 – 1.86 (m, 3H), 1.09 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.70, 172.14, 143.59, 135.38, 130.27, 128.76, 127.69, 127.52, 124.89, 122.81, 109.48, 78.69, 77.89, 72.19, 65.13, 62.40, 44.01, 25.24, 13.87. HRMS (ESI) m/z calcd for $C_{22}H_{22}N_2O_4Na$ $(M+Na)^+$ 401.1477, found 401.1479.

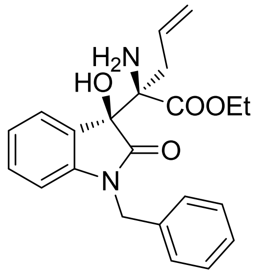
(S)-ethyl 2-amino-2-((S)-1-benzyl-3-hydroxy-2-oxoindolin-3-yl)pent-4-ynoate (*anti*-3d)



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.19 (m, 7H), 7.03 (t, J = 7.6 Hz, 1H), 6.70 (d, J = 7.8 Hz, 1H), 5.24 (s, 1H), 5.00 (d, J =

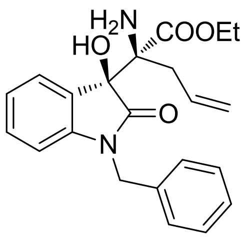
15.5 Hz, 1H), 4.60 (d, J = 15.5 Hz, 1H), 4.02 – 3.76 (m, 2H), 3.11 (qd, J = 16.4, 2.6 Hz, 2H), 2.52 (s, 2H), 2.06 (t, J = 2.6 Hz, 1H), 0.88 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.04, 172.65, 143.71, 135.40, 130.09, 128.77, 127.78, 127.69, 127.05, 125.06, 122.79, 109.33, 78.54, 72.41, 65.33, 61.81, 43.97, 23.73, 13.60. HRMS (ESI) m/z calcd for $C_{22}H_{22}N_2O_4Na$ $(M+Na)^+$ 401.1477, found 401.1476.

(R)-ethyl 2-amino-2-((S)-1-benzyl-3-hydroxy-2-oxoindolin-3-yl)pent-4-enoate (*syn*-3e)



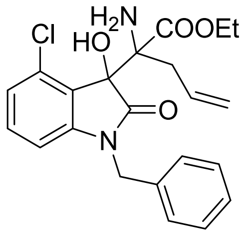
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, J = 7.4 Hz, 1H), 7.36 (d, J = 7.5 Hz, 2H), 7.30 (t, J = 7.5 Hz, 2H), 7.24 (m, 1H), 7.20 (t, J = 7.8 Hz, 1H), 7.02 (t, J = 7.6 Hz, 1H), 6.68 (d, J = 7.8 Hz, 1H), 5.74 – 5.52 (m, 1H), 5.20 (m, 3H), 4.98 (d, J = 15.7 Hz, 1H), 4.79 (d, J = 15.7 Hz, 1H), 4.24 – 4.04 (m, 2H), 3.28 (dd, J = 13.7, 6.3 Hz, 1H), 2.60 (dd, J = 13.7, 8.4 Hz, 1H), 1.72 (s, 2H), 1.16 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.52, 173.34, 143.89, 135.50, 131.56, 130.02, 128.73, 127.89, 127.61, 127.43, 125.12, 122.64, 120.69, 109.37, 78.96, 65.04, 62.17, 43.91, 38.83, 13.98. HRMS (ESI) m/z calcd for $C_{22}H_{24}N_2O_4Na$ $(M+Na)^+$ 403.1634, found 403.1652.

(S)-ethyl 2-amino-2-((S)-1-benzyl-3-hydroxy-2-oxoindolin-3-yl)pent-4-enoate (*anti*-3e)



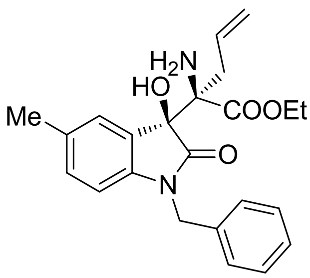
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, J = 7.4 Hz, 1H), 7.36 – 7.16 (m, 6H), 7.03 (t, J = 7.6 Hz, 1H), 6.71 (d, J = 7.8 Hz, 1H), 5.66 – 5.47 (m, 2H), 5.30 – 5.17 (m, 2H), 4.96 (d, J = 15.5 Hz, 1H), 4.62 (d, J = 15.5 Hz, 1H), 3.81 (m, 2H), 2.99 (dd, J = 13.3, 5.4 Hz, 1H), 2.76 (dd, J = 13.3, 9.5 Hz, 1H), 2.31 (s, 2H), 0.84 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.78, 173.44, 143.87, 135.60, 131.52, 129.73, 128.73, 127.73, 127.71, 125.50, 122.61, 121.30, 109.10, 65.21, 61.41, 43.90, 37.18, 13.58. HRMS (ESI) m/z calcd for $C_{22}H_{24}N_2O_4Na$ $(M+Na)^+$ 403.1634, found 403.1636.

ethyl 2-amino-2-(1-benzyl-4-chloro-3-hydroxy-2-oxoindolin-3-yl)pent-4-enoate (*syn*-3f+*anti*-3f)



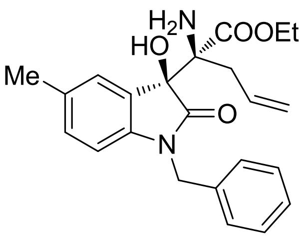
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.24 (m, 6H, *syn*; m, 6H, *anti*; overlap), 7.03 – 6.98 (m, 1H, *syn*; m, 1H, *anti*; overlap), 6.71 – 6.66 (m, 1H, *syn*; m, 1H, *anti*; overlap), 5.70 – 5.49 (m, 1H, *syn*; m, 1H, *anti*; overlap), 5.24 (m, 2H, *syn*; m, 2H, *anti*; overlap), 4.96 (d, *J* = 15.8 Hz, 1H, *syn*), 4.94 (t, *J* = 15.8 Hz, 1H, *anti*), 4.74 (d, *J* = 15.8 Hz, 1H, *syn*), 4.58 (d, *J* = 15.8 Hz, 1H, *anti*), 4.23 – 4.08 (m, 2H, *syn*), 3.95 – 3.68 (m, 2H, *anti*), 3.25 (dd, *J* = 13.7, 6.4 Hz, 1H, *syn*), 2.92 (dd, *J* = 13.3, 5.4 Hz, 1H, *anti*), 2.72 (dd, *J* = 13.3, 9.5 Hz, 1H, *anti*), 2.55 (dd, *J* = 13.7, 8.4 Hz, 1H, *syn*)1.18 (t, *J* = 7.1 Hz, 1H, *syn*), 0.89 (t, *J* = 7.1 Hz, 1H, *anti*). ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.75, 173.28, 173.18, 145.20, 145.17, 135.88, 135.59, 135.03, 134.95, 131.25, 131.18, 128.89, 128.87, 127.94, 127.83, 127.66, 127.38, 126.43, 126.29, 126.09, 122.51, 121.56, 120.92, 109.92, 109.70, 65.11, 64.94, 62.30, 61.61, 44.01, 38.85, 37.25, 14.00, 13.67. HRMS (ESI) m/z calcd for $C_{22}H_{23}N_2O_4NaCl$ $(M+Na)^+$ 437.1244, found 437.1250.

(R)-ethyl 2-amino-2-((S)-1-benzyl-3-hydroxy-5-methyl-2-oxoindolin-3-yl)pent-4-enoate (*syn*-3g)



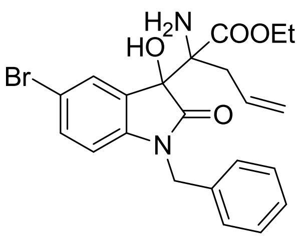
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.15 (m, 6H), 7.06 – 6.91 (m, 1H), 6.56 (d, *J* = 8.0 Hz, 1H), 5.65 (dddd, *J* = 16.0, 10.9, 8.3, 6.5 Hz, 1H), 5.28 – 5.12 (m, 2H), 4.94 (d, *J* = 15.7 Hz, 1H), 4.77 (d, *J* = 15.7 Hz, 1H), 4.29 – 4.03 (m, 2H), 3.27 (dd, *J* = 13.7, 6.5 Hz, 1H), 2.59 (dd, *J* = 13.7, 8.3 Hz, 1H), 2.30 (s, 3H), 1.19 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.52, 173.47, 141.48, 135.59, 132.21, 131.59, 130.28, 128.70, 127.78, 127.55, 127.39, 125.98, 120.66, 109.17, 79.21, 64.97, 62.15, 43.88, 38.82, 21.13, 14.01. HRMS (ESI) m/z calcd for $C_{23}H_{26}N_2O_4Na$ $(M+Na)^+$ 417.1790, found 417.1788.

(S)-ethyl 2-amino-2-((S)-1-benzyl-3-hydroxy-5-methyl-2-oxoindolin-3-yl)pent-4-enoate (*anti*-3g)



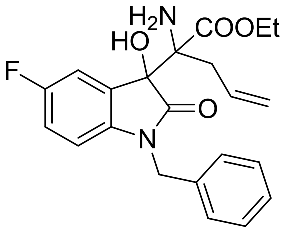
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.14 (m, 6H), 7.06 – 6.90 (m, 1H), 6.59 (d, *J* = 7.9 Hz, 1H), 5.71 – 5.50 (m, 1H), 5.36 – 5.13 (m, 2H), 4.92 (d, *J* = 15.5 Hz, 1H), 4.62 (d, *J* = 15.5 Hz, 1H), 3.99 – 3.67 (m, 2H), 2.99 (dd, *J* = 13.3, 5.4 Hz, 1H), 2.75 (dd, *J* = 13.3, 9.5 Hz, 1H), 2.31 (s, 3H), 0.88 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.74, 173.47, 141.45, 135.69, 132.12, 131.62, 129.97, 128.69, 127.72, 127.68, 127.64, 126.32, 121.27, 108.89, 65.18, 61.39, 43.88, 37.23, 21.15, 13.65. HRMS (ESI) m/z calcd for $C_{23}H_{26}N_2O_4Na$ $(M+Na)^+$ 417.1790, found 417.1786.

ethyl 2-amino-2-(1-benzyl-5-bromo-3-hydroxy-2-oxoindolin-3-yl)pent-4-enoate (*syn*-3h+*anti*-3h)



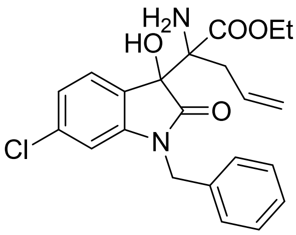
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, *J* = 2.0 Hz, 1H, *syn*), 7.50 (d, *J* = 2.0 Hz, 1H, *anti*), 7.37 – 7.22 (m, 6H, *syn*; m, 6H, *anti*; overlap), 6.57 (d, *J* = 8.3 Hz, 1H, *anti*), 6.53 (d, *J* = 8.3 Hz, 1H, *syn*), 5.71 – 5.48 (m, 1H, *syn*; m, 1H, *anti*; overlap), 5.32 – 5.17 (m, 2H, *syn*; m, 2H, *anti*; overlap), 4.96 (d, *J* = 15.8 Hz, 1H, *syn*), 4.92 (d, *J* = 15.6 Hz, 1H, *anti*), 4.76 (d, *J* = 15.8 Hz, 1H, *syn*), 4.62 (d, *J* = 15.6 Hz, 1H, *anti*), 4.24 – 4.11 (m, 2H, *syn*), 3.96 – 3.72 (m, 2H, *anti*), 3.24 (dd, *J* = 13.7, 6.5 Hz, 1H, *syn*), 2.93 (dd, *J* = 13.3, 5.4 Hz, 2H, *anti*), 2.72 (dd, *J* = 13.3, 9.5 Hz, 2H, *anti*), 2.55 (dd, *J* = 13.7, 8.3 Hz, 1H, *syn*), 1.19 (t, *J* = 7.1 Hz, 3H, *syn*), 0.90 (t, *J* = 7.1 Hz, 3H, *anti*). ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.29, 176.05, 173.26, 173.06, 142.97, 135.08, 135.00, 132.76, 132.49, 131.18, 131.11, 129.96, 128.84, 128.74, 128.43, 127.89, 127.78, 127.64, 127.35, 121.65, 120.98, 115.38, 115.33, 110.80, 110.53, 79.03, 76.92, 65.12, 64.96, 62.34, 61.62, 43.96, 38.81, 37.26, 14.00, 13.69. HRMS (ESI) m/z calcd for $C_{22}H_{24}N_2O_4Br$ (M^+) 459.0919, found 459.0918.

ethyl 2-amino-2-(1-benzyl-5-fluoro-3-hydroxy-2-oxoindolin-3-yl)pent-4-enoate (*anti*-3i+*syn*-3i)



[1]H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.23 (m, 5H, *syn*; m, 5H, *anti*; overlap), 7.18 (m, 1H, *syn*; m, 1H, *anti*; overlap), 6.92 (m, 1H, *syn*; m, 1H, *anti*; overlap), 6.60 (m, 1H, *syn*; m, 1H, *anti*; overlap), 5.70 – 5.48 (m, 1H, *syn*; m, 1H, *anti*; overlap), 5.31 – 5.15 (m, 2H, *syn*; m, 2H, *anti*; overlap), 4.97 (d, *J* = 15.7, 1H, *syn*), 4.95 (d, *J* = 15.7 Hz, 1H, *anti*), 4.77 (d, *J* = 15.7 Hz, 1H, *syn*), 4.60 (d, *J* = 15.7 Hz, 1H, *anti*), 4.23 – 4.09 (m, 2H, *syn*), 3.95 – 3.70 (m, 2H, *anti*), 3.26 (dd, *J* = 13.7, 6.4 Hz, 1H, *syn*), 2.94 (dd, *J* = 13.2, 5.4 Hz, 1H, *anti*), 2.71 (dd, *J* = 13.2, 9.5 Hz, 1H, *anti*), 2.57 (dd, *J* = 13.7, 8.5 Hz, 1H, *syn*), 1.17 (t, *J* = 7.1 Hz, 3H, *syn*), 0.87 (t, *J* = 7.1 Hz, 1H, *anti*). [13]C NMR (100 MHz, $CDCl_3$) δ 176.61, 176.29, 173.24, 173.15, 160.20, 157.81, 139.81 (d, *J* = 2.1 Hz), 139.76 (d, *J* = 2.1 Hz), 135.26, 135.17, 131.23, 131.10, 129.44 (d, *J* = 8.0 Hz), 128.83, 127.87, 127.75, 127.69, 127.39, 121.66, 121.01, 116.19 (d, *J* = 23.3 Hz), 115.90 (d, *J* = 23.4 Hz), 113.89 (d, *J* = 25.3 Hz), 113.48 (d, *J* = 25.2 Hz), 109.91 (d, *J* = 8.1 Hz), 109.60 (d, *J* = 8.0 Hz), 79.08, 77.24, 65.14, 64.94, 62.33, 61.58, 44.03, 38.69, 37.16, 31.94, 14.00, 13.64. HRMS (ESI) m/z calcd for $C_{22}H_{23}N_2O_4NaF$ $(M+Na)^+$ 421.1540, found 421.1535.

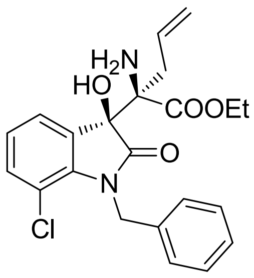
ethyl 2-amino-2-(1-benzyl-6-chloro-3-hydroxy-2-oxoindolin-3-yl)pent-4-enoate (*anti*-3j+*syn*-3j)



[1]H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.23 (m, 5H, *syn*; m, 5H, *anti*; overlap), 7.17 – 7.05 (m, 1H, *syn*; m, 1H, *anti*; overlap), 6.99 (m, 1H, *syn*), 6.93 (m, 1H, *anti*), 6.63 – 6.60 (m, 1H, *syn*), 6.58 (dd, *J* = 7.8, 0.8 Hz, 1H, *anti*), 5.65 – 5.42 (m, 1H, *syn*; m, 1H, *anti*; overlap), 5.25 – 5.14 (m, 2H, *syn*; m, 2H, *anti*; overlap), 5.06 (d, *J* = 15.6 Hz, 1H, *anti*), 4.92 (d, *J* = 15.4 Hz, 1H, *syn*), 4.68 (d, *J* = 15.6 Hz, 1H, *anti*), 4.59 (d, *J* = 15.5 Hz, 1H, *syn*), 3.92 (m, 2H, *syn*), 3.85 – 3.64 (m, 2H, *anti*), 3.08 (ddd, *J* = 14.0, 5.7, 1.3 Hz, 1H, *anti*), 2.96 – 2.86 (m, 1H, *syn*), 2.75 (m, 1H, *syn*; m, 1H, *anti*; overlap), 0.97 (t, *J* = 7.1 Hz, 3H, *anti*), 0.91 (t, *J* = 7.2 Hz, 1H, *syn*). [13]C NMR (100 MHz, $CDCl_3$) δ 176.61, 176.28, 172.88, 172.72, 145.89, 145.73, 135.21, 135.07, 131.97, 131.92, 131.78, 131.56, 130.67, 130.59,

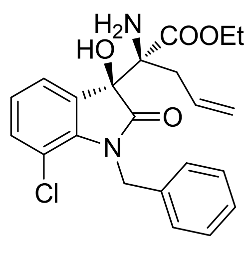
128.82, 128.79, 127.90, 127.81, 127.57, 127.29, 126.05, 125.91, 124.97, 124.88, 124.56, 121.28, 121.12, 107.62, 107.52, 79.74, 79.67, 67.28, 66.46, 62.12, 61.63, 44.37, 44.29, 40.53, 39.61, 13.75, 13.66. HRMS (ESI) m/z calcd for $C_{22}H_{23}N_2O_4NaCl$ $(M+Na)^+$ 437.1244, found 437.1248.

(R)-ethyl 2-amino-2-((S)-1-benzyl-7-chloro-3-hydroxy-2-oxoindolin-3-yl)pent-4-enoate (*syn*-3k)



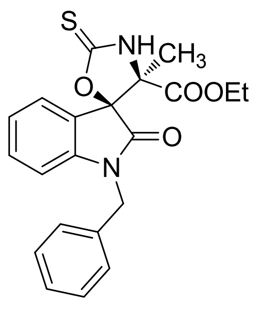
^1H NMR (400 MHz, $CDCl_3$) δ 7.36 (dd, *J* = 7.4, 1.1 Hz, 1H), 7.34 – 7.15 (m, 6H), 6.97 (dd, *J* = 8.2, 7.5 Hz, 1H), 5.72 – 5.52 (m, 1H), 5.41 – 5.13 (m, 5H), 4.16 (q, *J* = 7.1 Hz, 2H), 3.24 (dd, *J* = 13.7, 6.3 Hz, 1H), 2.57 (dd, *J* = 13.8, 8.5 Hz, 1H), 1.76 (s, 2H), 1.19 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.24, 173.13, 139.90, 137.18, 132.56, 131.34, 131.09, 128.50, 127.14, 126.68, 123.65, 123.53, 120.96, 115.66, 78.10, 65.12, 62.33, 45.07, 38.66, 13.97. HRMS (ESI) m/z calcd for $C_{22}H_{23}N_2O_4NaCl$ $(M+Na)^+$ 437.1244, found 437.1241.

(S)-ethyl 2-amino-2-((S)-1-benzyl-7-chloro-3-hydroxy-2-oxoindolin-3-yl)pent-4-enoate (*anti*-3k)



^1H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.16 (m, 7H), 6.99 (dd, *J* = 8.2, 7.5 Hz, 1H), 5.55 (m, 1H), 5.33 – 5.09 (m, 4H), 4.04 – 3.79 (m, 2H), 3.02 – 2.82 (m, 1H), 2.69 (dd, *J* = 13.3, 9.5 Hz, 1H), 1.00 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.65, 173.22, 139.91, 137.04, 132.30, 131.24, 130.89, 128.49, 127.21, 126.84, 124.11, 123.45, 121.55, 115.46, 76.37, 65.27, 61.71, 44.97, 37.21, 13.72. HRMS (ESI) m/z calcd for $C_{22}H_{23}N_2O_4NaCl$ $(M+Na)^+$ 437.1244, found 437.1239.

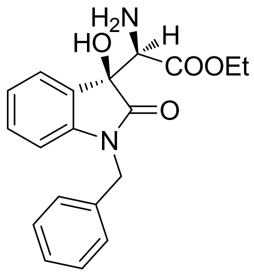
(3S)-ethyl 1-benzyl-4'-methyl-2-oxo-2'-thioxospiro[indoline-3,5'-oxazolidine]-4'-carboxylate (4b)



^1H NMR (400 MHz, DMSO) δ 11.09 (s, 1H), 7.64 – 7.24 (m, 6H), 7.24 – 6.91 (m, 3H), 5.06 (d, *J* = 15.7 Hz, 1H), 4.85 (d, *J* = 15.8 Hz, 1H), 4.05 – 3.65 (m, 2H), 1.57 (s, 3H), 0.71 (t, *J* = 6.9

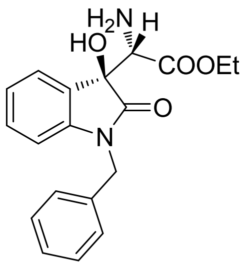
Hz, 3H). ^{13}C NMR (100 MHz, DMSO) δ 187.01, 169.36, 168.13, 142.82, 135.46, 132.03, 128.74, 127.71, 127.25, 124.32, 123.32, 122.40, 110.34, 86.35, 70.49, 61.91, 43.17, 19.74, 13.09. HRMS (ESI) m/z calcd for $C_{21}H_{20}N_2O_4NaS$ $(M+Na)^+$ 419.1041, found 419.1033.

(R)-ethyl 2-amino-2-((S)-1-benzyl-3-hydroxy-2-oxoindolin-3-yl)acetate (*syn*-3a)



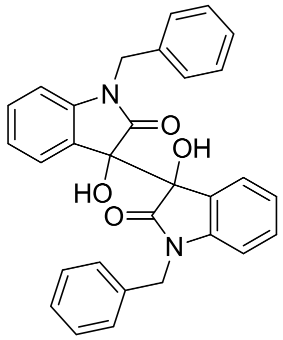
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 – 7.13 (m, 7H), 7.04 (t, J = 7.5 Hz, 1H), 6.67 (d, J = 7.8 Hz, 1H), 5.00 (d, J = 15.7 Hz, 1H), 4.72 (d, J = 15.7 Hz, 1H), 3.96 (q, J = 7.1 Hz, 2H), 3.92 (s, 1H), 0.93 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.27, 172.25, 143.66, 135.47, 130.11, 128.74, 127.65, 127.44, 124.38, 122.95, 109.41, 77.35, 77.03, 76.71, 75.04, 61.33, 60.16, 43.87, 13.67. HRMS (ESI) m/z calcd for $C_{19}H_{20}N_2O_4Na$ $(M+Na)^+$ 363.1321, found 363.1324.

(S)-ethyl 2-amino-2-((S)-1-benzyl-3-hydroxy-2-oxoindolin-3-yl)acetate (*anti*-3a)



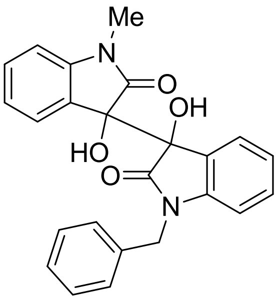
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (m, 6H), 7.19 (t, J = 7.7 Hz, 1H), 6.99 (t, J = 7.5 Hz, 1H), 6.72 (d, J = 7.8 Hz, 1H), 4.90 (s, 1H), 4.13 (s, 1H), 3.86 (m, 2H), 0.80 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.13, 171.11, 143.39, 135.49, 129.92, 128.75, 128.43, 127.76, 127.71, 123.84, 123.01, 109.36, 77.35, 77.03, 76.71, 75.03, 61.77, 58.74, 44.15, 13.55. HRMS (ESI) m/z calcd for $C_{19}H_{20}N_2O_4Na$ $(M+Na)^+$ 363.1321, found 363.1327.

1,1'-dibenzyl-3,3'-dihydroxy-[3,3'-biindoline]-2,2'-dione (5a)



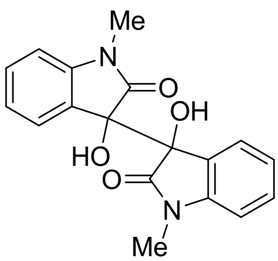
^{1}H NMR (400 MHz, DMSO) δ 7.27 (t, J = 7.7 Hz, 2H), 7.18 (m, 6H), 7.00 (s, 4H), 6.87 (m, 2H), 6.71 (d, J = 7.8 Hz, 2H), 6.46 (s, 2H), 4.83 (d, J = 16.0 Hz, 2H), 4.66 (d, J = 16.0 Hz, 2H). ^{13}C NMR (100 MHz, DMSO) δ 174.89, 143.17, 135.67, 130.05, 128.40, 127.08, 126.84, 126.62, 125.51, 122.19, 109.16, 77.30, 42.71. HRMS (ESI) m/z calcd for $C_{30}H_{24}N_2O_4Na$ $(M+Na)^+$ 499.1634, found 499.1646.

1-benzyl-3,3'-dihydroxy-1'-methyl-[3,3'-biindoline]-2,2'-dione



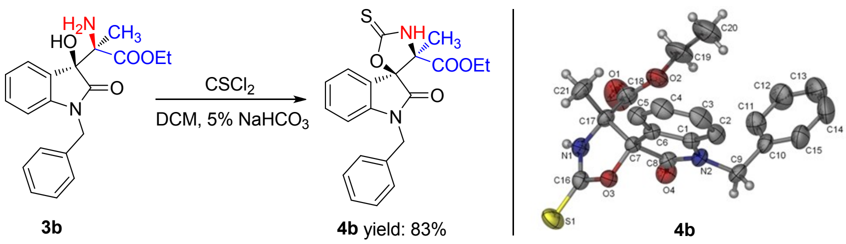
^1H NMR (400 MHz, DMSO) δ 7.37 (t, J = 7.7 Hz, 1H), 7.26 (t, J = 7.6 Hz, 2H), 7.17 – 7.16 (m, 3H), 7.03 – 6.97 (m, 2H), 6.86 – 6.71 (m, 3H), 6.65 (d, J = 7.8 Hz, 1H), 6.55 (s, 1H), 6.35 (s, 1H), 6.20 (s, 1H), 4.76 (d, J = 16.1 Hz, 1H), 4.51 (d, J = 16.1 Hz, 1H), 3.03 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ 180.27, 179.74, 149.32, 148.27, 140.80, 135.45, 135.25, 133.67, 132.27, 131.88, 131.80, 131.61, 131.25, 129.97, 127.43, 127.32, 114.24, 113.82, 83.52, 81.64, 47.79, 31.00. HRMS (ESI) m/z calcd for $C_{24}H_{20}N_2O_4Na$ $(M+Na)^+$ 423.1321, found 423.1329.

3,3'-dihydroxy-1,1'-dimethyl-[3,3'-biindoline]-2,2'-dione



^1H NMR (400 MHz, DMSO) δ 7.33 (t, J = 7.7 Hz, 2H), 6.91 (t, J = 7.6 Hz, 4H), 6.75 (s, 1H), 6.29 (s, 2H), 5.75 (s, 1H), 2.89 (s, 6H). ^{13}C NMR (100 MHz, DMSO) δ 174.55, 143.87, 130.07, 126.29, 125.06, 121.89, 108.35, 77.48, 54.87, 25.59. HRMS (ESI) m/z calcd for $C_{18}H_{16}N_2O_4Na$ $(M+Na)^+$ 347.1008, found 347.1016.

X-ray sturucure of deriviate of product **4b**



CCDC 1502570 (*syn*-**4b**) contains the supplementary crystallographic data for this paper. This data can be obtained from www.ccdc.cam.ac.uk/data_request/cif.

Crystal data and structure refinement for z.

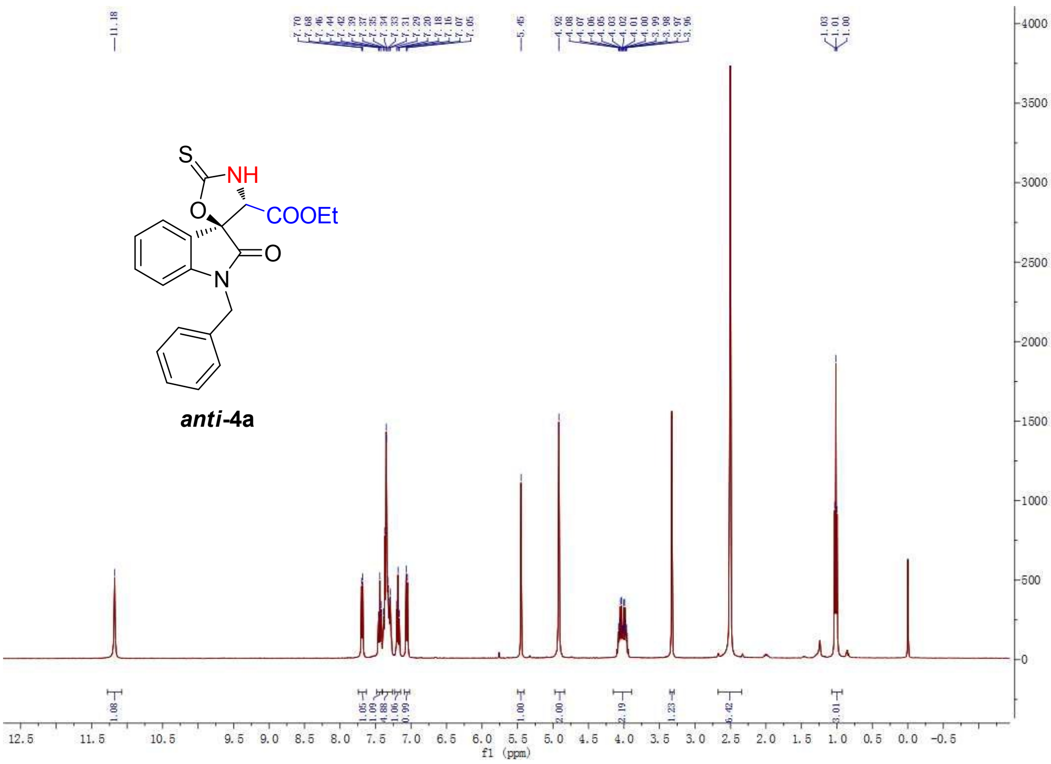
Identification code	z
Empirical formula	C21H20N2O4S
Formula weight	396.45
Temperature	296(2) K
Wavelength	0.71073 A
Crystal system, space group	Orthorhombic, P2(1)2(1)2(1)
Unit cell dimensions	a = 8.7225(7) A alpha = 90 deg.
	b = 10.1995(8) A beta = 90 deg.
	c = 22.6633(18) A gamma = 90deg.
Volume	2016.2(3) A^3
Z, Calculated density	4, 1.306 Mg/m^3
Absorption coefficient	0.189 mm^-1
F(000)	832
Crystal size	0.48 x 0.46 x 0.14 mm
Theta range for data collection	2.69 to 25.01 deg.
Limiting indices	-10<=h<=10, -12<=k<=12,-26<=l<=26
Reflections collected / unique	23366 / 3548 [R(int) = 0.0373]
Completeness to theta = 25.01	99.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9740 and 0.9145
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3548 / 8 / 253
Goodness-of-fit on F^2	1.036
Final R indices [I>2sigma(I)]	R1 = 0.0335, wR2 = 0.0838
R indices (all data)	R1 = 0.0364, wR2 = 0.0863
Absolute structure parameter	0.52(8)
Largest diff. peak and hole	0.196 and -0.205 e.A^-3

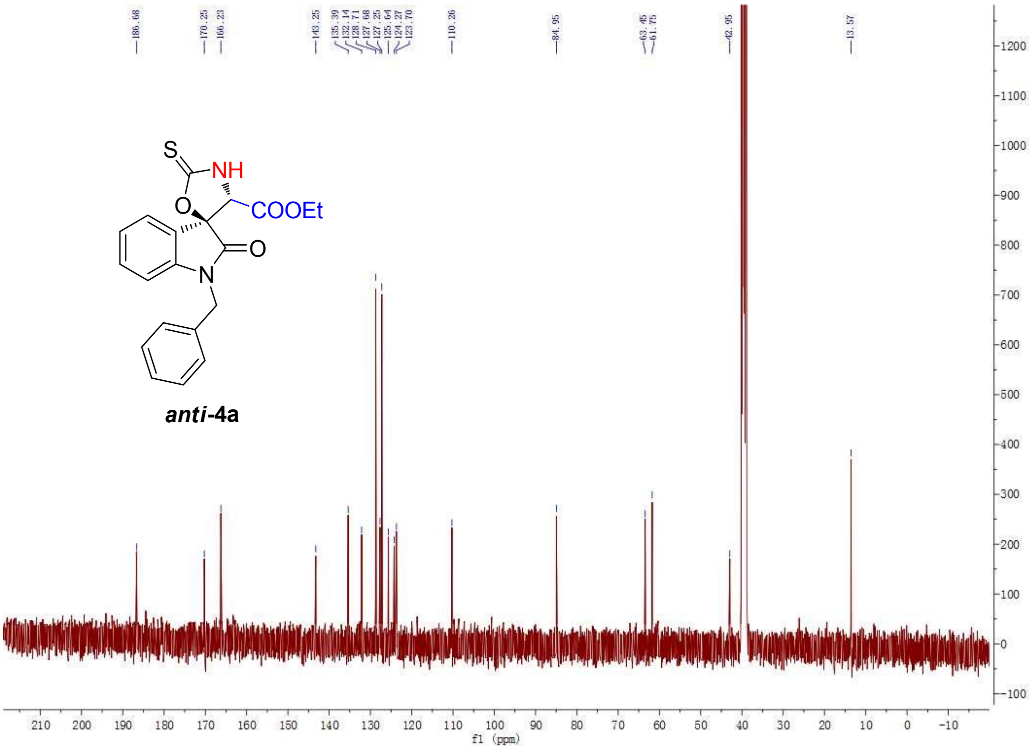
4. References

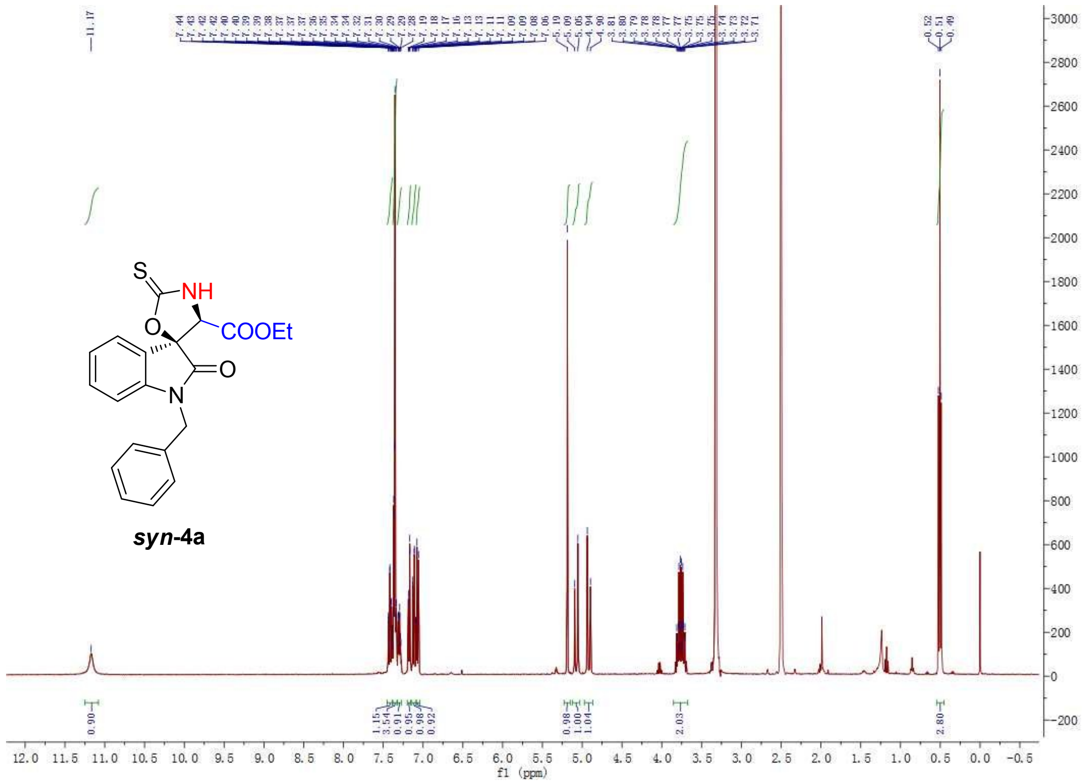
1. Doyle, M. P., Mckervey, M. A. and Ye, T. *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds*; Wiley: New York, (1998).

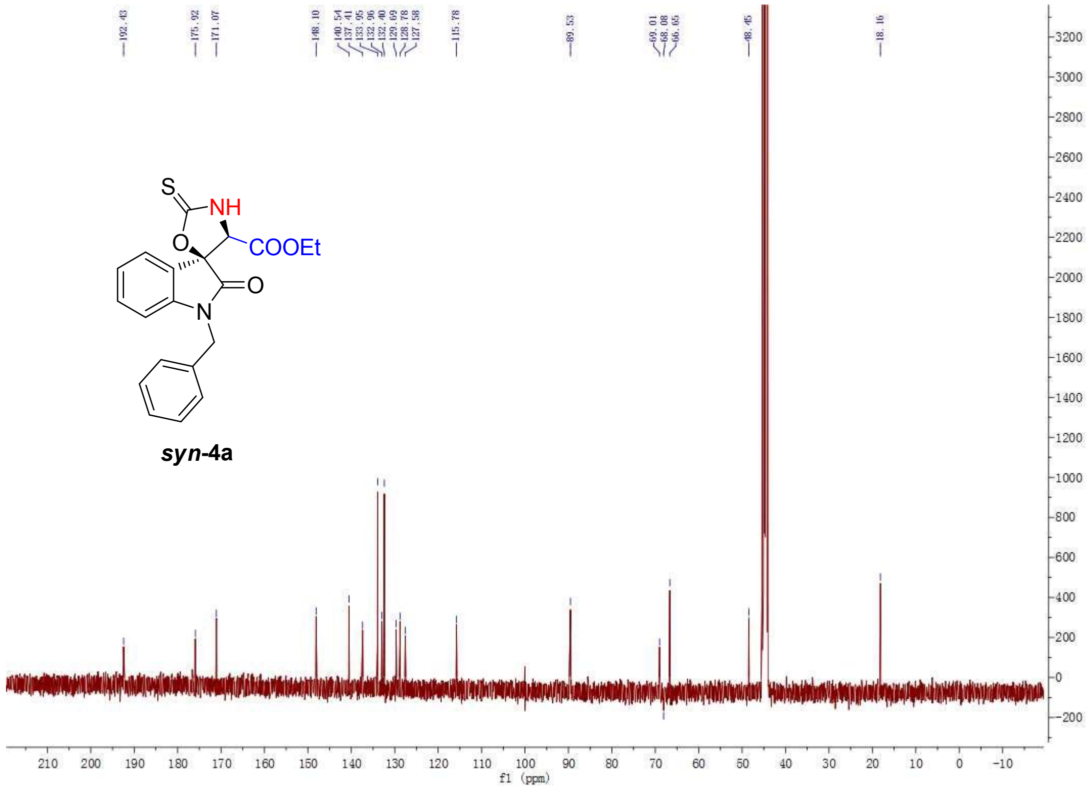
2. Xu, J.; Zhang, W.; Liu, Y.; Zhu, S.; Liu, M.; Hua, X.; Chen, S.; Lu, T.; Du, D., *RSC Advances* 2016, 6, 18601-18606.

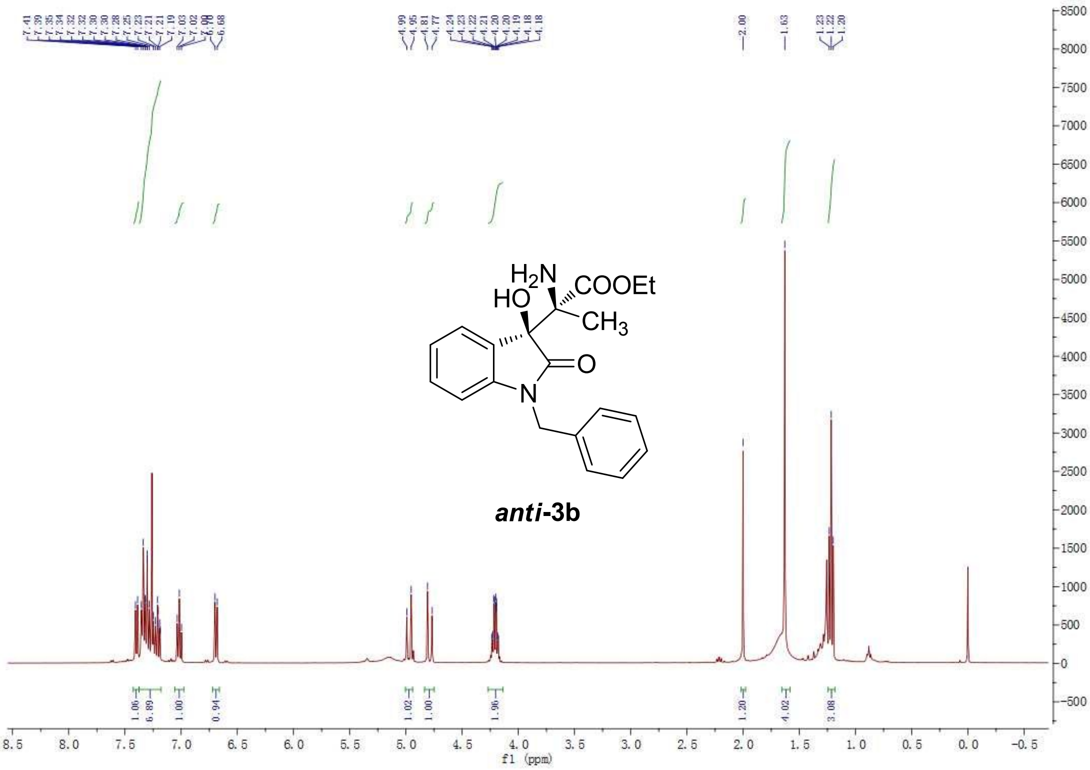
5. NMR spectra of the products






syn-4a
f1 (ppm)


syn-4a
f1 (ppm)



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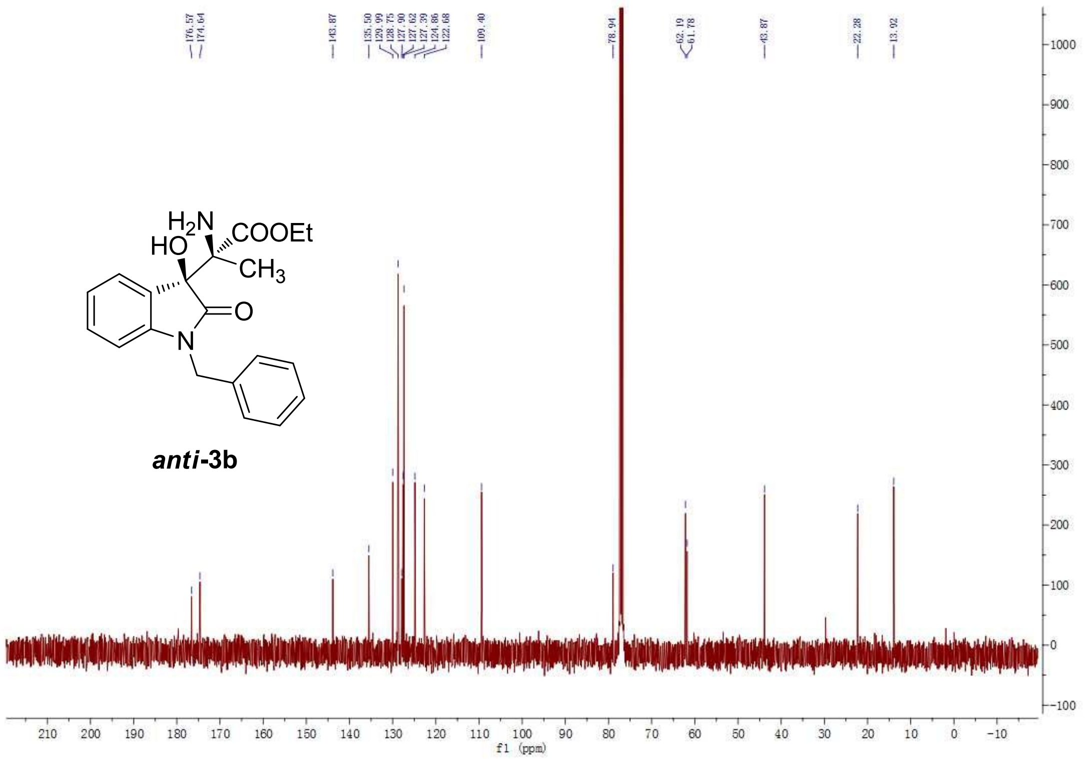

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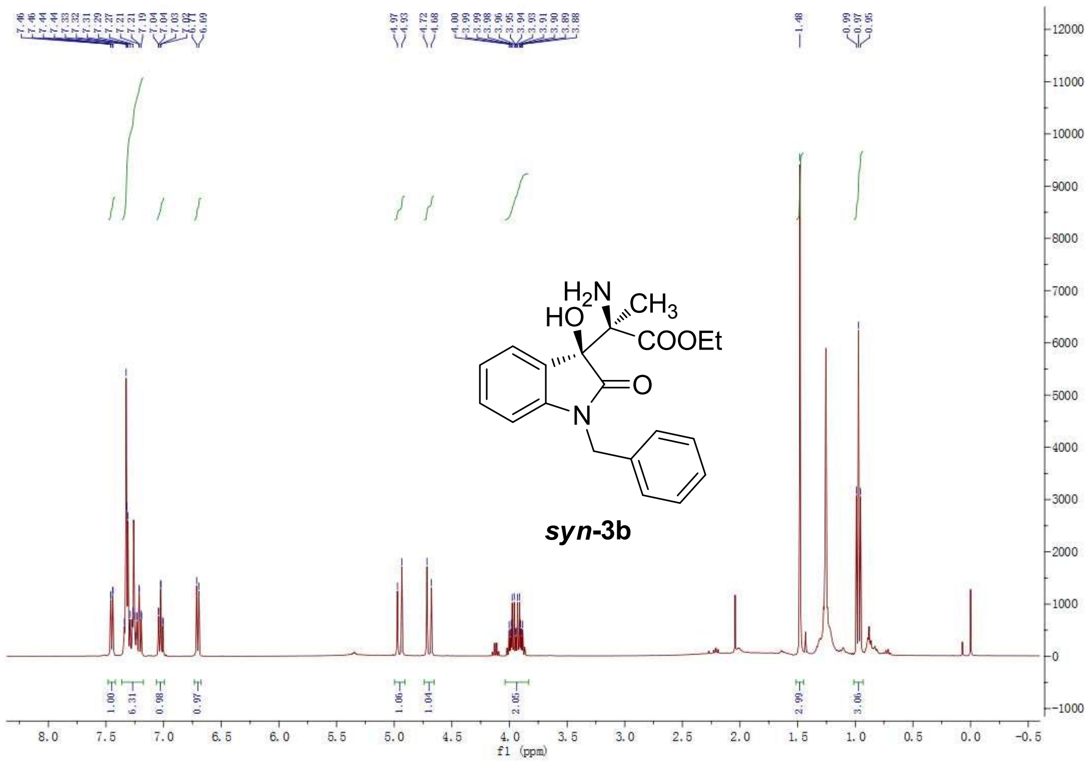

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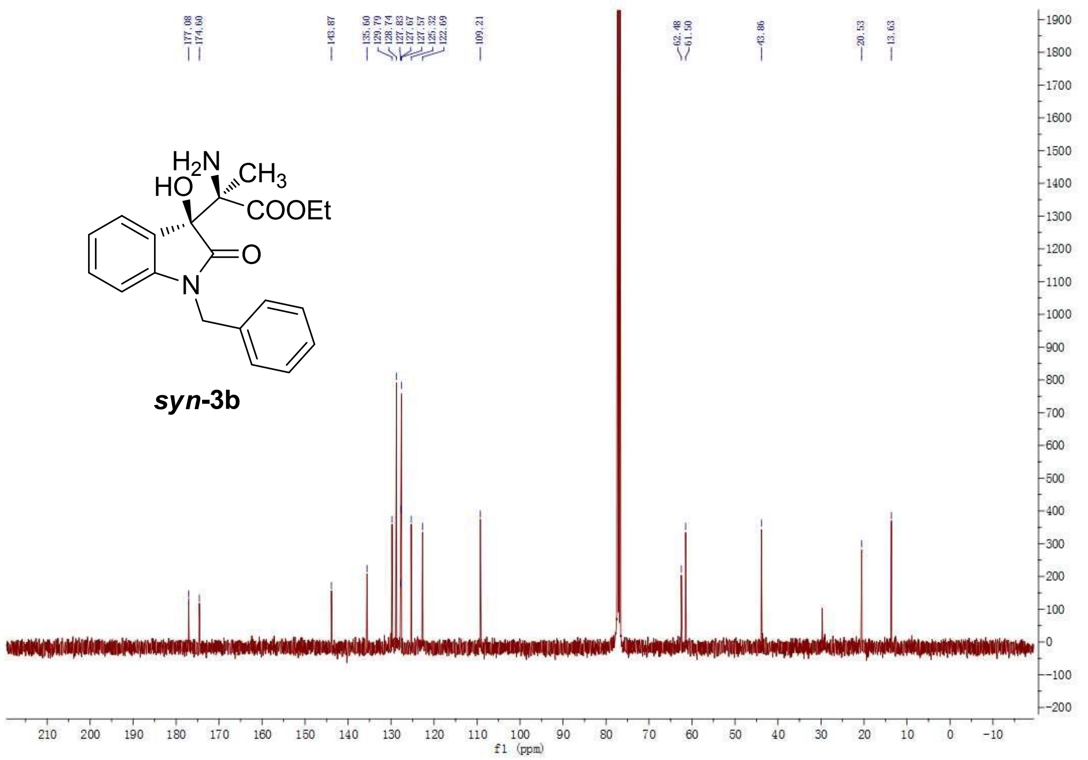
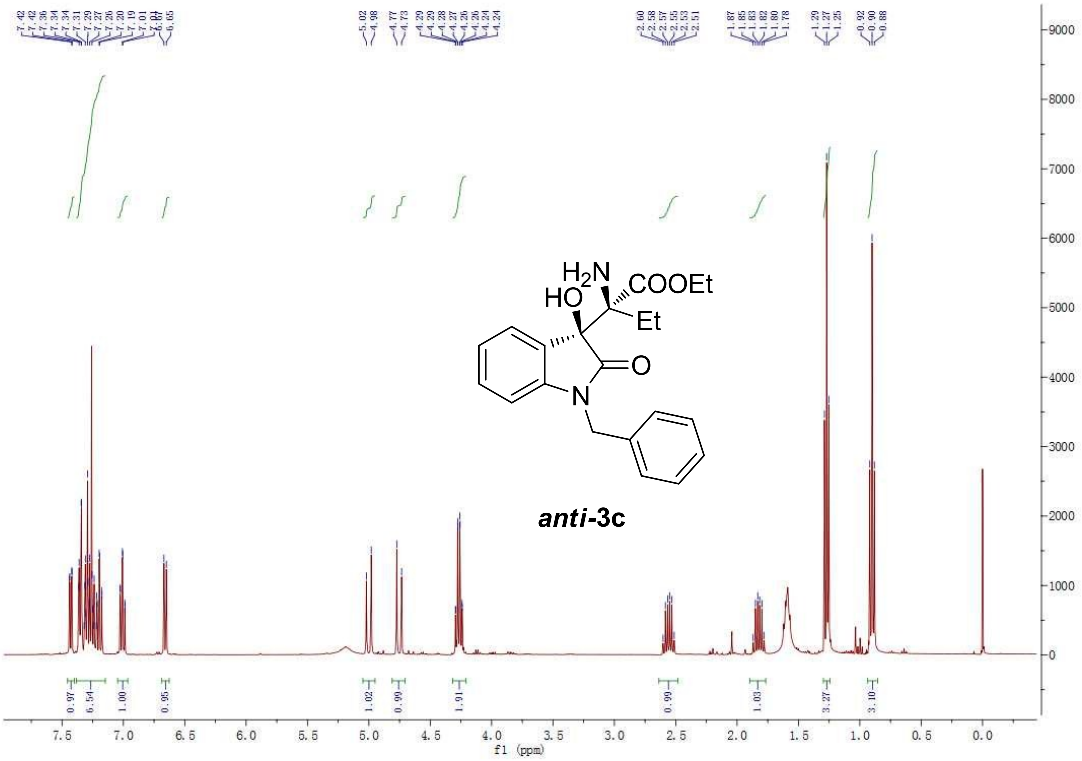


syn-3b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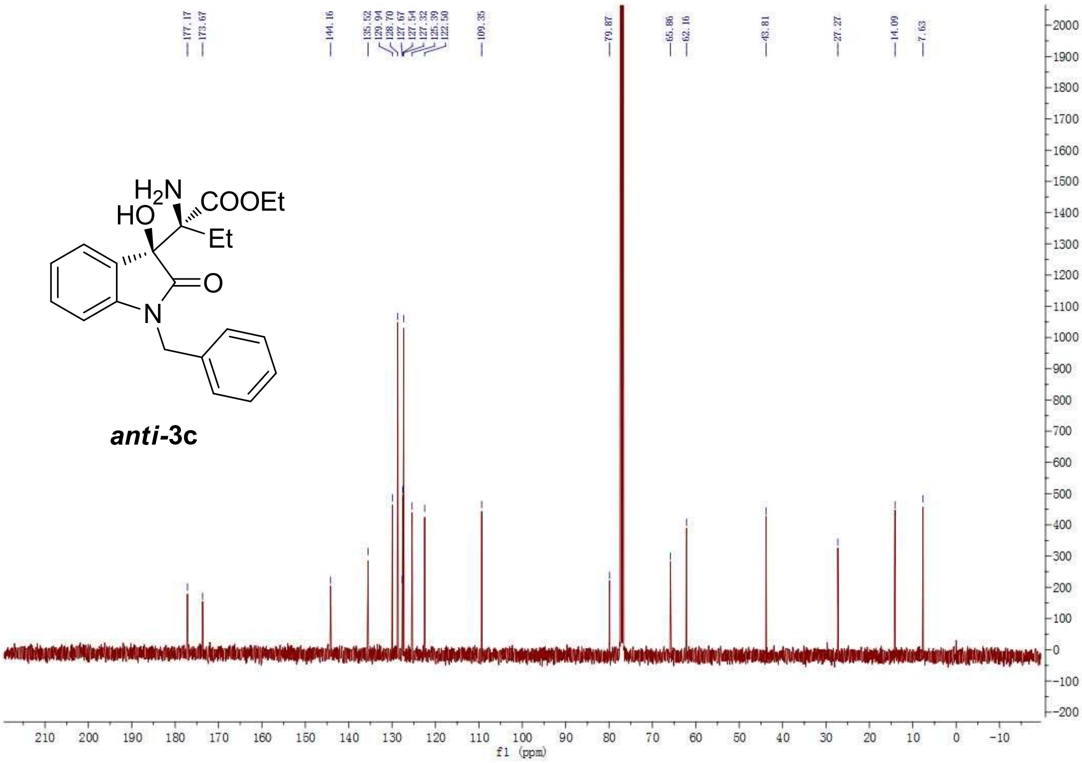
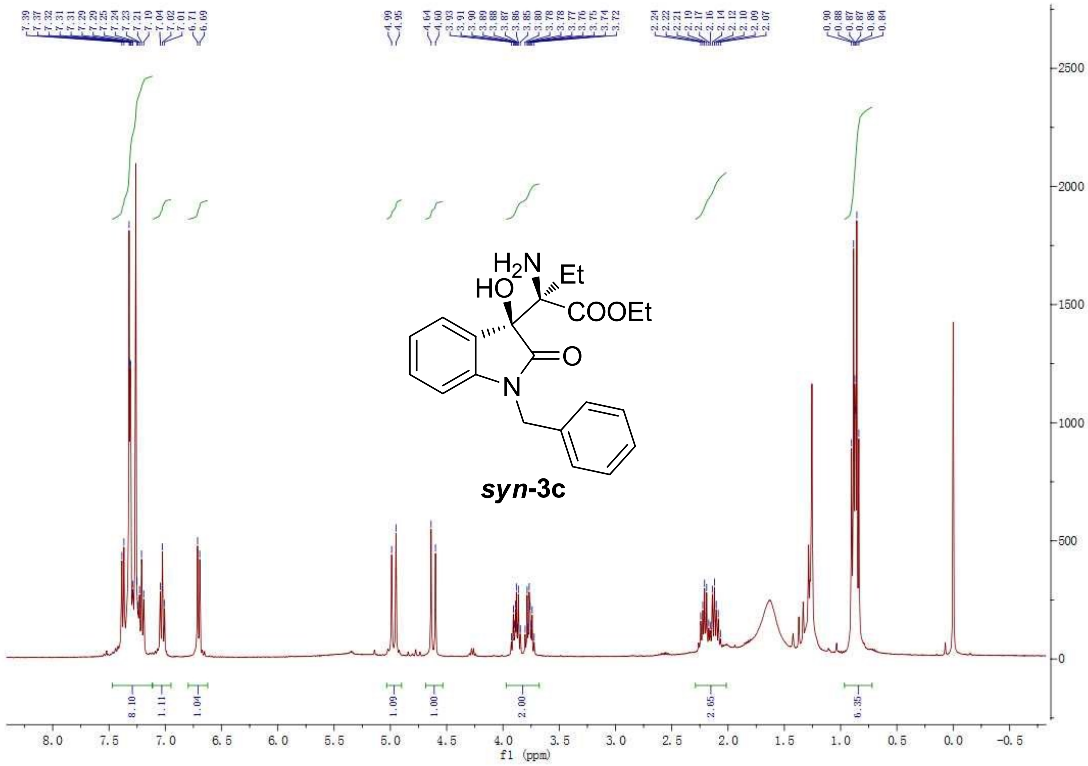
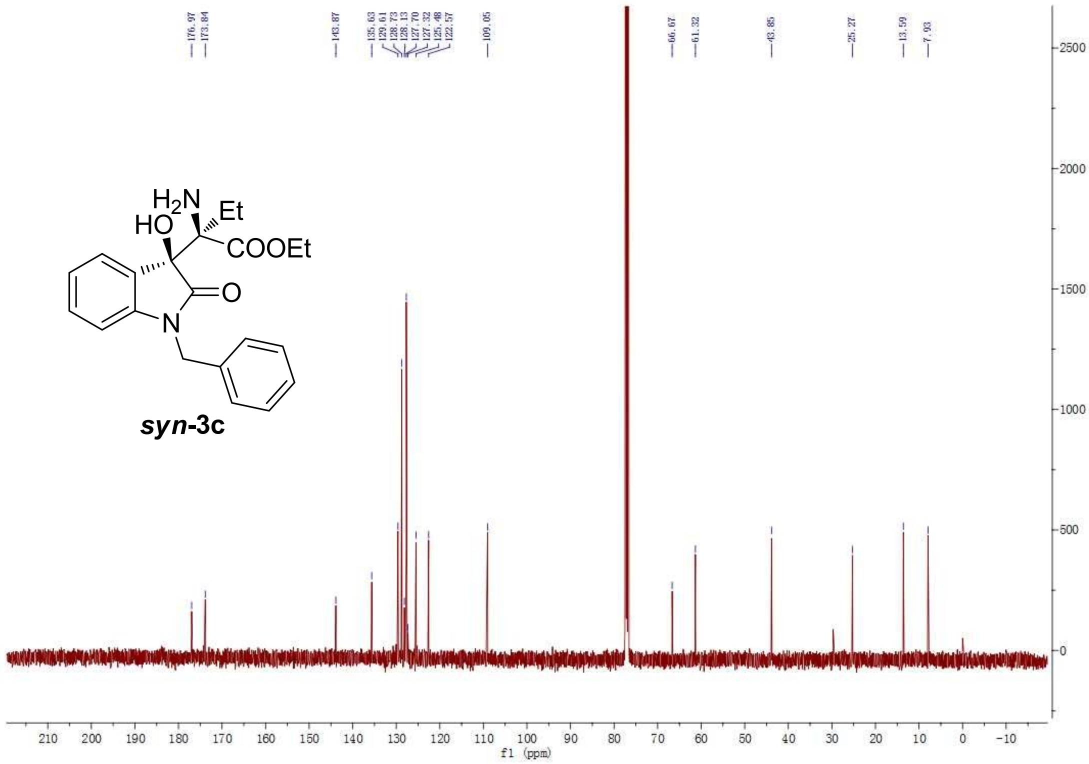
COOEt
HO
Et
O
N
anti-3c
f1 (ppm)


H2N
COOEt
HO
Et
O
N
anti-3c
f1 (ppm)


H2N
Et
HO
COOEt
O
N
syn-3c
f1 (ppm)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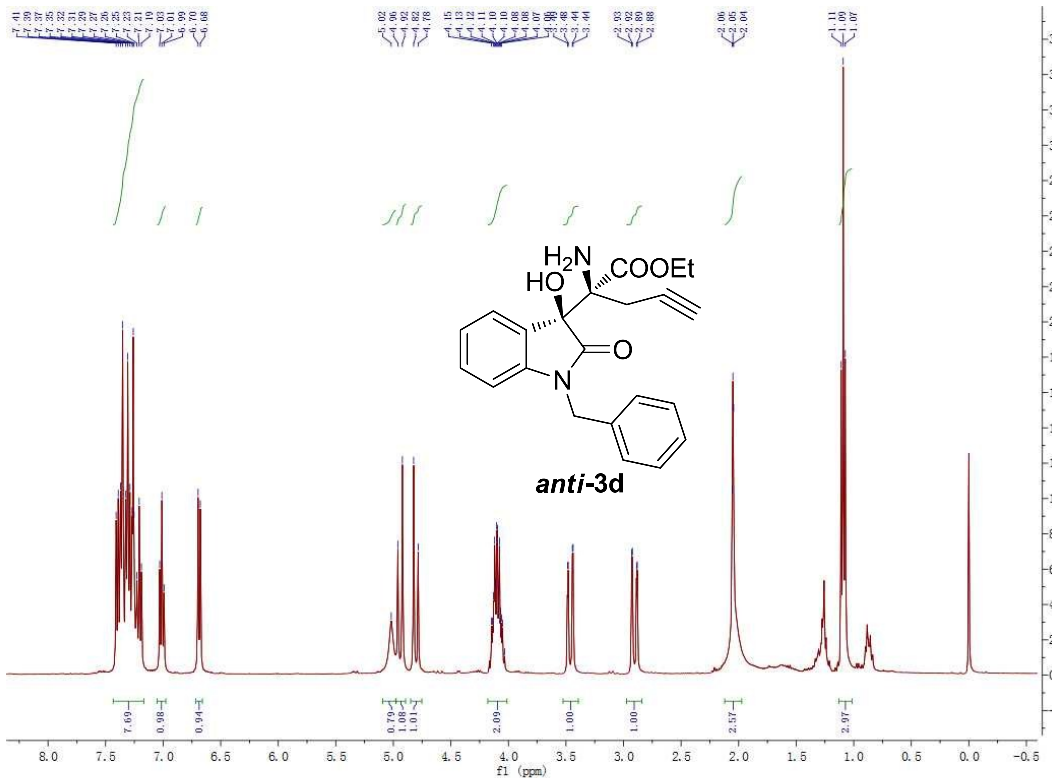
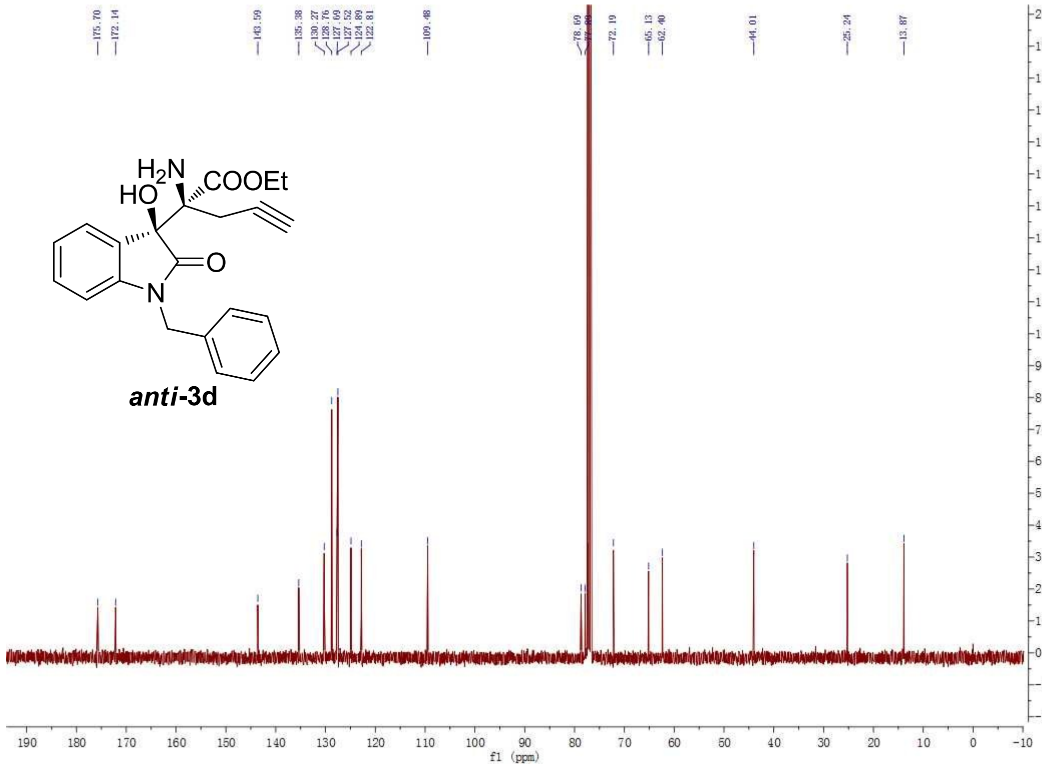
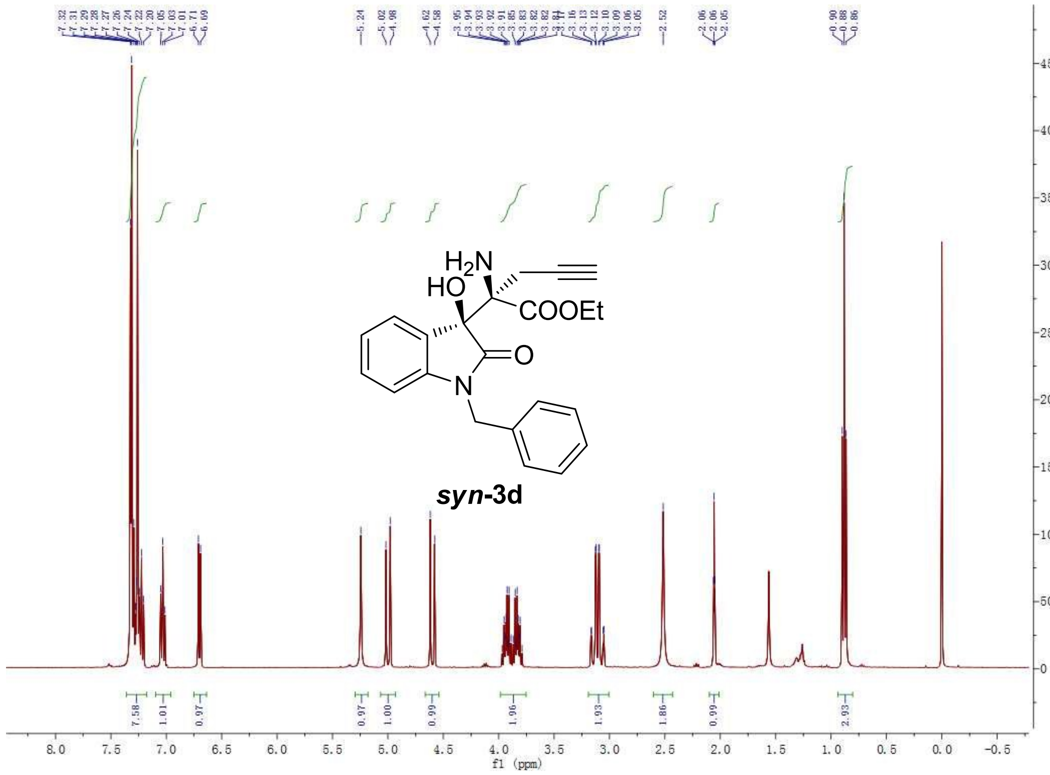
Et
HO
COOEt
O
N
syn-3c
f1 (ppm)



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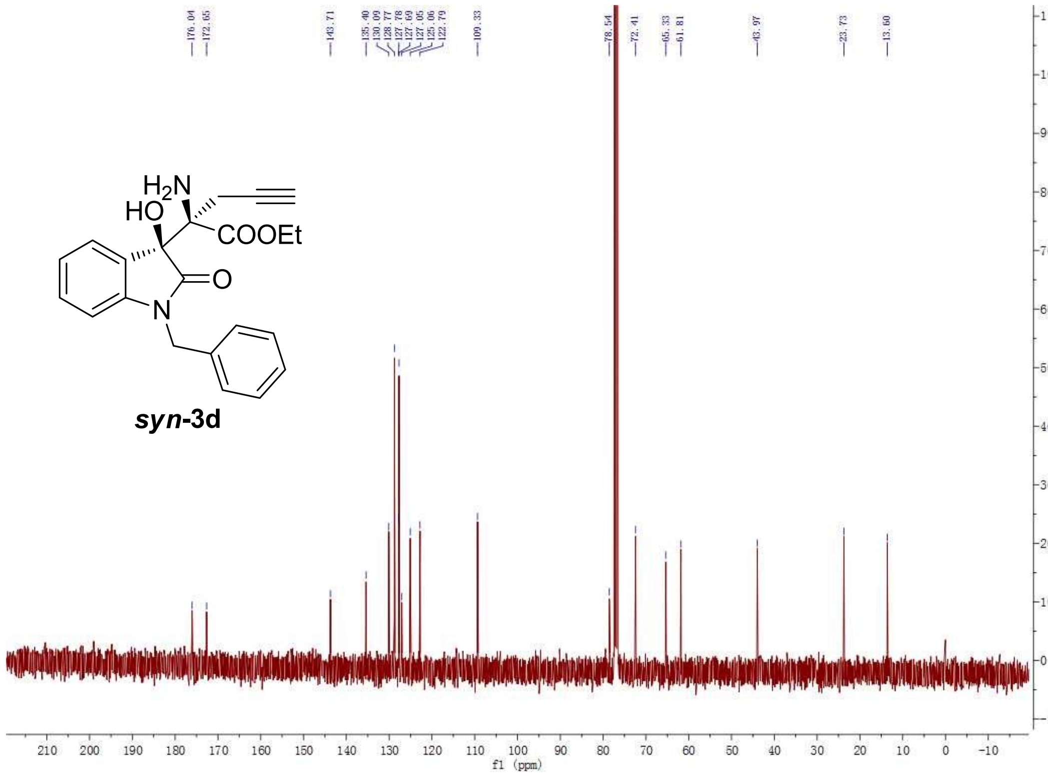
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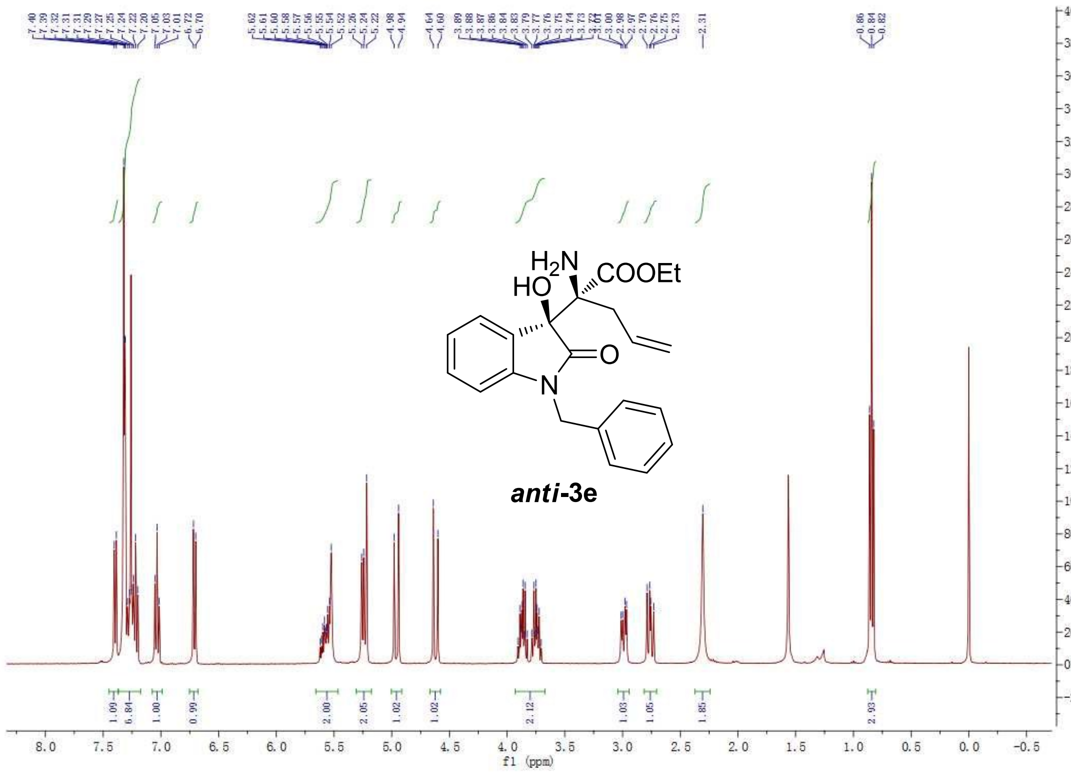
anti-3e
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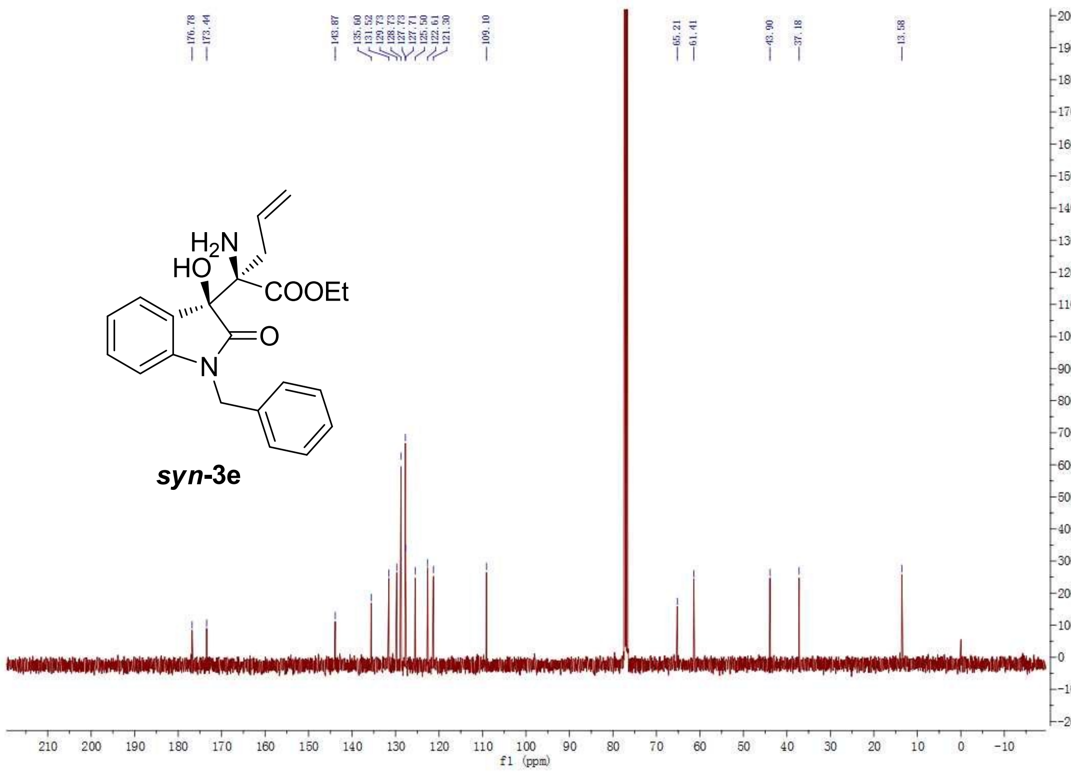
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173.44
143.87
135.60
131.52
129.73
128.73
127.73
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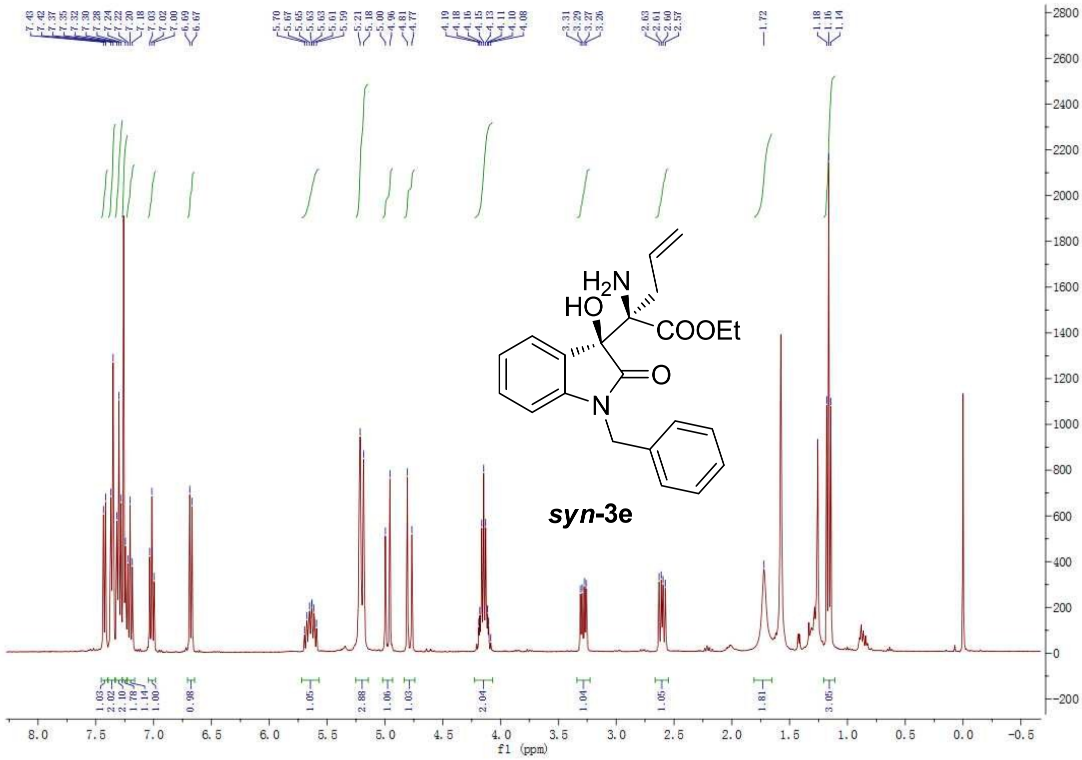
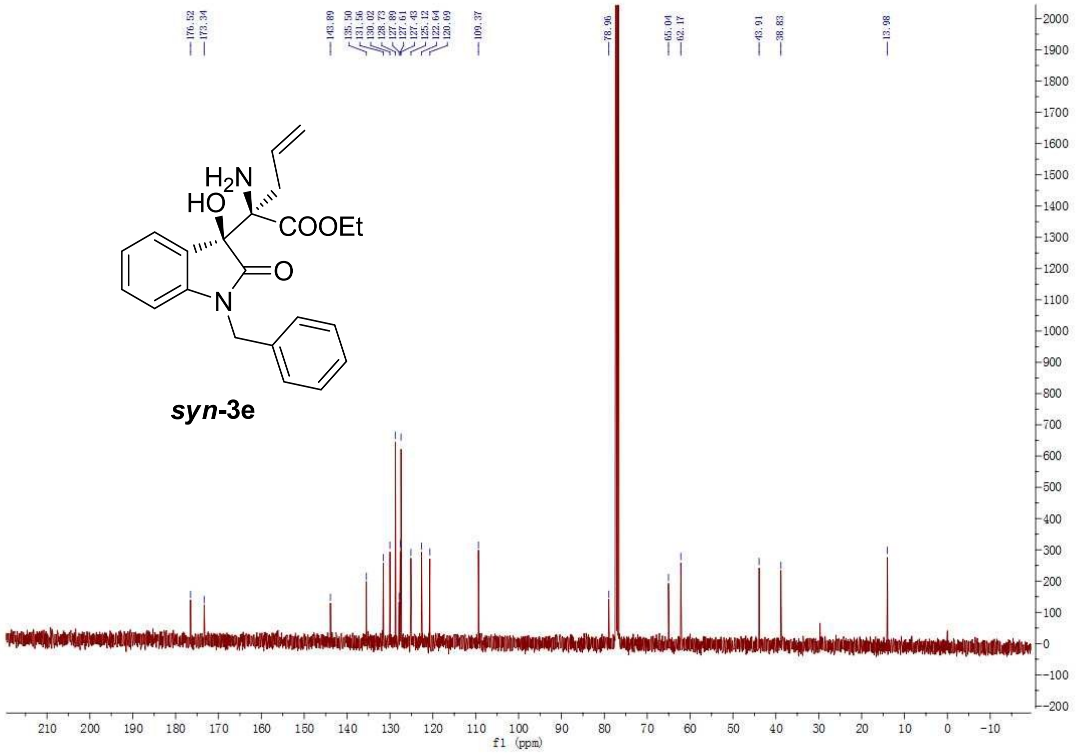
122.61
121.30
109.10
65.21
61.41
43.90
37.18
13.58
f1 (ppm)


H2N
HO
COOEt
O
N
syn-3e
f1 (ppm)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HO
COOEt
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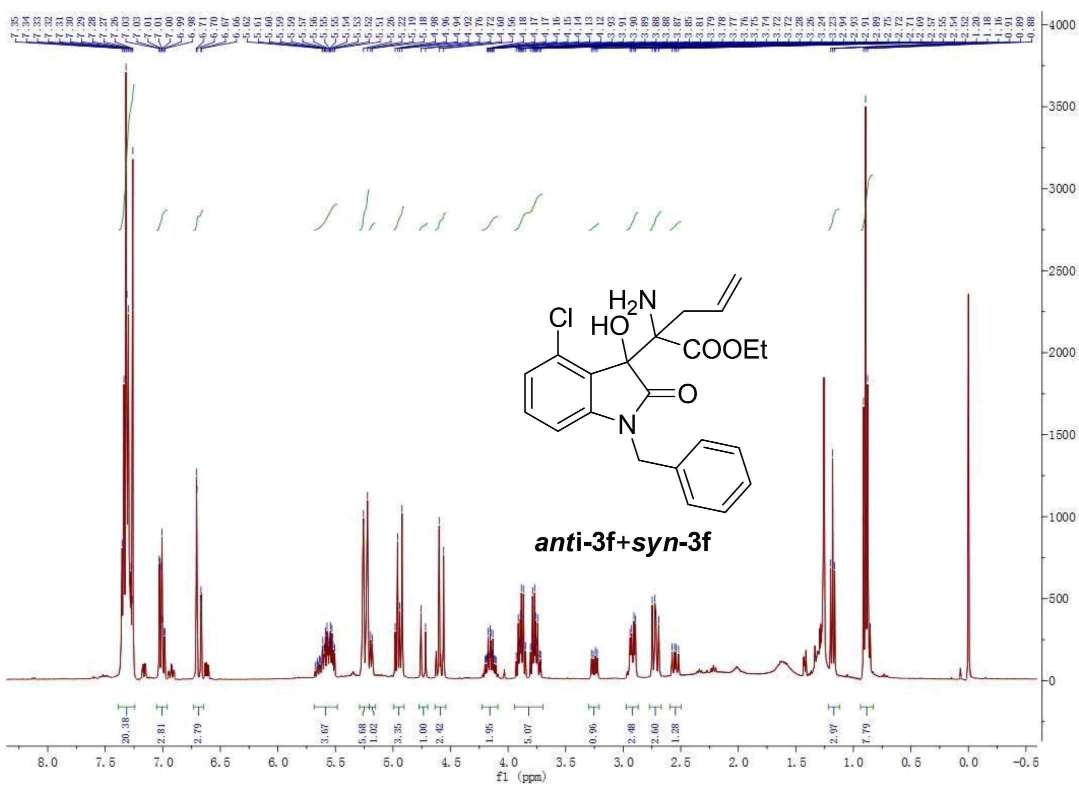
f1 (ppm)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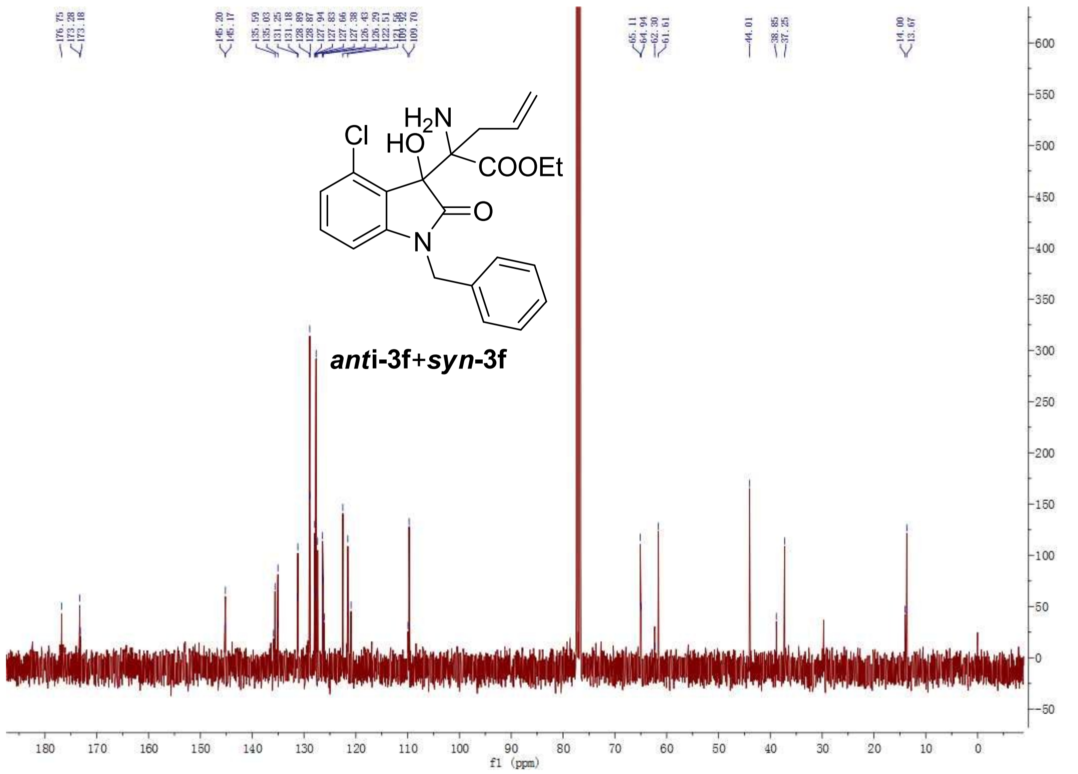
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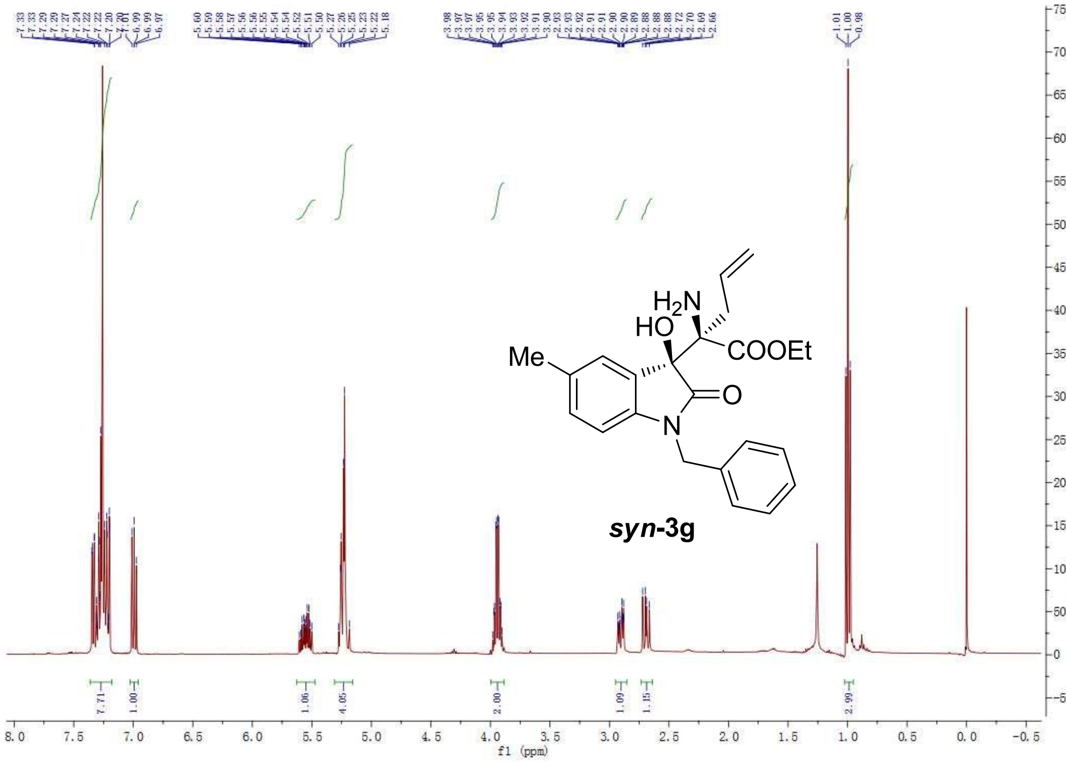
f1 (ppm)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N
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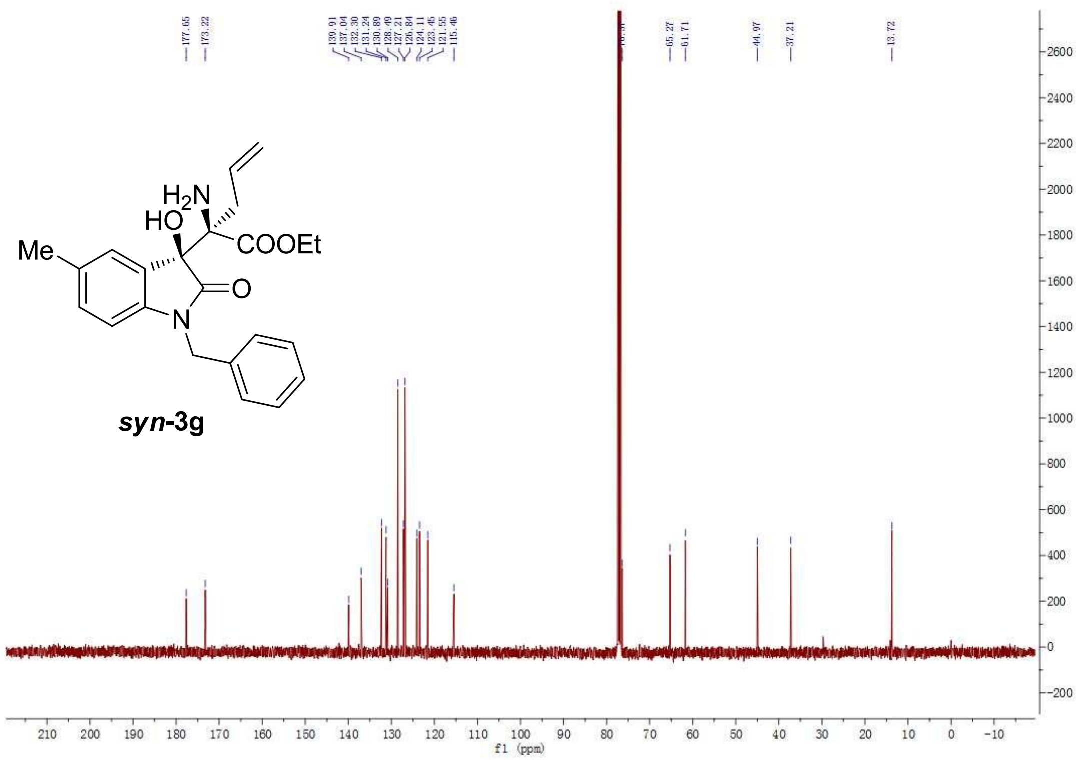
f1 (ppm)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Me
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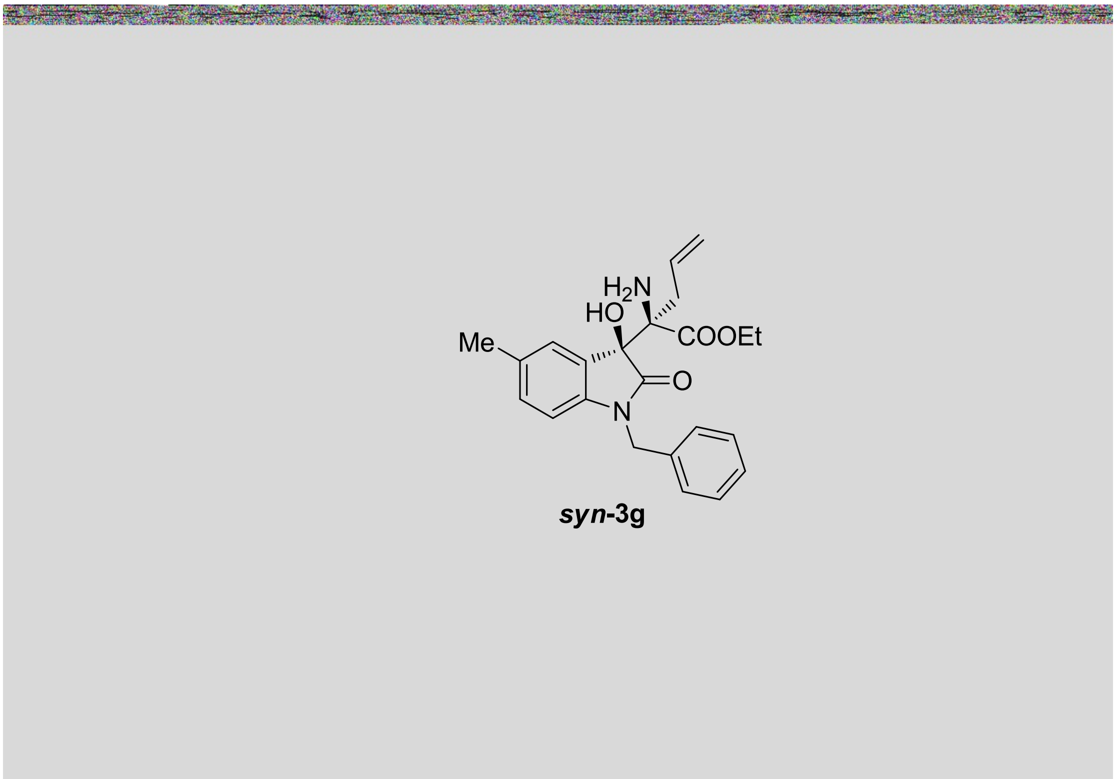
f1 (ppm)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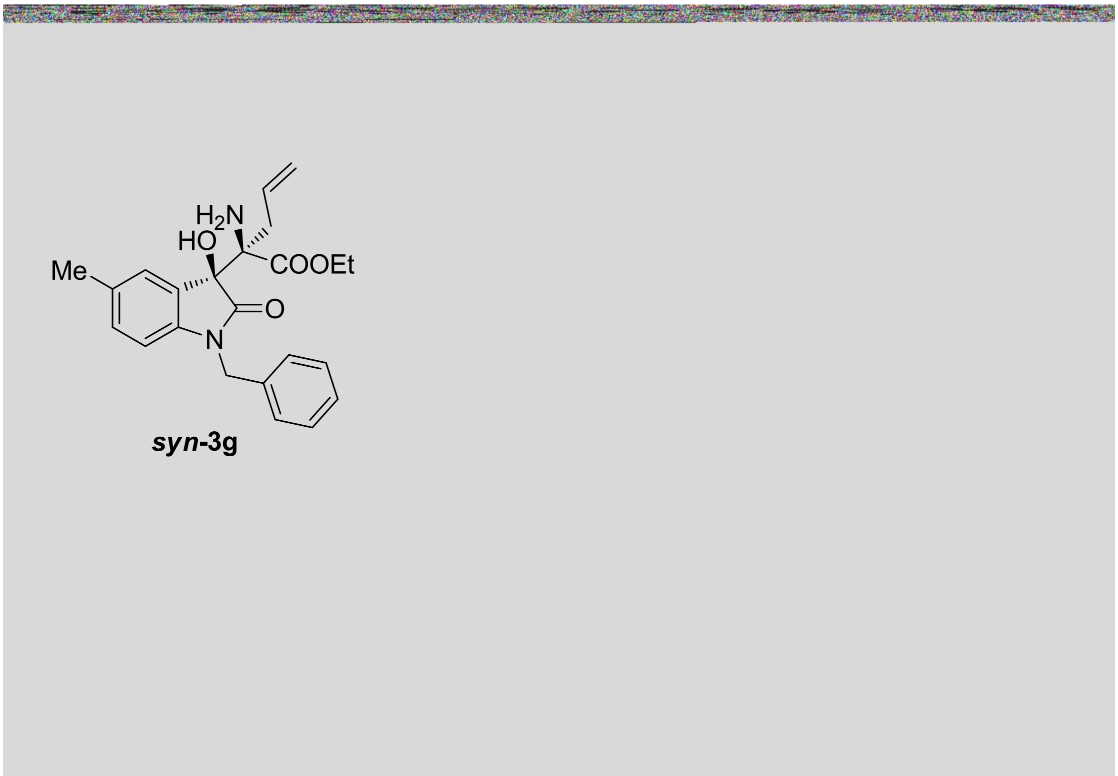
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N
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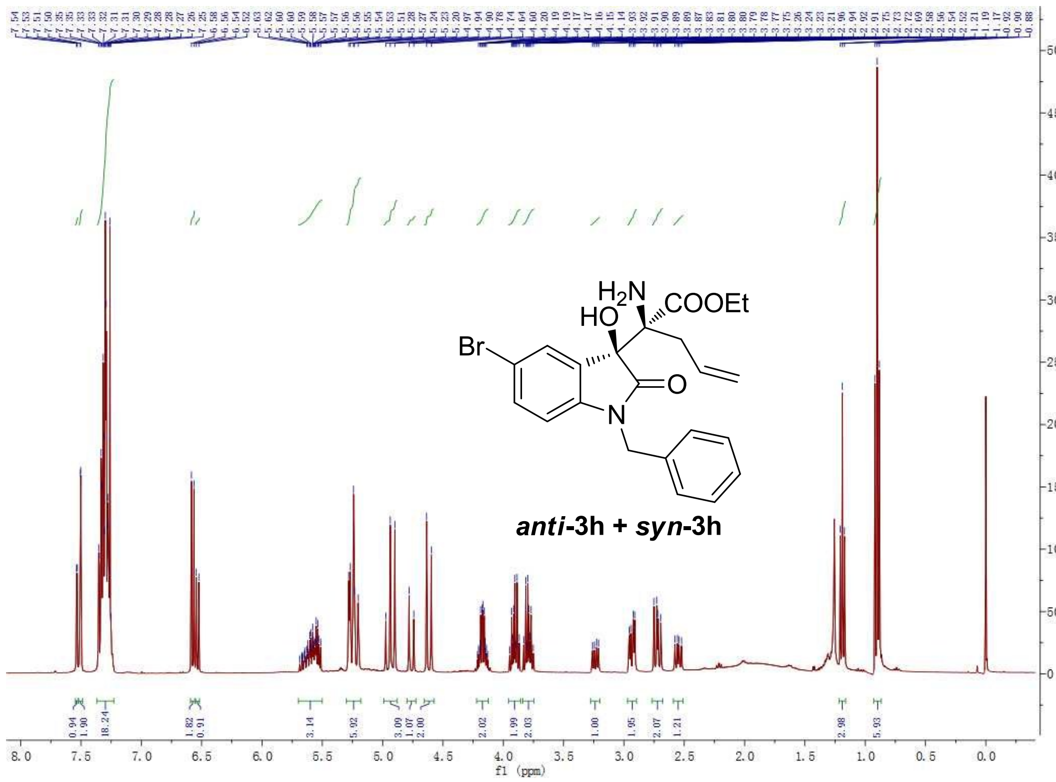

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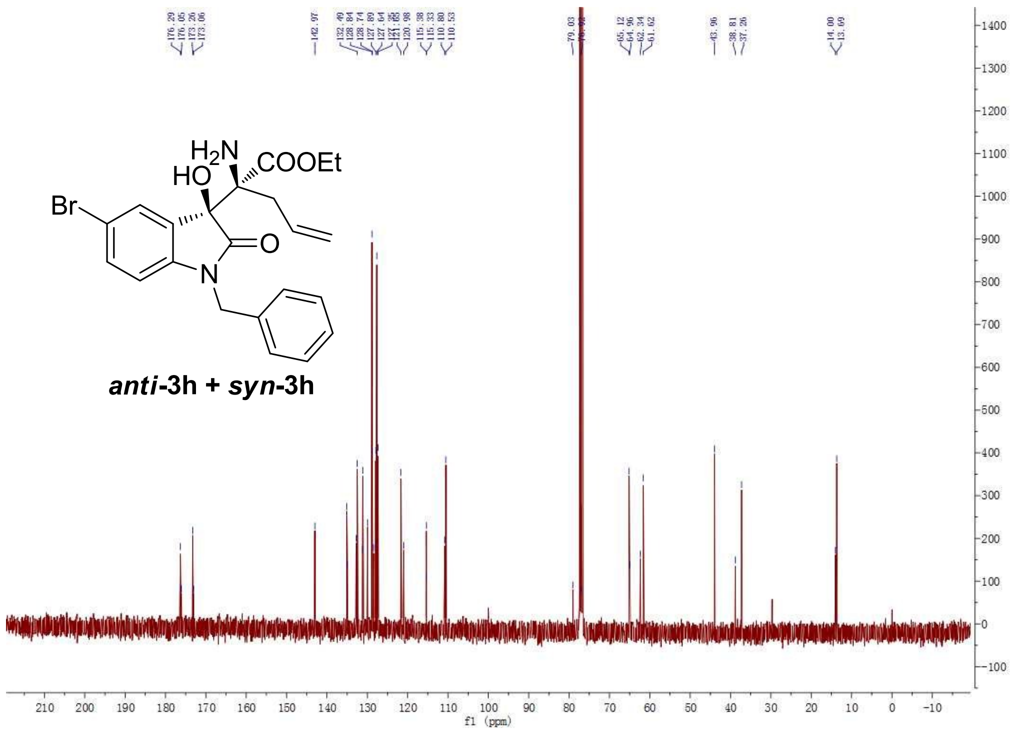
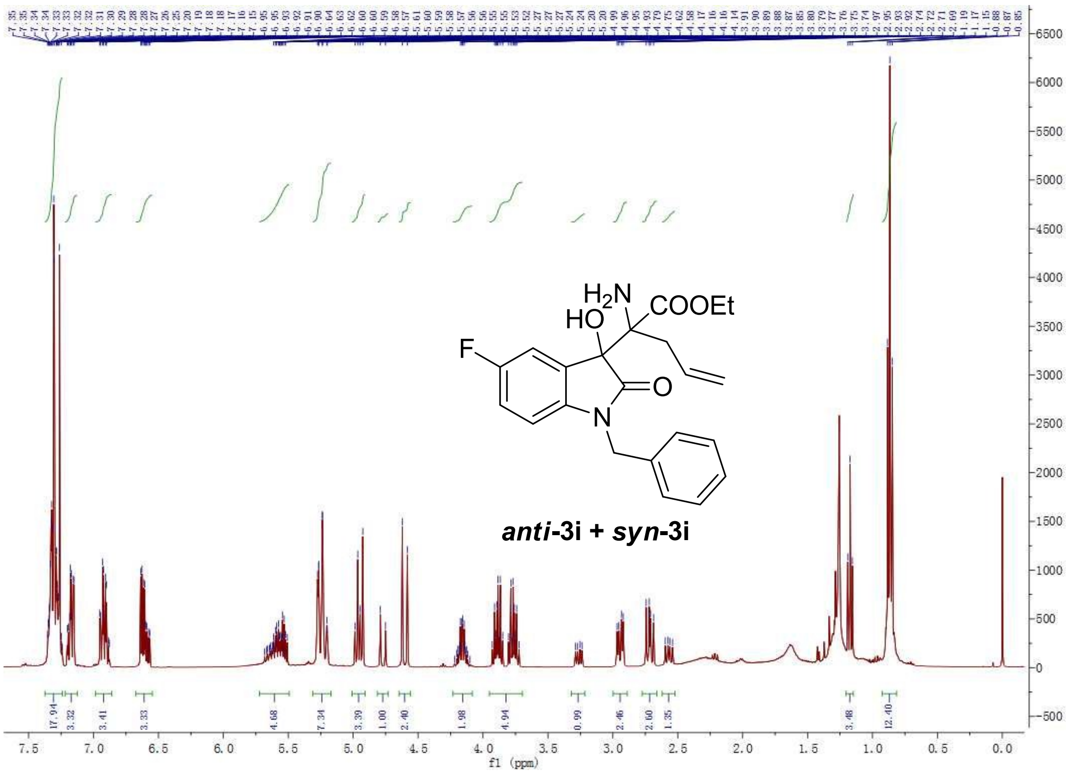


anti-3h + syn-3h
f1 (ppm)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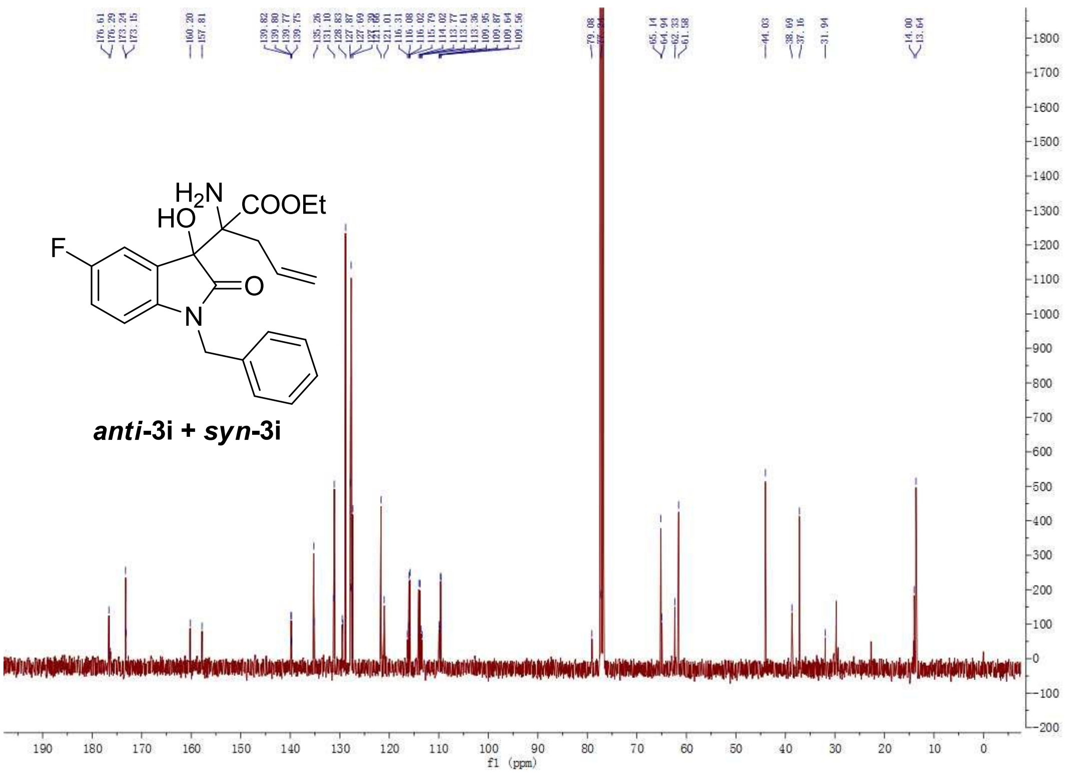
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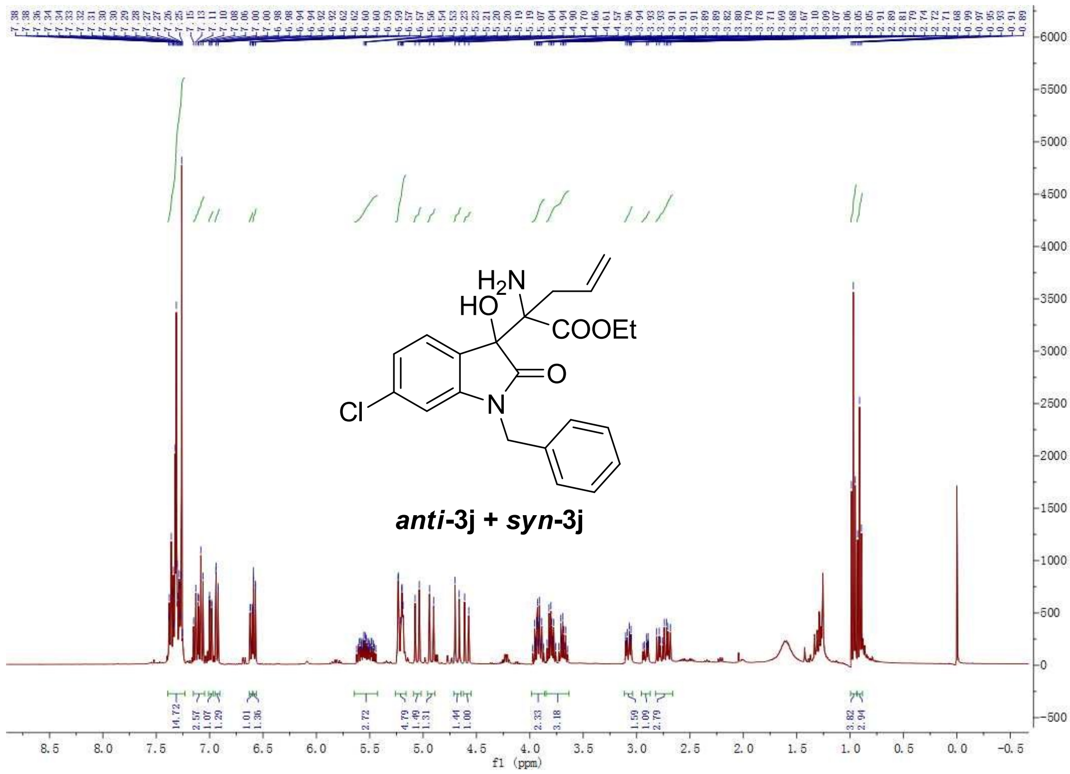
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Cl
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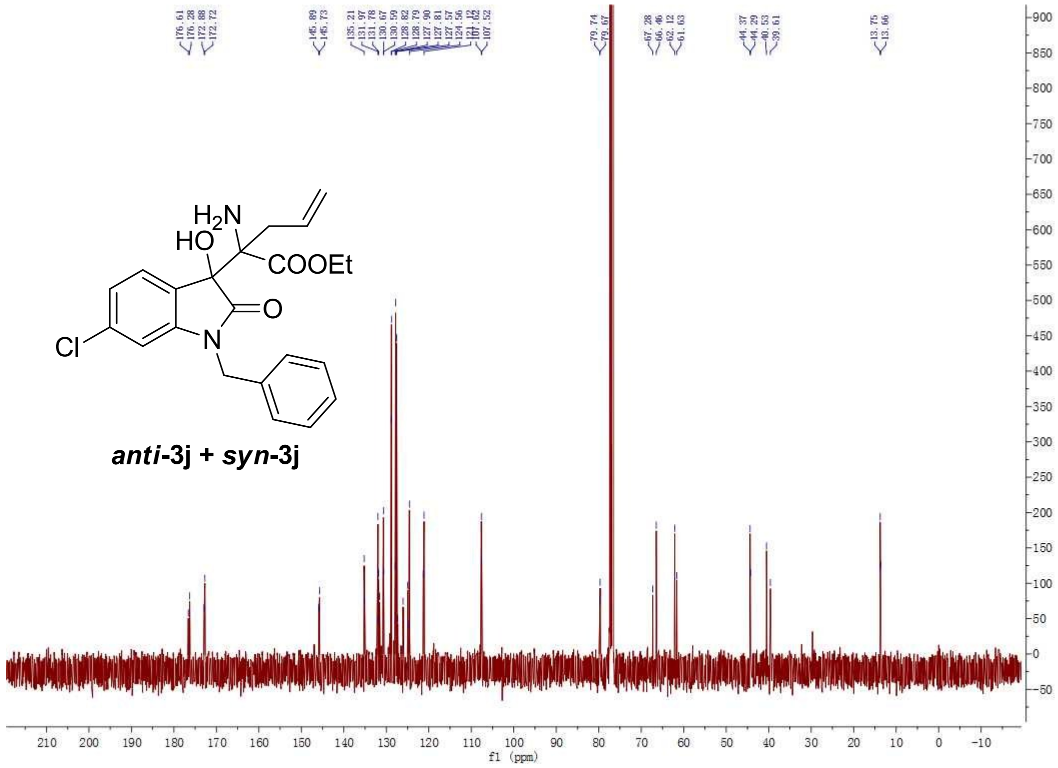
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Cl
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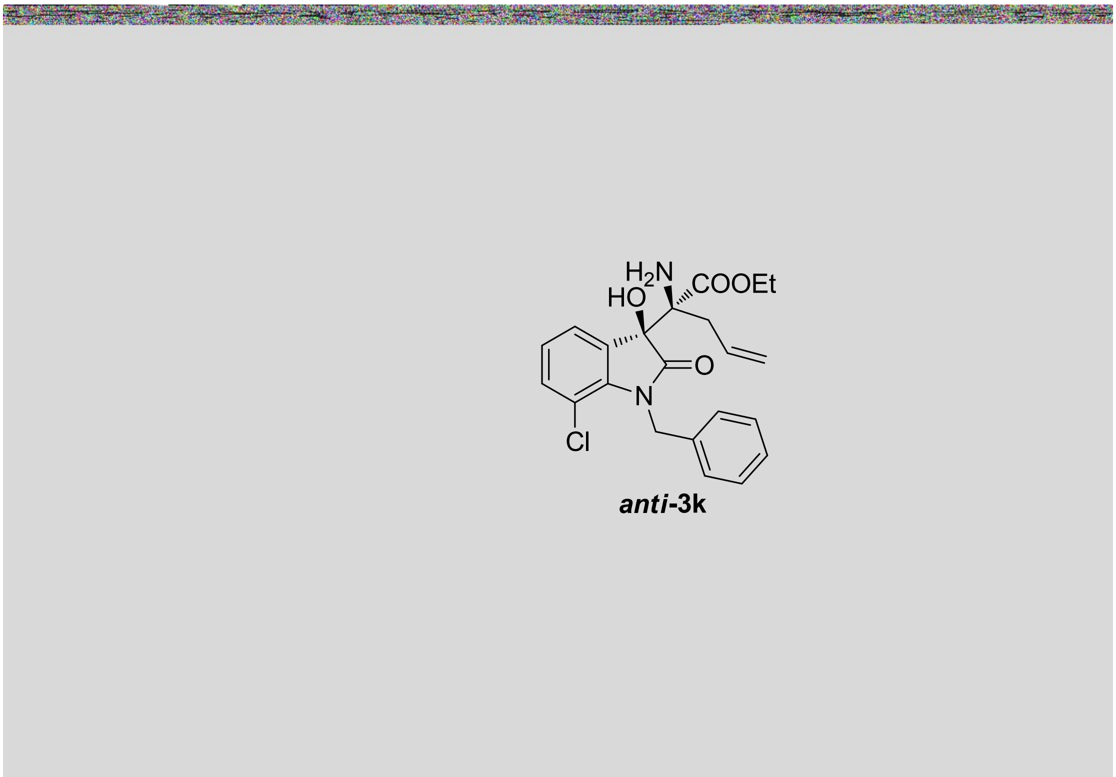
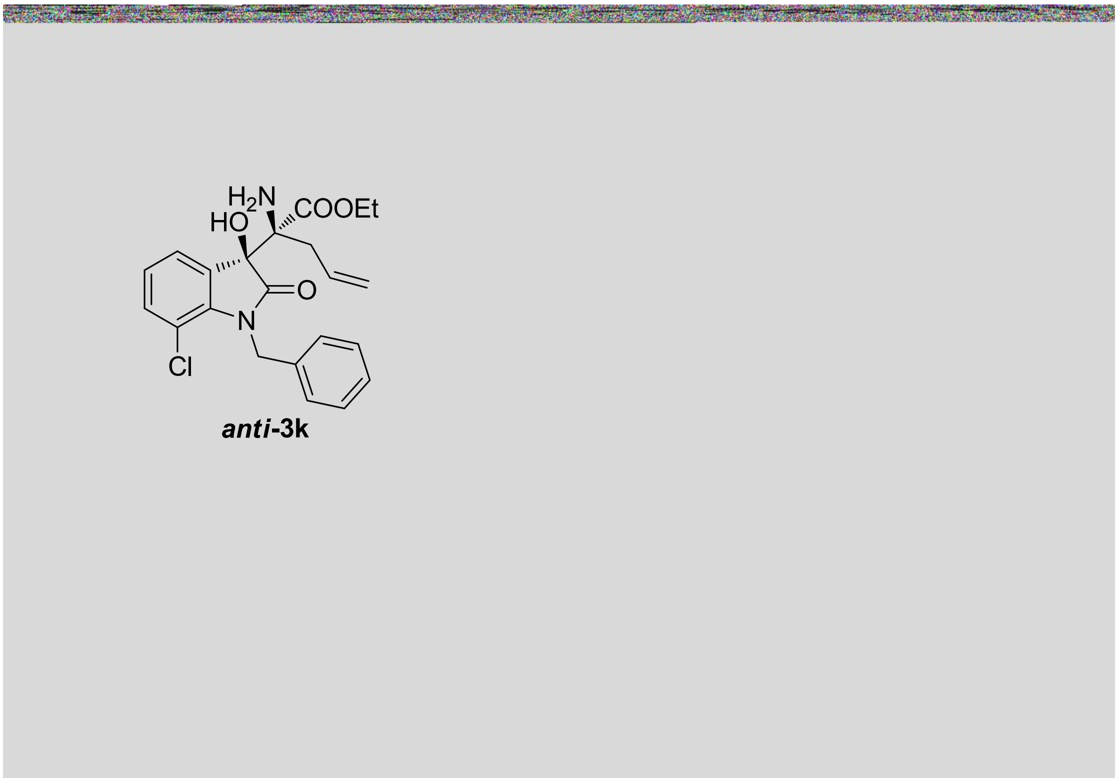
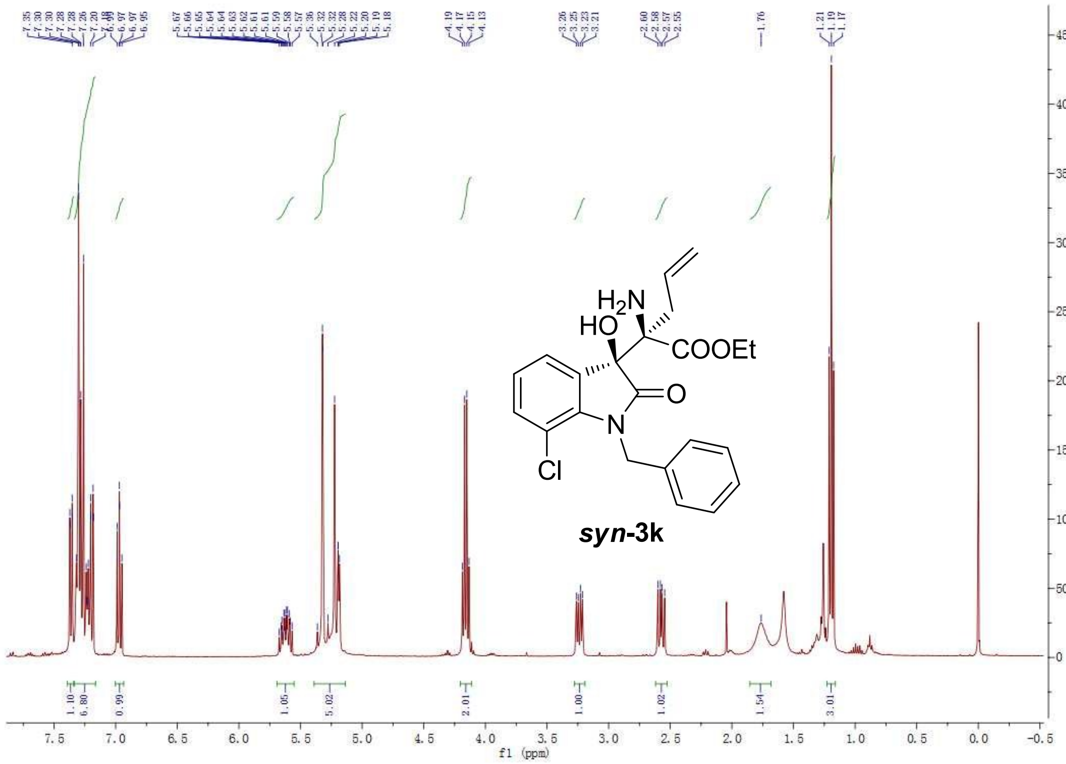
f1 (ppm)



***anti*-3k**



***anti*-3k**



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HO
COOEt
O
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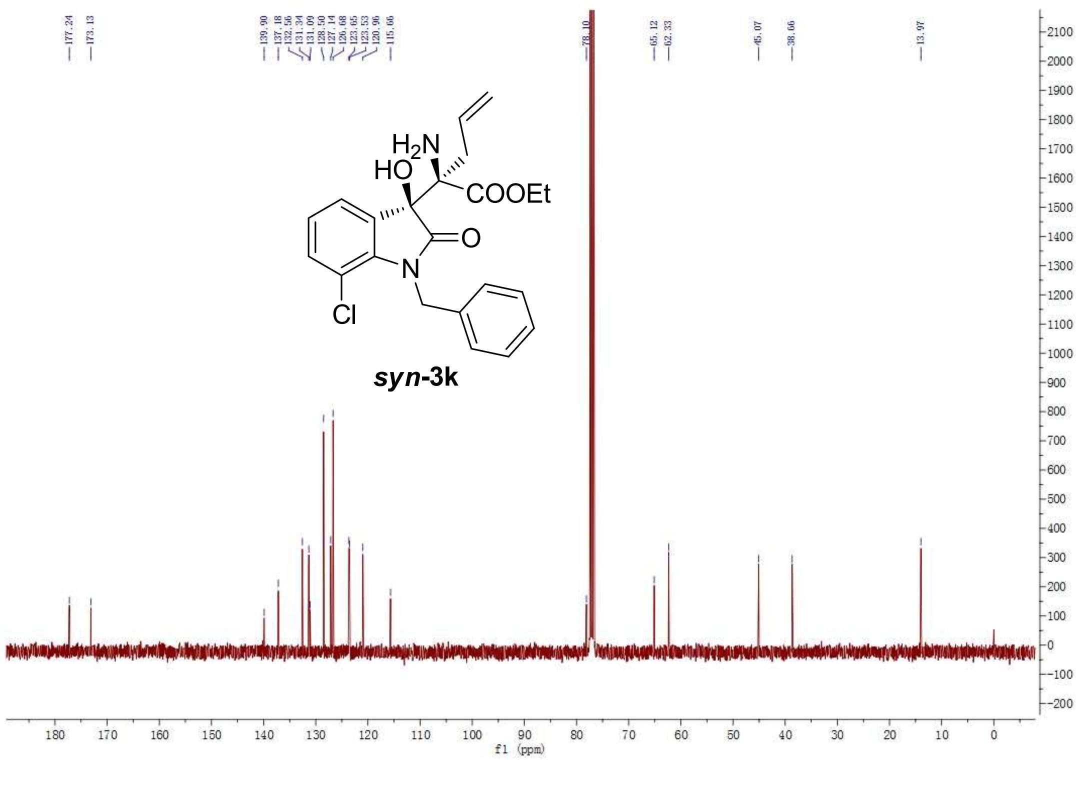
Cl
syn-3k
f1 (ppm)



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Cl
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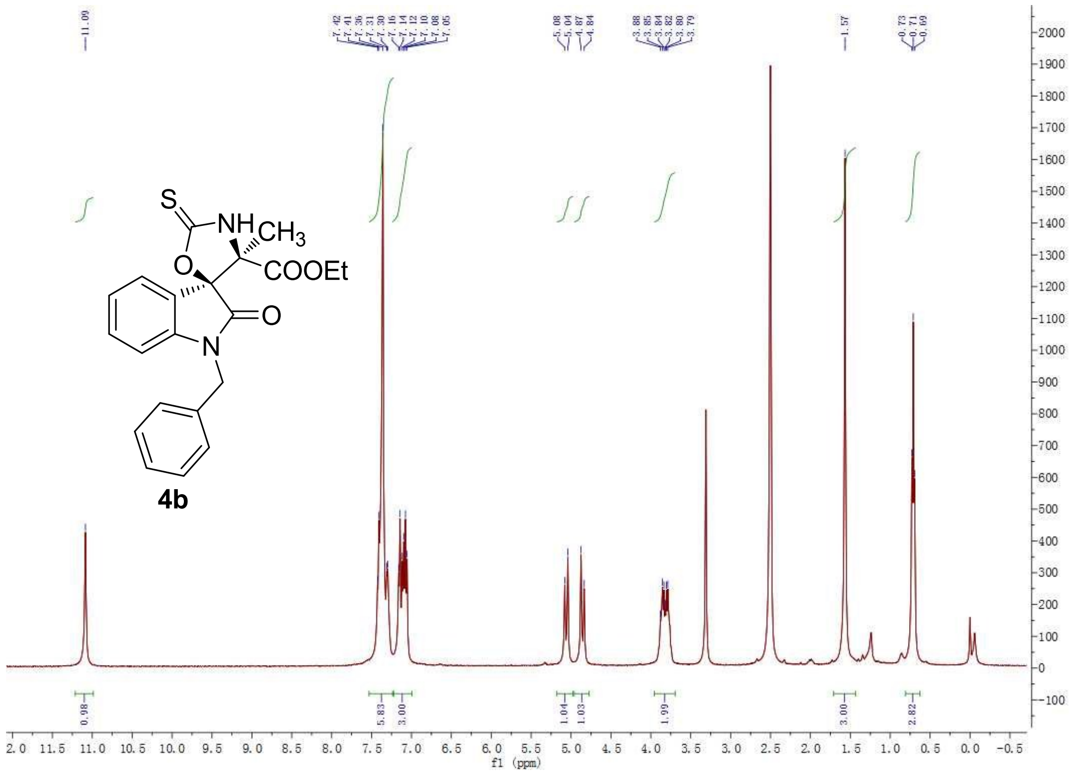
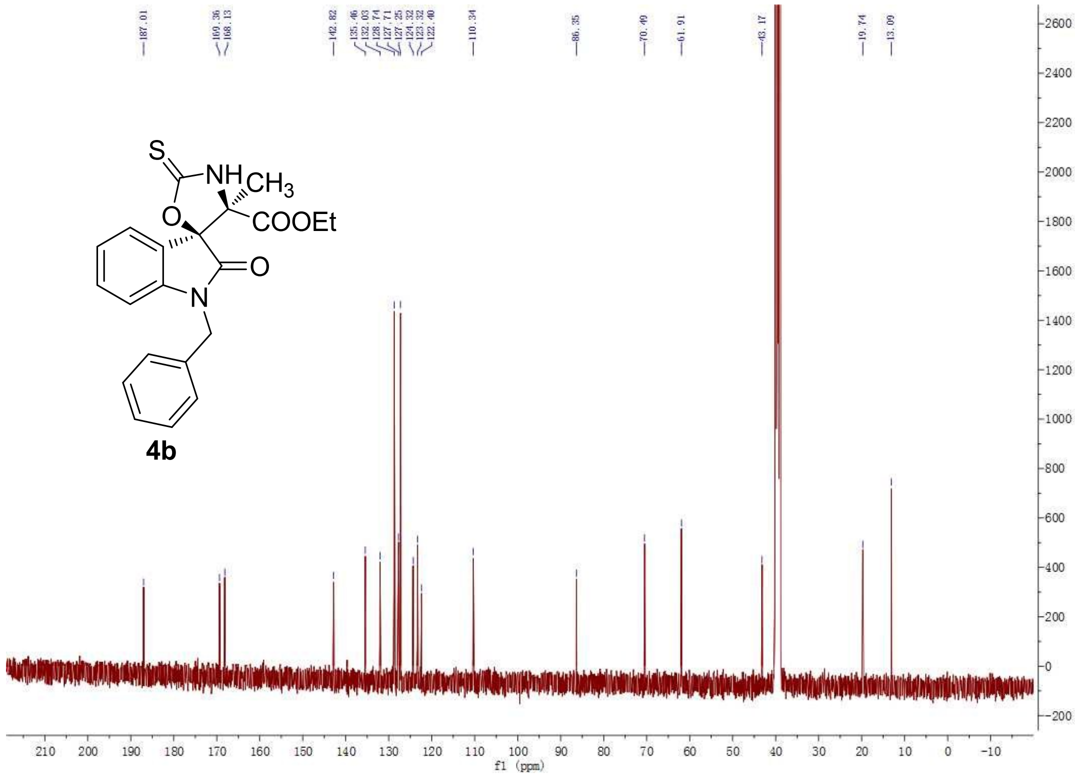
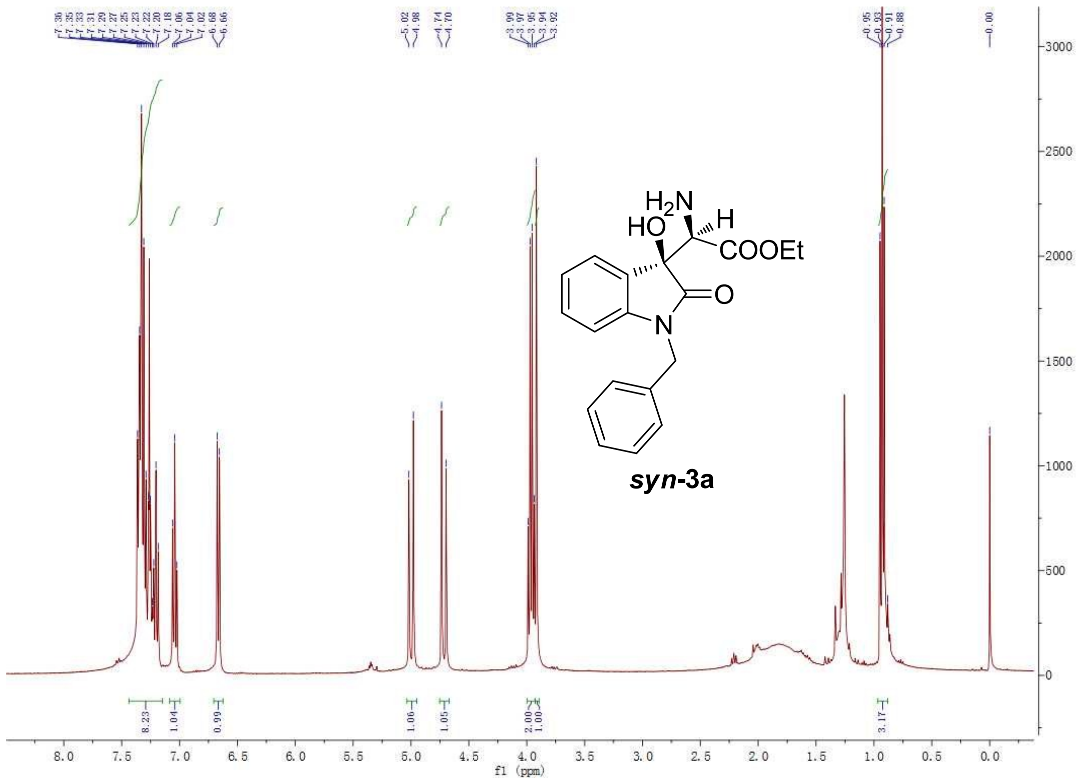
f1 (ppm)



4b



4b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1.06
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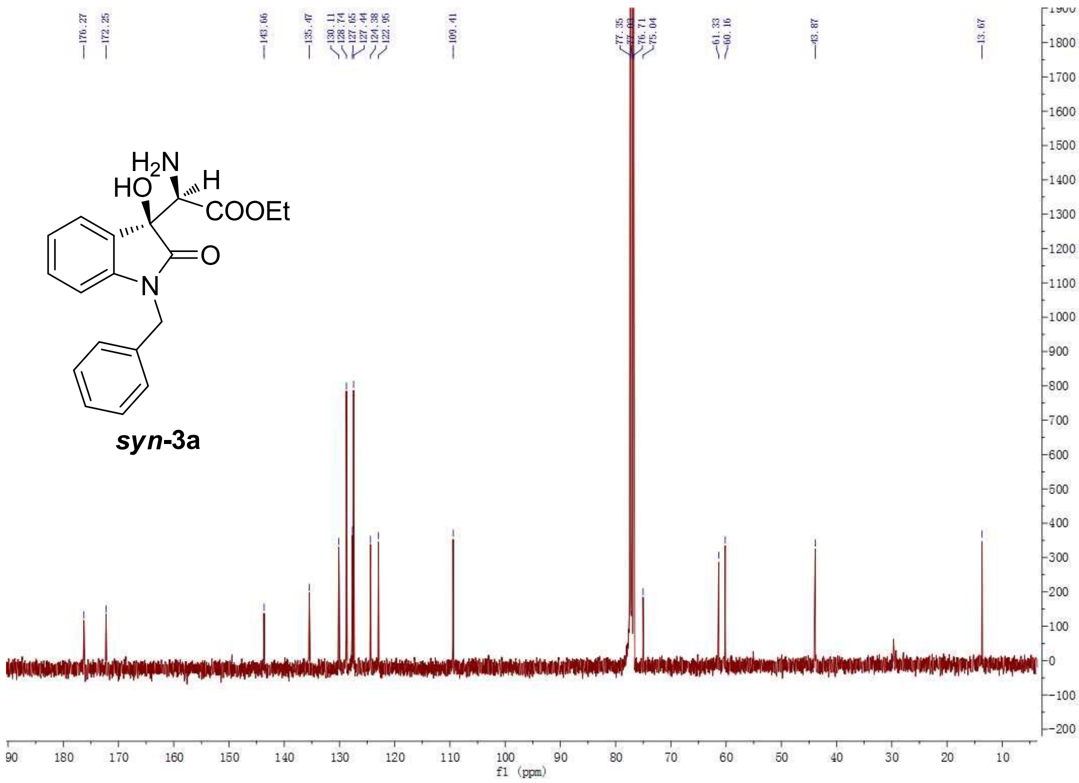
1.00
3.17
f1 (ppm)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HO
H
COOEt
O
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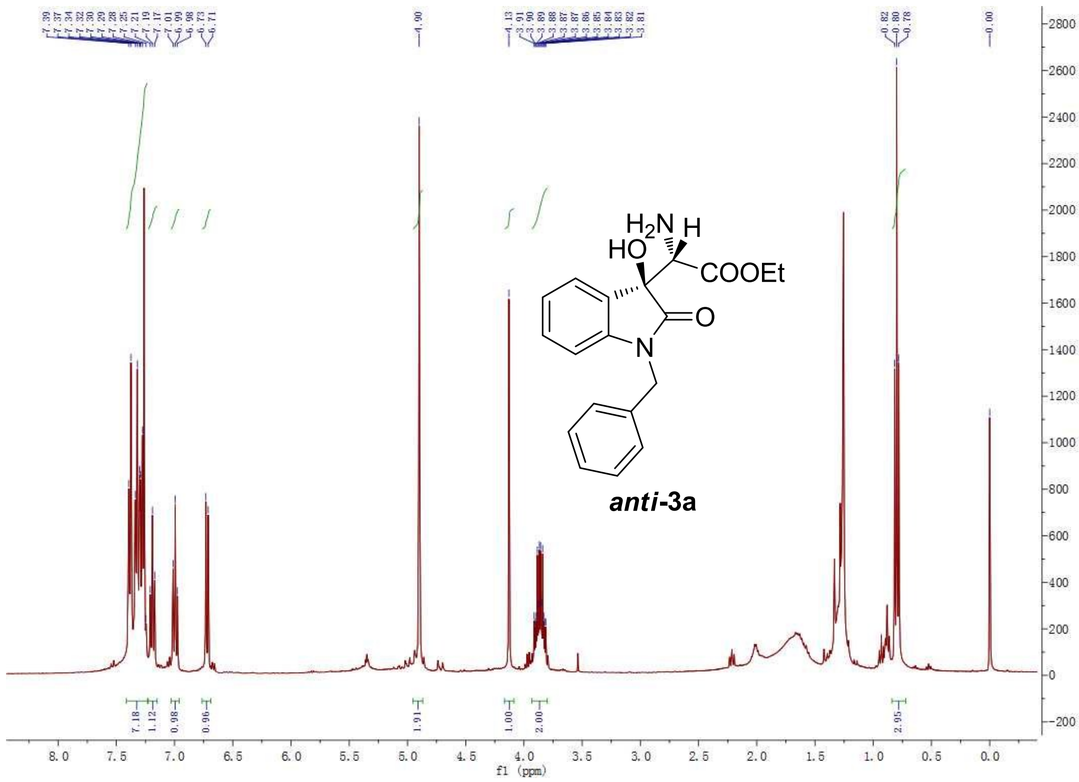
syn-3a
f1 (ppm)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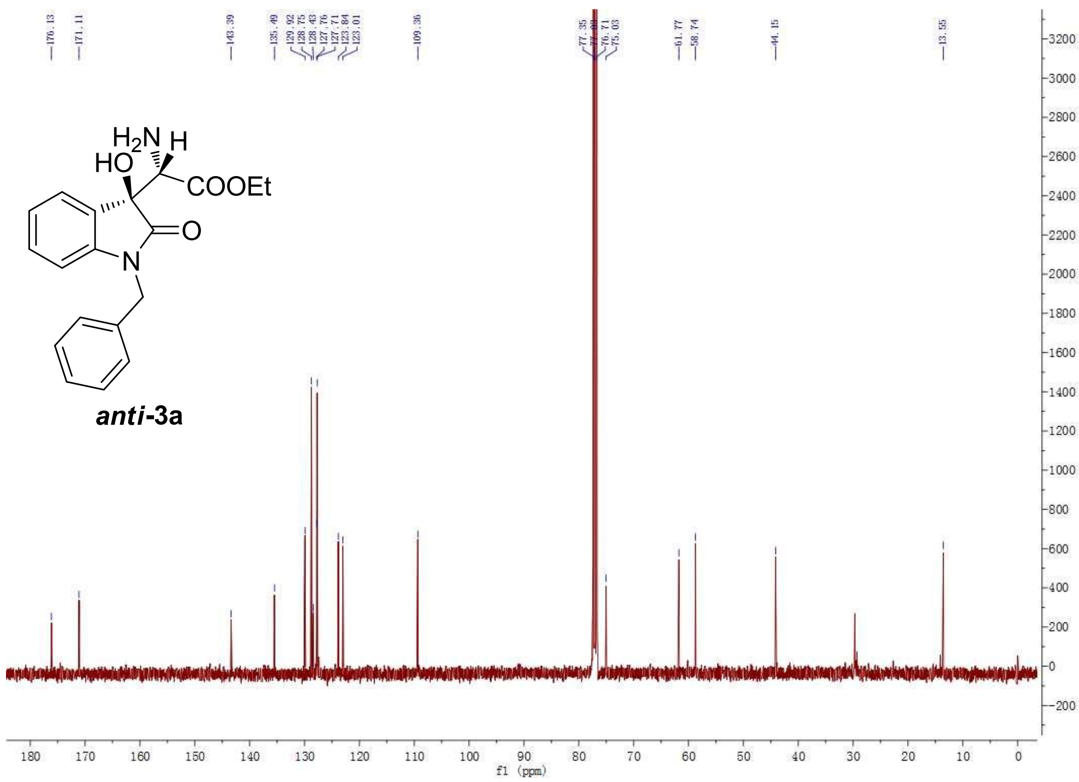
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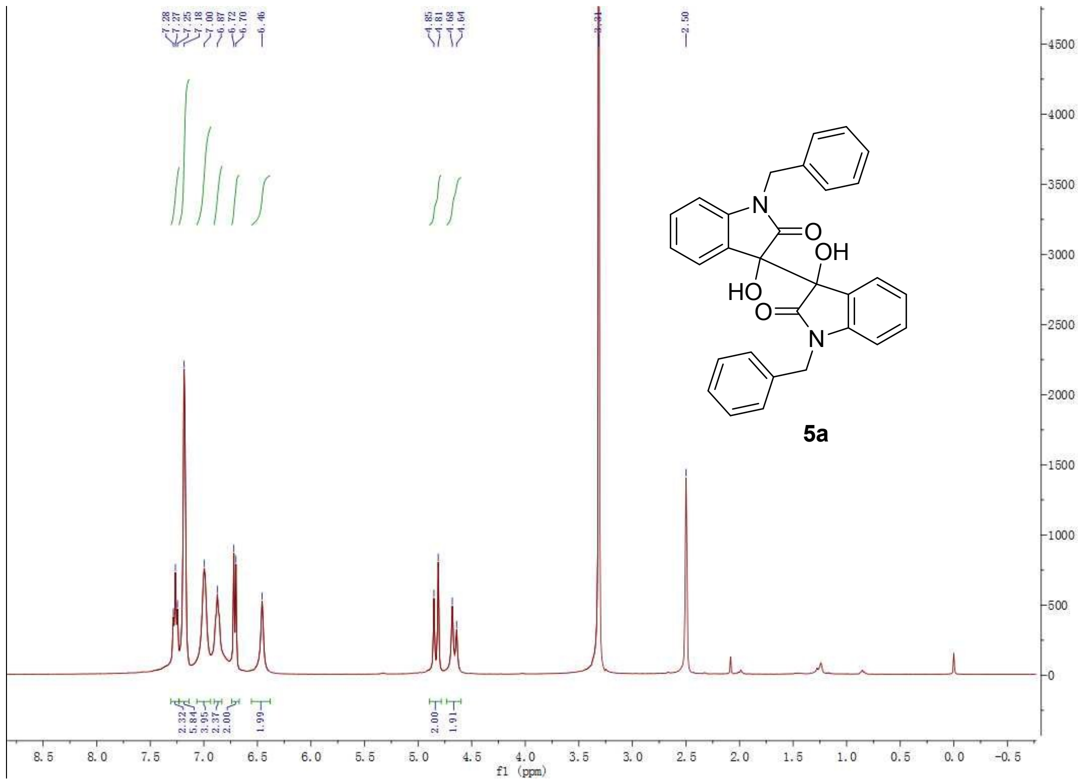

7.28
7.27
7.25
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6.87
6.72
6.70
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4.85
4.81
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4.64
3.31
2.50
N
O
OH
HO
O
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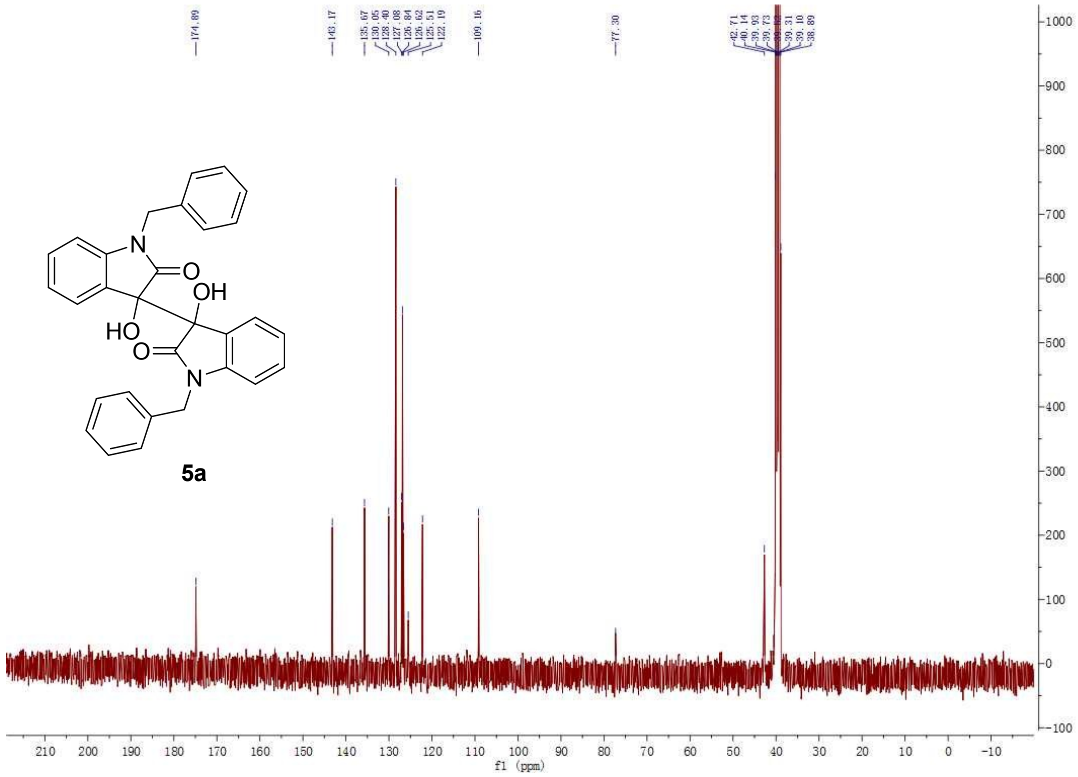
f1 (ppm)



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42.71
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39.31
39.10
38.89
N
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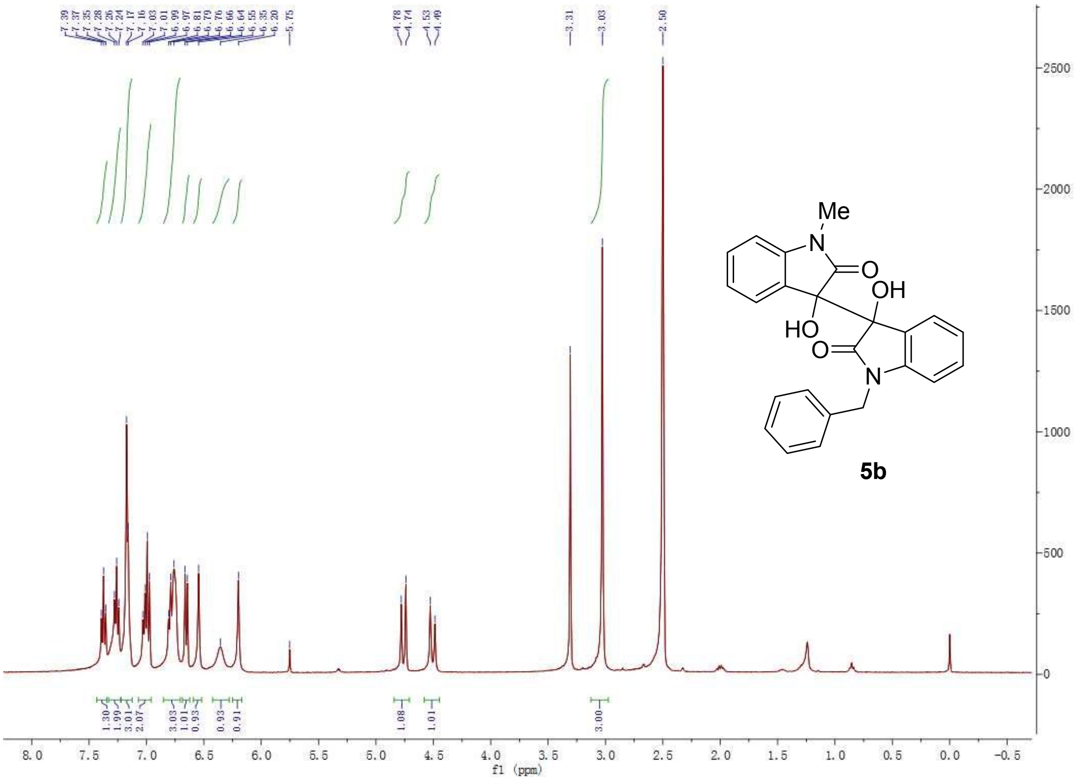
OH
HO
O
N
5a
f1 (ppm)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4.78 4.74 4.53 4.49
3.31
3.03
2.50
1.30 1.99 3.01 2.07 3.03 1.01 0.93 0.93 0.91
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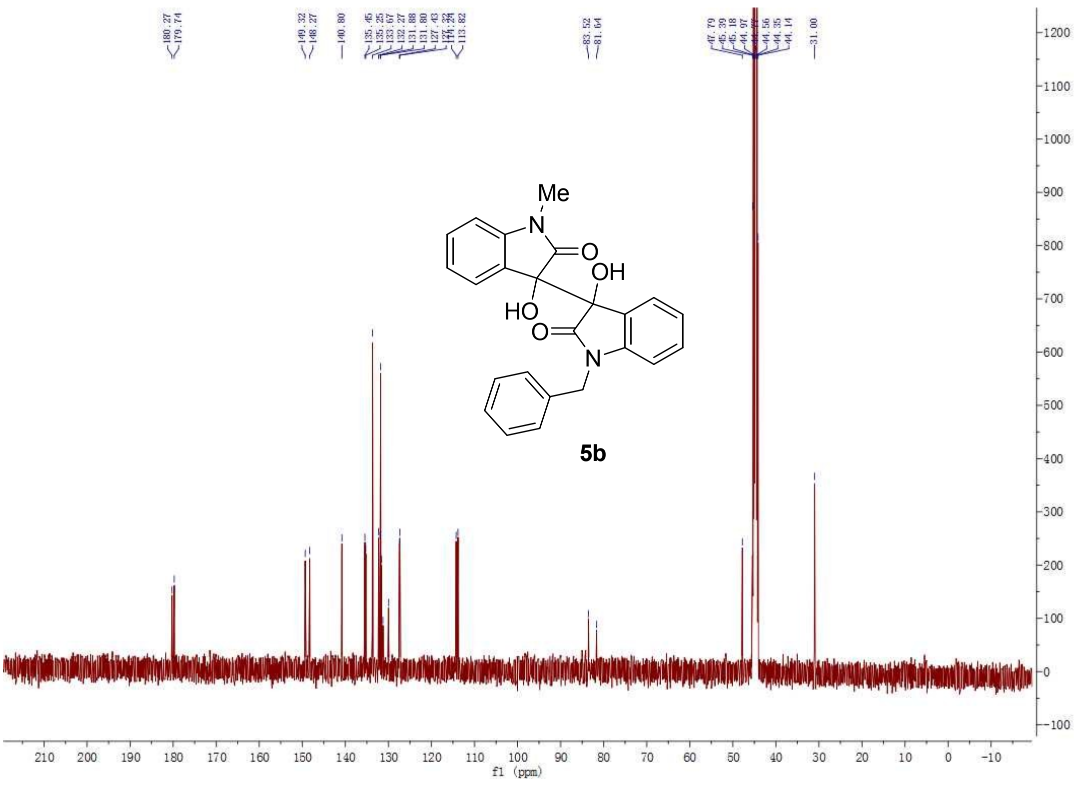
3.00
Me
N
O
OH
HO
O
N
5b
f1 (ppm)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149.32 148.27
140.80
135.45 135.25 133.67 132.27 131.88 131.80 127.43
113.82
83.52 81.64
47.79 45.39 45.18 44.97 44.56 44.35 44.14
31.00
Me
N
O
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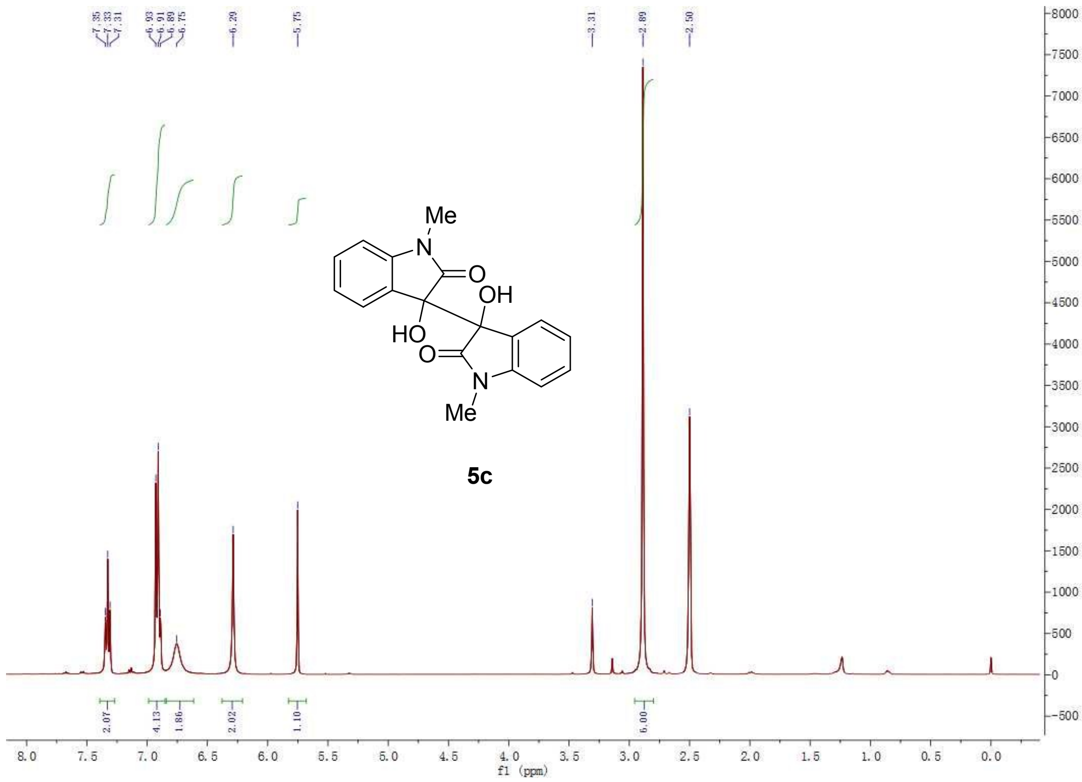
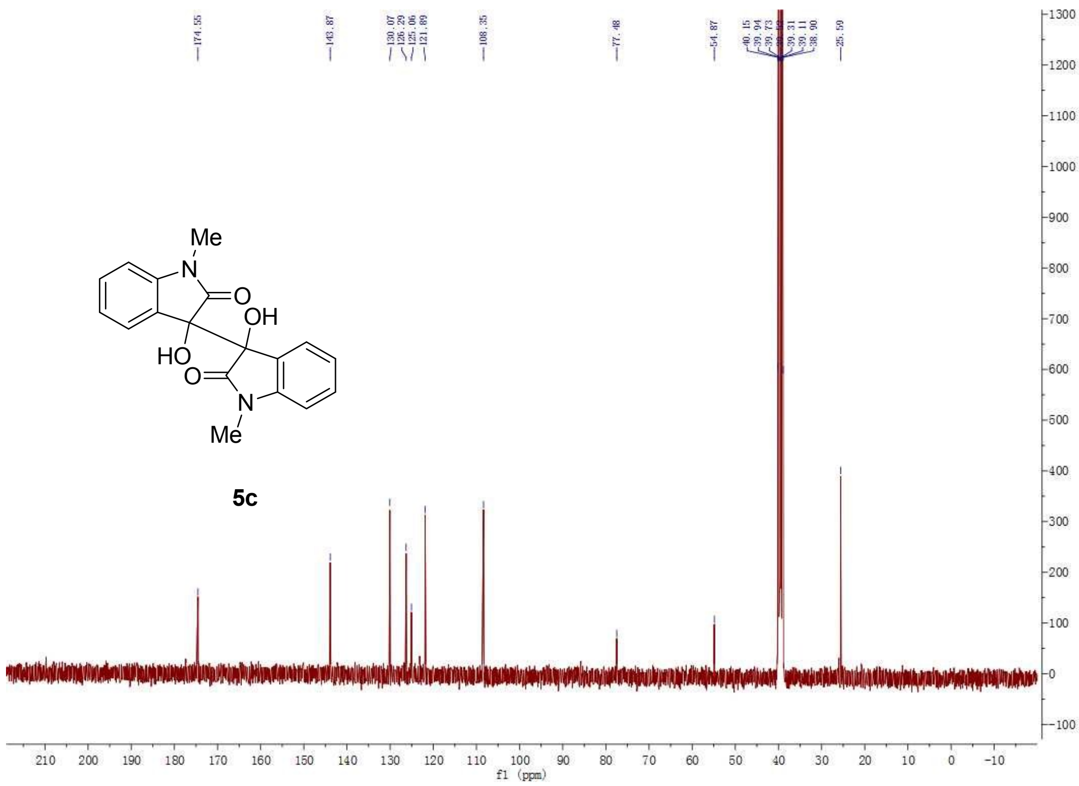
O
N
5b
f1 (ppm)





6. Computational details

Methods

The density functional theory (DFT) calculations were carried out by us using the Gaussian 09 program package.[1] The geometrical structures of intermediates were optimized using the M06 functional combined with the 6-311++G**basis. [2-3] The solvent effect of THF was considered by performing the single point calculations based on the gaseous structures using the SMD solvation model. [4]

References

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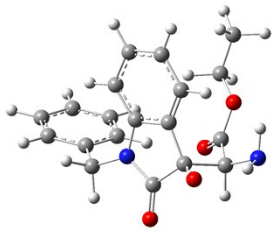

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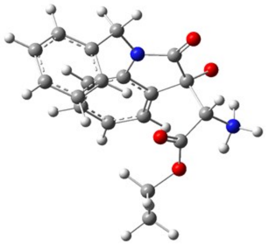

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