Supporting Information

Phosphine-catalyzed Asymmetric [4+1] Annulations of Activated *α,β*-Unsaturated Ketones with Morita-Baylis-Hillman Carbonates: Enantioselective Synthesis of Spirooxindoles Containing two Adjacent Quaternary Stereocenters

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CONTENTS

General Remarks:

Melting points were determined on a digital melting point apparatus and temperatures were uncorrected. Optical rotations were determined at 589 nm (sodium D line) by using a Perkin-Elmer-341 MC digital polarimeter; $[\alpha]_D$-values are given in unit of 10 deg^{-1} cm^2 g^{-1}. ^1H NMR spectra were recorded on a Varian Mercury-300 and 400 spectrometer for solution in $CDCl_3$ with tetramethylsilane (TMS) as an internal standard; coupling constants *J* are given in Hz. ^{13}C NMR spectra were recorded on a Varian Mercury-300 and 400 spectrophotometers (75 or 100 MHz) with complete proton decoupling spectrophotometers ($CDCl_3$: 77.0 ppm). Infrared spectra were recorded on a Perkin-Elmer PE-983 spectrometer with absorption in cm^{-1}. Flash column chromatography was performed using 300-400 mesh silica gel. For thin-layer chromatography (TLC), silica gel plates (Huanghai GF254) were used. Chiral HPLC was performed on a SHIMADZU SPD-10A *vp* series with chiral columns (Chiralpak AD-H, OD-H, and IC columns 4.6 × 250 mm, (Daicel Chemical Ind., Ltd.)) and chiral column (Phenomenex Lux 5μ Amylose-2 column 4.6 × 250 mm (PA-2), Phenomenex Lux 5μ Cellulose-2 column 4.6 × 250 mm (PC-2), (Phenomenex Ind., Ltd.)). Mass spectra were recorded by EI, ESI, MALDI and HRMS was measured on a HP-5989 instrument.

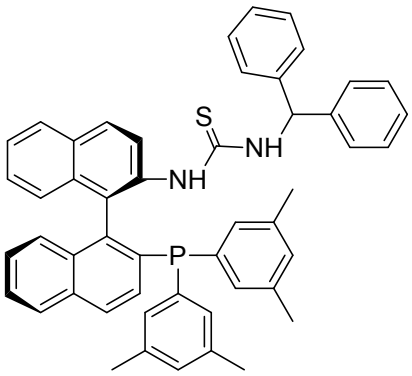
The catalysts TP were synthesized according to the known procedures.[1]

General procedure for the synthesis of *α,β*-unsaturated ketones 1:

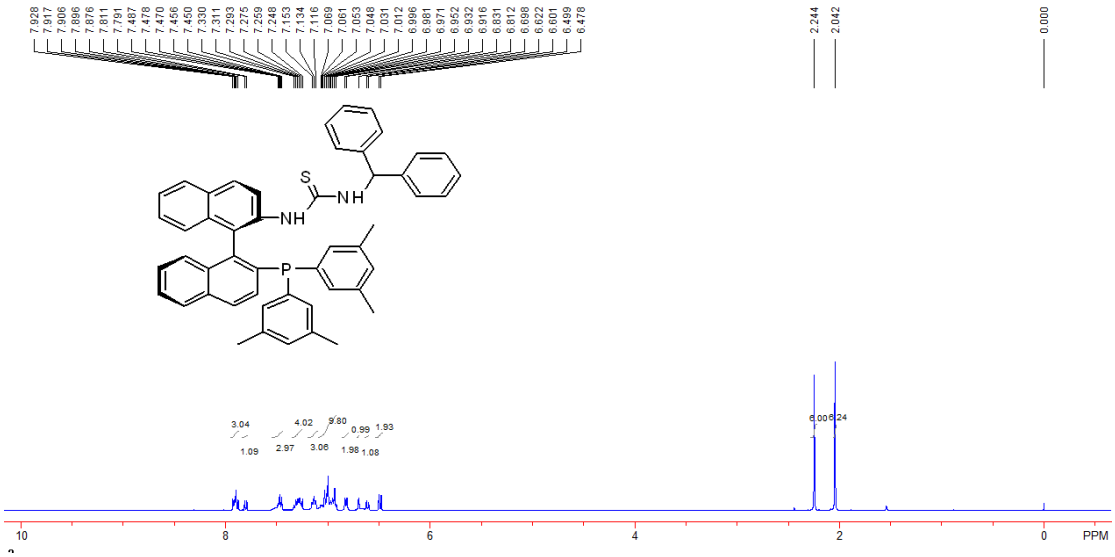
Into a 50 mL oven-dried three-necked bottle under Ar gas protection were added *N*-protected isatin or *N*-unprotected isatin (10 mmol), benzoylacetonitrile (10 mol), ethanol (15 mL) and triethanolamine (10 mmol). The reaction mixtures were stirred at room temperature for 48 h and the solvent was concentrated and purified by column chromatography on silica gel to give *α,β*-unsaturated ketones **1**.

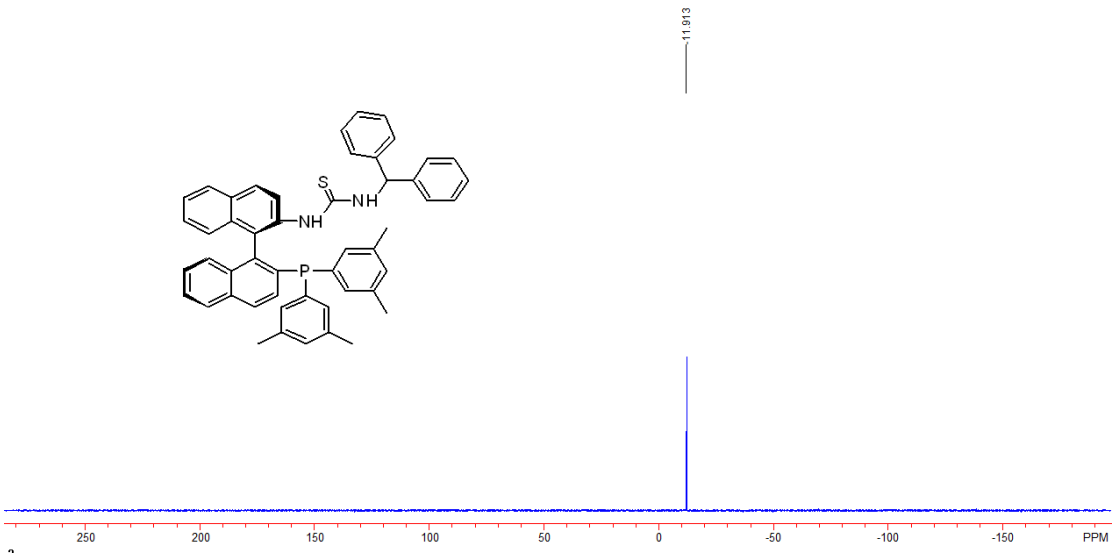
General procedure for the [4+1] reaction of *α,β*-unsaturated ketones 1 with MBH carbonates 2:

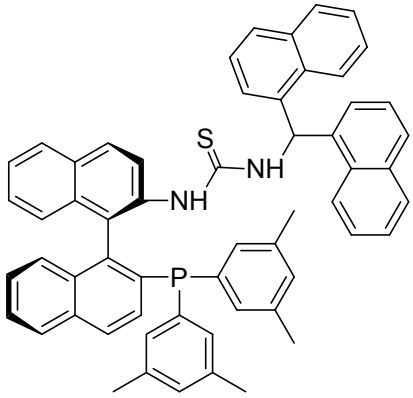
Into a 25 mL oven-dried reaction flask under argon atmosphere were added *α,β*-unsaturated ketones **1** (0.1 mmol) and MBH carbonates **2** (0.11 mmol), then catalyst **TP6** (0.02 mmol, 13 mg) in toluene (2 mL) was added and the reaction mixtures were stirred at room temperature for 12-48 h. After removal of the solvent under reduced pressure, the reaction mixture was purified by flash chromatography on silica gel (eluent: EtOAc:light petroleum ether = 1:8 to 1:4) to give the pure product **3**.



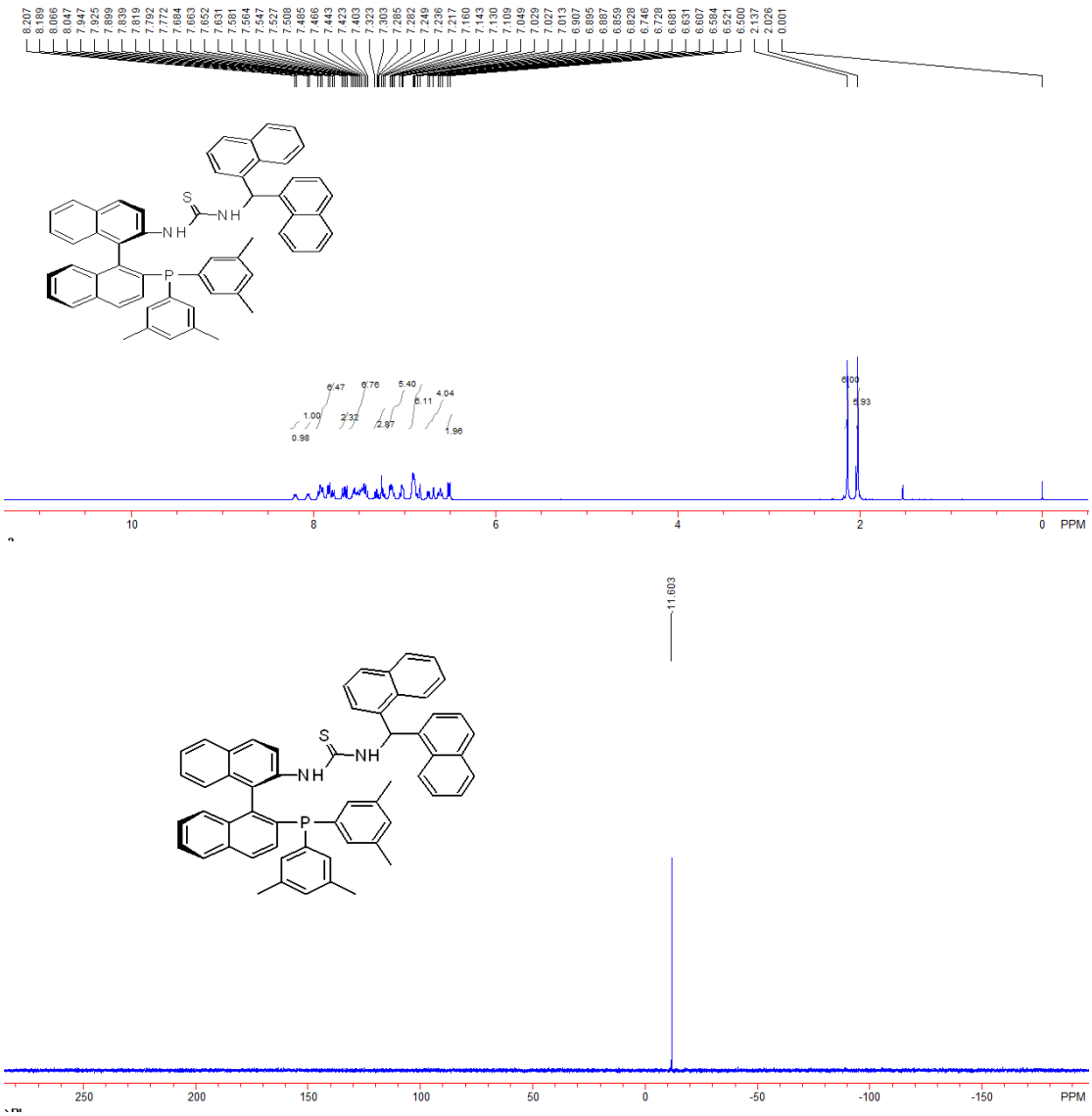
Catalyst TP9: A white solid power, Mp: 132-133 ^{o}C. ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 2.04 (s, 6H, CH_3), 2.24 (s, 6H, CH_3), 6.48-6.50 (m, 2H), 6.61 (d, *J* = 8.0 Hz, 1H), 6.70 (s, 1H), 6.81-6.83 (m, 2H), 6.92-7.15 (m, 13H), 7.25-7.33 (m, 4H), 7.45-7.51 (m, 3H), 7.80 (d, *J* = 8.0 Hz, 1H), 7.88-7.93 (m, 3H,). ^{31}P NMR (161.94 MHz, $CDCl_3$, 85% H_3PO_4): δ -11.91. IR (CH_2Cl_2) ν 696, 745, 817, 846, 1195, 1263, 1327, 1457, 1504, 1596, 2927, 3028, 3389 cm^{-1}. MS (ESI) m/e 735.3 (M^{+}+1). HRMS (ESI) calcd. for $C_{50}H_{44}N_2PS$: 735.2963, Found: 735.2957; $[\alpha]_D^{20}$ = 29.4 (c 0.45, CH_2Cl_2)].

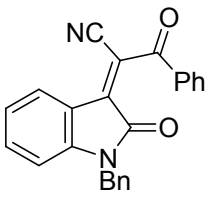




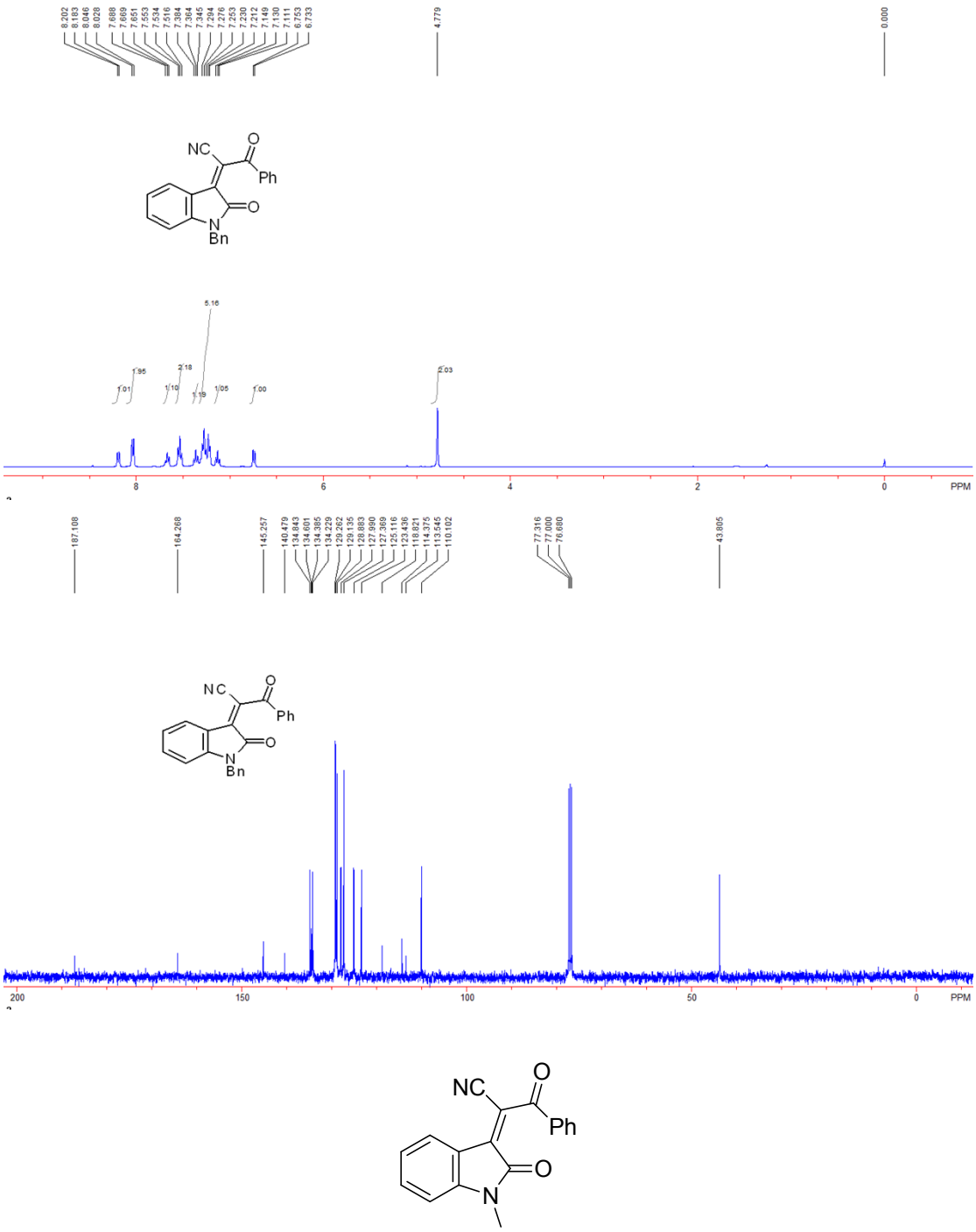


Catalyst TP10: A white solid power, Mp: 150-152 ^{o}C. ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 2.03 (s, 6H, CH_3), 2.14 (s, 6H, CH_3), 6.50-6.52 (m, 2H), 6.58-6.63 (m, 2H), 6.68 (s, 1H), 6.73-6.75 (m, 1H), 6.83 (s, 1H), 6.86-6.91 (m, 5H), 7.01-7.05 (m, 2H), 7.11-7.16 (m, 3H), 7.22-7.32 (m, 2H), 7.40-7.56 (m, 6H), 7.63-7.68 (m, 2H), 7.77-7.95 (m, 6H), 8.06 (d, *J* = 8.0 Hz, 1H), 8.20 (d, *J* = 8.0 Hz, 1H). ^{31}P NMR (161.94 MHz, $CDCl_3$, 85% H_3PO_4): δ -11.60. IR (CH_2Cl_2) ν 693, 747, 783, 817, 1193, 1250, 1265, 1501, 1597, 2910, 3049, 3389 cm^{-1}. MS (ESI) m/e 835.3 (M^{+}+1). HRMS (ESI) calcd. for $C_{58}H_{48}N_2PS$: 835.3276, Found: 835.3266; $[\alpha]_D^{20}$ = -40.2 (c 0.75, CH_2Cl_2)].

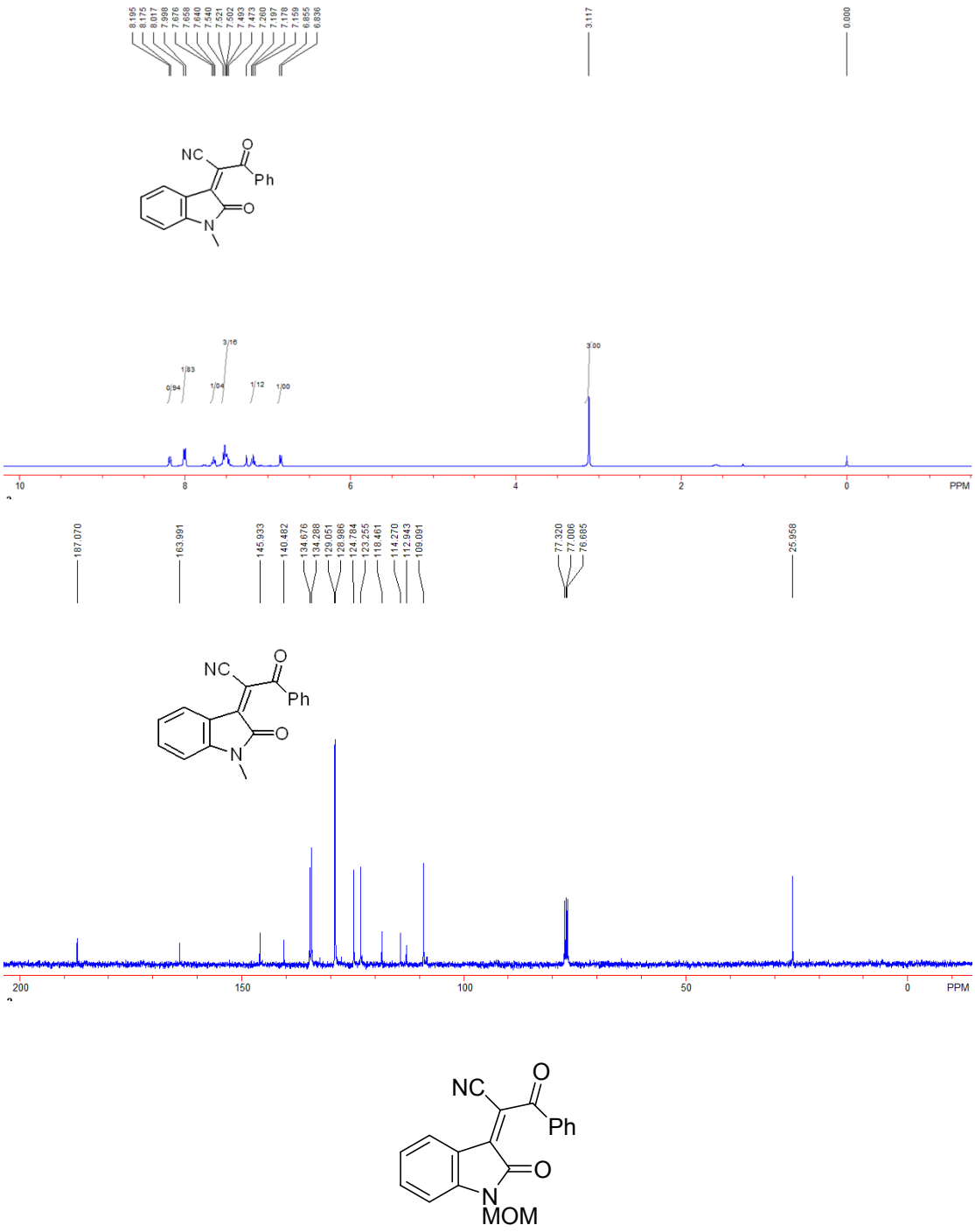




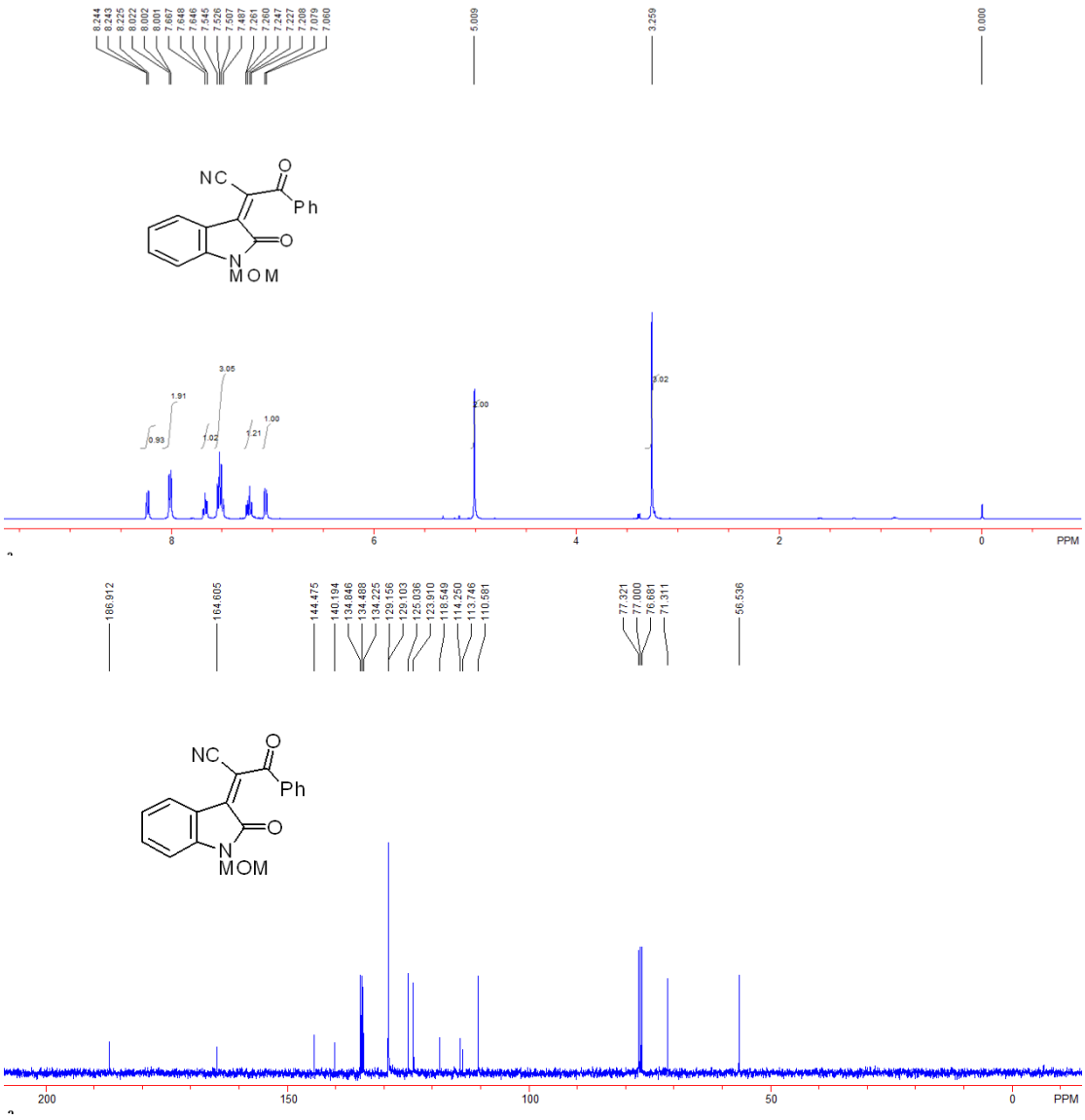
Compound 1a: A yellow solid, Mp: 124-125 ^{o}C. ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 4.78 (s, 2H, CH_2), 6.74 (d, J = 8.0 Hz, 1H, Ar), 7.11-7.15 (m, 1H, Ar), 7.21-7.29 (m, 5H, Ar), 7.35-7.38 (m, 1H, Ar), 7.52-7.55 (m, 2H, Ar), 7.65-7.69 (m, 1H, Ar), 8.04 (d, J = 7.2 Hz, 2H, Ar), 8.19 (d, J = 8.0 Hz, 1H, Ar). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 43.8, 110.1, 113.5, 114.4, 118.8, 123.4, 125.1, 127.4, 128.0, 128.9, 129.1, 129.3, 134.2, 134.4, 134.6, 134.8, 140.5, 145.3, 164.3, 187.1. IR (CH_2Cl_2) ν 701, 748, 1185, 1259, 1355, 1378, 1468, 1604, 1679, 1716, 2925 cm^{-1}. MS (ESI) m/e 365.1 (M^{+}+1). HRMS (ESI) calcd. for $C_{24}H_{17}N_2O_2$: 365.1290, Found: 365.1286.

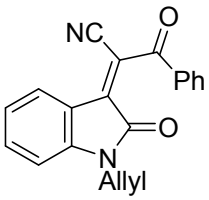


Compound 1b: A yellow solid, Mp: 120-121 ^{o}C. ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 3.12 (s, 3H, CH_3), 6.85 (d, J = 8.0 Hz, 1H, Ar), 7.18 (t, J = 7.6 Hz, 1H, Ar), 7.47-7.54 (m, 3H, Ar), 7.65 (t, J = 7.6 Hz, 1H, Ar), 8.01 (d, J = 8.0 Hz, 2H, Ar), 8.19 (d, J = 8.0 Hz, 1H, Ar). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 26.0, 109.1, 112.9, 114.3, 118.5, 123.3, 124.8, 129.0, 129.1, 134.3, 134.7, 140.5, 145.9, 164.0, 187.1. IR (CH_2Cl_2) ν 738, 752, 830, 103O, 1175, 1256, 1373, 1511, 1595, 1617, 1709, 1724, 2337, 2932 cm^{-1}. MS (ESI) m/e 289.1 (M^{+}+1). HRMS (ESI) calcd. for $C_{18}H_{13}N_2O_2$: 289.0977, Found: 289.0971.

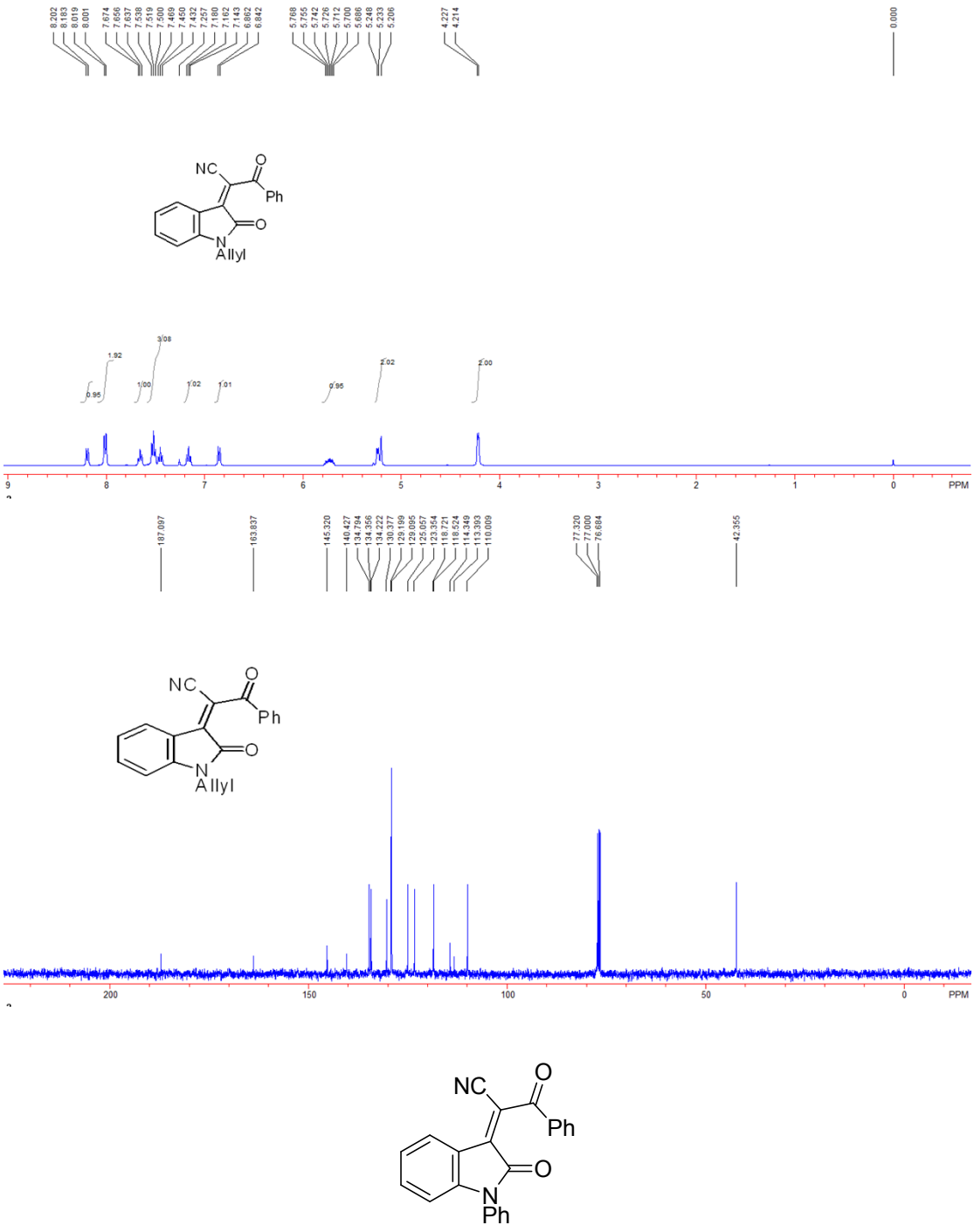


Compound 1c: A yellow solid, Mp: 154-155 ^{o}C. ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 3.26 (s, 3H, CH_3), 5.01 (s, 2H, CH_2), 7.07 (d, J = 8.0 Hz, 1H, Ar), 7.21-7.26 (m, 1H, Ar), 7.49-7.55 (m, 3H, Ar), 7.65-7.67 (m, 1H, Ar), 8.01 (d, J = 8.0 Hz, 2H, Ar), 8.23 (d, J = 7.6 Hz, 1H, Ar). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 56.5, 71.3, 110.6, 113.7, 114.3, 118.5, 123.9, 125.0, 129.1, 129.2, 134.2, 134.5, 140.2, 144.5, 164.6, 186.9. IR (CH_2Cl_2) ν 703, 751, 965, 1080, 1100, 1246, 1258, 1350, 1470, 1605, 1679, 1273, 2931 cm^{-1}. MS (ESI) m/e 319.1 (M^{+}+1). HRMS (ESI) calcd. for $C_{19}H_{15}N_2O_3$: 319.1083, Found: 319.1074.

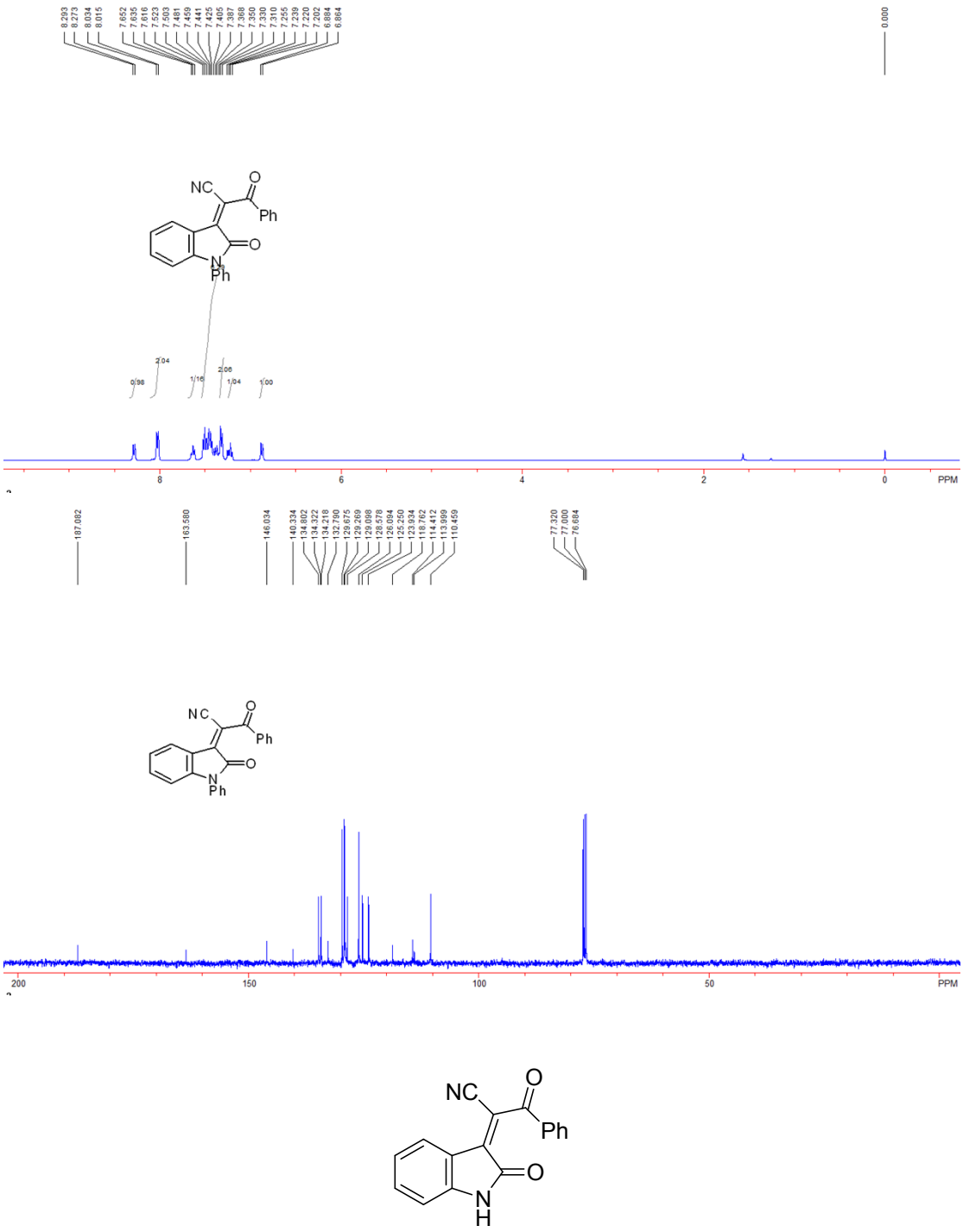




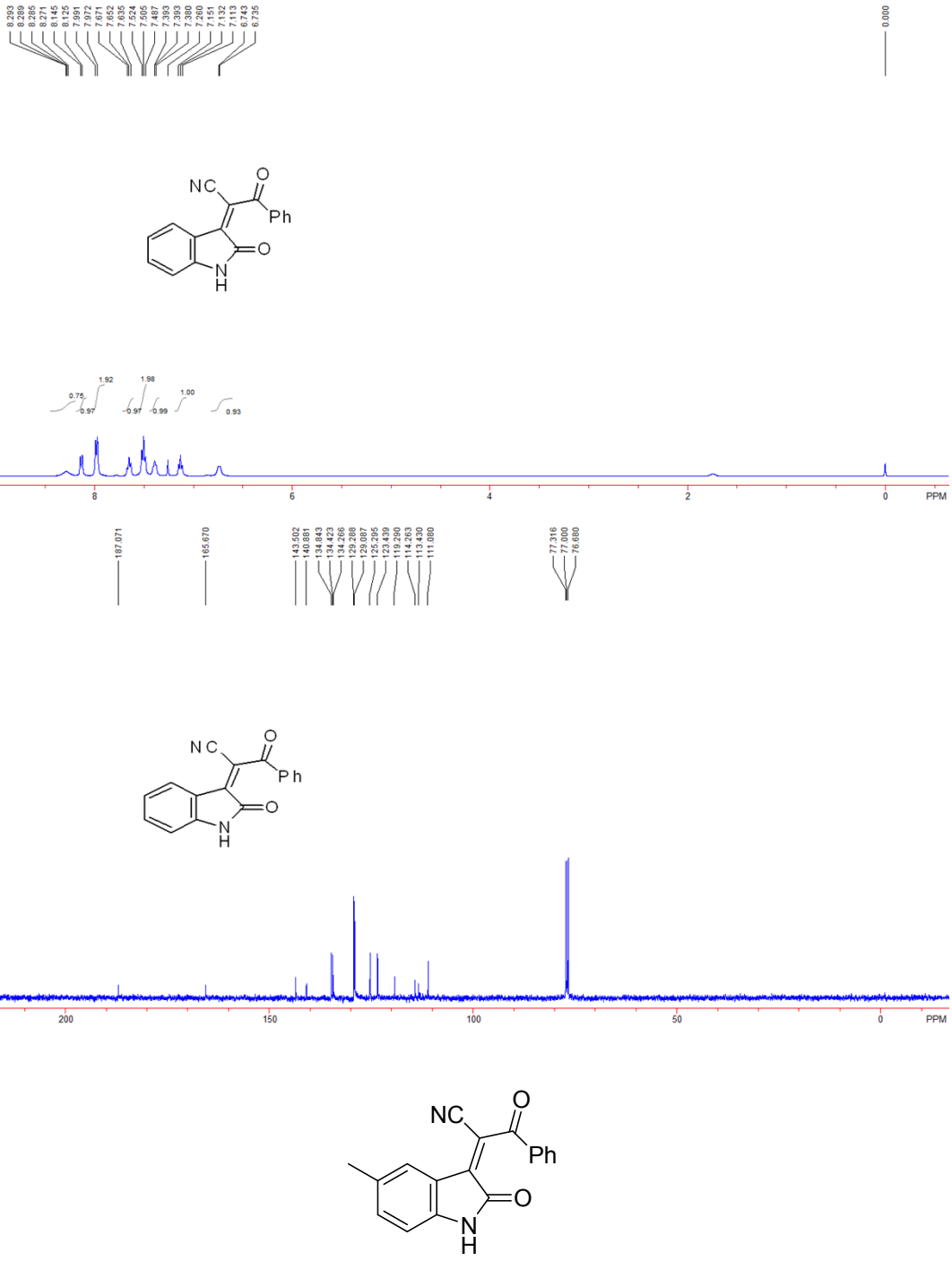
Compound 1d: A yellow solid, Mp: 86-187 ^{o}C. ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 4.22 (d, J = 5.2 Hz, 2H, CH_2), 5.21-5.25 (m, 2H, =CH), 5.69-5.77 (m, 1H, =CH), 6.85 (d, J = 8.0 Hz, 1H, Ar), 7.16 (t, J = 7.6 Hz, 1H, Ar), 7.26-7.54 (m, 3H, Ar), 7.66 (t, J = 7.6 Hz, 1H, Ar), 8.01 (d, J = 8.0 Hz, 2H, Ar), 8.19 (d, J = 8.0 Hz, 1H, Ar). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 42.4, 110.0, 113.4, 114.3, 118.5, 118.7, 123.4, 125.1, 129.1, 129.2, 130.4, 134.2, 134.4, 134.8, 140.4, 145.3, 163.8, 187.1. IR (CH_2Cl_2) ν 686, 703, 749, 1192, 1259, 1354, 1469, 1605, 1679, 1717 cm^{-1}. MS (ESI) m/e 315.1 (M^{+}+1). HRMS (ESI) calcd. for $C_{20}H_{15}N_2O_2$: 315.1134, Found: 315.1130.



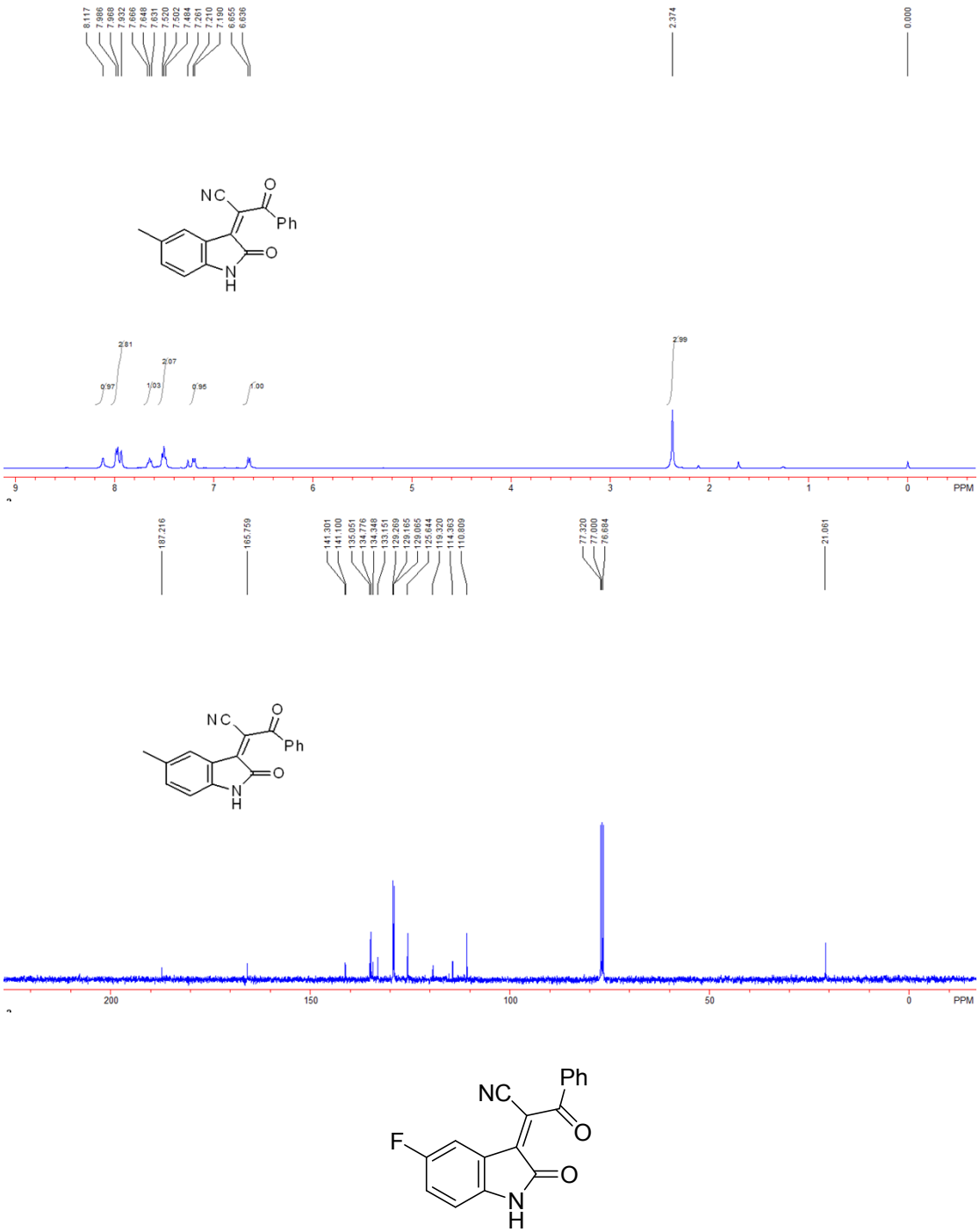
Compound 1e: A yellow solid, Mp: 164-165 ^{o}C. ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 6.87 (d, *J* = 8.0 Hz, 1H, Ar), 7.22 (t, *J* = 7.6 Hz, 1H, Ar), 7.3-7.33 (m, 2H, Ar), 7.35-7.52 (m, 6H, Ar), 7.62-7.65 (m, 1H, Ar), 8.02 (d, *J* = 8.0 Hz, 2H, Ar), 8.28 (d, *J* = 8.0 Hz, 1H, Ar). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 110.5, 114.0, 114.4, 118.8, 123.9, 125.3, 126.1, 128.6, 129.1, 129.3, 129.7, 1328, 134.2, 134.3, 134.8, 140.3, 146.3, 163.6, 187.1. IR (CH_2Cl_2) ν 699, 750, 1120, 1259, 1373, 1466, 1498, 1605, 1678, 1723 cm^{-1}. MS (ESI) m/e 351.1 (M^{+}+1). HRMS (ESI) calcd. for $C_{23}H_{15}N_2O_2$: 351.1134, Found: 351.1125.



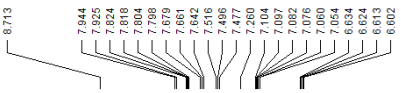
Compound 1f: A yellow solid, Mp: 192-193 ^{o}C. ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 6.74 (d, *J* = 3.2 Hz, 1H, Ar), 7.11-7.15 (m, 1H, Ar), 7.38-7.39 (m, 1H, Ar), 7.49-7.52 (m, 2H, Ar), 7.64-7.67 (m, 1H, Ar), 7.98 (d, *J* = 8.0 Hz, 2H, Ar), 8.14 (d, *J* = 8.0 Hz, 1H, Ar), 8.29 (br, 1H, NH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 111.1, 113.4, 114.3, 119.3, 123.4, 125.3, 129.1, 129.3, 134.3, 134.4, 134.8, 140.9, 143.5, 165.7, 187.1. IR (CH_2Cl_2) ν 704, 1258, 1339, 1467, 1610, 1681, 1726, 3295 cm^{-1}. MS (ESI) m/e 275.1 (M^{+}+1). HRMS (ESI) calcd. for $C_{17}H_{11}N_2O_2$: 275.0821, Found: 275.0817.



Compound 1g: A yellow solid, Mp: 231-232 ^{o}C. ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 2.37 (s, 3H, CH_3), 6.65 (d, J = 8.0 Hz, 1H, Ar), 7.16 (d, J = 8.0 Hz, 1H, Ar), 7.49-7.52 (m, 2H, Ar), 7.63-7.67 (m, 1H, Ar), 7.93-7.99 (m, 3H, Ar), 8.12 (s, 1H, NH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 21.1, 110.8, 114.4, 119.3, 125.6, 129.1, 129.2, 129.3, 133.2, 134.3, 134.8, 135.1, 141.1, 141.3, 165.8, 187.2. IR (CH_2Cl_2) ν 905, 1210, 1260, 1316, 1486, 1596, 1611, 1678, 1720, 3311. cm^{-1}. MS (ESI) m/e 289.1 (M^{+}+1). HRMS (ESI) calcd. for $C_{18}H_{13}N_2O_2$: 289.0977, Found: 289.0972.



Compound 1h: A yellow solid, Mp: 208-209 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 6.62 (dd, *J* = 8.0 Hz, *J* = 4.0 Hz, 1H, Ar), 7.08 (td, *J* = 8.4 Hz, *J* = 2.4 Hz, 1H, Ar), 7.48-7.52 (m, 2H, Ar), 7.64-7.68 (m, 1H, Ar), 7.81 (dd, *J* = 8.4 Hz, *J* = 2.4 Hz, 1H, Ar), 7.93-7.94 (m, 2H, Ar), 8.71 (s, 1H, NH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 112.2, 112.3 (*J* = 31.8 Hz), 113.7, 114.8, 119.9, (*J* = 9.6 Hz), 121.1 (*J* = 23.8 Hz), 129.2, 129.3, 133.9, 135.1, 139.7 (*J* = 2.1 Hz), 140.6 (*J* = 2.8 Hz), 159.2 (*J* = 241.1 Hz), 165.8, 186.7. ^{19}F NMR ($CDCl_3$, 376 MHz, $CFCl_3$) δ -118.08 - -118.02 (m). IR (CH_2Cl_2) ν 1174, 1263, 1481, 1598, 1678, 1727, 3303 cm^{-1}. MS (ESI) m/e 293.1 (M^++1). HRMS (ESI) calcd. for $C_{17}H_{10}FN_2O_2$: 293.0726, Found: 293.0722.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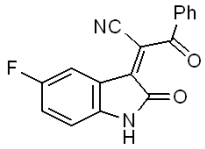
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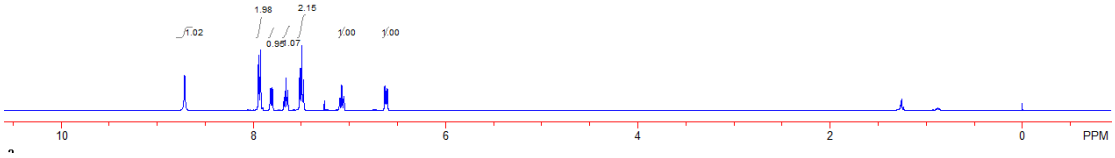
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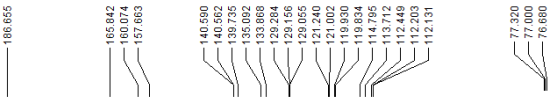
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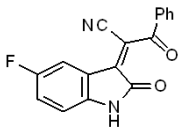
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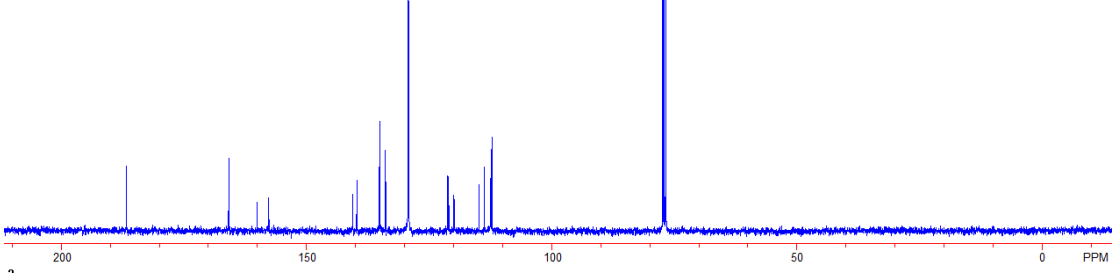
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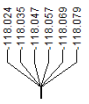
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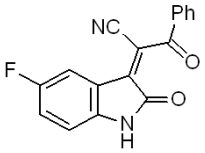
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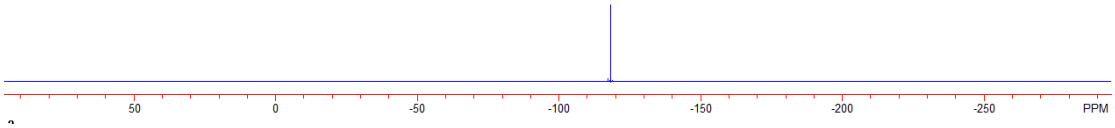
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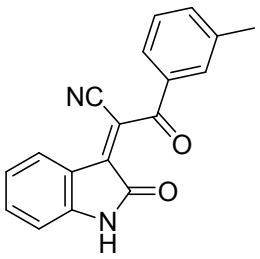
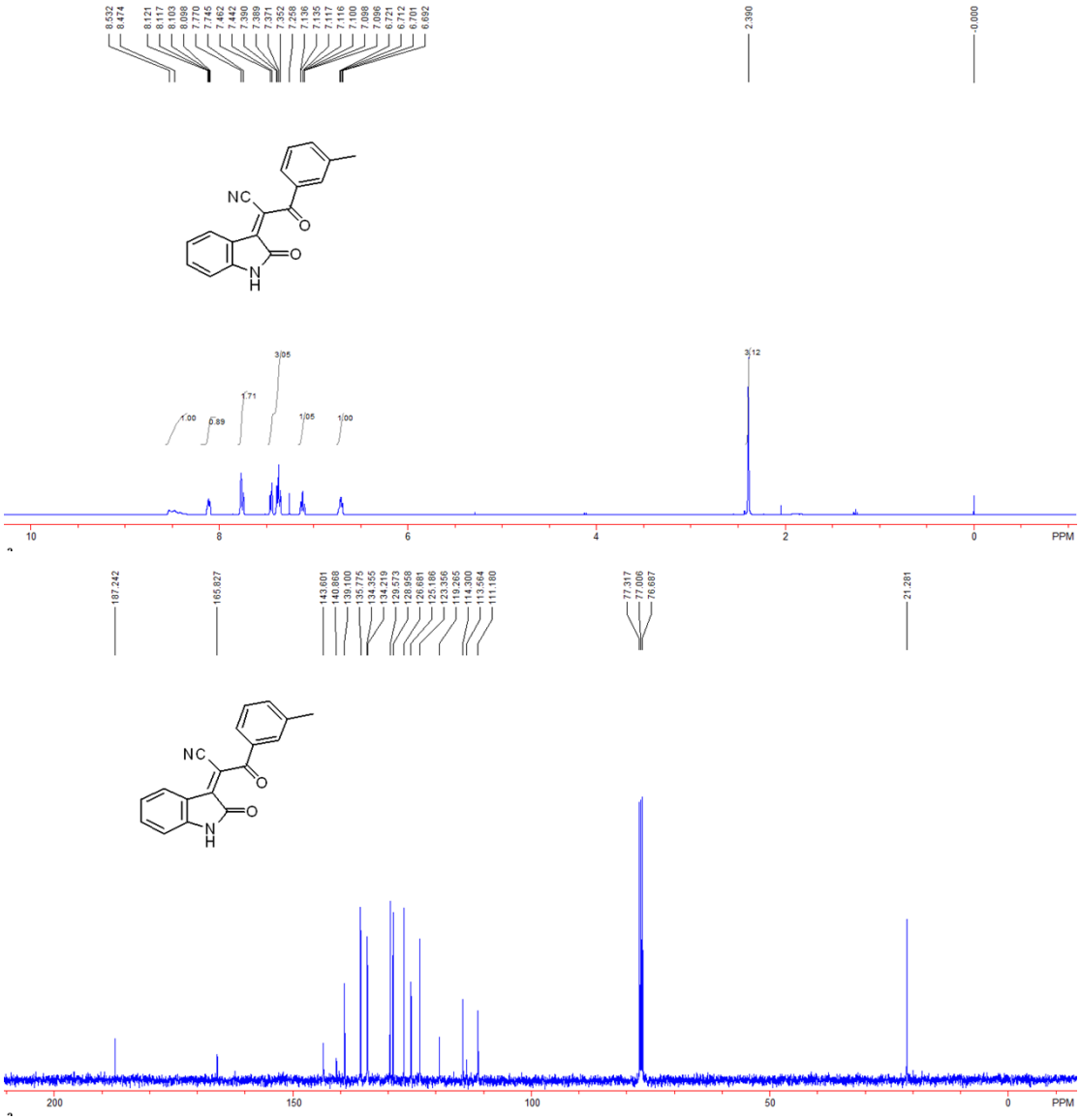
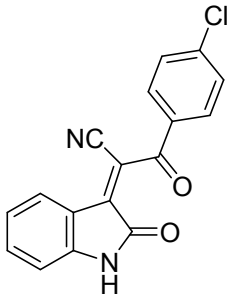
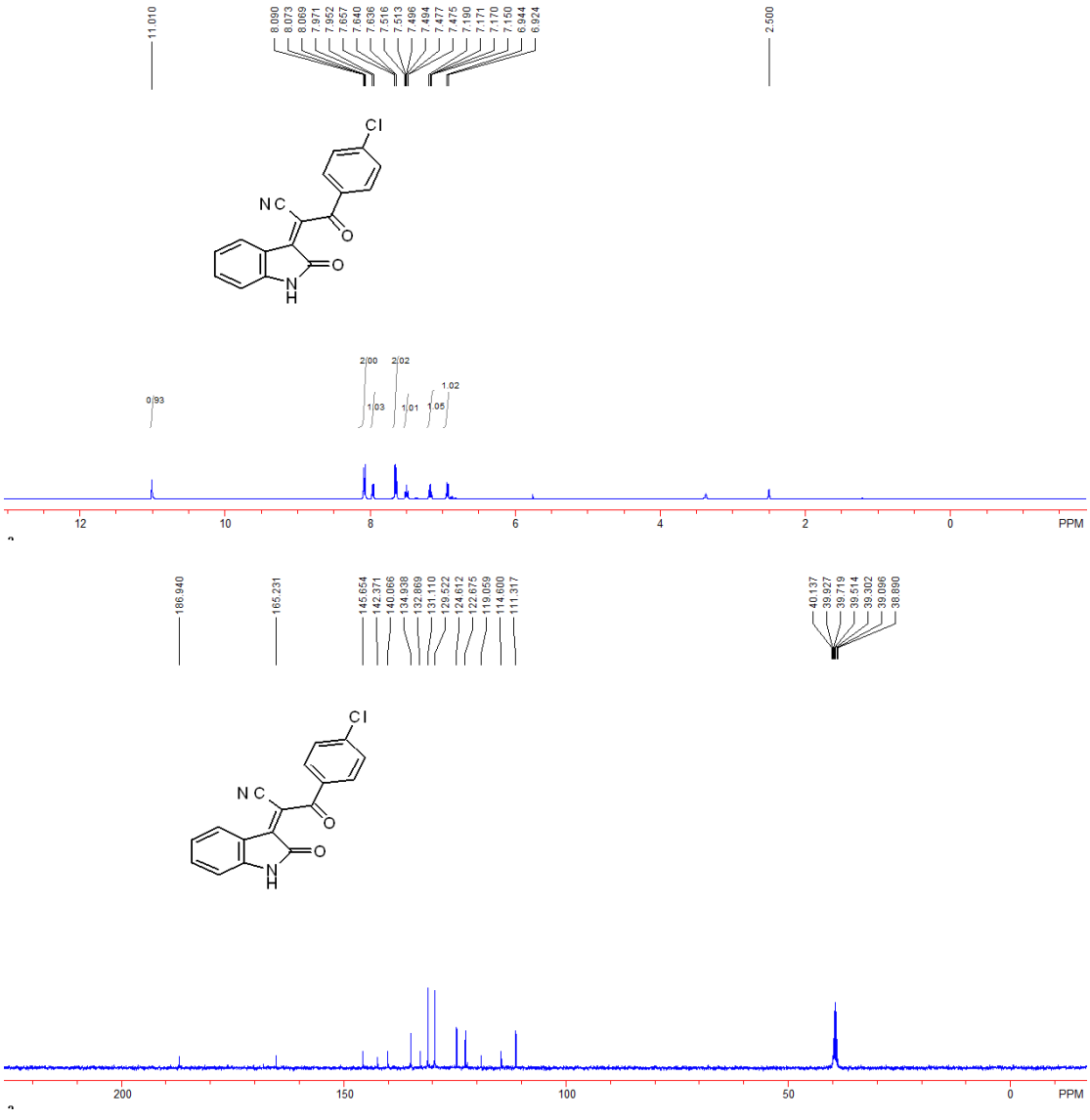


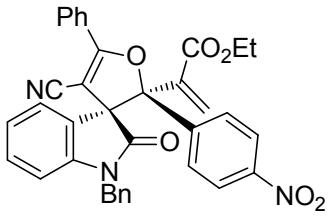
Compound 1j: A yellow solid, Mp: 178-179 ^{o}C. ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 2.39 (s, 3H, CH_3), 6.71 (dd, J = 8.0 Hz, J = 4.0 Hz, 1H, Ar), 7.10-7.14 (m, 1H, Ar), 7.35-7.36 (m, 3H, Ar), 7.75-7.77 (m, 2H, Ar), 8.10-8.12 (m, 1H, Ar), 8.47-8.53 (m, 1H, NH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 21.3, 111.2, 113.6, 114.3, 119.3, 123.4, 125.2, 126.7, 129.0, 129.6, 134.2, 134.4, 135.8, 139.1, 140.9, 143.6, 165.8, 187.2. IR (CH_2Cl_2) ν 1205, 1269, 1338, 1466, 1608, 1677, 1721, 3284 cm^{-1}. MS (ESI) m/e 289.1 (M^{+}+1). HRMS (ESI) calcd. for $C_{18}H_{13}N_2O_2$: 289.0977, Found: 289.0975.



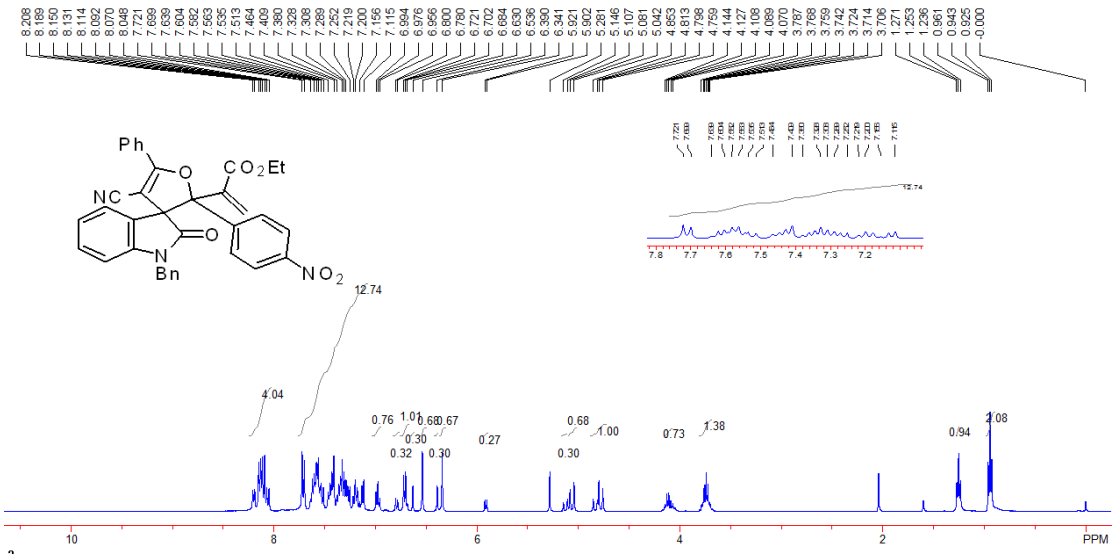


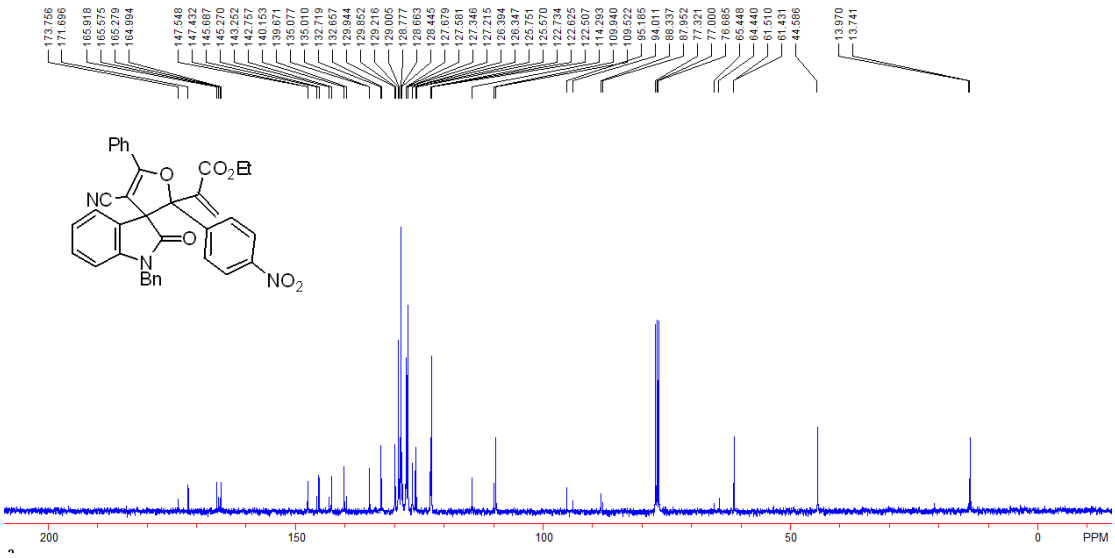
Compound 1k: A yellow solid, Mp: 189-190 °C. ^{1}H NMR (DMSO-d_6, 400 MHz, TMS) δ 6.93 (d, J = 8.0 Hz, 1H, Ar), 7.15-7.19 (m, 1H, Ar), 7.48-7.53 (m, 1H, Ar), 7.64-7.66 (m, 2H, Ar), 7.78 (d, J = 8.0 Hz, 1H, Ar), 8.07-8.09 (m, 2H, Ar), 11.01 (s, 1H, NH). ^{13}C NMR (DMSO-d_6, 100 MHz, TMS) δ 11.3, 114.6, 119.0, 122.7, 124.6, 129.5, 131.1, 132.9, 134.9, 140.1, 142.4, 145.6, 165.2, 186.9. IR (CH_2Cl_2) ν 748, 1093, 1258, 1339, 1467, 1587, 1609, 1680, 1727, 3296 cm^{-1}. MS (ESI) m/e 309.0 (M^++1). HRMS (ESI) calcd. for $C_{17}H_{10}ClN_2O_2$: 309.0431, Found: 309.0427.





Compound 3a: A white solid (58 mg, 97% yield), Mp: 100-103 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 0.94 (t, *J* = 7.2 Hz, 2.08H, CH_3), 1.25 (t, *J* = 7.2 Hz, 0.94H, CH_3), 3.70-3.79 (m, 1.38H, CH_2), 4.08-4.14 (m, 0.73H, CH_2), 4.76-4.85(m, 1H, CH), 4.78 (d, *J* = 16.0 Hz, 0.68H, CH), 5.13 (d, *J* = 16.0 Hz, 0.30H, CH), 5.91 (d, *J* = 8.0 Hz, 0.27H, Ar), 6.34 (s, 0.67H, =CH), 6.39 (s, 0.30H, =CH), 6.54 (s, 0.68H, =CH), 6.63 (s, 0.30H, =CH), 6.68-6.72 (m, 1H, Ar), 6.79 (d, *J* = 8.0 Hz, 0.32H, Ar), 6.96-6.99 (m, 0.76H, Ar), 7.12-7.72 (m, 12.74H, Ar), 8.05-8.21 (m, 4H, Ar). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 13.7, 14.0, 44.6, 61.4, 61.5, 64.4, 65.4, 88.0, 88.3, 94.0, 95.2, 109.5, 109.9, 114.3, 122.5, 122.6, 122.7, 125.6, 125.8, 126.3, 126.4, 127.2, 127.3, 127.6, 127.7, 128.4, 128.7, 128.8, 129.0, 129.2, 129.85, 129.94, 132.65, 132.72, 135.01, 135.08, 139.7, 140.2, 142.8, 143.3, 145.3, 145.7, 147.4, 147.5, 165.0, 165.3, 165.6, 165.9, 171.7, 173.8. IR (CH_2Cl_2) ν 690, 754, 853, 1023, 1177, 1347, 1467, 1487, 1521, 1609, 1716, 2206, 2931 cm^{-1}. MS (ESI) m/e 598.2 (M^++H). HRMS (ESI) calcd. for $C_{36}H_{28}N_3O_6$: 598.1978, Found: 598.1967. Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column [λ = 230 nm; eluent: Hexane/Isopropanol = 70/30; Flow rate: 0.70 mL/min; t_{major} = 13.63 min, t_{minor}= 31.03 min; ee% = 96%; $[\alpha]_D^{20}$ = -142.2(c 2.25, CH_2Cl_2)].





N2000 数据工作站

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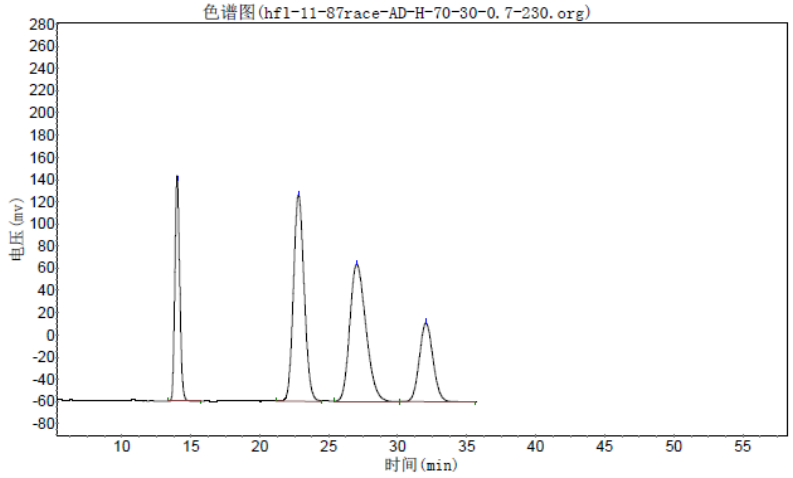
谱图文件:D:\4+1\Condition\hfl-11-87race-AD-H-70-30-0.7-230.org

实验者:
报告时间：2014-04-04,8:12:30
积分方法:面积归一法

使用仪器类型:气相色谱　　检测器:FID　　进样器:分流

柱温:程序升温



分析结果表

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2		22.832	185893.266	10097765.000	33.6066
3		27.065	123878.609	10108135.000	33.6411
4		32.065	71100.156	4910884.500	16.3440
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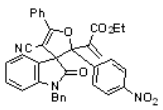

AD-H, 230
Hexane:iPrOH = 70:30
0.7 mL/min

实验时间：2013-10-11,17:26:45
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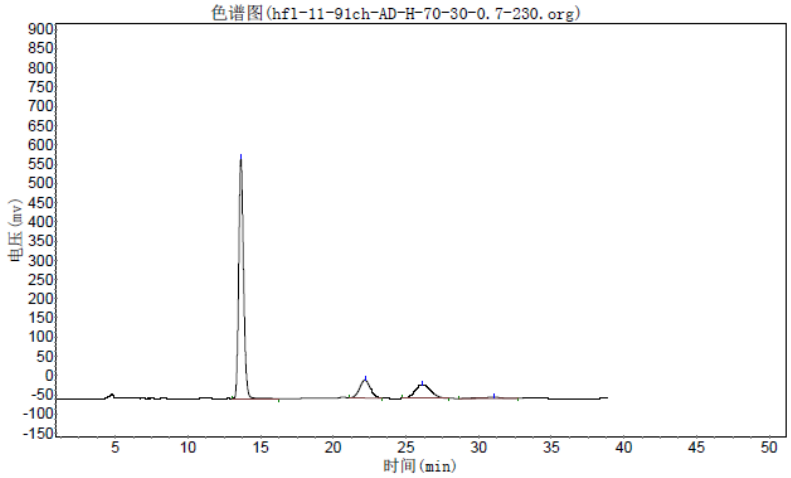
实验者:
报告时间：2014-04-04,8:11:54
积分方法:面积归一法

使用仪器类型:气相色谱　　检测器:FID　　进样器:分流

柱温:程序升温



分析结果表

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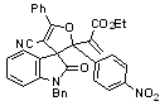
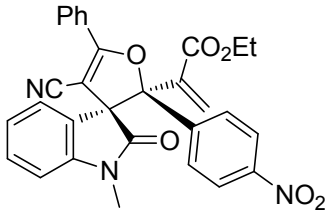
2		22.168	46618.242	2391233.750	12.0056
3		26.127	36052.727	2697262.750	13.5421
4		31.025	2992.300	315947.031	1.5863
总计			709878.831	19917672.531	100.0000



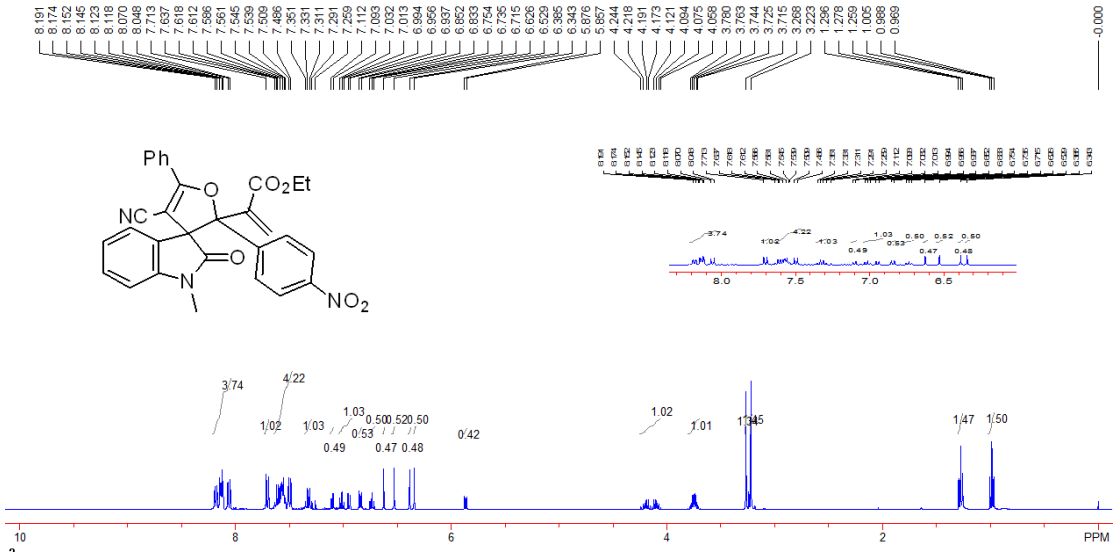
AD-H, 230
Hexane:iPrOH = 70:30
0.7 mL/min

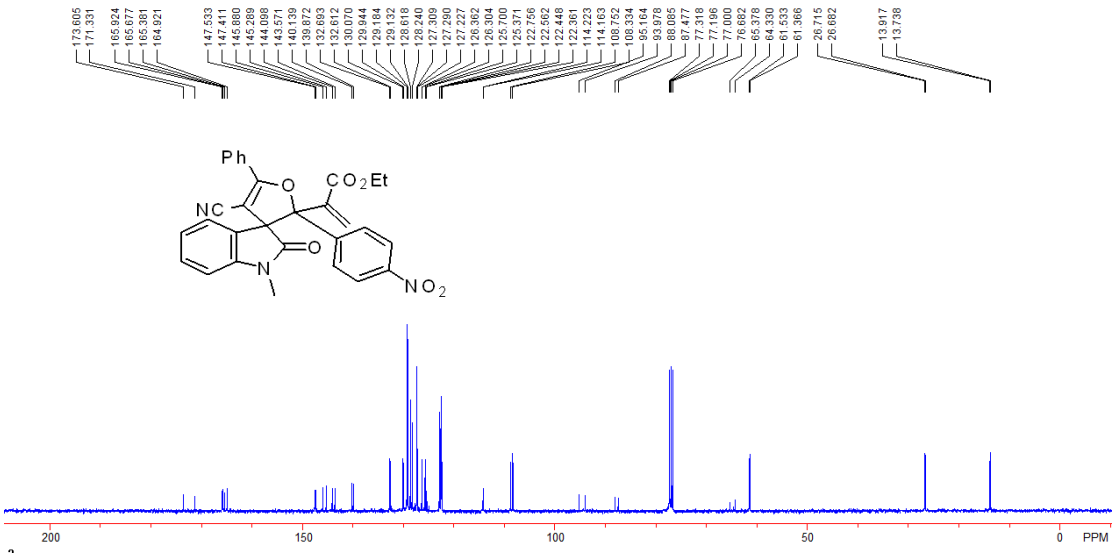
Translation: Enantiomeric excess was determined by HPLC with a Chiralcel AD-H column [λ = 230 nm; eluent: Hexane/Isopropanol = 60/40; Flow rate: 0.70 mL/min; t_{major} = 13.63 min, t_{minor}= 31.03 min; ee% = 96%.



Compound 3b: A white solid (51 mg, 97% yield), Mp: 80-83 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 0.99 (t, *J* = 7.2 Hz, 1.50H, CH_3), 1.28 (t, *J* = 7.2 Hz, 1.47H, CH_3), 3.22 (s, 1.45H, CH_3),

3.27 (s, 1.34H, CH_3), 3.72-3.78 (m, 1H, CH), 4.06-4.24 (m, 1H, CH), 5.87 (d, *J* = 8.0 Hz, 0.50H, Ar), 6.34 (s, 0.50H, =CH), 6.39 (s, 0.48H, =CH), 6.53 (s, 0.50H, =CH), 6.63 (s, 0.47H, =CH), 6.72-6.75 (m, 0.50H, Ar), 6.84 (d, *J* = 8.0 Hz, 0.50H, Ar), 6.95 (d, *J* = 8.0 Hz, 0.50H, Ar), 6.99-7.03 (m, 0.5H, Ar), 7.09-7.11 (m, 0.5H, Ar), 7.29-7.35 (m, 1H, Ar), 7.49-7.64 (m, 4H, Ar), 7.69-7.11 (m, 1H, Ar), 8.05-8.19 (m, 4H, Ar). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ. 13.7, 13.9, 26.68, 26.72, 61.4, 61.5, 64.3, 65.4, 87.5, 88.1, 94.0, 95.2, 108.3, 108.8, 114.17, 114.23, 122.26, 122.45, 122.6, 122.8, 125.4, 125.7, 126.3, 126.4, 127.2, 127.19, 127.31, 128.2, 128.6, 129.1, 129.2, 129.9, 130.1, 132.6, 132.7, 139.9, 140.1, 143.6, 144.1, 145.3, 145.9, 147.4, 147.5, 164.9, 165.4, 165.7, 165.9, 171.3, 173.6. IR (CH_2Cl_2) ν 730, 751, 832, 1032, 1171, 1253, 1371, 1509, 1593, 1615, 1709, 1725, 2343, 2925 cm^{-1}. MS (ESI) m/e 522.2 (M^++NH_4). HRMS (ESI) calcd. for $C_{30}H_{24}N_3O_6$: 522.1665, Found: 522.1654. Enantiomeric excess was determined by HPLC with a Chiralcel AD-H column [λ = 230 nm; eluent: Hexane/Isopropanol = 70/30; Flow rate: 0.70 mL/min; t_{major} = 13.14 min, t_{minor}= 21.17 min; ee% = 98%; $[\alpha]_D^{20}$ = -132.0 (c 2.00, CH_2Cl_2)].

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13.738
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NO2
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100
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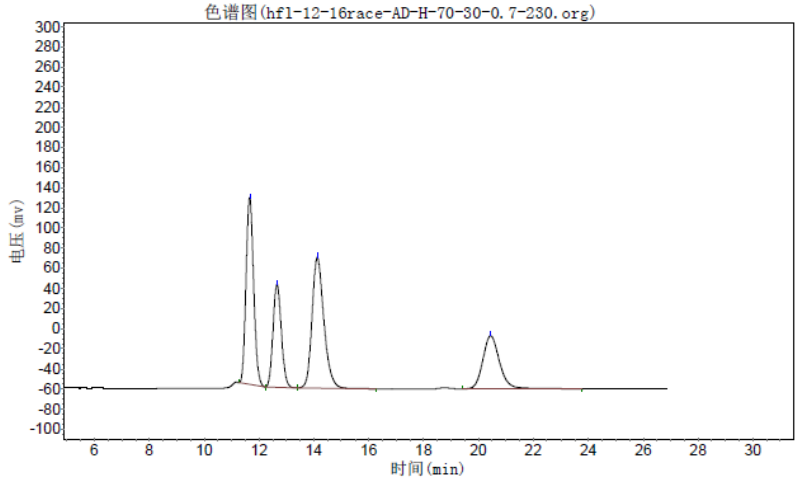
实验者：
报告时间：2014-04-04,7:57:29
积分方法:面积归一法

使用仪器类型:气相色谱　　检测器:FID　　进样器:分流

柱温:程序升温



分析结果表

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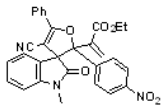
1		11.665	189587.984	3779123.500	30.9895
2		12.665	103662.688	2244303.000	18.4037
3		14.132	130428.445	3958148.500	32.4576
4		20.448	52557.215	2213269.500	18.1492
总计			476236.332	12194844.500	100.0000



AD-H, 230
Hexane:iPrOH = 70:30
0.7 mL/min

N2000 数据工作站 1

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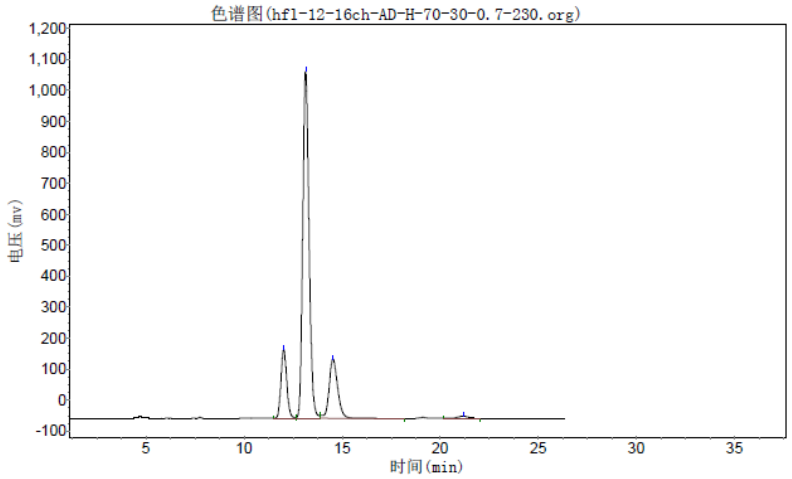
实验者:
报告时间：2014-04-04,7:58:57
积分方法:面积归一法

使用仪器类型:气相色谱　　检测器:FID　　进样器:分流

柱温:程序升温



分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
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2		13.142	1120231.250	24999124.000	70.0813
3		14.537	192057.234	5853081.500	16.4082
4		21.167	6722.053	261278.547	0.7325
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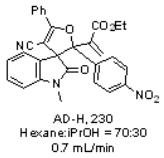
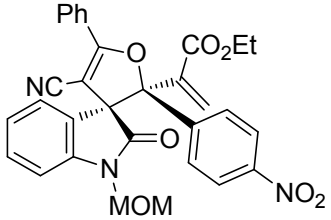
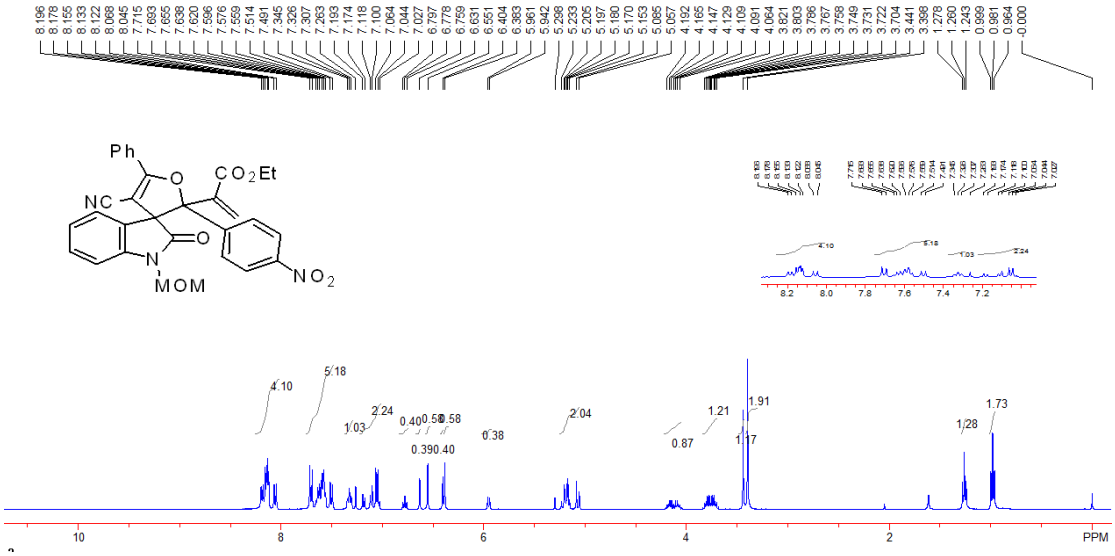


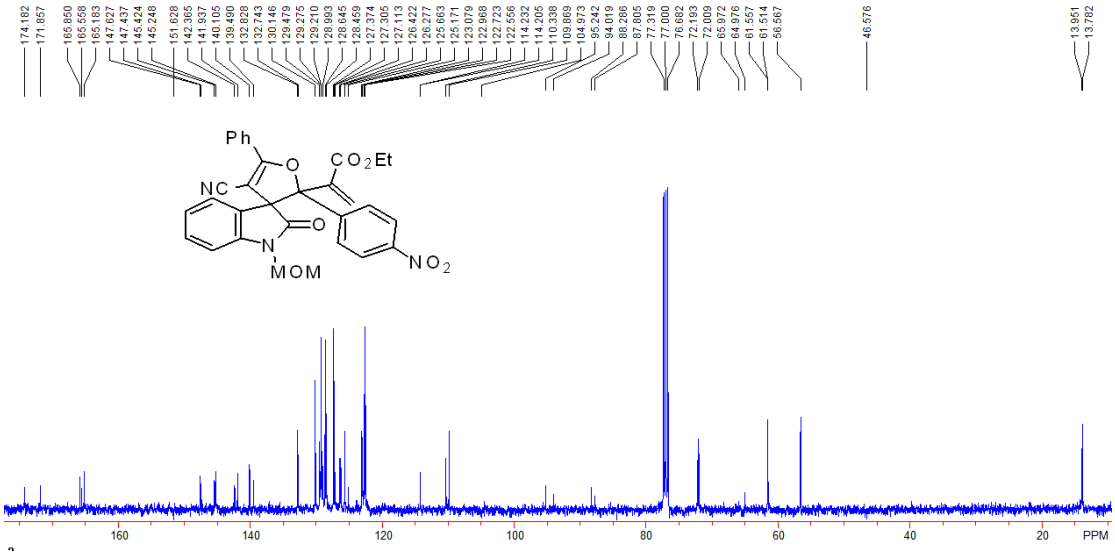
Translation: Enantiomeric excess was determined by HPLC with a Chiralcel AD-H column [λ = 230 nm; eluent: Hexane/Isopropanol = 60/40; Flow rate: 0.70 mL/min; t_{major} = 13.14 min, t_{minor}= 21.17 min; ee% = 98%.



Compound 3c: A white solid (51 mg, 92% yield), Mp: 100-103 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 0.98 (t, *J* = 7.2 Hz, 1.73H, CH_3), 1.26 (t, *J* = 7.2 Hz, 1.28H, CH_3), 3.40 (s, 1.91H, CH_3),

3.44 (s, 1.17H, CH_3), 3.70-3.82 (m, 1.21H, CH_2), 4.06-4.19 (m, 0.87H, CH_2), 5.06-5.23 (m, 2H, CH_2), 5.95 (d, J = 8.0 Hz, 0.38H, Ar), 6.38 (s, 0.58H, =CH), 6.40 (s, 0.40H, =CH), 6.55 (s, 0.58H, =CH), 6.63 (s, 0.39H, =CH), 6.76-6.80 (m, 0.4H, Ar), 7.03-7.19 (m, 2.24H, Ar), 7.31-7.35 (m, 1H, Ar), 7.49-7.72 (m, 5H, Ar), 8.05-8.20 (m, 4H, Ar). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ. 13.8, 14.0, 46.6, 56.5, 56.6, 61.5, 61.6, 65.0, 66.0, 72.0, 72.2, 87.8, 88.3, 94.0, 95.2, 105.0, 109.9, 110.3, 114.2, 122.6, 122.7, 123.0, 123.1, 125.2, 125.7, 126.3, 126.4, 127.1, 127.3, 127.4, 128.5, 128.6, 129.0, 129.2, 129.3, 129.5, 130.1, 132.7, 132.8, 139.5, 140.1, 141.9, 142.4, 145.2, 145.4, 147.4, 147.6, 151.6, 165.2, 165.6, 165.9, 171.9, 174.2. IR (CH_2Cl_2) ν 735, 750, 831, 1032, 1171, 1258, 1375, 1515, 1591, 1613, 1709, 1722, 2205, 29230 cm^{-1}. MS (ESI) m/e 569.2 (M^++NH_4). HRMS (ESI) calcd. for $C_{31}H_{29}N_4O_7$: 569.2036, Found: 569.2026. Enantiomeric excess was determined by HPLC with a Chiralcel AD-H column [λ = 230 nm; eluent: Hexane/Isopropanol = 70/30; Flow rate: 0.70 mL/min; t_{major} = 12.76 min, t_{minor}= 18.36 min; ee% = 98%; $[\alpha]_D^{20}$ = -93.3 (c 2.50, CH_2Cl_2)].





N2000 数据工作站

1

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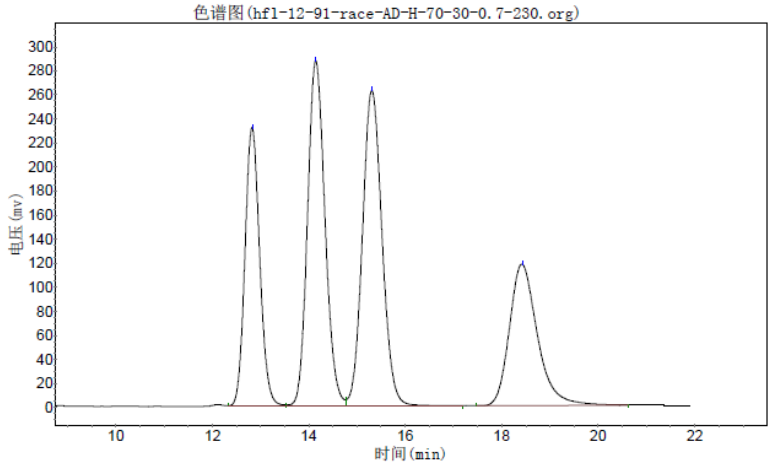
实验者：
报告时间：2014-04-03,21:34:15
积分方法:面积归一法

使用仪器类型:气相色谱　　检测器:FID　　进样器:分流

柱温:程序升温



分析结果表

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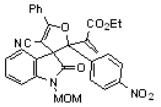
2		14.148	287394.125	7258004.500	29.7230
3		15.315	262253.156	7407689.500	30.3360
4		18.448	117634.641	4816752.000	19.7256
总计			899181.781	24418839.000	100.0000



AD-H, 230 nm
hexane/PrOH = 70:30
0.7 mL/min

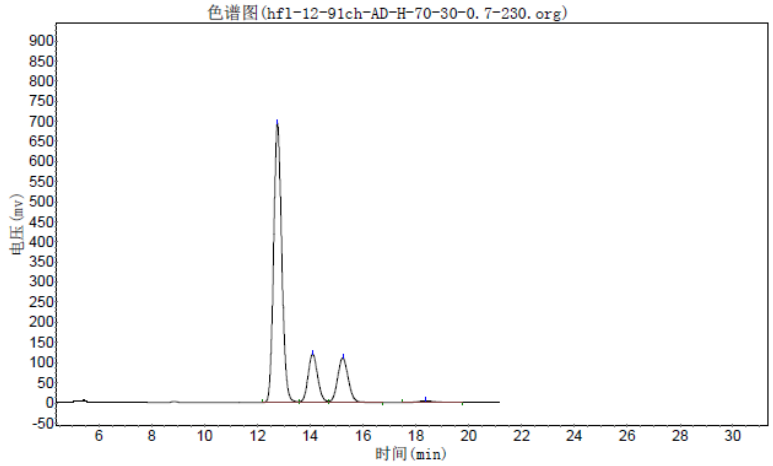
N2000 数据工作站 1

实验时间：2013-12-14,16:45:13
谱图文件:D:\4+1\底物拓展\hf1-12-91ch-AD-H-70-30-0.7-230.org
实验者：
报告时间：2014-04-03,21:35:30
积分方法:面积归一法

使用仪器类型:气相色谱　　检测器:FID　　进样器:分流

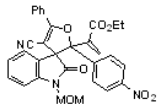
柱温:程序升温

色谱图(hf1-12-91ch-AD-H-70-30-0.7-230.org)



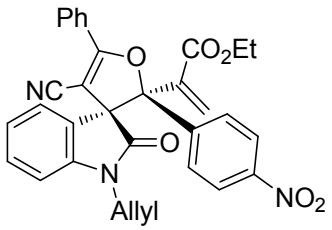
分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		12.757	694426.375	14760926.000	70.1403
2		14.090	120441.539	3043118.250	14.4602
3		15.230	110511.992	3075554.000	14.6143
4		18.363	3952.599	165251.891	0.7852
总计			929332.505	21044850.141	100.0000



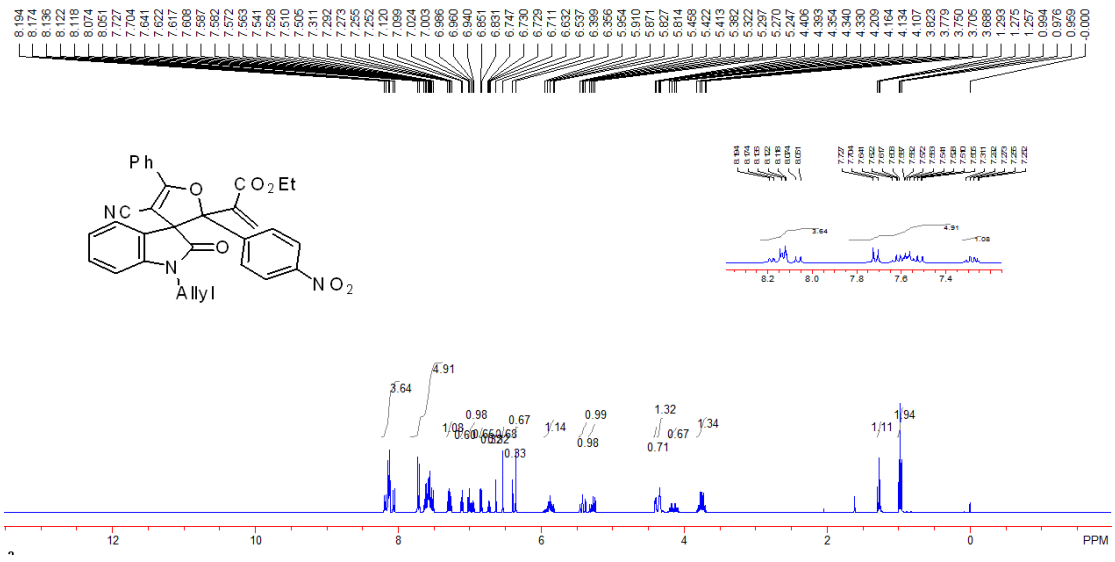
AD-H, 230 nm
hexane/^{i}PrOH = 70:30
0.7 mL/min

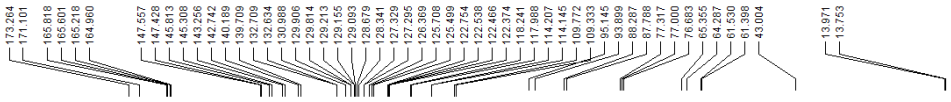
Translation: Enantiomeric excess was determined by HPLC with a Chiralcel AD-H column [λ = 230 nm; eluent: Hexane/Isopropanol = 60/40; Flow rate: 0.70 mL/min; t_{major} = 12.76 min, t_{minor}= 18.36 min; ee% = 98%.

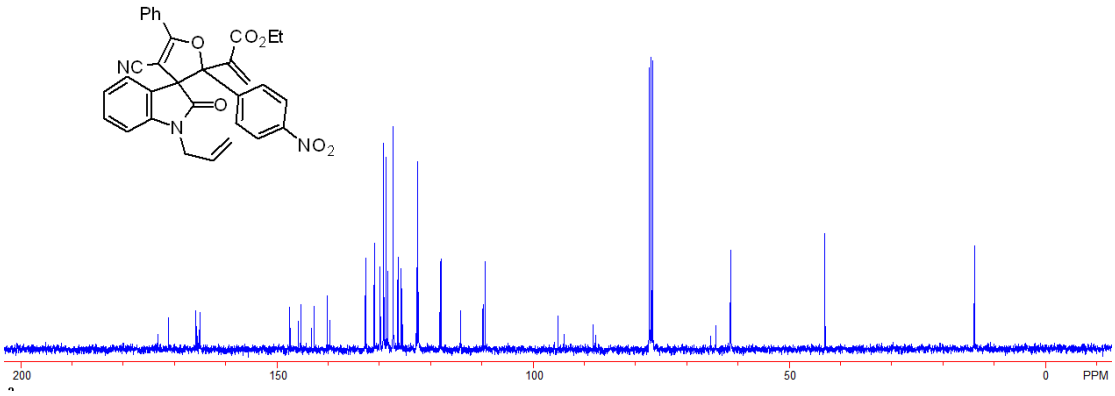


Compound 3d: A white solid (54 mg, 99% yield), Mp: 90-93 °C. ^{1}H NMR ($CDCl_3$, 400 MHz,

TMS) δ 0.98 (t, J = 7.2 Hz, 1.94H, CH_3), 1.28 (t, J = 7.2 Hz, 1.11H, CH_3), 3.69-3.82 (m, 1.34H, CH_2), 4.11-4.21 (m, 0.67H, CH_2), 4.33-4.35(m, 1.32H, CH_2), 4.39-4.41 (m, 0.71H, CH_2), 5.25-5.32 (m, 1H, =CH), 5.38-5.46 (m, 1H, =CH), 5.81-5.95 (m, 1H, =CH), 6.36 (s, 0.67H, =CH), 6.40 (s, 0.33H, =CH), 6.54 (s, 0.68H, =CH), 6.63 (s, 0.32H, =CH), 6.67-6.75 (m, 1H, Ar), 6.84 (d, J = 8.0 Hz, 0.65H, Ar), 6.94-7.02 (m, 1H, Ar), 7.11 (d, J = 8.0 Hz, 0.60H, Ar), 7.25-7.31 (m, 1H, Ar), 7.51-7.73 (m, 4.91H, Ar), 8.05-8.19 (m, 4H, Ar). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 13.8, 14.0, 443.0, 61.4, 61.5, 64.3, 65.4, 87.8, 88.3, 93.9, 95.1, 109.3, 109.8, 114.1, 114.2, 118.0, 118.2, 122.4, 122.47, 122.54, 122.8, 125.5, 125.7, 126.4, 127.29, 127.33, 128.3, 128.7, 129.1, 129.16, 129.21, 129.8, 129.9, 131.0, 132.6, 132.7, 139.7, 140.2, 142.7, 143.3, 145.3, 145.8, 147.4, 147.6, 165.0, 165.2, 165.6, 165.8, 171.1, 173.3. IR (CH_2Cl_2) ν 689, 734, 754, 853, 1022, 1178, 1209, 1349, 1467, 1487, 1520, 1608, 1716, 2201, 2919 cm^{-1}. MS (ESI) m/e 548.2 (M^++H). HRMS (ESI) calcd. for $C_{32}H_{26}N_3O_6$: 548.1822, Found: 548.1816. Enantiomeric excess was determined by HPLC with a Chiralcel AD-H column [λ = 230 nm; eluent: Hexane/Isopropanol = 70/30; Flow rate: 0.70 mL/min; t_{major} = 16.34 min, t_{minor}= 23.63 min; ee% = 98%; $[\alpha]_D^{20}$ = -111.5 (c 2.80, CH_2Cl_2)].







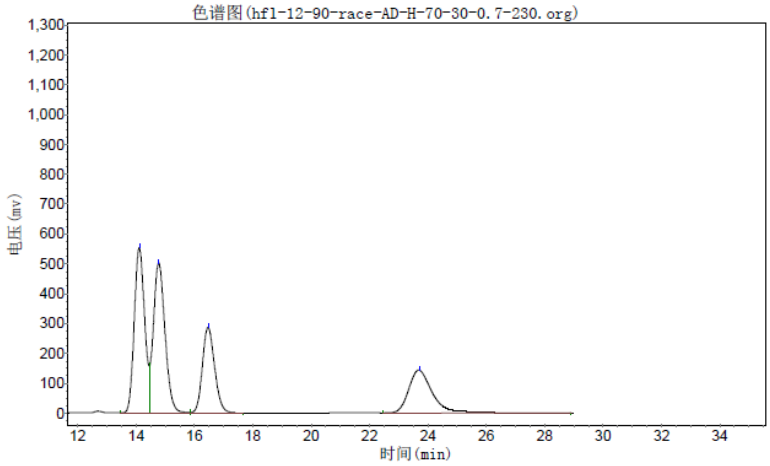
N2000 数据工作站 1

实验时间：2013-12-14,15:19:45
谱图文件:D:\4+1\底物拓展\hfl-12-90-race-AD-H-70-30-0.7-230.org

实验者：
报告时间：2014-04-03,21:36:18
积分方法:面积归一法

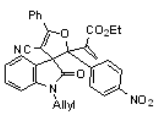
使用仪器类型:气相色谱　　检测器:FID　　进样器:分流

柱温:程序升温



分析结果表

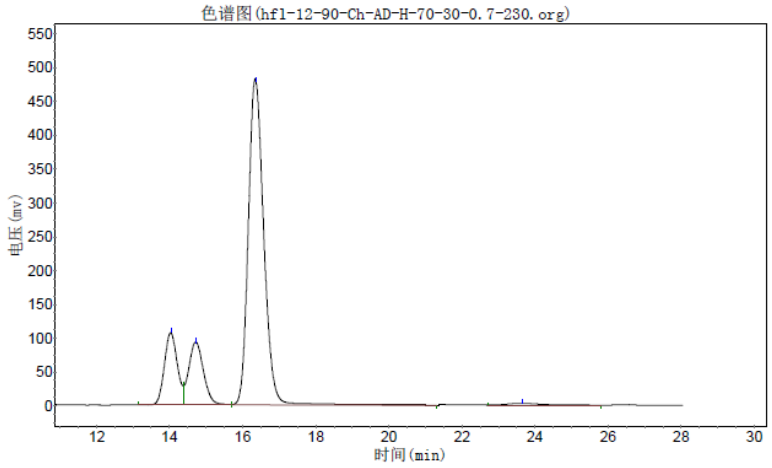
峰号	峰名	保留时间	峰高	峰面积	含量
1		14.115	552711.500	13811063.000	31.1681
2		14.782	502694.969	13979674.000	31.5486
3		16.465	286818.469	8385018.500	18.9229
4		23.698	143190.859	8135844.500	18.3605
总计			1485415.797	44311600.000	100.0000



AD-H, 230 nm
hexane/PrOH = 70:30
0.7 mL/min

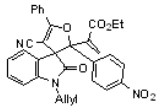
使用仪器类型:气相色谱　　检测器:FID　　进样器:分流

柱温:程序升温



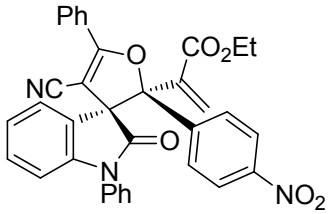
分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		14.032	106685.313	2675350.000	13.5908
2		14.732	93255.383	2613029.250	13.2742
3		16.365	481566.219	14221724.000	72.2466
4		23.665	2765.069	174865.219	0.8883
总计			684271.983	19684968.469	100.0000



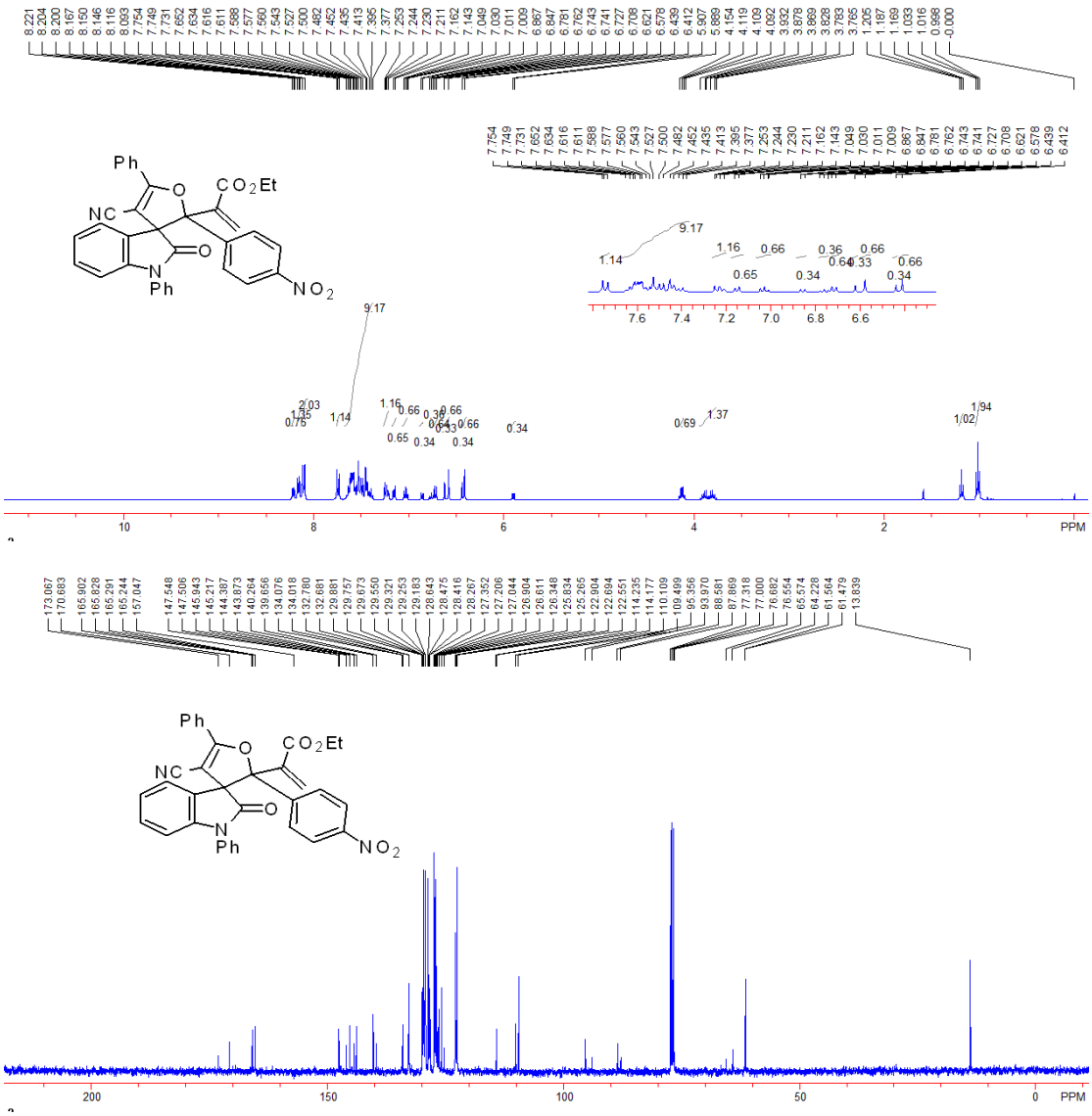
AD-H, 230 nm
hexane/PrOH = 70:30
0.7 mL/min

Translation: Enantiomeric excess was determined by HPLC with a Chiralcel AD-H column [λ = 230 nm; eluent: Hexane/Isopropanol = 60/40; Flow rate: 0.70 mL/min; t_{major} = 16.34 min, t_{minor}= 23.63 min; ee% = 98%.



Compound 3e: A white solid (52 mg, 90% yield), Mp: 80-83 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.02 (t, *J* = 7.2 Hz, 1.94H, CH_3), 1.19 (t, *J* = 7.2 Hz, 1.02H, CH_3), 3.77-3.93 (m, 1.37H, CH_2), 4.09-4.15 (m, 0.69H, CH_2), 5.90 (d, *J* = 7.2 Hz, 0.34H, Ar), 6.41 (s, 0.66H, =CH), 6.44 (s, 0.34H, =CH), 6.58 (s, 0.66H, =CH), 6.62 (s, 0.33H, =CH), 6.72 (d, *J* = 8.0 Hz, 0.64H, Ar), 6.74-

6.78 (m, 0.36H, Ar), 6.86 (d, J = 8.0 Hz, 0.34H, Ar), 7.01-7.05 (m, 0.66H, Ar), 7.15 (d, J = 8.0 Hz, 0.65H, Ar), 7.21-7.25 (m, 1H, Ar), 7.38-7.65 (m, 9H, Ar), 7.73-7.75 (m, 2H, Ar), 8.09-8.22 (m, 4H, Ar). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ. 13.8, 61.5, 61.6, 64.4, 65.6, 87.9, 88.6, 94.0, 95.4, 109.5, 110.1, 114.17, 114.23, 122.6. 122.7, 122.9, 125.3, 125.8, 126.3, 126.6, 126.9, 127.0, 127.2, 127.4, 128.3, 128.4, 128.5, 128.6, 129.2, 129.25, 129.32, 129.6, 129.7, 129.8, 129.9, 132.7, 132.8, 134.0, 134.1, 139.7, 140.3, 143.9, 144.4, 145.2, 145.9, 147.51, 147.55, 157.0, 165.2, 165.3, 165.8, 165.9. IR (CH_2Cl_2) ν 691, 700, 753, 854, 1026, 1177, 1198, 1298, 1324, 1348, 1497, 1521, 1608, 1724, 2211, 2983 cm^{-1}. MS (ESI) m/e 584.2 (M^++1). HRMS (ESI) calcd. for $C_{35}H_{26}N_3O_6$: 584.1822, Found: 584.1808. Enantiomeric excess was determined by HPLC with a Chiralcel IC column [λ = 214 nm; eluent: Hexane/Isopropanol = 70/30; Flow rate: 0.50 mL/min; t_{major} = 53.63 min, t_{minor}= 62.79 min; ee% = 97%; $[\alpha]_D^{20}$ = -178.0 (c 2.20, CH_2Cl_2)].



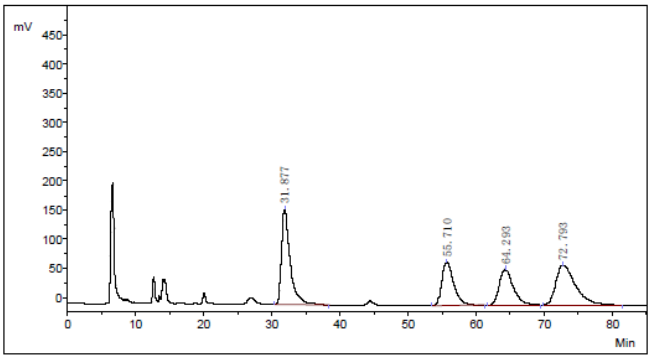
HPLC REPORT

Sample Name:hfl-13-31-rac-ic-7-3-0.5-214...che Date:2014-01-15

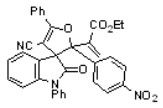
Time:12:23 Method:

Column: Flow Rate:

Wave Length: Mobile Phase:



No.	PeakNo	ID.Name	R.Time	PeakHeight	PeakArea	PerCent
1	1	Unknown	31.877	164082.5	14562189.5	31.7634
2	2	Unknown	55.710	74413.2	8969912.2	19.5654
3	3	Unknown	64.293	61785.7	8799123.8	19.1928
4	4	Unknown	72.793	68031.5	13514642.7	29.4784
Total				368312.8	45845868.2	100.0000



IC, 214 nm
Hexane:PrOH = 70:30
0.5 mL/min

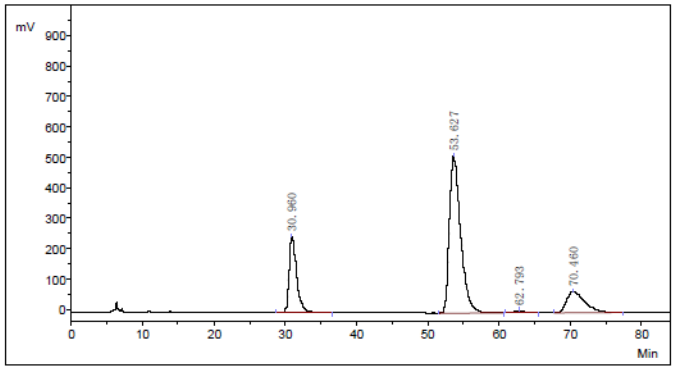
HPLC REPORT

Sample Name:hfl-13-31-chiral...che | Date:2014-01-15

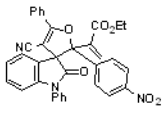
Time:13:48 | Method:

Column: | Flow Rate:

Wave Length: | Mobile Phase:

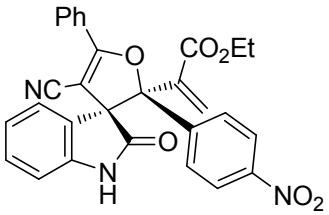


No.	PeakNo	ID. Name	R. Time	PeakHeight	PeakArea	PerCent
1	1	Unknown	30.960	248136.9	18562762.7	20.8442
2	2	Unknown	53.627	516766.5	57317027.4	64.3616
3	3	Unknown	62.793	6677.8	815620.6	0.9159
4	4	Unknown	70.460	68888.4	12359306.7	13.8783
Total				840469.4	89054717.4	100.0000



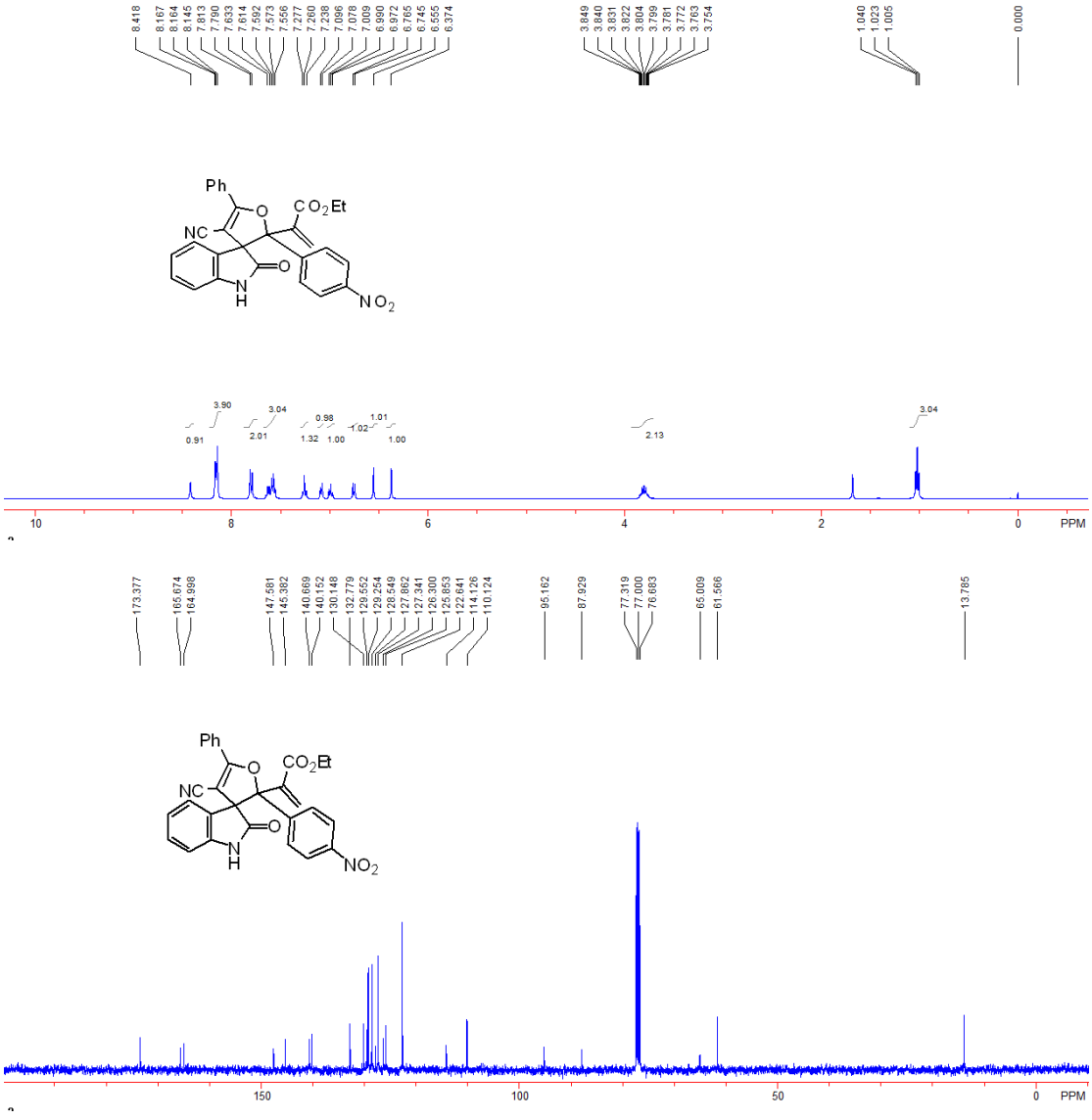
IC, 214 nm
Hexane:PrOH = 70:30
0.5 mL/min

Translation: Enantiomeric excess was determined by HPLC with a Chiralcel IC-H column [λ = 214 nm; eluent: Hexane/Isopropanol = 70/30; Flow rate: 0.50 mL/min; t_{major} = 53.63 min, t_{minor}= 62.79 min; ee% = 97%.



Compound 3f: A white solid (33 mg, 65% yield), Mp: 251-252 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.02 (t, *J* = 7.2 Hz, 3H, CH_3), 3.75-3.85 (m, 2H, CH_2), 6.37 (s, 1H, =CH), 6.56 (s, 1H, =CH), 6.76 (d, *J* = 8.0 Hz, 1H, Ar), 6.99 (t, *J* = 7.6 Hz, 1H, Ar), 7.09 (d, *J* = 7.2 Hz, 1H, Ar),

7.24-7.28 (m, 1H, Ar), 7.56-7.63 (m, 3H, Ar), 7.80 (d, J = 8.8 Hz, 2H, Ar), 8.15-8.17 (m, 4H, Ar), 8.42 (s, 1H, NH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 13.8, 61.6, 65.0, 87.9, 95.2, 110.1, 114.1, 122.6, 125.9, 126.3, 127.3, 127.9, 128.5, 129.3, 129.6, 130.1, 132.8, 140.2, 140.7, 145.4, 147.6, 165.0, 165.7, 173.4. IR (CH_2Cl_2) ν 688, 737, 799, 1016, 1097, 1178, 1260, 1348, 1473, 1521, 1618, 1713, 2209, 2293, 3311 cm^{-1}. MS (ESI) m/e 525.2 (M^++NH_4). HRMS (ESI) calcd. for $C_{29}H_{25}N_4O_6$: 525.1774, Found: 525.1765. Enantiomeric excess was determined by HPLC with a Chiralcel AD-H column [λ = 230 nm; eluent: Hexane/Isopropanol = 60/40; Flow rate: 0.70 mL/min; t_{major} = 80.08 min, t_{minor}= 13.40 min; ee% = 95%; $[\alpha]_D^{20}$ = -200.8 (c 1.50, CH_2Cl_2)].

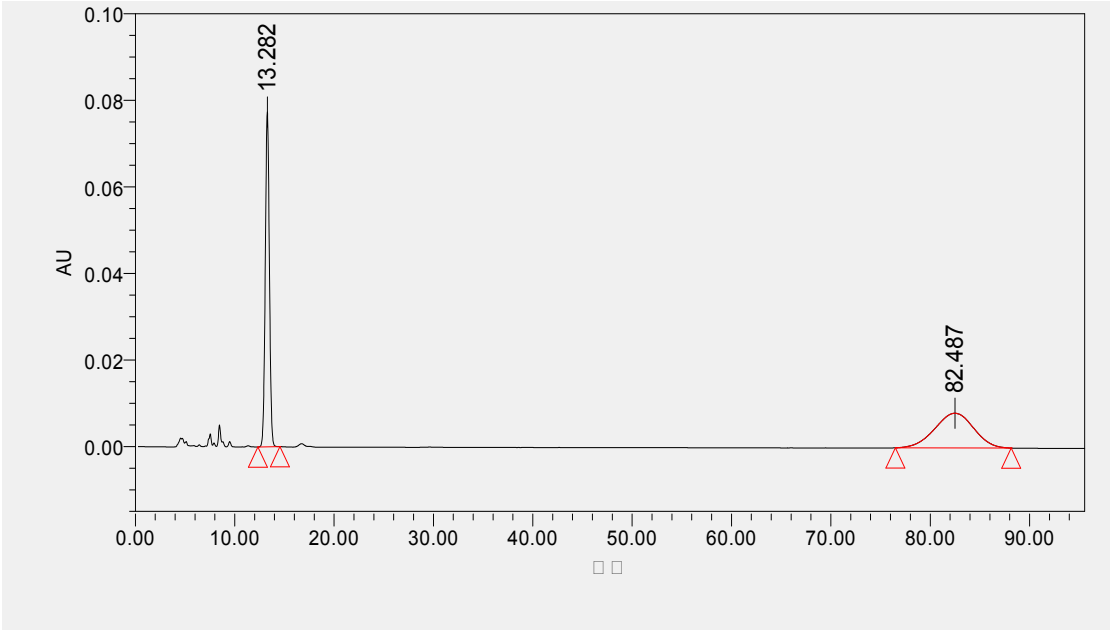


HPLC REPORT

Sample Name: hfl-13-21Race Date:####

Column: AD-H Mobile Phase:hex/ipr=60/40

Velocity(ml/min): 0.7 Detection Wavelength(nm):230



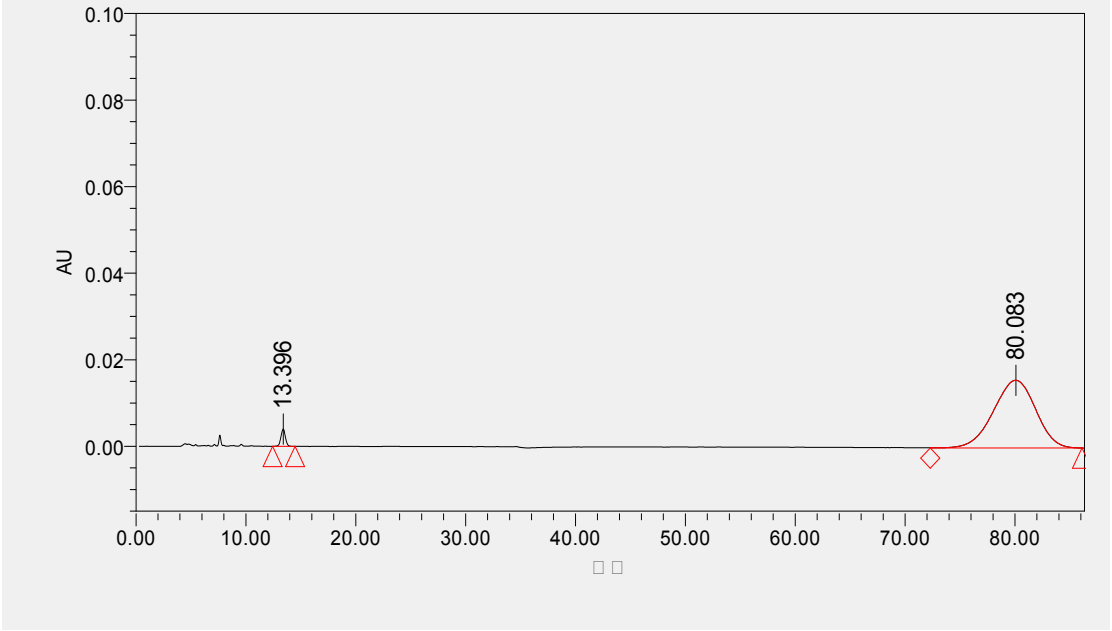
NO	R. Time	Peak Area	Percent	Peak Height
1	13.282	2231437	50.43	77421
2	82.487	2192993	49.57	8029

HPLC REPORT

Sample Name: hfl-13-21CH Date:####

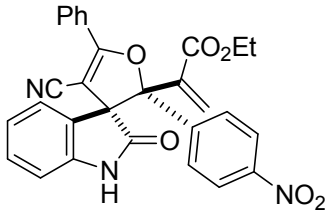
Column: AD-H Mobile Phase:hex/ipr=60/40

Velocity(ml/min): 0.7 Detection Wavelength(nm):230

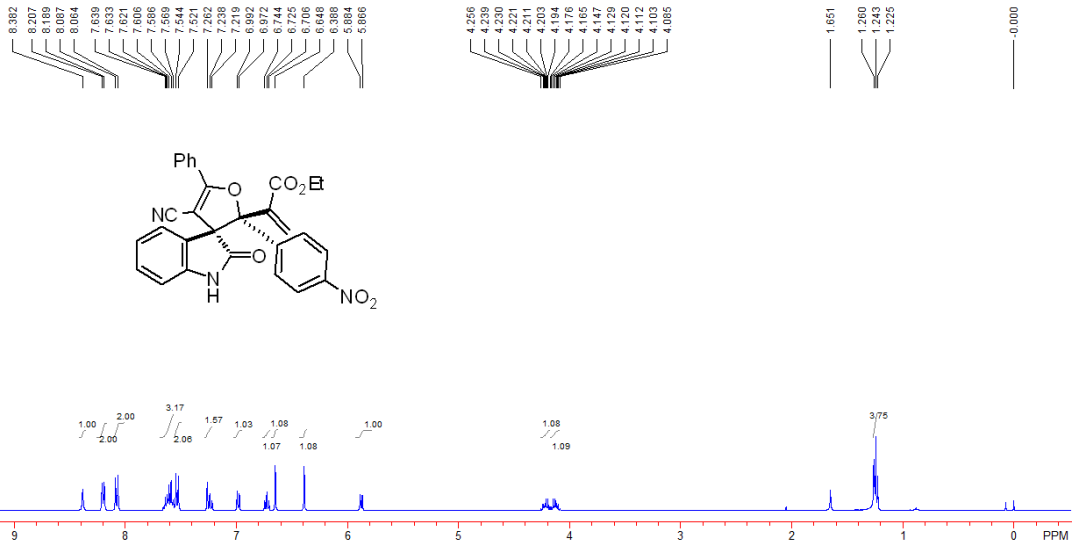


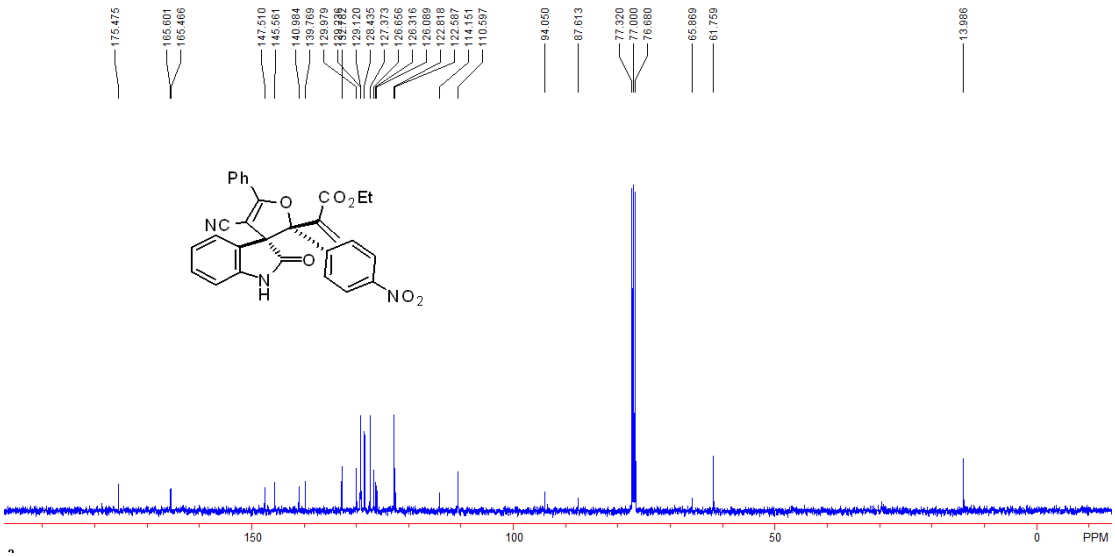
NO	R. Time	Peak Area	Percent	Peak Height
1	13.396	113437	2.64	3973

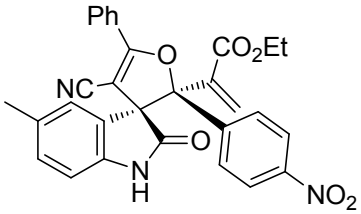
2	80.083	4179670	97.36	15649



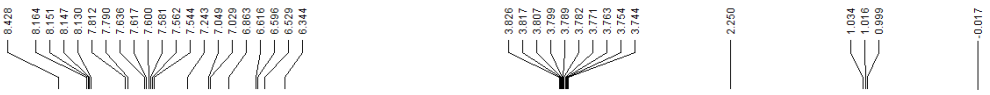
Compound 3f': A white solid (11 mg, 22% yield), Mp: 217-218 ^{o}C. ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.24 (t, *J* = 7.2 Hz, 3H, CH_3), 4.09-4.17 (m, 1H, CH_2), 4.18-4.26 (m, 1H, CH_2), 5.85 (d, *J* = 7.2 Hz, 1H, Ar), 6.39 (s, 1H, =CH), 6.65 (s, 1H, =CH), 6.73 (t, *J* = 7.6 Hz, 1H, Ar), 6.98 (d, *J* = 8.0 Hz, 1H, Ar), 7.22-7.25 (m, 1H, Ar), 7.52-7.64 (m, 5H, Ar), 8.08 (d, *J* = 8.8 Hz, 2H, Ar), 8.20 (d, *J* = 7.2 Hz, 2H, Ar), 8.38 (s, 1H, NH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 14.0, 61.8, 65.9, 87.6, 94.1, 110.6, 114.2, 122.6, 122.8, 126.1, 126.3, 126.7, 127.4, 128.4, 129.1, 129.2, 130.0, 132.8, 139.8, 141.0, 145.6, 147.5, 165.5, 165.6, 175.5. IR (CH_2Cl_2) ν 688, 753, 1186, 1324, 1349, 1472, 1523,1618, 1721, 2206, 2913, 3263 cm^{-1}. MS (ESI) m/e 508.2 (M^{+}+1). HRMS (ESI) calcd. for $C_{29}H_{22}N_3O_6$: 508.1509, Found:508.1504. $[\alpha]_D^{20}$ = -6.7 (c 0.45, CH_2Cl_2)].

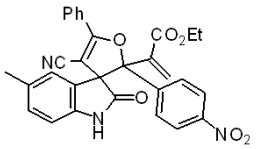


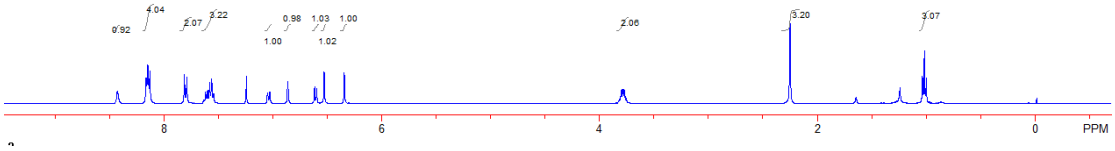


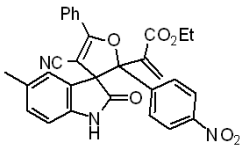


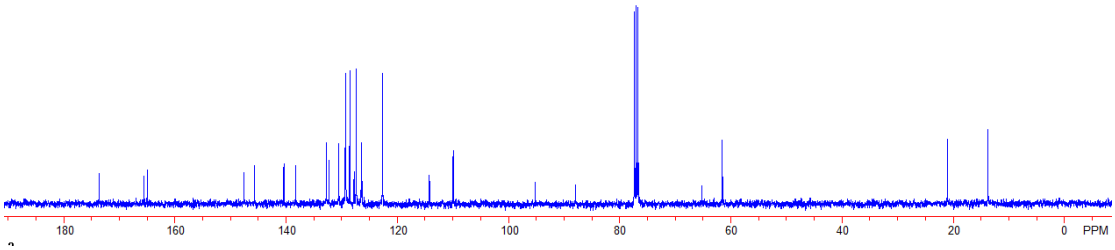
Compound 3g: A white solid (32 mg, 61% yield), Mp: 104-105 ^{o}C. ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.03 (t, *J* = 7.2 Hz, 3H, CH_3), 2.27 (s, 3H, CH_3), 3.76-3.84 (m, 2H, CH_2), 6.36 (s, 1H, =CH), 6.55 (s, 1H, =CH), 6.62 (d, *J* = 8.0 Hz, 1H, Ar), 6.88 (s, 1H, Ar), 7.06 (d, *J* = 8.0 Hz, 1H, Ar), 7.56-7.65 (m, 3H, Ar), 7.82 (d, *J* = 8.8 Hz, 2H, Ar), 8.15-8.18 (m, 4H, Ar), 8.45 (s, 1H, NH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 13.8, 21.0, 61.5, 65.2, 88.0, 95.2, 110.0, 114.2, 122.6, 126.4, 126.5, 127.4, 127.8, 128.5, 129.2, 129.4, 130.5, 132.3, 132.8, 138.3, 140.4, 145.6, 147.5, 165.0, 165.5, 173.6. IR (CH_2Cl_2) ν 692, 853, 1026, 1178, 1349, 1495, 1522, 1625, 1719, 2216, 2926, 3319 cm^{-1}. MS (ESI) m/e 522.2 (M^{+}+1). HRMS (ESI) calcd. for $C_{30}H_{24}N_3O_6$: 522.1665, Found: 522.1654. Enantiomeric excess was determined by HPLC with a Chiralcel AD-H column [λ = 230 nm; eluent: Hexane/Isopropanol = 60/40; Flow rate: 0.70 mL/min; t_{major} = 47.61 min, t_{minor}= 11.67 min; ee% = 95%; $[\alpha]_D^{20}$ = -211.7 (c 1.50, CH_2Cl_2)].









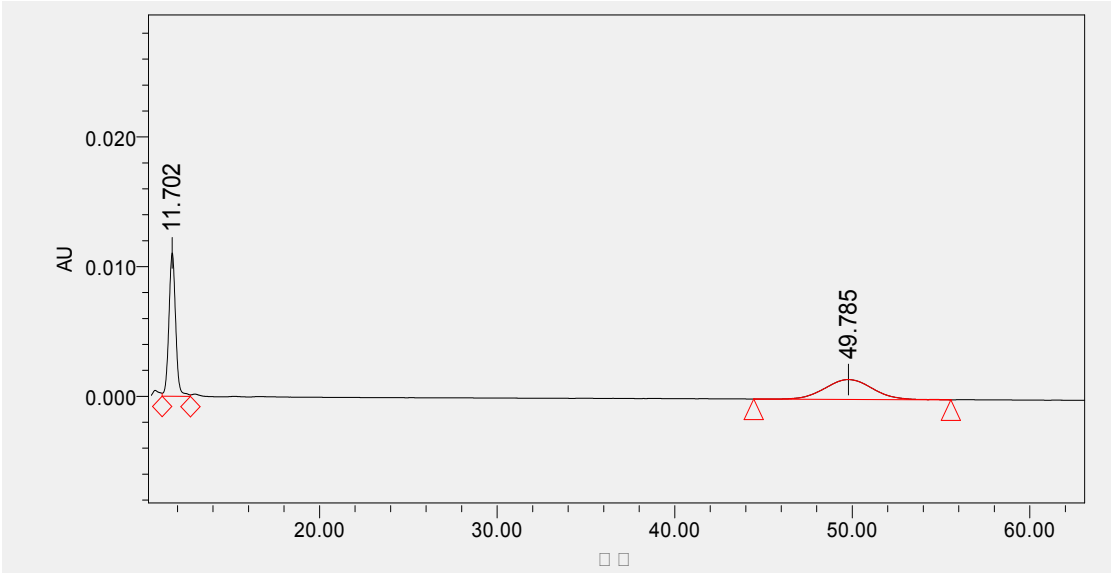


HPLC REPORT

Sample Name: hfl-13-27Race Date:####

Column: AD-H Mobile Phase:hex/ipr=60/40

Velocity(ml/min): 0.7 Detection Wavelength(nm):230



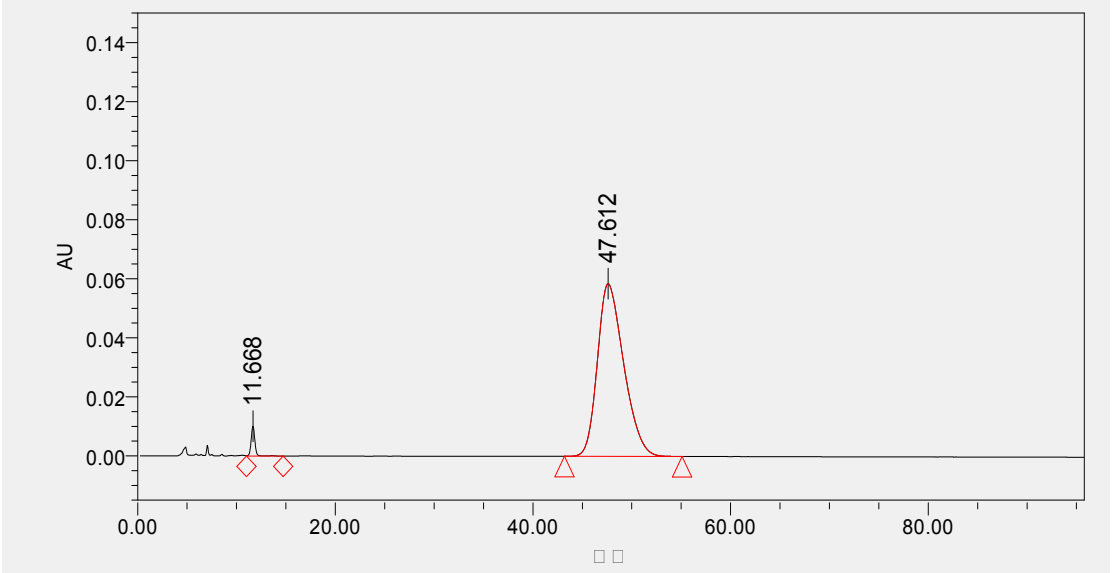
NO	R. Time	Peak Area	Percent	Peak Height
1	11.702	292128	50.60	11059
2	49.785	285189	49.40	1531

HPLC REPORT

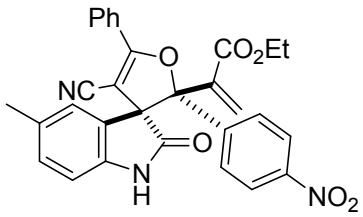
Sample Name: hfl-13-27CH Date:#####

Column: AD-H Mobile Phase:hex/ipr=60/40

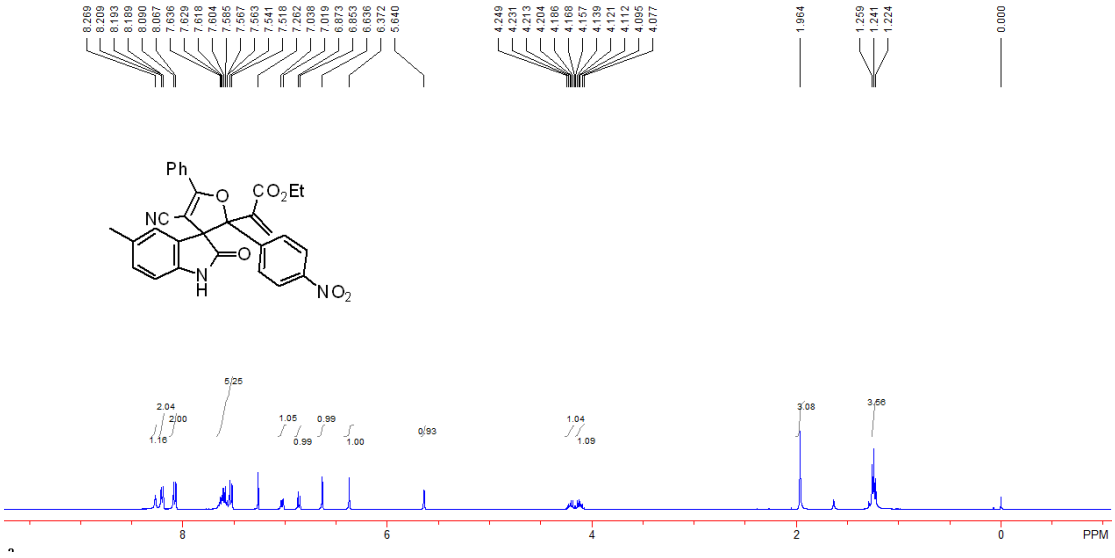
Velocity(ml/min): 0.7 Detection Wavelength(nm):230

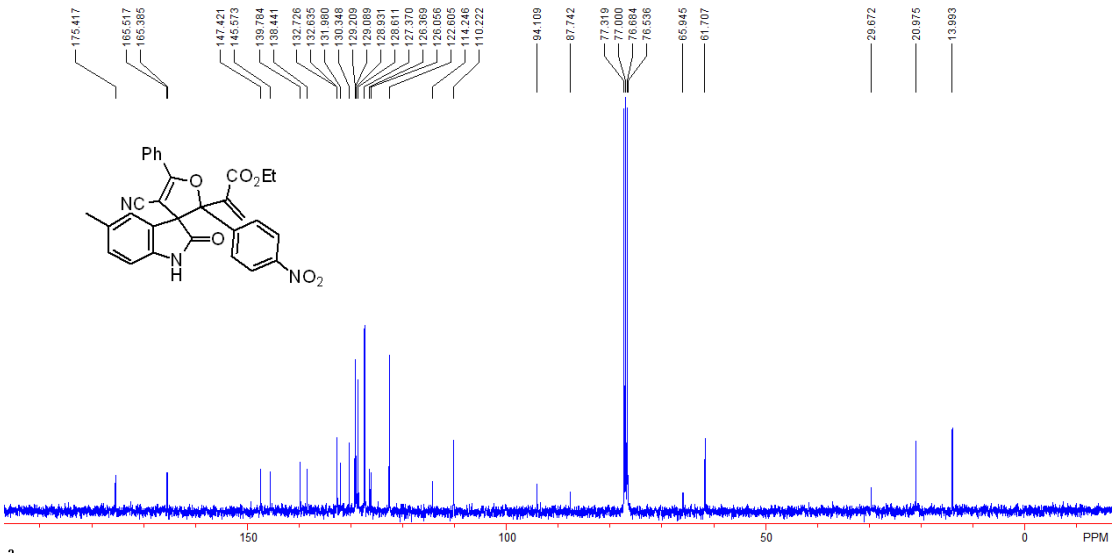


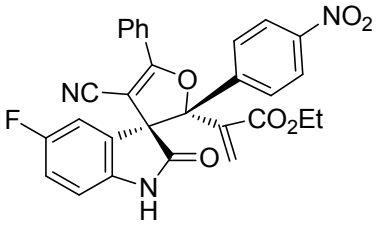
NO	R. Time	Peak Area	Percent	Peak Height
1	11.668	272728	2.46	10105
2	47.612	10818442	97.54	58496



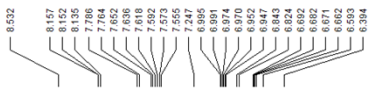
Compound 3g': A white solid (11 mg, 20% yield), Mp: 124-125 ^{o}C. ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.24 (t, *J* = 7.2 Hz, 3H, CH_3), 1.96 (s, 3H, CH_3), 4.08-4.16 (m, 1H, CH_2), 4.17-4.25 (m, 1H, CH_2), 5.64 (s, 1H, Ar), 6.37 (s, 1H, =CH), 6.64 (s, 1H, =CH), 6.50 (d, *J* = 8.0 Hz, 1H, Ar), 7.03 (d, *J* = 8.0 Hz, 1H, Ar), 7.52-7.64 (m, 5H, Ar), 8.08 (d, *J* = 8.8 Hz, 2H, Ar), 8.19-8.21 (m, 2H, Ar), 8.27 (s, 1H, NH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 14.0, 21.0, 61.7, 66.0, 87.7, 94.1, 110.2, 114.2, 122.6, 126.1, 126.4, 127.4, 128.6, 128.9, 129.2, 130.3, 132.0, 132.7, 138.4, 139.8, 145.6, 147.4, 165.4, 165.5, 175.4. IR (CH_2Cl_2) ν 697, 853, 1040, 1181, 1349, 1493, 1522, 1625, 1720, 2210, 2919, 3279 cm^{-1}. MS (ESI) m/e 522.2 (M^{+}+1). HRMS (ESI) calcd. for $C_{30}H_{24}N_3O_6$: 522.1665, Found: 522.1655. [α] $_D^{20}$ = -7.9 (c 0.65, CH_2Cl_2)].

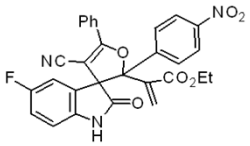


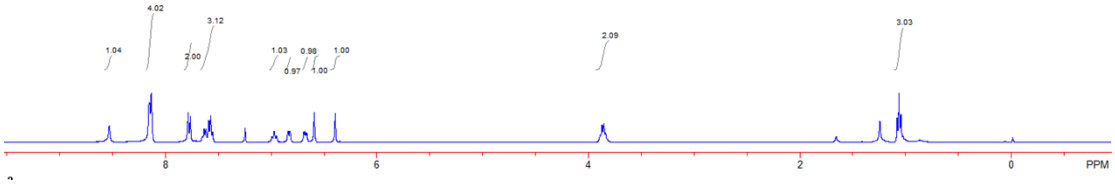


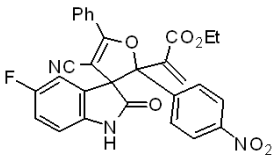


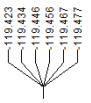
Compound 3h: A white solid (30 mg, 58% yield), Mp: 235-236 ^{o}C. ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.06 (t, *J* = 7.2 Hz, 3H, CH_3), 3.84-3.89 (m, 2H, CH_2), 6.39 (s, 1H, =CH), 6.59 (s, 1H, =CH), 6.68 (dd, *J* = 8.0 Hz, *J* = 4.0 Hz, 1H, Ar), 6.83 (d, *J* = 8.0 Hz, 1H, Ar), 6.95-7.00 (m, 1H, Ar), 7.56-7.65 (m, 3H, Ar), 7.78 (d, *J* = 8.8 Hz, 2H, Ar), 8.14-8.16 (m, 4H, Ar), 8.53 (s, 1H, NH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 13.8, 61.8, 65.4, 87.5, 95.1, 110.9 (*J* = 7.7 Hz), 113.6 (*J* = 25.4 Hz), 113.9, 116.7 (*J* = 23.4 Hz), 122.7, 126.0, 127.4, 128.5, 129.3, 130.0, 133.0, 136.7, 139.7, 145.0, 147.7, 158.8 (*J* = 240.8 Hz), 173.5. ^{19}F NMR ($CDCl_3$, 376 MHz, $CFCl_3$) δ -119.48--119.42 (m) IR (CH_2Cl_2) ν 691, 736, 853, 1026, 1182, 1348, 1487, 1521, 1631, 1713, 2215, 2927, 3304 cm^{-1}. MS (ESI) m/e 543.2 (M^++NH_4). HRMS (ESI) calcd. for $C_{29}H_{24}FN_4O_6$: 543.1680, Found: 543.1674. Enantiomeric excess was determined by HPLC with a Chiralcel AD-H column [λ = 230 nm; eluent: Hexane/Isopropanol = 60/40; Flow rate: 0.70 mL/min; t_{major} = 23.62 min, t_{minor}= 12.07 min; ee% = 90%; $[\alpha]_D^{20}$ = -61.8 (c 0.50, CH_2Cl_2)].

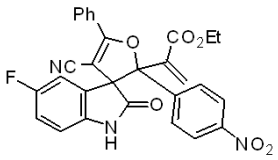


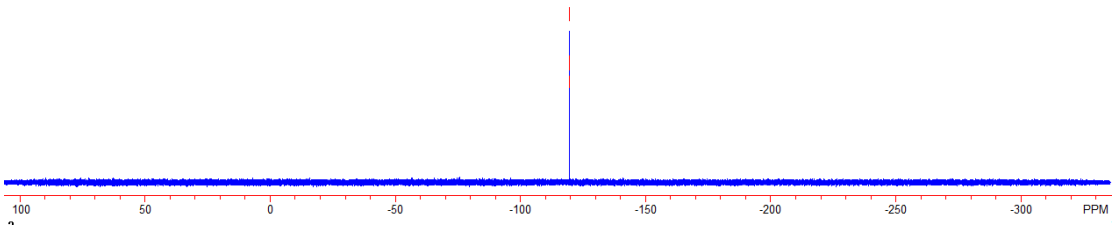










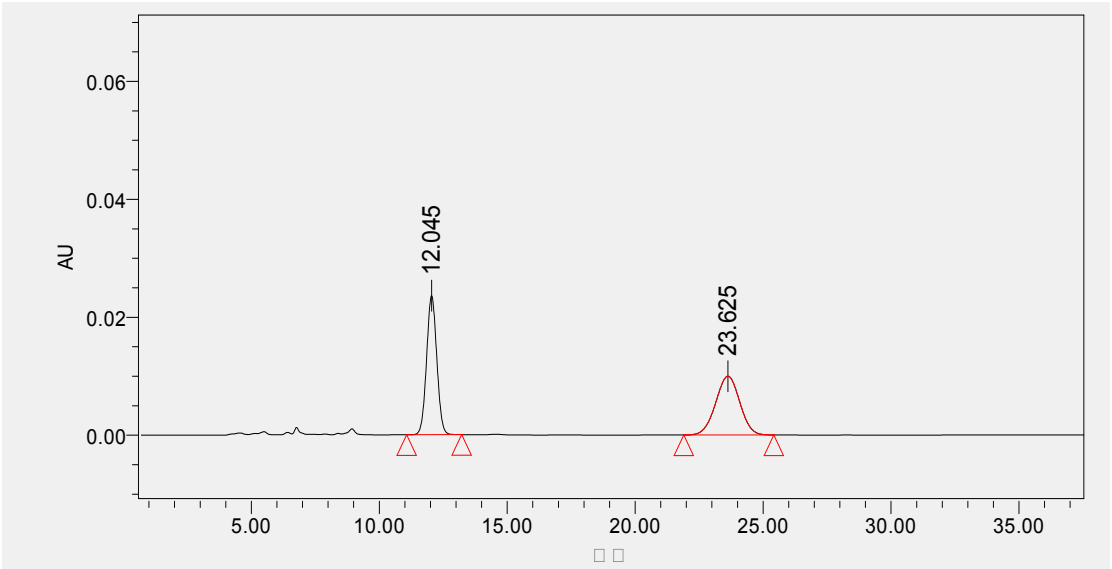


HPLC REPORT

Sample Name: hfl-13-34Race Date:####

Column: AD-H Mobile Phase:hex/ipr=60/40

Velocity(ml/min): 0.7 Detection Wavelength(nm):230



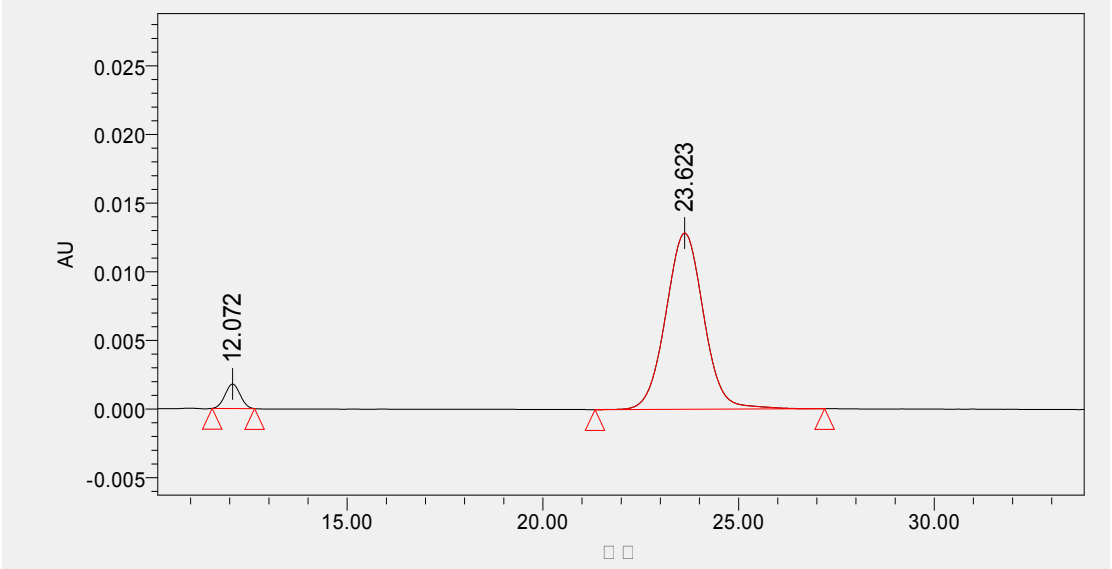
NO	R. Time	Peak Area	Percent	Peak Height
1	12.045	656238	50.19	23584
2	23.625	651171	49.81	9963

HPLC REPORT

Sample Name: hfl-13-34CH Date:####

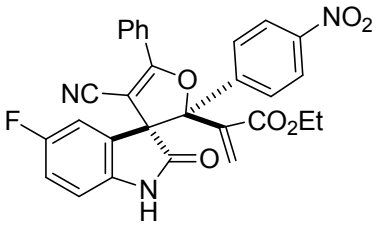
Column: AD-H Mobile Phase:hex/ipr=60/40

Velocity(ml/min): 0.7 Detection Wavelength(nm):230

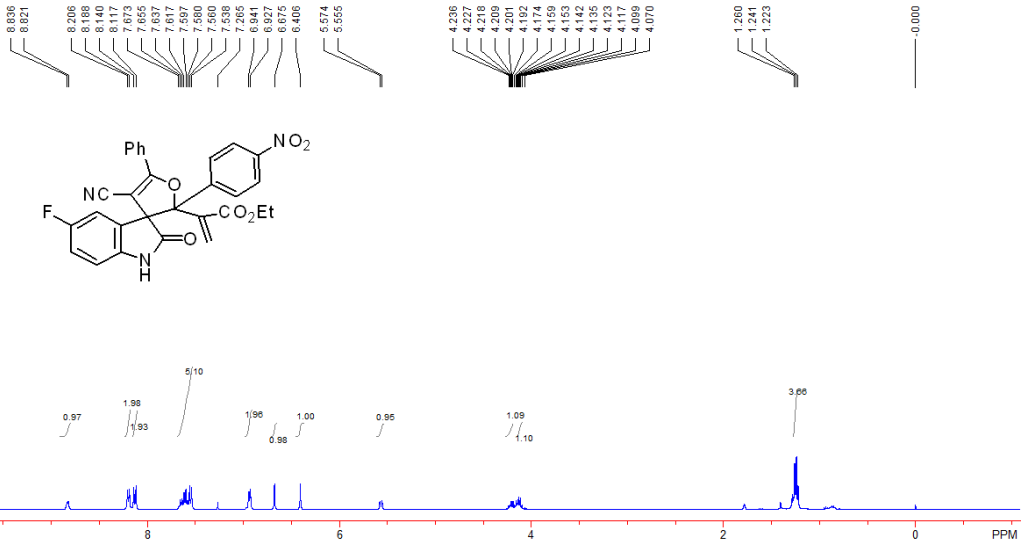


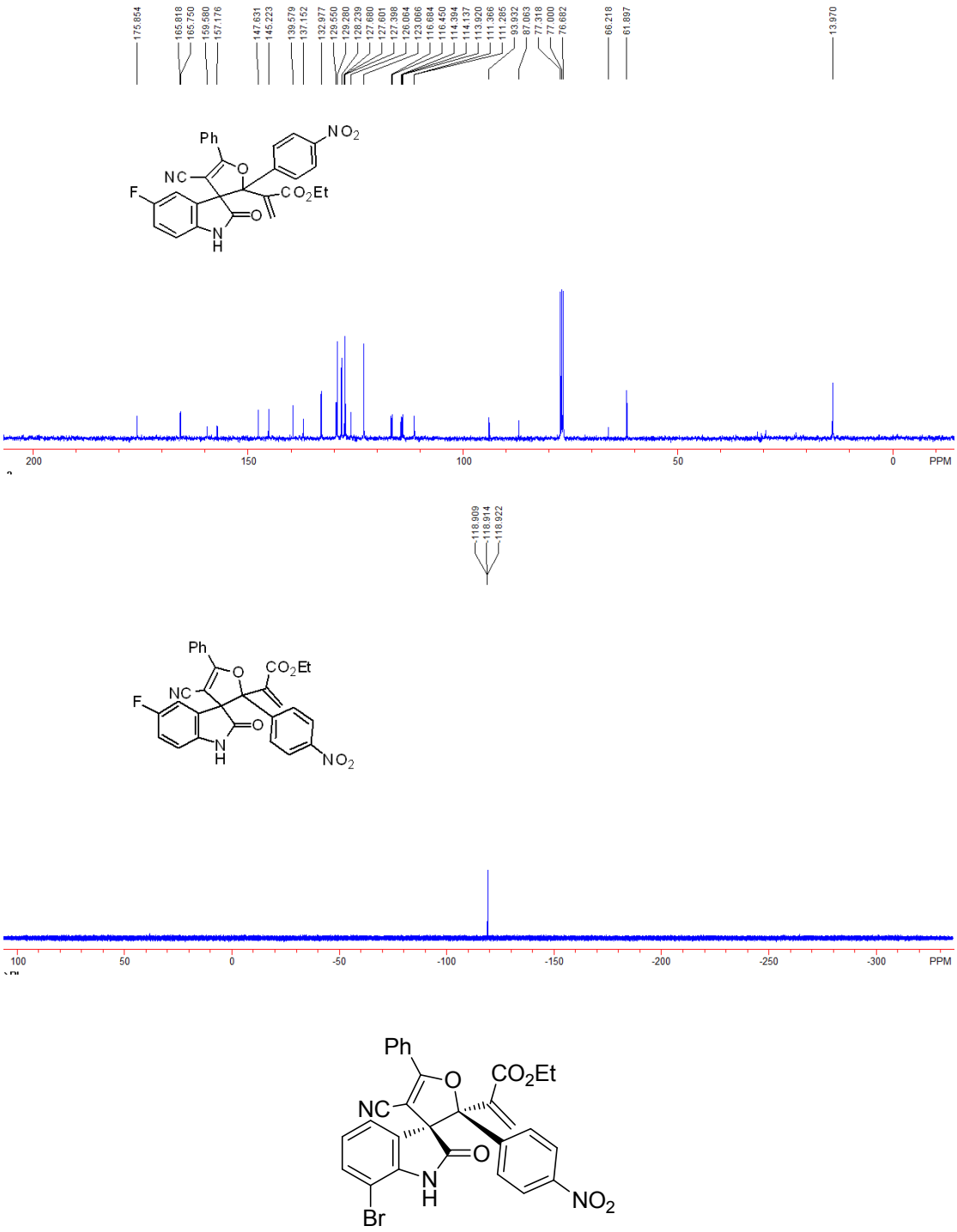
NO	R. Time	Peak Area	Percent	Peak Height

1	12.072	47730	5.24	1779
2	23.623	862578	94.76	12833



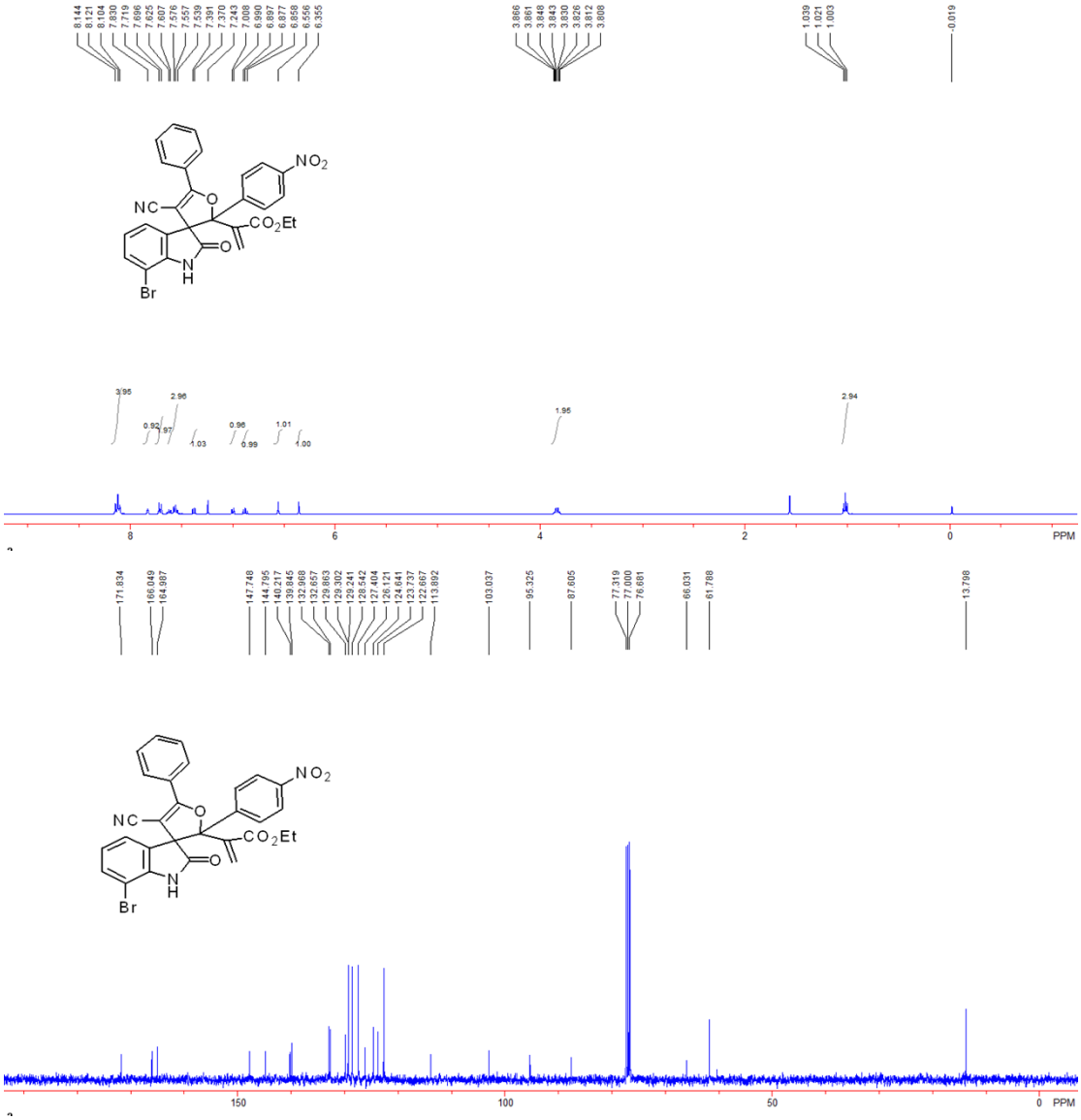
Compound 3h': A white solid (11 mg, 20% yield), Mp: 134-135 ^{o}C. ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.24 (t, *J* = 7.2 Hz, 3H, CH_3), 4.07-4.16 (m, 1H, CH_2), 4.17-4.24 (m, 1H, CH_2), 5.56 (d, *J* = 8.0 Hz, 1H, Ar), 6.41 (s, 1H, =CH), 6.68 (s, 1H, =CH), 6.93-6.94 (m, 2H, Ar), 7.54-7.67 (m, 5H, Ar), 8.13 (d, *J* = 8.8 Hz, 2H, Ar), 8.19-8.21 (m, 2H, Ar), 8.83 (d, *J* = 6.0 Hz, 1H, NH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 14.0, 61.9, 66.2, 87.1, 93.9, 111.3 (*J* = 8.1 Hz), 114.0 (*J* = 21.7 Hz), 114.4, 116.6 (*J* = 23.4 Hz), 123.1, 1261, 127.4, 127.6 (*J* = 7.9 Hz), 128.2, 129.3, 129.6, 133.0, 137.2, 140.0, 145.2, 147.6, 158.4 (*J* = 250.4 Hz), 165.75, 165.82, 175.9. ^{19}F NMR ($CDCl_3$, 376 MHz, $CFCl_3$) δ -119.48--119.42 (m) IR (CH_2Cl_2) ν 697, 735, 853, 1026, 1180, 1349, 1486, 1522, 1632, 1720, 2209, 2919, 3264 cm^{-1}. MS (ESI) m/e 543.2 (M^++NH_4). HRMS (ESI) calcd. for $C_{29}H_{24}FN_3O_6$: 543.1680, Found: 543.1675. [α] $_D^{20}$ = -0.3 (c 0.50, CH_2Cl_2)].





Compound 3i: A white solid (36 mg, 62% yield), Mp: 251-252 ^{o}C. ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.02 (t, J = 7.2 Hz, 3H, CH_3), 3.81-3.87 (m, 2H, CH_2), 6.36 (s, 1H, =CH), 6.56 (s, 1H, =CH), 6.86-6.90 (m, 1H, Ar), 7.00 (d, J = 8.0 Hz, 1H, Ar), 7.38 (d, J = 8.0 Hz, 1H, Ar), 7.54-7.63 (m, 3H, Ar), 7.21 (d, J = 8.8 Hz, 2H, Ar), 7.83 (s, 1H, NH), 8.10-8.14 (m, 4H, Ar). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 13.8, 61.8, 66.0, 87.6, 95.3, 103.0, 113.9, 112.7, 123.7, 124.6, 126.1, 127.4, 128.5, 129.2, 129.3, 129.9, 132.7, 133.0, 139.8, 140.2, 144.8, 147.7, 165.0, 166.0, 171.8. IR (CH_2Cl_2) ν 609, 741, 854, 1181, 1323, 1349, 1473, 1523, 1614, 1726, 2210, 2919, 3198 cm^{-1}.

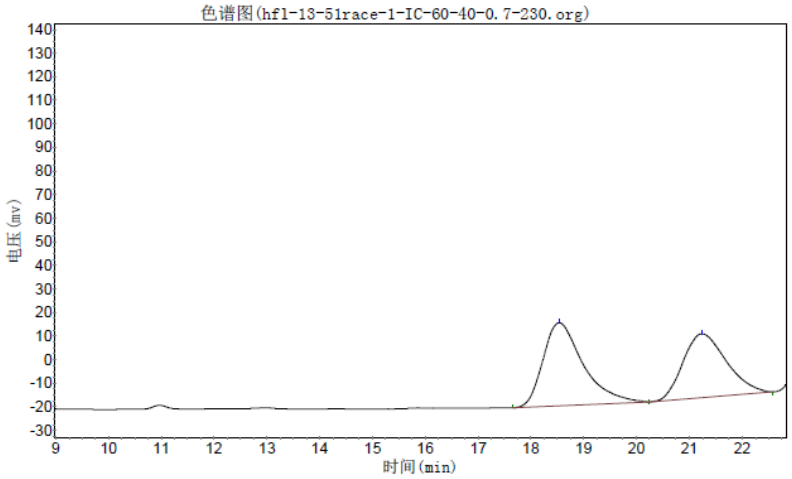
MS (ESI) m/e 603.1 (M^++NH_4). HRMS (ESI) calcd. for $C_{29}H_{24}BrN_4O_6$: 603.0879, Found: 603.0869. Enantiomeric excess was determined by HPLC with a Chiralcel IC column [λ = 230 nm; eluent: Hexane/Isopropanol = 70/30; Flow rate: 0.70 mL/min; t_{major} = 21.20 min, t_{minor}= 18.67 min; ee% = 96%; $[\alpha]_D^{20}$ = -70.9 (c 1.75, CH_2Cl_2)].



实验时间：2014-02-26,10:58:34
谱图文件:D:\4+1\底物拓展\hfl-13-51race-1-IC-60-40-0.7-230.org
实验者：
报告时间：2014-04-03,21:30:28
积分方法:面积归一法

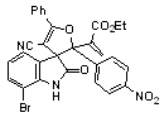
使用仪器类型:气相色谱　　检测器:FID　　进样器:分流

柱温:程序升温



分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		18.540	35418.227	1908325.500	51.4211
2		21.240	28740.555	1802849.500	48.5789
总计			64158.781	3711175.000	100.0000

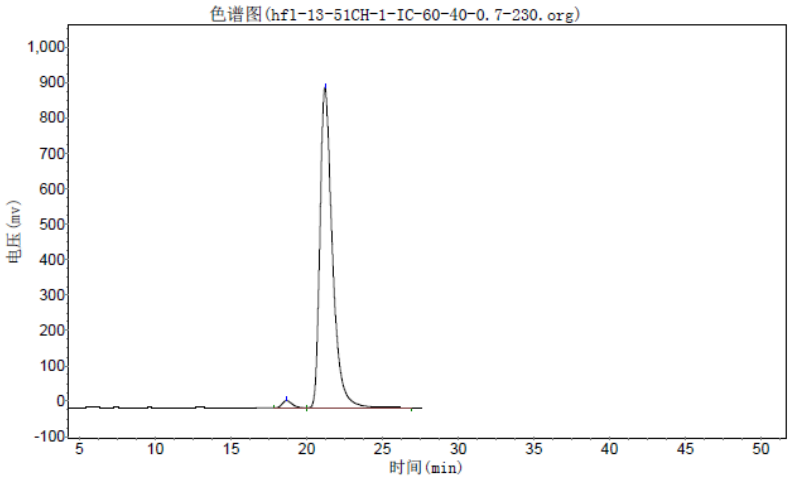


IC, 230 nm
hexane/ⁱPrOH = 60:40
0.7 mL/min

实验时间：2014-02-26,11:42:39
谱图文件:D:\4+1\底物拓展\hfl-13-51CH-1-IC-60-40-0.7-230.org
实验者：
报告时间：2014-04-03,21:31:26
积分方法:面积归一法

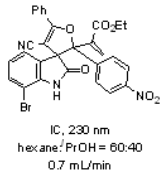
使用仪器类型:气相色谱　　检测器:FID　　进样器:分流

柱温:程序升温

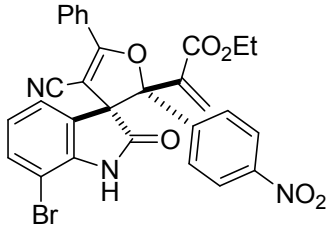


分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		18.673	20793.443	988233.000	1.8754
2		21.203	904908.750	51705584.000	98.1246
总计			925702.193	52693817.000	100.0000

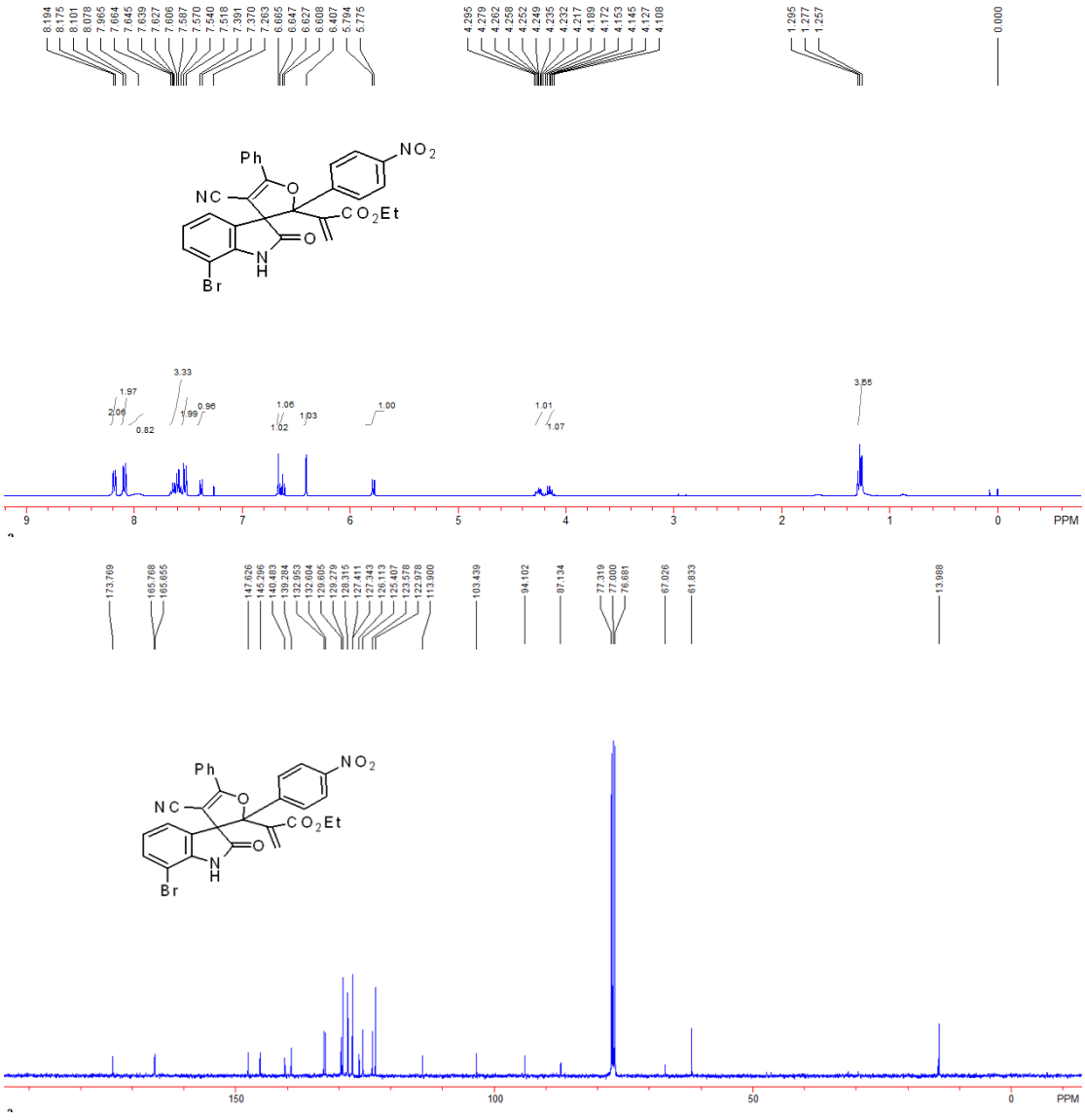


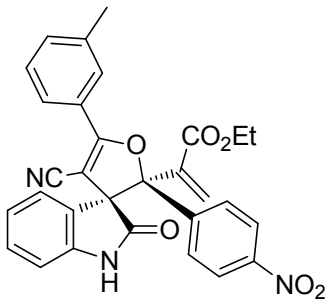
Translation: Enantiomeric excess was determined by HPLC with a Chiralcel IC-H column [λ = 230 nm; eluent: Hexane/Isopropanol = 60/40; Flow rate: 0.70 mL/min; t_{major} = 21.20 min, t_{minor}= 18.67 min; ee% = 96%.



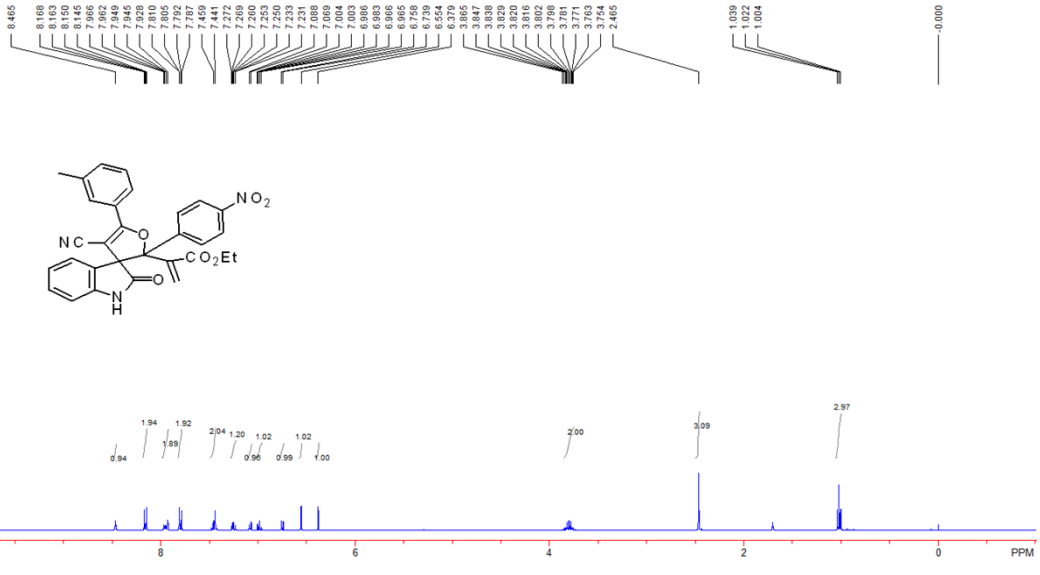
Compound 3i': A white solid (12 mg, 20% yield), Mp: 140-141 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.28 (t, *J* = 7.2 Hz, 3H, CH_3), 4.11-4.22 (m, 1H, CH_2), 4.23-4.30 (m, 1H, CH_2), 5.78 (d, *J*

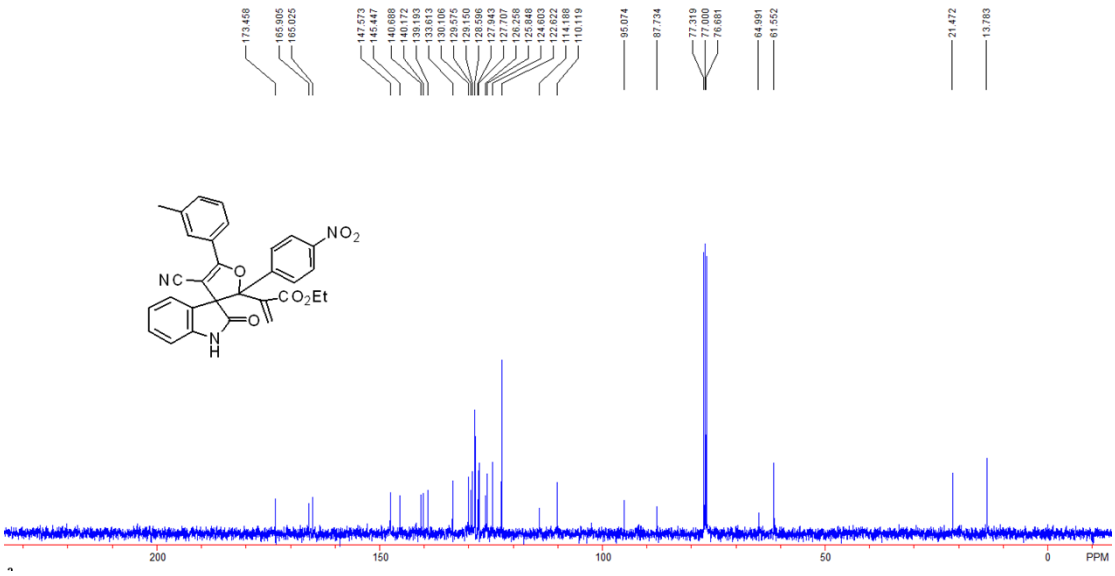
= 8.0 Hz, 1H, Ar), 6.41 (s, 1H, =CH), 6.61-6.65 (m, 1H, Ar), 6.67 (s, 1H, =CH), 7.38 (d, *J* = 8.0 Hz, 1H, Ar), 7.52-7.66 (m, 5H, Ar), 7.97 (br, 1H, NH), 8.08-8.10 (m, 2H, Ar), 8.18 (d, *J* = 8.0 Hz, 2H, Ar). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 14.0, 61.8, 67.0, 87.1, 94.1, 103.4, 113.9, 123.0, 123.6, 125.4, 126.1, 127.3, 127.4, 128.3, 129.3, 129.6, 132.6, 133.0, 139.3, 140.5, 145.3, 147.6, 165.7, 165.8, 173.8. IR (CH_2Cl_2) ν 689, 853, 1027, 1180, 1323, 1348, 1522, 1615, 1727, 2205, 2919, 3194 cm^{-1}. MS (ESI) m/e 603.1 (M^++NH_4). HRMS (ESI) calcd. for $C_{29}H_{24}BrN_4O_6$: 603.0879, Found: 603.0871. $[\alpha]_D^{20}$ = -4.9 (c 0.40, CH_2Cl_2)].





Compound 3j: A white solid (39 mg, 75% yield), Mp: 123-124 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.02 (t, *J* = 7.2 Hz, 3H, CH_3), 2.47 (s, 3H, CH_3), 3.75-3.87 (m, 2H, CH_2), 6.38 (s, 1H, =CH), 6.55 (s, 1H, =CH), 6.75 (d, *J* = 8.0 Hz, 1H, Ar), 6.97-7.00 (m, 1H, Ar), 7.08 (d, *J* = 8.0 Hz, 1H, Ar), 7.23-7.27 (m, 1H, Ar), 7.44-7.46 (m, 2H, Ar), 7.79-7.81 (m, 2H, Ar), 7.93-7.97 (m, 2H, Ar), 8.15-8.17 (m, 2H, Ar), 8.47 (s, 1H, NH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 13.8, 21.5, 61.6, 65.0, 87.7, 95.1, 110.1, 114.2, 122.6, 124.6, 125.8, 126.3, 127.7, 127.9, 128.6, 129.2, 129.6, 130.1, 133.6, 139.2, 140.2, 140.7, 145.4, 147.6, 165.0, 165.9, 173.5. IR (CH_2Cl_2) ν 750, 1178, 1205, 1324, 1348, 1473, 1522, 1619, 1723, 2206, 2919, 3296 cm^{-1}. MS (ESI) m/e 522.2 (M^++1). HRMS (ESI) calcd. for $C_{30}H_{24}N_3O_6$: 522.1665, Found: 522.1661. Enantiomeric excess was determined by HPLC with a Chiralcel AD-H column [λ = 230 nm; eluent: Hexane/Isopropanol = 60/40; Flow rate: 0.70 mL/min; t_{major} = 61.88 min, t_{minor}= 9.61 min; ee% = 81%; $[\alpha]_D^{20}$ = -185.3 (c 2.30, CH_2Cl_2)].



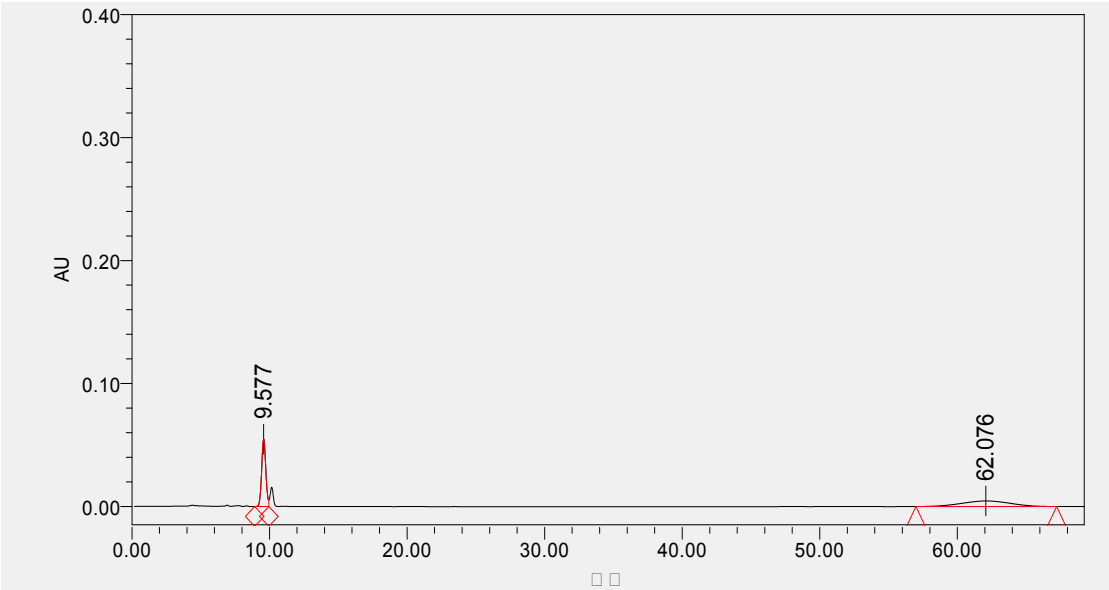


HPLC REPORT

Sample Name: hfl-13-45Race Date:####

Column: AD-H Mobile Phase:hex/ipr=60/40

Velocity(ml/min): 0.7 Detection Wavelength(nm):230



NO	R. Time	Peak Area	Percent	Peak Height
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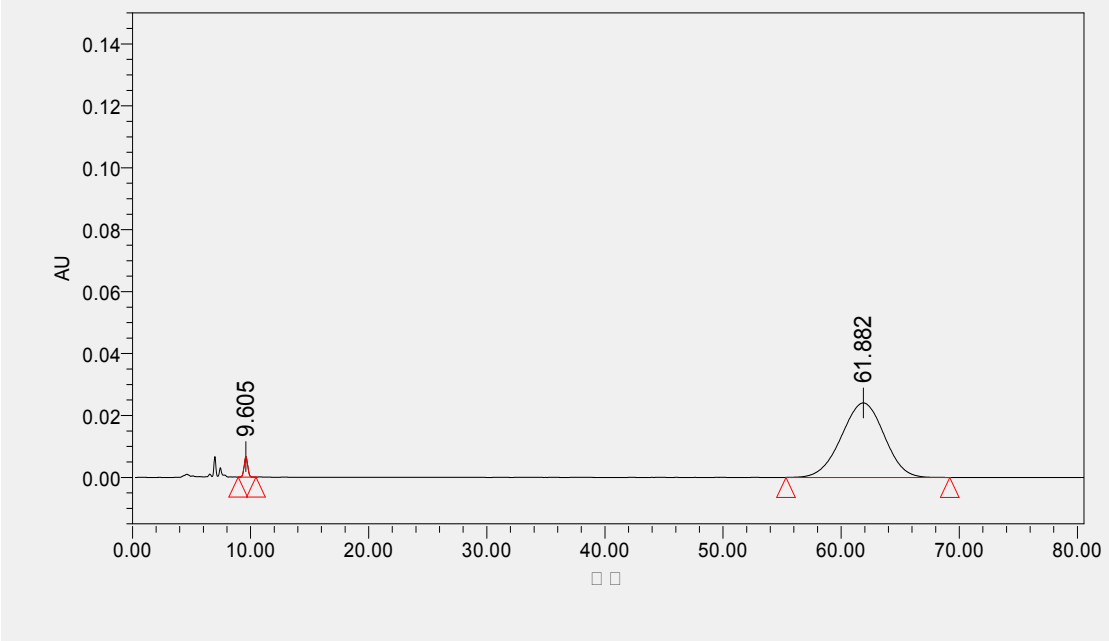
2	62.076	1126636	49.38	4538

HPLC REPORT

Sample Name: hfl-13-45CH Date:####

Column: AD-H Mobile Phase:hex/ipr=60/40

Velocity(ml/min): 0.7 Detection Wavelength(nm):230



NO	R. Time	Peak Area	Percent	Peak Height
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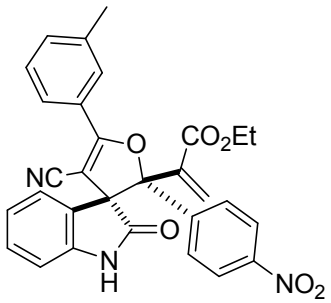
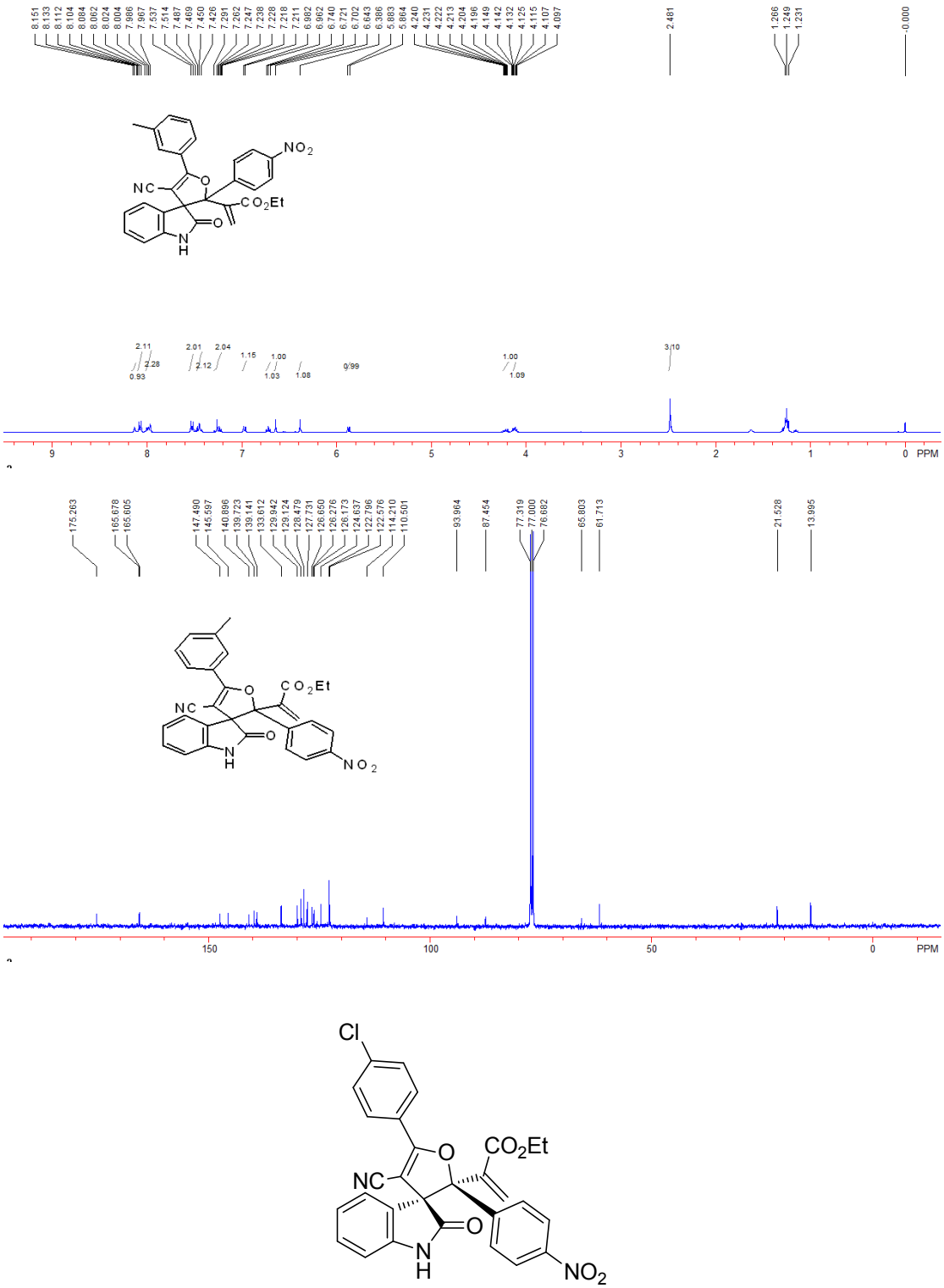
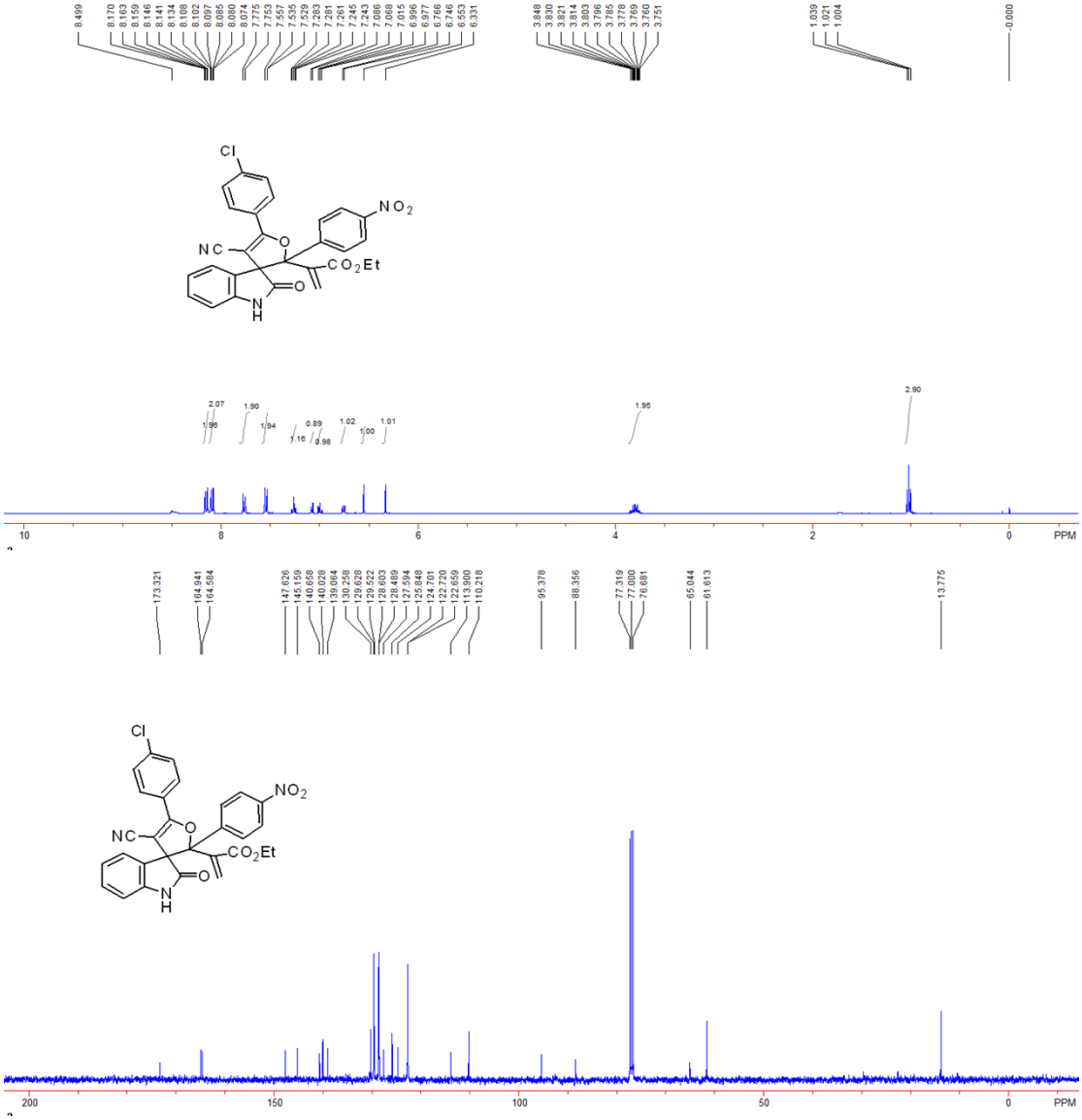


Compound 3j': A white solid (10 mg, 19% yield), Mp: 128-129 ^{o}C. ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.25 (t, *J* = 7.2 Hz, 3H, CH_3), 2.48 (s, 3H, CH_3), 4.10-4.14 (m, 1H, CH_2), 4.10-4.24 (m, 1H, CH_2), 5.88 (d, *J* = 8.0 Hz, 1H, Ar), 6.39 (s, 1H, =CH), 6.65 (s, 1H, =CH), 6.70-6.74 (m, 1H, Ar), 6.97 (d, *J* = 8.0 Hz, 1H, Ar), 7.22-7.29 (m, 1H, Ar), 7.43-7.49 (m, 2H, Ar), 7.53 (d, *J* = 8.0 Hz, 2H, Ar), 7.97-8.01 (m, 2H, Ar), 8.08 (d, *J* = 8.0 Hz, 2H, Ar), 8.14 (s, 1H, NH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 14.0, 21.5, 61.7, 65.8, 87.5, 94.0, 110.5, 114.2, 122.6, 122.8, 124.6, 126.2, 126.3, 126.7, 127.7, 128.5, 129.1, 129.9, 133.6, 139.1, 139.7, 140.9, 145.6, 147.5, 165.6, 165.7, 175.3. IR (CH_2Cl_2) ν 751, 1179, 1210, 1349, 1472, 1523, 1618, 1721, 2210, 2931, 3259. (ESI) m/e 522.2 (M^{+}+1). HRMS (ESI) calcd. for $C_{30}H_{24}N_3O_{26}$: 522.1665, Found: 522.1659. $[\alpha]_D^{20}$ = -10.0 (c 0.60, CH_2Cl_2)].



Compound 3k: A white solid (28 mg, 51% yield), Mp: 113-114 ^{o}C. ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.02 (t, *J* = 7.2 Hz, 3H, CH_3), 3.754-3.85 (m, 2H, CH_2), 6.33 (s, 1H, =CH), 6.55 (s, 1H, =CH), 6.68 (dd, *J* = 8.0 Hz, *J* = 4.0 Hz, 1H, Ar), 6.76 (d, *J* = 8.0 Hz, 1H, Ar), 6.98-7.09 (m, 1H, Ar), 7.24-7.28 (m, 1H, Ar), 7.55 (d, *J* = 8.8 Hz, 2H, Ar), 7.76 (d, *J* = 8.8 Hz, 2H, Ar), 8.07-8.11 (m, 2H, Ar), 8.13-8.17 (m, 2H, Ar), 8.50 (br, 1H, NH). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 13.8, 61.6, 65.0, 88.4, 95.4, 110.2, 113.9, 122.66, 122.7, 124.7, 125.8, 127.6, 128.5, 128.6, 129.5,

129.6, 130.3, 139.1, 140.0, 140.7, 145.2, 147.6, 164.6, 164.9, 173.3. IR (CH_2Cl_2) ν 749, 853, 1012, 1094, 1180, 1325, 1349, 1473, 1491, 1522, 1619, 1716, 2198, 2917, 3287 cm^{-1}. MS (ESI) m/e 559.1 (M^++NH_4). HRMS (ESI) calcd. for $C_{29}H_{24}ClN_4O_6$: 559.1384, Found: 559.1373. Enantiomeric excess was determined by HPLC with a Chiralcel AD-H column [λ = 230 nm; eluent: Hexane/Isopropanol = 60/40; Flow rate: 0.70 mL/min; t_{major} = 42.50 min, t_{minor}= 26.57 min; ee% = 90%; $[\alpha]_D^{20}$ = -54.6 (c 0.55, CH_2Cl_2)].



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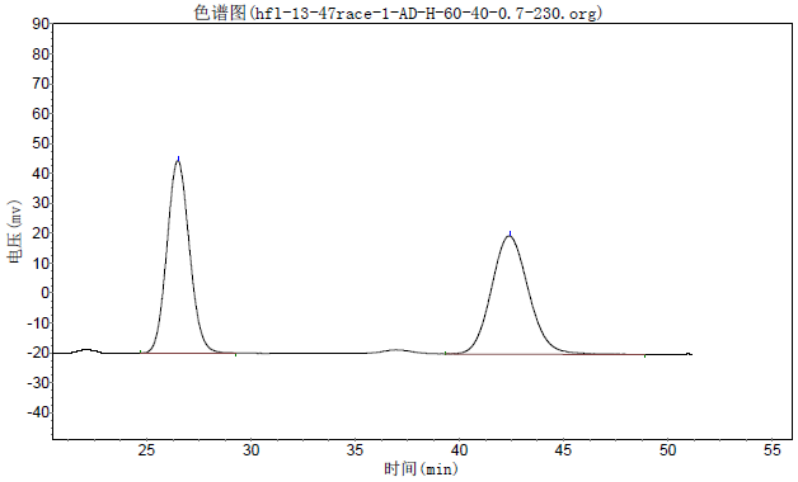
实验者:
报告时间：2014-04-03,21:32:02
积分方法:面积归一法

使用仪器类型:气相色谱　　检测器:FID　　进样器:分流

柱温:程序升温



分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
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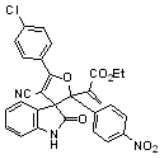
2		42.407	39533.828	4905505.500	50.1669
总计			104076.207	9778361.500	100.0000



AD-H, 230 nm
hexane:^{i}PrOH = 60:40
0.7 mL/min

实验时间：2014-02-18,12:22:14
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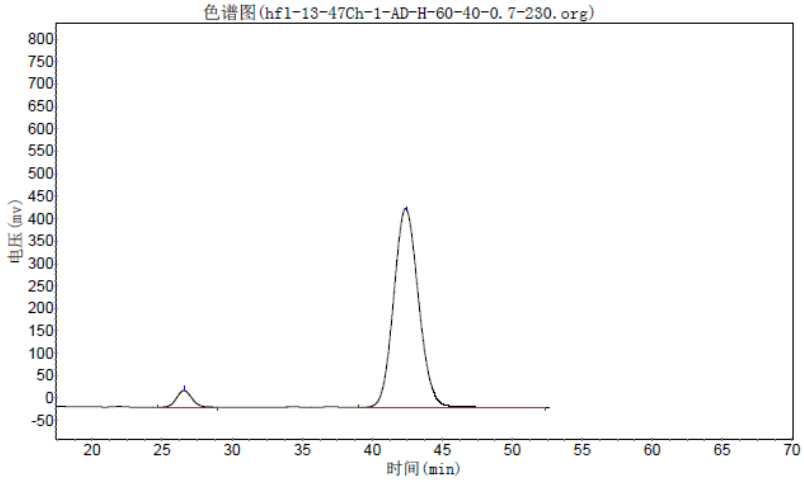
实验者：
报告时间：2014-04-03,21:32:49
积分方法:面积归一法

使用仪器类型:气相色谱　　检测器:FID　　进样器:分流

柱温:程序升温



分析结果表

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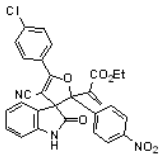
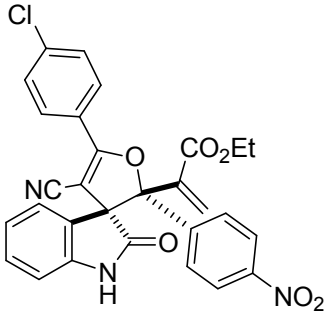


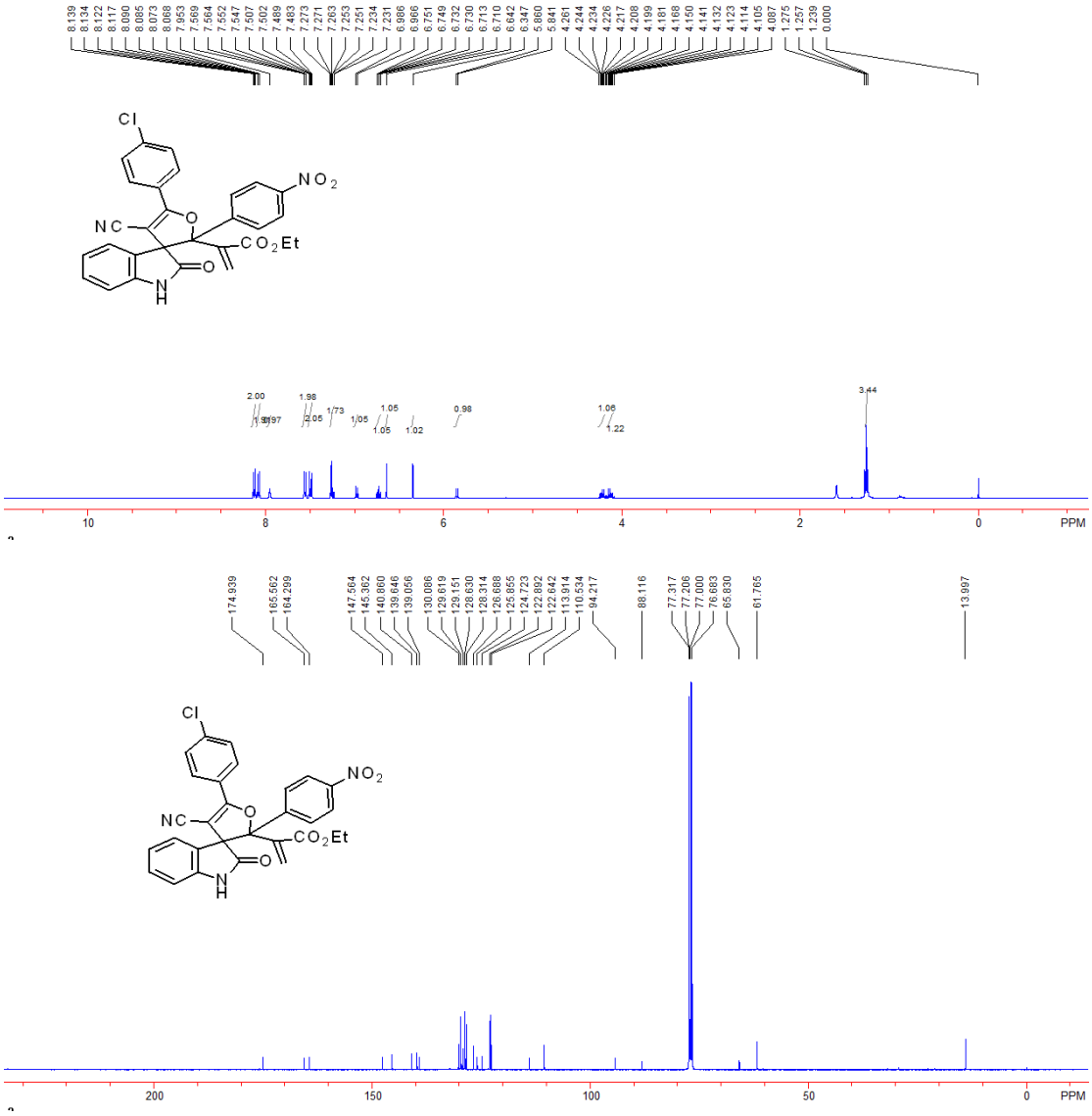
AD-H, 230 nm

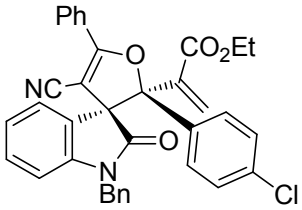
Translation: Enantiomeric excess was determined by HPLC with a Chiralcel AD-H column [λ = 230 nm; eluent: Hexane/Isopropanol = 60/40; Flow rate: 0.70 mL/min; t_{major} = 42.50 min, t_{minor}= 26.57 min; ee% = 90%.



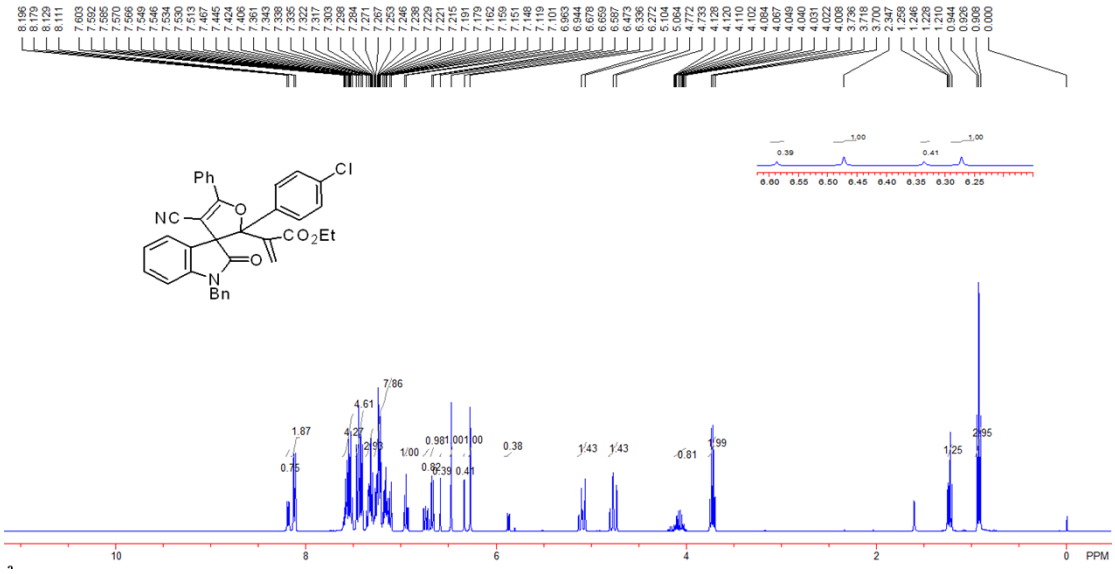
Compound 3k': A white solid (13 mg, 20% yield), Mp: 145-146 °C. ^{1}H NMR ($CDCl_3$, 400 MHz,

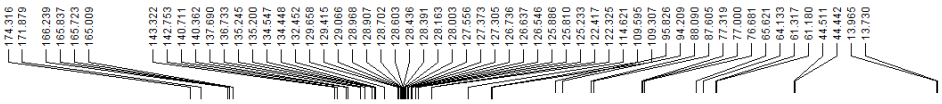
TMS) δ 1.26 (t, J = 7.2 Hz, 3H, CH_3), 4.09-4.17 (m, 1H, CH_2), 4.20-4.26 (m, 1H, CH_2), 5.85 (d, J = 8.0 Hz, 1H, Ar), 6.35 (s, 1H, =CH), 6.42 (s, 1H, =CH), 6.71-6.75 (m, 1H, Ar), 6.98 (d, J = 8.0 Hz, 1H, Ar), 7.23-7.27 (m, 1H, Ar), 7.49 (d, J = 8.0 Hz, 2H, Ar), 7.56 (d, J = 8.0 Hz, 2H, Ar), 8.53 (s, 1H, NH), 8.08 (d, J = 8.0 Hz, 2H, Ar), 8.13 (d, J = 8.0 Hz, 2H, Ar). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 14.0, 61.8, 65.8, 88.1, 94.2, 110.5, 113.9, 122.6, 122.9, 124.7, 125.9, 126.7, 128.3, 128.6, 129.2, 129.6, 130.1, 139.1, 139.6, 140.9, 145.4, 147.6, 164.3, 165.6, 175.0. IR (CH_2Cl_2) ν 753, 853, 1038, 1094, 1180, 1325, 1350, 1472, 1523, 1618, 1722, 2210, 2917, 3271 cm^{-1}. MS (ESI) m/e 542.1 (M^++NH_4). HRMS (ESI) calcd. for $C_{29}H_{21}ClN_3O_6$: 542.1119, Found: 542.1109. [α] $_D^{20}$ = -1.1 (c 0.45, CH_2Cl_2)].





Compound 3l: A white solid (53 mg, 90% yield), Mp: 90-92 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 0.93 (t, *J* = 7.2 Hz, 2.14H, CH_3), 1.23 (t, *J* = 7.2 Hz, 0.91H, CH_3), 3.73 (q, *J* = 7.2 Hz, 1.37H, CH_2), 4.02-4.13 (m, 0.60H, CH_2), 4.73-4.80 (m, 1H, CH), 5.06-5.13 (m, 1H, CH), 5.87 (d, *J* = 8.0 Hz, 0.26H, Ar), 6.27 (s, 0.70H, =CH), 6.34 (s, 0.30H, =CH), 6.47 (s, 0.70H, =CH), 6.59 (s, 0.28H, =CH), 6.67 (d, *J* = 8.0 Hz, 0.66H, Ar), 6.70-6.76 (m, 0.58H, Ar), 6.93-6.96 (m, 0.70H, Ar), 7.10-7.59 (m, 13.75H, Ar), 8.11-8.13 (m, 1.27H, Ar), 8.17-8.20 (m, 0.55H, Ar). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 13.7, 14.0, 44.4, 44.5, 61.2. 61.3, 64.1, 65.6, 87.6, 88.1, 94.2, 95.8, 109.3, 109.6, 114.6, 122.3, 122.4, 125.2, 125.8, 125.9, 126.5, 126.6, 126.7, 127.3, 127.4, 127.6, 128.0, 128.2, 128.39, 128.44, 128.6, 128.7, 128.9, 129.0, 129.1, 129.4, 129.7, 132.5, 134.4, 134.5, 135.20, 135.24, 136.7, 137.7, 140.4, 140.7, 142.8, 143.3, 165.0, 165.7, 165.8, 166.2, 171.9, 1743.3. IR (CH_2Cl_2) ν 689, 735, 1017, 1096, 1177, 1322, 1342, 1467, 1487, 1610, 1716, 2207, 2980 cm^{-1}. MS (ESI) m/e 587.2 (M^++H). HRMS (ESI) calcd. for $C_{36}H_{28}ClN_2O_4$: 587.1738, Found: 587.1724. Enantiomeric excess was determined by HPLC with a Chiralcel AD-H column [λ = 230 nm; eluent: Hexane/Isopropanol = 60/40; Flow rate: 0.70 mL/min; t_{major} = 11.88 min, t_{minor}= 13.46 min; ee% = 97%; $[\alpha]_D^{20}$ = -174.3(c 2.25, CH_2Cl_2)].

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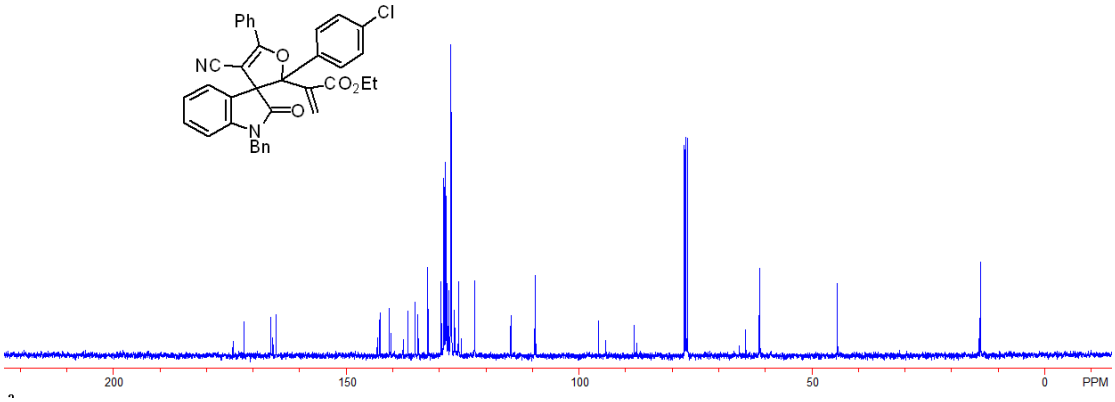
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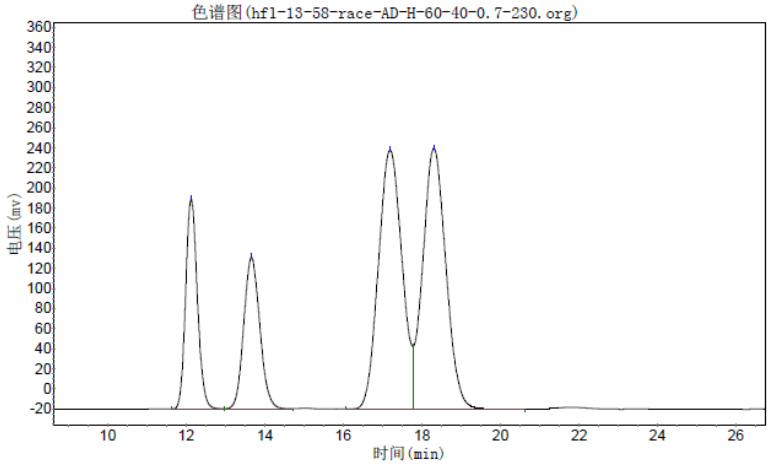
实验者：
报告时间：2014-04-03,21:23:20
积分方法:面积归一法

使用仪器类型:气相色谱　　检测器:FID　　进样器:分流

柱温:程序升温

色谱图(hfl-13-58-race-AD-H-60-40-0.7-230.org)



分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
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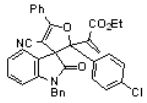
2		13.657	151276.453	4345292.500	14.3784
3		17.190	257859.359	10785860.000	35.6899
4		18.323	259506.688	10729728.000	35.5042
总计			877596.859	30221000.500	100.0000



AD-H, 230 nm
hexane/iPrOH = 60:40
0.7 mL/min

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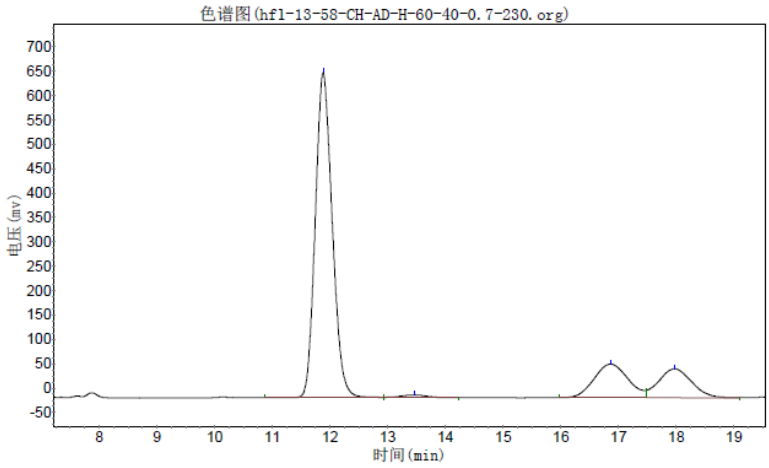
实验者：
报告时间：2014-04-03,21:25:00
积分方法:面积归一法

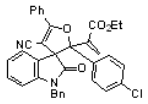
使用仪器类型:气相色谱　　检测器:FID　　进样器:分流

柱温:程序升温



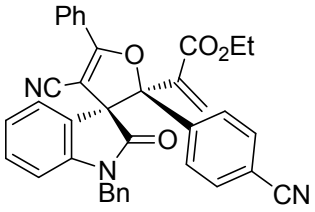
分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		11.875	666671.625	13578793.000	71.6601
2		13.457	5720.239	184074.906	0.9714
3		16.860	68912.609	2824197.500	14.9043
4		17.967	59163.742	2361819.500	12.4642
总计			800468.216	18948884.906	100.0000



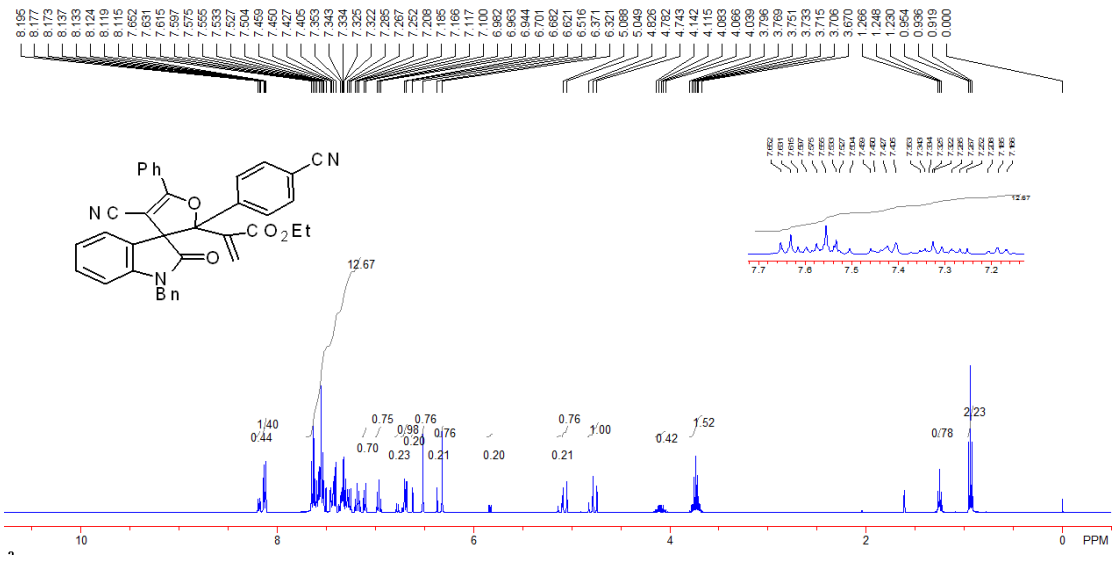
AD-H, 230 nm
hexane/ⁱPrOH = 60:40
0.7 mL/min

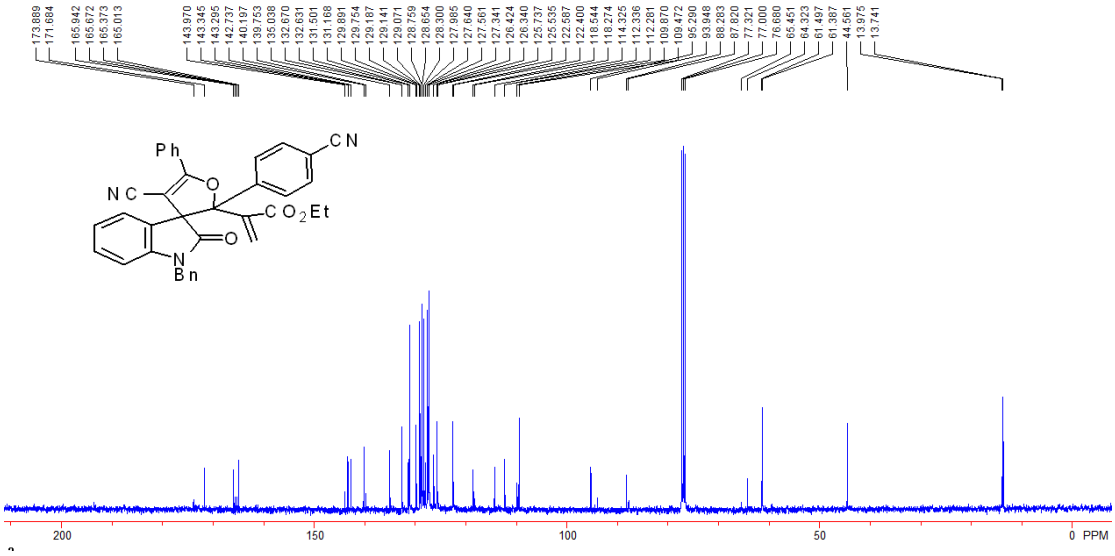
Translation: Enantiomeric excess was determined by HPLC with a Chiralcel AD-H column [λ = 230 nm; eluent: Hexane/Isopropanol = 60/40; Flow rate: 0.70 mL/min; t_{major} = 11.88 min, t_{minor}= 13.46 min; ee% = 97%.



Compound 3m: A white solid (57 mg, 98% yield), Mp: 89-94 °C. ^{1}H NMR ($CDCl_3$, 400 MHz,

TMS) δ 0.94 (t, J = 7.2 Hz, 2.23H, CH_3), 1.25 (t, J = 7.2 Hz, 0.78H, CH_3), .3.67-3.80 (m, 1.52H, CH_2), 4.04-4.14 (m, 0.42H, CH_2), 4.74-4.83 (m, 1H, CH), 5.09 (d, J = 16.0 Hz, 0.76H, CH), 5.12 (d, J = 16.0 Hz, 0.21H, CH), 5.83 (d, J = 8.0 Hz, 0.20H, Ar), 6.32 (s, 0.76H, =CH), 6.37 (s, 0.21H, =CH), 6.52 (s, 0.76H, =CH), 6.62 (s, 0.20H, =CH), 6.68-6.73 (m, 1H, Ar), 6.78 (d, J = 8.0 Hz, 0.23H, Ar), 6.94-6.98 (m, 0.75H, Ar), 7.10-7.12 (m, 0.70H, Ar), 7.25-7.65 (m, 12.67H, Ar), 8.12-8.14 (m, 1.40H, Ar), 8.17-8.20 (m, 0.44H, Ar). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 13.7, 14.0, 44.6, 61.4, 61.5, 64.3, 65.5, 87.8, 88.3, 93.9, 95.3, 109.5, 109.9, 112.28, 112.34, 114.3, 118.3, 118.5, 122.4, 122.6, 125.5, 125.7, 126.3, 126.4, 127.3, 127.56, 127.64, 128.0, 128.3, 128.7, 128.8, 129.07, 129.14, 129.2, 129.8, 129.9, 131.2, 131.5, 132.6, 132.7, 135.0, 139.8, 140.2, 142.7, 143.30, 143.35, 144.0, 165.0, 165.4, 165.7, 165.9, 171.7, 173.9. IR (CH_2Cl_2) ν 690, 736, 1023, 1184, 1208, 1324, 1342, 1609, 1716, 2209, 2229, 2976 cm^{-1}. MS (ESI) m/e 578.2 (M^++H). HRMS (ESI) calcd. for $C_{37}H_{28}N_3O_4$: 578.2080, Found: 578.2068. Enantiomeric excess was determined by HPLC with a Chiralcel AD-H column [λ = 230 nm; eluent: Hexane/Isopropanol = 60/40; Flow rate: 0.70 mL/min; t_{major} = 20.80 min, t_{minor}= 24.25 min; ee% = 98%; $[\alpha]_D^{20}$ = -139.2 (c 2.50, CH_2Cl_2)].





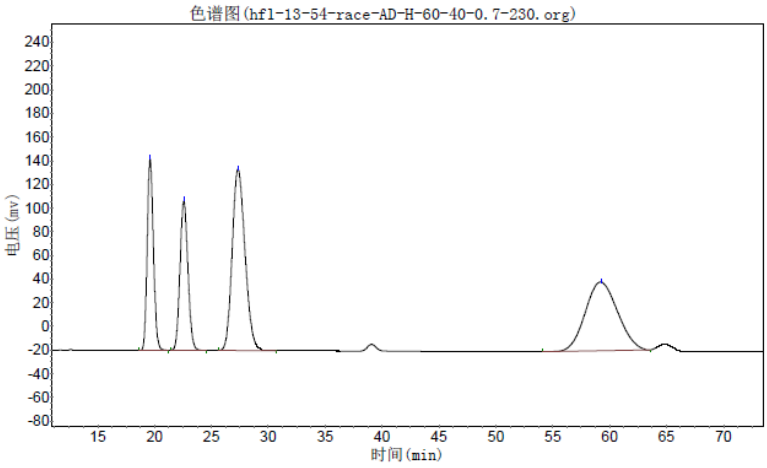
N2000 数据工作站 1

实验时间：2014-02-22,13:26:19
谱图文件:D:\4+1\底物拓展\hfl-13-54-race-AD-H-60-40-0.7-230.org

实验者：
报告时间：2014-04-03,21:28:10
积分方法:面积归一法

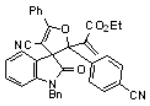
使用仪器类型:气相色谱　　检测器:FID　　进样器:分流

柱温:程序升温



分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		19.607	161600.922	6162635.500	17.0014
2		22.590	126042.930	6120869.000	16.8862
3		27.357	153056.750	12015781.000	33.1490
4		59.290	59009.367	11948505.000	32.9634
总计			499709.969	36247790.500	100.0000

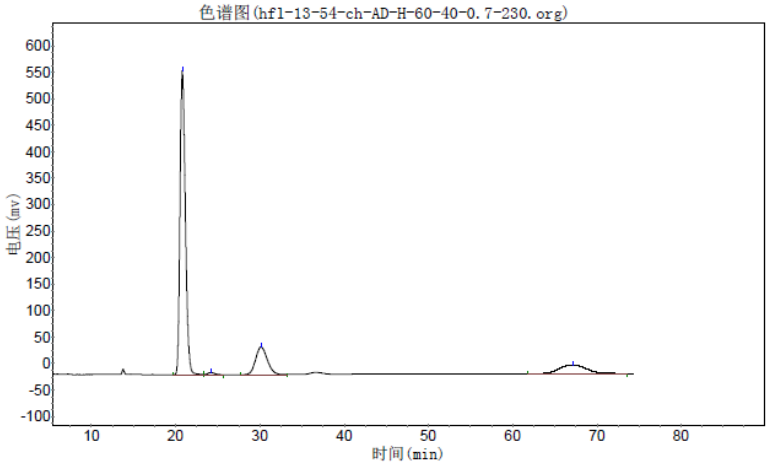


AD-H, 230 nm
hexane/iPrOH = 60:40
0.7 mL/min

实验时间：2014-02-22,14:54:58
谱图文件:D:\4+1\底物拓展\hfl-13-54-ch-AD-H-60-40-0.7-230.org
实验者：
报告时间：2014-04-03,21:29:39
积分方法:面积归一法

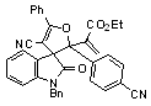
使用仪器类型:气相色谱　　检测器:FID　　进样器:分流

柱温:程序升温



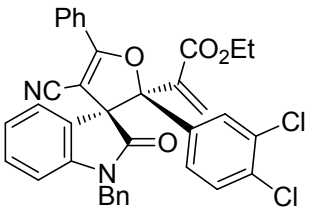
分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		20.797	574113.250	25321946.000	72.5386
2		24.245	3767.769	219364.516	0.6284
3		30.145	52003.379	5006292.500	14.3413
4		67.153	17648.635	4360652.500	12.4918
总计			647533.033	34908255.516	100.0000



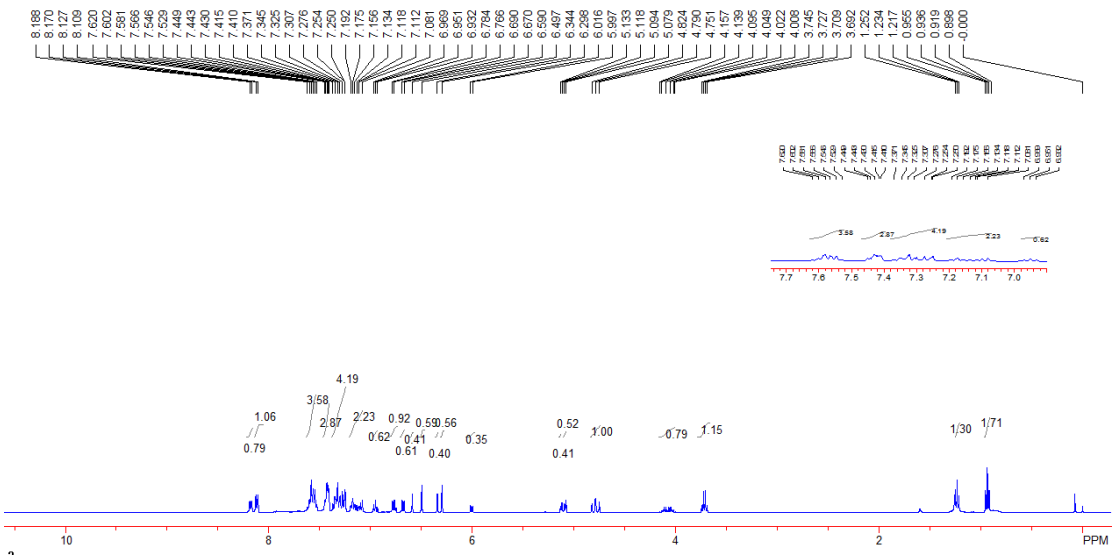
AD-H, 230 nm
hexane/^{i}PrOH = 60:40
0.7 mL/min

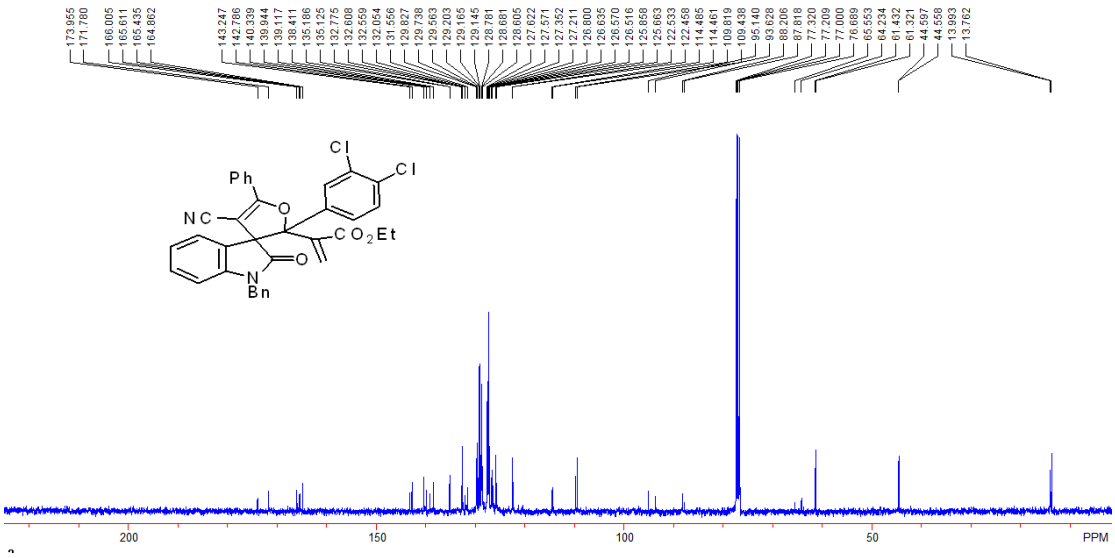
Translation: Enantiomeric excess was determined by HPLC with a Chiralcel AD-H column [λ = 230 nm; eluent: Hexane/Isopropanol = 60/40; Flow rate: 0.70 mL/min; t_{major} = 20.80 min, t_{minor}= 24.25 min; ee% = 98%.



Compound 3n: A white solid (53 mg, 85% yield), Mp: 70-74 °C. ^{1}H NMR ($CDCl_3$, 400 MHz,

TMS) δ 0.94 (t, J = 7.2 Hz, 1.71H, CH_3), 1.23 (t, J = 7.2 Hz, 1.30H, CH_3), 3.72 (q, J = 7.2 Hz, 1.15H, CH_2), 4.01-4.16 (m, 0.79H, CH_2), 4.75-4.82 (m, 1H, CH), 5.09 (d, J = 16.0 Hz, 0.52H, CH), 5.13 (d, J = 16.0 Hz, 0.41H, CH), 6.01 (d, J = 8.0 Hz, 0.35H, Ar), 6.30 (s, 0.56H, =CH), 6.34 (s, 0.40H, =CH), 6.50 (s, 0.59H, =CH), 6.59 (s, 0.41H, =CH), 6.68 (d, J = 8.0 Hz, 0.61H, Ar), 6.75-6.84 (m, 1H, Ar), 6.93-6.97 (m, 0.62H, Ar), 7.08-7.19(m, 2.23H, Ar), 7.25-7.37 (m, 4.19H, Ar), 7.41-7.45 (m, 2.87H, Ar), 7.53-7.62 (m, 3.58H, Ar), 8.12 (d, J = 7.2 Hz, 1.06H, Ar), 8.18 (d, J = 7.2 Hz, 0.79H, Ar),. ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 13.8, 14.0, 44.56, 44.60, 61.3, 61.4, 64.2, 65.6, 87.8, 88.2, 93.6, 95.1, 109.4, 109.8, 114.46, 114.49, 122.46, 122.53, 125.7, 125.9, 126.5, 126.57, 126.64, 126.8, 127.2, 127.4, 127.57, 127.62, 128.6, 128.7, 128.8, 129.1, 129.16, 129.20, 129.6, 129.7, 129.8, 131.6, 132.1, 132.55, 132.60, 132.8, 135.1, 135.2, 138.4, 139.1, 139.9, 140.3, 142.8, 143.2, 164.9, 165.4, 165.6, 166.0, 171.8, 174.0. IR (CH_2Cl_2) ν 690, 737, 755, 1029, 1180, 1319, 1342, 1468, 1487, 1610, 1633, 1716, 2198, 2988 cm^{-1}. MS (ESI) m/e 621.1 (M^++H). HRMS (ESI) calcd. for $C_{36}H_{27}Cl_2N_2O_4$: 621.1348, Found: 621.1332. Enantiomeric excess was determined by HPLC with a Chiralcel AD-H column [λ = 214 nm; eluent: Hexane/Isopropanol = 80/20; Flow rate: 0.50 mL/min; t_{major} = 20.01 min, t_{minor}= 21.83 min; ee% = 96%; $[\alpha]_D^{20}$ = -67.7 (c 2.50, CH_2Cl_2)].





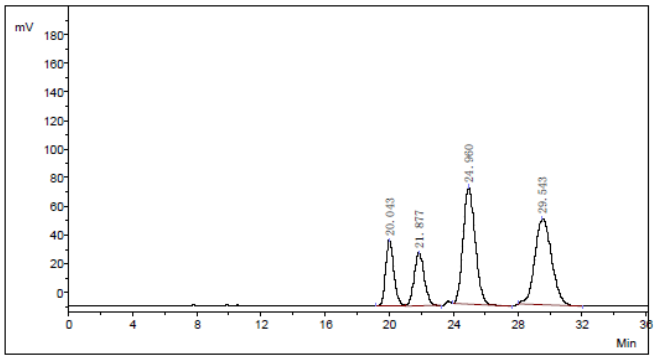
HPLC REPORT

Sample Name:hfl-13-55-rac-ad-h-8-2-0.5-214....che Date:2014-03-04

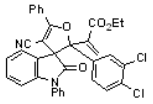
Time:14:58 Method:

Column: Flow Rate:

Wave Length: Mobile Phase:



No.	PeakNo	ID.Name	R.Time	PeakHeight	PeakArea	PerCent
1	1	Unknown	20.043	45323.0	1623421.5	13.6345
2	2	Unknown	21.877	36795.4	1642092.3	13.7913
3	3	Unknown	24.960	81482.2	4257812.4	35.7598
4	4	Unknown	29.543	59813.7	4383373.3	36.8143
Total				223414.2	11906699.4	100.0000



AD-H, 214 nm
Hexane:^{i}PrOH = 80:20
0.5 mL/min

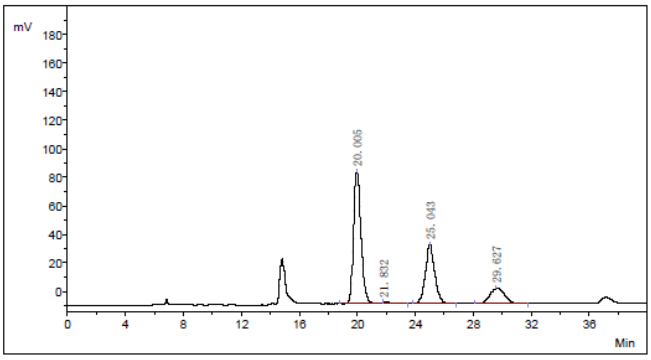
HPLC REPORT

Sample Name:hfl-13-55-ch.che | Date:2014-03-04

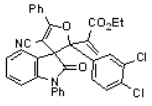
Time:14:03 | Method:

Column: | Flow Rate:

Wave Length: | Mobile Phase:

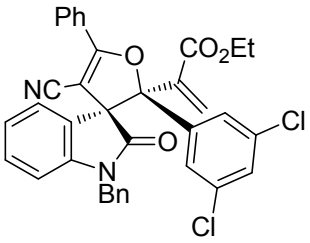


No.	PeakNo	ID. Name	R. Time	PeakHeight	PeakArea	PerCent
1	1	Unknown	20.005	92600.3	3336489.8	55.3561
2	2	Unknown	21.832	979.3	62289.0	1.0334
3	3	Unknown	25.043	41456.3	1852045.0	30.7275
4	4	Unknown	29.627	10631.2	776501.6	12.8830
Total				145667.1	6027325.4	100.0000



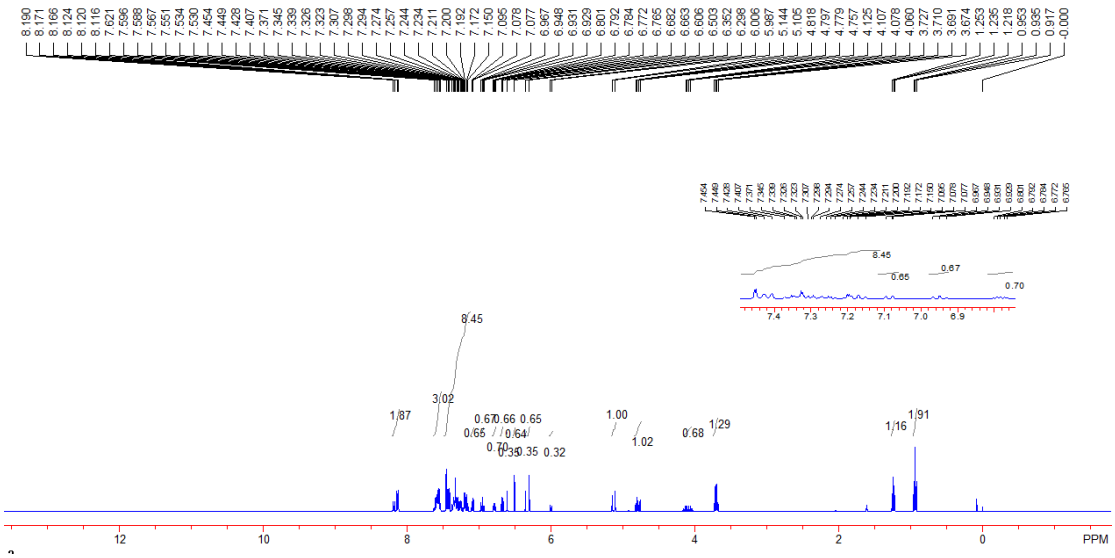
AD-H, 214 nm
Hexane/^{i}PrOH = 80:20
0.5 mL/min

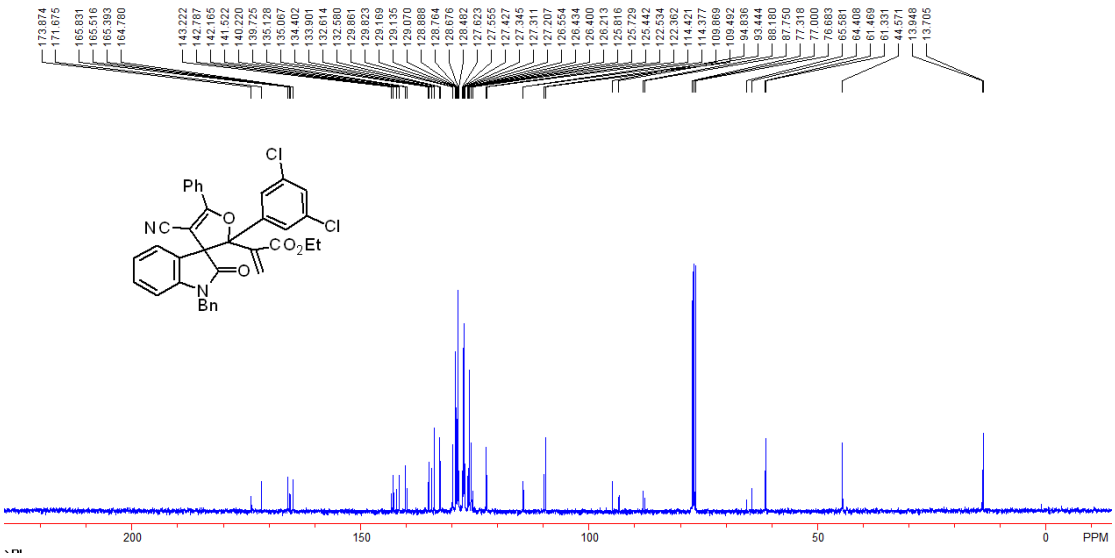
Translation: Enantiomeric excess was determined by HPLC with a Chiralcel AD-H column [λ = 214 nm; eluent: Hexane/Isopropanol = 80/20; Flow rate: 0.50 mL/min; t_{major} = 22.01 min, t_{minor}= 21.83 min; ee% = 96%.



Compound 3o: A white solid (55 mg, 89% yield), Mp: 73-76 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 0.94 (t, *J* = 7.2 Hz, 1.91H, CH_3), 1.24 (t, *J* = 7.2 Hz, 1.16H, CH_3), 3.70 (q, *J* = 7.2 Hz, 1.29H, CH_2), 4.03-4.15 (m, 0.68H, CH_2), 4.76-4.82 (m, 1H, CH), 5.12 (d, *J* = 16.0 Hz, 1H, CH),

6.00 (d, J = 8.0 Hz, 0.32H, Ar), 6.30 (s, 0.65H, =CH), 6.35 (s, 0.35H, =CH), 6.50 (s, 0.64H, =CH), 6.61 (s, 0.35H, =CH), 6.67 (d, J = 8.0 Hz, 0.66H, Ar), 6.77-6.80 (m, 0.70H, Ar), 6.93-6.97 (m, 0.67H, Ar), 7.08-7.10 (m, 0.65H, Ar), 7.15-7.45 (m, 8.45H, Ar), 6.77-6.80 (m, 0.70H, Ar), 7.53-7.62 (m, 3H, Ar), 8.12-8.19 (m, 2H, Ar). ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 13.7, 13.9, 44.6, 61.3, 61.5, 64.4, 65.6, 87.8, 88.2, 93.4, 94.8, 109.5, 109.9, 114.38, 114.42, 122.4, 122.5, 125.4, 125.7, 125.8, 126.2, 126.40, 126.43, 126.6, 127.2, 127.31, 127.35, 127.4, 127.56, 127.62, 128.5, 128.7, 128.8, 128.9, 129.07, 129.14, 129.2, 129.8, 129.9, 132.58, 132.61, 133.9, 134.4, 135.07, 135.13, 139.7, 140.2, 141.5, 142.2, 142.8, 143.2, 164.8, 165.4, 165.5, 165.8, 171.7, 173.9. IR (CH_2Cl_2) ν 695, 756, 801, 1181, 1310, 1362, 1488, 1611, 1719, 2209, 2972 cm^{-1}. MS (ESI) m/e 621.1 (M^++H). HRMS (ESI) calcd. for $C_{36}H_{27}Cl_2N_2O_4$: 621.1348, Found: 621.1336. Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column [λ = 230 nm; eluent: Hexane/Isopropanol = 60/40; Flow rate: 0.70 mL/min; t_{major} = 8.89 min, t_{minor}= 9.56 min; ee% = 81%; $[\alpha]_D^{20}$ = -111.7(c 2.20, CH_2Cl_2)].





N2000 数据工作站

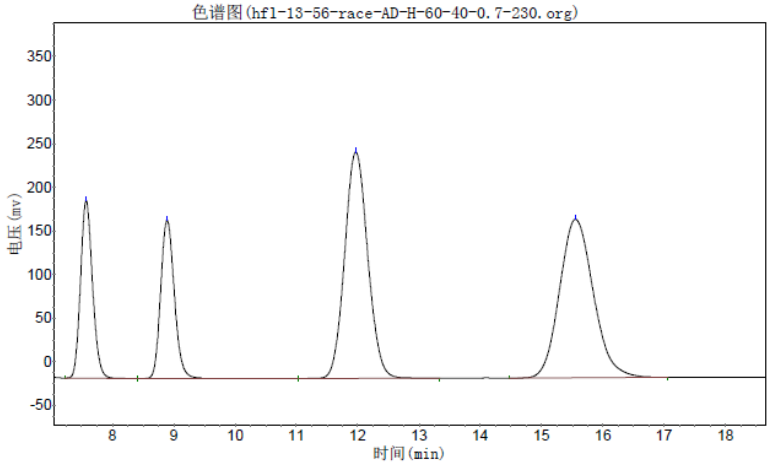
1

实验时间：2014-02-22,15:25:32
谱图文件:D:\4+1\底物拓展\hfl-13-56-race-AD-H-60-40-0.7-230.org

实验者：
报告时间：2014-04-03,21:26:28
积分方法:面积归一法

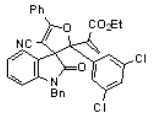
使用仪器类型:气相色谱　　检测器:FID　　进样器:分流

柱温:程序升温



分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		7.573	203983.078	2813995.250	14.4947
2		8.890	181092.734	2807757.500	14.4625
3		11.973	259548.000	6810623.500	35.0810
4		15.557	181496.125	6981629.000	35.9618
总计			826119.938	19414005.250	100.0000

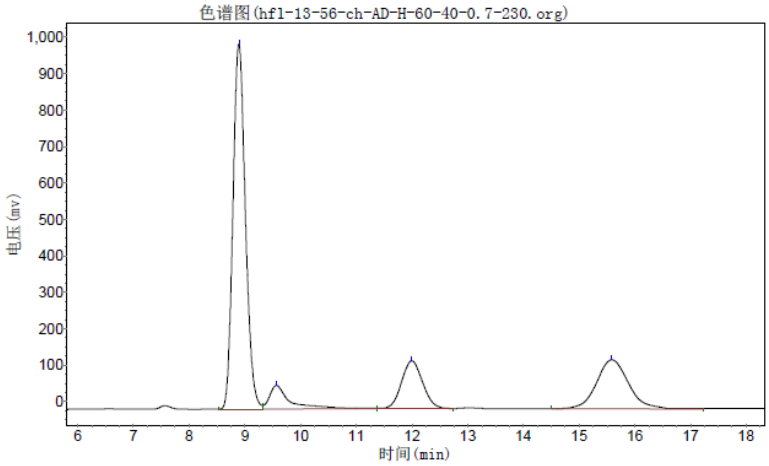


AD-H, 230 nm
hexane/PrOH = 60:40
0.7 mL/min

实验时间：2014-02-22,16:06:53
谱图文件:D:\4+1\底物拓展\hfl-13-56-ch-AD-H-60-40-0.7-230.org
实验者：
报告时间：2014-04-03,21:27:29
积分方法:面积归一法

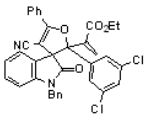
使用仪器类型:气相色谱　　检测器:FID　　进样器:分流

柱温:程序升温



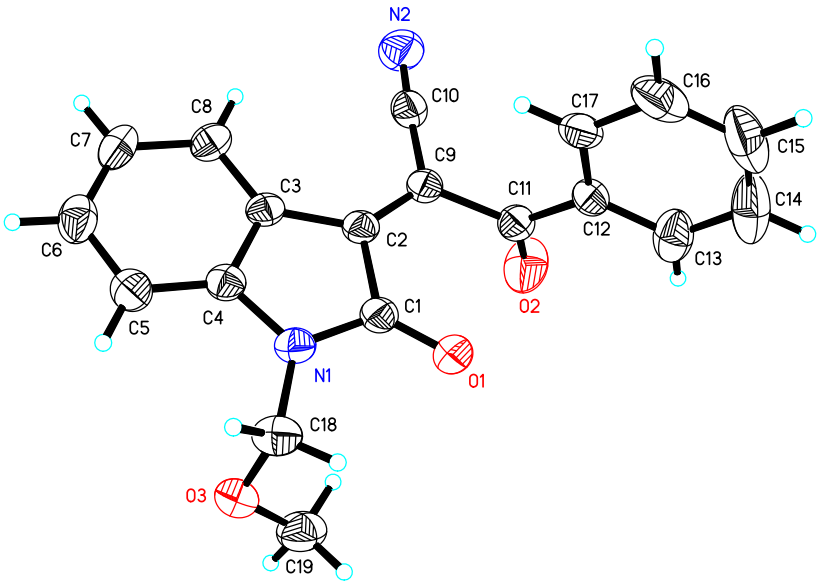
分析结果表

峰号	峰名	保留时间	峰高	峰面积	含量
1		8.890	1001705.063	15583911.000	59.7807
2		9.563	65010.211	1688397.500	6.4768
3		11.995	131010.414	3446028.000	13.2191
4		15.588	134377.047	5350124.000	20.5234
总计			1332102.734	26068460.500	100.0000

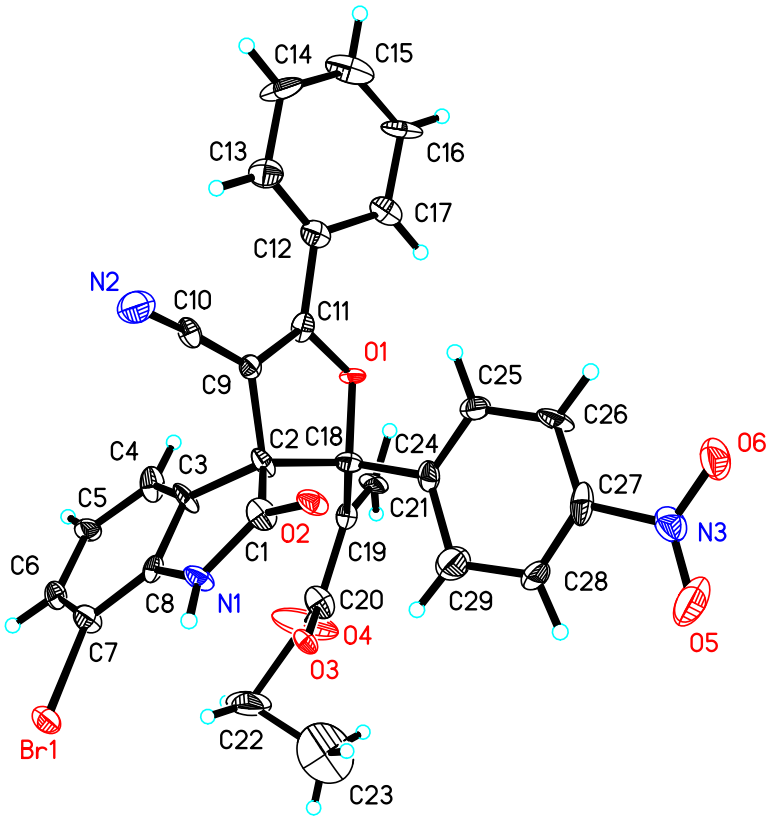


AD-H, 230 nm
hexane/iPrOH = 60:40
0.7 mL/min

Translation: Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column [λ = 230 nm; eluent: Hexane/Isopropanol = 60/40; Flow rate: 0.70 mL/min; t_{major} = 8.89 min, t_{minor}= 9.56 min; ee% = 81%.

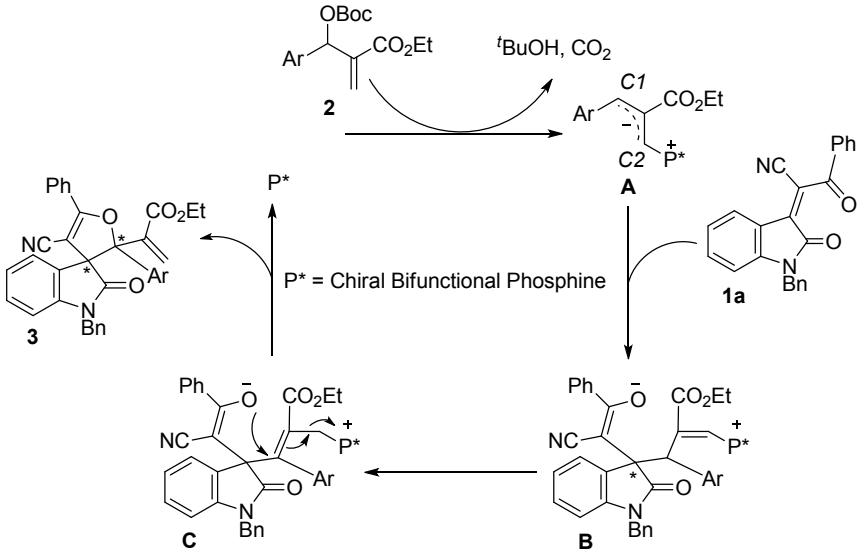


The crystal data of **1c** have been deposited in CCDC with number 991742. Empirical Formula: $C_{19}H_{14}N_2O_3$; Formula Weight: 318.32; Crystal Color, Habit: colorless, Crystal Dimensions: 0.176 x 0.123 x 0.105 mm; Crystal System: Orthorhombic; Lattice Parameters: a = 16.678(2)Å, b = 25.506(2)Å, c = 7.5764(8)Å, $\alpha = 90^o$, $\beta = 90^o$, $\gamma = 90^o$, V = 3223.0(6)Å^3; Space group: Iba2 : Z = 8; D_{calc}= 1.312 g/cm^3; F_{000} = 1328; Final R induces [I>2sigma(I)]: R1 = 0.0513; wR2 = 0.1164.



The crystal data of **3i** have been deposited in CCDC with number 990849. Empirical Formula: $C_{30}H_{22}BrCl_2N_3O_6$; Formula Weight: 671.31; Crystal Color, Habit: colorless, Crystal Dimensions: 0.280 x 0.120 x 0.050 mm; Crystal System: Orthorhombic; Lattice Parameters: a = 13.3390(14)Å, b = 15.360(16)Å, c = 30.918(3)Å, α = 90°, β = 90°, γ = 90°, V = 6334.7(11)Å^3; Space group: P2(1)2(1)2(1) : Z = 8; D_{calc}= 1.408 g/cm^3; F_{000} = 2720; Final R induces [I>2sigma(I)]: R1 = 0.0929; wR2 = 0.2276.

Initially the chiral bifunctional phosphine **TP6** attacks from *β* position of MBH carbonates **2** to take off carbon dioxide and *tert*-butyl alcohol, producing phosphorus ylide **A**, which undergoes the nucleophilic attack with α,β-unsaturated ketone **1a** to give the corresponding intermediate **B**. Subsequent hydrogen transfer produces **C**, which is followed by Michael addition and elimination of chiral bifunctional phosphine **TP6** to produce **3**. The possible transition states illustrated in Figure 1 may account for the observed stereochemical outcome. Presumably, the zwitterionic intermediate **A** is favored to approach **1a** *via* the *re*-face due to less steric hindrance of thiourea moiety in **TP6** with α,β-unsaturated ketone **1a** derived from isatin.



Scheme 1. A Proposed Mechanism

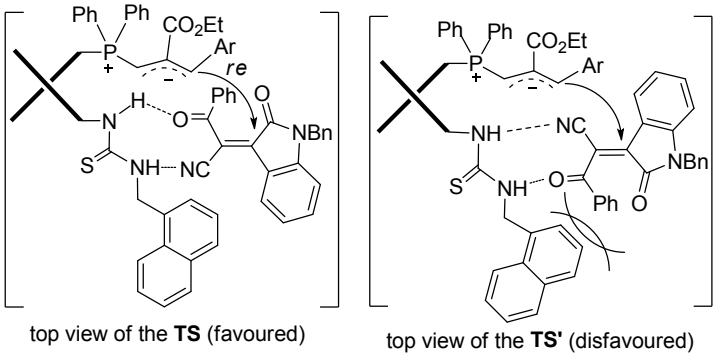


Figure 1. A plausible transition state

References

1. (a) Y.-L. Yang, C.-K. Pei and M. Shi, *Org. Biomol. Chem*., 2011, **9**, 3349; (b) D.-P. Deng, Y. Wei and M. Shi, *Eur. J. Org. Chem.* 2011, 1956; (c) D.-P. Deng and M. Shi, *Eur. J. Org. Chem.* 2012, 183; (d) X. Y. Han, Y. Q. Wang, F. R. Zhong and Y. X. Lu, *J. Am. Chem. Soc.* 2011, **133**, 1726; (e) X.-N. Zhang, G.-Q. Chen, X. Dong, Y. Wei and M. Shi, *Adv. Synth. Catal.*, 2013, **355**, 3351.