

**Enantioselective Synthesis of Spiro-oxindole-based 3,4-Dihydropyrroles via a
Michael/Cyclization Cascade of 3-Aminooxindoles with 2-Enoylpyridines**

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Supporting Information

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1. General remarks

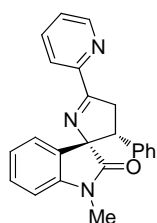
Reagents were purchased from commercial sources and were directly used unless otherwise noted. Catalysts **3a-d** were purchased from commercial sources [Daicel Chiral Technologies (China) Co., LTD]. Catalysts **3e-h** were prepared according to the known methods.^{1,2} Substrates **1** were prepared according to the known method.³ ¹H NMR and ¹³C NMR (400 and 100 MHz, respectively) spectra were recorded in CDCl₃. ¹H NMR chemical shifts are reported in ppm relative to tetramethylsilane (TMS) with the solvent resonance employed as the internal standard (CDCl₃ at 7.26 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet and m = multiplet), coupling constants (Hz) and integration. ¹³C NMR chemical shifts are reported in ppm relative to tetramethylsilane (TMS) with the solvent resonance as the internal standard (CDCl₃ at 77.16 ppm).

2. General procedure for the synthesis of compounds **4**, **5** and **8**

In a 5 mL of flame-dried vial with a stir bar, the mixture of 3-aminooxindoles **1** (0.2 mmol), 2-enoylpyridines **2** (0.3 mmol, 1.5 equiv.), Catalyst **3f** (0.02 mmol, 11.3 mg) in 2.0 mL of CH₂Cl₂ was stirred at 25 °C for the specified time. After completion of the reaction indicated by TLC, the mixture was directly purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 5:1~3:1) to afford the compounds **4**.

Then the mixture with compounds **4** and concentrated hydrochloric acid (10 equiv.) in 5.0 mL of MeOH was refluxed at 90 °C for 2 h. After completion of the reaction indicated by TLC, the mixture was added water (10 mL) and the pH was adjusted to 9 with saturated sodium bicarbonate solution. Then the mixture was extracted with EtOAc (5 mL × 4). After being dried over anhydrous Na₂SO₄, the mixture was concentrated, and the residue was purified by flash column chromatography (petroleum ether/ethyl acetate = 4:1~2:1) to give the products **5**.

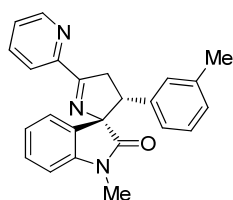
The procedure for the synthesis of compound **8** was similar with the above performance.



(2'S,3'R)-1-methyl-3'-phenyl-5'-(pyridin-2-yl)-3',4'-dihydrospiro[indoline-3,2'-pyrrol]-2-one 5a: Light yellow solid; 56.5 mg, 80% yield; 97:3 dr, >99% ee; $[\alpha]_D^{25} = -109.8$ (*c* 1.00, CHCl₃); mp 64.5-65.9 °C. The ee was determined by HPLC (Chiralpak AD-H, *i*-PrOH/hexane = 30/70, flow rate 1.0 mL/min, $\lambda = 254$

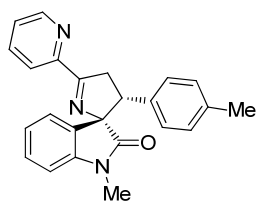
nm, major diastereomer: $t_{\text{minor}} = 5.8$ min, $t_{\text{major}} = 23.3$ min). ¹H NMR (400 MHz, CDCl₃): δ 2.84 (d,

$J = 1.8$ Hz, 3H), 3.82-3.89 (m, 1H), 4.01-4.11 (m, 2H), 6.71 (d, $J = 7.8$ Hz, 1H), 7.00-7.02 (m, 2H), 7.13-7.19 (m, 4H), 7.32-7.41 (m, 2H), 7.44 (d, $J = 7.3$ Hz, 1H), 7.74-7.78 (m, 1H), 8.23-8.25 (m, 1H), 8.71-8.73 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 26.0, 39.4, 54.7, 85.8, 108.2, 122.7, 123.2, 123.9, 125.5, 127.3, 127.7, 128.2, 129.6, 130.8, 135.7, 136.6, 144.4, 149.3, 152.6, 173.7, 180.3. HRMS (ESI-TOF) calcd. for $\text{C}_{23}\text{H}_{20}\text{N}_3\text{O}$ $[\text{M} + \text{H}]^+$ 354.1601; found: 354.1606.



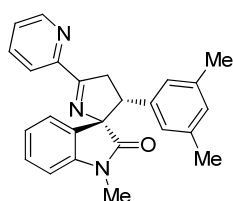
(2'S,3'R)-1-methyl-5'-(pyridin-2-yl)-3'-(*m*-tolyl)-3',4'-dihydrospiro[indoline-3,2'-pyrrol]-2-one 5b: White solid; 50.0 mg, 68% yield; >99:1 dr, >99% ee; $[\alpha]_{\text{D}}^{25} = -49.6$ (c 1.00, CHCl_3); mp 79.8-81.2 °C. The ee was determined by HPLC (Chiralpak OD-H, *i*-PrOH/hexane = 20/80, flow rate 1.0 mL/min,

$\lambda = 254$ nm, major diastereomer: $t_{\text{major}} = 27.2$ min). ^1H NMR (400 MHz, CDCl_3): δ 2.19 (s, 3H), 2.87 (s, 3H), 3.81-3.87 (m, 1H), 3.99-4.08 (m, 2H), 6.73 (d, $J = 7.8$ Hz, 1H), 6.78 (d, $J = 7.6$ Hz, 1H), 6.82 (s, 1H), 6.96 (d, $J = 7.4$ Hz, 1H), 7.01-7.04 (m, 1H), 7.16-7.20 (m, 1H), 7.33-7.36 (m, 1H), 7.37-7.41 (m, 1H), 7.43 (d, $J = 7.3$ Hz, 1H), 7.74-7.78 (m, 1H), 8.22-8.24 (m, 1H), 8.72-8.73 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 21.5, 26.0, 39.5, 54.5, 85.8, 108.1, 122.7, 123.2, 123.9, 124.6, 125.5, 128.0, 128.1, 128.5, 129.6, 131.0, 135.8, 136.5, 137.7, 144.5, 149.3, 152.7, 173.8, 180.4. HRMS (ESI-TOF) calcd. for $\text{C}_{24}\text{H}_{22}\text{N}_3\text{O}$ $[\text{M} + \text{H}]^+$ 368.1757; found: 368.1762.



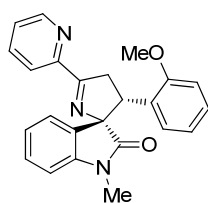
(2'S,3'R)-1-methyl-5'-(pyridin-2-yl)-3'-(*p*-tolyl)-3',4'-dihydrospiro[indoline-3,2'-pyrrol]-2-one 5c: White solid; 41.2 mg, 56% yield; >99:1 dr, >99% ee; $[\alpha]_{\text{D}}^{25} = -87.6$ (c 1.00, CHCl_3); mp 74.1-75.3 °C. The ee was determined by HPLC (Chiralpak OD-H, *i*-PrOH/hexane = 30/70, flow

rate 1.0 mL/min, $\lambda = 254$ nm, major diastereomer: $t_{\text{major}} = 15.8$ min). ^1H NMR (400 MHz, CDCl_3): δ 2.24 (d, $J = 5.1$ Hz, 3H), 2.86-2.88 (m, 3H), 3.80-3.88 (m, 1H), 3.98-4.08 (m, 2H), 6.71-6.74 (m, 1H), 6.89-6.97 (m, 4H), 7.14-7.20 (m, 1H), 7.32-7.45 (m, 3H), 7.73-7.79 (m, 1H), 8.22-8.25 (m, 1H), 8.71-8.73 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 21.1, 26.0, 39.6, 54.3, 85.7, 108.2, 122.7, 123.2, 123.9, 125.5, 127.5, 128.9, 129.5, 130.9, 132.6, 136.6, 136.8, 144.4, 149.2, 152.6, 173.8, 180.3. HRMS (ESI-TOF) calcd. for $\text{C}_{24}\text{H}_{22}\text{N}_3\text{O}$ $[\text{M} + \text{H}]^+$ 368.1757; found: 368.1754.



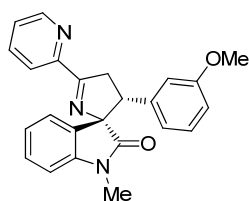
(2'S,3'R)-3'-(3,5-dimethylphenyl)-1-methyl-5'-(pyridin-2-yl)-3',4'-dihydrospiro[indoline-3,2'-pyrrol]-2-one 5d: Light yellow solid; 43.5 mg, 57% yield; >99:1 dr, 98% ee; $[\alpha]_{\text{D}}^{25} = -58.8$ (c 0.40, CHCl_3); mp 153.5-155.0 °C.

The ee was determined by HPLC (Chiralpak OD-H, *i*-PrOH/hexane = 30/70, flow rate 0.8 mL/min, $\lambda = 254$ nm, major diastereomer: $t_{\text{minor}} = 4.6$ min, $t_{\text{major}} = 19.6$ min). ^1H NMR (400 MHz, CDCl_3): δ 2.14 (s, 6H), 2.87-2.88 (m, 3H), 3.78-3.85 (m, 1H), 3.98-4.05 (m, 2H), 6.60 (s, 2H), 6.73 (d, $J = 7.8$ Hz, 1H), 6.77 (s, 1H), 7.15-7.19 (m, 1H), 7.32-7.39 (m, 2H), 7.42 (d, $J = 7.3$ Hz, 1H), 7.72-7.76 (m, 1H), 8.22 (d, $J = 7.9$ Hz, 1H), 8.71-8.72 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 21.3, 26.0, 39.5, 54.3, 85.7, 108.0, 122.6, 123.1, 123.9, 125.4, 128.8, 129.5, 131.1, 135.9, 136.5, 137.4, 144.5, 149.3, 152.7, 173.7, 180.3. HRMS (ESI-TOF) calcd. for $\text{C}_{25}\text{H}_{24}\text{N}_3\text{O}$ [$\text{M} + \text{H}$] $^+$ 382.1914; found: 382.1906.



(2'S,3'R)-3'-(2-methoxyphenyl)-1-methyl-5'-(pyridin-2-yl)-3',4'-dihydrospiro[indoline-3,2'-pyrrol]-2-one 5e: White solid; 65.0 mg, 85% yield; >99:1 dr, >99% ee; $[\alpha]_{\text{D}}^{25} = -169.6$ (c 1.00, CHCl_3); mp 65.7-67.2 °C. The ee was determined by HPLC (Chiralpak OD-H, *i*-PrOH/hexane = 30/70, flow rate

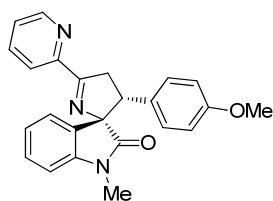
1.0 mL/min, $\lambda = 254$ nm, major diastereomer: $t_{\text{major}} = 12.2$ min). ^1H NMR (400 MHz, CDCl_3): δ 2.87 (d, $J = 1.2$ Hz, 3H), 3.19 (d, $J = 1.2$ Hz, 3H), 3.79 (dd, $J = 8.9$ Hz, 17.3 Hz, 1H), 4.00 (dd, $J = 11.6$ Hz, 17.3 Hz, 1H), 4.69 (t, $J = 10.2$ Hz, 1H), 6.60 (d, $J = 8.2$ Hz, 1H), 6.67 (d, $J = 7.8$ Hz, 1H), 6.87-6.91 (m, 1H), 7.09-7.14 (m, 2H), 7.23-7.27 (m, 1H), 7.37-7.43 (m, 2H), 7.58 (d, $J = 7.8$ Hz, 1H), 7.74-7.78 (m, 1H), 8.25 (d, $J = 7.8$ Hz, 1H), 8.71-8.72 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 26.0, 40.3, 46.0, 54.7, 85.6, 107.6, 110.0, 120.3, 122.6, 122.8, 124.4, 125.5, 128.0, 128.5, 128.8, 131.5, 136.6, 144.0, 149.2, 152.6, 157.7, 174.1, 180.1. HRMS (ESI-TOF) calcd. for $\text{C}_{24}\text{H}_{22}\text{N}_3\text{O}_2$ [$\text{M} + \text{H}$] $^+$ 384.1707; found: 384.1705.



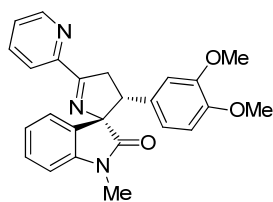
(2'S,3'R)-3'-(3-methoxyphenyl)-1-methyl-5'-(pyridin-2-yl)-3',4'-dihydrospiro[indoline-3,2'-pyrrol]-2-one 5f: Colourless oil; 46.8 mg, 61% yield; >99:1 dr, >99% ee; $[\alpha]_{\text{D}}^{25} = -136.7$ (c 1.00, CHCl_3). The ee was determined by HPLC (Chiralpak OD-H, *i*-PrOH/hexane = 30/70, flow rate

1.0 mL/min, $\lambda = 254$ nm, major diastereomer: $t_{\text{major}} = 16.1$ min). ^1H NMR (400 MHz, CDCl_3): δ 2.87 (s, 3H), 3.58 (s, 3H), 3.81-3.89 (m, 1H), 3.98-4.09 (m, 2H), 6.48 (s, 1H), 6.64 (d, $J = 7.7$ Hz, 1H), 6.68-6.70 (m, 1H), 6.73 (d, $J = 7.8$ Hz, 1H), 7.04-7.08 (m, 1H), 7.15-7.19 (m, 1H), 7.32-7.36 (m, 1H), 7.37-7.40 (m, 1H), 7.43 (d, $J = 7.3$ Hz, 1H), 7.73-7.78 (m, 1H), 8.22-8.24 (m, 1H), 8.71-8.73 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 26.1, 39.4, 54.6, 55.0, 85.7, 108.2, 112.6, 113.5, 119.9, 122.8, 123.2, 123.9, 125.6, 129.2, 129.6, 130.8, 136.7, 137.4, 144.5, 149.2, 152.5,

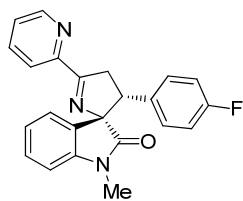
159.2, 173.6, 180.2. HRMS (ESI-TOF) calcd. for C₂₄H₂₂N₃O₂ [M + H]⁺ 384.1707; found: 384.1711.



(2'S,3'R)-3'-(4-methoxyphenyl)-1-methyl-5'-(pyridin-2-yl)-3',4'-dihydrospiro[indoline-3,2'-pyrrol]-2-one 5g: Yellow oil; 59.1 mg, 77% yield; 99:1 dr, 85% ee; $[\alpha]_D^{25} = -49.4$ (*c* 1.00, CHCl₃). The ee was determined by HPLC (Chiralpak AD-H, *i*-PrOH/hexane = 30/70, flow rate 1.0 mL/min, $\lambda = 254$ nm, major diastereomer: $t_{\text{minor}} = 8.9$ min, $t_{\text{major}} = 29.0$ min). ¹H NMR (400 MHz, CDCl₃): δ 2.87 (s, 3H), 3.72 (s, 3H), 3.78-3.86 (m, 1H), 3.95-4.06 (m, 2H), 6.68 (d, *J* = 8.2 Hz, 2H), 6.72 (d, *J* = 7.8 Hz, 1H), 6.94 (d, *J* = 8.5 Hz, 2H), 7.14-7.18 (m, 1H), 7.31-7.36 (m, 1H), 7.37-7.40 (m, 1H), 7.41-7.43 (m, 1H), 7.73-7.77 (m, 1H), 8.21-8.24 (m, 1H), 8.71-8.72 (m, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 26.1, 39.7, 54.1, 55.2, 85.8, 108.2, 113.5, 122.7, 123.2, 123.9, 125.5, 127.7, 128.7, 129.6, 130.8, 136.6, 144.4, 149.3, 152.6, 158.7, 173.9, 180.4. HRMS (ESI-TOF) calcd. for C₂₄H₂₂N₃O₂ [M + H]⁺ 384.1707; found: 384.1708.

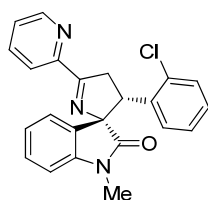


(2'S,3'R)-3'-(3,4-dimethoxyphenyl)-1-methyl-5'-(pyridin-2-yl)-3',4'-dihydrospiro[indoline-3,2'-pyrrol]-2-one 5h: White solid; 46.3 mg, 56% yield; >99:1 dr, >99% ee; $[\alpha]_D^{25} = -63.2$ (*c* 1.00, CHCl₃); mp 79.0-80.2 °C. The ee was determined by HPLC (Chiralpak OD-H, *i*-PrOH/hexane = 30/70, flow rate 1.0 mL/min, $\lambda = 254$ nm, major diastereomer: $t_{\text{major}} = 25.7$ min). ¹H NMR (400 MHz, CDCl₃): δ 2.87 (s, 3H), 3.54 (s, 3H), 3.79-3.85 (m, 4H), 3.95-4.05 (m, 2H), 6.35 (s, 1H), 6.68-6.73 (m, 3H), 7.15-7.19 (m, 1H), 7.32-7.40 (m, 2H), 7.44 (d, *J* = 7.3 Hz, 1H), 7.74-7.78 (m, 1H), 8.23 (d, *J* = 7.8 Hz, 1H), 8.72 (d, *J* = 4.4 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 26.1, 39.3, 54.4, 54.5, 55.8, 85.7, 108.1, 110.6, 110.7, 119.5, 122.7, 123.2, 124.0, 125.5, 128.1, 129.6, 130.9, 136.6, 144.6, 148.0, 148.2, 149.2, 152.6, 173.7, 180.4. HRMS (ESI-TOF) calcd. for C₂₅H₂₄N₃O₃ [M + H]⁺ 414.1812; found: 414.1815.



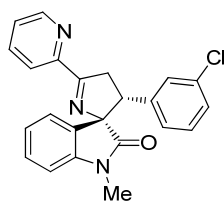
(2'S,3'R)-3'-(4-fluorophenyl)-1-methyl-5'-(pyridin-2-yl)-3',4'-dihydrospiro[indoline-3,2'-pyrrol]-2-one 5i: Yellow oil; 53.5 mg, 72% yield; >99:1 dr, >99% ee; $[\alpha]_D^{25} = -85.7$ (*c* 1.00, CHCl₃). The ee was determined by HPLC (Chiralpak OD-H, *i*-PrOH/hexane = 20/80, flow rate 1.0 mL/min, $\lambda = 254$ nm, major diastereomer: $t_{\text{major}} = 16.9$ min). ¹H NMR (400 MHz, CDCl₃): δ 2.86 (s, 3H), 3.83 (dd, *J* = 7.0 Hz, 15.2 Hz, 1H), 3.94-4.06 (m, 2H), 6.72 (d, *J* = 7.8 Hz, 1H),

6.80-6.84 (m, 2H), 6.96-6.99 (m, 2H), 7.15-7.18 (m, 1H), 7.32-7.43 (m, 3H), 7.73-7.77 (m, 1H), 8.22 (d, $J = 7.9$ Hz, 1H), 8.71 (d, $J = 4.5$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 26.0, 39.8, 54.0, 85.8, 108.3, 115.0 (d, $J = 21.1$ Hz, 1C), 122.7, 123.3, 123.9, 125.6, 129.3 (d, $J = 7.9$ Hz, 1C), 129.7, 130.5, 131.4 (d, $J = 3.2$ Hz, 1C), 136.7, 144.3, 149.2, 152.4, 162.1 (d, $J = 244.4$ Hz, 1C), 173.6, 180.2. HRMS (ESI-TOF) calcd. for $\text{C}_{23}\text{H}_{19}\text{FN}_3\text{O}$ $[\text{M} + \text{H}]^+$ 372.1507; found: 372.1514.



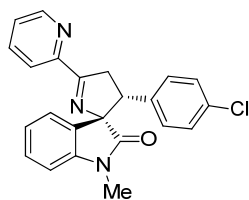
(2'S,3'R)-3'-(2-chlorophenyl)-1-methyl-5'-(pyridin-2-yl)-3',4'-dihydrospiro
of[indoline-3,2'-pyrrol]-2-one 5j: Yellow oil; 47.3 mg, 61% yield; >99:1
 dr, >99% ee; $[\alpha]_{\text{D}}^{25} = -63.1$ (c 1.00, CHCl_3). The ee was determined by HPLC
 (Chiralpak AD-H, *i*-PrOH/hexane = 10/90, flow rate 0.8 mL/min, $\lambda = 254$ nm,

major diastereomer: $t_{\text{major}} = 45.9$ min). ^1H NMR (400 MHz, CDCl_3): δ 2.94 (s, 3H), 3.92 (d, $J = 9.9$ Hz, 2H), 4.76 (t, $J = 9.9$ Hz, 1H), 6.70 (d, $J = 7.8$ Hz, 1H), 7.07-7.13 (m, 2H), 7.16-7.18 (m, 1H), 7.19-7.23 (m, 1H), 7.28-7.32 (m, 1H), 7.39-7.45 (m, 2H), 7.72-7.75 (m, 1H), 7.76-7.80 (m, 1H), 8.25 (d, $J = 8.0$ Hz, 1H), 8.71-8.72 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 26.2, 42.3, 48.9, 85.9, 108.1, 122.9, 123.0, 125.0, 125.6, 126.7, 128.4, 129.4, 129.5, 129.8, 130.2, 134.0, 134.9, 136.8, 143.9, 149.2, 152.4, 173.9, 179.7. HRMS (ESI-TOF) calcd. for $\text{C}_{23}\text{H}_{19}\text{ClN}_3\text{O}$ $[\text{M} + \text{H}]^+$ 388.1211; found: 388.1205.



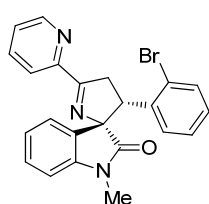
(2'S,3'R)-3'-(3-chlorophenyl)-1-methyl-5'-(pyridin-2-yl)-3',4'-dihydrospiro
ro[indoline-3,2'-pyrrol]-2-one 5k: White solid; 59.0 mg, 76% yield; 98:2
 dr, >99% ee; $[\alpha]_{\text{D}}^{25} = -120.1$ (c 1.00, CHCl_3); mp 63.9-65.1 °C. The ee was
 determined by HPLC (Chiralpak AD-H, *i*-PrOH/hexane = 30/70, flow rate

1.0 mL/min, $\lambda = 254$ nm, major diastereomer: $t_{\text{major}} = 21.1$ min). ^1H NMR (400 MHz, CDCl_3): δ 2.88 (s, 3H), 3.84 (dd, $J = 6.0$ Hz, 14.1 Hz, 1H), 3.94-4.05 (m, 2H), 6.75 (d, $J = 7.8$ Hz, 1H), 6.91-6.96 (m, 2H), 7.05-7.13 (m, 2H), 7.15-7.19 (m, 1H), 7.33-7.42 (m, 3H), 7.72-7.76 (m, 1H), 8.21 (d, $J = 7.9$ Hz, 1H), 8.70 (d, $J = 4.5$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 26.0, 39.6, 54.0, 85.6, 108.3, 122.7, 123.4, 123.8, 125.6, 125.8, 127.4, 128.0, 129.4, 129.8, 130.4, 133.9, 136.6, 138.2, 144.3, 149.2, 152.4, 173.4, 179.9. HRMS (ESI-TOF) calcd. for $\text{C}_{23}\text{H}_{19}\text{ClN}_3\text{O}$ $[\text{M} + \text{H}]^+$ 388.1211; found: 388.1213.



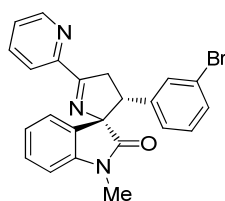
(2'S,3'R)-3'-(4-chlorophenyl)-1-methyl-5'-(pyridin-2-yl)-3',4'-dihydrospiro
piro[indoline-3,2'-pyrrol]-2-one 5l: White solid; 63.6 mg, 82%

yield; >99:1 dr, >99% ee; $[\alpha]_D^{25} = -58.8$ (*c* 1.00, CHCl₃); mp 77.5-78.6 °C. The ee was determined by HPLC (Chiralpak OD-H, *i*-PrOH/hexane = 30/70, flow rate 1.0 mL/min, $\lambda = 254$ nm, major diastereomer: $t_{\text{major}} = 13.2$ min). ¹H NMR (400 MHz, CDCl₃): δ 2.87 (d, *J* = 4.1 Hz, 3H), 3.81-3.89 (m, 1H), 3.95-4.04 (m, 2H), 6.72-6.74 (m, 1H), 6.94-6.96 (m, 2H), 7.10-7.19 (m, 3H), 7.33-7.42 (m, 3H), 7.74-7.77 (m, 1H), 8.21-8.23 (m, 1H), 8.70 (s, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 26.0, 39.6, 54.0, 85.7, 108.3, 122.6, 123.3, 123.8, 125.5, 128.3, 129.1, 129.7, 130.4, 133.0, 134.4, 136.5, 144.3, 149.3, 152.4, 173.5, 180.1. HRMS (ESI-TOF) calcd. for C₂₃H₁₉ClN₃O [M + H]⁺ 388.1211; found: 388.1220.



(2'*S*,3'*R*)-3'-(2-bromophenyl)-1-methyl-5'-(pyridin-2-yl)-3',4'-dihydrospiro[indoline-3,2'-pyrrol]-2-one 5m: White solid; 75.2 mg, 87% yield; >99:1 dr, 99% ee; $[\alpha]_D^{25} = -163.1$ (*c* 1.00, CHCl₃); mp 160.7-162.2 °C. The ee was determined by HPLC (Chiralpak AD-H, *i*-PrOH/hexane = 30/70, flow rate 1.0

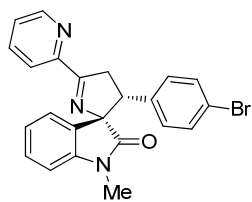
mL/min, $\lambda = 254$ nm, major diastereomer: $t_{\text{minor}} = 8.2$ min, $t_{\text{major}} = 12.9$ min). ¹H NMR (400 MHz, CDCl₃): δ 2.94 (s, 3H), 3.87 (dd, *J* = 10.4 Hz, 17.6 Hz, 1H), 3.95 (dd, *J* = 9.0 Hz, 17.6 Hz, 1H), 4.74 (t, *J* = 9.7 Hz, 1H), 6.69 (d, *J* = 7.8 Hz, 1H), 6.98-7.02 (m, 1H), 7.08-7.12 (m, 1H), 7.22-7.24 (m, 1H), 7.27-7.31 (m, 1H), 7.35-7.40 (m, 2H), 7.44 (d, *J* = 7.3 Hz, 1H), 7.71-7.77 (m, 2H), 8.24 (d, *J* = 8.0 Hz, 1H), 8.69-8.71 (m, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 26.2, 42.7, 51.4, 86.0, 108.1, 122.7, 122.9, 125.2, 125.5, 125.7, 127.3, 128.7, 129.5, 130.0, 130.1, 132.8, 135.9, 136.6, 143.8, 149.2, 152.4, 173.9, 179.6. HRMS (ESI-TOF) calcd. for C₂₃H₁₉BrN₃O [M + H]⁺ 432.0706; found: 432.0703.



(2'*S*,3'*R*)-3'-(3-bromophenyl)-1-methyl-5'-(pyridin-2-yl)-3',4'-dihydrospiro[indoline-3,2'-pyrrol]-2-one 5n: White solid; 51.9 mg, 60% yield; >99:1 dr, >99% ee; $[\alpha]_D^{25} = -129.3$ (*c* 1.00, CHCl₃); mp 73.1-74.6 °C. The ee was determined by HPLC (Chiralpak OD-H, *i*-PrOH/hexane = 30/70,

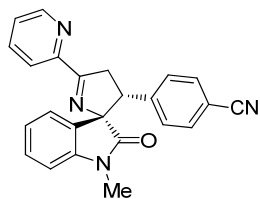
flow rate 1.0 mL/min, $\lambda = 254$ nm, major diastereomer: $t_{\text{major}} = 13.8$ min). ¹H NMR (400 MHz, CDCl₃): δ 2.89 (s, 3H), 3.82-3.90 (m, 1H), 3.94-4.04 (m, 2H), 6.76 (d, *J* = 7.8 Hz, 1H), 6.96-7.04 (m, 2H), 7.10 (s, 1H), 7.16-7.20 (m, 1H), 7.26-7.29 (m, 1H), 7.34-7.42 (m, 3H), 7.73-7.77 (m, 1H), 8.22 (d, *J* = 7.9 Hz, 1H), 8.71 (d, *J* = 4.2 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 26.1, 39.5, 53.9, 85.6, 108.3, 122.2, 122.7, 123.4, 123.8, 125.6, 126.2, 129.7, 129.9, 130.4, 130.9, 136.7, 138.4, 144.3, 149.2, 152.3, 173.4, 179.9. HRMS (ESI-TOF) calcd. for C₂₃H₁₉BrN₃O [M + H]⁺ 432.0706;

found: 432.0705.



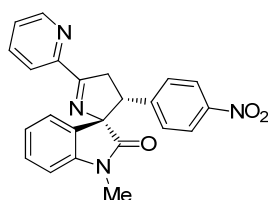
(2'S,3'R)-3'-(4-bromophenyl)-1-methyl-5'-(pyridin-2-yl)-3',4'-dihydro spiro[indoline-3,2'-pyrrol]-2-one 5o: White solid; 63.6 mg, 73% yield; >99:1 dr, >99% ee; $[\alpha]_D^{25} = -55.8$ (*c* 1.00, CHCl₃); mp 79.8-81.2 °C.

The ee was determined by HPLC (Chiralpak OD-H, *i*-PrOH/hexane = 20/80, flow rate 1.0 mL/min, $\lambda = 254$ nm, major diastereomer: $t_{\text{major}} = 21.4$ min). ¹H NMR (400 MHz, CDCl₃): δ 2.90 (s, 3H), 3.99-4.09 (m, 3H), 6.76 (d, *J* = 7.7 Hz, 1H), 6.89 (d, *J* = 8.3 Hz, 2H), 7.17-7.21 (m, 1H), 7.27 (d, *J* = 9.8 Hz, 2H), 7.35-7.39 (m, 1H), 7.43 (d, *J* = 7.4 Hz, 1H), 7.51-7.54 (m, 1H), 7.88-7.92 (m, 1H), 8.38 (d, *J* = 7.9 Hz, 1H), 8.79 (d, *J* = 4.5 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 26.0, 39.6, 54.0, 85.6, 108.3, 121.2, 122.6, 123.3, 123.8, 125.6, 129.4, 129.7, 130.3, 131.2, 134.8, 136.6, 144.3, 149.2, 152.3, 173.5, 180.0. HRMS (ESI-TOF) calcd. for C₂₃H₁₉BrN₃O [M + H]⁺ 432.0706; found: 432.0699.



4-((2'S,3'R)-1-methyl-2-oxo-5'-(pyridin-2-yl)-3',4'-dihydro spiro[indoline-3,2'-pyrrol]-3'-yl)benzotrile 5p: Light yellow solid; 43.9 mg, 58% yield; >99:1 dr, >99% ee; $[\alpha]_D^{25} = -69.1$ (*c* 1.00, CHCl₃); mp 192.7-194.2 °C. The ee was determined by HPLC (Chiralpak OD-H, *i*-PrOH/hexane =

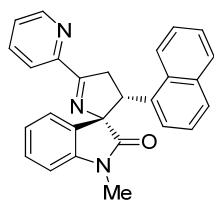
30/70, flow rate 0.8 mL/min, $\lambda = 254$ nm, major diastereomer: $t_{\text{minor}} = 16.6$ min, $t_{\text{major}} = 27.8$ min). ¹H NMR (400 MHz, CDCl₃): δ 2.86 (s, 3H), 3.88 (dd, *J* = 8.1 Hz, 16.3 Hz, 1H), 3.95-4.05 (m, 1H), 4.06-4.11 (m, 1H), 6.75 (d, *J* = 7.8 Hz, 1H), 7.11 (d, *J* = 8.1 Hz, 2H), 7.17-7.20 (m, 1H), 7.35-7.44 (m, 5H), 7.74-7.79 (m, 1H), 8.21 (d, *J* = 7.9 Hz, 1H), 8.71 (d, *J* = 4.7 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 26.1, 39.5, 54.4, 85.9, 108.5, 111.2, 118.8, 122.7, 123.5, 123.9, 125.7, 128.6, 130.0, 132.0, 136.7, 141.7, 144.2, 149.3, 152.2, 173.3, 179.8. HRMS (ESI-TOF) calcd. for C₂₄H₁₉N₄O [M + H]⁺ 379.1553; found: 379.1558.



(2'S,3'R)-1-methyl-3'-(4-nitrophenyl)-5'-(pyridin-2-yl)-3',4'-dihydro spiro[indoline-3,2'-pyrrol]-2-one 5q: Yellow oil; 45.4 mg, 57% yield; >99:1 dr, >99% ee; $[\alpha]_D^{25} = -46.2$ (*c* 1.00, CHCl₃). The ee was determined by HPLC (Chiralpak OD-H, *i*-PrOH/hexane = 30/70, flow

rate 1.0 mL/min, $\lambda = 254$ nm, major diastereomer: $t_{\text{major}} = 29.2$ min). ¹H NMR (400 MHz, CDCl₃): δ 2.86-2.87 (m, 3H), 3.89-3.95 (m, 1H), 4.02-4.09 (m, 1H), 4.12-4.17 (m, 1H), 6.76 (d, *J* = 7.8 Hz, 1H), 7.17-7.22 (m, 3H), 7.35-7.42 (m, 2H), 7.45 (d, *J* = 7.4 Hz, 1H), 7.75-7.79 (m, 1H), 7.99-8.01

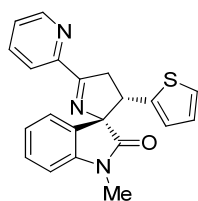
(m, 2H), 8.22 (d, $J = 8.0$ Hz, 1H), 8.71-8.72 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 26.1, 39.7, 54.1, 85.9, 108.5, 122.7, 123.4, 123.6, 123.9, 125.7, 128.7, 130.0, 130.1, 136.6, 143.9, 144.2, 147.2, 149.4, 152.2, 173.2, 179.8. HRMS (ESI-TOF) calcd. for $\text{C}_{23}\text{H}_{19}\text{N}_4\text{O}_3$ $[\text{M} + \text{H}]^+$ 399.1452; found: 399.1451.



(2'S,3'R)-1-methyl-3'-(naphthalen-1-yl)-5'-(pyridin-2-yl)-3',4'-dihydrospiro[indoline-3,2'-pyrrol]-2-one 5r: Yellow oil; 50.0 mg, 62% yield; 90:10

dr, >99% ee; $[\alpha]_{\text{D}}^{25} = -202.2$ (c 1.00, CHCl_3). The ee was determined by HPLC (Chiralpak OD-H, i -PrOH/hexane = 20/80, flow rate 1.0 mL/min, $\lambda =$

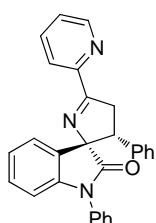
254 nm, major diastereomer: $t_{\text{major}} = 25.0$ min). ^1H NMR (400 MHz, CDCl_3): δ 2.65 (s, 3H), 3.92-4.02 (m, 1H), 4.19 (dd, $J = 10.7$ Hz, 17.6 Hz, 1H), 4.97 (t, $J = 9.8$ Hz, 1H), 6.43-6.45 (m, 1H), 7.05-7.09 (m, 1H), 7.16-7.21 (m, 2H), 7.28 (d, $J = 7.2$ Hz, 1H), 7.40-7.47 (m, 3H), 7.55-7.58 (m, 1H), 7.68 (d, $J = 8.2$ Hz, 1H), 7.72 (d, $J = 8.1$ Hz, 1H), 7.77-7.81 (m, 1H), 7.89 (d, $J = 7.3$ Hz, 1H), 8.30 (d, $J = 7.9$ Hz, 1H), 8.73-8.75 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 25.9, 42.2, 48.8, 86.3, 108.2, 122.8, 123.0, 123.9, 125.1, 125.2, 125.4, 125.5, 125.6, 127.8, 128.2, 128.6, 129.5, 130.9, 131.9, 132.3, 133.6, 136.6, 144.1, 149.3, 152.6, 173.9, 180.3. HRMS (ESI-TOF) calcd. for $\text{C}_{27}\text{H}_{22}\text{N}_3\text{O}$ $[\text{M} + \text{H}]^+$ 404.1757; found: 404.1755.



(2'S,3'S)-1-methyl-5'-(pyridin-2-yl)-3'-(thiophen-2-yl)-3',4'-dihydrospiro[indoline-3,2'-pyrrol]-2-one 5s: White solid; 39.5 mg, 55% yield; >99:1

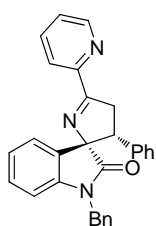
dr, >99% ee; $[\alpha]_{\text{D}}^{25} = -101.3$ (c 1.00, CHCl_3); mp 132.8-134.3 °C. The ee was determined by HPLC (Chiralpak OD-H, i -PrOH/hexane = 30/70, flow rate 1.0

mL/min, $\lambda = 254$ nm, major diastereomer: $t_{\text{major}} = 21.2$ min). ^1H NMR (400 MHz, CDCl_3): δ 2.96 (s, $J = 1.7$ Hz, 3H), 3.96-3.99 (m, 2H), 4.26 (t, $J = 10.1$ Hz, 1H), 6.74-6.75 (m, 1H), 6.79-6.85 (m, 2H), 7.01-7.03 (m, 1H), 7.15-7.19 (m, 1H), 7.36-7.41 (m, 3H), 7.72-7.77 (m, 1H), 8.20 (d, $J = 7.9$ Hz, 1H), 8.70-8.72 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 26.1, 41.2, 49.9, 85.2, 108.3, 122.6, 123.3, 123.9, 124.0, 124.8, 125.6, 126.8, 129.9, 130.2, 136.5, 139.0, 144.8, 149.3, 152.4, 173.3, 179.9. HRMS (ESI-TOF) calcd. for $\text{C}_{21}\text{H}_{18}\text{N}_3\text{OS}$ $[\text{M} + \text{H}]^+$ 360.1165; found: 360.1169.



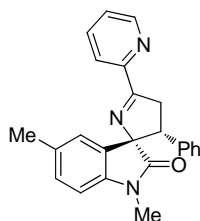
(2'S,3'R)-1,3'-diphenyl-5'-(pyridin-2-yl)-3',4'-dihydrospiro[indoline-3,2'-pyrrol]-2-one 5u: White solid; 50.7 mg, 61% yield; >99:1 dr, >99% ee; $[\alpha]_{\text{D}}^{25} = -121.5$ (c 1.00, CHCl_3); mp 82.9-84.2 °C. The ee was determined by HPLC (Chiralpak

OD-H, *i*-PrOH/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm, major diastereomer: t_{major} = 8.7 min). ^1H NMR (400 MHz, CDCl_3): δ 3.87 (dd, J = 6.9 Hz, 15.4 Hz, 1H), 4.04-4.17 (m, 2H), 6.61 (d, J = 7.6 Hz, 1H), 6.77 (d, J = 7.4 Hz, 2H), 7.07 (d, J = 7.0 Hz, 2H), 7.18-7.35 (m, 8H), 7.39-7.42 (m, 1H), 7.52 (d, J = 7.1 Hz, 1H), 7.76-7.80 (m, 1H), 8.30 (d, J = 7.9 Hz, 1H), 8.74 (d, J = 4.2 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 38.9, 56.1, 86.1, 109.3, 122.7, 123.6, 124.1, 125.6, 126.6, 127.5, 127.8, 128.1, 128.3, 129.5, 130.4, 134.0, 135.5, 136.6, 144.5, 149.3, 152.6, 173.0, 180.8. HRMS (ESI-TOF) calcd. for $\text{C}_{28}\text{H}_{22}\text{N}_3\text{O}$ $[\text{M} + \text{H}]^+$ 416.1757; found: 416.1759.



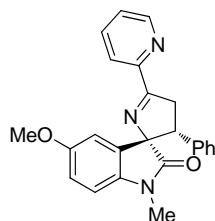
(2'S,3'R)-1-benzyl-3'-phenyl-5'-(pyridin-2-yl)-3',4'-dihydrospiro[indoline-3,2'-pyrrol]-2-one 5v: White solid; 48.1 mg, 56% yield; >99:1 dr, 97% ee; $[\alpha]_{\text{D}}^{25} = +10.7$ (c 1.00, CHCl_3); mp 73.0-74.3 °C. The ee was determined by HPLC (Chiralpak OD-H, *i*-PrOH/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm,

major diastereomer: t_{minor} = 41.4 min, t_{major} = 36.3 min). ^1H NMR (400 MHz, CDCl_3): δ 3.86-3.93 (m, 1H), 4.07-4.17 (m, 2H), 4.22 (d, J = 15.9 Hz, 1H), 5.07 (d, J = 16.0 Hz, 1H), 6.45-6.50 (m, 3H), 7.06-7.10 (m, 2H), 7.12-7.17 (m, 5H), 7.18-7.22 (m, 2H), 7.27-7.30 (m, 1H), 7.38-7.41 (m, 1H), 7.46-7.48 (m, 1H), 7.75-7.79 (m, 1H), 8.26-8.28 (m, 1H), 8.73-8.75 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 39.7, 43.8, 54.8, 85.9, 109.4, 122.8, 123.2, 124.0, 125.6, 126.6, 127.2, 127.5, 128.3, 128.5, 128.6, 129.6, 130.6, 135.1, 135.6, 136.6, 143.6, 149.3, 152.6, 173.9, 180.5. HRMS (ESI-TOF) calcd. for $\text{C}_{29}\text{H}_{24}\text{N}_3\text{O}$ $[\text{M} + \text{H}]^+$ 431.1914; found: 431.1914.



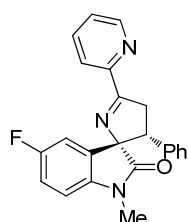
(2'S,3'R)-1,5-dimethyl-3'-phenyl-5'-(pyridin-2-yl)-3',4'-dihydrospiro[indoline-3,2'-pyrrol]-2-one 5w: Light yellow solid; 41.9 mg, 57% yield; 96:4 dr, >99% ee; $[\alpha]_{\text{D}}^{25} = -122.6$ (c 1.00, CHCl_3); mp 66.8-67.9 °C. The ee was determined by HPLC (Chiralpak OD-H, *i*-PrOH/hexane = 30/70, flow rate 1.0

mL/min, λ = 254 nm, major diastereomer: t_{major} = 12.9 min). ^1H NMR (400 MHz, CDCl_3): δ 2.39 (s, 3H), 2.83 (s, 3H), 3.83-3.90 (m, 1H), 4.00-4.10 (m, 2H), 6.61 (d, J = 7.9 Hz, 1H), 7.02-7.03 (m, 2H), 7.13-7.15 (m, 4H), 7.26 (s, 1H), 7.38-7.41 (m, 1H), 7.75-7.79 (m, 1H), 8.26 (d, J = 7.9 Hz, 1H), 8.73 (d, J = 4.5 Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 21.4, 26.0, 39.5, 54.6, 85.9, 108.0, 122.9, 124.7, 125.6, 127.3, 127.7, 128.2, 129.9, 130.7, 132.8, 135.9, 136.7, 142.1, 149.2, 152.5, 173.6, 180.2. HRMS (ESI-TOF) calcd. for $\text{C}_{24}\text{H}_{22}\text{N}_3\text{O}$ $[\text{M} + \text{H}]^+$ 368.1757; found: 368.1760.



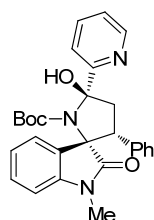
(2'S,3'R)-5-methoxy-1-methyl-3'-phenyl-5'-(pyridin-2-yl)-3',4'-dihydrospiro[indoline-3,2'-pyrrol]-2-one 5x: Light yellow solid; 48.0 mg, 63% yield; >99:1 dr, >99% ee; $[\alpha]_{\text{D}}^{25} = -83.8$ (*c* 1.00, CHCl_3); mp 69.0-70.2 °C.

The ee was determined by HPLC (Chiralpak OD-H, *i*-PrOH/hexane = 30/70, flow rate 1.0 mL/min, $\lambda = 254$ nm, major diastereomer: $t_{\text{major}} = 17.7$ min). ^1H NMR (400 MHz, CDCl_3): δ 2.82 (s, 3H), 3.84-3.88 (m, 4H), 4.00-4.08 (m, 2H), 6.63 (d, $J = 8.5$ Hz, 1H), 6.87 (d, $J = 8.4$ Hz, 1H), 7.02-7.06 (m, 3H), 7.14-7.15 (m, 3H), 7.38-7.41 (m, 1H), 7.75-7.78 (m, 1H), 8.24 (d, $J = 7.9$ Hz, 1H), 8.73 (d, $J = 4.5$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 26.1, 39.5, 54.9, 56.0, 86.2, 108.7, 111.1, 114.2, 122.8, 125.6, 127.3, 127.7, 128.2, 132.0, 135.8, 136.6, 137.9, 149.3, 152.6, 156.6, 173.4, 180.4. HRMS (ESI-TOF) calcd. for $\text{C}_{24}\text{H}_{22}\text{N}_3\text{O}_2$ $[\text{M} + \text{H}]^+$ 384.1707; found: 384.1699.



(2'S,3'R)-5-fluoro-1-methyl-3'-phenyl-5'-(pyridin-2-yl)-3',4'-dihydrospiro[indoline-3,2'-pyrrol]-2-one 5y: White solid; 43.1 mg, 58% yield; >99:1 dr, >99% ee; $[\alpha]_{\text{D}}^{25} = -38.5$ (*c* 1.00, CHCl_3); mp 77.9-79.4 °C. The ee was determined by

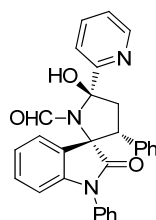
HPLC (Chiralpak OD-H, *i*-PrOH/hexane = 30/70, flow rate 1.0 mL/min, $\lambda = 254$ nm, major diastereomer: $t_{\text{major}} = 12.0$ min). ^1H NMR (400 MHz, CDCl_3): δ 2.83 (s, 3H), 3.85 (dd, $J = 14.1$ Hz, 18.4 Hz, 1H), 4.00-4.09 (m, 2H), 6.62-6.65 (m, 1H), 7.02-7.07 (m, 3H), 7.16-7.21 (m, 4H), 7.40-7.43 (m, 1H), 7.76-7.80 (m, 1H), 8.23 (d, $J = 7.9$ Hz, 1H), 8.74 (d, $J = 4.3$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 26.1, 39.6, 55.0, 86.0, 108.8 (d, $J = 7.9$ Hz, 1C), 112.2 (d, $J = 24.6$ Hz, 1C), 115.8 (d, $J = 23.4$ Hz, 1C), 122.8, 125.7, 127.5, 127.7, 128.3, 132.4 (d, $J = 7.7$ Hz, 1C), 135.3, 136.8, 140.4, 149.3, 152.3, 159.7 (d, $J = 240.3$ Hz, 1C), 173.4, 180.8. HRMS (ESI-TOF) calcd. for $\text{C}_{23}\text{H}_{19}\text{FN}_3\text{O}$ $[\text{M} + \text{H}]^+$ 372.1507; found: 372.1512.



(2'S,3'R,5'R)-tert-butyl 5'-hydroxy-1-methyl-2-oxo-3'-phenyl-5'-(pyridin-2-yl)spiro[indoline-3,2'-pyrrolidine]-1'-carboxylate 4a: White solid; $[\alpha]_{\text{D}}^{25} = +61.6$

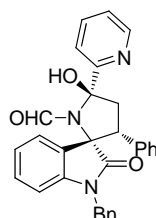
(*c* 1.00, CHCl_3), mp 95.7-97.2 °C. ^1H NMR (400 MHz, CDCl_3): δ 0.85 (s, 5.4H), 0.90 (s, 3.6H), 2.32 (dd, $J = 5.6$ Hz, 12.0 Hz, 1H), 2.74 (d, $J = 2.8$ Hz, 3H), 3.28-3.42 (m, 1H), 4.17 (dd, $J = 5.4$ Hz, 14.2 Hz, 0.4H), 4.27 (dd, $J = 5.6$ Hz, 14.4 Hz, 0.6H), 6.57-6.60 (m, 1H), 6.81-6.86 (m, 2.4H), 6.92 (s, 0.6H), 7.08-7.20 (m, 4H), 7.28-7.34 (m, 2H), 7.54 (d, $J = 7.2$ Hz, 0.4H), 7.62 (d, $J = 7.2$ Hz, 0.6H), 7.81-7.89 (m, 1H), 8.35-8.37 (m, 0.6H), 8.55-8.59 (m, 1.4H); ^{13}C NMR (100 MHz, CDCl_3): δ 25.5, 25.7, 27.6, 27.8, 45.3, 45.9, 53.4, 53.8,

73.1, 73.4, 80.6, 80.7, 90.4, 90.8, 107.7, 108.1, 120.9, 121.7, 122.0, 122.4, 122.9, 123.0, 123.1, 123.2, 127.7, 127.8, 127.9, 128.0, 128.1, 128.8, 130.1, 131.4, 134.0, 134.1, 138.0, 143.2, 143.5, 146.2, 146.6, 151.4, 152.2, 160.4, 161.6, 175.6. HRMS (ESI-TOF) calcd. for C₂₈H₃₀N₃O₄ [M + H]⁺ 472.2231; found: 472.2239.



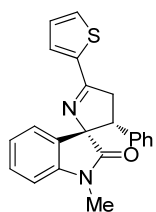
(2'S,3'R,5'R)-5'-hydroxy-2-oxo-1,3'-diphenyl-5'-(pyridin-2-yl)spiro[indoline-3,2'-pyrrolidine]-1'-carbaldehyde 4z: Light yellow solid; 38.8 mg, 84% yield;

85:15 dr, >99% ee; [α]_D²⁵ = +120.8 (*c* 1.00, CHCl₃); mp 143.1-144.4 °C. The ee was determined by HPLC (Chiralpak AD-H, *i*-PrOH/hexane = 10/90, flow rate 0.8 mL/min, λ = 254 nm, major diastereomer: t_{major} = 18.7 min). ¹H NMR (400 MHz, CDCl₃): δ 2.48 (dd, *J* = 5.6 Hz, 12.4 Hz, 1H), 3.54 (dd, *J* = 12.5 Hz, 14.0 Hz, 1H), 4.39 (dd, *J* = 5.6 Hz, 14.0 Hz, 1H), 6.53-6.55 (m, 1H), 6.78 (d, *J* = 7.2 Hz, 2H), 6.95-6.97 (m, 2H), 7.17-7.23 (m, 4H), 7.27-7.40 (m, 5H), 7.62-7.64 (m, 1H), 7.82 (s, 1H), 7.86-7.90 (m, 1H), 8.45 (d, *J* = 8.0 Hz, 1H), 8.59-8.62 (m, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 45.1, 53.2, 71.8, 90.4, 109.4, 122.6, 122.7, 123.6, 124.2, 126.4, 126.7, 128.1, 128.2, 128.3, 128.5, 129.1, 129.5, 133.5, 134.0, 138.9, 143.8, 146.8, 158.7, 160.7, 173.9. HRMS (ESI-TOF) calcd. for C₂₉H₂₄N₃O₃ [M + H]⁺ 462.1812; found: 462.1819.



(2'S,3'R,5'R)-1-benzyl-5'-hydroxy-2-oxo-3'-phenyl-5'-(pyridin-2-yl)spiro[indoline-3,2'-pyrrolidine]-1'-carbaldehyde 4a': Light yellow solid; 43.0 mg, 90% yield;

80:20 dr, >99% ee; [α]_D²⁵ = +128.9 (*c* 1.00, CHCl₃); mp 154.6-156.2 °C. The ee was determined by HPLC (Chiralpak AD-H, *i*-PrOH/hexane = 10/90, flow rate 0.8 mL/min, λ = 254 nm, major diastereomer: t_{major} = 48.5 min). ¹H NMR (400 MHz, CDCl₃): δ 2.45-2.50 (m, 1H), 3.56 (t, *J* = 13.4 Hz, 1H), 4.37-4.42 (m, 2H), 4.88 (d, *J* = 16.2 Hz, 1H), 6.41-6.43 (m, 1H), 6.56 (d, *J* = 7.4 Hz, 2H), 6.98 (d, *J* = 8.0 Hz, 2H), 7.09-7.19 (m, 7H), 7.27-7.30 (m, 1H), 7.40-7.43 (m, 1H), 7.57-7.59 (m, 1H), 7.77 (s, 1H), 7.92-7.96 (m, 1H), 8.42-8.44 (m, 1H), 8.60-8.61 (m, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 43.9, 45.7, 52.7, 71.5, 90.3, 109.5, 122.5, 122.7, 123.2, 124.2, 126.5, 127.1, 128.1, 128.4, 128.5, 128.7, 128.8, 129.2, 133.6, 135.2, 138.9, 143.1, 146.8, 158.7, 160.7, 174.4. HRMS (ESI-TOF) calcd. for C₃₀H₂₆N₃O₃ [M + H]⁺ 476.1969; found: 476.1967.

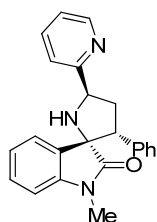


(2'S,3'R)-1-methyl-3'-phenyl-5'-(thiophen-2-yl)-3',4'-dihydrospiro[indoline-3,2'-pyrrol]-2-one 8: Light yellow solid; 30.0 mg, 42% yield; >99:1 dr, 83% ee;

$[\alpha]_D^{25} = +9.0$ (c 1.00, CHCl_3); mp 103.6-105.2 °C. The ee was determined by HPLC (Chiralpak OD-H, *i*-PrOH/hexane = 30/70, flow rate 0.8 mL/min, $\lambda = 254$ nm, major diastereomer: $t_{\text{minor}} = 25.9$ min, $t_{\text{major}} = 21.5$ min). ^1H NMR (400 MHz, CDCl_3): δ 3.22 (s, 3H), 3.66 (dd, $J = 7.2$ Hz, 16.6 Hz, 1H), 3.86 (dd, $J = 8.5$ Hz, 16.7 Hz, 1H), 4.20 (t, $J = 7.6$ Hz, 1H), 6.50 (d, $J = 7.4$ Hz, 1H), 6.68-6.74 (m, 2H), 6.98-7.00 (m, 2H), 7.10-7.16 (m, 5H), 7.52 (d, $J = 5.0$ Hz, 1H), 7.60 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 26.6, 42.2, 51.7, 85.0, 108.1, 122.3, 125.6, 127.0, 127.7, 127.8, 127.9, 128.3, 129.1, 130.8, 130.9, 138.3, 138.6, 143.6, 172.0, 177.0. HRMS (ESI-TOF) calcd. for $\text{C}_{22}\text{H}_{19}\text{N}_2\text{OS}$ $[\text{M} + \text{H}]^+$ 359.1213; found: 359.1211.

3. Procedure for the synthesis of compound 6

A mixture of **5a** (52.0 mg, 0.15 mmol) and 10% Pd/C (20.8 mg, 40% m/m) in MeOH (6 mL) was stirred vigorously under the atmosphere of hydrogen at room temperature for 12 h. Then, the mixture was filtered through a Celite plug, concentrated in vacuo, and the residue was purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 1/1) to furnish the compound **6** as a light yellow solid (40.5 mg, 76% yield).



(2'S,3'R,5'R)-1-methyl-3'-phenyl-5'-(pyridin-2-yl)spiro[indoline-3,2'-pyrrolidin-

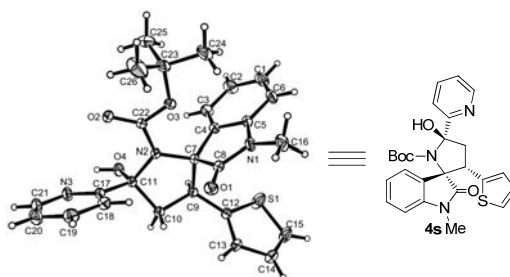
n]-2-one 6: Light yellow solid; 40.5 mg, 76% yield; 97:3 dr, >99% ee; $[\alpha]_D^{25} =$

+17.6 (c 1.00, CHCl_3); mp 52.6-54.1 °C. The ee was determined by HPLC

(Chiralpak AD-H, *i*-PrOH/hexane = 10/90, flow rate 0.8 mL/min, $\lambda = 254$ nm,

major diastereomer: $t_{\text{major}} = 31.1$ min). ^1H NMR (400 MHz, CDCl_3): δ 2.59-2.64 (m, 1H), 2.72 (s, 3H), 3.06-3.15 (m, 2H), 3.79 (dd, $J = 5.4$ Hz, 13.4 Hz, 1H), 5.04 (dd, $J = 5.5$ Hz, 10.6 Hz, 1H), 6.58 (d, $J = 7.7$ Hz, 1H), 6.85 (d, $J = 7.3$ Hz, 2H), 7.05-7.11 (m, 3H), 7.16-7.21 (m, 2H), 7.25-7.29 (m, 1H), 7.56 (d, $J = 7.3$ Hz, 1H), 7.73-7.76 (m, 1H), 8.02 (d, $J = 7.9$ Hz, 1H), 8.53 (d, $J = 4.4$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 26.0, 37.7, 57.9, 63.9, 72.9, 107.9, 121.8, 122.3, 122.6, 123.0, 127.3, 127.6, 127.8, 129.2, 131.8, 135.7, 137.2, 143.9, 148.3, 163.4, 178.3. HRMS (ESI-TOF) calcd. for $\text{C}_{23}\text{H}_{22}\text{N}_3\text{O}$ $[\text{M} + \text{H}]^+$ 356.1757; found: 356.1755.

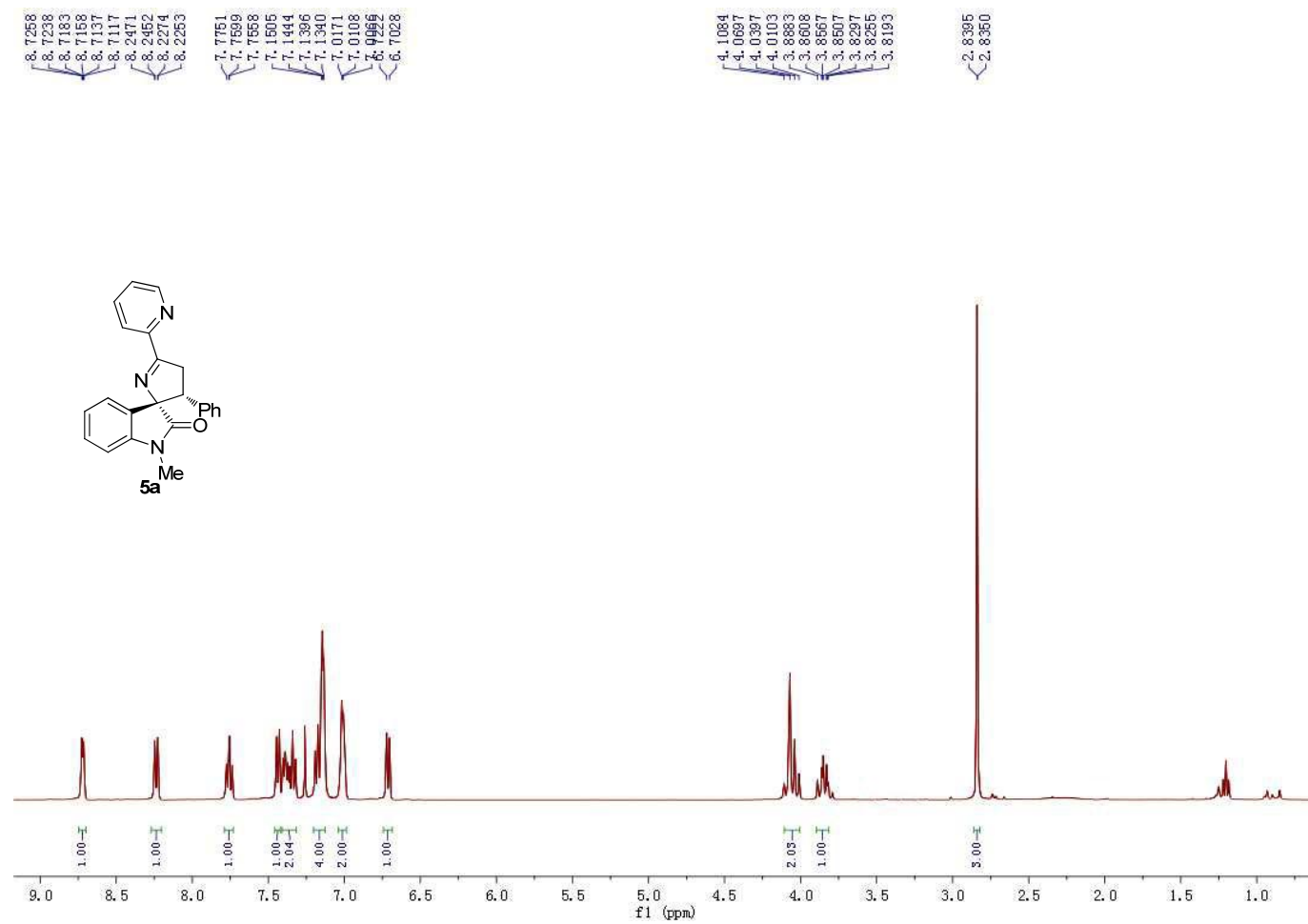
4. Crystallographic information for compound 4s

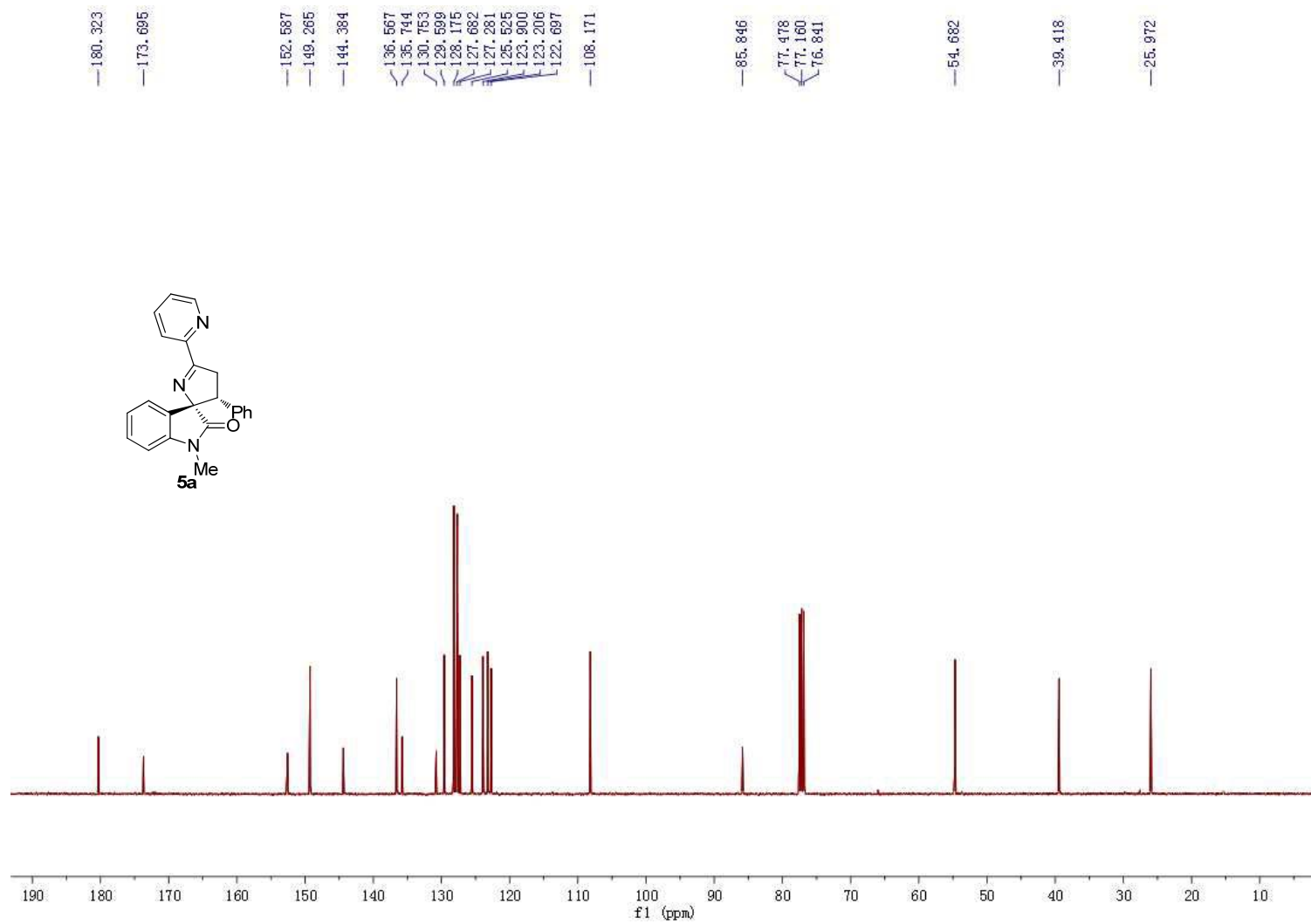


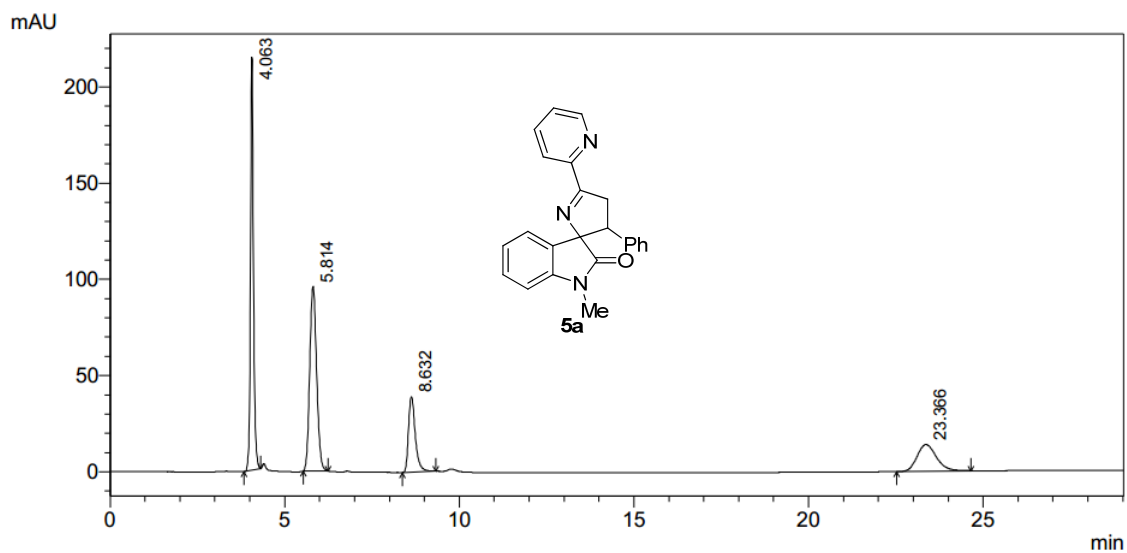
Compound 4s	Data
Empirical formula	C ₂₆ H ₂₇ N ₃ O ₄ S
Formula weight	477.56
Temperature/K	290(2)
Crystal system	Trigonal
Space group	P3 ₂
a/Å	9.32980(10)
b/Å	9.32980(10)
c/Å	25.5998(2)
α/°	90
β/°	90
γ/°	120
Volume/Å ³	1929.80(4)
Z	3
ρ _{calc} /cm ³	1.233
μ/mm ⁻¹	1.408
F(000)	756.0
Crystal size/mm ³	0.220 × 0.170 × 0.150
Radiation	CuKα (λ = 1.54184)
2θ range for data collection/°	10.366 to 142.666
Index ranges	-11 ≤ h ≤ 8, -11 ≤ k ≤ 11, -30 ≤ l ≤ 31
Reflections collected	10333
Independent reflections	4820 [R _{int} = 0.0246, R _{sigma} = 0.0277]
Data/restraints/parameters	4820/1/313
Goodness-of-fit on F ²	1.035
Final R indexes [I ≥ 2σ (I)]	R ₁ = 0.0342, wR ₂ = 0.0916
Final R indexes [all data]	R ₁ = 0.0344, wR ₂ = 0.0918
Largest diff. peak/hole / e Å ⁻³	0.22/-0.34
Flack parameter	0.023(7)

5. NMR and HPLC spectra for compounds 4, 5, 6 and 8

NMR and HPLC of 5a

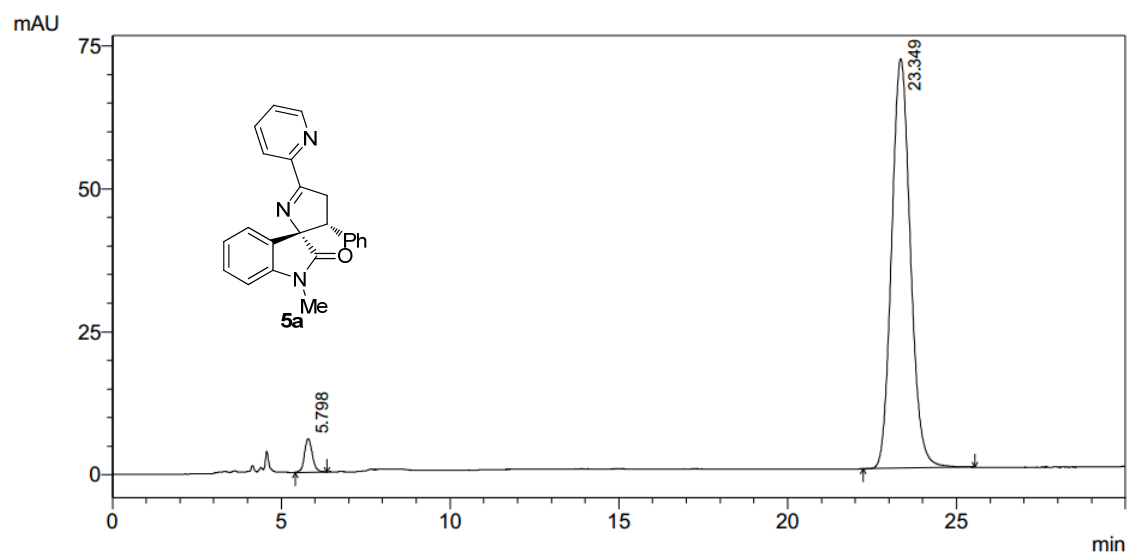






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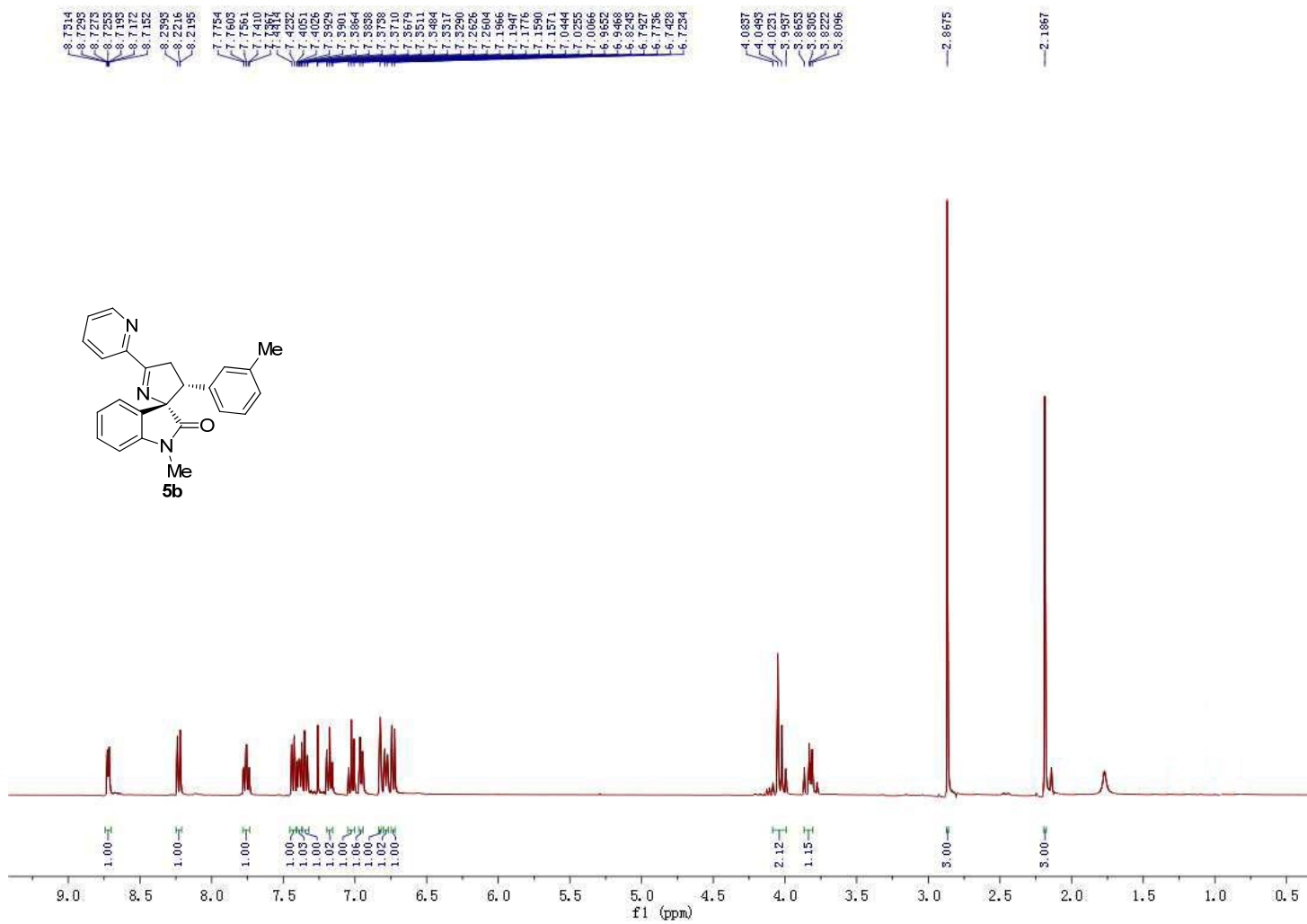
ID#	Ret. time	Area	Height	Area %
1	4.063	1290219	214746	35.138
2	5.814	1315927	95891	35.838
3	8.632	529787	39259	14.428
4	23.366	535901	13900	14.595

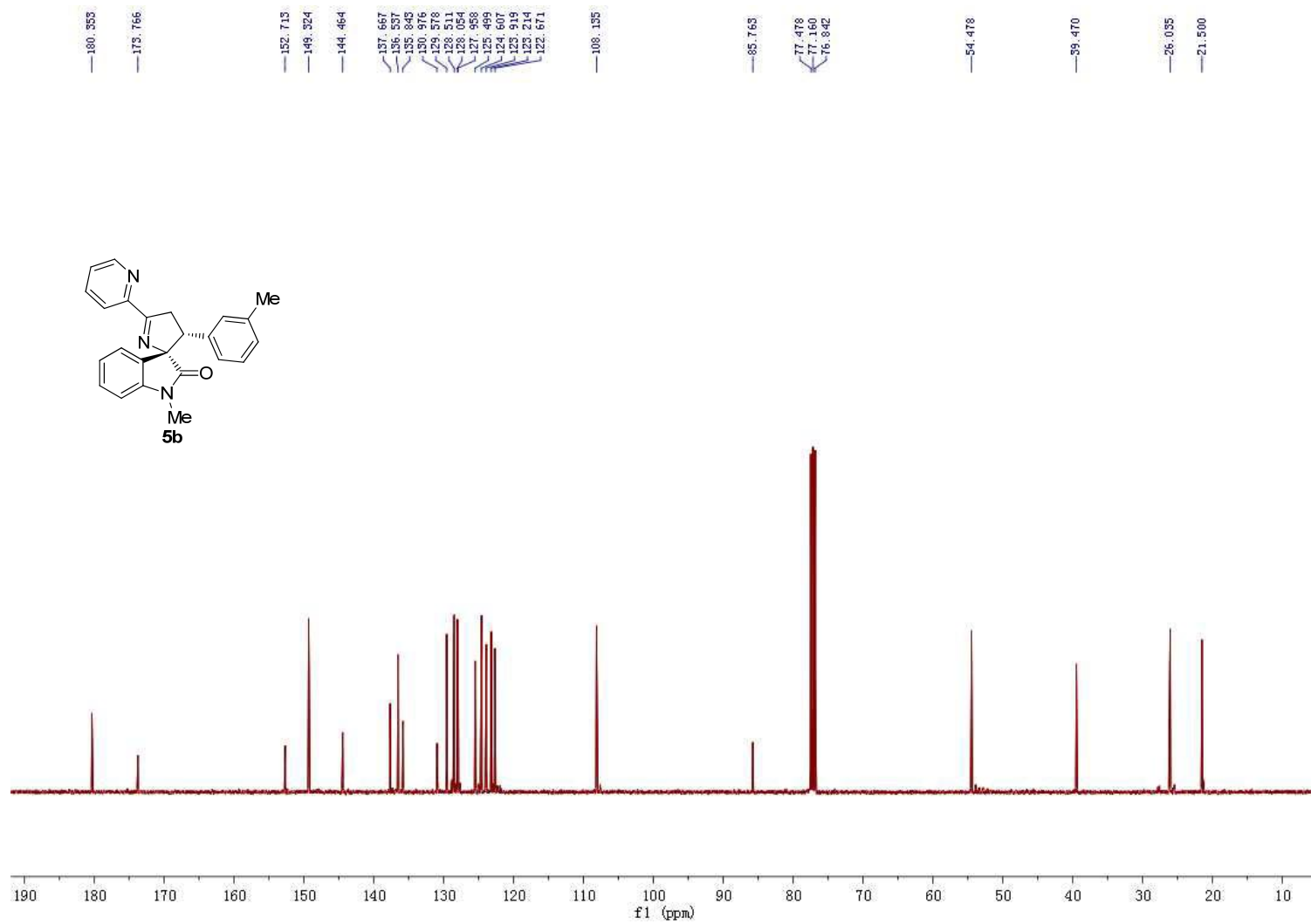


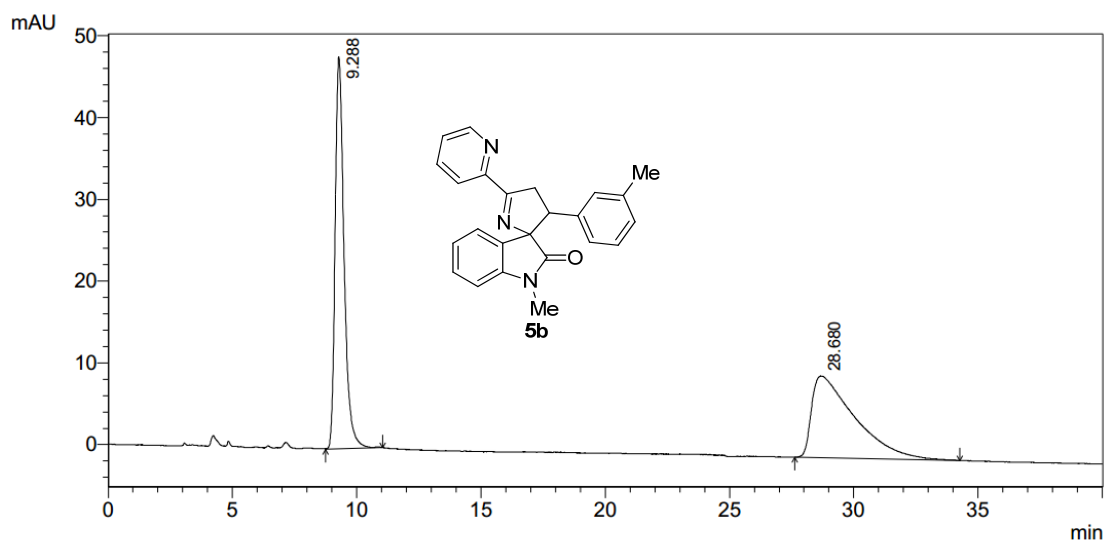
PDA

ID#	Ret. time	Area	Height	Area %
1	5.798	95159	5861	3.317
2	23.349	2773723	71652	96.683

NMR and HPLC of 5b

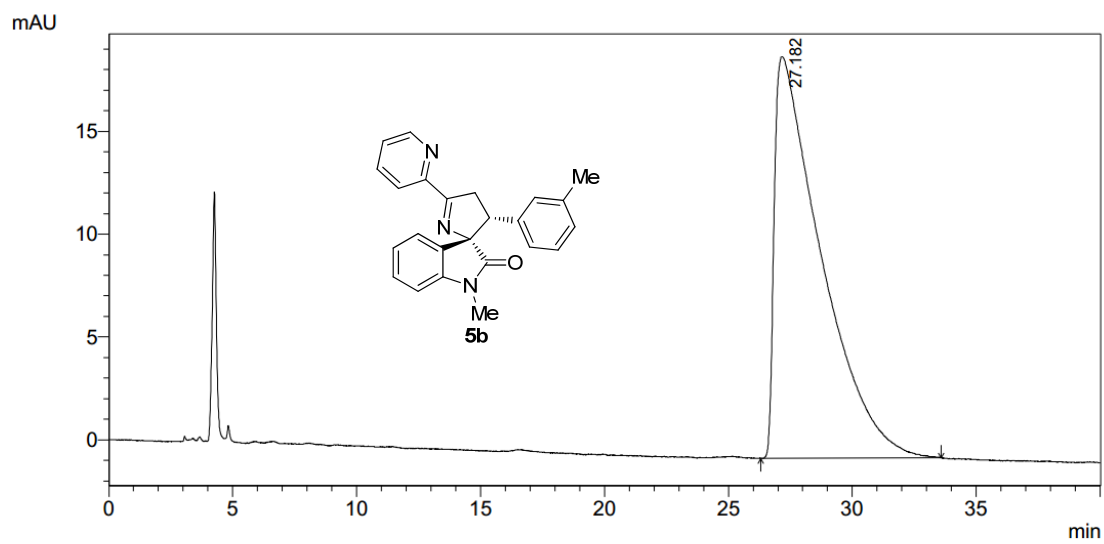






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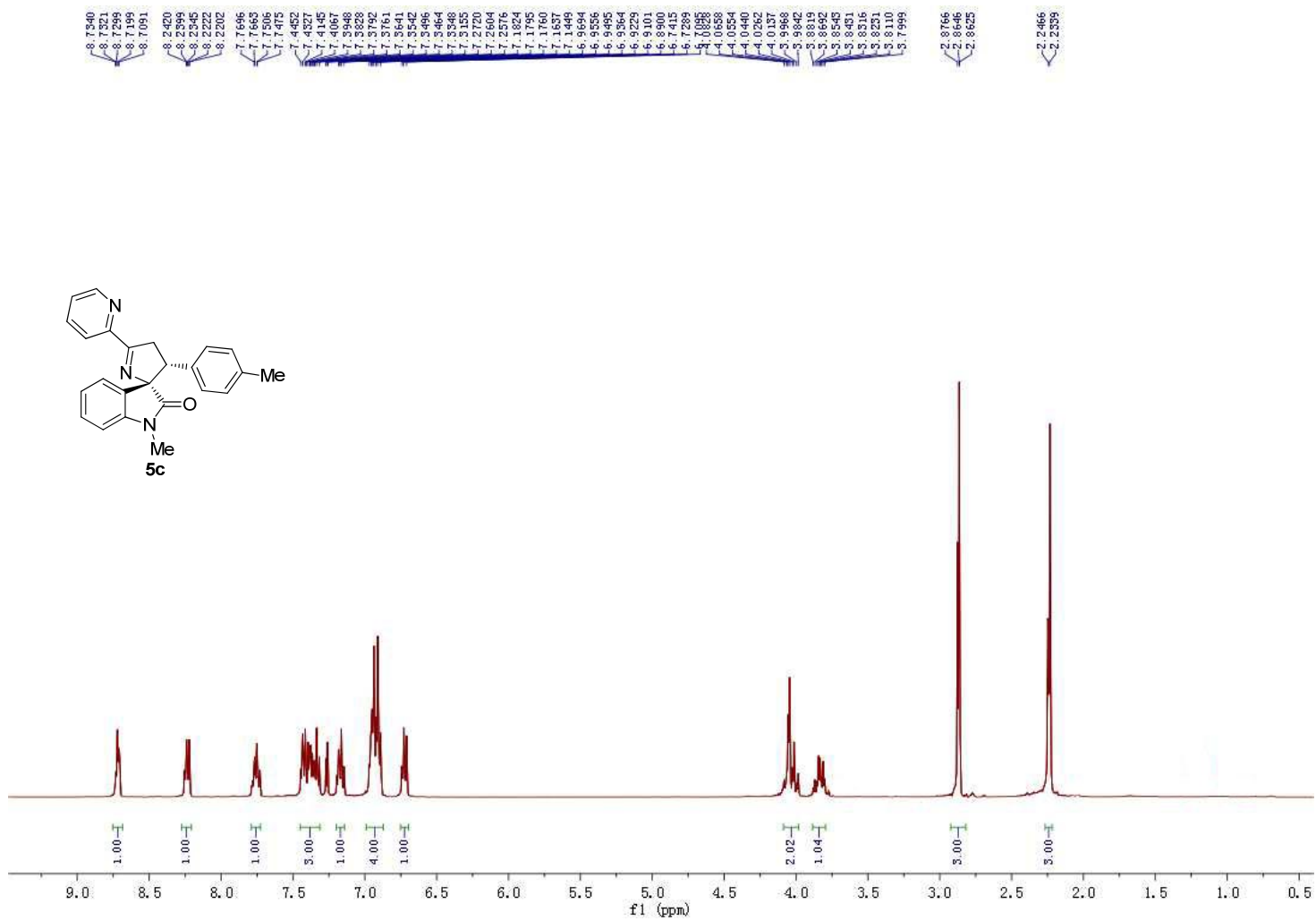
ID#	Ret. time	Area	Height	Area %
1	9.288	1194159	47945	49.758
2	28.680	1205769	9994	50.242

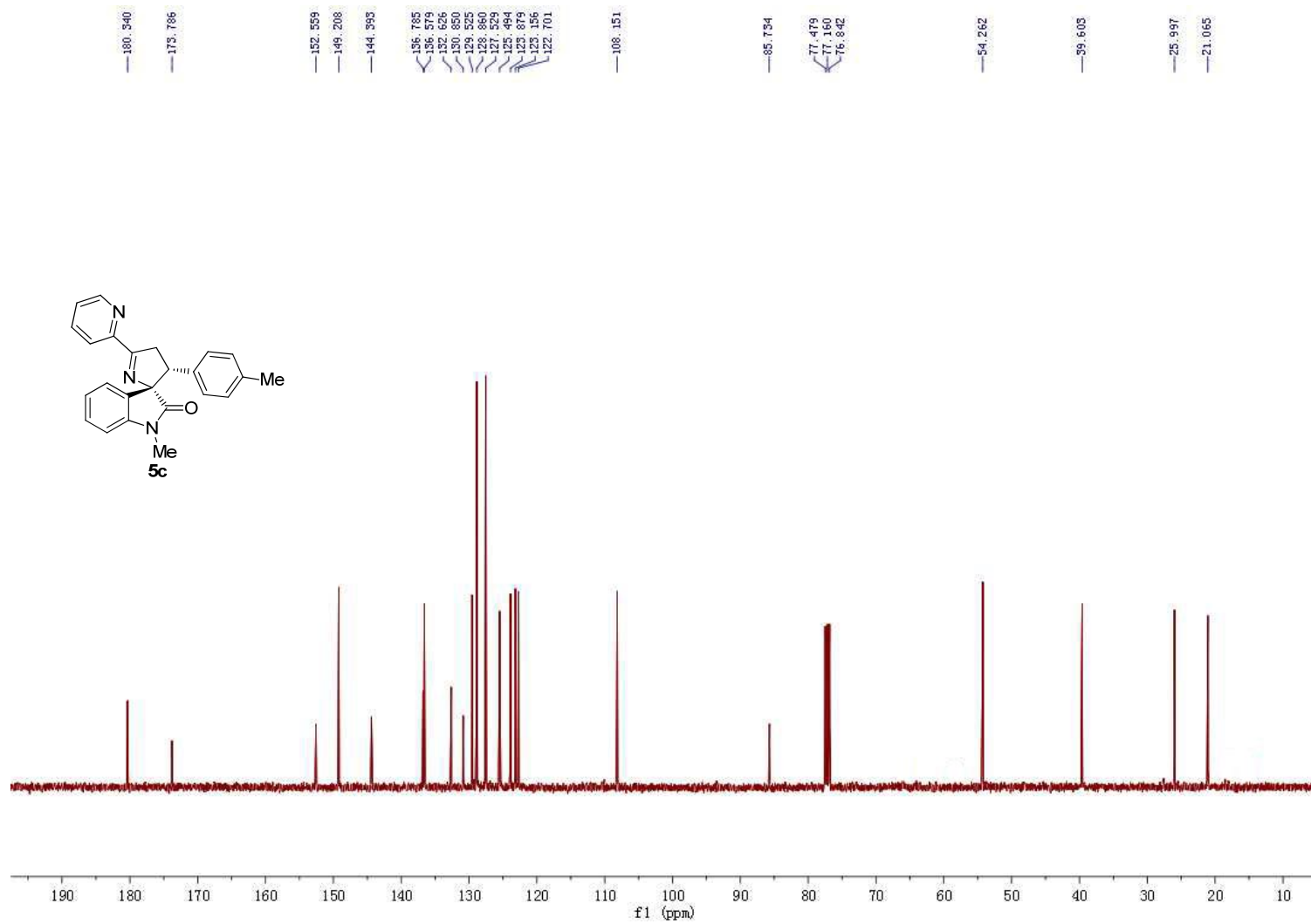


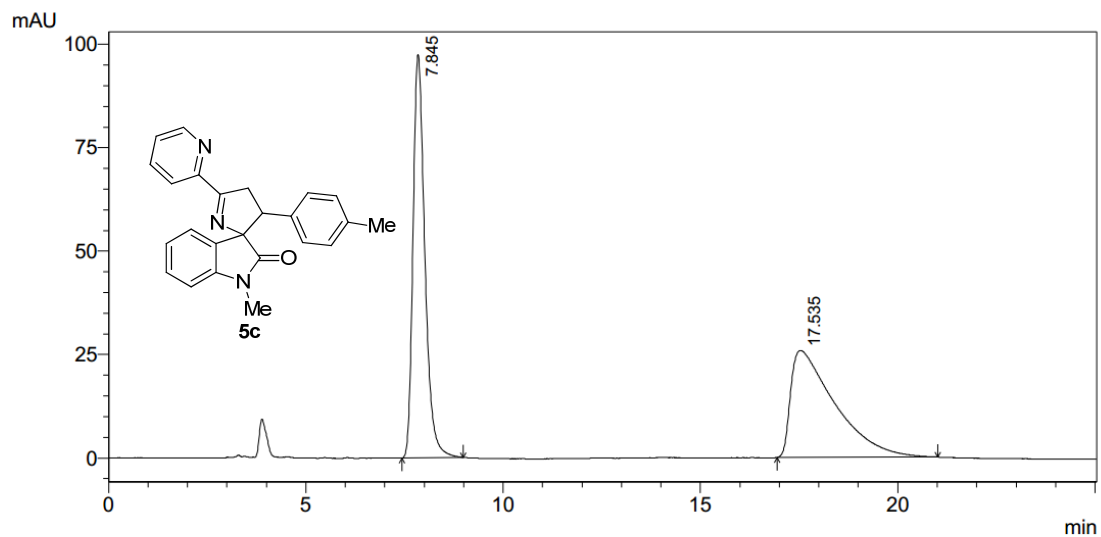
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ID#	Ret. time	Area	Height	Area %
1	27.182	2554951	19530	100.000

NMR and HPLC of 5c

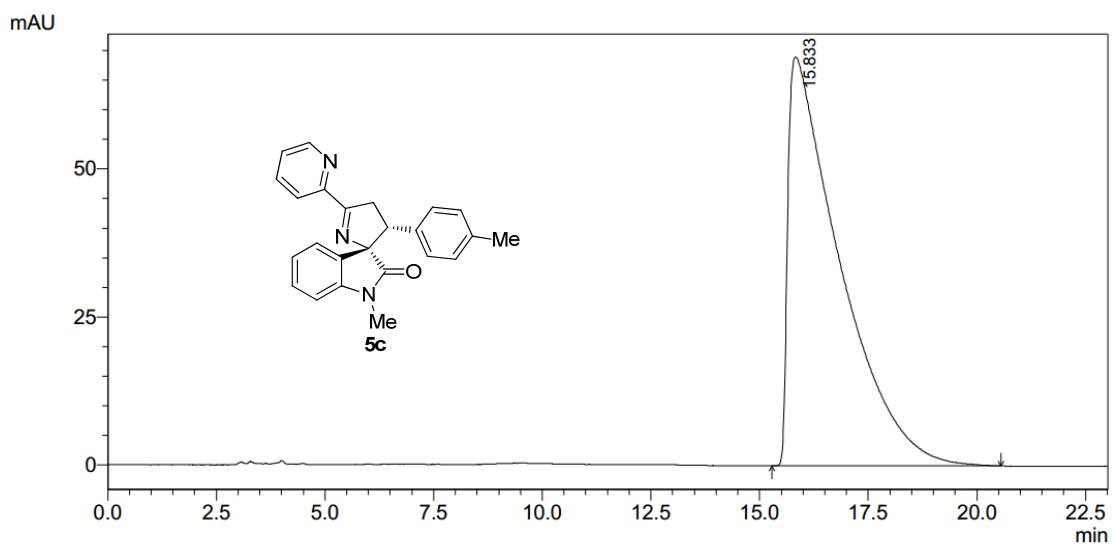






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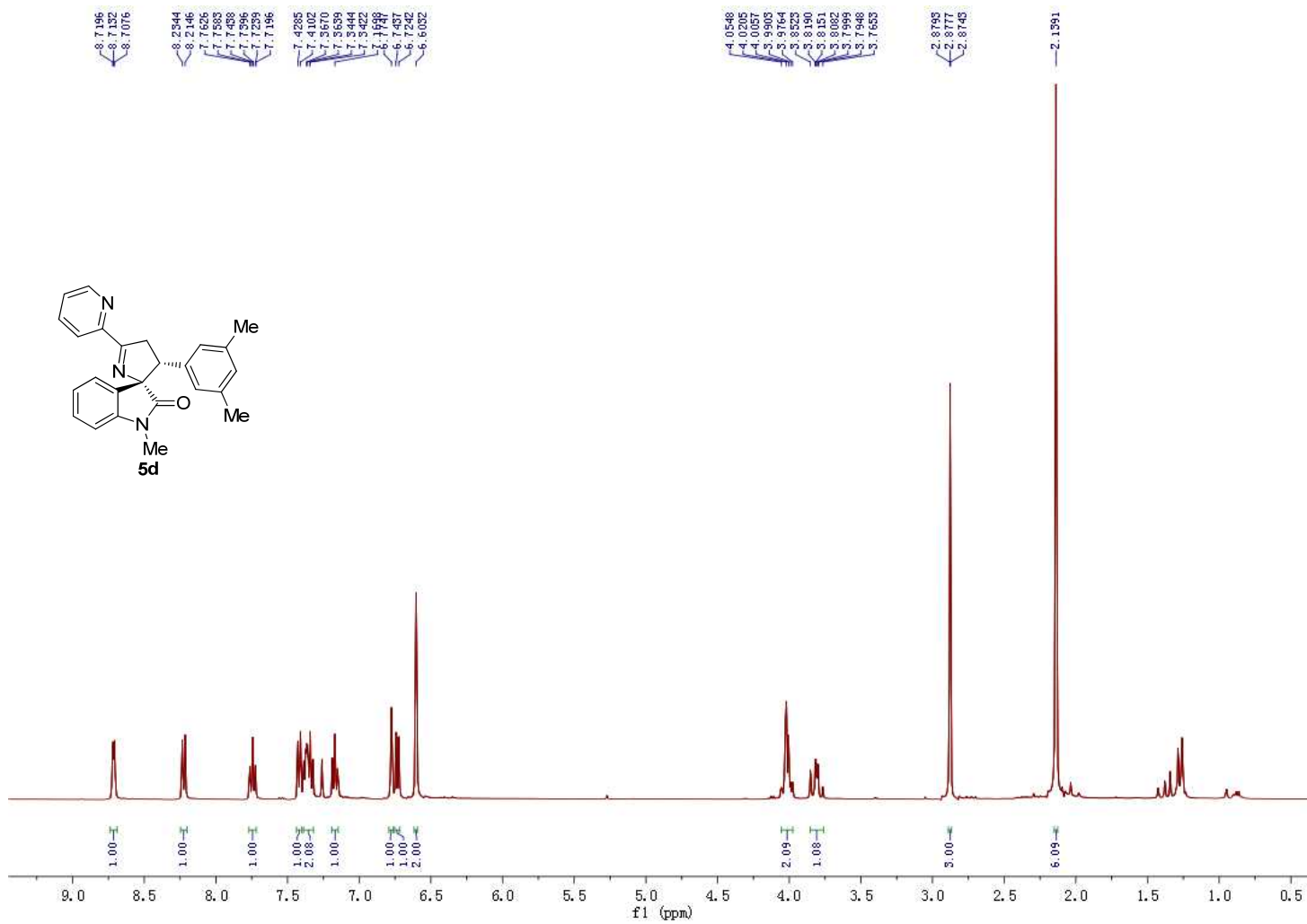
ID#	Ret. time	Area	Height	Area %
1	7.845	2033383	97576	50.257
2	17.535	2012552	25872	49.743

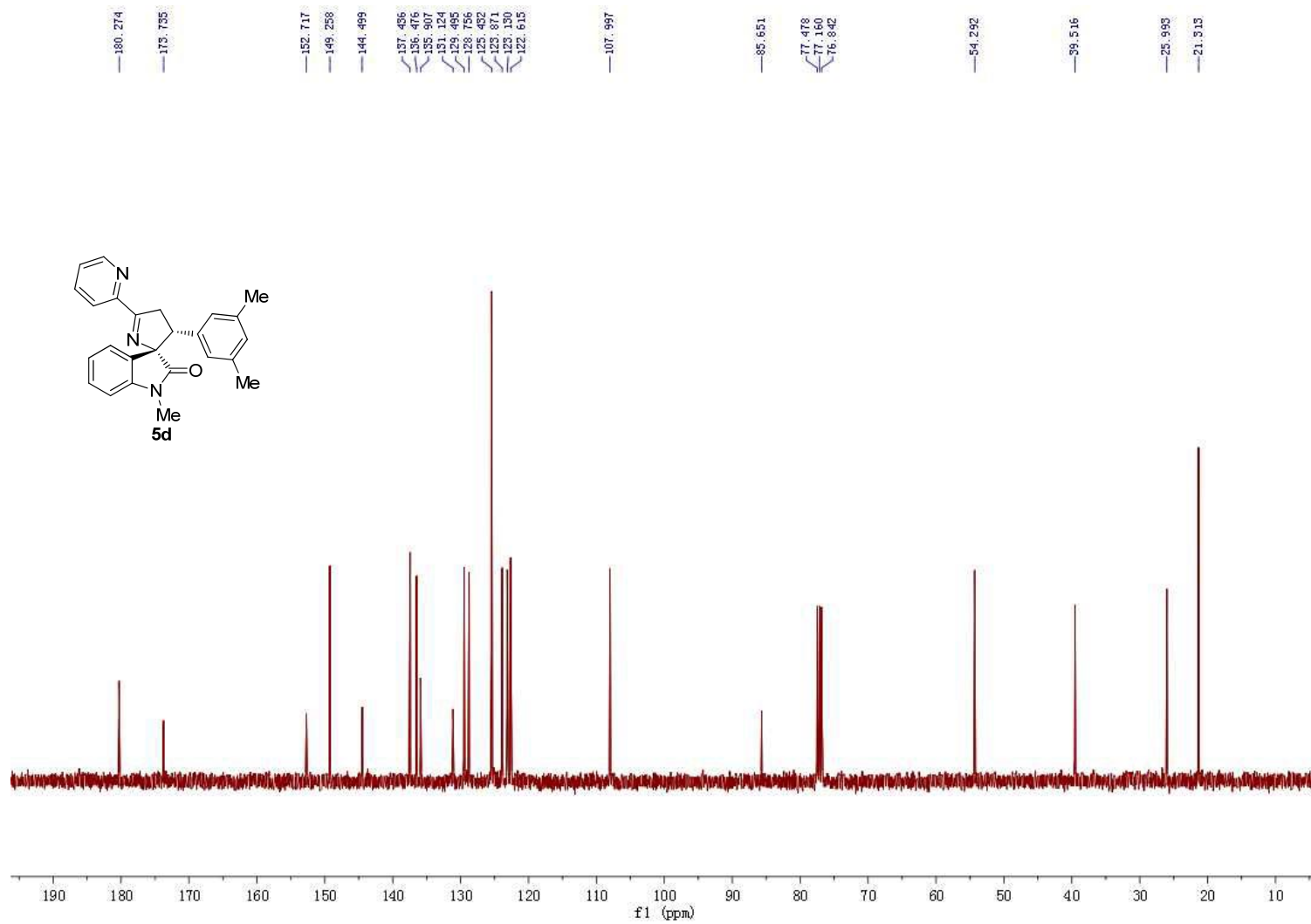


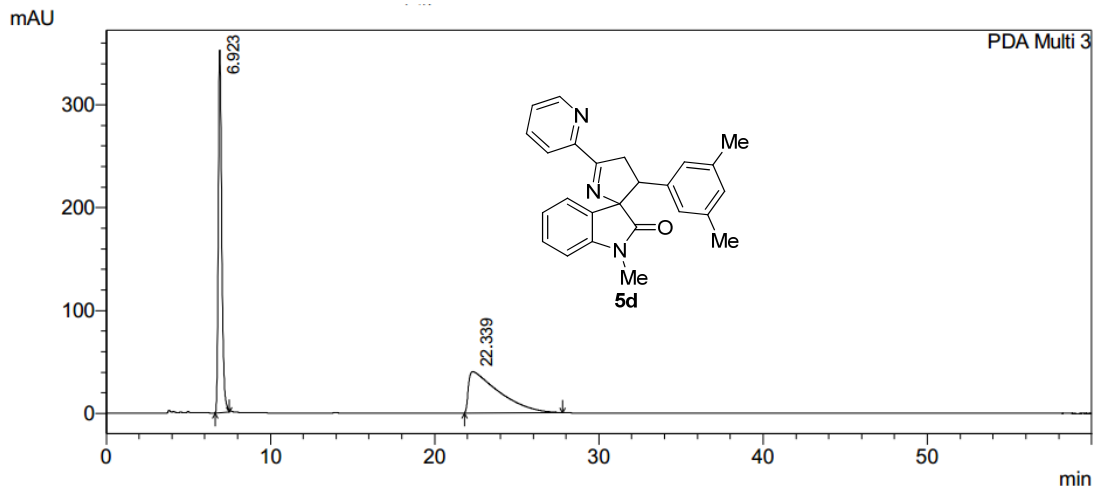
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ID#	Ret. time	Area	Height	Area %
1	15.833	5716510	69087	100.000

NMR and HPLC of 5d





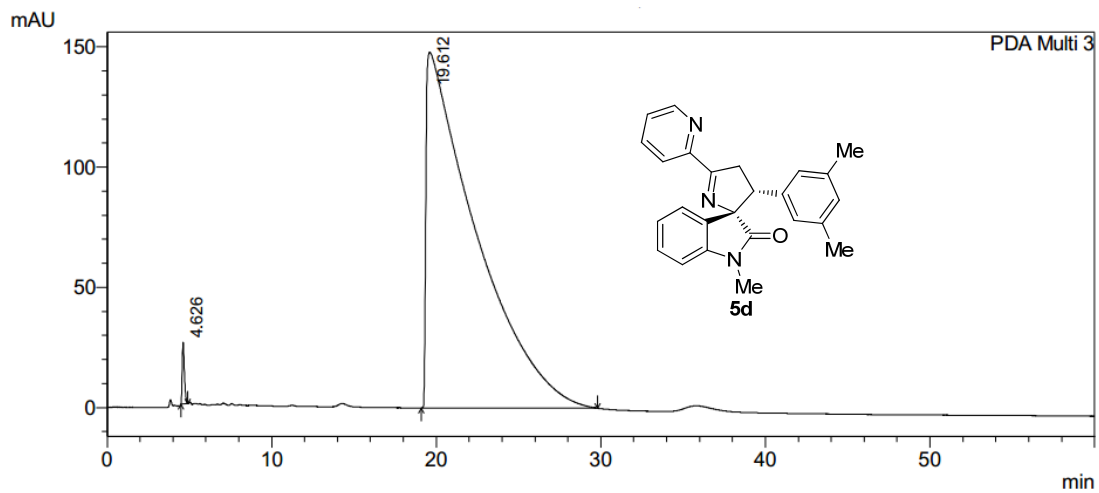


1 PDA Multi 3/254nm 4nm

Quantitative Results

PDA

ID#	Name	Ret. Time	Area	Height	Conc.
1	RT6.923	6.923	5168892	352324	50.045
2	RT22.339	22.339	5159503	40128	49.955



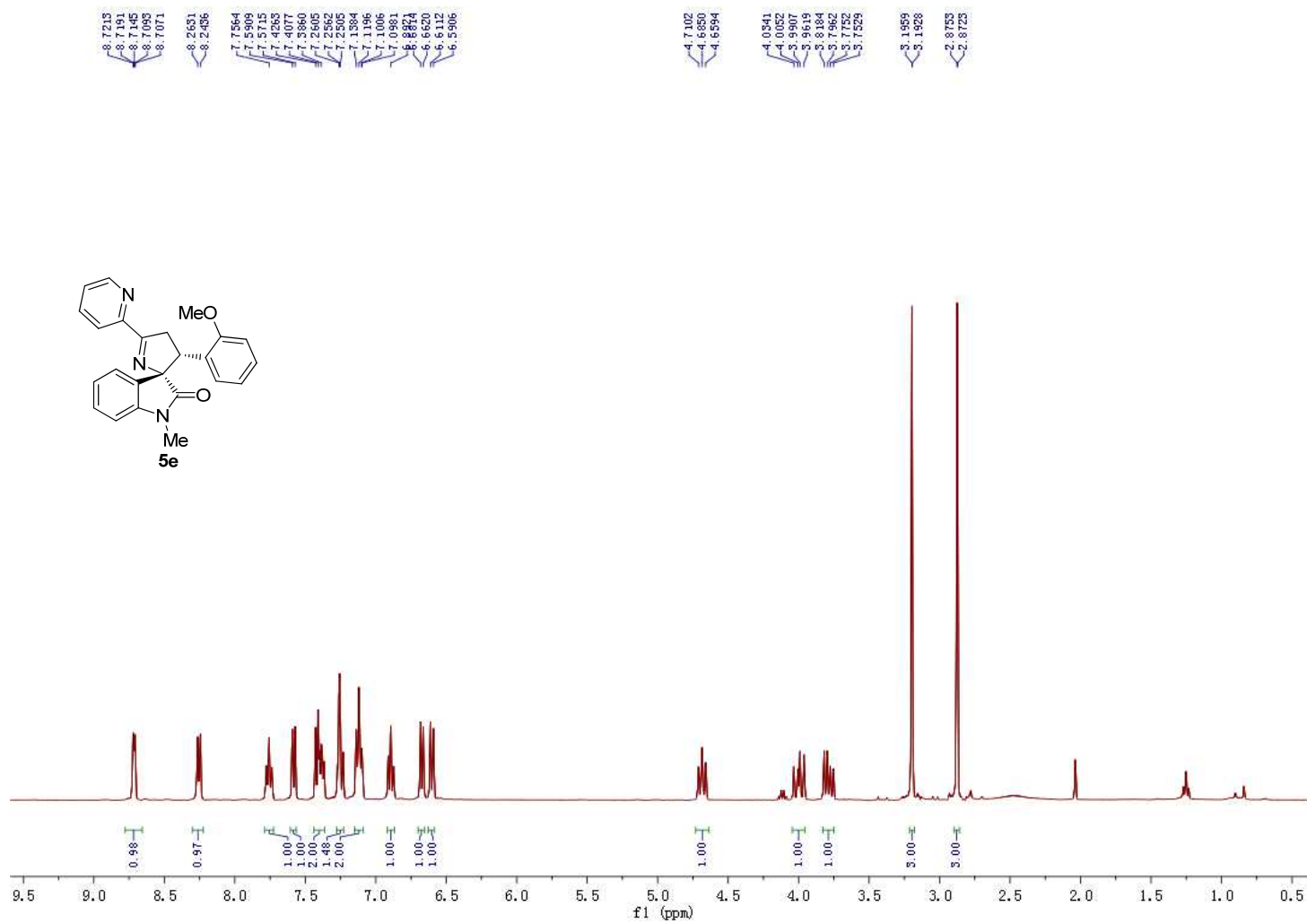
1 PDA Multi 3/254nm 4nm

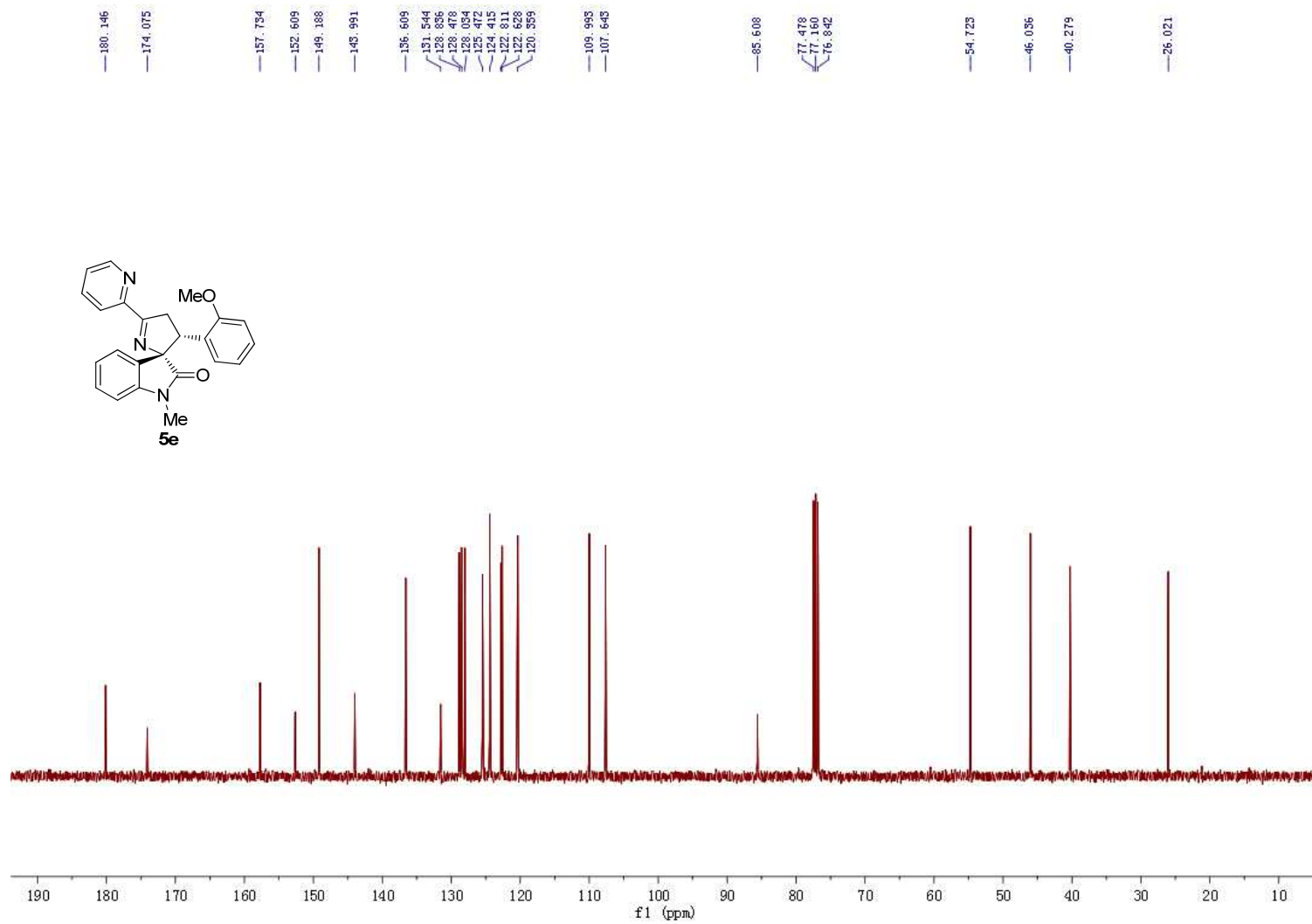
Quantitative Results

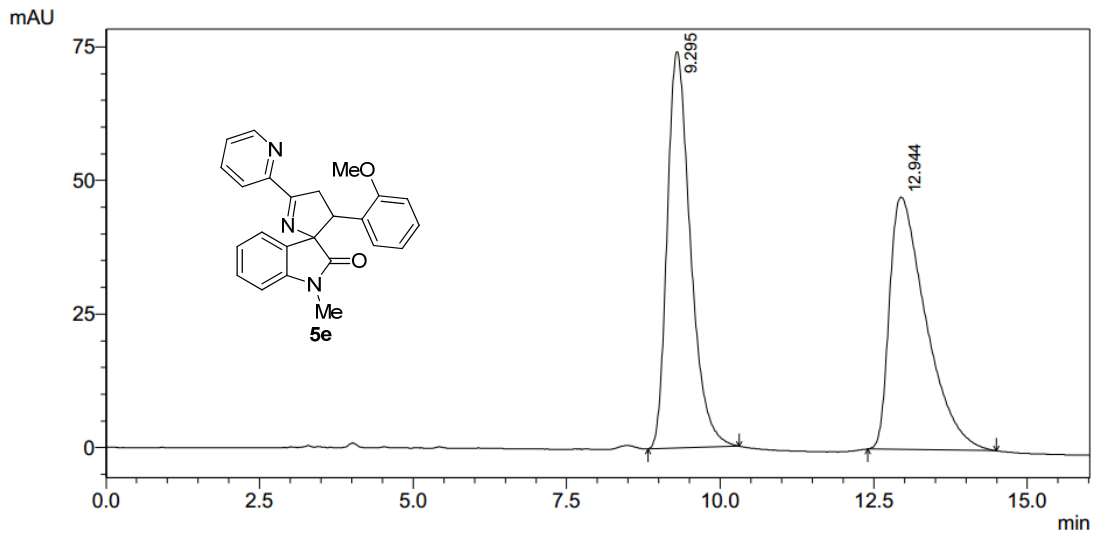
PDA

ID#	Name	Ret. Time	Area	Height	Conc.
1	RT4.626	4.626	238736	25720	0.765
2	RT19.612	19.612	30979944	147860	99.235

NMR and HPLC of 5e

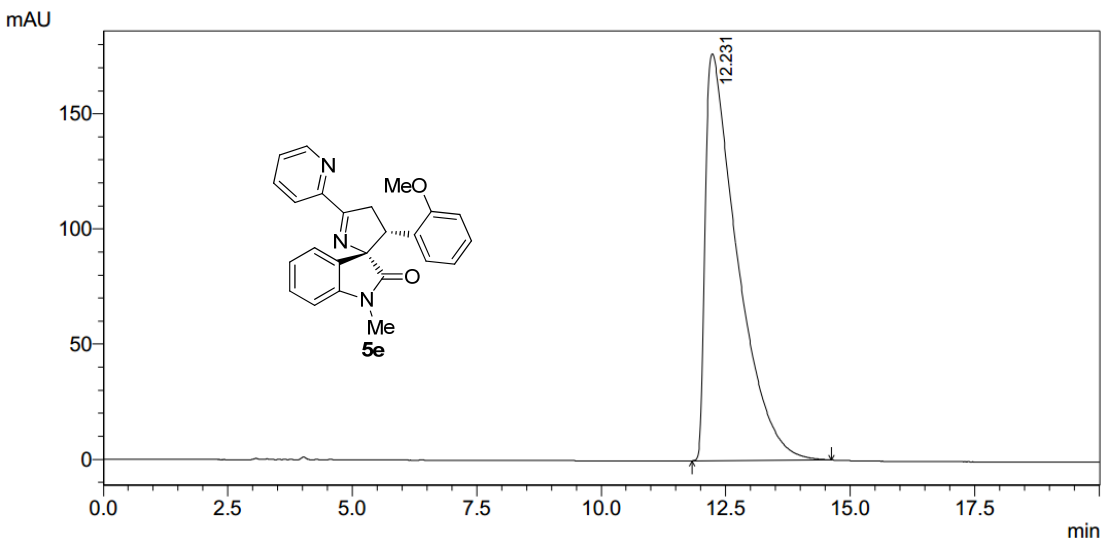






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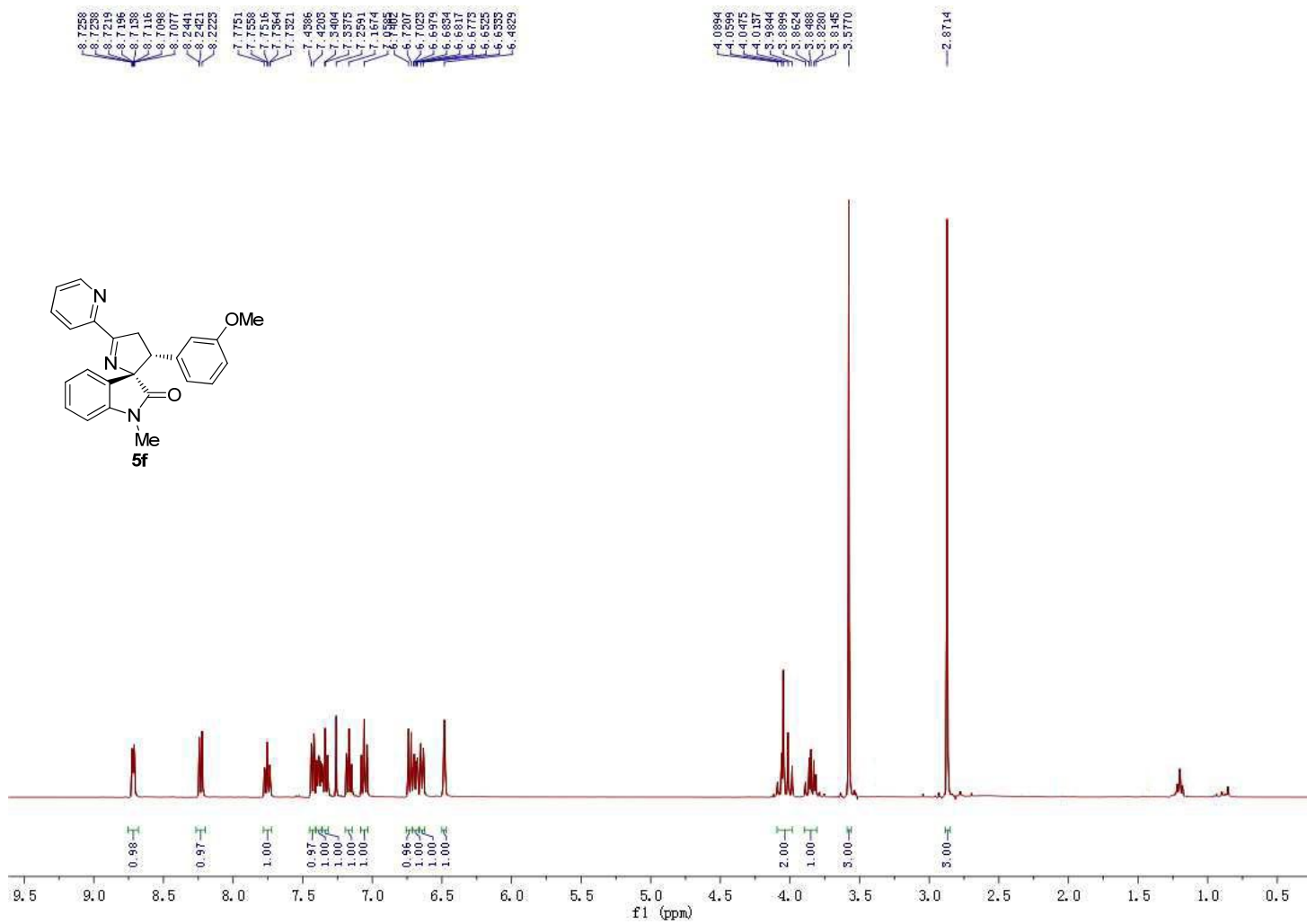
ID#	Ret. time	Area	Height	Area %
1	9.295	1957104	74212	50.110
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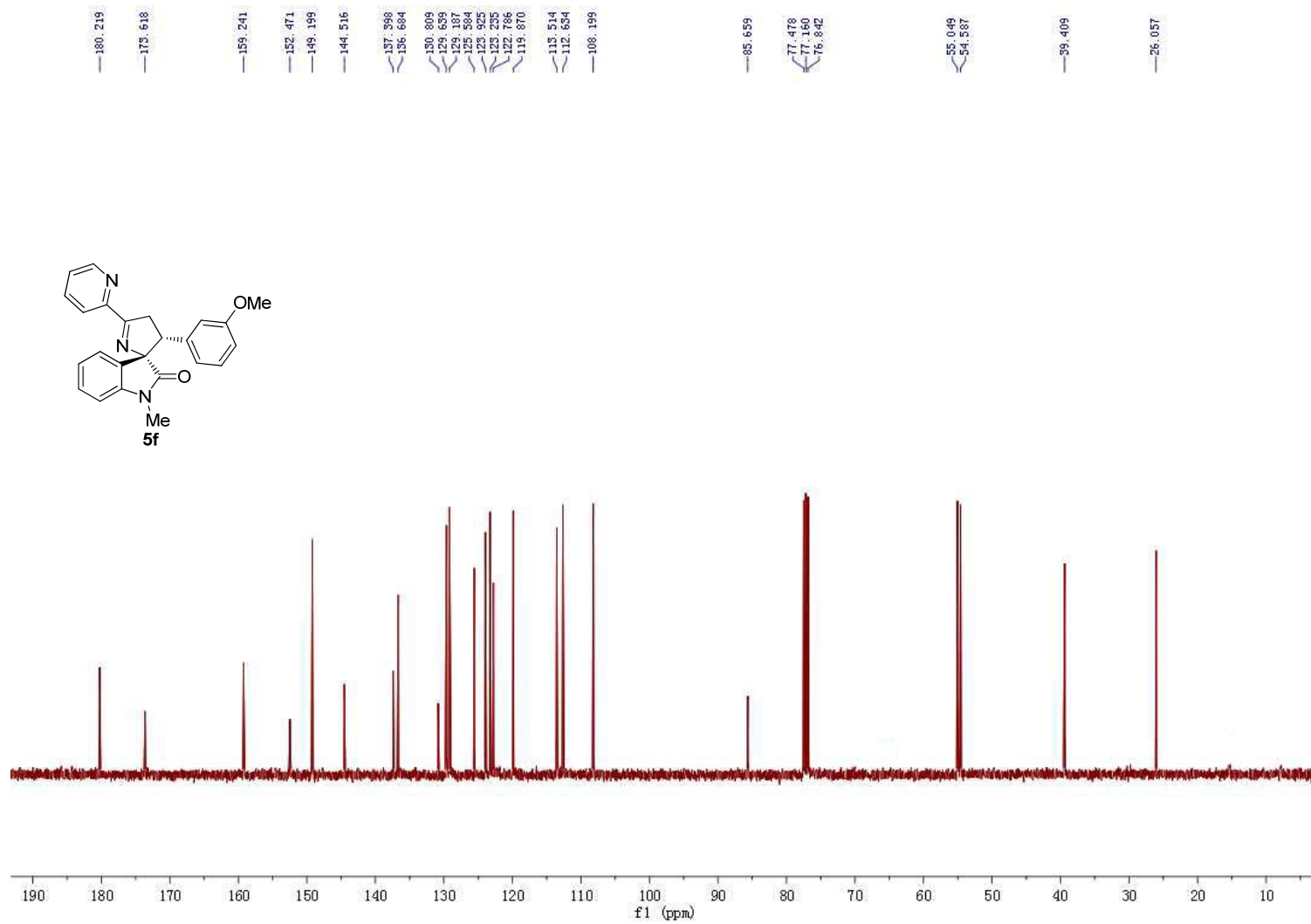


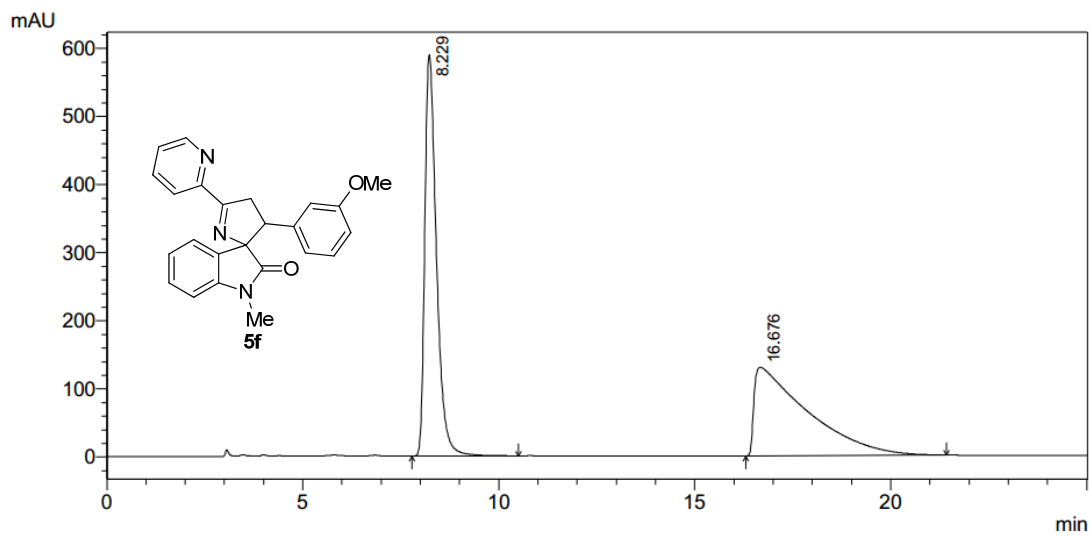
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ID#	Ret. time	Area	Height	Area %
1	12.231	7913284	176727	100.000

NMR and HPLC of 5f

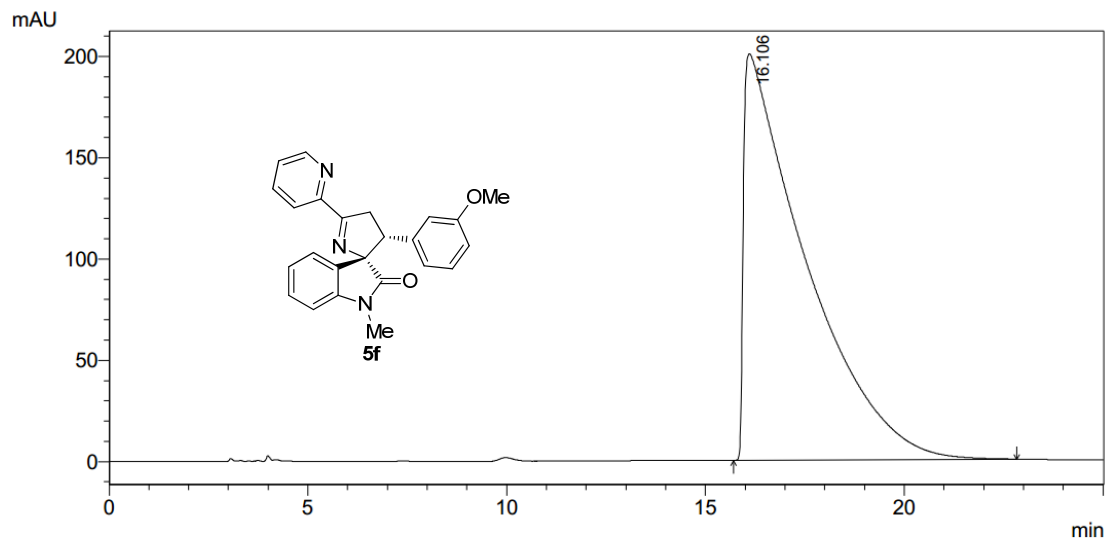






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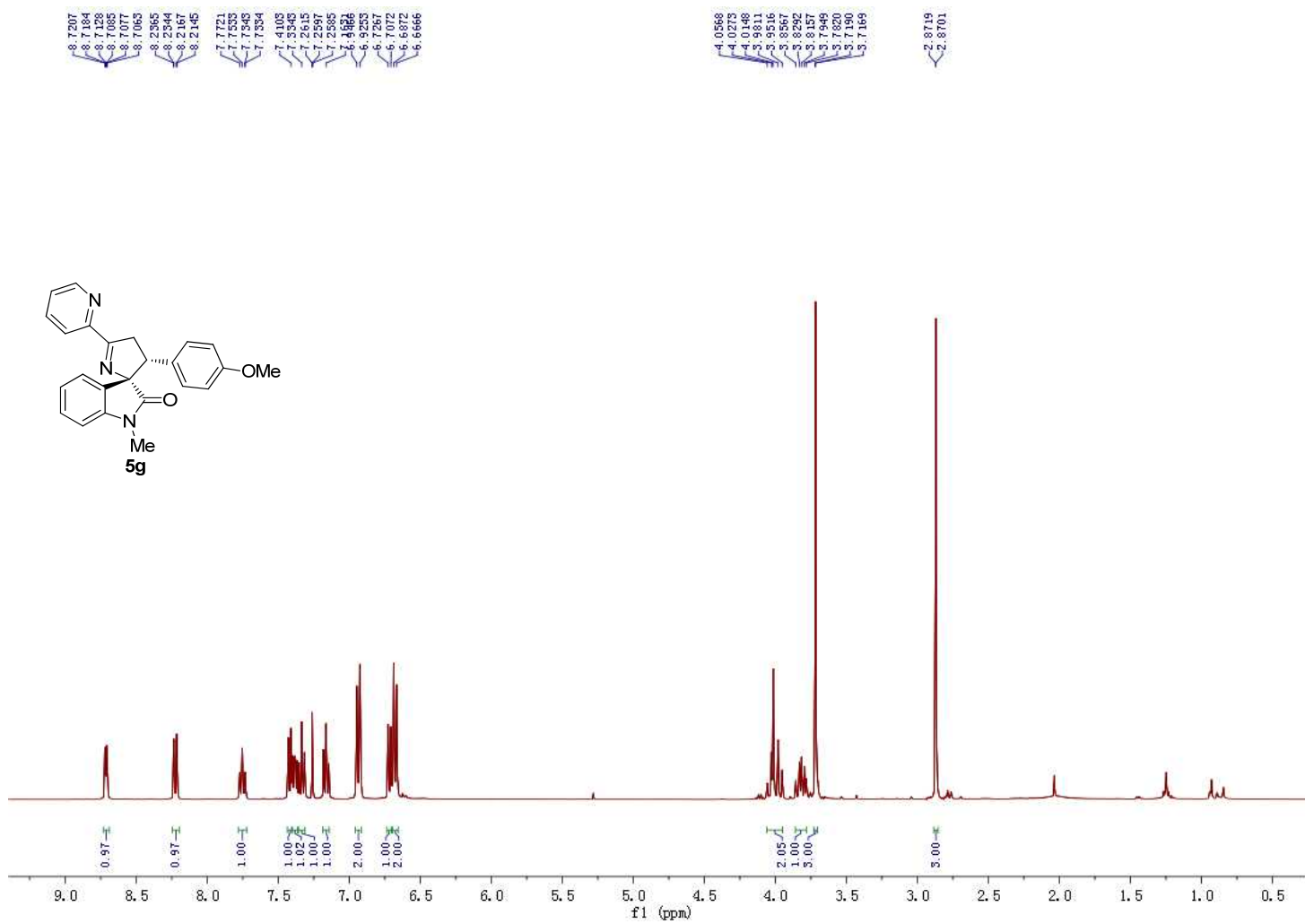
ID#	Ret. time	Area	Height	Area %
1	8.229	12189906	589744	49.823
2	16.676	12276492	129965	50.177

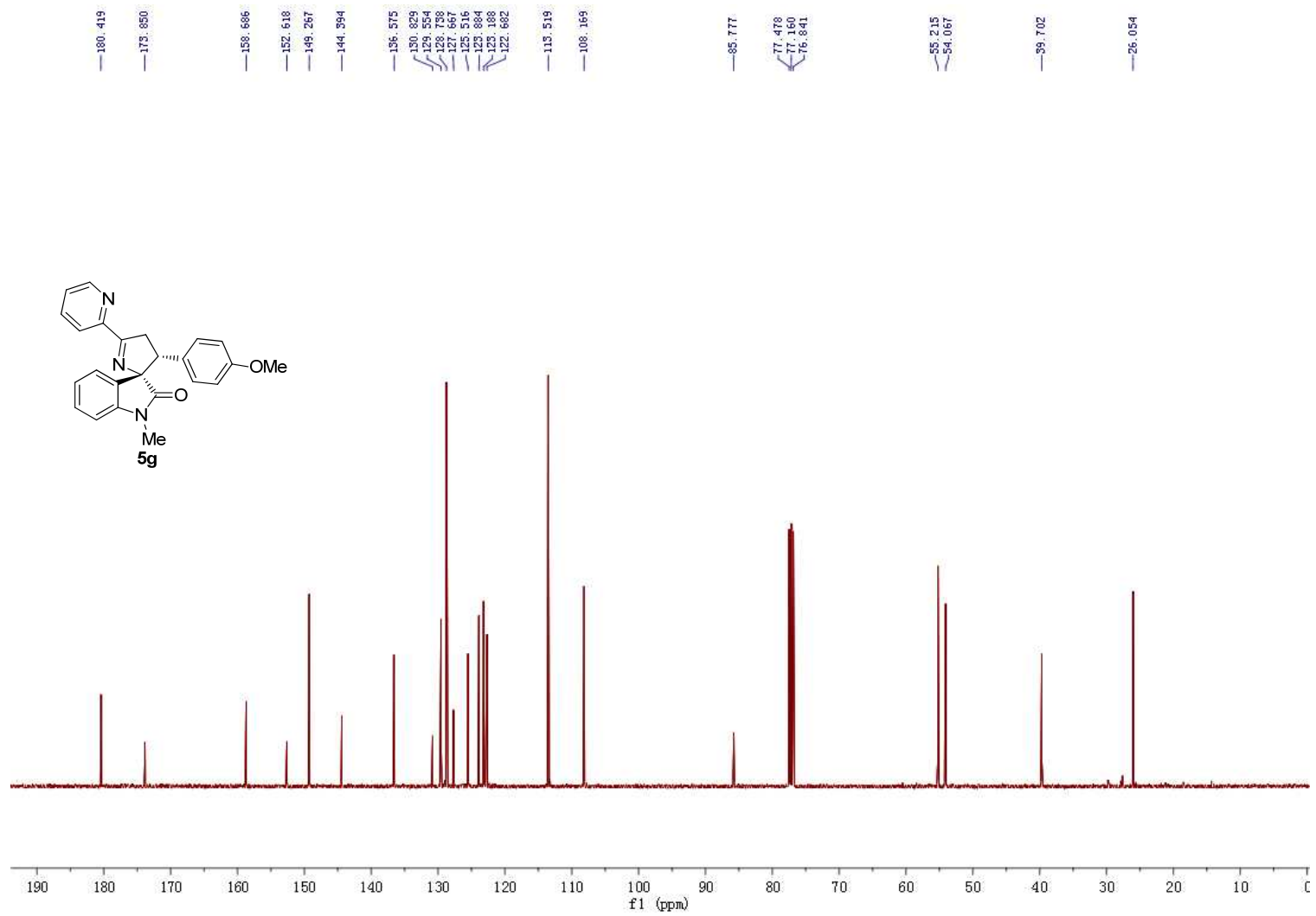


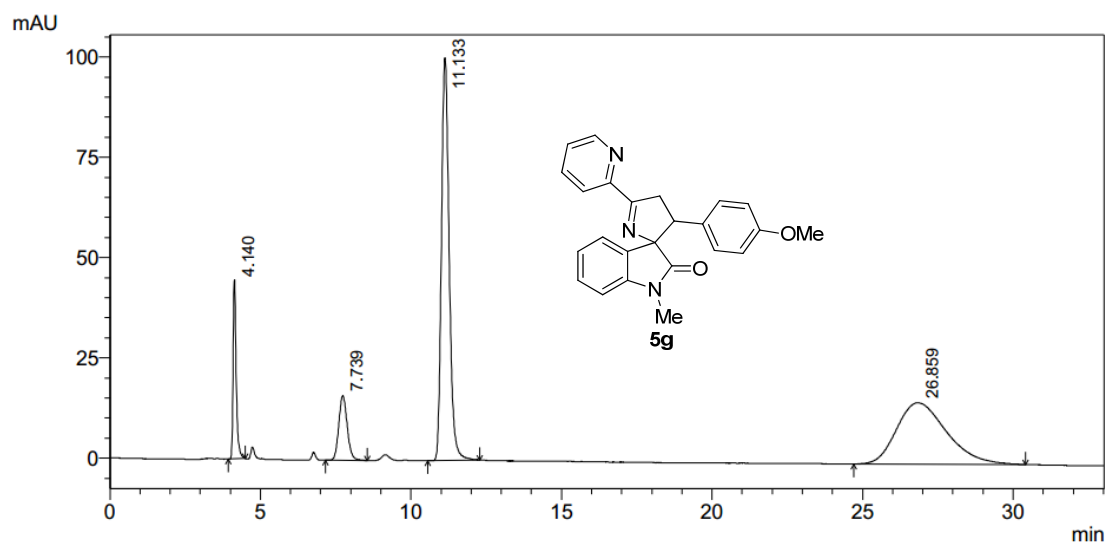
PDA

ID#	Ret. time	Area	Height	Area %
1	16.106	21735242	200696	100.000

NMR and HPLC of 5g

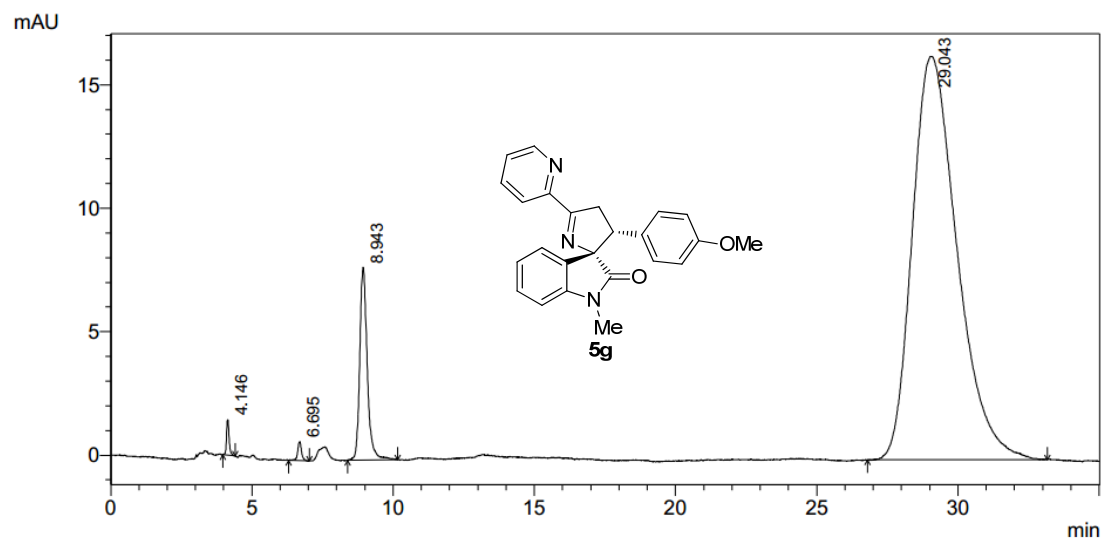






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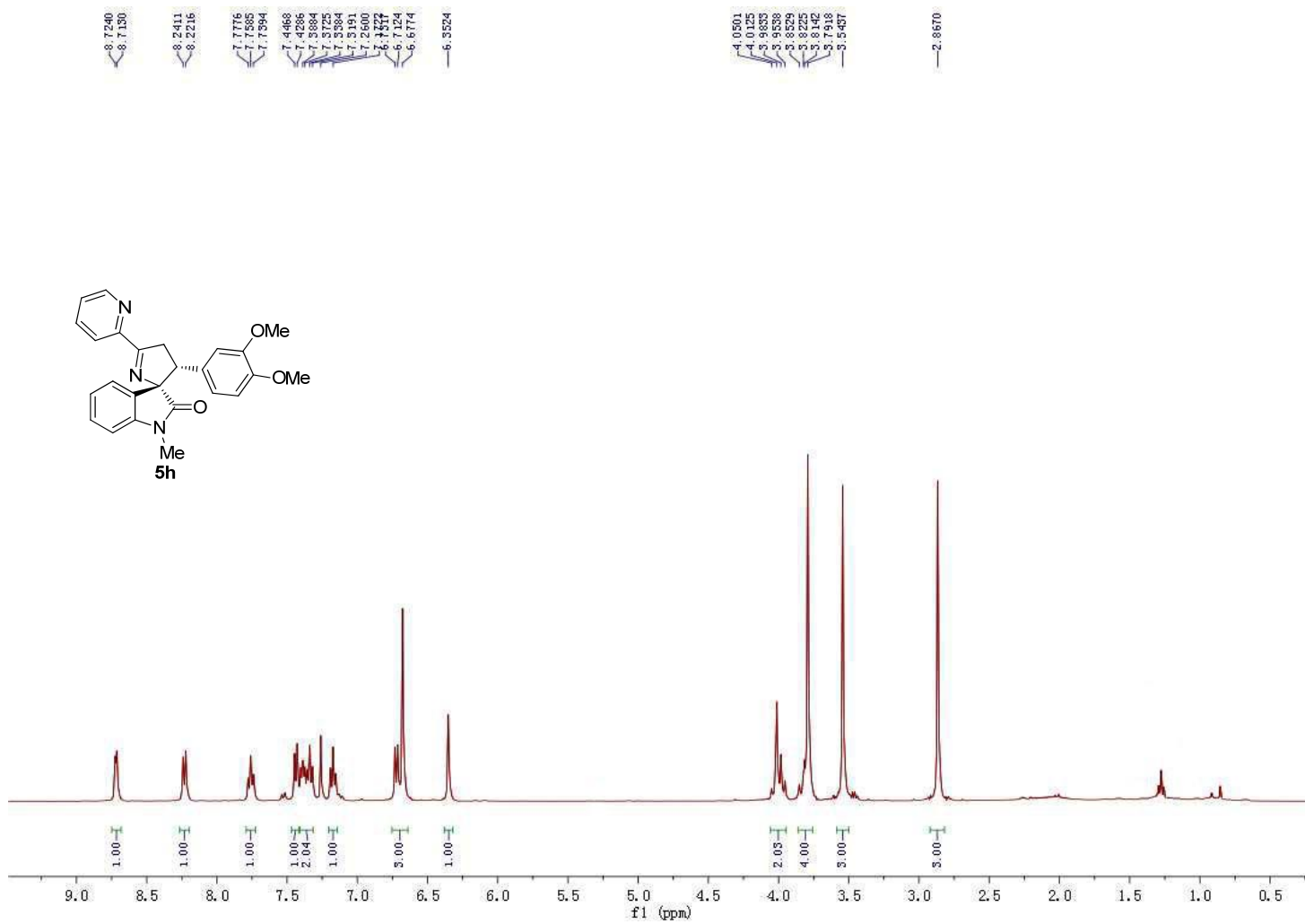
ID#	Ret. time	Area	Height	Area %
1	4.140	316663	44636	7.577
2	7.739	314973	16153	7.537
3	11.133	1783728	100450	42.682
4	26.859	1763723	15285	42.204

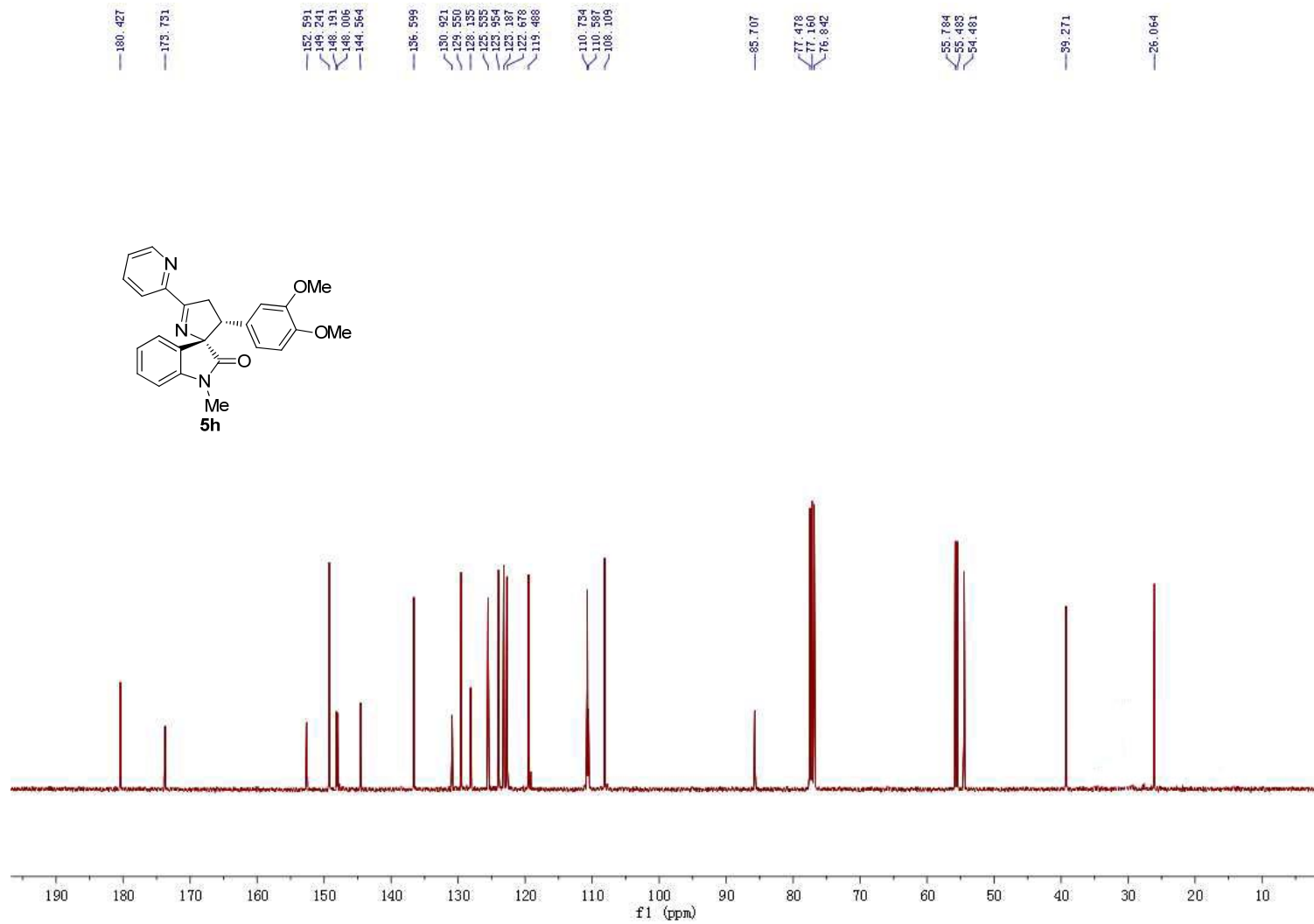


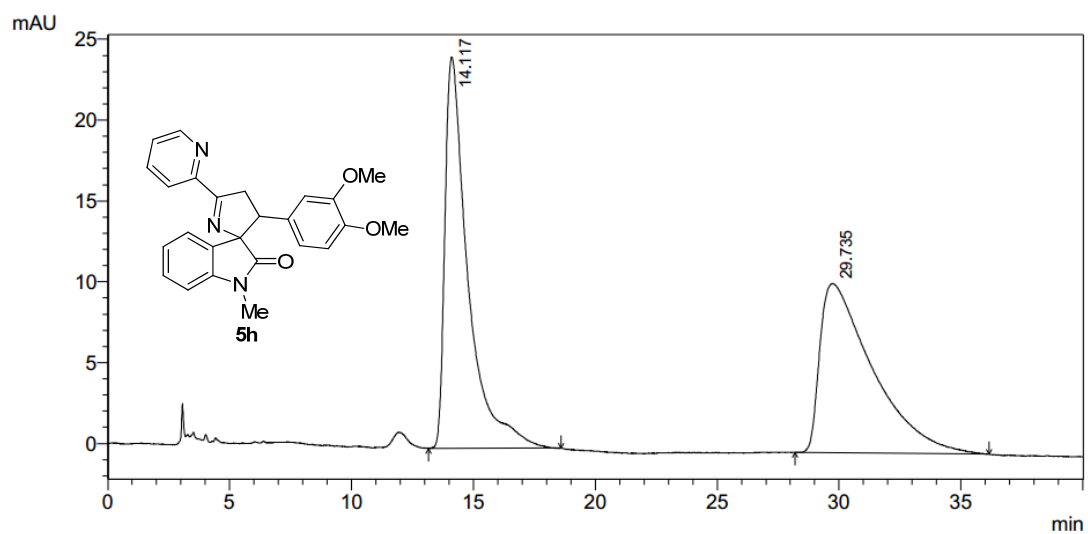
PDA

ID#	Ret. time	Area	Height	Area %
1	4.146	8836	1441	0.451
2	6.695	7105	775	0.362
3	8.943	143987	7802	7.341
4	29.043	1801428	16342	91.846

NMR and HPLC of 5h

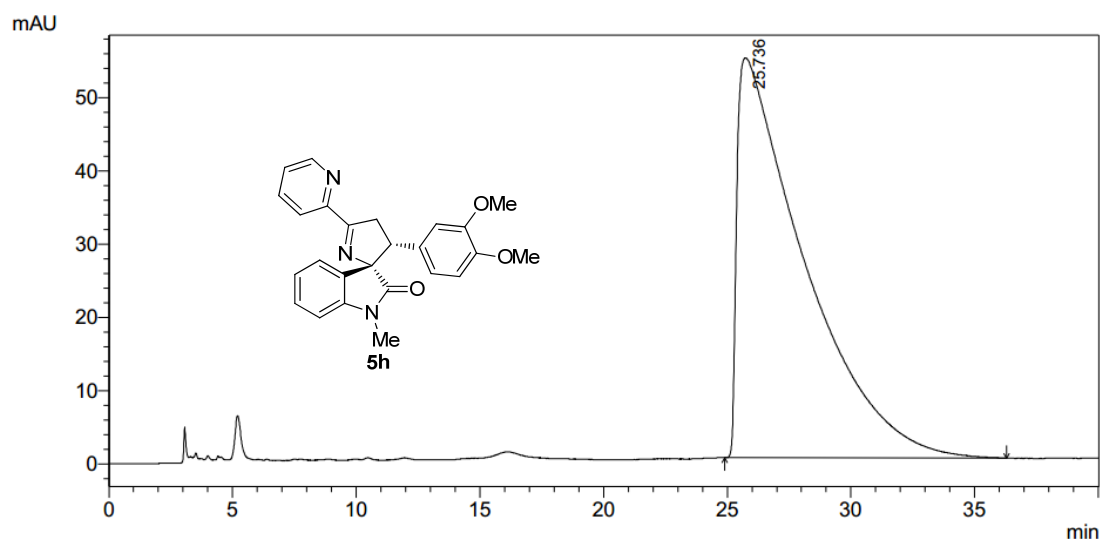






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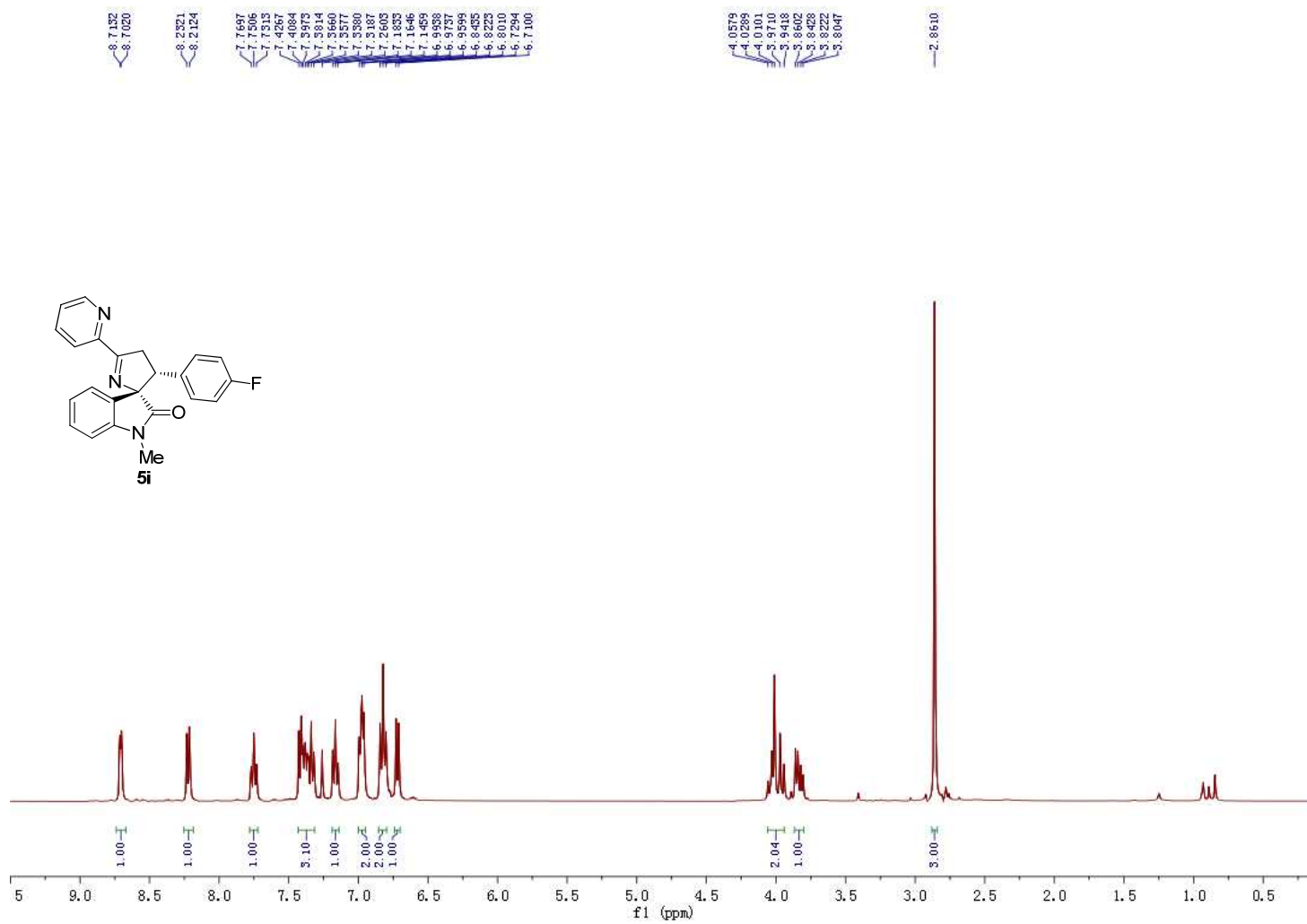
ID#	Ret. time	Area	Height	Area %
1	14.117	1586373	24203	50.183
2	29.735	1574802	10465	49.817

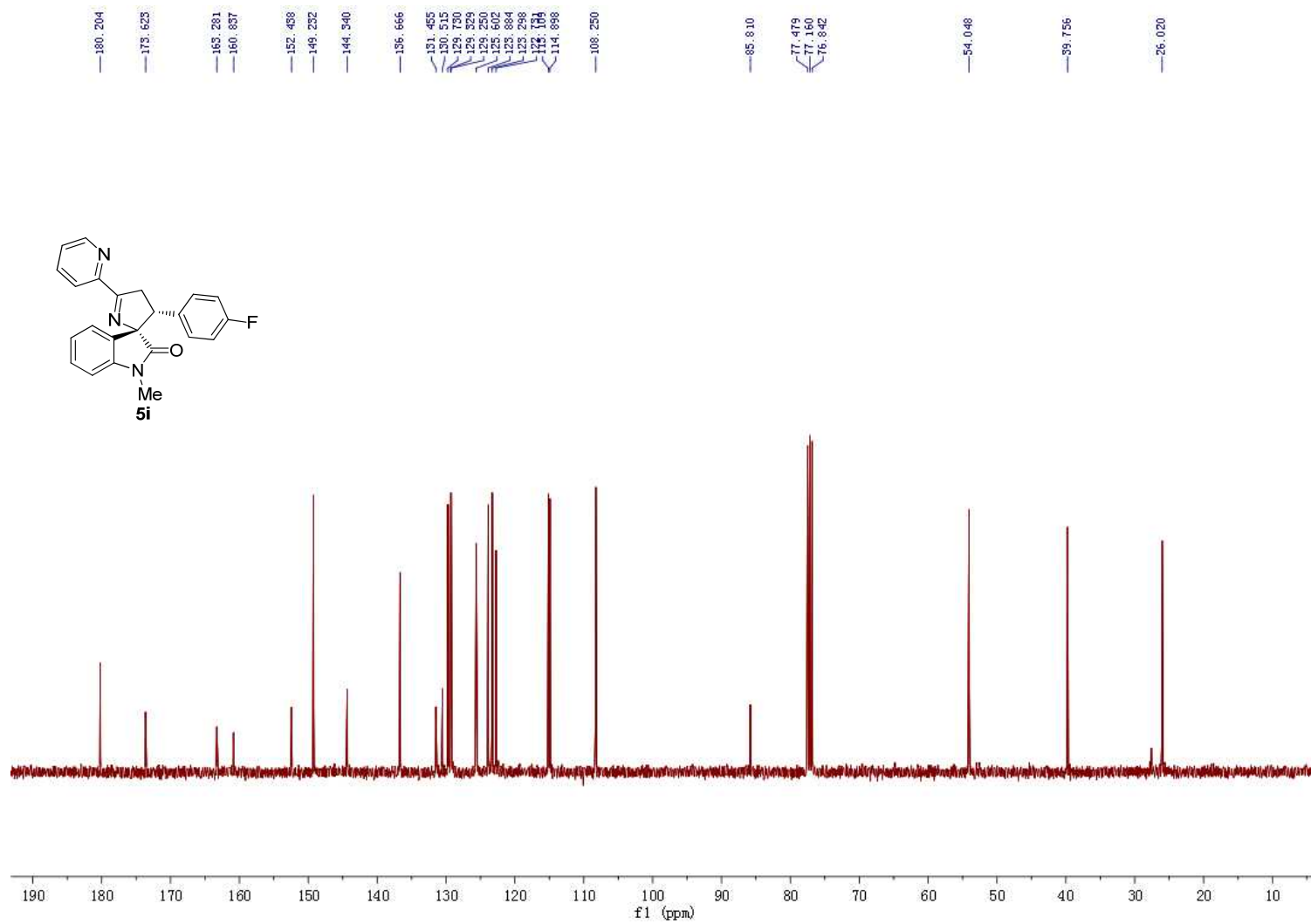


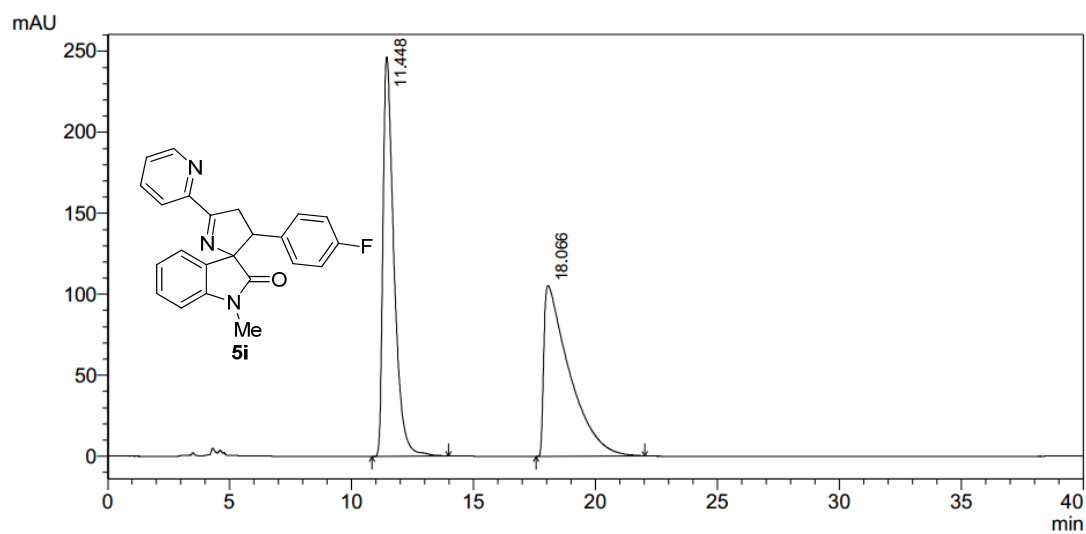
PDA

ID#	Ret. time	Area	Height	Area %
1	25.736	10297328	54595	100.000

NMR and HPLC of 5i

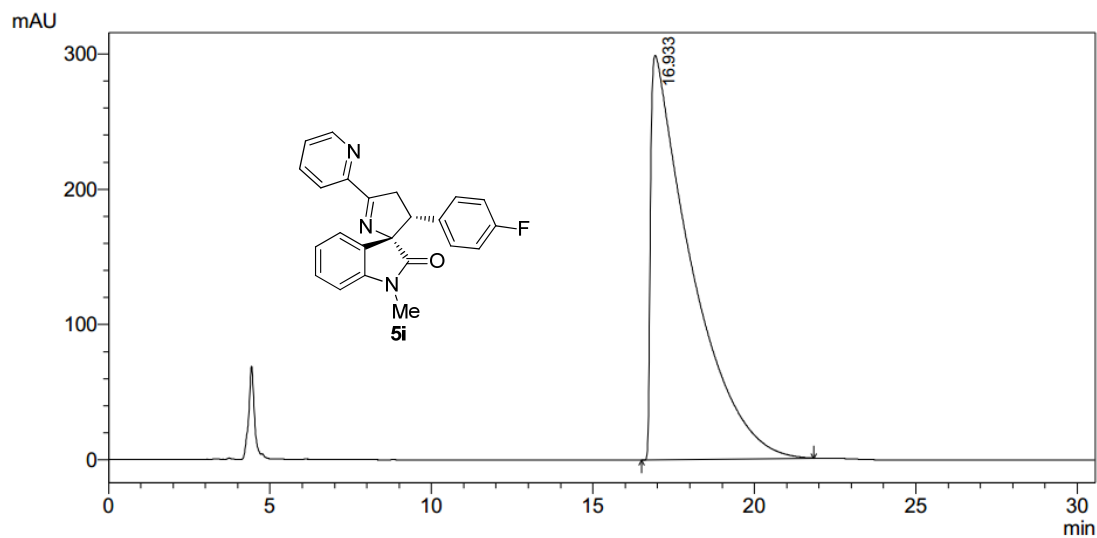






PDA

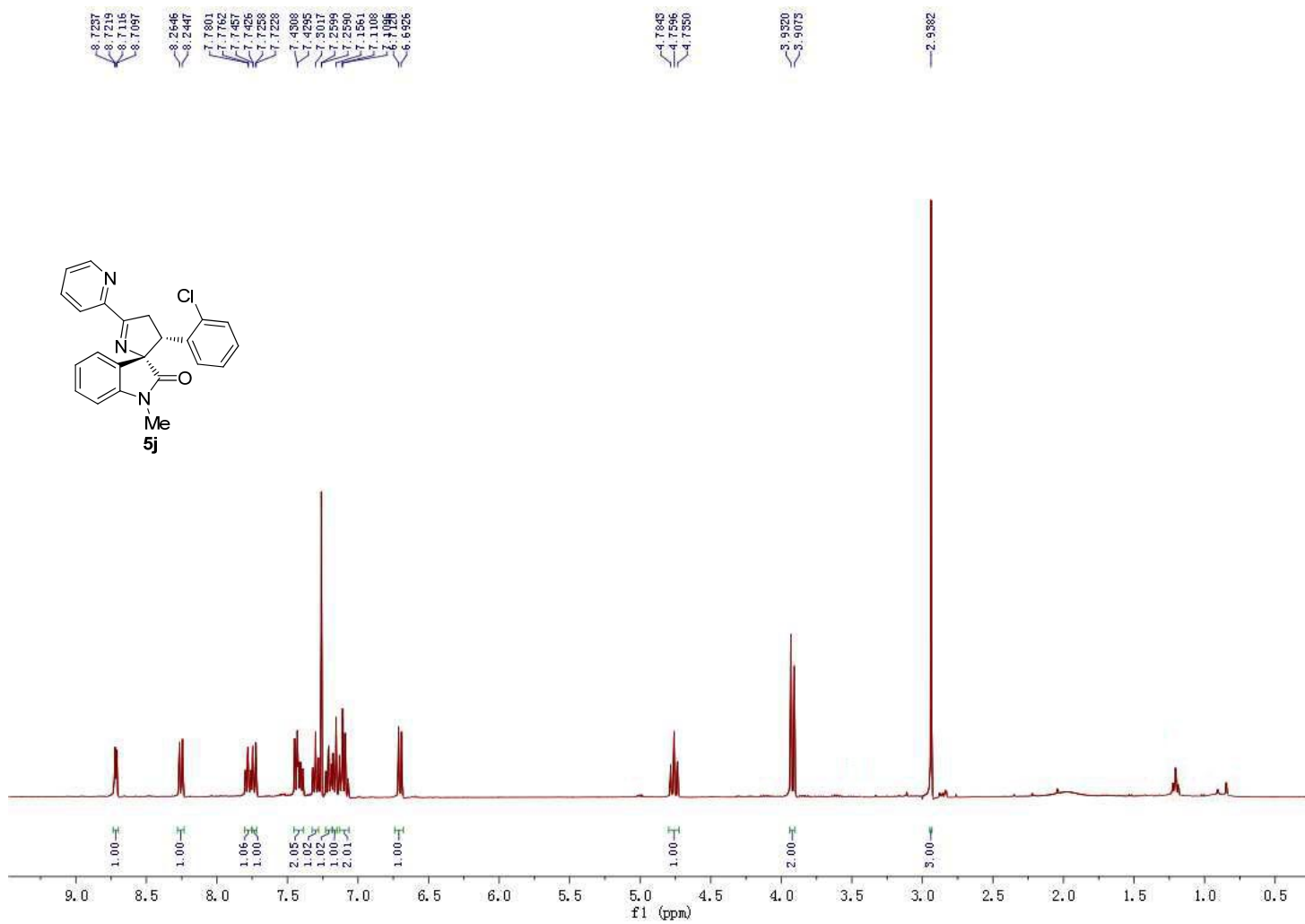
ID#	Ret. time	Area	Height	Area %
1	11.448	7744409	246768	50.227
2	18.066	7674324	105389	49.773

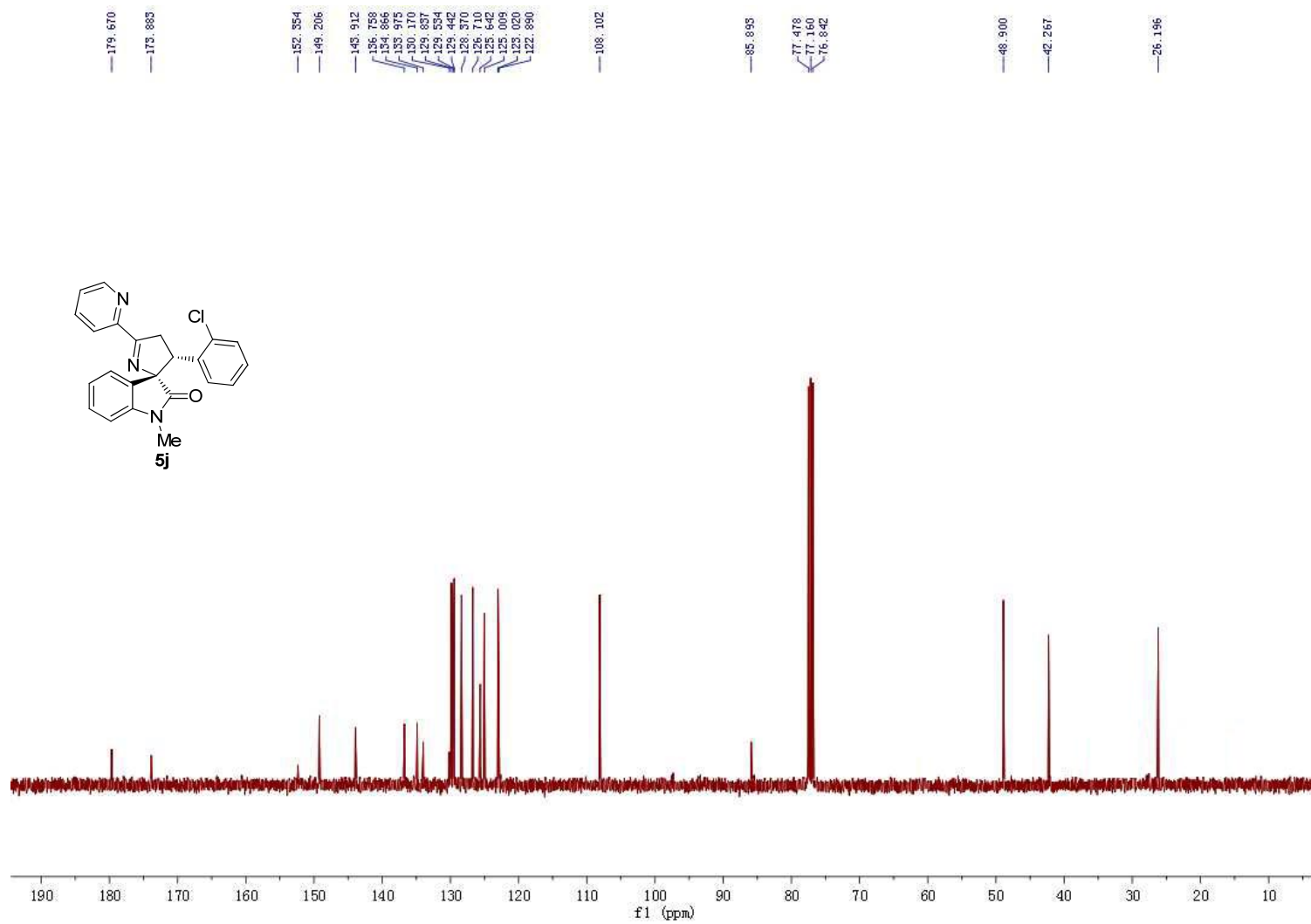


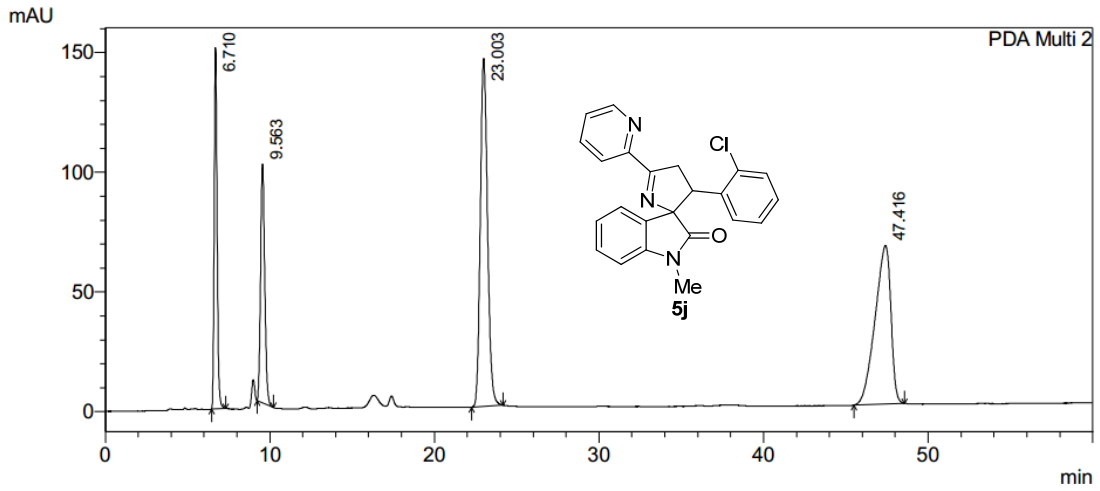
PDA

ID#	Ret. time	Area	Height	Area %
1	16.933	26059021	299242	100.000

NMR and HPLC of 5j



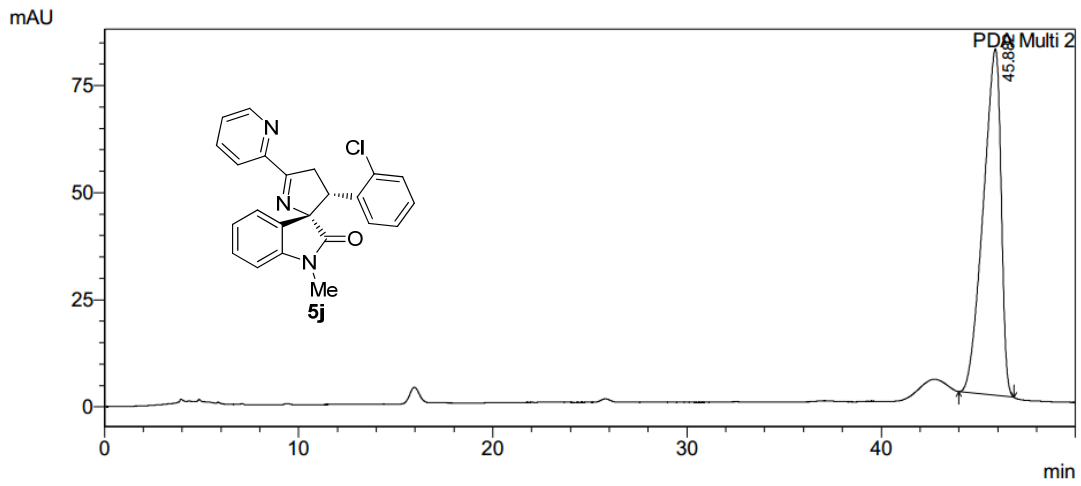




1 PDA Multi 2/254nm 4nm

Quantitative Results

ID#	Name	Ret. Time	Area	Height	Conc.
1	RT6.710	6.710	1846820	150800	14.849
2	RT9.563	9.563	1751370	99709	14.082
3	RT23.003	23.003	4419197	145500	35.533
4	RT47.416	47.416	4419604	66293	35.536

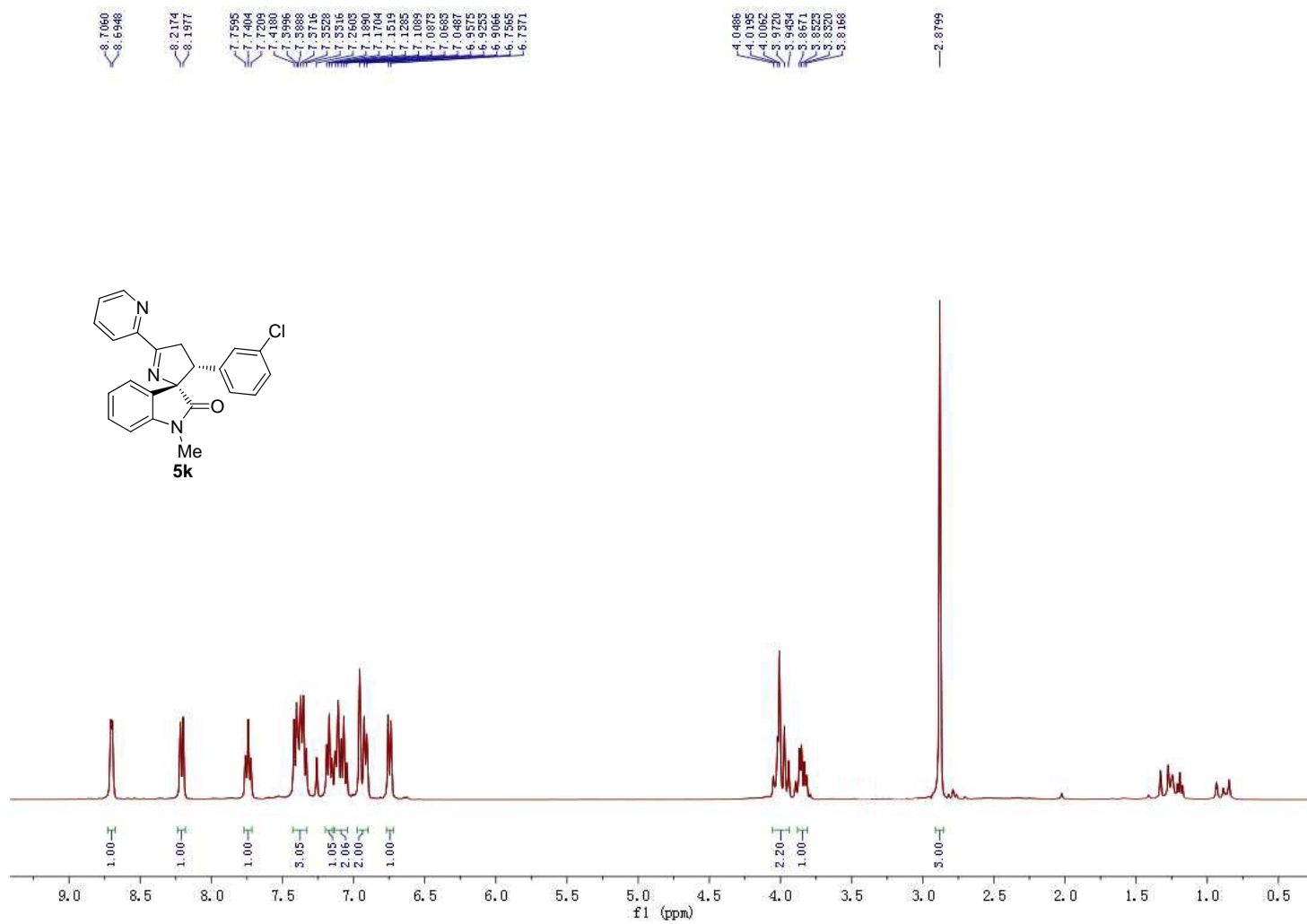


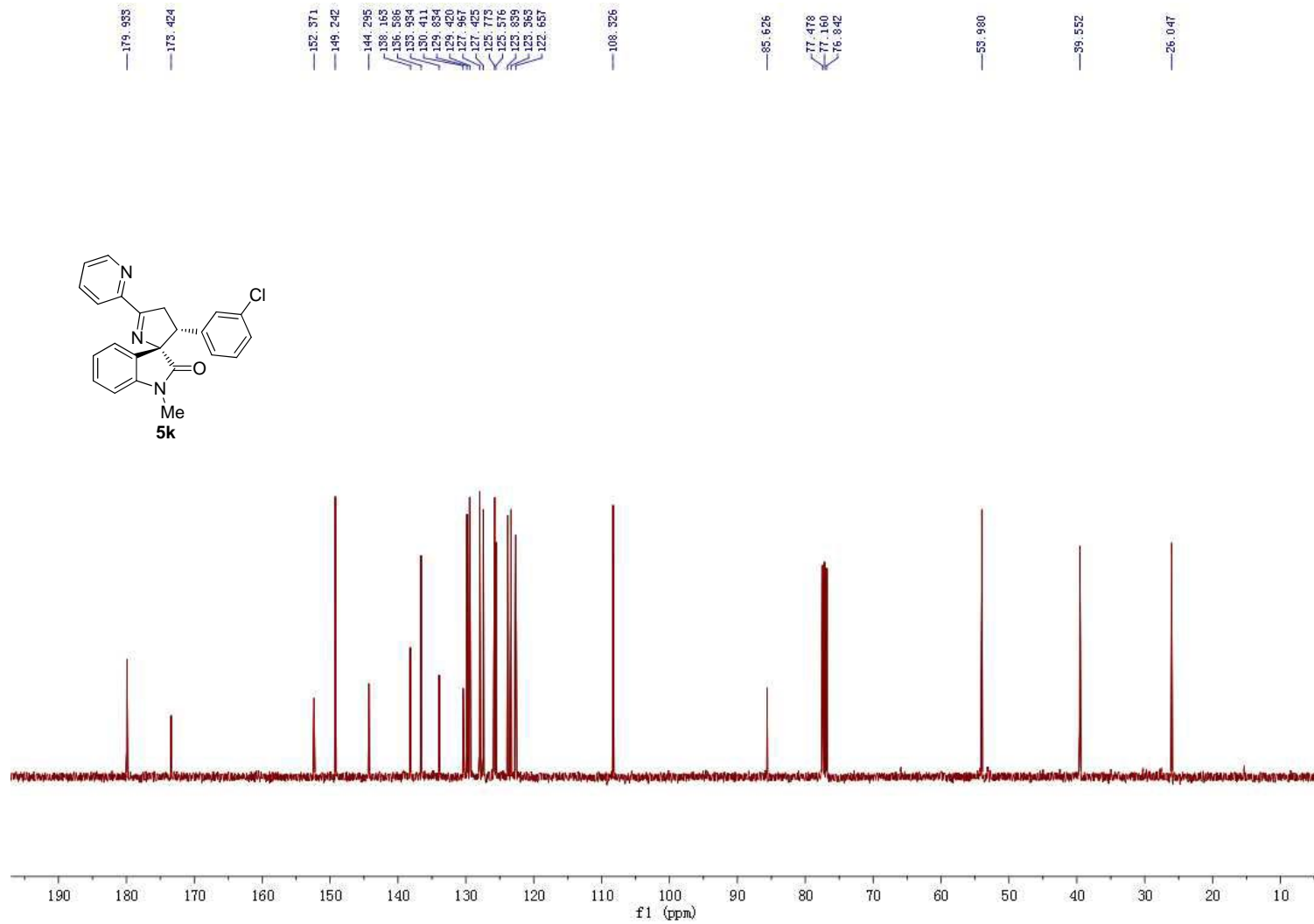
1 PDA Multi 2/254nm 4nm

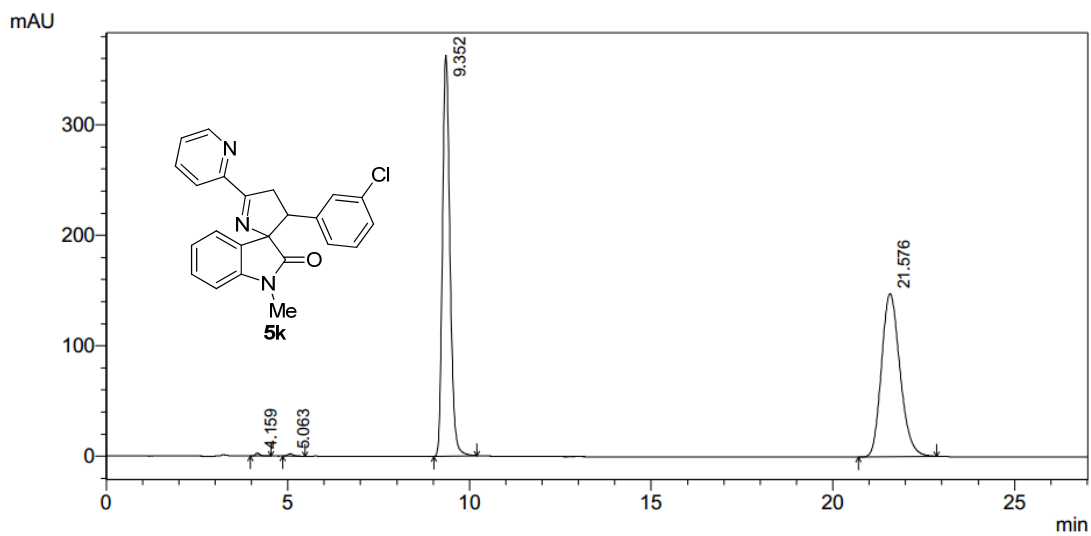
Quantitative Results

ID#	Name	Ret. Time	Area	Height	Conc.
1	RT45.882	45.882	5164903	80806	100.000

NMR and HPLC of 5k

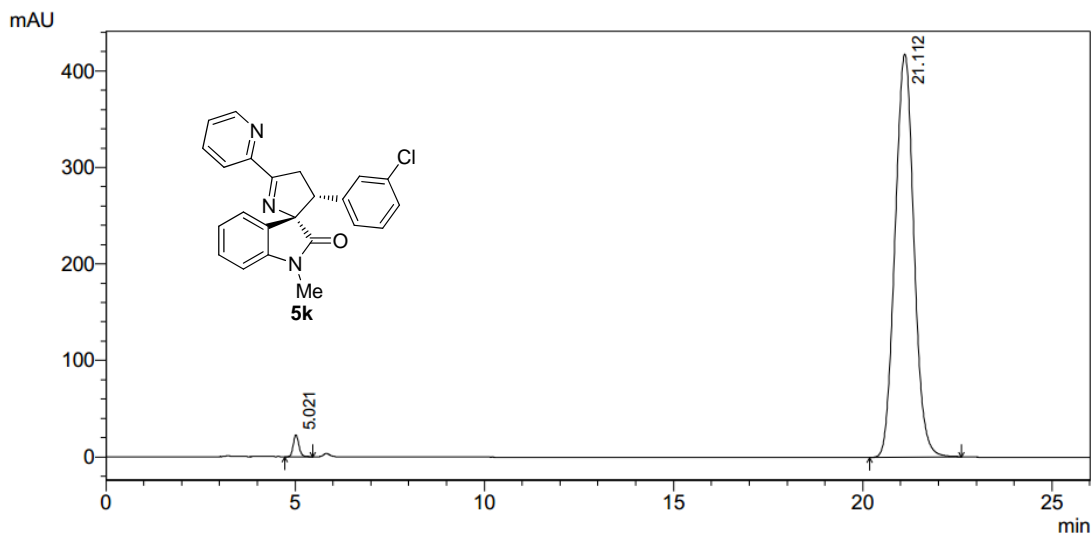






PDA

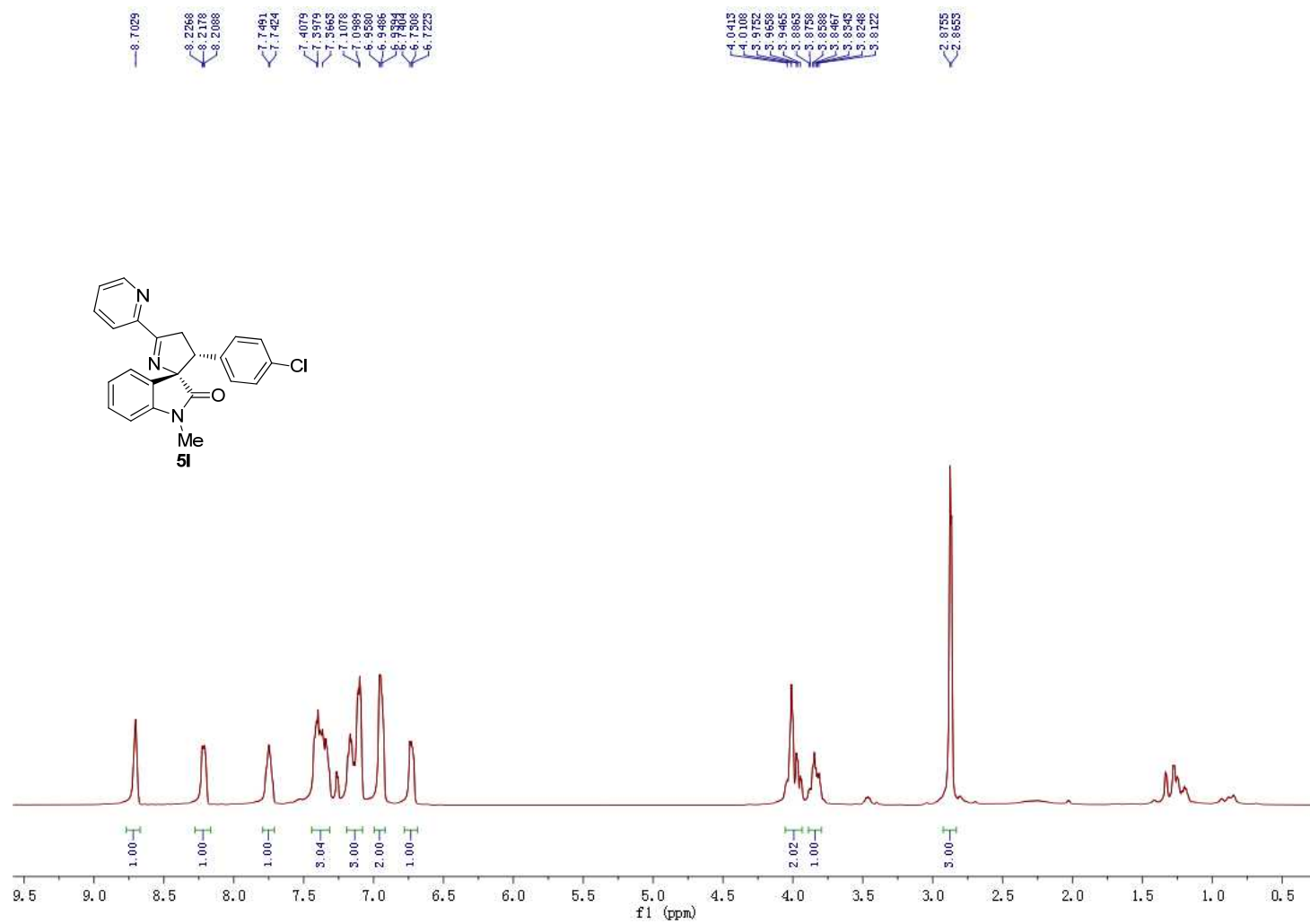
ID#	Ret. time	Area	Height	Area %
1	4.159	23515	2793	0.224
2	5.063	22551	2064	0.214
3	9.352	5228212	363003	49.707
4	21.576	5243847	147734	49.855

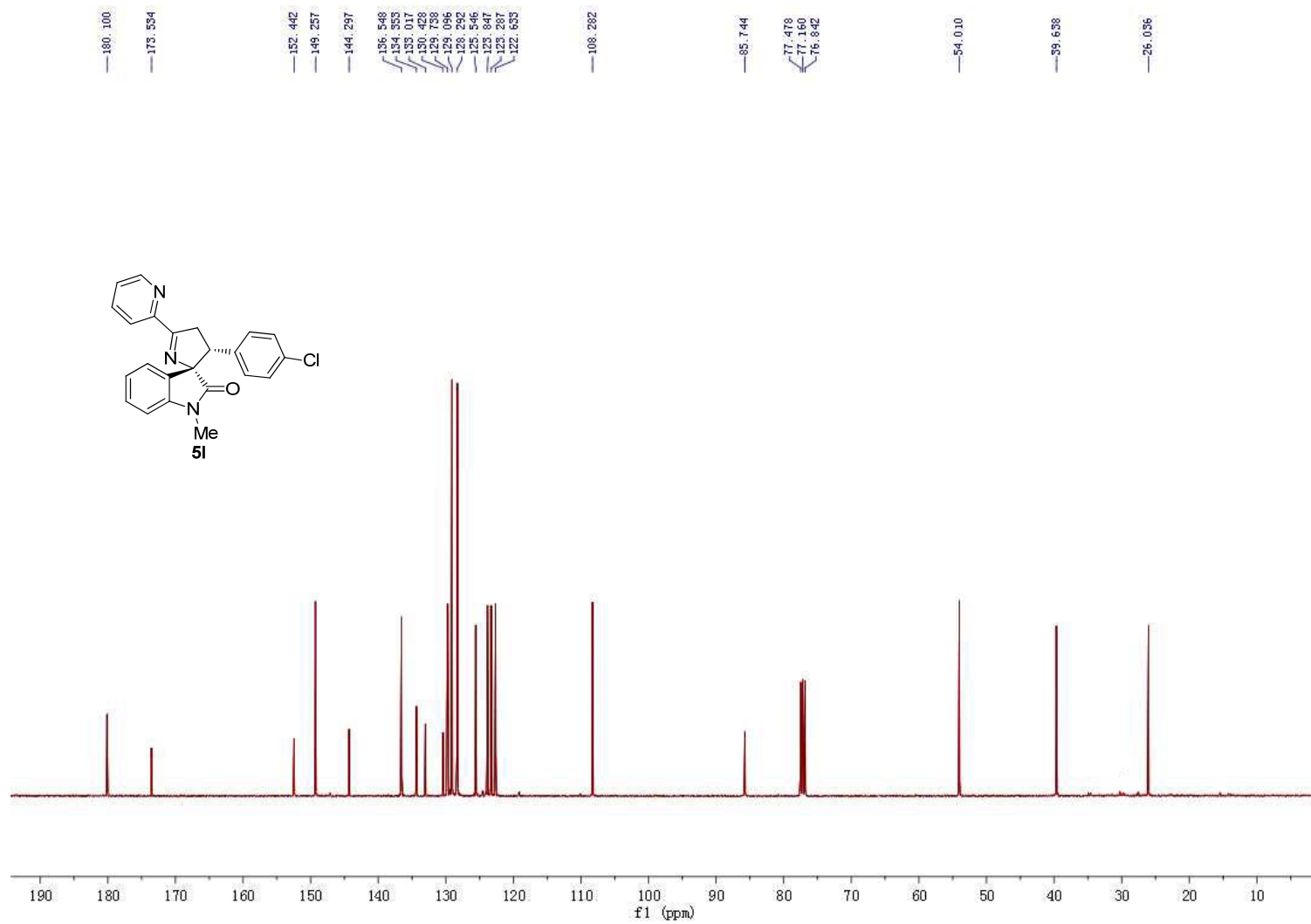


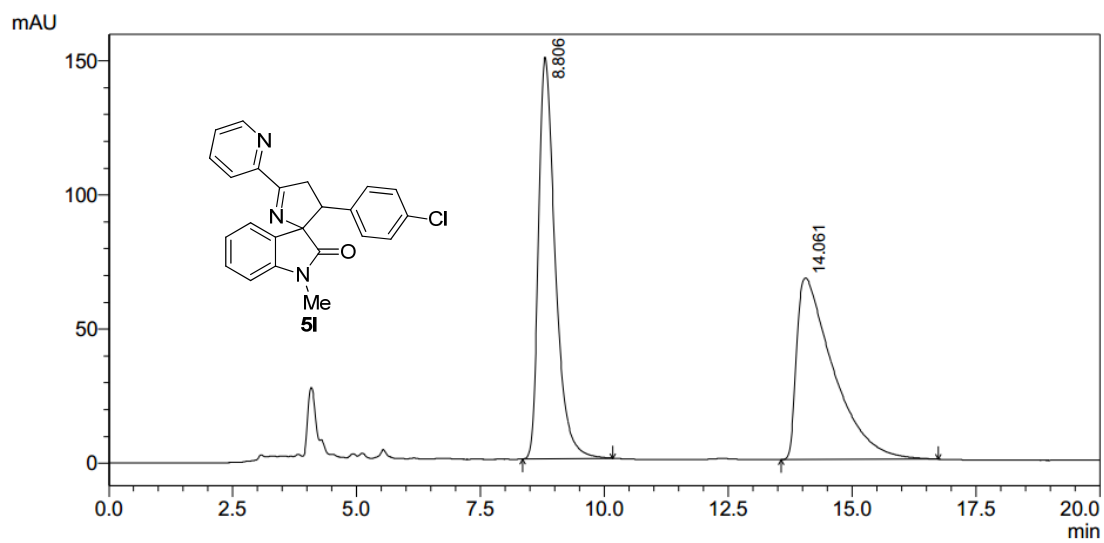
PDA

ID#	Ret. time	Area	Height	Area %
1	5.021	237496	22769	1.615
2	21.112	14469236	418249	98.385

NMR and HPLC of 5l

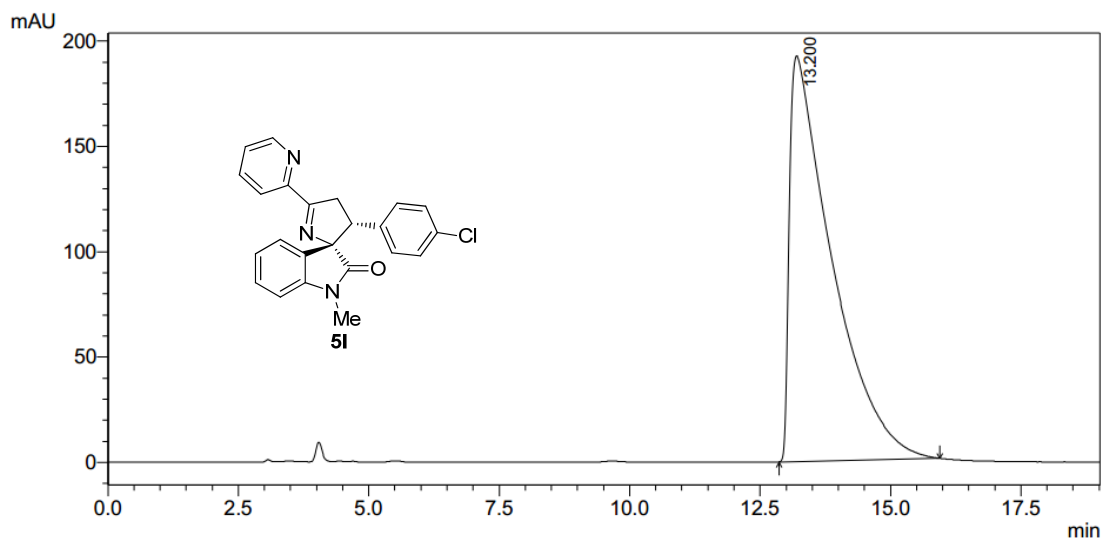






PDA

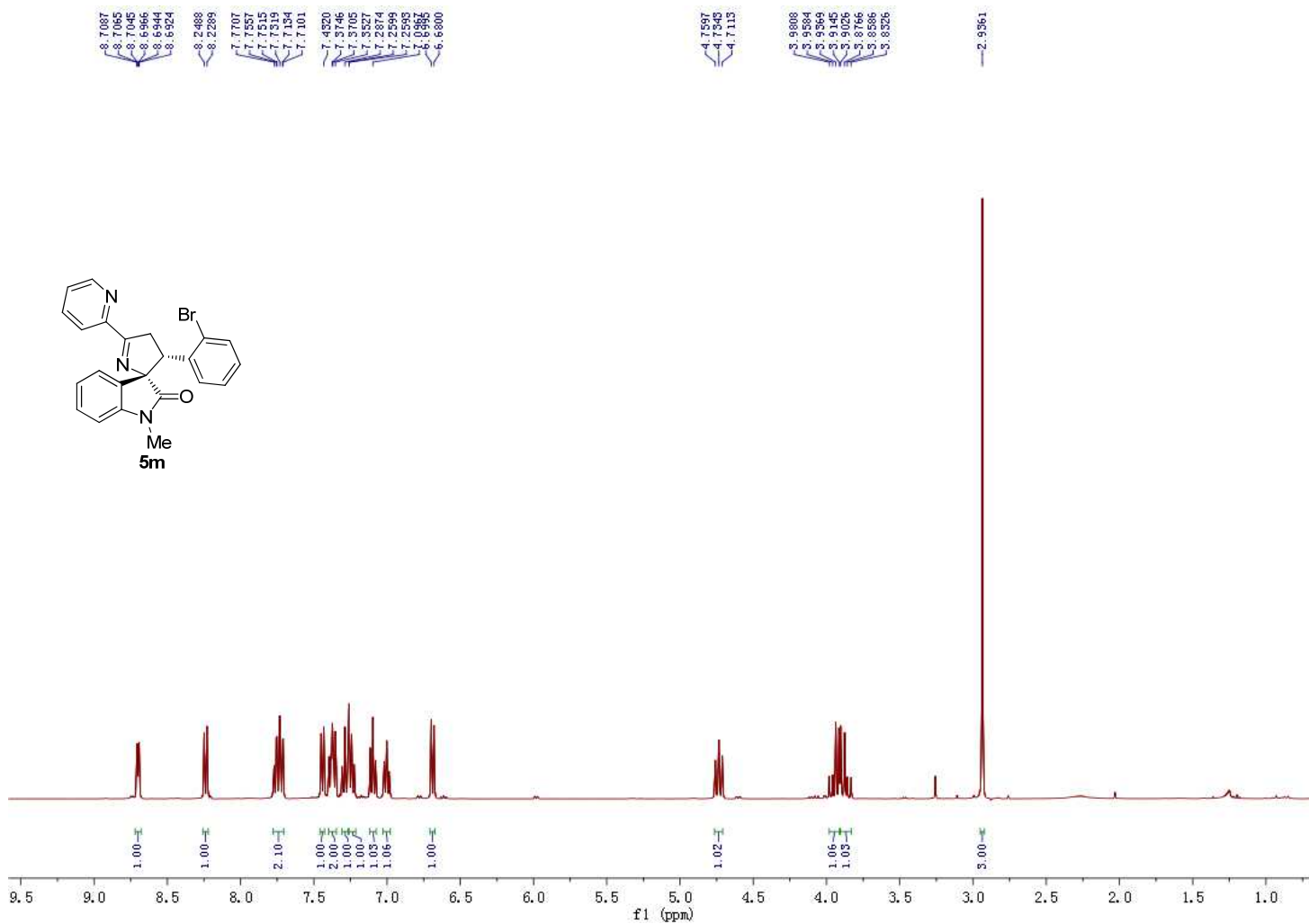
ID#	Ret. time	Area	Height	Area %
1	8.806	3513091	149787	50.104
2	14.061	3498462	67696	49.896

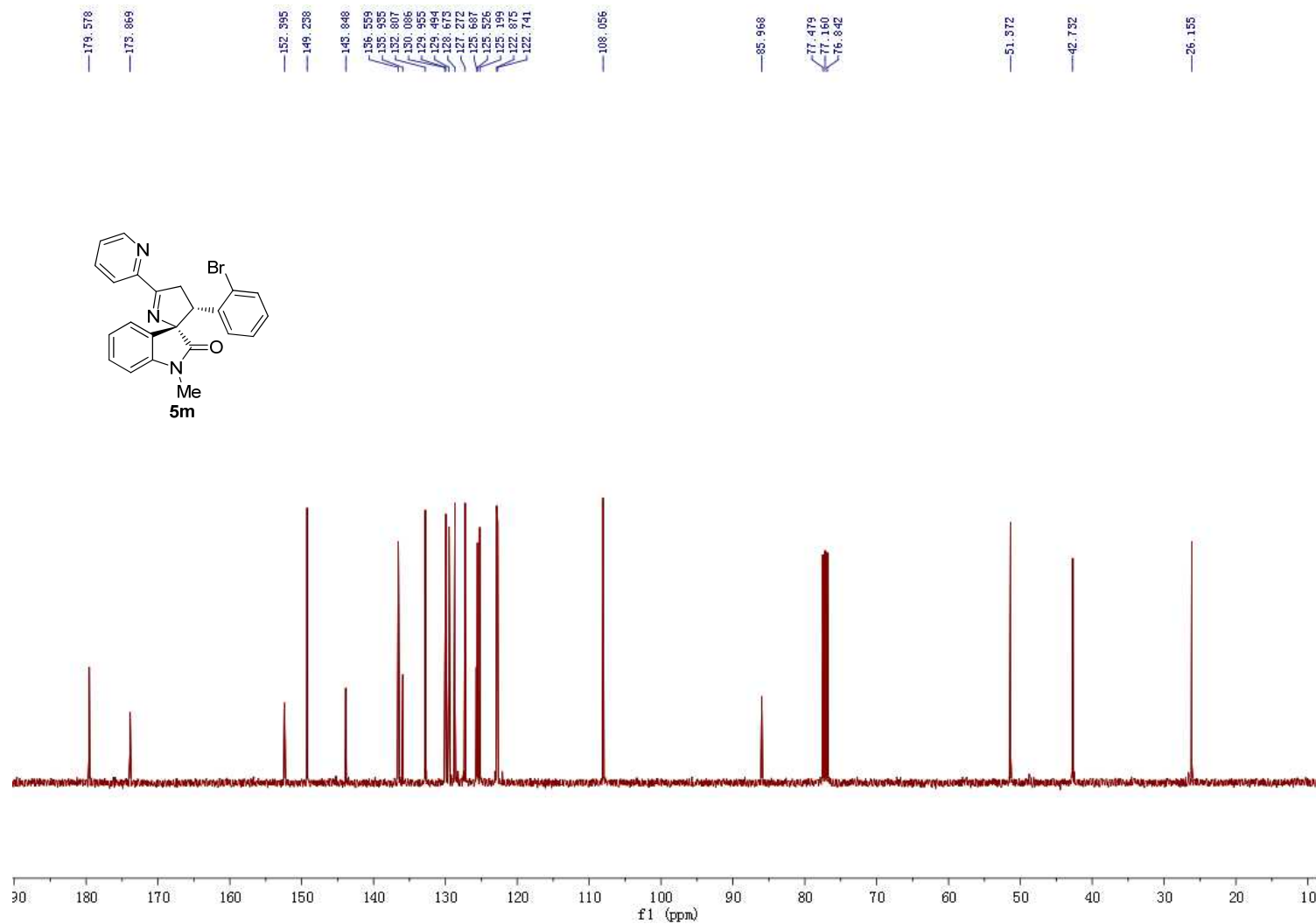


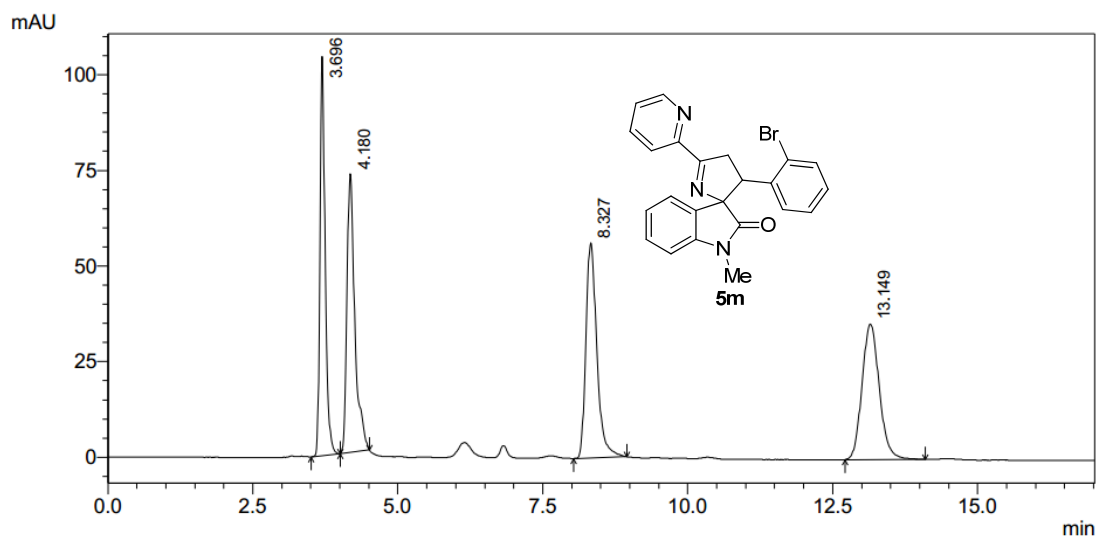
PDA

ID#	Ret. time	Area	Height	Area %
1	13.200	10931002	192678	100.000

NMR and HPLC of 5m

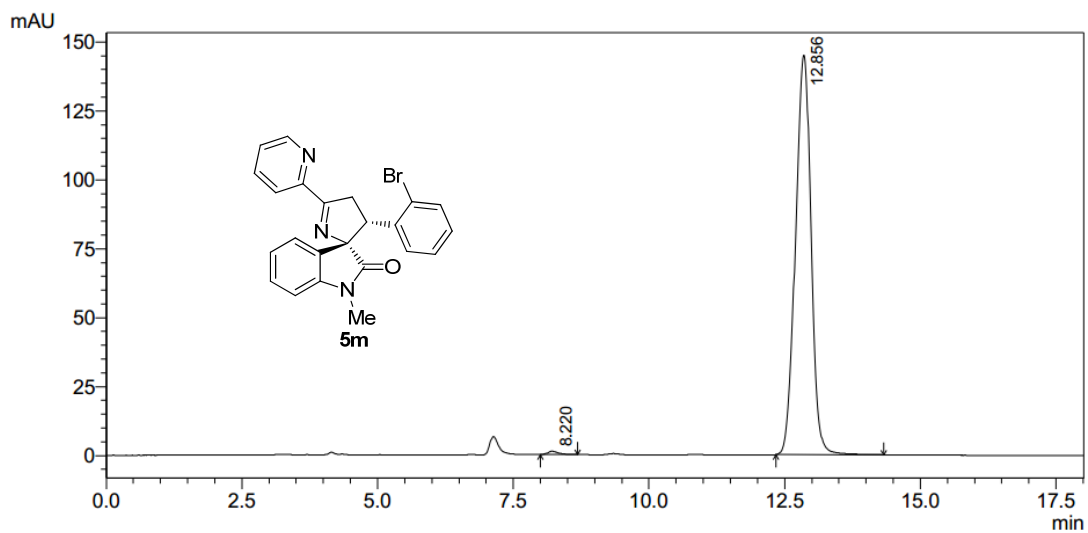






PDA

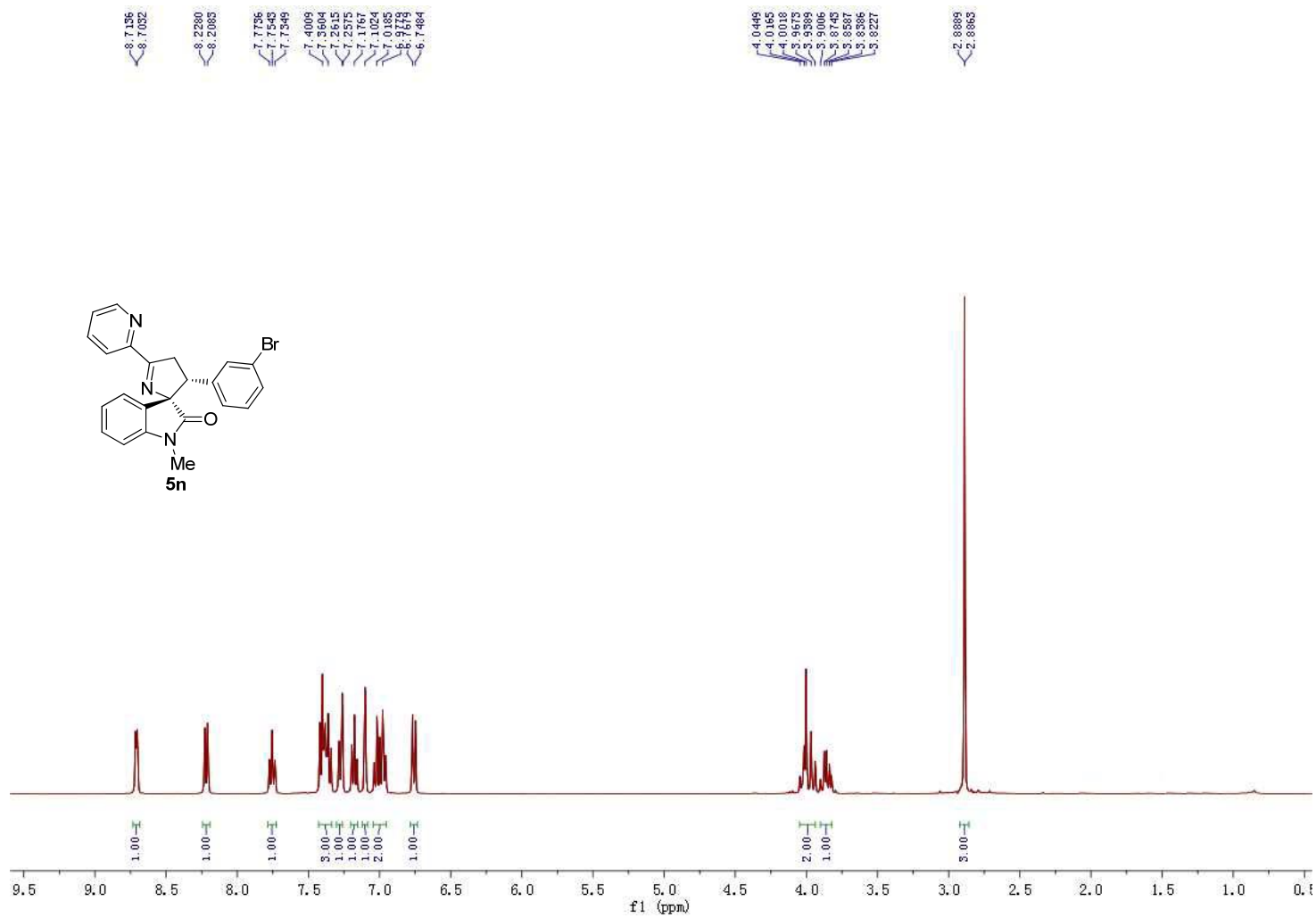
ID#	Ret. time	Area	Height	Area %
1	3.696	656289	104479	23.275
2	4.180	689055	72798	24.437
3	8.327	738095	56237	26.176
4	13.149	736322	35444	26.113

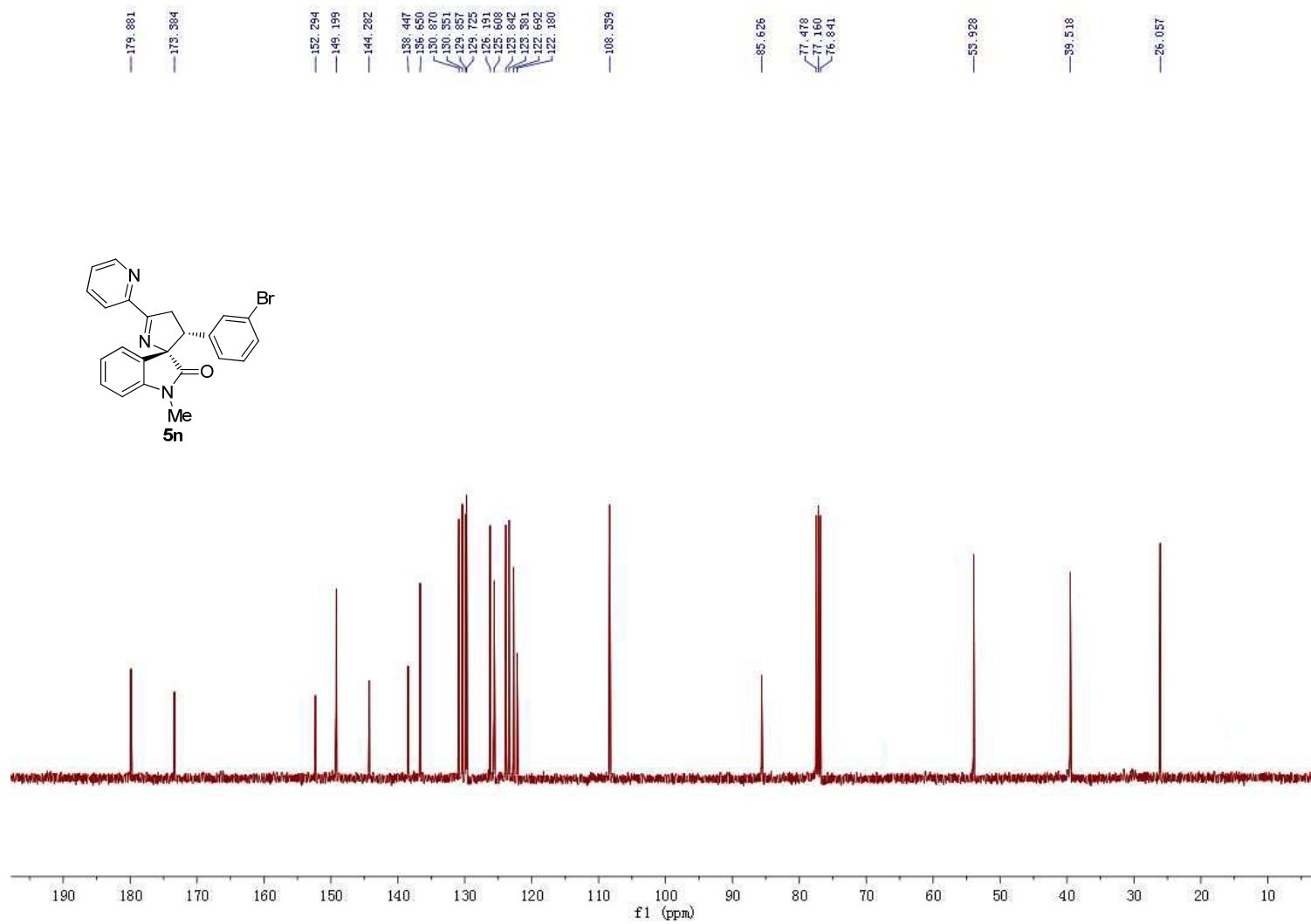


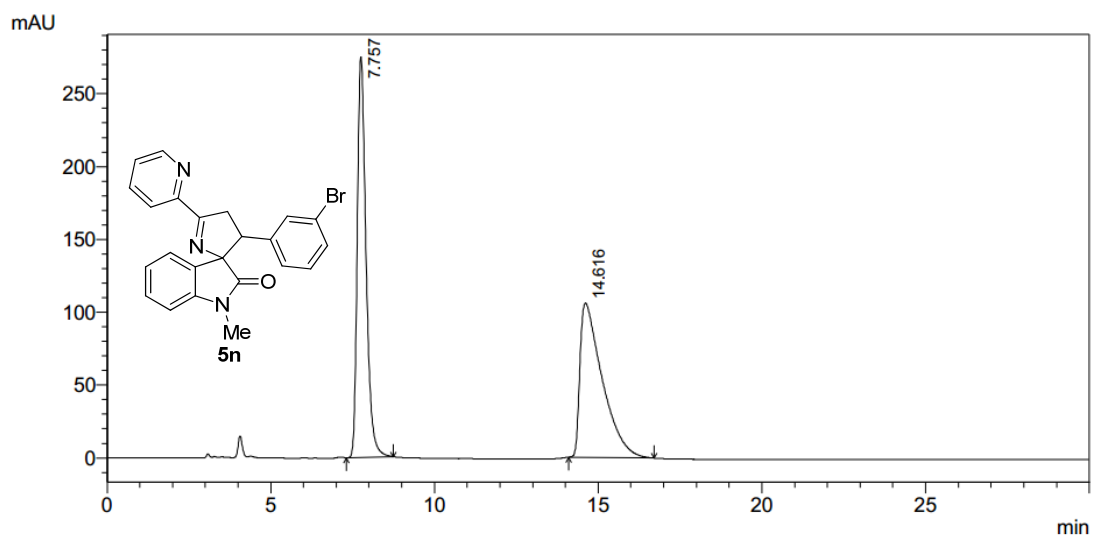
PDA

ID#	Ret. time	Area	Height	Area %
1	8.220	16550	1188	0.567
2	12.856	2900354	145014	99.433

NMR and HPLC of 5n

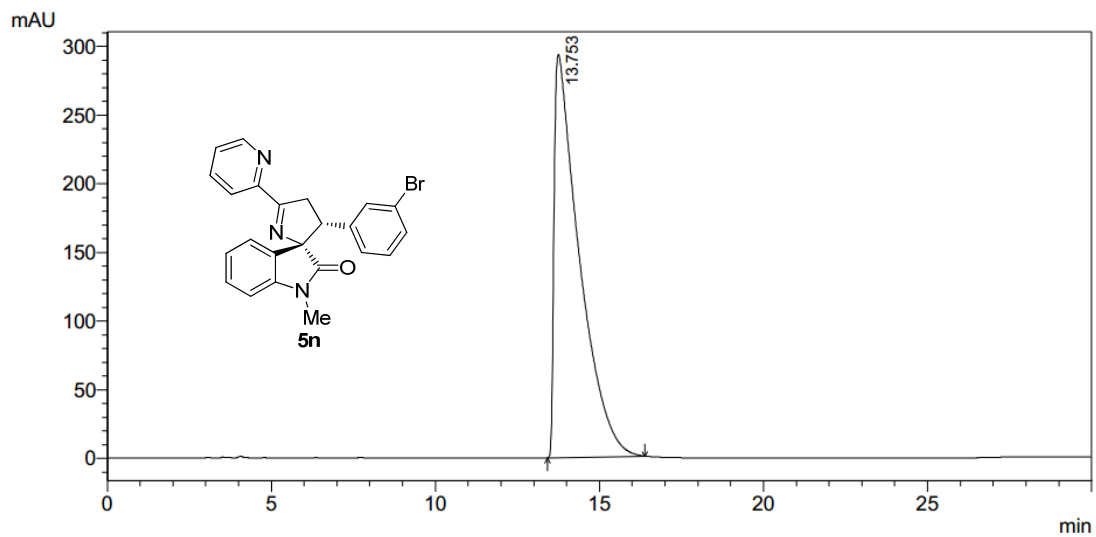






PDA

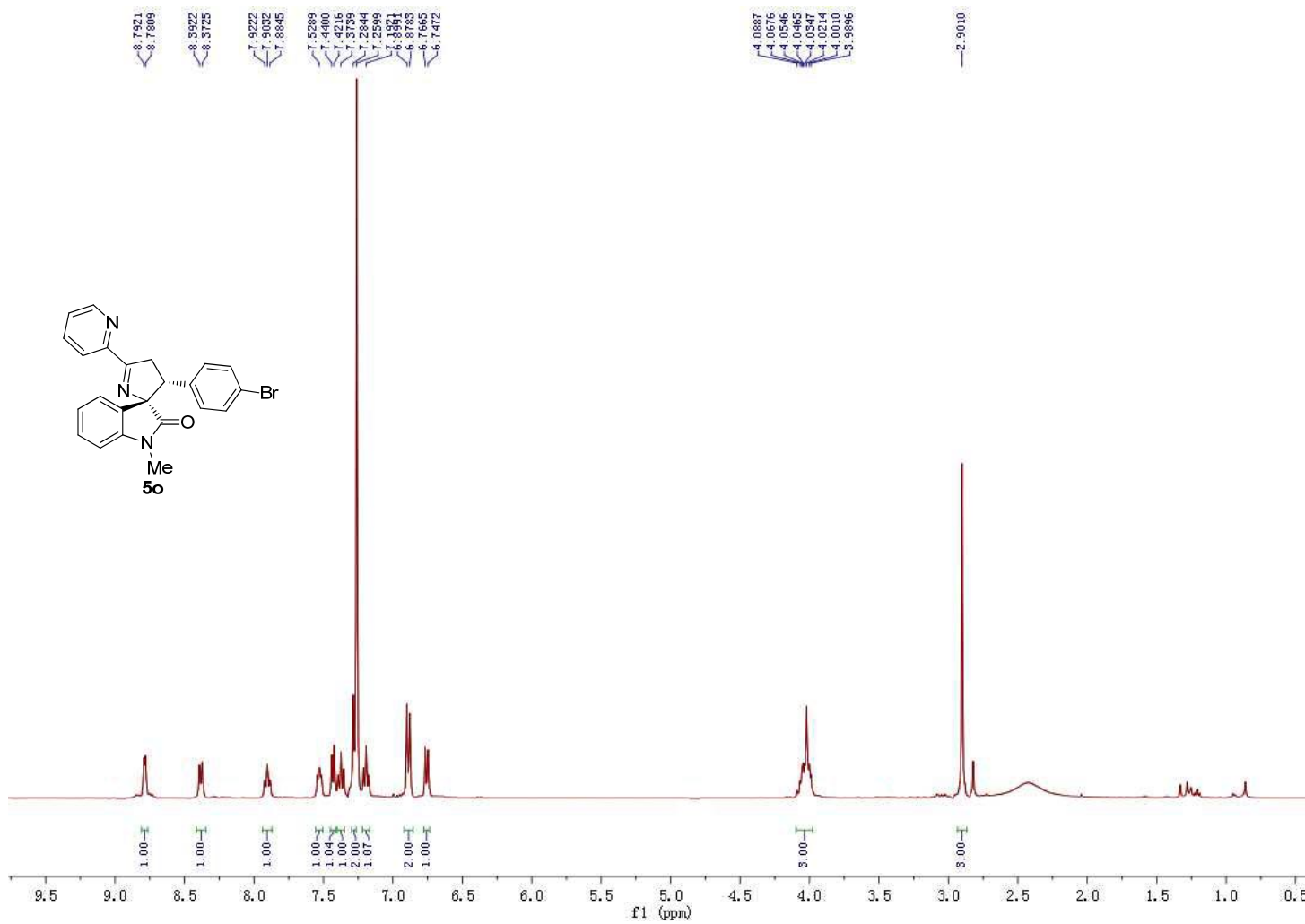
ID#	Ret. time	Area	Height	Area %
1	7.757	5119655	275148	50.538
2	14.616	5010684	105933	49.462

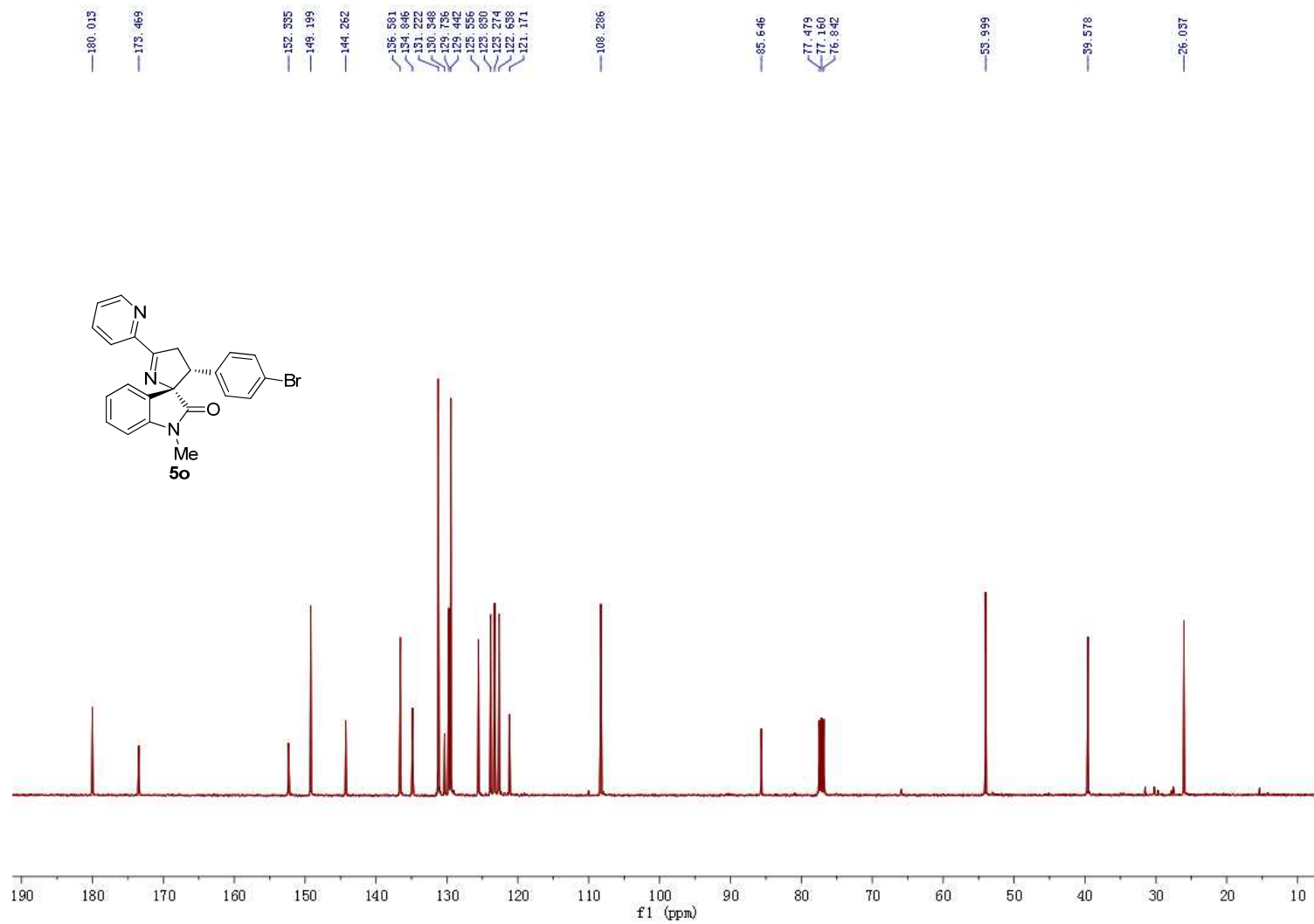


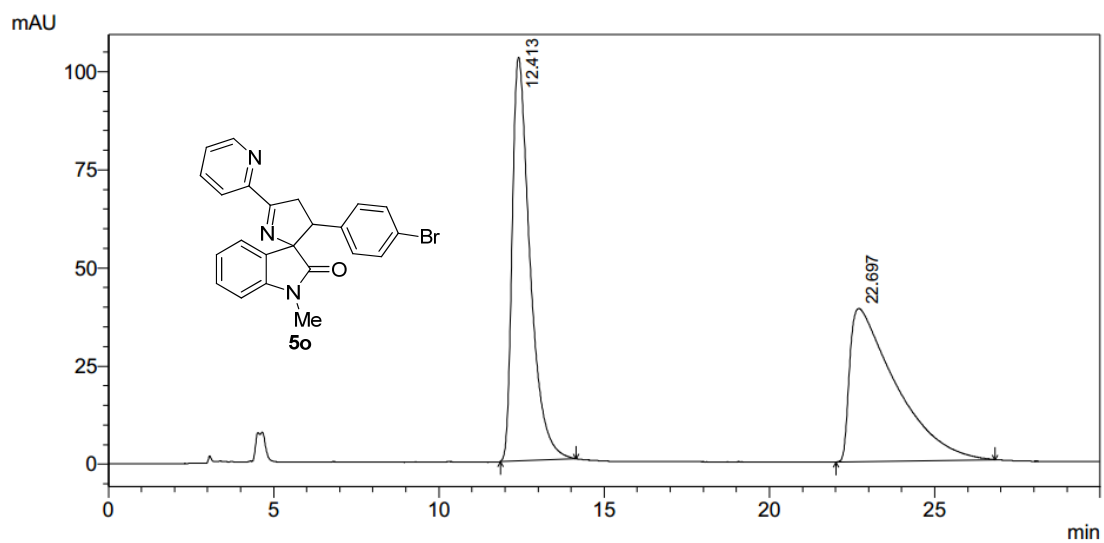
PDA

ID#	Ret. time	Area	Height	Area %
1	13.753	15601717	293880	100.000

NMR and HPLC of 5o

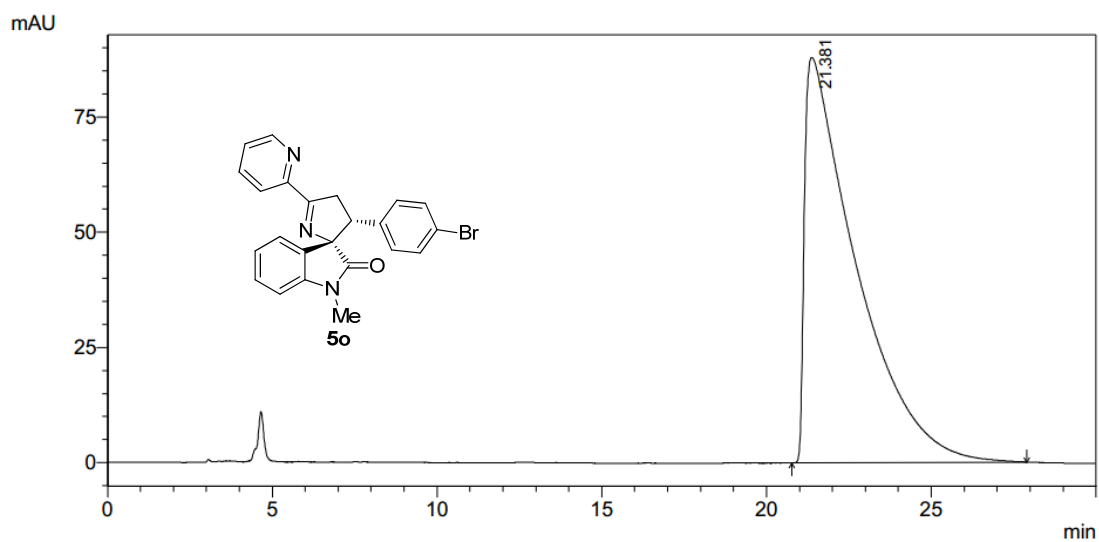






PDA

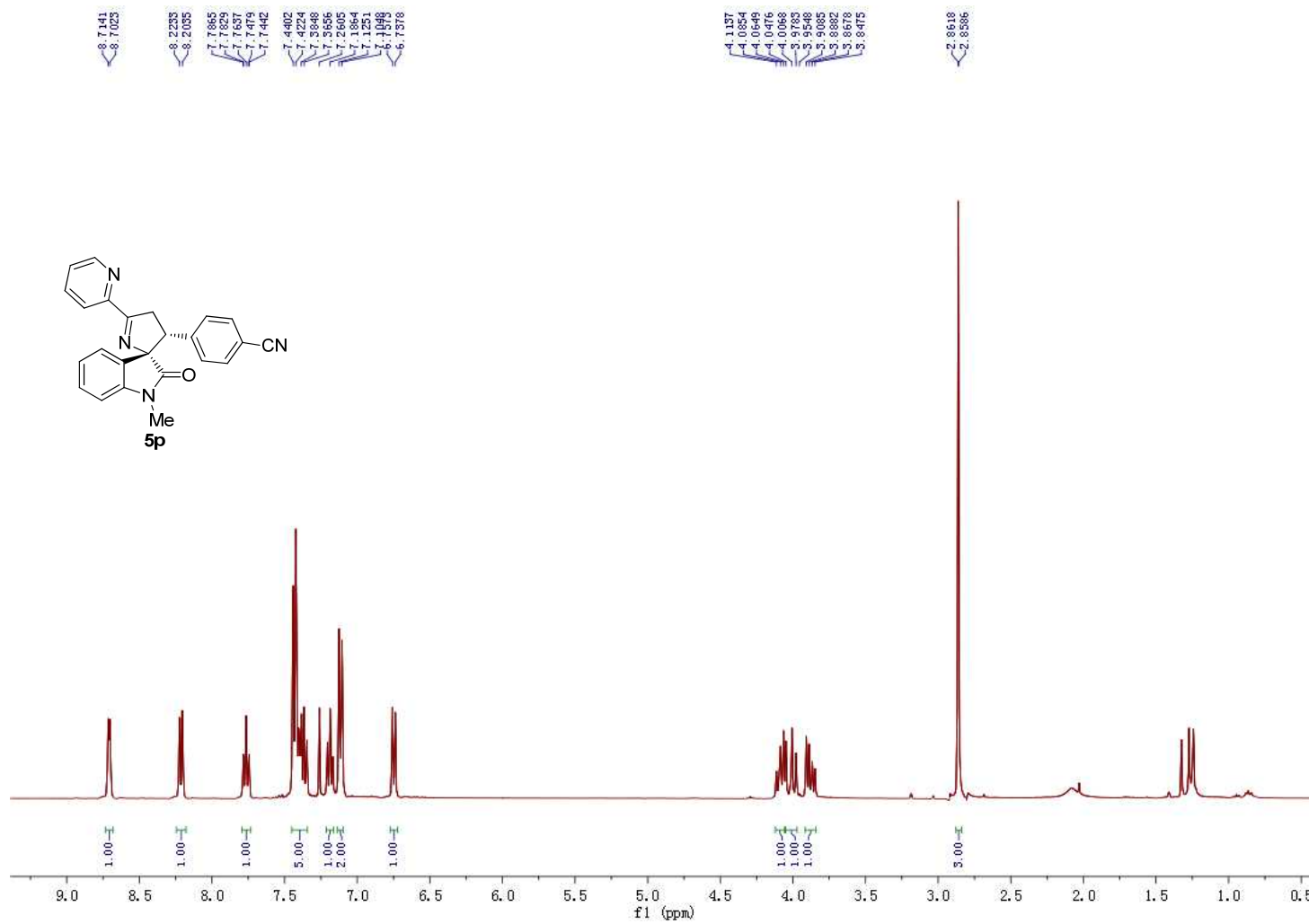
ID#	Ret. time	Area	Height	Area %
1	12.413	3847015	102860	50.327
2	22.697	3796983	39057	49.673

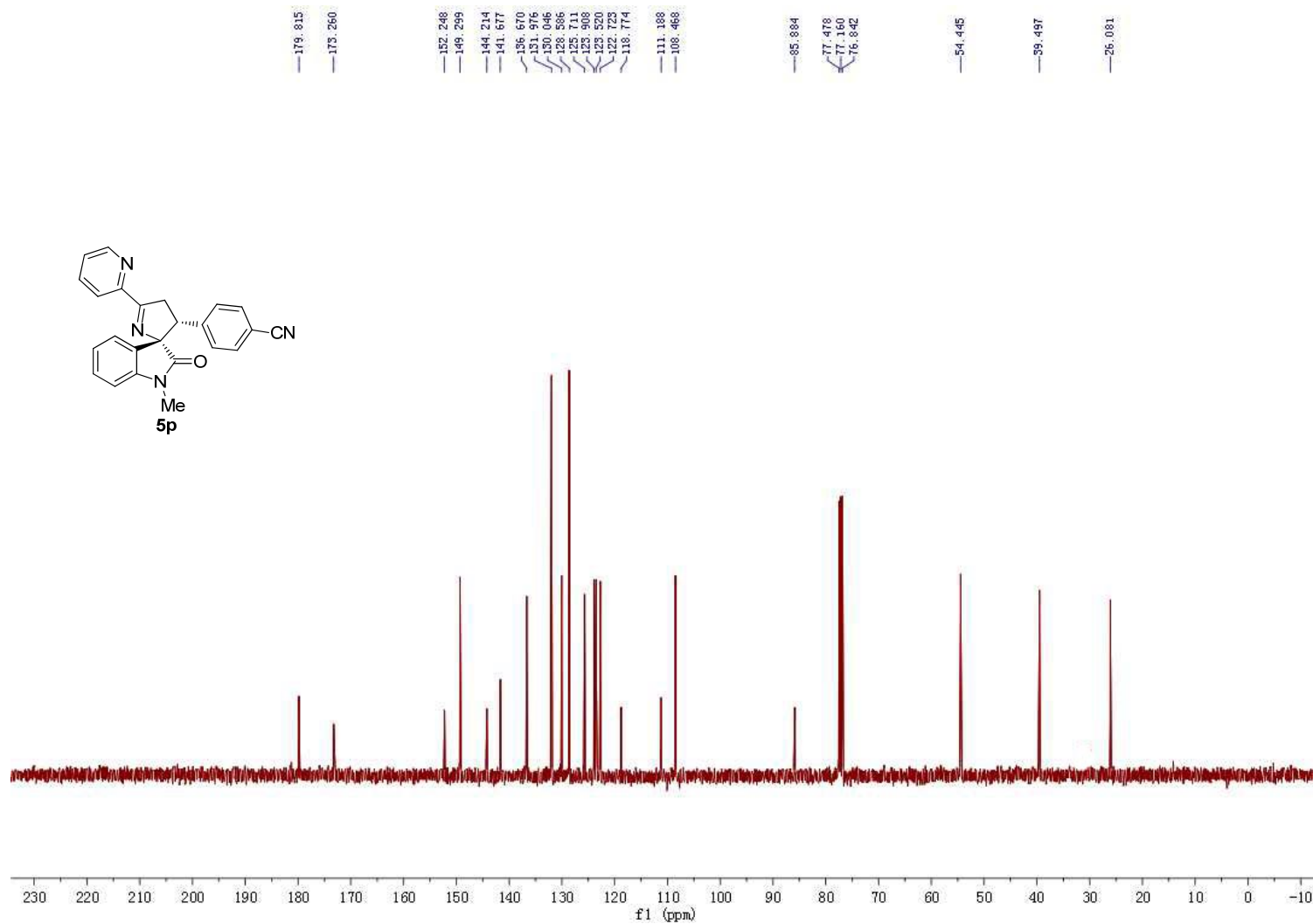


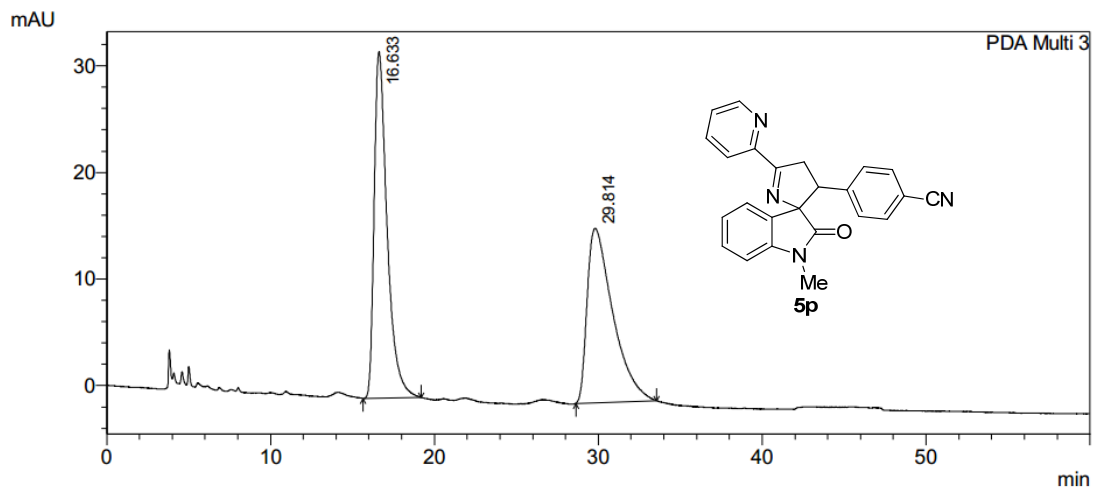
PDA

ID#	Ret. time	Area	Height	Area %
1	21.381	9562397	87961	100.000

NMR and HPLC of 5p



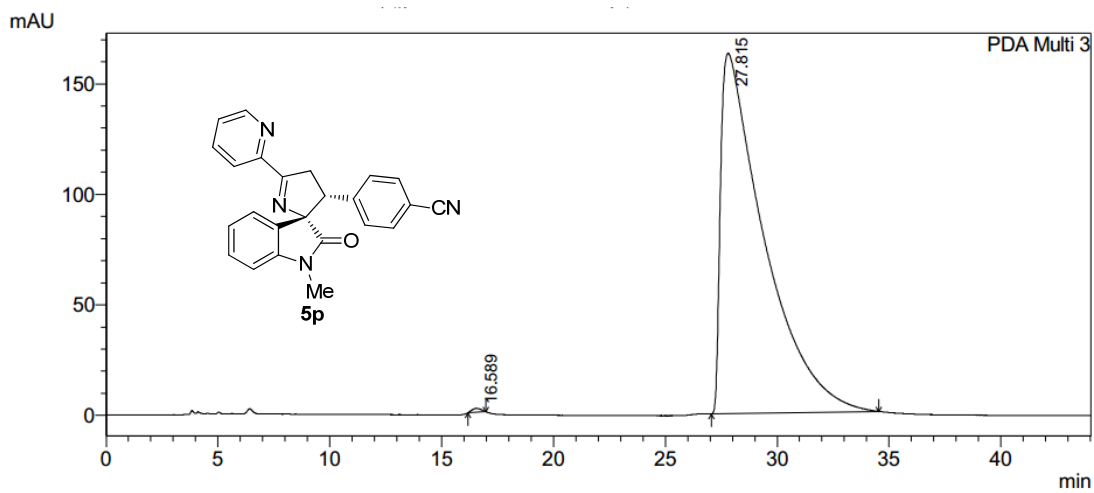




1 PDA Multi 3/254nm 4nm

Quantitative Results

ID#	Name	Ret. Time	Area	Height	Conc.
1	RT16.633	16.633	1784969	32497	49.974
2	RT29.814	29.814	1786813	16364	50.026

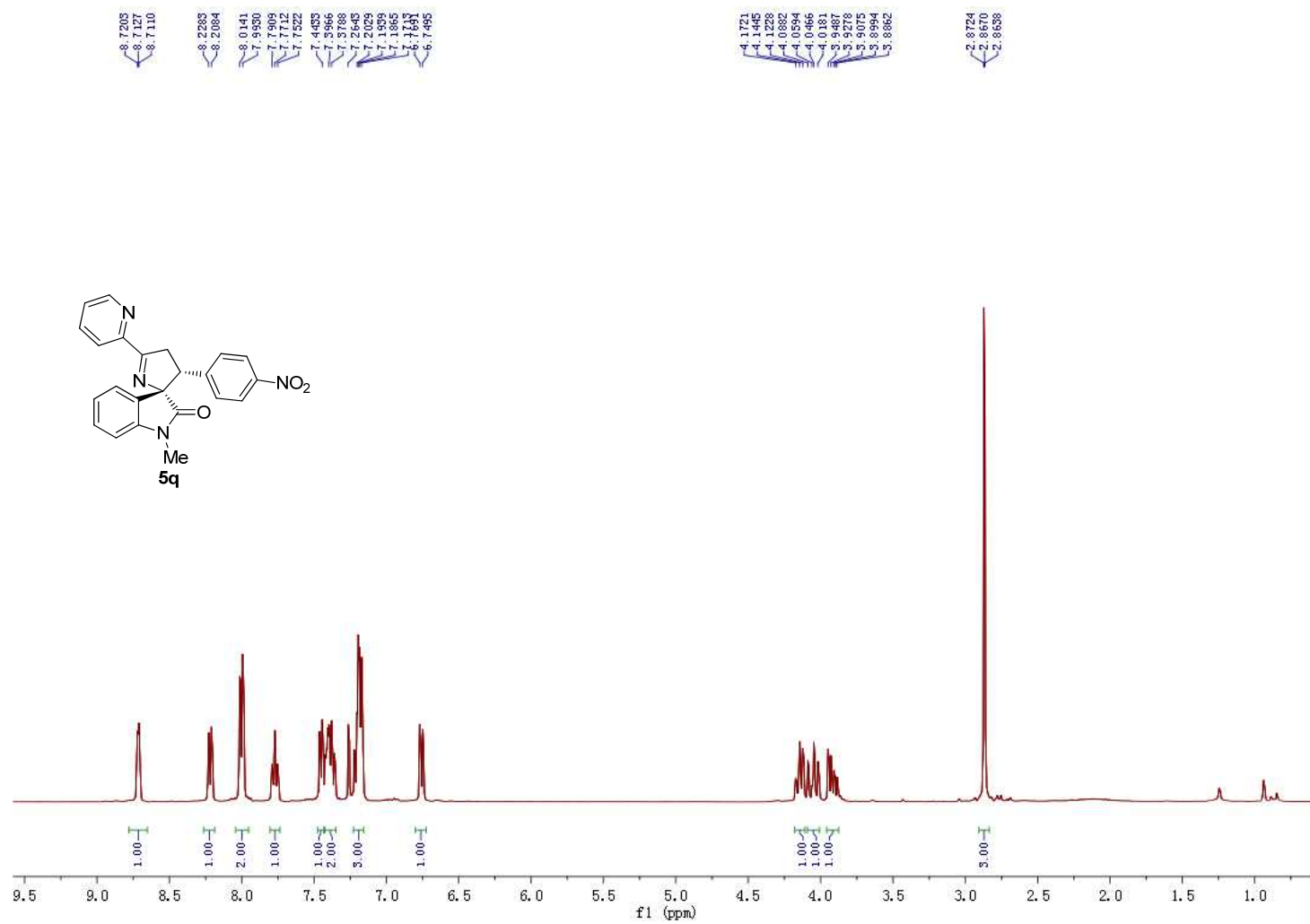


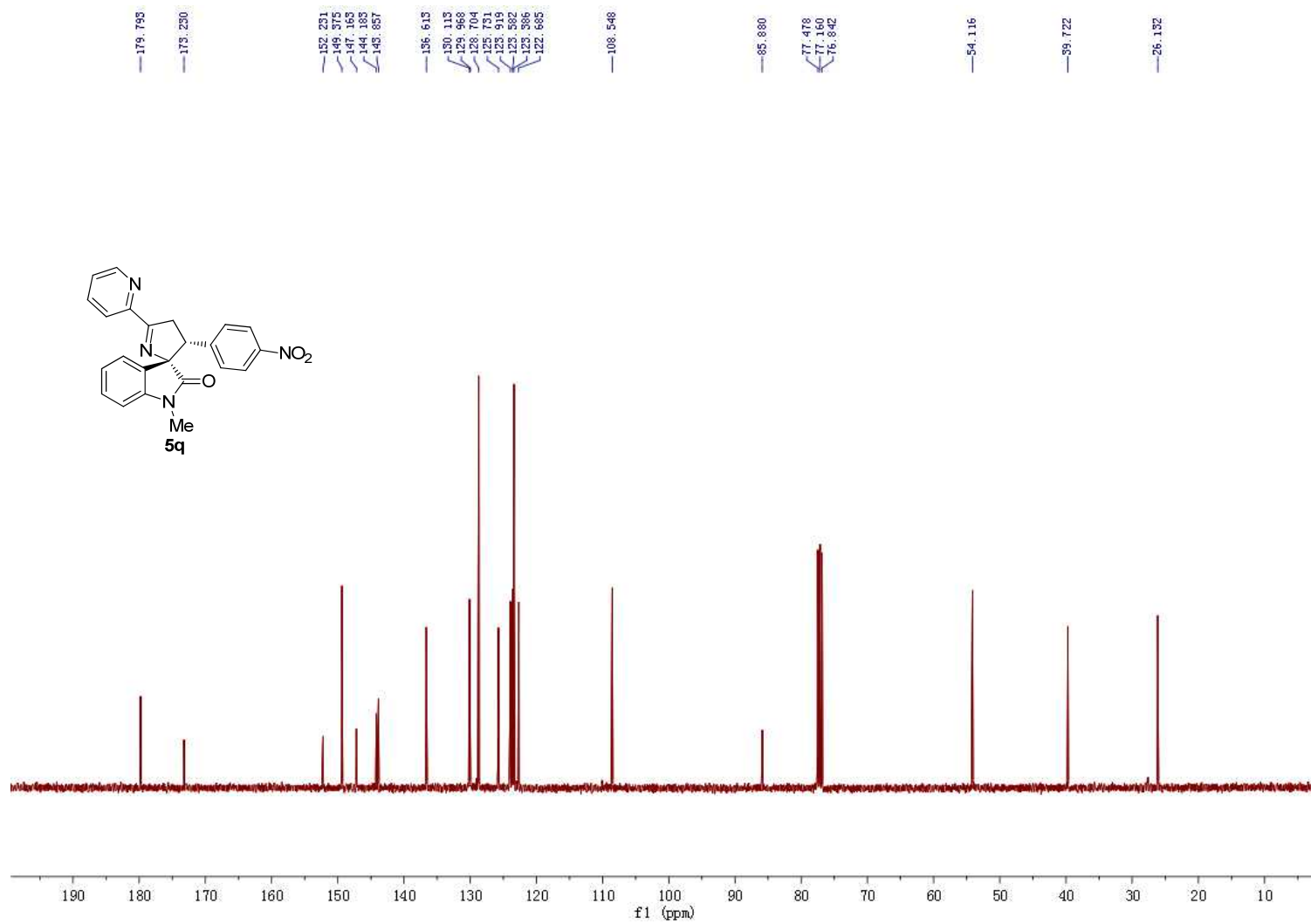
1 PDA Multi 3/254nm 4nm

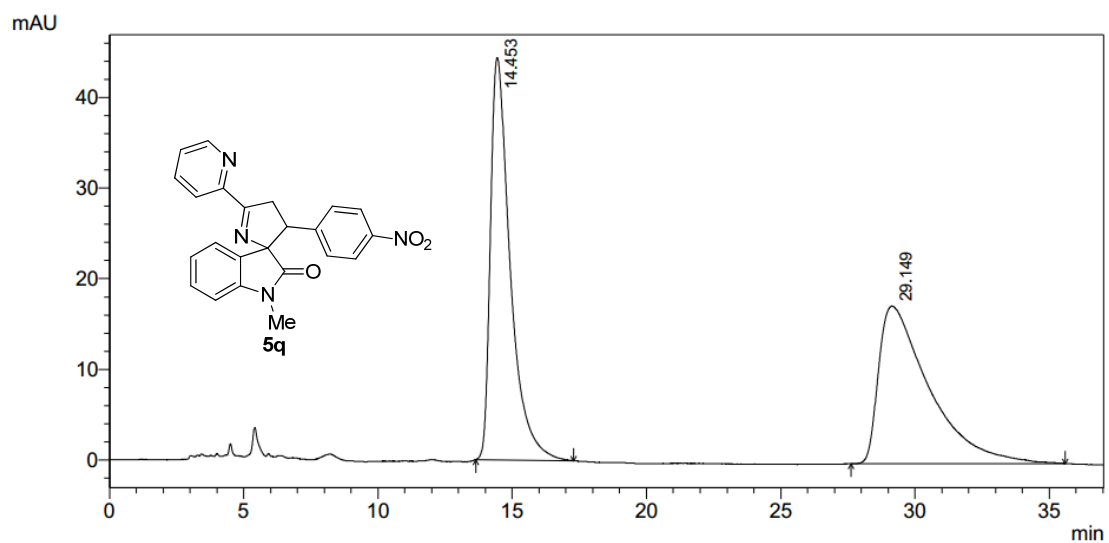
Quantitative Results

ID#	Name	Ret. Time	Area	Height	Conc.
1	RT16.589	16.589	50628	1733	0.230
2	RT27.815	27.815	21989299	163009	99.770

NMR and HPLC of 5q

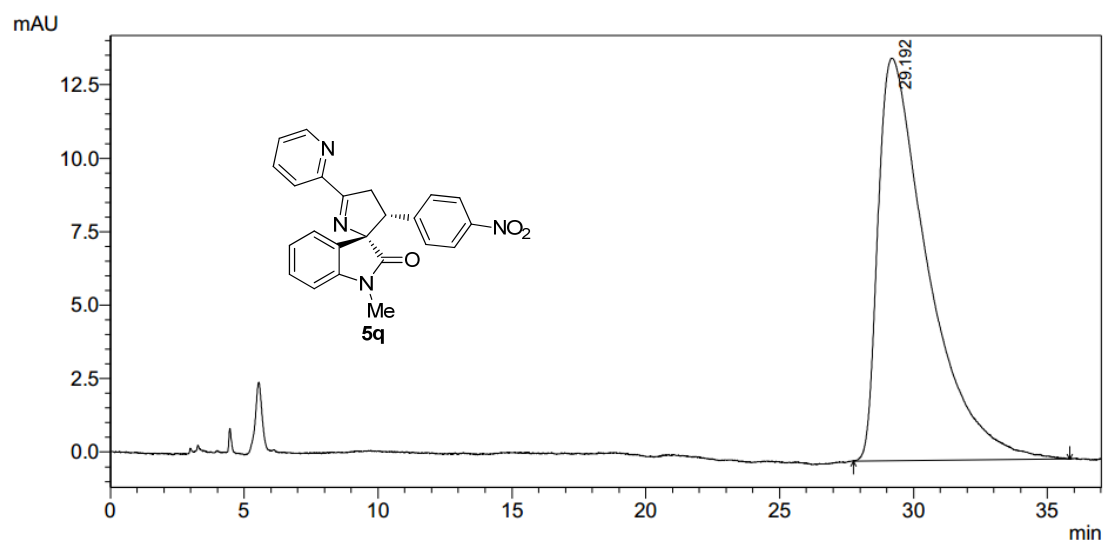






PDA

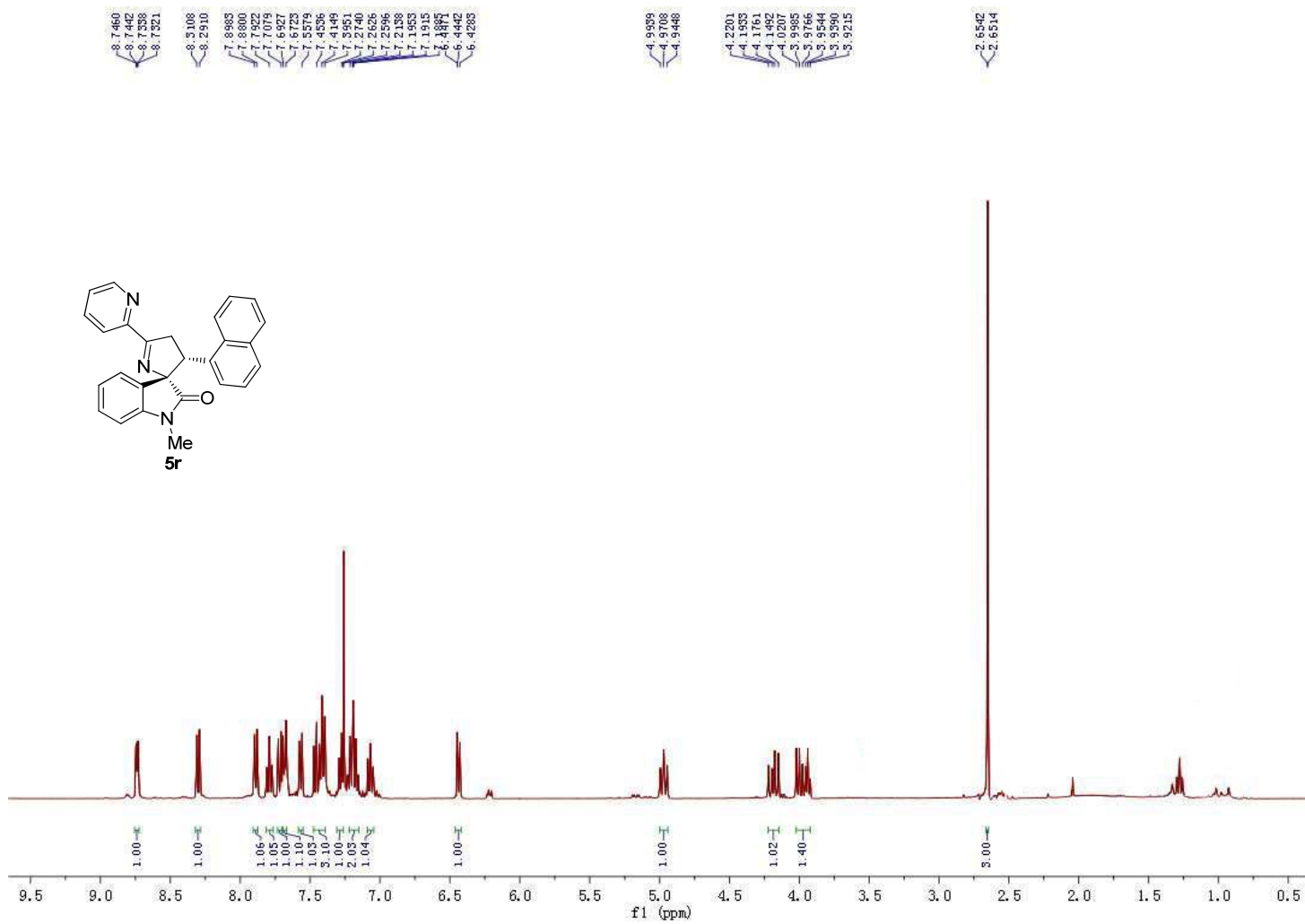
ID#	Ret. time	Area	Height	Area %
1	14.453	2275958	44408	50.011
2	29.149	2274917	17381	49.989

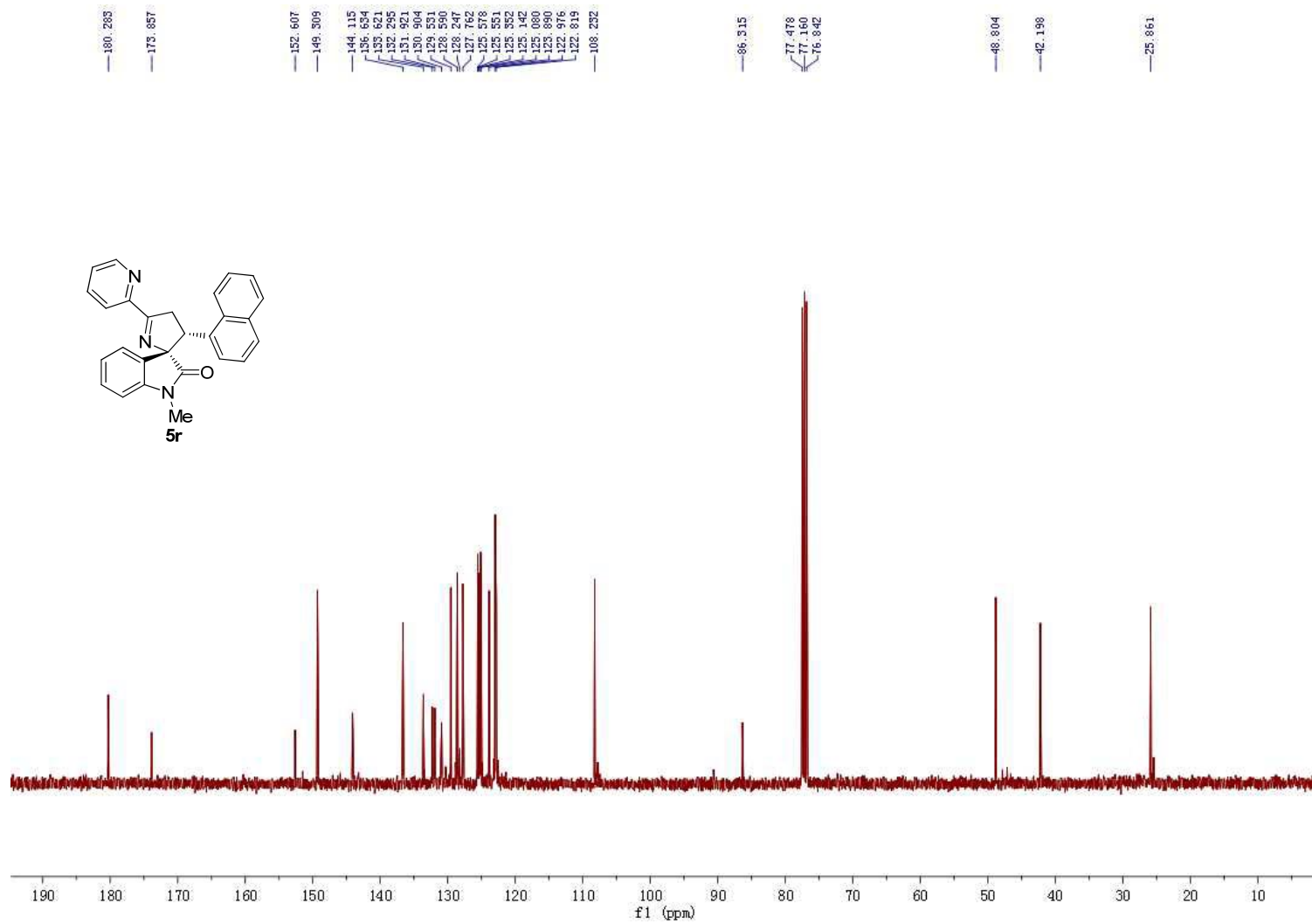


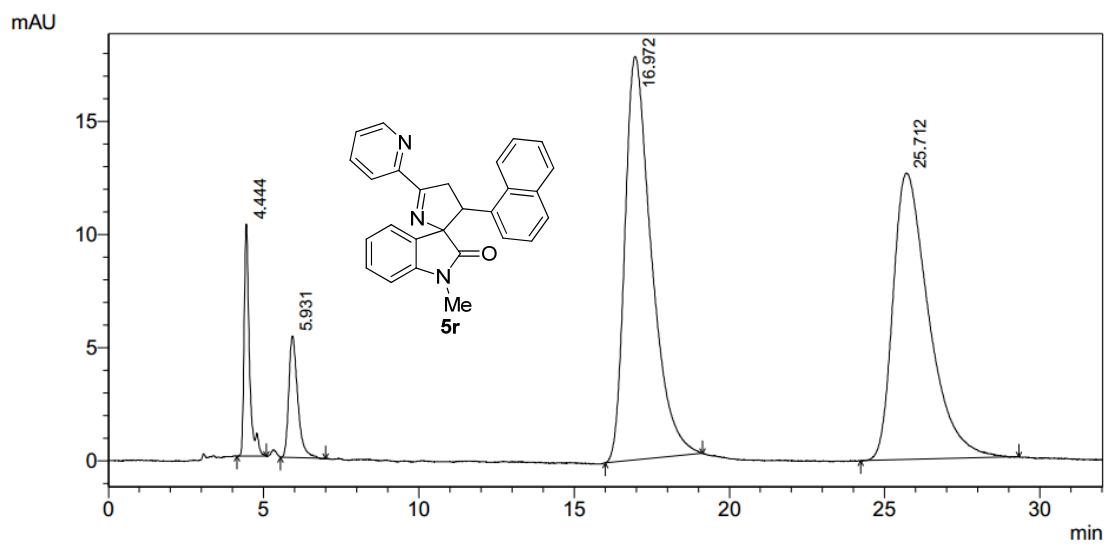
PDA

ID#	Ret. time	Area	Height	Area %
1	29.192	1765708	13698	100.000

NMR and HPLC of 5r

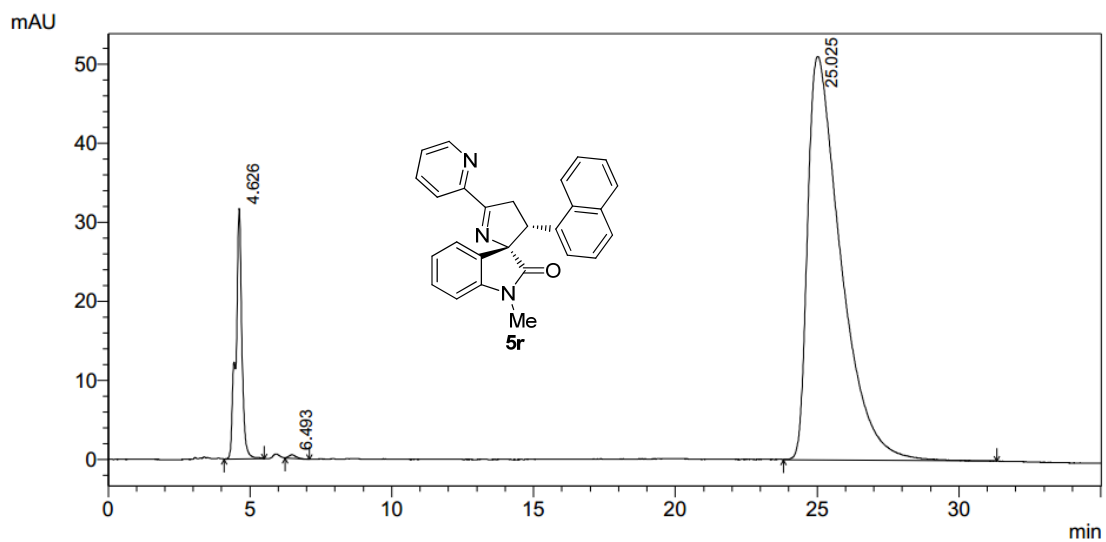






PDA

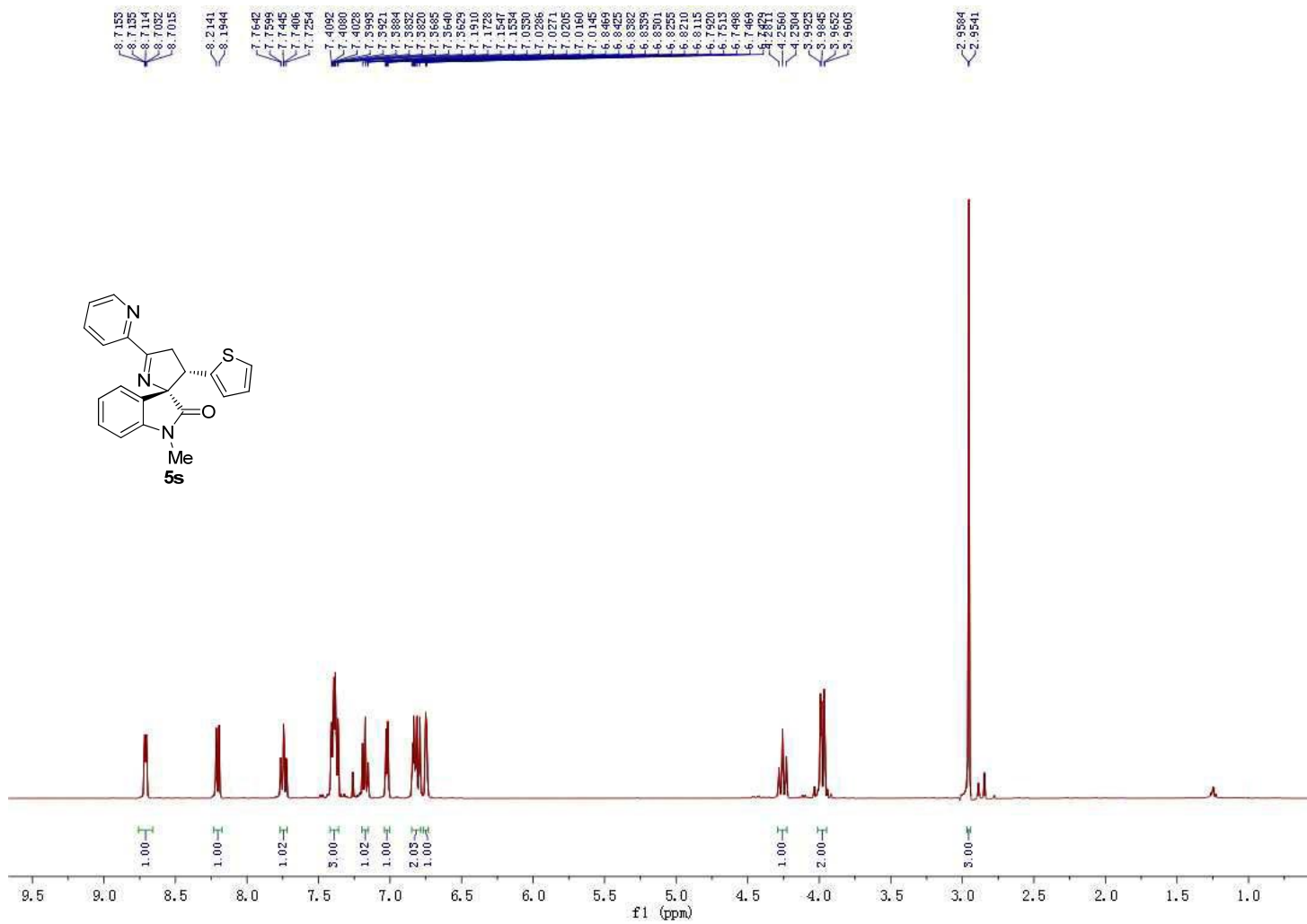
ID#	Ret. time	Area	Height	Area %
1	4.444	120986	10259	5.261
2	5.931	107199	5365	4.662
3	16.972	1059227	17840	46.061
4	25.712	1012229	12678	44.017

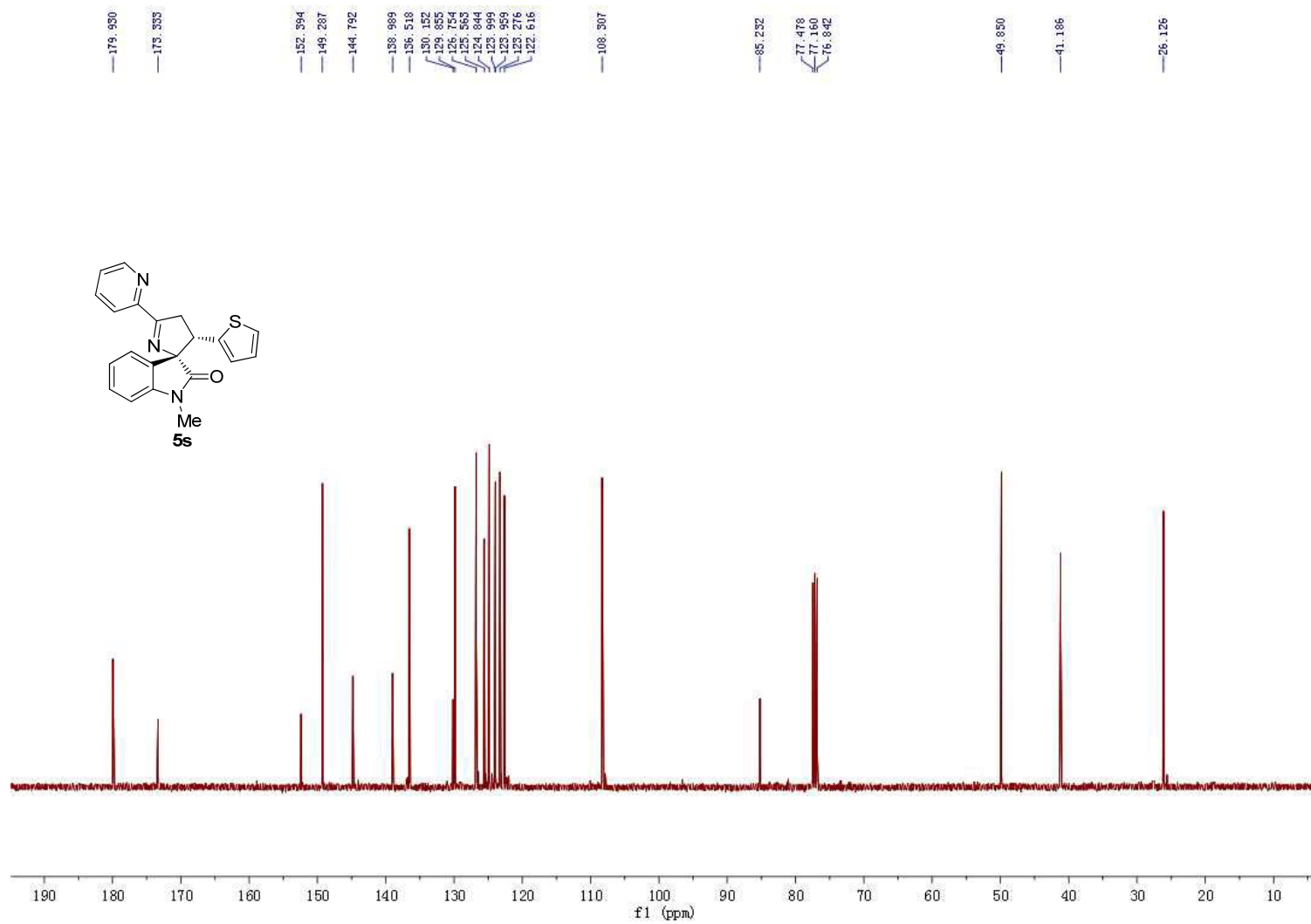


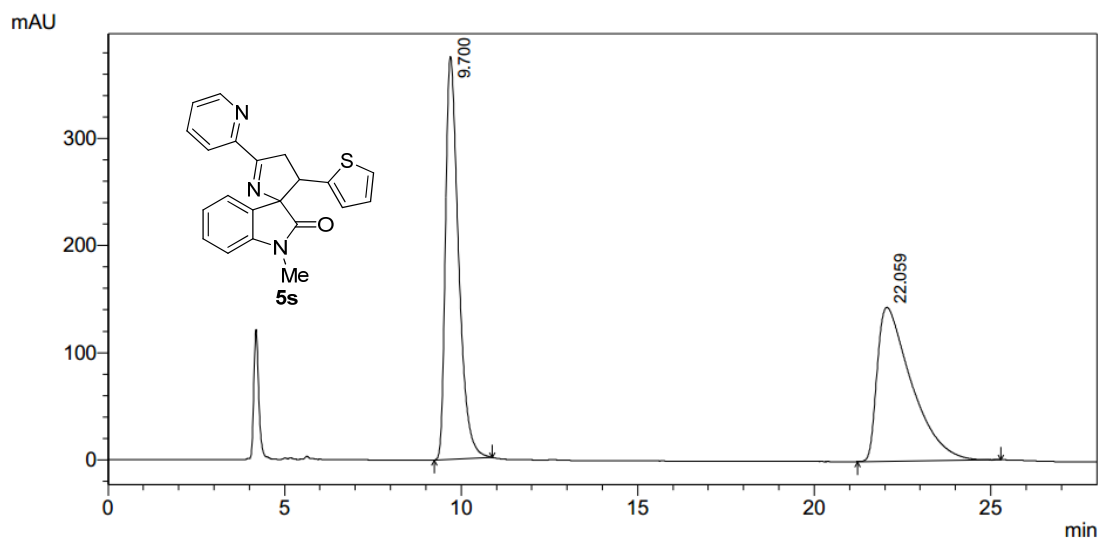
PDA

ID#	Ret. time	Area	Height	Area %
1	4.626	469055	31648	10.137
2	6.493	7033	434	0.152
3	25.025	4150994	51016	89.711

NMR and HPLC of 5s

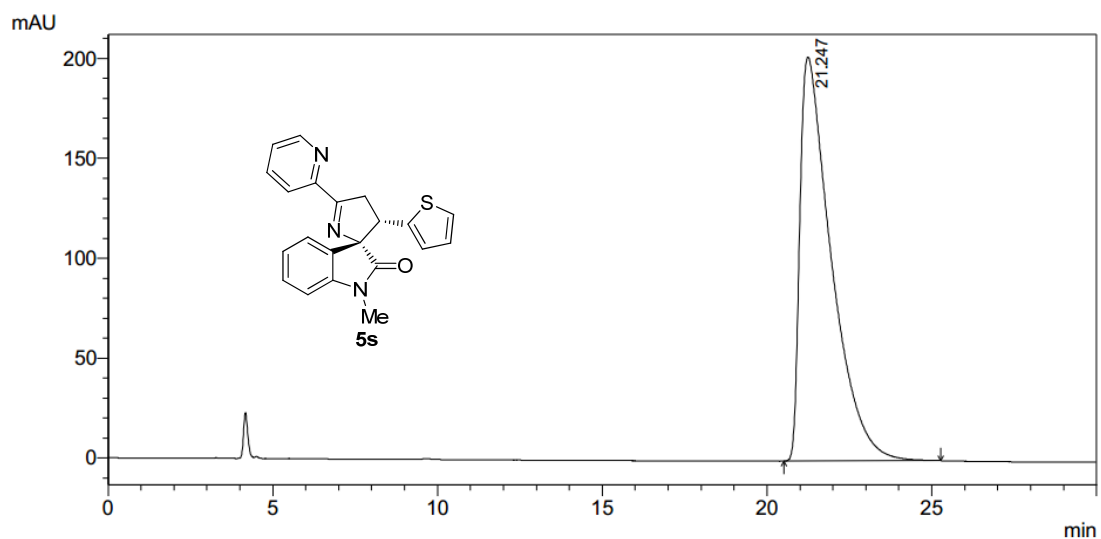






PDA

ID#	Ret. time	Area	Height	Area %
1	9.700	9721428	376399	50.052
2	22.059	9701339	143738	49.948



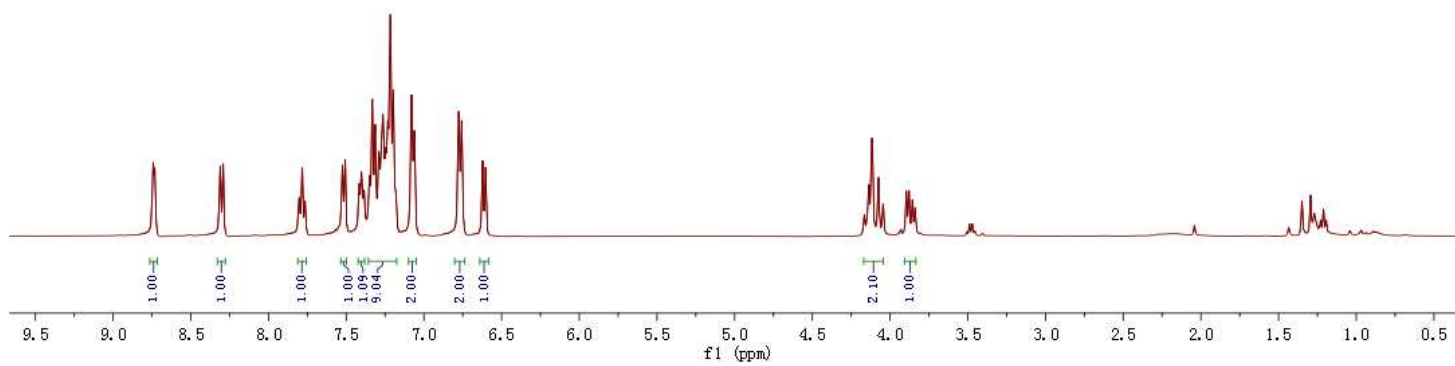
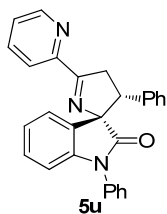
PDA

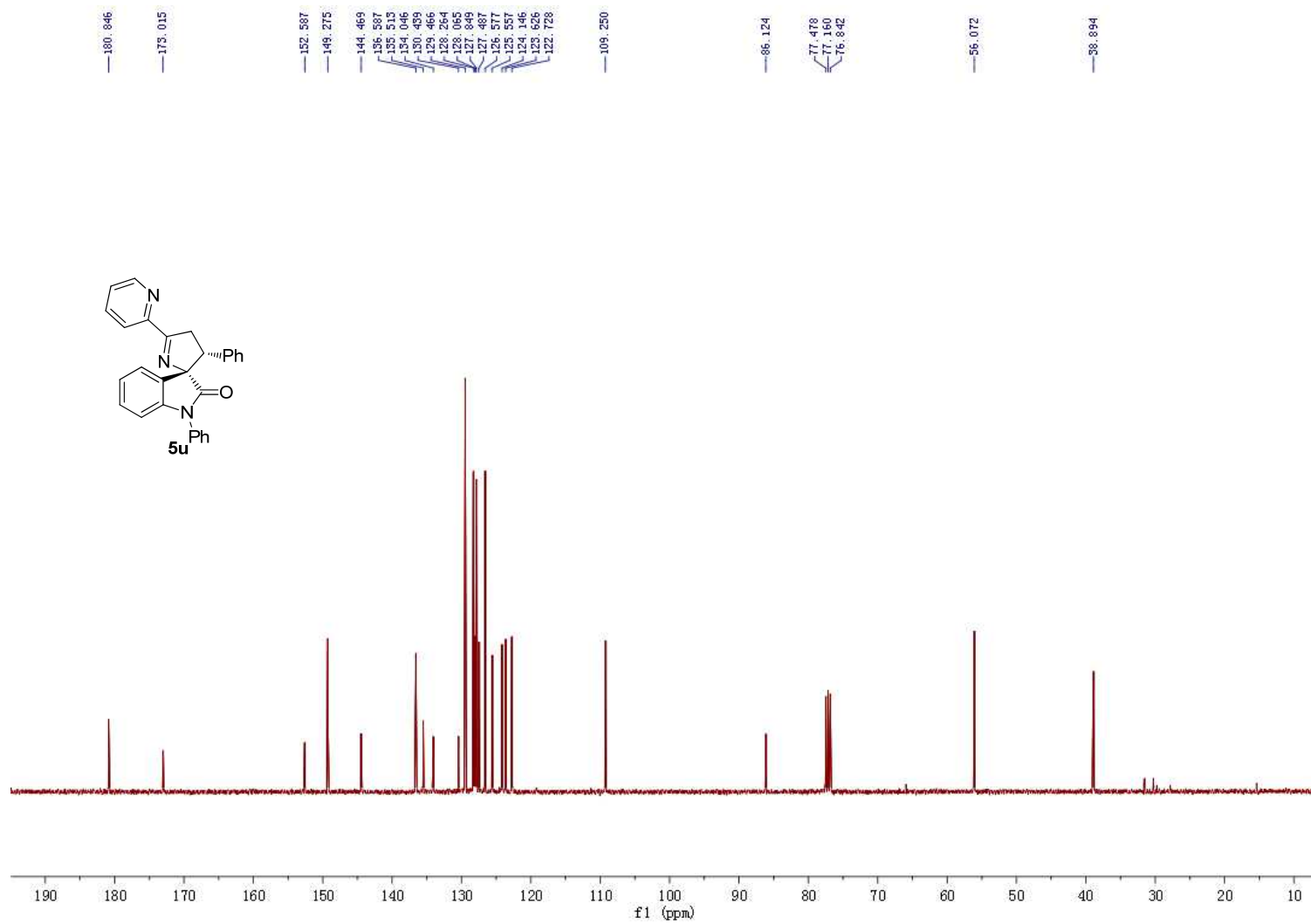
ID#	Ret. time	Area	Height	Area %
1	21.247	13382021	202286	100.000

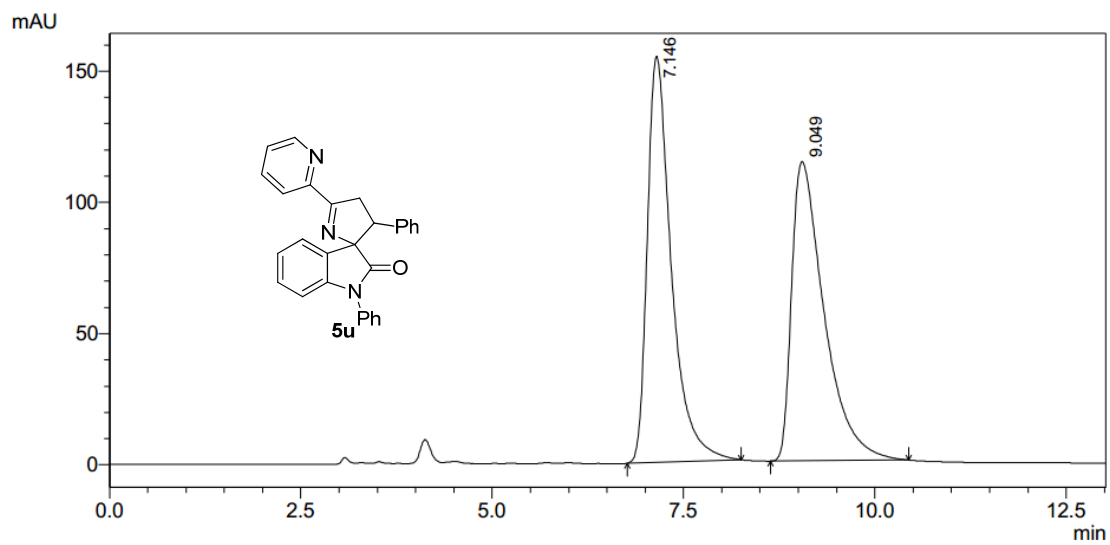
NMR and HPLC of 5u

8.7423
8.7318
8.3110
8.2913
7.8074
7.7885
7.7644
7.3917
7.3180
7.2884
7.2684
7.2520
7.2157
7.1973
7.0783
6.7522
6.6215
6.6027

4.1658
4.1361
4.1168
4.0744
4.0448
3.8949
3.8776
3.8564
3.8390

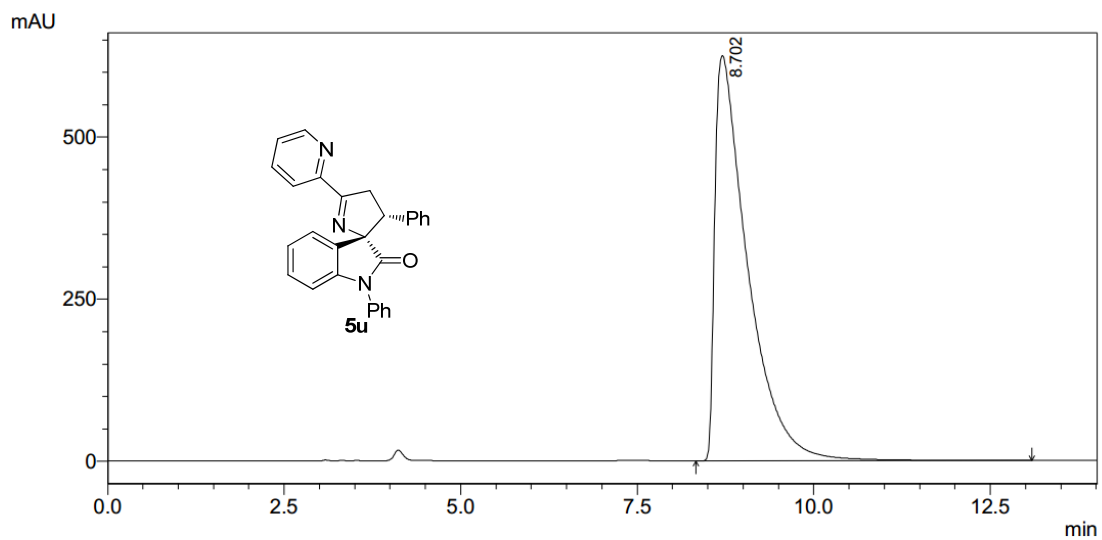






PDA

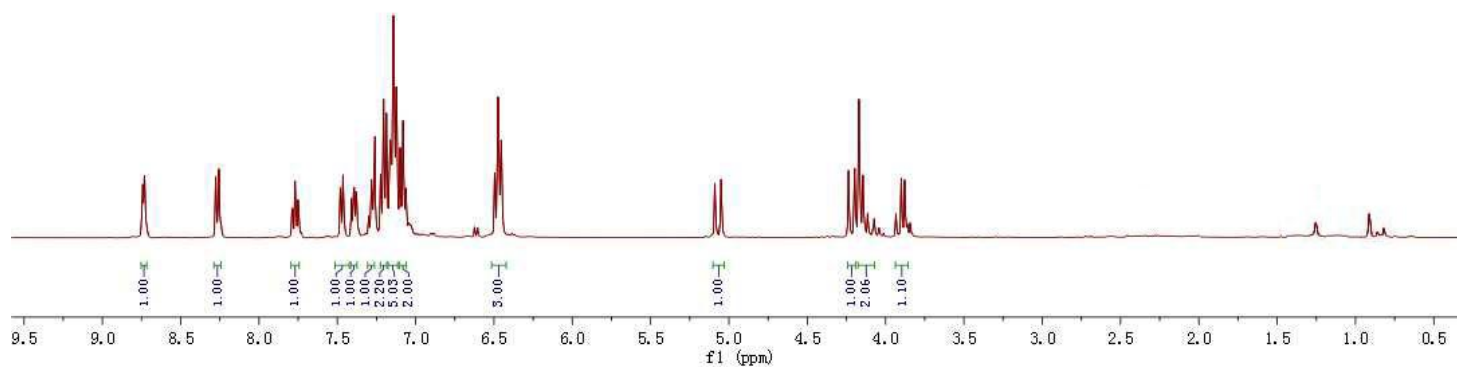
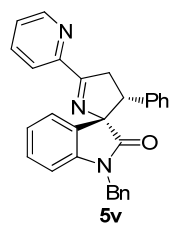
ID#	Ret. time	Area	Height	Area %
1	7.146	3384054	154871	50.139
2	9.049	3365259	114086	49.861

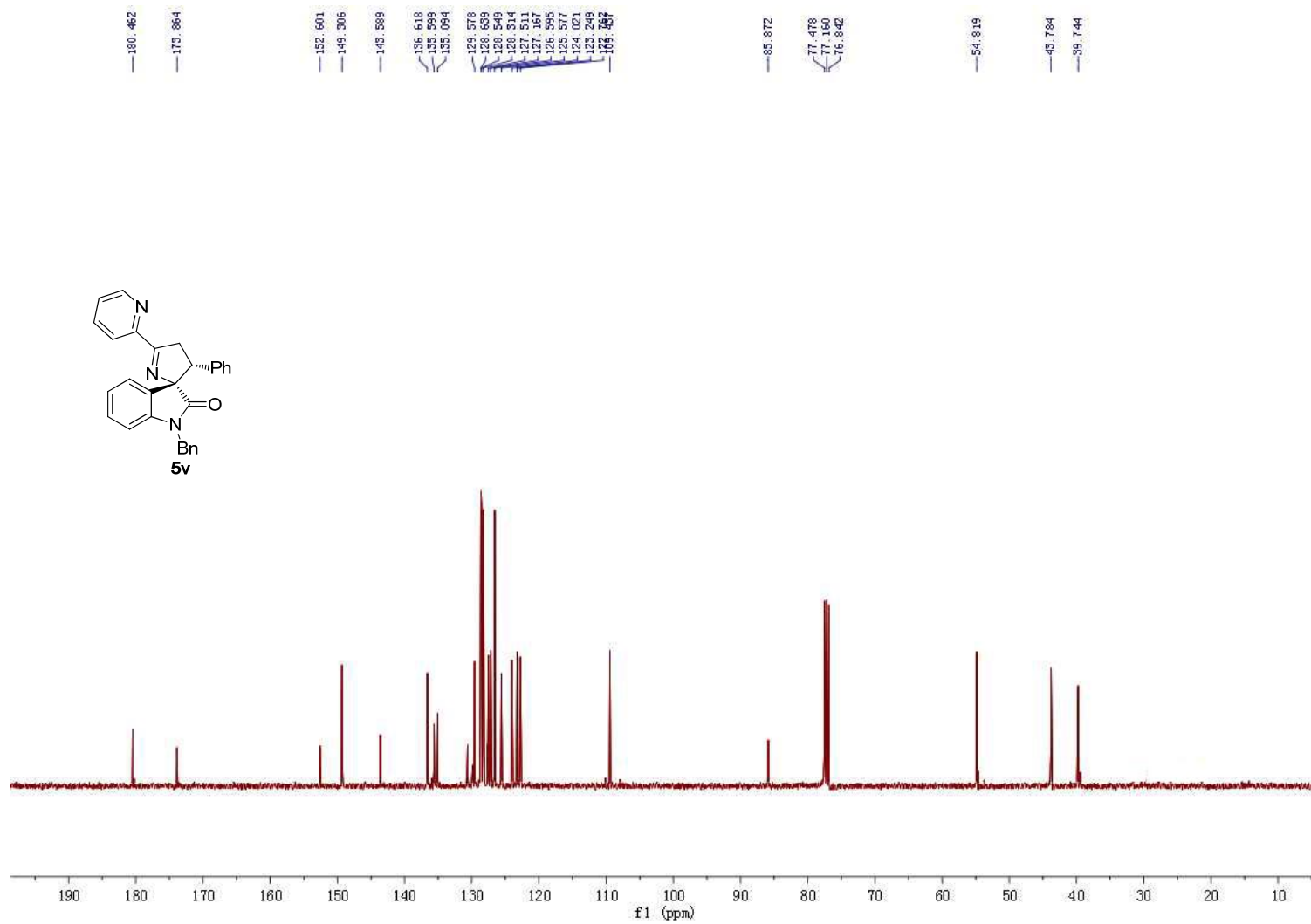


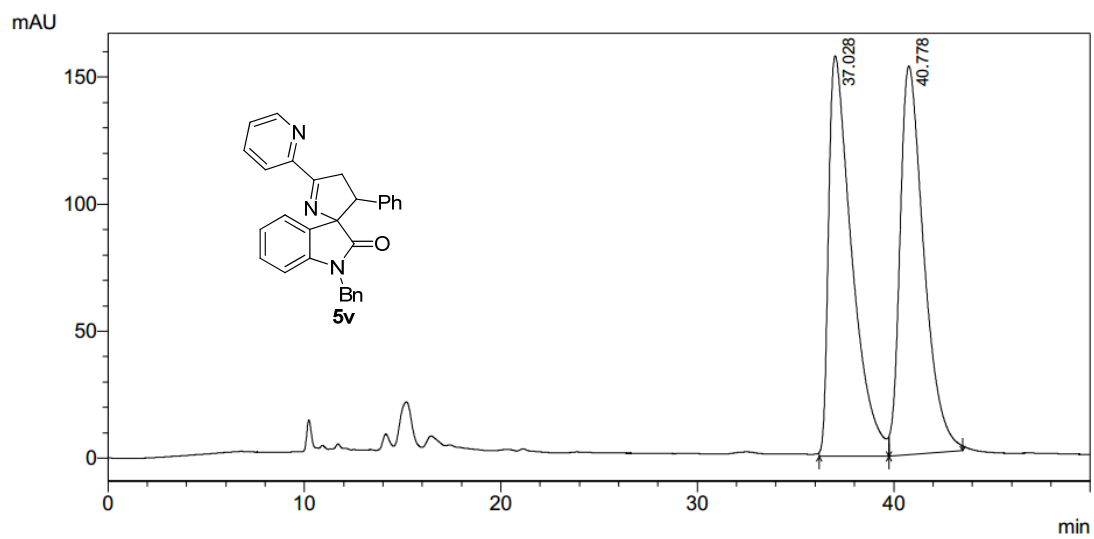
PDA

ID#	Ret. time	Area	Height	Area %
1	8.702	20185893	625328	100.000

NMR and HPLC of 5v

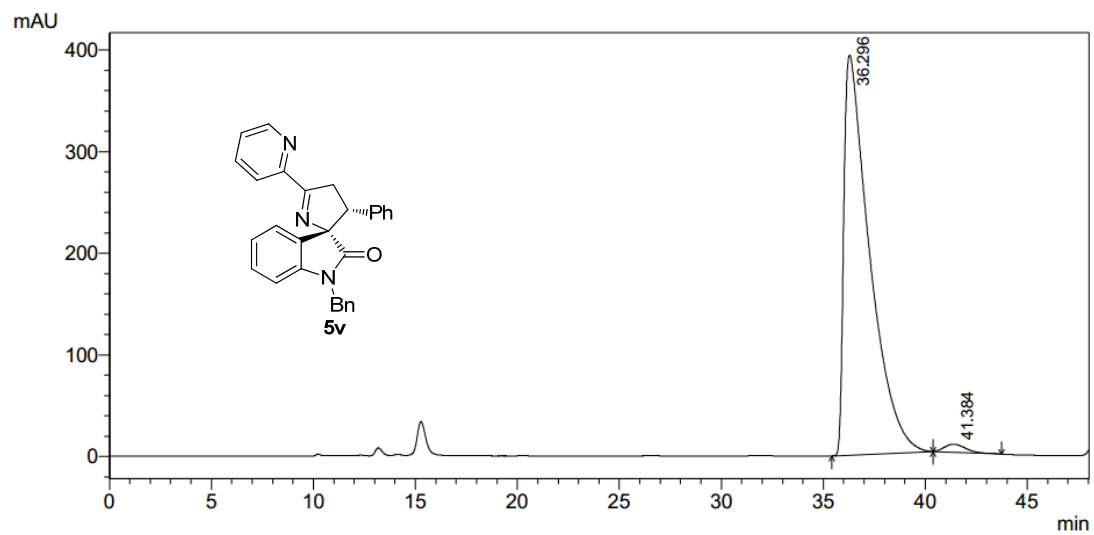






PDA

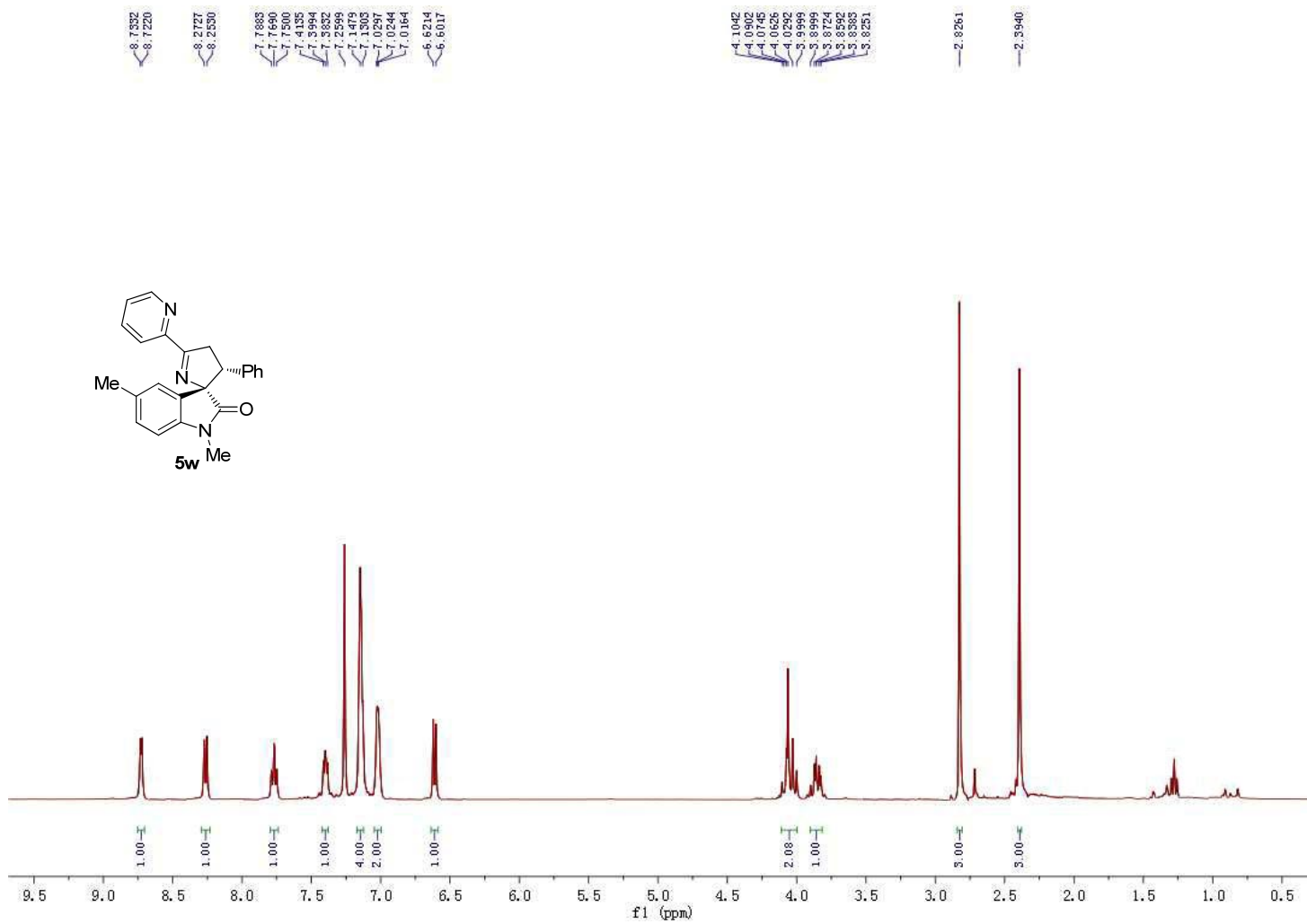
ID#	Ret. time	Area	Height	Area %
1	37.028	12944247	157636	49.983
2	40.778	12953298	152996	50.017

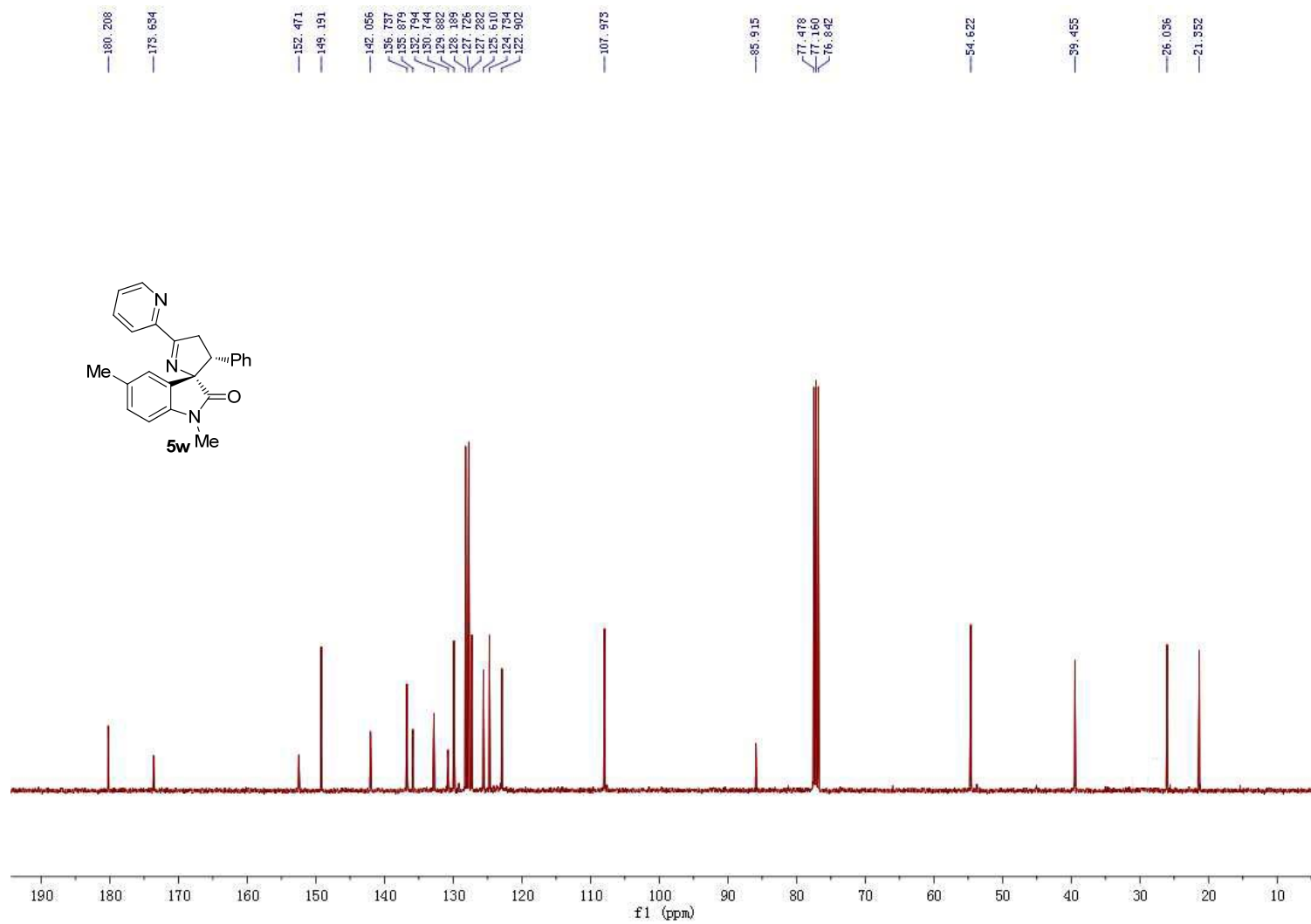


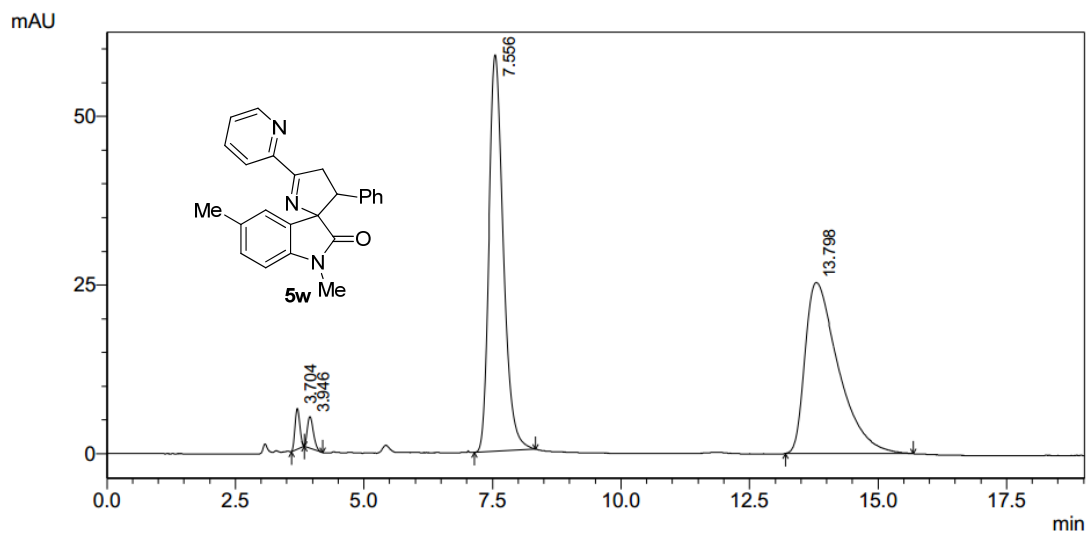
PDA

ID#	Ret. time	Area	Height	Area %
1	36.296	34448760	393789	98.370
2	41.384	570756	7858	1.630

NMR and HPLC of 5w

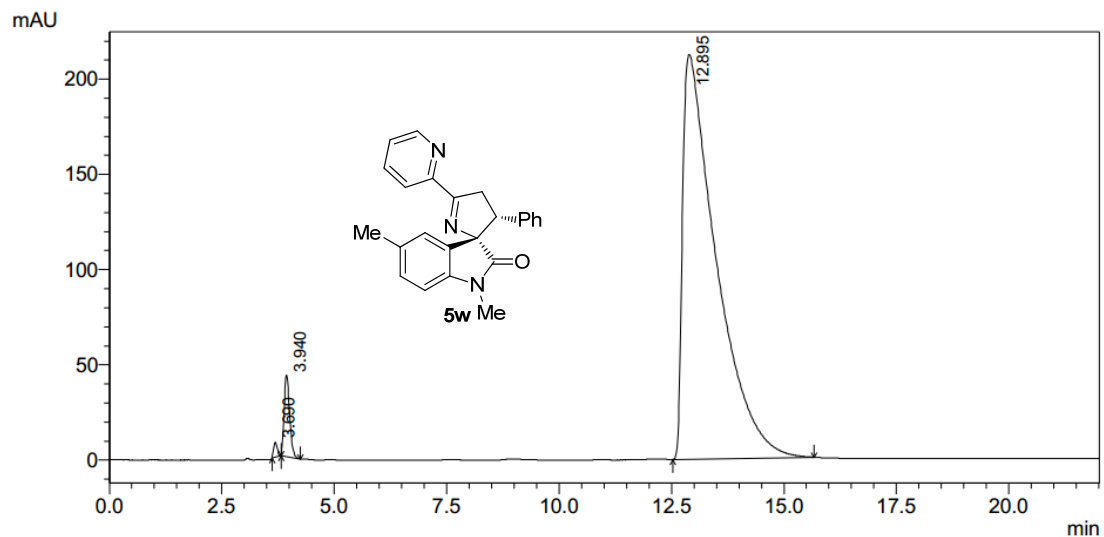






PDA

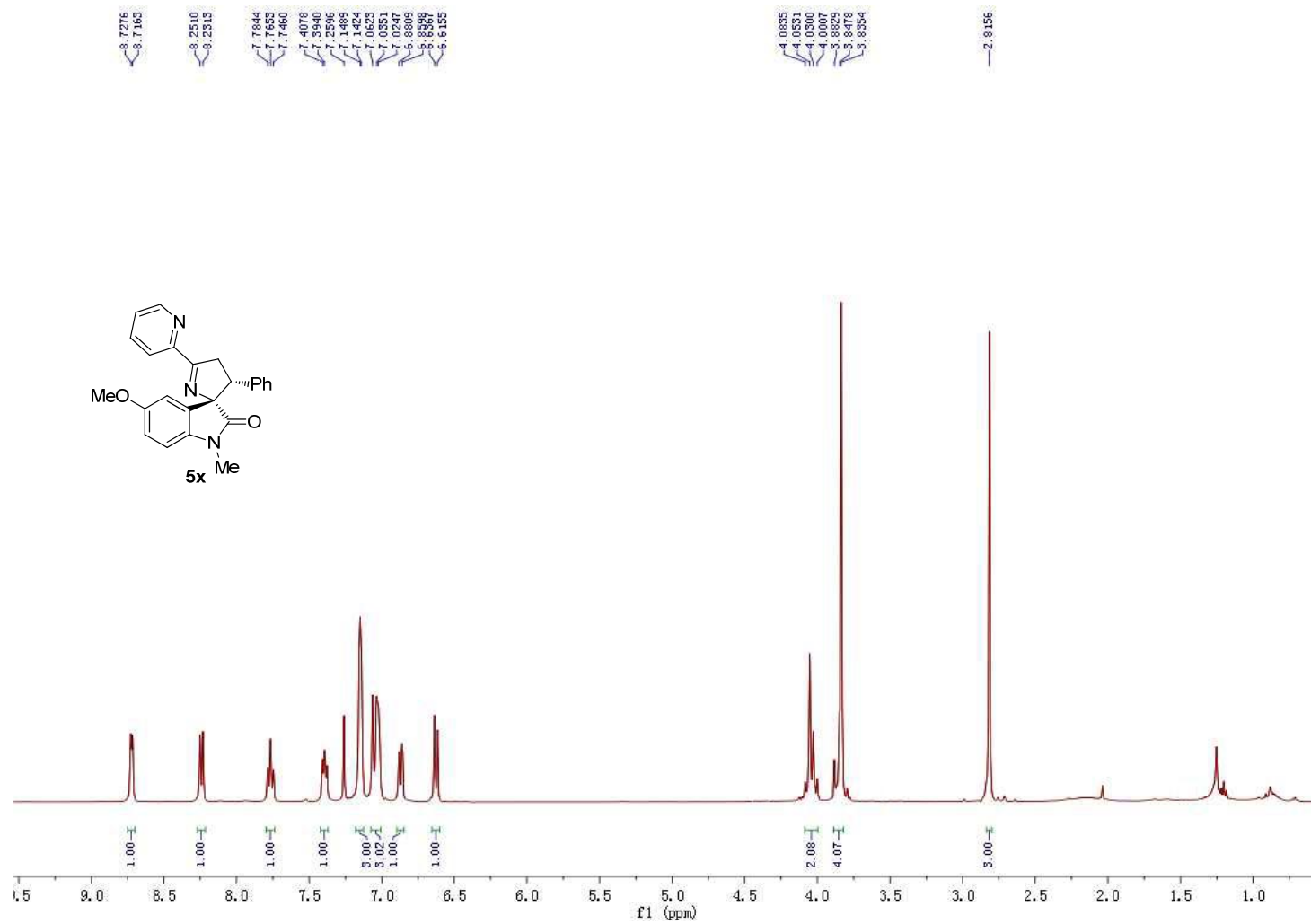
ID#	Ret. time	Area	Height	Area %
1	3.704	39153	6053	1.652
2	3.946	37673	4676	1.589
3	7.556	1146966	58831	48.381
4	13.798	1146926	25374	48.379

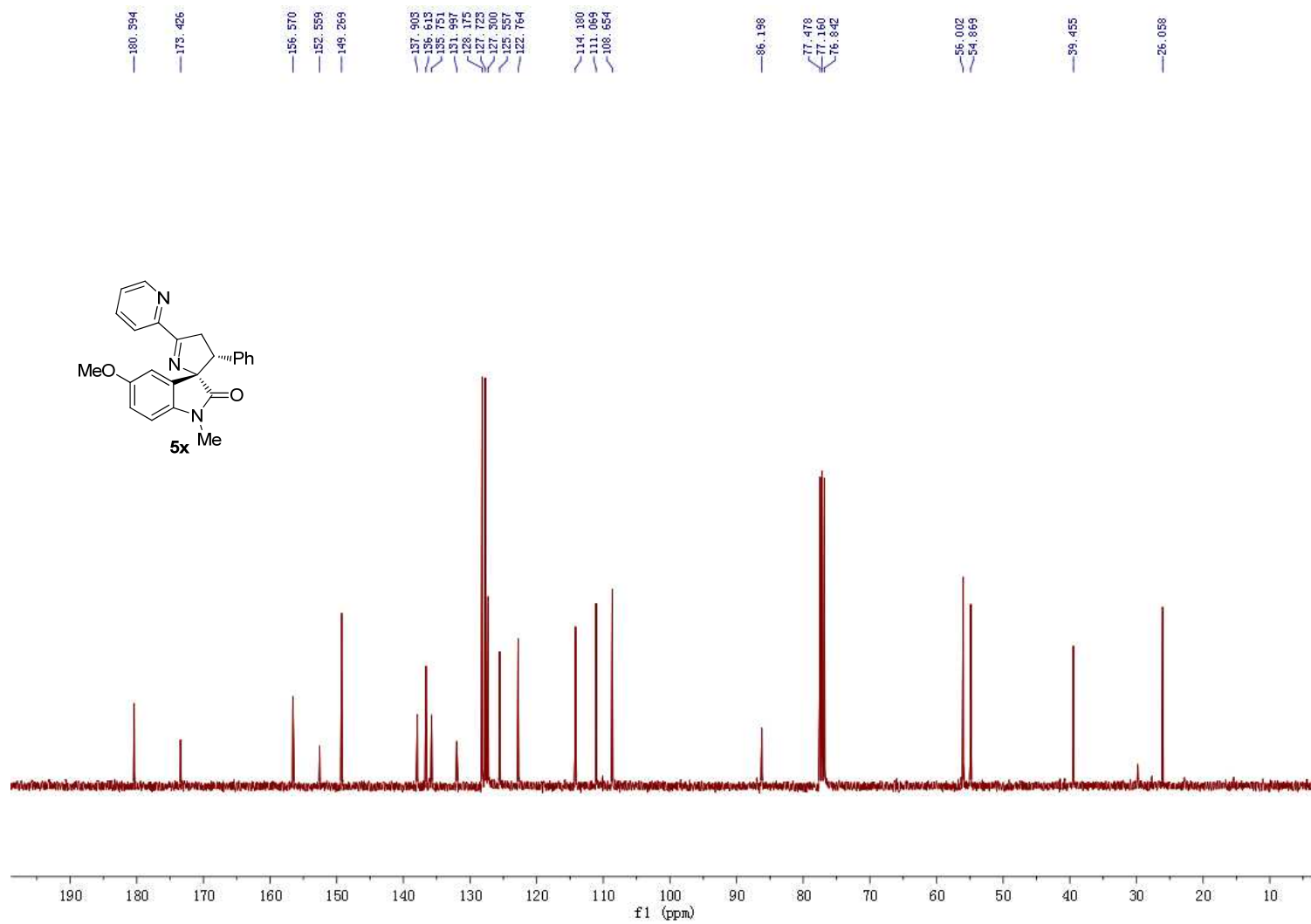


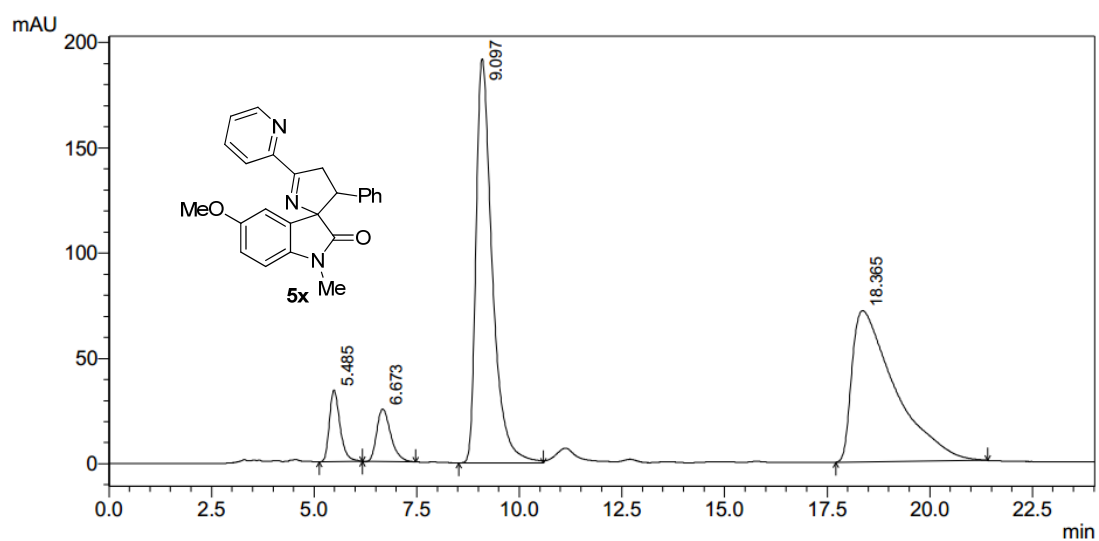
PDA

ID#	Ret. time	Area	Height	Area %
1	3.690	43005	7740	0.377
2	3.940	360487	42568	3.160
3	12.895	11004205	212520	96.463

NMR and HPLC of 5x

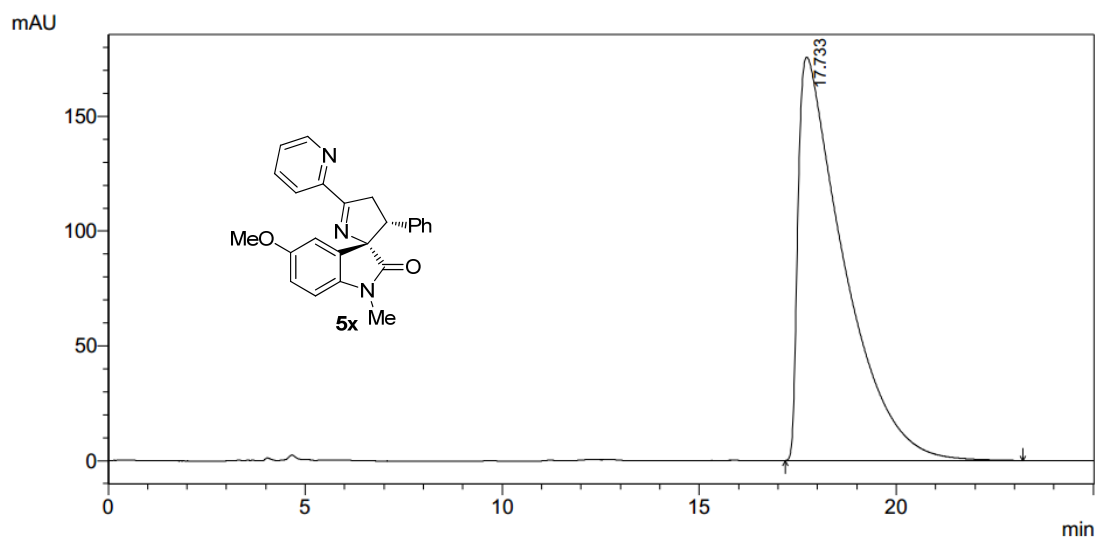






PDA

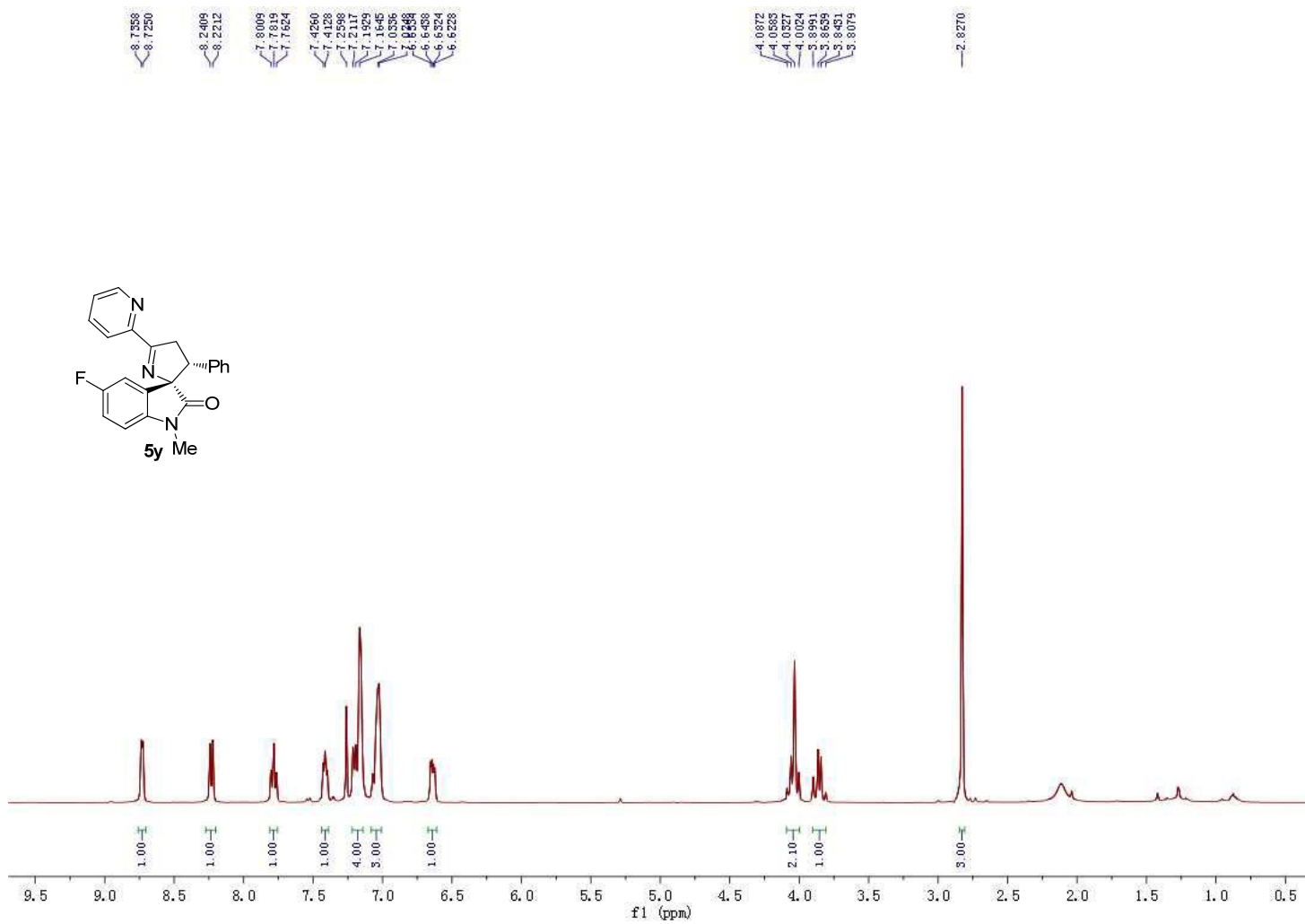
ID#	Ret. time	Area	Height	Area %
1	5.485	613139	33945	5.222
2	6.673	592358	25012	5.045
3	9.097	5276890	191952	44.940
4	18.365	5259562	71762	44.793

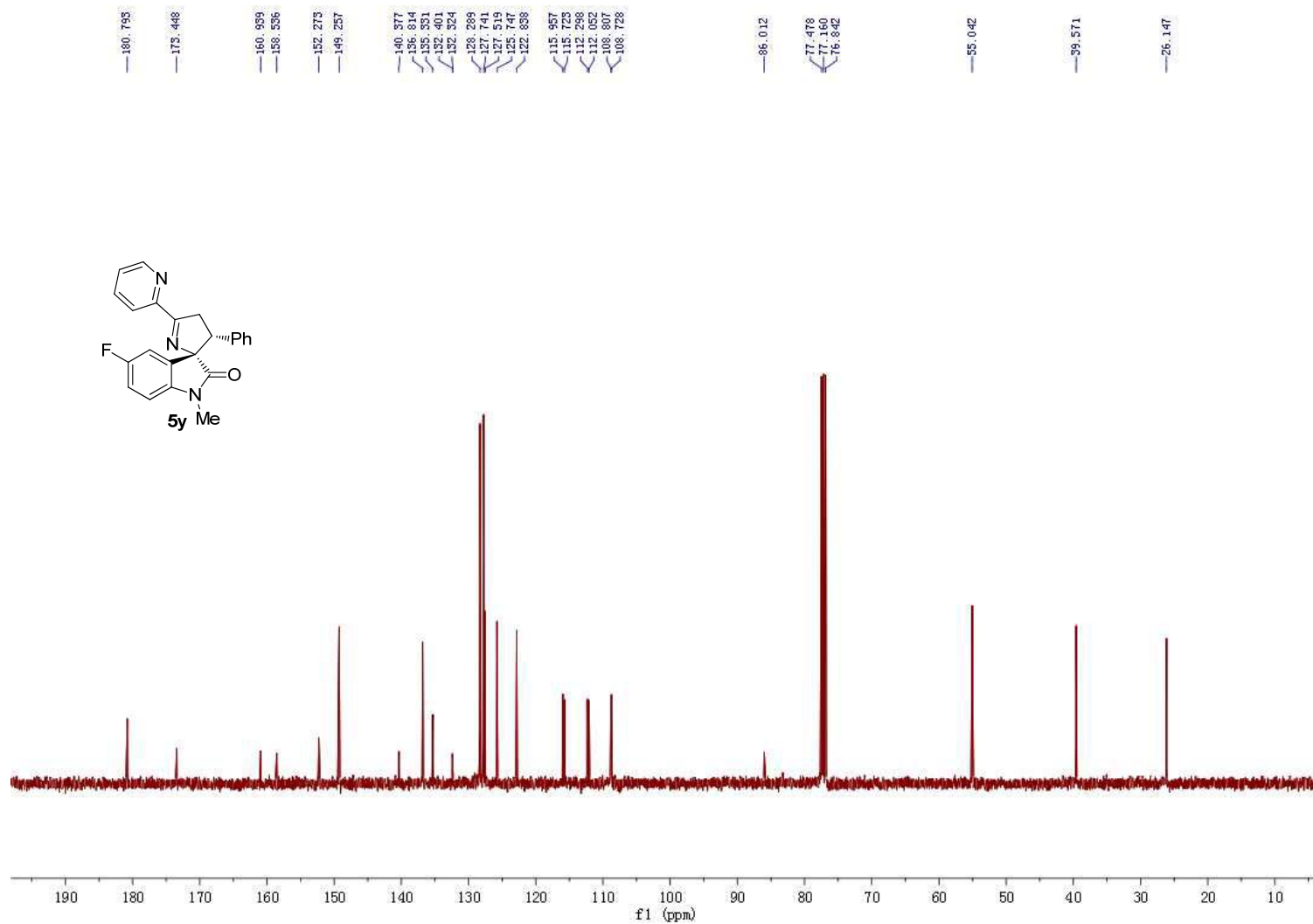


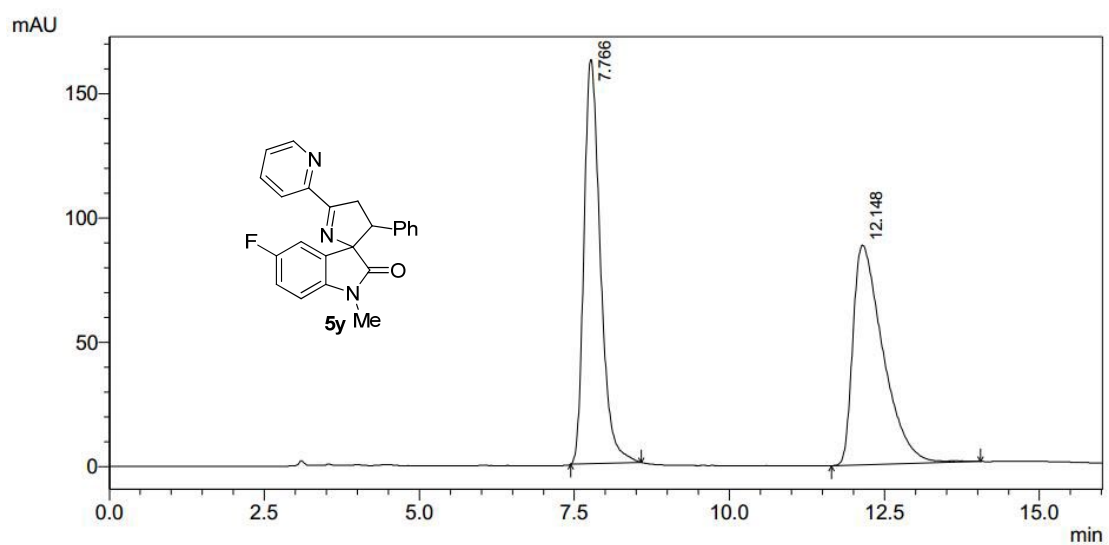
PDA

ID#	Ret. time	Area	Height	Area %
1	17.733	14206882	175795	100.000

NMR and HPLC of 5y

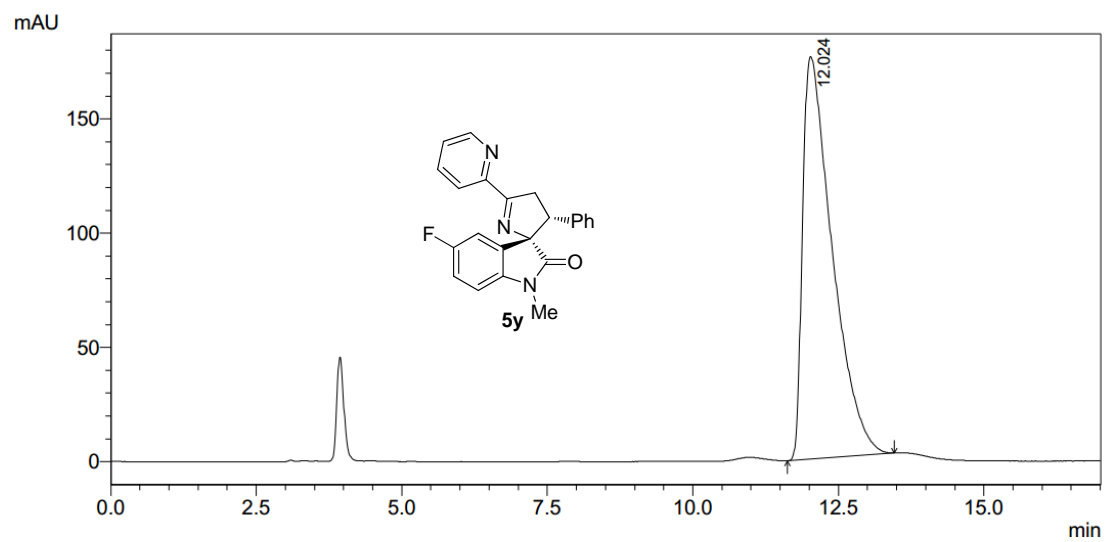






PDA

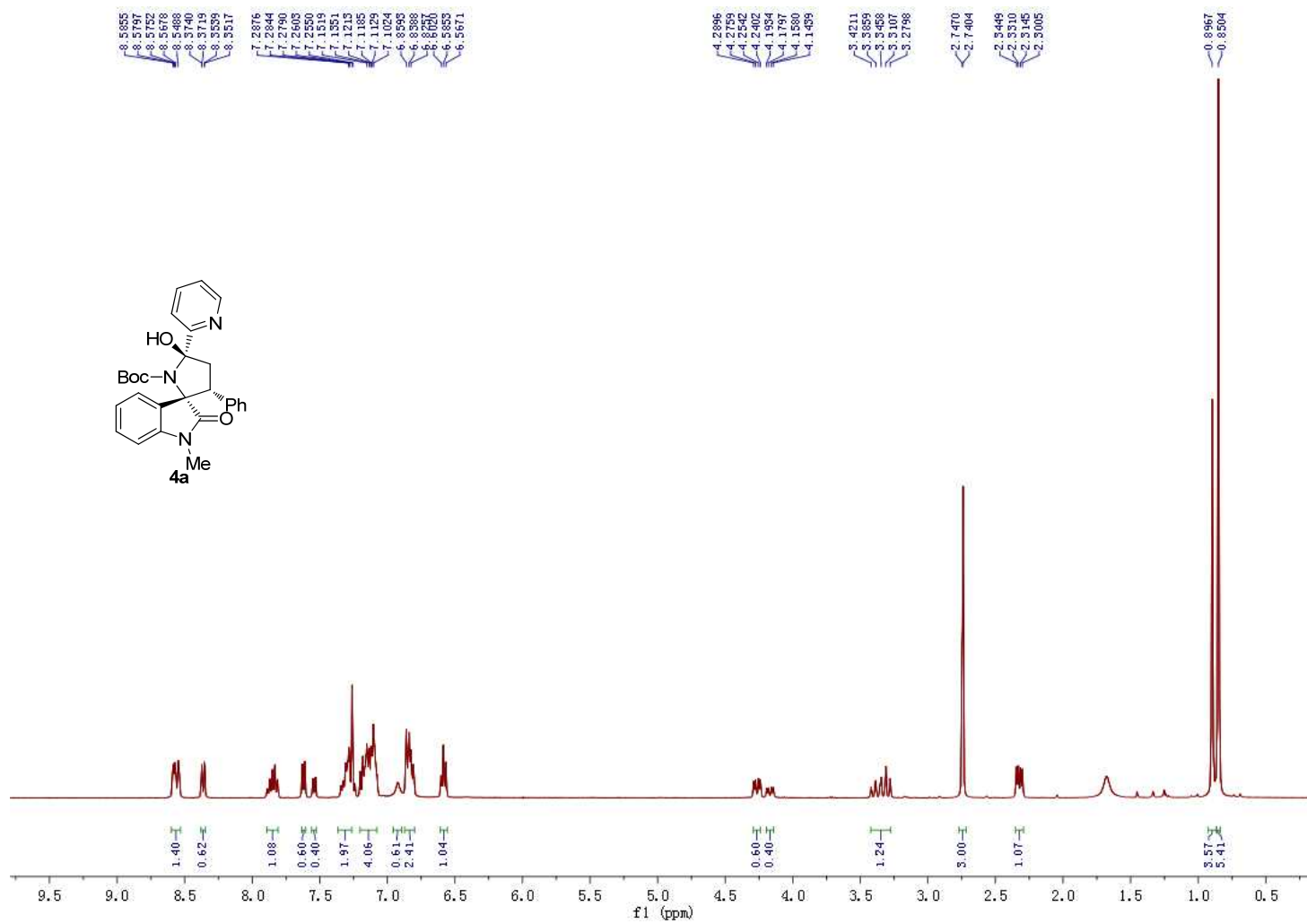
ID#	Ret. time	Area	Height	Area %
1	7.766	2987618	162593	49.979
2	12.148	2990094	88304	50.021

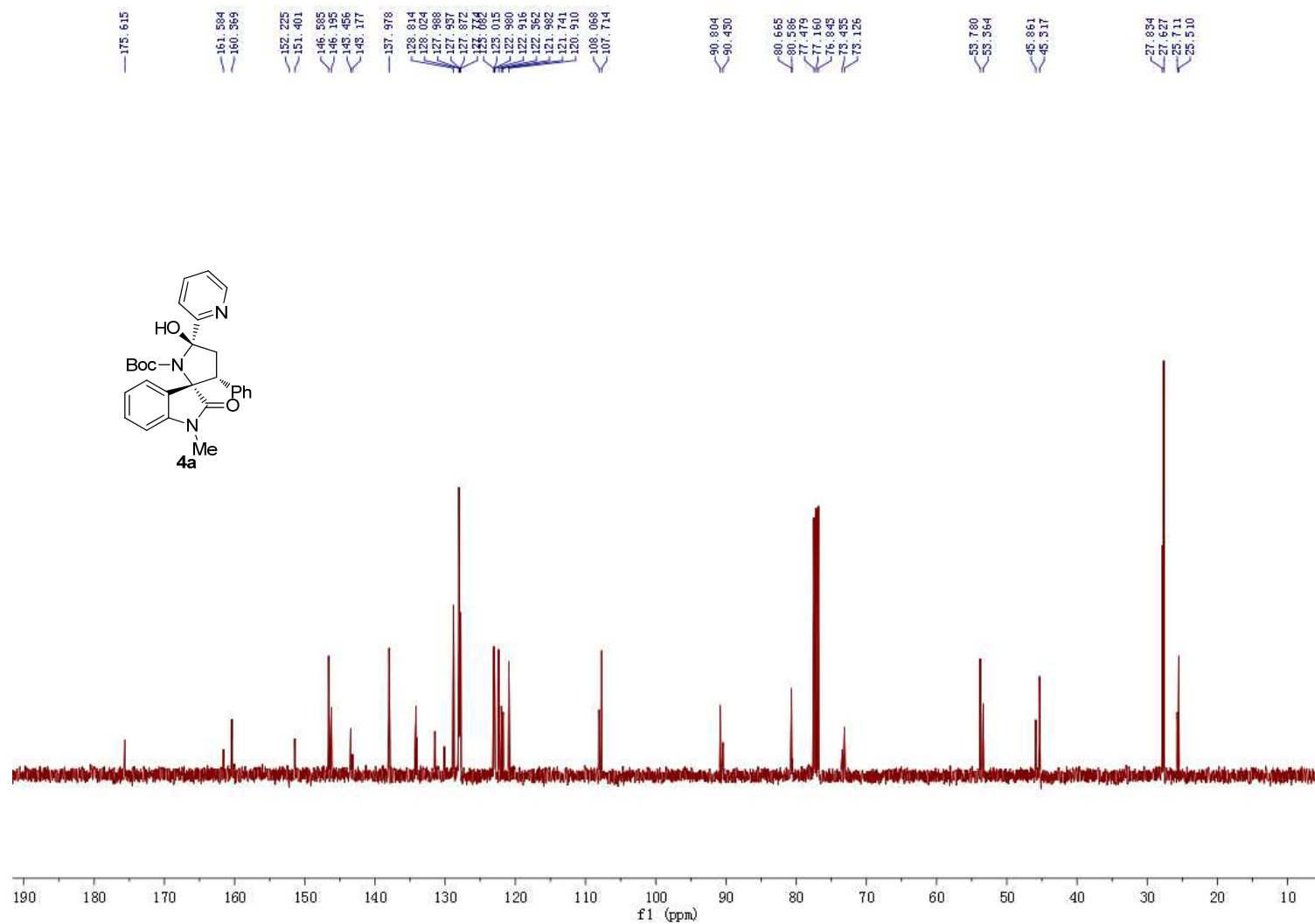


PDA

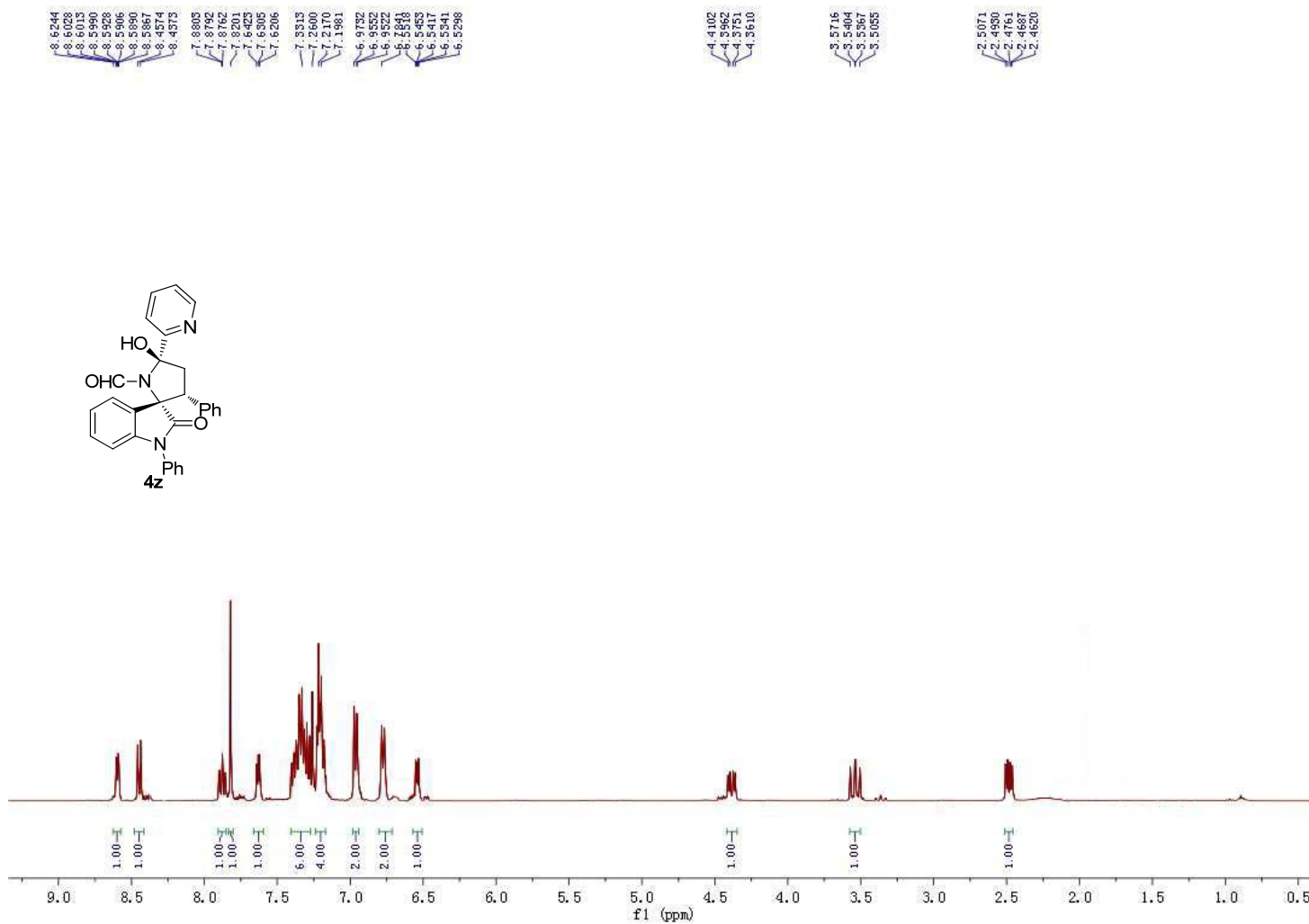
ID#	Ret. time	Area	Height	Area %
1	12.024	6239557	176210	100.000

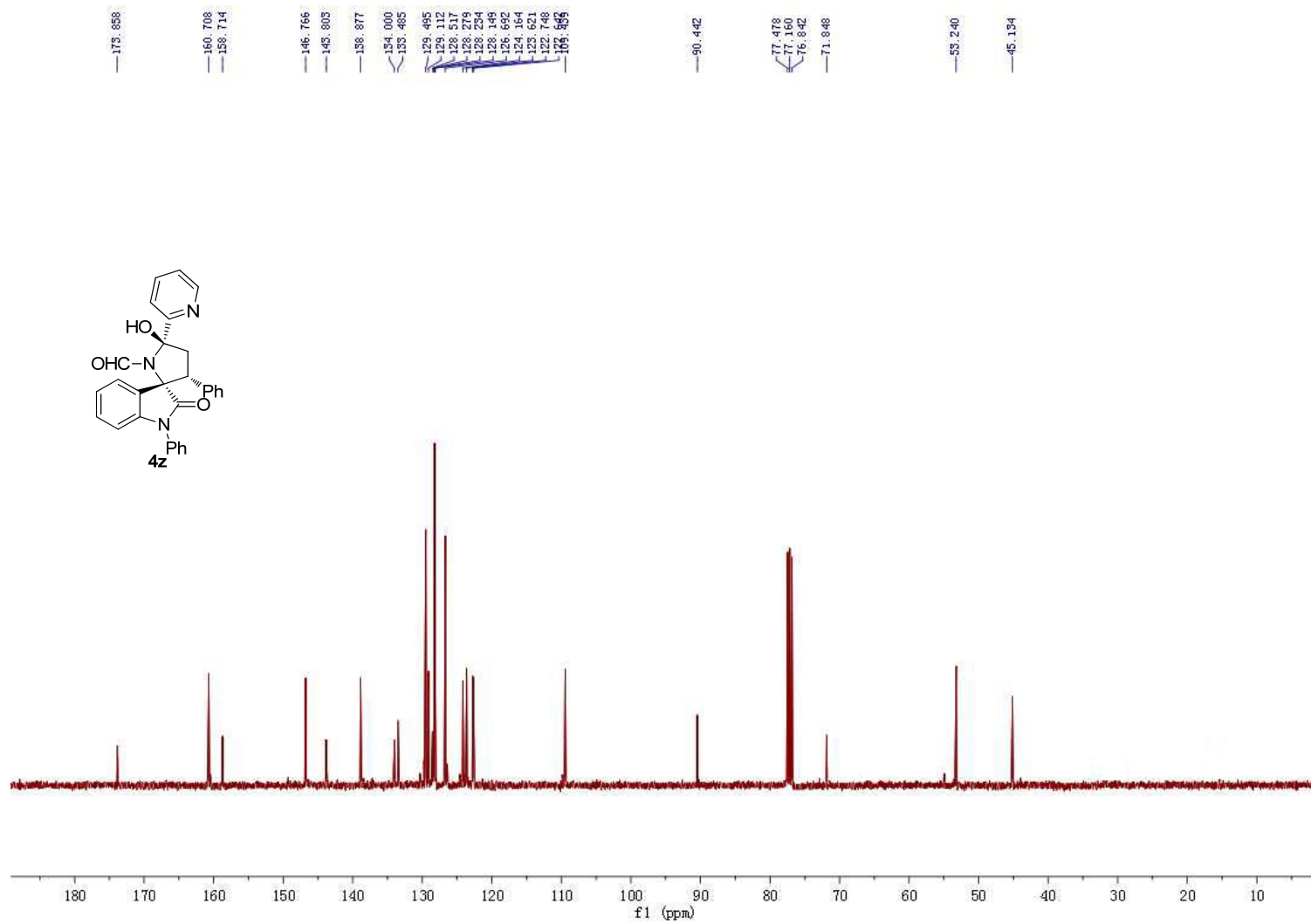
NMR and HPLC of 4a

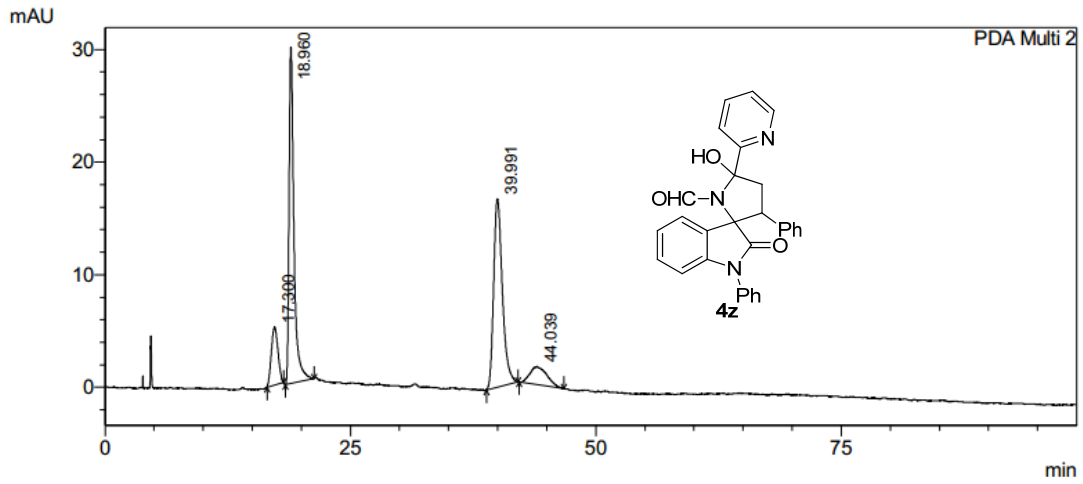




NMR and HPLC of 4z



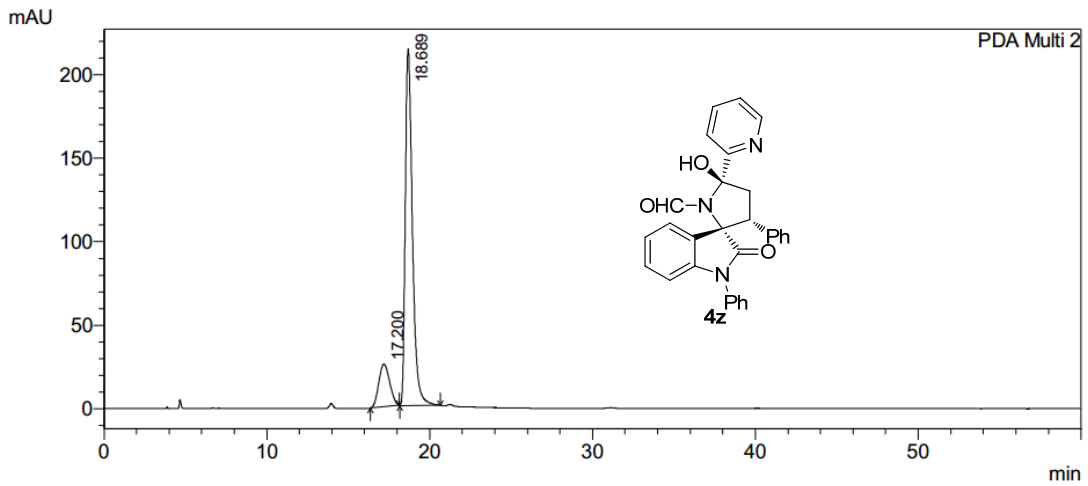




Quantitative Results

PDA

ID#	Name	Ret. Time	Area	Height	Conc.
1	RT17.300	17.300	242008	5130	9.686
2	RT18.960	18.960	1030691	29847	41.254
3	RT39.991	39.991	1032165	16733	41.313
4	RT44.039	44.039	193550	1605	7.747

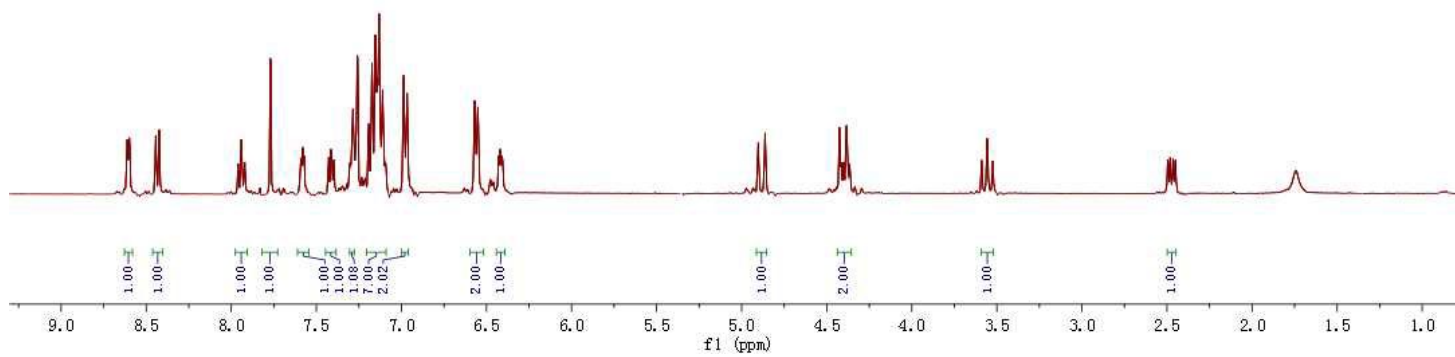
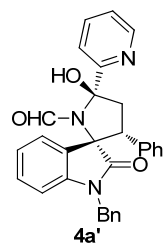


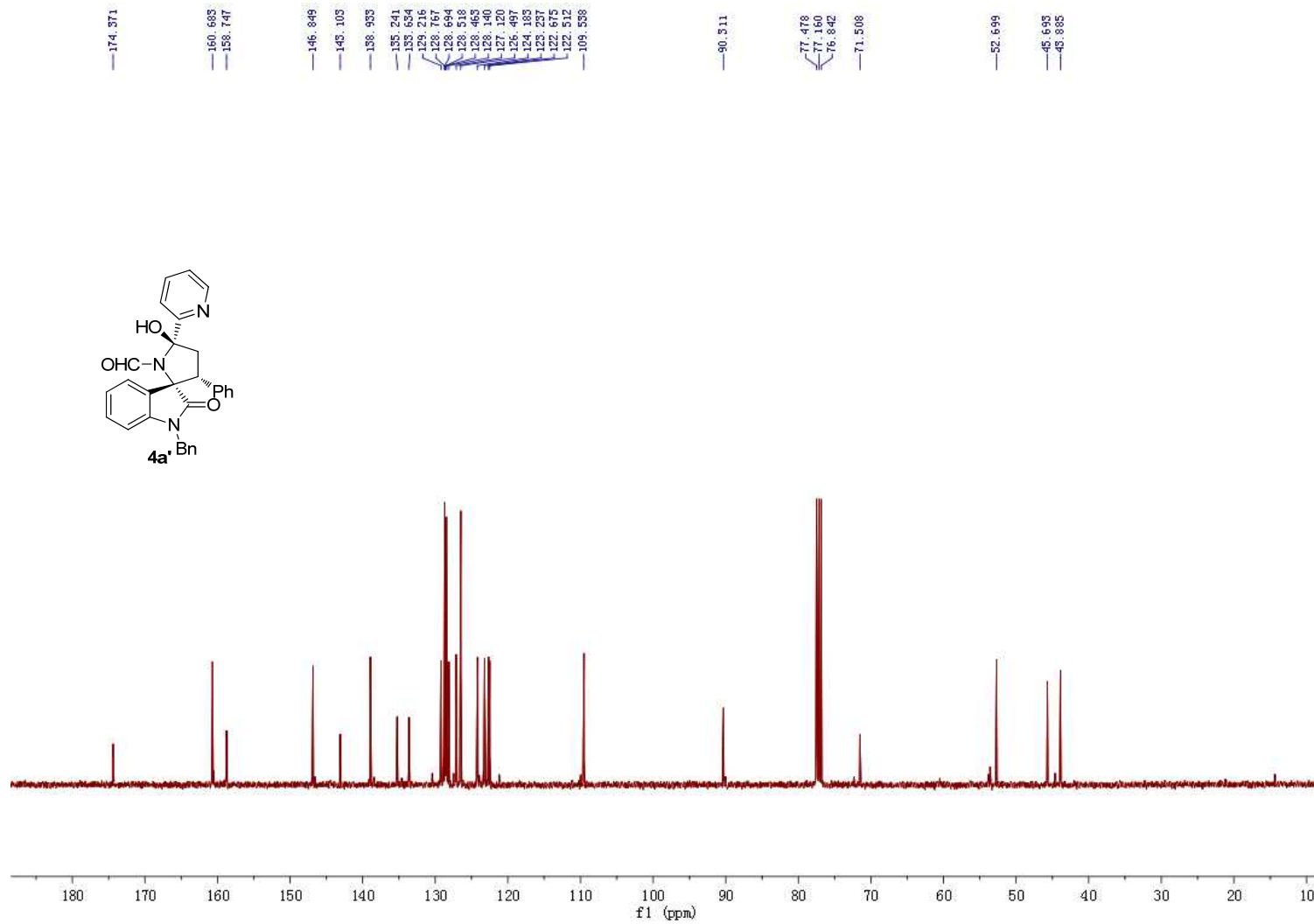
Quantitative Results

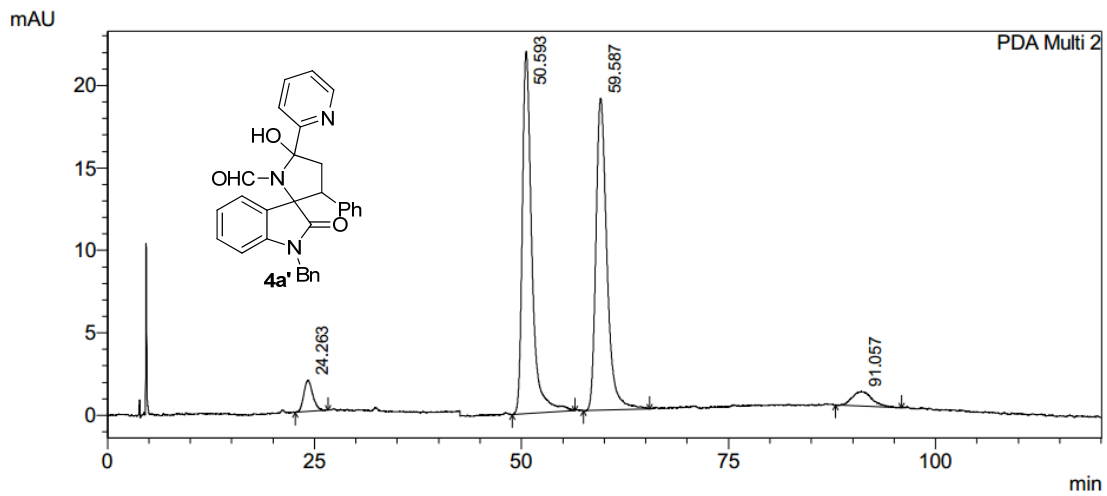
PDA

ID#	Name	Ret. Time	Area	Height	Conc.
1	RT17.200	17.200	1187283	25581	15.458
2	RT18.689	18.689	6493303	213332	84.542

NMR and HPLC of 4a'





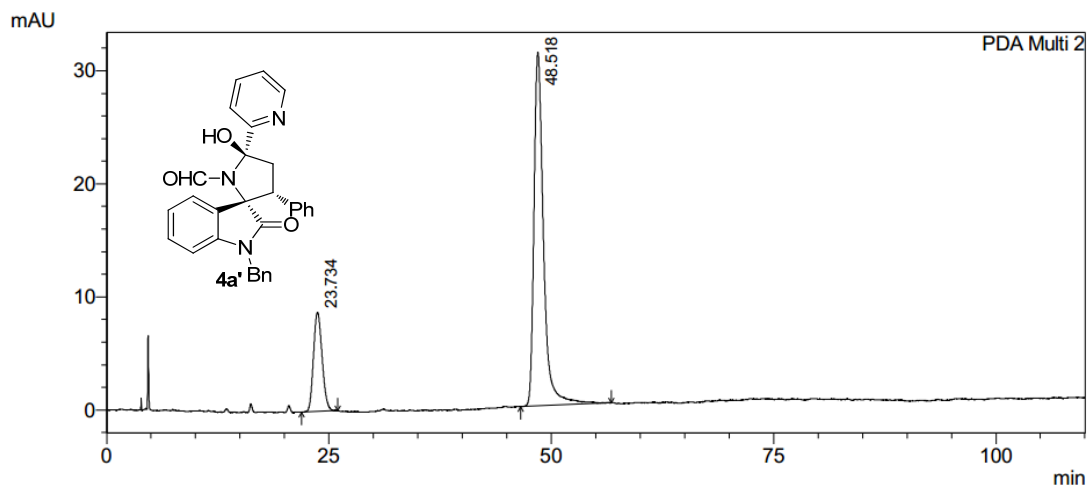


1 PDA Multi 2/254nm 4nm

Quantitative Results

PDA

ID#	Name	Ret. Time	Area	Height	Conc.
1	RT24.263	24.263	140044	1898	3.706
2	RT50.593	50.593	1747267	21948	46.239
3	RT59.587	59.587	1745079	18918	46.182
4	RT91.057	91.057	146350	881	3.873



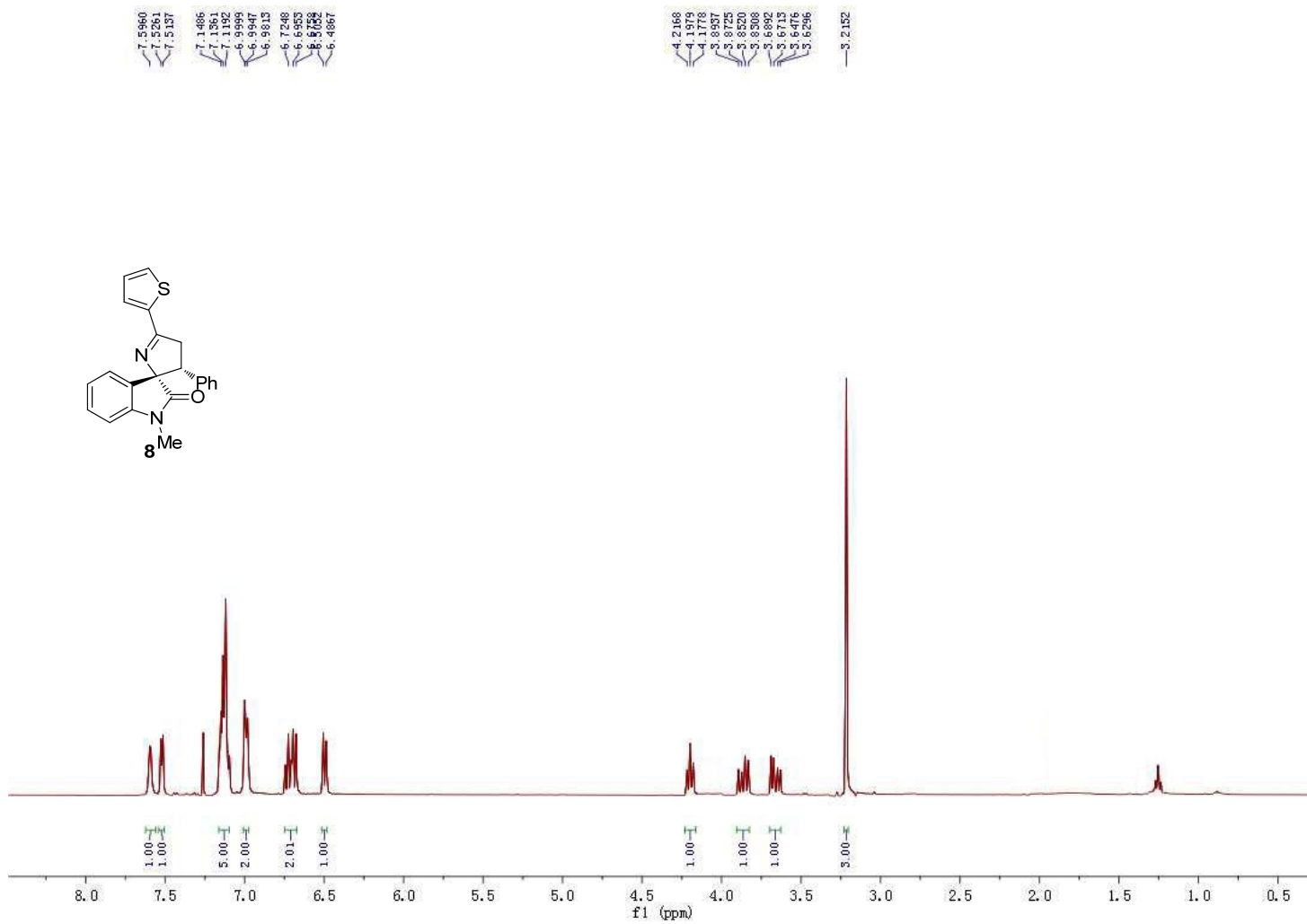
1 PDA Multi 2/254nm 4nm

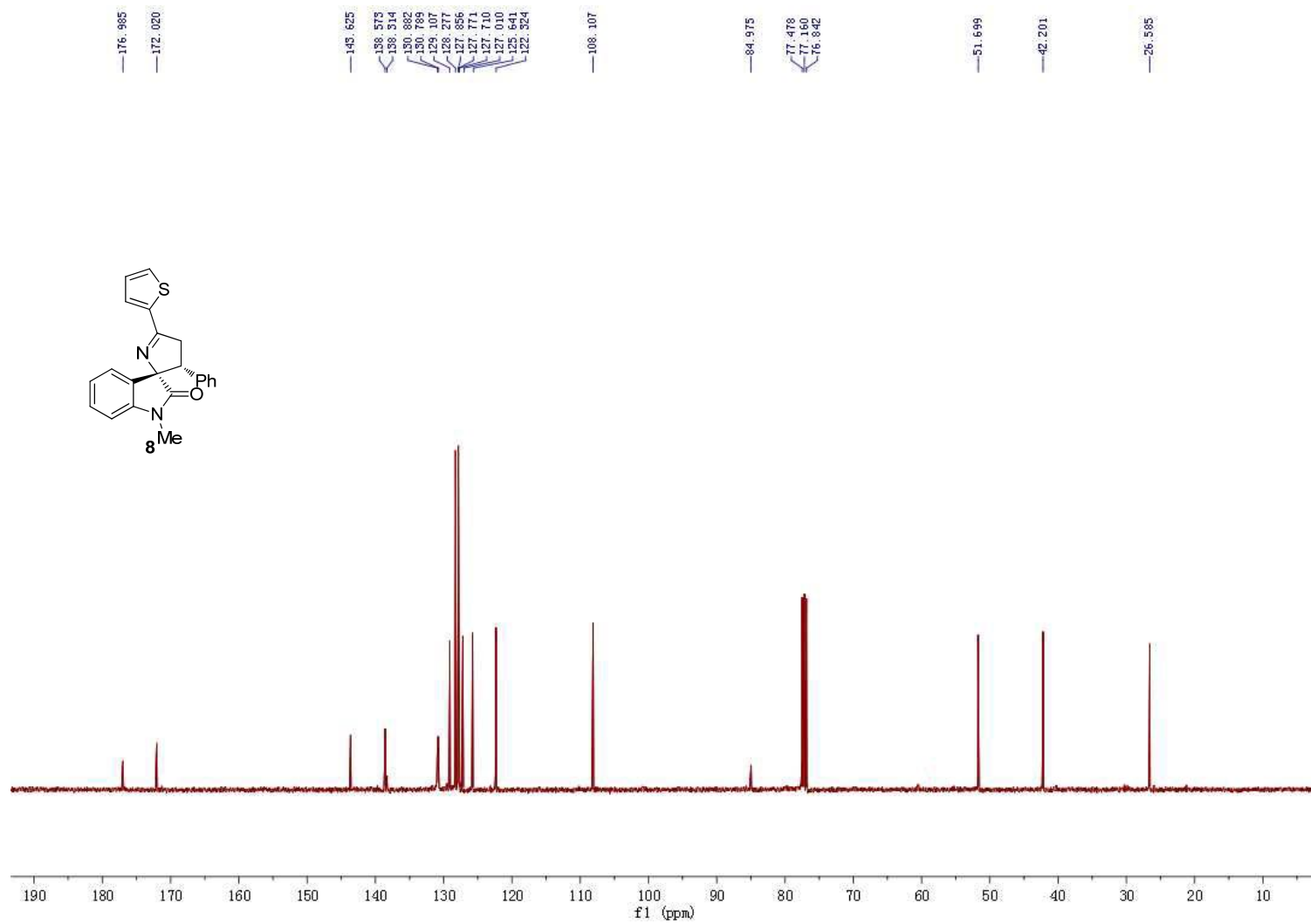
Quantitative Results

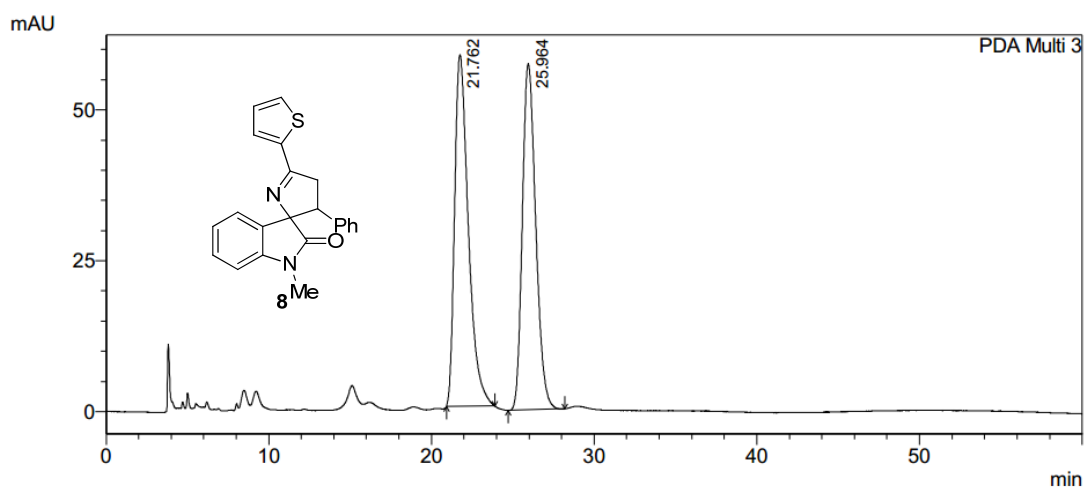
PDA

ID#	Name	Ret. Time	Area	Height	Conc.
1	RT23.734	23.734	590885	8756	20.176
2	RT48.518	48.518	2337823	31272	79.824

NMR and HPLC of 8



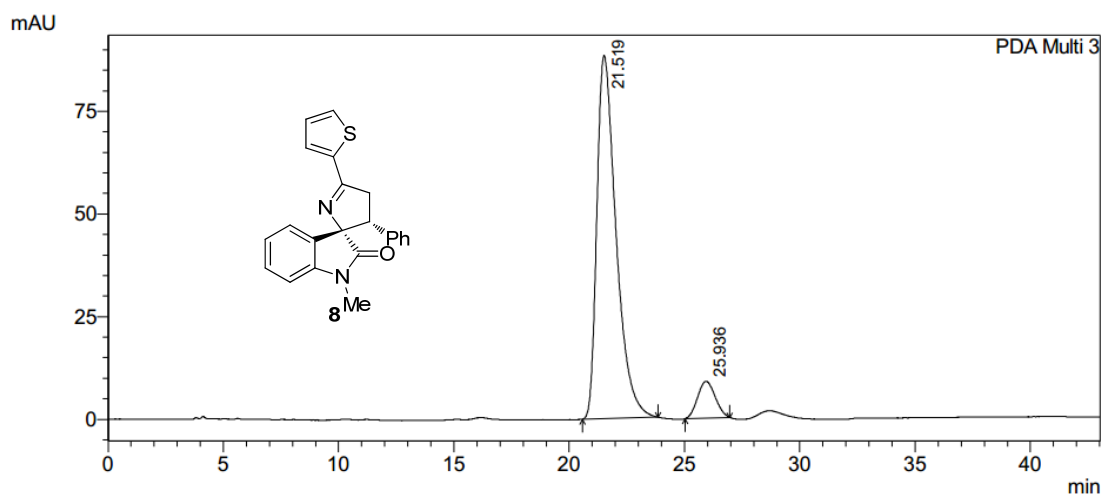




1 PDA Multi 3/254nm 4nm

Quantitative Results

ID#	Name	Ret. Time	Area	Height	Conc.
1	RT21.762	21.762	3416589	58236	51.025
2	RT25.964	25.964	3279323	57364	48.975

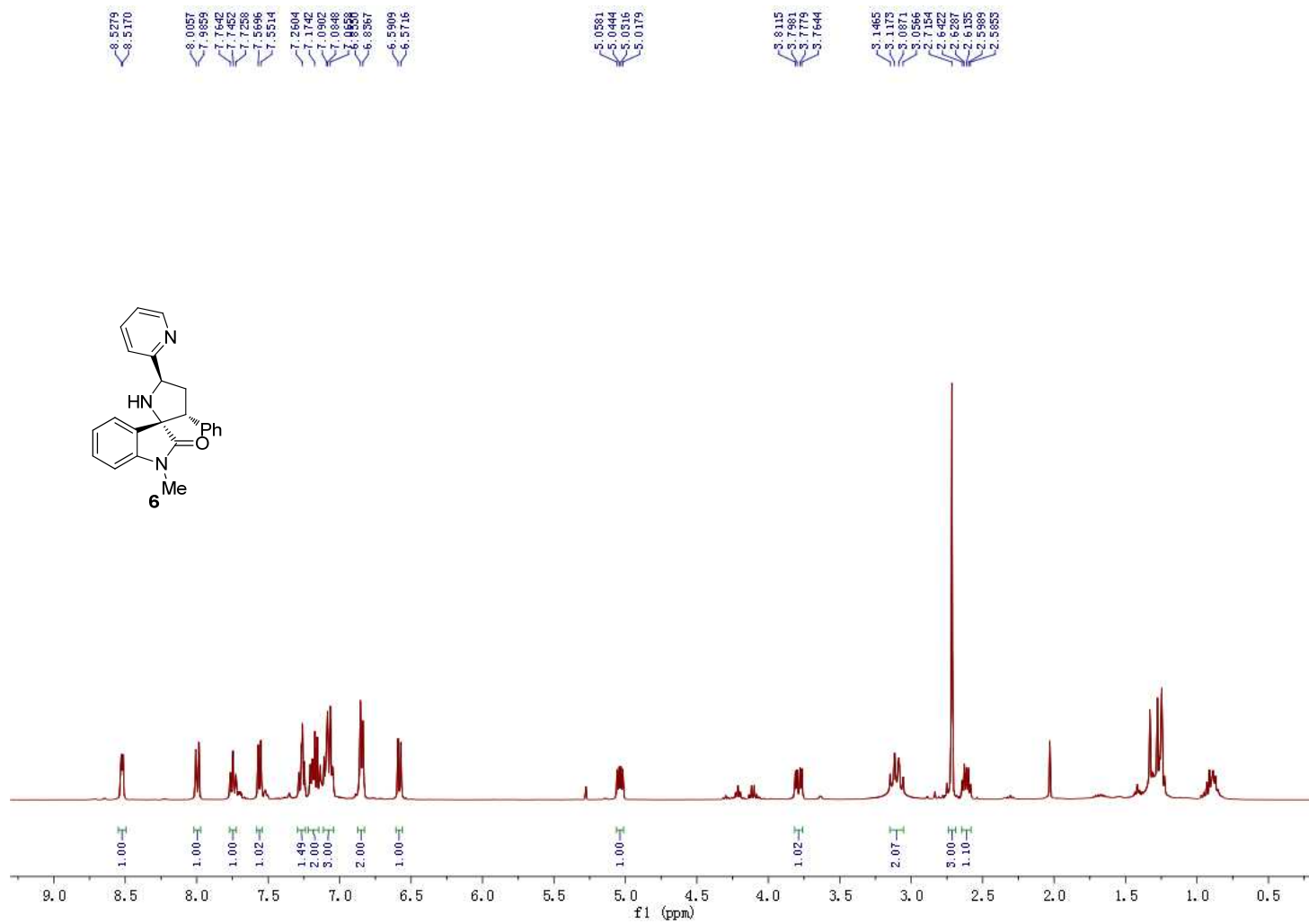


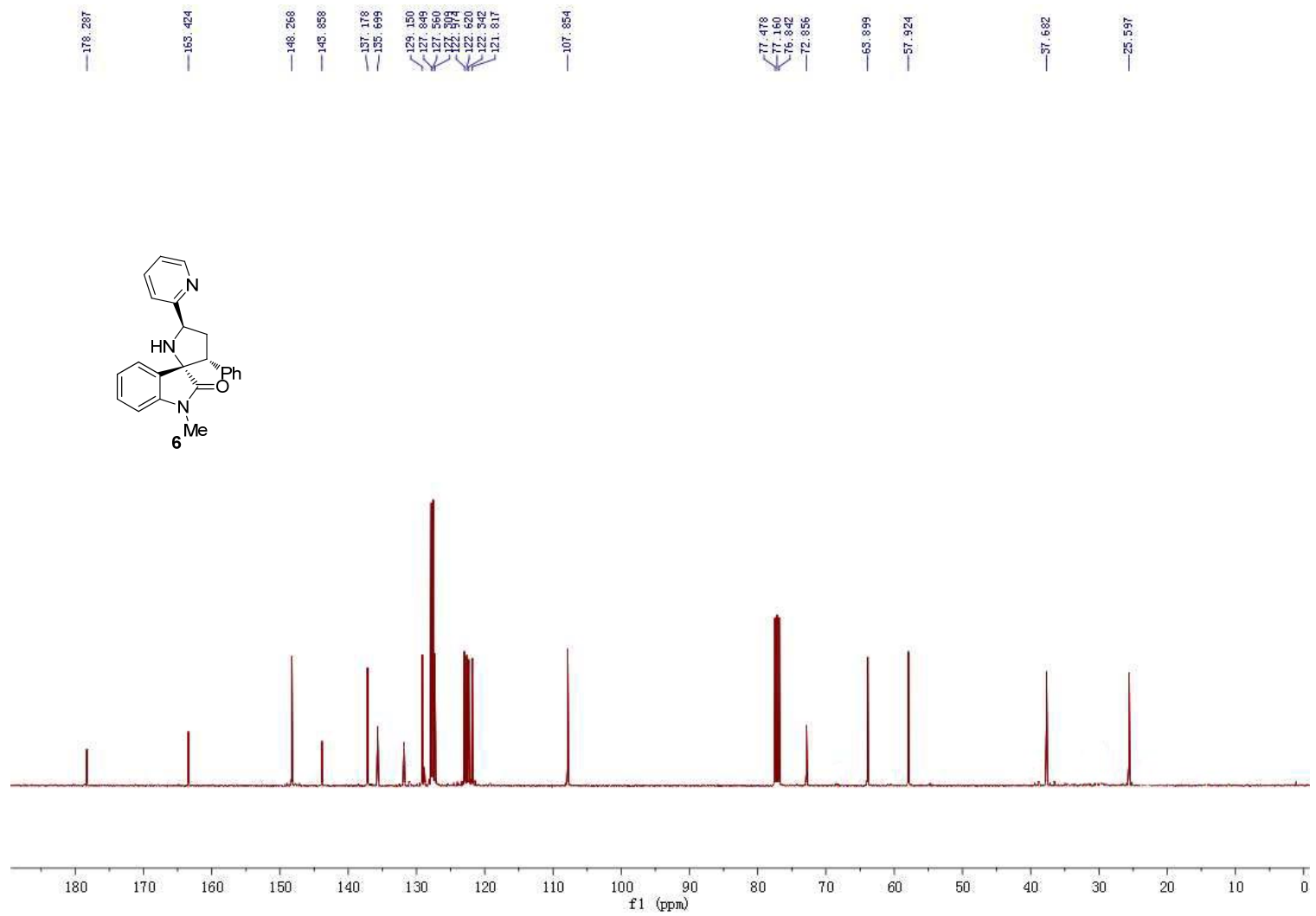
1 PDA Multi 3/254nm 4nm

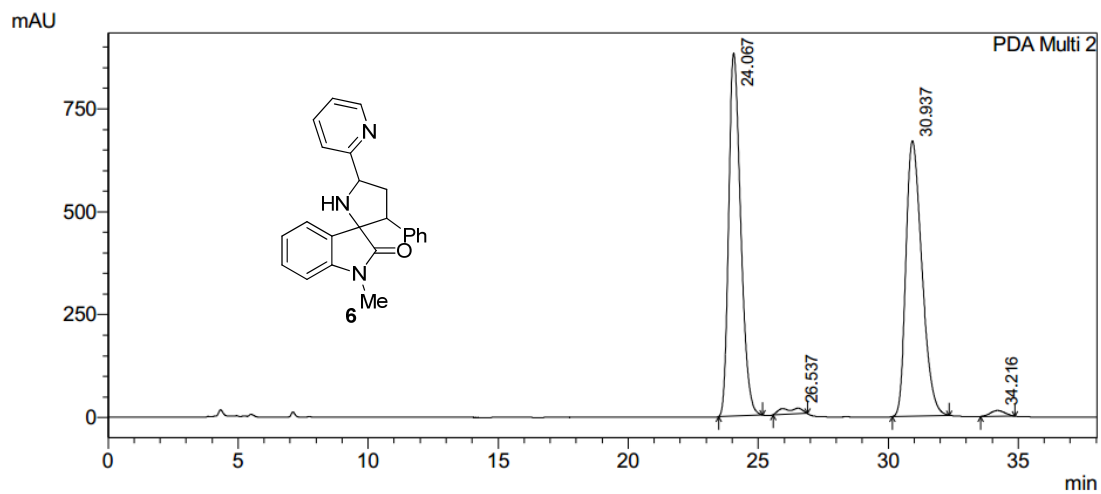
Quantitative Results

ID#	Name	Ret. Time	Area	Height	Conc.
1	RT21.519	21.519	5121066	88451	91.489
2	RT25.936	25.936	476420	8978	8.511

NMR and HPLC of 6



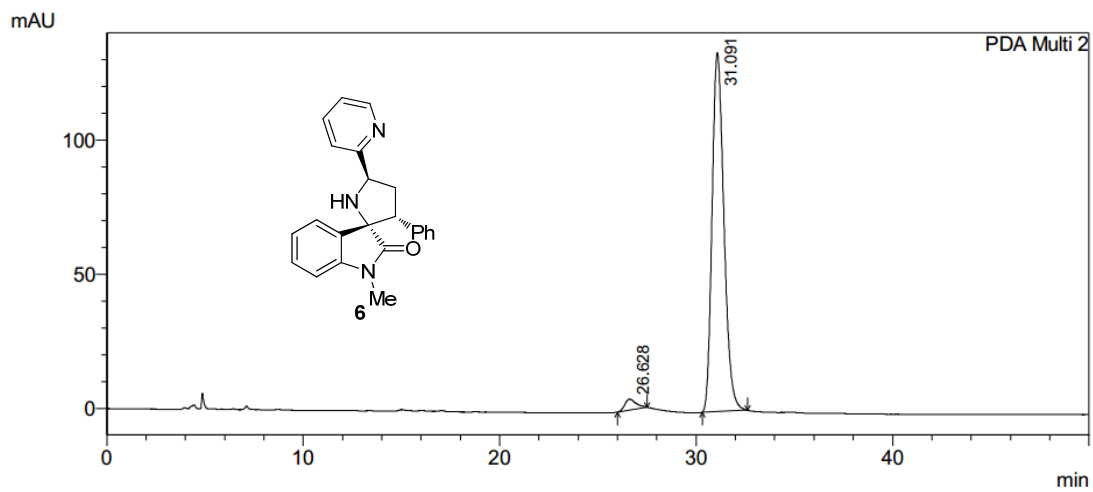




Quantitative Results

PDA

ID#	Name	Ret. Time	Area	Height	Conc.
1	RT24.067	24.067	28414969	881831	48.792
2	RT26.537	26.537	738635	13502	1.268
3	RT30.937	30.937	28553809	668788	49.030
4	RT34.216	34.216	529764	13777	0.910

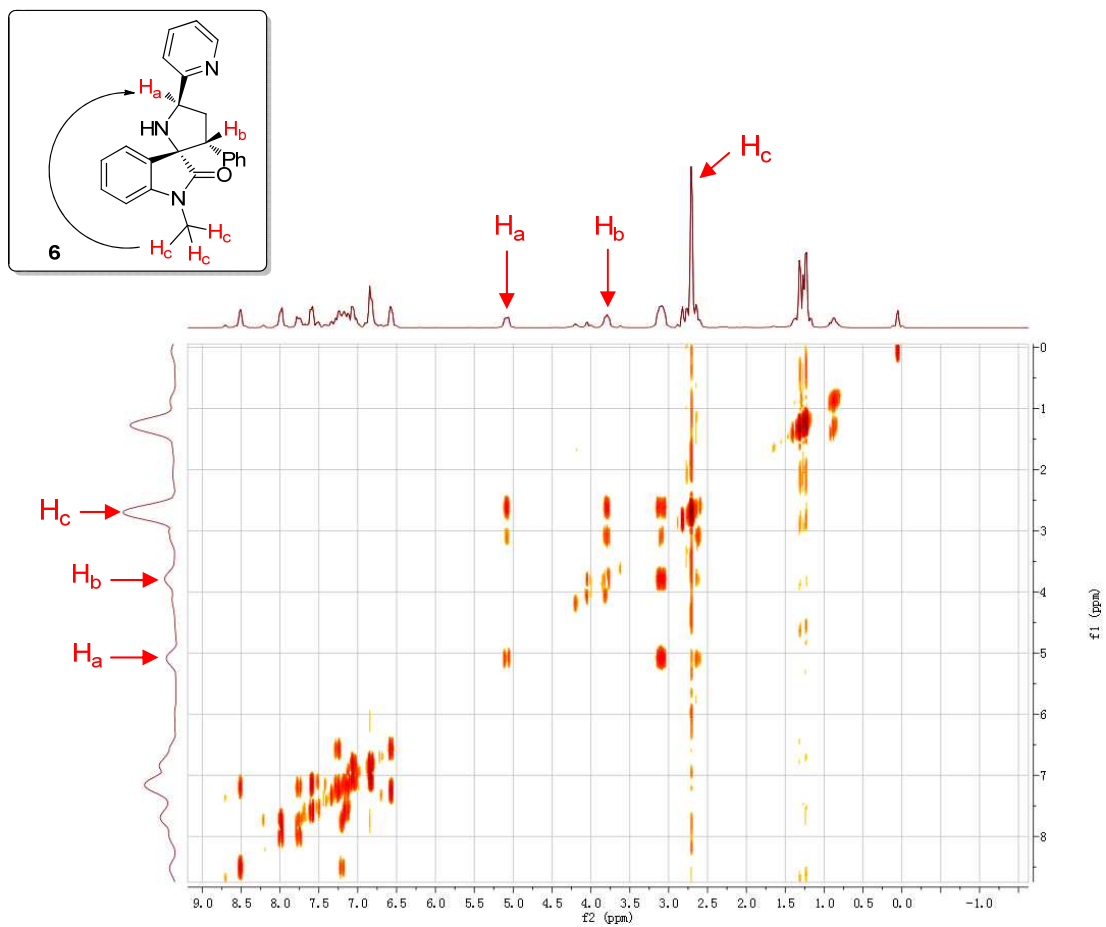


Quantitative Results

PDA

ID#	Name	Ret. Time	Area	Height	Conc.
1	RT26.628	26.628	162233	4101	2.829
2	RT31.091	31.091	5572988	133476	97.171

6. NOESY spectra for compound 6



7. References

- (1) B.-J. Li, L. Jiang, M. Liu, Y.-C. Chen, L.-S. Ding and Y. Wu, *Synlett*, 2005, **4**, 603.
- (2) E. Massolo, M. Benaglia, A. Genoni, R. Annunziata, G. Celentano and N. Gaggero, *Org. Biomol. Chem.*, 2015, **13**, 5591.
- (3) T. Emura, T. Esaki, K. Tachibana and M. Shimizu, *J. Org. Chem.*, 2006, **71**, 8559.