

Supporting Information

Asymmetric Michael addition reactions of pyrrolones with chalcones catalyzed by vicinal primary-diamine salts

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Contents

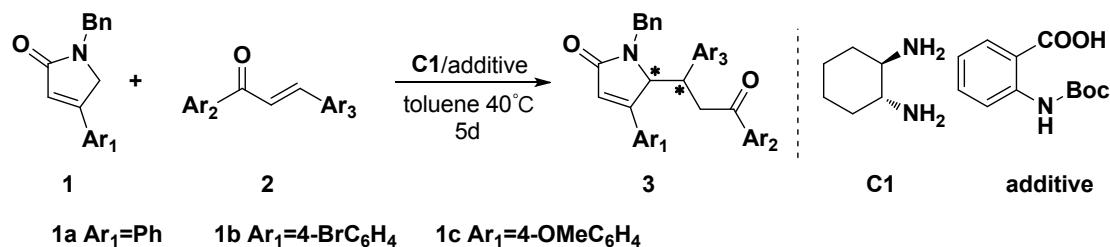
| | |
|---|----|
| A. General information | 2 |
| B. Experimental procedures and characterization data of products..... | 2 |
| a General procedure for the synthesis of products..... | 2 |
| b Characterization data | 3 |
| c NMR Spectra..... | 14 |
| d HPLC Spectra | 32 |

A. General information

¹H NMR spectra were recorded on a Bruker AVANCE III-400 spectrometer. Chemical shifts (in ppm) were referenced to the solvent residual signal ($\delta = 7.26$ ppm) of CDCl₃. ¹³C NMR spectra were obtained by using the same NMR spectrometer and were calibrated to CDCl₃ ($\delta = 77.00$ ppm). High Resolution Mass spectra were recorded using a Fourier Transform Ion Cyclotron Resonance Mass Spectrometer (APEX IV, Bruker). Unless otherwise noted, materials obtained from commercial suppliers were used without further purification. Column chromatography was carried out on silica gel (particle size 200–300 mesh ASTM).

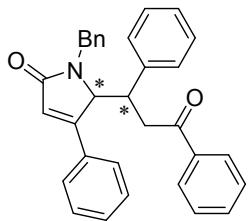
B. Experimental procedures and characterization data of products

a. General procedure for the synthesis of products



Pyrrolone **1** (0.15 mmol), chalcone **2** (0.225 mmol) was dissolved in toluene (1.5 mL), and the catalyst **C1** (0.03 mmol), acid additive (0.06 mmol) was added. The mixture was reacted at 40 °C for 5 days. After the completion of the reaction as indicated by TLC, the mixture was cooled to room temperature and the solvent was evaporated. 10 mL of CH₂Cl₂ was added and the mixture was washed with 5% HCl, 2% NaOH, saturated NaCl, the organic phase was dried with anhydrous Na₂SO₄. The mixture was filtered, the solvent was evaporated in vacuo to afford the crude product. Chromatography on silica gel (ethyl acetate-dichloromethane-petroleum ether=1:1:4) gave the corresponding product **3** as a colourless oil.

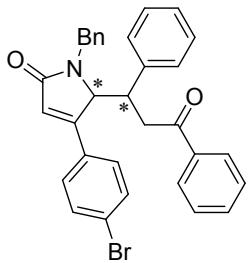
b. Characterization data



N-Benzyl-5-(3-oxo-1,3-diphenylpropyl)-4-phenyl-1H-pyrrol-2(5H)-one (3a)

Yield 65%, colourless oil; ^1H NMR (400 MHz, CDCl_3): (syn) δ 7.89 (d, $J = 7.7$ Hz, 2H), 7.62 (t, $J = 7.4$ Hz, 1H), 7.50 (t, $J = 7.6$ Hz, 2H), 7.30 (m, 4H), 7.28 – 7.20 (m, 4H), 7.18 – 7.11 (m, 2H), 7.09 (d, $J = 7.1$ Hz, 1H), 7.03 (t, $J = 7.4$ Hz, 2H), 6.65 (d, $J = 7.5$ Hz, 2H), 6.22 (s, 1H), 5.49 (dd, $J = 15.3$ Hz, 1H), 4.91 (d, $J = 1.6$ Hz, 1H), 4.34 (d, $J = 15.4$ Hz, 1H), 4.16 (td, $J = 7.3, 2.3$ Hz, 1H), 3.46 – 3.29 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3): (syn) δ 197.57, 171.86, 160.48, 137.67, 137.00, 136.70, 133.43, 132.48, 129.52, 128.95, 128.71, 128.58, 128.14, 128.08, 128.01, 127.94, 127.79, 127.37, 126.92, 122.43, 64.53, 45.67, 40.94, 37.41; ES-HRMS: Calcd for $\text{C}_{32}\text{H}_{28}\text{NO}_2$ $[\text{M}+\text{H}]^+$, 458.2114, Found 458.2105.

The enantiomeric excess was determined by HPLC analysis. (OD-H, hexane:IPA= 85:15, flow rate:1.0 mL/min) : t_{R} 9.90min (minor) , t_{R} 20.71min (major) , ee 95%

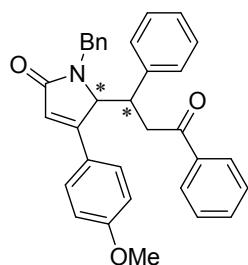


N-Benzyl-5-(3-oxo-1,3-diphenylpropyl)-4-(4-bromophenyl)-1H-pyrrol-2(5H)-one (3b)

Yield 40%, colourless oil; ^1H NMR (400 MHz, CDCl_3): (syn) δ 7.89 (d, $J = 7.6$ Hz, 2H), 6.80-7.80(m, 15H), 6.66 (d, $J = 7.4$ Hz, 2H), 6.22 (s, 1H), 5.48 (d, $J = 15.3$ Hz, 1H), 4.87 (m, 1H), 4.32 (d, $J = 15.4$ Hz, 1H), 4.18 – 4.06 (m, 1H), 3.37 (d, $J = 7.1$ Hz,

2H). ^{13}C NMR (100 MHz, CDCl_3): (syn) δ 197.48, 171.52, 159.14, 139.11, 137.51, 137.04, 136.84, 136.64, 133.52, 132.42, 131.79, 128.98, 128.84, 128.75, 128.21, 128.15, 127.98, 127.93, 123.93, 122.89, 64.38, 45.72, 40.91, 37.30; ES-HRMS: Calcd for $\text{C}_{32}\text{H}_{27}\text{BrNO}_2$ [$\text{M}+\text{H}]^+$, 536.1219, Found 536.1199.

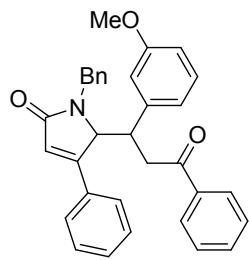
The enantiomeric excess was determined by HPLC analysis. (OD-H, hexane:IPA=85:15, flow rate:1.0 mL/min) : t_{R} 11.41min (minor), t_{R} 26.52min (major), ee 90%



N-Benzyl-5-(3-oxo-1,3-diphenylpropyl)-4-methoxyphenyl-1H-pyrrol-2(5H)-one (3c)

Yield 55%, colourless oil; ^1H NMR (400 MHz, CDCl_3): (syn) δ 7.95 – 7.86 (m, 2H), 7.62 (t, $J = 7.4$ Hz, 1H), 7.50 (t, $J = 7.7$ Hz, 2H), 7.30 (m, 3H), 7.24 (m, 2H), 7.19 – 7.10 (m, 3H), 7.07 (t, $J = 7.2$ Hz, 2H), 6.79 (d, $J = 8.8$ Hz, 2H), 6.69 (d, $J = 7.1$ Hz, 2H), 6.12 (s, 1H), 5.49 (d, $J = 15.4$ Hz, 1H), 4.87 (d, $J = 2.1$ Hz, 1H), 4.34 (d, $J = 15.4$ Hz, 1H), 4.14 (td, $J = 7.2, 2.6$ Hz, 1H), 3.83 (s, 3H), 3.41 (d, $J = 7.3$ Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3): (syn) δ 197.70, 172.31, 160.73, 160.10, 137.75, 137.09, 136.71, 133.44, 128.93, 128.90, 128.71, 128.11, 128.07, 127.95, 127.72, 126.94, 125.00, 120.41, 114.03, 64.29, 55.36, 45.84, 41.27, 37.86; ES-HRMS: Calcd for $\text{C}_{33}\text{H}_{30}\text{NO}_3$ [$\text{M}+\text{H}]^+$, 488.2220, Found 488.2202.

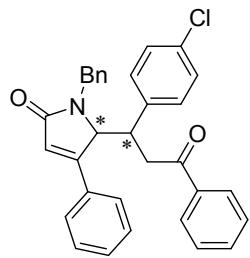
The enantiomeric excess was determined by HPLC analysis. (OD-H, hexane:IPA=85:15, flow rate:1.0 mL/min) : t_{R} 12.07min (minor), t_{R} 27.83min (major), ee 90%



N-Benzyl-5-(1-(3-methoxyphenyl)-3-oxo-3-phenylpropyl)-4-phenyl-1H-pyrrol-2(5H)-one (3d)

Yield 70%, colourless oil; ^1H NMR (400 MHz, CDCl_3): (syn) δ 7.79 (d, $J = 7.8$ Hz, 2H), 6.80-7.65 (m, 15H), 6.65 (m, 2H), 6.35 (s, 1H), 5.27 (d, $J = 14.9$ Hz, 1H), 4.90 (m, 1H), 4.09 (m, 1H), 3.91 (d, $J = 14.9$ Hz, 1H), 3.76 (s, 3H), 3.32 (ddd, $J = 24.2$, 17.9, 7.1 Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3): (syn) δ 197.37, 171.66, 159.71, 159.36, 140.98, 137.22, 136.51, 133.31, 132.45, 130.20, 129.56, 129.18, 128.96, 128.62, 128.49, 128.18, 127.97, 127.33, 123.37, 120.26, 114.34, 112.20, 65.11, 55.19, 45.00, 40.65, 35.55; ES-HRMS: Calcd for $\text{C}_{33}\text{H}_{30}\text{NO}_3$ [$\text{M}+\text{H}]^+$, 488.2220, Found 488.2220.

The enantiomeric excess was determined by HPLC analysis. (OD-H, hexane:IPA= 85:15, flow rate:1.0 mL/min) : t_{R} 12.39min (minor), t_{R} 30.86min (major), ee 90%

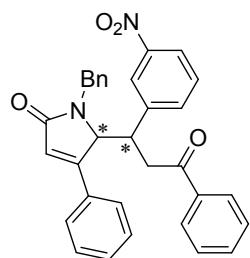


N-Benzyl-5-(1-(4-chlorophenyl)-3-oxo-3-phenylpropyl)-4-phenyl-1H-pyrrol-2(5H)-one (3e)

Yield 62%, colourless oil; ^1H NMR (400 MHz, CDCl_3): (syn) δ 7.92 – 7.84 (m, 2H), 7.63 (t, $J = 7.4$ Hz, 1H), 7.50 (t, $J = 7.7$ Hz, 2H), 7.35 – 7.30 (m, 4H), 7.29 – 7.24 (m, 4H), 7.20 – 7.15 (m, 2H), 7.00 (t, $J = 5.5$ Hz, 2H), 6.56 (d, $J = 8.4$ Hz, 2H), 6.23 (s, 1H), 5.46 (d, $J = 15.4$ Hz, 1H), 4.87 (d, $J = 2.1$ Hz, 1H), 4.34 (d, $J = 15.4$ Hz, 1H),

4.10 (td, $J = 7.2, 2.7$ Hz, 1H), 3.36 (d, $J = 7.2$ Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3): (syn) δ 197.23, 171.93, 160.25, 136.90, 136.55, 136.22, 133.56, 132.80, 132.36, 129.74, 129.32, 128.98, 128.76, 128.71, 128.18, 128.11, 127.93, 127.87, 127.36, 122.51, 64.41, 45.96, 40.62, 37.65; ES-HRMS: Calcd for $\text{C}_{32}\text{H}_{27}\text{ClNO}_2$ [M+H] $^+$, 492.1724, Found 492.1727.

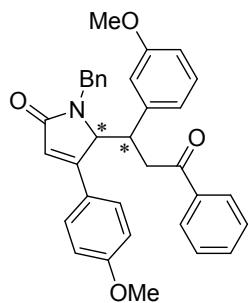
The enantiomeric excess was determined by HPLC analysis. (OD-H, hexane:IPA=85:15, flow rate:1.0 mL/min) : t_{R} 10.19min (minor) , t_{R} 20.38min (major) , ee 81%



***N*-Benzyl-5-(1-(3-nitrophenyl)-3-oxo-3-phenylpropyl)-4-phenyl-1*H*-pyrrol-2(*5H*)-one (3f)**

Yield 75%, colourless oil; ^1H NMR (400 MHz, CDCl_3): (syn) δ 7.89 (d, $J = 7.4$ Hz, 2H), 7.22-7.55 (m, 15H), 7.14 (m, 2H), 6.23 (s, 1H), 5.37 (d, $J = 15.3$ Hz, 1H), 4.87 (m, 1H), 4.40 (d, $J = 15.4$ Hz, 1H), 4.24 (m, 1H), 3.41 (d, $J = 7.1$ Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3): (syn) δ 196.82, 171.79, 160.02, 147.77, 140.00, 136.76, 136.27, 134.76, 134.25, 133.80, 129.98, 129.32, 129.14, 128.95, 128.88, 128.84, 128.77, 128.17, 128.06, 127.98, 127.49, 127.27, 123.02, 122.82, 122.05, 64.70, 46.13, 40.78, 36.96; ES-HRMS: Calcd for $\text{C}_{32}\text{H}_{27}\text{N}_2\text{O}_4$ [M+H] $^+$, 503.1965, Found 503.1971.

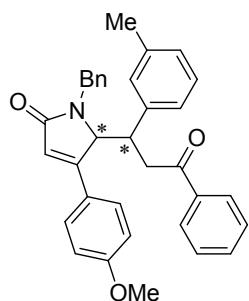
The enantiomeric excess was determined by HPLC analysis. (OD-H, hexane:IPA=75:25, flow rate:0.3 mL/min) : t_{R} 48.27min (minor) , t_{R} 81.21min (major) , ee 92%



N-Benzyl-5-(1-(3-methoxyphenyl)-3-oxo-3-phenylpropyl)-4-(4-methoxyphenyl)-1H-pyrrol-2(5H)-one (3g)

Yield 64%, colourless oil; ^1H NMR (400 MHz, CDCl_3): (syn) δ 7.92 – 7.86 (m, 2H), 7.50 (t, J = 7.7 Hz, 2H), 7.41 (dd, J = 17.8, 8.3 Hz, 3H), 7.28 – 7.20 (m, 5H), 7.02 – 6.91 (m, 2H), 6.87 – 6.80 (m, 2H), 6.29 (s, 1H), 6.16 (s, 2H), 5.48 (d, J = 15.4 Hz, 1H), 4.84 (d, J = 2.1 Hz, 1H), 4.30 (d, J = 15.4 Hz, 1H), 4.14 (td, J = 7.4, 2.7 Hz, 1H), 3.82 (s, 3H), 3.58 (s, 3H), 3.34 (qd, J = 18.0, 7.2 Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3): (syn) δ 197.65, 172.10, 160.73, 160.05, 159.24, 139.44, 137.09, 136.73, 133.41, 129.05, 128.91, 128.70, 128.43, 128.17, 127.94, 127.73, 125.10, 120.58, 120.46, 114.62, 113.94, 112.54, 64.53, 55.34, 54.92, 45.54, 41.00, 37.24; ES-HRMS: Calcd for $\text{C}_{34}\text{H}_{32}\text{NO}_4$ [$\text{M}+\text{H}]^+$, 518.2325, Found 518.2326.

The enantiomeric excess was determined by HPLC analysis. (OD-H, hexane:IPA = 85:15, flow rate:1.0 mL/min) : t_{R} 14.63min (minor), t_{R} 40.45min (major), ee 93%

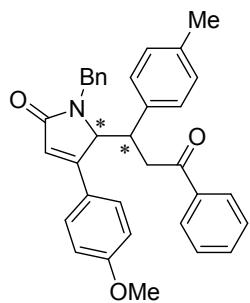


N-Benzyl-5-(1-(3-methylphenyl)-3-oxo-3-phenylpropyl)-4-(4-methoxyphenyl)-1H-pyrrol-2(5H)-one (3h)

Yield 55%; colourless oil; ^1H NMR (400 MHz, CDCl_3): (syn) δ 7.89 (d, J = 7.3 Hz, 2H), 7.50 (t, J = 7.7 Hz, 2H), 7.30 (m, 5H), 6.95 (m, 4H), 6.78 (t, J = 6.8 Hz, 2H), 6.38

(s, 1H), 6.14 (s, 1H), 5.43 (d, $J = 15.4$ Hz, 1H), 4.83 (m, 1H), 4.34 (d, $J = 15.4$ Hz, 1H), 4.12 (td, $J = 7.1, 2.7$ Hz, 1H), 3.82 (s, 3H), 3.35 (m, 2H), 2.11 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3): (syn) δ 197.74, 172.15, 160.70, 160.19, 139.56, 137.73, 137.46, 137.22, 136.79, 133.37, 128.96, 128.89, 128.68, 128.38, 128.21, 127.96, 127.70, 127.31, 125.26, 124.78, 120.60, 113.88, 64.80, 55.33, 45.67, 40.96, 37.33, 21.28; ES-HRMS: Calcd for $\text{C}_{34}\text{H}_{32}\text{NO}_3$ [$\text{M}+\text{H}]^+$, 502.2376, Found 502.2373.

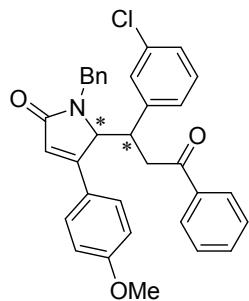
The enantiomeric excess was determined by HPLC analysis. (OD-H, hexane:IPA=85:15, flow rate:1.0 mL/min) : t_{R} 10.72min (minor) , t_{R} 22.10min (major) , ee 85%



N-Benzyl-5-(1-(p-tolyl)-3-oxo-3-phenylpropyl)-4-(4-methoxyphenyl)-1H-pyrrol-2(5H)-one (3i)

Yield 60%, colourless oil; ^1H NMR (400 MHz, CDCl_3): (syn) δ 7.89 (d, $J = 8.0$ Hz, 2H), 7.62 (t, $J = 7.3$ Hz, 1H), 7.50 (t, $J = 7.6$ Hz, 2H), 7.28 (m, 3H), 7.20 (m, 4H), 6.88 (d, $J = 7.8$ Hz, 2H), 6.81 (d, $J = 8.6$ Hz, 2H), 6.58 (d, $J = 7.8$ Hz, 2H), 6.11 (s, 1H), 5.48 (d, $J = 15.4$ Hz, 1H), 4.86 (d, $J = 1.0$ Hz, 1H), 4.33 (d, $J = 15.4$ Hz, 1H), 4.07 (t, $J = 6.2$ Hz, 1H), 3.84 (s, 3H), 3.50 – 3.32 (m, 2H), 2.25 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3): (syn) δ 197.79, 172.40, 160.75, 160.12, 137.14, 136.48, 134.58, 133.37, 128.97, 128.85, 128.71, 128.68, 128.07, 127.98, 127.95, 127.66, 125.08, 120.31, 114.01, 64.22, 55.34, 45.95, 41.13, 38.35, 20.96; ES-HRMS: Calcd for $\text{C}_{34}\text{H}_{32}\text{NO}_3$ [$\text{M}+\text{H}]^+$, 502.2376, Found 502.2374.

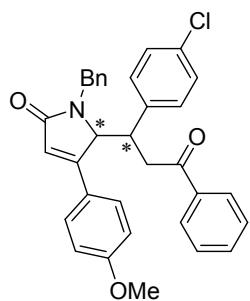
The enantiomeric excess was determined by HPLC analysis. (OD-H, hexane:IPA=85:15, flow rate:1.0 mL/min) : t_{R} 10.20min (minor) , t_{R} 20.41min (major) , ee 85%



N-Benzyl-5-(1-(3-chlorophenyl)-3-oxo-3-phenylpropyl)-4-(4-methoxyphenyl)-1H-pyrrol-2(5H)-one (3j)

Yield 82%, colourless oil; ^1H NMR (400 MHz, CDCl_3): (syn) δ 7.88 (d, $J = 7.7$ Hz, 2H), 7.63 (t, $J = 7.2$ Hz, 1H), 7.51 (t, $J = 7.5$ Hz, 2H), 7.32 (m, 3H), 7.28 (m, 2H), 7.10 (t, $J = 7.7$ Hz, 3H), 7.02 (t, $J = 7.7$ Hz, 1H), 6.81 (d, $J = 8.2$ Hz, 3H), 6.62 (d, $J = 7.6$ Hz, 1H), 6.53 (s, 1H), 6.15 (s, 1H), 5.39 (d, $J = 15.4$ Hz, 1H), 4.81 (s, 1H), 4.34 (d, $J = 15.3$ Hz, 1H), 4.11 (t, $J = 6.6$ Hz, 1H), 3.84 (s, 3H), 3.38 – 3.27 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3): (syn) δ 197.25, 172.22, 160.95, 159.96, 140.01, 137.02, 136.52, 133.88, 133.58, 129.28, 128.99, 128.91, 128.75, 128.39, 128.16, 127.96, 127.84, 127.13, 126.38, 124.83, 120.69, 114.14, 64.60, 55.38, 45.92, 40.86, 37.23; ES-HRMS: Calcd for $\text{C}_{33}\text{H}_{29}\text{ClNO}_3$ [M+H] $^+$, 522.1830, Found 522.1830.

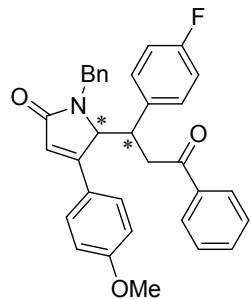
The enantiomeric excess was determined by HPLC analysis. (OD-H, hexane:IPA=92:8, flow rate:1.0 mL/min) : t_{R} 25.87min (minor), t_{R} 57.63min (major), ee 83%



N-Benzyl-5-(1-(4-chlorophenyl)-3-oxo-3-phenylpropyl)-4-(4-methoxyphenyl)-1H-pyrrol-2(5H)-one (3k)

Yield 64%, colourless oil; ^1H NMR (400 MHz, CDCl_3): (syn) δ 7.88 (d, $J = 7.6$ Hz, 2H), 7.63 (t, $J = 7.4$ Hz, 1H), 7.51 (t, $J = 7.7$ Hz, 2H), 7.30 (m, 3H), 7.26 – 7.20 (m, 2H), 7.15 (d, $J = 8.7$ Hz, 2H), 7.03 (d, $J = 8.4$ Hz, 2H), 6.82 (d, $J = 8.7$ Hz, 2H), 6.59 (d, $J = 8.4$ Hz, 2H), 6.12 (s, 1H), 5.45 (d, $J = 15.4$ Hz, 1H), 4.83 (d, $J = 2.3$ Hz, 1H), 4.33 (d, $J = 15.4$ Hz, 1H), 4.08 (td, $J = 7.1, 2.4$ Hz, 1H), 3.84 (s, 3H), 3.46 – 3.30 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3): (syn) δ 197.37, 172.39, 160.89, 159.91, 136.98, 136.54, 136.29, 133.58, 132.76, 129.41, 128.94, 128.89, 128.76, 128.14, 128.08, 127.94, 127.81, 124.81, 120.47, 114.14, 64.21, 55.40, 46.10, 40.92, 37.99; ES-HRMS: Calcd for $\text{C}_{33}\text{H}_{29}\text{ClNO}_3$ [M+H] $^+$, 522.1830, Found 522.1833.

The enantiomeric excess was determined by HPLC analysis. (OD-H, hexane:IPA=90:10, flow rate:1.0 mL/min) : t_R 18.24min (minor), t_R 38.63min (major), ee 87%

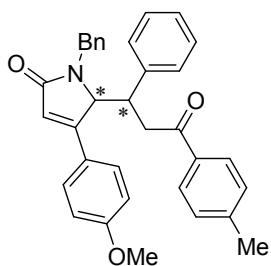


N-Benzyl-5-(1-(4-fluorophenyl)-3-oxo-3-phenylpropyl)-4-(4-methoxyphenyl)-1H-pyrrol-2(5H)-one (3l)

Yield 55%, colourless oil; ^1H NMR (400 MHz, CDCl_3): (syn) δ 7.90 – 7.86 (m, 2H), 7.63 (t, $J = 7.4$ Hz, 1H), 7.51 (t, $J = 7.7$ Hz, 2H), 7.30 (m, 3H), 7.23 (m, 2H), 7.17 (d, $J = 8.8$ Hz, 2H), 6.83 (d, $J = 8.8$ Hz, 2H), 6.77 (t, $J = 8.7$ Hz, 2H), 6.63 (m, 2H), 6.12 (s, 1H), 5.46 (d, $J = 15.4$ Hz, 1H), 4.84 (d, $J = 1.9$ Hz, 1H), 4.34 (d, $J = 15.4$ Hz, 1H), 4.09 (td, $J = 7.2, 2.3$ Hz, 1H), 3.84 (s, 3H), 3.43 (dd, $J = 18.2, 7.1$ Hz, 1H), 3.36 (dd, $J = 18.1, 7.7$ Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3): (syn) δ 197.49, 172.44, 161.71(d, $J = 244.0$ Hz), 160.88, 160.00, 137.02, 136.60, 133.54, 129.63, 129.55, 128.92(d, $J = 1.5$ Hz), 128.75, 128.07, 127.94, 127.78, 124.88, 120.42, 114.97, 114.76, 114.14,

64.25, 55.39, 46.12, 40.81, 38.34; ES-HRMS: Calcd for $C_{33}H_{29}FNO_3$ [M+H]⁺, 506.2126, Found 506.2126.

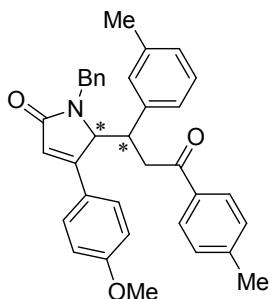
The enantiomeric excess was determined by HPLC analysis. (OD-H, hexane:IPA=85:15, flow rate:1.0 mL/min) : t_R 13.20min (minor), t_R 29.05min (major), ee 85%



N-Benzyl-5-(3-oxo-1-phenyl-3-(p-tolyl)propyl)-4-(4-methoxyphenyl)-1H-pyrrol-2(5H)-one (3m)

Yield 69%; colourless oil; ¹H NMR (400 MHz, CDCl₃): (syn) δ 7.81 (d, J = 8.2 Hz, 2H), 7.39 (d, J = 8.7 Hz, 2H), 7.34 – 7.04 (m, 12H), 6.81 (m, 2H), 6.11 (s, 1H), 5.48 (d, J = 15.4 Hz, 1H), 4.89 (d, J = 1.9 Hz, 1H), 4.35 (d, J = 15.4 Hz, 1H), 4.15 (m, 1H), 3.82 (s, 3H), 3.38 (m, 2H), 2.45 (s, 3H). ¹³C NMR (100 MHz, CDCl₃): (syn) δ 197.33, 172.37, 160.75, 160.17, 144.28, 137.86, 137.18, 134.31, 129.38, 128.94, 128.88, 128.45, 128.16, 128.09, 127.96, 127.70, 126.91, 125.04, 120.37, 114.05, 64.31, 55.35, 45.91, 41.41, 37.85, 21.70; ES-HRMS: Calcd for $C_{34}H_{32}NO_3$ [M+H]⁺, 502.2376, Found 502.2373.

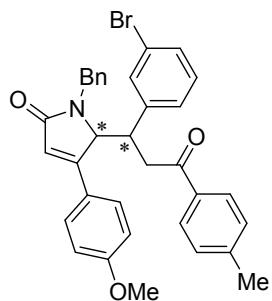
The enantiomeric excess was determined by HPLC analysis. (OD-H, hexane:IPA=95:5, flow rate:1.0 mL/min) : t_R 39.43min (minor), t_R 93.11min (major), ee 84%



N-Benzyl-5-(1-(3-bromophenyl)-3-oxo-3-(p-tolyl)propyl)-4-(4-methoxyphenyl)-1H-pyrrol-2(5H)-one (3n)

Yield 66%; colourless oil ; ^1H NMR (400 MHz, CDCl_3): (syn+anti) δ 7.81 (d, $J = 8.0$ Hz, 1H), 7.74 (d, $J = 8.0$ Hz, 1H), 7.38 (t, $J = 12.4$ Hz, 1H), 7.35 – 7.27 (m, 3H), 7.22 (dd, $J = 11.2, 8.6$ Hz, 2H), 7.10 (d, $J = 8.8$ Hz, 1H), 6.99 – 6.87 (m, 2H), 6.78 (t, $J = 7.3$ Hz, 2H), 6.53 (d, $J = 7.4$ Hz, 0H), 6.38 (s, 0H), 6.27 (s, 0H), 6.13 (s, 0H), 5.43 (d, $J = 15.3$ Hz, 0H), 5.23 (d, $J = 14.9$ Hz, 0H), 4.84 (s, 1H), 4.35 (d, $J = 15.3$ Hz, 0H), 4.21 – 4.03 (m, 1H), 3.82 (dd, $J = 13.1, 8.6$ Hz, 3H), 3.50 (dd, $J = 17.8, 9.3$ Hz, 0H), 3.33 (d, $J = 7.2$ Hz, 1H), 2.94 (dd, $J = 17.8, 5.0$ Hz, 0H), 2.45 (s, 1H), 2.42 (s, 1H). ^{13}C NMR (100 MHz, CDCl_3): (syn+anti) δ 197.37, 197.13, 172.23, 172.15, 161.15, 160.69, 160.26, 159.15, 144.22, 144.10, 139.65, 138.16, 137.81, 137.41, 137.36, 137.27, 134.34, 134.17, 129.36, 129.28, 128.97, 128.91, 128.88, 128.86, 128.44, 128.39, 128.24, 128.18, 128.15, 128.10, 127.92, 127.90, 127.69, 127.61, 127.31, 125.28, 125.22, 124.80, 121.21, 120.53, 114.58, 113.89, 65.35, 64.79, 55.40, 55.33, 45.73, 45.05, 41.04, 40.80, 37.28, 34.95, 21.70, 21.65, 21.52, 21.29; ES-HRMS: Calcd for $\text{C}_{34}\text{H}_{31}\text{BrNO}_3$ [M+H] $^+$, 516.2533, Found 516.2534.

The enantiomeric excess was determined by HPLC analysis. (OD-H, hexane:IPA= 85:15, flow rate:1.0 mL/min) : t_{R} 9.88min (minor) , t_{R} 18.34min (major) , ee 85%

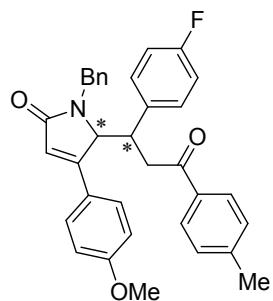


N-Benzyl-5-(1-(3-bromophenyl)-3-oxo-3-(p-tolyl)propyl)-4-(4-methoxyphenyl)-1H-pyrrol-2(5H)-one (3o)

Yield 64%, colourless oil; ^1H NMR (400 MHz, CDCl_3): (syn) δ 7.78 (d, $J = 8.0$ Hz, 2H), 7.37 – 7.20 (m, 8H), 7.11 (d, $J = 8.5$ Hz, 2H), 6.96 (t, $J = 8.0$ Hz, 1H), 6.81 (d, J

= 8.6 Hz, 2H), 6.66 (d, J = 6.5 Hz, 2H), 6.14 (s, 1H), 5.37 (d, J = 15.3 Hz, 1H), 4.81 (s, 1H), 4.38 – 4.27 (d, J = 15.3 Hz, 1H), 4.08 (td, J = 7.0, 2.2 Hz, 1H), 3.84 (s, 3H), 3.37 – 3.21 (m, 2H), 2.46 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3): (syn) δ 196.85, 172.26, 160.94, 160.01, 144.47, 140.40, 137.07, 134.08, 131.31, 130.01, 129.54, 129.42, 128.98, 128.91, 128.20, 128.09, 127.82, 126.84, 124.85, 122.12, 120.69, 114.14, 64.66, 55.37, 45.95, 40.90, 37.05, 21.71, 1.02; ES-HRMS: Calcd for $\text{C}_{34}\text{H}_{31}\text{BrNO}_3$ [M+H] $^+$, 580.1481, Found 580.1478.

The enantiomeric excess was determined by HPLC analysis. (OD-H, hexane:IPA= 85:15, flow rate:1.0 mL/min) : t_R 13.07min (minor) , t_R 23.90min (major) , ee 86%



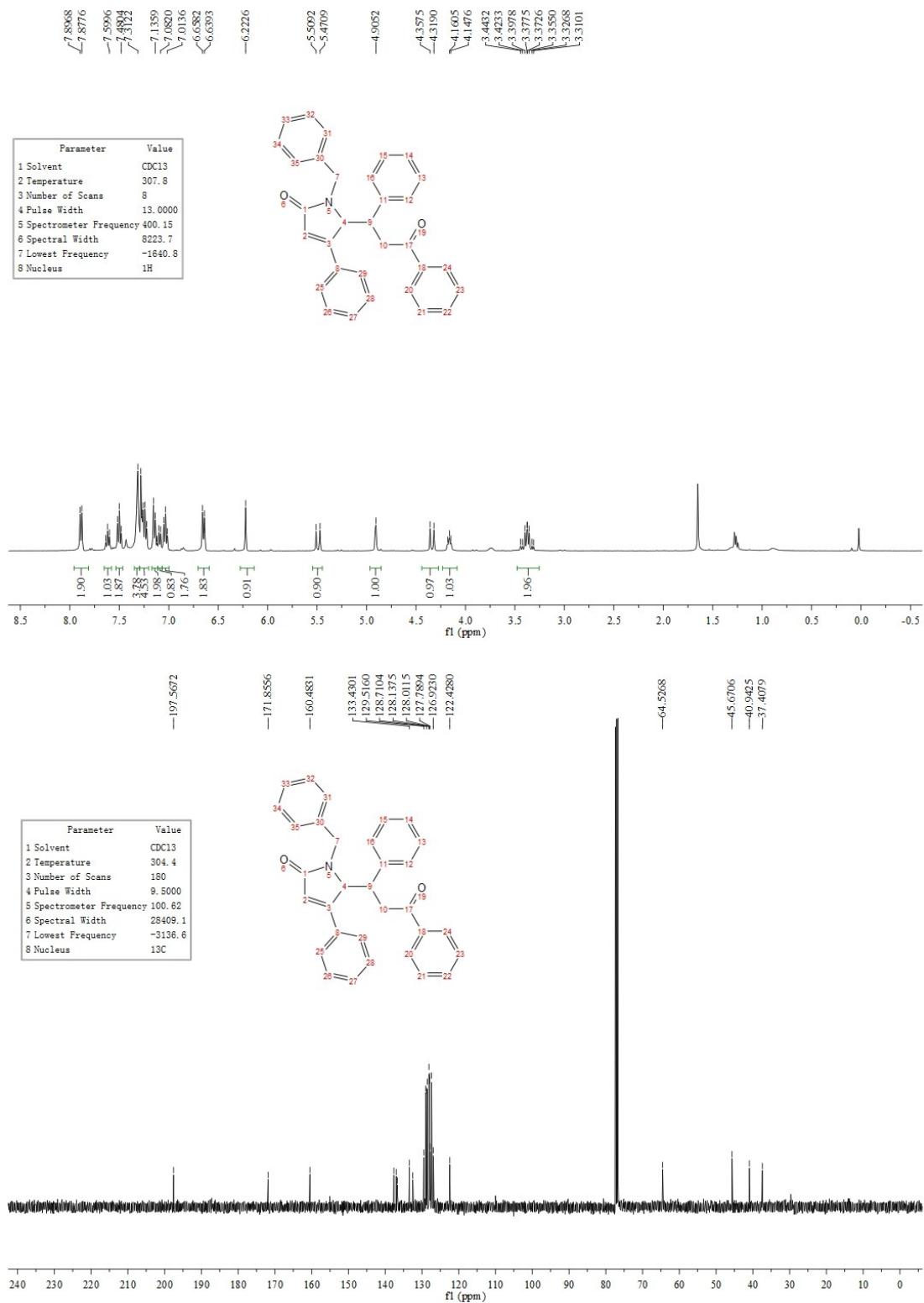
N-Benzyl-5-(1-(4-fluorophenyl)-3-oxo-3-(p-tolyl)propyl)-4-(4-methoxyphenyl)-1H-pyrrol-2(5H)-one (3p)

Yield 90%, colourless oil; ^1H NMR (400 MHz, CDCl_3): (syn) δ 7.77 (t, J = 16.7 Hz, 2H), 7.30 (m, 5H), 7.26 – 7.21 (m, 2H), 7.18 (d, J = 8.8 Hz, 2H), 6.83 (d, J = 8.8 Hz, 2H), 6.76 (m, J = 8.6 Hz, 2H), 6.63 (m, 2H), 6.11 (s, 1H), 5.45 (d, J = 15.4 Hz, 1H), 4.84 (d, J = 2.2 Hz, 1H), 4.33 (d, J = 15.4 Hz, 1H), 4.07 (dt, J = 20.2, 10.1 Hz, 1H), 3.84 (s, 3H), 3.37 (m, 2H), 2.46 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3): (syn) δ 197.12, 172.50, 160.87, 160.06, 144.44, 137.06, 134.16, 133.55, 129.64, 129.56, 129.42, 128.91, 128.10, 128.07, 127.76, 124.90, 120.37, 114.93, 114.72, 114.12, 64.25, 55.38, 46.15, 40.87, 38.24, 21.70; ES-HRMS: Calcd for $\text{C}_{34}\text{H}_{31}\text{FNO}_3$ [M+H] $^+$, 520.2282, Found 520.2283.

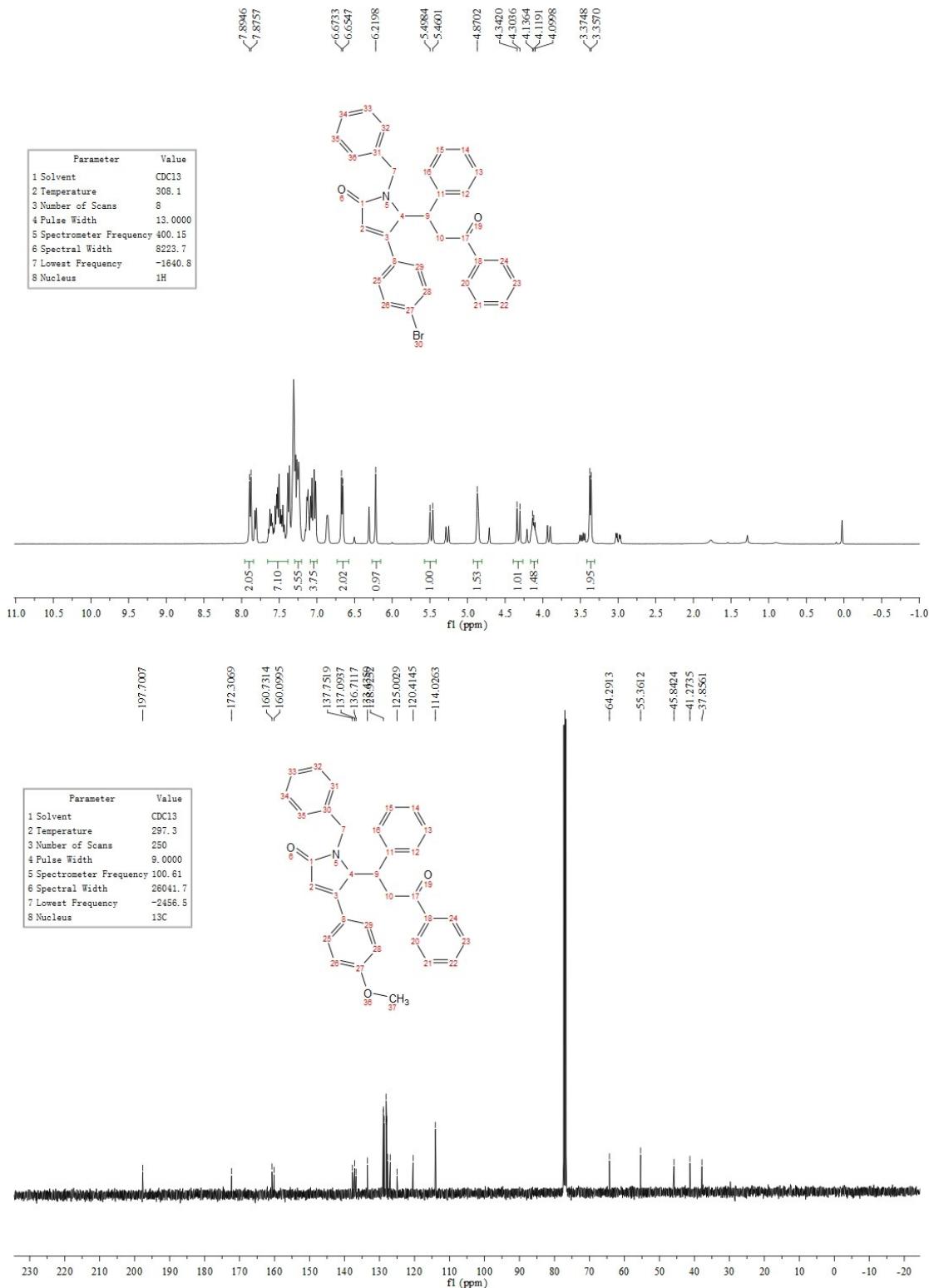
The enantiomeric excess was determined by HPLC analysis. (OD-H, hexane:IPA=92:8, flow rate:1.0 mL/min) : t_R 20.47min (minor), t_R 50.49min (major), ee 87%

c NMR Spectra

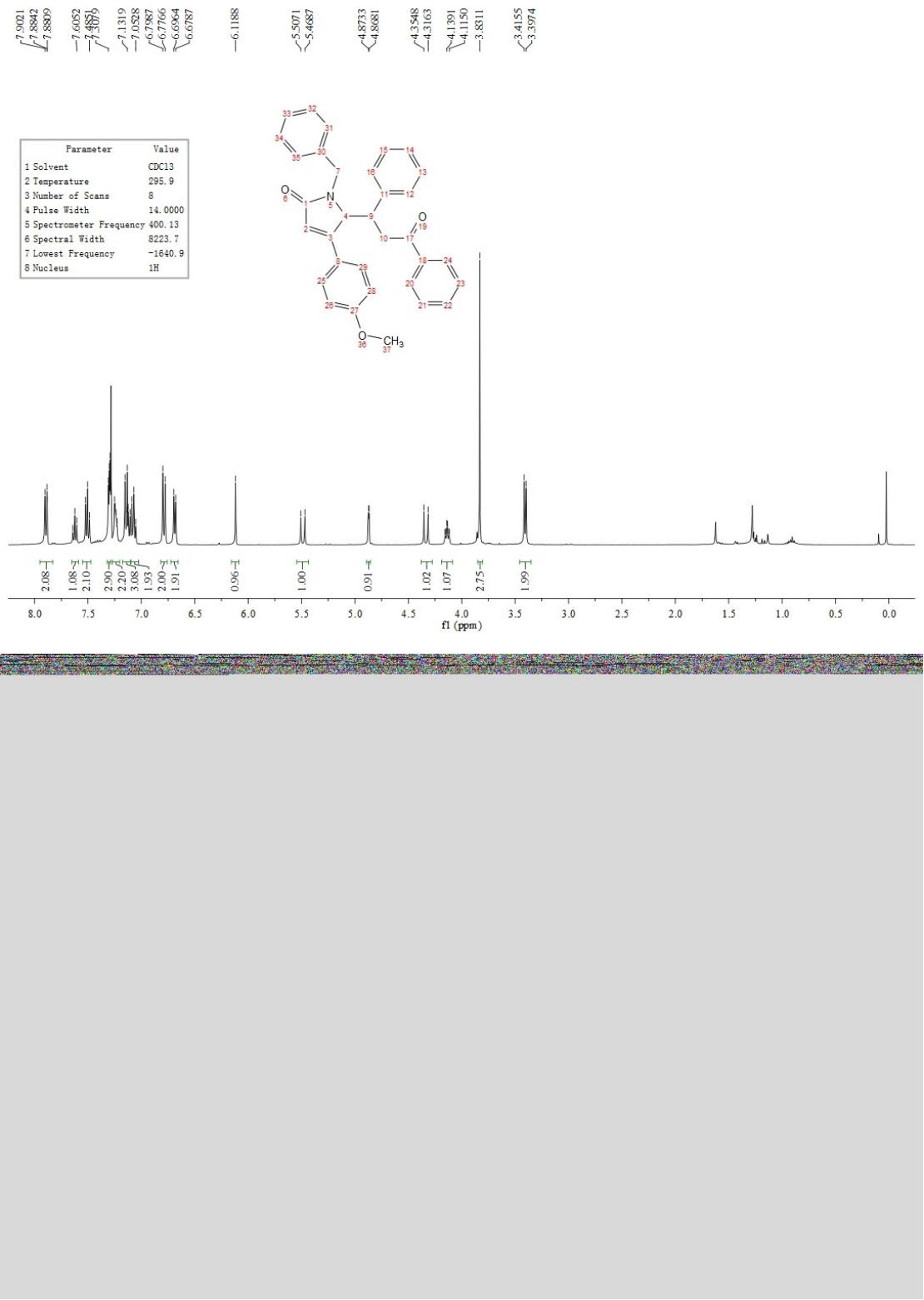
¹H NMR and ¹³C NMR spectra of 3a

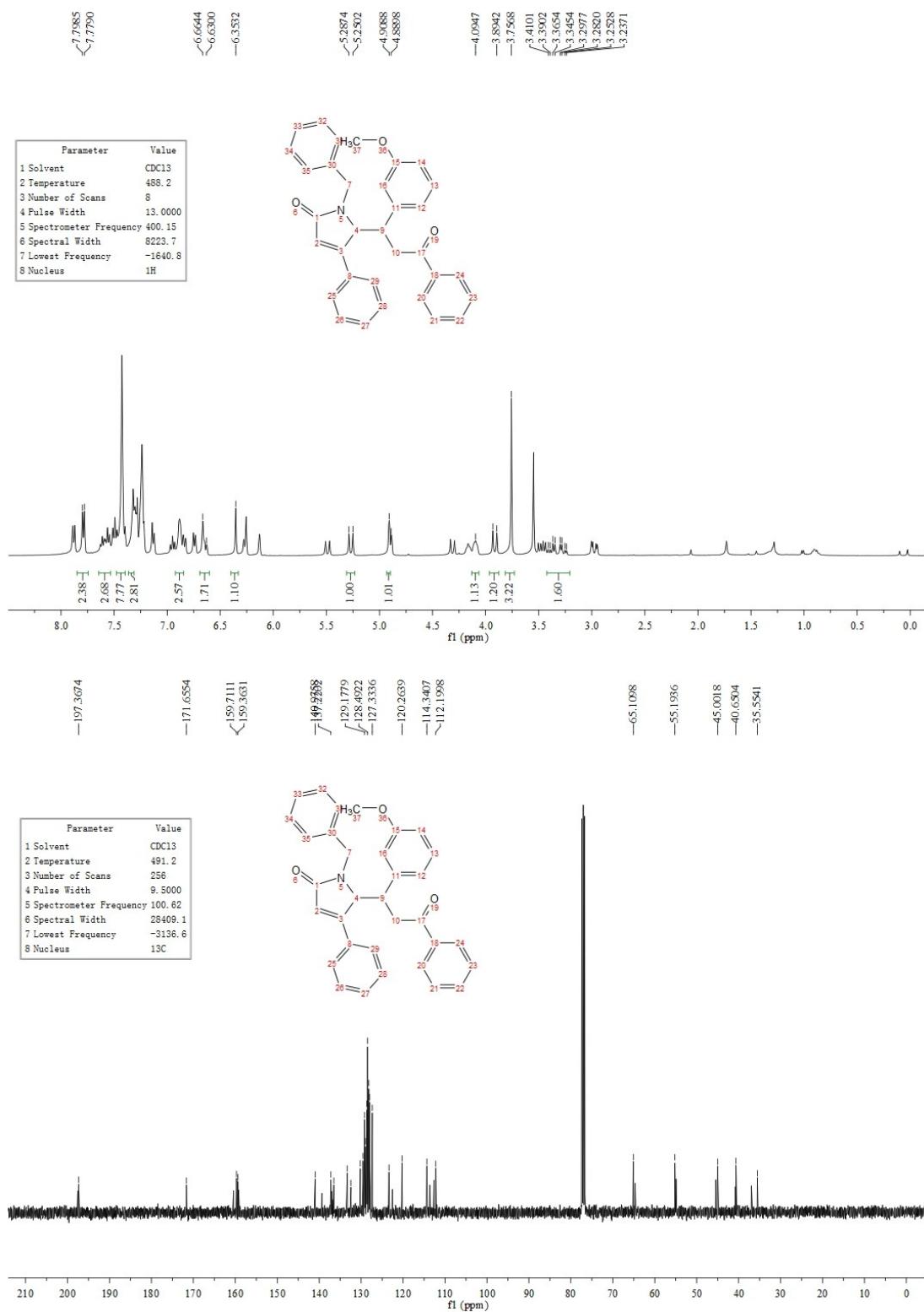


¹H NMR and ¹³C NMR spectra of 3b



¹H NMR and ¹³C NMR spectra of 3c

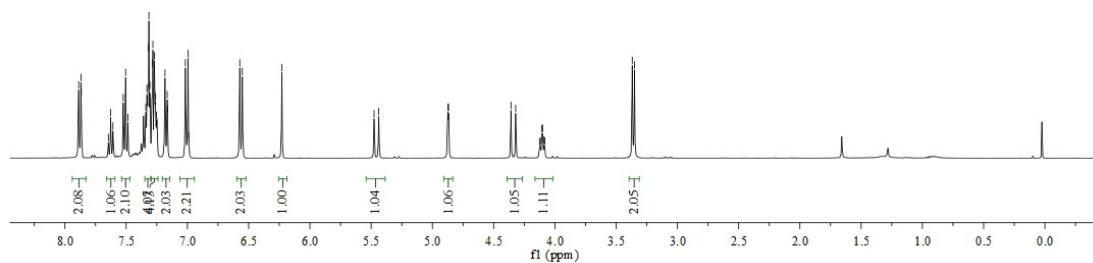
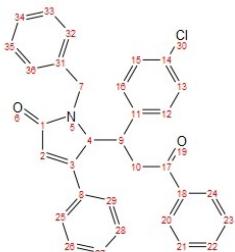




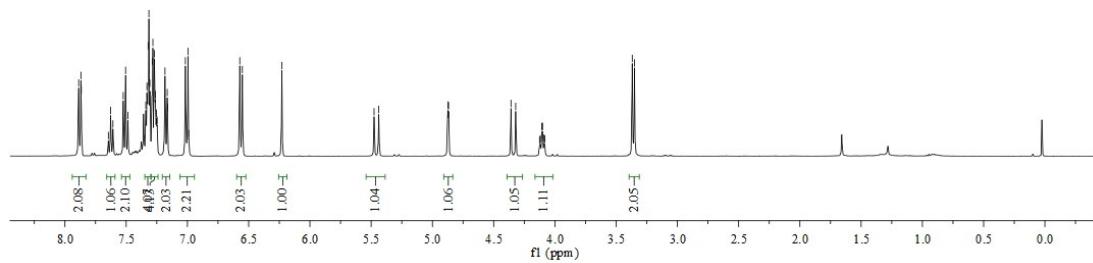
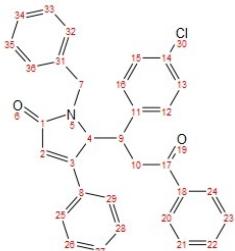
¹H NMR and ¹³C NMR spectra of 3e



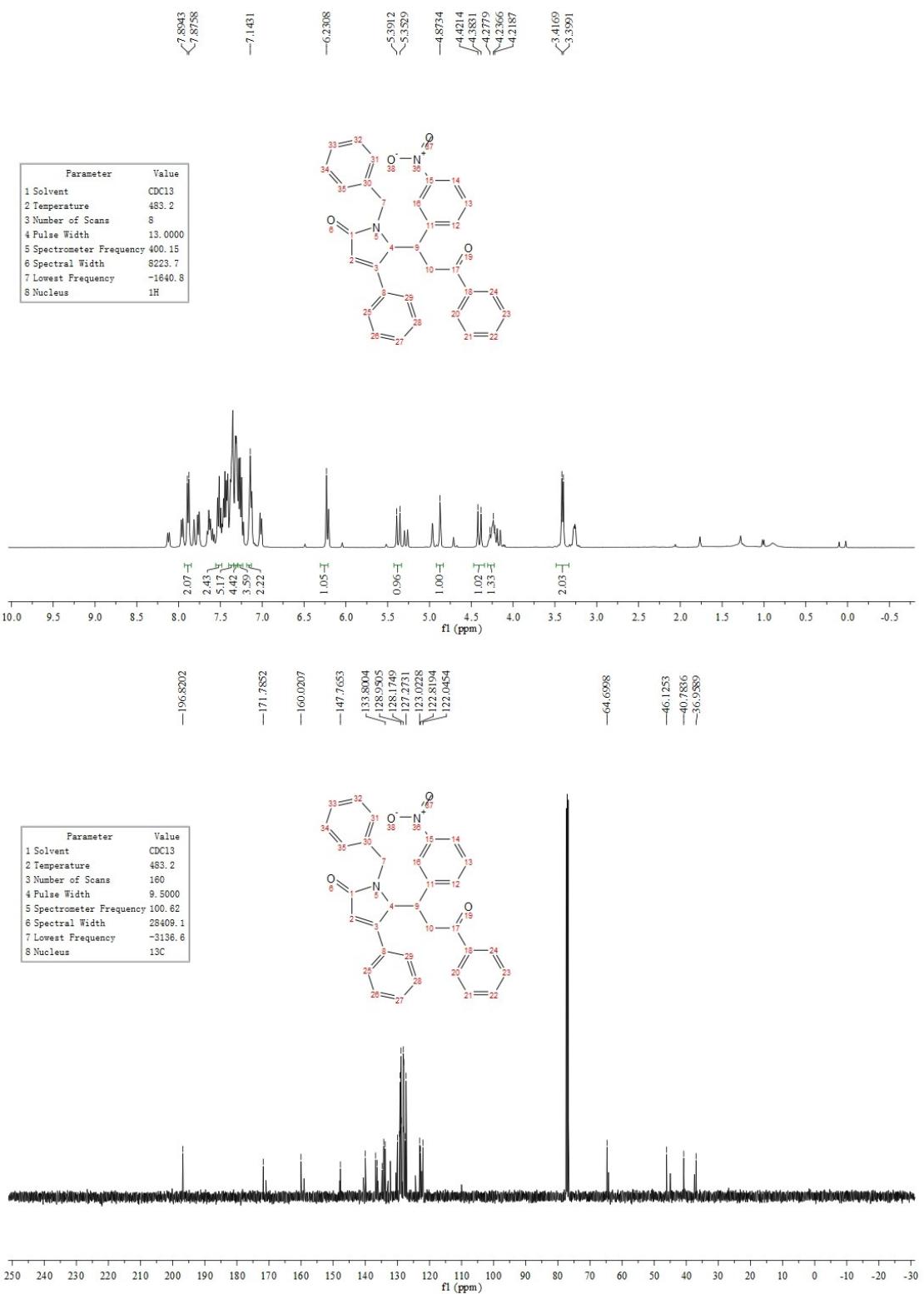
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| 3 Number of Scans | 8 |
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| 5 Spectrometer Frequency | 400.15 |
| 6 Spectral Width | 8223.7 |
| 7 Lowest Frequency | -1640.8 |
| 8 Nucleus | 1H |



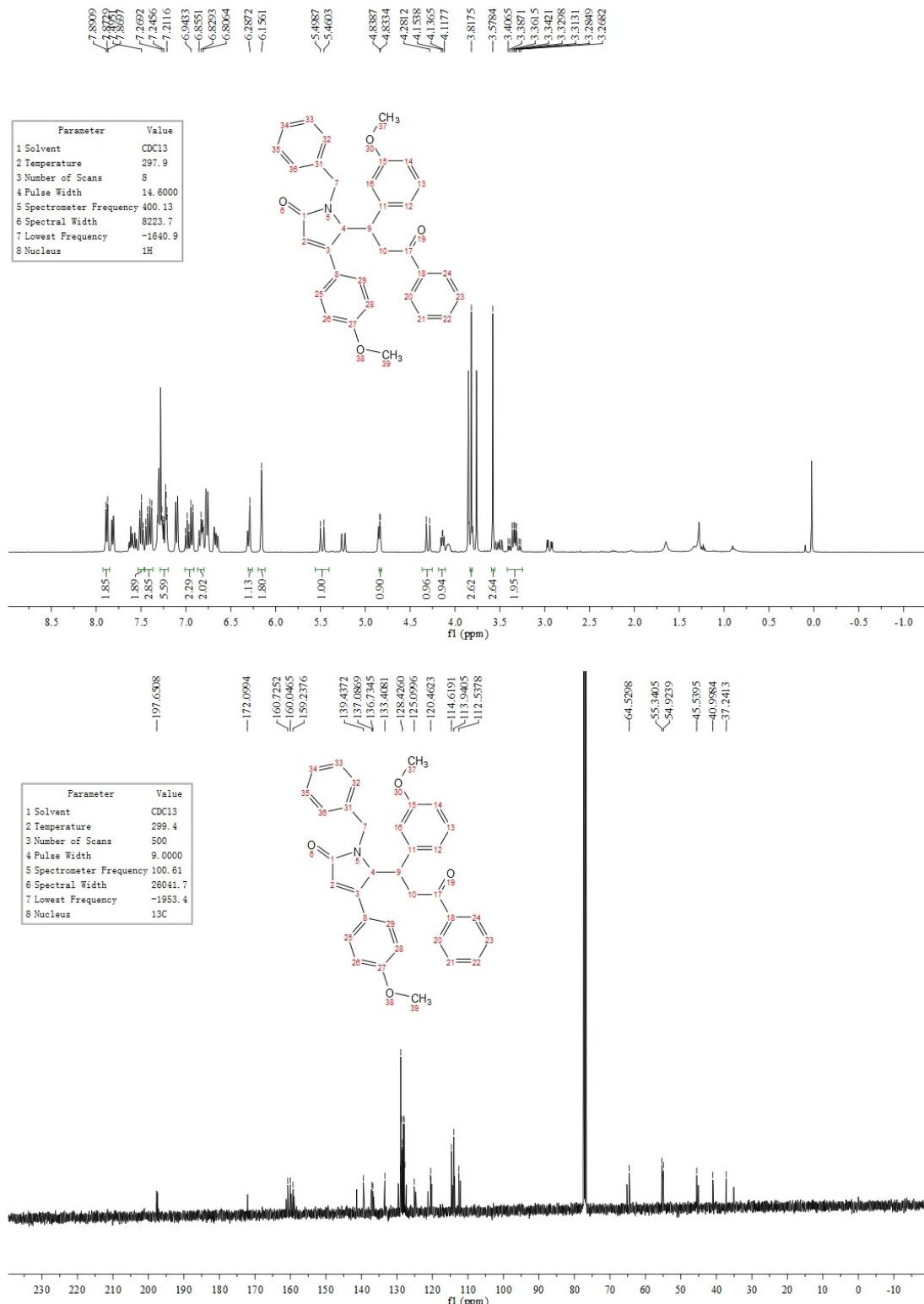
| Parameter | Value |
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| 3 Number of Scans | 8 |
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| 6 Spectral Width | 8223.7 |
| 7 Lowest Frequency | -1640.8 |
| 8 Nucleus | 1H |



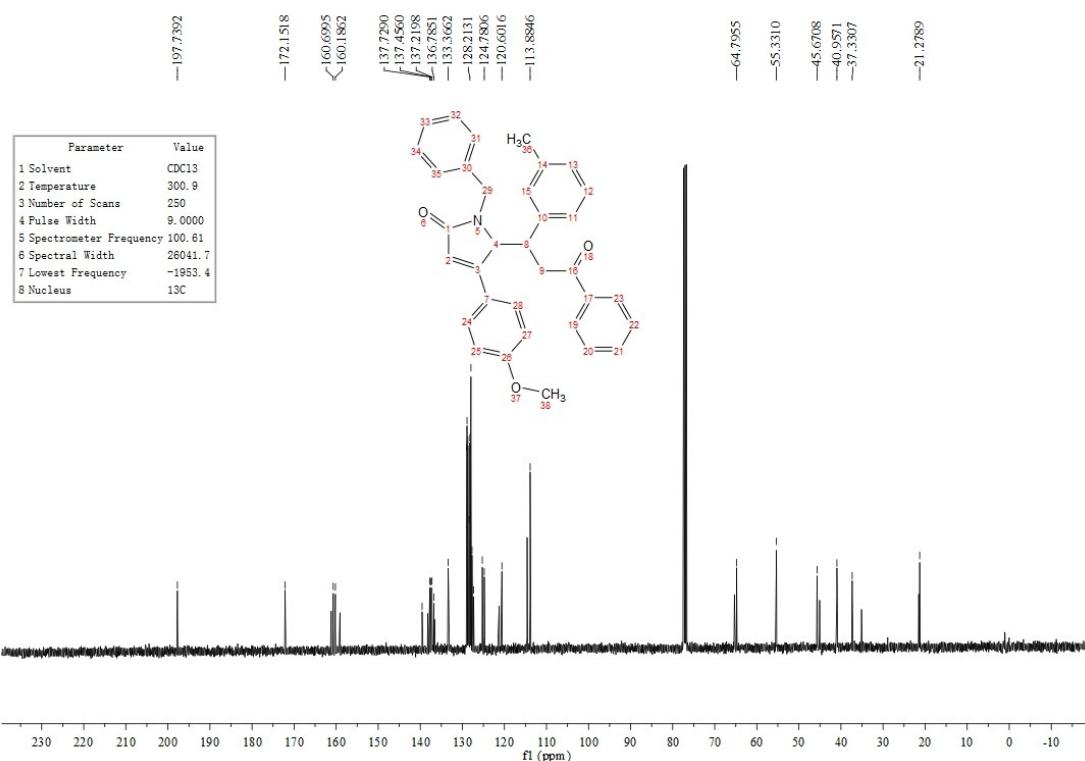
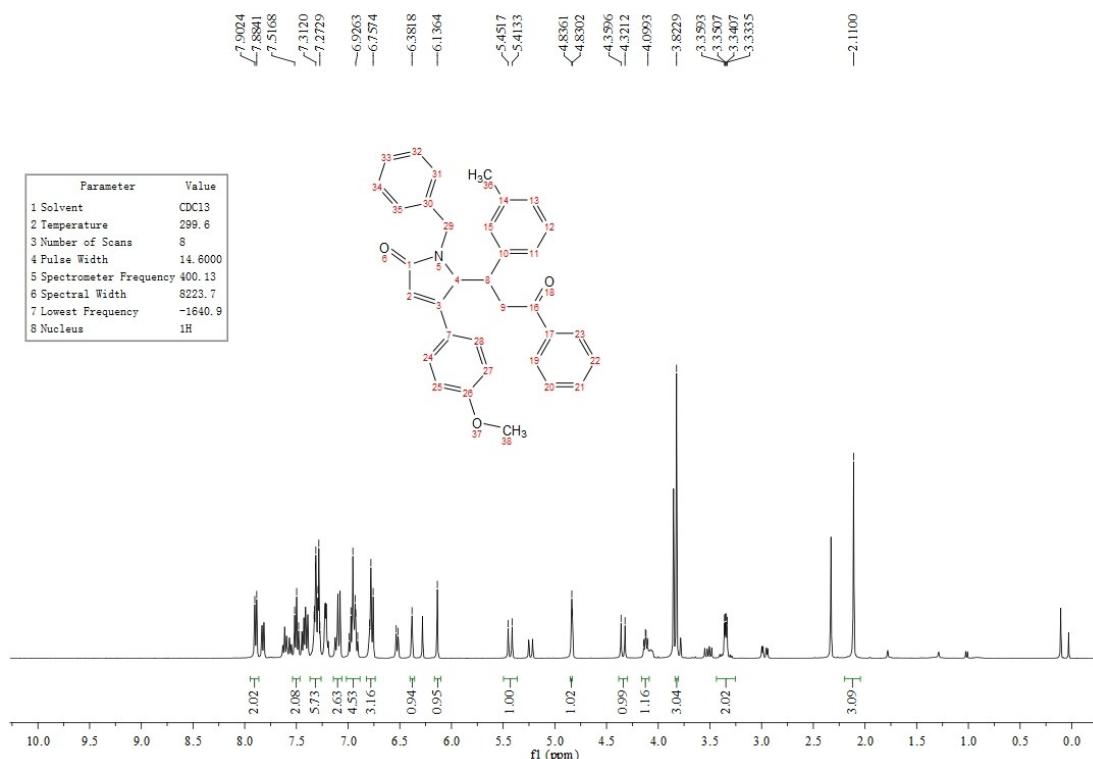
¹H NMR and ¹³C NMR spectra of 3f



¹H NMR and ¹³C NMR spectra of 3g



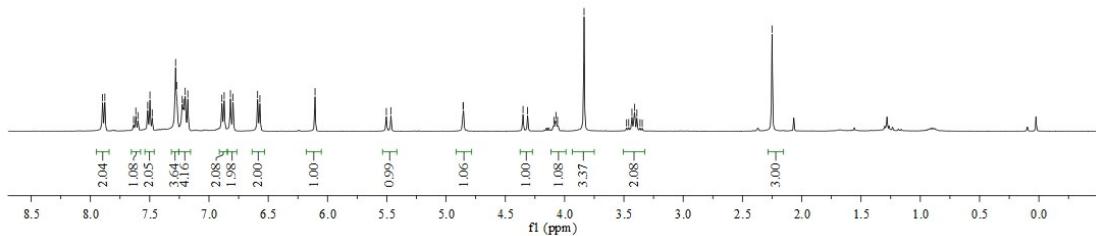
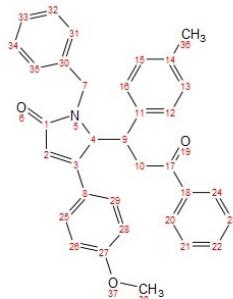
¹H NMR and ¹³C NMR spectra of 3h



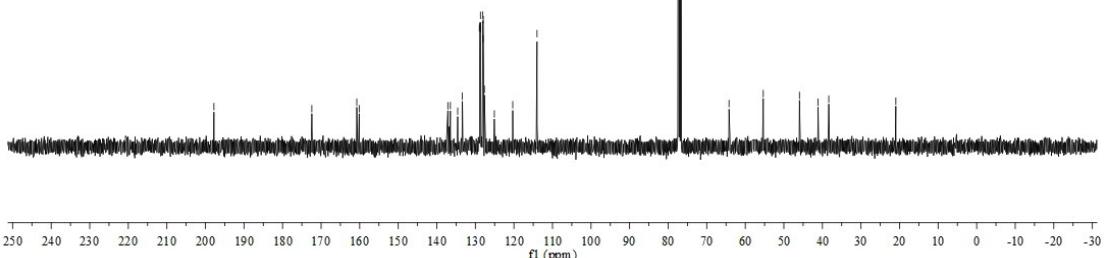
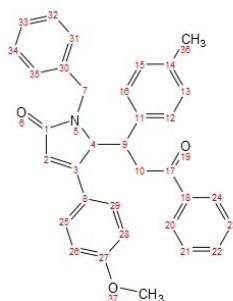
¹H NMR and ¹³C NMR spectra of 3i

| | | | |
|----------------------|----------------------|----------------------|----------------------|
| $\tilde{A}^{\mu\nu}$ | $\tilde{A}^{\mu\nu}$ | $\tilde{A}^{\mu\nu}$ | $\tilde{A}^{\mu\nu}$ |
| \tilde{A}^{00} | \tilde{A}^{01} | \tilde{A}^{02} | \tilde{A}^{03} |
| \tilde{A}^{10} | \tilde{A}^{11} | \tilde{A}^{12} | \tilde{A}^{13} |
| \tilde{A}^{20} | \tilde{A}^{21} | \tilde{A}^{22} | \tilde{A}^{23} |
| \tilde{A}^{30} | \tilde{A}^{31} | \tilde{A}^{32} | \tilde{A}^{33} |
| \tilde{A}^{00} | \tilde{A}^{01} | \tilde{A}^{02} | \tilde{A}^{03} |
| \tilde{A}^{10} | \tilde{A}^{11} | \tilde{A}^{12} | \tilde{A}^{13} |
| \tilde{A}^{20} | \tilde{A}^{21} | \tilde{A}^{22} | \tilde{A}^{23} |
| \tilde{A}^{30} | \tilde{A}^{31} | \tilde{A}^{32} | \tilde{A}^{33} |

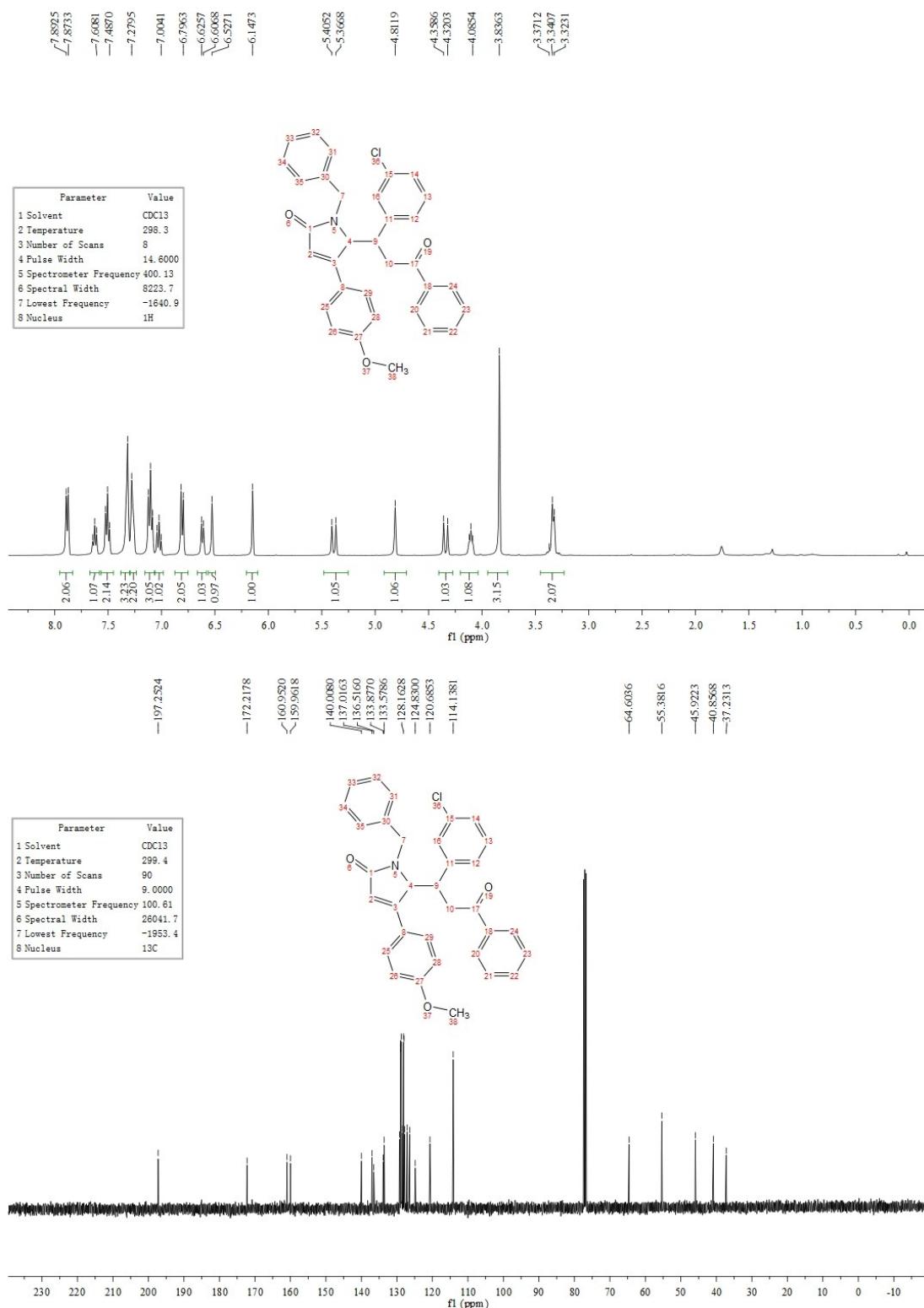
| Parameter | Value |
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| 3 Number of Scans | 8 |
| 4 Pulse Width | 13.0000 |
| 5 Spectrometer Frequency | 400.15 |
| 6 Spectral Width | 8223.7 |
| 7 Lowest Frequency | -1640.8 |
| 8 Nucleus | 1H |



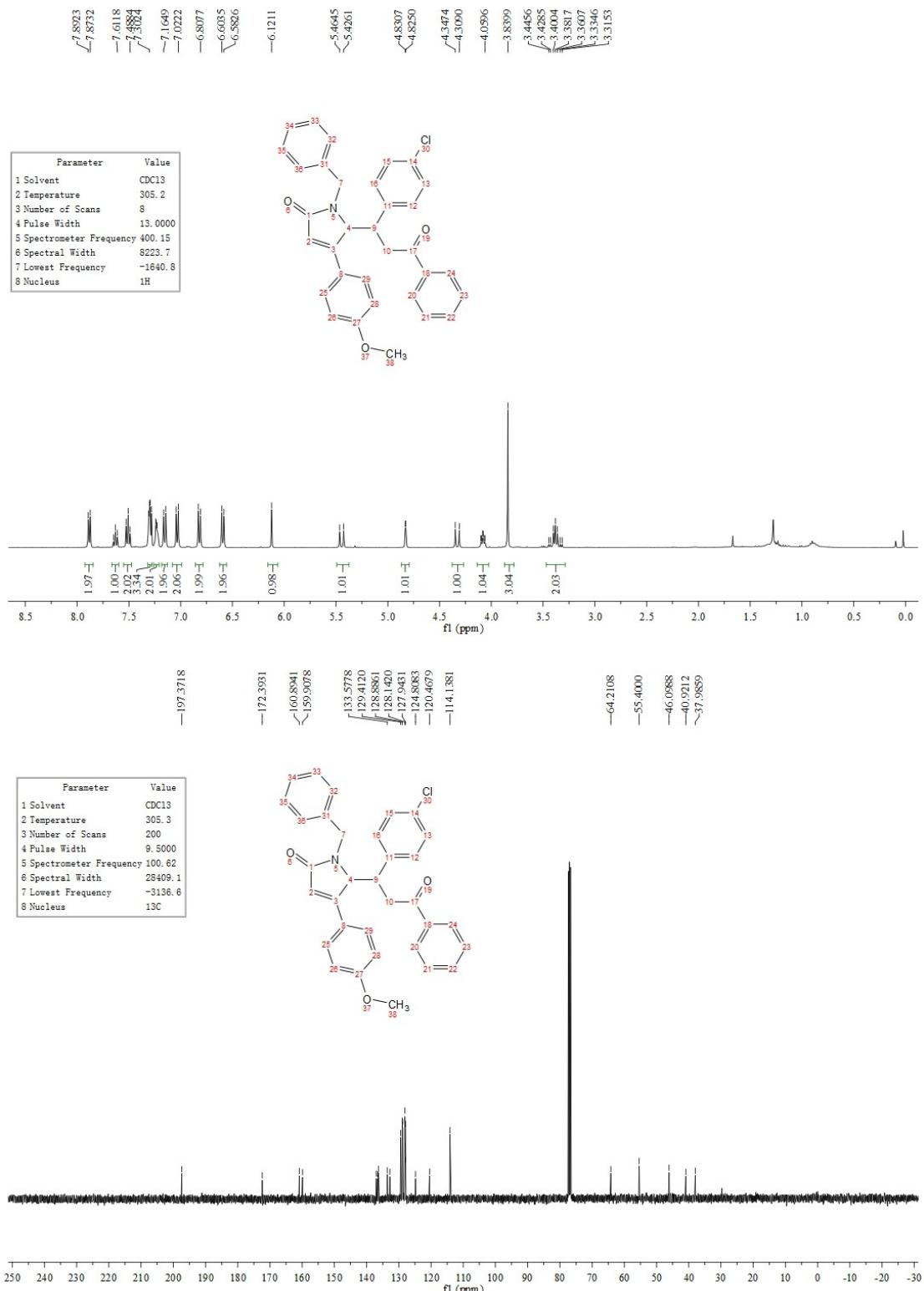
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| 2 Temperature | 307.6 |
| 3 Number of Scans | 200 |
| 4 Pulse Width | 9.5000 |
| 5 Spectrometer Frequency | 100.62 |
| 6 Spectral Width | 28409.1 |
| 7 Lowest Frequency | -3136.6 |
| 8 Nucleus | 13C |



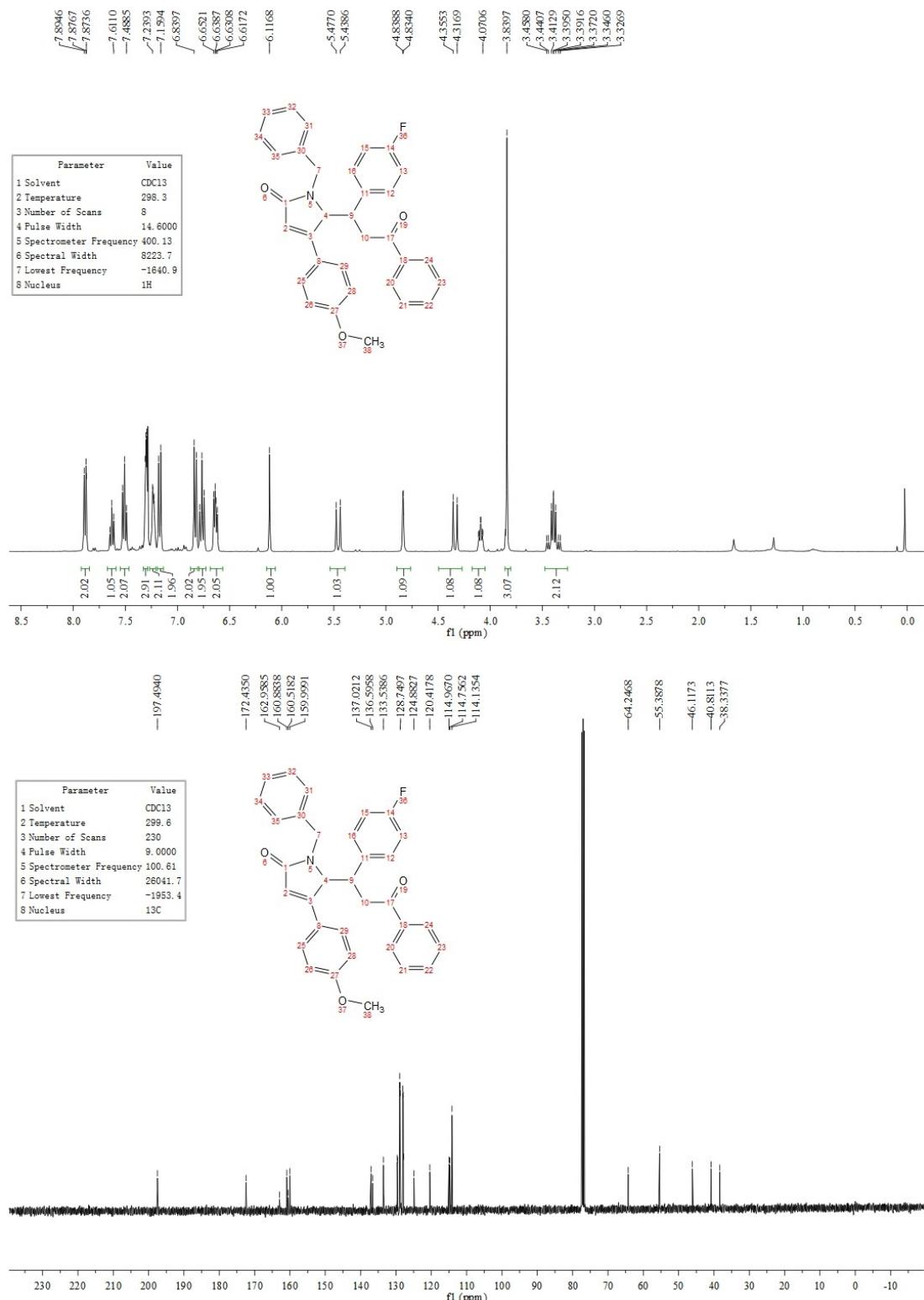
¹H NMR and ¹³C NMR spectra of 3j



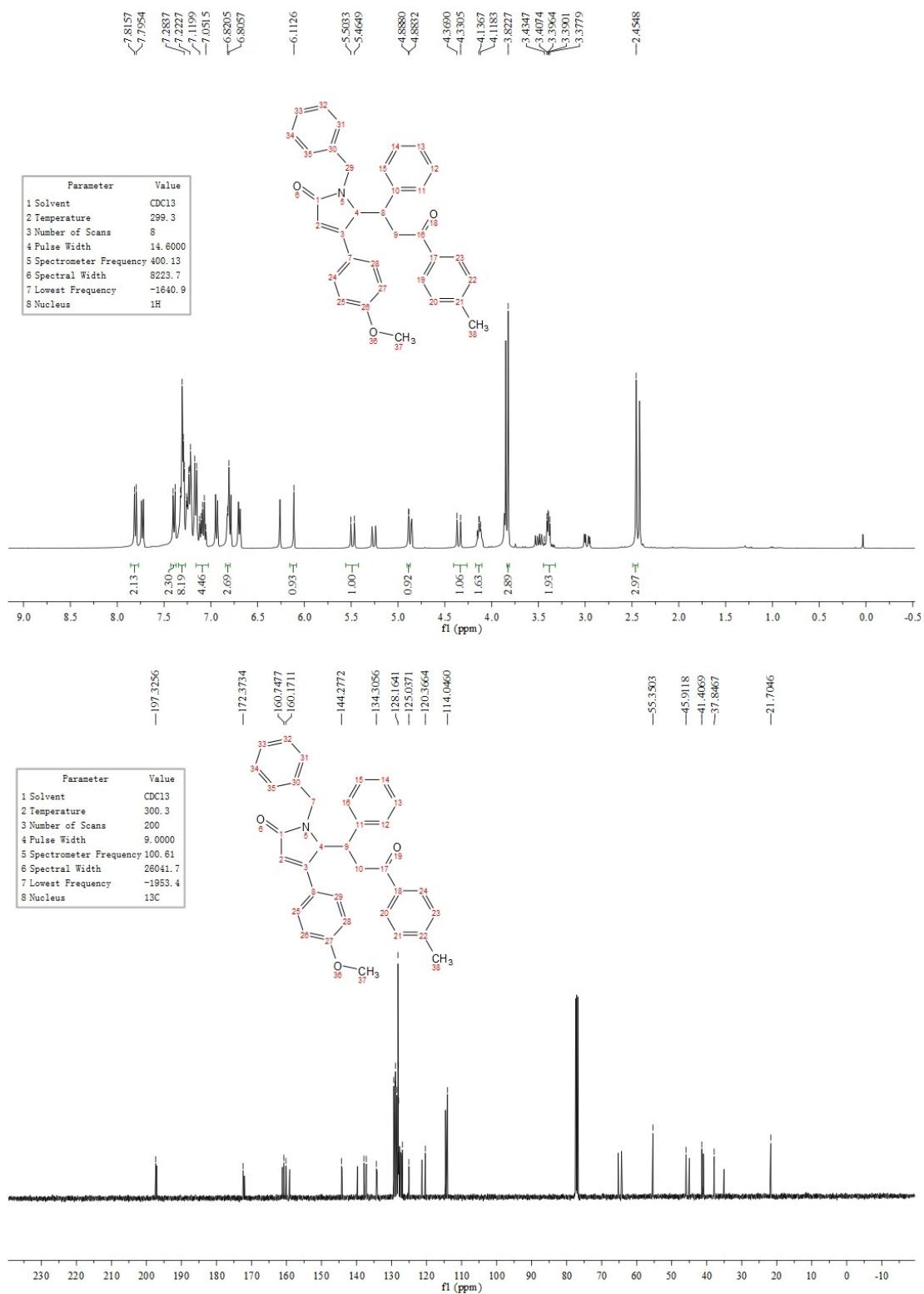
¹H NMR and ¹³C NMR spectra of 3k



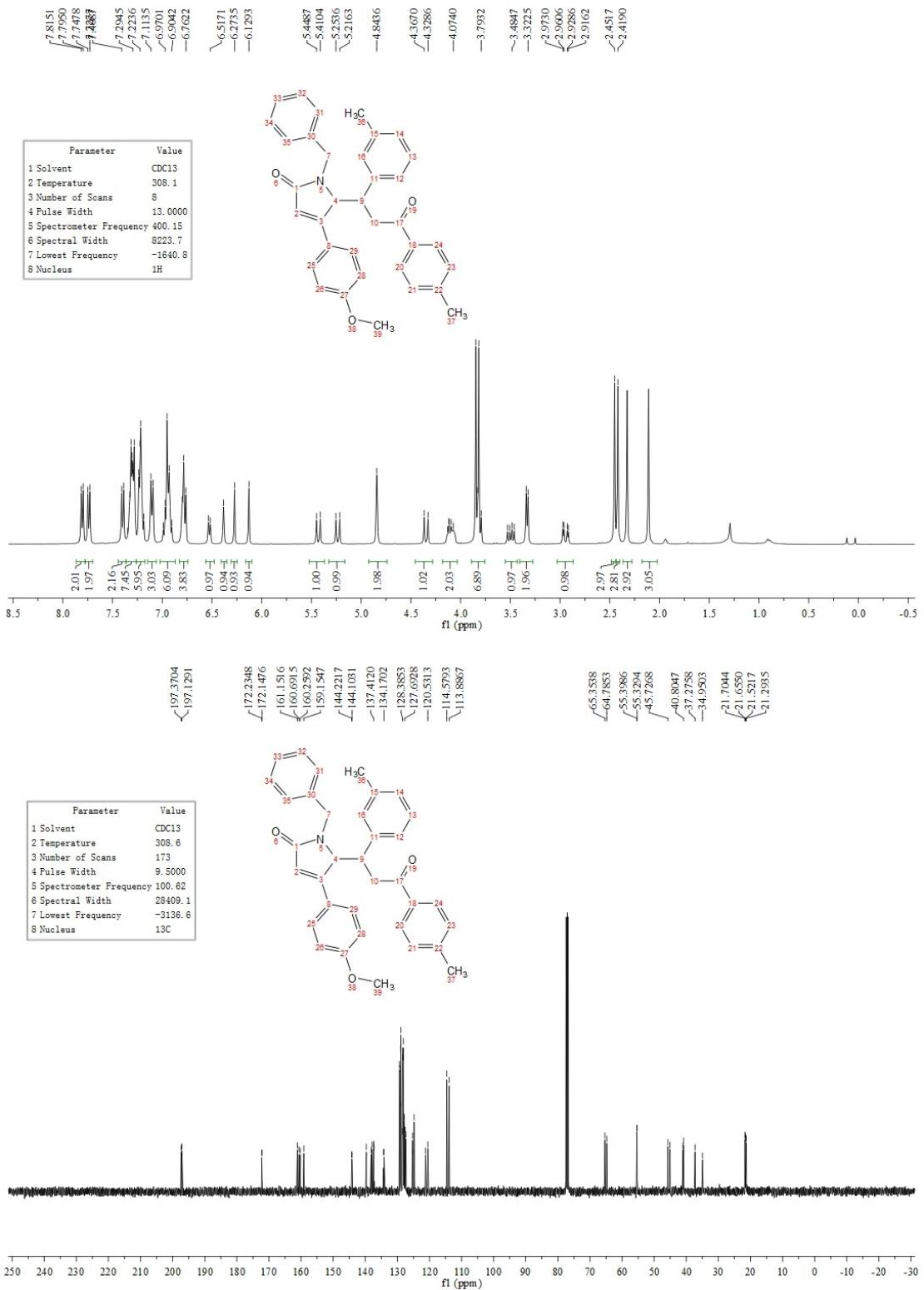
¹H NMR and ¹³C NMR spectra of 3l



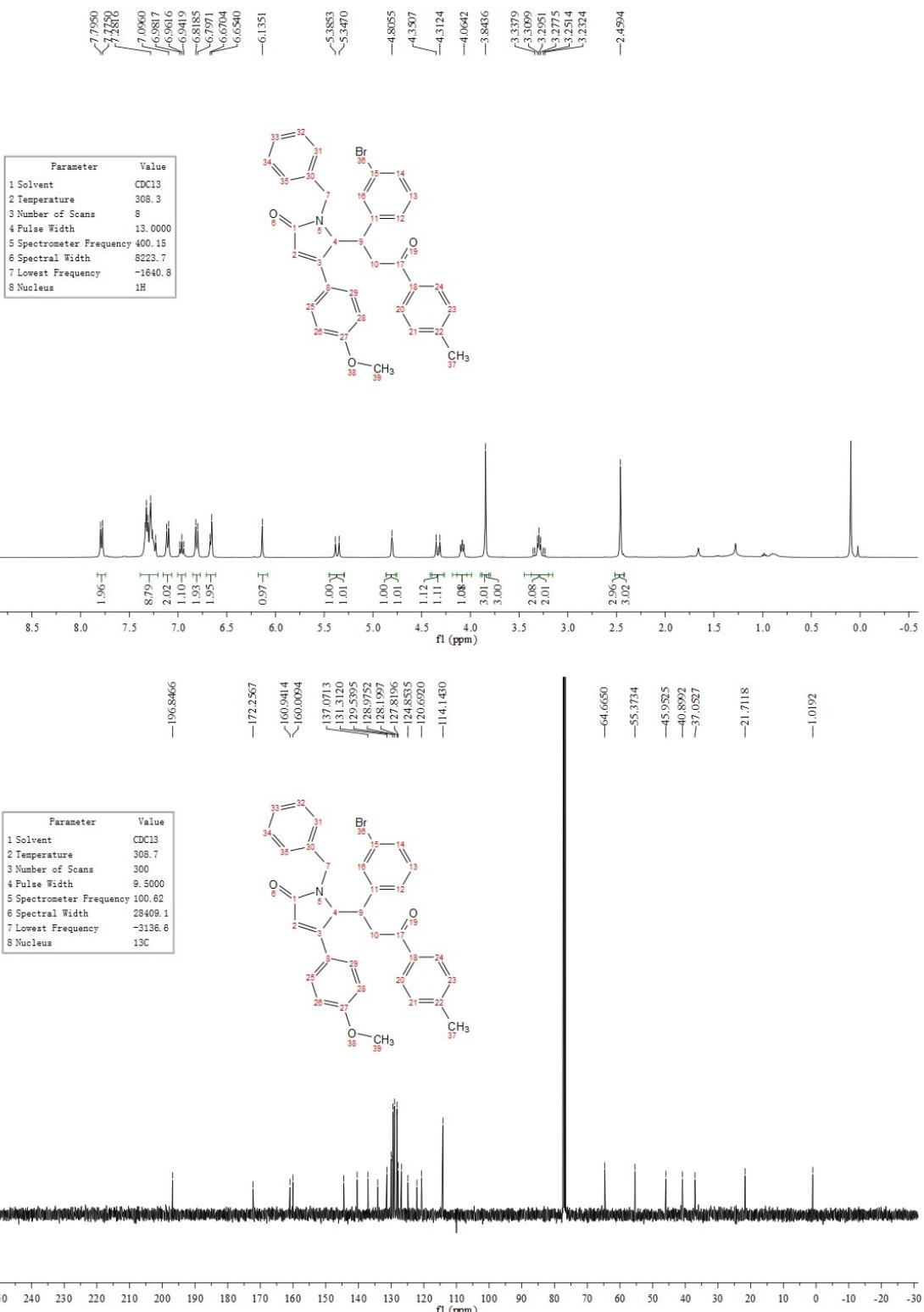
¹H NMR and ¹³C NMR spectra of 3m



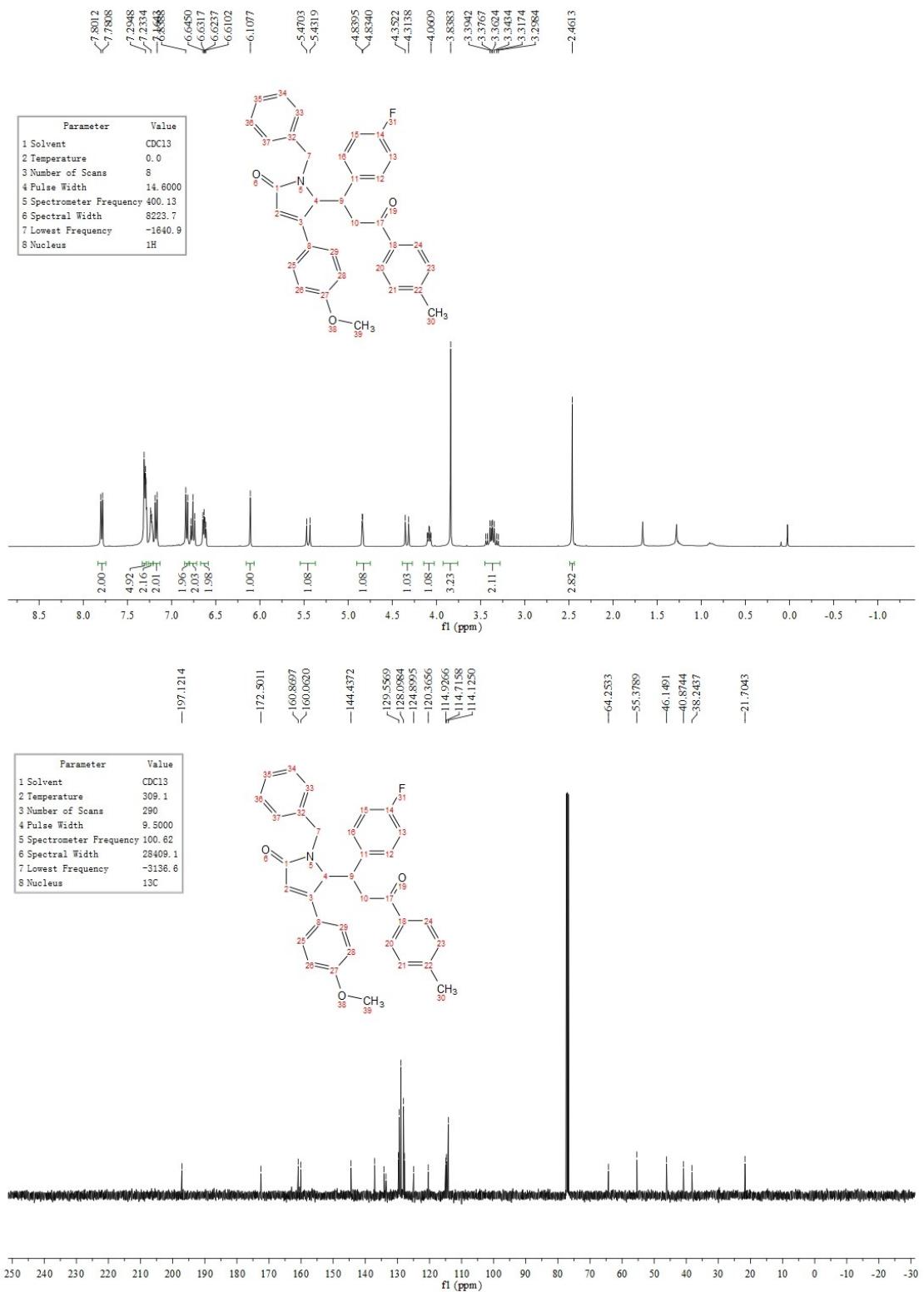
¹H NMR and ¹³C NMR spectra of 3n



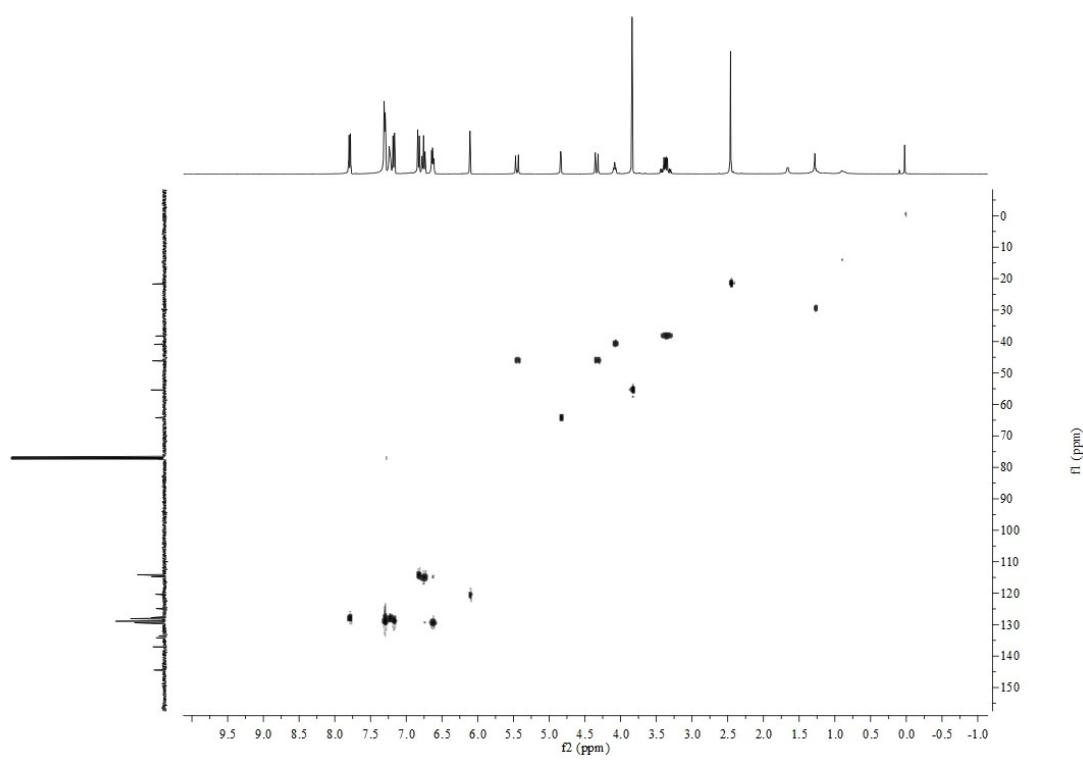
¹H NMR and ¹³C NMR spectra of 3o



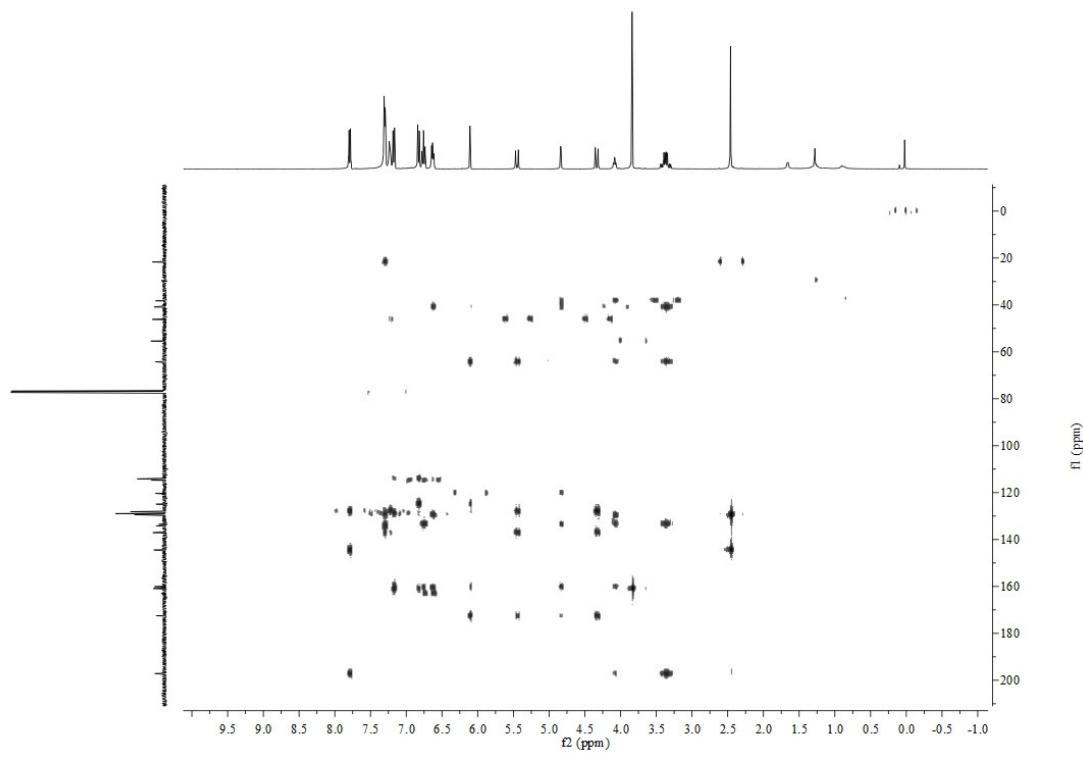
¹H NMR and ¹³C NMR spectra of 3p



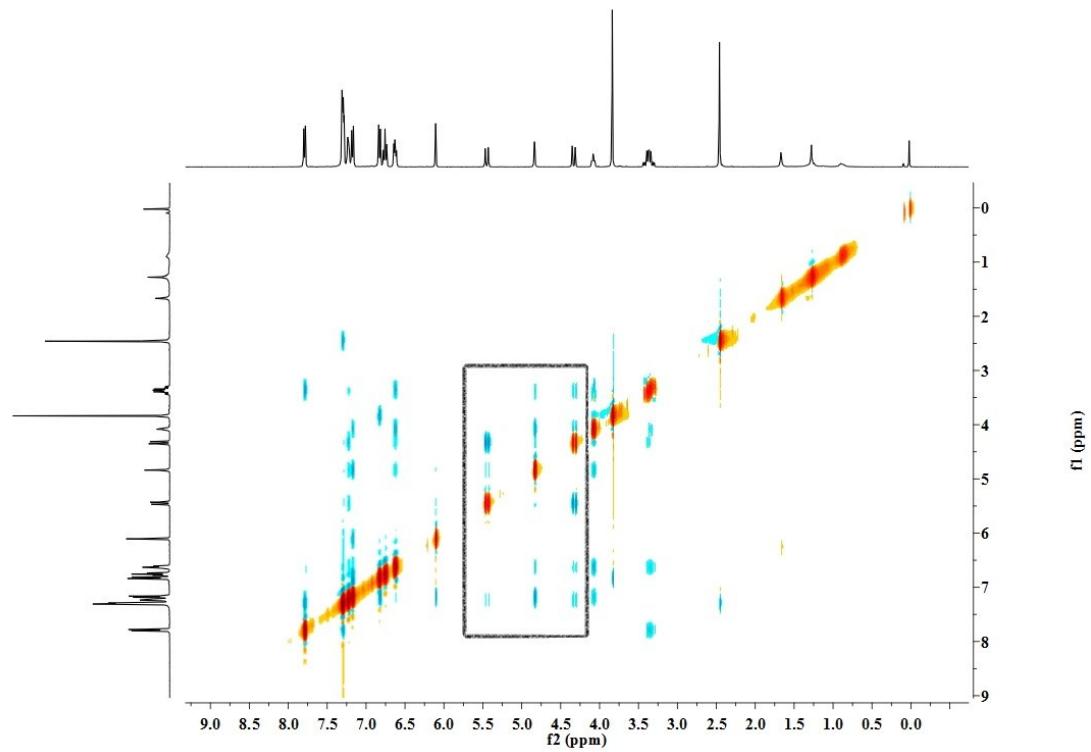
HSQC of 3p₁



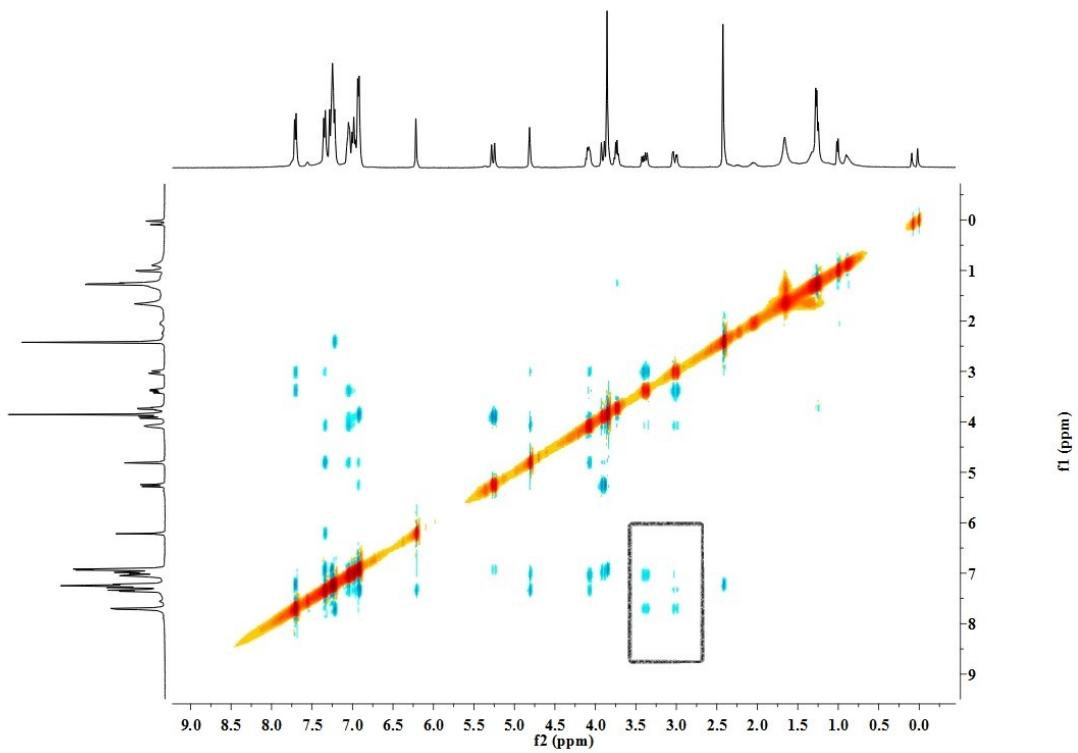
HMBC of 3p_1



NOE of 3p₁

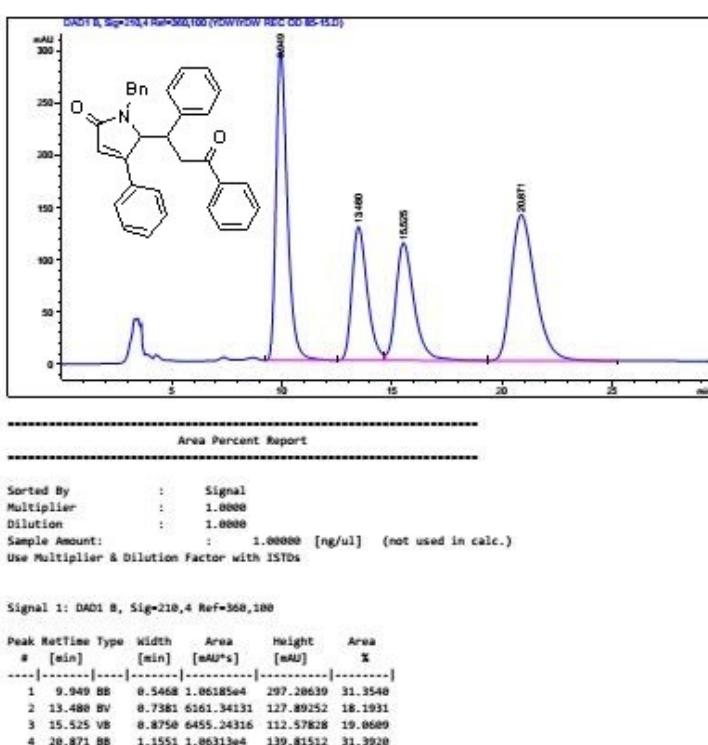


NOE of 4-3p₂

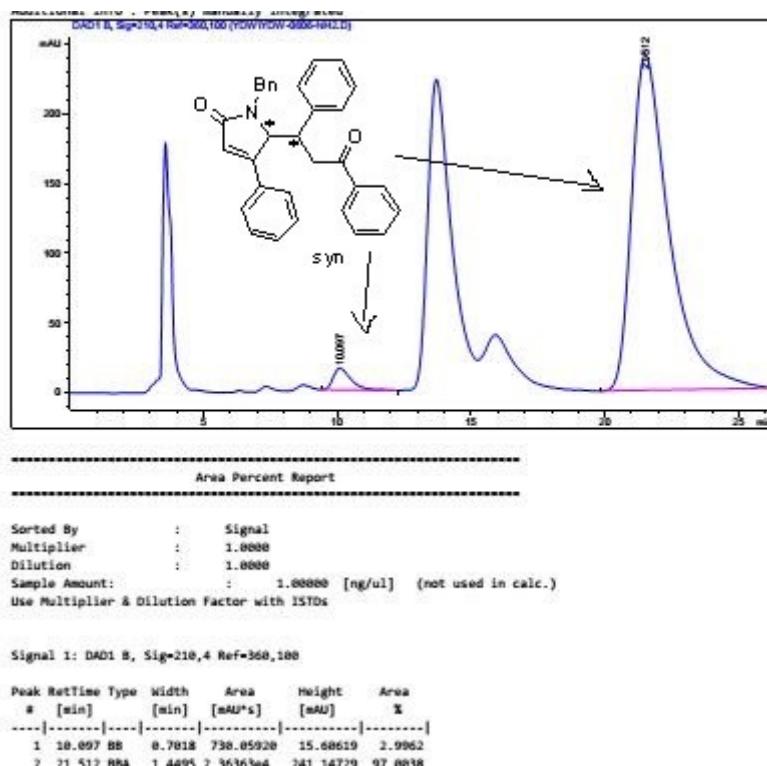


d HPLC Spectra

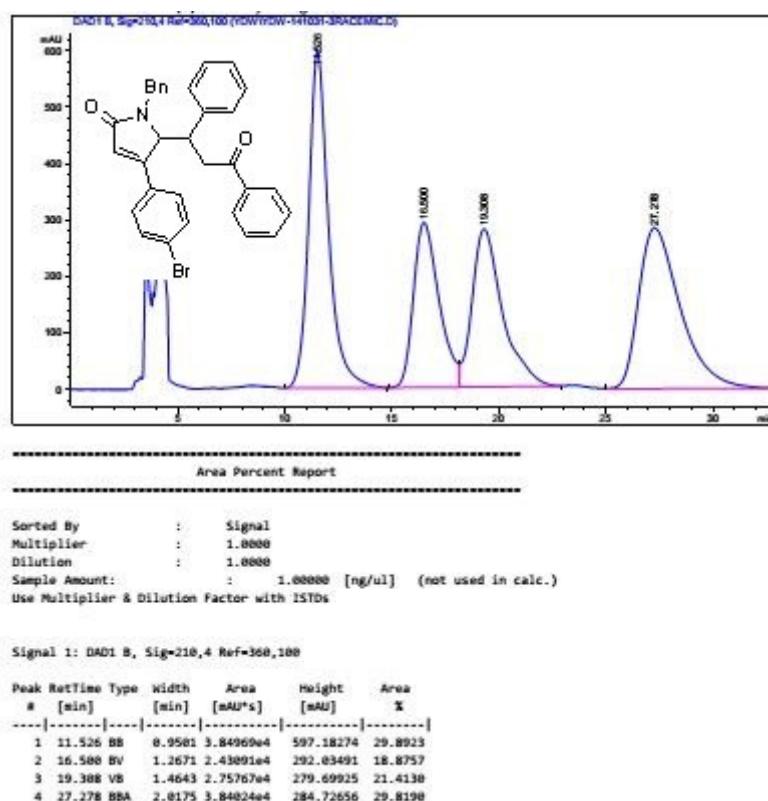
3a (racemate)



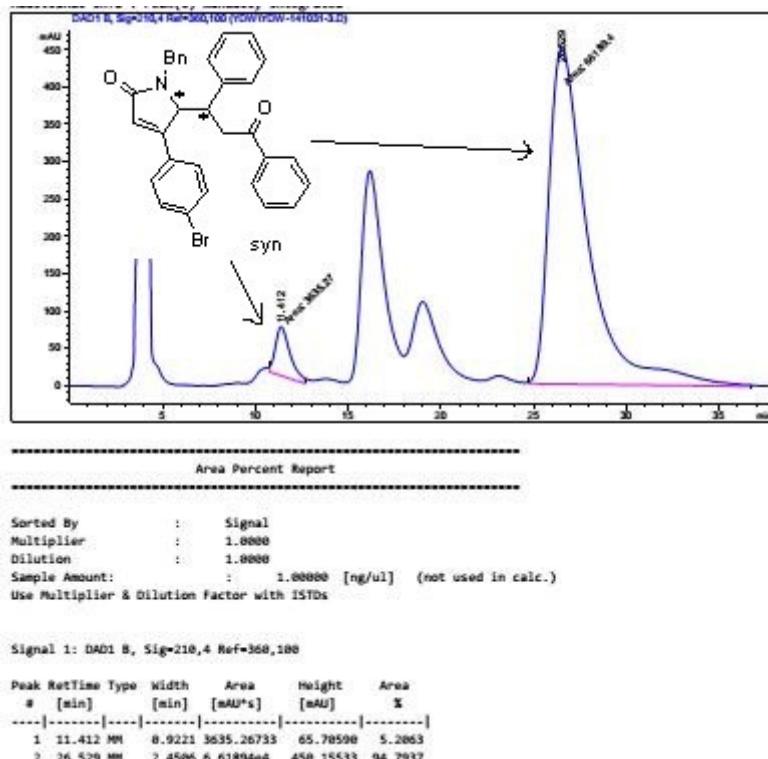
3a (chiral synthesis)



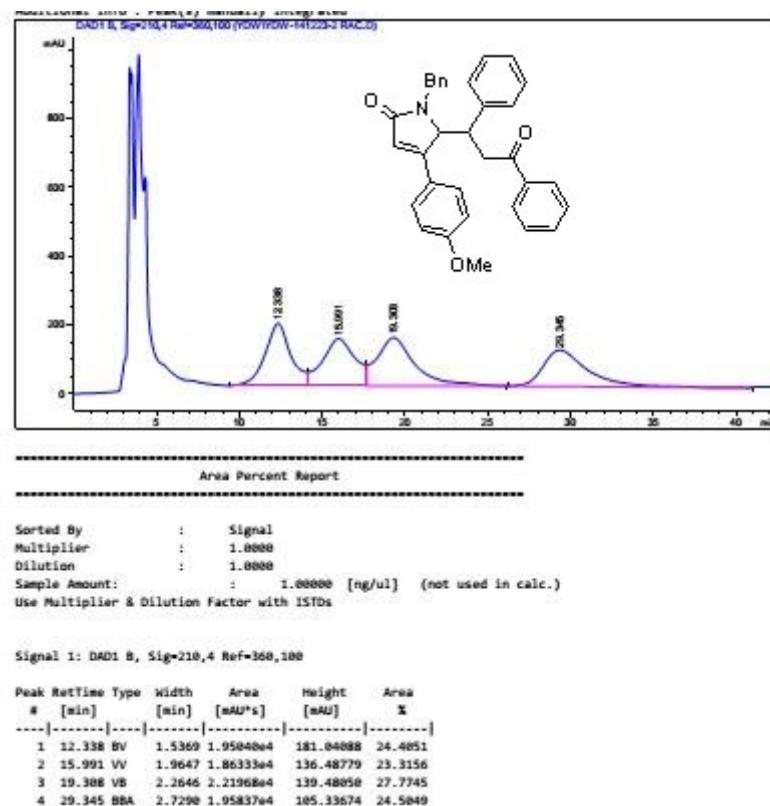
3b (racemate)



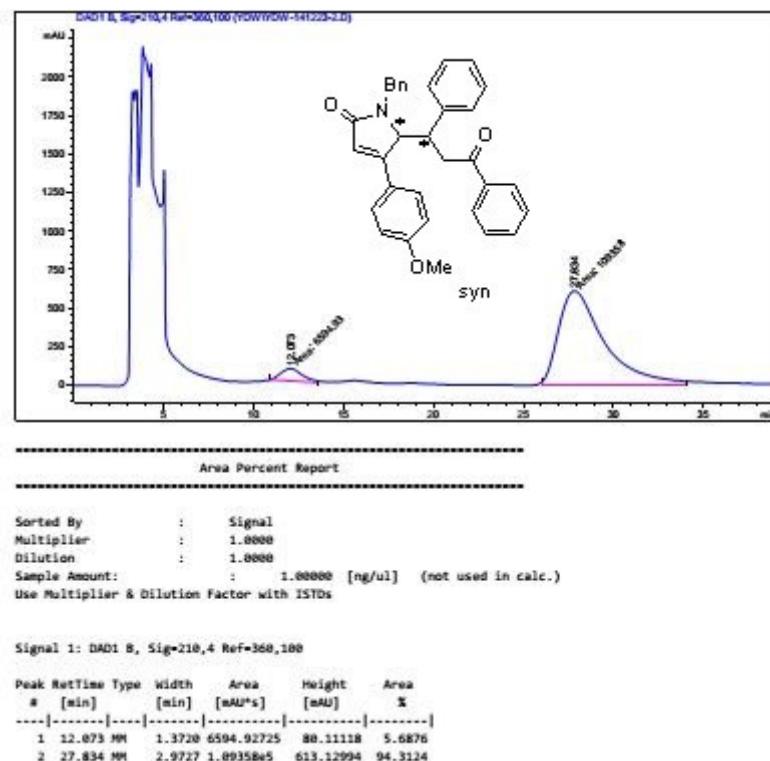
3b (chiral synthesis)



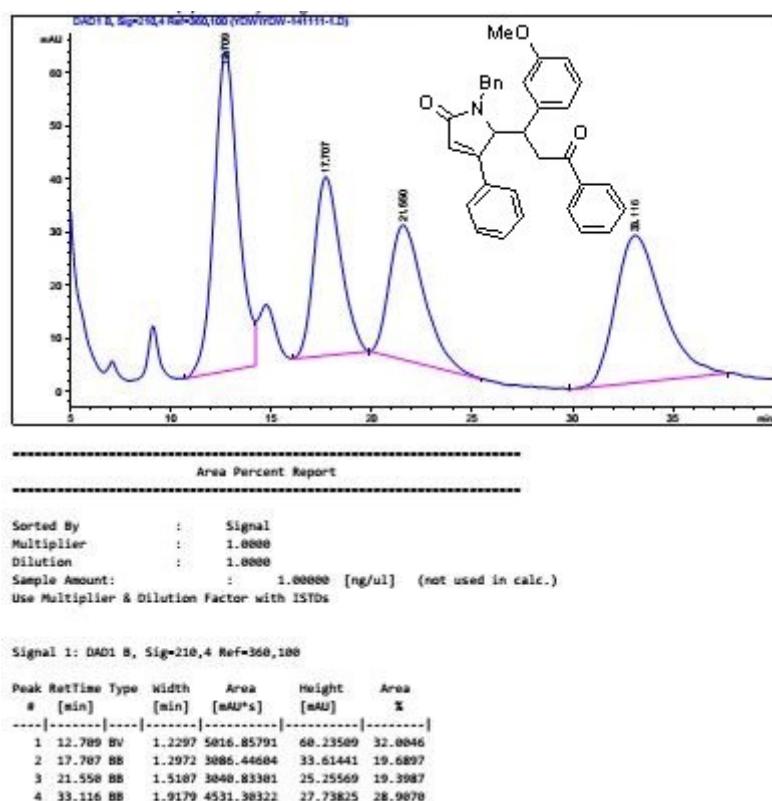
3c (racemate)



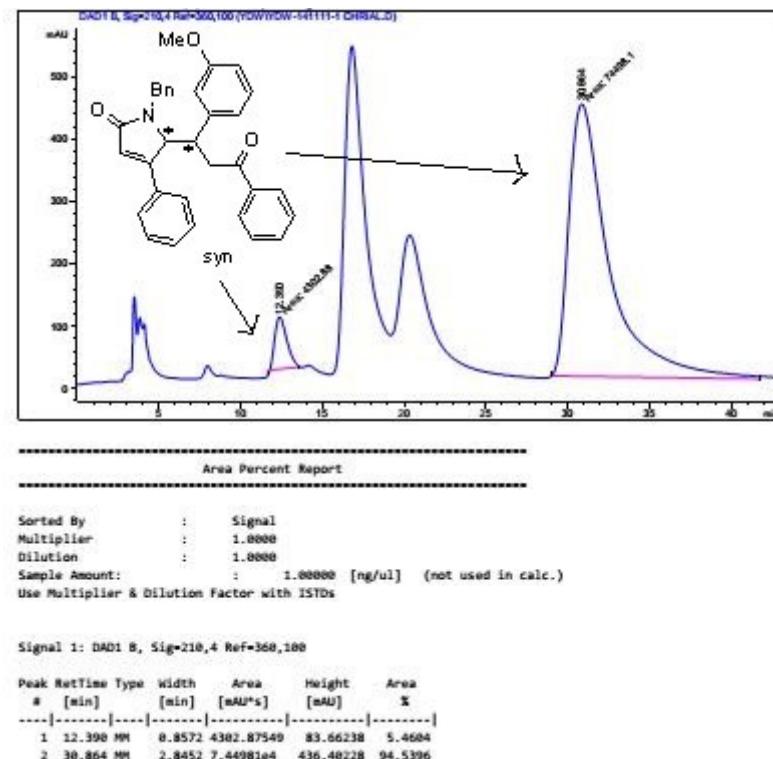
3c (chiral synthesis) (TLC)



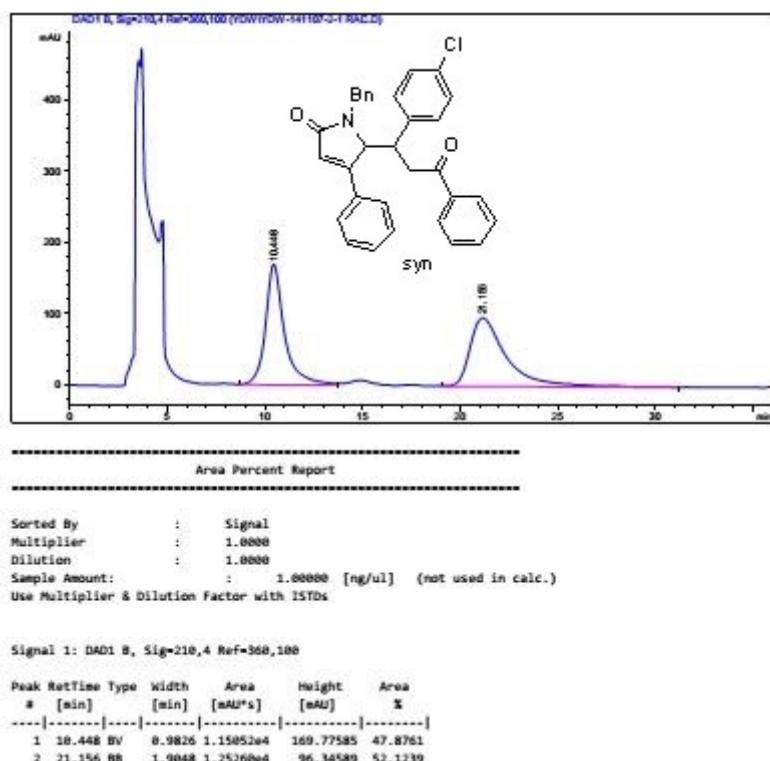
3d (racemate)



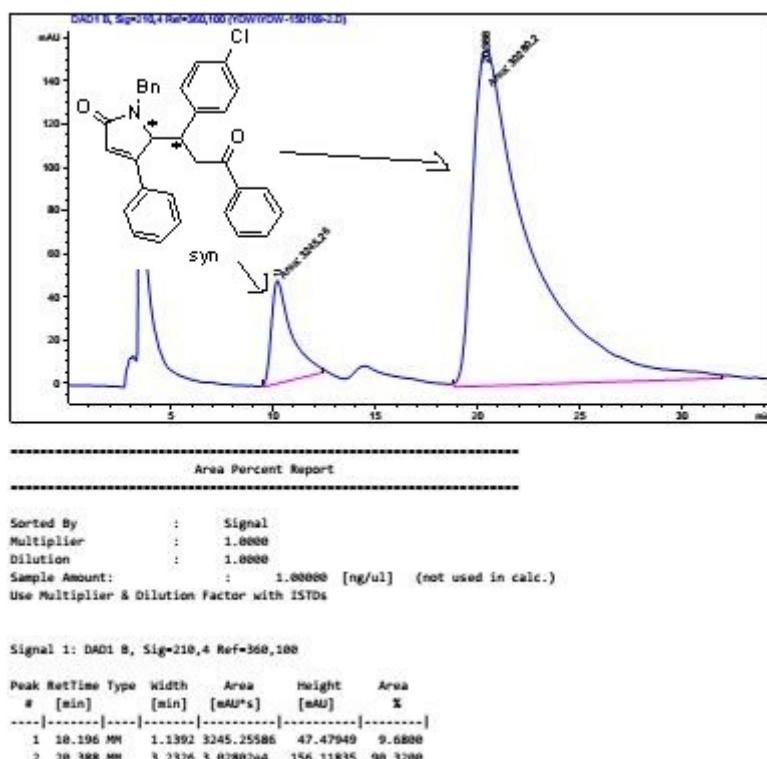
3d (chiral synthesis)



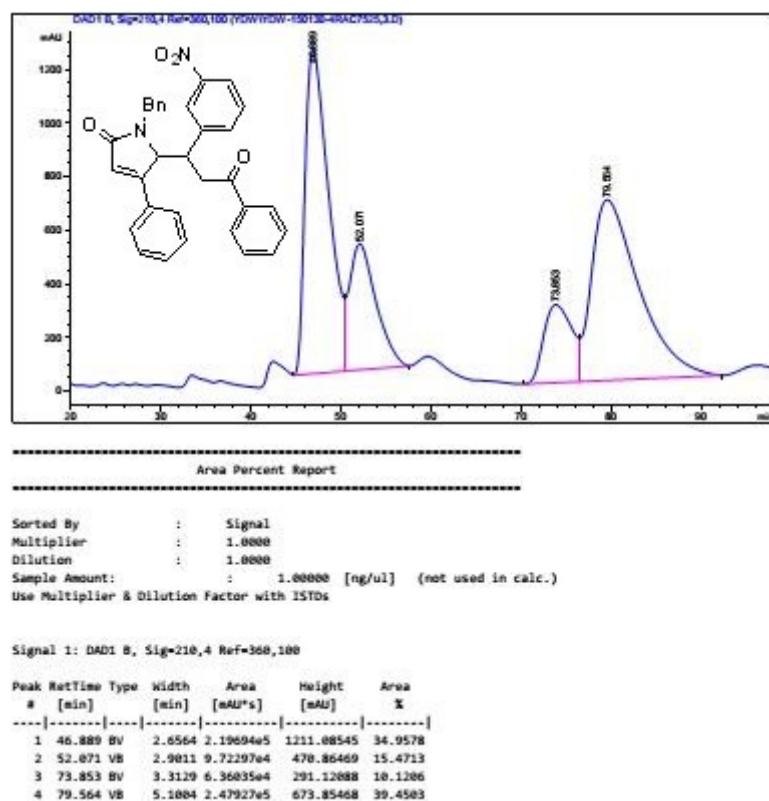
3e (racemate) (TLC)



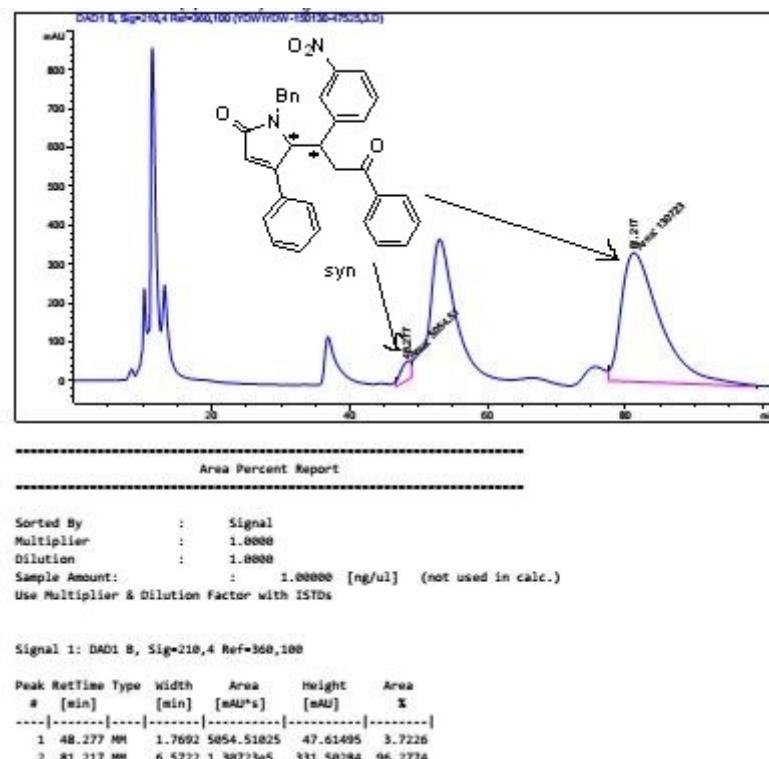
3e (chiral synthesis) (TLC)



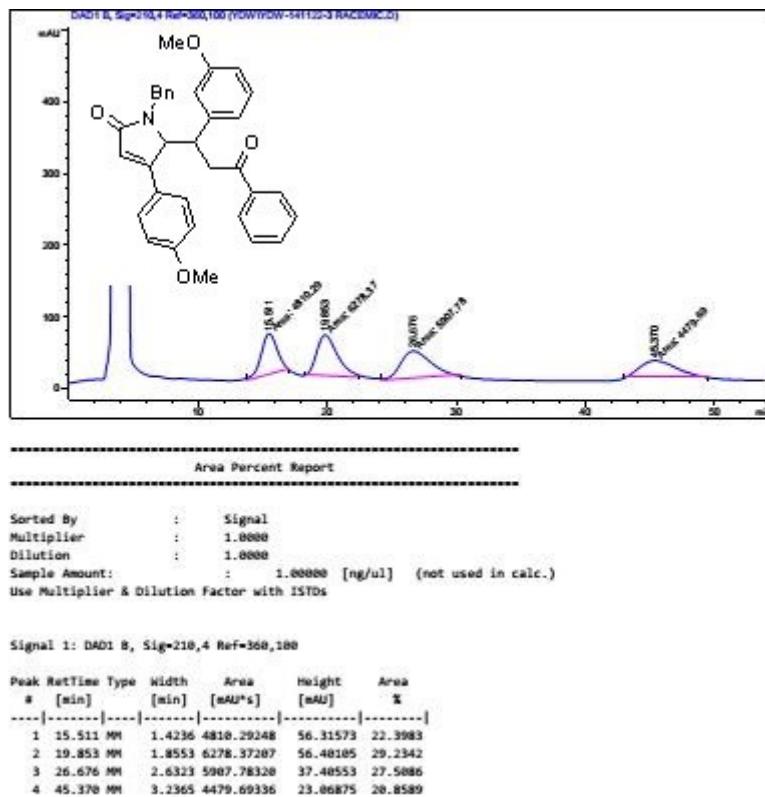
3f (racemate)



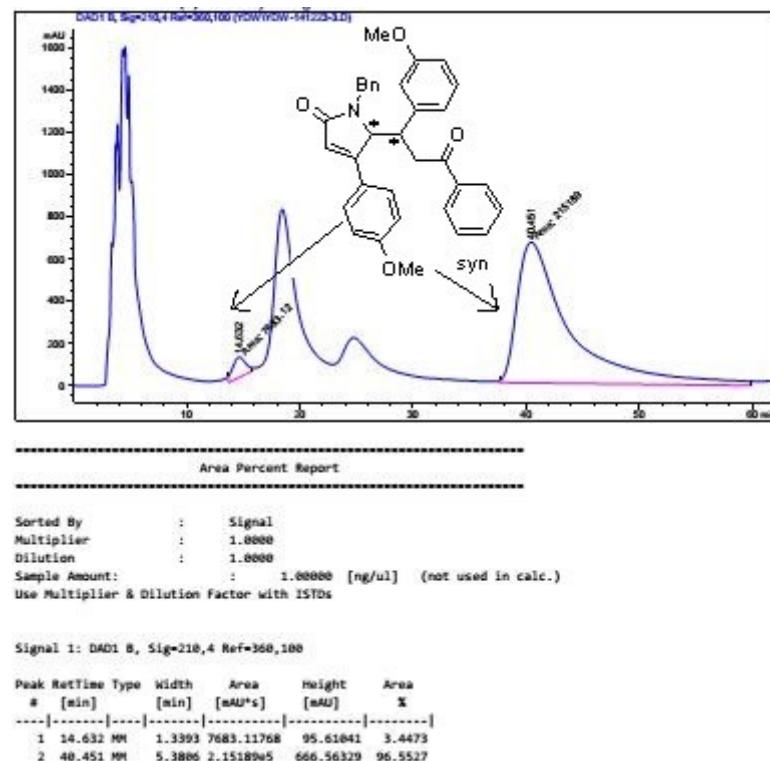
3f (chiral synthesis)



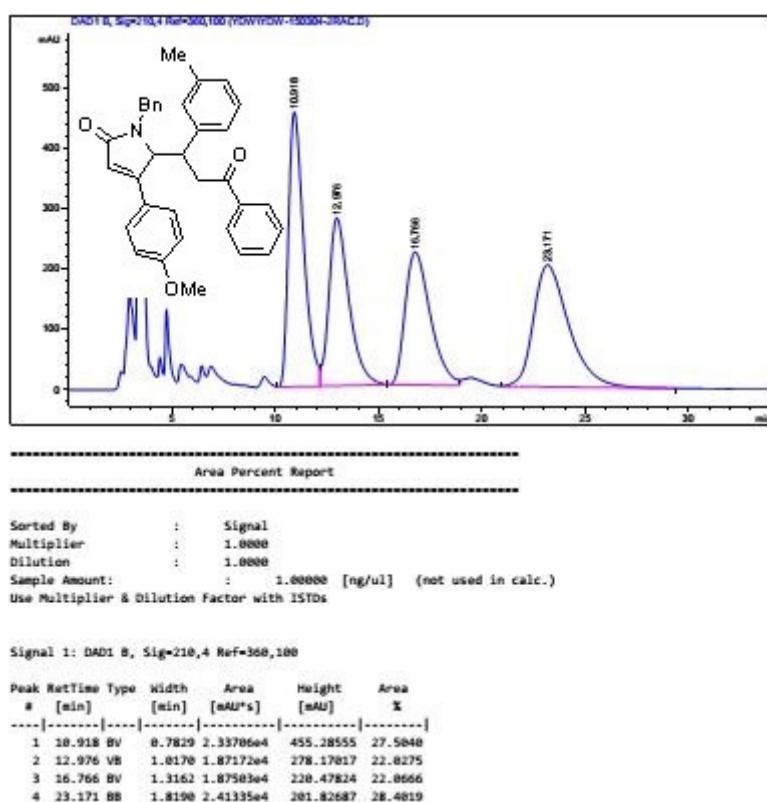
3g (racemate)



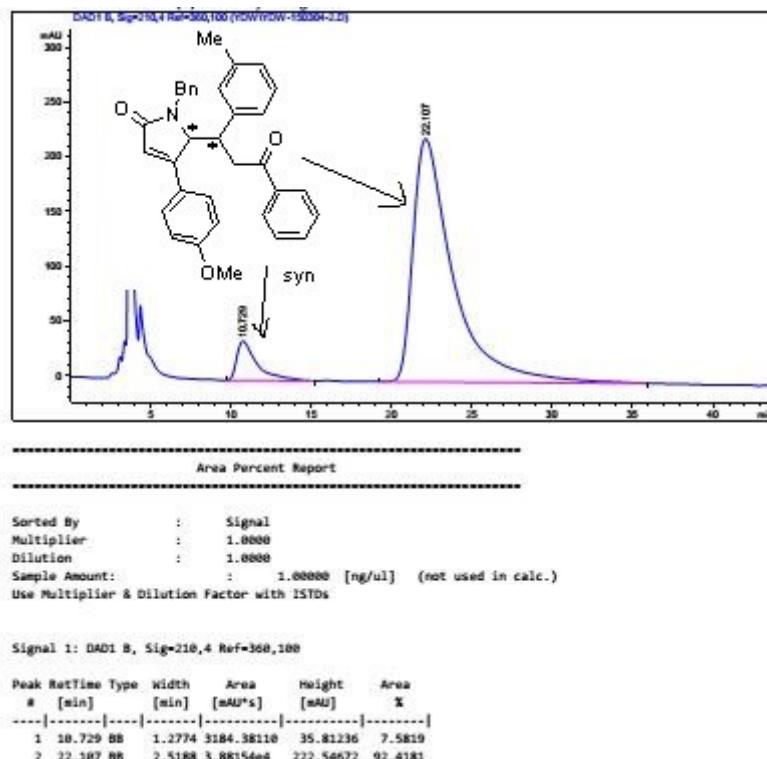
3g (chiral synthesis)



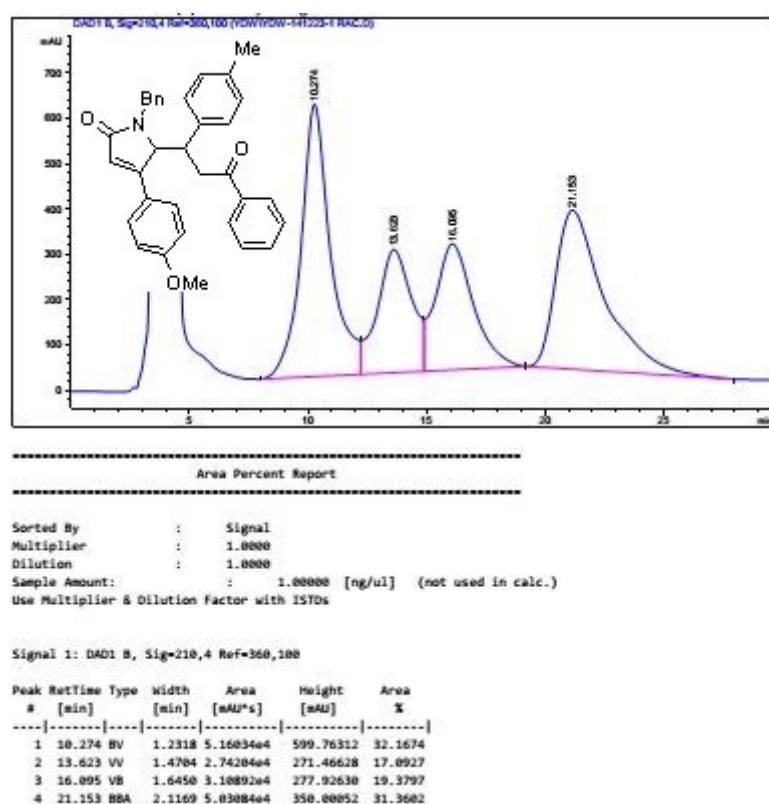
3h (racemate)



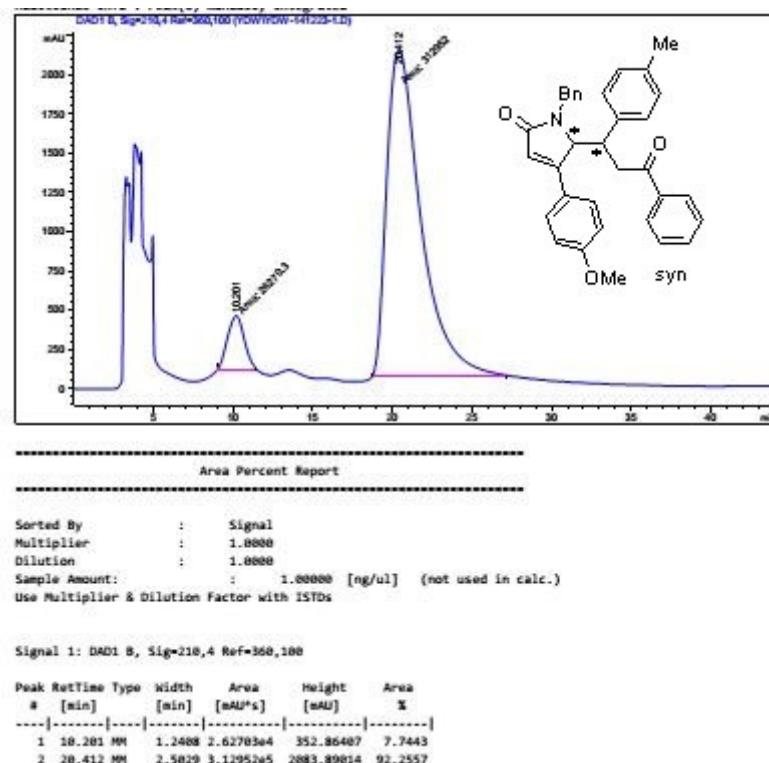
3h (chiral synthesis) (TLC)



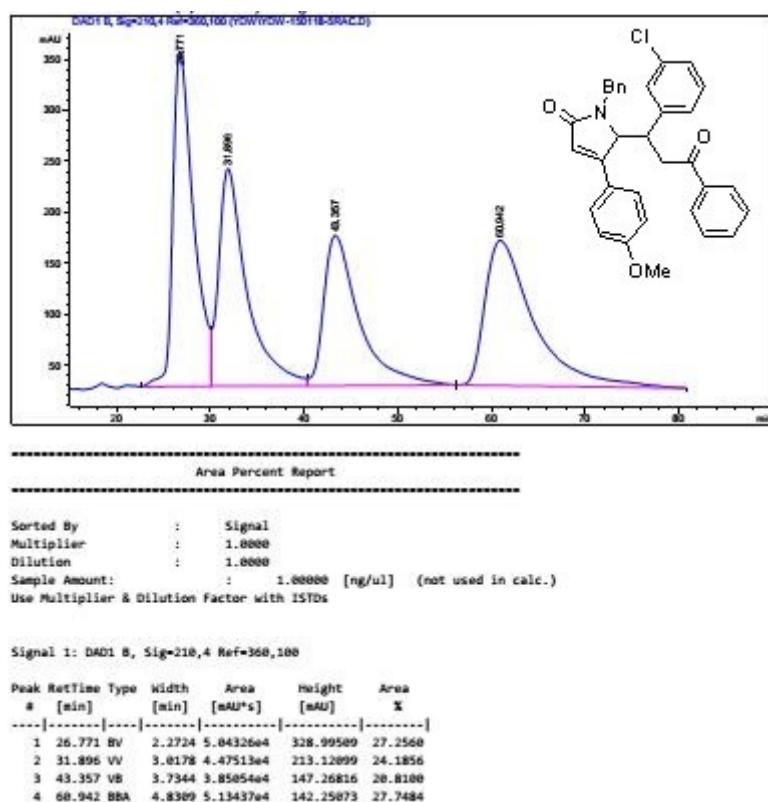
3i (racemate)



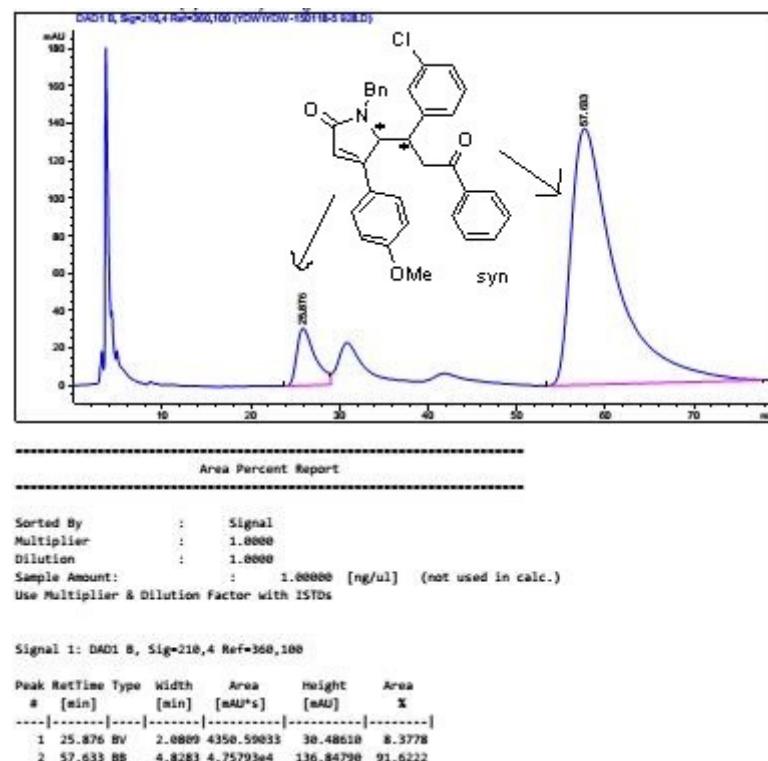
3i (chiral synthesis) (TLC)



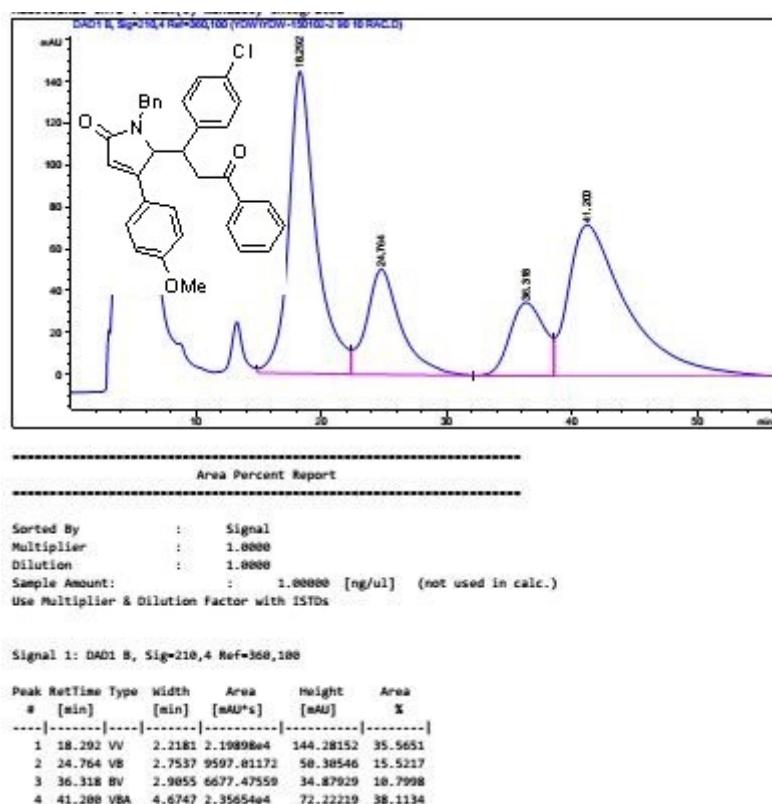
3j (racemate)



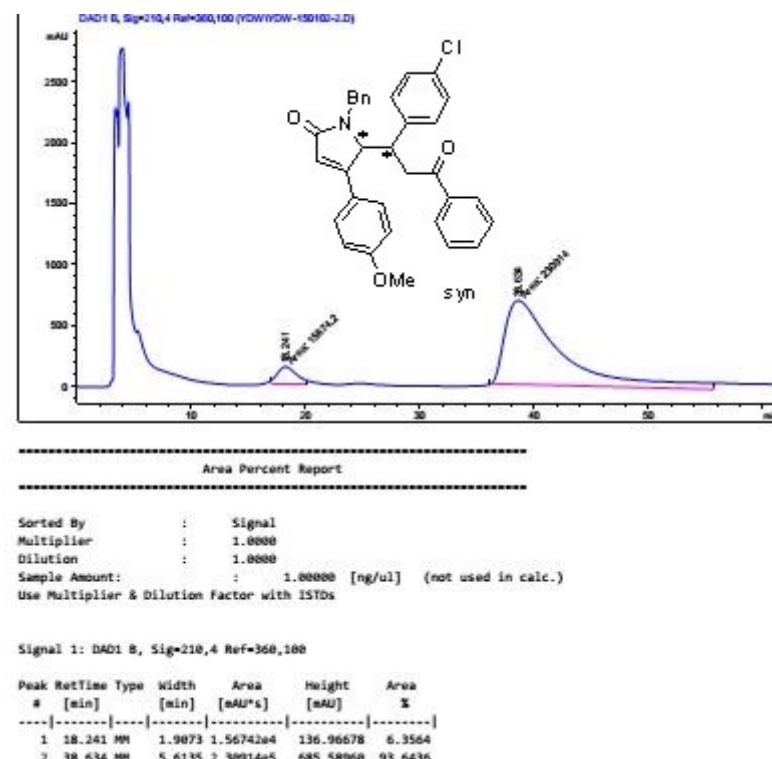
3j (chiral synthesis)



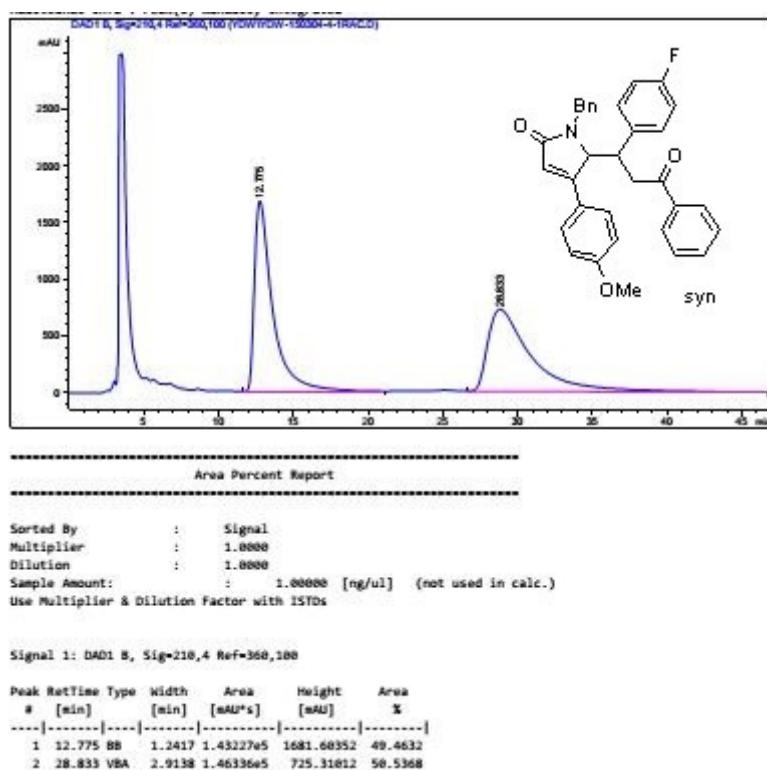
3k (racemate)



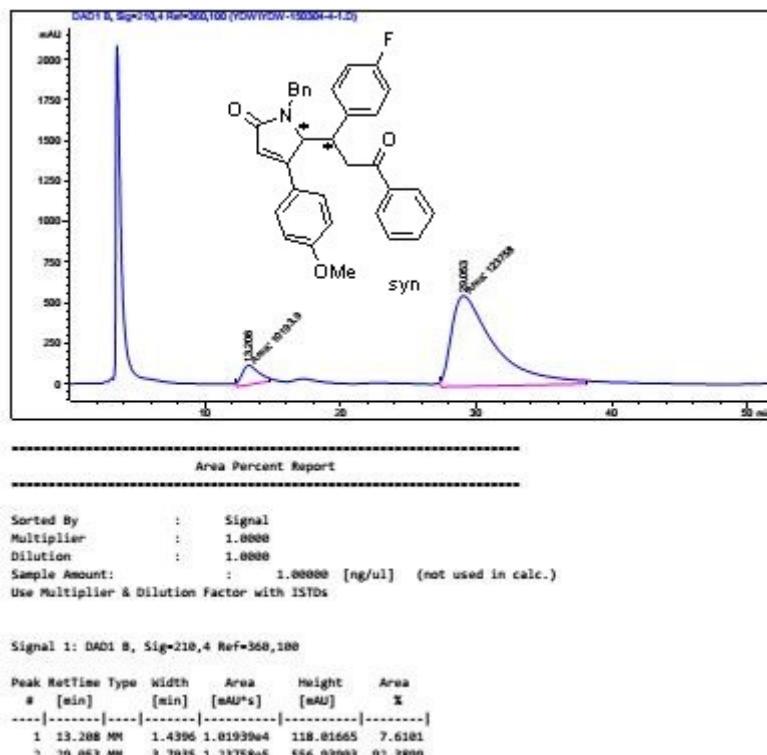
3k (chiral synthesis) (TLC)



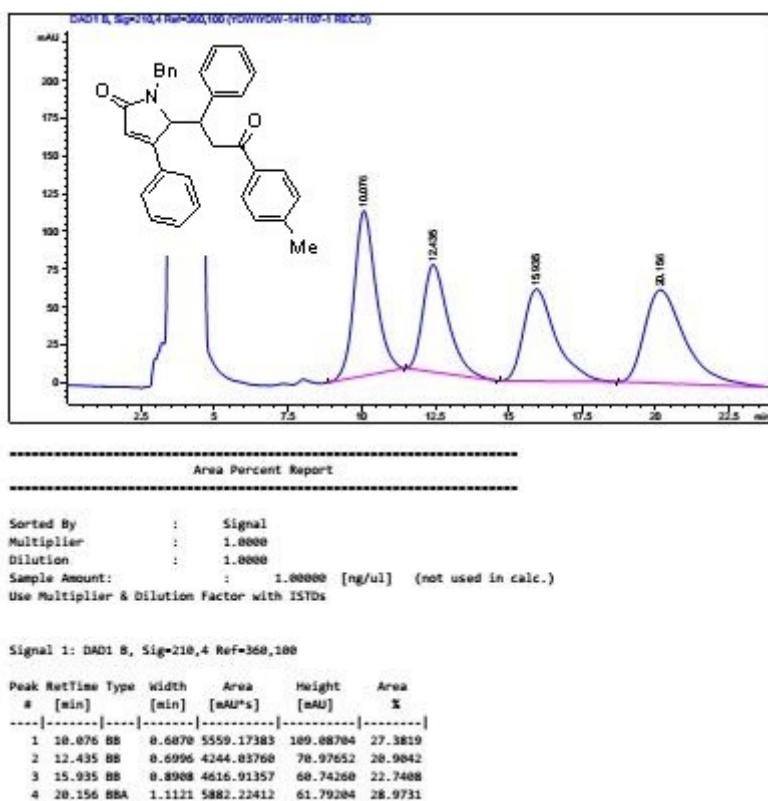
3l (racemate) (TLC)



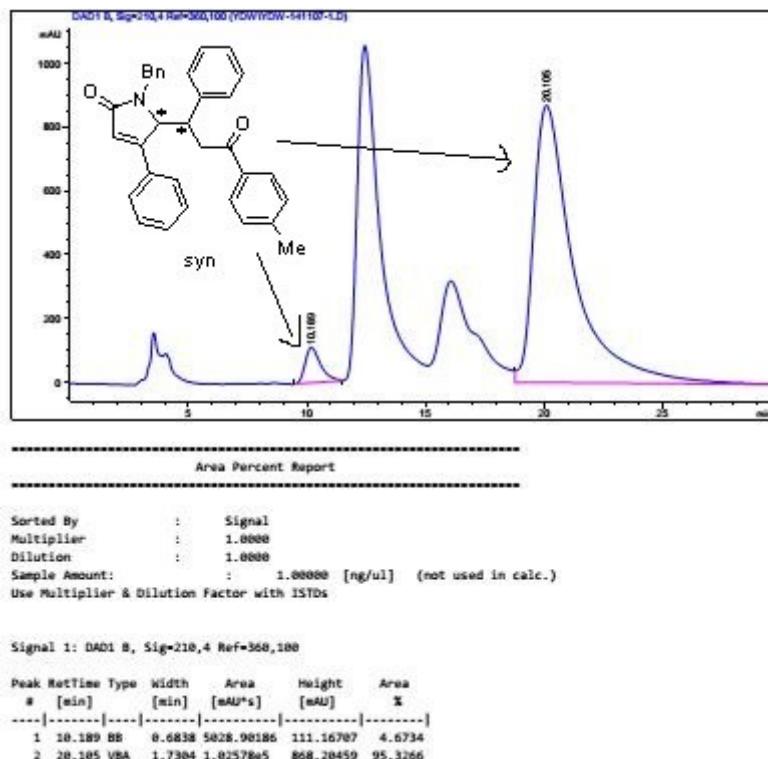
3l (chiral synthesis) (TLC)



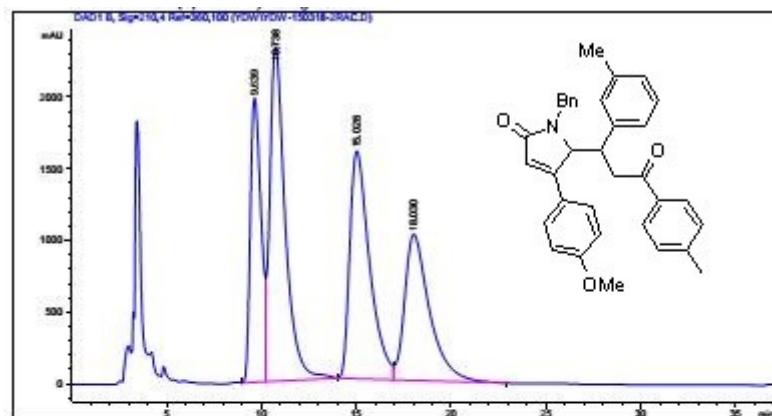
3m (racemate)



3m (chiral synthesis)



3n (racemate)



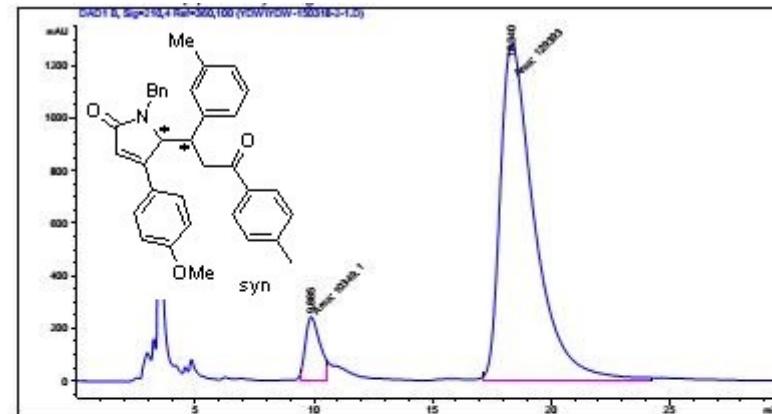
Area Percent Report

```
Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Sample Amount: : 1.00000 [ng/uL] (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs
```

Signal 1: DAD1 B, Sig=210,4 Ref=360,100

| Peak # | RetTime | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------|------|-------------|--------------|--------------|---------|
| 1 | 9.639 | BV | 0.6825 | 7.78954e4 | 1979.83748 | 18.6821 |
| 2 | 10.738 | VB | 0.8487 | 1.31915e5 | 2329.24689 | 31.5398 |
| 3 | 15.028 | BV | 1.0923 | 1.15353e5 | 1586.44918 | 27.5792 |
| 4 | 18.038 | VB | 1.3516 | 9.31871e4 | 1818.35791 | 22.2797 |

3n (chiral synthesis) (TLC)



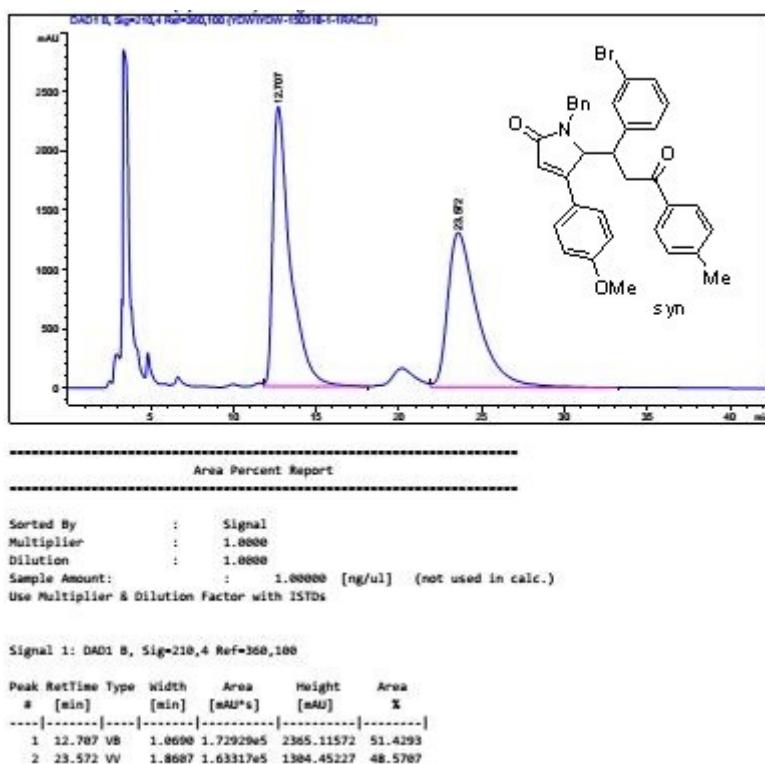
Area Percent Report

```
Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Sample Amount: : 1.00000 [ng/uL] (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs
```

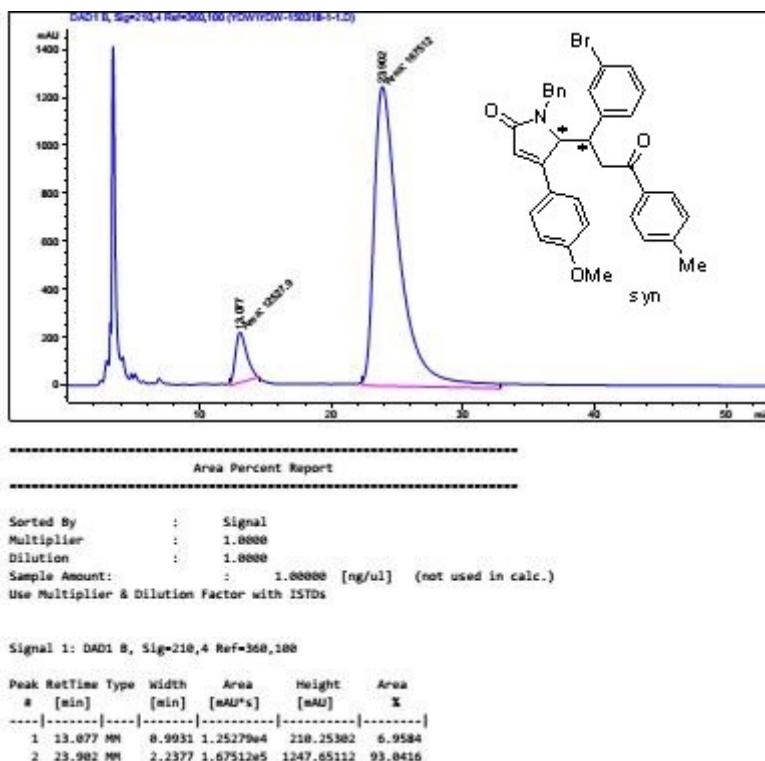
Signal 1: DAD1 B, Sig=210,4 Ref=360,100

| Peak # | RetTime | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------|------|-------------|--------------|--------------|---------|
| 1 | 9.885 | MM | 0.7097 | 1.03491e4 | 243.03778 | 7.4058 |
| 2 | 18.348 | MM | 1.6763 | 1.29393e5 | 1286.47488 | 92.5942 |

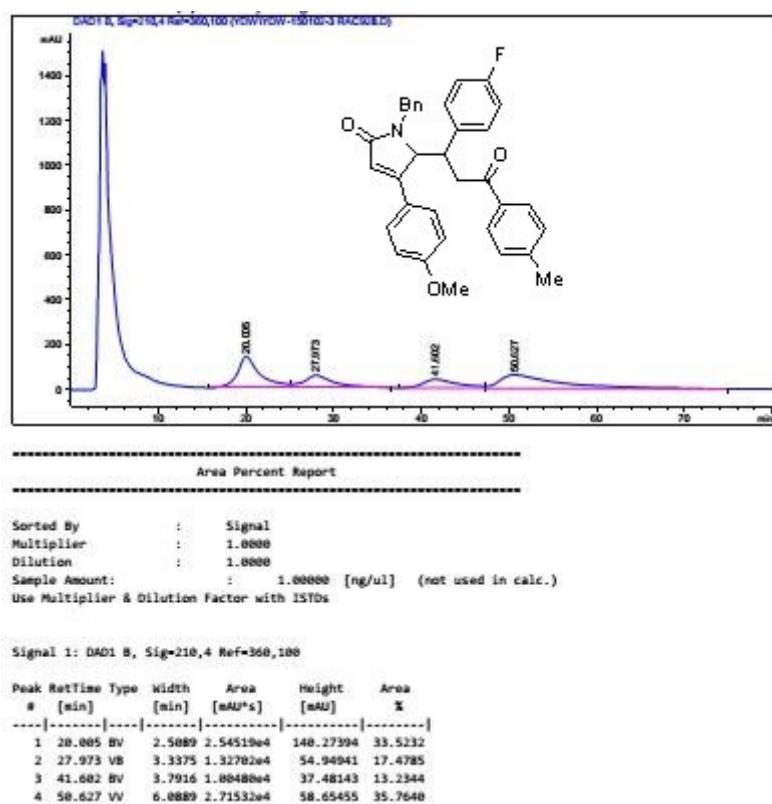
4-3o (racemate) (TLC)



4-3o (chiral synthesis) (TLC)



3p (racemate)



3p (chiral synthesis) (TLC)

