

Supporting Information

Direct Enantioselective Vinylogous Aldol/Cyclization Cascade Reaction of Allyl Pyrazoleamides with Isatins: Asymmetric Construction of Spirocyclic Oxindole– Dihydropyranones

Tian-Ze Li, Yu Jiang, Yu-Qing Guan, Feng Sha*, and Xin-Yan Wu*

*Key Laboratory for Advanced Materials and Institute of Fine Chemicals, East China
University of Science and Technology, 130 Meilong Road, Shanghai 200237, P. R. China*

xinyanwu@ecust.edu.cn

Table of Contents

1. General Information.....	S2
2. General Procedure for the Cascade Reaction and Characterization of the Products	S2
3. Control Reaction of α,β -Unsaturated Pyrazoleamide 1a' with 2d	S11
4. Preparation and Characterization of the Substrates	S11
5. References.....	S14
6. Copies of NMR Spectra of the Products.....	S15
7. Copies of NMR Spectra of the the Substrates.....	S38
8. Copies of HPLC Spectra of the Products.....	S47

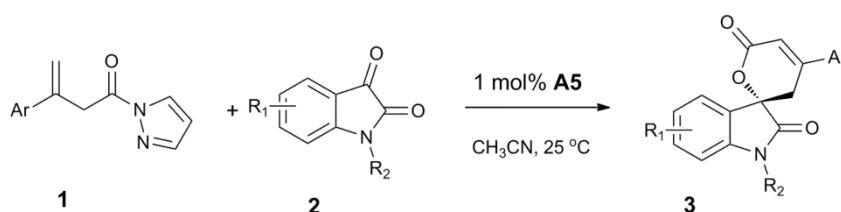
1. General Information

Melting points were taken without correction. ^1H NMR and ^{13}C NMR spectra were recorded on Bruker 400 spectrometer and the chemical shifts were referenced to tetramethylsilane (δ 0.00 ppm) using d_6 -DMSO or CDCl_3 as solvent. IR spectra were recorded on Nicolet Magna-I 550 spectrometer. High resolution mass spectra (HRMS) were performed on an electron spray ionization time-of-flight (ESI-TOF) mass spectrometer. Optical rotations were measured on a WZZ-2A digital polarimeter at the wavelength of the sodium D-line (589 nm). HPLC analysis was performed on Waters equipment using Daicel Chiralpak AD-H, Chiralcel OD-H Chiralpak or AS-H column column.

Toluene, THF, and ether were freshly distilled from sodium-benzophenone. Ethyl acetate, CH_2Cl_2 , DMF, and CH_3CN were freshly distilled from CaH_2 . Thin-layer chromatography (TLC) was performed on 10-40 μm silica gel plates. Column chromatography was performed, using silica gel (300-400 mesh) eluted with ethyl acetate and CH_2Cl_2 .

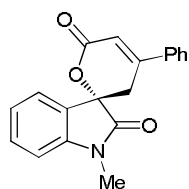
Catalysts **A1-A3**,¹ **A4**,² **A5-A7**³ and **A8**⁴ were prepared according to literature procedures.

2. General Procedure for the Cascade Reaction and Characterization of the Products

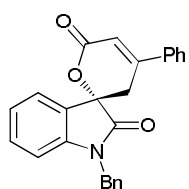


To a solution of catalyst **A5** (0.002 mmol, 0.8 mg) and allyl pyrazoleamide **1** (0.3 mmol) in 2 mL of CH_3CN was added isatin derivative **2** (0.2 mmol) at $25\text{ }^\circ\text{C}$, and the resulting mixture was stirred at this temperature until the reaction completed (monitored by TLC). The solvent was removed under reduced pressure and the residue was purified by column chromatography (20/1 CH_2Cl_2 /ethyl acetate) to give the desired product **3**.

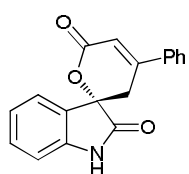
(S)-1-methyl-4'-phenylspiro[indoline-3,2'-pyran]-2,6'(3'H)-dione (3aa). Yield: 99% (60.5 mg), white solid, mp $192.2\text{-}193.2\text{ }^\circ\text{C}$, 91% ee, $[\alpha]_{\text{D}}^{20} +50.2$ (c 0.48, CH_3CN); ^1H NMR (400 MHz, CDCl_3): δ 7.54-7.52 (m, 2H), 7.47-7.41 (m, 4H), 7.37



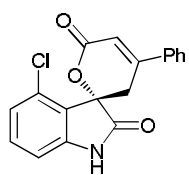
(td, $J = 8.0$ Hz, 1.2 Hz, 1H), 7.04 (td, $J = 7.6$ Hz, 0.8 Hz, 1H), 6.87 (d, $J = 7.6$ Hz, 1H), 6.57 (s, 1H), 3.34 (dd, $J = 18.0$ Hz, 1.6 Hz, 1H), 3.20 (s, 3H), 3.09 (dd, $J = 18.0$ Hz, 1.2 Hz, 1H); HPLC analysis (Daicel Chiralcel OD-H column, *n*-Hexane/*i*-PrOH = 65:35, 0.9 mL/min, $\lambda = 254$ nm): $t_R = 27.5$ min (minor), 31.2 min (major).



(S)-1-benzyl-4'-phenylspiro[indoline-3,2'-pyran]-2,6'(3'H)-dione (3ab). Yield: 98 % (74.6 mg), white solid, mp 185.9-186.3 °C, 91% ee, $[\alpha]_D^{20} +36.4$ (c 0.58, CH₃CN); ¹H NMR (400 MHz, *d*₆-DMSO): δ 7.81 (d, $J = 7.6$ Hz, 2H), 7.63 (d, $J = 7.2$ Hz, 1H), 7.52-7.47 (m, 3H), 7.38-7.28 (m, 6H), 7.09 (t, $J = 7.2$ Hz, 1H), 7.01 (d, $J = 8.0$ Hz, 1H), 6.73 (s, 1H), 4.36 (d, $J = 16.0$ Hz, 1H), 4.89 (d, $J = 16.0$ Hz, 1H), 3.53 (d, $J = 18.4$ Hz, 1H), 3.42 (d, $J = 18.4$ Hz, 1H); ¹³C NMR (100 MHz, *d*₆-DMSO): δ 172.7, 163.2, 152.2, 142.2, 135.7, 135.4, 131.0, 130.9, 128.9, 128.8, 127.6, 127.5, 127.2, 126.6, 124.4, 123.3, 113.6, 110.1, 79.7, 42.9, 31.1; IR (KBr, cm⁻¹): ν 2922, 1724, 1620, 1496, 1361, 1257, 1075, 696; HRMS calcd for C₂₅H₂₀NO₃[M+H]: 382.1443, found 382.1439; HPLC analysis (Daicel Chiralcel OD-H column, *n*-Hexane/*i*-PrOH = 65:35, 0.9 mL/min, $\lambda = 254$ nm): $t_R = 19.2$ min (minor), 23.6 min (major).

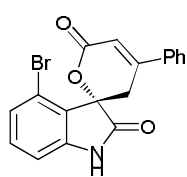


(S)-4'-phenylspiro[indoline-3,2'-pyran]-2,6'(3'H)-dione (3ad). Yield: 98% (57.2 mg), white solid, mp 125.3-126.4 °C, 94% ee, $[\alpha]_D^{20} +50.1$ (c 0.40, CH₃CN); ¹H NMR (400 MHz, *d*₆-DMSO): δ 10.80 (s, 1H), 7.77 (d, $J = 8.0$ Hz, 2H), 7.54-7.44 (m, 4H), 7.34 (t, $J = 8.0$ Hz, 1H), 7.03 (t, $J = 7.6$ Hz, 1H), 6.94 (d, $J = 7.6$ Hz, 1H), 6.67 (s, 1H), 3.41 (d, $J = 18.4$ Hz, 1H), 3.31 (d, $J = 18.4$ Hz, 1H); ¹³C NMR (100 MHz, *d*₆-DMSO): δ 174.2, 163.4, 152.0, 141.8, 135.5, 131.0, 130.9, 128.9, 128.1, 126.6, 124.5, 122.5, 113.7, 110.5, 80.0, 31.1; IR (KBr, cm⁻¹): ν 3270, 1724, 1620, 1472, 1262, 1121, 1054, 759; HRMS calcd for C₁₈H₁₄NO₃[M+H]: 292.0974, found 292.0966; HPLC analysis (Daicel Chiralpak AD-H column, *n*-Hexane/*i*-PrOH = 80:20, 0.9 mL/min, $\lambda = 254$ nm): $t_R = 32.1$ min (minor), 34.9 min (major).



(S)-4-chloro-4'-phenylspiro[indoline-3,2'-pyran]-2,6'(3'H)-dione (3ae). Yield: 98% (63.7 mg), white solid, mp 203.9-204.0 °C, 88% ee, $[\alpha]_D^{20} +102.7$ (c 0.49, CH₃CN); ¹H NMR (400 MHz, *d*₆-DMSO): δ 10.91 (s, 1H), 7.76 (d, $J = 6.0$ Hz, 2H), 7.65 (d, $J = 1.2$ Hz, 1H),

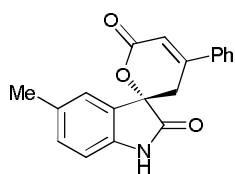
7.48-7.40 (m, 4H), 6.95 (d, $J = 8.4$ Hz, 1H), 6.67 (s, 1H), 3.50 (d, $J = 18.4$ Hz, 1H), 3.33 (d, $J = 18.4$ Hz, 1H); ^{13}C NMR (100 MHz, d_6 -DMSO): δ 174.0, 163.1, 151.8, 140.8, 135.4, 130.9, 130.8, 129.9, 129.0, 126.6, 126.4, 124.9, 113.5, 112.1, 79.8, 30.7; IR (KBr, cm^{-1}): ν 3266, 1724, 1621, 1475, 1262, 1078, 767, 610; HRMS calcd for $\text{C}_{18}\text{H}_{11}\text{ClNO}_3[\text{M}-\text{H}]$: 324.0433, found 324.0425; HPLC analysis (Daicel Chiralpak AS-H column, n -Hexane/EtOH = 60:40, 0.9 mL/min, $\lambda = 254$ nm): $t_{\text{R}} = 18.1$ min (major), 27.6 min (minor).



(S)-4-bromo-4'-phenylspiro[indoline-3,2'-pyran]-2,6'(3'H)-dione

(3af). Yield: 98% (72.4 mg), white solid, mp 222.3-222.9 °C, 84% ee, $[\alpha]_{\text{D}}^{20} +45.9$ (c 0.61, CH_3CN); ^1H NMR (400 MHz, d_6 -DMSO): δ 10.94 (s, 1H), 7.76 (d, $J = 6.8$ Hz, 2H), 7.50-7.46 (m, 4H), 7.23 (d, $J =$

8.0 Hz, 1H), 7.08 (s, 1H), 6.66 (s, 1H), 3.44 (d, $J = 18.4$ Hz, 1H), 3.33 (d, $J = 18.4$ Hz, 1H); ^{13}C NMR (100 MHz, d_6 -DMSO): δ 174.0, 163.1, 152.0, 143.5, 135.4, 130.9, 128.9, 127.4, 126.6, 126.4, 125.1, 123.7, 113.6, 113.4, 79.6, 30.7; IR (KBr, cm^{-1}): ν 3265, 1720, 1614, 1449, 1261, 1105, 769; HRMS calcd for $\text{C}_{18}\text{H}_{11}\text{BrNO}_3[\text{M}-\text{H}]$: 367.9928, found 367.9930; HPLC analysis (Daicel Chiralpak AS-H column, n -Hexane/EtOH = 60:40, 0.9 mL/min, $\lambda = 254$ nm): $t_{\text{R}} = 9.4$ min (major), 12.4 min (minor).

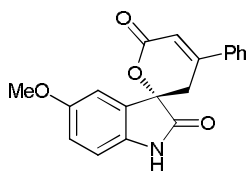


(S)-5-methyl-4'-phenylspiro[indoline-3,2'-pyran]-2,6'(3'H)-dione

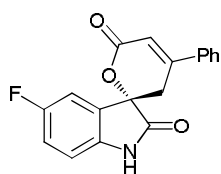
(3ag). Yield: 98% (60.4 mg), white solid, mp 230.9-231.6 °C, 97% ee, $[\alpha]_{\text{D}}^{20} +90.0$ (c 0.45, CH_3CN); ^1H NMR (400 MHz, d_6 -DMSO): δ 10.68 (s, 1H), 7.79-7.77 (m, 2H), 7.50-7.44 (m, 3H),

7.35 (s, 1H), 7.15 (d, $J = 7.6$ Hz, 1H), 6.82 (d, $J = 8.0$ Hz, 1H), 6.66 (s, 1H), 3.38 (d, $J = 18.4$ Hz, 1H), 3.28 (d, $J = 18.4$ Hz, 1H), 2.24 (s, 3H); ^{13}C NMR (100 MHz, d_6 -DMSO): δ 174.2, 163.4, 151.9, 139.2, 135.5, 131.5, 131.1, 130.8, 128.9, 128.2, 126.6, 125.0, 113.6, 110.3, 80.0, 31.1, 20.6; IR (KBr, cm^{-1}): ν 3278, 1720, 1626, 1494, 1262, 1157, 1051, 768, 687; HRMS calcd for $\text{C}_{19}\text{H}_{14}\text{NO}_3[\text{M}-\text{H}]$: 304.0979, found 304.0962; HPLC analysis (Daicel Chiralpak AS-H column, n -Hexane/EtOH = 60:40, 0.9 mL/min, $\lambda = 254$ nm): $t_{\text{R}} = 25.7$ min (major), 36.8 min (minor).

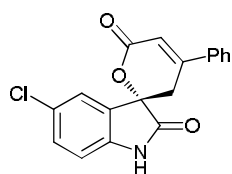
(S)-5-methoxy-4'-phenylspiro[indoline-3,2'-pyran]-2,6'(3'H)-dione (3ah). Yield: 97% (62.1 mg), white solid, mp 213.6-213.9 °C, 92% ee, $[\alpha]_{\text{D}}^{20} +96.0$ (c 0.52, CH_3CN); ^1H NMR (400 MHz, d_6 -DMSO): δ 10.59 (s, 1H), 7.78-7.76 (m, 2H),



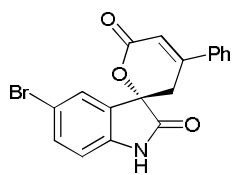
7.50-7.44 (m, 3H), 7.21 (d, $J = 2.0$ Hz, 1H), 6.92 (dd, $J = 8.4$ Hz, $J = 2.0$ Hz, 1H), 6.85 (d, $J = 8.4$ Hz, 1H), 6.65 (s, 1H), 3.71 (s, 3H), 3.45 (d, $J = 18.4$ Hz, 1H), 3.28 (d, $J = 18.4$ Hz, 1H); ^{13}C NMR (100 MHz, d_6 -DMSO): δ 174.3, 163.4, 155.3, 151.8, 135.5, 134.8, 130.8, 129.1, 128.9, 126.6, 115.6, 113.6, 111.5, 111.1, 80.3, 55.6, 31.1; IR (KBr, cm^{-1}): ν 3265, 1721, 1490, 1264, 1204, 1054, 870, 768; HRMS calcd for $\text{C}_{19}\text{H}_{14}\text{NO}_4[\text{M}-\text{H}]$: 320.0928, found 320.0925; HPLC analysis (Daicel Chiralpak AD-H column, n -Hexane/ i -PrOH = 80:20, 0.9 mL/min, $\lambda = 254$ nm): $t_{\text{R}} = 35.1$ min (minor), 55.2 min (major).



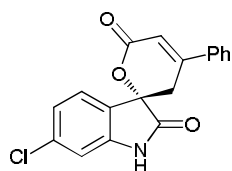
(S)-5-fluoro-4'-phenylspiro[indoline-3,2'-pyran]-2,6'(3'H)-dione (3ai). Yield: 99% (61.3 mg), white solid, mp 232.7-233.6 °C, 90% ee, $[\alpha]_{\text{D}}^{20} +31.6$ (c 0.44, CH_3CN); ^1H NMR (400 MHz, d_6 -DMSO): δ 10.80 (s, 1H), 7.79-7.77 (m, 2H), 7.51-7.45 (m, 4H), 7.20 (td, $J = 8.8$ Hz, $J = 2.4$ Hz, 1H), 6.95-6.92 (m, 1H), 6.66 (s, 1H), 3.47 (d, $J = 18.4$ Hz, 1H), 3.33 (d, $J = 18.4$ Hz, 1H); ^{13}C NMR (100 MHz, d_6 -DMSO): δ 174.3, 163.2, 158.2 (d, $J = 236.9$ Hz), 151.7, 138.0, 135.4, 130.9, 129.5 (d, $J = 8.1$ Hz), 128.9, 126.6, 117.4 (d, $J = 23.2$ Hz), 113.6, 112.6 (d, $J = 25.1$ Hz), 111.5 (d, $J = 7.9$ Hz), 80.0, 30.8; IR (KBr, cm^{-1}): ν 3269, 1724, 1627, 1488, 1262, 1189, 1051, 767, 687; HRMS calcd for $\text{C}_{18}\text{H}_{11}\text{FNO}_3[\text{M}-\text{H}]$: 308.0728, found 308.0719; HPLC analysis (Daicel Chiralpak AS-H column, n -Hexane/EtOH = 60:40, 0.9 mL/min, $\lambda = 254$ nm): $t_{\text{R}} = 15.2$ min (major), 30.7 min (minor).



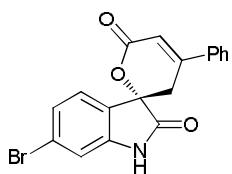
(S)-5-chloro-4'-phenylspiro[indoline-3,2'-pyran]-2,6'(3'H)-dione (3aj). Yield: 98% (63.7 mg), white solid, mp 203.9-204.0 °C, 86% ee, $[\alpha]_{\text{D}}^{20} +102.7$ (c 0.49, CH_3CN); ^1H NMR (400 MHz, d_6 -DMSO): δ 10.91 (s, 1H), 7.76 (d, $J = 6.0$ Hz, 2H), 7.65 (d, $J = 1.2$ Hz, 1H), 7.48-7.40 (m, 4H), 6.95 (d, $J = 8.4$ Hz, 1H), 6.67 (s, 1H), 3.50 (d, $J = 18.4$ Hz, 1H), 3.33 (d, $J = 18.4$ Hz, 1H); ^{13}C NMR (100 MHz, d_6 -DMSO): δ 174.0, 163.1, 151.8, 140.8, 135.4, 130.9, 130.8, 129.9, 129.0, 126.6, 126.4, 124.9, 113.5, 112.1, 79.8, 30.7; IR (KBr, cm^{-1}): ν 3266, 1724, 1621, 1475, 1262, 1078, 767, 610; HRMS calcd for $\text{C}_{18}\text{H}_{11}\text{ClNO}_3[\text{M}-\text{H}]$: 324.0433, found 324.425; HPLC analysis (Daicel Chiralpak AS-H column, n -Hexane/EtOH = 60:40, 0.9 mL/min, $\lambda = 254$ nm): $t_{\text{R}} = 18.1$ min (major), 27.6 min (minor).



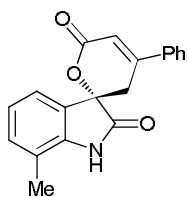
(S)-5-bromo-4'-phenylspiro[indoline-3,2'-pyran]-2,6'(3'H)-dione (3ak). Yield: 98% (72.6 mg), white solid, mp 236.5-237.2 °C, 86% ee, $[\alpha]_D^{20} +101.4$ (*c* 0.60, CH₃CN); ¹H NMR (400 MHz, *d*₆-DMSO): δ 10.91 (s, 1H), 7.79-7.77 (m, 3H), 7.55-7.46 (m, 4H), 6.90 (d, *J* = 8.4 Hz, 1H), 6.66 (s, 1H), 3.51 (d, *J* = 18.4 Hz, 1H), 3.32 (d, *J* = 18.4 Hz, 1H); ¹³C NMR (100 MHz, *d*₆-DMSO): δ 173.9, 163.1, 151.8, 141.2, 135.4, 133.7, 130.9, 130.2, 128.9, 127.6, 126.6, 114.0, 113.5, 112.6, 79.8, 30.7; IR (KBr, cm⁻¹): ν 3266, 1721, 1618, 1474, 1261, 1048, 766, 607; HRMS calcd for C₁₈H₁₁BrNO₃[M-H]: 367.9928, found 367.9920; HPLC analysis (Daicel Chiralpak AS-H column, *n*-Hexane/EtOH = 60:40, 0.9 mL/min, λ = 254 nm): *t*_R = 24.0 min (major), 29.5 min (minor).



(S)-6-chloro-4'-phenylspiro[indoline-3,2'-pyran]-2,6'(3'H)-dione (3al). Yield: 99% (64.3 mg), white solid, mp 236.2-237.1 °C, 92% ee, $[\alpha]_D^{20} +51.6$ (*c* 0.53, CH₃CN); ¹H NMR (400 MHz, *d*₆-DMSO): δ 10.96 (s, 1H), 7.77-7.75 (m, 2H), 7.55 (d, *J* = 8.0 Hz, 1H), 7.51-7.45 (m, 3H), 7.09 (td, *J* = 8.0 Hz, *J* = 1.6 Hz, 1H), 6.96 (s, 1H), 6.66 (s, 1H), 3.44 (d, *J* = 18.4 Hz, 1H), 3.33 (d, *J* = 18.0 Hz, 1H); ¹³C NMR (100 MHz, *d*₆-DMSO): δ 174.1, 163.2, 152.0, 143.4, 135.4, 135.3, 130.9, 128.9, 126.9, 126.6, 126.1, 122.2, 113.6, 110.7, 79.5, 30.8; IR (KBr, cm⁻¹): ν 3277, 2922, 1741, 1617, 1448, 1262, 1048, 761; HRMS calcd for C₁₈H₁₁ClNO₃[M-H]: 324.0433, found 324.0425; HPLC analysis (Daicel Chiralpak AS-H column, *n*-Hexane/EtOH = 60:40, 0.9 mL/min, λ = 254 nm): *t*_R = 21.6 min (major), 31.9 min (minor).

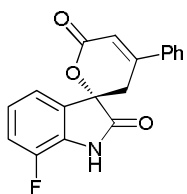


(S)-6-bromo-4'-phenylspiro[indoline-3,2'-pyran]-2,6'(3'H)-dione (3am). Yield: 97% (71.6 mg), white solid, mp 231.8-232.9 °C, 92% ee, $[\alpha]_D^{20} +52.5$ (*c* 0.60, CH₃CN); ¹H NMR (400 MHz, *d*₆-DMSO): δ 10.94 (s, 1H), 7.80 (d, *J* = 6.8 Hz, 2H), 7.52-7.44 (m, 3H), 7.35-7.28 (m, 2H), 6.95 (d, *J* = 7.2 Hz, 1H), 6.65 (d, *J* = 2.0 Hz, 1H), 3.70 (dd, *J* = 18.8 Hz, *J* = 2.0 Hz, 1H), 3.39 (d, *J* = 18.8 Hz, 1H); ¹³C NMR (100 MHz, *d*₆-DMSO): δ 174.3, 163.2, 150.7, 144.1, 135.1, 132.9, 130.9, 128.9, 126.6, 126.4, 125.2, 119.3, 113.0, 110.0, 80.5, 28.1; IR (KBr, cm⁻¹): ν 3133, 1715, 1613, 1447, 1218, 1055, 768; HRMS calcd for C₁₈H₁₁BrNO₃[M-H]: 367.9928, found 367.9912; HPLC analysis (Daicel Chiralpak AS-H column, *n*-Hexane/EtOH = 60:40, 0.9 mL/min, λ = 254 nm): *t*_R = 20.4 min (major), 29.6 min (minor).



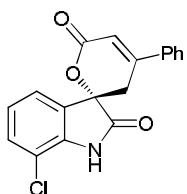
(S)-7-methyl-4'-phenylspiro[indoline-3,2'-pyran]-2,6'(3'H)-dione

(3an). Yield: 98% (60.0 mg), white solid, mp 271.7-272.7 °C, 94% ee, $[\alpha]_D^{20} +16.6$ (*c* 0.48, CH₃CN); ¹H NMR (400 MHz, *d*₆-DMSO): δ 10.82 (s, 1H), 7.78-7.76 (m, 2H), 7.49-7.44 (m, 3H), 7.34 (d, *J* = 7.6 Hz, 1H), 7.10 (d, *J* = 7.6 Hz, 1H), 6.94 (t, *J* = 7.6 Hz, 1H), 6.66 (s, 1H), 3.39 (d, *J* = 18.4 Hz, 1H), 3.30 (d, *J* = 18.4 Hz, 1H), 2.23 (s, 3H); ¹³C NMR (100 MHz, *d*₆-DMSO): δ 174.7, 163.4, 152.0, 140.3, 135.5, 132.1, 130.9, 128.9, 127.9, 126.6, 122.5, 121.8, 120.0, 113.6, 80.2, 31.1, 16.3; IR (KBr, cm⁻¹): ν 3263, 1727, 1627, 1448, 1261, 1074, 767; HRMS calcd for C₁₉H₁₄NO₃[M-H]: 304.0979, found 304.0967; HPLC analysis (Daicel Chiralpak AS-H column, *n*-Hexane/EtOH = 60:40, 0.9 mL/min, λ = 254 nm): *t*_R = 15.4 min (major), 33.0 min (minor).



(S)-7-fluoro-4'-phenylspiro[indoline-3,2'-pyran]-2,6'(3'H)-dione

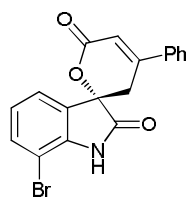
(3ao). Yield: 98% (60.6 mg), white solid, mp 253.6-255.1 °C, 88% ee, $[\alpha]_D^{20} +32.9$ (*c* 0.50, CH₃CN); ¹H NMR (400 MHz, *d*₆-DMSO): δ 11.34 (s, 1H), 7.79-7.77 (m, 2H), 7.51-7.44 (m, 3H), 7.40 (d, *J* = 7.6 Hz, 1H), 7.30 (d, *J* = 9.2 Hz, 1H), 7.09-7.03 (m, 1H), 6.68 (s, 1H), 3.46 (d, *J* = 18.4 Hz, 1H), 3.37 (d, *J* = 18.4 Hz, 1H); ¹³C NMR (100 MHz, *d*₆-DMSO): δ 174.0, 163.1, 152.1, 146.6 (d, *J* = 242.0 Hz), 135.4, 130.9, 130.9 (d, *J* = 3.6 Hz), 129.1, 128.9, 126.6, 123.6 (d, *J* = 5.7 Hz), 120.6 (d, *J* = 3.0 Hz), 118.0 (d, *J* = 17.9 Hz), 113.5, 79.9 (d, *J* = 3.1 Hz), 30.9; IR (KBr, cm⁻¹): ν 3187, 1747, 1693, 1644, 1491, 1207, 1073, 767; HRMS calcd for C₁₈H₁₁FNO₃[M-H]: 308.0728, found 308.0730; HPLC analysis (Daicel Chiralpak AS-H column, *n*-Hexane/EtOH = 60:40, 0.9 mL/min, λ = 254 nm): *t*_R = 14.1 min (major), 35.3 min (minor).



(S)-7-chloro-4'-phenylspiro[indoline-3,2'-pyran]-2,6'(3'H)-dione

(3ap). Yield: 99% (64.3 mg), white solid, mp 269.5-269.6 °C, 85% ee, $[\alpha]_D^{20} -30.5$ (*c* 0.53, CH₃CN); ¹H NMR (400 MHz, *d*₆-DMSO): δ 11.25 (s, 1H), 7.79-7.77 (m, 2H), 7.53-7.43 (m, 5H), 7.07 (t, *J* = 8.0 Hz, 1H), 6.67 (s, 1H), 3.47 (d, *J* = 18.4 Hz, 1H), 3.38 (d, *J* = 18.4 Hz, 1H); ¹³C NMR (100 MHz, *d*₆-DMSO): δ 174.2, 163.1, 152.0, 139.6, 135.4, 130.9, 130.9, 129.9, 128.9, 126.7, 123.9, 123.3, 114.7, 113.5, 80.3, 30.8; IR (KBr, cm⁻¹): ν 3178, 2970, 1746, 1691, 1620, 1382, 1276, 1058, 765; HRMS calcd for C₁₈H₁₁ClNO₃[M-H]: 324.0433, found 324.0420; HPLC analysis (Daicel Chiralpak AS-H column, *n*-Hexane/EtOH =

60:40, 0.9 mL/min, $\lambda = 254$ nm): $t_R = 15.2$ min (major), 45.2 min (minor).

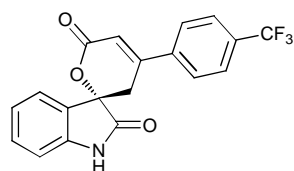


(S)-7-bromo-4'-phenylspiro[indoline-3,2'-pyran]-2,6'(3'H)-dione

(3aq). Yield: 99% (73.2 mg), white solid, mp 271.5-273.2 °C, 82% ee,

$[\alpha]_D^{20} -14.2$ (c 0.56, CH₃CN); ¹H NMR (400 MHz, *d*₆-DMSO): δ 11.11 (s, 1H), 7.79-7.77 (m, 2H), 7.57-7.44 (m, 5H), 7.00 (t, $J = 8.0$

Hz, 1H), 6.67 (s, 1H), 3.47 (d, $J = 18.4$ Hz, 1H), 3.38 (d, $J = 18.4$ Hz, 1H); ¹³C NMR (100 MHz, *d*₆-DMSO): δ 174.1, 163.1, 152.0, 141.3, 135.4, 133.8, 130.9, 129.8, 128.9, 126.7, 124.2, 123.7, 113.5, 102.8, 80.6, 30.8; IR (KBr, cm⁻¹): ν 3221, 2970, 1736, 1701, 1618, 1383, 1261, 1056, 767; HRMS calcd for C₁₈H₁₁BrNO₃[M-H]: 367.9928, found 367.9917; HPLC analysis (Daicel Chiralpak AS-H column, *n*-Hexane/EtOH = 60:40, 0.9 mL/min, $\lambda = 254$ nm): $t_R = 17.1$ min (major), 52.7 min (minor).

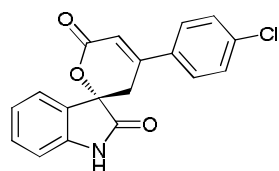


(S)-4'-(4-(trifluoromethyl)phenyl)spiro[indoline-3,2'-pyran]-2,6'(3'H)-dione (3bd). Yield: 98% (70.0 mg), white solid, mp 248.8-250.3 °C, 95% ee, $[\alpha]_D^{20} +56.5$ (c 0.58,

CH₃CN); ¹H NMR (400 MHz, *d*₆-DMSO): δ 10.80 (s, 1H), 7.99 (d, $J = 8.0$ Hz, 2H), 7.81 (d, $J = 8.0$ Hz, 2H), 7.55 (d, $J = 7.6$ Hz, 1H), 7.35 (t, $J = 7.6$ Hz, 1H), 7.04 (t, $J = 7.6$ Hz, 1H), 6.93 (d, $J = 8.0$ Hz, 1H), 6.78 (s, 1H), 3.48 (d, $J = 18.0$ Hz, 1H), 3.36 (d, $J = 18.0$ Hz, 1H); ¹³C NMR (100 MHz, *d*₆-DMSO): δ 174.1,

163.1, 150.5, 141.8, 139.6, 131.1, 130.4 (q, $J = 31.9$ Hz), 127.9, 127.5, 125.7, 125.7, 124.6, 122.5, 116.0, 110.6, 80.0, 31.0; IR (KBr, cm⁻¹): ν 3270, 1736, 1620, 1473, 1326, 1121, 1070, 751; HRMS calcd for C₁₉H₁₃F₃NO₃[M+H]: 360.0848, found 360.0822; HPLC analysis (Daicel Chiralpak AS-H column, *n*-Hexane/EtOH = 60:40, 0.9 mL/min, $\lambda = 254$ nm): $t_R = 9.8$ min (major), 13.3 min (minor).

(S)-4'-(4-chlorophenyl)spiro[indoline-3,2'-pyran]-2,6'(3'H)-dione (3cd). Yield:

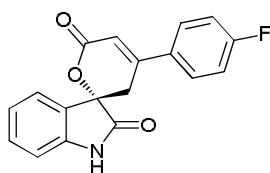


99% (64.2 mg), white solid, mp 242.9-243.7 °C, 93% ee, $[\alpha]_D^{20} +63.6$ (c 0.52, CH₃CN); ¹H NMR (400 MHz, *d*₆-DMSO): δ 10.77 (s, 1H), 7.81 (d, $J = 8.4$ Hz, 2H), 7.52 (d, $J = 8.4$ Hz,

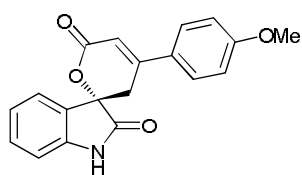
3H), 7.35 (t, $J = 7.6$ Hz, 1H), 7.03 (t, $J = 7.6$ Hz, 1H), 6.92 (d, $J = 7.6$ Hz, 1H), 6.69 (s, 1H), 3.40 (d, $J = 18.0$ Hz, 1H), 3.26 (d, $J = 18.4$ Hz, 1H); ¹³C NMR (100 MHz, *d*₆-DMSO): δ 174.1, 163.3, 150.7, 141.8, 135.6, 134.3, 131.0, 128.9, 128.5, 128.0, 124.6, 122.5, 114.2, 110.5, 79.9, 30.9; IR (KBr, cm⁻¹): ν 3398, 1736, 1619, 1365, 1217, 1093, 770; HRMS calcd for C₁₈H₁₁ClNNO₃[M+Na]: 348.0403,

found 348.0413; HPLC analysis (Daicel Chiralpak AS-H column, *n*-Hexane/EtOH = 60:40, 0.9 mL/min, $\lambda = 254$ nm): $t_R = 14.9$ min (major), 18.3 min (minor).

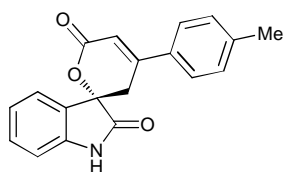
(S)-4'-(4-fluorophenyl)spiro[indoline-3,2'-pyran]-2,6'(3'H)-dione (3dd) Yield: 99%



(60.9 mg), white solid, mp 239.6-240.8 °C, 92% ee, $[\alpha]_D^{20} +49.7$ (*c* 0.48, CH₃CN); ¹H NMR (400 MHz, *d*₆-DMSO): δ 10.78 (s, 1H), 7.88-7.84 (m, 2H), 7.52 (d, *J* = 7.6 Hz, 1H), 7.36-7.28 (m, 3H), 7.02 (t, *J* = 7.6 Hz, 1H), 6.93 (d, *J* = 7.6 Hz, 1H), 6.66 (s, 1H), 3.40 (d, *J* = 18.4 Hz, 1H), 3.31 (d, *J* = 18.4 Hz, 1H); ¹³C NMR (100 MHz, *d*₆-DMSO): δ 174.2, 163.6 (d, *J* = 247.8), 163.4, 150.9, 141.8, 132.0 (d, *J* = 2.9 Hz), 131.0, 129.2 (d, *J* = 8.7 Hz), 128.1, 124.5, 122.5, 115.9 (d, *J* = 21.6 Hz), 113.6, 110.5, 79.9, 31.1; IR (KBr, cm⁻¹): ν 3268, 1735, 1600, 1473, 1236, 1054, 835, 753; HRMS calcd for C₁₈H₁₃FNO₃[M+H]: 310.0879, found 310.0862; HPLC analysis (Daicel Chiralpak AS-H column, *n*-Hexane/EtOH = 80:20, 0.9 mL/min, $\lambda = 254$ nm): $t_R = 42.8$ min (major), 49.8 min (minor).

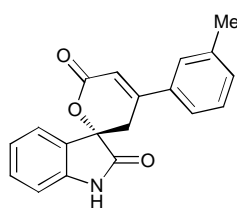


(S)-4'-(4-methoxyphenyl)spiro[indoline-3,2'-pyran]-2,6'(3'H)-dione (3ed). Yield: 93% (59.7 mg), white solid, mp 254.3-255.0 °C, 92% ee, $[\alpha]_D^{20} +49.7$ (*c* 0.48, CH₃CN); ¹H NMR (400 MHz, *d*₆-DMSO): δ 10.76 (s, 1H), 7.76 (d, *J* = 8.4 Hz, 2H), 7.50 (d, *J* = 7.2 Hz, 1H), 7.34 (t, *J* = 7.6 Hz, 1H), 7.03-6.99 (m, 3H), 6.92 (d, *J* = 7.6 Hz, 1H), 6.58 (s, 1H), 3.80 (s, 3H), 3.35 (d, *J* = 18.4 Hz, 1H), 3.26 (d, *J* = 18.4 Hz, 1H); ¹³C NMR (100 MHz, *d*₆-DMSO): δ 174.2, 163.6, 161.5, 151.5, 141.8, 130.9, 128.4, 128.3, 127.5, 124.5, 122.5, 114.3, 111.2, 110.5, 79.8, 55.4, 30.9; IR (KBr, cm⁻¹): ν 3266, 1736, 1602, 1515, 1472, 1248, 1183, 1026, 827, 732; HRMS calcd for C₁₉H₁₅KNO₄[M+K]: 360.0638, found 360.0622; HPLC analysis (Daicel Chiralpak AS-H column, *n*-Hexane/EtOH = 60:40, 0.9 mL/min, $\lambda = 254$ nm): $t_R = 22.1$ min (major), 34.1 min (minor).



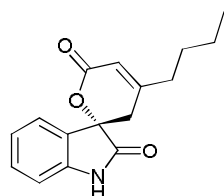
(S)-4'-(*p*-tolyl)spiro[indoline-3,2'-pyran]-2,6'(3'H)-dione (3fd). Yield: 97% (59.1 mg), white solid, mp 233.3-235.1 °C, 93% ee, $[\alpha]_D^{20} +80.1$ (*c* 0.47, CH₃CN); ¹H NMR (400 MHz, *d*₆-DMSO): δ 10.8 (s, 1H), 7.67 (d, *J* = 2.0 Hz, 2H), 7.51 (d, *J* = 7.2 Hz, 1H), 7.34 (t, *J* = 7.2 Hz, 1H), 7.26 (d, *J* = 8.0 Hz, 2H), 7.01 (t, *J* = 7.2 Hz, 1H), 6.93 (d, *J* = 7.6 Hz, 1H), 6.62 (s, 1H), 3.36 (d, *J* = 18.4 Hz, 1H), 3.26 (d, *J* = 18.4

Hz, 1H), 2.33 (s, 3H); ^{13}C NMR (100 MHz, d_6 -DMSO): δ 174.2, 163.5, 151.9, 141.8, 141.0, 132.6, 130.9, 129.5, 128.2, 126.5, 124.5, 122.5, 112.6, 110.5, 79.9, 31.0, 20.9; IR (KBr, cm^{-1}): ν 3369, 1707, 1618, 1263, 1095, 818, 769; HRMS calcd for $\text{C}_{19}\text{H}_{15}\text{NNaO}_3[\text{M}+\text{Na}]$: 328.0950, found 328.0948; HPLC analysis (Daicel Chiralpak AS-H column, *n*-Hexane/EtOH = 60:40, 0.9 mL/min, λ = 254 nm): t_{R} = 16.6 min (major), 25.7 min (minor).



(S)-4'-(*m*-tolyl)spiro[indoline-3,2'-pyran]-2,6'(3'*H*)-dione (3gd)

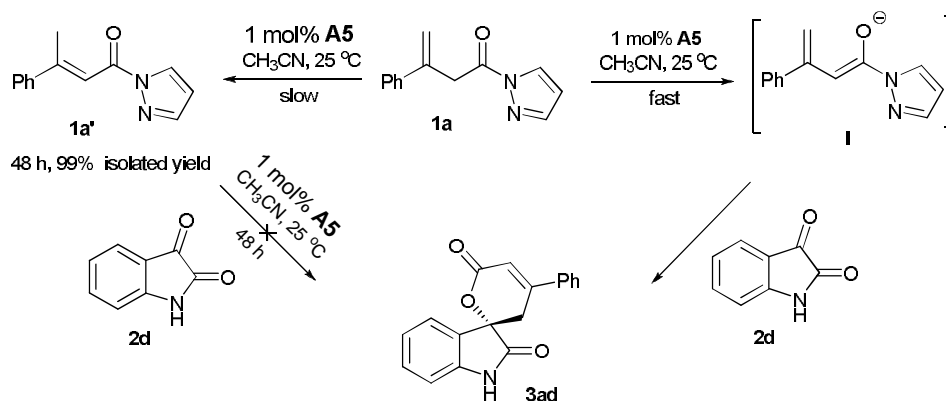
Yield: 98% (60.4 mg), white solid, mp 192.6-193.6 °C, 95% ee, $[\alpha]_{\text{D}}^{20}$ +40.0 (c 0.47, CH_3CN); ^1H NMR (400 MHz, d_6 -DMSO): δ 10.79 (s, 1H), 7.61-7.51 (m, 3H), 7.36-7.26 (m, 3H), 7.03 (t, J = 7.6 Hz, 1H), 6.94 (d, J = 7.6 Hz, 1H), 6.66 (s, 1H), 3.39 (d, J = 17.6 Hz, 1H), 3.39 (d, J = 17.6 Hz), 2.33 (s, 3H); ^{13}C NMR (100 MHz, d_6 -DMSO): δ 174.2, 163.4, 152.1, 141.8, 138.3, 135.4, 131.5, 131.0, 128.8, 128.2, 127.2, 124.5, 123.7, 122.5, 113.4, 110.5, 79.9, 31.2, 20.9; IR (KBr, cm^{-1}): ν 3274, 1727, 1620, 1473, 1252, 1093, 865, 680; HRMS calcd for $\text{C}_{19}\text{H}_{15}\text{NNaO}_3[\text{M}+\text{Na}]$: 328.0950, found 328.0981; HPLC analysis (Daicel Chiralpak AS-H column, *n*-Hexane/EtOH = 60:40, 0.9 mL/min, λ = 254 nm): t_{R} = 18.6 min (major), 35.4 min (minor).



(S)-4'-butylspiro[indoline-3,2'-pyran]-2,6'(3'*H*)-dione (3hd)

Yield: 94% (50.9 mg), viscous liquid, 88% ee, $[\alpha]_{\text{D}}^{20}$ + 15.3 (c 0.39, CH_3CN); ^1H NMR (400 MHz, CDCl_3): δ 9.01 (s, 1H), 7.37 (d, J = 7.6 Hz, 1H), 7.29-7.25 (m, 1H), 7.00 (t, J = 7.6 Hz, 1H), 6.92 (d, J = 7.6 Hz, 1H), 6.05 (s, 1H), 2.91 (d, J = 18.0 Hz, 1H), 2.61 (d, J = 18.0 Hz, 1H), 2.30 (t, J = 7.6 Hz, 2H), 1.55-1.47 (m, 2H), 1.41-1.32 (m, 2H), 0.92 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 174.8, 163.1, 158.5, 140.3, 130.9, 128.1, 124.0, 123.2, 115.2, 111.1, 80.2, 36.4, 34.0, 28.1, 22.2, 13.7; IR (KBr, cm^{-1}): ν 3261, 2959, 1739, 1473, 1246, 1047, 762; HRMS calcd for $\text{C}_{16}\text{H}_{17}\text{NNaO}_3[\text{M}+\text{Na}]$: 294.1106, found 294.1104; HPLC analysis (Daicel Chiralpak AS-H column, *n*-Hexane/EtOH = 60:40, 0.9 mL/min, λ = 254 nm): t_{R} = 6.65 min (major), 18.1 min (minor).

3. Control Reaction of α,β -Unsaturated Pyrazoleamide **1a'** with **2d**

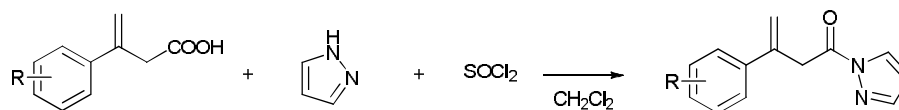


Allyl pyrazoleamide **1a** can be transformed to the corresponding α,β -unsaturated pyrazoleamide isomer **1a'** under the typical reaction condition without the addition of isatin. The results indicated that the isomerization rate of transforming **1a** to **1a'** is much slower than the rate of the tandem reaction between **1a** and isatin. As predicted, **1a'** is an unreactive nucleophile in the vinylogous aldol reaction, probably because it couldn't be deprotonated by the tertiary amine to form the key intermediates **I**.

(*E*)-3-phenyl-1-(1*H*-pyrazol-1-yl)but-2-en-1-one(**1a'**).

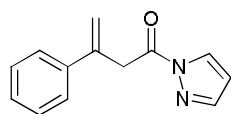
To a solution of catalyst **A5** (0.02 mmol, 8.4 mg) in 20 mL of CH_3CN was added allyl pyrazoleamide **1a** (0.2 mmol, 0.42 g) at 25°C , and the resulting mixture was stirred at this temperature for 48 h. The solvent was removed under reduced pressure and the residue was purified by column chromatography (10/1 petroleum ether/ethyl acetate) to give 0.42 g (99%) colorless liquid; ^1H NMR (400 MHz, CDCl_3): δ 8.35 (d, $J = 2.8$ Hz, 1H), 7.70 (s, 1H), 7.61-7.57 (m, 3H), 7.38-7.36 (m, 3H), 6.42-6.41 (m, 1H), 2.71 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 163.0, 160.2, 143.1, 141.9, 129.5, 128.4, 128.2, 126.4, 114.6, 109.2, 18.7; IR (KBr, cm^{-1}): ν 3164, 1697, 1610, 1382, 1099, 1030, 765, 694; HRMS calcd for $\text{C}_{13}\text{H}_{12}\text{N}_2\text{NaO}$ [$\text{M}+\text{Na}$]: 235.0847, found 235.0844.

4. Preparation and Characterization of the Substrates

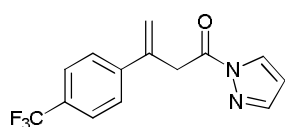


A CH_2Cl_2 (5 mL) solution of thionyl chloride (13 mmol) were added dropwise to a mixture of 10 mmol pyrazole, 40 mmol allyl carboxylic acid and 25 mL CH_2Cl_2 . The resultant solution was stirred for 2 h at room temperature. After being quenched with 0.1 M HCl solution (3×10 mL), washed with 0.1 M NaOH solution (3×10 mL)

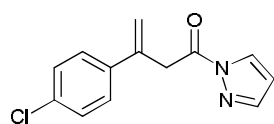
and aq NaCl, the organic phase was separated, dry over anhydrous MgSO₄, filtered and concentrated under reduced pressure, the crude product was purified by chromatography on silica gel with petroleum ether-ethyl acetate as eluent.



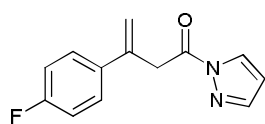
3-phenyl-1-(1H-pyrazol-1-yl)but-3-en-1-one (1a). Yield: 85% (1.80 g), colorless liquid; ¹H NMR (400 MHz, CDCl₃): δ 8.22 (d, *J* = 2.8 Hz, 1H), 7.73 (s, 1H), 7.47 (d, *J* = 7.6 Hz, 2H), 7.33-7.24 (m, 3H), 6.43 (d, *J* = 1.2 Hz, 1H), 5.63 (s, 1H), 5.29 (s, 1H), 4.38 (s, 2H); ¹³C NMR (100 MHz, CDCl₃): δ 169.7, 144.1, 140.3, 139.6, 128.4, 128.4, 127.8, 125.8, 117.0, 109.8, 40.1; IR (KBr, cm⁻¹): ν 1736, 1383, 1353, 1200, 1089, 914, 774, 704; HRMS calcd for C₁₃H₁₂N₂NaO [M+Na]: 235.0847, found 235.0843.



1-(1H-pyrazol-1-yl)-3-(4-(trifluoromethyl)phenyl)but-3-en-1-one (1b). Yield: 81% (2.27 g), colorless liquid; ¹H NMR (400 MHz, CDCl₃): δ 8.22 (d, *J* = 2.8 Hz, 1H), 7.75 (s, 1H), 7.58 (s, 4H), 6.46-6.45 (m, 1H), 5.70 (s, 1H), 5.42 (s, 1H), 4.41 (s, 2H); ¹³C NMR (100 MHz, CDCl₃): δ 169.3, 144.3, 143.3, 139.4, 129.7 (q, *J* = 32.2 Hz), 128.5, 126.2, 125.4 (q, *J* = 3.7 Hz), 122.7, 119.2, 110.0, 30.0; IR (KBr, cm⁻¹): ν 3129, 1736, 1619, 1384, 1327, 1121, 915, 764; HRMS calcd for C₁₄H₁₂F₃N₂O [M+H]: 281.0902, found 281.0905.

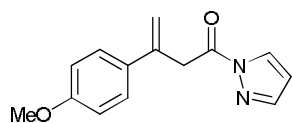


3-(4-chlorophenyl)-1-(1H-pyrazol-1-yl)but-3-en-1-one (1c). Yield: 89% (2.20 g), colorless liquid; ¹H NMR (400 MHz, CDCl₃): δ 8.22 (d, *J* = 2.8 Hz, 1H), 7.74 (s, 1H), 7.40 (d, *J* = 8.8 Hz, 2H), 7.28 (d, *J* = 8.4 Hz, 2H), 6.45-6.44 (m, 1H), 5.61 (s, 1H), 5.31 (s, 1H), 4.35 (s, 2H); ¹³C NMR (100 MHz, CDCl₃): δ 169.4, 144.2, 139.3, 138.1, 133.6, 128.5, 128.4, 127.1, 117.6, 109.9, 40.0; IR (KBr, cm⁻¹): ν 1736, 1493, 1383, 1200, 1089, 914, 838, 766; HRMS calcd for C₁₃H₁₁ClN₂NaO [M+Na]: 269.0458, found 269.0459.

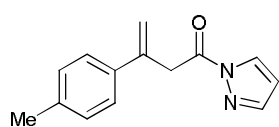


3-(4-fluorophenyl)-1-(1H-pyrazol-1-yl)but-3-en-1-one (1d). Yield: 86% (1.98 g), colorless liquid; ¹H NMR (400 MHz, CDCl₃): δ 8.23 (d, *J* = 2.8 Hz, 1H), 7.74 (s, 1H), 7.46-7.42 (m, 2H), 7.00 (m, 2H), 6.45-6.44 (m, 1H), 5.57 (s, 1H), 5.28 (s, 1H), 4.36 (s, 2H); ¹³C NMR (100 MHz, CDCl₃): δ 169.5, 162.4 (d, *J* = 245.3 Hz), 144.1, 139.4, 135.8 (d, *J* = 3.2 Hz), 128.4, 127.5 (d, *J* = 8.0 Hz), 117.0, 115.2 (d, *J* = 21.3 Hz), 109.9, 40.2; IR (KBr, cm⁻¹): ν 1736, 1511, 1383, 1237, 1084, 915, 842, 765; HRMS calcd for C₁₃H₁₁FN₂NaO [M+Na]: 253.0753, found 253.0758.

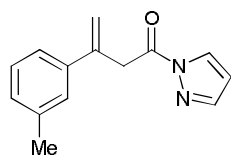
3-(4-methoxyphenyl)-1-(1H-pyrazol-1-yl)but-3-en-1-one(1e). Yield: 84% (2.03 g),



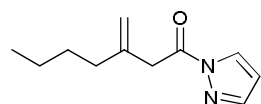
colorless liquid; ^1H NMR (400 MHz, CDCl_3): δ 8.23 (s, 1H), 7.74 (s, 1H), 7.41 (d, $J = 8.0$ Hz, 2H), 6.84 (d, $J = 8.0$ Hz, 2H), 6.36-6.33 (m, 1H), 5.55 (s, 1H), 5.20 (s, 1H), 4.35 (s, 2H), 3.78 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 169.8, 159.3, 144.0, 139.6, 132.0, 128.4, 126.9, 115.3, 113.7, 109.8, 55.1, 40.1; IR (KBr, cm^{-1}): ν 2835, 1736, 1608, 1514, 1250, 1032, 914, 765; HRMS calcd for $\text{C}_{14}\text{H}_{15}\text{N}_2\text{O}_2[\text{M}+\text{H}]$: 243.1134, found 243.1134.



1-(1H-pyrazol-1-yl)-3-(p-tolyl)but-3-en-1-one (1f). Yield: 90% (2.04 g), colorless liquid; ^1H NMR (400 MHz, CDCl_3): δ 8.23 (d, $J = 2.8$ Hz, 1H), 7.73 (s, 1H), 7.37 (d, $J = 8.0$ Hz, 2H), 7.12 (d, $J = 8.0$ Hz, 2H), 7.43-7.42 (m, 1H), 5.60 (s, 1H), 5.24 (s, 1H), 4.36 (s, 2H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 169.7, 144.0, 140.1, 137.6, 136.7, 129.1, 128.4, 125.6, 116.1, 109.8, 40.1, 21.0; IR (KBr, cm^{-1}): ν 1736, 1515, 1383, 1088, 915, 832, 608; HRMS calcd for $\text{C}_{14}\text{H}_{14}\text{N}_2\text{NaO} [\text{M}+\text{Na}]$: 249.1004, found 249.1004.



1-(1H-pyrazol-1-yl)-3-(m-tolyl)but-3-en-1-one (1g). Yield: 88% (1.99 g), colorless liquid; ^1H NMR (400 MHz, CDCl_3): δ 8.23 (d, $J = 2.8$ Hz, 1H), 7.74 (s, 1H), 7.29-7.13 (m, 3H), 7.08 (d, $J = 7.2$ Hz, 1H), 8.44-8.43 (m, 1H), 5.61 (s, 1H), 5.26 (s, 1H), 4.37 (s, 2H), 2.33 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 169.7, 144.0, 140.5, 139.7, 137.9, 128.6, 128.4, 128.3, 126.6, 122.9, 116.8, 109.8, 40.2, 21.4; IR (KBr, cm^{-1}): ν 1736, 1383, 1352, 1120, 1088, 916, 769, 723; HRMS calcd for $\text{C}_{14}\text{H}_{14}\text{N}_2\text{NaO} [\text{M}+\text{Na}]$: 249.1004, found 249.1003.

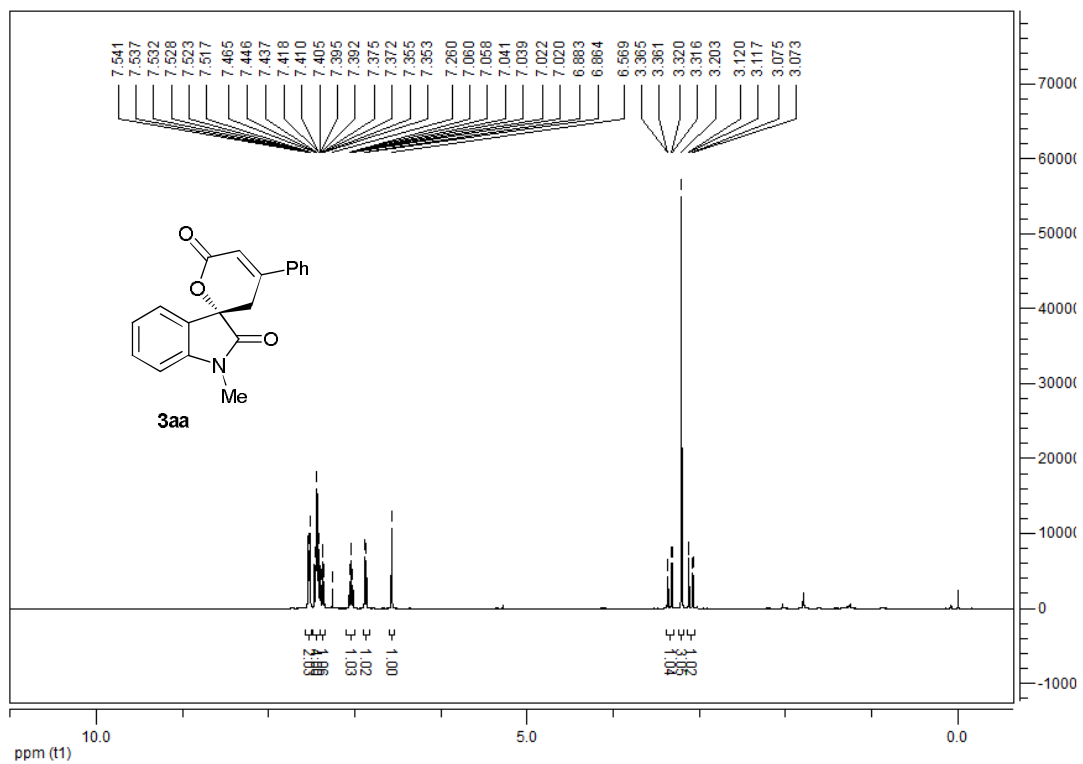


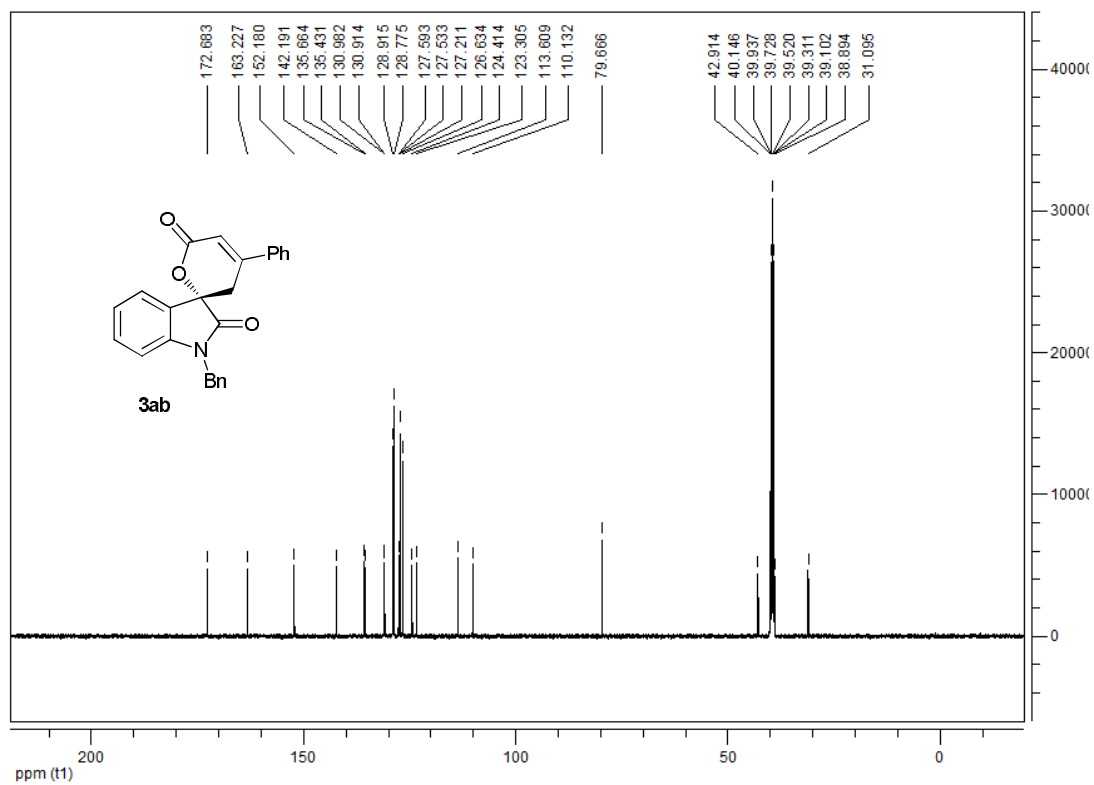
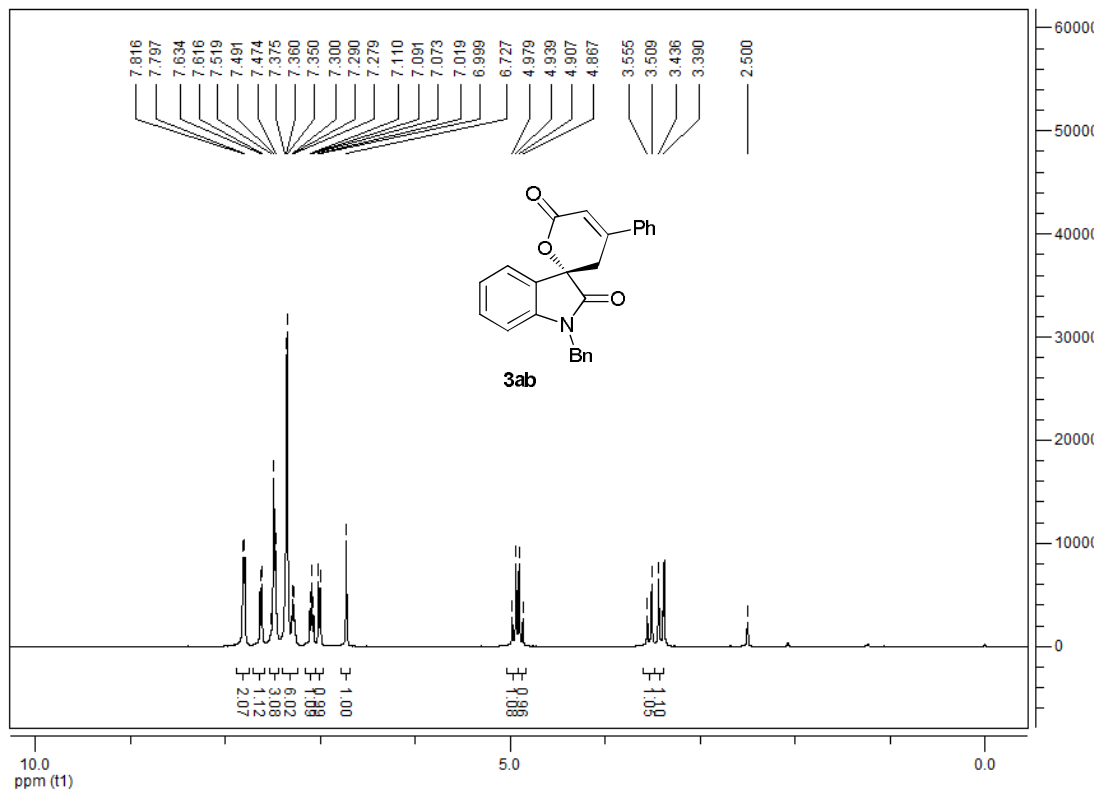
3-methylene-1-(1H-pyrazol-1-yl)heptan-1-one (1h). Yield: 90% (1.28 g), colorless liquid, ^1H NMR (400 MHz, CDCl_3): δ 8.22 (s, 1H), 7.66 (s, 1H), 6.39 (s, 1H), 4.95 (s, 1H), 4.90 (s, 1H), 3.82 (s, 2H), 2.12 (t, $J = 7.6$ Hz, 2H), 1.46-1.38 (m, 2H), 1.33-1.24 (m, 2H), 0.86 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 169.9, 143.8, 142.0, 128.2, 114.0, 109.6, 40.6, 35.7, 29.4, 22.1, 13.8; IR (KBr, cm^{-1}): ν 2958, 1739, 1383, 1200, 1088, 919, 768; HRMS calcd for $\text{C}_{11}\text{H}_{17}\text{N}_2\text{O} [\text{M}+\text{H}]$: 193.1341, found 193.1346.

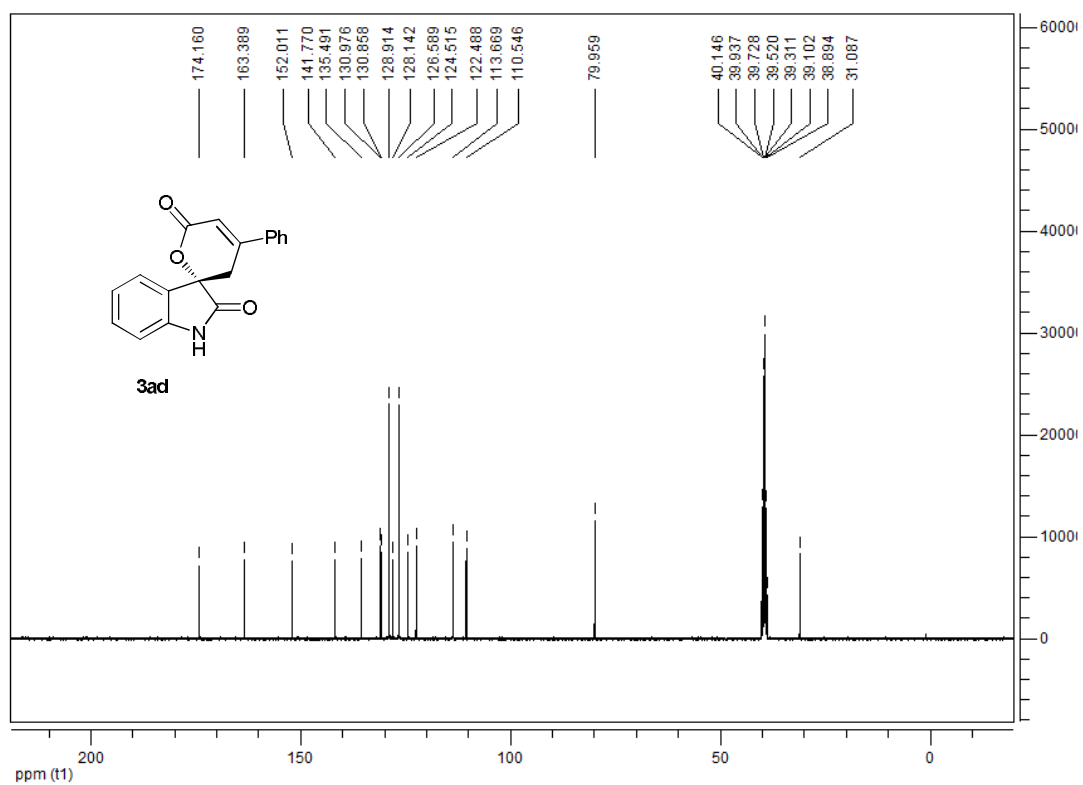
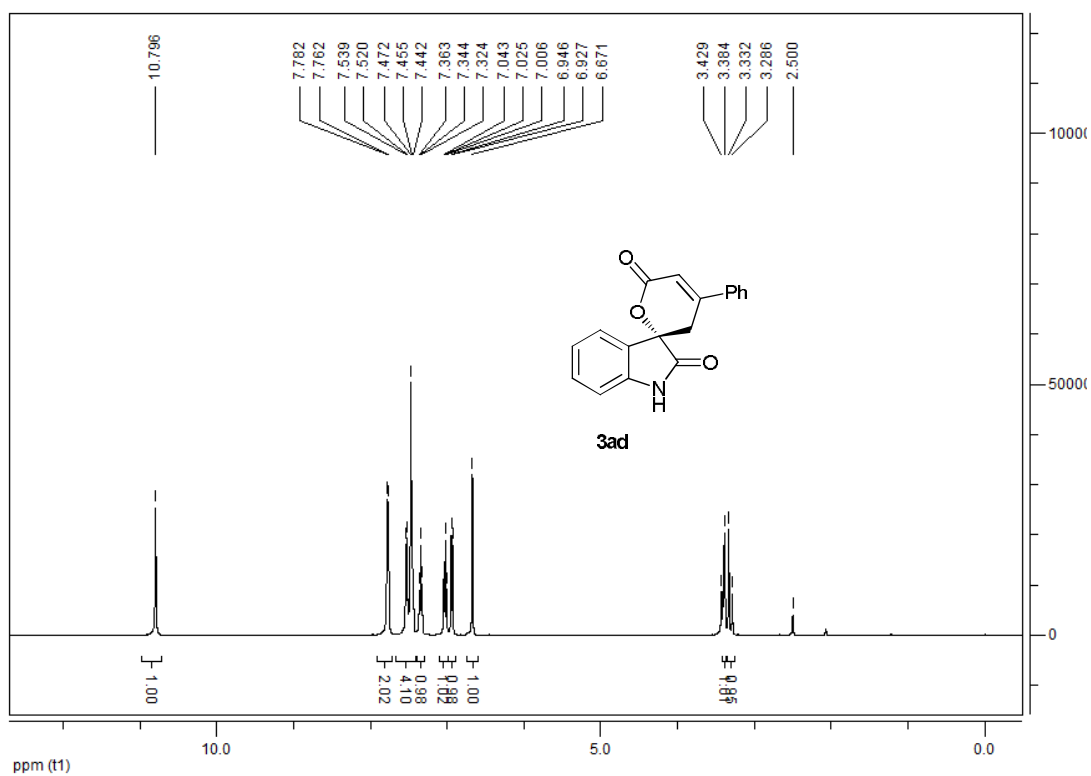
5. References

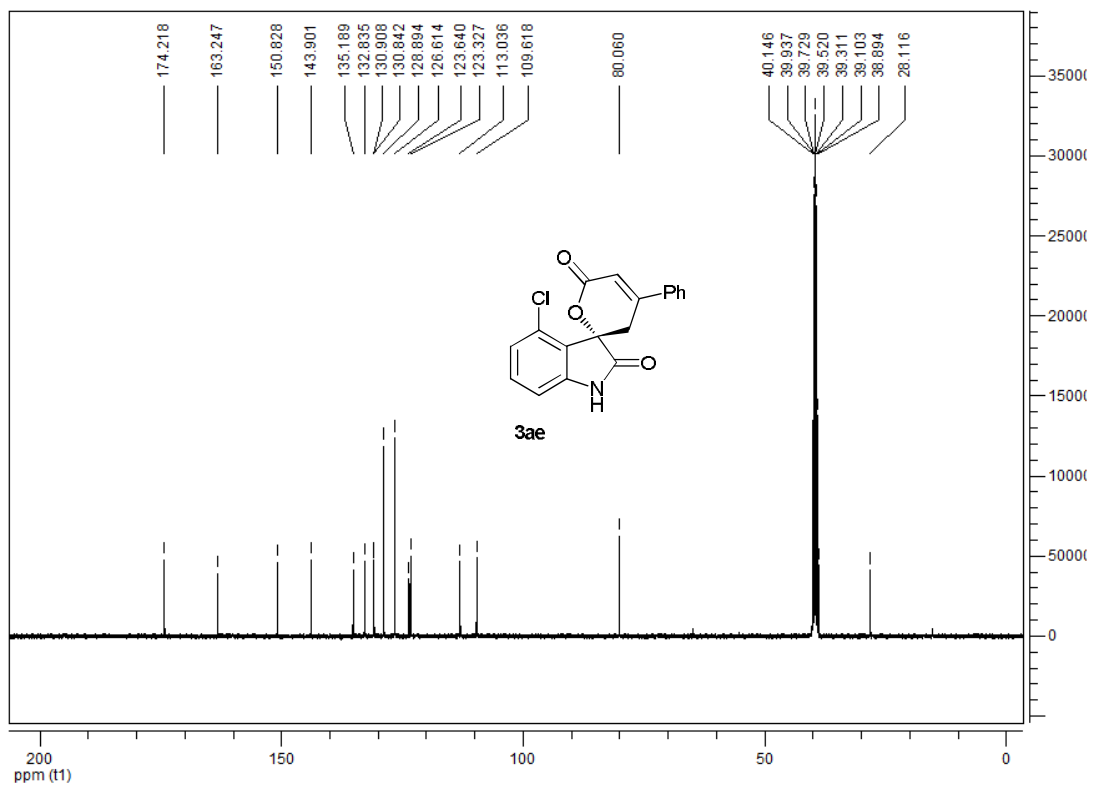
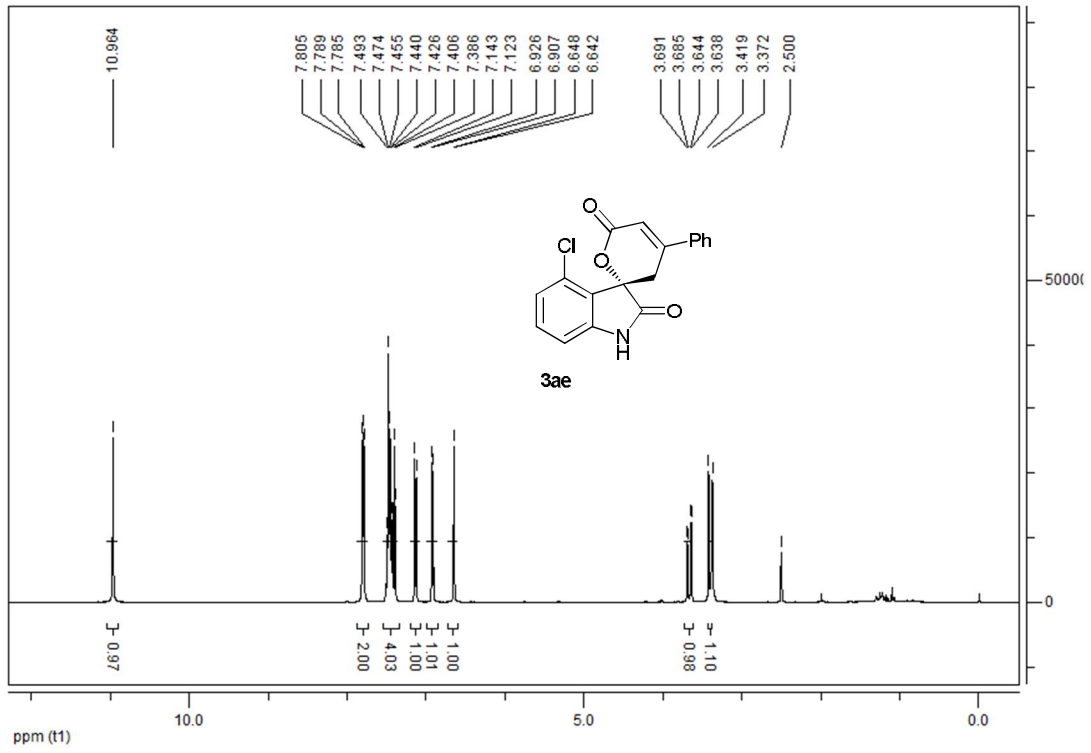
1. (a) B. Vakulya, S. Varga, A. Csámpai and T. Soós, *Org. Lett.*, 2005, **7**, 1967-1969; (b) M. Shi, Z.-Y. Lei, M.-X. Zhao and J.-W. Shi, *Tetrahedron Lett.*, 2007, **48**, 5743-5746; (c) W. Yang and D.-M. Du, *Org. Lett.*, 2010, **12**, 5450-5453.
2. T.-Y. Liu, J. Long, B.-J. Li, L. Jiang, R. Li, Y. Wu, L.-S. Ding and Y.-C. Chen, *Org. Biomol. Chem.*, 2006, **4**, 2097-2099.
3. (a) T. Okino, Y. Hoashi, T. Furukawa, X. Xu and Y. Takemoto, *J. Am. Chem. Soc.*, 2004, **127**, 119-125; (b) Y. Wang, Y. Xing, X. Liu, H. Ji, M. Kai, Z. Chen, J. Yu, D. Zhao, H. Ren and R. Wang, *J. Med. Chem.*, 2012, **55**, 6224-6236; (c) S.-Z. Nie, Z.-P. Hu, Y.-N. Xuan, J.-J. Wang, X.-M. Li and M. Yan, *Tetrahedron: Asymmetry*, 2010, **21**, 2055-2059.
4. W. Yang and D.-M. Du, *Adv. Synth. Catal.*, 2011, **353**, 1241-1246.

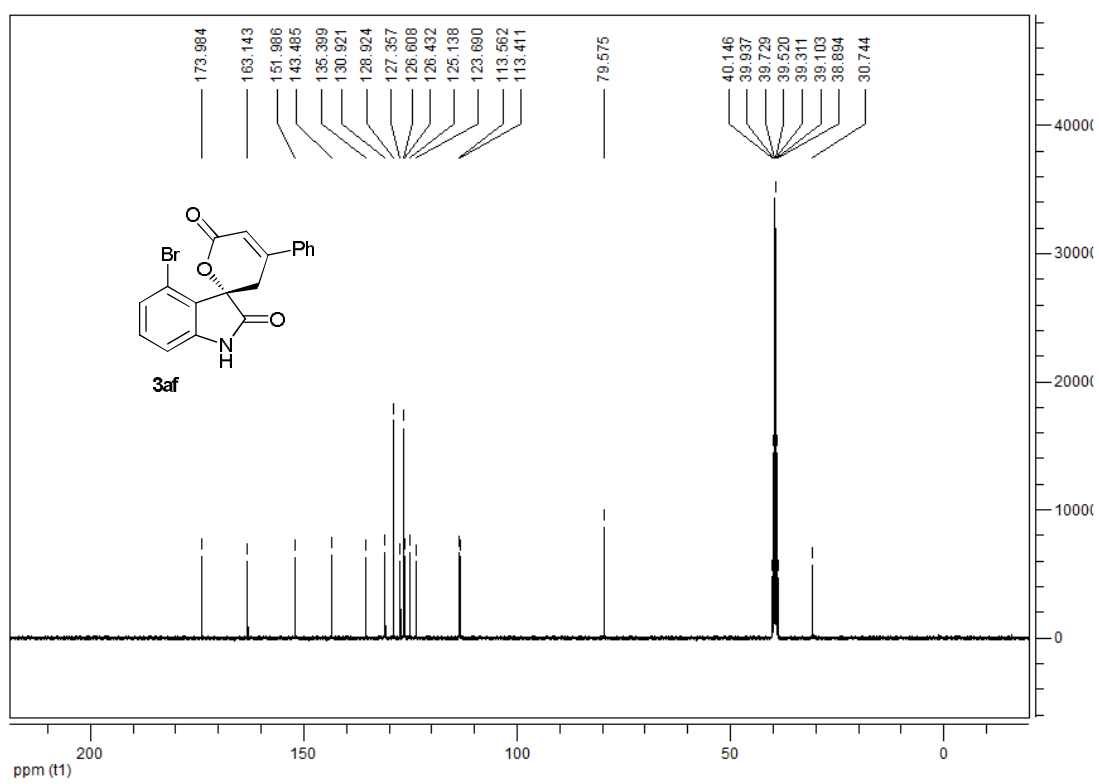
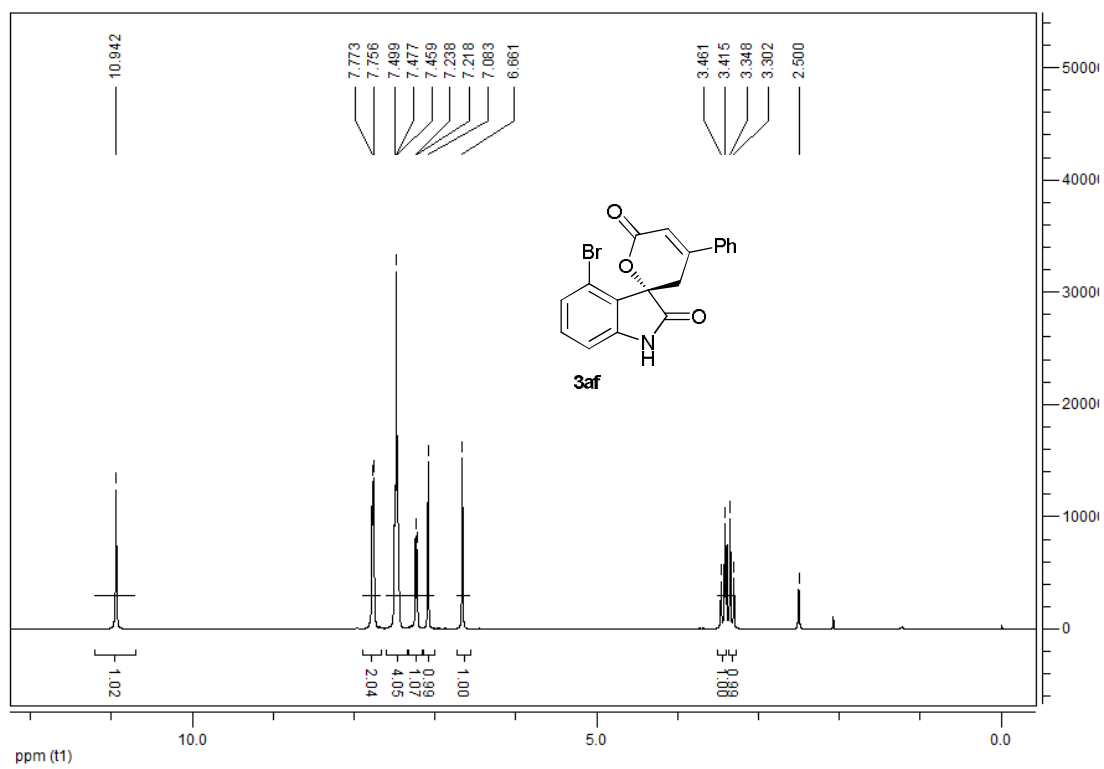
6. Copies of NMR Spectra of the Products

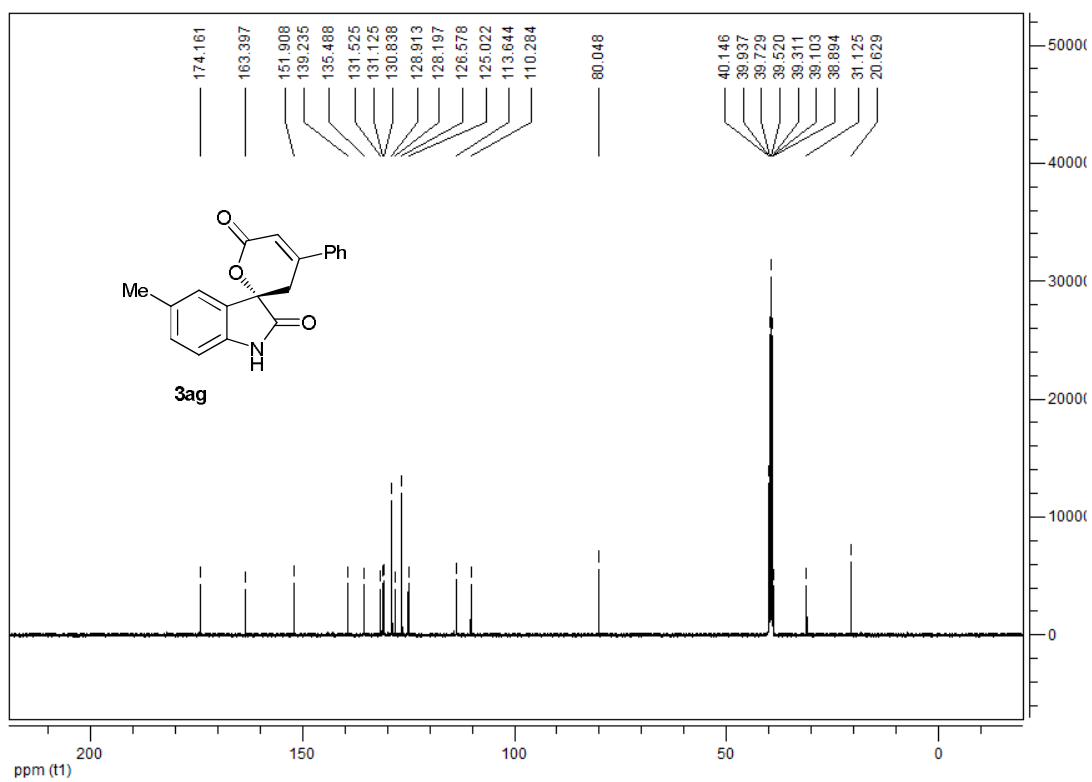
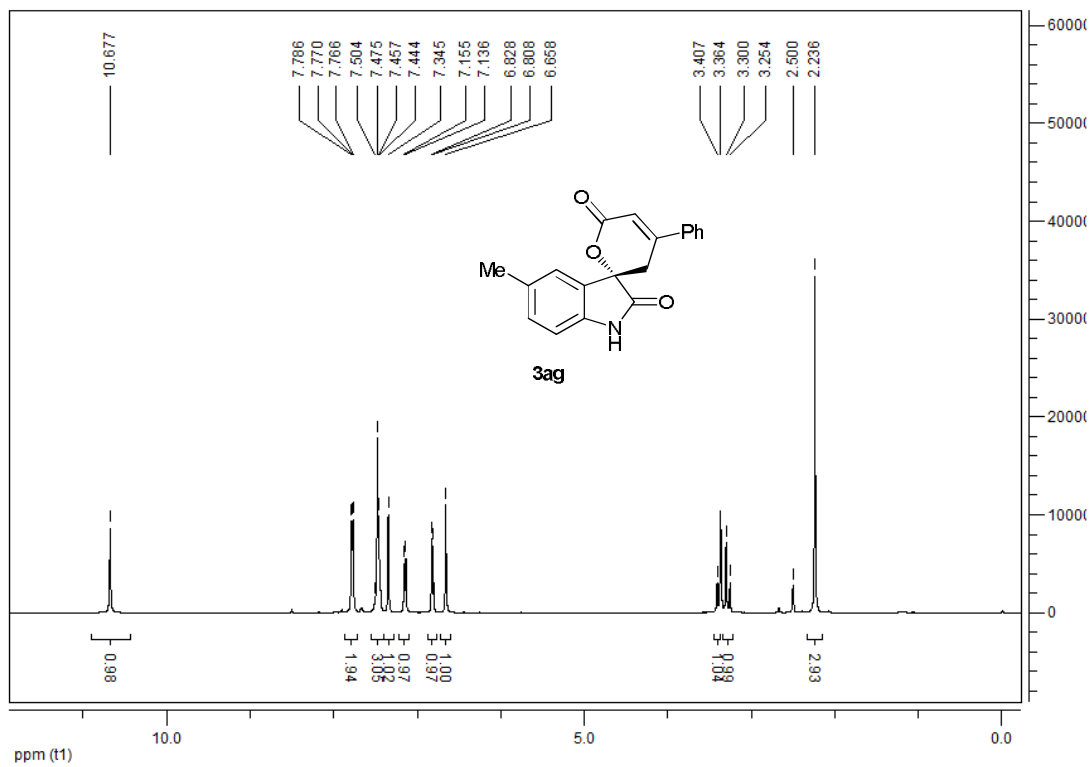


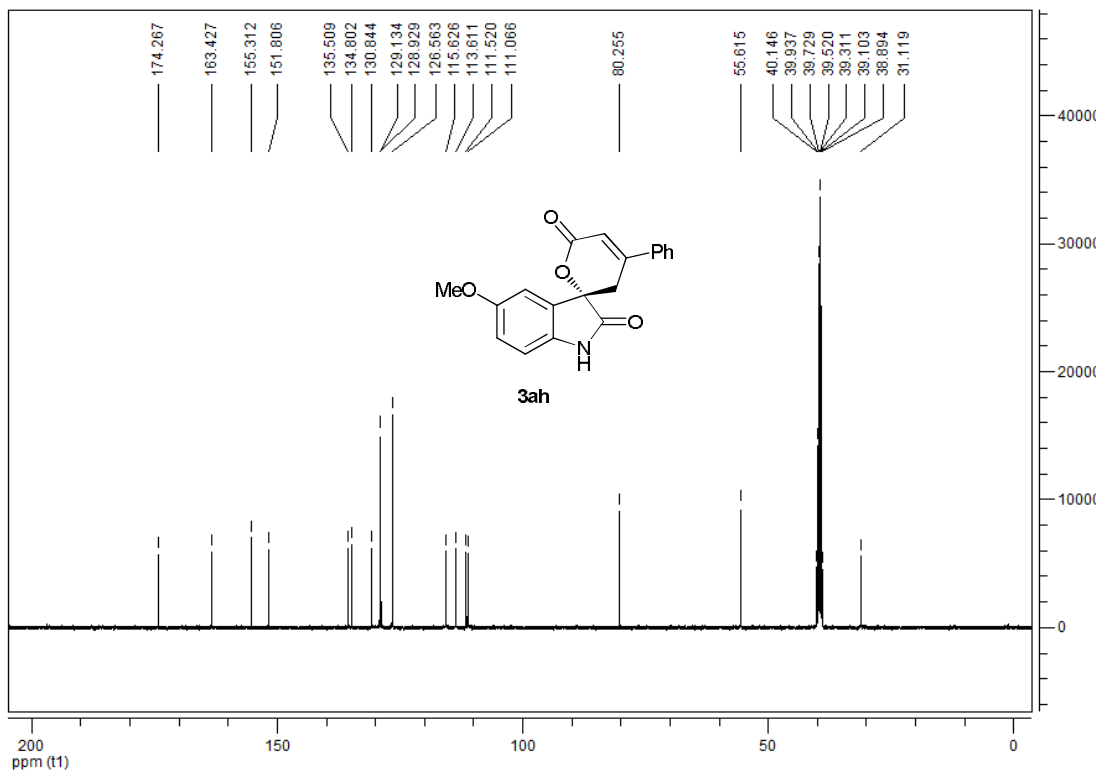
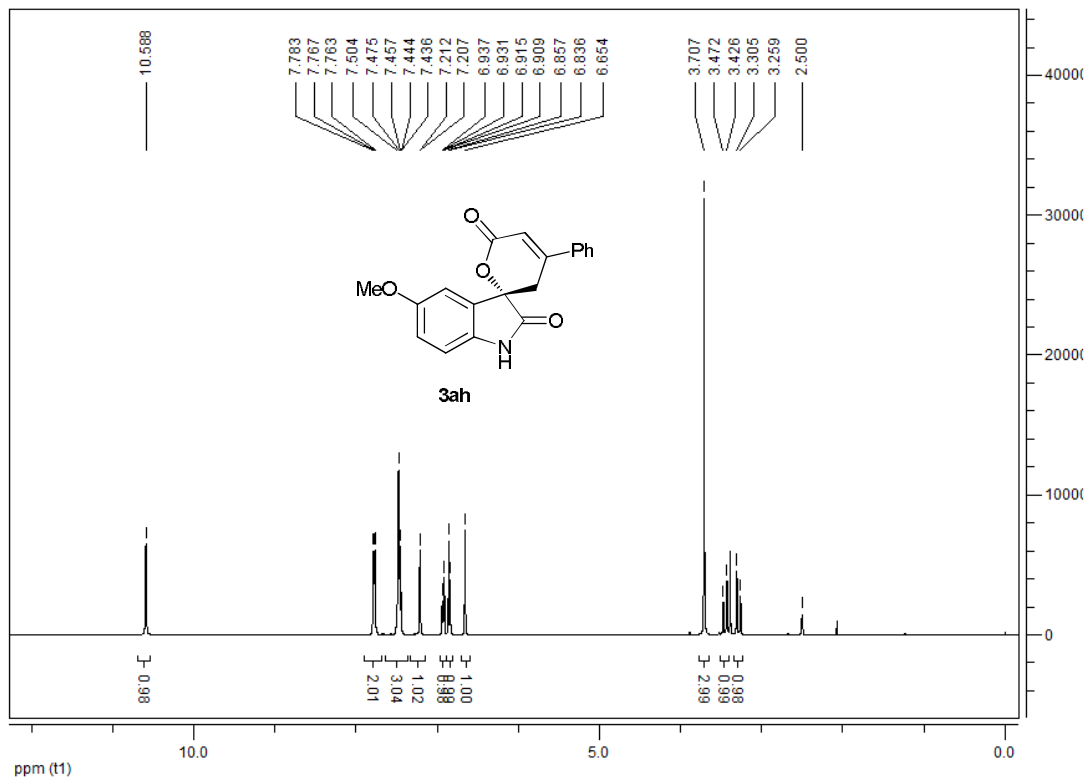


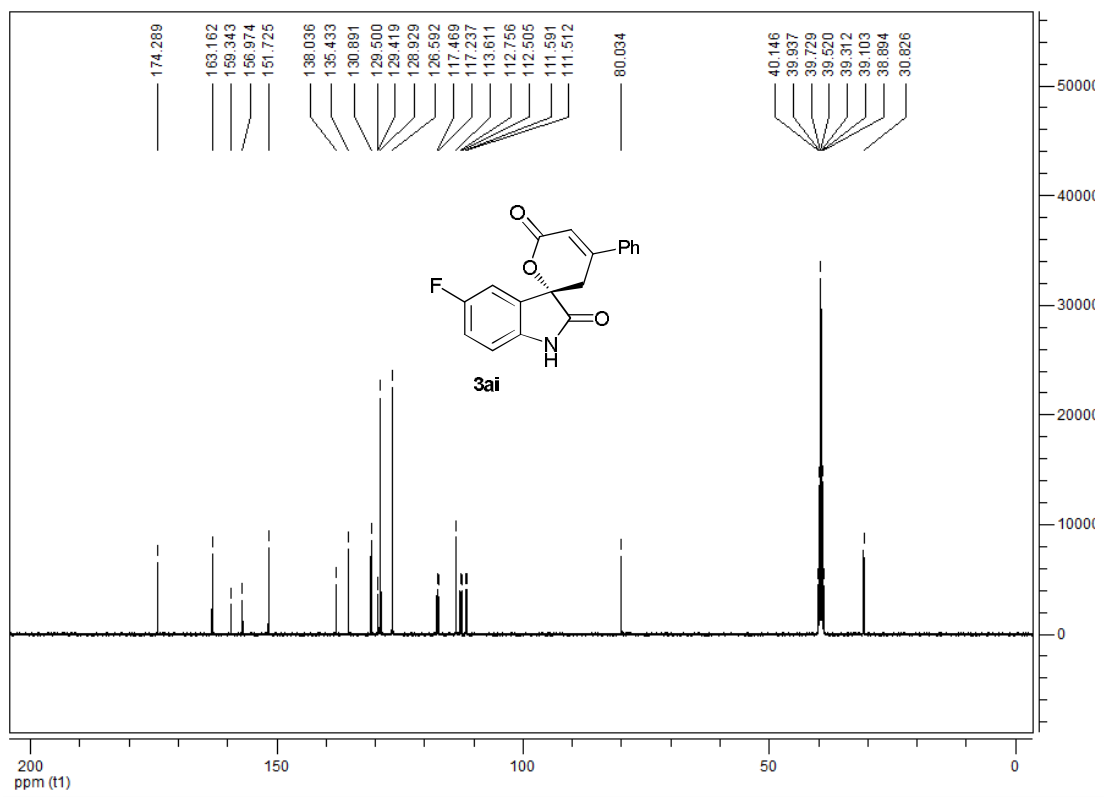
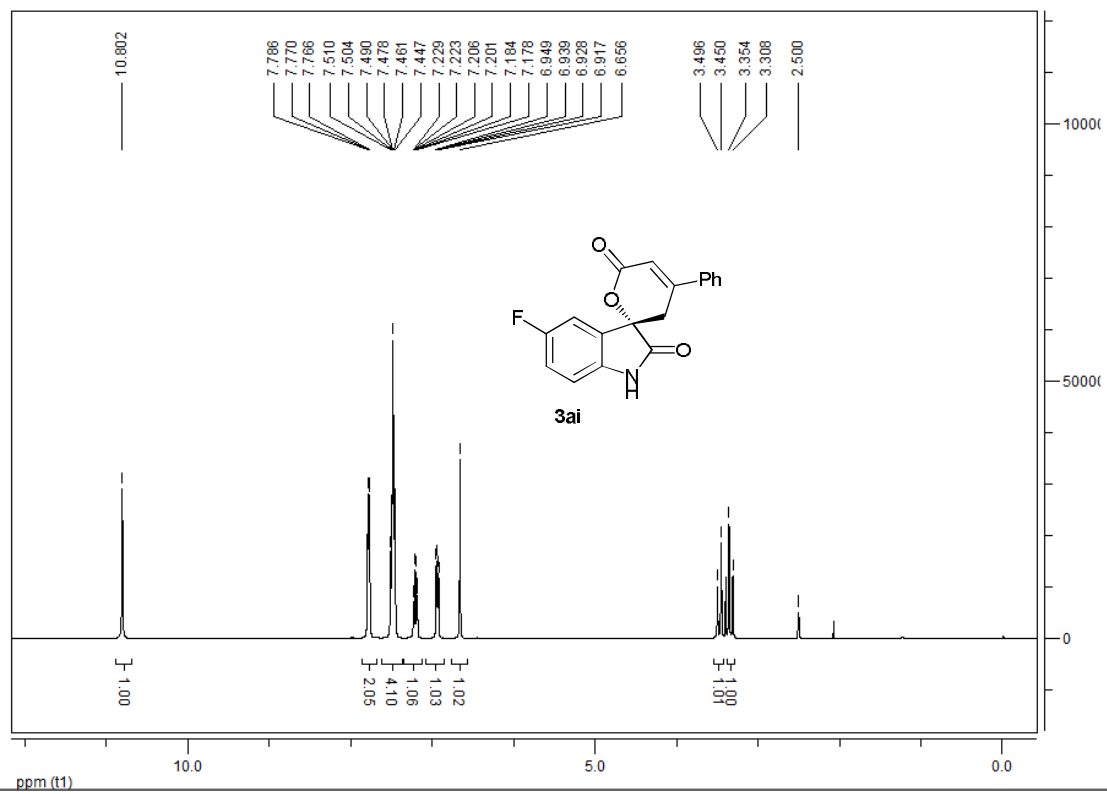


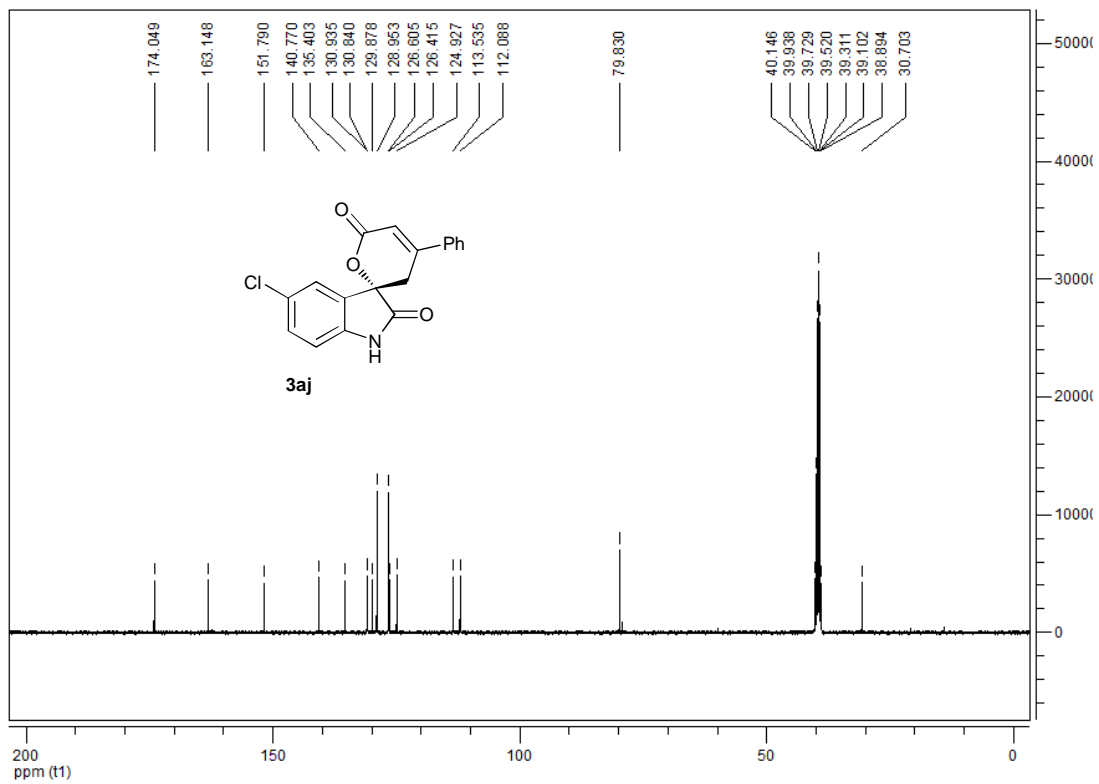
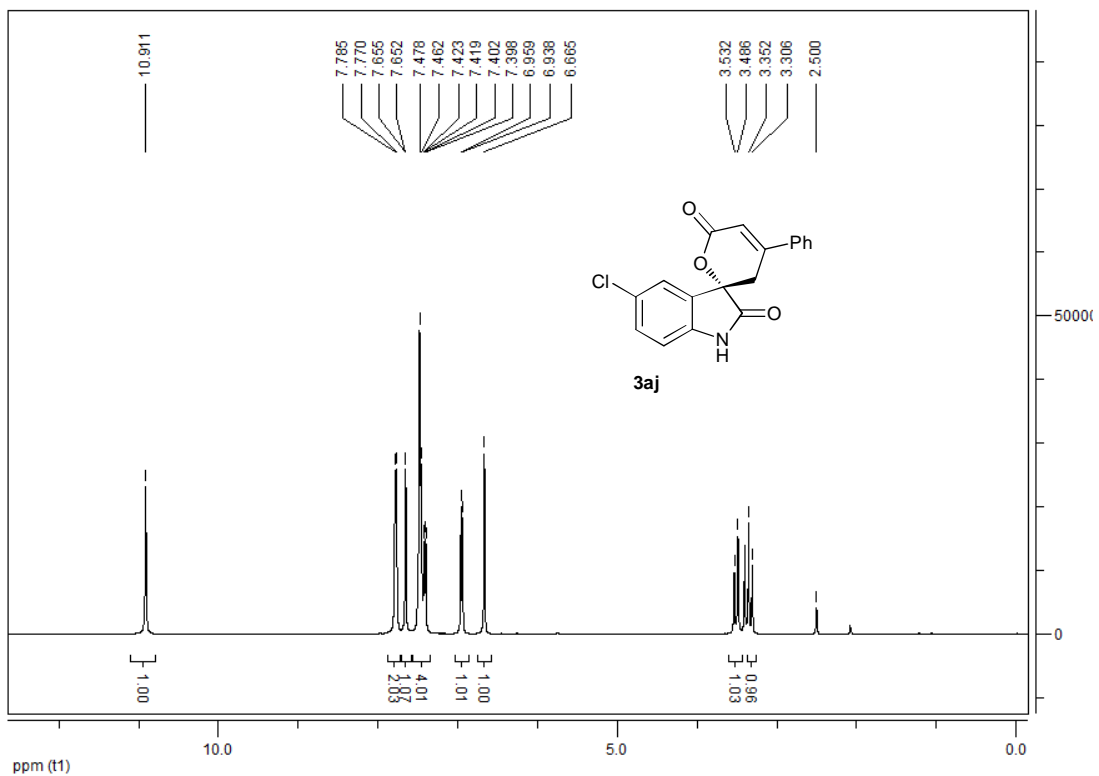


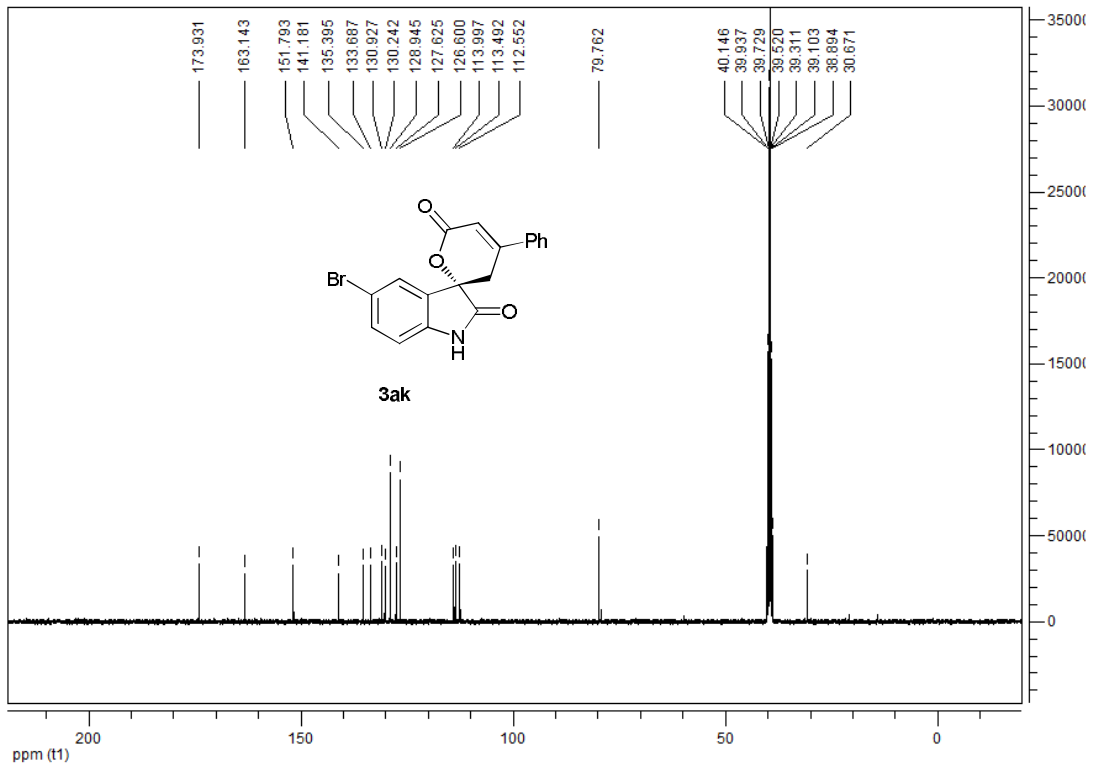
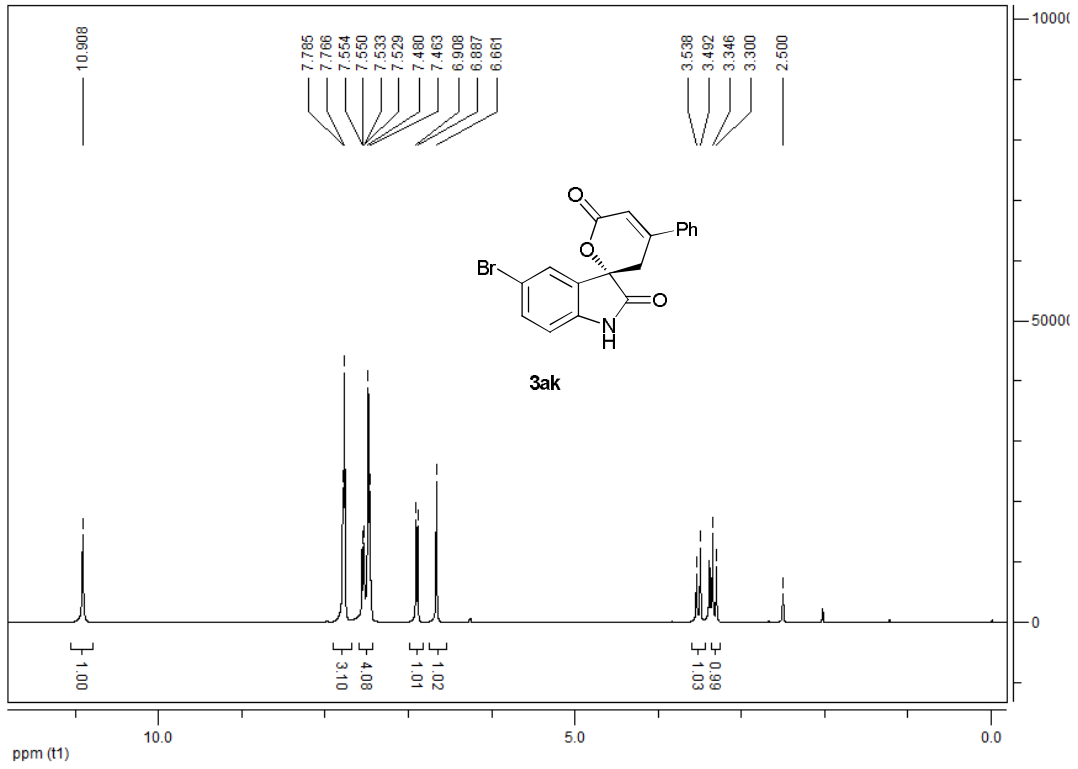


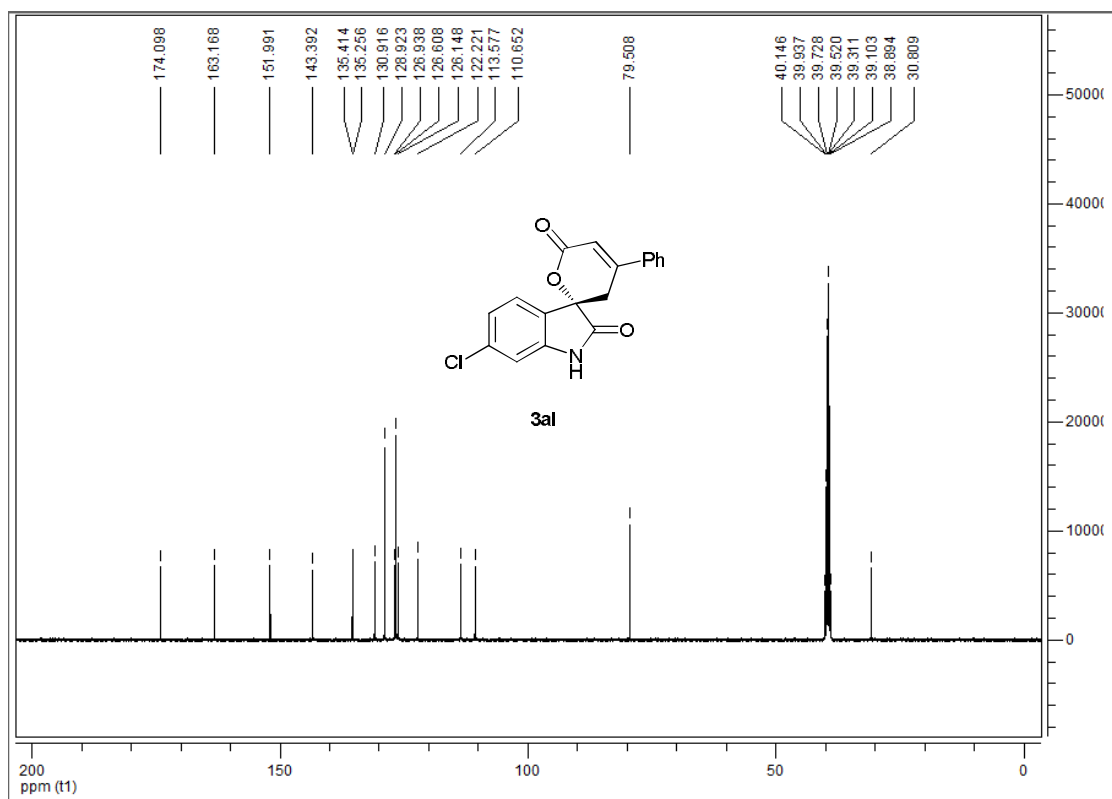
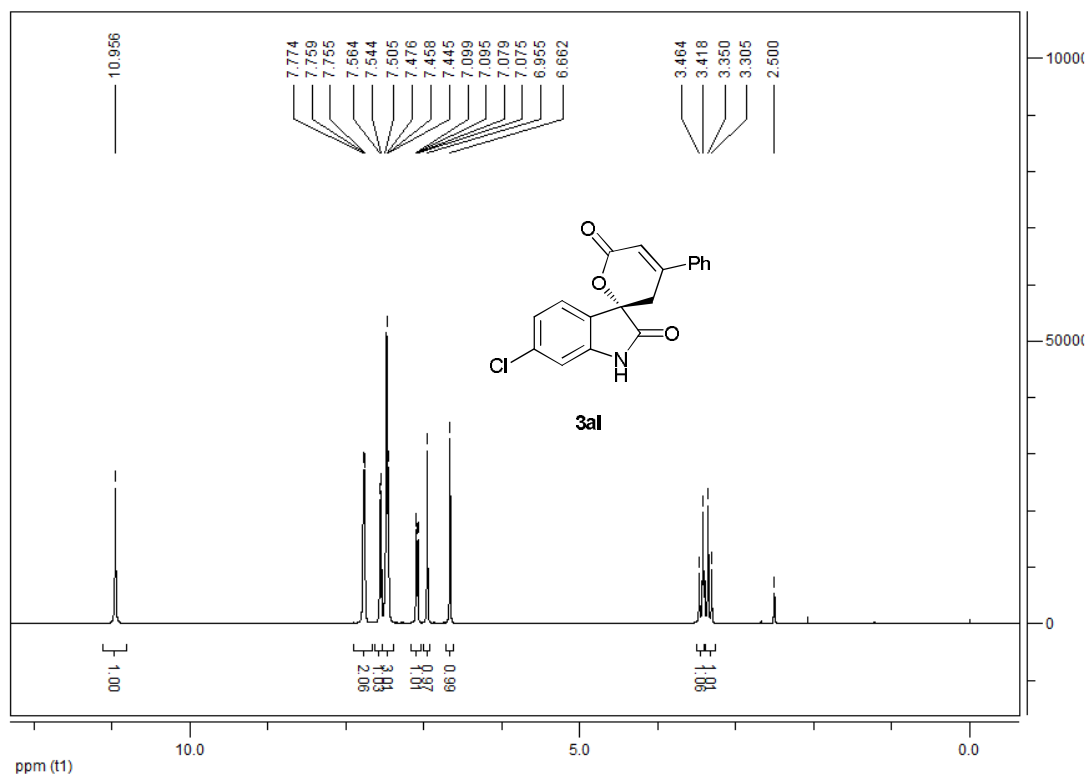


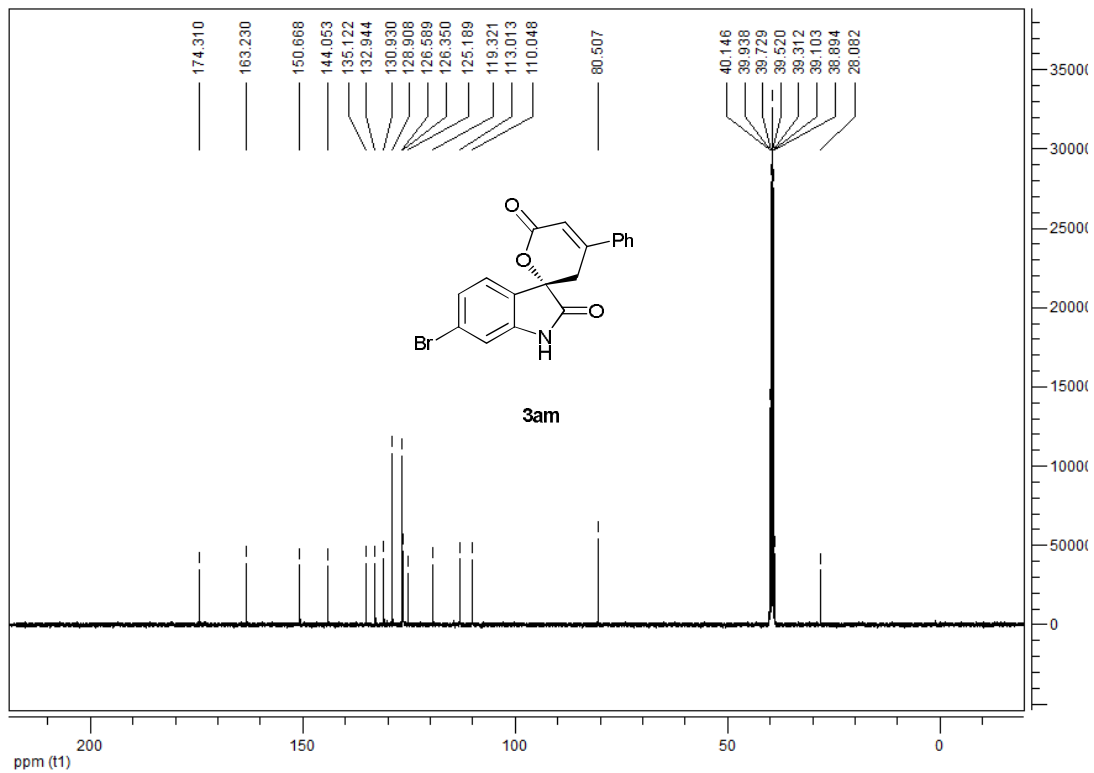
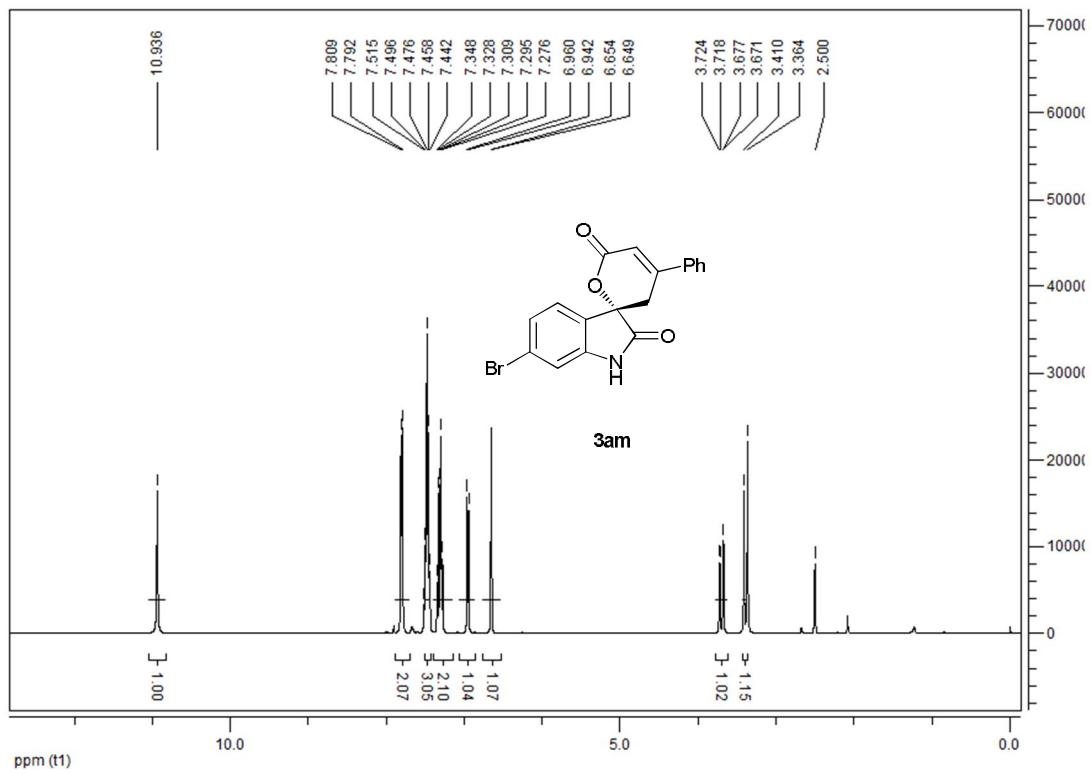


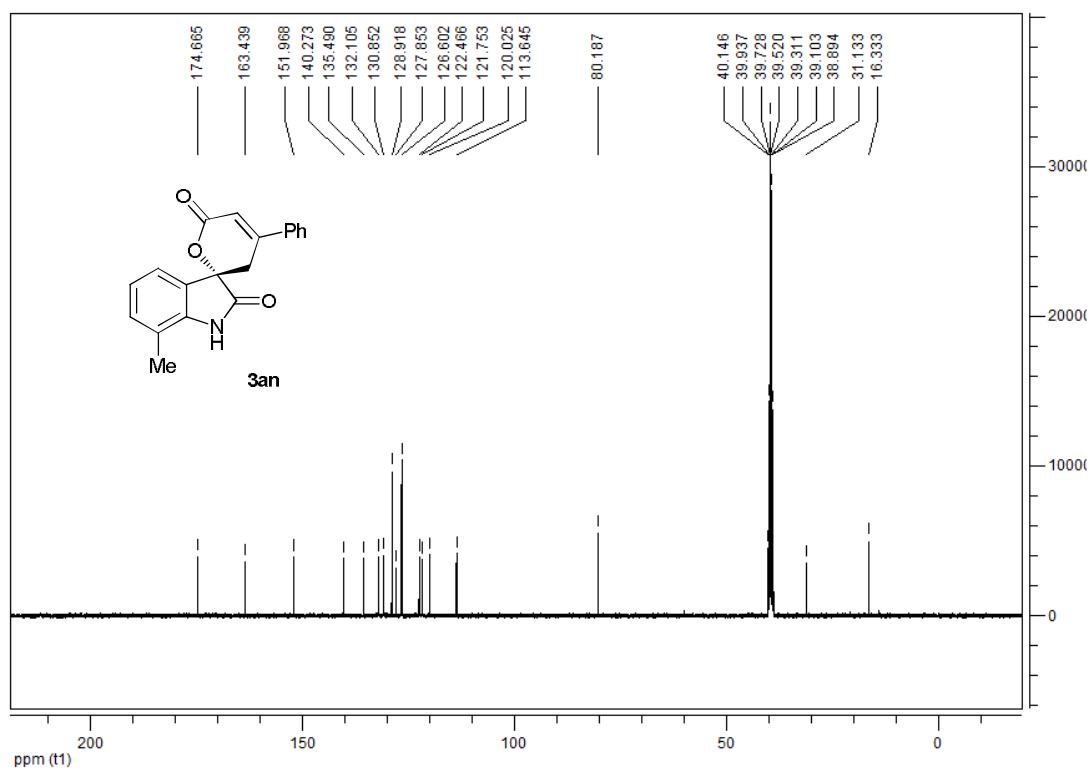
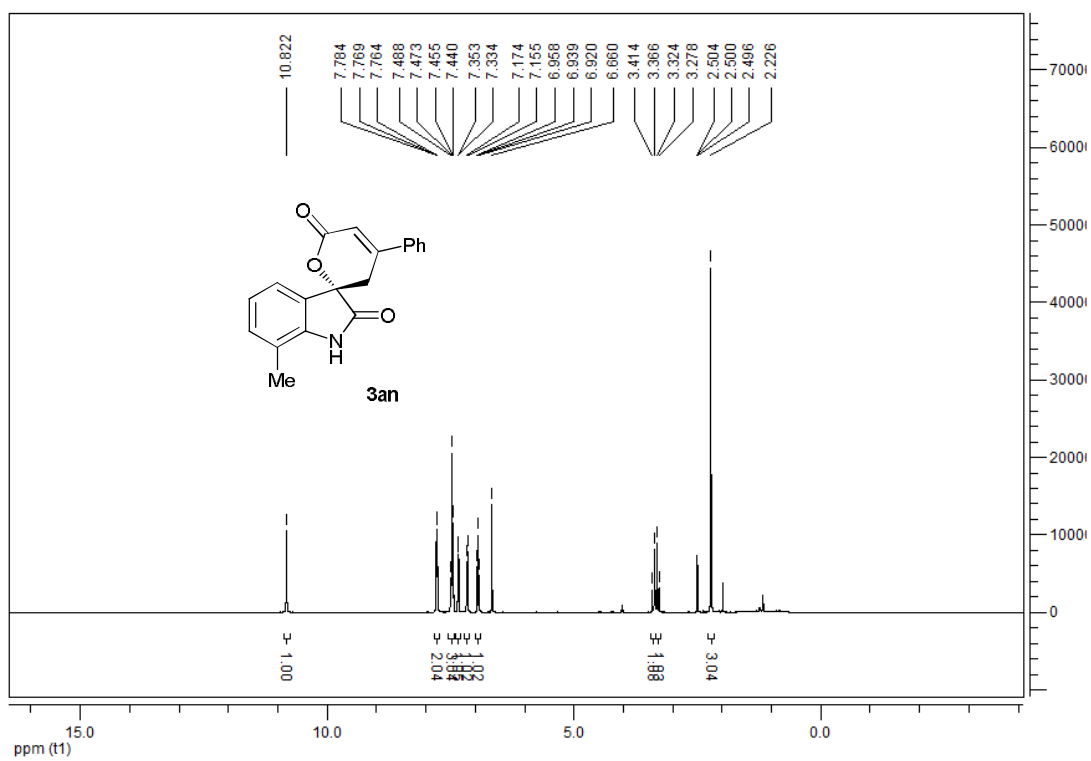


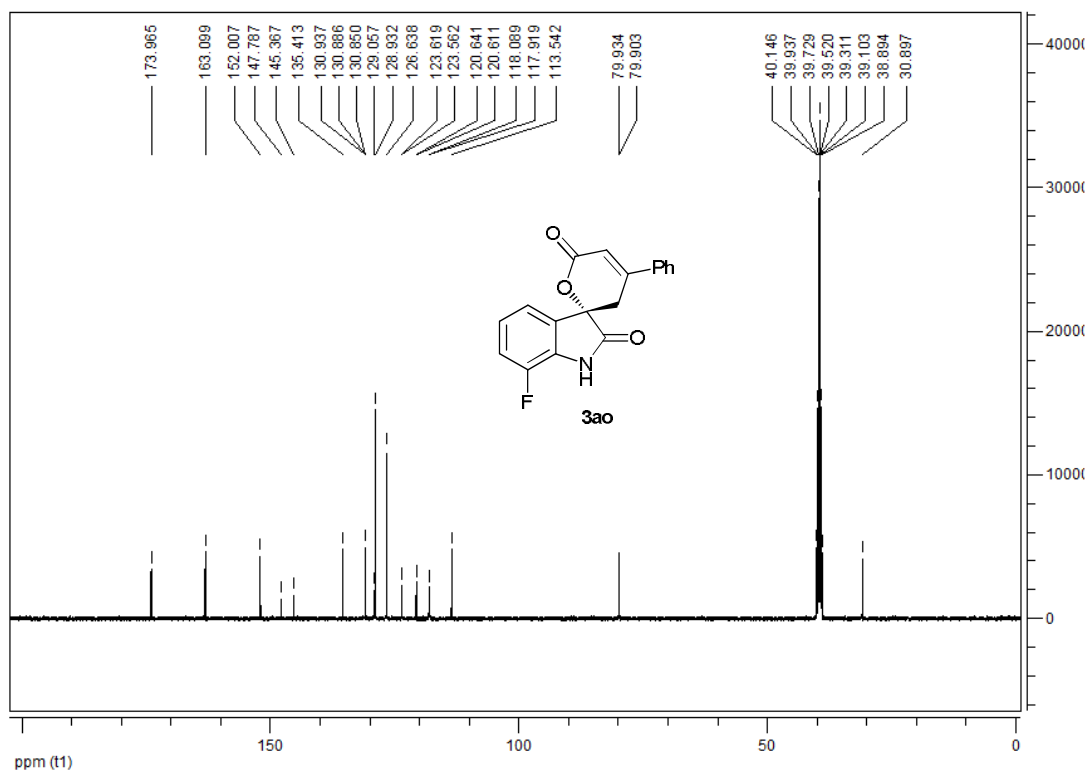
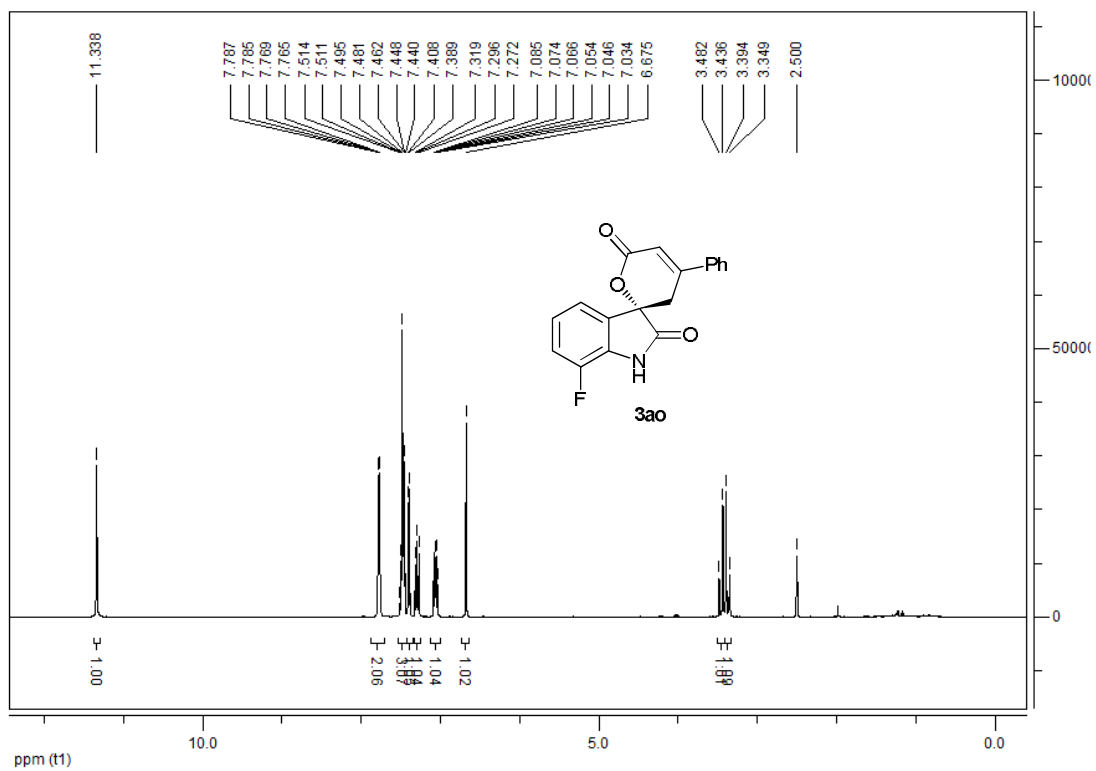


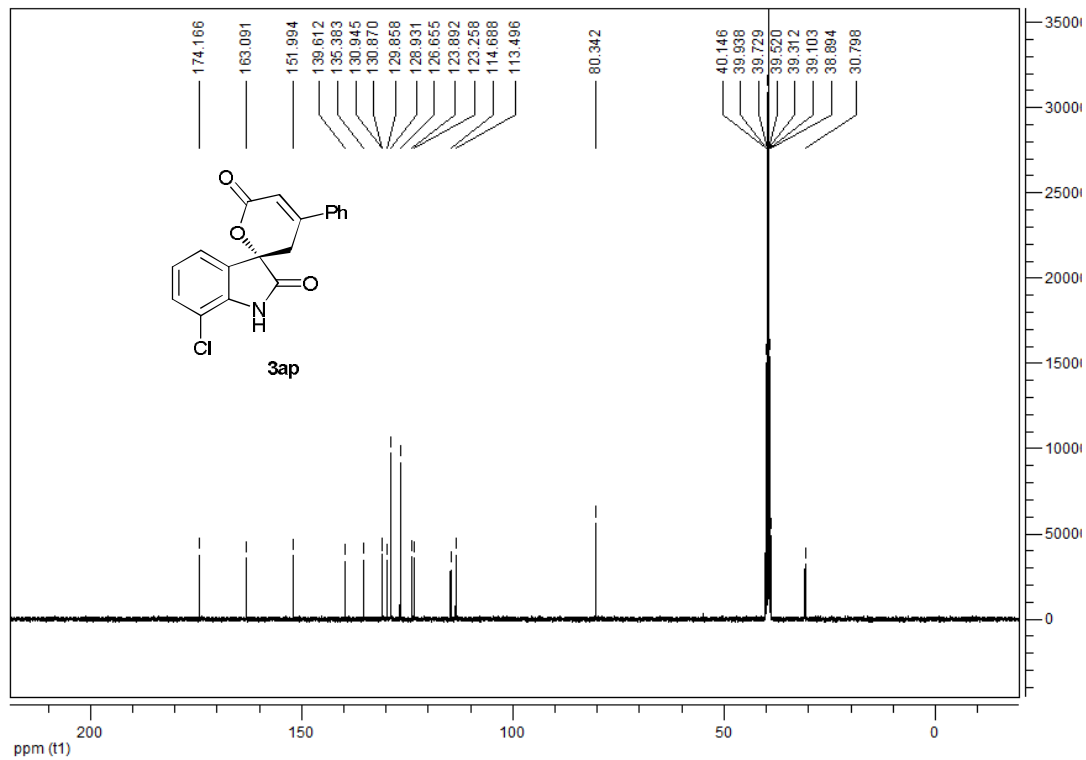
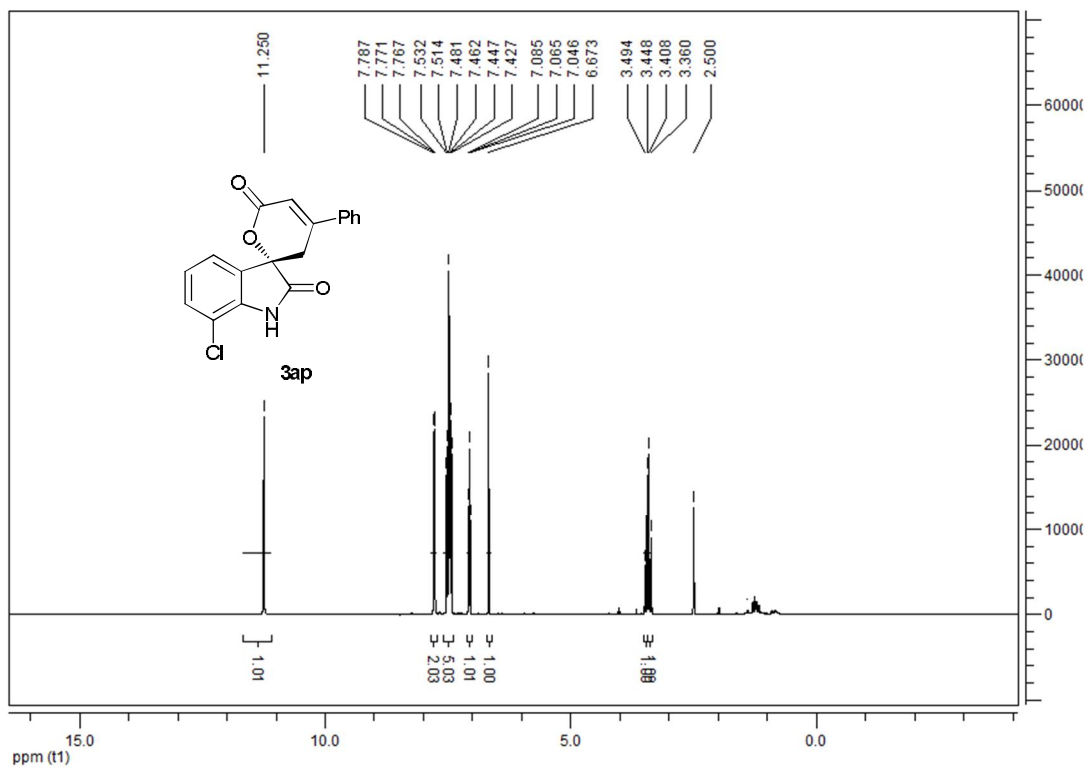


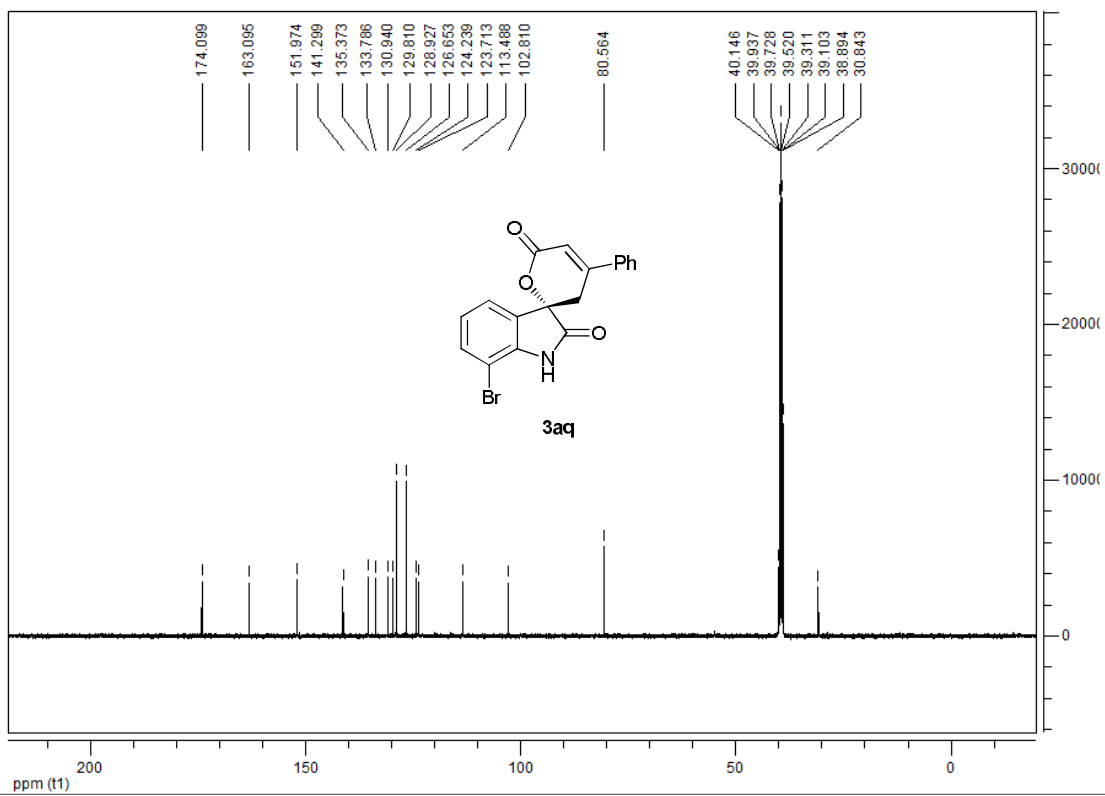
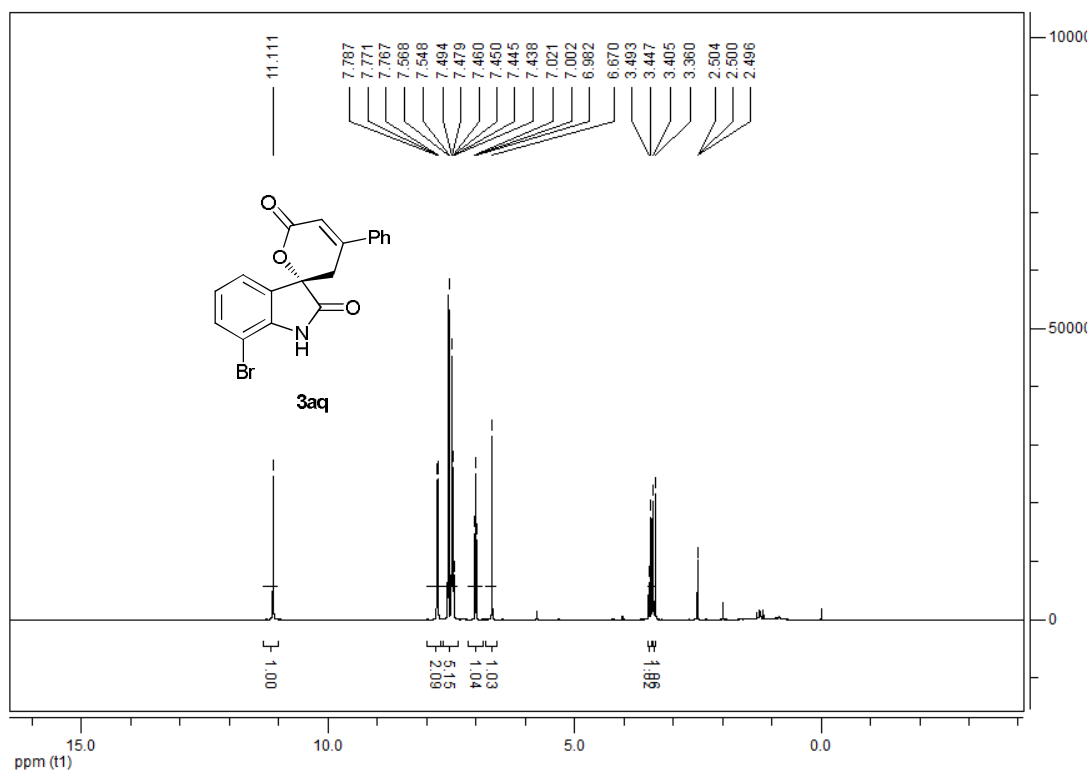


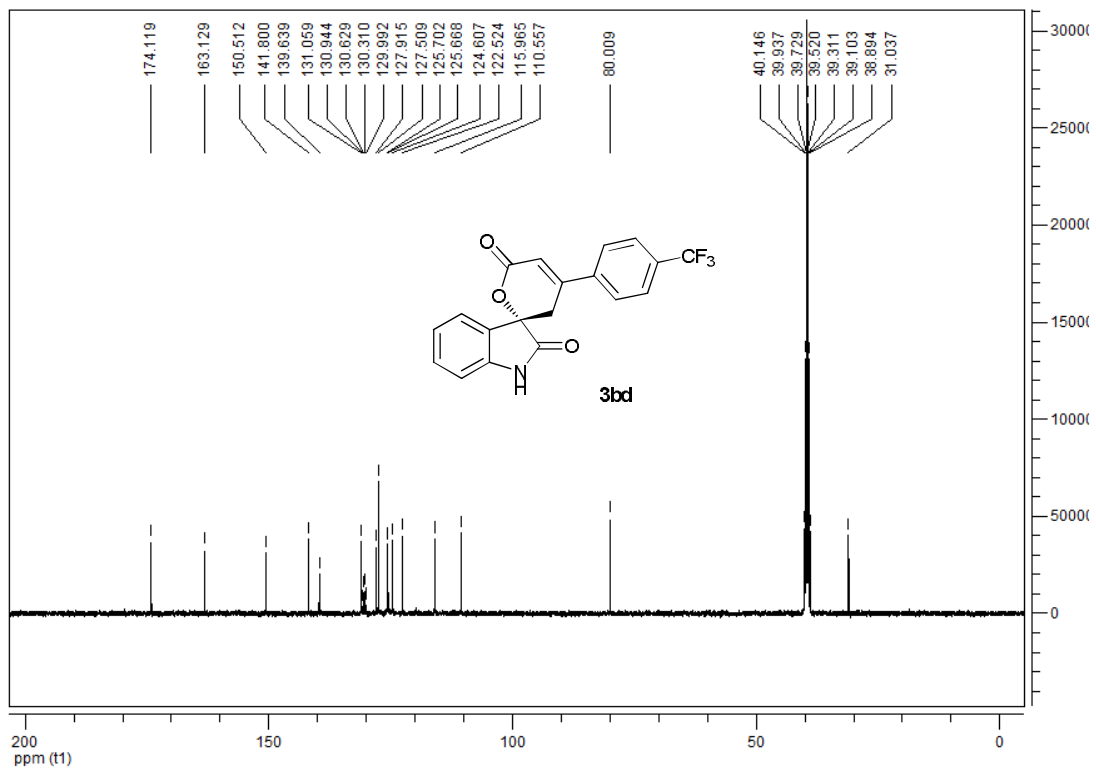
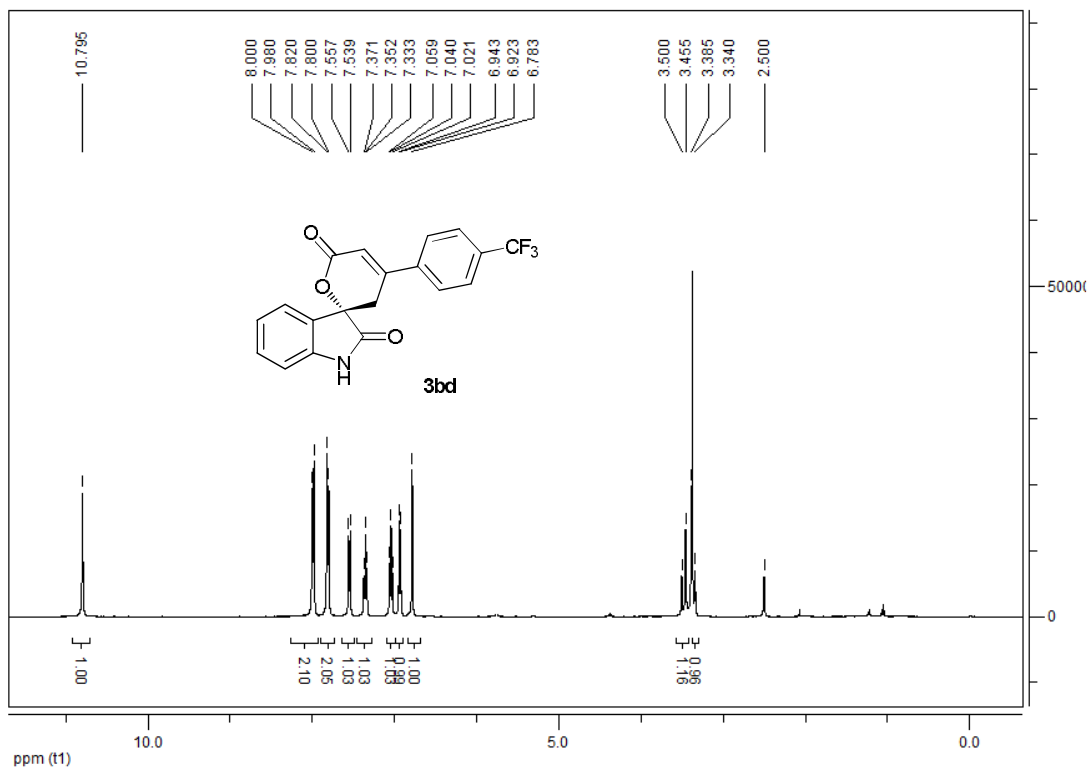


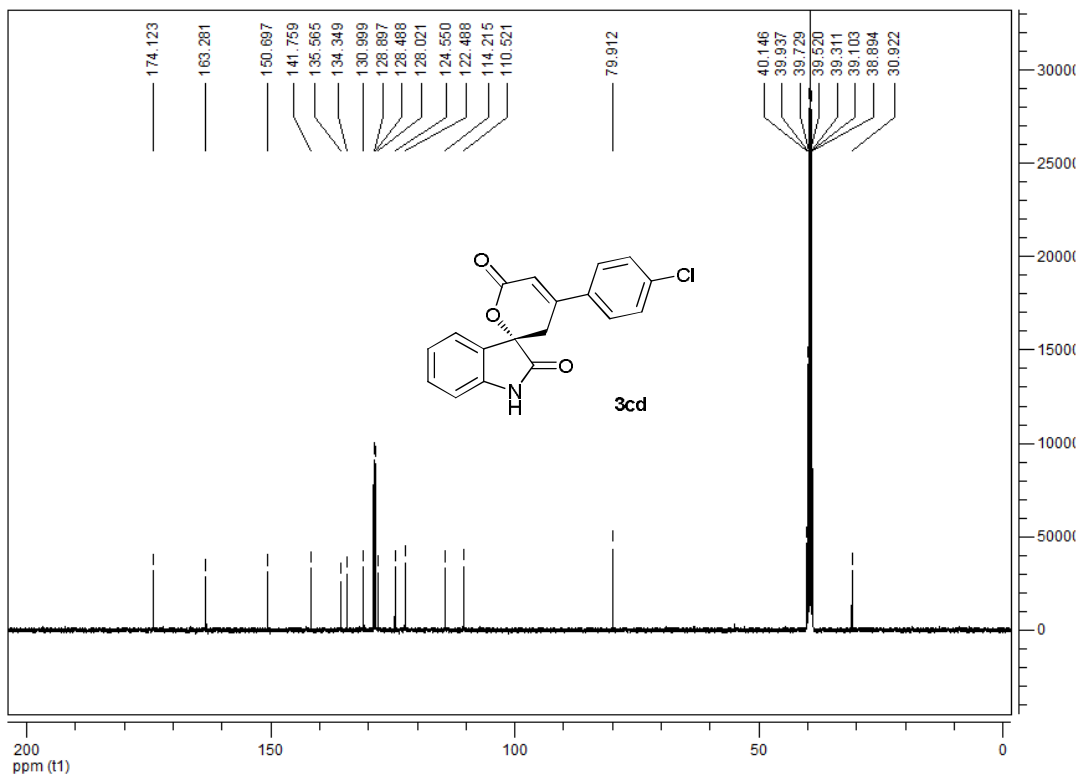
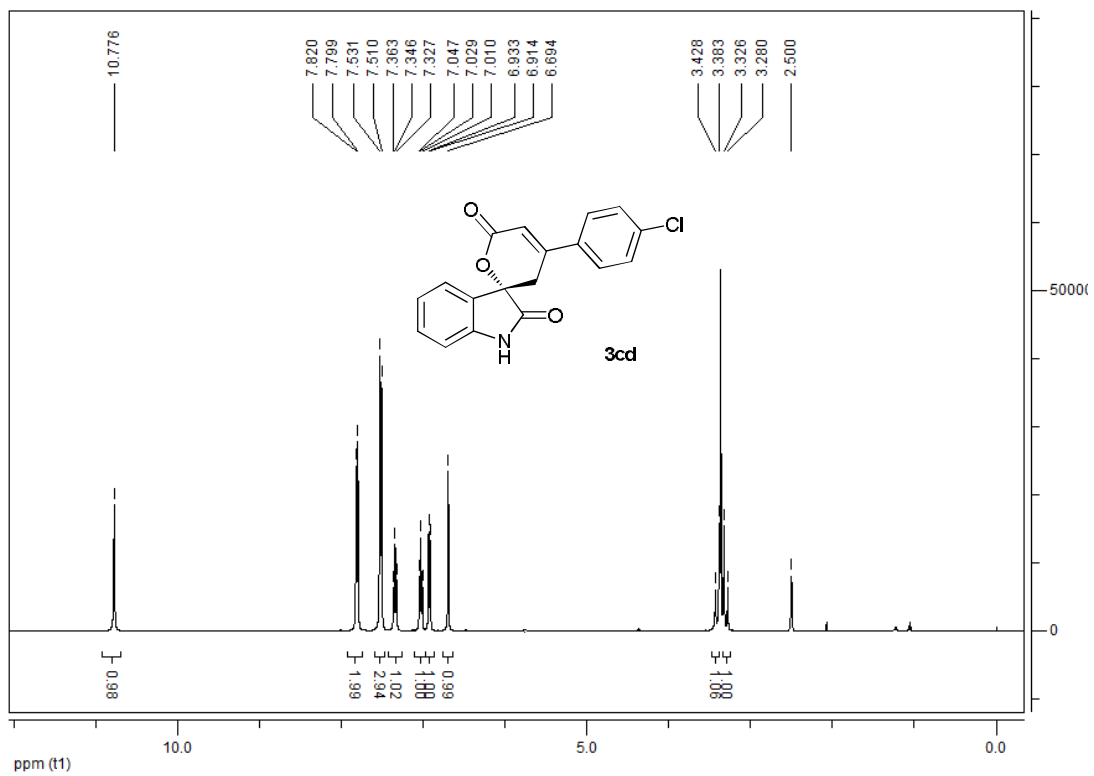


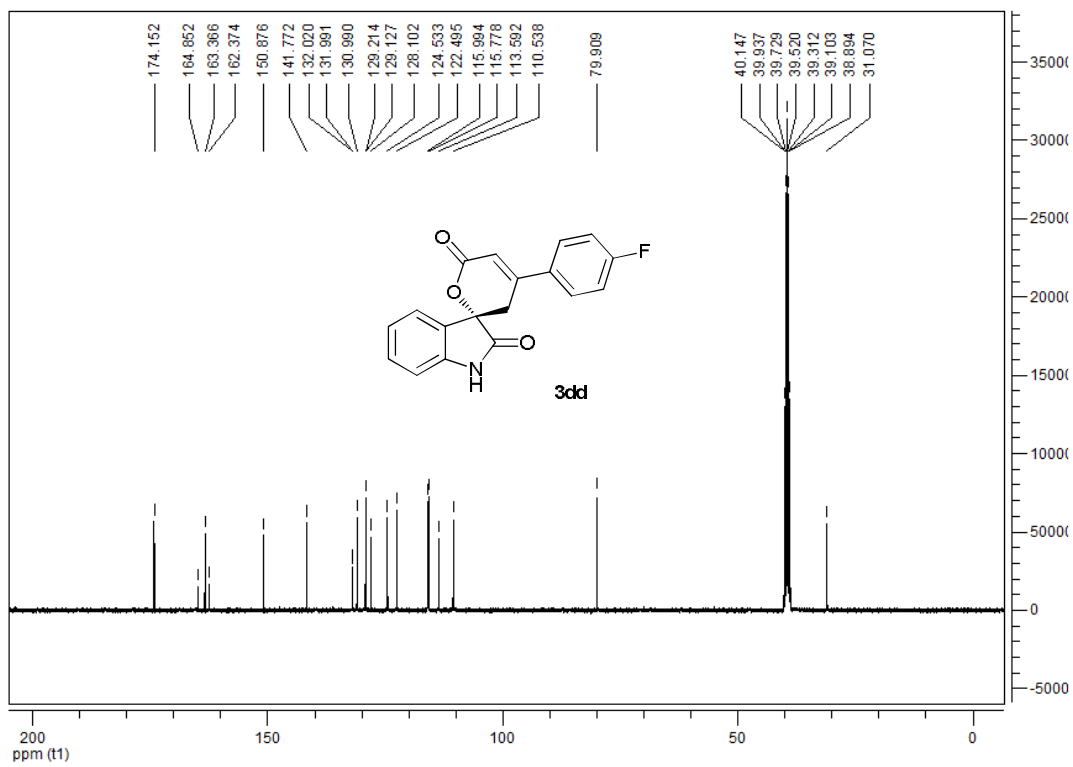
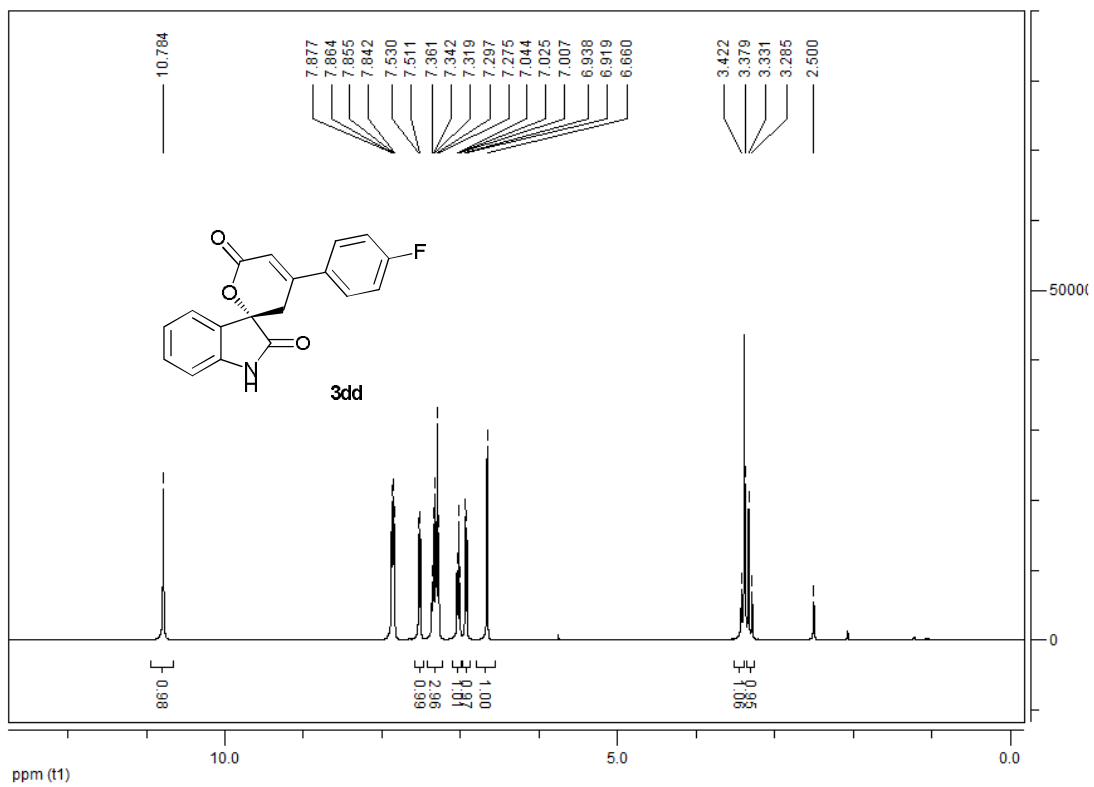


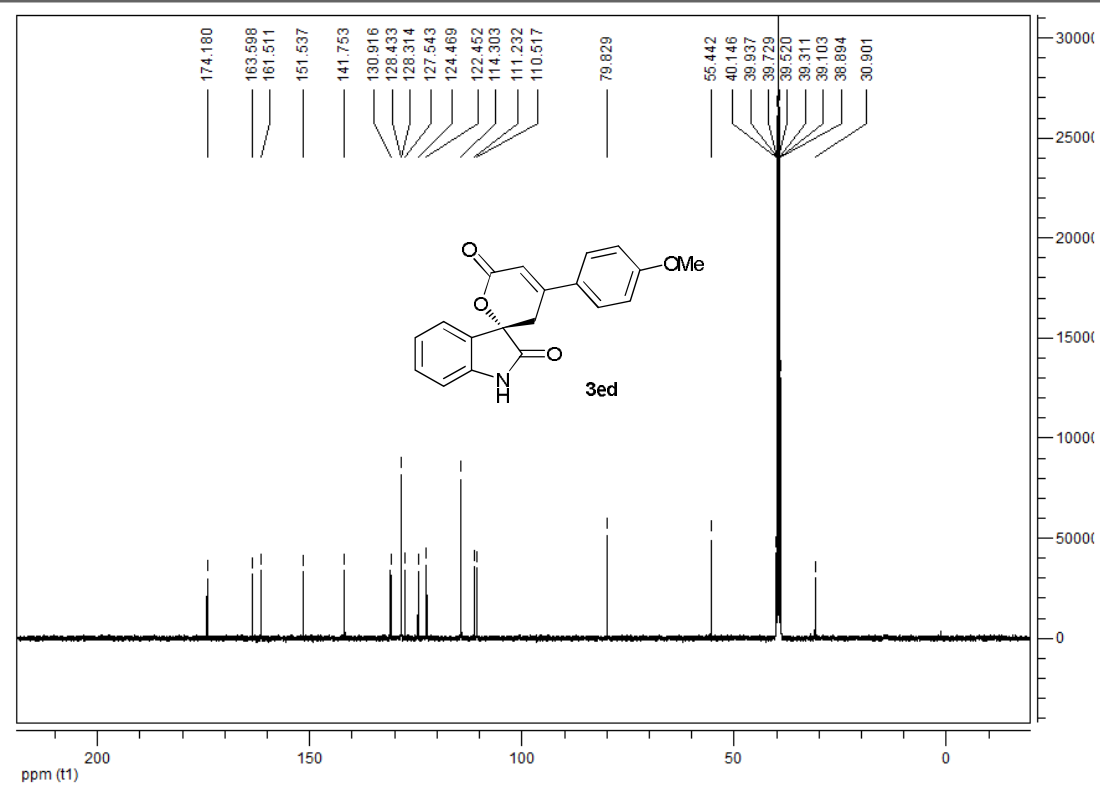
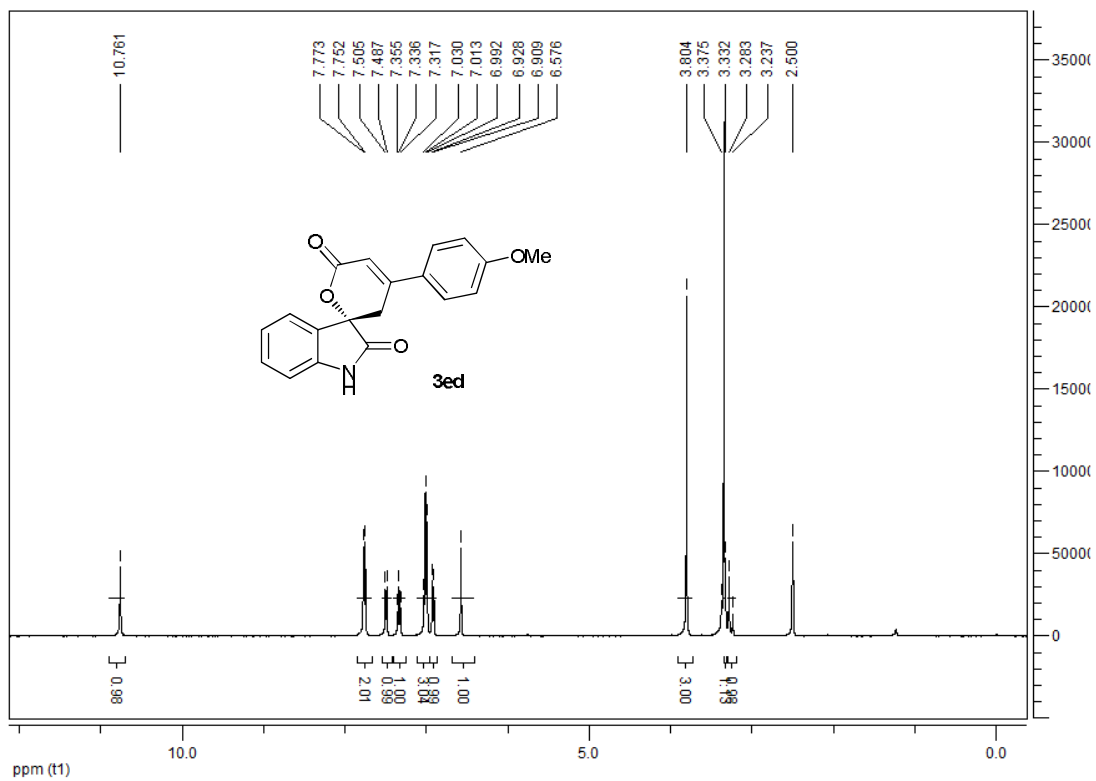


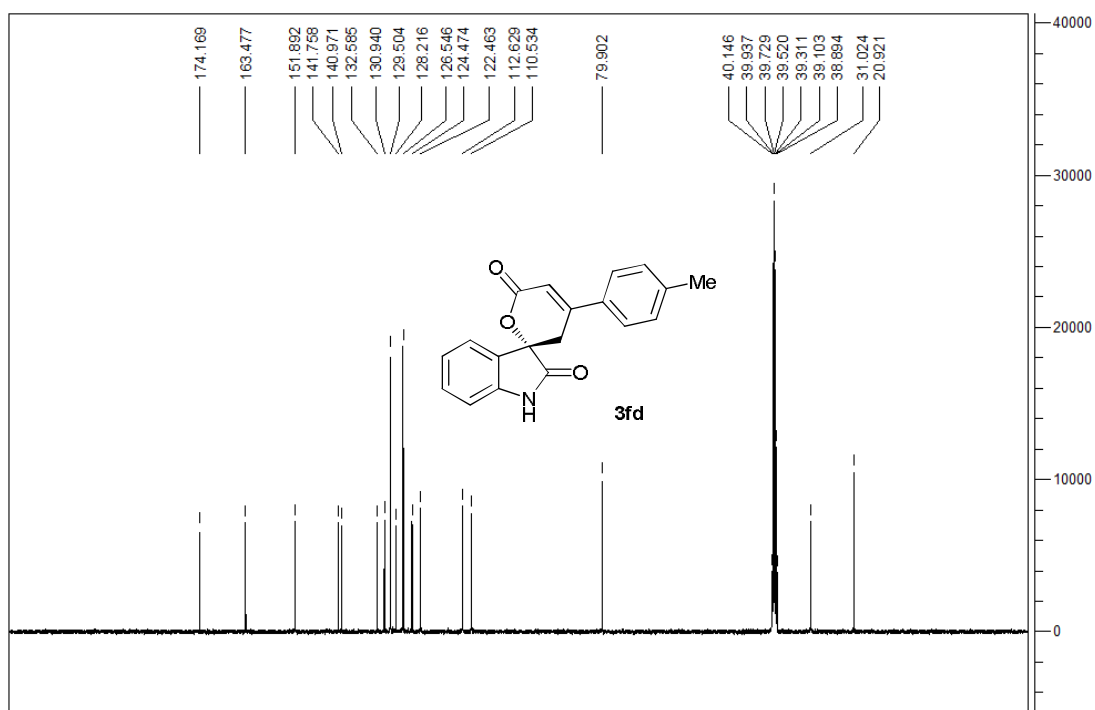
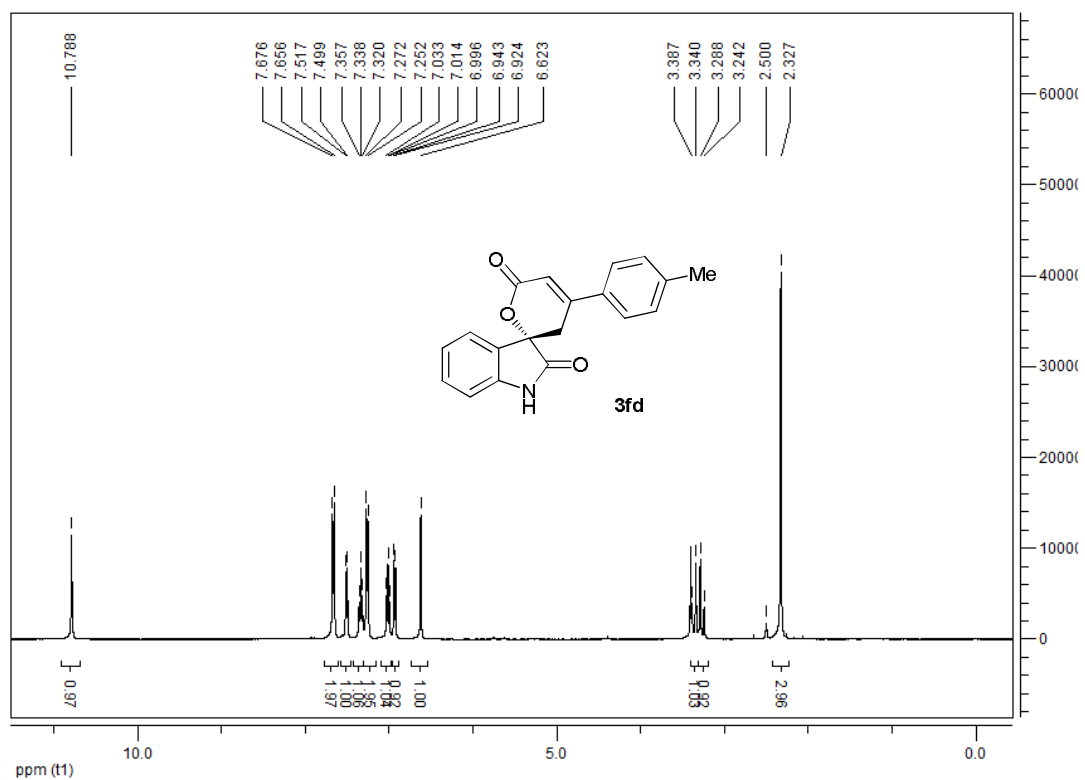


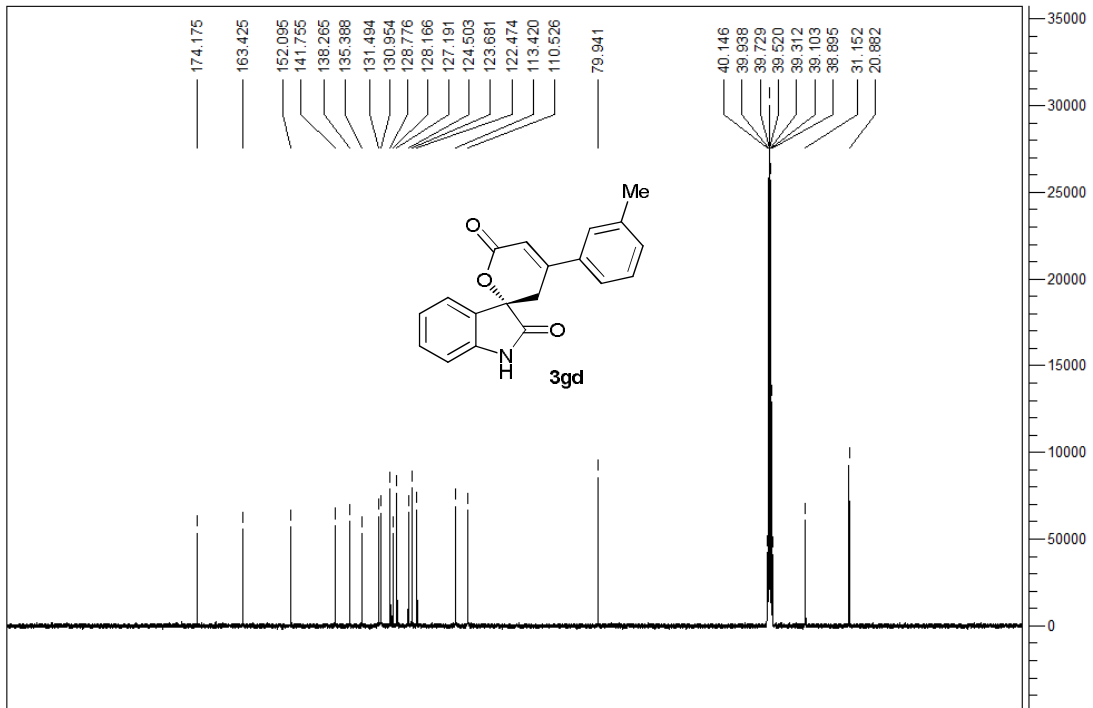
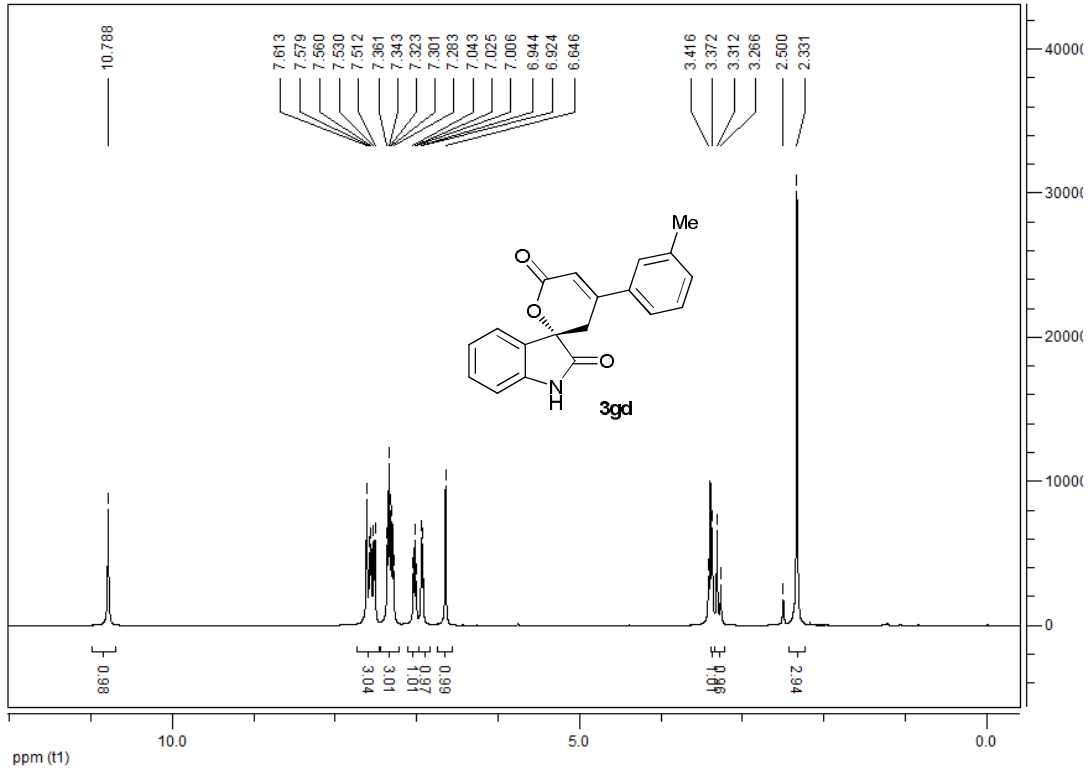


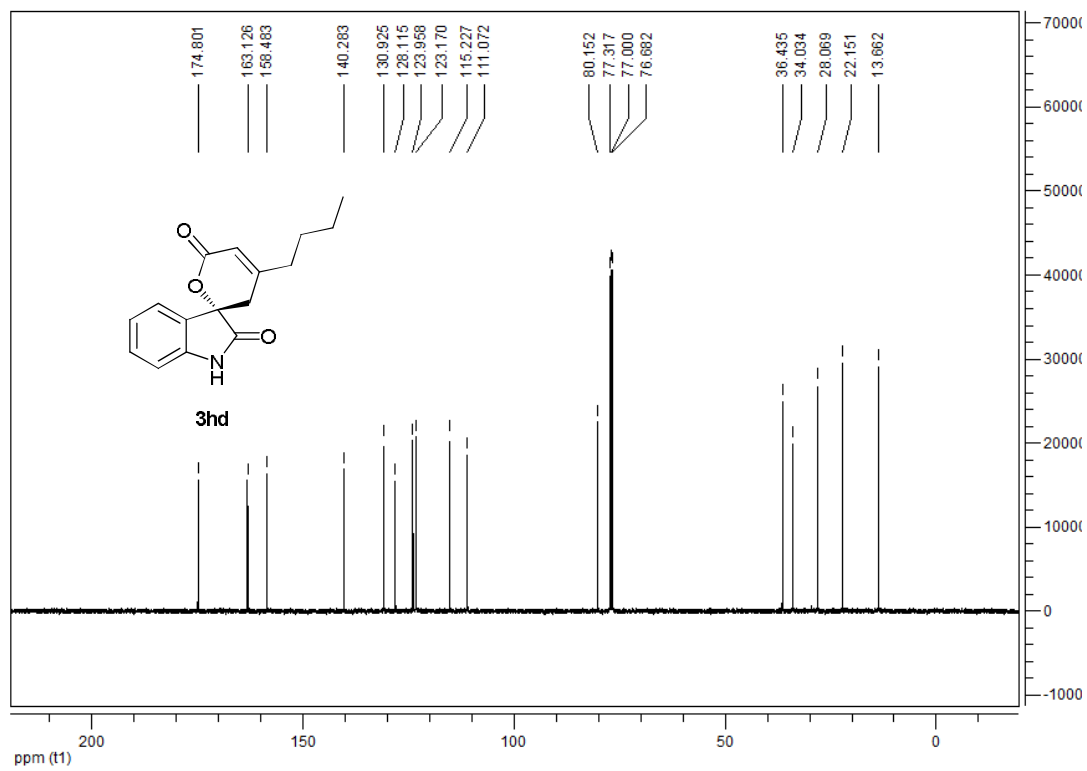
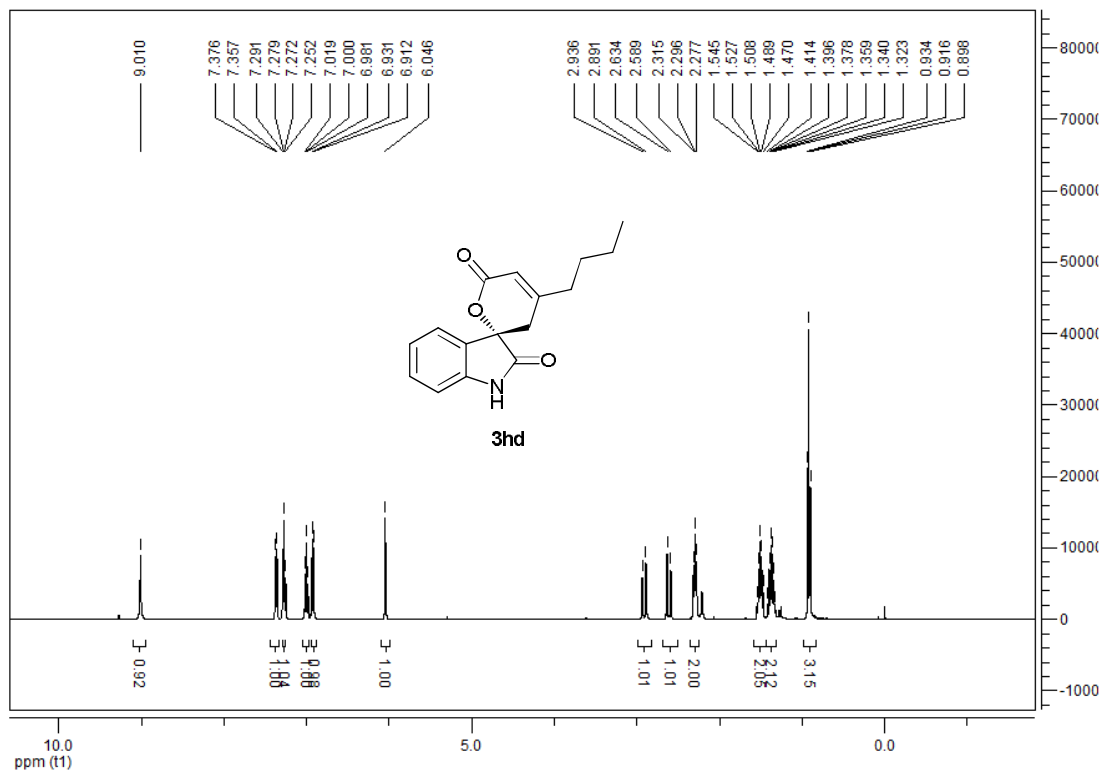




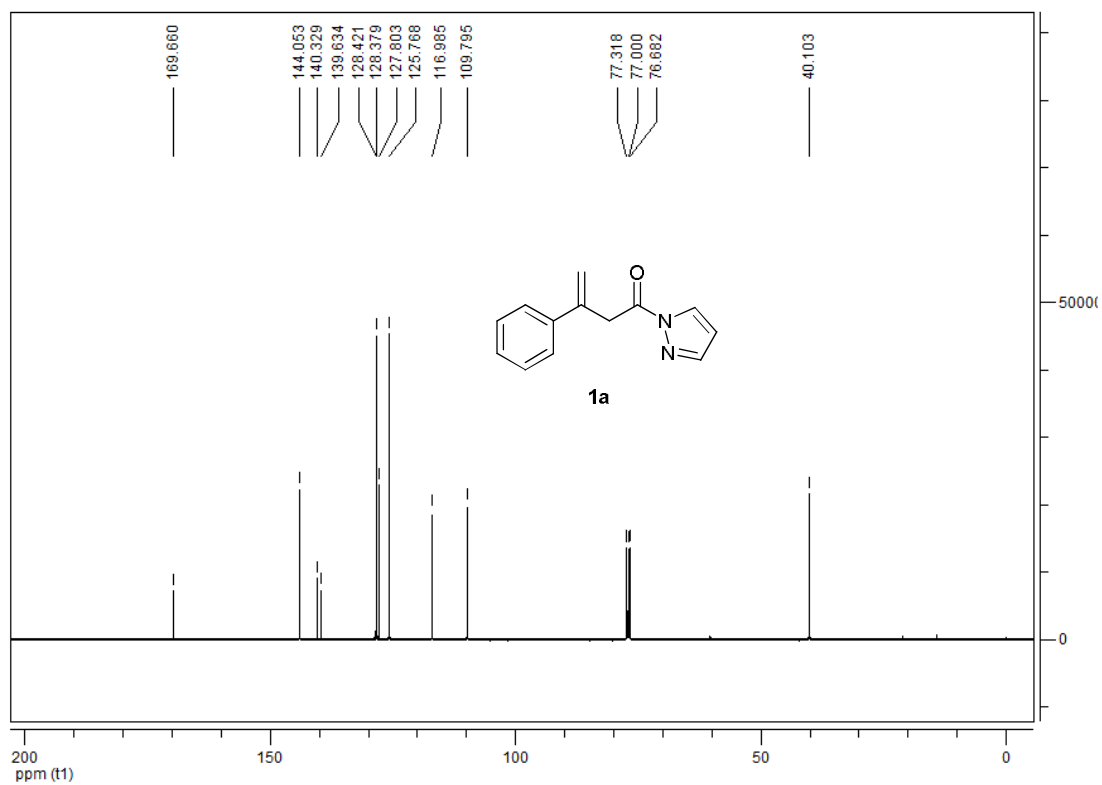
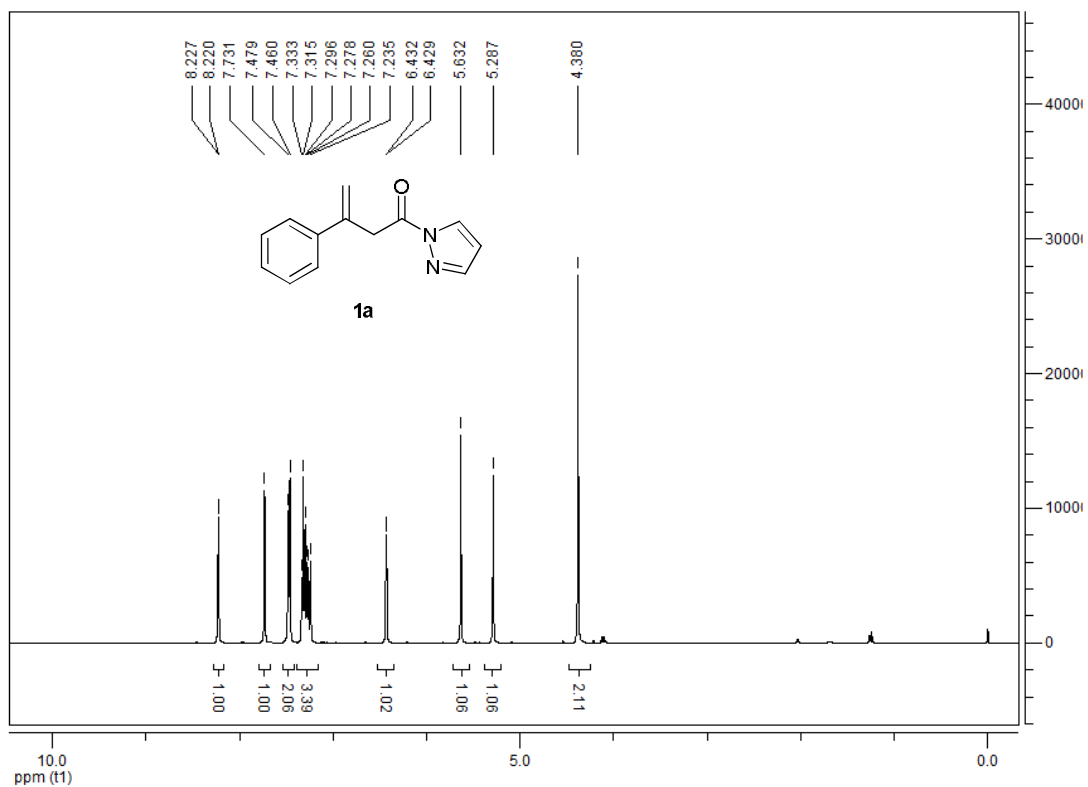


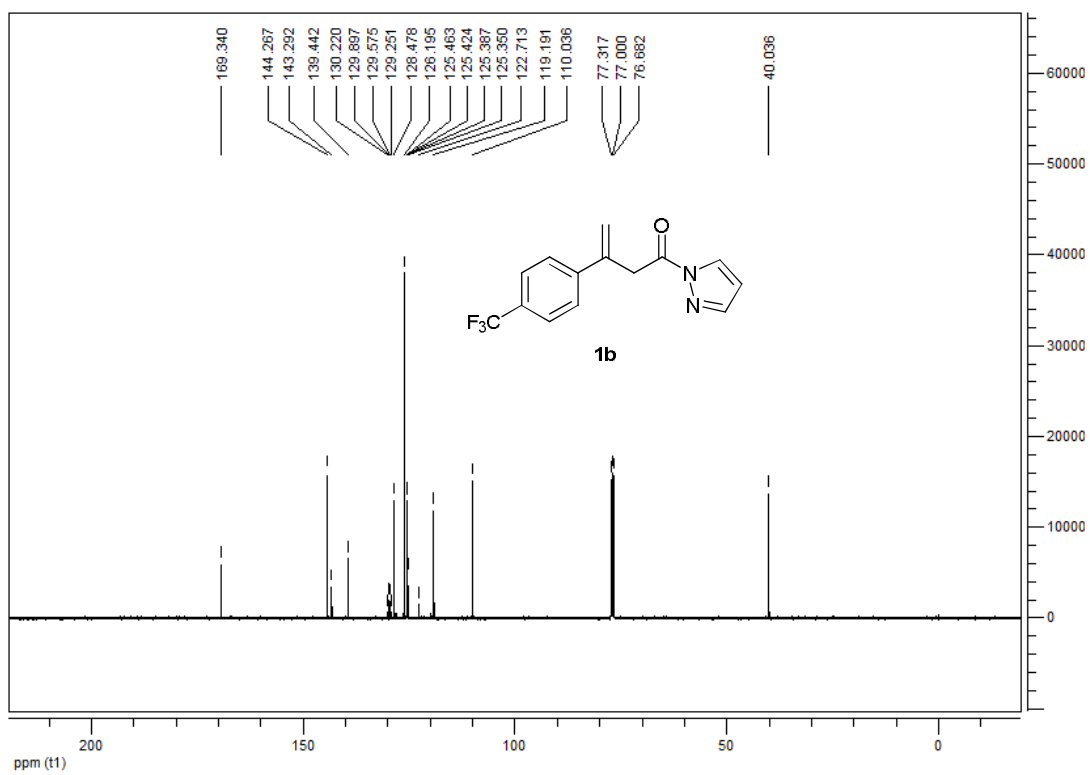
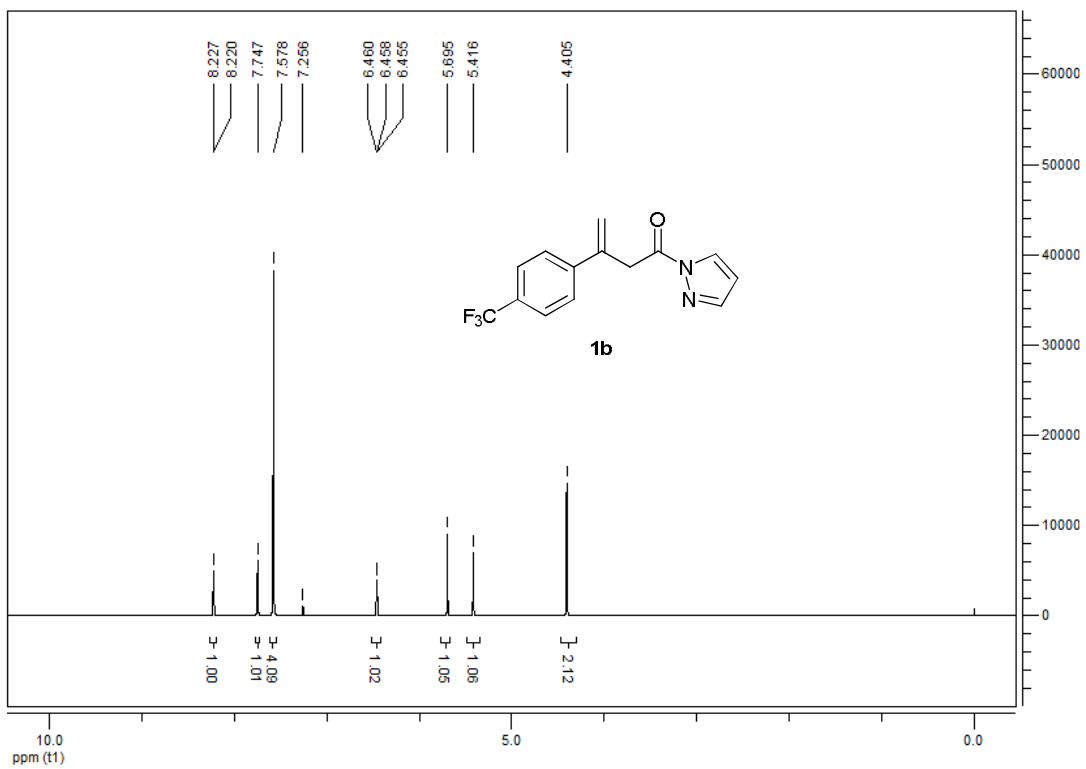


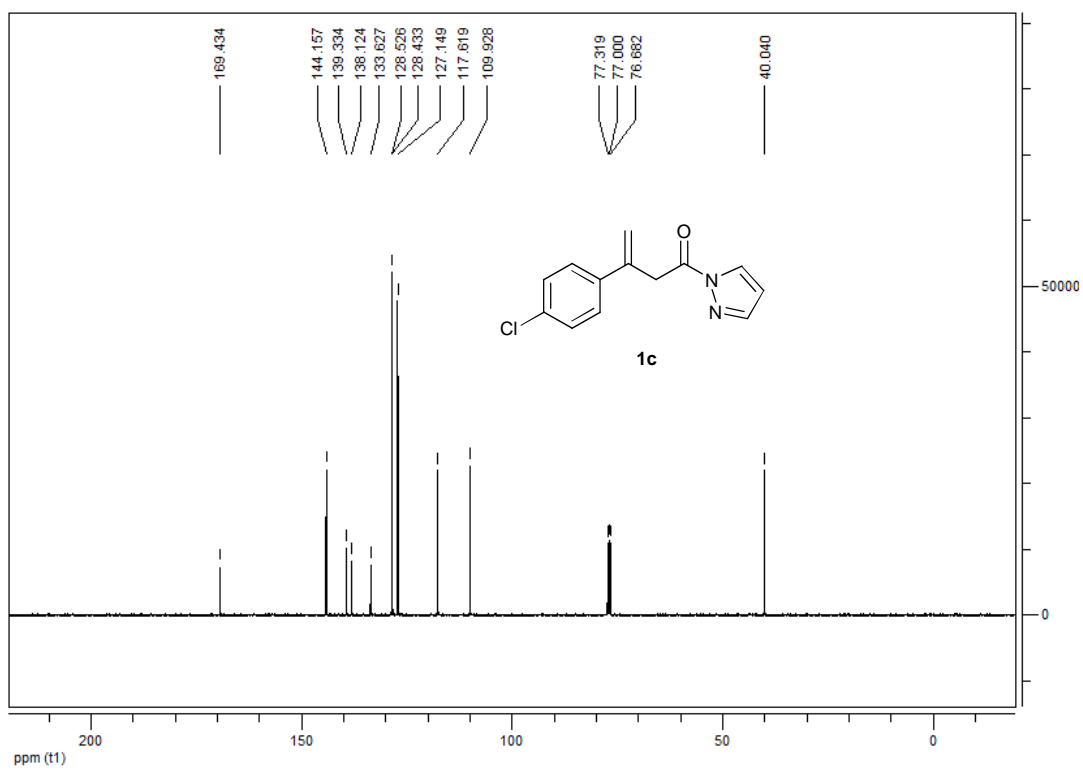
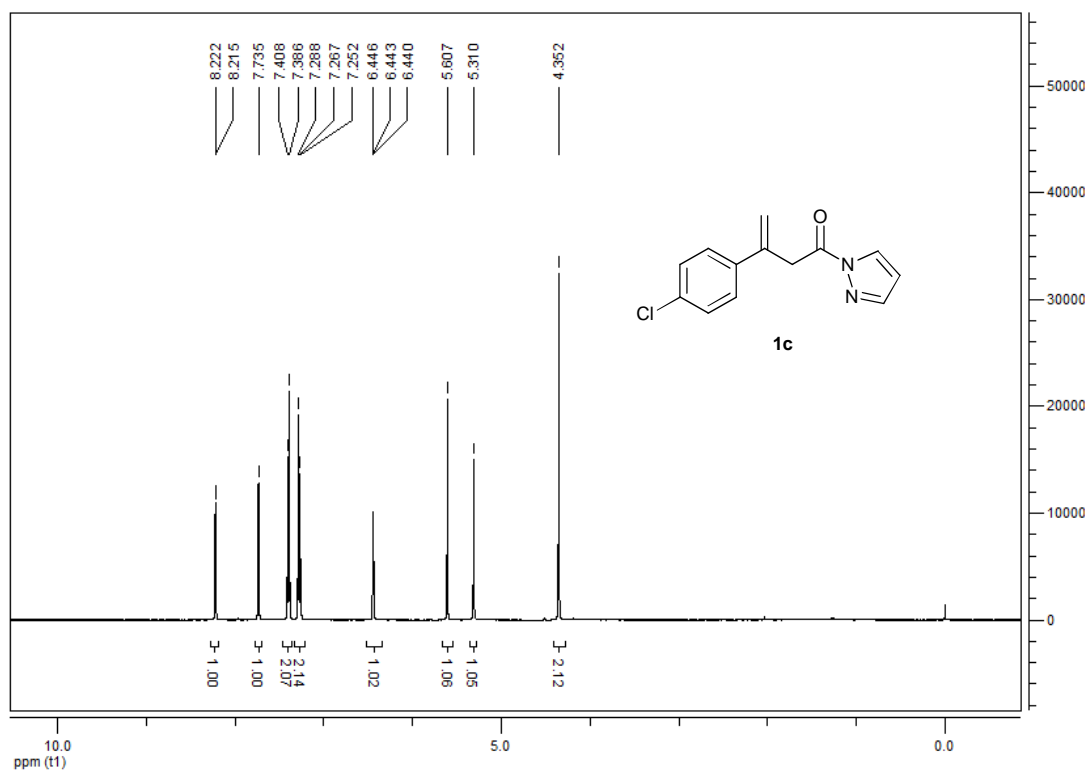


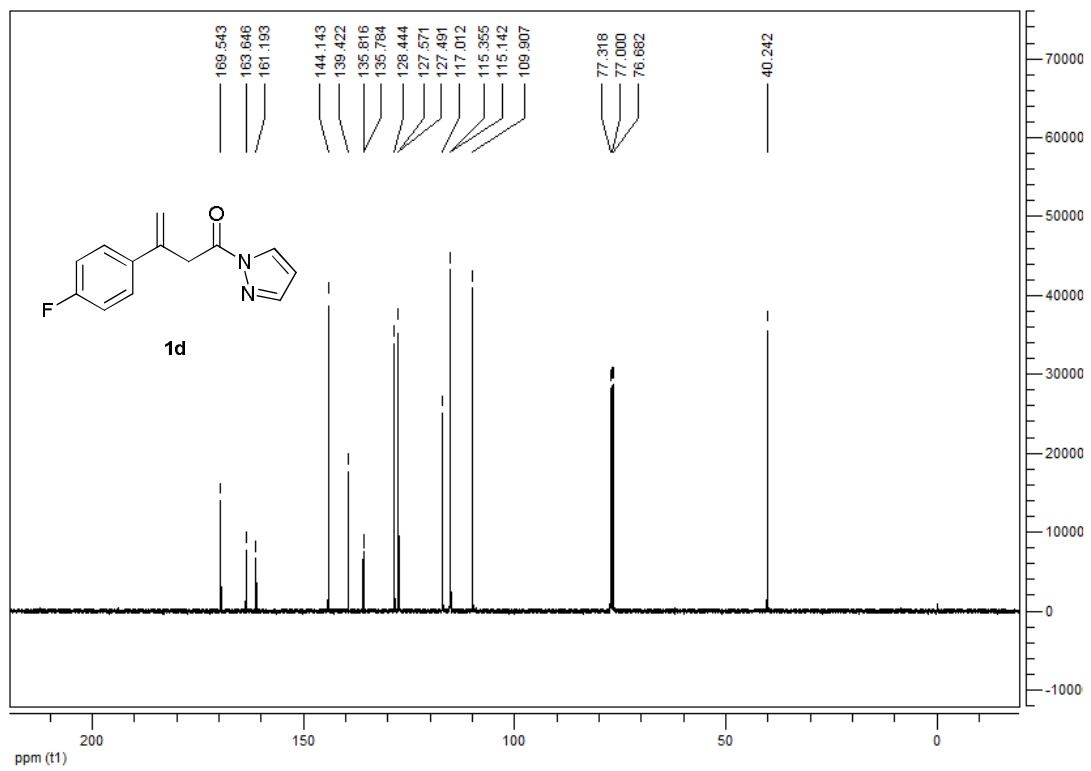
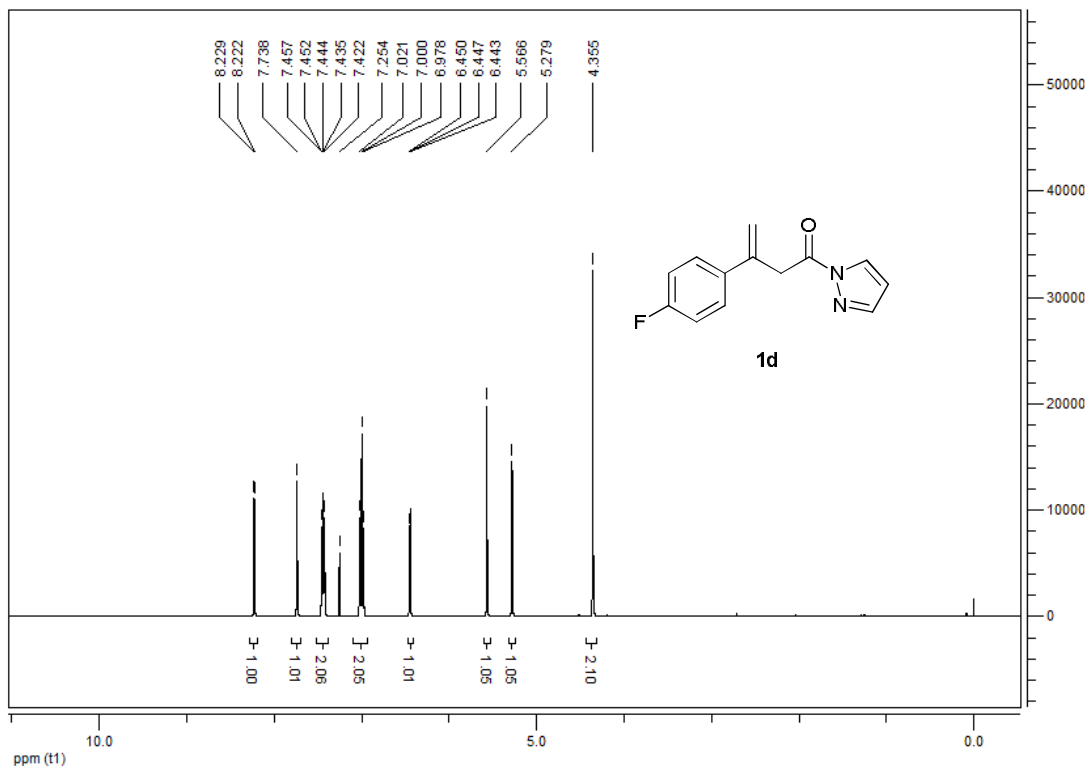


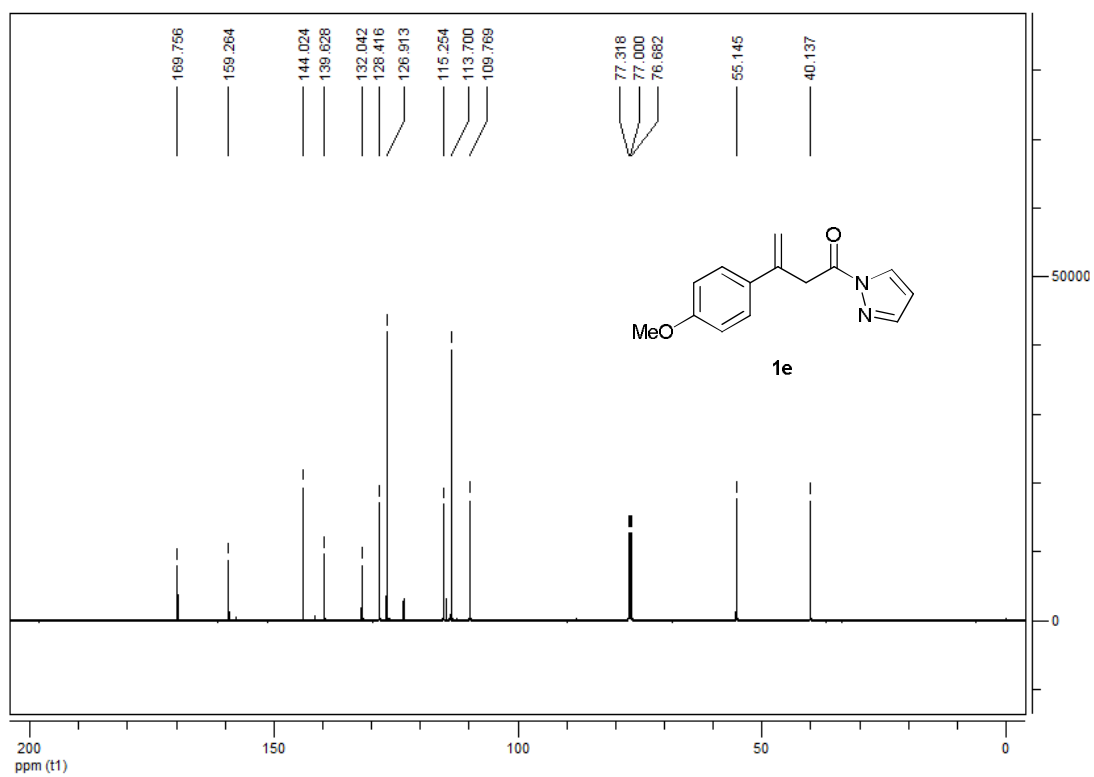
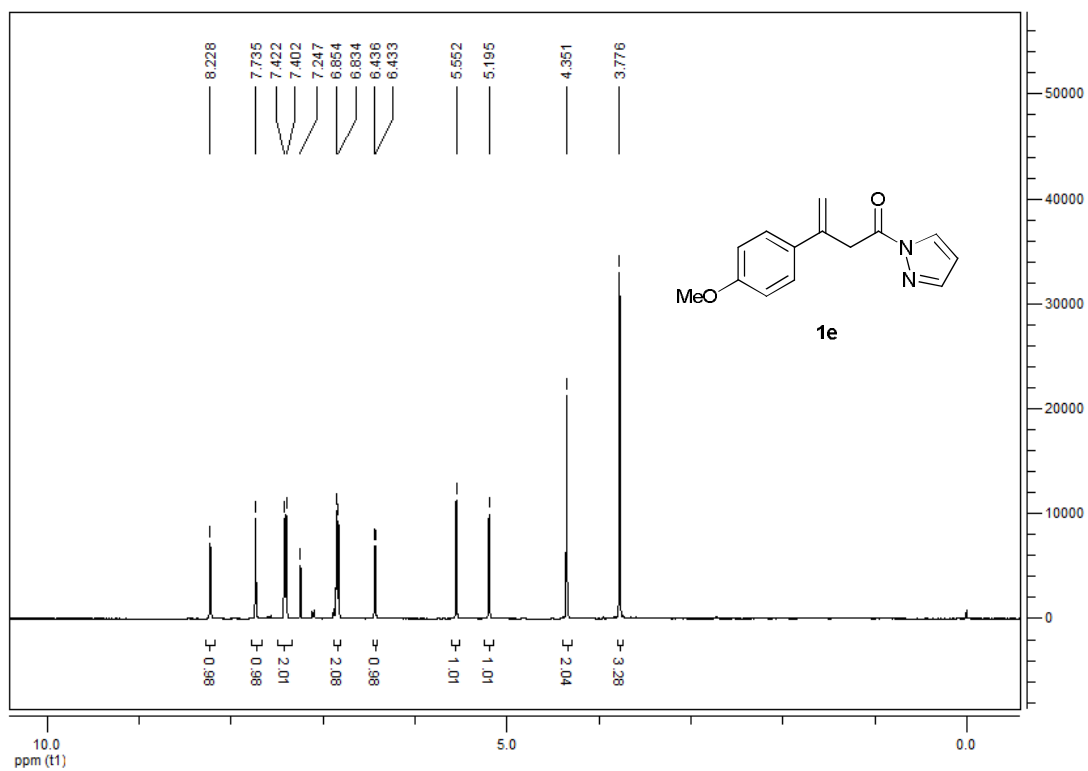
7. Copies of NMR Spectra of the the Substrates

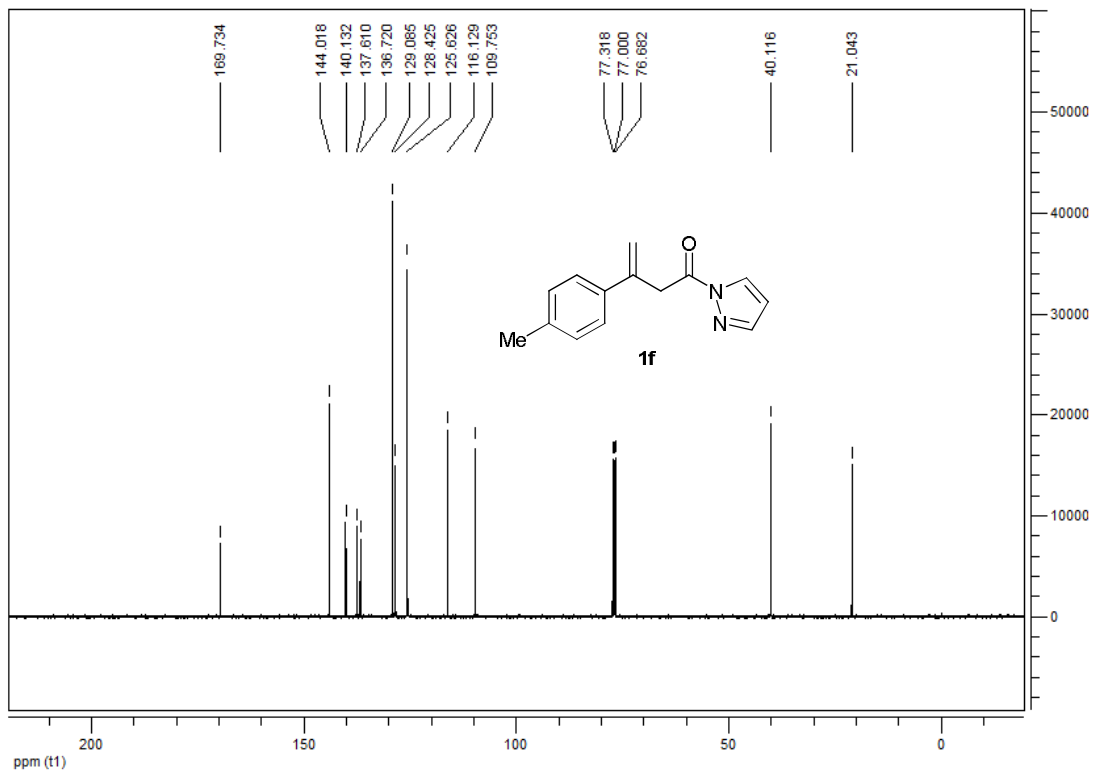
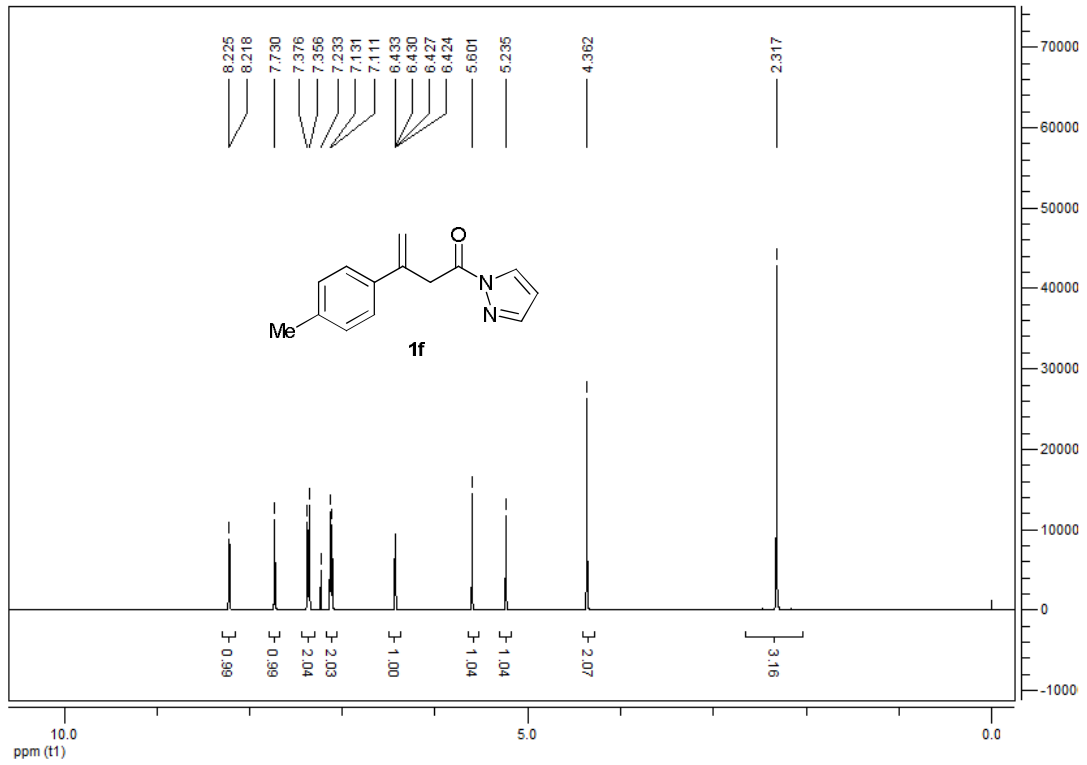


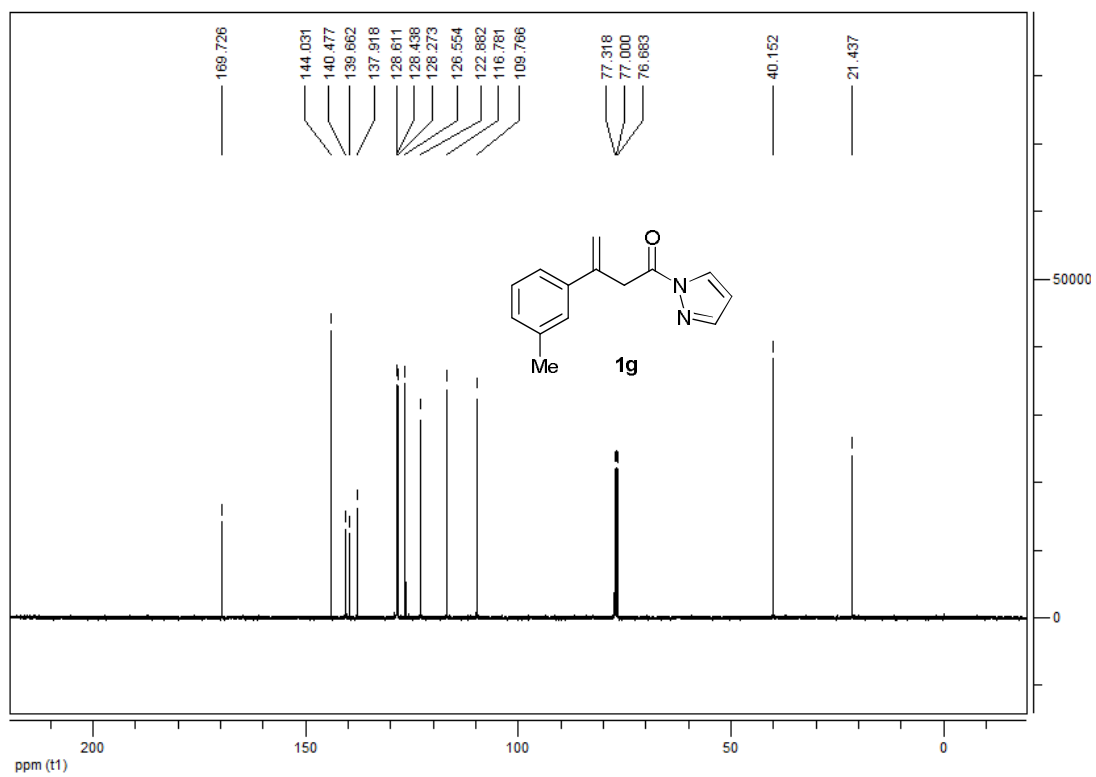
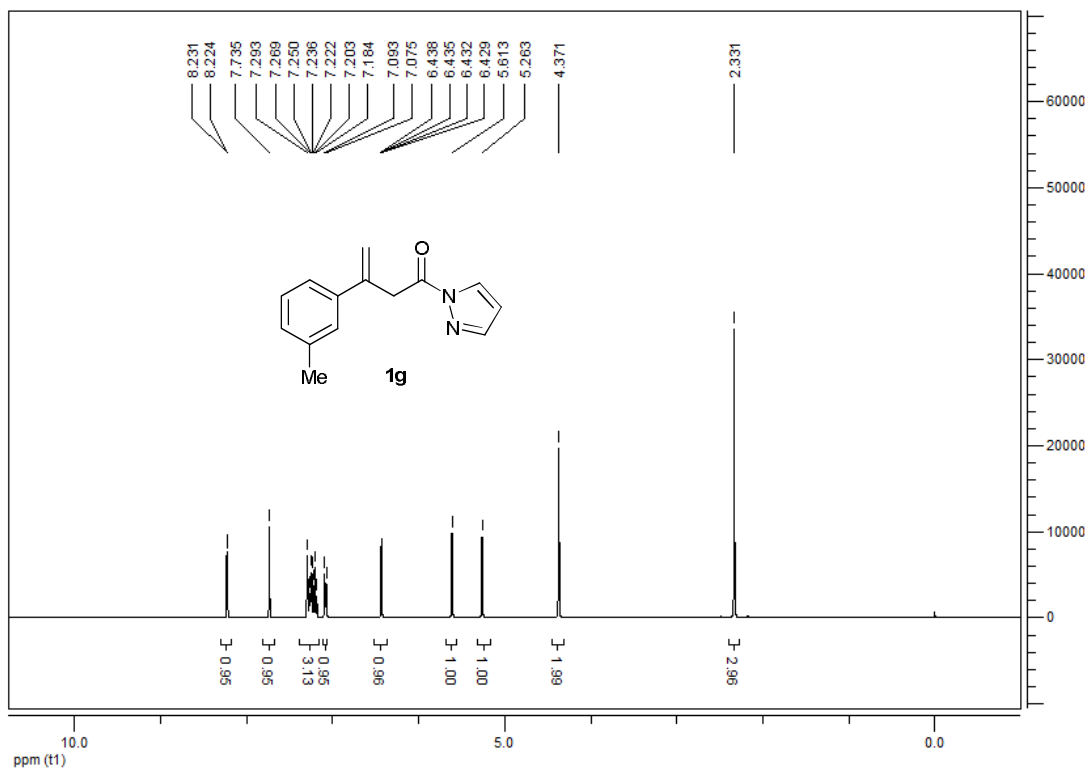


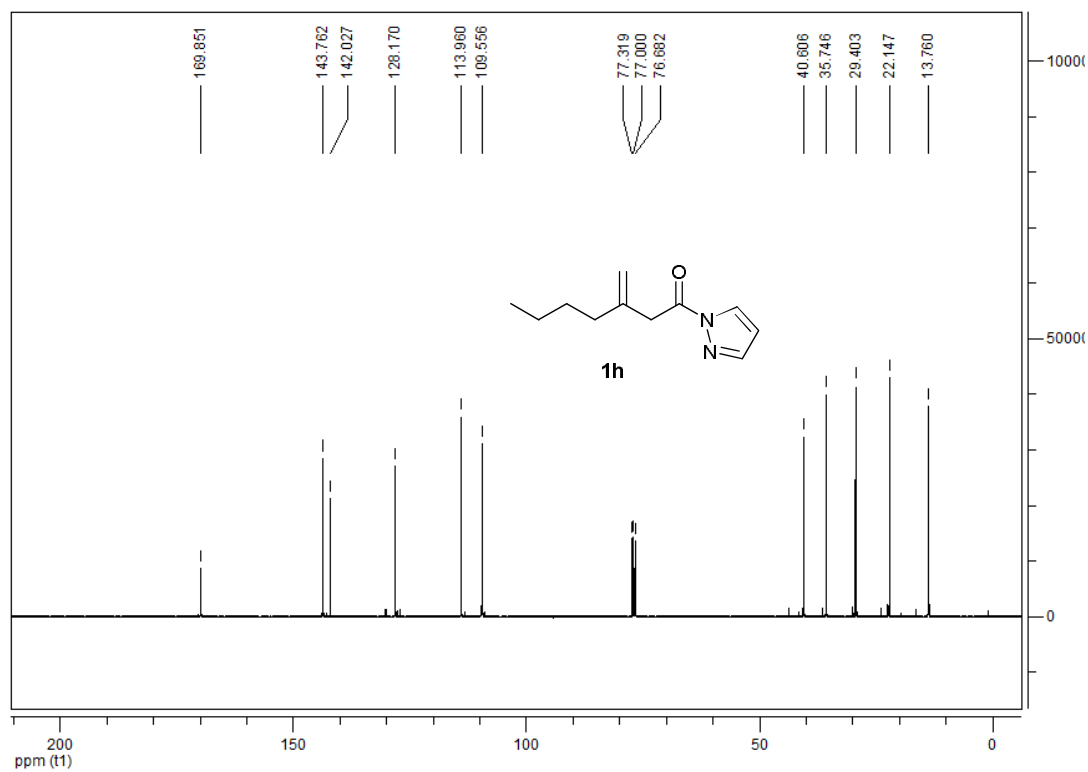
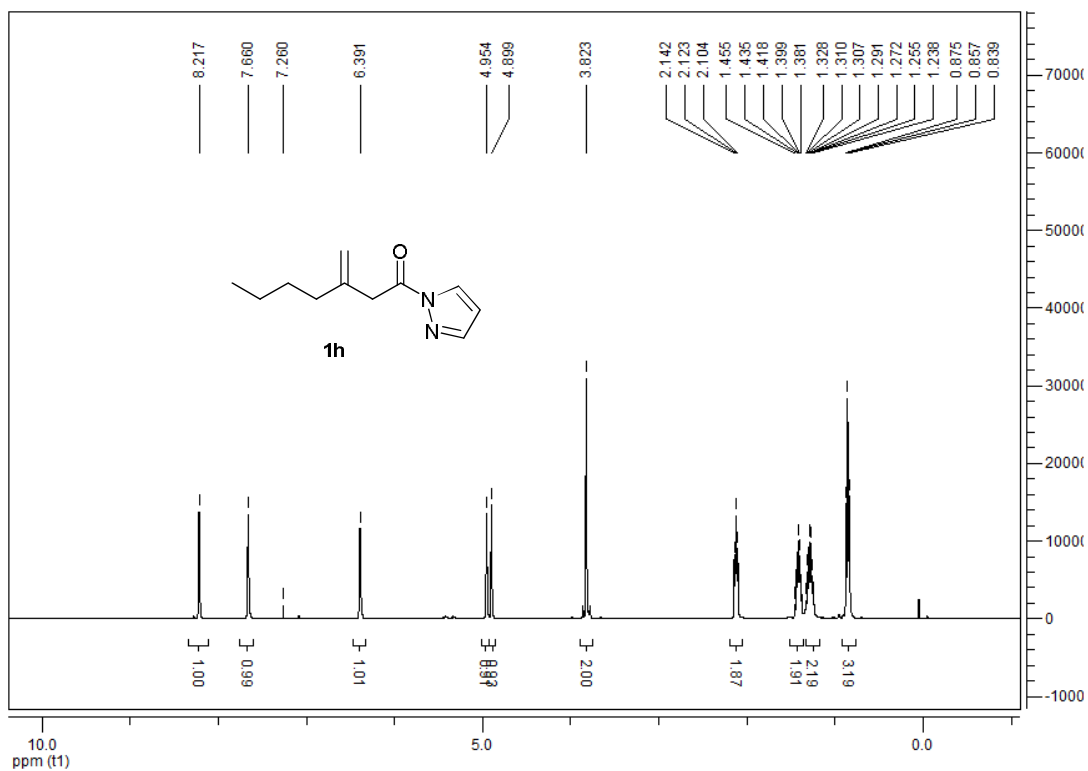


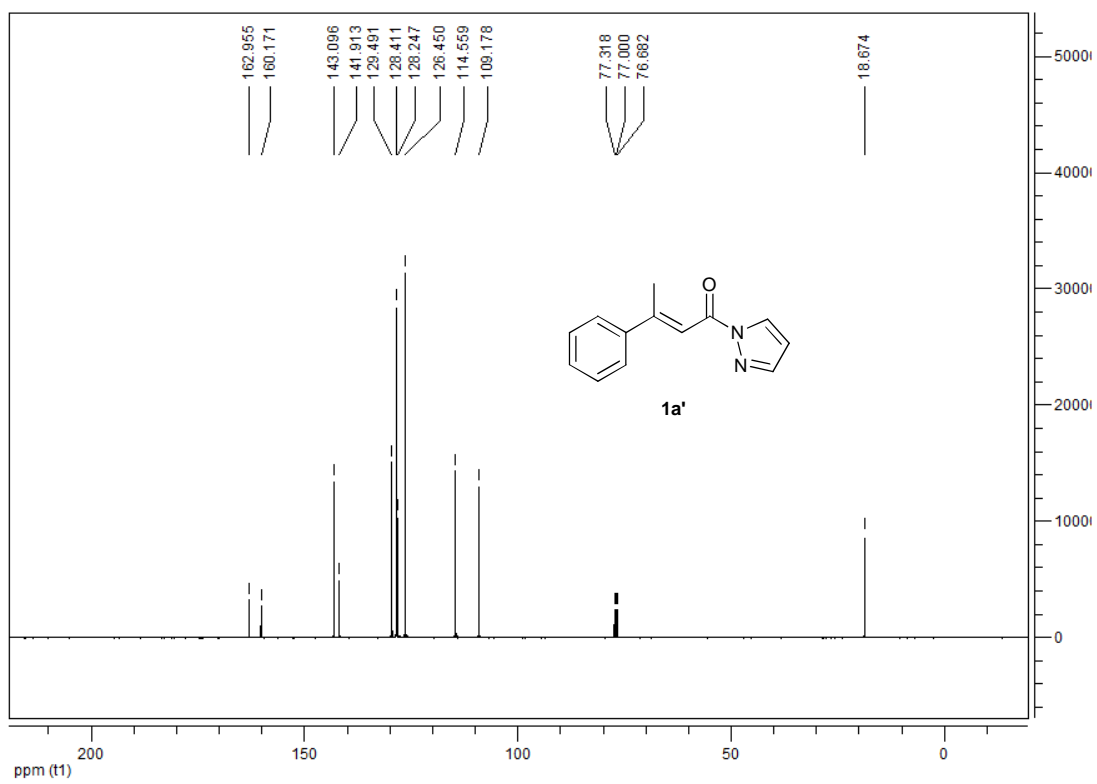
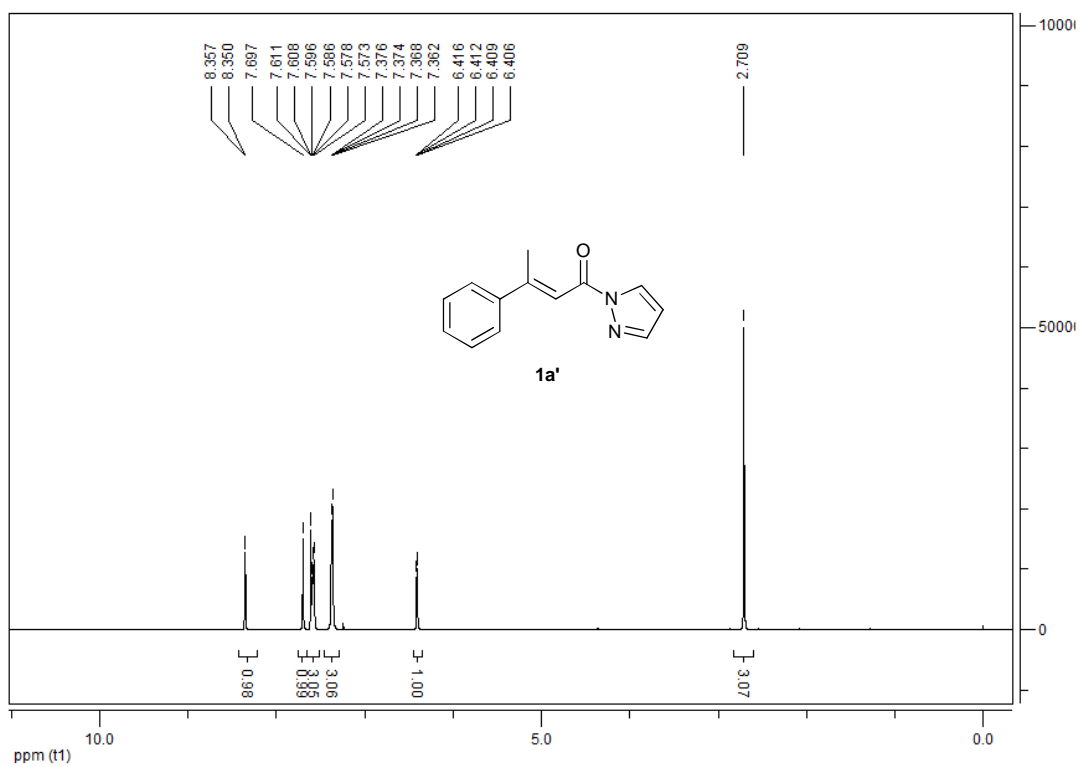




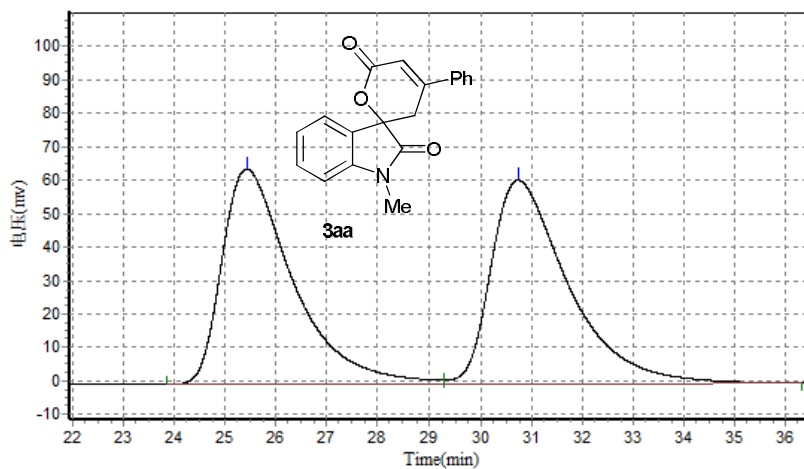






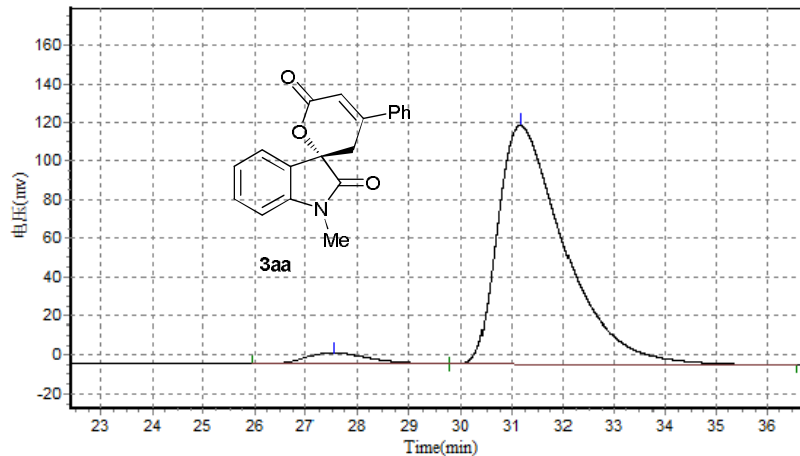


8. Copies of HPLC Spectra of the Products



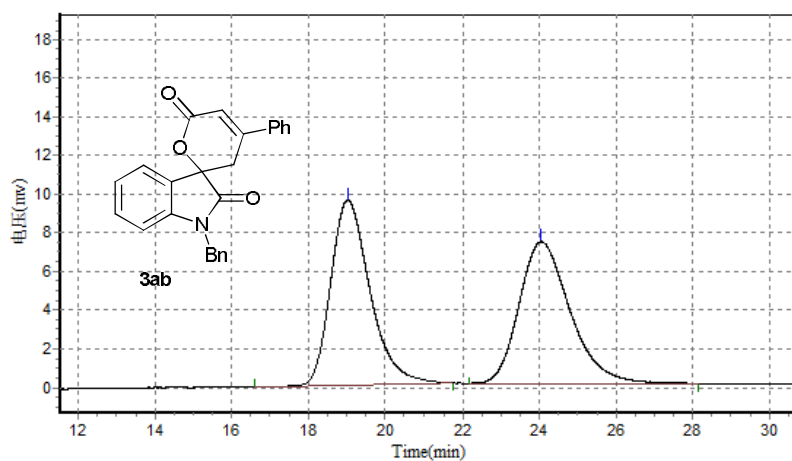
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		25.423	64283.477	6259666.000	49.2683
2		30.740	60854.992	6445590.000	50.7317
Total			125138.469	12705256.000	100.0000



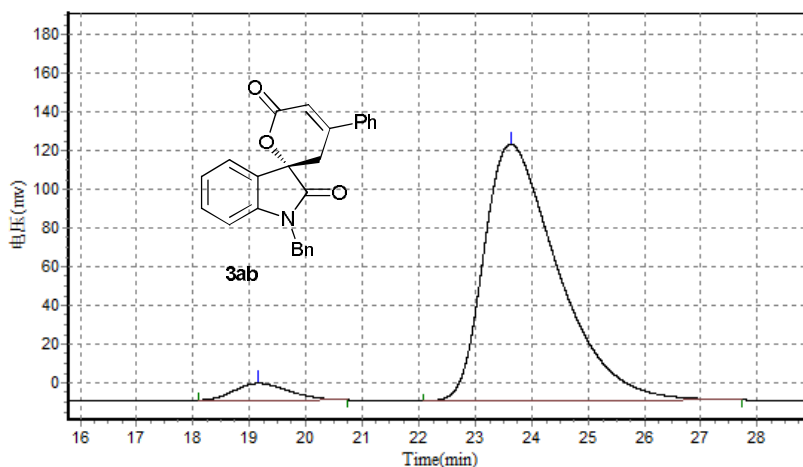
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		27.532	5927.883	507569.563	4.3325
2		31.165	123544.539	11207894.000	95.6675
Total			129472.422	11715463.563	100.0000



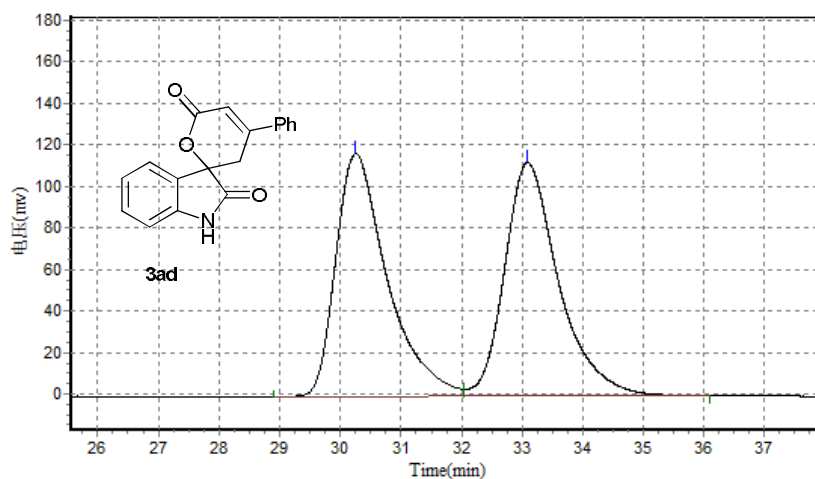
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		19.027	9569.344	681083.313	50.1323
2		24.038	7332.167	677488.688	49.8677
Total			16901.511	1358572.000	100.0000



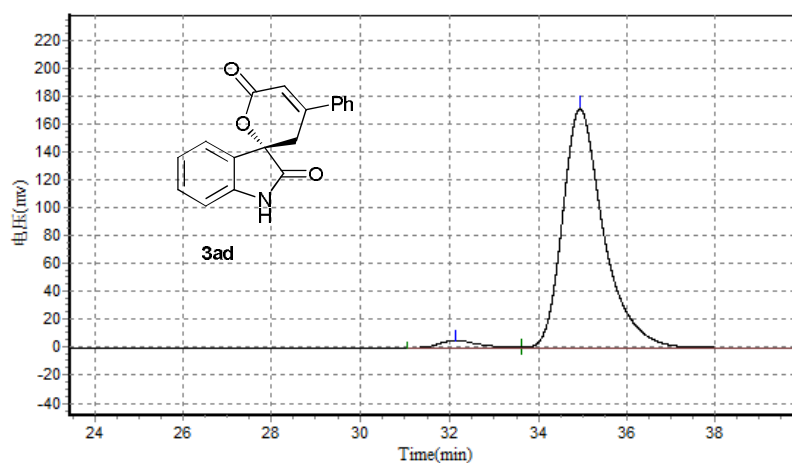
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		19.168	8604.880	578129.625	4.5689
2		23.620	132085.656	12075368.000	95.4311
Total			140690.536	12653497.625	100.0000



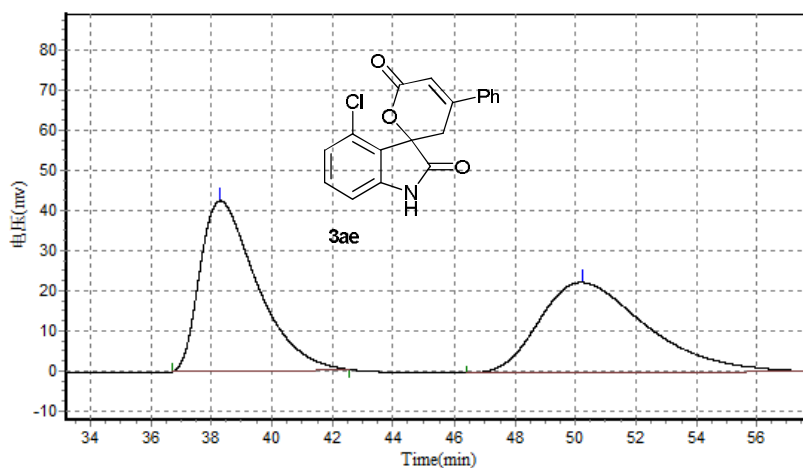
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		30.262	116630.703	6876079.000	49.6043
2		33.082	112269.078	6985788.000	50.3957
Total			228899.781	13861867.000	100.0000



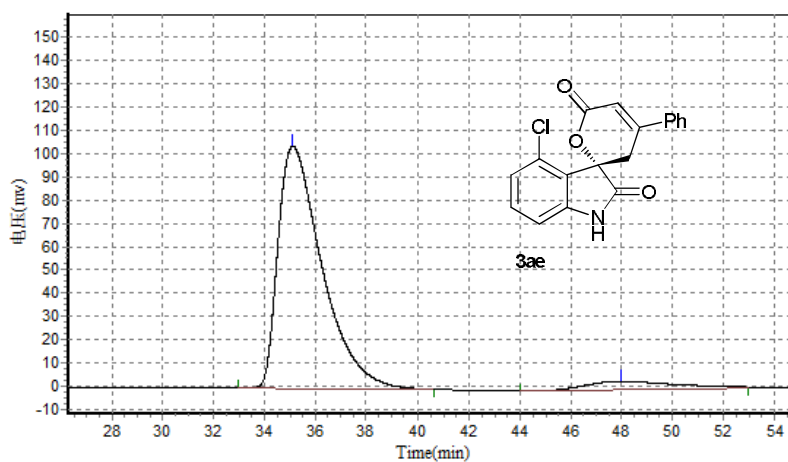
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		32.123	5399.264	330483.500	2.9153
2		34.948	171162.313	11005803.000	97.0847
Total			176561.576	11336286.500	100.0000



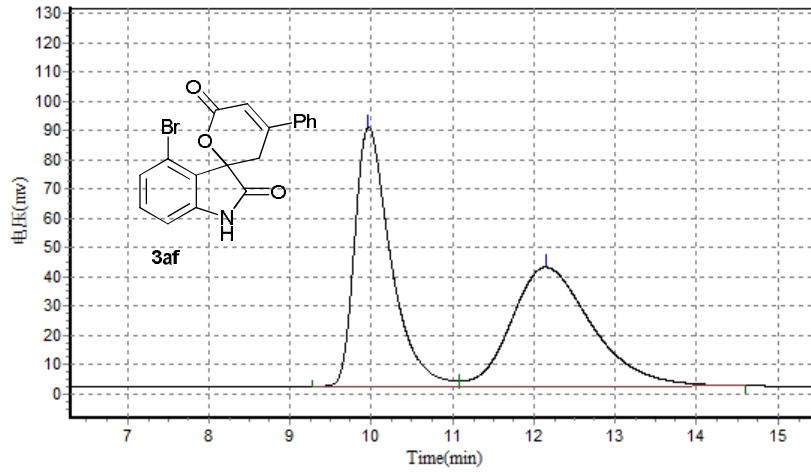
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		38.293	42360.832	5526875.500	50.1769
2		50.208	22386.371	5487906.000	49.8231
Total			64747.203	11014781.500	100.0000



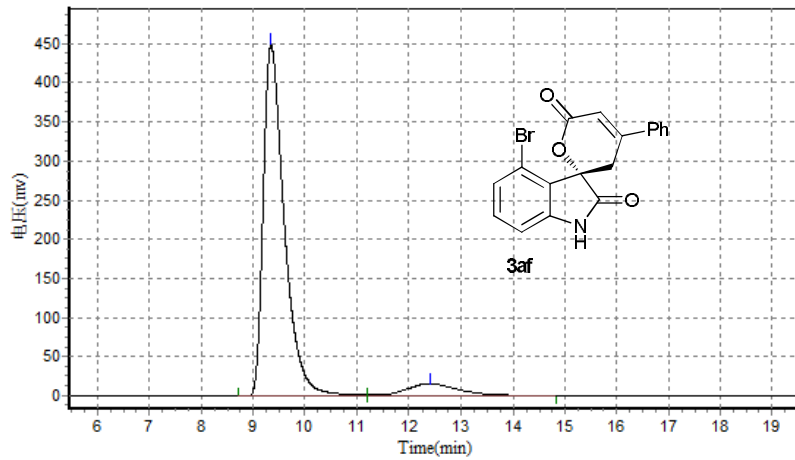
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		35.117	104106.352	12506568.000	94.3455
2		48.003	3437.008	749569.188	5.6545
Total			107543.360	13256137.188	100.0000



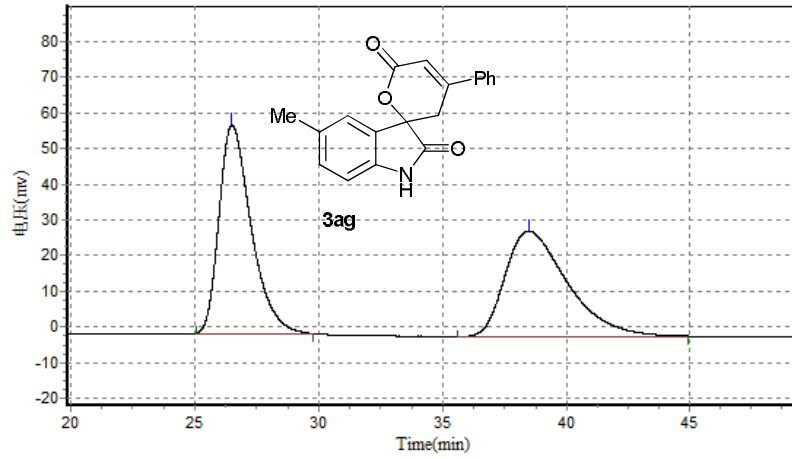
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		9.973	88795.227	2745785.250	49.5894
2		12.143	40713.438	2791254.750	50.4106
Total			129508.664	5537040.000	100.0000



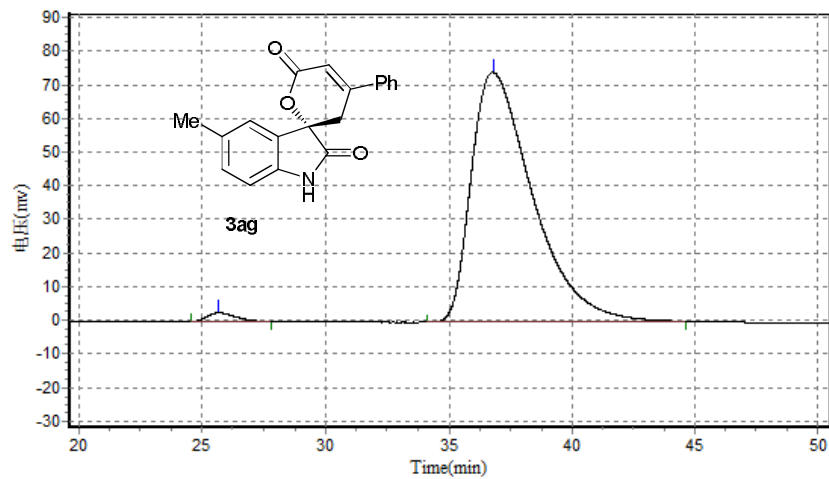
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		9.352	448155.250	12630039.000	92.1243
2		12.390	15388.225	1079740.125	7.8757
Total			463543.475	13709779.125	100.0000



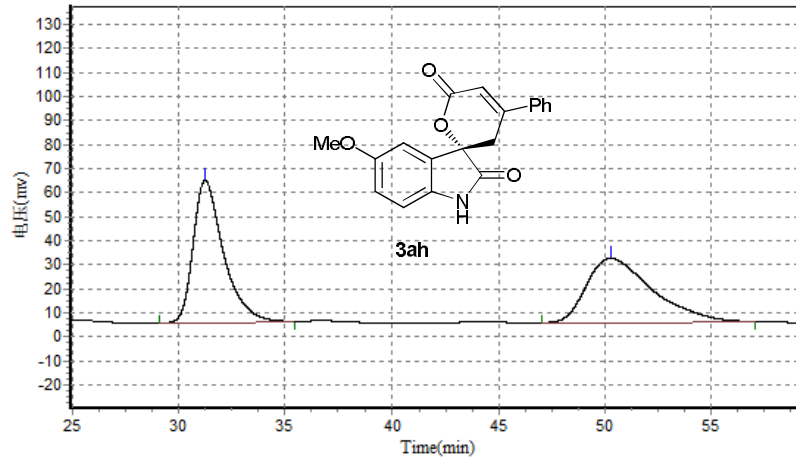
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		26.503	58588.211	5298666.500	50.6718
2		38.480	29557.637	5158166.000	49.3282
Total			88145.848	10456832.500	100.0000



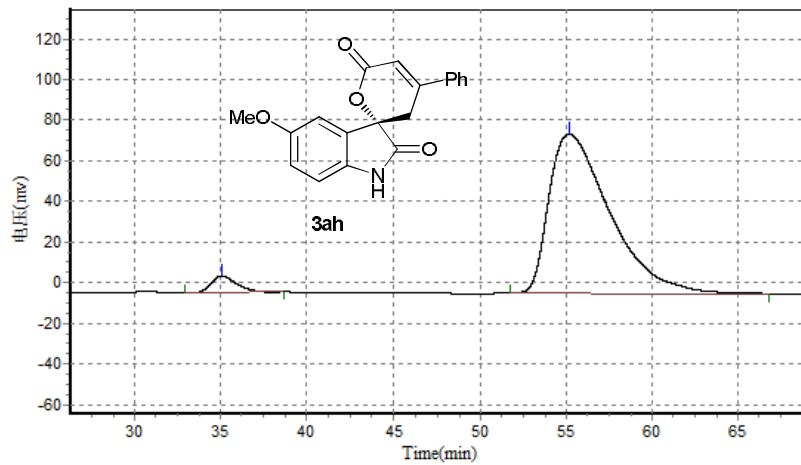
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		25.678	2686.233	225917.906	1.7215
2		36.785	74114.477	12897374.000	98.2785
Total			76800.709	13123291.906	100.0000



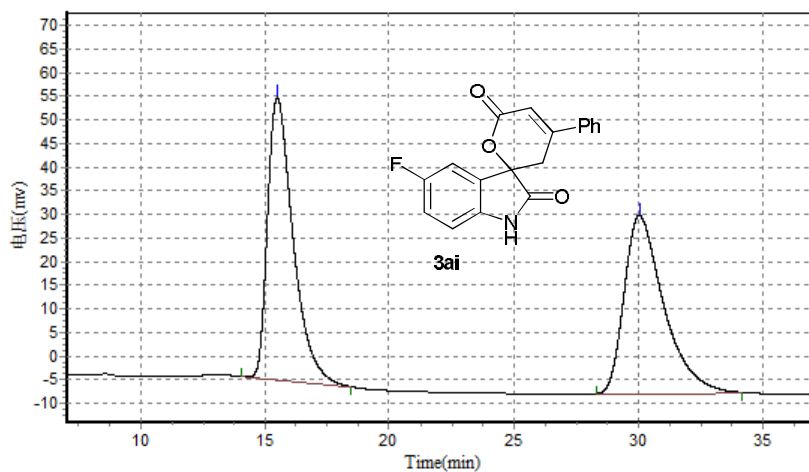
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		31.230	59315.523	5866317.500	50.6228
2		50.267	26623.018	5721965.000	49.3772
Total			85938.541	11588282.500	100.0000



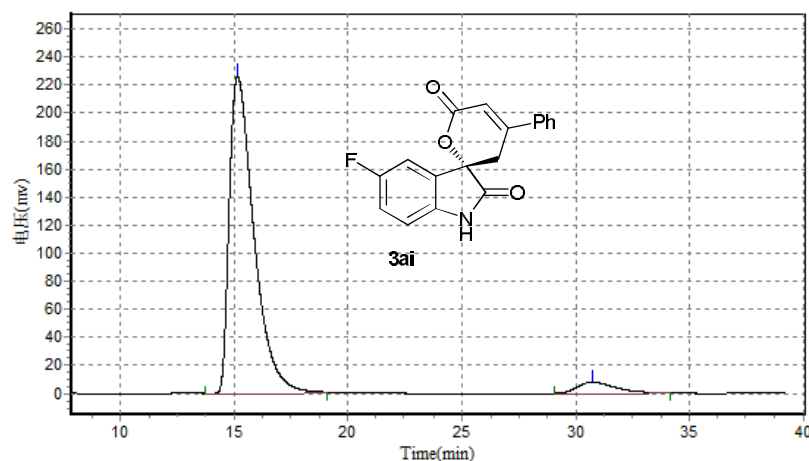
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		35.070	8221.466	820627.688	4.1122
2		55.193	78173.711	19135268.000	95.8878
Total			86395.177	19955895.688	100.0000



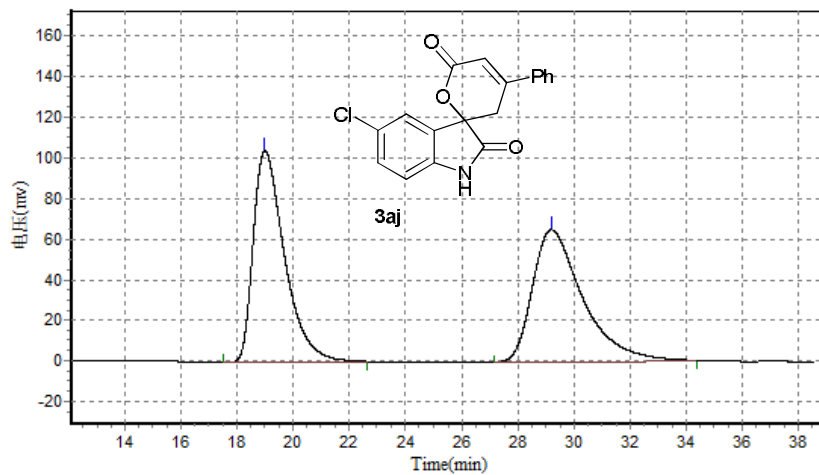
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		15.503	59718.336	4272878.500	50.6095
2		30.045	37720.148	4169966.750	49.3905
Total			97438.484	8442845.250	100.0000



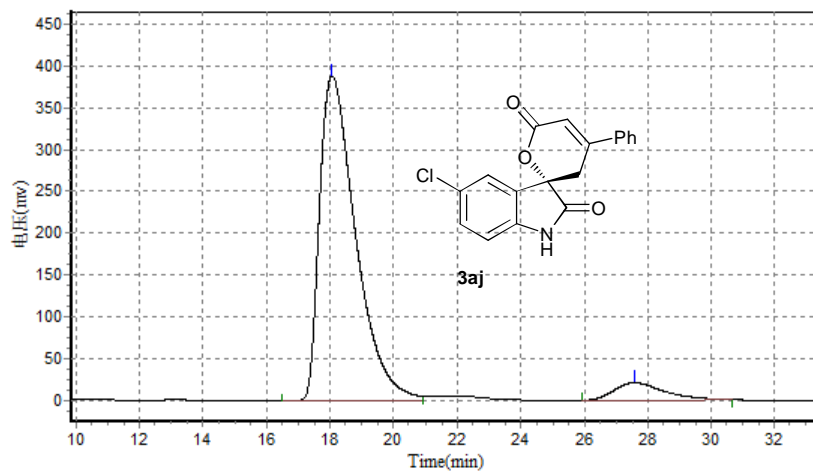
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		15.168	226079.406	16983002.000	94.8085
2		30.728	8041.277	929949.563	5.1915
Total			234120.683	17912951.563	100.0000



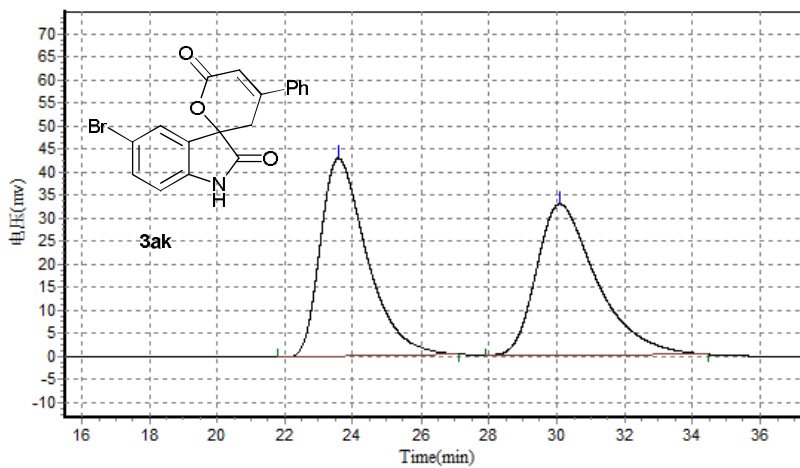
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		18.990	104296.086	8084320.000	50.0585
2		29.177	64900.984	8065422.500	49.9415
Total			169197.070	16149742.500	100.0000



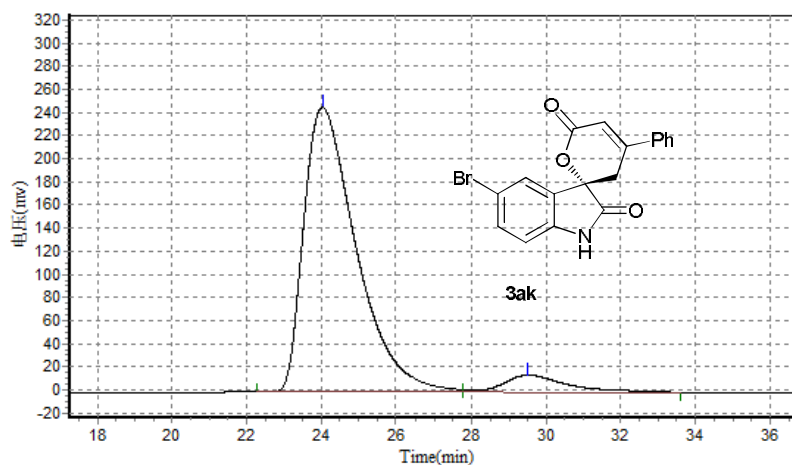
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		18.073	387834.563	30642214.000	93.1196
2		27.568	20752.867	2264084.000	6.8804
Total			408587.430	32906298.000	100.0000



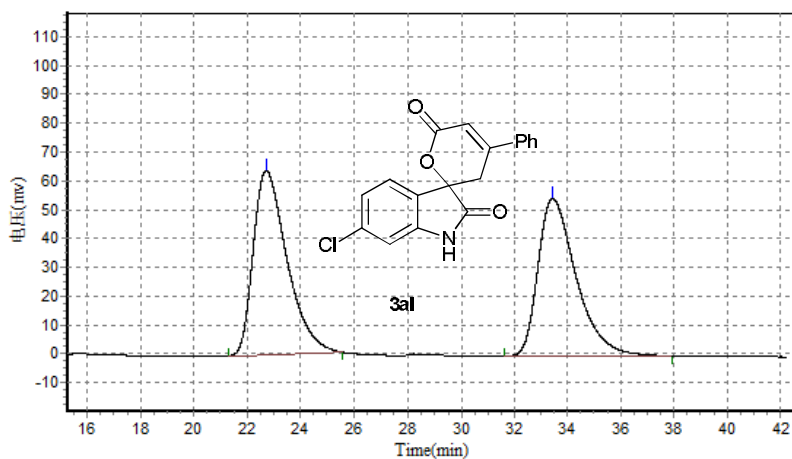
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		23.583	42890.621	4087179.750	50.2472
2		30.083	32763.549	4046968.500	49.7528
Total			75654.170	8134148.250	100.0000



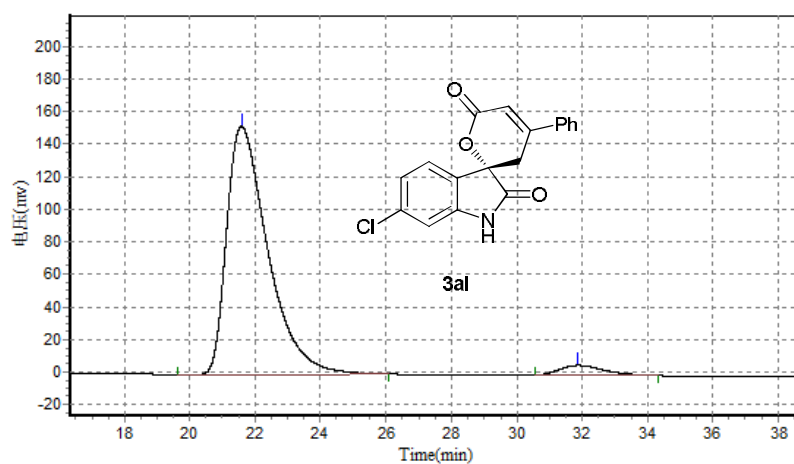
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		24.038	245629.688	24008240.000	93.1927
2		29.515	14745.289	1753693.125	6.8073
Total			260374.977	25761933.125	100.0000



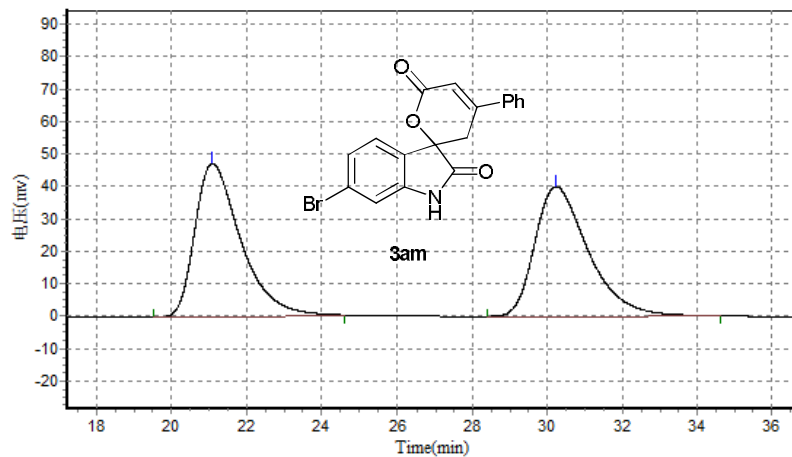
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		22.718	63858.203	5614878.000	50.8699
2		33.437	54557.031	5422837.500	49.1301
Total			118415.234	11037715.500	100.0000



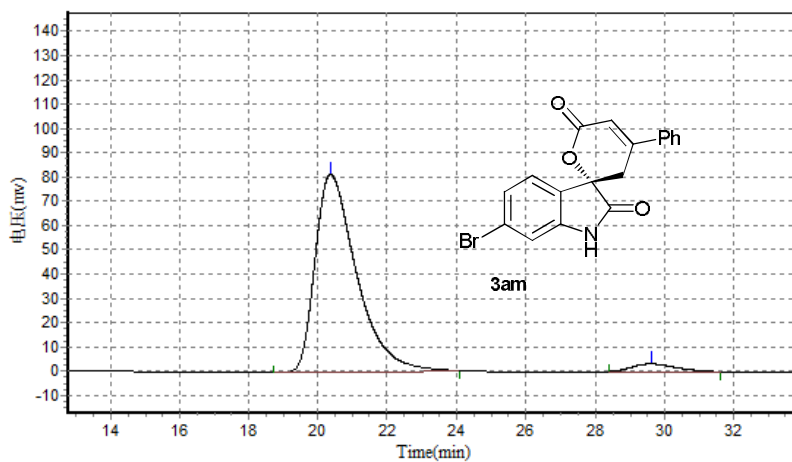
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		21.583	152342.563	13347878.000	95.9035
2		31.863	6051.785	570151.688	4.0965
Total			158394.348	13918029.688	100.0000



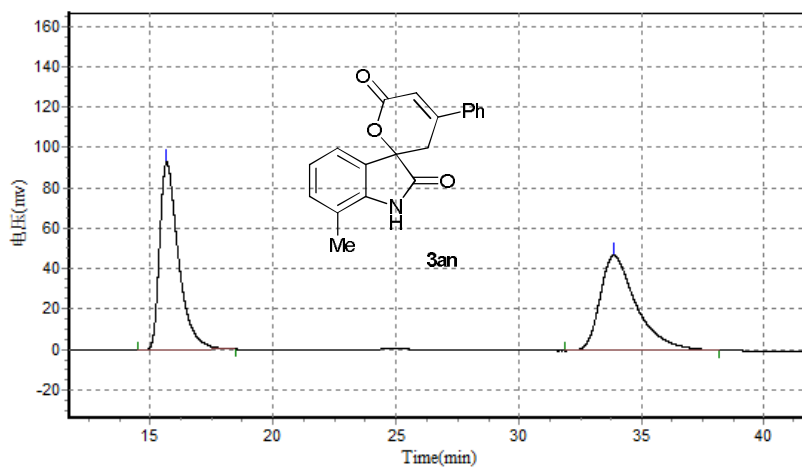
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		21.087	47209.508	3996776.000	50.2066
2		30.228	39983.508	3963884.500	49.7934
Total			87193.016	7960660.500	100.0000



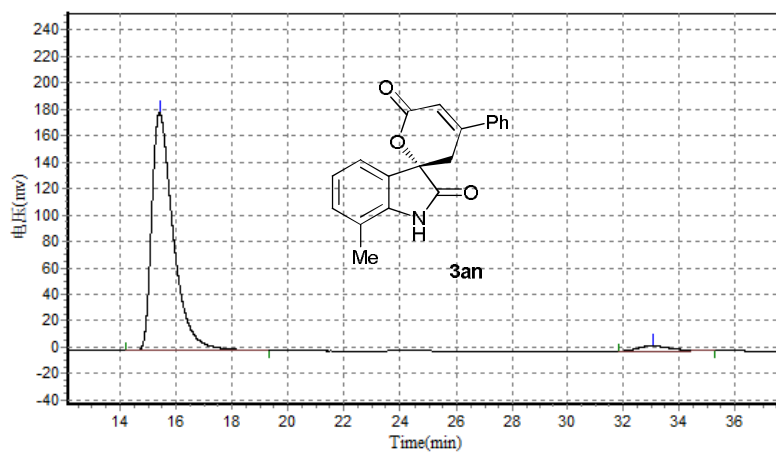
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		20.375	81386.898	6755831.000	95.9409
2		29.633	3226.972	285825.781	4.0591
Total			84613.871	7041656.781	100.0000



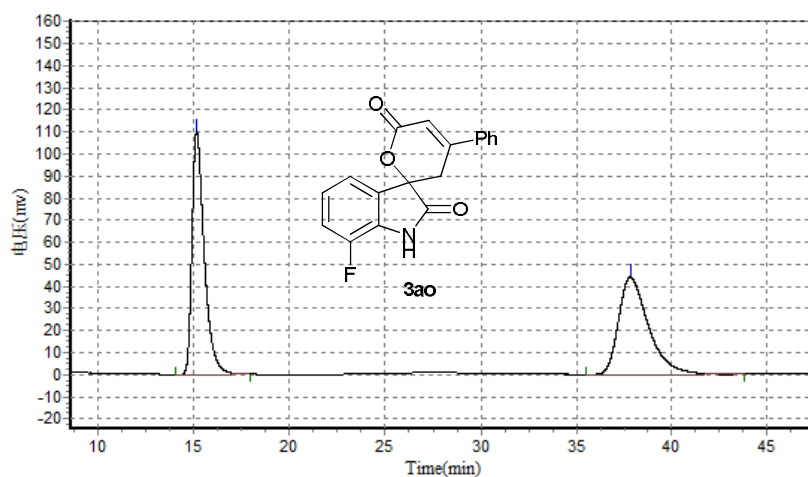
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		15.675	92881.789	4958927.500	50.5899
2		33.872	47144.340	4843274.500	49.4101
Total			140026.129	9802202.000	100.0000



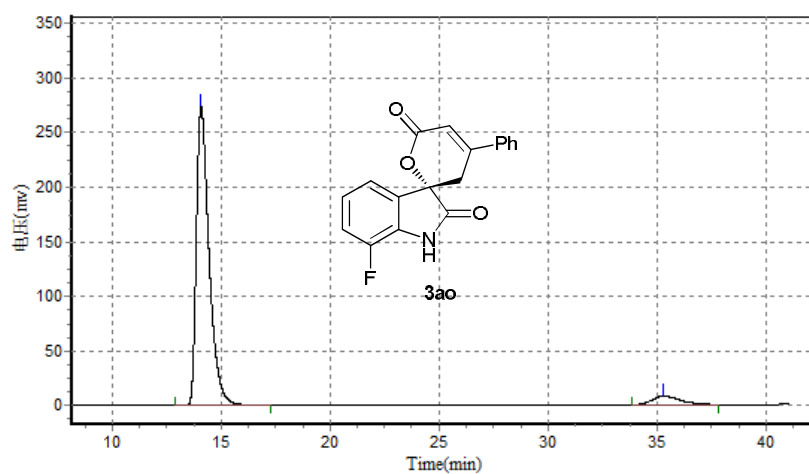
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		15.420	180590.719	9653887.000	97.0255
2		33.033	3777.073	295957.063	2.9745
Total			184367.792	9949844.063	100.0000



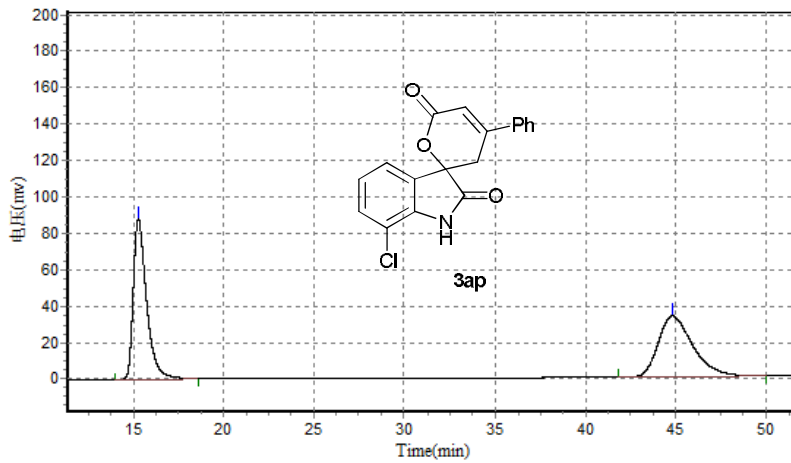
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		15.148	110255.930	4907262.500	50.6830
2		37.823	44102.844	4775007.000	49.3170
Total			154358.773	9682269.500	100.0000



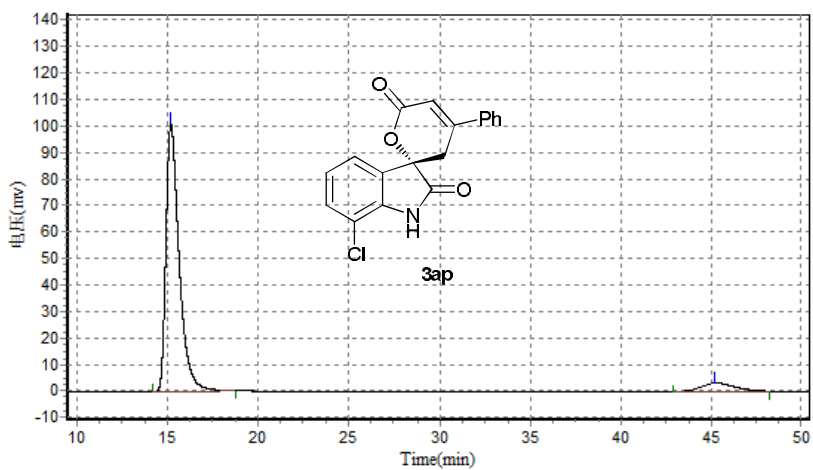
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		14.065	274775.438	11203871.000	93.8684
2		35.317	7964.771	731844.500	6.1316
Total			282740.209	11935715.500	100.0000



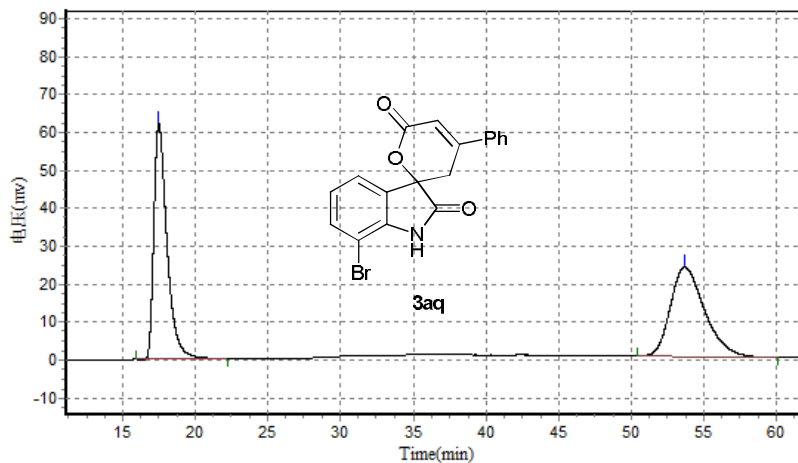
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		15.255	87861.969	4469438.500	50.5265
2		44.823	33218.957	4376296.000	49.4735
Total			121080.926	8845734.500	100.0000



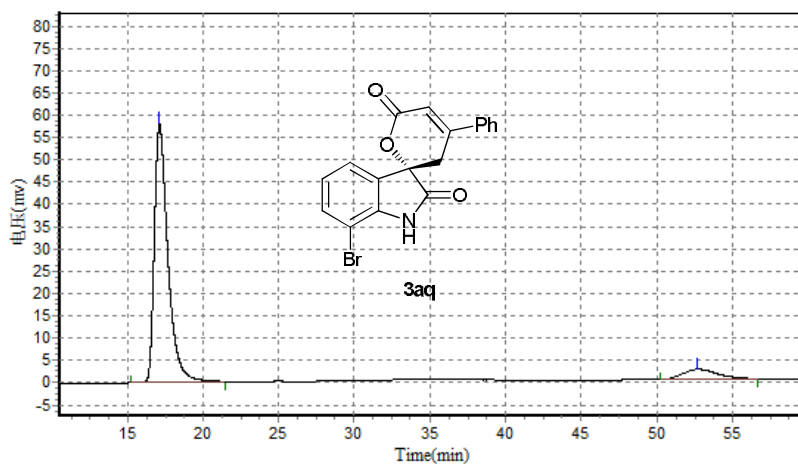
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		15.188	100707.688	5102755.000	92.6228
2		45.237	3136.021	406420.188	7.3772
Total			103843.708	5509175.188	100.0000



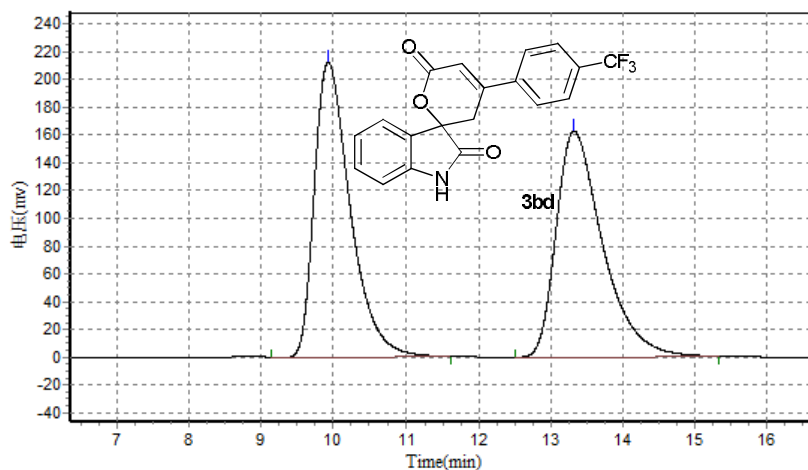
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		17.533	62238.250	3907139.750	50.7213
2		53.690	23353.363	3796013.000	49.2787
Total			85591.613	7703152.750	100.0000



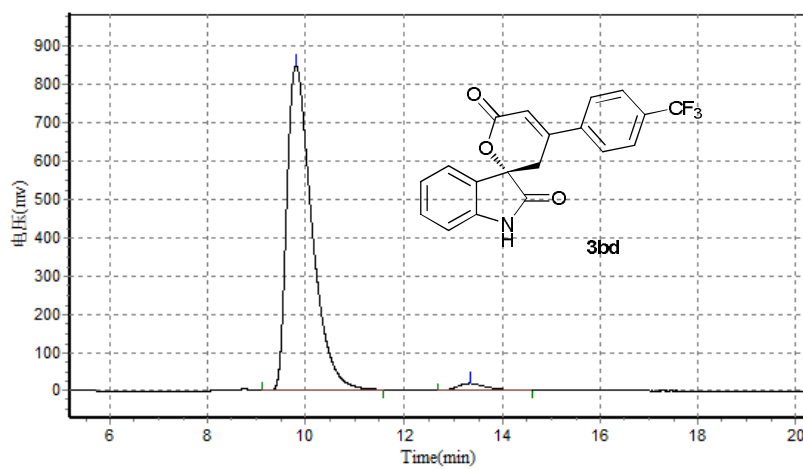
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		17.098	57754.734	3594863.500	90.8792
2		52.675	2225.175	360788.344	9.1208
Total			59979.909	3955651.844	100.0000



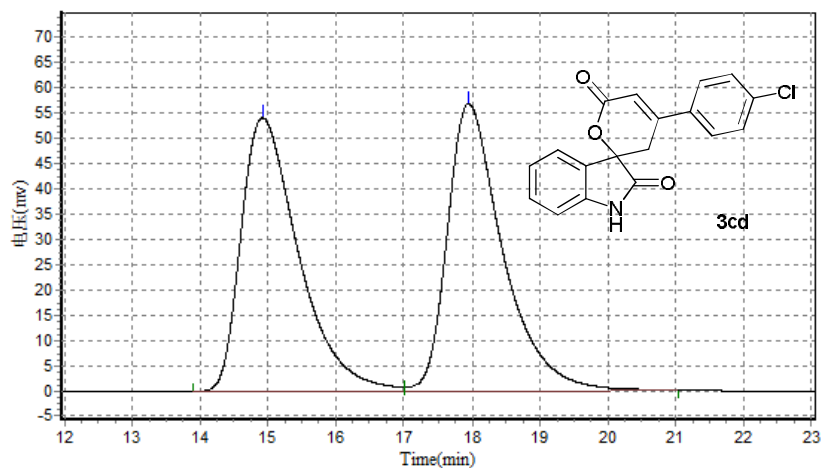
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		9.927	211862.188	7327057.500	50.1551
2		13.330	162372.641	7281735.000	49.8449
Total			374234.828	14608792.500	100.0000



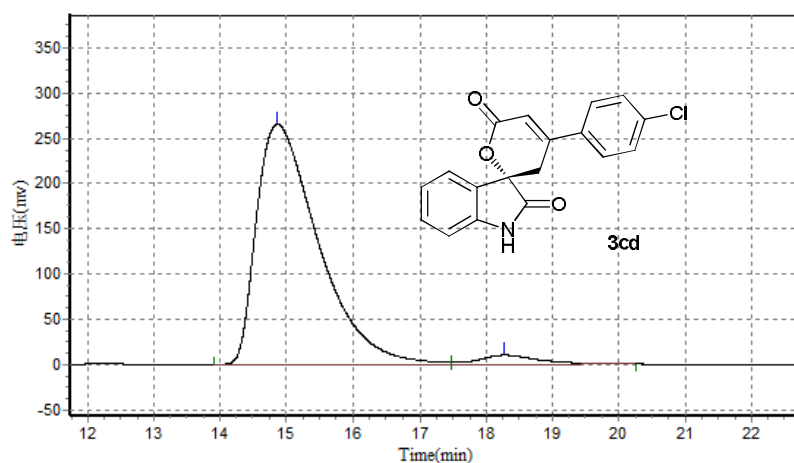
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		9.802	846723.188	30064930.000	97.4088
2		13.335	18671.775	799778.500	2.5912
Total			865394.963	30864708.500	100.0000



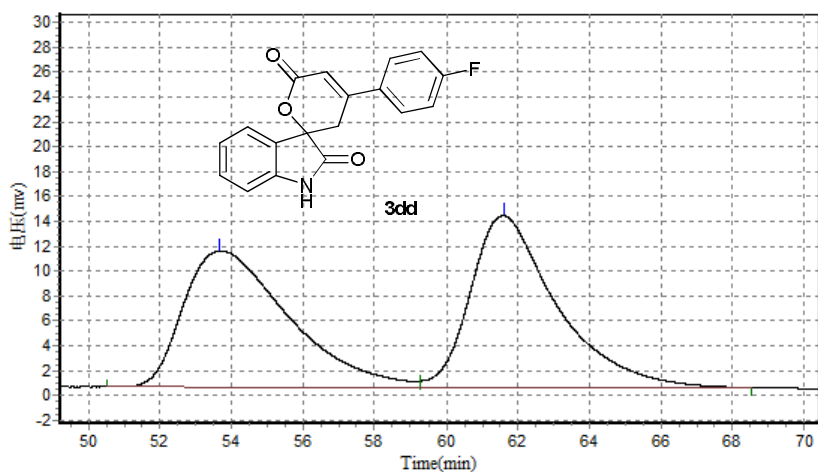
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		14.915	54062.020	3183149.750	49.7358
2		17.938	56769.484	3216965.250	50.2642
Total			110831.504	6400115.000	100.0000



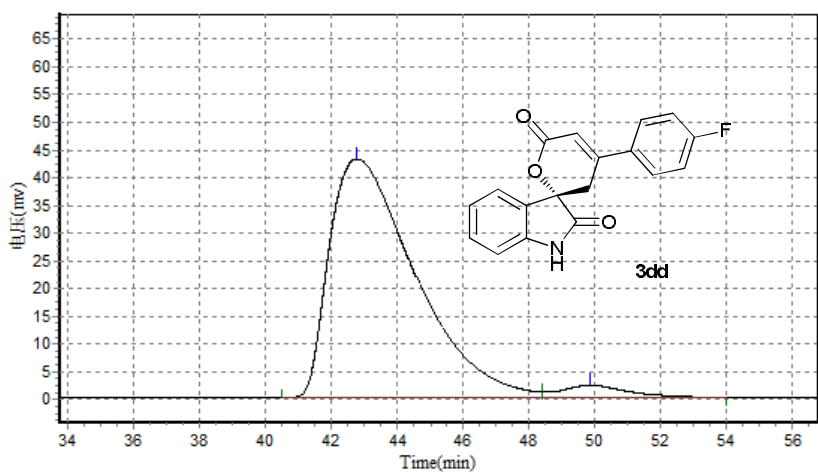
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		14.865	265343.313	17229668.000	96.5428
2		18.268	9947.638	617001.000	3.4572
Total			275290.950	17846669.000	100.0000



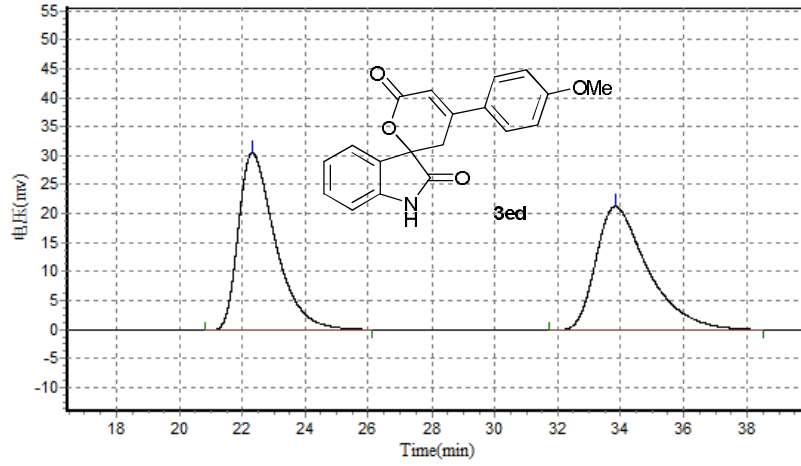
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		53.673	10972.609	2240754.750	49.0582
2		61.603	13818.933	2326787.250	50.9418
Total			24791.542	4567542.000	100.0000



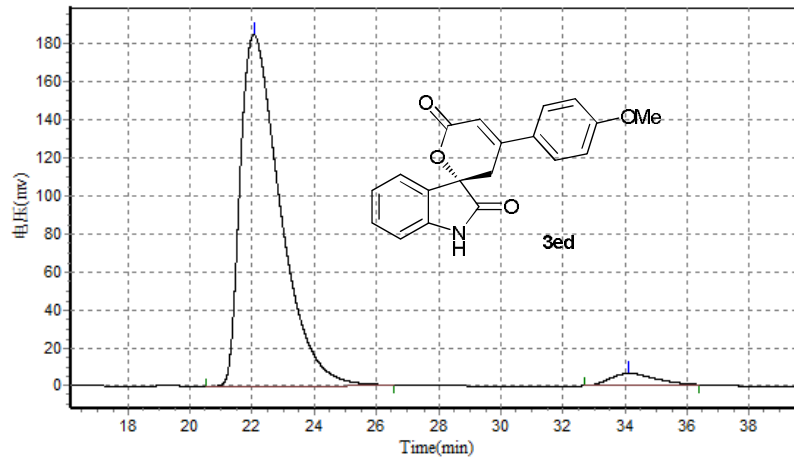
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		42.795	43033.180	7750841.500	96.1608
2		49.848	2221.133	309447.563	3.8392
Total			45254.313	8060289.063	100.0000



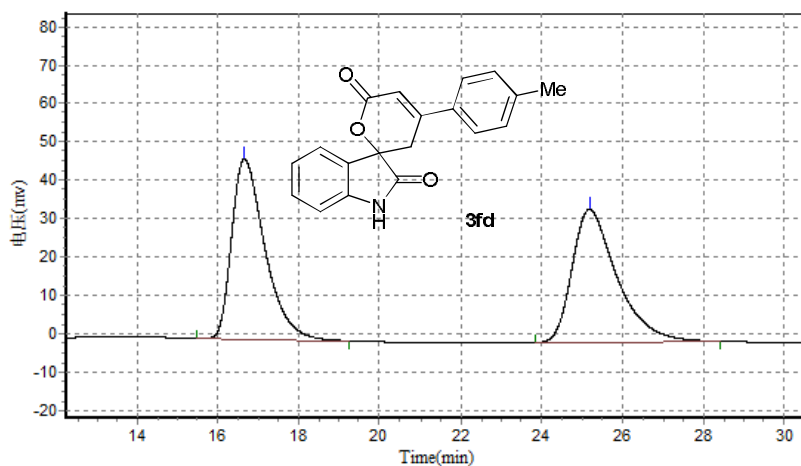
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		22.315	30562.031	2499027.500	50.2270
2		33.835	21389.068	2476439.000	49.7730
Total			51951.100	4975466.500	100.0000



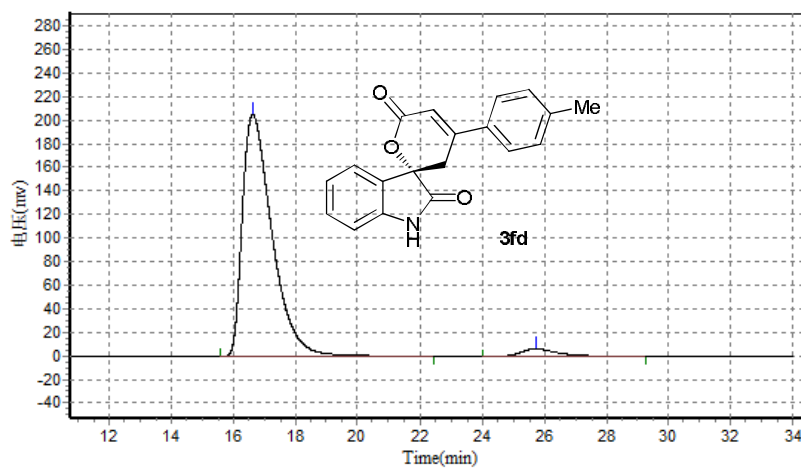
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		22.053	184507.109	16559878.000	96.3107
2		34.137	6226.667	634341.438	3.6893
Total			190733.776	17194219.438	100.0000



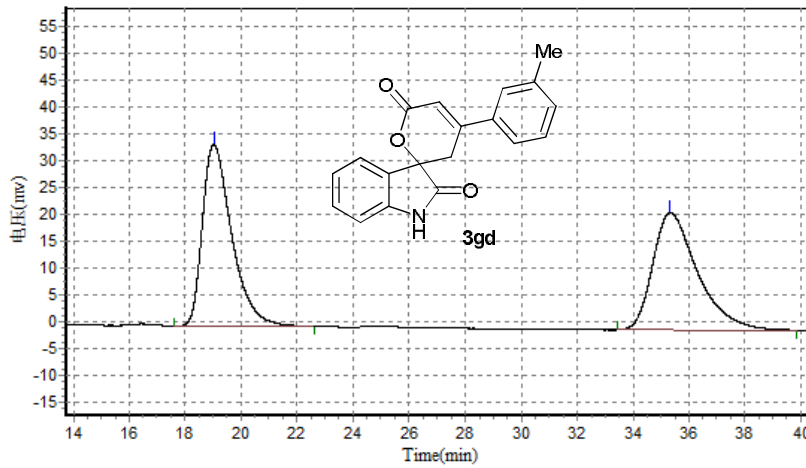
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		16.657	46989.043	2688806.000	50.1241
2		25.177	34604.715	2675492.750	49.8759
Total			81593.758	5364298.750	100.0000



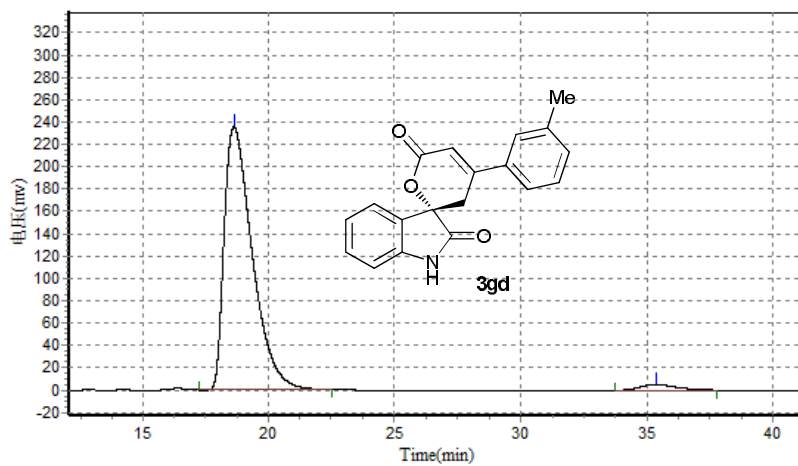
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		16.632	204797.734	13655593.000	96.3905
2		25.732	6168.125	511351.031	3.6095
Total			210965.859	14166944.031	100.0000



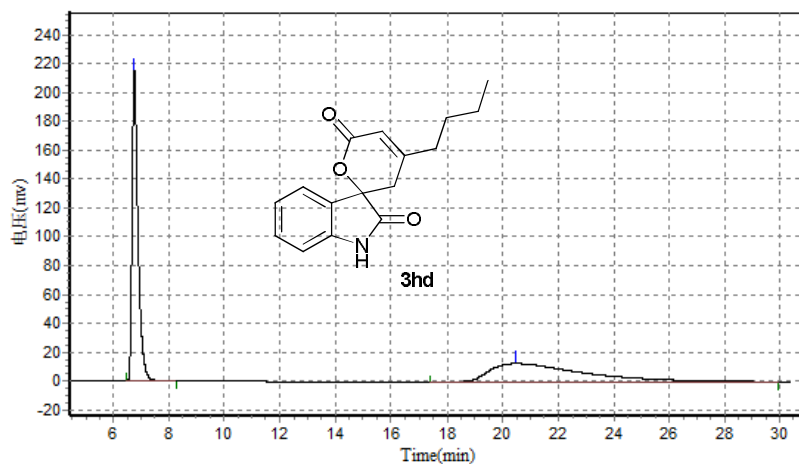
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		19.023	34024.535	2471100.000	50.3623
2		35.320	21879.656	2435549.750	49.6377
Total			55904.191	4906649.750	100.0000



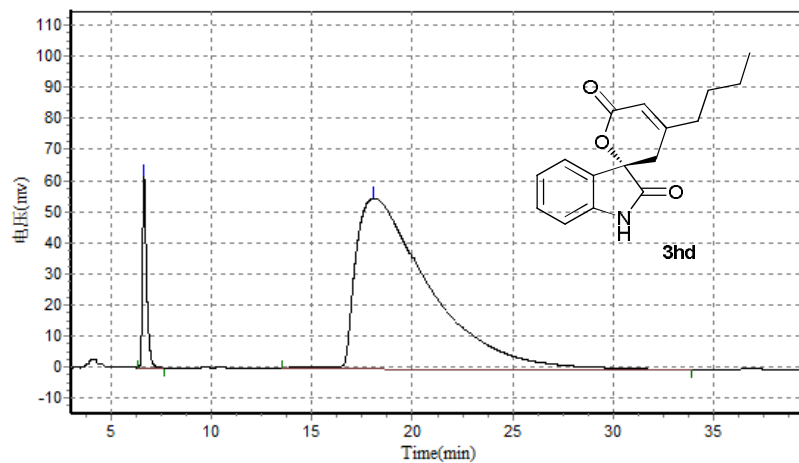
Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		18.608	235680.531	18345082.000	97.2656
2		35.375	5020.489	515726.750	2.7344
Total			240701.020	18860808.750	100.0000



Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		6.763	215936.344	3214875.500	52.6582
2		20.450	12538.112	2890299.500	47.3418
Total			228474.456	6105175.000	100.0000



Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		6.652	61564.234	872776.813	5.9339
2		18.097	54813.113	13835417.000	94.0660
Total			116377.348	14708193.813	100.0000