Electronic Supplementary Information

An NHC-Catalyzed [3+2] Cyclization of β-Disubstituted Enals with Benzoyl Cyanides

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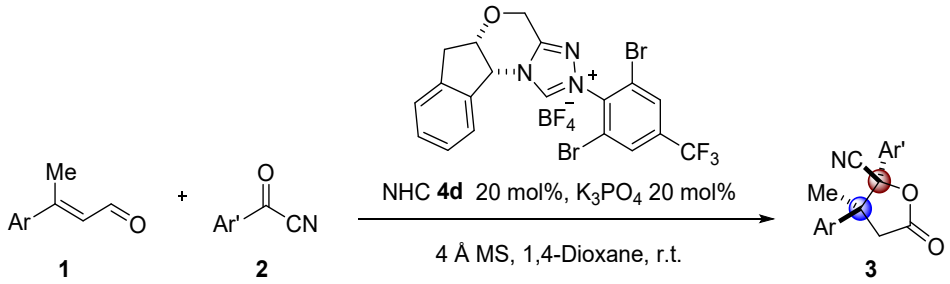
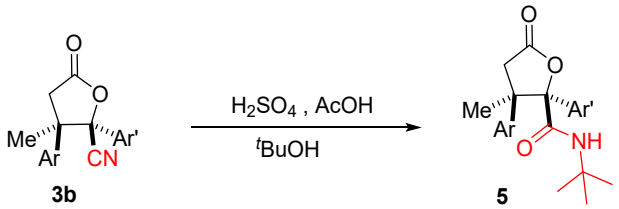
General Methods and Materials

All solvents were distilled according to general practice prior to use. All reagents were purchased and used without further purification unless specified otherwise. Solvents for flash column chromatography were technical grade and distilled prior to use. Analytical thin-layer chromatography (TLC) was performed using Huanghai silica gel plates with HSGF 254. Visualization of the developed chromatogram was performed by UV absorbance (254 nm) and appropriate stains. Flash column chromatography was performed using Qingdao Haiyang Chemical HG/T2354-92 silica gel (200-300 mesh) with the indicated solvent system according to standard techniques. ^{1}H NMR and ^{13}C NMR data were recorded on Bruker 400 and 500 MHz (100 MHz for ^{13}C, 376MHz for ^{19}F) nuclear resonance spectrometers unless otherwise specified, respectively. Chemical shifts (δ) in ppm are reported as quoted relative to the residual signals of chloroform (^{1}H 7.26 ppm and ^{13}C 77.16 ppm). Multiplicities are described as: s (singlet), bs (broad singlet), d (doublet), t (triplet), q (quartet), m (multiplet); and coupling constants (J) are reported in Hertz (Hz). ^{13}C NMR spectra were recorded with total proton decoupling. Chiral HPLC was recorded on a Shimadzu LC-20A spectrometer using Daicel Chiralcel TM columns. HRMS (ESI) analysis was performed by The Analytical Instrumentation Center at Peking University; Shenzhen Graduate School and (HRMS) data were reported with ion mass/charge (m/z) ratios as values in atomic mass units. β-Disubstituted enals were synthesized by the procedure published by Yonggui Robin Chi[1] and Benjamin List.[2] According to the standard procedure, racemic samples were prepared by utilizing the corresponding achiral NHC catalyst. The absolute stereochemistry of the desired product was determined by X-ray crystallographic analysis of **3b**.

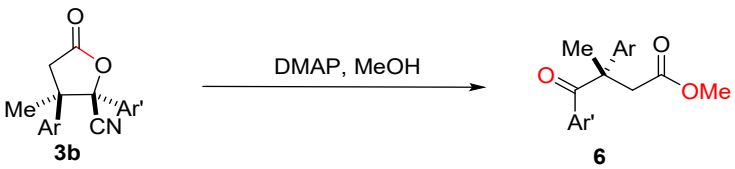
General Procedure



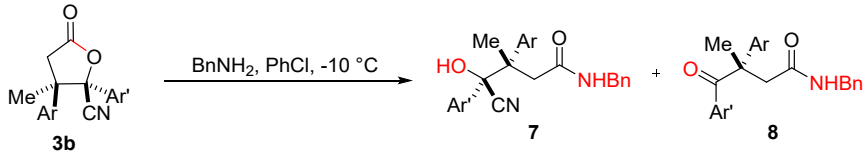
To an oven-dried test tube, NHC precursor **4d** (12 mg, 0.02 mmol, 0.2 equiv.), 4Å molecular sieves (100 mg) and K_3PO_4 (4.2 mg, 0.02 mmol, 0.2 equiv.) were stirred in anhydrous 1,4-dioxane (1.0 ml). The reaction vessel was sealed with a rubber septum, degassed, back-filled with argon and stirred at r.t. for 1 hour. Enals **1** (0.15 mmol, 1.5 equiv.) was slowly added and the mixture was stirred at r.t. for 10 min. Benzoyl cyanide **2** (0.1 mmol, 1.0 equiv.) was slowly added and the reaction was stirred at 25 ℃ for 18-24 h. Upon complete consumption of compound **2**, judged by TLC or GC, the reaction mixture was filtered through a plug of silica gel and concentrated. The residue was purified by silica gel flash column chromatography [eluent: hexane/Et_2O = 10:1 (200mL) to afford the desired product **3**. Er was determined by chiral HPLC.



To a solution of **3b** (0.1 mmol, 35.3 mg) in AcOH (1 mL) was added ^{t}BuOH (0.2 mmol, 20 μL) and concentrated sulfuric acid (0.1 mL) in turn at 0℃. The mixture was stirred at rt for 12 hours, and poured into ice water (1 mL). The mixture was neutralized with saturated $NaHCO_3$, and then extracted with DCM (2*8 mL). The combined organic extract was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude mixture was purified by column chromatography (silica gel, hexane/ethyl acetate) to provide **5**.

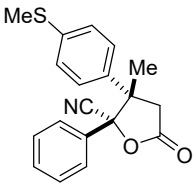


DMAP (4-(Dimethylamino)pyridine) (13.4 mg, 0.11 mmol) was added to a stirred solution of compound **3b** (35.3 mg, 0.1 mmol) in methanol (1.0 mL). The solution was stirred at room temperature overnight. The methanol was removed *in vacuo* and the product **6** was isolated by flash column chromatography (hexane/ethyl acetate).



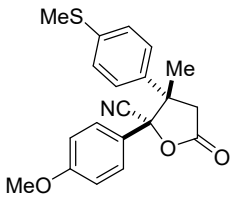
$BnNH_2$ (9.3 μl) was added to a solution of **3b** (35.3 mg, 0.1 mmol) in PhCl (1.0 mL) at -10 °C and the reaction mixture was stirred at this temperature for about 12 hours, then the reaction mixtures were directly loaded onto a short silica gel column, followed by gradient elution with PE/EA mixture. Removing the solvent in vacuo, afforded products **7** and **8**.

(2S,3S)-3-methyl-3-(4-(methylthio)phenyl)-5-oxo-2-phenyltetrahydrofuran-2-carbonitrile (**3a**)



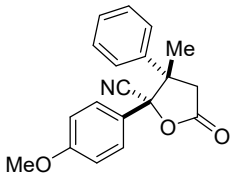
Yellow solid, yield: 85%. er: 89:11, dr: >20:1, determined by chiral HPLC. **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.57-7.41 (m, 3H), 7.35 (d, J = 7.2 Hz, 2H), 7.29 (d, J = 8.4 Hz, 2H), 7.19 (d, J = 8.0 Hz, 2H), 3.80 (d, J = 16.8 Hz, 1H), 2.79 (d, J = 16.4 Hz, 1H), 2.54 (s, 3H), 1.22 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.31, 140.01, 132.75, 130.84, 130.22, 128.48, 127.57, 126.42, 126.07, 117.05, 87.35, 51.95, 41.19, 22.64, 15.21. **HRMS** (ESI-TOF) [M+Na$^+$] calculated for $[C_{19}H_{17}O_2NNaS]^+$ 346.0878, observed 346.0873. **HPLC** (Chiralpak-AD column, 90: 10 hexane/ethanol, flow rate: 1.0 mL/min): tmajor = 15.201 min; tminor = 17.554 min.

(2S,3S)-2-(4-methoxyphenyl)-3-methyl-3-(4-(methylthio)phenyl)-5-oxotetrahydrofuran-2-carbonitrile (**3b**)



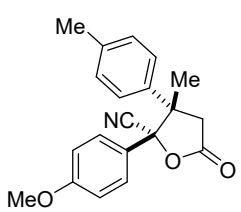
Yellow solid yield: 90%. er: 95:5, dr: 19:1, determined by chiral HPLC. **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.32-7.24 (m, 4H), 7.20-7.12 (m, 2H), 7.00-6.95 (m, 2H), 3.88 (s, 3H), 3.83-3.74 (m, 1H), 2.78 (d, J = 16.8 Hz, 1H), 2.53 (s, 3H), 1.23 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.43, 160.94, 139.86, 133.06, 127.96, 127.47, 126.08, 122.49, 117.12, 113.81, 87.37, 55.45, 52.08, 41.09, 22.71, 15.23. **HRMS** (ESI-TOF) [M+Na$^+$] calculated for $[C_{20}H_{19}NNaO_3S]^+$ 376.0983, observed 376.0978. **HPLC** (Chiralpak-IA column, 97: 3 hexane/ethanol, flow rate: 1.0 mL/min): tmajor = 28.346 min; tminor = 31.022min.

(2S,3S)-2-(4-methoxyphenyl)-3-methyl-5-oxo-3-phenyltetrahydrofuran-2-carbonitrile (**3c**)



White solid, yield: 82%. er: 91:9, dr: 14:1, determined by chiral HPLC. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.47-7.41 (m, 3H), 7.35-7.29 (m, 2H), 7.28-7.24 (m, 2H), 7.02-6.94 (m, 2H), 3.89 (s, 3H), 3.83 (d, J = 16.0 Hz, 1H), 2.81 (d, J = 16.0 Hz, 1H), 1.27 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.55, 160.94, 136.84, 128.80, 128.09, 127.01, 126.66, 122.57, 117.07, 113.77, 87.39, 55.45, 52.44, 41.08, 22.89. **HRMS** (ESI-TOF) [M+Na$^+$] calculated for $[C_{19}H_{17}NNaO_3]^+$ 330.1106, observed 330.1101. **HPLC** (Chiralpak-AD column, 95: 5 hexane/ethanol, flow rate: 1.0 mL/min): tmajor = 20.488 min; tminor = 13.340 min.

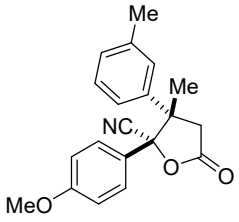
(2S,3S)-2-(4-methoxyphenyl)-3-methyl-5-oxo-3-(p-tolyl)tetrahydrofuran-2-carbonitrile (**3d**)



White solid, yield: 88%. er: 93:7, dr: 15:1, determined by chiral HPLC. **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.34-7.26 (m, 2H), 7.24 (d, J = 8.4 Hz, 2H), 7.15 (d, J = 8.4 Hz, 2H), 6.97 (d, J = 8.0 Hz, 2H), 3.89 (s, 3H), 3.81 (d, J = 16.8 Hz, 1H), 2.78 (d, J = 16.4 Hz, 1H), 2.41 (s, 3H), 1.23 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.69, 160.87, 138.72, 133.73, 129.46, 128.01, 126.91, 122.68, 117.17, 113.73,

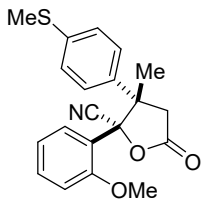
87.49, 55.43, 52.14, 41.14, 22.81, 21.03. **HRMS** (ESI-TOF) [M+Na$^+$] calculated for [$C_{20}H_{19}NNaO_3$]$^+$ 344.1263, observed 344.1258. **HPLC** (Chiralpak-AD column, 95: 5 hexane/ethanol, flow rate: 1.0 mL/min): tmajor = 16.383 min; tminor = 10.723 min.

(2S,3S)-2-(4-methoxyphenyl)-3-methyl-5-oxo-3-(m-tolyl)tetrahydrofuran-2-carbonitrile (**3e**)



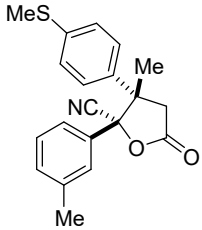
White solid, yield: 89%. er: 92:8, dr: 20:1, determined by chiral HPLC. **^{1}H NMR** (400 MHz, Chloroform-d) *δ*7.35-7.25 (m, 3H), 7.25-7.20 (m, 1H), 7.09-7.01 (m, 2H), 7.01-6.94 (m, 2H), 3.89 (s, 3H), 3.82 (d, *J* = 16.4 Hz, 1H), 2.79 (d, *J* = 16.8 Hz, 1H), 2.40 (s, 3H), 1.25 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) *δ* 172.66, 160.93, 138.44, 136.84, 129.49, 128.65, 128.16, 127.70, 124.03, 122.69, 117.10, 113.68, 87.42, 55.45, 52.35, 41.10, 22.97, 21.63. **HRMS** (ESI-TOF) [M+Na$^+$] calculated for [$C_{20}H_{19}NNaO_3$]$^+$ 344.1263, observed 344.1259. **HPLC** (Chiralpak-AD column, 95: 5 hexane/ethanol, flow rate: 1.0 mL/min): tmajor = 14.810 min; tminor = 9.441 min.

(2R,3S)-2-(2-methoxyphenyl)-3-methyl-3-(4-(methylthio)phenyl)-5-oxotetrahydrofuran-2-carbonitrile (**3f**)



Yellow solid, yield: 60%. er: 90:10, dr: 10:1, determined by chiral HPLC. **^{1}H NMR** (400 MHz, Chloroform-d) *δ* 7.49 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.46-7.38 (m, 3H), 7.34-7.29 (m, 2H), 7.07 (td, *J* = 7.6, 1.2 Hz, 1H), 6.95-6.85 (m, 1H), 3.66 (d, *J* = 17.2 Hz, 1H), 3.39 (s, 3H), 2.74 (d, *J* = 17.2 Hz, 1H), 2.53 (s, 3H), 1.27 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) *δ* 172.66, 155.88, 138.85, 135.23, 131.40, 127.62, 127.04, 125.80, 120.73, 119.99, 116.66, 111.57, 85.47, 54.80, 51.27, 42.51, 22.29, 15.51. **HRMS** (ESI-TOF) [M+Na$^+$] calculated for [$C_{20}H_{19}NNaO_3S$]$^+$ 376.0983, observed 376.0979. **HPLC** (Chiralpak-AD column, 97: 3 hexane/ethanol, flow rate: 1.0 mL/min): tmajor = 16.651 min; tminor = 18.829 min.

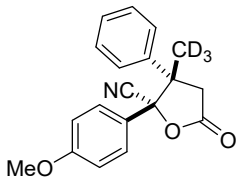
(2S,3S)-3-methyl-3-(4-(methylthio)phenyl)-5-oxo-2-(m-tolyl)tetrahydrofuran-2-carbonitrile (**3g**)



Yellow solid, yield: 95%. er: 90:10, dr: 15:1, determined by chiral HPLC. **^{1}H NMR** (400 MHz, Chloroform-d) *δ* 7.41-7.10 (m, 8H), 3.79 (d, *J* = 16.8 Hz, 1H), 2.78 (d, *J* = 16.8 Hz, 1H), 2.54 (s, 3H), 2.41 (s,

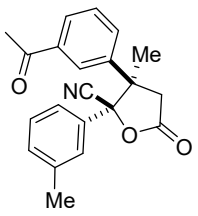
3H), 1.22 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.44, 139.96, 138.43, 132.87, 130.93, 130.71, 128.35, 127.61, 126.85, 126.01, 123.60, 117.11, 87.37, 51.90, 41.19, 22.68, 21.51, 15.23. **HRMS** (ESI-TOF) [M+H$^+$] calculated for $[C_{20}H_{20}NO_2S]^+$ 338.1215, observed 338.1209. **HPLC** (Chiralpak-AD column, 97: 3 hexane/ethanol, flow rate: 1.0 mL/min): tmajor = 8.871 min; tminor = 9.872 min.

(2S,3S)-2-(4-methoxyphenyl)-3-(methyl-d3)-5-oxo-3-phenyltetrahydrofuran-2-carbonitrile (**3h**)



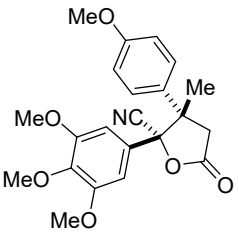
White solid, yield: 80%. er: 90:10, dr: >20:1, determined by chiral HPLC. NaNa **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.47-7.40 (m, 3H), 7.33-7.23 (m, 4H), 7.01-6.94 (m, 2H), 3.89 (s, 3H), 3.83 (d, *J* = 16.4, 1H), 2.81 (d, *J* = 16.4 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.55, 160.93, 136.81, 128.80, 128.08, 127.01, 126.65, 122.57, 117.06, 113.77, 87.38, 55.44, 52.34 (q, *J* = 6.6 Hz), 41.05, 29.70. **HRMS** (ESI-TOF) [M+Na$^+$] calculated for $[C_{19}H_{14}D_3NNaO_3]^+$ 333.1294, observed 333.1288. **HPLC** (Chiralpak-OD column, 95: 5 hexane/ethanol, flow rate: 1.0 mL/min): tmajor = 21.306 min; tminor = 24.121 min.

(2S,3S)-3-(3-acetylphenyl)-3-methyl-5-oxo-2-(m-tolyl)tetrahydrofuran-2-carbonitrile (**3i**)



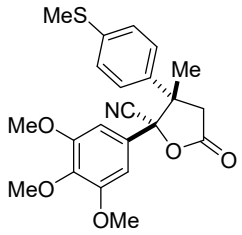
Yellow solid, yield: 96%. er: 90:10, dr: 11:1, determined by chiral HPLC. **^{1}H NMR** (400 MHz, Chloroform-d) δ 8.01 (dt, *J* = 7.2, 1.6 Hz, 1H), 7.85 (t, *J* = 2.0 Hz, 1H), 7.61-7.49 (m, 2H), 7.41-7.30 (m, 2H), 7.17-7.13 (m, 2H), 3.86 (d, *J* = 16.8 Hz, 1H), 2.86 (d, *J* = 16.8 Hz, 1H), 2.61 (s, 3H), 2.41 (s, 1H), 1.28 (s, 3H). **^{13}C NMR** (101 MHz, CDCl3) δ 197.27, 172.06, 138.63, 137.72, 137.34, 131.41, 131.24, 130.40, 129.17, 128.93, 128.47, 127.06, 126.95, 123.62, 116.93, 87.10, 52.39, 41.01, 26.66, 23.04, 21.50. **HRMS** (ESI-TOF) [M+Na$^+$] calculated for $[C_{21}H_{19}NNaO_3]^+$ 356.1263, observed 356.1257. **HPLC** (Chiralpak-OD column, 90: 10 hexane/ethanol, flow rate: 1.0 mL/min): tmajor = 19.314 min; tminor = 22.236 min.

(2S,3S)-3-(4-methoxyphenyl)-3-methyl-5-oxo-2-(3,4,5-trimethoxyphenyl)tetrahydrofuran-2-carbonitrile (**3j**)



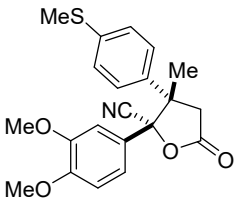
Yellow solid, yield: 87%. er: 90:10, dr: 20:1, determined by chiral HPLC. **^{1}H NMR** (500 MHz, Chloroform-d) δ 7.30 (d, J = 5.6 Hz, 2H), 6.95 (d, J = 7.2 Hz, 2H), 6.45 (s, 2H), 3.89 (s, 3H), 3.84 (s, 3H),3.80 (s, 6H), 3.79-3.74 (m, 1H), 2.75 (d, J = 12.6 Hz, 1H), 1.21 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 172.35, 160.00, 153.13, 128.86, 127.96, 126.23, 117.16, 113.85, 103.67, 87.36, 60.95, 56.35, 55.36, 51.86, 41.42, 22.44. **HRMS** (ESI-TOF) [M+Na$^+$] calculated for $[C_{22}H_{23}NNaO_6]^+$ 420.1423, observed 420.1418. **HPLC** (Chiralpak-IA column, 90: 10 hexane/ethanol, flow rate: 1.0 mL/min): tmajor = 15.785 min; tminor = 13.703 min.

(2S,3S)-3-methyl-3-(4-(methylthio)phenyl)-5-oxo-2-(3,4,5-trimethoxyphenyl)tetrahydrofuran-2-carbonitrile (**3k**)



Yellow oil, yield: 93%. er: 91:9, dr: 13:1, determined by chiral HPLC. **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.29 (s, 4H), 6.47 (s, 2H), 3.90 (s, 3H), 3.81 (s, 6H), 3.79-3.76 (m, 1H), 2.77 (d, J = 16.8 Hz, 1H), 2.52 (s, 3H), 1.23 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.24, 153.11, 140.30, 139.17, 132.39, 127.95, 126.04, 125.80, 117.02, 103.49, 87.12, 60.98, 56.34, 52.05, 41.21, 22.38, 15.22. **HRMS** (ESI-TOF) [M+Na$^+$] calculated for $[C_{22}H_{23}NNaO_4S]^+$ 436.1195, observed 436.1189. **HPLC** (Chiralpak-OD column, 90: 10 hexane/ethanol, flow rate: 1.0 mL/min): tmajor = 15.232 min; tminor = 17.988 min.

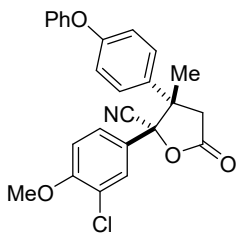
(2S,3S)-2-(3,4-dimethoxyphenyl)-3-methyl-3-(4-(methylthio)phenyl)-5-oxotetrahydrofuran-2-carbonitrile (**3l**)



Yellow oil, yield: 90%. er: 90:10, dr: 19:1, determined by chiral HPLC. **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.31-7.26 (m, 2H), 7.25-7.18 (m, 2H), 6.93-6.88(m, 2H), 6.79-6.74 (m, 1H), 3.95 (s,

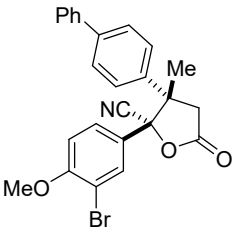
3H), 3.85 (s, 3H), 3.79 (d, *J* = 16.4 Hz, 1H), 2.78 (d, *J* = 16.8 Hz, 1H), 2.53 (s, 3H), 1.23 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.40, 150.39, 148.70, 140.04, 132.81, 127.69, 125.94, 122.81, 119.33, 117.11, 110.63, 109.36, 87.25, 56.13, 56.03, 52.12, 41.13, 22.60, 15.23. **HRMS** (ESI-TOF) [M+Na$^+$] calculated for $[C_{21}H_{21}NNaO_4S]^+$ 406.1089, observed 406.1086. **HPLC** (Chiralpak-AD column, 90: 10 hexane/ethanol, flow rate: 1.0 mL/min): tmajor = 20.330 min; tminor = 18.370 min.

(2S,3S)-2-(3-chloro-4-methoxyphenyl)-3-methyl-5-oxo-3-(4-phenoxyphenyl)tetrahydrofuran-2-carbonitrile (**3m**)



Yellow solid, yield: 96%. er: 91:9, dr>20:1, determined by chiral HPLC. **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.46-7.37 (m, 3H), 7.26-7.15 (m, 4H), 7.13-7.07 (m, 2H), 7.08-7.02 (m, 2H), 6.99 (d, *J* = 8.8 Hz, 1H), 3.98 (s, 3H), 3.88 (d, *J* = 16.8 Hz, 1H), 2.80 (d, *J* = 16.4 Hz, 1H), 1.25 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.02, 158.19, 156.40, 156.06, 130.50, 129.98, 128.55, 128.23, 126.25, 124.16, 123.58, 122.92, 119.75, 118.15, 116.79, 111.54, 86.65, 56.35, 52.00, 41.14, 22.79. **HRMS** (ESI-TOF) [M+Na$^+$] calculated for $[C_{25}H_{20}ClNNaO_4]^+$ 456.0979, observed 456.0974. **HPLC** (Chiralpak-IA column, 95: 5 hexane/ethanol, flow rate: 1.0 mL/min): tmajor =19.030 min; tminor = 22.399 min.

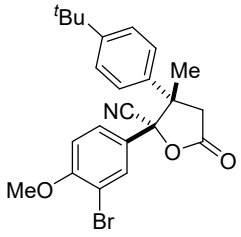
(2S,3S)-3-([1,1'-biphenyl]-4-yl)-2-(3-bromo-4-methoxyphenyl)-3-methyl-5-oxotetrahydrofuran-2-carbonitrile (**3n**)



Yellow solid, yield: 90%. er: 93:7. dr: 19:1, determined by chiral HPLC. **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.72-7.67 (m, 2H), 7.67-7.62 (m, 2H), 7.61 (d, *J* = 2.4 Hz, 1H), 7.53-7.47 (m, 2H), 7.44-7.40 (m, 1H), 7.38-7.32 (m, 2H), 7.31-7.25 (m, 1H), 6.97 (d, *J* = 8.8 Hz, 1H), 3.99 (s, 3H), 3.90-3.81 (m, 1H), 2.85 (d, *J* = 16.8 Hz, 1H), 1.30 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.08, 157.33, 141.79, 139.79, 135.18, 131.33, 128.93, 127.87, 127.51, 127.44, 127.12, 127.08, 124.01, 116.79, 111.90, 111.30, 86.44, 56.46, 52.31, 41.08, 22.72. **HRMS** (ESI-TOF) [M+Na$^+$] calculated for $[C_{25}H_{20}BrNNaO_3]^+$ 484.0524, observed 484.0521. **HPLC** (Chiralpak-

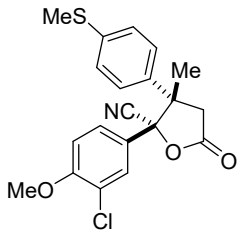
AD column, 92: 8 hexane/ethanol, flow rate: 1.0 mL/min): tmajor = 16.396 min; tminor = 20.473 min.

(2S,3S)-2-(3-bromo-4-methoxyphenyl)-3-(4-(tert-butyl)phenyl)-3-methyl-5-oxotetrahydrofuran-2-carbonitrile (**3o**)



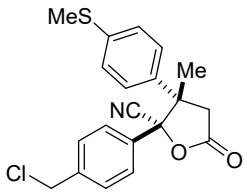
White solid, yield: 85%. er: 90:10, dr: 11:1, determined by chiral HPLC. **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.56 (d, J = 2.4 Hz, 1H), 7.49-7.42 (m, 2H), 7.25 (dd, J = 8.4, 2.4 Hz, 1H), 7.20-7.17 (m, 2H), 6.94 (d, J = 8.8 Hz, 1H), 3.96 (s, 3H), 3.79 (d, J = 16.8 Hz, 1H), (m, 1H), 2.75 (d, J = 16.8 Hz, 1H), 1.37 (s, 9H), 1.24 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.26, 157.18, 152.01, 133.12, 131.20, 127.01, 126.74, 125.75, 124.18, 116.82, 111.77, 111.22, 86.43, 56.41, 52.04, 41.09, 34.58, 31.20, 22.63. **HRMS** (ESI-TOF) [M+Na$^+$] calculated for $[C_{23}H_{24}BrNNaO_3]^+$ 464.0837, observed 464.0832. **HPLC** (Chiralpak-OD column, 97: 3 hexane/ethanol, flow rate: 1.0 mL/min): tmajor = 13.673 min; tminor = 18.124 min.

(2S,3S)-2-(3-chloro-4-methoxyphenyl)-3-methyl-3-(4-(methylthio)phenyl)-5-oxotetrahydrofuran-2-carbonitrile (**3p**)



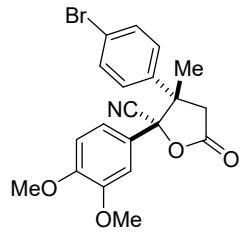
Yellow solid, yield: 92%. er: 90:10, dr: 12:1, determined by chiral HPLC. **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.44-7.37 (m, 1H), 7.35-7.26 (m, 2H), 7.21-7.15 (m, 3H), 6.99 (d, J = 8.4 Hz, 1H), 3.98 (s, 3H), 3.78 (d, J = 16.8 Hz, 1H), 2.79 (d, J = 16.4 Hz, 1H), 2.54 (s, 3H), 1.24 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.00, 156.40, 140.20, 132.56, 128.21, 127.42, 126.24, 126.12, 123.54, 122.93, 116.74, 111.51, 86.54, 56.35, 52.08, 41.00, 22.60, 15.20. **HRMS** (ESI-TOF) [M+Na$^+$] calculated for $[C_{20}H_{18}ClNNaO_3S]^+$ 410.0594, observed 410.0589. **HPLC** (Chiralpak-AD column, 92: 8 hexane/ethanol, flow rate: 1.0 mL/min): tmajor = 21.147 min; tminor = 17.764 min.

(2S,3S)-2-(4-(chloromethyl)phenyl)-3-methyl-3-(4-(methylthio)phenyl)-5-oxotetrahydrofuran-2-carbonitrile (**3q**)



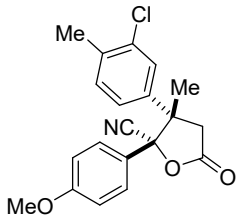
Yellow solid, yield: 87%. er: 90:10, dr: 8:1, determined by chiral HPLC. **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.53-7.47 (m, 2H), 7.37-7.33 (m, 2H), 7.32-7.26 (m, 2H), 7.22-7.17 (m, 2H), 4.65 (s, 2H), 3.80 (d, J = 16.8 Hz, 1H), 2.79 (d, J = 16.8 Hz, 1H), 2.54 (s, 3H), 1.23 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.12, 140.17, 139.68, 132.50, 131.01, 128.59, 127.54, 126.84, 126.08, 116.87, 87.07, 51.99, 45.17, 41.14, 22.57, 15.18. **HRMS** (ESI-TOF) [M+H$^+$] calculated for $[C_{20}H_{19}ClNO_2S]^+$ 372.0825, observed 372.0816. **HPLC** (Chiralpak-AD column, 92: 8 hexane/ethanol, flow rate: 1.0 mL/min): tmajor = 37.669 min; tminor = 23.731 min.

(2S,3S)-3-(4-bromophenyl)-2-(3,4-dimethoxyphenyl)-3-methyl-5-oxotetrahydrofuran-2-carbonitrile (**3r**)



Yellow solid, yield: 80%. er: 91:9, dr: 11:1, determined by chiral HPLC. **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.57 (d, J = 8.8 Hz, 2H), 7.18 (d, J = 8.4 Hz, 2H), 6.96-6.86 (m, 2H), 6.82-6.74 (m, 1H), 3.95 (s, 3H), 3.86 (s, 3H), 3.76 (d, J = 16.4 Hz, 1H), 2.80 (d, J = 16.8 Hz, 1H), 1.24 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.00, 150.54, 148.80, 135.70, 131.85, 128.98, 123.34, 122.48, 119.44, 116.92, 110.69, 109.35, 86.98, 56.16, 56.04, 52.24, 41.02, 24.06, 22.67. **HRMS** (ESI-TOF) [M+H$^+$] calculated for $[C_{20}H_{19}BrNO_4]^+$ 416.0497, observed 416.0493. **HPLC** (Chiralpak-AD column, 95: 5 hexane/ethanol, flow rate: 1.0 mL/min): tmajor = 29.818 min; tminor = 25.782 min.

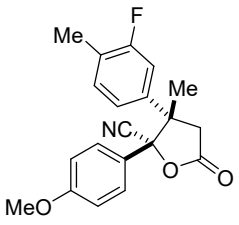
(2S,3S)-3-(3-chloro-4-methylphenyl)-2-(4-methoxyphenyl)-3-methyl-5-oxotetrahydrofuran-2-carbonitrile (**3s**)



Yellow solid, yield: 75%. er: 91:9. dr: 11:1, determined by chiral HPLC. ^{1}H NMR (400 MHz, Chloroform-d) δ 7.36 (d, J = 8.4 Hz, 1H), 7.29-7.24 (m, 2H), 7.10-7.08 (m, 1H), 6.96 (d, J = 9.0 Hz, 2H), 3.87 (s, 3H), 3.74 (d, J = 16.4 Hz, 1H), 2.77 (d, J = 16.4 Hz,

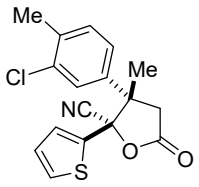
1H), 2.39 (s, 3H), 1.21 (s, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.22, 161.02, 136.52, 135.42, 135.04, 129.55, 129.34, 128.06, 125.75, 122.29, 116.96, 113.76, 87.19, 55.44, 52.02, 41.02, 22.89, 20.31. **HRMS** (ESI-TOF) [M+Na$^+$] calculated for $[C_{20}H_{18}ClNNaO_3]^+$ 378.0873, observed 378.0868. **HPLC** (Chiralpak-AD column, 97:3 hexane/ethanol, flow rate: 1.0 mL/min): tmajor = 26.867 min; tminor = 13.782 min.

(2S,3S)-3-(3-fluoro-4-methylphenyl)-2-(4-methoxyphenyl)-3-methyl-5-oxotetrahydrofuran-2-carbonitrile (**3t**)



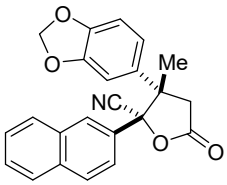
White solid, yield: 89%. er: 93:7, dr:10:1, determined by chiral HPLC. **^{1}H NMR** (400 MHz, Chloroform-d) *δ* 7.33-7.28 (m, 3H), 7.02-6.95 (m, 3H), 6.85 (dd, *J* = 11.2, 2.0 Hz, 1H), 3.89 (s, 3H), 3.74 (d, *J* = 16.8 Hz, 1H), 2.79 (d, *J* = 16.4 Hz, 1H), 2.33 (s, 3H), 1.22 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) *δ* 172.19, 161.14 (d, *J* = 244.2 Hz), 161.02, 136.60 (d, *J* = 6.9 Hz), 131.79 (d, *J* = 5.5 Hz), 128.03, 126.63, 125.68 (d, *J* = 17.1 Hz), 122.34 (d, *J* = 2.6 Hz), 116.97, 114.09 (d, *J* = 24.0 Hz), 113.85, 87.21, 55.46, 52.05 (d, *J* = 1.7 Hz), 41.11, 22.92, 14.27 (d, *J* = 3.1 Hz). **HRMS** (ESI-TOF) [M+Na$^+$] calculated for $[C_{20}H_{18}FNNaO_3]^+$ 362.1168, observed 362.1162. **HPLC** (Chiralpak-AD column, 95:5 hexane/ethanol, flow rate: 1.0 mL/min): tmajor = 19.971 min; tminor = 11.329 min.

(2S,3S)-3-(3-chloro-4-methylphenyl)-3-methyl-5-oxo-2-(thiophen-2-yl)tetrahydrofuran-2-carbonitrile (**3u**)



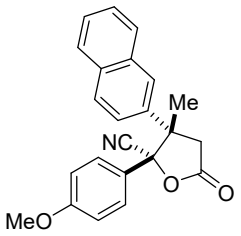
Yellow oil, yield: 85%. er: 91:9, dr: 6:1, determined by chiral HPLC. **^{1}H NMR** (400 MHz, Chloroform-d) *δ* 7.53 (dd, *J* = 5.2, 1.2 Hz, 1H), 7.34-7.27 (m, 2H), 7.21 (dd, *J* = 3.6, 1.2 Hz, 1H), 7.17-7.11 (m, 2H), 3.70 (d, *J* = 17.2 Hz, 1H), 2.85 (d, *J* = 16.8 Hz, 1H), 2.42 (s, 3H), 1.41 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) *δ* 171.31, 137.11, 136.49, 135.00, 133.33, 131.38, 129.16, 128.16, 127.53, 127.13, 124.84, 116.14, 85.09, 52.28, 40.74, 23.70, 19.76. **HRMS** (ESI-TOF) [M+Na$^+$] calculated for $[C_{17}H_{14}ClNNaO_2S]^+$ 354.0331, observed 354.0328. **HPLC** (Chiralpak-IC column, 98: 2 hexane/ethanol, flow rate: 1.0 mL/min): tmajor = 18.814 min; tminor = 16.204 min.

(2S,3S)-3-(benzo[d][1,3]dioxol-5-yl)-3-methyl-2-(naphthalen-2-yl)-5-oxotetrahydrofuran-2-carbonitrile (**3v**)



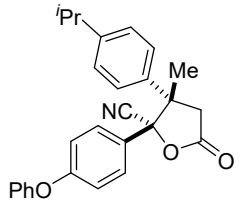
Yellow solid, yield: 75%. er: 91:9, dr: 10:1, determined by chiral HPLC. **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.99-7.87 (m, 4H), 7.66-7.57 (m, 2H), 7.43 (dd, J = 8.8, 2.0 Hz, 1H), 6.87 (d, J = 8.4 Hz, 1H), 6.81-6.71 (m, 2H), 6.05 (dd, J = 12.0, 1.6 Hz, 2H), 3.79 (d, J = 16.8 Hz, 1H), 2.83 (d, J = 16.8 Hz, 1H), 1.24 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.35, 148.19, 148.02, 133.75, 132.34, 130.43, 128.54, 128.35, 128.15, 127.75, 127.65, 127.17, 126.65, 123.22, 120.93, 117.11, 108.30, 107.72, 101.64, 87.66, 52.41, 41.54, 23.24. **HRMS** (ESI-TOF) [M+Na$^+$] calculated for $[C_{23}H_{17}NNaO_4]^+$ 394.1055, observed 394.1052. **HPLC** (Chiralpak-AD column, 90: 10 hexane/ethanol, flow rate: 1.0 mL/min): tmajor = 37.044 min; tminor = 15.146 min.

(2S,3S)-2-(4-methoxyphenyl)-3-methyl-3-(naphthalen-2-yl)-5-oxotetrahydrofuran-2-carbonitrile (**3w**)



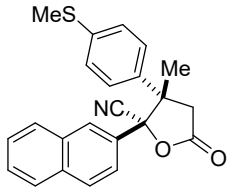
White solid, yield: 91%. er: 92:8, dr: 7:1, determined by chiral HPLC. **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.95-7.82 (m, 3H), 7.76 (s, 1H), 7.62-7.53 (m, 2H), 7.39-7.29 (m, 3H), 6.99 (d, J = 8.8 Hz, 2H), 3.99 (d, J = 16.4 Hz, 1H), 3.91 (s, 3H), 2.91 (d, J = 16.8 Hz, 1H), 1.37 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.53, 161.01, 134.30, 132.96, 132.94, 128.52, 128.36, 128.20, 127.53, 127.03, 126.77, 126.67, 124.21, 122.65, 117.13, 113.80, 87.44, 55.47, 52.65, 41.28, 23.06. **HRMS** (ESI-TOF) [M+Na$^+$] calculated for $[C_{23}H_{19}NNaO_3]^+$ 380.1263, observed 380.1258. **HPLC** (Chiralpak-OD column, 95: 5 hexane/ethanol, flow rate: 1.0 mL/min): tmajor = 20.201 min; tminor = 25.058 min.

(2S,3S)-3-(4-isopropylphenyl)-3-methyl-5-oxo-2-(4-phenoxyphenyl)tetrahydrofuran-2-carbonitrile (**3x**)



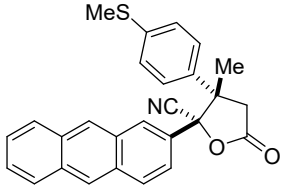
Yellow oil, yield: 92%. er: 93:7, dr: 15:1, determined by chiral HPLC. **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.48-7.35 (m, 2H), 7.36-7.23 (m, 4H), 7.22-7.13 (m, 3H), 7.12-7.05 (m, 2H), 77.04-7.00 (m, 2H), 3.80 (d, J = 16.8 Hz, 1H), 2.93 (p, J = 6.8 Hz, 1H), 2.75 (d, J = 16.0 Hz, 1H), 1.26 (d, J = 6.8 Hz, 6H), 1.23 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ172.47, 159.20, 155.77, 149.49, 133.70, 129.99, 128.09, 126.98, 126.80, 124.97, 124.32, 119.81, 117.57, 117.05, 87.17, 51.99, 41.15, 33.58, 23.77, 23.75, 22.70.**HRMS** (ESI-TOF) [M+Na$^+$] calculated for $[C_{27}H_{25}NNaO_3]^+$ 434.1732, observed 434.1728. **HPLC** (Chiralpak-OD column, 95: 5 hexane/ethanol, flow rate: 1.0 mL/min): tmajor = 8.823 min; tminor = 16.896 min.

(2S,3S)-3-methyl-3-(4-(methylthio)phenyl)-2-(naphthalen-2-yl)-5-oxotetrahydrofuran-2-carbonitrile (**3y**)



Yellow oil, yield: 90%. er: 90:10, dr: 13:1, determined by chiral HPLC. **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.97-7.86 (m, 4H), 7.67-7.57 (m, 2H), 7.39 (dd, J = 8.8, 2.0 Hz, 1H), 7.35-7.26 (m, 2H), 7.26-7.18 (m, 2H), 3.86 (d, J = 16.8 Hz, 1H), 2.84 (d, J = 16.8 Hz, 1H), 2.55 (s, 3H), 1.26 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.36, 140.10, 133.75, 132.81, 132.36, 128.54, 128.39, 128.15, 127.76, 127.65, 127.16, 126.46, 126.08, 123.08, 117.10, 87.52, 52.21, 41.25, 22.73, 15.22. **HRMS** (ESI-TOF) [M+Na$^+$] calculated for $[C_{23}H_{19}NNaO_2S]^+$ 396.1034, observed 396.1031. **HPLC** (Chiralpak-AD column, 95: 5 hexane/ethanol, flow rate: 1.0 mL/min): tmajor = 33.118 min; tminor = 21.190 min.

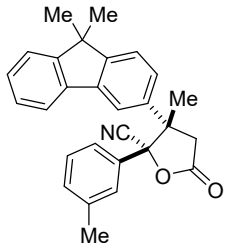
(2S,3S)-2-(anthracen-2-yl)-3-methyl-3-(4-(methylthio)phenyl)-5-oxotetrahydrofuran-2-carbonitrile (**3z**)



Yellow solid, yield: 95%. er: 92:8, dr: 6:1, determined by chiral HPLC. **^{1}H NMR** (400 MHz, Chloroform-d) δ 8.50 (d, J = 3.6 Hz, 2H), 8.11-8.02 (m, 4H), 7.60-7.52 (m, 2H), 7.37-7.23 (m, 5H), 3.87 (d, J = 16.8 Hz, 1H), 2.85 (d, J = 16.8 Hz, 1H), 2.56 (s, 3H), 1.30 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.39, 140.10, 132.87, 132.64,

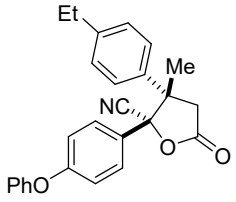
132.27, 131.25, 130.04, 128.82, 128.30, 128.21, 127.66, 127.56, 127.49, 127.11, 126.41, 126.39, 126.19, 126.08, 122.24, 117.07, 87.61, 52.33, 41.26, 22.79, 15.23. **HRMS** (ESI-TOF) [M+Na$^+$] calculated for $[C_{27}H_{21}NNaO_2S]^+$ 446.1191, observed 446.1184. **HPLC** (Chiralpak-OD column, 85: 15 hexane/ethanol, flow rate: 1.0 mL/min): tmajor = 12.939 min; tminor = 14.537 min.

(2S,3S)-3-(9,9-dimethyl-9H-fluoren-3-yl)-3-methyl-5-oxo-2-(m-tolyl)tetrahydrofuran-2-carbonitrile (**3aa**)



Yellow solid, yield: 95%. er: 90:10, dr: 12:1, determined by chiral HPLC. **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.83-7.76 (m, 2H), 7.51-7.47 (m, 1H), 7.42-7.38 (m, 2H), 7.38-7.33 (m, 3H), 7.26 (d, J = 2.0 Hz, 1H), 7.20-7.13 (m, 2H), 3.94 (dd, J = 16.8, 1.2 Hz, 1H), 2.87 (d, J = 16.8 Hz, 1H), 2.41 (s, 3H), 1.53 (s, 3H), 1.48 (s, 3H), 1.33 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.65, 153.87, 140.02, 138.31, 138.16, 135.05, 130.98, 130.83, 128.24, 127.92, 127.21, 127.00, 125.94, 123.79, 122.72, 121.70, 120.43, 120.08, 117.19, 87.67, 52.62, 47.02, 41.45, 27.06, 26.92, 22.79, 21.52. **HRMS** (ESI-TOF) [M+Na$^+$] calculated for $[C_{28}H_{25}NNaO_2]^+$ 430.1783, observed 430.1780. **HPLC** (Chiralpak-AD column, 97: 3 hexane/ethanol, flow rate: 1.0 mL/min): tmajor = 8.662 min; tminor = 7.205 min.

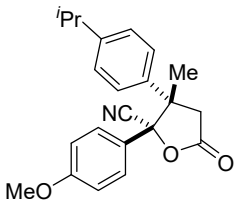
(2S,3S)-3-(4-ethylphenyl)-3-methyl-5-oxo-2-(4-phenoxyphenyl)tetrahydrofuran-2-carbonitrile (**3ab**)



Green solid, yield: 90%. er: 93:7, dr: 20:1, determined by chiral HPLC. **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.47-7.39 (m, 2H), 7.33-7.29 (m, 2H), 7.29-7.26 (m, 2H), 7.25-7.19 (m, 3H), 7.13-7.08 (m, 2H), 7.08-7.03 (m, 2H), 3.83 (d, J = 16.8 Hz, 1H), 2.79 (d, J = 16.8 Hz, 1H), 2.71 (q, J = 7.6 Hz, 2H), 1.29 (t, J = 7.6 Hz, 3H), 1.26 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.51, 159.27, 155.84, 145.01, 133.69, 130.05, 128.29, 128.17, 127.02, 125.00, 124.39, 119.87, 117.64, 117.10, 87.28, 52.09, 41.20, 28.34, 22.76, 15.20. **HRMS** (ESI-TOF) [M+Na$^+$] calculated for

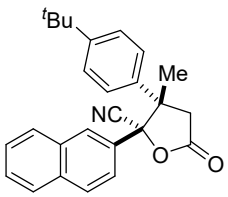
$[C_{26}H_{23}NNaO_3]^+$ 420.1576, observed 420.1571. **HPLC** (Chiralpak-OD column, 97: 3 hexane/ethanol, flow rate: 1.0 mL/min): tmajor = 12.946 min; tminor = 24.425 min.

(2S,3S)-3-(4-isopropylphenyl)-2-(4-methoxyphenyl)-3-methyl-5-oxotetrahydrofuran-2-carbonitrile (**3ac**)



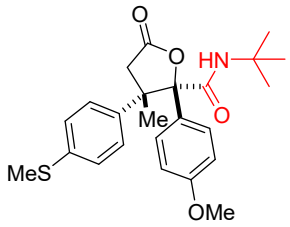
White oil, yield: 88%. er: 90:10, dr: 13:1, determined by chiral HPLC. **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.33-7.25 (m, 4H), 7.22-7.13 (m, 2H), 7.01-6.94 (m, 2H), 3.89 (s, 3H), 3.82 (d, J = 16.8 Hz, 1H), 2.97 (m, 1H), 2.78 (d, J = 16.8 Hz, 1H), 1.30 (d, J = 6.8 Hz, 6H), 1.23 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.70, 160.86, 149.46, 133.99, 127.99, 127.02, 126.81, 122.76, 117.19, 113.74, 87.44, 55.44, 52.13, 41.23, 33.66, 23.85, 22.84. **HRMS** (ESI-TOF) [M+Na$^+$] calculated for $[C_{22}H_{23}NNaO_3]^+$ 372.1576, observed 372.1571. **HPLC** (Chiralpak-OD column, 95: 5 hexane/ethanol, flow rate: 1.0 mL/min): tmajor = 8.547 min; tminor = 11.431 min.

(2S,3S)-3-(4-(tert-butyl)phenyl)-3-methyl-2-(naphthalen-2-yl)-5-oxotetrahydrofuran-2-carbonitrile (**3ad**)



White solid, yield: 74%. er: 90:10, dr:10:1, determined by chiral HPLC. **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.97-7.87 (m, 4H), 7.68-7.55 (m, 2H), 7.16 (d, J = 8.8 Hz, 2H), 7.39 (dd, J = 8.4, 1.6 Hz, 1H), 7.25 (d, J = 8.4 Hz, 2H), 3.90 (d, J = 16.0 Hz, 1H), 2.84 (d, J = 16.8 Hz, 1H), 1.39 (s, 9H), 1.27 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.63, 151.97, 133.72, 133.42, 132.37, 128.55, 128.44, 128.32, 127.75, 127.55, 127.09, 126.98, 126.41, 125.71, 123.20, 117.19, 87.55, 52.17, 41.42, 34.63, 31.27, 22.85. **HRMS** (ESI-TOF) [M+Na$^+$] calculated for $[C_{26}H_{25}NNaO_2]^+$ 406.1783, observed 406.1779. **HPLC** (Chiralpak-AD column, 95: 5 hexane/ethanol, flow rate: 1.0 mL/min): tmajor = 8.423 min; tminor = 7.613 min.

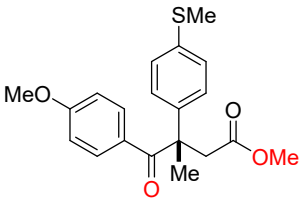
(2S,3S)-N-(tert-butyl)-2-(4-methoxyphenyl)-3-methyl-3-(4-(methylthio)phenyl)-5-oxotetrahydrofuran-2-carboxamide (**5**)



Yellow solid, yield: 66%. er: 91:9, dr: 2:1, determined by chiral HPLC. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.69 (d, J = 7.2 Hz, 1H), 7.15-7.05 (m, 3H), 7.03 (d, J = 7.2 Hz, 2H), 6.62 (d, J = 7.2 Hz, 2H), 3.74 (s, 3H), 3.19 (d, J = 13.2 Hz, 1H), 2.46

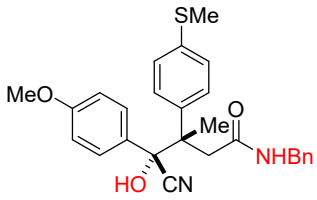
(s, 3H), 2.45 (s, 1H), 1.35 (s, 9H), 1.26 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ174.05, 167.80, 159.45, 137.69, 135.37, 128.67, 127.50, 127.16, 125.52, 112.86, 90.97, 55.20, 51.66, 50.99, 41.38, 28.58, 24.40, 15.65. **HRMS** (ESI-TOF) [M+Na$^+$] calculated for $[C_{24}H_{29}NNaO_4S]^+$ 450.1715, observed 450.1709. **HPLC** (Chiralpak-AD column, 95: 5 hexane/ethanol, flow rate: 1.0 mL/min): tmajor = 5.763 min; tminor = 6.333 min.

Methyl(S)-4-(4-methoxyphenyl)-3-methyl-3-(4-(methylthio)phenyl)-4-oxobutanoate (**6**)



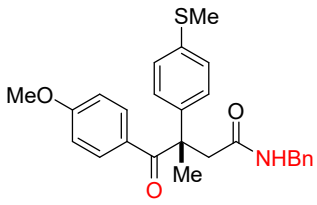
Yellow solid, yield: 94%. er: 92:8, determined by chiral HPLC. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.54-7.48 (m, 2H), 7.27-7.21 (m, 4H), 6.77-6.70 (m, 2H), 3.79 (s, 3H), 3.56 (s, 3H), 3.09 (d, J = 15.6 Hz, 1H), 2.88 (d, J = 15.6 Hz, 1H), 2.49 (s, 3H), 1.87 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 200.22, 171.72, 162.32, 139.51, 137.58, 132.00, 128.46, 126.73, 126.69, 113.24, 55.32, 52.76, 51.41, 45.33, 23.77, 15.49. **HRMS** (ESI-TOF) [M+H$^+$] calculated for $[C_{20}H_{22}NaO_4S]^+$ 381.1136, observed 381.1132. **HPLC** (Chiralpak-OD column, 95: 5 hexane/ethanol, flow rate: 1.0 mL/min): tmajor = 10.349 min; tminor = 12.910 min.

(3S,4R)-N-benzyl-4-cyano-4-hydroxy-4-(4-methoxyphenyl)-3-methyl-3-(4-(methylthio)phenyl)butanamide (**7**)



Yellow solid, yield: 38%. er: 90:10, dr: >20:1, determined by chiral HPLC. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.35 (br, 1H), 7.40-7.31 (m, 3H), 7.27-7.23 (m, 2H), 7.10-7.02 (m, 2H), 6.99 (m, 2H), 6.95-6.87 (m, 2H), 6.71-6.58 (m, 2H), 6.24 (t, J = 5.6 Hz, 1H), 4.48 (qd, J = 14.8, 6.0 Hz, 2H), 3.88-3.82 (m, 1H), 3.78 (s, 3H), 2.73 (d, J = 15.6 Hz, 1H), 2.46 (s, 3H), 1.40 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.38, 159.50, 138.69, 137.99, 137.04, 128.89, 128.87, 128.66, 127.95, 127.92, 127.85, 125.49, 121.67, 112.38, 80.98, 55.26, 48.29, 47.07, 44.31, 16.65, 15.48. **HRMS** (ESI-TOF) [M+Na$^+$] calculated for $[C_{27}H_{28}N_2NaO_3S]^+$ 483.1718, observed 483.1715. **HPLC** (Chiralpak-AD column, 95: 5 hexane/ethanol, flow rate: 1.0 mL/min): tmajor = 23.242 min; tminor = 24.843 min.

(S)-N-benzyl-4-(4-methoxyphenyl)-3-methyl-3-(4-(methylthio)phenyl)-4-oxobutanamide (**8**)



White solid, yield: 42%. er: 91:9, determined by chiral HPLC. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.60-7.42 (m, 2H), 7.34-7.25 (m, 3H), 7.21 (s, 4H), 7.13-6.98 (m, 2H), 6.85-6.59 (m, 2H), 6.17 (t, J = 5.6 Hz, 1H), 4.46-4.14 (m, 2H), 3.80 (s, 3H), 3.07 (d, J = 13.6 Hz, 1H), 2.64 (d, J = 13.6 Hz, 1H), 2.49 (s, 3H), 1.88 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 201.60, 170.40, 162.58, 139.73, 138.26, 137.77, 132.29, 128.56, 128.17, 127.64, 127.28, 126.84, 126.49, 113.32, 55.37, 53.54, 48.54, 43.46, 22.93, 15.42. **HRMS** (ESI-TOF) [M+H$^+$] calculated for $[C_{26}H_{27}NNaO_3S]^+$ 456.1609, observed 456.1604. **HPLC** (Chiralpak-AD column, 95: 5 hexane/ethanol, flow rate: 1.0 mL/min): tmajor = 15.842 min; tminor = 17.851 min.

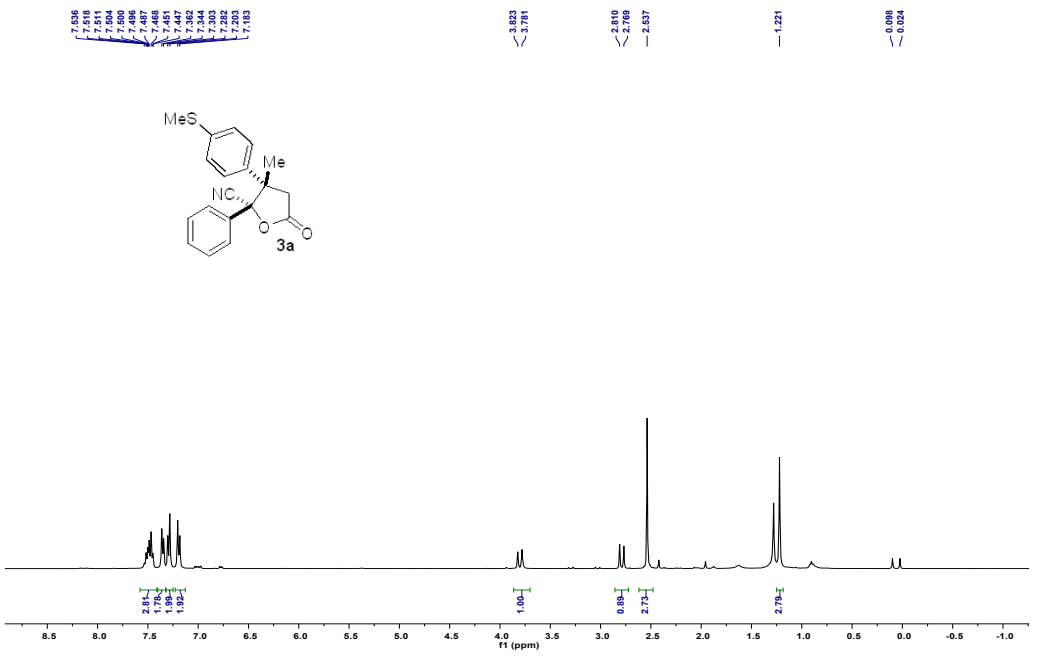
Reference

(1) Mo, J.; Chen, X.; Chi, Y. R. *J. Am. Chem. Soc.* **2012**, *134*, 8810.

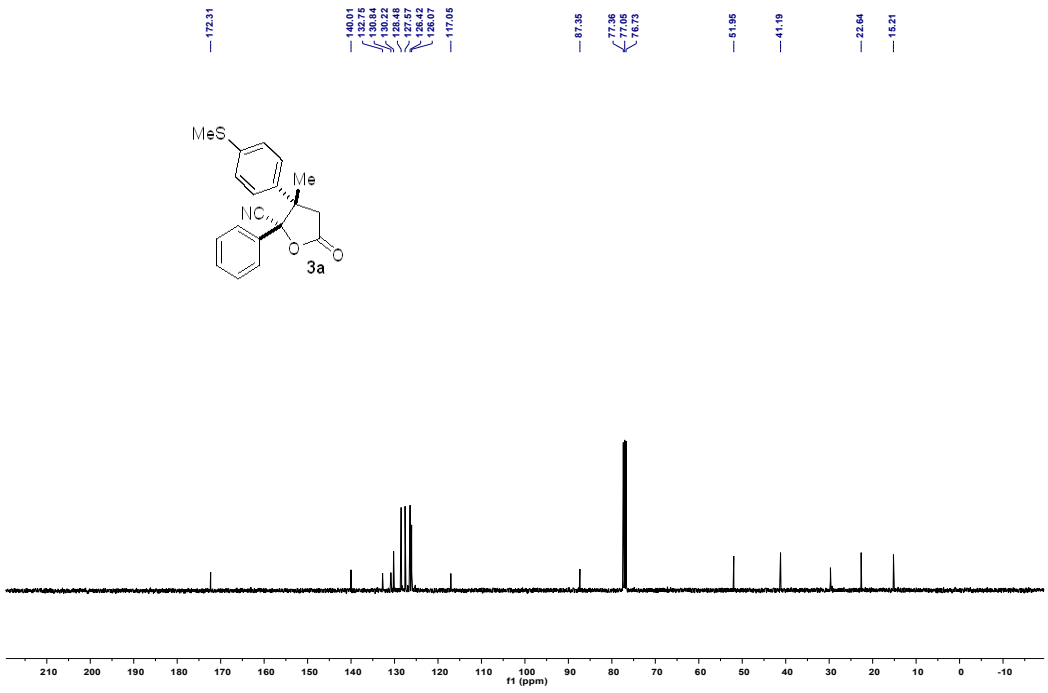
(2) M Stadler.; B List. *Synlett* **2008**, *4*, 597.

NMR spectra

3a

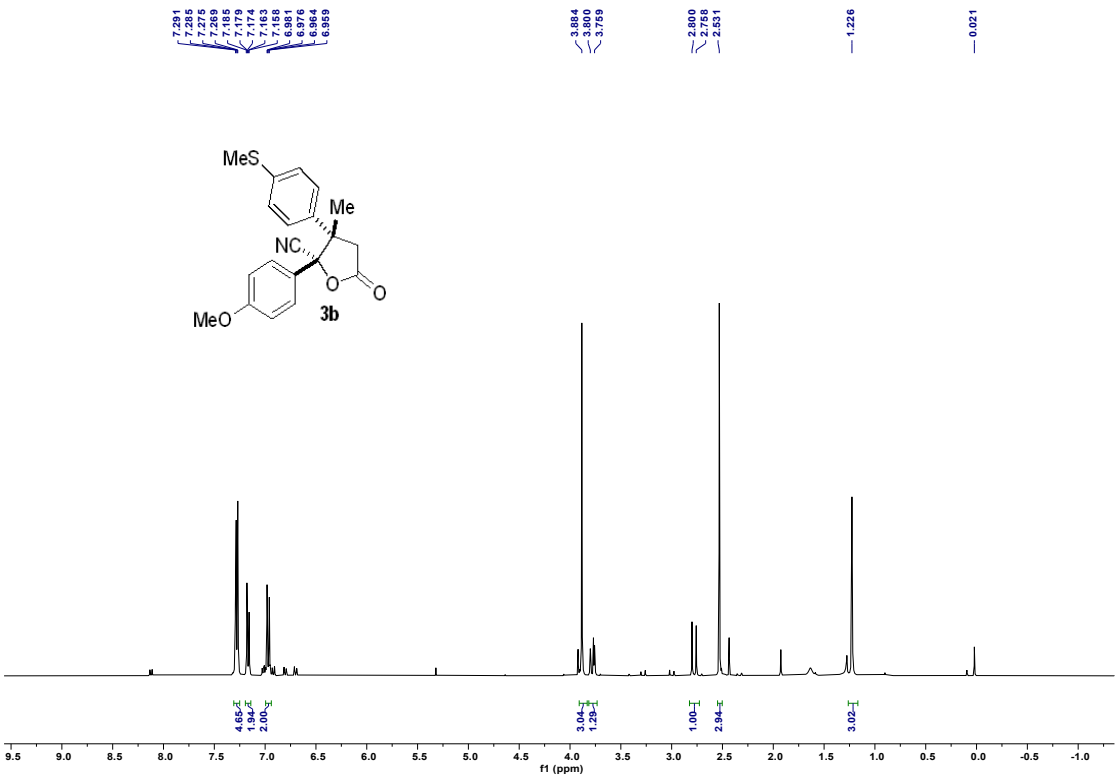


^{1}H NMR (400 MHz, $CDCl_3$)

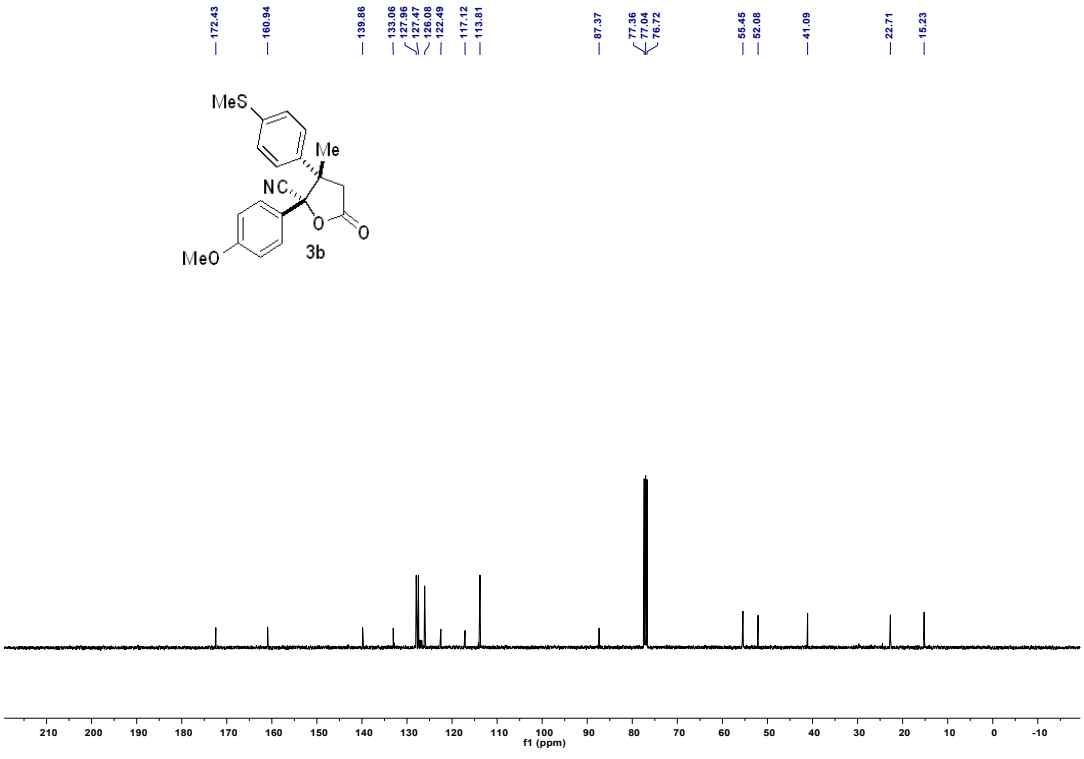


^{13}C NMR (101 MHz, $CDCl_3$)

3b

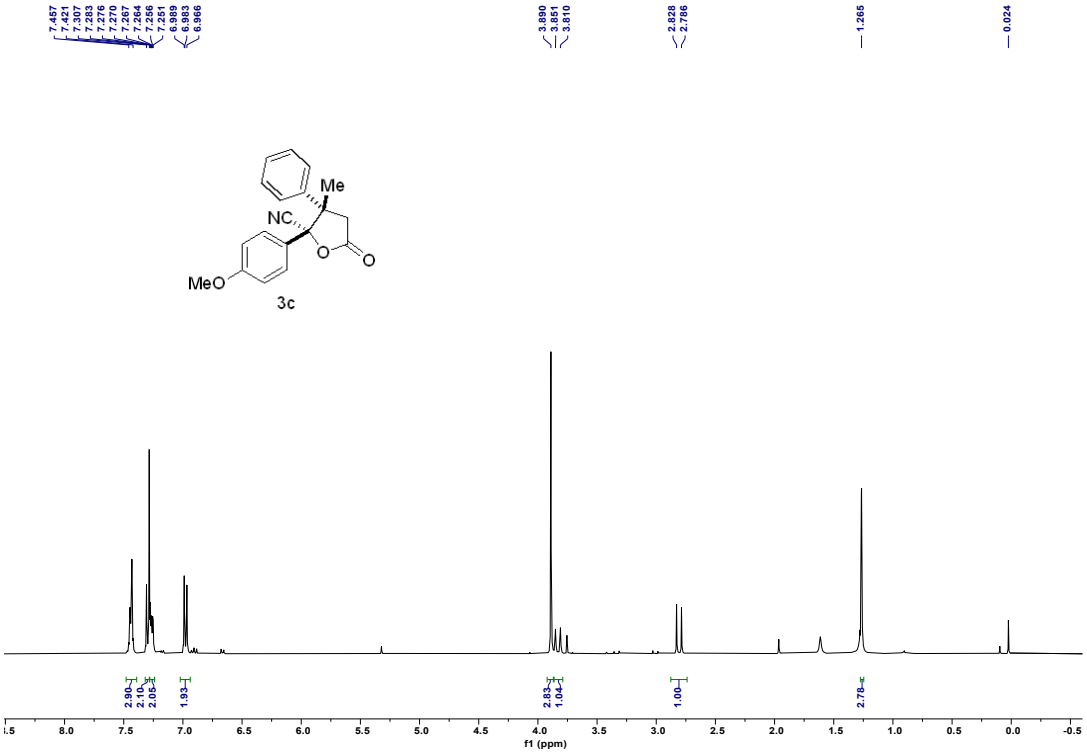


^{1}H NMR (400 MHz, $CDCl_3$)

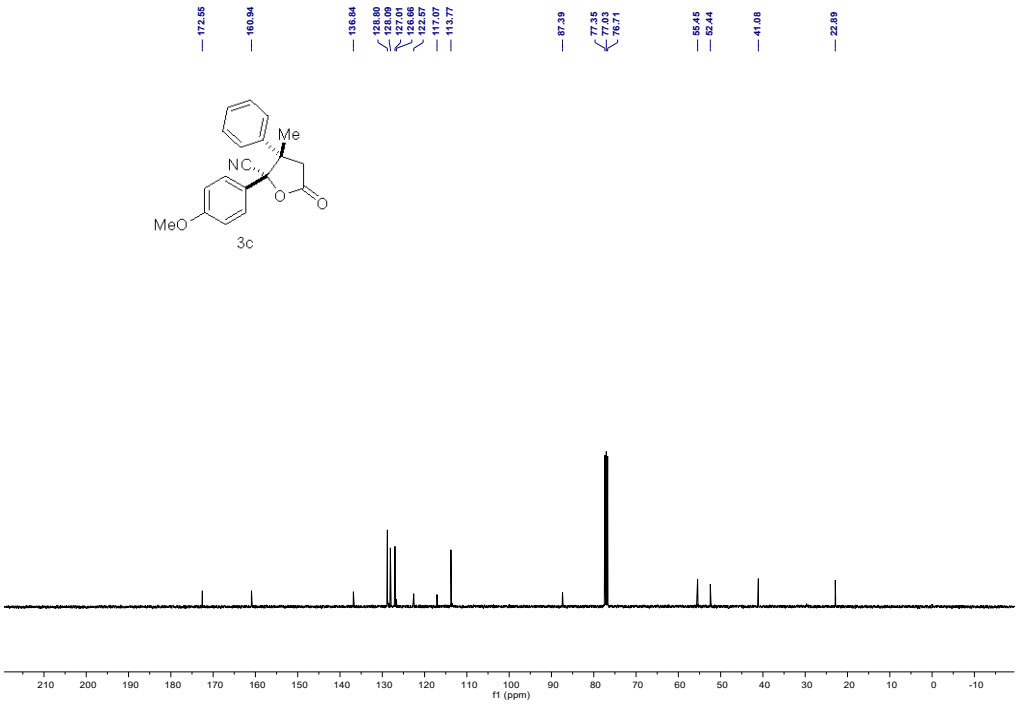


^{13}C NMR (101 MHz, $CDCl_3$)

3c

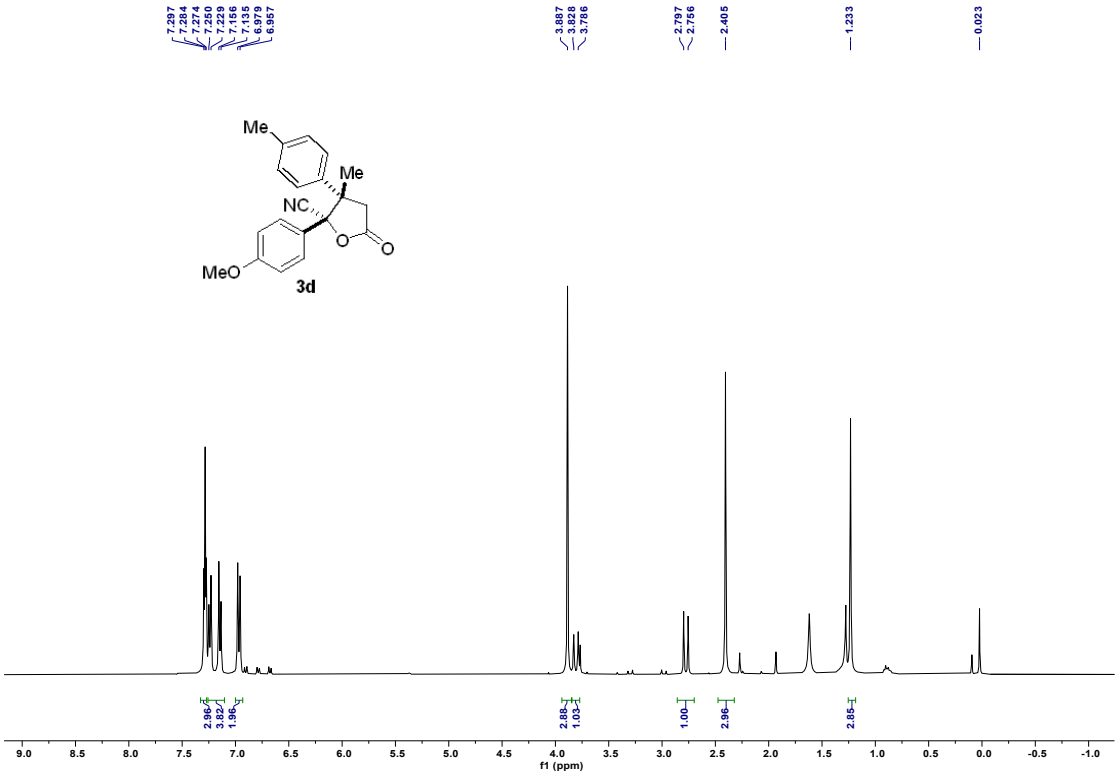


^{1}H NMR (400 MHz, $CDCl_3$)

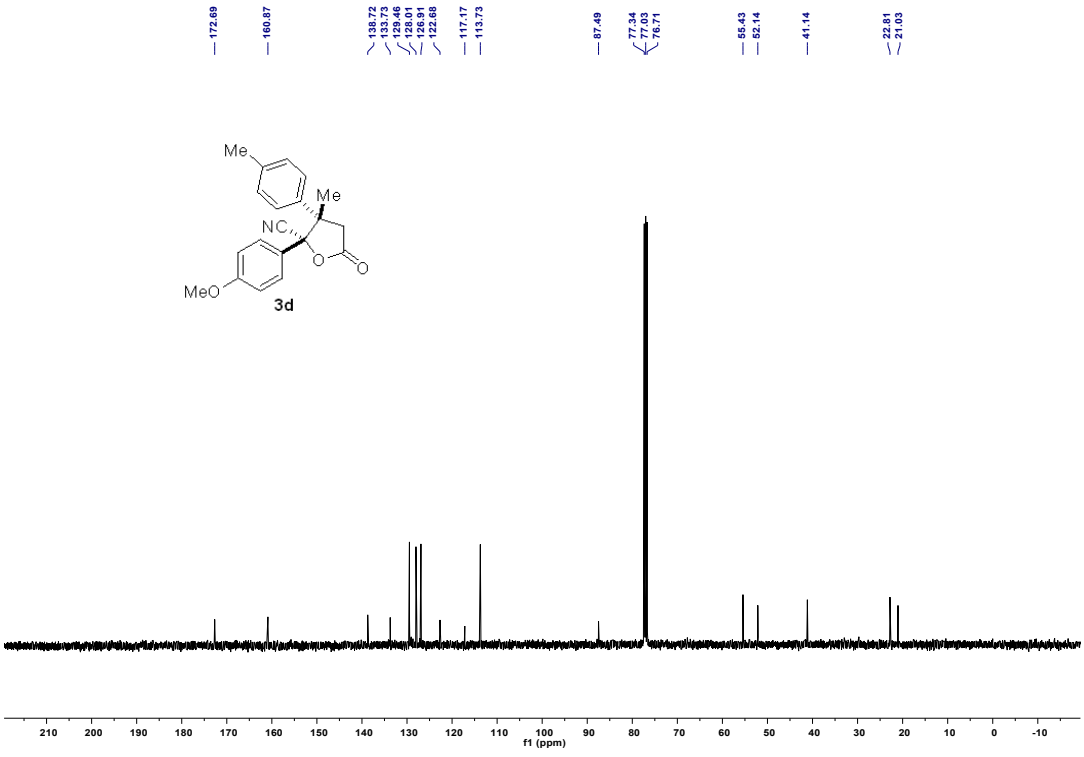


^{13}C NMR (101 MHz, $CDCl_3$)

3d

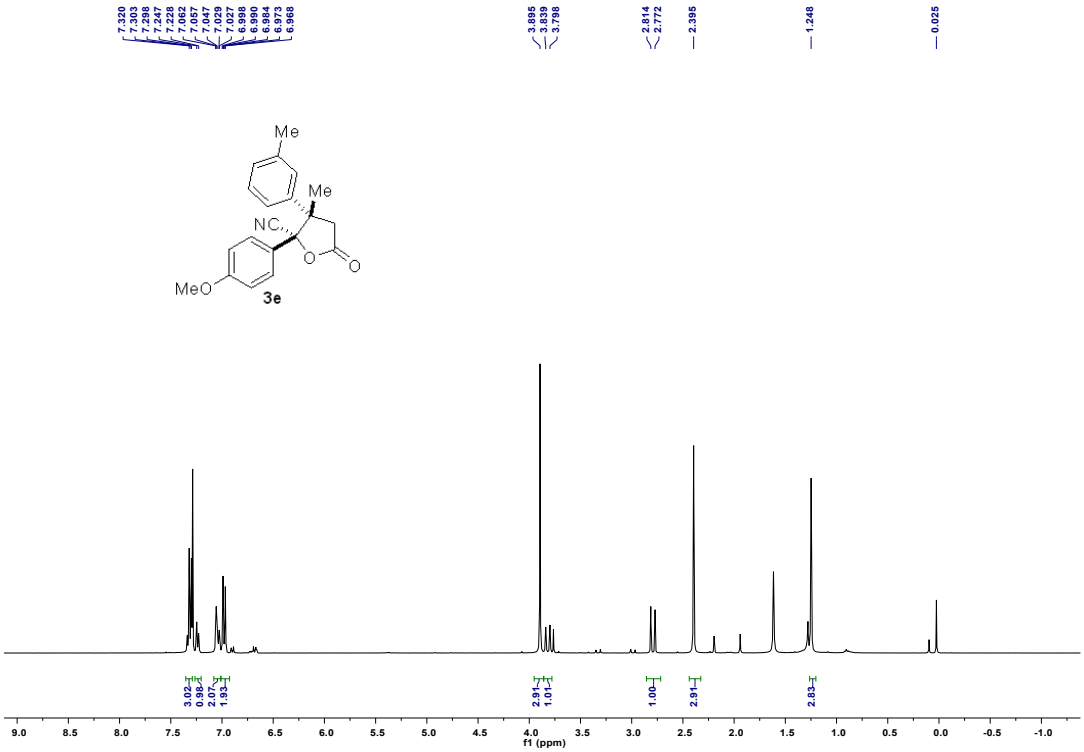


^{1}H NMR (400 MHz, $CDCl_3$)

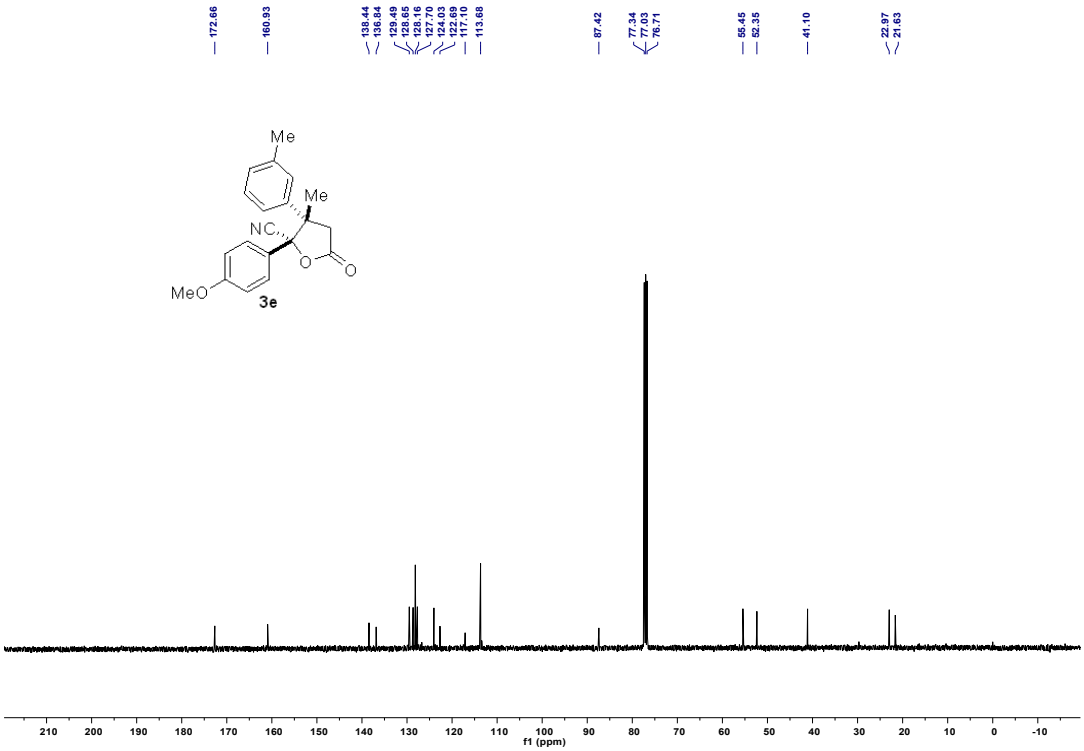


^{13}C NMR (101 MHz, $CDCl_3$)

3e

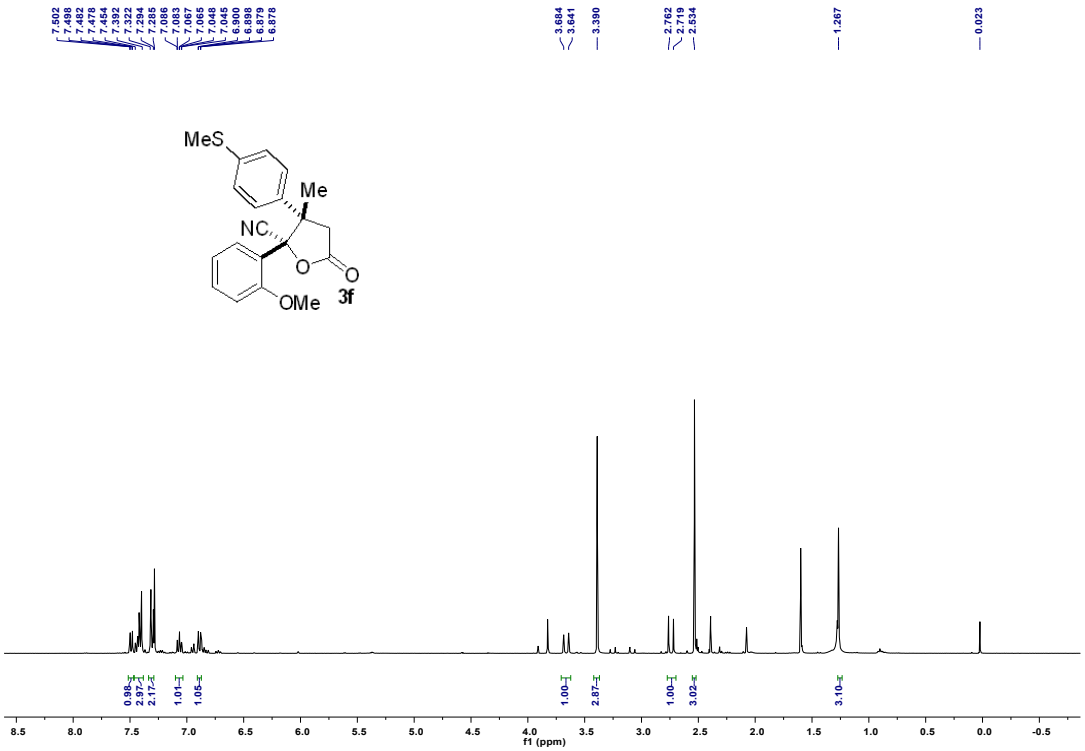


^{1}H NMR (400 MHz, $CDCl_3$)

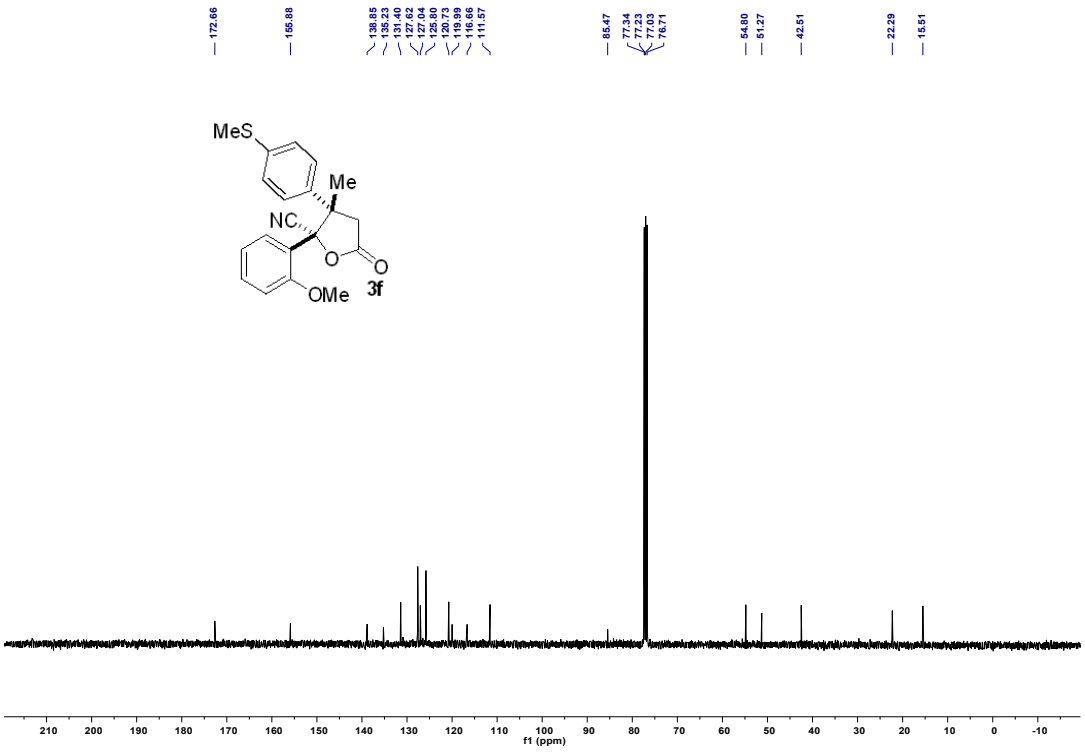


^{13}C NMR (101 MHz, $CDCl_3$)

3f

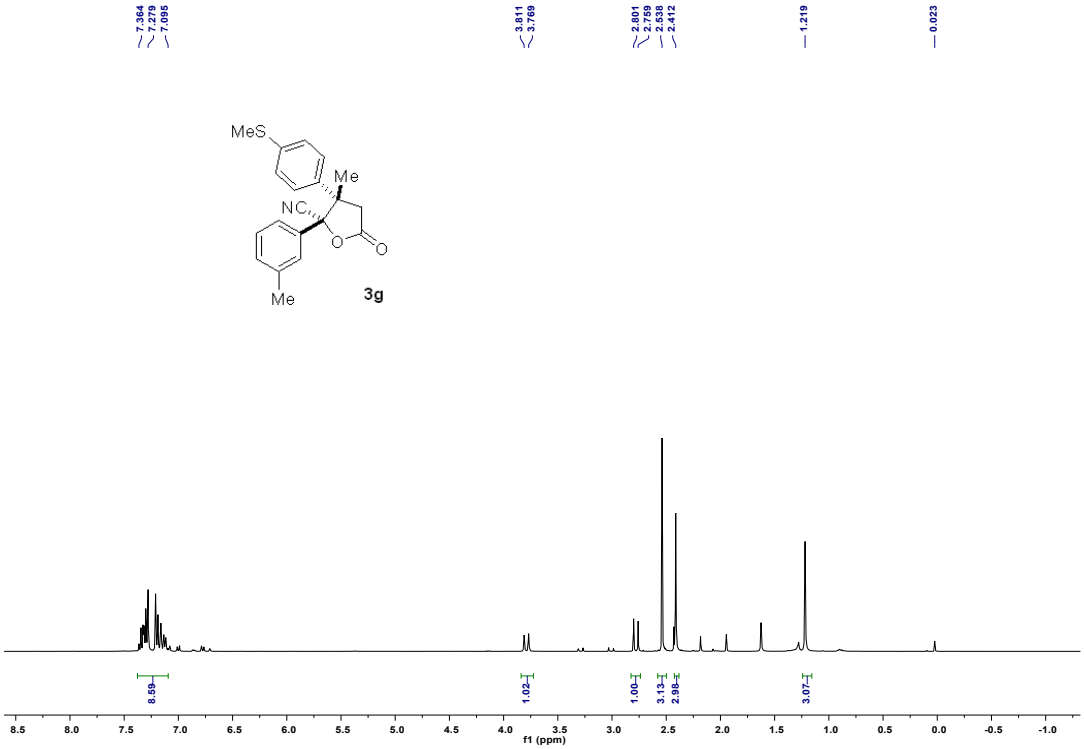


^{1}H NMR (400 MHz, $CDCl_3$)

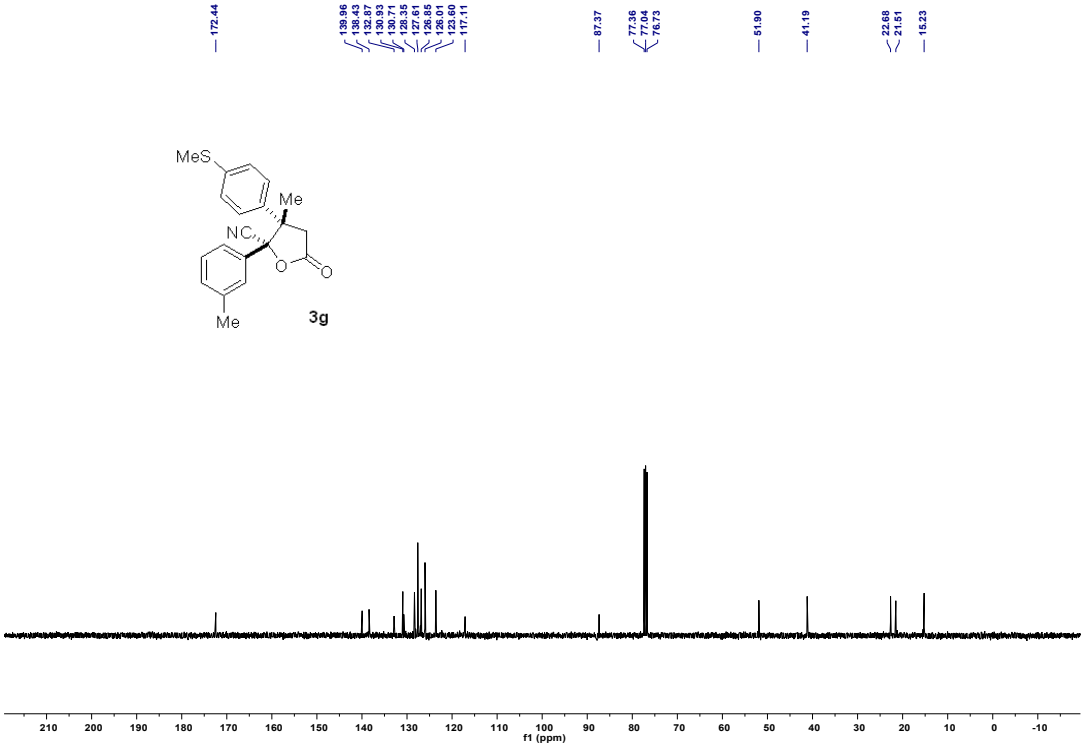


^{13}C NMR (101 MHz, $CDCl_3$)

3g

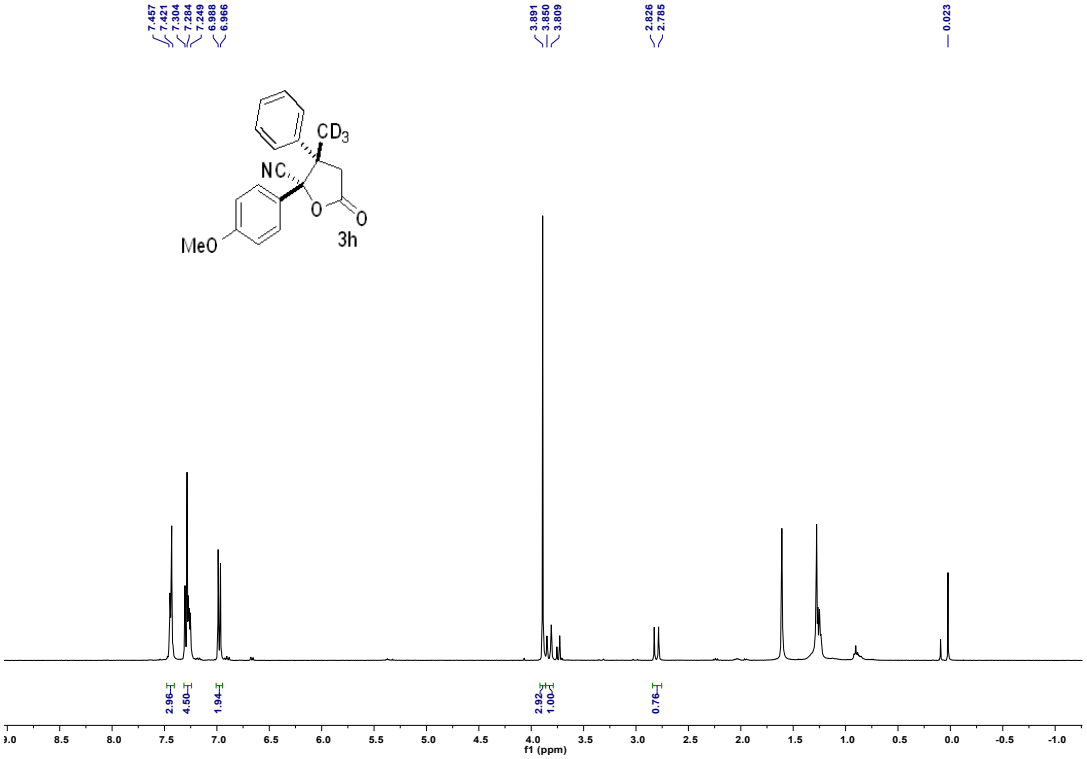


^{1}H NMR (400 MHz, $CDCl_3$)

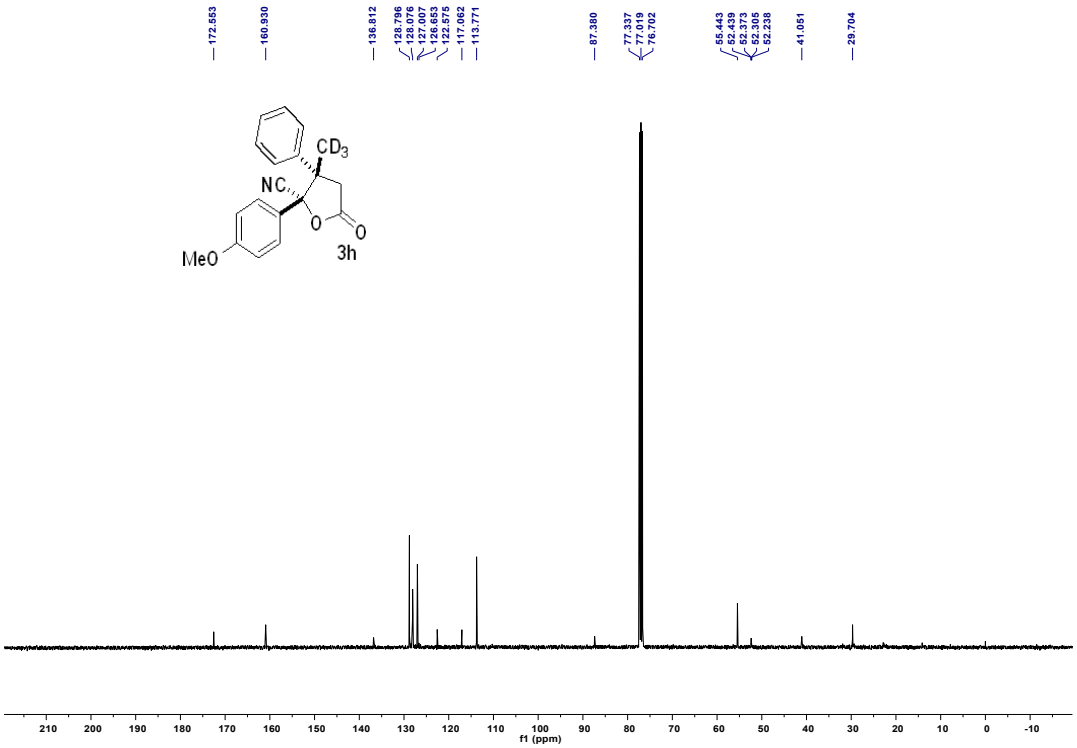


^{13}C NMR (101 MHz, $CDCl_3$)

3h

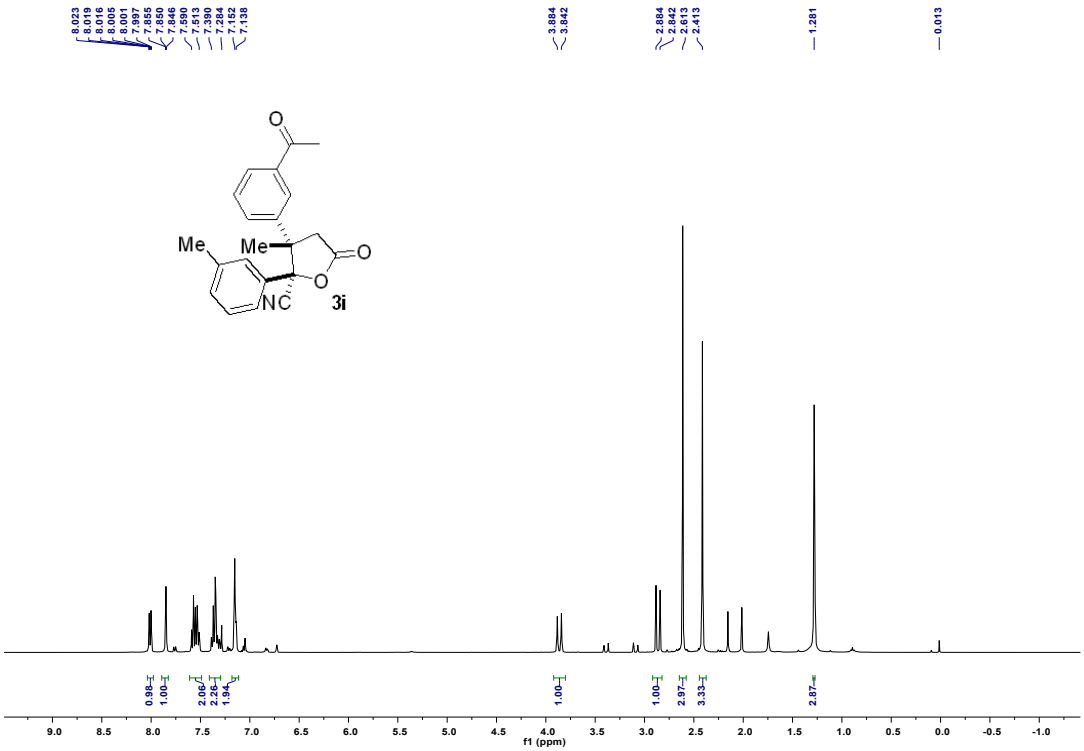


^{1}H NMR (400 MHz, $CDCl_3$)

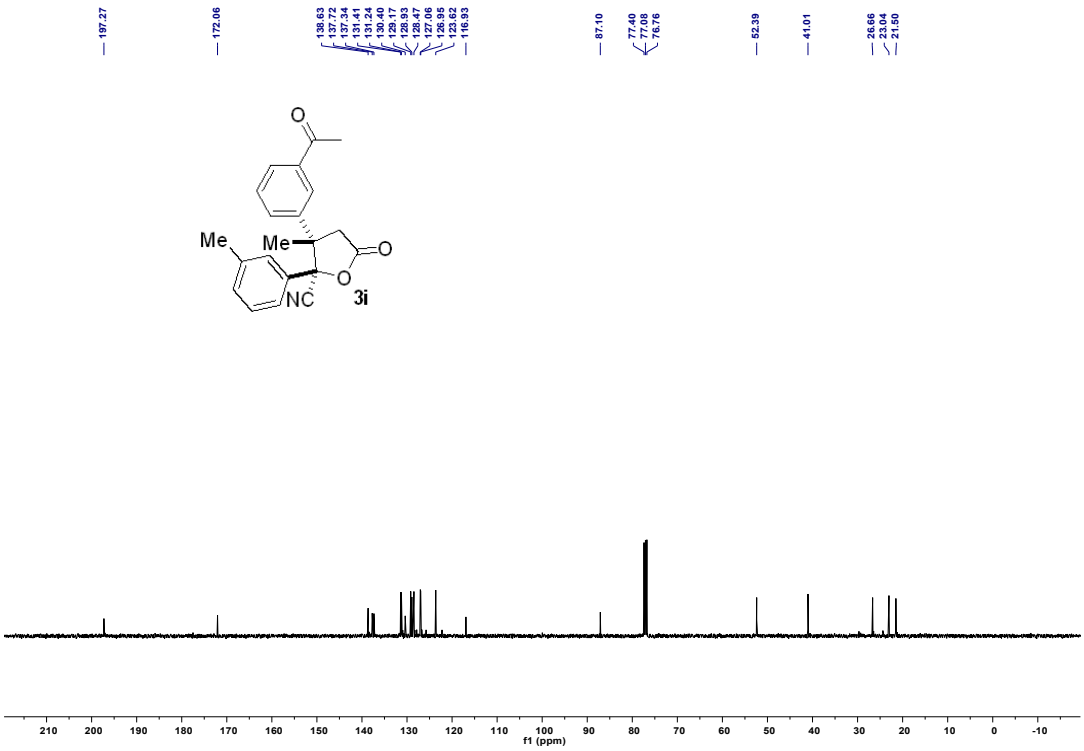


^{13}C NMR (101 MHz, $CDCl_3$)

3i

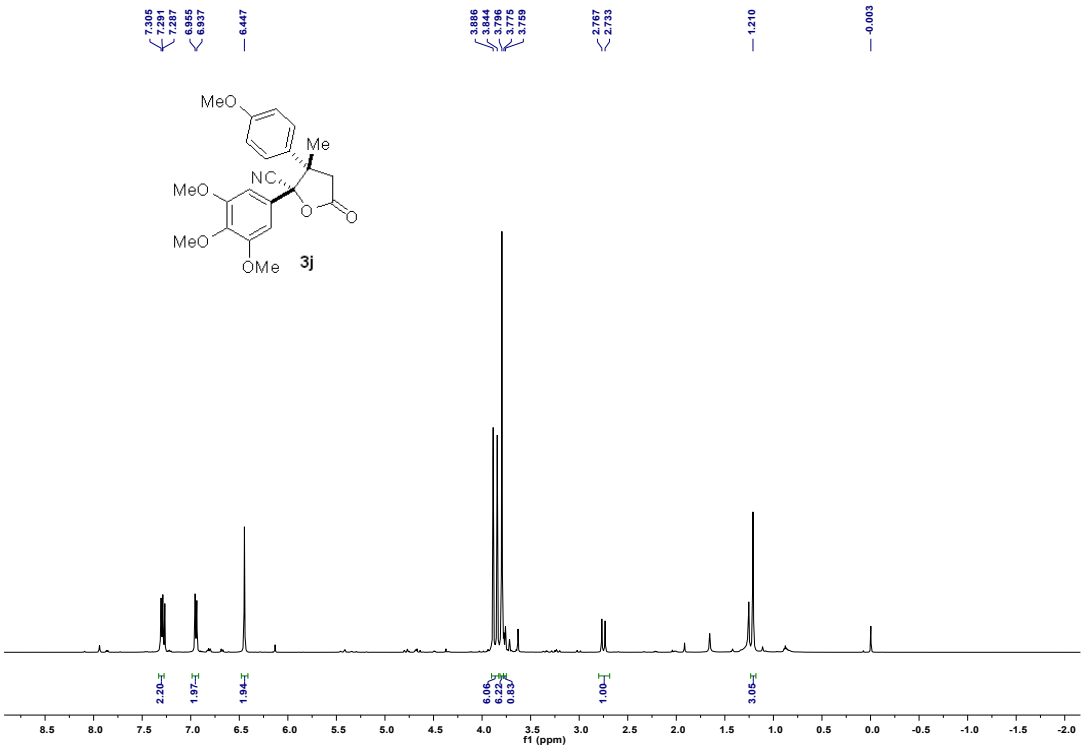


^{1}H NMR (400 MHz, $CDCl_3$)

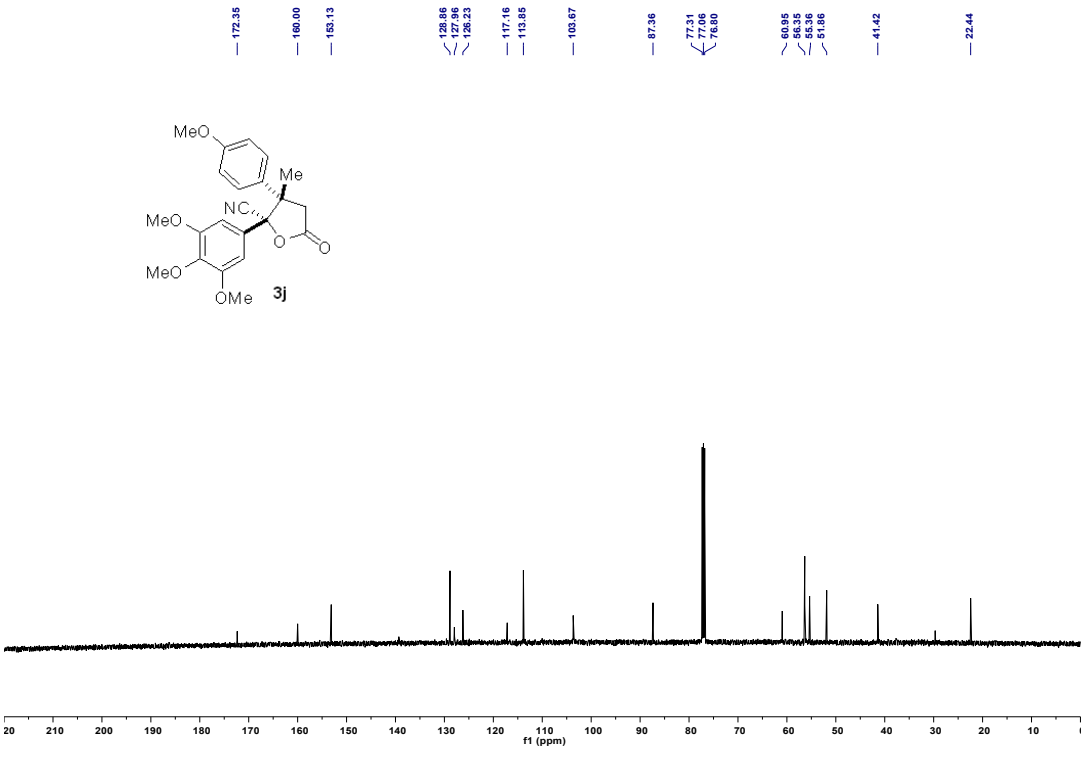


^{13}C NMR (101 MHz, $CDCl_3$)

3j

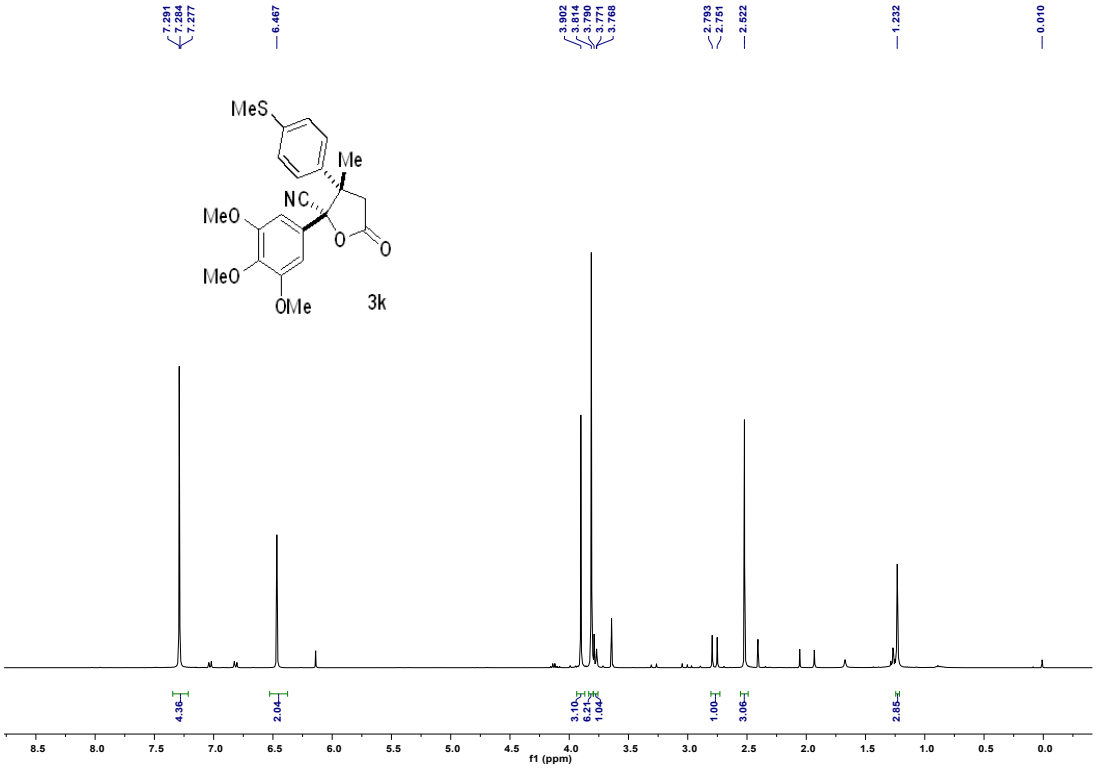


^{1}H NMR (500 MHz, $CDCl_3$)

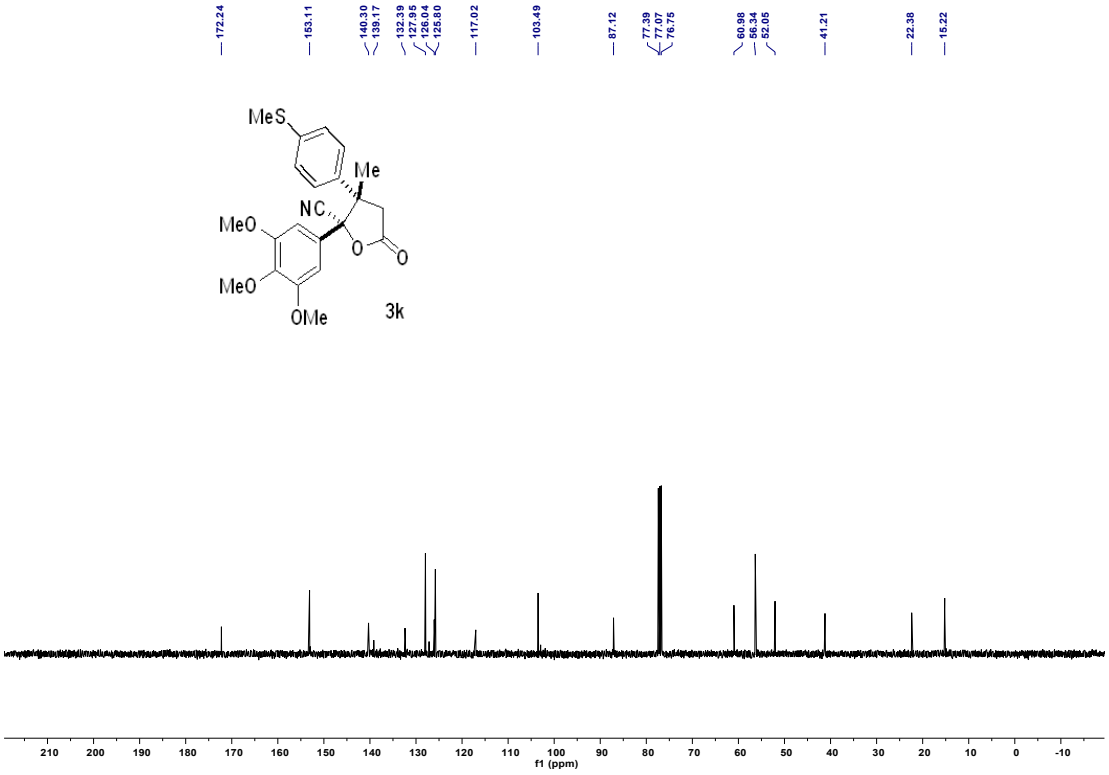


^{13}C NMR (126 MHz, $CDCl_3$)

3k

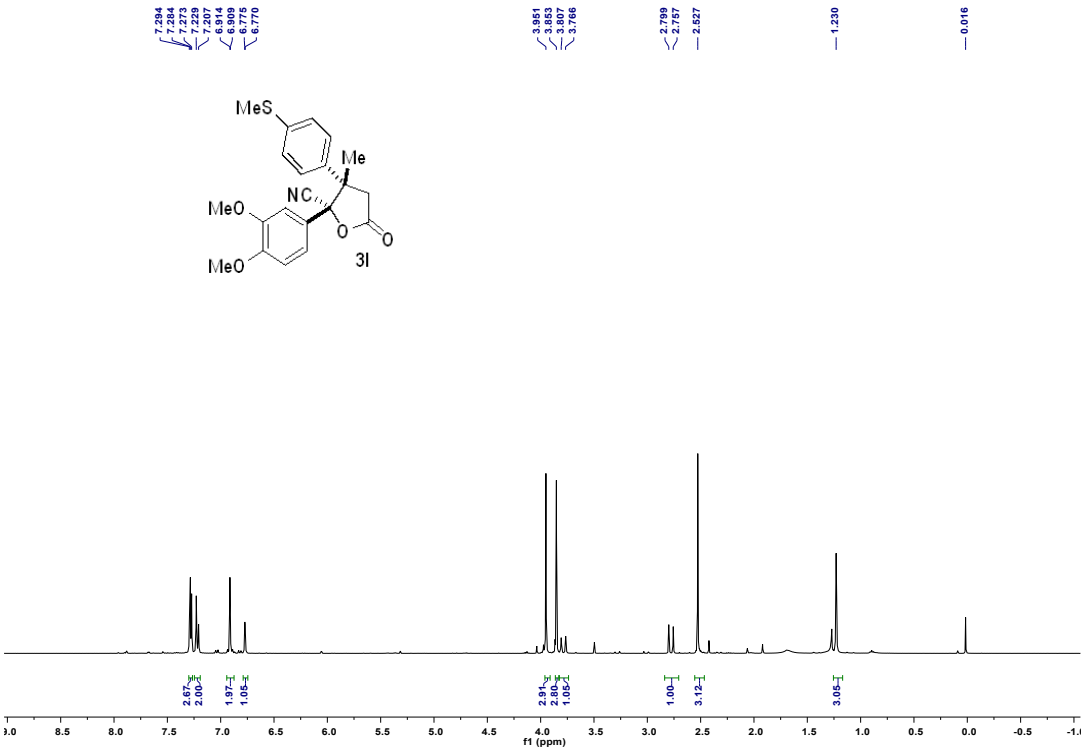


^{1}H NMR (400 MHz, $CDCl_3$)

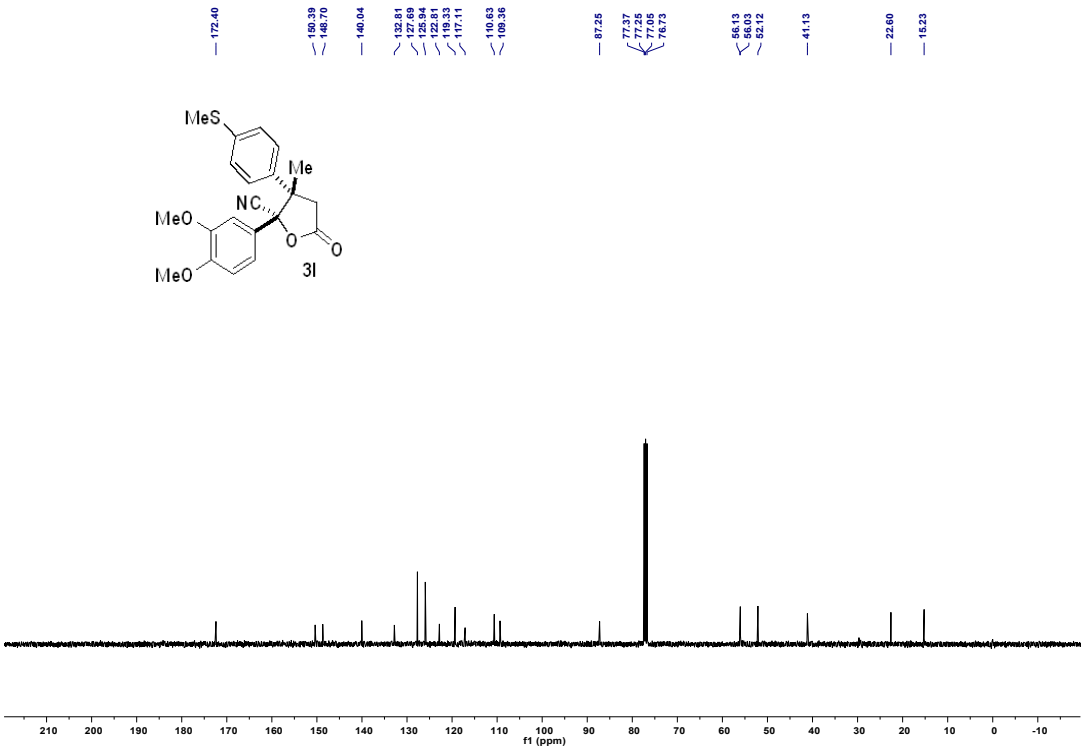


^{13}C NMR (101 MHz, $CDCl_3$)

3l

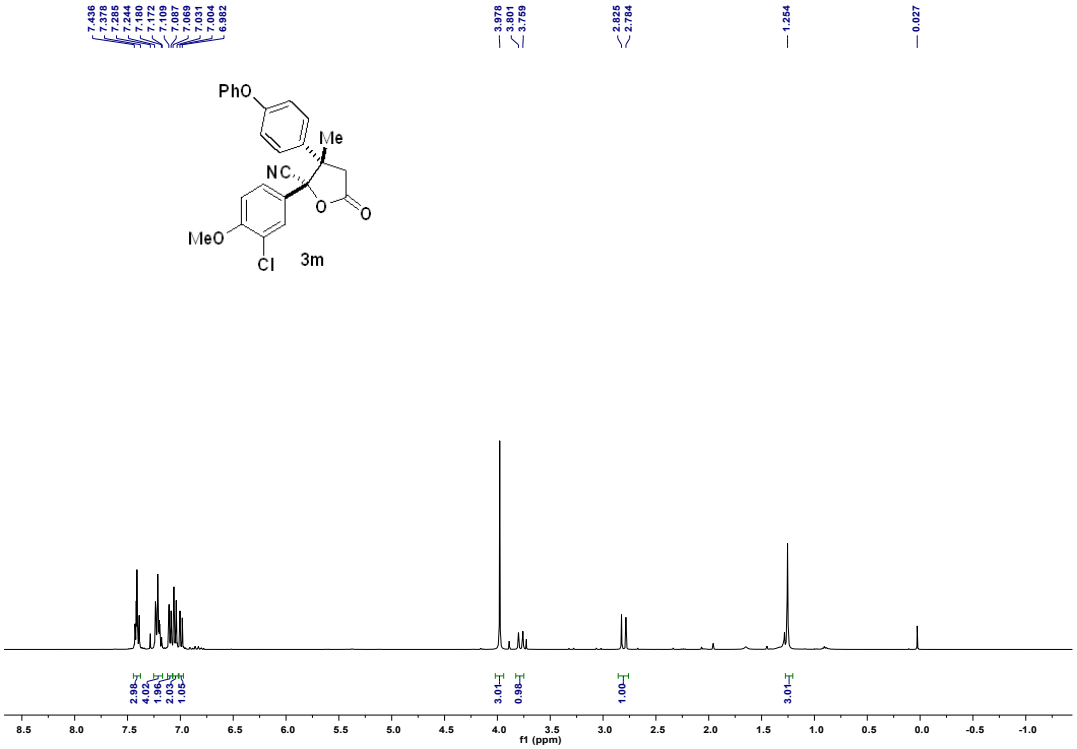


^{1}H NMR (400 MHz, $CDCl_3$)

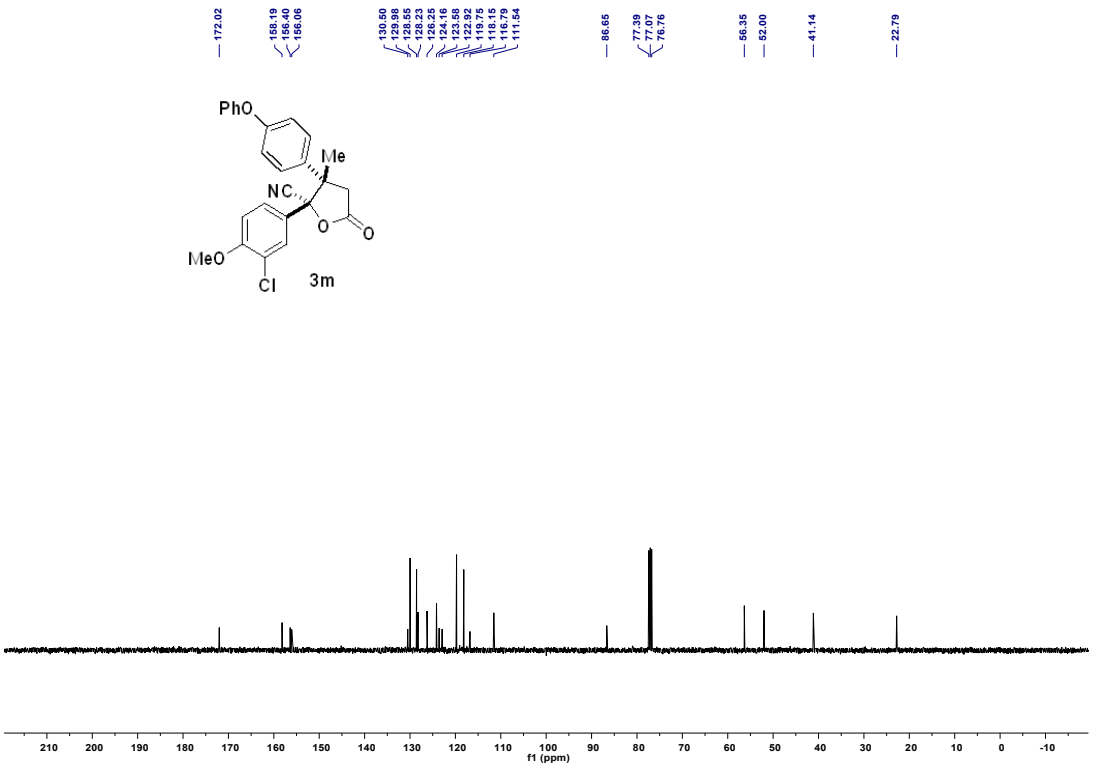


^{13}C NMR (101 MHz, $CDCl_3$)

3m

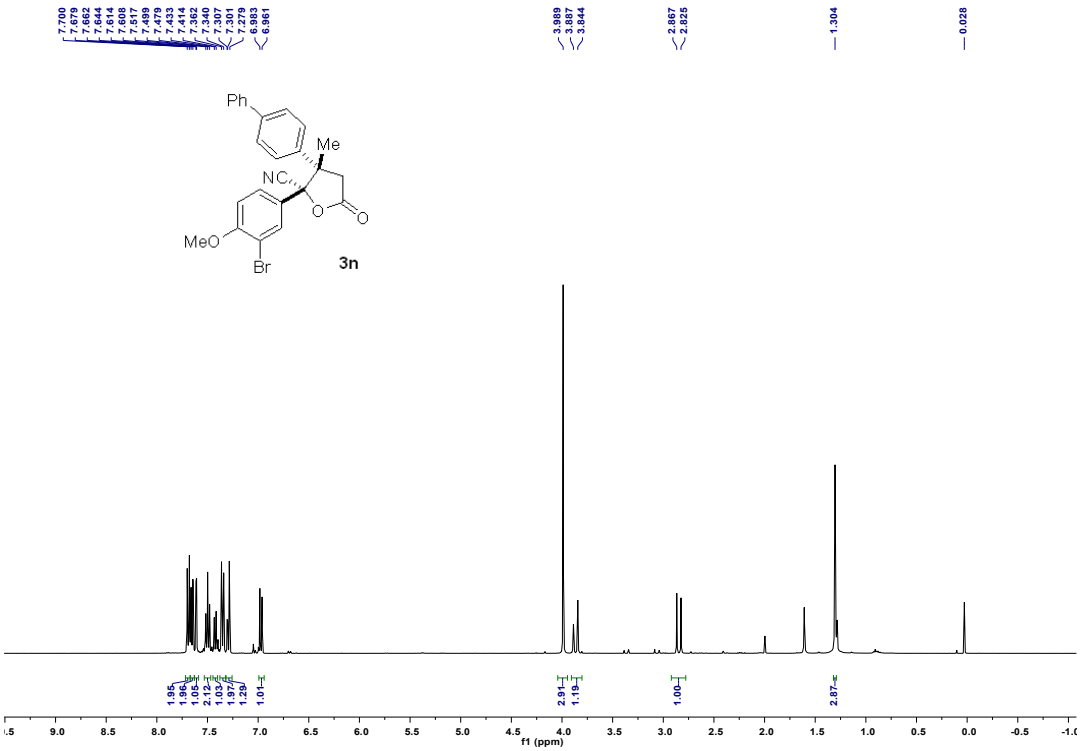


^{1}H NMR (400 MHz, $CDCl_3$)

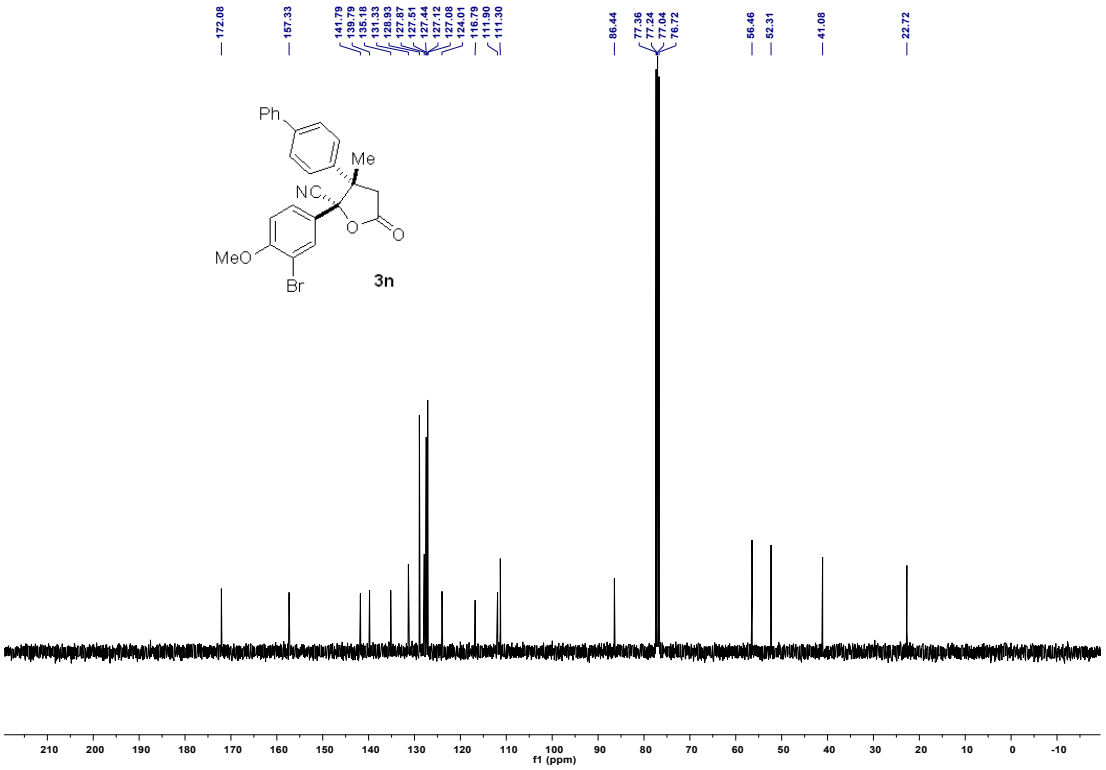


^{13}C NMR (101 MHz, $CDCl_3$)

3n

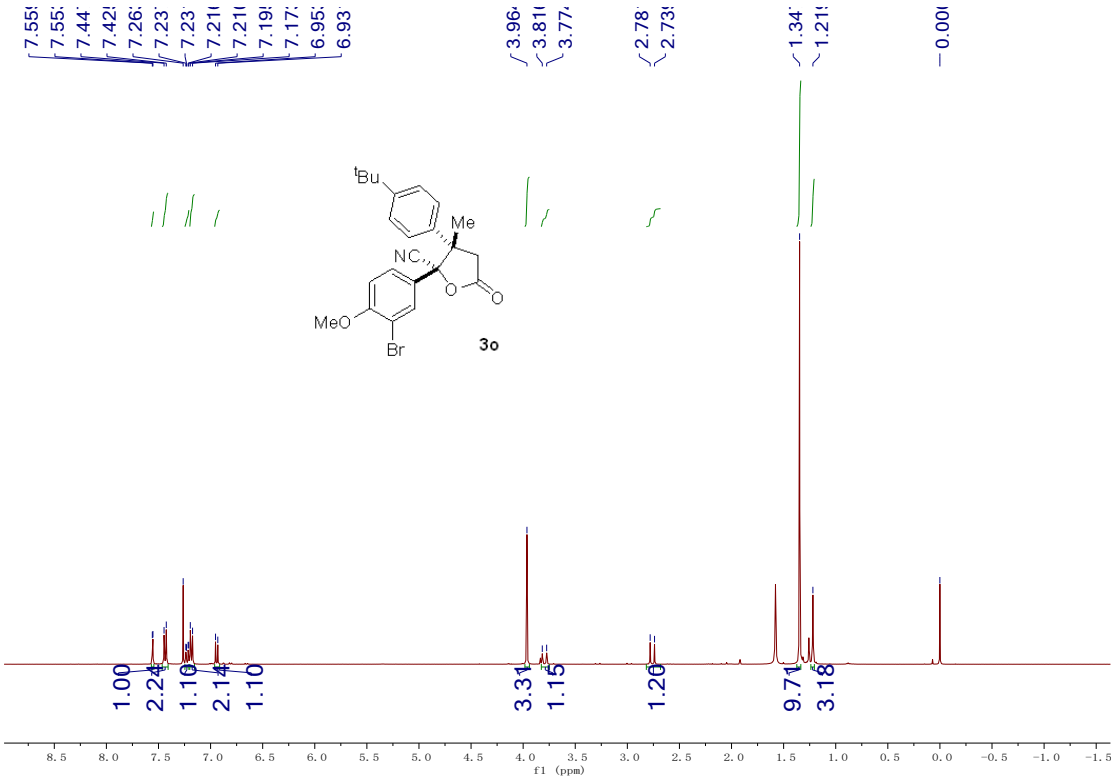


^{1}H NMR (400 MHz, $CDCl_3$)

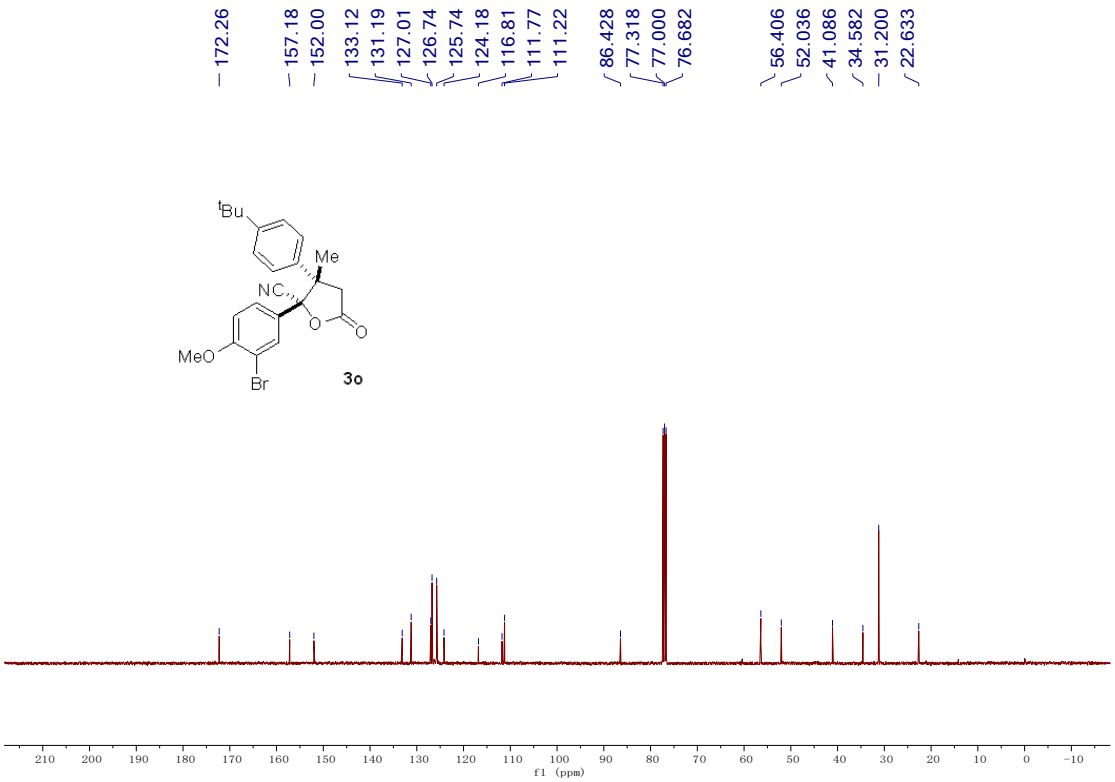


^{13}C NMR (101 MHz, $CDCl_3$)

3o

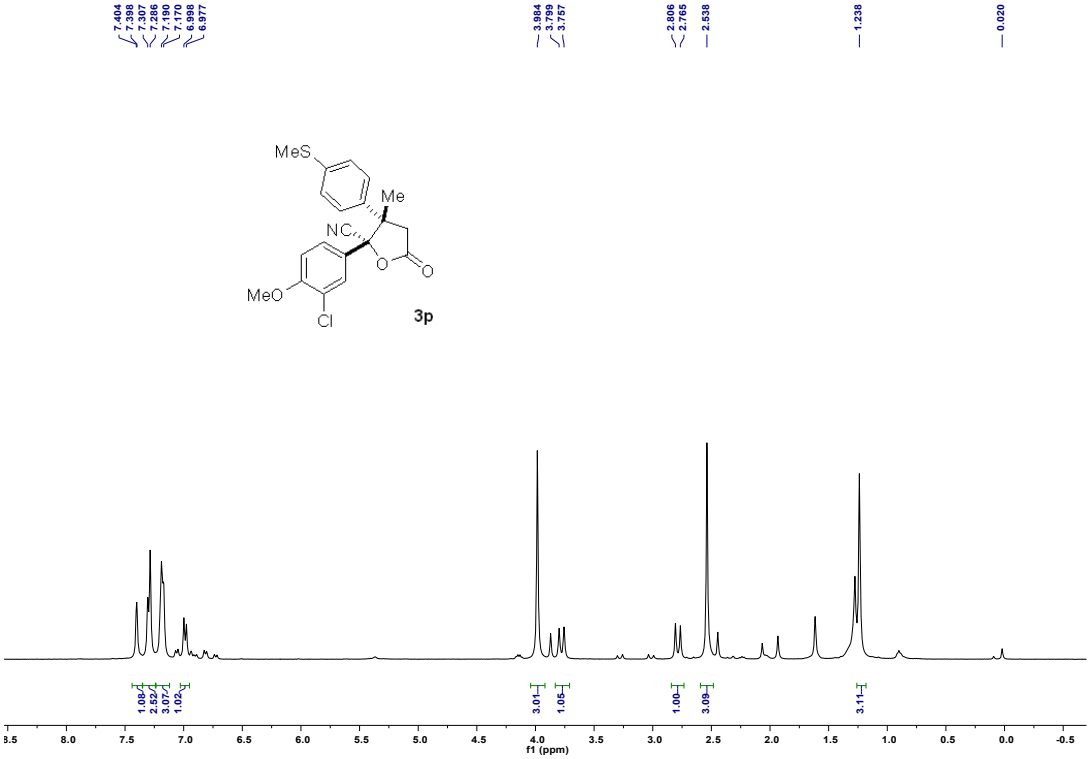


^{1}H NMR (400 MHz, $CDCl_3$)

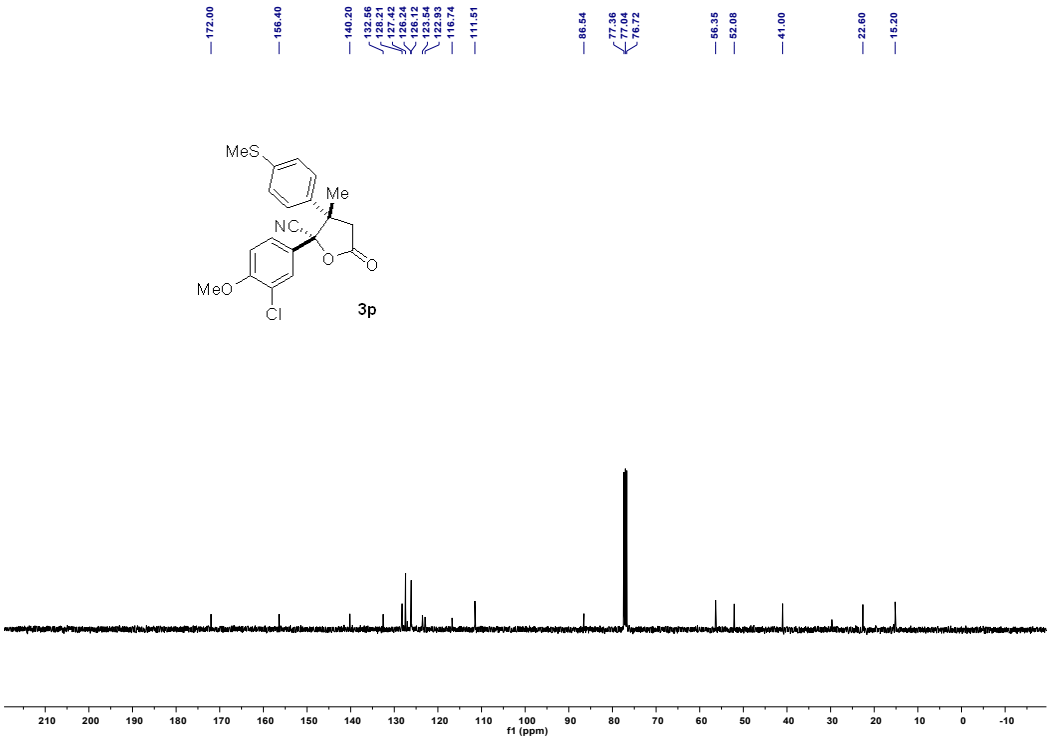


^{13}C NMR (101 MHz, $CDCl_3$)

3p

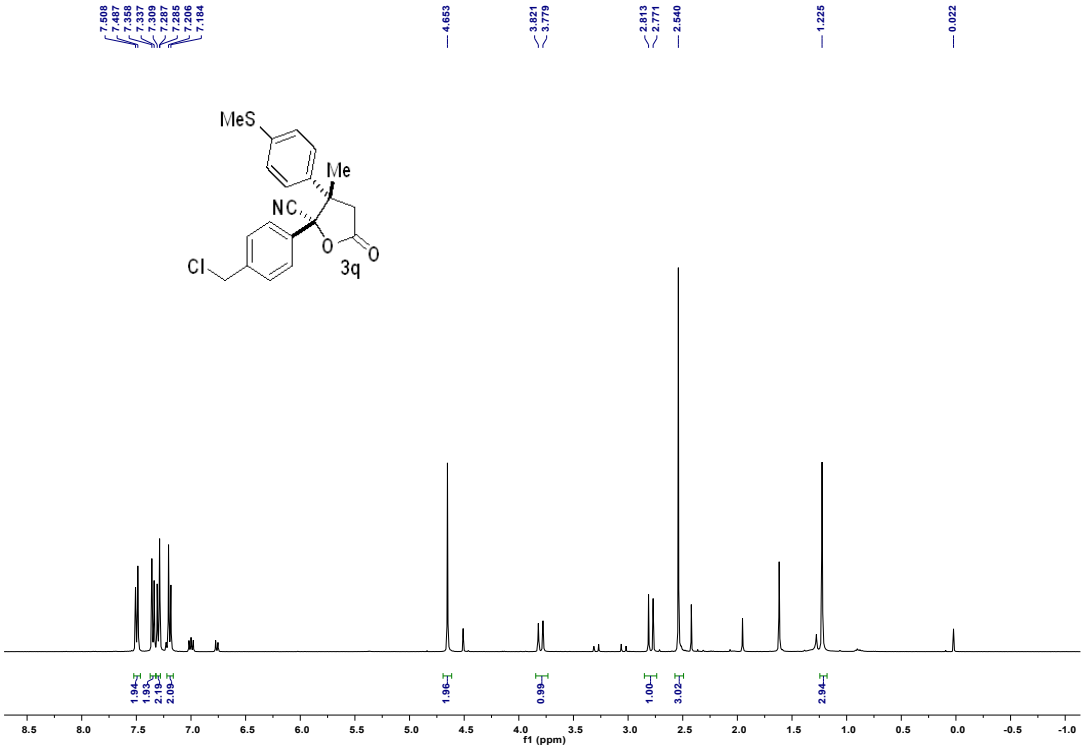


^{1}H NMR (400 MHz, $CDCl_3$)

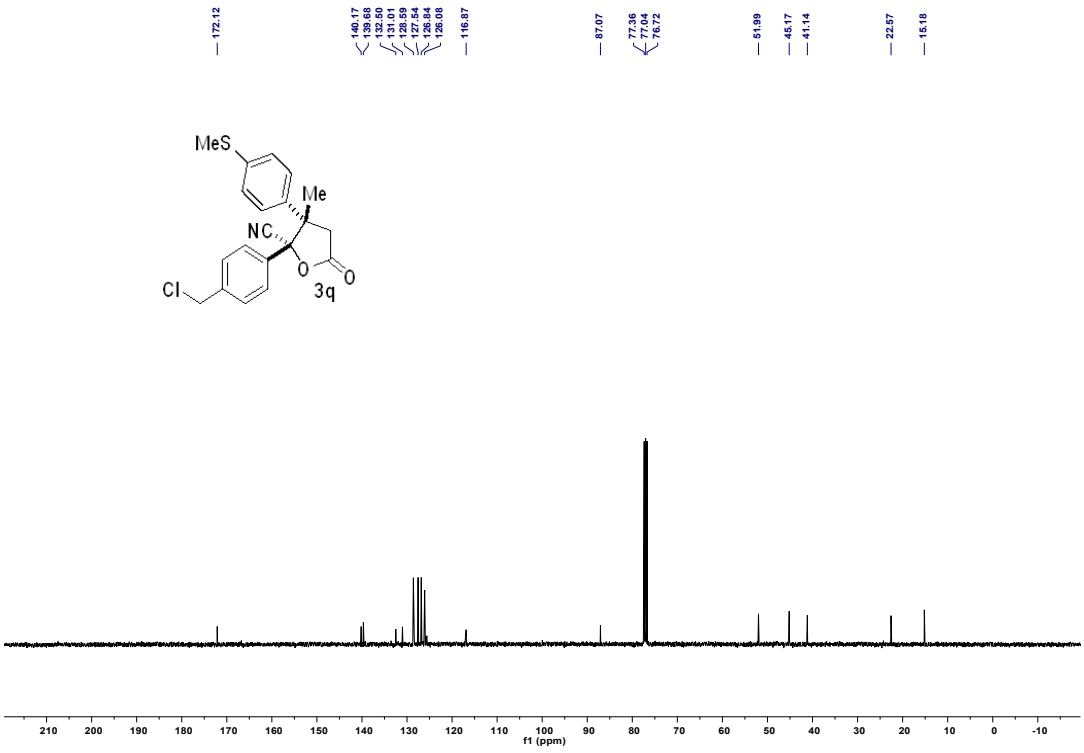


^{13}C NMR (101 MHz, $CDCl_3$)

3q

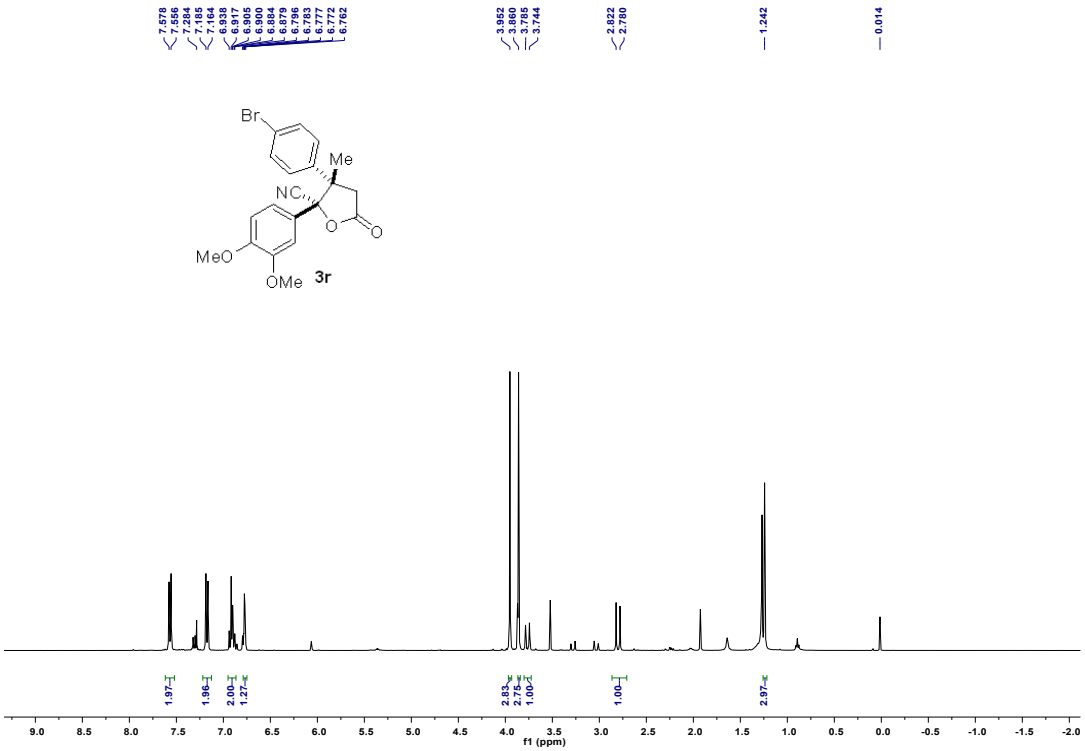


^{1}H NMR (400 MHz, $CDCl_3$)

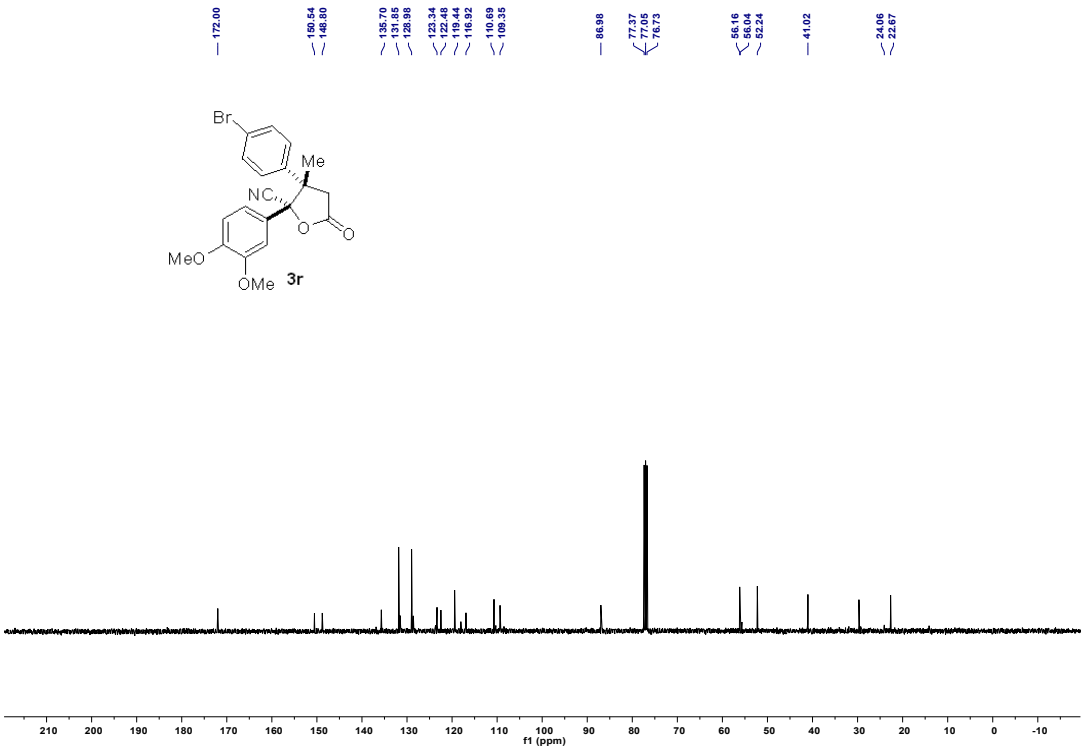


^{13}C NMR (101 MHz, $CDCl_3$)

3r

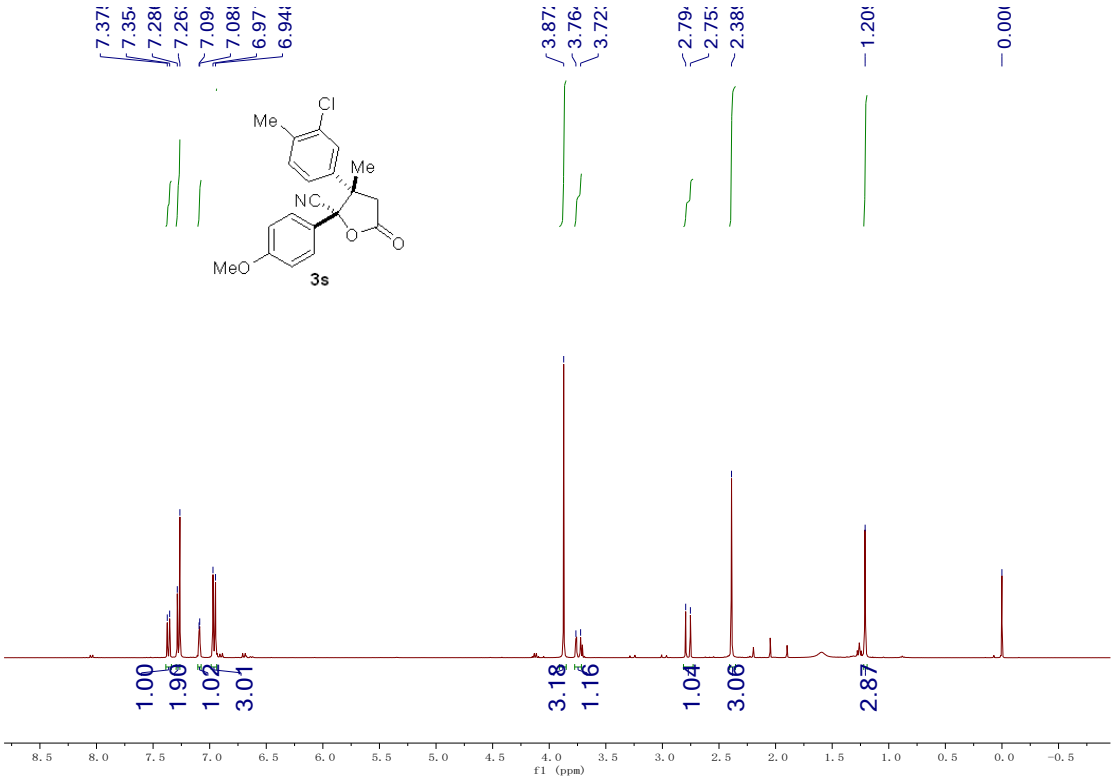


^{1}H NMR (400 MHz, $CDCl_3$)

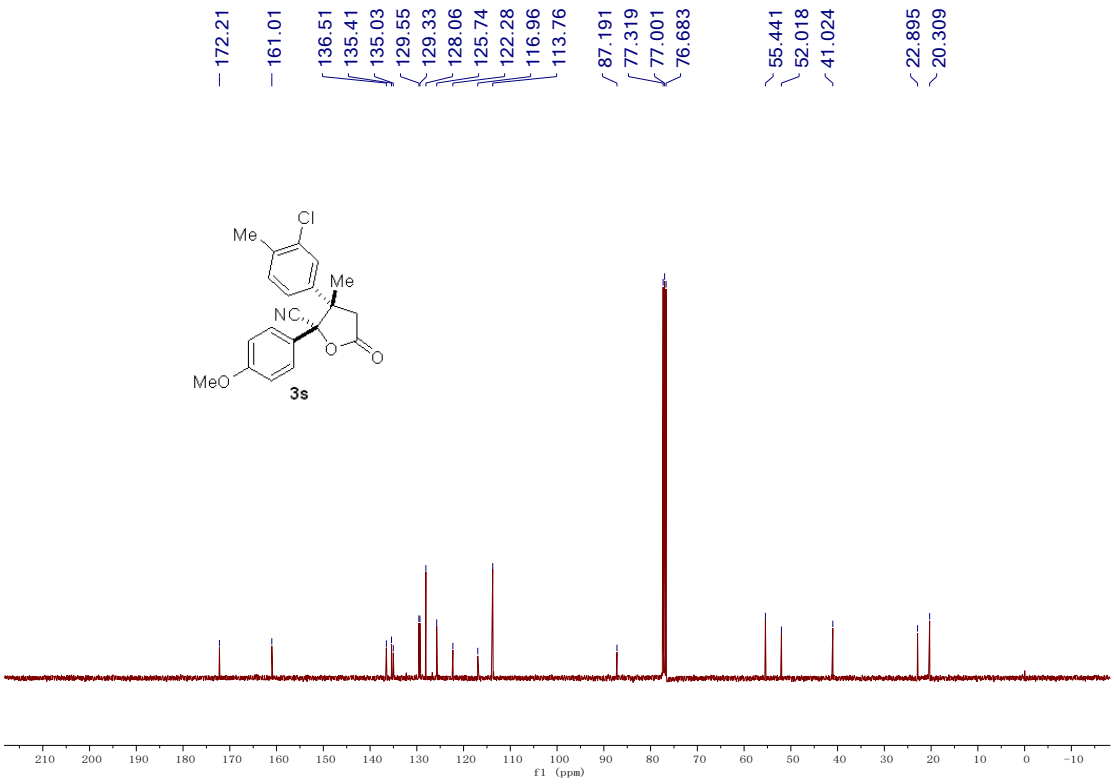


^{13}C NMR (101 MHz, $CDCl_3$)

3s

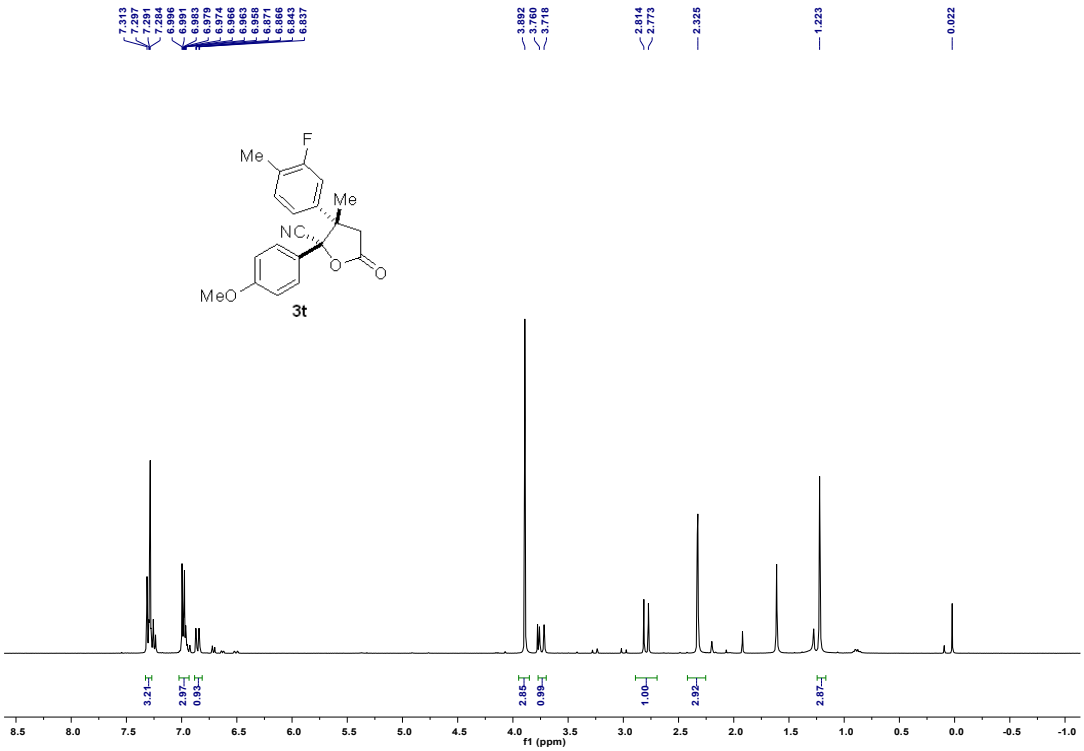


^{1}H NMR (400 MHz, $CDCl_3$)

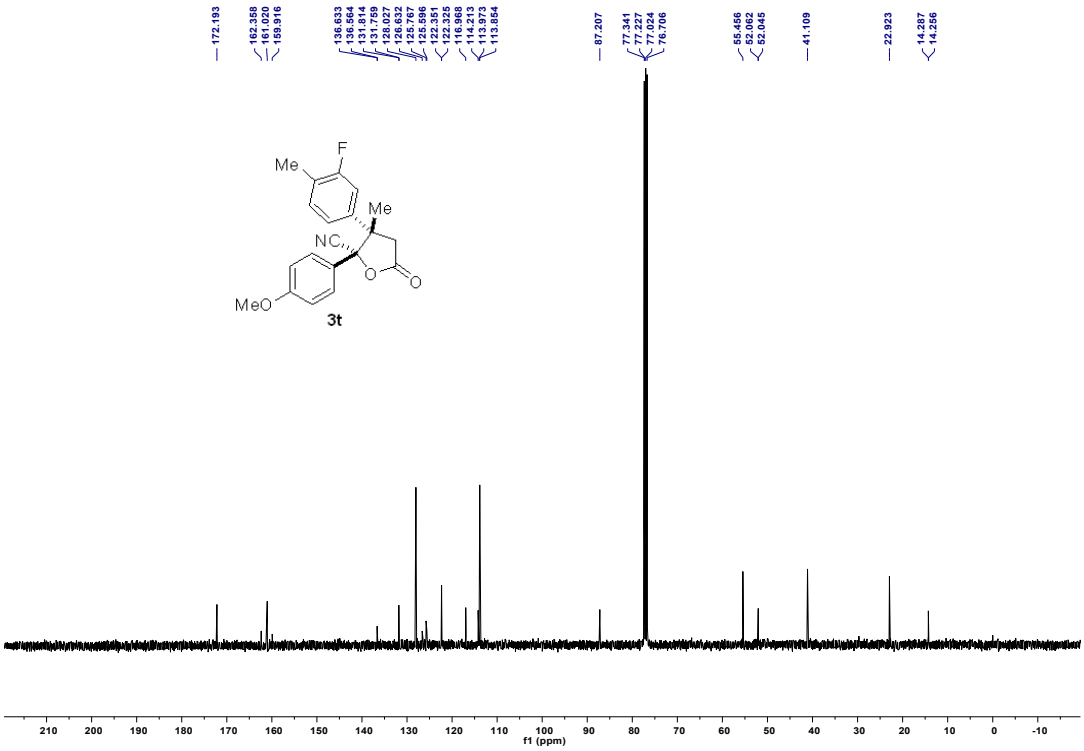


^{13}C NMR (101 MHz, $CDCl_3$)

3t

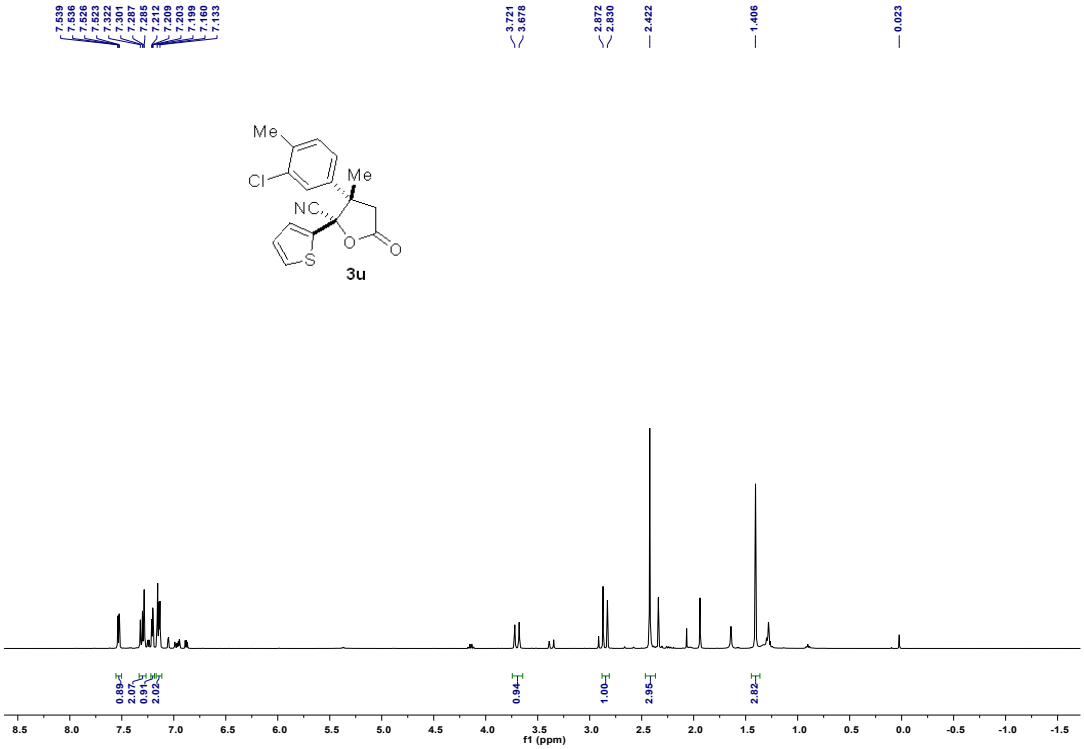


^{1}H NMR (400 MHz, $CDCl_3$)

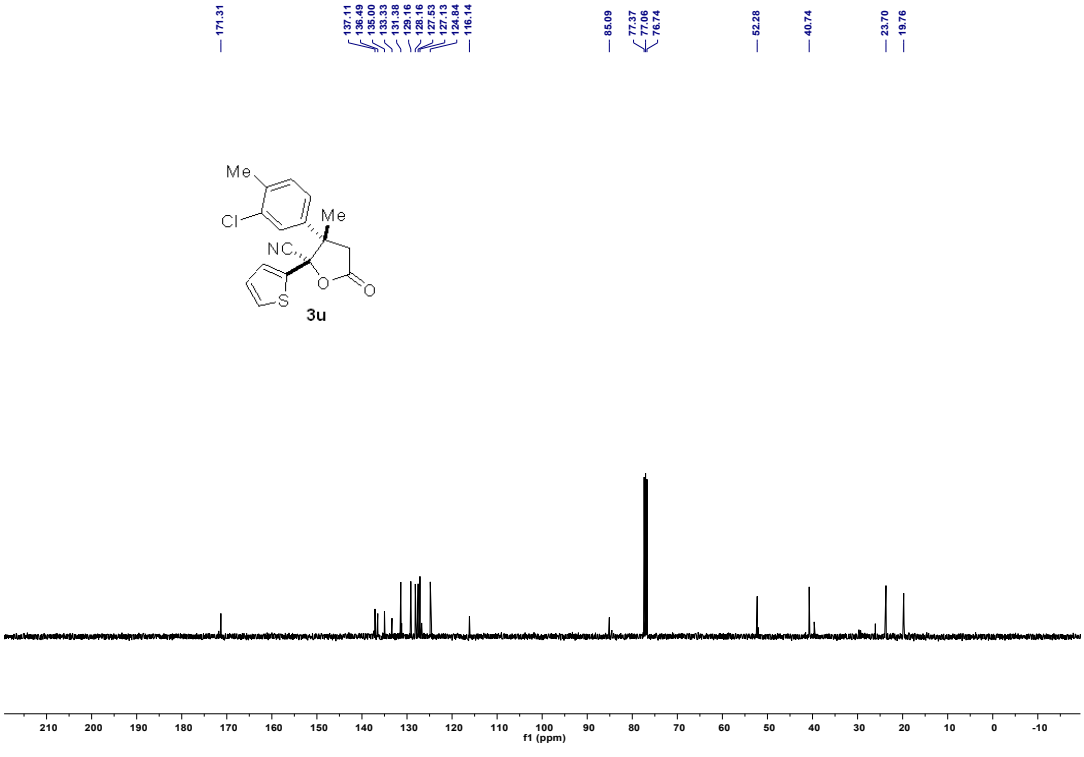


^{13}C NMR (101 MHz, $CDCl_3$)

3u

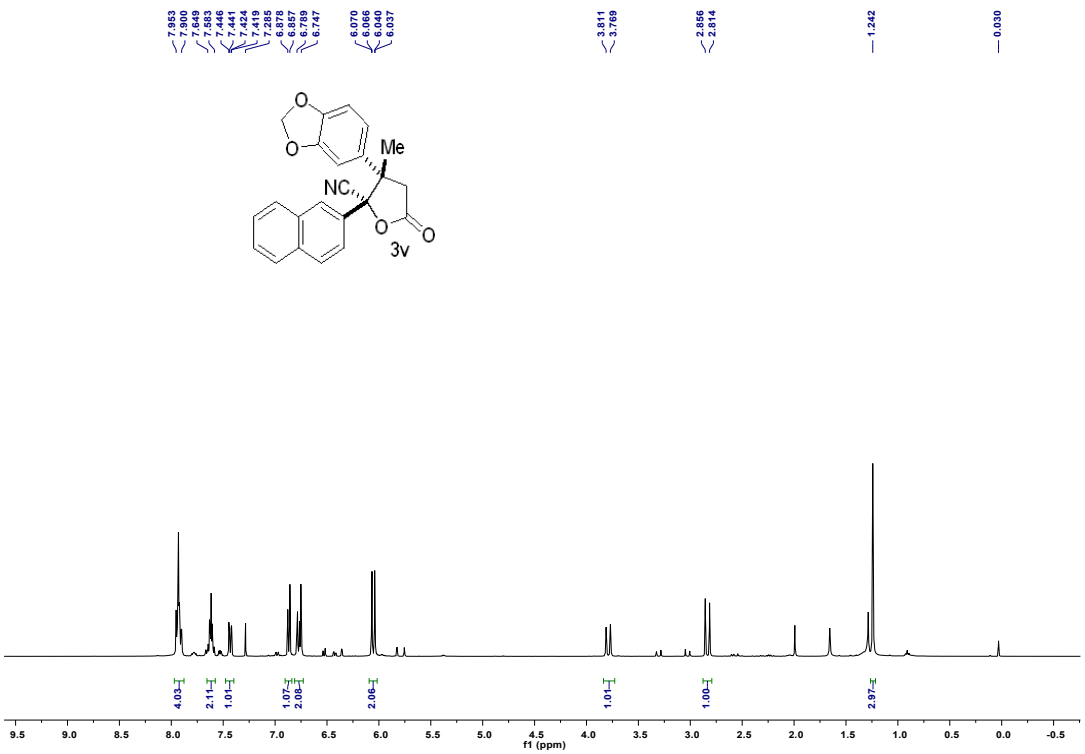


^{1}H NMR (400 MHz, $CDCl_3$)

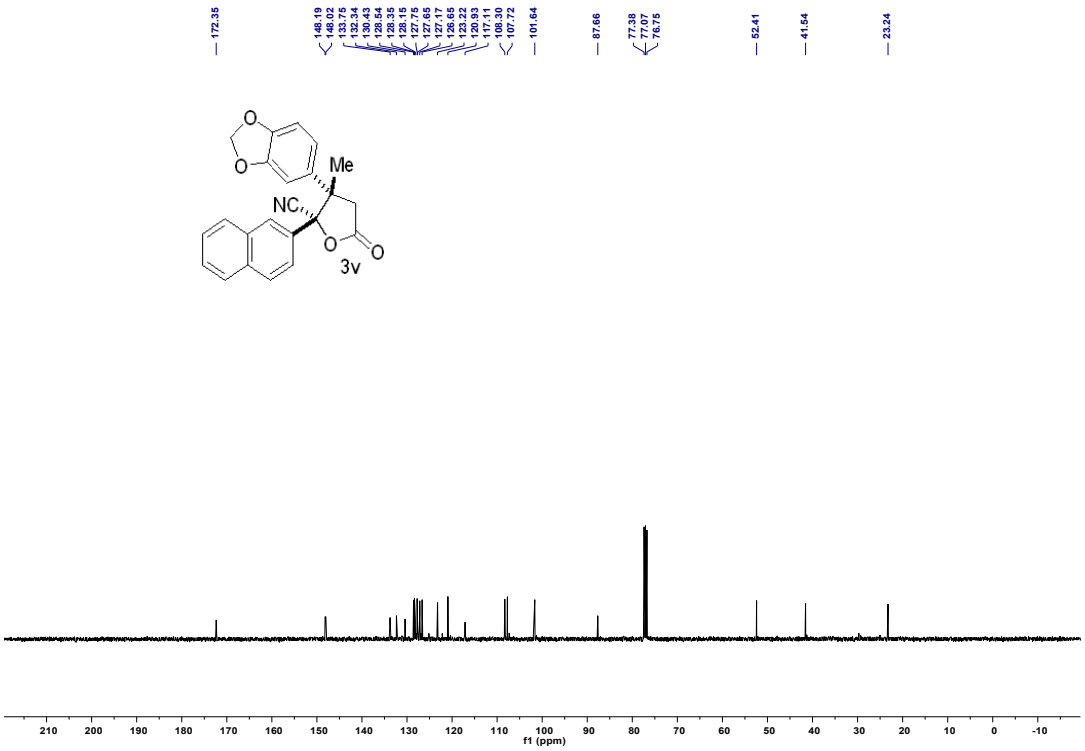


^{13}C NMR (101 MHz, $CDCl_3$)

3v

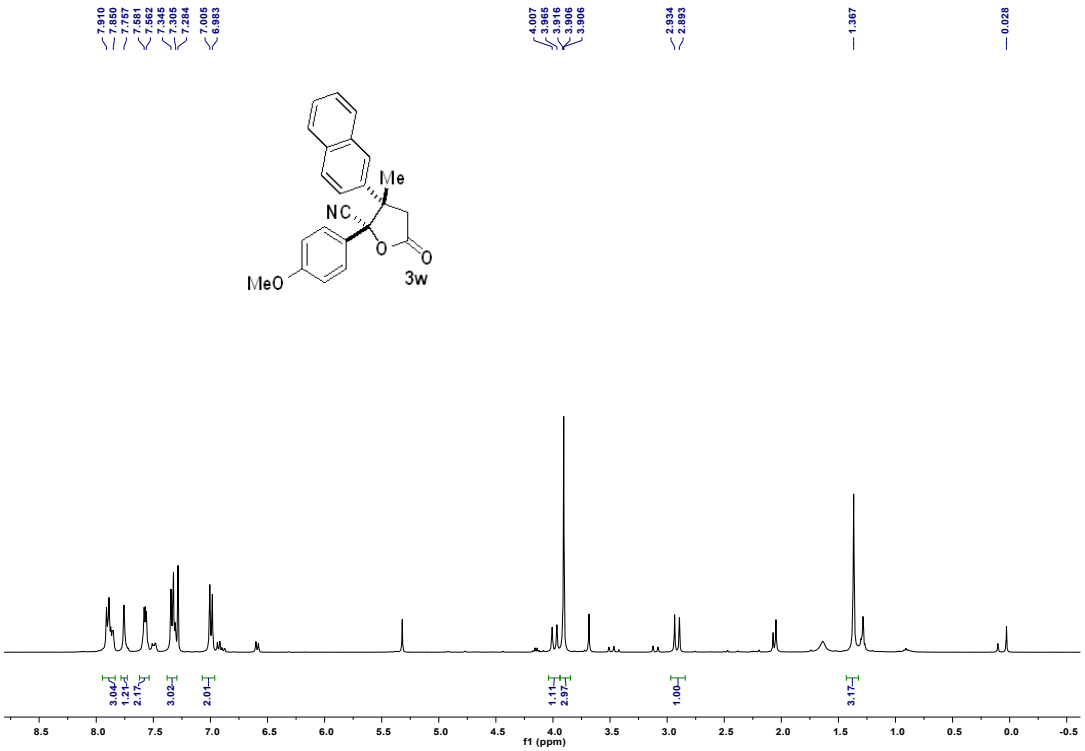


^{1}H NMR (400 MHz, $CDCl_3$)

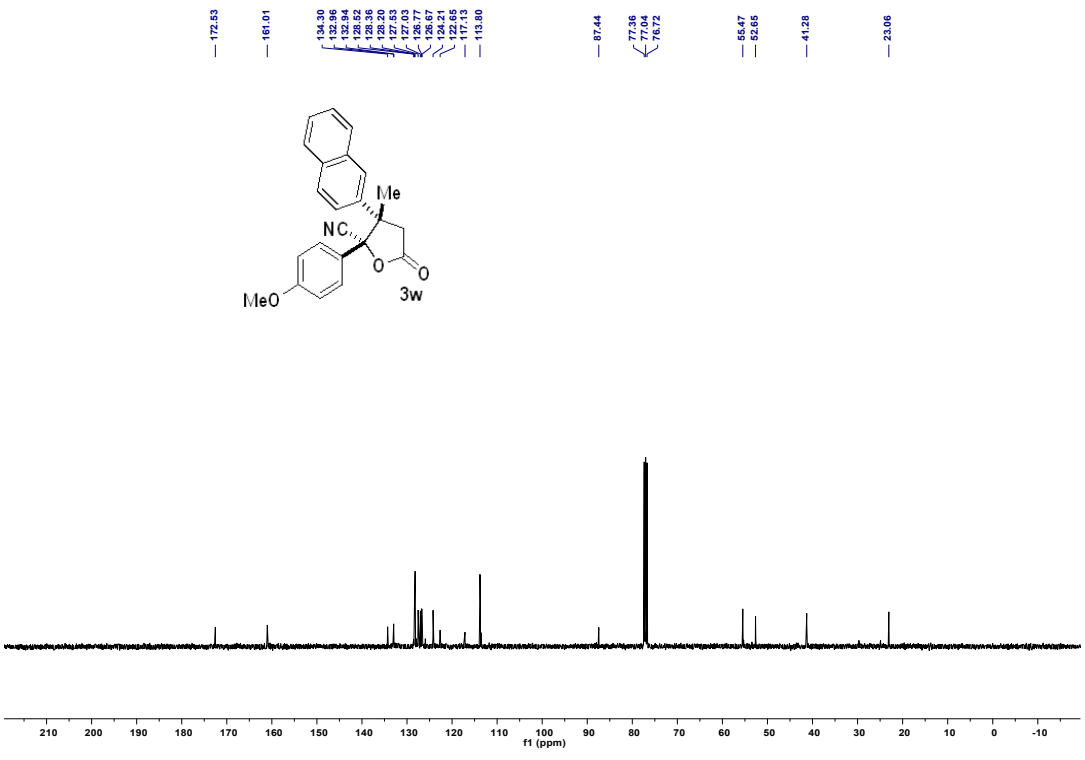


^{13}C NMR (101 MHz, $CDCl_3$)

3w

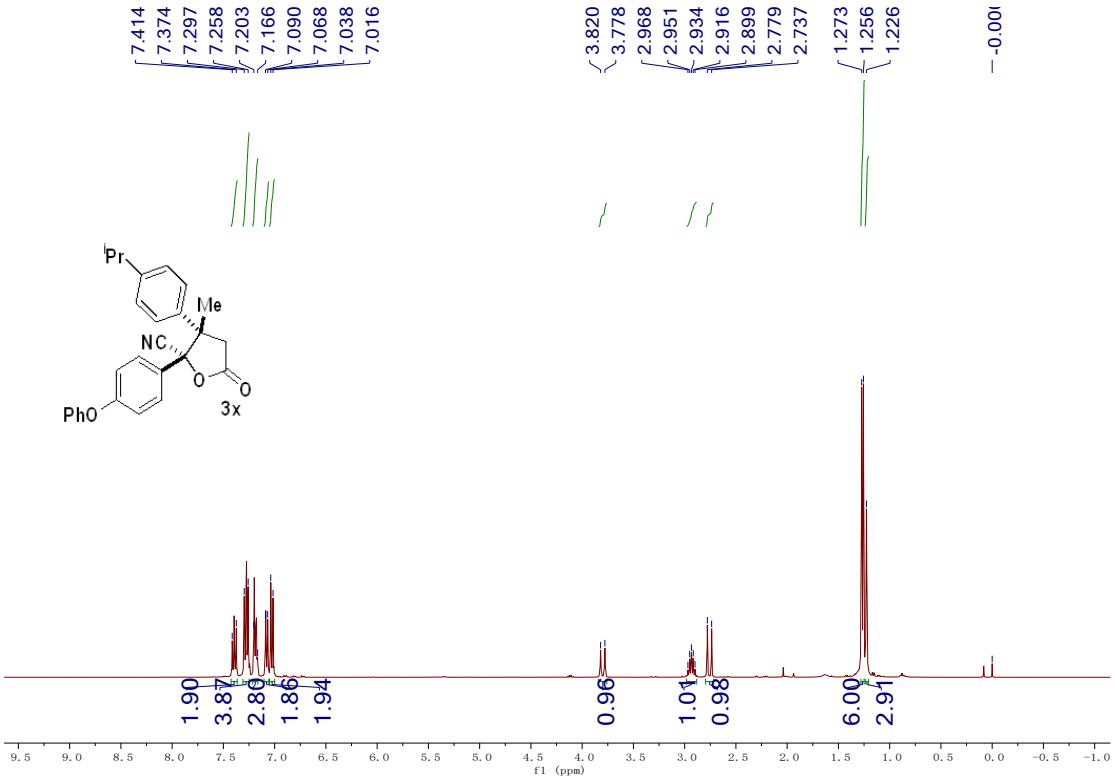


^{1}H NMR (400 MHz, $CDCl_3$)

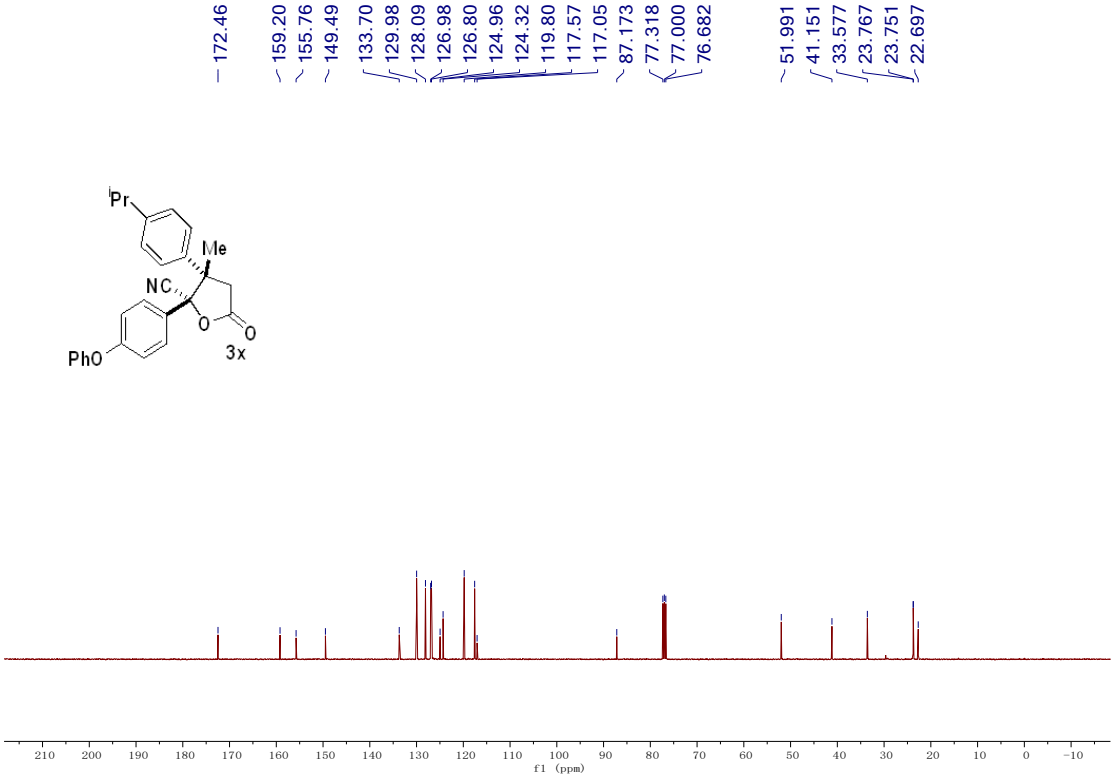


^{13}C NMR (101 MHz, $CDCl_3$)

3x

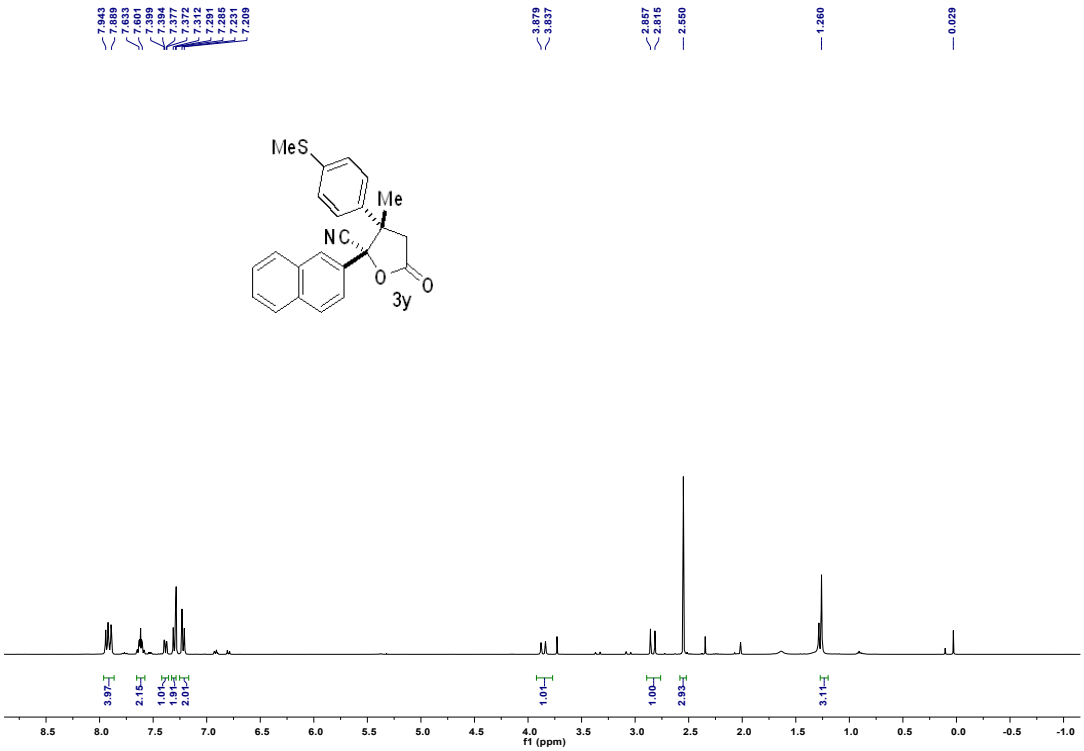


^{1}H NMR (400 MHz, $CDCl_3$)

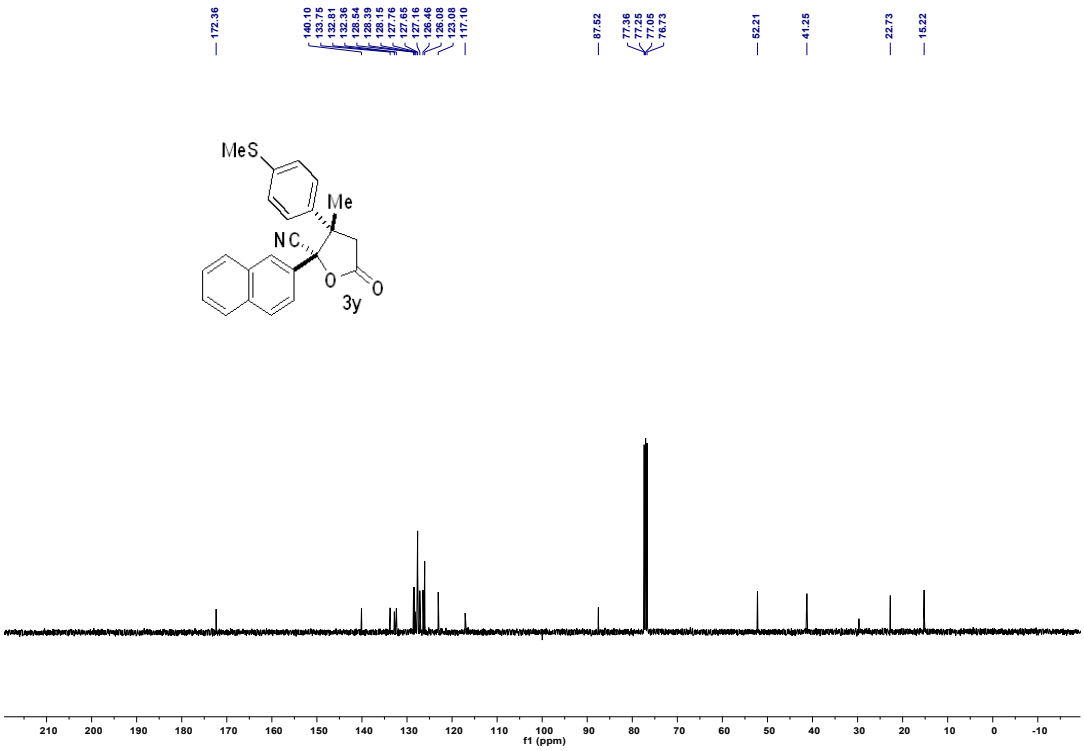


^{13}C NMR (101 MHz, $CDCl_3$)

3y

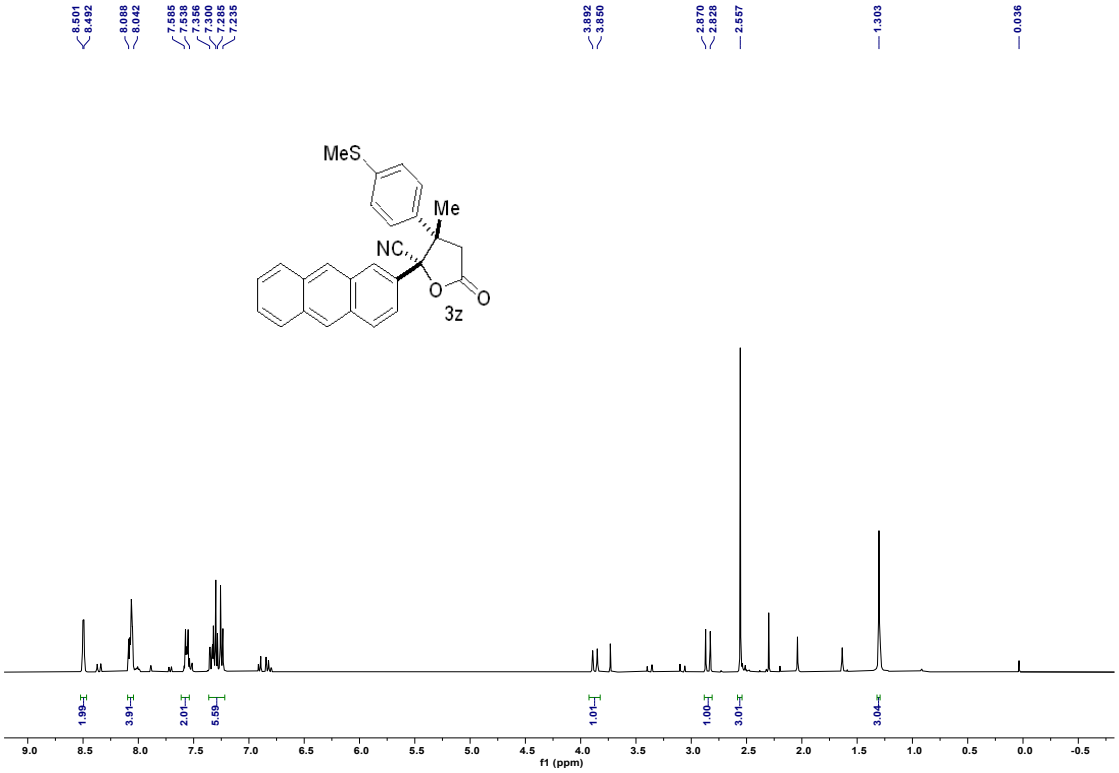


^{1}H NMR (400 MHz, $CDCl_3$)

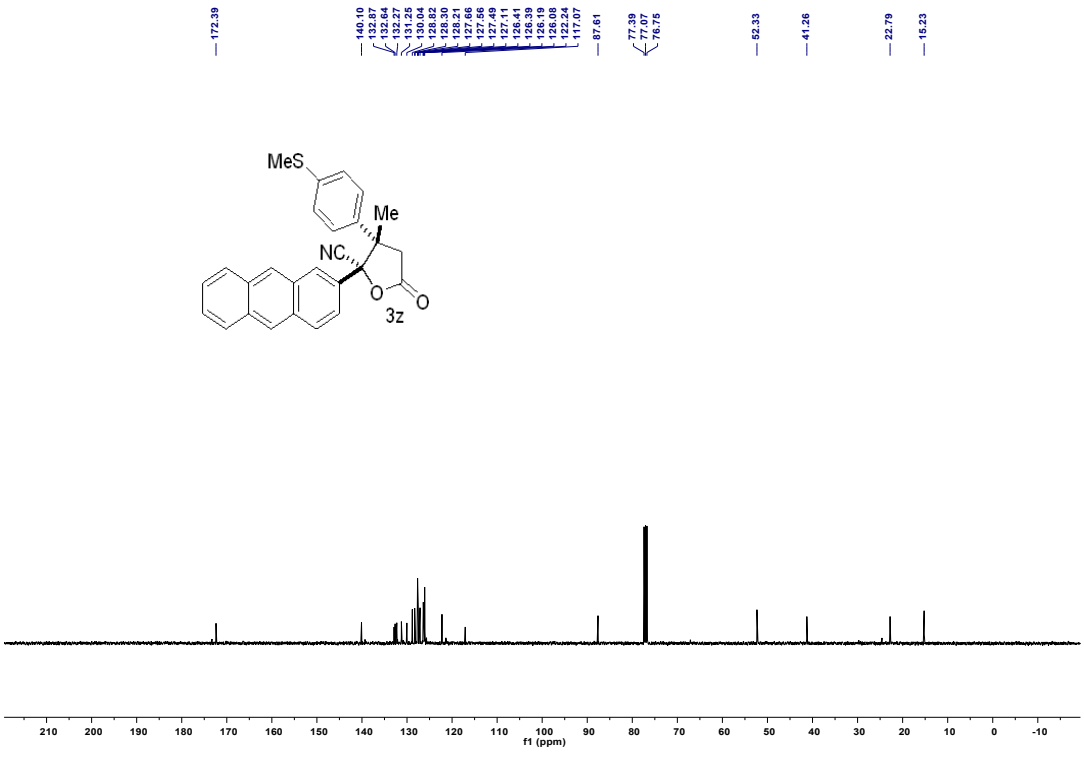


^{13}C NMR (101 MHz, $CDCl_3$)

3z

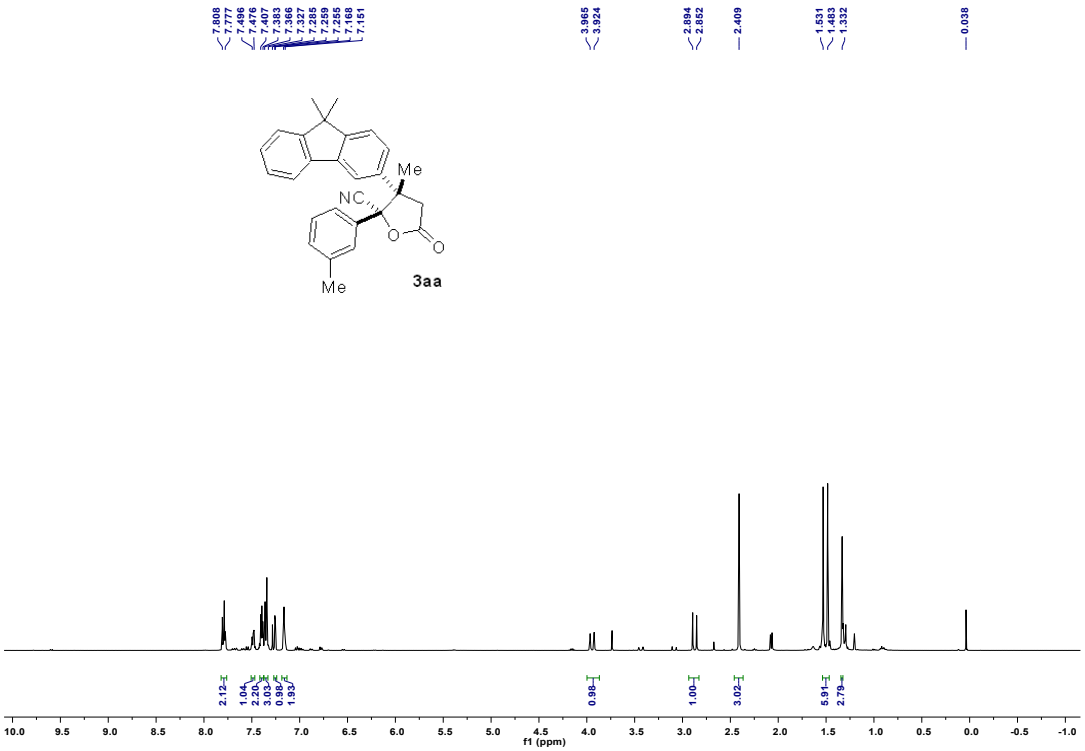


^{1}H NMR (400 MHz, $CDCl_3$)

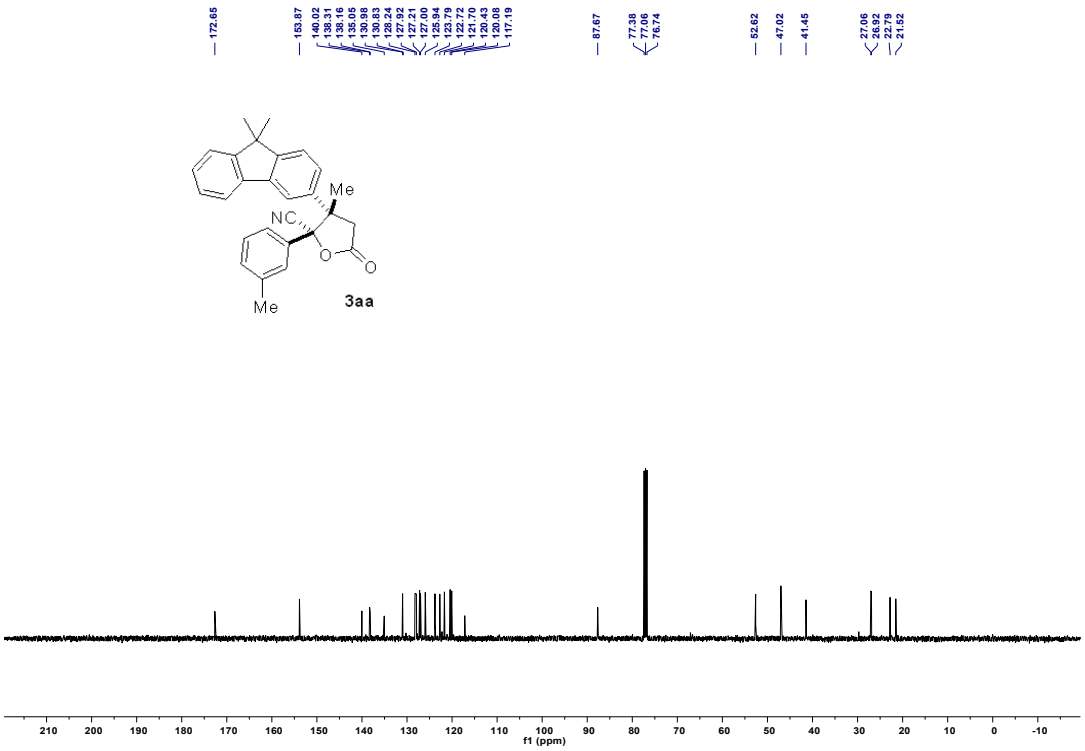


^{13}C NMR (101 MHz, $CDCl_3$)

3aa

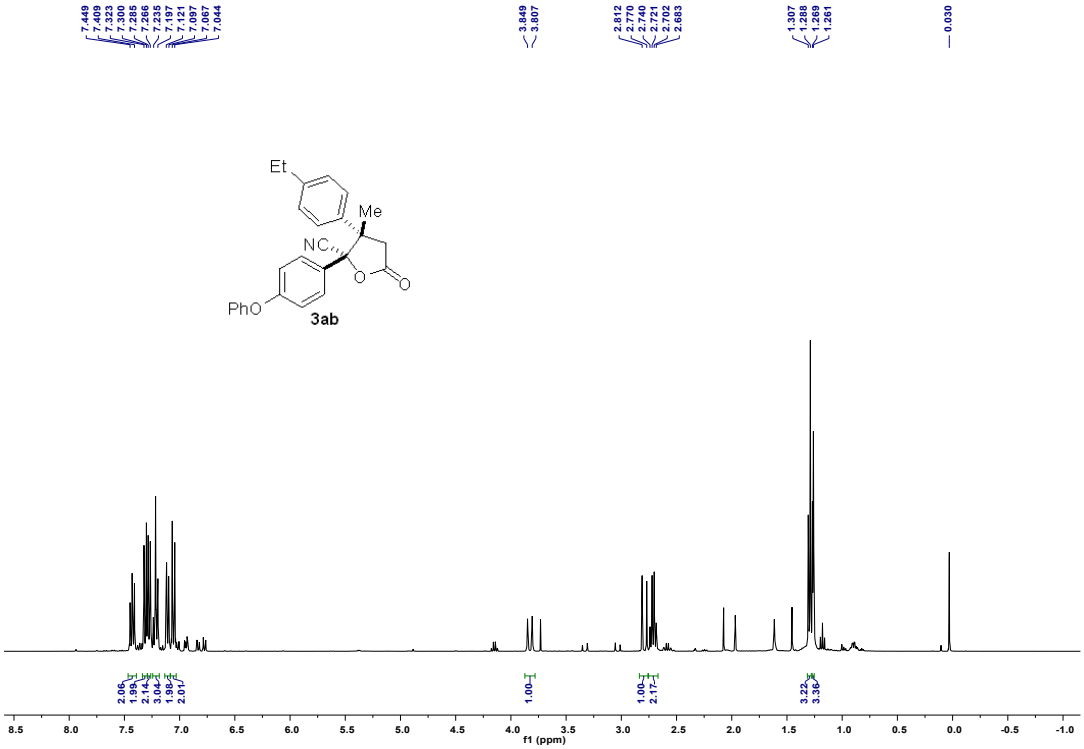


^{1}H NMR (400 MHz, $CDCl_3$)

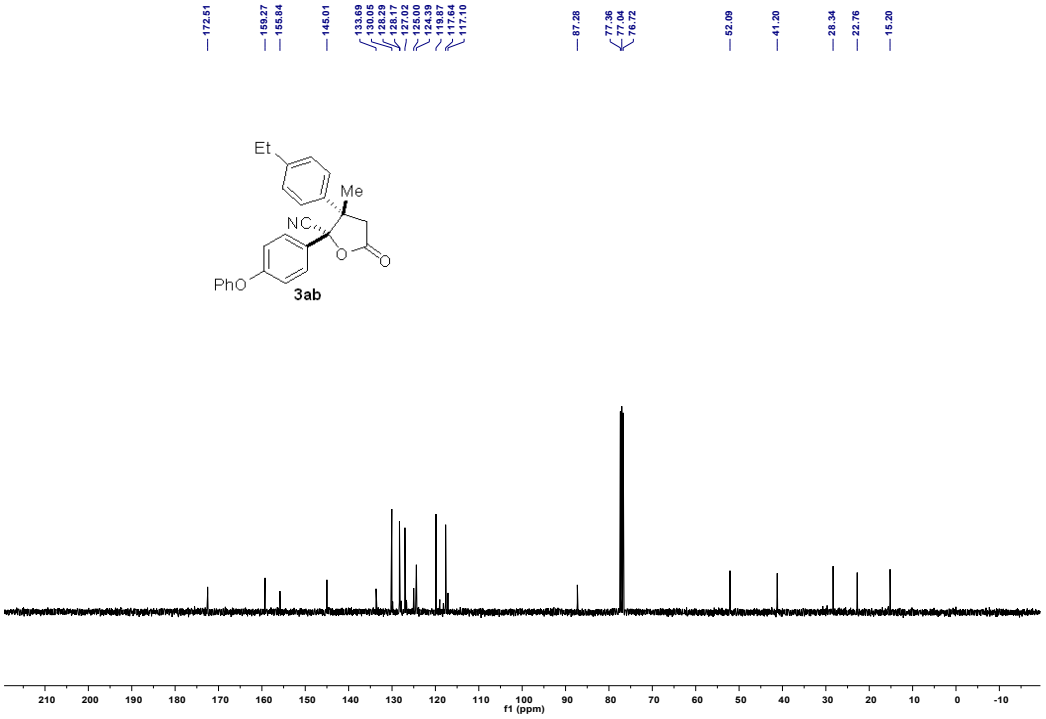


^{13}C NMR (101 MHz, $CDCl_3$)

3ab

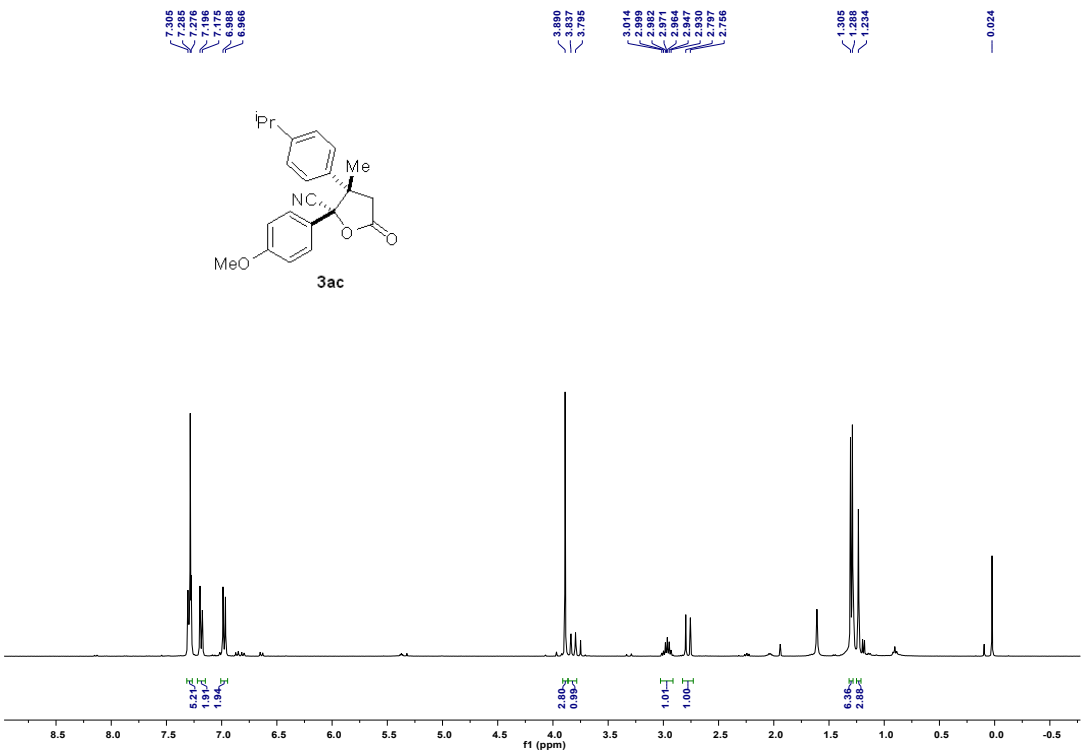


^{1}H NMR (400 MHz, $CDCl_3$)

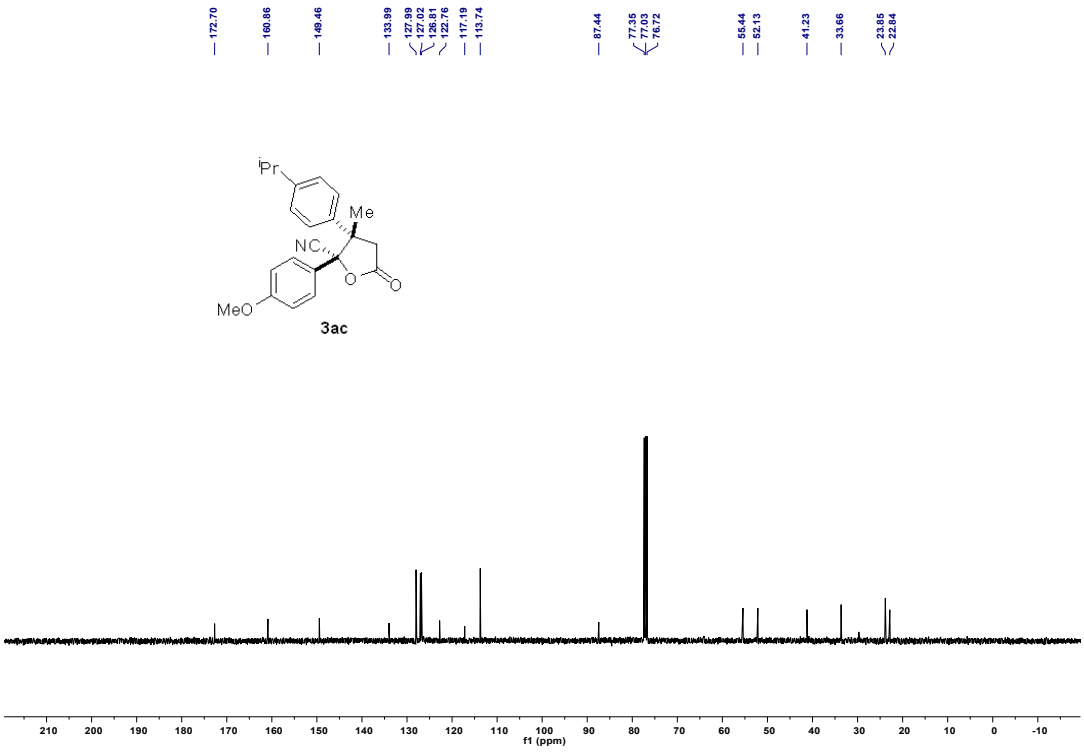


^{13}C NMR (101 MHz, $CDCl_3$)

3ac

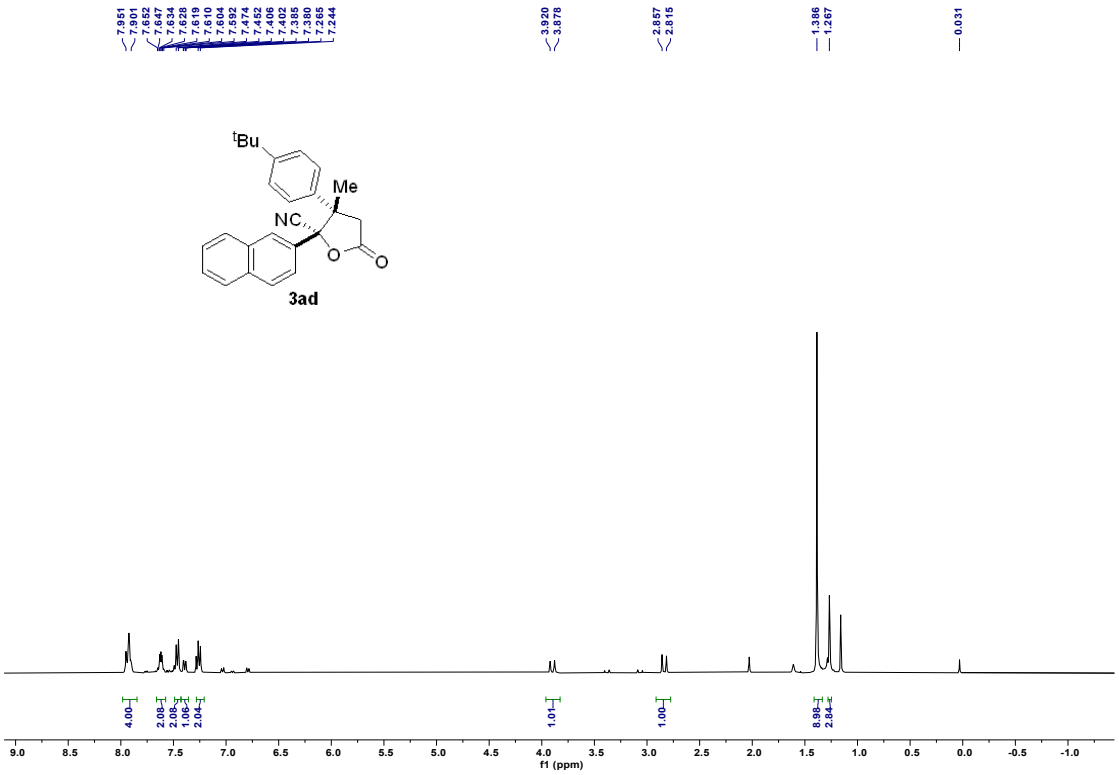


^{1}H NMR (400 MHz, $CDCl_3$)

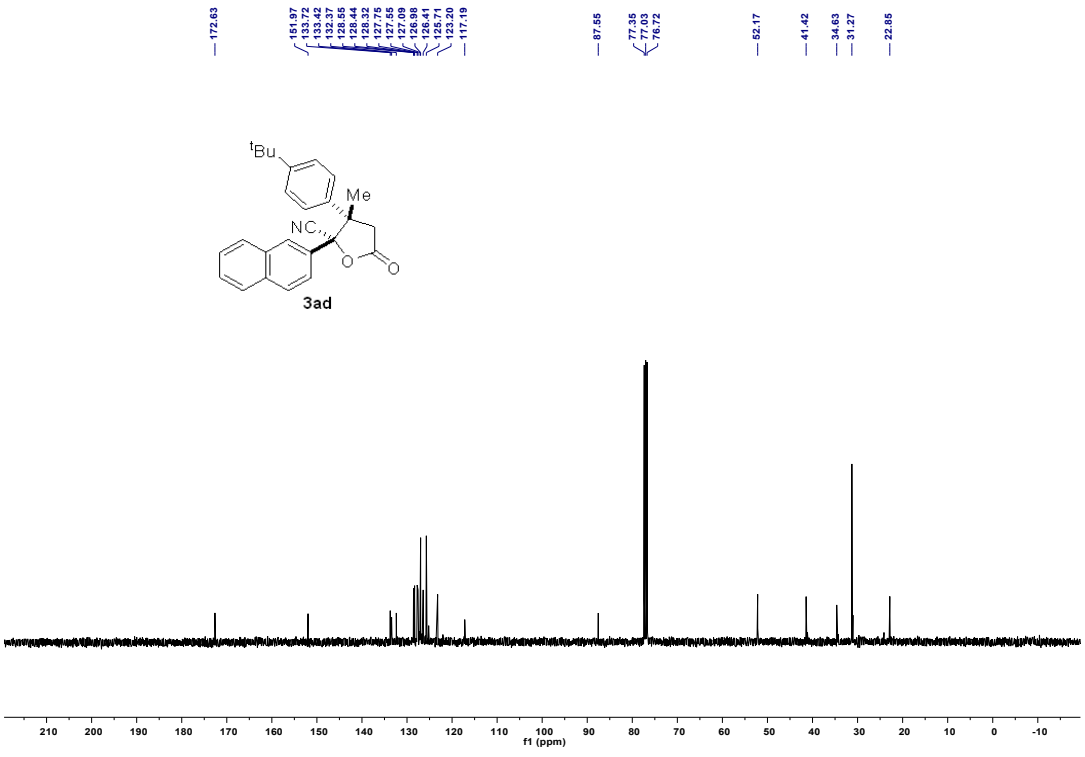


^{13}C NMR (101 MHz, $CDCl_3$)

3ad

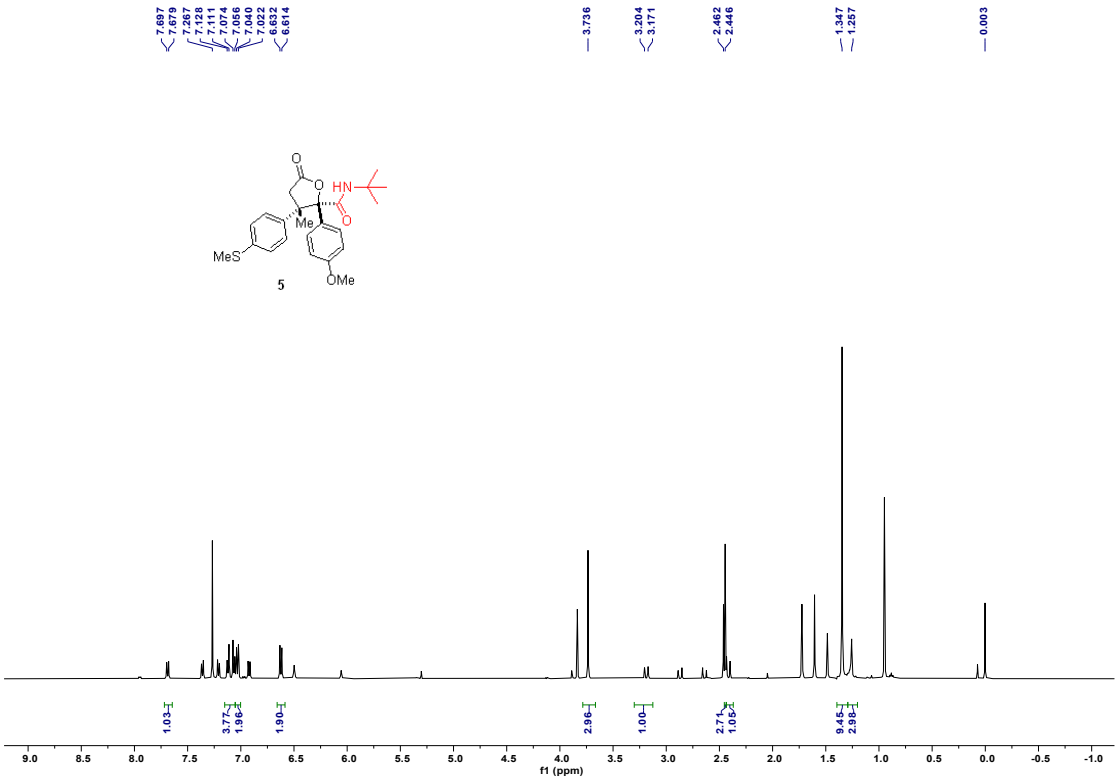


^{1}H NMR (400 MHz, $CDCl_3$)

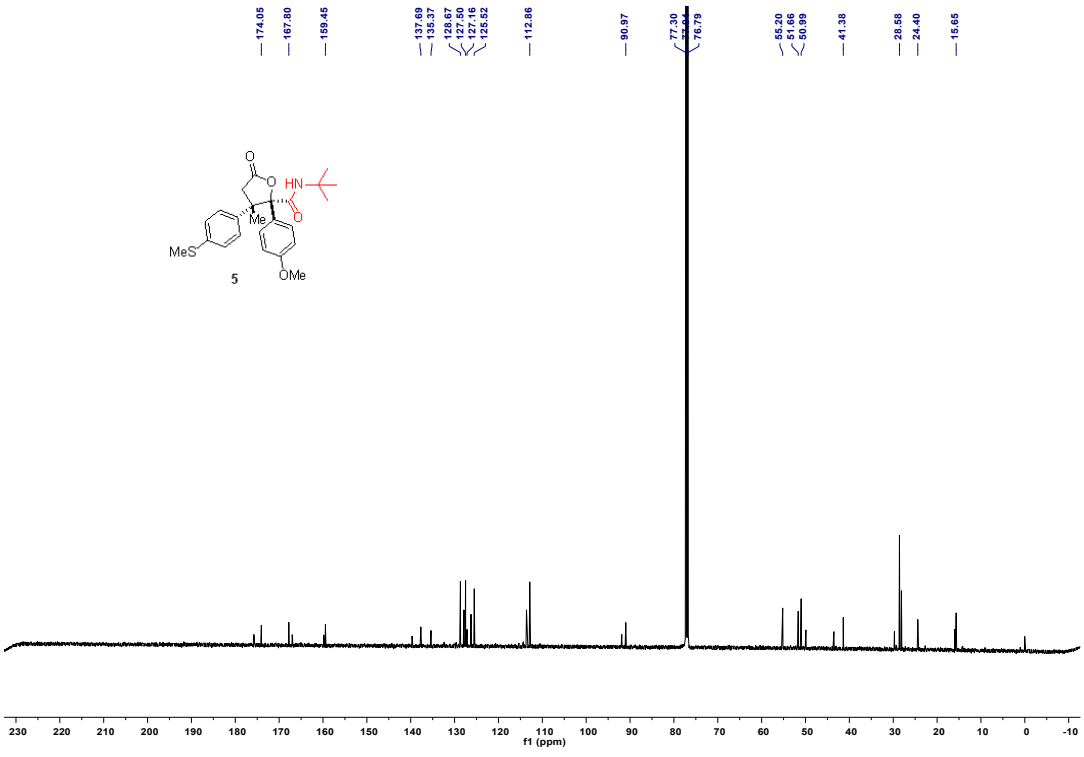


^{13}C NMR (101 MHz, $CDCl_3$)

5

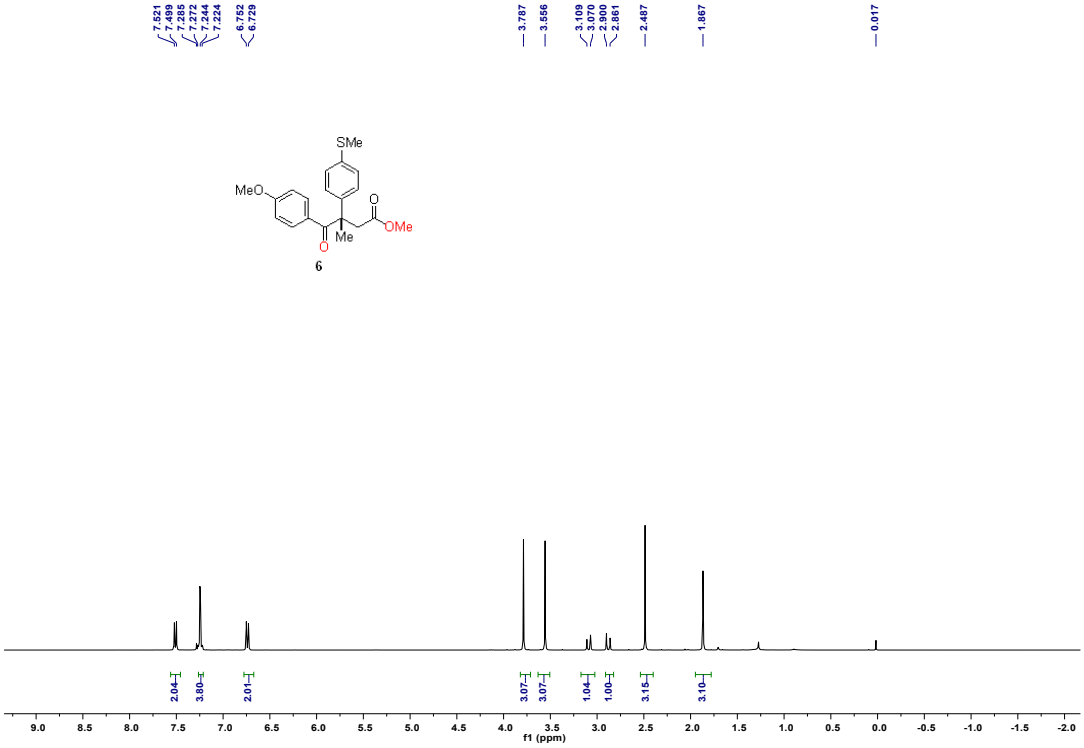


^{1}H NMR (500 MHz, $CDCl_3$)

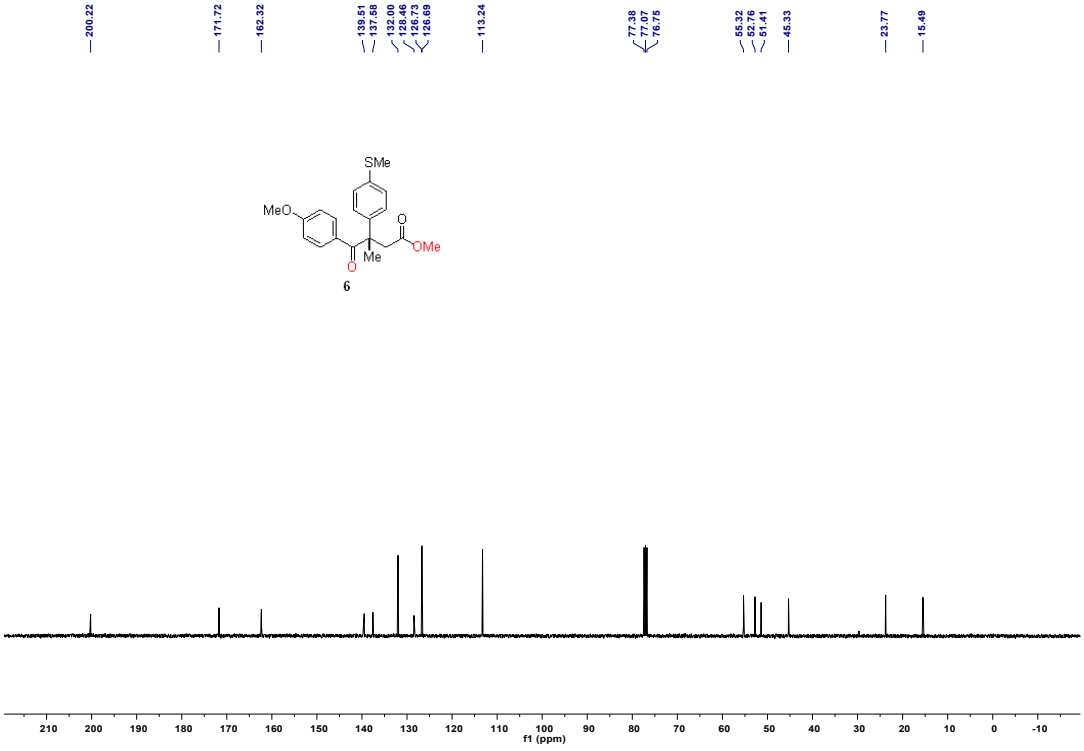


^{13}C NMR (126 MHz, $CDCl_3$)

6

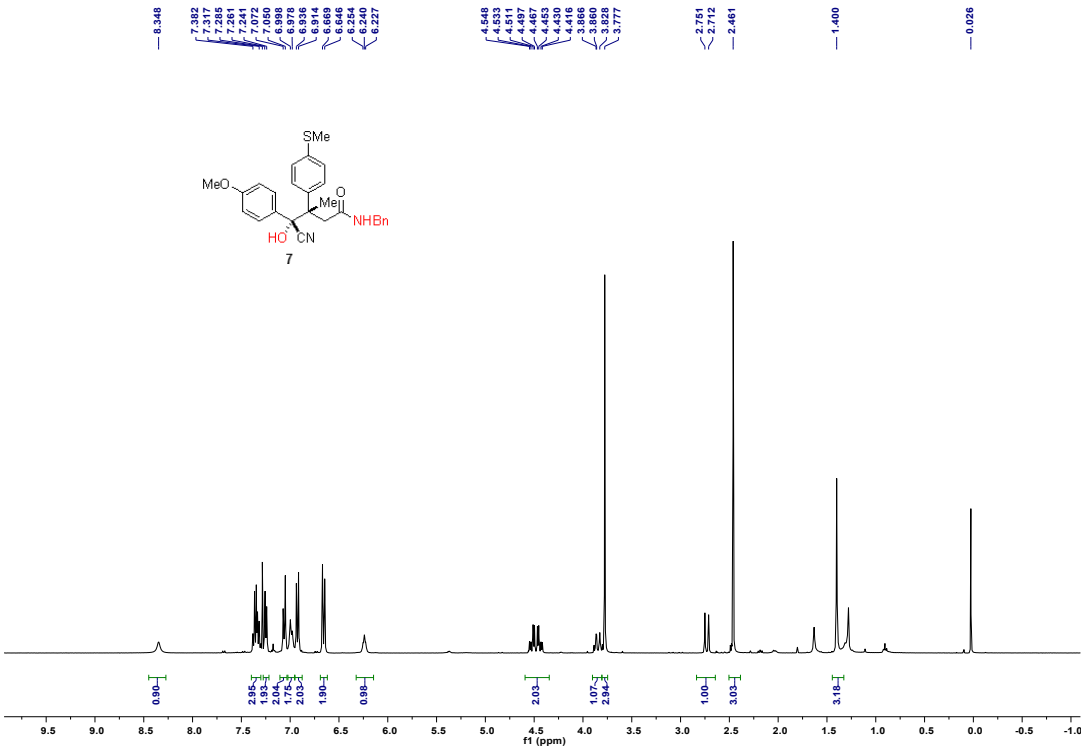


^{1}H NMR (400 MHz, $CDCl_3$)

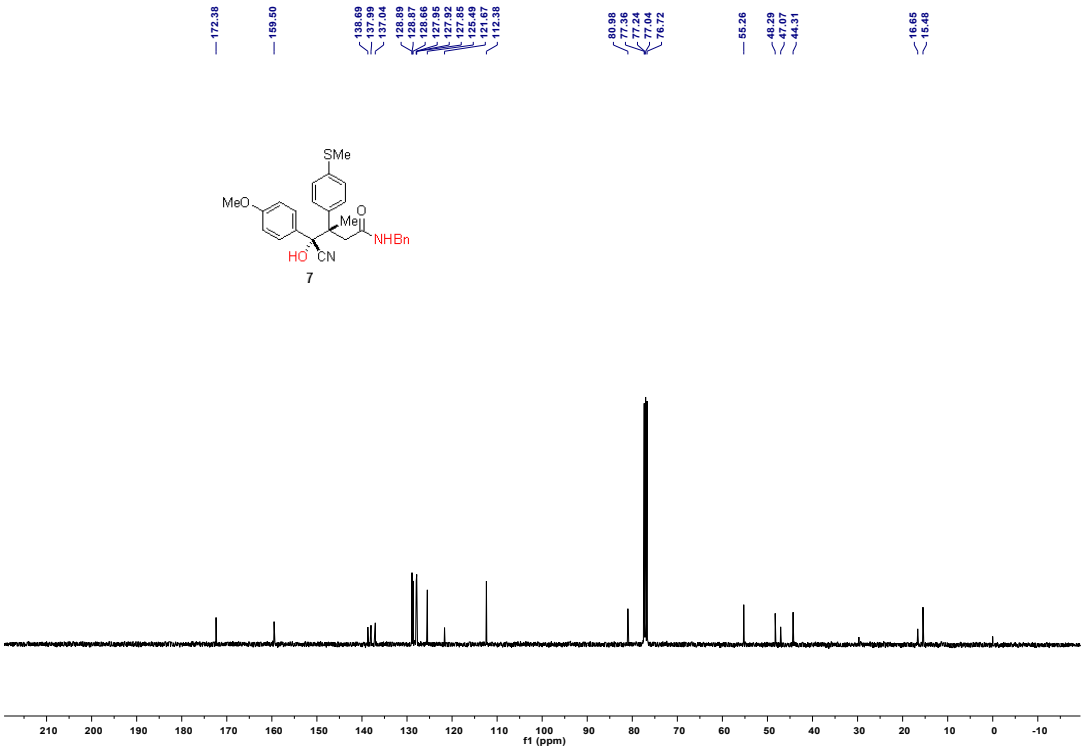


^{13}C NMR (101 MHz, $CDCl_3$)

7

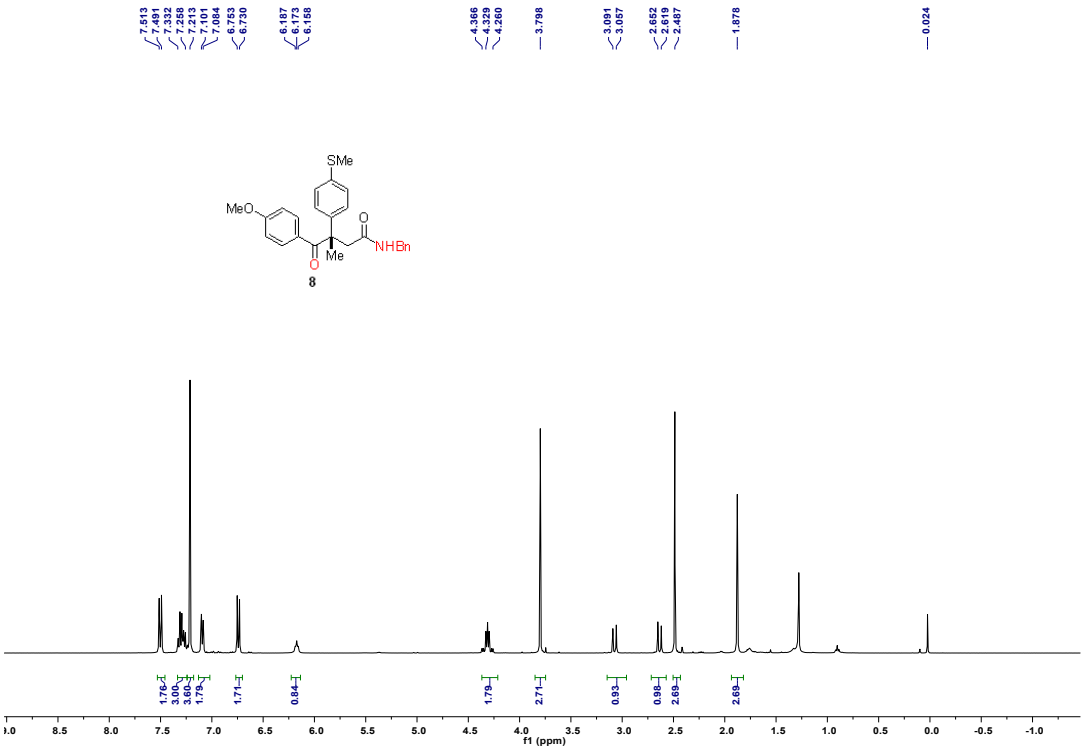


^{1}H NMR (400 MHz, $CDCl_3$)

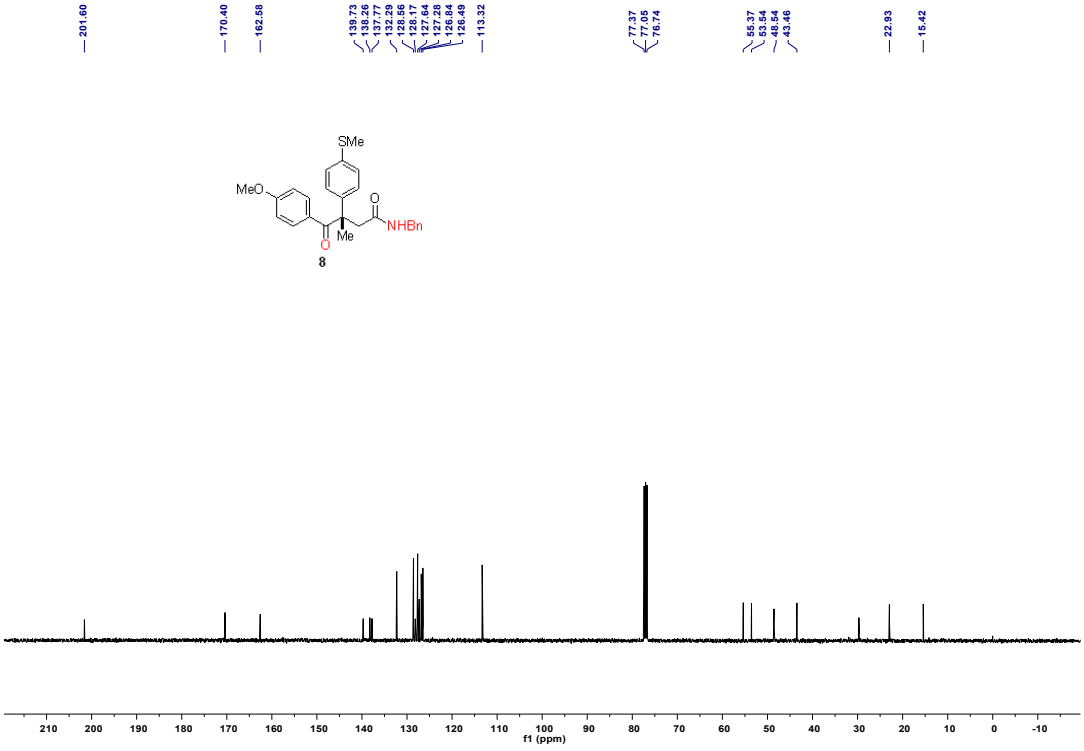


^{13}C NMR (101 MHz, $CDCl_3$)

8



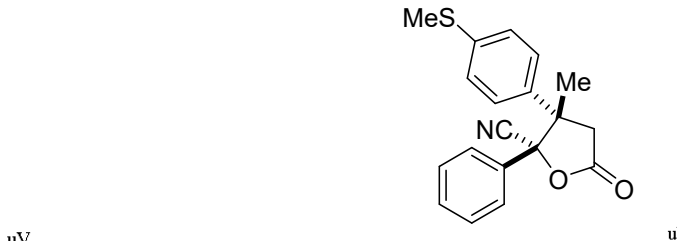
^{1}H NMR (400 MHz, $CDCl_3$)

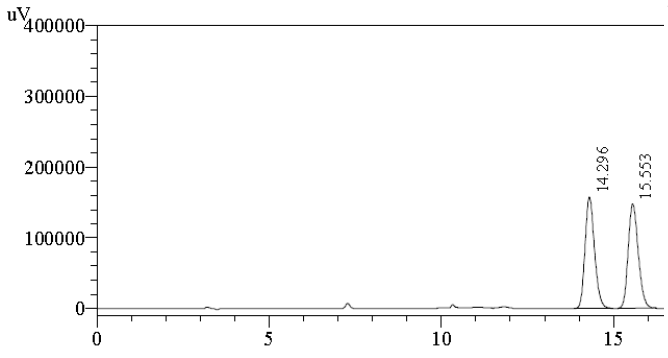


^{13}C NMR (101 MHz, $CDCl_3$)

HPLC spectra

(2S,3S)-3-methyl-3-(4-(methylthio)phenyl)-5-oxo-2-phenyltetrahydrofuran-2-carbonitrile (**3a**)





1 PDA Multi 1 / 254nm 4nm

PeakTal

PDA Ch1 254nm 4nm

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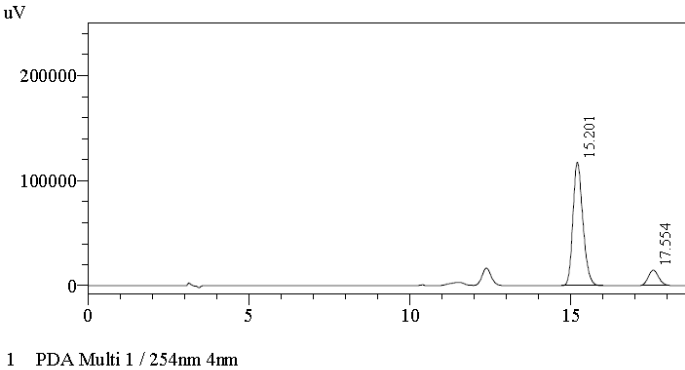
2	15.553	2993613	147817	
Total		5998005	305153	



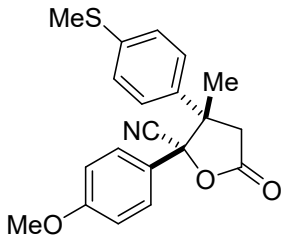
1 PDA Multi 1 / 254nm 4nm

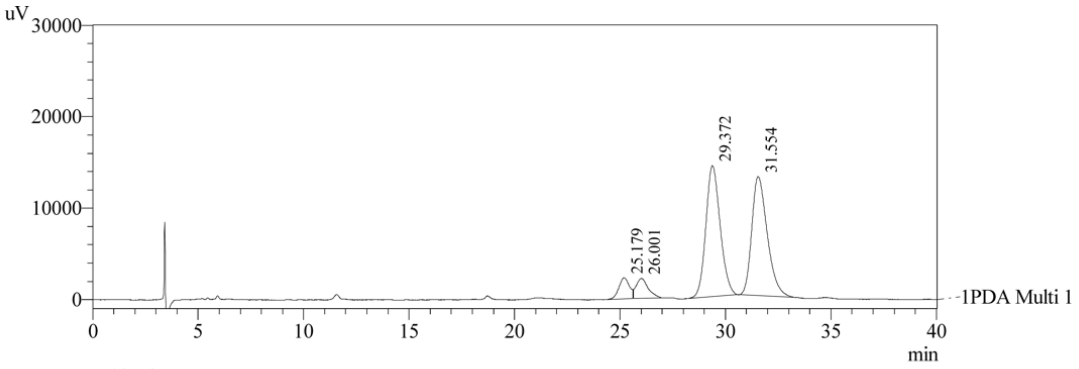
PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %
1	15.201	2527421	117419	89.2
2	17.554	303105	14234	10.7
Total		2830525	131653	100.0

(2S,3S)-2-(4-methoxyphenyl)-3-methyl-3-(4-(methylthio)phenyl)-5-oxotetrahydrofuran-2-carbonitrile (**3b**)



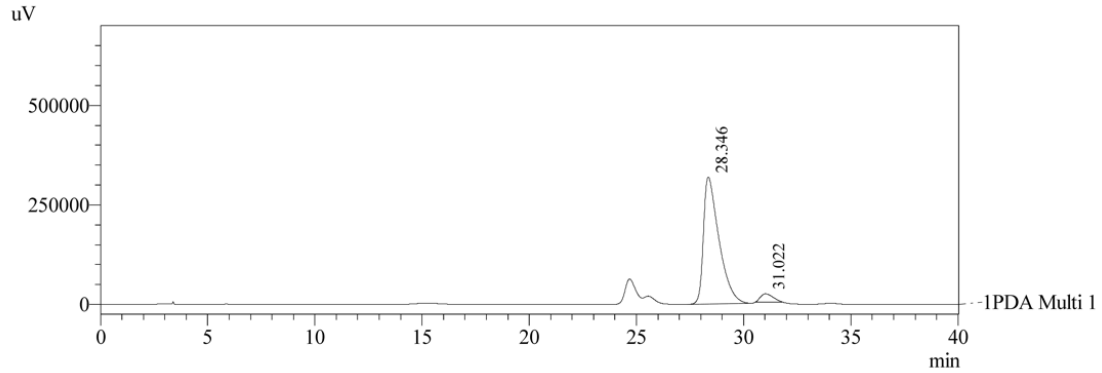


1 PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	25.179	81665	2323	5.407	7.294
2	26.001	85964	2186	5.691	6.864
3	29.372	675053	14307	44.692	44.929
4	31.554	667790	13028	44.211	40.912
Total		1510471	31843	100.000	100.000



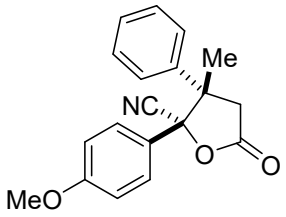
1 PDA Multi 1 / 254nm 4nm

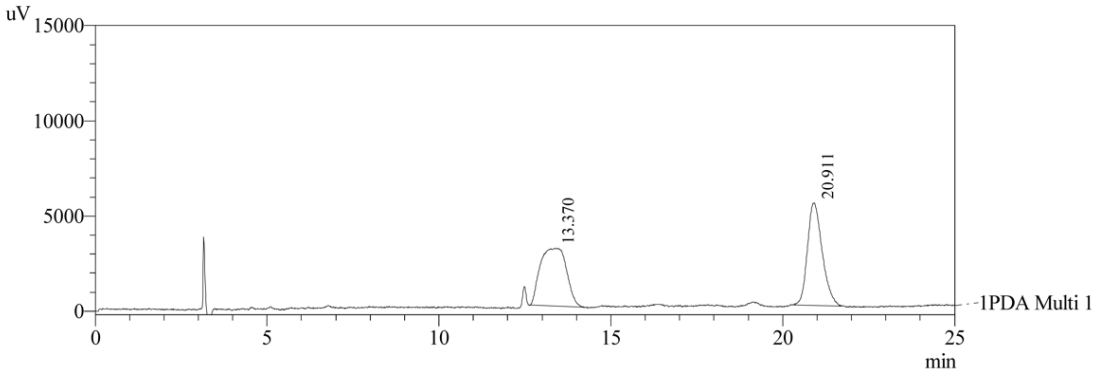
PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	28.346	16068157	319028	94.884	93.790
2	31.022	866458	21123	5.116	6.210
Total		16934616	340150	100.000	100.000

(2S,3S)-2-(4-methoxyphenyl)-3-methyl-5-oxo-3-phenyltetrahydrofuran-2-carbonitrile (**3c**)





1 PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.370	160473	3030	49.958	35.986
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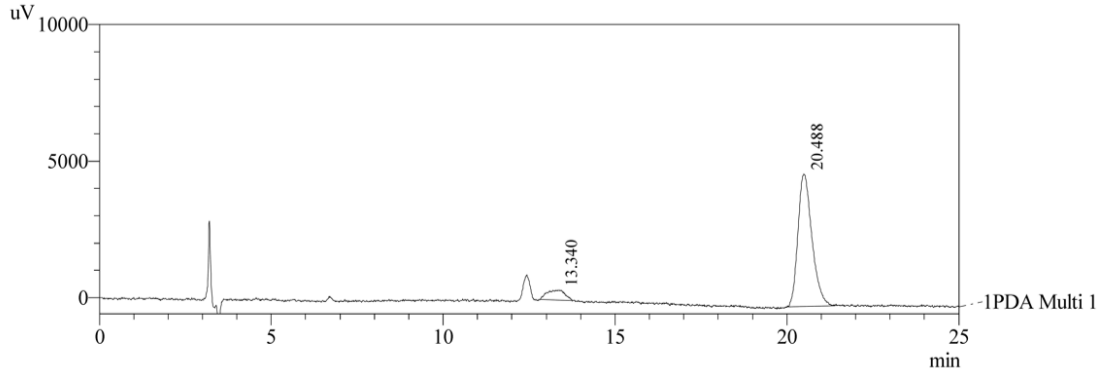
Total		321216	8419	100.000	100.000



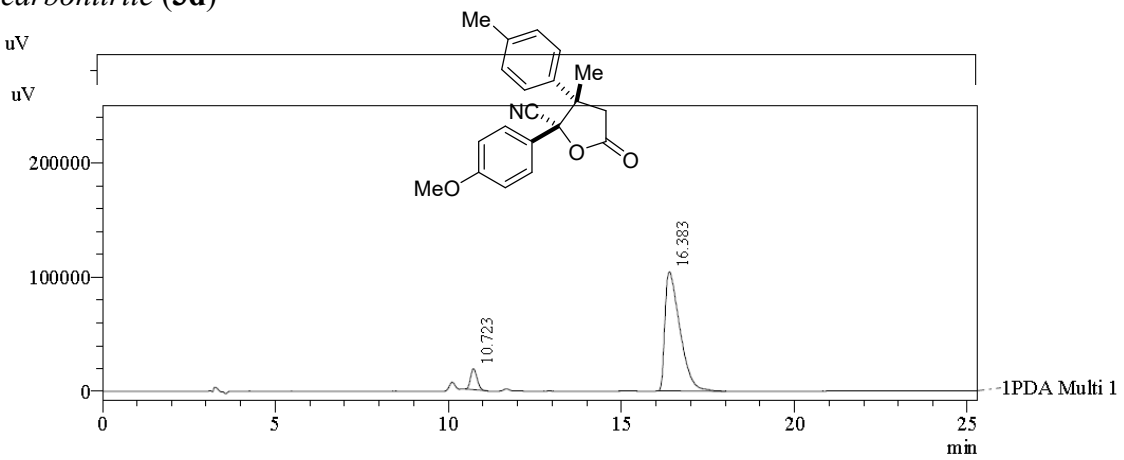
1 PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.340	13128	366	8.727	7.010
2	20.488	137299	4857	91.273	92.990
Total		150427	5224	100.000	100.000

(2S,3S)-2-(4-methoxyphenyl)-3-methyl-5-oxo-3-(p-tolyl)tetrahydrofuran-2-carbonitrile (**3d**)



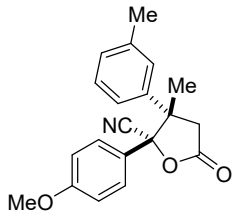
1 PDA Multi 1 / 254nm 4nm

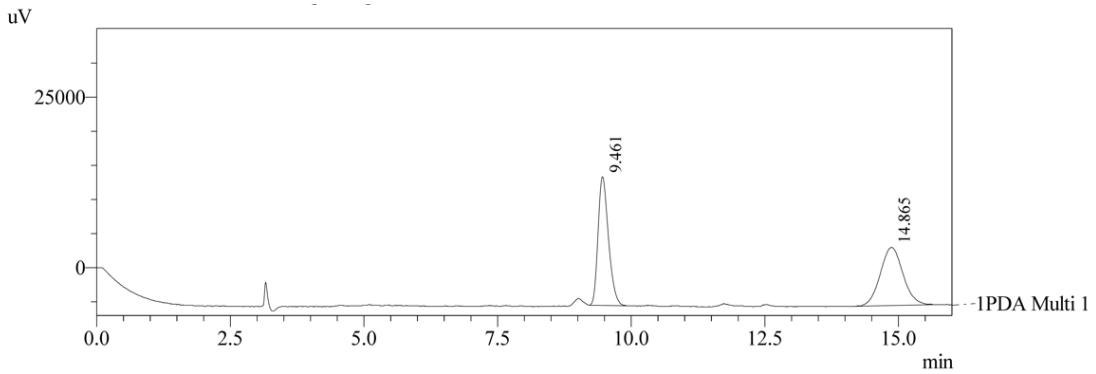
PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.723	242627	18487	7.186	15.041
2	16.383	3133682	104426	92.814	84.959
Total		3376309	122912	100.000	100.000

(2S,3S)-2-(4-methoxyphenyl)-3-methyl-5-oxo-3-(m-tolyl)tetrahydrofuran-2-carbonitrile (**3e**)



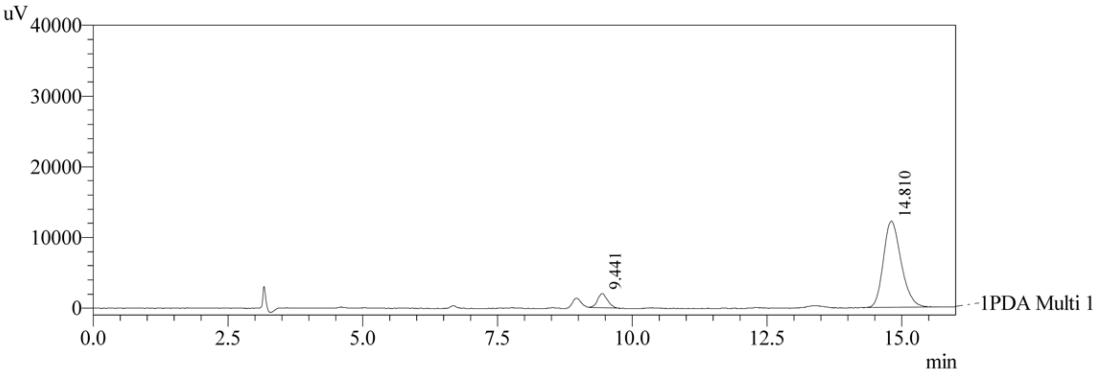


1 PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.461	255308	18831	50.421	68.895
2	14.865	251042	8502	49.579	31.105
Total		506350	27333	100.000	100.000



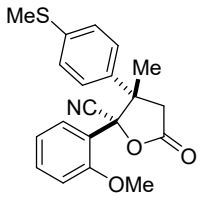
1 PDA Multi 1 / 254nm 4nm

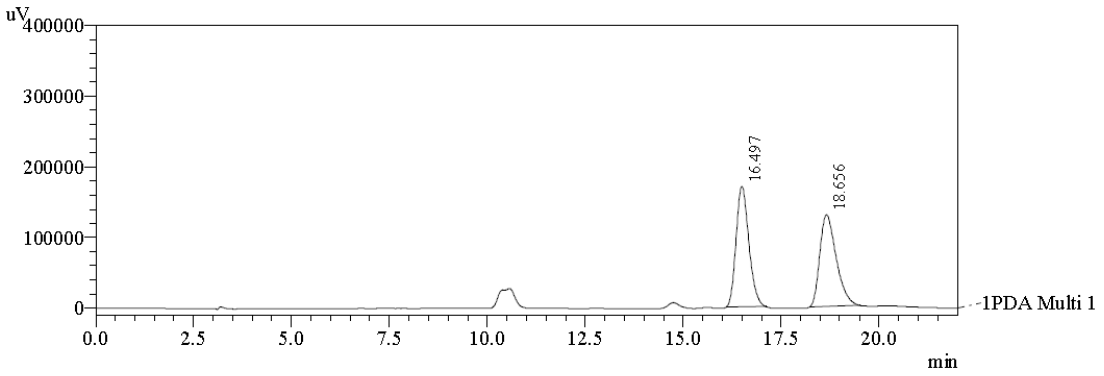
PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.441	25419	1974	8.319	13.895
2	14.810	280133	12233	91.681	86.105
Total		305552	14207	100.000	100.000

(2R,3S)-2-(2-methoxyphenyl)-3-methyl-3-(4-(methylthio)phenyl)-5-oxotetrahydrofuran-2-carbonitrile (**3f**)



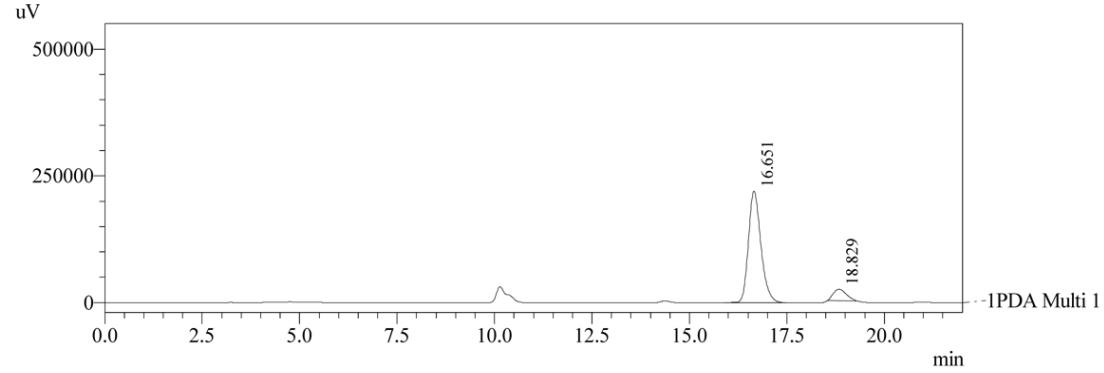


1 PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.497	3879175	170510	50.663	56.853
2	18.656	3777583	129403	49.337	43.147
Total		7656758	299913	100.000	100.000



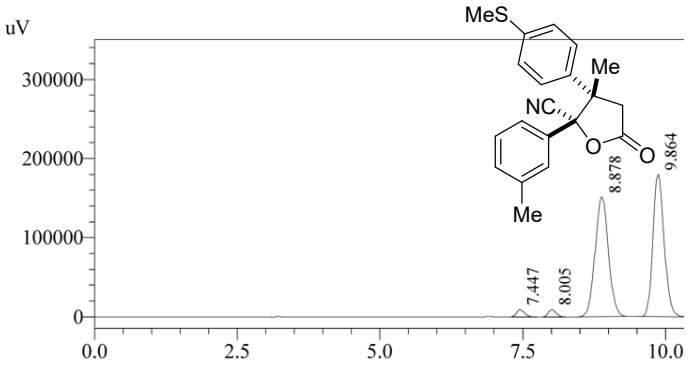
1 PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.651	4914344	220206	90.165	90.590
2	18.829	536054	22873	9.835	9.410
Total		5450398	243079	100.000	100.000

(2S,3S)-3-methyl-3-(4-(methylthio)phenyl)-5-oxo-2-(m-tolyl)tetrahydrofuran-2-carbonitrile (**3g**)

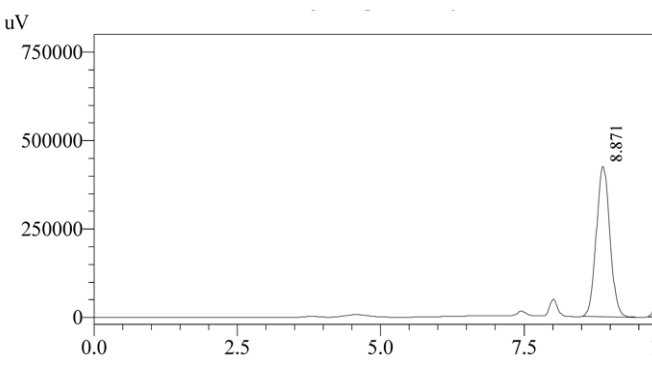


1 PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area
1	7.447	87012	9088	
2	8.005	86951	9453	
3	8.878	2458572	151168	
4	9.864	2463722	179629	
Total		5096256	349339	100.000



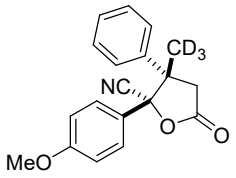
1 PDA Multi 1 / 254nm 4nm

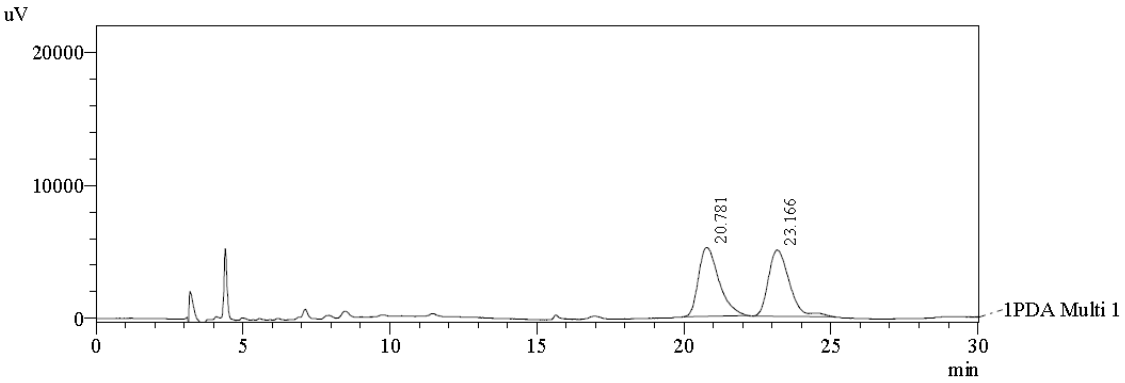
PeakT

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height
1	8.871	7021692	425574
2	9.872	764684	58478
Total		7786377	484052

(2S,3S)-2-(4-methoxyphenyl)-3-(methyl-d_3)-5-oxo-3-phenyltetrahydrofuran-2-carbonitrile (**3h**)



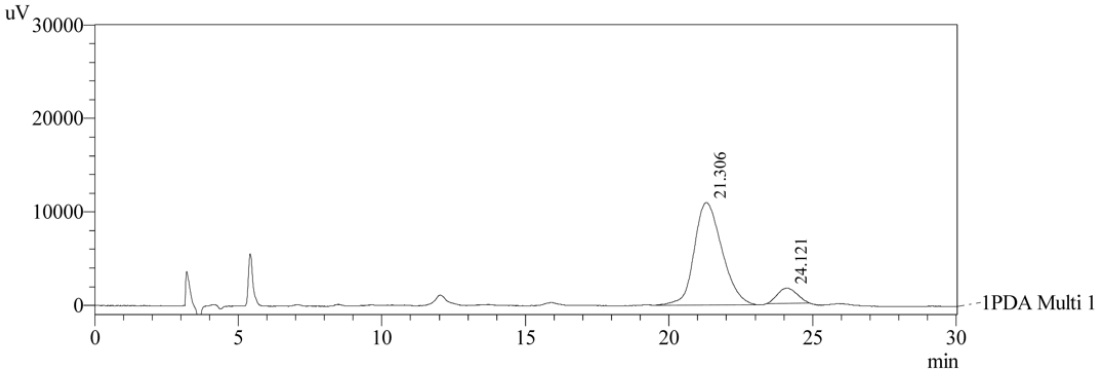


1 PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	20.781	253025	5199	50.451	51.057
2	23.166	248505	4984	49.549	48.943
Total		501530	10184	100.000	100.000



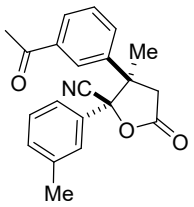
1 PDA Multi 1 / 254nm 4nm

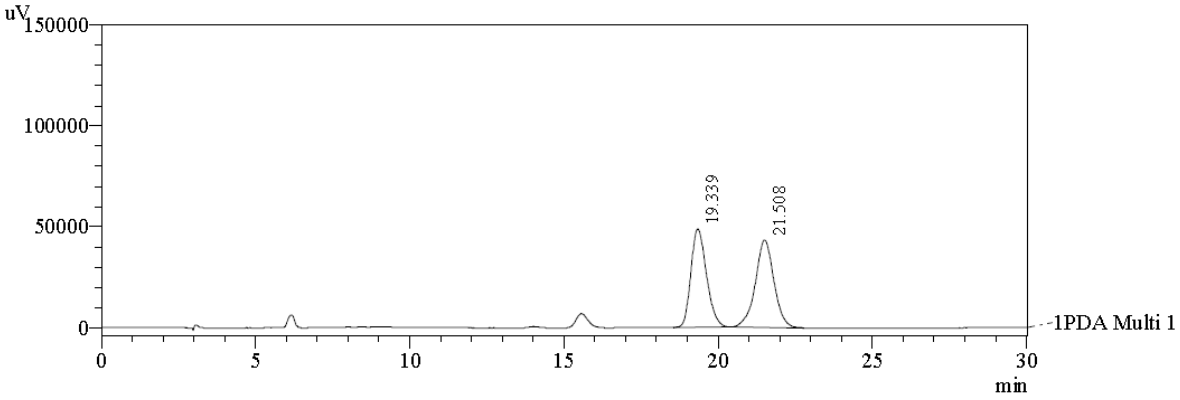
PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	21.306	738208	10957	90.483	87.046
2	24.121	77646	1631	9.517	12.954
Total		815854	12587	100.000	100.000

(2S,3S)-3-(3-acetylphenyl)-3-methyl-5-oxo-2-(m-tolyl)tetrahydrofuran-2-carbonitrile (**3i**)



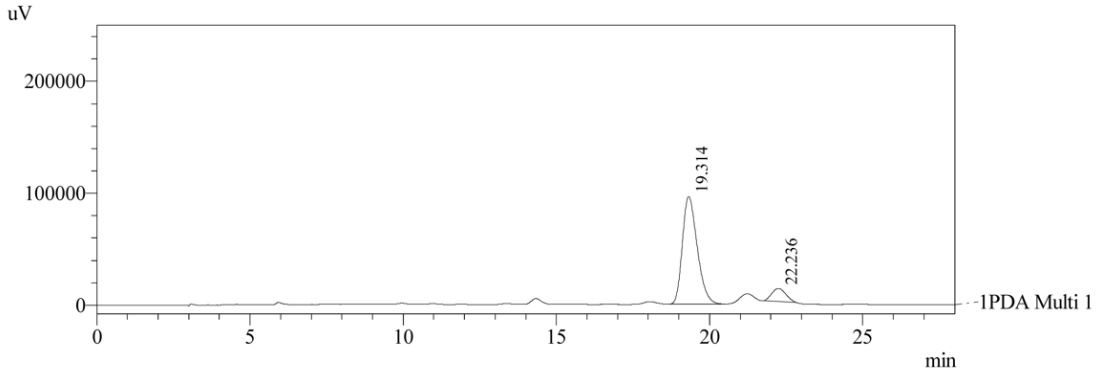


1 PDA

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	19.339	1712919	48606	48.506	52.903
2	21.508	1818402	43272	51.494	47.097
Total		3531321	91878	100.000	100.000



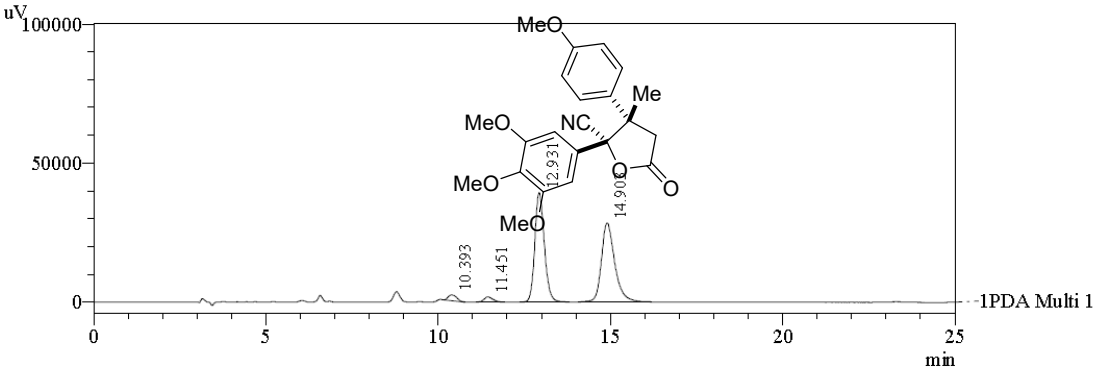
1 PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	19.314	3246700	96210	90.035	89.398
2	22.236	359354	11410	9.965	10.602
Total		3606054	107620	100.000	100.000

(2S,3S)-3-(4-methoxyphenyl)-3-methyl-5-oxo-2-(3,4,5-trimethoxyphenyl)tetrahydrofuran-2-carbonitrile (**3j**)

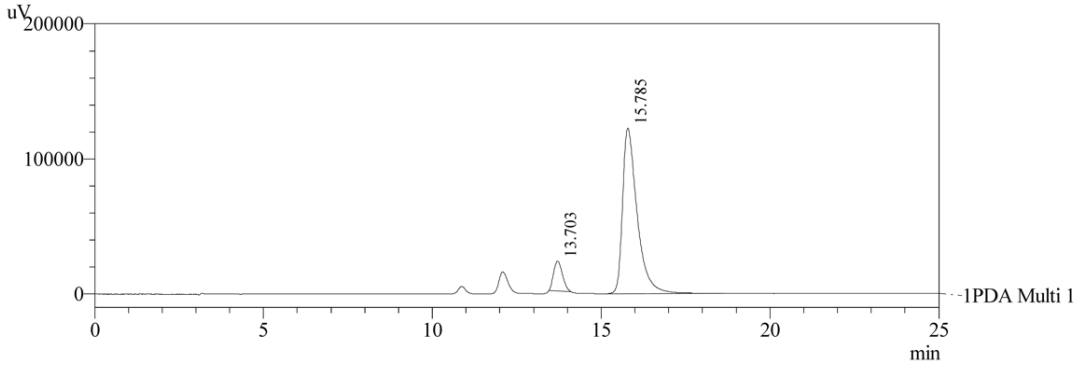


1 PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.393	35914	2099	2.249	2.923
2	11.451	34875	1871	2.184	2.605
3	12.931	759987	39436	47.593	54.927
4	14.903	766077	28391	47.974	39.544
Total		1596853	71796	100.000	100.000



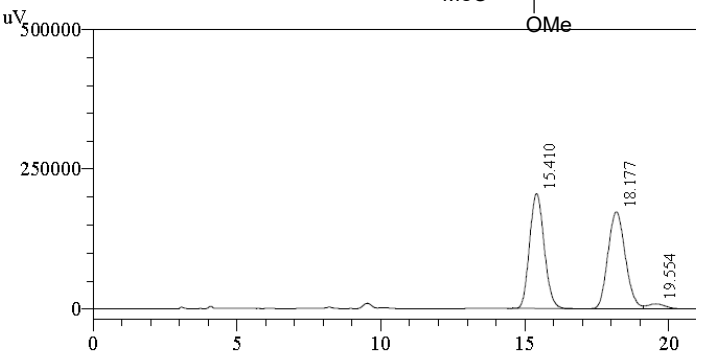
1 PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.703	405697	22221	9.898	15.364
2	15.785	3693268	122405	90.102	84.636
Total		4098965	144626	100.000	100.000

(2S,3S)-3-methyl-3-(4-(methylthio)phenyl)-5-oxo-2-(3,4,5-trimethoxyphenyl)tetrahydrofuran-2-carbonitrile (**3k**)

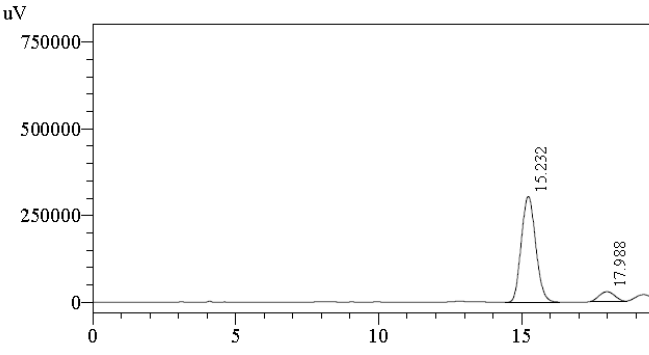


1 PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area
1	15.410	7274910	205567	
2	18.177	7260097	173076	
3	19.554	373276	8704	
4	23.540	383242	7185	
Total		15291525	394532	100.000



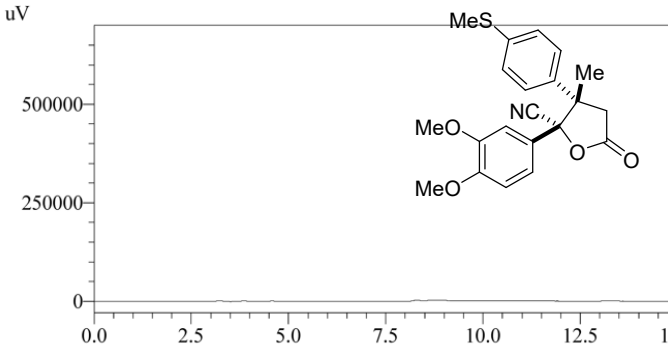
1 PDA Multi 1 / 254nm 4nm

PeakTa

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	
1	15.232	10693402	304409	
2	17.988	1013734	27639	
Total		11707136	332048	

(2S,3S)-2-(3,4-dimethoxyphenyl)-3-methyl-3-(4-(methylthio)phenyl)-5-oxotetrahydrofuran-2-carbonitrile (**3l**)

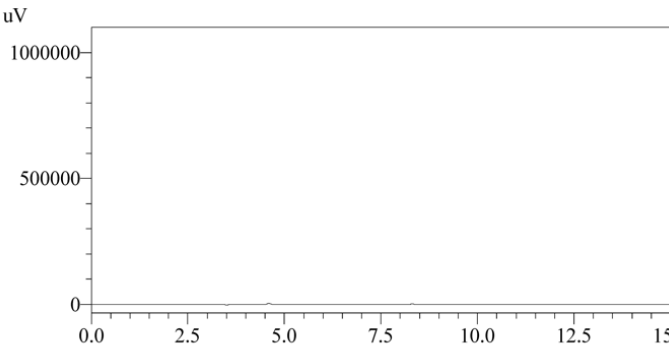


1 PDA Multi 1 / 254nm 4nm

PeakTabl

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Ar
1	15.451	310783	12974	
2	16.432	311783	12608	
3	18.067	8208124	307821	
4	20.000	8265830	268529	
Total		17096520	601933	



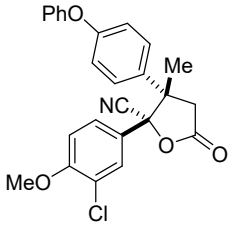
1 PDA Multi 1 / 254nm 4nm

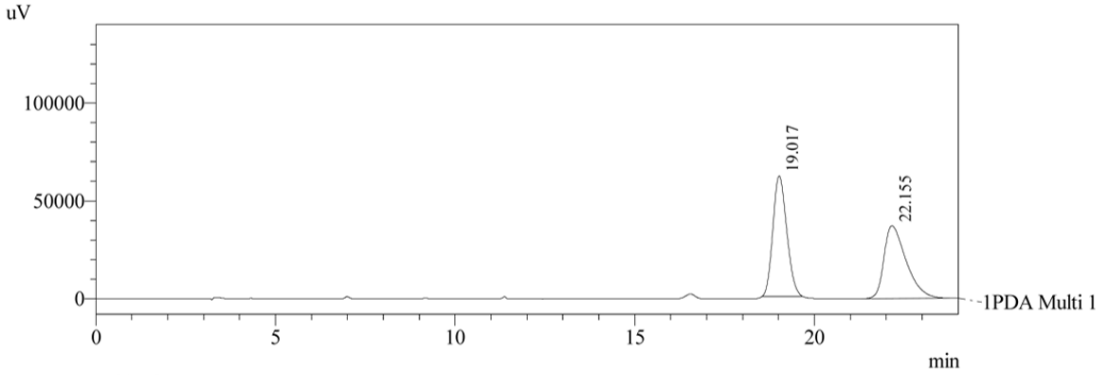
PeakTabl

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Are
1	18.370	1710138	65545	
2	20.330	15740572	491702	
Total		17450710	557247	

(2S,3S)-2-(3-chloro-4-methoxyphenyl)-3-methyl-5-oxo-3-(4-phenoxyphenyl)tetrahydrofuran-2-carbonitrile (**3m**)



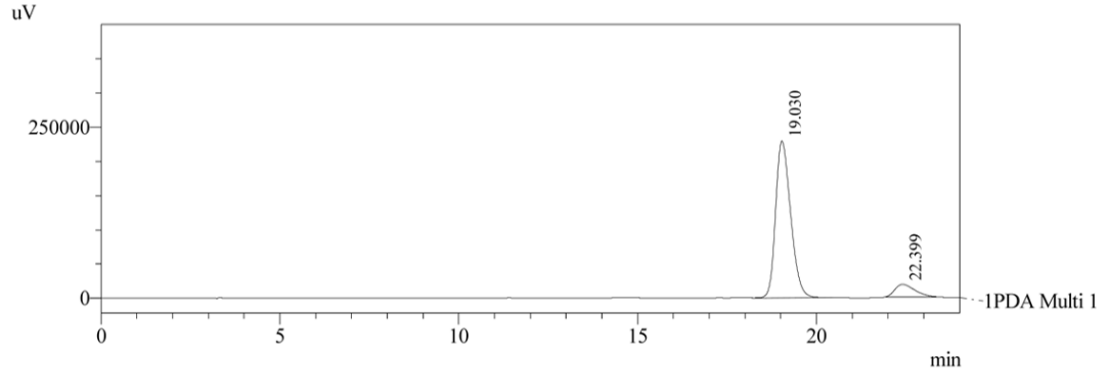


1 PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	19.017	1653754	61395	50.888	62.275
2	22.155	1596056	37192	49.112	37.725
Total		3249810	98587	100.000	100.000



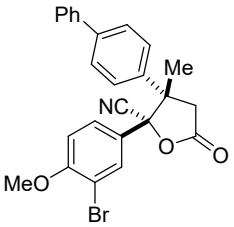
1 PDA Multi 1 / 254nm 4nm

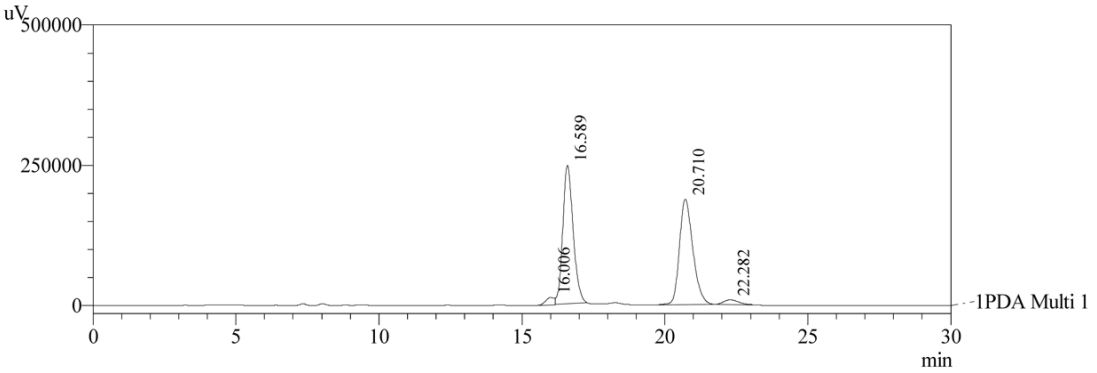
PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	19.030	6707689	229032	90.661	92.654
2	22.399	690933	18158	9.339	7.346
Total		7398622	247191	100.000	100.000

(2S,3S)-3-([1,1'-biphenyl]-4-yl)-2-(3-borom-4-methoxyphenyl)-3-methyl-5-oxotetrahydrofuran-2-carbonitrile (**3n**)



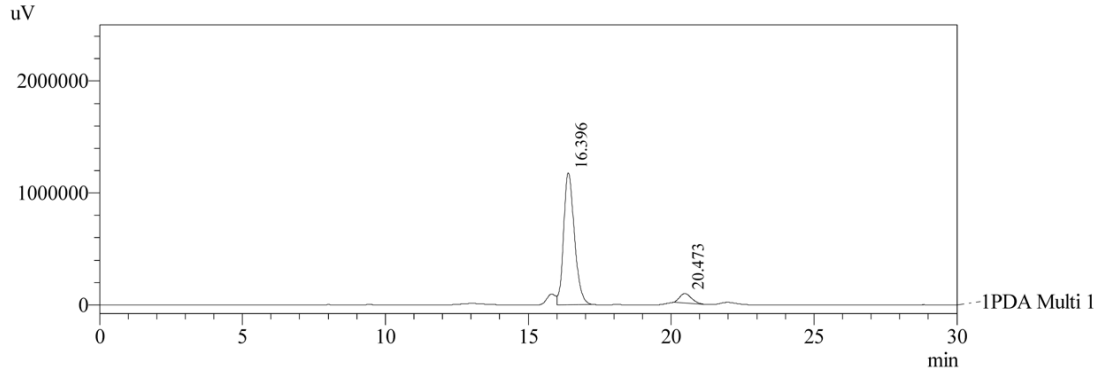


1 PDA M

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.006	298058	13475	2.304	2.955
2	16.589	6222718	246649	48.111	54.088
3	20.710	6118978	187621	47.309	41.144
4	22.282	294387	8268	2.276	1.813
Total		12934141	456013	100.000	100.000



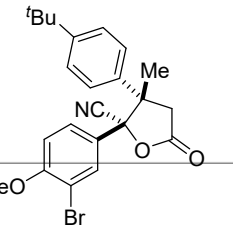
1 PDA Multi 1 / 254nm 4nm

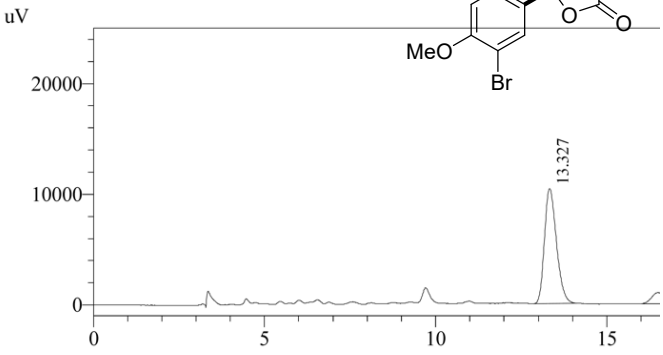
PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.396	31097151	1180117	92.663	93.286
2	20.473	2462075	84938	7.337	6.714
Total		33559226	1265055	100.000	100.000

(2S,3S)-2-(3-bromo-4-methoxyphenyl)-3-(4-(tert-butyl)phenyl)-3-methyl-5-oxotetrahydrofuran-2-carbonitrile (**3o**)



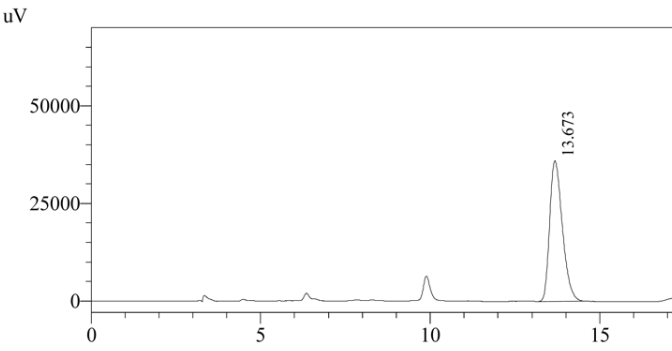


1 PDA Multi 1 / 254nm 4nm

PeakTa

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	A
1	13.327	254100	10410	
2	16.489	26728	1014	
3	17.330	252736	7622	
4	18.475	28169	905	
Total		561732	19952	100.000



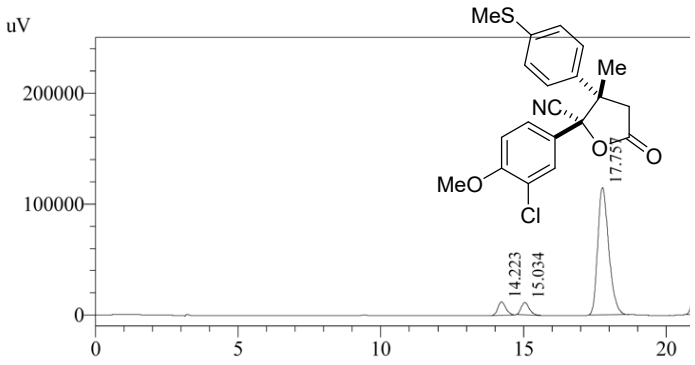
1 PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Are
1	13.673	939571	36056	
2	18.124	104369	3366	
Total		1043940	39422	

(2S,3S)-2-(3-chloro-4-methoxyphenyl)-3-methyl-3-(4-(methylthio)phenyl)-5-oxotetrahydrofuran-2-carbonitrile (**3p**)

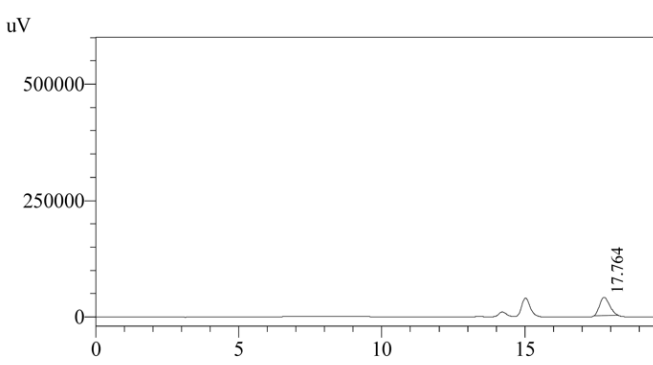


1 PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area
1	14.223	229825	12037	
2	15.034	217561	11125	
3	17.757	3095090	114822	
4	21.239	3107039	97650	
Total		6649515	235635	100.000



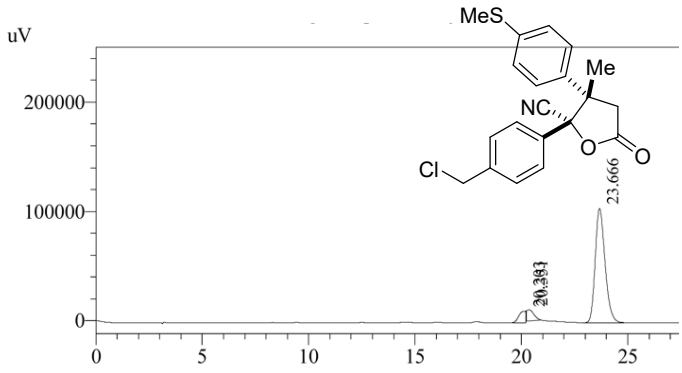
1 PDA Multi 1 / 254nm 4nm

PeakT

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	
1	17.764	964022	39557	
2	21.147	9171695	280830	
Total		10135717	320387	100.000

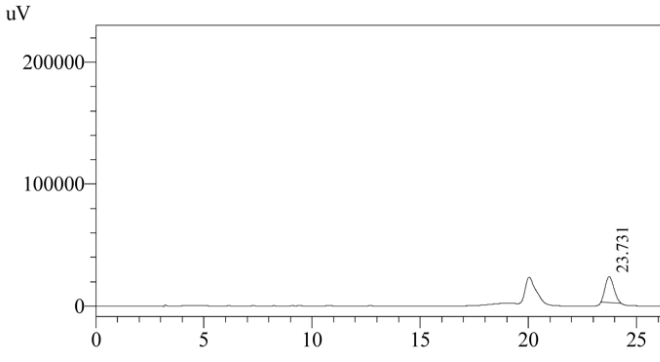
(2S,3S)-2-(4-(chloromethyl)phenyl)-3-methyl-3-(4-(methylthio)phenyl)-5-oxotetrahydrofuran-2-carbonitrile (**3q**)



1 PDA M PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area
1	20.203	235377	10706	
2	20.351	235867	10126	
3	23.666	3359657	104387	
4	37.695	3382110	64876	
Total		7213012	190095	

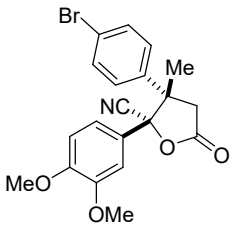


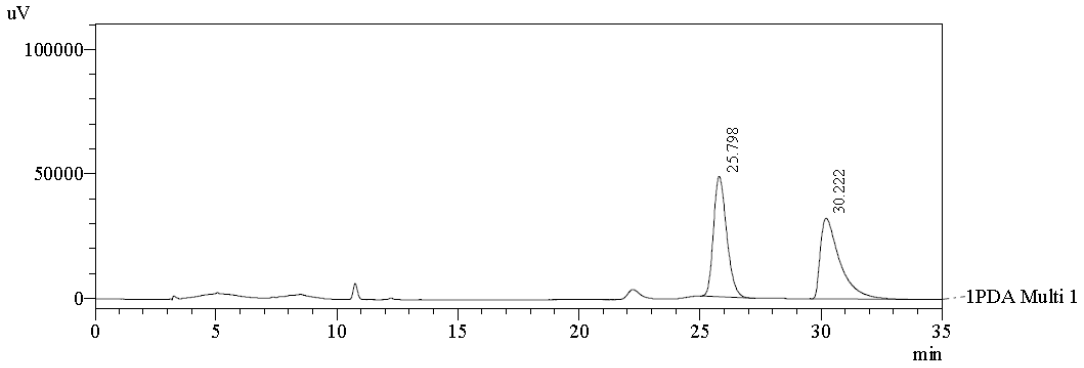
1 PDA Multi 1 / 254nm 4nm PeakT

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	
1	23.731	590582	21223	
2	37.669	5340896	101448	
Total		5931478	122670	

(2S,3S)-3-(4-bromophenyl)-2-(3,4-dimethoxyphenyl)-3-methyl-5-oxotetrahydrofuran-2-carbonitrile (**3r**)



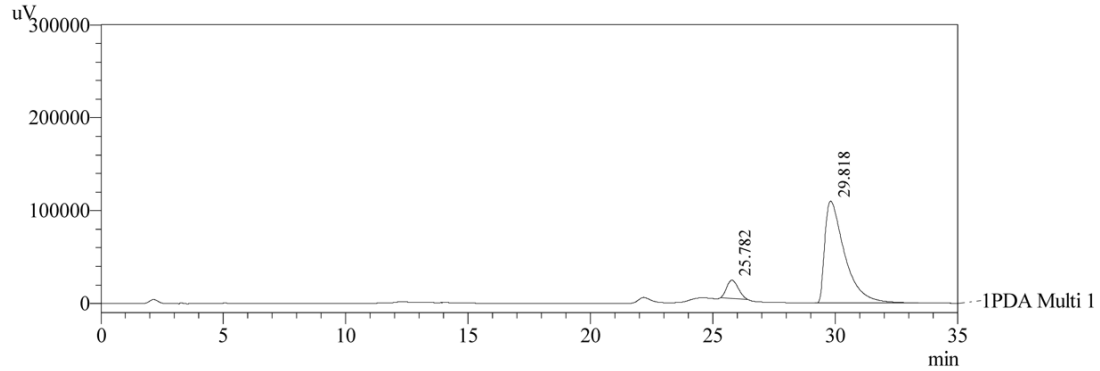


1 PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	25.798	1817718	48241	50.017	59.866
2	30.222	1816478	32340	49.983	40.134
Total		3634196	80581	100.000	100.000



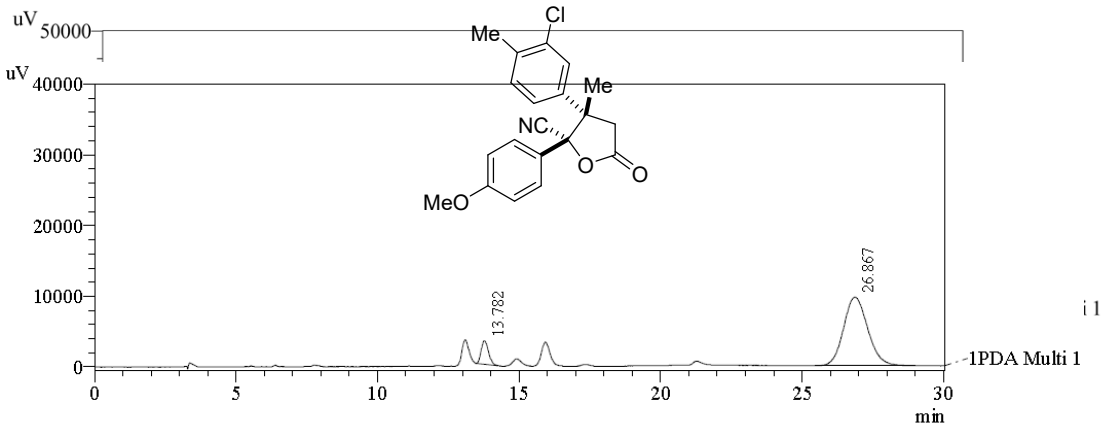
1 PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	25.782	637564	19542	9.334	15.129
2	29.818	6193131	109631	90.666	84.871
Total		6830695	129173	100.000	100.000

(2S,3S)-3-(3-chloro-4-methylphenyl)-2-(4-methoxyphenyl)-3-methyl-5-oxotetrahydrofuran-2-carbonitrile (**3s**)



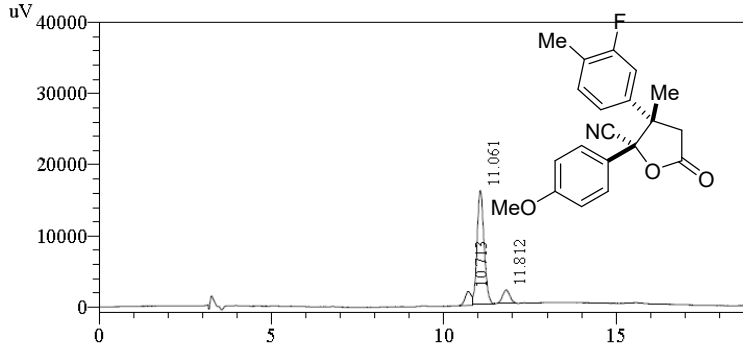
1 PDA Multi 1 / 254nm 4nm

PeakTable

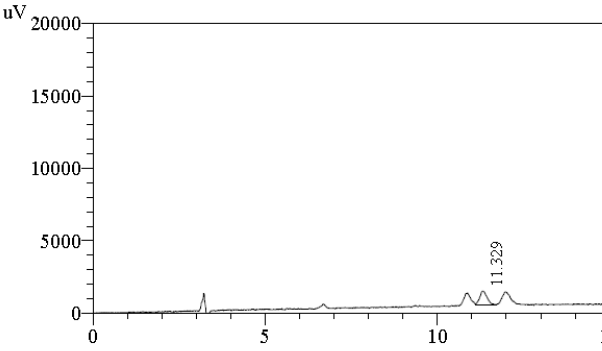
PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.782	59871	3354	9.339	25.603
2	26.867	581229	9745	90.661	74.397
Total		641099	13099	100.000	100.000

(2S,3S)-3-(3-fluoro-4-methylphenyl)-2-(4-methoxyphenyl)-3-methyl-5-oxotetrahydrofuran-2-carbonitrile （**3t**）



1 PDA Multi 1 / 254nm 4nm



1 PDA Multi 1 / 254nm 4nm

PeakTable

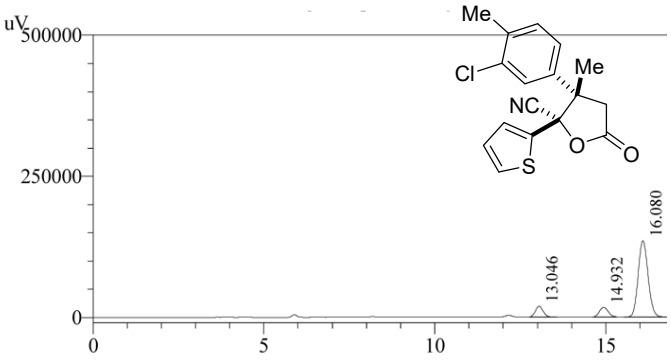
PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %
1	10.713	24524	1983	4.87
2	11.061	225836	16006	44.86
3	11.812	25755	1840	5.11
4	19.434	227289	7907	45.15
Total		503404	27736	100.000

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height
1	11.329	14971	969
2	19.971	188993	6418
Total		203964	7387

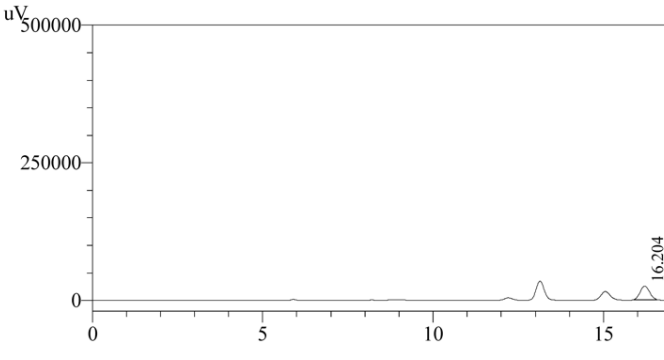
(2S,3S)-3-(3-chloro-4-methylphenyl)-3-methyl-5-oxo-2-(thiophen-2-yl)tetrahydrofuran-2-carbonitrile (**3u**)



1 PDA M PeakTab

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Ar
1	13.046	305451	19242	
2	14.932	306784	17287	
3	16.080	2732496	135900	
4	18.684	2848765	126343	
Total		6193496	298772	

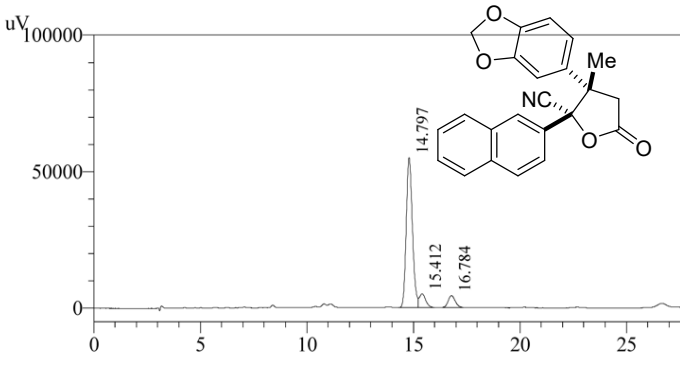


1 PDA Multi 1 / 254nm 4nm PeakTab

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Ar
1	16.204	464749	24587	
2	18.814	4466340	188353	
Total		4931089	212940	

(2S,3S)-3-(benzo[d][1,3]dioxol-5-yl)-3-methyl-2-(naphthalen-2-yl)-5-oxotetrahydrofuran-2-carbonitrile (**3v**)

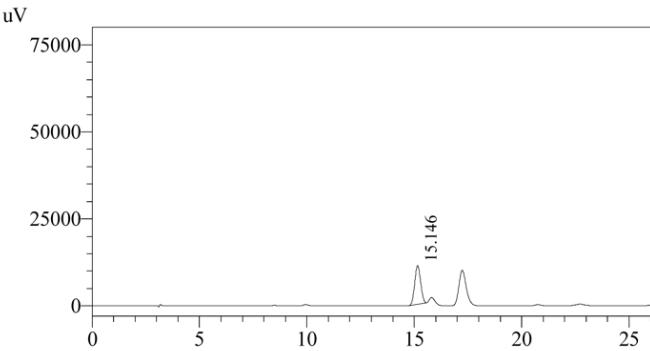


1 PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Are	
1	14.797	1113448	54997		
2	15.412	106374	5008		
3	16.784	97296	4288		
4	35.821	1099223	21827		
Total		2416341	86120	100.000	100.000



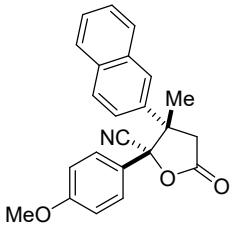
1 PDA M

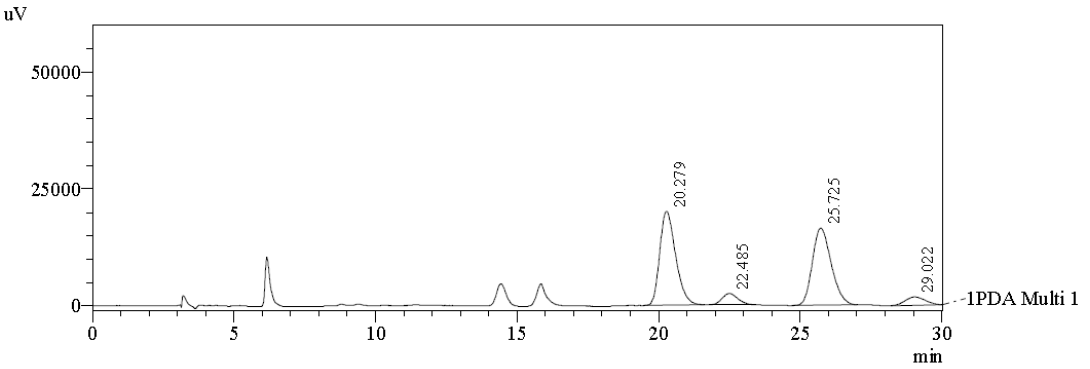
PeakT

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	
1	15.146	211731	11095	
2	37.044	2094657	39249	
Total		2306388	50344	

(2S,3S)-2-(4-methoxyphenyl)-3-methyl-3-(naphthalen-2-yl)-5-oxotetrahydrofuran-2-carbonitrile (**3w**)



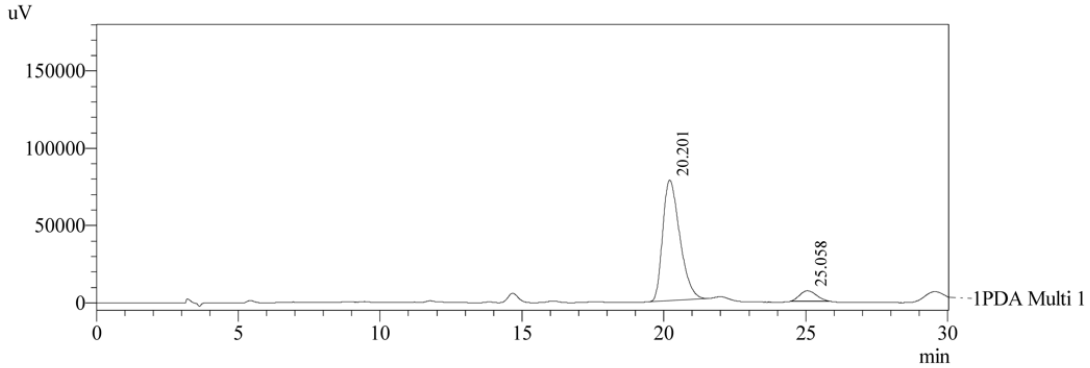


1 PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	20.279	785618	20092	45.386	49.271
2	22.485	93617	2415	5.408	5.923
3	25.725	763834	16494	44.128	40.448
4	29.022	87900	1777	5.078	4.358
Total		1730968	40779	100.000	100.000



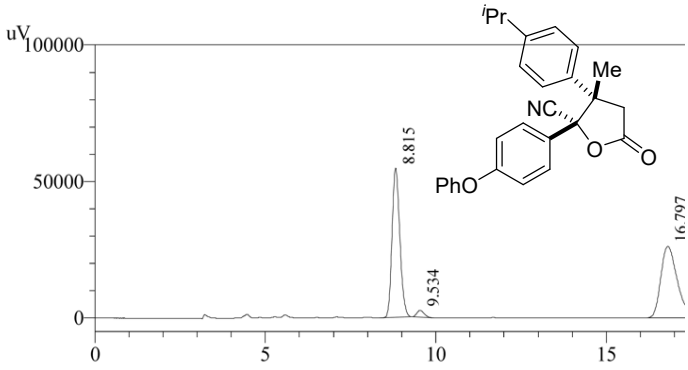
1 PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	20.201	3276494	78005	92.086	91.933
2	25.058	281579	6845	7.914	8.067
Total		3558073	84850	100.000	100.000

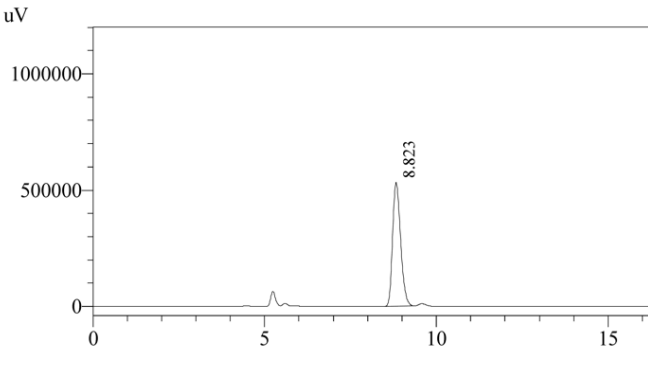
(2S,3S)-3-(4-isopropylphenyl)-3-methyl-5-oxo-2-(4-phenoxyphenyl)tetrahydrofuran-2-carbonitrile (**3x**)



1 PDA M PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area
1	8.815	867645	54837	
2	9.534	38060	2533	
3	16.797	873587	26285	
4	17.472	41220	2824	
Total		1820511	86479	1

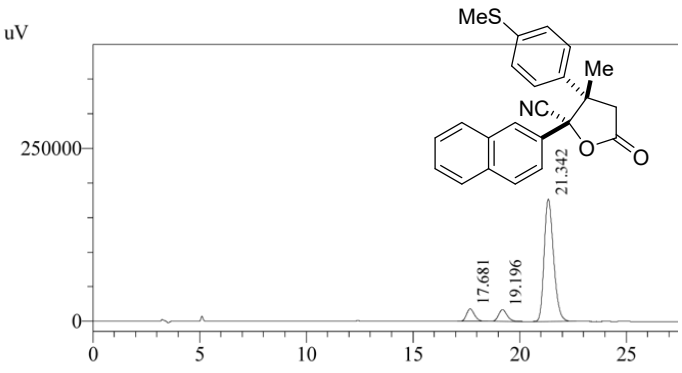


1 PDA Multi 1 / 254nm 4nm PeakT

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height
1	8.823	8640767	532609
2	16.896	678910	23177
Total		9319676	555786

(2S,3S)-3-methyl-3-(4-(methylthio)phenyl)-2-(naphthalen-2-yl)-5-oxotetrahydrofuran-2-carbonitrile (**3y**)

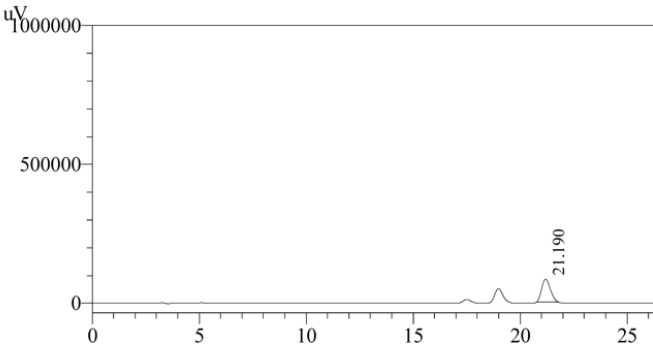


1 PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area
1	17.681	476542	18259	
2	19.196	479007	17116	
3	21.342	5444585	177041	
4	33.626	5451314	114943	
Total		11851447	327358	100.000



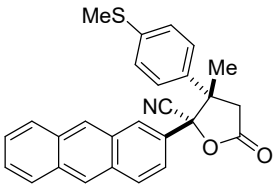
1 PDA Multi 1 / 254nm 4nm

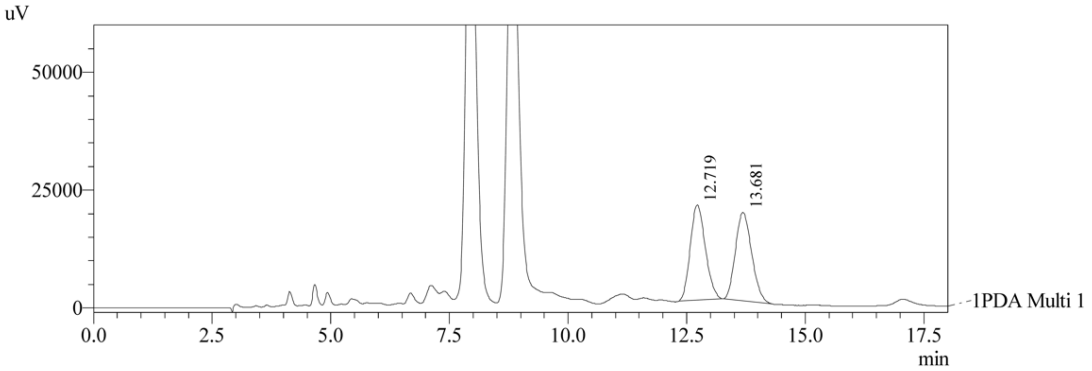
PeakTa

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	
1	21.190	2329330	82337	
2	33.118	21187295	434419	
Total		23516625	516756	

(2S,3S)-2-(anthracen-2-yl)-3-methyl-3-(4-(methylthio)phenyl)-5-oxotetrahydrofuran-2-carbonitrile (**3z**)



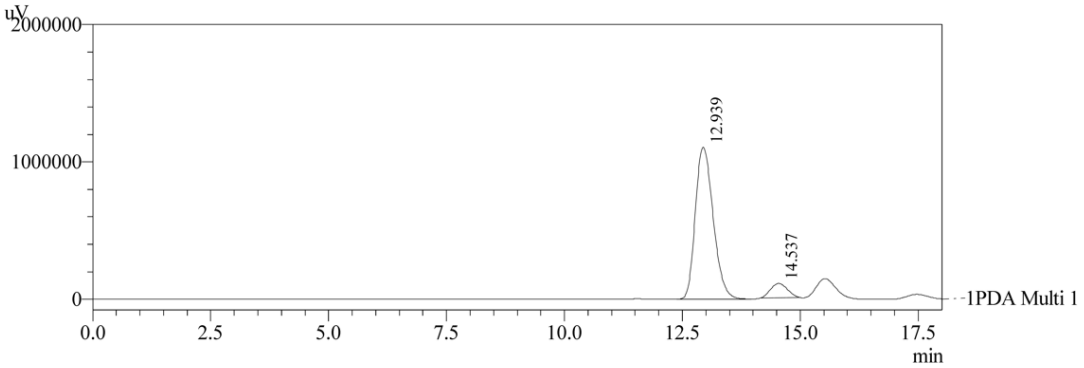


1 PDA M

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.719	448081	20200	49.981	51.843
2	13.681	448416	18763	50.019	48.157
Total		896498	38963	100.000	100.000



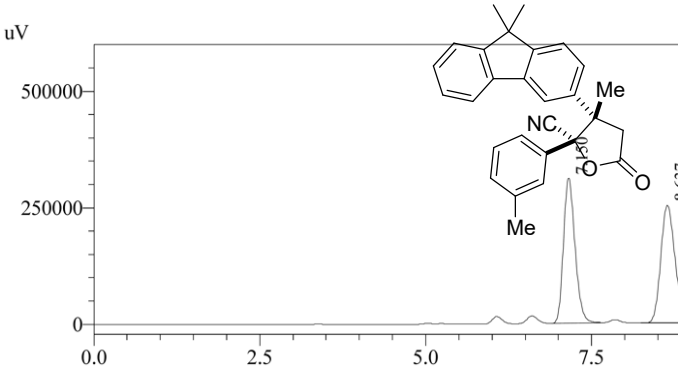
1 PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.939	29188691	1106475	91.825	91.384
2	14.537	2598553	104325	8.175	8.616
Total		31787244	1210800	100.000	100.000

(2S,3S)-3-(9,9-dimethyl-9H-fluoren-3-yl)-3-methyl-5-oxo-2-(m-tolyl)tetrahydrofuran-2-carbonitrile (**3aa**)

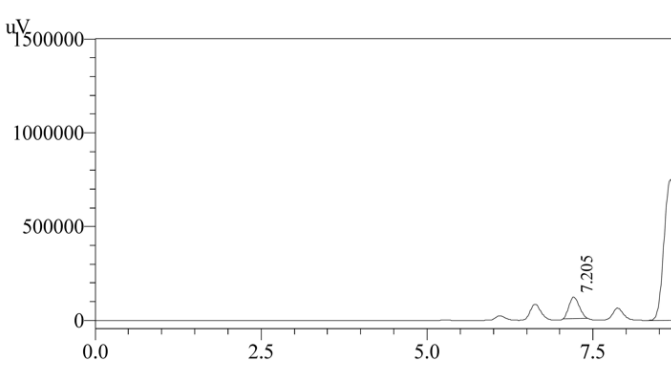


1 PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Are
1	7.150	3783340	311793	
2	8.637	3820688	252328	
Total		7604028	564121	



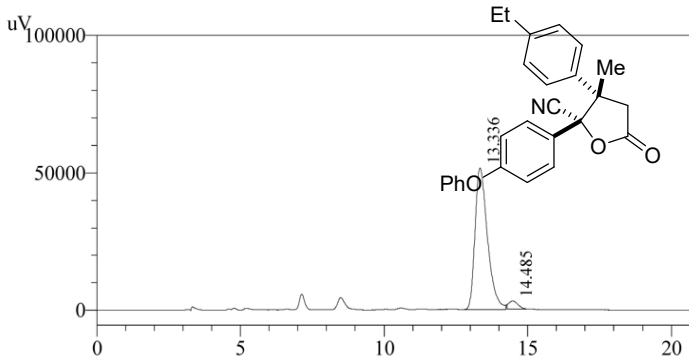
1 PDA M

PeakTab

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	A
1	7.205	1239588	114655	
2	8.662	11444083	749762	
Total		12683672	864417	

(2S,3S)-3-(4-ethylphenyl)-3-methyl-5-oxo-2-(4-phenoxyphenyl)tetrahydrofuran-2-carbonitrile (**3ab**)

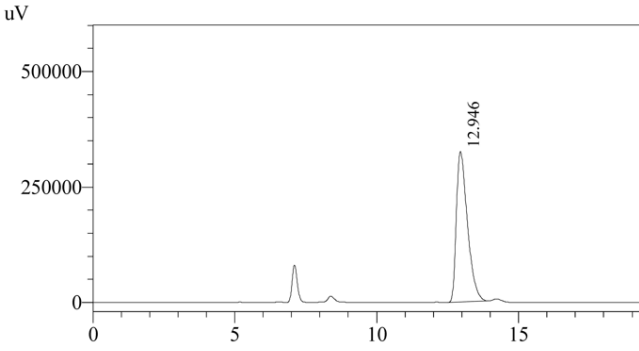


1 PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area
1	13.336	1559847	51623	
2	14.485	70285	3001	
3	24.739	1567179	31901	
4	29.060	64857	1460	
Total		3262169	87986	100.000



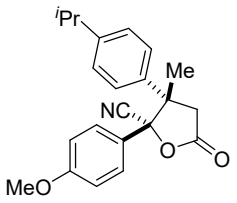
1 PDA Multi 1 / 254nm 4nm

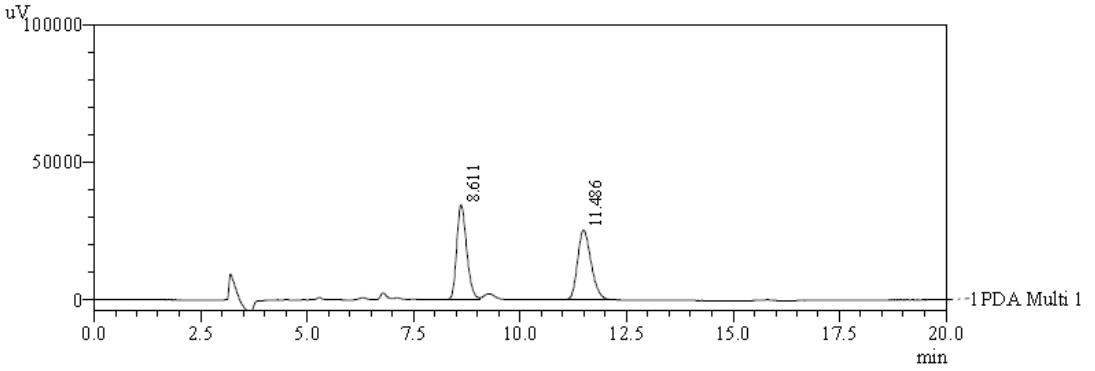
PeakT

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	
1	12.946	8863404	325443	
2	24.425	717852	17171	
Total		9581256	342614	

(2S,3S)-3-(4-isopropylphenyl)-2-(4-methoxyphenyl)-3-methyl-5-oxotetrahydrofuran-2-carbonitrile (**3ac**)



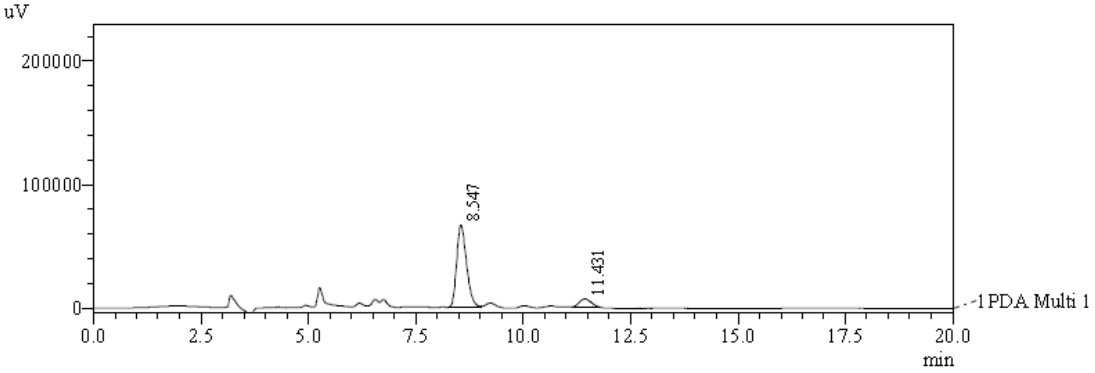


1 PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.611	566453	34554	50.435	57.792
2	11.486	556678	25237	49.565	42.208
Total		1123130	59791	100.000	100.000



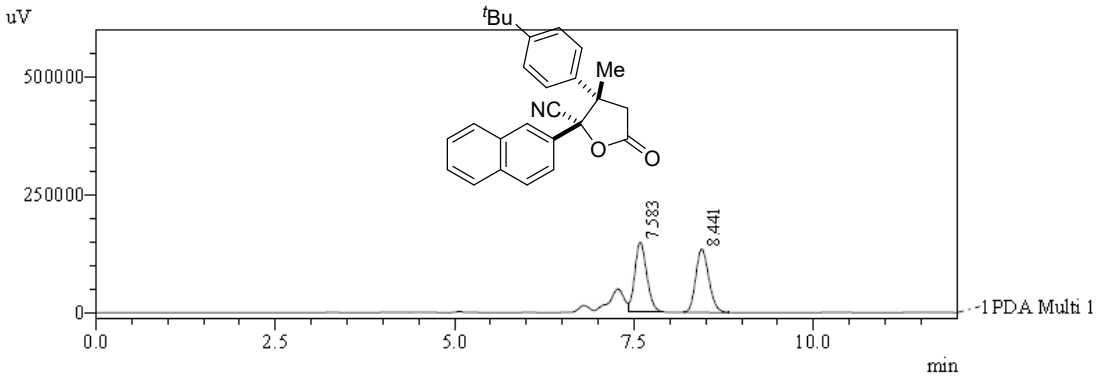
1 PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.547	1082066	66811	90.175	91.316
2	11.431	117899	6353	9.825	8.684
Total		1199965	73164	100.000	100.000

(2S,3S)-3-(4-(tert-butyl)phenyl)-3-methyl-2-(naphthalen-2-yl)-5-oxotetrahydrofuran-2-carbonitrile (**3ad**)

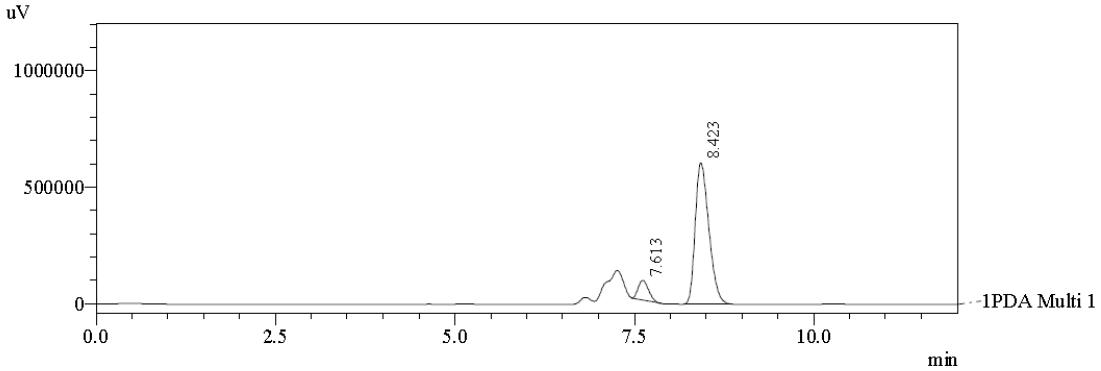


1 PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.583	1702544	147627	49.797	52.306
2	8.441	1716432	134608	50.203	47.694
Total		3418975	282235	100.000	100.000



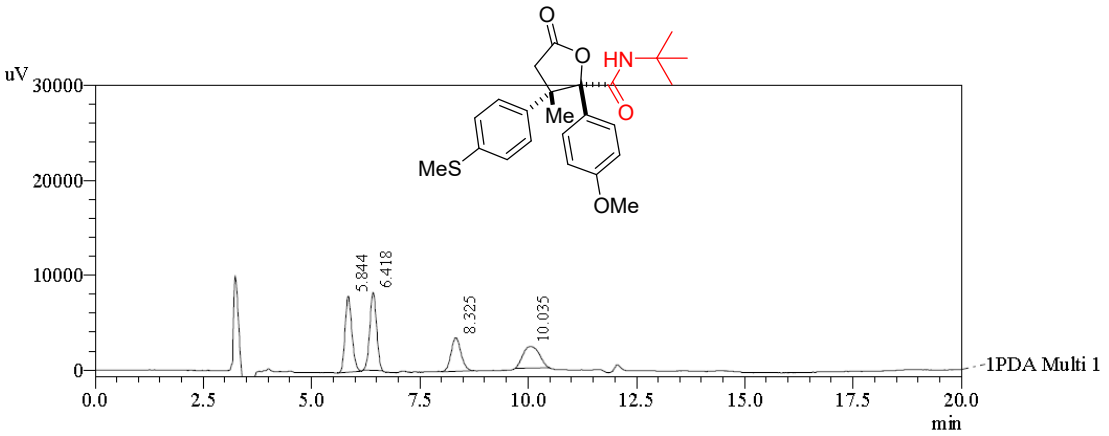
1 PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.613	842377	83456	9.518	12.115
2	8.423	8008083	605409	90.482	87.885
Total		8850460	688865	100.000	100.000

(*2S,3S)-N-(tert-butyl)-2-(4-methoxyphenyl)-3-methyl-3-(4-(methylthio)phenyl)-5-oxotetrahydrofuran-2-carboxamide* (**5**)

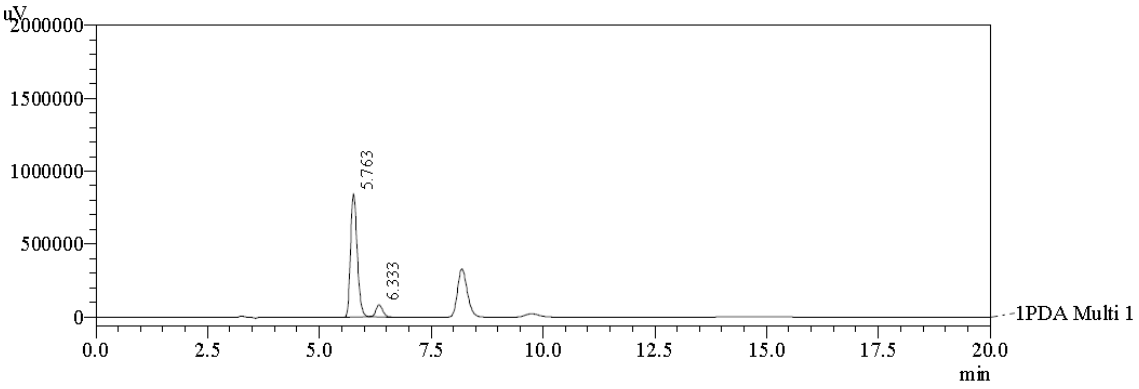


1 PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.844	88251	7998	29.897	36.229
2	6.418	90638	8259	30.705	37.409
3	8.325	56989	3548	19.306	16.070
4	10.035	59307	2272	20.092	10.291
Total		295186	22076	100.000	100.000



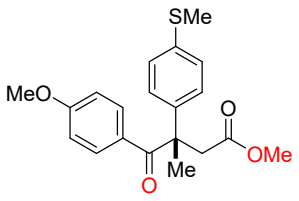
1 PDA Multi 1 / 254nm 4nm

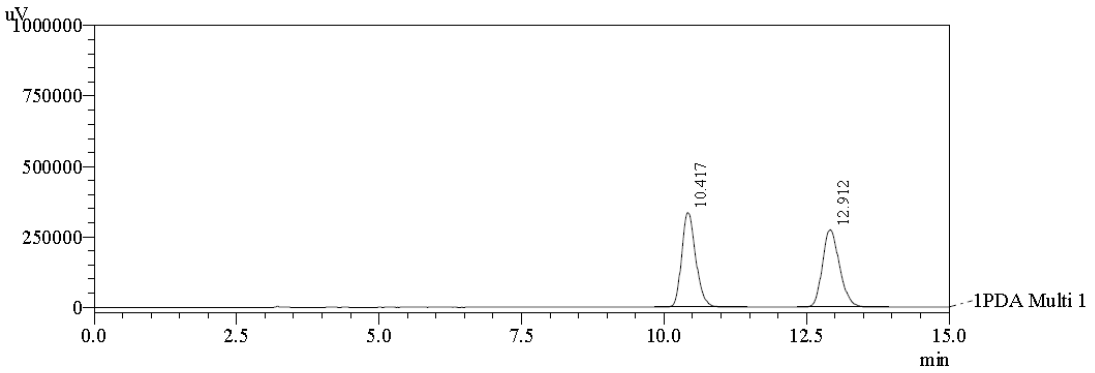
PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.763	8779226	847415	91.277	91.179
2	6.333	839042	81987	8.723	8.821
Total		9618268	929401	100.000	100.000

Methyl(S)-4-(4-methoxyphenyl)-3-methyl-3-(4-(methylthio)phenyl)-4-oxobutanoate (**6**)



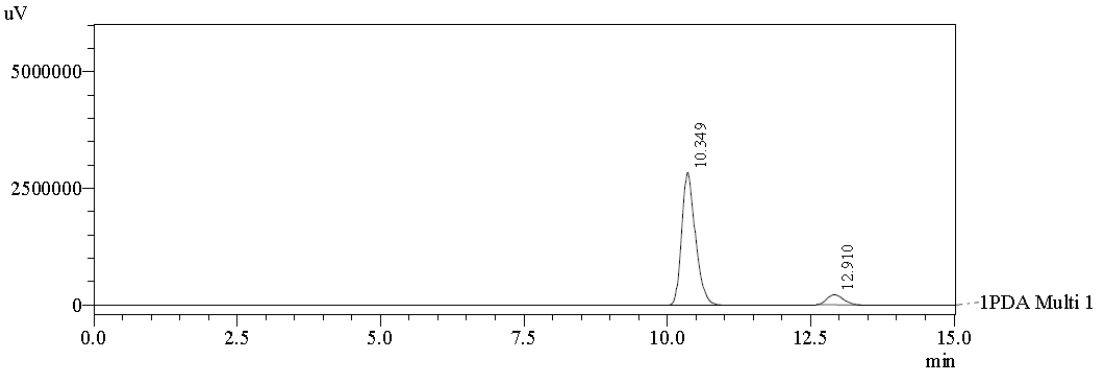


1 PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.417	5791150	336294	50.124	54.995
2	12.912	5762476	275208	49.876	45.005
Total		11553626	611502	100.000	100.000



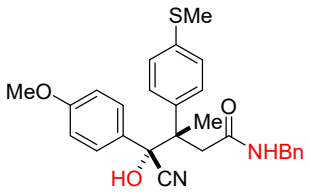
1 PDA Multi 1 / 254nm 4nm

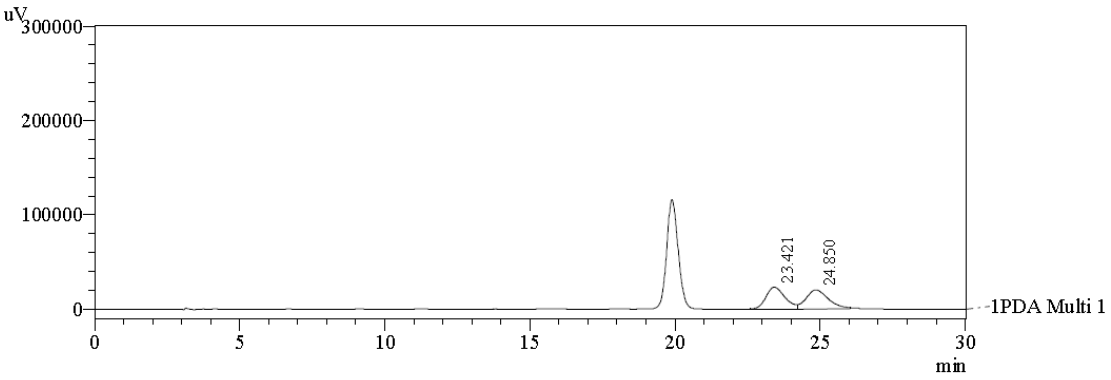
PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.349	47239143	2831609	91.642	92.902
2	12.910	4308609	216347	8.358	7.098
Total		51547753	3047955	100.000	100.000

(3S,4R)-N-benzyl-4-cyano-4-hydroxy-4-(4-methoxyphenyl)-3-methyl-3-(4-(methylthio)phenyl)butanamide (**7**)



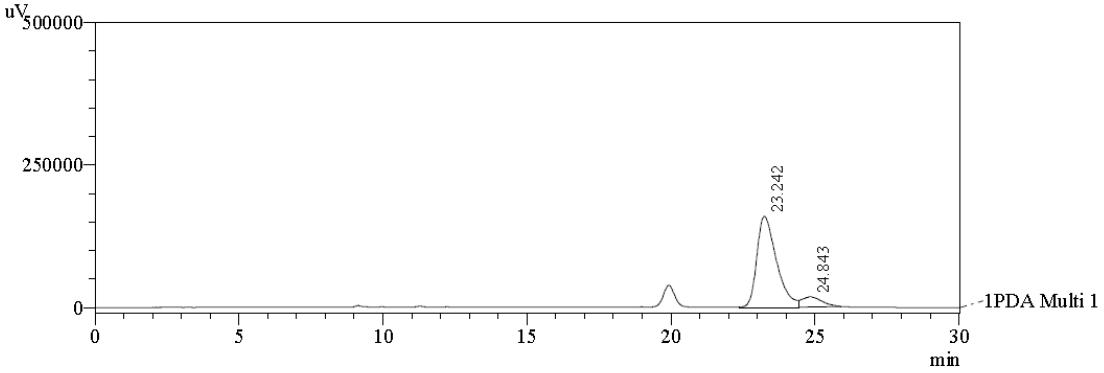


1 PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	23.421	1075315	23276	49.621	53.473
2	24.850	1091726	20252	50.379	46.527
Total		2167041	43528	100.000	100.000



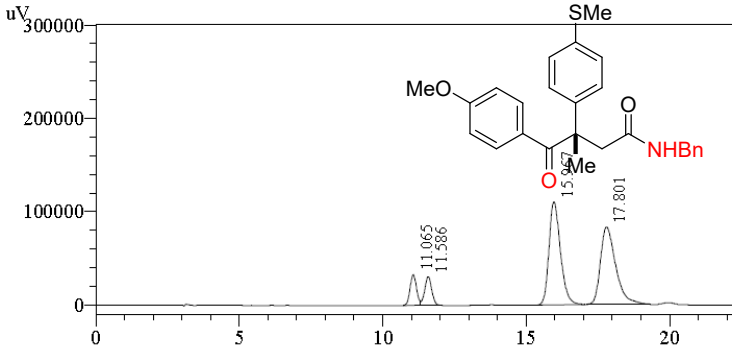
1 PDA

PeakTable

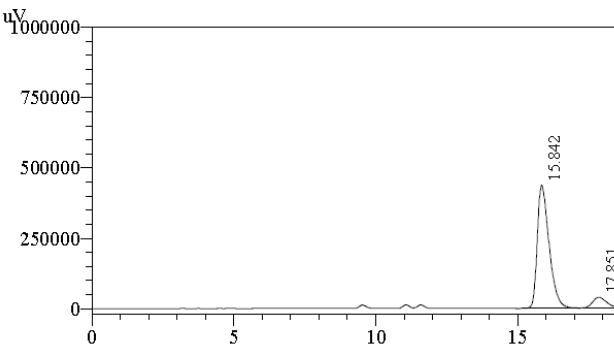
PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	23.242	7656186	160224	89.961	90.153
2	24.843	854401	17501	10.039	9.847
Total		8510587	177725	100.000	100.000

(S)-N-benzyl-4-(4-methoxyphenyl)-3-methyl-3-(4-(methylthio)phenyl)-4-oxobutanamide (**8**)



1 PDA Multi 1 / 254nm 4nm



1 PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %
1	11.065	515135	32758	7.21
2	11.586	515102	30352	7.21
3	15.967	3053579	109934	42.7
4	17.801	3060479	82799	42.8
Total		7144295	255843	100.000

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height
1	15.842	12635676	438089
2	17.851	1258625	37424
Total		13894301	475513