An Access to Highly Enantioselective and Diastereoselective Spirooxindole Dihydrofuran Fused Pyrazolones

Prakash K. Warghude, Abhijeet S. Sabale and Ramakrishna G. Bhat*

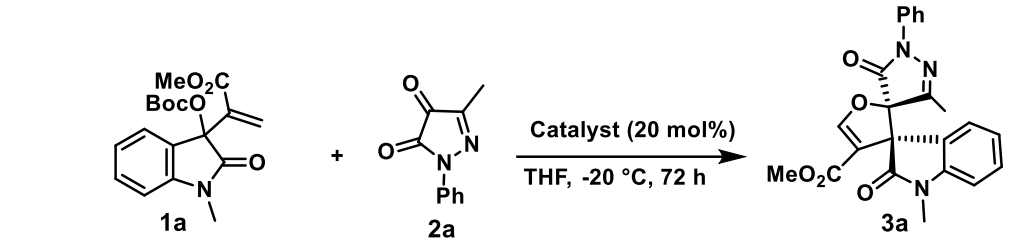
Department of Chemistry, Main Building, Indian Institute of Science Education and Research (IISER)-Pune, Dr. Homi Bhabha Road, Pashan, Pune, 411008, Maharashtra, India,

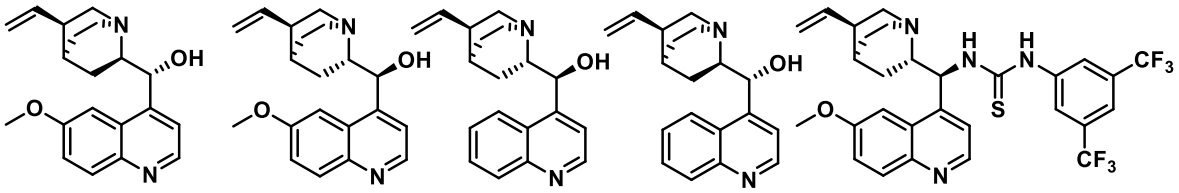
rgb@iiserpune.ac.in

General Experimental Method

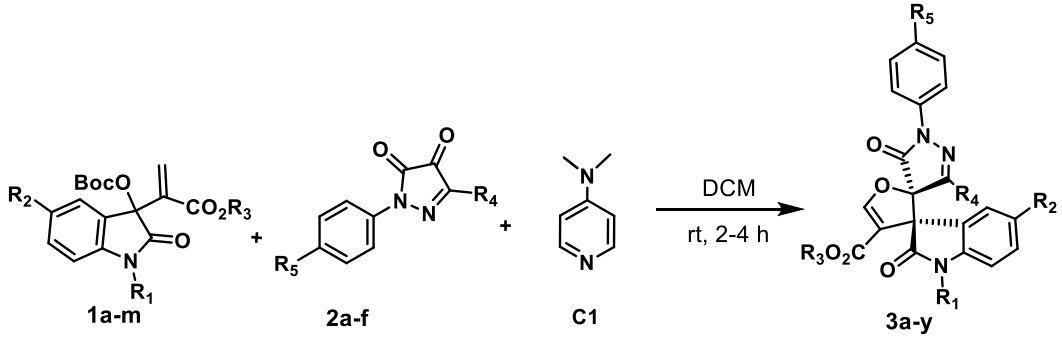
Unless otherwise stated, all the reagents were purchased from commercial suppliers and used without purification. Isatins and pyrazolones were purchased from Aldrich, TCI chemicals and Alfa-aeser. HPLC grade solvents were purchased from RANKEM. All the reactions were carried out in oven dried glassware. Thin-layer chromatography (TLC) was performed using silica gel 60 GF_{254} pre-coated aluminum backed plates (2.5 mm). Visualization was accomplished by irradiation with UV light at 254 nm and the solution of Phosphomolybdic Acid (PMA) was used to stain products. The column chromatography was performed using silica gel (200-300 mesh) eluting with petroleum ether and ethyl acetate. The NMR spectra were recorded using tetramethylsilane as the internal standard. ^{1}H NMR spectra were recorded at 400 MHz, and ^{13}C NMR spectra were recorded at 100 MHz (Bruker and Jeol). Chemical shifts (δ) are reported in ppm downfield from $CDCl_3$ (δ = 7.26 ppm) for ^{1}H NMR and relative to the central $CDCl_3$ resonance (δ = 77.16 ppm) for ^{13}C NMR spectroscopy. For ^{1}H NMR, data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, dd = double doublet, t = triplet, q = quartet, br = broad, m = multiplet), coupling constants (*J*) are given in Hz and integration. IR spectra were obtained using FT-IR spectrophotometer as neat and are reported in cm^{-1}. All the samples were analyzed by High-resolution mass spectrometer (HRMS) using ESI TOF. Optical rotations were measured at 589 nm at 25 °C. Optical rotation was measured in $CHCl_3$ solution. HPLC analysis was performed using an Agilent 1200 infinity series HPLC System with a diode array detector. Enantiomeric excess was determined by HPLC analysis on Chiralpak IC (4.6 mm × 250 mm) and Chiralpak IA (4.6 mm × 250 mm) columns in comparison with authentic racemic materials using *n*-hexane and isopropanol as eluents. Data were analyzed by using Agilent EZChrom Elite and Agilent OpenLAB software. Melting points were measured using BUCHI M-560 melting point instrument. All melting points were measured in open glass capillary and values are uncorrected. Catalysts **C2, C3, C4, C6, C7, C8** were synthesized according to the literature procedures.[1] Morita-Baylis-Hillman carbonates **1a-1m** were prepared according to the literature procedure.[3] Substituted pyrazonlone 4, 5-diones were synthesized according to the literature procedure.[4]

Appendix-I: Screening of catalysts with free hydroxyl group



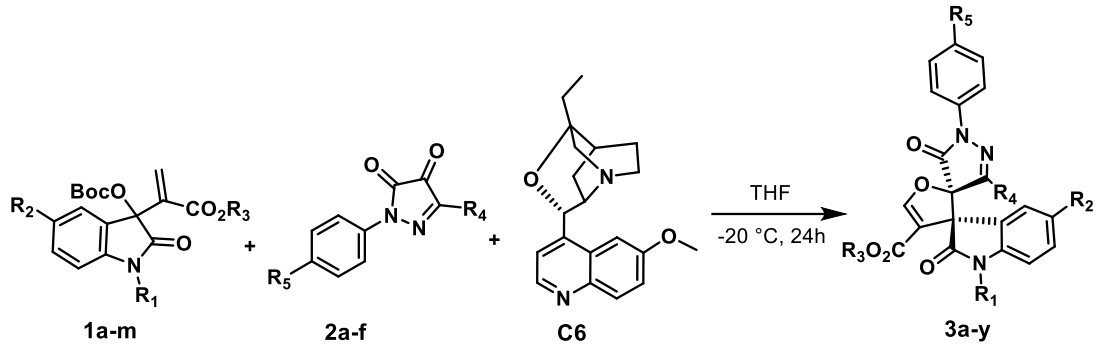


General procedure A for the racemic synthesis of spiro-oxindole-pyrazolone dihydrofuran



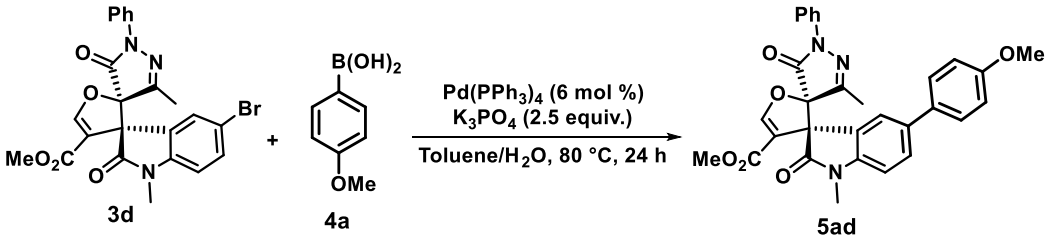
To a solution of Morita-Baylis-Hillman carbonate **1a** (50 mg, 1.0 equiv.) in 1 mL of DCM, pyrazole-4, 5-dione **2a** (27 mg, 1.0 equiv.) and DMAP **C1** (4.0 mg, 0.2 equiv.) were added at room temperature. The resulting mixture was stirred for 2 h. After completion of the reaction (monitored by TLC), solvent was evaporated under reduced pressure and the residue was purified by silica gel (100-200 mesh) using column chromatography (petroleum ether/ethyl acetate 70:30) to obtain the desired product **3a** as white solid in 98% yield (59 mg).

General procedure B for the asymmetric synthesis of spiro-oxindole-pyrazolone dihydrofuran



To a solution of Morita-Baylis-Hillman carbonate **1a** (50 mg, 1.0 equiv.) in 1 mL of THF, pyrazole-4, 5-dione **2a** (27 mg, 1.0 equiv.) and catalyst **C6,** (9.3 mg, 0.2 equiv.) were added at -20 °C. The resulting mixture was stirred for 24 h. After completion of the reaction (monitored by TLC) the solvent was evaporated under reduced pressure and the residue was purified by silica gel (100-200 mesh) using column chromatography (petroleum ether/ethyl acetate 70:30) to obtain desired product **3a** as white solid in 75% yield (45 mg).

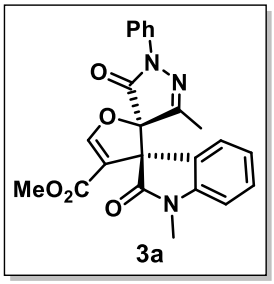
Procedure for the synthesis of 5ad (Suzuki coupling reaction)-Application of this protocol



To a solution of **3d** (38 mg, 1.0 equiv.) in toluene/H_2O (1 mL/0.3 mL) at RT was added 4-methoxy phenylboronic acid **4a** (18 mg, 1.5 equiv.), $Pd(PPh_3)_4$ (5.5 mg, 0.06 equiv.) and K_3PO_4 (41 mg, 2.5 equiv.) sequentially under argon atmosphere. The reaction mixture was heated to 80 °C and maintained at this temperature for stirring 24 h. After which, the reaction mixture was cooled to room temperature and filtered through celite bed and the solvent was evaporated under reduce pressure. The residue was purified by column chromatography (silica gel 100-200 mesh) to afford the desired compound **5ad** as white solid (28 mg, 60 % isolated yield).

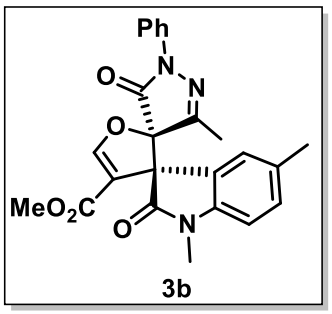
Characterization Data :

Methyl (2'*R*, 3*S*)-1, 3''-dimethyl-2, 5''-dioxo-1''-phenyl-1'', 5''-dihydrodispiro[indoline-3, 3'-furan-2', 4''-pyrazole]-4'-carboxylate (3a)



The compound **3a** was obtained following the general procedure B, starting from **1a**, **2a** and catalyst **C6**. **3a** was purified by column chromatography (Silica gel, petroleum ether/EtOAc 70:30) as white solid (45 mg, 75%, *d.r.* >20:1), R_f (petroleum ether/EtOAc 70:30) = 0.3, **MP**: 127-130 °C, **HPLC:** CHIRAPAK IC column, *n*-hexane/iso-propanol = 80/20, flow rate = 0.6 mL/min, λ = 254 nm, tR(major) = 24.68 min, tR(minor) = 33.08 min, 93% *ee*. $[\alpha]_D^{25}$= +374.2 (c 1.0, $CHCl_3$). **^{1}H NMR (400 MHz, $CDCl_3$):** δ (ppm) 7.83 (s, 1H), 7.50 (dd, *J* = 8.8, 1.0 Hz, 2H), 7.45 (d, *J* = 8.2 Hz, 1H), 7.33 – 7.26 (m, 3H), 7.16 – 7.10 (m, 1H), 7.04 (td, *J* = 7.7, 0.7 Hz, 1H), 6.78 (d, *J* = 7.8 Hz, 1H), 3.59 (s, 3H), 3.22 (s, 3H), 2.35 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ (ppm) 172.9, 167.1, 162.3, 159.3, 157.6, 143.9, 137.0, 130.3, 128.9, 127.0, 125.7, 123.3, 122.9, 119.1, 113.8, 108.5, 93.2, 63.2, 51.8, 27.1, 16.1. **FTIR (cm^{-1}):** 3099, 2950, 1713, 1615, 1490, 1350, 1277, 1196, 1120, 1040, 991, 922, 746, 689, 643, 605. **HRMS (**ESI TOF) *m/z* calcd. For $C_{23}H_{20}N_3O_5$ [M+H] 418.1403, found 418.1403

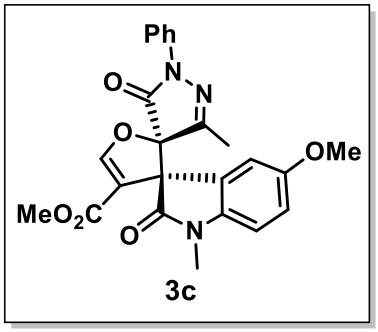
Methyl (2'*R*, 3*S*)-1,3'',4-trimethyl-2, 5''-dioxo-1''-phenyl-1'', 5''-dihydrodispiro[indoline-3, 3'-furan-2', 4''-pyrazole]-4'-carboxylate (3b)



The compound **3b** was obtained following the general procedure B, starting from **1b**, **2a** and catalyst **C6**. **3b** was purified by column chromatography (Silica gel, petroleum ether/EtOAc

70:30) as light brown solid (55 mg, 92%, *d.r*. >20:1), $\mathbf{R_f}$ (petroleum ether/EtOAc 70:30) = 0.35, **MP**: 189-191 °C, **HPLC:** CHIRAPAK IC column, n-hexane/iso-propanol = 80/20, flow rate = 0.6 mL/min, λ = 254 nm, tR(major) = 35.89 min, tR(minor) = 49.68 min, 90% *ee*. $[\boldsymbol{a}]_{\boldsymbol{D}}^{\mathbf{25}}$ = +308.04 (c 1.0, $CHCl_3$). **^{1}H NMR (400 MHz, $CDCl_3$):** δ (ppm) 7.83 (s, 1H), 7.50 (dt, *J* = 8.9, 1.7 Hz, 2H), 7.33 – 7.24 (m, 3H), 7.17 – 7.09 (m, 1H), 7.07 – 7.01 (m, 1H), 6.65 (d, *J* = 7.9 Hz, 1H), 3.59 (s, 3H), 3.18 (s, 3H), 2.32 (s, 3H), 2.26 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ (ppm) 172.8, 167.2, 162.3, 159.4, 157.3, 141.5, 136.9, 132.3, 130.5, 128.8, 127.5, 125.6, 123.0, 118.8, 113.7, 108.2, 93.2, 63.2, 51.7, 27.0, 21.2, 16.0. **FTIR (cm^{-1}):** 2924, 2858, 1713, 1620, 1496, 1440, 1350, 1279, 1189, 1042. 1114, 992, 925, 801, 741, 691, 639. **HRMS (**ESI TOF) *m/z* calcd. For $C_{24}H_{22}N_3O_5$ [M+H] 432.1559, found 432.1551.

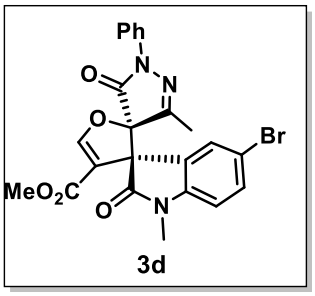
Methyl (2'*R*, 3*S*)-4-methoxy-1, 3''-dimethyl-2, 5''-dioxo-1''-phenyl-1'', 5''-dihydrodispiro [indoline-3, 3'-furan-2', 4''-pyrazole]-4'-carboxylate (3c)



3c

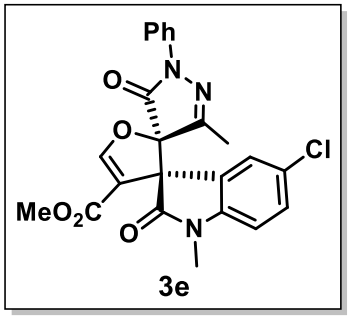
The compound **3c** was obtained following the general procedure B, starting from **1c**, **2a** and catalyst **C6**. **3c** was purified by column chromatography (Silica gel, petroleum ether/EtOAc 70:30) as light brown solid (52 mg, 88%, *d.r*. >20:1), $\boldsymbol{R_f}$ (petroleum ether/EtOAc 70:30) = 0.20, **MP**: 164-168 °C, **HPLC:** CHIRAPAK IC column, *n*-hexane/iso-propanol = 80/20, flow rate = 0.6 mL/min, λ = 254 nm, tR(major) = 61.75 min, tR(minor) = 68.16 min, 91% *ee*. $[\boldsymbol{a}]_{\boldsymbol{D}}^{\mathbf{25}}$ = +285.8 (c 1.0, $CHCl_3$). **^{1}H NMR (400 MHz, $CDCl_3$):** δ (ppm) 7.83 (s, 1H), 7.58 – 7.51 (m, 2H), 7.34 – 7.25 (m, 2H), 7.18 – 7.09 (m, 1H), 7.08 (d, *J* = 2.5 Hz, 1H), 6.79 (dd, *J* = 8.5, 2.6 Hz, 1H), 6.68 (d, *J* = 8.5 Hz, 1H), 3.72 (s, 3H), 3.60 (s, 3H), 3.18 (s, 3H), 2.33 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ (ppm) 172.6, 167.1, 162.3, 159.4, 157.3, 156.0, 137.4, 137.0, 128.9, 125.6, 124.3, 118.9, 115.4, 113.7, 108.9, 93.3, 63.4, 55.9, 51.8, 27.1, 16.0. **FTIR (cm^{-1}):** 3096, 2925, 2854, 1716, 1622, 1495, 1446, 1353, 1286, 1200, 1123, 1035, 923, 792, 746, 691, 638. **HRMS (**ESI-TOF) *m/z* calcd. For $C_{24}H_{22}N_3O_6$ [M+H] 448.1509, found 448.1506

Methyl (2'*R*, 3*R*)-4-bromo-1,3''-dimethyl-2, 5''-dioxo-1''-phenyl-1'', 5''-dihydrodispiro[indoline-3, 3'-furan-2', 4''-pyrazole]-4'-carboxylate (3d)



The compound **3d** was obtained following the general procedure B, starting from **1d**, **2a** and catalyst **C6**. **3c** was purified by column chromatography (Silica gel, petroleum ether/EtOAc 70:30) as light yellow solid (53 mg, 91%, *d.r*. 90:10), R_f (petroleum ether/EtOAc 70:30) = 0.32, **MP**: 185-188 °C, **HPLC:** CHIRAPAK IC column, *n*-hexane/iso-propanol = 80/20, flow rate = 0.6 mL/min, λ = 254 nm, tR(major) = 24.37 min, tR(minor) = 29.65 min, 88% *ee*. $[\alpha]_D^{25}$ = +171.0 (c 1.0, $CHCl_3$) **^{1}H NMR (400 MHz, $CDCl_3$):** δ (ppm) 7.83 (s, 1H), 7.60 (d, *J* = 1.9 Hz, 1H), 7.56 – 7.52 (m, 2H), 7.40 (dd, *J* = 8.3, 2.1 Hz, 1H), 7.36 – 7.30 (m, 2H), 7.20 – 7.12 (m, 1H), 6.66 (d, *J* = 8.3 Hz, 1H), 3.63 (s, 3H), 3.19 (s, 3H), 2.33 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ (ppm) 172.4, 166.8, 162.2, 159.5, 159.5, 157.2, 142.9, 136.8, 133.2, 130.1, 129.0, 125.9, 125.2, 119.0, 115.7, 113.5, 109.9, 92.9, 63.0, 52.0, 51.9, 27.1, 16.1. **FTIR (cm^{-1}):** 3099, 2926, 1719, 1618, 1488, 1347, 1277, 1203, 1119, 990, 915, 813, 743, 689, 642. **HRMS** (ESI TOF) *m/z* calcd. For $C_{23}H_{19}BrN_3O_5$ [M+H] 496.0508, 498.0488 found 496.0517, 498.0493

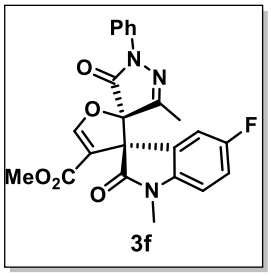
Methyl (2'R, 3R)-4-chloro-1, 3''-dimethyl-2, 5''-dioxo-1''-phenyl-1'', 5'' dihydrodispiro[indoline-3, 3'-furan-2', 4''-pyrazole]-4'-carboxylate (3e)



The compound **3e** was obtained following the general procedure B, starting from **1e**, **2a** and catalyst **C6**. **3e** was purified by column chromatography (Silica gel, petroleum ether/EtOAc 75:25) as light brown solid (54 mg, 91%, *d.r*. >20:1), R_f (petroleum ether/EtOAc 70:30) =

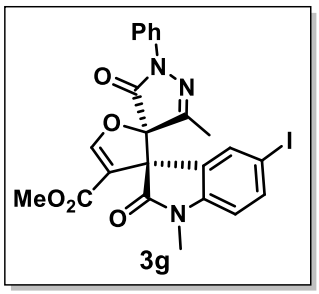
0.35, **MP**: 195-197 °C, **HPLC:** CHIRAPAK IC column, *n*-hexane/iso-propanol = 80/20, flow rate = 0.6 mL/min, λ = 254 nm, tR(major) = 22.80 min, tR(minor) = 29.33 min, 92% *ee*. $[\boldsymbol{a}]_{\boldsymbol{D}}^{\mathbf{25}}$ = +285.6 (c 1.0, $CHCl_3$)**; ^{1}H NMR (400 MHz, $CDCl_3$):** δ (ppm): 7.83 (s, 1H), 7.58 – 7.52 (m, 2H), 7.47 (d, *J* = 2.1 Hz, 1H), 7.32 (dd, *J* = 8.5, 7.6 Hz, 2H), 7.28 – 7.22 (m, 1H), 7.16 (d, *J* = 7.4 Hz, 1H), 6.71 (d, *J* = 8.3 Hz, 1H), 3.63 (s, 3H), 3.20 (s, 3H), 2.34 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ (ppm) 172.5, 166.7, 162.2, 159.4, 157.3, 142.4, 136.8, 130.3, 129.0, 128.4, 127.4, 125.9, 125.0, 119.0, 118.9, 118.9, 118.9, 113.6, 109.4, 92.9, 63.0, 52.0, 27.2, 16.1. **FTIR (cm^{-1}):** 3098, 2923, 1717, 1620, 1490, 1440, 1347, 1277, 1202, 1119, 992, 916, 815, 743, 689, 642. **HRMS** (ESI TOF) *m/z* calcd. For $C_{23}H_{19}ClN_3O_5$ [M+H] 452.1013 found 452.1011

Methyl (2'*R*, 3*R*)-4-fluoro-1, 3''-dimethyl-2, 5''-dioxo-1''-phenyl-1'', 5''-dihydrodispiro[indoline-3, 3'-furan-2', 4''-pyrazole]-4'-carboxylate (3f)



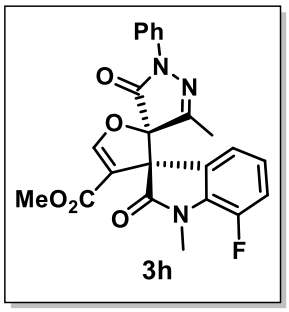
Following general procedure using 1**f**, **2a** and catalyst **C6, 3f** was obtained after column chromatography (silica gel, petroleum ether/EtOAc 75:25) as light brown solid (53 mg, 89%, *d.r*. >20:1), $\boldsymbol{R_f}$ (petroleum ether/EtOAc 70:30) = 0.25, **MP**: 176-178 °C, **HPLC:** CHIRAPAK IC column, *n*-hexane/iso-propanol = 80/20, flow rate = 0.6 mL/min, λ = 254 nm, tR(major) = 23.29 min, tR(minor) = 30.66 min, 92% *ee*. $[\boldsymbol{a}]_{\boldsymbol{D}}^{\mathbf{25}}$ = +388.9 (c 1.0, $CHCl_3$); **^{1}H NMR (400 MHz, $CDCl_3$):** δ (ppm) 7.83 (s, 1H), 7.58 – 7.51 (m, 2H), 7.35 – 7.28 (m, 2H), 7.26 – 7.22 (m, 1H), 7.18 – 7.11 (m, 1H), 6.99 (td, *J* = 8.7, 2.6 Hz, 1H), 6.71 (dd, *J* = 8.6, 4.1 Hz, 1H), 3.62 (s, 3H), 3.20 (s, 3H), 2.34 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ (ppm) 172.6, 166.7, 162.2, 159.4, 159.11 (d, $J_{C\text{-}F}$ = 240 Hz) , 157.4, 139.9, 136.9, 129.0, 125.01 (d, *J* = 8.6 Hz), 118.9, 116.76 (d, *J* = 23.6 Hz), 115.30 (d, *J* = 26.1 Hz), 113.7, 108.98 (d, *J* = 8.0 Hz), 93.0, 77.5, 77.2, 76.8, 63.3, 51.9, 27.2, 16.1. **^{19}F NMR (377 MHz, $CDCl_3$):** δ (ppm) -119.6. **FTIR (cm^{-1}):** 3093, 2928, 1720, 1625, 1494, 1450, 1351, 1276, 1123, 1041, 993, 919, 799, 747, 691, 640. **HRMS** (ESI TOF) *m/z* calcd. For $C_{23}H_{19}FN_3O_5$ [M+H] 436.1309 found 436.1310

Methyl (2'R, 3R)-4-iodo-1, 3''-dimethyl-2, 5''-dioxo-1''-phenyl-1'', 5''-dihydrodispiro[indoline-3, 3'-furan-2', 4''-pyrazole]-4'-carboxylate (3g)



The compound **3g** was obtained following the general procedure B, starting from **1g**, **2a** and catalyst **C6**. **3g** was purified by column chromatography (Silica gel, petroleum ether/EtOAc 75:25) as light brown solid (51 mg, 89%, *d.r.* >20:1), $\boldsymbol{R_f}$ (petroleum ether/EtOAc 70:30) = 0.34, **MP**: 166-170 °C, **HPLC:** CHIRAPAK IC column, *n*-hexane/iso-propanol = 80/20, flow rate = 0.6 mL/min, λ = 254 nm, tR(major) = 28.18 min, tR(minor) = 32.25 min, 91% *ee*. $[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{25}}$ = +130.6 (c 1.0, $CHCl_3$); **^{1}H NMR (400 MHz, $CDCl_3$):** δ (ppm) 7.83 (s, 1H), 7.75 (d, *J* = 1.7 Hz, 1H), 7.63 – 7.50 (m, 3H), 7.39 – 7.30 (m, 2H), 7.19 – 7.12 (m, 1H), 6.55 (dd, *J* = 8.2, 1.7 Hz, 1H), 3.63 (s, 3H), 3.18 (s, 3H), 2.32 (s, 3H**). ^{13}C NMR (100 MHz, $CDCl_3$):** δ (ppm) 172.2, 166.8, 162.2, 159.6, 157.1, 143.6, 139.1, 136.7, 135.4, 129.0, 125.9, 125.4, 119.0, 113.4, 110.5, 93.0, 85.5, 62.8, 51.9, 27.1, 16.0. **FTIR (cm^{-1}):** 3100, 2923, 2857, 1717, 1623, 1487, 1346, 1277, 1199, 1121, 1040, 990, 915, 811, 746, 689, 643, 605**. HRMS** (ESI TOF) *m/z* calcd. For $C_{23}H_{19}IN_3O_5$ [M+H] 544.0369 found 544.0369

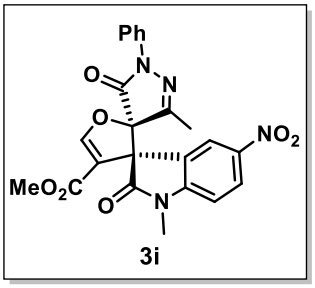
Methyl (2'*R*, 3*S*)-7-fluoro-1, 3''-dimethyl-2, 5''-dioxo-1''-phenyl-1'', 5''-dihydrodispiro[indoline-3, 3'-furan-2', 4''-pyrazole]-4'-carboxylate (3h)



The compound **3h** was obtained following the general procedure B, starting from **1h**, **2a** and catalyst **C6**. **3h** was purified by column (Silica gel, petroleum ether/EtOAc 80:20) as light brown solid (54 mg, 90%, *d.r.* >20:1), $\boldsymbol{R_f}$ (petroleum ether/EtOAc 70:30) = 0.53, **MP**: 165-168 °C, **HPLC:** CHIRAPAK IC column, *n*-hexane/iso-propanol = 80/20, flow rate = 0.6

mL/min, λ = 254 nm, tR(major) = 19.88 min, tR(minor) = 30.43 min, 93% *ee*. $[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{25}}$ = +302.8 (c 1.0, $CHCl_3$); **^{1}H NMR (400 MHz, $CDCl_3$):** δ (ppm) 7.82 (s, 1H), 7.58 – 7.49 (m, 2H), 7.35 – 7.28 (m, 2H), 7.25 – 7.22 (m, 1H), 7.15 (tt, *J* = 7.0, 1.1 Hz, 1H), 7.05 – 6.93 (m, 2H), 3.62 (s, 3H), 3.42 (d, *J* = 2.8 Hz, 3H), 2.34 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ (ppm) 172.6, 166.8, 162.2, 159.3, 157.4, 147.60 (d, $J_{C\text{-}F}$ = 243.8 Hz), 136.9, 130.6 (d, $J_{C\text{-}F}$ = 9 Hz), 129.0, 126.1, 125.8, 123.25 (d, $J_{C\text{-}F}$ = 6.5 Hz), 122.94 (d, *J* = 3.3 Hz), 119.0, 118.4, 118.2, 113.9, 93.1, 63.3, 51.9, 29.63 (d, $J_{C\text{-}F}$ = 6.2 Hz), 16.1. **^{19}F NMR (377 MHz, $CDCl_3$):** δ (ppm) -136.1. **FTIR (cm^{-1}):** 2922, 2859, 1718, 1626, 1486, 1349, 1281, 1243, 1188, 1122, 990, 913, 850, 740, 691, 643. **HRMS**(ESI TOF) *m/z* calcd. For $C_{23}H_{19}FN_3O_5$ [M+H] 436.1309 found 436.1313

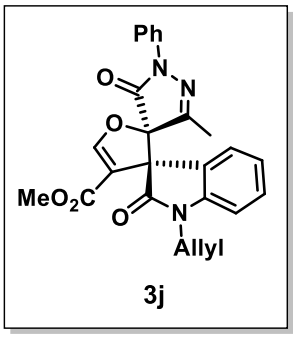
Methyl (2'*R*, 3*S*)-1, 3''-dimethyl-4-nitro-2, 5''-dioxo-1''-phenyl-1'', 5''-dihydrodispiro[indoline-3, 3'-furan-2',4''-pyrazole]-4'-carboxylate (3i)



3i

The compound **3i** was obtained following the general procedure B, starting from **1i**, **2a** and catalyst **C6**. **3e** was purified by column chromatography (Silica gel, petroleum ether/EtOAc 70:30) as light brown solid (54 mg, 92%, *d.r*. >20:1), $\boldsymbol{R_f}$ (petroleum ether/EtOAc 70:30) = 0.15, **MP**: 192-194 °C, **HPLC:** CHIRAPAK IC column, *n*-hexane/iso-propanol = 80/20, flow rate = 0.6 mL/min, λ = 254 nm, tR(major) = 36.25 min, tR(minor) = 46.02 min, 90% *ee*. $[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{25}}$ = +13.0 (c 1.03, $CHCl_3$); **^{1}H NMR (400 MHz, $CDCl_3$):** δ (ppm) 8.37 (d, *J* = 2.3 Hz, 1H), 8.27 (dd, *J* = 8.6, 2.1 Hz, 1H), 7.86 (s, 1H), 7.55 (dt, *J* = 8.9, 1.7 Hz, 2H), 7.30 (t, *J* = 7.9 Hz, 2H), 7.14 (t, *J* = 7.4 Hz, 1H), 6.88 (d, *J* = 8.6 Hz, 1H), 3.64 (s, 3H), 3.28 (s, 3H), 2.38 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ (ppm) 172.8, 165.9, 161.9, 159.2, 157.3, 148.8, 143.5, 136.7, 128.9, 127.1, 125.8, 124.4, 123.0, 118.5, 113.6, 108.1, 92.3, 62.7, 52.0, 27.4, 16.1. **FTIR (cm^{-1}):** 3100, 2926, 2856, 1723, 1613, 1496, 1444, 1337, 1292, 1199, 1124, 993, 923, 831, 743, 691, 643. **HRMS** (ESI TOF) *m/z* calcd. For $C_{23}H_{19}N_4O_7$ [M+H] 463.1254 found 463.1253

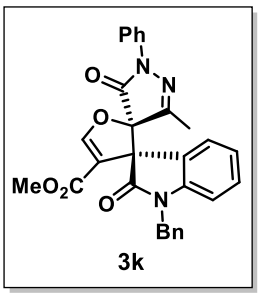
Methyl (2'*R*, 3*S*)-1-allyl-3''-methyl-2, 5''-dioxo-1''-phenyl-1'', 5''-dihydrodispiro[indoline-3, 3'-furan-2', 4''-pyrazole]-4'-carboxylate (3j)



3j

The compound **3j** was obtained following the general procedure B, starting from **1j**, **2a** and catalyst **C6**. **3j** was purified by column chromatography (Silica gel, petroleum ether/EtOAc 85:15) as light yellow solid (53 mg, 90%, *d.r.* >20:1), R_f (petroleum ether/EtOAc 70:30) = 0.44, **MP**: 148-151 °C, **HPLC:** CHIRAPAK IC column, *n*-hexane/iso-propanol = 80/20, flow rate = 0.6 mL/min, λ = 254 nm, tR(major) = 25.18 min, tR(minor) = 30.05 min, 91% *ee*. $[\alpha]_D^{25}$ = +349.4 (c 1.0, $CHCl_3$); **^{1}H NMR (400 MHz, $CDCl_3$):** δ(ppm) 7.85 (s, 1H), 7.52 – 7.42 (m, 3H), 7.32 – 7.26 (m, 2H), 7.23 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.17 – 7.10 (m, 1H), 7.03 (td, *J* = 7.6, 1.0 Hz, 1H), 6.75 (d, *J* = 7.8 Hz, 1H), 5.86 – 5.70 (m, 1H), 5.22 – 5.09 (m, 2H), 4.42 (ddt, *J* = 16.7, 5.0, 1.7 Hz, 1H), 4.24 (ddt, *J* = 16.7, 4.6, 1.8 Hz, 1H), 3.60 (s, 3H), 2.34 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ (ppm) 172.7, 167.1, 162.3, 159.4, 157.8, 143.0, 136.9, 130.6, 130.2, 128.9, 127.0, 125.7, 123.3, 122.8, 119.1, 117.5, 113.7, 109.4, 93.4, 63.4, 51.8, 42.8, 16.2. **FTIR (cm^{-1}):** 3094, 2923, 2857, 2314, 1719, 1618, 1490, 1356, 1285, 1237, 1187, 1124, 988, 923, 751, 687. **HRMS**(ESI TOF) *m/z* calcd. For $C_{25}H_{22}N_3O_5$ [M+H] 444.1559 found 444.1561

Methyl (2'*R*, 3*S*)-1-benzyl-3''-methyl-2, 5''-dioxo-1''-phenyl-1'', 5''-dihydrodispiro[indoline-3, 3'-furan-2', 4''-pyrazole]-4'-carboxylate (3k)

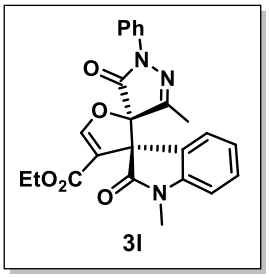


3k

The compound **3k** was obtained following the general procedure B, starting from **1k**, **2a** and catalyst **C6**. **3k** was purified by column chromatography (Silica gel, petroleum ether/EtOAc

85:15) as light brown solid (48 mg, 82%, *d.r*. >20:1), $\boldsymbol{R_f}$ (petroleum ether/EtOAc 70:30) = 0.47, **MP**: 139-141 °C, **HPLC:** CHIRAPAK IC column, *n*-hexane/iso-propanol = 80/20, flow rate = 0.9 mL/min, λ = 254 nm, tR(major) = 13.62 min, tR(minor) = 17.92 min, 93% *ee*. $[\boldsymbol{a}]_{\boldsymbol{D}}^{\boldsymbol{25}}$ = +59.2 (c 1.0, $CHCl_3$); **^{1}H NMR (400 MHz, $CDCl_3$):** δ (ppm) 7.86 (s, 1H), 7.51 – 7.45 (m, 2H), 7.43 (dd, *J* = 7.4, 0.9 Hz, 1H), 7.32 – 7.26 (m, 2H), 7.16 (ddt, *J* = 7.5, 4.3, 1.7 Hz, 5H), 7.13 – 7.06 (m, 2H), 7.03 (td, *J* = 7.6, 0.9 Hz, 1H), 6.61 (d, *J* = 7.8 Hz, 1H), 5.05 (d, *J* = 15.9 Hz, 1H), 4.78 (d, *J* = 16.0 Hz, 1H), 3.58 (s, 3H), 2.36 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ (ppm) 172.9, 166.9, 162.3, 159.2, 158.5, 142.5, 137.0, 135.0, 130.3, 128.9, 128.9, 127.7, 127.1, 126.8, 125.7, 123.6, 122.8, 119.0, 114.0, 109.5, 93.4, 63.8, 51.8, 44.3, 16.3. **FTIR (cm^{-1}):** 2923, 1718, 1607, 1492, 1357, 1281, 1234, 1178, 1126, 987, 917, 836, 743, 695, 643. **HRMS** (ESI TOF) *m/z* calcd. For $C_{29}H_{24}N_3O_5$ [M+H] 494.1716 found 494.1713

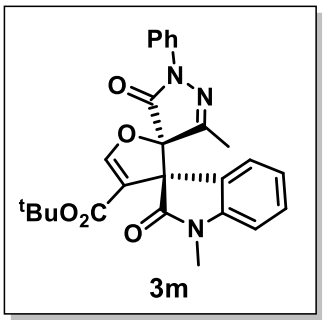
Ethyl (2'*R*, 3*S*)-1, 3''-dimethyl-2, 5''-dioxo-1''-phenyl-1'', 5''-dihydrodispiro[indoline-3, 3'-furan-2', 4''-pyrazole]-4'-carboxylate (3l)



3l

The compound **3l** was obtained following the general procedure B, starting from **1l**, **2a** and catalyst **C6**. **3l** was purified by column chromatography (Silica gel, petroleum ether/EtOAc 80:20) as light brown solid (55 mg, 92%, d.r. >20:1), $\boldsymbol{R_f}$ (petroleum ether/EtOAc 70:30) = 0.41, **MP**: 189-191 °C, **HPLC:** CHIRAPAK IC column, *n*-hexane/iso-propanol = 80/20, flow rate = 0.6 mL/min, λ = 254 nm, tR(minor) = 25.51 min, tR(major) = 30.98 min, 90% *ee*. $[\boldsymbol{a}]_{\boldsymbol{D}}^{\boldsymbol{25}}$ = +391 (c 1.0, $CHCl_3$); **^{1}H NMR (400 MHz, $CDCl_3$):** δ(ppm) 7.84 (s, 1H), 7.54 – 7.49 (m, 2H), 7.48 – 7.43 (m, 1H), 7.33 – 7.24 (m, 3H), 7.13 (t, *J* = 7.4 Hz, 1H), 7.04 (td, *J* = 7.6, 1.0 Hz, 1H), 6.77 (d, *J* = 7.8 Hz, 1H), 4.00 (qq, *J* = 7.4, 3.7 Hz, 2H), 3.20 (s, 3H), 2.35 (s, 3H), 1.06 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ (ppm) 173.0, 167.1, 161.8, 159.1, 157.7, 143.9, 137.0, 130.2, 128.9, 127.0, 125.7, 123.6, 122.8, 119.0, 114.3, 108.4, 93.2, 63.2, 60.6, 27.0, 16.2, 14.0. **FTIR (cm^{-1}):** 2924, 1722, 1622, 1492, 1368, 1290, 1125, 1030, 950, 820,754, 690, 599**. HRMS** (ESI TOF) *m/z* calcd. For $C_{24}H_{22}N_3O_5$ [M+H] 432.1559 found 432.1557

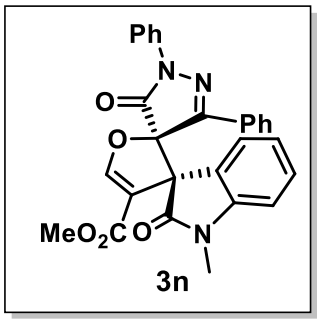
tert-butyl (2'*R*, 3*S*)-1, 3''-dimethyl-2,5''-dioxo-1''-phenyl-1'',5''-dihydrodispiro[indoline-3, 3'-furan-2', 4''-pyrazole]-4'-carboxylate (3m)



3m

The compound **3m** was obtained following the general procedure B, starting from **1m**, **2a** and catalyst **C6**. **3m** was purified by column chromatography (Silica gel, petroleum ether/EtOAc 85:15 as light brown solid (54 mg, 92%, *d.r.* >20:1), R_f (petroleum ether/EtOAc 70:30) = 0.5, **MP**: 65-68 °C, **HPLC:** CHIRAPAK IC column, *n*-hexane/iso-propanol = 80/20, flow rate = 0.6 mL/min, λ = 254 nm, tR(minor) = 15.32 min, tR(major) = 15.94 min, 88% *ee*. $[\alpha]_D^{25}$ = +345.6 (c 1.0, $CHCl_3$); **^{1}H NMR (400 MHz, $CDCl_3$):** δ(ppm) 7.79 (s, 1H), 7.54 – 7.43 (m, 3H), 7.33 – 7.23 (m, 3H), 7.17 – 7.09 (m, 1H), 7.04 (td, *J* = 7.6, 1.0 Hz, 1H), 6.74 (d, *J* = 7.8 Hz, 1H), 3.18 (s, 3H), 2.35 (s, 3H), 1.16 (s, 9H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ (ppm) 173.1, 167.2, 161.0, 159.0, 157.8, 143.8, 137.0, 130.0, 128.9, 127.0, 125.6, 124.1, 122.7, 119.0, 115.5, 108.2, 93.3, 81.3, 63.3, 27.9, 26.9, 16.1. **FTIR (cm^{-1}):** 3093, 2928, 1720, 1625, 1494, 1450, 1351, 1276, 1123, 1041, 993, 919, 799, 747, 691, 640. **HRMS** (ESI TOF) *m/z* calcd. For $C_{26}H_{26}N_3O_5$ [M+H] 460.1872 found 460.1871

Methyl (2'*R*, 3*S*)-1-methyl-2, 5''-dioxo-1'', 3''-diphenyl-1'', 5''-dihydrodispiro[indoline-3, 3'-furan-2', 4''-pyrazole]-4'-carboxylate (3n)

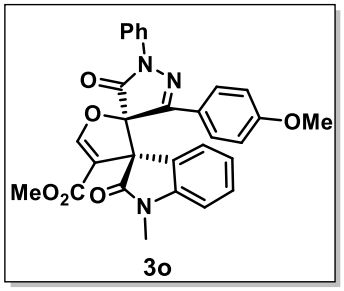


3n

The compound **3n** was obtained following the general procedure B, starting from **1a**, **2b** and catalyst **C6**. **3n** was purified by column chromatography (Silica gel, petroleum ether/EtOAc 70:30) as brown solid (62 mg, 90%, *d.r.* >20:1), R_f (petroleum ether/EtOAc 70:30) = 0.29,

MP: 183-186 °C, **HPLC:** CHIRAPAK IC column, *n*-hexane/iso-propanol = 80/20, flow rate = 0.6 mL/min, λ = 254 nm, tR(major) = 21.74 min, tR(minor) = 30.06 min, 96% *ee*. $[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{25}}$ = +310.6 (c 1.0, $CHCl_3$); **^{1}H NMR (400 MHz, $CDCl_3$):** δ (ppm) 7.93 (s, 1H), 7.77 – 7.64 (m, 2H), 7.45 – 7.31 (m, 6H), 7.28 – 7.21 (m, 2H), 7.19 – 7.13 (m, 1H), 7.09 (tt, *J* = 7.0, 1.1 Hz, 1H), 6.88 (td, *J* = 7.7, 1.0 Hz, 1H), 6.65 (d, *J* = 7.7 Hz, 1H), 3.51 (s, 3H), 2.68 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ (ppm) 172.0, 167.8, 162.5, 160.5, 154.2, 144.6, 136.6, 131.1, 130.4, 130.3, 128.9, 128.0, 128.0, 126.2, 126.1, 122.7, 122.6, 119.5, 112.4, 108.4, 94.4, 63.5, 51.7, 26.4. **FTIR (cm^{-1}):** 3061, 2953, 1719, 1616, 1491, 1346, 1276, 1193, 1116, 987, 925, 800, 744, 684, 598. **HRMS** (ESI TOF) *m/z* calcd. For $C_{28}H_{22}N_3O_5$ [M+H] 480.1559 found 480.1564

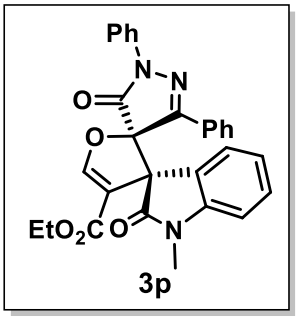
Methyl (2'*R*, 3*S*)- 3''-(4-methoxyphenyl)-1-methyl-2, 5''-dioxo-1''-phenyl-1'', 5''-dihydrodispiro[indoline-3, 3'-furan-2', 4''-pyrazole]-4'-carboxylate (3o)



3o

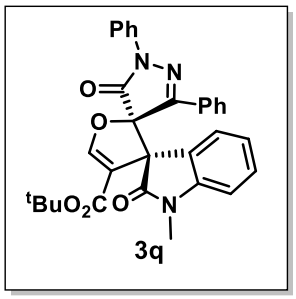
The compound **3o** was obtained following the general procedure B, starting from **1a**, **2c** and catalyst **C6**. **3o** was purified by column chromatography (Silica gel, petroleum ether/EtOAc 70:30) as brown solid (68 mg, 93%, *d.r.* >20:1), $\boldsymbol{R_f}$ (petroleum ether/EtOAc 70:30) = 0.17, **MP**: 197-199 °C, **HPLC:** CHIRAPAK IC column, *n*-hexane/iso-propanol = 80/20, flow rate = 0.6 mL/min, λ = 254 nm, tR(major) = 39.91 min, tR(minor) = 57.83 min, 97% *ee*. $[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{25}}$ = +174.6 (c 1.0, $CHCl_3$); **^{1}H NMR (400 MHz, $CDCl_3$):** δ(ppm) 7.92 (s, 1H), 7.72 – 7.66 (m, 2H), 7.44 – 7.34 (m, 3H), 7.27 – 7.21 (m, 2H), 7.19 – 7.12 (m, 2H), 7.09 (d, *J* = 7.4 Hz, 1H), 6.90 – 6.83 (m, 3H), 6.64 (d, *J* = 7.7 Hz, 1H), 3.80 (s, 3H), 3.51 (s, 3H), 2.72 (s, 3H). **^{13}C NMR (100MHz, $CDCl_3$):** δ (ppm) 172.2, 167.7, 162.5, 161.9, 160.5, 153.9, 144.6, 136.7, 130.3, 129.7, 128.9, 126.2, 126.0, 123.0, 122.7, 122.7, 119.5, 113.4, 112.3, 108.3, 94.7, 63.5, 55.5, 51.7, 26.5. **FTIR (cm^{-1}):** 3096, 2920, 2856, 1720, 1608, 1493, 1461, 1349, 1302, 1257, 1186, 1118, 1026, 969, 924, 834, 737, 682, 612. **HRMS** (ESI TOF) *m/z* calcd. For $C_{29}H_{24}N_3O_6$ [M+H] 510.1665 found 510.1662

Ethyl (2'R, 3S)-1-methyl-2, 5''-dioxo-1'', 3''-diphenyl-1'', 5''-dihydrodispiro[indoline-3, 3'-furan-2', 4''-pyrazole]-4'-carboxylate (3p)



The compound **3p** was obtained following the general procedure B, starting from **1l**, **2b** and catalyst **C6**. **3p** was purified by column chromatography (Silica gel, petroleum ether/EtOAc 70:30) as brown solid (62 mg, 93%, *d.r.* >20:1), R_f (petroleum ether/EtOAc 70:30) = 0.35, **MP**: 133-137 °C, **HPLC:** CHIRAPAK IA column, *n*-hexane/iso-propanol = 80/20, flow rate = 0.6 mL/min, λ = 254 nm, tR(minor) = 16.06 min, tR(major) = 25.68 min, 97% *ee*. $[\alpha]_D^{25}$ = +270.4 (c 1.0, $CHCl_3$); **^{1}H NMR (400 MHz, $CDCl_3$):** δ(ppm) 8.00 (s, 1H), 7.83 – 7.76 (m, 2H), 7.53 – 7.40 (m, 6H), 7.36 – 7.28 (m, 2H), 7.26 – 7.15 (m, 2H), 6.96 (td, *J* = 7.7, 1.0 Hz, 1H), 6.72 (d, *J* = 7.7 Hz, 1H), 3.99 (qd, *J* = 7.1, 2.6 Hz, 2H), 2.77 (s, 3H), 1.06 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ (ppm) 172.1, 167.8, 162.0, 160.3, 154.3, 144.7, 136.6, 131.1, 130.5, 130.3, 128.9, 128.0, 128.0, 126.2, 126.1, 122.9, 122.7, 119.5, 112.8, 108.3, 94.4, 63.5, 60.5, 26.4, 14.1. **FTIR (cm^{-1}):** 3060, 2923, 1718, 1617, 1490, 1375, 1336, 1277, 1110, 1020, 961, 810, 777, 684, 596. **HRMS** (ESI TOF) *m/z* calcd. For $C_{29}H_{24}N_3O_5$ [M+H] 494.1716 found 494.1714

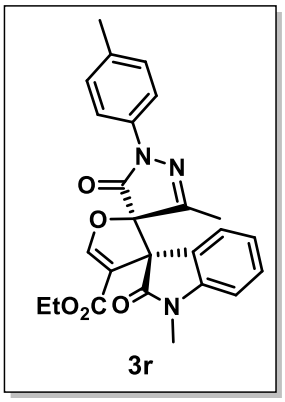
Tert-butyl (2'*R*, 3*S*)-1-methyl-2, 5''-dioxo-1'', 3''-diphenyl-1'', 5''-dihydrodispiro[indoline-3, 3'-furan-2', 4''-pyrazole]-4'-carboxylate (3q)



The compound **3q** was obtained following the general procedure B, starting from **1m**, **2b** and catalyst **C6**. **3q** was purified by column chromatography (Silica gel, petroleum ether/EtOAc 80:20) as brown solid (61 mg, 91%, *d.r.* >20:1), R_f (petroleum ether/EtOAc 70:30) = 0.53,

MP: 188-192 °C, **HPLC:** CHIRAPAK IC column, *n*-hexane/iso-propanol = 80/20, flow rate = 0.6 mL/min, λ = 254 nm, tR(major) = 15.78 min, tR(minor) = 26.61min, 96% *ee*. $[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{25}}$ = +111.8 (c 0.5, $CHCl_3$); **^{1}H NMR (400 MHz, $CDCl_3$):**δ(ppm) 7.94 (s, 1H), 7.83 – 7.76 (m, 2H), 7.53 – 7.38 (m, 6H), 7.36 – 7.27 (m, 2H), 7.28 – 7.19 (m, 1H), 7.17 (d, *J* = 7.4 Hz, 1H), 6.97 (td, *J* = 7.6, 1.0 Hz, 1H), 6.70 (d, *J* = 7.7 Hz, 1H), 2.77 (s, 3H), 1.13 (s, 9H). **^{13}C NMR(100 MHz, $CDCl_3$):** δ (ppm) 172.2, 161.1, 159.9, 154.4, 144.7, 136.6, 131.0, 130.6, 130.1, 128.9, 128.0, 128.0, 126.2, 126.0, 123.5, 122.6, 119.5, 114.3, 108.1, 94.5, 81.1, 63.5, 27.9, 26.3. **FTIR (cm^{-1}):** 3063, 2923, 2857, 1722, 1628, 1491, 1364, 1262, 1106, 1026, 963, 922, 813, 746, 686, 596. **HRMS** (ESI TOF) *m/z* calcd. For $C_{31}H_{28}N_3O_5$ [M+H] 522.2029 found 522.2040

Ethyl (2'*R*, 3*S*)-1, 3''-dimethyl-2, 5''-dioxo-1''-(p-tolyl)-1'', 5''-dihydrodispiro[indoline-3, 3'-furan-2', 4''-pyrazole]-4'-carboxylate (3r)

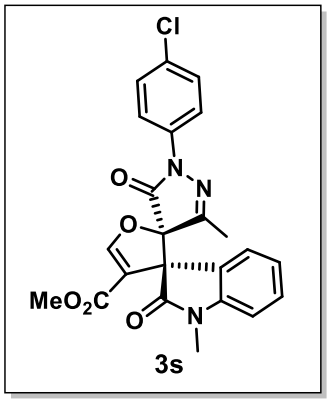


3r

The compound **3r** was obtained following the general procedure B, starting from **1m**, **2d** and catalyst **C6**. **3r** was purified by column chromatography (Silica gel, petroleum ether/EtOAc 75:25) as brown solid (58 mg, 94%, *d.r*. >20:1), $\boldsymbol{R_f}$ (petroleum ether/EtOAc 70:30) = 0.41, **MP**: 179-180 °C, **HPLC:** CHIRAPAK IC column, *n*-hexane/iso-propanol = 80/20, flow rate = 0.6 mL/min, λ = 254 nm, tR(major) = 15.35 min, tR(minor) = 20.86 min, 95% *ee*. $[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{25}}$ = +332.6 (c 1.0, $CHCl_3$); **^{1}H NMR (400 MHz, $CDCl_3$):** δ(ppm) 7.84 (s, 1H), 7.47 – 7.43 (m, 1H), 7.39 – 7.34 (m, 2H), 7.27 (td, *J* = 7.8, 1.2 Hz, 1H), 7.09 (d, *J* = 8.2 Hz, 2H), 7.03 (td, *J* = 7.7, 1.0 Hz, 1H), 6.77 (d, *J* = 7.8 Hz, 1H), 4.00 (qq, *J* = 7.3, 3.7 Hz, 2H), 3.20 (s, 3H), 2.34 (s, 3H), 2.28 (s, 3H), 1.06 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ (ppm) 173.0, 167.0, 161.9, 159.2, 157.5, 143.9, 135.5, 134.5, 130.2, 129.4, 127.0, 123.6, 122.8, 119.1, 114.2, 108.4, 93.2, 63.2, 60.6, 27.0, 21.1, 16.1, 14.0. **FTIR (cm^{-1}):** 2920, 2860, 2190, 1717,

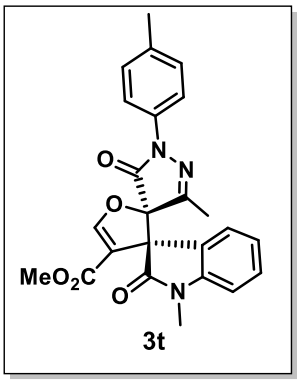
1621, 1509, 1463, 1368, 1279, 1112, 1026, 955, 897, 817, 748, 610. **HRMS** (ESI TOF) *m/z* calcd. For $C_{25}H_{24}N_3O_5$ [M+H] 446.1716 found 446.1723

Methyl (2'*R*, 3*S*)-1''-(4-chlorophenyl)-1, 3''-dimethyl-2, 5''-dioxo-1'', 5''dihydrodispiro[indoline-3, 3'-furan-2', 4''-pyrazole]-4'-carboxylate (3s)



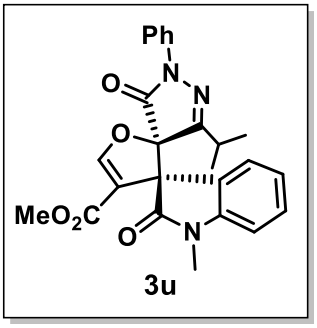
The compound **3s** was obtained following the general procedure B, starting from **1a**, **2e** and catalyst **C6**. **3s** was purified by column (Silica gel, petroleum ether/EtOAc 70:30) as off white solid (53mg, 90%, *d.r.* >20:1), $\boldsymbol{R_f}$ (petroleum ether/EtOAc 70:30) = 0.34, **MP**: 215-218 °C, **HPLC:** CHIRAPAK IC column, *n*-hexane/iso-propanol = 80/20, flow rate = 0.6 mL/min, λ = 254 nm, tR(major) = 31.79 min, tR(minor) = 41.26 min, 92% *ee*. $[\boldsymbol{a}]_{\boldsymbol{D}}^{\boldsymbol{25}}$ = +331 (c 1.0, $CHCl_3$); **^{1}H NMR (400 MHz, $CDCl_3$):** δ(ppm) 7.82 (s, 1H), 7.51 – 7.46 (m, 2H), 7.43 – 7.39 (m, 1H), 7.32 – 7.22 (m, 3H), 7.03 (td, *J* = 7.6, 1.0 Hz, 1H), 6.79 (d, *J* = 7.8 Hz, 1H), 3.59 (s, 3H), 3.21 (s, 3H), 2.34 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ (ppm) 172.7, 166.8, 162.1, 159.0, 157.9, 143.7, 135.4, 130.7, 130.3, 128.9, 126.8, 123.1, 122.7, 119.9, 113.8, 108.4, 93.0, 63.2, 51.7, 26.9, 16.0. **FTIR (cm^{-1}):** 3102, 2923, 2856, 1717, 1619, 1489, 1351, 1278, 1194, 1123, 1036, 993, 928, 829, 747, 610. **HRMS** (ESI TOF) *m/z* calcd. For $C_{25}H_{24}N_3O_5$ [M+H] 452.1013 found 452.1013

Methyl (2'*R*, 3*S*)-1,3''-dimethyl-2, 5''-dioxo-1''-(p-tolyl)-1'', 5''-dihydrodispiro[indoline-3, 3'-furan-2', 4''-pyrazole]-4'-carboxylate (3t)



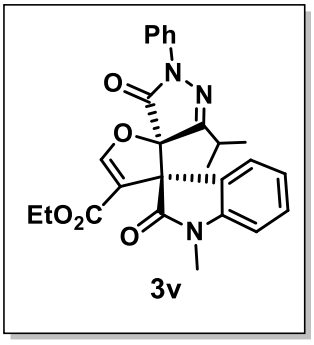
The compound **3t** was obtained following the general procedure B, starting from **1a**, **2d** and catalyst **C6**. **3t** was purified by column chromatography (Silica gel, petroleum ether/EtOAc 70:30) as off white solid (53mg, 90%, *d.r.* >20:1), R_f (petroleum ether/EtOAc 70:30) = 0.32, **MP**: 201-204 °C, **HPLC:** CHIRAPAK IC column, *n*-hexane/iso-propanol = 80/20, flow rate = 0.6 mL/min, λ = 254 nm, tR(major) = 33.60 min, tR(minor) = 48.37 min, 88% *ee*. $[\alpha]_D^{25}$ = +201.16 (c 1.0, $CHCl_3$); **^{1}H NMR (400 MHz, $CDCl_3$):** δ(ppm) 7.83 (s, 1H), 7.47 – 7.42 (m, 1H), 7.39 – 7.33 (m, 2H), 7.30 – 7.24 (m, 1H), 7.09 (d, *J* = 8.2 Hz, 2H), 7.03 (td, *J* = 7.6, 1.0 Hz, 1H), 6.77 (d, *J* = 7.8 Hz, 1H), 3.58 (s, 3H), 3.20 (s, 3H), 2.33 (s, 3H), 2.28 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ (ppm) 172.8, 166.8, 162.2, 159.2, 157.2, 143.8, 135.4, 134.4, 130.2, 129.3, 126.9, 123.2, 122.7, 119.0, 113.7, 108.4, 93.1, 63.0, 51.6, 26.9, 20.9, 16.0. **FTIR (cm^{-1}):** 2922, 2312, 1722, 1621, 1511, 1468, 1355, 1281, 1197, 1127, 1037, 991, 928, 821, 753, 695, 609. **HRMS** (ESI TOF) *m/z* calcd. For $C_{24}H_{22}N_3O_5$ [M+H] 432.1559 found 432.1559

Methyl (2'*R*, 3*S*)-3''-isopropyl-1-methyl-2, 5''-dioxo-1''-phenyl-1'', 5''-dihydrodispiro[indoline-3, 3'-furan-2', 4''-pyrazole]-4'-carboxylate (3u)



The compound **3u** was obtained following the general procedure B, starting from **1a**, **2f** and catalyst **C6**. **3u** was purified by column (Silica gel, petroleum ether/EtOAc 70:30) as off white solid (57mg, 89%, *d.r.* >20:1), $\boldsymbol{R_f}$ (petroleum ether/EtOAc 70:30) = 0.36, **MP**: 157-159 °C, **HPLC:** CHIRAPAK IC column, *n*-hexane/iso-propanol = 80/20, flow rate = 0.9 mL/min, λ = 254 nm, tR(minor) = 8.58 min, tR(major) = 9.33 min, 86% *ee*. $[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{25}}$ = +275 (c 1.0, $CHCl_3$); **^{1}H NMR (400 MHz, $CDCl_3$):** δ(ppm) 7.86 (s, 1H), 7.50 – 7.40 (m, 3H), 7.32 – 7.26 (m, 2H), 7.26 – 7.23 (m, 1H), 7.15 – 7.09 (m, 1H), 7.00 (td, *J* = 7.7, 1.0 Hz, 1H), 6.77 (d, *J* = 7.7 Hz, 1H), 3.59 (s, 3H), 3.27 (p, *J* = 6.8 Hz, 1H), 3.20 (s, 3H), 1.26 (d, *J* = 6.7 Hz, 3H), 1.23 (d, *J* = 6.9 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ (ppm) 173.1, 167.7, 164.6, 162.4, 159.9, 144.1, 136.9, 130.3, 128.9, 126.7, 125.6, 123.3, 122.9, 119.1, 119.1, 119.0, 119.0, 113.1, 108.5, 94.3, 63.3, 51.8, 29.8, 27.0, 22.9, 19.3. **FTIR (cm^{-1}):** 3991, 2927, 1719, 1622, 1493, 1351, 1265, 1217, 1128, 991, 909, 733**. HRMS** (ESI TOF) *m/z* calcd. For $C_{25}H_{24}N_3O_5$ [M+H] 446.1716 found 446.1716

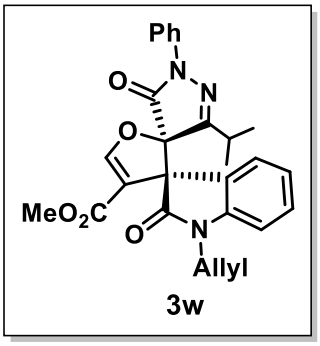
Ethyl (2'*R*, 3*S*)- 3''-isopropyl-1-methyl-2, 5''-dioxo-1''-phenyl-1'', 5''-dihydrodispiro[indoline-3, 3'-furan-2', 4''-pyrazole]-4'-carboxylate (3v)



The compound **3v** was obtained following the general procedure B, starting from **1l**, **2f** and catalyst **C6**. **3v** was purified by column chromatography (Silica gel, petroleum ether/EtOAc 70:30) as off white solid (53mg, 83%, *d.r.* >20:1), $\boldsymbol{R_f}$ (petroleum ether/EtOAc 70:30) = 0.45, **MP**: 166-167 °C, **HPLC:** CHIRAPAK IC column, *n*-hexane/iso-propanol = 80/20, flow rate = 0.9 mL/min, λ = 254 nm, tR(minor) = 8.63 min, tR(major) = 10.43 min, 88% *ee*. $[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{25}}$ = +277 (c 1.0, $CHCl_3$); **^{1}H NMR (400 MHz, $CDCl_3$):** δ(ppm) 7.87 (s, 1H), 7.51 – 7.41 (m, 3H), 7.32 – 7.27 (m, 2H), 7.25 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.16 – 7.09 (m, 1H), 7.00 (td, *J* = 7.7, 1.0 Hz, 1H), 6.76 (d, *J* = 7.7 Hz, 1H), 4.00 (qd, *J* = 7.1, 2.9 Hz, 2H), 3.28 (p, *J* = 6.8 Hz, 1H), 3.19 (s, 3H), 1.27 (d, *J* = 6.7 Hz, 3H), 1.23 (d, *J* = 6.9 Hz, 3H), 1.06 (t, *J* = 7.1 Hz,

3H).**^{13}C NMR (100 MHz, $CDCl_3$):** δ (ppm) 173.1, 167.6, 164.7, 161.8, 159.6, 144.0, 136.9, 130.1, 128.7, 126.7, 125.5, 123.5, 122.7, 118.9, 113.5, 108.2, 94.2, 63.2, 60.4, 29.7, 26.8, 22.8, 19.1, 13.9. **FTIR (cm^{-1}):** 2926, 1717, 1624, 1493, 1347, 1267, 1218, 1125, 1019, 908, 808, 736. **HRMS** (ESI TOF) *m/z* calcd. For $C_{26}H_{25}N_3O_5$ [M+H] 460.1872 found 460.1872

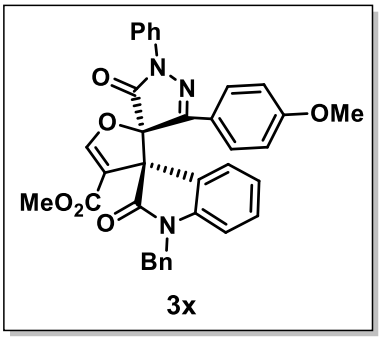
Methyl (2'*R*, 3*S*)-1-allyl-3''-isopropyl-2, 5''-dioxo-1''-phenyl-1'', 5''-dihydrodispiro[indoline-3, 3'-furan-2', 4''-pyrazole]-4'-carboxylate (3w)



3w

The compound **3w** was obtained following the general procedure B, starting from **1j**, **2f** and catalyst **C6**. **3w** was purified by column chromatography (Silica gel, petroleum ether/EtOAc 80:20) as off white solid (51mg, 81%, *d.r.* >20:1), R_f (petroleum ether/EtOAc 70:30) = 0.59, **MP**: 169-170 °C, **HPLC:** CHIRAPAK IC column, *n*-hexane/iso-propanol = 80/20, flow rate = 0.6 mL/min, λ = 254 nm, tR(minor) = 10.29 min, tR(major) = 10.98 min, 90% *ee*. $[\alpha]_D^{25}$ = +175 (c 1.0, $CHCl_3$); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.86 (s, 1H), 7.49 – 7.41 (m, 3H), 7.32 – 7.26 (m, 2H), 7.22 (td, *J* = 7.8, 1.3 Hz, 1H), 7.16 – 7.10 (m, 1H), 7.00 (td, *J* = 7.6, 1.0 Hz, 1H), 6.73 (d, *J* = 7.8 Hz, 1H), 5.77 (ddt, *J* = 17.2, 10.3, 4.9 Hz, 1H), 5.23 – 5.12 (m, 2H), 4.38 (ddt, *J* = 16.6, 5.0, 1.7 Hz, 1H), 4.26 (ddt, *J* = 16.6, 4.6, 1.8 Hz, 1H), 3.59 (s, 3H), 3.24 (h, *J* = 6.8 Hz, 1H), 1.26 (d, *J* = 6.6 Hz, 3H), 1.24 (d, *J* = 6.9 Hz, 3H). **^{13}C NMR ($CDCl_3$, 100 MHz)**: δ (ppm) 173.0, 167.7, 164.8, 162.4, 159.8, 143.2, 137.0, 130.5, 130.2, 128.9, 126.9, 125.6, 123.5, 122.8, 119.1, 117.7, 113.3, 109.4, 94.5, 63.5, 51.7, 42.8, 30.2, 22.6, 19.2. **HRMS** (ESI TOF) *m/z* calcd. For $C_{27}H_{26}N_3O_5$ [M+H] 472.1872 found 472.1872.

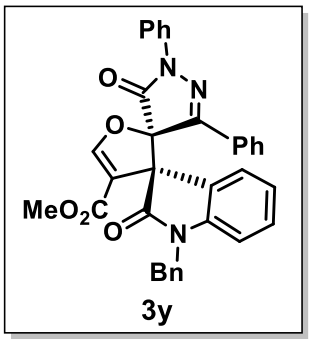
Methyl (2'*R*, 3*S*)-1-benzyl- 3'' -(4-methoxyphenyl)- 2, 5''-dioxo-1''-phenyl-1'', 5''-dihydrodispiro[indoline-3, 3'-furan-2', 4''-pyrazole]-4'-carboxylate (3x)



3x

The compound **3x** was obtained following the general procedure B, starting from **1k**, **2c** and catalyst **C6**. **3x** was purified by column chromatography (Silica gel, petroleum ether/EtOAc 70:30) as yellow solid (59mg, 85%, *d.r.* >20:1), R_f (petroleum ether/EtOAc 70:30) = 0.35, **MP**: 172-174 °C, **HPLC:** CHIRAPAK IC column, *n*-hexane/iso-propanol = 80/20, flow rate = 0.6 mL/min, λ = 290 nm, tR(major) = 25.45 min, tR(minor) = 37.80 min, 98% *ee*. $[\alpha]_D^{25}$ = +60 (c 0.1, $CHCl_3$); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.02 (s, 1H), 7.86 – 7.81 (m, 2H), 7.50 – 7.44 (m, 3H), 7.34 – 7.27 (m, 2H), 7.21 – 7.03 (m, 7H), 6.96 – 6.88 (m, 3H), 6.54 (d, *J* = 7.8 Hz, 1H), 4.60 (d, *J* = 15.9 Hz, 1H), 4.48 (d, *J* = 15.9 Hz, 1H), 3.86 (s, 3H), 3.58 (s, 3H). **^{13}C NMR ($CDCl_3$, 100 MHz):** δ (ppm) 172.4, 167.7, 162.3, 161.8, 160.2, 154.2, 143.6, 136.6, 135.0, 130.1, 129.6, 128.8, 128.6, 127.4, 126.9, 126.4, 125.8, 123.1, 122.9, 122.5, 119.3, 113.3, 112.9, 109.3, 94.8, 63.6, 55.3, 51.6, 44.1. **HRMS** (ESI TOF) *m/z* calcd. For $C_{35}H_{28}N_3O_6$ [M+H] 586.1978 found 586.1978.

Methyl (2'*R*, 3*S*)-1-benzyl-2, 5''-dioxo-1'', 3''-diphenyl-1'', 5''-dihydrodispiro[indoline-3, 3'-furan-2', 4''-pyrazole]-4'-carboxylate (3y)



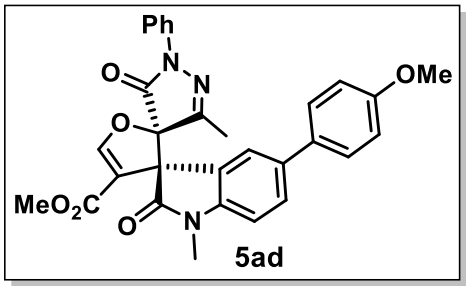
3y

The compound **3y** was obtained following the general procedure B, starting from **1k**, **2b** and catalyst **C6**. **3y** was purified by column chromatography (Silica gel, petroleum ether/EtOAc

70:30) as white solid (55mg, 84%, *d.r.* >20:1), R_f (petroleum ether/EtOAc 70:30) = 0.47, **MP**: 134.6-136.4 °C, **HPLC:** CHIRAPAK IC column, *n*-hexane/iso-propanol = 80/20, flow rate = 0.6 mL/min, λ = 254 nm, tR(major) = 19.18 min, tR(minor) = 22.08 min, 92% *ee*. $[\alpha]_D^{25}$ = +158 (c 1.0, $CHCl_3$); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.02 (s, 1H), 7.89 – 7.84 (m, 2H), 7.47 (tdd, *J* = 7.2, 3.1, 1.4 Hz, 4H), 7.43 – 7.38 (m, 2H), 7.35 – 7.28 (m, 2H), 7.21 – 7.14 (m, 4H), 7.14 – 7.01 (m, 3H), 6.94 (td, *J* = 7.6, 0.9 Hz, 1H), 6.55 (d, *J* = 7.7 Hz, 1H), 4.55 (d, *J* = 16.0 Hz, 1H), 4.46 (d, *J* = 15.9 Hz, 1H), 3.57 (s, 3H). **^{13}C NMR ($CDCl_3$, 100 MHz):** δ (ppm) 172.2, 167.8, 162.2, 160.2, 154.5, 143.6, 136.5, 134.9, 131.0, 130.4, 130.1, 128.8, 128.6, 127.9, 127.9, 127.4, 126.9, 126.4, 126.0, 123.0, 122.6, 119.4, 112.9, 109.4, 94.5, 63.6, 51.6, 44.0. **HRMS** (ESI TOF) *m/z* calcd. For $C_{34}H_{26}N_3O_5$ [M+H] 556.1872 found 556.1872

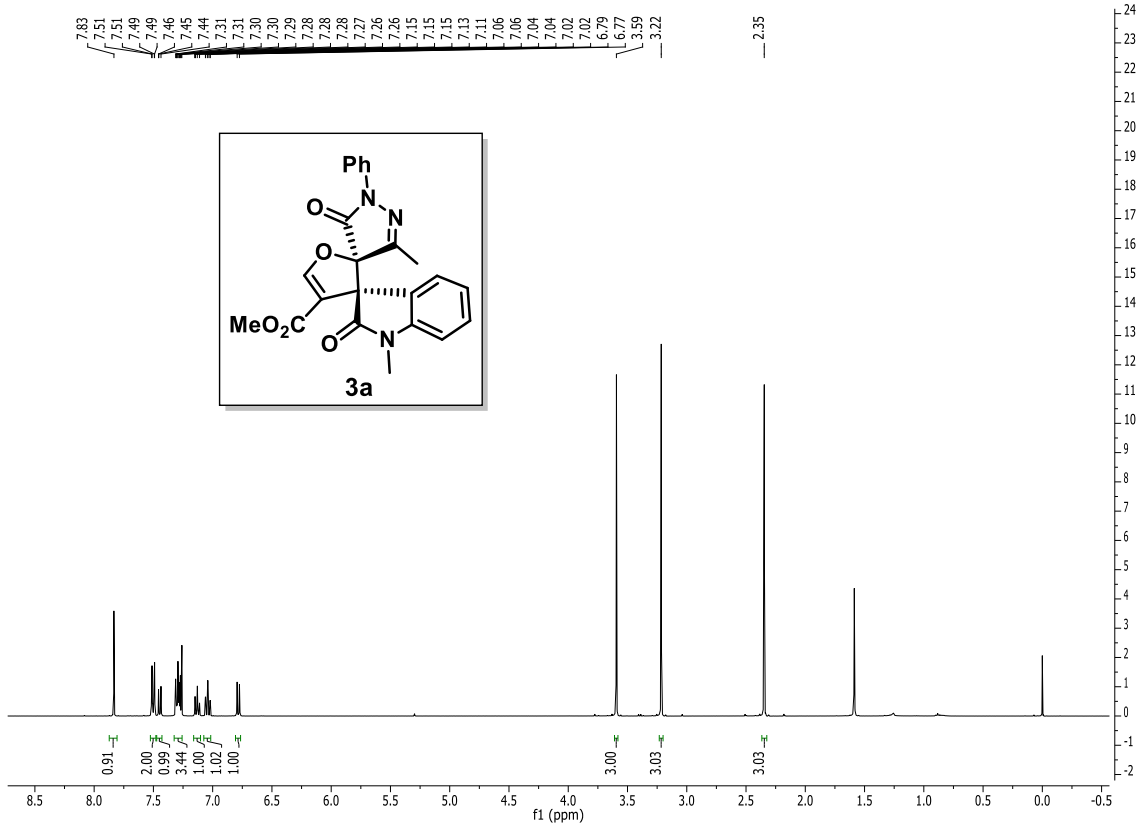
Procedure for the synthesis of 5ad (Suzuki coupling reaction)

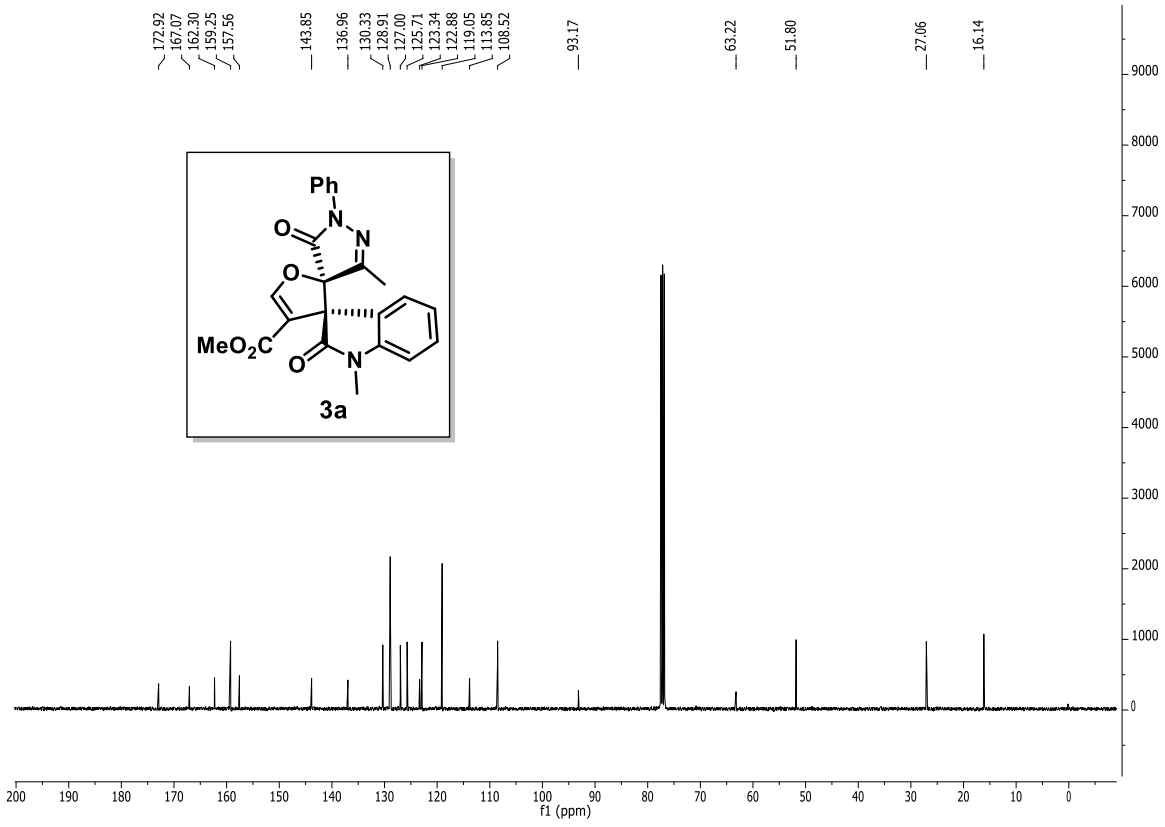
Methyl (2'*R*, 3*S*)-5-(4-methoxyphenyl)-1, 3''-dimethyl-2, 5''-dioxo-1''-phenyl-1'', 5''-dihydrodispiro[indoline-3, 3'-furan-2', 4''-pyrazole]-4'-carboxylate

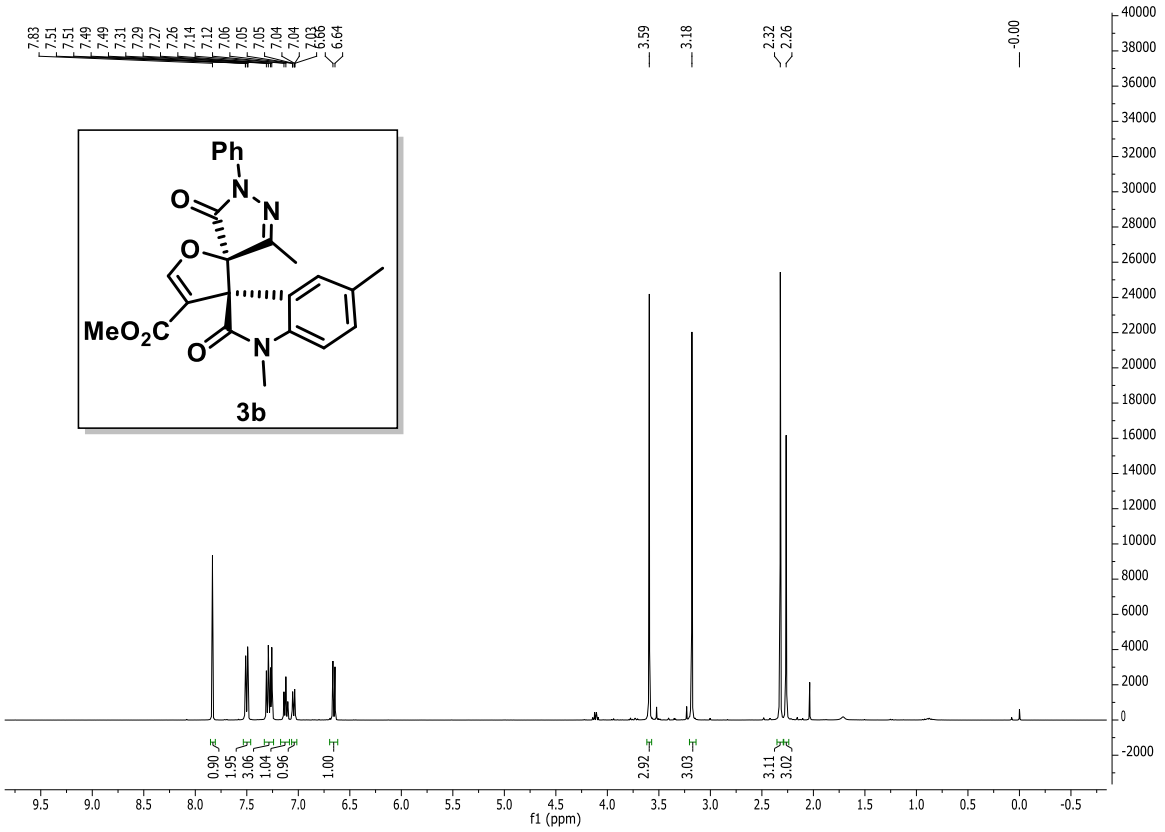


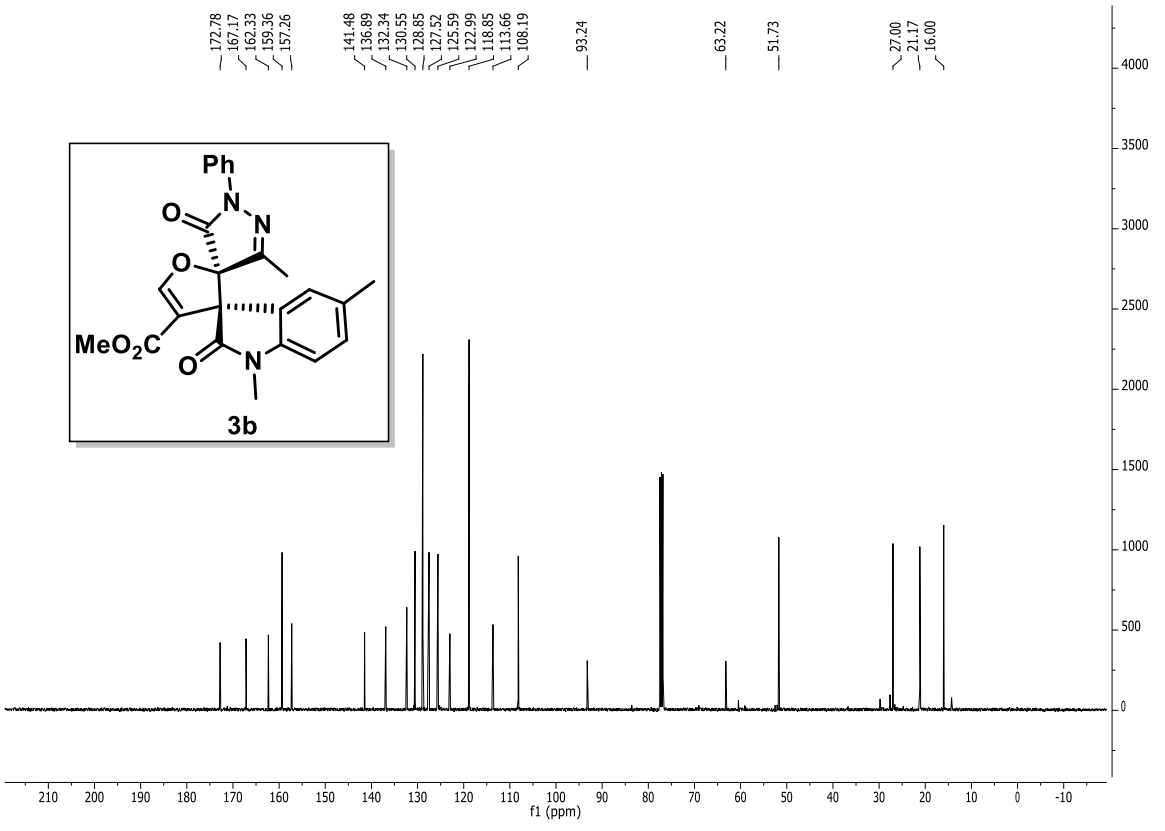
White solid (28 mg, 60%, *d.r.* >20:1), R_f (petroleum ether/EtOAc 70:30) = 0.32, **HPLC:** CHIRAPAK IC column, *n*-hexane/iso-propanol = 80/20, flow rate = 0.6 mL/min, λ = 290nm, tR(minor) = 57.60 min, tR(major) = 40.59 min, 91% *ee*. $[\alpha]_D^{25}$ = +3.00 (c 1.0, $CHCl_3$); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.84 (s, 1H), 7.63 (d, *J* = 1.6 Hz, 1H), 7.45 (tt, *J* = 6.7, 2.0 Hz, 5H), 7.25 – 7.20 (m, 2H), 7.12 – 7.07 (m, 1H), 6.97 – 6.92 (m, 2H), 6.82 (d, *J* = 8.1 Hz, 1H), 3.85 (s, 3H), 3.59 (s, 3H), 3.24 (s, 3H), 2.36 (s, 3H).**^{13}C NMR (100 MHz, $CDCl_3$):** δ (ppm) 173.0, 167.3, 162.3, 159.4, 159.1, 157.6, 142.6, 136.9, 135.9, 133.3, 128.9, 128.5, 128.1, 125.8, 123.8, 119.1, 114.3, 113.7, 108.6, 93.4, 63.5, 55.5, 51.8, 27.2, 16.1.**HRMS** (ESI TOF) *m/z* calcd. For $C_{30}H_{25}N_3O_6$ [M+H] 524.1822 found 524.1821.

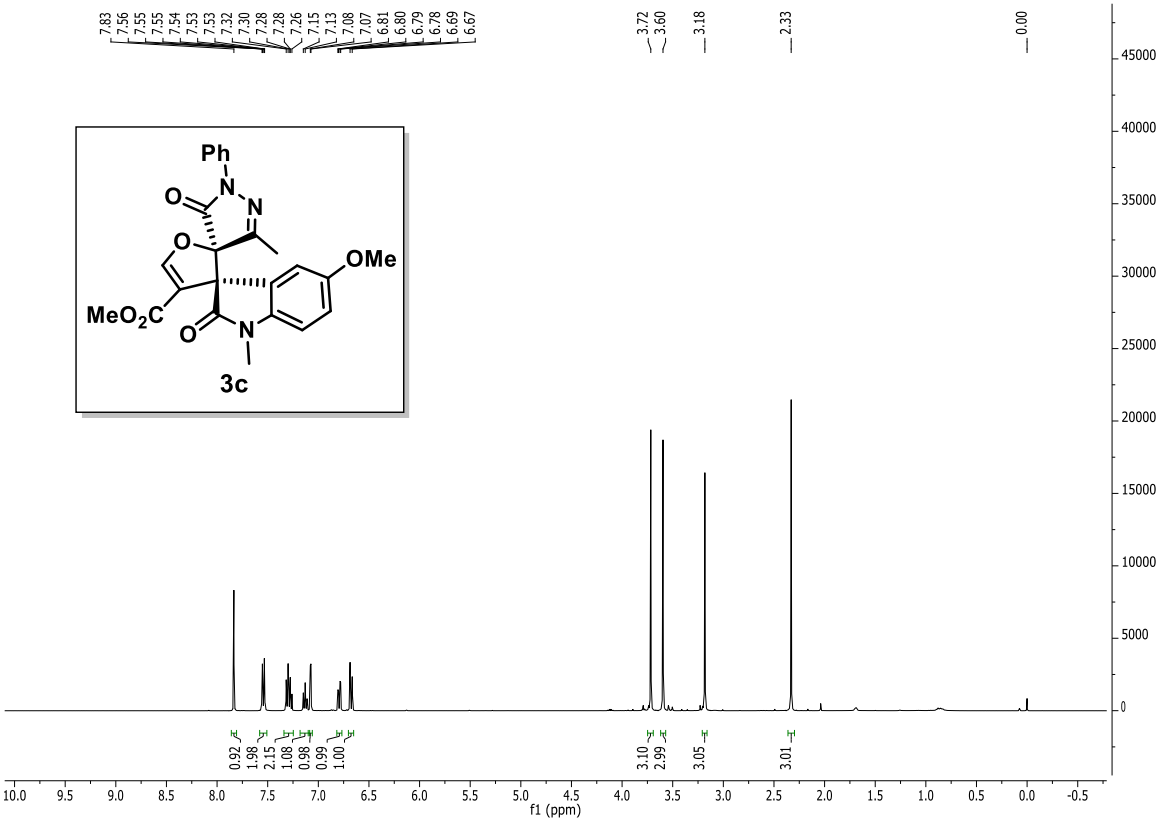
Copies of ^{1}H and ^{13}C Spectra (3a-3y) and 5ad

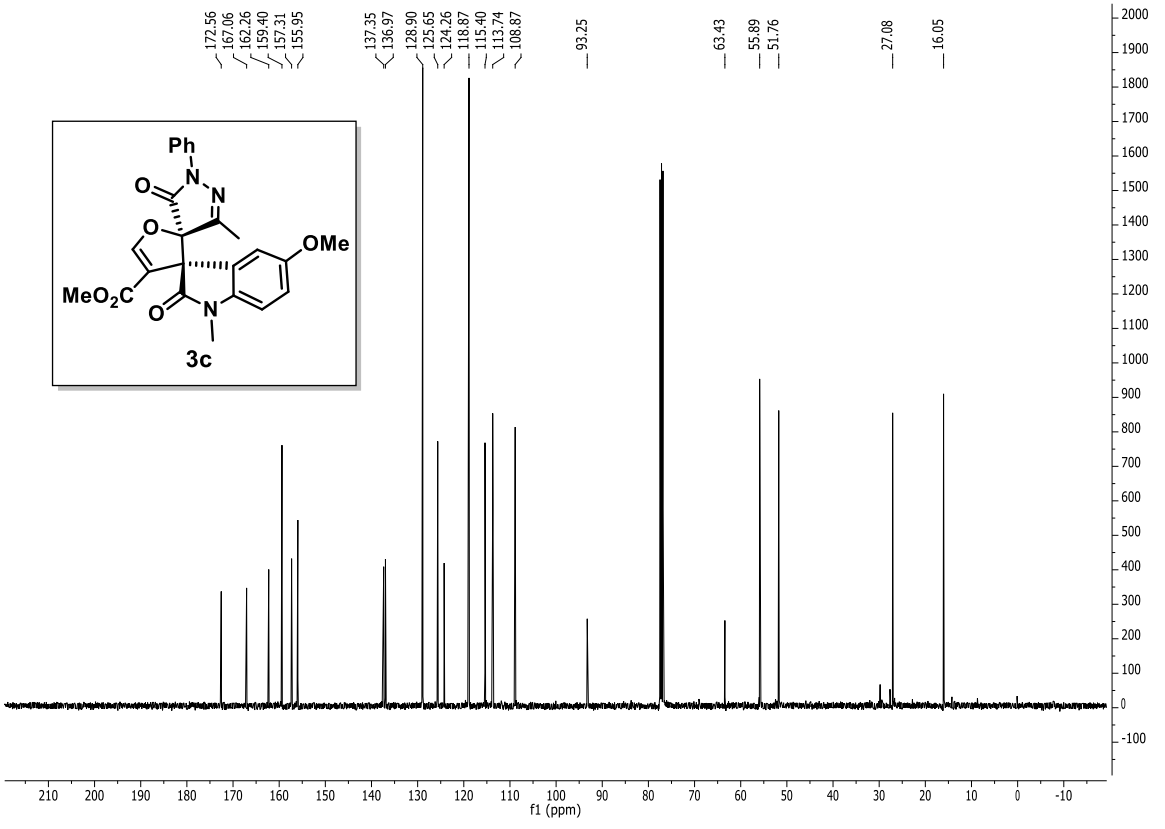


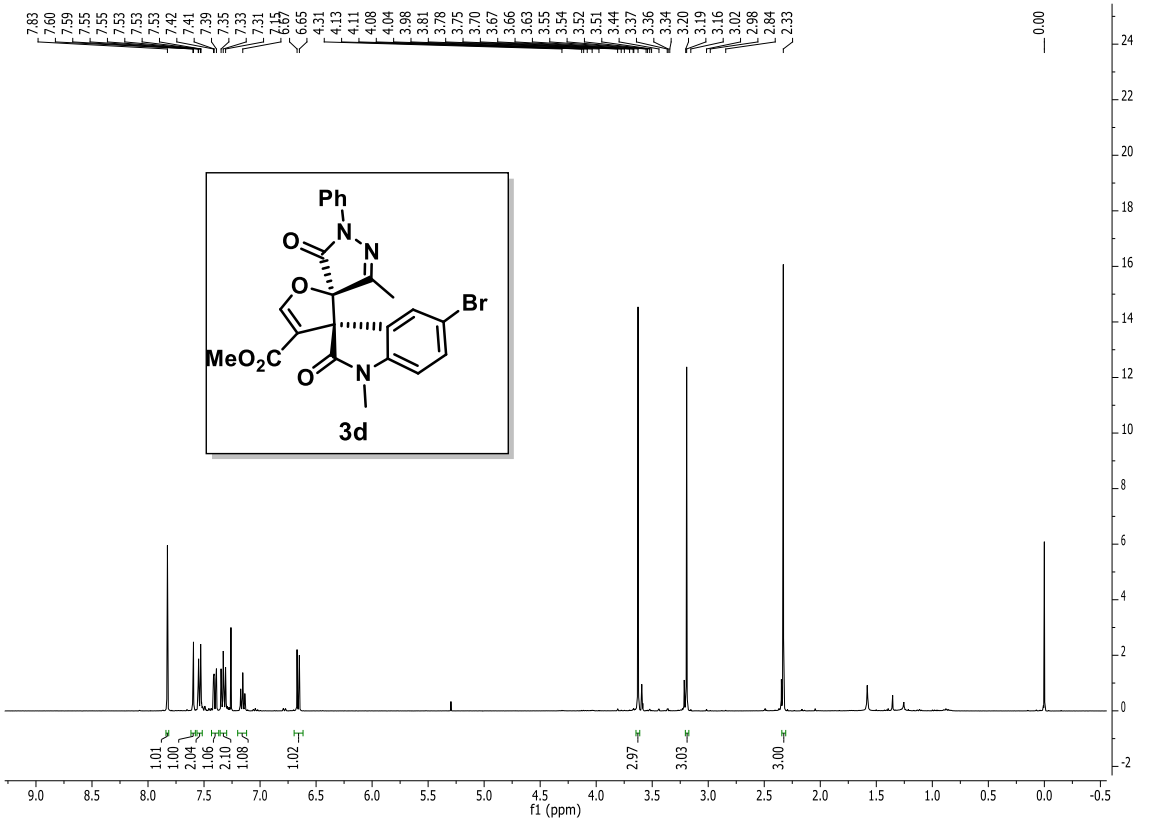


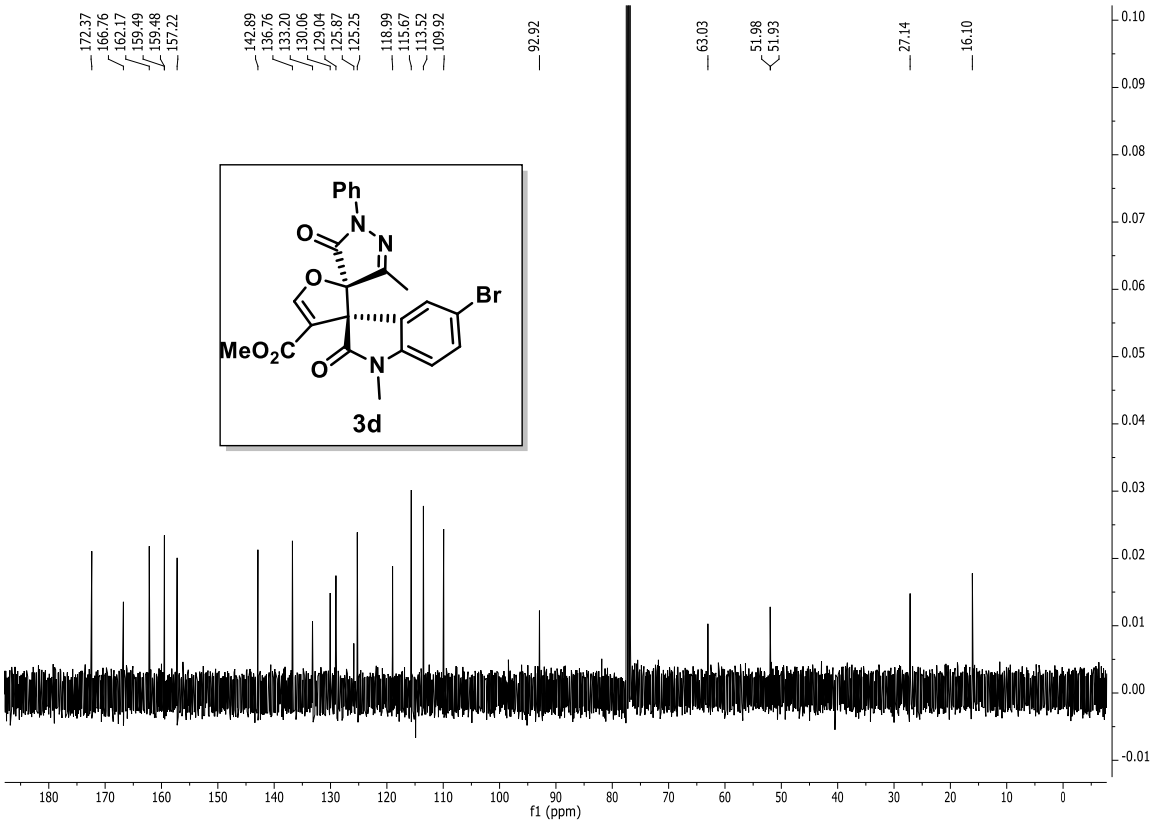

7.83
7.51
7.51
7.49
7.49
7.31
7.29
7.27
7.26
7.14
7.12
7.06
7.05
7.05
7.04
7.04
7.03
6.66
6.64
3.59
3.18
2.32
2.26
-0.00
Ph
N
N
O
O
MeO2C
O
N
3b
0.90
1.95
3.06
1.04
0.96
1.00
2.92
3.03
3.11
3.02
f1 (ppm)

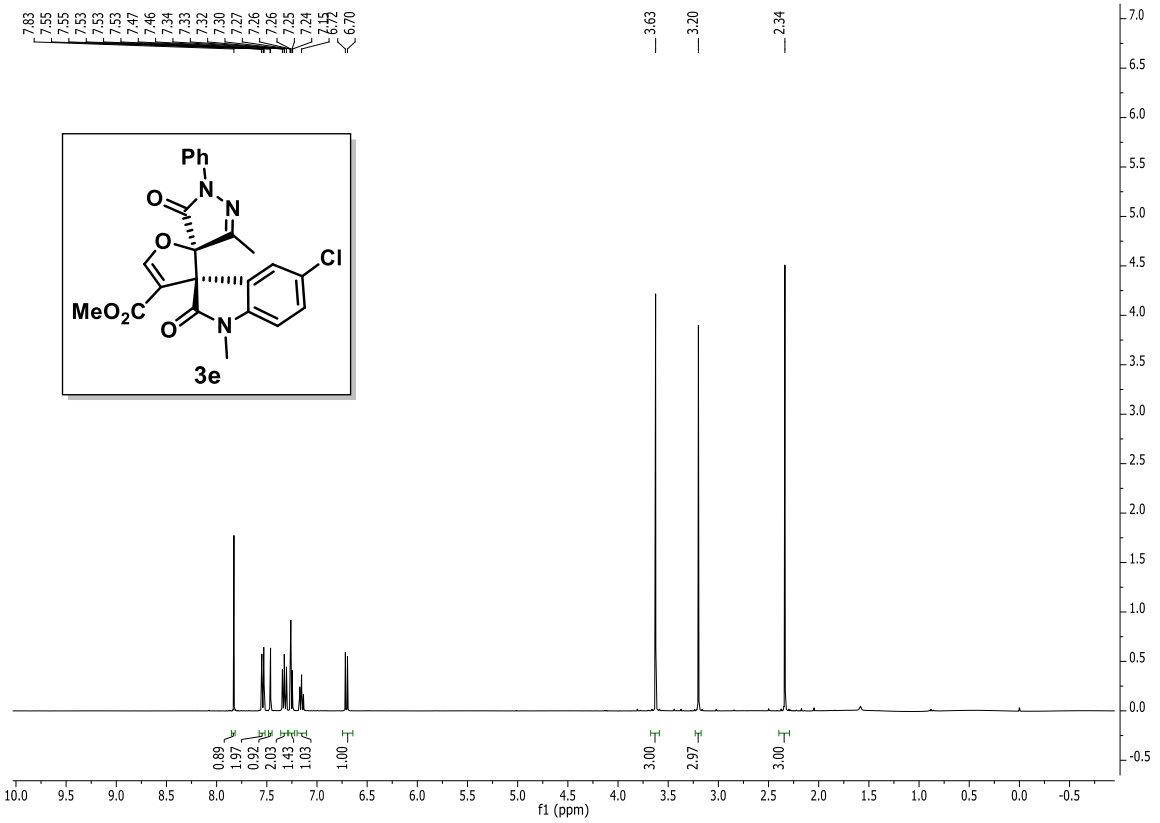

172.78
167.17
162.33
159.36
157.26
141.48
136.89
132.34
130.55
128.85
127.52
125.59
122.99
118.85
113.66
108.19
93.24
63.22
51.73
27.00
21.17
16.00
Ph
N
N
O
O
MeO2C
O
N
3b
f1 (ppm)

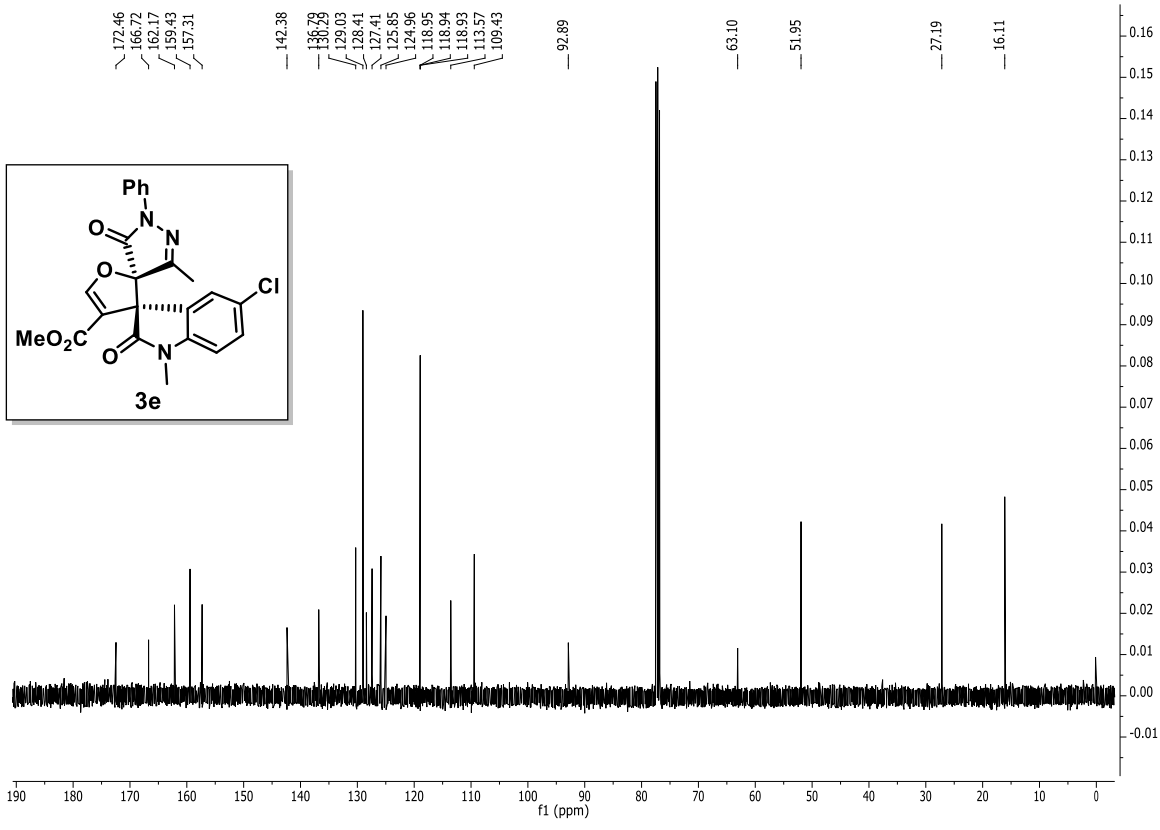

7.83
7.56
7.55
7.55
7.54
7.53
7.53
7.32
7.30
7.28
7.28
7.26
7.15
7.13
7.08
7.07
6.81
6.80
6.79
6.78
6.69
6.67
3.72
3.60
3.18
2.33
0.00
Ph
N
N
O
O
OMe
MeO2C
O
N
3c
0.92
1.98
2.15
1.08
0.98
0.99
1.00
3.10
2.99
3.05
3.01
f1 (ppm)

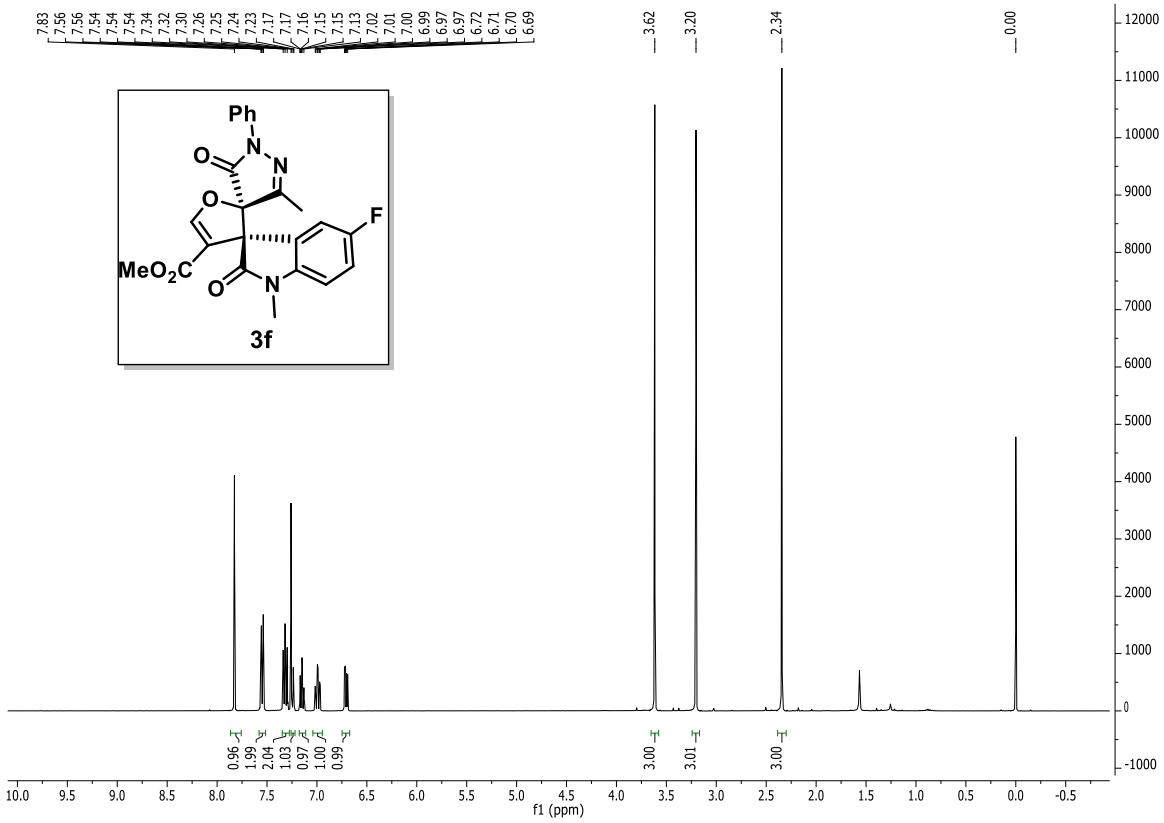

172.56
167.06
162.26
159.40
157.31
155.95
137.35
136.97
128.90
125.65
124.26
118.87
115.40
113.74
108.87
93.25
63.43
55.89
51.76
27.08
16.05
Ph
N
N
O
O
OMe
MeO2C
O
N
3c
f1 (ppm)

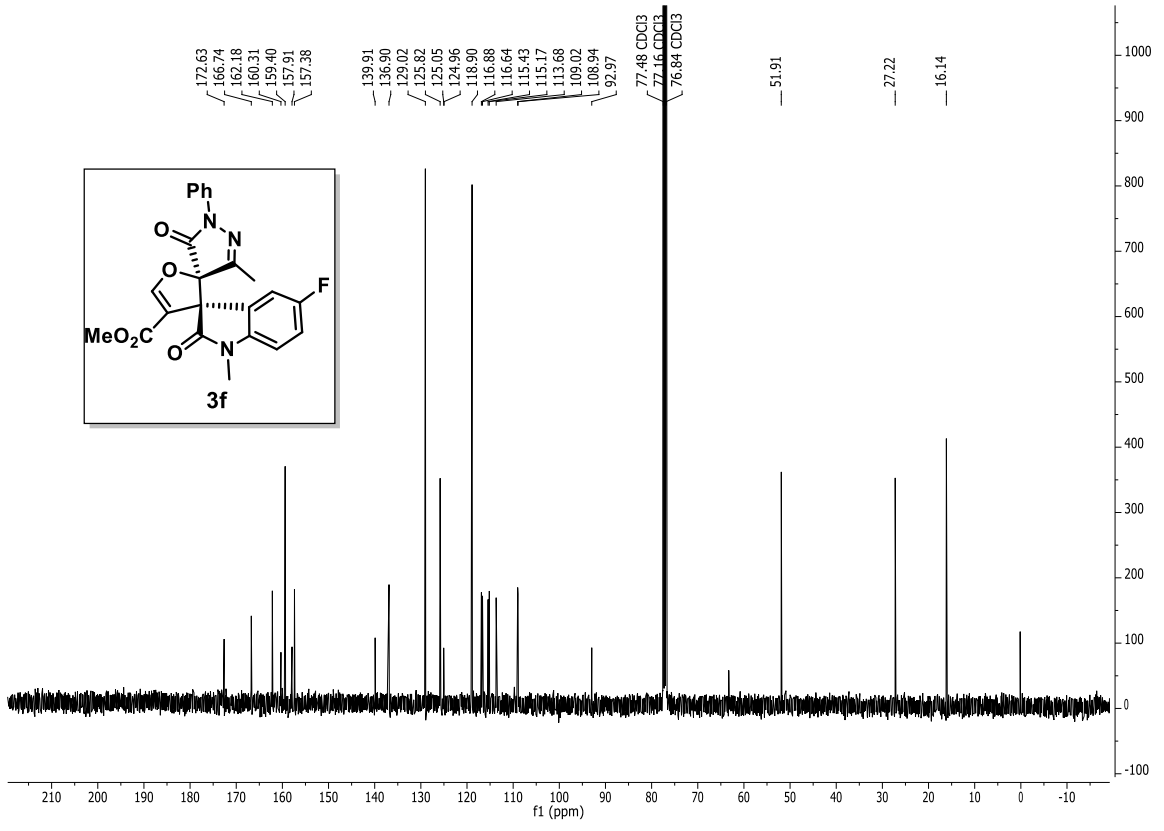

7.83
7.60
7.59
7.55
7.55
7.53
7.53
7.53
7.42
7.41
7.39
7.35
7.33
7.31
7.15
6.67
6.65
4.31
4.13
4.11
4.08
4.04
3.98
3.81
3.78
3.75
3.70
3.67
3.66
3.63
3.55
3.54
3.52
3.51
3.44
3.37
3.36
3.34
3.20
3.19
3.16
3.02
2.98
2.84
2.33
0.00
Ph
N
N
O
O
O
Br
MeO2C
O
N
3d
1.01
1.00
2.04
1.06
2.10
1.08
1.02
2.97
3.03
3.00
f1 (ppm)

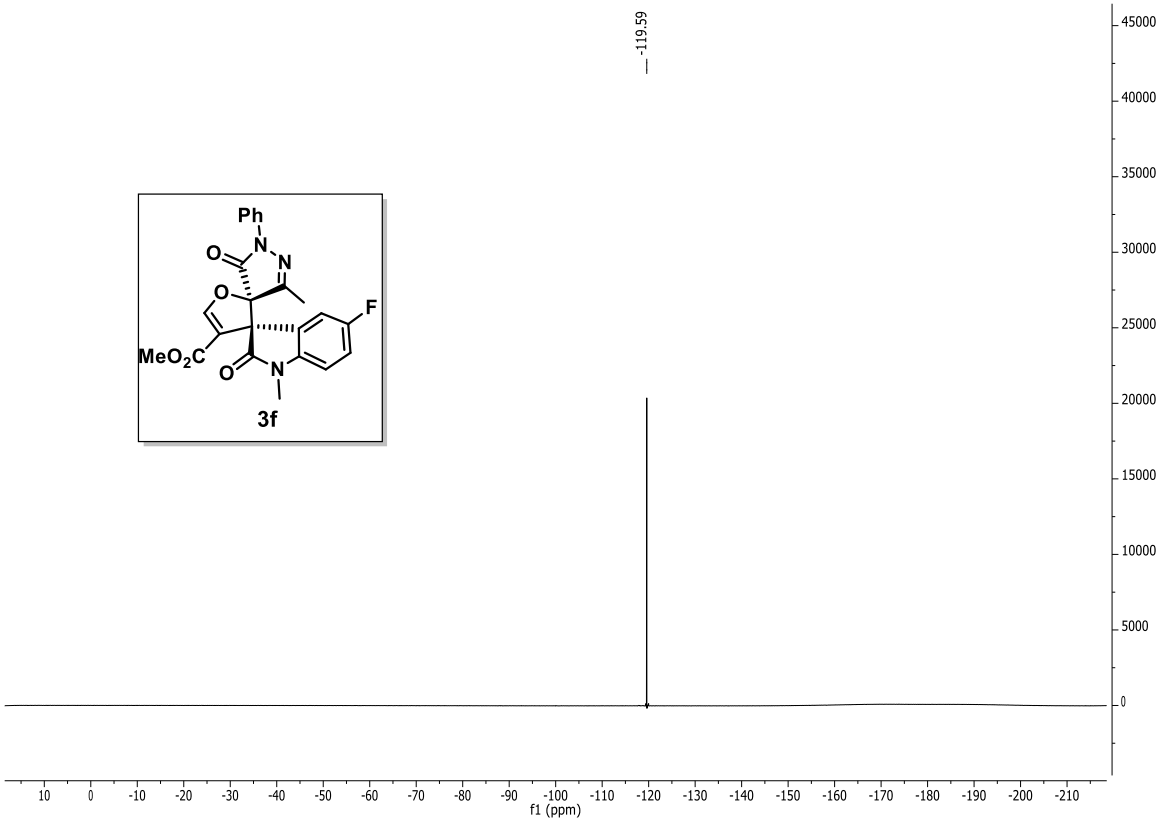

172.37
166.76
162.17
159.49
159.48
157.22
142.89
136.76
133.20
130.06
129.04
125.87
125.25
118.99
115.67
113.52
109.92
92.92
63.03
51.98
51.93
27.14
16.10
Ph
N
N
O
O
O
Br
MeO2C
O
N
3d
f1 (ppm)


7.83
7.55
7.55
7.53
7.53
7.53
7.47
7.46
7.34
7.33
7.32
7.30
7.27
7.26
7.26
7.25
7.24
7.15
7.12
6.70
3.63
3.20
2.34
Ph
N
N
O
O
Cl
MeO2C
O
N
3e
0.89
1.97
0.92
2.03
1.43
1.03
1.00
3.00
2.97
3.00
f1 (ppm)

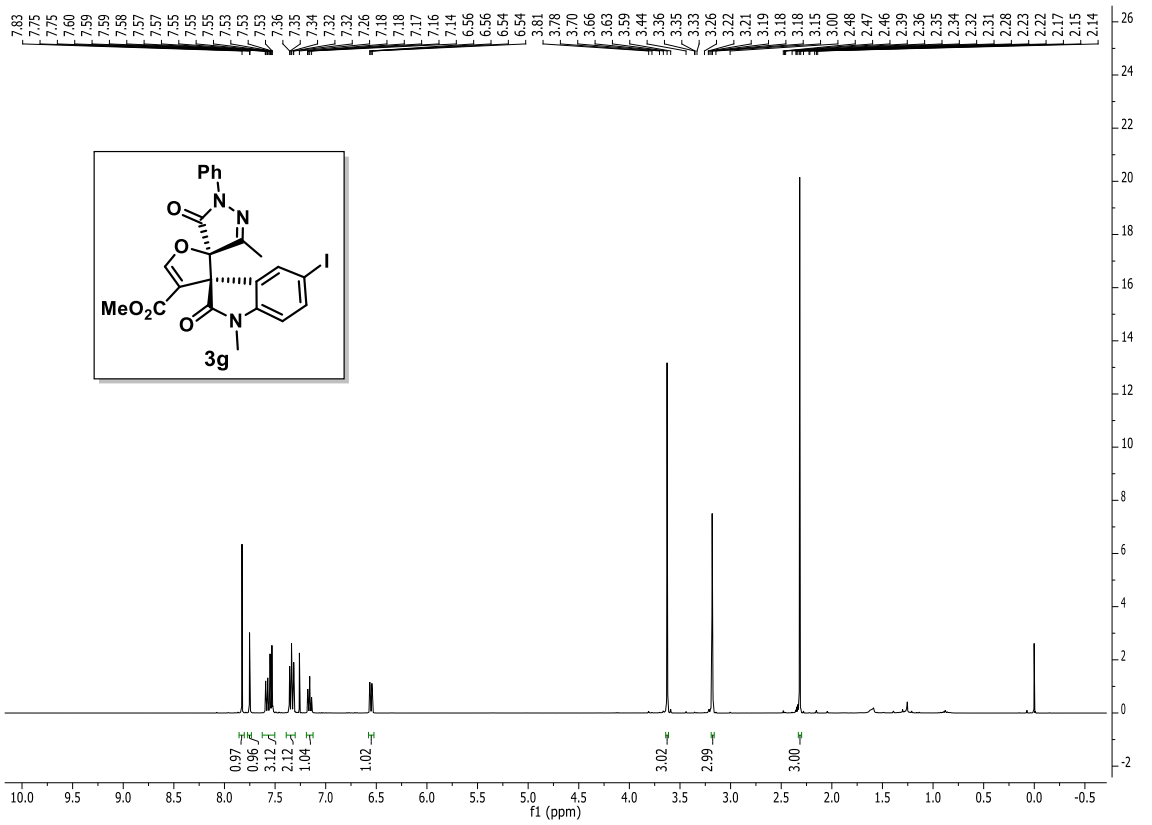

172.46
166.72
162.17
159.43
157.31
142.38
136.79
130.29
129.03
128.41
127.41
125.85
124.96
118.95
118.94
118.93
113.57
109.43
92.89
63.10
51.95
27.19
16.11
Ph
N
N
O
O
Cl
MeO2C
O
N
3e
f1 (ppm)

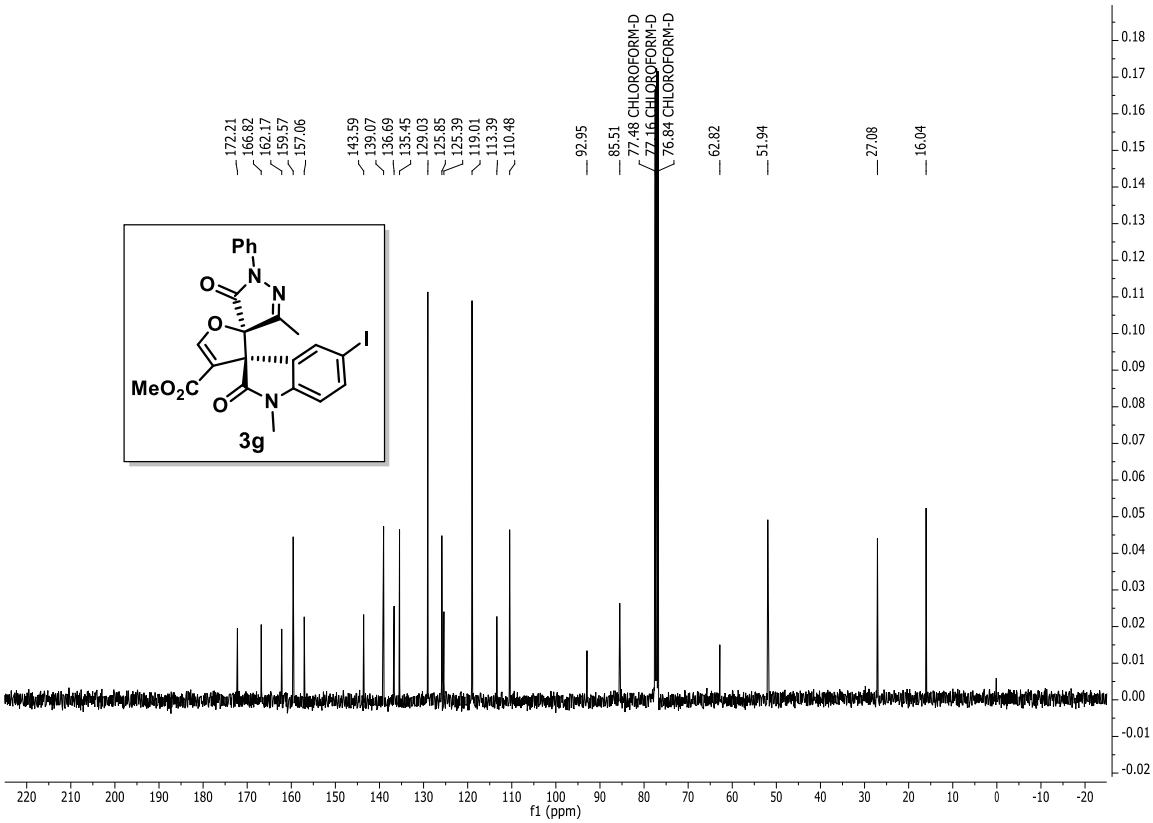

7.83
7.56
7.56
7.54
7.54
7.54
7.34
7.32
7.30
7.26
7.25
7.24
7.23
7.17
7.17
7.16
7.15
7.15
7.13
7.02
7.01
7.00
6.99
6.97
6.72
6.71
6.70
6.69
3.62
3.20
2.34
0.00
Ph
N
N
O
O
O
F
MeO2C
O
N
3f
0.96
1.99
2.04
1.03
0.97
1.00
0.99
3.00
3.01
3.00
f1 (ppm)

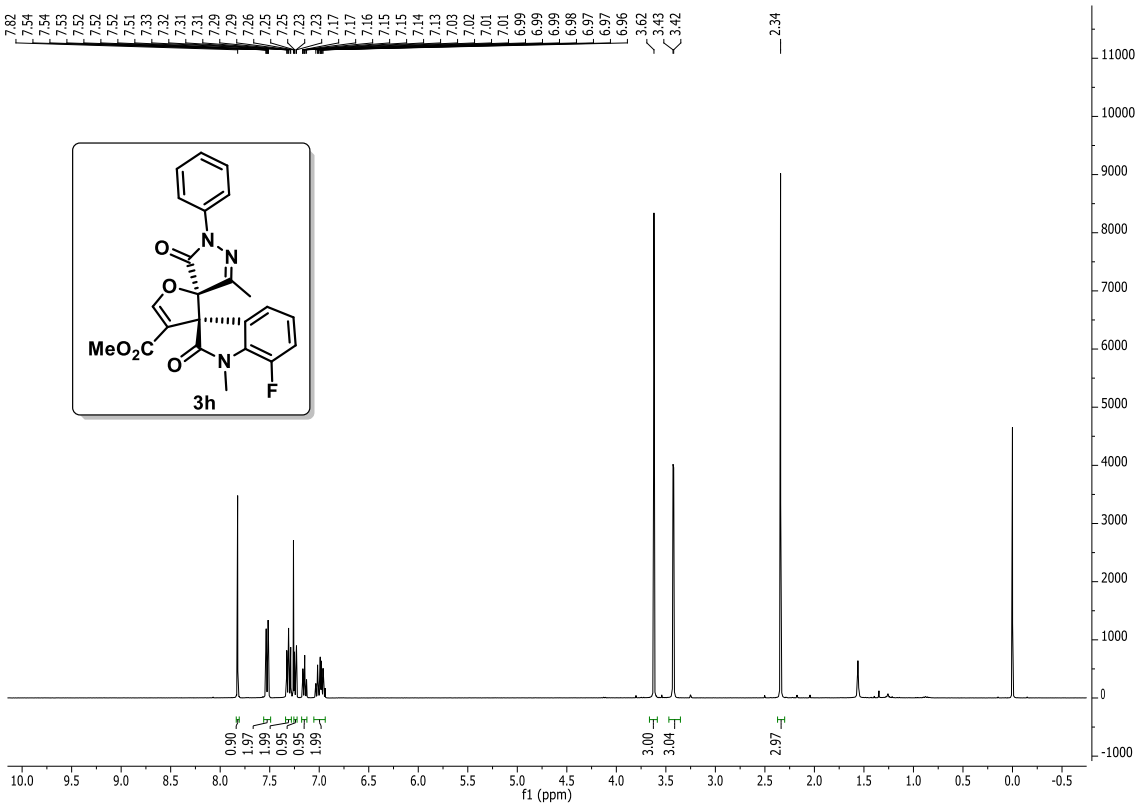

172.63
166.74
162.18
160.31
159.40
157.91
157.38
139.91
136.90
129.02
125.82
125.05
124.96
118.90
116.88
116.64
115.43
115.17
113.68
109.02
108.94
92.97
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
51.91
27.22
16.14
Ph
N
N
O
O
O
F
MeO2C
O
N
3f
f1 (ppm)

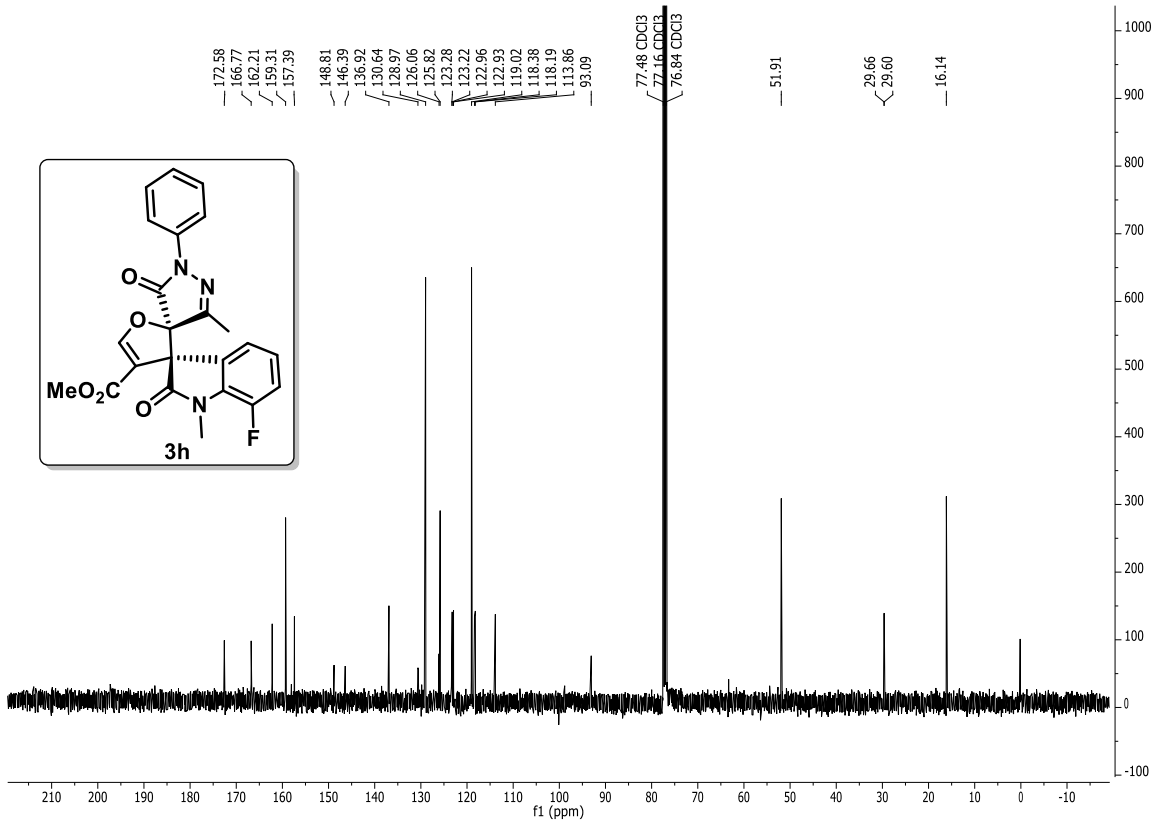


^{19}F-NMR Spectrum of **3f**

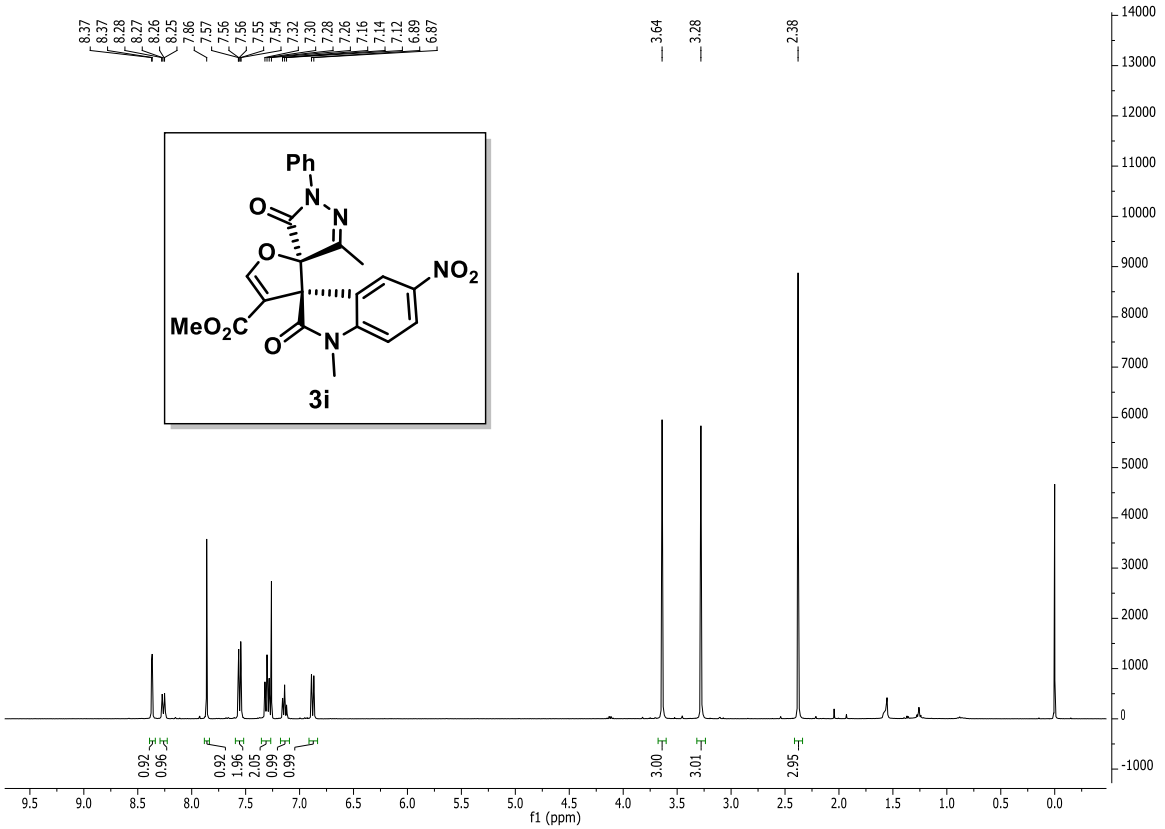

Ph
O
N
N
O
I
MeO2C
O
N
3g
f1 (ppm)

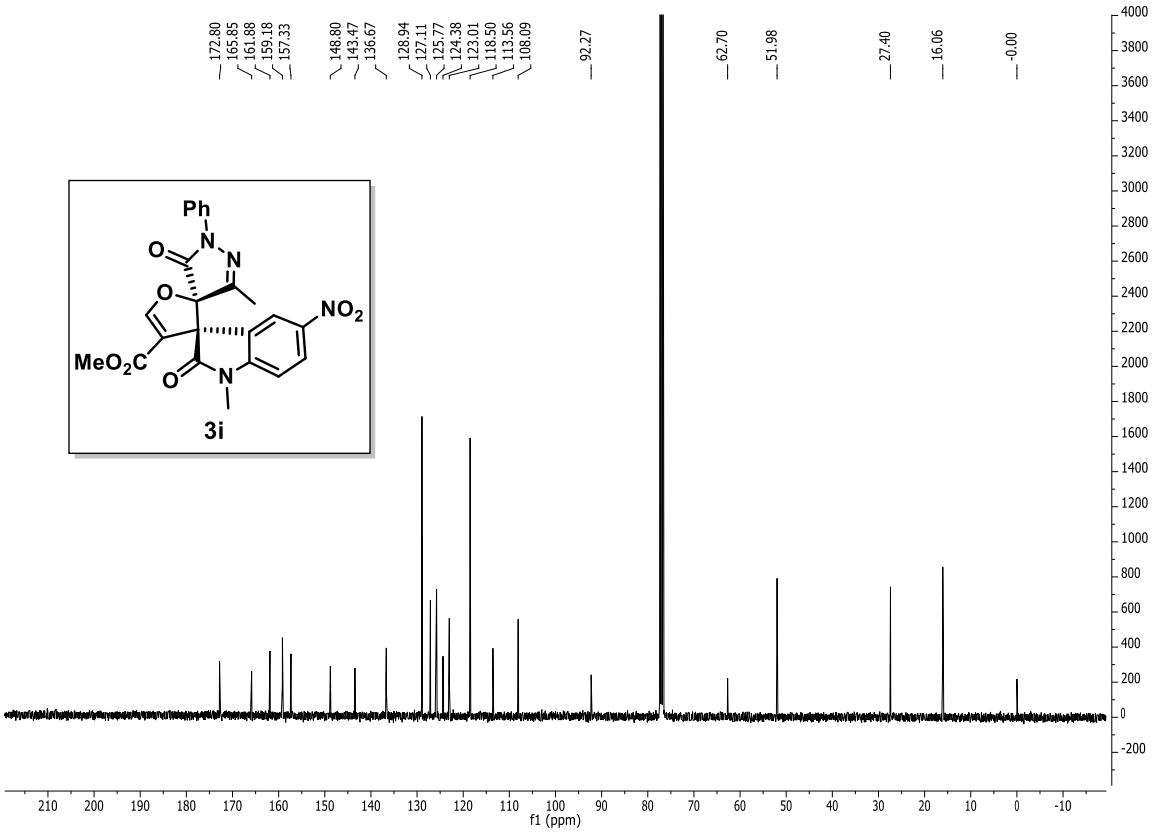

172.21
166.82
162.17
159.57
157.06
143.59
139.07
136.69
135.45
129.03
125.85
125.39
119.01
113.39
110.48
92.95
85.51
77.48 CHLOROFORM-D
77.16 CHLOROFORM-D
76.84 CHLOROFORM-D
62.82
51.94
27.08
16.04
Ph
O
N
N
O
I
MeO2C
O
N
3g
f1 (ppm)

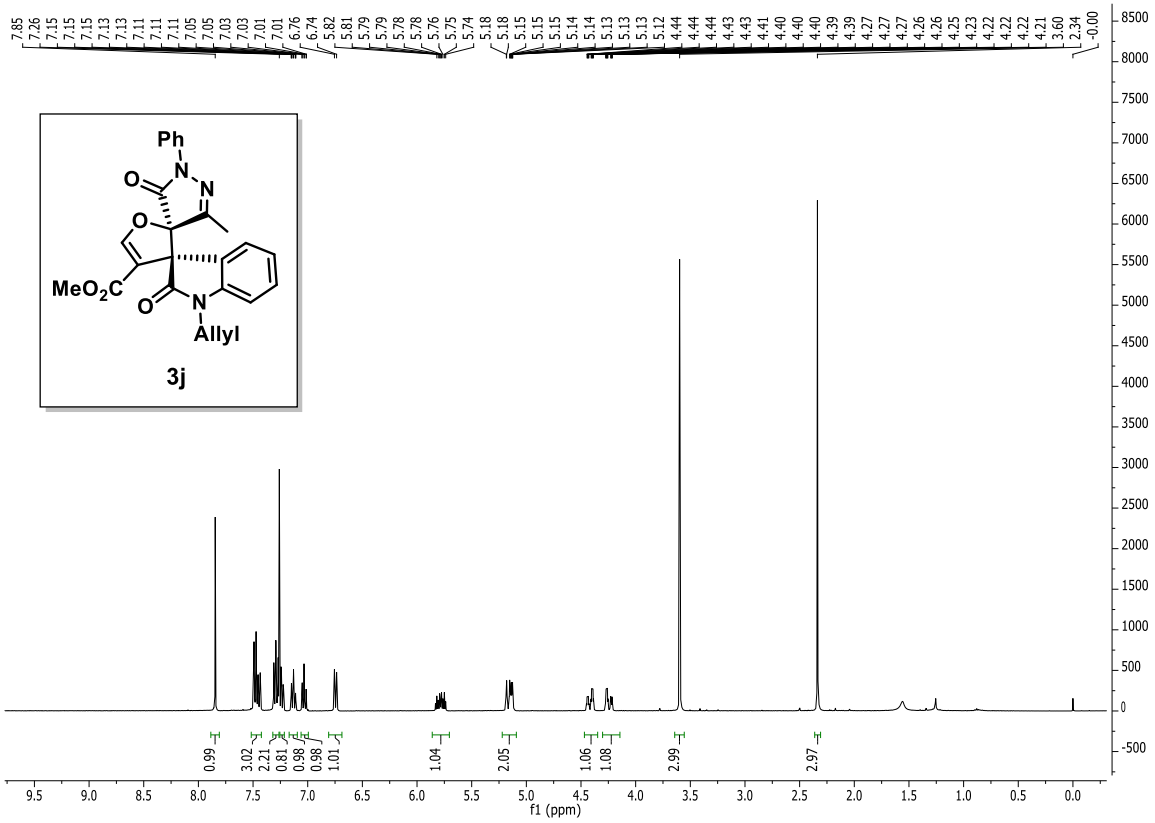

7.82
7.54
7.54
7.53
7.52
7.52
7.52
7.51
7.33
7.32
7.31
7.31
7.29
7.29
7.26
7.25
7.25
7.23
7.23
7.17
7.17
7.16
7.15
7.15
7.14
7.13
7.03
7.02
7.01
7.01
6.99
6.99
6.98
6.97
6.97
6.96
3.62
3.43
3.42
2.34
MeO2C
F
3h
0.90
1.97
1.99
0.95
0.95
1.99
3.00
3.04
2.97
f1 (ppm)

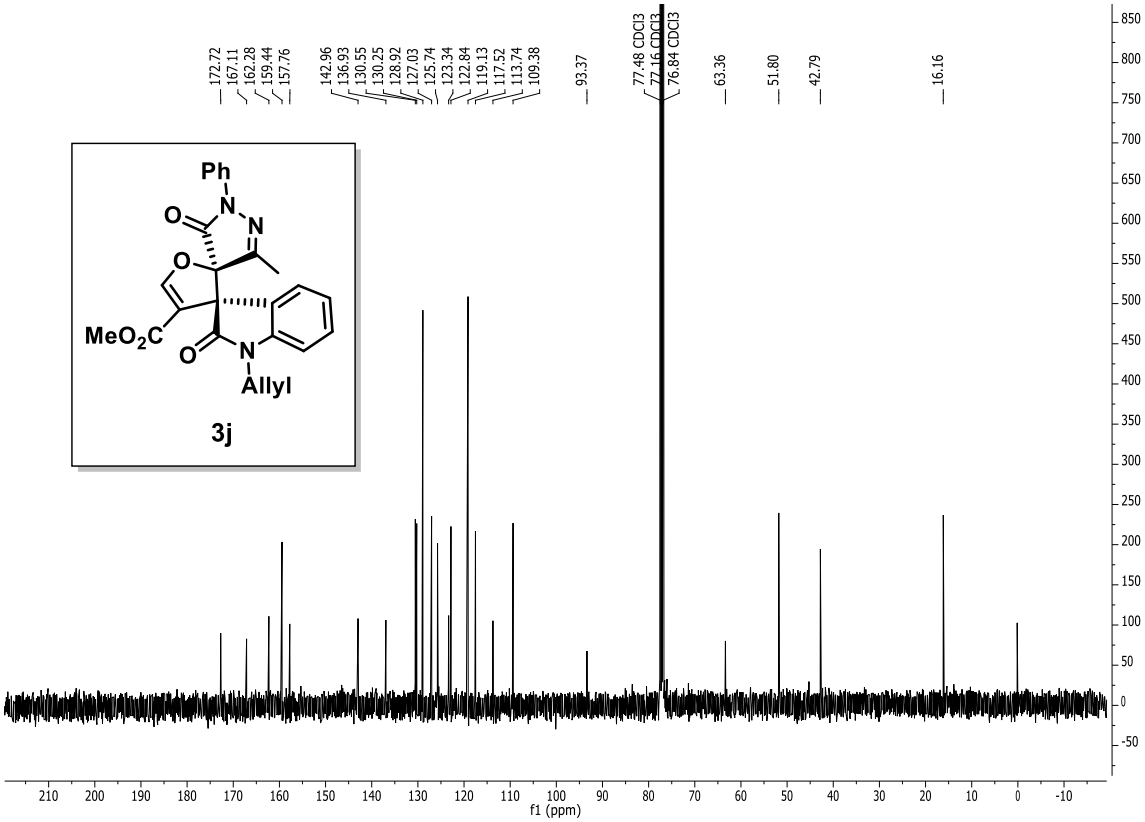

172.58
166.77
162.21
159.31
157.39
148.81
146.39
136.92
130.64
128.97
126.06
125.82
123.28
123.22
122.96
122.93
119.02
118.38
118.19
113.86
93.09
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
51.91
29.66
29.60
16.14
MeO2C
F
3h
f1 (ppm)

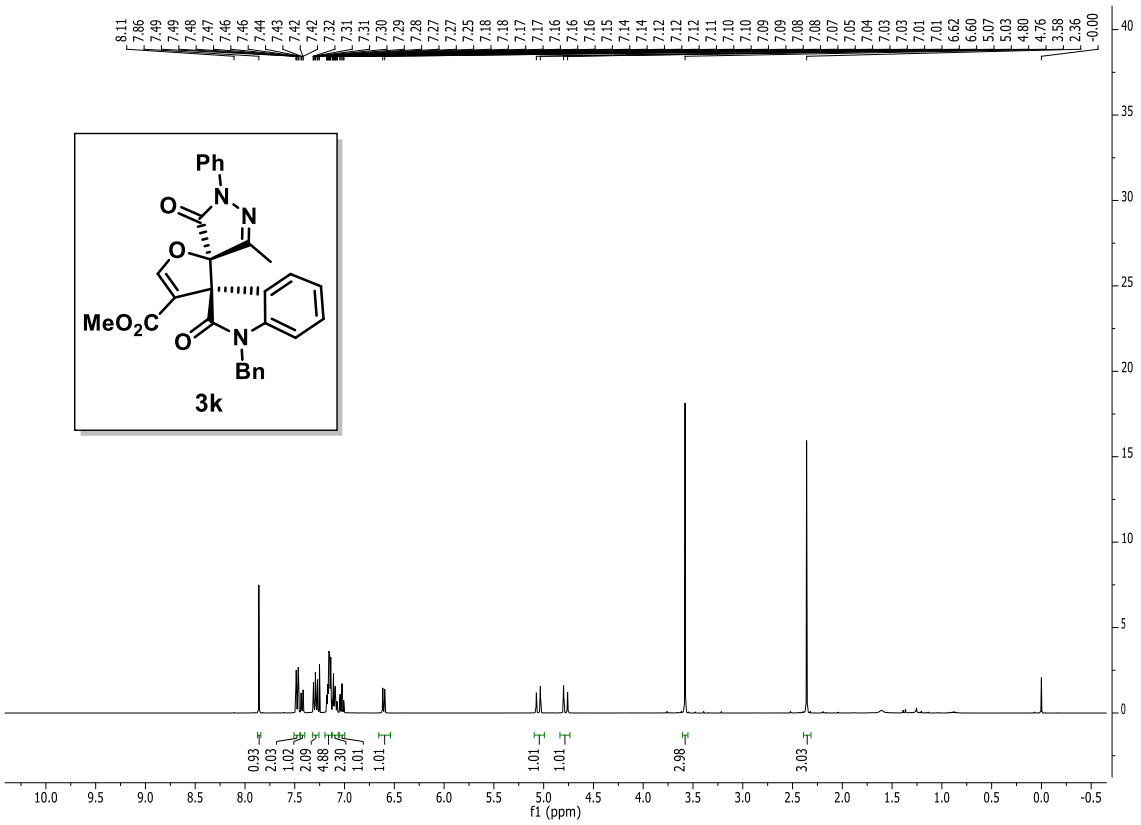
^{19}F-NMR Sprectrum of **3h**

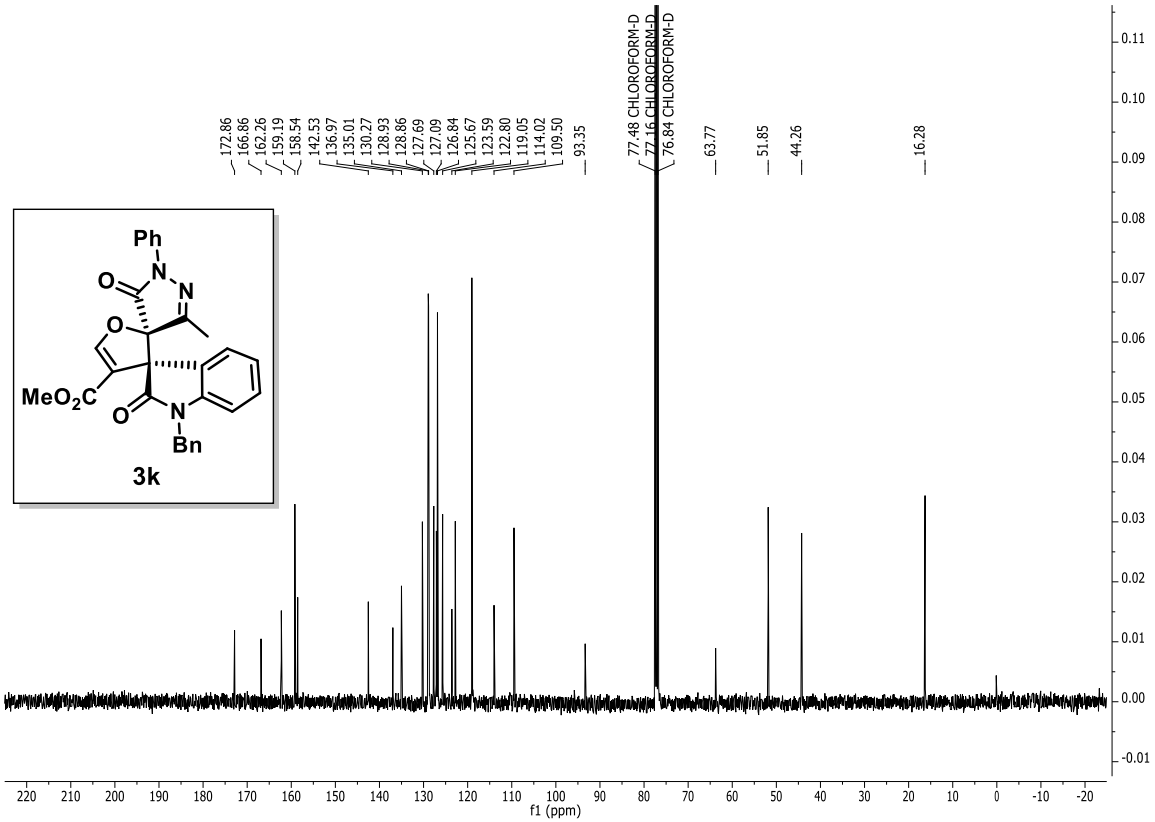

8.37
8.37
8.28
8.27
8.26
8.25
7.86
7.57
7.56
7.56
7.55
7.54
7.32
7.30
7.28
7.26
7.16
7.14
7.12
6.89
6.87
3.64
3.28
2.38
Ph
N
N
O
O
NO2
MeO2C
O
N
3i
0.92
0.96
0.92
1.96
2.05
0.99
0.99
3.00
3.01
2.95
f1 (ppm)

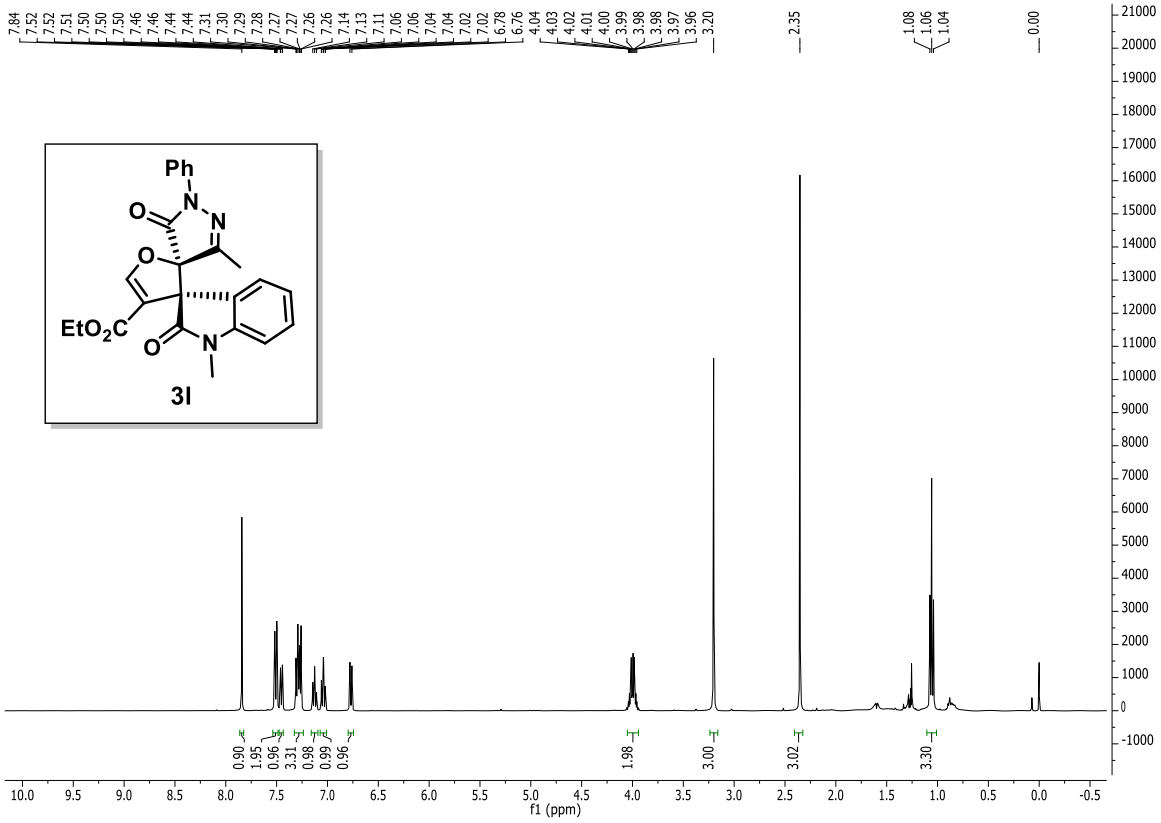

172.80
165.85
161.88
159.18
157.33
148.80
143.47
136.67
128.94
127.11
125.77
124.38
123.01
118.50
113.56
108.09
92.27
62.70
51.98
27.40
16.06
-0.00
Ph
N
N
O
O
NO2
MeO2C
O
N
3i
f1 (ppm)

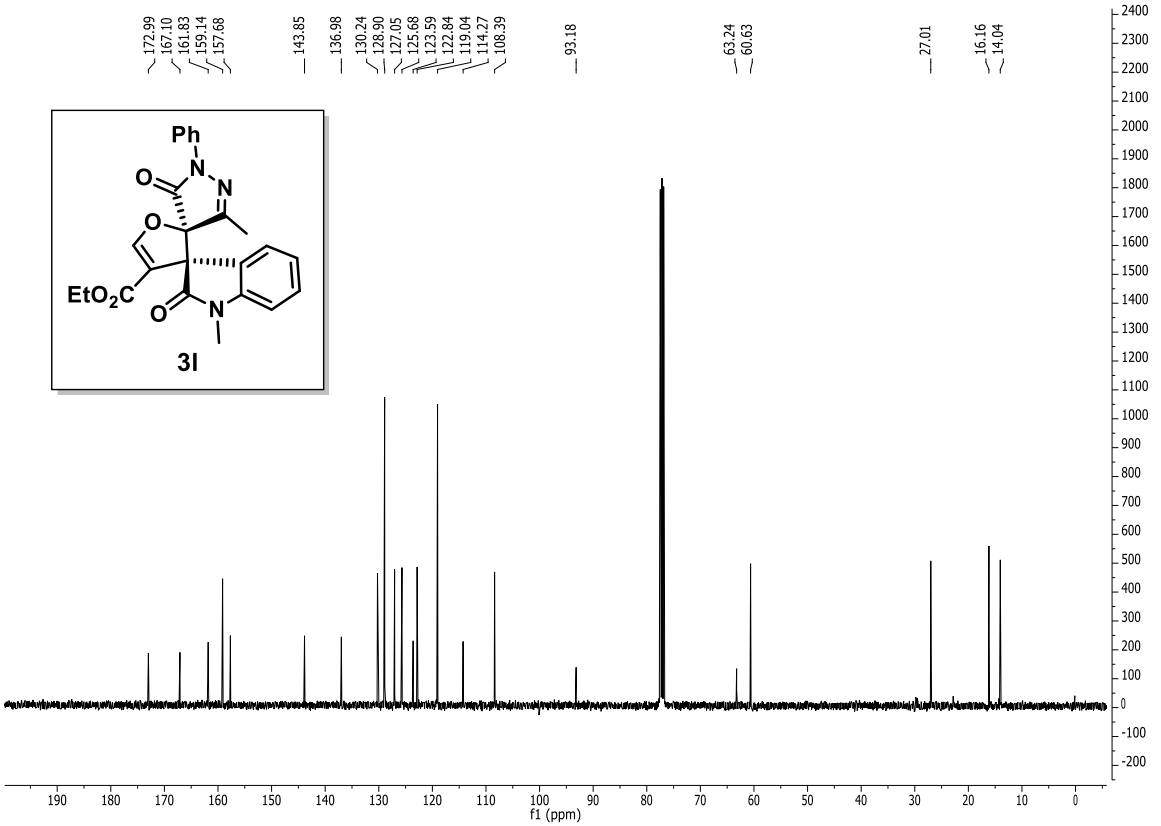

Ph
N
N
O
O
O
MeO2C
N
Allyl
3j
f1 (ppm)

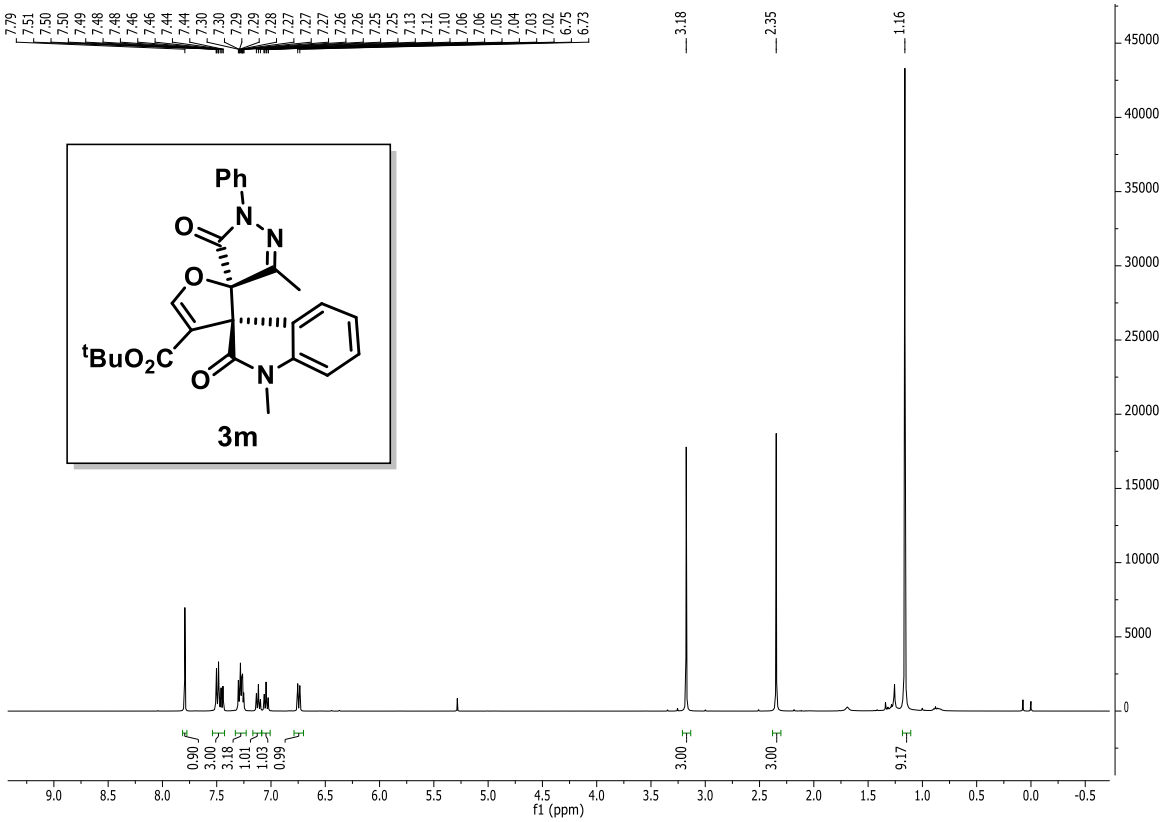

Ph
N
N
O
O
O
MeO2C
N
Allyl
3j
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
f1 (ppm)

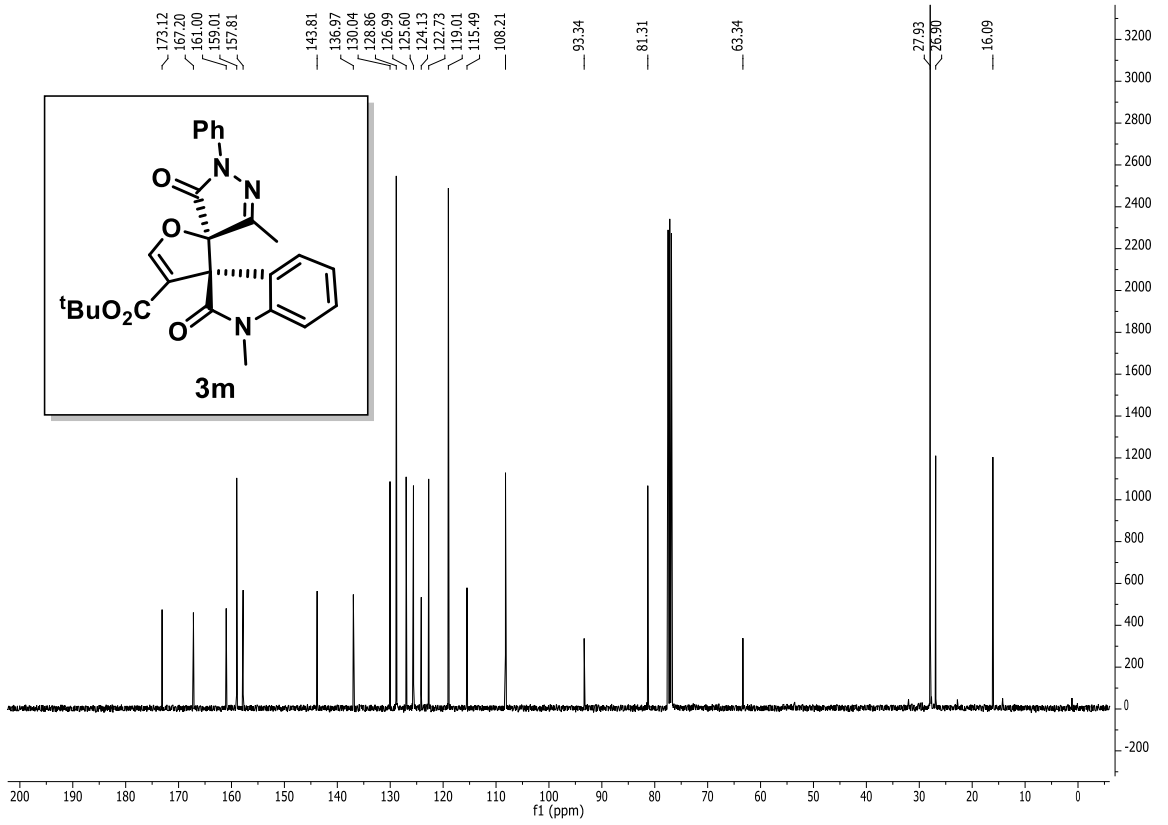

Ph
N
N
O
O
MeO2C
O
N
Bn
3k
f1 (ppm)

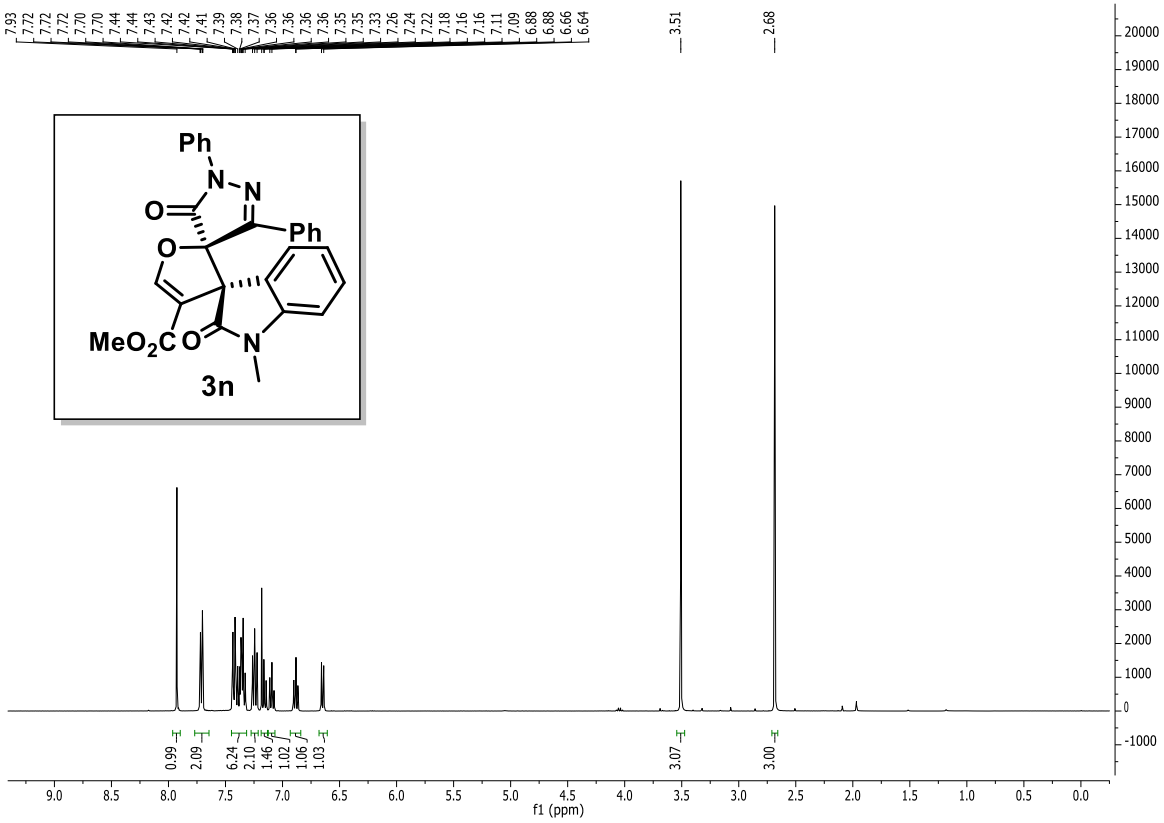

Ph
N
N
O
O
MeO2C
O
N
Bn
3k
77.48 CHLOROFORM-D
77.16 CHLOROFORM-D
76.84 CHLOROFORM-D
f1 (ppm)

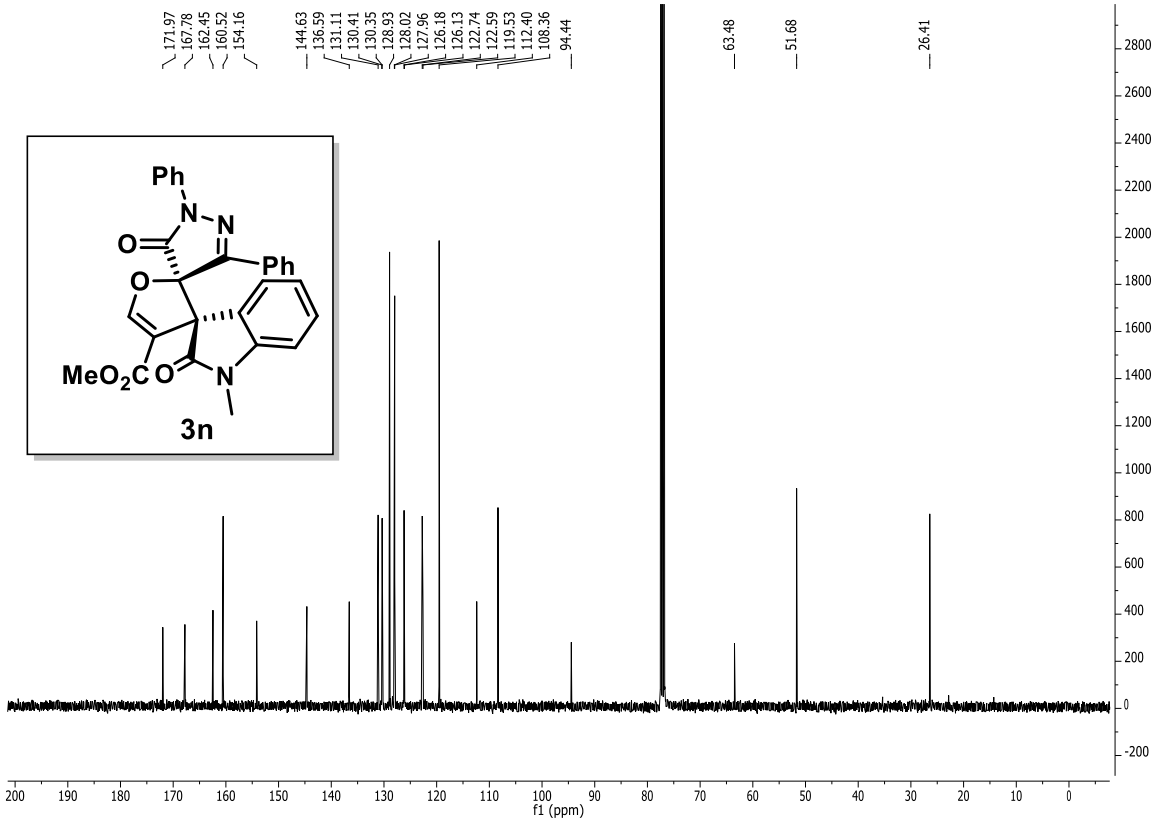

7.84 7.52 7.52 7.51 7.50 7.50 7.50 7.46 7.46 7.44 7.44 7.31 7.30 7.29 7.28 7.27 7.27 7.26 7.26 7.14 7.13 7.11 7.06 7.06 7.04 7.04 7.02 7.02 6.78 6.76 4.04 4.03 4.02 4.01 4.00 3.99 3.98 3.98 3.97 3.96 3.20 2.35 1.08 1.06 1.04 0.00
Ph
O
N
N
O
EtO2C
O
N
3l
0.90 1.95 0.96 3.31 0.98 0.99 0.96 1.98 3.00 3.02 3.30
f1 (ppm)

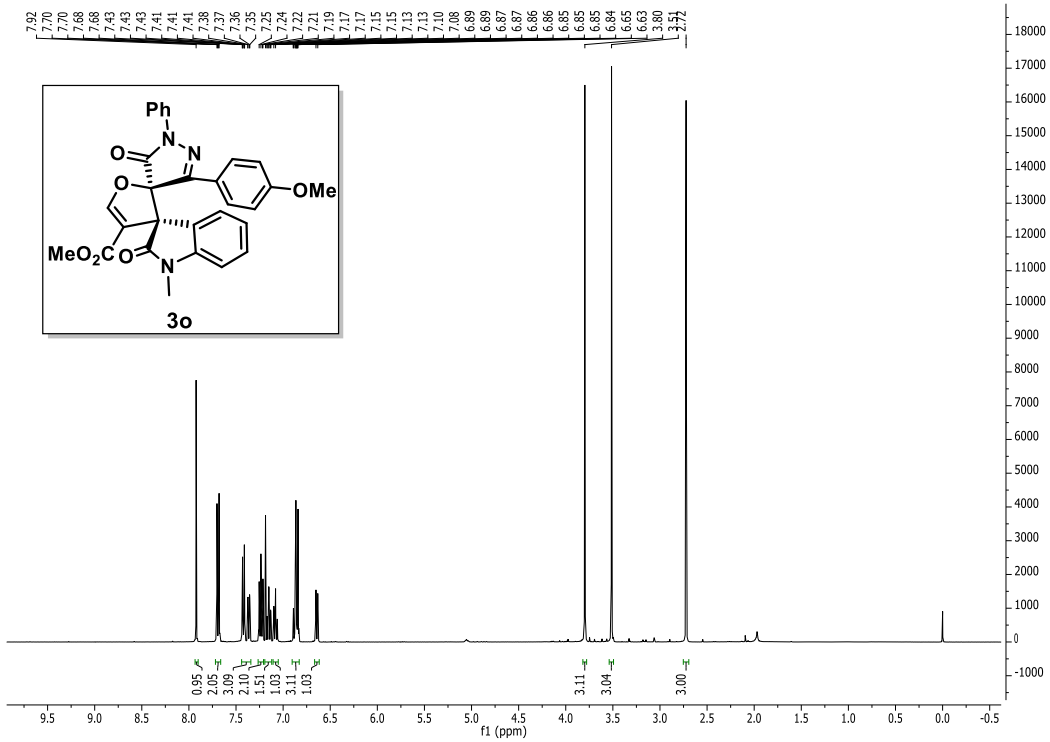

172.99 167.10 161.83 159.14 157.68 143.85 136.98 130.24 128.90 127.05 125.68 123.59 122.84 119.04 114.27 108.39 93.18 63.24 60.63 27.01 16.16 14.04
Ph
O
N
N
O
EtO2C
O
N
3l
f1 (ppm)

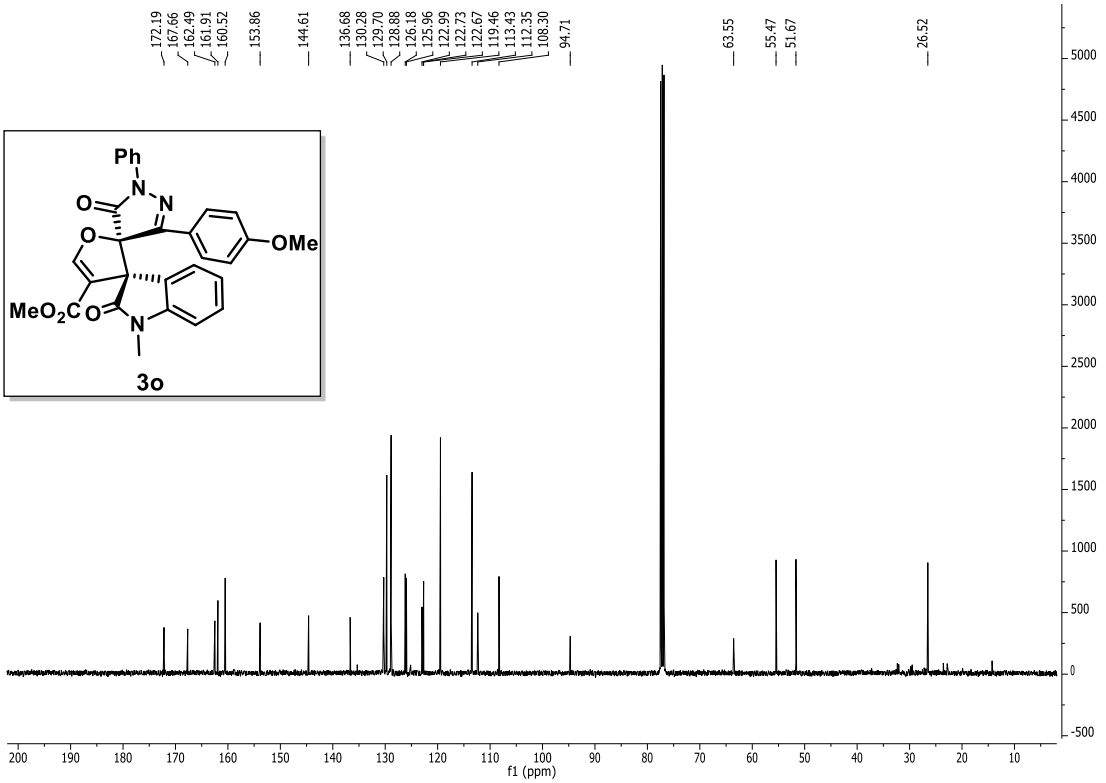

7.79
7.51
7.50
7.50
7.49
7.48
7.48
7.46
7.46
7.46
7.44
7.44
7.30
7.30
7.29
7.29
7.28
7.27
7.27
7.27
7.26
7.26
7.25
7.25
7.13
7.12
7.10
7.06
7.06
7.05
7.04
7.03
7.02
6.75
6.73
3.18
2.35
1.16
Ph
N
N
O
O
O
$^{t}BuO_2C$
O
N
3m
0.90
3.00
3.18
1.01
1.03
0.99
3.00
3.00
9.17
f1 (ppm)

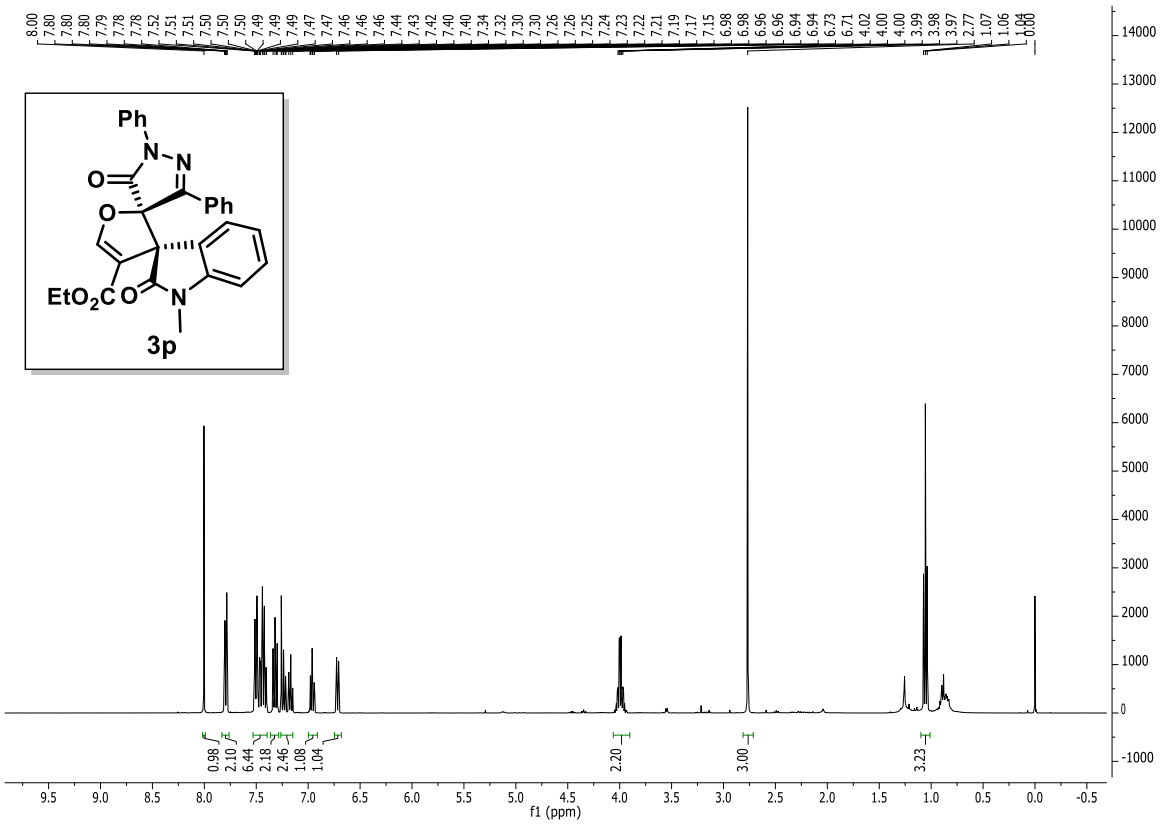

173.12
167.20
161.00
159.01
157.81
143.81
136.97
130.04
128.86
126.99
125.60
124.13
122.73
119.01
115.49
108.21
93.34
81.31
63.34
27.93
26.90
16.09
Ph
N
N
O
O
O
$^{t}BuO_2C$
O
N
3m
f1 (ppm)

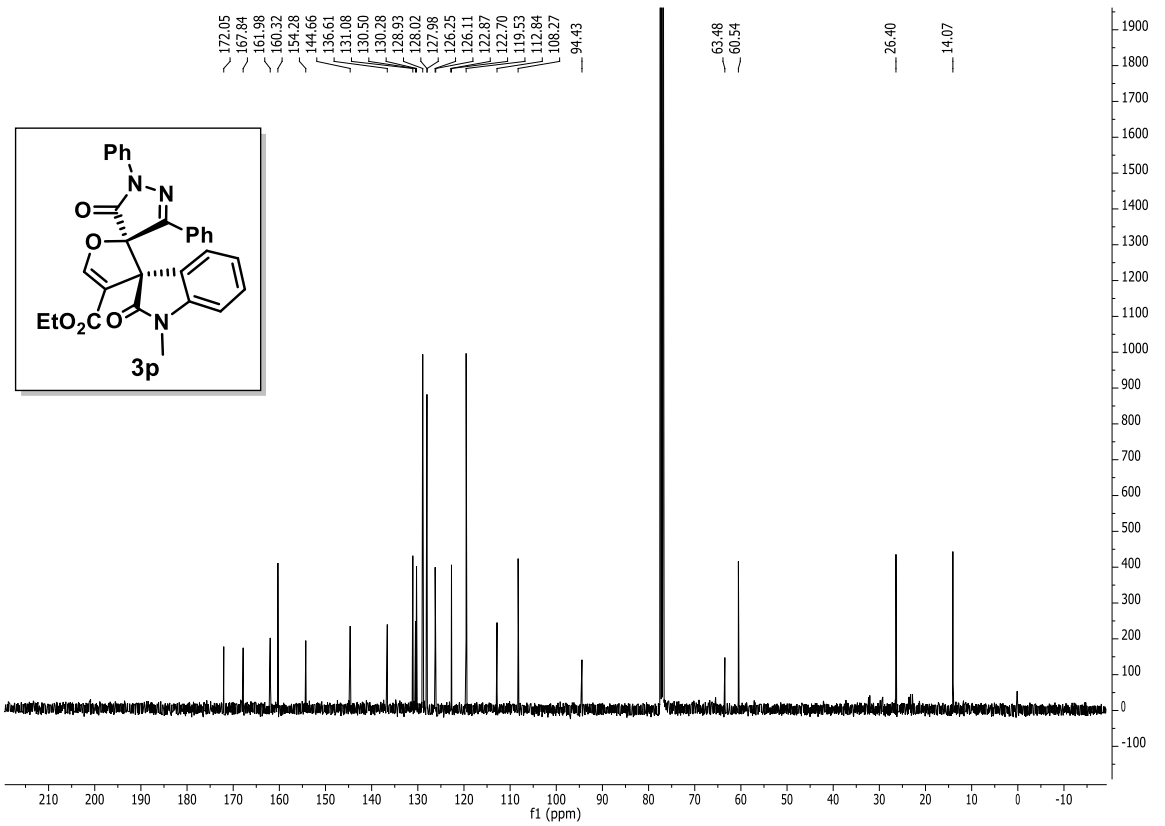

7.93
7.72
7.72
7.72
7.70
7.70
7.44
7.44
7.43
7.42
7.42
7.41
7.39
7.38
7.37
7.36
7.36
7.36
7.26
7.35
7.35
7.33
7.26
7.24
7.22
7.18
7.16
7.16
7.11
7.09
6.88
6.88
6.66
6.64
3.51
2.68
Ph
N
N
O
Ph
O
MeO2C O
N
3n
0.99
2.09
6.24
2.10
1.46
1.02
1.06
1.03
3.07
3.00
f1 (ppm)

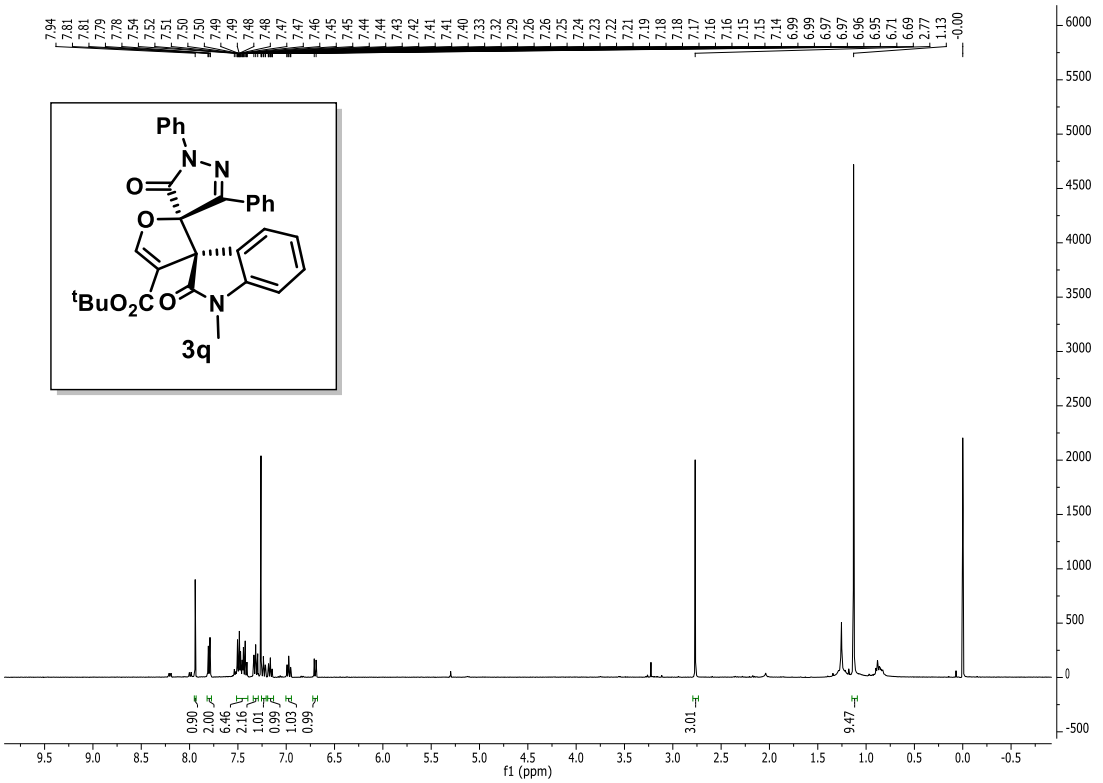

171.97
167.78
162.45
160.52
154.16
144.63
136.59
131.11
130.41
130.35
128.93
128.02
127.96
126.18
126.13
122.74
122.59
119.53
112.40
108.36
94.44
63.48
51.68
26.41
Ph
N
N
O
Ph
O
MeO2C O
N
3n
f1 (ppm)

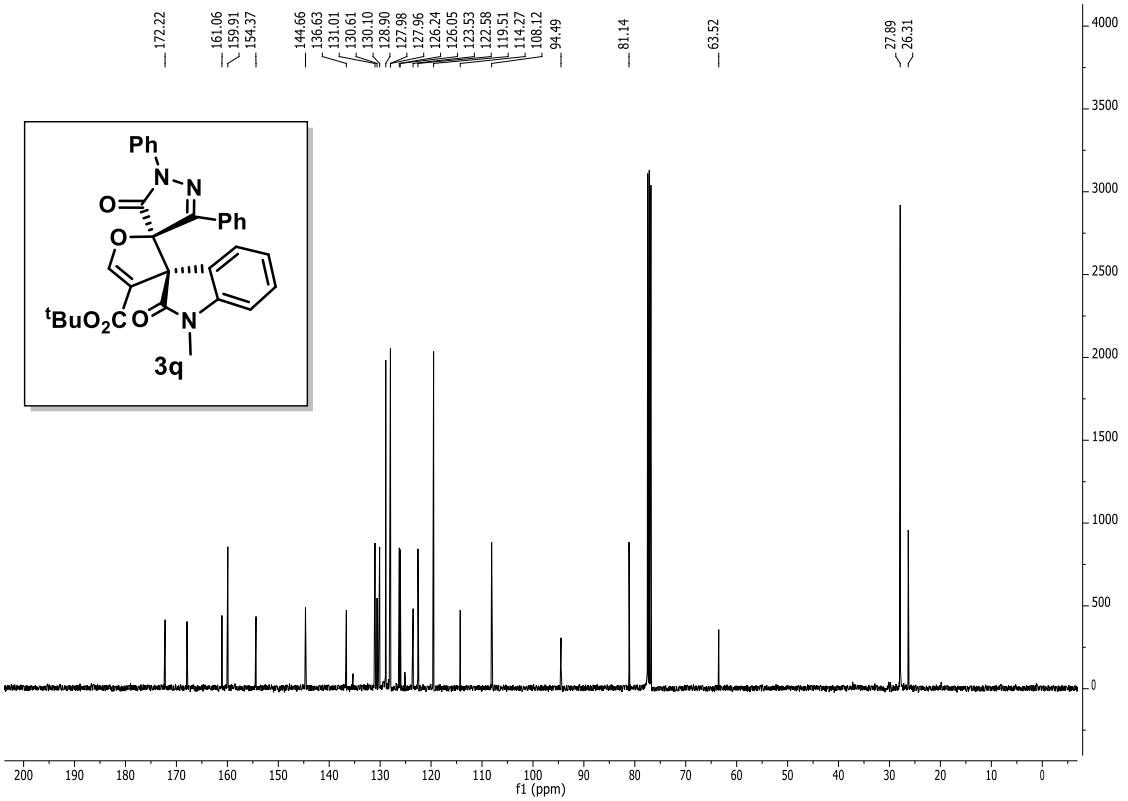

Ph
N
N
O
O
OMe
MeO2C
O
N
3o
f1 (ppm)

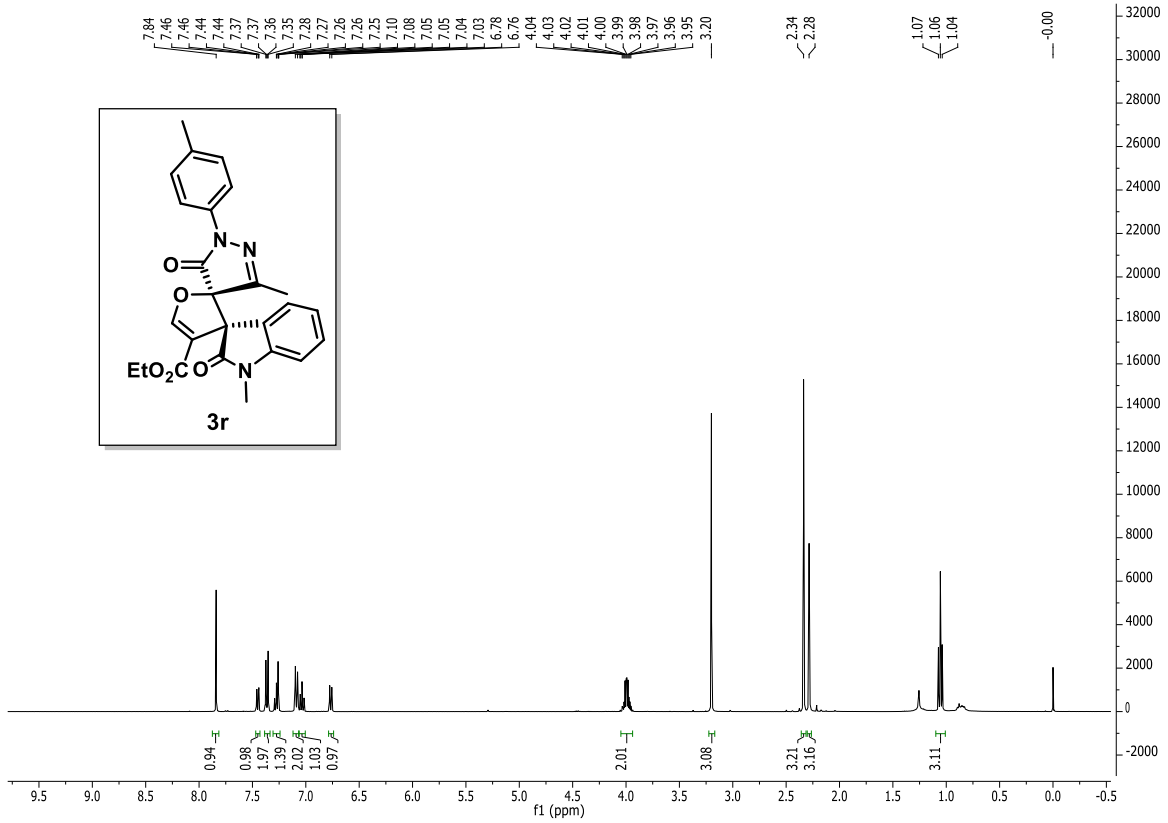

Ph
N
N
O
O
OMe
MeO2C
O
N
3o
f1 (ppm)

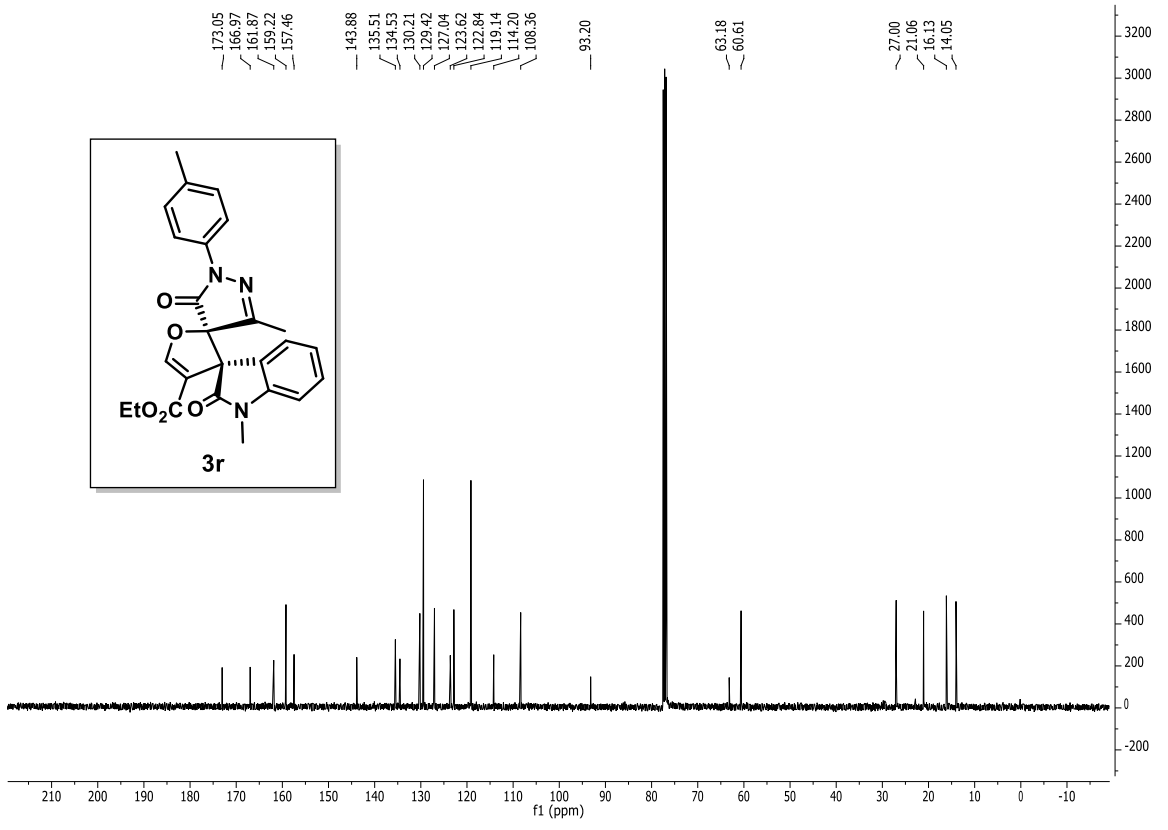

Ph
N
N
O
Ph
O
EtO2C
O
N
3p
f1 (ppm)

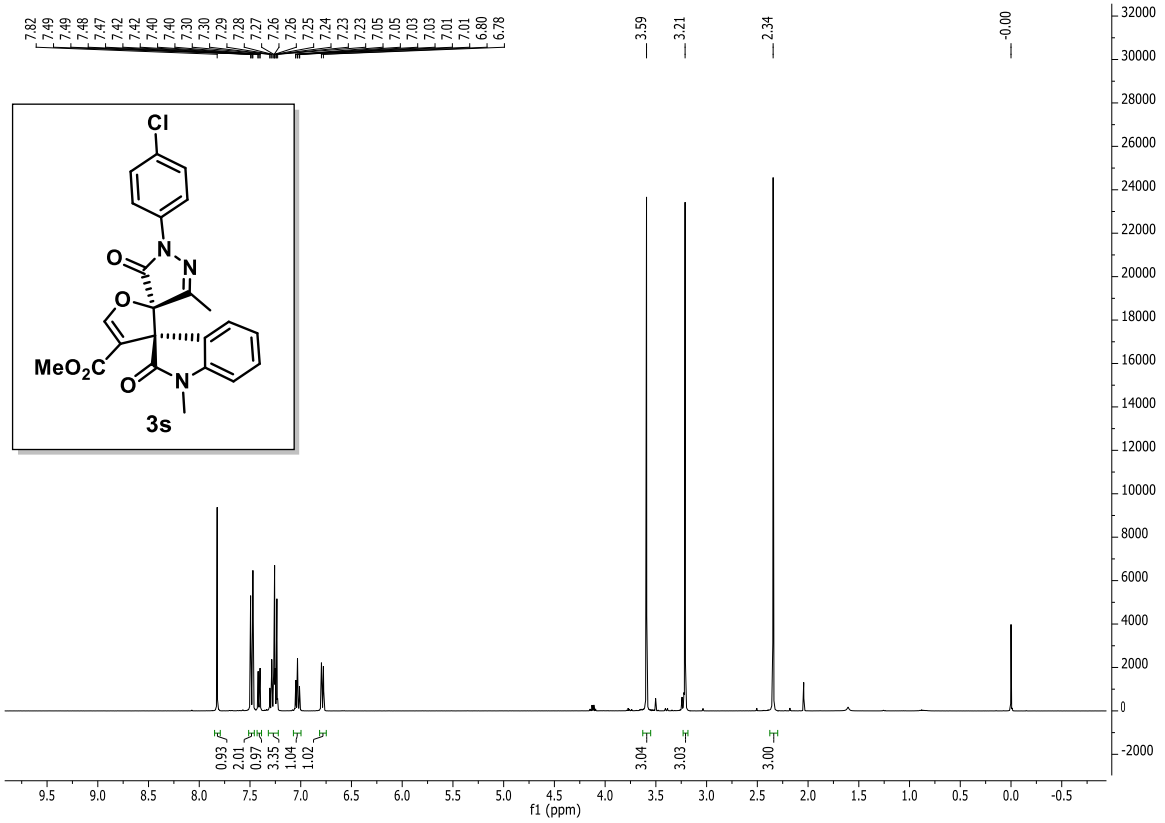

Ph
N
N
O
Ph
O
EtO2C
O
N
3p
f1 (ppm)

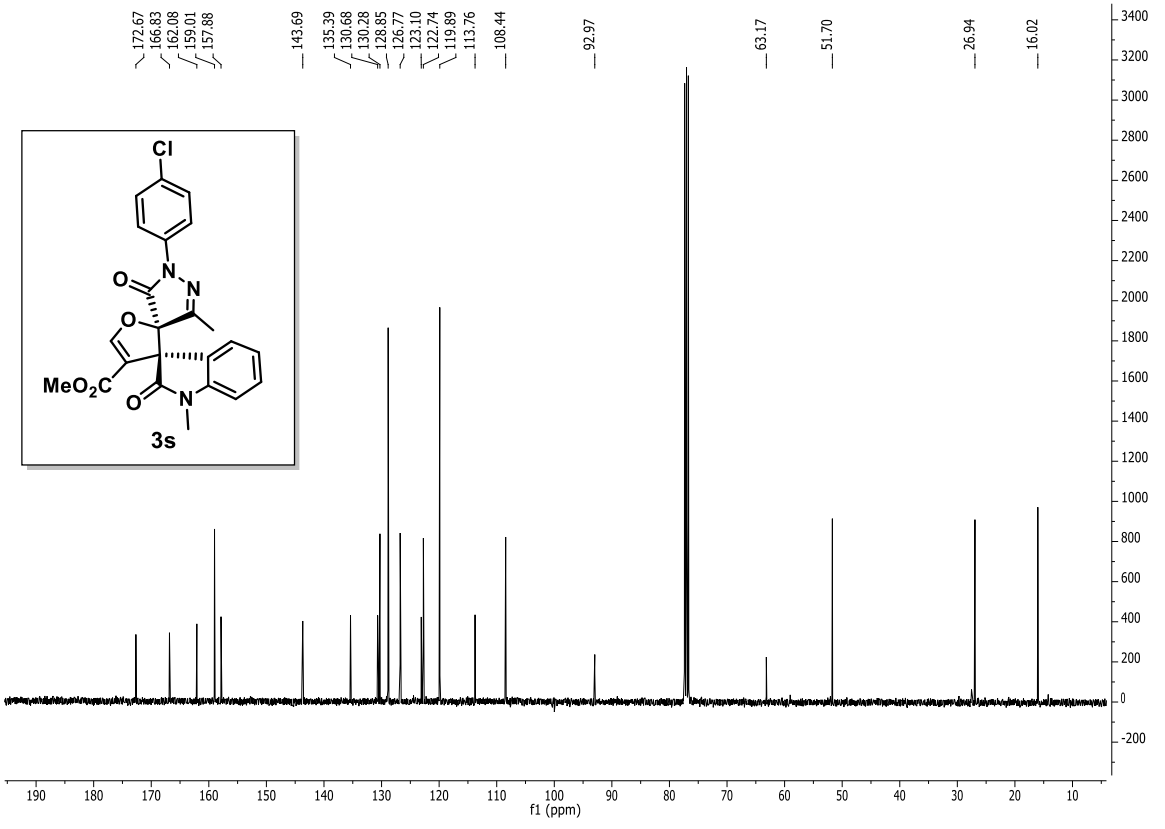

Ph
N
N
O
Ph
O
tBuO2C
O
N
3q
f1 (ppm)

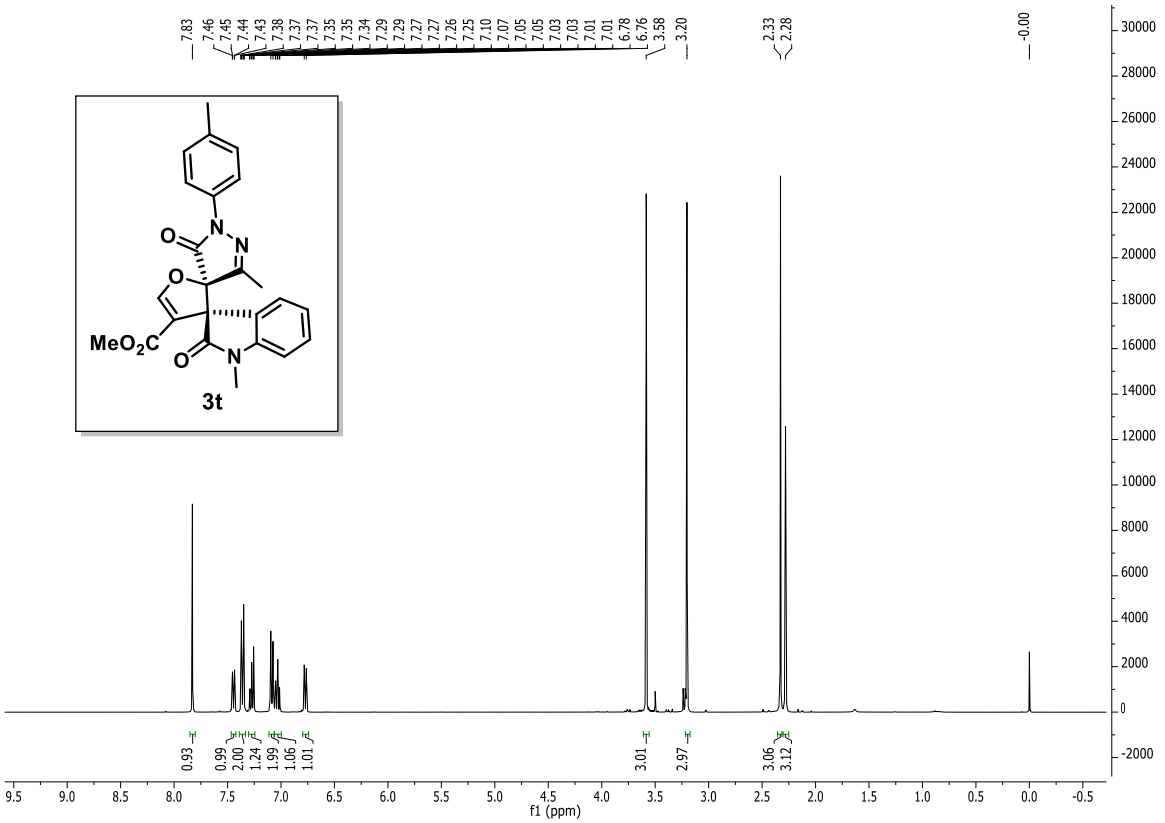

Ph
N
N
O
Ph
O
tBuO2C
O
N
3q
f1 (ppm)

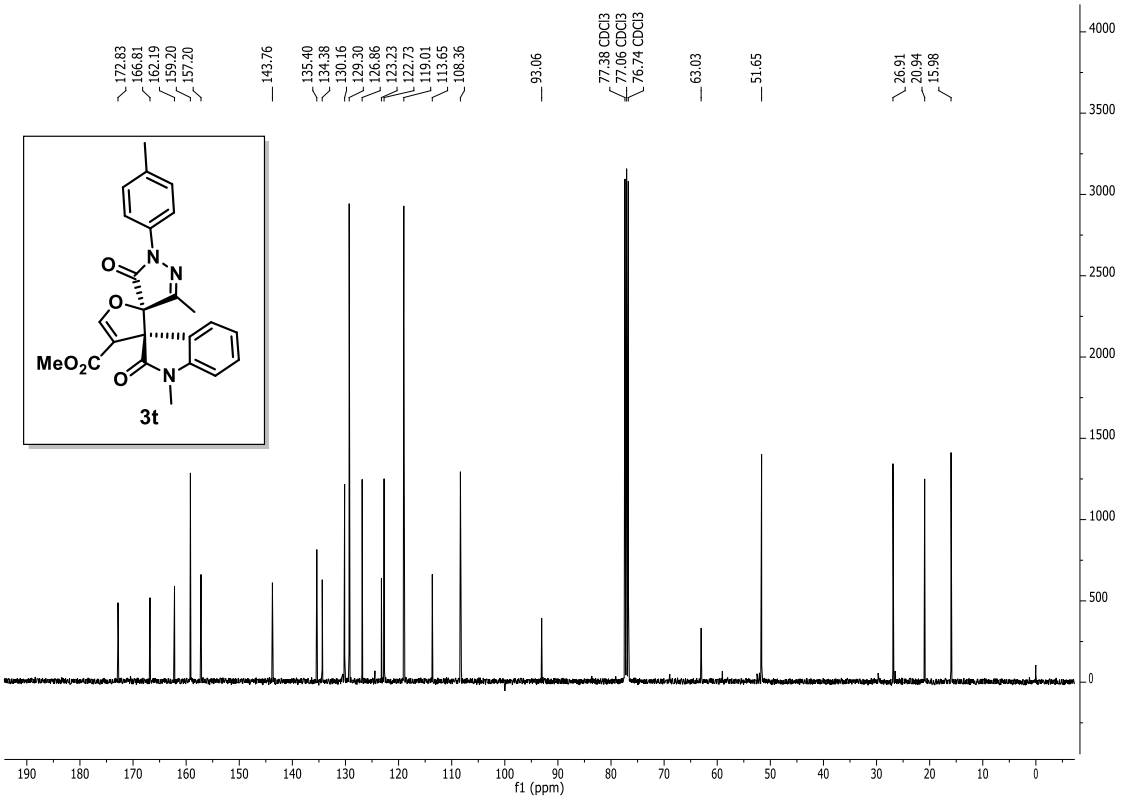

7.84 7.46 7.46 7.44 7.44 7.37 7.37 7.36 7.35 7.28 7.27 7.26 7.26 7.25 7.10 7.08 7.05 7.05 7.04 7.03 6.78 6.76 4.04 4.03 4.02 4.01 4.00 3.99 3.98 3.97 3.96 3.95 3.20 2.34 2.28 1.07 1.06 1.04 -0.00
EtO2C
3r
0.94 0.98 1.97 1.39 2.02 1.03 0.97 2.01 3.08 3.21 3.16 3.11
f1 (ppm)

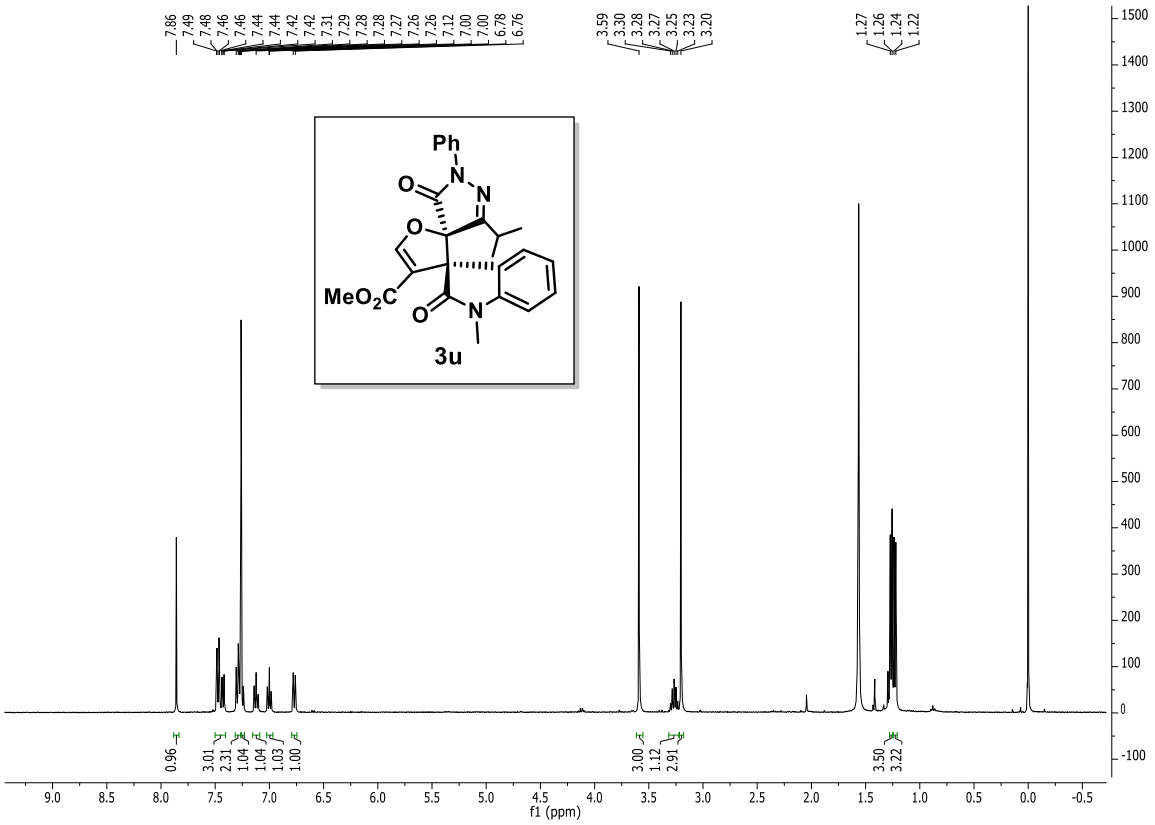

173.05 166.97 161.87 159.22 157.46 143.88 135.51 134.53 130.21 129.42 127.04 123.62 122.84 119.14 114.20 108.36 93.20 63.18 60.61 27.00 21.06 16.13 14.05
EtO2C
3r
f1 (ppm)

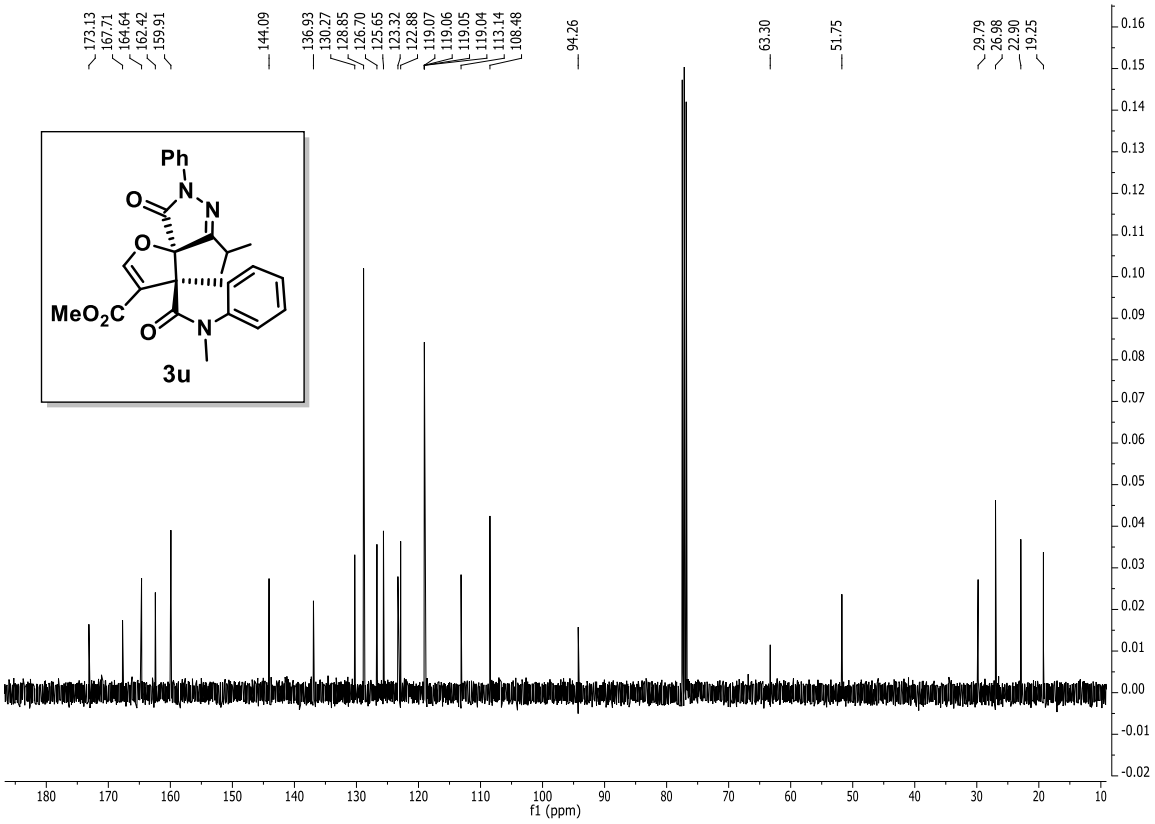

7.82
7.49
7.49
7.48
7.47
7.42
7.42
7.40
7.40
7.30
7.30
7.29
7.28
7.27
7.26
7.26
7.25
7.24
7.23
7.23
7.05
7.05
7.03
7.03
7.01
7.01
6.80
6.78
3.59
3.21
2.34
-0.00
Cl
N
N
O
O
O
MeO2C
O
N
3s
0.93
2.01
0.97
3.35
1.04
1.02
3.04
3.03
3.00
f1 (ppm)

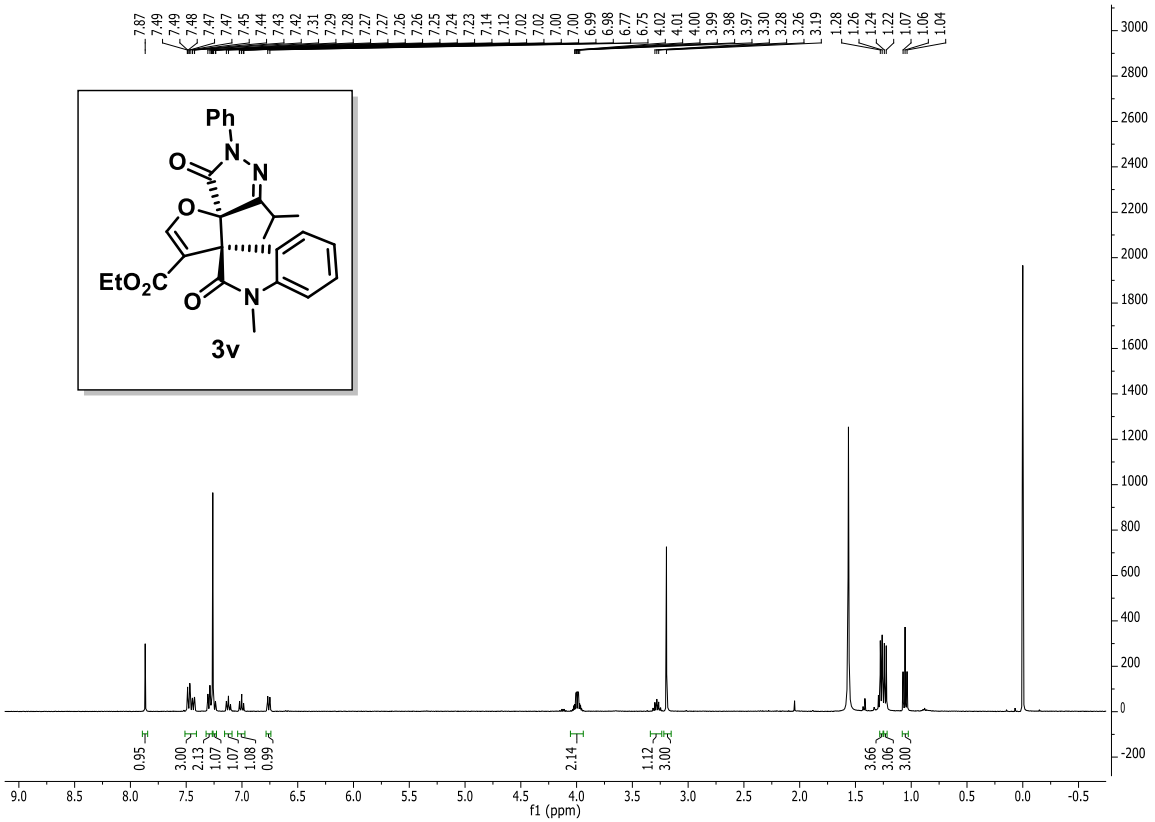

172.67
166.83
162.08
159.01
157.88
143.69
135.39
130.68
130.28
128.85
126.77
123.10
122.74
119.89
113.76
108.44
92.97
63.17
51.70
26.94
16.02
Cl
N
N
O
O
O
MeO2C
O
N
3s
f1 (ppm)

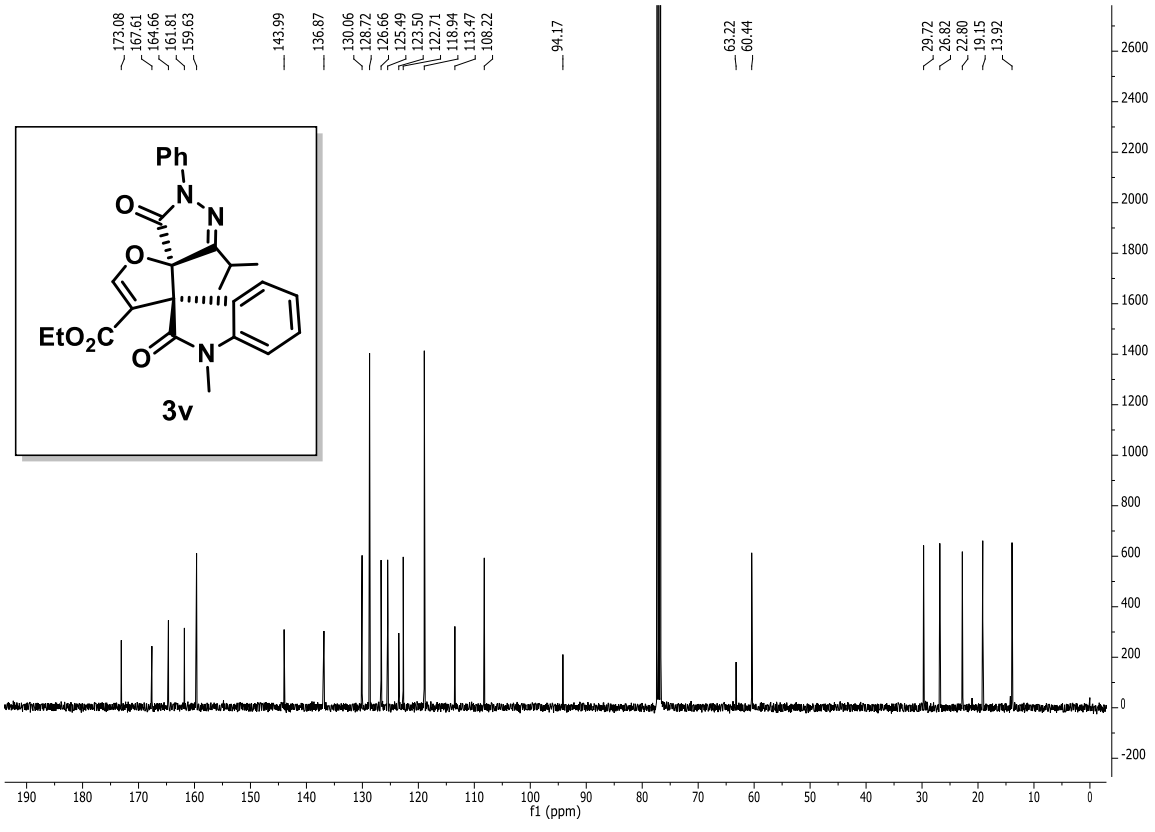

7.83
7.46
7.45
7.44
7.43
7.38
7.37
7.37
7.35
7.35
7.34
7.29
7.29
7.27
7.27
7.26
7.25
7.10
7.07
7.05
7.05
7.03
7.03
7.01
7.01
6.78
6.76
3.58
3.20
2.33
2.28
-0.00
0.93
0.99
2.00
1.24
1.99
1.06
1.01
3.01
2.97
3.06
3.12
f1 (ppm)
MeO2C
3t

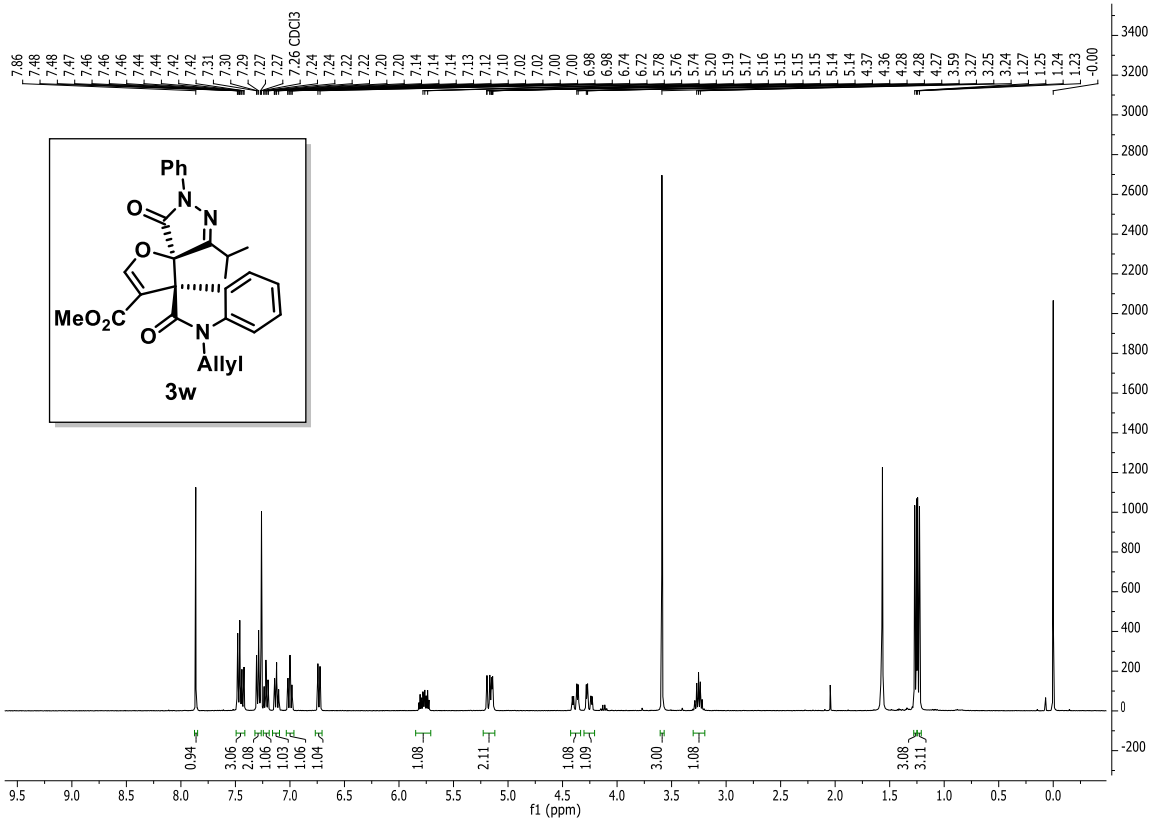

172.83
166.81
162.19
159.20
157.20
143.76
135.40
134.38
130.16
129.30
126.86
123.23
122.73
119.01
113.65
108.36
93.06
77.38 CDCl3
77.06 CDCl3
76.74 CDCl3
63.03
51.65
26.91
20.94
15.98
f1 (ppm)
MeO2C
3t

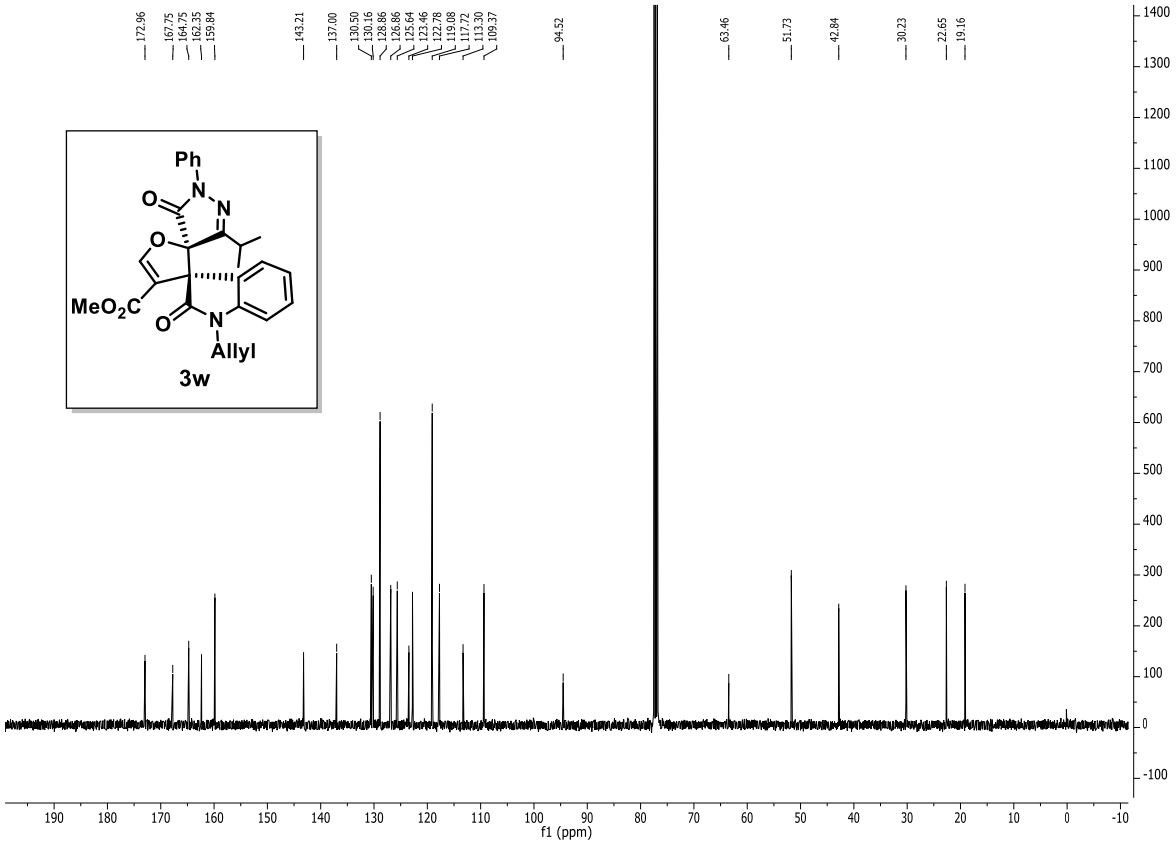

7.86
7.49
7.48
7.46
7.46
7.46
7.44
7.44
7.42
7.42
7.31
7.29
7.28
7.28
7.27
7.26
7.26
7.12
7.00
7.00
6.78
6.76
3.59
3.30
3.28
3.27
3.25
3.23
3.20
1.27
1.26
1.24
1.22
Ph
N
N
O
O
MeO2C
O
N
3u
0.96
3.01
2.31
1.04
1.04
1.03
1.00
3.00
1.12
2.91
3.50
3.22
f1 (ppm)

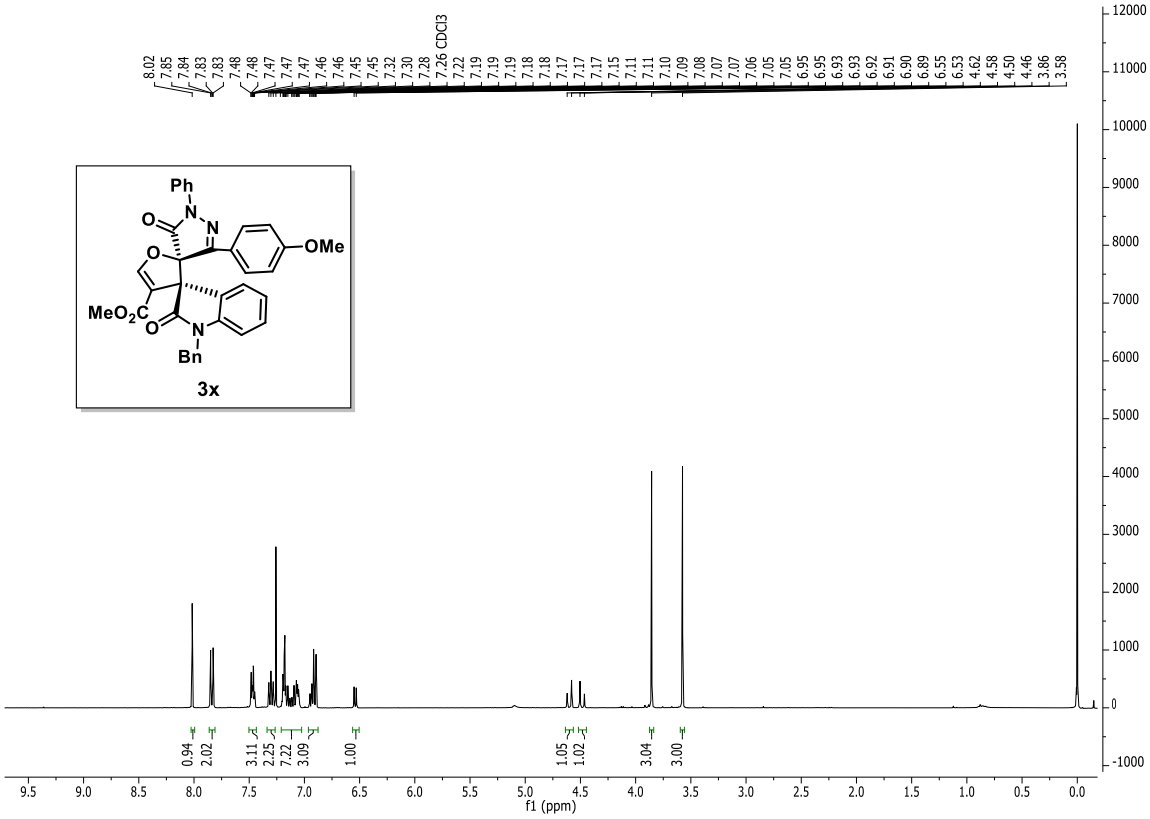

173.13
167.71
164.64
162.42
159.91
144.09
136.93
130.27
128.85
126.70
125.65
123.32
122.88
119.07
119.06
119.05
119.04
113.14
108.48
94.26
63.30
51.75
29.79
26.98
22.90
19.25
Ph
N
N
O
O
MeO2C
O
N
3u
f1 (ppm)

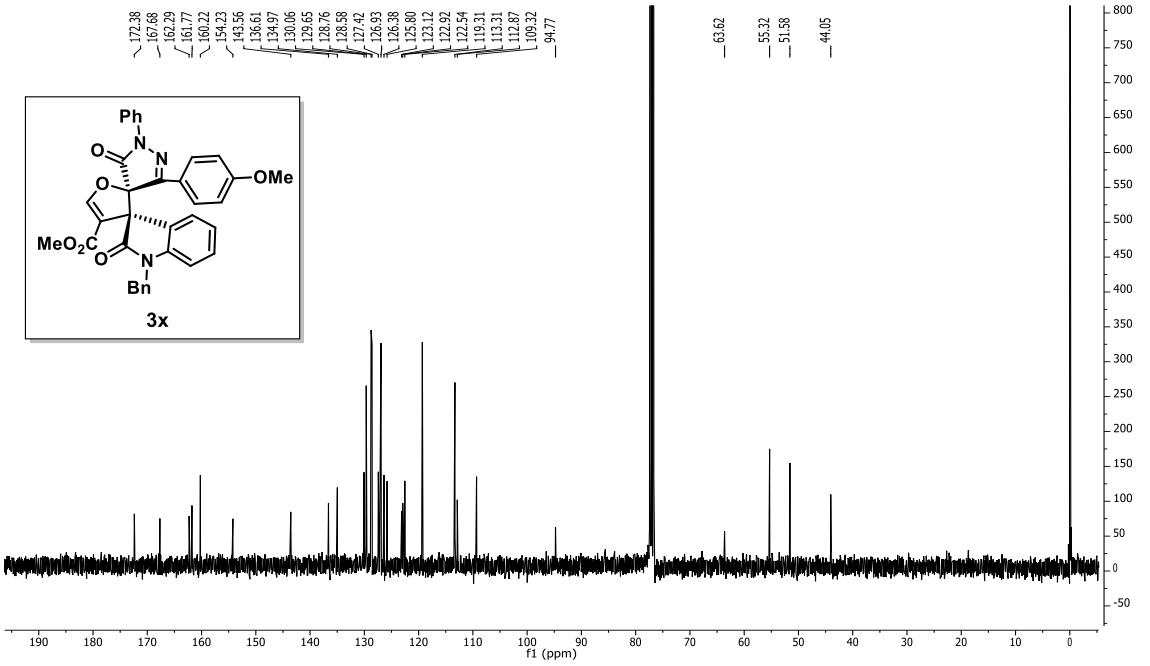

7.87
7.49
7.49
7.48
7.47
7.47
7.47
7.45
7.44
7.43
7.42
7.31
7.29
7.28
7.27
7.27
7.26
7.26
7.25
7.24
7.23
7.14
7.12
7.02
7.02
7.00
7.00
6.99
6.98
6.77
6.75
4.02
4.01
4.00
3.99
3.98
3.97
3.30
3.28
3.26
3.19
1.28
1.26
1.24
1.22
1.07
1.06
1.04
Ph
N
N
O
O
O
EtO2C
O
N
3v
0.95
3.00
2.13
1.07
1.07
1.08
0.99
2.14
1.12
3.00
3.66
3.06
3.00
f1 (ppm)

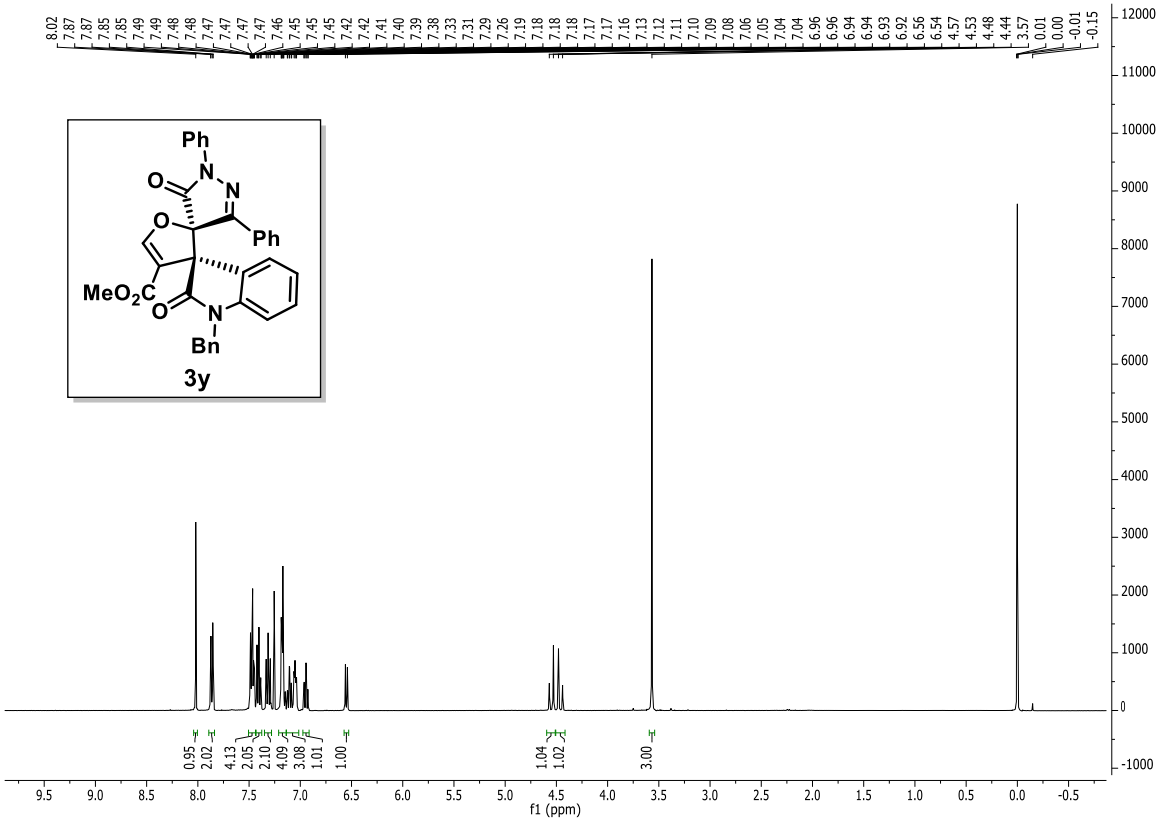

173.08
167.61
164.66
161.81
159.63
143.99
136.87
130.06
128.72
126.66
125.49
123.50
122.71
118.94
113.47
108.22
94.17
63.22
60.44
29.72
26.82
22.80
19.15
13.92
Ph
N
N
O
O
O
EtO2C
O
N
3v
f1 (ppm)

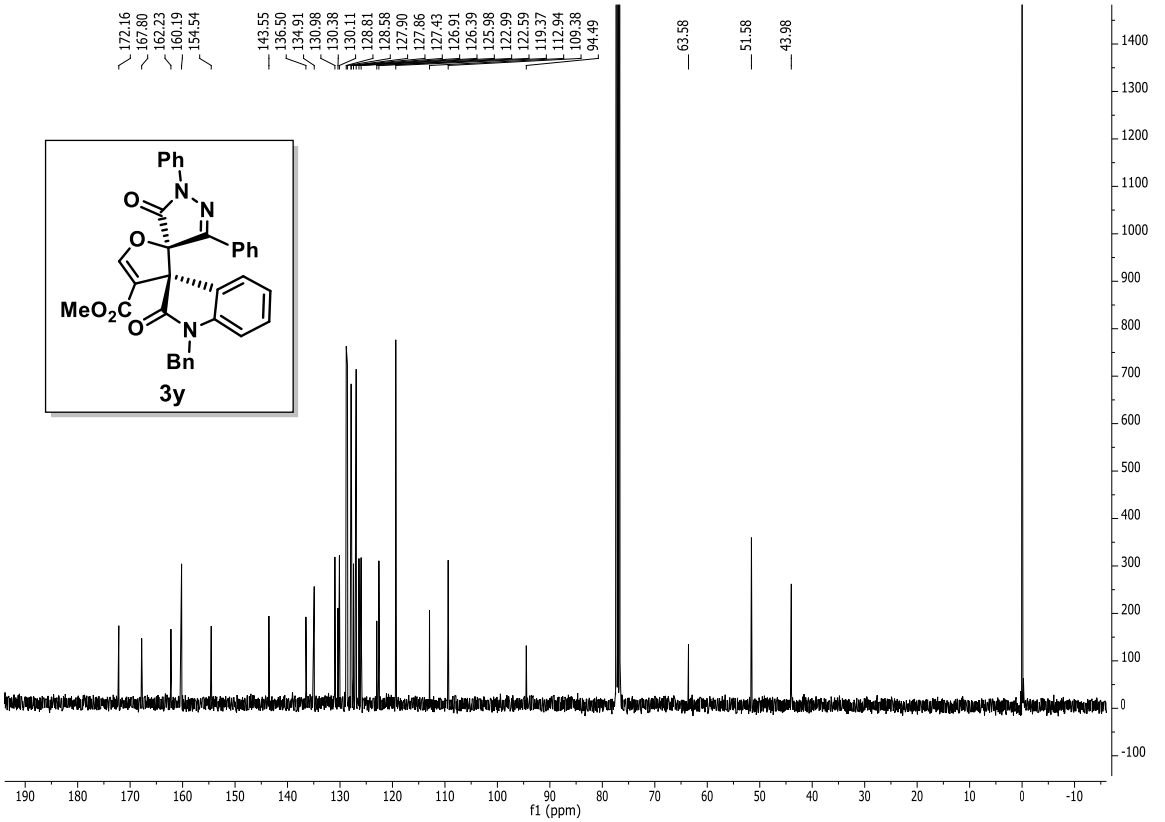

Ph
N
N
O
O
O
MeO2C
N
Allyl
3w
f1 (ppm)

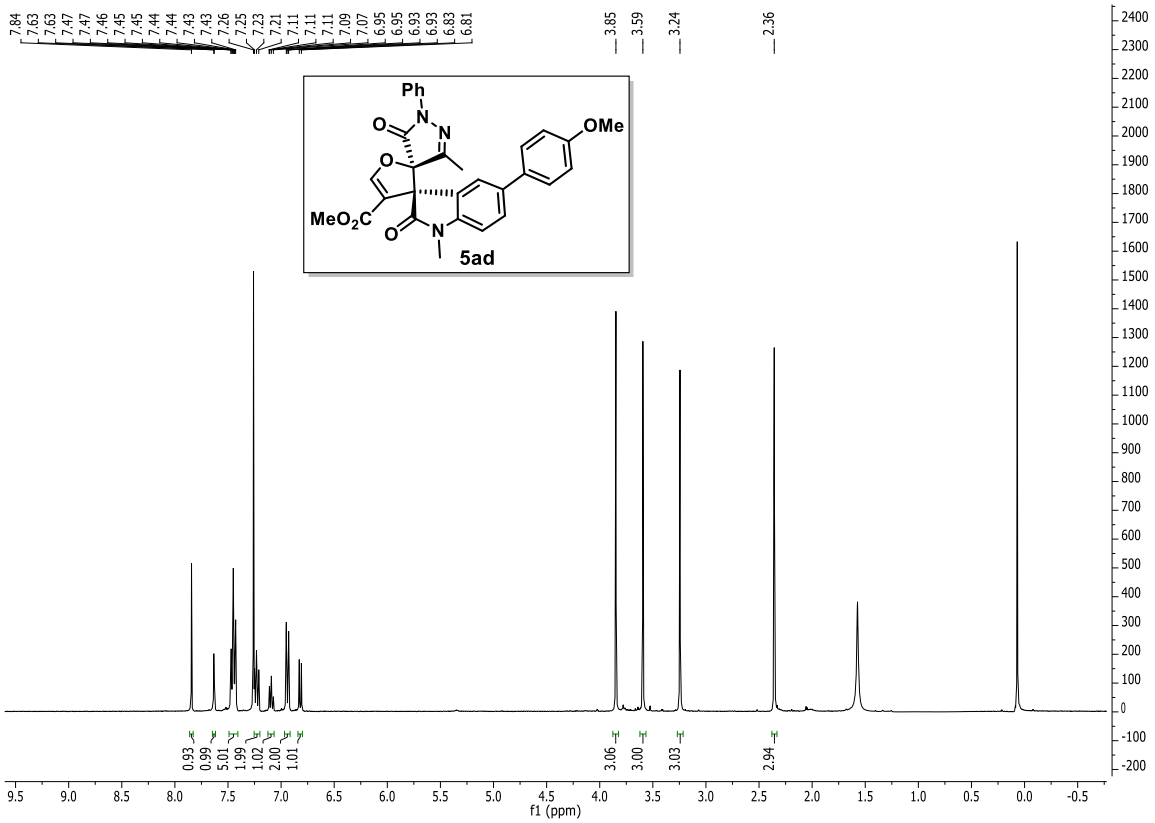

Ph
N
N
O
O
O
MeO2C
N
Allyl
3w
f1 (ppm)

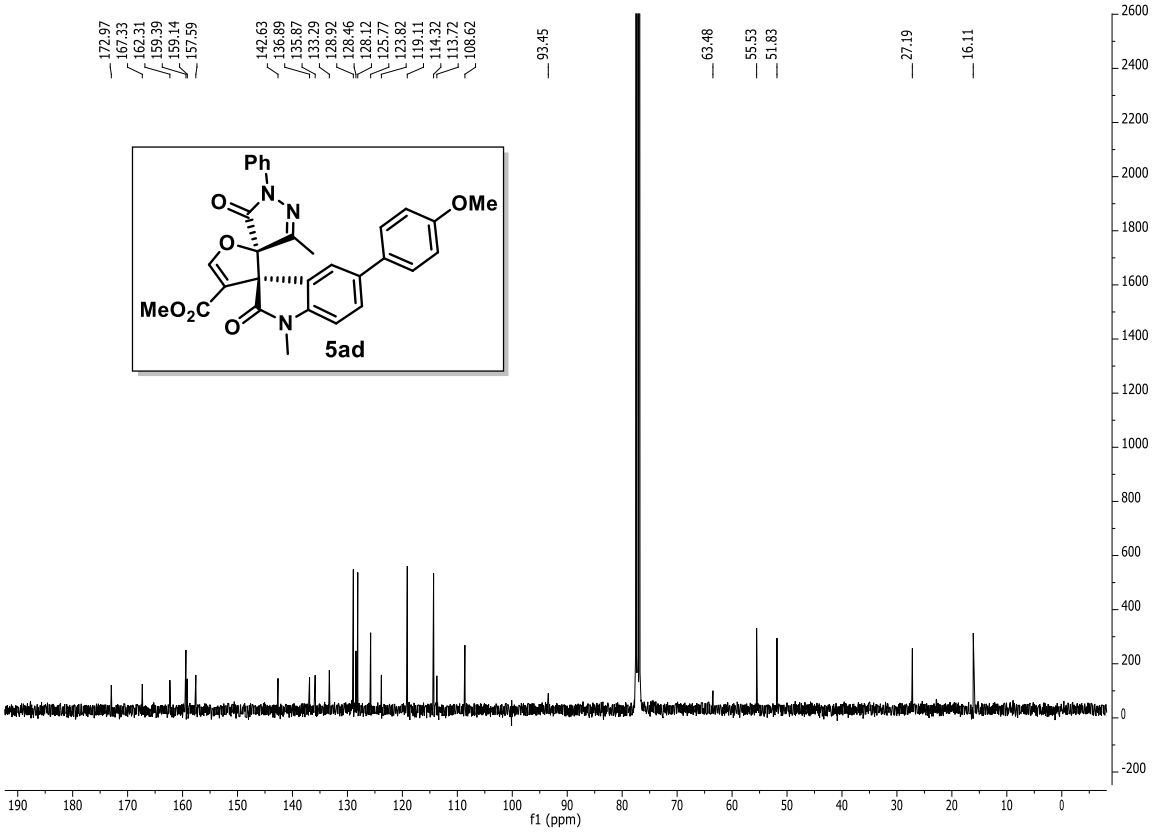

Ph
N
N
O
O
OMe
MeO2C
O
N
Bn
3x
f1 (ppm)


Ph
N
N
O
O
OMe
MeO2C
O
N
Bn
3x
f1 (ppm)

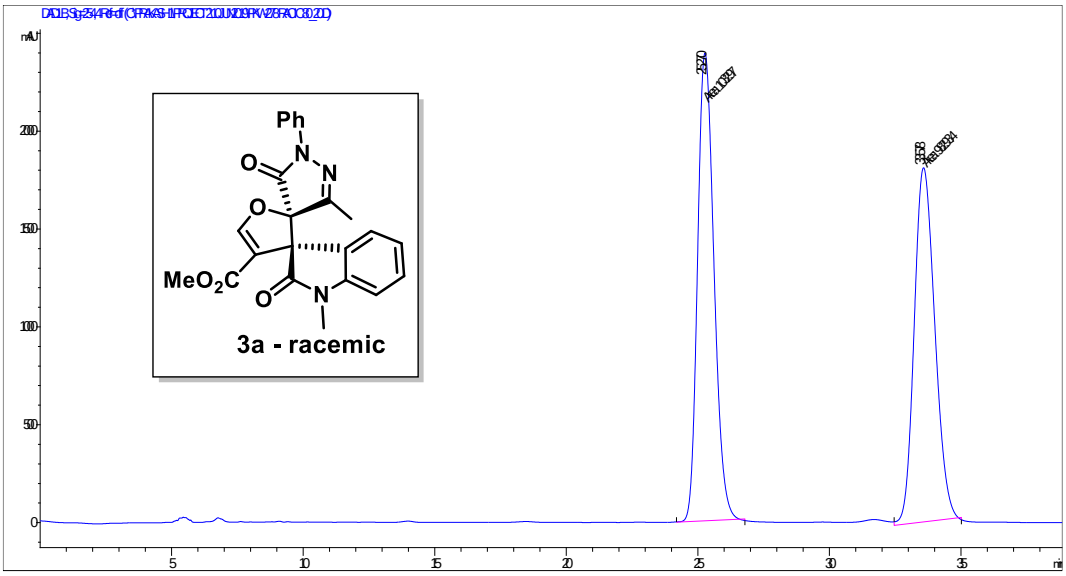

Ph
N
N
O
O
Ph
MeO2C
O
N
Bn
3y
f1 (ppm)


Ph
N
N
O
O
Ph
MeO2C
O
N
Bn
3y
f1 (ppm)

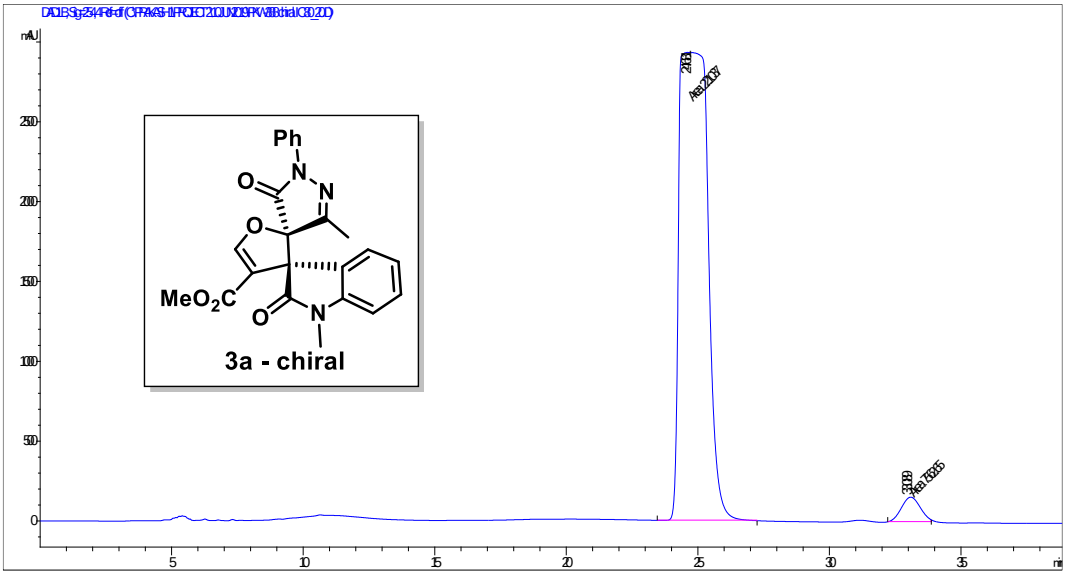

7.84
7.63
7.63
7.47
7.47
7.46
7.45
7.45
7.44
7.44
7.43
7.43
7.26
7.25
7.23
7.21
7.11
7.11
7.11
7.09
7.07
6.95
6.95
6.93
6.93
6.83
6.81
3.85
3.59
3.24
2.36
Ph
N
N
O
O
OMe
MeO2C
O
N
5ad
0.93
0.99
5.01
1.99
1.02
2.00
1.01
3.06
3.00
3.03
2.94
f1 (ppm)


172.97
167.33
162.31
159.39
159.14
157.59
142.63
136.89
135.87
133.29
128.92
128.46
128.12
125.77
123.82
119.11
114.32
113.72
108.62
93.45
63.48
55.53
51.83
27.19
16.11
Ph
N
N
O
O
OMe
MeO2C
O
N
5ad
f1 (ppm)

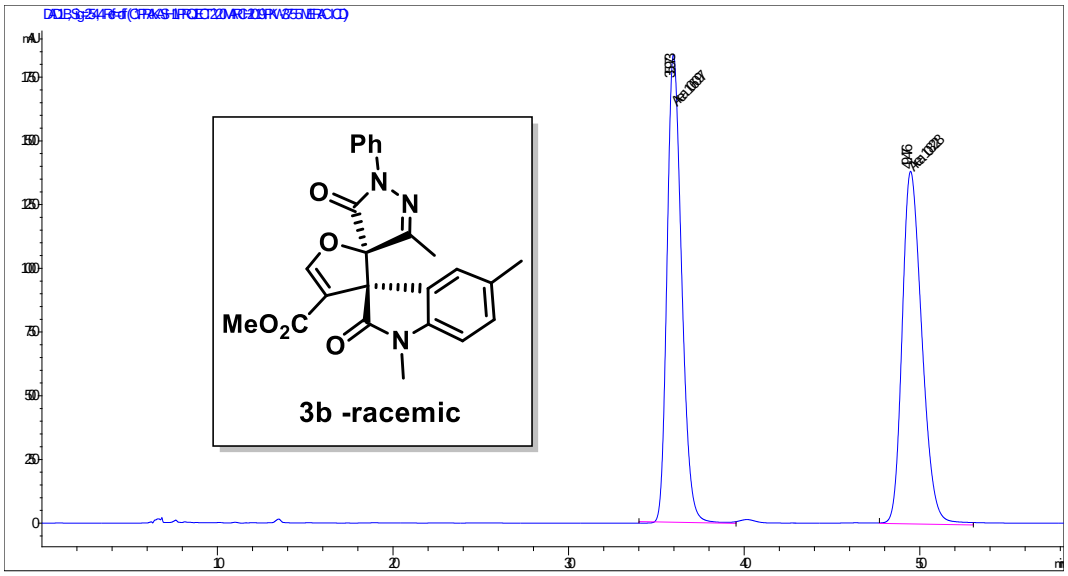
HPLC Chromatograms (3a-3y) and 5ad



#	Time	Area	Height	Width	Area%	Symmetry
1	25.27	103296.5	2389.5	0.7205	51.241	0.784
2	33.578	98293.4	1809.3	0.9055	48.759	0.809

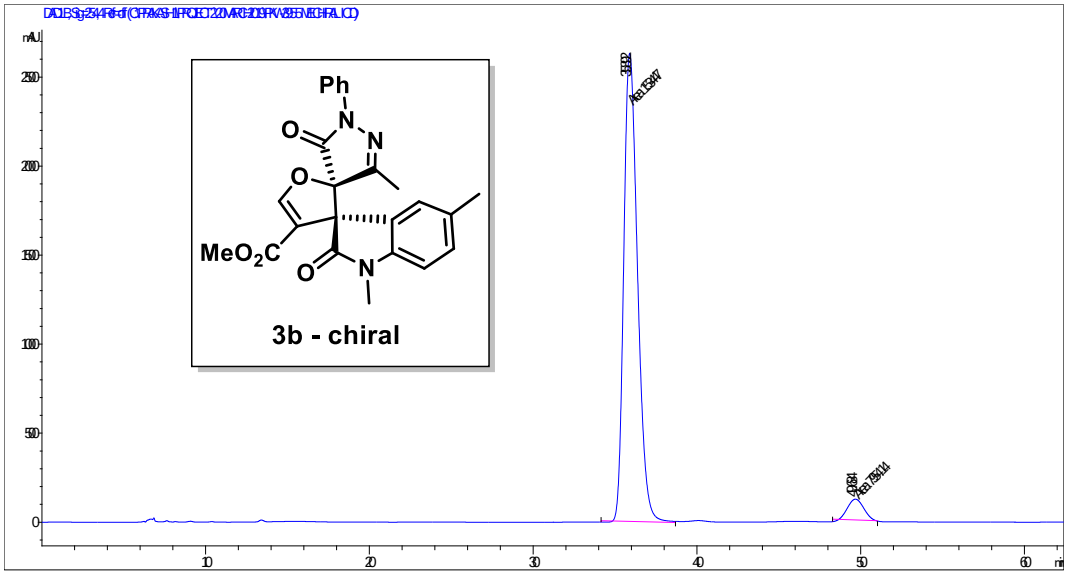


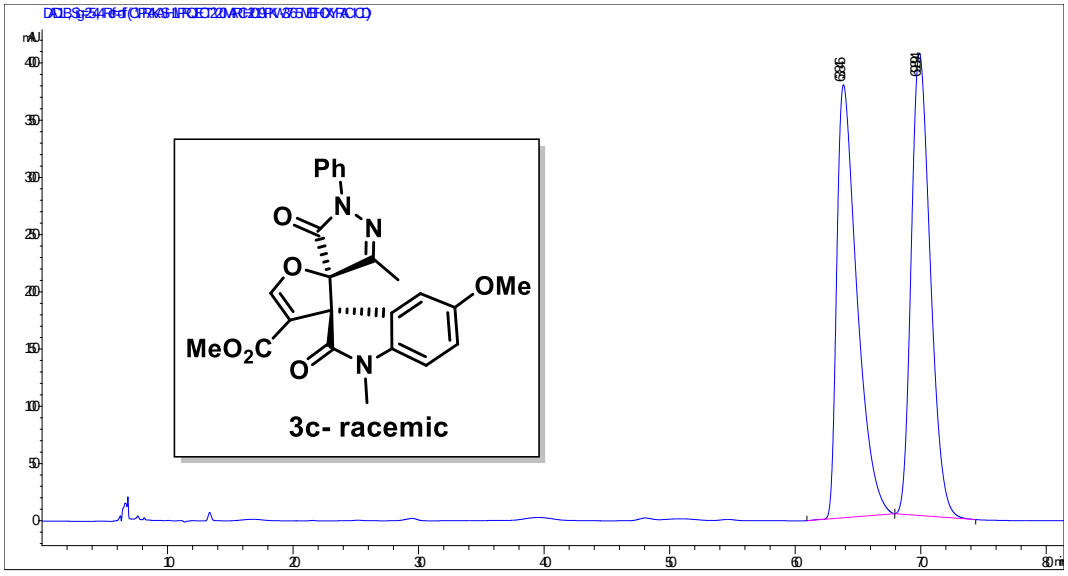
#	Time	Area	Height	Width	Area%	Symmetry
1	24.681	221036.5	2930.6	1.2571	96.692	0.555
2	33.089	7562.6	153.1	0.8234	3.308	0.938



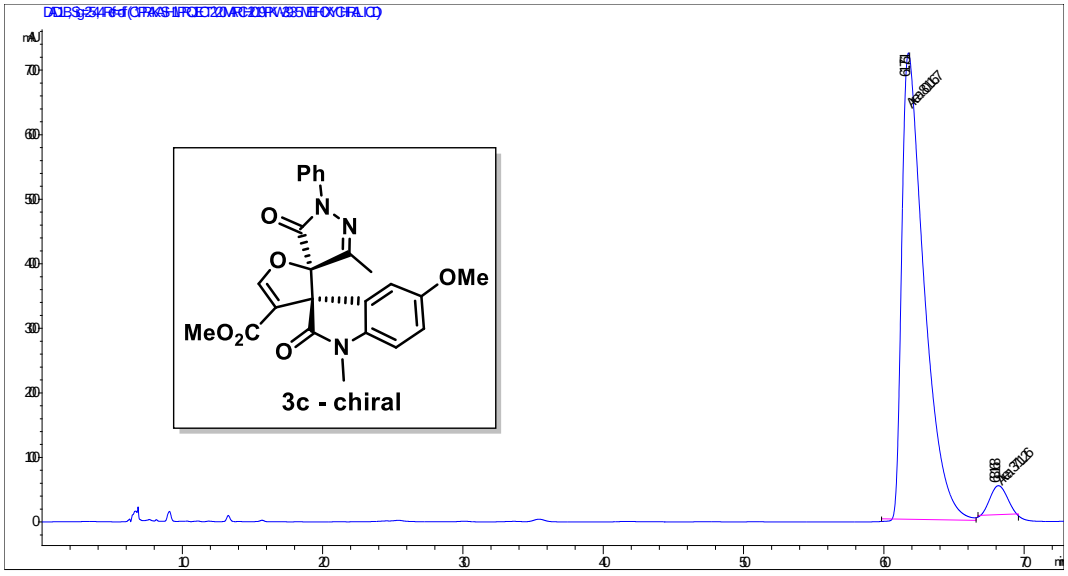
#	Time	Area	Height	Width	Area%	Symmetry
1	35.973	106096.6	1836.6	0.9628	49.503	0.748
2	49.476	108227.6	1383.7	1.3036	50.497	0.711

#	Time	Area	Height	Width	Area%	Symmetry
1	35.892	153447	2629.3	0.9727	95.072	0.717
2	49.684	7954.1	117.1	1.1319	4.928	0.898

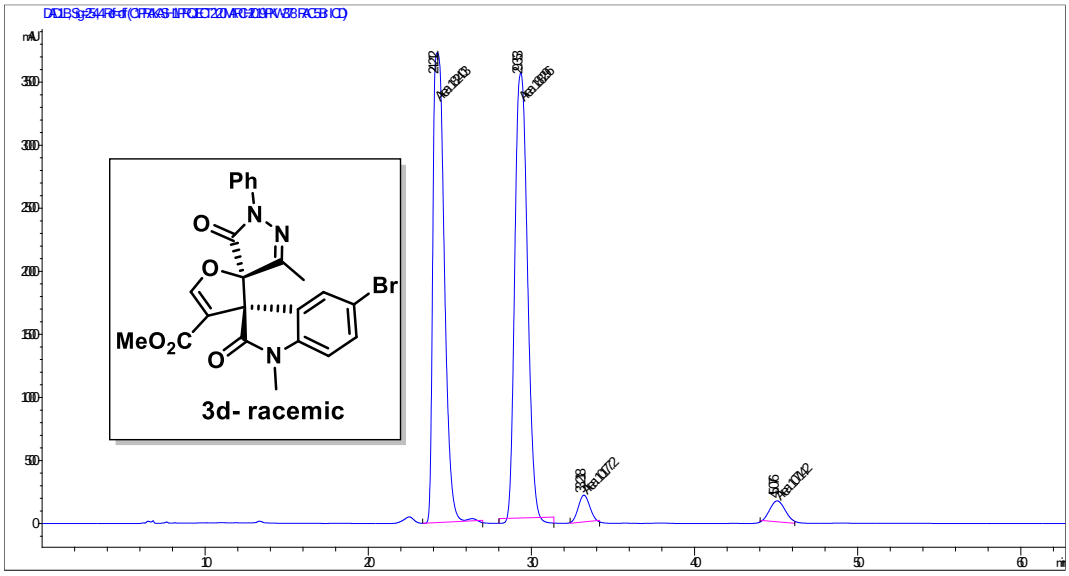




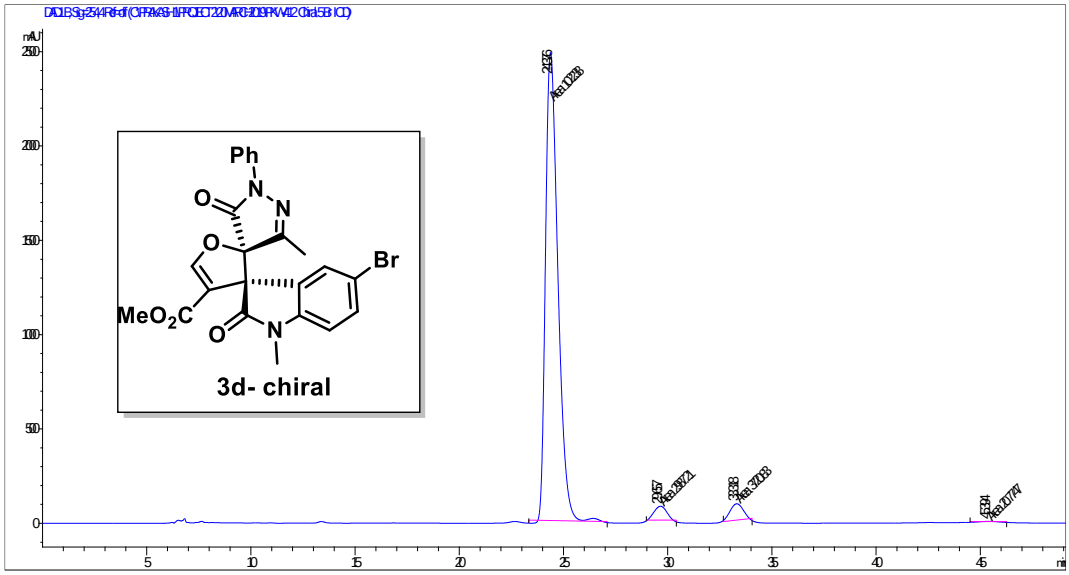
#	Time	Area	Height	Width	Area%	Symmetry
1	63.846	42433.1	378.5	1.6601	49.744	0.455
2	69.894	42869.9	404.2	1.6195	50.256	0.703



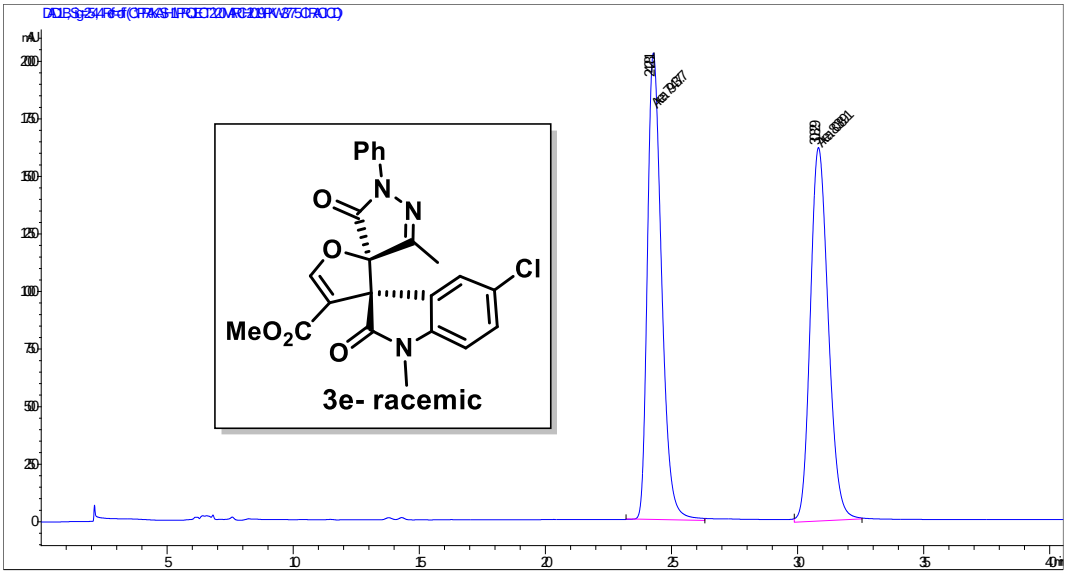
#	Time	Area	Height	Width	Area%	Symmetry
1	61.751	80116.7	722.4	1.8483	95.573	0.405
2	68.168	3711.3	44.9	1.3772	4.427	0.964



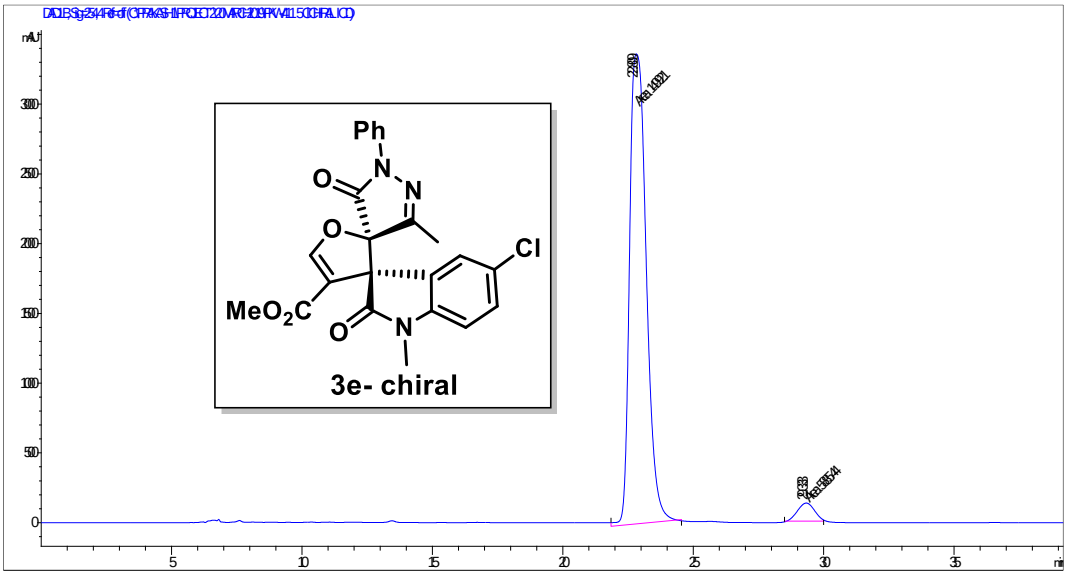
#	Time	Area	Height	Width	Area%	Symmetry
1	24.212	182402.9	3725.5	0.816	46.580	0.542
2	29.353	188295.7	3531.3	0.8887	48.085	0.874
3	33.218	10177.2	212	0.8002	2.599	1.007
4	45.076	10714.2	165.8	1.0767	2.736	0.827



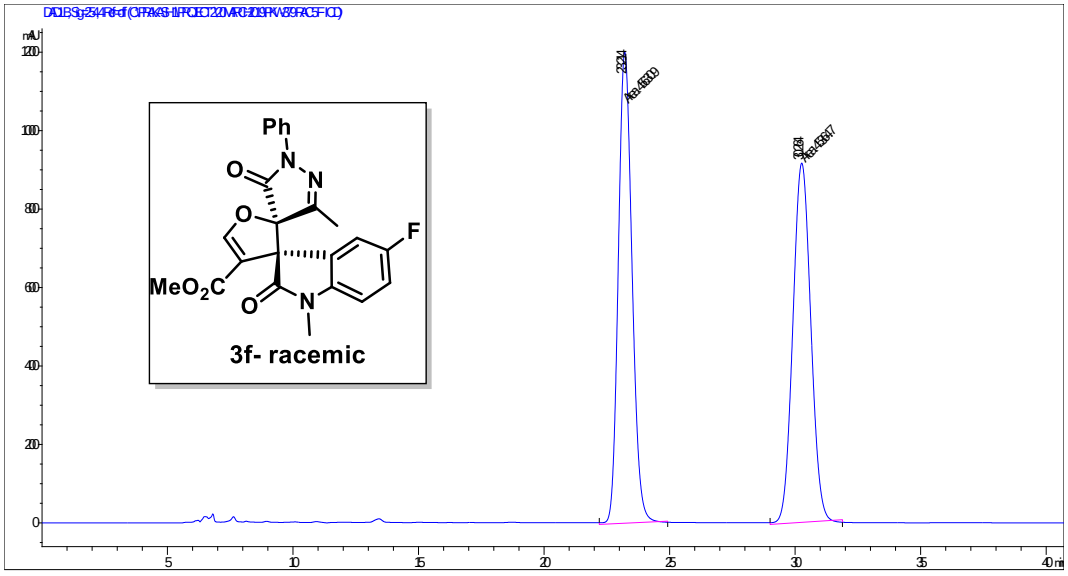
#	Time	Area	Height	Width	Area%	Symmetry
1	24.376	102237.9	2480.2	0.687	93.825	0.633
2	29.657	2987.2	73	0.682	2.741	1.052
3	33.318	3720.8	86.5	0.7165	3.415	1.098
4	45.394	20.8	9.6E-1	0.3602	0.019	0.973



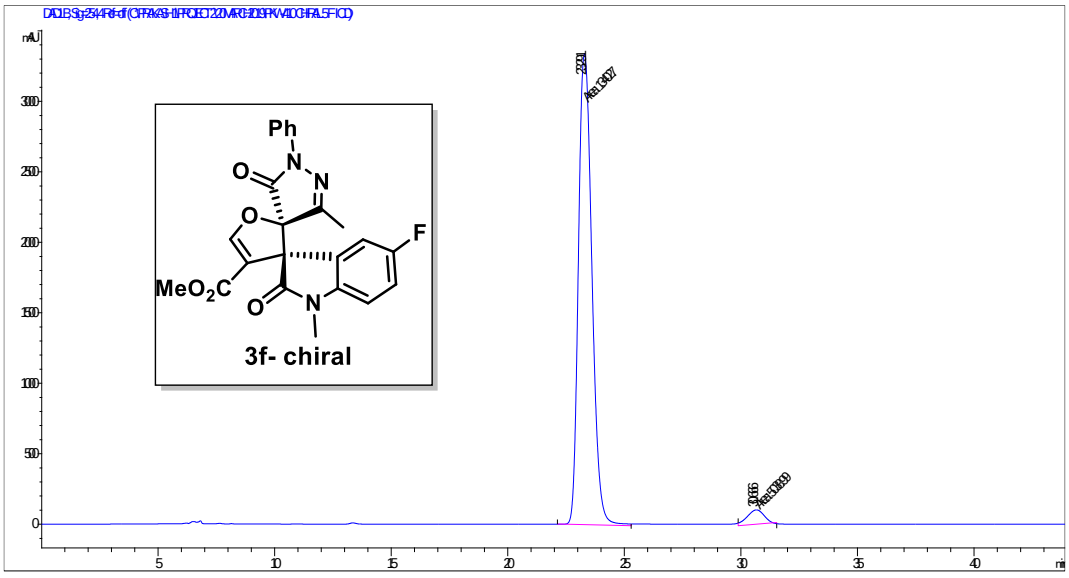
#	Time	Area	Height	Width	Area%	Symmetry
1	24.281	79437.7	2025.9	0.6535	49.702	0.68
2	30.829	80389.1	1622.2	0.8259	50.298	0.801



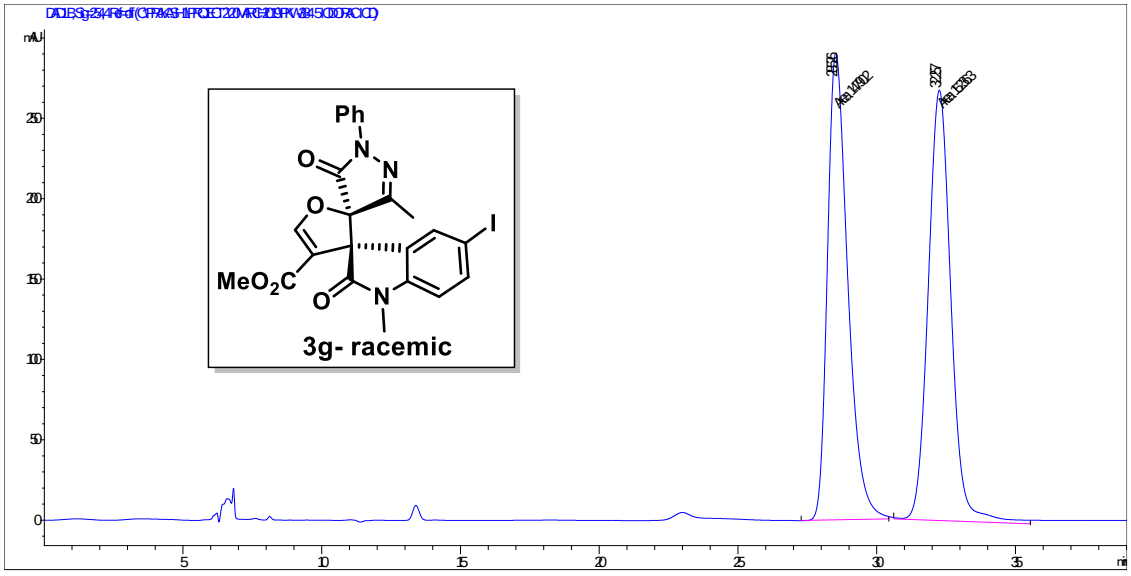
#	Time	Area	Height	Width	Area%	Symmetry
1	22.809	149920.7	3370.3	0.7414	96.223	0.626
2	29.333	5885.4	130.5	0.7515	3.777	1.031



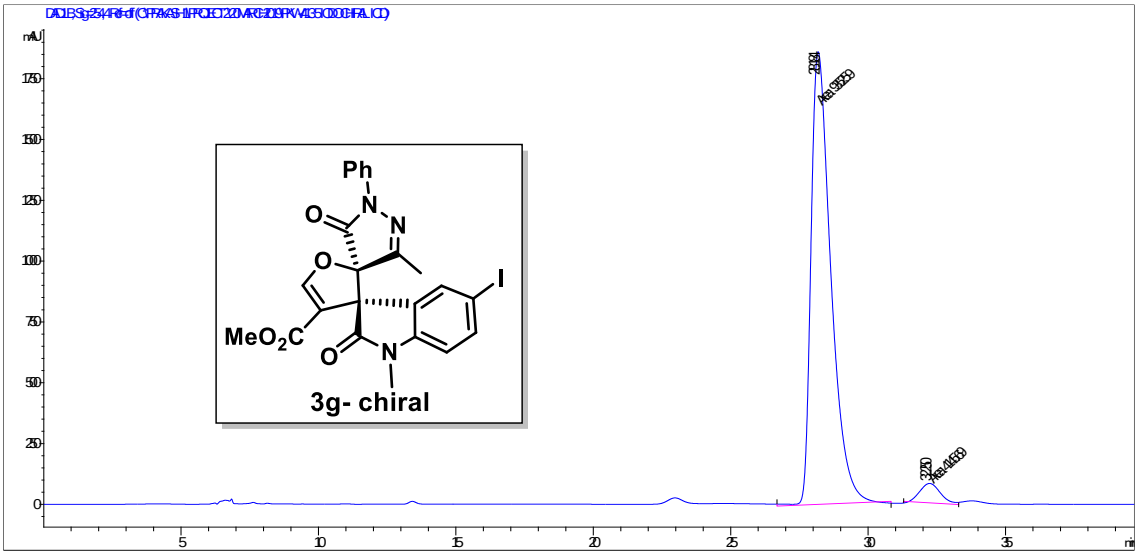
#	Time	Area	Height	Width	Area%	Symmetry
1	23.214	45630.9	1200.8	0.6333	50.146	0.85
2	30.264	45364.7	915.7	0.8257	49.854	0.953



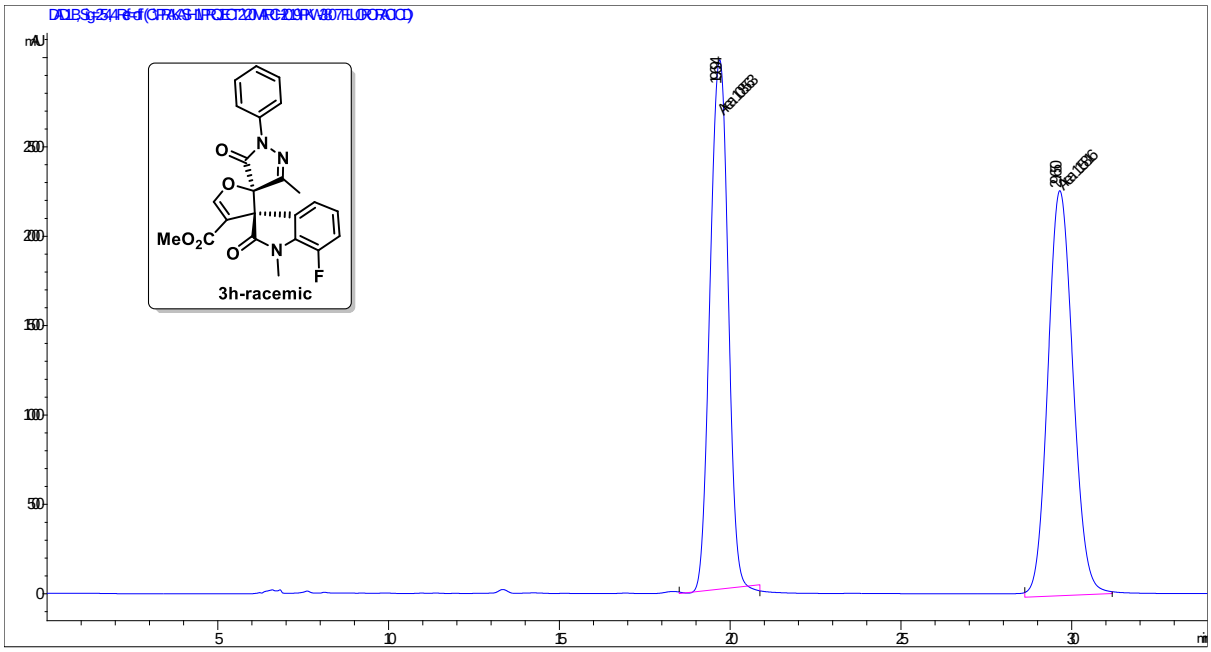
#	Time	Area	Height	Width	Area%	Symmetry
1	23.291	134026.7	3342.8	0.6682	96.377	0.782
2	30.666	5039	101.3	0.8293	3.623	1.285



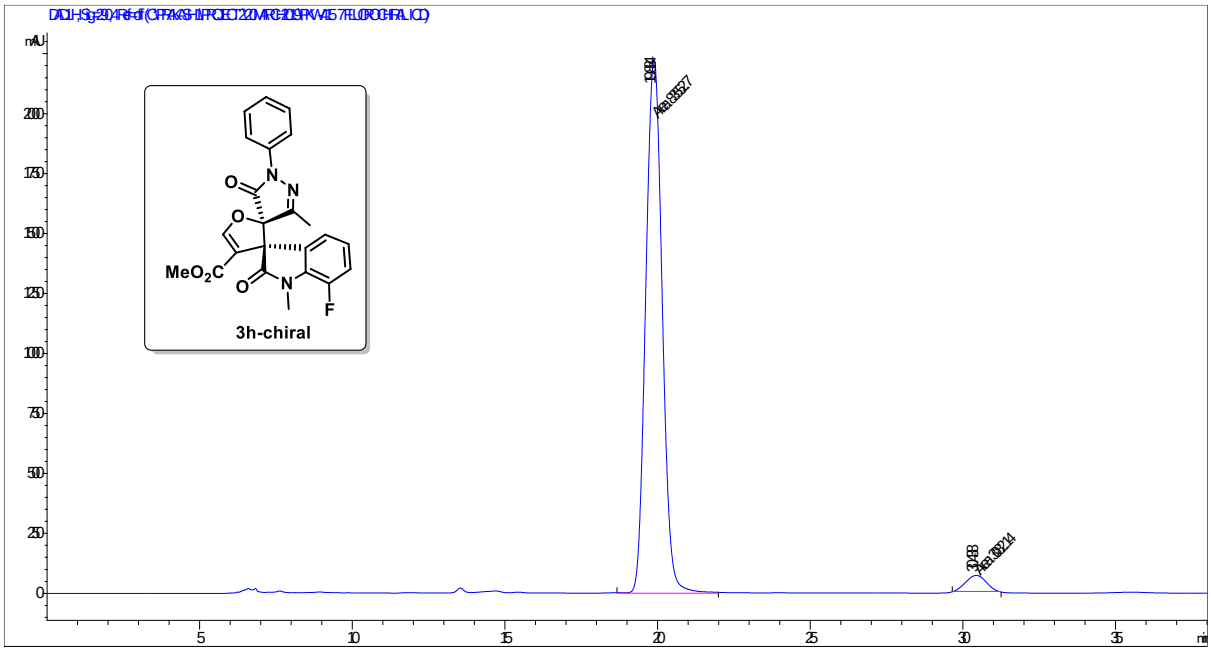
#	Time	Area	Height	Width	Area%	Symmetry
1	28.526	14796.2	290.4	0.7784	49.930	0.647
2	32.257	14837.9	266.7	0.8632	50.070	0.919



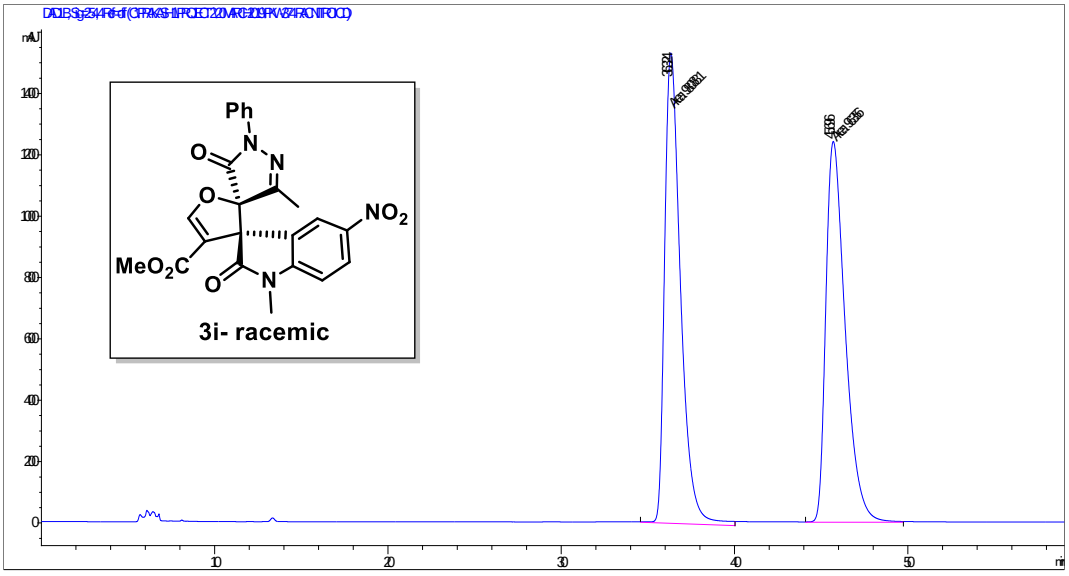
#	Time	Area	Height	Width	Area%	Symmetry
1	28.184	93525.9	1860.8	0.8377	95.755	0.545
2	32.25	4145.7	79.7	0.867	4.245	0.84



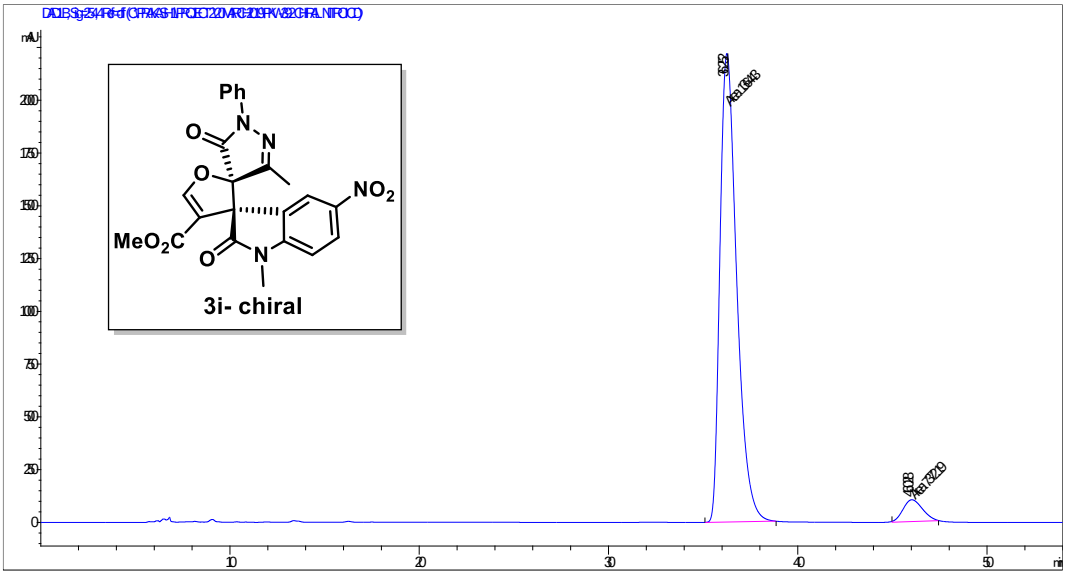
#	Time	Area	Height	Width	Area%	Symmetry
1	19.694	108562.6	2961.4	0.611	48.384	1.096
2	29.65	115815.9	2266.2	0.8517	51.616	0.87



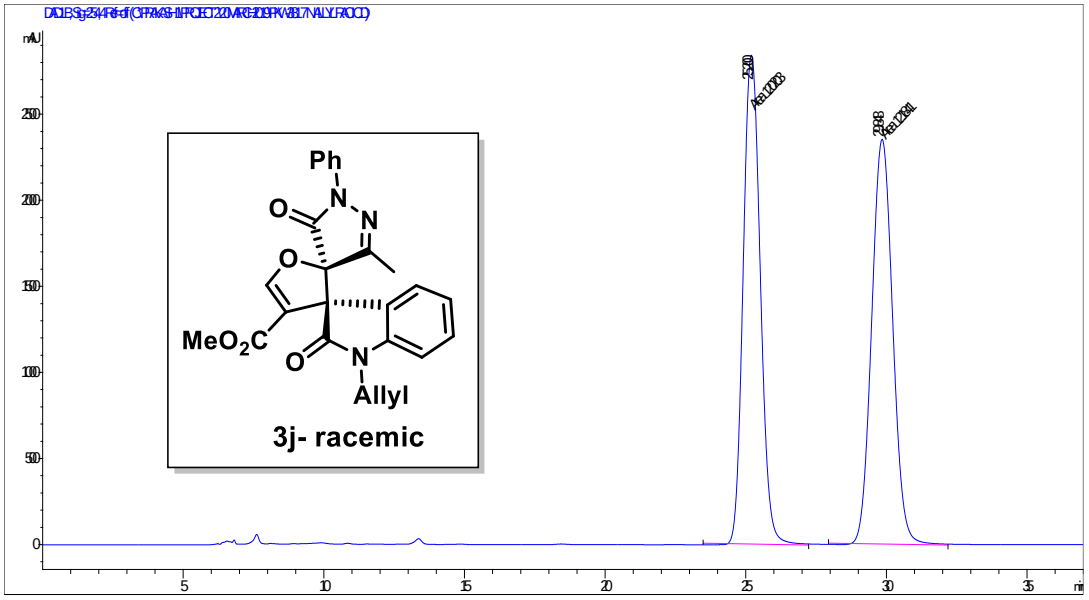
#	Time	Area	Height	Width	Area%	Symmetry
1	19.884	83552.7	2226	0.6256	96.442	0.952
2	30.438	3082.1	67.2	0.7649	3.558	1.046



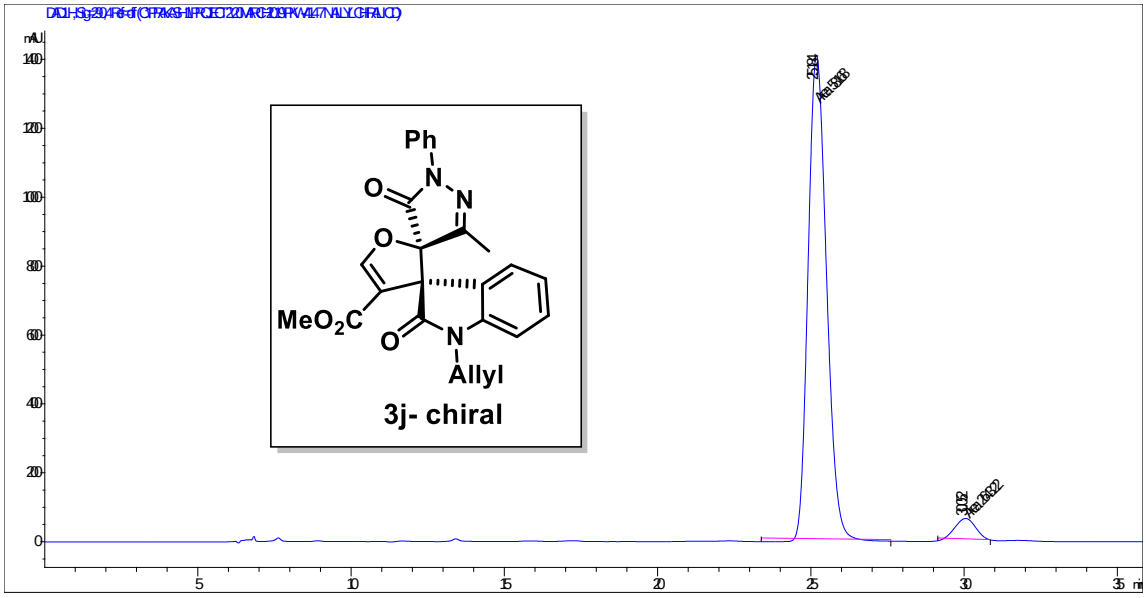
#	Time	Area	Height	Width	Area%	Symmetry
1	36.324	98088.1	1532.9	1.0665	50.445	0.606
2	45.696	96356	1241.5	1.2936	49.555	0.597



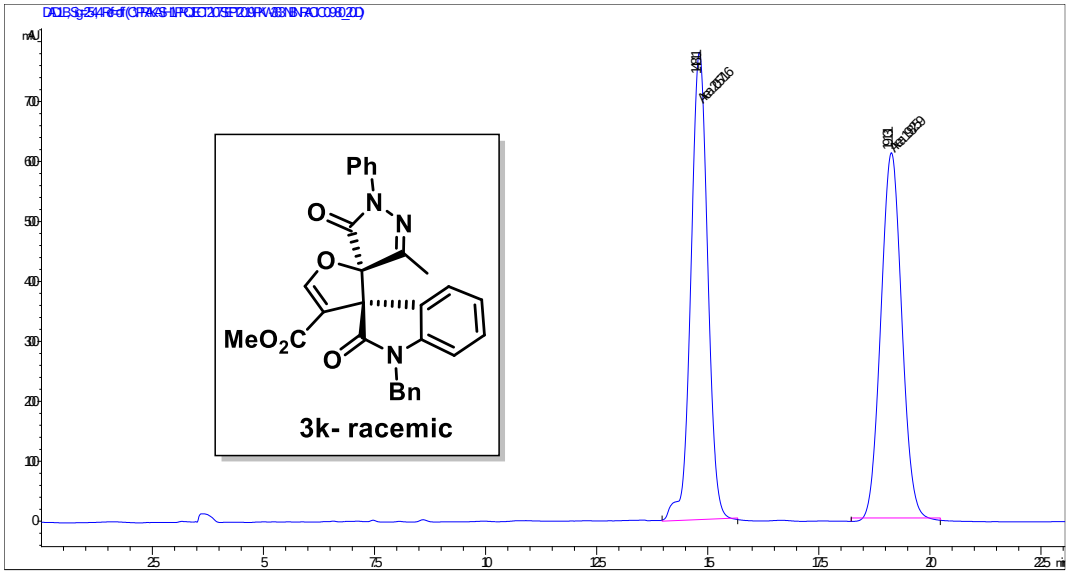
#	Time	Area	Height	Width	Area%	Symmetry
1	36.252	136443.3	2219.6	1.0245	94.874	0.663
2	46.028	7372.2	103.2	1.1909	5.126	0.818



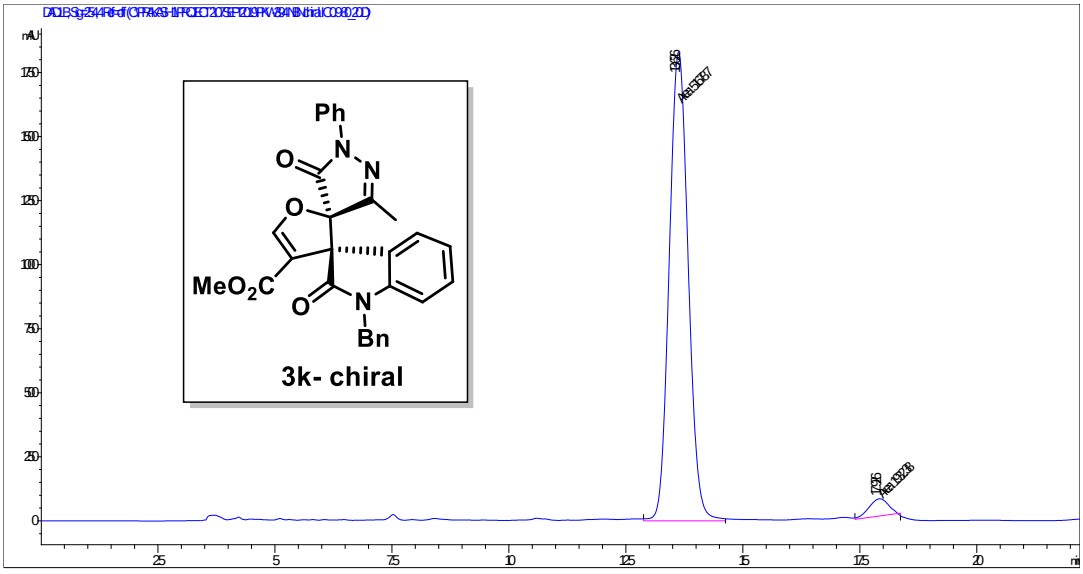
#	Time	Area	Height	Width	Area%	Symmetry
1	25.2	120203.1	2839.4	0.7056	49.662	0.876
2	29.848	121840.5	2350.7	0.8639	50.338	0.937



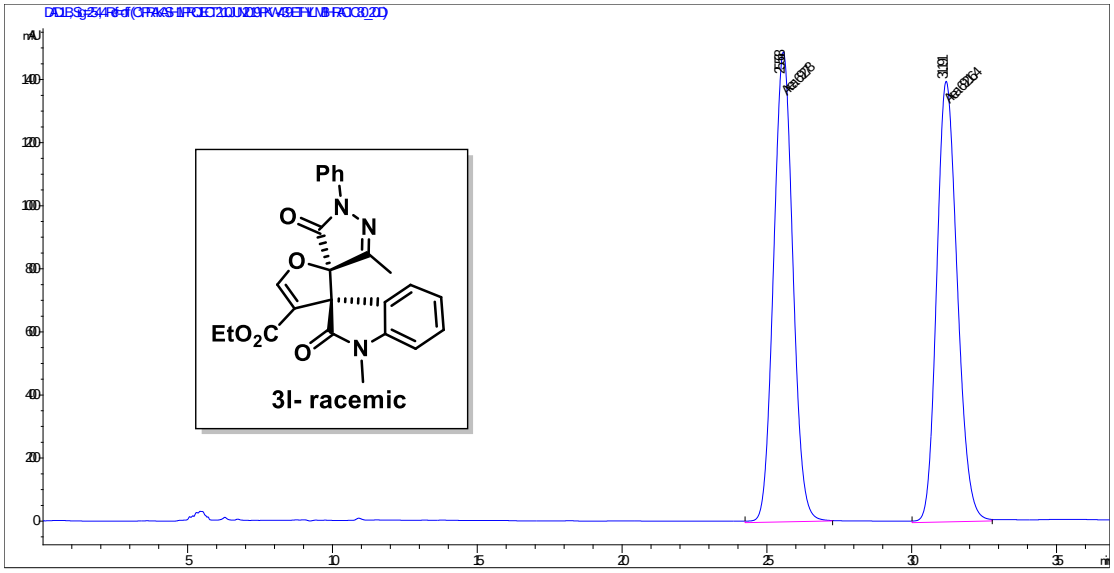
#	Time	Area	Height	Width	Area%	Symmetry
1	25.184	58168	1403.5	0.6907	95.653	0.808
2	30.052	2643.2	59	0.7463	4.347	0.99



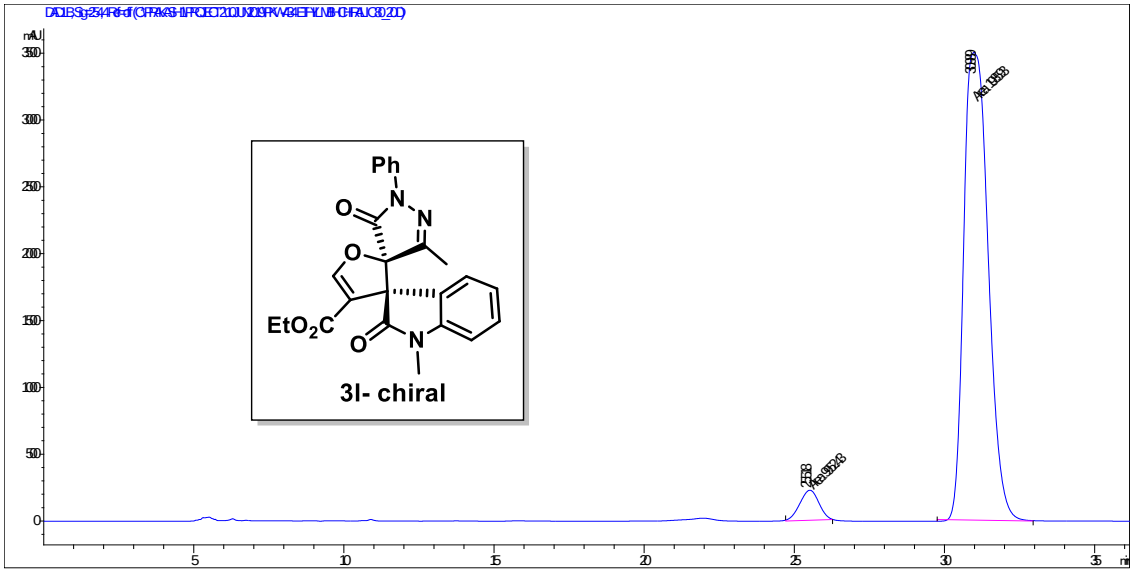
#	Time	Area	Height	Width	Area%	Symmetry
1	14.811	20571.6	779.9	0.4396	50.923	1.01
2	19.131	19825.9	609.3	0.5423	49.077	0.963



#	Time	Area	Height	Width	Area%	Symmetry
1	13.626	51678.7	1831.2	0.4704	96.396	0.923
2	17.926	1932.4	66.9	0.4811	3.604	1.304

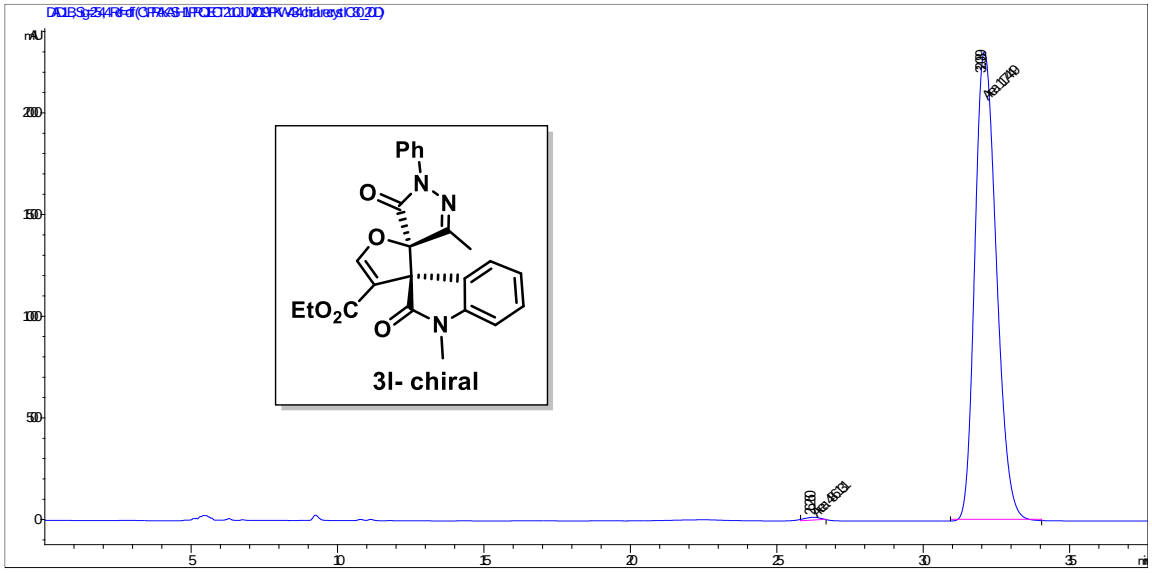


#	Time	Area	Height	Width	Area%	Symmetry
1	25.568	69278	1490	0.7749	50.022	0.971
2	31.191	69216.4	1397	0.8258	49.978	0.815

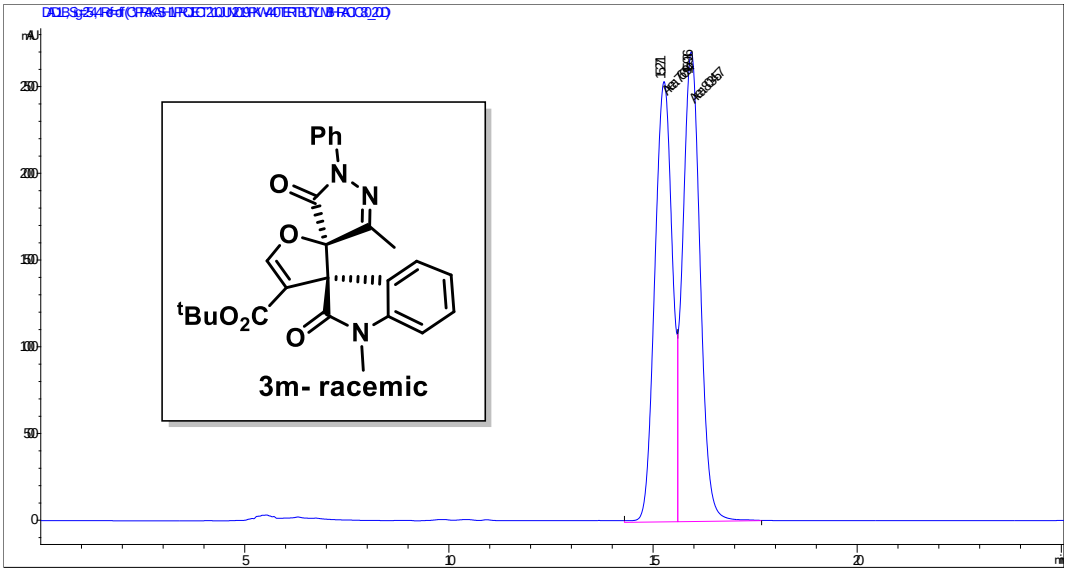


#	Time	Area	Height	Width	Area%	Symmetry
1	25.518	9952.4	225	0.7371	4.772	1.109
2	30.989	198592.6	3502.8	0.9449	95.228	0.715

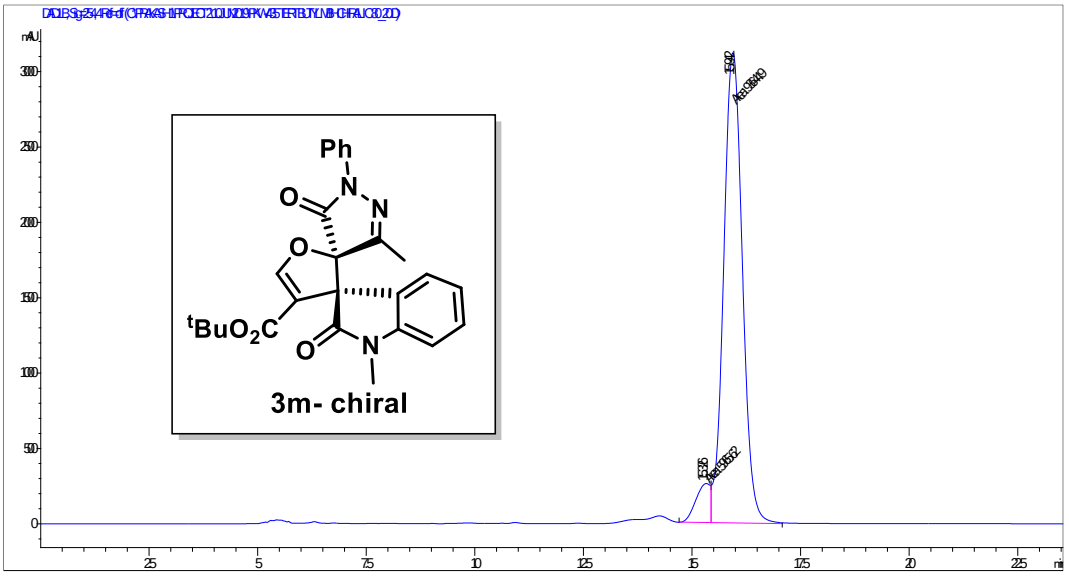
3l- after recrystalization



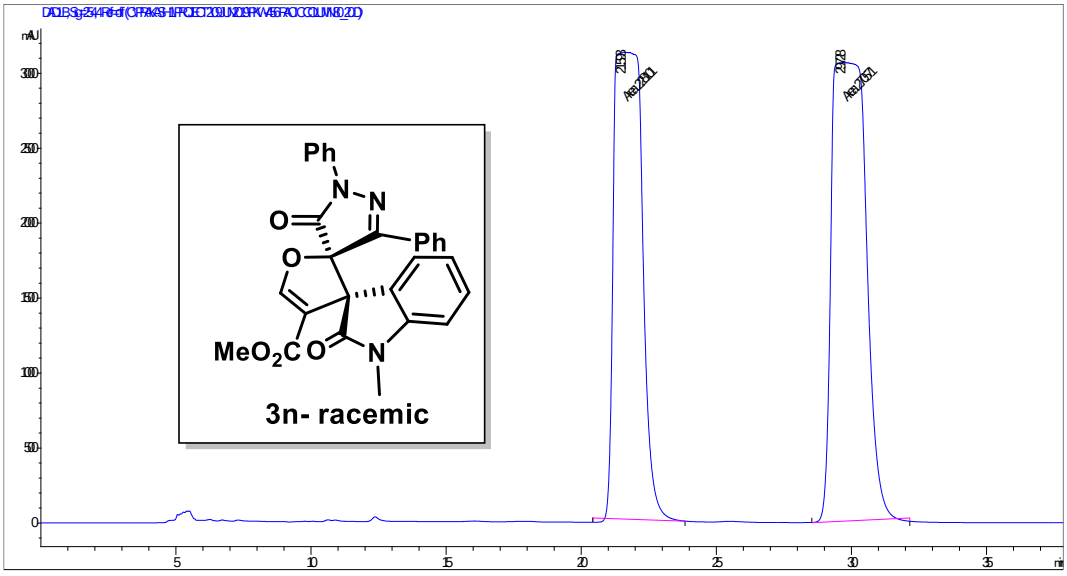
#	Time	Area	Height	Width	Area%	Symmetry
1	26.26	486.1	13.6	0.5963	0.412	1.658
2	32.089	117448.7	2298.9	0.8515	99.588	0.764



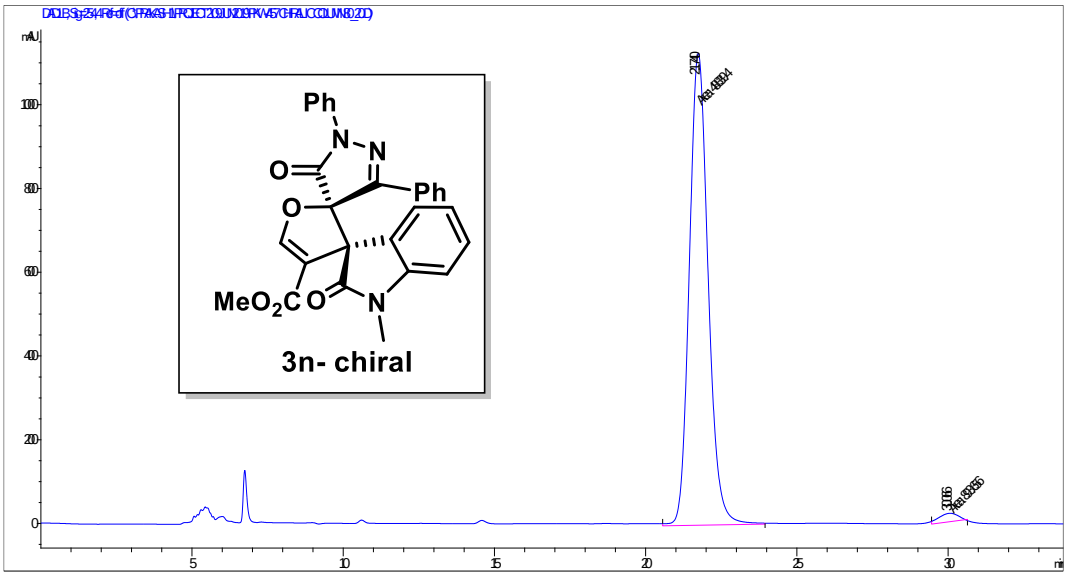
#	Time	Area	Height	Width	Area%	Symmetry
1	15.271	76094	2538	0.4997	48.641	1.088
2	15.936	80345.7	2707.3	0.4946	51.359	0.901



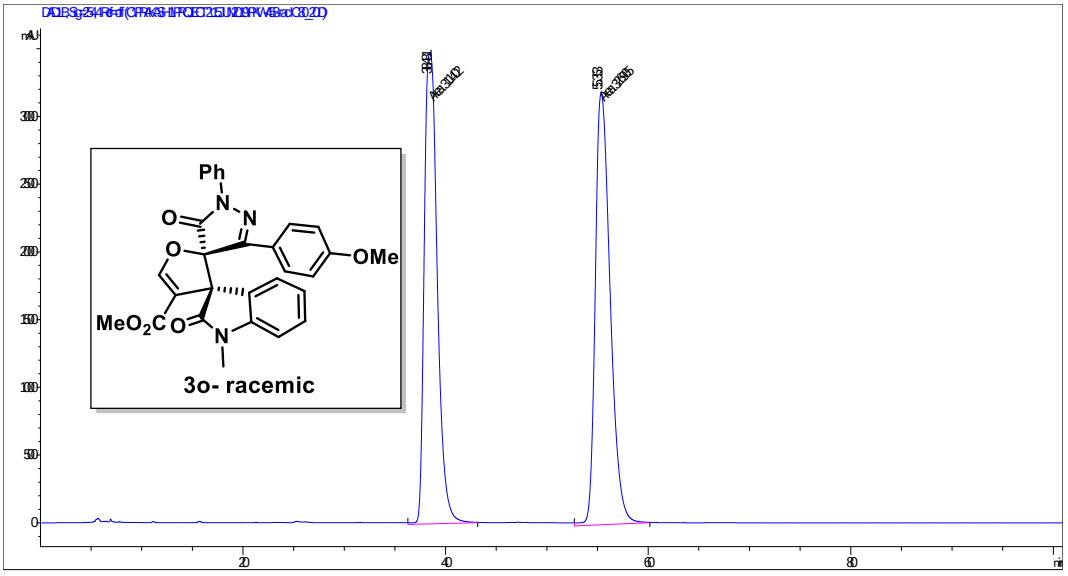
#	Time	Area	Height	Width	Area%	Symmetry
1	15.326	5965.6	258.5	0.3846	5.989	2.328
2	15.942	93644.9	3119.5	0.5003	94.011	0.93



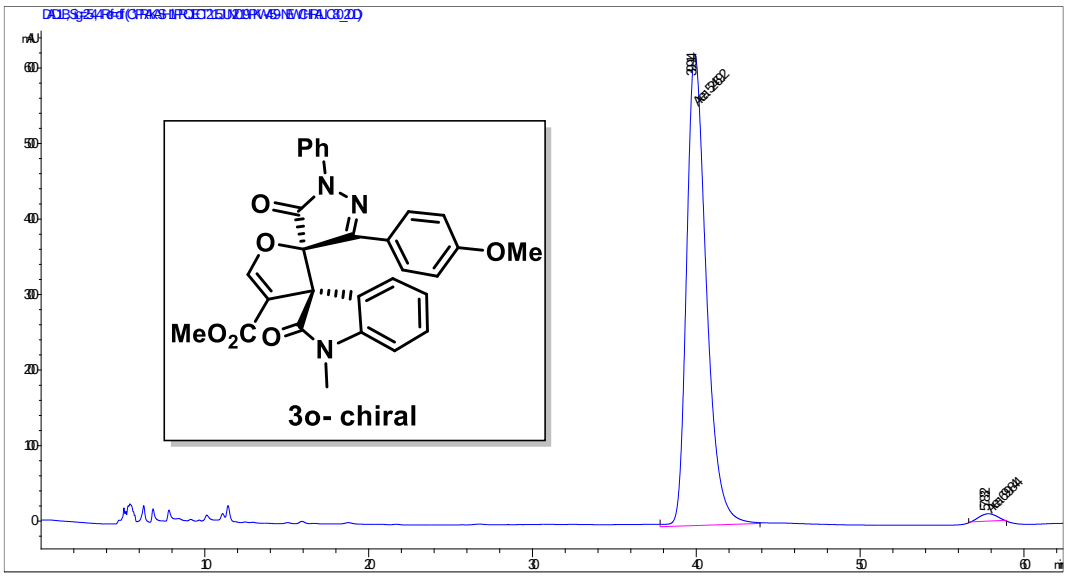
#	Time	Area	Height	Width	Area%	Symmetry
1	21.593	228100.6	3114.6	1.2206	45.742	0.577
2	29.728	270571.4	3061.5	1.473	54.258	0.57



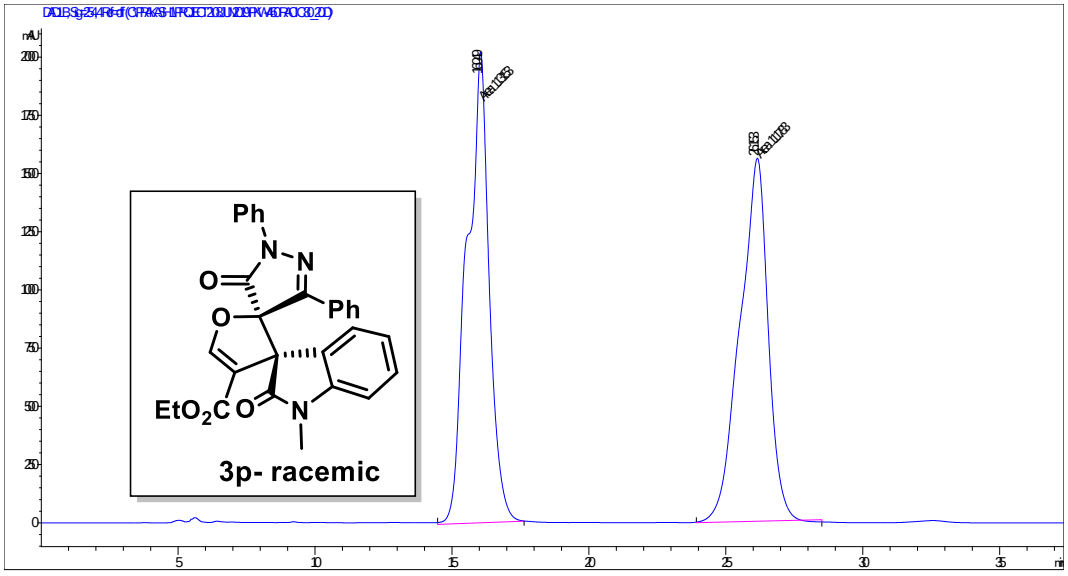
#	Time	Area	Height	Width	Area%	Symmetry
1	21.74	48839.4	1127.2	0.7222	98.203	0.863
2	30.066	893.7	20.2	0.7373	1.797	1.552



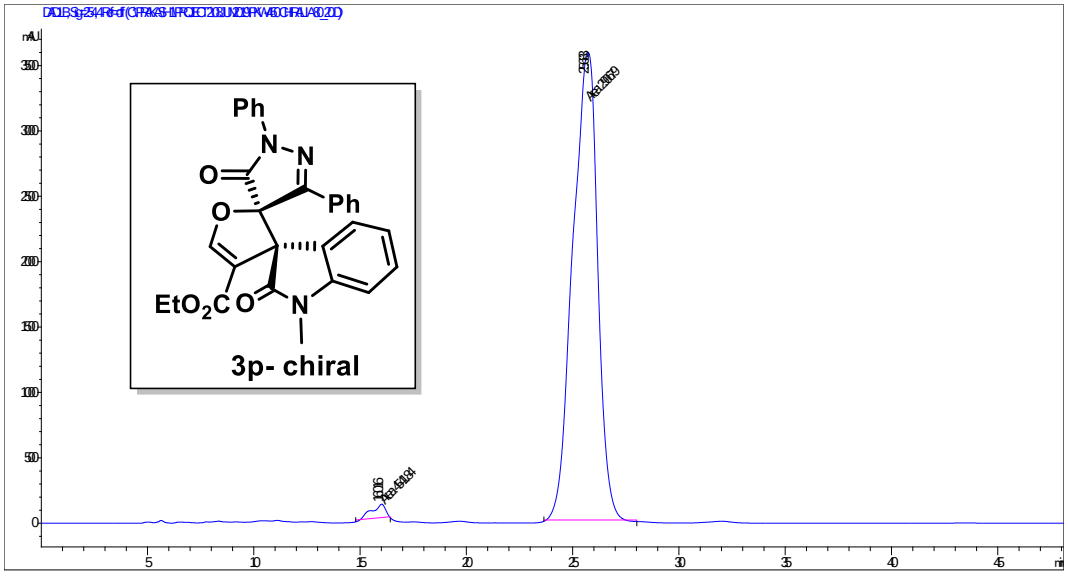
#	Time	Area	Height	Width	Area%	Symmetry
1	38.481	311402.1	3482	1.4905	48.786	0.789
2	55.353	326905	3189.2	1.7084	51.214	0.626



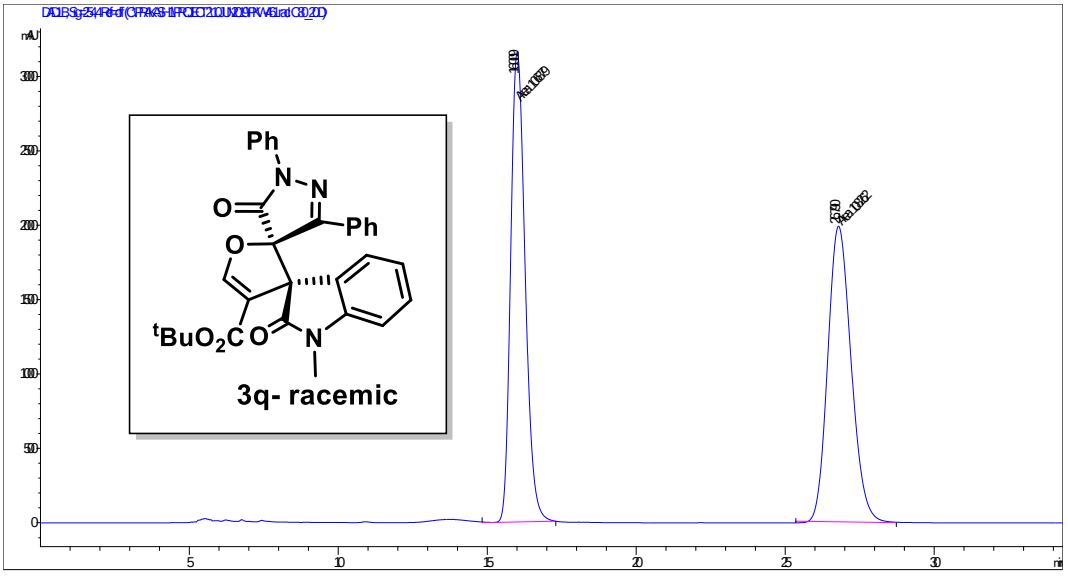
#	Time	Area	Height	Width	Area%	Symmetry
1	39.914	52469.2	623.8	1.4019	98.684	0.687
2	57.832	699.8	9.6	1.2128	1.316	1.091



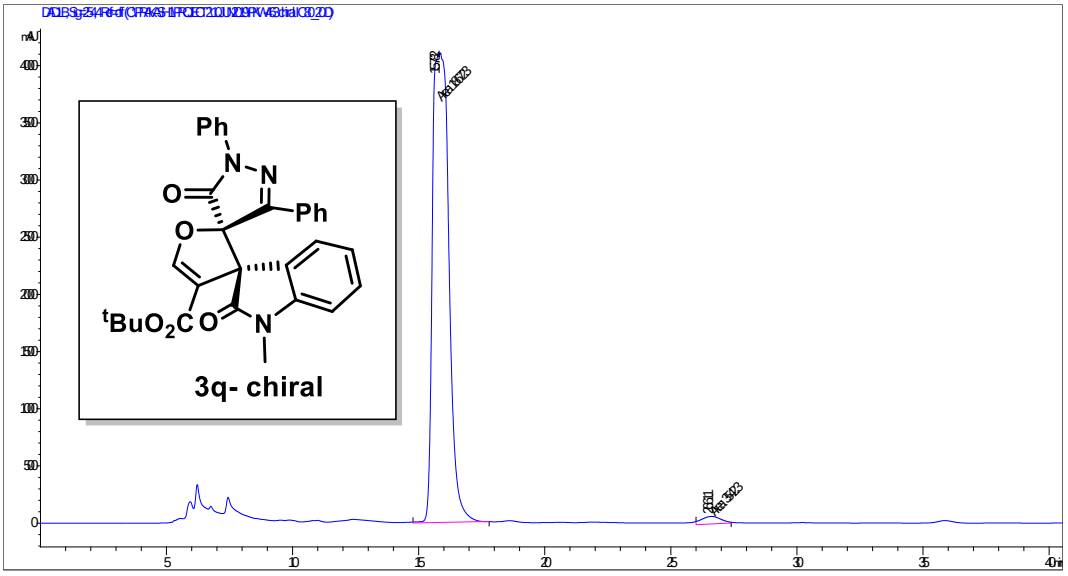
#	Time	Area	Height	Width	Area%	Symmetry
1	16.049	113152.8	2021.3	0.933	50.304	1.469
2	26.153	111783.4	1559	1.195	49.696	1.535



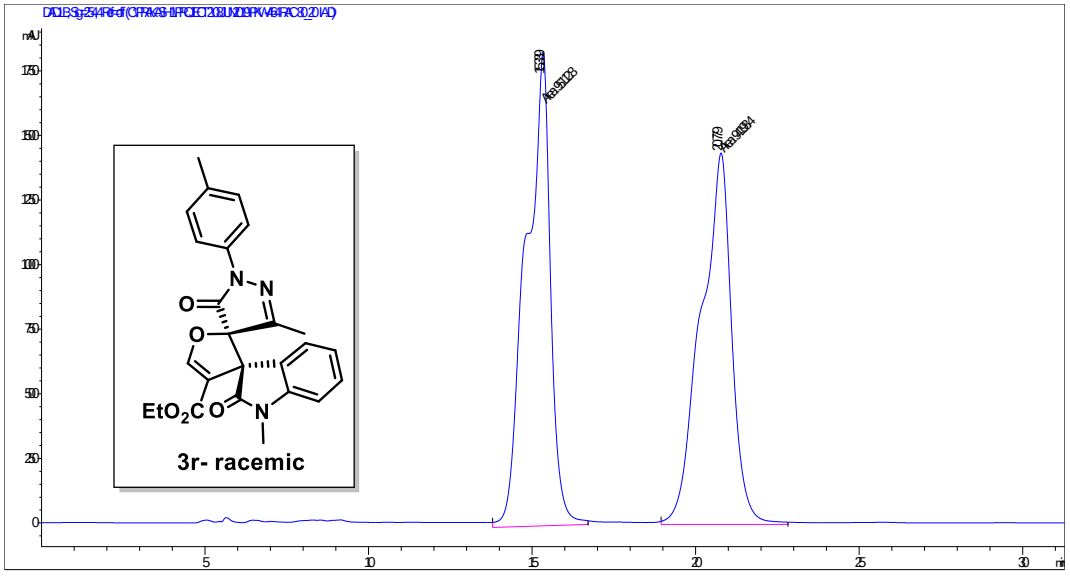
#	Time	Area	Height	Width	Area%	Symmetry
1	16.016	4541.8	102	0.7418	1.538	2.694
2	25.683	290678.5	3574.9	1.3552	98.462	1.319



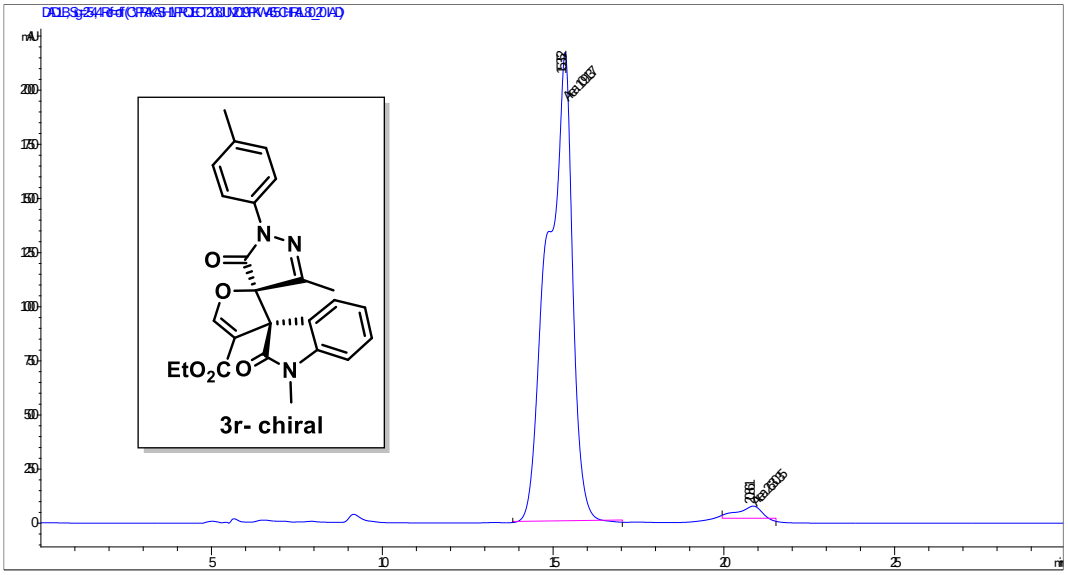
#	Time	Area	Height	Width	Area%	Symmetry
1	16.009	106878.5	3158.5	0.564	49.679	0.807
2	26.79	108261.6	1987.1	0.908	50.321	0.823



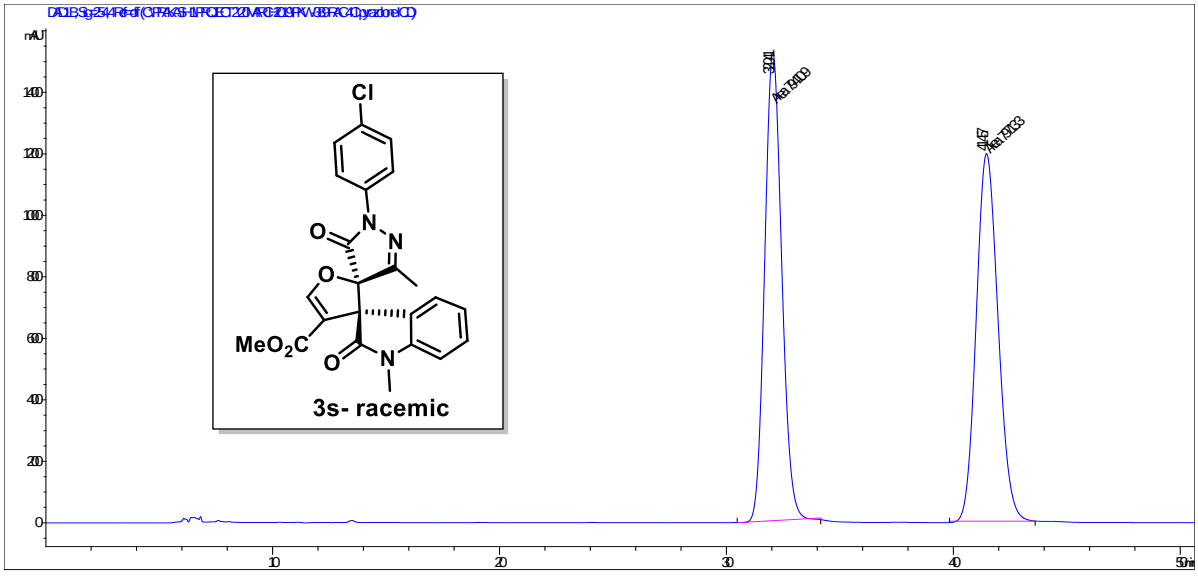
#	Time	Area	Height	Width	Area%	Symmetry
1	15.782	186723.4	4110.7	0.7571	98.138	0.559
2	26.611	3542.3	65.9	0.8953	1.862	1.062



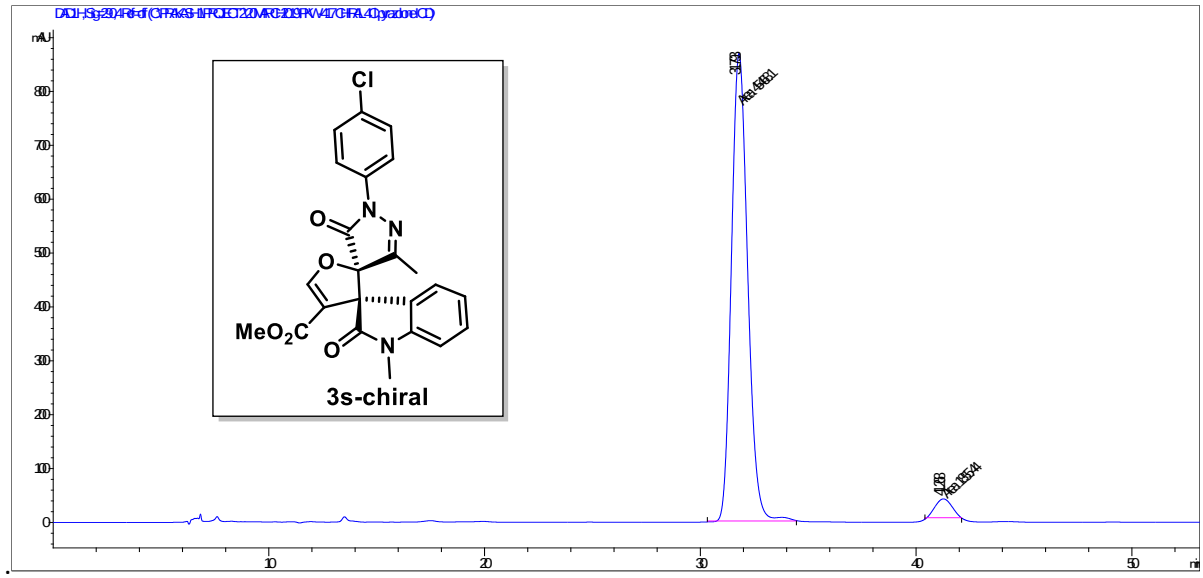
#	Time	Area	Height	Width	Area%	Symmetry
1	15.339	95112.8	1833.9	0.8644	50.242	2.081
2	20.779	94198.4	1437.3	1.0923	49.758	1.739



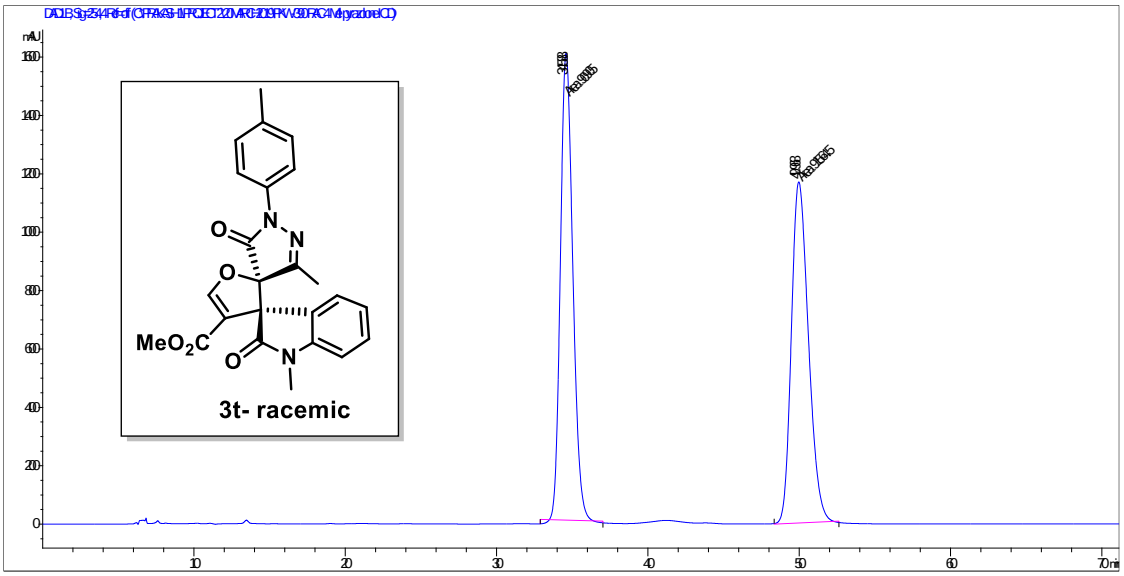
#	Time	Area	Height	Width	Area%	Symmetry
1	15.352	109136.8	2163.4	0.8408	97.647	2.116
2	20.861	2630.3	56.3	0.7792	2.353	2.092



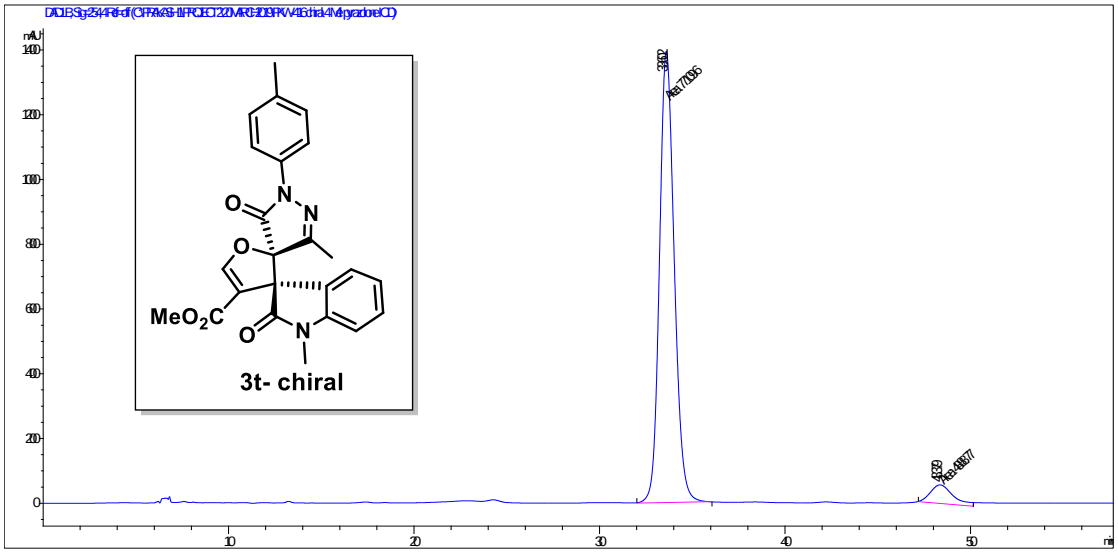
#	Time	Area	Height	Width	Area%	Symmetry
1	32.041	79410.9	1523.9	0.8685	49.905	0.88
2	41.457	79713.3	1195.5	1.1113	50.095	0.857



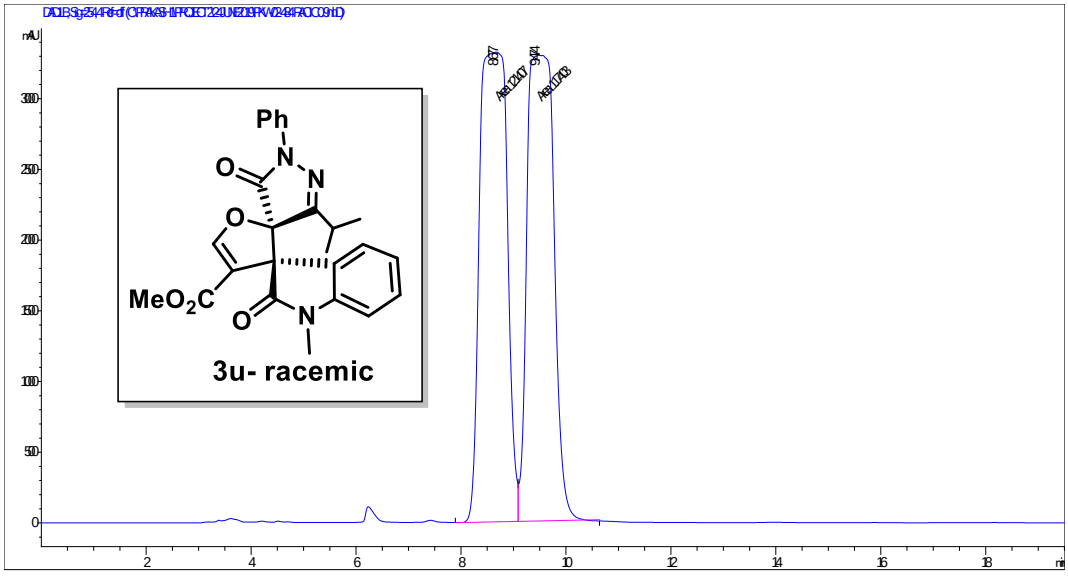
#	Time	Area	Height	Width	Area%	Symmetry
1	31.793	45468.1	868	0.8731	96.079	0.833
2	41.268	1855.4	34.9	0.8853	3.921	0.96



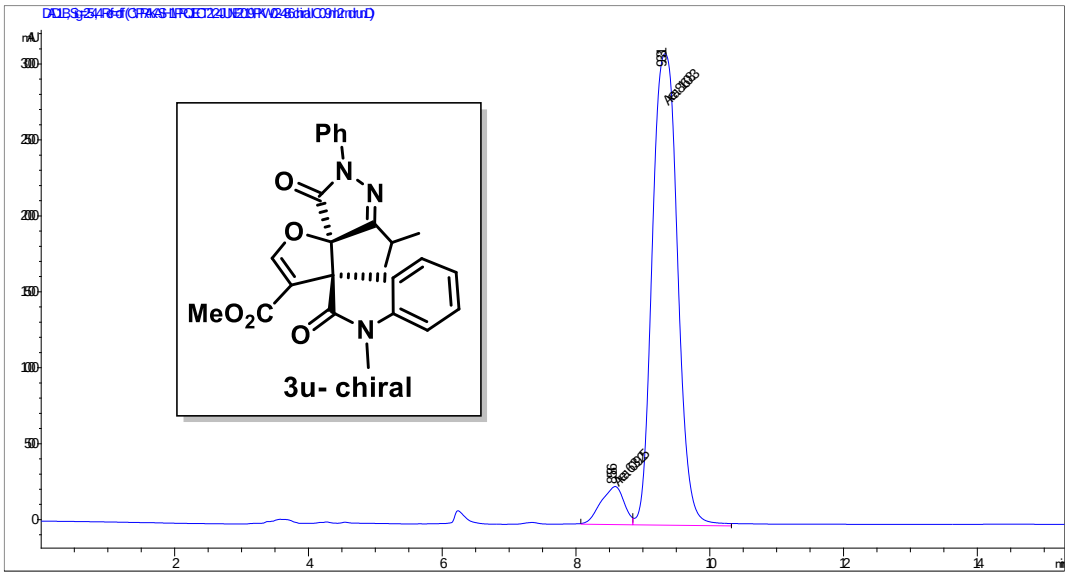
#	Time	Area	Height	Width	Area%	Symmetry
1	34.588	90905	1599.3	0.9474	49.819	0.807
2	49.968	91564.5	1168.5	1.306	50.181	0.747



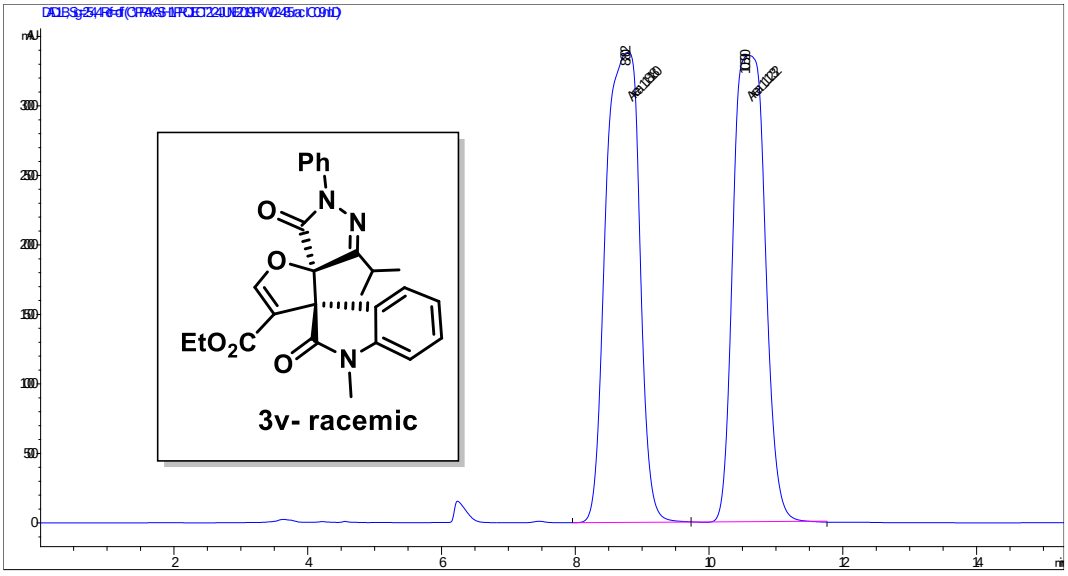
#	Time	Area	Height	Width	Area%	Symmetry
1	33.602	77109.6	1394.4	0.9217	94.038	0.831
2	48.379	4888.8	57.3	1.4211	5.962	0.685



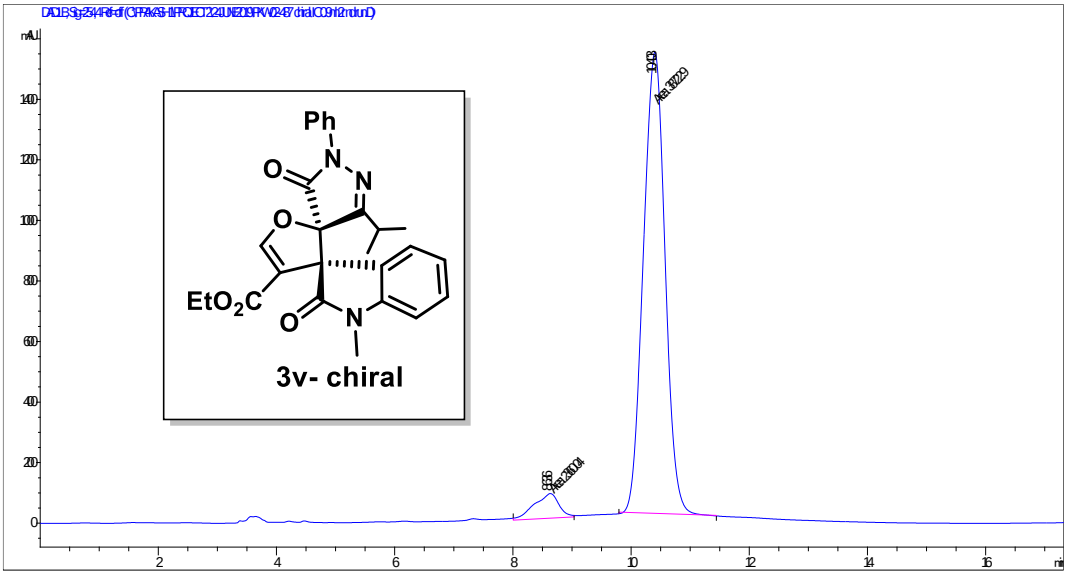
#	Time	Area	Height	Width	Area%	Symmetry
1	8.677	121406.8	3321.9	0.6091	50.838	1.431
2	9.474	117402.7	3293.4	0.5941	49.162	0.717



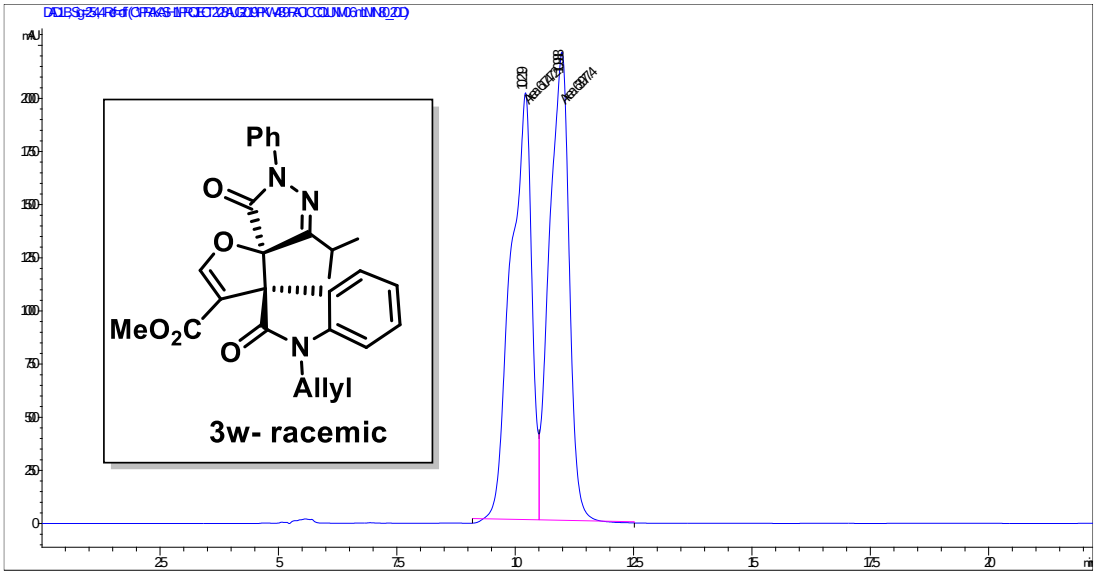
#	Time	Area	Height	Width	Area%	Symmetry
1	8.586	6039.2	250.7	0.4014	6.890	1.532
2	9.331	81608.3	3104.8	0.4381	93.110	0.959



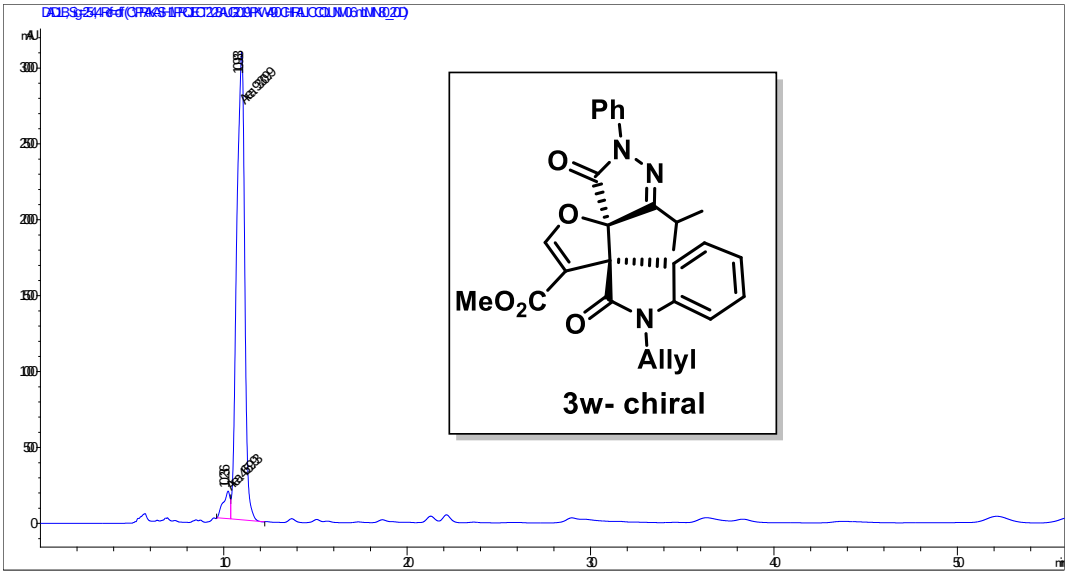
#	Time	Area	Height	Width	Area%	Symmetry
1	8.802	118180.5	3383.5	0.5821	51.514	1.902
2	10.59	111231.9	3355.2	0.5525	48.486	0.888



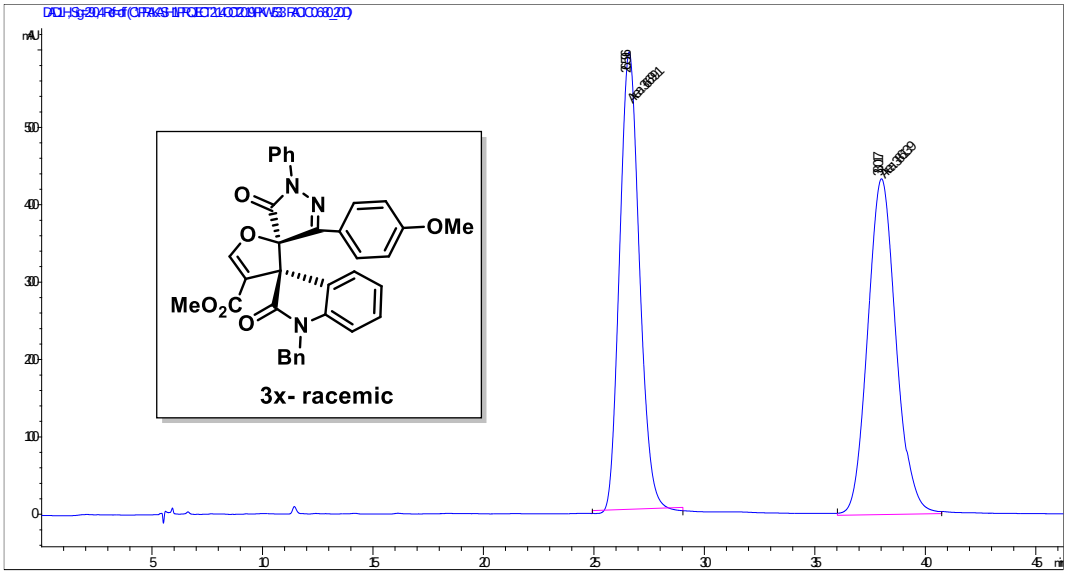
#	Time	Area	Height	Width	Area%	Symmetry
1	8.636	2360	81.2	0.4847	5.745	1.856
2	10.403	38722.9	1522.8	0.4238	94.255	1.073



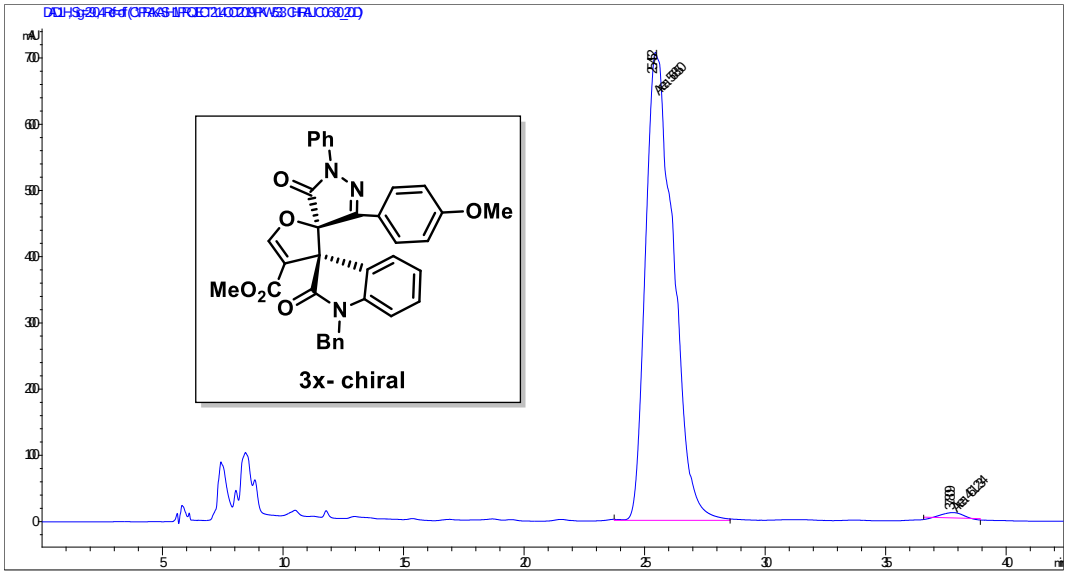
#	Time	Area	Height	Width	Area%	Symmetry
1	10.219	61747.2	2007.6	0.5126	49.113	2.168
2	10.988	63977.4	2202.6	0.4841	50.887	1.585



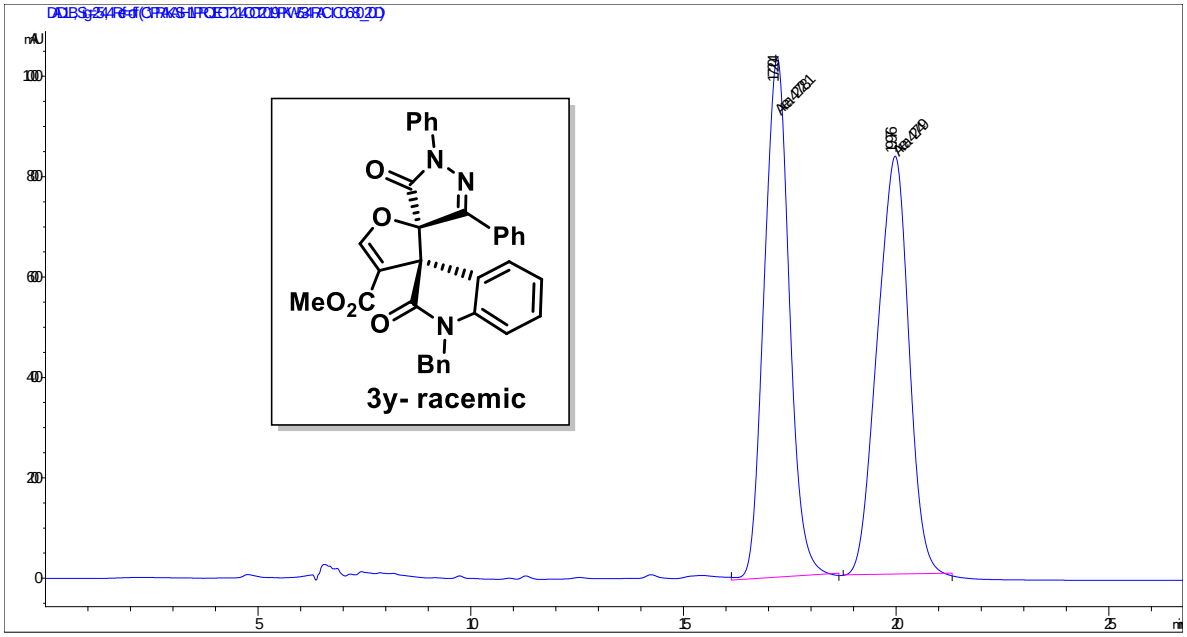
#	Time	Area	Height	Width	Area%	Symmetry
1	10.236	4659.9	181.5	0.4279	4.756	2.439
2	10.983	93309.9	3079.9	0.5049	95.244	1.567



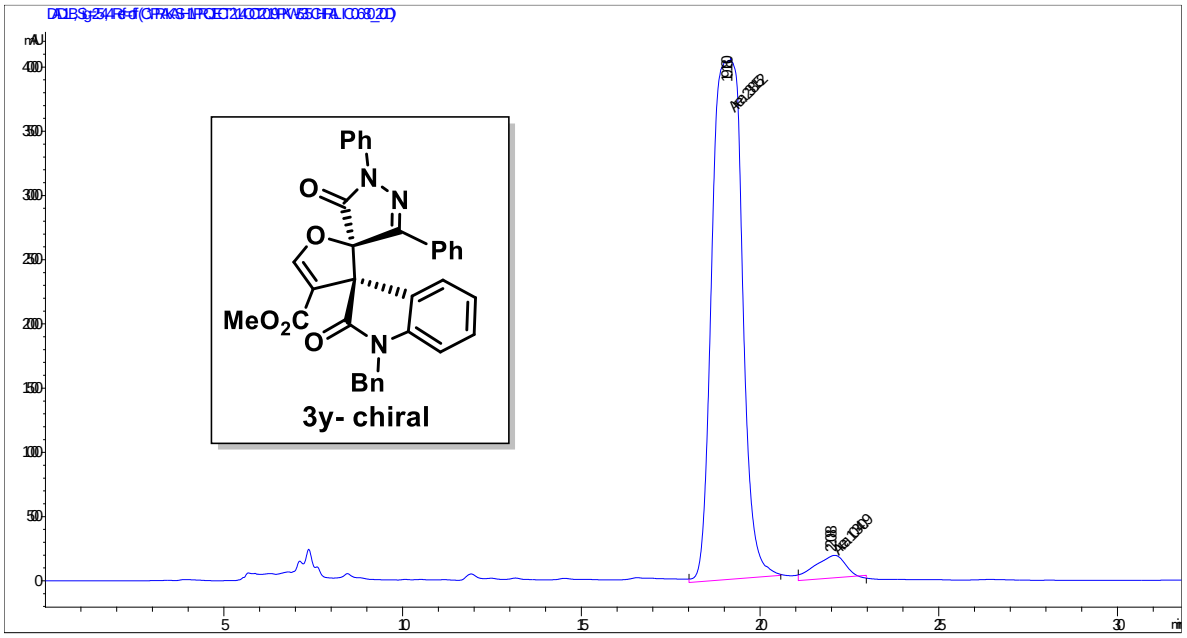
#	Time	Area	Height	Width	Area%	Symmetry
1	26.596	36699.1	591	1.035	48.729	0.885
2	38.017	38613.9	434	1.4829	51.271	0.914



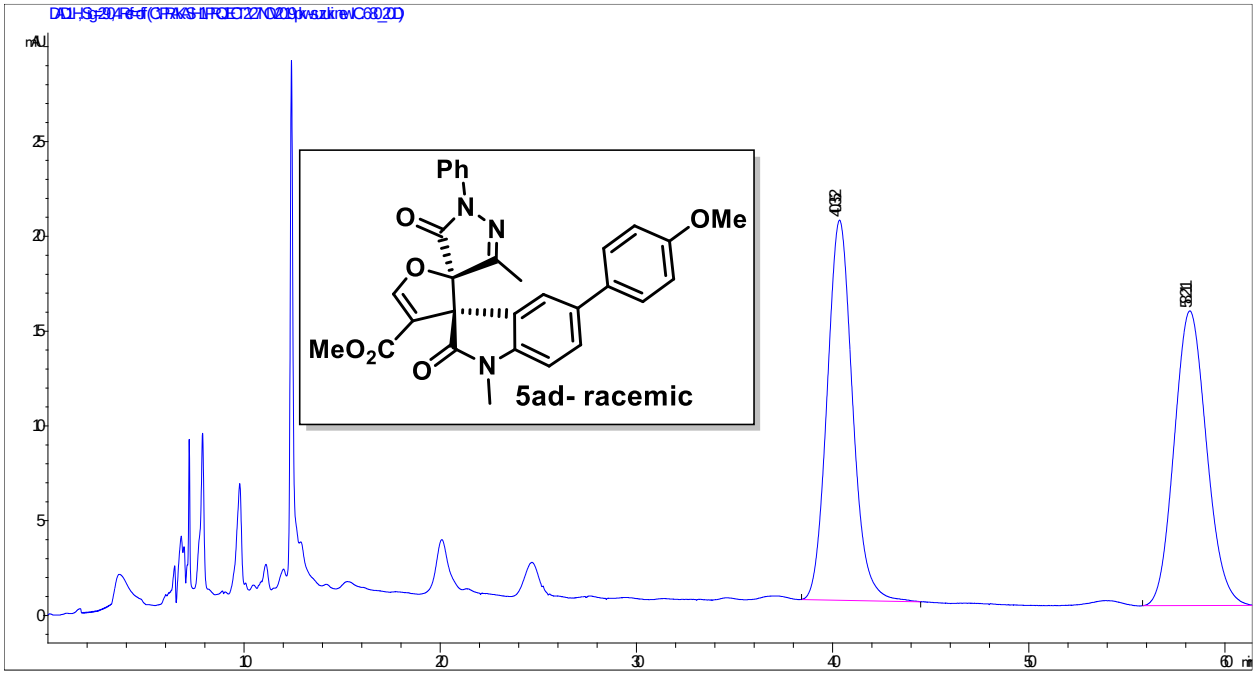
#	Time	Area	Height	Width	Area%	Symmetry
1	25.452	56850	706.8	1.3405	99.195	0.553
2	37.809	461.2	8.2	0.942	0.805	1.083



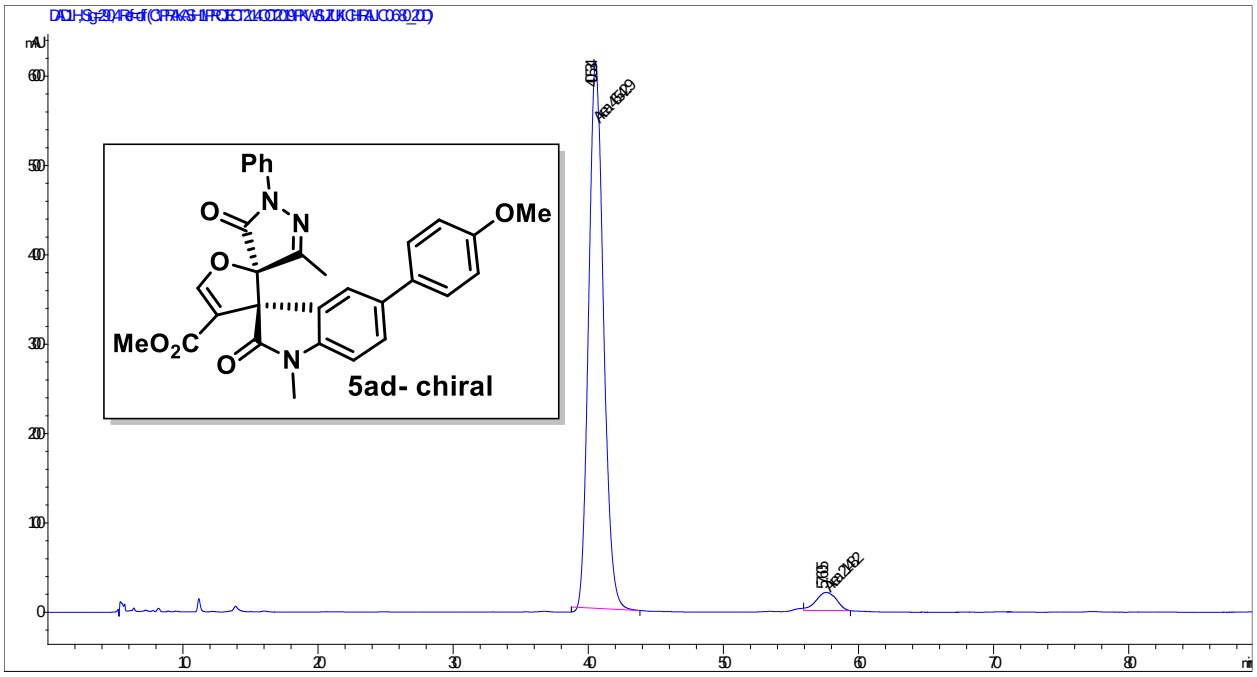
#	Time	Area	Height	Width	Area%	Symmetry
1	17.204	42728.1	1035.5	0.6877	49.988	1.023
2	19.976	42749	832.5	0.8558	50.012	1.236



#	Time	Area	Height	Width	Area%	Symmetry
1	19.18	238151.7	4056.7	0.9784	95.839	1.461
2	22.088	10340.9	175.3	0.9832	4.161	1.946



#	Time	Area	Height	Width	Area%	Symmetry
1	40.352	1805.6	20	1.2067	50.358	0.9
2	58.211	1779.9	15.5	1.3417	49.642	0.909



#	Time	Area	Height	Width	Area%	Symmetry
1	40.534	46542.9	611.4	1.2688	95.588	0.823
2	57.605	2148.2	20.4	1.7512	4.412	0.996

Molecular Structure of compound 3a using Single Crystal X-ray analysis

Datablock: T1_a

Bond precision: C-C = 0.0046 A Wavelength=1.54178

Cell: a=11.2231(13) b=8.1552(9) c=11.9835(14)
alpha=90 beta=115.450(5) gamma=90

Temperature: 100 K

	Calculated	Reported
Volume	990.4(2)	990.4(2)
Space group	P 21	P 21
Hall group	P 2yb	P 2yb
Moiety formula	C23 H19 N3 O5	?
Sum formula	C23 H19 N3 O5	C23 H19 N3 O5
Mr	417.41	417.41
Dx,g cm-3	1.400	1.400
Z	2	2
Mu (mm-1)	0.832	0.832
F000	436.0	436.0
F000'	437.43	
h,k,lmax	14,10,15	14,10,14
Nref	4279[2294]	4111
Tmin,Tmax	0.890,0.928	0.633,0.754
Tmin'	0.890	

Correction method= # Reported T Limits: Tmin=0.633 Tmax=0.754 AbsCorr = MULTI-SCAN

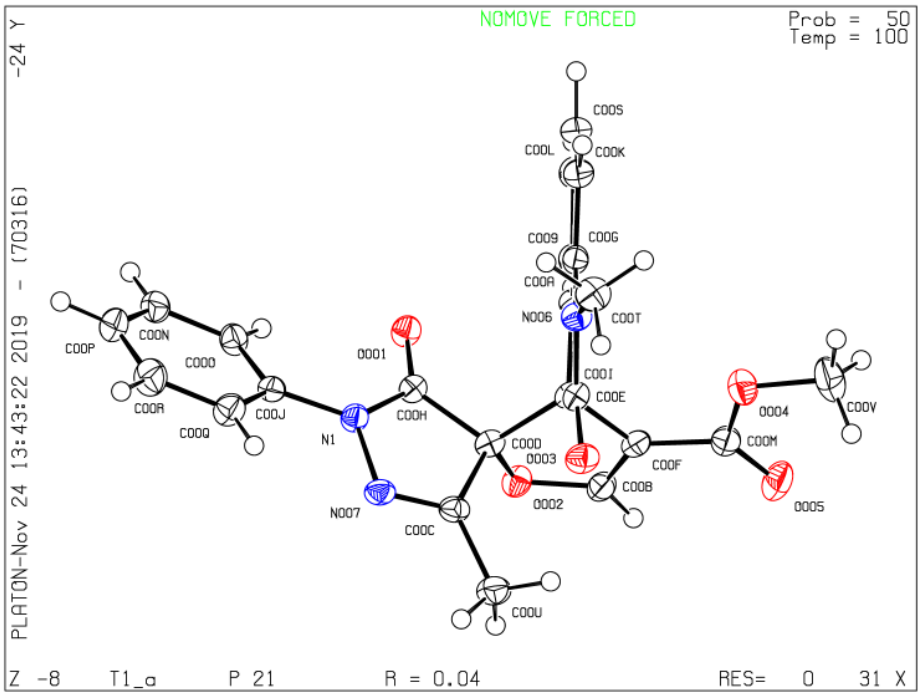
Data completeness= 1.79/0.96 Theta(max)= 78.820

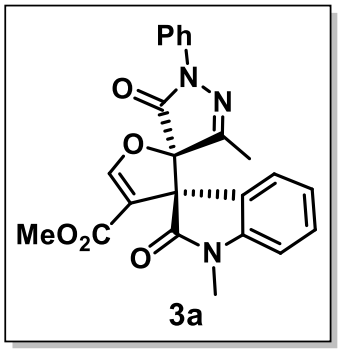
R(reflections)= 0.0368(3820) wR2(reflections)= 0.0954(4111)

S = 1.071 Npar= 284

Flack Parameter Value (CIF) -0.03(11)

Molecular Stricture of compound 3a using Single Crystal X-ray analysis





3a

Refrences

1] Choudhury, A. R.; Mukherjee, S. *Org. Biomol. Chem*. **2012**, *10*, 7313-7320

2] Zhan, G.; Shi, M.-L.; He, Q.; Lin, W. J.; Ouyang, Q.; Du, W.; Chen, Y. C. *Angew. Chem., Int. Ed*. **2016**, *55*, 2147-2151

3] (a) Zhong, N.J.; Wei, F.; Xuan, Q. Q.; Liu, L.; Wang, D.; Chen, Y. J. *Chem. Commun*. **2013**, *49*, 11071-11073; (b) Fan, X.; Yang, H.; Shi, M. *Adv. Synth. Catal*. **2017**, *359*, 49-57.

4] (a) Kaya, U.; Chauhan, P.; Mahajan, S.; Deckers, K.; Valkonen, A.; Rissanen, K.; Enders, D. *Angew. Chem., Int. Ed*. **2017**, *56*, 15358−15362. (b) Chauhan, P.; Mahajan, S.; Kaya, U.; Peuronen, A.; Rissanen, K.; Enders, D. *J. Org. Chem*. **2017**, *82*, 7050−7058. (c) Mahajan, S.; Chauhan, P.; Kaya, U.; Deckers, K.; Rissanen, K.; Enders, D. *Chem. Commun*. **2017**, *53*, 6633−6636. (d) Ray, B.; Mukherjee, S. *J. Org. Chem*. **2018**, *83*, 10871−10880.