Supporting Information

Strain-release driven spirocyclization of bicyclo[1.1.0]butanes: access to 6,7-diazaspiro[3.4]octane

Qin Jiang, Jianyang Dong,* Fang Lei, Dejiang Yu, Ting Li, Huaming Sun, and Dong Xue*

E-mail: jydong@snnu.edu.cn; xuedong_welcome@snnu.edu.cn

Table of contents

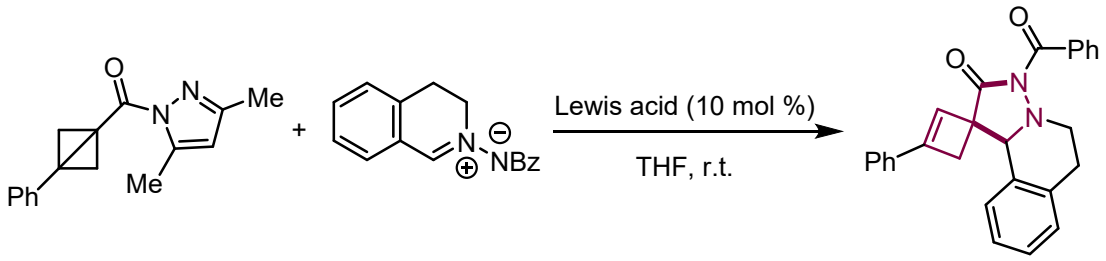
1. General information

Commercially available reagents were used without further purification unless otherwise stated. All reactions were carried out under argon atmosphere with dry solvents under anhydrous conditions, all solvents were purchased from Energy Chemical and stored over molecular sieves. Analytical thin-layer chromatography (TLC) was conducted with TLC plates (Silica gel 60 F254, Qingdao Haiyang) and visualization on TLC was achieved by UV light or Phosphomolybdic acid. Flash column chromatography was performed on silica gel 200-300 mesh with freshly distilled solvents. Nuclear magnetic resonance (NMR) spectra were recorded on a Bruker 600, 400 and JEOL 400 MHz in Chloroform-*d* solvent. All chemical shifts in ^{1}H NMR spectra were given in parts per million (ppm) relative to the residual or Chloroform-*d* (7.26 ppm) as internal standards and coupling constants (*J*) were given in Hertz (Hz). ^{13}C NMR chemical shifts were reported in ppm relative to the central peak of Chloroform-*d* (77.16 ppm) as internal standards. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, q = quartet, m = multiplet, dd = doublet of doublets, dt = doublet of triplets), coupling constant (Hz), and integration. HRMS data were obtained by ESI or APCI method with Bruker mass spectrometer (MAXIS). The absolute configurations of **3a** were assigned by the X-ray analysis and the configurations of other cycloaddition products were assigned by analogy. The X-ray single-crystal determination was performed on Bruker D8 VENTURE X-ray single crystal diffractometer. Melting points (M. p.) were recorded on an Electrothermal WRX-4 melting point apparatus.

1a-1i were prepared according to the literature procedure.[1] **2a, 3j-3ac** were prepared according to the literature procedure.[2]

2. Optimization of reaction conditions

Table S1. The screening of Lewis acid.[a]



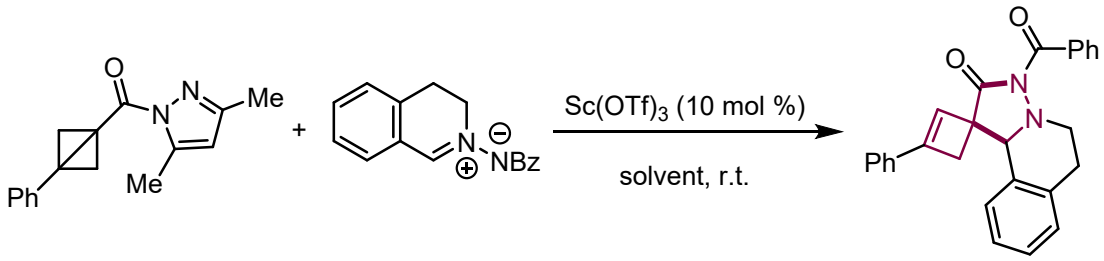
1a **2a** **3a**

entry	Lewis acid	d.r.	yield (%)
1	$Sc(OTf)_3$	1.7:1	78
2	$Cu(OTf)_2$	2.7:1	63

3	$Yb(OTf)_3$	2.0:1	57
4	$Mg(OTf)_2$	--	trace
5	$Zn(OTf)_2$	1.8:1	78
6	$Eu(OTf)_3$	1.5:1	72
7	$Lu(OTf)_3$	1.5:1	64
8	$La(OTf)_3$	--	trace
9	$Bi(OTf)_3$	1.7:1	74

[a]Reaction conditions: **1a** (0.1 mmol), **2a** (0.15 mmol), Lewis acid (10 mol%), THF (2.0 mL), Ar, room temperature (r.t.), 12 h. Yields were determined by ^{1}H NMR spectroscopy with CH_2Br_2 as an internal standard.

Table S2. The screening of solvent.[a]

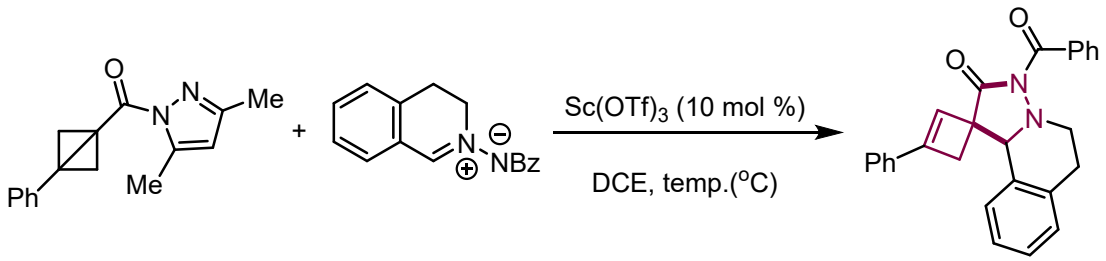


1a **2a** **3a**

entry	solvent	d.r.	yield (%)
1	THF	1.7:1	78
2	1,4-Dioxane	1.3:1	86
3	1,3-Dioxane	1.4:1	86
4	DME	1.0:1	76
5	DCM	1.4:1	84
6	DCE	1.7:1	87 (84[b])
7	MeOH	1.3:1	58
8	MeCN	1.3:1	75
9	EtOAc	1.3:1	69
10	PhCl	1.2:1	68
11[c]	DCE	3.0:1	68
11[d]	DCE	4.6:1	51

[a]Reaction conditions: **1a** (0.1 mmol), **2a** (0.15 mmol), $Sc(OTf)_3$ (10 mol%), solvent (2.0 mL), Ar, room temperature (r.t.), 12 h. Yields were determined by ^{1}H NMR spectroscopy with CH_2Br_2 as an internal standard. [b]Isolated yield. [c]$Sc(OTf)_3$ (5 mol%). [d]$Sc(OTf)_3$ (2.5 mol%).

Table S3. Investigation of reaction temperature.[a]

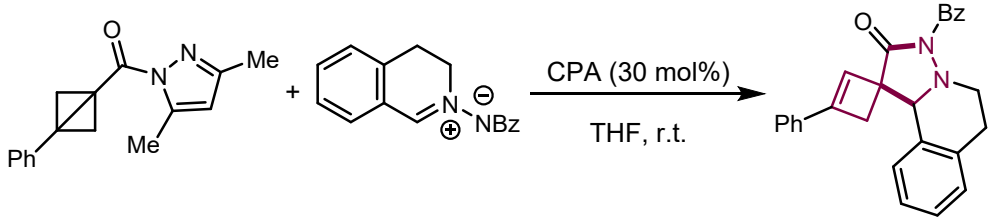


1a **2a** **3a**

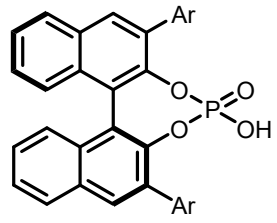
entry	temp.(°C)	d.r.	yield (%)
1	0	2.0:1	58
2	r.t.	1.7:1	87 (84[b])
3	40	1.5:1	86
4	50	1.3:1	87
5	60	1.3:1	84

[a]Reaction conditions: **1a** (0.1 mmol), **2a** (0.15 mmol), $Sc(OTf)_3$ (10 mol%), solvent (2.0 mL), Ar, 12 h. Yields were determined by ^1H NMR spectroscopy with CH_2Br_2 as an internal standard. [b] Isolated yield.

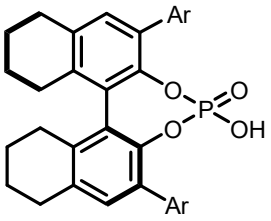
Table S4. The screening of chiral phosphoric acid.[a]



1a **2a** **3a**



C1: Ar = phenanthrenyl
C2: Ar = 4-OMePh
C3: Ar = 4-^{t}BuPh
C4: Ar = 2,4,6-trimethyl-Ph
C5: Ar = 2,4,6-tri-^{i}Pr-Ph



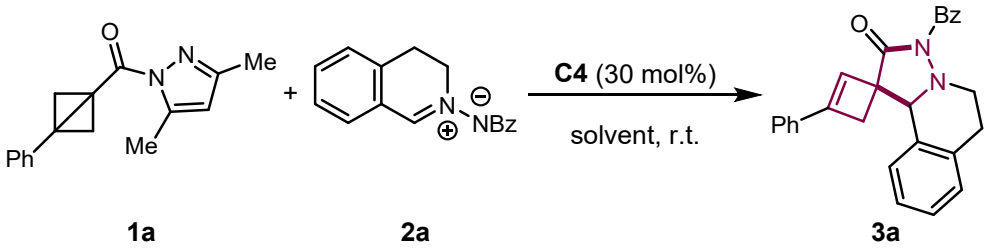
C6: Ar = phenanthrenyl

entry	CPA	d.r.	*ee* (%)	yield (%)
1	**C1**	5.4:1	56/29	54
2	**C2**	1.9:1	44/22	48
3	**C3**	1.4:1	17/8	44
4	**C4**	3.3:1	78/49	63
5	**C5**	2.7:1	40/78	40

6	**C6**	5.0:1	56/29	20

[a]Reaction conditions: **1a** (0.1 mmol), **2a** (0.15 mmol), CPA (30 mol%), THF (2.0 mL), Ar, room temperature (r.t.), 12 h. Yields were determined by ^{1}H NMR spectroscopy with CH_2Br_2 as an internal standard. The d.r. values were measured by ^{1}H NMR and the *ee*. values were determined by HPLC on a chiral stationary phase.

Table S5. Screening of solvent using CPA **C4**.[a]

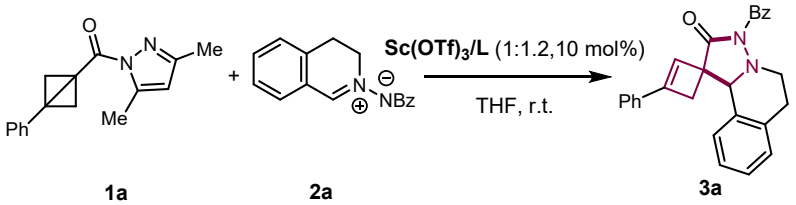


1a **2a** **3a**

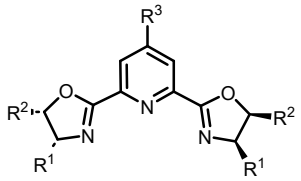
entry	solvent	d.r.	*ee* (%)	yield (%)
1	THF	3.3:1	78/49	63
2	2Me-THF	2.3:1	74/44	59
3	1,3-dioxane	1.8:1	65/48	61
4	1,4-dioxane	1.7:1	82/63	66
5	DME	1.3:1	58/54	54
6	MeCN	2.0:1	3/14	57
7	DCE	1.9:1	35/12	70
8	DCM	1.9:1	35/12	70
9	EtOAc	1.7:1	56/46	61
10	PhCl	1.5:1	34/8	50

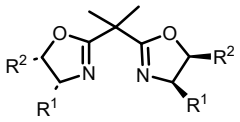
[a]Reaction conditions: **1a** (0.1 mmol), **2a** (0.15 mmol), **C4** (30 mol%), solvent (2.0 mL), Ar, room temperature (r.t.), 12 h. Yields were determined by ^{1}H NMR spectroscopy with CH_2Br_2 as an internal standard. The d.r. values were measured by ^{1}H NMR and the *ee*. values were determined by HPLC on a chiral stationary phase.

Table S6. Screening of chiral ligand using $Sc(OTf)_3$.



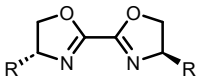
1a **2a** **3a**

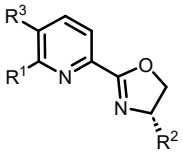




(*S*)-**L1**:R^1 = Me, R^2 = H, R^3 = H, 84% yield, dr 1.8/1, *ee* 0/3
(*S*)-**L2**:R^1 = *i*-Pr, R^2 = H, R^3 = Br, 81% yield, dr 1.9/1, *ee* 0/0
(*R*)-**L3**:R^1 = ^{t}Bu, R^2 = H, R^3 = H, 73% yield, dr 1.6/1, *ee* 0/0
(*R*)-**L5**:R^1 = Ph, R^2 = H, R^3 = H, 73% yield, dr 1.6/1, *ee* 0/0
(*R*)-**L6**:R^1 = Bn, R^2 = H, R^3 = H, 73% yield, dr 1.6/1, *ee*

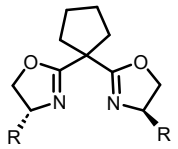
(*R*)-**L7**:R^1 = Ph, R^2 = H, 81% yield, dr 1.8/1, *ee* 0/0
(*R*)-**L8**:R^1 = ^{t}Bu, R^2 = H, 81% yield, dr 1.8/1, *ee* 0/2

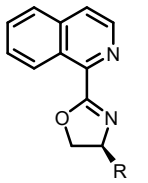




(*S*)-**L9**:R = ^{t}Bu, 87% yield, dr 1.7/1, *ee* 0/2
(*S*)-**L10**:R = *i*-Pr, 94% yield, dr 1.6/1,*ee* 0/0
(*S*)-**L11**:R = Bn, 81% yield, dr 1.6/1, *ee* 0/0

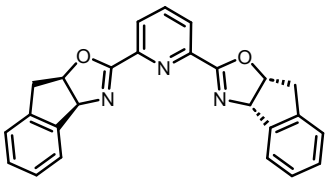
(*S*)-**L12**:R^1 = Me, R^2 = i-Pr, R^3 = H, 88% yield, dr 1.7/1, *ee* 0/3
(*S*)-**L13**:R^1 = ^{t}Bu, R^2 = H, R^3 = CF_3, 90% yield, dr 1.6/1, *ee* 0/0

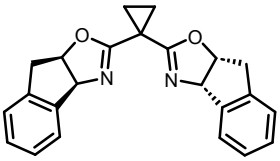




(*R*)-**L14**:R = Ph, 74% yield, dr 1.7/1, *ee* 4/8
(*S*)-**L15**:R = Bn, 82% yield, dr 1.6/1, *ee 0/2*

(S)-**L16: R = ^{t}Bu** 79% yield, dr 1.7/1, *ee* 0/0
(S)-**L17: R = Ph** 79% yield, dr 1.7/1, *ee* 2/2

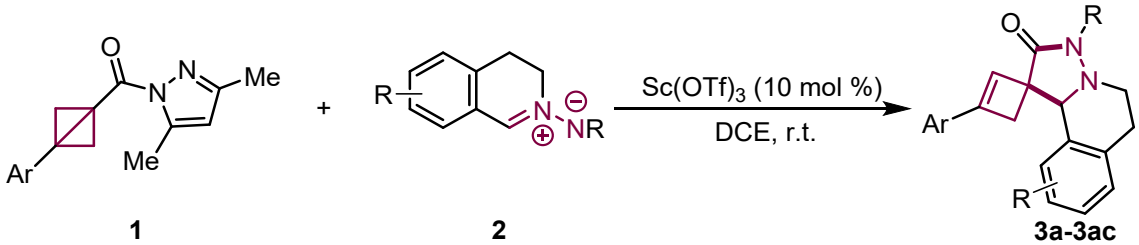




L18: 91% yield, dr 1.9/1, *ee* 0/0

L19: 81% yield, dr 1.8/1, *ee* 0/0

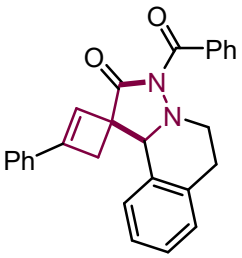
3. General procedure for reactions



1 **2** **3a-3ac**

To a 10 mL reaction vial equipped with a magnetic stir bar was added compounds **1** (0.2 mmol, 1.0 equiv.), **2** (0.3 mmol, 1.5 equiv.), $Sc(OTf)_3$ (10 mol%), and the tube was evacuated and backfilled with argon three times. DCE (4.0 mL) was added under argon atmosphere. The mixture was then stirred rapidly for 12 hours. Upon completion of the reaction, the reaction mixture was filtered through celite pad and concentrated in vacuo to give the crude product. The crude product was purified by silica gel chromatography to afford the product **3a-3ac.**

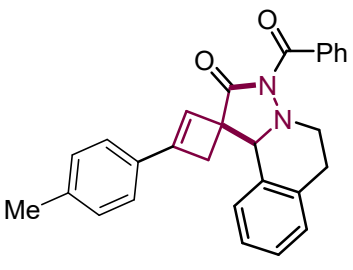
3'-benzoyl-3-phenyl-6',10b'-dihydro-5′*H*-spiro[cyclobutane-1,1'-pyrazolo[5,1-*a*]isoquinolin]-2-en-2'(3′*H*)-one (3a)



3a

The crude product was purified by column chromatography on silica gel (PE/EtOAc = 4:1). D.r. 1.7:1, yellow solid, 68.2 mg, 84% yield. M. p. 171.0 – 172.4 °C. 63% and 82% *ee* was determined by HPLC analysis (chiral IB column, 15% IPA in hexane, rate: 1.0 mL/min, 254 nm). Retention time: t (minor) = 29.71 and 42.33 min, t (major) = 35.69 and 58.07 min. **^{1}H NMR** (400 MHz, Chloroform-*d*, ppm): δ 7.71 (d, *J* = 7.7 Hz, 2H), 7.55 – 7.48 (m, 1H), 7.42 (t, *J* = 7.6 Hz, 2H), 7.37 – 7.23 (m, 5H), 7.23 – 7.14 (m, 3H), 7.14 – 7.01 (m, 1H), 6.39 (s, 0.62H), 5.98 (s, 0.37H), 5.04 (s, 0.37H), 4.98 (s, 0.63H), 3.80 – 3.59 (m, 1H), 3.41 – 3.15 (m, 2H), 3.14 – 2.96 (m, 1H), 2.93 – 2.73 (m, 1.69H), 2.42 (d, *J* = 12.5 Hz, 0.69H). **^{13}C NMR** (101 MHz, Chloroform-*d,* ppm) δ 175.9 and 175.3, 166.6 and 166.5, 150.7 and 149.0, 134.0 and 133.9, 133.2, 132.8 and 132.7, 132.1 and 132.0, 131.8 and 130.9, 129.1 and 129.0, 128.9, 128.7 and 128.6, 128.4, 128.0 and 127.9, 127.8 and 127.6, 126.7 and 126.3, 126.0 and 125.8, 125.3 and 125.2, 124.1, 62.9 and 62.8, 54.7 and 54.1, 50.2 and 50.0, 38.1 and 37.3, 29.0 and 28.7. **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{27}H_{23}N_2O_2$ 407.1754; Found 407.1746.

3'-benzoyl-3-(*p*-tolyl)-6',10b'-dihydro-5'*H*-spiro[cyclobutane-1,1'-pyrazolo[5,1-*a*]isoquinolin]-2-en-2'(3'*H*)-one (3b)

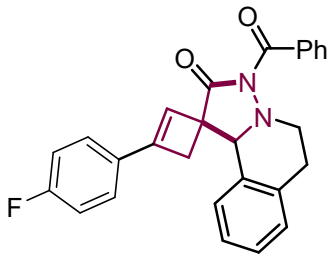


3b

The crude product was purified by column chromatography on silica gel (PE/EtOAc = 4:1). D.r. 1.5:1, yellow solid, 72.2 mg, 86% yield. M. p. 83.8 – 84.6 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*, ppm): δ 7.73 (d, *J* = 7.5 Hz, 2H), 7.56 – 7.47 (m, 1H), 7.48 – 7.39 (m, 2H), 7.25 – 7.15 (m, 5H), 7.15 – 7.04 (m, 3H), 6.34 (s, 0.56H),

5.93 (s, 0.46H), 5.05 (s, 0.44H), 4.99 (s, 0.56H), 3.78 – 3.63 (m, 1H), 3.39 – 3.14 (m, 2H), 3.14 – 2.96 (m, 1H), 2.93 – 2.74 (m, 1.7H), 2.41 (d, *J* = 12.4 Hz, 0.62H), 2.33 (s, 3H). **^{13}C NMR** (101 MHz, Chloroform-*d,* ppm) δ 176.0 and 175.4, 166.5 and 166.4, 150.6 and 148.9, 139.0 and 138.9, 134.0 and 133.9, 133.2, 132.0 and 131.9, 131.8 and 130.9, 130.2 and 130.1, 129.1, 129.0 and 128.9, 128.6 and 128.5, 127.9, 127.6 and 127.5, 126.6 and 126.2, 125.9 and 125.8, 125.2 and 125.1, 124.8 and 122.9, 62.9 and 62.8, 54.6 and 54.0, 50.1 and 49.9, 38.0 and 37.3, 28.9 and 28.6, 21.5. **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{28}H_{25}N_2O_2$ 421.1911; Found 421.1904.

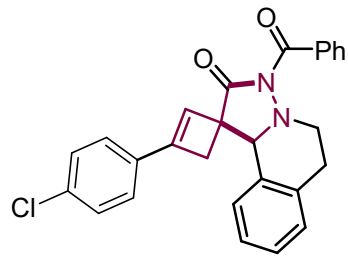
3'-benzoyl-3-(4-fluorophenyl)-6',10b'-dihydro-5'*H*-spiro[cyclobutane-1,1'-pyrazolo[5,1-*a*]isoquinolin]-2-en-2'(3'*H*)-one (3c)



3c

The crude product was purified by column chromatography on silica gel (PE/EtOAc = 4:1). D.r. 2.1:1 yellow solid, 51.7 mg, 61% yield. M. p. 91.4 – 92.6 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*, ppm): δ 7.71 (d, *J* = 7.6 Hz, 2H), 7.57 – 7.48 (m, 1H), 7.48 – 7.36 (m, 2H), 7.29 – 7.17 (m, 4H), 7.17 – 7.05 (m, 2H), 7.05 – 6.84 (m, 2H), 6.33 (s, 0.63H), 5.92 (s, 41H), 5.03 (s, 0.35H), 4.98 (s, 0.63H), 3.77 – 3.56 (m, 1H), 3.42 – 3.12 (m, 2H), 3.12 – 2.95 (m, 1H), 2.89 – 2.74 (m, 1.67H), 2.39 (d, *J* = 12.5 Hz, 0.61H). **^{13}C NMR** (100 MHz, Chloroform-*d*, ppm): δ 175.8 and 175.2, 166.5, 163.1 (d, *J* = 249.2 Hz), 149.5 and 147.9, 133.9 and 133.8, 133.2, 132.1 and 132.0, 131.8 and 130.8, 129.0 and 128.9, 128.8 and 128.7, 128.0, 127.8 and 127.7, 127.2, 127.1 and 127.0, 126.7 and 126.3, 125.9 and 125.8, 123.6 (d, *J* = 2.3 Hz), 115.6 and 115.4, 62.9 and 62.8, 54.6 and 54.0, 50.2 and 50.0, 38.1 and 37.3, 28.9 and 28.6. **^{19}F NMR** (376 MHz, Chloroform-*d,* ppm) δ -111.30 – -111.43 (m) and -111.43 – -111.55 (m). **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{27}H_{22}FN_2O_2$ 425.1660; Found 425.1656.

3'-benzoyl-3-(4-chlorophenyl)-6',10b'-dihydro-5'*H*-spiro[cyclobutane-1,1'-pyrazolo[5,1-*a*]isoquinolin]-2-en-2'(3'*H*)-one (3d)

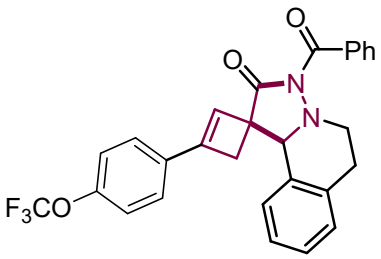


3d

The crude product was purified by column chromatography on silica gel (PE/EtOAc = 4:1). D.r. 1.6:1, yellow solid, 58.9 mg, 67% yield. M. p. 93.3 – 95.3 °C. **^{1}H NMR** (400 MHz, Chloroform-*d,* ppm) δ 7.71 (d, *J* = 7.6 Hz, 2H), 7.55 – 7.48 (m, 1H), 7.48 – 7.38 (m, 2H), 7.29 – 7.08 (m, 8H), 6.39 (s, 0.68H), 5.98 (s,

0.37H), 5.03 (s, 0.34H), 4.98 (s, 0.66H), 3.77 – 3.58 (m, 1H), 3.39 – 2.95 (m, 3H), 2.89 – 2.74 (m, 1.66H), 2.39 (d, *J* = 12.4 Hz, 0.63H). **^{13}C NMR** (100 MHz, Chloroform-*d*, ppm): δ 175.7 and 175.0, 166.5, 149.4 and 147.8, 134.9 and 134.8, 133.89 and 133.85, 133.2, 132.2 and 132.1, 131.7 and 130.8, 131.21 and 131.17, 129.01 and 128.95, 128.8 128.72 and 128.70, 128.0, 127.8 and 127.7, 126.53 and 126.50, 126.3, 125.9 and 125.73, 124.8, 62.9 and 62.8, 54.8 and 54.2, 50.2 and 50.0, 38.0 and 37.2, 28.9 and 28.6. **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{27}H_{22}ClN_2O_2$ 441.1364; Found 441.1362.

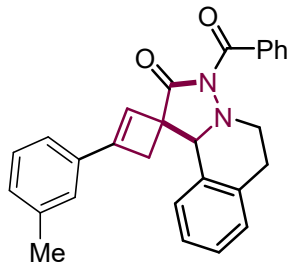
3'-benzoyl-3-(4-(trifluoromethoxy)phenyl)-6',10b'-dihydro-5'*H*-spiro [cyclobutane-1,1'-pyrazolo[5,1-*a*]isoquinolin]-2-en-2'(3'*H*)-one (3e)



3e

The crude product was purified by column chromatography on silica gel (PE/EtOAc = 4:1). D.r. 1.6:1, yellow solid, 60.8 mg, 62% yield. M. p. 77.6 – 78.8 °C. **^{1}H NMR** (400 MHz, Chloroform-*d,* ppm) δ 7.71 (d, *J* = 7.7 Hz, 2H), 7.60 – 7.47 (m, 1H), 7.42 (t, *J* = 7.5 Hz, 2H), 7.32 – 7.24 (m, 2H), 7.24 – 7.19 (m, 2H), 7.18 – 7.03 (m, 4H), 6.41 (s, 0.57H), 5.99 (s, 0.44H), 5.04 (s, 0.42H), 4.99 (s, 0.58H), 3.81 – 3.57 (m, 1H), 3.44 – 3.13 (m, 2H), 3.13 – 2.94 (m, 1H), 2.90 – 2.72 (m, 1.77H), 2.41 (d, *J* = 12.5 Hz, 0.59H). **^{13}C NMR** (100 MHz, Chloroform-*d*, ppm): δ 175.5 and 174.9, 166.4 and 166.3, 149.5 and 149.4, 149.1 and 147.5, 133.8 and 133.7, 133.2 and 133.1, 132.0 and 131.9, 131.6 and 130.7, 131.4 and 131.3, 129.0 and 128.9, 128.7 and 128.6, 127.9, 127.8 and 127.6, 126.9 and 126.2, 126.7 and 126.6, 125.8 and 125.7, 125.0, 120.9, 120.4 (q, *J* = 257.6 Hz), 62.8 and 62.7, 54.7 and 54.1, 50.2 and 49.9, 38.0 and 37.2, 28.8 and 28.6. **^{19}F NMR** (376 MHz, Chloroform-*d,* ppm) δ -57.77 (s). **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{28}H_{22}F_3N_2O_3$ 491.1577; Found 491.1572.

3'-benzoyl-3-(*m*-tolyl)-6',10b'-dihydro-5'*H*-spiro[cyclobutane-1,1'-pyrazolo[5,1-*a*]isoquinolin]-2-en-2'(3'*H*)-one (3f)

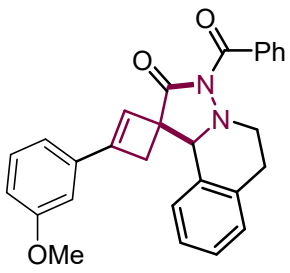


3f

The crude product was purified by column chromatography on silica gel (PE/EtOAc = 4:1). D.r. 1.5:1, yellow solid, 56.3 mg, 67% yield. M. p. 84.4 – 86.9 °C. **^{1}H NMR** (400 MHz, Chloroform-*d,* ppm) δ 7.74 – 7.67 (m, 2H), 7.57 – 7.48 (m, 1H), 7.45 – 7.38 (m, 2H), 7.23 – 7.14 (m, 4H), 7.14 – 7.05 (m, 4H), 6.37 (s, 0.58H), 5.96 (s, 0.41H), 5.03 (s, 0.41H),

4.98 (s, 0.59H), 3.74 – 3.61 (m, 1H), 3.38 – 3.14 (m, 2H), 3.13 – 2.97 (m, 1H), 2.90 – 2.75 (m, 1.68H), 2.41 (d, *J* = 12.4 Hz, 0.59H), 2.30 (s, 3H). **^{13}C NMR** (100 MHz, Chloroform-*d*, ppm): δ 175.9 and 175.3, 166.6 and 166.5, 150.8 and 149.2, 138.1 and 138.0, 134.0 and 133.9, 133.2, 132.8 and 132.7, 132.1 and 132.0, 131.9 and 130.9, 129.8 and 129.7, 129.0 and 128.9, 128.7 and 128.6, 128.3, 128.0, 127.7 and 127.6, 126.7 and 126.3, 126.0 and 125.9, 125.8 and 125.7, 123.8, 122.4 and 122.3, 62.9 and 62.8, 54.7 and 54.1, 50.2 and 49.9, 38.1 and 37.4, 29.0 and 28.7, 21.4. **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{28}H_{25}N_2O_2$ 421.1911; Found 421.1903.

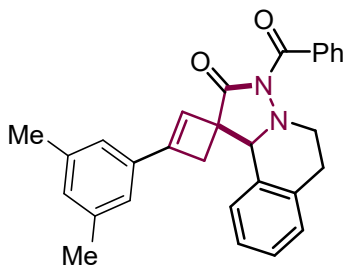
3'-benzoyl-3-(3-methoxyphenyl)-6',10b'-dihydro-5'*H*-spiro[cyclobutane-1,1'-pyrazolo[5,1-*a*]isoquinolin]-2-en-2'(3'*H*)-one (3g)



3g

The crude product was purified by column chromatography on silica gel (PE/EtOAc = 3:1). D.r. 1.5:1, yellow solid, 58.4 mg, 67% yield. M. p. 65.5 – 66.9 °C. **^{1}H NMR** (400 MHz, Chloroform-*d,* ppm) δ 7.76 – 7.67 (m, 2H), 7.60 – 7.48 (m, 1H), 7.42 (t, *J* = 7.6 Hz, 2H), 7.24 – 7.04 (m, 5H), 6.91 – 6.80 (m, 2H), 6.78 (s, 1H), 6.39 (s, 0.54H), 5.98 (s, 0.49H), 5.03 (s, 0.46H), 4.98 (s, 0.54H), 3.77 (d, *J* = 2.6 Hz, 3H), 3.74 – 3.63 (m, 1H), 3.42 – 3.13 (m,2H), 3.13 – 2.95 (m, 1H), 2.93 – 2.71 (m, 1.62H), 2.40 (d, *J* = 12.5 Hz, 0.55H). **^{13}C NMR** (100 MHz, Chloroform-*d*, ppm): δ 175.9 and 175.2, 166.6 and 166.5, 159.7, 150.6 and 149.0, 134.2 and 134.1, 134.0 and 133.9, 133.2, 132.1 and 132.0, 131.8 and 130.9, 129.5, 129.0 and 128.9, 128.7 and 128.6, 128.0, 127.8 and 127.6, 126.7, 126.4 and 126.3, 126.0 and 125.8, 124.5, 117.9 and 117.8, 114.8 and 110.5, 62.9 and 62.8, 55.3, 54.7 and 54.1, 50.2 and 50.0, 38.2 and 37.4, 29.0 and 28.7. **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{28}H_{25}N_2O_3$ 437.1860; Found 437.1858.

3'-benzoyl-3-(3,5-dimethylphenyl)-6',10b'-dihydro-5'*H*-spiro[cyclobutane-1,1'-pyrazolo[5,1-*a*]isoquinolin]-2-en-2'(3'*H*)-one (3h)

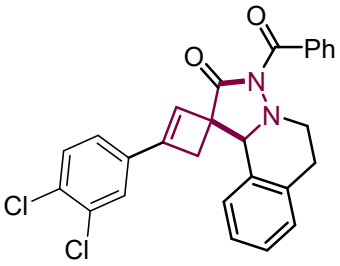


3h

The crude product was purified by column chromatography on silica gel (PE/EtOAc = 4:1). D.r. 1.4:1, yellow solid, 54.7 mg, 63% yield. M. p. 89.6 – 90.6 °C. **^{1}H NMR** (400 MHz, Chloroform-*d,* ppm) δ 7.72 (d, *J* = 7.7 Hz, 2H), 7.53 (t, *J* = 7.5 Hz, 1H), 7.43 (t, *J* = 7.6 Hz, 2H), 7.24 – 7.16 (m, 3H), 7.16 – 7.07 (m, 1H), 6.95 – 6.89 (m, 3H), 6.36 (s, 0.53H), 5.96 (s, 0.45H), 5.04 (s, 0.46H),

4.99 (s, 0.54H), 3.76 – 3.65 (m, 1H), 3.37 – 3.15 (m, 2H), 3.14 – 2.99 (m, 1H), 2.91 – 2.75 (m, 1.69H), 2.42 (d, *J* = 12.4 Hz, 0.61H), 2.27 (s, 6H). **^{13}C NMR** (100 MHz, Chloroform-*d*, ppm): δ 175.9 and 175.3, 166.5 and 166.4, 150.9 and 149.2, 137.9, 133.9 and 133.8, 133.1, 132.7 and 132.6, 132.0 and 131.9, 131.8 and 130.9, 130.7 and 130.6, 129.0 and 128.9, 128.6 and 128.5, 127.9, 127.6 and 127.5, 126.6 and 126.3, 126.0 and 125.8, 125.6 and 123.6, 123.0, 62.9 and 62.8, 54.6 and 54.0, 50.1 and 49.9, 38.0 and 37.3, 28.9 and 28.6, 21.2. **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{29}H_{27}N_2O_2$ 435.2067; Found 435.2061.

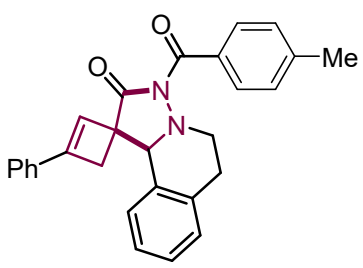
3'-benzoyl-3-(3,5-dichlorophenyl)-6',10b'-dihydro-5'*H*-spiro[cyclobutane-1,1'-pyrazolo[5,1-*a*]isoquinolin]-2-en-2'(3'*H*)-one (3i)



3i

The crude product was purified by column chromatography on silica gel (PE/EtOAc = 4:1). D.r. 1.6:1, yellow solid, 50.4 mg, 53% yield. M. p. 98.6 – 99.7 °C. **^{1}H NMR** (400 MHz, Chloroform-*d,* ppm) δ 7.76 – 7.67 (m, 2H), 7.55 – 7.48 (m, 1H), 7.45 – 7.38 (m, 2H), 7.38 – 7.27 (m, 2H), 7.24 – 7.16 (m, 2H), 7.16 – 7.05 (m, 3H), 6.44 (s, 0.58H), 6.02 (s, 0.39H), 5.03 (s, 0.40H), 4.99 (s, 0.60H), 3.72 – 3.63 (m, 1H), 3.33 – 3.11 (m, 2H), 3.10 – 2.94 (m, 1H), 2.88 – 2.73 (m, 1.60H), 2.37 (d, *J* = 12.5 Hz, 0.61H). **^{13}C NMR** (100 MHz, Chloroform-*d*, ppm): δ 175.4 and 174.7, 166.5, 148.3 and 146.7, 133.8 and 133.7, 133.3 and 133.2, 133.0 and 132.9, 132.8, 132.6 and 132.5, 132.2 and 132.1, 131.6 and 130.6, 130.5 and 130.4, 129.0 and 128.9, 128.8 and 128.7, 128.3, 128.0, 127.9 and 127.7, 127.1, 126.7 and 126.3, 125.8 and 125.7, 124.5 and 124.4, 62.8 and 62.7, 54.9 and 54.3, 50.3 and 50.1, 37.9 and 37.2, 28.9 and 28.7. **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{27}H_{21}Cl_2N_2O_2$ 475.0975; Found 475.0966.

3'-(4-methylbenzoyl)-3-phenyl-6',10b'-dihydro-5'*H*-spiro[cyclobutane-1,1'-pyrazolo[5,1-*a*]isoquinolin]-2-en-2'(3'*H*)-one (3j)

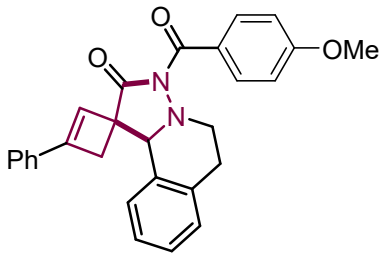


3j

The crude product was purified by column chromatography on silica gel (PE/EtOAc = 4:1). D.r. 1.8:1, yellow solid, 62.2 mg, 74% yield. M. p. 158.0 – 158.9 °C. **^{1}H NMR** (400 MHz, Chloroform-*d,* ppm) δ 7.64 (d, *J* = 7.9 Hz, 2H), 7.30 – 7.24 (m, 5H), 7.24 – 7.13 (m, 5H), 7.13 – 7.02 (m, 1H), 6.39 (s, 0.64H), 5.98 (s, 0.36H), 5.03 (s, 0.37H), 4.97 (s, 0.63H), 3.73 – 3.61 (m, 1H), 3.37 – 3.14 (m, 2H),

3.13 – 2.96 (m, 1H), 2.88 – 2.76 (m, 1.65H), 2.42 (s, 0.53H), 2.38 (s, 3H). **^{13}C NMR** (100 MHz, Chloroform-*d*, ppm): δ 175.8 and 175.2, 166.5 and 165.4, 150.5 and 148.9, 142.9 and 142.8, 133.2, 132.8 and 132.7, 131.8 and 131.0, 130.9 and 130.8, 129.3 and 129.2, 128.9 and 128.8, 128.7, 128.6 and 128.5, 128.4, 127.7 and 127.5, 126.6 and 126.2, 126.0 and 125.8, 126.0 and 124.2, 125.2 and 125.1, 62.9 and 62.8, 54.7 and 54.1, 50.2 and 50.0, 38.1 and 37.3, 28.9 and 28.6, 21.8 and 21.7. **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{28}H_{25}N_2O_2$ 421.1911; Found 421.1901.

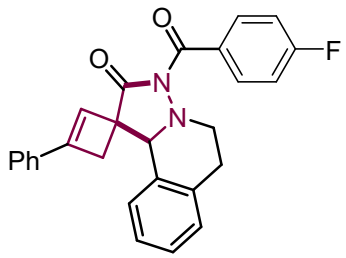
3'-(4-methoxybenzoyl)-3-phenyl-6',10b'-dihydro-5'*H*-spiro[cyclobutane-1,1'-pyrazolo[5,1-*a*]isoquinolin]-2-en-2'(3'*H*)-one (3k)



3k

The crude product was purified by column chromatography on silica gel (PE/EtOAc = 3:1). D.r. 1.6:1, yellow solid, 71.5 mg, 82% yield. M. p. 92.3 – 93.7 °C. **^{1}H NMR** (400 MHz, Chloroform-*d,* ppm) δ 7.82 – 7.74 (m, 2H), 7.32 – 7.24 (m, 5H), 7.21 – 7.14 (m, 3H), 7.14 – 7.03 (m, 1H), 6.94 – 6.85 (m, 2H), 6.40 (s, 0.56H), 5.99 (s, 0.37H), 5.03 (s, 0.38H), 4.98 (s, 0.62H), 3.83 (s, 3H), 3.71 – 3.59 (m, 1H), 3.37 – 3.15 (m, 2H), 3.14 – 2.99 (m, 1H), 2.89 – 2.78 (m, 1.60H), 2.41 (d, *J* = 12.5 Hz, 0.67H). **^{13}C NMR** (100 MHz, Chloroform-*d*, ppm): δ 175.9 and 175.2, 165.9, 163.1 and 163.0, 150.6 and 148.9, 133.3 and 133.2, 132.9 and 132.8, 132.0 and 131.0, 131.9 and 131.8, 129.0 and 128.9, 128.7 and 128.6, 128.4, 127.7 and 127.5, 126.7 and 126.3, 126.1 and 126.0, 125.9 and 125.7, 125.8 and 124.2, 125.2 and 125.1, 113.3, 63.0 and 62.9, 55.5, 54.8 and 54.2, 50.4 and 50.2, 38.2 and 37.3, 29.0 and 28.6. **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{28}H_{25}N_2O_3$ 437.1860; Found 437.1858.

3'-(4-fluorobenzoyl)-3-phenyl-6',10b'-dihydro-5'*H*-spiro[cyclobutane-1,1'-pyrazolo[5,1-*a*]isoquinolin]-2-en-2'(3'*H*)-one (3l)

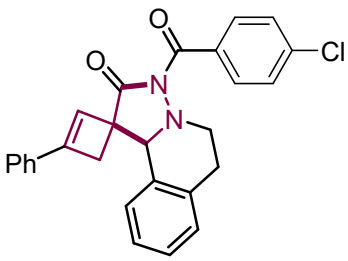


3l

The crude product was purified by column chromatography on silica gel (PE/EtOAc = 4:1). D.r. 1.3:1, yellow solid, 54.3 mg, 64% yield. M. p. 173.1 – 173.7 °C. **^{1}H NMR** (400 MHz, Chloroform-*d,* ppm) δ 7.83 – 7.71 (m, 2H), 7.31 – 7.25 (m, 5H), 7.23 – 7.14 (m, 3H), 7.14 – 7.05 (m, 3H), 6.39 (s, 0.55H), 5.98 (s, 0.43H), 5.03 (s, 0.40H), 4.98 (s, 0.60H), 3.72 – 3.58 (m, 1H), 3.38 – 3.16 (m, 2H), 3.16 – 2.97 (m, 1H), 2.89 – 2.76 (m, 1.54H), 2.42 (d, *J* = 12.5 Hz, 0.63H). **^{13}C NMR** (100 MHz, Chloroform-*d*, ppm): δ 176.0 and 175.3, 165.3, 165.1

(d, J = 253.2 Hz) and 165.0 (d, J = 253.2 Hz), 150.7 and 149.1, 133.1, 132.7 and 132.6, 131.9 and 131.7, 131.9 and 131.8, 131.7 and 130.8, 129.9 (t, J = 3.3 Hz), 129.1 and 129.0, 128.7 and 128.6, 128.4, 127.8 and 127.6, 126.7 and 126.3, 126.0 and 124.0, 125.9 and 125.8, 125.2 and 125.1, 115.2 (d, J = 22.0 Hz) and 115.1 (d, J = 22.0 Hz), 62.9 and 62.8, 54.7 and 54.1, 50.3 and 50.0, 38.1 and 37.3, 28.9 and 28.6. **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -106.16 – -106.27 (m) and -106.31 – -106.43 (m). **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{27}H_{22}FN_2O_2$ 425.1660; Found 425.1671.

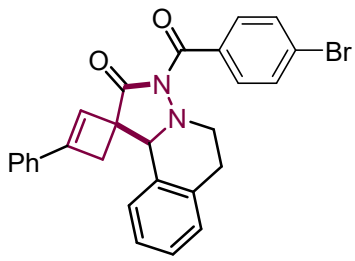
3'-(4-chlorobenzoyl)-3-phenyl-6',10b'-dihydro-5'*H*-spiro[cyclobutane-1,1'-pyrazolo[5,1-*a*]isoquinolin]-2-en-2'(3'*H*)-one (3m)



3m

The crude product was purified by column chromatography on silica gel (PE/EtOAc = 4:1). D.r. 1.4:1, yellow solid, 48.4 mg, 55% yield. M. p. 169.9 – 170.7 °C. **^{1}H NMR** (400 MHz, Chloroform-*d,* ppm) δ 7.72 – 7.63 (m, 2H), 7.42 – 7.36 (m, 2H), 7.32 – 7.25 (m, 5H), 7.23 – 7.04 (m, 4H), 6.38 (s, 0.56H), 5.97 (s, 0.40H), 5.03 (s, 0.42H), 4.97 (s, 0.58H), 3.71 – 3.59 (m, 1H), 3.37 – 3.13 (m, 2H), 3.13 – 2.97 (m, 1H), 2.89 – 2.76 (m, 1.64H), 2.42 (d, J = 12.5 Hz, 0.58H). **^{13}C NMR** (100 MHz, Chloroform-*d*, ppm): δ 176.0 and 175.4, 165.4, 150.8 and 149.1, 138.4 and 138.3, 133.1, 132.8 and 132.7, 132.2 and 132.1, 131.7 and 130.7, 130.6 and 130.5, 129.1 and 129.0, 128.8 and 128.7, 128.5, 128.3, 127.8 and 127.7, 126.7 and 126.3, 126.0 and 125.8, 125.3 and 125.2, 123.9, 63.0 and 62.9, 54.6 and 54.0, 50.3 and 50.0, 38.1 and 37.3, 28.9 and 28.6. **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{27}H_{22}ClN_2O_2$ 441.1364; Found 441.1359.

3'-(4-bromobenzoyl)-3-phenyl-6',10b'-dihydro-5'*H*-spiro[cyclobutane-1,1'-pyrazolo[5,1-*a*]isoquinolin]-2-en-2'(3'*H*)-one (3n)

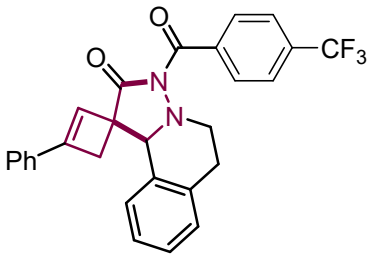


3n

The crude product was purified by column chromatography on silica gel (PE/EtOAc = 4:1). D.r. 1.8:1, yellow solid, 65.0 mg, 67% yield. M. p. 162.8 – 164.3 °C. **^{1}H NMR** (400 MHz, Chloroform-*d,* ppm) δ 7.63 – 7.58 (m, 2H), 7.58 – 7.53 (m, 2H), 7.32 – 7.25 (m, 5H), 7.24 – 7.18 (m, 2H), 7.18 – 7.05 (m, 2H), 6.38 (s, 0.60H), 5.98 (s, 0.41H), 5.03 (s, 0.40H), 4.97 (s, 0.60H), 3.71 – 3.58 (m, 1H), 3.37 – 3.14 (m, 2H), 3.14 – 2.97 (m, 1H), 2.89 – 2.76 (m, 1.62H), 2.42 (d, J = 12.5 Hz, 0.63H). **^{13}C NMR** (100 MHz, Chloroform-*d*, ppm): δ 176.0 and

175.4, 165.5, 150.8 and 149.1, 133.1, 132.7 and 132.6, 132.5 and 131.6, 131.3, 130.7 and 130.6, 129.1 and 129.0, 128.8 and 128.7, 128.5, 127.8 and 127.7, 127.0 and 126.9, 126.8 and 126.4, 126.0, 125.9 and 125.8, 125.3 and 125.2, 123.9, 62.9 and 62.8, 54.6 and 54.0, 50.3 and 50.0, 38.1 and 37.3, 28.9 and 28.6. **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{27}H_{22}BrN_2O_2$ 485.0859; Found 485.0851.

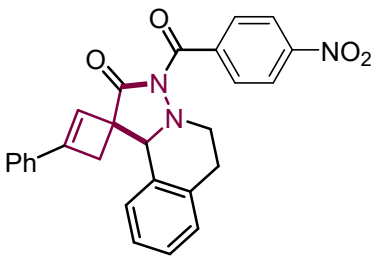
3-phenyl-3'-(4-(trifluoromethyl)benzoyl)-6',10b'-dihydro-5'*H*-spiro[cyclobutane-1,1'-pyrazolo[5,1-*a*]isoquinolin]-2-en-2'(3'*H*)-one (3o)



3o

The crude product was purified by column chromatography on silica gel (PE/EtOAc = 4:1). D.r. 1.6:1, yellow solid, 50.2 mg, 53% yield. M. p. 90.0 – 91.8 °C. **^{1}H NMR** (400 MHz, Chloroform-*d,* ppm) δ 7.79 (d, *J* = 8.1 Hz, 2H), 7.68 (d, *J* = 8.2 Hz, 2H), 7.32 – 7.23 (m, 5H), 7.24 – 7.14 (m, 3H), 7.14 – 7.05 (m, 1H), 6.38 (s, 0.61H), 5.98 (s, 0.38H), 5.05 (s, 0.41H), 4.99 (s, 0.62H), 3.76 – 3.63 (m, 1H), 3.37 – 2.99 (m, 3H), 2.89 – 2.76 (m, 1.55H), 2.44 (d, *J* = 12.5 Hz, 0.64H). **^{13}C NMR** (100 MHz, Chloroform-*d*, ppm): δ 176.1 and 175.5, 165.2 and 165.1, 150.8 and 149.2, 137.4, 133.0, 132.6 and 132.5, 131.5 and 130.6, 129.3 and 129.2, 129.1 and 129.0, 128.7 and 128.6, 128.4, 127.8 and 127.7, 126.8 and 126.4, 125.9, 125.8 and 125.7, 125.2 and 125.1, 125.0 (q, *J* = 3.7 Hz), 123.8, 123.7 (q, *J* = 272.8 Hz), 62.9 and 62.8, 54.5 and 53.9, 50.1 and 49.9, 38.0 and 37.4, 28.9 and 28.6. **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -63.02 (s) and -63.03 (s). **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{28}H_{22}F_3N_2O_2$ 475.1628; Found 475.1619.

3'-(4-nitrobenzoyl)-3-phenyl-6',10b'-dihydro-5'*H*-spiro[cyclobutane-1,1'-pyrazolo[5,1-*a*]isoquinolin]-2-en-2'(3'*H*)-one (3p)

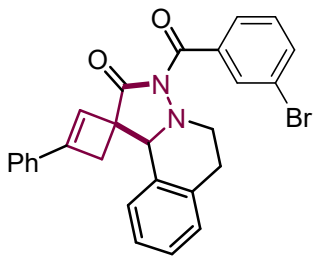


3p

The crude product was purified by column chromatography on silica gel (PE/EtOAc = 3:1). D.r. 1.4:1, yellow solid, 28.0 mg, 31% yield. M. p. 175.0 – 176.2 °C. **^{1}H NMR** (400 MHz, Chloroform-*d,* ppm) δ 8.35 – 8.24 (m, 2H), 7.87 – 7.78 (m, 2H), 7.31 – 7.21 (m, 7H), 7.19 – 7.06 (m, 2H), 6.38 (s, 0.67H), 5.98 (s, 0.39H), 5.05 (s, 0.39H), 4.99 (s, 0.64H), 3.76 – 3.64 (m, 1H), 3.39 – 3.16 (m, 2H), 3.16 – 2.99 (m, 1H), 2.92 – 2.77 (m, 1.55H), 2.45 (d, *J* = 12.5 Hz, 0.59H). **^{13}C NMR** (100 MHz, Chloroform-*d*, ppm): δ 176.2 and 175.6,

164.4, 151.0 and 149.5, 139.9 and 139.8, 133.0, 132.6, 131.4 and 130.4, 129.7 and 129.6, 129.3 and 129.2, 128.8 and 128.7, 128.5, 128.0 and 127.8, 126.9 and 126.5, 125.9 and 125.8, 125.6, 125.3 and 125.2, 123.6, 123.3, 63.0 and 62.9, 54.5 and 53.8, 50.2 and 49.9, 38.0 and 37.4, 28.9 and 28.7. **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{27}H_{22}N_3O_4$ 452.1605; Found 452.1602.

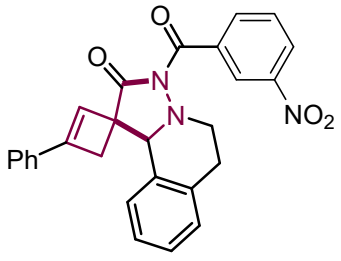
3'-(3-bromobenzoyl)-3-phenyl-6',10b'-dihydro-5'*H*-spiro[cyclobutane-1,1'-pyrazolo[5,1-*a*]isoquinolin]-2-en-2'(3'*H*)-one (3q)



3q

The crude product was purified by column chromatography on silica gel (PE/EtOAc = 4:1). D.r. 1.5:1, yellow solid, 68.9 mg, 71% yield. M. p. 86.1 – 87.9 °C. **^{1}H NMR** (400 MHz, Chloroform-*d,* ppm) δ 7.84 (s, 1H), 7.65 – 7.59 (m, 2H), 7.32 – 7.24 (m, 6H), 7.23 – 7.03 (m, 4H), 6.38 (s, 0.58H), 5.97 (s, 0.42H), 5.02 (s, 0.41H), 4.97 (s, 0.60H), 3.70 – 3.59 (m, 1H), 3.35 – 3.14 (m, 2H), 3.14 – 2.97 (m, 1H), 2.88 – 2.76 (m, 1.65H), 2.42 (d, *J* = 12.5 Hz, 0.60H). **^{13}C NMR** (100 MHz, Chloroform-*d*, ppm): δ 175.9 and 175.3, 164.8, 150.7 and 149.1, 135.81 and 135.79, 134.86 and 134.79, 133.1 and 133.0, 132.7 and 132.6, 131.72 and 131.68, 131.6 and 130.6, 129.5, 129.03 and 129.00, 128.70 and 128.63, 128.4, 127.77 and 127.64, 127.49 and 127.43, 126.70 and 126.30, 125.90 and 123.88, 125.83 and 125.76, 125.19 and 125.16, 121.95, 62.8 and 62.8, 54.5 and 53.9, 50.2 and 49.9, 38.0 and 37.3, 28.9 and 28.6. **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{27}H_{22}BrN_2O_2$ 485.0859; Found 485.0854.

3'-(3-nitrobenzoyl)-3-phenyl-6',10b'-dihydro-5'*H*-spiro[cyclobutane-1,1'-pyrazolo[5,1-*a*]isoquinolin]-2-en-2'(3'*H*)-one (3r)

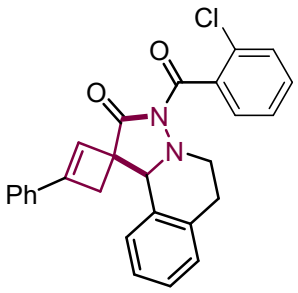


3r

The crude product was purified by column chromatography on silica gel (PE/EtOAc = 3:1). D.r. 1.4:1, yellow solid, 34.3 mg, 38% yield. M. p. 181.5 – 182.4 °C. **^{1}H NMR** (400 MHz, Chloroform-*d,* ppm) δ 8.53 (d, *J* = 2.1 Hz, 1H), 8.37 (d, *J* = 8.2 Hz, 1H), 8.00 (d, *J* = 7.7 Hz, 1H), 7.62 (t, *J* = 8.0 Hz, 1H), 7.32 – 7.20 (m, 7H), 7.20 – 7.04 (m, 2H), 6.39 (s, 0.61H), 5.98 (s, 0.40H), 5.06 (s, 0.44H), 5.01 (s, 0.58H), 3.76 – 3.65 (m, 1H), 3.40 – 3.17 (m, 2H), 3.17 – 3.01 (m, 1H), 2.93 – 2.77 (m, 1.67H), 2.45 (d, *J* = 12.5 Hz, 0.63H). **^{13}C NMR** (100 MHz, Chloroform-*d*, ppm): δ 176.3 and 175.7, 164.0, 151.0 and 149.3, 147.8, 135.6, 134.7 and 134.6,

133.1 and 133.0, 132.6 and 132.5, 131.4 and 130.5, 129.2 and 129.1, 128.8 and 128.7, 128.5, 128.0 and 127.8, 126.9 and 126.5, 126.4 and 126.3, 126.0 and 125.8, 125.7, 125.3 and 125.2, 124.1 and 124.0, 123.7, 63.0 and 62.9, 54.5 and 53.9, 50.2 and 49.9, 38.1 and 37.5, 28.9 and 28.7. **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{27}H_{22}N_3O_4$ 452.1605; Found 452.1602.

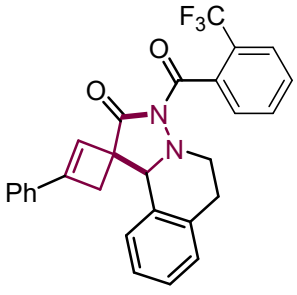
3'-(2-chlorobenzoyl)-3-phenyl-6',10b'-dihydro-5'*H*-spiro[cyclobutane-1,1'-pyrazolo[5,1-*a*]isoquinolin]-2-en-2'(3'*H*)-one (3s)



3s

The crude product was purified by column chromatography on silica gel (PE/EtOAc = 4:1). D.r. 2.4:1, yellow solid, 52.8 mg, 60% yield. M. p. 110.3 – 112.7 °C. **^{1}H NMR** (400 MHz, Chloroform-*d,* ppm) δ 7.42 – 7.33 (m, 4H), 7.29 – 7.18 (m, 7H), 7.16 – 7.03 (m, 2H), 6.33 (s, 0.73H), 5.95 (s, 0.32H), 5.01 (s, 0.32H), 4.97 (s, 0.71H), 3.87 – 3.76 (m, 1H), 3.46 – 3.22 (m, 1.41H), 3.19 – 2.96 (m, 1.46H), 2.91 – 2.75 (m, 1.53H), 2.43 (d, *J* = 12.5 Hz, 0.72H). **^{13}C NMR** (100 MHz, Chloroform-*d*, ppm): δ 175.5 and 175.0, 163.1, 150.7 and 149.1, 135.1, 133.2 and 133.1, 132.7 and 131.6, 131.2 and 131.1, 130.7, 129.5, 129.0 and 128.9, 128.7 and 128.6, 128.4 and 128.3, 128.2, 127.7 and 127.6, 127.1 and 127.0, 126.7 and 126.3, 125.9, 125.8 and 125.7, 125.2 and 125.1, 123.8, 62.7, 54.5 and 53.8 ,49.7 and 49.3 ,37.8 and 37.2, 28.9 and 28.8. **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{27}H_{22}ClN_2O_2$ 441.1364; Found 441.1365.

3-phenyl-3'-(2-(trifluoromethyl)benzoyl)-6',10b'-dihydro-5'*H*-spiro[cyclobutane-1,1'-pyrazolo[5,1-*a*]isoquinolin]-2-en-2'(3'*H*)-one (3t)

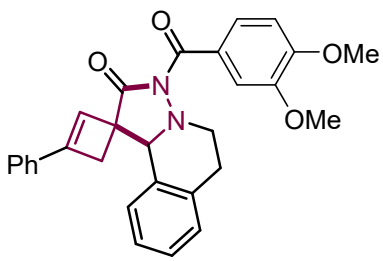


3t

The crude product was purified by column chromatography on silica gel (PE/EtOAc = 4:1). D.r. 2.6:1, yellow solid, 55.0 mg, 58% yield. M. p. 95.7 – 96.9 °C. **^{1}H NMR** (400 MHz, Chloroform-*d,* ppm) δ 7.70 (d, *J* = 7.9 Hz, 1H), 7.62 (t, *J* = 7.6 Hz, 1H), 7.55 (t, *J* = 7.8 Hz, 1H), 7.44 (d, *J* = 7.5 Hz, 1H), 7.28 – 7.19 (m, 7H), 7.16 – 7.04 (m, 2H), 6.29 (s, 0.69H), 5.93 (s, 0.25H), 4.98 (s, 0.29H), 4.94 (s, 0.71H), 3.94 – 3.74 (m, 1H), 3.48 – 3.32 (m, 1H), 3.22 (d, *J* = 12.4 Hz, 0.32H), 3.14 – 2.96 (m, 1.33H), 2.91 (d, *J* = 16.5 Hz, 1H), 2.70 (d, *J* = 12.4 Hz, 0.77H), 2.43 (d, *J* = 12.4 Hz, 0.77H). **^{13}C NMR** (100 MHz, Chloroform-*d*, ppm): δ 175.7 and 175.2, 163.3, 150.7 and 149.1, 134.1 (q, *J* = 3.9 Hz), 133.2 and 133.1, 132.5, 132.0 and 131.9, 131.4 and 130.5,

129.8 and 129.7, 129.1 and 129.0, 128.7 and 128.6, 128.4 and 128.3, 127.7 and 127.6, 127.3, 126.3 (q, J = 4.5 Hz), 126.2 and 126.1, 125.8, 125.7 and 125.6, 125.1 and 125.0, 123.9 (q, J = 273.6 Hz), 123.5, 62.5, 54.4 and 53.7, 49.0 and 48.6, 37.7 and 37.2, 28.8 and 28.7. **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{28}H_{22}F_3N_2O_2$ 475.1628; Found 475.1625.

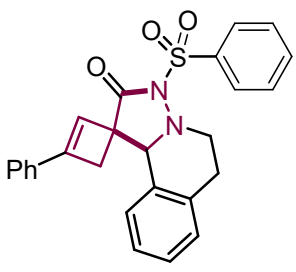
3'-(3,4-dimethoxybenzoyl)-3-phenyl-6',10b'-dihydro-5'*H*-spiro[cyclobutane-1,1'-pyrazolo[5,1-*a*]isoquinolin]-2-en-2'(3'*H*)-one (3u)



3u

The crude product was purified by column chromatography on silica gel (PE/EtOAc = 3:1). D.r. 1.5:1, yellow solid, 51.3 mg, 55% yield. M. p. 78.3 – 79.6 °C. **^{1}H NMR** (400 MHz, Chloroform-*d,* ppm) δ 7.46 (d, J = 8.5 Hz, 1H), 7.37 (s, 1H), 7.34 – 7.25 (m, 5H), 7.24 – 7.04 (m, 4H), 6.86 (d, J = 8.5 Hz, 1H), 6.41 (s, 0.58H), 6.00 (s, 0.41H), 5.05 (s, 0.42H), 4.99 (s, 0.59H), 3.91 (s, 6H), 3.74 – 3.61 (m, 1H), 3.38 – 3.17 (m, 2H), 3.15 – 2.98 (m, 1H), 2.93 – 2.75 (m, 1.65H), 2.41 (d, J = 12.5 Hz, 0.59H). **^{13}C NMR** (100 MHz, Chloroform-*d*, ppm): δ 175.9 and 175.3, 165.9, 152.7 and 152.6, 150.5 and 148.9, 148.4 and 148.3, 133.2 and 133.1, 132.8 and 132.7, 131.9 and 130.9, 128.9 and 128.8, 128.7 and 128.6, 128.4, 127.7 and 127.5, 126.6 and 126.2, 126.0 and 125.8, 125.7 and 125.6, 125.2 and 125.1, 124.1 and 124.0, 123.9, 112.4, 109.8, 62.9, 56.2 and 56.1, 56.0, 54.7 and 54.1, 50.4 and 50.2, 38.2 and 37.2, 28.9 and 28.5. **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{29}H_{27}N_2O_4$ 467.1965; Found 467.1959.

3-phenyl-3'-(phenylsulfonyl)-6',10b'-dihydro-5'*H*-spiro[cyclobutane-1,1'-pyrazolo[5,1-*a*]isoquinolin]-2-en-2'(3'*H*)-one (3v)

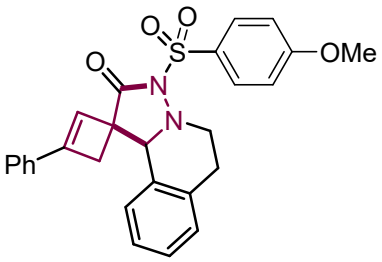


3v

The crude product was purified by column chromatography on silica gel (PE/EtOAc = 5:1). D.r. 5.5:1, yellow solid, 50.4 mg, 57% yield. M. p. 80.7 – 82.2 °C. **^{1}H NMR** (400 MHz, Chloroform-*d,* ppm) δ 8.15 – 8.04 (m, 2H), 7.67 (t, J = 7.4 Hz, 1H), 7.55 (t, J = 7.7 Hz, 2H), 7.31 – 7.16 (m, 7H), 7.06 – 6.88 (m, 2H), 6.10 (s, 0.83H), 5.96 (s, 0.15H), 4.26 (s, 0.19H), 4.21 (s, 0.81H), 3.85 – 3.71 (m, 1H), 3.39 – 3.26 (m, 1.22H), 3.26 – 3.13 (m, 1H), 2.94 – 2.77 (m, 2H), 2.39 (d, J = 12.6 Hz, 0.88H). **^{13}C NMR** (100 MHz, Chloroform-*d*, ppm): δ 176.0 and 175.3, 150.4 and 148.9, 138.3, 134.3, 133.3, 132.7 and 132.6, 131.4 and 130.5, 129.3, 129.1 and 129.0, 128.8 and 128.7, 128.4, 128.1,

127.8 and 127.7, 126.6 and 126.1, 125.8 and 125.7, 125.6 and 123.3, 125.18, 64.3, 54.4 and 53.5, 52.3 and 51.9, 37.0 and 36.9, 29.3 and 29.2. **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{26}H_{23}N_2O_3S$ 443.1424; Found 443.1427.

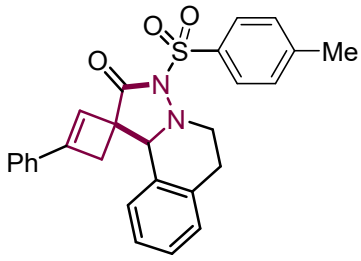
3'-((4-methoxyphenyl)sulfonyl)-3-phenyl-6',10b'-dihydro-5'*H*-spiro[cyclobutane-1,1'-pyrazolo[5,1-*a*]isoquinolin]-2-en-2'(3'*H*)-one (3w)



3w

The crude product was purified by column chromatography on silica gel (PE/EtOAc = 4:1). D.r. 5.1:1, yellow solid, 53.8 mg, 57% yield. M. p. 167.9 – 168.4 °C. **^{1}H NMR** (400 MHz, Chloroform-*d,* ppm) δ 8.09 – 7.97 (m, 2H), 7.30 – 7.15 (m, 7H), 7.06 – 6.90 (m, 4H), 6.12 (s, 0.81H), 5.96 (s, 0.16H), 4.31 (s, 0.18H), 4.25 (s, 0.79H), 3.87 (s, 3H), 3.80 – 3.71 (m, 1H), 3.39 – 3.14 (m, 2.26H), 2.94 – 2.76 (m, 2H), 2.39 (d, *J* = 12.6 Hz, 0.79H). **^{13}C NMR** (100 MHz, Chloroform-*d*, ppm): δ 176.0 and 175.3, 164.2, 150.3 and 148.8, 133.4 and 133.3, 132.7 and 132.6, 130.6 and 130.5, 129.8, 129.0 and 128.9, 128.7 and 128.6, 128.4, 127.8 and 127.6, 126.6 and 126.1, 125.9 and 125.6, 125.6, 125.1, 123.4, 114.4, 64.4, 64.3 and 55.8, 54.5 and 53.6, 52.2 and 51.9, 37.0 and 36.9, 29.3 and 29.2. **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{27}H_{25}N_2O_4S$ 473.1530; Found 473.1538.

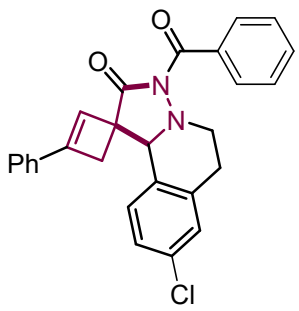
3-phenyl-3'-tosyl-6',10b'-dihydro-5'*H*-spiro[cyclobutane-1,1'-pyrazolo[5,1-*a*]isoquinolin]-2-en-2'(3'*H*)-one (3x)



3x

The crude product was purified by column chromatography on silica gel (PE/EtOAc = 5:1). D.r. 4.4:1, yellow solid, 56.5 mg, 62% yield. M. p. 175.5 – 176.2 °C. **^{1}H NMR** (400 MHz, Chloroform-*d,* ppm) δ 7.97 (d, *J* = 7.9 Hz, 2H), 7.35 – 7.17 (m, 9H), 7.07 – 6.88 (m, 2H), 6.13 (s, 0.88H), 5.96 (s, 0.18H), 4.29 (s, 0.19H), 4.24 (s, 0.71H), 3.82 – 3.67 (m, 1H), 3.37 – 3.16 (m, 2H), 2.91 – 2.77 (m, 2H), 2.42 (s, 3H), 2.40 – 2.29 (m, 1H). **^{13}C NMR** (100 MHz, Chloroform-*d*, ppm): δ 176.0 and 175.3, 150.3 and 148.8, 145.4, 137.7 and 135.3, 133.4, 132.7 and 132.6, 131.5 and 130.5, 129.9, 129.0 and 128.9, 128.7 and 128.6, 128.4, 128.2, 127.8 and 127.6, 126.6 and 126.1, 125.6 and 125.5, 125.1 and 125.0, 123.4, 64.3, 54.4 and 53.4, 52.2 and 51.8, 36.9 and 36.8, 29.3 and 29.2, 21.84. **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{27}H_{25}N_2O_3S$ 457.1580; Found 457.1576.

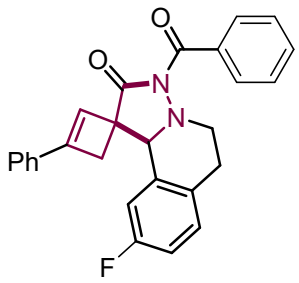
3'-benzoyl-8'-chloro-3-phenyl-6',10b'-dihydro-5'*H*-spiro[cyclobutane-1,1'-pyrazolo[5,1-a]isoquinolin]-2-en-2'(3'*H*)-one (3y)



3y

The crude product was purified by column chromatography on silica gel (PE/EtOAc = 5:1). D.r. 2.6:1, yellow solid, 59.8 mg, 68% yield. M. p. 83.1 – 84.9 °C. **^{1}H NMR** (400 MHz, Chloroform-*d,* ppm) δ 7.73 – 7.68 (m, 2H), 7.56 – 7.49 (m, 1H), 7.46 – 7.39 (m, 2H), 7.34 – 7.27 (m, 5H), 7.22 – 7.10 (m, 3H), 6.38 (s, 0.70H), 5.99 (s, 0.27H), 4.98 (s, 0.29H), 4.93 (s, 0.71H), 3.80 – 3.64 (m, 1H), 3.38 – 3.13 (m, 1.61H), 3.11 – 2.95 (m, 1H), 2.89 – 2.77 (m, 1.76H), 2.44 (d, *J* = 12.6 Hz, 0.75H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 175.4 and 174.8, 166.4, 151.1 and 149.5, 133.8 and 133.7, 133.6 and 132.7, 132.6 and 132.5, 132.24 and 132.2, 132.1 and 131.9, 131.8, 130.1 and 130.0, 129.1 and 129.0, 128.9, 128.8 and 128.4, 128.0 and 127.92, 127.96, 125.9 and 125.7, 125.4 and 123.6, 125.2, 62.6 and 62.5, 54.6 and 53.9, 49.8 and 49.6, 38.1 and 37.5, 28.4 and 28.0. **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{27}H_{22}ClN_2O_2$ 441.1364; Found 441.1360.

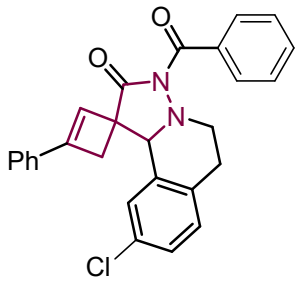
3'-benzoyl-9'-fluoro-3-phenyl-6',10b'-dihydro-5'*H*-spiro[cyclobutane-1,1'-pyrazolo[5,1-a]isoquinolin]-2-en-2'(3'*H*)-one (3z)



3z

The crude product was purified by column chromatography on silica gel (PE/EtOAc = 5:1). D.r. 2.5:1, yellow solid, 61.0 mg, 72% yield. M. p. 88.4 – 90.2 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.73 – 7.65 (m, 2H), 7.55 – 7.46 (m, 1H), 7.45 – 7.36 (m, 2H), 7.34 – 7.21 (m, 5H), 7.20 – 7.09 (m, 1H), 6.96 – 6.83 (m, 2H), 6.37 (s, 0.71H), 5.98 (s, 0.29H), 4.98 (s, 0.30H), 4.94 (s, 0.70H), 3.74 – 3.62 (m, 1H), 3.37 – 3.14 (m, 1.77H), 3.09 – 2.94 (m, 1H), 2.87 – 2.77 (m, 1.73H), 2.43 (d, *J* = 12.6 Hz, 0.74H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 175.4 and 174.8, 166.4 and 166.3, 161.3 (d, *J* = 245.0 Hz) and 160.9 (d, *J* = 245.0 Hz), 151.0 and 149.3, 133.8 and 133.7, 133.6 (d, *J* = 7.5 Hz) and 132.7 (d, *J* = 7.5 Hz), 132.5 and 132.4, 132.1 and 132.0, 130.2 and 130.1, 129.1 and 129.0, 128.9, 128.8, 128.4, 127.9, 125.5 and 123.7, 125.2, 115.1 (d, *J* = 21.4 Hz) and 115.0 (d, *J* = 21.4 Hz), 112.5 (d, *J* = 22.4 Hz) and 112.35 (d, *J* = 22.4 Hz), 62.7 and 62.6, 54.5 and 53.9, 50.0 and 49.8, 38.0 and 37.4, 28.2 and 27.9. **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -115.4 – -115.6 (m). **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{27}H_{22}FN_2O_2$ 425.1660; Found 425.1658.

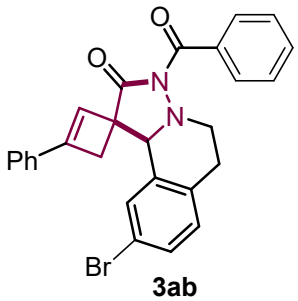
3'-benzoyl-9'-chloro-3-phenyl-6',10b'-dihydro-5'*H*-spiro[cyclobutane-1,1'-pyrazolo[5,1-a]isoquinolin]-2-en-2'(3'*H*)-one (3aa)



3aa

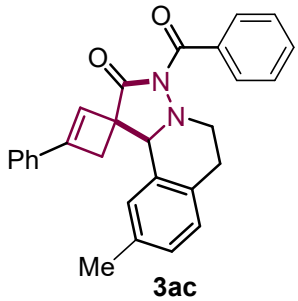
The crude product was purified by column chromatography on silica gel (PE/EtOAc = 5:1). D.r. 2.3:1, yellow solid, 63.4 mg, 72% yield. M. p. 79.6 – 80.4 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.69 (d, *J* = 7.7 Hz, 2H), 7.51 (dd, *J* = 8.5, 6.4 Hz, 1H), 7.41 (t, *J* = 7.6 Hz, 2H), 7.32 – 7.25 (m, 5H), 7.23 – 7.17 (m, 1H), 7.12 – 7.03 (m, 2H), 6.36 (s, 0.69H), 5.96 (s, 0.29H), 4.99 (s, 0.32H), 4.94 (s, 0.68H), 3.76 – 3.63 (m, 1H), 3.39 – 3.09 (m, 1.77H), 3.09 – 2.94 (m, 1H), 2.87 – 2.77 (m, 1.73H), 2.40 (d, *J* = 12.5 Hz, 0.72H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 175.5 and 174.8, 166.5 and 166.4, 150.8 and 149.2, 135.2 and 135.1, 133.8 and 133.7, 133.4 and 133.3, 132.5 and 132.4, 132.2 and 132.1, 130.3 and 129.4, 129.2 and 129.1, 129.0 and 128.9, 128.6 and 128.5, 128.5, 127.9, 127.3 and 127.0, 127.0 and 126.6, 125.6 and 123.7, 125.2, 62.5 and 62.4, 54.5 and 53.9, 49.7 and 49.4, 37.9 and 37.3, 28.8 and 28.5. **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{27}H_{22}ClN_2O_2$ 441.1364; Found 441.1360.

3'-benzoyl-9'-bromo-3-phenyl-6',10b'-dihydro-5'*H*-spiro[cyclobutane-1,1'-pyrazolo[5,1-a]isoquinolin]-2-en-2'(3'*H*)-one (3ab)



3ab

The crude product was purified by column chromatography on silica gel (PE/EtOAc = 5:1). D.r. 3.7:1, yellow solid, 70.7 mg, 73% yield. M. p. 78.4 – 79.3 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.72 – 7.64 (m, 2H), 7.53 – 7.47 (m, 1H), 7.41 (t, *J* = 7.6 Hz, 2H), 7.35 – 7.25 (m, 7H), 7.08 (d, *J* = 8.2 Hz, 1H), 6.36 (s, 0.77H), 5.97 (s, 0.19H), 4.97 (s, 0.26H), 4.92 (s, 0.74H), 3.78 – 3.62 (m, 1H), 3.37 – 3.12 (m, 1.54H), 3.10 – 2.94 (m, 1H), 2.85 – 2.77 (m, 1.74H), 2.42 (d, *J* = 12.5 Hz, 0.86H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 175.4 and 174.7, 166.4, 151.1 and 149.6, 134.0 and 133.0, 133.8 and 133.7, 132.6 and 132.5, 132.3, 132.2 and 132.1, 130.9 and 130.8, 130.4 and 130.3, 129.1 and 129.0, 128.9 and 128.8, 128.6, 128.4, 128.0, 125.4 and 123.6, 125.2, 120.1 and 119.8, 62.44 and 62.3, 54.6 and 53.9, 49.7 and 49.5, 38.1 and 37.5, 28.5 and 28.0. **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{27}H_{22}BrN_2O_2$ 485.0859; Found 485.0861.



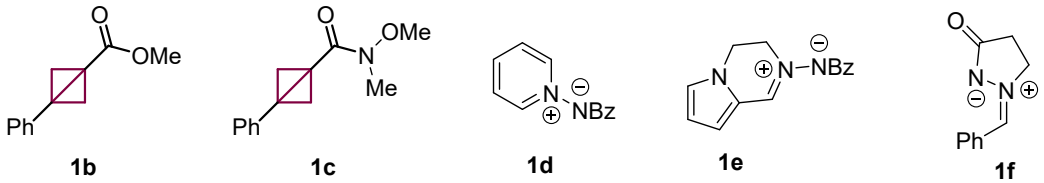
3ac

3'-benzoyl-9'-methyl-3-phenyl-6',10b'-dihydro-5'*H*-spiro[cyclobutane-1,1'-pyrazolo[5,1-a]isoquinolin]-2-en-

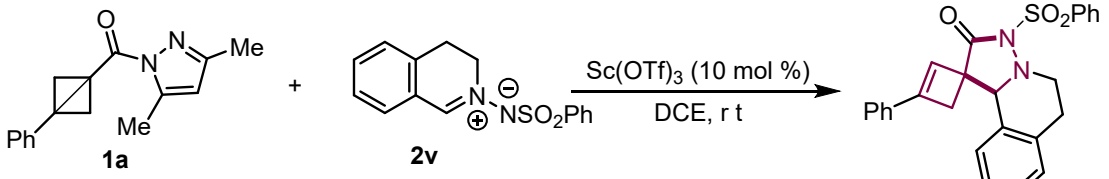
2'(3'*H*)-one (3ac)

The crude product was purified by column chromatography on silica gel (PE/EtOAc = 5:1). D.r. 2.9:1, yellow solid, 57.1 mg, 68% yield. M. p. 81.2 – 82.6 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.77 – 7.67 (m, 2H), 7.53 – 7.45 (m, 1H), 7.40 (dd, *J* = 8.2, 6.8 Hz, 2H), 7.33 – 7.21 (m, 5H), 7.07 (t, *J* = 7.6 Hz, 1H), 7.04 – 6.92 (m, 2H), 6.38 (s, 0.71H), 5.98 (s, 0.24H), 4.98 (s, 0.28H), 4.93 (s, 0.72H), 3.72 – 3.60 (m, 1H), 3.35 – 3.08 (m, 1.87H), 3.06 – 2.95 (m, 0.79H), 2.86 – 2.75 (m, 1.78H), 2.42 (d, *J* = 12.4 Hz, .0.76H), 2.19 (s, 0.76H), 2.15 (s, 2.18H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 176.0 and 175.3, 166.5, 150.6 and 149.0, 136.0 and 135.7, 134.0 and 133.9, 132.9 and 132.8, 132.0 and 131.9, 131.6 and 130.6, 130.1 and 130.0, 128.9, 128.8, 128.6 and 128.5, 128.4, 128.3, 127.9, 126.4 and 126.3, 126.0 and 124.1, 125.2 and 125.1, 62.9, 54.7 and 54.1, 50.3 and 50.0, 38.0 and 37.4, 28.5 and 28.2, 21.2 and 21.1. **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{28}H_{25}N_2O_2$ 421.1911; Found 421.1917.

Unsuccessful examples:



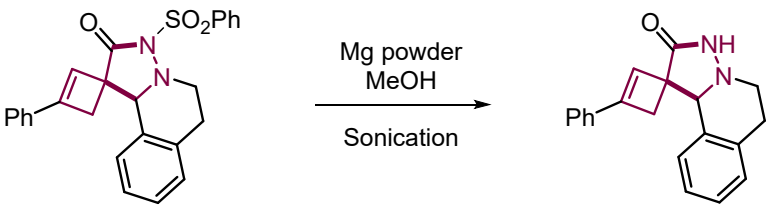
4. Gram-scale reaction



4 mmol, 1 eq. 6 mmol, 1.5 eq. **3v**, 50% (0.884 g) 4.9:1 d.r.

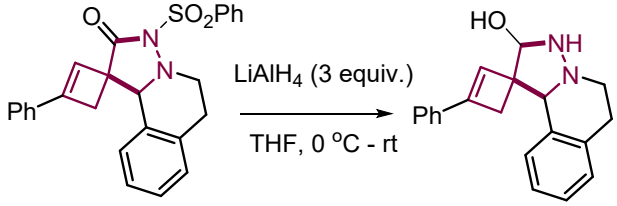
To a 10 mL reaction vial equipped with a magnetic stir bar was added compounds **1a** (4.0 mmol, 1.0 equiv.), **2** (6 mmol, 1.5 equiv.), $Sc(OTf)_3$ (10 mol%), and the tube was evacuated and backfilled with argon three times. DCE was added under argon atmosphere. The mixture was then stirred rapidly for 12 hours. Upon completion of the reaction, the mixture was purified by column chromatography on silica gel (PE/EtOAc = 5:1) to afford **3v** (0.884 g, 50% yield, 4.9:1 d.r.) as a yellow solid.

5. Post-functionalizations



3v 4.9:1 d.r. **4**, 69% 4.9:1 d.r.

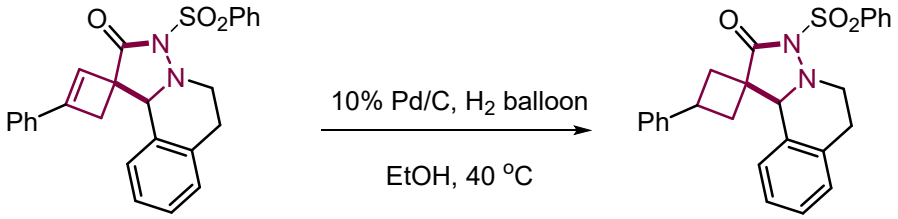
To a dry Schlenk tube equipped with a magnetic stir bar, was added **3v** (88.4 mg, 0.2 mmol) and Mg-powder (57.6 mg, 12 equiv.). The tube was capped with a septum, evacuated and refilled with Ar for 3 times. Then, absolute MeOH (4 mL) was added and the reaction was sonicated at room temperature until no more starting material remained monitored by TLC (around 25-30 min). The solution was cooled to 0 °C and slowly quenched with saturated NH_4Cl. The aqueous phases were extracted with DCM (3 × 10 mL). The combined organic phases were washed with saturated brine (20 mL), then dried over Na_2SO_4, concentrated under reduced pressure. The residue was purified by silica gel column chromatography (DCM/MeOH = 20:1) to afford **4** (41.7 mg, 69%, 4.9:1 d.r.) as white solid. M. p. 182.1 – 182.9 °C. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 10.06 (s, 0.21H), 10.02 (s, 0.73H), 7.36 – 7.28 (m, 5H), 7.25 – 7.17 (m, 2H), 7.12 – 7.05 (m, 2H), 6.48 (s, 0.86H), 6.06 (s, 0.16H), 4.80 (s, 1H), 3.26 – 3.15 (m, 1H), 3.05 – 2.94 (m, 1.35H), 2.90 – 2.71 (m, 2.27H), 2.56 (d, J = 12.5 Hz, 0.93H), 2.08 (d, J = 12.6 Hz, 0.93H). **^{13}C NMR** (100 MHz, DMSO-d_6) δ 176.2, 148.0, 133.9, 133.4, 132.6, 129.0, 128.9, 127.5, 127.3, 126.2, 125.9, 125.2, 125.1, 64.6, 52.8, 52.4, 36.4, 28.9. **HRMS** (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{20}H_{18}N_2ONa$ 325.1311; Found 325.1306.



3v 4.9:1 d.r. **5**, 54% 2.4:1 d.r.

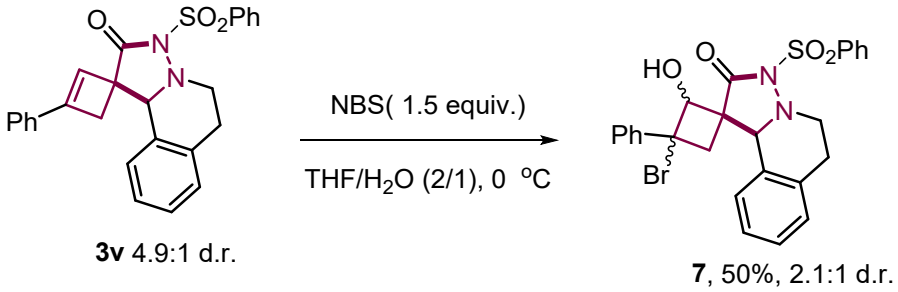
Under Ar atmosphere, a solution of **3v** (88.4 mg, 0.2 mmol) in DCM (2.0 mL) was stirred at 0 °C, followed by the drop-wise addition of $LiAlH_4$ (1.0 M in THF, 0.3 mL, 0.3 mmol). The mixture was then warmed to room temperature and continued to stir for 2h until the consumption of the **3v** (monitored by TLC). The solution was cooled to 0 °C and slowly quenched with saturated NH_4Cl. The aqueous phases were extracted with DCM (3 × 10 mL). The combined organic phases were washed with saturated brine (20 mL), then dried over Na_2SO_4, concentrated under reduced pressure. The residue was

purified by silica gel column chromatography (PE/Acetone = 10:1) to afford **5** (32.8 mg, 54%, 2.4:1 d.r.) as yellow oily liquid. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.44 – 7.27 (m, 5H), 7.20 – 7.02 (m, 4H), 6.50 (d, *J* = 2.0 Hz, 0.67H), 5.97 (d, *J* = 2.0 Hz, 0.37H), 4.92 (s, 0.36H), 4.88 (s, 0.63H), 4.14 – 3.91 (m, 1H), 3.37 – 3.16 (m, 1.48H), 3.10 – 2.84 (m, 1.51H), 2.83 – 2.74 (m, 0.68H), 2.60 – 2.45 (m, 1.57H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 151.2 and 150.6, 147.6 and 146.3, 136.3 and 135.8, 134.4 and 134.2, 133.7 and 133.5, 129.2, 128.9 and 128.8, 128.7 and 128.6, 128.5 and 128.4, 127.4 and 126.4, 126.6 and 126.1, 126.3 and 125.8, 125.1 and 125.0, 67.4 and 65.7, 61.2 and 60.3, 49.3 and 48.1, 43.4 and 36.2, 26.8 and 25.6. **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{20}H_{20}N_2O$ 305.1648; Found 305.1655.



3v 4.9:1 d.r. **6,** 64%, 1:1 d.r.

An oven-dried test tube charged with Pd/C (30 mg, 10%), **3v** (66.3 mg, 0.15 mmol), and EtOH (1.5 mL) was replaced with hydrogen 3 times. The reaction mixture was stirred (1 atm of hydrogen) at rt for 24 h. The reaction mixture was filtered over celite and washed with ethyl acetate and the solvent was evaporated under reduced pressure. The resulting residue was purified by flash chromatography over silica gel (petroleum ether/EtOAc = 5:1) to afford the desired product **6** (42.9 mg, 64%, 1:1 d.r.) as white solid. M. p. 146.3 – 147.9 °C. **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 8.07 (dd, *J* = 15.9, 7.9 Hz, 2H), 7.70 – 7.60 (m, 1H), 7.53 (q, *J* = 7.4 Hz, 2H), 7.35 – 7.09 (m, 8H), 6.95 (d, *J* = 7.6 Hz, 1H), 4.07 (s, 0.50H), 3.85 (d, *J* = 12.3 Hz, 0.89H), 3.75 – 3.64 (m, 1H), 3.34 – 3.19 (m, 1H), 3.19 – 3.06 (m, 1.56H), 3.00 – 2.78 (m, 1.57H), 2.70 – 2.62 (m, 0.49H) 2.53 – 2.37 (m, 1.62H), 2.35 – 2.24 (m, 1H), 1.99 (t, *J* = 10.9 Hz, 0.51H). **^{13}C NMR** (151 MHz, Chloroform-*d*) δ 178.5 and 177.2, 144.3 and 143.8, 138.3 and 138.2, 134.4 and 134.1, 134.3, 131.2 and 131.1, 129.3 and 129.2, 129.1 and 129.0, 128.5 and 128.4, 128.3 and 128.2, 128.1 and 128.0, 126.9 and 126.6, 126.8 and 126.42, 126.5 and 126.0, 124.4, 66.6 and 65.8, 52.3 and 51.6, 47.2 and 46.2, 36.8 and 36.5, 35.4 and 35.0, 34.9 and 33.6, 29.1. **HRMS** (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{26}H_{25}N_2O_3S$ 445.1580; Found 445.1576.

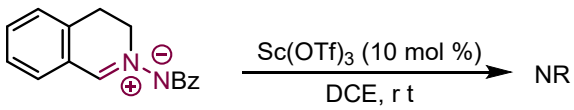


3v 4.9:1 d.r. **7**, 50%, 2.1:1 d.r.

An oven-dried test tube charged with **3v** (88.4 mg, 0.20 mmol), THF (1.5 mL) and H_2O (0.75 mL) was added NBS (53.4 mg, 0.3 mmol) at 0 °C. After stirring for 5 h at the same temperature, the reaction mixture was quenched by the addition of sat. aq. Na_2SO_3 and diluted with EtOAc. After the layers were separated, the aqueous layer was extracted with EtOAc. The combined organic solution was washed with brine, dried over Na_2SO_4, filtered, and concentrated to give a residue. The resulting residue was purified by flash chromatography over silica gel (CH_2Cl_2/EtOH = 100:1) to afford the desired product **7** (54.0 mg, 50%, 2.1:1 d.r.) as colorless oil. (major) **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.99 – 7.92 (m, 2H), 7.67 – 7.55 (m, 1H), 7.55 – 7.42 (m, 4H), 7.41 – 7.24 (m, 6H), 7.16 – 7.07 (m, 1H), 4.90 (s, 1H), 3.90 (s, 1H), 3.72 – 3.64 (m, 1H), 3.34 – 3.15 (m, 2H), 3.07 – 2.95 (m, 1H), 2.95 – 2.82 (m, 1H), 2.34 (s, 1H), 2.04 – 1.88 (m, 1H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 172.9, 139.0, 138.3, 134.4, 134.3, 129.8, 129.3, 128.73, 128.7, 128.1, 128.0, 127.5, 126.9, 126.7, 78.2, 64.1, 53.8, 52.9, 49.0, 39.3, 28.9. (minor) **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.07 – 7.95 (m, 2H), 7.68 – 7.61 (m, 1H), 7.53 (t, *J* = 7.8 Hz, 2H), 7.28 – 7.09 (m, 5H), 6.98 – 6.87 (m, 3H), 6.60 – 6.53 (m, 1H), 5.38 (s, 1H), 4.22 (s, 1H), 3.65 – 3.53 (m, 1H), 3.24 – 2.98 (m, 4H), 2.93 – 2.79 (m, 1H), 2.56 – 2.44 (m, 1H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 177.0, 138.4, 138.0, 134.7, 134.6, 129.7, 129.6, 129.5, 128.5, 128.4, 128.1, 128.0, 127.9, 127.2, 126.2, 77.4, 64.7, 59.0, 53.4, 49.2, 39.4, 28.7. **HRMS** (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{26}H_{23}BrN_2O_4SNa$ 561.0454; Found 561.0453.

6. Mechanistic studies

A) Control experiment: reaction without **1a**

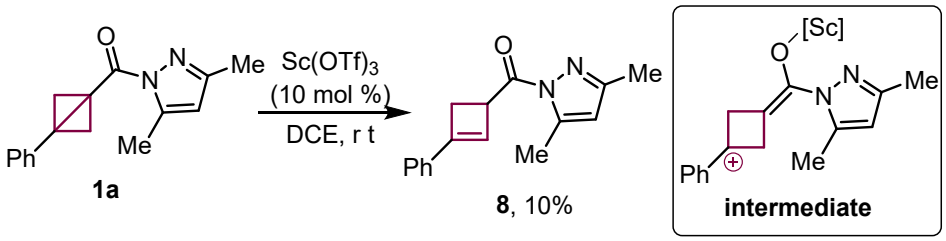


2a

To a 10 mL reaction vial equipped with a magnetic stir bar was added compounds **2a** (0.15 mmol), $Sc(OTf)_3$ (0.01 mmol), and the tube was evacuated and backfilled with

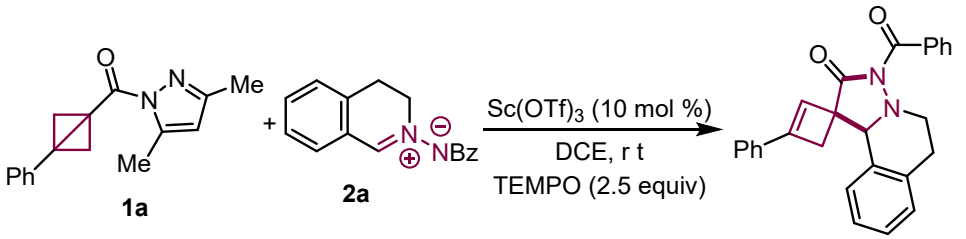
argon three times. DCE was added under argon atmosphere. The mixture was then stirred rapidly for 12 hours monitored by TLC and ^{1}H NMR analysis, showing that no product was formed in the reaction.

B) Control experiment: reaction without **2a**



To a 10 mL reaction vial equipped with a magnetic stir bar was added compound **1a** (0.2 mmol, 1.0 equiv.), $Sc(OTf)_3$ (10 mol%), and the tube was evacuated and backfilled with argon three times. DCE was added under argon atmosphere. Upon completion of reaction, the reaction mixture was concentrated in vacuo to give the crude product. The crude product was purified by column chromatography on silica gel (PE/EtOAc = 20:1) to afford **8** (5.1 mg, 10% yield) a yellow oil. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.38 (d, *J* = 7.6 Hz, 2H), 7.37 – 7.28 (m, 2H), 7.30 – 7.22 (m, 1H), 6.43 (s, 1H), 5.96 (s, 1H), 4.71 (d, *J* = 3.7 Hz, 1H), 3.16 (d, *J* = 3.4 Hz, 2H), 2.55 (s, 3H), 2.26 (s, 3H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 173.5, 152.2, 148.2, 144.1, 134.0, 128.4, 128.3, 125.5, 124.9, 111.0, 42.9, 32.6, 14.5, 14.0.

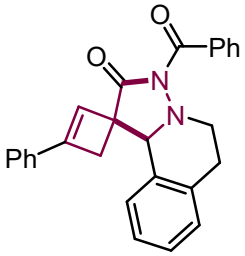
C) TEMPO radical trapping experiment



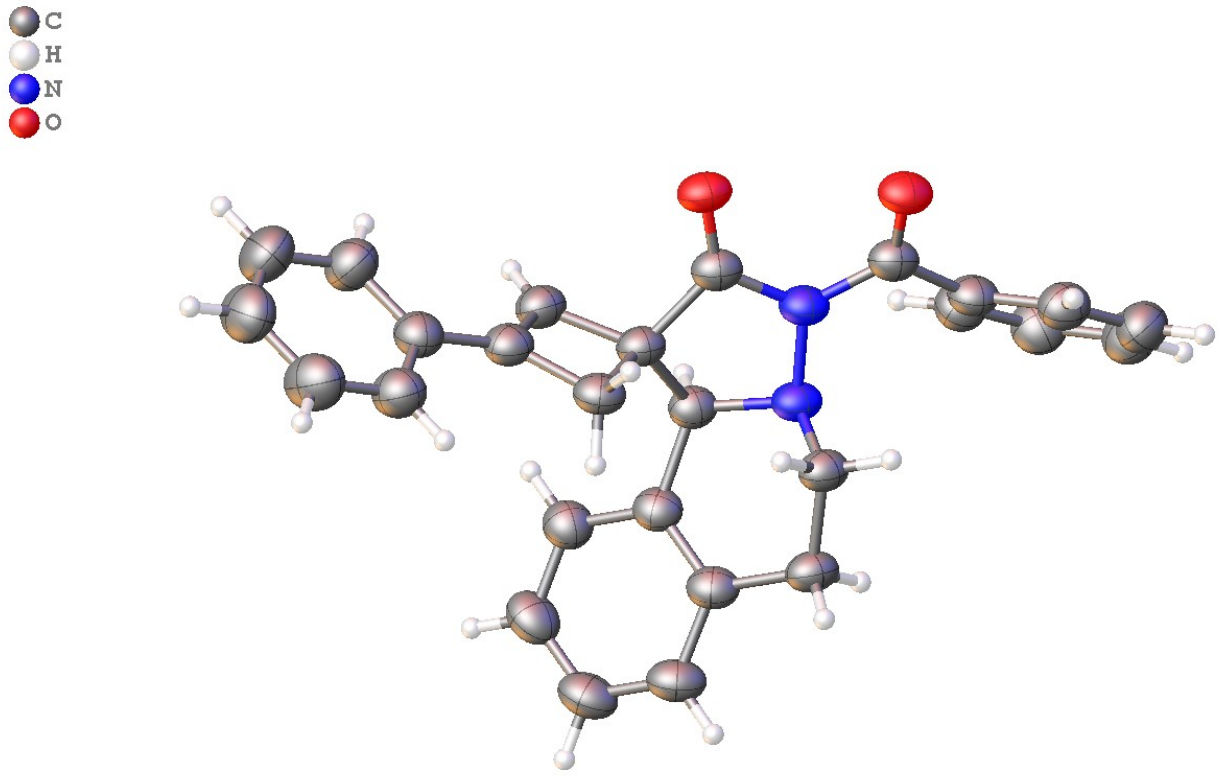
To a 10 mL reaction vial equipped with a magnetic stir bar was added compounds **1a** (0.2 mmol, 1.0 equiv.), **2a** (0.3 mmol, 1.5 equiv.), 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO) (0.5 mmol, 2.5 equiv.), $Sc(OTf)_3$ (10 mol%), and the tube was evacuated and backfilled with argon three times. DCE was added under argon atmosphere. The mixture was then stirred rapidly for 12 hours. Upon completion of the reaction, the crude product was purified by column chromatography on silica gel (PE/EtOAc = 4:1) to afford **3a** (47.9 mg, 59% yield, 2.0:1 d.r.) a yellow solid.

7. X-ray crystallographic data

The structure of **3a** were determined by the X-ray diffraction analysis of single crystal, which recrystallized from a mixed solution of CH_2Cl_2 and *n*-hexane. CCDC 2427337, contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.



3a



ORTEP of **3a**
(CCDC: 2427337)
Thermal probability ellipsoids shown at the 40% probability level.

Table S7. Crystal data and structure refinement for **3a**.

Identification code	**3a**
CCDC Deposit number	2427337
Empirical formula	$C_{27}H_{22}N_2O_2$
Formula weight	406.46
Temperature/K	200.00
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	15.0680(11)
b/Å	6.3158(5)
c/Å	22.0503(16)
α/°	90
β/°	100.439(3)
γ/°	90
Volume/Å^3	2063.7(3)
Z	4
ρ_{calc}g/cm^3	1.308
μ/mm^{-1}	0.658
F(000)	856.0
Crystal size/mm^3	0.3 × 0.2 × 0.1
Radiation	CuKα (λ = 1.54178)
2Θ range for data collection/°	8.154 to 136.58
Index ranges	$-18 \le h \le 18$, $-7 \le k \le 7$, $-26 \le l \le 26$
Reflections collected	29808
Independent reflections	3783 [R_{int} = 0.0827, R_{sigma} = 0.0546]
Data/restraints/parameters	3783/0/280
Goodness-of-fit on F^2	1.093
Final R indexes [I>=2σ (I)]	R_1 = 0.0574, wR_2 = 0.1540
Final R indexes [all data]	R_1 = 0.0824, wR_2 = 0.1616
Largest diff. peak/hole / e Å^{-3}	0.24/-0.25

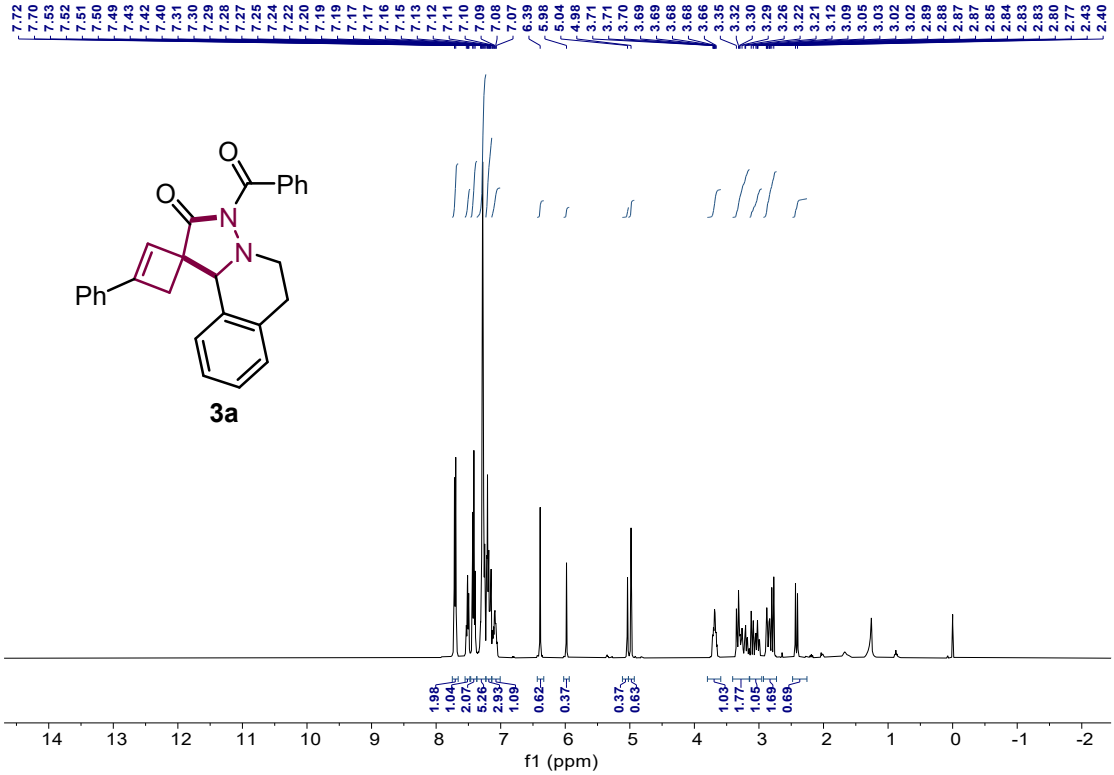
8. References

[1] Y. Liang, F. Paulus, C. G. Daniliuc, F. Glorius, *Angew. Chem. Int. Ed*. 2023, **62**, e202305043.

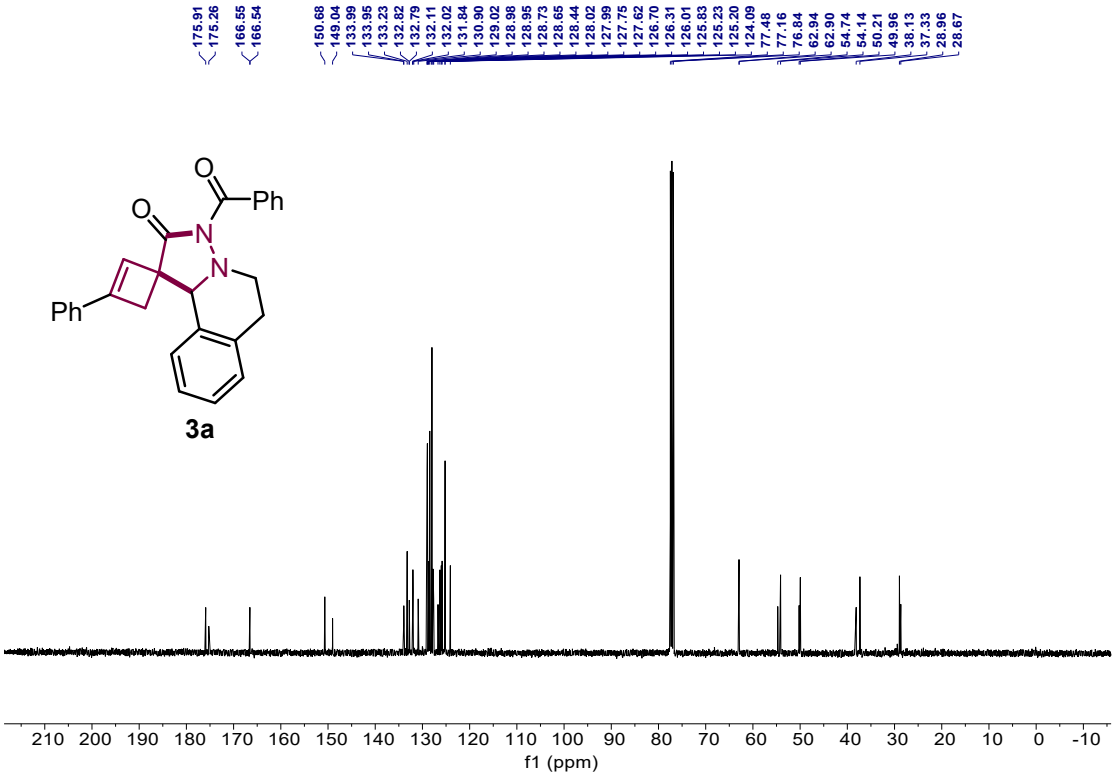
[2] a) L. Zhang, H. Liu, G. Qiao, Z. Hou, Y. Liu, Y. Xiao and H. Guo, *J. Am. Chem. Soc.*, 2015, **137**, 4316–4319; b) C. Chen, X.-X. Yang, Z. Zhao, B. Han, W. Du, Y.-C. Chen, *Chem. Commun*., 2022, **58**, 5502–5505; c) X. Xu, Y. Zhong, Q. Xing, Z. Gao, J. Gou, B. Yu, *Org. Lett.,* 2020*,* **22***,* 5176–5181.

9. NMR spectra of the products

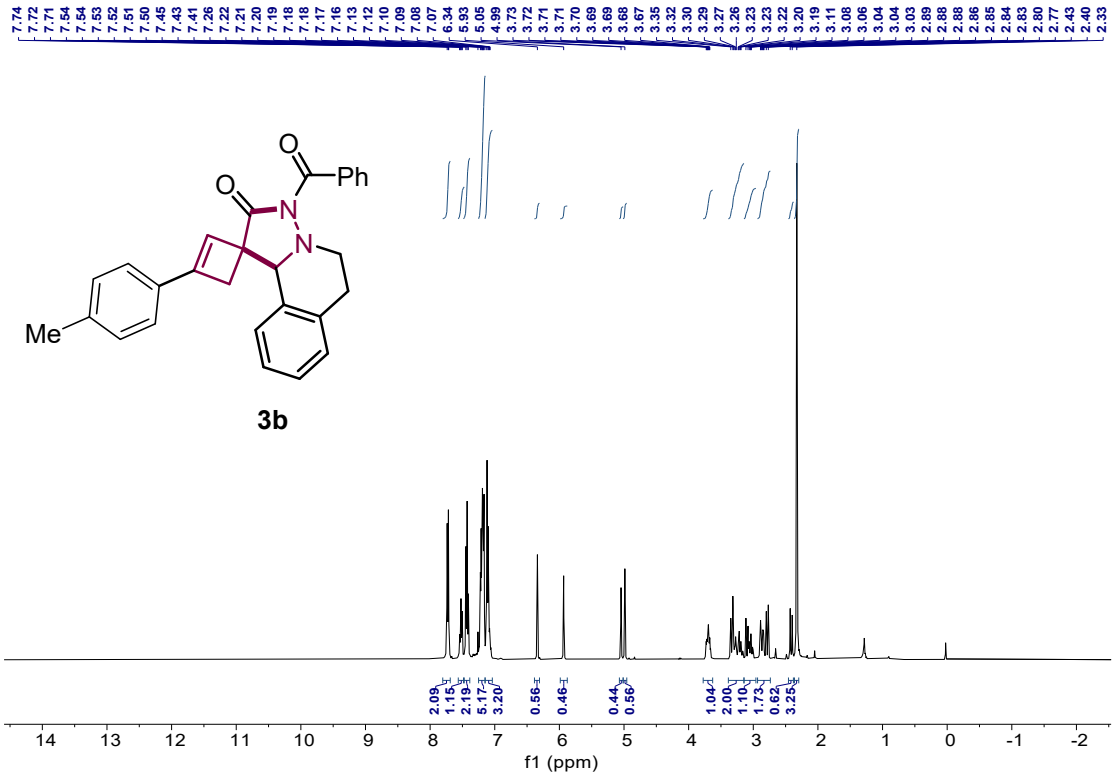
^{1}H NMR (400 MHz, Chloroform-*d*) of **3a**



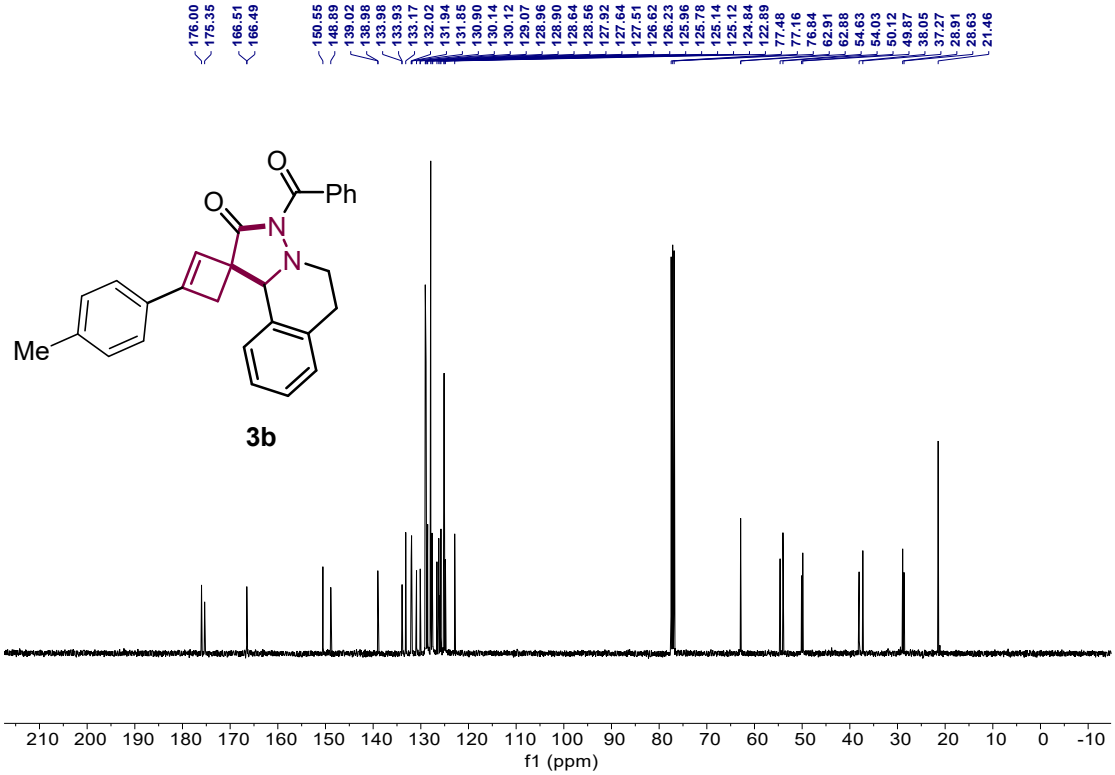
^{13}C NMR (100 MHz, Chloroform-*d*) of **3a**



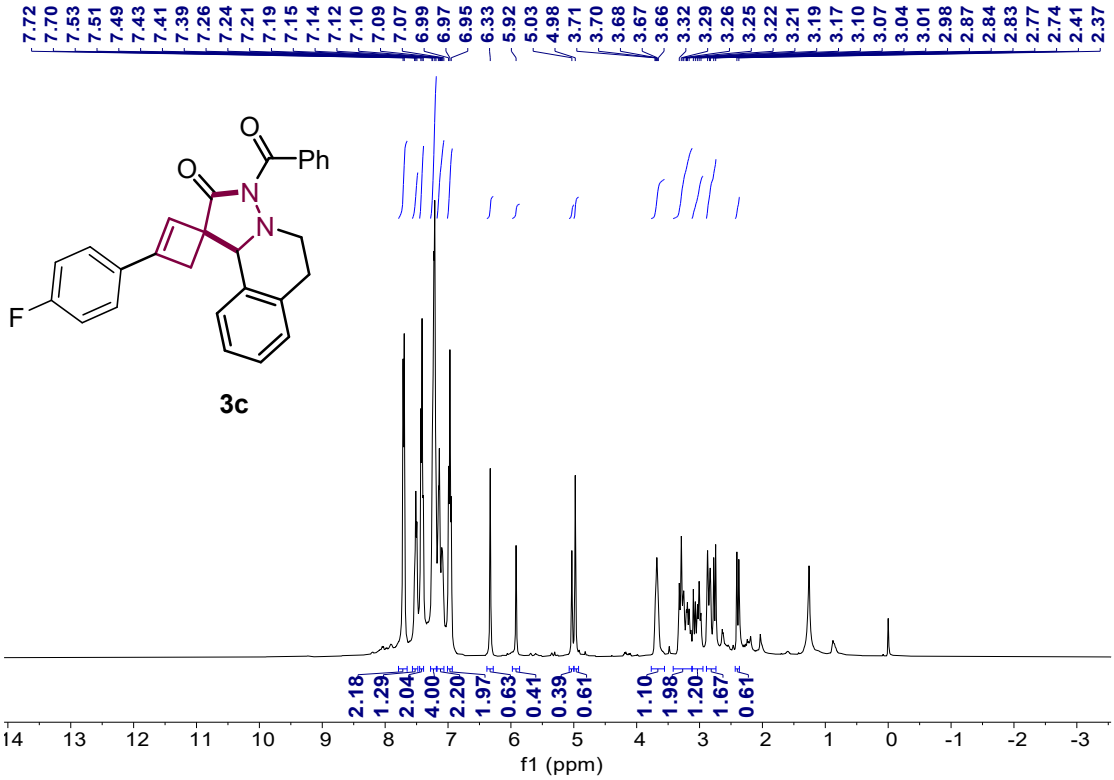
^{1}H NMR (400 MHz, Chloroform-*d*) of **3b**



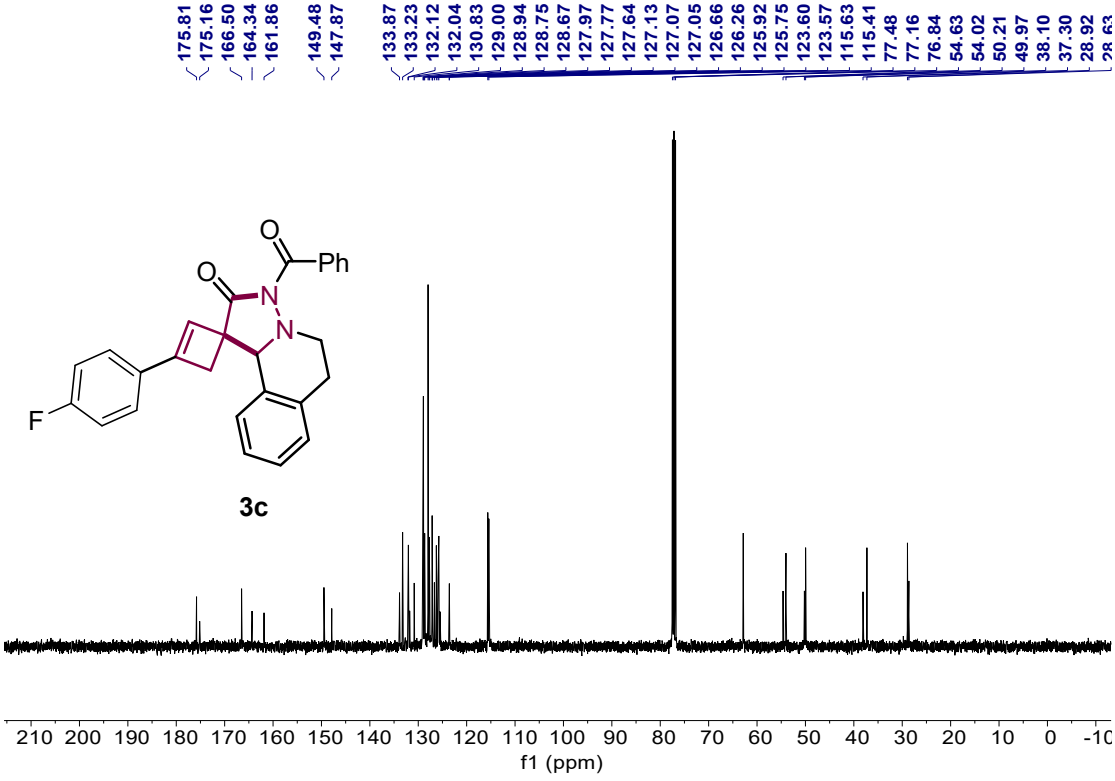
^{13}C NMR (100 MHz, Chloroform-*d*) of **3b**



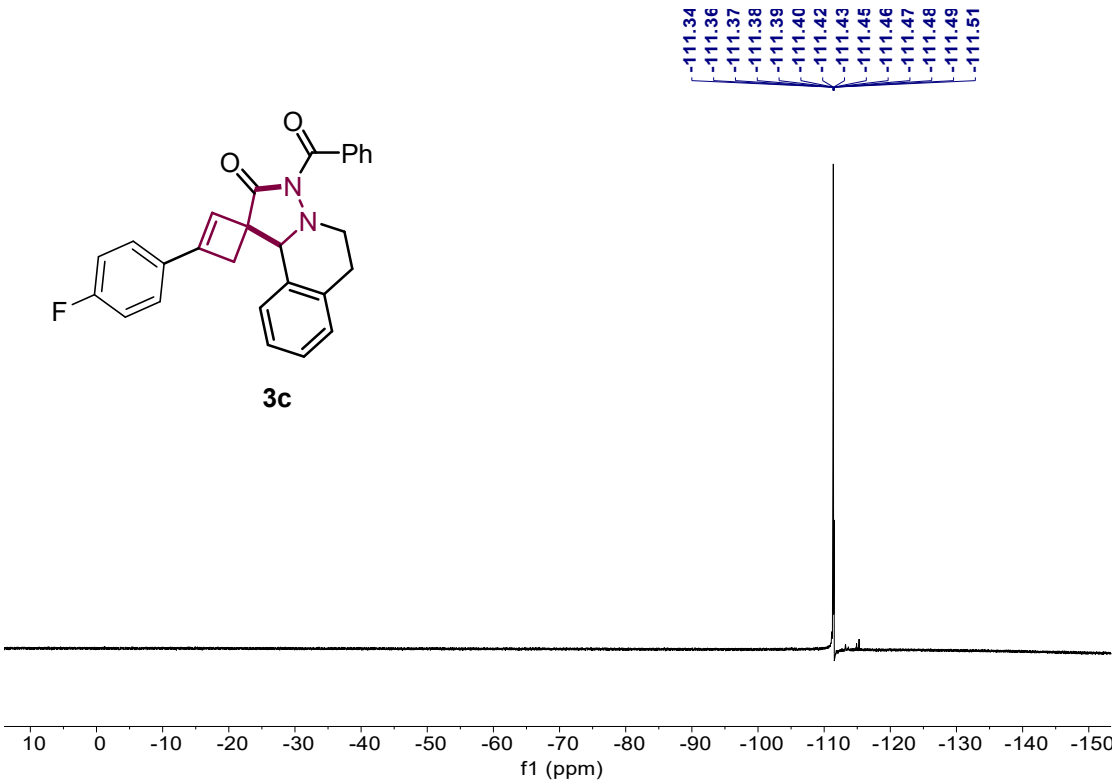
^{1}H NMR (400 MHz, Chloroform-*d*) of **3c**



^{13}C NMR (100 MHz, Chloroform-*d*) of **3c**

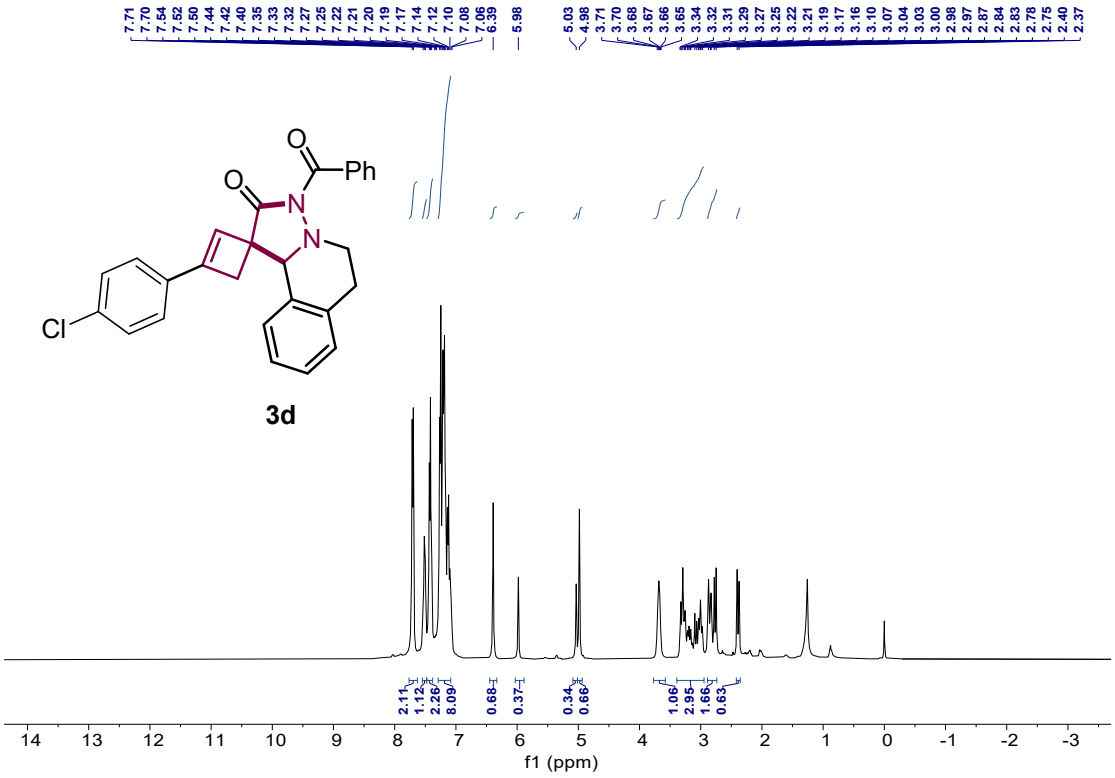


^{19}F NMR (376 MHz, Chloroform-*d*) of **3c**

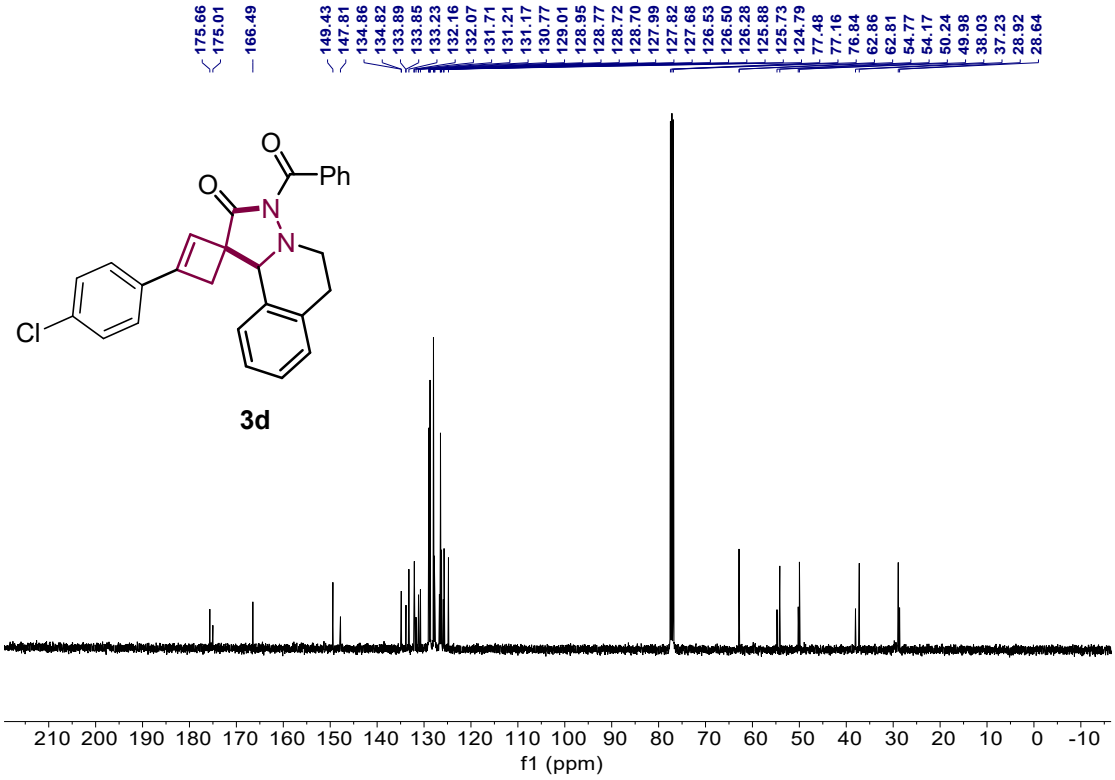


3c

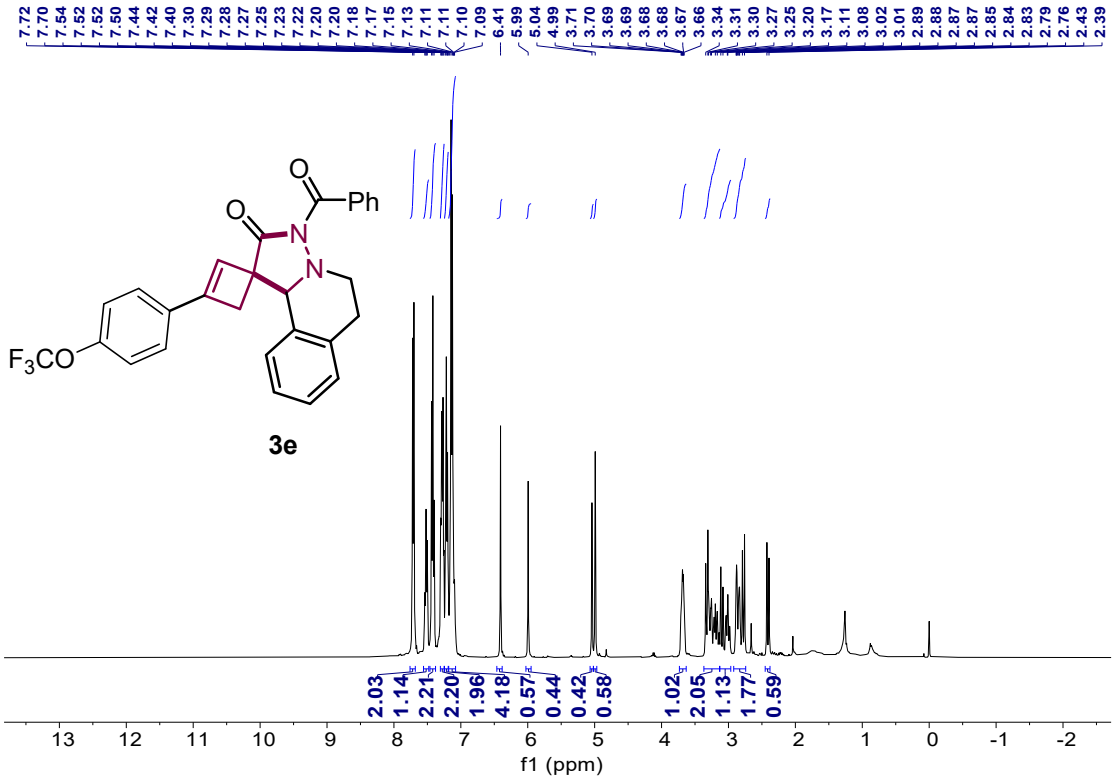
^{1}H NMR (400 MHz, Chloroform-*d*) of **3d**



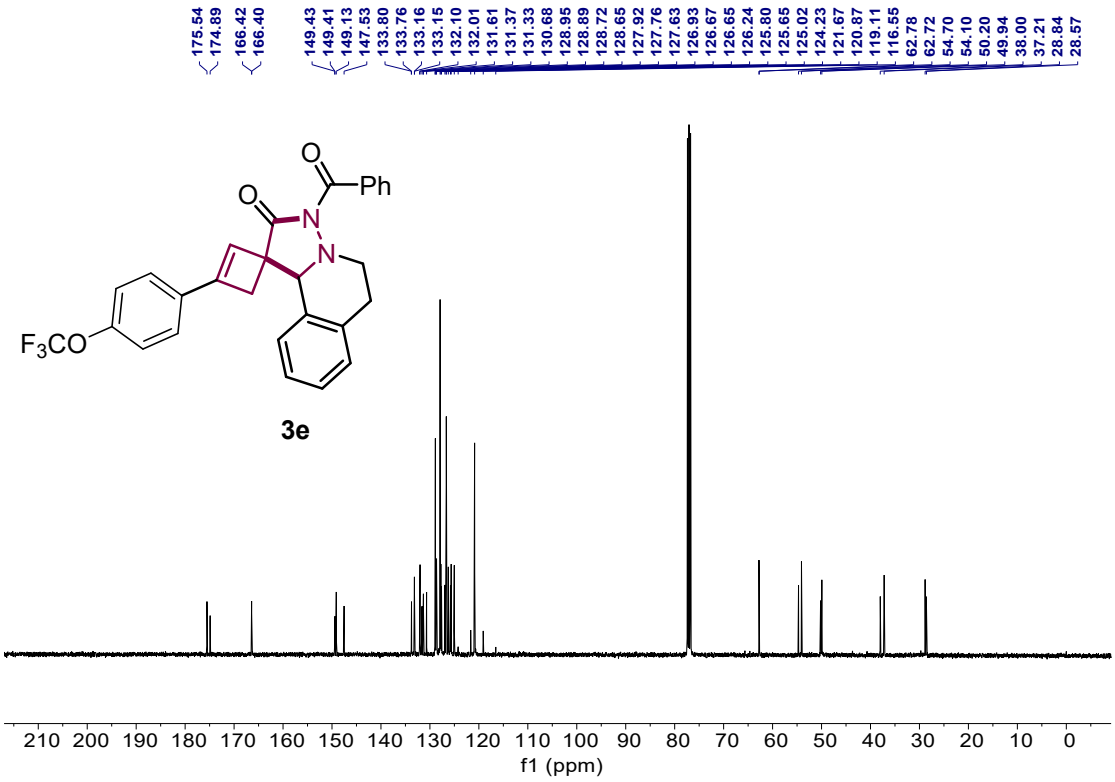
^{13}C NMR (100 MHz, Chloroform-*d*) of **3d**



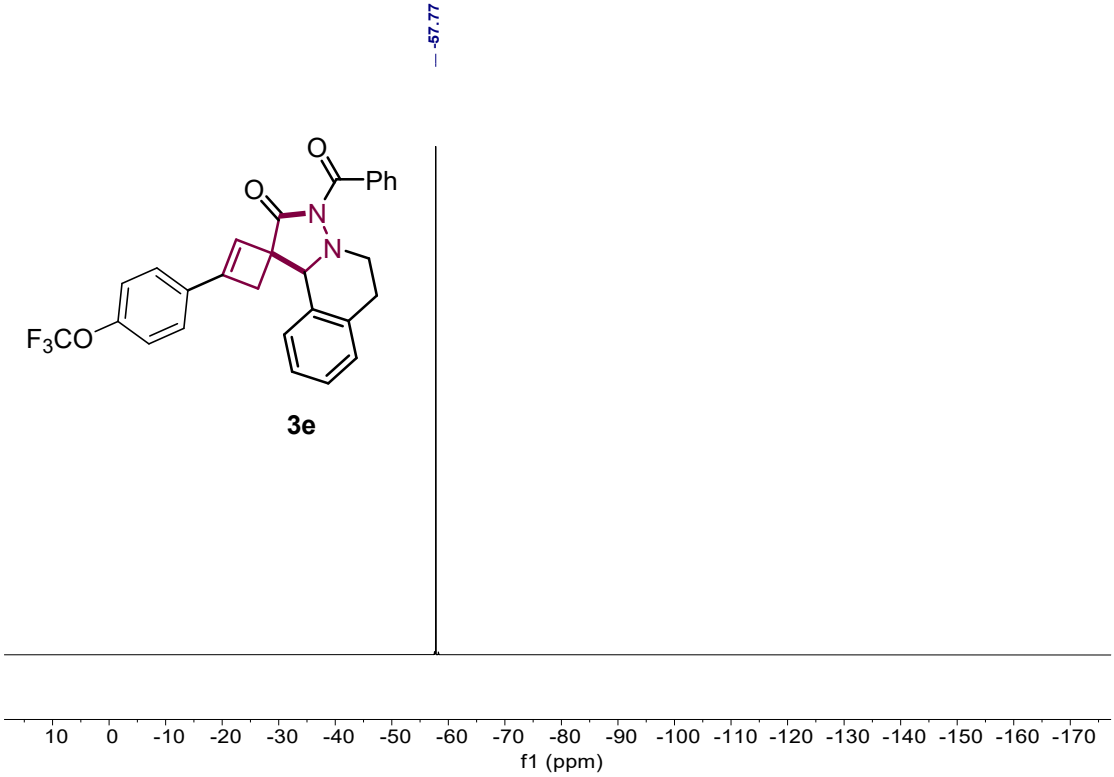
^{1}H NMR (400 MHz, Chloroform-*d*) of **3e**



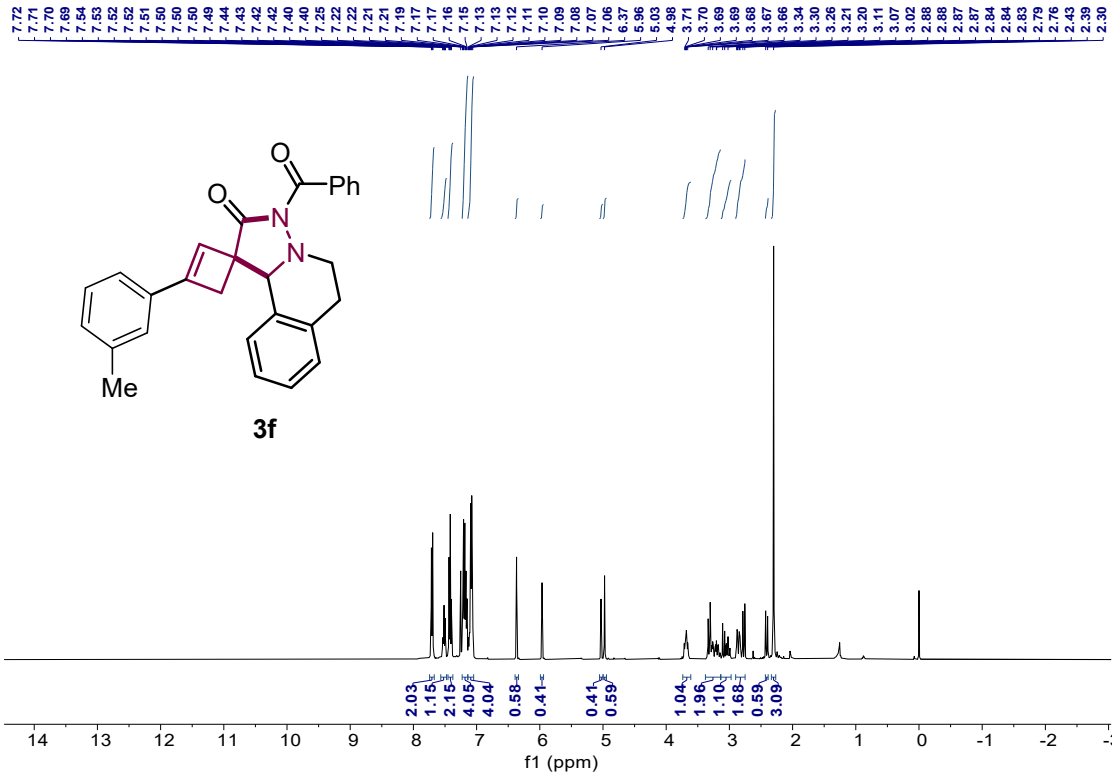
^{13}C NMR (100 MHz, Chloroform-*d*) of **3e**



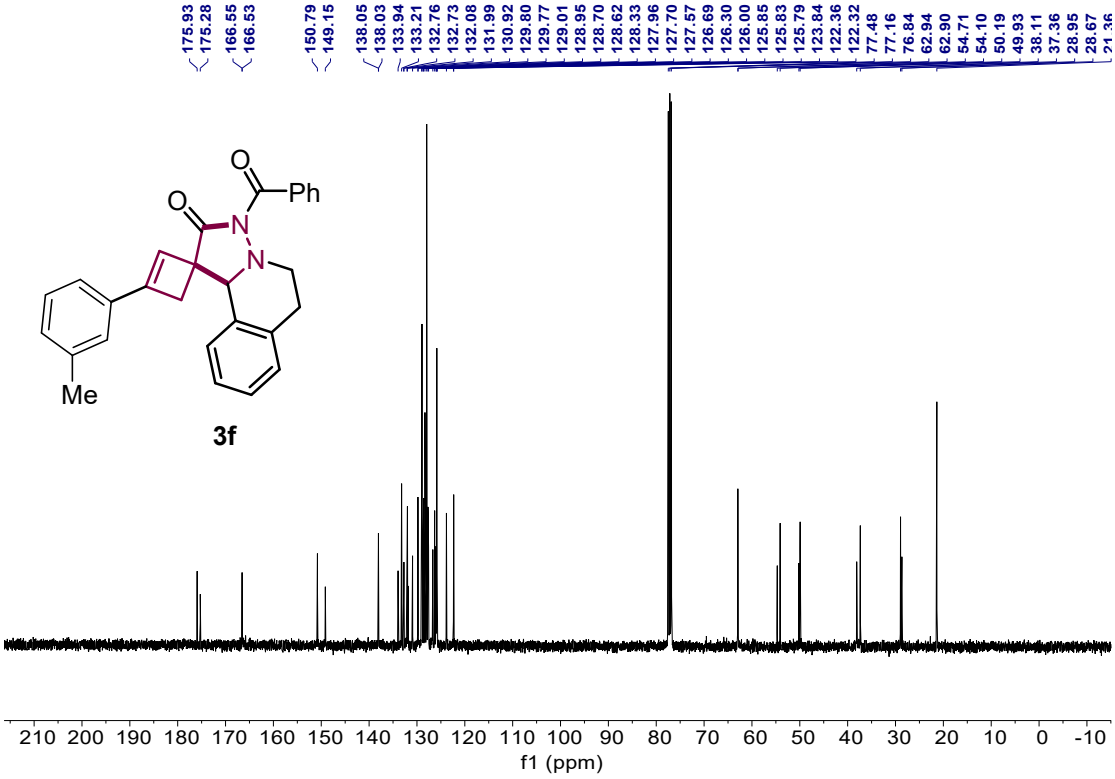
^{19}F NMR (376 MHz, Chloroform-*d*) of **3e**



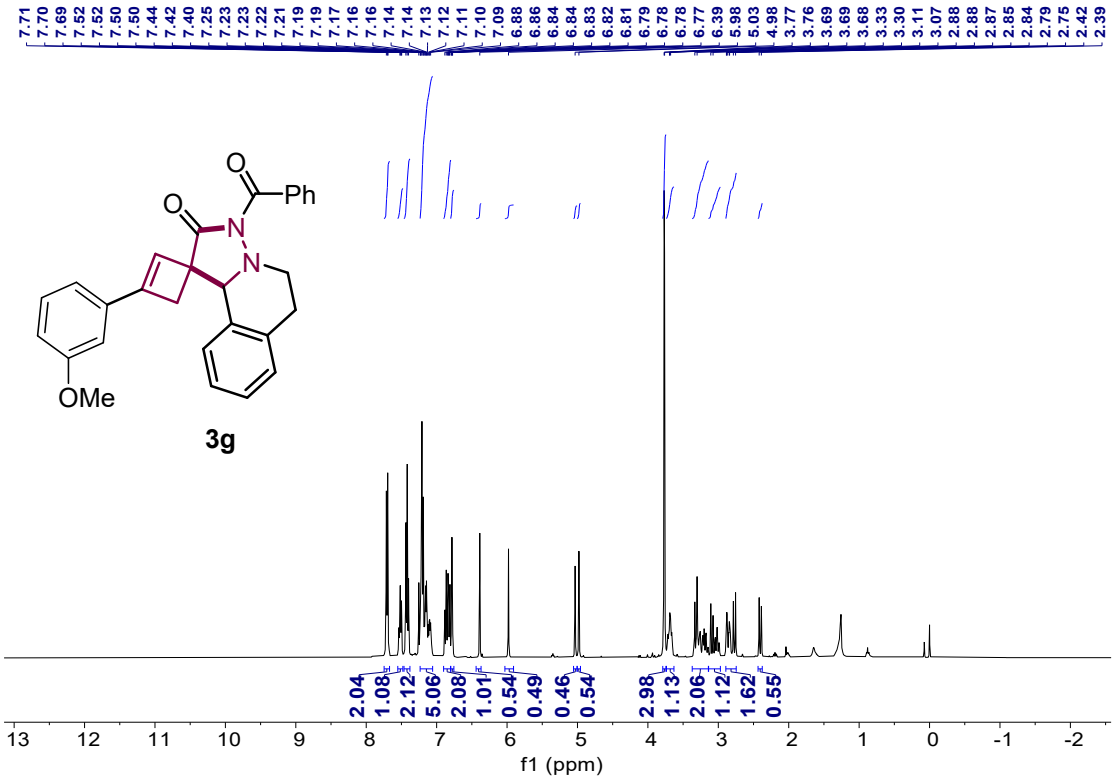
^{1}H NMR (400 MHz, Chloroform-*d*) of **3f**



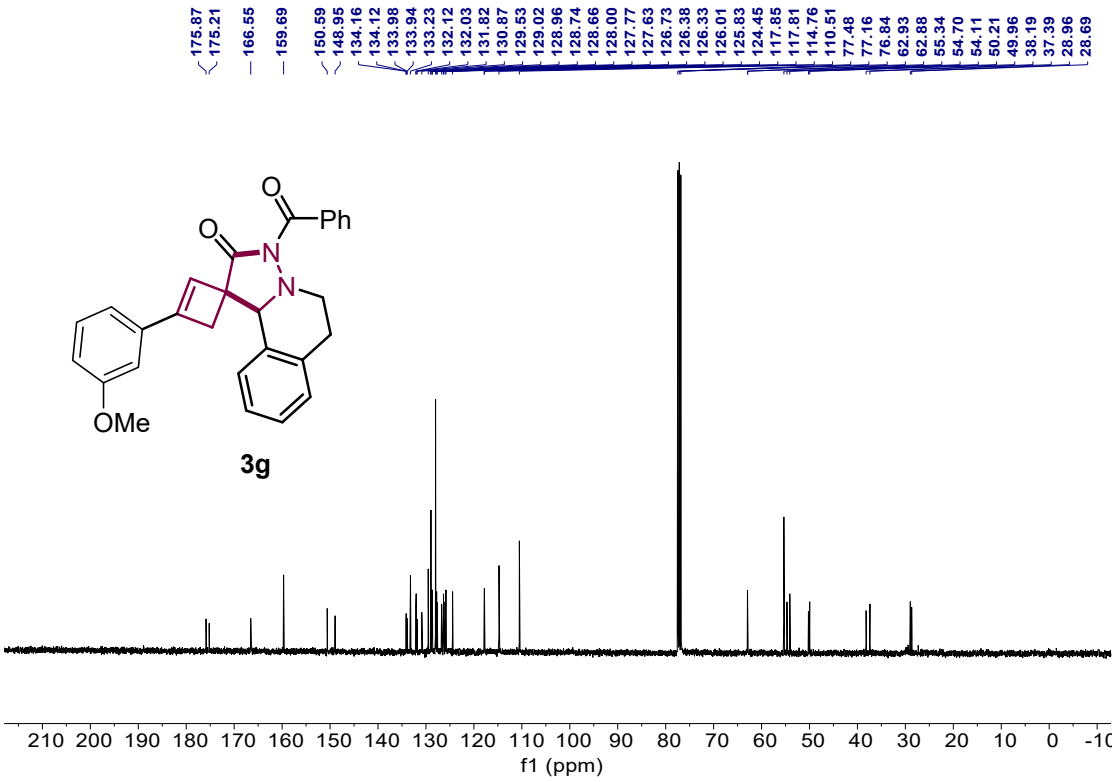
^{13}C NMR (100 MHz, Chloroform-*d*) of **3f**



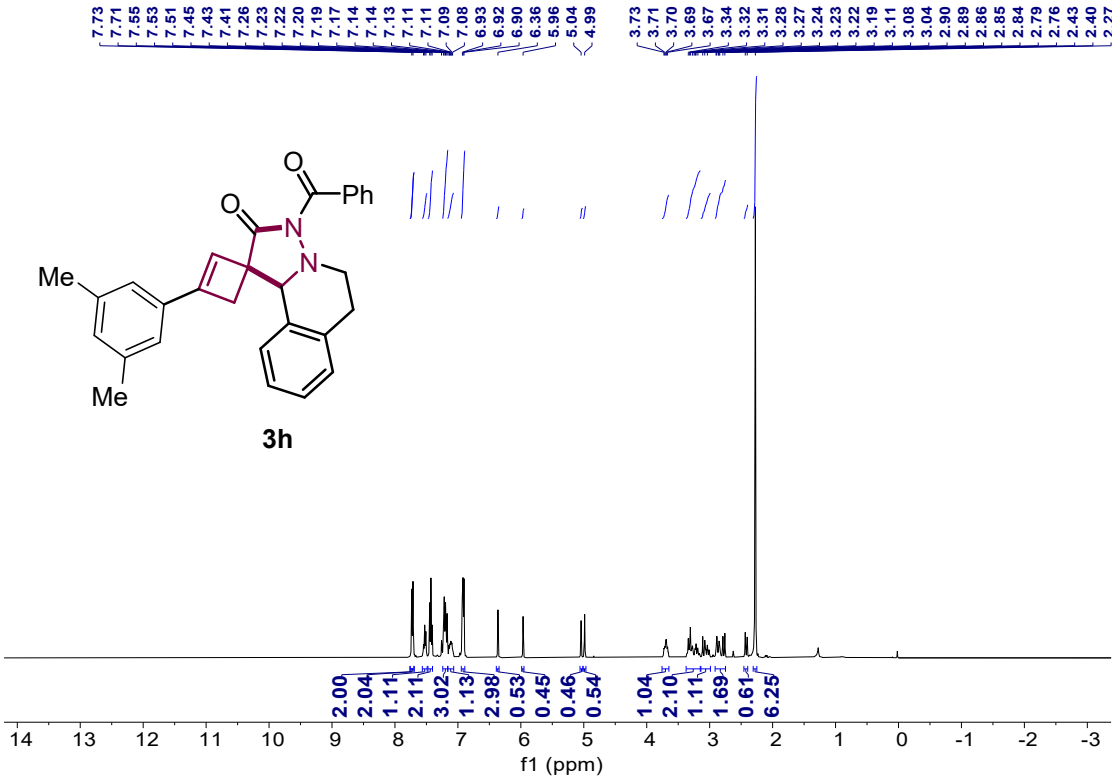
^{1}H NMR (400 MHz, Chloroform-*d*) of **3g**



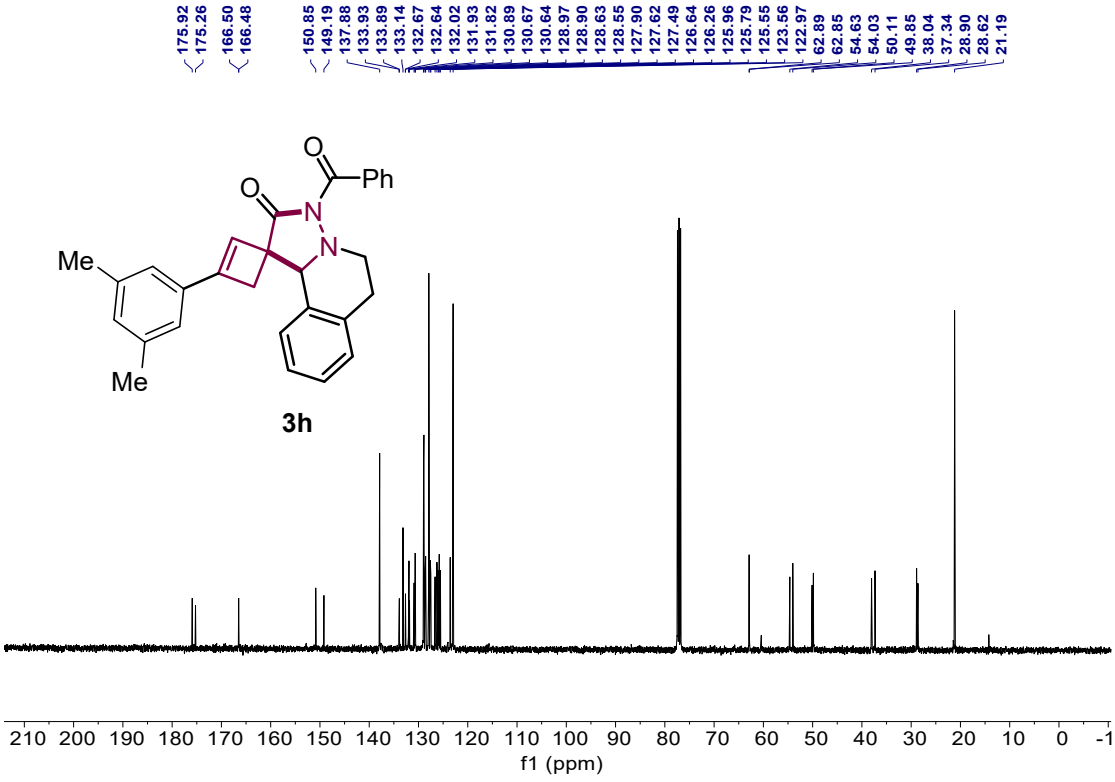
^{13}C NMR (100 MHz, Chloroform-*d*) of **3g**



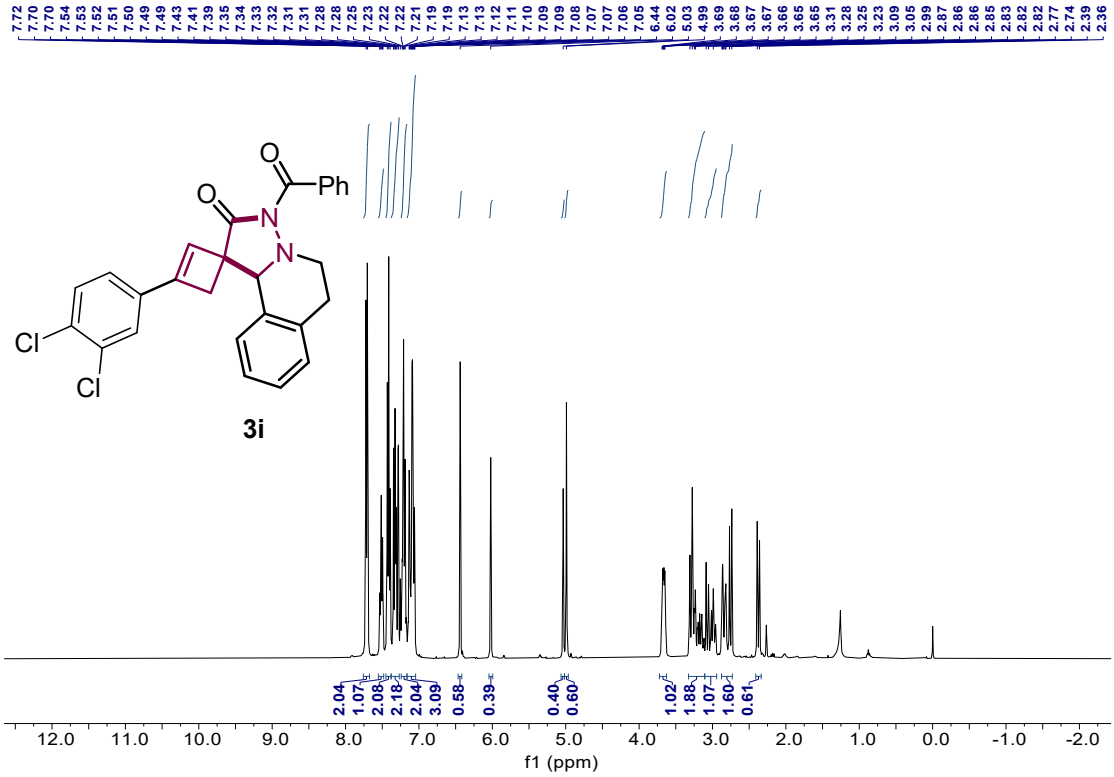
^{1}H NMR (400 MHz, Chloroform-*d*) of **3h**



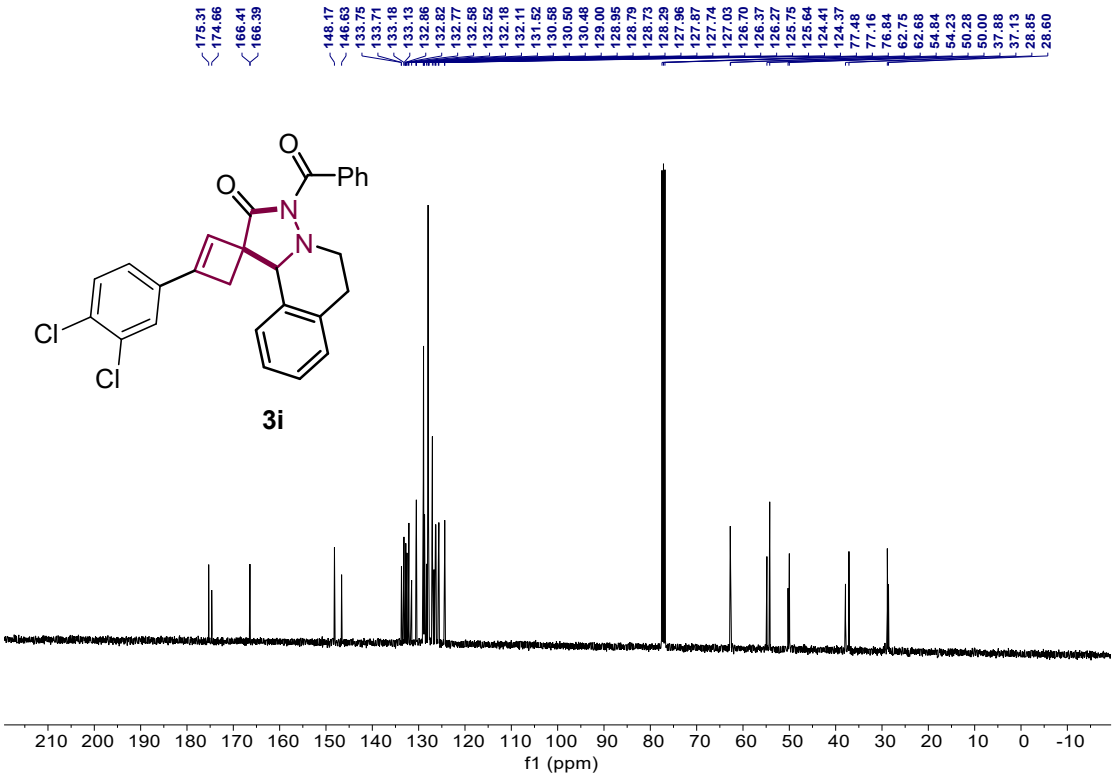
^{13}C NMR (100 MHz, Chloroform-*d*) of **3h**



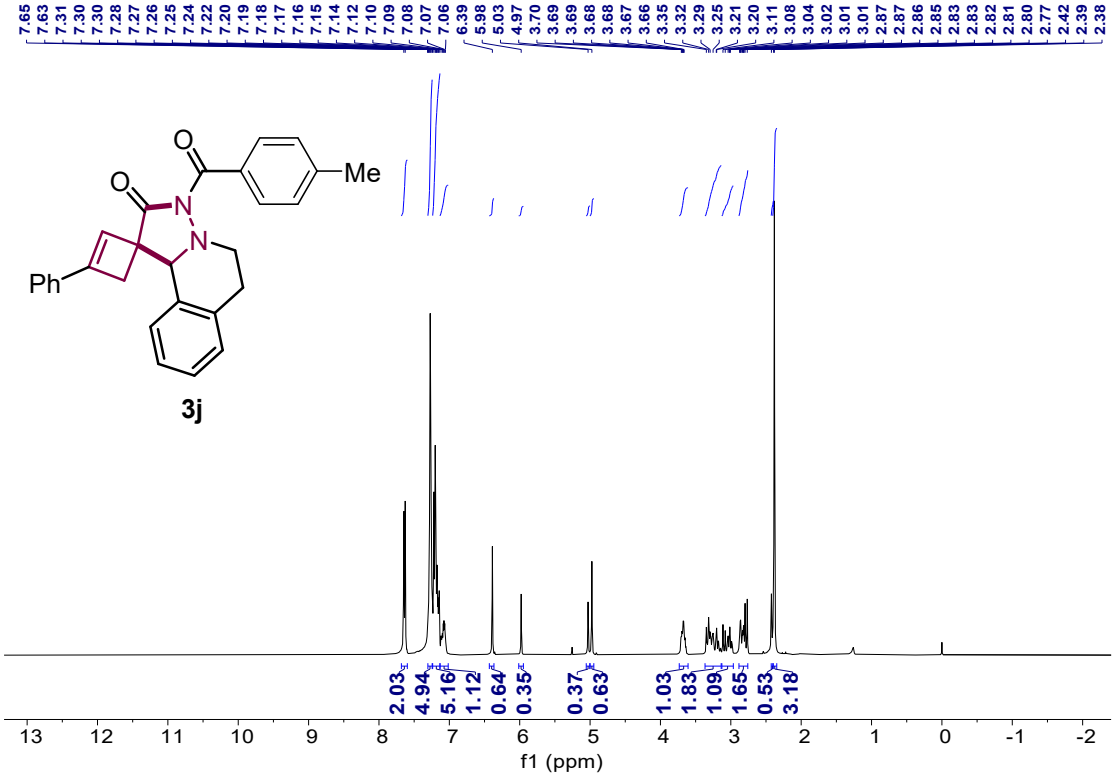
^{1}H NMR (400 MHz, Chloroform-*d*) of **3i**



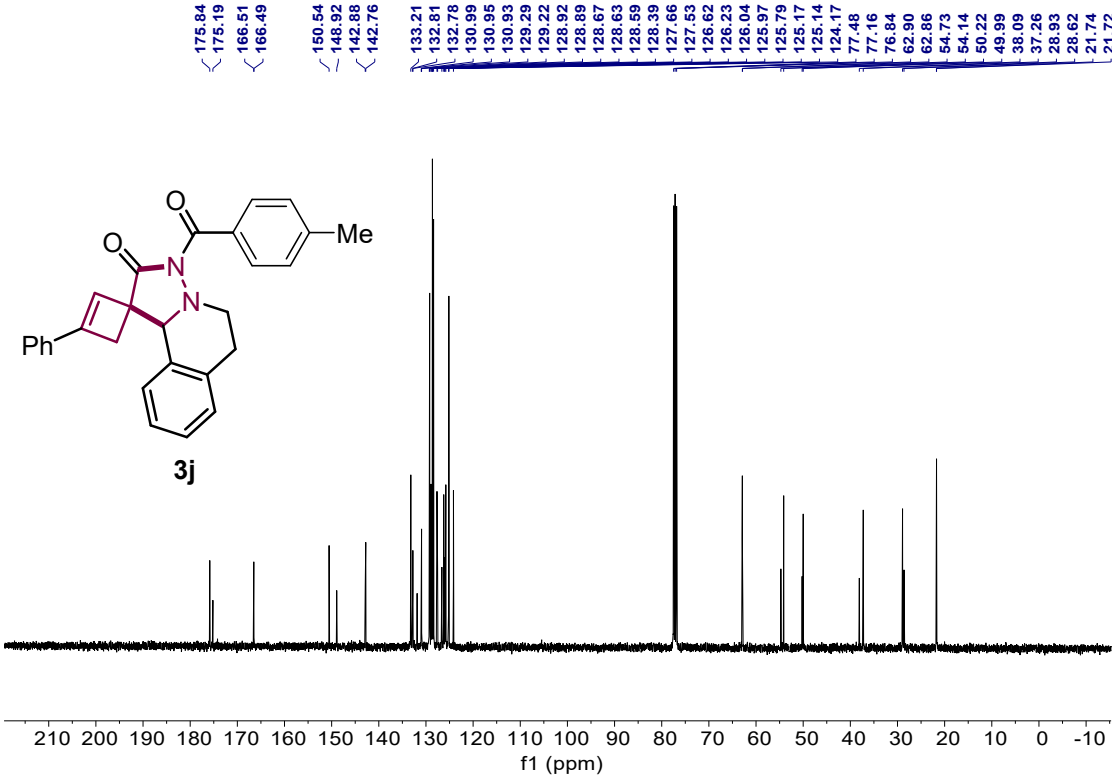
^{13}C NMR (100 MHz, Chloroform-*d*) of **3i**



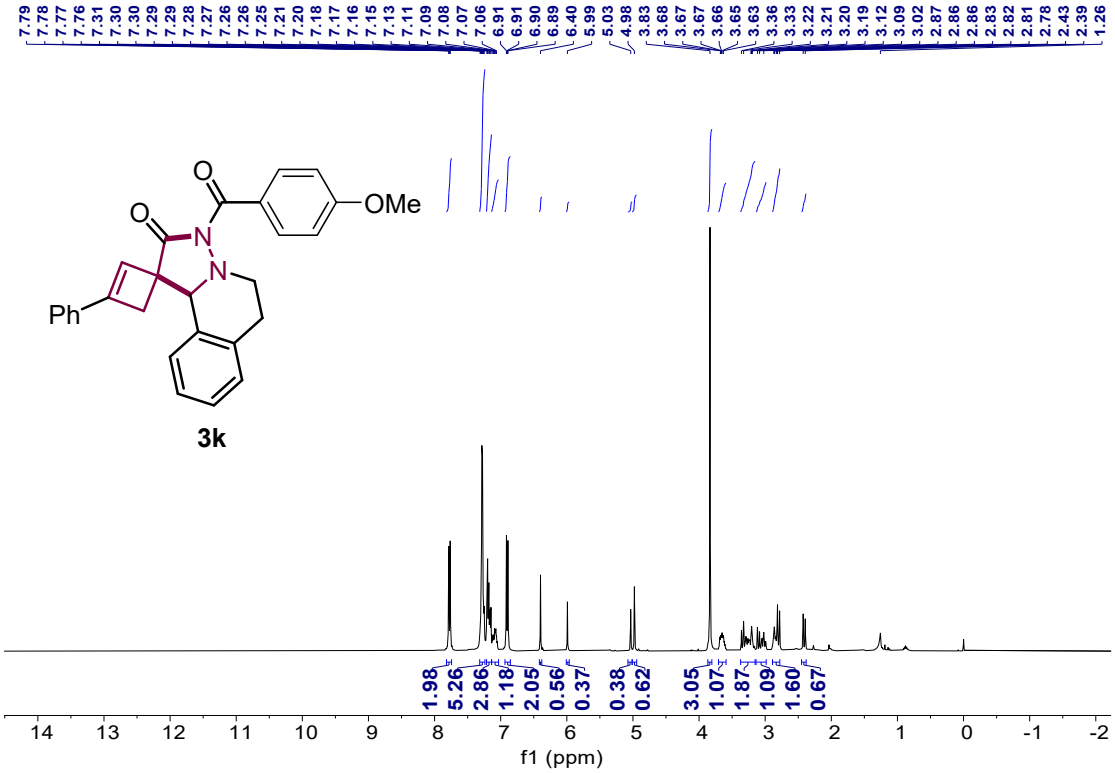
^{1}H NMR (400 MHz, Chloroform-*d*) of **3j**



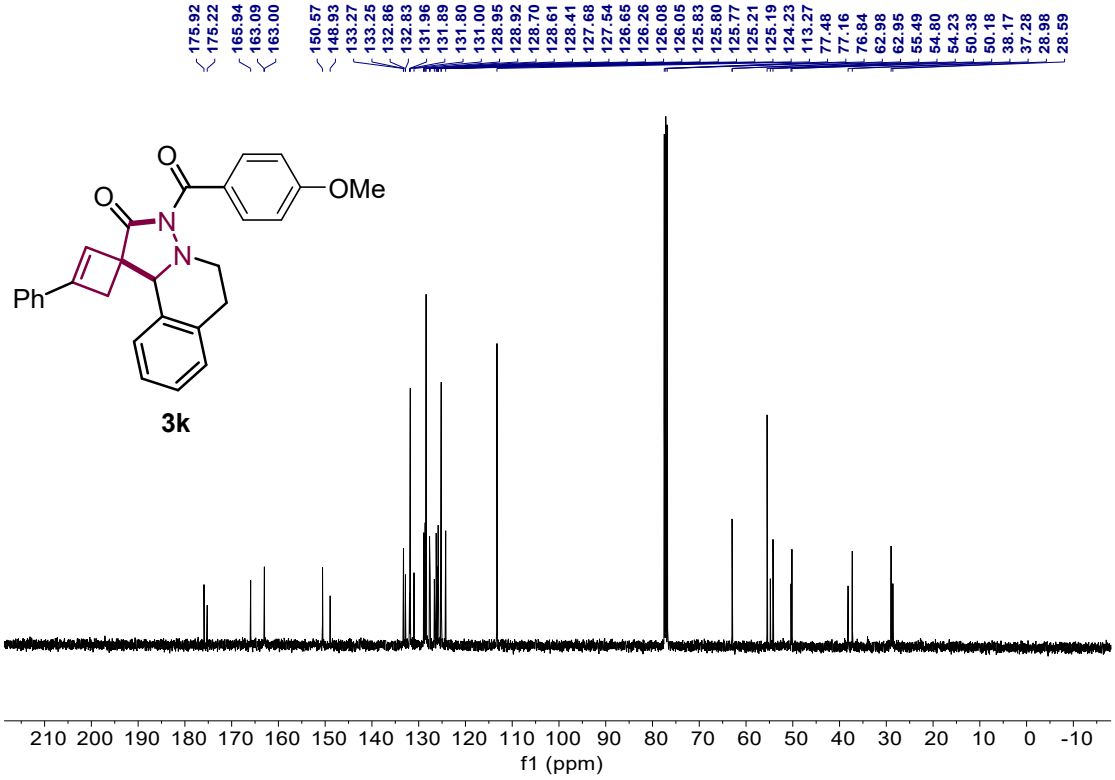
^{13}C NMR (100 MHz, Chloroform-*d*) of **3j**



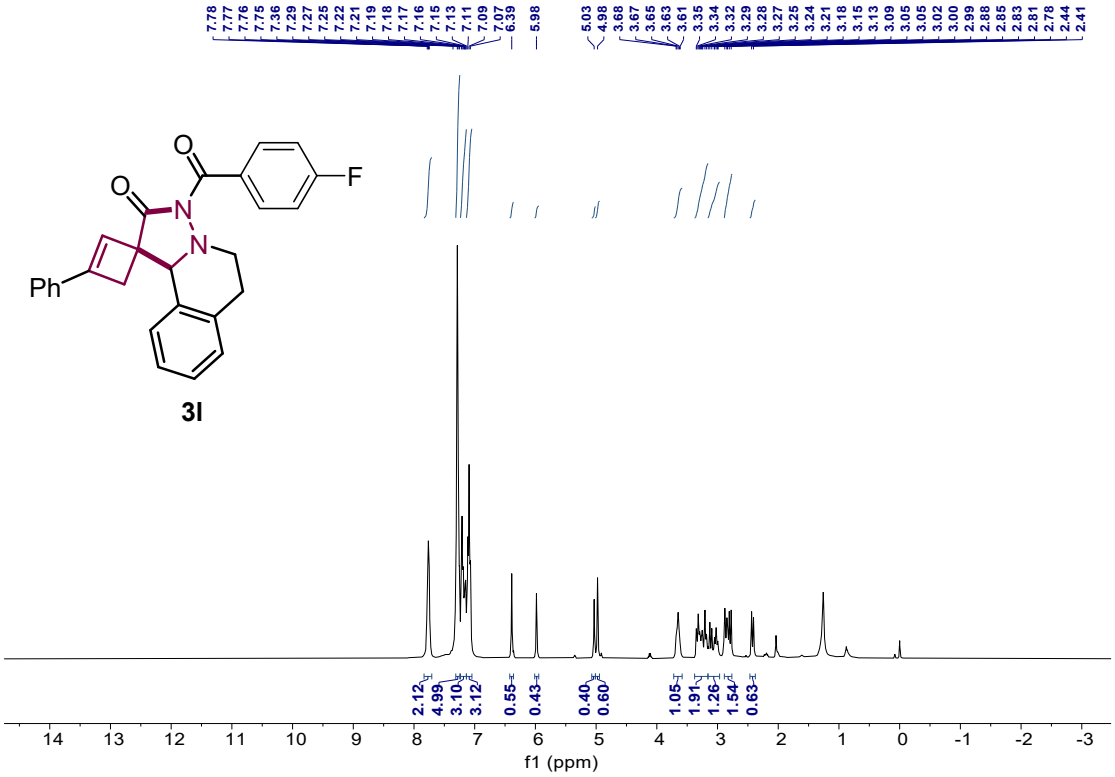
^{1}H NMR (400 MHz, Chloroform-*d*) of **3k**



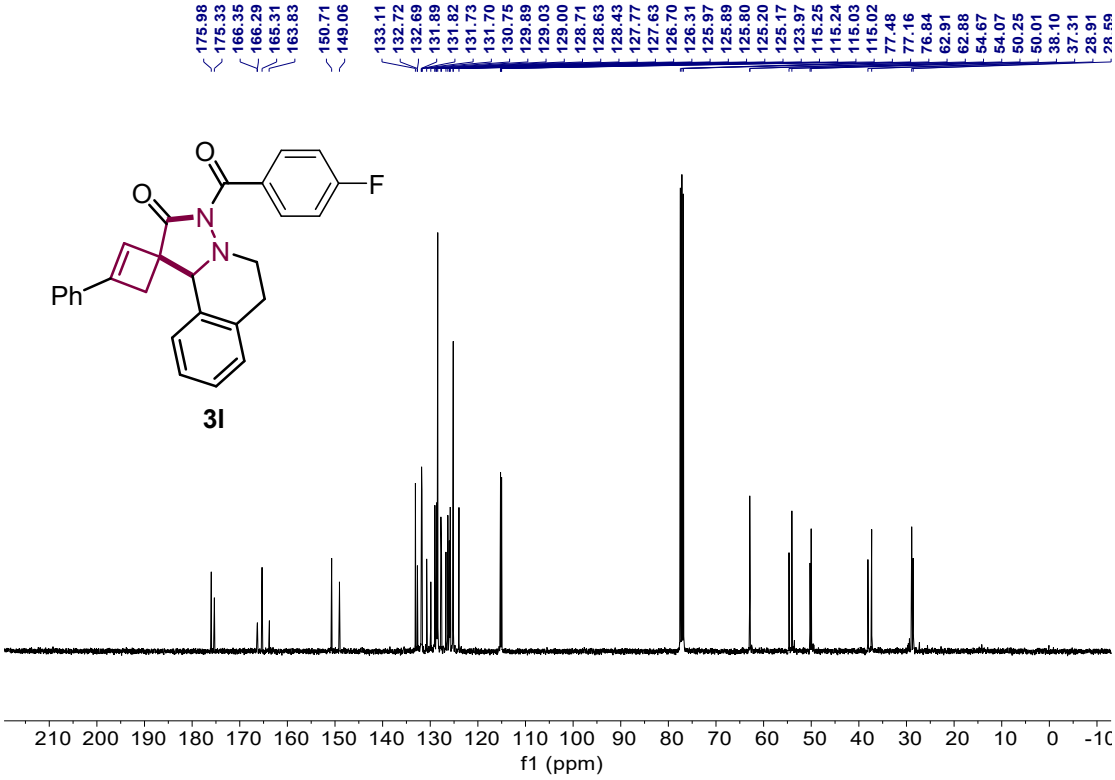
^{13}C NMR (100 MHz, Chloroform-*d*) of **3k**



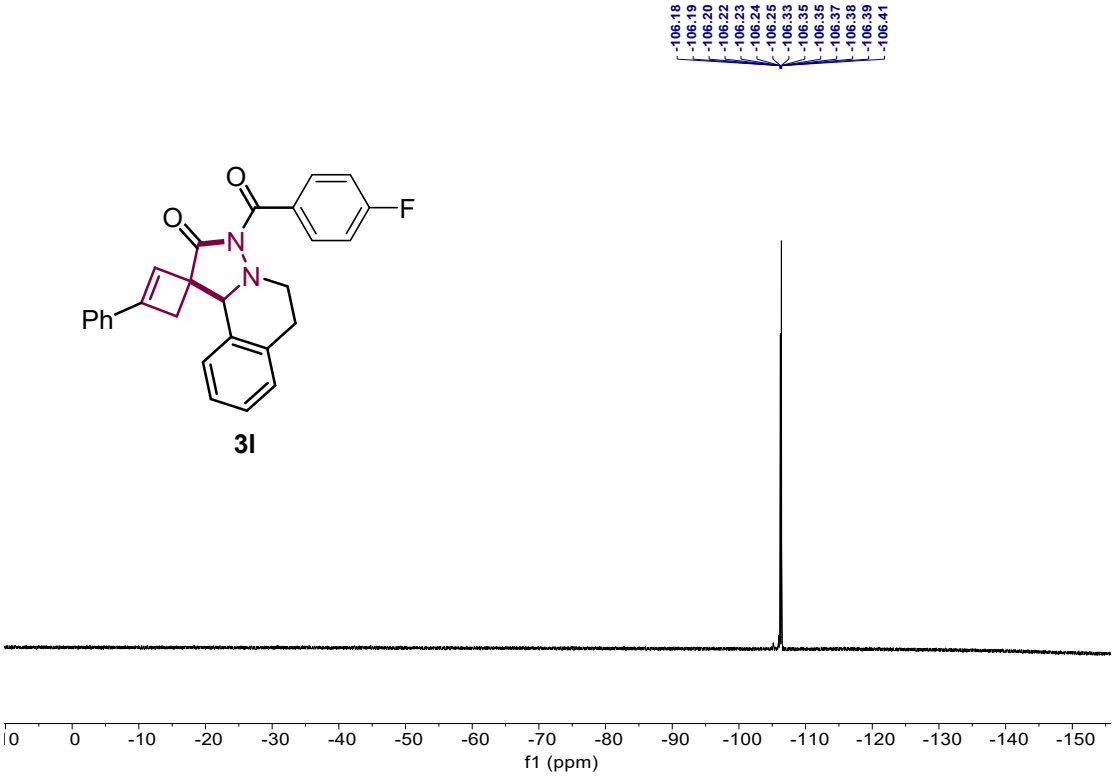
^{1}H NMR (400 MHz, Chloroform-*d*) of **3l**



^{13}C NMR (100 MHz, Chloroform-*d*) of **3l**

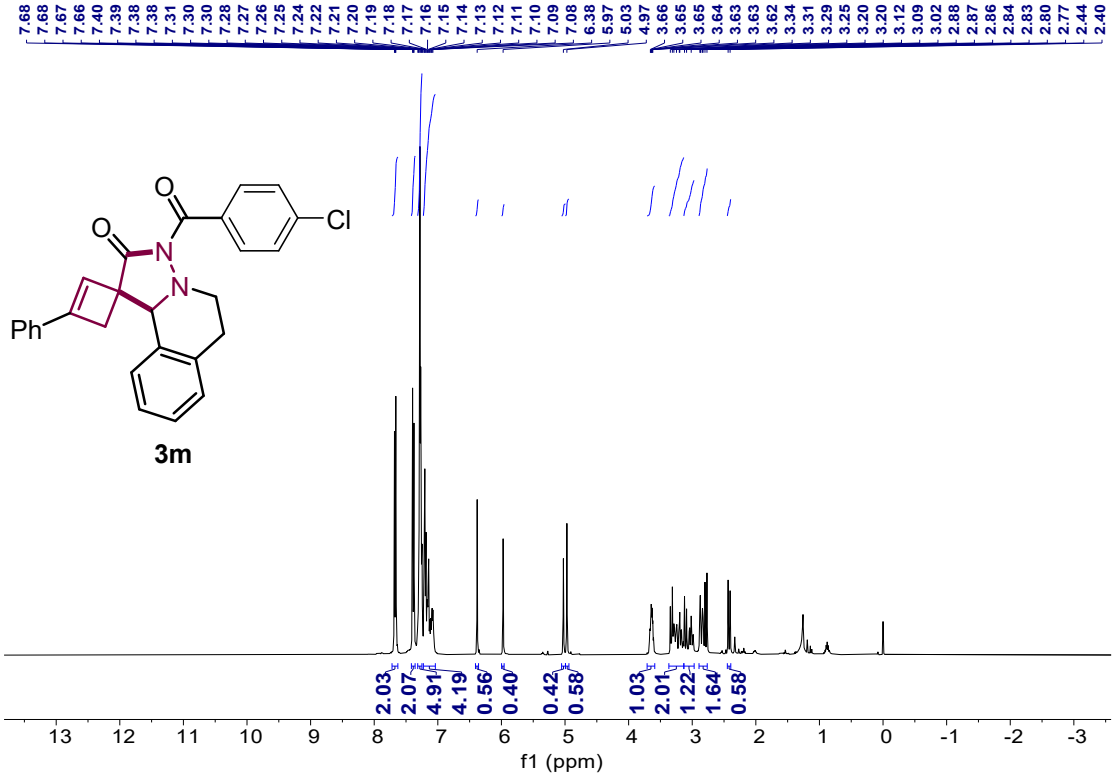


^{19}F NMR (376 MHz, Chloroform-*d*) of **3l**

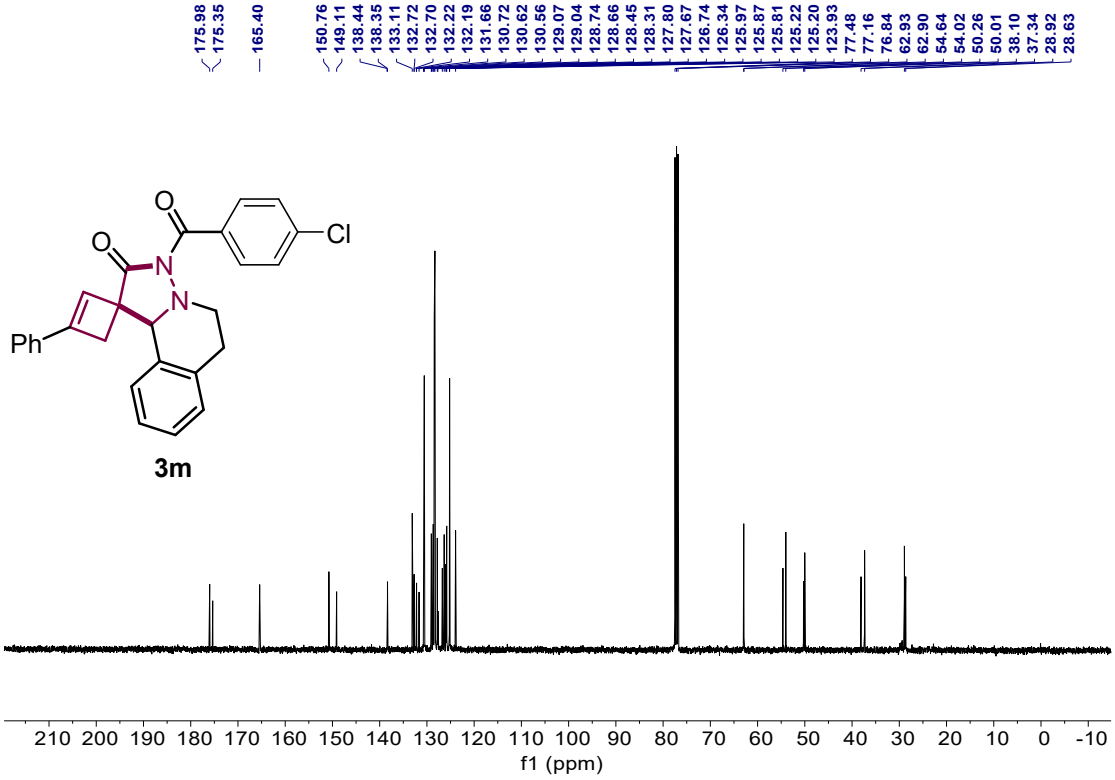


3l

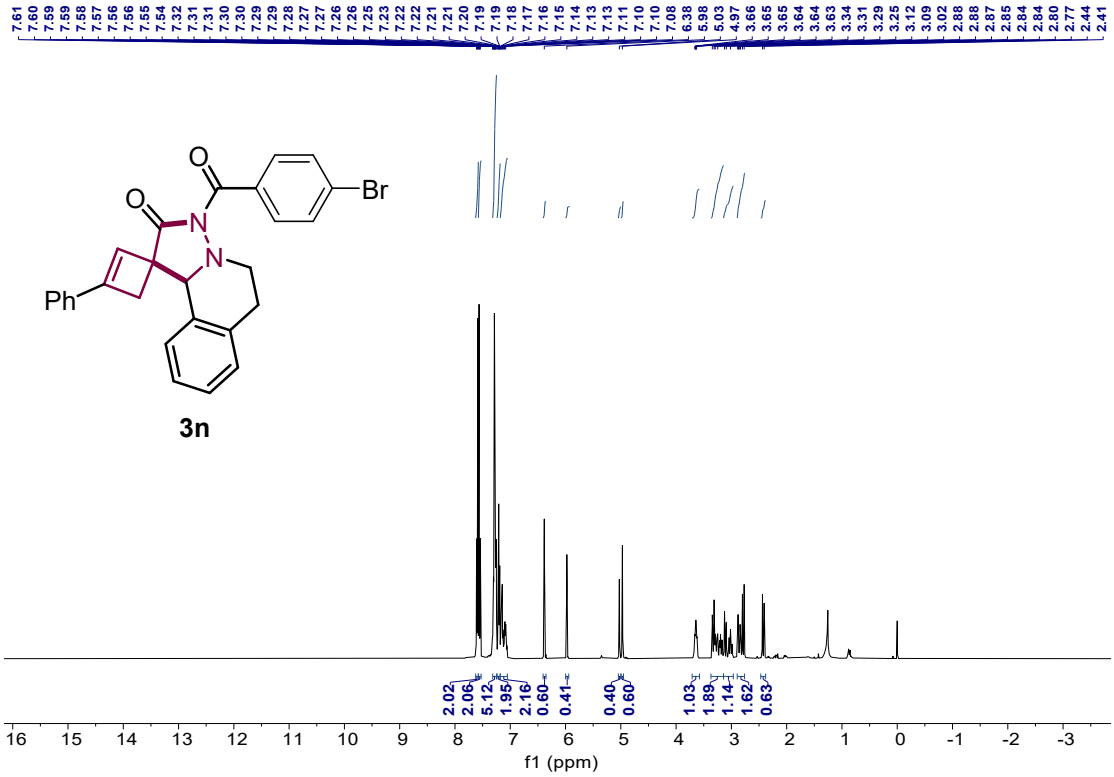
[1]H NMR (400 MHz, Chloroform-*d*) of **3m**



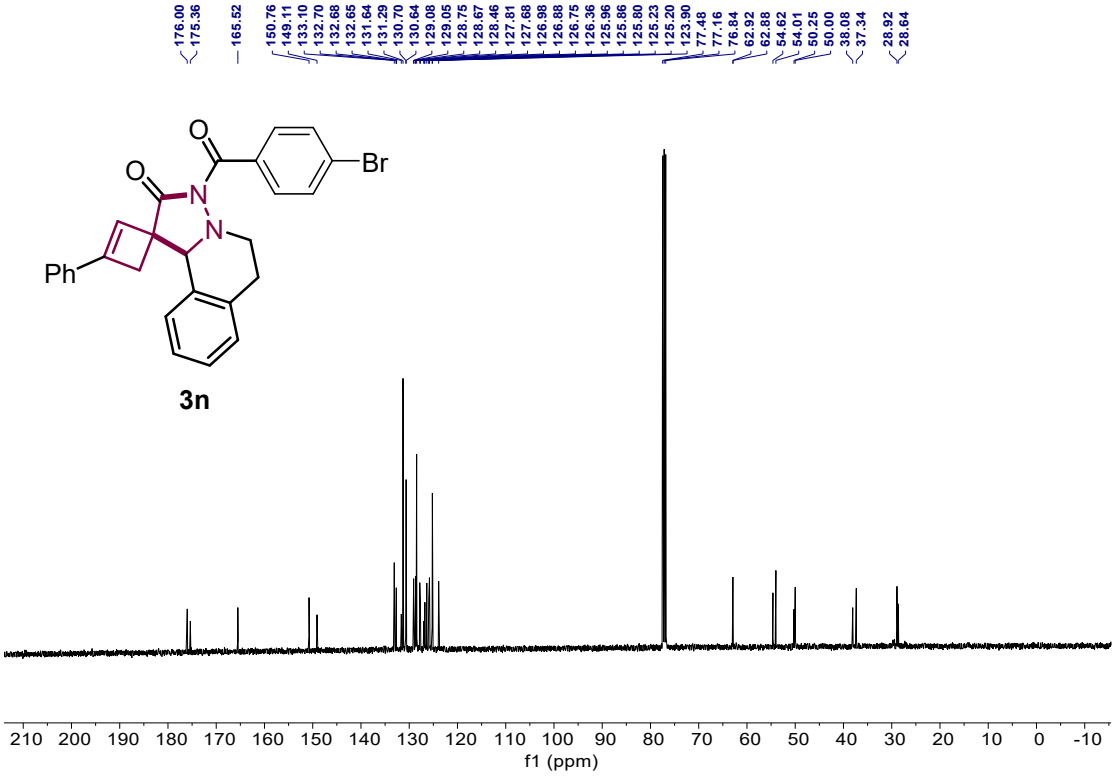
[13]C NMR (100 MHz, Chloroform-*d*) of **3m**



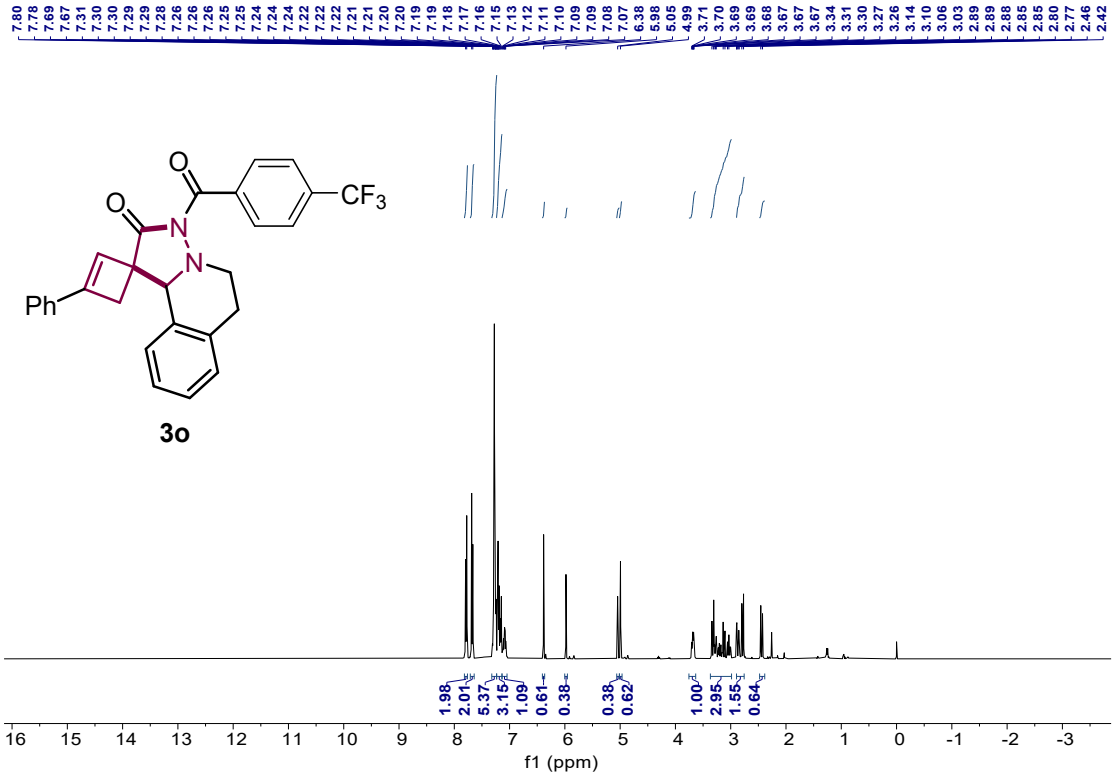
^{1}H NMR (400 MHz, Chloroform-*d*) of **3n**



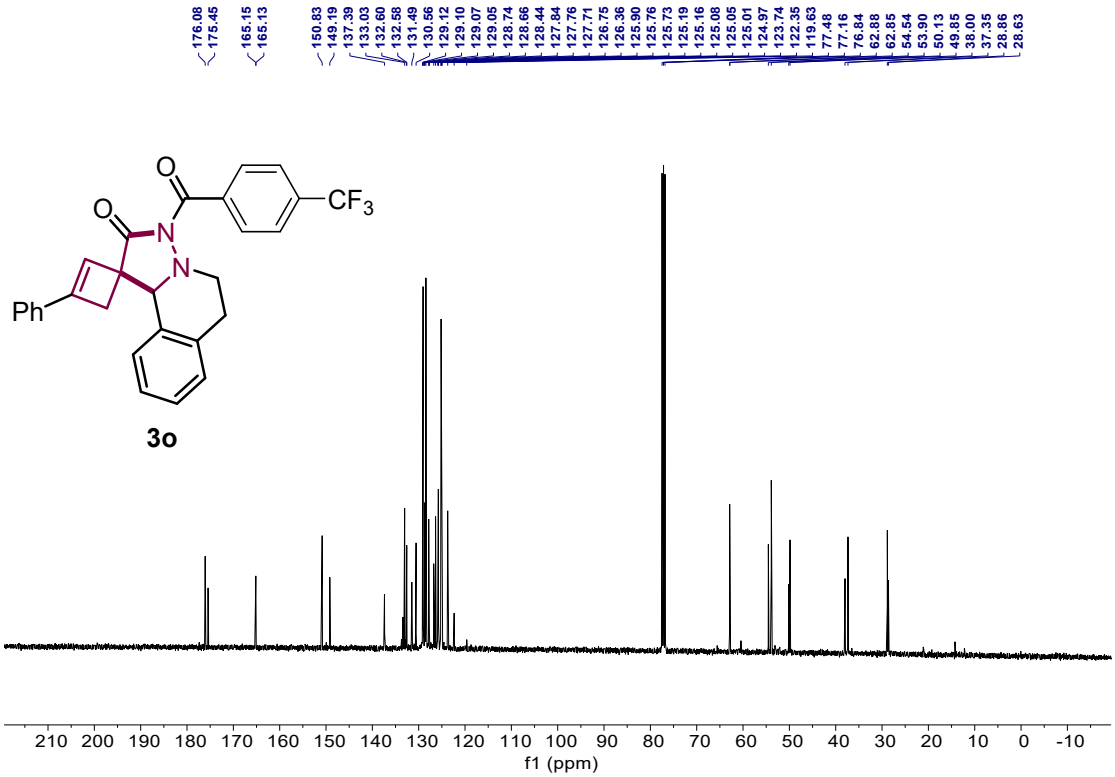
^{13}C NMR (100 MHz, Chloroform-*d*) of **3n**



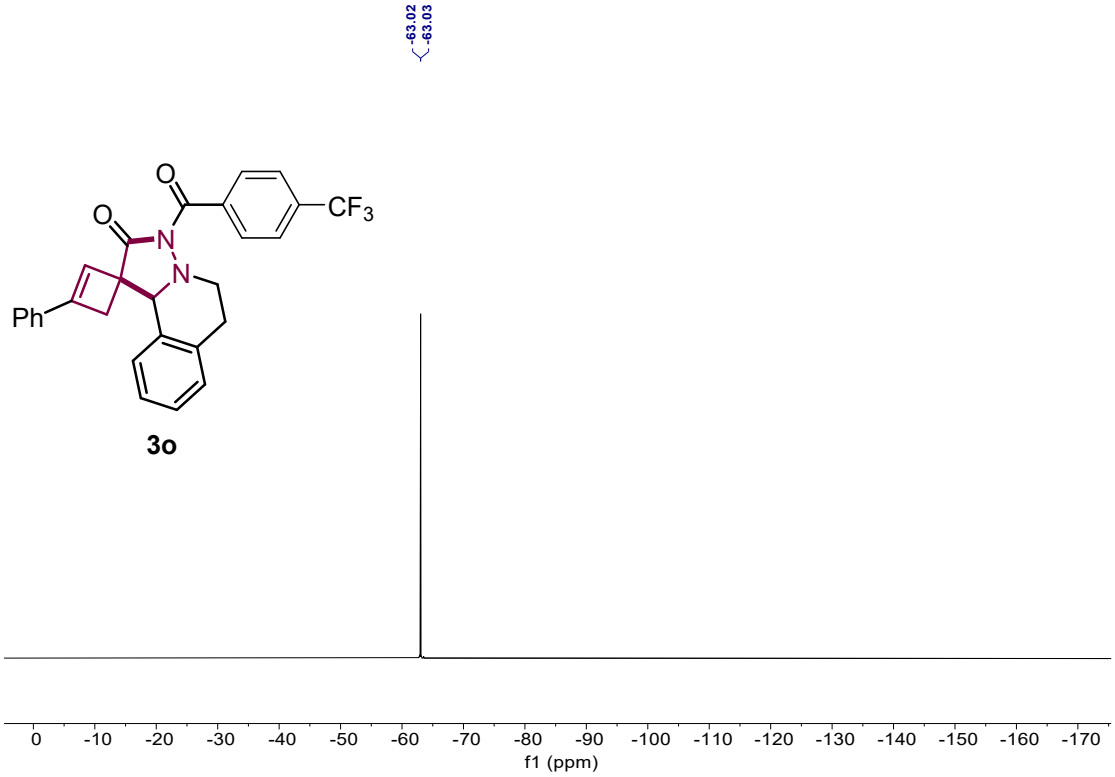
^{1}H NMR (400 MHz, Chloroform-*d*) of **3o**



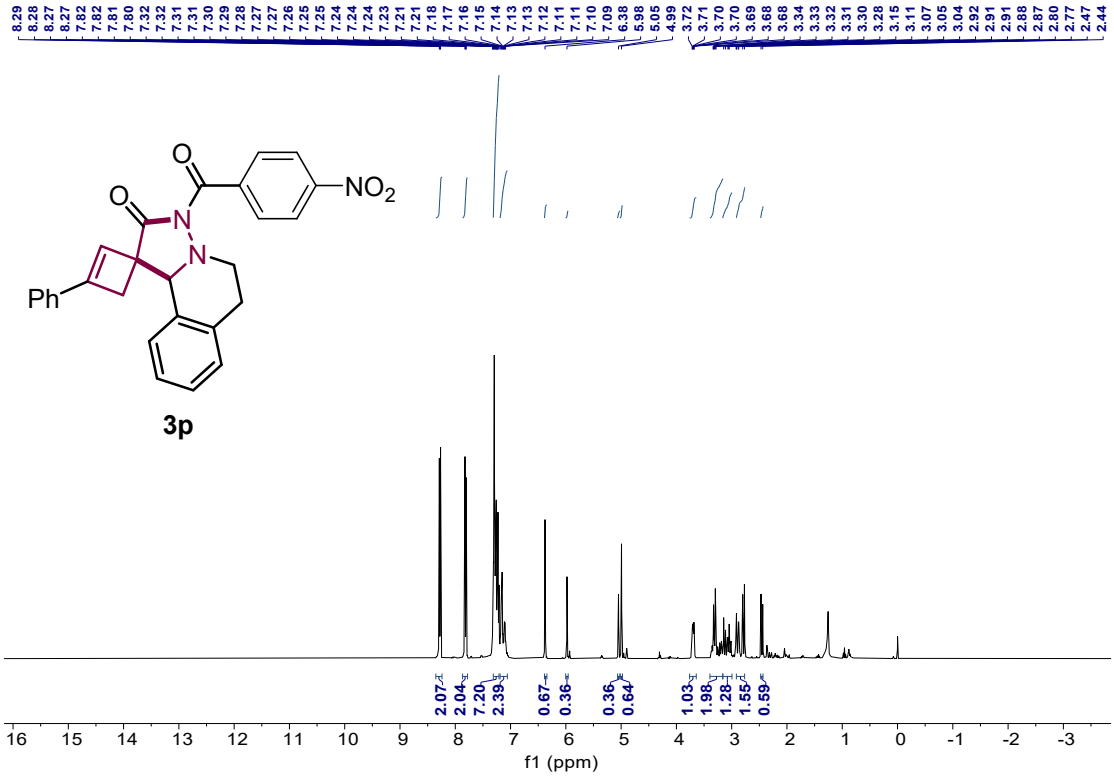
^{13}C NMR (100 MHz, Chloroform-*d*) of **3o**



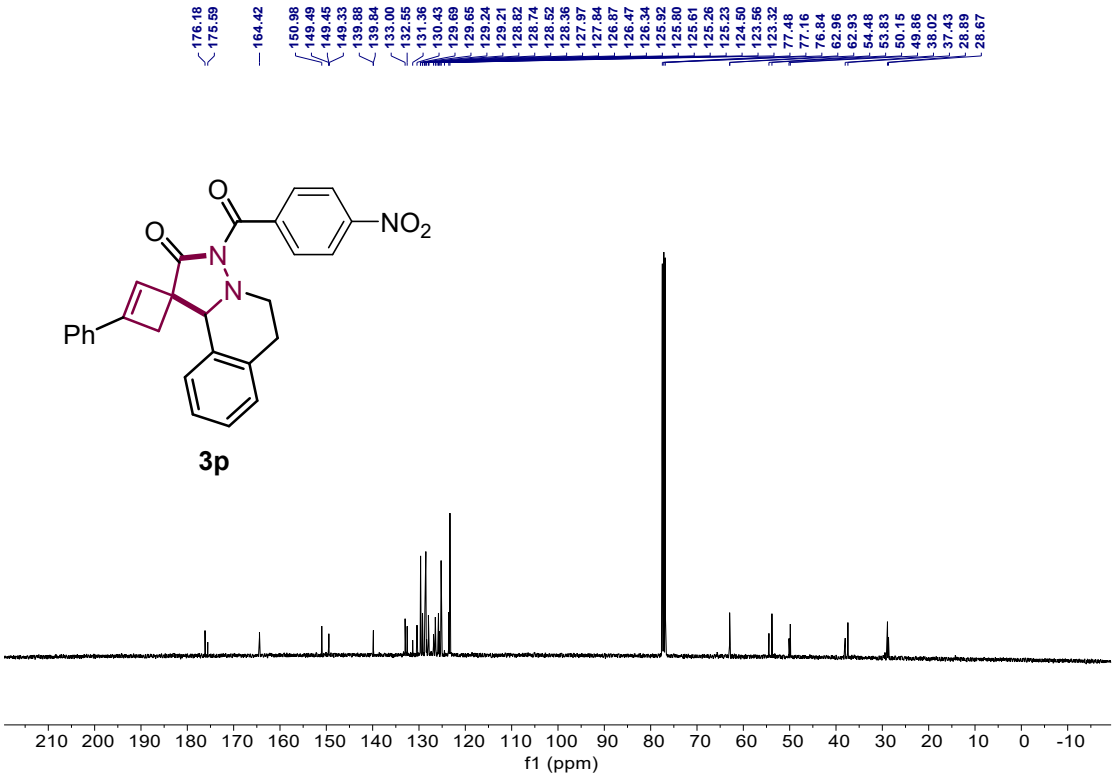
^{19}F NMR (376 MHz, Chloroform-*d*) of **3o**



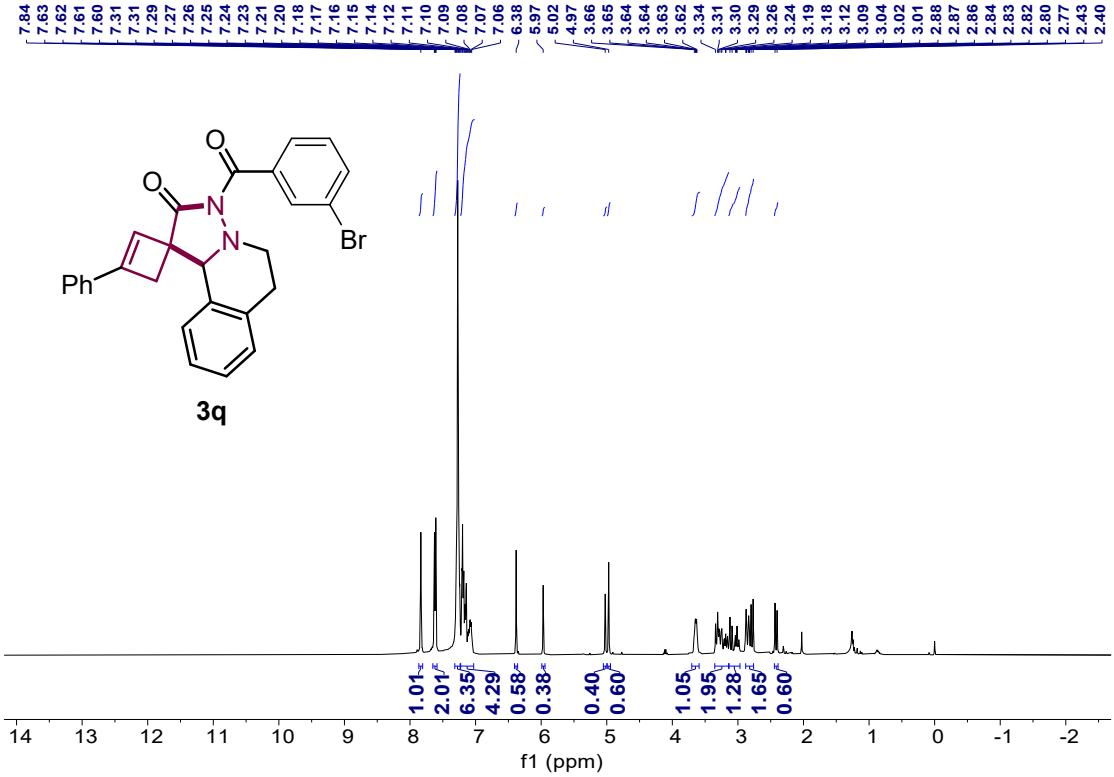
^{1}H NMR (400 MHz, Chloroform-*d*) of **3p**



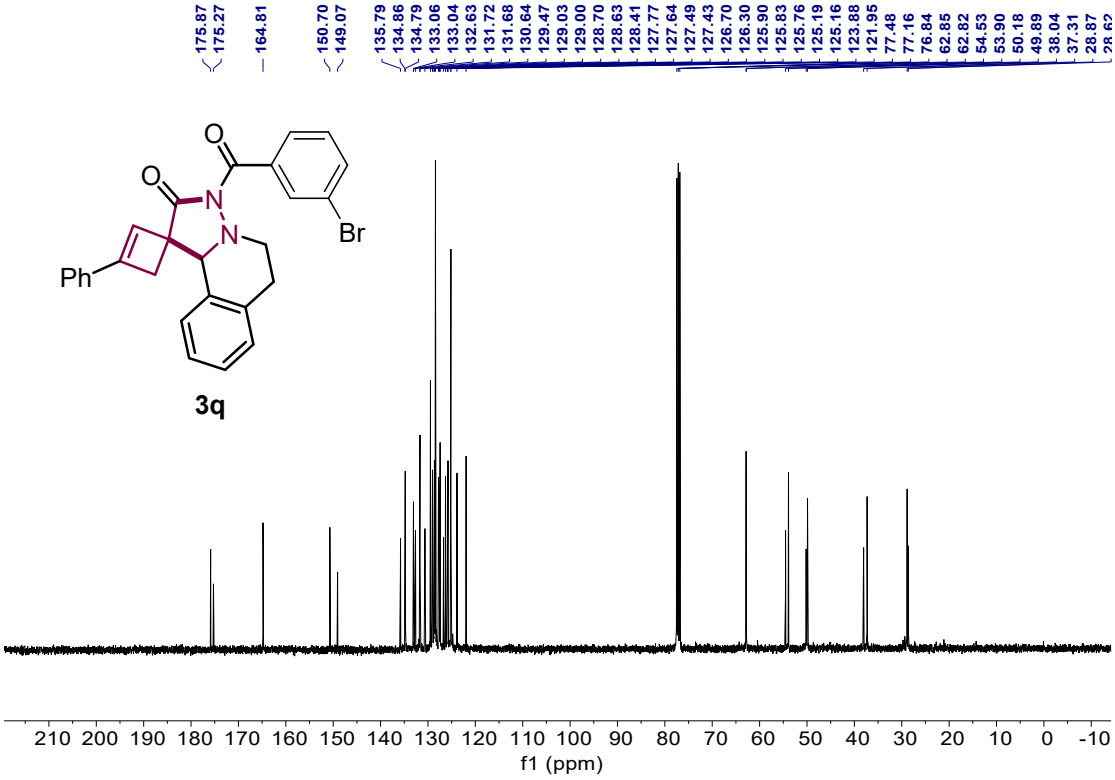
^{13}C NMR (100 MHz, Chloroform-*d*) of **3p**



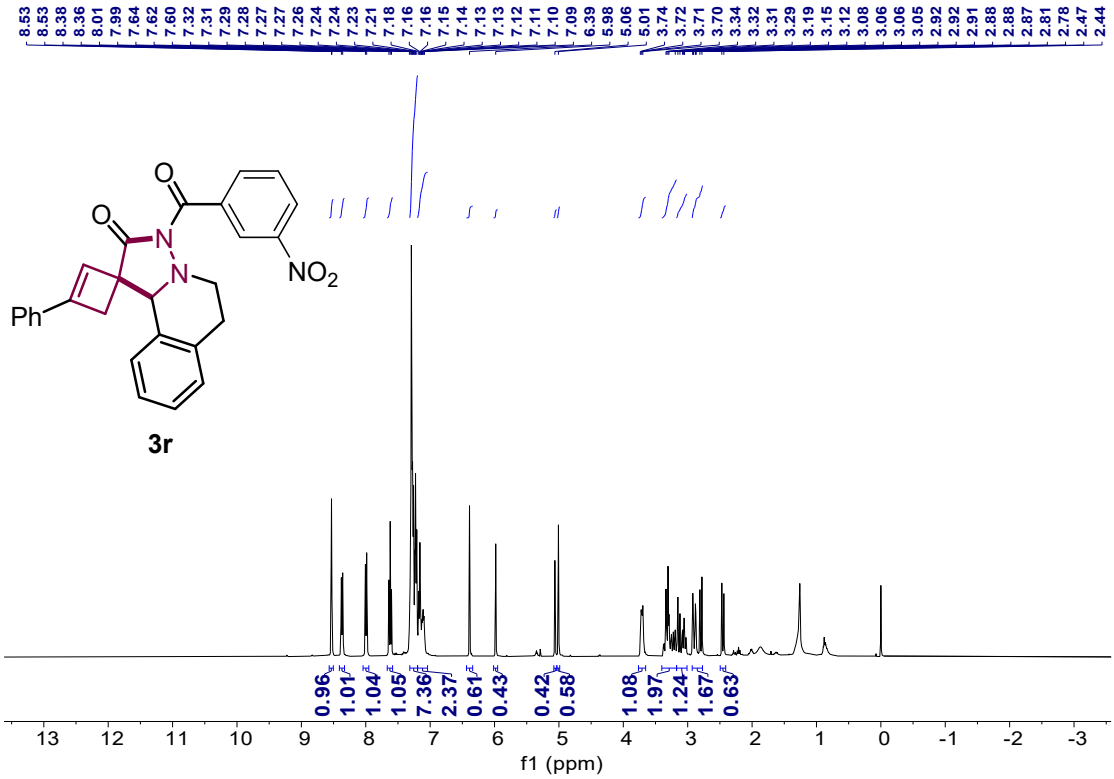
^{1}H NMR (400 MHz, Chloroform-*d*) of **3q**



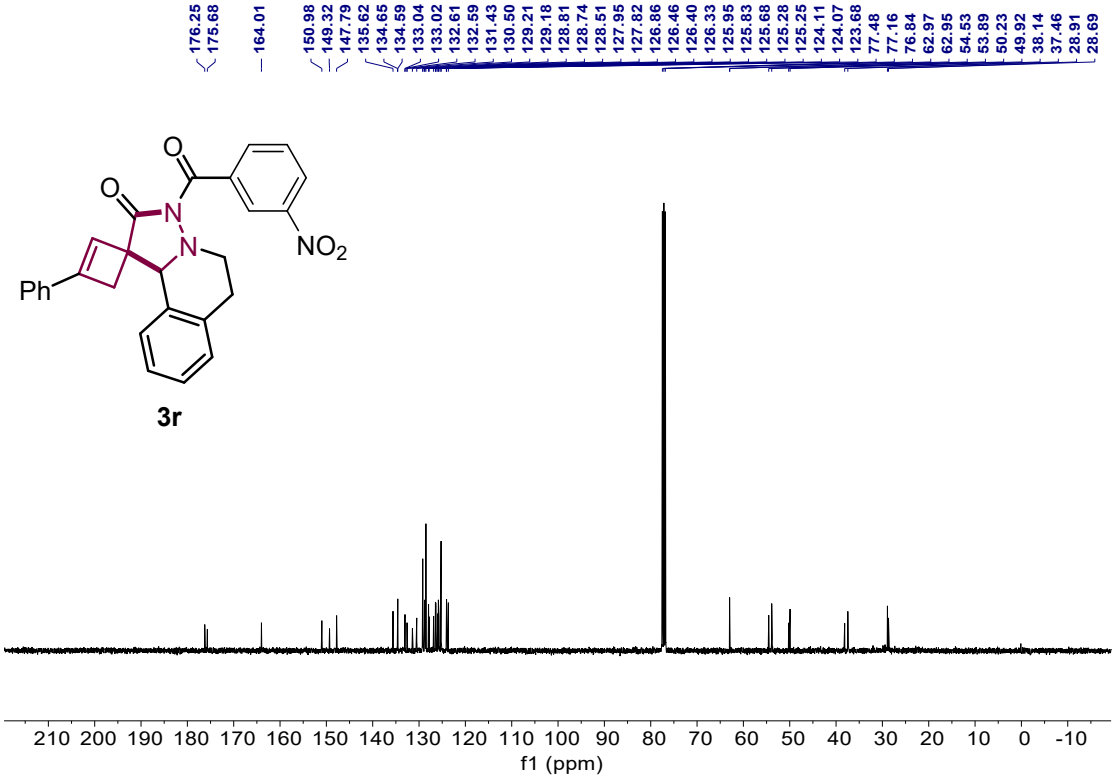
^{13}C NMR (100 MHz, Chloroform-*d*) of **3q**



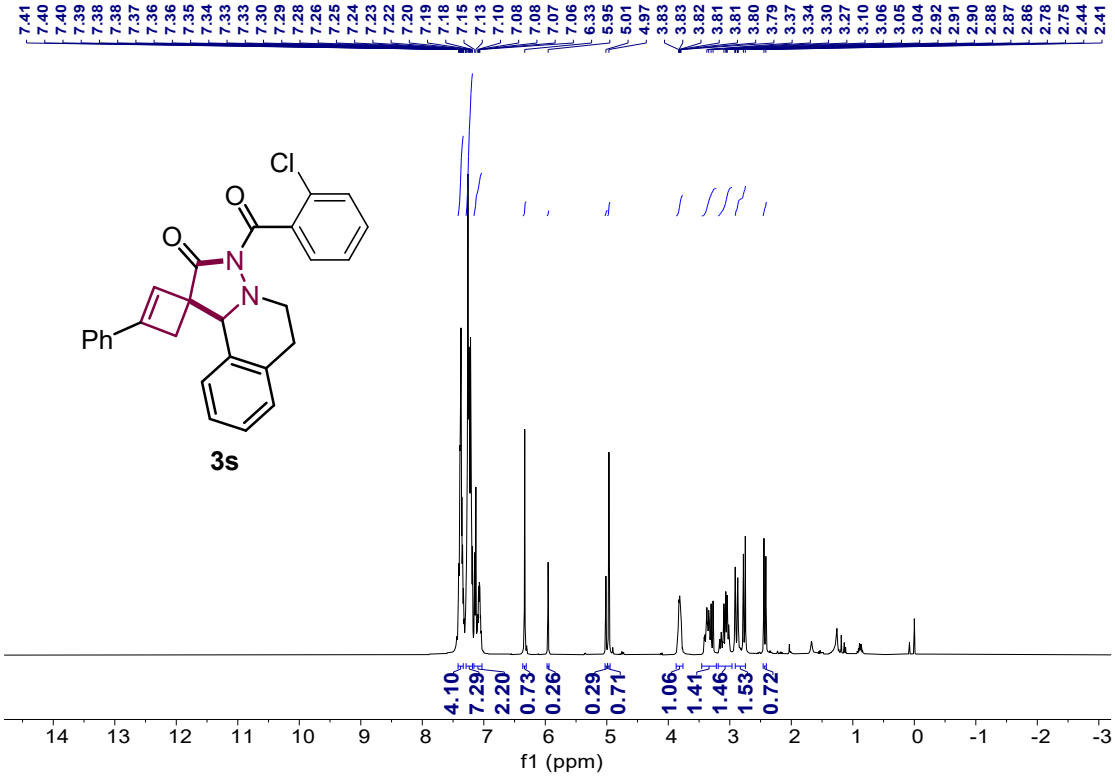
^{1}H NMR (400 MHz, Chloroform-*d*) of **3r**



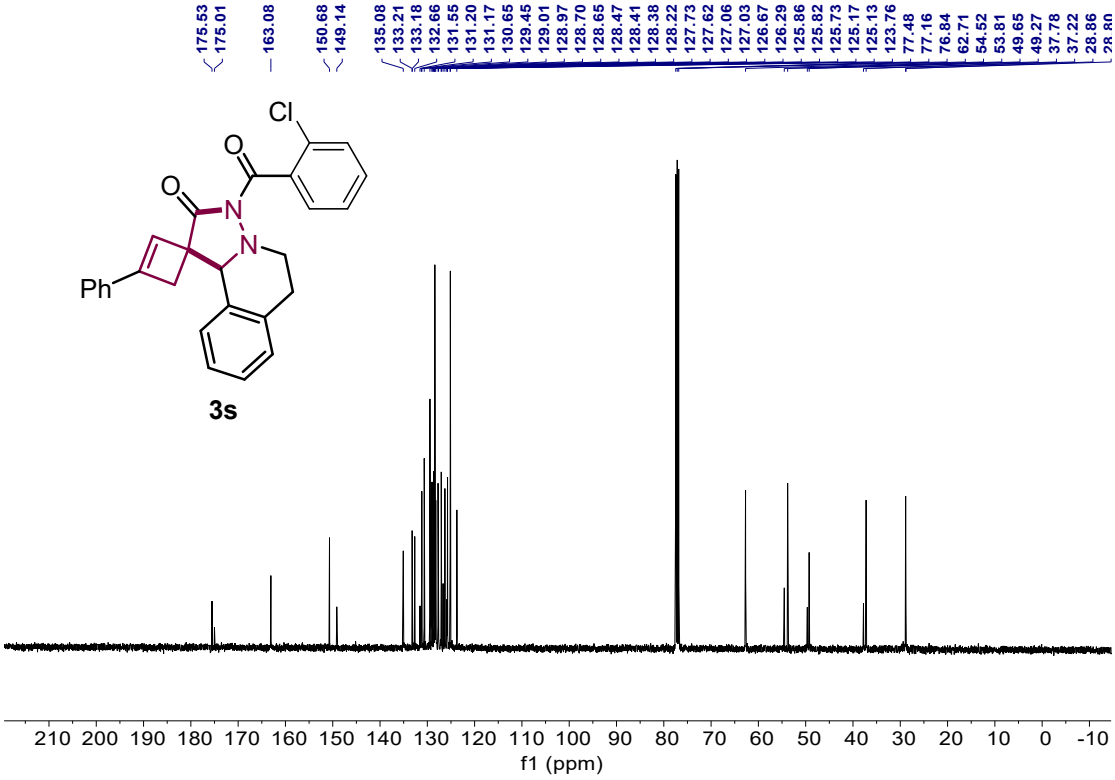
^{13}C NMR (100 MHz, Chloroform-*d*) of **3r**



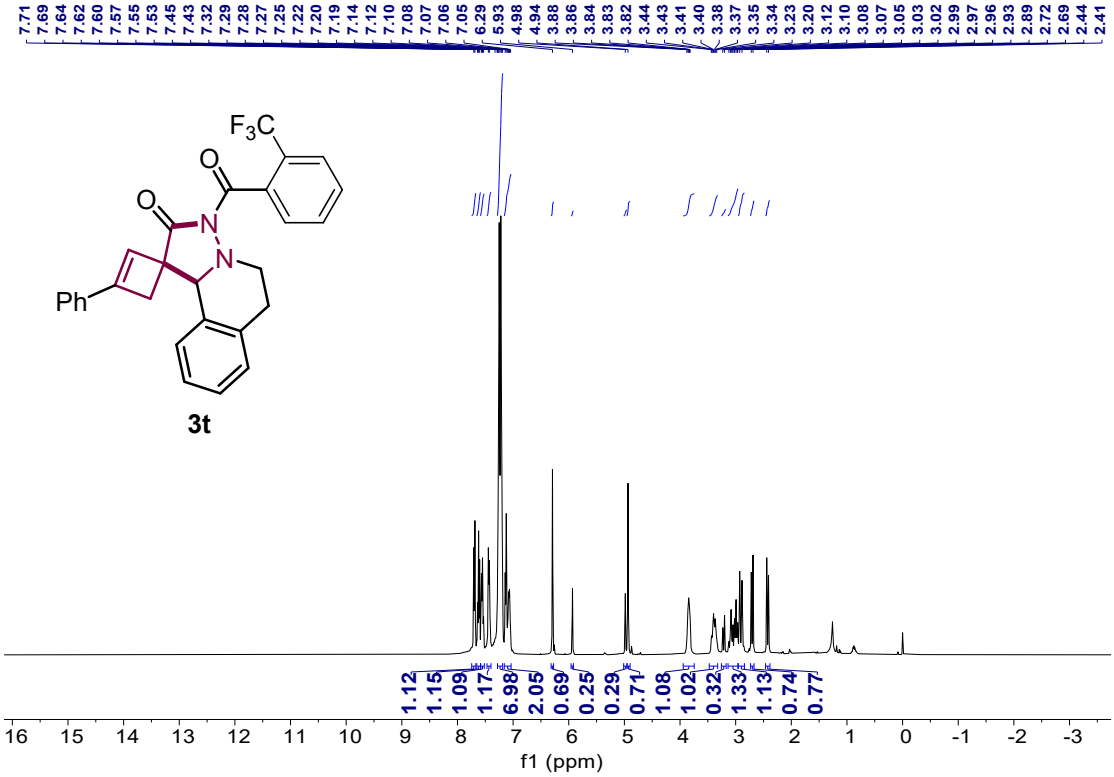
^{1}H NMR (400 MHz, Chloroform-*d*) of **3s**



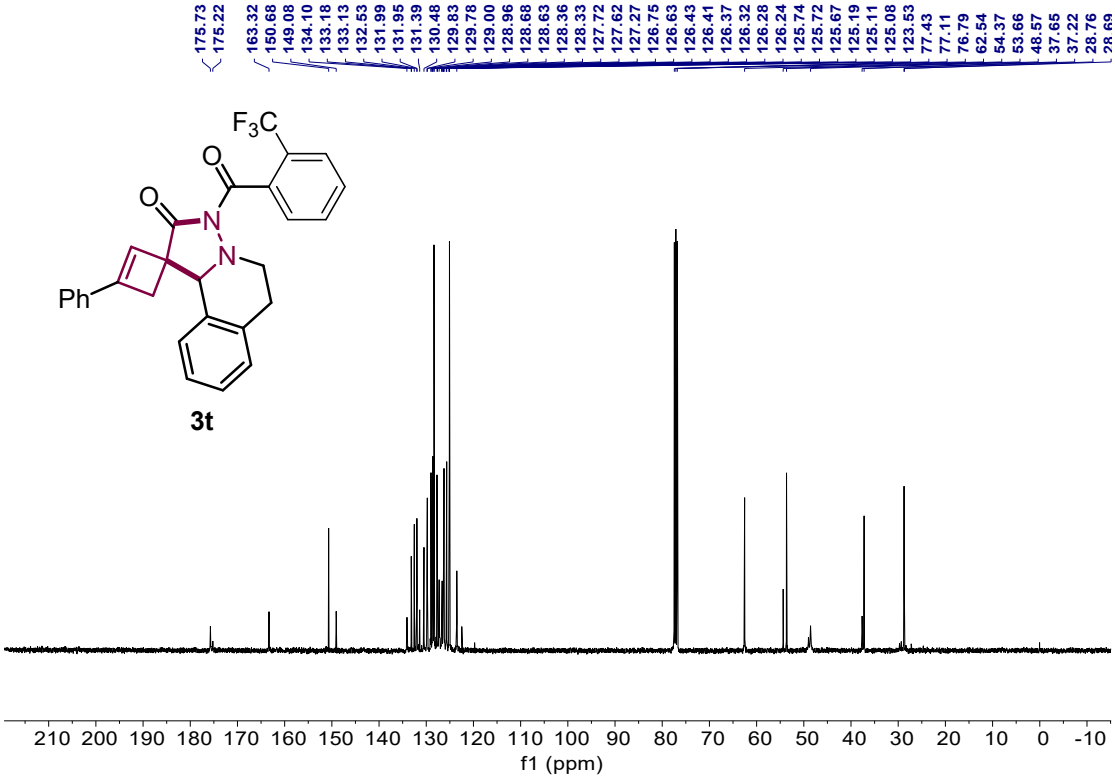
^{13}C NMR (100 MHz, Chloroform-*d*) of **3s**



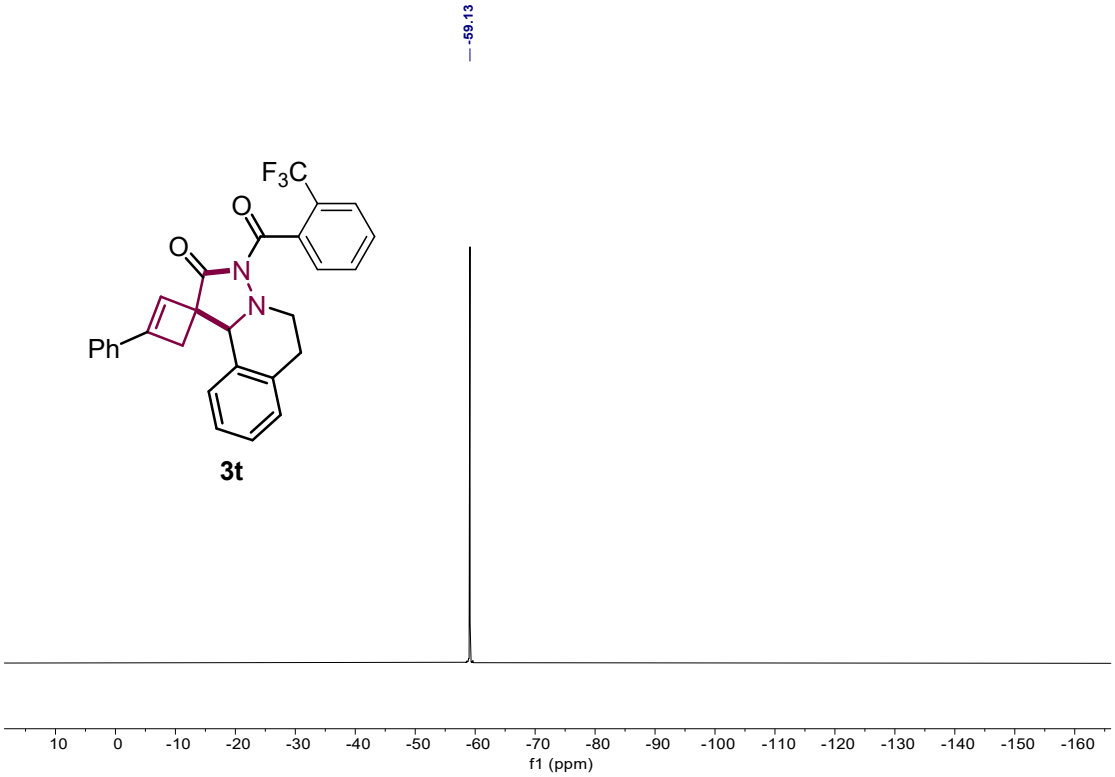
^{1}H NMR (400 MHz, Chloroform-*d*) of **3t**



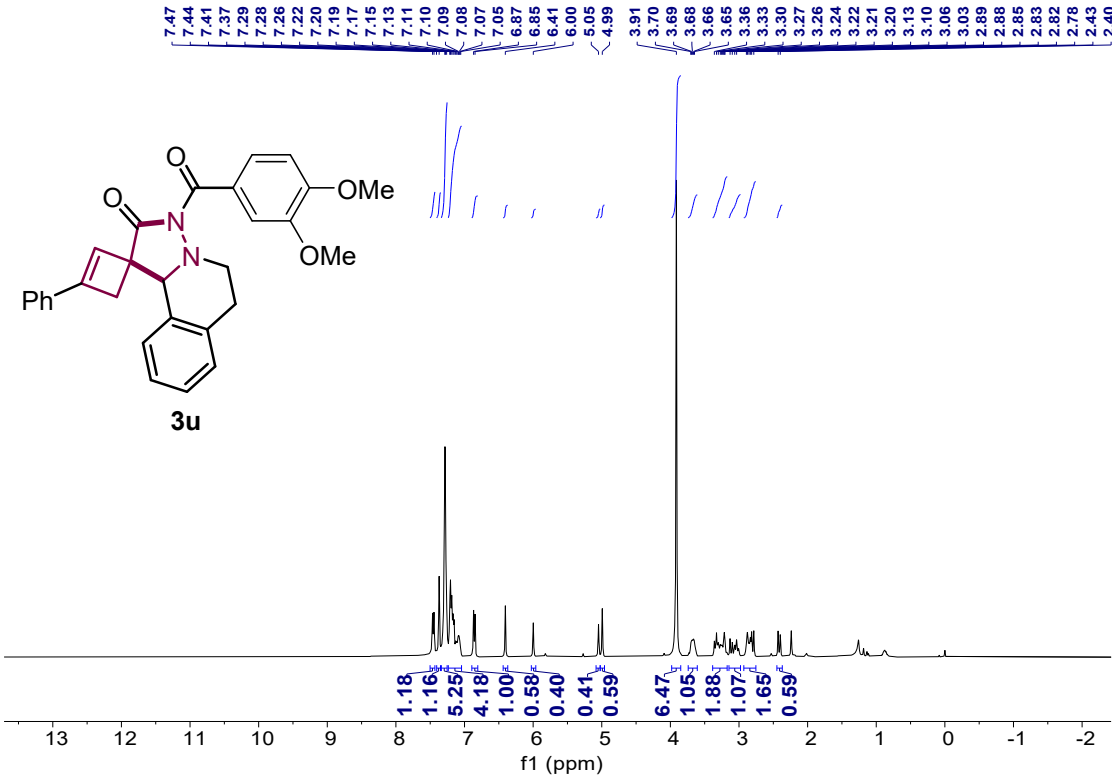
^{13}C NMR (100 MHz, Chloroform-*d*) of **3t**



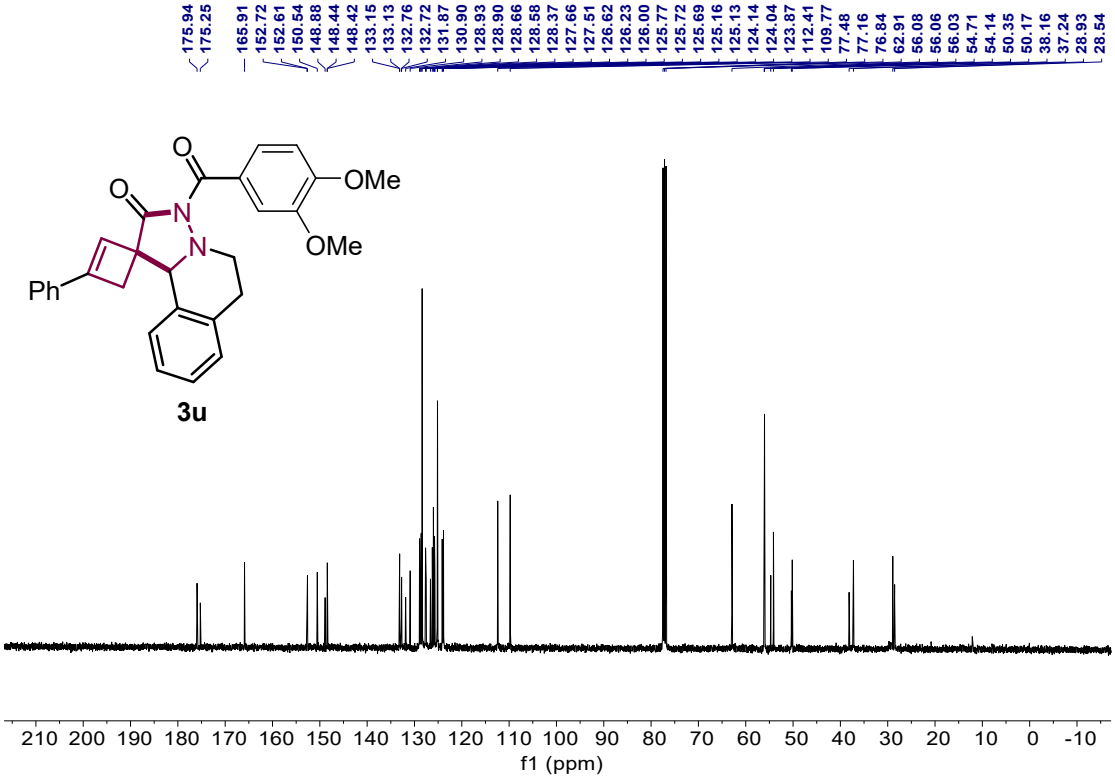
^{19}F NMR (376 MHz, Chloroform-*d*) of **3t**



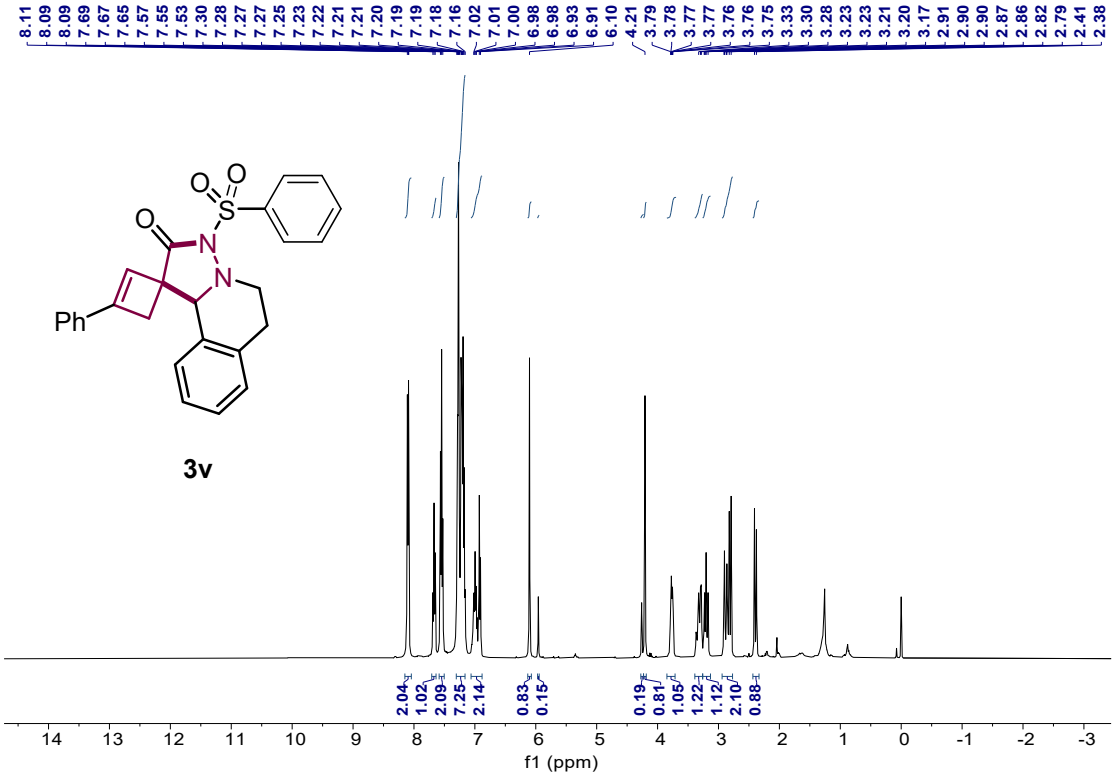
^{1}H NMR (400 MHz, Chloroform-*d*) of **3u**



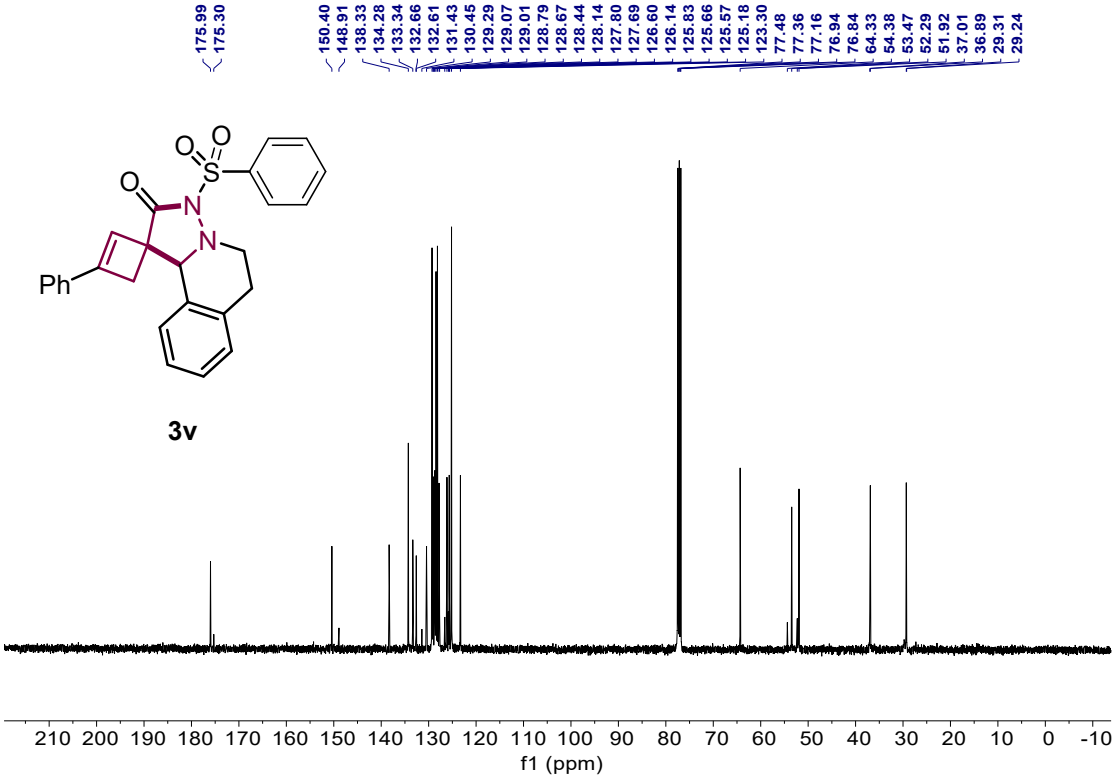
^{13}C NMR (100 MHz, Chloroform-*d*) of **3u**



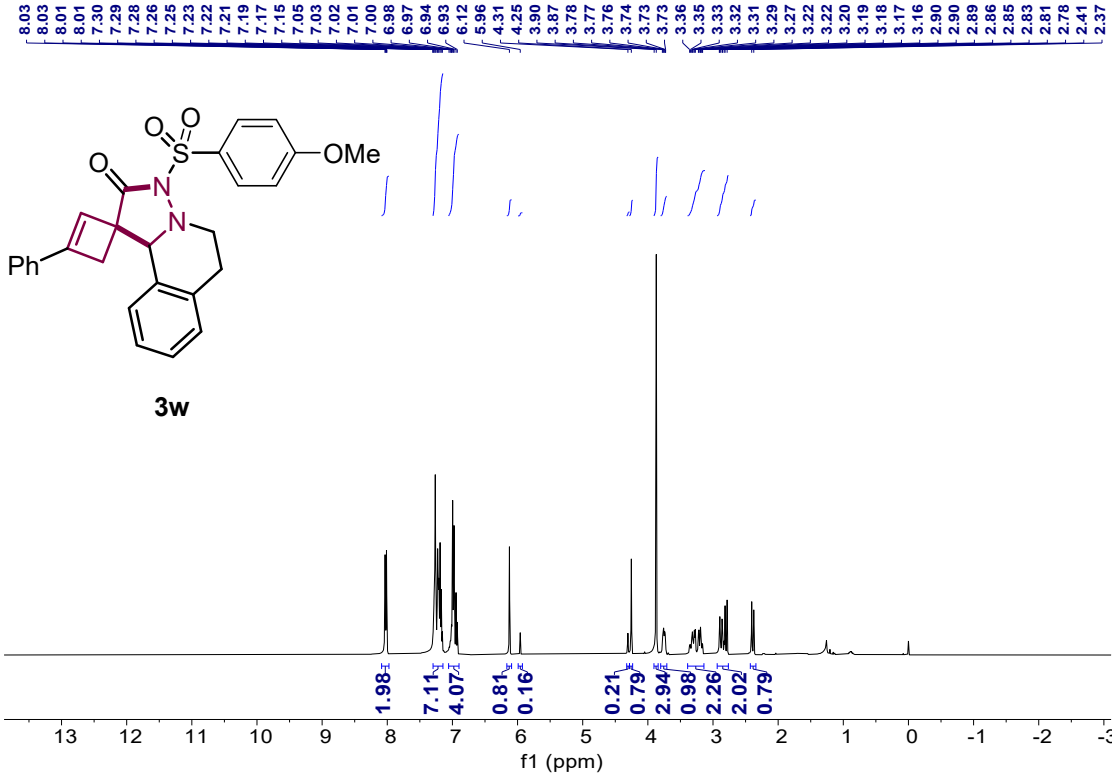
^{1}H NMR (400 MHz, Chloroform-*d*) of **3v**



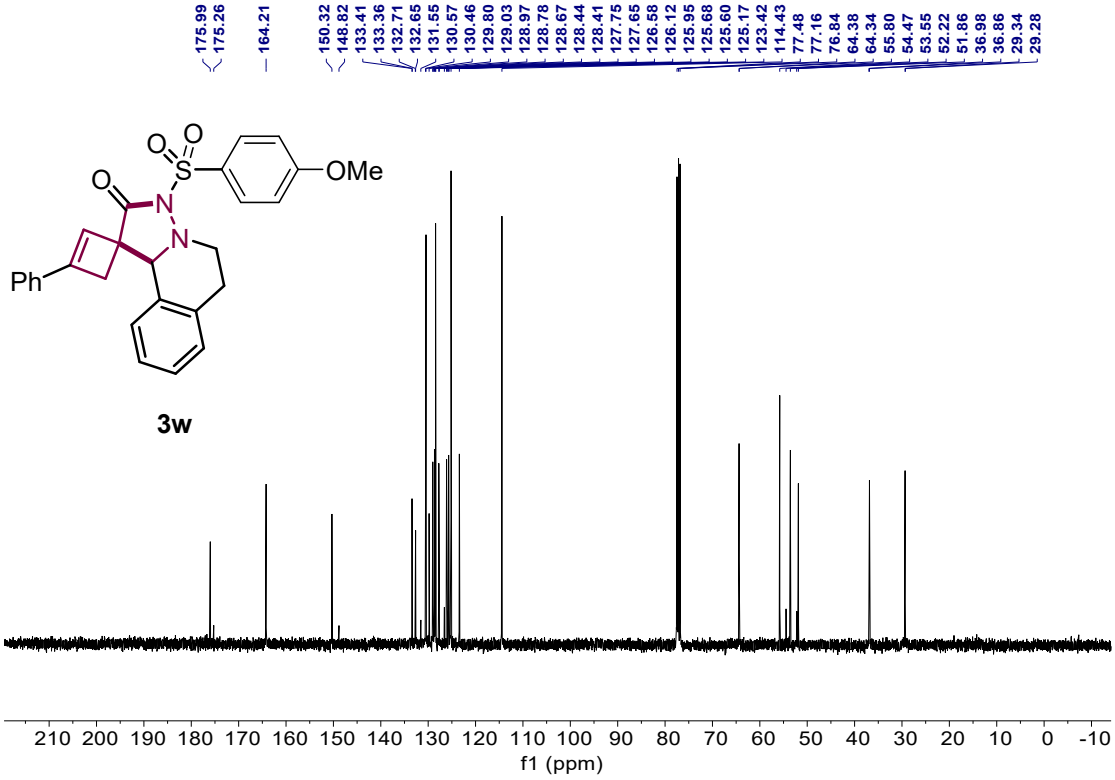
^{13}C NMR (100 MHz, Chloroform-*d*) of **3v**



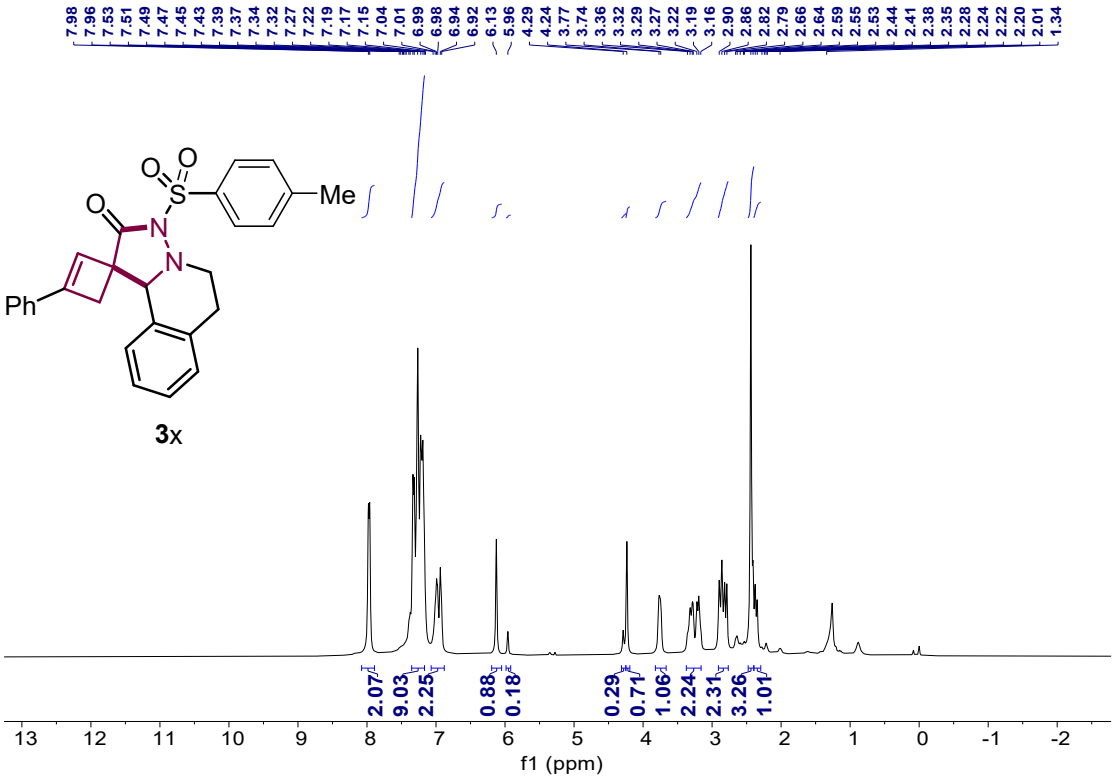
^{1}H NMR (400 MHz, Chloroform-*d*) of **3w**



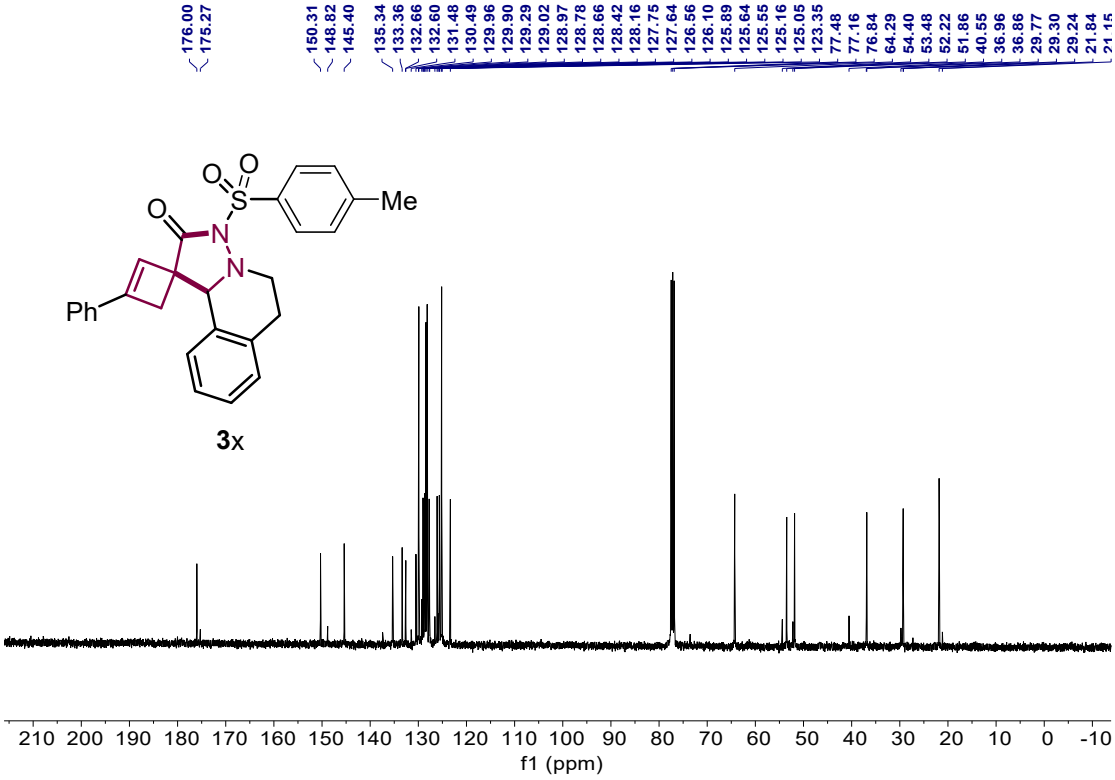
^{13}C NMR (100 MHz, Chloroform-*d*) of **3w**



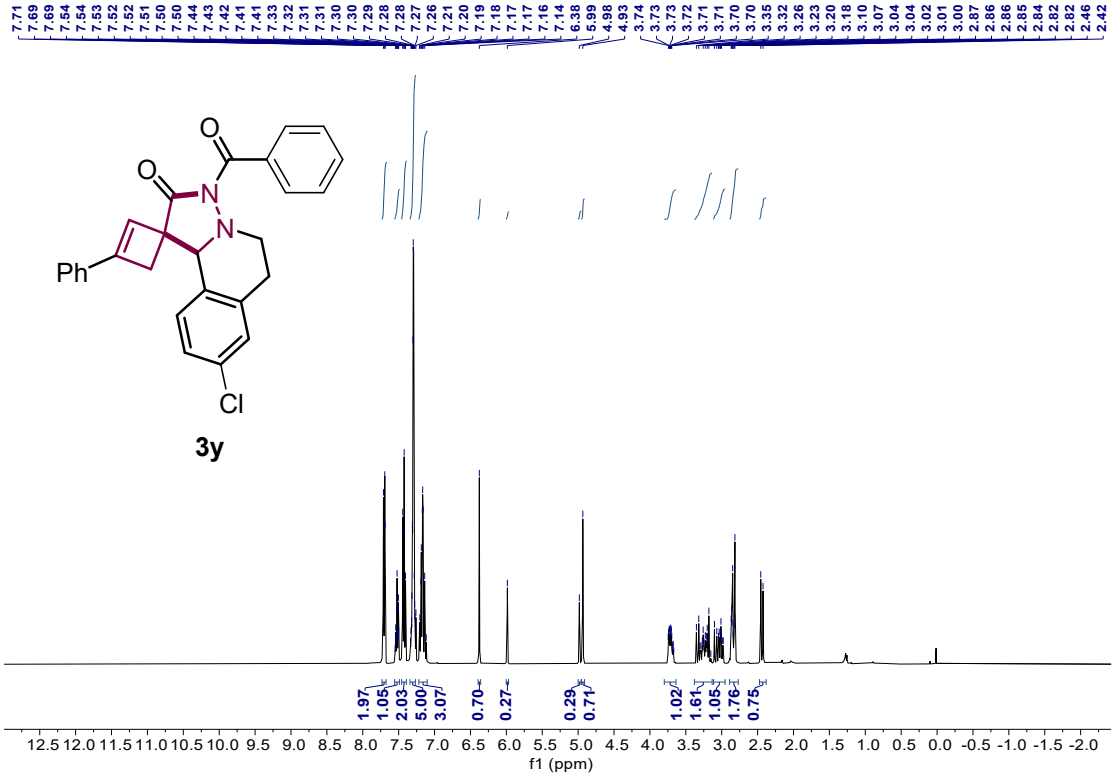
^{1}H NMR (400 MHz, Chloroform-*d*) of **3x**



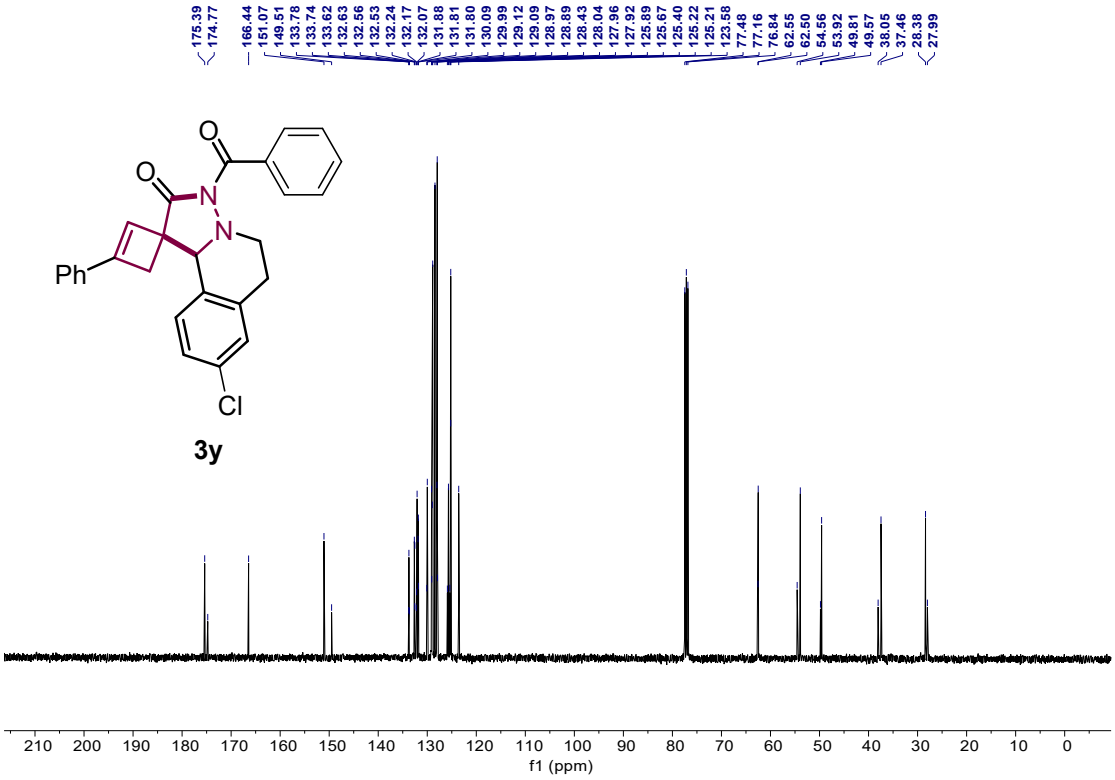
^{13}C NMR (100 MHz, Chloroform-*d*) of **3x**



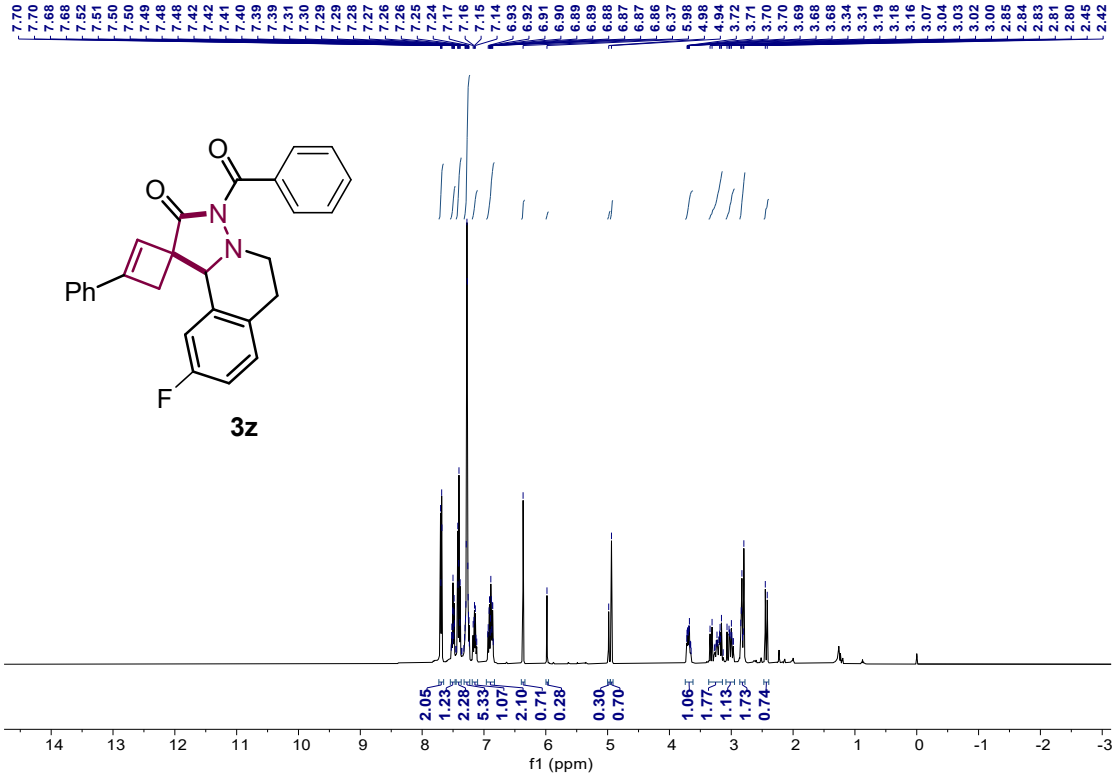
^{1}H NMR (400 MHz, Chloroform-*d*) of **3y**



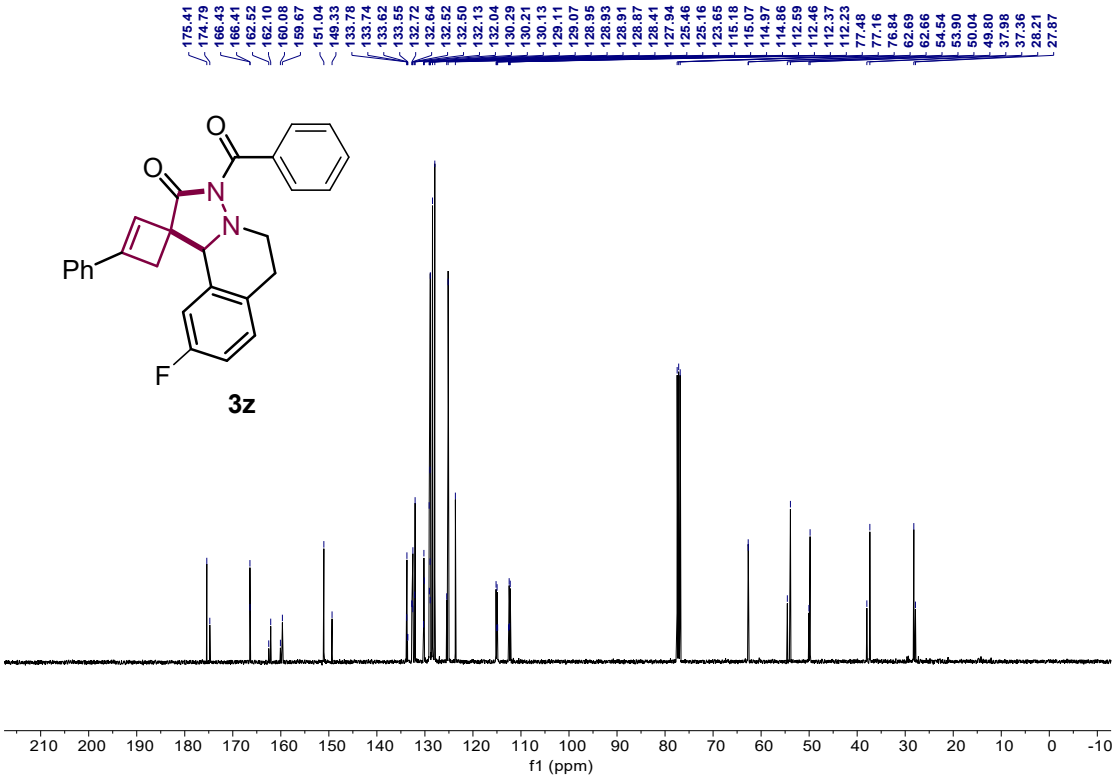
^{13}C NMR (100 MHz, Chloroform-*d*) of **3y**



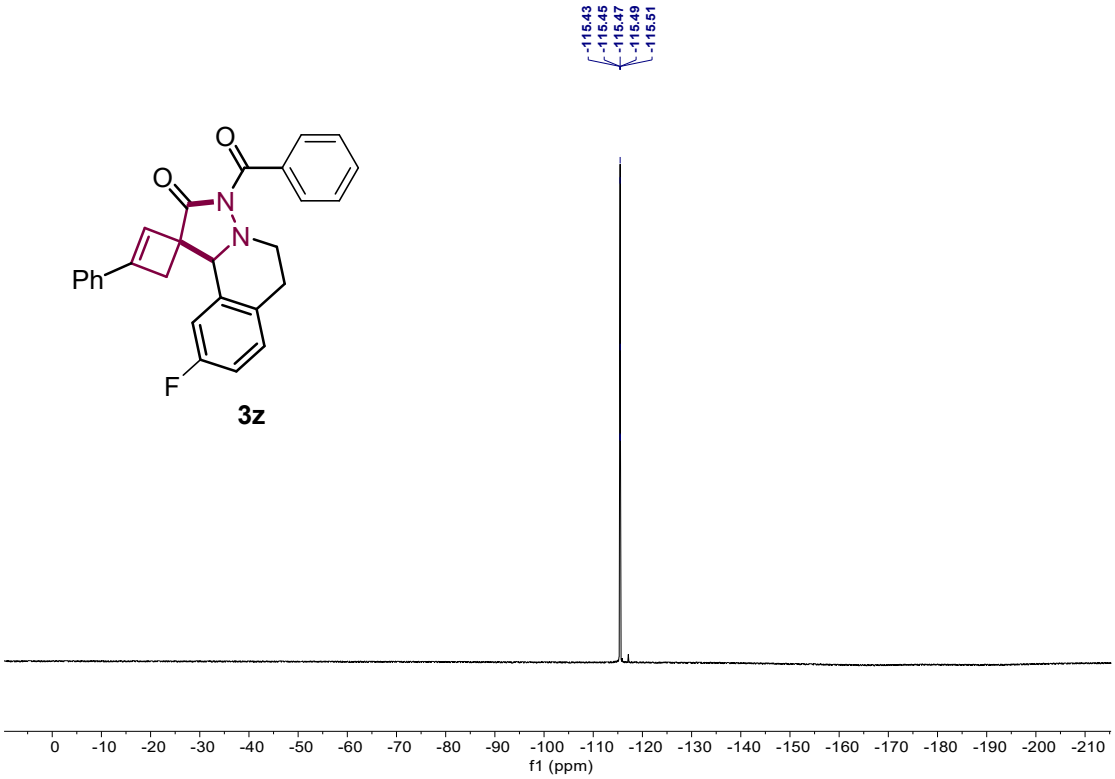
^{1}H NMR (400 MHz, Chloroform-*d*) of **3z**



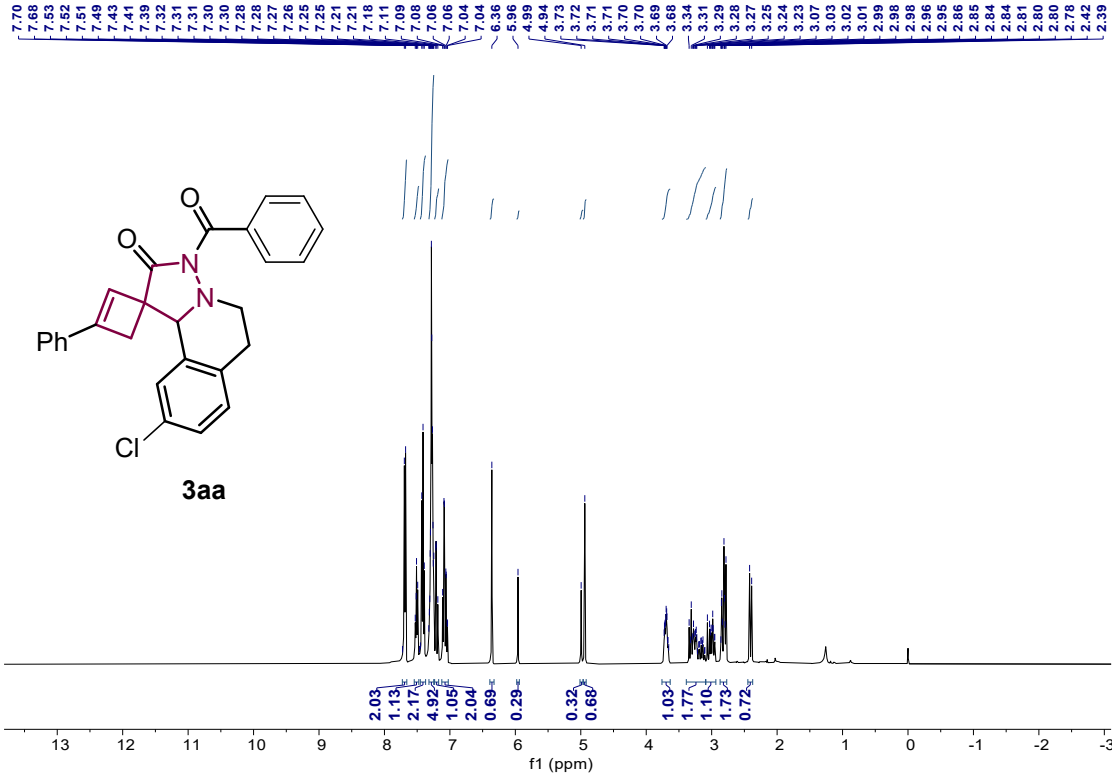
^{13}C NMR (100 MHz, Chloroform-*d*) of **3z**



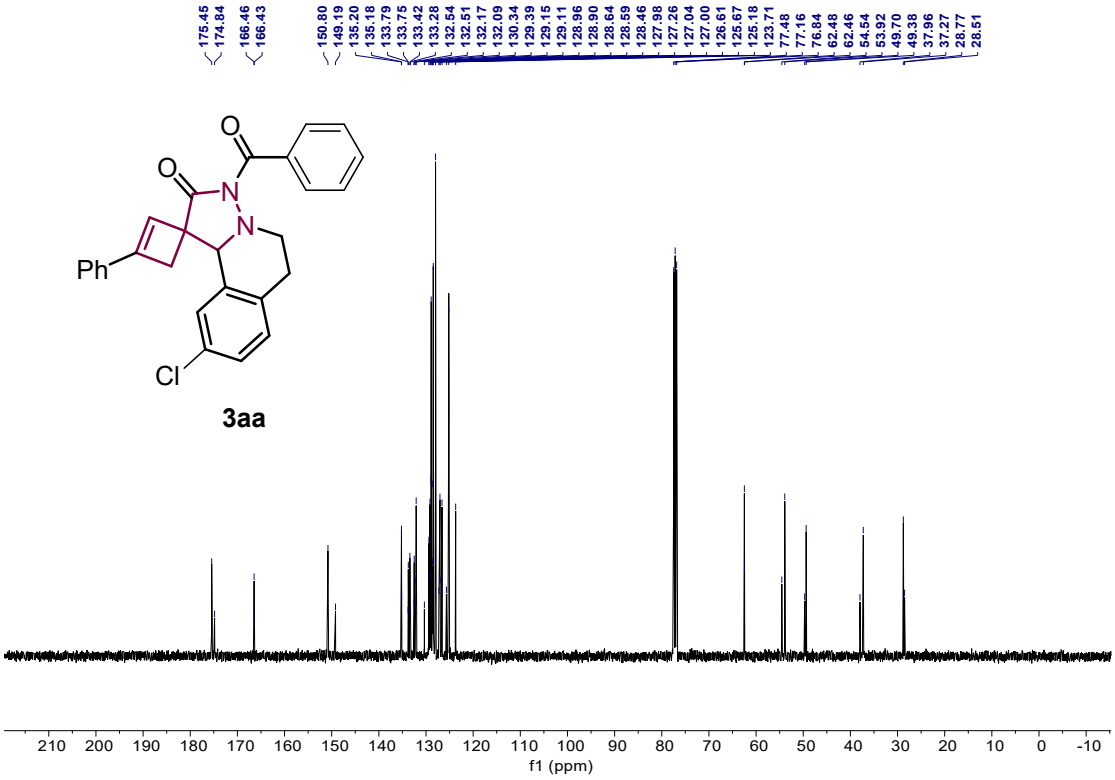
^{19}F NMR (376 MHz, Chloroform-*d*) of **3z**



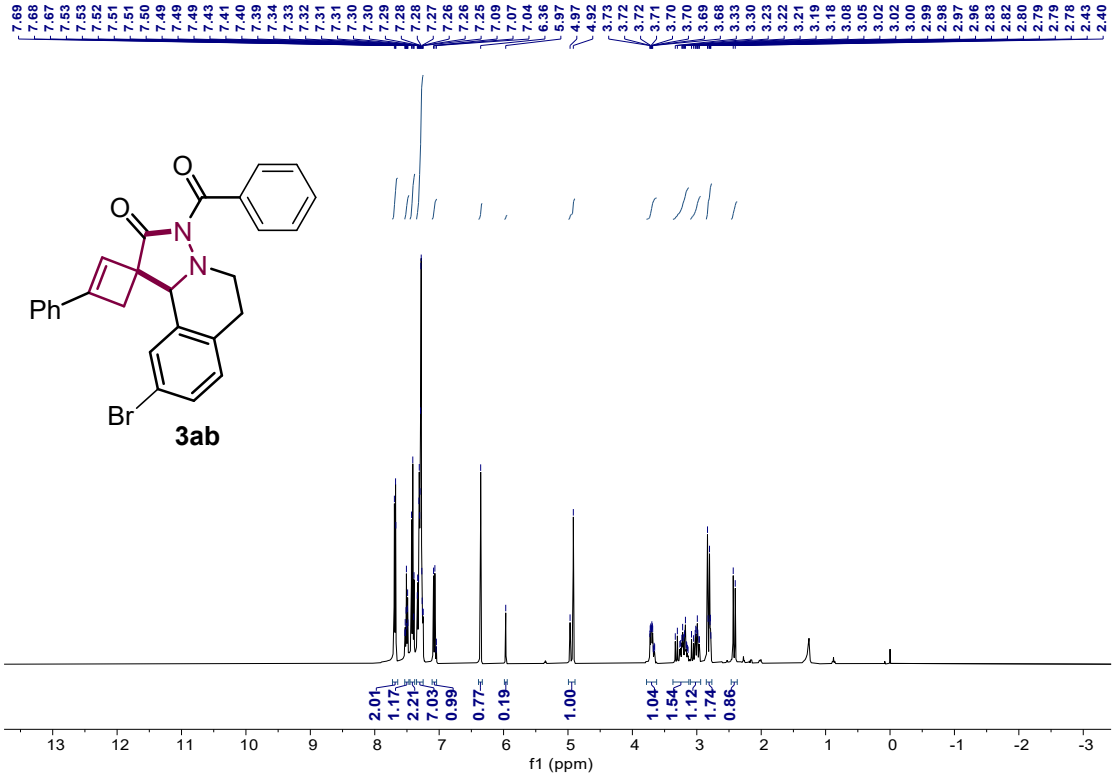
^{1}H NMR (400 MHz, Chloroform-*d*) of **3aa**



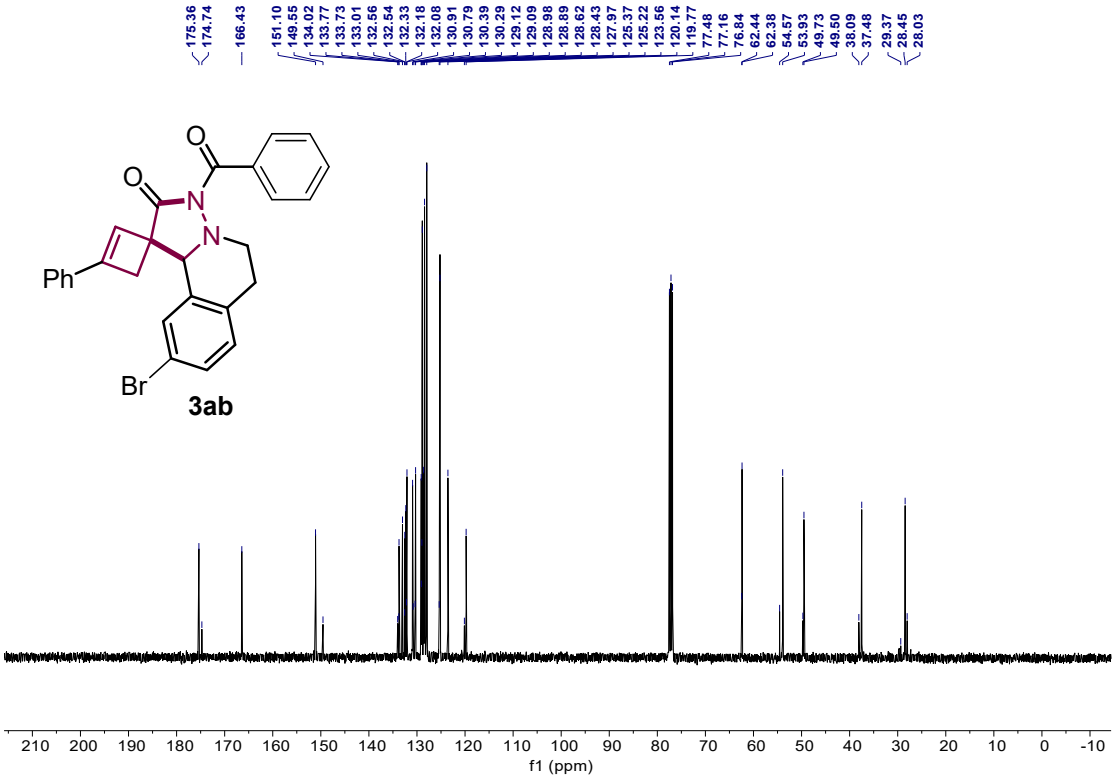
^{13}C NMR (100 MHz, Chloroform-*d*) of **3aa**



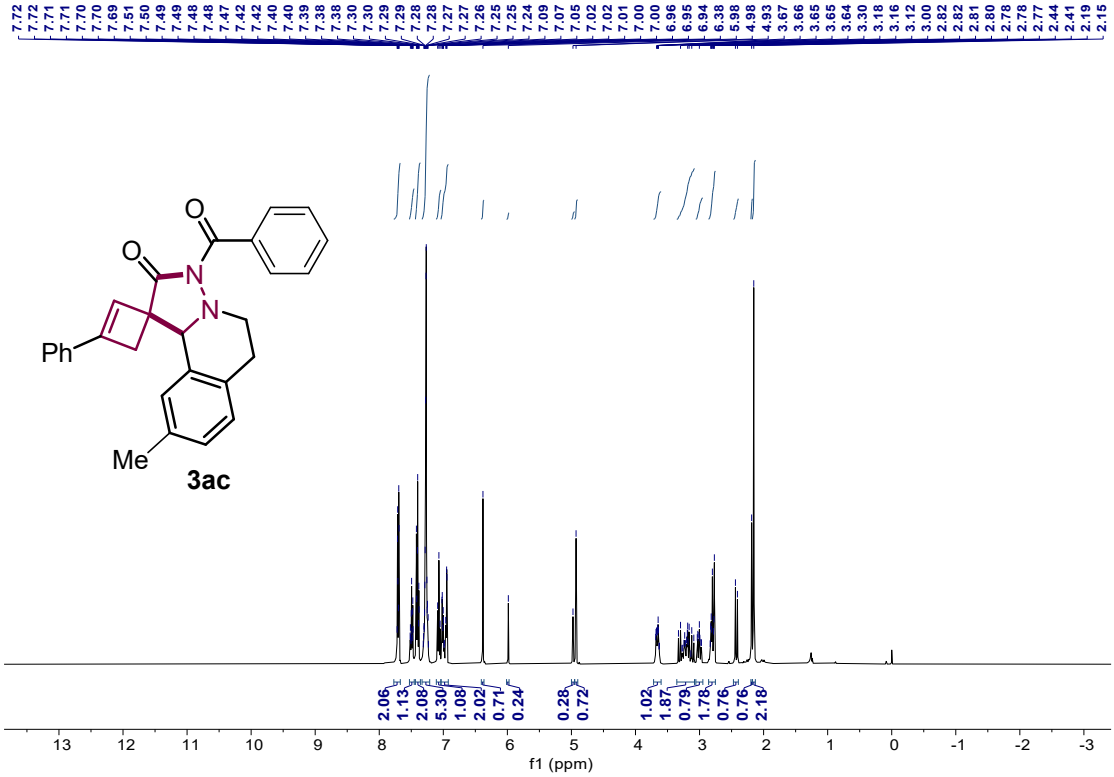
^{1}H NMR (400 MHz, Chloroform-*d*) of **3ab**



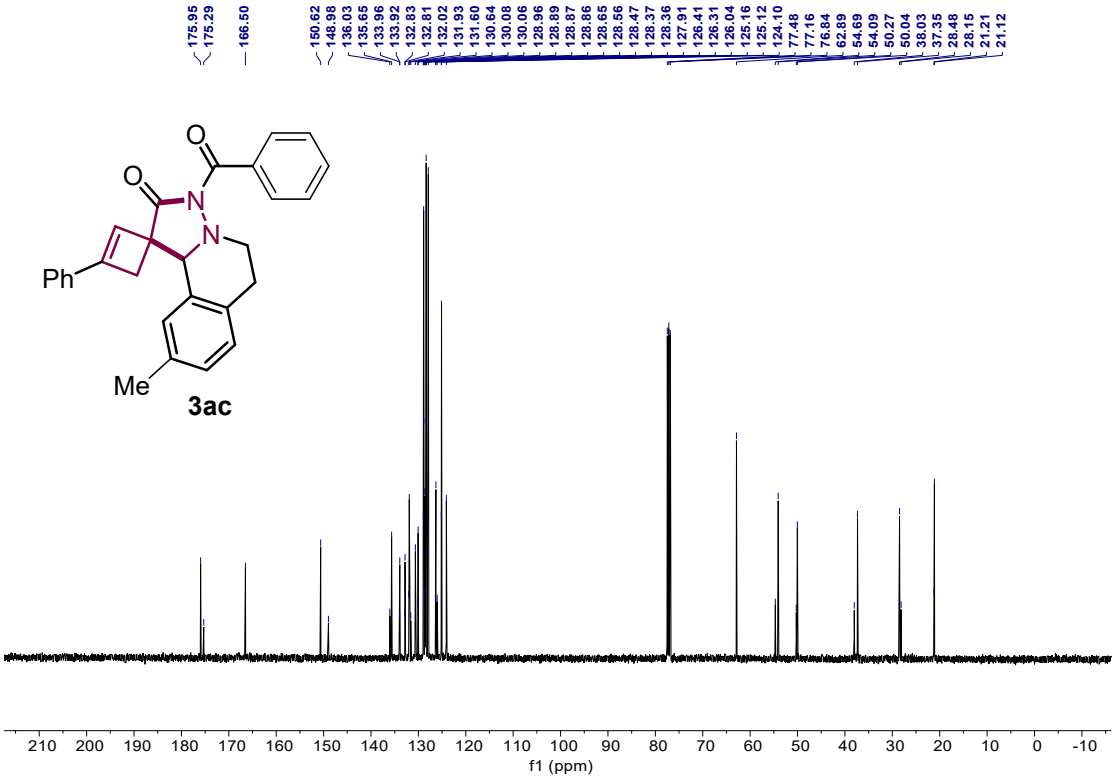
^{13}C NMR (100 MHz, Chloroform-*d*) of **3ab**



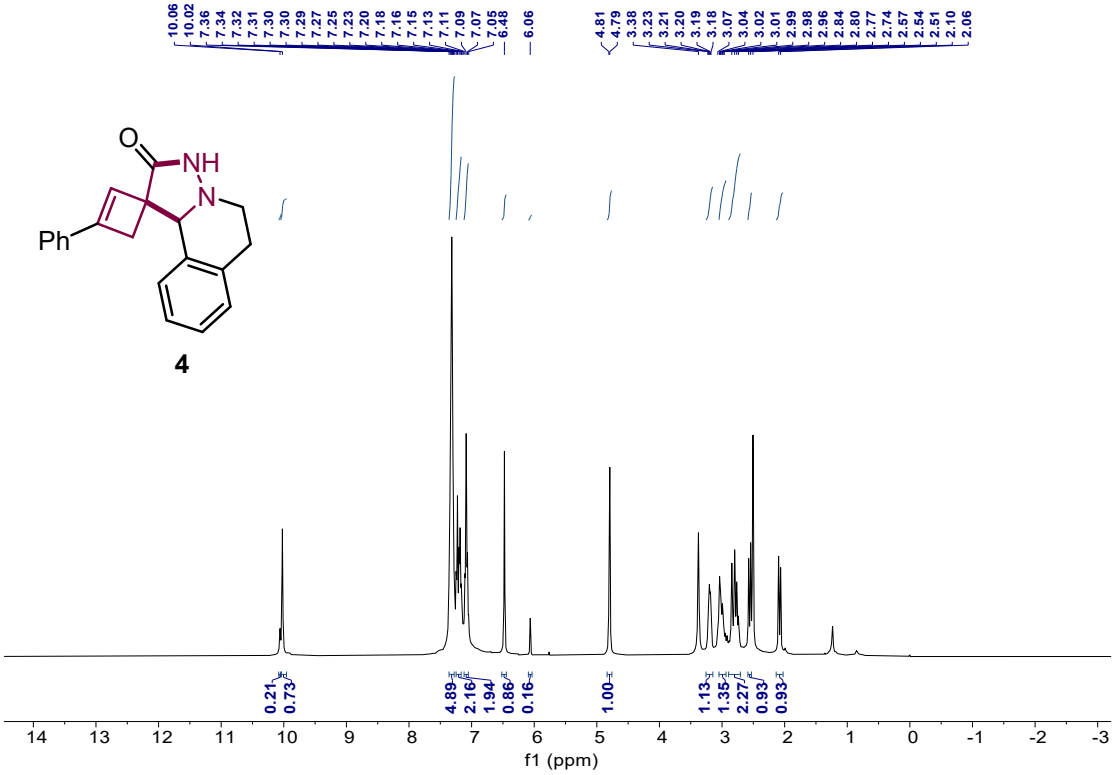
^{1}H NMR (400 MHz, Chloroform-*d*) of **3ac**



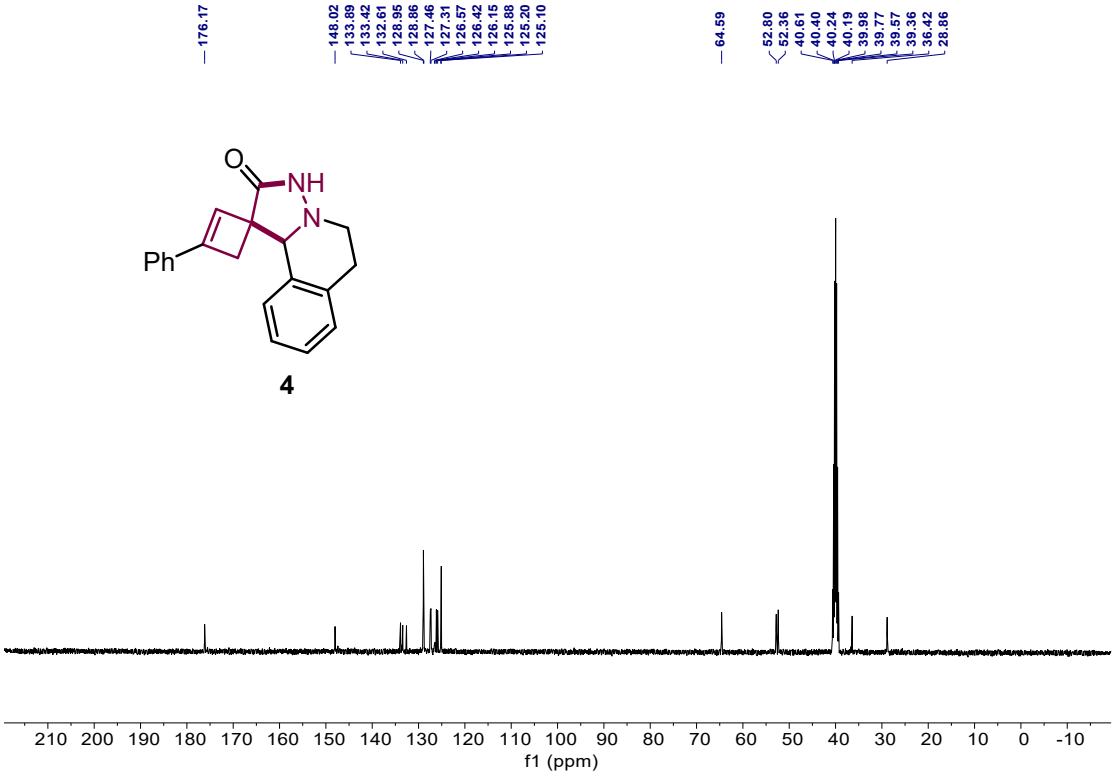
^{13}C NMR (100 MHz, Chloroform-*d*) of **3ac**



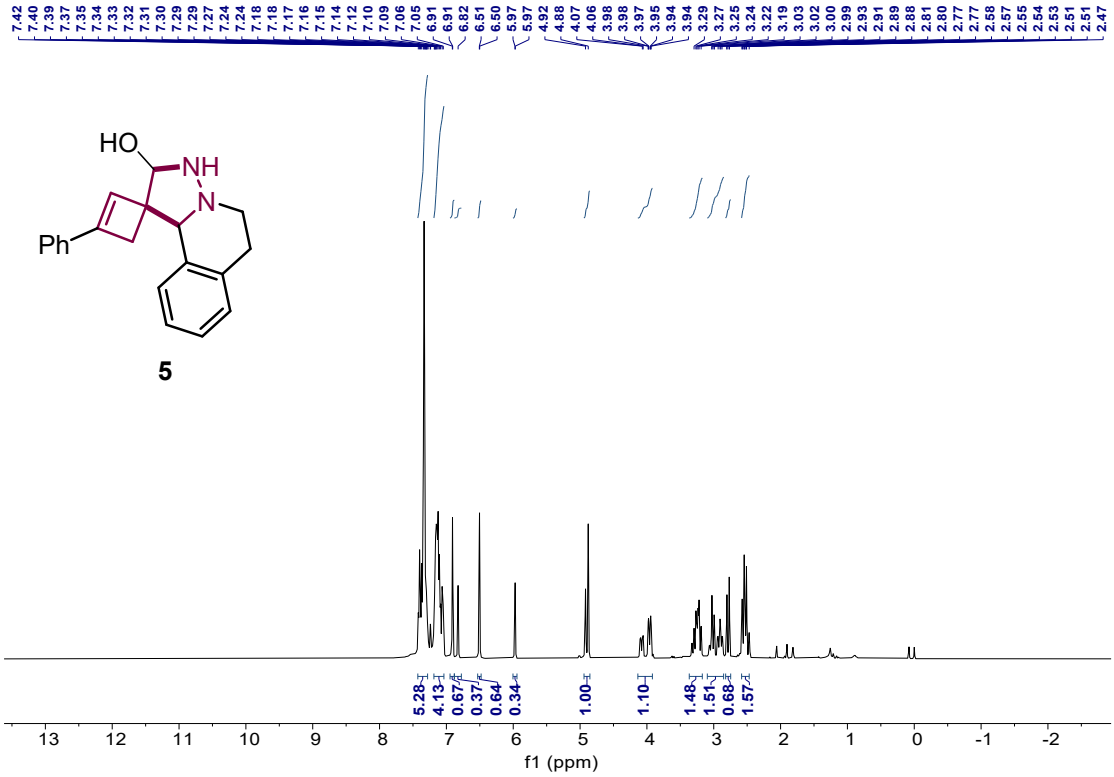
^{1}H NMR (400 MHz, DMSO-d_6)) of **4**



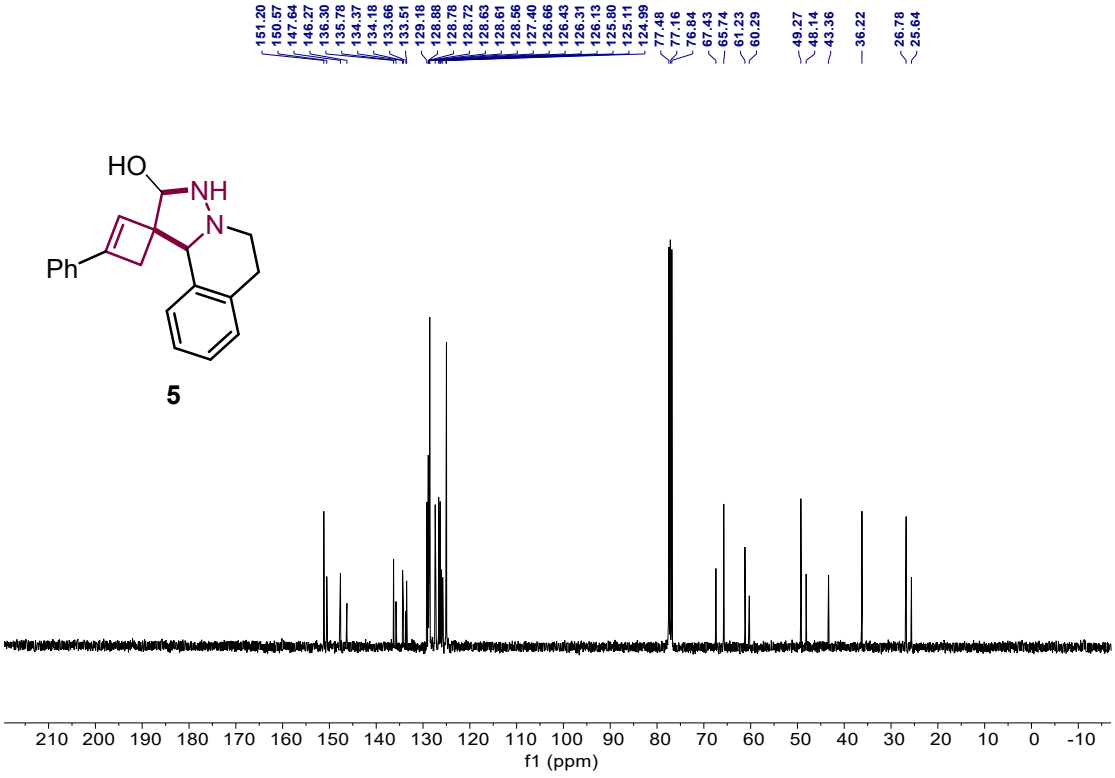
^{13}C NMR (100 MHz, DMSO-d_6)) of **4**



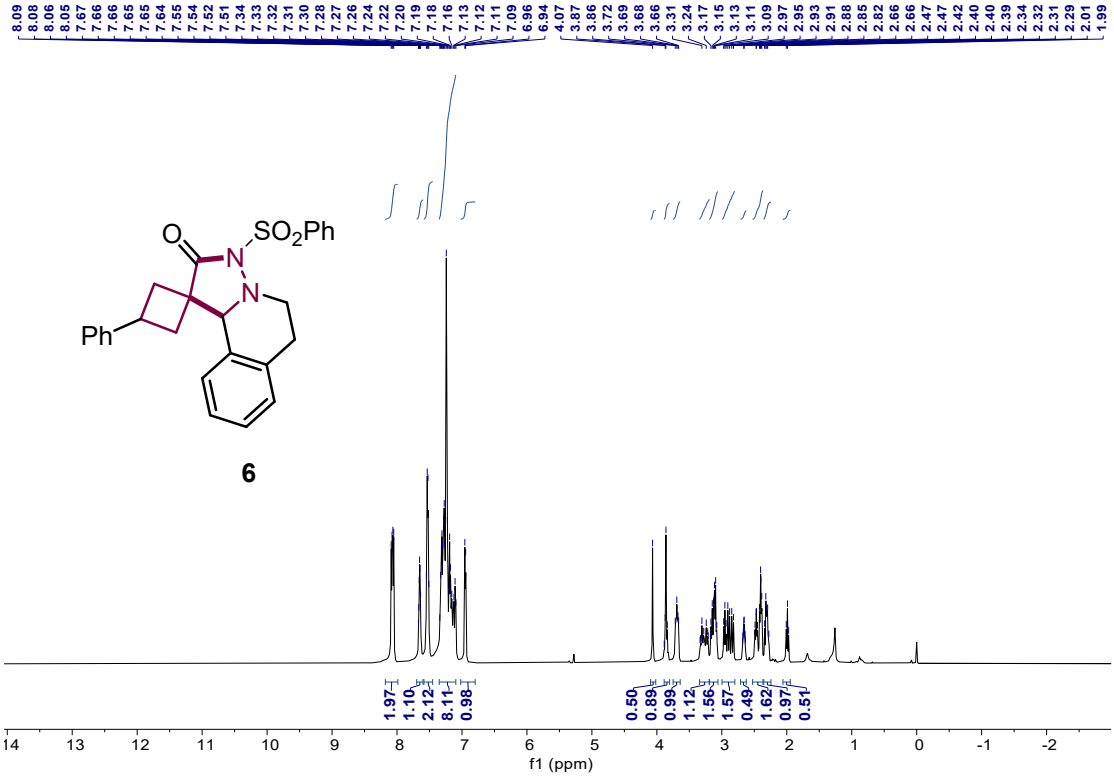
^{1}H NMR (400 MHz, Chloroform-*d*) of **5**



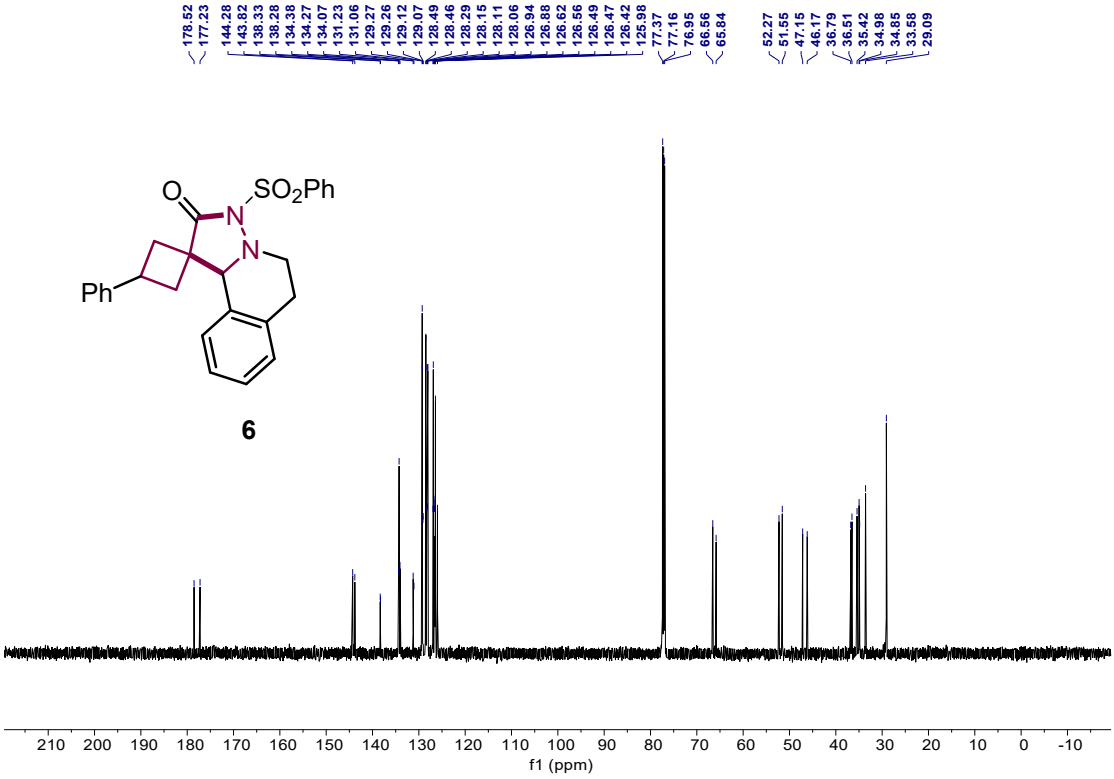
^{13}C NMR (100 MHz, Chloroform-*d*) of **5**



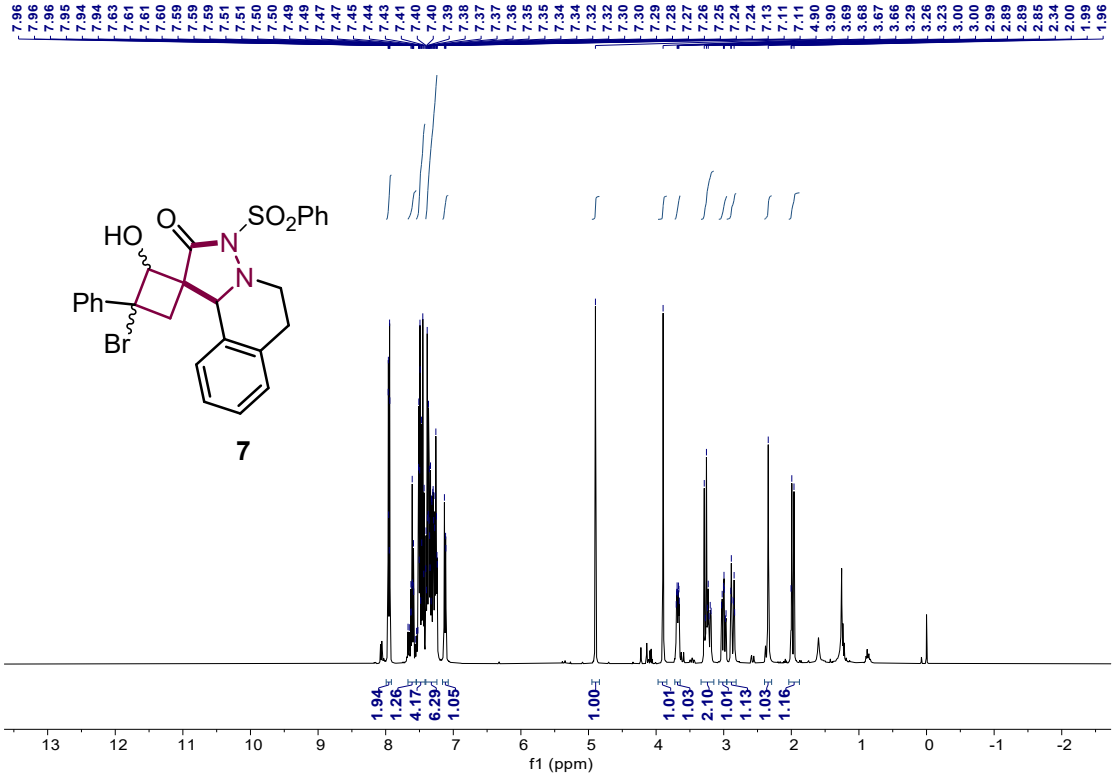
^{1}H NMR (600 MHz, Chloroform-*d*) of **6**



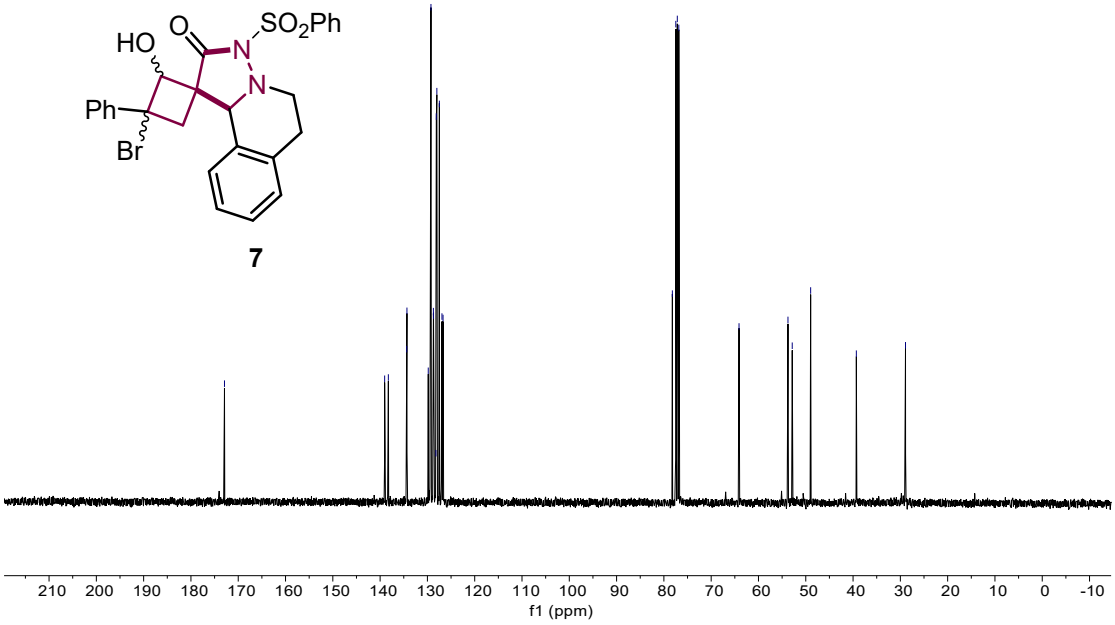
^{13}C NMR (151 MHz, Chloroform-*d*) of **6**



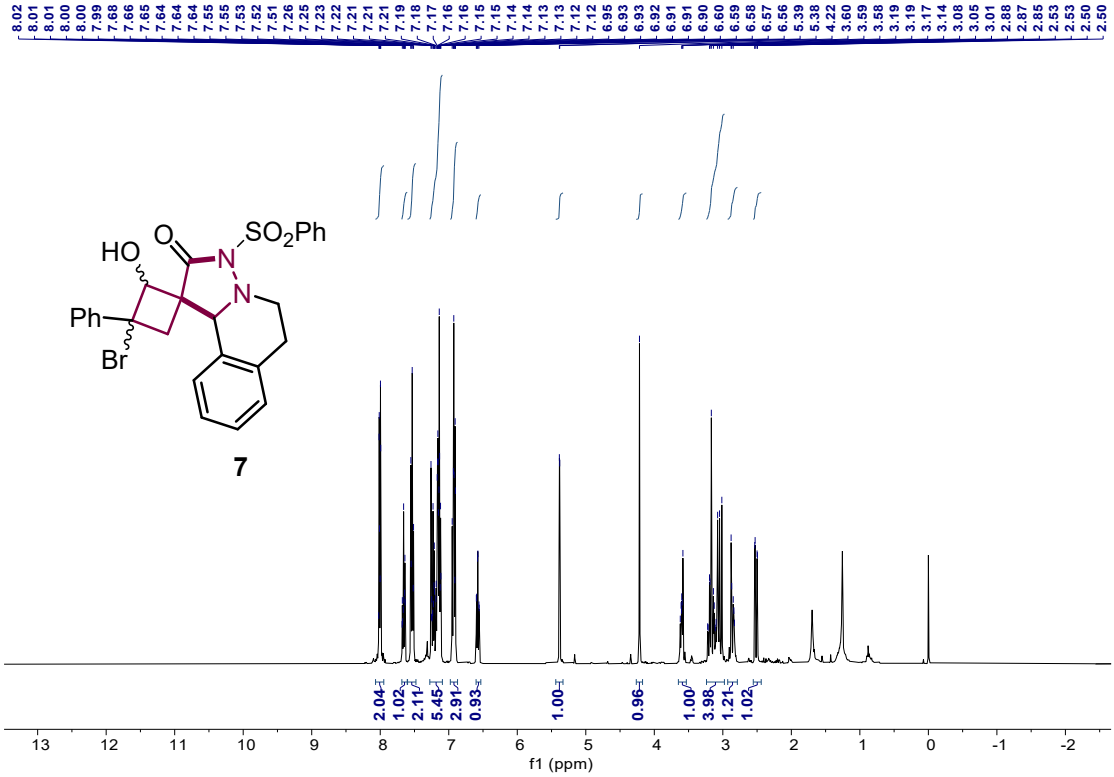
^{1}H NMR (400 MHz, Chloroform-*d*) of **7** (major)



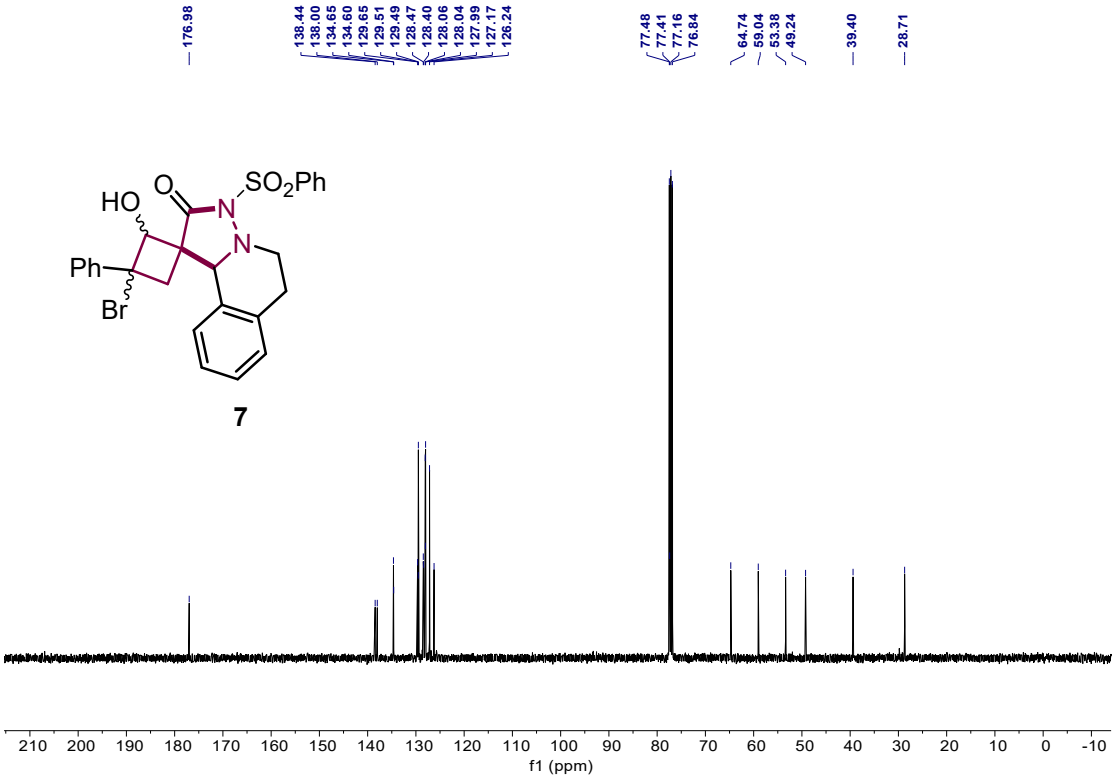
^{13}C NMR (100 MHz, Chloroform-*d*) of **7**(major)



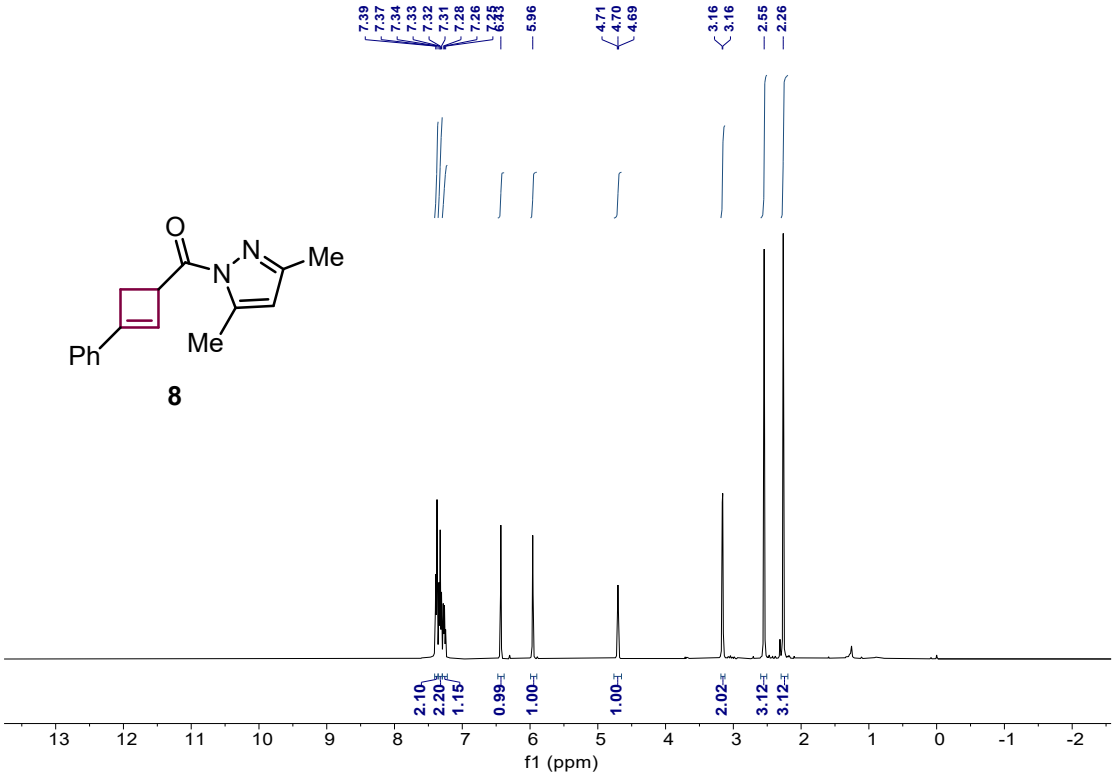
^{1}H NMR (400 MHz, Chloroform-*d*) of **7** (minor)



^{13}C NMR (100 MHz, Chloroform-*d*) of **7**(minor)

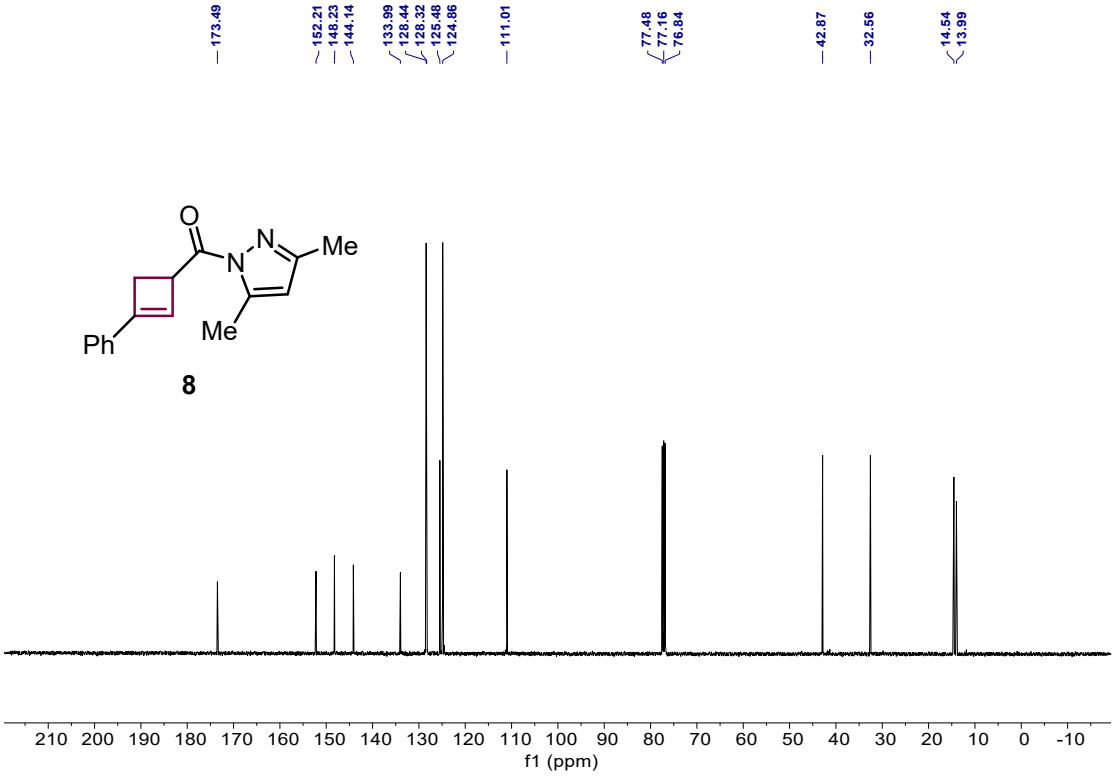


^{1}H NMR (400 MHz, Chloroform-*d*) of **8**



8

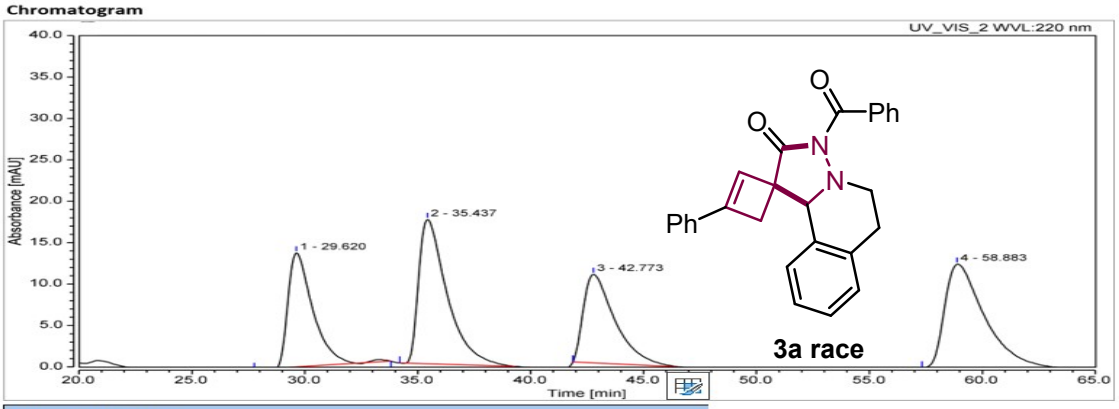
^{13}C NMR (100 MHz, Chloroform-*d*) of **8**



8

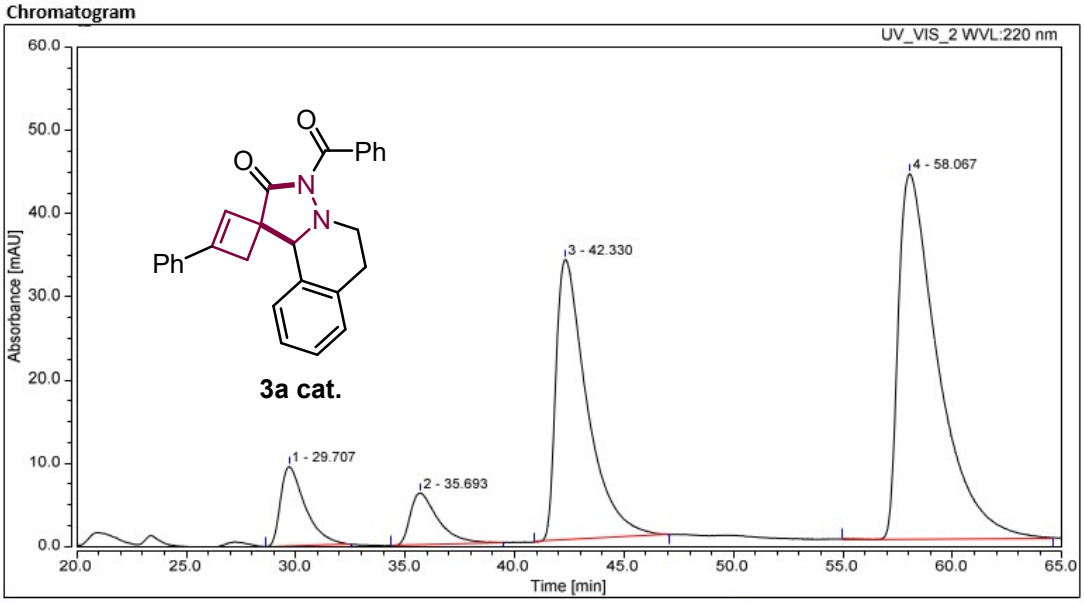
10. Copies of HPLC spectra of the product 3a

HPLC spectra of **3a**



Integration Results

No.	Retention Time min	Area mAU*min	Relative Area %	Relative Height %
1	29.620	17.433	20.32	25.29
2	35.437	25.338	29.54	32.00
3	42.773	17.281	20.15	19.65
4	58.883	25.720	29.99	23.06
Total:		**85.772**	**100.00**	**100.00**



Integration Results

No.	Retention Time min	Area mAU*min	Relative Area %	Relative Height %
1	29.707	12.434	7.38	10.20
2	35.693	9.147	5.43	6.65
3	42.330	55.491	32.93	36.17
4	58.067	91.424	54.26	46.98
Total:		**168.496**	**100.00**	**100.00**