Supporting Information

Synthesis of spirocyclic oxazole derivatives from 2-arylidene cycloalkanones and α-halohydroxamates

Huiyang Wan,[a] Shuangshuang Xia,[a] Xinghua Liu,[a] Yongchan Jian,[a] Yuanyuan An,*[a] Yubin Wang*[a]

[a] *School of Pharmaceutical Sciences, Nanjing Tech University, Nanjing 211816, P.R. China*

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1. General Information

1) Reagents and Solvents: All solvents were purified and dried according to standard methods. PE refers to petroleum ether (b.p. 60~90 °C) and EA refers to ethyl acetate. 2-Arylidene cycloalkanones[1] and α-halohydroxamates[2] were prepared according to reported procedures. Unless otherwise indicated, all other reagents and solvents were obtained from commercial suppliers and used without further purification.

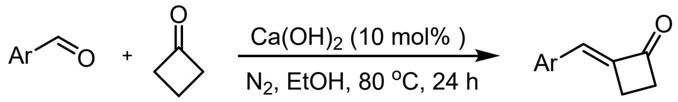
2) Chromatography: Flash column chromatography was carried out using commercially available 300-400 mesh under pressure and conducted by eluting with PE/EA, which are listed as volume/volume ratios.

3) Data Collection: ^{1}H, ^{13}C and ^{19}F NMR spectra were collected on BRUKER AVANCE III 400 spectrometer (^{1}H NMR 400 MHz, ^{13}C NMR 100 MHz, ^{19}F NMR 376 MHz) using $CDCl_3$ as solvent. Chemical shifts of ^{1}H NMR were recorded in parts per million (ppm, δ) relative to tetramethylsilane (δ = 0.00 ppm) with the solvent resonance as an internal standard ($CDCl_3$, δ = 7.26 ppm). Data are reported as follows: chemical shift in ppm (δ), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, brs = broad singlet, m = multiplet), coupling constant (Hz), and integration. Chemical shifts of ^{13}C NMR were reported in ppm with the solvent as the internal standard ($CDCl_3$, δ = 77.0 ppm). High Resolution Mass measurement was performed on Waters Acquity UPLC/XEVO G2-XS QTOF with electron spray ionization (ESI) as the ion source.

2. Experimental Procedures

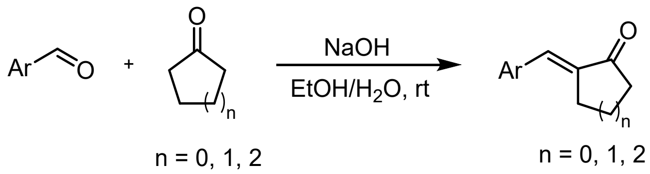
1) General Procedures for the Preparation of *exo*-α,β-unsaturated ketone.[1-2]

(a) Method A



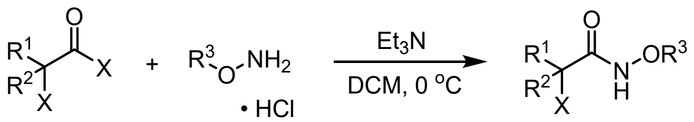
To a 50 mL round-bottomed flask was added aldehyde (10.0 mmol, 1.0 equiv), cyclobutanone (30.0 mmol, 3.0 equiv), 10 mol% of $Ca(OH)_2$ and anhydrous EtOH (20 mL) sequentially. The reaction mixture was heated at 80 °C under N_2 atmosphere for 24 hours. The resulting mixture was then evaporated in vacuo to afford crude product, which was further purified by chromatography on silica gel (PE/EA = 40/1) to afford 2-arylidene cyclobutanones in 55% yield.

b) Method B



To a 50 mL round-bottomed flask was added aldehyde (10.0 mmol, 1.0 equiv), ketone (20.0 mmol, 2.0 equiv) and anhydrous EtOH (20 mL), then a solution of NaOH (12.0 mmol, 1.2 equiv.) in $EtOH/H_2O$ (1:1) was added. The mixture was stirred at room temperature for 12 hours. Thereafter, the mixture was carefully quenched with HCl (4 M) until neutral pH was reached. The resulting mixture was extracted with DCM, washed with a saturated aqueous solution of $NaHCO_3$, brine, dried over Na_2SO_4, and evaporated in vacuo. The residue was purified by chromatography on silica gel (PE/EA = 40/1) to afford the desired 2-arylidene cycloalkanones in 89% yield.

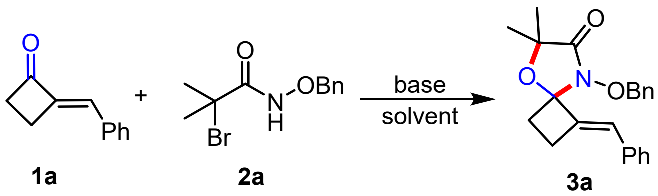
2) General Procedures for the Preparation of α-Halohydroxamates.[3]



To a suspension of the O-benzyloxyamine hydrochloride and triethylamine in

DCM (0.25 M), α-haloacid halide was added dropwise at 0°C. The reaction mixture was stirred at this temperature until complete consumption of starting material (detected by TLC). The mixture was warmed to room temperature and quenched with water. The organic phase was washed with water, brine, dried over Na_2SO_4, filtered and evaporated in vacuo. The residue was purified by chromatography on silica gel (PE/EA = 8/1) to afford the desired α-halohydroxamates in 88% yield.

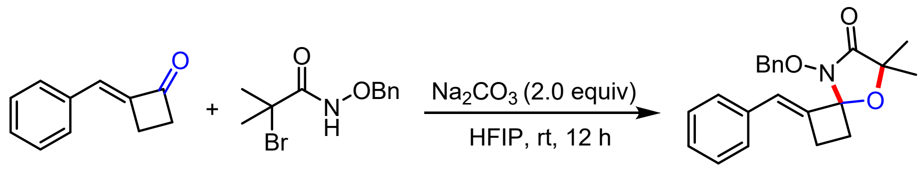
3) Optimization of the reaction conditions. [a]



entry	base	solvent	T(°C)	Yield [b](%)
1	Na_2CO_3	TFE	50	20
2	Na_2CO_3	toluene	50	trace
3	Na_2CO_3	THF	50	trace
4	Na_2CO_3	CH_3CN	50	trace
5	Na_2CO_3	HFIP	50	73
6	NaOAc	HFIP	50	16
7	NaOH	HFIP	50	40
8	^{t}BuOK	HFIP	50	38
9	Cs_2CO_3	HFIP	50	47
10[c]	Na_2CO_3	HFIP	50	68
11[d]	Na_2CO_3	HFIP	50	72
12[e]	Na_2CO_3	HFIP	50	64
13	Na_2CO_3	HFIP	rt	79
14	Na_2CO_3	HFIP	40	75
15	Na_2CO_3	HFIP	60	79
17[f]	Na_2CO_3	HFIP	rt	90
18[g]	Na_2CO_3	HFIP	rt	91

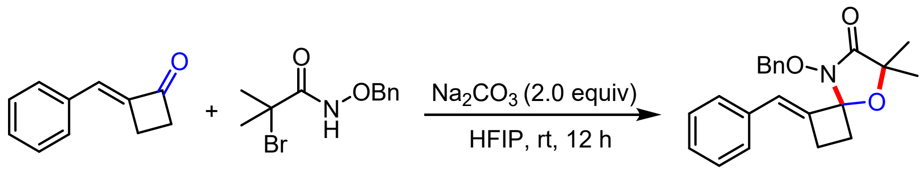
[a] Reaction conditions: **1a** (0.3 mmol), **2a** (0.45 mmol), base (2.0 equiv) in solvent (3.0 mL) for 12 h at 50°C. [b] Isolated yield. [c] 1.5 equiv of Na_2CO_3 was used. [d] 2.5 equiv of Na_2CO_3 was used. [e] 2.0 equiv of Na_2CO_3 was used and the reaction time was 36 h. [f] 2.0 equiv of **2a** was used. [g] 2.5 equiv of **2a** was used. Abbreviations: TFE = 2,2,2-trifluoroethanol, THF = tetrahydrofuran, HFIP = 1,1,1,3,3,3-hexafluoroisopropanol.

4) General procedure for the synthesis of product 3.



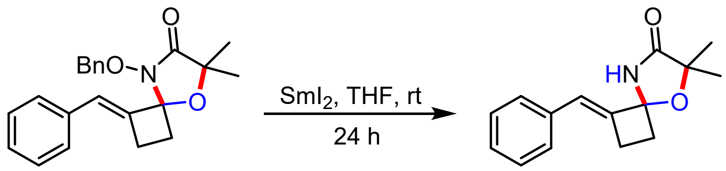
To a solution of (*E*)-2-benzylidenecyclobutan-1-one **1a** (0.3 mmol) and N-(benzyloxy)-2-bromo-2-methylpropanamide **2a** (0.6 mmol, 2.0 equiv) in HFIP (3.0 mL) was added Na_2CO_3 (0.6 mmol, 2.0 equiv). The reaction mixture was stirred at room temperature for 12 h. After completion of the reaction (monitored by TLC), the reaction mixture was concentrated in vacuo. The residue was purified by flash column chromatography (PE/EA = 20/1) to afford **3a** (94.2 mg) in 90% yield.

5) Gram-Scale Synthetic of Compound 3a.

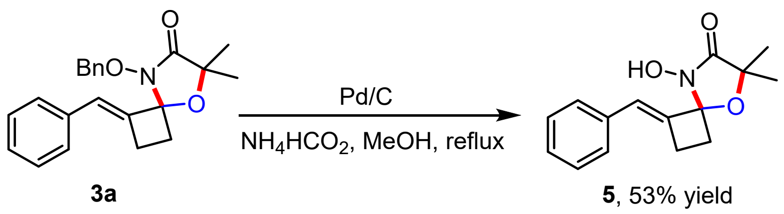


To a 100 mL round-bottomed flask was added (*E*)-2-benzylidenecyclobutan-1-one **1a** (4 mmol, 1.0 equiv), N-(benzyloxy)-2-bromo-2-methylpropanamide **2a** (8 mmol, 2.0 equiv), Na_2CO_3 (8 mmol, 2.0 equiv), and HFIP (40.0 mL) sequentially. The reaction was then stirred at room temperature for 24 hours. The reaction mixture was filtered through celite and washed with ethyl acetate. After that, the solution was concentrated under reduced pressure and the resulting residue was purified by flash column chromatography (PE/EA = 20/1) to afford **3a** (1.172 g) in 84% yield.

6）Synthetic transformation of the cycloaddition product 3a.[4]



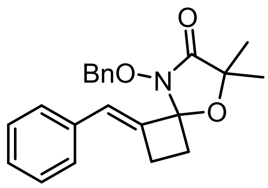
To a solution of **3a** (105 mg, 0.3 mmol) in anhydrous THF (0.1 mL) added SmI_2 21.0 mL (0.1 M in THF). The reaction mixture was stirred at room temperature for 24 h under nitrogen atmosphere. The reaction was quenched with saturated solution of ammonium chloride (20 mL) and extracted with ethyl acetate. The organic phase was evaporated under reduced pressure and the resulting residue was purified via flash column chromatography (PE/EA = 4/1) to afford compound **4** as a white solid in 60% yield.



To a solution of **3a** (105 mg, 0.3 mmol) in MeOH (3.0 mL) added ammonium formate (152 mg, 2.4 mmol) and Pd/C. The reaction mixture was stirred at 60 ℃ for 24 hours. The volatiles were removed under reduced pressure and the residue was purified via flash column chromatography (PE/EA = 2/1) to afford compound **5** (41 mg) as a solid in 53% yield.

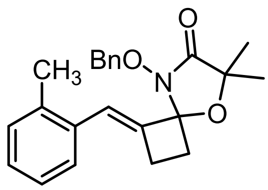
3. Characterization Data for the Products

(*E*)-1-Benzylidene-8-(benzyloxy)-6,6-dimethyl-5-oxa-8-azaspiro[3.4]octan-7-one (3a)



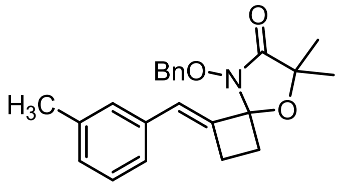
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40-7.28 (m, 10H), 6.55 (t, *J* = 2.6 Hz, 1H), 5.20 (d, *J* = 10.0 Hz, 1H), 5.01 (d, *J* = 10.0 Hz, 1H), 2.84-2.72 (m, 3H), 2.53-2.45 (m, 1H), 1.53 (s, 3H), 1.41 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.0, 141.9, 134.7, 133.4, 128.6, 128.0, 127.6, 127.5, 127.4, 126.8, 125.2, 93.7, 78.1, 76.7, 33.4, 24.9, 24.5, 24.4 ppm. HRMS(ESI) *m/z* calcd for $[C_{22}H_{23}NO_3 + H]^+$ 350.1756, found 350.1750.

(*E*)-8-(Benzyloxy)-6,6-dimethyl-1-(2-methylbenzylidene)-5-oxa-8-azaspiro[3.4]octan-7-one (3b)



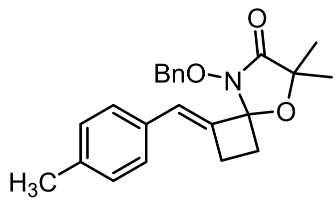
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44-7.39 (m, 2H), 7.35-7.28 (m, 4H), 7.22-7.16 (m, 3H), 6.79 (t, *J* = 2.5 Hz, 1H), 5.22 (d, *J* = 9.8 Hz, 1H), 5.04 (d, *J* = 9.8 Hz, 1H), 2.81-2.69 (m, 3H), 2.52-2.43 (m, 1H), 2.34 (s, 3H), 1.54 (s, 3H), 1.42 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.9, 142.2, 135.4, 133.4, 133.0, 129.5, 128.6, 128.0, 127.5, 126.8, 126.5, 124.9, 122.5, 93.6, 78.1, 76.7, 33.2, 24.8, 24.4, 24.3, 18.7 ppm. HRMS(ESI) *m/z* calcd for $[C_{23}H_{25}NO_3 + H]^+$ 364.1913, found 364.1913.

(*E*)-8-(Benzyloxy)-6,6-dimethyl-1-(3-methylbenzylidene)-5-oxa-8-azaspiro[3.4]octan-7-one (3c)



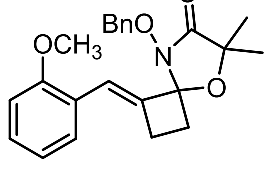
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41-7.37 (m, 2H), 7.32-7.24 (m, 4H), 7.14-7.09 (m, 3H), 6.54 (t, *J* = 2.6 Hz, 1H), 5.20 (d, *J* = 10.0 Hz, 1H), 5.00 (d, *J* = 9.9 Hz, 1H), 2.84-2.71 (m, 3H), 2.52–2.45 (m, 1H), 2.36 (s, 3H), 1.53 (s, 3H), 1.41 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.9, 141.6, 137.1, 134.7, 133.5, 128.6, 128.3, 128.0, 127.6, 127.5, 125.3, 124.5, 93.7, 78.1, 76.7, 33.4, 24.9, 24.5, 24.4, 20.4 ppm. HRMS(ESI) *m/z* calcd for $[C_{23}H_{25}NO_3 + Na]^+$ 386.1732, found 386.1733.

(*E*)-8-(Benzyloxy)-6,6-dimethyl-1-(4-methylbenzylidene)-5-oxa-8-azaspiro[3.4]octan-7-one (3d)



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40-7.37 (m, 2H), 7.33-7.29 (m, 3H), 7.22 (d, *J* = 8.1 Hz, 2H), 7.17 (d, *J* = 8.0 Hz, 2H), 6.54 (t, *J* = 2.5 Hz, 1H), 5.19 (d, *J* = 10.0 Hz, 1H), 5.00 (d, *J* = 9.9 Hz, 1H), 2.82-2.71 (m, 3H), 2.54-2.35 (m, 1H), 2.35 (s, 3H), 1.53 (s, 3H), 1.41 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.9, 140.6, 136.8, 133.4, 131.9, 128.6, 128.3, 128.0, 127.4, 127.4, 125.1, 93.7, 78.1, 76.6, 33.4, 24.8, 24.4, 24.4, 20.3 ppm. HRMS(ESI) *m/z* calcd for $[C_{23}H_{25}NO_3 + H]^+$ 364.1913, found 364.1907.

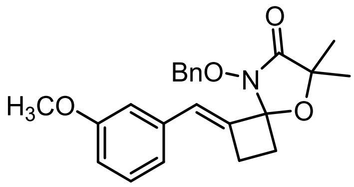
(*E*)-8-(Benzyloxy)-1-(2-methoxybenzylidene)-6,6-dimethyl-5-oxa-8-azaspiro[3.4]octan-7-one (3e)



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44-7.41 (m, 2H), 7.36-7.31 (m, 4H), 7.29-7.25 (m, 1H), 7.05 (t, *J* = 2.6 Hz, 1H), 6.98-6.94 (m, 1H), 6.91-6.89 (m,1H), 5.25 (d, *J* = 9.8

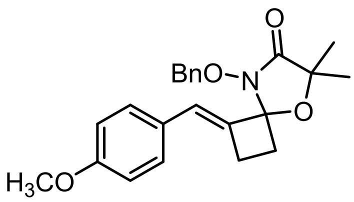
Hz, 1H), 5.04 (d, J = 9.8 Hz, 1H), 3.83 (s, 3H), 2.85-2.72 (m, 3H), 2.52-2.42 (m, 1H), 1.55 (s, 3H), 1.42 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.8, 155.9, 141.3, 133.6, 128.6, 128.1, 127.9, 127.4, 127.4, 123.5, 119.8, 119.3, 109.7, 93.7, 78.1, 76.7, 54.4, 33.1, 24.9, 24.4 ppm. HRMS(ESI) *m/z* calcd for $[C_{23}H_{25}NO_4 + H]^+$ 380.1862, found 380.1854.

(*E*)-8-(Benzyloxy)-1-(3-methoxybenzylidene)-6,6-dimethyl-5-oxa-8-azaspiro[3.4]octan-7-one (3f)



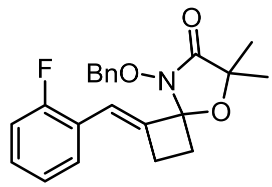
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40-7.36 (m, 2H), 7.34-7.25 (m, 4H), 6.93-6.91 (m, 1H), 6.86-6.82 (m, 2H), 6.53 (t, J = 2.6 Hz, 1H), 5.20 (d, J = 10.0 Hz, 1H), 5.00 (d, J = 10.0 Hz, 1H), 3.82 (s, 3H), 2.86-2.71 (m, 3H), 2.52–2.45 (m, 1H), 1.53 (s, 3H), 1.41 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.0, 158.6, 142.3, 136.0, 133.4, 128.6, 128.5, 128.0, 127.5, 125.1, 120.0, 112.9, 112.3, 93.6, 78.1, 76.7, 54.2, 33.3, 24.8, 24.5, 24.4 ppm. HRMS(ESI) *m/z* calcd for $[C_{23}H_{25}NO_4 + H]^+$ 380.1862, found 380.1859.

(*E*)-8-(Benzyloxy)-1-(4-methoxybenzylidene)-6,6-dimethyl-5-oxa-8-azaspiro[3.4]octan-7-one (3g)



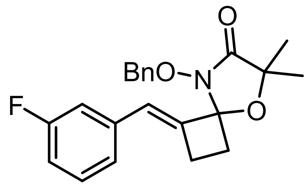
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44-7.40 (m, 2H), 7.34-7.28 (m, 5H), 6.94-6.91 (m, 2H), 6.54 (t, J = 2.7 Hz, 1H), 5.22 (d, J = 9.9 Hz, 1H), 5.03 (d, J = 10.0 Hz, 1H), 3.85 (s, 3H), 2.82-2.74 (m, 3H), 2.57-2.45 (m, 1H), 1.55 (s, 3H), 1.44 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.9, 158.2, 138.9, 133.5, 128.8, 128.6, 127.9, 127.6, 127.4, 124.7, 113.0, 93.7, 78.1, 76.6, 54.2, 33.4, 24.8, 24.4, 24.3 ppm. HRMS(ESI) *m/z* calcd for $[C_{23}H_{25}NO_4 + H]^+$ 380.1862, found 380.1853.

(*E*)-8-(Benzyloxy)-1-(2-fluorobenzylidene)-6,6-dimethyl-5-oxa-8-azaspiro[3.4]octan-7-one (3h)



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41-7.13 (m, 7H), 7.15-7.04 (m, 2H), 6.77 (t, *J* = 2.6 Hz, 1H), 5.22 (d, *J* = 10.0 Hz, 1H), 5.02 (d, *J* = 10.0 Hz, 1H), 2.82-2.71 (m, 3H), 2.52-2.42 (m, 1H), 1.53 (s, 3H), 1.41 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.0, 159.2 (d, J_{CF} = 248.7 Hz), 144.1, 133.5, 128.7, 128.4 (d, J_{CF} = 19.3 Hz), 128.0, 127.8 (d, J_{CF} = 3.1 Hz), 127.5, 123.0 (d, J_{CF} = 3.6 Hz), 122.5 (d, J_{CF} = 21.5 Hz), 117 (d, J_{CF} = 5.0 Hz), 114.7 (d, J_{CF} = 21.9 Hz), 93.5, 78.1, 76.8, 33.1, 24.9, 24.5, 24.3 ppm. ^{19}F NMR(376 MHz, $CDCl_3$) δ -116.73 ppm. HRMS(ESI) *m/z* calcd for $[C_{22}H_{22}FNO_3 + H]^+$ 368.1662, found 368.1664.

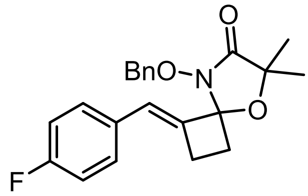
(*E*)-8-(Benzyloxy)-1-(3-fluorobenzylidene)-6,6-dimethyl-5-oxa-8-azaspiro[3.4]octan-7-one (3i)



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39-7.26 (m, 6H), 7.07-6.95 (m, 3H), 6.48 (t, *J* = 2.8 Hz, 1H), 5.19 (d, *J* = 10.1 Hz, 1H), 5.01 (d, *J* = 10.1 Hz, 1H), 2.81-2.70 (m, 3H), 2.54-2.45 (m, 1H), 1.52 (s, 3H), 1.41 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.1, 161.8 (d, J_{CF} = 244.1 Hz), 143.6, 136.8 (d, J_{CF} = 7.8 Hz), 133.4, 129.0 (d, J_{CF} = 8.3 Hz), 128.7, 128.0, 127.5, 124.0 (d, J_{CF} = 2.7 Hz), 123.3 (d, J_{CF} = 2.7 Hz), 113.8 (d, J_{CF} = 21.8 Hz), 113.6 (d, J_{CF} = 7.4 Hz), 93.5, 78.0, 76.7, 33.3, 24.8, 24.5, 24.4 ppm. ^{19}F NMR (376 MHz, $CDCl_3$) δ -112.29 ppm. HRMS(ESI) *m/z* calcd for $[C_{22}H_{22}FNO_3 + H]^+$ 368.1662, found 368.1659.

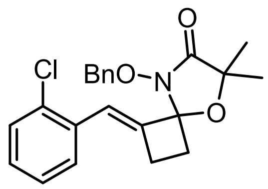
(*E*)-8-(Benzyloxy)-1-(4-fluorobenzylidene)-6,6-dimethyl-5-oxa-8-azaspiro[3.4]oct

an-7-one (3j)



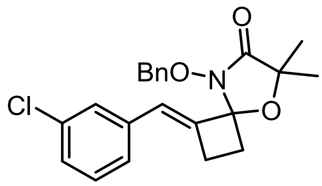
[1]H NMR (400 MHz, $CDCl_3$) δ 7.39-7.36 (m, 2H), 7.33-7.25 (m, 5H), 7.08-7.02 (m, 2H), 6.49 (t, J = 2.6 Hz 1H), 5.20 (d, J = 10.1 Hz, 1H), 5.01 (d, J = 10.1 Hz, 1H), 2.80-2.71 (m, 3H), 2.55-2.43 (m, 1H), 1.53 (s, 3H), 1.42 (s, 3H) ppm. [13]C NMR (100 MHz, $CDCl_3$) δ 170.1, 161.2 (d, J_{CF} = 246.9 Hz), 141.3, 133.4, 130.9 (d, J_{CF} = 3.3 Hz), 129.0 (d, J_{CF} = 8.0 Hz), 128.6, 128.0, 127.5, 124.0, 114.7, 114.5, 93.6, 78.0, 76.7, 33.4, 24.8, 24.4, 24.3 ppm. [19]F NMR (376 MHz, $CDCl_3$) δ -113.14 ppm. HRMS(ESI) *m/z* calcd for $[C_{22}H_{22}FNO_3 + H]^+$ 368.1662, found 368.1659.

(*E*)-8-(Benzyloxy)-1-(2-chlorobenzylidene)-6,6-dimethyl-5-oxa-8-azaspiro[3.4]octan-7-one (3k)



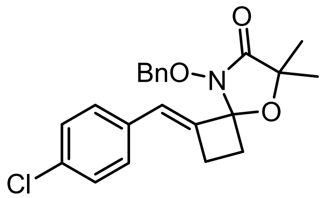
[1]H NMR (400 MHz, $CDCl_3$) δ 7.42-7.37 (m, 4H), 7.34-7.19 (m, 5H), 6.99 (t, J = 2.7 Hz, 1H), 5.25 (d, J = 9.9 Hz, 1H), 5.06 (d, J = 10.0 Hz, 1H), 2.83-2.67 (m, 3H), 2.52-2.42 (m, 1H), 1.55 (s, 3H), 1.42 (s, 3H) ppm. [13]C NMR (100 MHz, $CDCl_3$) δ 170.0, 144.5, 133.5, 132.8, 132.3, 128.9, 128.6, 128.0, 127.9, 127.7, 127.5, 125.7, 121.4, 93.5, 78.1, 76.8, 33.0, 24.9, 24.3, 24.2 ppm. HRMS(ESI) *m/z* calcd for $[C_{22}H_{22}ClNO_3 + Na]^+$ 406.1186, found 406.1183.

(*E*)-8-(Benzyloxy)-1-(3-chlorobenzylidene)-6,6-dimethyl-5-oxa-8-azaspiro[3.4]octan-7-one (3l)



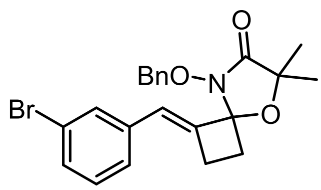
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42-7.36 (m, 2H), 7.33-7.21 (m, 6H), 7.17-7.15 (m, 1H), 6.43 (t, *J* = 2.6 Hz, 1H), 5.19 (d, *J* = 10.2 Hz, 1H), 5.00 (d, *J* = 10.2 Hz, 1H), 2.81-2.70 (m, 3H), 2.54-2.45 (m, 1H), 1.52 (s, 3H), 1.41 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.1, 143.8, 136.4, 133.4, 133.4, 128.8, 128.7, 128.0, 127.5, 127.2, 126.8, 125.5, 123.7, 93.5, 78.0, 76.7, 33.3, 24.8, 24.5, 24.4 ppm. HRMS(ESI) *m/z* calcd for $[C_{22}H_{22}ClNO_3 + Na]^+$ 406.1186, found 406.1181.

(*E*)-8-(Benzyloxy)-1-(4-chlorobenzylidene)-6,6-dimethyl-5-oxa-8-azaspiro[3.4]octan-7-one (3m)



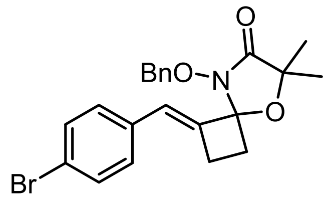
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.36 (m, 2H), 7.33-7.26 (m, 5H), 7.23-7.21 (m, 2H), 6.46 (t, *J* = 2.6 Hz 1H), 5.19 (d, *J* = 10.1 Hz, 1H), 5.00 (d, *J* = 10.1 Hz, 1H), 2.79-2.70 (m, 3H), 2.54-2.43 (m, 1H), 1.52 (s, 3H), 1.41 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.2, 143.7, 134.5, 134.3, 133.6, 129.8, 129.7, 129.2, 128.9, 128.6, 125.0, 94.7, 79.1, 77.8, 34.5, 26.0, 25.5, 25.5 ppm. HRMS(ESI) *m/z* calcd for $[C_{22}H_{22}ClNO_3 + H]^+$ 384.1336, found 384.1360.

(*E*)-8-(Benzyloxy)-1-(3-bromobenzylidene)-6,6-dimethyl-5-oxa-8-azaspiro[3.4]octan-7-one (3n)



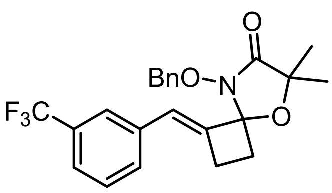
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42-7.36 (m, 4H), 7.33-7.28 (m, 3H), 7.24-7.19 (m, 2H), 6.42 (t, 1H), 5.19 (d, *J* = 10.2 Hz, 1H), 5.00 (d, *J* = 10.2 Hz, 1H), 2.80-2.70 (m, 3H), 2.53-2.44 (m, 1H), 1.52 (s, 3H), 1.41 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.1, 143.8, 136.7, 133.4, 130.2, 129.7, 129.1, 128.7, 128.1, 127.5, 125.9, 123.6, 121.7, 93.5, 78.0, 76.8, 33.3, 24.9, 24.5, 24.4 ppm. HRMS(ESI) *m/z* calcd for $[C_{22}H_{22}BrNO_3 + H]^+$ 428.0861, found 428.0862.

(*E*)-8-(Benzyloxy)-1-(4-bromobenzylidene)-6,6-dimethyl-5-oxa-8-azaspiro[3.4]octan-7-one (3o)



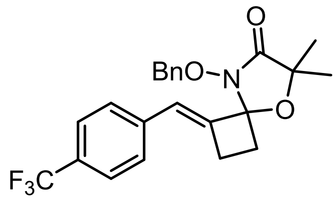
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49-7.47 (m, 2H), 7.38-7.26 (m, 5H), 7.16-7.14 (m, 2H), 6.44 (t, *J* = 2.5 Hz, 1H), 5.19 (d, *J* = 10.1 Hz, 1H), 5.00 (d, *J* = 10.1 Hz, 1H), 2.79-2.70 (m, 3H), 2.53-2.43 (m, 1H), 1.52 (s, 3H), 1.41(s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.1, 142.9, 133.6, 133.4, 130.7, 128.8, 128.7, 128.1, 127.5, 124.0, 120.8, 93.6, 78.0, 76.8, 33.4, 24.9, 24.5, 24.4 ppm. HRMS(ESI) *m/z* calcd for $[C_{22}H_{22}BrNO_3 + H]^+$ 428.0861, found 428.0859.

(*E*)-8-(Benzyloxy)-6,6-dimethyl-1-(3-(trifluoromethyl)benzylidene)-5-oxa-8-azaspiro[3.4]octan-7-one (3p)



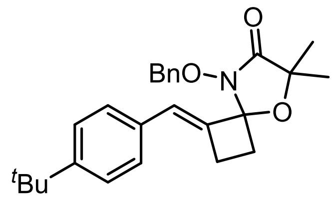
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54-7.44 (m, 4H), 7.39-7.36 (m, 2H), 7.31-7.23 (m, 3H), 6.49 (t, *J* = 2.5 Hz, 1H), 5.20 (d, *J* = 10.4 Hz, 1H), 5.02 (d, *J* = 10.3 Hz, 1H), 2.81-2.71 (m, 3H), 2.55-2.46 (m, 1H), 1.53 (s, 3H), 1.42 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.2, 144.3, 135.4, 133.5, 130.3, 130.1, 128.7, 128.1, 128.0, 127.5, 124.0 (q, J_{CF} = 3.7 Hz), 123.6, 123.3 (q, J_{CF} = 3.8 Hz), 93.5, 78.0, 76.8, 33.3, 24.9, 24.5, 24.4 ppm. ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.81 ppm. HRMS(ESI) *m/z* calcd for $[C_{23}H_{22}F_3NO_3 + H]^+$ 418.1630, found 418.1625.

(*E*)-8-(Benzyloxy)-6,6-dimethyl-1-(4-(trifluoromethyl)benzylidene)-5-oxa-8-azaspiro[3.4]octan-7-one (3q)



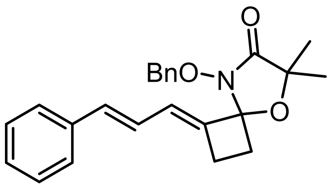
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, *J* = 8.1 Hz, 2H), 7.39-7.36 (m, 4H), 7.32-7.24 (m, 3H), 6.52 (t, *J* = 2.6 Hz, 1H), 5.20 (d, *J* = 10.2 Hz, 1H), 5.01 (d, *J* = 10.2 Hz, 1H), 2.83-2.71 (m, 3H), 2.56-2.46 (m, 1H), 1.53 (s, 3H), 1.42 (s, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.2, 145.2, 138.1, 133.4, 128.7, 128.1, 127.5, 127.5, 124.5 (q, J_{CF} = 3.8 Hz) 123.7, 93.5, 78.0, 76.8, 33.3, 24.9, 24.6, 24.4 ppm. ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.58 ppm. HRMS(ESI) *m/z* calcd for $[C_{23}H_{22}F_3NO_3 + H]^+$ 418.1630, found 418.1626.

(*E*)-8-(Benzyloxy)-1-(4-(tert-butyl)benzylidene)-6,6-dimethyl-5-oxa-8-azaspiro[3.4]octan-7-one (3r)



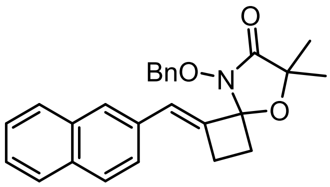
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41-7.39 (m, 4H), 7.34-7.27 (m, 5H), 6.57 (t, *J* = 2.8 Hz, 1H), 5.19 (d, *J* = 9.9 Hz, 1H), 4.99 (d, *J* = 9.9 Hz, 1H), 2.87-2.71 (m, 3H), 2.52-2.45 (m, 1H), 1.53 (s, 3H), 1.41 (s, 3H), 1.33 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.9, 150.0, 140.9, 133.4, 132.0, 128.6, 128.0, 127.5, 127.2, 125.0, 124.5, 93.7, 78.1, 76.7, 33.6, 33.4, 30.2, 24.8, 24.5, 24.4 ppm. HRMS(ESI) *m/z* calcd for $[C_{26}H_{31}NO_3 + H]^+$ 406.2382, found 406.2373.

(*E*)-8-(Benzyloxy)-6,6-dimethyl-1-((E)-3-phenylallylidene)-5-oxa-8-azaspiro[3.4]octan-7-one (3s)



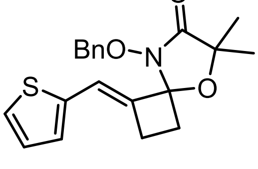
^{1}H NMR (400 MHz, CDCl$_3$) δ 7.44-7.40 (m, 4H), 7.38-7.32 (m, 5H), 7.28-7.23 (m, 1H), 6.76-6.69 (m, 1H), 6.60 (d, *J* = 15.7 Hz, 1H), 6.38-6.34 (m, 1H), 5.18 (d, *J* = 10.0 Hz, 1H), 5.00 (d, *J* = 9.9 Hz, 1H), 2.70-2.53 (m, 3H), 2.44-2.35 (m, 1H), 1.50 (s, 3H), 1.40 (s, 3H) ppm. ^{13}C NMR (100 MHz, CDCl$_3$) δ 169.9, 143.2, 135.9, 133.8, 133.5, 128.7, 128.0, 127.7, 127.5, 127.0, 125.6, 125.3, 122.5, 93.1, 78.0, 76.6, 31.9, 24.8, 24.3, 21.8 ppm. HRMS(ESI) *m/z* calcd for $[C_{24}H_{25}NO_3 + H]^+$ 376.1913, found 376.1906.

(*E*)-8-(Benzyloxy)-6,6-dimethyl-1-(naphthalen-2-ylmethylene)-5-oxa-8-azaspiro[3.4]octan-7-one (3t)



^{1}H NMR ((400 MHz, CDCl$_3$) δ 8.07-8.05 (m, 1H), 7.86-7.77 (m, 2H), 7.53-7.41 (m, 4H), 7.35-7.25 (m, 4H), 5.28 (d, *J* = 10.0 Hz, 1H), 5.11 (d, *J* = 10.0 Hz, 1H), 2.78-2.69 (m, 3H), 2.53-2.44 (m, 1H), 1.61 (s, 3H), 1.46 (s, 3H) ppm. ^{13}C NMR (100 MHz, CDCl$_3$) δ 171.2, 144.8, 134.5, 133.8, 131.9, 131.4, 129.7, 129.1, 128.7, 128.6, 128.5, 126.4, 126.0, 125.8, 125.4, 123.7, 122.8, 94.7, 79.2, 77.9, 34.2, 26.0, 25.5, 25.4 ppm. HRMS(ESI) *m/z* calcd for $[C_{26}H_{25}NO_3 + Na]^+$ 422.1732, found 422.1733.

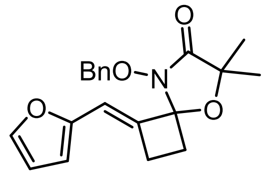
(*E*)-8-(Benzyloxy)-6,6-dimethyl-1-(thiophen-2-ylmethylene)-5-oxa-8-azaspiro[3.4]octan-7-one (3u)



^{1}H NMR (400 MHz, CDCl$_3$) δ 7.39-7.28 (m, 6H), 7.05-7.00 (m, 2H), 6.75 (t, *J* = 2.5

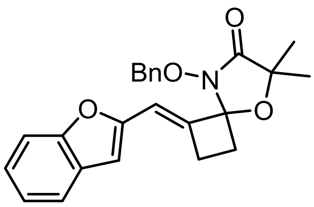
Hz, 1H), 5.18 (d, J = 10.0 Hz, 1H), 4.99 (d, J = 10.0 Hz, 1H), 2.77-2.62 (m, 3H), 2.51-2.43 (m, 1H), 1.51 (s, 3H), 1.40 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.0, 140.0, 138.7, 133.4, 128.7, 128.0, 127.5, 126.6, 126.2, 125.7, 118.7, 93.3, 78.1, 76.7, 32.7, 24.9, 24.3, 23.9 ppm. HRMS(ESI) *m/z* calcd for $[C_{20}H_{21}NO_3S + H]^+$ 356.1320, found 356.1317.

(*E*)-8-(Benzyloxy)-1-(furan-2-ylmethylene)-6,6-dimethyl-5-oxa-8-azaspiro[3.4]octan-7-one (3v)



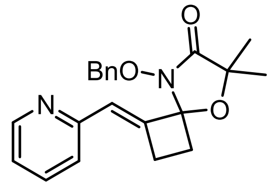
^1H NMR (400 MHz, $CDCl_3$) δ 7.47-7.30 (m, 6H), 6.43-6.37 (m, 2H), 6.28 (d, J = 3.4 Hz, 1H), 5.17 (d, J = 10.0 Hz, 1H), 5.00 (d, J = 10.0 Hz, 1H), 2.82-2.67 (m, 3H), 2.51– 2.39 (m, 1H), 1.49 (s, 3H), 1.40 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.2, 151.9, 142.9, 141.5, 134.6, 129.8, 129.1, 128.6, 114.7, 111.6, 110.3, 94.5, 79.1, 77.8, 34.0, 26.0, 25.5, 25.0 ppm. HRMS(ESI) *m/z* calcd for $[C_{20}H_{21}NO_4 + H]^+$ 340.1549, found 340.1544.

(*E*)-1-(Benzofuran-2-ylmethylene)-8-(benzyloxy)-6,6-dimethyl-5-oxa-8-azaspiro[3.4]octan-7-one (3w)



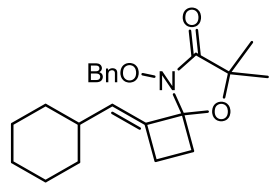
^1H NMR (400 MHz, $CDCl_3$) δ 7.56-7.54 (m, 1H), 7.47-7.44 (m, 1H), 7.41-7.38 (m, 2H), 7.32-7.20 (m, 5H), 6.62 (s, 1H), 6.47 (t, J = 2.8 Hz, 1H), 5.18 (d, J = 10.1 Hz, 1H), 5.03 (d, J = 10.1 Hz, 1H), 2.99-2.72 (m, 3H), 2.53-2.45 (m, 1H), 1.52 (s, 3H), 1.42 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.1, 154.0, 152.6, 144.7, 133.4, 128.7, 128.0, 127.5, 127.5, 123.8, 122.0, 120.1, 113.7, 110.1, 105.5, 93.2, 78.0, 76.7, 32.8, 24.9, 24.4, 24.3 ppm. HRMS(ESI) *m/z* calcd for $[C_{24}H_{23}NO_4 + H]^+$ 390.1705, found 390.1702.

(*E*)-8-(Benzyloxy)-6,6-dimethyl-1-(pyridin-2-ylmethylene)-5-oxa-8-azaspiro[3.4]octan-7-one (3x)



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56-7.54 (m, 1H), 7.47-7.44 (m, 1H), 7.41-7.38 (m, 2H), 7.32-7.20 (m, 5H), 6.62 (s, 1H), 6.47 (t, *J* = 2.8 Hz, 1H), 5.18 (d, *J* = 10.1 Hz, 1H), 5.03 (d, *J* = 10.1 Hz, 1H), 2.99-2.72 (m, 3H), 2.53-2.45 (m, 1H), 1.52 (s, 3H), 1.42 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.0, 155.0, 149.8, 148.6, 136.3, 134.5, 129.8, 129.1, 128.6, 126.3, 123.3, 122.1, 94.6, 79.1, 77.9, 34.4, 26.0, 25.5 ppm. HRMS(ESI) *m/z* calcd for $[C_{21}H_{22}N_2O_3 + H]^+$ 351.1709, found 351.1703.

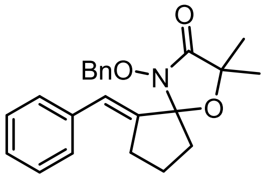
(*E*)-8-(benzyloxy)-1-(cyclohexylmethylene)-6,6-dimethyl-5-oxa-8-azaspiro[3.4]octan-7-one (3y)



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45-7.43 (m, 2H), 7.39-7.37 (m, 3H), 5.68 (dt, *J* = 8.7, 8.7 Hz, 1H), 5.18 (d, *J* = 9.7 Hz, 1H), 4.96 (d, *J* = 9.6 Hz, 1H), 2.65-2.58 (m, 1H), 2.54-2.45 (m, 1H), 2.37-2.30 (m, 1H), 2.19-2.10 (m, 1H), 1.75-1.64 (m, 5H), 1.46 (s, 3H), 1.37 (s, 3H), 1.32-1.24 (m, 2H), 1.19-1.11 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.6, 138.8, 133.5, 132.6, 128.5, 128.0, 127.5, 93.1, 78.0, 76.5, 36.6, 32.0, 31.5, 31.3, 24.9, 24.8, 24.8, 24.8, 24.2, 21.5 ppm. HRMS(ESI) *m/z* calcd for $[C_{22}H_{29}NO_3 + Na]^+$ 378.2045, found 378.2042.

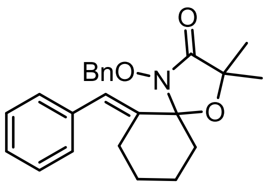
(*E*)-6-Benzylidene-4-(benzyloxy)-2,2-dimethyl-1-oxa-4-azaspiro[4.4]nonan-3-one

(3z)



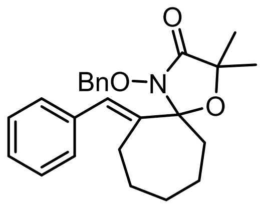
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42-7.34 (m, 10H), 6.73 (t, J = 2.7 Hz, 1H), 5.22 (d, J = 9.8 Hz, 1H), 5.01 (d, J = 9.9 Hz, 1H), 2.87-2.79 (m, 1H), 2.72-2.63 (m, 1H), 2.23-2.16 (m, 1H), 1.96-1.83 (m, 3H), 1.60 (s, 3H), 1.50 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.3, 141.2, 135.6, 133.4, 128.5, 127.9, 127.4, 127.4, 126.5, 126.2, 98.4, 77.7, 76.1, 35.4, 28.7, 25.5, 24.9, 21.0 ppm. HRMS(ESI) *m/z* calcd for $[C_{23}H_{25}NO_3 + H]^+$ 364.1913, found 364.1906.

(*E*)-6-Benzylidene-4-(benzyloxy)-2,2-dimethyl-1-oxa-4-azaspiro[4.5]decan-3-one (3aa)



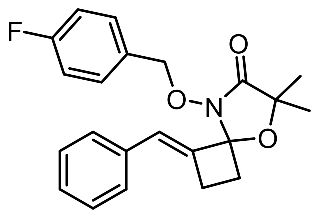
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51-7.46 (m, 2H), 7.42-7.36 (m, 3H), 7.32-7.25 (m, 2H), 7.22-7.14 (m, 3H), 6.56 (d, J = 1.8 Hz, 1H), 5.28 (d, J = 10.1 Hz, 1H), 5.10 (d, J = 10.0 Hz, 1H), 2.87-2.81 (m, 1H), 2.27-2.19 (m, 1H), 2.02-1.94 (m, 1H), 1.89-1.64 (m, 4H), 1.44 (s, 3H), 1.39 (s, 3H), 1.27-1.23 (m, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.3, 139.3, 135.8, 133.5, 128.8, 128.0, 127.9, 127.5, 127.1, 125.7, 122.6, 92.8, 77.7, 76.1, 36.5, 26.2, 25.9, 24.8, 23.5, 20.9 ppm. HRMS(ESI) *m/z* calcd for $[C_{24}H_{27}NO_3 + H]^+$ 378.2069, found 378.2065.

(*E*)-6-Benzylidene-4-(benzyloxy)-2,2-dimethyl-1-oxa-4-azaspiro[4.6]undecan-3-one (3ab)



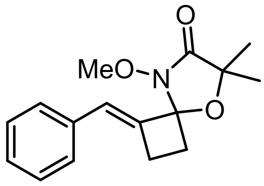
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43-7.41 (m, 2H), 7.37-7.32 (m, 5H), 7.30-7.23 (m, 3H), 6.96 (s, 1H), 5.16 (d, J = 9.6 Hz, 1H), 4.98 (d, J = 9.6 Hz, 1H), 2.70-2.64 (m, 1H), 2.34-2.24 (m, 2H), 1.96-1.90 (m, 1H), 1.87-1.84 (m, 1H), 1.75-1.67 (m, 2H), 1.62-1.58 (m, 2H), 1.56-1.54 (m, 1H), 1.54 (s, 3H), 1.49 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.8, 142.2, 136.0, 133.3, 128.8, 128.7, 128.0, 127.6, 127.5, 127.3, 126.0, 94.5, 77.5, 75.9, 37.7, 29.5, 29.3, 26.5, 25.5, 25.0, 21.5 ppm. HRMS(ESI) *m/z* calcd for $[C_{25}H_{29}NO_3 + H]^+$ 392.2226, found 392.2219.

(*E*)-1-Benzylidene-8-(4-fluorophenoxy)-6,6-dimethyl-5-oxa-8-azaspiro[3.4]octan-7-one (3ac)



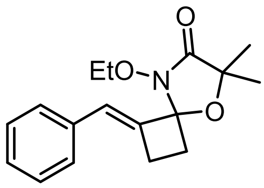
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39-7.28 (m, 7H), 7.00-6.95 (m, 2H), 6.52 (t, J = 2.5 Hz, 1H), 5.14 (d, J = 10.2 Hz, 1H), 4.98 (d, J = 10.2 Hz, 1H), 2.88-2.73 (m, 3H), 2.55-2.47 (m, 1H), 1.52 (s, 3H), 1.41 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.2, 162.1 (d, $^1J_{CF}$ = 246.5 Hz), 141.7, 134.6, 130.6 (d, $^3J_{CF}$ = 8.4 Hz), 129.4 (d, $^3J_{CF}$ = 3.2 Hz), 127.6, 127.4, 126.9, 125.2, 114.5 (d, $^2J_{CF}$ = 21.4 Hz), 93.6, 77.2, 76.7, 33.4, 24.9, 24.5, 24.3 ppm. ^{19}F NMR (376 MHz, $CDCl_3$) δ -112.29 ppm. HRMS(ESI) m/z calcd for $[C_{22}H_{22}FNO_3 + Na]^+$ 390.1481, found 390.1479.

(*E*)-1-Benzylidene-8-methoxy-6,6-dimethyl-5-oxa-8-azaspiro[3.4]octan-7-one (3ad)



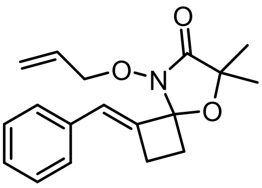
^{1}H NMR (400 MHz, CDCl3) δ 7.39-7.27 (m, 5H), 6.62 (t, *J* = 2.6 Hz, 1H), 3.92 (s, 3H), 2.92-2.83 (m, 3H), 2.59-2.49 (m, 1H), 1.53 (s, 3H), 1.41 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 143.1, 135.7, 128.6, 128.4, 127.9, 126.2, 94.5, 77.7, 64.9, 34.4, 25.8, 25.5, 25.4 ppm. HRMS(ESI) *m/z* calcd for $[C_{16}H_{19}NO_3 + H]^+$ 274.1443, found 274.1442.

(*E*)-1-Benzylidene-8-ethoxy-6,6-dimethyl-5-oxa-8-azaspiro[3.4]octan-7-one (3ae)



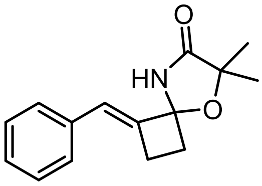
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.29 (m, 5H), 6.64-6.57 (t, *J* = 3.0 Hz, 1H), 4.25-4.06 (m, 2H), 2.92-2.82 (m, 3H), 2.60-2.49 (m, 1H), 1.53 (s, 3H), 1.41 (s, 3H), 1.29 (t, *J* = 7.1 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 143.2, 135.7, 128.6, 128.4, 127.9, 126.0, 94.6, 77.7, 73.0, 34.4, 25.9, 25.6, 25.4, 13.9 ppm. HRMS(ESI) *m/z* calcd for $[C_{17}H_{21}NO_3 + H]^+$ 288.1600, found 288.1601.

(*E*)-8-(Allyloxy)-1-benzylidene-6,6-dimethyl-5-oxa-8-azaspiro[3.4]octan-7-one (3af)



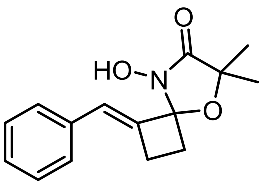
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39-7.28 (m, 5H), 6.61 (t, *J* = 2.6 Hz, 1H), 6.06-5.96 (m, 1H), 5.33-5.27 (m, 2H), 4.65-4.50 (m, 2H), 2.92-2.82 (m, 3H), 2.61-2.49 (m, 1H), 1.52 (s, 3H), 1.41 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 143.0, 135.7, 131.8, 128.6, 128.4, 127.9, 126.3, 120.8, 94.6, 78.1, 77.7, 34.4, 25.9, 25.5, 25.4 ppm. HRMS(ESI) *m/z* calcd for $[C_{18}H_{21}NO_3 + Na]^+$ 322.1419, found 322.1418.

(*E*)-1-Benzylidene-6,6-dimethyl-5-oxa-8-azaspiro[3.4]octan-7-one (4)



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (s, 1H), 7.36-7.23 (m, 5H), 6.54 (t, J = 2.7 Hz, 1H), 2.99-2.90 (m, 1H), 2.81-2.54 (m, 3H), 1.50 (s, 3H), 1.44 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.5, 145.1, 135.9, 128.7, 128.4, 127.8, 125.0, 93.1, 79.8, 38.1, 25.9, 25.8, 25.4 ppm. HRMS(ESI) *m/z* calcd for $[C_{15}H_{17}NO_2 + H]^+$ 244.1338, found 244.1333.

(*E*)-1-benzylidene-8-hydroxy-6,6-dimethyl-5-oxa-8-azaspiro[3.4]octan-7-one (5)



^{1}H NMR (400 MHz, $CDCl_3$) δ 10.49 (s, 1H), 7.34-7.33 (m, 4H), 7.27-7.26 (m, 2H), 6.54 (t, J = 2.7, 1H), 3.00-2.86 (m, 3H), 2.57-2.50 (m, 1H), 1.50 (s, 3H), 1.41 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.4, 140.8, 134.8, 127.5, 127.4, 126.7, 125.22, 95.1, 77.6, 33.0, 24.9, 24.7, 24.5 ppm. HRMS(ESI) *m/z* calcd for $[C_{15}H_{17}NO_3 + H]^+$ 260.1287, found 260.1282.

4. Reference

1) L. Yu, Y. Wu, H. Cao, X. Zhang, X. Shi, J. Luan, T. Chen, Y. Pan and Q. Xu, *Green. Chem.*, 2014, **16**, 287-293.

2) B. B. C. Peters, J. Jongcharoenkamol, S. Krajangsri and P. G. Andersson, *Org. Lett.*, 2021, **23**, 242-246.

3) C. S. Jeffrey, K. L. Barnes, J. A. Eickhoff and C. R. Carson, *J. Am. Chem. Soc.*, 2011, **133**, 7688-7691.

4) A. Acharya, D. Anumandla and C. S. Jeffrey, *J. Am. Chem. Soc.*, 2015, **137**, 14858-14860.

5. ^{1}H NMR and ^{13}C NMR Spectra of Compounds

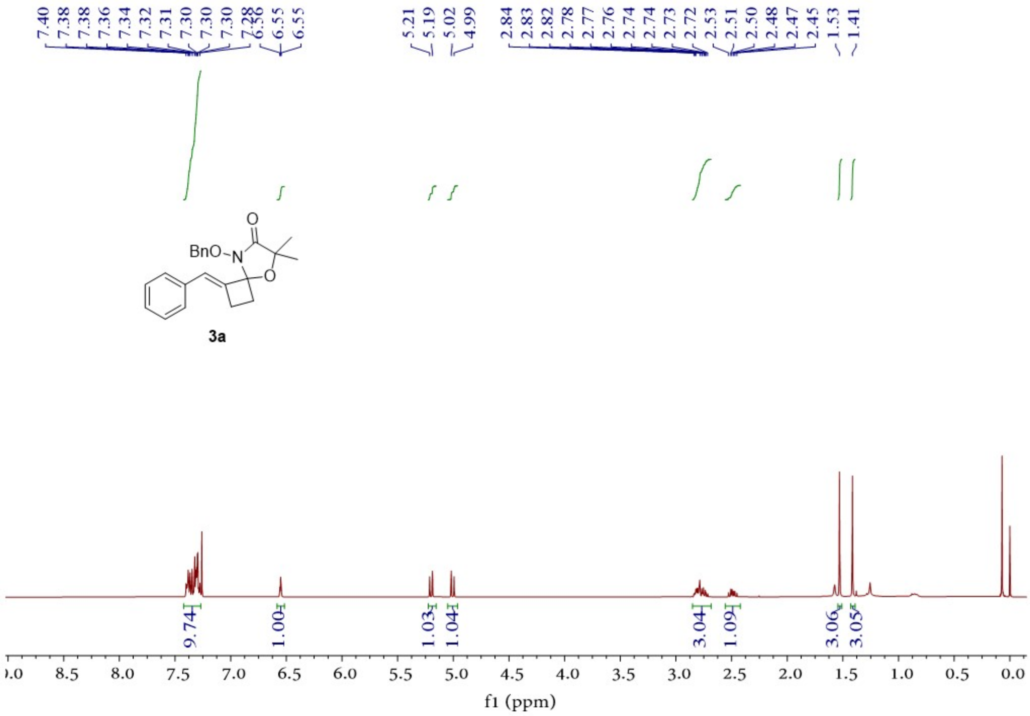


Fig. S1 ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3a**.

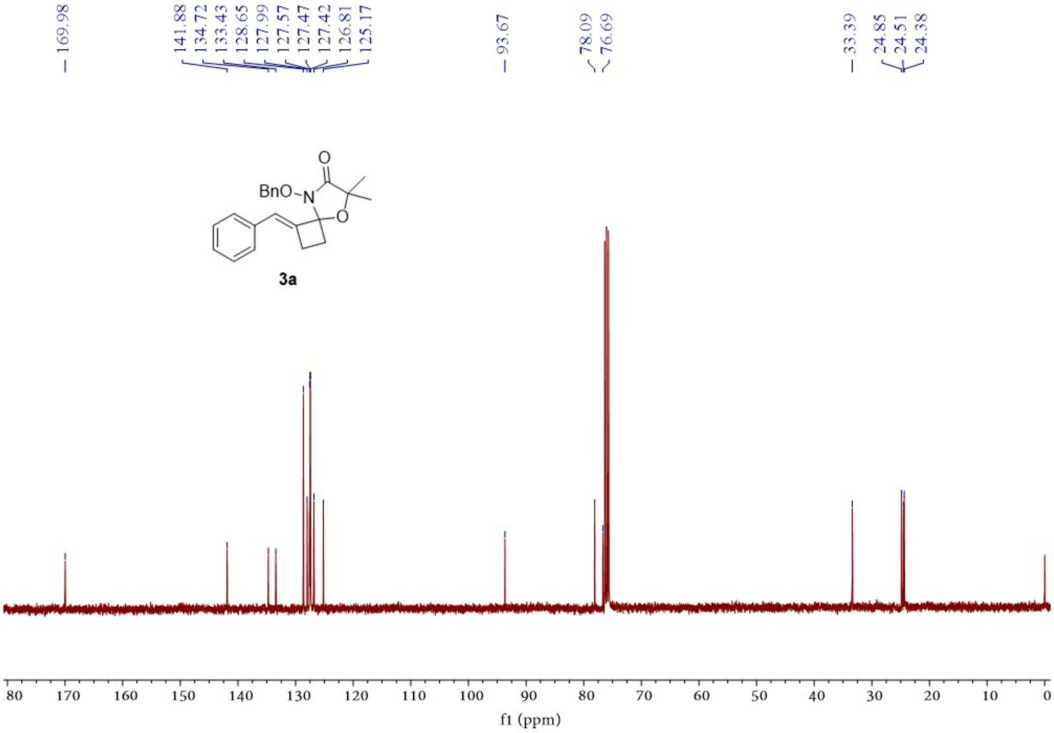


Fig. S2 ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3a**.

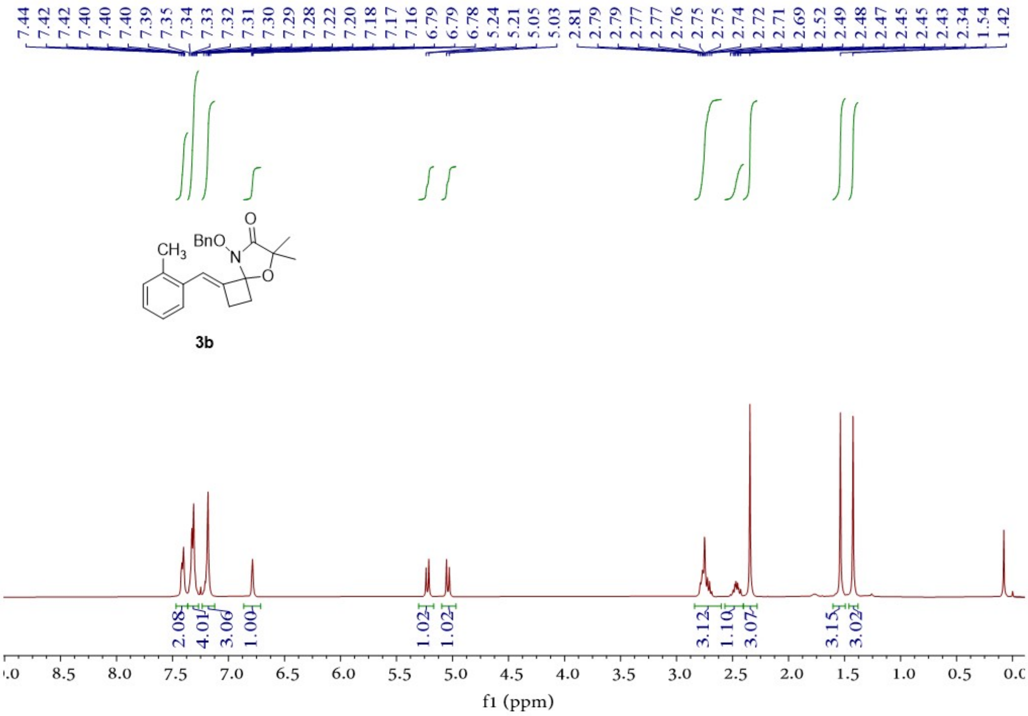


Fig. S3 ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3b**.

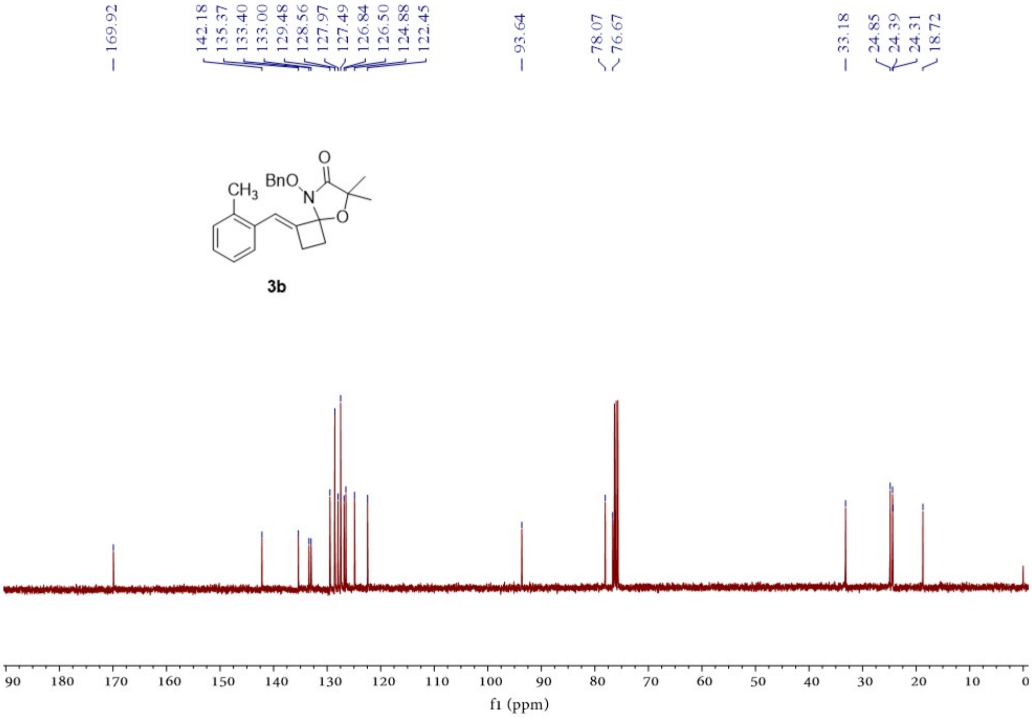


Fig. S4 ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3b**.

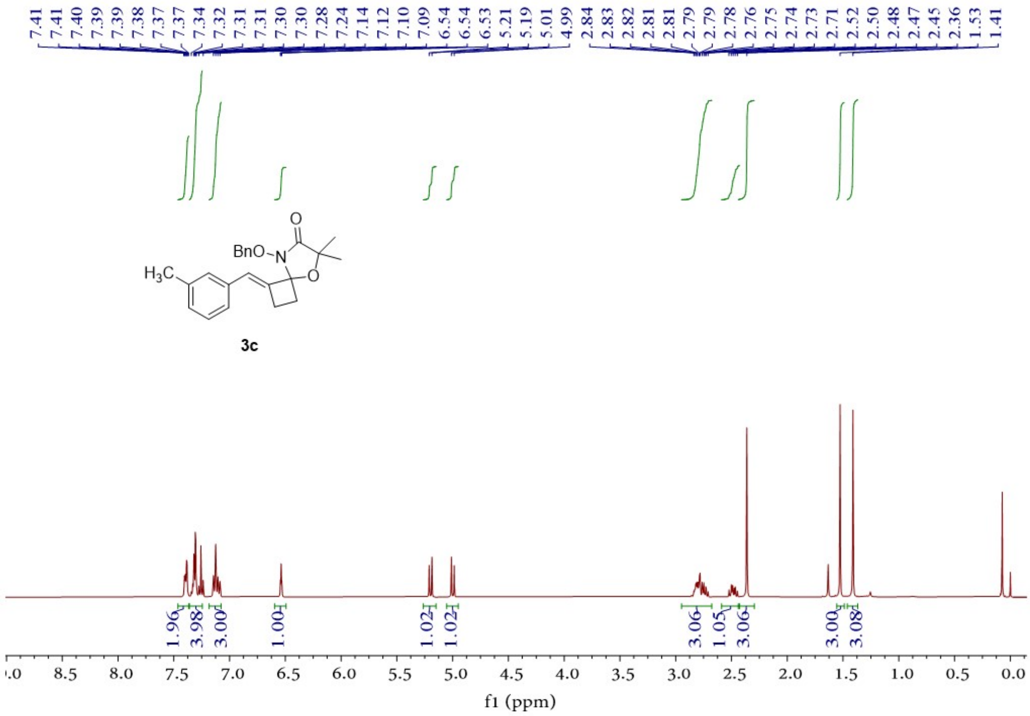


Fig. S5 ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3c**.

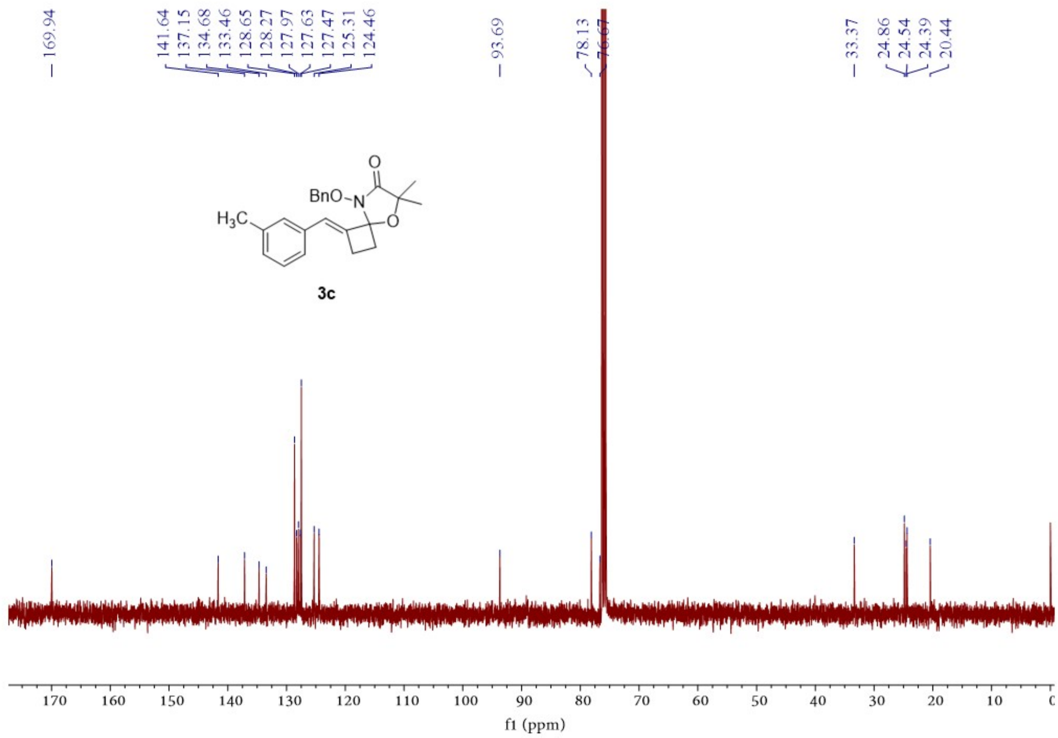


Fig. S6 ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3c**.

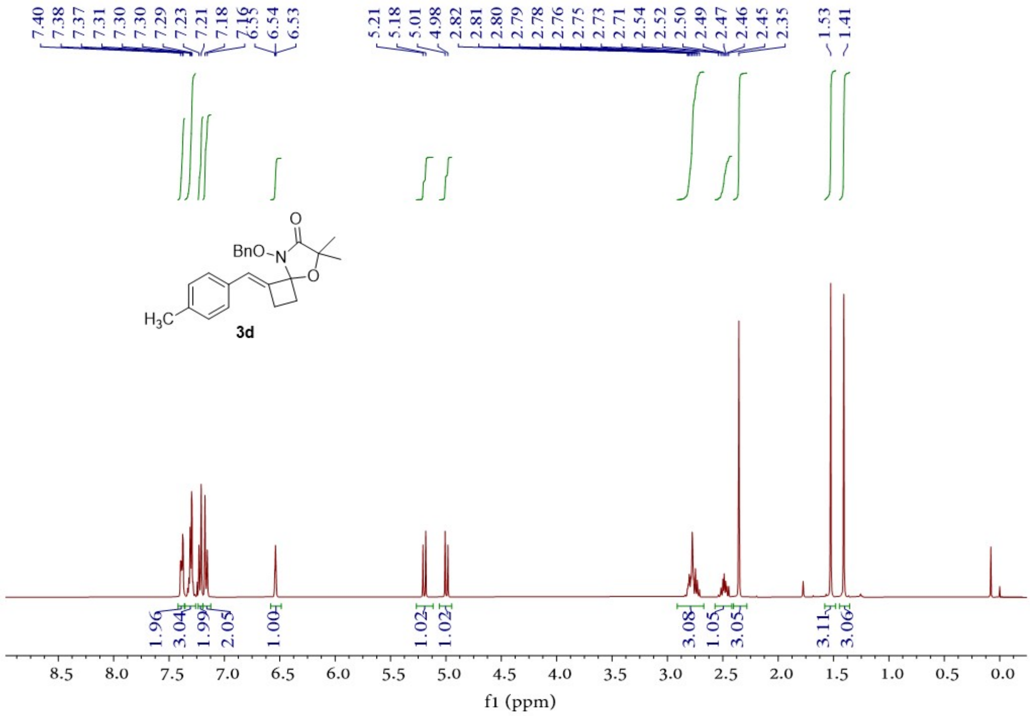


Fig. S7 ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3d**.

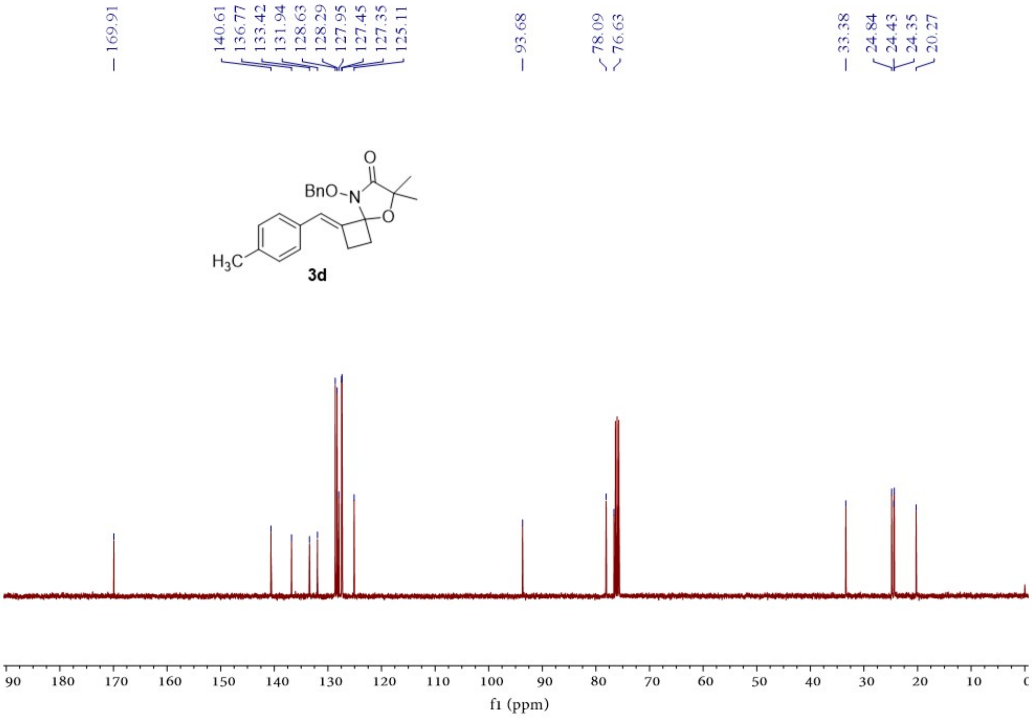


Fig. S8 ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3d**.

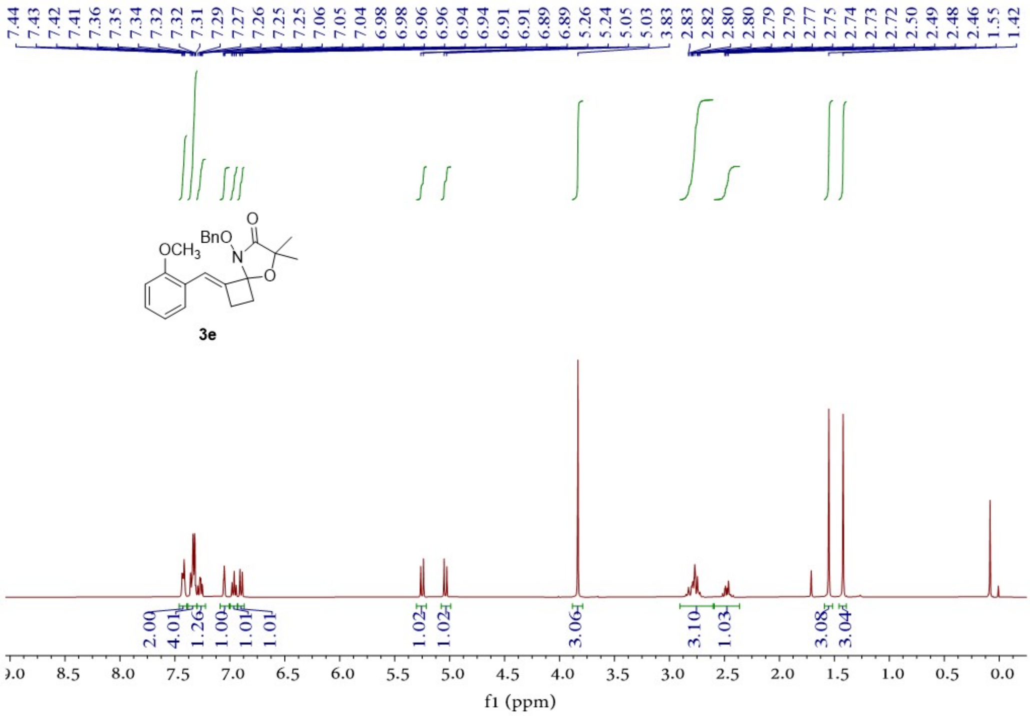


Fig. S9 ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3e**.

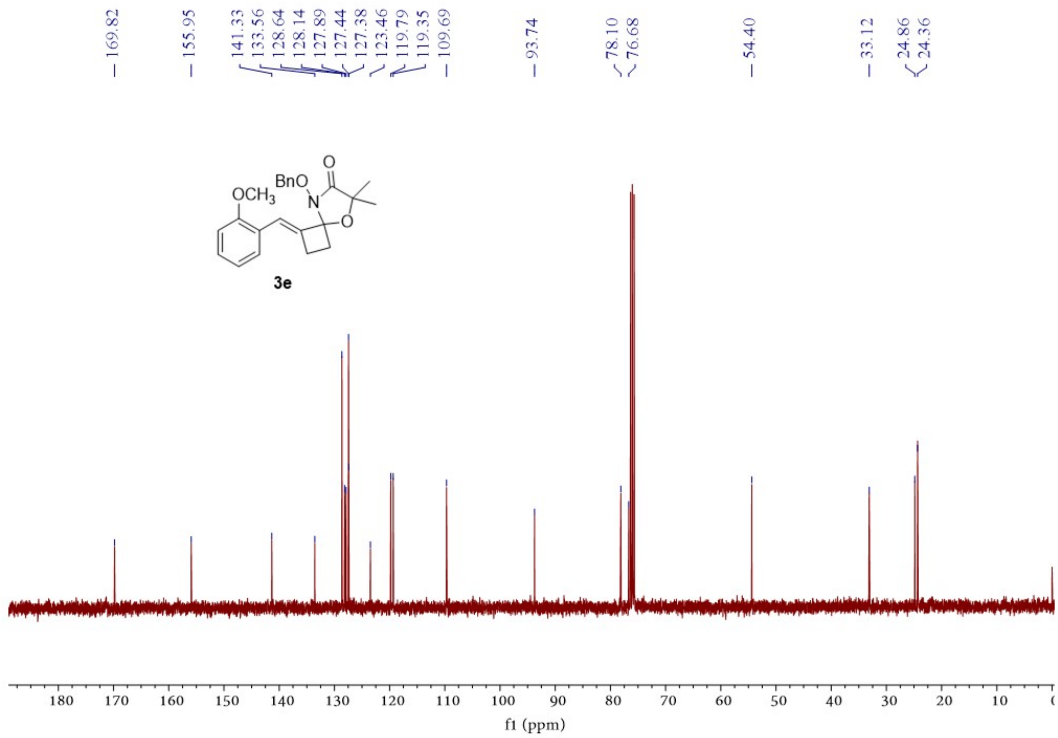


Fig. S10 ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3e**.

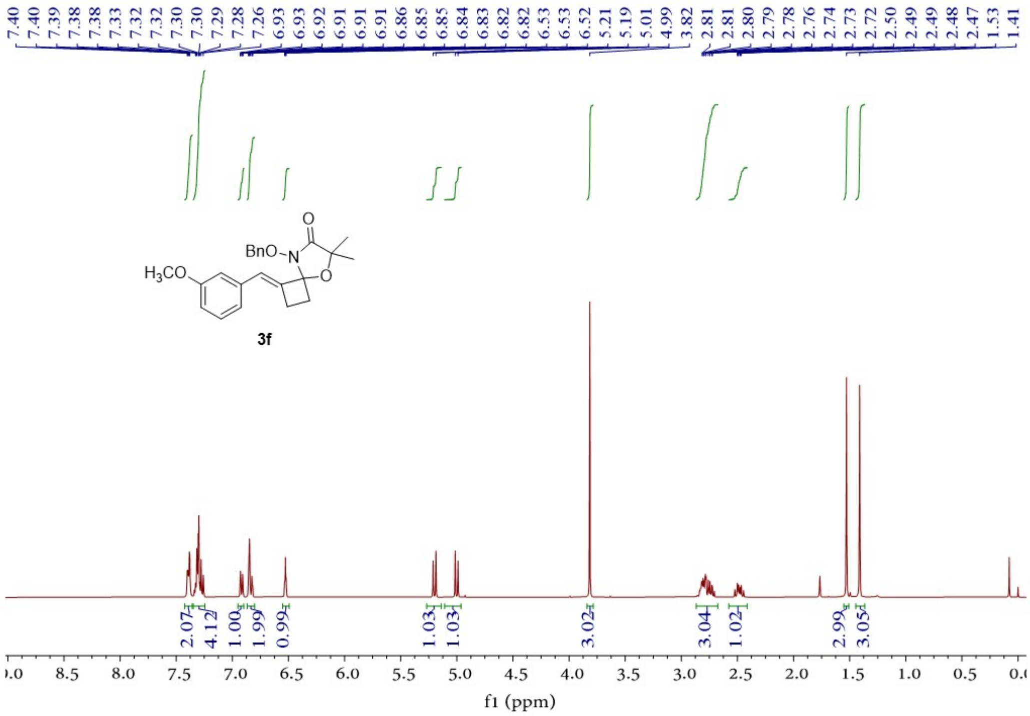


Fig. S11 [1]H NMR (400 MHz, $CDCl_3$) spectrum of **3f**.

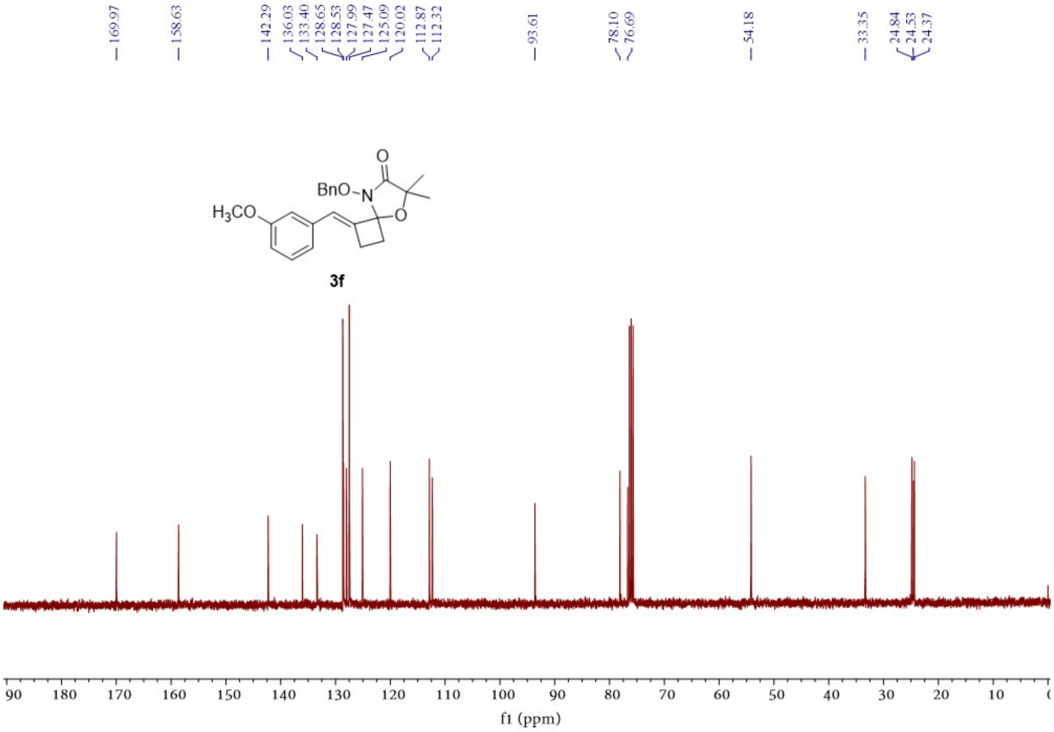


Fig. S12 [13]C NMR (100 MHz, $CDCl_3$) spectrum of **3f**.

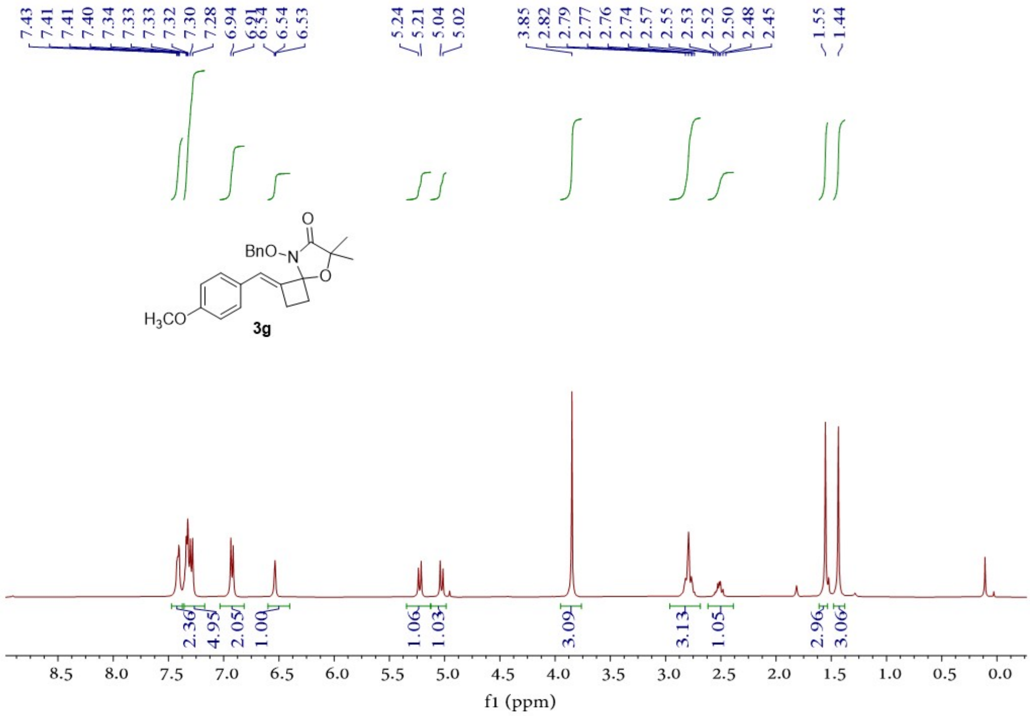


Fig. S13 ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3g**.

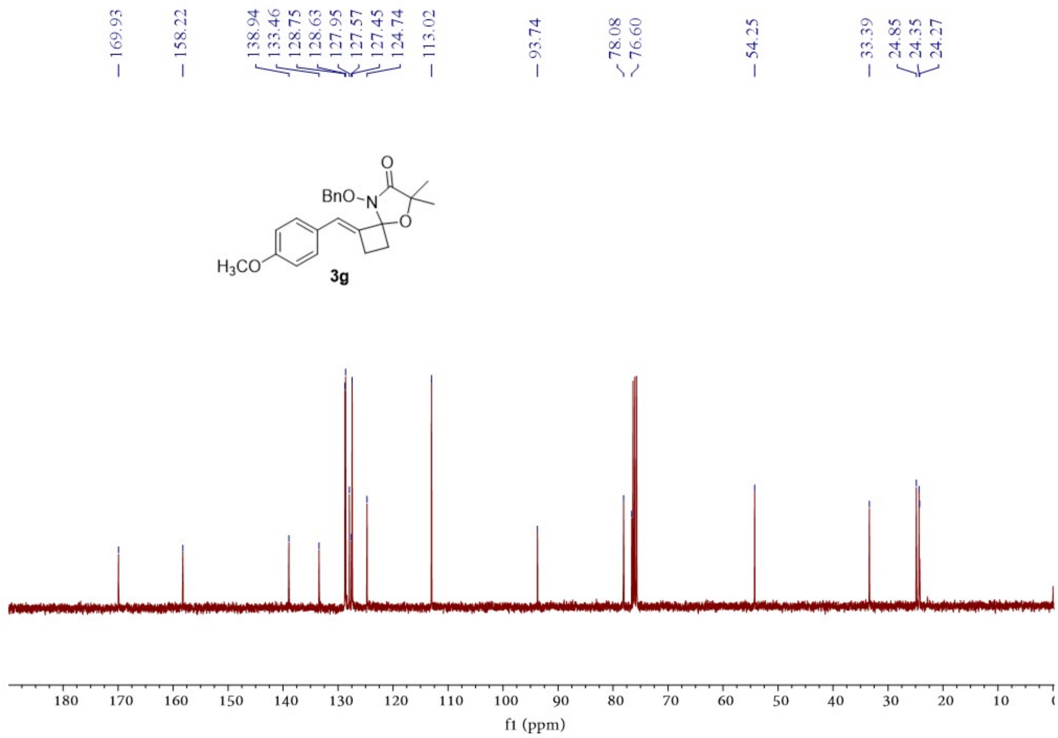


Fig. S14 ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3g**.

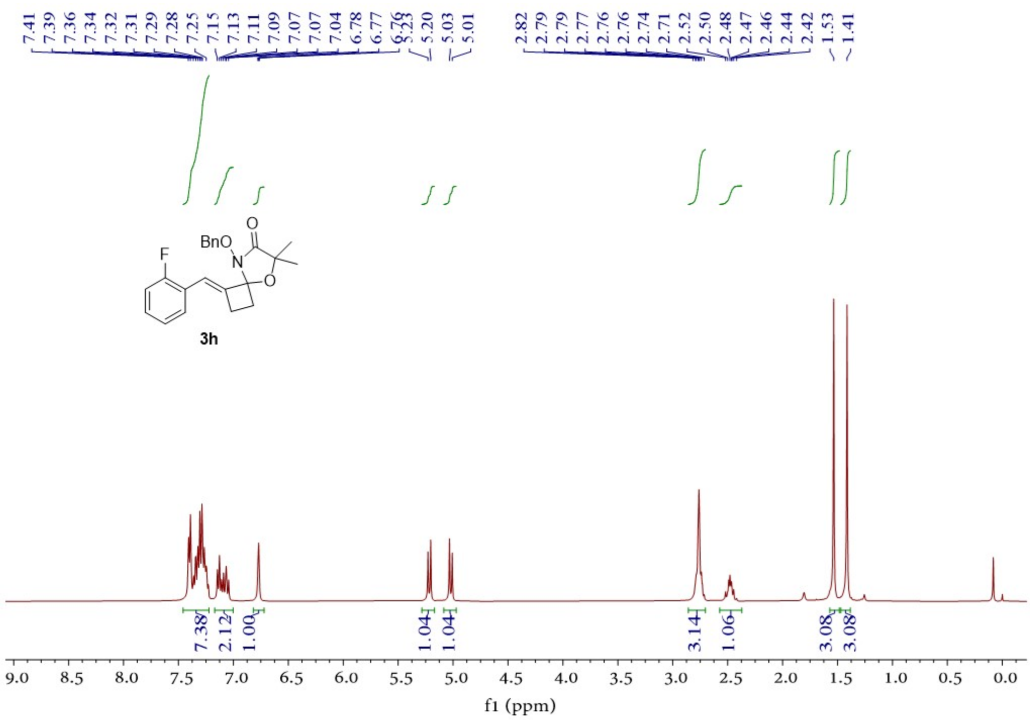


Fig. S15 [1]H NMR (400 MHz, $CDCl_3$) spectrum of **3h**.

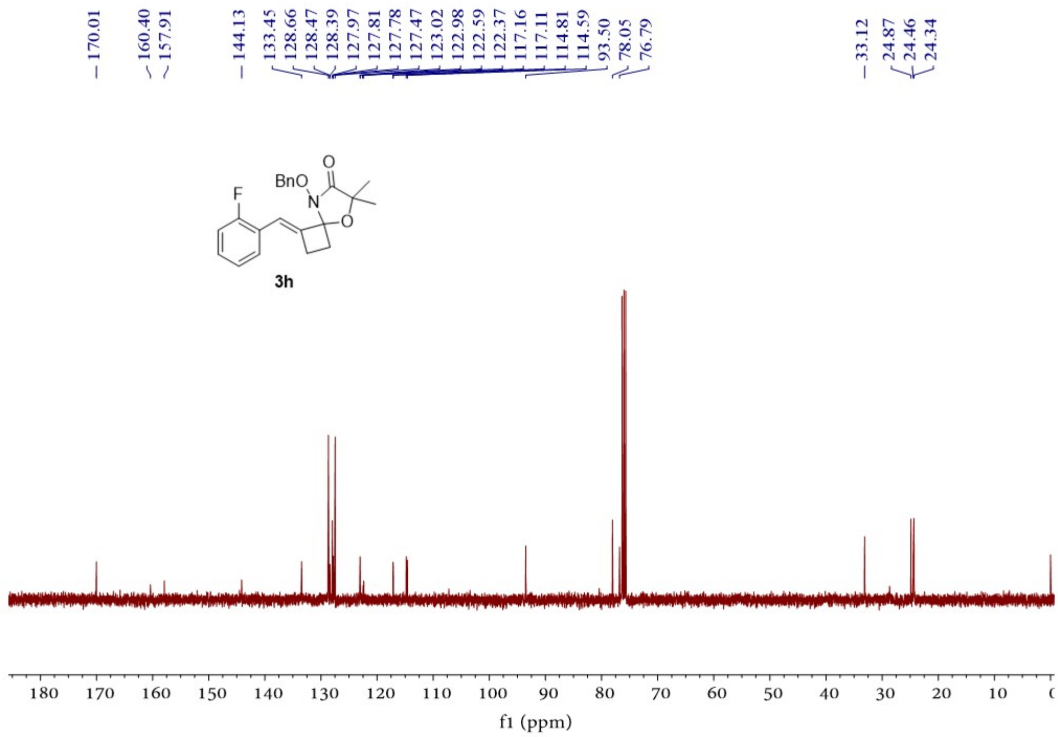


Fig. S16 [13]C NMR (100 MHz, $CDCl_3$) spectrum of **3h**.

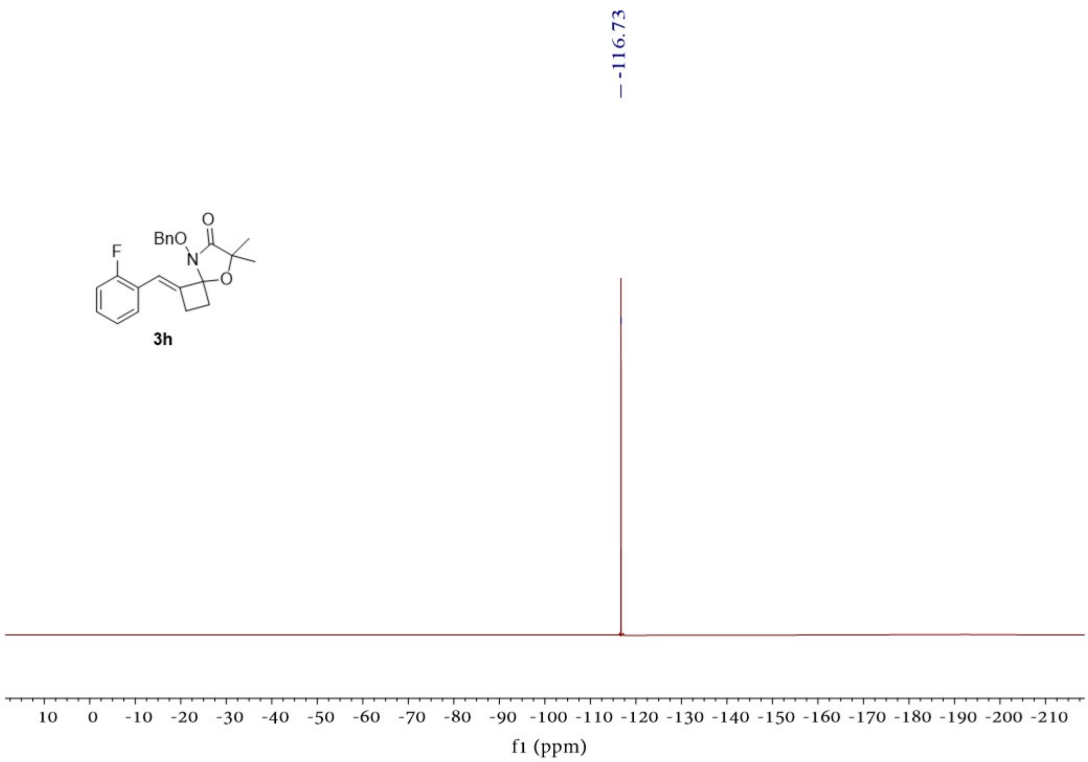


Fig. S17 [19]F NMR (376 MHz, $CDCl_3$) spectrum of **3h**.

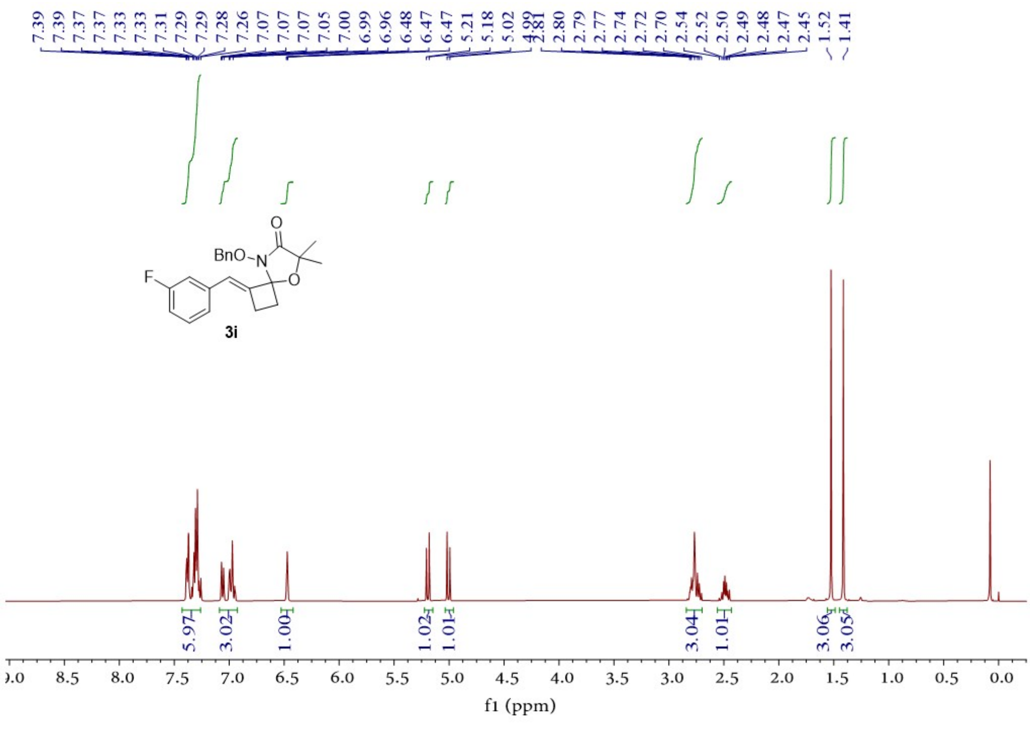


Fig. S18 [1]H NMR (400 MHz, $CDCl_3$) spectrum of **3i**.

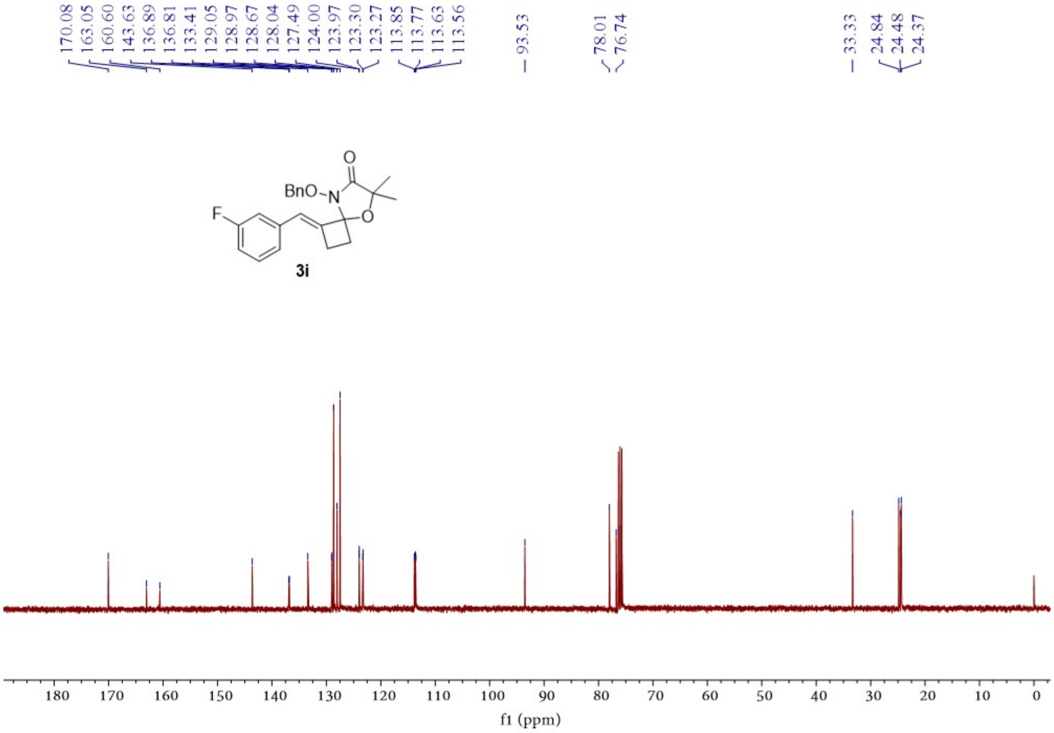


Fig. S19 ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3i**.

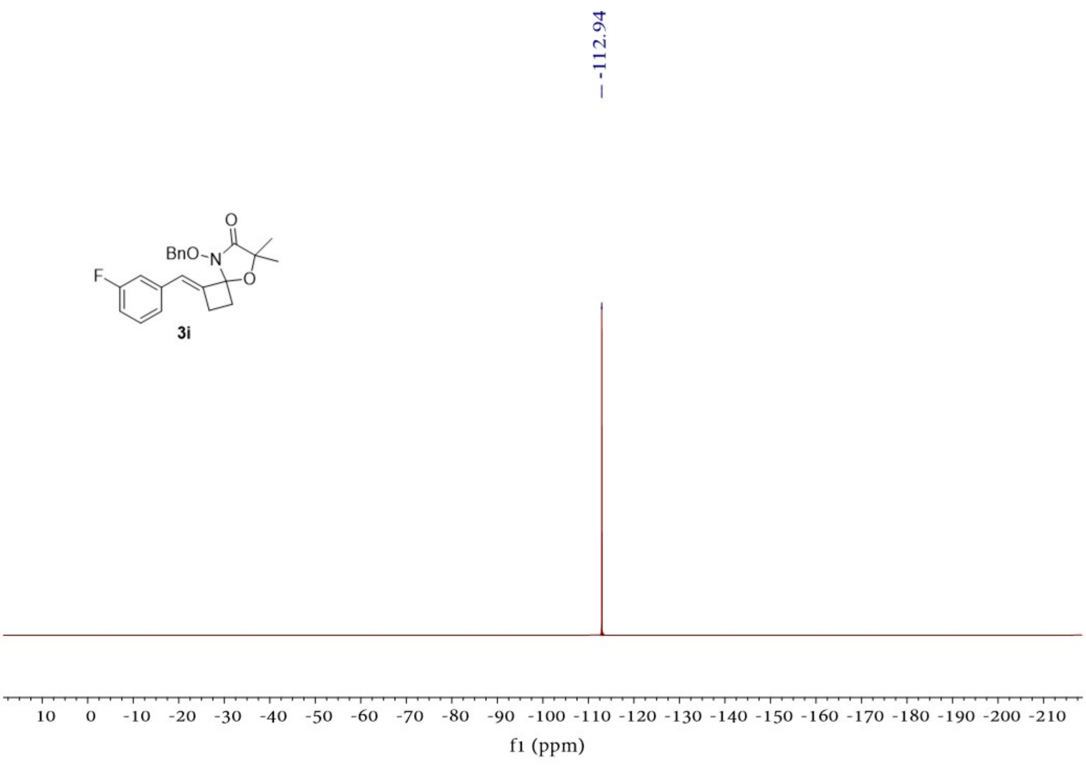


Fig. S20 ^{19}F NMR (376 MHz, $CDCl_3$) spectrum of **3i**.

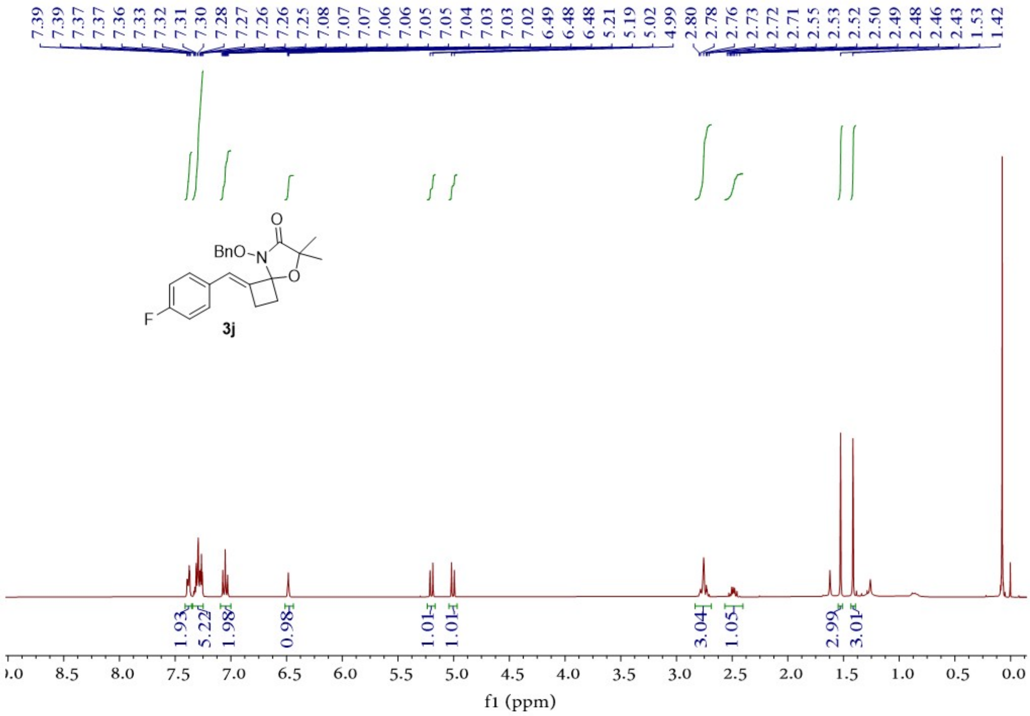


Fig. S21 ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3j**.

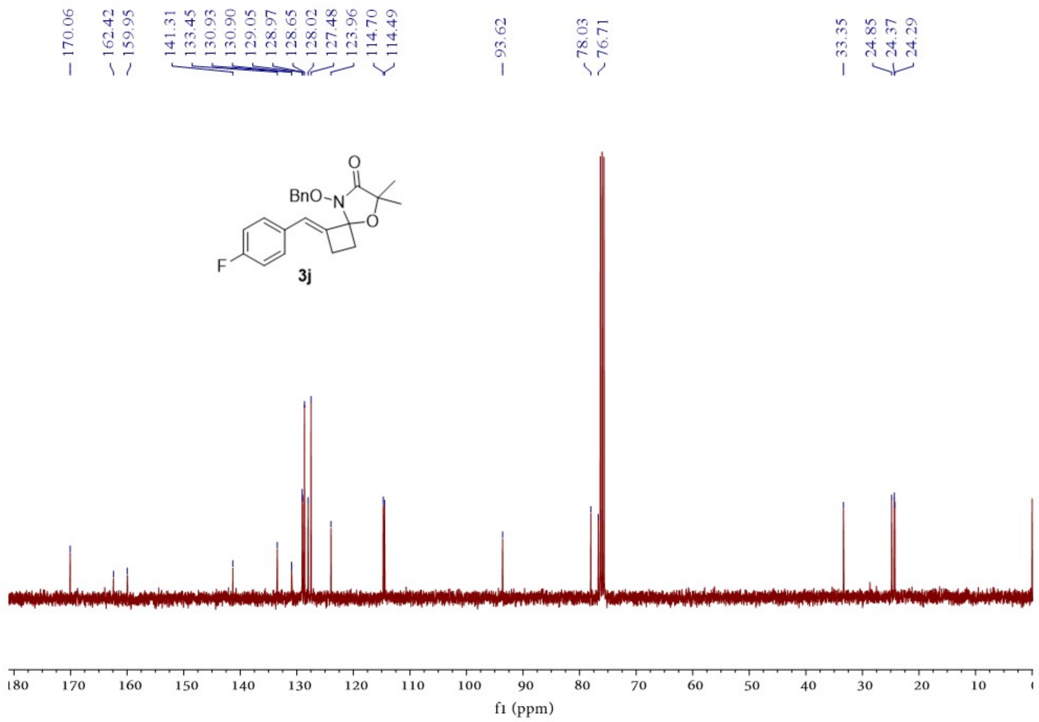


Fig. S22 ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3j**.

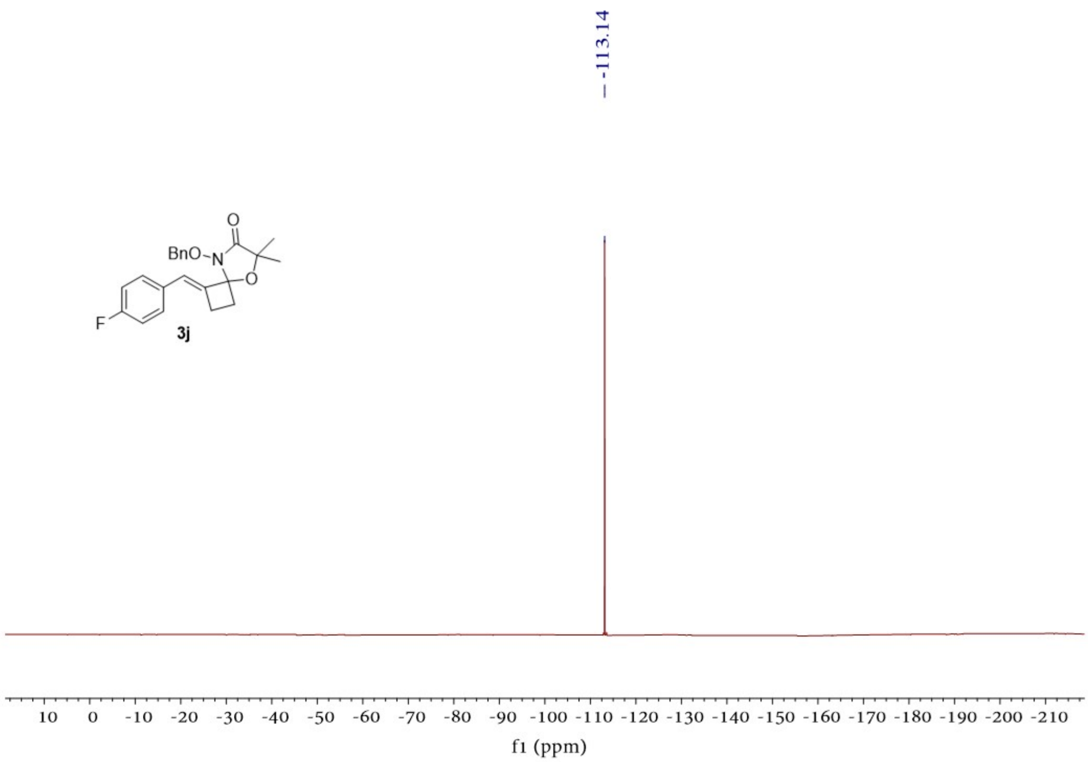


Fig. S23 [19]F NMR (376 MHz, $CDCl_3$) spectrum of **3j**.

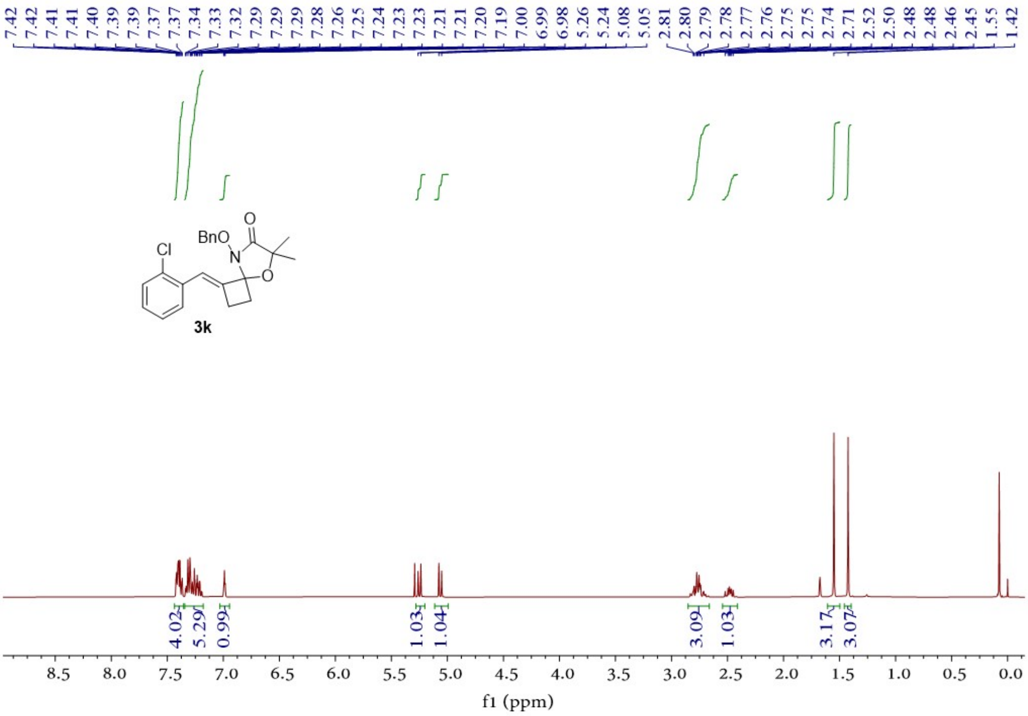


Fig. S24 [1]H NMR (400 MHz, $CDCl_3$) spectrum of **3k**.

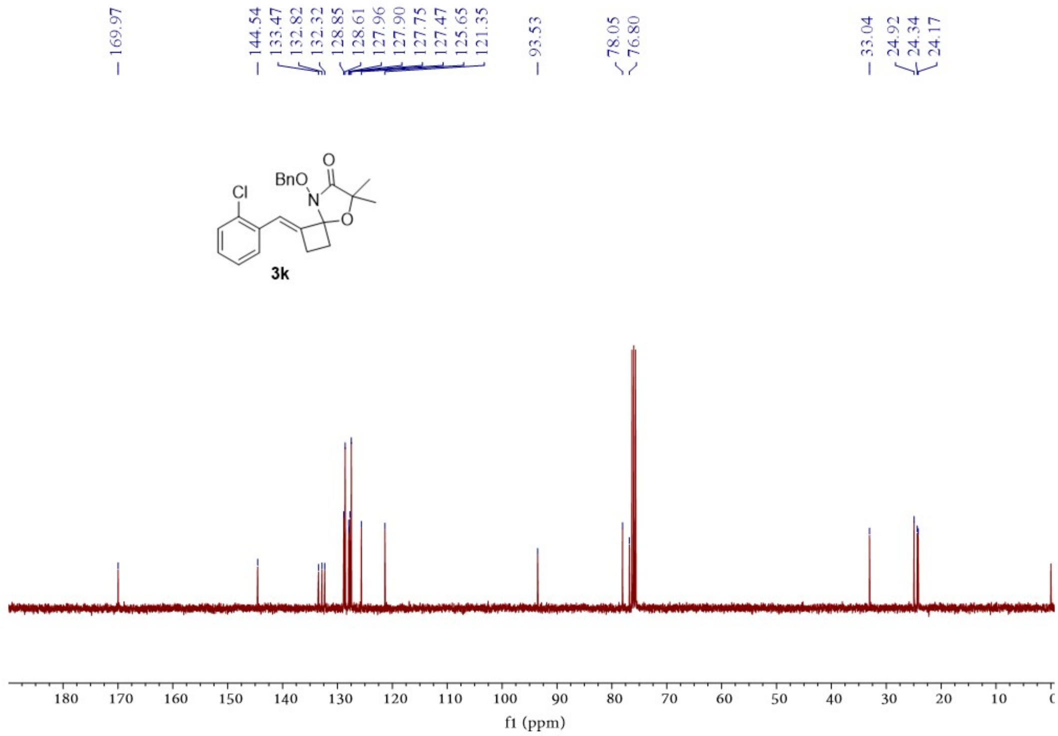


Fig. S25 ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3k**.

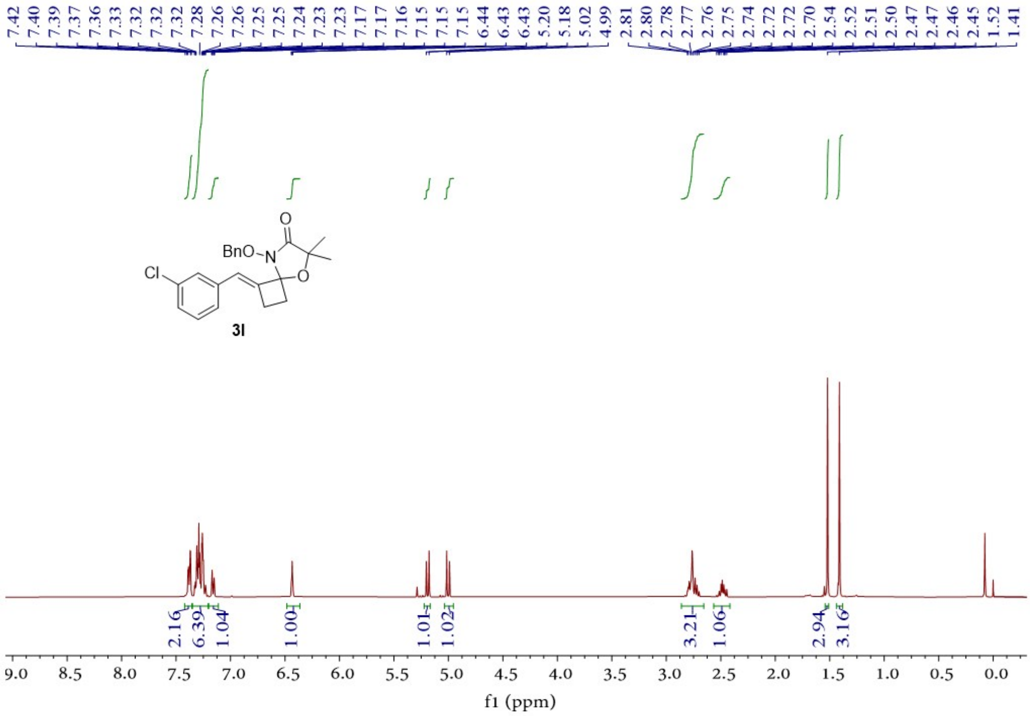


Fig. S26 ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3l**.

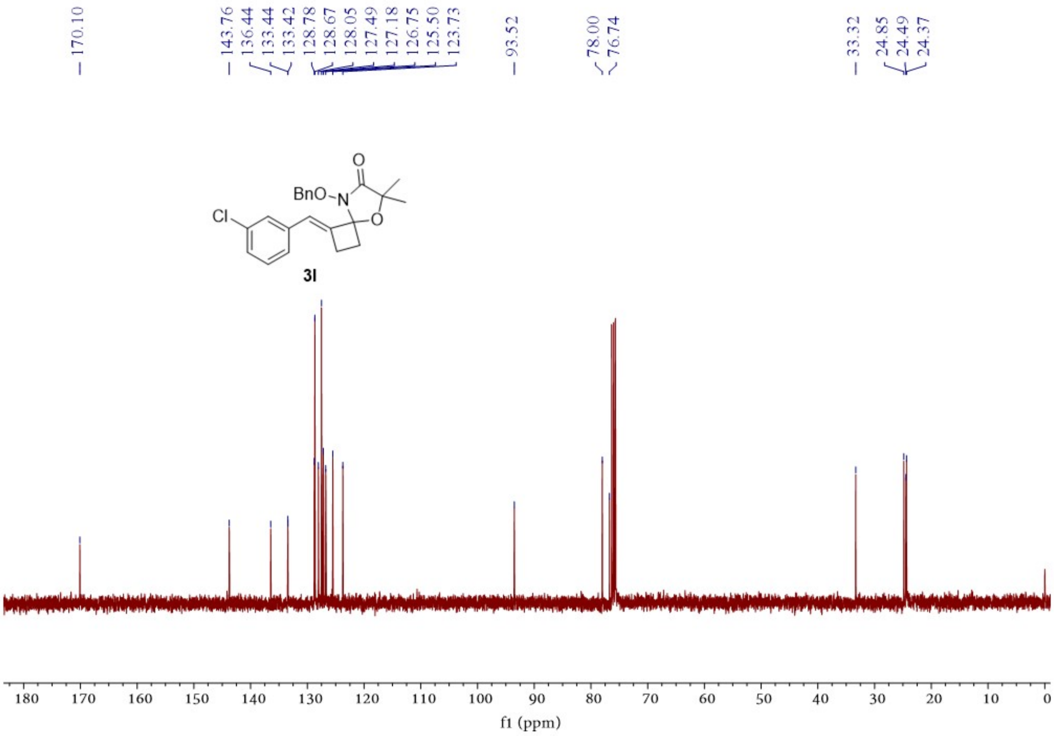


Fig. S27 ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3l**.

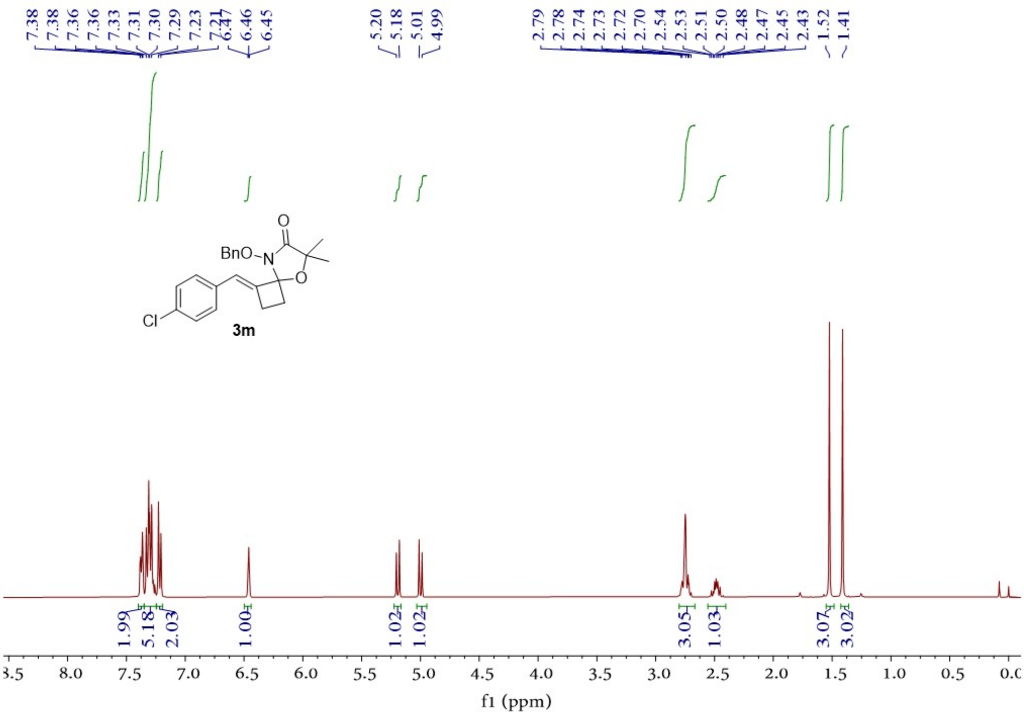


Fig. S28 ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3m**.

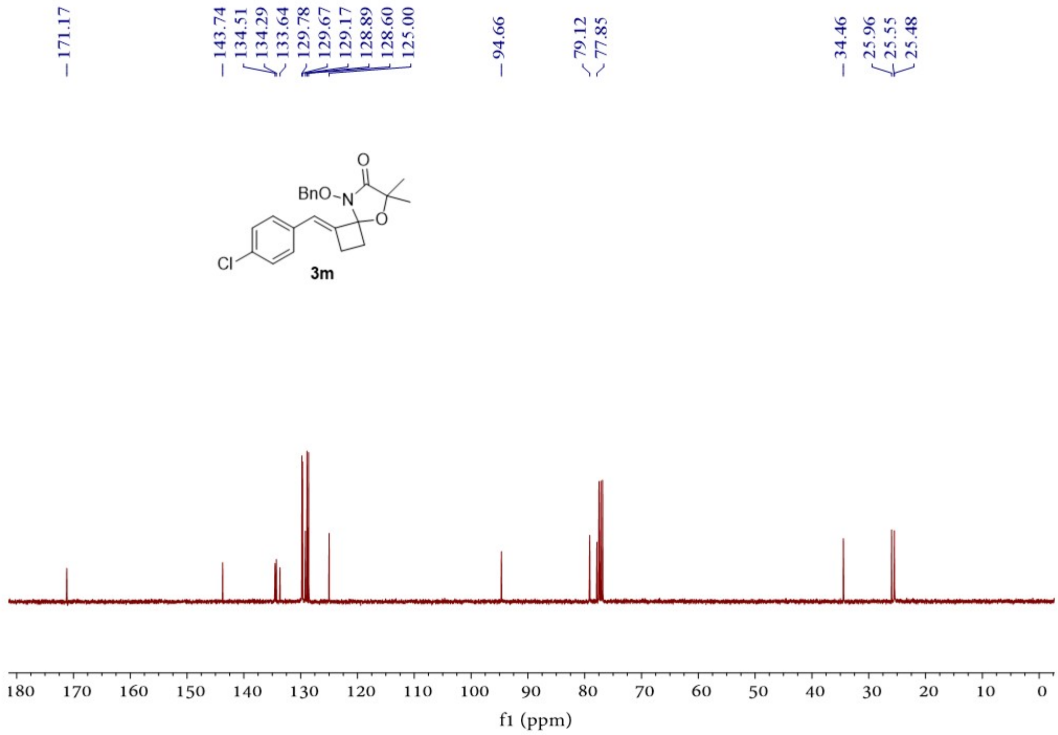


Fig. S29 ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3m**.

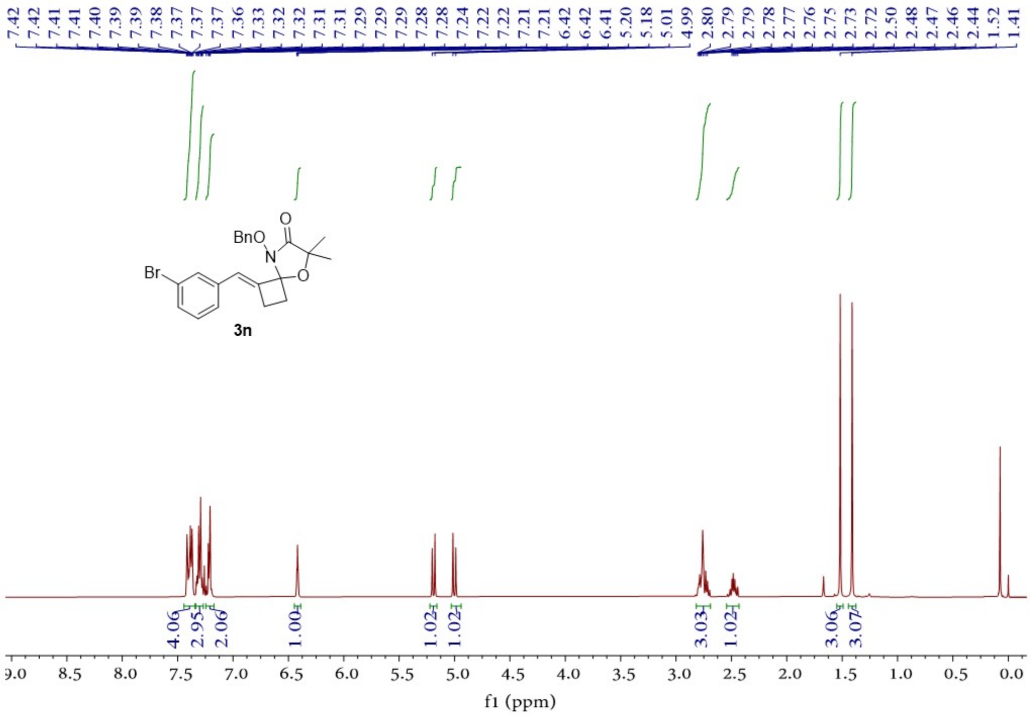


Fig. S30 ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3n**.

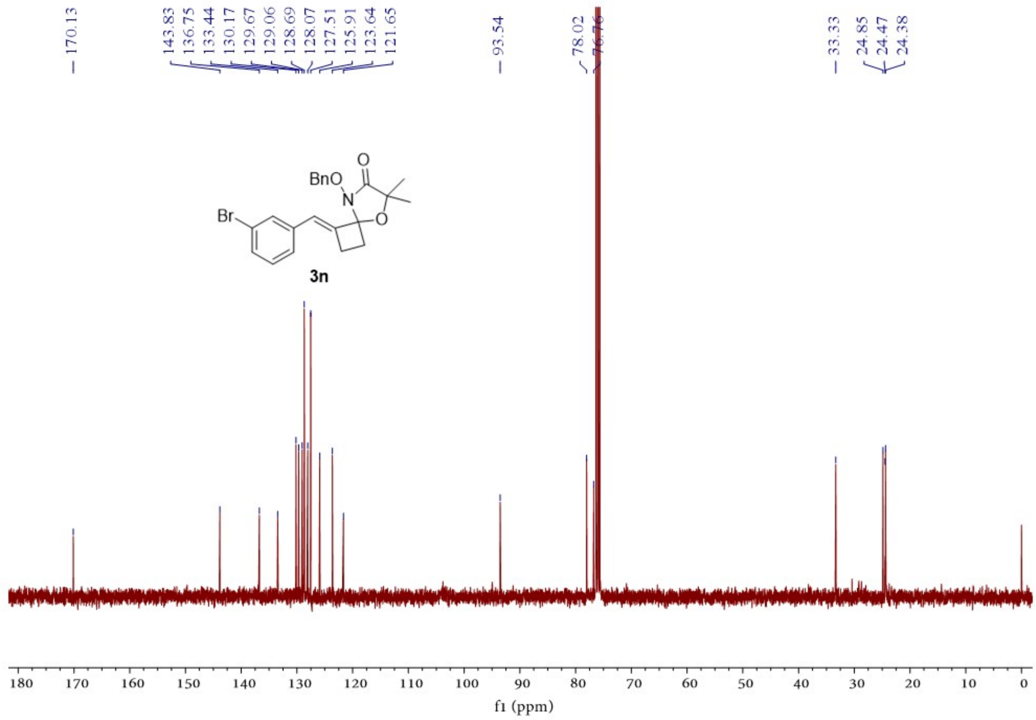


Fig. S31 ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3n**.

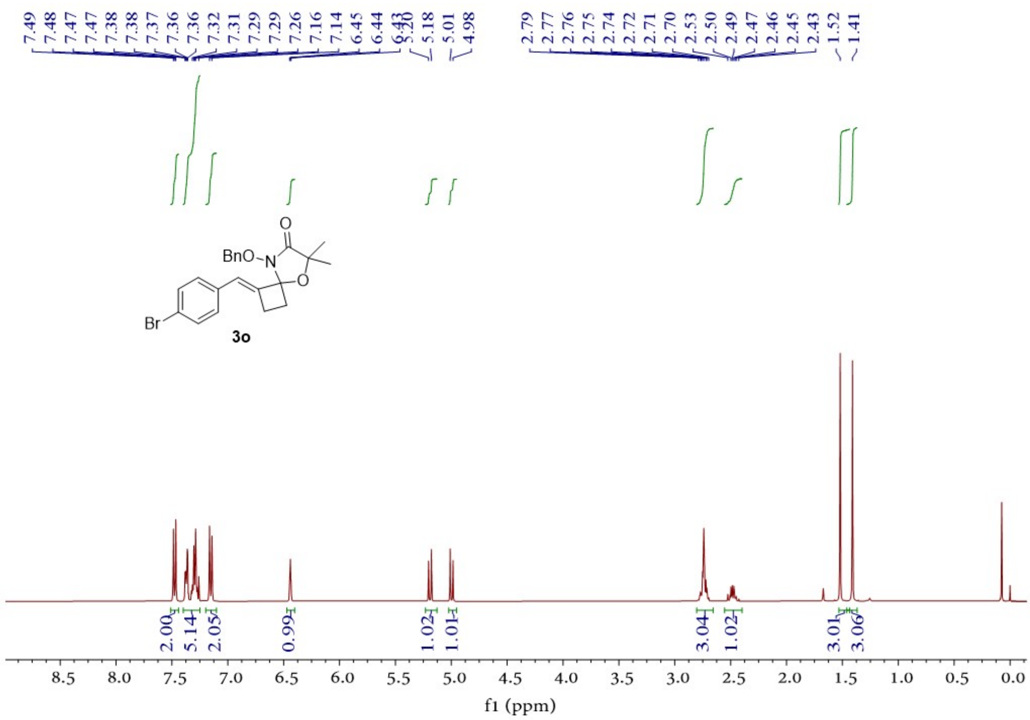


Fig. S32 ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3o**.

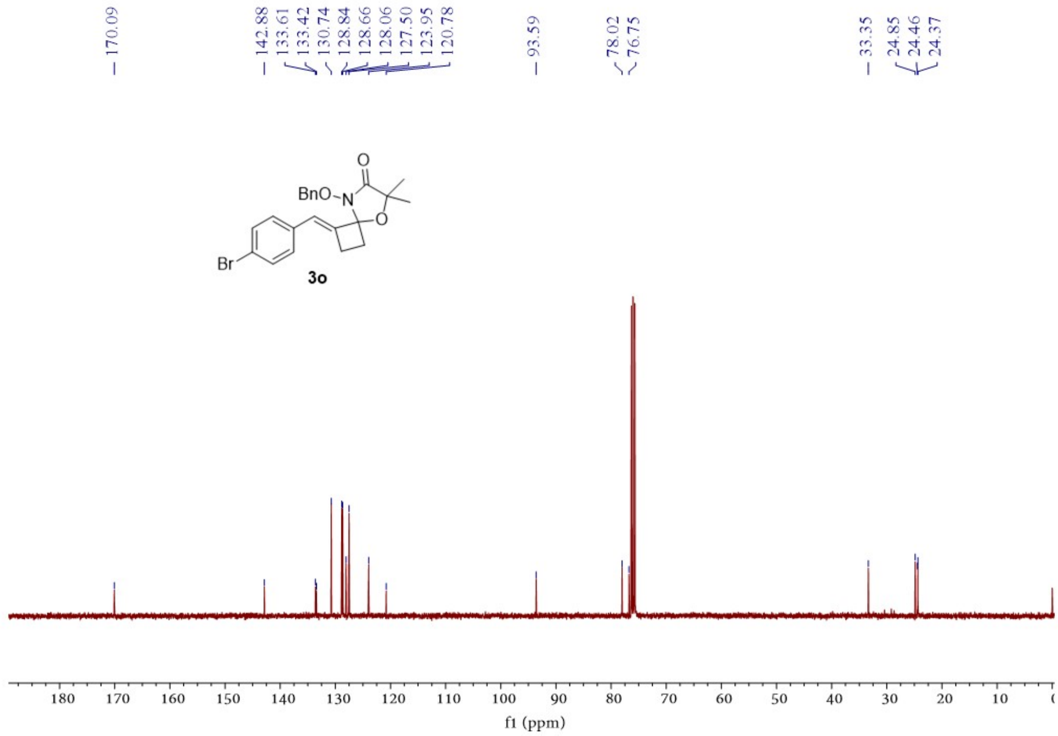


Fig. S33 ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3o**.

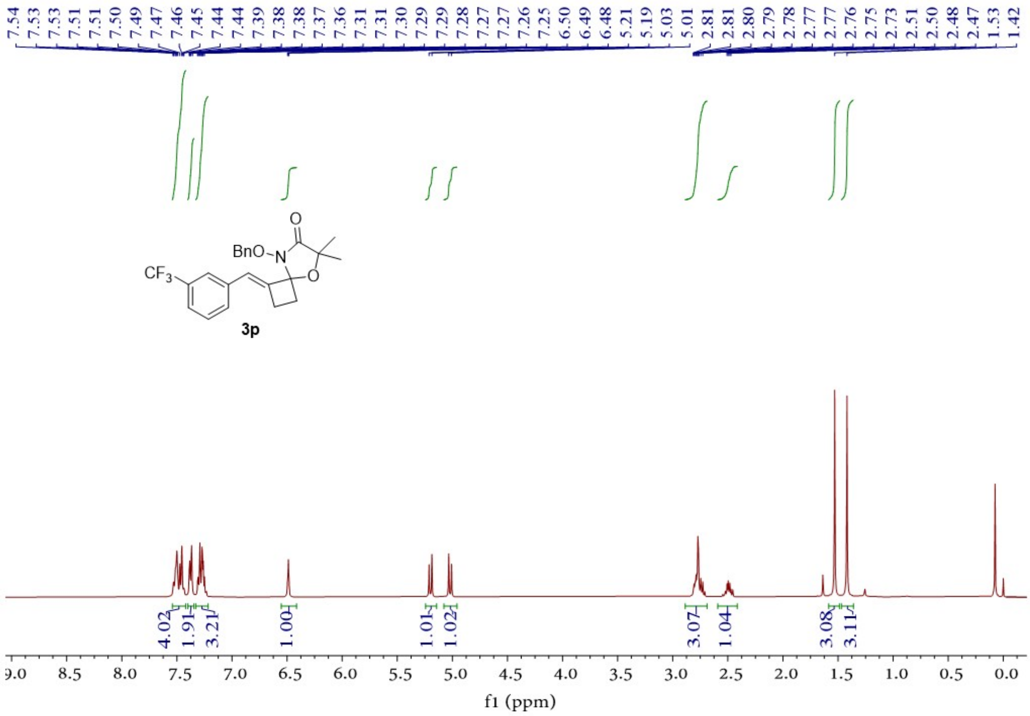


Fig. S34 ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3p**.

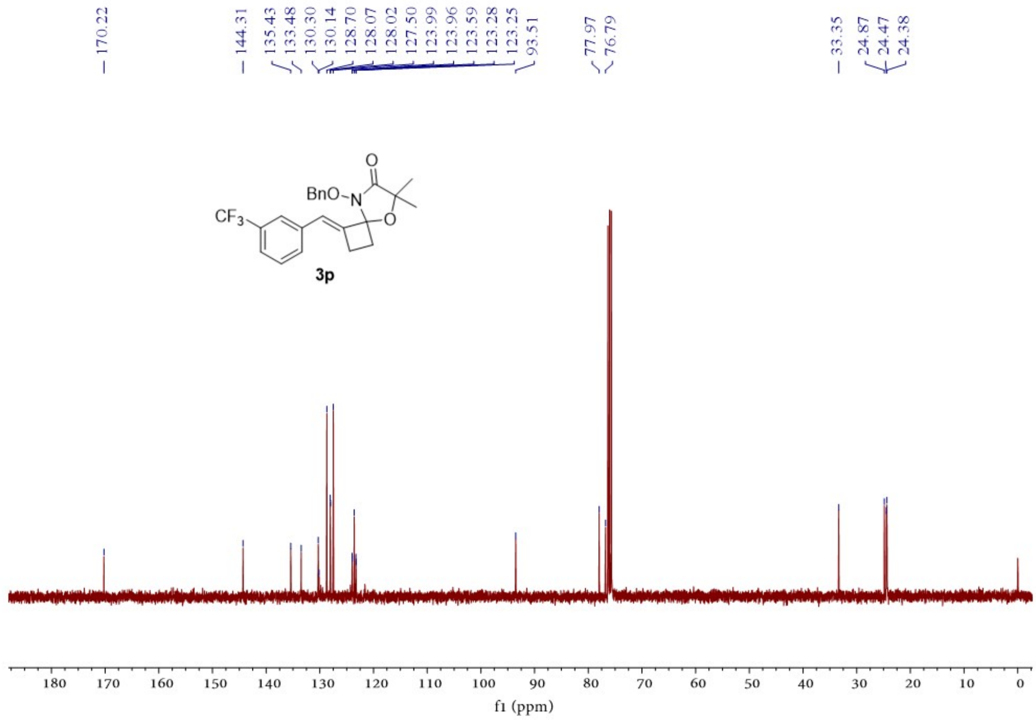


Fig. S35 ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3p**.

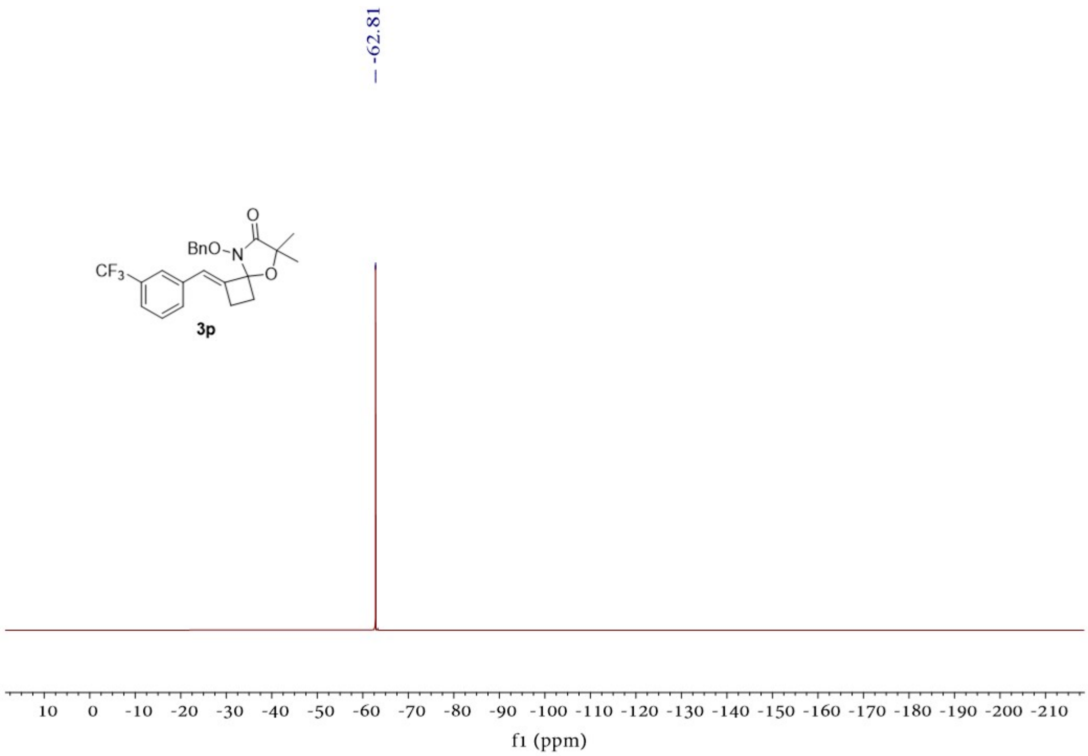


Fig. S36 ^{19}F NMR (376 MHz, $CDCl_3$) spectrum of **3p**.

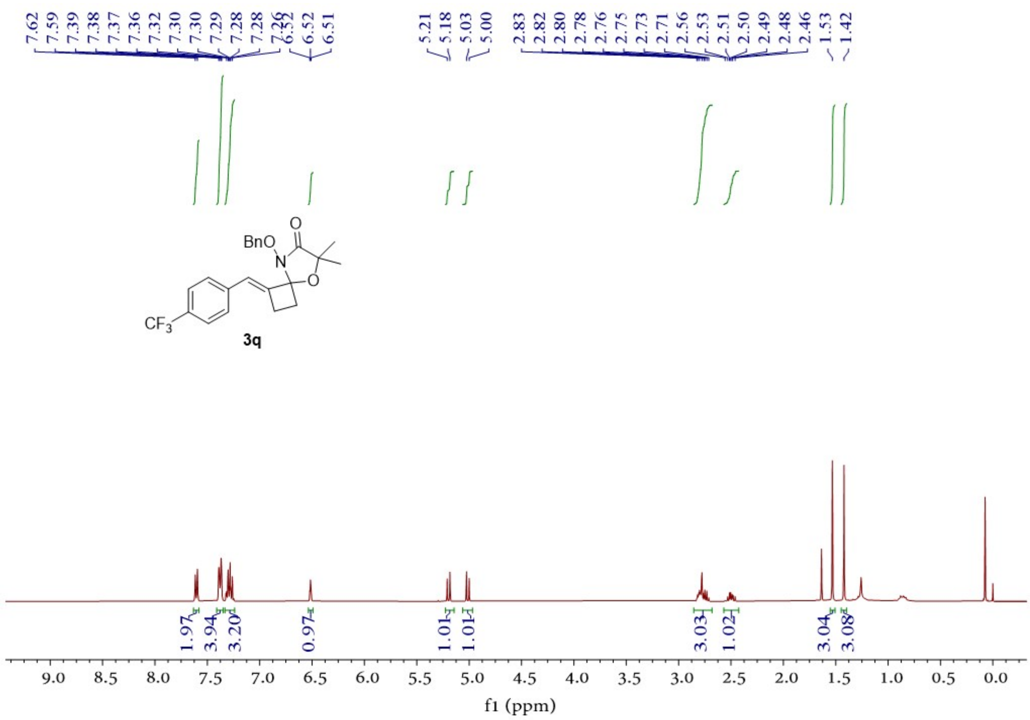


Fig. S37 ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3q**.

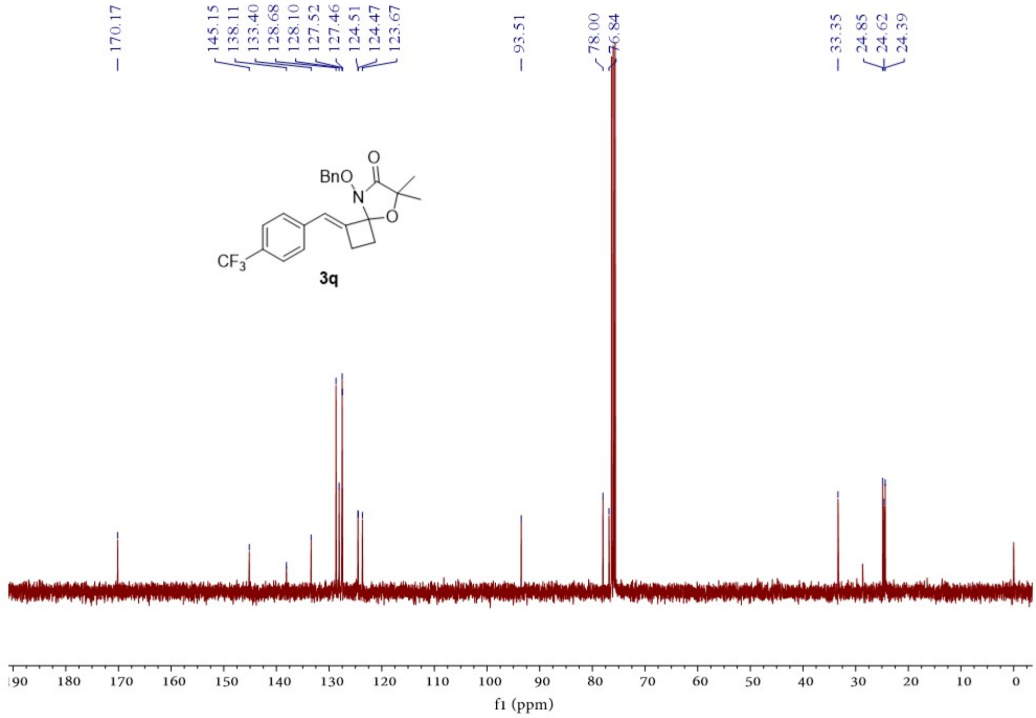


Fig. S38 ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3q**.

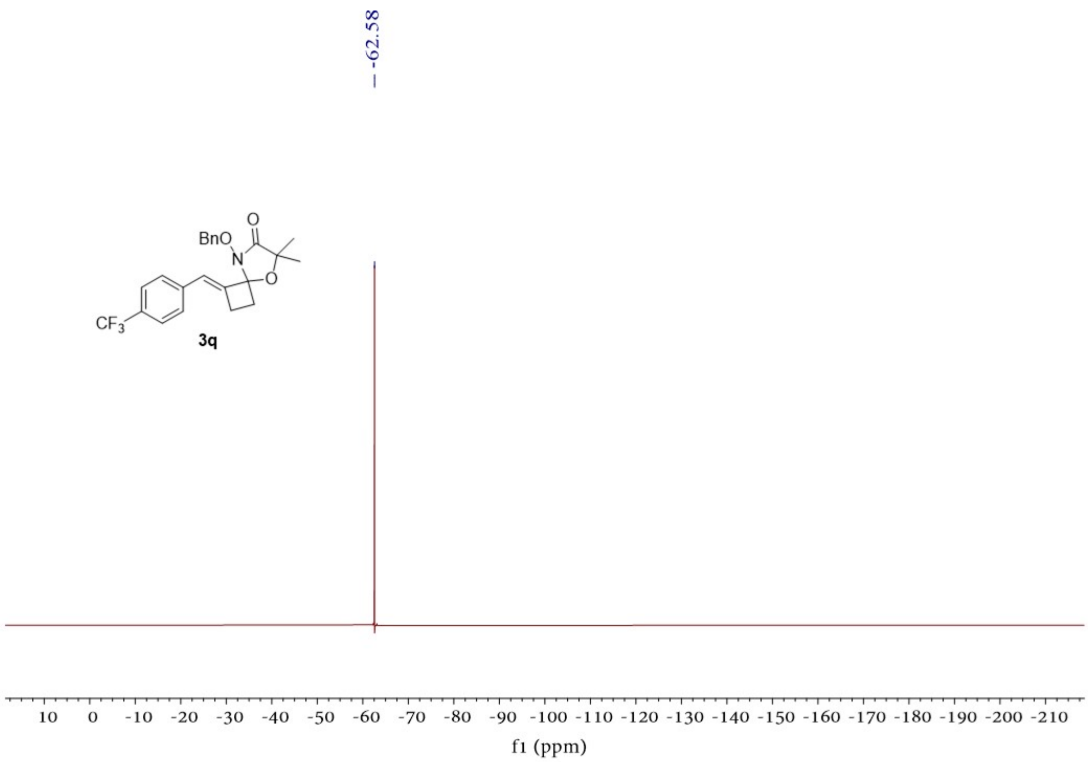


Fig. S39 ^{19}F NMR (376 MHz, $CDCl_3$) spectrum of **3q**.

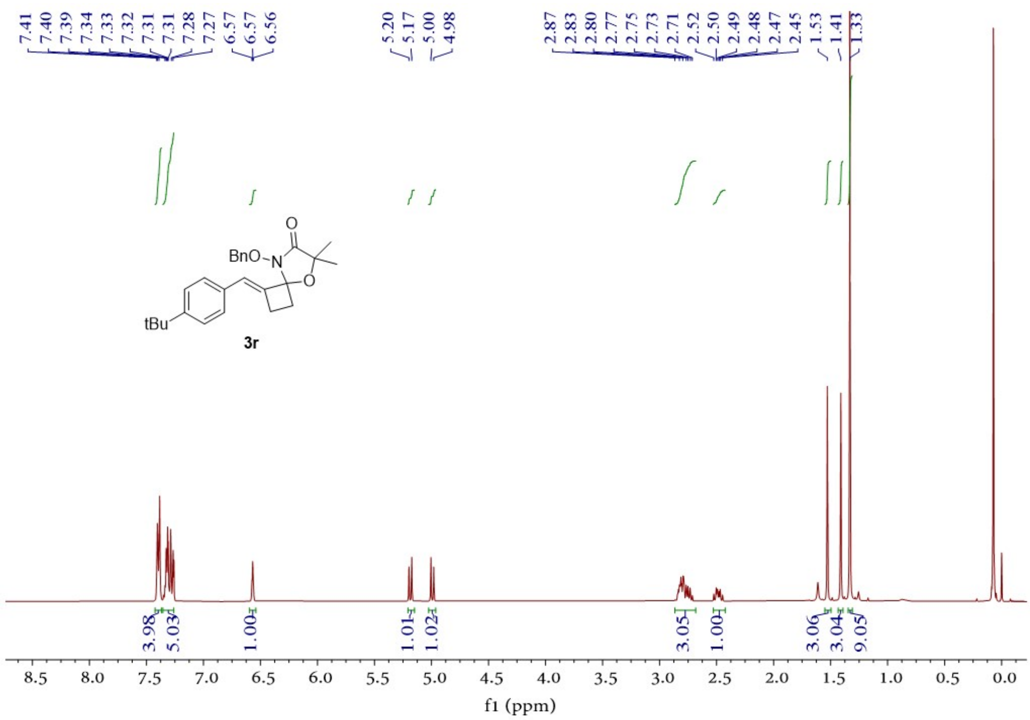


Fig. S40 ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3r**.

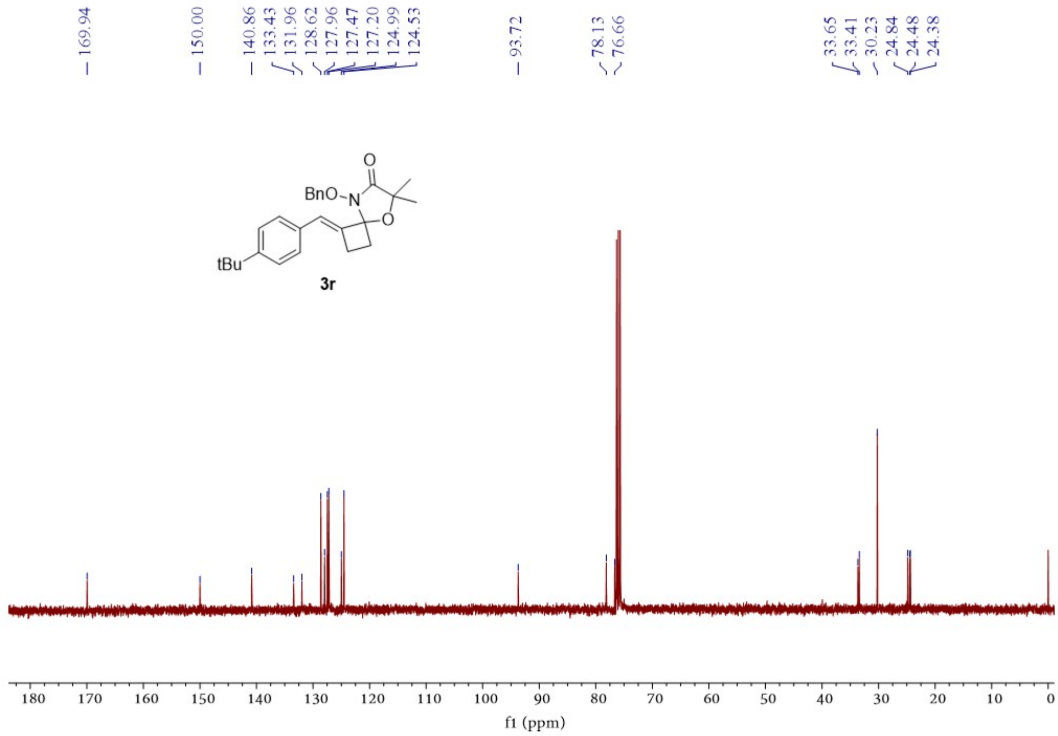


Fig. S41 ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3r**.

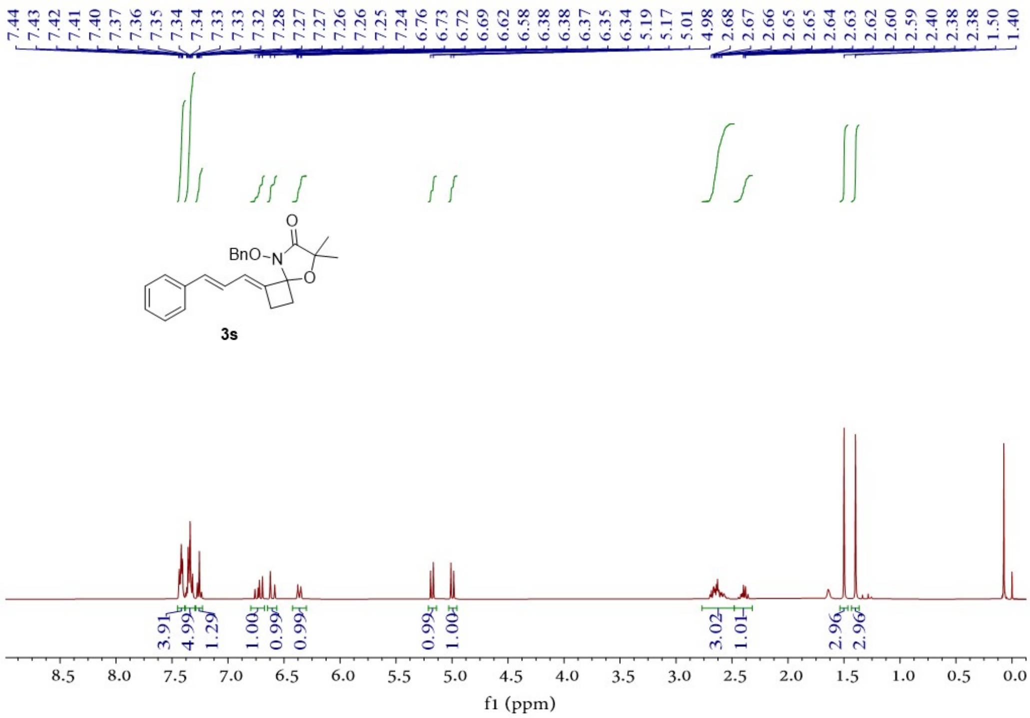


Fig. S42 ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3s**.

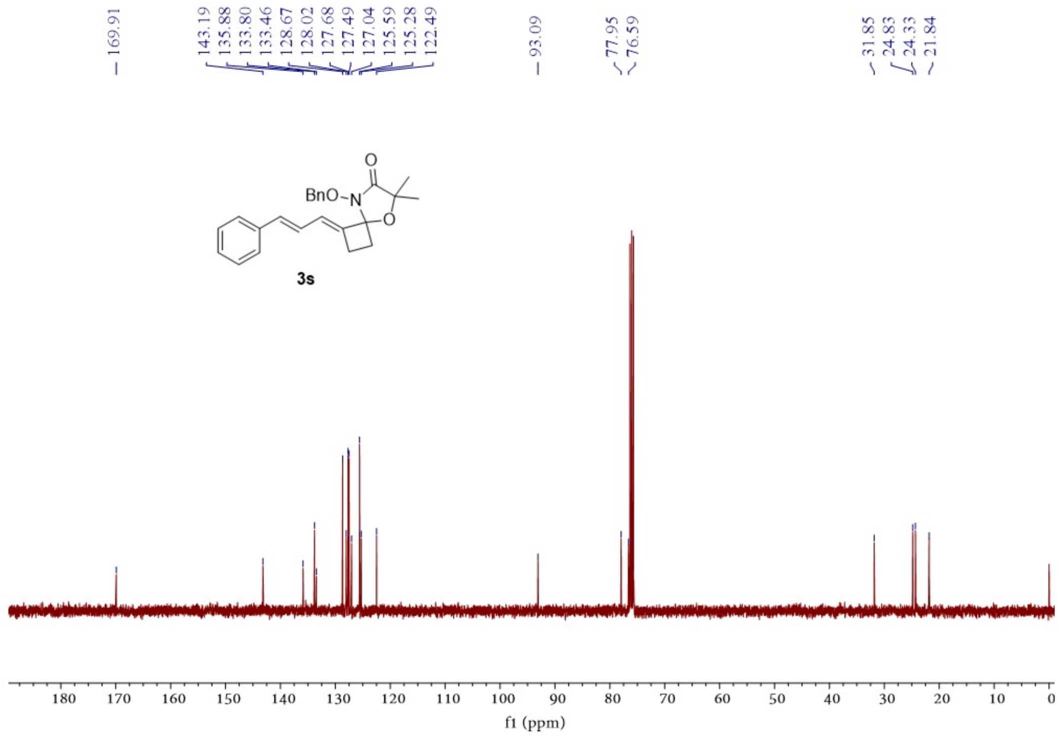


Fig. S43 ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3s**.

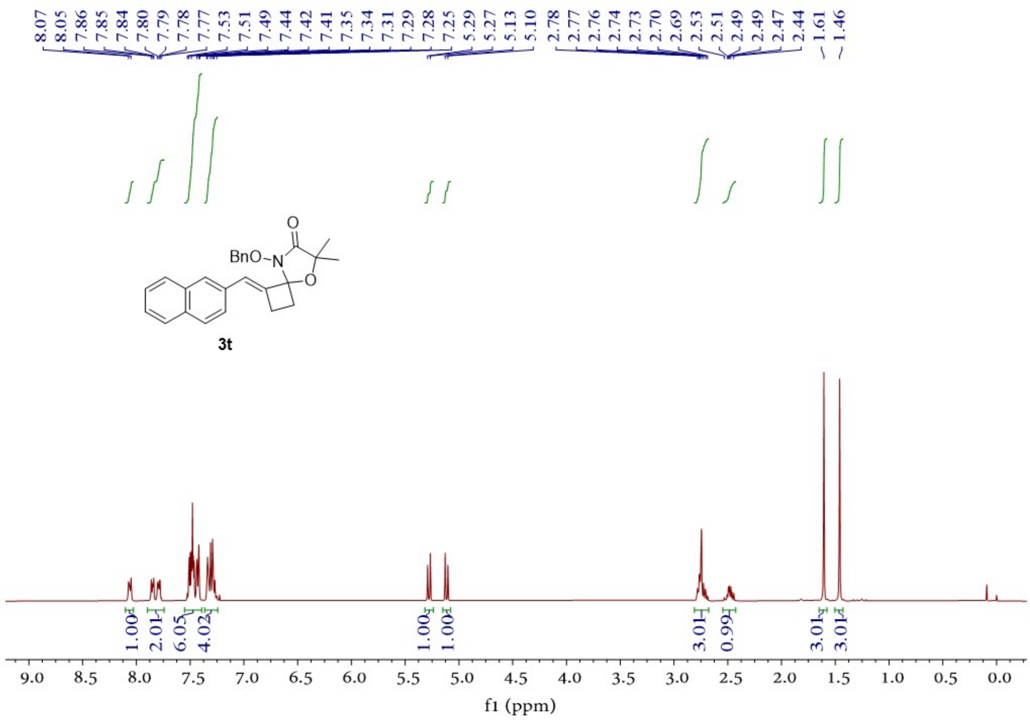


Fig. S44 ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3t**.

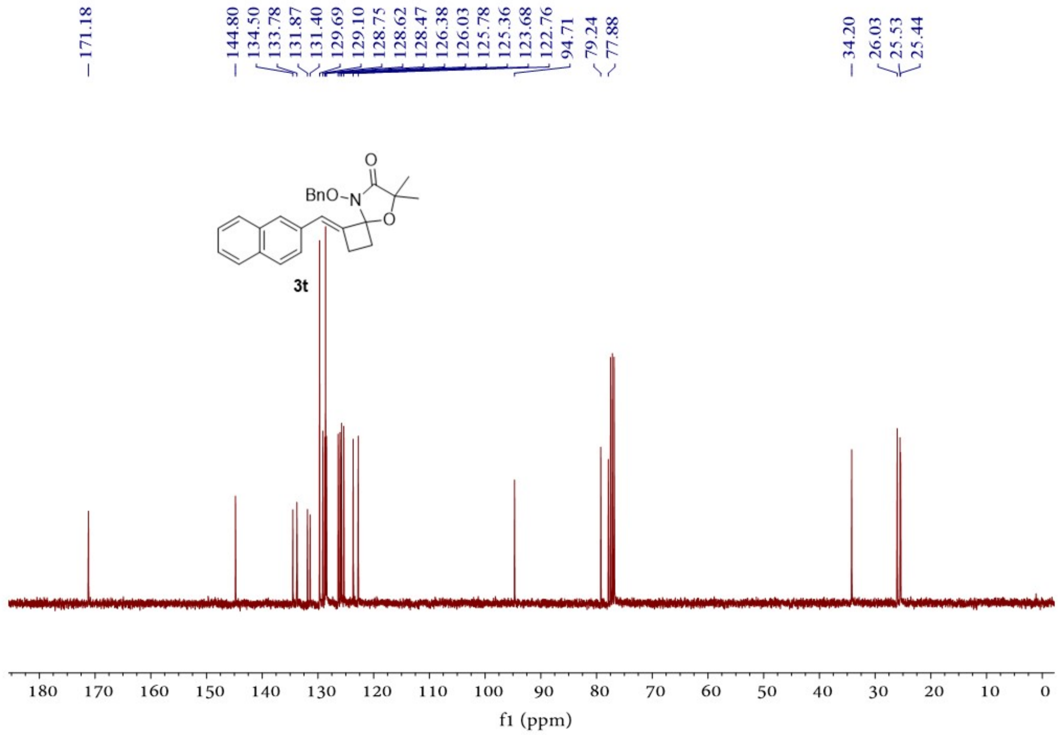


Fig. S45 [13]C NMR (100 MHz, $CDCl_3$) spectrum of **3t**.

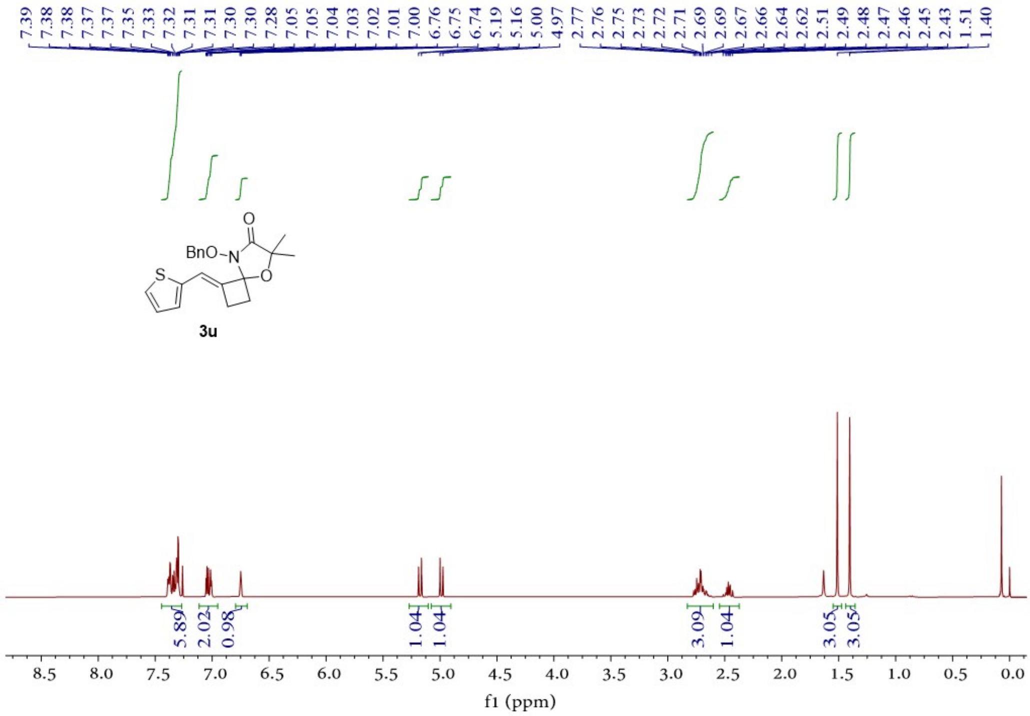


Fig. S46 [1]H NMR (400 MHz, $CDCl_3$) spectrum of **3u**.

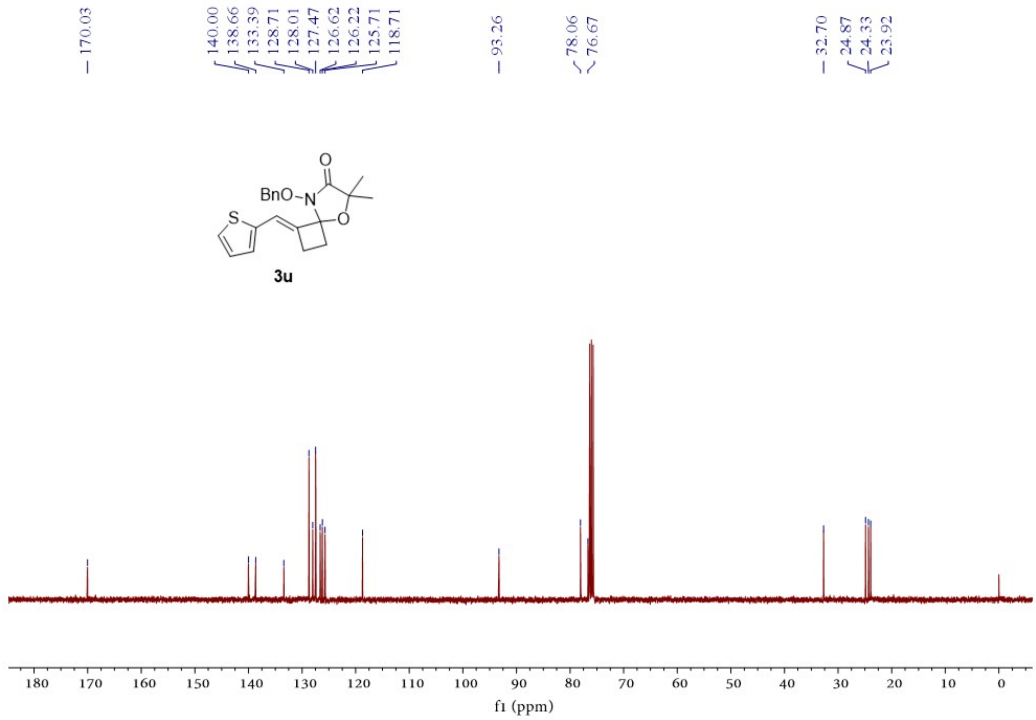


Fig. S47 ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3u**.

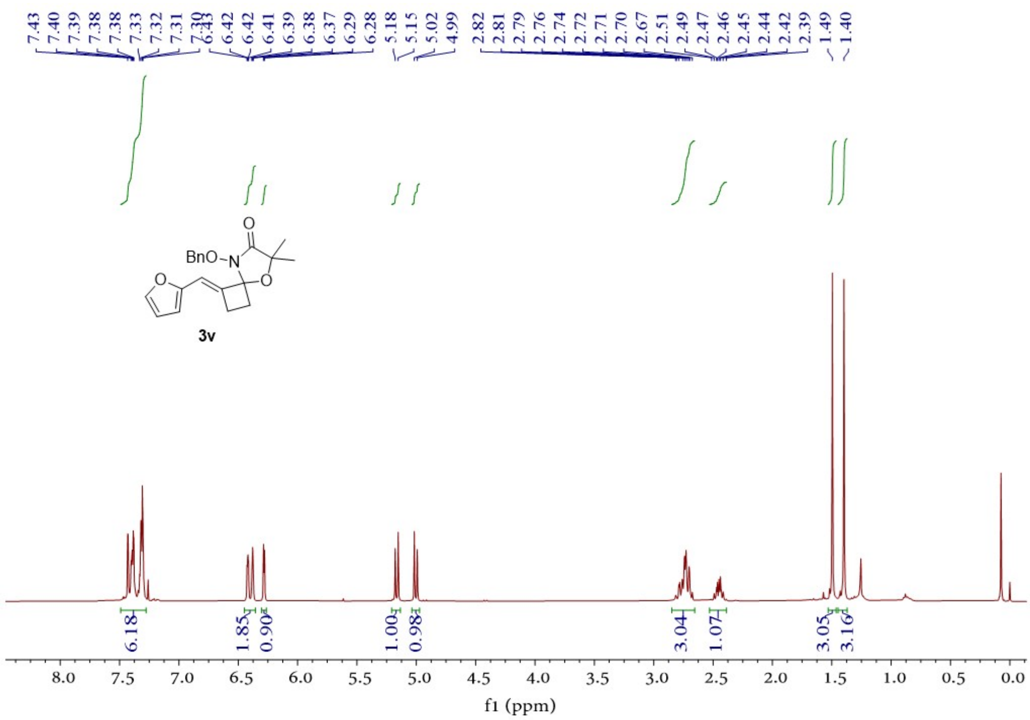


Fig. S48 ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3v**.

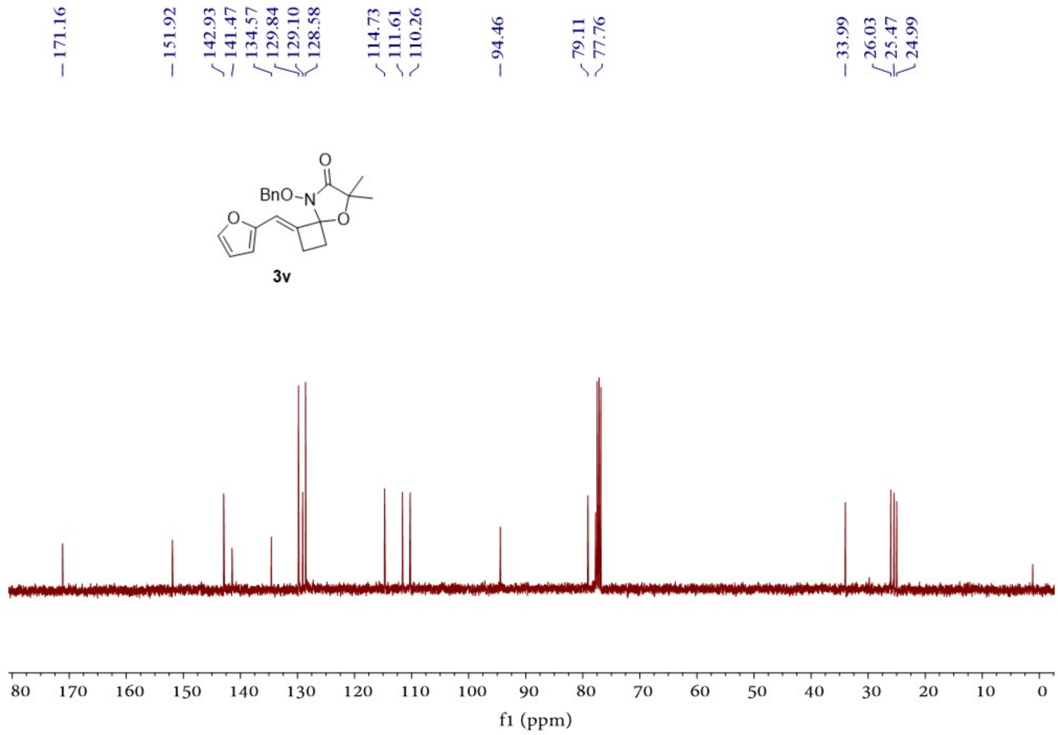


Fig. S49 ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3v**.

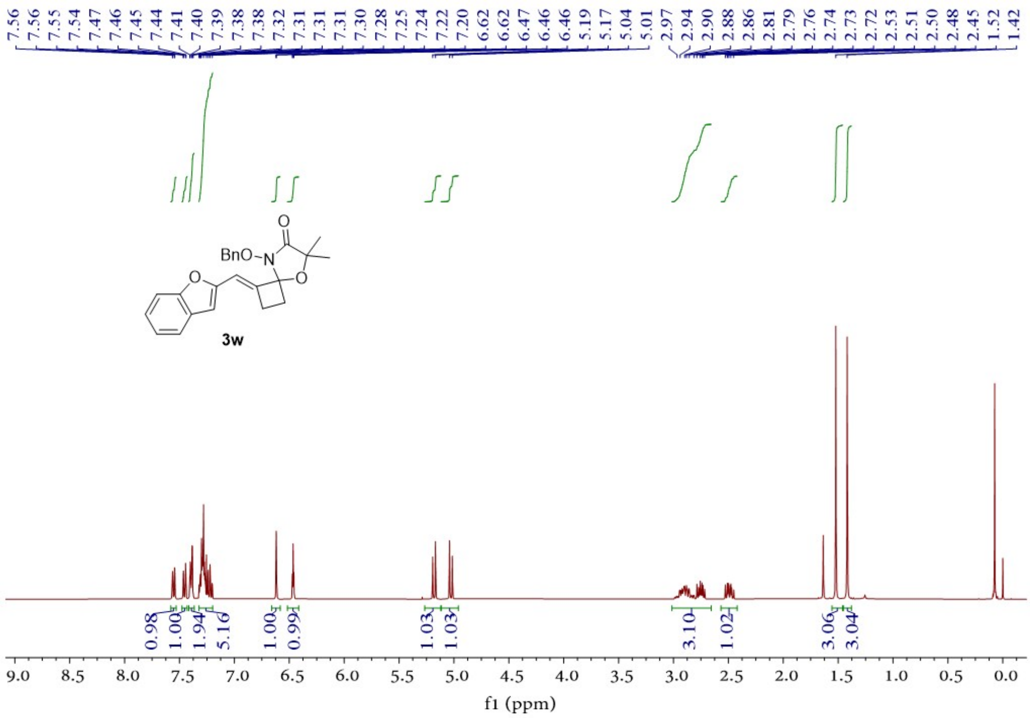


Fig. S50 ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3w**.

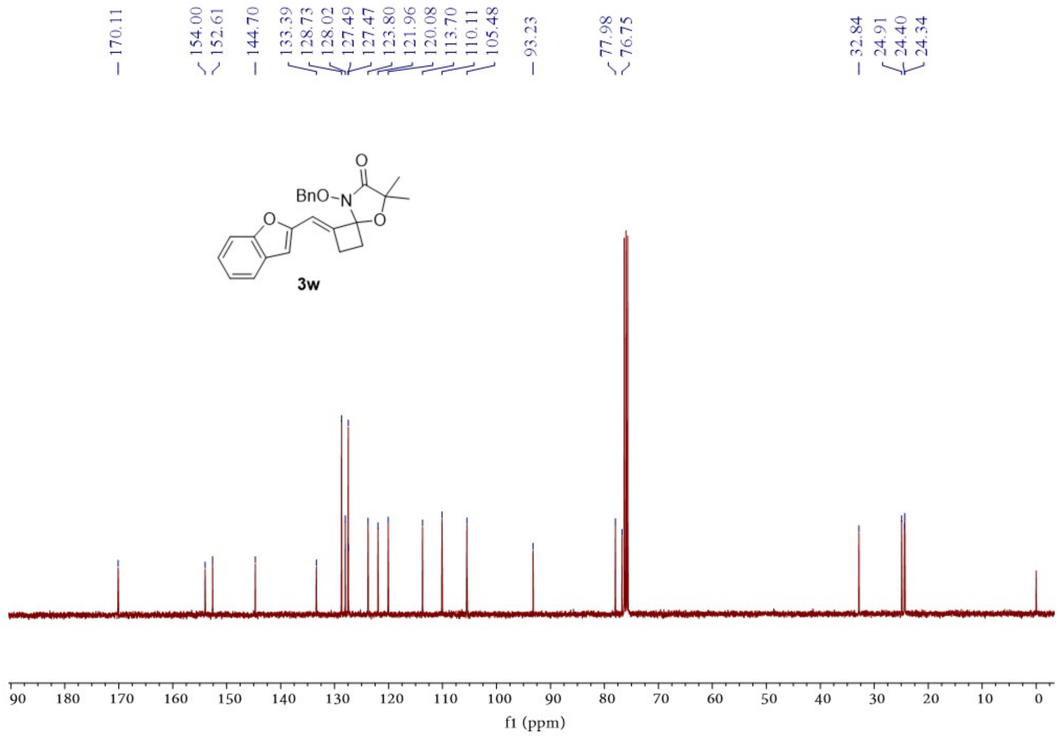


Fig. S51 ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3w**.

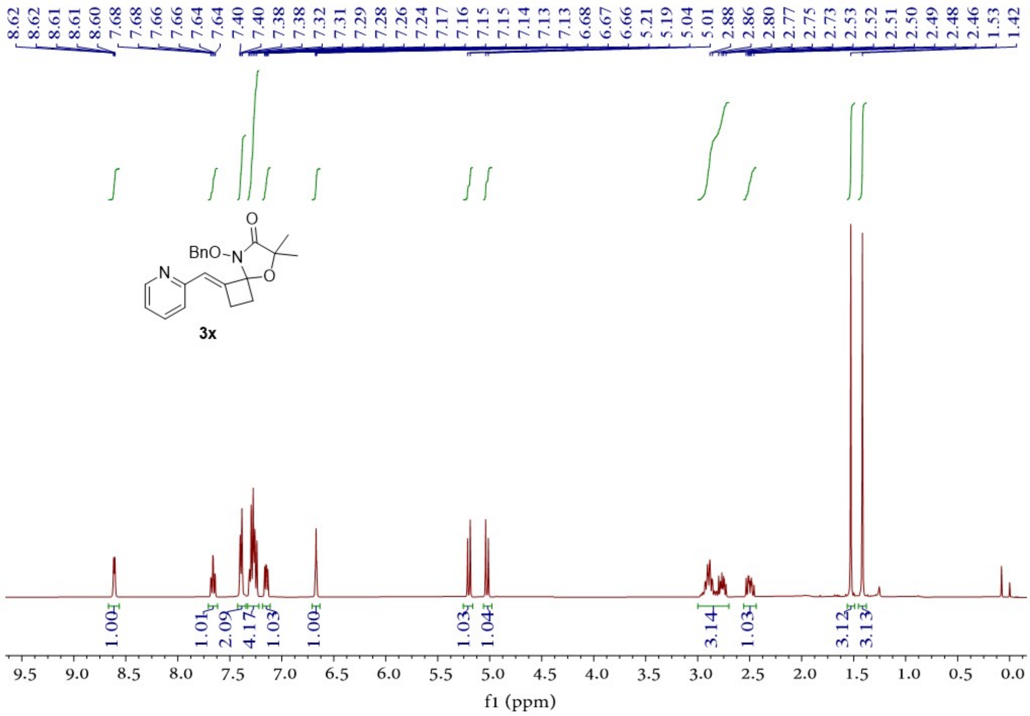


Fig. S52 ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3x**.

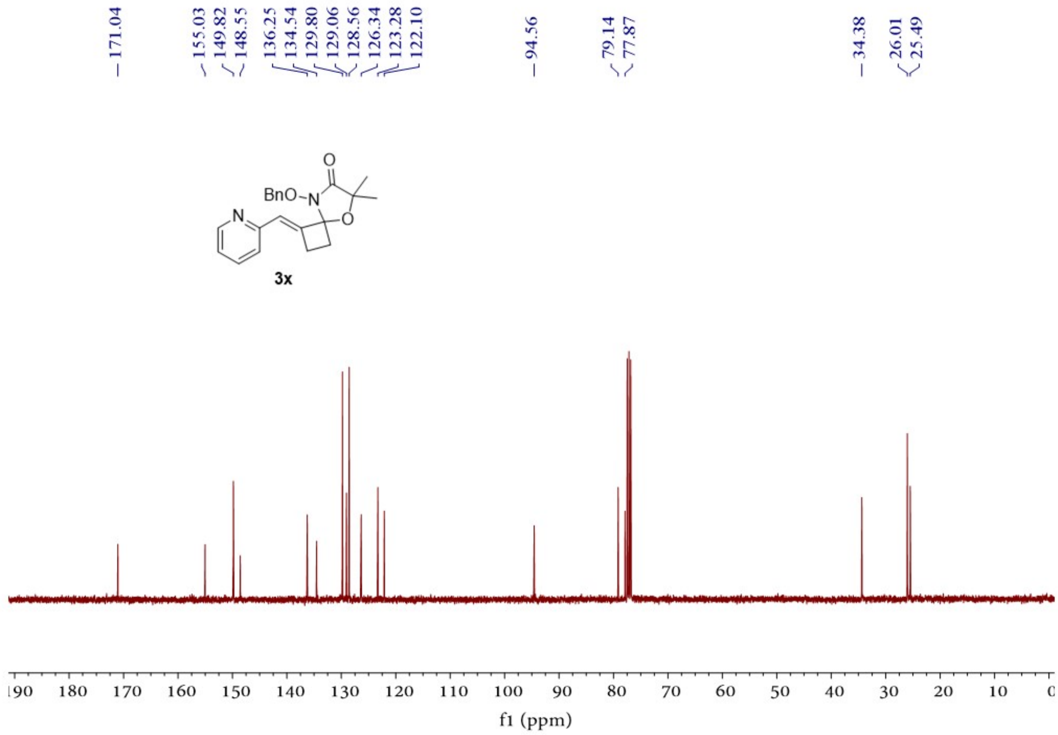


Fig. S53 ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3x**.

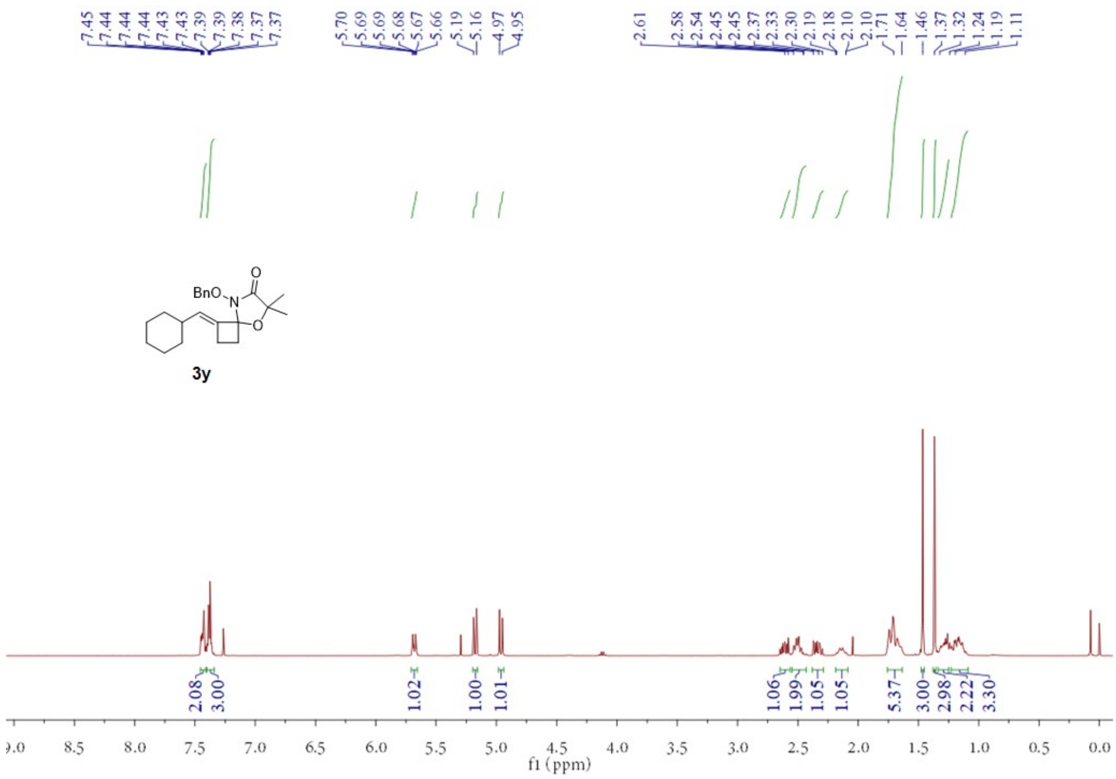


Fig. S54 ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3y**.

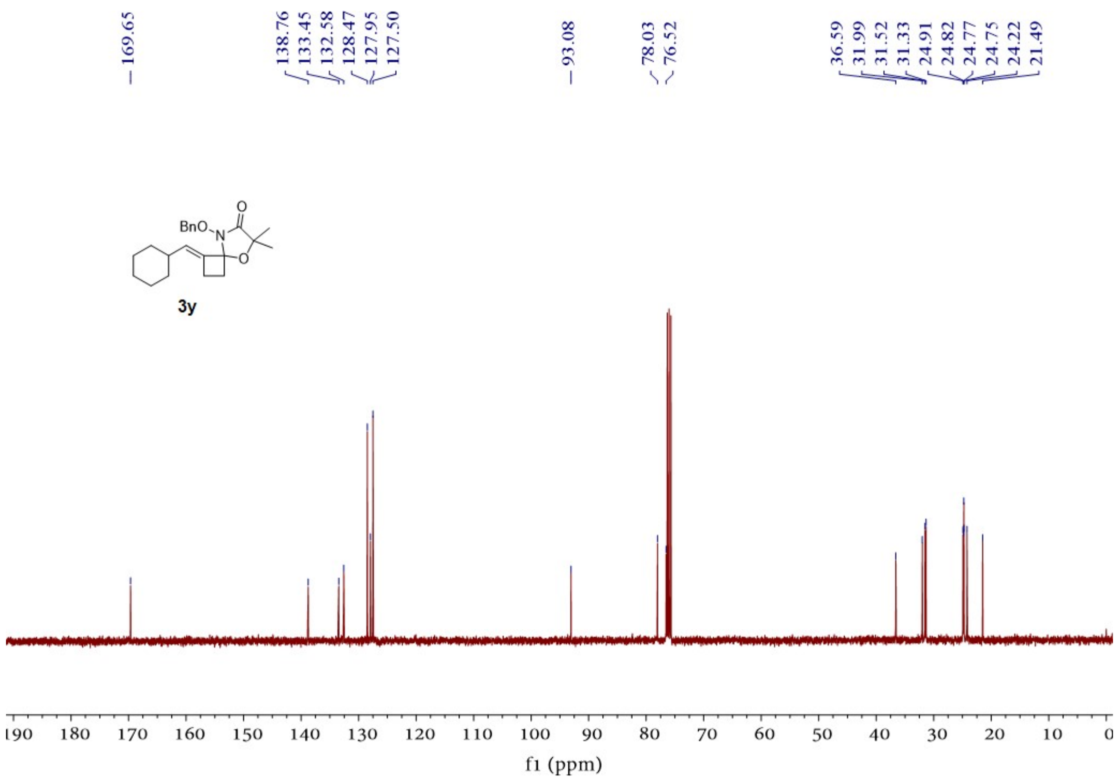


Fig. S55 ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3y**.

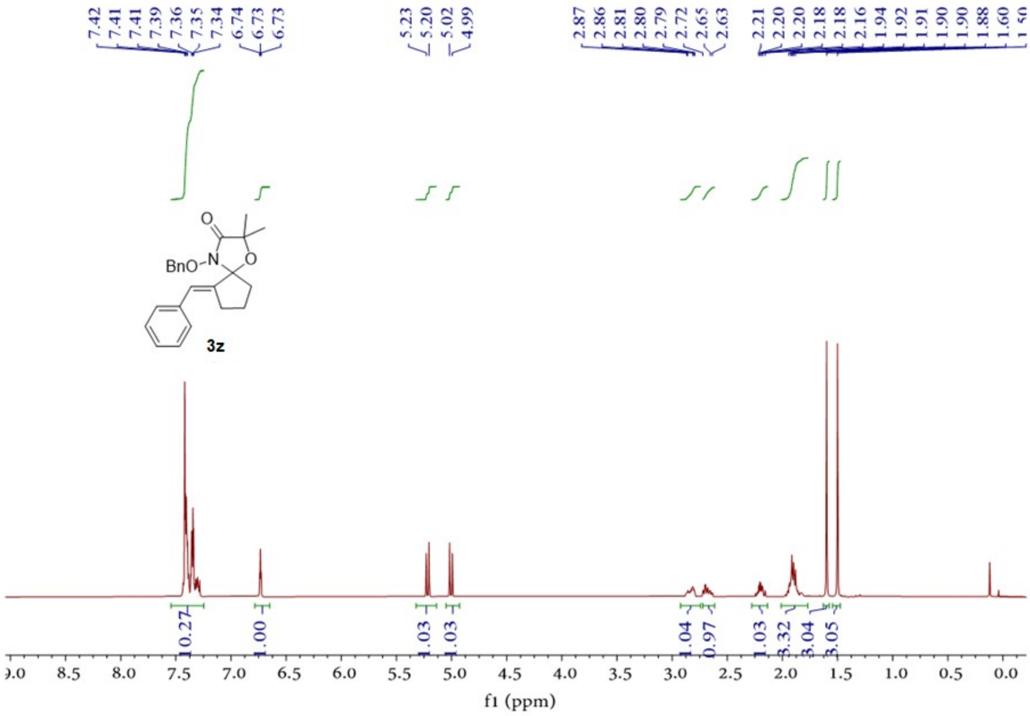


Fig. S56 ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3z**.

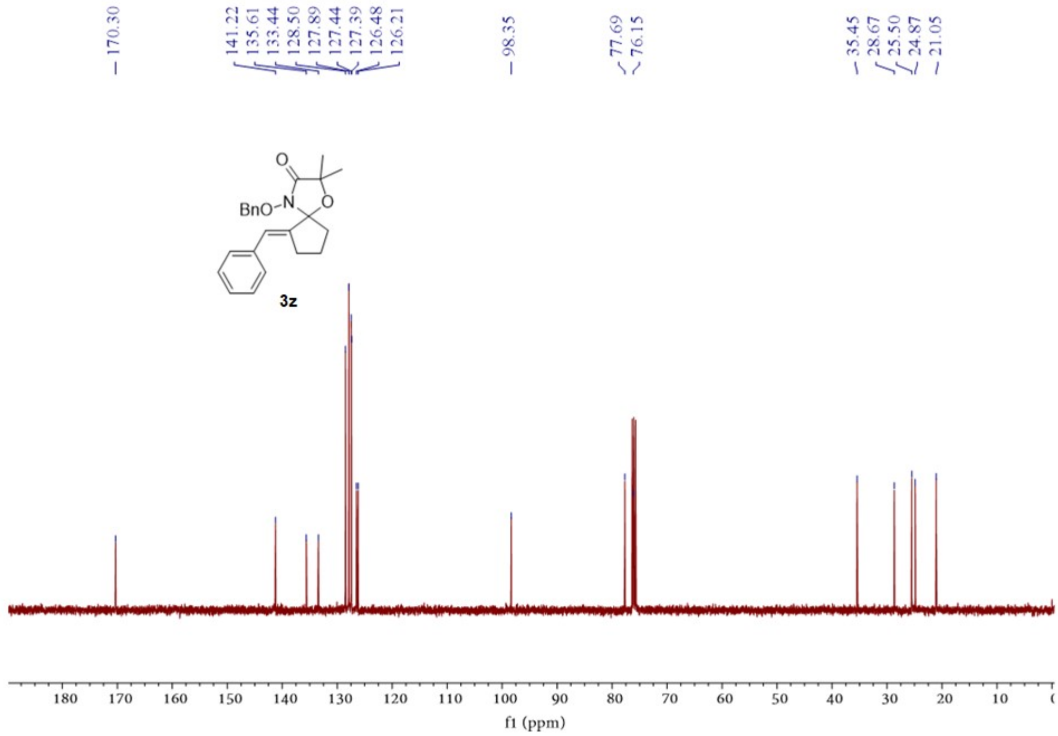


Fig. S57 ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3z**.

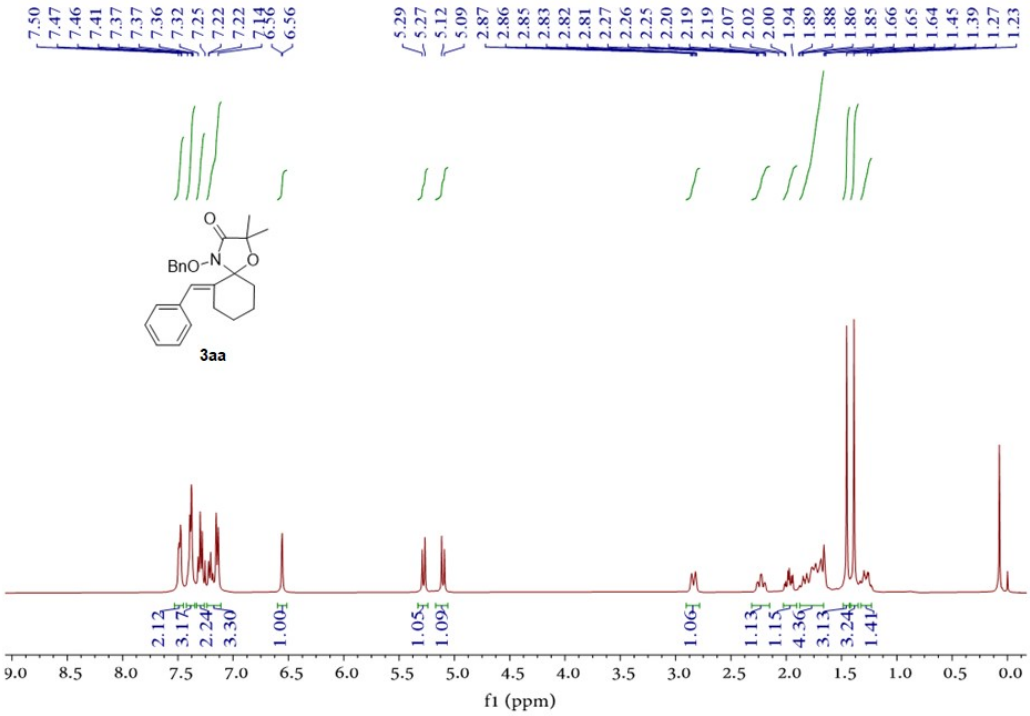


Fig. S58 ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3aa**.

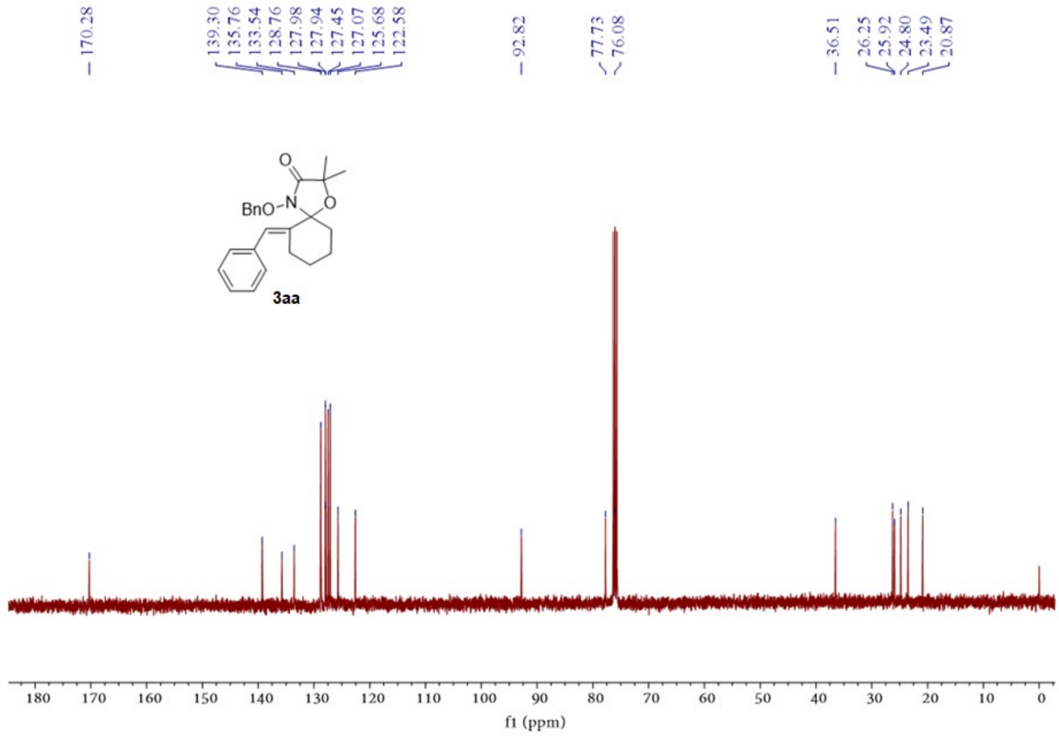


Fig. S59 ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3aa**.

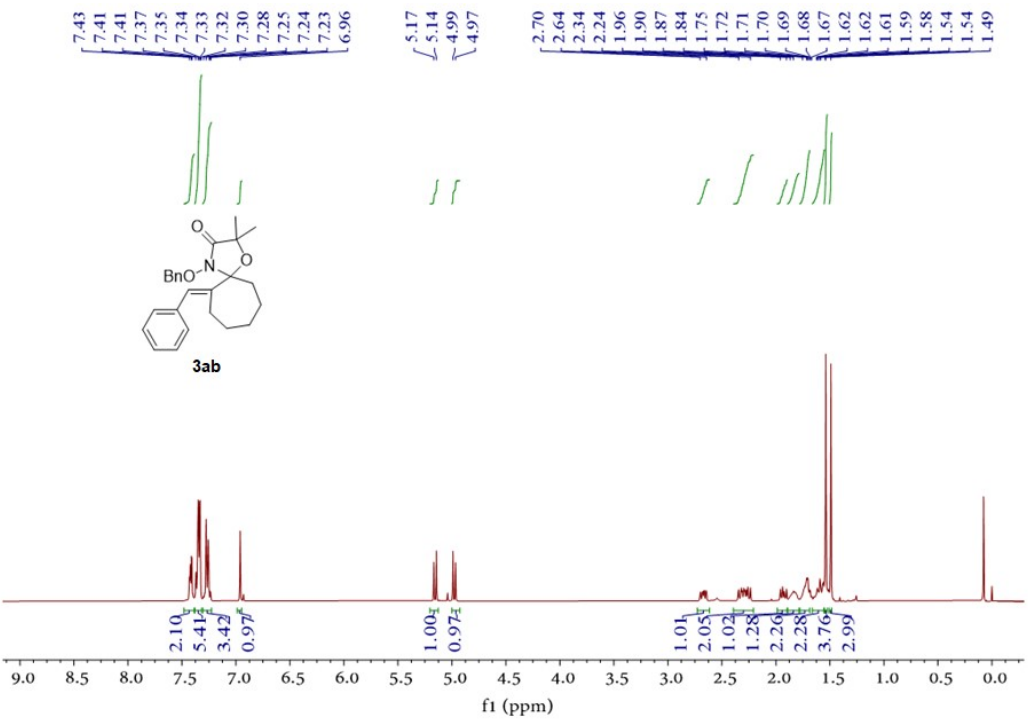


Fig. S60 ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3ab**.

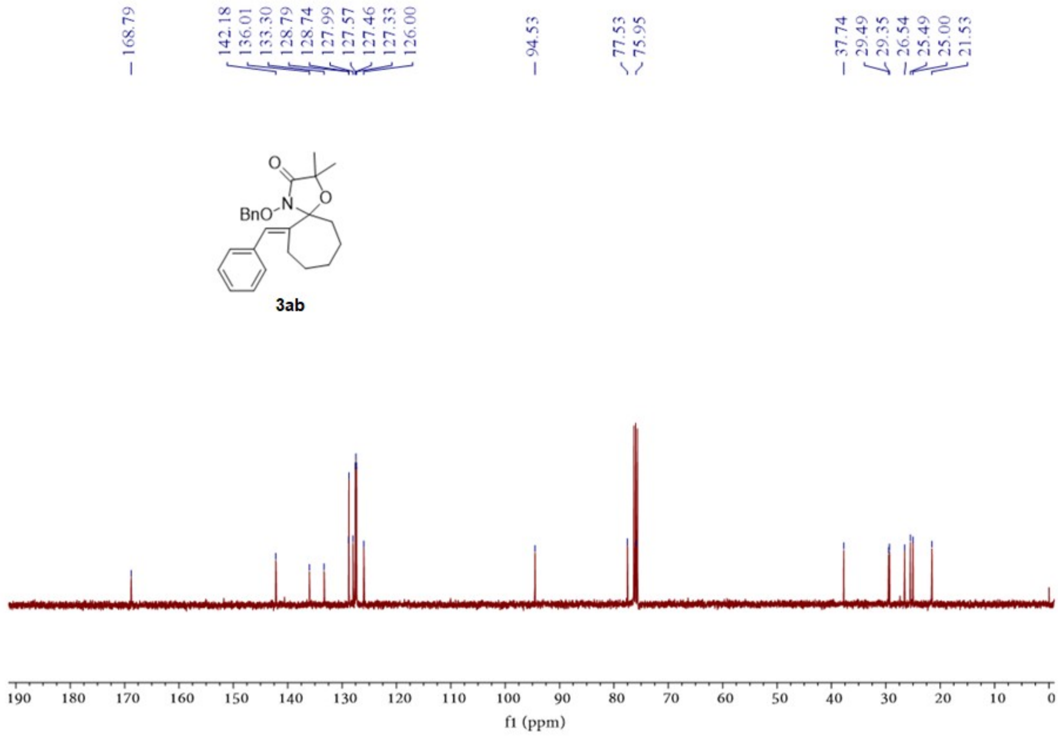


Fig. S61 ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3ab**.

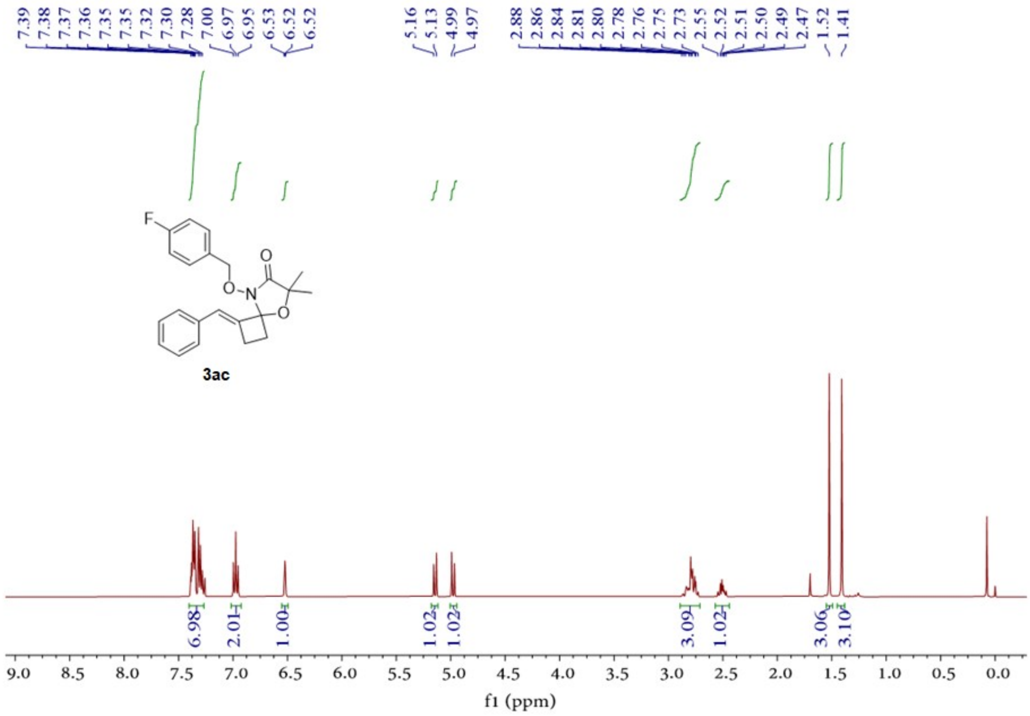


Fig. S62 ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3ac**.

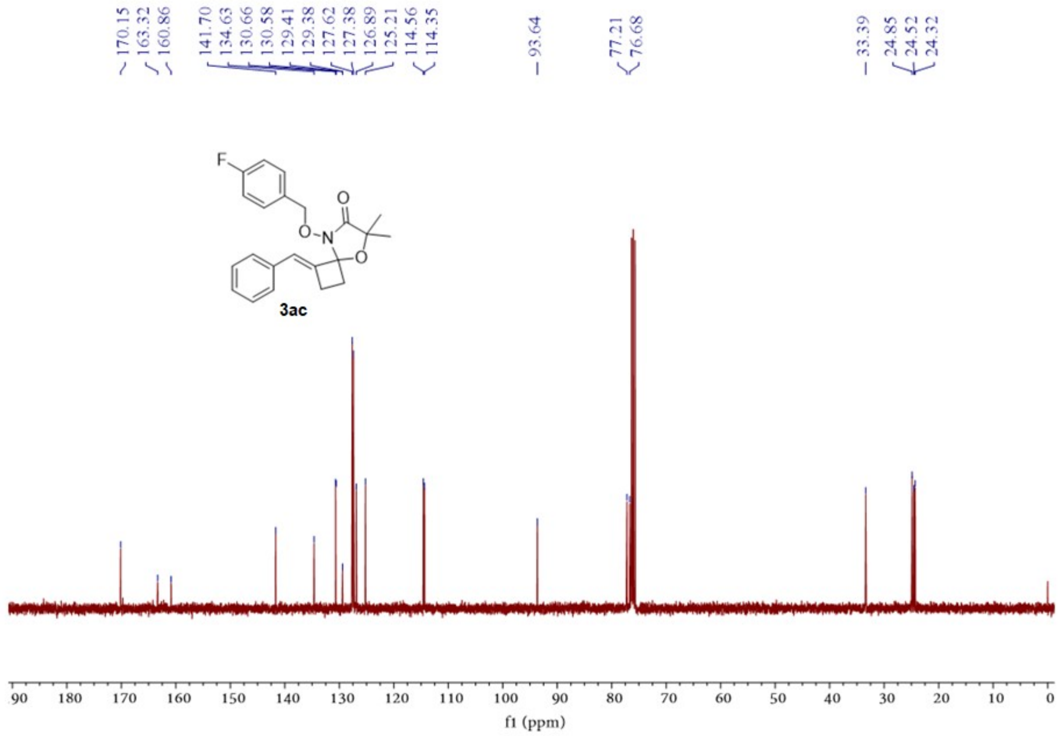


Fig. S63 ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3ac**.

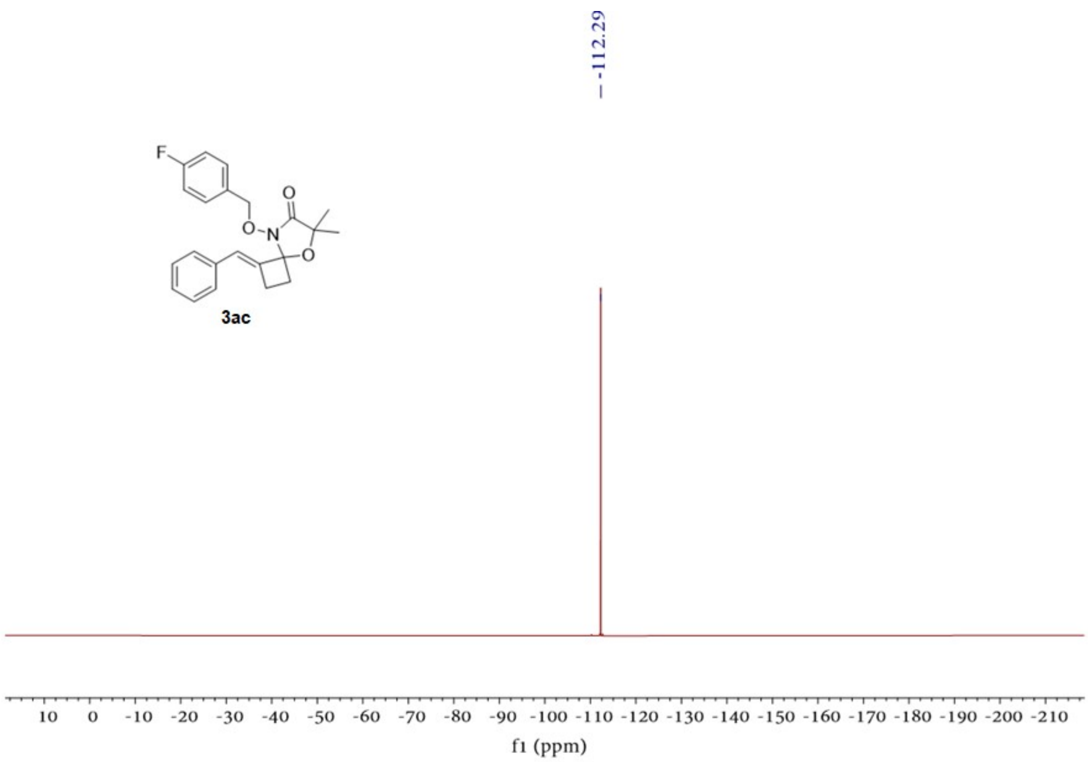


Fig. S64 ^{19}F NMR (376 MHz, $CDCl_3$) spectrum of **3ac**.

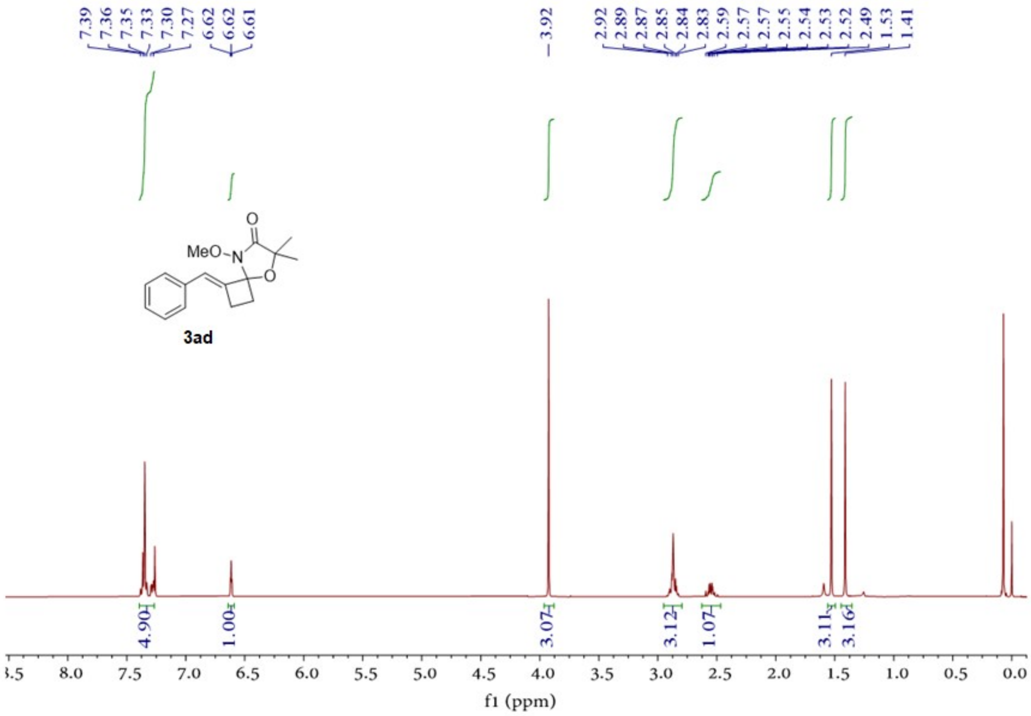


Fig. S65 ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3ad**.

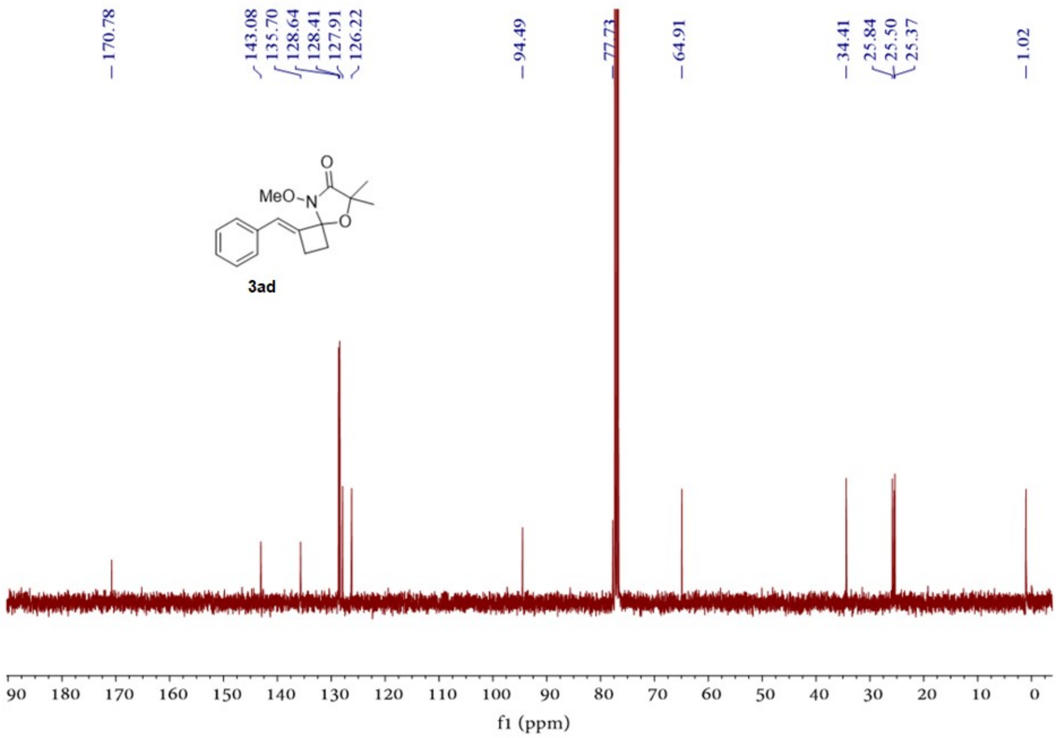


Fig. S66 ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3ad**.

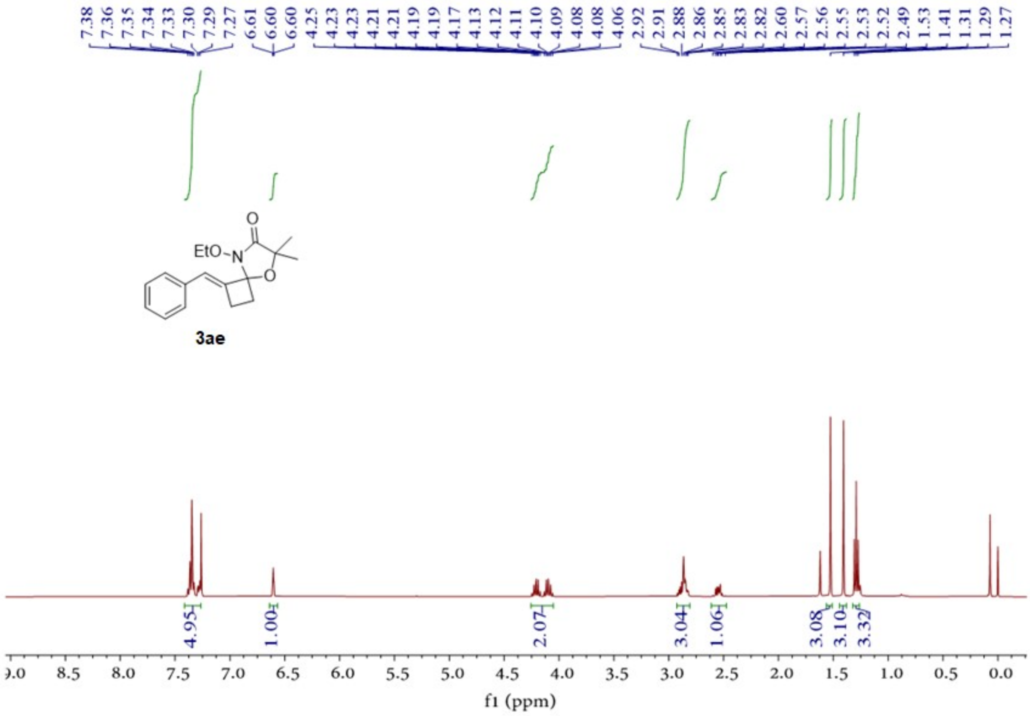


Fig. S67 ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3ae**.

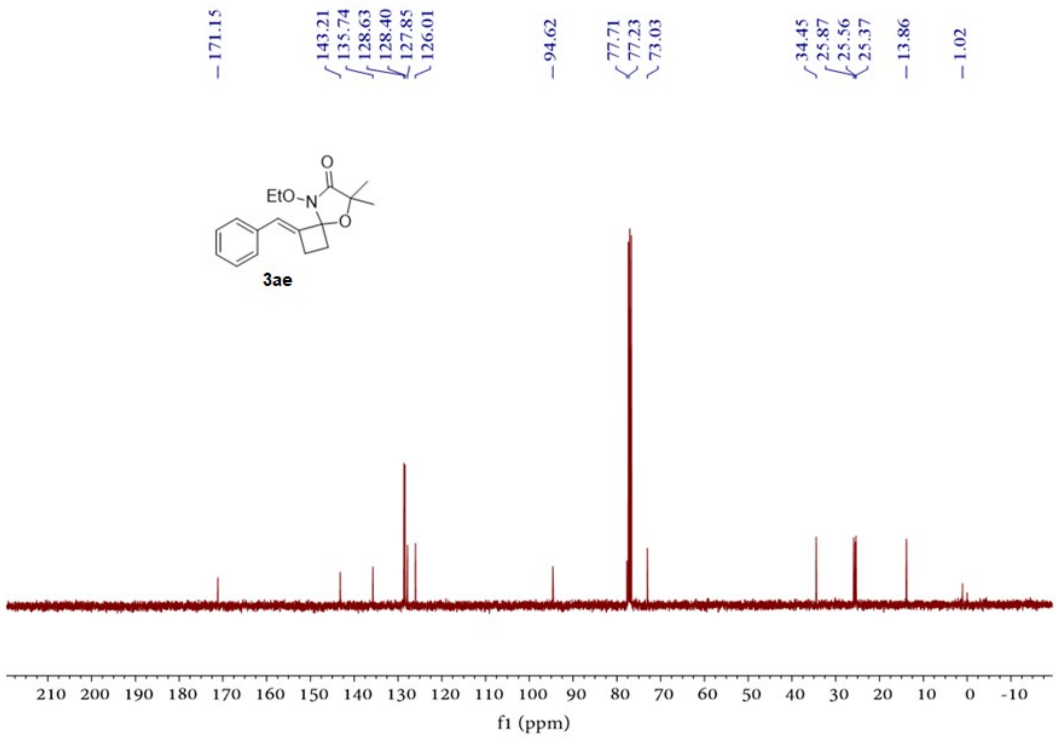


Fig. S68 ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3ae**.

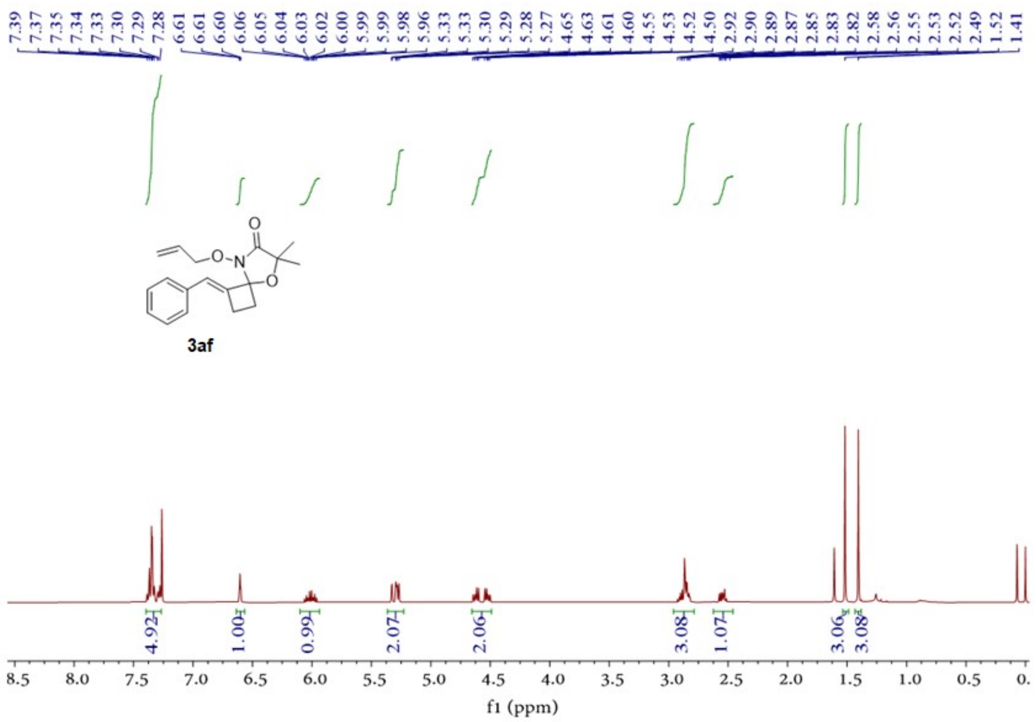


Fig. S69 ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3af**.

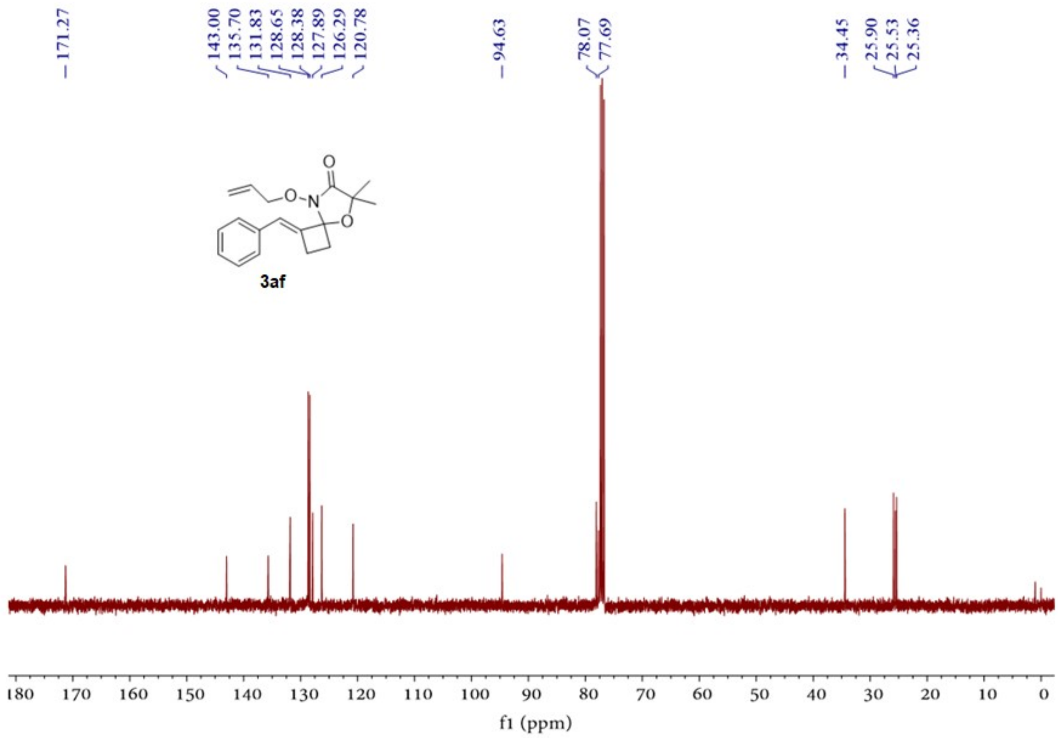


Fig. S70 ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3af**.

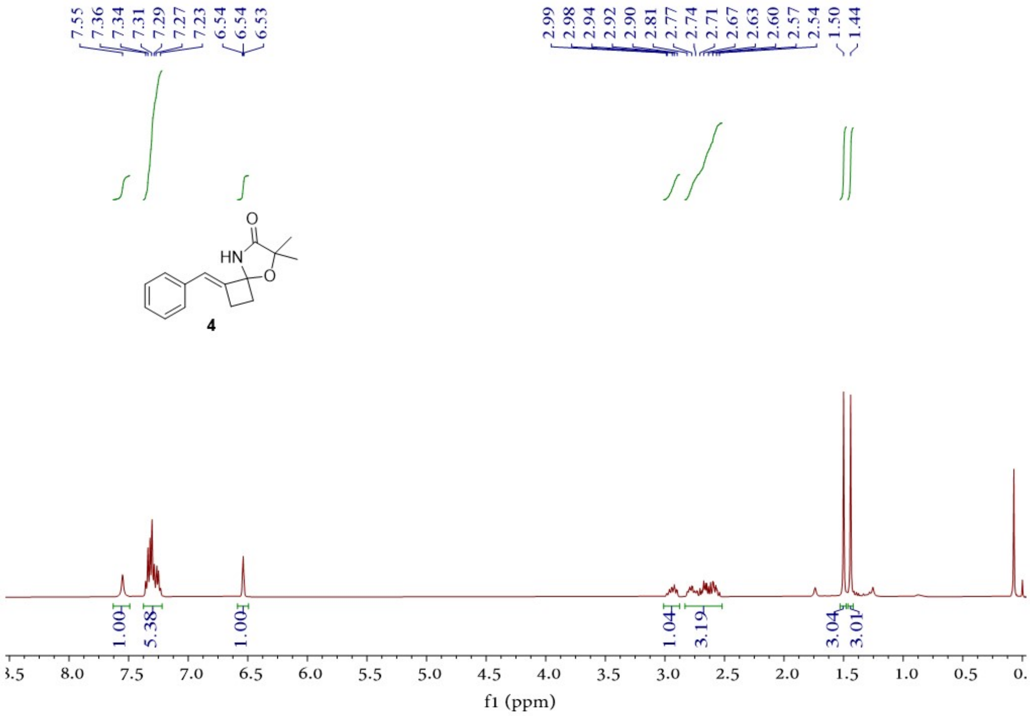


Fig. S71 [1]H NMR (400 MHz, $CDCl_3$) spectrum of **4**.

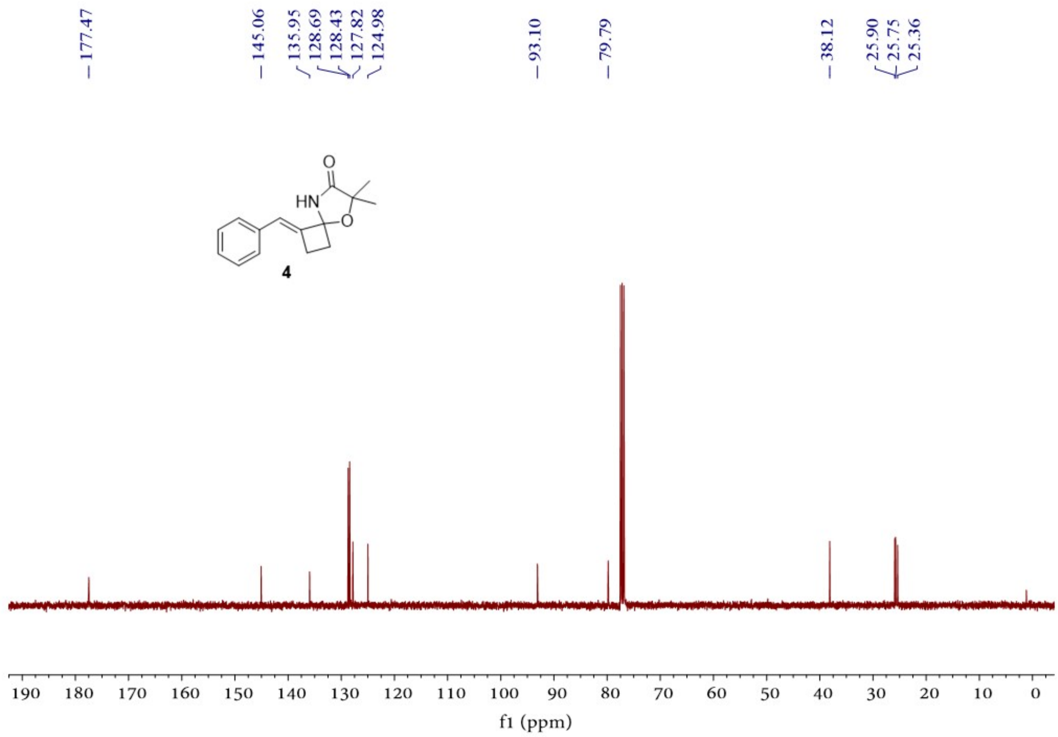


Fig. S72 [13]C NMR (100 MHz, $CDCl_3$) spectrum of **4**.

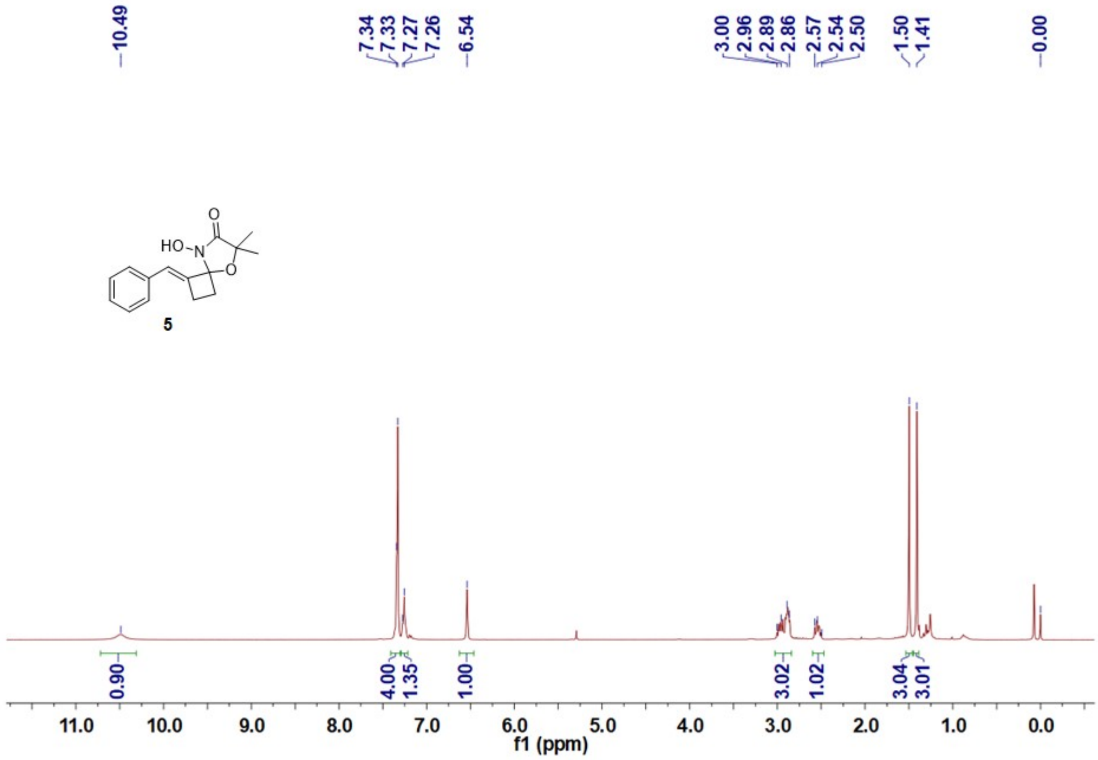


Fig. S73 [1]H NMR (400 MHz, $CDCl_3$) spectrum of **5**.

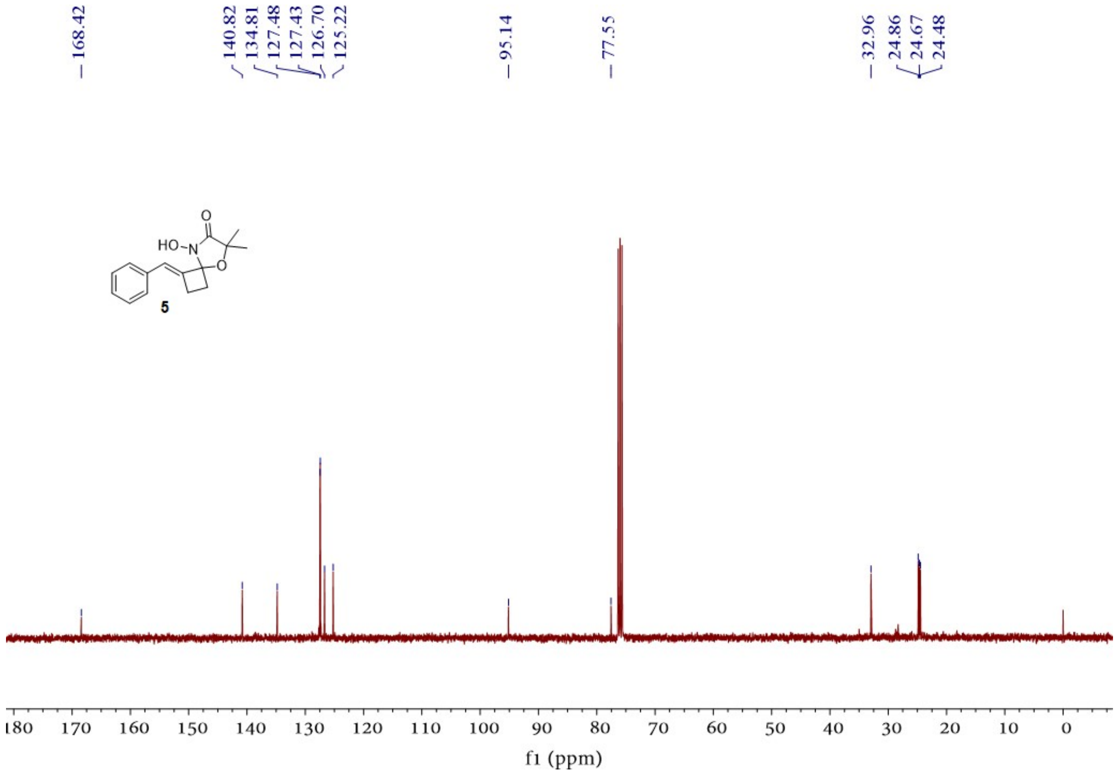


Fig. S74 [13]C NMR (100 MHz, $CDCl_3$) spectrum of **5**.