Spirocyclic sulfamidate imines via palladium-catalysed asymmetric (3 + 2) cycloaddition reactions.

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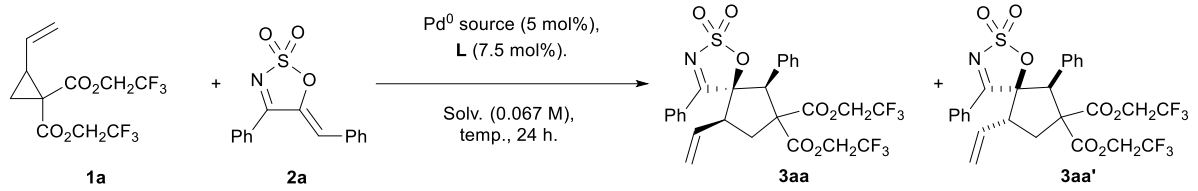
Supporting information

1. General

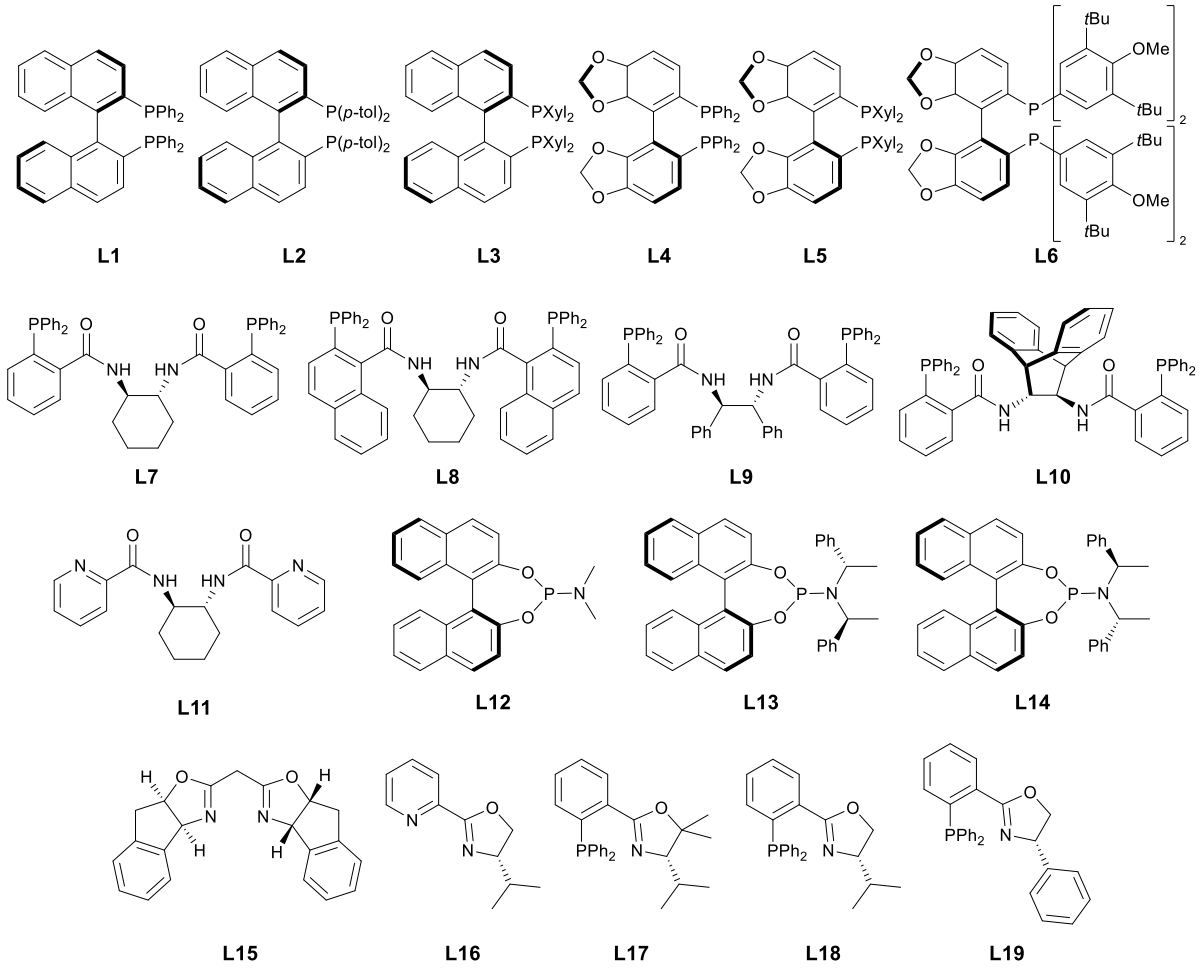
Reagents and solvents were acquired from commercial suppliers and were used either without further purification or purified by standard techniques. Anhydrous solvents were passed through activated alumina for dryness before being stored under N_2 over 4 Å molecular sieves. Anhydrous THF was obtained by distillation from a sodium/benzophenone ketyl still under nitrogen. Air- and moisture-sensitive reactions were performed in oven-dried glassware under an inert N_2 atmosphere. For thin-layer chromatography (TLC), silica gel plates were obtained from Merck & Co., visualised under UV light and/or by treatment with either potassium permanganate or cerium molybdate TLC stain solution, followed by heating. Purification was carried out using flash column chromatography (FCC) with silica gel 60 (0.04 – 0.06) mm obtained from Chem-Supply. Solvent used for NMR analysis was deuterated chloroform ($CDCl_3$) with 0.1% w/v tetramethylsilane (TMS), obtained from Sigma–Aldrich. ^{1}H, ^{19}F, and ^{13}C NMR spectra were recorded with either a Bruker Avance III 400 spectrometer (400 MHz for ^{1}H NMR and 100 MHz for ^{13}C NMR) or a Bruker Avance Neo 500 spectrometer equipped with a BBO Prodigy N_2 cryoprobe (500 MHz for ^{1}H NMR, 125 MHz for ^{13}C NMR, and 470 MHz for ^{19}F NMR). Trifluorotoluene was used as an external reference for ^{19}F NMR analysis and was referenced to 0.00 ppm. Abbreviations used in the descriptions of NMR resonances include: singlet (s), doublet (d), triplet (t), quartet (q), heptet (h), multiplet (m), broad singlet (br s), doublet of doublet (dd), doublet of doublet of doublet (ddd). High-performance liquid chromatography (HPLC) was performed using a Shimadzu Nexera X2 UHPLC equipped with a PDA detector. Melting point analysis was carried out using a Buchi Melting Point M-560 instrument.

2. Table of reaction optimisation results[a]



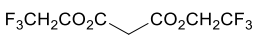
	Entry	Pd^0 source	Ligand	Solvent	Temp.	Yield[b]	*d.r.* (**3aa** : **3aa'**)[c]	*e.r.* (**3aa** : **ent-3aa**)[d]
Preliminary ligand screen	1	Pd_2dba_3•$CHCl_3$	**L1**	THF	RT	71% (67%)	4.0 : 1	12 : 88
	2	Pd_2dba_3•$CHCl_3$	**L2**	THF	RT	80% (82%)	5.5 : 1	17 : 83
	3	Pd_2dba_3•$CHCl_3$	**L3**	THF	RT	92% (84%)	2.9 : 1	25 : 75
	4	Pd_2dba_3•$CHCl_3$	**L4**	THF	RT	59% (72%)	4.0 : 1	83 : 17
	5	Pd_2dba_3•$CHCl_3$	**L5**	THF	RT	86% (82%)	3.1 : 1	83 : 17
	6	Pd_2dba_3•$CHCl_3$	**L6**	THF	RT	18% (27%)	1 : 1.3	90 : 10
	7[e]	Pd_2dba_3•$CHCl_3$	**L7**	THF	RT	58% (32%)	7.0 : 1	67 : 33
	8	Pd_2dba_3•$CHCl_3$	**L8**	THF	RT	13% (11%)	5.3 : 1	58 : 42
	9	Pd_2dba_3•$CHCl_3$	**L9**	THF	RT	0%	_	_
	10	Pd_2dba_3•$CHCl_3$	**L10**	THF	RT	29% (23%)	6.5 : 1	19 : 81
	11	Pd_2dba_3•$CHCl_3$	**L11**	THF	RT	0%	_	_
	12	Pd_2dba_3•$CHCl_3$	**L12**	THF	RT	53% (54%)	1.7 : 1	54 : 46
	13	Pd_2dba_3•$CHCl_3$	**L13**	THF	RT	61% (49%)	1.6 : 1	61 : 39
	14	Pd_2dba_3•$CHCl_3$	**L14**	THF	RT	83% (77%)	3.1 : 1	74 : 26
	15	Pd_2dba_3•$CHCl_3$	**L15**	THF	RT	0%	_	_
	16	Pd_2dba_3•$CHCl_3$	**L16**	THF	RT	0%	_	_
	17[f]	Pd_2dba_3•$CHCl_3$	**L17**	THF	RT	96% (69%)	1 : 2.4	63 : 37
	18	Pd_2dba_3•$CHCl_3$	**L18**	THF	RT	90% (93%)	1 : 2.5	55 : 45
	19	Pd_2dba_3•$CHCl_3$	**L19**	THF	RT	94% (89%)	1 : 1.7	49 : 51
Solvent screen	20	Pd_2dba_3•$CHCl_3$	**L1**	Dioxane	RT	60% (63%)	7.6 : 1	13 : 87
	21	Pd_2dba_3•$CHCl_3$	**L1**	DME	RT	92% (87%)	4.6 : 1	11 : 89
	22	Pd_2dba_3•$CHCl_3$	**L1**	MTBE	RT	88% (77%)	4.4 : 1	14 : 86
	23	Pd_2dba_3•$CHCl_3$	**L1**	2-Me-THF	RT	89% (81%)	4.5 : 1	12 : 88
	24	Pd_2dba_3•$CHCl_3$	**L1**	CH_2Cl_2	RT	77% (68%)	2.8 : 1	25 : 75
	25	Pd_2dba_3•$CHCl_3$	**L1**	$CHCl_3$	RT	81% (75%)	3.2 : 1	22 : 78
	26	Pd_2dba_3•$CHCl_3$	**L1**	DCE	RT	78% (62%)	2.5 : 1	24 : 76
	27	Pd_2dba_3•$CHCl_3$	**L1**	PhMe	RT	71% (36%)	7.2 : 1	7 : 93
	28	Pd_2dba_3•$CHCl_3$	**L1**	Benzene	RT	67% (65%)	7.9 : 1	6 : 94
	29	Pd_2dba_3•$CHCl_3$	**L1**	MeCN	RT	90% (83%)	2.5 : 1	24 : 76
	30	Pd_2dba_3•$CHCl_3$	**L1**	DMF	RT	72% (65%)	2.3 : 1	22 : 78
	31	Pd_2dba_3•$CHCl_3$	**L1**	DMSO	RT	73% (71%)	2.6 : 1	24 : 76
	32	Pd_2dba_3•$CHCl_3$	**L1**	MeOH	RT	0%	_	_
Ligand screen	33	Pd_2dba_3•$CHCl_3$	**L2**	PhMe	RT	87% (81%)	8.7 : 1	89 : 11
	34	Pd_2dba_3•$CHCl_3$	**L3**	PhMe	RT	91% (74%)	7.1 : 1	88 : 12
	35	Pd_2dba_3•$CHCl_3$	**L4**	PhMe	RT	80% (76%)	7.1 : 1	90 : 10
	36	Pd_2dba_3•$CHCl_3$	**L5**	PhMe	RT	98% (84%)	7.3 : 1	94 : 6
	37	Pd_2dba_3•$CHCl_3$	**L6**	PhMe	RT	31% (34%)	1 : 1.2	94 : 6
Further fine tunings	38	Pd_2dba_3•$CHCl_3$	**L5**	PhMe	0 °C	84% (92%)	3.8 : 1	90 : 10
	39	Pd_2dba_3•$CHCl_3$	**L5**	PhMe	−10 °C	81% (85%)	2.7 : 1	81 : 19
	40[g]	Pd_2dba_3•$CHCl_3$	**L5**	PhMe	RT	88% (84%)	5.4 : 1	93 : 7
	41[h]	Pd_2dba_3•$CHCl_3$	**L5**	PhMe	RT	83% (77%)	8.5 : 1	94 : 6
	42[i]	Pd_2dba_3•$CHCl_3$	**L5**	PhMe	RT	75% (71%)	8.0 : 1	94 : 6
	43[h,j]	Pd_2dba_3•$CHCl_3$	**L5**	PhMe	RT	99% (99%)	8.0 : 1	95 : 5
	44[h,j,k]	$Pd(OAc)_2$	**L5**	PhMe	RT	41% (42%)	3.9 : 1	84 : 16
	45[h,j]	$[Pd(\pi\text{-}C_3H_5)Cl]_2$	**L5**	PhMe	RT	61% (68%)	5.5 : 1	89 : 11
	46[h,j,k]	$Pd(\pi\text{-}C_3H_5)Cp$	**L5**	PhMe	RT	75% (67%)	8.3 : 1	95 : 5
	47[h,j,k]	Pd(π-cinnamyl)Cp	**L5**	PhMe	RT	80% (76%)	7.6 : 1	95 : 5
	48[h,j,l]	Pd_2dba_3•$CHCl_3$	**L5**	PhMe	RT	100% (89%)	7.7 : 1	95 : 5
	49[h,j,m]	Pd_2dba_3•$CHCl_3$	**L5**	PhMe	RT	22% (23%)	6.5 : 1	88 : 12

[a]Reaction conditions: **1a** (0.12 mmol, 1.2 equiv.), **2a** (0.1 mmol, 1.0 equiv.), Pd_2dba_3•$CHCl_3$ (2.5 mol%), **Ligand** (7.5 mol% or 15 mol%), solvent (0.067 M wrt **2a**), rt, 24 h. [b]Yield determined by ^1H NMR integration against an internal standard (1,3,5-trimethoxybenzene), isolated yield in parentheses. [c]Determined by ^1H NMR analysis of the crude reaction mixture. [d]Enantiomeric ratio determined by chiral HPLC. [e]Reaction time: 6 h. [f]Reaction conditions: **1a** (0.1 mmol, 1.0 equiv.), **2a** (0.11 mmol, 1.1 equiv.), Pd_2dba_3•$CHCl_3$ (2.5 mol%), **Ligand** (7.5 mol%), solvent (0.067 M wrt **VCP**), rt, 24 h. [g]Concentration: 0.134 M wrt **2a**. [h]Concentration: 0.034 M wrt **2a**. [i]Concentration: 0.017M wrt **2a**. [j]1.5 equiv. of **1a** used. [k]Monomeric Pd source (5 mol%) used. [l]Pd_2dba_3•$CHCl_3$ (1.5 mol%) and **Ligand** (5 mol%) used. [m]Pd_2dba_3•$CHCl_3$ (0.5 mol%) and **Ligand** (2 mol%) used.



3. Synthesis of vinylcyclopropanes

Bis(2,2,2-trifluoroethyl) malonate (S1)



Procedure:[1]

A suspension of malonic acid (3.235 g, 30.993 mmol), 2,2,2-trifluoroethanol (10.6 mL, 145.480 mmol), $MgSO_4$ (3.777 g, 31.376 mmol), and H_2SO_4 (0.7 mL, 13.132 mmol) in anhydrous benzene (15 mL) was stirred at reflux for 72 h. The reaction mixture was then cooled to rt and filtered. The eluent was diluted with benzene, then washed with sat. aq. Na_2CO_3, water, and brine. The organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The desired clear oil product was then used directly without further purification (5.200 g, 59%).

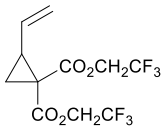
R_f: 0.53 (25% CH_2Cl_2 in hex).

^{1}H NMR (500 MHz, $CDCl_3$): δ 4.55 (q, *J* = 8.2 Hz, 4H), 3.61 (s, 2H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 164.1, 122.5 (q, *J* = 277.2 Hz), 61.2 (q, *J* = 37.2 Hz), 40.2.

The NMR spectroscopic data agreed with those reported.[1]

Bis(2,2,2-trifluoroethyl) 2-vinylcyclopropane-1,1-dicarboxylate (1a)



Procedure:[1]

A suspension of **S1** (4.900 g, 18.225 mmol), *trans*-1,4-dibromo-2-butene (4.138 g, 19.345 mmol), and Cs_2CO_3 (15.086 g, 46.288 mmol) in anhydrous THF (150 mL) was heated at reflux for 24 h. The reaction mixture was then allowed to cool to rt, filtered, then diluted with Et_2O. The ethereal mixture was then washed successively with saturated aqueous $NaHCO_3$, water, and brine. The organic layer was then dried over Na_2SO_4, filtered, then concentrated *in vacuo*. Purification by FCC (40% CH_2Cl_2 in hexane) afforded the desired product as a clear oil (1.990 g, 34%).

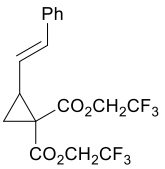
R_f = 0.24 (30% CH_2Cl_2 in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.47 (ddd, *J* = 17.1, 10.0, 7.7 Hz, 1H), 5.35 (ddd, *J* = 17.0, 1.5, 0.6 Hz, 1H), 5.23 (ddd, *J* = 10.0, 1.6, 0.7 Hz, 1H), 4.62–4.44 (m, 4H), 2.74 (app q, *J* = 8.0 Hz, 1H), 1.90 (dd, *J* = 8.0, 5.2 Hz, 1H), 1.74 (dd, *J* = 9.1, 5.2 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 167.5, 165.2, 131.3, 122.6 (q, *J* = 277.5 Hz), 120.3, 61.3 (q, *J*, = 37.1), 61.2 (q, *J* = 37.1), 35.1, 32.9, 21.5.

The NMR spectroscopic data agreed with those reported.[1]

Bis(2,2,2-trifluoroethyl) (*E*)-2-styrylcyclopropane-1,1-dicarboxylate (1b)



Procedure:[1]

A solution of **1a** (164.5 mg, 0.514 mmol), styrene (1.1 mL, 9.601 mmol), and Grubbs catalyst 2nd generation (11.7 mg, 0.0138 mmol) in anhydrous CH_2Cl_2 (4 mL) was heated at reflux for 1 h. The reaction mixture was allowed to cool to rt, then concentrated *in vacuo*. Purification by FCC (10% EtOAc in hexane) afforded the desired product as a yellow oil (168.8 mg, 82%).

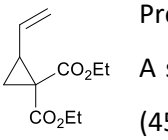
R_f = 0.32 (10% EtOAc in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38–7.22 (m, 5H), 6.69 (dd, *J* = 15.9, 0.8, 1H), 5.83 (dd, *J* = 15.8, 8.4, 1H), 4.64–4.43 (m, 4H), 2.91 (app q, *J* = 9.1 Hz, 1H), 2.03 (dd, *J* = 8.0, 5.3 Hz, 1H), 1.85 (dd, *J* = 9.1, 5.3 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 167.5, 165.4, 136.2, 135.4, 128.6, 128.0, 126.3, 122.6 (two overlapping q, *J* = 277.2 Hz), 122.5, 61.3 (two overlapping q, *J* = 37.0 Hz), 35.3, 33.4, 22.3.

The NMR spectroscopic data agreed with those reported.[1]

Diethyl 2-vinylcyclopropane-1,1-dicarboxylate (1c)



Procedure:[2]

A suspension of diethyl malonate (0.300 mL, 1.970 mmol), *trans*-1,4-dibromo-2-butene (454.8 mg, 2.126 mmol), and Cs_2CO_3 (1.674 g, 5.138 mmol) in anhydrous THF (10 mL) was heated at reflux overnight. The reaction mixture was then allowed to cool to rt, filtered, then diluted with Et_2O. The ethereal mixture was then washed successively with saturated aqueous $NaHCO_3$, water, and brine. The organic layer was then dried over $MgSO_4$, filtered, then concentrated *in vacuo*. Purification by FCC (50% CH_2Cl_2 in hexane) afforded the desired product as a clear oil (304.4 mg, 73%).

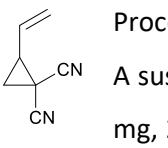
R_f = 0.22 (50% CH_2Cl_2 in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.44 (ddd, *J* 17.1, 10.1, 8.3 Hz, 1H), 5.30 (ddd, *J* = 17.1, 1.7, 0.7 Hz, 1H), 5.14 (ddd, *J* = 10.2, 1.7, 0.7 Hz, 1H), 4.28–4.12 (m, 4H), 2.57 (app q, *J* = 9.1 Hz, 1H), 1.69 (dd, *J* = 7.5, 4.9 Hz, 1 H), 1.55 (dd, *J* = 9.0, 4.9 Hz), 1.27 (t, *J* = 7.1 Hz, 3H), 1.27 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 169.7, 167.4, 133.2, 118.4, 61.6, 61.5, 35.9, 31.1, 20.4, 14.2, 14.1.

The NMR spectroscopic data agreed with those reported.[3]

2-Vinylcyclopropane-1,1-dicarbonitrile (1d)



Procedure:[2]

A suspension of malononitrile (0.130 mL, 2.064 mmol), *trans*-1,4-dibromo-2-butene (501.6 mg, 2.345 mmol), and Cs_2CO_3 (1.858 g, 5.701 mmol) in anhydrous THF (10 mL) was heated at reflux overnight. The reaction mixture was then allowed to cool to rt, filtered, then diluted with Et_2O. The ethereal mixture was then washed successively with saturated aqueous $NaHCO_3$, water, and

brine. The organic layer was then dried over $MgSO_4$, filtered, then concentrated *in vacuo*. Purification by FCC (50% CH_2Cl_2 in hexane) afforded the desired product as a clear oil (85.4 mg, 33%).

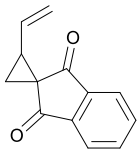
R_f = 0.21 (50% CH_2Cl_2 in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.66–5.50 (m, 3 H), 2.69 (app q, *J* = 9.0 Hz, 1H), 2.07 (dd, *J* = 9.1, 6.2 Hz, 1H), 1.83 (dd, *J* = 8.3, 6.2 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 129.7, 123.1, 115.0, 113.4, 33.3, 23.4, 5.7.

The NMR spectroscopic data agreed with those reported.[2]

2-Vinylspiro[cyclopropane-1,2'-indene]-1',3'-dione (1e)



Procedure:[4]

A suspension of 1,3-indandione (301.4 mg, 2.062 mmol), *trans*-1,4-dibromo-2-butene (444.0 mg, 2.076 mmol), and K_2CO_3 (616.4 mg, 4.460 mmol) in anhydrous DMF (20 mL) was stirred at rt and monitored by TLC. Upon completion, the reaction mixture was diluted with EtOAc, followed by the addition of water. The mixture was extracted with EtOAc, then the combined organic extracts were washed with H_2O and brine. The organic layer was dried over $MgSO_4$, filtered, then concentrated *in vacuo*. Purification by FCC (20% EtOAc in hexane) afforded the desired product as a red orange solid (279.4 mg, 68%).

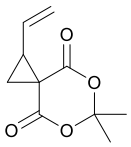
R_f = 0.34 (20% EtOAc in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.97–7.92 (m, 2H), 7.80–7.77 (m, 2H), 6.03 (ddd, *J* = 17.1, 10.3, 9.5 Hz, 1H), 5.30 (ddd, *J* = 17.2, 1.51, 0.6 Hz, 1H), 5.16 (ddd *J* = 10.3, 1.5, 0.6 Hz, 1H), 2.86–2.79 (app q, *J* = 8.0 Hz, 1H), 2.15 (dd, *J* = 8.8, 4.0 Hz, 1H), 2.00 (dd, *J* = 8.1, 4.0 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 198.0, 197.1, 142.5, 141.8, 134.9, 134.8, 133.0, 122.50, 122.46, 118.5, 42.2, 40.2, 24.6.

The NMR spectroscopic data agreed with those reported.[4]

6,6-Dimethyl-1-vinyl-5,7-dioxaspiro[2.5]octane-4,8-dione (1f)



Procedure:[5]

To a stirring solution of Meldrum's acid (572.1 mg, 3.969 mmol) in anhydrous DMF (4 mL) at 0 °C was added K_2CO_3 (750.7 mg, 5.432 mmol), and the resulting suspension was stirred at the same temperature for 10 min. *trans*-1,4-Dibromo-2-butene (1.071 g, 5.007 mmol) was then added, and the reaction mixture was stirred for an additional 20 min at 0 °C, then 45 min at rt. A second portion of K_2CO_3 (798.6 mg, 5.778 mmol) was then added, then the reaction mixture was stirred at rt overnight. Upon completion, indicated by TLC, the reaction was quenched with 1M HCl and extracted with EtOAc. The combined organic extracts were washed with water and brine, then

the organic layer was dried over $MgSO_4$, filtered, then concentrated *in vacuo*. Purification by FCC (20% EtOAc in hexane) afforded the desired product as a white solid (285.5 mg, 37%).

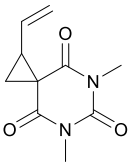
R_f = 0.27 (20% EtOAc in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.77 (dd, *J* = 17.1, 10.3, 9.5 Hz, 1H), 5.47 (ddd, *J* = 17.1, 1.3, 0.6 Hz, 1H), 5.35 (dd, *J* = 10.3, 1.3 Hz, 1H), 2.78 (app q, *J* = 9.1 Hz, 1H), 2.38 (dd, *J* = 9.1, 4.5 Hz, 1H), 2.23 (dd, *J* = 8.6, 4.5 Hz, 1H), 1.79 (app s, 3H), 1.73 (app s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 167.6, 165.2, 131.4, 121.9, 105.2, 43.1, 31.6, 27.7, 27.6, 24.7.

The NMR spectroscopic data agreed with those reported.[5]

5,7-Dimethyl-1-vinyl-5,7-diazaspiro[2.5]octane-4,6,8-trione (1g)



Procedure:[4]

A suspension of 1,3-dimethylbarbituric acid (310.1 mg, 1.986 mmol), *trans*-1,4-dibromo-2-butene (475.8 mg, 2.224 mmol), and K_2CO_3 (580.9 mg, 4.203 mmol) in anhydrous DMF (13 mL) was stirred at rt and monitored by TLC. Upon completion, the reaction mixture was diluted with EtOAc, followed by the addition of water. The mixture was extracted with EtOAc, then the combined organic extracts were washed with H_2O and brine. The organic layer was dried over $MgSO_4$, filtered, then concentrated *in vacuo*. Purification by FCC (20% EtOAc in hexane) afforded the desired product as a white solid (122.7 mg, 30%).

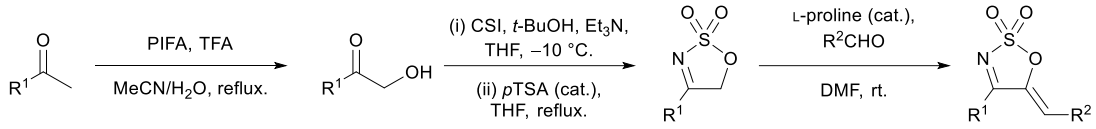
R_f = 0.32 (20% EtOAc in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.94 (ddd, *J* = 17.2, 10.3, 9.3 Hz, 1H), 5.41 (ddd, *J* = 17.2, 1.5, 0.6 Hz, 1H), 5.28 (dd, *J* = 10.3, 1.6 Hz, 1H), 3.33 (s, 3H), 3.32 (s, 3H), 2.85 (app q, *J* = 9.1 Hz, 1H), 2.31 (dd, *J* = 9.2, 3.9 Hz, 1H), 2.18 (dd, *J* = 8.7, 3.8 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 168.1, 166.2, 151.8, 131.8, 121.2, 45.1, 35.3, 28.9, 28.7, 27.4.

The NMR spectroscopic data agreed with those reported.[2]

4. Synthesis of 1-azadienes



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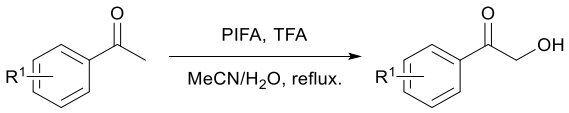
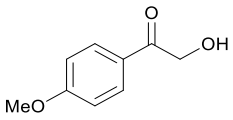
a. Synthesis of α-hydroxyketones



General procedure A:[6]

To a stirring solution of acetophenone (1.0 equiv.) and TFA (2.0 equiv.) in a 5:1 mixture of MeCN/H_2O (0.17 M wrt the acetophenone) was added $PhI(OCOCF_3)_2$ (2.0 equiv.). The resulting solution was then heated to reflux, monitored by TLC. Upon completion, the reaction mixture was allowed to cool to rt, then MeCN was removed under reduced pressure. The remaining aqueous solution was extracted with CH_2Cl_2, then the combined organic extracts were washed with water and brine. The organic layer was dried over $MgSO_4$, filtered, then concentrated *in vacuo*, followed by purification by FCC.

2-Hydroxy-1-(4-methoxyphenyl)ethan-1-one (S2a)



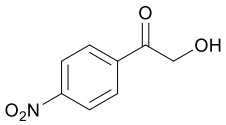
The titled compound was prepared following the General procedure A using 4'-methoxyacetophenone (3.198 g, 21.298 mmol), TFA (3.2 mL, 41.789 mmol), and $PhI(OCOCF_3)_2$ (17.398 g, 40.457 mmol) in 5:1 MeCN/H_2O (120 mL). Purification by FCC (30%–50% EtOAc in hexane) furnished **S2a** as an orange solid (2.297 g, 65%).

R_f = 0.17 (30% EtOAc in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91 (d, *J* = 9.0 Hz, 2H), 6.97 (d, *J* = 9.0 Hz, 2H), 4.82 (s, 2H), 3.89 (s, 3H).

The NMR spectroscopic data agreed with those reported.[7]

2-Hydroxy-1-(4-nitrophenyl)ethan-1-one (S2b)



The titled compound was prepared following the General procedure A using 4'-nitroacetophenone (3.305 g, 20.009 mmol), TFA (3.2 mL, 41.789 mmol), and $PhI(OCOCF_3)_2$ (17.175 g, 39.934 mmol) in 5:1 MeCN/H_2O (150 mL). Purification by FCC (40% EtOAc in hexane) furnished **S2b** as an orange solid (679.0 mg, 19%).

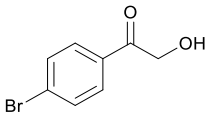
R_f = 0.21 (40% EtOAc in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.37 (d, *J* = 8.9 Hz, 2H), 8.10 (d, *J* = 8.8 Hz, 2H), 4.94 (s, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): 197.2, 151.0, 137.8, 128.9, 124.3, 66.0.

The NMR spectroscopic data agreed with those reported.[8]

1-(4-Bromophenyl)-2-hydroxyethan-1-one (S2c)



Procedure:[9]

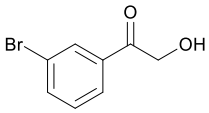
To a stirring solution of 2,4'-dibromoacetophenone (2.828 g, 10.174 mmol) in DMF (100 mL) at 0 °C was added $NaNO_2$ (896.3 mg, 12.990 mmol) in one portion, and the resulting solution was stirred at the same temperature for 4 h. Upon completion, as indicated by TLC, the reaction was quenched with H_2O, then extracted with EtOAc. The combined organic layers were washed with H_2O and brine, dried over $MgSO_4$, filtered, then concentrated *in vacuo*. Purification by FCC afforded **S2c** as an orange oil (776.5 mg, 35%).

R_f = 0.27 (30% EtOAc in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79 (d, *J* = 8.6 Hz, 2H), 7.66 (d, *J* = 8.6 Hz, 2H), 4.85 (s, 2H), 3.45 (s, 1H).

The NMR spectroscopic data agreed with those reported.[8]

1-(3-Bromophenyl)-2-hydroxyethan-1-one (S2d)



The titled compound was prepared following the General procedure A using 3'-bromoacetophenone (0.67 mL, 5.016 mmol), TFA (0.77 mL, 10.555 mmol), and $PhI(OCOCF_3)_2$ (4.327 g, 10.061 mmol) in 5:1 MeCN/H_2O (30 mL). Purification by FCC (25% EtOAc in hexane) furnished **S2d** as a yellow oil (322.3 mg, 30%).

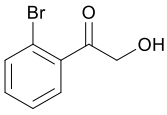
R_f = 0.26 (25% EtOAc in hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.07 (s, 1H), 7.85 (d, *J* = 7.8 Hz, 1H), 7.77 (d, *J* = 7.9 Hz, 1H), 7.41 (t, *J* = 7.9 Hz, 1H), 4.87 (s, 2H).

^{13}C NMR (125 MHz, $CDCl_3$): 197.5, 137.4, 135.2, 131.0, 130.8, 126.4, 123.5, 65.8.

The NMR spectroscopic data agreed with those reported.[8]

1-(2-bromophenyl)-2-hydroxyethan-1-one (S2e)



The titled compound was prepared following the General procedure A using 2'-bromoacetophenone (0.66 mL, 4.895 mmol), TFA (0.77 mL, 10.555 mmol), and $PhI(OCOCF_3)_2$ (4.415 g, 10.267 mmol) in 5:1 MeCN/H_2O (30 mL). Purification by FCC (30% EtOAc in hexane) furnished **S2e** as a yellow oil (460.9 mg, 44%).

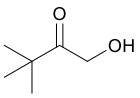
R_f = 0.28 (30% EtOAc in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70–7.67 (m, 1H), 7.56–7.53 (m, 2H), 7.45–7.37 (m, 2H), 4.79 (s, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): 201.5, 136.8, 134.5, 133.0, 129.4, 127.6, 119.9, 68.0.

The NMR spectroscopic data agreed with those reported.[10]

1-Hydroxy-3,3-dimethylbutan-2-one (S2f)



Procedure:[11]

To a reaction vessel containing 1-bromopinacolone (1.50 mL, 11.151 mmol) and a stir bar at 0 °C was slowly added an aqueous solution of 1 M NaOH (13 mL) over 20 mL, and the resulting mixture was stirred at the same temp for 1 h. The reaction mixture was then extracted with EtOAc, then the combined organic extracts were washed with water and brine. The combined organic layer was dried over $MgSO_4$, filtered, then concentrated *in vacuo*. The crude material was then used directly in the subsequent step without further purifications (1.192 g, 90%).

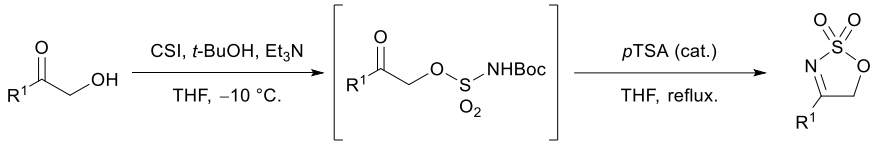
R_f = 0.26 (30% EtOAc in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 4.40 (s, 2H), 1.19 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$): 215.2, 63.9, 42.1, 26.2.

The NMR spectroscopic data agreed with those reported.[12]

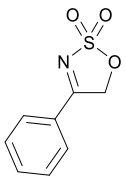
b. Synthesis of methylene active cyclic sulfamidate imines



General procedure B:

To a stirring solution of *t*-BuOH (1.5 equiv.) in THF (1.0 M wrt CSI) at −10 °C was added chlorosulfonyl isocyanate (CSI) (1.2 equiv.) dropwise, followed by rapid stirring at the same temperature for 30 min. A solution of α-hydroxy ketone (1.0 equiv.) in THF (final conc. 0.5 M wrt α-hydroxy ketone) was then added to the CSI/*t*-BuOH mixture, followed by the dropwise addition of Et_3N (1.2 equiv.). The resulting solution was then stirred at −10 °C and monitored by TLC. Upon completion, the reaction was quenched with water, extracted with EtOAc, then the combined organic extracts were washed with water and brine. The combined layer was dried over $MgSO_4$, filtered, and then concentrated *in vacuo*. The crude reaction mixture was then dissolved in THF (0.1 M) and *p*TSA was then added (10 mol%). The resulting mixture was heated at reflux overnight. Upon completion, the reaction mixture was allowed to cool down to rt, then quenched with sat. aq. $NaHCO_3$, followed by extraction with EtOAc. The combined organic extracts were then washed with water and brine, dried over $MgSO_4$, filtered, then concentrated *in vacuo*, followed by purification by either FCC or by recrystallisation.

4-Phenyl-5*H*-1,2,3-oxathiazole 2,2-dioxide (S3a)



The titled compound was prepared following the General procedure B using 2-hydroxyacetophenone (4.836 g, 35.520 mmol), CSI (3.8 mL, 43.657 mmol), *t*-BuOH (5.0 mL, 52.280 mmol), and Et_3N (8.0 mL, 57.397 mmol) in THF (70 mL), then *p*TSA•H_2O (796

mg, 4.185 mmol) in THF (70 mL). Recrystallisation of the crude residue from 1:2 THF/*n*-hexane at −20 °C afforded **S3a** as a light-yellow solid (3.600 g, 51%).

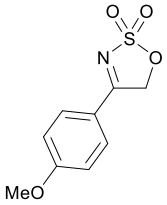
R_f = 0.15 (20% EtOAc in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.97 – 7.89 (m, 2H), 7.74 (ddt, J = 7.9, 7.1, 1.3 Hz, 1H), 7.66 – 7.54 (m, 2H), 5.59 (s, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 175.3, 135.9, 129.7, 128.9, 127.2, 74.3.

The NMR spectroscopic data agreed with those reported.[13]

4-(4-Methoxyphenyl)-5H-1,2,3-oxathiazole 2,2-dioxide (S3b)



The titled compound was prepared following the General procedure B using **S2a** (2.297 g, 13.821 mmol), CSI (1.50 mL, 17.233 mmol), *t*-BuOH (2.00 mL, 20.912 mmol), and Et_3N (3.00 mL, 21.524 mmol) in THF (50 mL), then *p*TSA•H_2O (282.4 mg, 1.485 mmol) in THF (60 mL). Recrystallisation of the crude residue from 1:2 THF/*n*-hexane at −20 °C afforded **S3b** as a dark orange solid (1.075 mg, 34%).

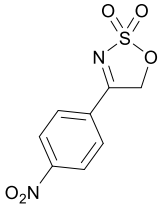
R_f = 0.06 (20% EtOAc in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 – 7.74 (m, 2H), 7.11 – 6.99 (m, 2H), 5.54 (s, 2H), 3.93 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 174.1, 165.9, 131.3, 119.5, 115.2, 74.0, 55.8.

The NMR spectroscopic data agreed with those reported.[13]

4-(4-Nitrophenyl)-5*H*-1,2,3-oxathiazole 2,2-dioxide (S3c)



The titled compound was prepared following the General procedure B using **S2b** (679.0 mg, 3.748 mmol), CSI (0.41 mL, 4.710 mmol), *t*-BuOH (0.55 mL, 5.751 mmol), and Et_3N (0.80 mL, 5.740 mmol) in THF (20 mL), then *p*TSA•H_2O (92.0 mg, 0.484 mmol) in THF (20 mL). Recrystallisation of the crude residue from 1:2 THF/*n*-hexane at −20 °C afforded **S3c** as a dark orange solid (552.5 mg, 61%).

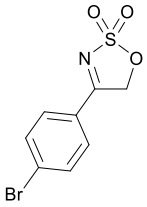
R_f = 0.11 (20% EtOAc in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.64 – 8.31 (m, 2H), 8.23 – 8.09 (m, 2H), 5.63 (s, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 173.4, 151.8, 132.3, 130.0, 124.8, 74.1.

The NMR spectroscopic data is in good agreement with those reported in DMSO-d_6.[13]

4-(4-Bromophenyl)-5*H*-1,2,3-oxathiazole 2,2-dioxide (S3d)



The titled compound was prepared following the General procedure B using **S2c** (776.5 mg, 3.611 mmol), CSI (0.36 mL, 4.300 mmol), *t*-BuOH (0.52 mL, 5.437 mmol), and Et_3N (0.75 mL, 5.380 mmol) in THF (25 mL), then *p*TSA•H_2O (80.3 mg, 0.422 mmol) in THF (25 mL). Recrystallisation of the crude residue from 1:2 THF/*n*-hexane at −20 °C afforded **S3d** as a white solid (264.6 mg, 27%).

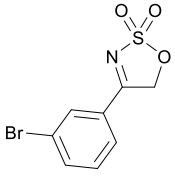
R_f = 0.15 (20% EtOAc in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87 – 7.67 (m, 4H), 5.55 (s, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 174.3, 133.2, 131.6, 130.1, 126.0, 74.0.

The NMR spectroscopic data are in good agreement with those reported in DMSO-d_6.[14]

4-(3-Bromophenyl)-5H-1,2,3-oxathiazole 2,2-dioxide (S3e)



The titled compound was prepared following the General procedure B using **S2d** (322.3 mg, 1.499 mmol), CSI (0.16 mL, 1.838 mmol), *t*-BuOH (0.22 mL, 2.300 mmol), and Et_3N (0.31 mL, 2.224 mmol) in THF (5 mL), then *p*TSA•H_2O (20.8 mg, 0.109 mmol) in THF (10 mL). Recrystallisation of the crude residue from 1:2 THF/*n*-hexane at −20 °C afforded **S3e** as an off-white yellow solid (206.2 mg, 50%).

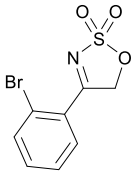
R_f = 0.11 (20% EtOAc in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.07 (t, *J* = 1.8 Hz, 1H), 7.85 (dddd, *J* = 9.9, 7.9, 1.9, 1.1 Hz, 2H), 7.48 (t, *J* = 7.9 Hz, 1H), 5.55 (s, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 174.1, 138.7, 131.7, 131.2, 129.1, 127.3, 123.9, 74.1.

The NMR spectroscopic data are in good agreement with those reported in DMSO-d_6.[14]

4-(2-Bromophenyl)-5*H*-1,2,3-oxathiazole 2,2-dioxide (S3f)



The titled compound was prepared following the General procedure B using **S2e** (460.9 mg, 2.143 mmol), CSI (0.22 mL, 2.528 mmol), *t*-BuOH (0.31 mL, 3.241 mmol), and Et_3N (0.45 mL, 3.229 mmol) in THF (9 mL), then *p*TSA•H_2O (32.4 mg, 0.1780 mmol) in THF (15 mL). Purification by FCC (20% EtOAc in hexane) afforded **S3f** as an off-white semi-solid (141.9 mg, 24%).

Mp: 132–136 °C.

R_f = 0.17 (20% EtOAc in hexane).

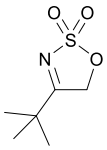
IR (neat): 1574, 1351, 1190, 977, 753, 662 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.23 – 8.06 (m, 1H), 7.84 – 7.71 (m, 1H), 7.58 – 7.47 (m, 2H), 5.80 (s, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 176.5, 135.5, 135.3, 133.1, 128.8, 128.4, 123.1, 76.6.

HRESI-MS (ESI –ve): Found 273.9167, calc for $C_8H_5NO_3SBr$ 273.9174 $[M - H]^-$.

4-(*tert*-Butyl)-5*H*-1,2,3-oxathiazole 2,2-dioxide (S3g)



The titled compound was prepared following the General procedure B using **S2f** (1.192 g, 10.257 mmol), CSI (1.10 mL, 12.638 mmol), *t*-BuOH (1.50 mL, 15.684 mmol), and Et_3N (2.1 mL, 15.067 mmol) in THF (21 mL), then *p*TSA•H_2O (211.2 mg, 1.110 mmol) in THF (25 mL). Recrystallisation of the crude residue from 1:2 THF/*n*-hexane at −20 °C afforded **S3g** as a clear colourless solid (184.1 mg, 10%).

R_f = 0.16 (20% EtOAc in hexane).

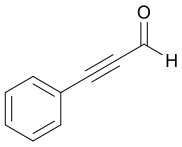
^{1}H NMR (400 MHz, $CDCl_3$): δ 5.17 (s, 2H), 1.34 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 190.7, 73.9, 36.9, 27.3.

The NMR spectroscopic data agreed with those reported.[13]

c. Synthesis of aldehydes

3-Phenylpropiolaldehyde (S4a)



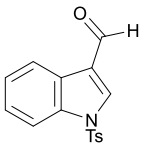
Procedure:[15]

A solution of phenylpropargyl aldehyde diethyl acetal (0.80 mL, 3.881 mmol) in a solution of 5% H_2SO_4 (1.0 mL) and glacial acetic (1.0 mL) was stirred at reflux with removal of EtOH for 1.5 h, after which the solution was allowed to cool to rt. The reaction mixture was neutralised with saturated aqueous $NaHCO_3$, followed by extraction with EtOAc. The combined organic layers were then washed with brine, dried over $MgSO_4$, filtered, then concentrated *in vacuo* to give **S4a** (415.2 mg, 82%) as a dark orange oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.43 (s, 1H), 7.67 – 7.58 (m, 2H), 7.57 – 7.46 (m, 1H), 7.46 – 7.38 (m, 2H).

The NMR spectroscopic data agreed with those reported.[16]

1-Tosyl-1*H*-indole-3-carbaldehyde (S4b)



Procedure:[17]

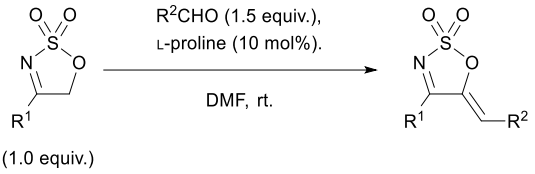
To a solution of Indole-3-carboxaldehyde (617.6 mg, 4.255 mmol) in CH_2Cl_2 (10 mL) at 0 °C was added Et_3N (1.2 mL, 8.610 mmol), and the resulting mixture was stirred at the same temperature for 15 min. *p*-Toluenesulfonyl chloride (877.5 mg, 4.603 mmol) was then added in one portion, and the reaction mixture was stirred at rt for 70 h. The reaction mixture was then diluted with CH_2Cl_2, washed sequentially with saturated aqueous NH_4Cl, $NaHCO_3$, and brine. The organic layer was then dried over $MgSO_4$, filtered, and concentrated *in vacuo* to give **S4b** (1.062 g, 83%) as a purple solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ 10.10 (s, 1H), 8.25 (ddd, *J* = 7.6, 1.6, 0.7 Hz, 1H), 8.22 (s, 1H), 7.98 – 7.91 (m, 1H), 7.89 – 7.81 (m, 2H), 7.44 – 7.33 (m, 2H), 7.33 – 7.27 (m, 2H), 2.38 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 185.3, 146.2, 136.2, 135.3, 134.4, 130.3, 127.2, 126.3, 125.1, 122.6, 122.4, 113.3, 21.7.

The NMR spectroscopic data agreed with those reported.[17]

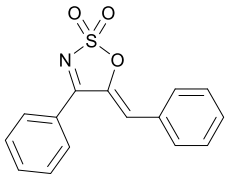
d. Synthesis of the 1-azadiene



General procedure C:[18]

A solution of 4-substituted-5*H*-1,2,3-oxathiazole 2,2-dioxide (1.0 equiv.), aldehyde (1.5 equiv.), and L-proline (10 mol%) in anhydrous DMF (0.5 M) was stirred at rt and monitored by TLC. Upon completion, water was added to stop the reaction, and the resulting mixture was extracted with EtOAc. The combined organic layers were washed with water and brine, dried over $MgSO_4$, filtered, then concentrated *in vacuo*. Purification by either FCC or recrystallisation was then carried out to afford the desired product.

(*Z*)-5-benzylidene-4-phenyl-5*H*-1,2,3-oxathiazole 2,2-dioxide (2a)



The titled compound was prepared following the General procedure C using **S3a** (1.375 g, 6.973 mmol), benzaldehyde (1.5 mL, 14.760 mmol), and L-proline (91.6 mg, 0.796 mmol) in DMF (15 mL). Recrystallisation from THF/hexane (1:2 v/v) at −20 °C afforded the desired product as an orange crystal (1.547 g, 78%).

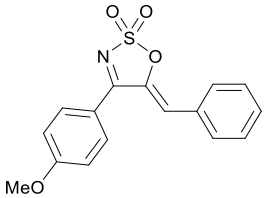
R_f = 0.25 (30% Et_2O in hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.90 – 7.81 (m, 2H), 7.79 (ddd, *J* = 5.3, 2.7, 1.4 Hz, 2H), 7.77 – 7.68 (m, 1H), 7.66 – 7.58 (m, 2H), 7.47 (tt, *J* = 3.8, 2.5 Hz, 3H), 6.67 (s, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 172.1, 143.5, 133.9, 131.8, 131.6, 131.1, 130.0, 129.6, 129.4, 128.2, 120.9.

The NMR spectroscopic data agreed with those reported.[18]

(*Z*)-5-benzylidene-4-(4-methoxyphenyl)-5*H*-1,2,3-oxathiazole 2,2-dioxide (2b)



The titled compound was prepared following the General procedure C using **S3b** (342.1 mg, 1.506 mmol), benzaldehyde (0.23 mL, 2.263 mmol), and L-proline (20.4 mg, 0.177 mmol) in DMF (3 mL). Recrystallisation from THF/hexane (1:2 v/v) at −20 °C afforded the desired product as a brick-red crystal (257.0 mg, 54%).

Mp: 184–186 °C.

R_f = 0.21 (30% Et_2O in hexane).

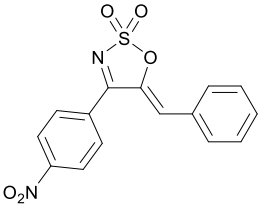
IR (neat): 1600, 1499, 1365, 1253, 1197, 1170, 1130, 981, 845, 759, 660 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.90 – 7.81 (m, 2H), 7.83 – 7.74 (m, 2H), 7.52 – 7.42 (m, 3H), 7.16 – 7.05 (m, 2H), 6.68 (s, 1H), 3.94 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 171.0, 164.4, 143.3, 132.2, 131.3, 131.3, 131.1, 129.1, 120.2, 120.1, 114.9, 55.7.

HRESI-MS (ESI +ve): Found 316.0641, calc for $C_{16}H_{14}NO_4S$ 316.0644 $[M + H]^+$.

(*Z*)-5-benzylidene-4-(4-nitrophenyl)-5*H*-1,2,3-oxathiazole 2,2-dioxide (2c)



The titled compound was prepared following the General procedure C using **S3c** (499.2 mg, 1.511 mmol), benzaldehyde (0.30 mL, 2.951 mmol), and L-proline (27.4 mg, 0.238 mmol) in DMF (3 mL). Recrystallisation from THF/hexane (1:2 v/v) at −20 °C afforded the desired product as a dark orange solid (344.3 mg, 68%).

Mp: 198–202 °C.

R_f = 0.21 (15% EtOAc in hexane).

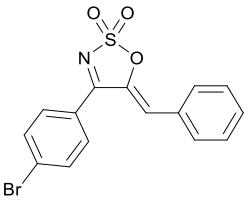
IR (neat): 1531, 1379, 1332, 1203, 1132, 985, 872, 850, 717, 655 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.58 – 8.34 (m, 2H), 8.17 – 7.93 (m, 2H), 7.86 – 7.73 (m, 2H), 7.57 – 7.39 (m, 3H), 6.57 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 168.9, 149.7, 141.7, 132.5, 131.2, 130.6, 129.9, 129.4, 128.3, 123.4, 120.2.

HRESI-MS (ESI –ve): Found 329.0236, calc for $C_{15}H_9N_2O_5S$ 329.0232 $[M – H]^-$.

(*Z*)-5-benzylidene-4-(4-bromophenyl)-5*H*-1,2,3-oxathiazole 2,2-dioxide (2d)



The titled compound was prepared following the General procedure C using **S3d** (255.8 mg, 0.926 mmol), benzaldehyde (0.15 mL, 1.476 mmol), and L-proline (11.0 mg, 0.096 mmol) in DMF (2 mL). Recrystallisation from THF/hexane (1:2 v/v) at −20 °C afforded the desired product as an orange crystal (232.6 mg, 69%).

Mp: 185–193 °C.

R_f = 0.24 (10% EtOAc in hexane).

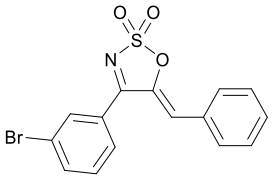
IR (neat): 1635, 1568, 1397, 1331, 1199, 982, 868, 758, 656, , 652 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 – 7.75 (m, 4H), 7.75 – 7.69 (m, 2H), 7.54 – 7.39 (m, 3H), 6.62 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 170.9, 143.0, 132.8, 131.8, 131.5, 131.2, 130.8, 129.2, 129.0, 126.7, 120.7.

HRESI-MS (ESI –ve): Found 361.9486, calc for $C_{15}H_9NO_3SBr$ 361.9487 $[M - H]^-$.

(*Z*)-5-benzylidene-4-(3-bromophenyl)-5*H*-1,2,3-oxathiazole 2,2-dioxide (2e)



The titled compound was prepared following the General procedure C using **S3e** (165.9 mg, 0.601 mmol), benzaldehyde (0.10 mL, 0.984 mmol), and L-proline (14.0 mg, 0.124 mmol) in DMF (2 mL). Recrystallisation from THF/hexane (1:2 v/v) at −20 °C afforded the desired product as an orange crystal (124.2 mg, 57%).

Mp: 166–172 °C.

R_f = 0.25 (15% EtOAc in hexane).

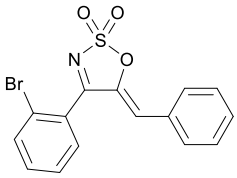
IR (neat): 1635, 1516, 1495, 1368, 1352, 1198, 1190, 1136, 991, 871, 761, 682 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.98 (t, *J* = 1.8 Hz, 1H), 7.93 – 7.70 (m, 4H), 7.59 – 7.37 (m, 4H), 6.62 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 170.4, 143.0, 136.5, 132.5, 131.8, 131.5, 130.8, 130.7, 129.8, 129.2, 128.3, 123.5, 120.8.

HRESI-MS (ESI –ve): Found 361.9474, calc for $C_{15}H_9NO_3SBr$ 361.9487 $[M - H]^+$.

(*Z*)-5-benzylidene-4-(2-bromophenyl)-5*H*-1,2,3-oxathiazole 2,2-dioxide (2f)



The titled compound was prepared following the General procedure C using **S3f** (141.9 mg, 0.514 mmol), benzaldehyde (0.10 mL, 0.984 mmol), and L-proline (8.8 mg, 0.076 mmol) in DMF (1 mL). Recrystallisation from THF/hexane (1:2 v/v) at −20 °C afforded the desired product as a dark orange crystal (80.8 mg, 57%).

Mp: 138–141 °C.

R_f = 0.17 (15% EtOAc in hexane).

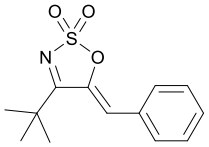
IR (neat): 1644, 1535, 1379, 1333, 1196, 1145, 983, 868, 754, 652 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88 – 7.76 (m, 1H), 7.76 – 7.70 (m, 2H), 7.61 – 7.38 (m, 6H), 6.23 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 171.8, 143.4, 134.0, 133.1, 131.8, 131.5, 130.6, 130.5, 129.3, 129.2, 127.7, 121.7, 120.2.

HRESI-MS (ESI +ve): Found 363.9640, calc for $C_{15}H_{11}NO_3SBr$ 363.9643 $[M + H]^+$.

(*Z*)-5-benzylidene-4-(tert-butyl)-5*H*-1,2,3-oxathiazole 2,2-dioxide (2g)



The titled compound was prepared following the General procedure C using **S3g** (174.5 mg, 0.985 mmol), benzaldehyde (0.15 mL, 1.476 mmol), and L-proline (10.4 mg, 0.090 mmol) in DMF (2 mL). Purification by FCC (10% EtOAc in hexane) afforded the desired product as an off-white solid (106.3 mg, 41%).

Mp: 133–137 °C.

R_f = 0.16 (10% EtOAc in hexane).

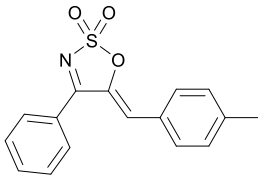
IR (neat): 1638, 1527, 1366, 1198, 1164, 1002, 876, 758, 658, , 652 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93 – 7.66 (m, 2H), 7.61 – 7.36 (m, 3H), 6.77 (s, 1H), 1.54 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 182.0, 142.0, 131.4, 131.2, 130.7, 129.1, 118.2, 37.5, 29.7.

HRESI-MS (ESI +ve): Found 288.0672, calc for $C_{13}H_{15}NO_3SNa$ 288.0670 $[M + Na]^+$.

(*Z*)-5-(4-methylbenzylidene)-4-phenyl-5*H*-1,2,3-oxathiazole 2,2-dioxide (2h)



The titled compound was prepared following the General procedure C using **S3a** (300.8 mg, 1.525 mmol), *p*-tolualdehyde (0.27 mL, 2.890 mmol), and L-proline (20.0 mg, 0.174 mmol) in DMF (3 mL). Recrystallisation from THF/hexane (1:2 v/v) at −20 °C afforded the desired product as a dark-yellow crystal (292.9 mg, 64%).

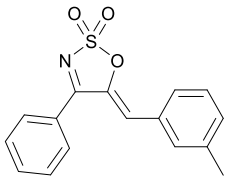
R_f = 0.36 (20% EtOAc in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87 – 7.79 (m, 2H), 7.77 – 7.65 (m, 3H), 7.65 – 7.56 (m, 2H), 7.27 (d, *J* = 8.0 Hz, 3H), 6.64 (s, 1H), 2.42 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 171.9, 142.8, 142.6, 133.5, 131.5, 130.0, 129.8, 129.3, 128.2, 128.1, 121.0, 21.7.

The NMR spectroscopic data agreed with those reported.[18]

(*Z*)-5-(3-methylbenzylidene)-4-phenyl-5*H*-1,2,3-oxathiazole 2,2-dioxide (2i)



The titled compound was prepared following the General procedure C using **S3a** (318.7 mg, 1.616 mmol), *m*-tolualdehyde (0.27 mL, 2.290 mmol), and L-proline (25.1 mg, 0.218 mmol) in DMF (3 mL). Recrystallisation from THF/hexane (1:2 v/v) at −20 °C afforded the desired product as a yellow crystal (287.6 mg, 59%).

Mp: 150–152 °C.

R_f = 0.27 (15% EtOAc in hexane).

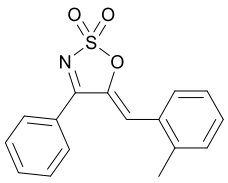
IR (neat): 1637, 1516, 1487, 1367, 1348, 1200, 1176, 1130, 984, 869, 769, 666, , 652 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89 – 7.78 (m, 2H), 7.78 – 7.68 (m, 1H), 7.66 – 7.55 (m, 4H), 7.35 (t, *J* = 7.6 Hz, 1H), 7.28 (d, *J* = 7.7 Hz, 1H), 6.64 (s, 1H), 2.41 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 171.9, 143.1, 139.0, 133.6, 132.5, 131.9, 130.9, 129.8, 129.3, 129.0, 128.7, 128.0, 121.0, 21.4.

HRESI-MS (ESI +ve): Found 300.0685, calc for $C_{16}H_{14}NO_3S$ 300.0694 $[M + H]^+$.

(*Z*)-5-(2-methylbenzylidene)-4-phenyl-5*H*-1,2,3-oxathiazole 2,2-dioxide (2j)



The titled compound was prepared following the General procedure C using **S3a** (301.5 mg, 1.529 mmol), *o*-tolualdehyde (0.27 mL, 2.335 mmol), and L-proline (23.8 mg, 0.207 mmol) in DMF (3 mL). Recrystallisation from THF/hexane (1:2 v/v) at −20 °C afforded the desired product as a yellow crystal (327.3 mg, 72%).

Mp: 145–150 °C.

R_f = 0.25 (30% Et_2O in hexane).

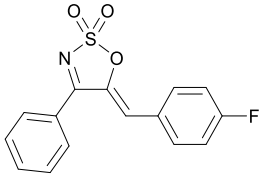
IR (neat): 1595, 1507, 1485, 1360, 1176, 1128, 979, 823, 708, 664 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.17 – 8.04 (m, 1H), 7.97 – 7.80 (m, 2H), 7.79 – 7.68 (m, 1H), 7.70 – 7.54 (m, 2H), 7.40 – 7.29 (m, 2H), 7.29 – 7.19 (m, 1H), 6.92 (s, 1H), 2.34 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 171.9, 143.4, 138.8, 133.7, 131.4, 130.8, 130.6, 129.8, 129.6, 129.3, 128.1, 126.9, 117.6, 20.0.

HRESI-MS (ESI +ve): Found 322.0500, calc for $C_{16}H_{13}NO_3SNa$ 322.0514 $[M + Na]^+$.

(*Z*)-5-(4-fluorobenzylidene)-4-phenyl-5*H*-1,2,3-oxathiazole 2,2-dioxide (2k)



The titled compound was prepared following the General procedure C using **S3a** (299.9 mg, 1.521 mmol), 4-fluorobenzaldehyde (0.25 mL, 2.331 mmol), and L-proline (25.4 mg, 0.221 mmol) in DMF (3 mL). Recrystallisation from THF/hexane (1:2 v/v) at −20 °C afforded the desired product as a yellow crystal (253.0 mg, 55%).

Mp: 142–148 °C.

R_f = 0.45 (40% EtOAc in hexane).

IR (neat): 1597, 1526, 1487, 1368, 1194, 1130, 984, 869, 815, 708, 663 cm^{-1}.

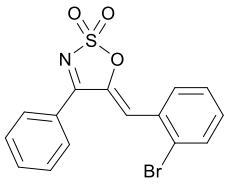
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87 – 7.75 (m, 4H), 7.77 – 7.68 (m, 1H), 7.68 – 7.57 (m, 2H), 7.24 – 7.06 (m, 2H), 6.63 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 171.8, 165.6, 163.0, 143.0, 133.7, 133.7, 133.6, 129.8, 129.4, 127.9, 127.3, 127.3, 119.3, 116.7, 116.4.

^{19}F NMR (376 MHz, $CDCl_3$): δ -105.78 (t, *J* = 7.3 Hz).

HRESI-MS (ESI +ve): Found 304.0435, calc for $C_{15}H_{11}NO_3SF$ 304.0444 $[M + H]^+$.

(*Z*)-5-(2-bromobenzylidene)-4-phenyl-5*H*-1,2,3-oxathiazole 2,2-dioxide (2l)



The titled compound was prepared following the General procedure C using **S3a** (304.1 mg, 1.542 mmol), 2-bromobenzaldehyde (0.27 mL, 2.313 mmol), and L-proline (17.3 mg, 0.150 mmol) in DMF (3 mL). Recrystallisation from THF/hexane (1:2 v/v) at −20 °C afforded the desired product as a light-orange crystal (344.8 mg, 61%).

Mp: 159–163 °C.

R_f = 0.42 (20% EtOAc in hexane).

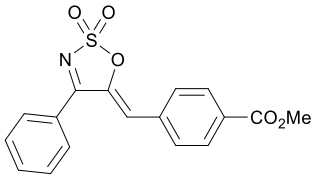
IR (neat): 1595, 1518, 1386, 1197, 1109, 985, 872, 760, 702, 656 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.18 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.96 – 7.87 (m, 2H), 7.80 – 7.69 (m, 1H), 7.65 (qd, *J* = 7.8, 1.6 Hz, 3H), 7.46 (td, *J* = 7.7, 1.3 Hz, 1H), 7.30 (td, *J* = 7.7, 1.7 Hz, 1H), 7.22 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 171.9, 143.9, 134.0, 133.4, 132.3, 131.8, 130.8, 130.0, 129.4, 128.2, 127.7, 126.6, 118.2.

HRESI-MS (ESI –ve): Found 361.9500, calc for $C_{15}H_9NO_3SBr$ 361.9487 $[M - H]^-$.

Methyl (*Z*)-4-((2,2-dioxido-4-phenyl-5*H*-1,2,3-oxathiazol-5-ylidene)methyl)benzoate (2m)



The titled compound was prepared following the General procedure C using **S3a** (253.6 mg, 1.286 mmol), methyl 4-formylbenzoate (384.8 mg, 2.344 mmol), and L-proline (19.4 mg, 0.169 mmol) in DMF (3 mL). Trituration of the crude reaction mixture with warm THF followed by vacuum filtration afforded the desired product as an off-white powder (260.6 mg, 59%).

Mp: 236–237 °C.

R_f = 0.26 (20% EtOAc in hexane).

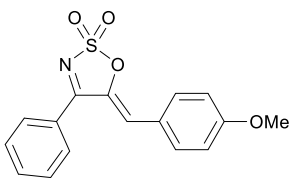
IR (neat): 1703, 1523, 1277, 1193, 1114, 983, 875, 768 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.16 – 8.06 (m, 2H), 7.92 – 7.80 (m, 4H), 7.80 – 7.69 (m, 1H), 7.69 – 7.55 (m, 2H), 6.68 (s, 1H), 3.95 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 171.8, 166.1, 144.2, 135.0, 133.9, 132.2, 131.1, 130.2, 129.9, 129.5, 127.7, 118.8, 52.5.

HRESI-MS (ESI +ve): Found 398.0670, calc for $C_{18}H_{17}NO_6SNa$ 398.0674 $[M + Na + MeOH]^+$.

(*Z*)-5-(4-methoxybenzylidene)-4-phenyl-5*H*-1,2,3-oxathiazole 2,2-dioxide (2n)



The titled compound was prepared following the General procedure C using **S3a** (415.4 mg, 2.106 mmol), *p*-anisaldehyde (0.38 mL, 3.126 mmol), and L-proline (26.4 mg, 0.229 mmol) in DMF (4 mL). Recrystallisation from THF/hexane (1:2 v/v) at −20 °C afforded the desired product as a vibrant yellow crystal (327.8 mg, 53%).

Mp: 143–147 °C.

R_f = 0.17 (20% EtOAc in hexane).

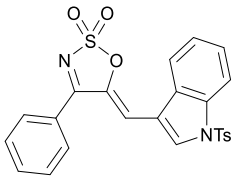
IR (neat): 1595, 1507, 1485, 1360, 1176, 1128, 979, 823, 708, 664 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): 7.84 – 7.80 (m, 2H), 7.79 – 7.74 (m, 3H), 7.74 – 7.68 (m, 1H), 7.65 – 7.56 (m, 2H), 7.01 – 6.89 (m, 2H), 6.63 (s, 1H), 3.88 (s, 4H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 171.9, 162.6, 142.3, 133.8, 133.6, 130.0, 129.5, 128.5, 123.9, 121.2, 115.0, 55.8.

HRESI-MS (ESI +ve): Found 316.0645, calc for $C_{16}H_{14}NO_4S$ 316.0644 $[M + H]^+$.

(*Z*)-4-phenyl-5-((1-tosyl-1*H*-indol-3-yl)methylene)-5*H*-1,2,3-oxathiazole 2,2-dioxide (2o)



The titled compound was prepared following the General procedure C using **S3a** (304.2 mg, 1.543 mmol), **S4b** (566.9 mg, 1.894 mmol), and L-proline (19.5 mg, 0.169 mmol) in DMF (3 mL). Recrystallisation from THF/hexane (1:2 v/v) at −20 °C afforded the desired product as a vibrant yellow crystal (613.8 mg, 76%).

Mp: 194–208 °C.

R_f = 0.18 (20% EtOAc in hexane).

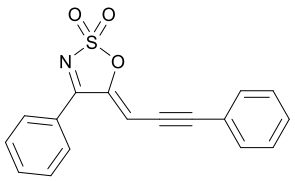
IR (neat): 1639, 1514, 1487, 1370, 1352, 1273, 1186, 1171, 1138, 1124, 966, 879, 806, 757, 660, 568, 536 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.40 (d, *J* = 0.9 Hz, 1H), 8.03 (dt, *J* = 8.3, 0.8 Hz, 1H), 7.92 – 7.82 (m, 4H), 7.80 – 7.69 (m, 1H), 7.66 – 7.58 (m, 2H), 7.54 (dt, *J* = 7.8, 1.0 Hz, 1H), 7.41 (ddd, *J* = 8.4, 7.2, 1.2 Hz, 1H), 7.35 – 7.27 (m, 3H), 6.87 (d, *J* = 0.8 Hz, 1H), 2.37 (s, 4H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 170.6, 145.9, 143.4, 134.6, 133.7, 130.5, 130.3, 129.7, 129.4, 128.7, 128.0, 127.2, 126.0, 124.2, 118.7, 114.0, 113.5, 110.1, 21.7.

HRESI-MS (ESI +ve): Found 479.0732, calc for $C_{24}H_{16}N_2O_5S_2$ 479.0735 $[M + H]^+$.

(*Z*)-4-phenyl-5-(3-phenylprop-2-yn-1-ylidene)-5*H*-1,2,3-oxathiazole 2,2-dioxide (2p)



The titled compound was prepared following the General procedure C using **S3a** (501.1 mg, 2.541 mmol), **S4a** (415.2 mg, 3.189 mmol), and L-proline (35.7 mg, 0.310 mmol) in DMF (6 mL). Purification by FCC (20% EtOAc in hexane) followed by recrystallisation from EtOAc/hexane (9:1) afforded the desired product as a dark orange crystal (91.1 mg, 11%).

Mp: 130–131 °C.

R_f = 0.18 (30% Et_2O in hexane).

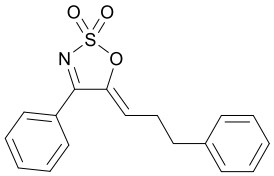
IR (neat): 2186, 1527, 1376, 1342, 1200, 1136, 981, 867, 703, 658 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91 – 7.78 (m, 2H), 7.71 (ddt, *J* = 8.3, 7.0, 1.3 Hz, 1H), 7.67 – 7.51 (m, 6H), 7.51 – 7.31 (m, 3H), 6.15 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 169.5, 150.6, 134.1, 132.4, 130.3, 129.8, 129.5, 128.7, 127.3, 121.5, 107.9, 101.0, 82.6.

HRESI-MS (ESI +ve): Found 310.0545, calc for $C_{17}H_{12}NO_3S$ 480.1821 $[M + H]^+$.

(*Z*)-4-phenyl-5-(3-phenylpropylidene)-5*H*-1,2,3-oxathiazole 2,2-dioxide (2q)



The titled compound was prepared following the General procedure C using **S3a** (302.4 mg, 1.533 mmol), hydrocinnamaldehyde (0.30 mL, 2.278 mmol), and L-proline (19.3 mg, 0.168 mmol) in DMF (3 mL). Purification by FCC (10% EtOAc in hexane) afforded the desired product as a dark orange oil (95.3 mg, 20%).

R_f = 0.12 (10% EtOAc in hexane).

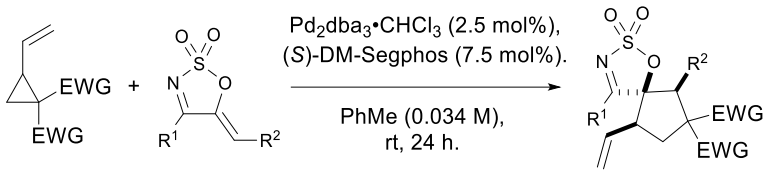
IR (neat): 1690, 1377, 1197, 1179, 976, 696 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74 – 7.63 (m, 3H), 7.56 – 7.48 (m, 3H), 7.32 (dd, *J* = 8.1, 6.7 Hz, 2H), 7.25 – 7.16 (m, 3H), 5.93 (t, *J* = 7.5 Hz, 1H), 2.90 – 2.81 (m, 2H), 2.77 (tdd, *J* = 8.4, 6.2, 1.5 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 170.4, 145.9, 139.8, 133.8, 129.8, 129.3, 128.8, 128.3, 126.7, 123.3, 34.2, 29.0.

HRESI-MS (ESI –ve): Found 312.0687, calc for $C_{17}H_{14}NO_3S$ 312.0694 $[M – H]^-$.

5. Synthesis of spirocyclic sulfamidate imines

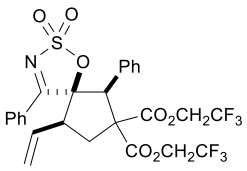


General procedure D:

To a reaction vial charged with a magnetic stirrer containing Pd_2dba_3•$CHCl_3$ (2.5 mol%) and (*S*)-DM-Segphos (7.5 mol%) was added anhydrous PhMe (0.003 M wrt Pd_2dba_3•$CHCl_3$). The resulting mixture was sonicated for a few seconds to fully dissolve the solid material and then stirred for 15 min at rt, affording a vinous-coloured solution. The catalyst solution was then transferred via a cannula to the reaction vial containing neat VCP (1.5 equiv.) and 1-azadiene (1.0 equiv.), rinsing twice with anhydrous PhMe (0.034 M wrt 1-azadiene final concentration). The reaction mixture was then stirred at rt and monitored by TLC. Upon completion, the reaction mixture was concentrated *in vacuo*, then purified by FCC.

(Note: Racemate samples for HPLC were prepared following General procedure D using (*rac*)-BINAP as ligand.)

Bis(2,2,2-trifluoroethyl) (5*R*,6*S*,9*S*)-4,6-diphenyl-9-vinyl-1-oxa-2-thia-3-azaspiro[4.4]non-3-ene-7,7-dicarboxylate 2,2-dioxide (3aa)



The titled compound was prepared following General procedure D using VCP **1a** (80.2 mg, 0.250 mmol), 1-azadiene **2a** (47.8 mg, 0.168 mmol), Pd_2dba_3•$CHCl_3$ (4.2 mg, 0.004 mmol), and (*S*)-DM-Segphos (10.8 mg, 0.015 mmol). Purification by FCC (20% Et_2O in hexane) afforded a mixture of **3aa** and **3aa'** as a colourless oily residue (100.2 mg, 8.2 : 1 *dr*, 99%).

Chiral HPLC: Chiralpak® IG-3, 10% isopropanol/hexanes, 0.5 mL.min^{-1}, 254 nm, t_r (minor dia) = 18.8 & 20.9 min, t_r (major dia) = 22.4 & 34.6 min.

R_f = 0.14 (30% Et_2O in hexane).

IR (neat): 1749, 1560, 1374, 1280, 1203, 1160, 1099, 939, 853, 762, 658 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) (8.3 : 1 mixture of two diastereoisomers, distinguishable resonances of the major diastereoisomer): δ 8.14 – 8.05 (m, 2H), 7.79 – 7.69 (m, 1H), 7.66 – 7.57 (m, 2H), 7.31 – 7.18 (m, 4H), 7.15 – 7.06 (m, 2H), 5.89 (ddd, *J* = 16.9, 10.2, 7.6 Hz, 1H), 5.26 (dd, *J* = 10.2, 1.2 Hz, 1H), 5.26 (s, 1H), 5.11 (dt, *J* = 17.0, 1.0 Hz, 1H), 4.71 (dq, *J* = 12.5, 8.2 Hz, 1H), 4.47 (ddq, *J* = 12.5, 9.4, 8.2 Hz, 2H), 3.54 – 3.45 (m, 1H), 3.44 (d, *J* = 13.2 Hz, 1H), 3.43 – 3.32 (m, 1H), 2.53 (dd, *J* = 13.2, 5.6 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) (8.3 : 1 mixture of two diastereoisomers, distinguishable resonances of the major diastereoisomer): δ 176.7, 170.4, 166.3, 134.9, 130.7, 130.5, 130.5, 129.9, 129.6, 129.3, 128.6,

127.3, 122.3 (q, *J* = 276.3 Hz), 122.0 (q, *J* = 275.0 Hz), 121.6, 106.2, 63.1, 62.2 (q, *J* = 37.4 Hz), 61.5 (q, *J* = 37.4 Hz), 58.2, 52.6, 39.4.

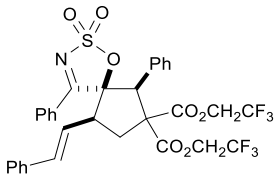
^{1}H NMR (400 MHz, $CDCl_3$) (8.3 : 1 mixture of two diastereoisomers, distinguishable resonances of the minor diastereoisomer): δ 7.87 – 7.78 (m, 2H), 7.51 (t, J = 7.8 Hz, 2H), 5.60 (ddd, *J* = 17.0, 10.3, 7.6 Hz, 1H), 5.22 – 5.14 (m, 1H), 5.10 (s, 1H), 5.02 (dt, *J* = 10.4, 1.0 Hz, 1H), 2.33 (dd, *J* = 14.2, 6.6 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) (8.3 : 1 mixture of two diastereoisomers, distinguishable resonances of the minor diastereoisomer): δ 179.0, 169.2, 166.8, 134.3, 133.2, 130.6, 130.5, 129.2, 129.2, 128.6, 120.2, 106.1, 63.5, 56.9, 54.6, 38.6.

^{19}F NMR (470 MHz, $CDCl_3$): δ -73.71 – -73.87 (m), -74.08 – -74.22 (m).

HRESI-MS (ESI +ve): Found 628.0849, calc for $C_{26}H_{21}F_6NO_7SNa$ 628.0841 $[M + Na]^+$.

Bis(2,2,2-trifluoroethyl) (5*R*,6*S*,9*S*)-4,6-diphenyl-9-((*E*)-styryl)-1-oxa-2-thia-3-azaspiro[4.4]non-3-ene-7,7-dicarboxylate 2,2-dioxide (3ba)



The titled compound was prepared following General procedure D using VCP **1b** (65.6 mg, 0.166 mmol), 1-azadiene **2a** (32.4 mg, 0.114 mmol), Pd_2dba_3•$CHCl_3$ (2.9 mg, 0.003 mmol), and (*S*)-DM-Segphos (5.5 mg, 0.008 mmol). Purification by FCC (20% Et_2O in hexane) afforded **3ba** as an ivory colour semi-solid (51.1 mg, >20 : 1 *dr*, 66%) and **3ba'** as a beige oil (20.9 mg, >20 : 1 *dr*, 28%).

Chiral HPLC: Chiralpak® IG-3, 20% isopropanol/hexanes, 1.5 mL.min^{-1}, 254 nm, t_r (major dia) = 27.2 & 64.6 min.

R_f = 0.16 (20% EtOAc in hexane).

IR (neat): 1750, 1559, 1373, 1281, 1246, 1201, 1155, 1100, 940, 762, 701, 658 cm^{-1}.

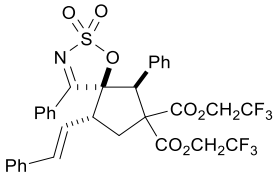
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.21 – 8.04 (m, 2H), 7.81 – 7.67 (m, 1H), 7.60 (dd, *J* = 8.5, 7.3 Hz, 2H), 7.38 – 7.19 (m, 8H), 7.13 (dq, *J* = 6.6, 2.3, 1.8 Hz, 2H), 6.39 (d, *J* = 15.9 Hz, 1H), 6.25 (dd, *J* = 15.8, 8.3 Hz, 1H), 5.31 (s, 1H), 4.71 (dq, *J* = 12.6, 8.2 Hz, 1H), 4.49 (ddq, *J* = 14.4, 12.5, 8.2 Hz, 2H), 3.79 – 3.60 (m, 1H), 3.51 (t, *J* = 13.6 Hz, 1H), 3.39 (dq, *J* = 12.5, 8.3 Hz, 1H), 2.59 (dd, *J* = 14.0, 6.5 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 176.8, 170.4, 166.3, 135.8, 135.8, 134.9, 130.8, 130.5, 129.9, 129.6, 129.3, 128.7, 128.6, 128.3, 127.2, 126.8, 122.3 (q, *J* = 277.5 Hz), 122.0 (q, *J* = 277.1), 121.7, 106.6, 63.2, 62.2 (q, *J* = 37.3 Hz), 61.5 (q, *J* = 37.3 Hz), 58.1, 52.4, 39.9.

^{19}F NMR (376 MHz, $CDCl_3$): δ -73.60 – -73.86 (m), -74.10 (q, J = 6.7, 6.2 Hz).

HRESI-MS (ESI +ve): Found 704.1157, calc for $C_{32}H_{25}F_6NO_7SNa$ 704.1154 $[M + Na]^+$.

Bis(2,2,2-trifluoroethyl) (5*R*,6*S*,9*R*)-4,6-diphenyl-9-((*E*)-styryl)-1-oxa-2-thia-3-azaspiro[4.4]non-3-ene-7,7-dicarboxylate 2,2-dioxide (3ba')



The titled compound was prepared following General procedure D using VCP **1b** (65.6 mg, 0.166 mmol), 1-azadiene **2a** (32.4 mg, 0.114 mmol), Pd_2dba_3•$CHCl_3$ (2.9 mg, 0.003 mmol), and (*S*)-DM-Segphos (5.5 mg, 0.008 mmol). Purification by FCC (20% Et_2O in hexane) afforded **3ba** as an ivory colour semi-solid (51.1 mg, >20 : 1 *dr*, 66%) and **3ba'** as a beige oil (20.9 mg, >20 : 1 *dr*, 28%).

R_f = 0.25 (20% EtOAc in hexane).

IR (neat): 1749, 1560, 1368, 1283, 1234, 1203, 1156, 1107, 938, 753, 694, 664 cm^{-1}.

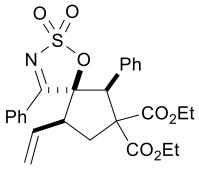
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82 – 7.73 (m, 2H), 7.53 – 7.44 (m, 1H), 7.43 – 7.35 (m, 4H), 7.31 (dt, *J* = 4.7, 1.9 Hz, 3H), 7.23 – 7.13 (m, 3H), 6.91 (td, *J* = 5.0, 4.4, 3.2 Hz, 2H), 6.38 (dd, *J* = 15.8, 1.1 Hz, 1H), 5.71 (dd, *J* = 15.8, 8.7 Hz, 1H), 5.29 (s, 1H), 4.71 (dq, *J* = 12.6, 8.1 Hz, 1H), 4.65 – 4.49 (m, 2H), 4.40 (dq, *J* = 12.7, 8.1 Hz, 1H), 3.89 (dddd, *J* = 8.8, 7.7, 4.7, 1.2 Hz, 1H), 3.76 – 3.55 (m, 2H), 2.36 (dd, J = 14.4, 4.8 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 179.3, 169.7, 166.6, 135.4, 134.8, 133.7, 130.8, 130.3, 130.1, 129.3, 129.3, 129.2, 128.9, 128.5, 128.3, 126.3, 124.3, 122.3 (q, *J* = 277.5 Hz)*, 122.10 (q, *J* = 277.3 Hz)*, 106.6, 63.6, 61.67 (two overlapping quartets, *J* = 35.5 Hz), 55.7, 54.2, 39.3.

**Note: outermost resonances of these quartets were not observed due to their low intensities.*

^{19}F NMR (376 MHz, $CDCl_3$): δ -73.72 (t, *J* = 8.4 Hz), -73.80 (t, *J* = 8.3 Hz).

Diethyl (5*R*,6*S*,9*S*)-4,6-diphenyl-9-vinyl-1-oxa-2-thia-3-azaspiro[4.4]non-3-ene-7,7-dicarboxylate 2,2-dioxide (3ca)



The titled compound was prepared following General procedure D using VCP **1c** (28.7 mg, 0.135 mmol), 1-azadiene **2a** (25.9 mg, 0.098 mmol), Pd_2dba_3•$CHCl_3$ (2.3 mg, 0.002 mmol), and (*S*)-DM-Segphos (4.7 mg, 0.007 mmol). Purification by FCC (20% EtOAc in hexane) afforded a mixture of **3ca** and **3ca'** as a beige semi-solid residue (30.6 mg, 2.4 : 1 *dr*, 68%).

Chiral HPLC: Chiralpak® IG-3, 40% isopropanol/hexanes, 0.4 $mL.min^{-1}$, 274 nm, t_r (minor dia) = 22.8 & 23.7 min, t_r (major dia) = 21.2 & 418 min.

R_f = 0.15 (20% EtOAc in hexane).

IR (neat): 1716, 1556, 1369, 1263, 1201, 1184, 1089, 941, 858, 765 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) (2.6 : 1 mixture of two diastereoisomers, distinguishable resonances of the major diastereoisomer): δ 8.24 – 8.10 (m, 2H), 7.76 – 7.66 (m, 1H), 7.68 – 7.56 (m, 2H), 7.30 – 7.15 (m, 3H), 7.11 (dt, *J* = 6.7, 1.6 Hz, 2H), 5.89 (ddd, *J* = 16.9, 10.2, 7.6 Hz, 1H), 5.31 (s, 1H), 5.21 (dd, J = 10.2, 1.4 Hz, 1H), 5.06 (d, *J* = 17.1, 1.0 Hz, 1H), 4.36 (dq, J = 10.8, 7.1 Hz, 1H), 4.32 – 4.14 (m, 1H), 3.98 – 3.84 (m, 1H), 3.59 – 3.29 (m, 3H), 2.52 – 2.40 (m, 1H), 1.26 (t, *J* = 7.1 Hz, 5H), 0.72 (t, *J* = 7.2 Hz, 3H).

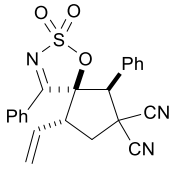
^{13}C NMR (100 MHz, $CDCl_3$) (2.6 : 1 mixture of two diastereoisomers, distinguishable resonances of the major diastereoisomer): δ 177.2, 172.4, 168.4, 134.7, 131.9, 130.9, 130.1, 129.5, 128.6, 128.2, 127.5, 120.9, 107.0, 63.3, 62.7, 61.7, 58.1, 52.7, 39.6, 13.9, 13.2.

^{1}H NMR (400 MHz, $CDCl_3$) (2.6 : 1 mixture of two diastereoisomers, distinguishable resonances of the minor diastereoisomer): δ 7.90 – 7.81 (m, 2H), 7.55 – 7.45 (m, 2H), 5.63 (ddd, *J* = 17.0, 10.4, 7.5 Hz, 1H), 5.16 (dt, *J* = 17.0, 1.2 Hz, 1H), 5.05 (s, 1H), 4.98 (dt, *J* = 10.3, 1.2 Hz, 1H), 4.19 – 4.05 (m, 1H), 3.81 (dq, *J* = 10.7, 7.2 Hz, 1H), 2.23 (dd, *J* = 14.0, 7.1 Hz, 1H), 1.22 (t, *J* = 7.2 Hz, 3H), 0.95 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) (2.6 : 1 mixture of two diastereoisomers, distinguishable resonances of the minor diastereoisomer): δ 179.5, 171.3, 168.8, 134.0, 133.9, 131.5, 131.3, 131.1, 130.6, 129.0, 128.9, 128.6, 128.6, 128.1, 119.5, 106.9, 63.7, 62.3, 61.8, 57.0, 54.6, 38.7, 13.9, 13.5.

HRESI-MS (ESI +ve): Found 520.1403, calc for $C_{26}H_{27}NO_7SNa$ 520.1406 $[M + Na]^+$.

(5*R*,6*S*,9*R*)-4,6-Diphenyl-9-vinyl-1-oxa-2-thia-3-azaspiro[4.4]non-3-ene-7,7-dicarbonitrile 2,2-dioxide (3da')



The titled compound was prepared following General procedure D using VCP **1d** (18.0 mg, 0.152 mmol), 1-azadiene **2a** (29.2 mg, 0.102 mmol), Pd_2dba_3•$CHCl_3$ (2.5 mg, 0.002 mmol), and (*S*)-DM-Segphos (6.3 mg, 0.009 mmol). Purification by FCC (30% EtOAc in hexane) afforded a mixture of **3da** and **3da'** as a light yellow semi-solid (33.8 mg, 2.8 : 1 *dr*, 82%).

Chiral HPLC: Chiralpak® IG-3, 10% isopropanol/hexanes, 1.0 mL.min^{-1}, 273 nm, t_r (minor dia) = 28.9 & 30.8 min, t_r (major dia) = 34.0 & 35.1 min.

R_f = 0.17 (30% EtOAc in hexane).

IR (neat): 1591, 1558, 1366, 1203, 1182, 935, 836, 482 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) (2.5 : 1 mixture of two diastereoisomers, distinguishable resonances of the major diastereoisomer): δ 7.81 (dq, J = 7.2, 1.4 Hz, 2H), 7.79 – 7.69 (m, 1H), 7.65 – 7.49 (m, 2H), 7.49 – 7.28 (m, 5H), 5.79 (ddd, *J* = 16.8, 10.4, 6.2 Hz, 1H), 5.40 (dd, *J* = 17.1, 1.8 Hz, 1H), 5.26 (dd, *J* = 10.5, 1.7 Hz, 1H), 4.28 (s, 1H), 4.15 – 4.01 (m, 1H), 3.32 – 3.22 (m, 1H), 2.84 (dd, *J* = 13.8, 11.3 Hz, 1H).

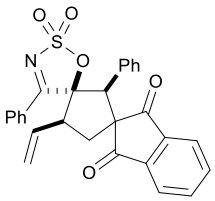
^{13}C NMR (100 MHz, $CDCl_3$) (1.1 : 1 mixture of two diastereoisomers, distinguishable resonances of the major diastereoisomer): δ 177.2, 172.4, 168.4, 134.7, 131.9, 130.9, 130.1, 129.5, 128.6, 128.2, 127.5, 120.9, 107.0, 63.3, 62.7, 61.7, 58.1, 52.7, 39.6, 13.9, 13.2.

^{1}H NMR (400 MHz, $CDCl_3$) (2.5 : 1 mixture of two diastereoisomers, distinguishable resonances of the minor diastereoisomer): δ 5.95 – 5.83 (m, 1H), 5.39 – 5.32 (m, 1H), 5.19 (d, J = 17.0 Hz, 1H), 4.34 (s, 1H), 3.78 (dt, J = 11.1, 8.5 Hz, 1H), 3.20 (ddd, J = 14.3, 8.6, 2.5 Hz, 1H), 3.00 (ddd, J = 14.3, 11.1, 1.7 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) (1.1 : 1 mixture of two diastereoisomers, distinguishable resonances of the minor diastereoisomer): δ 179.5, 171.3, 168.8, 134.0, 133.9, 131.5, 131.3, 131.1, 130.6, 129.0, 128.9, 128.6, 128.6, 128.1, 119.5, 106.9, 63.7, 62.3, 61.8, 57.0, 54.6, 38.7, 13.9, 13.5.

HRESI-MS (ESI +ve): Found 426.0896, calc for $C_{22}H_{17}N_3O_3SNa$ 426.0888 $[M + Na]^+$.

(2'*S*,3'*R*,4'*S*)-2',4''-Diphenyl-4'-vinyldispiro[indene-2,1'-cyclopentane-3',5''-[1,2,3]oxathiazole]-1,3-dione 2'',2''-dioxide (3ea)



The titled compound was prepared following General procedure D using VCP **1e** (31.4 mg, 0.158 mmol), 1-azadiene **2a** (30.7 mg, 0.108 mmol), Pd_2dba_3•$CHCl_3$ (2.8 mg, 0.003 mmol), and (*S*)-DM-Segphos (5.0 mg, 0.007 mmol). Purification by FCC (30% EtOAc in hexane) afforded a mixture of **3ea** and **3ea'** as a colourless oily residue (44.6 mg, 1.1 : 1 *dr*, 86%).

Chiral HPLC: Chiralpak® IG-3, 25% isopropanol/hexanes, 1.5 mL.min^{-1}, 226 nm, t_r = 18.8, 20.9, 22.4 & 34.6 min.

R_f = 0.23 (30% EtOAc in hexane).

IR (neat): 1742, 1704, 1591, 1559, 1372, 1266, 1200, 916, 819 cm^{-1}.

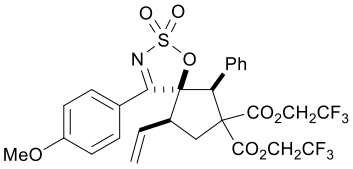
^{1}H NMR (400 MHz, $CDCl_3$) (1.1 : 1 mixture of two diastereoisomers, distinguishable resonances of the major diastereoisomer): δ 7.81 (dq, J = 7.2, 1.4 Hz, 2H), 7.79 – 7.69 (m, 1H), 7.65 – 7.49 (m, 2H), 7.49 – 7.28 (m, 5H), 5.79 (ddd, *J* = 16.8, 10.4, 6.2 Hz, 1H), 5.40 (dd, *J* = 17.1, 1.8 Hz, 1H), 5.26 (dd, *J* = 10.5, 1.7 Hz, 1H), 4.28 (s, 1H), 4.15 – 4.01 (m, 1H), 3.32 – 3.22 (m, 1H), 2.84 (dd, *J* = 13.8, 11.3 Hz, 1H).

^{1}H NMR (400 MHz, $CDCl_3$) (2.5 : 1 mixture of two diastereoisomers, distinguishable resonances of the minor diastereoisomer): δ 5.95 – 5.83 (m, 1H), 5.39 – 5.32 (m, 1H), 5.19 (d, J = 17.0 Hz, 1H), 4.34 (s, 1H), 3.78 (dt, J = 11.1, 8.5 Hz, 1H), 3.20 (ddd, J = 14.3, 8.6, 2.5 Hz, 1H), 3.00 (ddd, J = 14.3, 11.1, 1.7 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) (1.1 : 1 mixture of two diastereoisomers, the resonances of the each diastereoisomer were undistinguishable): δ 204.0, 200.6, 200.5, 198.7, 179.0, 177.3, 142.9, 142.1, 141.1, 140.5, 136.6, 136.5, 135.9, 135.7, 134.7, 134.6, 133.3, 131.6, 131.1, 131.1, 130.6, 129.8, 129.7, 129.7, 129.6, 129.3, 128.9, 128.8, 128.4, 128.3, 127.8, 127.5, 123.7, 123.6, 123.3, 123.3, 121.1, 119.8, 107.5, 106.0, 63.9, 63.0, 61.6, 54.9, 54.1, 38.1, 37.0.

HRESI-MS (ESI +ve): Found 506.1021, calc for $C_{28}H_{21}NO_5SNa$ 506.1038 $[M + Na]^+$.

Bis(2,2,2-trifluoroethyl) (5*R*,6*S*,9*S*)-4-(4-methoxyphenyl)-6-phenyl-9-vinyl-1-oxa-2-thia-3-azaspiro[4.4]non-3-ene-7,7-dicarboxylate 2,2-dioxide (3ab)



The titled compound was prepared following General procedure D using VCP **1a** (51.0 mg, 0.159 mmol), 1-azadiene **2b** (33.1 mg, 0.105 mmol), Pd_2dba_3•$CHCl_3$ (2.7 mg, 0.003 mmol), and (*S*)-DM-Segphos (6.0 mg, 0.008 mmol). Purification by FCC (20% EtOAc in hexane) afforded a mixture of **3ab** and **3ab'** as a light yellow oily residue (42.0 mg, 6.0 : 1 *dr*, 63%).

Chiral HPLC: Chiralpak® IG-3, 5% isopropanol/hexanes, 1.5 mL.min^{-1}, 300 nm, t_r (minor dia) = 20.8 & 22.1 min, t_r (major dia) = 24.5 & 42.7 min.

R_f = 0.12 (20% EtOAc in hexane).

IR (neat): 1749, 1605, 1541, 1369, 1276, 1243, 1201, 1171, 832 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) (6.0 : 1 mixture of two diastereoisomers, distinguishable resonances of the major diastereoisomer): δ 8.27 – 8.12 (m, 2H), 7.32 – 7.15 (m, 4H), 7.16 – 7.02 (m, 4H), 5.94 – 5.80 (m, 1H), 5.32 (s, 1H), 5.22 (dd, *J* = 10.2, 1.3 Hz, 1H), 5.06 (dt, *J* = 17.0, 0.9 Hz, 1H), 4.72 (dq, *J* = 12.6, 8.2 Hz, 1H), 4.49 (ddq, *J* = 18.5, 12.5, 8.2 Hz, 2H), 3.95 (s, 3H), 3.57 – 3.30 (m, 3H), 2.57 – 2.49 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) (6.0 : 1 mixture of two diastereoisomers, distinguishable resonances of the major diastereoisomer): δ 175.1, 170.7, 166.4, 165.2, 132.8, 130.8, 130.6, 129.2, 128.5, 122.3 (q, *J* = 277.4 Hz), 122.0 (q, *J* = 277.0 Hz), 121.4, 119.1, 115.1, 105.8, 63.2, 61.82 (two overlapping quartets, *J* = 37.4 Hz). 58.8, 55.8, 53.0, 39.5.

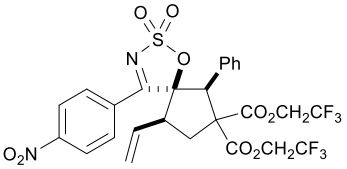
^{1}H NMR (400 MHz, $CDCl_3$) (6.0 : 1 mixture of two diastereoisomers, distinguishable resonances of the minor diastereoisomer): δ 7.94 – 7.85 (m, 2H), 7.02 – 6.95 (m, 2H), 5.68 (ddd, *J* = 17.3, 10.4, 7.2 Hz, 1H), 5.06 (s, 1H), 3.91 (s, 3H), 2.38 (dd, *J* = 14.2, 7.1 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) (6.0 : 1 mixture of two diastereoisomers, distinguishable resonances of the minor diastereoisomer): δ 177.2, 169.2, 166.8, 164.8, 133.4, 120.3, 119.9, 114.6, 105.9, 63.5, 57.9, 55.8, 54.3, 38.4.

^{19}F NMR (376 MHz, $CDCl_3$): δ -73.75 (dt, *J* = 23.1, 9.0 Hz), -74.06 – -74.16 (m).

HRESI-MS (ESI +ve): Found 658.0944, calc for $C_{27}H_{23}F_6NO_8SNa$ 658.0946 $[M + Na]^+$.

Bis(2,2,2-trifluoroethyl) (5*R*,6*S*,9*S*)-4-(4-nitrophenyl)-6-phenyl-9-vinyl-1-oxa-2-thia-3-azaspiro[4.4]non-3-ene-7,7-dicarboxylate 2,2-dioxide (3ac)



The titled compound was prepared following General procedure D using VCP **1a** (61.1 mg, 0.191 mmol), 1-azadiene **2c** (42.5 mg, 0.129 mmol), Pd_2dba_3•$CHCl_3$ (3.3 mg, 0.003 mmol), and (*S*)-DM-Segphos (7.3 mg, 0.010 mmol). In a slight deviation from the General procedure D, this reaction mixture was stirred at reflux for 24 h. Purification by FCC (10–30% EtOAc in hexane) afforded a mixture of **3ac** and **3ac'** as a light yellow oily residue (57.1 mg, 2.5 : 1 *dr*, 68%).

Chiral HPLC: Chiralpak® IG-3, 5% isopropanol/hexanes, 1.5 mL.min^{-1}, 254 nm, t_r (minor dia) = 13.0 & 13.4 min, t_r (major dia) = 15.8 & 23.7 min.

R_f = 0.21 (15% EtOAc in hexane).

IR (neat): 1750, 1530, 1382, 1281, 1242, 1205, 1165, 852 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) (2.5 : 1 mixture of two diastereoisomers, distinguishable resonances of the major diastereoisomer): δ 8.51 – 8.41 (m, 2H), 8.29 – 8.18 (m, 2H), 7.40 – 7.18 (m, 3H), 7.15 – 7.05 (m, 2H), 5.90 (dddd, J = 17.0, 10.3, 5.3, 2.1 Hz, 1H), 5.31 (dd, J = 10.3, 1.0 Hz, 1H), 5.15 (d, J = 17.2 Hz, 1H), 5.11 (s, 1H), 4.71 (dqd, J = 12.5, 8.1, 4.2 Hz, 1H), 4.62 – 4.31 (m, 3H), 3.50 – 3.32 (m, 3H), 2.62 – 2.47 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) (2.5 : 1 mixture of two diastereoisomers, distinguishable resonances of the major diastereoisomer): δ 175.5, 170.4, 166.0, 151.0, 132.8, 131.4, 130.8, 130.4, 130.2, 128.9, 124.6, 122.2 (q, *J* = 277.3 Hz)*, 122.1, 121.9 (q, *J* = 277.1 Hz)*, 106.1, 63.2, 62.3 (q, *J* = 37.3 Hz), 61.6 (q, *J* = 37.4 Hz), 57.9, 52.4, 39.5.

**Note: outermost resonances of these quartets were not observed due to their low intensities.*

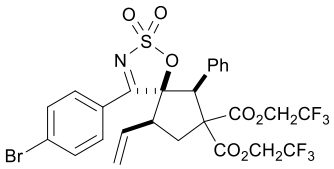
^{1}H NMR (400 MHz, $CDCl_3$) (2.5 : 1 mixture of two diastereoisomers, distinguishable resonances of the minor diastereoisomer): δ 8.40 – 8.31 (m, 2H), 7.99 – 7.89 (m, 2H), 7.15 – 7.03 (m, 5H), 5.51 (ddd, *J* = 16.9, 10.2, 8.2 Hz, 1H), 5.20 (d, *J* = 17.2 Hz, 1H), 5.07 (s, 1H), 5.04 (dt, *J* = 10.3, 0.9 Hz, 1H), 3.86 – 3.73 (m, 1H), 3.69 (dt, *J* = 12.5, 8.1 Hz, 1H), 3.57 (dd, *J* = 14.3, 7.7 Hz, 1H), 2.29 (dd, *J* = 14.4, 5.0 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) (2.5 : 1 mixture of two diastereoisomers, distinguishable resonances of the minor diastereoisomer): δ 177.8, 169.4, 166.3, 150.5, 130.2, 130.1, 129.7, 129.1, 124.1, 121.1, 106.2, 63.4, 55.7, 54.8, 38.9.

^{19}F NMR (376 MHz, $CDCl_3$): δ -73.80 (dq, *J* = 19.1, 8.3, 7.8 Hz), -74.12 (t, *J* = 8.5 Hz).

HRESI-MS (ESI +ve): Found 673.0681, calc for $C_{26}H_{20}F_6N_2O_9SNa$ 673.0691 $[M + Na]^+$.

Bis(2,2,2-trifluoroethyl) (5*R*,6*S*,9*S*)-4-(4-bromophenyl)-6-phenyl-9-vinyl-1-oxa-2-thia-3-azaspiro[4.4]non-3-ene-7,7-dicarboxylate 2,2-dioxide (3ad)



The titled compound was prepared following General procedure D using VCP **1a** (51.6 mg, 0.161 mmol), 1-azadiene **2d** (40.2 mg, 0.110 mmol), Pd_2dba_3•$CHCl_3$ (2.8 mg, 0.003 mmol), and (*S*)-DM-Segphos (6.8 mg, 0.009 mmol). In a slight deviation from the General procedure D, this reaction mixture was stirred at reflux for 24 h. Purification by FCC (10% EtOAc in hexane) afforded a mixture of **3ad** and **3ad'** as a colourless oily residue (33.9 mg, 4.2 : 1 *dr*, 45%).

Chiral HPLC: Chiralpak® IG-3, 5% isopropanol/hexanes, 1.5 mL.min^{-1}, 254 nm, t_r (minor dia) = 7.5 & 8.1 min, t_r (major dia) = 9.6 & 13.9 min.

R_f = 0.23 (10% EtOAc in hexane).

IR (neat): 1749, 1584, 1549, 1376, 1280, 1242, 1203, 1163, 1105, 660 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) (4.2 : 1 mixture of two diastereoisomers, distinguishable resonances of the major diastereoisomer): δ 8.06 – 7.95 (m, 2H), 7.82 – 7.73 (m, 2H), 7.31 – 7.19 (m, 3H), 7.13 – 7.01 (m, 2H), 5.87 (ddd, *J* = 16.8, 10.3, 1.6 Hz, 1H), 5.26 (dd, *J* = 10.3, 1.1 Hz, 1H), 5.21 (s, 1H), 5.09 (dd, *J* = 16.9, 1.1 Hz, 1H), 4.71 (dq, *J* = 12.6, 8.2 Hz, 1H), 4.47 (ddq, *J* = 14.6, 12.6, 8.2 Hz, 2H), 3.52 – 3.31 (m, 3H), 2.62 – 2.44 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) (4.2 : 1 mixture of two diastereoisomers, distinguishable resonances of the major diastereoisomer): δ 175.7, 170.5, 166.2, 133.1, 132.6, 131.3, 130.7, 130.5, 128.7, 125.9, 122.3 (q, *J* = 277.5 Hz)*, 122.0 (q, *J* = 277.1 Hz)*, 121.8, 106.0, 63.1, 62.0 (two overlapping quartets, *J* = 36.7 Hz), 58.3, 52.7, 39.5.

**Note: outermost resonances of these quartets were not observed due to their low intensities.*

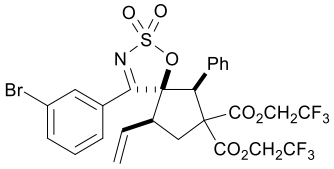
^{1}H NMR (400 MHz, $CDCl_3$) (4.2 : 1 mixture of two diastereoisomers, distinguishable resonances of the minor diastereoisomer): 7.73 – 7.64 (m, 4H), 5.58 (ddd, *J* = 17.0, 10.3, 7.7 Hz, 1H), 5.03 (s, 1H), 3.93 – 3.70 (m, 3H), 2.31 (dd, *J* = 14.3, 6.2 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) (4.2 : 1 mixture of two diastereoisomers, distinguishable resonances of the minor diastereoisomer): δ 178.0, 169.3, 166.6, 131.8, 130.3, 129.4, 106.0, 39.5.

^{19}F NMR (376 MHz, $CDCl_3$): δ -73.77 (t, J = 8.3 Hz), -74.12 (t, J = 8.4 Hz).

HRESI-MS (ESI +ve): Found 705.9920, calc for $C_{26}H_{20}F_6BrNO_3SNa$ 705.9946 $[M + Na]^+$.

Bis(2,2,2-trifluoroethyl) (5*R*,6*S*,9*S*)-4-(3-bromophenyl)-6-phenyl-9-vinyl-1-oxa-2-thia-3-azaspiro[4.4]non-3-ene-7,7-dicarboxylate 2,2-dioxide (3ae)



The titled compound was prepared following General procedure D using VCP **1a** (47.0 mg, 0.147 mmol), 1-azadiene **2e** (35.4 mg, 0.097 mmol), Pd_2dba_3•$CHCl_3$ (2.6 mg, 0.003 mmol), and (*S*)-DM-Segphos (5.0 mg, 0.007 mmol). Purification by FCC (15% EtOAc in hexane) afforded a mixture of **3ae** and **3ae'** as an off-white semi-solid (62.6 mg, 4.1 : 1 *dr*, 94%).

Chiral HPLC: Chiralpak® IG-3, 5% isopropanol/hexanes, 1.5 $mL.min^{-1}$, 254 nm, t_r (minor dia) = 7.4 & 8.0 min, t_r (major dia) = 8.6 & 13.2 min.

R_f = 0.19 (15% EtOAc in hexane).

IR (neat): 1749, 1587, 1554, 1379, 1280, 1240, 1201, 1158, 1101, 658 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) (4.1 : 1 mixture of two diastereoisomers, distinguishable resonances of the major diastereoisomer): δ 8.25 (t, *J* = 1.9 Hz, 1H), 8.05 (ddd, *J* = 7.9, 1.9, 1.0 Hz, 1H), 7.87 (ddd, *J* = 8.1, 1.9, 0.9 Hz, 1H), 7.51 (t, *J* = 8.0 Hz, 1H), 7.34 – 7.19 (m, 3H), 7.13 – 7.05 (m, 2H), 5.87 (dddd, *J* = 16.9,

10.4, 6.3, 1.6 Hz, 1H), 5.28 (dd, *J* = 10.3, 1.1 Hz, 1H), 5.19 (s, 1H), 5.16 – 5.09 (m, 1H), 4.71 (dqd, *J* = 12.5, 8.1, 1.2 Hz, 1H), 4.61 – 4.33 (m, 2H), 3.45 – 3.31 (m, 3H), 2.62 – 2.44 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) (4.1 : 1 mixture of two diastereoisomers, distinguishable resonances of the major diastereoisomer): δ 175.6, 170.4, 166.2, 137.7, 132.8, 131.0, 130.5, 130.5, 130.3, 129.5, 128.7, 127.9, 123.9, 122.3 (q, *J* = 277.5 Hz), 122.0 (q, *J* = 277.1 Hz), 121.9, 106.1, 63.2, 62.89 – 60.78 (two overlapping quartets, *J* = 37.4 Hz), 58.1, 52.5, 39.4.

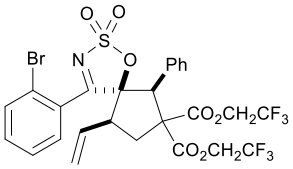
^{1}H NMR (400 MHz, $CDCl_3$) (4.1 : 1 mixture of two diastereoisomers, distinguishable resonances of the minor diastereoisomer): δ 7.97 (t, *J* = 1.9 Hz, 1H), 7.77 (ddd, *J* = 8.0, 2.0, 0.9 Hz, 1H), 7.69 (ddd, *J* = 7.9, 1.8, 1.0 Hz, 1H), 7.40 (t, *J* = 8.0 Hz, 1H), 5.55 (ddd, *J* = 16.9, 10.3, 7.8 Hz, 1H), 5.19 (ddd, *J* = 17.0, 1.4, 0.7 Hz, 1H), 5.06 (s, 1H), 5.06 (dt, *J* = 10.2, 1.0 Hz, 1H), 3.50 (dd, *J* = 14.3, 7.8 Hz, 1H), 2.30 (dd, *J* = 14.4, 5.9 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) (4.1 : 1 mixture of two diastereoisomers, distinguishable resonances of the minor diastereoisomer): δ 177.9, 169.3, 166.6, 136.9, 133.3, 133.0, 130.6, 130.4, 129.4, 129.0, 128.8, 128.6, 63.5, 56.3, 54.6, 38.6.

^{19}F NMR (376 MHz, $CDCl_3$): δ -73.78 (q, J = 8.7, 8.0 Hz), -74.13 (t, J = 9.0 Hz).

HRESI-MS (ESI +ve): Found 705.9929, calc for $C_{26}H_{20}F_6NO_7BrSNa$ 705.9946 $[M + Na]^+$.

Bis(2,2,2-trifluoroethyl) (5*R*,6*S*,9*S*)-4-(2-bromophenyl)-6-phenyl-9-vinyl-1-oxa-2-thia-3-azaspiro[4.4]non-3-ene-7,7-dicarboxylate 2,2-dioxide (3af)



The titled compound was prepared following General procedure D using VCP **1a** (47.8 mg, 0.149 mmol), 1-azadiene **2f** (36.3 mg, 0.100 mmol), Pd_2dba_3•$CHCl_3$ (2.6 mg, 0.003 mmol), and (*S*)-DM-Segphos (5.4 mg, 0.007 mmol). Purification by FCC (20% EtOAc in hexane) afforded **3ab** as an of-white semi-solid (49.1 mg, >20 : 1 *dr*, 72%).

Chiral HPLC: Chiralpak® IG-3, 5% isopropanol/hexanes, 1.5 mL.min^{-1}, 214 nm, t_r = 9.5 & 10.9 min.

R_f = 0.12 (20% EtOAc in hexane).

IR (neat): 1753, 1616, 1380, 1281, 1240, 1203, 1149, 939, 758, 657 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82 – 7.72 (m, 1H), 7.57 – 7.39 (m, 3H), 7.30 (s, 6H), 6.19 – 6.01 (m, 1H), 5.46 (dd, *J* = 10.6, 0.9 Hz, 1H), 5.41 (dt, *J* = 17.2, 0.9 Hz, 1H), 4.64 (s, 1H), 4.62 – 4.52 (m, 1H), 4.34 (dp, *J* = 12.5, 8.3 Hz, 2H), 3.42 – 3.28 (m, 2H), 3.21 (dq, *J* = 12.5, 8.3 Hz, 1H), 2.54 – 2.39 (m, 1H).

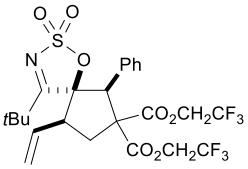
^{13}C NMR (100 MHz, $CDCl_3$): δ 178.2, 169.4, 166.0, 135.1, 133.0, 131.1, 130.9, 130.6, 129.3, 128.8, 128.6, 128.3, 127.4, 122.4, 122.24 (q, *J* = 277.4 Hz)*, 121.6, 106.6, 63.5, 56.5, 50.0, 39.1.

**Note: outermost resonances of these quartets were not observed due to their low intensities.*

^{19}F NMR (376 MHz, $CDCl_3$): δ -73.86 (t, J = 8.6 Hz), -74.10 (t, J = 8.3 Hz).

HRESI-MS (ESI +ve): Found 705.9934, calc for $C_{26}H_{20}F_6BNO_7SNa$ 705.9946 $[M + Na]^+$.

Bis(2,2,2-trifluoroethyl) (5*R*,6*S*,9*S*)-4-(*tert*-butyl)-6-phenyl-9-vinyl-1-oxa-2-thia-3-azaspiro[4.4]non-3-ene-7,7-dicarboxylate 2,2-dioxide (3ag).



The titled compound was prepared following General procedure D using VCP **1a** (51.1 mg, 0.160 mmol), 1-azadiene **2g** (30.0 mg, 0.113 mmol), Pd_2dba_3•$CHCl_3$ (3.0 mg, 0.003 mmol), and (*S*)-DM-Segphos (6.2 mg, 0.009 mmol). Purification by FCC (10–20% EtOAc in hexane) afforded a mixture of **3ag** and **3ag'** as an off-white semi-solid (27.2 mg, 1.0 : 1 *dr*, 41%).

Chiral HPLC: Chiralpak® IG-3, 5% isopropanol/hexanes, 1.5 mL.min^{-1}, 206 nm, t_r (minor dia, unresolved) = 6.0 min, t_r (major dia) = 6.6 & 7.3 min.

R_f = 0.12 (10% EtOAc in hexane).

IR (neat): 1749, 1591, 1375, 1281, 1205, 1158, 762, 702 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) (4.1 : 1 mixture of two diastereoisomers, distinguishable resonances of the major diastereoisomer): δ 8.25 (t, *J* = 1.9 Hz, 1H), 8.05 (ddd, *J* = 7.9, 1.9, 1.0 Hz, 1H), 7.87 (ddd, *J* = 8.1, 1.9, 0.9 Hz, 1H), 7.51 (t, *J* = 8.0 Hz, 1H), 7.34 – 7.19 (m, 3H), 7.13 – 7.05 (m, 2H), 5.87 (dddd, *J* = 16.9, 10.4, 6.3, 1.6 Hz, 1H), 5.28 (dd, *J* = 10.3, 1.1 Hz, 1H), 5.19 (s, 1H), 5.16 – 5.09 (m, 1H), 4.71 (dqd, *J* = 12.5, 8.1, 1.2 Hz, 1H), 4.61 – 4.33 (m, 2H), 3.45 – 3.31 (m, 3H), 2.62 – 2.44 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) (4.1 : 1 mixture of two diastereoisomers, distinguishable resonances of the major diastereoisomer): δ 175.6, 170.4, 166.2, 137.7, 132.8, 131.0, 130.5, 130.5, 130.3, 129.5, 128.7, 127.9, 123.9, 122.3 (q, *J* = 277.5 Hz), 122.0 (q, *J* = 277.1 Hz), 121.9, 106.1, 63.2, 62.89 – 60.78 (two overlapping quartets, *J* = 37.4 Hz), 58.1, 52.5, 39.4.

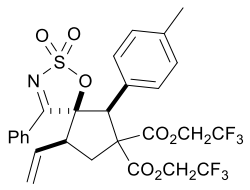
^{1}H NMR (400 MHz, $CDCl_3$) (4.1 : 1 mixture of two diastereoisomers, distinguishable resonances of the minor diastereoisomer): δ 7.97 (t, *J* = 1.9 Hz, 1H), 7.77 (ddd, *J* = 8.0, 2.0, 0.9 Hz, 1H), 7.69 (ddd, *J* = 7.9, 1.8, 1.0 Hz, 1H), 7.40 (t, *J* = 8.0 Hz, 1H), 5.55 (ddd, *J* = 16.9, 10.3, 7.8 Hz, 1H), 5.19 (ddd, *J* = 17.0, 1.4, 0.7 Hz, 1H), 5.06 (s, 1H), 5.06 (dt, *J* = 10.2, 1.0 Hz, 1H), 3.50 (dd, *J* = 14.3, 7.8 Hz, 1H), 2.30 (dd, *J* = 14.4, 5.9 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) (4.1 : 1 mixture of two diastereoisomers, distinguishable resonances of the minor diastereoisomer): δ 177.9, 169.3, 166.6, 136.9, 133.3, 133.0, 130.6, 130.4, 129.4, 129.0, 128.8, 128.6, 63.5, 56.3, 54.6, 38.6.

^{19}F NMR (376 MHz, $CDCl_3$): δ -73.80 (d, *J* = 9.1 Hz), -74.12 (t, *J* = 9.0 Hz).

HRESI-MS (ESI +ve): Found 608.1145, calc for $C_{24}H_{25}F_6NO_7SNa$ 608.1154 $[M + Na]^+$.

Bis(2,2,2-trifluoroethyl) (5*R*,6*S*,9*S*)-4-phenyl-6-(p-tolyl)-9-vinyl-1-oxa-2-thia-3-azaspiro[4.4]non-3-ene-7,7-dicarboxylate 2,2-dioxide (3ah)



The titled compound was prepared following General procedure D using VCP **1a** (54.0 mg, 0.169 mmol), 1-azadiene **2h** (33.1 mg, 0.111 mmol), Pd_2dba_3•$CHCl_3$ (2.7 mg, 0.003 mmol), and (*S*)-DM-Segphos (6.5 mg, 0.009 mmol). Purification by FCC (20% EtOAc in hexane) afforded a mixture of **3ah** and **3ah'** as an off white semi-solid (72.0 mg, 7.6 : 1 *dr*, quant.).

Chiral HPLC: Chiralpak® IG-3, 2% isopropanol/hexanes, 1.5 mL.min^{-1}, 254 nm, t_r (minor dia) = 14.2 & 15.6 min, t_r (major dia) = 17.1 & 29.3 min.

R_f = 0.29 (20% EtOAc in hexane).

IR (neat): 1750, 1560, 1374, 1282, 1242, 1203, 1163, 658 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) (9.8 : 1 mixture of two diastereoisomers, distinguishable resonances of the major diastereoisomer): δ 8.15 – 8.02 (m, 2H), 7.77 – 7.68 (m, 1H), 7.60 (dd, *J* = 8.5, 7.3 Hz, 2H), 7.03 (d, *J* = 8.2 Hz, 2H), 6.98 (d, *J* = 8.4 Hz, 2H), 5.89 (ddd, *J* = 17.0, 10.3, 7.6 Hz, 1H), 5.25 (dd, *J* = 10.2, 1.2 Hz, 1H), 5.22 (s, 1H), 5.10 (dt, *J* = 17.1, 0.9 Hz, 1H), 4.69 (dq, *J* = 12.6, 8.2 Hz, 1H), 4.47 (ddt, *J* = 15.6, 12.5, 8.2 Hz, 2H), 3.53 – 3.37 (m, 3H), 2.56 – 2.46 (m, 1H), 2.25 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) (9.8 : 1 mixture of two diastereoisomers, distinguishable resonances of the major diastereoisomer): δ 176.9, 170.4, 166.4, 139.2, 134.8, 130.6, 130.4, 129.9, 129.6, 129.3, 127.5, 127.3, 122.3 (q, *J* = 277.5 Hz), 122.0 (q, *J* = 277.1 Hz), 121.6, 106.4, 63.1, 62.1 (q, *J* = 37.3 Hz), 61.5 (q, *J* = 37.3 Hz), 58.0, 52.6, 39.4, 21.1.

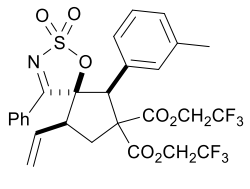
^{1}H NMR (400 MHz, $CDCl_3$) (9.8 : 1 mixture of two diastereoisomers, distinguishable resonances of the minor diastereoisomer): δ 7.85 – 7.78 (m, 2H), 7.69 – 7.61 (m, 1H), 7.55 – 7.47 (m, 2H), 7.15 – 7.06 (m, 2H), 5.60 (ddd, *J* = 17.0, 10.4, 7.6 Hz, 1H), 5.22 – 5.13 (m, 1H), 5.05 (s, 1H), 5.01 (dt, *J* = 10.3, 1.1 Hz, 1H), 3.99 – 3.77 (m, 2H), 2.32 (dd, *J* = 14.2, 6.8 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) (9.8 : 1 mixture of two diastereoisomers, distinguishable resonances of the minor diastereoisomer): δ 179.0, 169.2, 166.8, 139.1, 134.3, 133.3, 130.6, 130.5, 129.2, 128.7, 127.2, 120.1, 106.3, 63.4, 56.8, 54.5, 38.6.

^{19}F NMR (376 MHz, $CDCl_3$): δ -73.71 – -73.85 (m), -74.13 (t, J = 9.4 Hz).

HRESI-MS (ESI +ve): Found 642.0977, calc for $C_{27}H_{23}F_6NO_7SNa$ 642.0997 $[M + Na]^+$.

Bis(2,2,2-trifluoroethyl) (5*R*,6*S*,9*S*)-4-phenyl-6-(m-tolyl)-9-vinyl-1-oxa-2-thia-3-azaspiro[4.4]non-3-ene-7,7-dicarboxylate 2,2-dioxide (3ai)



The titled compound was prepared following General procedure D using VCP **1a** (49.4 mg, 0.154 mmol), 1-azadiene **2i** (31.7 mg, 0.106 mmol), Pd_2dba_3•$CHCl_3$ (2.6 mg, 0.003 mmol), and (*S*)-DM-Segphos (7.0 mg, 0.010 mmol). Purification

by FCC (20% EtOAc in hexane) afforded a mixture of **3aib** and **3ai'** as a light-yellow oily residue (65.7 mg, 10.0 : 1 *dr*, 97%).

Chiral HPLC: Chiralpak® IG-3, 5% isopropanol/hexanes, 1.5 mL.min^{-1}, 254 nm, t_r (minor dia, overlapping peaks) = 8.5 min, t_r (major dia) = 9.8 & 12.9 min.

R_f = 0.14 (15% EtOAc in hexane).

IR (neat): 1750, 1591, 1560, 1374, 1282, 1241, 1202, 1162, 1103, 658 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) (16.7 : 1 mixture of two diastereoisomers, distinguishable resonances of the major diastereoisomer): δ 8.15 – 8.03 (m, 2H), 7.79 – 7.69 (m, 1H), 7.66 – 7.56 (m, 2H), 7.14 – 7.03 (m, 2H), 6.96 – 6.84 (m, 2H), 5.88 (ddd, *J* = 17.0, 10.2, 7.6 Hz, 1H), 5.25 (dd, *J* = 10.2, 1.2 Hz, 1H), 5.20 (s, 1H), 5.10 (dt, *J* = 17.0, 1.0 Hz, 1H), 4.69 (dq, J = 12.6, 8.1 Hz, 1H), 4.47 (ddq, *J* = 17.8, 12.5, 8.2 Hz, 2H), 3.55 – 3.28 (m, 3H), 2.58 – 2.45 (m, 1H), 2.23 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) (16.7 : 1 mixture of two diastereoisomers, distinguishable resonances of the major diastereoisomer): δ 176.9, 170.4, 166.4, 138.4, 134.8, 131.2, 130.6, 130.5, 130.0, 129.9, 129.6, 128.4, 127.6, 127.3, 122.3 (q, *J* = 277.4 Hz), 122.04 (q, *J* = 277.1 Hz), 121.6, 106.3, 63.1, 62.2 (q, *J* = 37.4 Hz), 61.5 (q, *J* = 37.3 Hz), 58.2, 52.6, 39.4, 21.2.

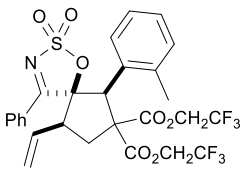
^{1}H NMR (400 MHz, $CDCl_3$) (16.7 : 1 mixture of two diastereoisomers, distinguishable resonances of the minor diastereoisomer): δ 7.84 – 7.78 (m, 2H), 7.67 – 7.63 (m, 1H), 7.52 – 7.48 (m, 2H), 5.58 (ddd, *J* = 17.1, 10.3, 7.7 Hz, 1H), 5.16 (dt, *J* = 17.2, 1.0 Hz, 1H), 5.06 (s, 1H), 5.00 (dt, *J* = 10.3, 1.0 Hz, 1H), 2.35 – 2.29 (m, 1H), 2.25 (s, 4H).

^{13}C NMR (100 MHz, $CDCl_3$) (16.7 : 1 mixture of two diastereoisomers, distinguishable resonances of the minor diastereoisomer): δ 179.0, 169.3, 166.8, 134.2, 133.2, 129.2, 128.8, 120.1, 106.3, 63.5, 56.7, 54.6, 38.7, 21.3.

^{19}F NMR (376 MHz, $CDCl_3$): δ -73.80 (t, *J* = 9.0 Hz), -74.12 (t, *J* = 8.0 Hz).

HRESI-MS (ESI +ve): Found 642.0977, calc for $C_{27}H_{23}F_6NO_7SNa$ 642.0997 $[M + Na]^+$.

Bis(2,2,2-trifluoroethyl) (5*R*,6*S*,9*S*)-4-phenyl-6-(o-tolyl)-9-vinyl-1-oxa-2-thia-3-azaspiro[4.4]non-3-ene-7,7-dicarboxylate 2,2-dioxide (3aj)



The titled compound was prepared following General procedure D using VCP **1a** (50.5 mg, 0.158 mmol), 1-azadiene **2j** (31.1 mg, 0.104 mmol), Pd_2dba_3•$CHCl_3$ (2.6 mg, 0.003 mmol), and (*S*)-DM-Segphos (5.3 mg, 0.007 mmol). Purification by FCC (20% EtOAc in hexane) afforded **3aj** as an off-white semi-solid (52.6 mg, >20 : 1 *dr*, 82%).

Chiral HPLC: Chiralpak® IG-3, 5% isopropanol/hexanes, 1.5 mL.min^{-1}, 266 nm, t_r (minor dia) = 9.6 & 19.6 min, t_r (major dia) = 10.9 & 24.6 min.

R_f = 0.15 (15% EtOAc in hexane).

IR (neat): 1747, 1561, 1373, 1283, 1202, 1162, 661 cm^{-1}.

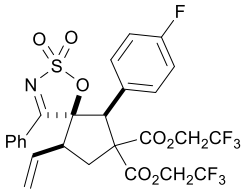
^{1}H NMR (400 MHz, $CDCl_3$) (16.1 : 1 mixture of two diastereoisomers, distinguishable resonances of the major diastereoisomer): δ 8.38 – 8.16 (m, 2H), 7.80 – 7.72 (m, 1H), 7.62 (dd, *J* = 8.5, 7.3 Hz, 2H), 7.33 – 7.28 (m, 1H), 7.18 – 7.07 (m, 2H), 7.03 – 6.91 (m, 1H), 5.89 (ddd, *J* = 17.1, 10.3, 7.9 Hz, 1H), 5.71 (s, 1H), 5.25 (dd, *J* = 10.3, 1.2 Hz, 1H), 5.12 (dt, *J* = 17.1, 1.0 Hz, 1H), 4.80 – 4.64 (m, 1H), 4.62 – 4.47 (m, 1H), 4.45 – 4.30 (m, 1H), 3.62 (ddd, *J* = 13.8, 7.9, 6.0 Hz, 1H), 3.44 (t, *J* = 13.8 Hz, 1H), 3.18 (dq, *J* = 12.5, 8.3 Hz, 1H), 2.55 (dd, *J* = 13.9, 6.0 Hz, 1H), 1.80 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) (16.1 : 1 mixture of two diastereoisomers, distinguishable resonances of the major diastereoisomer): δ 176.3, 171.0, 166.2, 137.6, 135.3, 131.1, 130.7, 130.4, 130.4, 129.7, 129.5, 128.9, 127.1, 125.9, 122.3 (q, *J* = 277.6 Hz), 122.0 (q, *J* = 276.9 Hz), 121.6, 106.2, 64.0, 62.2 (q, *J* = 37.4 Hz), 61.4 (q, *J* = 37.3 Hz), 52.9, 52.5, 39.9, 19.9.

^{19}F NMR (376 MHz, $CDCl_3$): δ -73.61 – -73.90 (m), -74.20 (t, J = 8.0 Hz).

HRESI-MS (ESI +ve): Found 642.0986, calc for $C_{27}H_{23}F_6NO_7SNa$ 642.0997 $[M + Na]^+$.

Bis(2,2,2-trifluoroethyl) (5*R*,6*S*,9*S*)-6-(4-fluorophenyl)-4-phenyl-9-vinyl-1-oxa-2-thia-3-azaspiro[4.4]non-3-ene-7,7-dicarboxylate 2,2-dioxide (3ak)



The titled compound was prepared following General procedure D using VCP **1a** (50.7 mg, 0.158 mmol), 1-azadiene **2k** (32.6 mg, 0.107 mmol), Pd_2dba_3•$CHCl_3$ (2.8 mg, 0.003 mmol), and (*S*)-DM-Segphos (5.9 mg, 0.008 mmol). Purification by FCC (20% EtOAc in hexane) afforded a mixture of **3ak** and **3ak'** as an off-white semi-solid (64.7 mg, 6.9 : 1 *dr*, 97%).

Chiral HPLC: Chiralpak® IG-3, 5% isopropanol/hexanes, 1.5 $mL.min^{-1}$, 254 nm, t_r (minor dia) = 9.3 & 12.7 min, t_r (major dia) = 11.0 & 21.3 min.

R_f = 0.17 (20% EtOAc in hexane).

IR (neat): 1745, 1559, 1380, 1199, 1150, 658 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) (9.7 : 1 mixture of two diastereoisomers, distinguishable resonances of the major diastereoisomer): δ 8.13 – 8.05 (m, 2H), 7.79 – 7.70 (m, 1H), 7.61 (t, *J* = 7.9 Hz, 2H), 7.15 – 7.03 (m, 2H), 6.99 – 6.86 (m, 2H), 5.87 (ddd, *J* = 17.0, 10.3, 7.8 Hz, 1H), 5.26 (s, 1H), 5.26 (dd, *J* = 10.2, 1.1 Hz, 1H), 5.11 (d, *J* = 17.1 Hz, 1H), 4.69 (dq, *J* = 12.6, 8.2 Hz, 1H), 4.48 (ddq, *J* = 32.4, 12.6, 8.2 Hz, 2H), 3.63 – 3.46 (m, 2H), 3.42 (t, *J* = 13.5 Hz, 1H), 2.55 (dd, *J* = 13.6, 6.1 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) (9.7.1 : 1 mixture of two diastereoisomers, distinguishable resonances of the major diastereoisomer): δ 176.7, 170.2, 166.3, 163.2 (d, *J* = 249.5 Hz), 135.1, 132.4 (d, *J* = 8.4 Hz),

130.3, 129.8 (d, *J* = 12.8 Hz), 127.1, 126.5 (d, *J* = 3.4 Hz), 122.3 (q, *J* = 277.5 Hz), 120.0 (q, *J* = 277.0 Hz), 121.8, 115.7 (d, *J* = 21.5 Hz), 106.2, 63.1, 57.5, 52.5, 62.2 (q, *J* = 37.3 Hz), 61.6 (q, *J* = 37.4 Hz), 39.4.

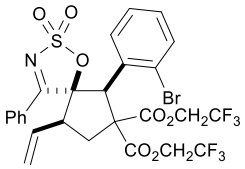
^{1}H NMR (400 MHz, $CDCl_3$) (9.7 : 1 mixture of two diastereoisomers, distinguishable resonances of the minor diastereoisomer): δ 7.85 – 7.79 (m, 2H), 7.70 – 7.65 (m, 1H), 7.53 (t, *J* = 7.9 Hz, 2H), 7.25 – 7.18 (m, 2H), 5.63 (ddd, *J* = 17.4, 10.3, 7.3 Hz, 1H), 5.21 (dd, *J* = 17.0, 1.6 Hz, 1H), 5.08 – 5.04 (m, 1H), 5.04 (s, 1H), 4.05 – 3.88 (m, 2H), 2.41 – 2.27 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) (9.7 : 1 mixture of two diastereoisomers, distinguishable resonances of the minor diastereoisomer): δ 178.7, 169.0, 166.7, 134.6, 133.1, 130.6, 129.3, 120.3, 106.0, 63.4, 56.6, 54.3, 38.5.

^{19}F NMR (376 MHz, $CDCl_3$): δ -73.81 (t, *J* = 8.3 Hz), -74.08 – -74.23 (m), -111.75 (q, *J* = 6.9 Hz).

HRESI-MS (ESI +ve): Found 646.0745, calc for $C_{26}H_{20}F_7NO_7SNa$ 646.0746 $[M + Na]^+$.

Bis(2,2,2-trifluoroethyl) (5*R*,6*R*,9*S*)-6-(2-bromophenyl)-4-phenyl-9-vinyl-1-oxa-2-thia-3-azaspiro[4.4]non-3-ene-7,7-dicarboxylate 2,2-dioxide (3al)



The titled compound was prepared following General procedure D using VCP **1a** (49.7 mg, 0.155 mmol), 1-azadiene **2l** (38.2 mg, 0.105 mmol), Pd_2dba_3•$CHCl_3$ (2.7 mg, 0.003 mmol), and (*S*)-DM-Segphos (6.0 mg, 0.008 mmol). Purification by FCC (20% EtOAc in hexane) afforded a mixture of **3al** and **3al'** as a colourless semi-solid (70.3 mg, 10.7 : 1 *dr*, 97%).

Chiral HPLC: Chiralpak® IG-3, 5% isopropanol/hexanes, 1.5 mL.min^{-1}, 266 nm, t_r (minor dia) = 10.6 & 21.2 min, t_r (major dia) = 9.6 & 23.4 min.

R_f = 0.26 (20% EtOAc in hexane).

IR (neat): 1751, 1559, 1374, 1283, 1202, 1161, 760, 657 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) (13.5 : 1 mixture of two diastereoisomers, distinguishable resonances of the major diastereoisomer): δ 8.46 – 8.28 (m, 2H), 7.79 – 7.70 (m, 1H), 7.65 – 7.57 (m, 2H), 7.44 (dd, *J* = 8.1, 1.4 Hz, 1H), 7.38 (dd, *J* = 8.1, 1.8 Hz, 1H), 7.34 – 7.26 (m, 1H), 7.11 (ddd, *J* = 8.1, 7.3, 1.7 Hz, 1H), 6.22 (s, 1H), 5.89 – 5.77 (m, 1H), 5.24 (dd, *J* = 10.2, 1.1 Hz, 1H), 5.07 (dt, *J* = 17.1, 1.0 Hz, 1H), 4.73 (dq, *J* = 12.6, 8.2 Hz, 1H), 4.59 (dq, *J* = 12.6, 8.2 Hz, 1H), 4.37 (dq, *J* = 12.5, 8.2 Hz, 1H), 3.62 (ddd, *J* = 13.7, 7.9, 5.9 Hz, 1H), 3.47 – 3.33 (m, 2H), 2.55 (dd, *J* = 13.9, 5.9 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) (13.5 : 1 mixture of two diastereoisomers, distinguishable resonances of the major diastereoisomer): δ 176.2, 170.2, 166.1, 135.4, 133.3, 132.8, 131.1, 131.0, 130.5, 130.1, 129.5, 127.1, 127.0, 126.3, 122.3 (q, *J* = 277.5 Hz)*, 121.9 (q, *J* = 277.1 Hz)*, 121.9, 105.6, 63.9, 62.3 (q, *J* = 37.4 Hz), 61.6 (q, *J* = 37.4 Hz), 55.5, 52.7, 40.0.

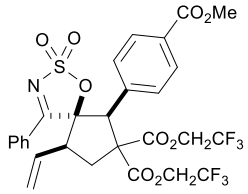
^{1}H NMR (400 MHz, $CDCl_3$) (13.5 : 1 mixture of two diastereoisomers, distinguishable resonances of the minor diastereoisomer): δ 7.99 – 7.94 (m, 2H), 7.70 – 7.65 (m, 1H), 7.54 (t, *J* = 7.9 Hz, 2H), 5.58 (s, 1H), 5.33 (dd, *J* = 17.3, 1.7 Hz, 1H), 5.17 (dd, *J* = 10.7, 1.7 Hz, 1H), 4.20 – 4.11 (m, 1H), 3.13 (dd, *J* = 14.2, 8.0 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) (13.5 : 1 mixture of two diastereoisomers, distinguishable resonances of the minor diastereoisomer): δ 178.0, 167.8, 167.5, 134.8, 133.4, 132.4, 131.3, 129.2, 105.0, 64.0, 56.2, 54.3, 38.4.

^{19}F NMR (376 MHz, $CDCl_3$): δ -73.80 (t, *J* = 8.4 Hz), -74.09 (t, *J* = 8.4 Hz).

HRESI-MS (ESI +ve): Found 705.9941, calc for $C_{26}H_{20}F_6NBrO_7SNa$ 705.9946 $[M + Na]^+$.

Bis(2,2,2-trifluoroethyl) (5*R*,6*S*,9*S*)-6-(4-(methoxycarbonyl)phenyl-4-phenyl-9-vinyl-1-oxa-2-thia-3-azaspiro[4.4]non-3-ene-7,7-dicarboxylate 2,2-dioxide (3am)



The titled compound was prepared following General procedure D using VCP **1a** (50.5 mg, 0.158 mmol), 1-azadiene **2m** (36.5 mg, 0.106 mmol), Pd_2dba_3•$CHCl_3$ (2.6 mg, 0.003 mmol), and (*S*)-DM-Segphos (5.2 mg, 0.007 mmol). Purification by FCC (20% EtOAc in hexane) afforded a mixture of **3am** and **3am'** as a colourless oily residue (67.4 mg, 5.1 : 1 *dr*, 96%).

Chiral HPLC: Chiralpak® IG-3, 5% isopropanol/hexanes, 1.5 mL.min^{-1}, 254 nm, t_r (minor dia) = 31.5 & 35.4 min, t_r (major dia) = 38.0 & 62.3 min.

R_f = 0.26 (20% EtOAc in hexane).

IR (neat): 1752, 1724, 1560, 1377, 1203, 1167, 768, 658 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) (11.4 : 1 mixture of two diastereoisomers, distinguishable resonances of the major diastereoisomer): δ 8.12 – 8.07 (m, 2H), 7.92 – 7.88 (m, 2H), 7.78 – 7.73 (m, 1H), 7.65 – 7.57 (m, 2H), 7.21 – 7.15 (m, 2H), 5.88 (ddd, *J* = 17.1, 10.3, 7.8 Hz, 1H), 5.31 (s, 1H), 5.27 (dd, *J* = 10.3, 1.1 Hz, 1H), 5.13 (dt, *J* = 17.1, 1.0 Hz, 1H), 4.71 (dq, *J* = 12.6, 8.2 Hz, 1H), 4.48 (ddq, *J* = 27.1, 12.4, 8.1 Hz, 2H), 3.87 (s, 3H), 3.60 – 3.39 (m, 3H), 2.57 (dd, *J* = 13.7, 6.1 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) (11.4 : 1 mixture of two diastereoisomers, distinguishable resonances of the major diastereoisomer): δ 176.4, 170.2, 166.3, 166.1, 135.6, 135.2, 131.0, 130.6, 130.2, 129.9, 129.8, 129.8, 127.0, 122.3 (q, *J* = 277.4 Hz), 121.9 (q, *J* = 277.1 Hz), 121.9, 105.9, 63.0, 61.9 (two overlapping quartets, *J* = 37.4 Hz), 58.0, 52.6, 52.2, 39.5.

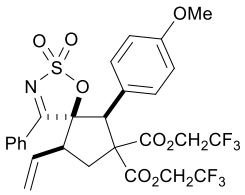
^{1}H NMR (400 MHz, $CDCl_3$) (11.4 : 1 mixture of two diastereoisomers, distinguishable resonances of the minor diastereoisomer): δ 7.85 – 7.77 (m, 2H), 7.72 – 7.63 (m, 1H), 7.57 – 7.48 (m, 2H), 7.34 – 7.26 (m, 2H), 5.88 (ddd, *J* = 17.1, 10.3, 7.8 Hz, 11H), 5.65 (ddd, *J* = 17.0, 10.4, 7.4 Hz, 1H), 5.27 – 5.18 (m, 1H), 5.08 (s, 1H), 5.08 (ddd, *J* = 10.5, 1.4, 0.7 Hz, 1H), 2.42 – 2.33 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) (11.4 : 1 mixture of two diastereoisomers, distinguishable resonances of the minor diastereoisomer): δ 178.5, 168.9, 166.6, 166.4, 135.3, 134.6, 133.0, 130.8, 129.7, 129.3, 120.4, 105.7, 63.5, 57.1, 54.5, 38.5.

^{19}F NMR (376 MHz, $CDCl_3$): δ -73.80 (t, J = 8.9 Hz), -74.07 – -74.16 (m).

HRESI-MS (ESI +ve): Found 686.0883, calc for $C_{28}H_{23}F_6NO_9SNa$ 686.0895 $[M + Na]^+$.

Bis(2,2,2-trifluoroethyl) (5*R*,6*S*,9*S*)-6-(4-methoxyphenyl)-4-phenyl-9-vinyl-1-oxa-2-thia-3-azaspiro[4.4]non-3-ene-7,7-dicarboxylate 2,2-dioxide (3an)



The titled compound was prepared following General procedure D using VCP **1a** (51.9 mg, 0.162 mmol), 1-azadiene **2n** (34.4 mg, 0.109 mmol), Pd_2dba_3•$CHCl_3$ (2.8 mg, 0.003 mmol), and (*S*)-DM-Segphos (6.4 mg, 0.009 mmol). Purification by FCC (20% EtOAc in hexane) afforded a mixture of **3an** and **3an'** as a light yellow oil (61.5 mg, 9.1 : 1 *dr*, 89%).

Chiral HPLC: Chiralpak® IG-3, 5% isopropanol/hexanes, 1.5 mL.min^{-1}, 266 nm, t_r (minor dia) = 15.5 & 17.6 min, t_r (major dia) = 16.3 & 33.0 min.

R_f = 0.15 (20% EtOAc in hexane).

IR (neat): 1748, 1560, 1515, 1377, 1279, 1242, 1201, 1165, 764, 659 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) (12.6 : 1 mixture of two diastereoisomers, distinguishable resonances of the major diastereoisomer): δ 8.18 – 7.98 (m, 2H), 7.78 – 7.69 (m, 1H), 7.68 – 7.55 (m, 2H), 7.10 – 6.97 (m, 2H), 6.78 – 6.69 (m, 2H), 5.89 (ddd, *J* = 17.0, 10.3, 7.7 Hz, 1H), 5.25 (dd, *J* = 10.3, 1.1 Hz, 1H), 5.22 (s, 1H), 5.10 (dt, *J* = 17.1, 0.9 Hz, 1H), 4.70 (dq, *J* = 12.5, 8.2 Hz, 1H), 4.55 – 4.41 (m, 2H), 3.72 (s, 3H), 3.61 – 3.33 (m, 3H), 2.52 (dd, *J* = 13.2, 5.7 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) (12.6 : 1 mixture of two diastereoisomers, distinguishable resonances of the major diastereoisomer): δ 177.0, 170.4, 166.5, 160.2, 134.9, 131.7, 130.6, 129.8, 129.6, 127.3, 122.4, 122.3 (q, *J* = 277.3 Hz), 122.1 (q, *J* = 276.9 Hz), 121.5, 114.0, 106.6, 63.1, 62.1 (q, *J* = 37.3 Hz), 61.5 (q, *J* = 37.3 Hz), 57.7, 55.2, 52.5, 39.3.

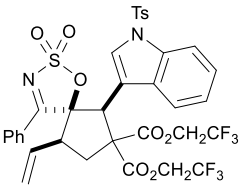
^{1}H NMR (400 MHz, $CDCl_3$) (12.6 : 1 mixture of two diastereoisomers, distinguishable resonances of the minor diastereoisomer): δ 7.85 – 7.79 (m, 2H), 7.54 – 7.48 (m, 2H), 7.19 – 7.13 (m, 2H), 5.60 (ddd, *J* = 17.0, 10.3, 7.5 Hz, 1H), 5.06 – 4.99 (m, 2H), 3.94 – 3.84 (m, 2H), 3.73 (s, 3H), 2.32 (dd, J = 14.2, 6.9 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) (12.6 : 1 mixture of two diastereoisomers, distinguishable resonances of the minor diastereoisomer): δ 179.1, 169.2, 166.9, 160.1, 134.3, 133.3, 131.9, 130.5, 129.2, 122.0, 120.1, 106.4, 63.4, 56.5, 54.3, 38.5.

^{19}F NMR (376 MHz, $CDCl_3$): δ -73.79 (t, *J* = 8.3 Hz), -74.06 (t, *J* = 8.8 Hz).

HRESI-MS (ESI +ve): Found 658.0937, calc for $C_{27}H_{23}F_6NO_8SNa$ 658.0946 $[M + Na]^+$.

Bis(2,2,2-trifluoroethyl) (5*R*,6*S*,9*S*)-4-phenyl-6-(1-tosyl-1*H*-indol-3-yl)-9-vinyl-1-oxa-2-thia-3-azaspiro[4.4]non-3-ene-7,7-dicarboxylate 2,2-dioxide (3ao)



The titled compound was prepared following General procedure D using VCP **1a** (49.9 mg, 0.156 mmol), 1-azadiene **2o** (49.6 mg, 0.104 mmol), Pd_2dba_3•$CHCl_3$ (2.8 mg, 0.003 mmol), and (*S*)-DM-Segphos (5.3 mg, 0.007 mmol). Purification by FCC (20% EtOAc in hexane) afforded a mixture of **3ao** and **3ao'** as a colourless oily residue (66.3 mg, 10.6 : 1 *dr*, 80%).

Chiral HPLC: Chiralpak® IG-3, 10% isopropanol/hexanes, 0.75 mL.min^{-1}, 206 nm, t_r (minor dia) = 18.3 min, t_r (major dia plus one unresolved peak of minor dia) = 19.5 & 50.5 min.

R_f = 0.11 (20% EtOAc in hexane).

IR (neat): 1750, 1559, 1448, 1371, 1281, 1243, 1203, 1166, 672, 577 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) (14.3 : 1 mixture of two diastereoisomers, distinguishable resonances of the major diastereoisomer): δ 8.04 – 7.96 (m, 2H), 7.94 (d, *J* = 8.1 Hz, 2H), 7.88 (dd, *J* = 8.3, 1.0 Hz, 1H), 7.79 (s, 1H), 7.68 (t, *J* = 7.5 Hz, 1H), 7.53 (t, *J* = 7.7 Hz, 2H), 7.32 – 7.15 (m, 4H), 7.14 – 7.03 (m, 1H), 5.91 (ddd, *J* = 17.0, 10.2, 7.7 Hz, 1H), 5.71 (s, 1H), 5.27 (dd, *J* = 10.2, 1.1 Hz, 1H), 5.12 (dt, *J* = 17.0, 0.9 Hz, 1H), 4.72 (dq, *J* = 12.5, 8.1 Hz, 1H), 4.48 (dq, *J* = 12.6, 8.2 Hz, 1H), 4.25 (dq, *J* = 12.5, 8.2 Hz, 1H), 3.60 – 3.39 (m, 2H), 3.17 (dq, *J* = 12.4, 8.1 Hz, 1H), 2.56 (dd, *J* = 13.2, 5.7 Hz, 1H), 2.32 (s, 3H).

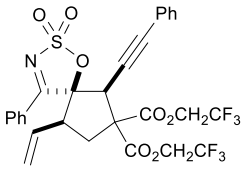
^{13}C NMR (100 MHz, $CDCl_3$) (14.3 : 1 mixture of two diastereoisomers, distinguishable resonances of the major diastereoisomer): δ 176.7, 170.5, 166.1, 145.4, 135.0, 134.7, 130.4, 130.1, 130.0, 129.7, 129.6, 127.7, 127.1, 126.9, 125.0, 123.3, 122.3 (q, *J* = 277.4 Hz), 121.8 (q, *J* = 277.3 Hz), 121.8, 118.4, 113.2, 105.9, 63.9, 62.3 (q, *J* = 37.4 Hz), 61.1 (q, *J* = 37.3 Hz), 52.9, 48.4, 39.3, 21.5.

^{1}H NMR (400 MHz, $CDCl_3$) (14.3 : 1 mixture of two diastereoisomers, distinguishable resonances of the minor diastereoisomer): δ 7.87 – 7.82 (m, 2H), 7.76 (s, 1H), 7.42 (dd, *J* = 8.4, 7.5 Hz, 2H), 5.62 (ddd, *J* = 17.0, 10.3, 7.7 Hz, 1H), 5.45 (s, 1H), 5.25 – 5.19 (m, 1H), 5.04 (dt, *J* = 10.3, 1.0 Hz, 1H), 3.96 – 3.85 (m, 1H), 3.74 (dq, *J* = 12.6, 8.2 Hz, 1H), 2.41 (dd, *J* = 14.2, 6.6 Hz, 1H), 2.26 (s, 3H).

^{19}F NMR (376 MHz, $CDCl_3$): δ -73.79 (t, *J* = 8.3 Hz), -74.06 (t, *J* = 8.8 Hz).

HRESI-MS (ESI +ve): Found 797.1094, calc for $C_{35}H_{27}F_6N_2O_9S_2$ 797.1062 $[M - H]^-$.

Bis(2,2,2-trifluoroethyl) (5*R*,6*S*,9*S*)-4-phenyl-6-(phenylethynyl)-9-vinyl-1-oxa-2-thia-3-azaspiro[4.4]non-3-ene-7,7-dicarboxylate 2,2-dioxide (3ap)



The titled compound was prepared following General procedure D using VCP **1a** (53.9 mg, 0.168 mmol), 1-azadiene **2p** (34.3 mg, 0.111 mmol), Pd_2dba_3•$CHCl_3$ (2.8 mg, 0.003 mmol), and (*S*)-DM-Segphos (6.0 mg, 0.008 mmol). Purification by FCC (20% EtOAc in hexane) afforded a mixture of **3ap** and **3ap'** as an orange oily residue (43.2 mg, 5.0 : 1 *dr*, 62%).

Chiral HPLC: Chiralpak® IG-3, 4% isopropanol/hexanes, 0.75 mL.min^{-1}, 254 nm, t_r (minor dia) = 24.0 & 25.6 min, t_r (major dia) = 22.6 & 27.5 min.

R_f = 0.11 (20% EtOAc in hexane).

IR (neat): 1745, 1560, 1373, 1284, 1238, 1200, 1152, 934, 756, 657 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) (10.4 : 1 mixture of two diastereoisomers, distinguishable resonances of the major diastereoisomer): δ 8.16 – 8.06 (m, 2H), 7.77 – 7.67 (m, 1H), 7.65 – 7.55 (m, 2H), 7.48 – 7.40 (m, 2H), 7.33 – 7.21 (m, 3H), 5.82 (ddd, *J* = 17.0, 10.2, 7.6 Hz, 1H), 5.24 (dd, *J* = 10.3, 1.1 Hz, 1H), 5.15 (s, 1H), 5.05 (dt, *J* = 17.0, 1.0 Hz, 1H), 4.74 (dqd, *J* = 12.8, 8.2, 6.3 Hz, 2H), 4.59 (dq, *J* = 12.5, 8.1 Hz, 1H), 4.23 (dq, *J* = 12.6, 8.2 Hz, 1H), 3.43 – 3.27 (m, 2H), 2.52 – 2.41 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) (10.4 : 1 mixture of two diastereoisomers, distinguishable resonances of the major diastereoisomer): δ 175.4, 169.6, 165.5, 135.0, 132.0, 130.0, 129.8, 129.7, 129.1, 128.3, 126.9, 122.4 (q, *J* = 277.2 Hz), δ 122.3 (q, *J* = 277.7 Hz), 121.9, 121.4, 104.6, 89.8, 77.9, 62.4, 62.3 (q, *J* = 37.4 Hz), 62.1 (q, *J* = 37.2 Hz), 52.0, 47.4, 39.0.

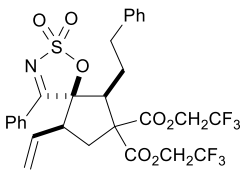
^{1}H NMR (400 MHz, $CDCl_3$) (10.4 : 1 mixture of two diastereoisomers, distinguishable resonances of the minor diastereoisomer): δ 7.90 – 7.85 (m, 2H), 7.69 – 7.65 (m, 1H), 7.55 (t, *J* = 7.8 Hz, 2H), 5.57 (ddd, *J* = 17.2, 10.3, 7.1 Hz, 1H), 4.83 (s, 1H), 4.44 (dq, *J* = 12.6, 8.2 Hz, 1H), 3.94 (dt, *J* = 9.7, 7.9 Hz, 1H), 2.27 (dd, *J* = 13.9, 9.7 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) (10.4 : 1 mixture of two diastereoisomers, distinguishable resonances of the minor diastereoisomer): δ 177.1, 167.7, 165.9, 134.7, 132.8, 130.6, 129.4, 128.2, 127.7, 120.3, 104.2, 89.9, 62.7, 53.6, 47.9, 38.2.

^{19}F NMR (376 MHz, $CDCl_3$): δ -73.59 (t, *J* = 8.5 Hz), -73.74 (t, *J* = 8.4 Hz).

HRESI-MS (ESI +ve): Found 652.0839, calc for $C_{28}H_{21}F_6NO_7SNa$ 652.0841 $[M + Na]^+$.

Bis(2,2,2-trifluoroethyl) (5*R*,6*S*,9*S*)-6-phenethyl-4-phenyl-9-vinyl-1-oxa-2-thia-3-azaspiro[4.4]non-3-ene-7,7-dicarboxylate 2,2-dioxide (3aq)



The titled compound was prepared following General procedure D using VCP **1a** (46.9 mg, 0.146 mmol), 1-azadiene **2q** (28.4 mg, 0.091 mmol), Pd_2dba_3•$CHCl_3$ (2.0 mg, 0.002 mmol), and (*S*)-DM-Segphos (5.0 mg, 0.007

mmol). Purification by FCC (20% EtOAc in hexane) afforded a mixture of **3aq** and **3aq'** as a light yellow oily residue (7.1 mg, 9.6 : 1 *dr*, 12%).

Chiral HPLC: Chiralpak® IG-3, 2.5% isopropanol/hexanes, 1.5 mL.min^{-1}, 254 nm, t_r (minor dia) = 15.2 & 24.6 min, t_r (major dia) = 16.4 & 23.0 min.

R_f = 0.16 (15% EtOAc in hexane).

IR (neat): 2922, 2852, 1751, 1558, 1373, 1283, 1238, 1200, 1165, 1093, 658 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) (10.6 : 1 mixture of two diastereoisomers, distinguishable resonances of the major diastereoisomer): δ 7.97 – 7.88 (m, 2H), 7.65 (ddt, *J* = 8.6, 7.2, 1.2 Hz, 1H), 7.54 – 7.41 (m, 2H), 7.18 – 6.88 (m, 6H), 5.73 (ddd, *J* = 17.0, 10.2, 7.9 Hz, 1H), 5.15 (dd, *J* = 10.2, 1.2 Hz, 1H), 5.09 (s, 0H), 4.87 (dt, *J* = 17.1, 1.0 Hz, 1H), 4.76 – 4.44 (m, 4H), 4.04 (t, *J* = 6.5 Hz, 1H), 3.32 – 3.10 (m, 2H), 2.57 – 2.39 (m, 3H), 1.98 – 1.83 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) (10.6 : 1 mixture of two diastereoisomers, distinguishable resonances of the major diastereoisomer): δ 177.1, 170.4, 166.6, 139.8, 135.0, 130.4, 130.0, 129.6, 128.4, 128.3, 126.9, 126.3, 122.4* (d, *J* = 277.4 Hz), 121.5, 106.8, 61.9, 61.6 (two overlapping q, *J* = 37.3 Hz). 52.7, 52.4, 39.5, 33.1, 28.1.

**Note: outermost resonances of this quartet were not observed due to their low intensities. The second quartet was not observed.*

^{1}H NMR (400 MHz, $CDCl_3$) (10.6 : 1 mixture of two diastereoisomers, distinguishable resonances of the minor diastereoisomer): δ 7.89 – 7.84 (m, 2H), 7.51 (t, *J* = 7.9 Hz, 3H), 5.67 – 5.57 (m, 1H), 5.28 – 5.22 (m, 1H), 5.10 – 5.04 (m, 1H).

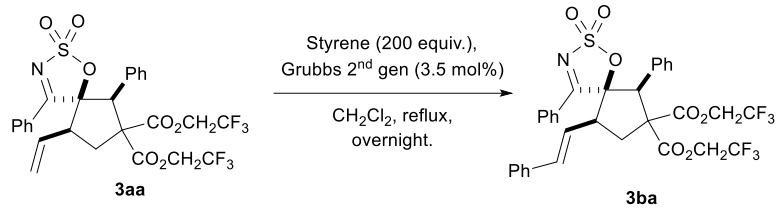
^{13}C NMR (100 MHz, $CDCl_3$) (10.4 : 1 mixture of two diastereoisomers, distinguishable resonances of the minor diastereoisomer): δ 177.1, 167.7, 165.9, 134.7, 132.8, 130.5, 129.4, 128.9, 128.3, 128.2, 121.6, 120.3, 104.2, 89.9, 77.2, 53.6, 47.9, 38.2..

^{19}F NMR (376 MHz, $CDCl_3$): δ -73.47 (t, *J* = 8.2 Hz), -73.74 (t, *J* = 8.2 Hz).

HRESI-MS (ESI +ve): Found 656.1131, calc for $C_{28}H_{25}F_6NO_7SNa$ 656.1154 $[M + Na]^+$.

6. Post-synthetic modifications

a. Olefin cross-metathesis

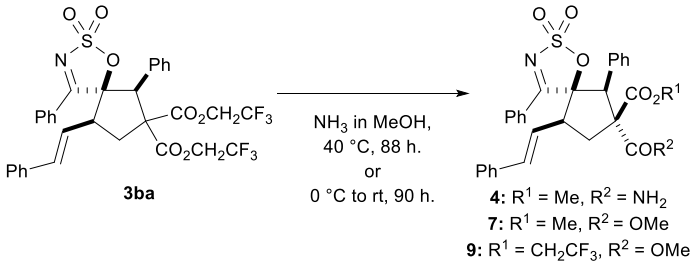


Procedure:

A mixture of **3aa** (651.1 mg, 1.075 mmol), styrene (25 mL, 218.2 mmol), and Grubbs catalyst 2nd generation (31.7 mg) in anhydrous CH_2Cl_2 (30 mL) was stirred at reflux overnight. The reaction mixture was then allowed to cool to rt, then concentrated *in vacuo*. Purification by FCC (15–30% EtOAc in hexane) afforded the major diastereoisomeric product **3ba** as a white foam (529.4 mg, 72%).

For the characterisation data of **3ba**, vide supra.

b. Regioselective transesterification/amidation



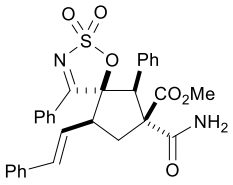
Procedure (40 °C):[1]

Ammonia solution (7N in MeOH, 2.0 mL) was added to **3ba** (31.9 mg, 0.047 mmol) at rt. The resulting solution was then stirred at 40 °C for 88 h, before being concentrated *in vacuo*. Purification by FCC (50% EtOAc in hexane) afforded **4** as a colourless residue (24.2 mg, 97%).

Procedure (0 °C to rt):[1]

Ammonia solution (7N in MeOH, 2.5 mL) was added to **3ba** (35.6 mg, 0.052 mmol) at 0 °C. The resulting solution was then allowed to slowly warm to rt, and stirred for 90 h, before being concentrated *in vacuo*. Purification by FCC (50% EtOAc in hexane) afforded **4** as a colourless residue (10.4 mg, 37%), **7** as a white semi-solid (5.5 mg, 19%), and **9** as a colourless residue (8.0 mg, 11.0 : 1 *dr*, 25%).

Methyl (5*R*,6*S*,7*S*,9*S*)-7-carbamoyl-4,6-diphenyl-9-((*E*)-styryl)-1-oxa-2-thia-3-azaspiro[4.4]non-3-ene-7-carboxylate 2,2-dioxide (4)



R_f = 0.24 (50% EtOAc in hexane).

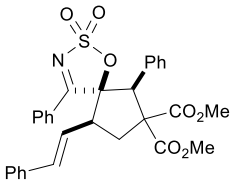
IR (neat): 1734, 1678, 1557, 1368, 1200, 1186, 939, 887, 765, 700 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.36 – 8.07 (m, 2H), 7.77 – 7.65 (m, 1H), 7.68 – 7.49 (m, 2H), 7.38 – 7.30 (m, 2H), 7.31 – 7.14 (m, 5H), 7.14 – 7.05 (m, 2H), 6.61 (s, 1H), 6.39 (d, *J* = 15.9 Hz, 1H), 6.34 – 6.19 (m, 1H), 5.23 (s, 1H), 3.98 (dt, *J* = 12.7, 7.6 Hz, 1H), 3.51 (s, 3H), 3.35 (t, *J* = 13.1 Hz, 1H), 2.72 – 2.52 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 177.6, 174.0, 171.0, 136.2, 135.2, 134.8, 131.6, 130.5, 130.2, 129.5, 129.0, 128.6, 128.4, 128.1, 127.3, 126.7, 123.0, 107.6, 63.5, 60.3, 53.5, 53.0, 40.6.

HRESI-MS (ESI +ve): Found 533.1365, calc for $C_{29}H_{26}N_2O_6SNa$ 533.1409 $[M + Na]^+$.

Dimethyl (5*R*,6*S*,9*S*)-4,6-diphenyl-9-((*E*)-styryl)-1-oxa-2-thia-3-azaspiro[4.4]non-3-ene-7,7-dicarboxylate 2,2-dioxide (7)



R_f = 0.25 (20% EtOAc in hexane).

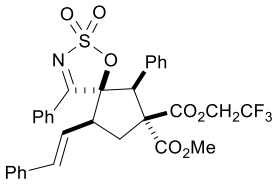
IR (neat): 1728, 1589, 1558, 1366, 1259, 1200, 1173, 893, 764, 700 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.22 – 8.13 (m, 2H), 7.78 – 7.68 (m, 1H), 7.67 – 7.56 (m, 2H), 7.36 – 7.17 (m, 8H), 7.17 – 7.07 (m, 2H), 6.36 (d, *J* = 15.9 Hz, 1H), 6.26 (dd, *J* = 15.9, 8.1 Hz, 1H), 5.36 (s, 1H), 3.84 (s, 3H), 3.64 (ddd, *J* = 14.1, 8.1, 6.4 Hz, 1H), 3.48 (t, *J* = 13.6 Hz, 1H), 3.27 (s, 3H), 2.53 (dd, *J* = 13.8, 6.4 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 177.2, 173.0, 168.8, 136.1, 135.2, 134.7, 131.7, 130.7, 130.1, 130.1, 129.5, 128.8, 128.6, 128.3, 128.1, 127.5, 126.7, 122.6, 107.2, 63.4, 58.2, 53.8, 52.6, 52.5, 40.1.

HRESI-MS (ESI +ve): Found 568.1382, calc for $C_{30}H_{27}NO_7SNa$ 568.1406 $[M + Na]^+$.

7-methyl 7-(2,2,2-trifluoroethyl) (5*R*,6*S*,7*S*,9*S*)-4,6-diphenyl-9-((*E*)-styryl)-1-oxa-2-thia-3-azaspiro[4.4]non-3-ene-7,7-dicarboxylate 2,2-dioxide (9)



R_f = 0.30 (20% EtOAc in hexane).

IR (neat): 1734, 1559, 1373, 1255, 1182, 1163, 896, 762, 701 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) (11.0 : 1 mixture of two diastereoisomers, distinguishable resonances of the major diastereoisomer): δ 8.28 – 8.12 (m, 2H), 7.81 – 7.66 (m, 1H), 7.71 – 7.55 (m, 2H), 7.40 – 7.16 (m, 7H), 7.16 – 7.05 (m, 2H), 6.37 (d, *J* = 15.9 Hz, 1H), 6.25 (dd, *J* = 15.9, 8.3 Hz, 1H), 5.38 (s, 1H), 4.57 (dq, *J* = 12.4, 8.3 Hz, 1H), 3.85 (s, 4H), 3.68 (ddd, *J* = 14.2, 8.3, 6.5 Hz, 1H), 3.45 (t, *J* = 13.9 Hz, 1H), 3.26 (dq, *J* = 12.5, 8.3 Hz, 1H), 2.62 – 2.46 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) (11.0 : 1 mixture of two diastereoisomers, distinguishable resonances of the major diastereoisomer): δ 177.0, 172.1, 167.2, 135.9, 135.5, 134.8, 131.3, 130.6, 130.1, 129.6,

129.0, 128.6, 128.5, 128.5, 128.2, 127.3, 126.8, 122.2, 122.1* (d, *J* = 277.4 Hz), 106.9, 63.2, 61.0 (q, *J* = 37.2 Hz), 58.2, 53.8, 52.5, 40.0.

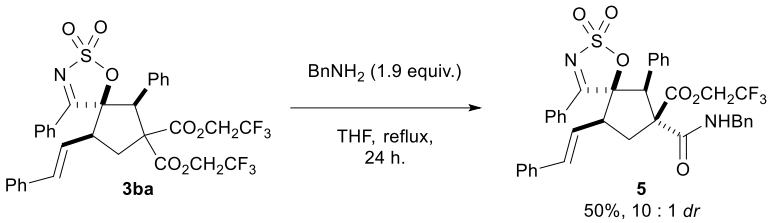
**Note: outermost resonances of this quartet were not observed due to their low intensities.*

^{1}H NMR (400 MHz, $CDCl_3$) (11.0 : 1 mixture of two diastereoisomers, distinguishable resonances of the minor diastereoisomer): δ 5.88 (ddd, *J* = 17.0, 10.2, 7.9 Hz, 1H), 5.38 (s, 11H), 5.33 (s, 1H), 5.24 (dd, *J* = 10.4, 1.2 Hz, 1H), 5.08 (dt, *J* = 17.1, 1.0 Hz, 1H), 3.83 (s, 3H), 3.37 (t, *J* = 13.6 Hz, 1H), 2.52 – 2.45 (m, 1H).

^{19}F NMR (376 MHz, $CDCl_3$): δ -74.13 (t, *J* = 8.2 Hz).

HRESI-MS (ESI +ve): Found 614.1487, calc for $C_{31}H_{27}NO_7SF_3$ 614.1460 $[M + H]^+$.

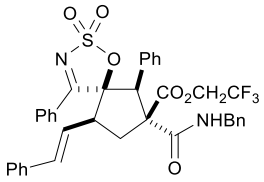
c. Regioselective amidation



Procedure:

A solution of **3ba** (32.8 mg, 0.048 mmol) and benzylamine (0.01 mL, 0.092 mmol) in anhydrous THF (0.6 mL) was stirred at reflux for 24 h. Upon completion, indicated by TLC, the reaction mixture was allowed to cool to rt and then quenched with saturated aqueous NH_4Cl. The mixture was extracted with EtOAc, then the combined extracts were then washed with brine. The organic layer was dried over $MgSO_4$, filtered, then concentrated *in vacuo*. Purification by FCC (40% Et_2O in hexane) afforded **5** as an orange oil (17.2 mg, 9.5 : 1 *dr*, 50%).

2,2,2-Trifluoroethyl (5*R*,6*S*,9*S*)-7-(benzylcarbamoyl)-4,6-diphenyl-9-((*E*)-styryl)-1-oxa-2-thia-3-azaspiro[4.4]non-3-ene-7-carboxylate 2,2-dioxide (5)



R_f = 0.13 (40% Et_2O in hexane).

IR (neat): 1751, 1672, 1558, 1373, 1284, 1201, 1184, 1167, 763, 699 cm^{-1}.

^{1}H NMR (400 MHz, C_6D_6): (9.5 : 1 mixture of two diastereoisomers, distinguishable resonances of the major diastereoisomer): δ 8.19 – 8.07 (m, 2H), 7.35 – 7.26 (m, 4H), 7.12 – 6.86 (m, 14H), 6.52 (dd, *J* = 15.8, 8.7 Hz, 1H), 6.13 (d, *J* = 15.8 Hz, 1H), 5.92 (t, *J* = 5.8 Hz, 1H), 5.89 (s, 1H), 4.46 (dd, *J* = 14.7, 6.3 Hz, 1H), 4.14 – 4.01 (m, 2H), 3.89 (ddd, *J* = 12.8, 8.7, 6.8 Hz, 1H), 3.46 (t, *J* = 13.1 Hz, 1H), 3.16 (dq, *J* = 12.7, 8.5 Hz, 1H), 2.43 – 2.34 (m, 1H).

^{13}C NMR (100 MHz, C_6D_6) (9.5 : 1 mixture of two diastereoisomers, distinguishable resonances of the major diastereoisomer): δ 177.0, 170.0, 169.0, 137.6, 136.2, 135.3, 134.1, 132.2, 130.6, 130.1, 129.1,

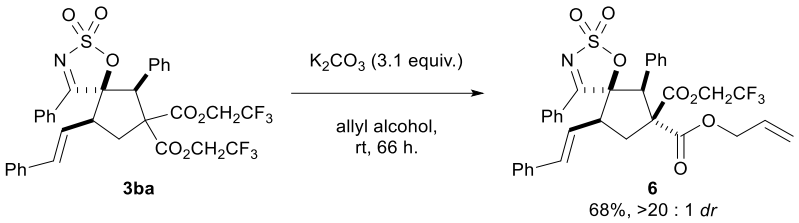
128.7, 128.6, 128.6, 128.6, 128.5, 128.5, 128.0, 127.9, 127.9, 127.7, 127.6, 127.5, 127.4, 126.9, 122.8, 122.5 (d, *J* = 277.5 Hz), 107.1, 64.1, 60.93 (q, *J* = 36.8 Hz), 59.1, 53.4, 44.6, 41.1.

^{1}H NMR (400 MHz, C_6D_6) (9.5 : 1 mixture of two diastereoisomers, distinguishable resonances of the minor diastereoisomer): δ 5.79 (s, 1H), 4.94 (dd, J = 10.2, 1.4 Hz, 1H), 4.75 (d, J = 16.5 Hz, 1H), 4.42 – 4.35 (m, 1H), 3.68 (dt, J = 14.4, 7.2 Hz, 1H), 3.39 – 3.28 (m, 3H), 2.27 (dd, J = 13.4, 6.7 Hz, 1H).

^{19}F NMR (376 MHz, C_6D_6): δ -73.30 (t, *J* = 8.2 Hz).

HRESI-MS (ESI +ve): Found 687.1777, calc for $C_{37}H_{30}F_3N_2O_6S$ 687.1777 $[M - H]^-$.

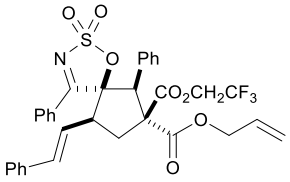
d. Regioselective transesterification



Procedure:

To a solution of **3ba** (81.1 mg, 0.119 mmol) in anhydrous allyl alcohol (8 mL) was added anhydrous K_2CO_3 (50.4 mg, 0.365 mmol), and the reaction mixture was stirred at rt for 66 h. Upon the complete consumption of **3ba**, as indicated by ESI-MS, the reaction mixture was quenched with water, and the resulting mixture was extracted with EtOAc. The combined extracts were then washed with brine, then the organic layer was dried over $MgSO_4$, filtered, before being concentrated *in vacuo*. Purification by FCC (20% EtOAc in hexane) afforded **6** as a colourless oil (52.0 mg, 68%).

7-Allyl 7-(2,2,2-trifluoroethyl) (5*R*,6*S*,7*S*,9*S*)-4,6-diphenyl-9-((*E*)-styryl)-1-oxa-2-thia-3-azaspiro[4.4]non-3-ene-7,7-dicarboxylate 2,2-dioxide (6)



R_f = 0.25 (20% EtOAc in hexane).

IR (neat): 1732, 1591, 1559, 1373, 1250, 1201, 1164, 1100, 939, 762, 658 cm^{-1}.

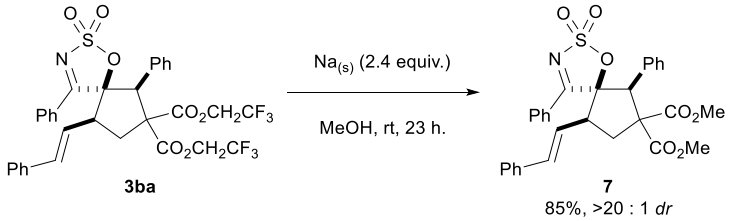
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.17 (d, *J* = 7.9 Hz, 2H), 7.72 (t, *J* = 7.5 Hz, 1H), 7.60 (t, *J* = 7.8 Hz, 2H), 7.39 – 7.17 (m, 8H), 7.17 – 7.08 (m, 2H), 6.37 (d, *J* = 15.9 Hz, 1H), 6.25 (dd, *J* = 15.8, 8.3 Hz, 1H), 5.87 (ddt, *J* = 16.7, 10.3, 6.1 Hz, 1H), 5.39 (s, 1H), 5.37 – 5.31 (m, 1H), 5.28 (d, *J* = 10.3 Hz, 1H), 4.71 (dt, *J* = 9.1, 4.8 Hz, 2H), 4.51 (dq, *J* = 12.5, 8.3 Hz, 1H), 3.69 (ddd, *J* = 14.3, 8.4, 6.6 Hz, 1H), 3.47 (t, *J* = 13.6 Hz, 1H), 3.29 (dq, *J* = 12.1, 8.1 Hz, 1H), 2.57 (dd, *J* = 13.9, 6.5 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 177.0, 171.3, 167.2, 136.0, 135.5, 134.8, 131.4, 130.6, 130.6, 130.1, 129.6, 129.1, 128.6, 128.5, 128.2, 127.3, 126.8, 122.2, 122.1 (q, *J* = 277.4 Hz), 120.1, 107.0, 67.9, 63.3, 61.1 (q, *J* = 37.2 Hz), 58.1, 52.4, 40.1.

^{19}F NMR (376 MHz, $CDCl_3$): δ -73.82 (t, *J* = 8.2 Hz).

HRESI-MS (ESI +ve): Found 662.1432, calc for $C_{33}H_{28}F_3NO_7SNa$ 622.1436 $[M + Na]^+$.

e. Double transesterification

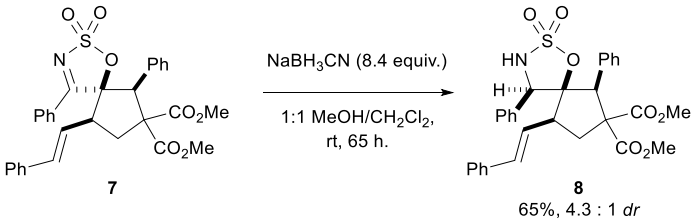


Procedure:

To a reaction vessel containing anhydrous MeOH (3 mL) was added $Na_{(s)}$ (16.3 mg, 0.709 mmol) at rt, and the mixture was stirred at the rt for 15 min. A solution of **3ba** (199.1 mg, 0.292 mmol) in anhydrous MeOH (4 mL) was then transferred via a cannula to the NaOMe solution, rinsed twice with MeOH (2 x 4 mL). The reaction mixture was then stirred at rt and monitored by TLC. Upon completion, the reaction was quenched with saturated aqueous $NaHCO_3$ and extracted with EtOAc. The combined extracts were then washed with brine, then the organic layer was dried over $MgSO_4$, filtered, before being concentrated *in vacuo*. The desired product **7** (135.5 mg, 85%) was then used without further purification.

For the characterisation data of **7**, vide supra.

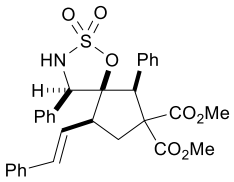
f. Diastereoselective imine reduction



Procedure:

To a solution of **7** (18.9 mg, 0.035 mmol) in a 1:1 $MeOH/CH_2Cl_2$ (4 mL) at 0 °C was added $NaBH_3CN$ (18.3 mg) in one portion. The resulting mixture was allowed to warm to rt, and stirred for 65 h. Upon completion, indicated by TLC, the reaction mixture was concentrated *in vacuo*. The crude residue was then dissolved in EtOAc and washed with water and brine. The organic layer was dried over $MgSO_4$, filtered, then concentrated *in vacuo*. Purification by FCC (25% EtOAc in hexane, alumina column) afforded **8** as a colourless oil (14.4 mg, 4.3 : 1 *dr*, 65%).

Dimethyl (4*S*,5*R*,6*S*,9*S*)-4,6-diphenyl-9-((*E*)-styryl)-1-oxa-2-thia-3-azaspiro[4.4]nonane-7,7-dicarboxylate 2,2-dioxide (8)



R_f = 0.16 (15% EtOAc in hexane).

IR (neat): 2953, 2922, 2852, 1726, 1346, 1266, 1191, 1162, 889, 760, 698 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) (4.3 : 1 mixture of two diastereoisomers, distinguishable resonances of the major diastereoisomer): δ 7.59 – 7.27 (m, 15H), 6.60 (dd, *J* = 16.0, 9.0 Hz, 1H), 6.23 (d, *J* = 16.0 Hz, 1H), 4.82 (d, *J* = 8.5 Hz, 1H), 4.68 (d, *J* = 8.5 Hz, 1H), 4.52 (s, 1H), 3.67 (s, 3H), 3.26 – 3.16 (m, 4H), 2.40 (ddd, *J* = 13.3, 9.1, 7.3 Hz, 1H), 2.12 (dd, *J* = 14.0, 7.2 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) (4.3 : 1 mixture of two diastereoisomers, distinguishable resonances of the major diastereoisomer): δ 172.4, 169.2, 136.5, 134.7, 133.2, 130.7, 129.7, 128.9, 128.8, 128.6, 128.6, 128.1, 127.5, 126.6, 125.0, 104.4, 62.9, 62.2, 55.8, 53.3, 52.5, 47.5, 38.8.

^{1}H NMR (400 MHz, $CDCl_3$) (4.3 : 1 mixture of two diastereoisomers, distinguishable resonances of the minor diastereoisomer): δ 7.03 – 6.99 (m, 2H), 6.76 (d, *J* = 15.9 Hz, 1H), 6.51 (dd, *J* = 15.9, 9.1 Hz, 1H), 5.14 (d, *J* = 9.6 Hz, 1H), 4.34 (d, *J* = 9.6 Hz, 1H), 3.96 (s, 1H), 3.66 (s, 3H), 3.08 (s, 3H), 3.03 – 2.88 (m, 1H), 2.33 (dd, *J* = 13.8, 6.8 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) (4.3 : 1 mixture of two diastereoisomers, distinguishable resonances of the minor diastereoisomer): δ 169.2, 136.4, 135.7, 133.8, 131.7, 129.5, 128.8, 128.1, 127.0, 126.8, 124.6, 104.1, 63.3, 62.5, 54.5, 53.3, 52.3, 51.0, 38.4.

HRESI-MS (ESI +ve): Found 570.1565, calc for $C_{30}H_{29}NO_7SNa$ 570.1562 $[M + Na]^+$.

7. Crystallographic data

Crystal data and structure refinement	
Formula	$C_{36.5}H_{31}N_2O_9F_6S_2Cl_3$
$D_{calc.}$/ g cm^{-3}	1.437
□/mm-1	0.390
Formula Weight	926.10
Colour	colourless
Shape	prism-shaped
Size/mm^3	0.21×0.20×0.15
T/K	230.00(10)
Crystal System	orthorhombic
Flack Parameter	0.00(3)
Hooft Parameter	0.00(3)
Space Group	$P2_12_12$
a/Å	10.4362(4)
b/Å	22.4430(8)
c/Å	18.2762(7)
α/°	90
β/°	90
γ/°	90
V/Å^3	4280.7(3)
Z	4
Z'	1
Wavelength/Å	0.71073
Radiation type	Mo K_α
Θ_{min}/°	2.247
Θ_{max}/°	25.348
Measured Refl's.	88507
Indep't Refl's	7833
Refl's I≥2 σ(I)	5572
R_{int}	0.0570
Parameters	747
Restraints	1034
Largest Peak	0.344
Deepest Hole	-0.267
GooF	1.032
wR_2 (all data)	0.1937
wR_2	0.1717
R_1 (all data)	0.0876
R_1	0.0636

Single colourless prism-shaped crystals **3ao** were used as supplied. A suitable crystal with dimensions 0.21 × 0.20 × 0.15 mm^3 was selected and mounted on a SuperNova, Dual, Cu at home/near, EosS2 diffractometer. The crystal was kept at a steady *T* = 230.00(10) K during data collection. The structure was solved with the ShelXT[19] solution program using dual methods and by using Olex2 1.5[20] as the graphical interface. The model was refined with ShelXL 2019/2[21] using full matrix least squares minimisation on F^2.

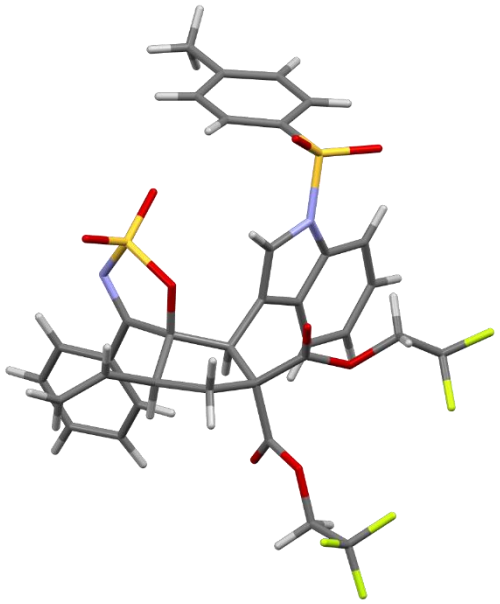


Figure S1. X-ray crystal structure of **(5*R*,6*S*,9*S*)-3ao**

Initial data collection on this sample at 130 K revealed an incommensurately modulated structure with a similar orthorhombic unit cell to this structure refinement presented here with q vector of approximately 0.2 along the a axis. With our currently available radiation source (Mo only) and detector technology (CCD) we were unable to collect suitable data for either handling as an incommensurately modulated structure or the supercell approach given the closeness and relative weakness of the 1st order satellites to the main reflections (only first order satellites could be seen). As such, we have presented this refinement at 230 K on a higher temperature non-modulated phase (phase change occur around 190 K).

Preliminary investigation of a refinement at 130 K by the super cell approach aided our understanding of the zones of the structure with the largest modulated features and helped to develop a disorder model to approximate these features in the 230 K dataset. The worst affected zones are the Tos-substituted indolyl, the Ph substituent and the dichloromethane solvent molecules that line a channel. Both the indolyl and Ph substituents were treated with three and two site positional disorder models, respectively. For the indolyl group, the occupancies were fixed on the basis of the ADP appearances, whereas for the Ph group these were refined. Both of these groups required the used of rigid body restraints implemented via the OLEX2 FragmentDB tool. For the minor components of the indolyl groups isotropic ADPs were used (with the exception of the heavier S atoms that allowed for stable anisotropic refinement). For the CF3 groups, the large ADPs showed signs of more moderate modulation effects and gave the appearance of suitable disorder models being achievable, but we could not develop models for these and they are presented with no restraints applied. Two sites for the dichloromethane solvent could be refined reasonably with refined occupancies, while the remaining sites along the solvent channel were treated with a solvent mask.

Further details are provided in the _refine_special_details field of the CIF file.

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9. NMR spectra of novel compounds

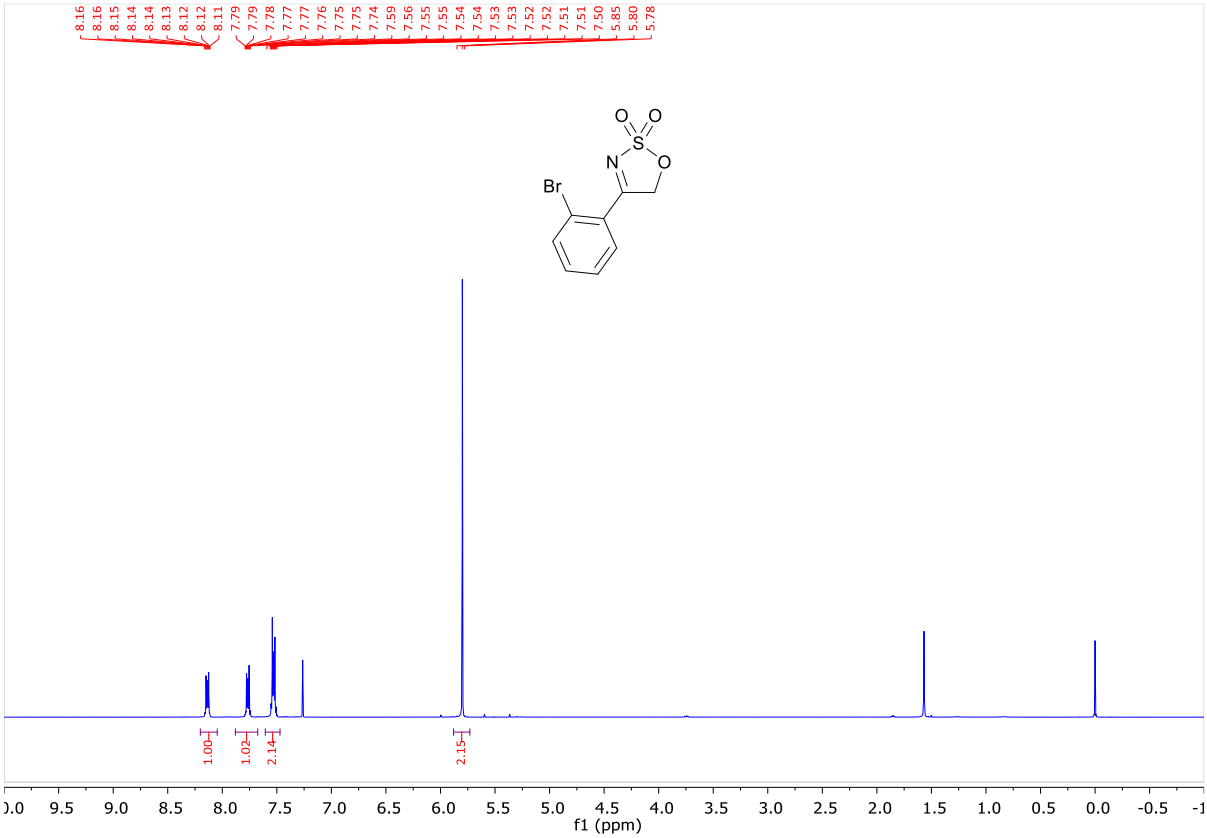


Figure S3. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of **S3f.**

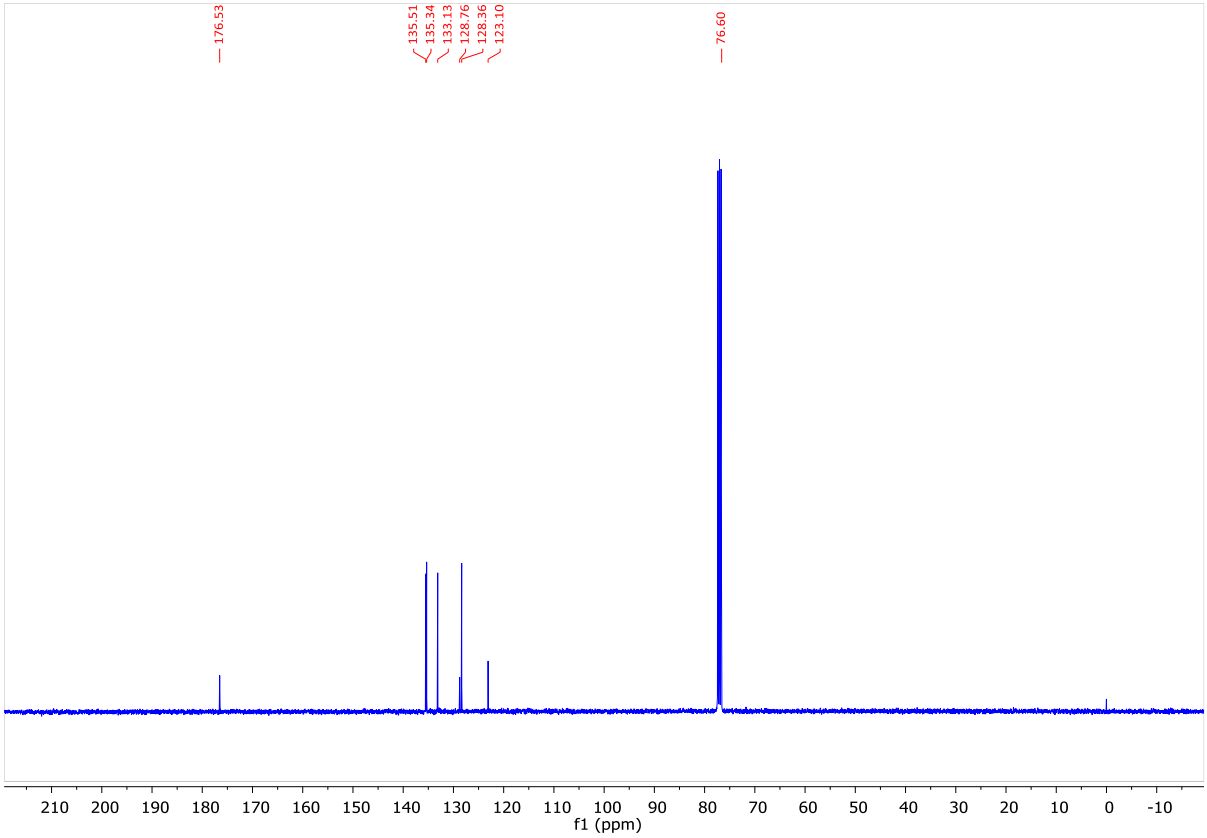


Figure S4. ^{13}C NMR spectrum ($CDCl_3$, 100 MHz) of **S3f**.

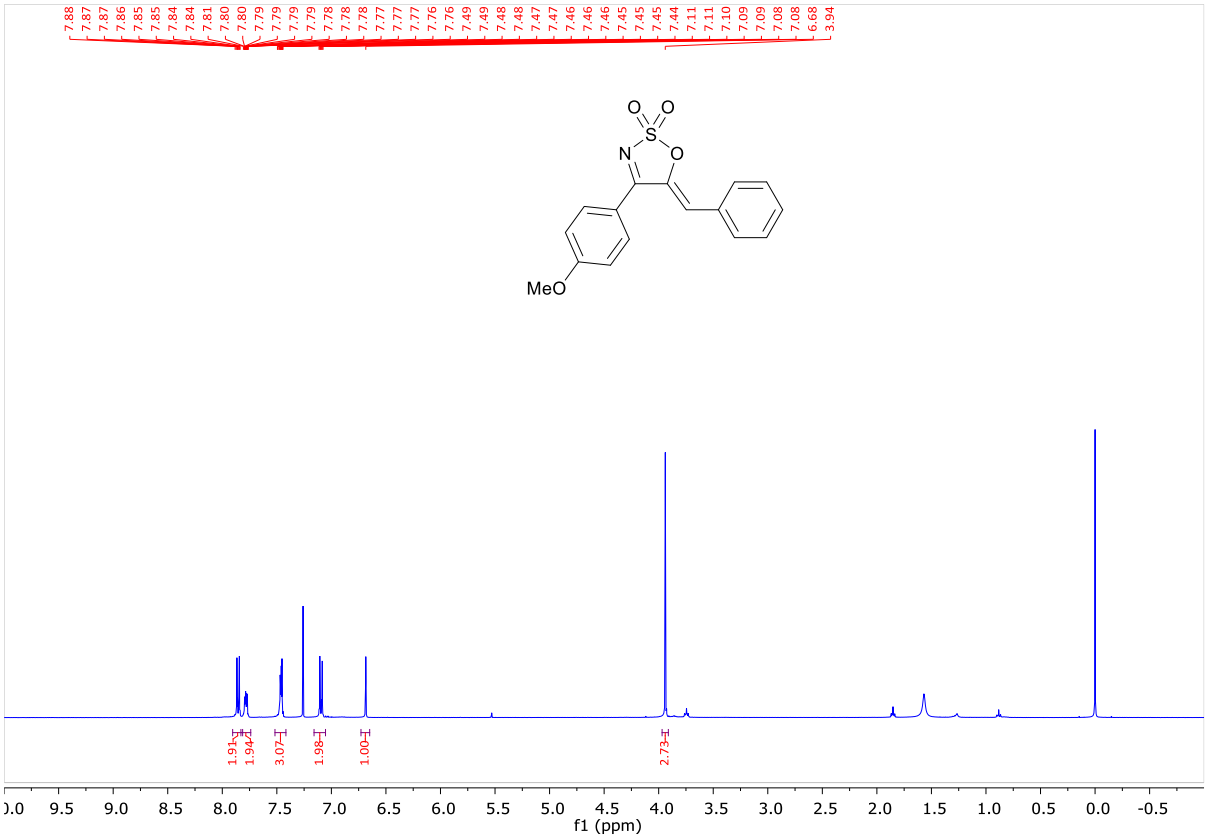


Figure S5. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of **2b.**

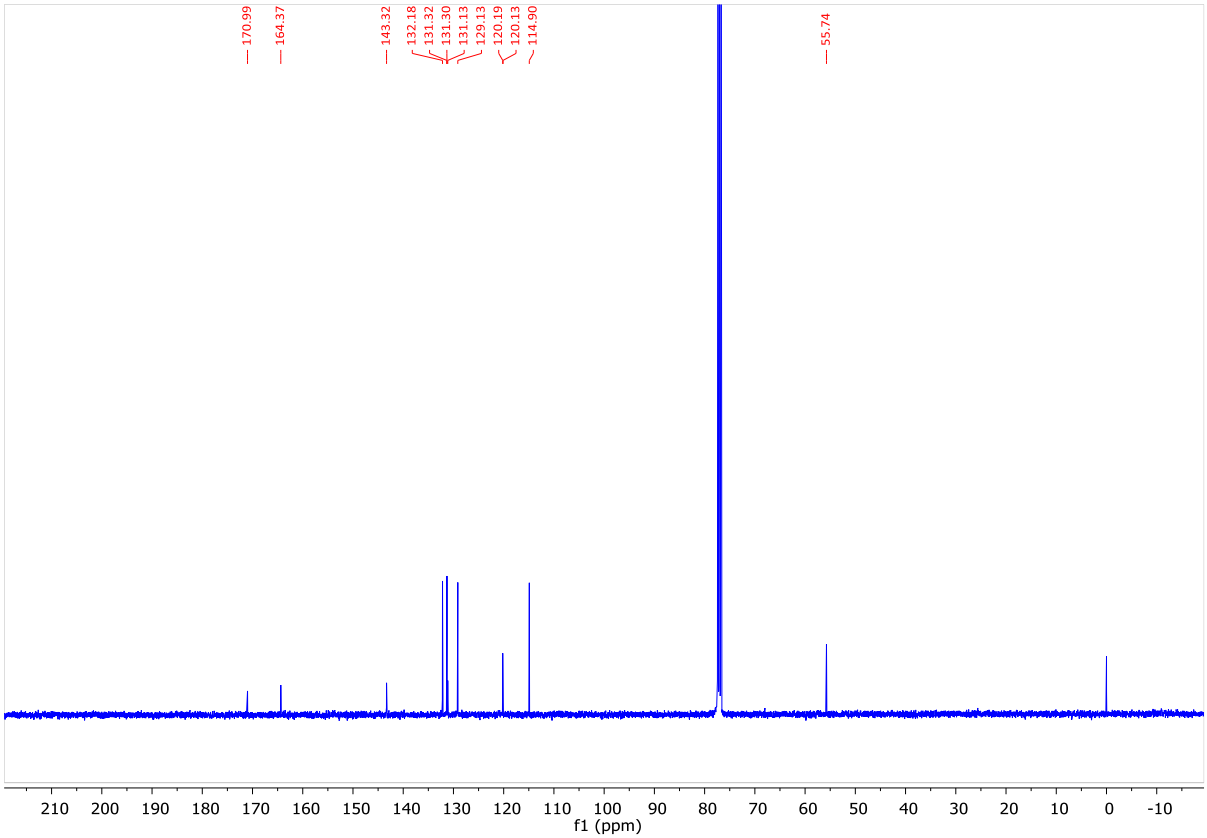


Figure S6. ^{13}C NMR spectrum ($CDCl_3$, 100 MHz) of **2b**.

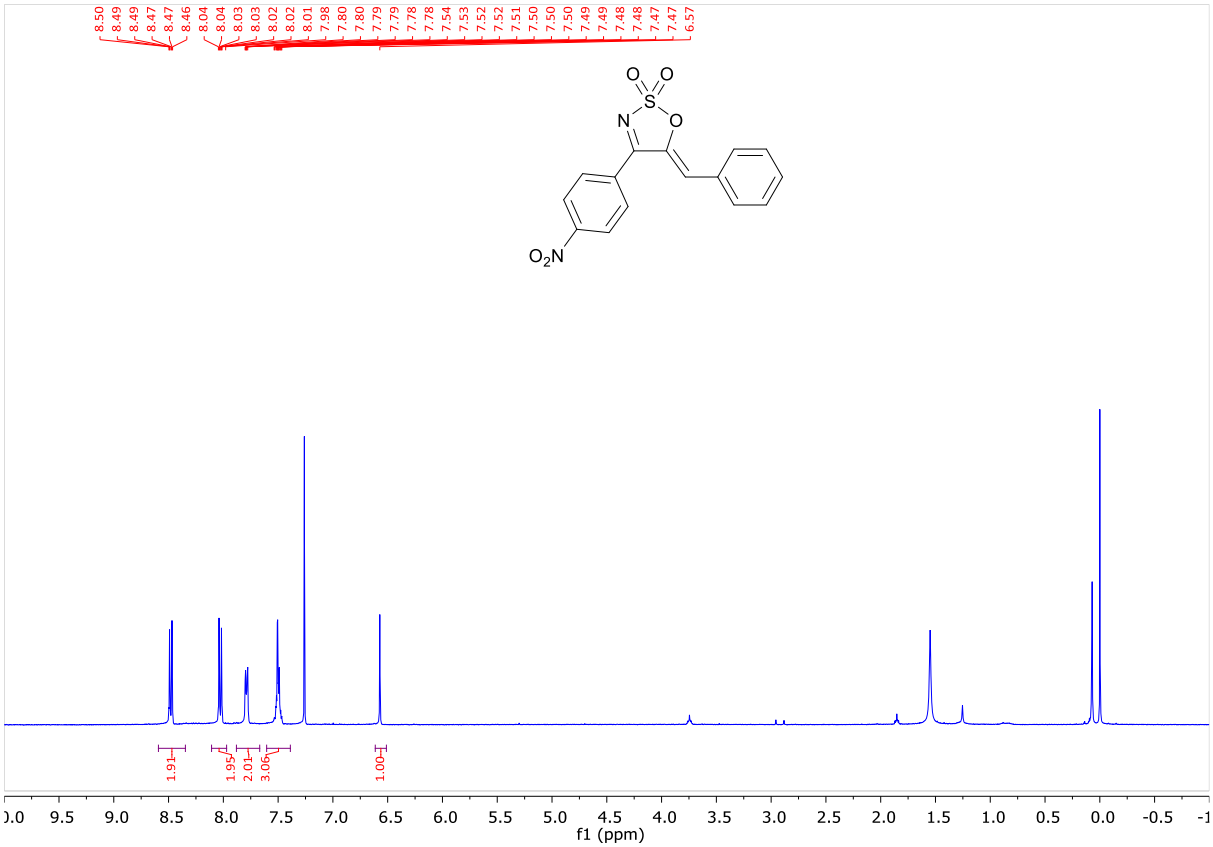


Figure S7. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of **2c.**

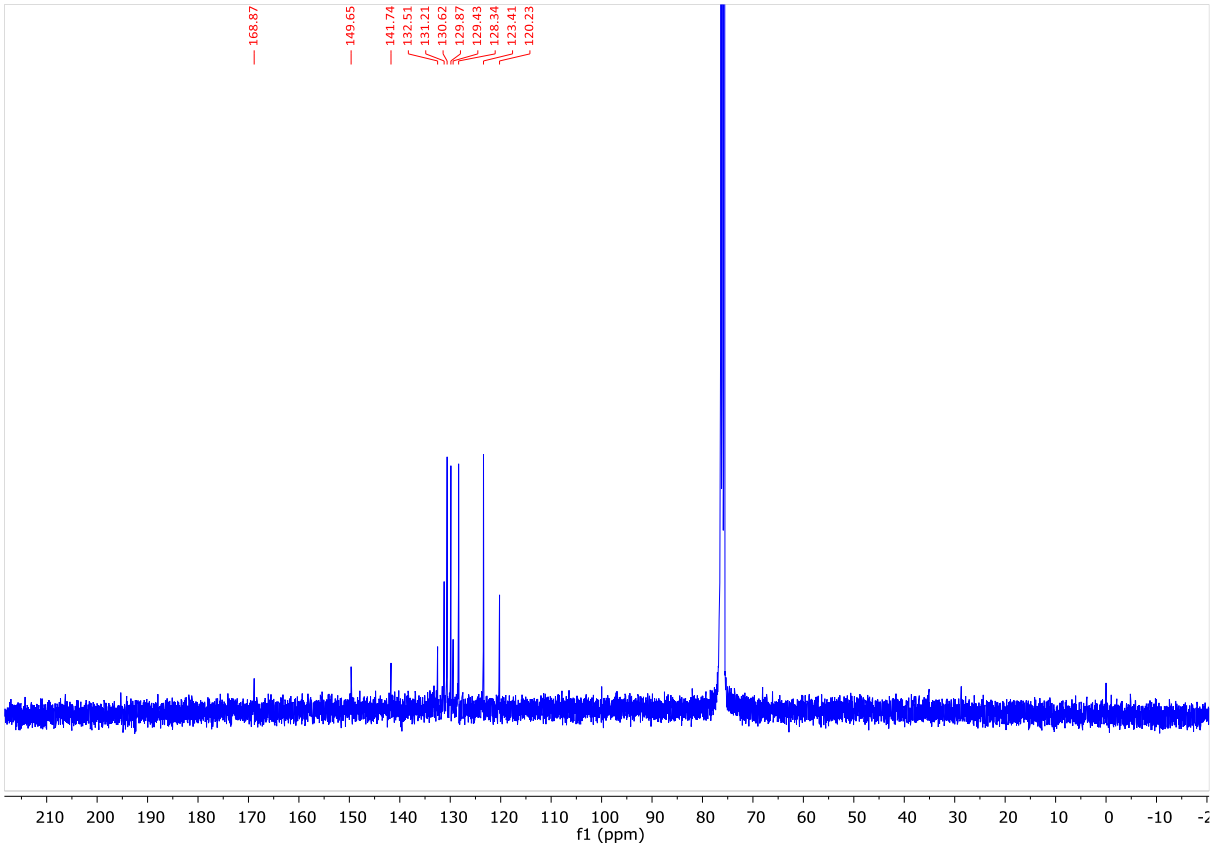


Figure S8. ^{13}C NMR spectrum ($CDCl_3$, 100 MHz) of **2c**.

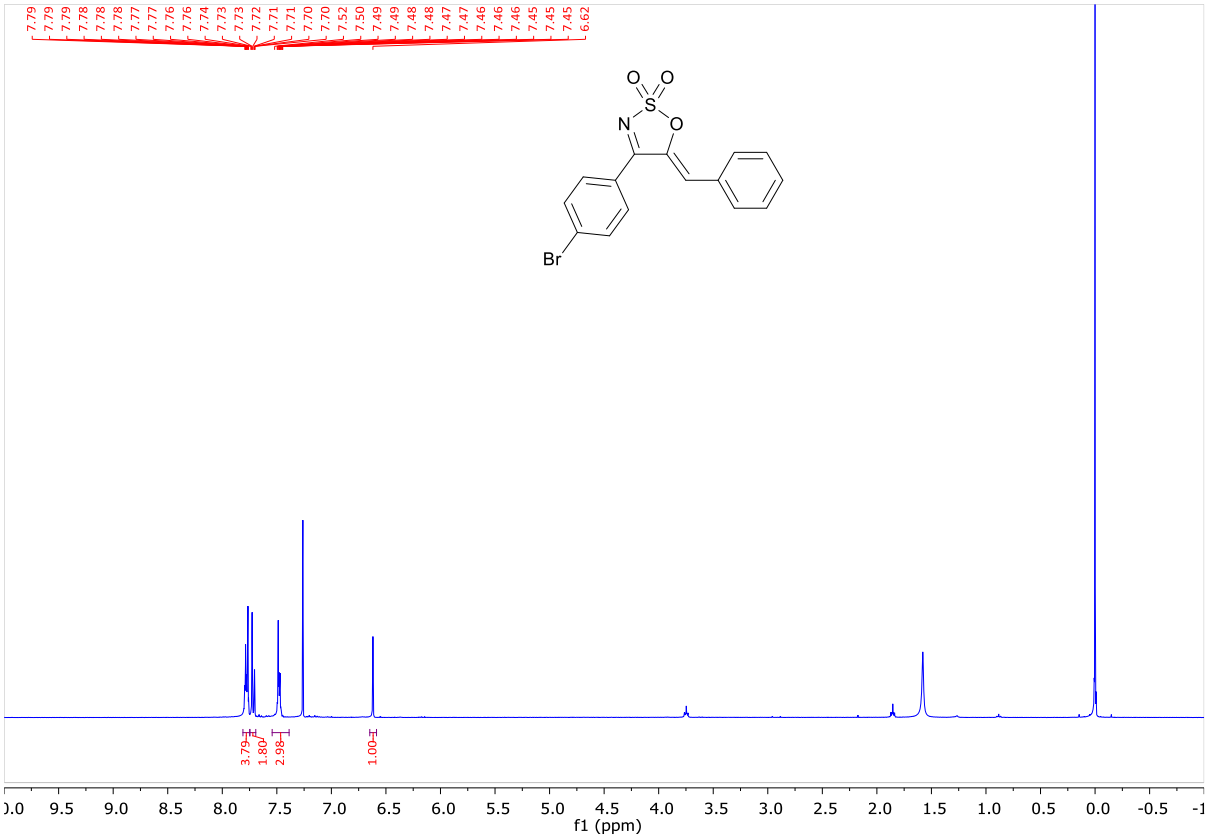


Figure S9. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of **2d.**

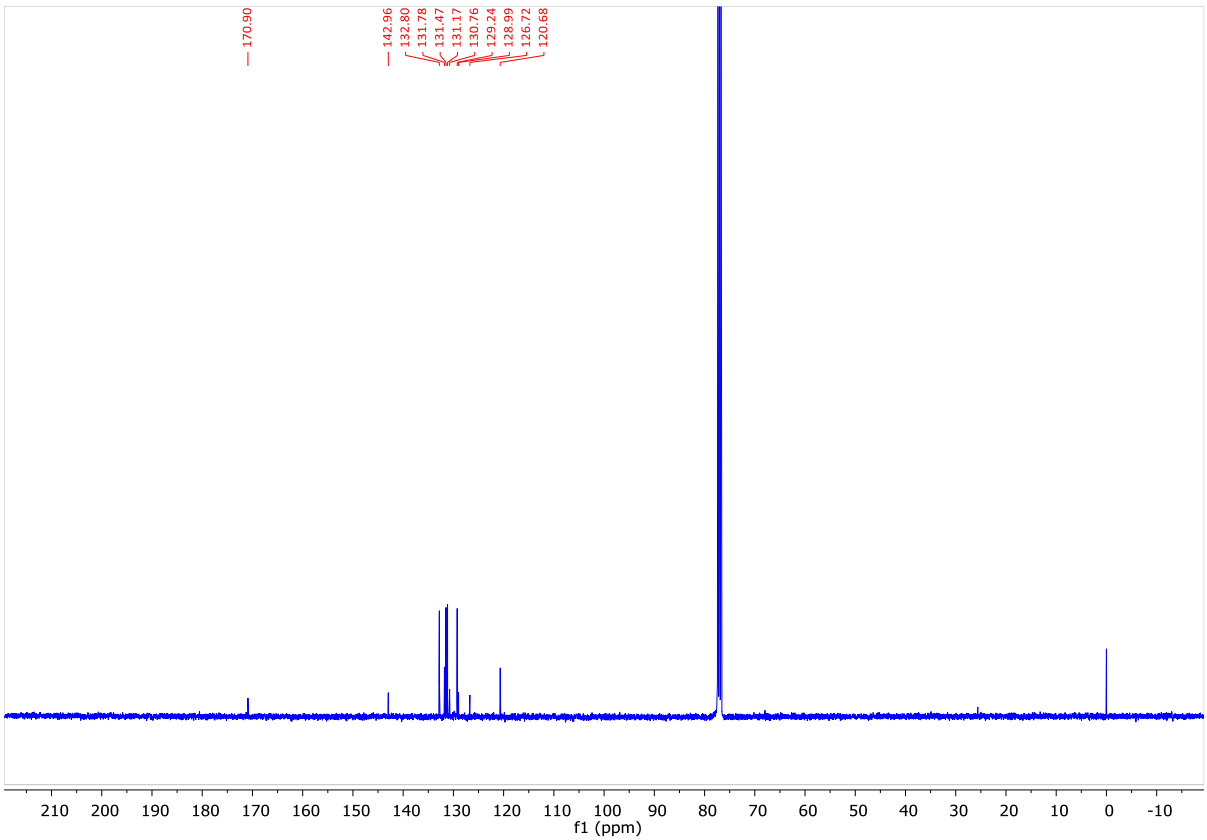


Figure S10. ^{13}C NMR spectrum ($CDCl_3$, 100 MHz) of **2d**.

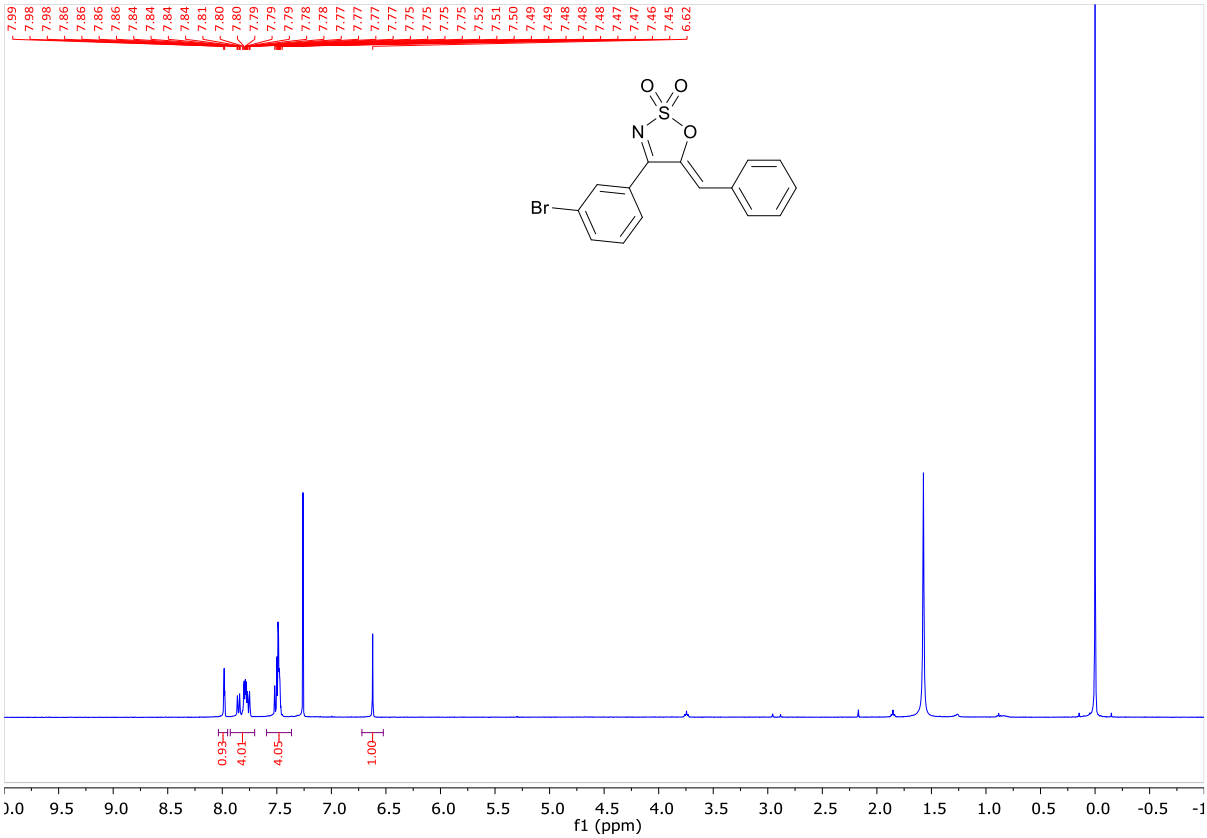


Figure S11. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of **2e.**

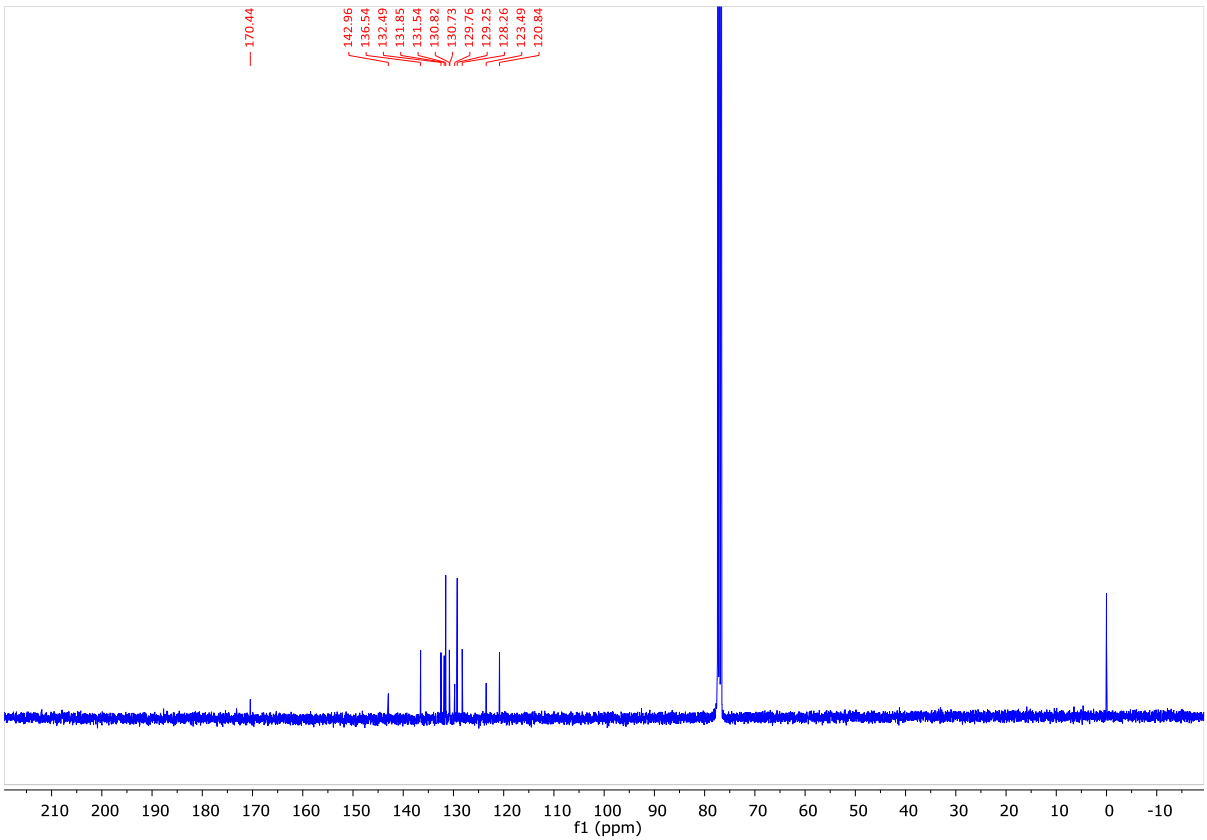


Figure S12. ^{13}C NMR spectrum ($CDCl_3$, 100 MHz) of **2e**.

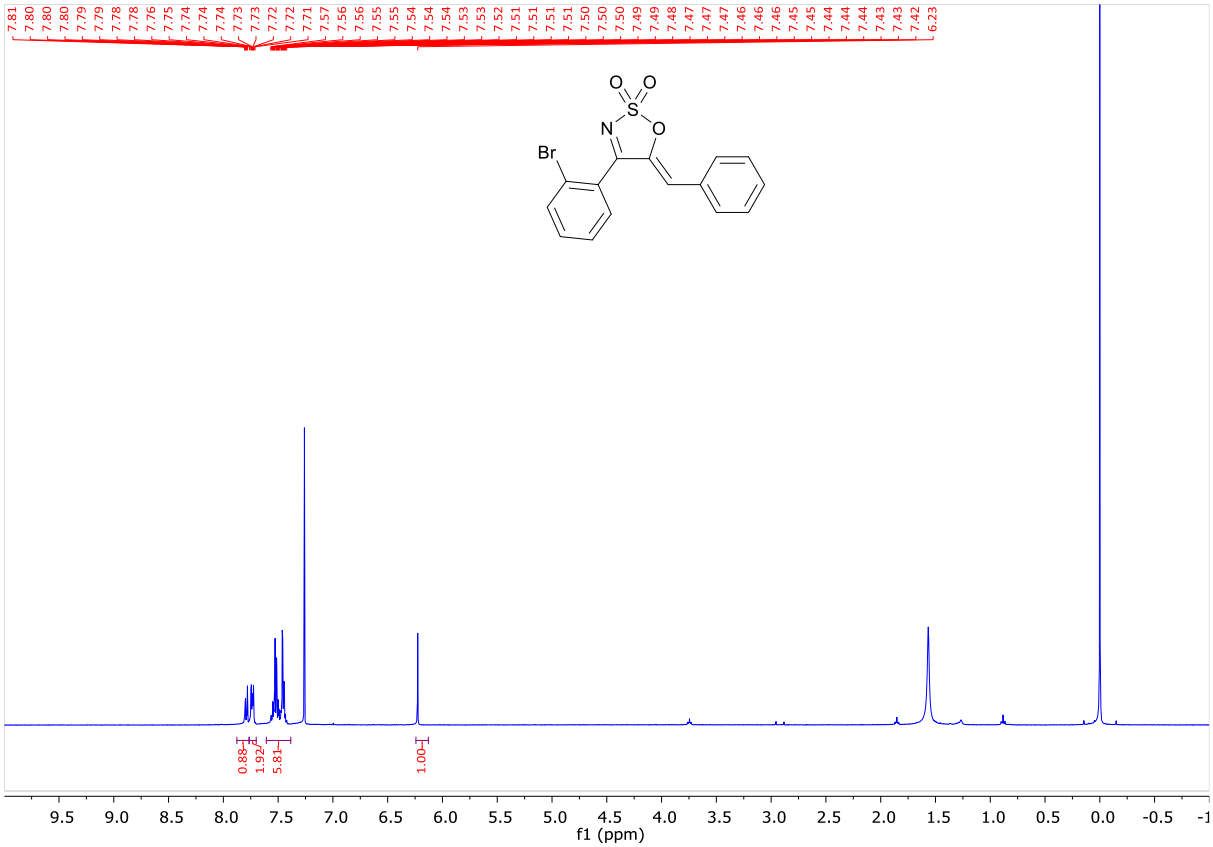


Figure S13. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of **2f.**

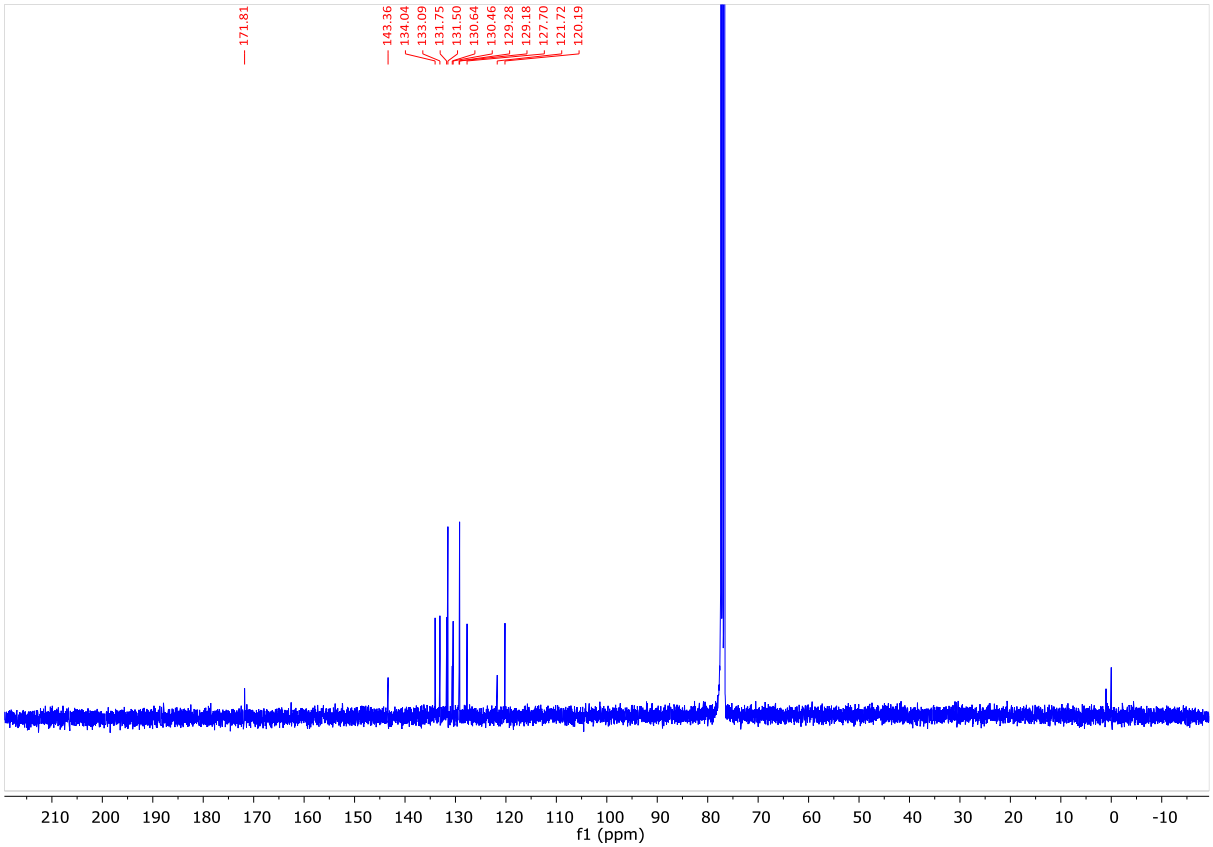


Figure S14. ^{13}C NMR spectrum ($CDCl_3$, 100 MHz) of **2f**.

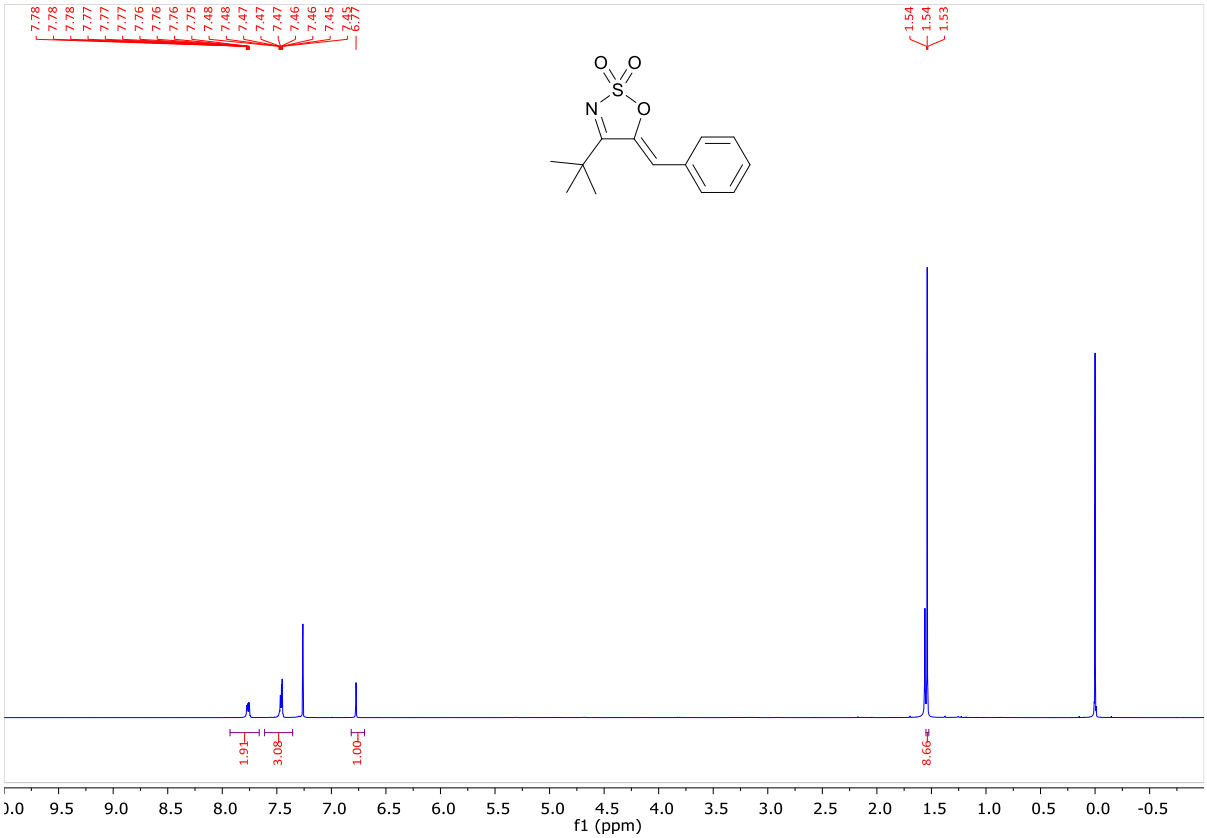


Figure S15. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of **2g.**

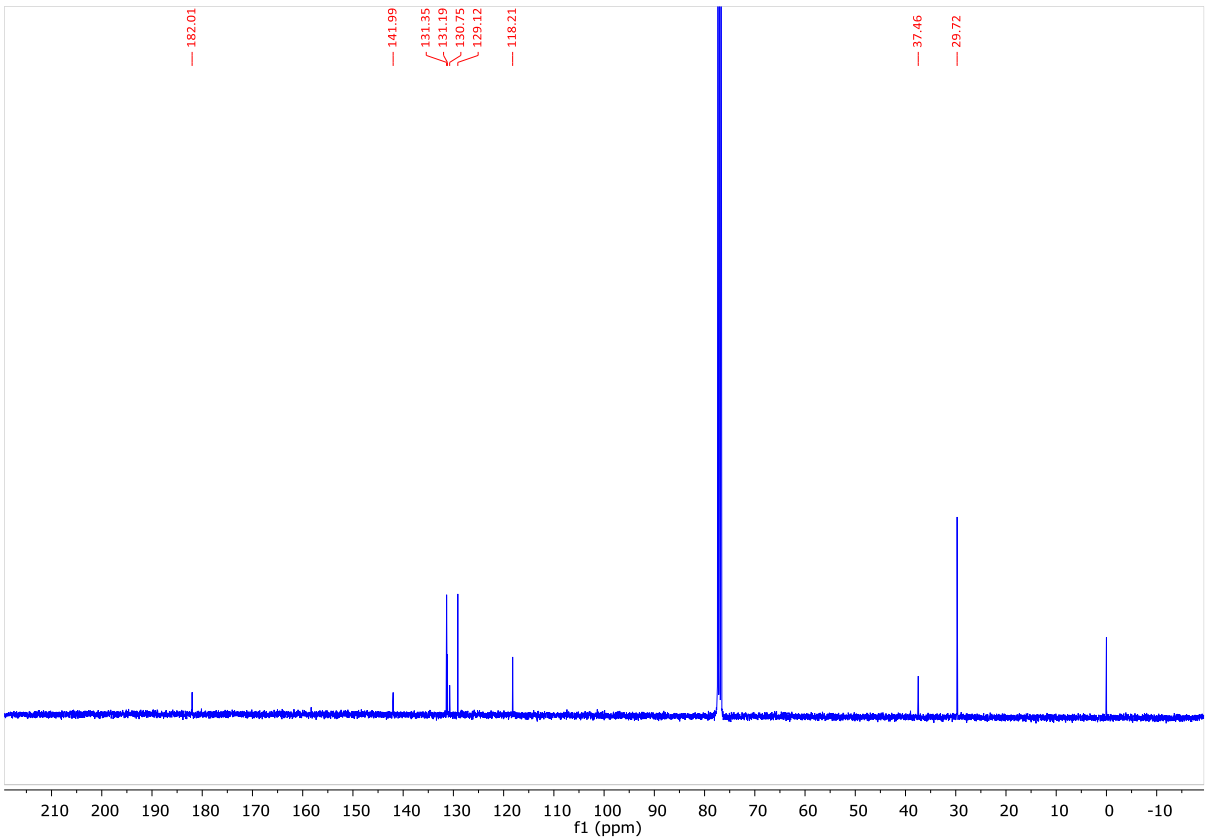


Figure S16. ^{13}C NMR spectrum ($CDCl_3$, 100 MHz) of **2g**.

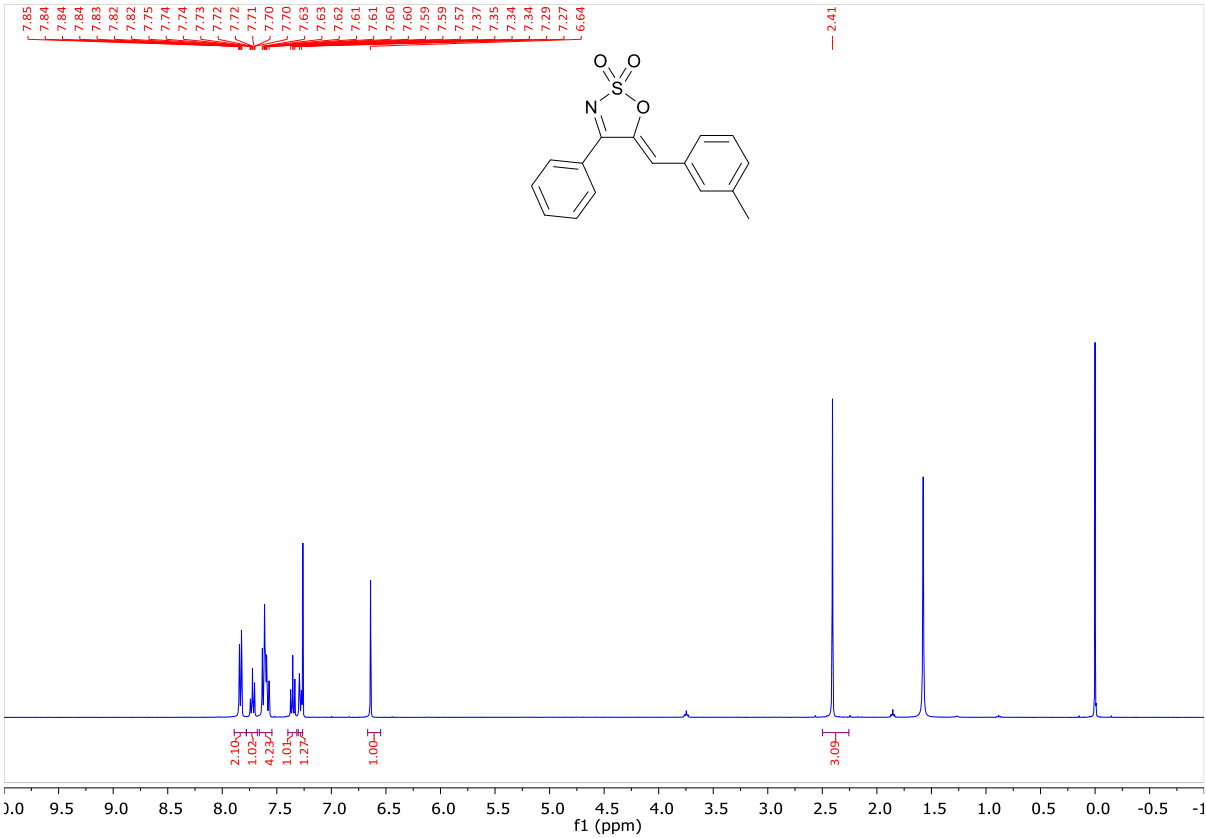


Figure S17. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of **2i.**

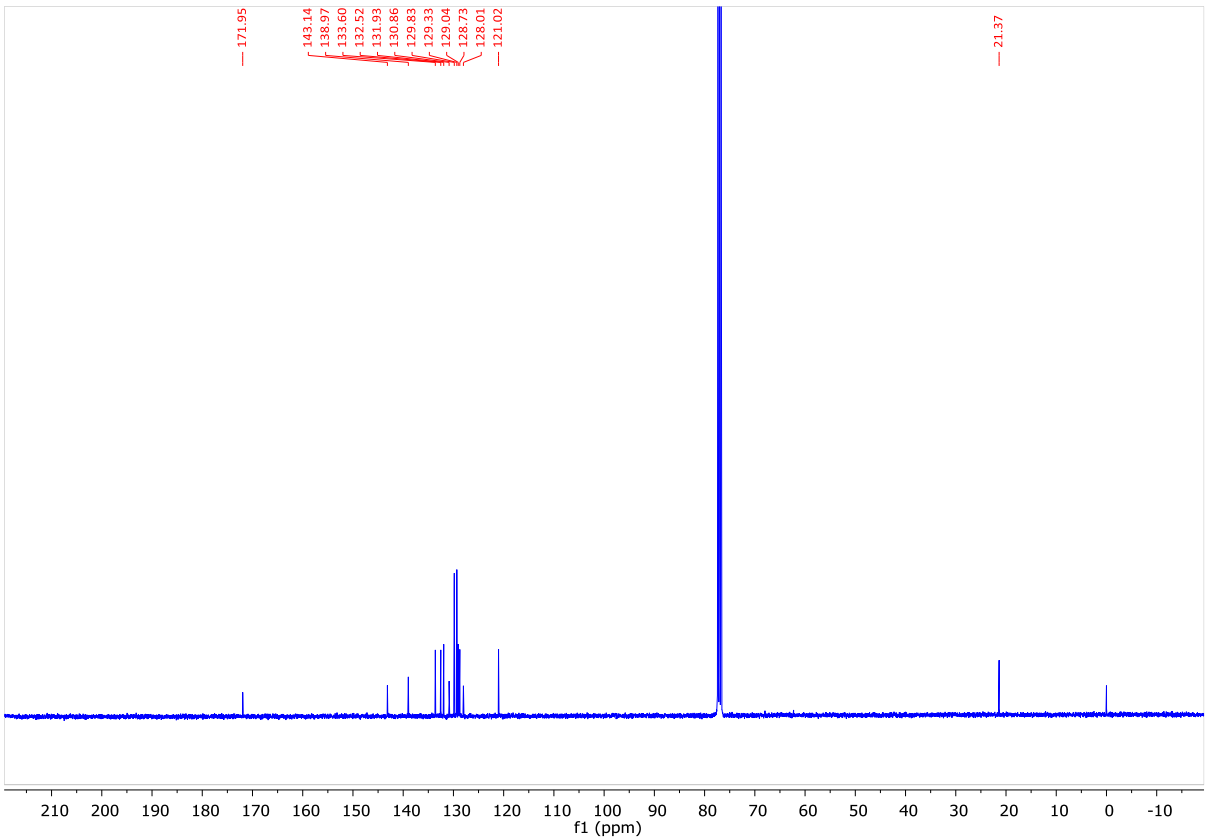


Figure S18. ^{13}C NMR spectrum ($CDCl_3$, 100 MHz) of **2i**.

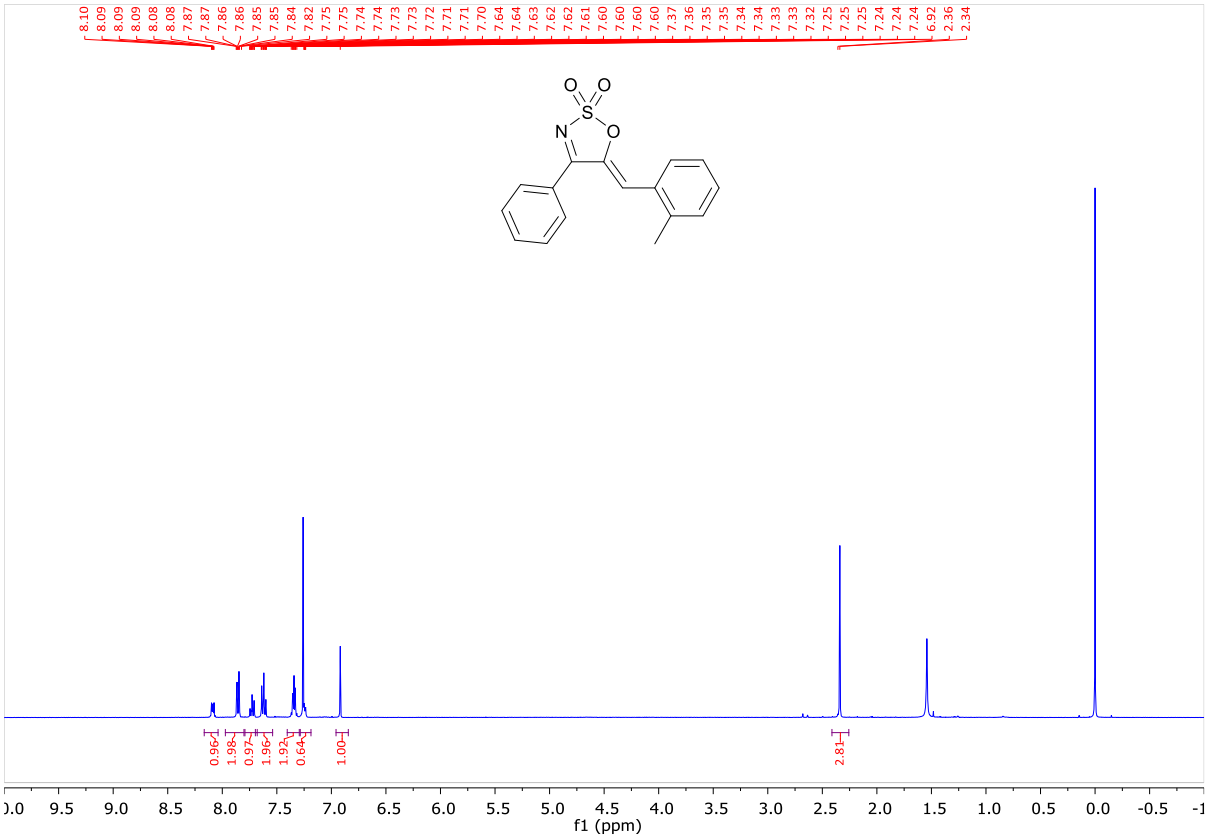


Figure S19. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of **2j.**

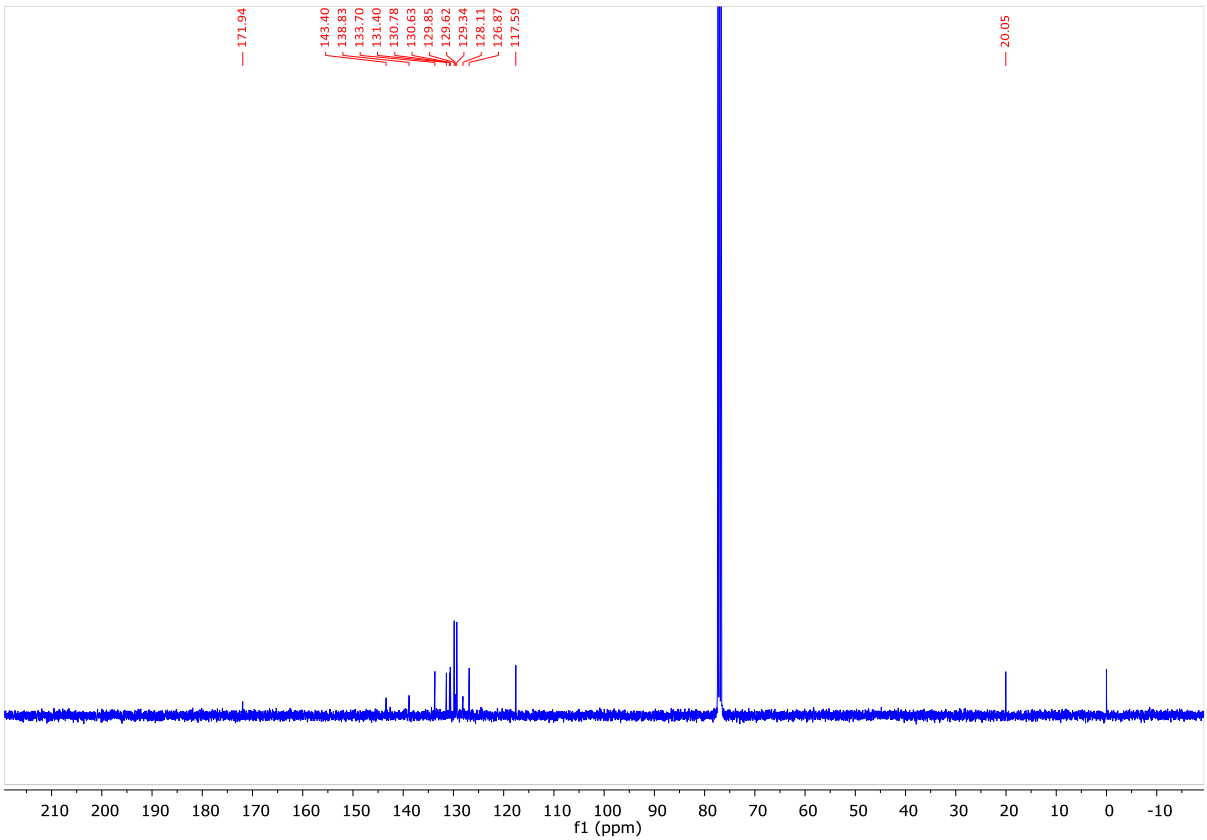


Figure S20. ^{13}C NMR spectrum ($CDCl_3$, 100 MHz) of **2j**.

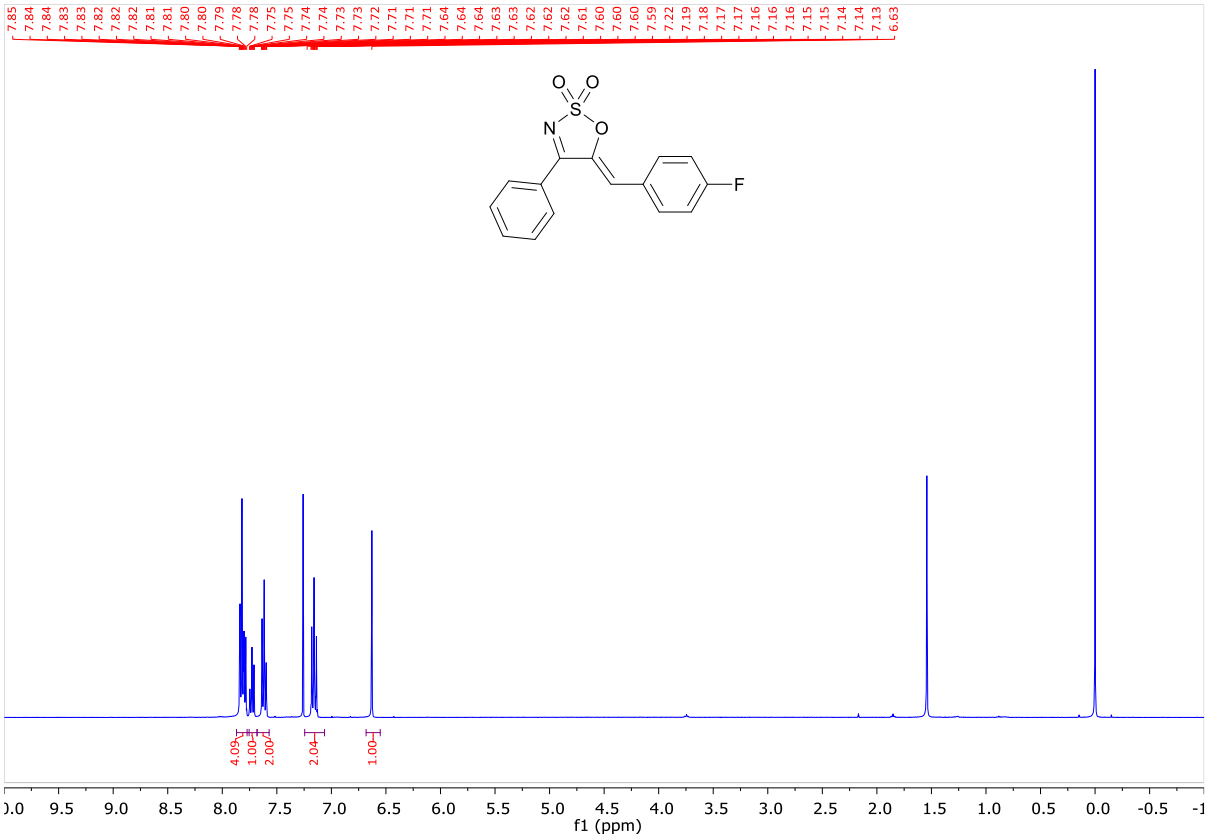


Figure S21. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of **2k.**

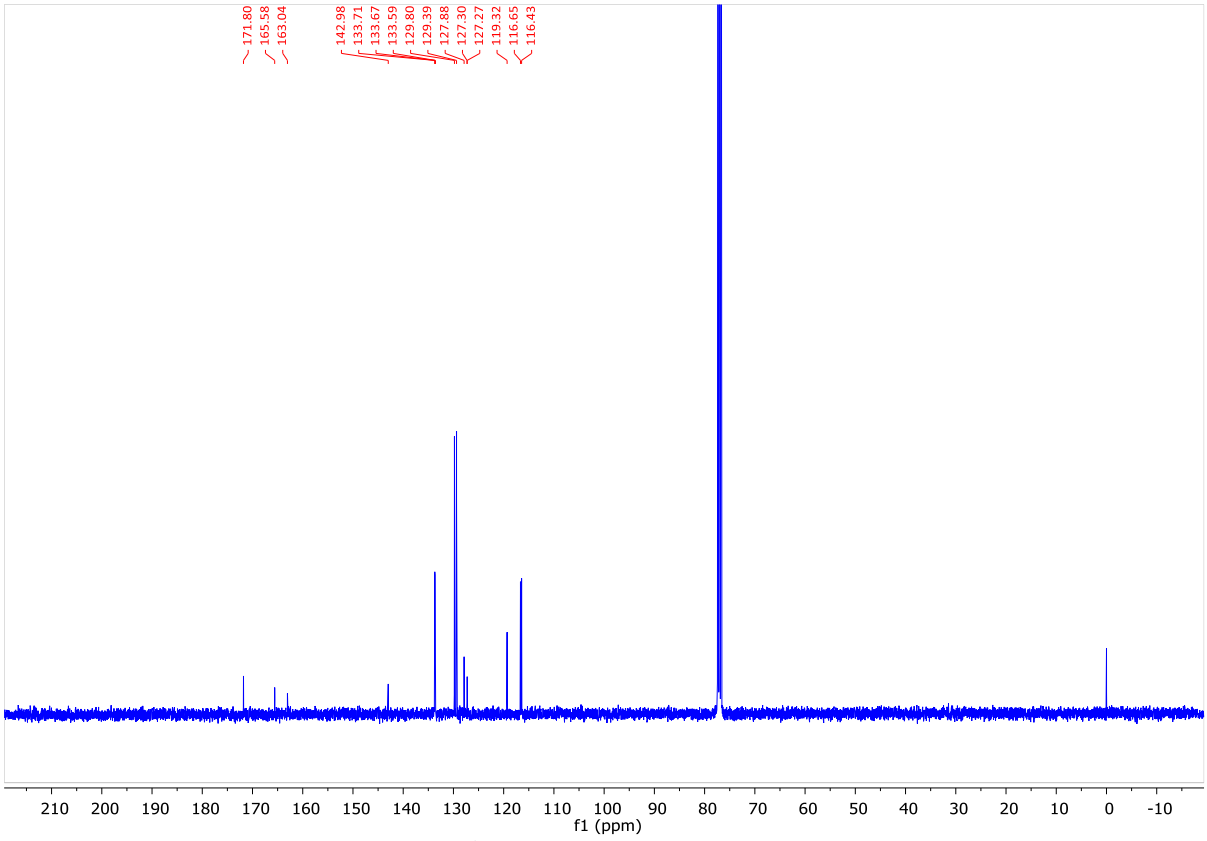


Figure S22. ^{13}C NMR spectrum ($CDCl_3$, 100 MHz) of **2k**.

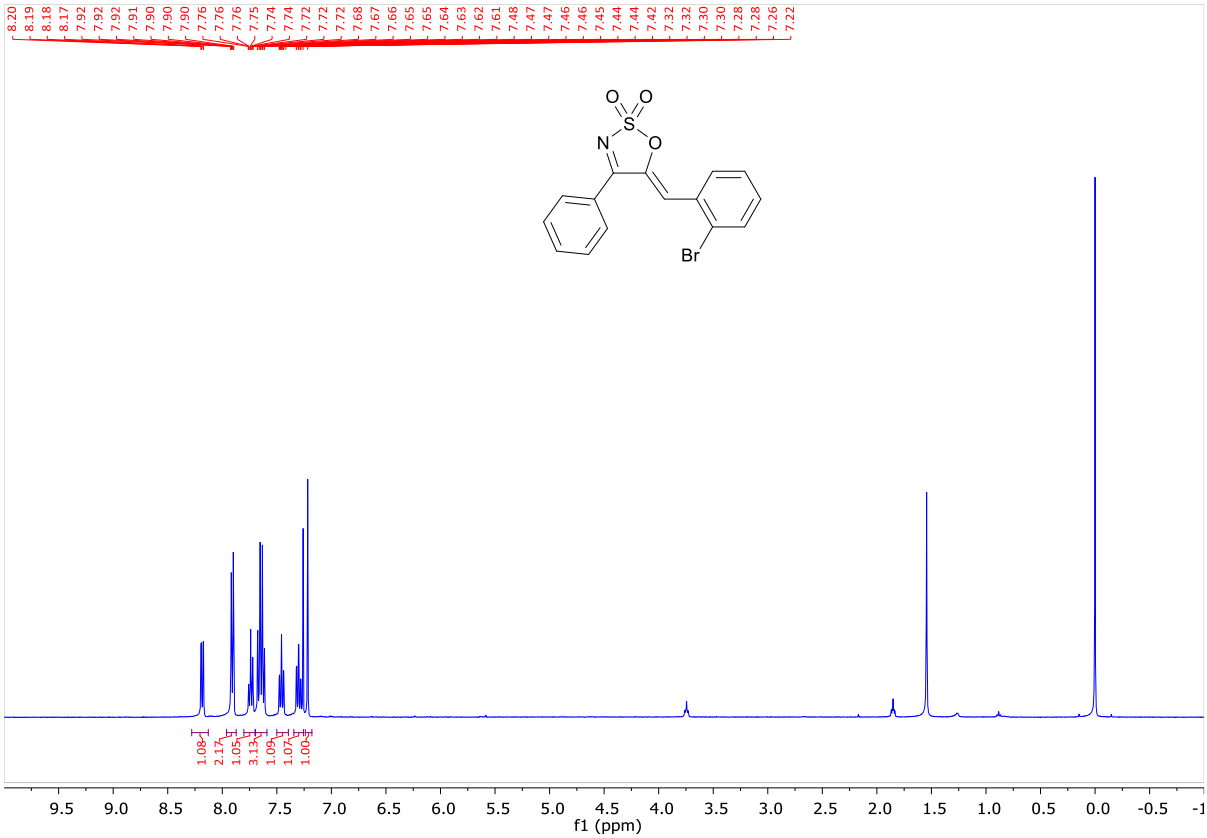


Figure S23. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of **2l.**

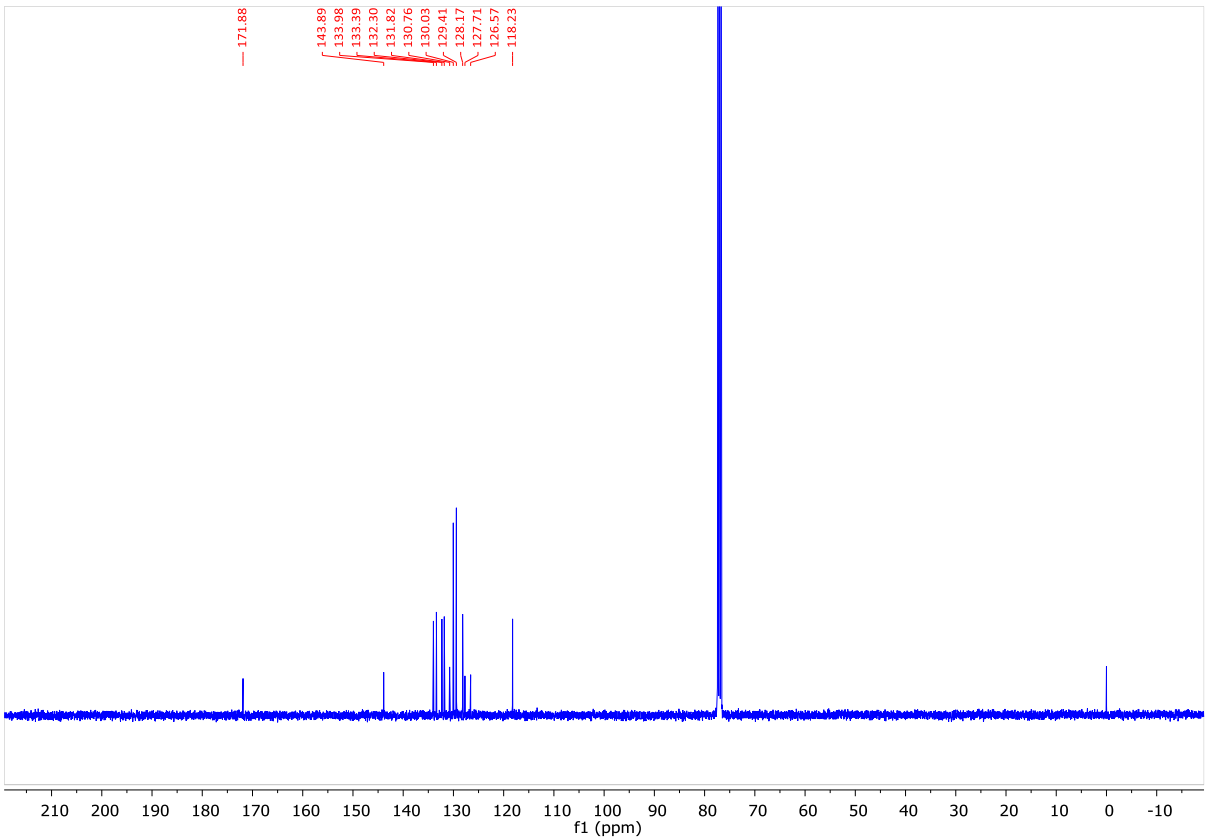


Figure S24. ^{13}C NMR spectrum ($CDCl_3$, 100 MHz) of **2l**.

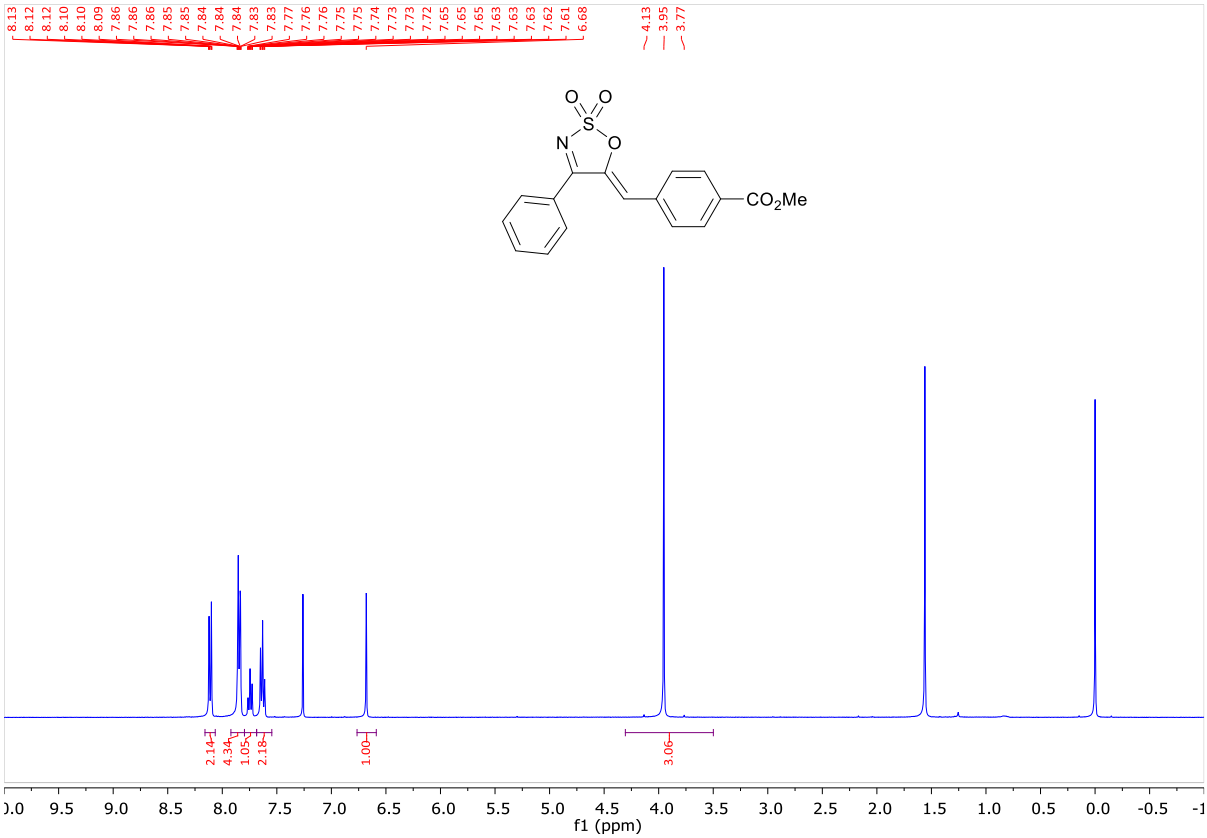


Figure S25. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of **2m.**

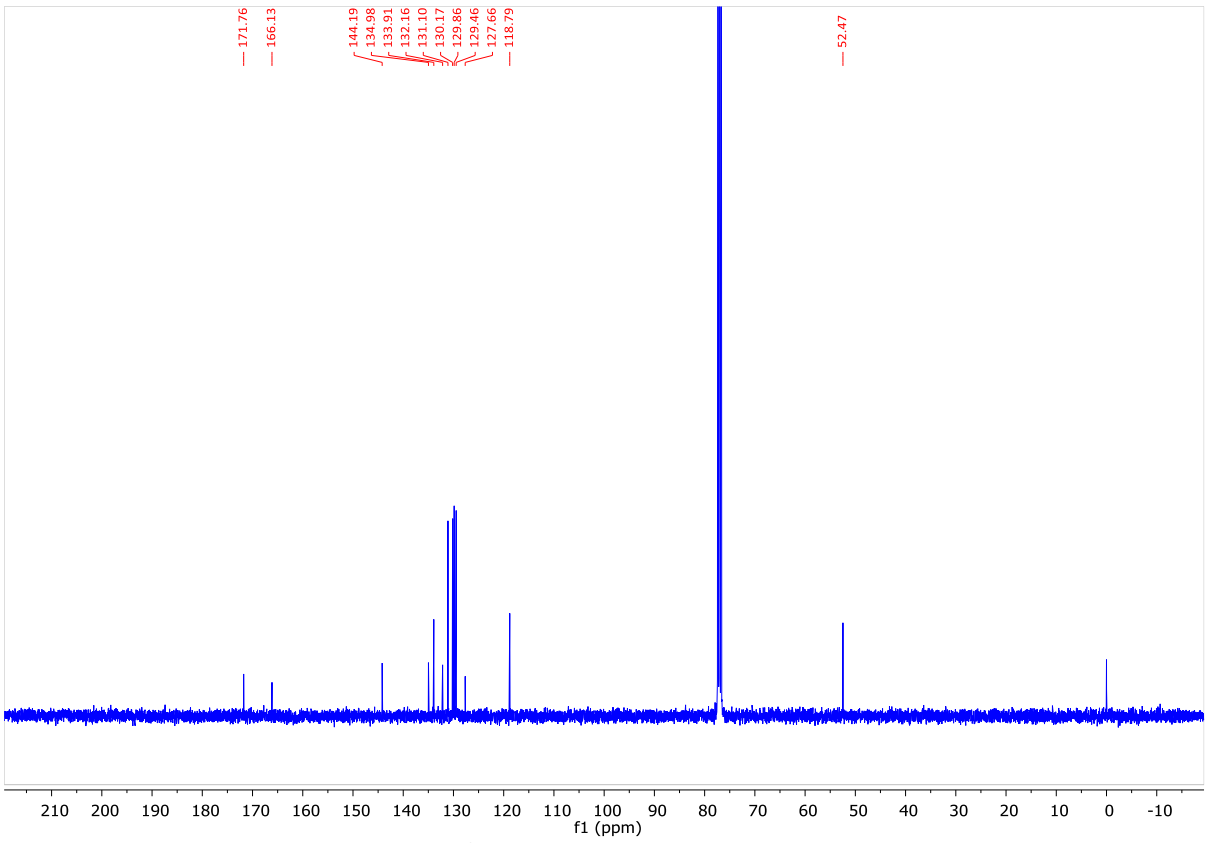


Figure S26. ^{13}C NMR spectrum ($CDCl_3$, 100 MHz) of **2m**.

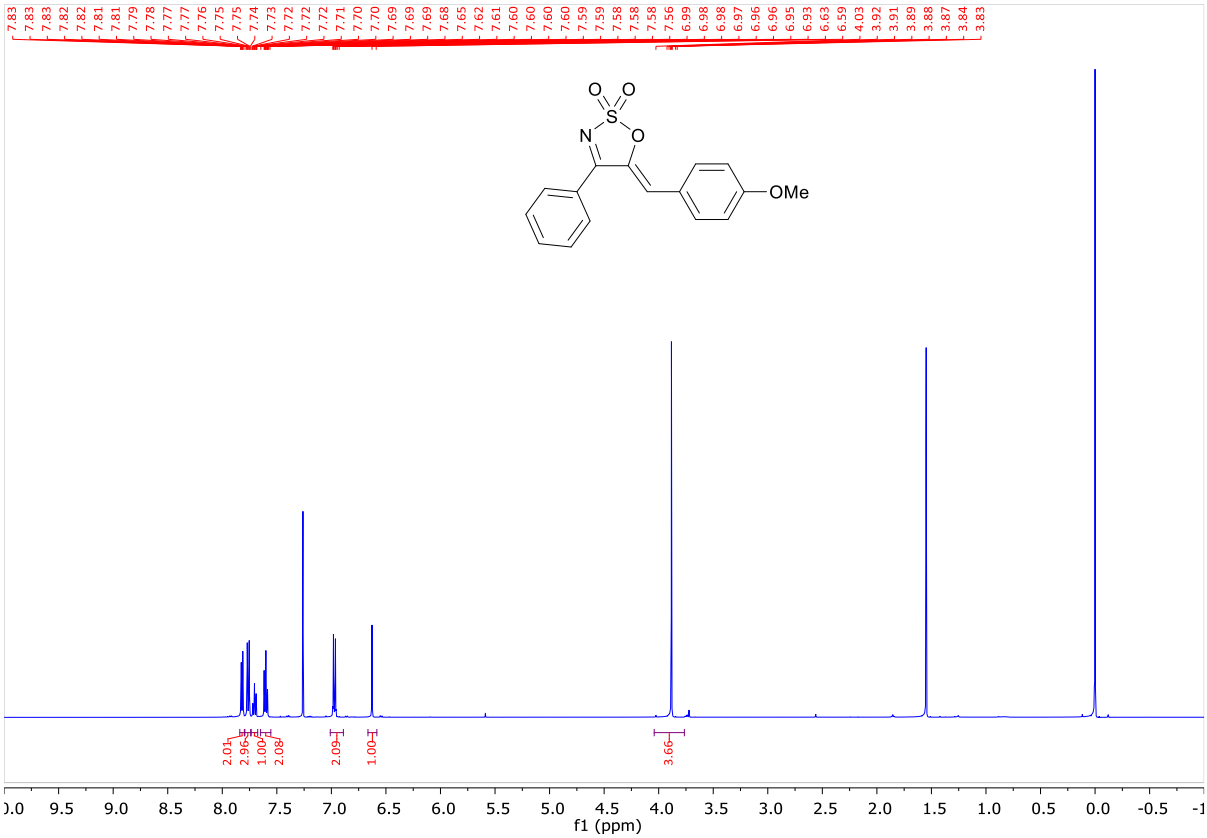


Figure S27. ^{1}H NMR spectrum ($CDCl_3$, 500 MHz) of **2n.**

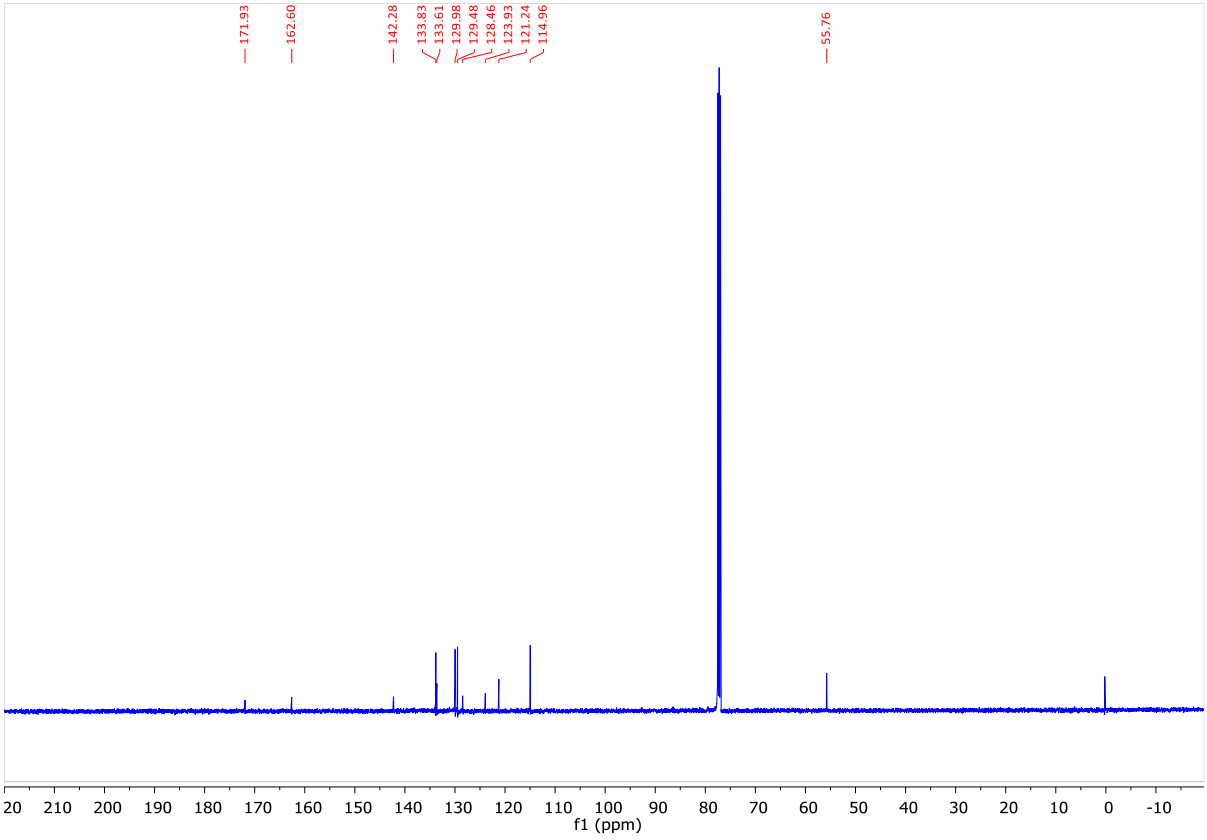


Figure S28. ^{13}C NMR spectrum ($CDCl_3$, 125 MHz) of **2n**.

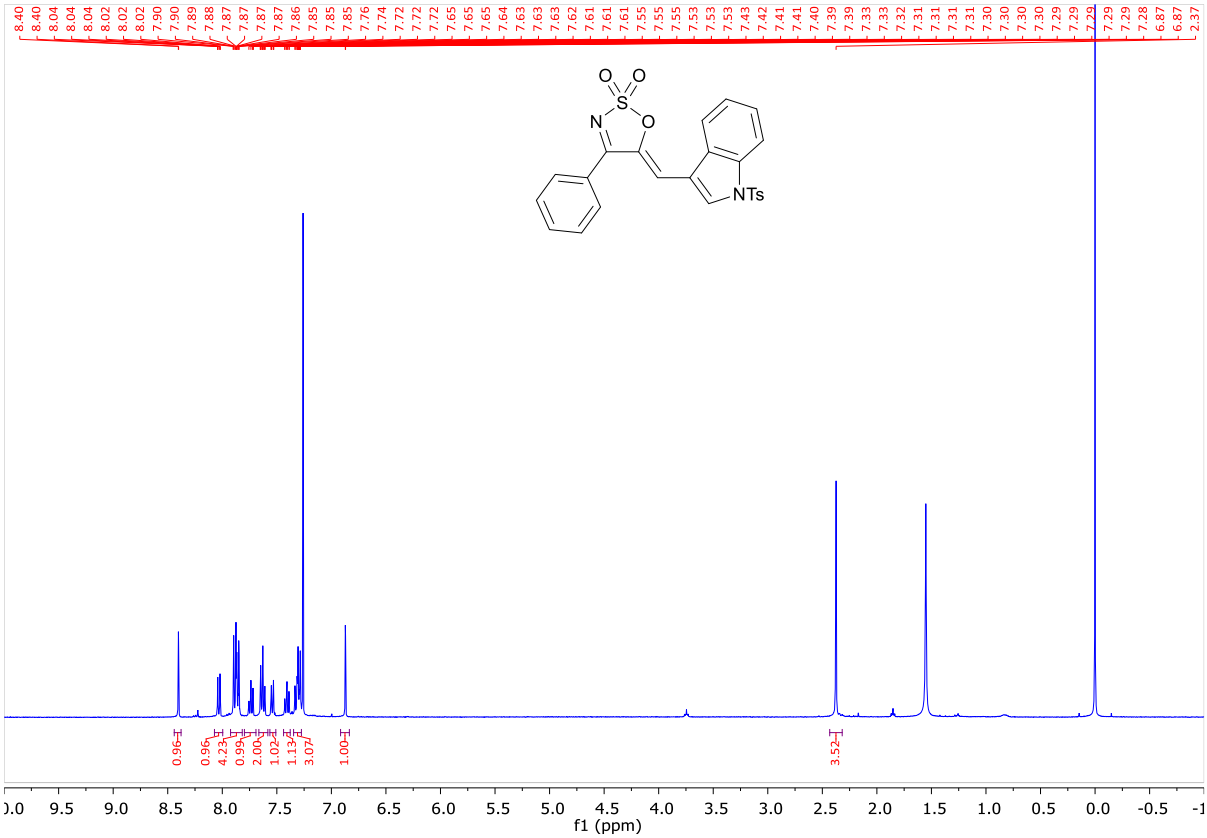


Figure S29. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of **2o.**

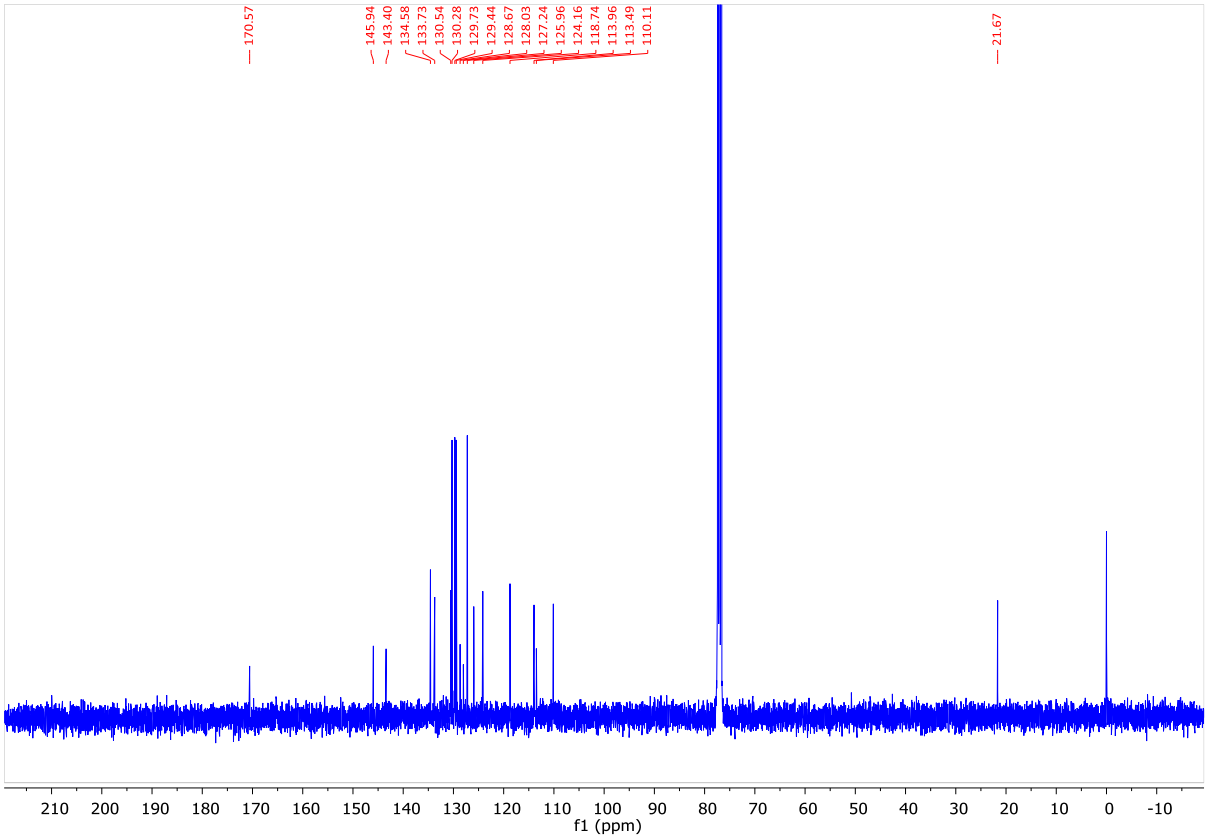


Figure S30. ^{13}C NMR spectrum ($CDCl_3$, 100 MHz) of **2o**.

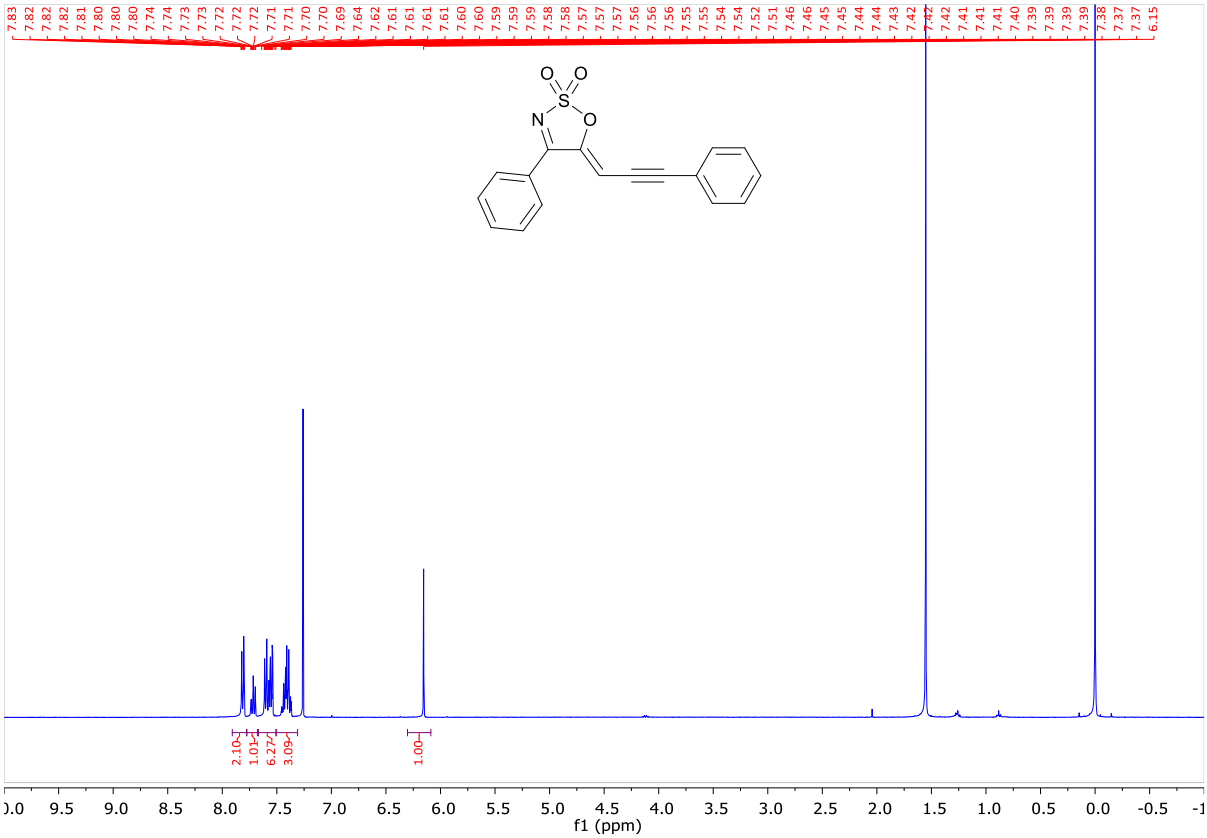


Figure S31. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of **2p.**

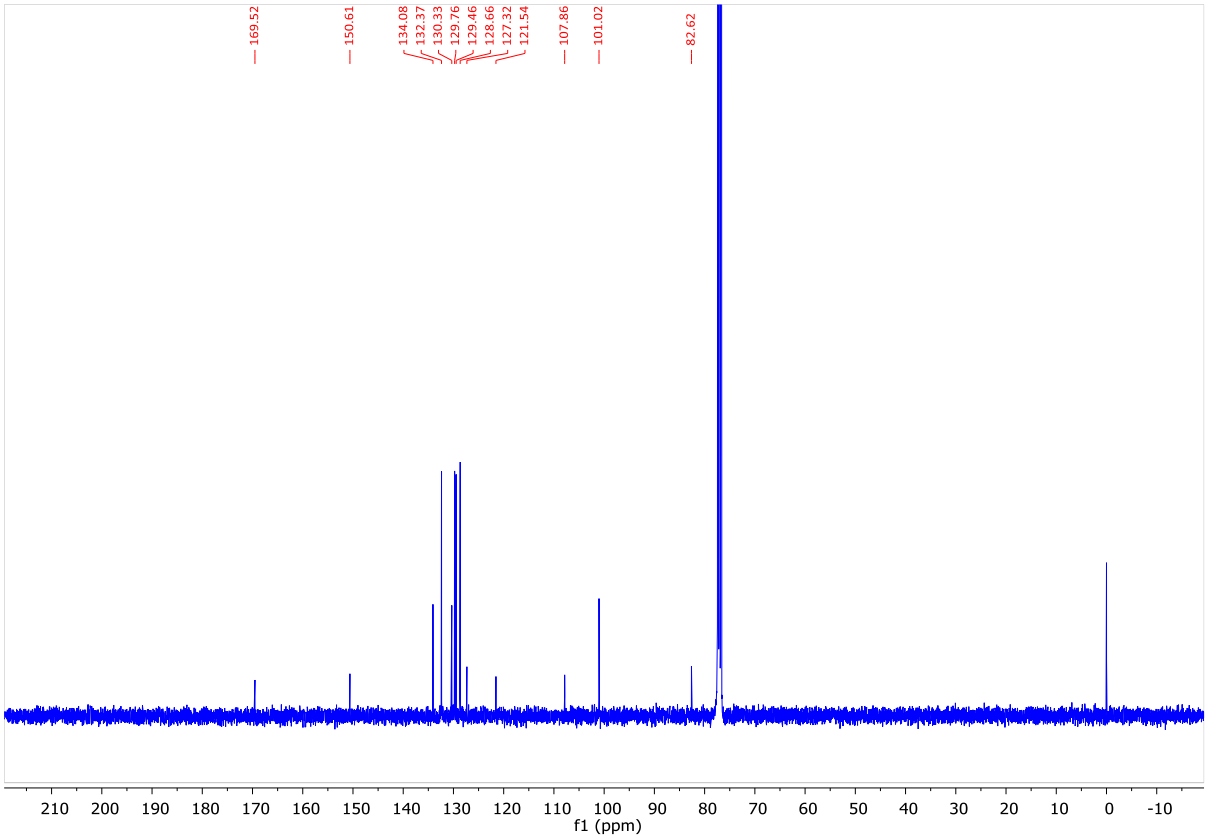


Figure S32. ^{13}C NMR spectrum ($CDCl_3$, 100 MHz) of **2p**.

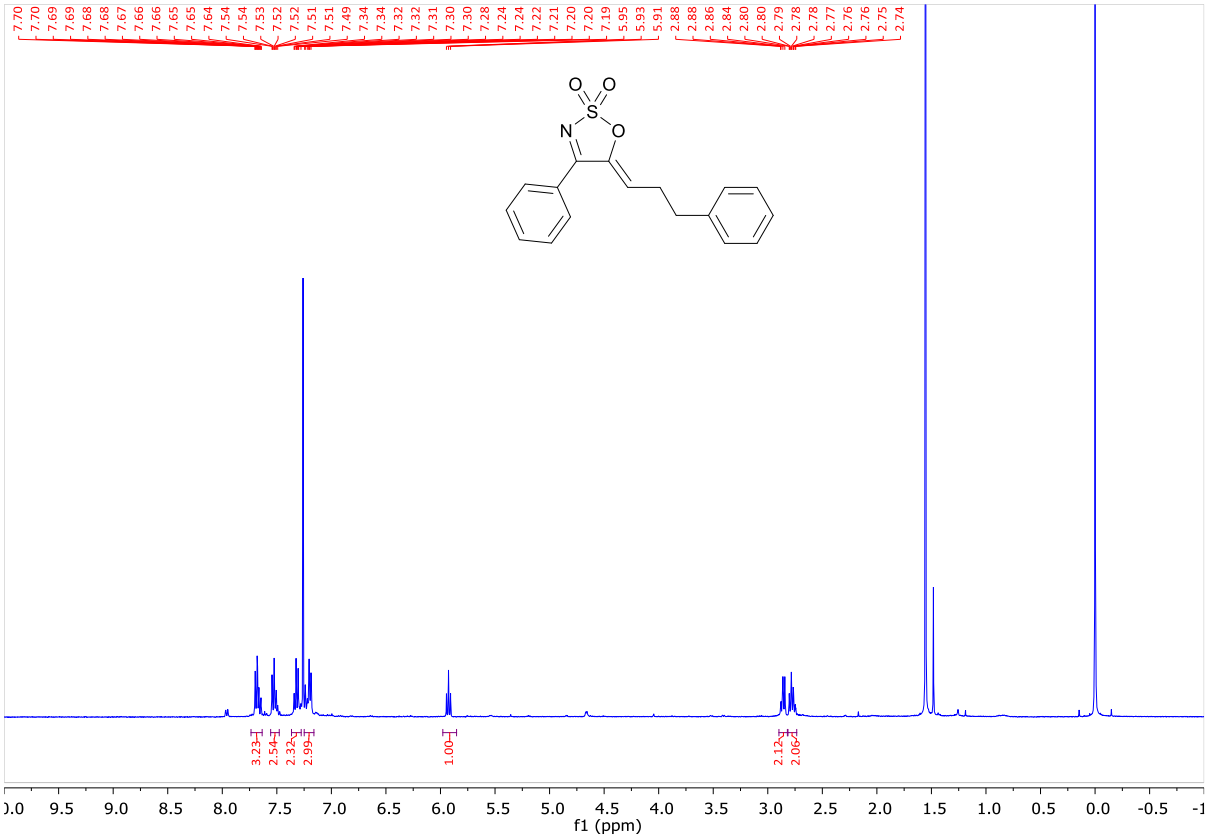


Figure S33. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of **2q.**

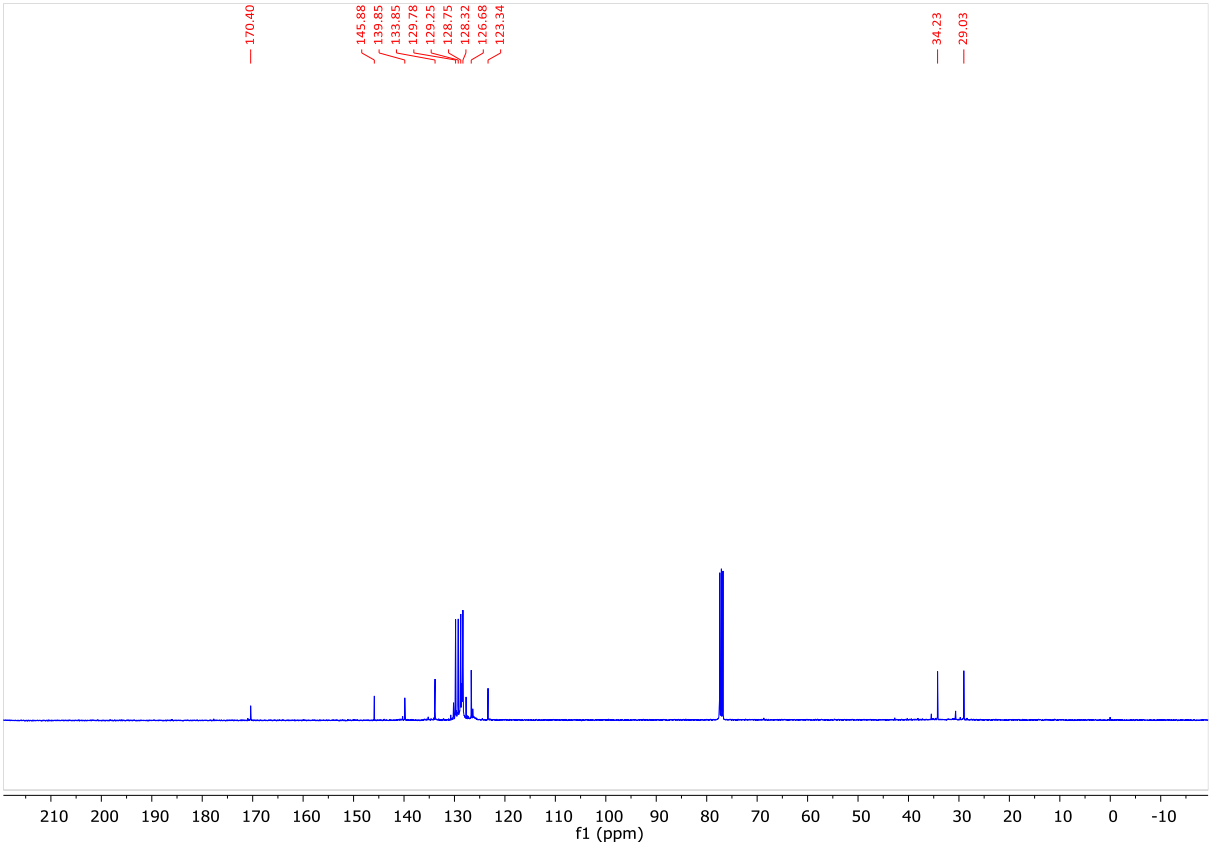


Figure S34. ^{13}C NMR spectrum ($CDCl_3$, 100 MHz) of **2q**.

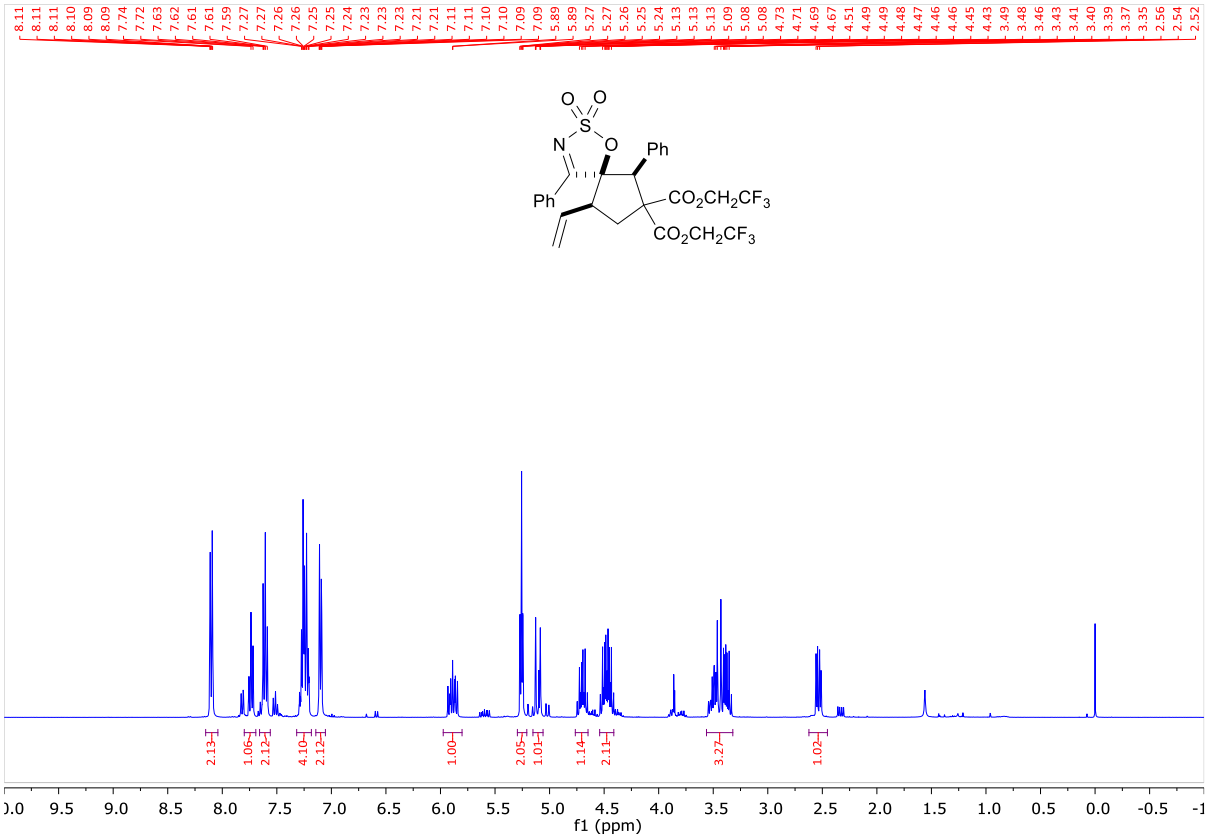


Figure S35. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of **3aa.**

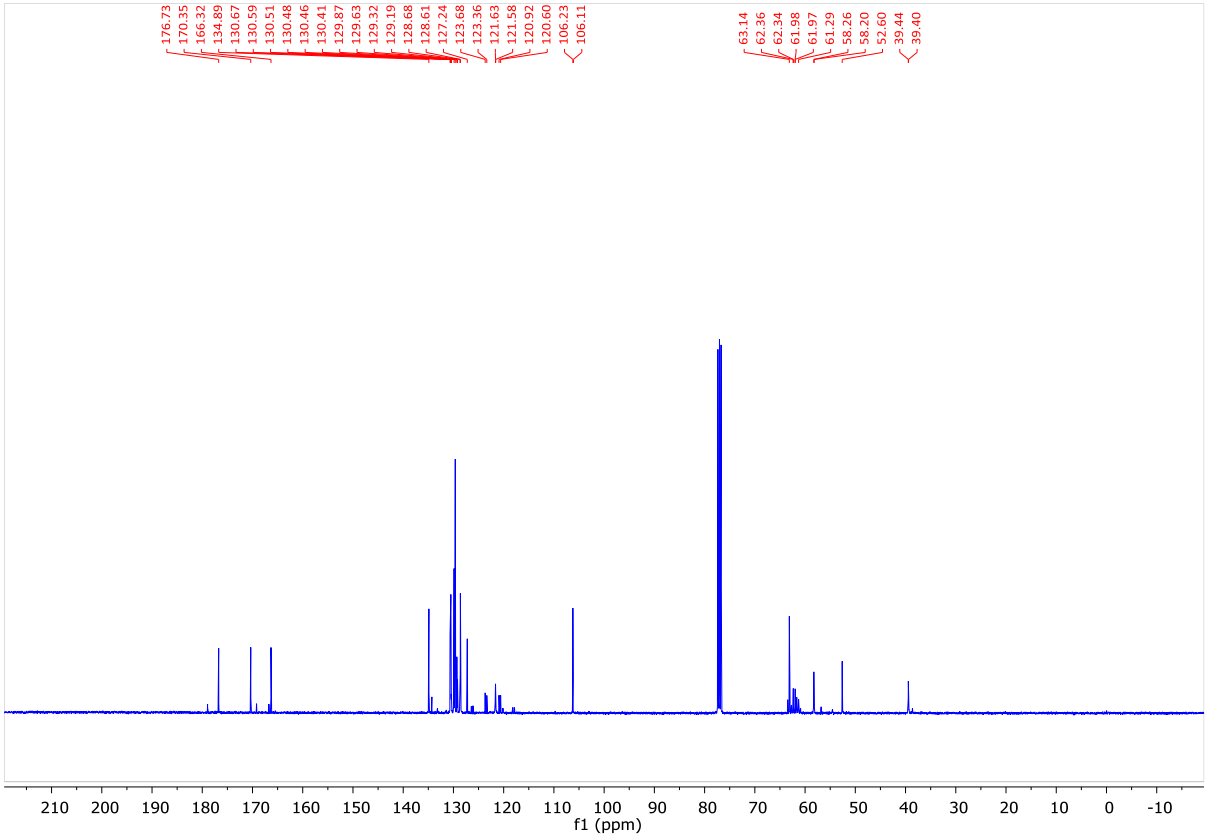


Figure S36. ^{13}C NMR spectrum ($CDCl_3$, 125 MHz) of **3aa**.

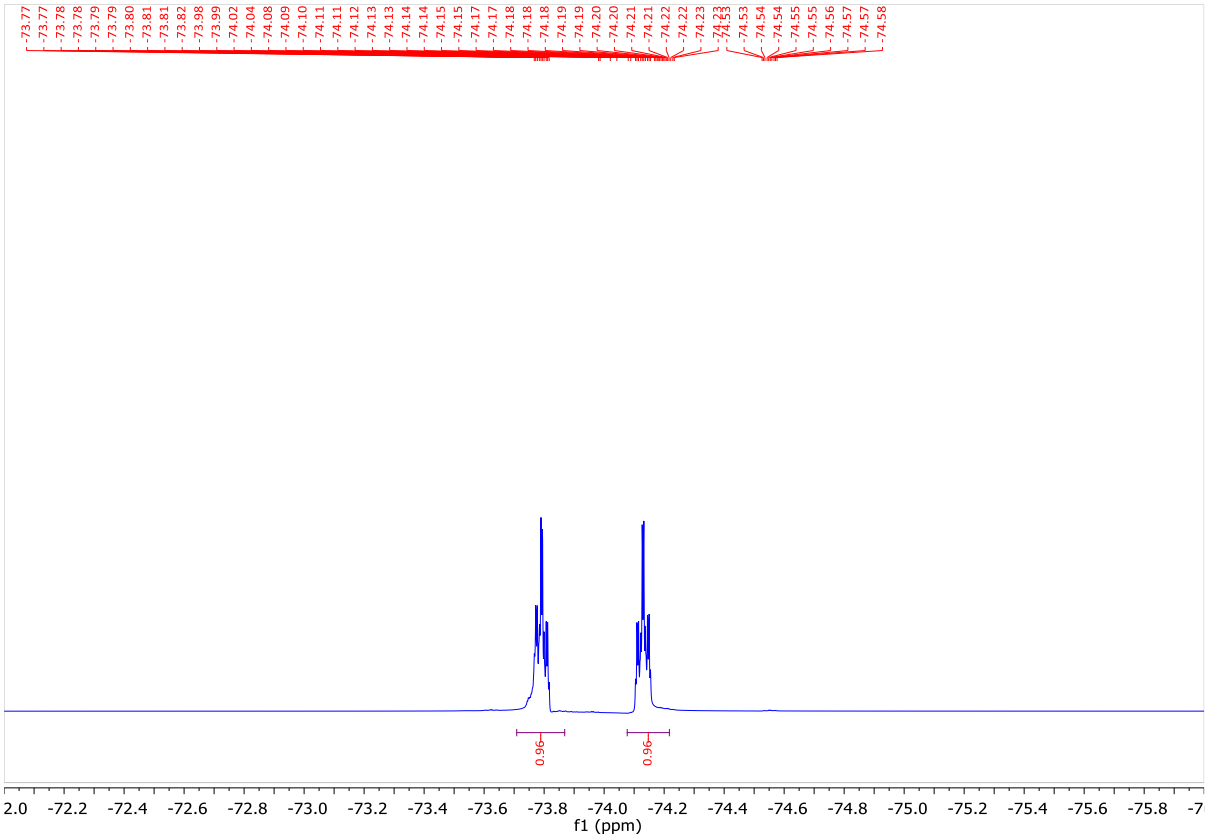


Figure S37. ^{19}F NMR spectrum ($CDCl_3$, 470 MHz) of **3aa.**

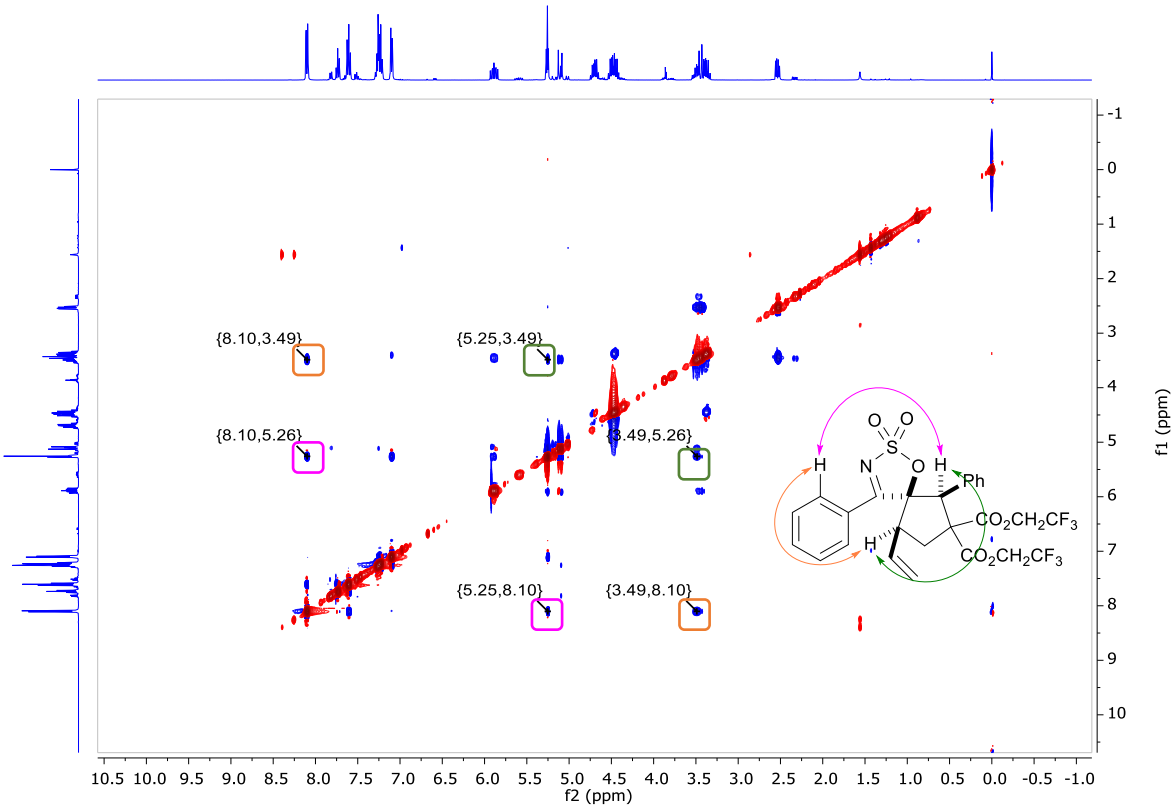


Figure S38. 2D NOESY spectrum ($CDCl_3$, 400 MHz) of **3aa.**

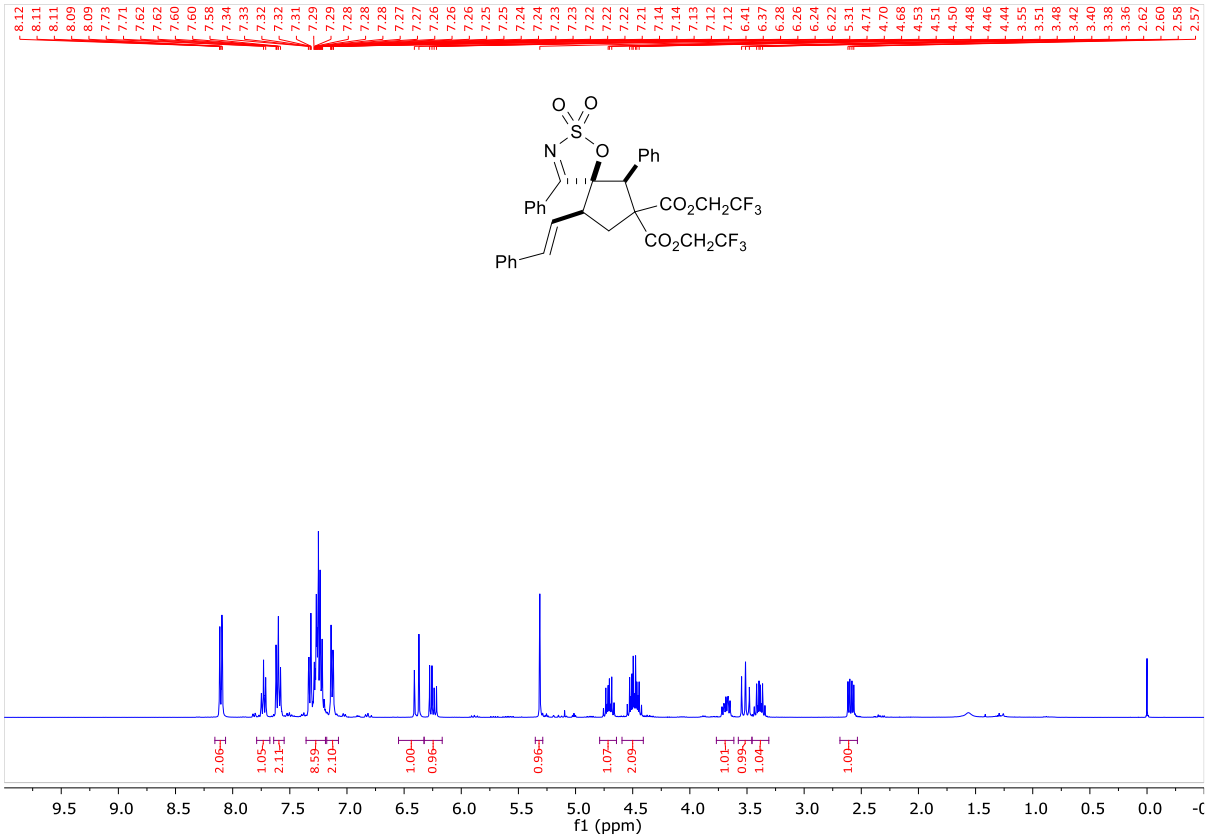


Figure S39. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of **3ba.**

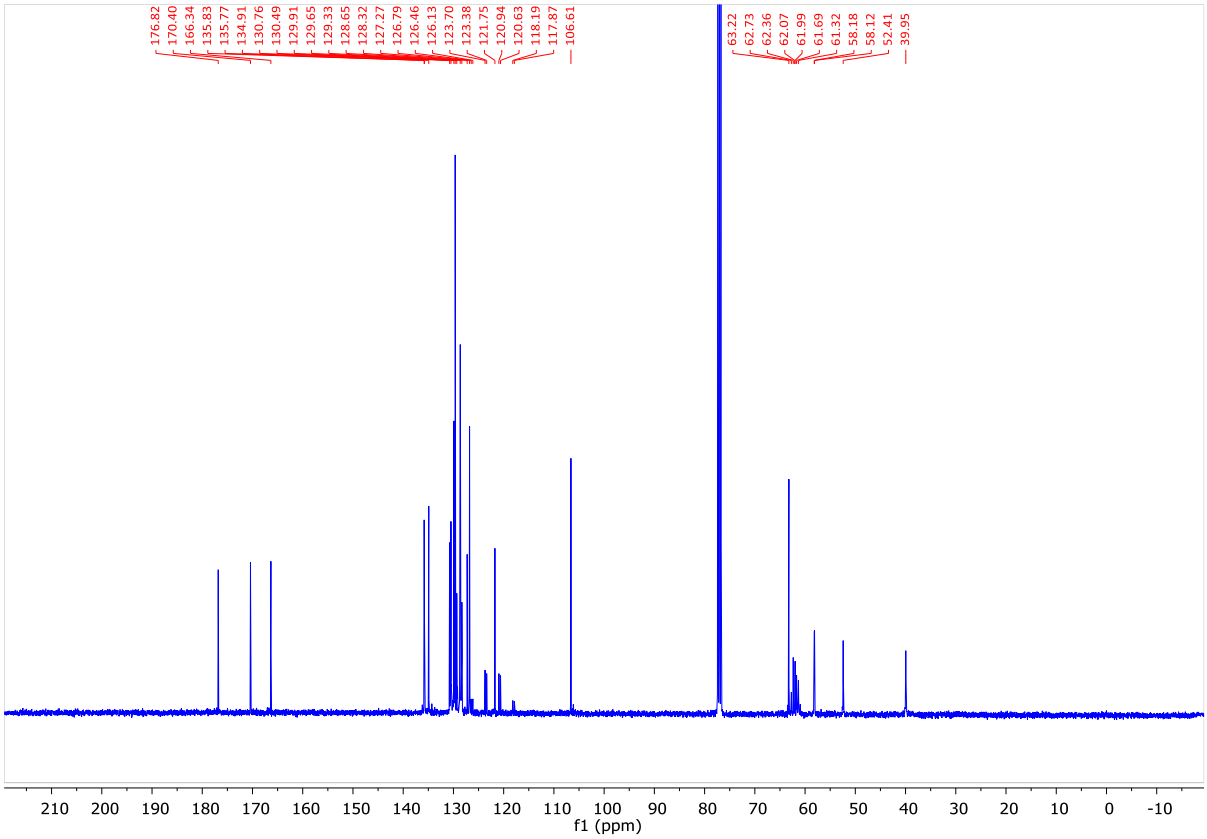


Figure S40. ^{13}C NMR spectrum ($CDCl_3$, 100 MHz) of **3ba**.

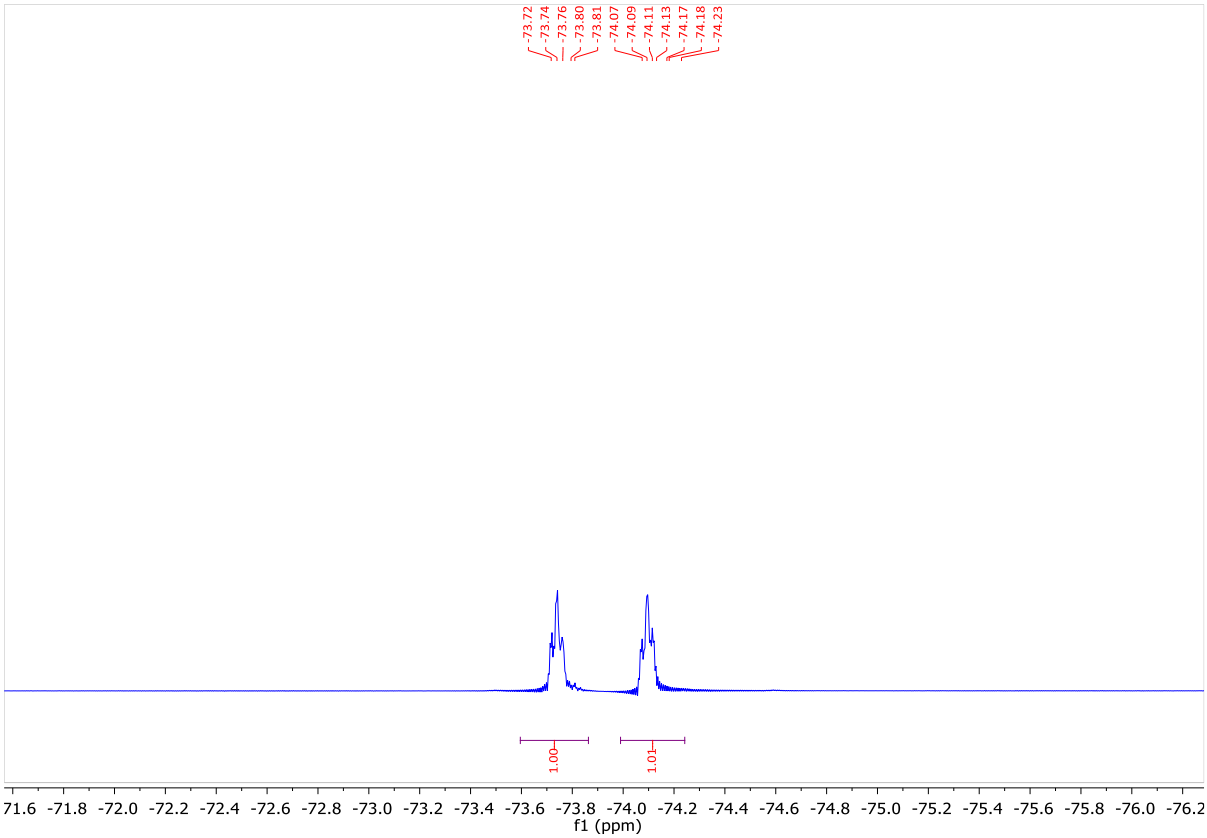


Figure S41. ^{19}F NMR spectrum ($CDCl_3$, 470 MHz) of **3ba.**

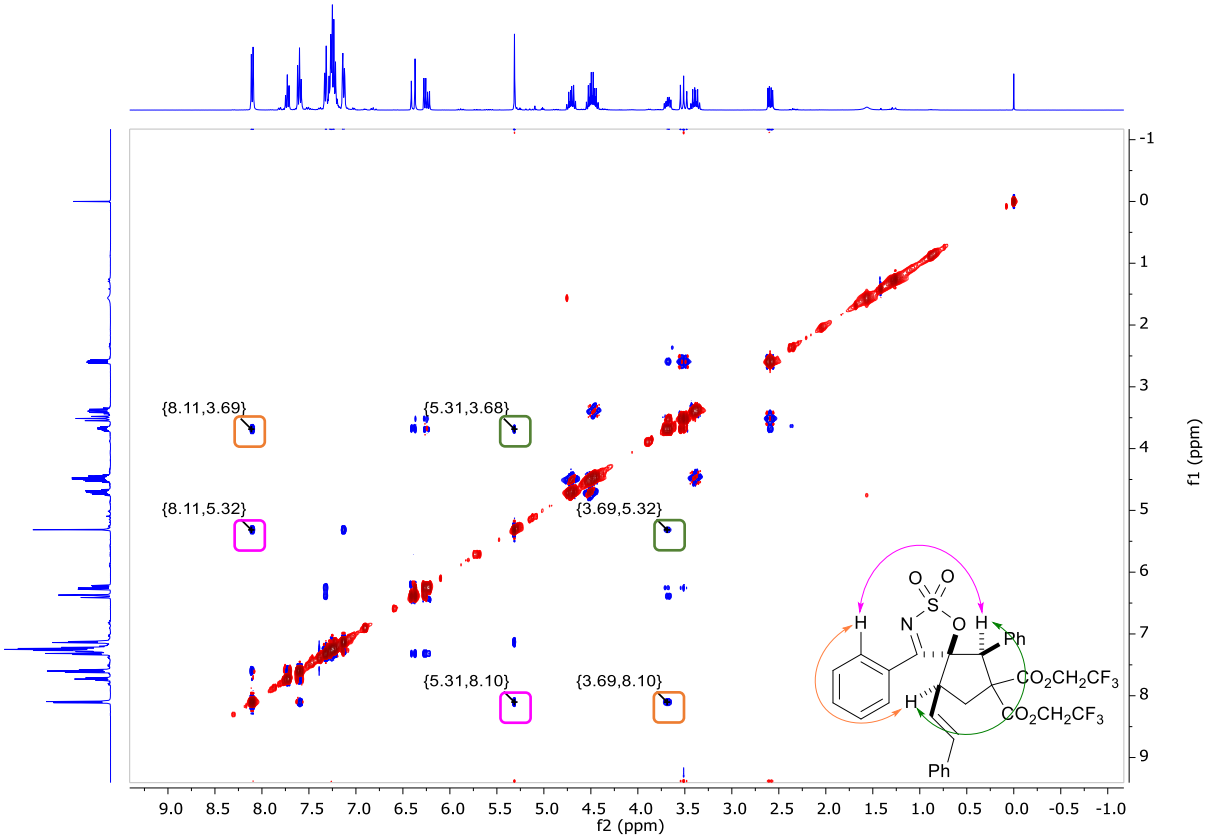


Figure S42. 2D NOESY spectrum ($CDCl_3$, 400 MHz) of **3ba.**

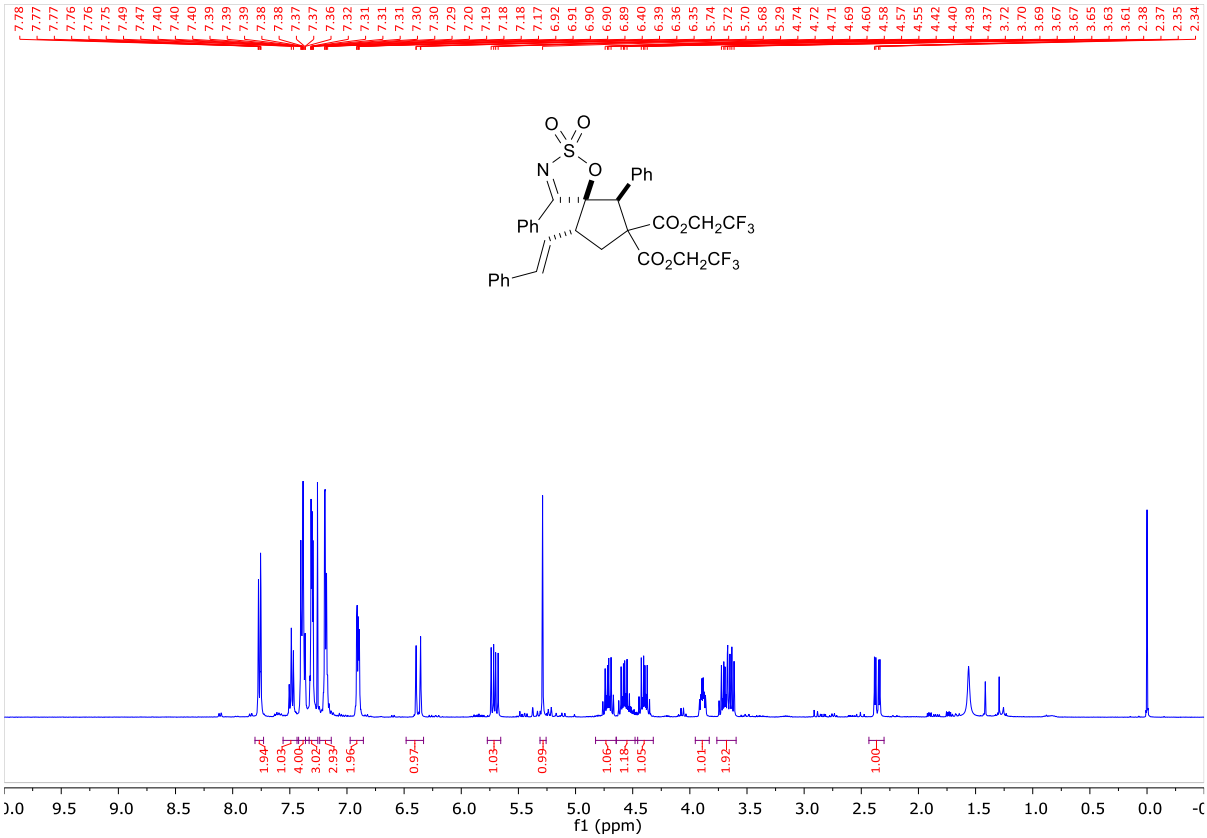


Figure S43. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of **3ba'**.

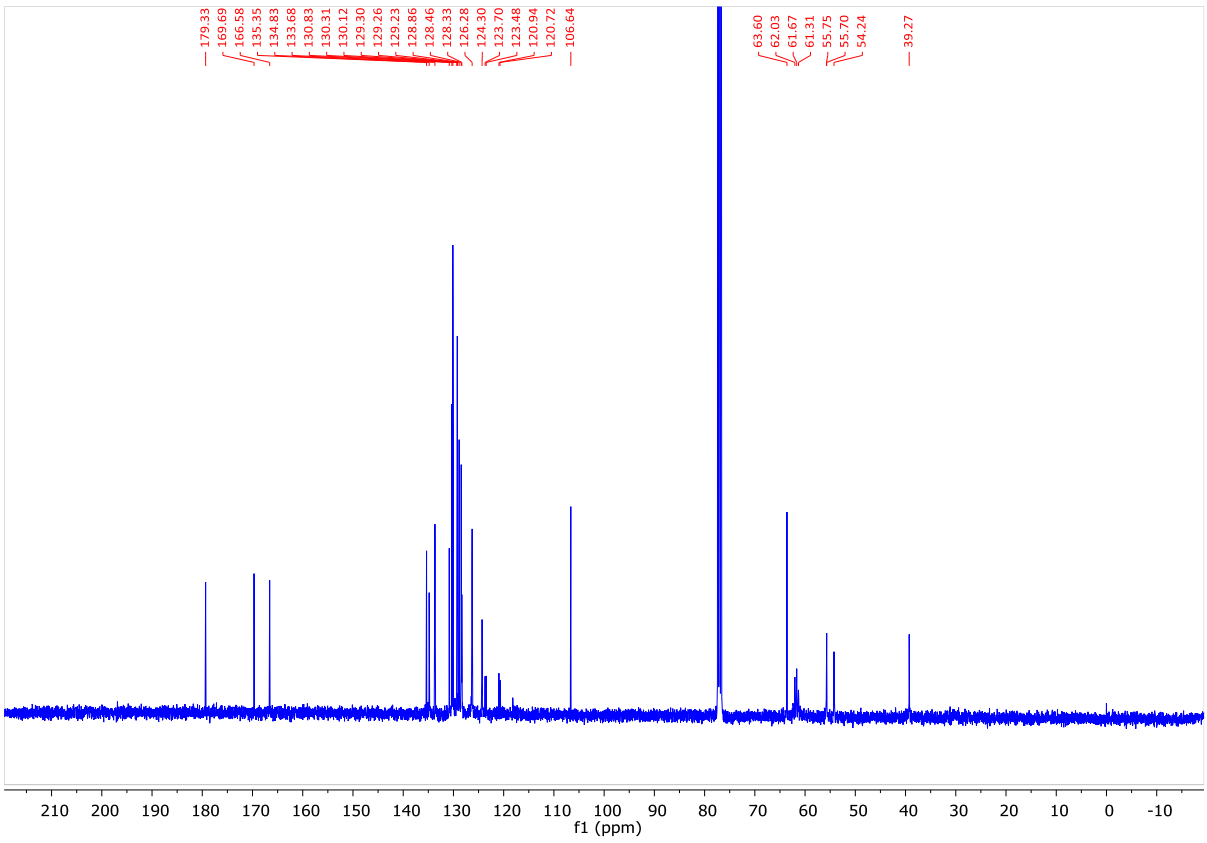


Figure S44. ^{13}C NMR spectrum ($CDCl_3$, 100 MHz) of **3ba'**.

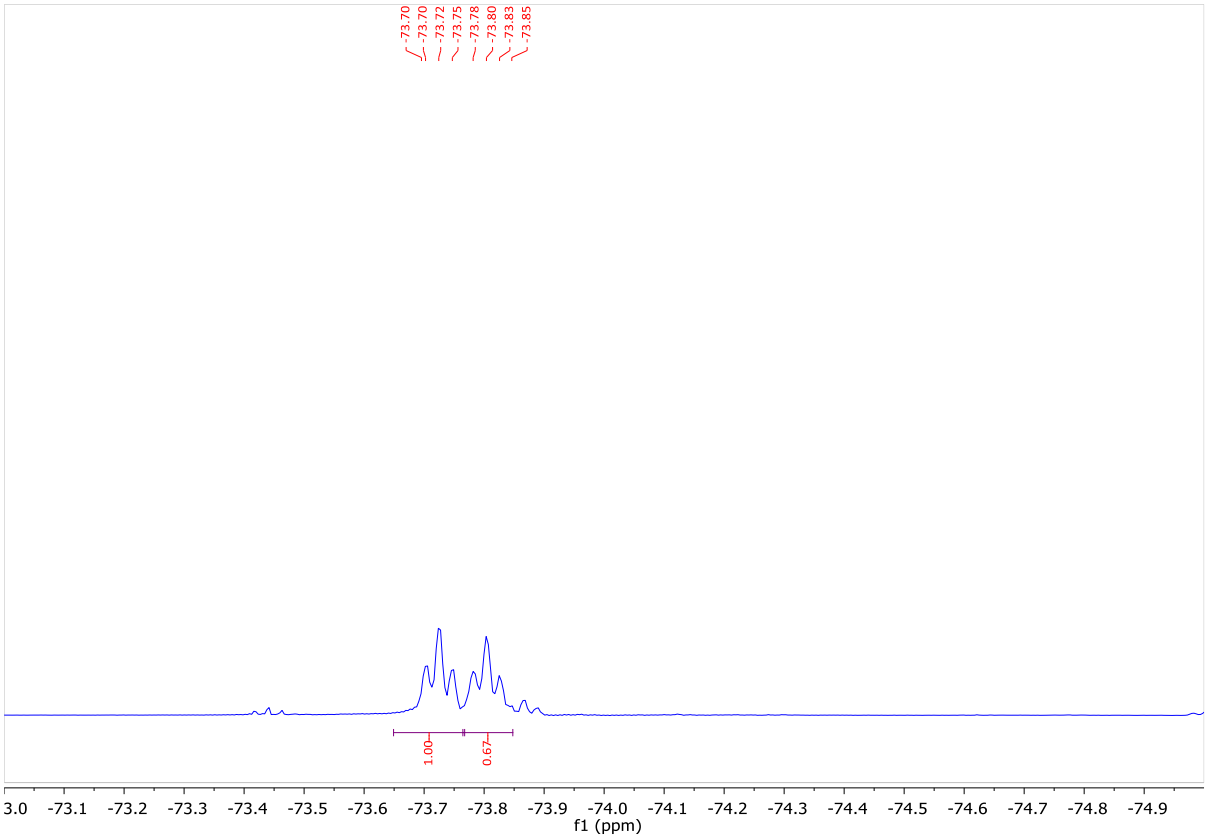


Figure S45. ^{19}F NMR spectrum ($CDCl_3$, 376 MHz) of **3ba'.**

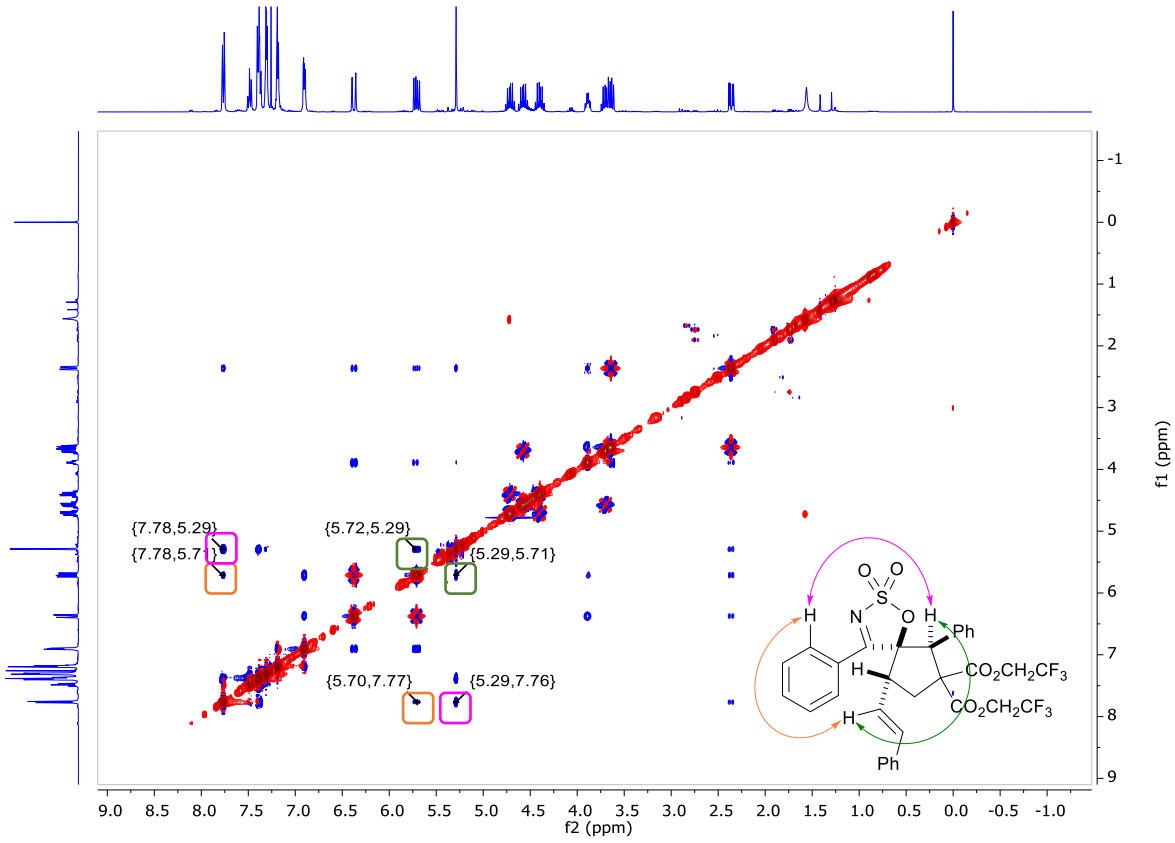


Figure S46. 2D NOESY spectrum ($CDCl_3$, 400 MHz) of **3ba'.**

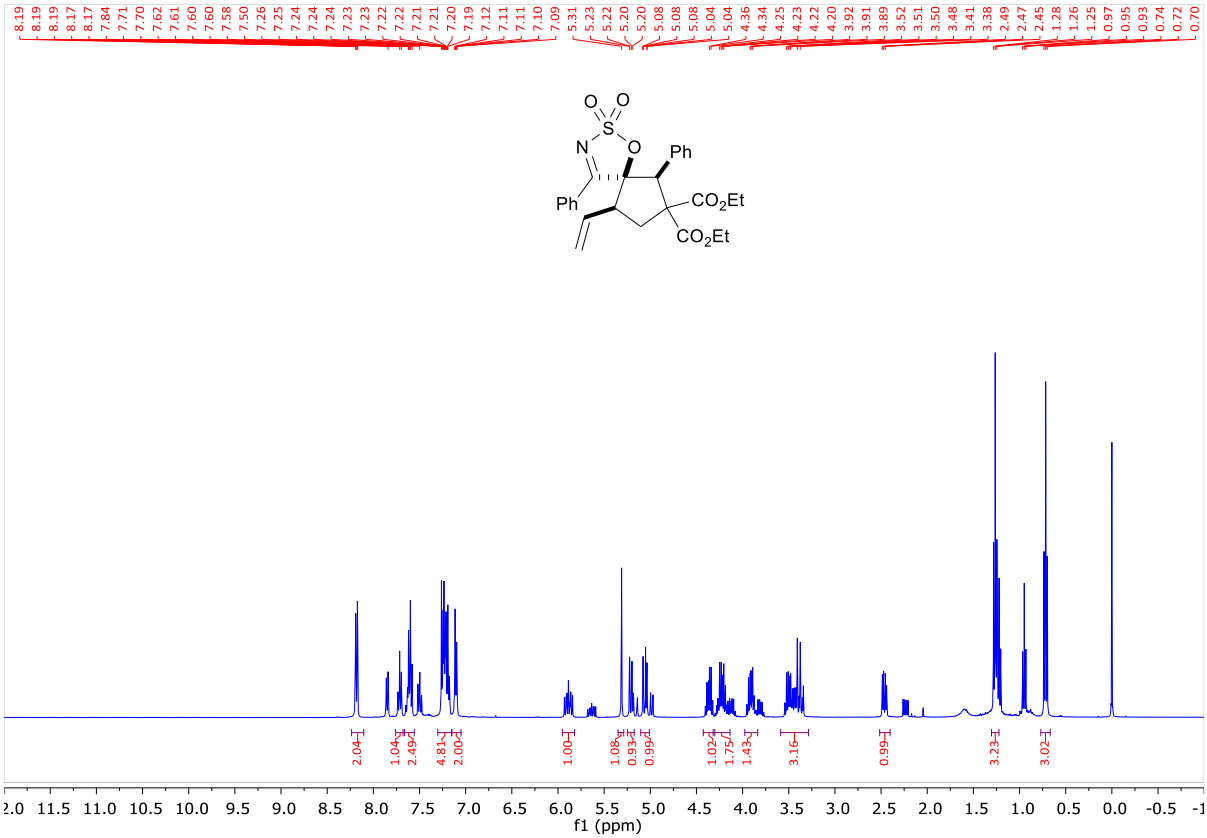


Figure S47. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of **3ca**.

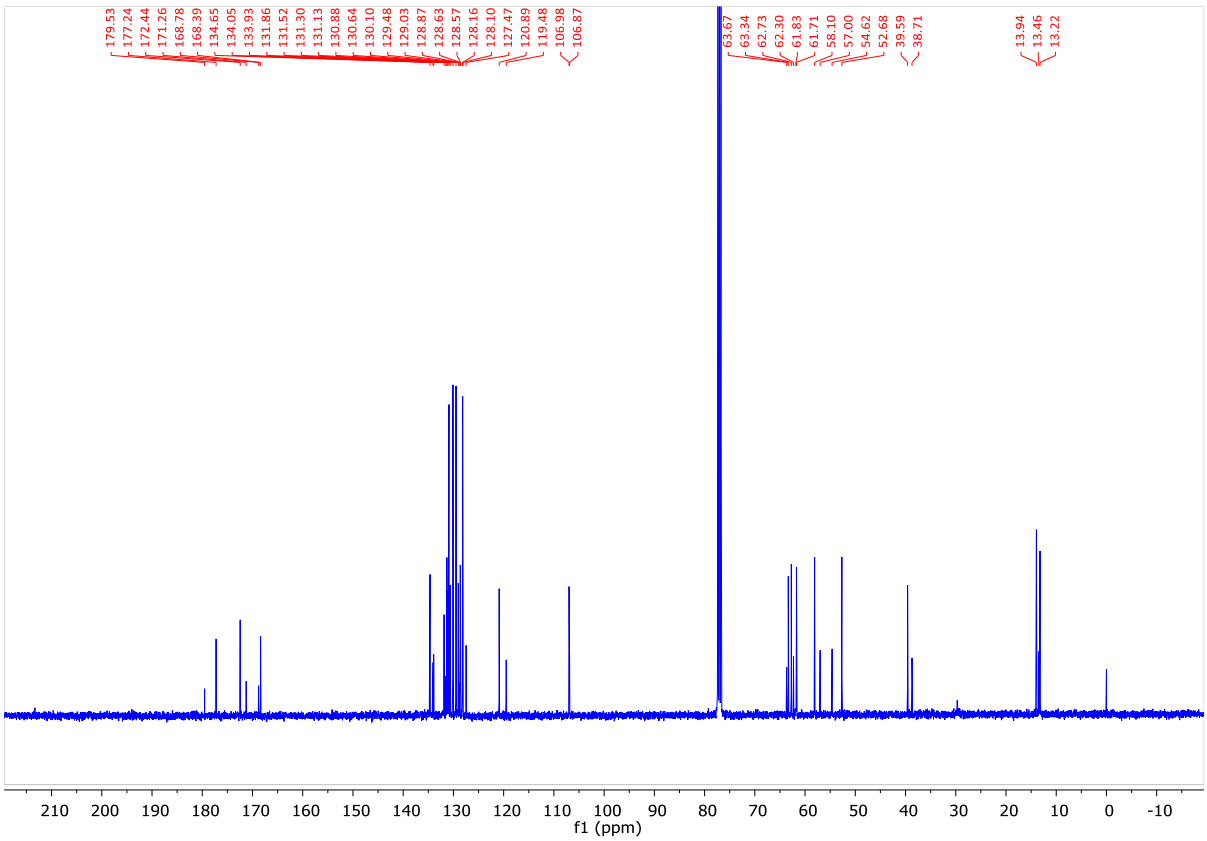


Figure S48. ^{13}C NMR spectrum ($CDCl_3$, 100 MHz) of **3ca**.

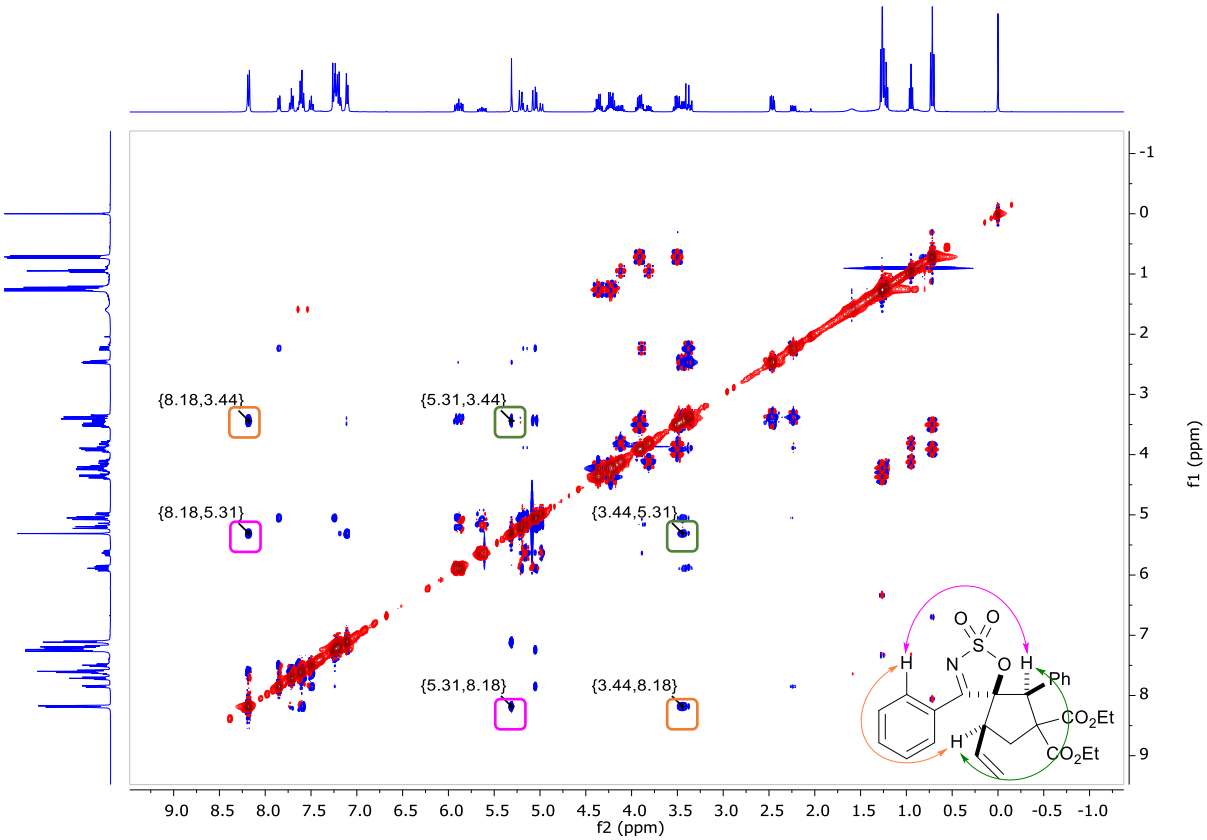


Figure S49. 2D NOESY spectrum ($CDCl_3$, 400 MHz) of **3ca.**

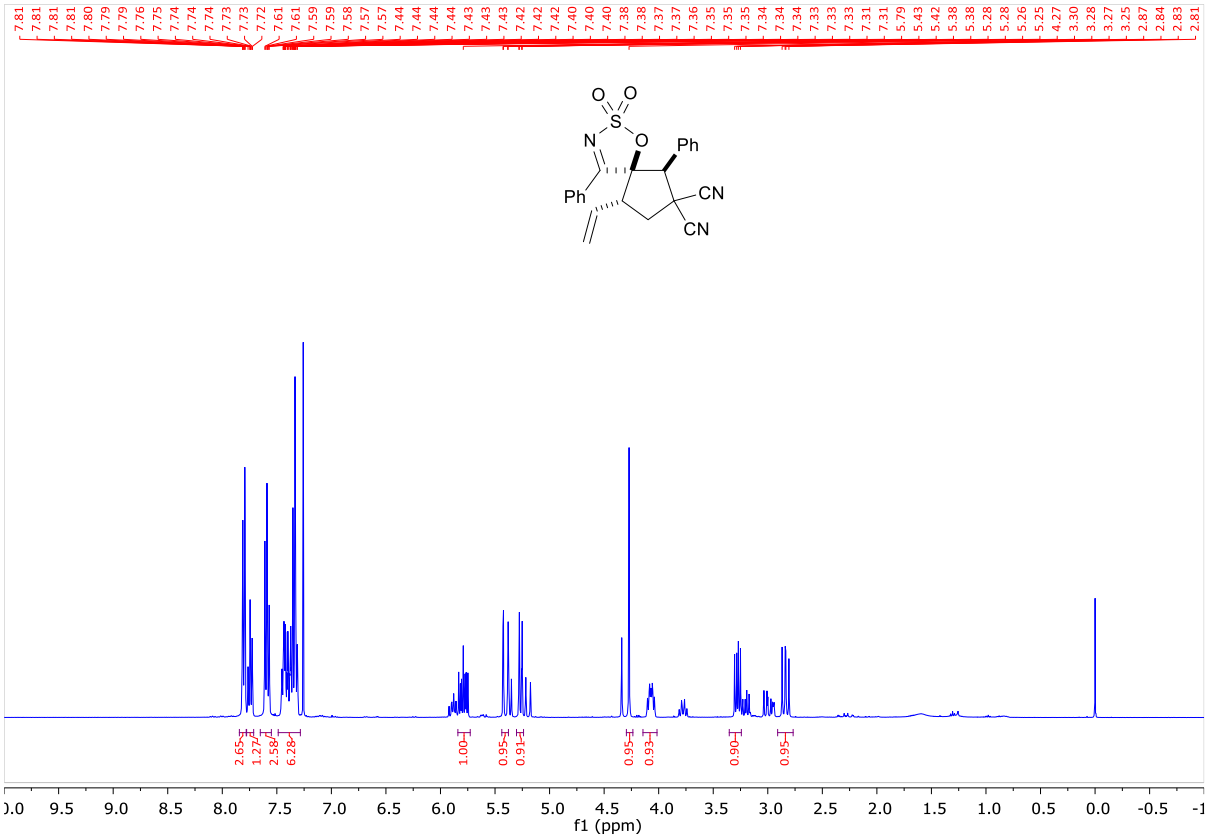


Figure S50. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of **3da'**.

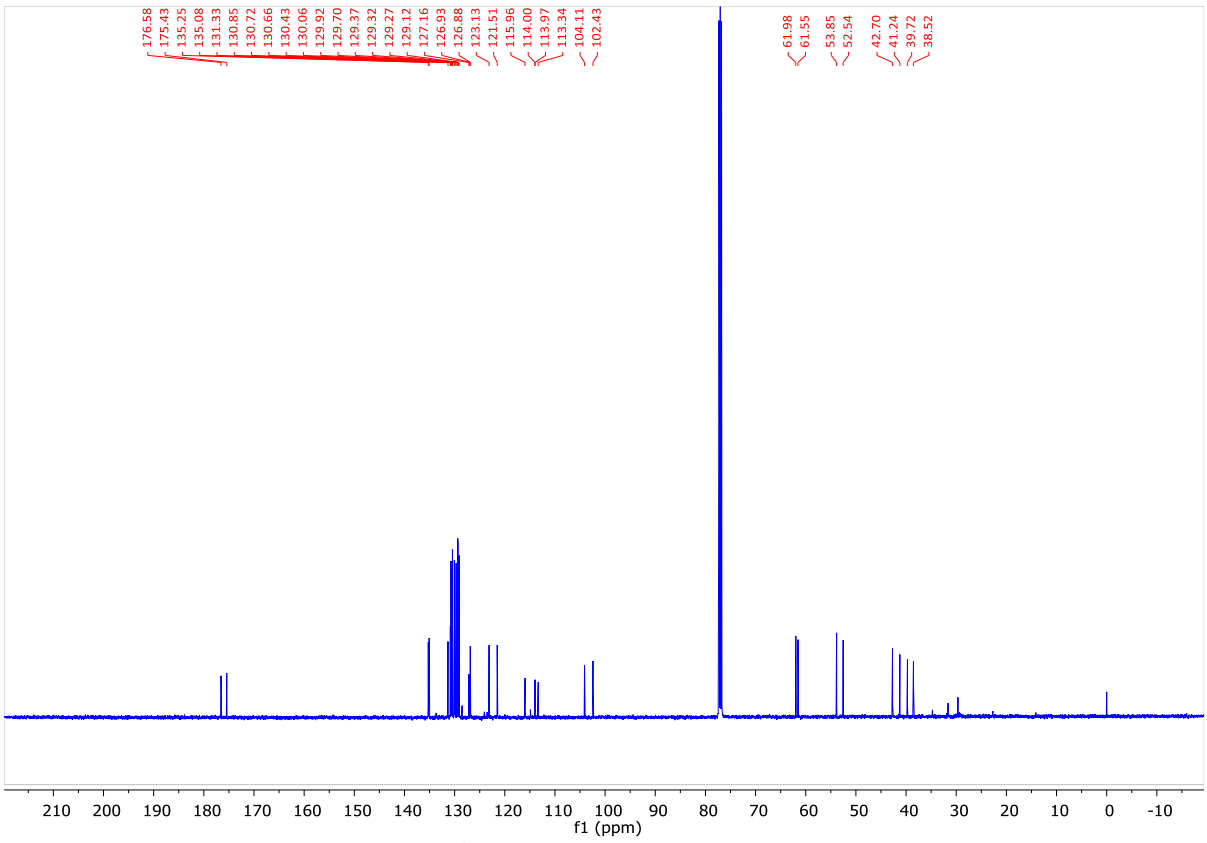


Figure S51. ^{13}C NMR spectrum ($CDCl_3$, 100 MHz) of **3da'**.

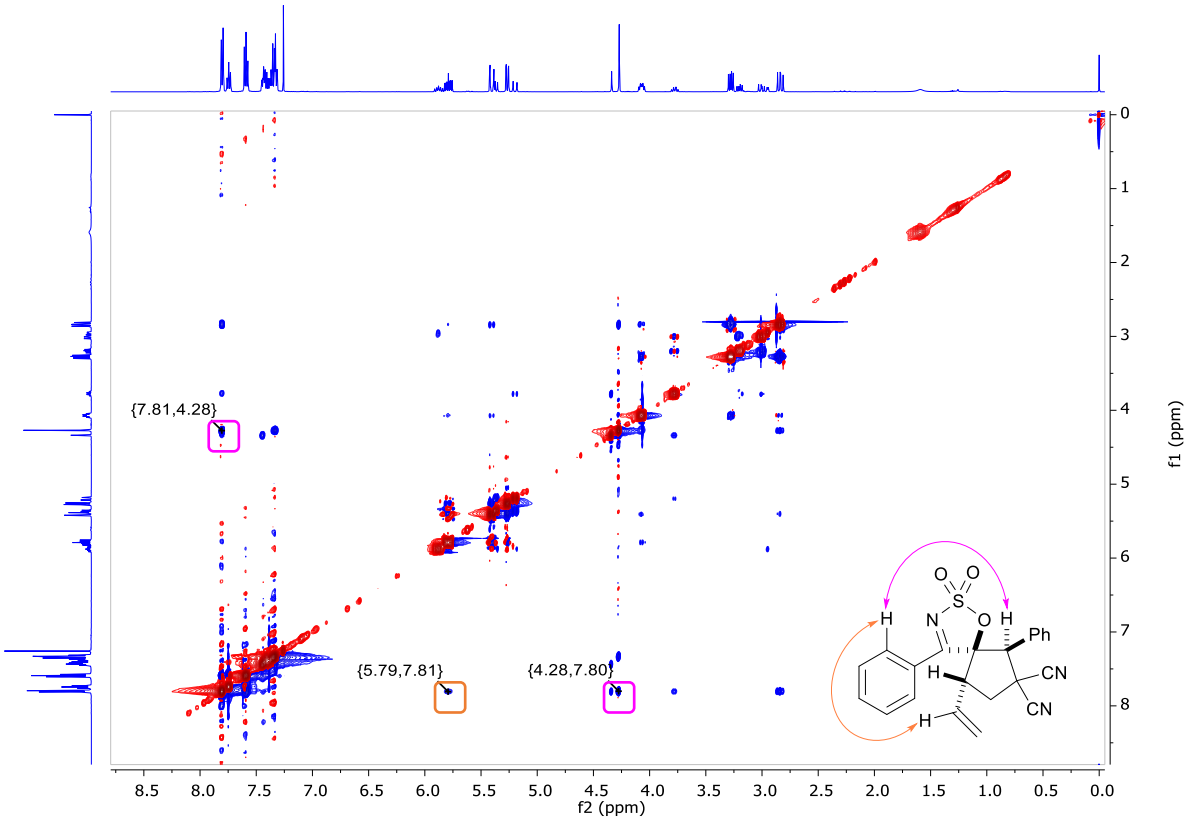


Figure S52. 2D NOESY spectrum ($CDCl_3$, 500 MHz) of **3da'.**

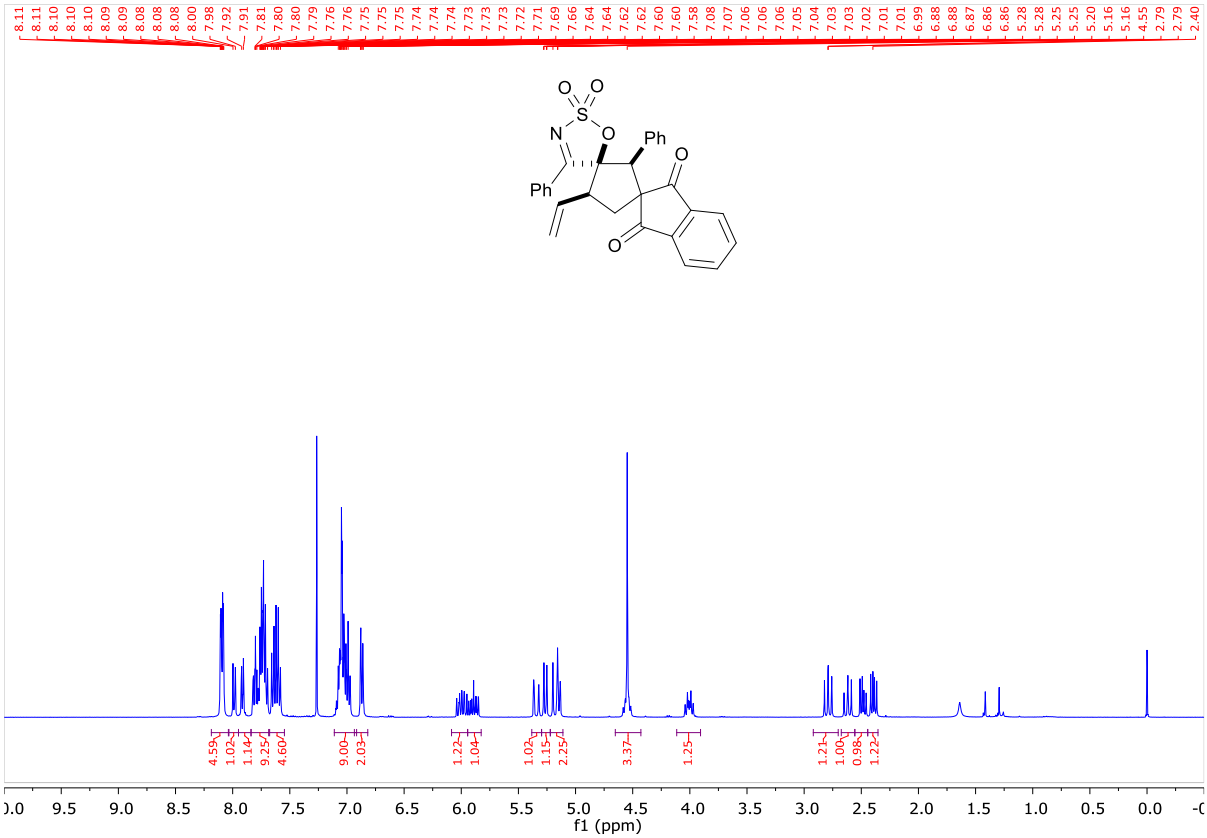


Figure S53. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of **3ea**.

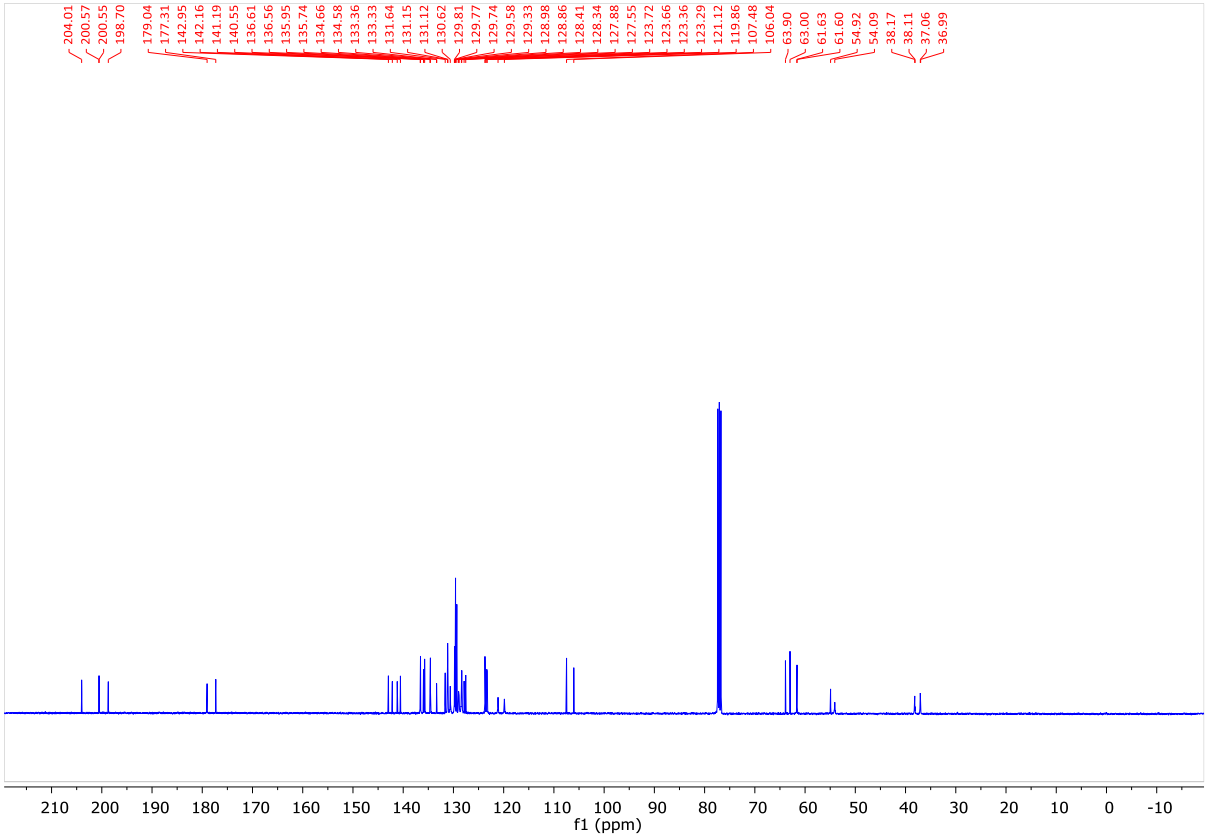


Figure S54. ^{13}C NMR spectrum ($CDCl_3$, 100 MHz) of **3ea**.

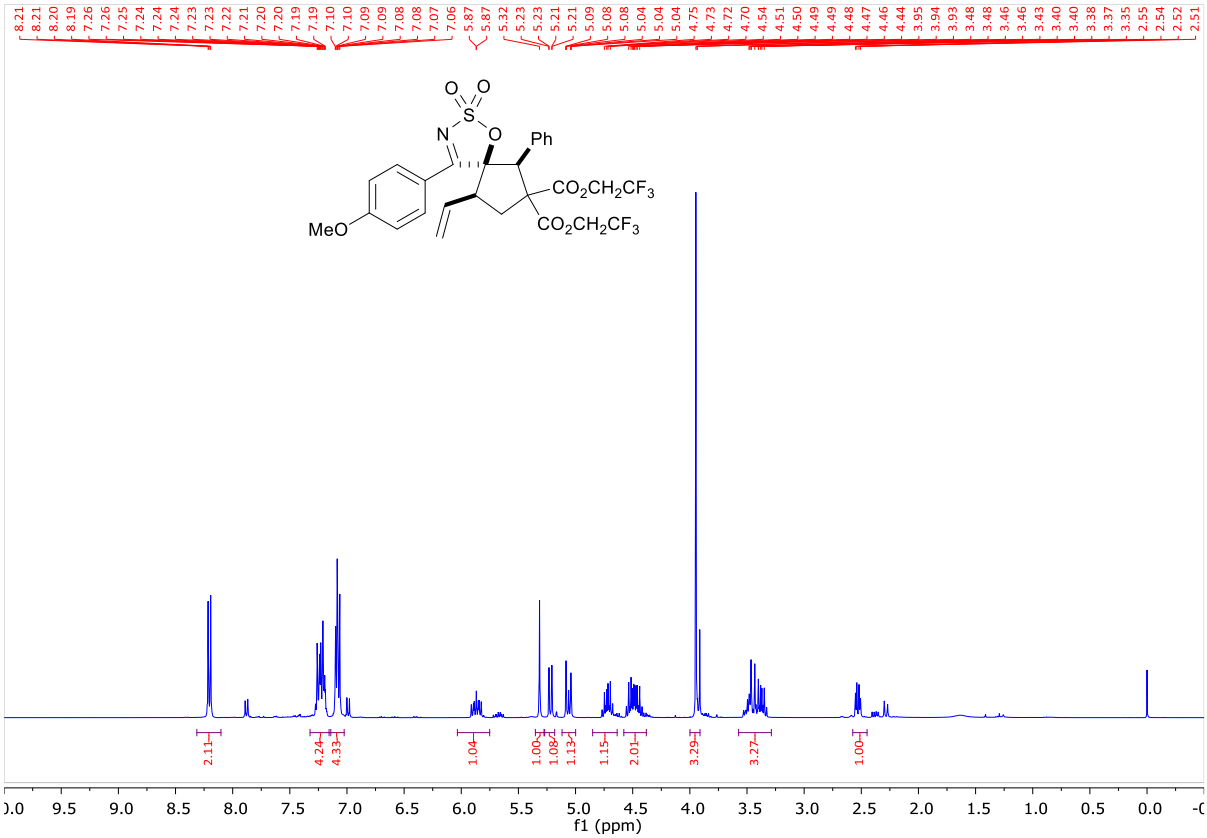


Figure S55. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of **3ab**.

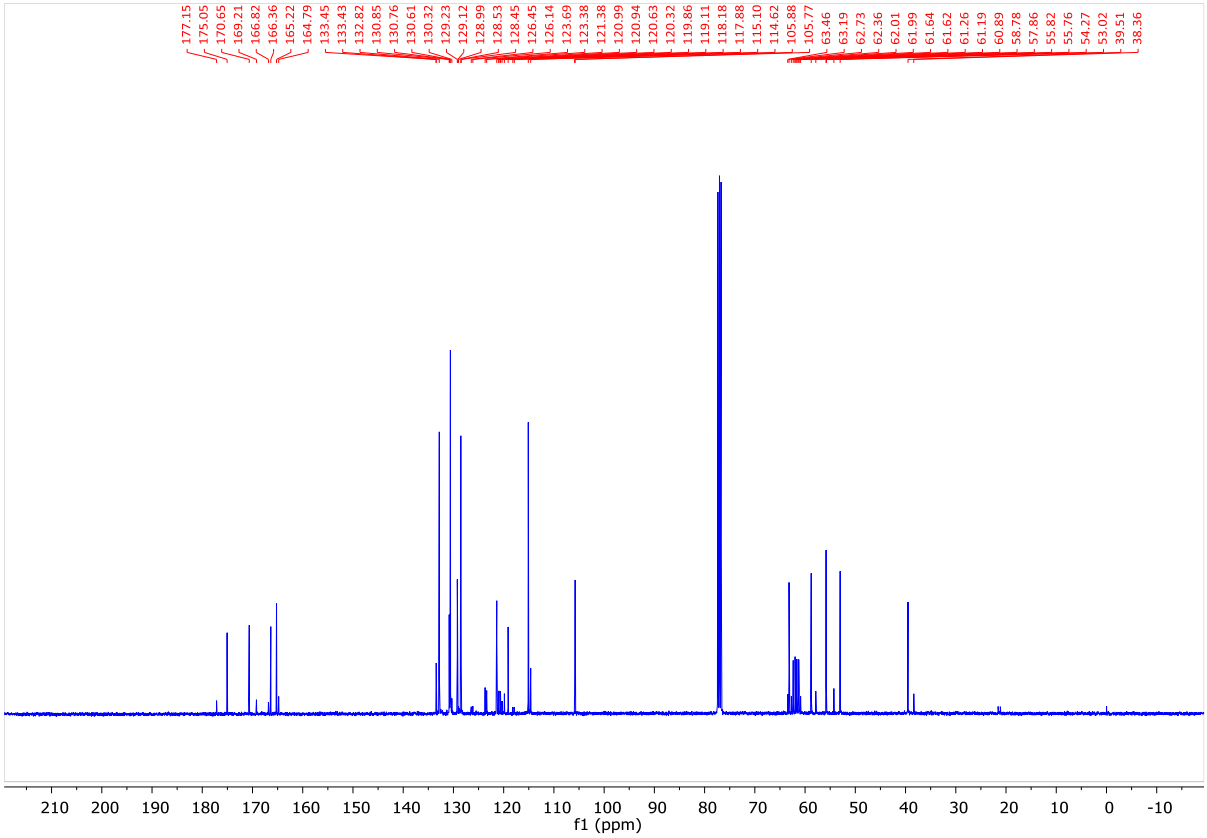


Figure S56. ^{13}C NMR spectrum ($CDCl_3$, 100 MHz) of **3ab**.

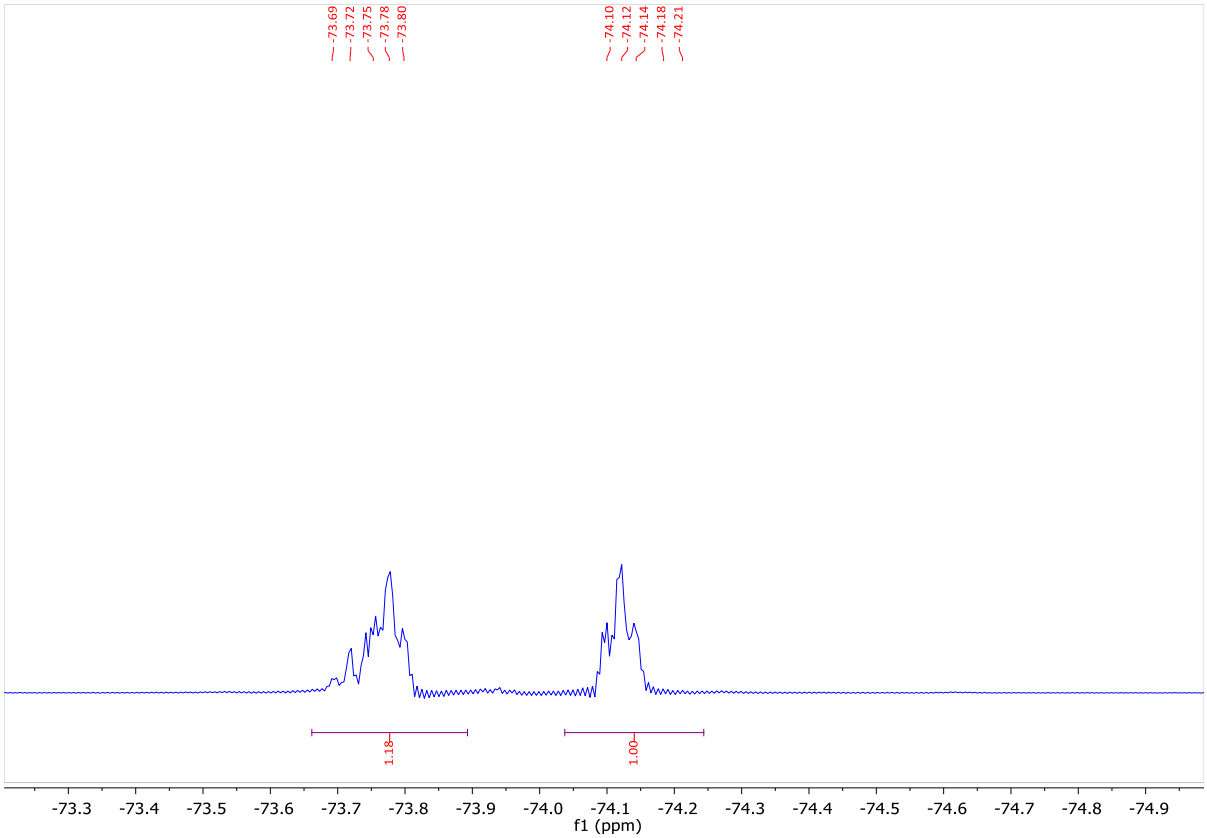


Figure S57. ^{19}F NMR spectrum ($CDCl_3$, 376 MHz) of **3ab.**

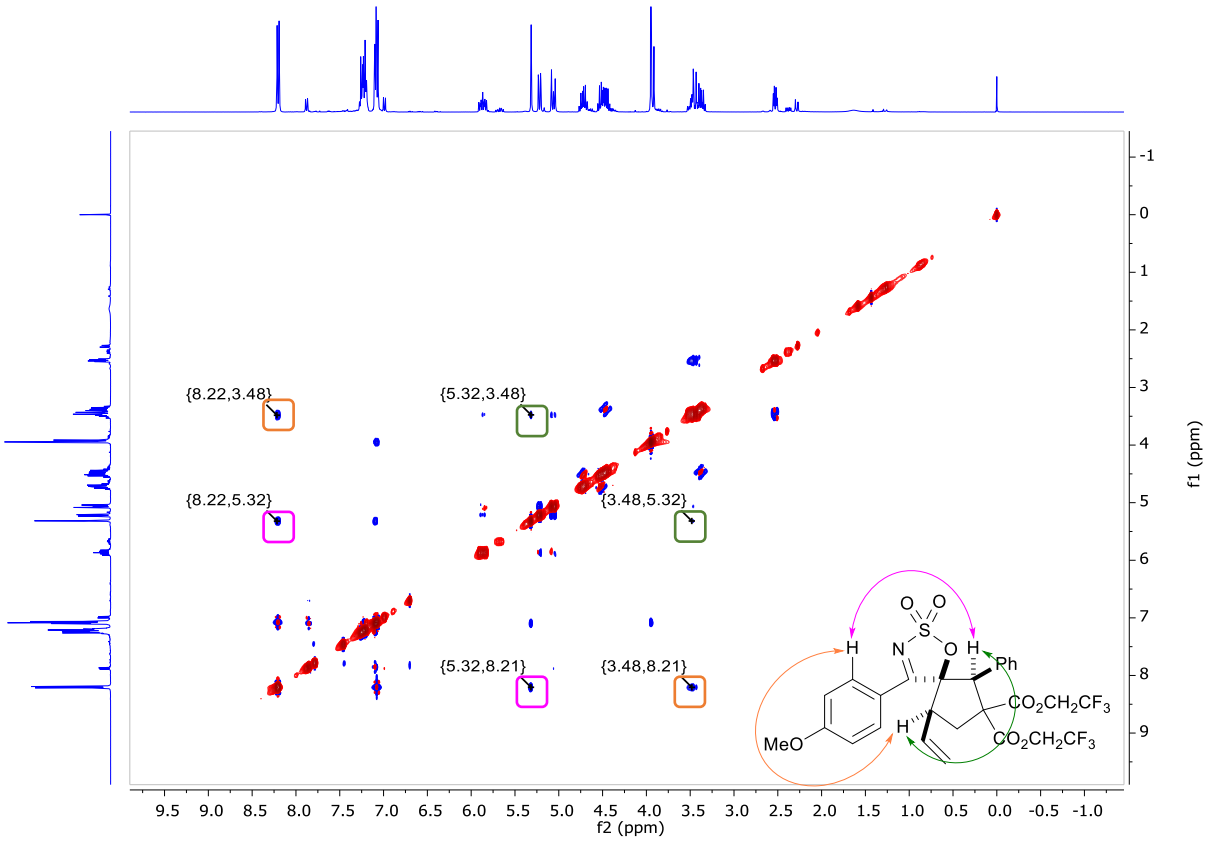


Figure S58. 2D NOESY spectrum ($CDCl_3$, 400 MHz) of **3ab.**

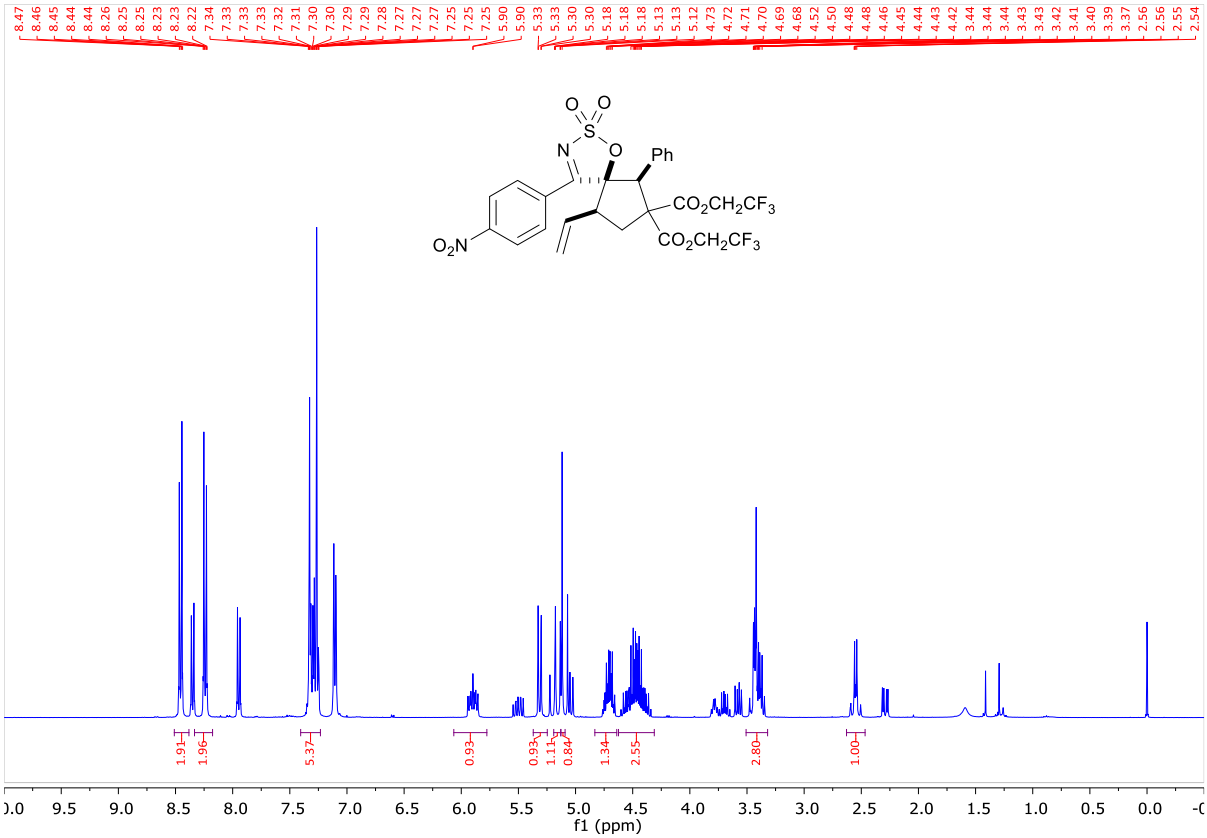


Figure S59. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of **3ac**.

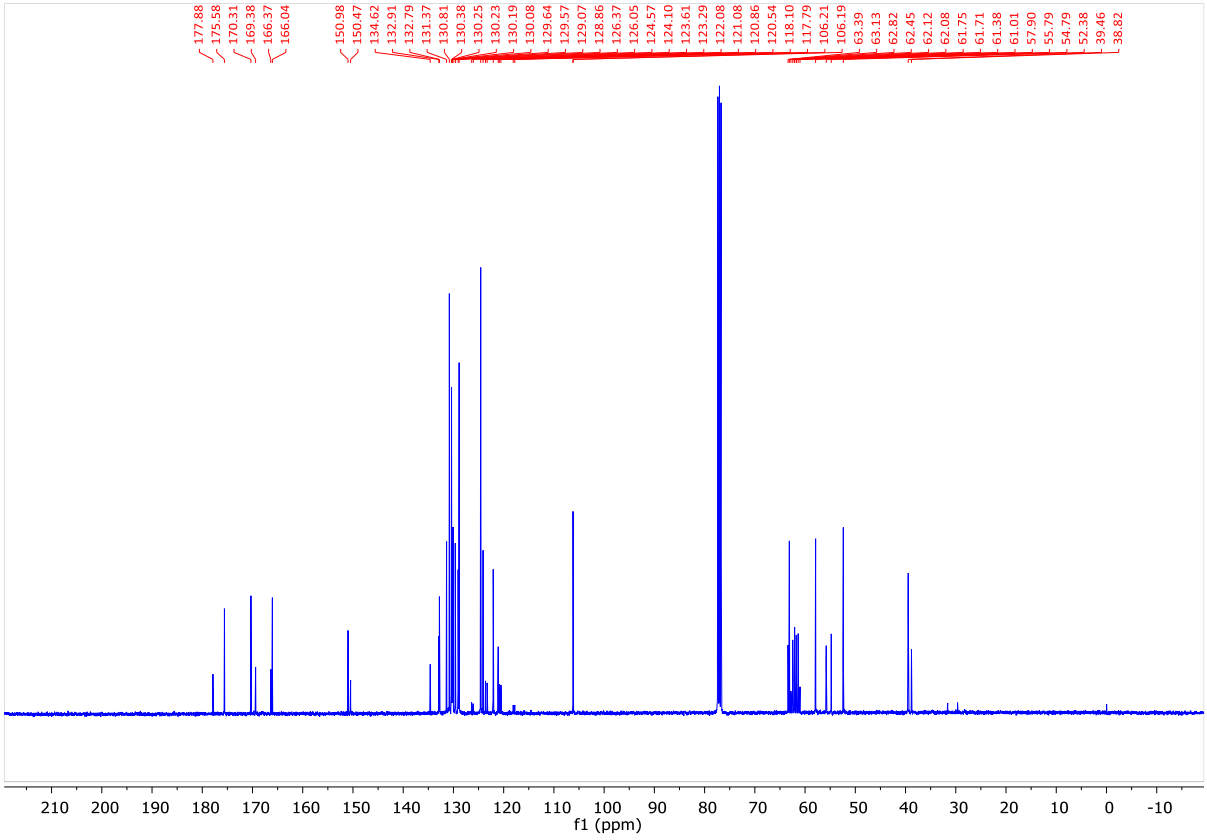


Figure S60. ^{13}C NMR spectrum ($CDCl_3$, 100 MHz) of **3ac**.

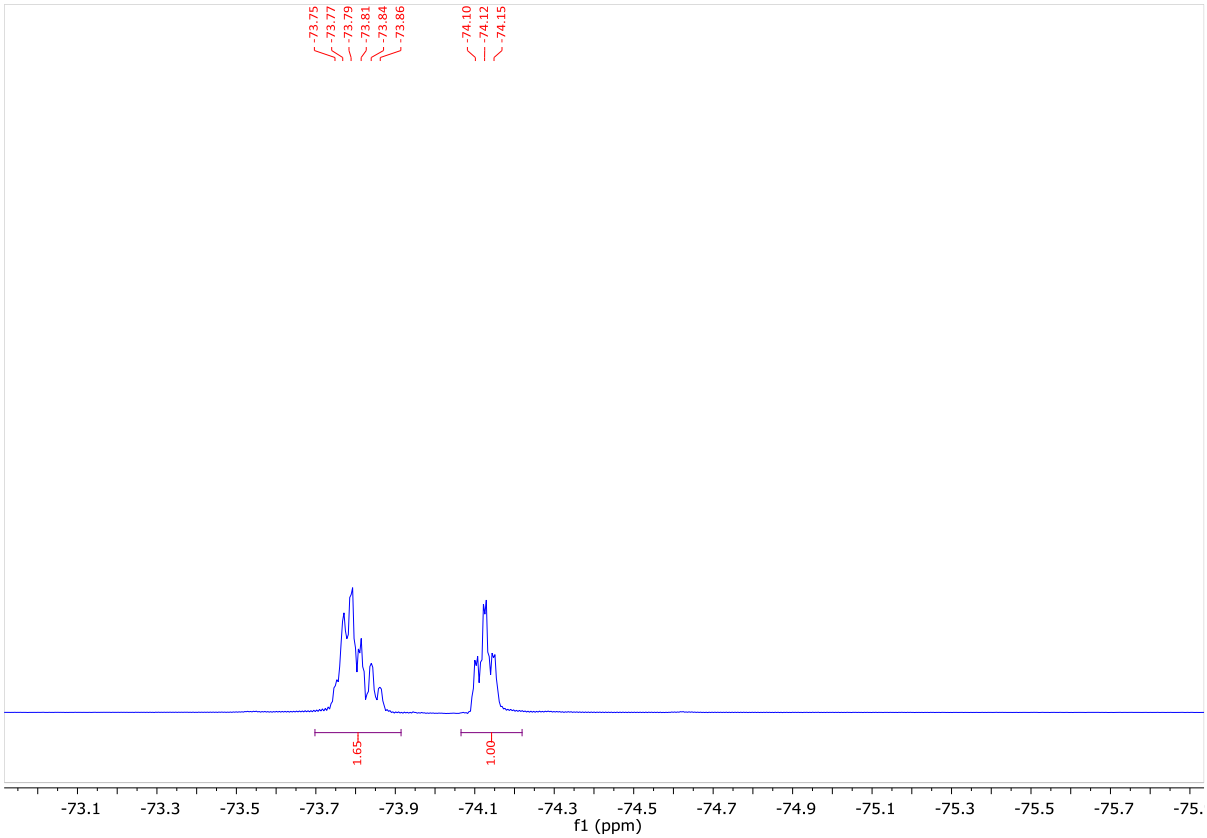


Figure S61. ^{19}F NMR spectrum ($CDCl_3$, 376 MHz) of **3ac.**

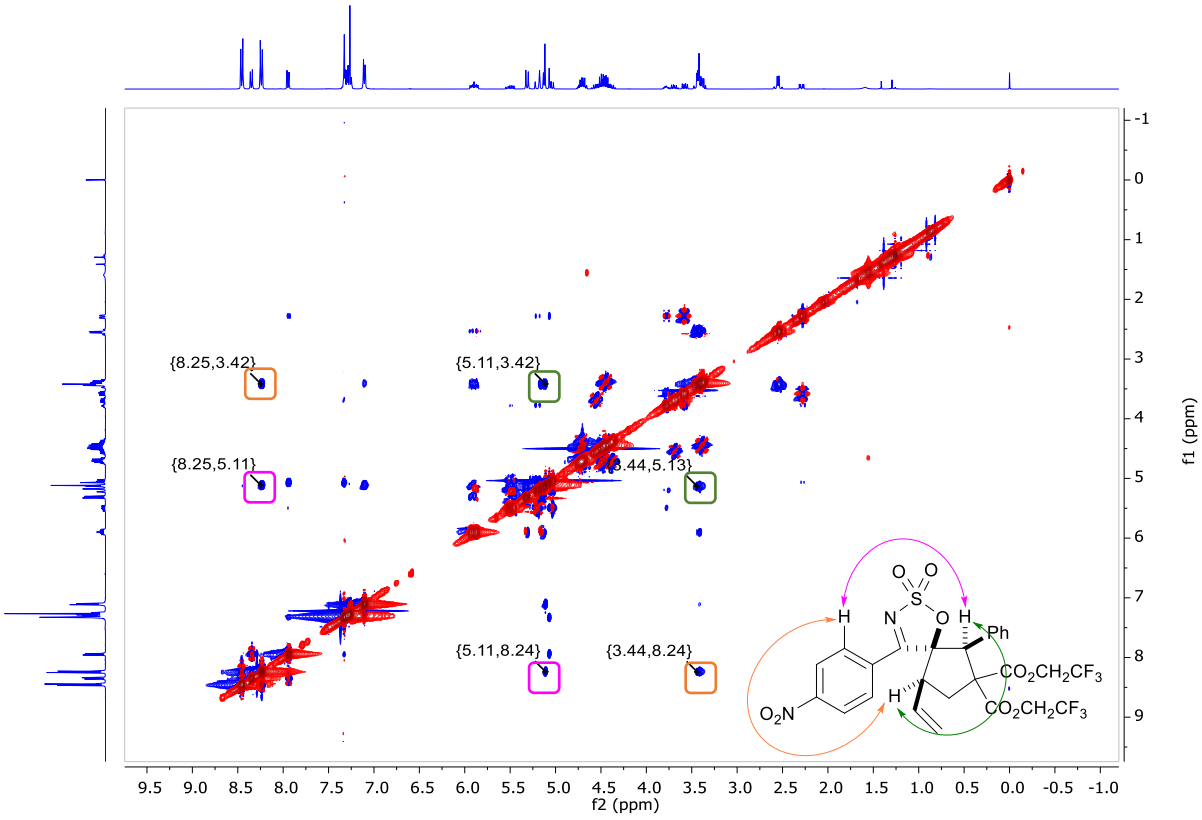


Figure S62. 2D NOESY spectrum ($CDCl_3$, 400 MHz) of **3ac.**

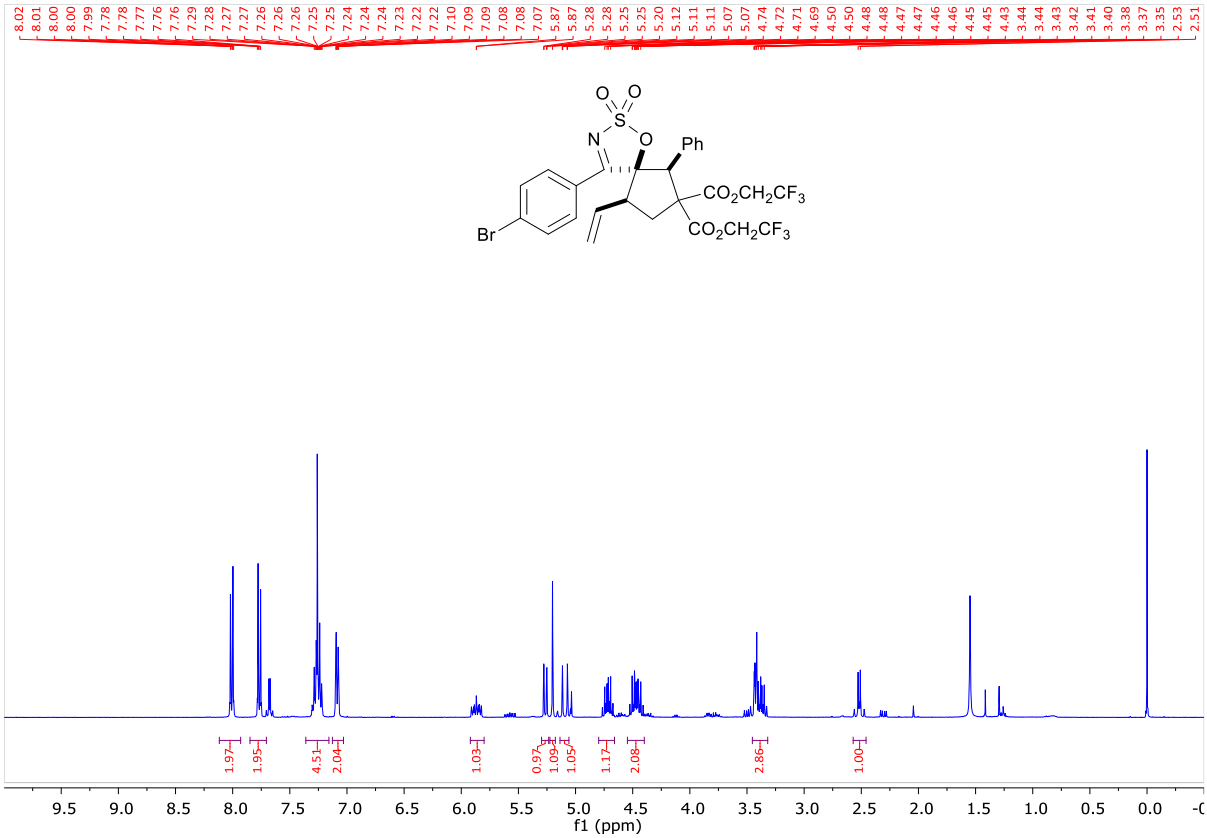


Figure S63. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of **3ad**.

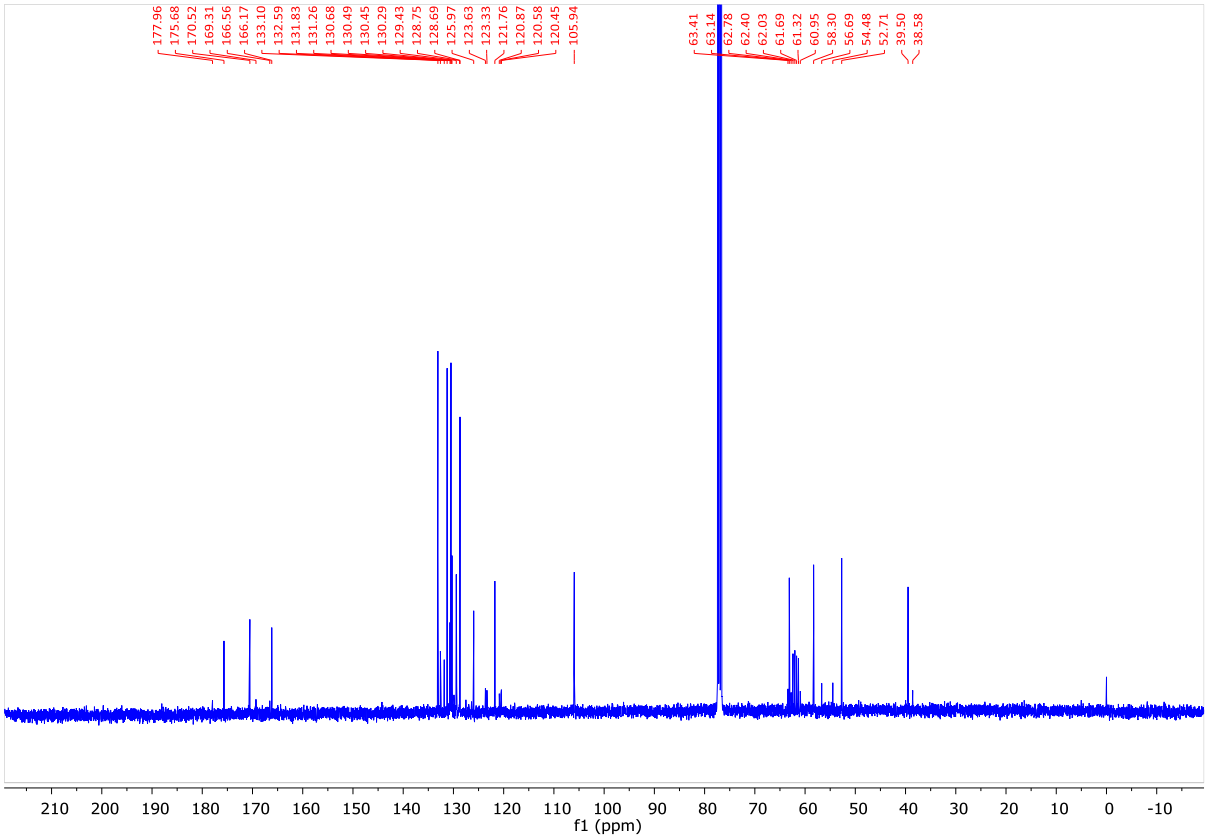


Figure S64. ^{13}C NMR spectrum ($CDCl_3$, 100 MHz) of **3ad**.

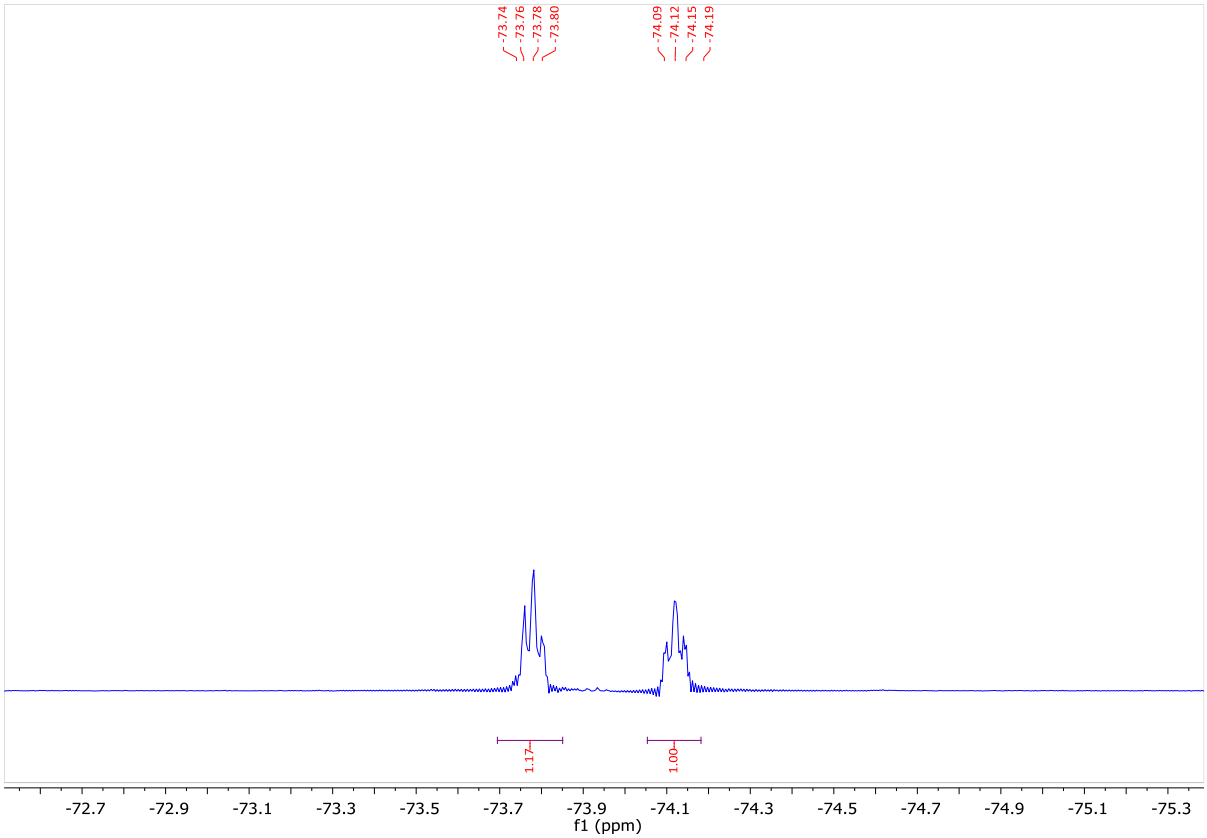


Figure S65. ^{19}F NMR spectrum ($CDCl_3$, 376 MHz) of **3ad.**

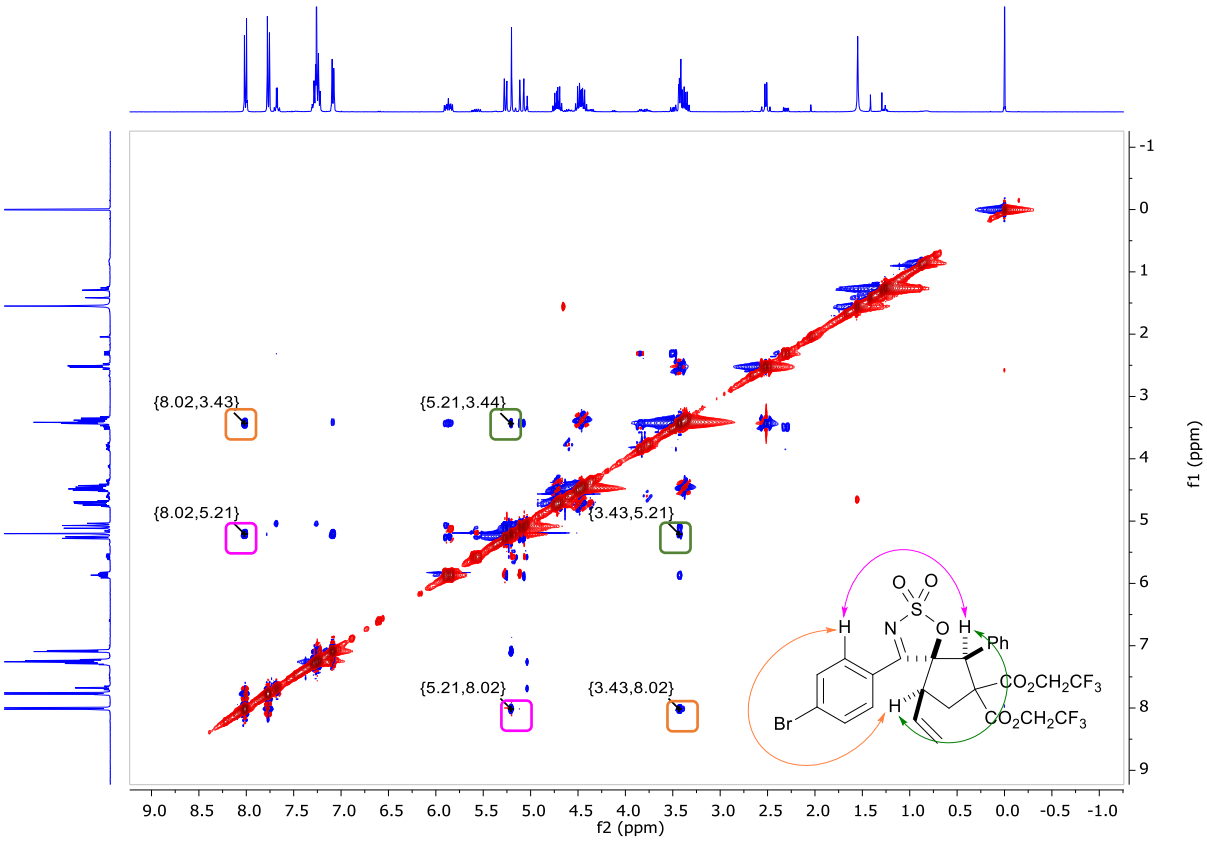


Figure S66. 2D NOESY spectrum ($CDCl_3$, 400 MHz) of **3ad.**

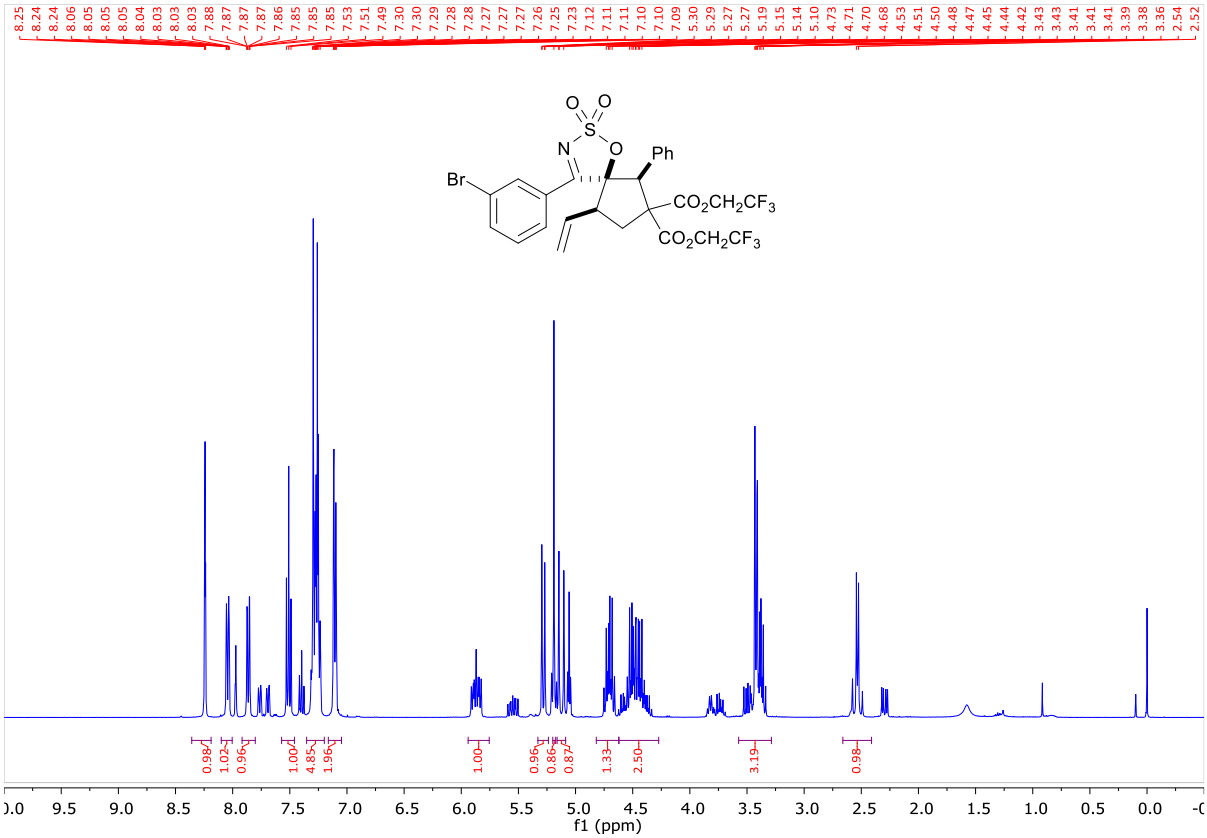


Figure S67. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of **3ae**.

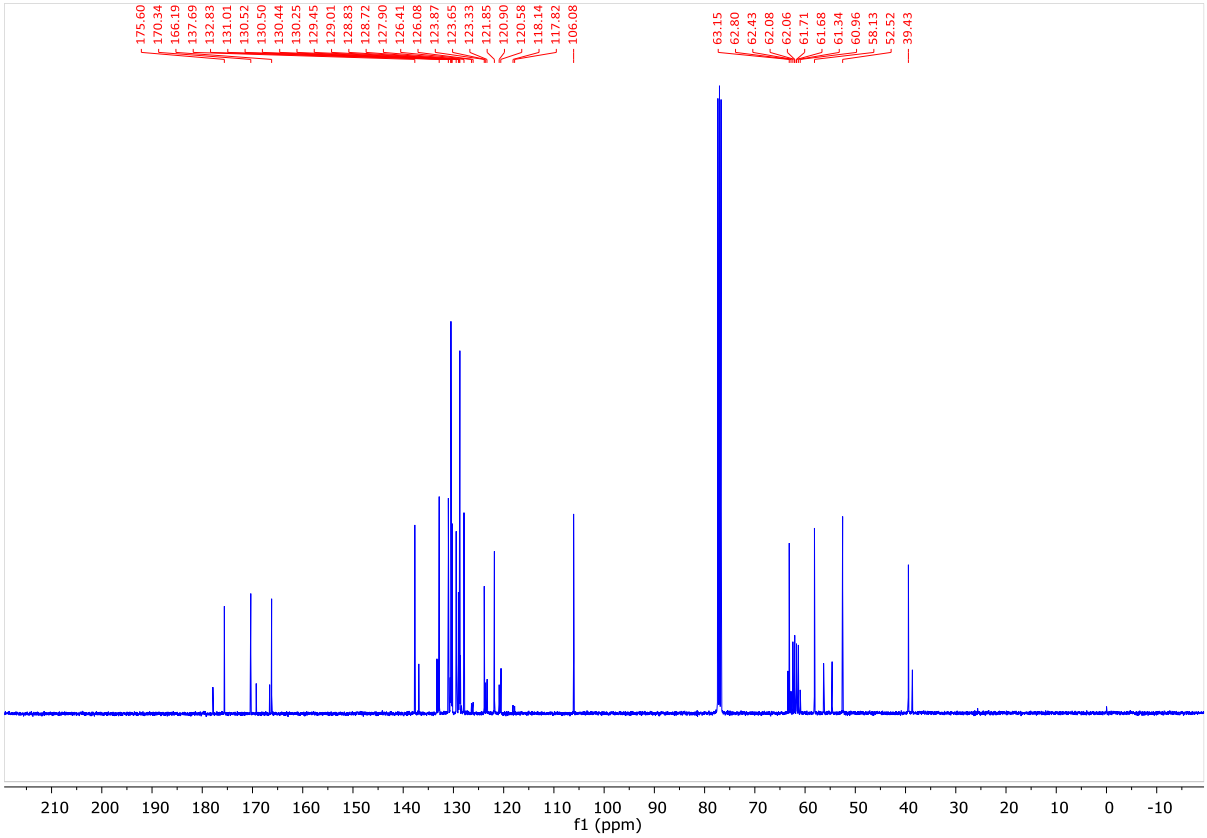


Figure S68. ^{13}C NMR spectrum ($CDCl_3$, 100 MHz) of **3ae**.

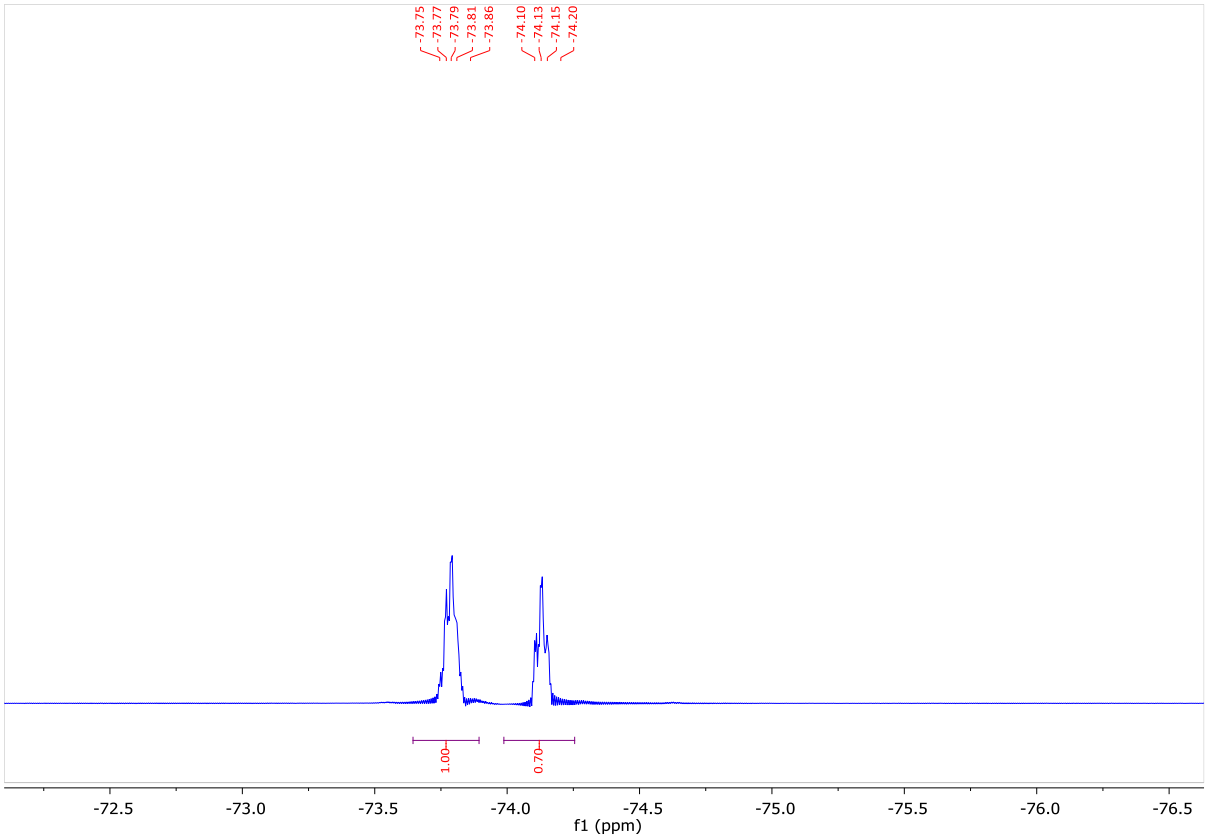


Figure S69. ^{19}F NMR spectrum ($CDCl_3$, 376 MHz) of **3ae.**

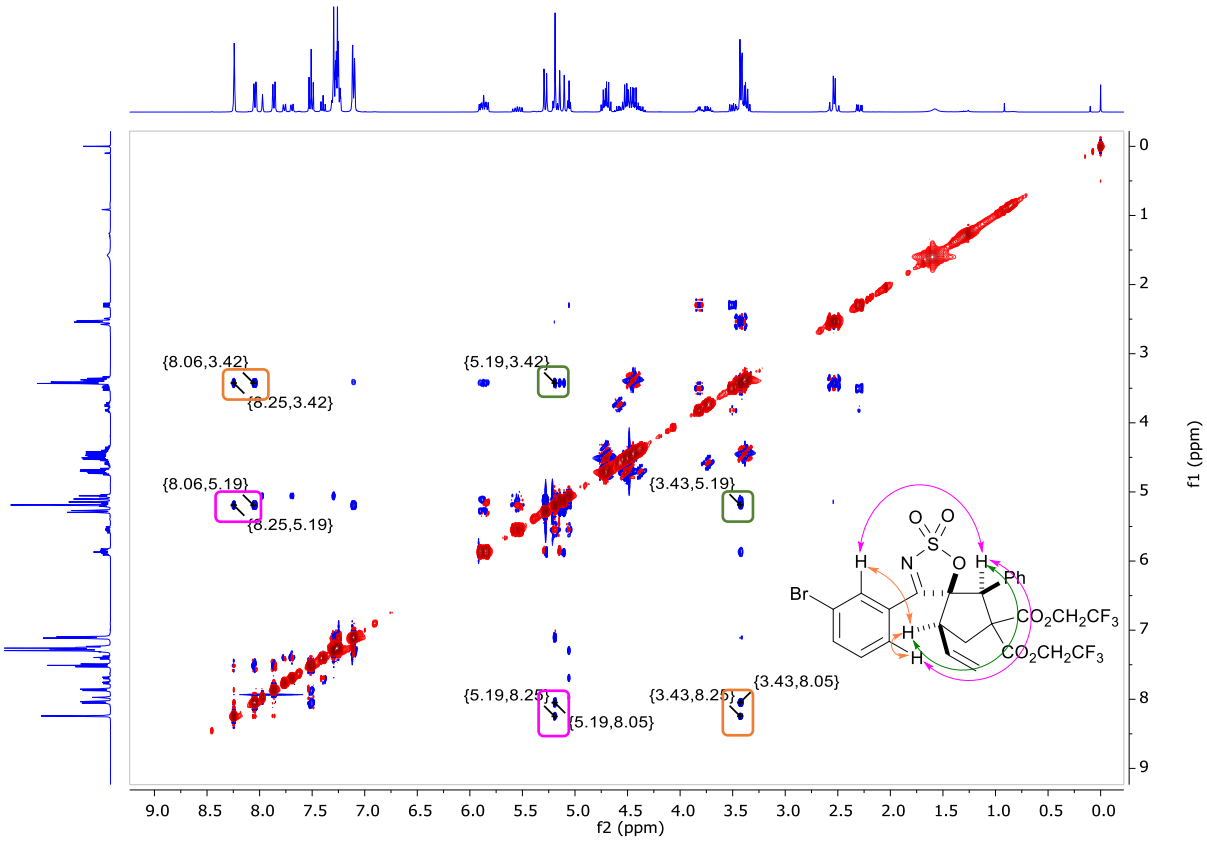


Figure S70. 2D NOESY spectrum ($CDCl_3$, 400 MHz) of **3ae.**

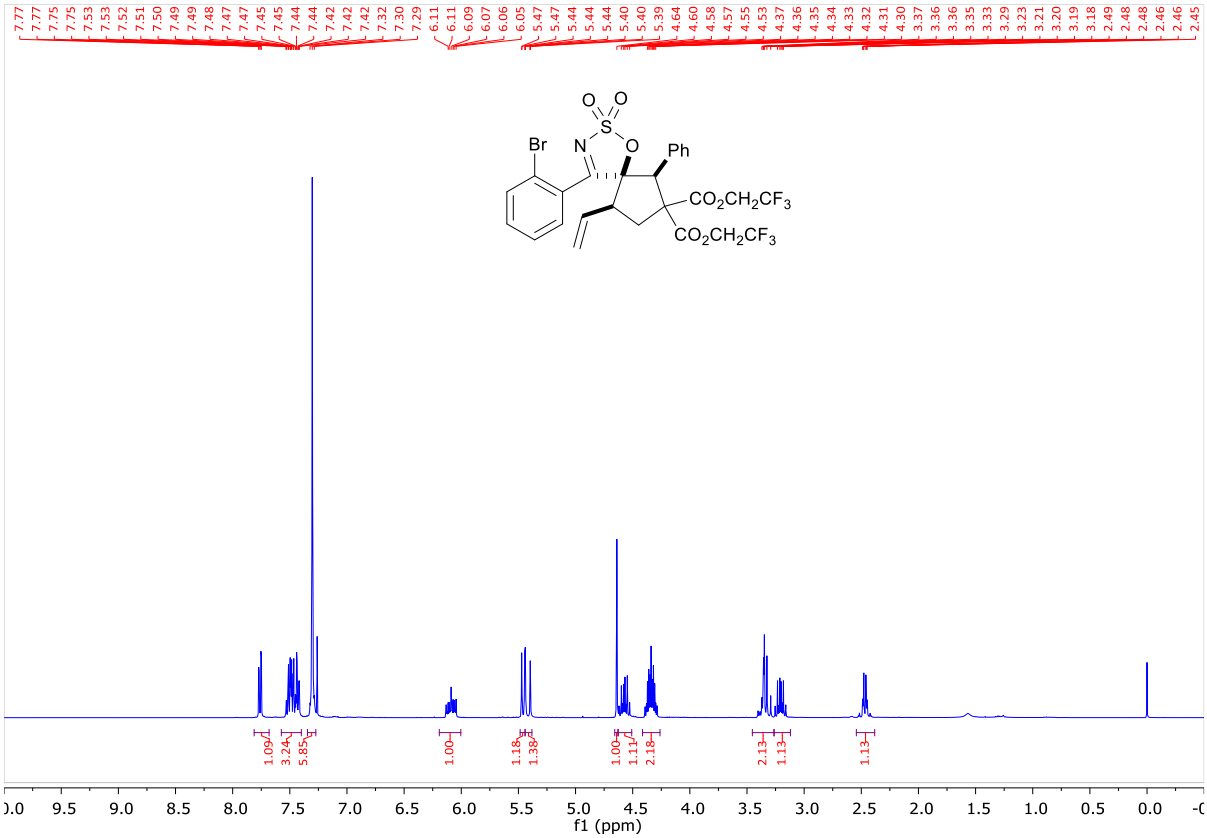


Figure S71. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of **3af**.

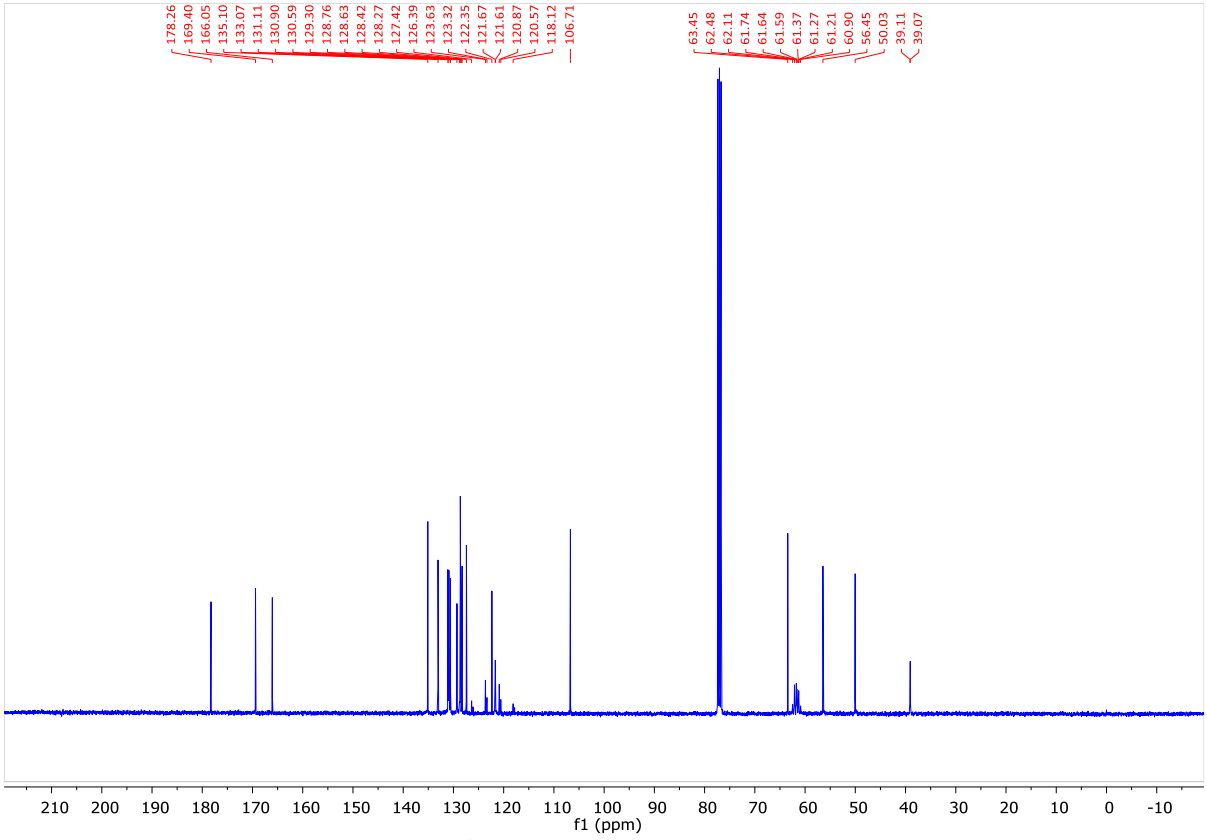


Figure S72. ^{13}C NMR spectrum ($CDCl_3$, 100 MHz) of **3af**.

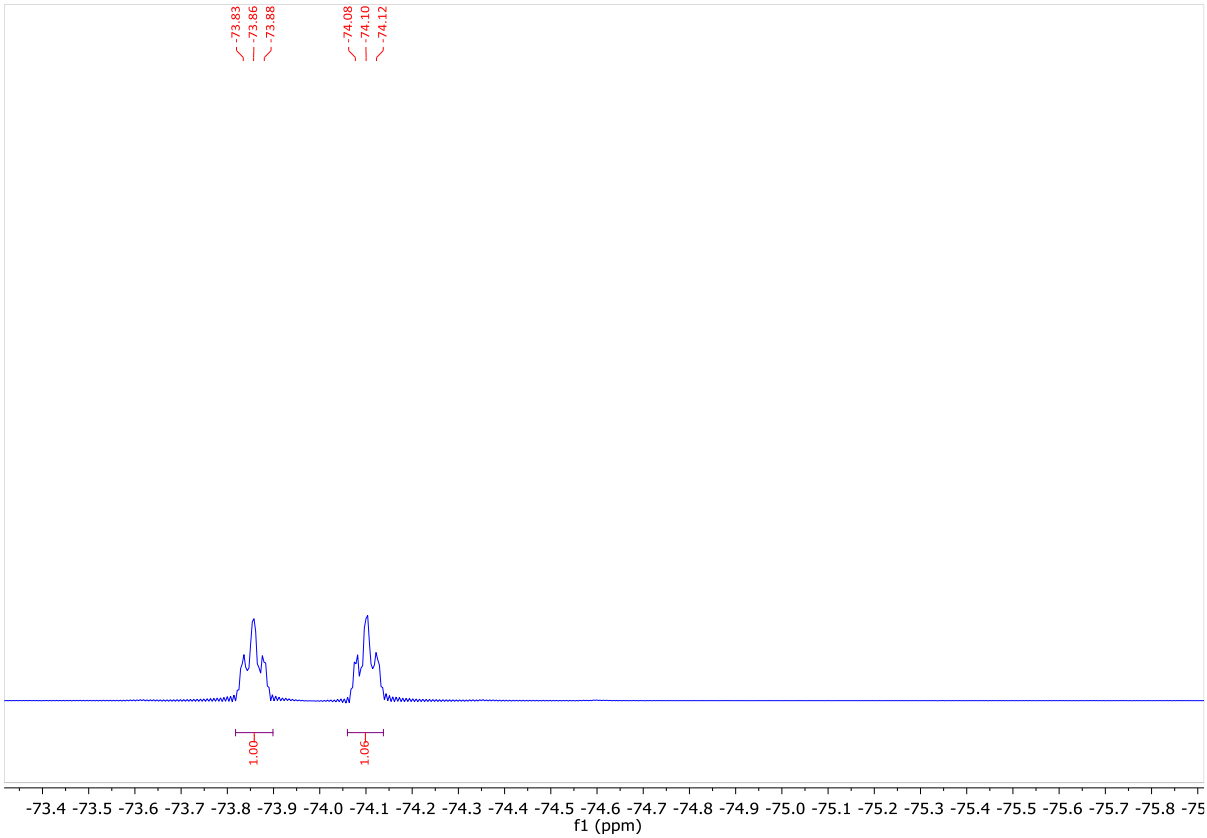


Figure S73. ^{19}F NMR spectrum ($CDCl_3$, 376 MHz) of **3af.**

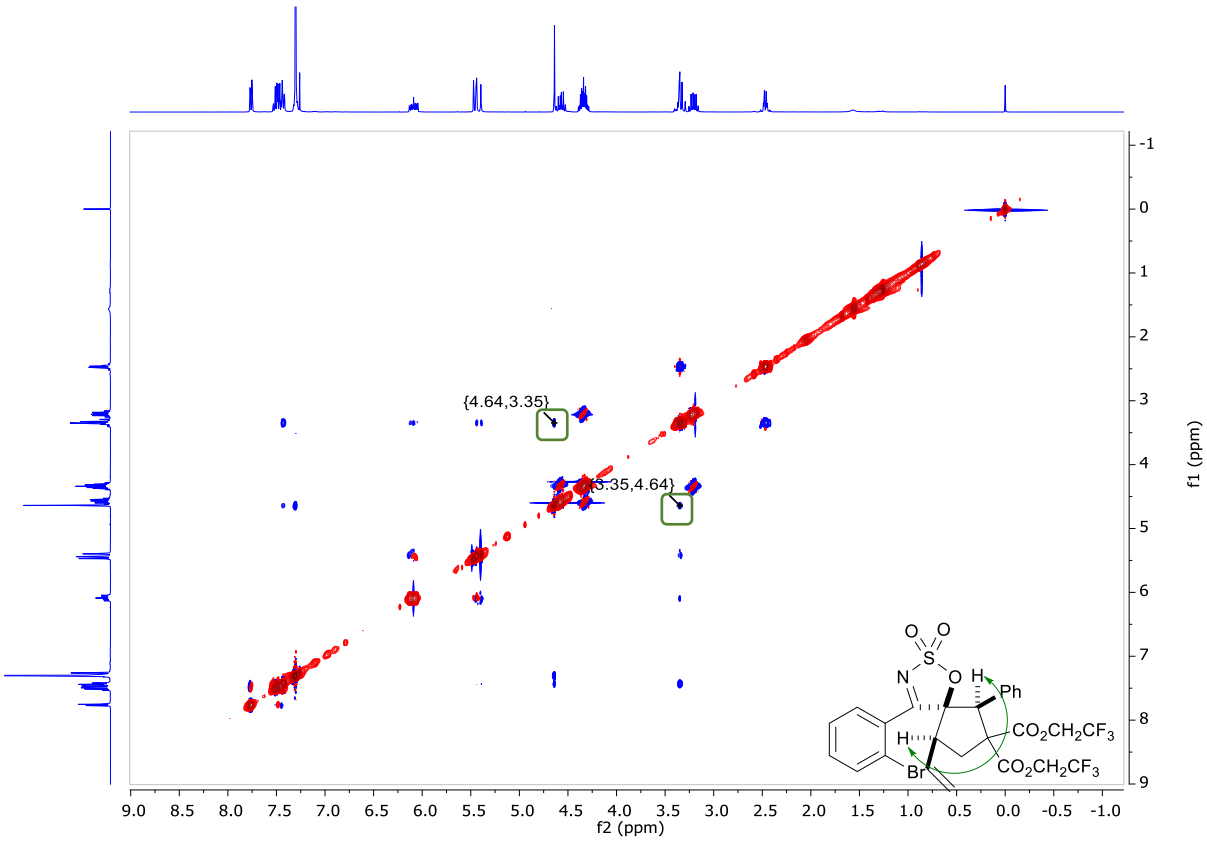


Figure S74. 2D NOESY spectrum ($CDCl_3$, 400 MHz) of **3af.**

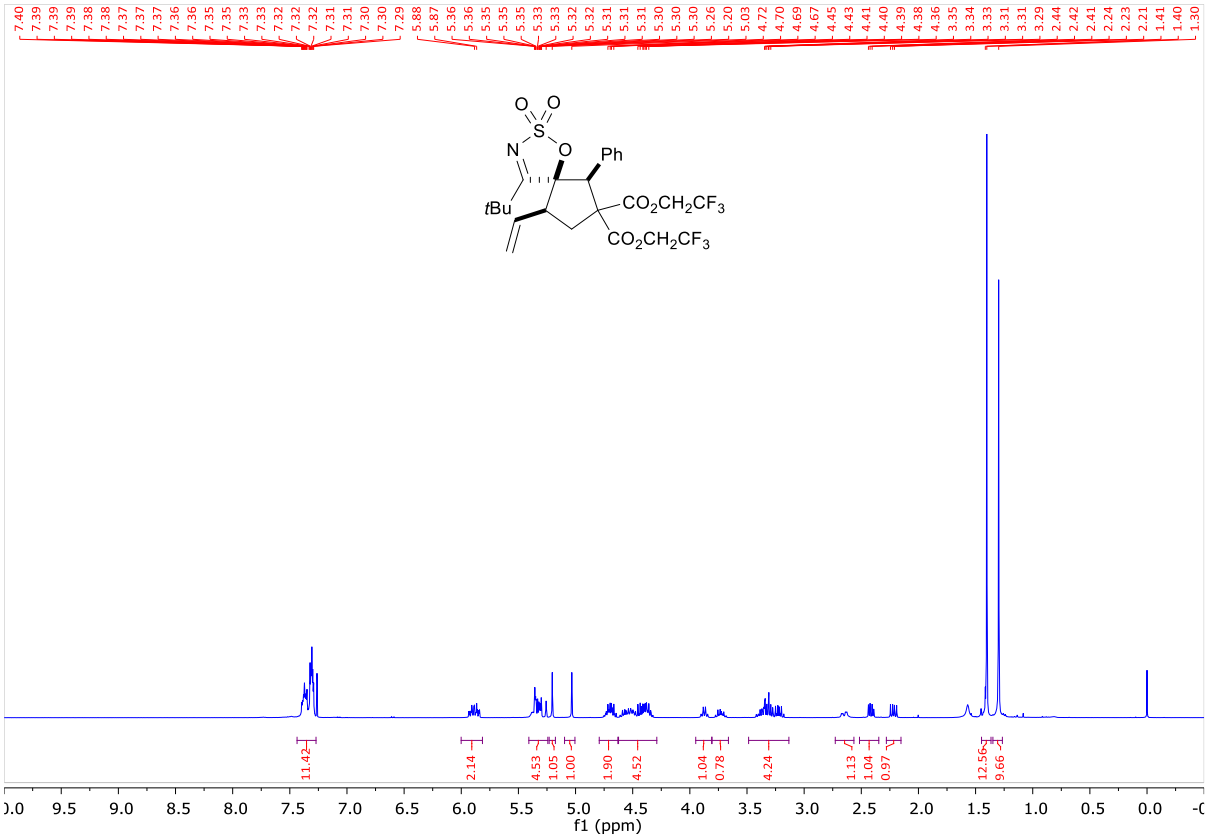


Figure S75. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of **3ag**.

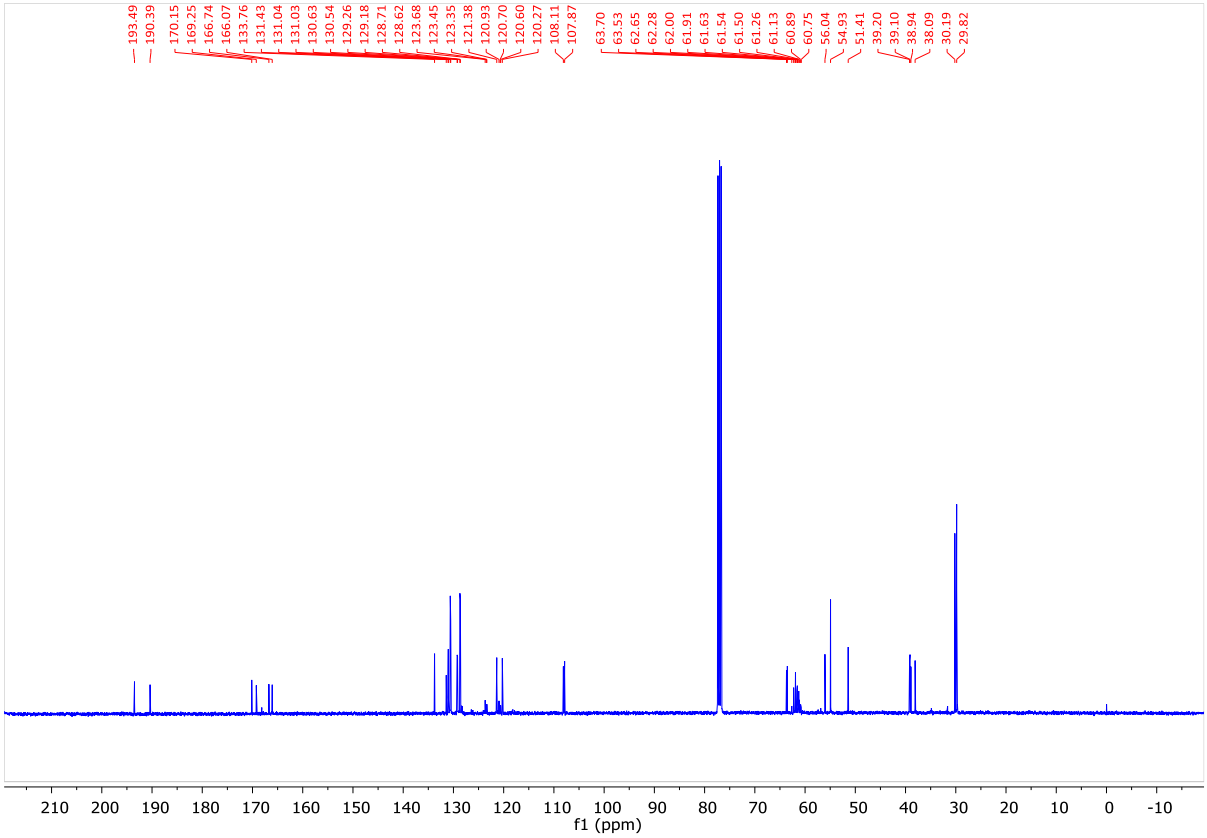


Figure S76. ^{13}C NMR spectrum ($CDCl_3$, 100 MHz) of **3ag**.

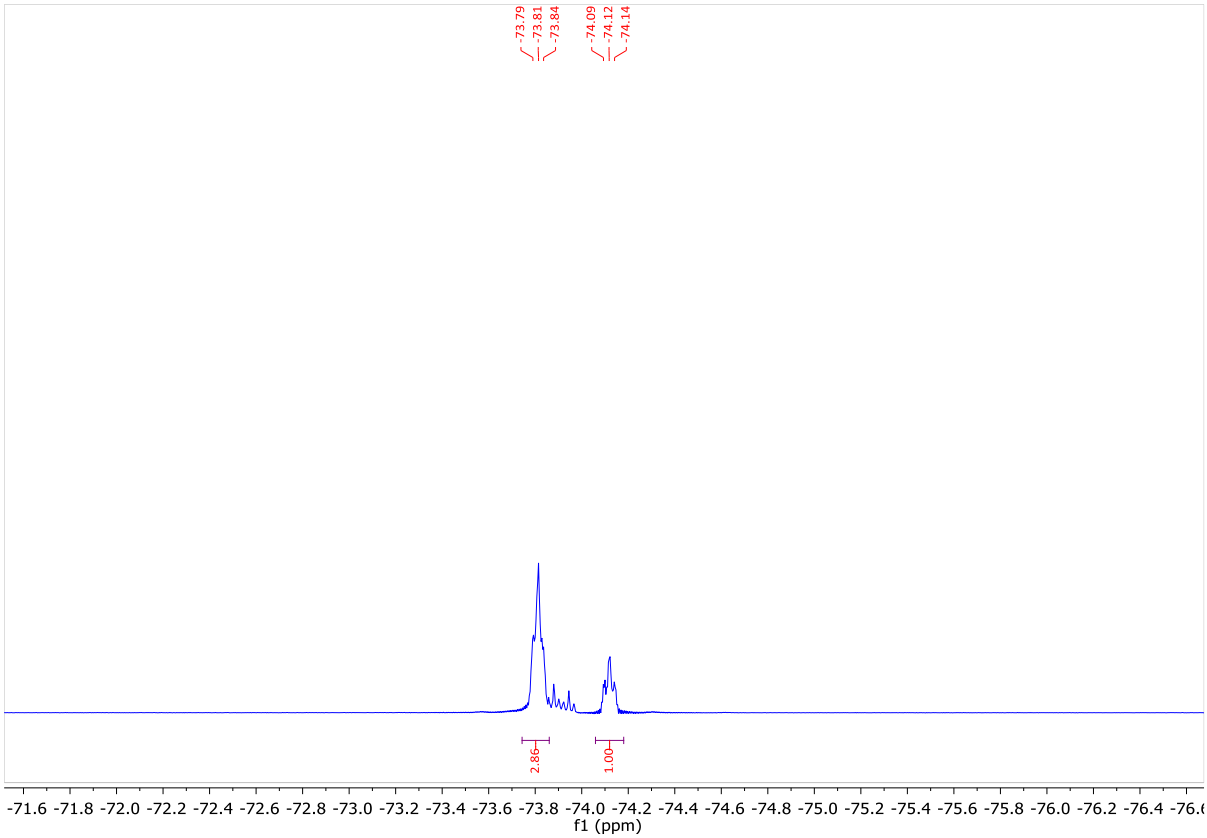


Figure S77. ^{19}F NMR spectrum ($CDCl_3$, 376 MHz) of **3ag.**

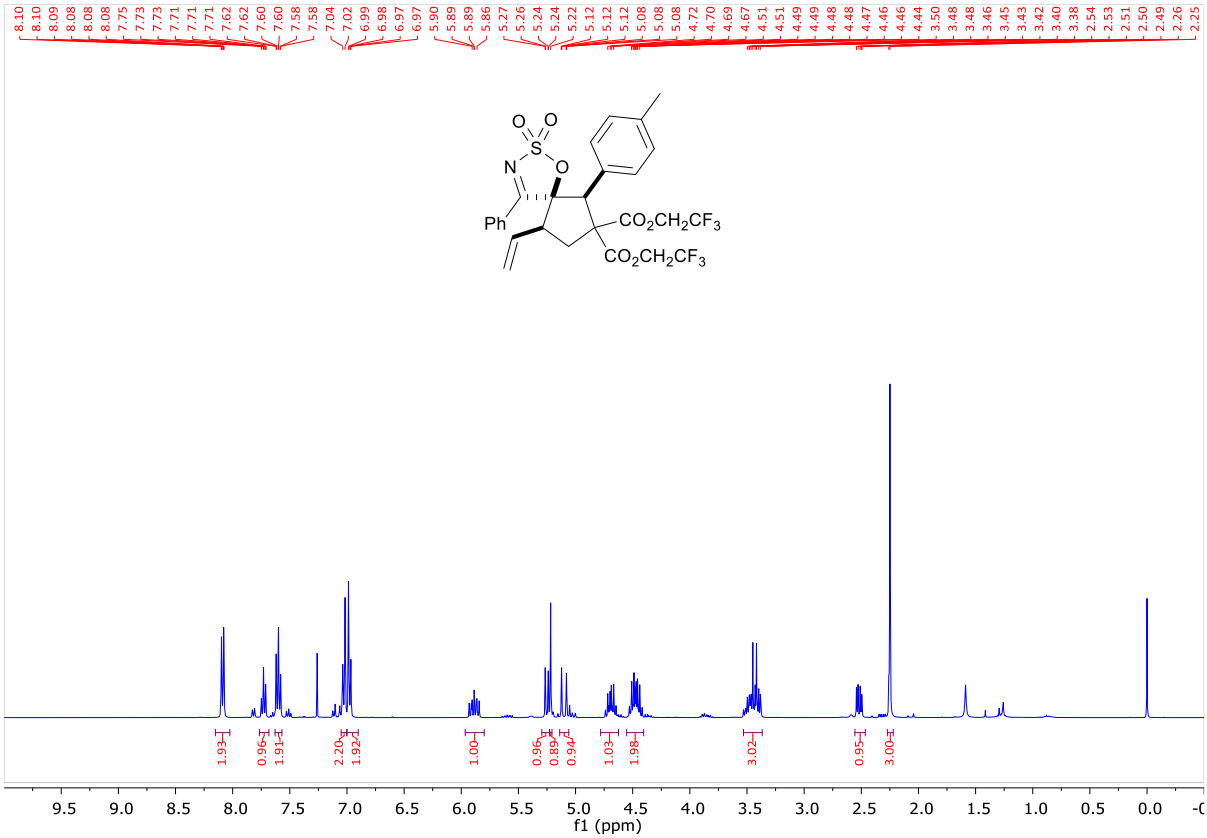


Figure S78. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of **3ah**.

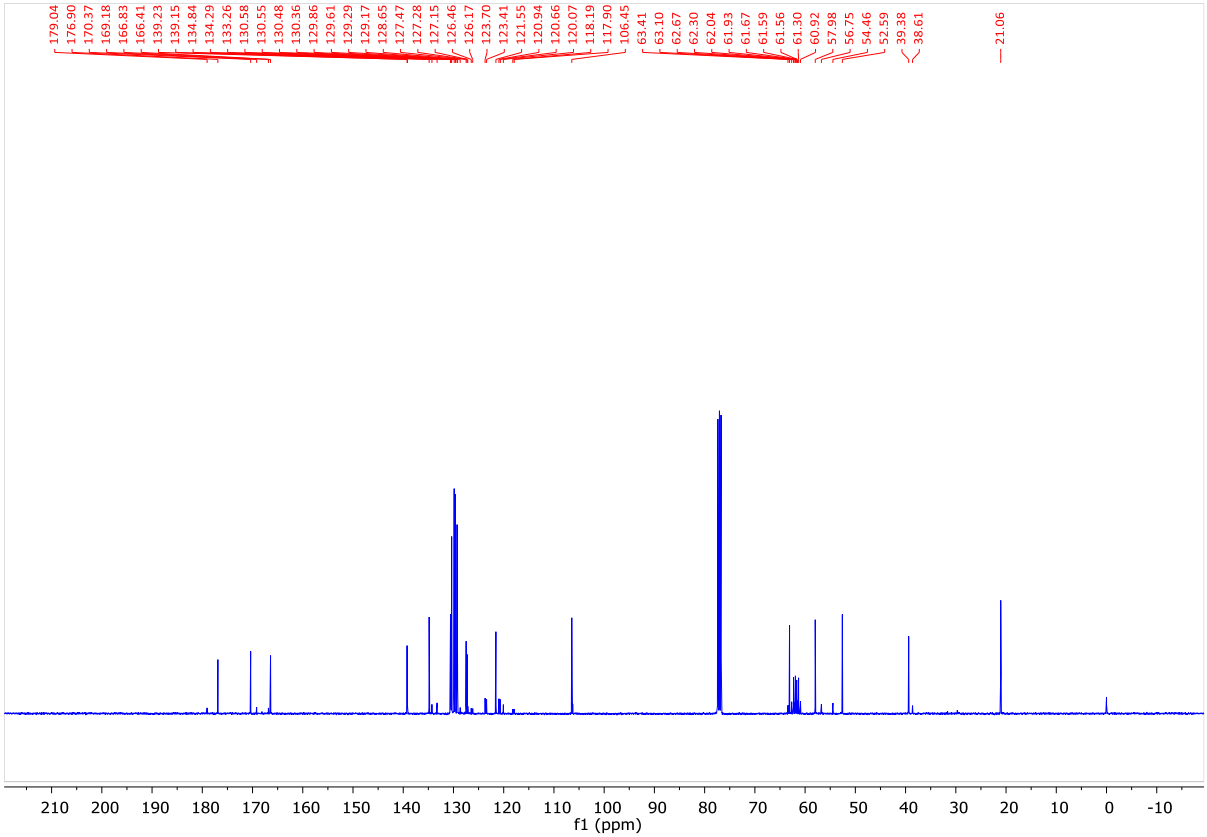


Figure S79. ^{13}C NMR spectrum ($CDCl_3$, 100 MHz) of **3ah**.

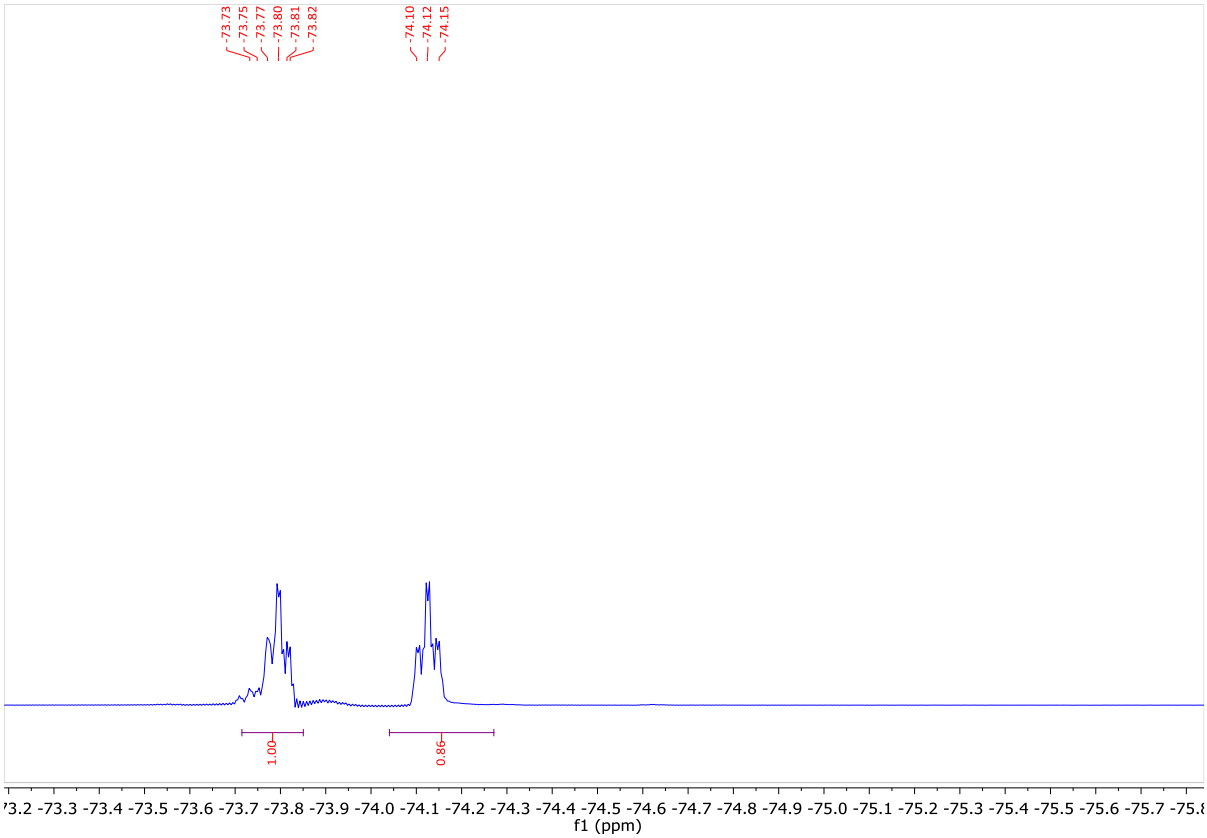


Figure S80. ^{19}F NMR spectrum ($CDCl_3$, 376 MHz) of **3ah.**

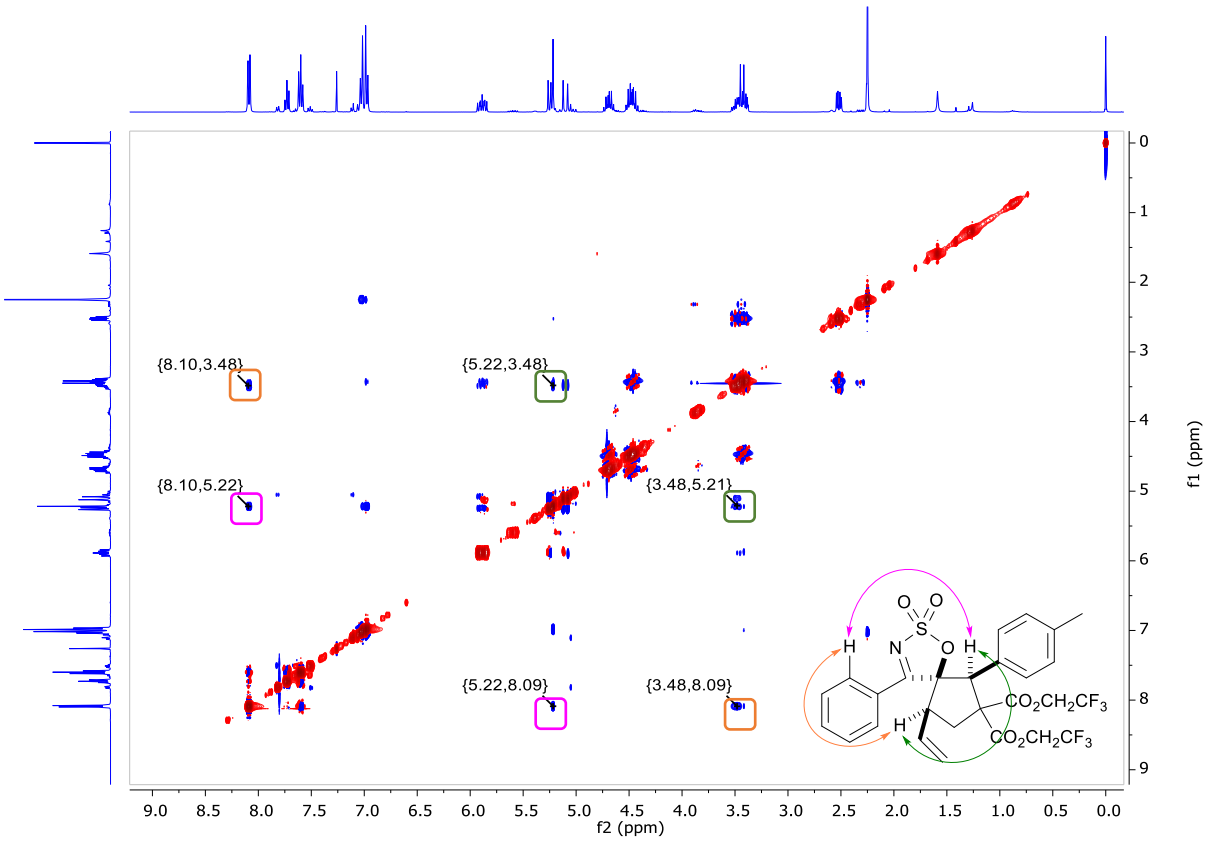


Figure S81. 2D NOESY spectrum ($CDCl_3$, 400 MHz) of **3ah.**

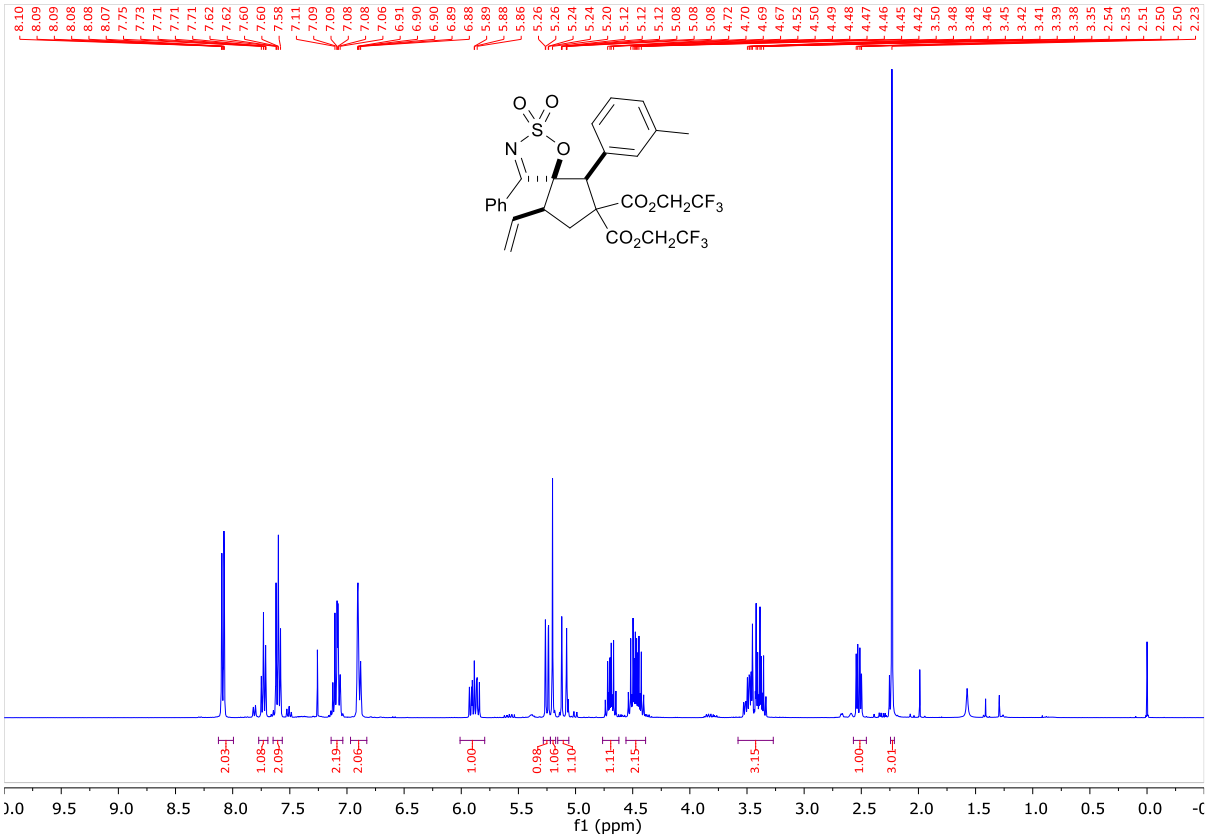


Figure S82. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of **3ai**.

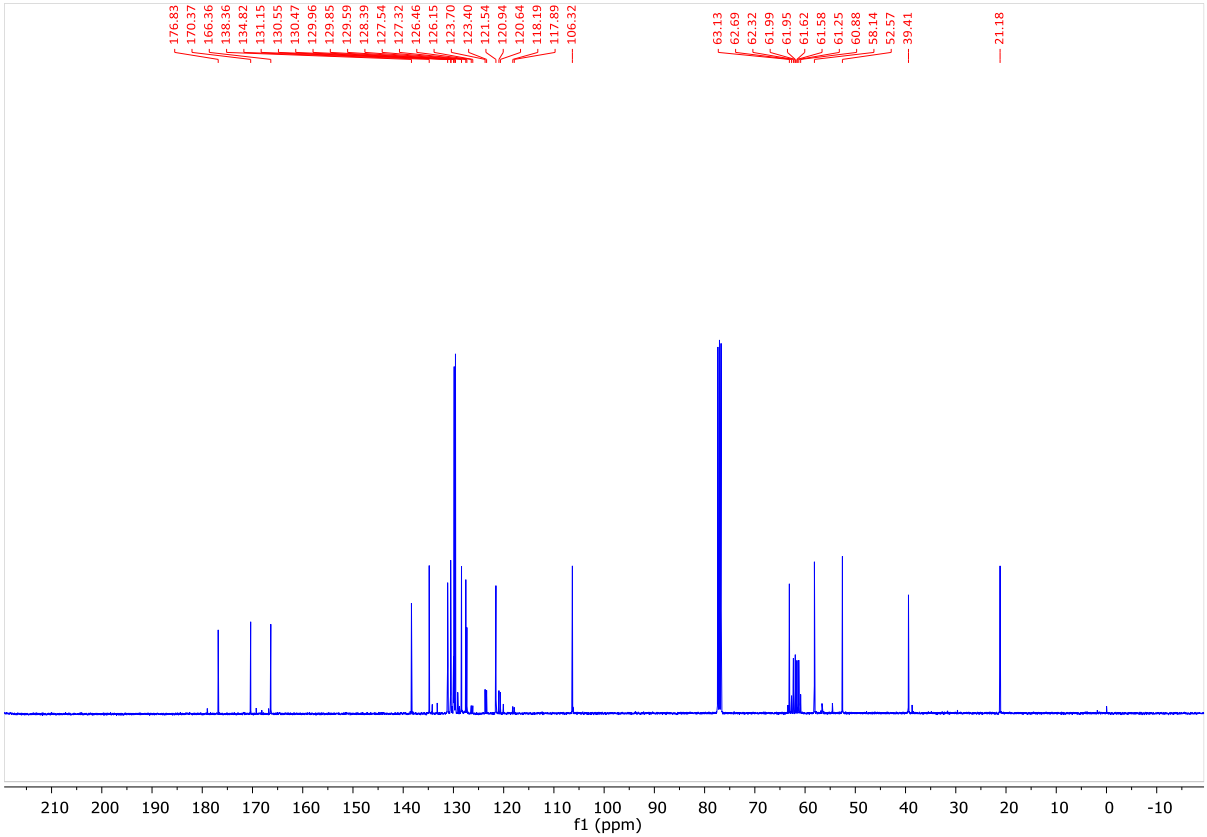


Figure S83. ^{13}C NMR spectrum ($CDCl_3$, 100 MHz) of **3ai**.

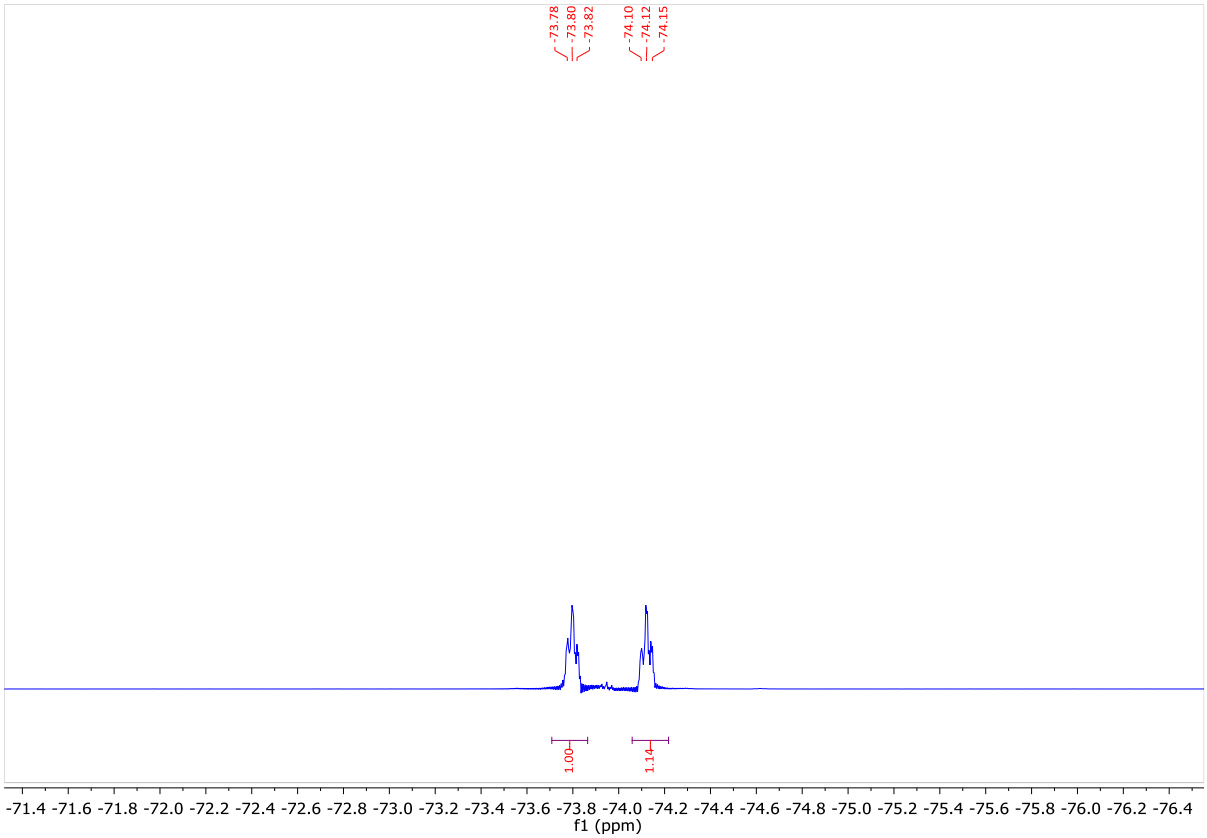


Figure S84. ^{19}F NMR spectrum ($CDCl_3$, 376 MHz) of **3ai.**

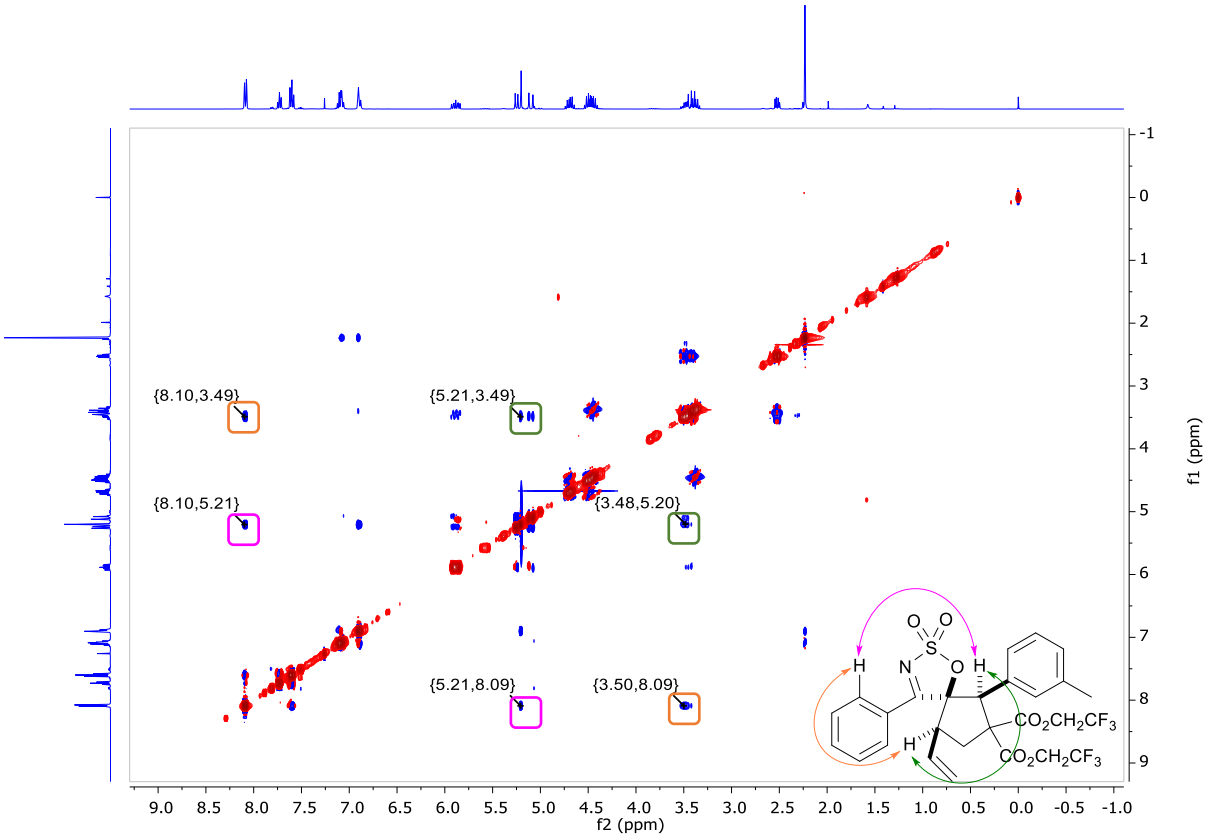


Figure S85. 2D NOESY spectrum ($CDCl_3$, 400 MHz) of **3ai.**

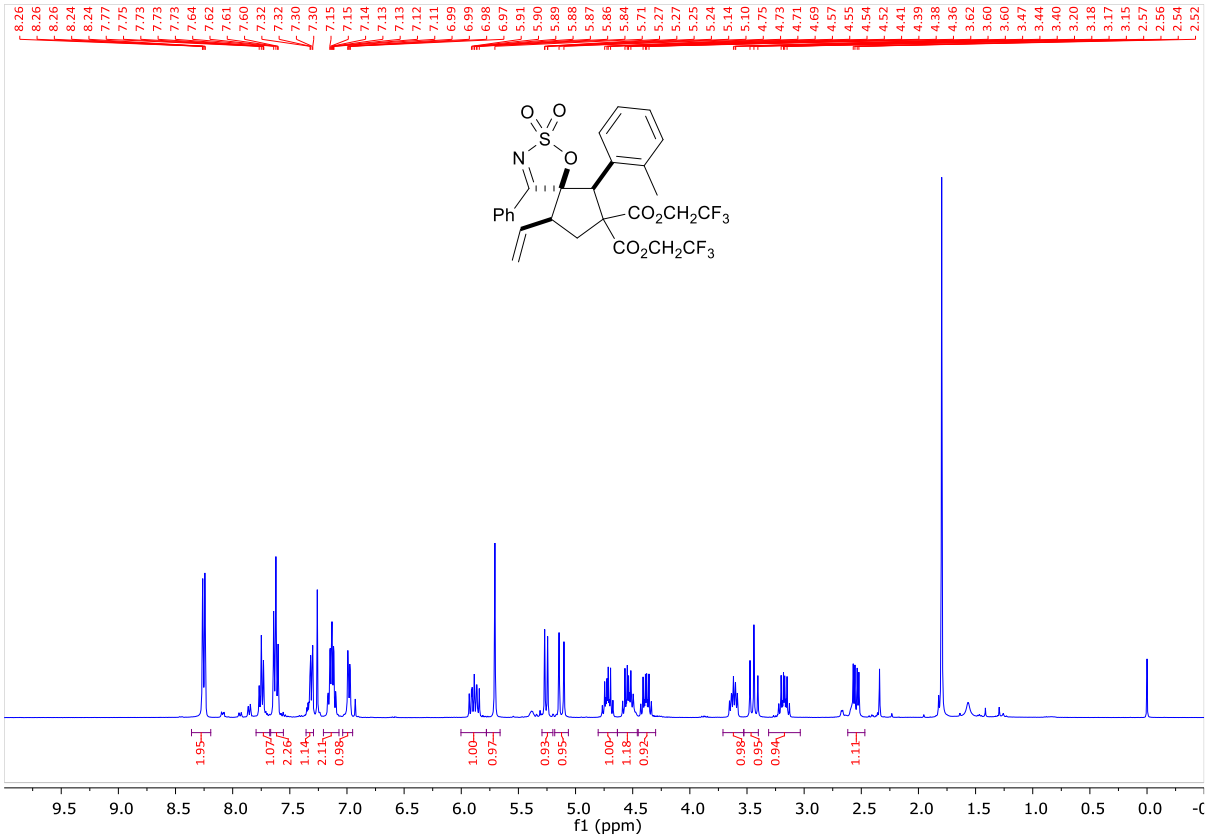


Figure S86. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of **3aj**.

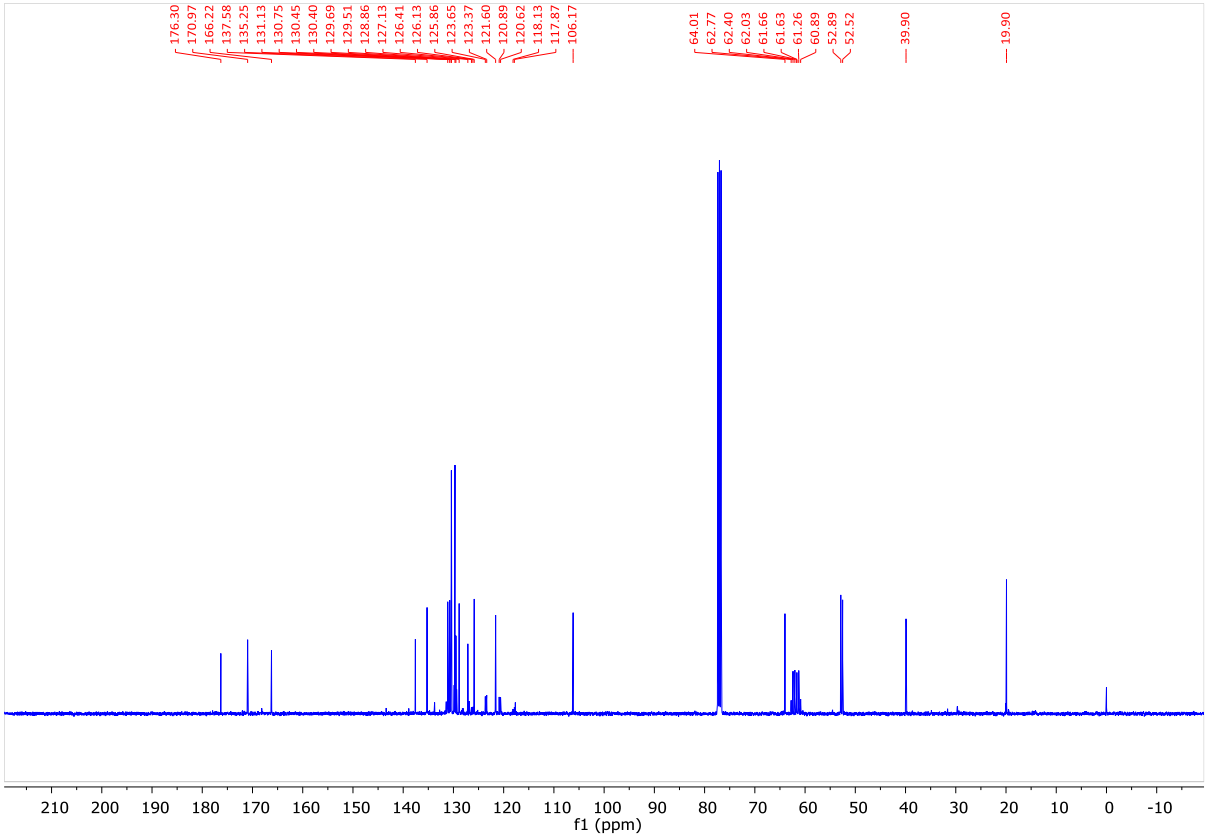


Figure S87. ^{13}C NMR spectrum ($CDCl_3$, 100 MHz) of **3aj**.

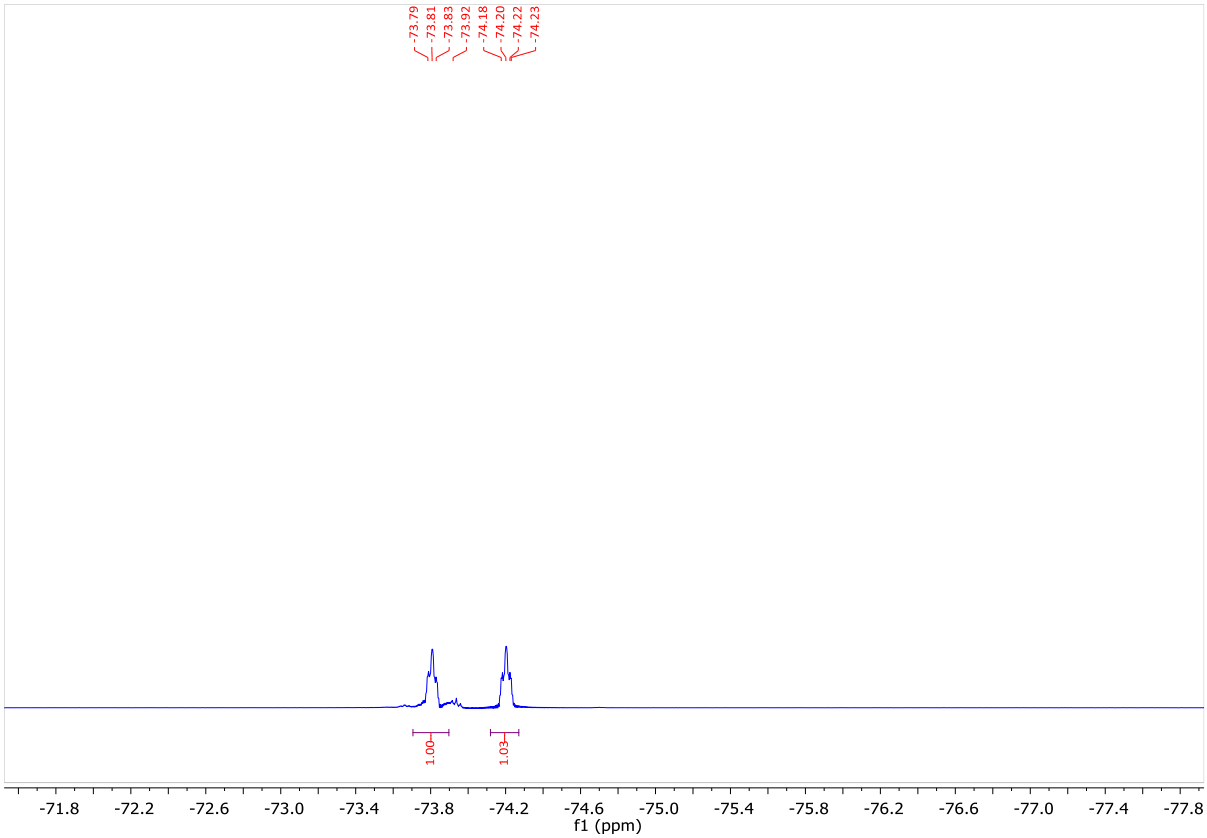


Figure S88. ^{19}F NMR spectrum ($CDCl_3$, 376 MHz) of **3aj.**

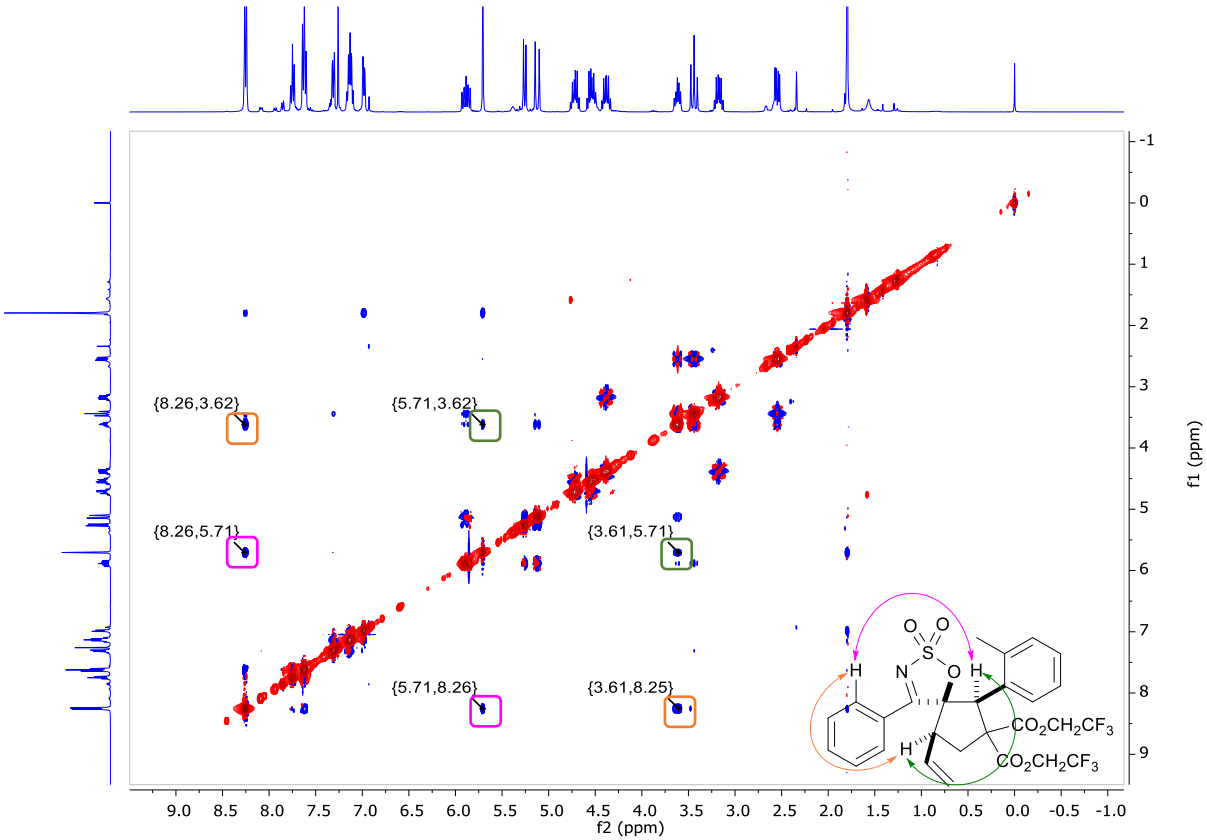


Figure S89. 2D NOESY spectrum ($CDCl_3$, 400 MHz) of **3aj.**

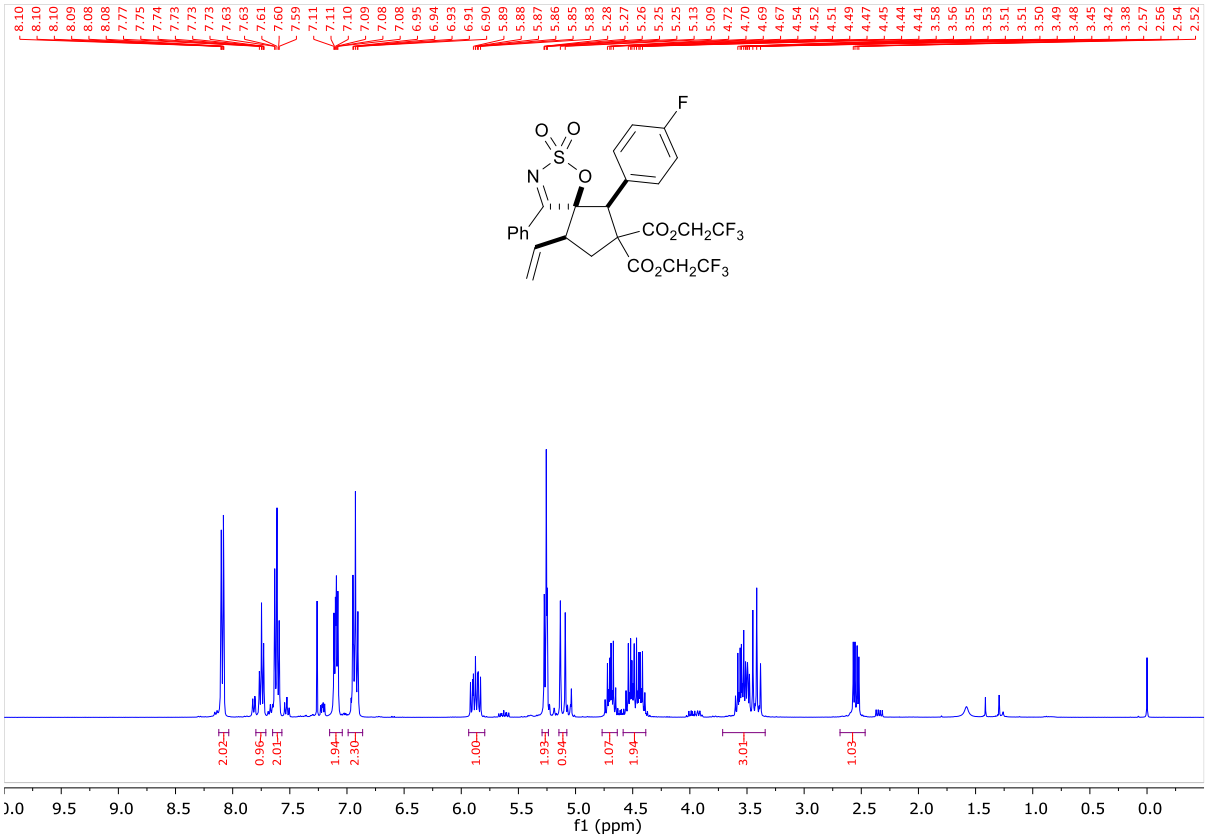


Figure S90. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of **3ak**.

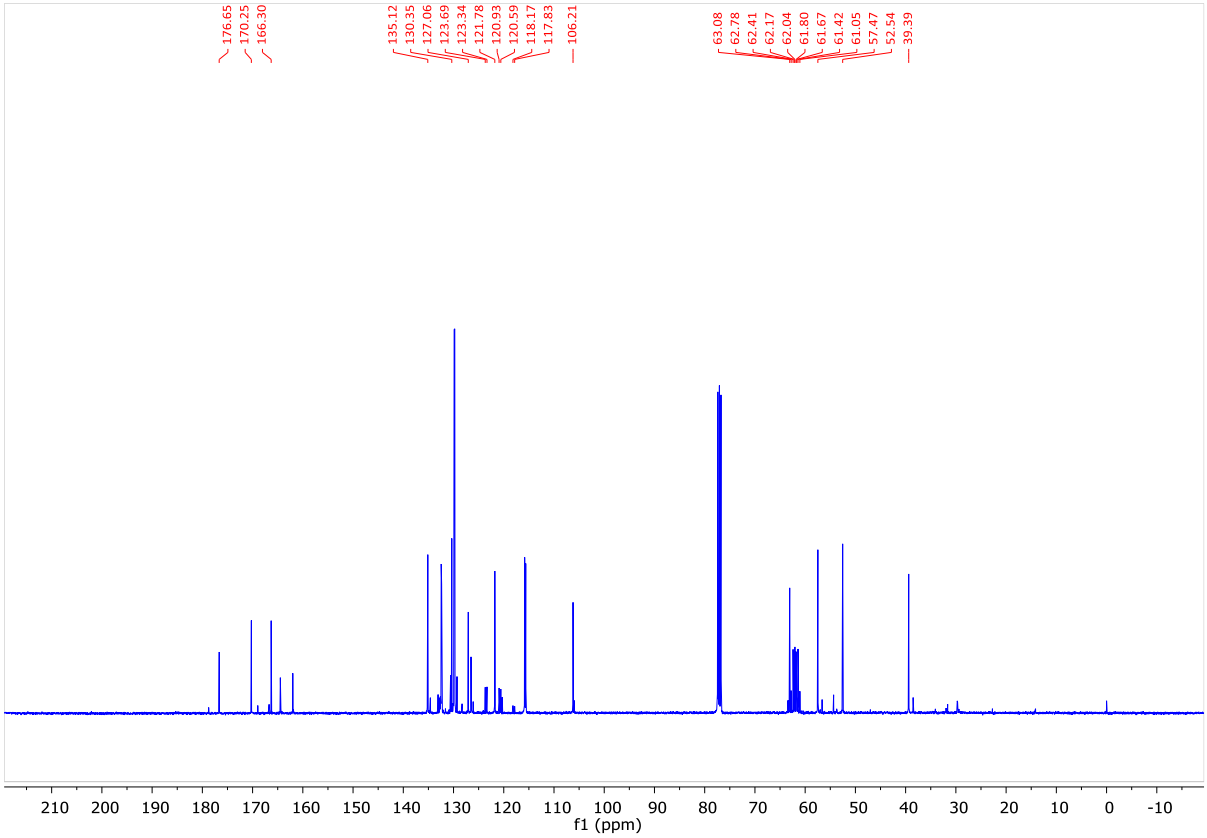


Figure S91. ^{13}C NMR spectrum ($CDCl_3$, 100 MHz) of **3ak**.

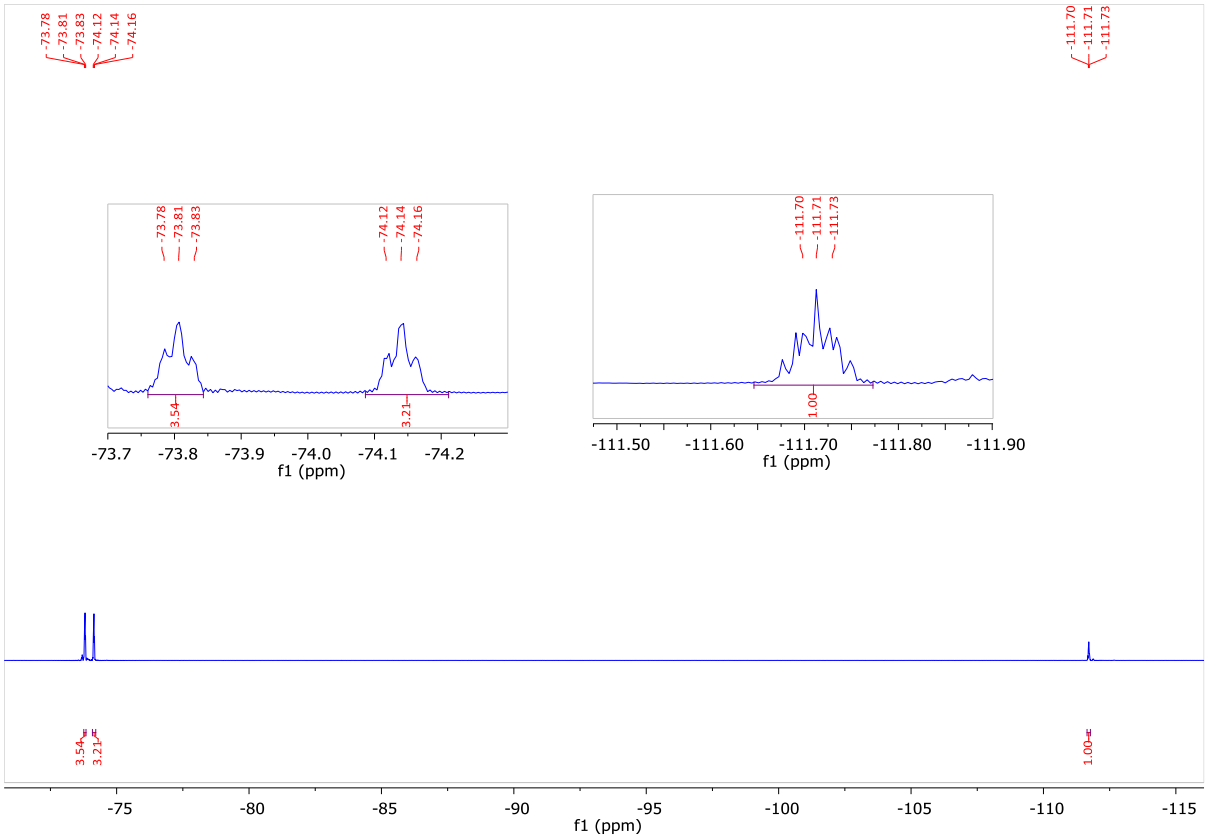


Figure S92. ^{19}F NMR spectrum ($CDCl_3$, 376 MHz) of **3ak.**

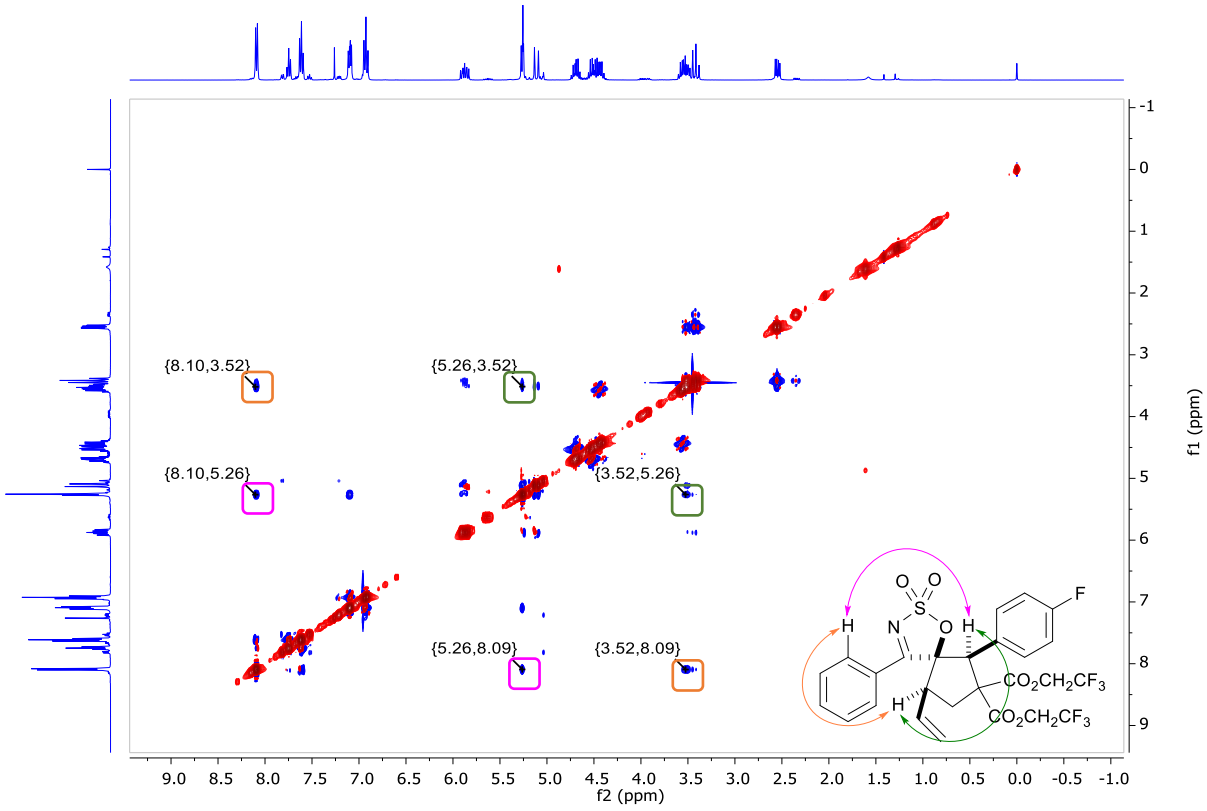


Figure S93. 2D NOESY spectrum ($CDCl_3$, 400 MHz) of **3ak.**

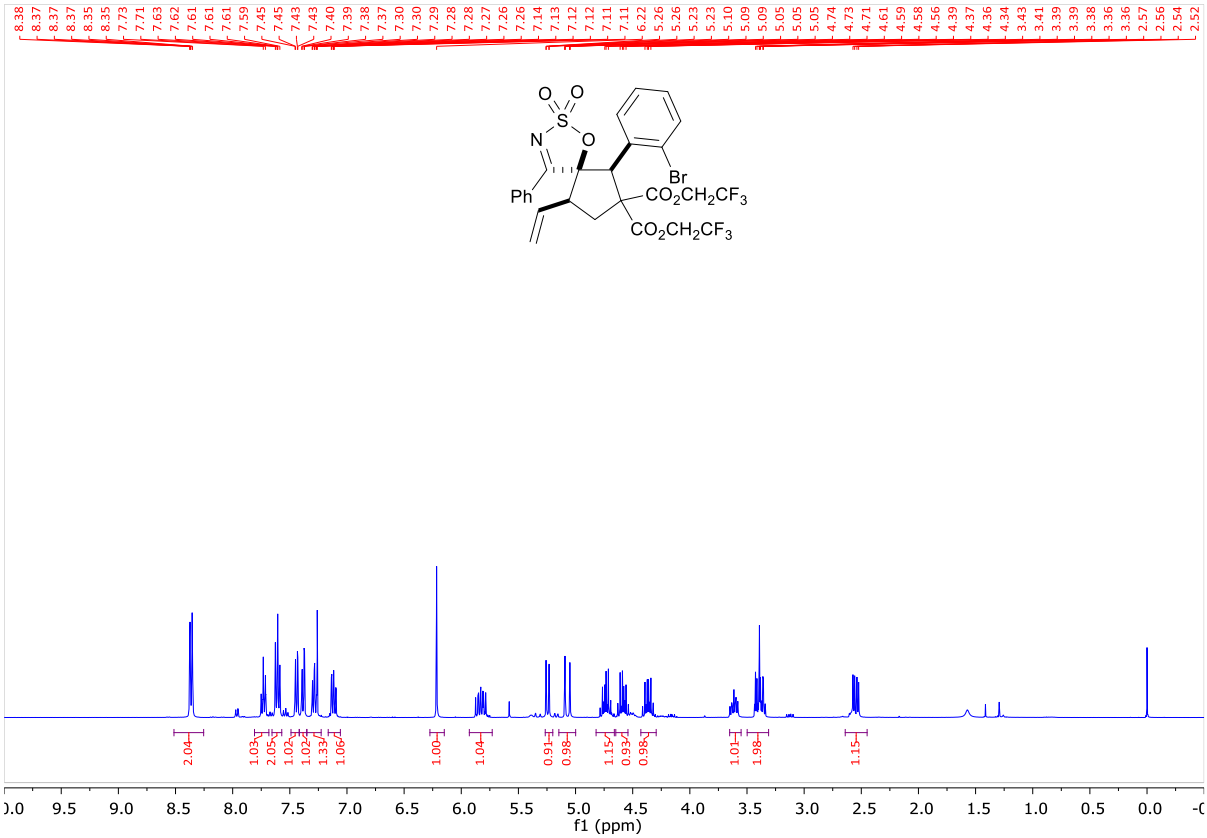


Figure S94. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of **3al**.

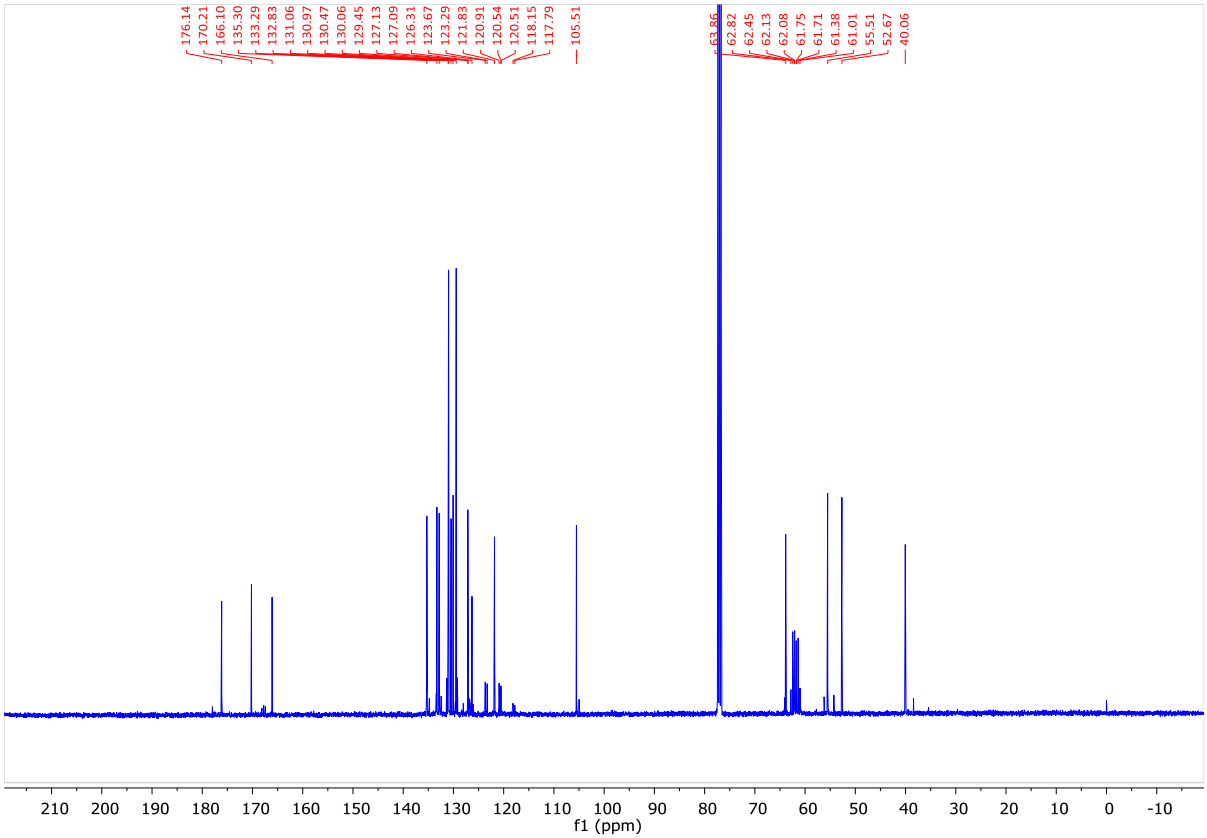


Figure S95. ^{13}C NMR spectrum ($CDCl_3$, 100 MHz) of **3al**.

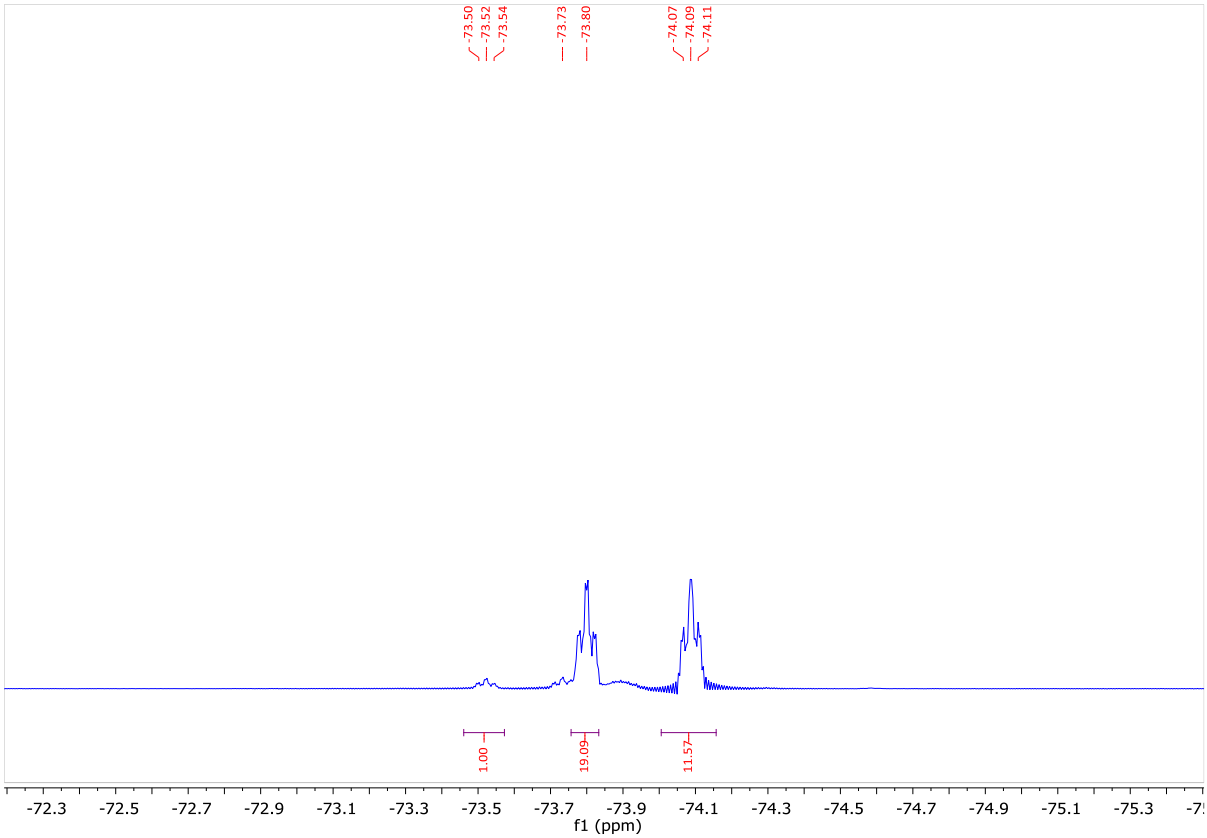


Figure S96. ^{19}F NMR spectrum ($CDCl_3$, 376 MHz) of **3al.**

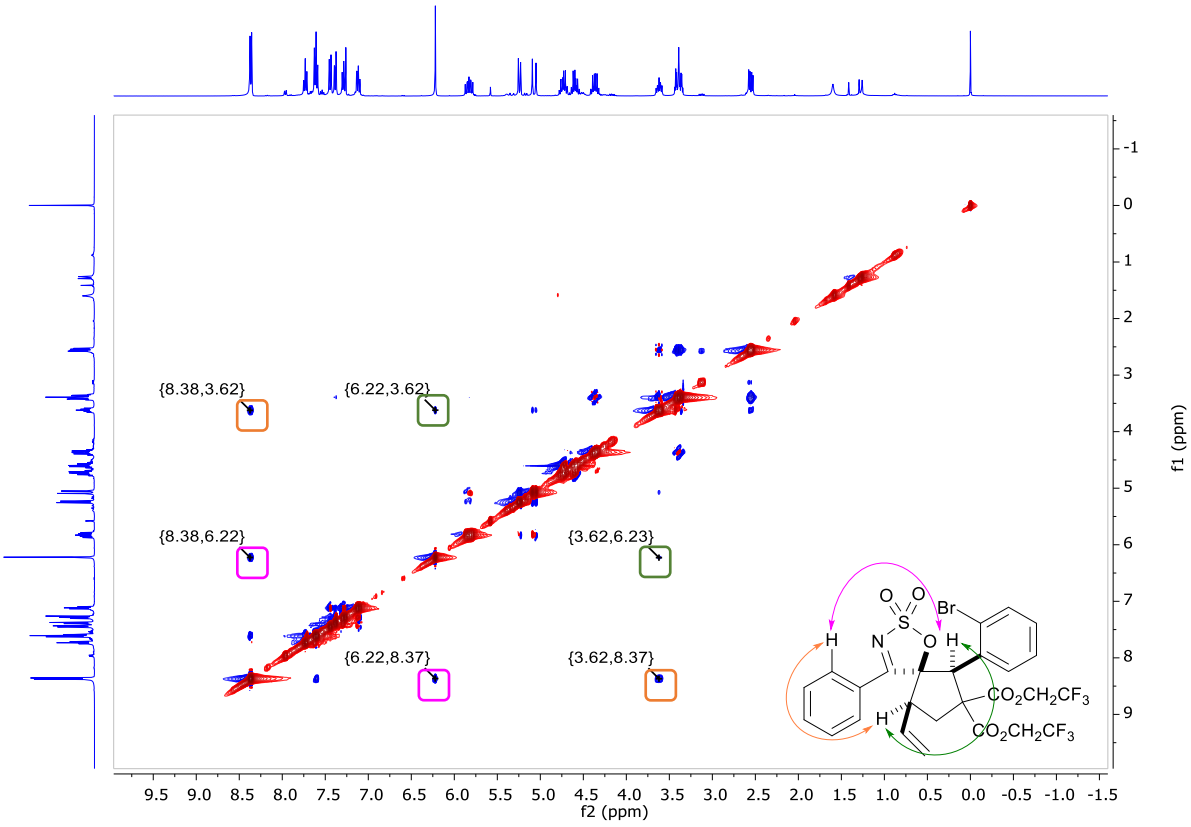


Figure S97. 2D NOESY spectrum ($CDCl_3$, 400 MHz) of **3al.**

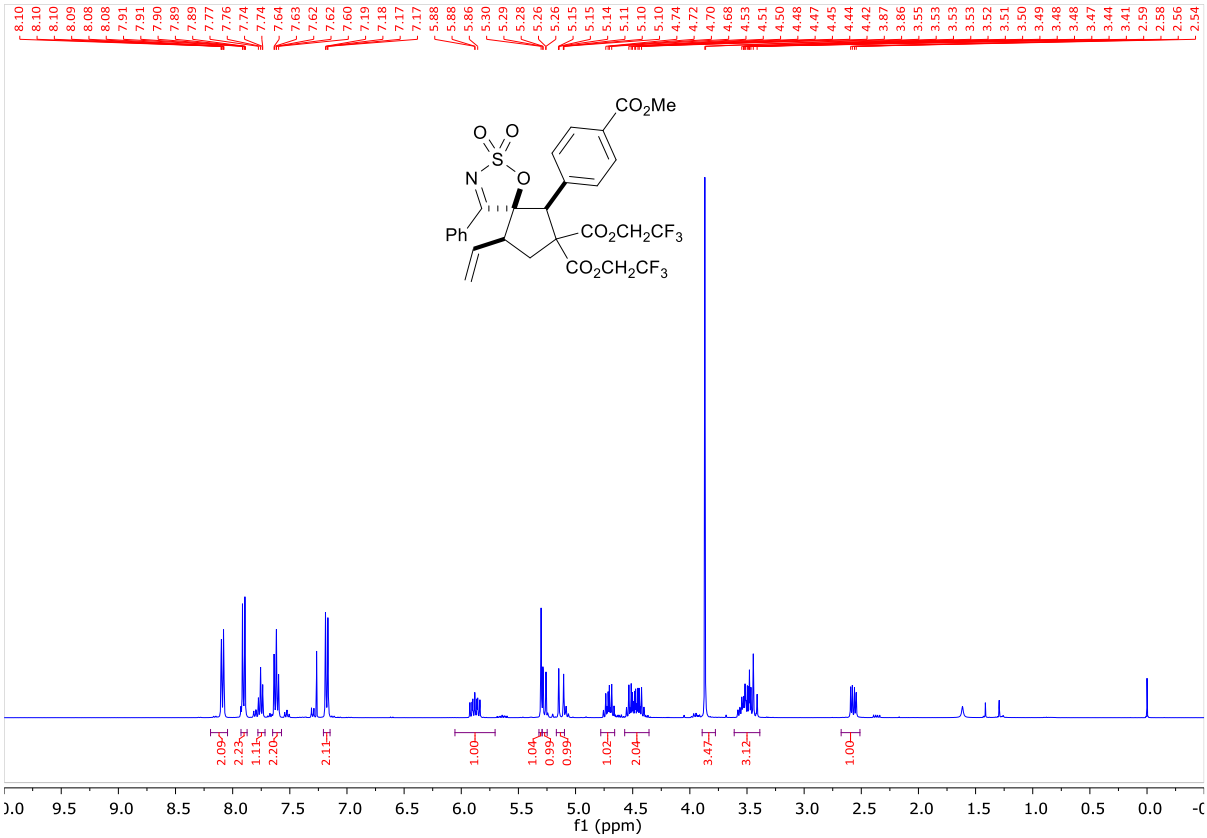


Figure S98. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of **3am**.

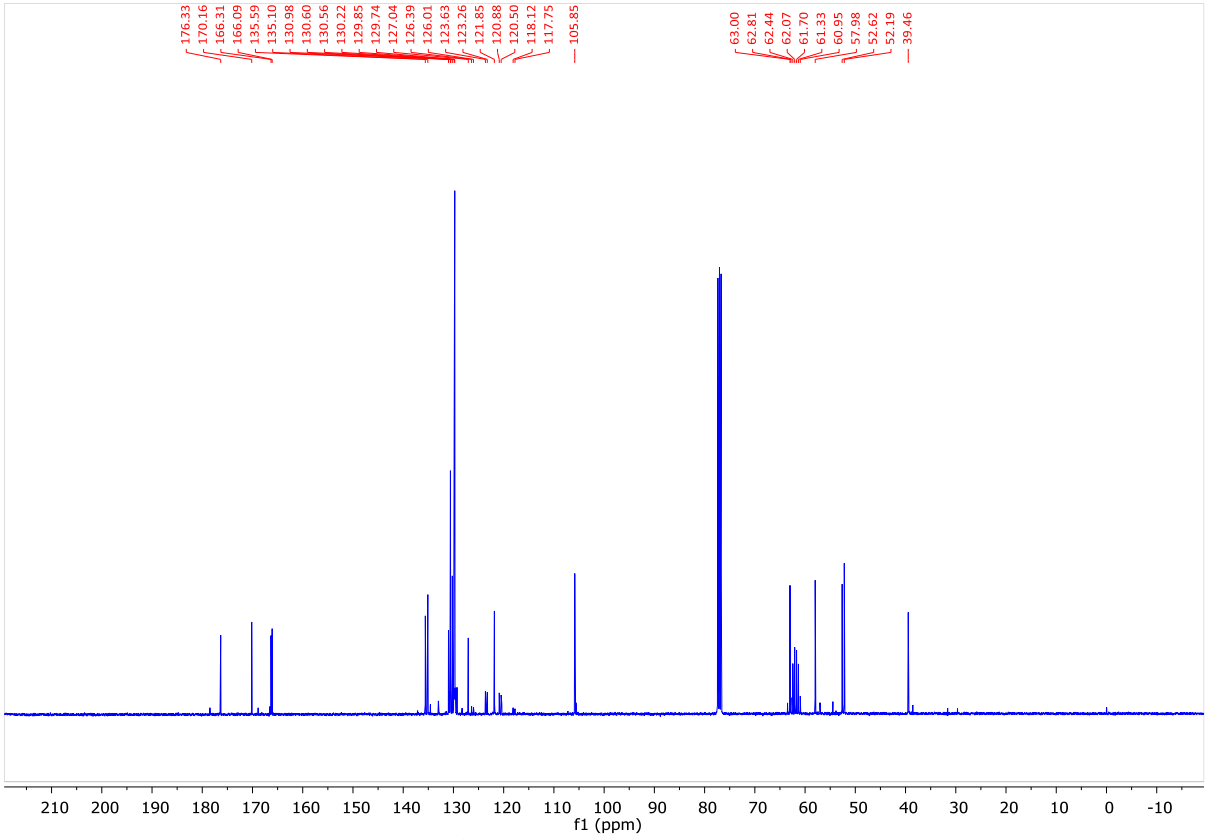


Figure S99. ^{13}C NMR spectrum ($CDCl_3$, 100 MHz) of **3am**.

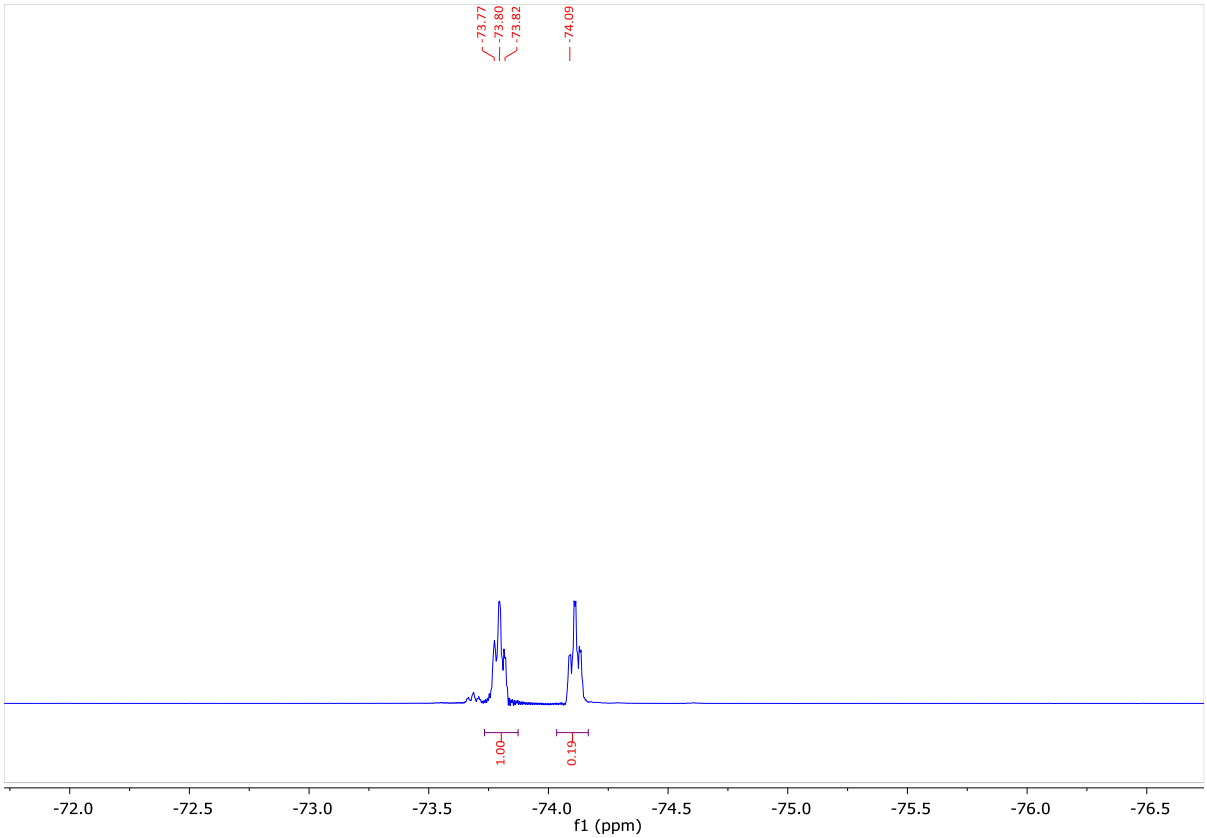


Figure S100. ^{19}F NMR spectrum ($CDCl_3$, 376 MHz) of **3am.**

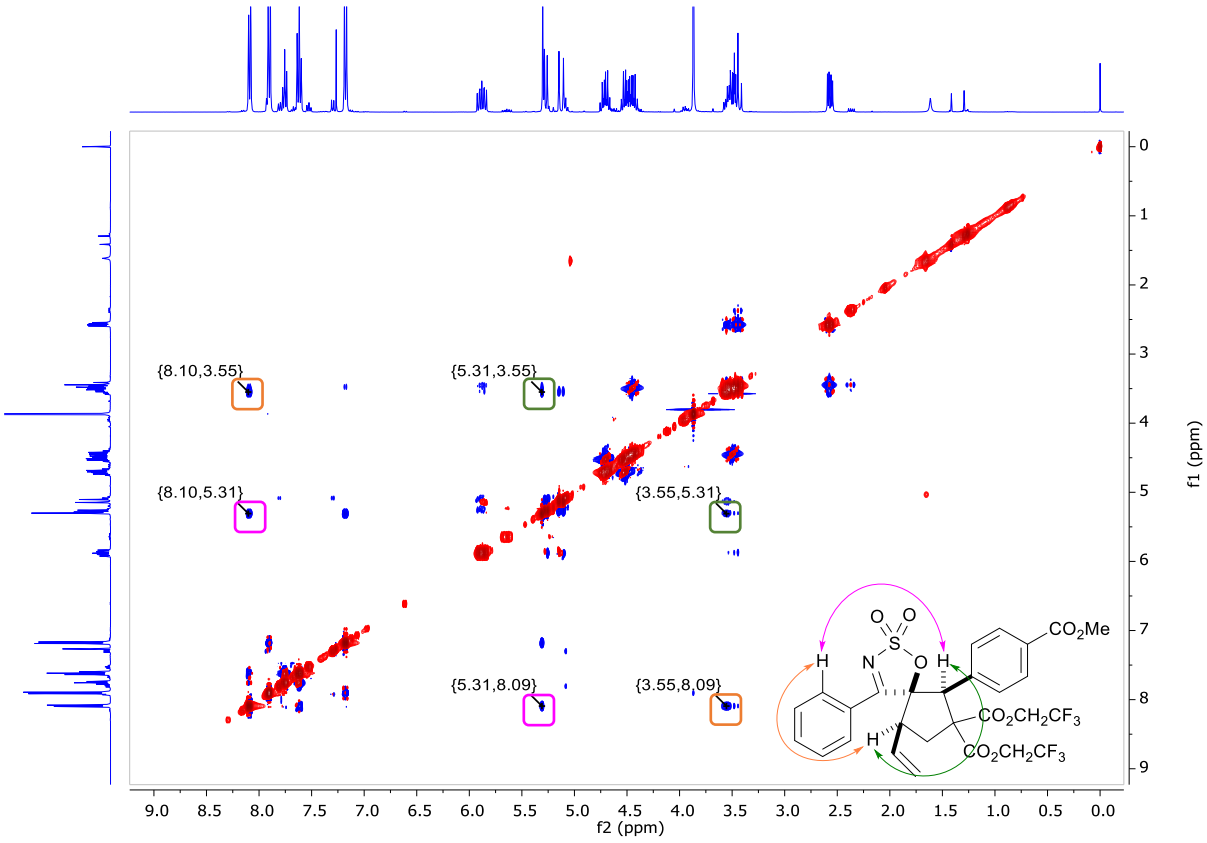


Figure S101. 2D NOESY spectrum ($CDCl_3$, 400 MHz) of **3am.**

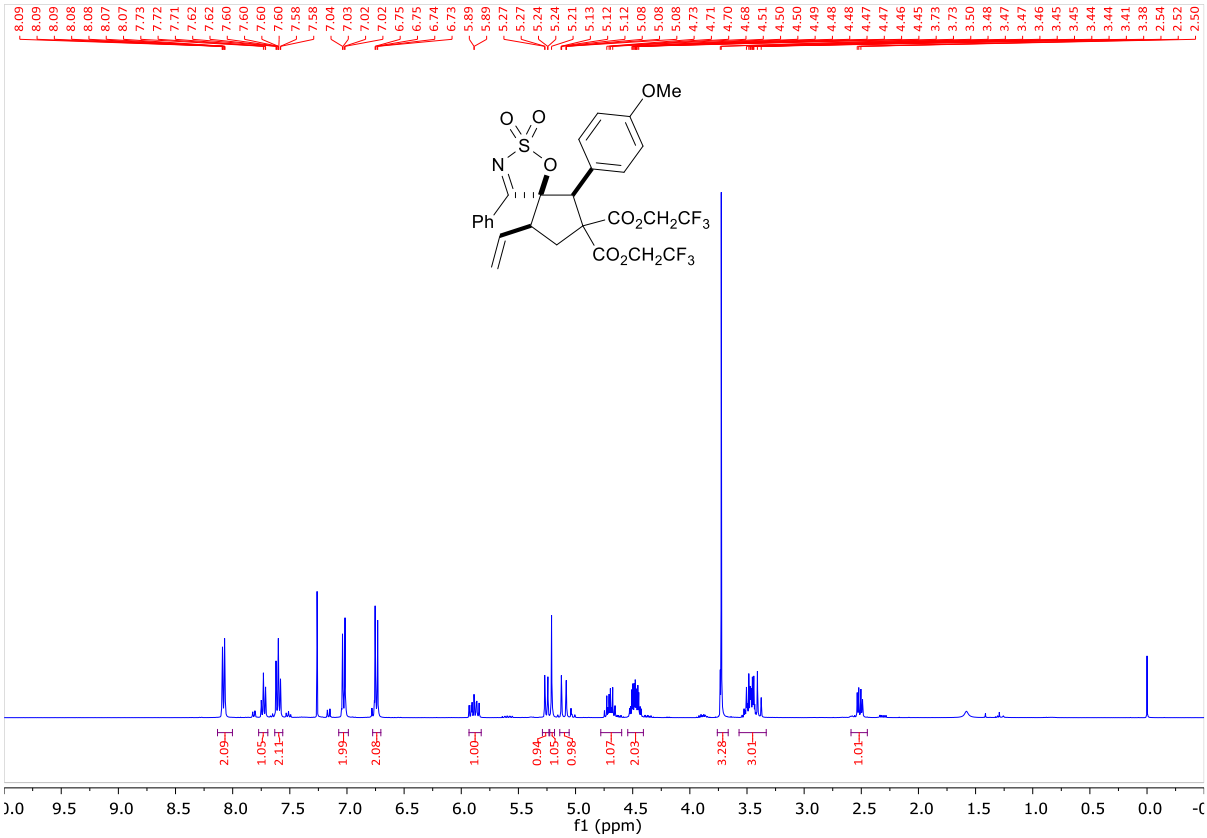


Figure S102. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of **3an.**

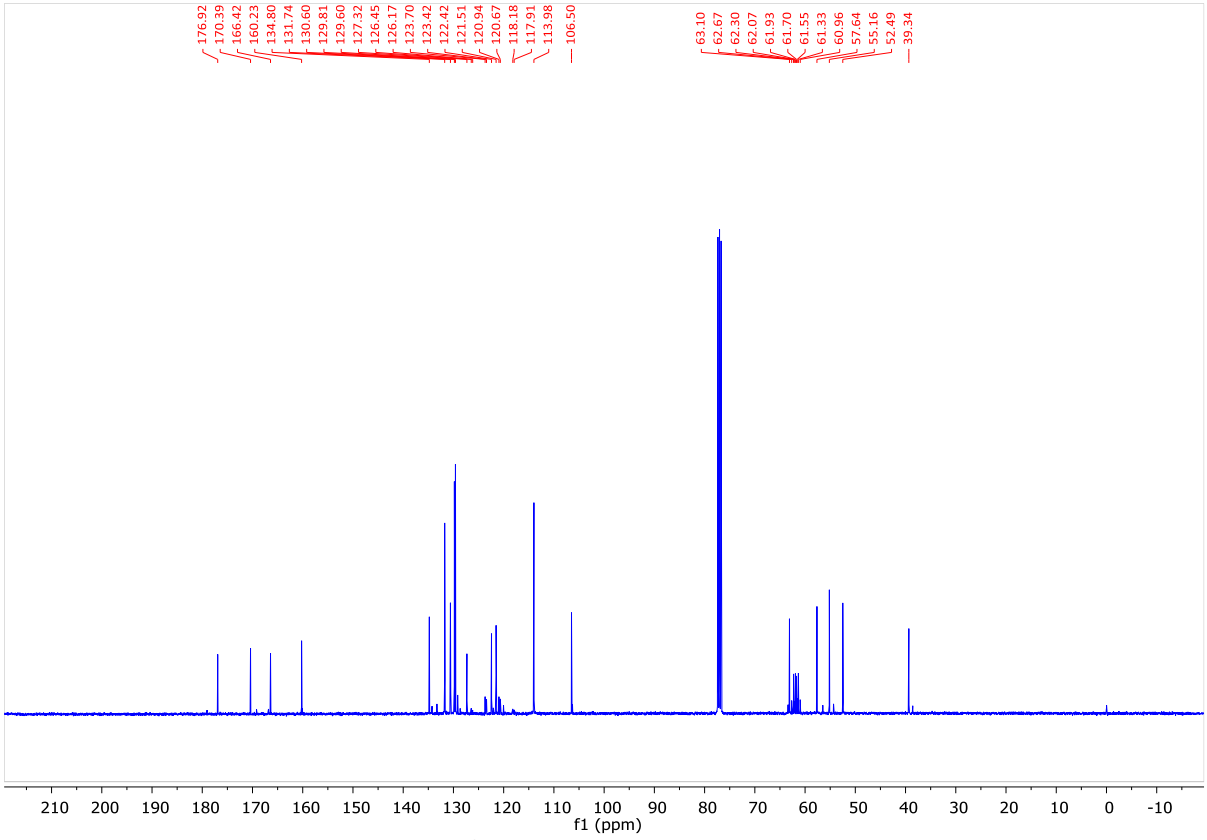


Figure S103. ^{13}C NMR spectrum ($CDCl_3$, 100 MHz) of **3an**.

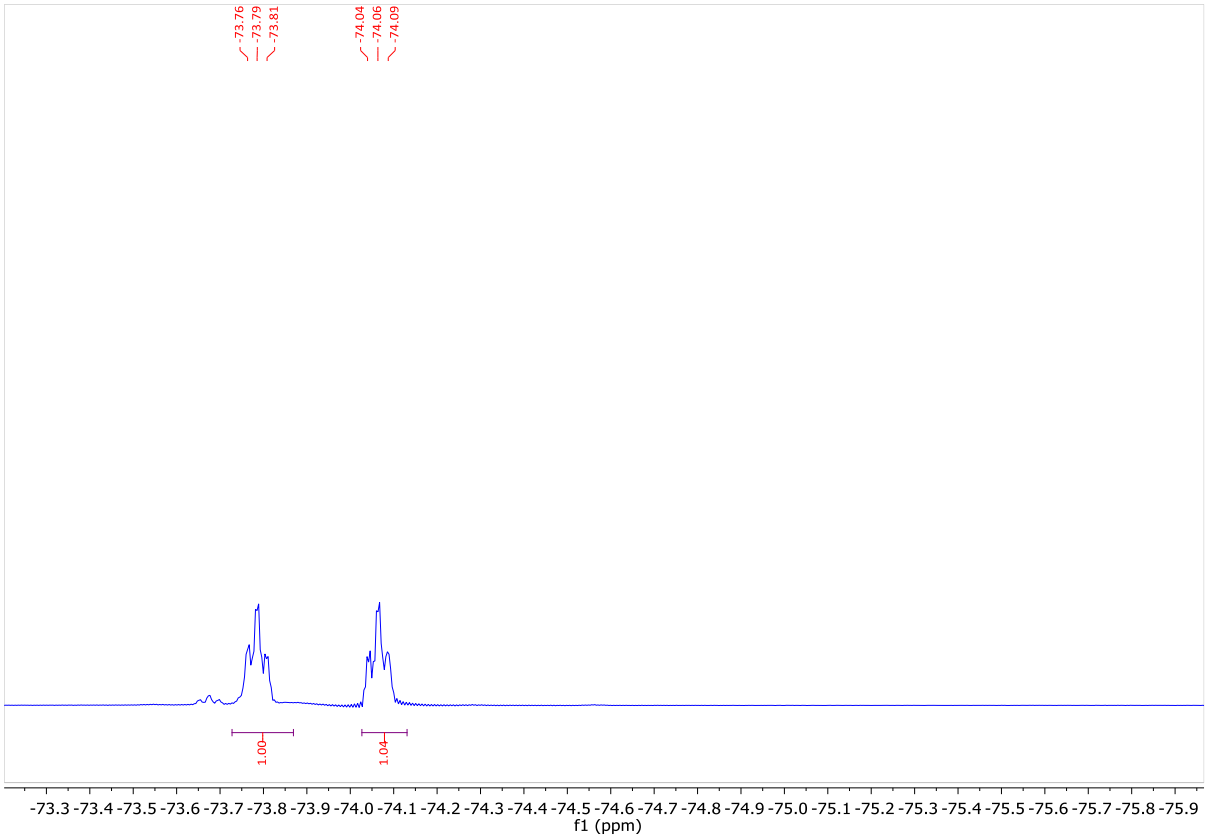


Figure S104. ^{19}F NMR spectrum ($CDCl_3$, 376 MHz) of **3an.**

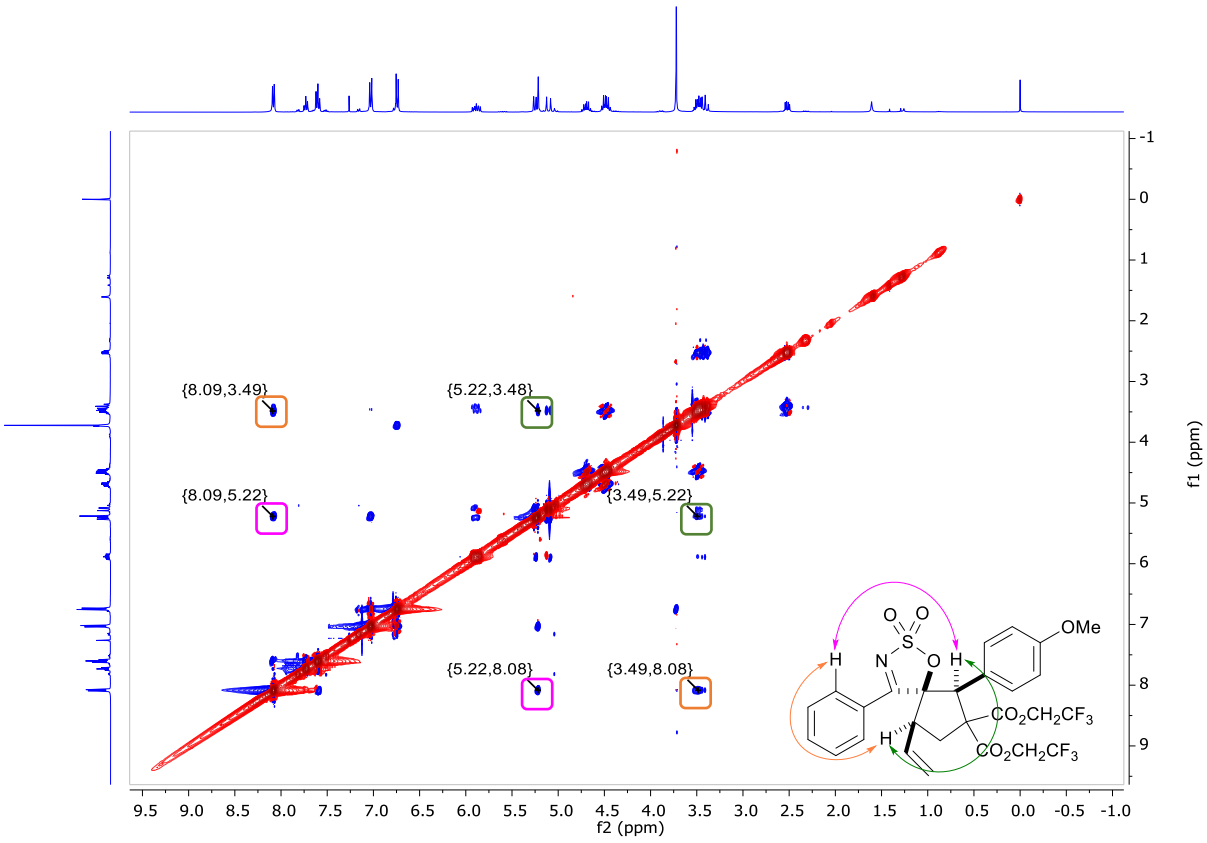


Figure S105. 2D NOESY spectrum ($CDCl_3$, 400 MHz) of **3an.**

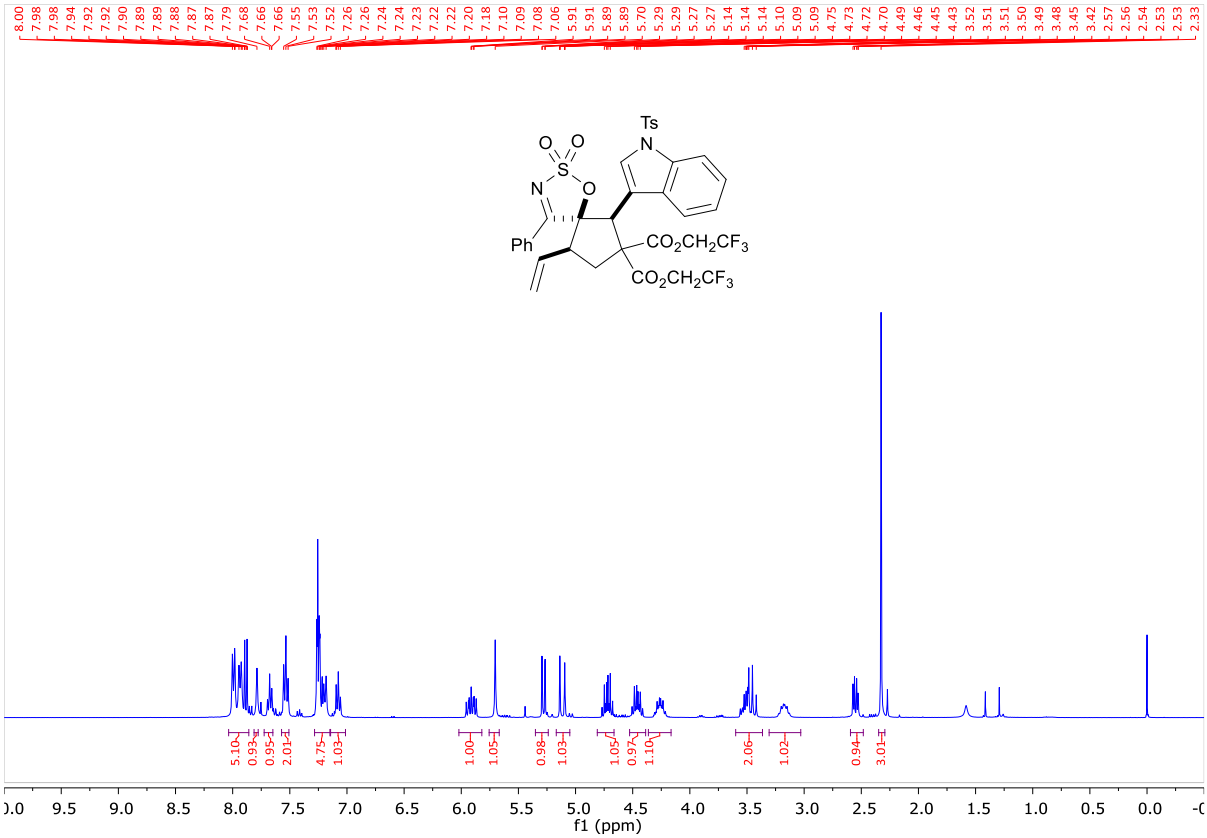


Figure S106. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of **3ao.**

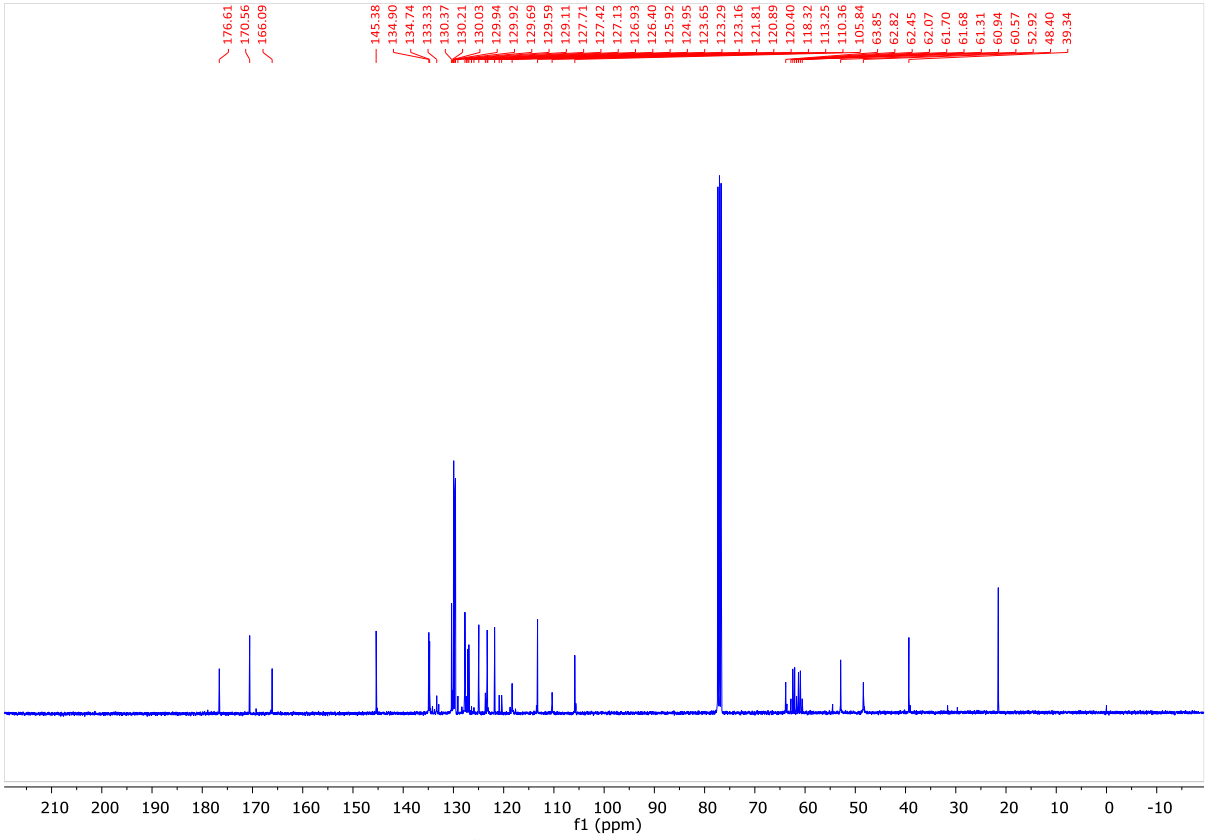


Figure S107. ^{13}C NMR spectrum ($CDCl_3$, 100 MHz) of **3ao**.

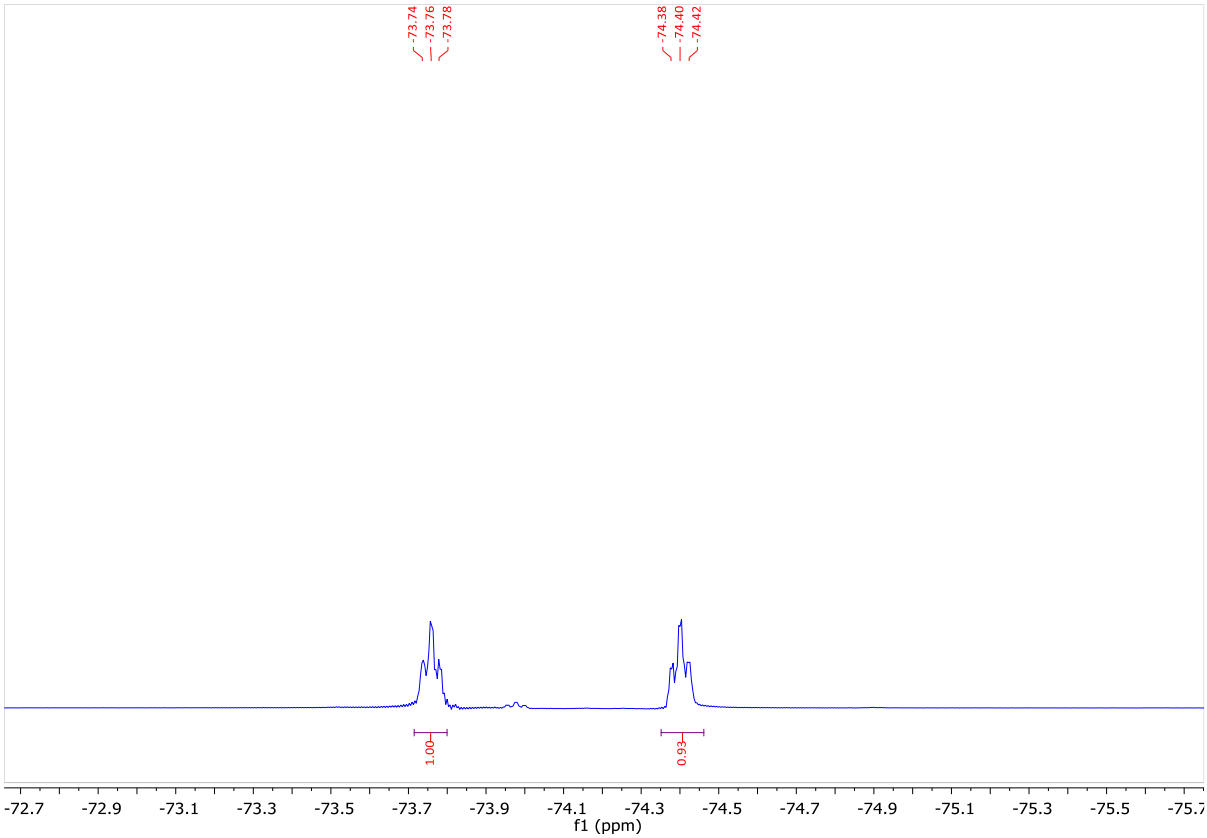


Figure S108. ^{19}F NMR spectrum ($CDCl_3$, 376 MHz) of **3ao.**

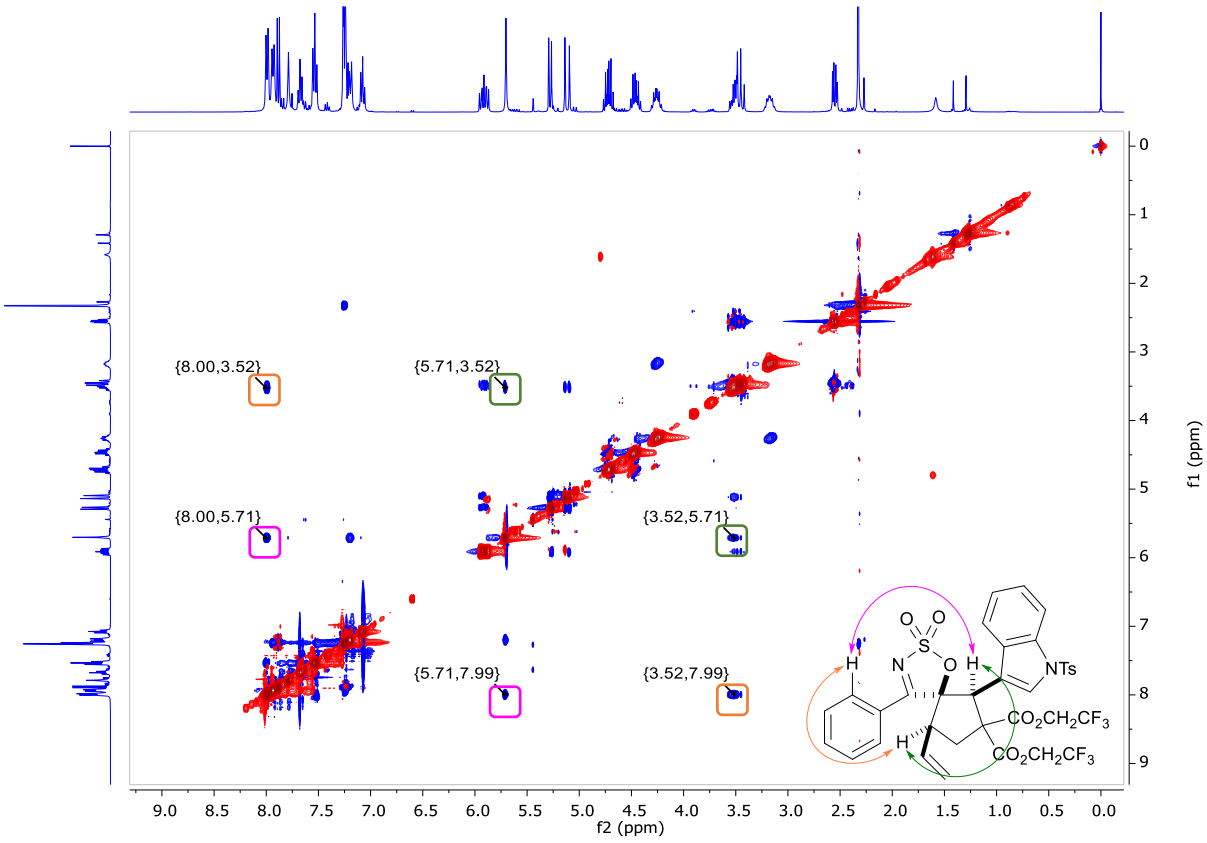


Figure S109. 2D NOESY spectrum ($CDCl_3$, 400 MHz) of **3ao.**

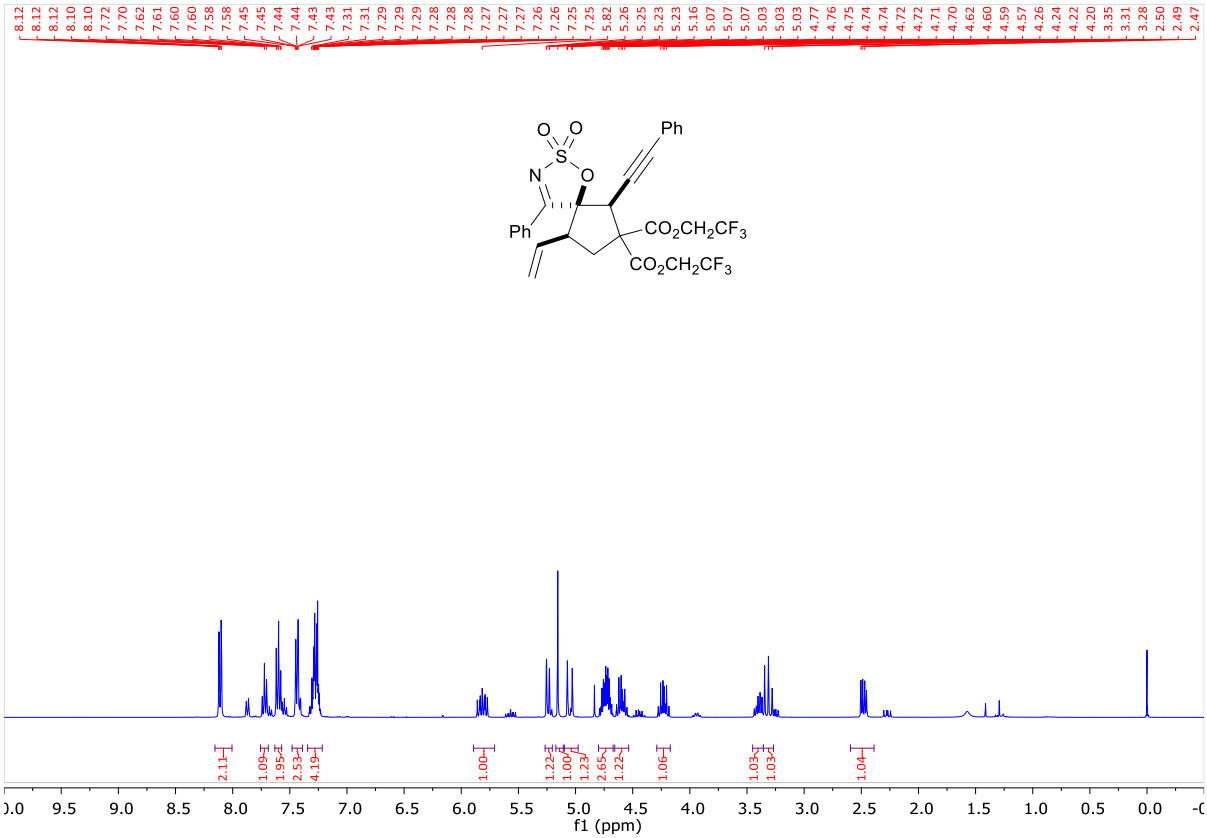


Figure S110. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of **3ap.**

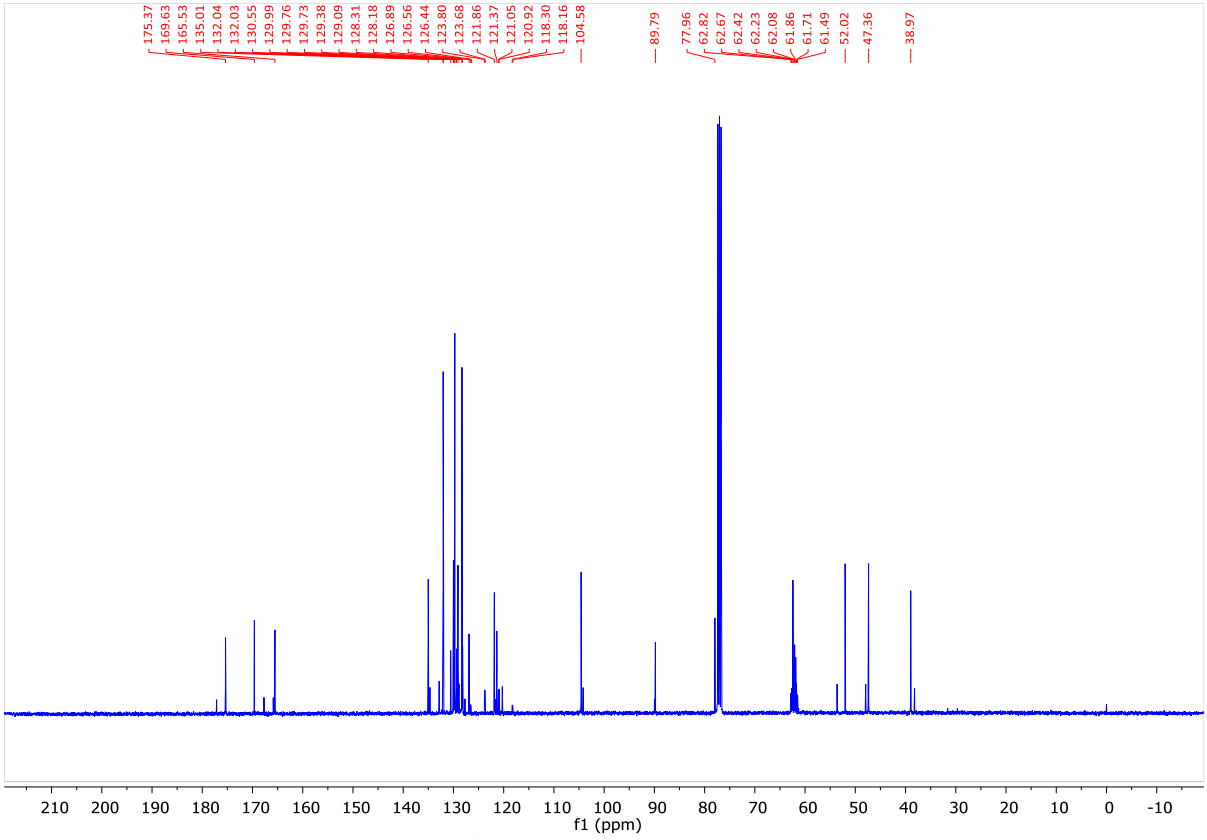


Figure S111. ^{13}C NMR spectrum ($CDCl_3$, 100 MHz) of **3ap**.

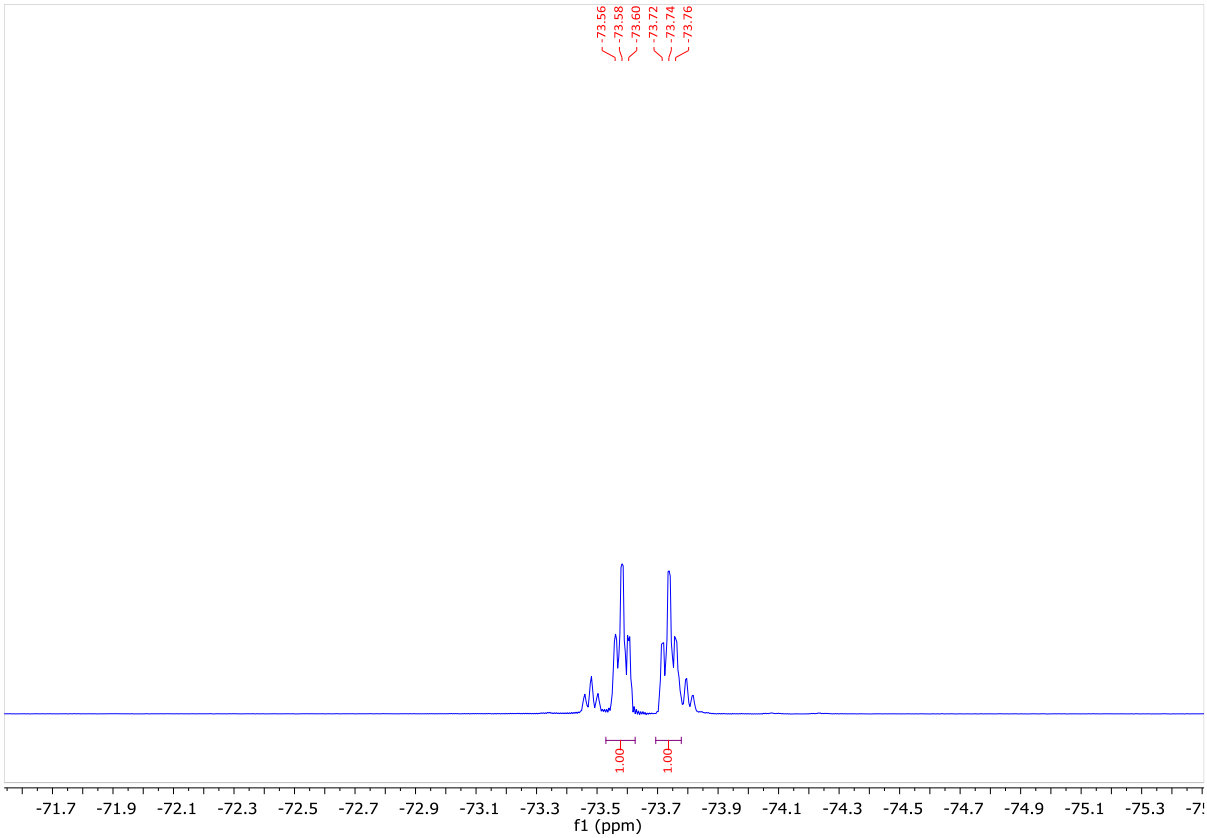


Figure S112. ^{19}F NMR spectrum ($CDCl_3$, 376 MHz) of **3ap.**

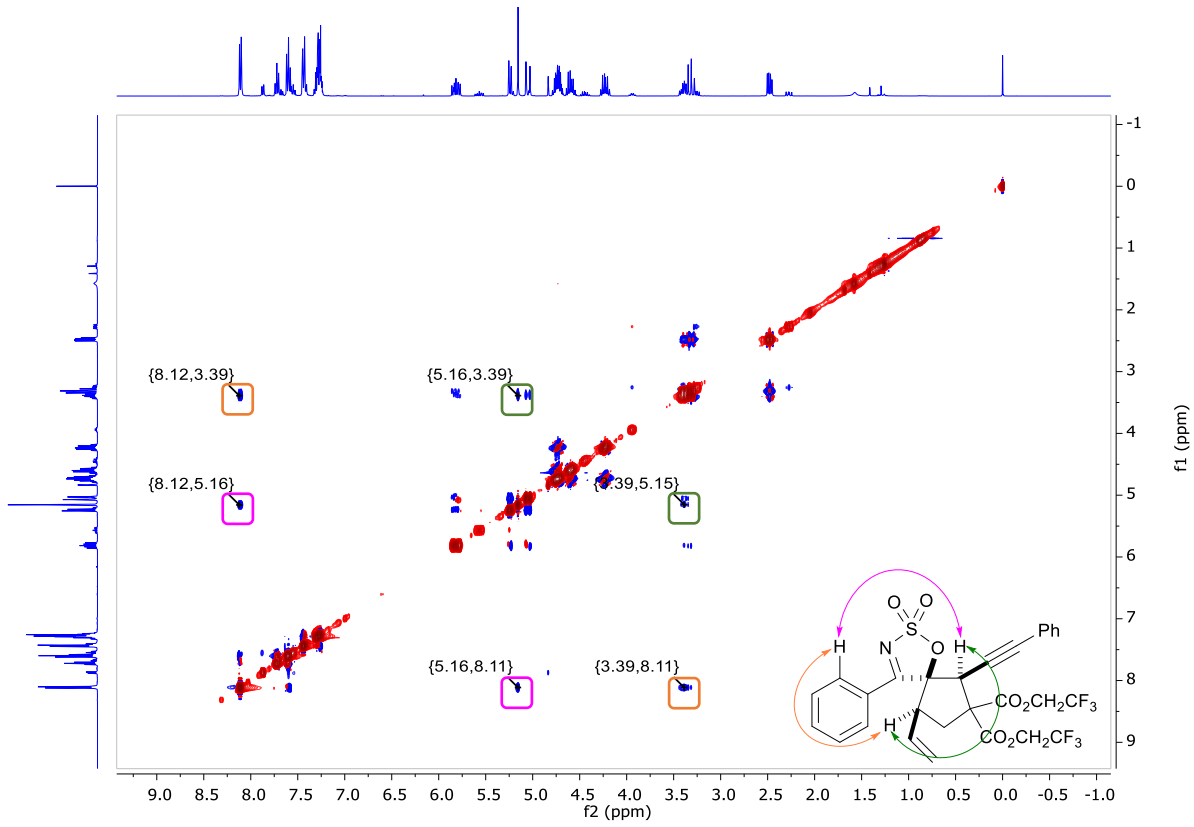


Figure S113. 2D NOESY spectrum ($CDCl_3$, 400 MHz) of **3ap.**

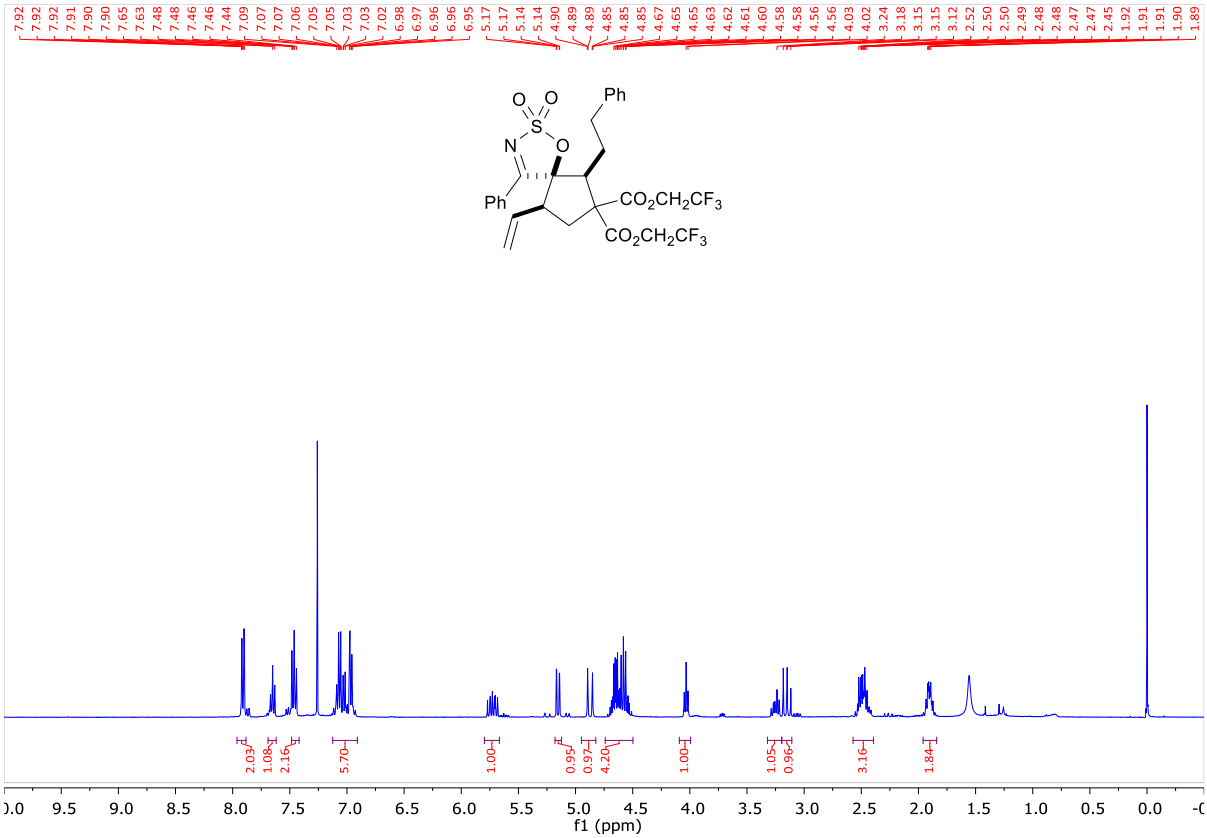


Figure S114. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of **3aq.**

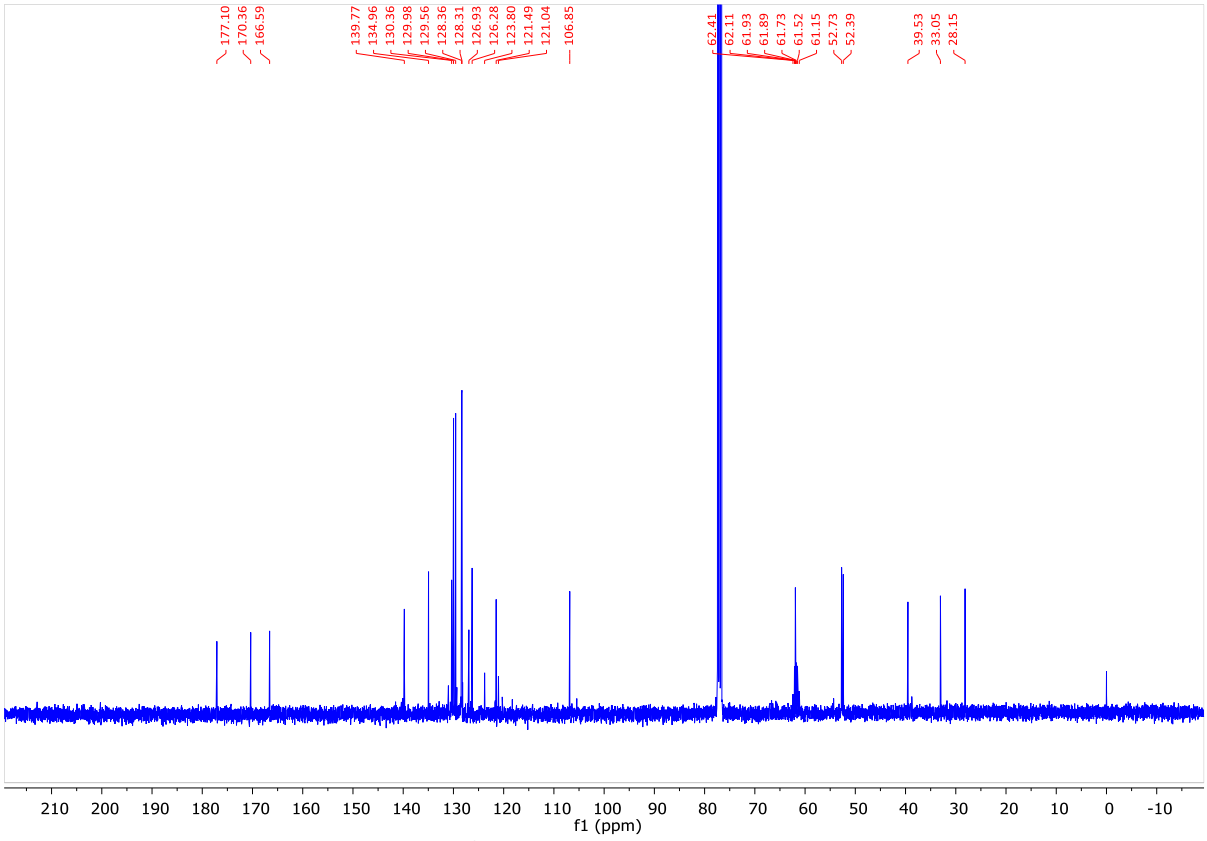


Figure S115. ^{13}C NMR spectrum ($CDCl_3$, 100 MHz) of **3aq**.

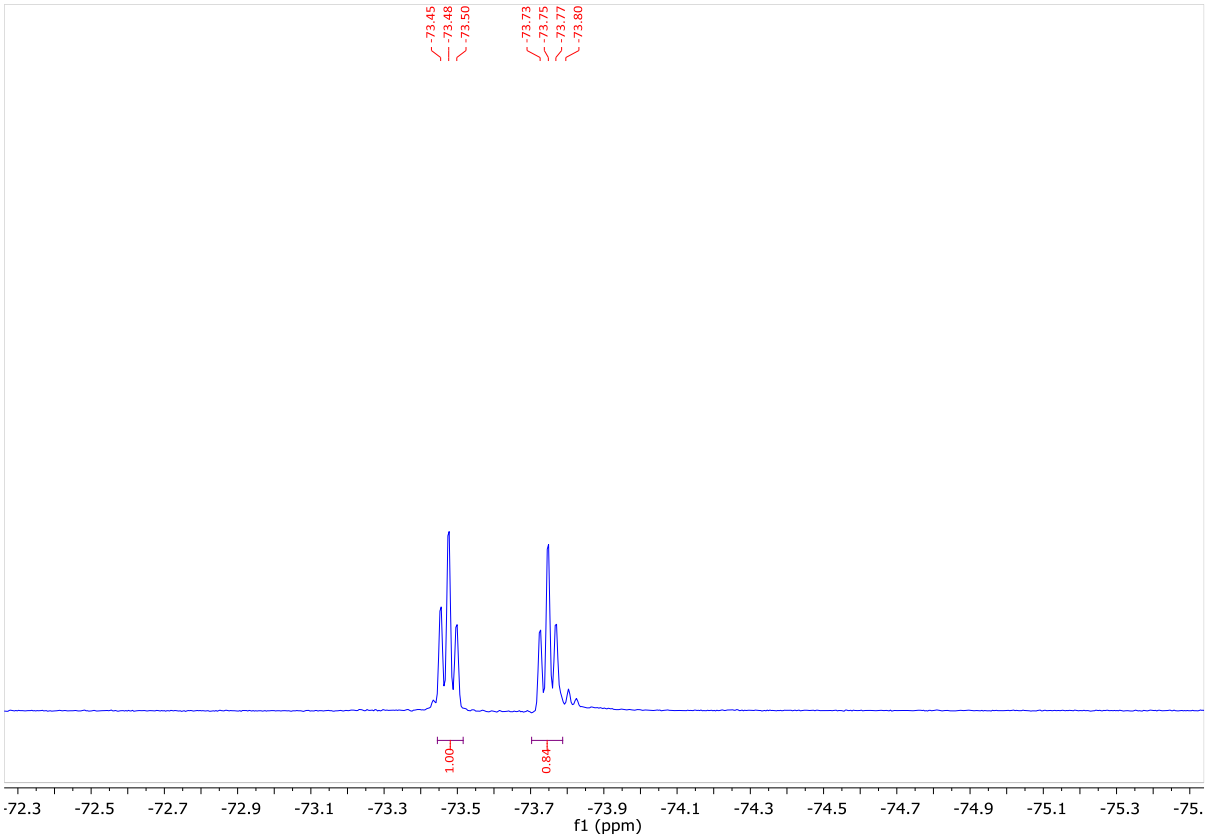


Figure S116. ^{19}F NMR spectrum ($CDCl_3$, 376 MHz) of **3aq.**

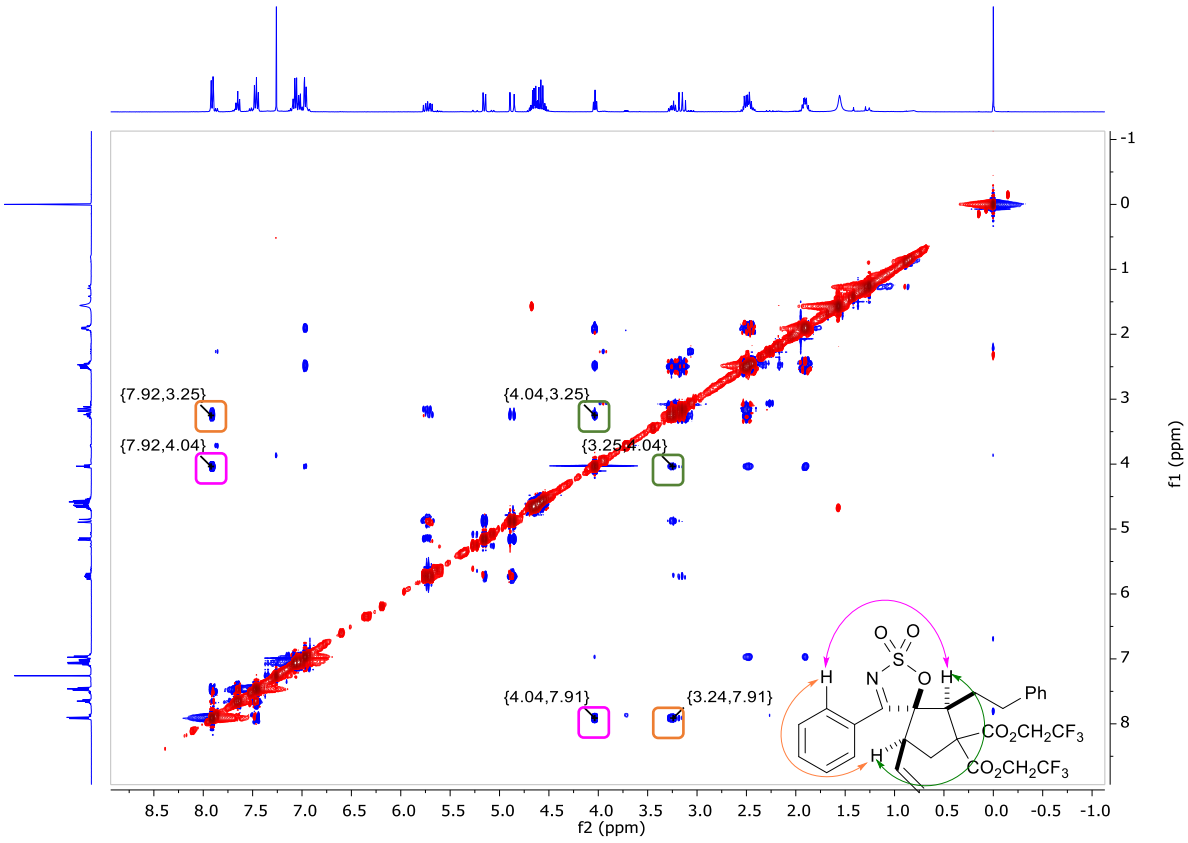


Figure S117. 2D NOESY spectrum ($CDCl_3$, 400 MHz) of **3aq.**

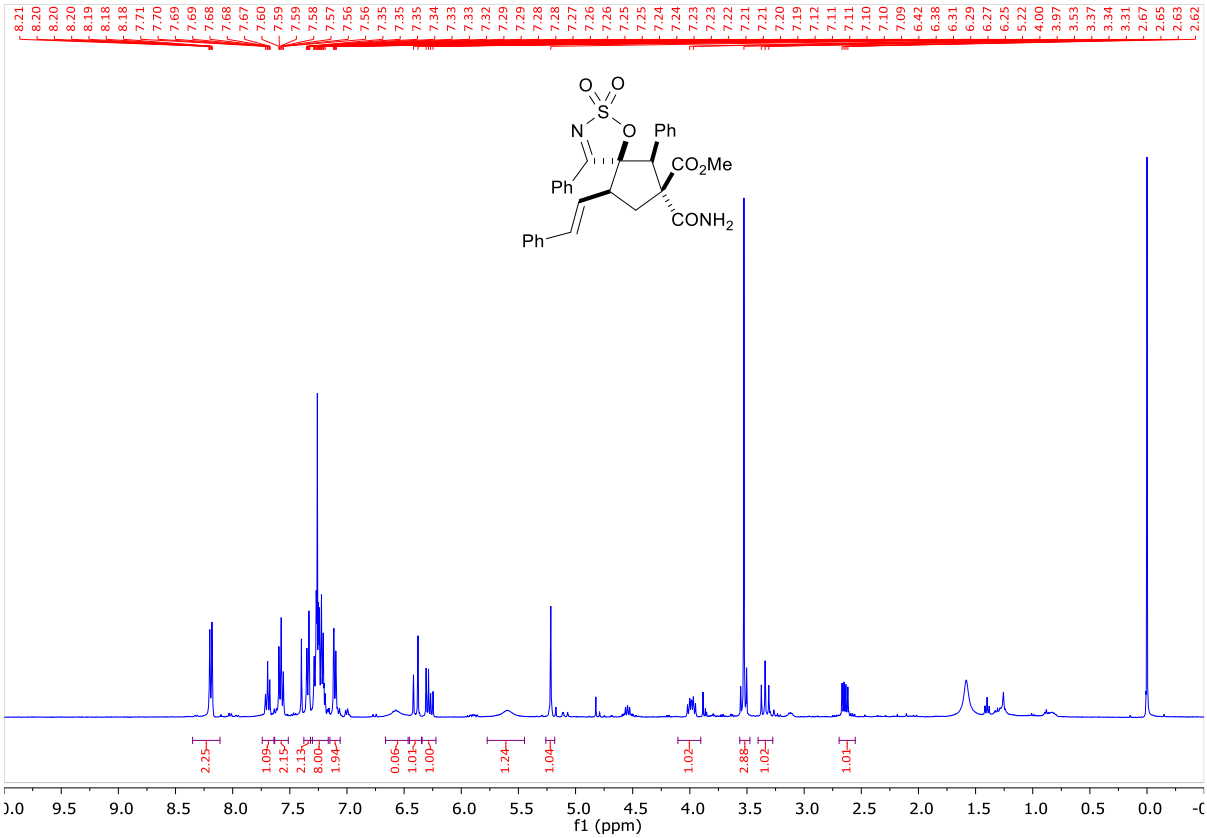


Figure S118. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of **4.**

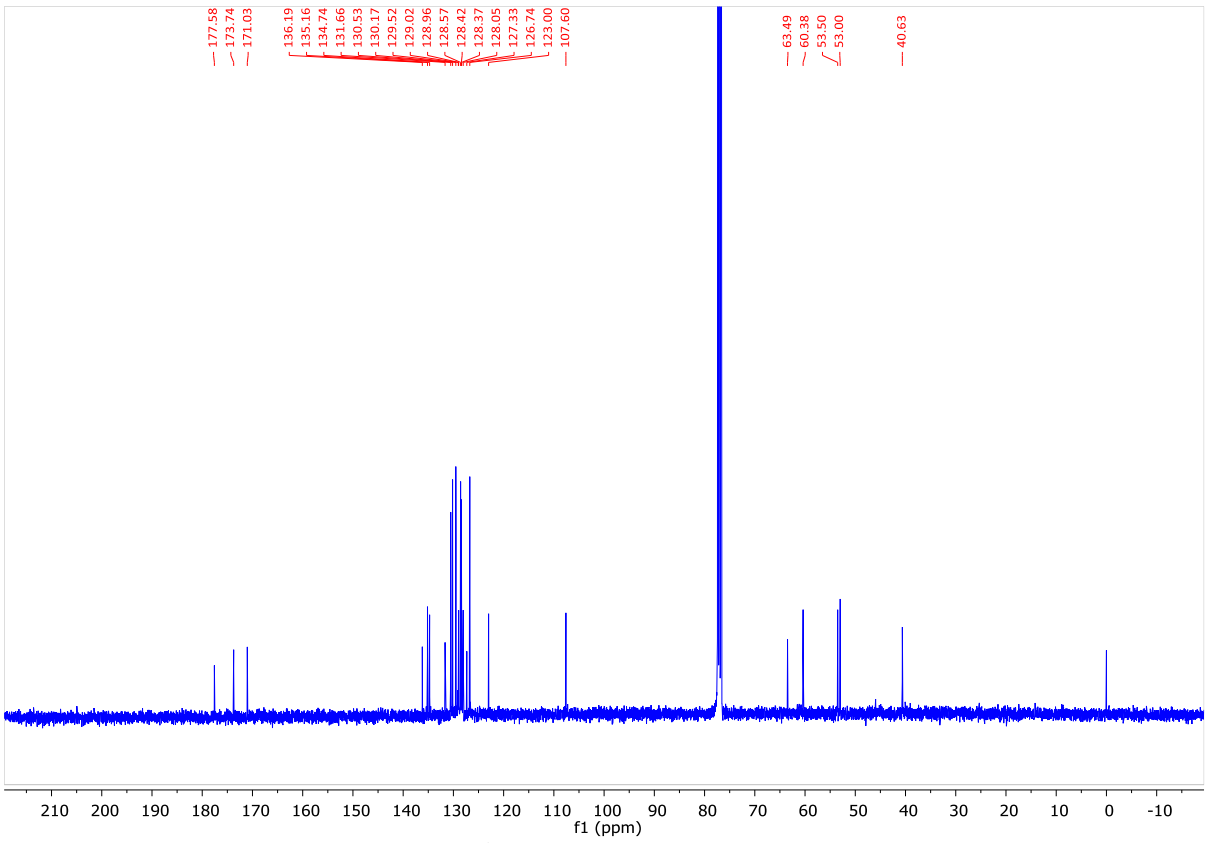


Figure S119. ^{13}C NMR spectrum ($CDCl_3$, 100 MHz) of **4**.

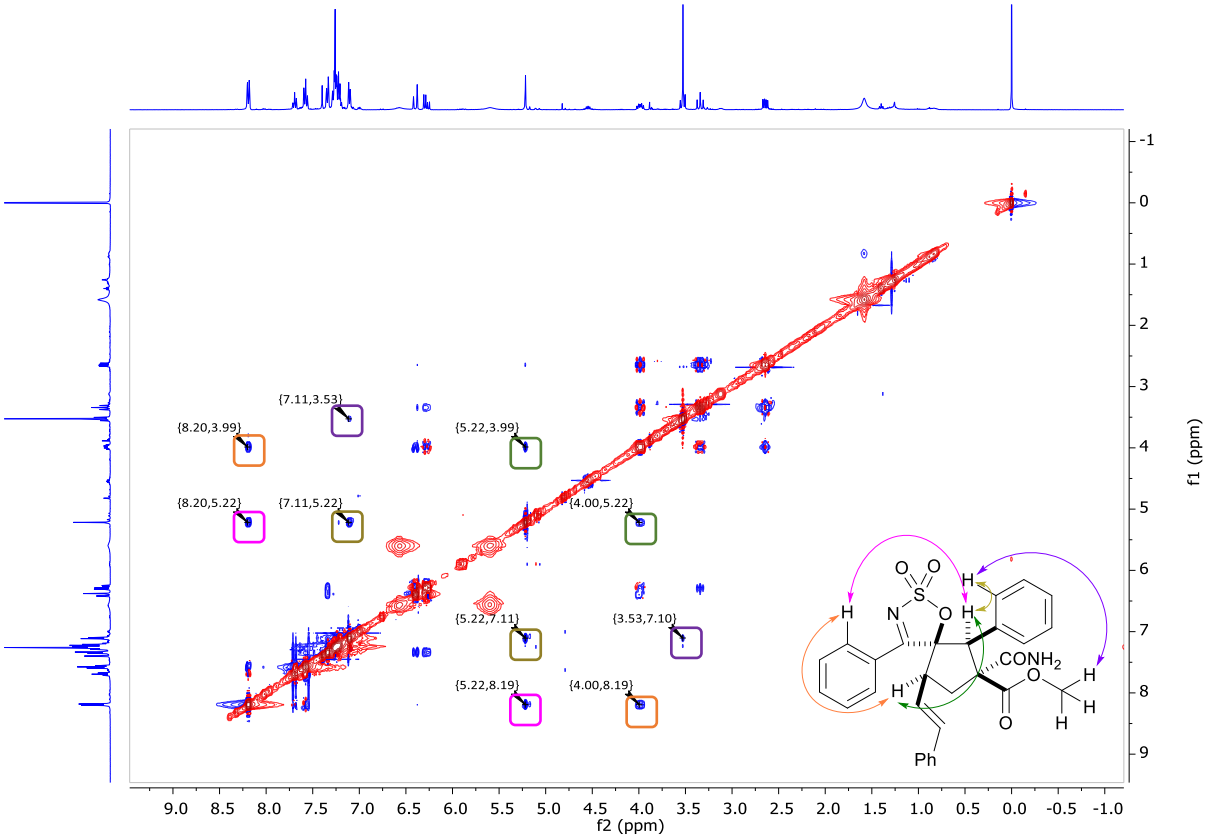


Figure S120. 2D NOESY spectrum ($CDCl_3$, 400 MHz) of **4.**

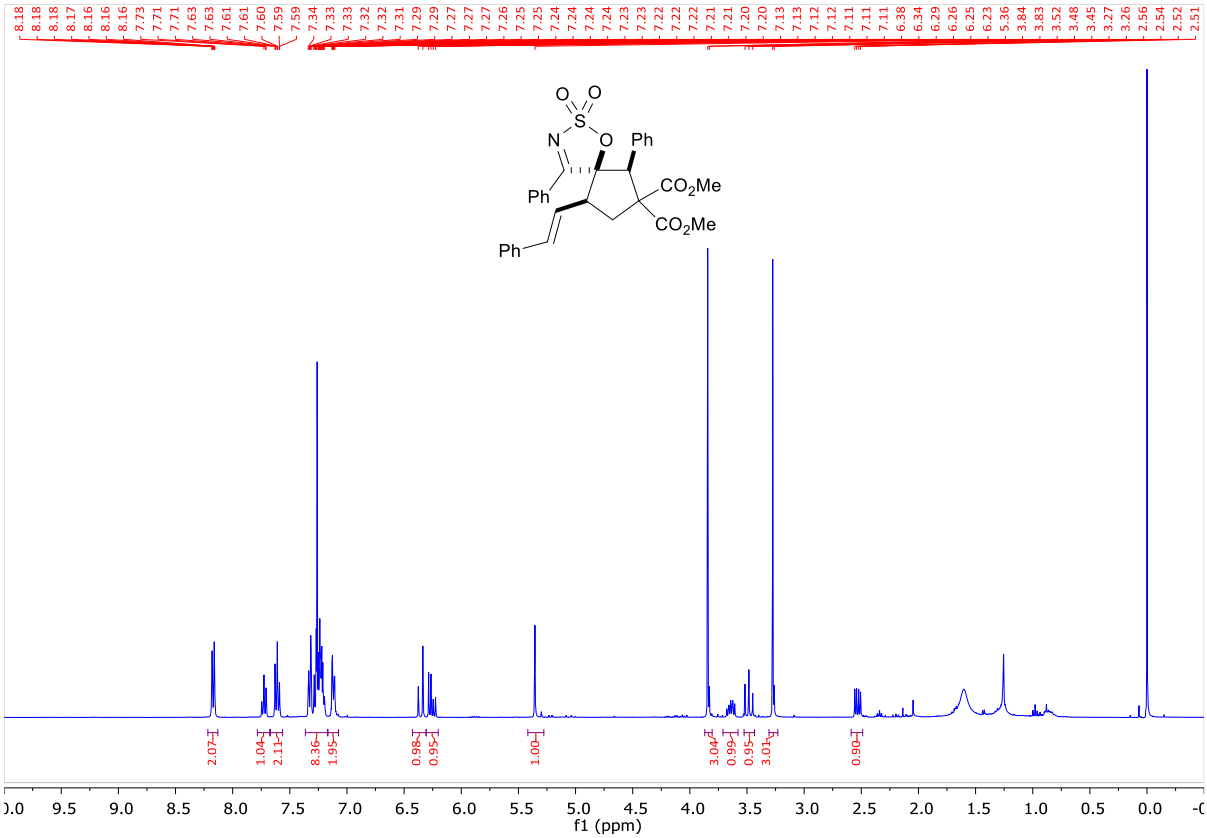


Figure S121. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of **7.**

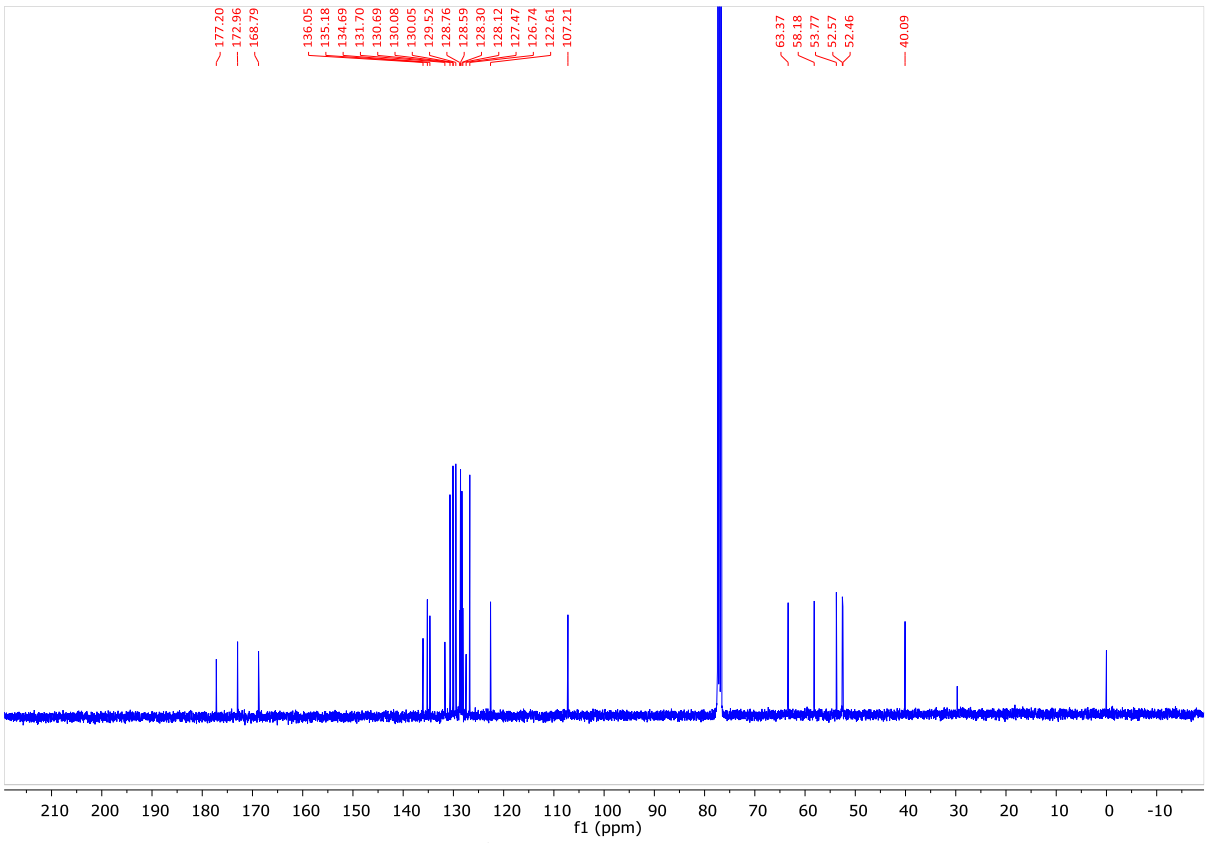


Figure S122. ^{13}C NMR spectrum ($CDCl_3$, 100 MHz) of **7.**

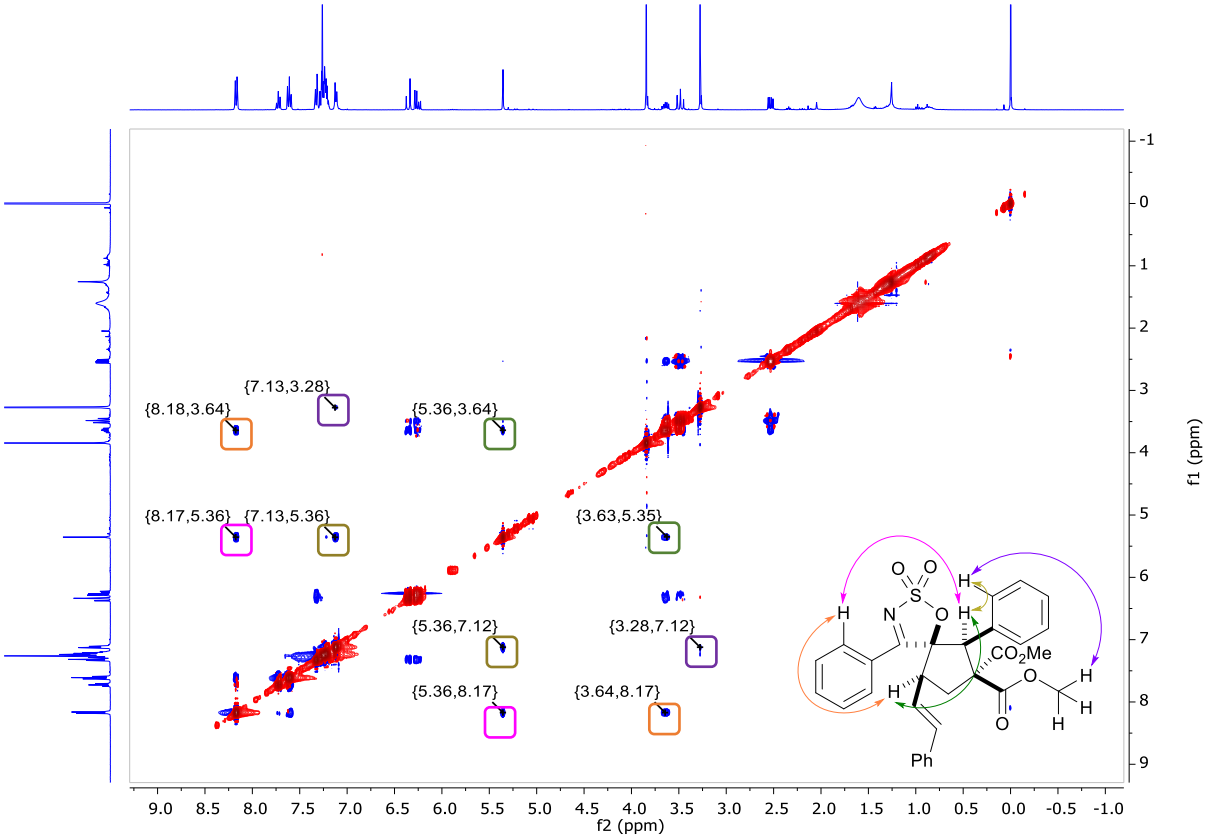


Figure S123. 2D NOESY spectrum ($CDCl_3$, 400 MHz) of **7.**

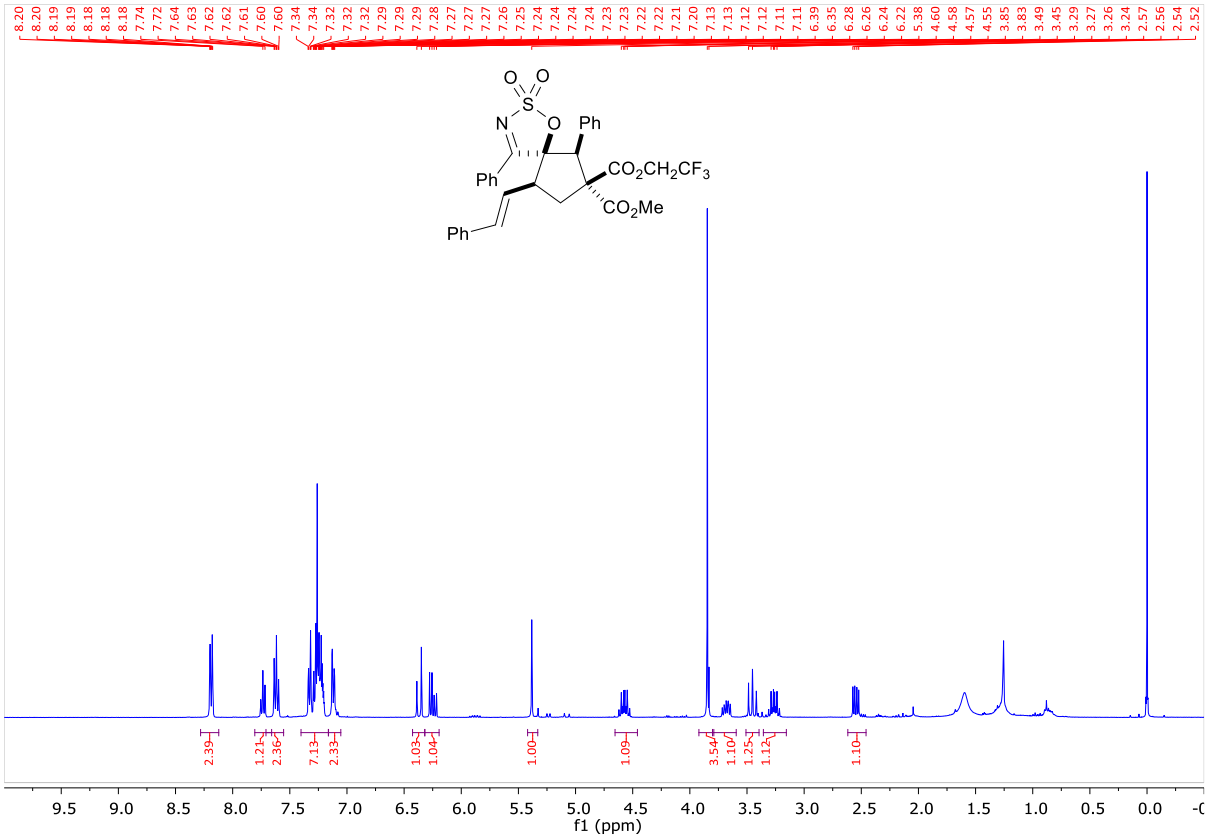


Figure S124. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of **9.**

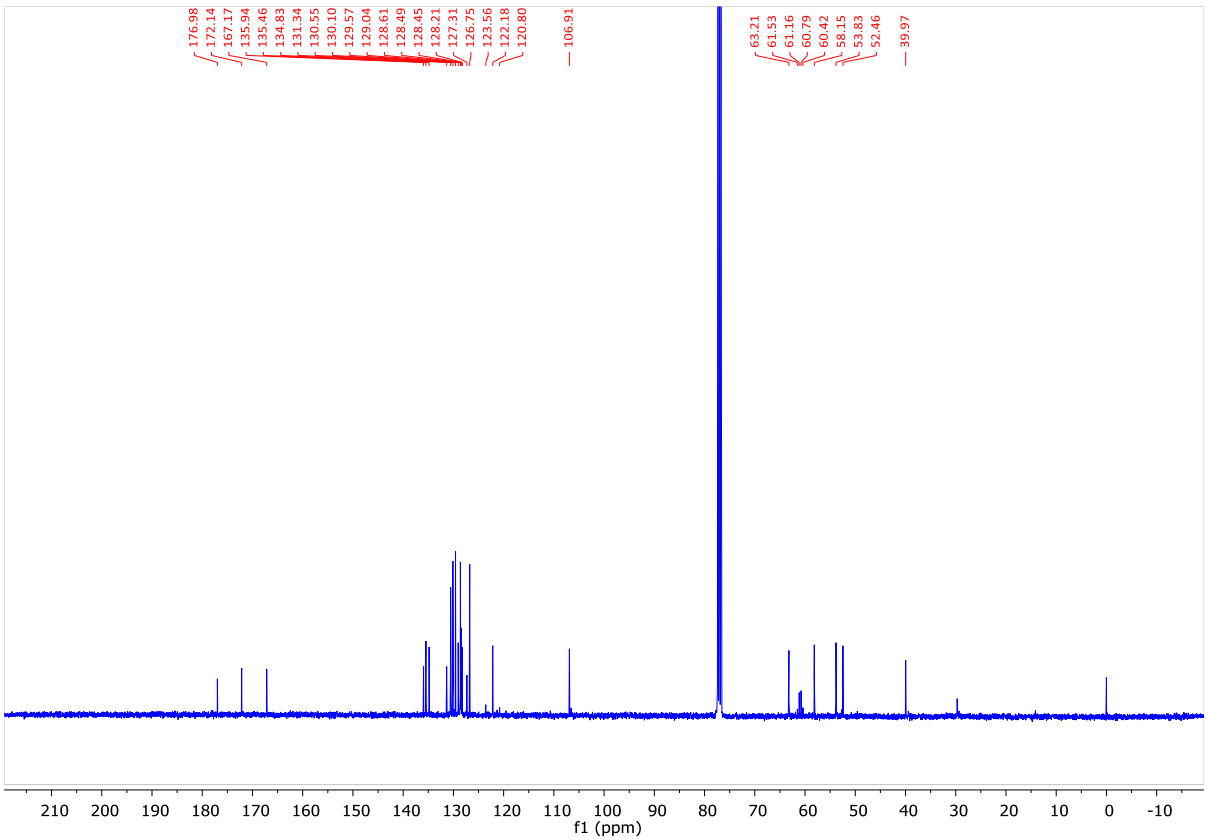


Figure S125. ^{13}C NMR spectrum ($CDCl_3$, 100 MHz) of **9.**

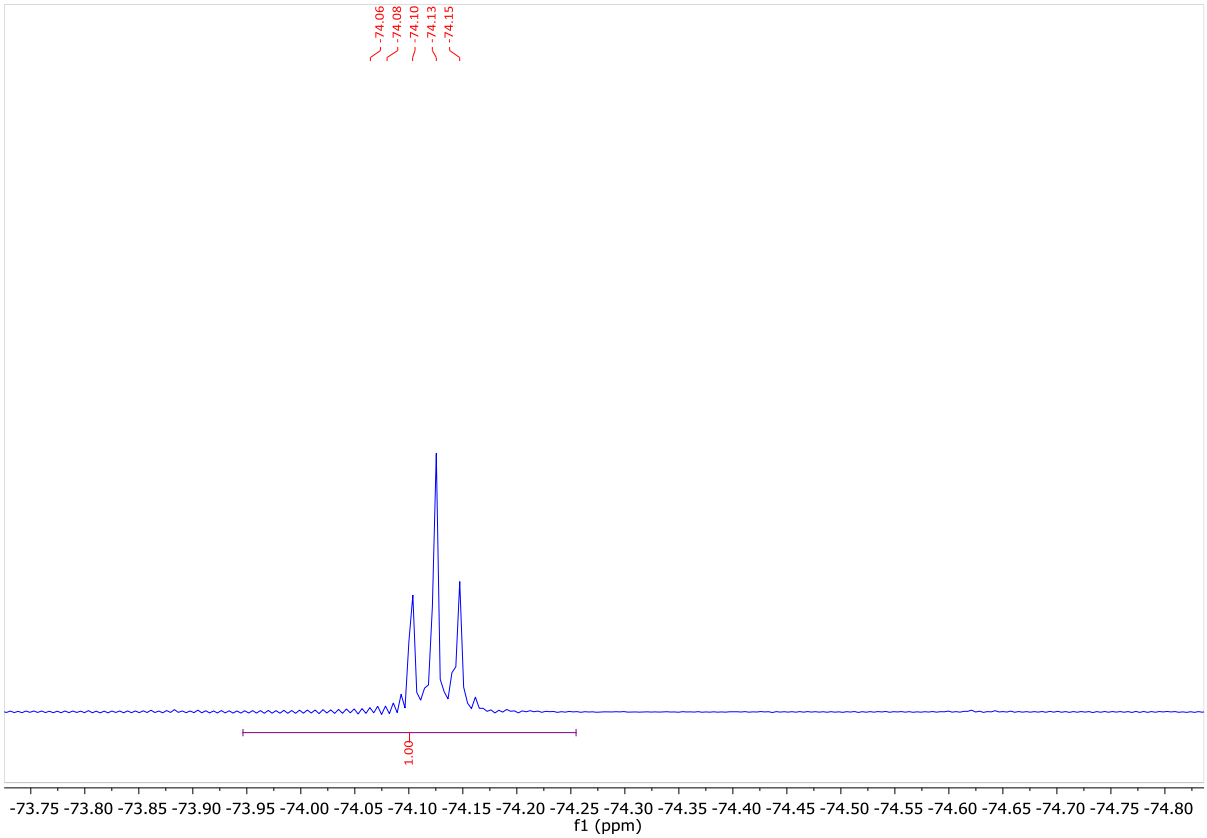


Figure S126. ^{19}F NMR spectrum ($CDCl_3$, 376 MHz) 9.

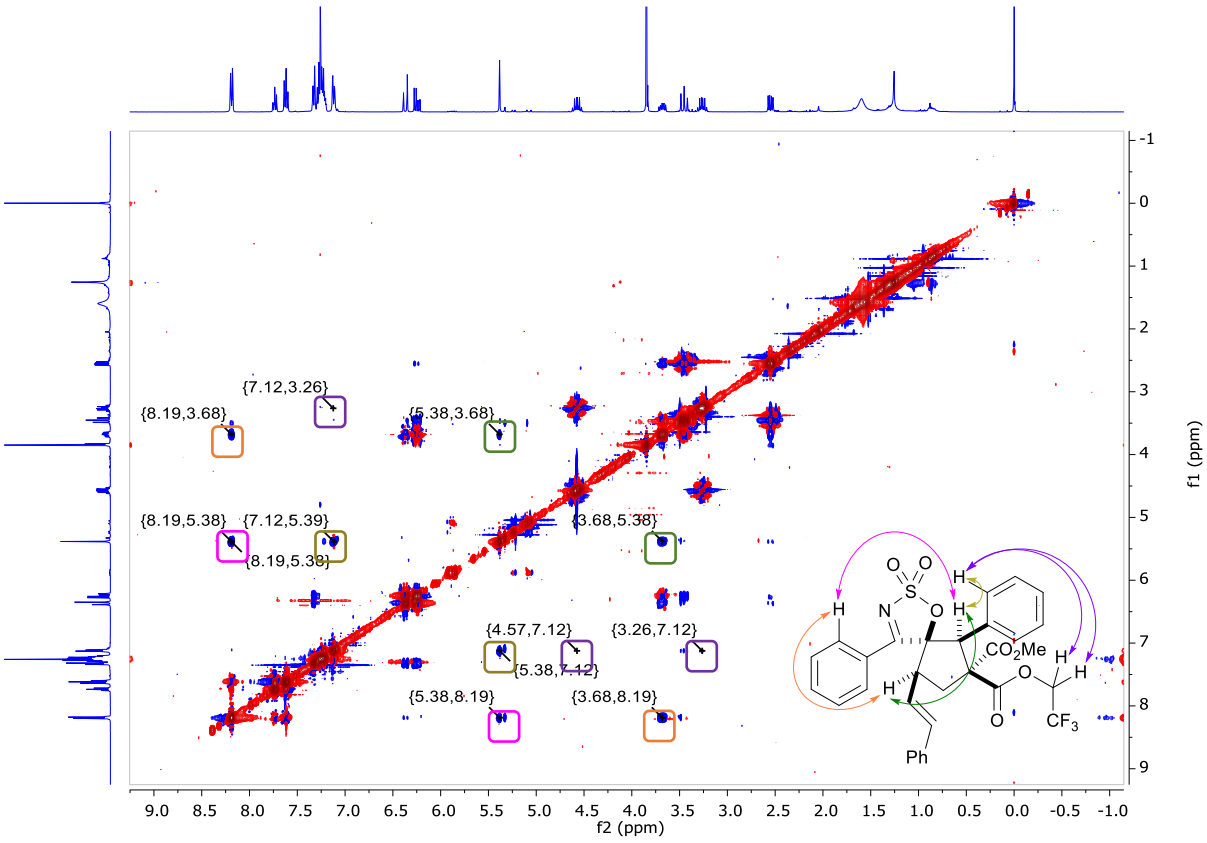


Figure S127. 2D NOESY spectrum ($CDCl_3$, 400 MHz) of **9.**

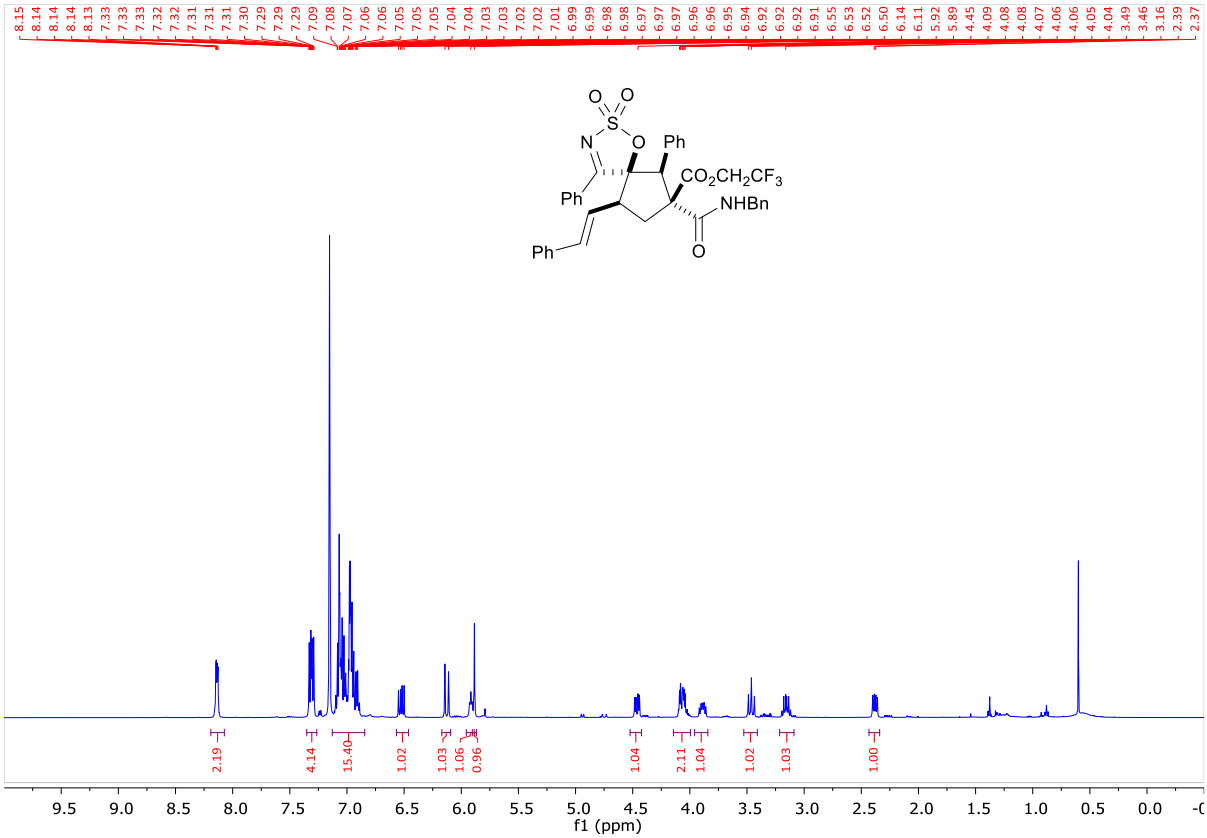


Figure S128. ^{1}H NMR spectrum (C_6D_6, 400 MHz) of **5.**

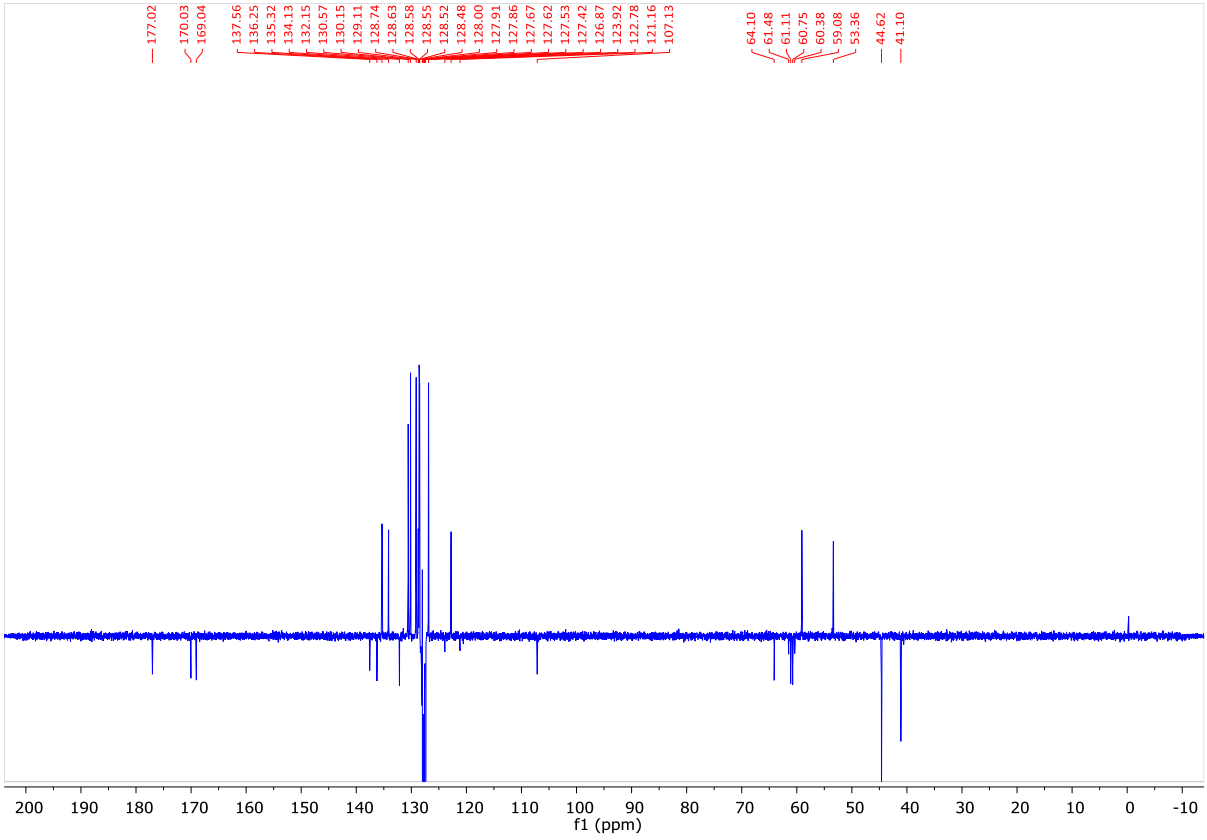


Figure S129. ^{13}C NMR spectrum (C_6D_6, 100 MHz) of **5**.

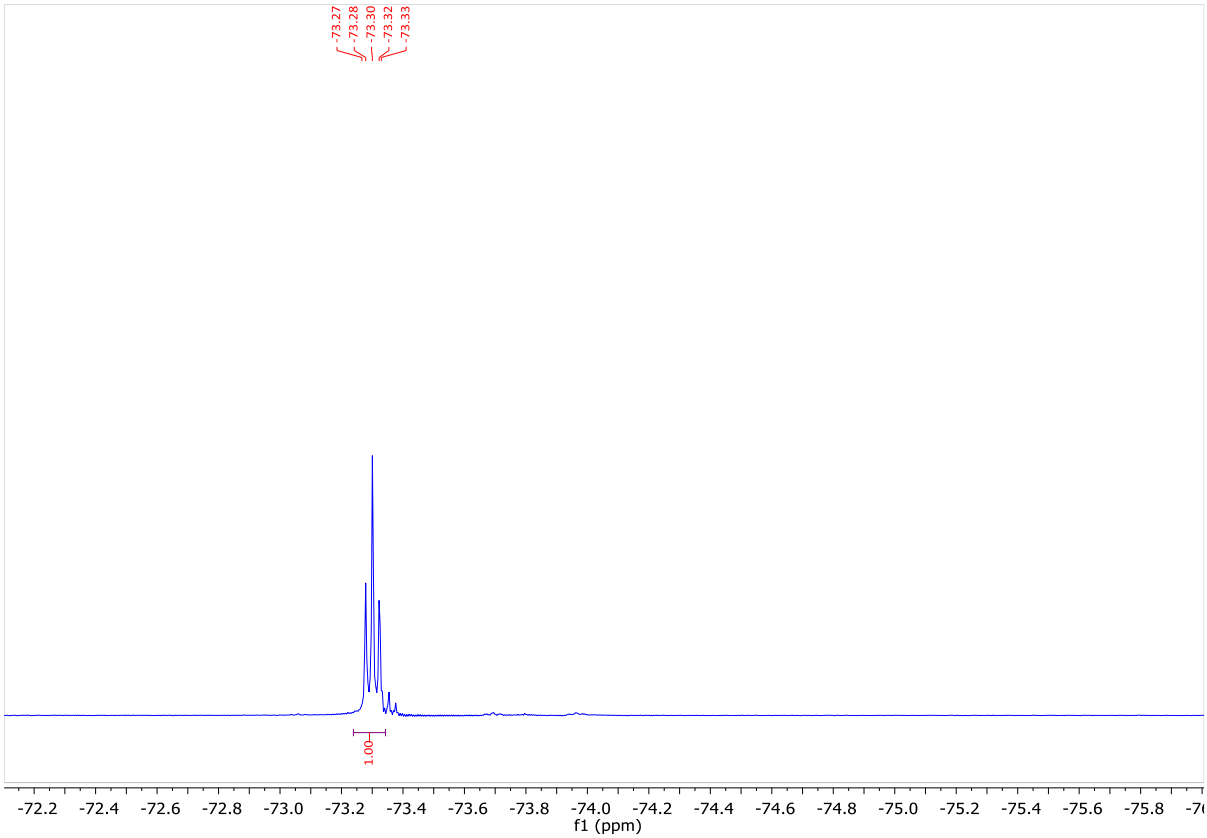


Figure S130. ^{19}F NMR spectrum (C_6D_6, 376 MHz) of **5.**

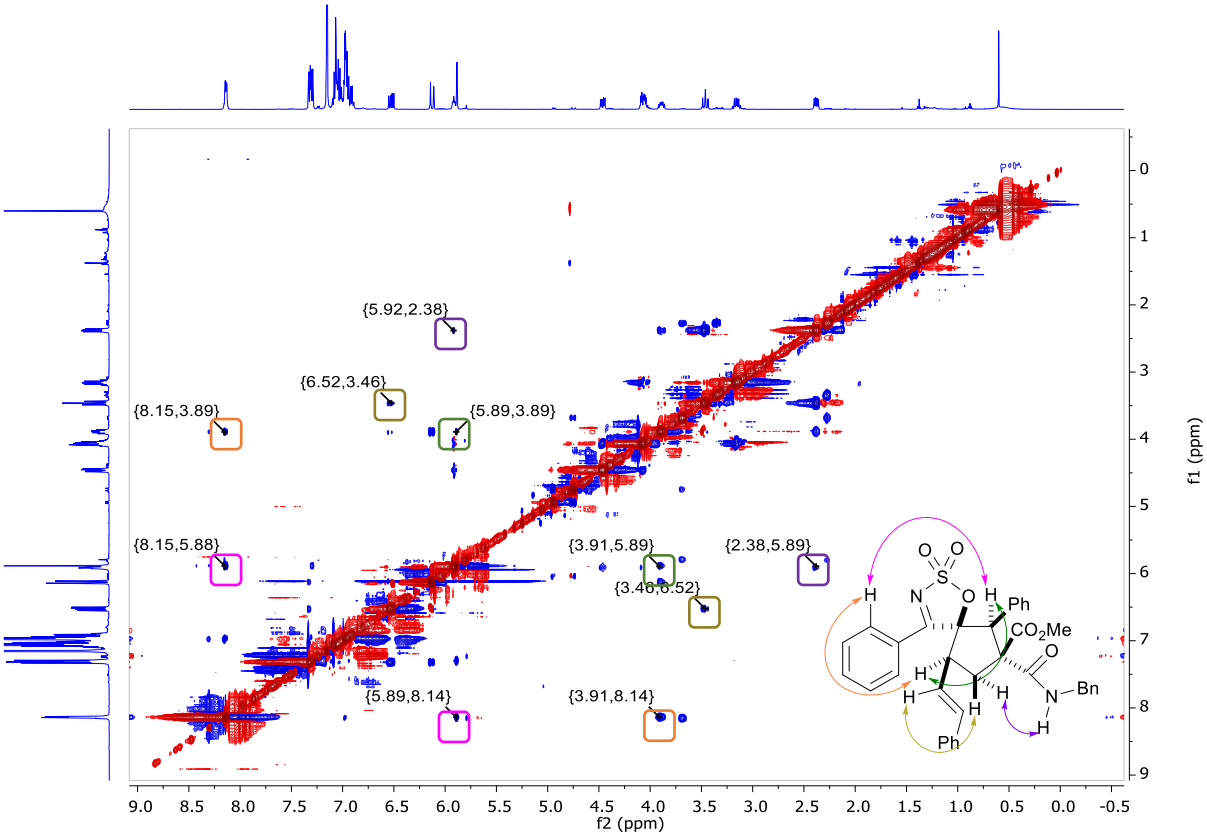


Figure S131. 2D NOESY spectrum (C_6D_6, 500 MHz) of **5.**

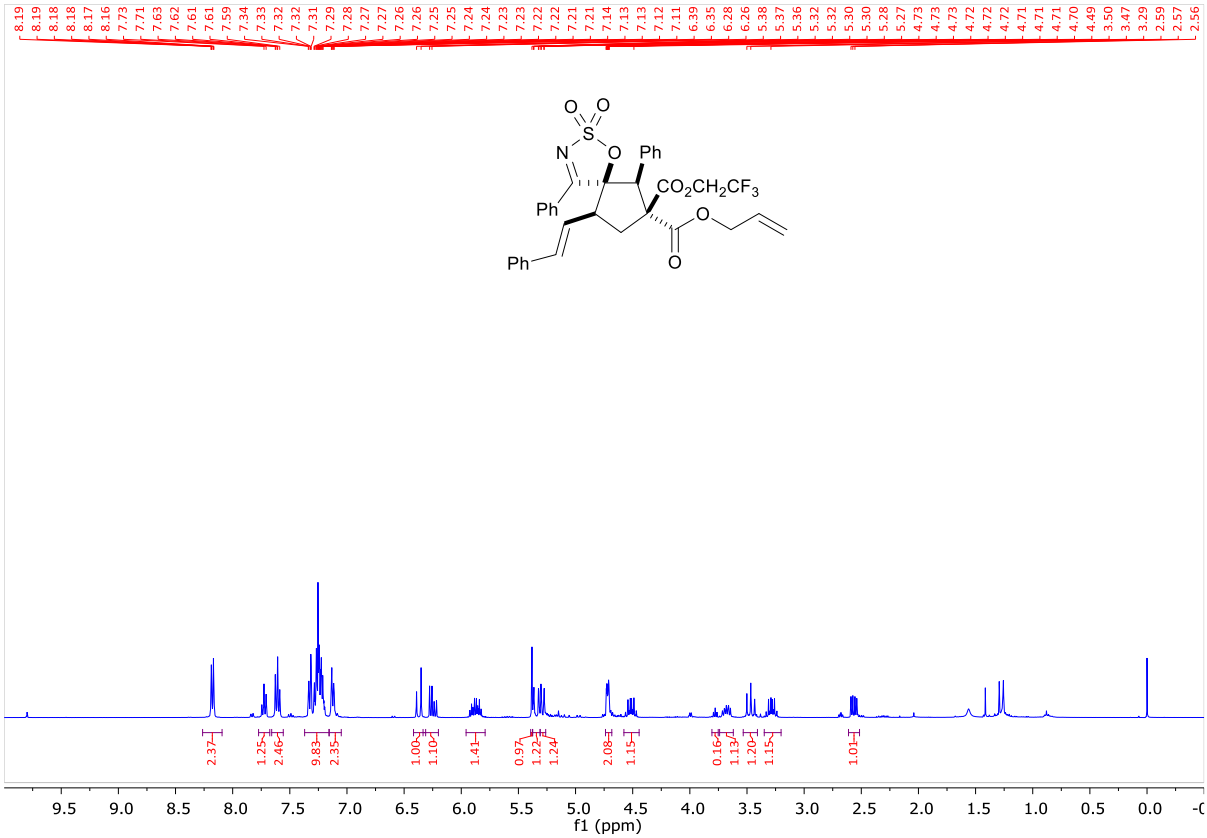


Figure S132. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of **6.**

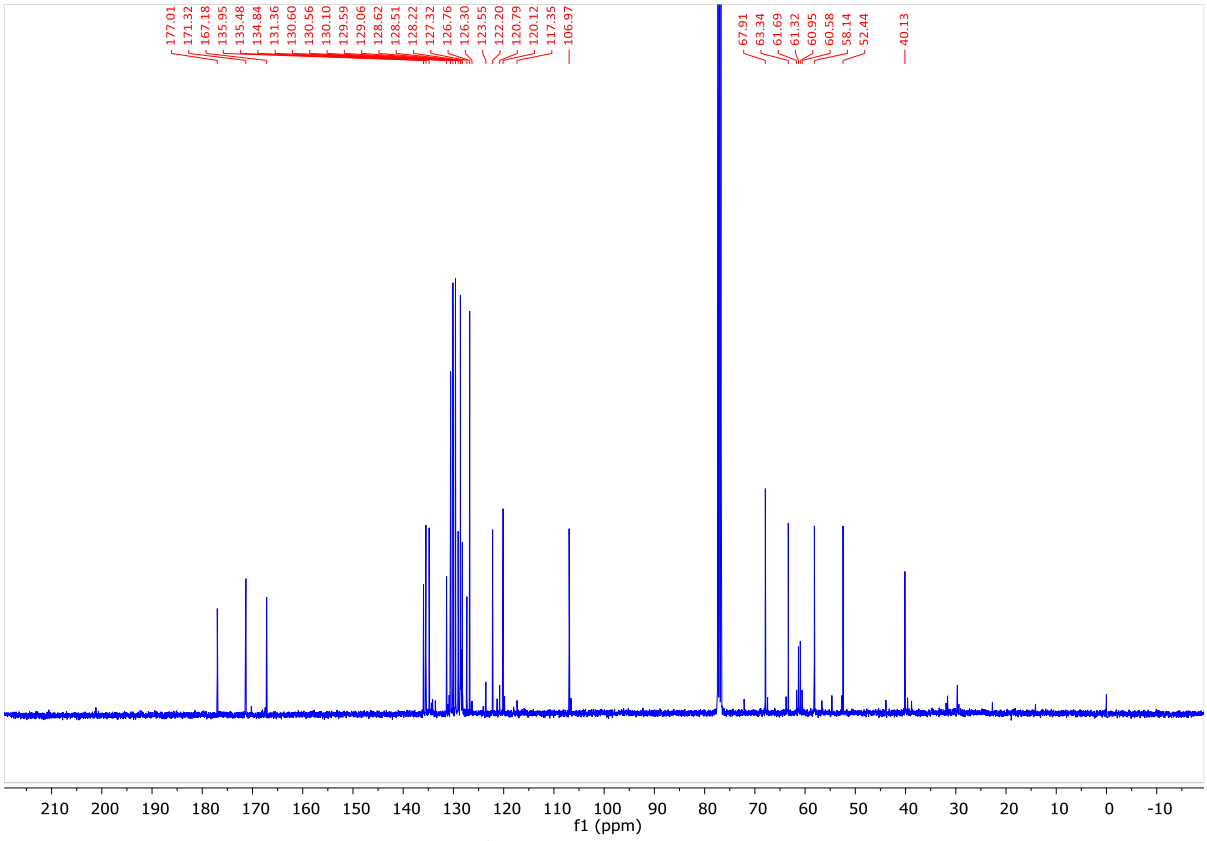


Figure S133. ^{13}C NMR spectrum ($CDCl_3$, 100 MHz) of **6**.

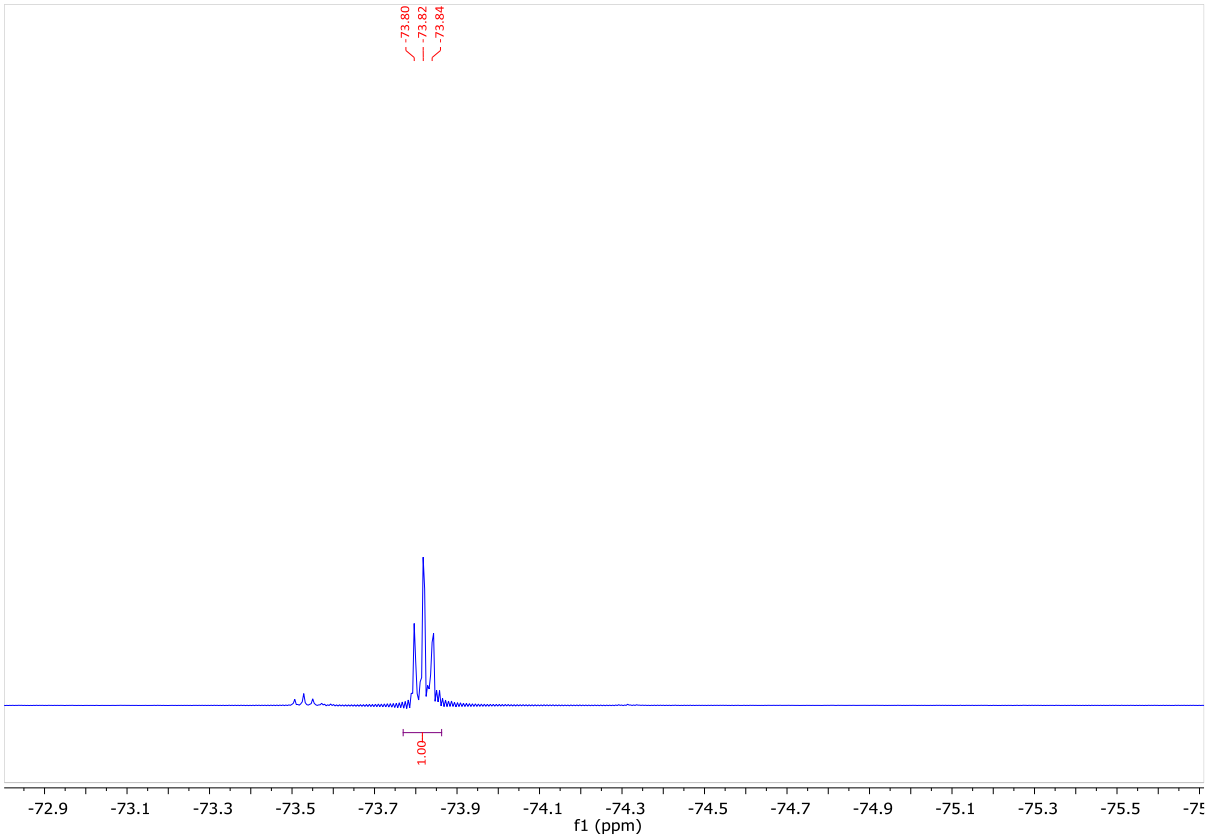


Figure S134. ^{19}F NMR spectrum ($CDCl_3$, 376 MHz) of **6.**

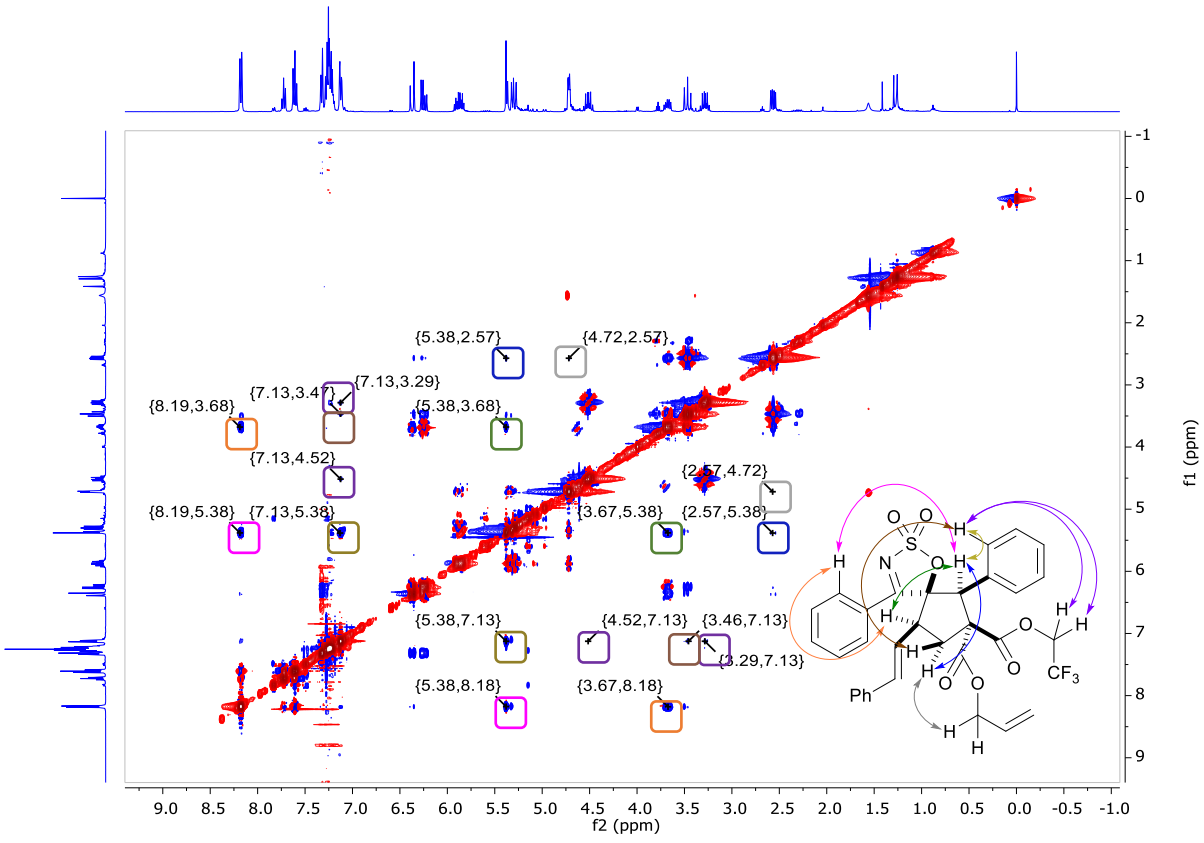


Figure S135. 2D NOESY spectrum ($CDCl_3$, 400 MHz) of **6.**

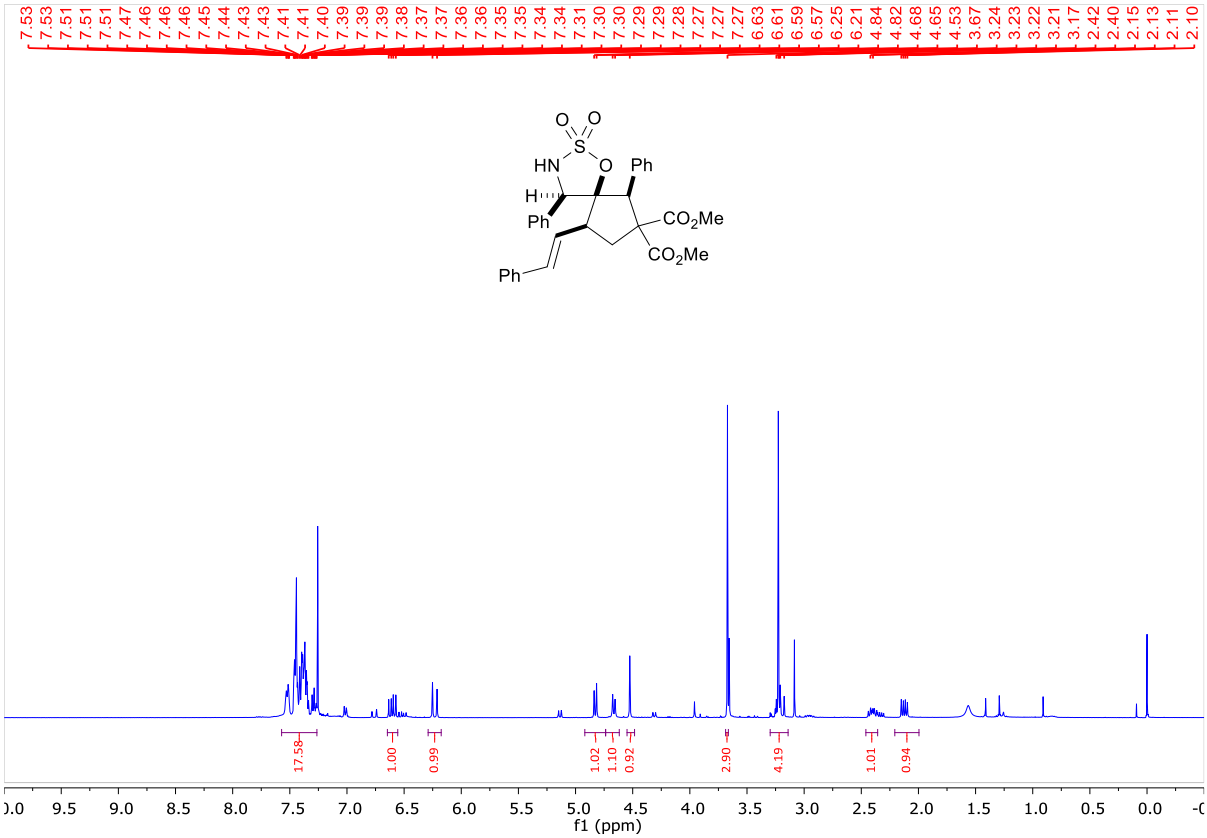


Figure S136. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of **8.**

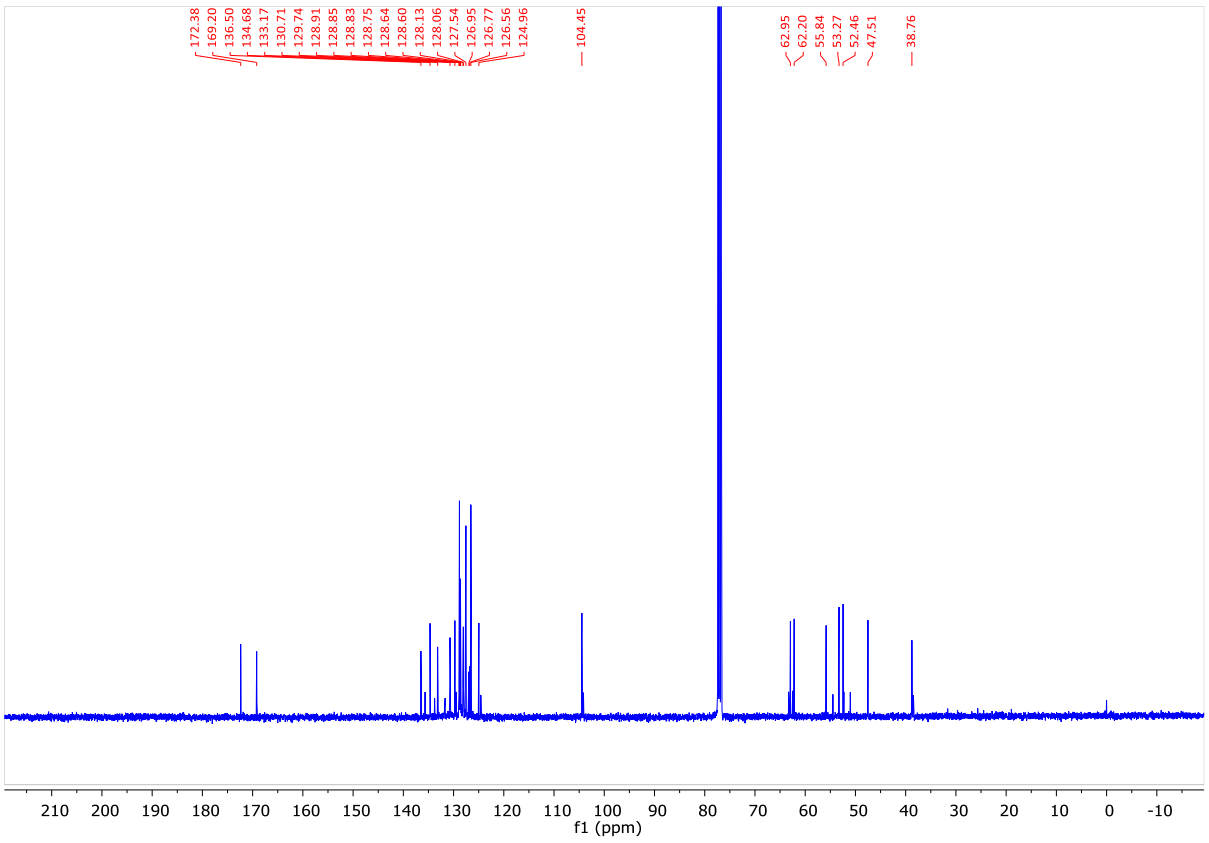


Figure S137. ^{13}C NMR spectrum ($CDCl_3$, 100 MHz) of **8**.

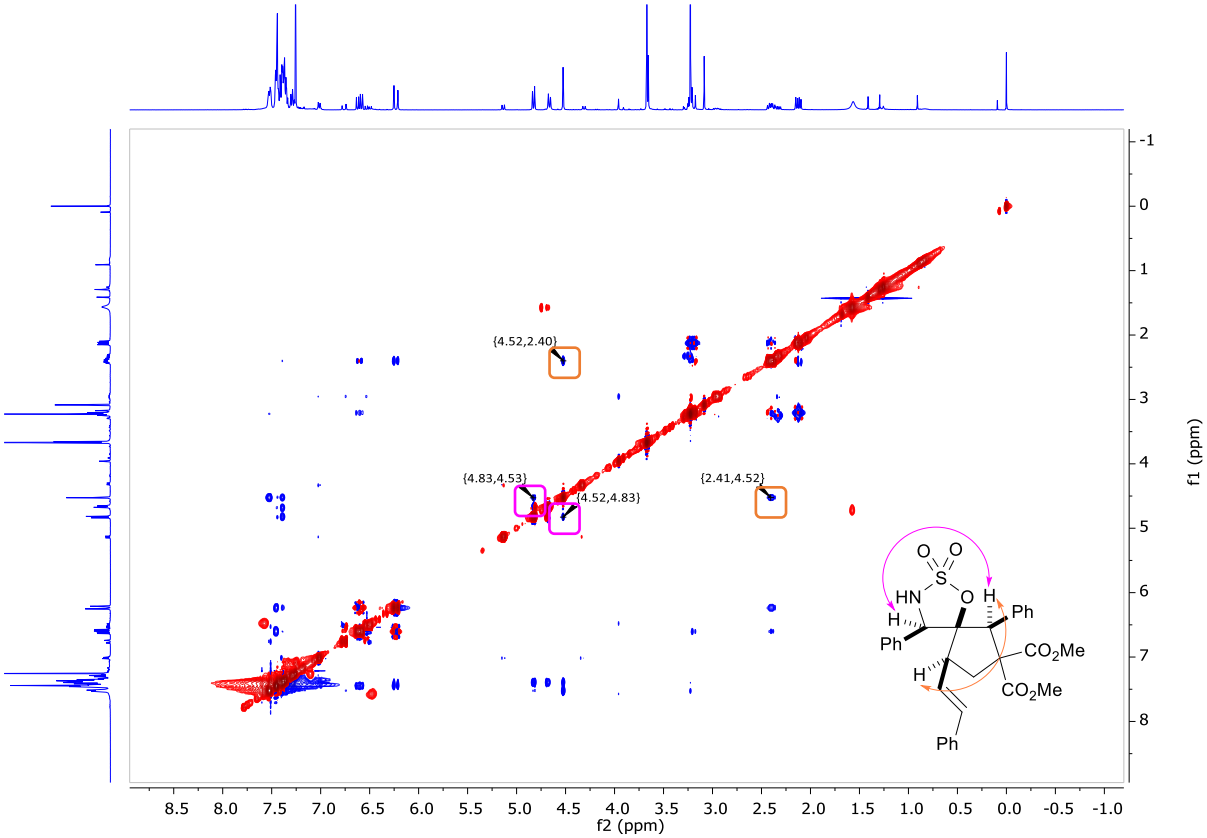
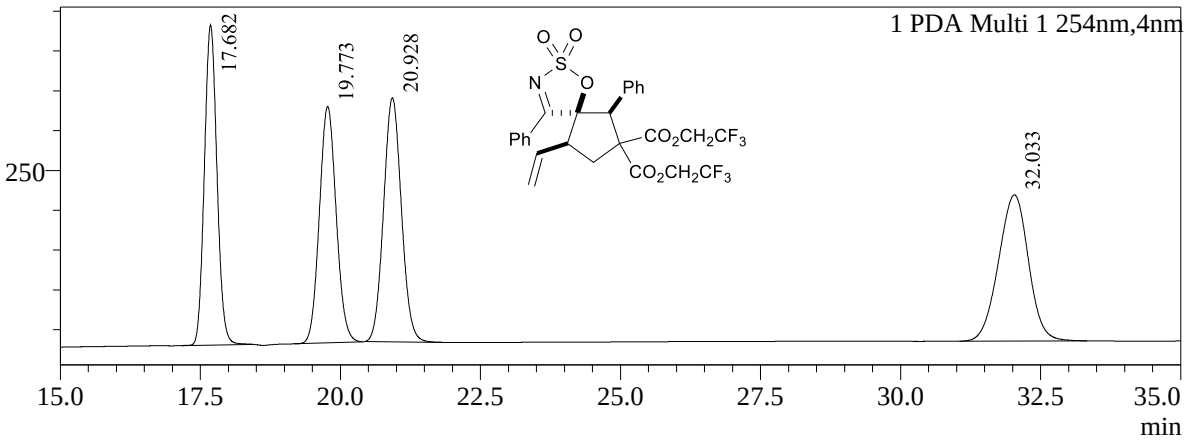


Figure S138. 2D NOESY spectrum ($CDCl_3$, 400 MHz) of **8.**

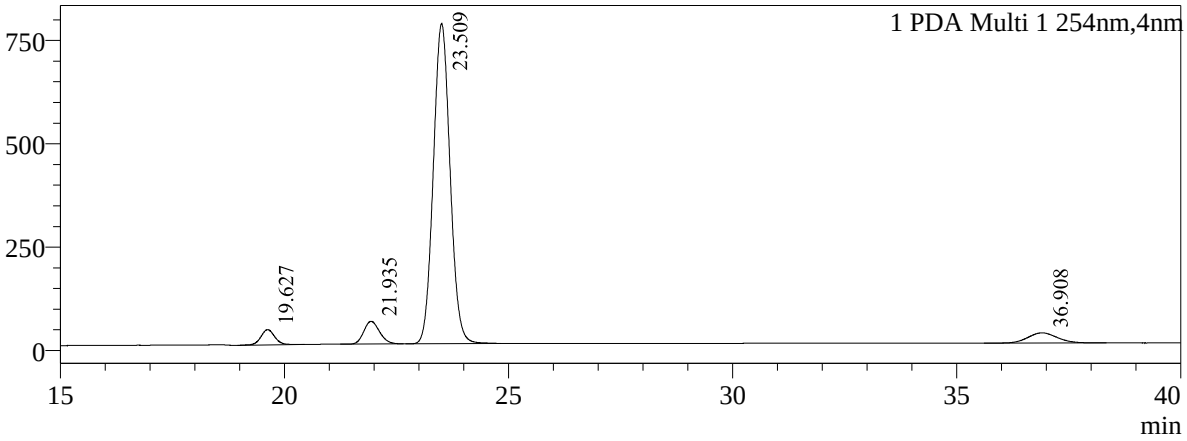
10. HPLC chromatograms

(*rac*)-3aa



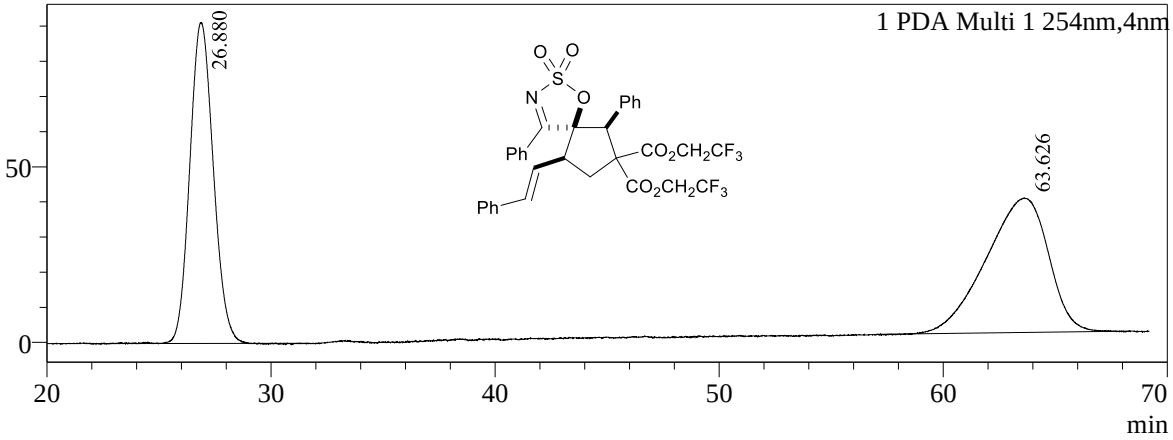
Peak#	Ret. Time	Area%	Name
1	17.682	24.082	Minor dia
2	19.773	23.752	Minor dia
3	20.928	25.986	Major dia
4	32.033	26.180	Major dia
Total		100.000	

(5*R*,6*S*,9*S*)-3aa



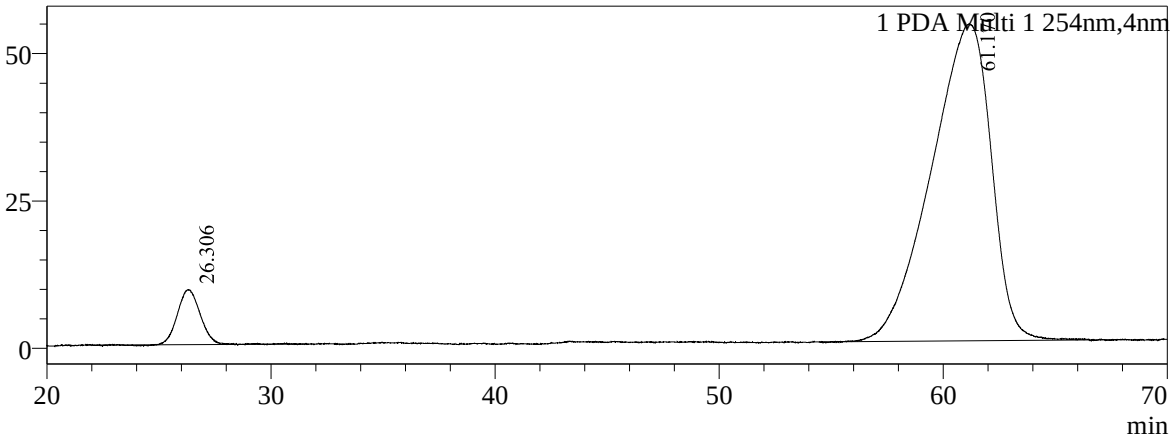
Peak#	Ret. Time	Area%	Name
1	19.627	3.481	Minor dia
2	21.935	5.739	Minor dia
3	23.509	85.992	Major dia
4	36.908	4.788	Major dia
Total		100.000	

(*rac*)-3ba



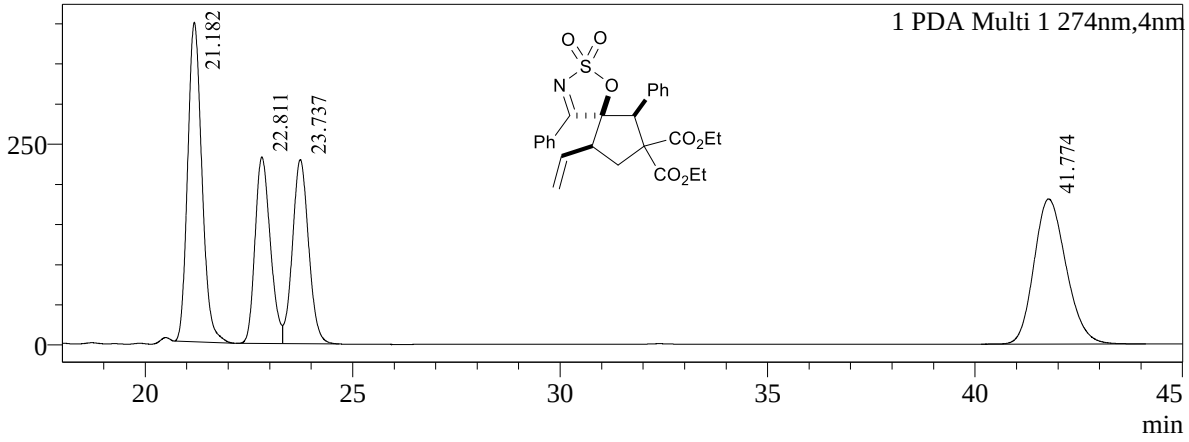
Peak#	Ret. Time	Area%	Name
1	26.880	47.378	
2	63.626	52.622	
Total		100.000	

(5*R*,6*S*,9*S*)-3ba



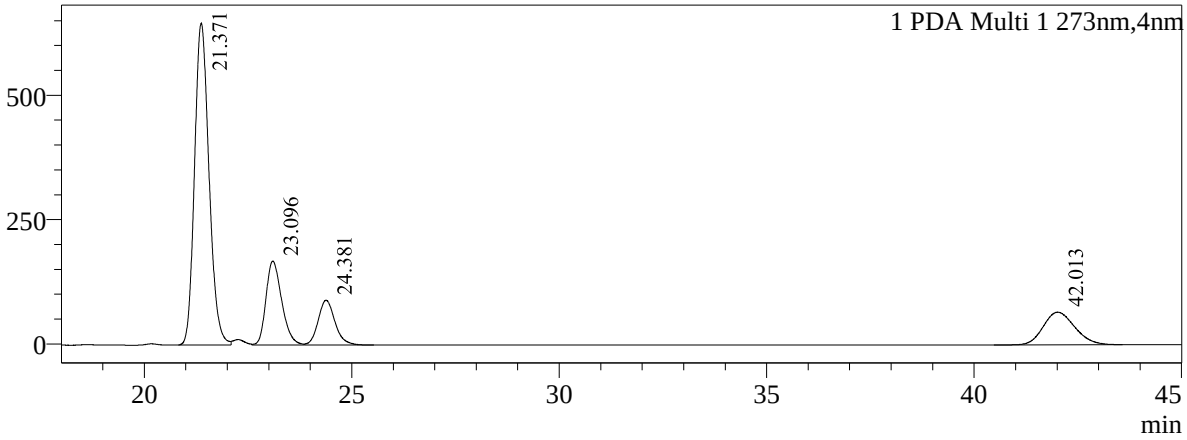
Peak#	Ret. Time	Area%	Name
1	26.306	6.231	
2	61.170	93.769	
Total		100.000	

(*rac*)-3ca



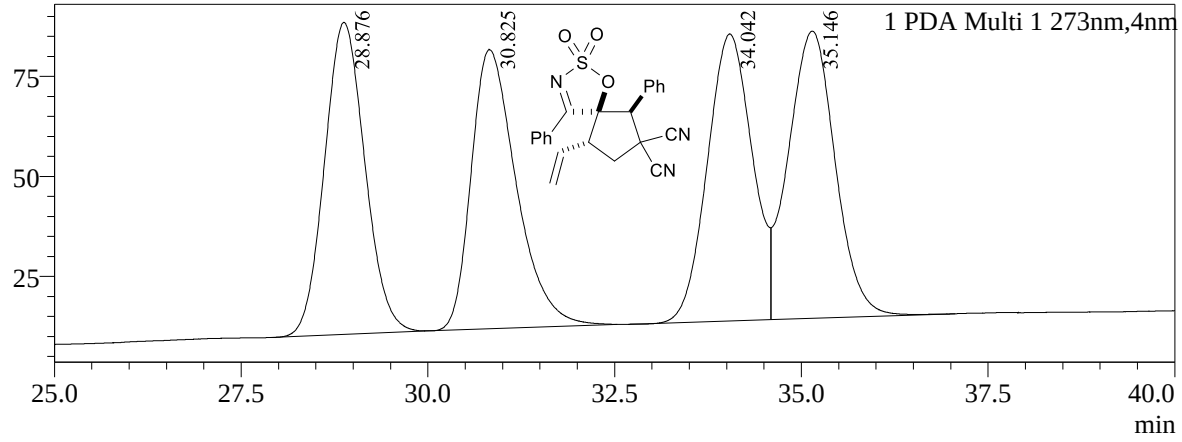
Peak#	Ret. Time	Area%	Name
1	21.182	30.285	Major dia
2	22.811	18.985	Minor dia
3	23.737	19.763	Minor dia
4	41.774	30.966	Major dia
Total		100.000	

(5*R*,6*S*,9*S*)-3ca



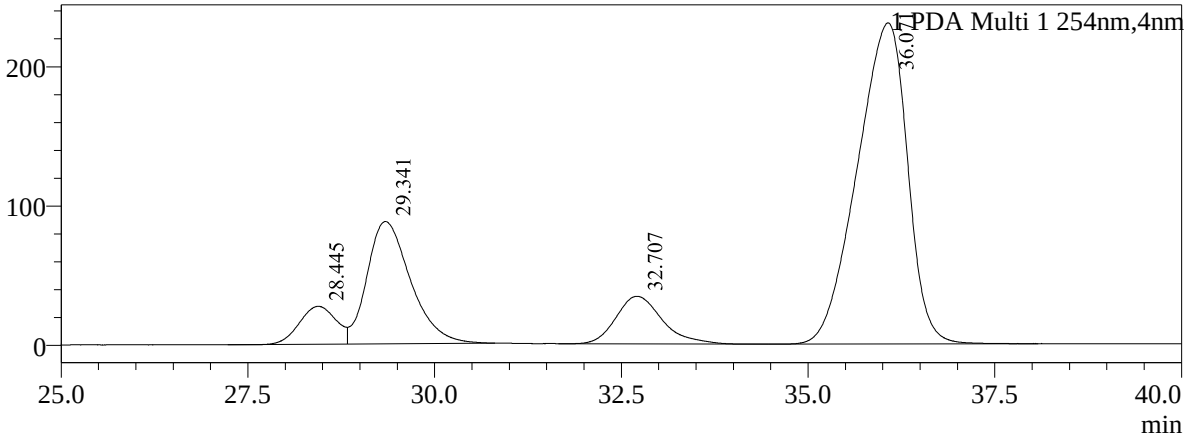
Peak#	Ret. Time	Area%	Name
1	21.371	60.010	Major dia
2	23.096	17.030	Minor dia
3	24.381	9.724	Minor dia
4	42.013	13.236	Major dia
Total		100.000	

(*rac*)-3da′



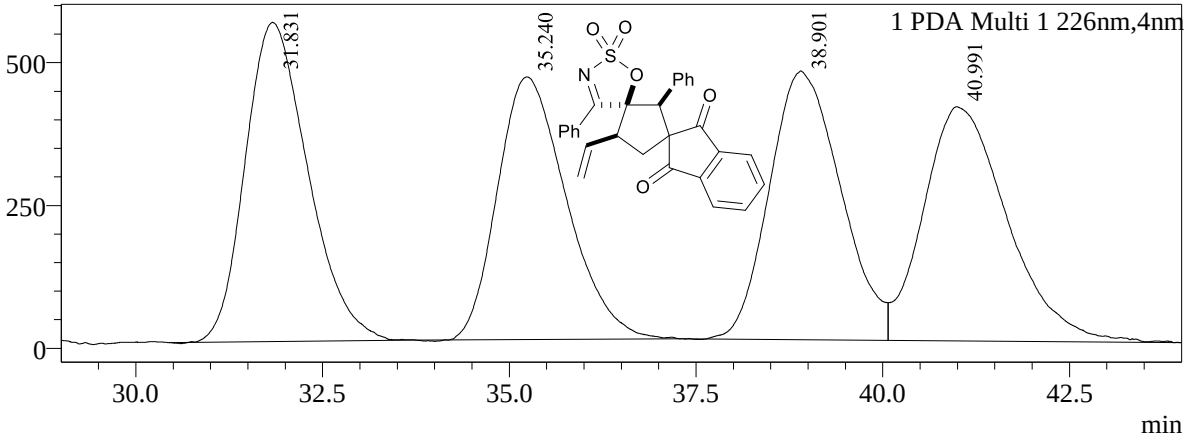
Peak#	Ret. Time	Area%	Name
1	28.876	24.410	Minor dia
2	30.825	24.385	Minor dia
3	34.042	25.030	Major dia
4	35.146	26.176	Major dia
Total		100.000	

(5*R*,6*S*,9*R*)-3da′



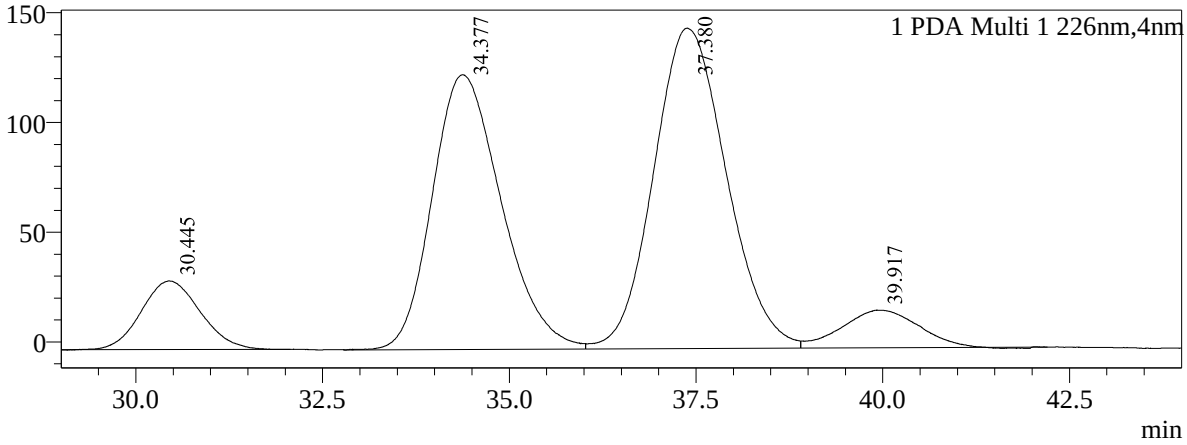
Peak#	Ret. Time	Area%	Name
1	28.445	5.622	Minor dia
2	29.341	21.274	Minor dia
3	32.707	8.769	Major dia
4	36.071	64.335	Major dia
Total		100.000	

(*rac*)-3ea



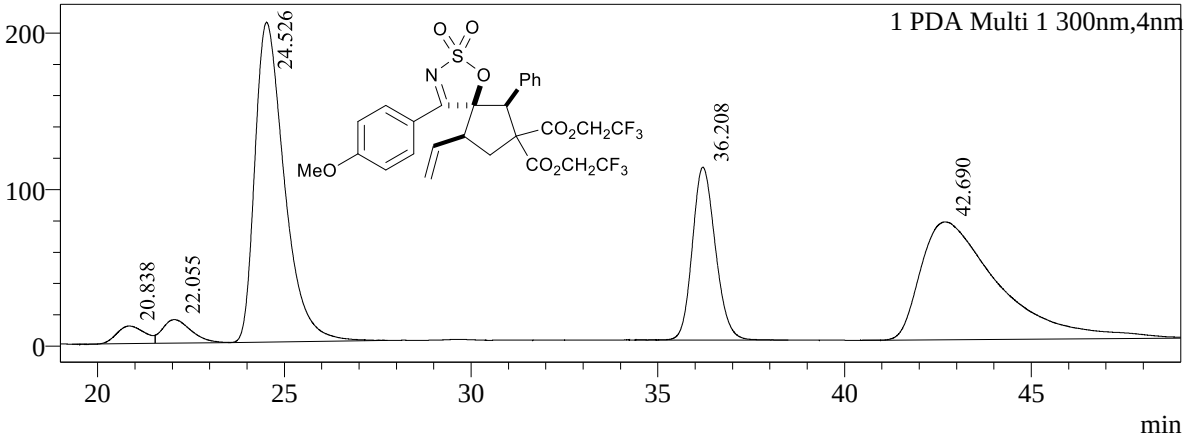
Peak#	Ret. Time	Area%	Name
1	31.831	26.015	
2	35.240	23.553	
3	38.901	24.969	
4	40.991	25.464	
Total		100.000	

(2′*S*,3′*R*,4′*S*)-3ea



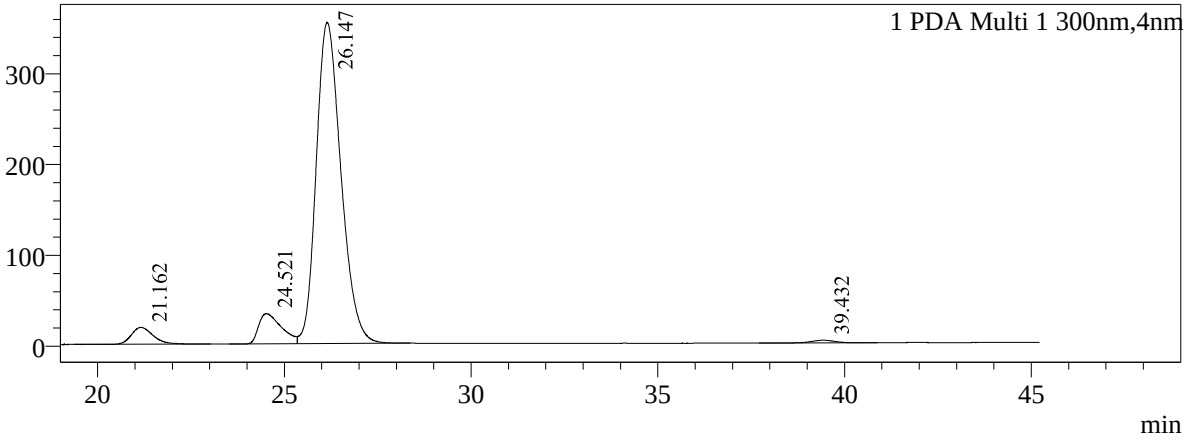
Peak#	Ret. Time	Area%	Name
1	30.445	8.207	
2	34.377	38.633	
3	37.380	47.351	
4	39.917	5.810	
Total		100.000	

(*rac*)-3ab



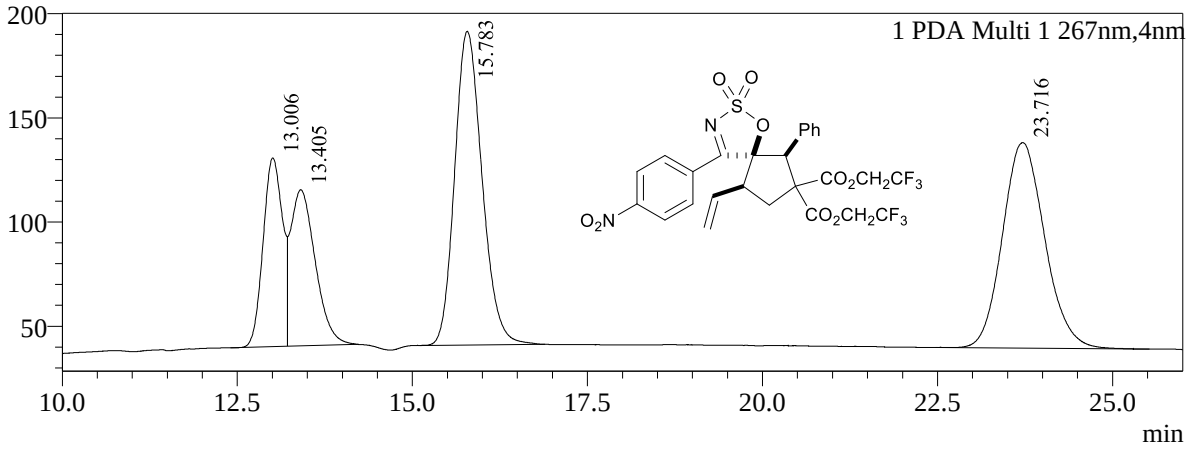
Peak#	Ret. Time	Area%	Name
1	20.838	2.071	Minor dia
2	22.055	2.805	Minor dia
3	24.526	39.514	Major dia
4	36.208	16.705	SM
5	42.690	38.905	Major dia
Total		100.000	

(5*R*,6*S*,9*S*)-3ab



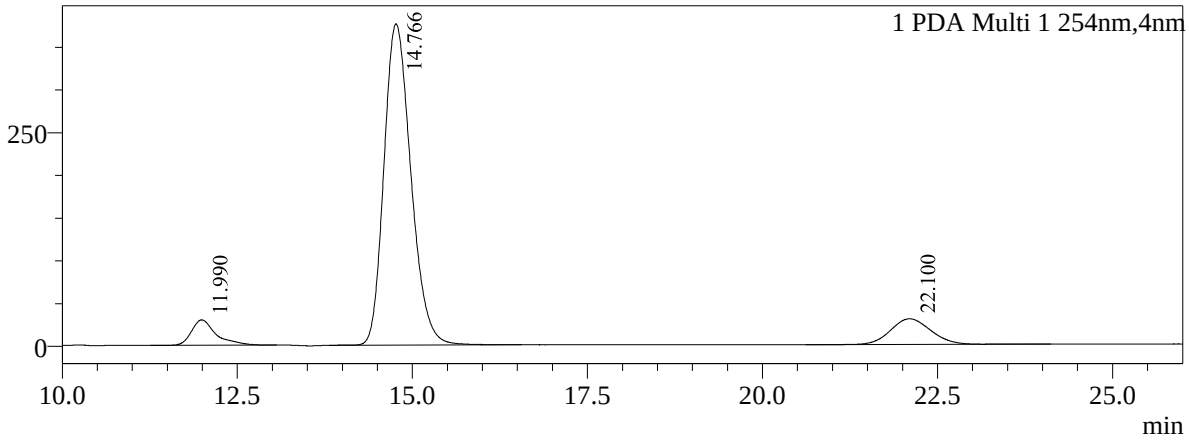
Peak#	Ret. Time	Area%	Name
1	21.162	4.057	Minor dia
2	24.521	7.605	Minor dia
3	26.147	87.659	Major dia
4	39.432	0.679	Major dia
Total		100.000	

(*rac*)-3ac



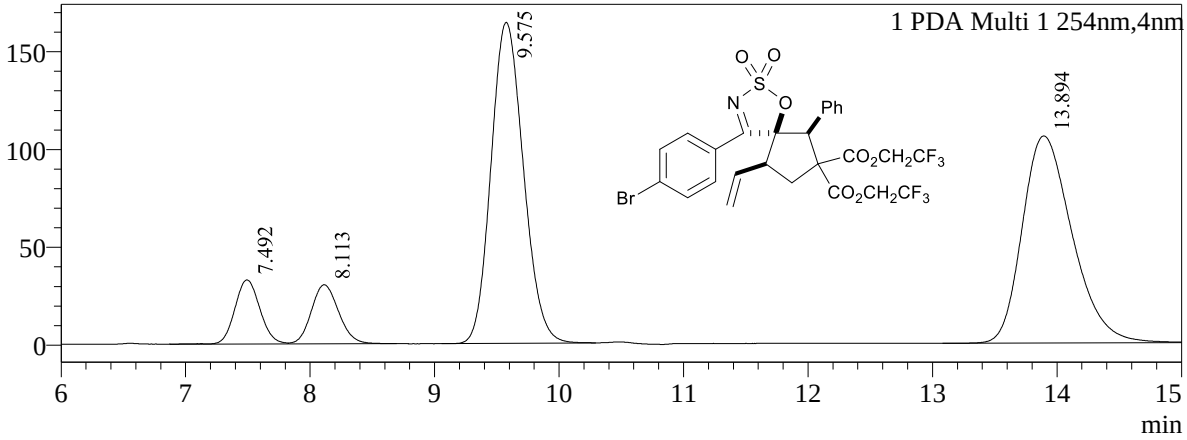
Peak#	Ret. Time	Area%	Name
1	13.006	14.910	Minor dia
2	13.405	15.453	Minor dia
3	15.783	34.640	Major dia
4	23.716	34.998	Major dia
Total		100.000	

(5*R*,6*S*,9*S*)-3ac



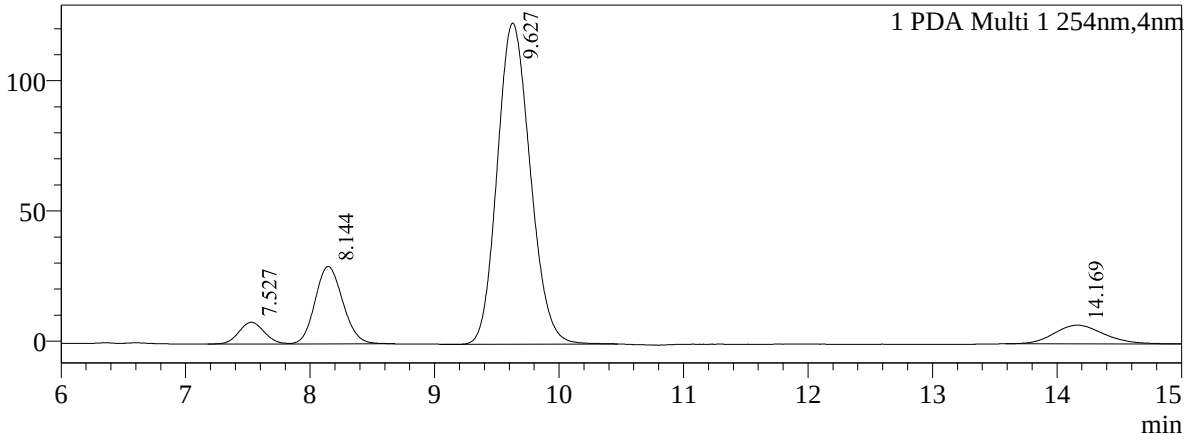
Peak#	Ret. Time	Area%	Name
1	11.990	5.952	Minor dia
2	14.766	84.131	Major dia
3	22.100	9.917	Major dia
Total		100.000	

(*rac*)-3ad



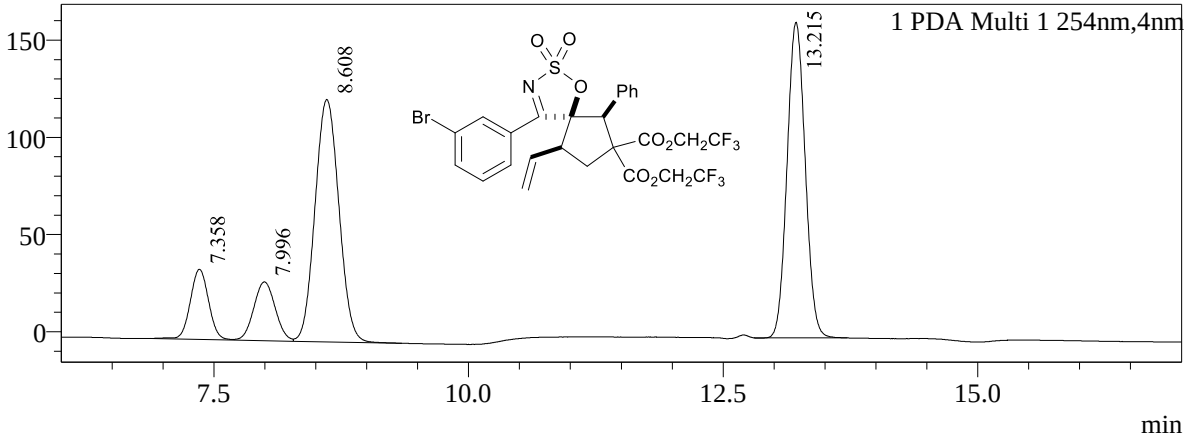
Peak#	Ret. Time	Area%	Name
1	7.492	6.677	Minor dia
2	8.113	6.728	Minor dia
3	9.575	43.438	Major dia
4	13.894	43.158	Major dia
Total		100.000	

(5*R*,6*S*,9*S*)-3ad



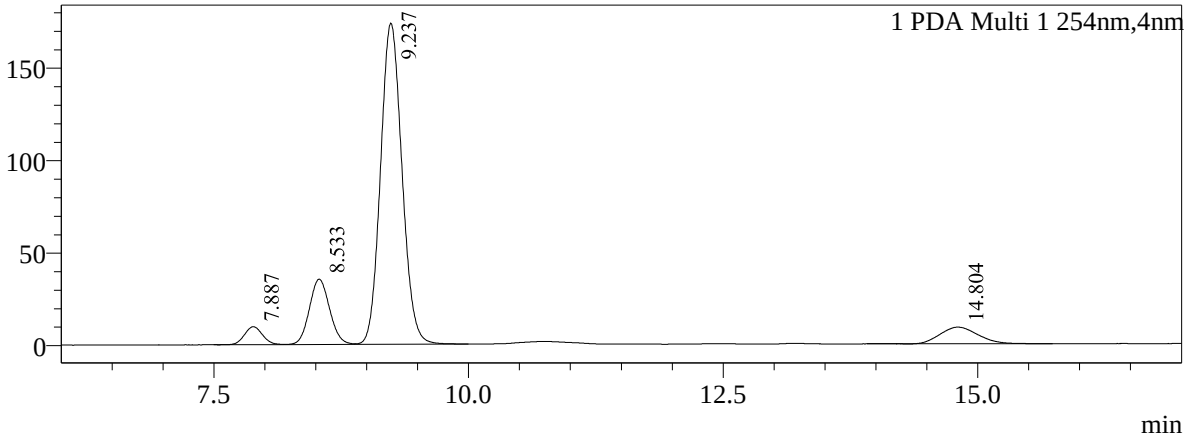
Peak#	Ret. Time	Area%	Name
1	7.527	3.866	Minor dia
2	8.144	15.099	Minor dia
3	9.627	74.431	Major dia
4	14.169	6.605	Major dia
Total		100.000	

(*rac*)-3ae



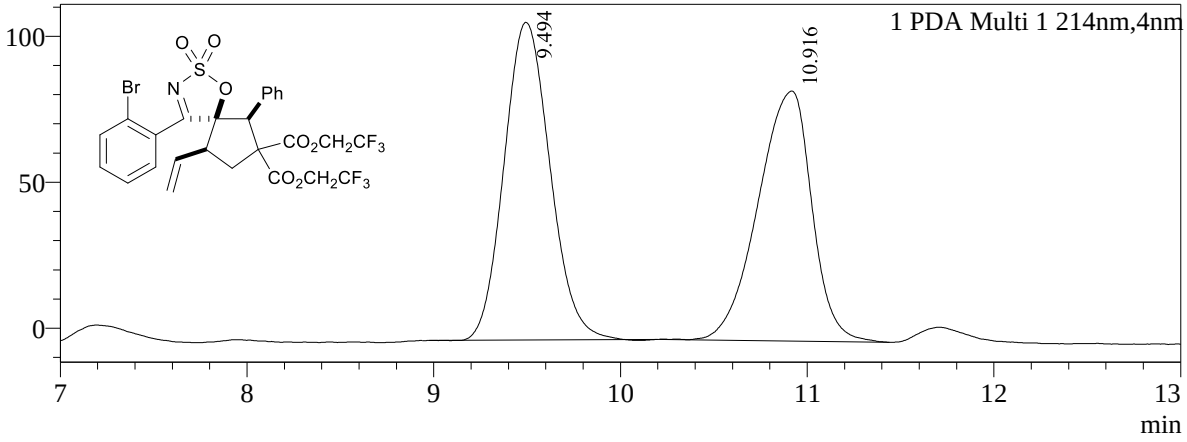
Peak#	Ret. Time	Area%	Name
1	7.358	9.131	Minor dia
2	7.996	8.959	Minor dia
3	8.608	41.194	Major dia
4	13.215	40.716	Major dia
Total		100.000	

(5*R*,6*S*,9*S*)-3ae



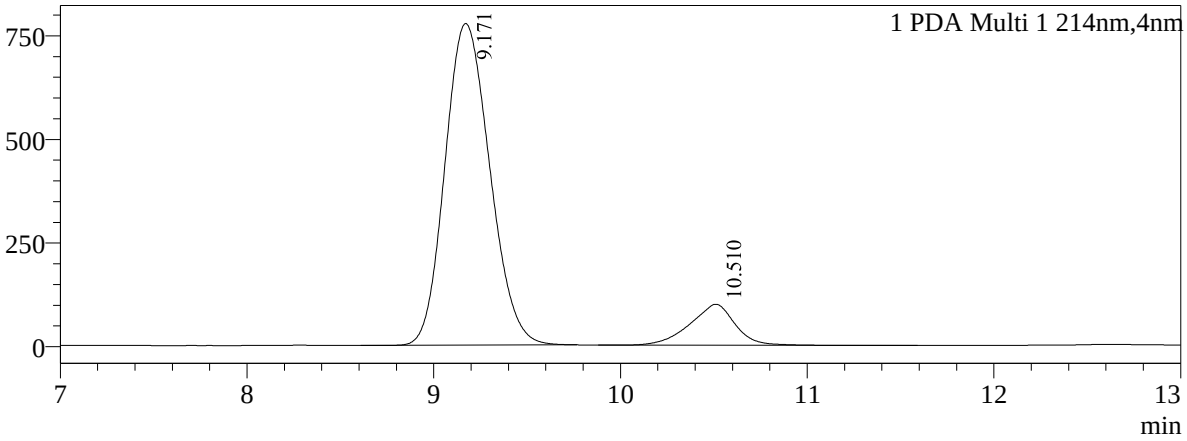
Peak#	Ret. Time	Area%	Name
1	7.887	3.557	Minor dia
2	8.533	14.404	Minor dia
3	9.237	75.166	Major dia
4	14.804	6.874	Major dia
Total		100.000	

(*rac*)-3af



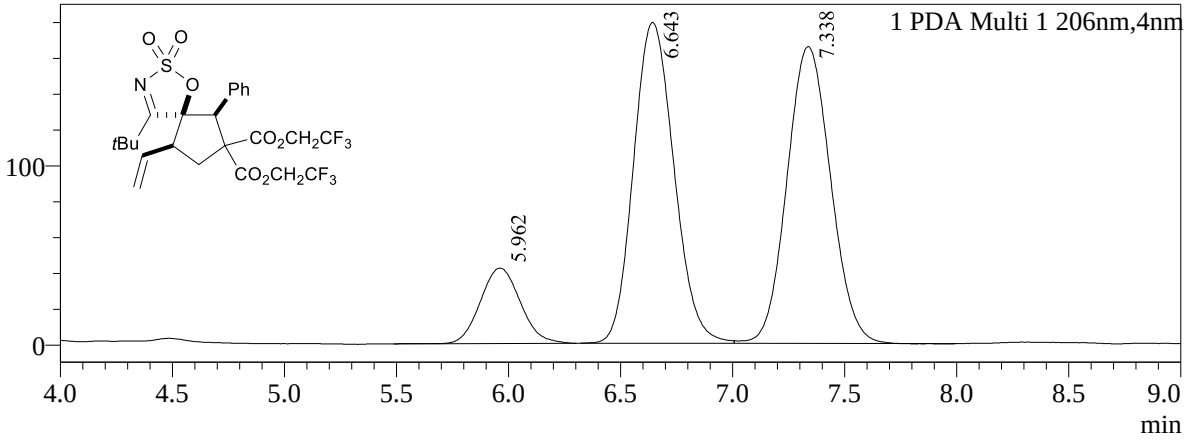
Peak#	Ret. Time	Area%	Name
1	9.494	51.966	
2	10.916	48.034	
Total		100.000	

(5*R*,6*S*,9*S*)-3af



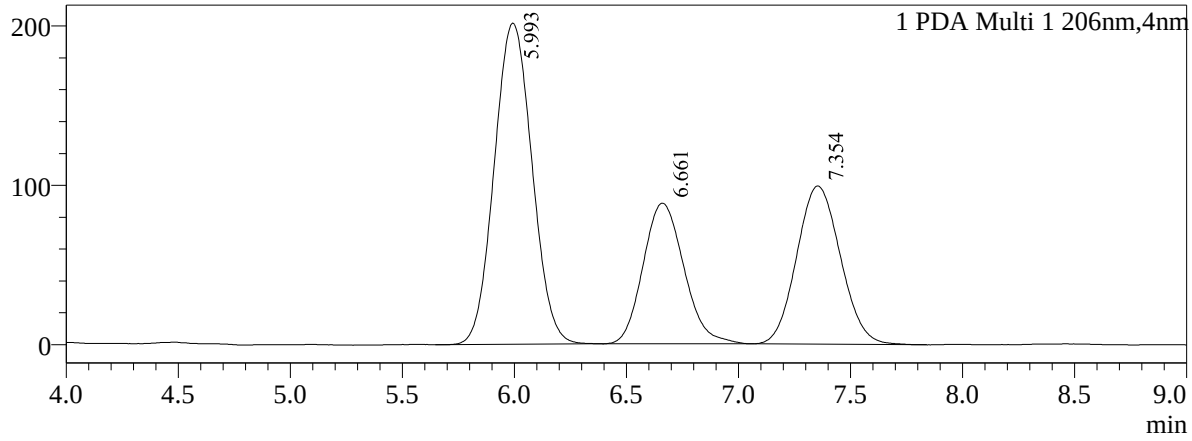
Peak#	Ret. Time	Area%	Name
1	9.171	88.736	
2	10.510	11.264	
Total		100.000	

(*rac*)-3ag



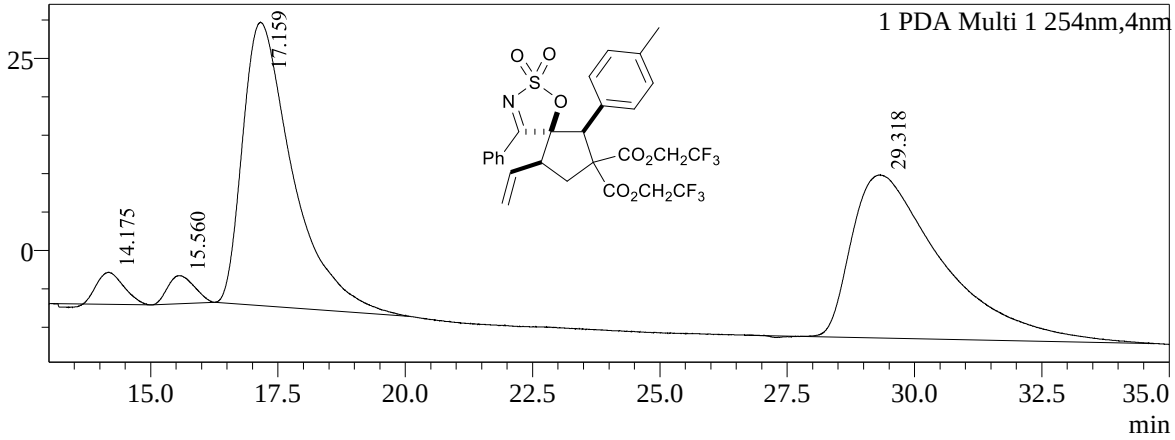
Peak#	Ret. Time	Area%	Name
1	5.962	10.381	Overlapping peaks of the minor dia
2	6.643	44.821	Major dia
3	7.338	44.798	Major dia
Total		100.000	

(5*R*,6*S*,9*S*)-3ag



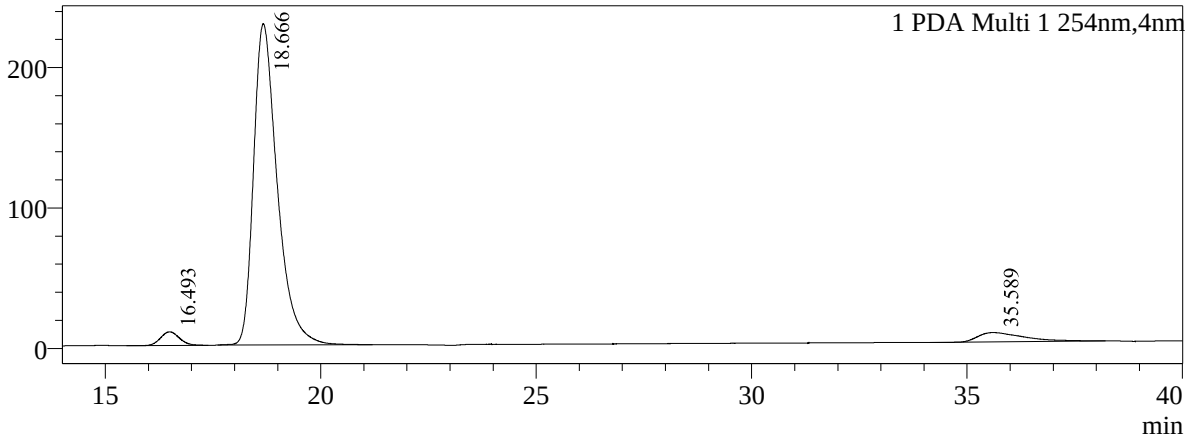
Peak#	Ret. Time	Area%	Name
1	5.993	48.927	Overlapping peaks of the minor dia
2	6.661	23.135	Major dia
3	7.354	27.937	Major dia
Total		100.000	

(*rac*)-3ah



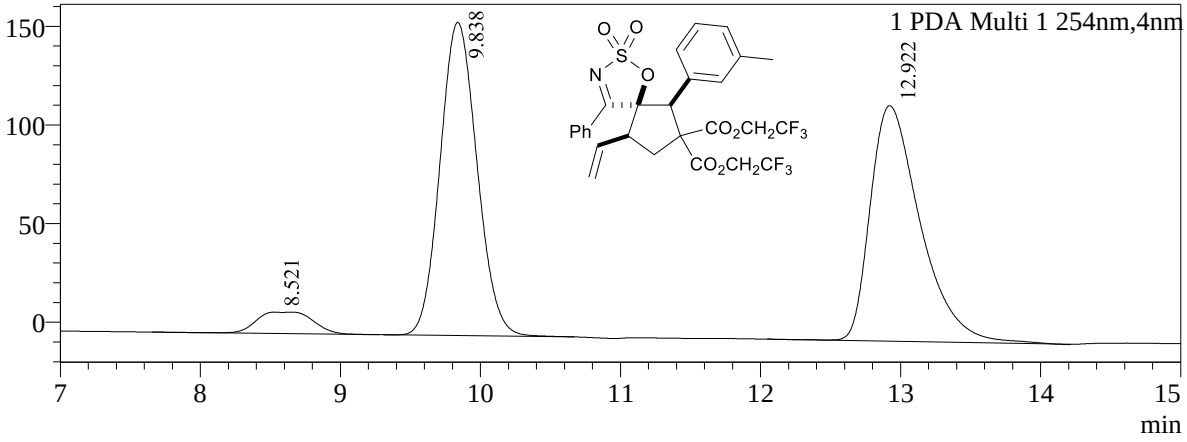
Peak#	Ret. Time	Area%	Name
1	14.175	2.691	Minor dia
2	15.560	2.453	Minor dia
3	17.159	46.529	Major dia
4	29.318	48.327	Major dia
Total		100.000	

(5*R*,6*S*,9*S*)-3ah



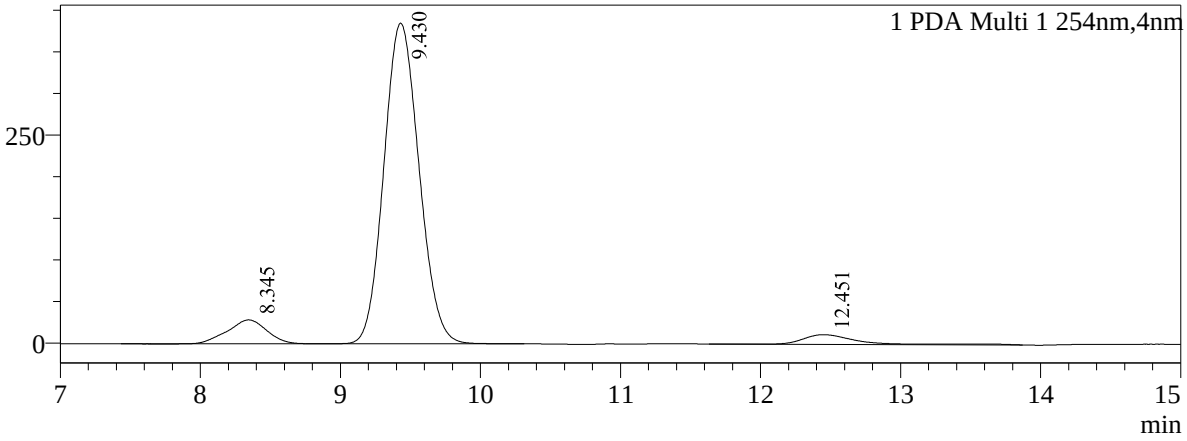
Peak#	Ret. Time	Area%	Name
1	16.493	3.080	Minor dia
2	18.666	91.835	Major dia
3	35.589	5.085	Major dia
Total		100.000	

(*rac*)-3ai



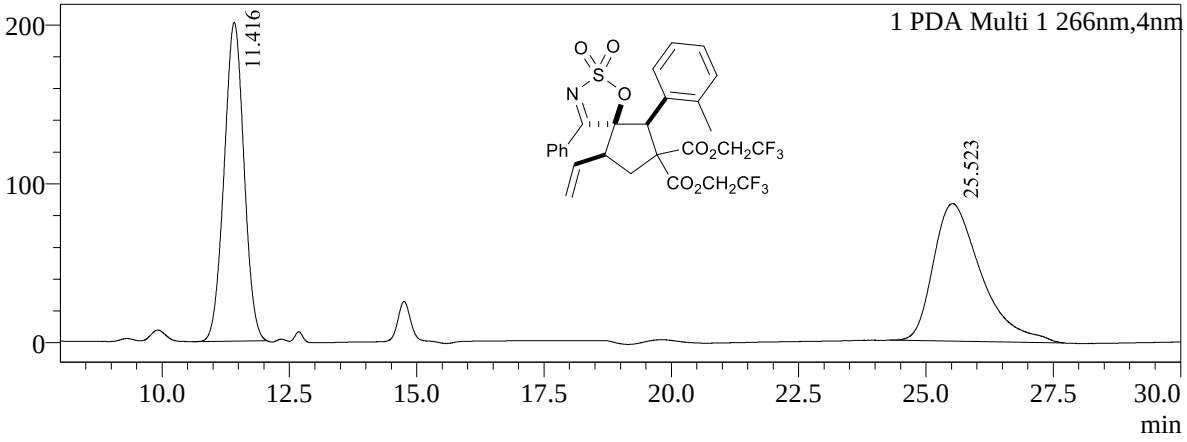
Peak#	Ret. Time	Area%	Name
1	8.521	4.869	Overlapping peaks of the minor dia
2	9.838	47.120	Major dia
3	12.922	48.011	Major dia
Total		100.000	

(5*R*,6*S*,9*S*)-3ai



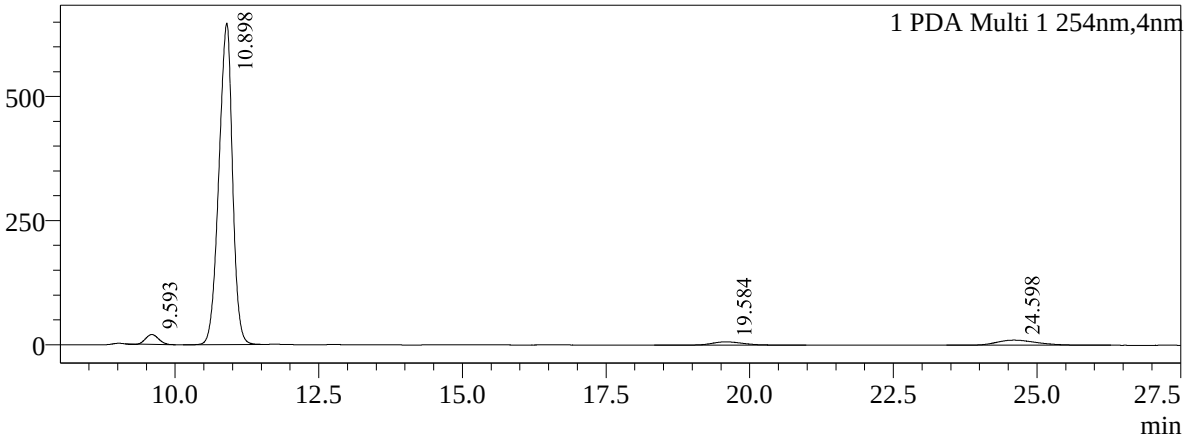
Peak#	Ret. Time	Area%	Name
1	8.345	7.346	Overlapping peaks of the minor dia
2	9.430	88.490	Major dia
3	12.451	4.164	Major dia
Total		100.000	

(*rac*)-3aj



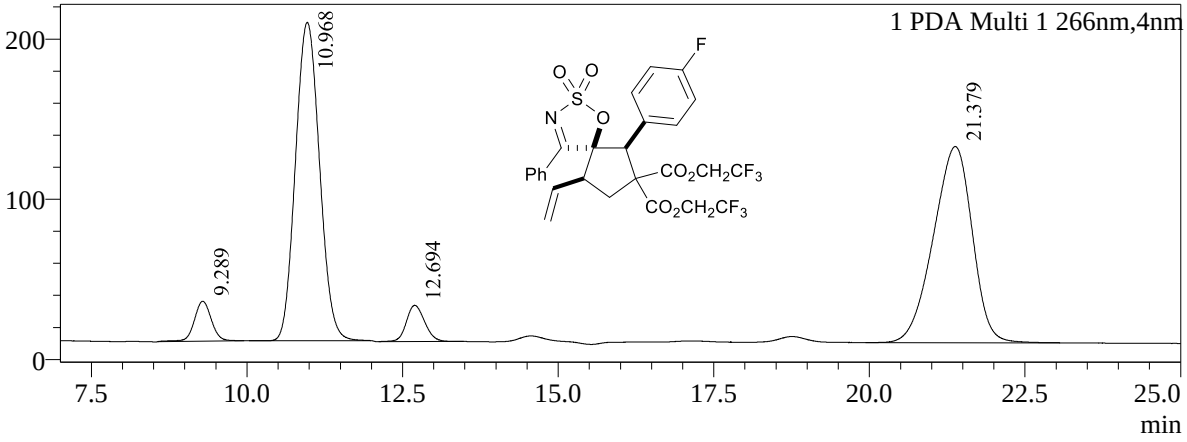
Peak#	Ret. Time	Area%	Name
1	11.416	49.044	Major dia
2	25.523	50.956	Major dia
Total		100.000	

(5*R*,6*S*,9*S*)-3aj



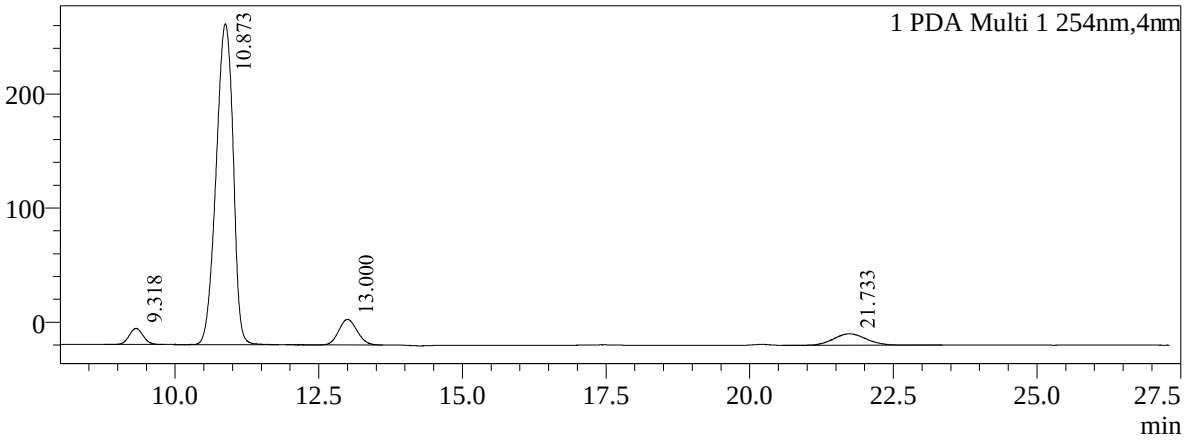
Peak#	Ret. Time	Area%	Name
1	9.593	2.539	Minor dia
2	10.898	91.193	Major dia
3	19.584	2.020	Minor dia
4	24.598	4.249	Major dia
Total		100.000	

(*rac*)-3ak



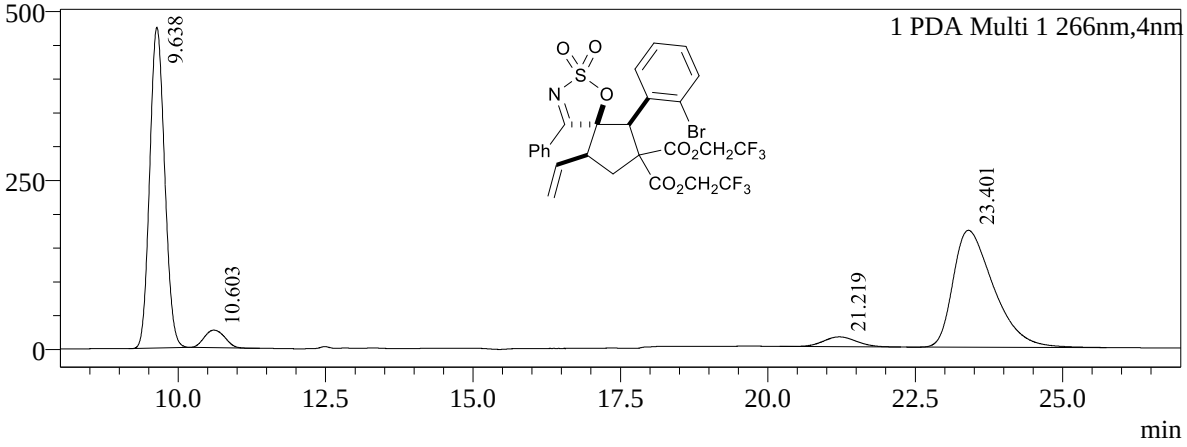
Peak#	Ret. Time	Area%	Name
1	9.289	4.118	Minor dia
2	10.968	46.041	Major dia
3	12.694	3.977	Minor dia
4	21.379	45.864	Major dia
Total		100.000	

(5*R*,6*S*,9*S*)-3ak



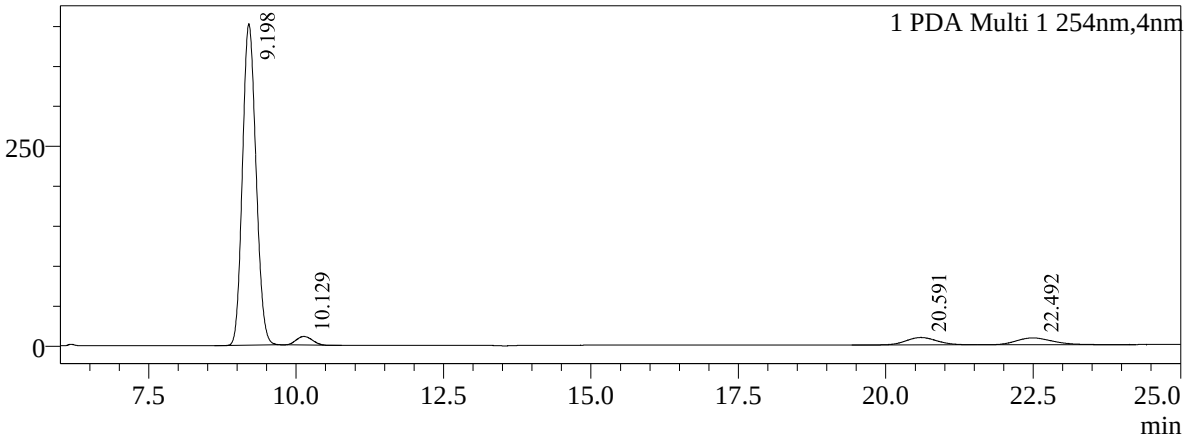
Peak#	Ret. Time	Area%	Name
1	9.318	3.376	Minor dia
2	10.873	83.688	Major dia
3	13.000	7.185	Minor dia
4	21.733	5.751	Major dia
Total		100.000	

(*rac*)-3al



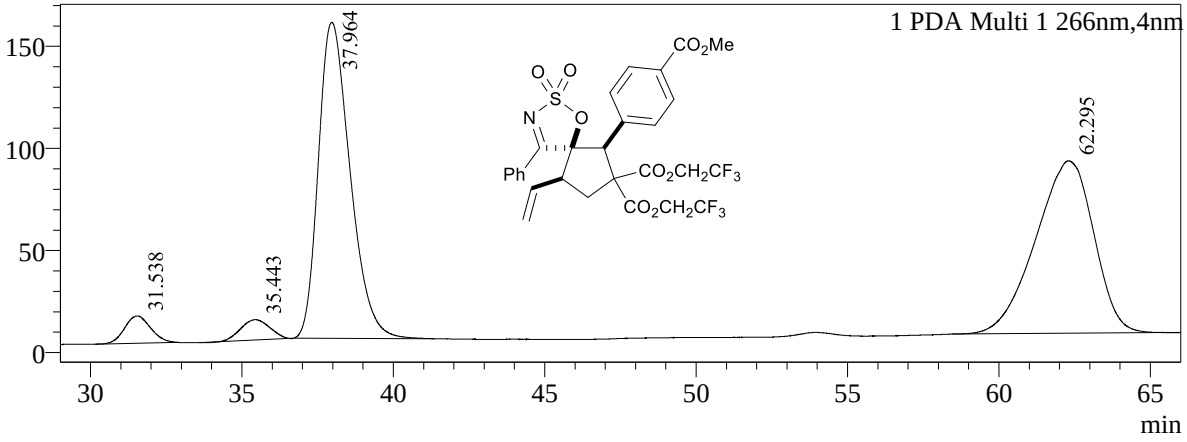
Peak#	Ret. Time	Area%	Name
1	9.638	46.878	Major dia
2	10.603	3.494	Minor dia
3	21.219	3.193	Minor dia
4	23.401	46.434	Major dia
Total		100.000	

(5*R*,6*R*,9*S*)-3al



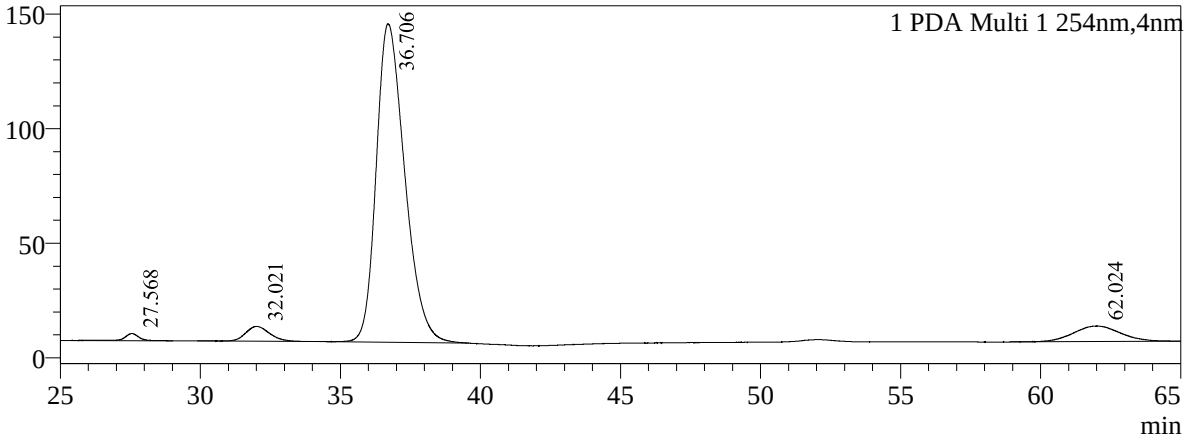
Peak#	Ret. Time	Area%	Name
1	9.198	87.726	Major dia
2	10.129	2.755	Minor dia
3	20.591	4.583	Minor dia
4	22.492	4.937	Major dia
Total		100.000	

(*rac*)-3am



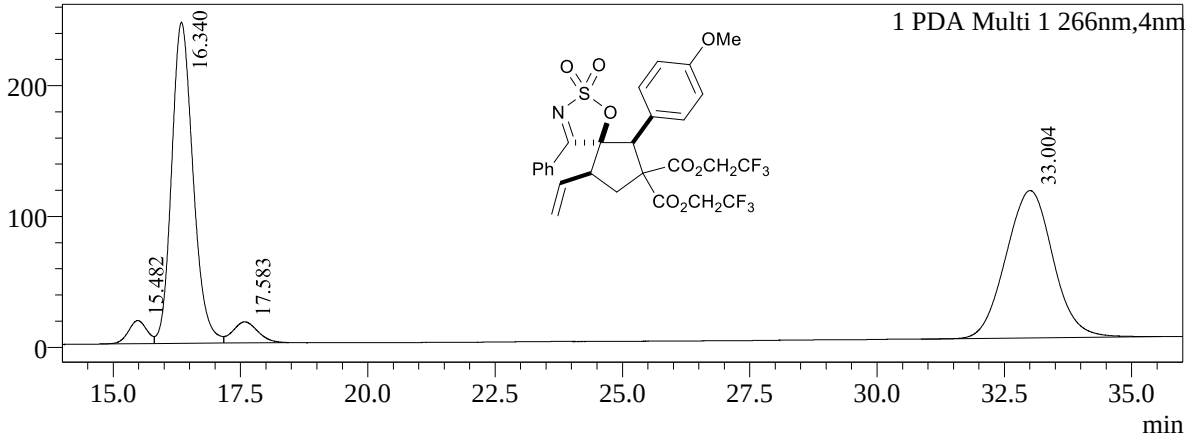
Peak#	Ret. Time	Area%	Name
1	31.538	3.331	Minor dia
2	35.443	2.776	Minor dia
3	37.964	46.839	Major dia
4	62.295	47.055	Major dia
Total		100.000	

(5*R*,6*S*,9*S*)-3am



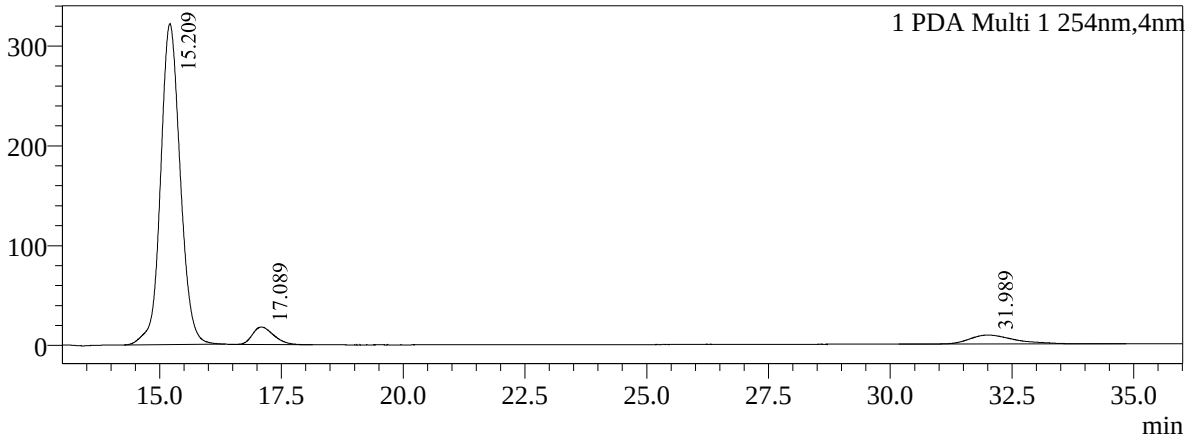
Peak#	Ret. Time	Area%	Name
1	27.568	1.003	Minor dia
2	32.021	3.447	Minor dia
3	36.706	88.330	Major dia
4	62.024	7.220	Major dia
Total		100.000	

(*rac*)-3an



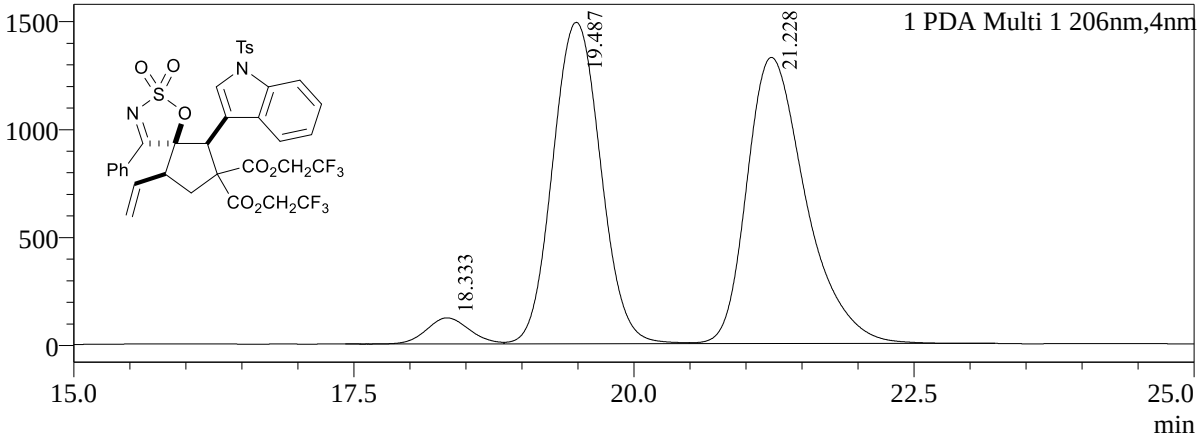
Peak#	Ret. Time	Area%	Name
1	15.482	2.926	Minor dia
2	16.340	46.582	Major dia
3	17.583	3.580	Minor dia
4	33.004	46.913	Major dia
Total		100.000	

(5*R*,6*S*,9*S*)-3an



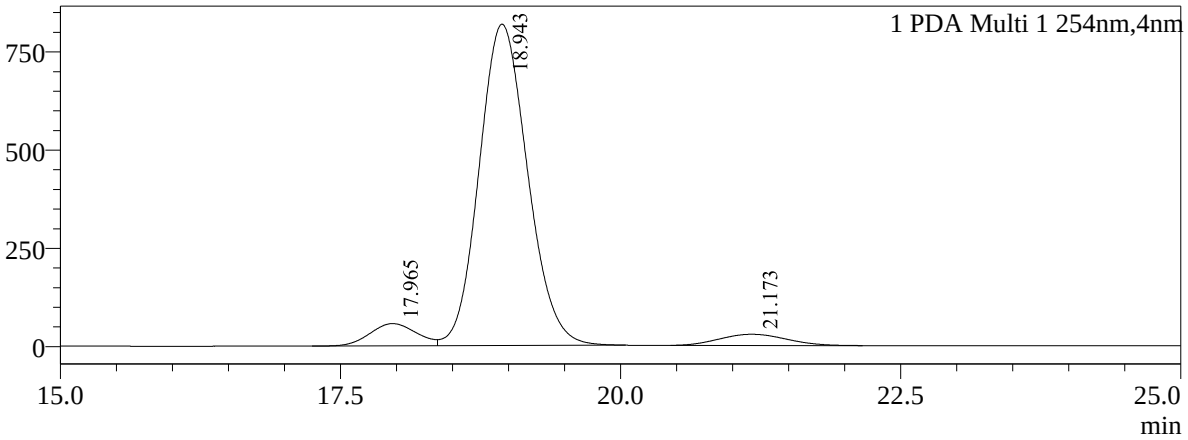
Peak#	Ret. Time	Area%	Name
1	15.209	89.202	Major dia
2	17.089	5.213	Minor dia
3	31.989	5.585	Major dia
Total		100.000	

(*rac*)-3ao



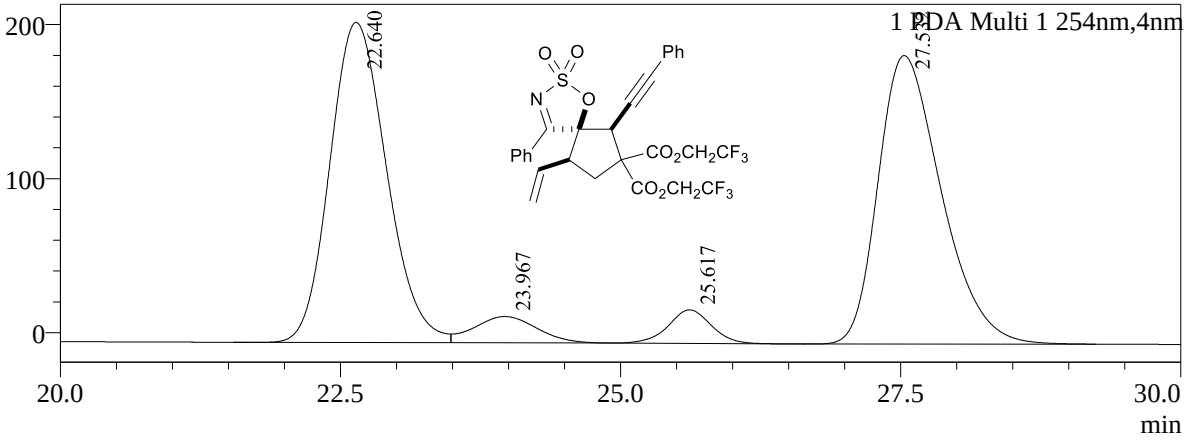
Peak#	Ret. Time	Area%	Name
1	18.333	3.295	Minor dia
2	19.487	46.222	Major dia
3	21.228	50.483	Major dia
Total		100.000	

(5*R*,6*S*,9*S*)-3ao



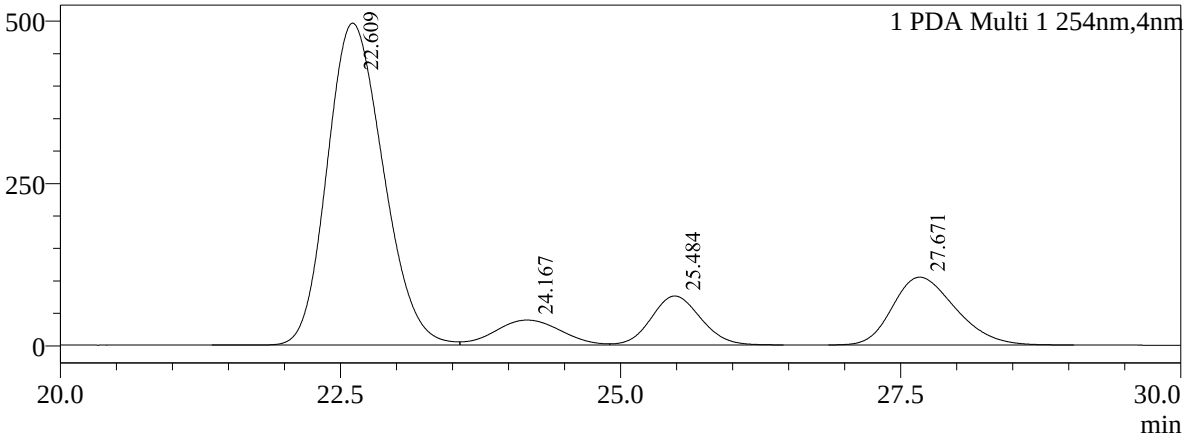
Peak#	Ret. Time	Area%	Name
1	17.965	6.004	Minor dia
2	18.943	89.667	Major dia
3	21.173	4.329	Major dia
Total		100.000	

(*rac*)-3ap



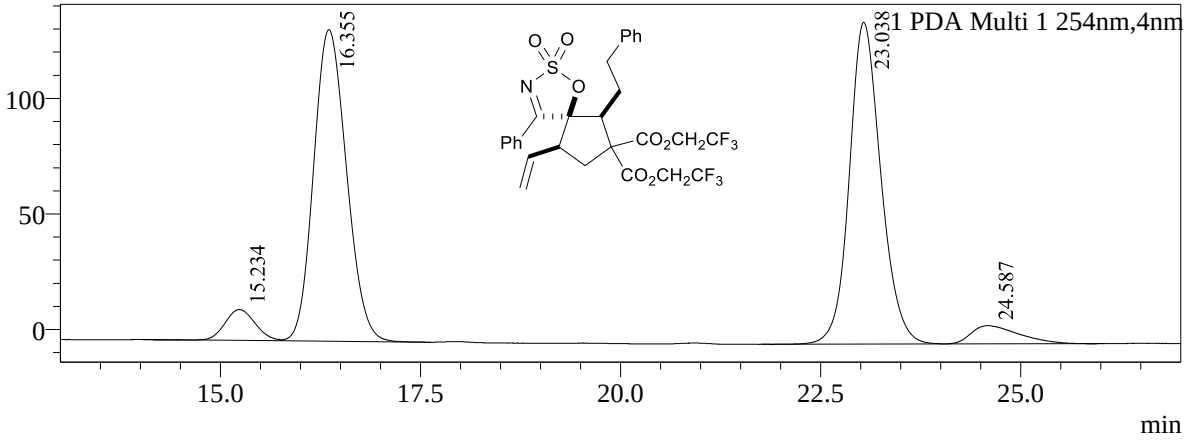
Peak#	Ret. Time	Area%	Name
1	22.640	46.005	Major dia
2	23.967	4.150	Minor dia
3	25.617	3.655	Minor dia
4	27.532	46.190	Major dia
Total		100.000	

(5*R*,6*S*,9*S*)-3ap



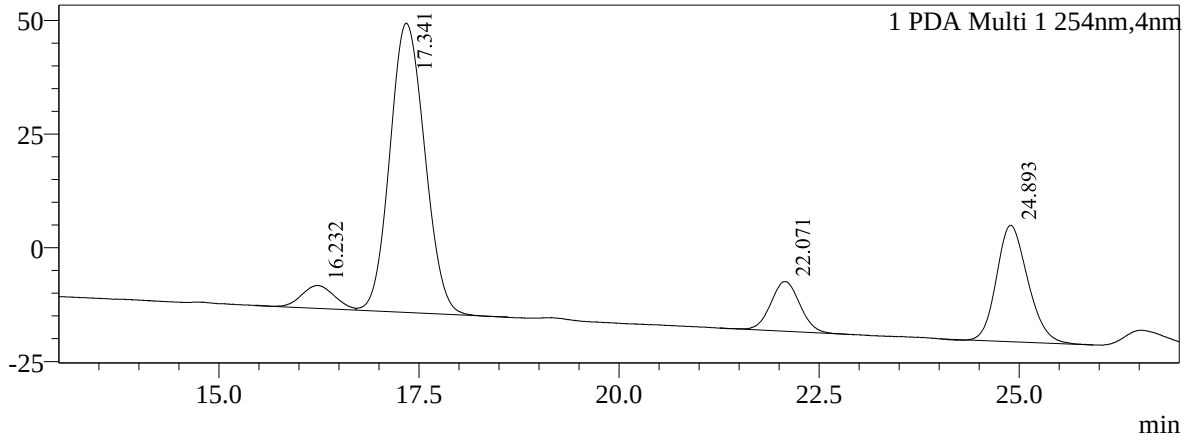
Peak#	Ret. Time	Area%	Name
1	22.609	68.375	Major dia
2	24.167	6.188	Minor dia
3	25.484	9.182	Minor dia
4	27.671	16.255	Major dia
Total		100.000	

(*rac*)-3aq



Peak#	Ret. Time	Area%	Name
1	15.234	4.182	Minor dia
2	16.355	46.165	Major dia
3	23.038	45.756	Major dia
4	24.587	3.897	Minor dia
Total		100.000	

(5*R*,6*S*,9*S*)-3aq



Peak#	Ret. Time	Area%	Name
1	16.232	4.739	Minor dia
2	17.341	63.375	Major dia
3	22.071	9.096	Major dia
4	24.893	22.790	Minor dia
Total		100.000	