Supporting Information

Energy-, time-, and labor-saving synthesis of α-ketiminophosphonates: Machine-learning-assisted simultaneous multiparameter screening for electrochemical oxidation

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CONTENTS:

General methods

^{1}H-, ^{13}C-NMR, and ^{31}P-NMR spectra were recorded with a JEOL JMN ECS400 FT NMR, JNM ECA600 FT NMR (^{1}H-NMR 400 MHz, ^{13}C-NMR 100, 150 MHz, or ^{31}P-NMR 240 MHz). ^{1}H-NMR spectra are reported as follows: chemical shift in ppm relative to the chemical shift of $CHCl_3$ at 7.26 ppm, integration, multiplicities (s = singlet, d = doublet, t = triplet, m = multiplet), and coupling constants (Hz). ^{13}C-NMR spectra reported in ppm relative to the central line of triplet for $CDCl_3$ at 77.16 ppm. ESI-MS spectra were obtained with JMS-T100LC (JEOL). Optical rotations were measured with JASCO P-1030 polarimeter. HPLC analyses were performed on a JASCO HPLC system (JASCO PU 980 pump and UV-975 UV/Vis detector). FT-IR spectra were recorded on a JASCO FT-IR system (FT/IR4100). Column chromatography on SiO_2 was performed with Kanto Silica Gel 60 (40-100 μm). Cyclic voltammetry was carried out on a BAS CV-620E voltammetric analyzer using a platinum disk as the working electrode, platinum wire as the counter electrode, and $Ag/AgNO_3$ as the reference electrode at a scan rate of 100 mV s^{-1}. Commercially available organic and inorganic compounds were used without further purification. Cyclic sulfonamides **1** were prepared according to the known literature procedure.[1] GPyOpt (a programming library in Python for Bayesian Optimization) was used to suggest the next parameters to examine from the previously collected dataset. Jupyter Notebook was also used to analyze data.

General for electrochemical reactions

The electro-oxidation was carried out using Pt plate electrodes (1.3 × 1.5 cm^2) connected to Pt wire (Figure S1 (a)). The electrochemical reactions were performed in a 12 mL reaction vessel equipped with two Pt electrodes. The two electrodes are connected to DC power supply (KIKUSUI PMX 35-1A) (Figure S1 (b)). The electrochemical reactions were carried out under air (1 atm.), and at constant current.

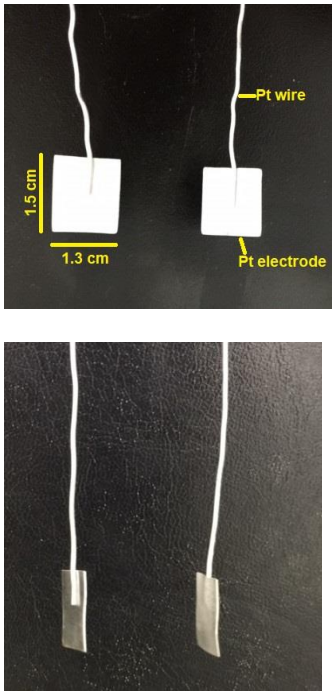


Figure S1 (a): Pt electrodes

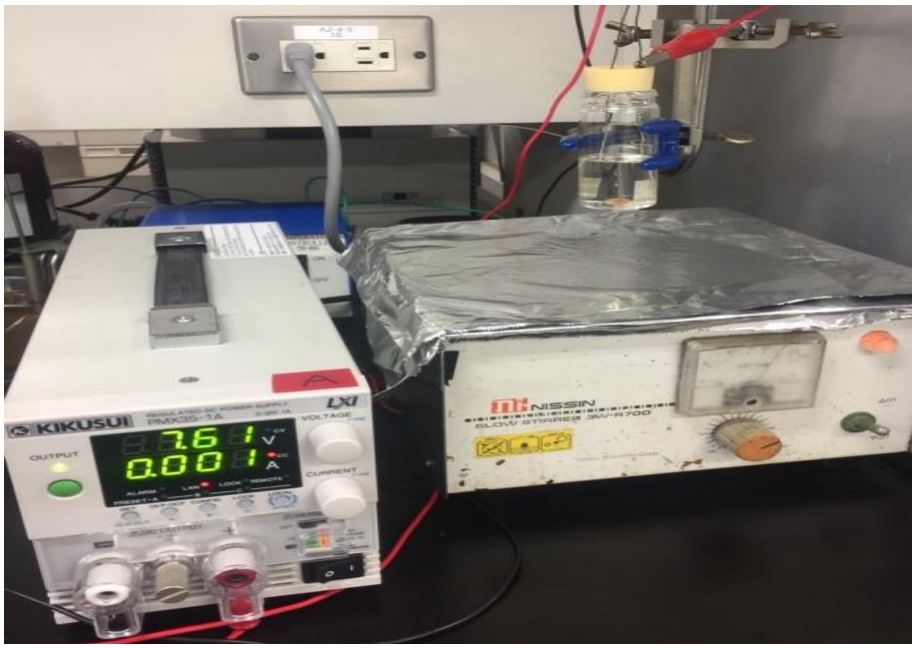
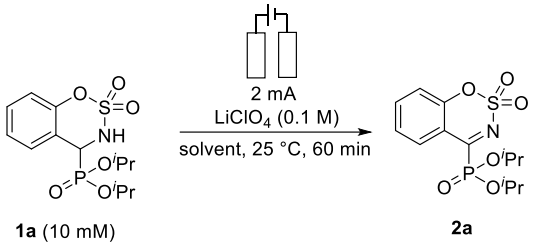


Figure S1 (b): DC power supply (KIKUSUI PMX 35.0-1.0A)

General procedure for the electrochemical synthesis of cyclic sulfonyl ketimines 2

In a reaction vessel (12 mL) equipped with a stirring bar, a mixture of substrates **1** (0.0624 mmol), $LiClO_4$ (1.14 mmol), and MeCN (6.0 mL) were added. The cell was equipped with platinum plates as the cathode and anode and performed in a KIKUSUI PMX 35-1A. The reaction mixture was stirred and electrolyzed at a constant current of 3 mA at 45 °C for 2 h. Upon completion, the solvent was removed under reduced pressure to afford the crude product, which was dissolved in AcOEt and washed with distilled water, and dried over Na_2SO_4. After removal solvent under reduced pressure, the residue was further purified by silica gel chromatography (Hexane/Acetone = 4/1 to 2/1) to afford the desired products **2.**

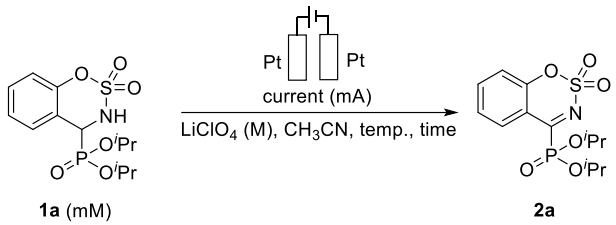
Table S1. Screening of electrolytes, solvents, and electrodes[a]



entry	electrodes	electrolyte	solvent	conversion (%)[b]	NMR yield (%)[b]
1	Pt(+)/Pt(-)	$LiClO_4$	CH_3CN	40	22
2	Pt(+)/Pt(-)	Et_4NClO_4	CH_3CN	78	6
3	Pt(+)/Pt(-)	Bu_4NClO_4	CH_3CN	40	9
4	Pt(+)/Pt(-)	Bu_4NBF_4	CH_3CN	50	5
5	Pt(+)/Pt(-)	Bu_4NPF_6	CH_3CN	47	4
6	Pt(+)/Pt(-)	$LiClO_4$	CH_3OH	0	0
7	Pt(+)/Pt(-)	$LiClO_4$	DMF	20	0
8	Pt(+)/Pt(-)	$LiClO_4$	THF	5	0
9	Pt(+)/Pt(-)	$LiClO_4$	Acetone	35	14
10	C(+)/Pt(-)	$LiClO_4$	CH_3CN	10	0
11	C(+)/C(-)	$LiClO_4$	CH_3CN	0	0

[a]Reaction conditions: undivided cell, **1a** (10 mM), $LiClO_4$ (0.1 M), constant current = 2 mA, under air. [b]1,3,5-Trimethoxybenzene was used as an internal standard.

Table S2. Table 1 in the manuscript



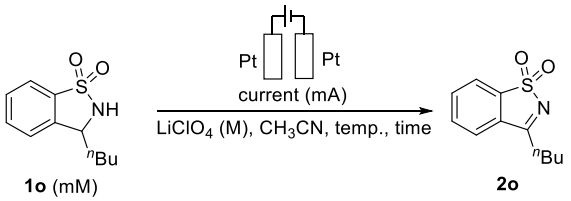
entry	current (mA)	**1a** (mM)	$LiClO_4$ (M)	Temp. (°C)	Time (min)	NMR yield (%)[b]
1	1	10	0.05	60	180	8.4 (≈ 8)
2	2	20	0.2	25	60	16
3	3	10	0.1	40	120	65
4	4	15	0.1	40	60	38
5	5	5	0.05	25	120	26
6	4	11	0.22	50	130	60
7	3	11	0.13	45	120	66
8	1	18	0.05	45	120	3
9	3	9.7	0.12	45	120	65
10	5	10	0.21	45	120	41
11	2	10	0.06	45	120	50
12	**3**	**10.4**	**0.19**	**45**	**120**	**72** (71)[c]
13	3	10.4	0.25	45	120	64
14	3	10.5	0.05	45	120	60

[a]Reaction conditions: undivided cell, Pt anode, Pt cathode, **1a**, $LiClO_4$, CH_3CN (6 mL), under air. [b]1,3,5-Trimethoxybenzene was used as an internal standard. [c]Isolated yield. [d]During the BO using all parameters and yields in entries 1 to 12, the outcome in entry 12 shows a trend of saturation close to highest yield. Additional investigations in entries 13 and 14 support the saturation.

Bayesian Optimization using GPyOpt for Table S2

```
import numpy as np
import GPy
import GPyOpt
import warnings
warnings.filterwarnings('ignore')

X = np.array([[ 1,  10,  0.05,  60,  180],
              [ 2,  20,  0.2,  25,  60],
              [ 3,  10,  0.1,  40,  120],
              [ 4,  15,  0.1,  40,  60],
              [ 5,  5,  0.05,  25,  120],
              [ 4,  11,  0.22,  50,  130],
             [ 3,  11,  0.13,  45,  120],
             [ 1,  18,  0.05,  45,  120],
             [3,  9.7,  0.12,  45,  120],
             [ 5,  10,  0.21,  45,  120],
             [2,  10,  0.06,  45,  120],
             [3,  10.4,  0.19,  45,  120],
             [3,  10.4,  0.25,  45,  120],
             [3,  10.5,  0.05,  45,  120]])

Y = -np.array([8.4,  16,  65,  38,  26,  60,  66,  3,  65,  41,  50,  72,  64,  60])[:, np.newaxis]

initial_x = X
initial_y = Y

bounds = [{'name': 'current', 'type': 'continuous', 'domain': (1,6)},
          {'name': 'int_molarity', 'type': 'continuous', 'domain': (5,30)},
          {'name': 'electrolyte', 'type': 'continuous', 'domain': (0.05,0.25)},
          {'name': 'temp', 'type': 'continuous', 'domain': (20,80)},
          {'name': 'time', 'type': 'continuous', 'domain': (60,240)}]

myBopt = GPyOpt.methods.BayesianOptimization(f=None,
                                             domain=bounds,
                                             X = initial_x,
                                             Y = initial_y,
                                             acquisition_type='EI',

                                             )

next_x = myBopt.suggest_next_locations()
print(next_x)
```

Table S3. Table 2 in the manuscript



1o (mM) **2o**

entry	current (mA)	**1o** (mM)	$LiClO_4$ (M)	Temp. (℃)	Time (min)	NMR yield (%)[b]
1	1	10	0.05	60	180	46
2	2	20	0.2	25	60	22
3	3	10	0.1	40	120	62
4	4	15	0.1	40	60	53
5	5	5	0.05	25	120	14
6	4	10	0.12	60	180	29
7	**3**	**11.7**	**0.22**	**40**	**120**	**67 (66)[c]**
8	3	13	0.25	40	120	67
9	2	12.6	0.25	40	120	52

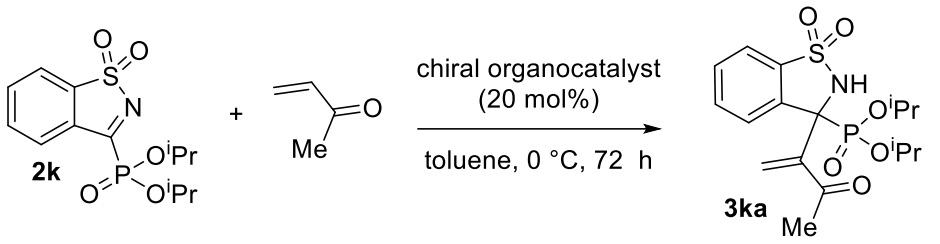
[a]Reaction conditions: undivided cell, Pt anode, Pt cathode, **1o**, $LiClO_4$, CH_3CN (6 mL), under air. [b]1,3,5-Trimethoxybenzene was used as an internal standard. [c]Isolated yield. [d]During the BO using all parameters and yields in entries 1 to 7, the outcome in entry 7 shows a trend of saturation close to highest yield. Additional investigations in entries 8 and 9 support the saturation.

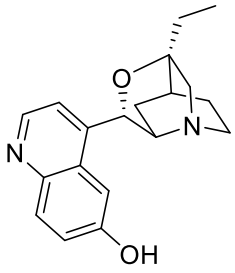
Bayesian Optimization using GPyOpt for Table S3

```
import numpy as np
import GPy
import GPyOpt
import warnings
warnings.filterwarnings('ignore')

X = np.array([[ 1,  10,  0.05,  60,  180],
              [ 2,  20,  0.2,  25,  60],
              [ 3,  10,  0.1,  40,  120],
              [ 4,  15,  0.1,  40,  60],
              [ 5,  5,  0.05,  25,  120],
             [ 4,  10,  0.12,  60,  180],
              [ 3,  11.7,  0.22,  40,  120],
             [ 3,  13,  0.25,  40,  120],
             [ 2,  12.6,  0.25,  40,  120]])

Y = -np.array([46,22,62,53,14,29,67,67,52])[:, np.newaxis]

initial_x = X
initial_y = Y

bounds = [{'name': 'current', 'type': 'continuous', 'domain': (1,6)},
          {'name': 'Init_molarity', 'type': 'continuous', 'domain': (5,30)},
          {'name': 'electrolyte', 'type': 'continuous', 'domain': (0.05,0.25)},
          {'name': 'temp', 'type': 'continuous', 'domain': (20,80)},
          {'name': 'time', 'type': 'continuous', 'domain': (60,240)}]

myBopt = GPyOpt.methods.BayesianOptimization(f=None,
                                             domain=bounds,
                                             X = initial_x,
                                             Y = initial_y,
                                             acquisition_type='EI',

                                             )

next_x = myBopt.suggest_next_locations()
print(next_x)
```

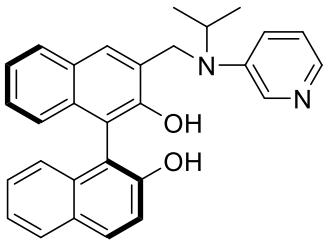
Table S4. Screening of organocatalysts for enantioselective reactions of **2k**

For aza-MBH reaction

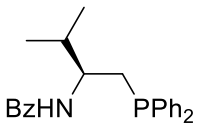




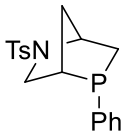
β-ICD[2]
3ka: 71% yield, 70% ee



Sasai catalyst[3]
3ka: 72% yield, 38% ee

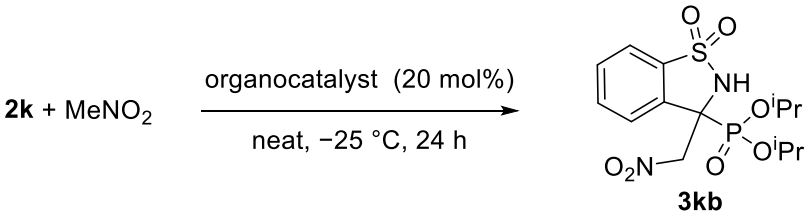


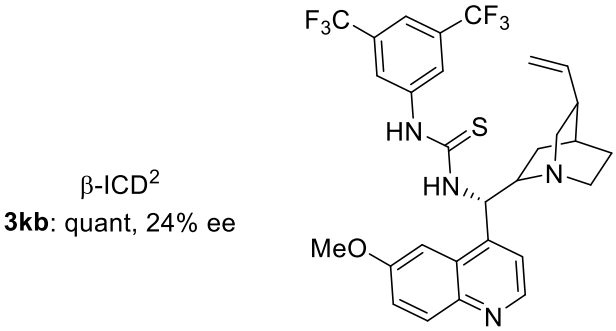
Wu catalyst[4]
3ka: trace



Kwon catalyst[5]
3ka: complex mixture

For aza-Henry reaction

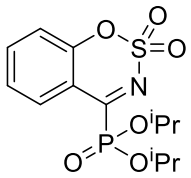




β-ICD[2]
3kb: quant, 24% ee

quinine-derived thiourea catalyst
3kb: quant, 21% ee

1,2,3-Benzoxathiazine-2,2-dioxide-4-diisopropylphosphonate (2a)

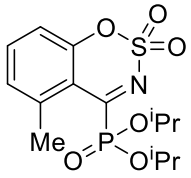


2a: 71% yield

^{1}H and ^{13}C NMR charts were consistent with previously reported data.[1a]

^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.51 (d, *J* = 7.8 Hz, 1H), 7.76-7.72 (m, 1H), 7.44-7.41 (m, 1H), 7.30 (d, *J* = 8.2 Hz, 1H), 4.96-4.88 (m, 2H), 1.43 (d, *J* = 6.2 Hz, 6H), 1.40 (d, *J* = 6.2 Hz, 6H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 173.6 (d, $J_{C\text{-}P}$ = 199.4 Hz), 154.4 (d, $J_{C\text{-}P}$ = 8.6 Hz), 137.7, 131.5, 126.3, 119.1, 115.9 (d, $J_{C\text{-}P}$ = 24.9 Hz), 75.2 (d, $J_{C\text{-}P}$ = 6.7 Hz), 24.1 (d, $J_{C\text{-}P}$ = 3.8 Hz), 23.9 (d, $J_{C\text{-}P}$ = 4.8 Hz)

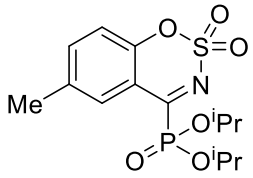
1,2,3-Benzoxathiazine-2,2-dioxide-5-methyl-4-diisopropylphosphonate (2b)



2b: 85% yield

^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.34 (d, *J* = 7.6 Hz, 1H), 7.58 (d, *J* = 7.6 Hz, 1H), 7.31 (t, *J* = 7.6 Hz, 1H), 4.94-4.89 (m, 2H), 2.40 (s, 3H), 1.42 (d, *J* = 6.2 Hz, 6H), 1.40 (d, *J* = 6.2 Hz, 6H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 173.8 (d, $J_{C\text{-}P}$ = 199.4 Hz), 152.6 (d, $J_{C\text{-}P}$ = 9.6 Hz), 139.2, 128.8 (d, $J_{C\text{-}P}$ = 2.9 Hz), 125.6, 115.6 (d, $J_{C\text{-}P}$ = 24.0 Hz), 75.0 (d, $J_{C\text{-}P}$ = 7.7 Hz), 24.1 (d, $J_{C\text{-}P}$ = 3.8 Hz), 23.8 (d, $J_{C\text{-}P}$ = 4.8 Hz), 15.0; ^{31}P NMR (240 MHz, $CDCl_3$) δ 0.2; HRMS (ESI) calcd for 384.0641: *m/z* ([M+Na^+]), found 384.0641; IR (KBr) 2988, 1544, 1403, 1253, 1101, 1005 cm^{-1}.

1,2,3-Benzoxathiazine-2,2-dioxide-6-methyl-4-diisopropylphosphonate (2c)

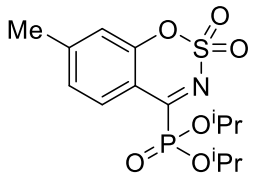


2c: 95% yield

^{1}H and ^{13}C NMR charts were consistent with previously reported data.[6]

^{1}H-NMR (400 MHz, $CDCl_3$)δ 8.3-8.27 (m, 1H), 7.54-7.52 (m, 1H), 7.20-7.17 (m, 1H), 4.95-4.87 (m, 2H), 2.44 (s, 3H), 1.43 (d, *J* = 6.2 Hz, 6H), 1.40 (d, *J* = 6.2 Hz, 6H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 173.6 (d, $J_{C\text{-}P}$ = 199.4 Hz), 152.4 (d, $J_{C\text{-}P}$ = 8.6 Hz), 138.6, 136.5, 131.2, 115.7 (d, $J_{C\text{-}P}$ = 24.0 Hz), 118.8, 75.1 (d, $J_{C\text{-}P}$ = 6.7 Hz), 24.1 (d, $J_{C\text{-}P}$ = 3.8 Hz), 23.9 (d, $J_{C\text{-}P}$ = 5.8 Hz), 21.1

1,2,3-Benzoxathiazine-2,2-dioxide-7-methyl-4-diisopropylphosphonate (2d)

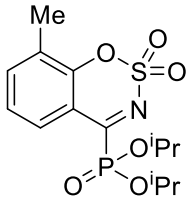


2d: 72% yield

^{1}H and ^{13}C NMR charts were consistent with previously reported data.[1a]

^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.38 (d, *J* = 8.2 Hz, 1H), 7.21 (d, *J* = 8.2 Hz, 1H), 7.09 (s, 1H), 4.94-4.86 (m, 2H), 2.49 (s, 3H), 1.42 (d, *J* = 6.2 Hz, 6H), 1.39 (d, *J* = 6.2 Hz, 6H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 173.2 (d, $J_{C\text{-}P}$ = 200.3 Hz), 154.5 (d, $J_{C\text{-}P}$ = 9.6 Hz), 150.6, 131.2 127.3, 119.3 (d, $J_{C\text{-}P}$ = 3.8 Hz), 113.6 (d, $J_{C\text{-}P}$ = 24.9 Hz), 75.0 (d, $J_{C\text{-}P}$ = 7.7 Hz), 24.1 (d, $J_{C\text{-}P}$ = 3.8 Hz), 23.9 (d, $J_{C\text{-}P}$ = 4.8 Hz), 22.4

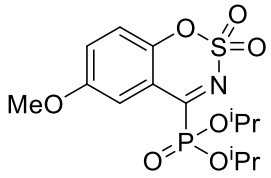
1,2,3-Benzoxathiazine-2,2-dioxide-8-methyl-4-diisopropylphosphonate (2e)



2e: 92% yield

^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.34 (d, *J* = 7.8 Hz, 1H), 7.58 (d, *J* = 8.0 Hz, 1H), 7.33-7.29 (m, 1H), 4.95-4.87 (m, 2H), 2.40 (s, 3H), 1.42 (d, *J* = 6.2 Hz, 6H), 1.39 (d, *J* = 6.2 Hz, 6H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 173.9 (d, $J_{C\text{-}P}$ = 200.3 Hz), 152.7 (d, $J_{C\text{-}P}$ = 8.6 Hz), 139.3, 128.9 (d, $J_{C\text{-}P}$ = 14.4 Hz), 125.6, 115.7 (d, $J_{C\text{-}P}$ = 24.9 Hz), 75.0 (d, $J_{C\text{-}P}$ = 6.7 Hz), 24.1 (d, $J_{C\text{-}P}$ = 2.9 Hz), 23.9 (d, $J_{C\text{-}P}$ = 5.8 Hz), 15.0; ^{31}P NMR (240 MHz, $CDCl_3$) δ 0.2; HRMS (ESI) calcd for *m/z* 384.0641: ([M+Na^+]), found *m/z* 384.0640; IR (KBr) 2985, 1545, 1403, 1253, 1178, 1006 cm^{-1}.

1,2,3-Benzoxathiazine-2,2-dioxide-6-methoxy-4-diisopropylphosphonate (2f)

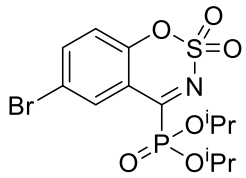


2f: 75% yield

^{1}H and ^{13}C NMR charts were consistent with previously reported data.[1a]

^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.02-8.01 (m, 1H), 7.29-7.26 (m, 1H), 7.23-7.21 (m, 1H), 4.94-4.89 (m, 2H), 3.87 (s, 3H), 1.44 (d, *J* = 6.2 Hz, 6H), 1.41 (d, *J* = 6.2 Hz, 6H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 173.3 (d, $J_{C\text{-}P}$ = 200.3 Hz), 157.06, 148.3 (d, $J_{C\text{-}P}$ = 7.7 Hz), 125.3, 120.1, 116.2 (d, $J_{C\text{-}P}$ = 24.0 Hz), 113.3, 75.1 (d, $J_{C\text{-}P}$ = 7.7 Hz), 56.2, 24.1 (d, $J_{C\text{-}P}$ = 2.9 Hz), 23.9 (d, $J_{C\text{-}P}$ = 5.8 Hz)

1,2,3-Benzoxathiazine-2,2-dioxide-6-bromo-4-diisopropylphosphonate (2g)

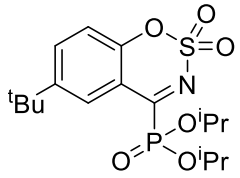


2g: 75% yield

^{1}H and ^{13}C NMR charts were consistent with previously reported data.[7]

^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.65-8.61 (m, 1H), 7.85-7.82 (m, 1H), 7.21-7.19 (m, 1H), 4.97-4.90 (m, 2H), 1.44 (d, *J* = 6.2 Hz, 6H), 1.42 (d, *J* = 6.2 Hz, 6H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 172.6 (d, $J_{C\text{-}P}$ = 200.3 Hz), 153.2 (d, $J_{C\text{-}P}$ = 8.6 Hz), 140.4, 133.7, 120.8, 119.1, 117.0 (d, $J_{C\text{-}P}$ = 24.0 Hz), 75.5 (d, $J_{C\text{-}P}$ = 7.7 Hz), 24.2 (d, $J_{C\text{-}P}$ = 3.8 Hz), 23.9 (d, $J_{C\text{-}P}$ = 4.8 Hz)

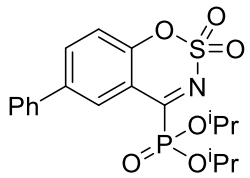
1,2,3-Benzoxathiazine-2,2-dioxide-6-*tert*-butyl-4-diisopropylphosphonate (2h)



2h: 98% yield

^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.52-8.49 (m, 1H), 7.77-7.75 (m, 1H), 7.22 (d, *J* = 8.7 Hz, 1H), 4.96-4.88 (m, 2H), 1.43 (d, *J* = 6.4 Hz, 6H), 1.41 (d, *J* = 6.4 Hz, 6H), 1.36 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 173.7 (d, $J_{C\text{-}P}$ = 200.3 Hz), 152.2 (d, $J_{C\text{-}P}$ = 8.6 Hz), 149.7, 135.3, 128.1, 118.2 115.4 (d, $J_{C\text{-}P}$ = 24.0 Hz), 74.9 (d, $J_{C\text{-}P}$ = 6.7 Hz), 35.1, 31.2, 24.2 (d, $J_{C\text{-}P}$ = 3.8 Hz), 23.9 (d, $J_{C\text{-}P}$ = 5.8 Hz); ^{31}P NMR (240 MHz, $CDCl_3$) δ 0.6; HRMS (ESI) calcd for *m/z* 426.1111: ([M+Na^+]), found *m/z* 426.1110; IR (KBr) 2970, 1547, 1401, 1254, 1192, 1002 cm^{-1}.

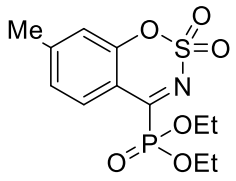
1,2,3-Benzoxathiazine-2,2-dioxide-6-phenyl-4-diisopropylphosphonate (2i)



2i: 73% yield

^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.75-8.73 (m, 1H), 7.96-7.93 (m, 1H), 7.58 (d, *J* = 7.3 Hz, 2H), 7.51-7.46 (m, 2H), 7.43 (d, *J* = 6.9 Hz, 1H), 7.37 (d, *J* = 8.2 Hz, 1H), 4.96-4.92 (m, 2H), 1.44 (d, *J* = 6.2 Hz, 6H), 1.42 (d, *J* = 6.2 Hz, 6H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 173.6 (d, $J_{C\text{-}P}$ = 199.4 Hz), 153.5 (d, $J_{C\text{-}P}$ = 8.6 Hz), 139.8, 138.3, 136.2, 129.6, 129.4, 128.6, 127.2, 119.4, 116.0 (d, $J_{C\text{-}P}$ = 24.0 Hz), 75.2 (d, $J_{C\text{-}P}$ = 7.7 Hz), 29.8, 24.2 (d, $J_{C\text{-}P}$ = 2.9 Hz), 23.9 (d, $J_{C\text{-}P}$ = 5.8 Hz); ^{31}P NMR (240 MHz, $CDCl_3$) δ 0.0; HRMS (ESI) calcd for *m/z* 446.0798: ([M+Na^+]), found *m/z* 446.0797; IR (KBr) 2925, 1544, 1401, 1261, 1191, 1006 cm^{-1}.

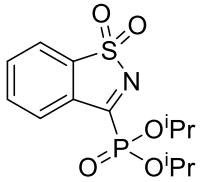
1,2,3-Benzoxathiazine-2,2-dioxide-7-methyl-4-diethylphosphonate (2j)



2j: 79% yield

^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.36 (d, J = 8.2 Hz, 1H), 7.22 (d, J = 8.2 Hz, 1H), 7.11 (s, 1H), 4.39-4.31 (m, 4H), 2.49 (s, 3H), 1.41 (t, J = 7.1 Hz, 6H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 172.5 (d, $J_{C\text{-}P}$ = 198.4 Hz), 154.5 (d, $J_{C\text{-}P}$ = 9.6 Hz), 150.8, 131.1, 127.5, 119.3 (d, $J_{C\text{-}P}$ = 3.8 Hz), 113.6 (d, $J_{C\text{-}P}$ = 24.9 Hz), 65.5 (d, $J_{C\text{-}P}$ = 6.7 Hz), 22.5, 16.4 (d, $J_{C\text{-}P}$ = 5.8 Hz); ^{31}P NMR (240 MHz, $CDCl_3$) δ 1.7; HRMS (ESI) calcd for *m/z* 356.0328: ([M+Na^+]), found *m/z* 356.0322; IR (KBr) 2965, 1623, 1527, 1397, 1260, 1198, 1021 cm^{-1}.

Diisopropyl-(1,1-dioxidobenzo[d]isothiazol-3-yl)phosphonate (2k)

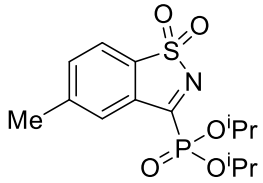


2k: 71% yield

^{1}H and ^{13}C NMR charts were consistent with previously reported data.[1a]

^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.22-8.19 (m, 1H), 7.94-7.92 (m, 1H), 7.77-7.75 (m, 2H), 4.98-4.93 (m, 2H), 1.44-1.41 (m, 12H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 168.3 (d, $J_{C\text{-}P}$ = 205.1 Hz), 138.7, 134.3 (d, $J_{C\text{-}P}$ = 40.0 Hz), 130.2 (d, $J_{C\text{-}P}$ = 25.9 Hz), 127.8, 123.0, 75.1 (d, $J_{C\text{-}P}$ = 6.7 Hz), 24.1 (d, $J_{C\text{-}P}$ = 3.8 Hz), 24.0 (d, $J_{C\text{-}P}$ = 4.8 Hz)

Diisopropyl-(5-methyl-1,1-dioxidobenzo[d]isothiazol-3-yl)phosphonate (2l)

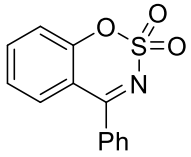


2l: 72% yield

^{1}H and ^{13}C NMR charts were consistent with previously reported data.[1a]

^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.00 (s, 1H), 7.79 (d, J = 7.8 Hz, 1H), 7.54 (d, J = 7.8 Hz, 1H), 4.97-4.92 (m, 2H), 2.52 (s, 3H), 1.43 (d, J = 6.2 Hz, 6H), 1.41 (d, J = 6.2 Hz, 7H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 168.3 (d, $J_{C\text{-}P}$ = 203.2 Hz), 146.0, 136.0, 134.7, 130.7 (d, $J_{C\text{-}P}$ = 24.9 Hz), 128.1, 122.8, 75.1 (d, $J_{C\text{-}P}$ = 6.7 Hz), 24.1 (d, $J_{C\text{-}P}$ = 3.8 Hz), 23.9 (d, $J_{C\text{-}P}$ = 5.8 Hz), 21.9

4-Phenyl-1,2,3-benzoxathiazine-2,2-dioxide (2m)

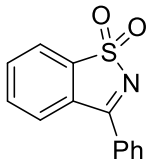


2m: 87% yield

^{1}H and ^{13}C NMR charts were consistent with previously reported data.[1b]

^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.72-7.84 (m, 3H), 7.62-7.72 (m, 2H), 7.52-7.62 (m, 2H), 7.33-7.47 (m, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 176.5, 154.7, 137.0, 133.8, 133.3, 131.9, 130.7, 129.0, 125.8, 119.6, 116.7

3-Phenyl-1,2-benzisothiazole 1,1-dioxide (2n)

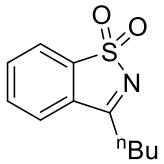


2n: 94% yield

^{1}H and ^{13}C NMR charts were consistent with previously reported data.[1b]

^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 7.5 Hz, 1H), 7.98 (d, *J* = 7.8 Hz, 2H), 7.91 (d, *J* = 7.5 Hz, 1H), 7.82-7.75 (m, 2H), 7.73-7.69 (m, 1H), 7.64-7.60 (m, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 171.2, 141.2, 133.8, 133.6, 130.7, 130.5, 129.6, 129.4, 126.7, 123.2

3-(*n*-Butyl)-1,2-benzisothiazole 1,1-dioxide (2o)

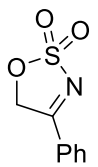


2o: 66% yield

^{1}H and ^{13}C NMR charts were consistent with previously reported data.[8]

^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.93-7.91 (m, 1H), 7.75-7.69 (m, 3H), 2.97 (t, *J* = 7.3 Hz, 2H), 1.90-1.86 (m, 2H), 1.54-1.49 (m, 2H), 0.99 (t, *J* = 7.6 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 176.5, 139.9, 134.0, 133.6, 131.5, 124.0, 122.6, 31.0, 27.6, 22.5, 13.9

4-Phenyl-5H-[1,2,3]oxathiazole 2,2-Dioxide (2p)

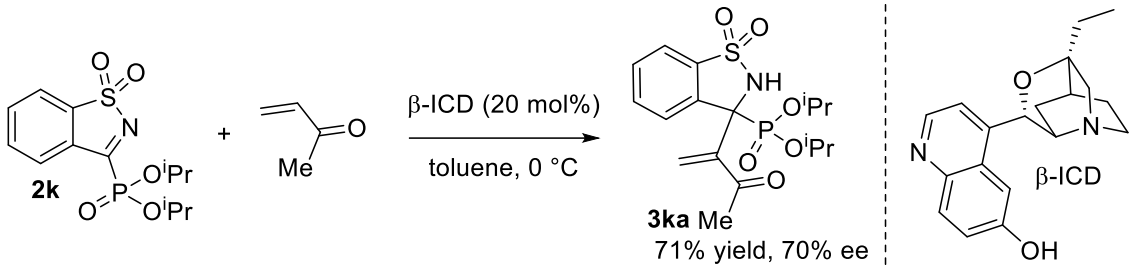


2p: 80% yield

^{1}H and ^{13}C NMR charts were consistent with previously reported data.[9]

^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.93-7.91 (m, 2H), 7.77-7.72 (m, 1H), 7.59 (t, *J* = 7.8 Hz, 2H), 5.59 (s, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 175.5, 136.1, 129.8, 129.1, 127.3, 74.5

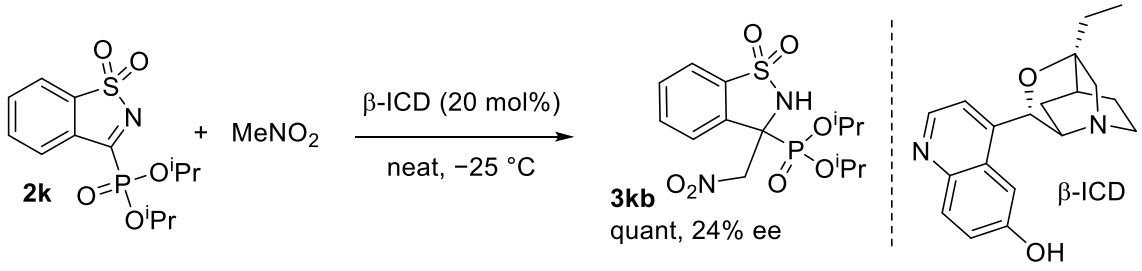
Diisopropyl-(1,1-dioxido-3-(3-oxobut-1-en-2-yl)-2,3-dihydrobenzo[d]isothiazol-3-yl)phosphonate (3ka)



Methyl vinyl ketone (27 μL, 0.33 mmol) was added to a mixture of diisopropyl (1,1-dioxidobenzo[d]isothiazol-3-yl)phosphonate (**2k**) (35.1 mg, 0.11 mmol) and β-ICD (6.8 mg, 0.022 mol) in toluene (1 mL) at 0 ºC under nitrogen atmosphere. After stirring 0 ºC for 72 h, toluene (10 mL) was added to the mixture. Subsequently the diluted reaction mixture was filtrated with a pad of silica gel using acetone as an eluent, the filtrate was condensed *in vacuo*, the obtained residue was purified by PTLC (eluent: EtOAc only x 2) to give the title compound **3ka** (31.4 mg, 71% yield).

^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 7.6 Hz, 1H), 7.85 (d, *J* = 7.6 Hz, 1H), 7.71 (t, *J* = 7.6 Hz, 1H), 7.63 (t, *J* = 7.6 Hz, 1H), 7.60 (brs, 1H), 6.28-6.24 (m, 1H), 6.15-6.12 (m, 1H), 4.80-4.72 (m, 1H), 4.52-4.55 (m, 1H), 2.46 (s, 3H), 1.32 (d, *J* = 6.0 Hz, 3H), 1.25-1.21 (m, 6H), 0.90 (d, *J* = 6.0 Hz, 3H); ^{13}C-NMR (150 MHz, $CDCl_3$) δ 201.3, 142.6, 135.6, 134.7, 132.7, 130.4, 130.0, 127.7, 122.1, 74.1 (d, $J_{C\text{-}P}$ = 7.2 Hz), 73.9 (d, $J_{C\text{-}P}$ = 7.2 Hz), 66.3 (d, $J_{C\text{-}P}$ = 167.6 Hz), 28.7, 24.2, 23.7 (d, $J_{C\text{-}P}$ = 5.8 Hz), 23.2 (d, $J_{C\text{-}P}$ = 5.8 Hz); ^{31}P NMR (240 MHz, $CDCl_3$) δ 14.6; HRMS (ESI) calcd for *m/z* 424.0954: ([M+Na^+]), found *m/z* 424.0953; IR (KBr) 2982, 2936, 1737, 1453, 1376, 1304, 1249, 1171, 1103, 994 cm^{-1}; $[\alpha]_D^{18}$ = +15.4 (c 3.9 $CHCl_3$ for 70% ee); HPLC conditions: Daicel Chiralpak IE column, *n*-hexane/^{i}PrOH = 50/50, 1.0 mL/min, 224 nm, tR = 31.9 min (major isomer) and 44.6 min (minor isomer).

Diisopropyl-(3-(nitromethyl)-1,1-dioxido-2,3-dihydrobenzo[d]isothiazol-3-yl)phosphonate (3kb)



Nitrometane (0.1 mL, 1.9 mmol) was added to a mixture of diisopropyl

(1,1-dioxidobenzo[d]isothiazol-3-yl)phosphonate (**2k**) (35.1 mg, 0.11 mmol) and β-ICD (6.8 mg, 0.022 mol) at –25 ºC under nitrogen atmosphere. After stirring –25 ºC for 24 h, toluene (10 mL) was added to the mixture. Subsequently the diluted reaction mixture was filtrated with a pad of silica gel using EtOAc as an eluent, the filtrate was condensed *in vacuo*, the obtained residue was purified by SiO_2 column chromatography (eluent: EtOAc/*n*-hexane = 1/3) to give the title compound **3kb** (43.2 mg, quant).

^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.88-7.83 (m, 2H), 7.77-7.68 (m, 2H), 5.81 (brs, 1H), 5.10-4.89 (m, 2H), 4.87-4.85 (m, 1H), 4.45-4.37 (m, 1H), 1.37 (d, *J* = 6.0 Hz, 3H), 1.30 (d, *J* = 6.0 Hz, 3H), 1.27 (d, *J* = 6.0 Hz, 3H), 0.83 (d, *J* = 6.0 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 135.4 (d, $J_{C\text{-}P}$ = 4.8 Hz), 133.7, 131.9 (d, $J_{C\text{-}P}$ = 4.8 Hz), 125.4, 122.2, 78.0 (d, $J_{C\text{-}P}$ = 9.6 Hz), 75.1 (d, $J_{C\text{-}P}$ = 7.6 Hz), 75.0(d, $J_{C\text{-}P}$ = 7.6 Hz), 62.4 (d, $J_{C\text{-}P}$ = 162 Hz), 24.3 (d, $J_{C\text{-}P}$ = 5.8 Hz), 24.2 (d, $J_{C\text{-}P}$ = 5.8 Hz), 23.7 (d, $J_{C\text{-}P}$ = 5.8 Hz), 23.0 (d, $J_{C\text{-}P}$ = 5.8 Hz); ^{31}P NMR (240 MHz, $CDCl_3$) δ ; HRMS (ESI) calcd for *m/z* 415.0699: ([M+Na^+]), found *m/z* 415.0700; IR (KBr) 3102, 1562, 1376, 1306, 1230, 1016 cm^{-1}; $[\alpha]_D^{25}$ = +6.8 (c 6.5 $CHCl_3$ for 24% ee); HPLC conditions: Daicel Chiralpak IE column, *n*-hexane/^{i}PrOH = 50/50, 1.0 mL/min, 275 nm, tR = 14.7 min (minor isomer) and 20.8 min (major isomer).

General procedure for the electrochemical synthesis of cyclic sulfonyl ketamine 2o with one gram of 1o

In a reaction vessel (12 mL) equipped with a stirring bar, a mixture of the substrate **1o** (1.0 g, 4.44 mmol), $LiClO_4$ (1.14 mmol), and MeCN (6.0 mL) were added. The cell was equipped with platinum plates as the cathode and anode and performed in a KIKUSUI PMX 35-1A. The reaction mixture was stirred and electrolyzed at a constant current of 20 mA at 40 °C for 16 h. Upon completion, the solvent was removed under reduced pressure to afford the crude product, which was dissolved in AcOEt and washed with distilled water, and dried over Na_2SO_4. After removal solvent under reduced pressure, the residue was further purified by silica gel chromatography (Hexane/Acetone = 4/1) to afford the desired products **2o** (53%, 521 mg).

Cyclic voltammograms

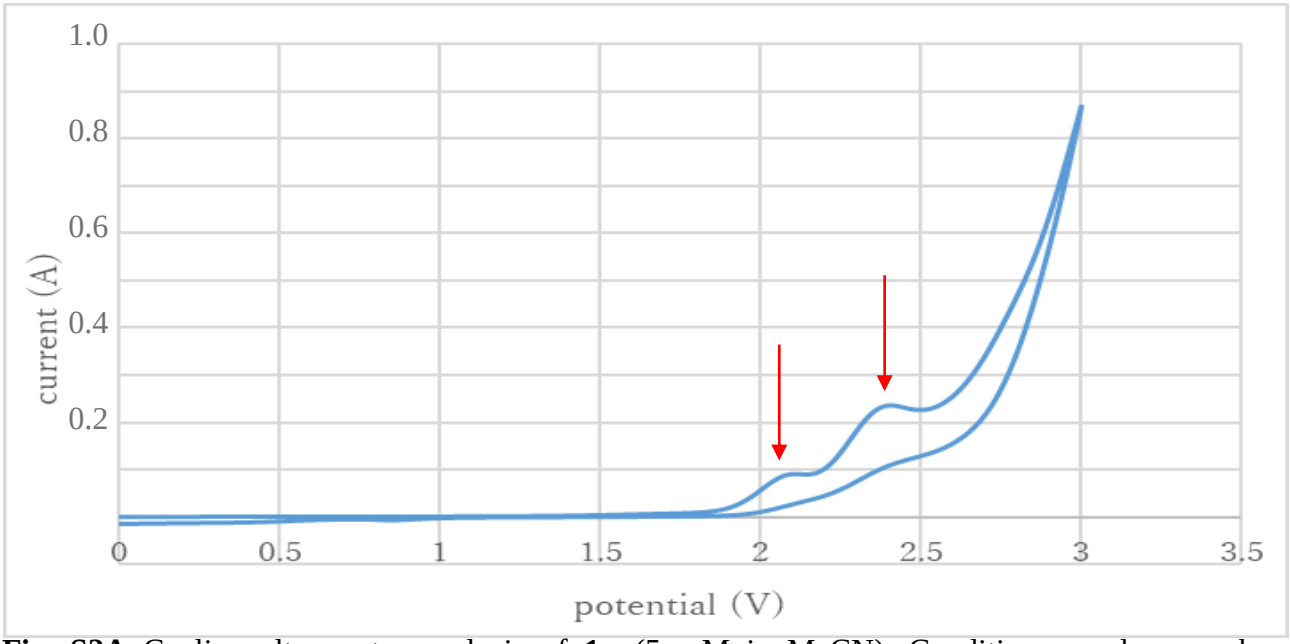


Fig. S2A Cyclic voltammetry analysis of **1n** (5 mM in MeCN). Conditions: a glassy carbon working electrode, a $Ag/AgNO_3$ reference electrode, and a platinum wire counter electrode, $LiClO_4$ (0.1 M in MeCN), 100 mV/s scan rate

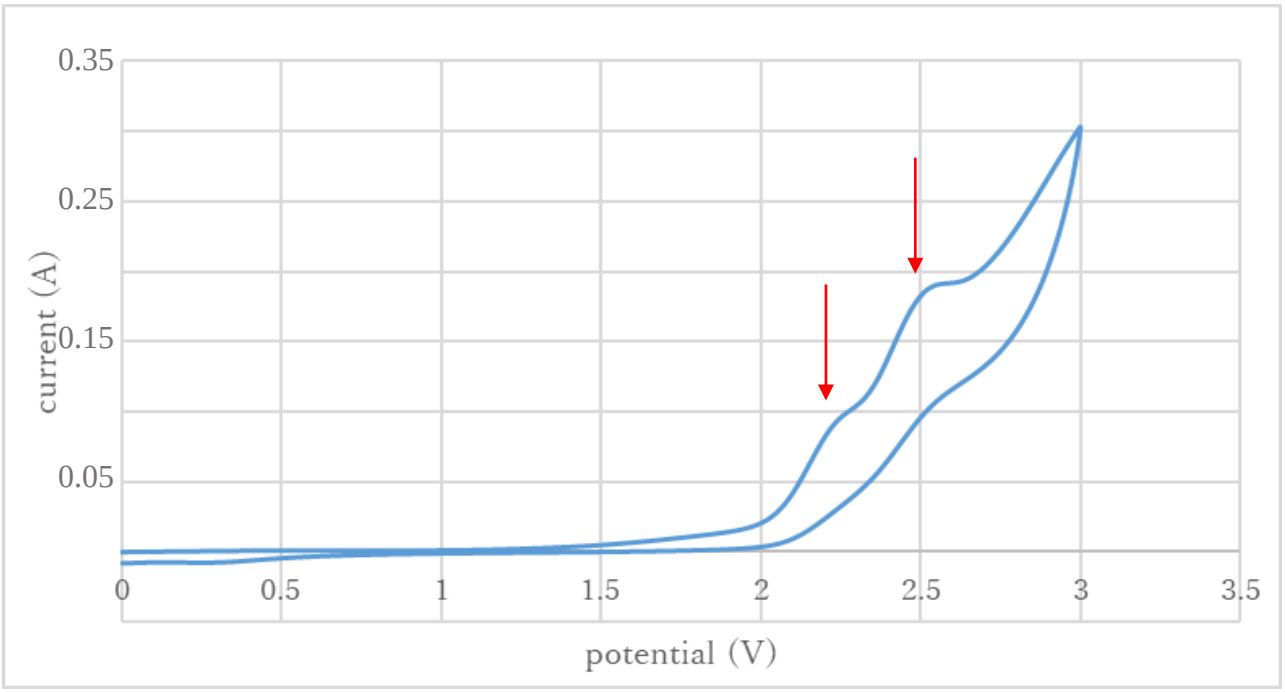


Fig. S2B Cyclic voltammetry analysis of **1n** (5 mM in MeCN). Conditions: a glassy carbon working electrode, a $Ag/AgNO_3$ reference electrode, and a platinum wire counter electrode, $^nBu_4NPF_6$ (0.1 M in MeCN), 100 mV/s scan rate

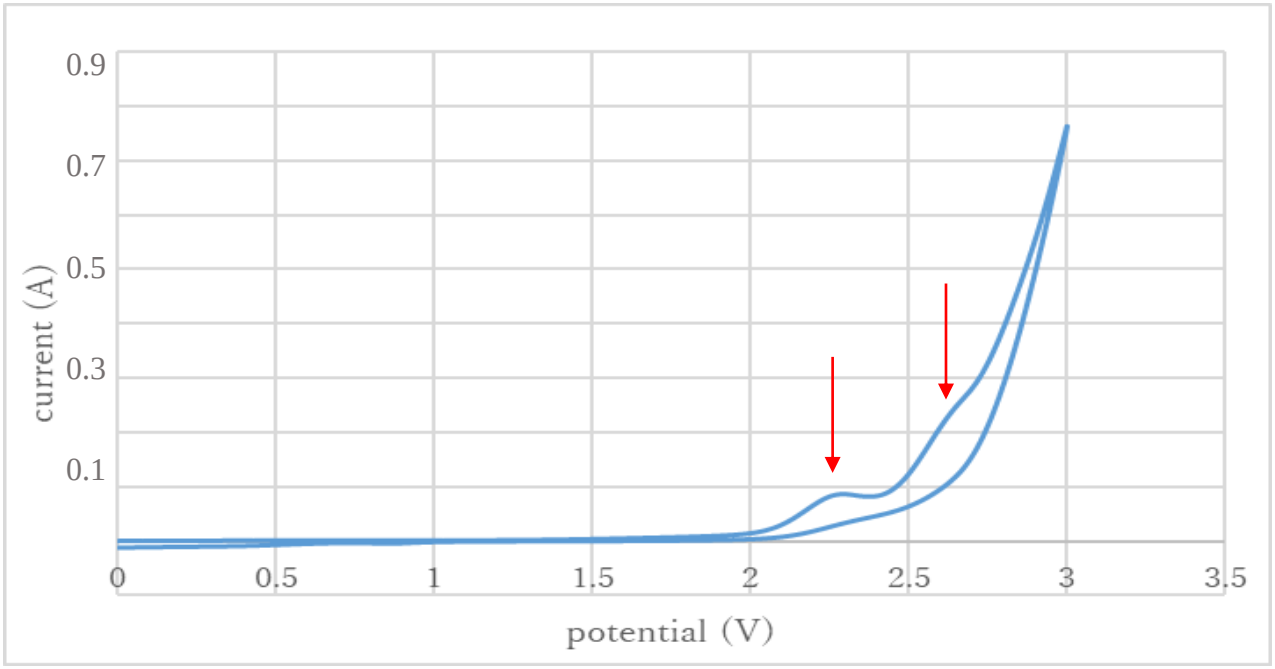


Fig. S2C Cyclic voltammetry analysis of **1o** (5 mM in MeCN). Conditions: a glassy carbon working electrode, a $Ag/AgNO_3$ reference electrode, and a platinum wire counter electrode, $LiClO_4$ (0.1 M in MeCN), 100 mV/s scan rate

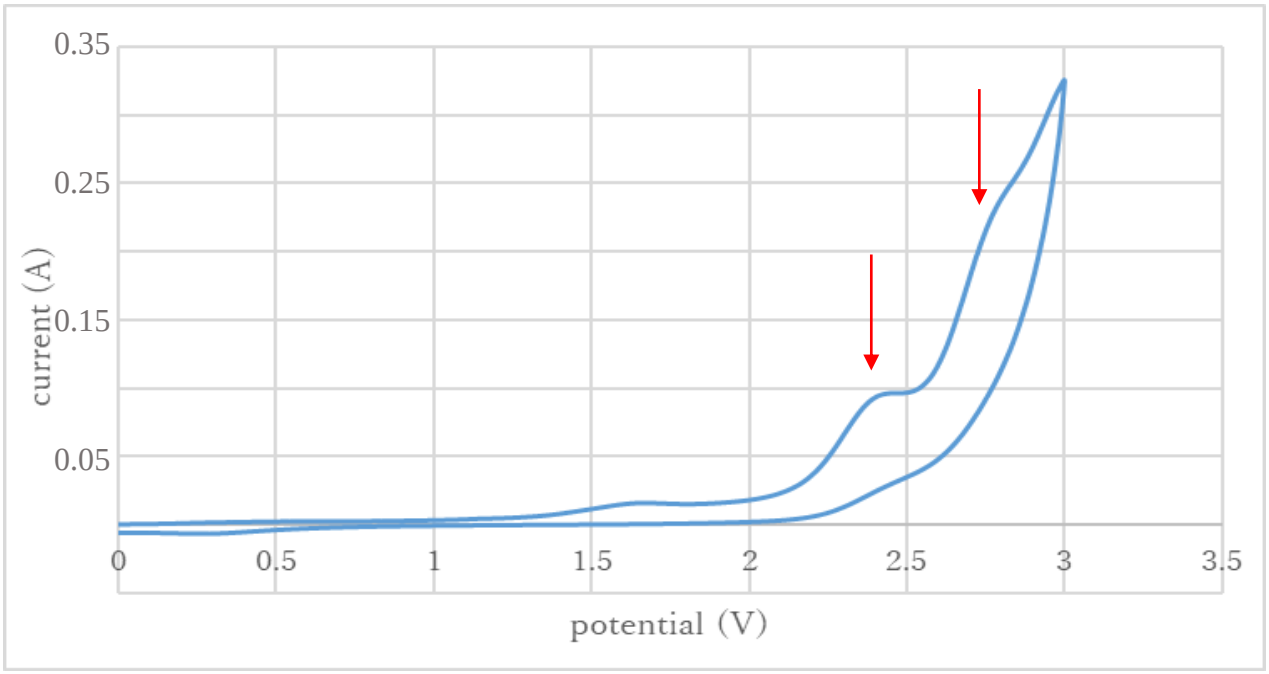


Fig. S2D Cyclic voltammetry analysis of **1o** (5 mM in MeCN). Conditions: a glassy carbon working electrode, a $Ag/AgNO_3$ reference electrode, and a platinum wire counter electrode, $^{n}Bu_4NPF_6$ (0.1 M in MeCN), 100 mV/s scan rate

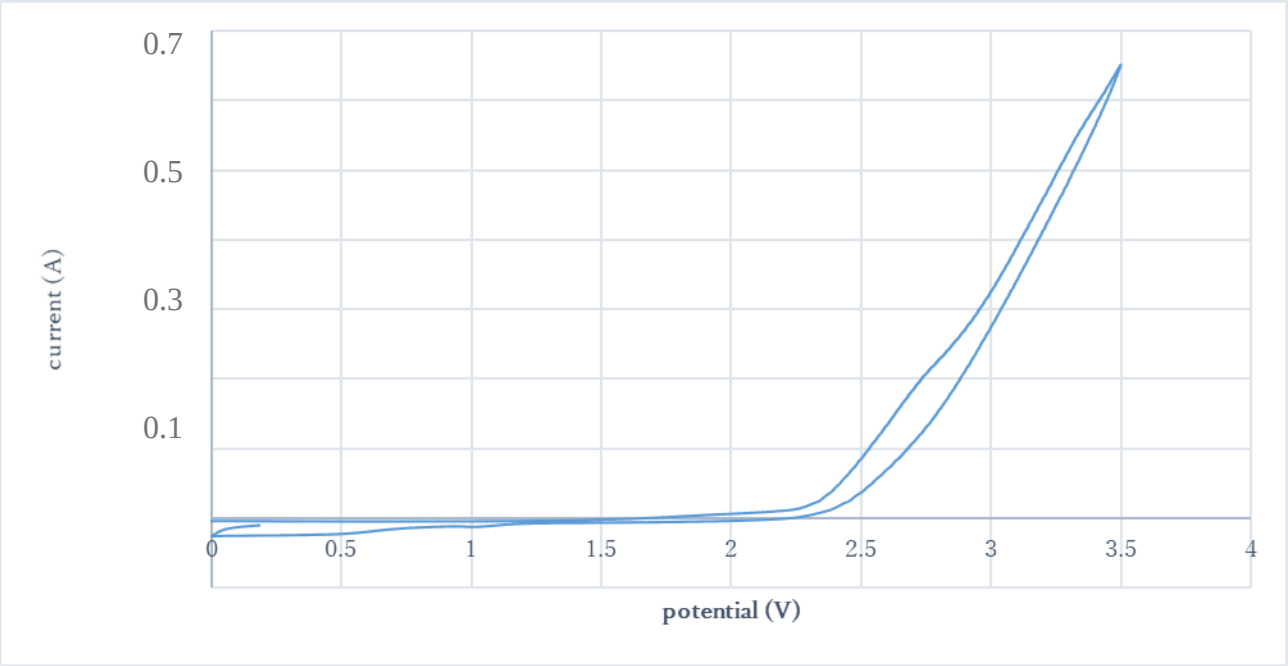


Fig. S2E Cyclic voltammetry analysis of **2n** (5 mM in MeCN). Conditions: a glassy carbon working electrode, a $Ag/AgNO_3$ reference electrode, and a platinum wire counter electrode, $LiClO_4$ (0.1 M in MeCN), 100 mV/s scan rate

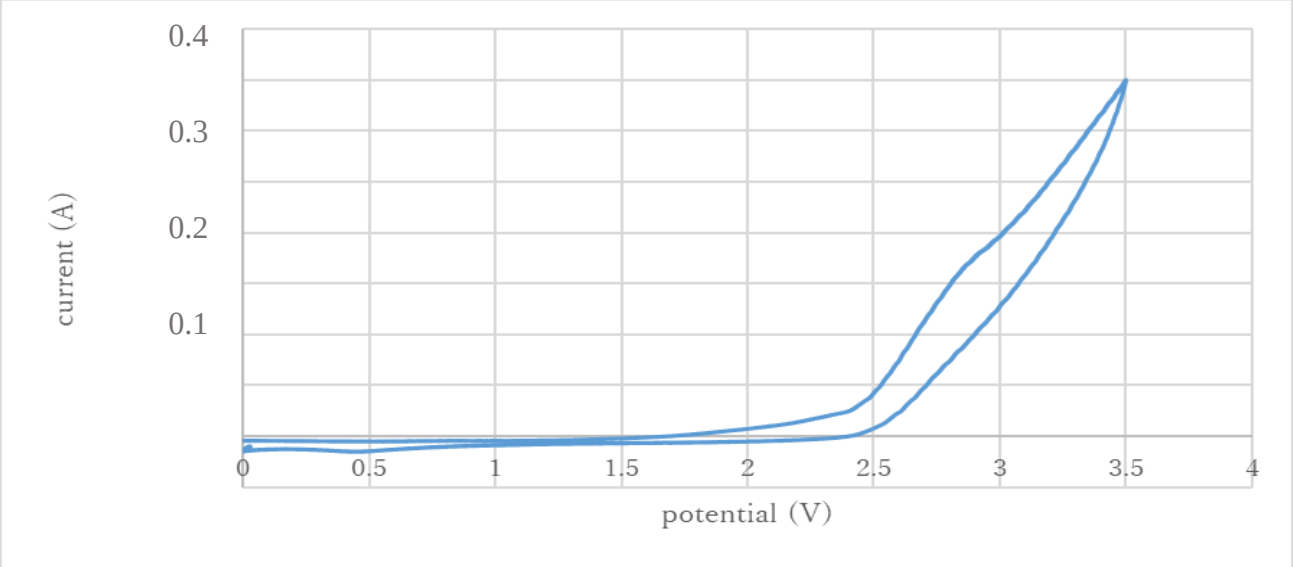


Fig. S2F Cyclic voltammetry analysis of **2n** (5 mM in MeCN). Conditions: a glassy carbon working electrode, a $Ag/AgNO_3$ reference electrode, and a platinum wire counter electrode, $^{n}Bu_4NPF_6$ (0.1 M in MeCN), 100 mV/s scan rate

References

1. (*a*) Z. Yan, B. Wu, X. Gao, M.-W. Chen and Y.-G. Zhou, *Org. Lett.*, 2016, **18**, 692–695; (*b*) Z.-Y. Ming, K.-R. Li, F.-J. Meng, L. Shi and W.-F. Jiang, *Tetrahedron Lett.*, 2020, **61**, 152059.
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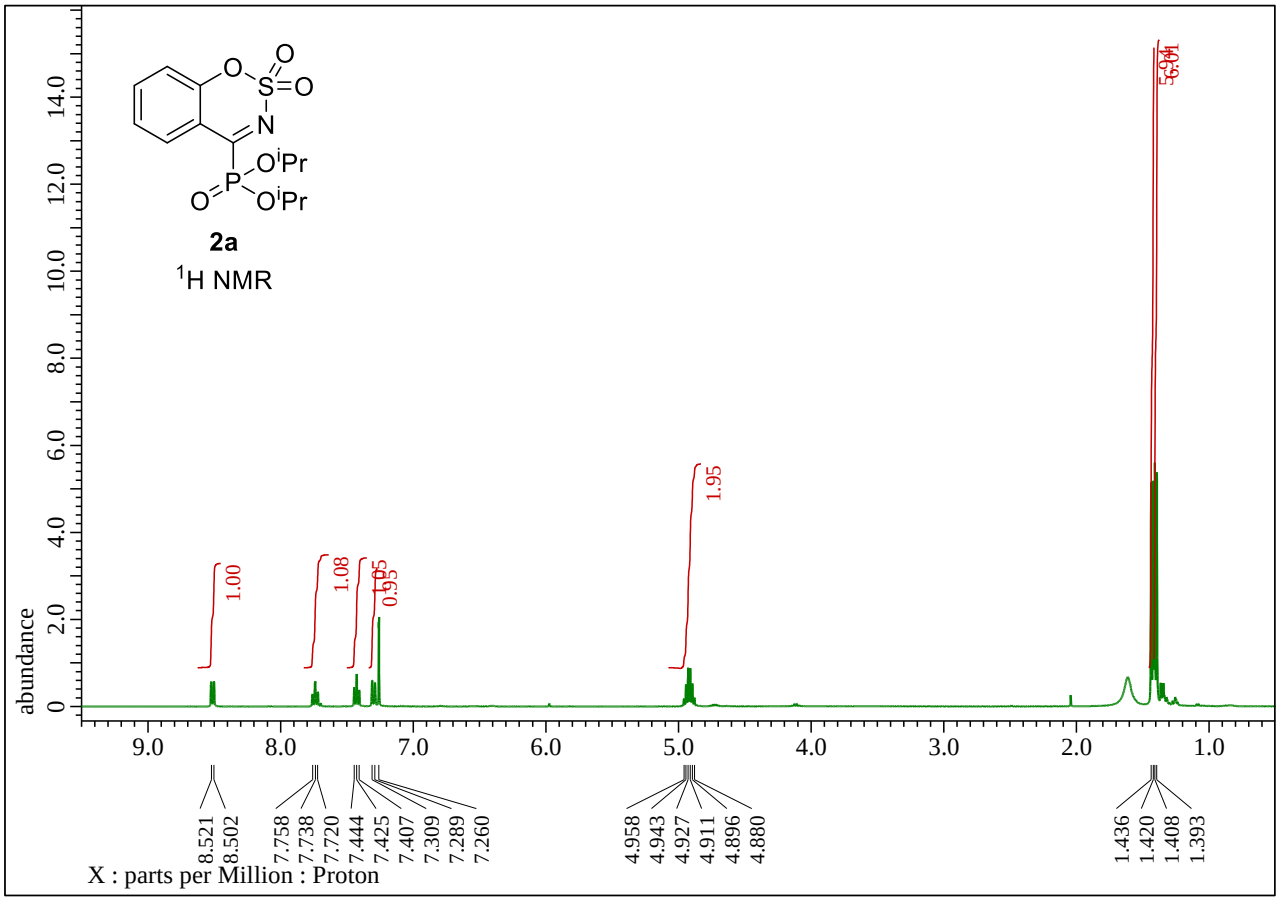
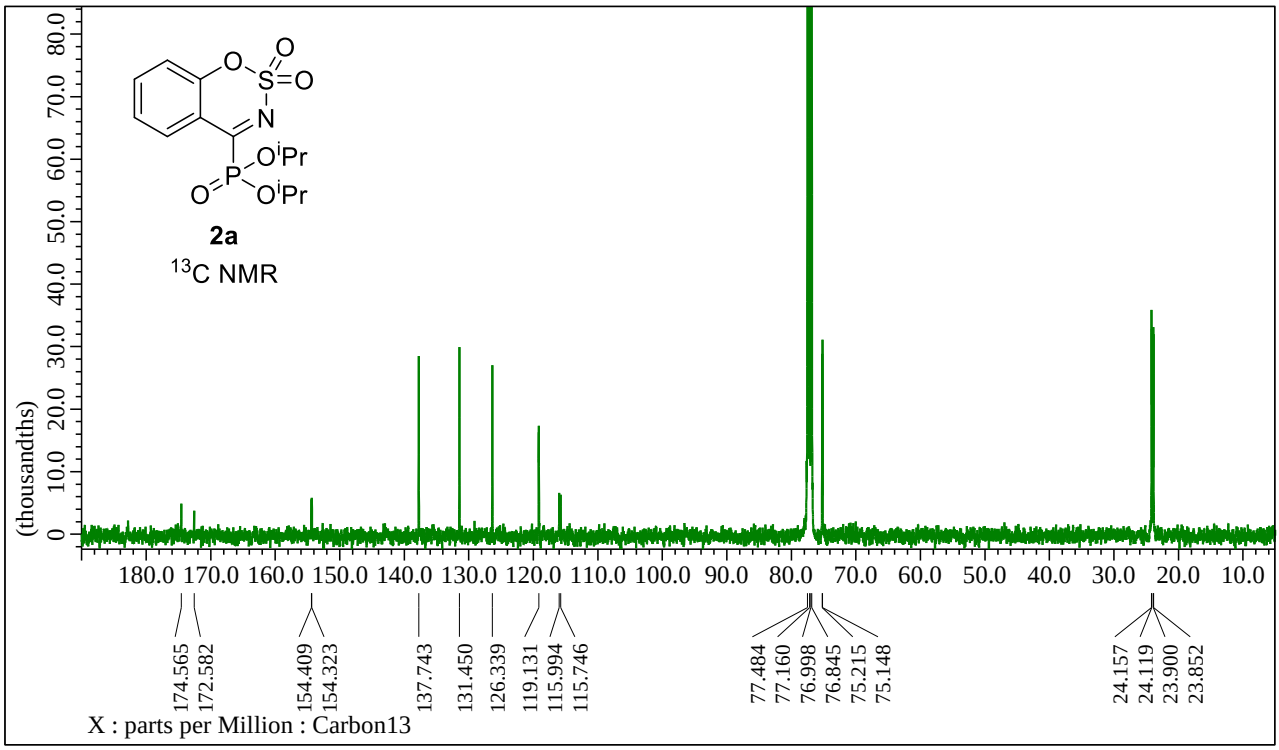
NMR charts

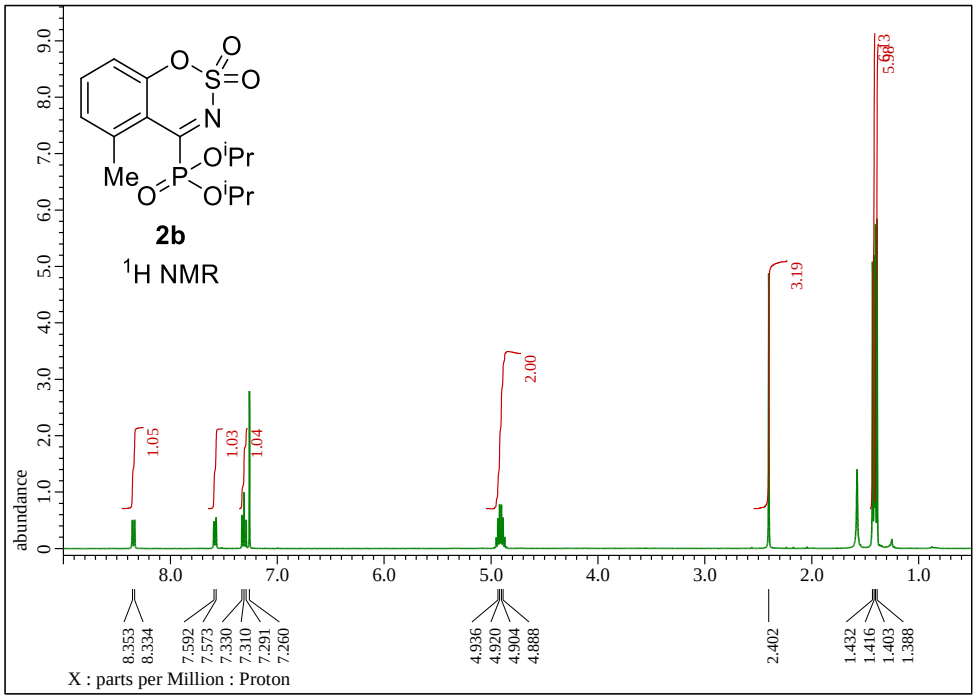
^{1}H-NMR (400 MHz, $CDCl_3$) chart of **2a**



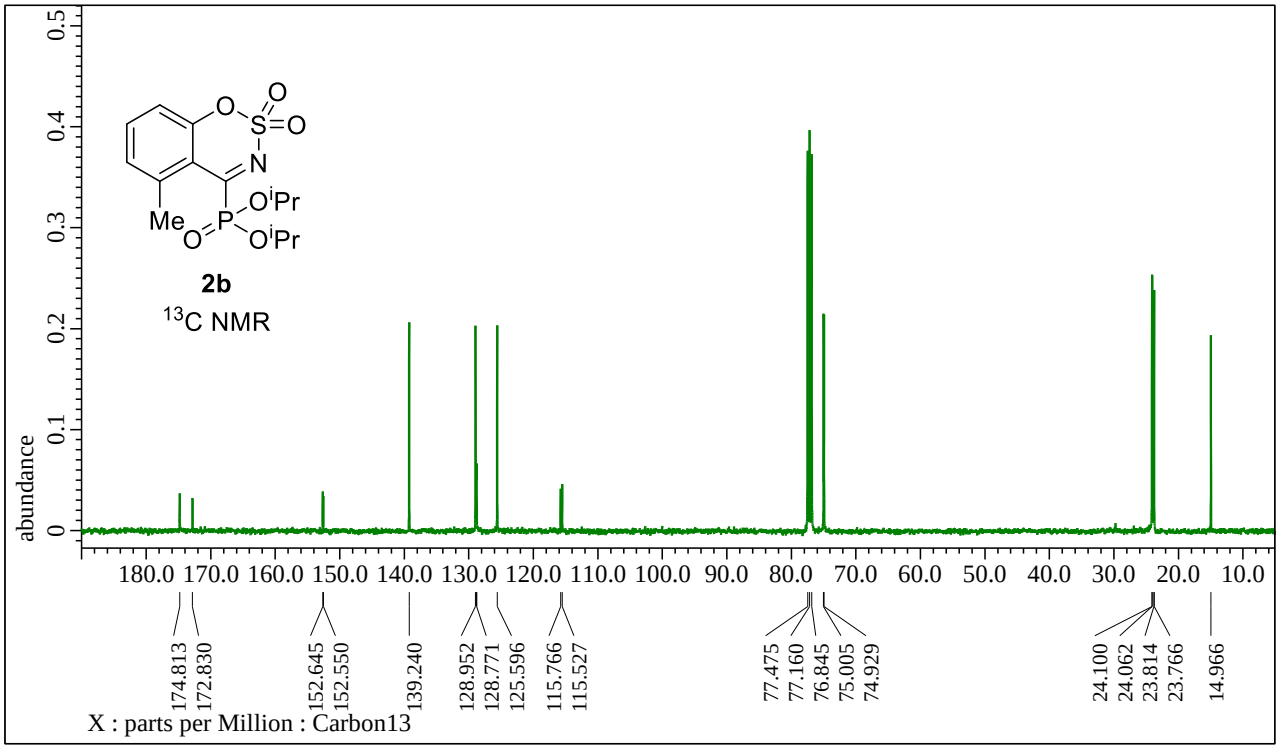
^{13}C-NMR (100 MHz, $CDCl_3$) chart of **2a**



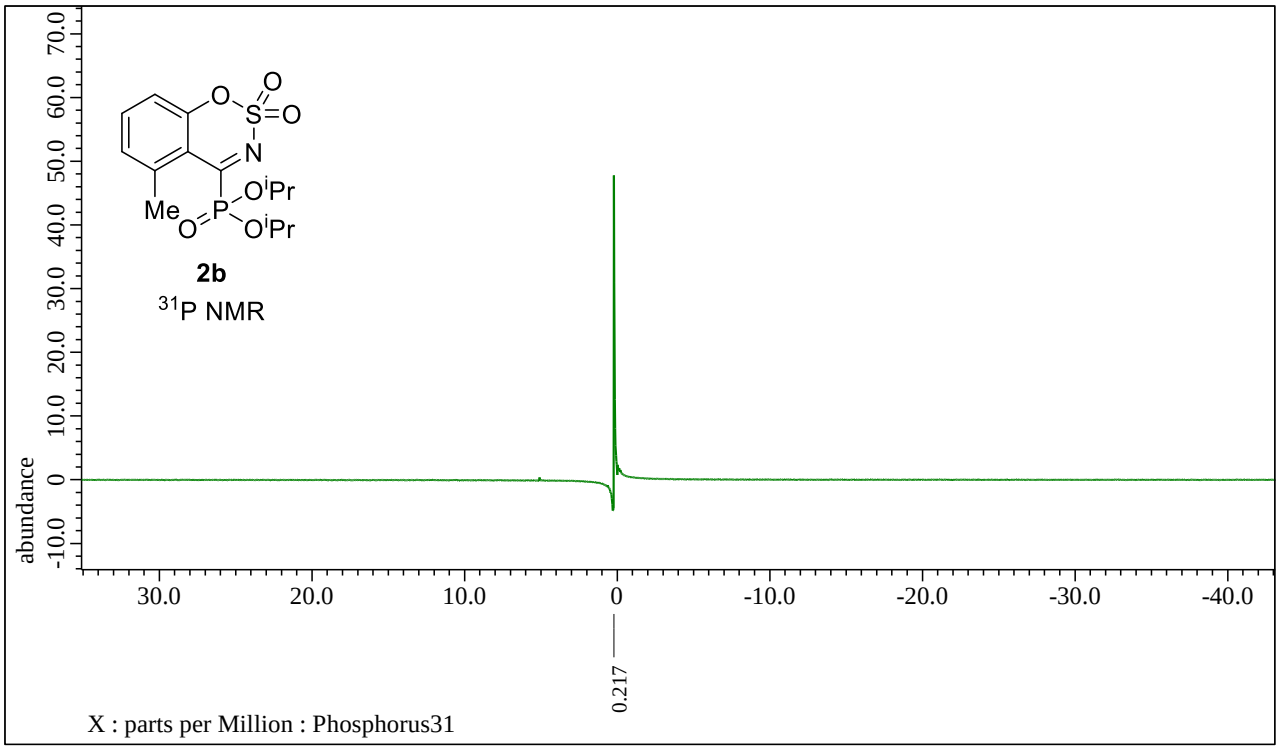
^{1}H-NMR (400 MHz, $CDCl_3$) chart of **2b**



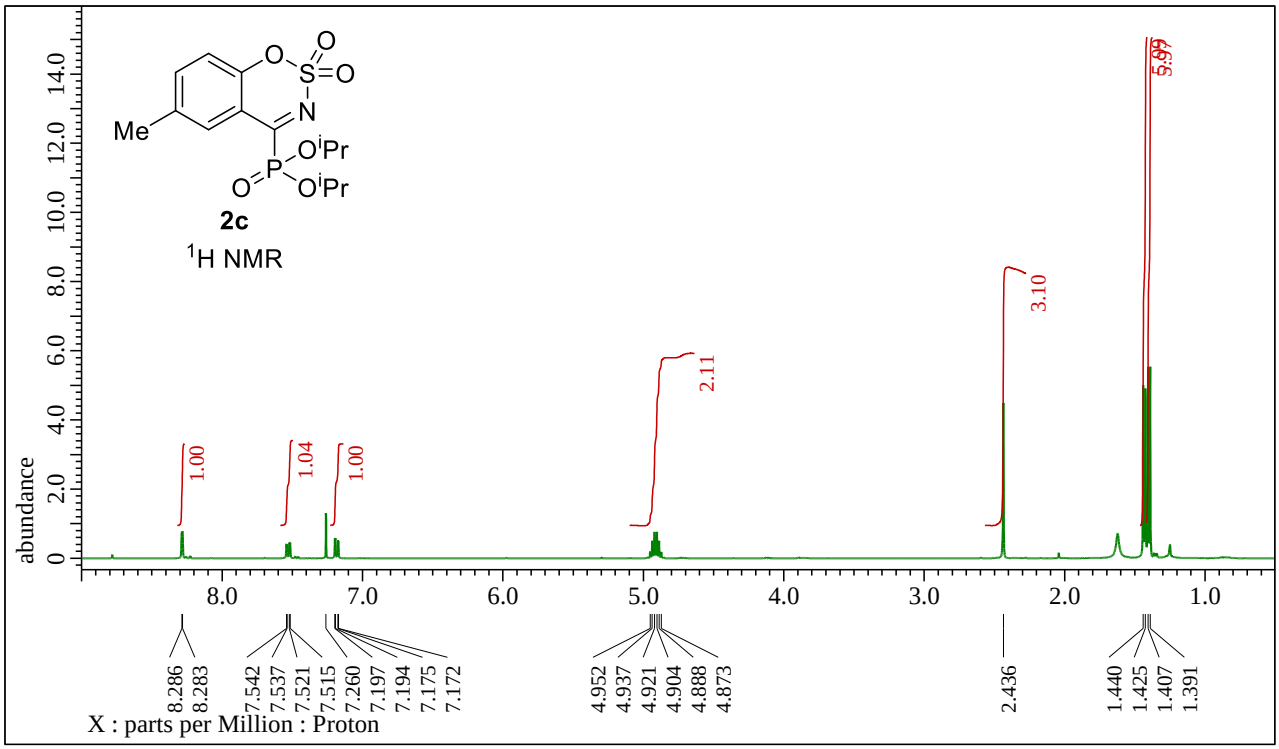
^{13}C-NMR (100 MHz, $CDCl_3$) chart of **2b**



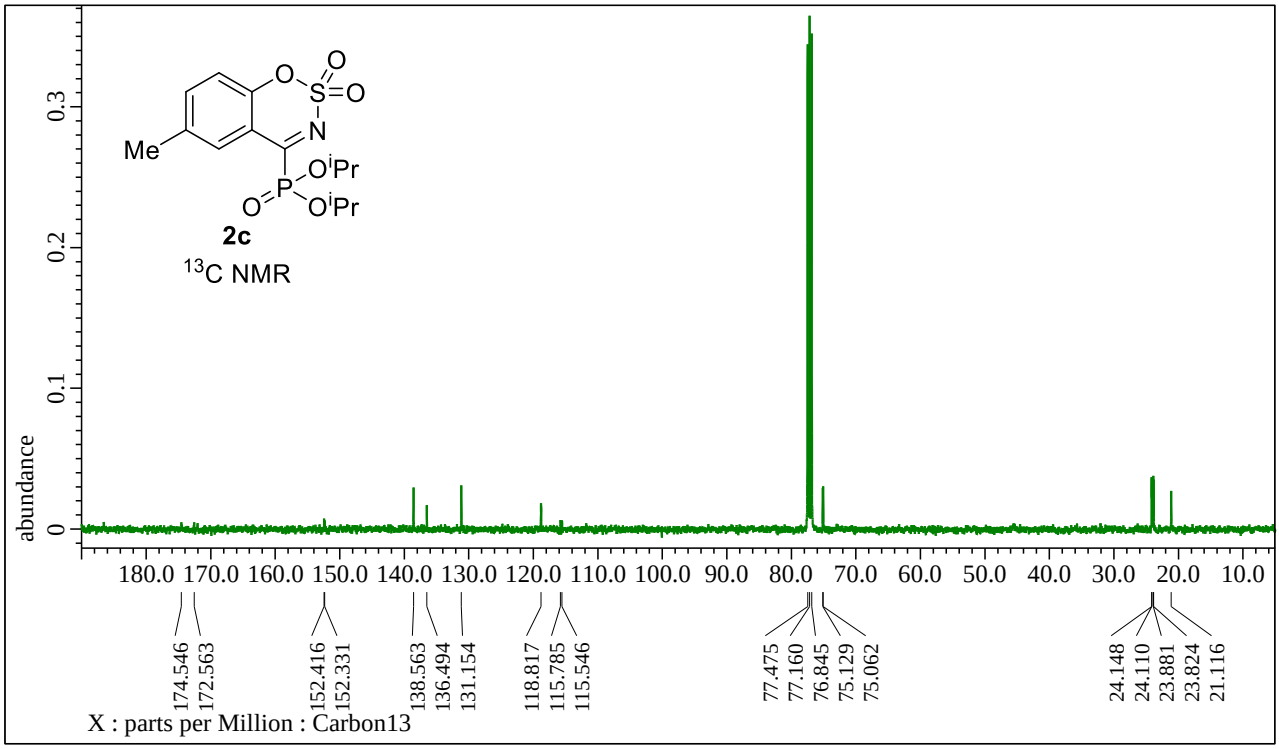
^{31}P-NMR (240 MHz, $CDCl_3$) chart of **2b**



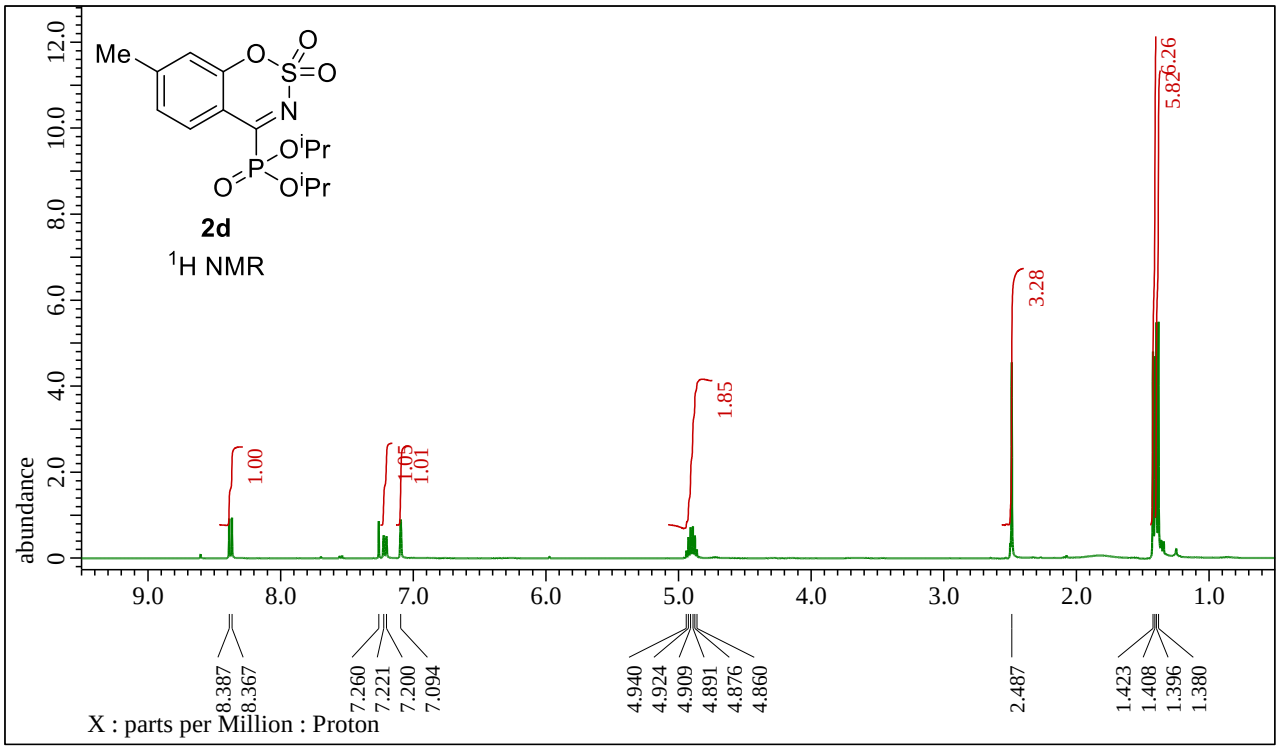
^{1}H-NMR (400 MHz, $CDCl_3$) chart of **2c**



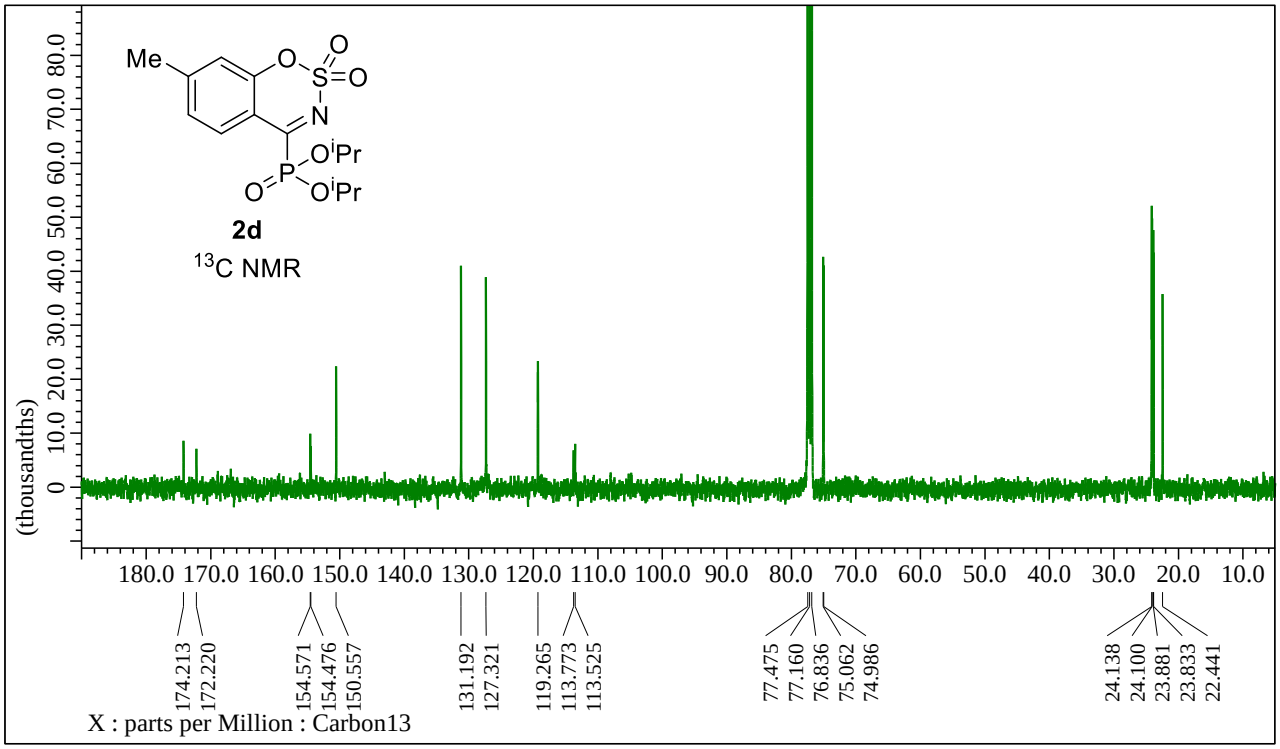
^{13}C-NMR (100 MHz, $CDCl_3$) chart of **2c**



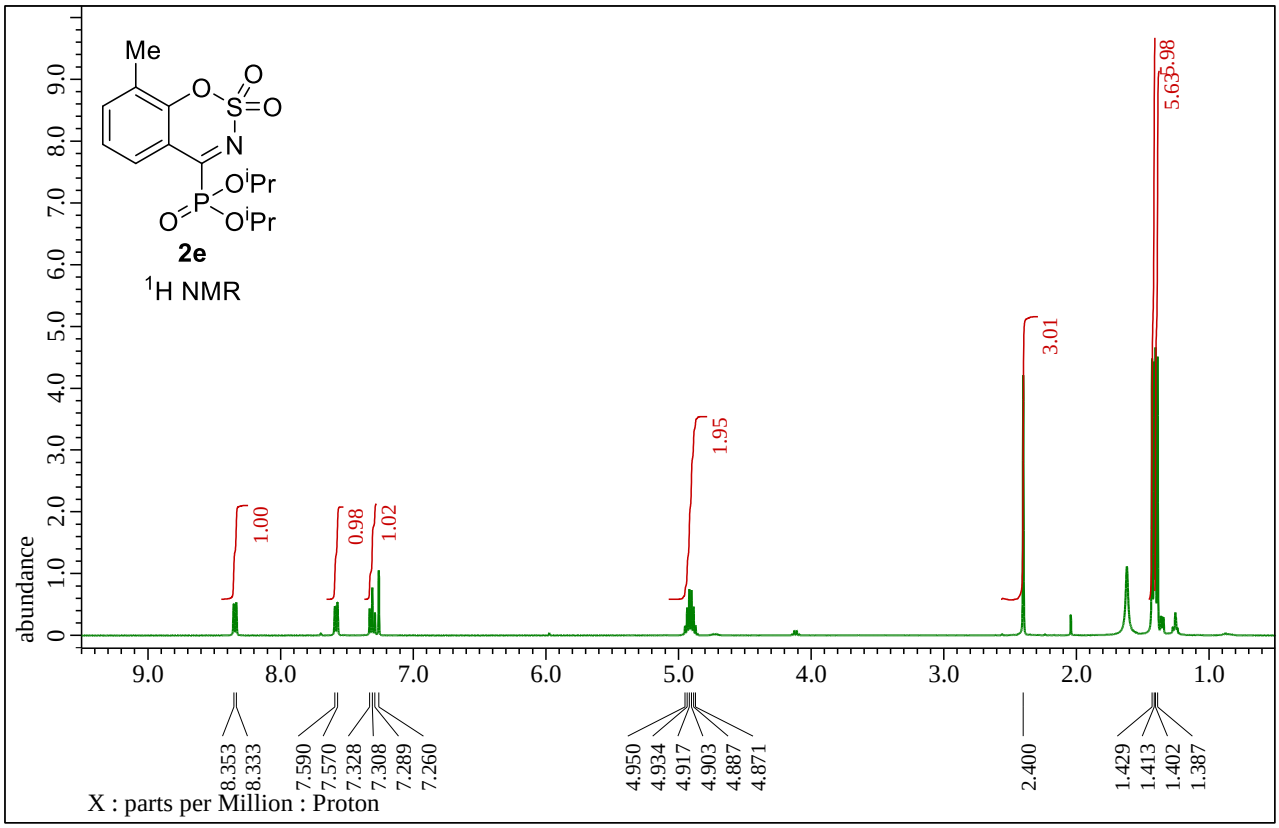
^{1}H-NMR (400 MHz, $CDCl_3$) chart of **2d**



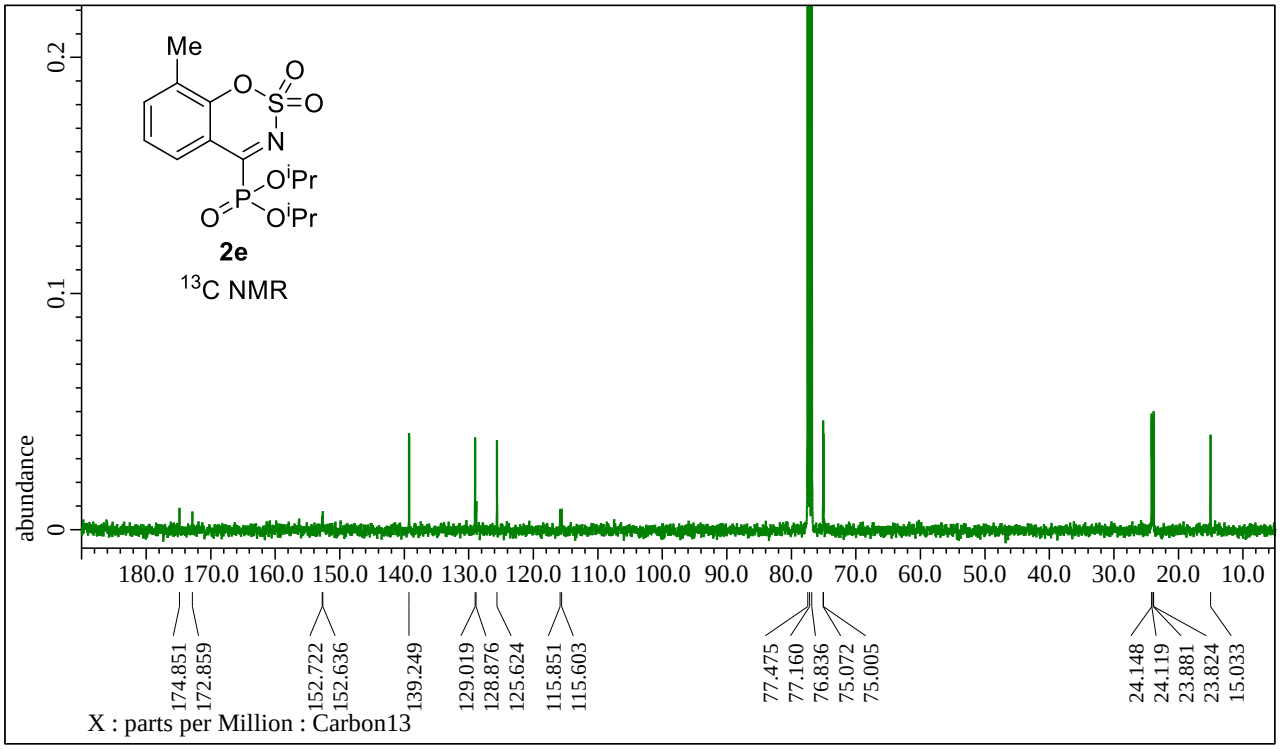
^{13}C-NMR (100 MHz, $CDCl_3$) chart of **2d**



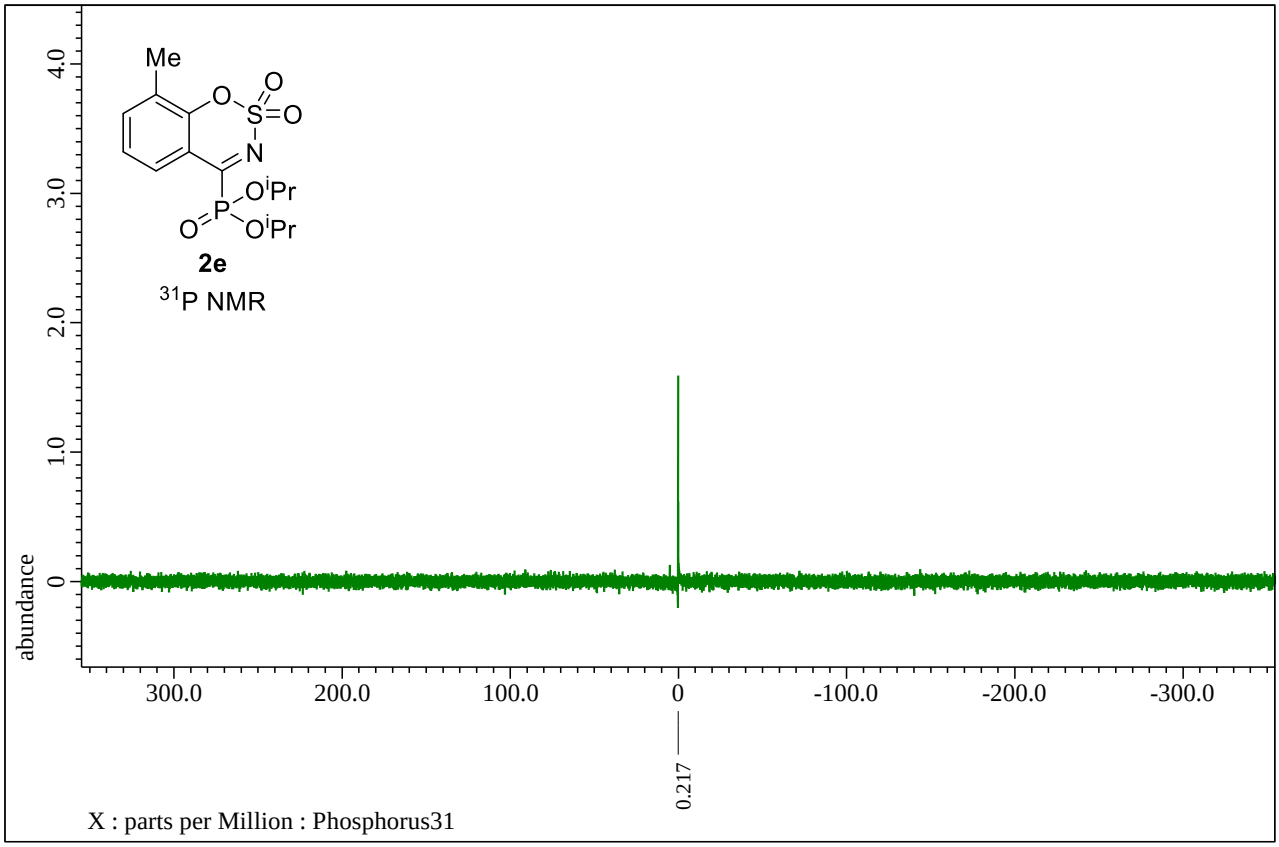
^{1}H-NMR (400 MHz, $CDCl_3$) chart of **2e**



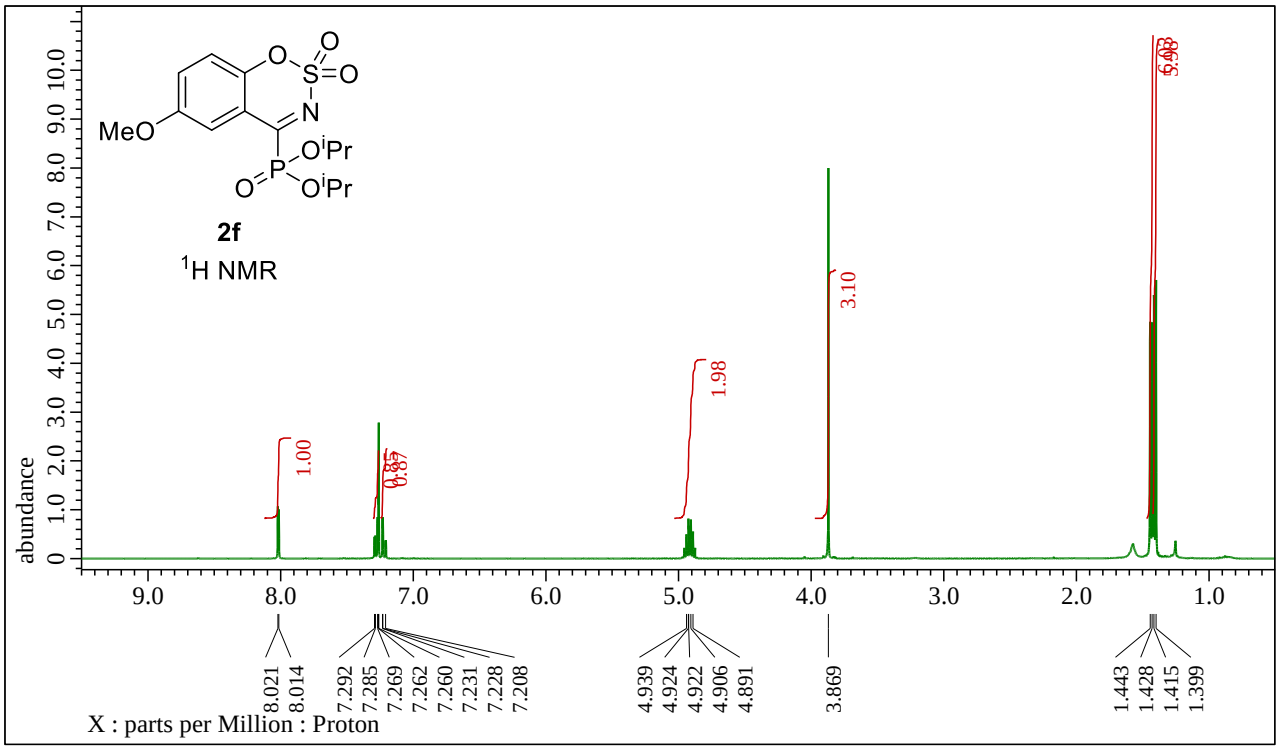
^{13}C-NMR (100 MHz, $CDCl_3$) chart of **2e**



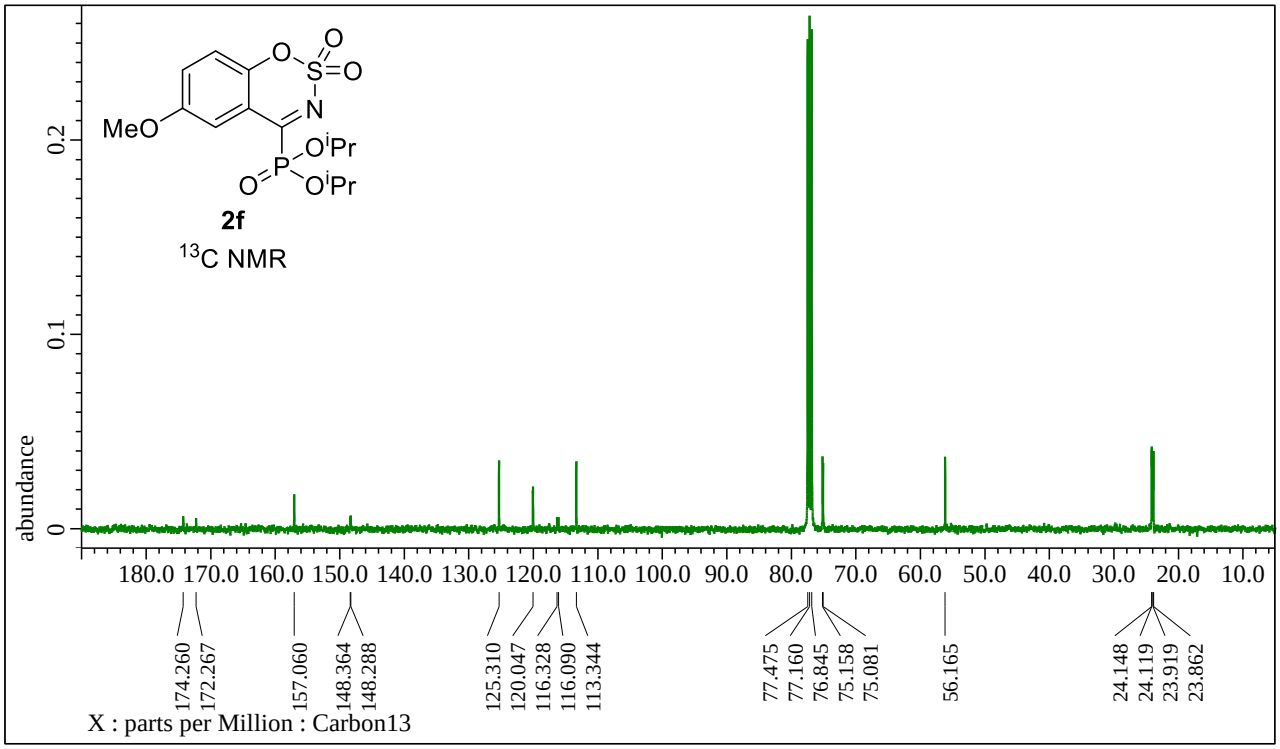
^{31}P-NMR (240 MHz, $CDCl_3$) chart of **2e**



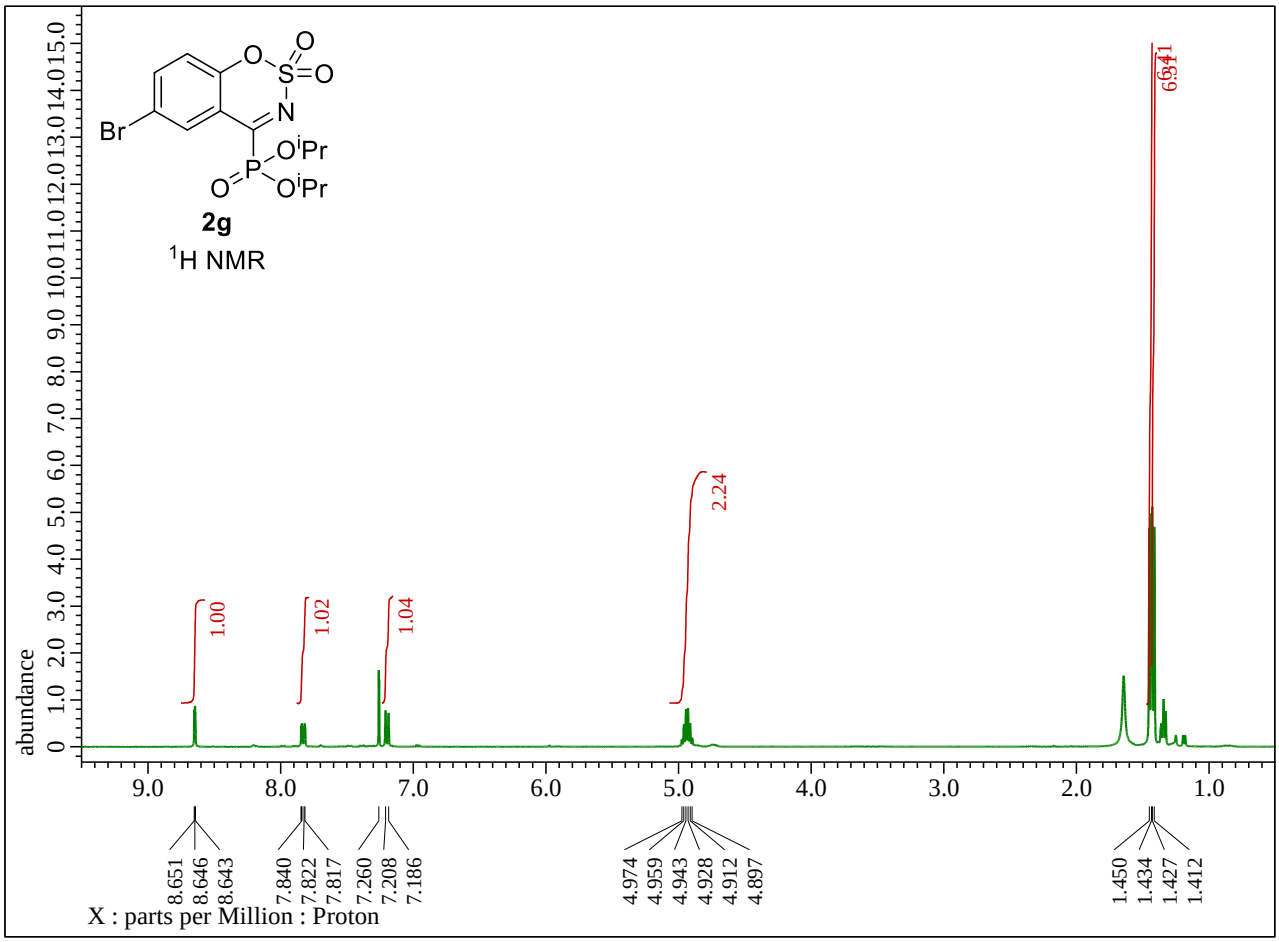
^{1}H-NMR (400 MHz, $CDCl_3$) chart of **2f**



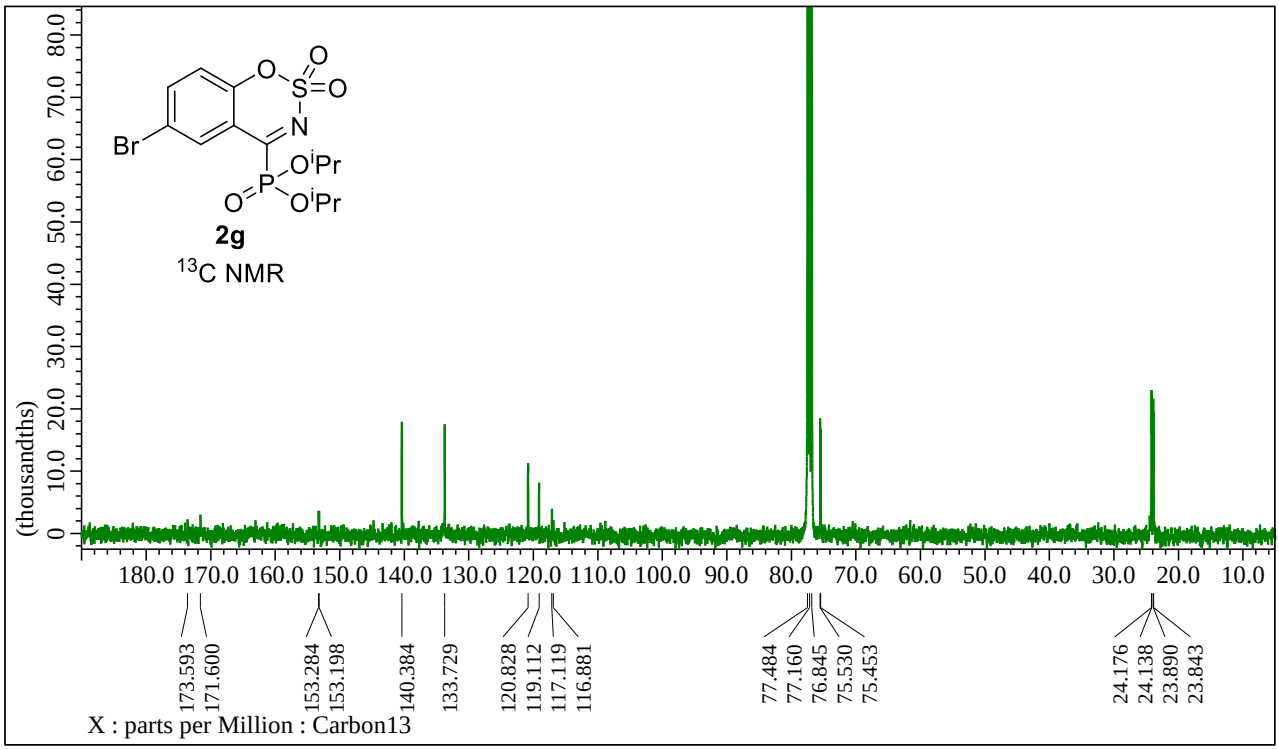
^{13}C-NMR (100 MHz, $CDCl_3$) chart of **2f**



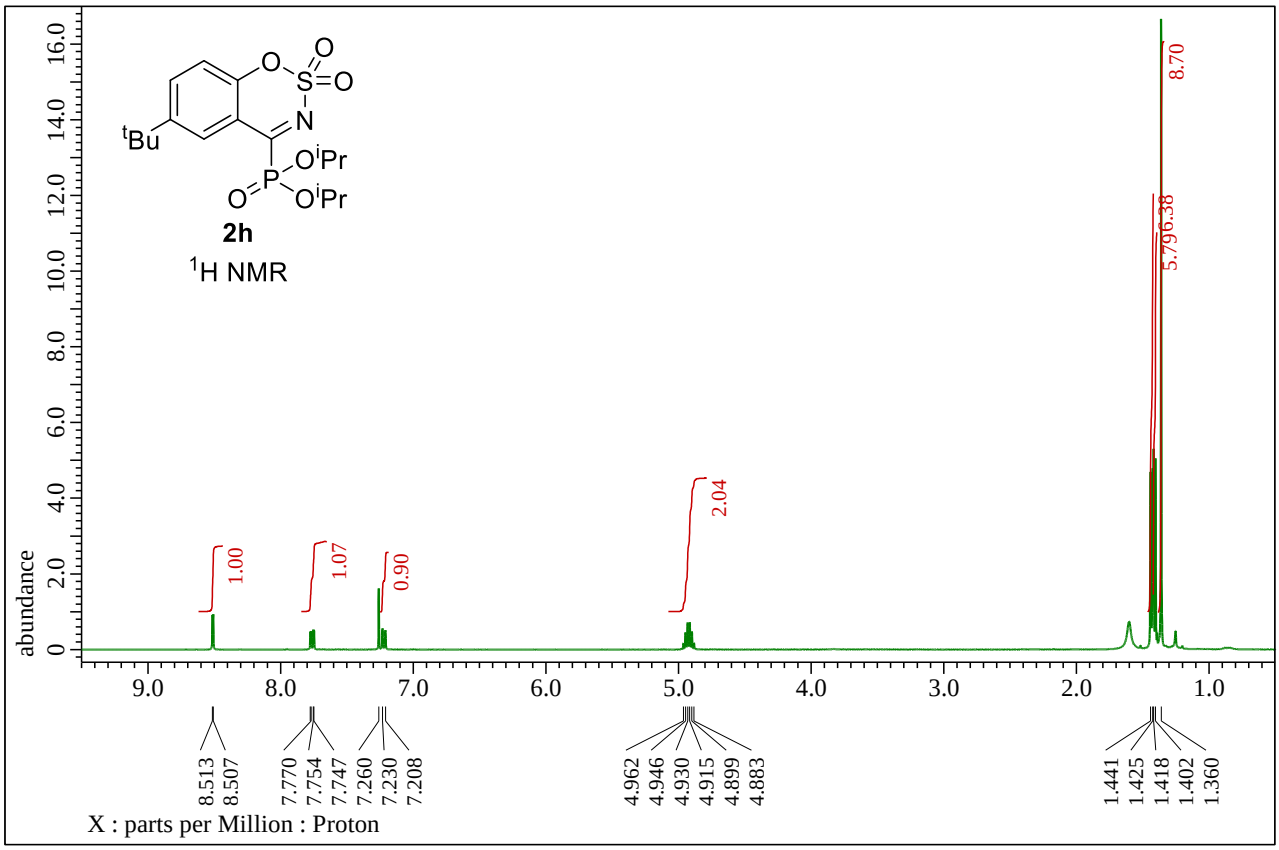
^{1}H-NMR (400 MHz, $CDCl_3$) chart of **2g**



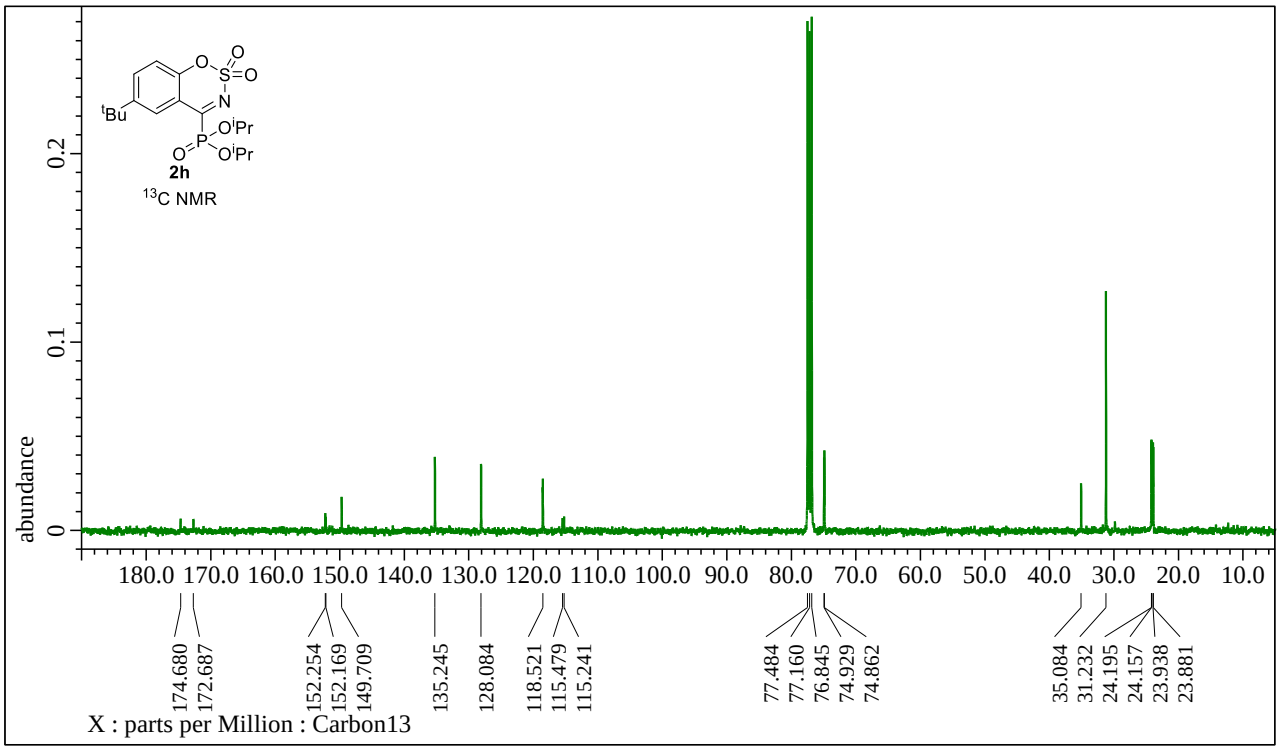
^{13}C-NMR (100 MHz, $CDCl_3$) chart of **2g**



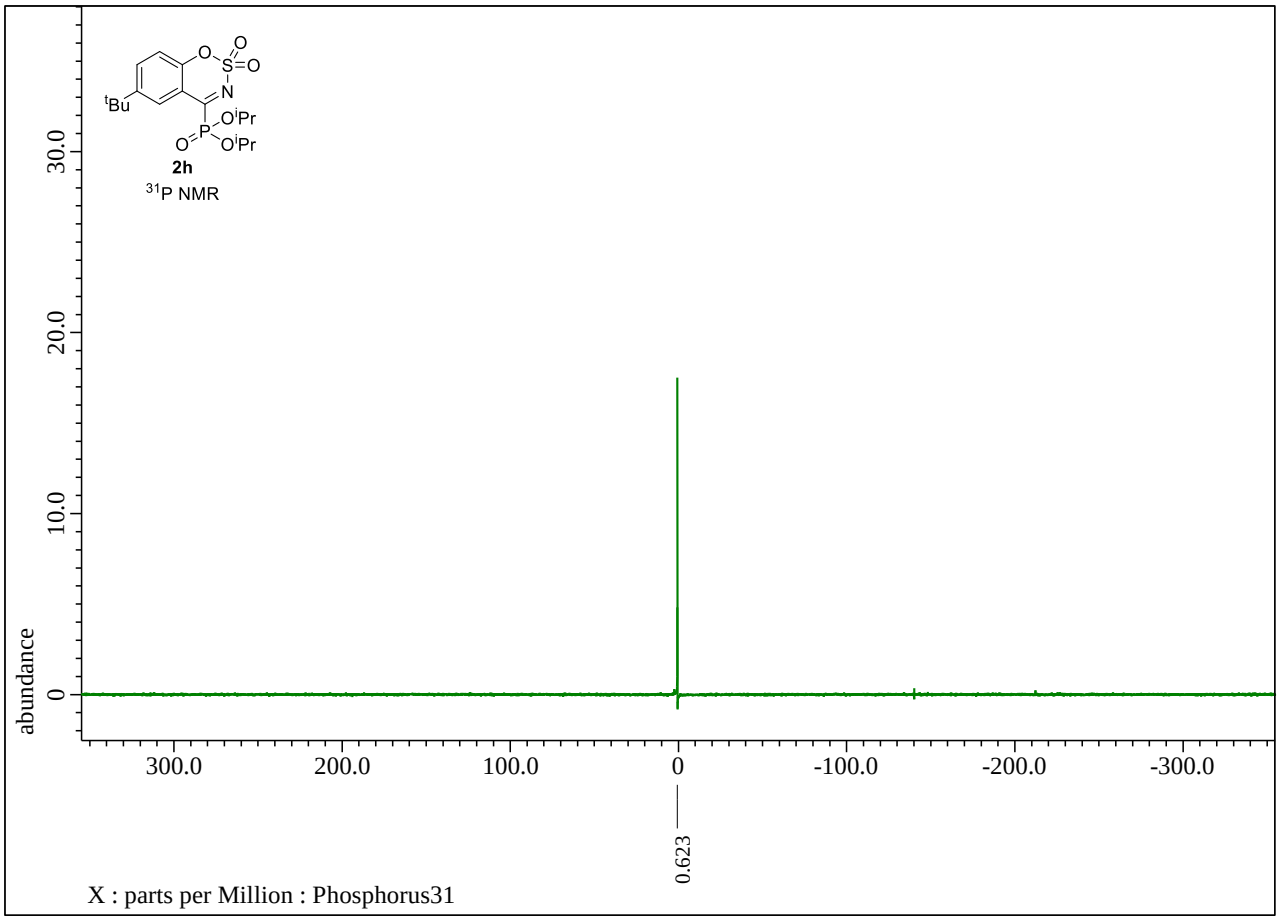
^{1}H-NMR (400 MHz, $CDCl_3$) chart of **2h**



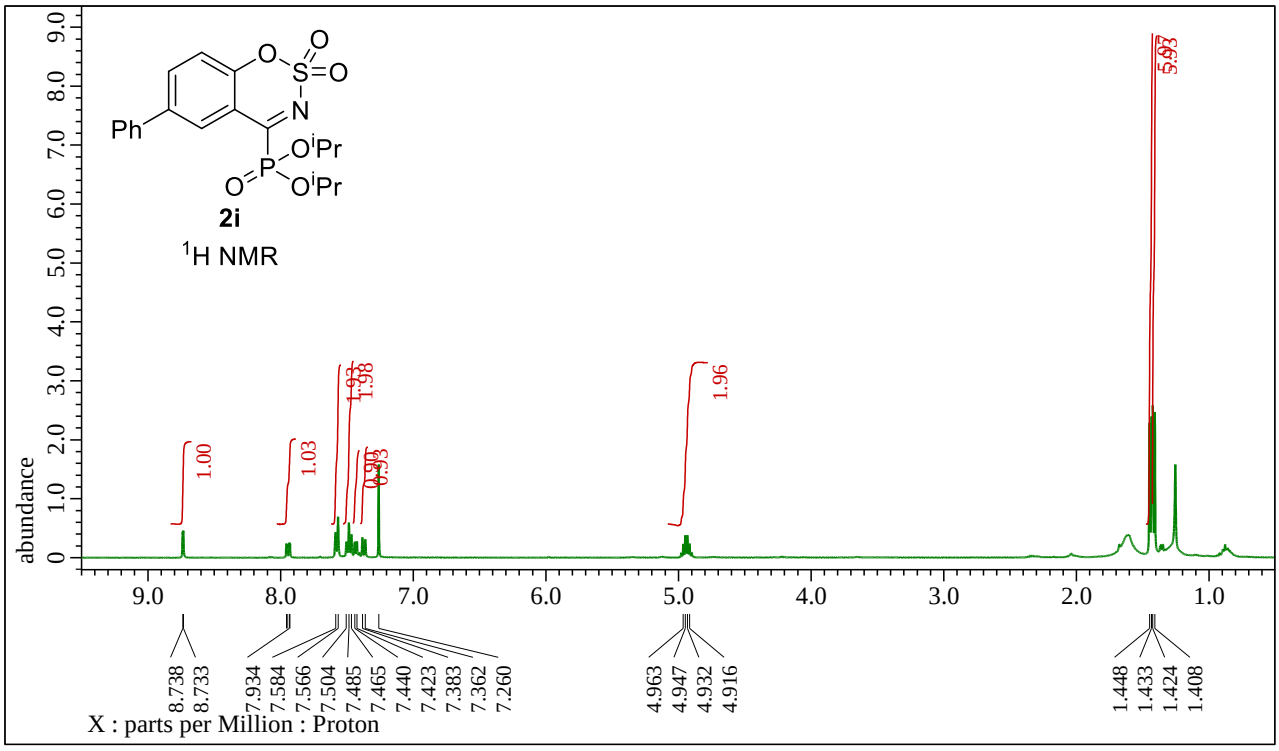
^{13}C-NMR (100 MHz, $CDCl_3$) chart of **2h**



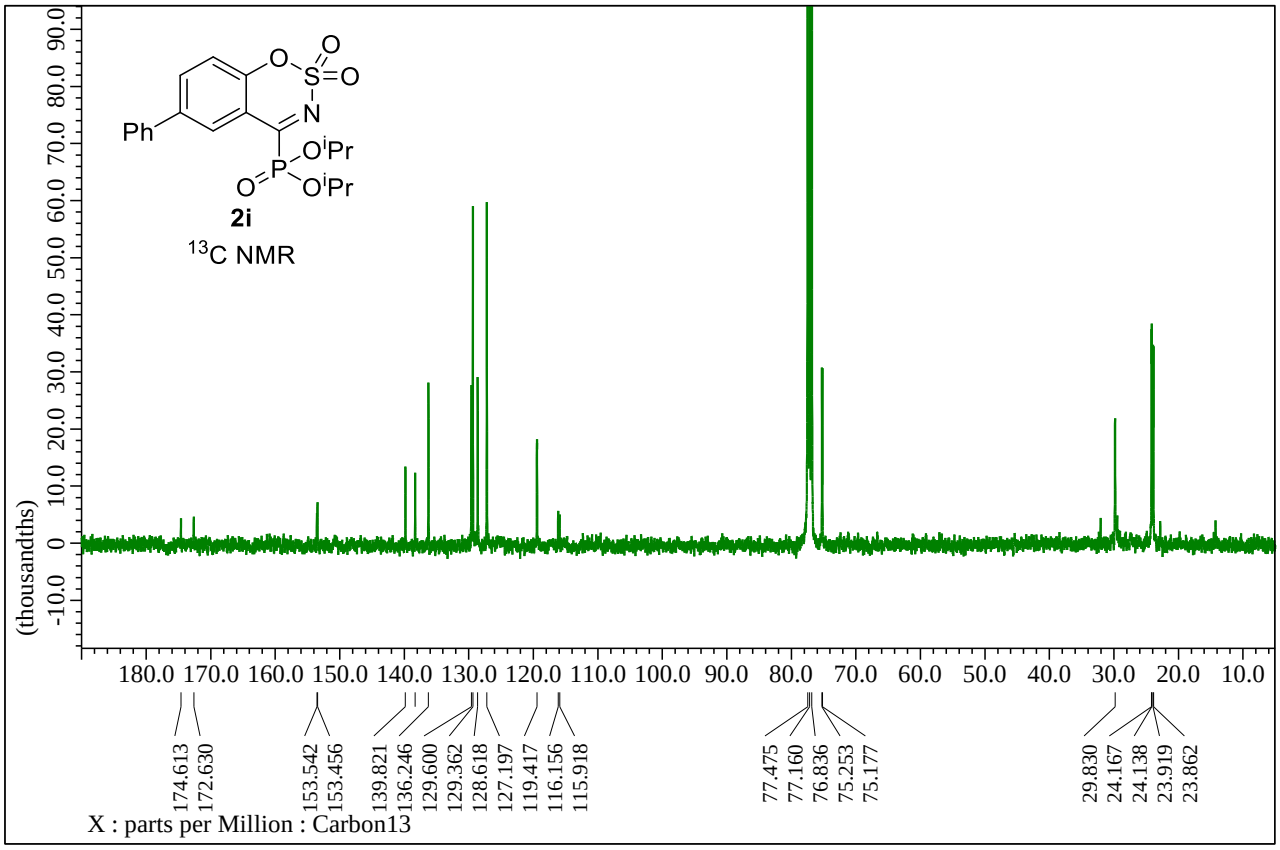
^{31}P-NMR (240 MHz, $CDCl_3$) chart of **2h**



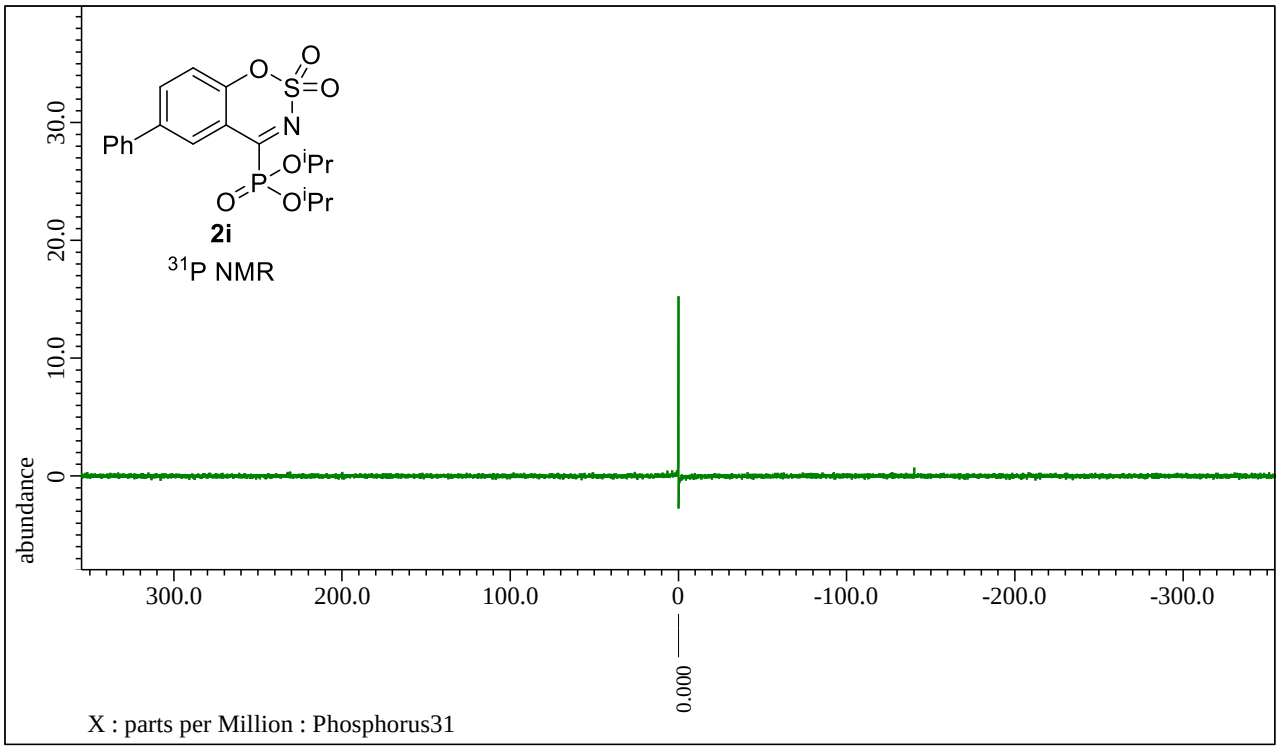
^{1}H-NMR (400 MHz, $CDCl_3$) chart of **2i**



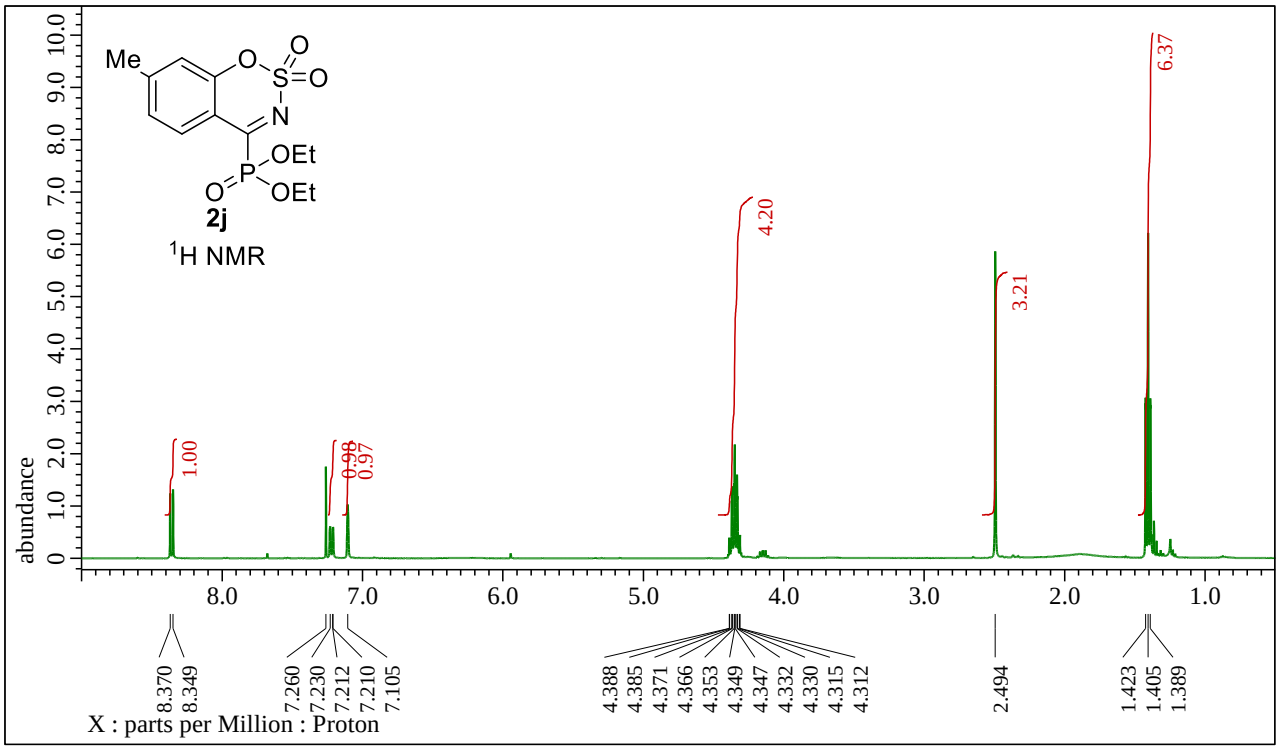
^{13}C-NMR (100 MHz, $CDCl_3$) chart of **2i**



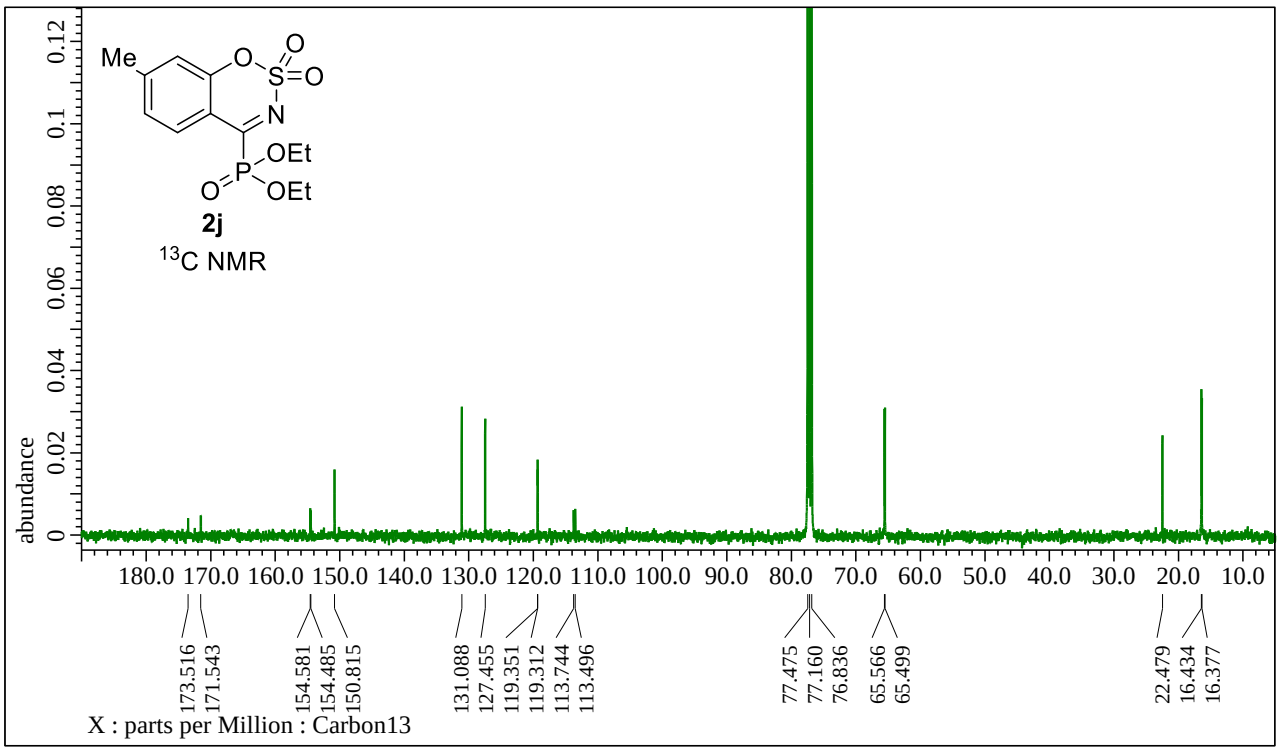
^{31}P-NMR (240 MHz, $CDCl_3$) chart of **2i**



^{1}H-NMR (400 MHz, $CDCl_3$) chart of **2j**



^{13}C-NMR (100 MHz, $CDCl_3$) chart of **2j**



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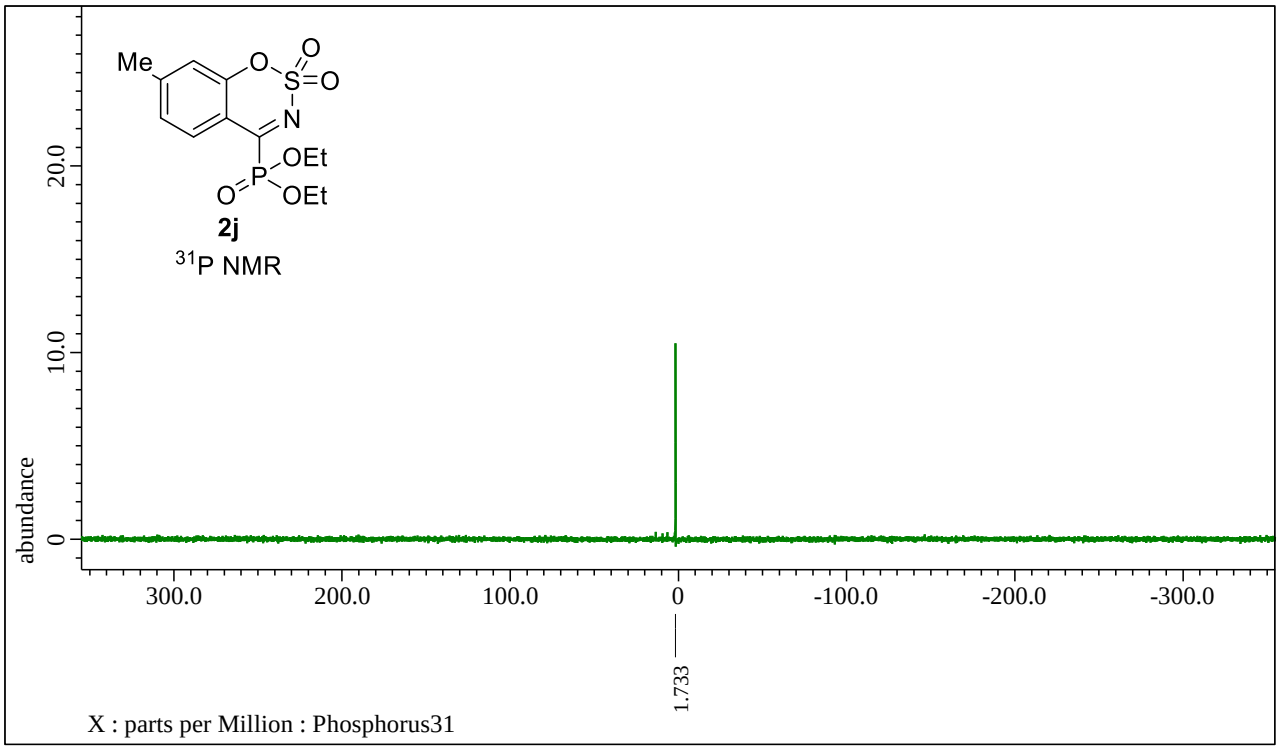
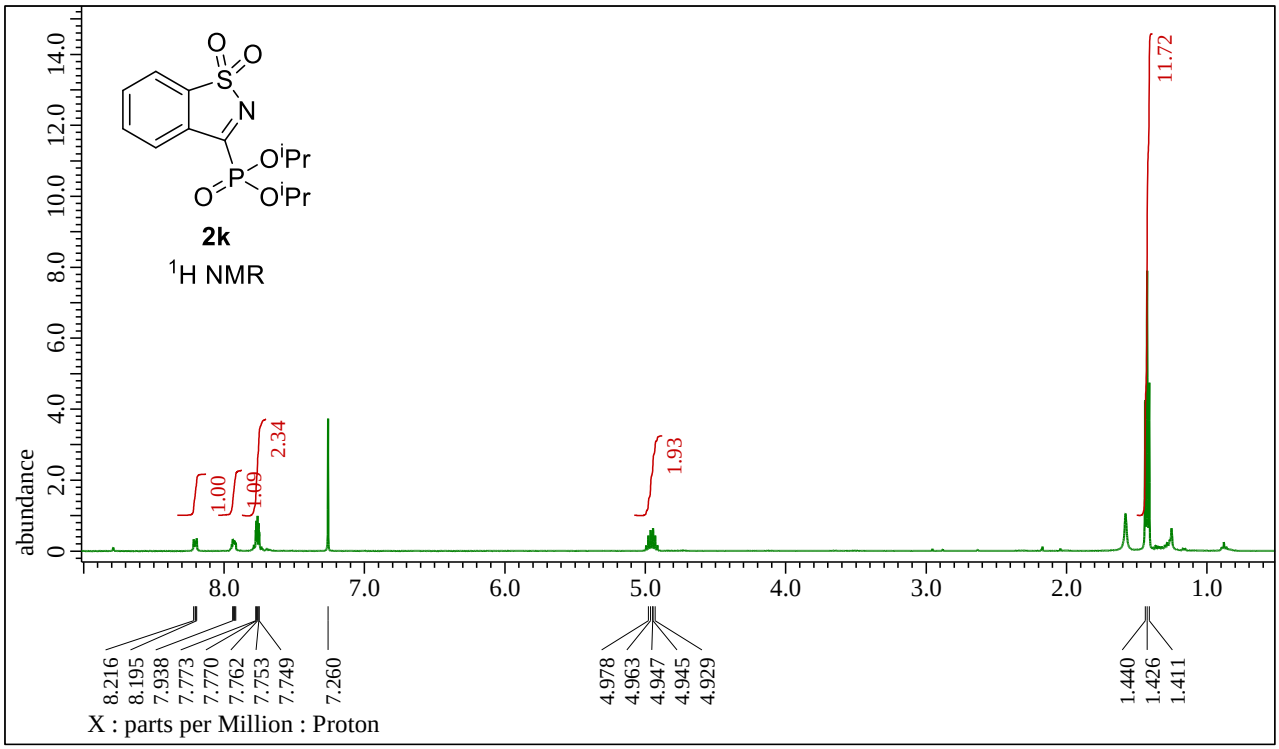
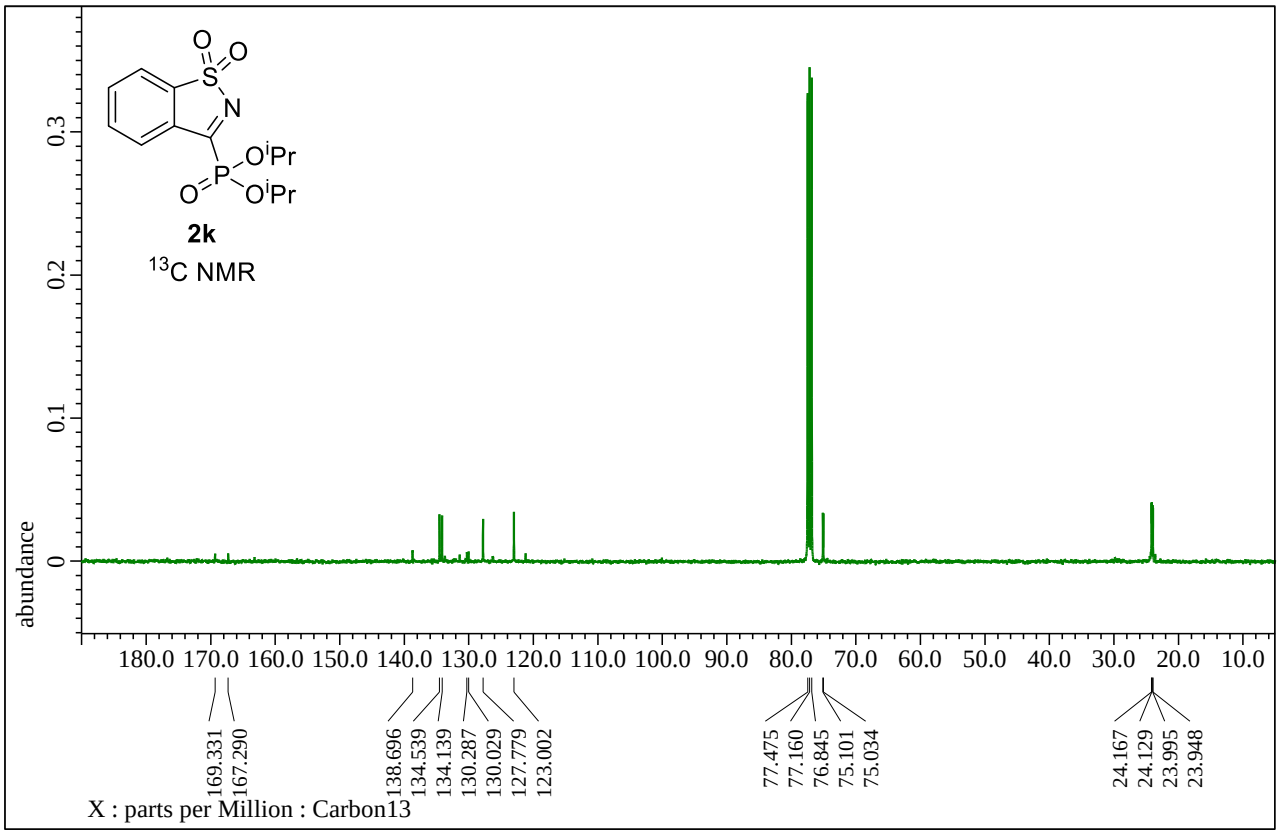


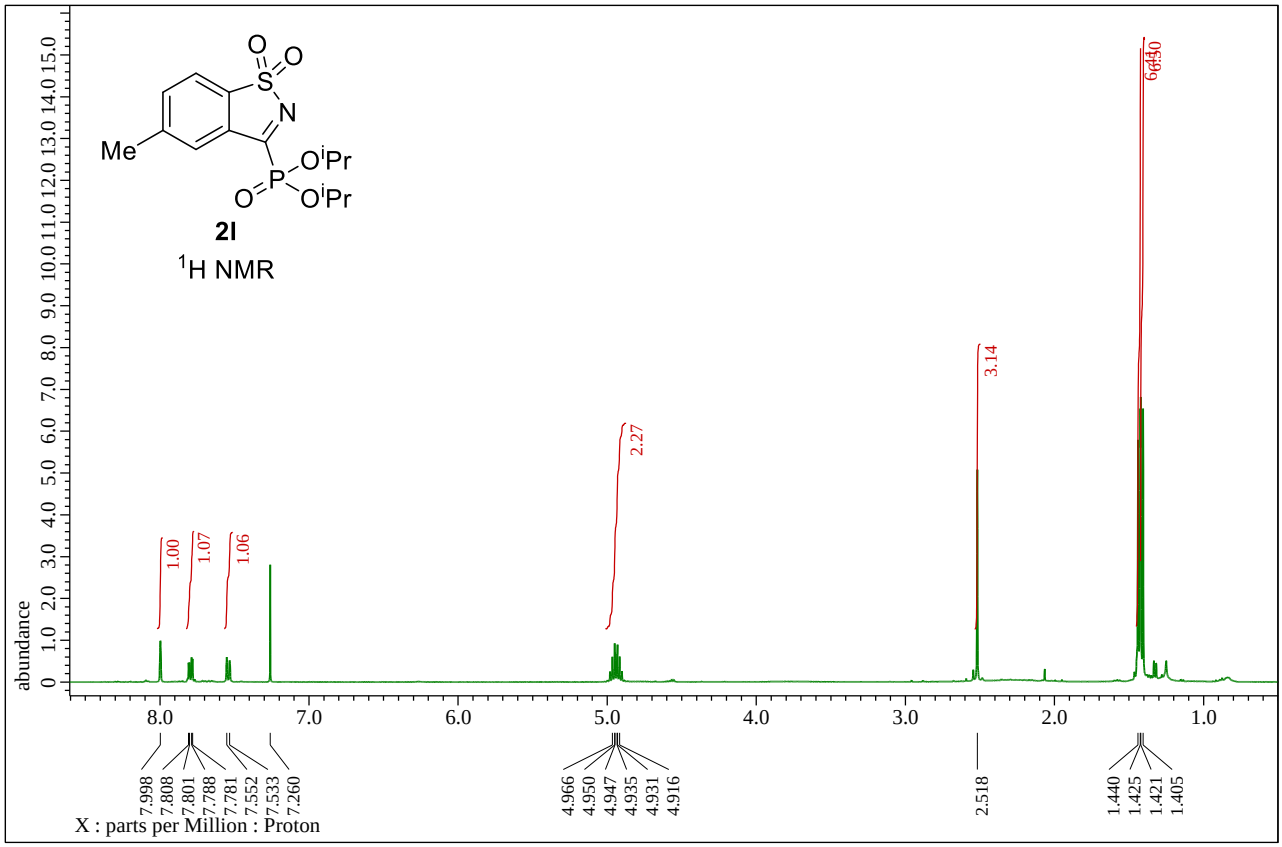
^{1}H-NMR (400 MHz, $CDCl_3$) chart of **2k**



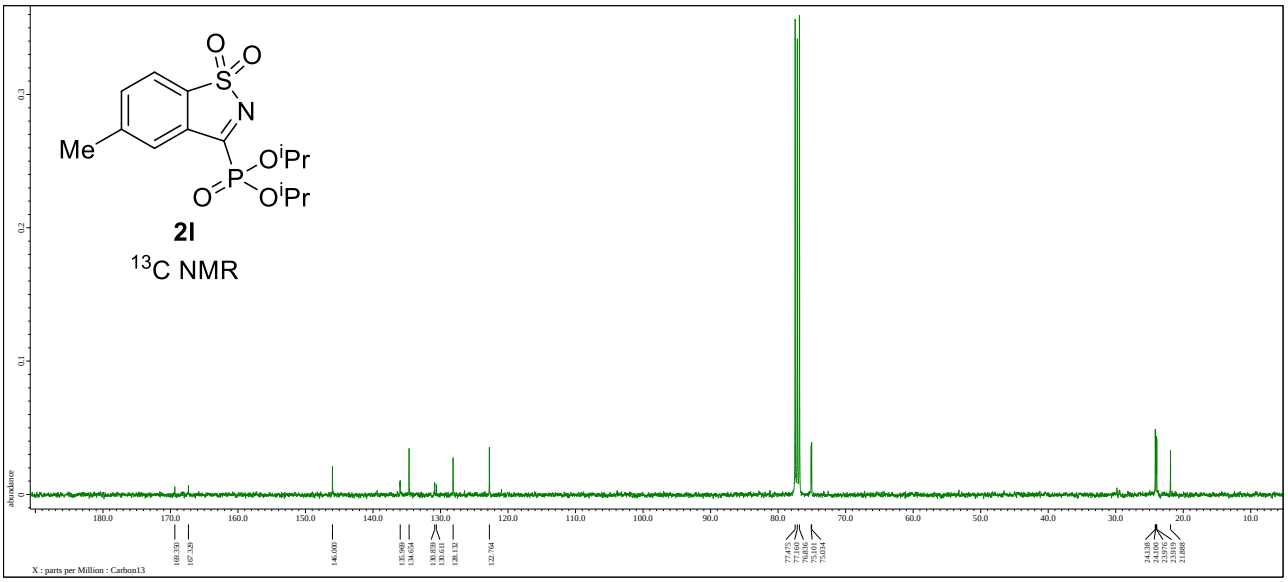
^{13}C-NMR (100 MHz, $CDCl_3$) chart of **2k**



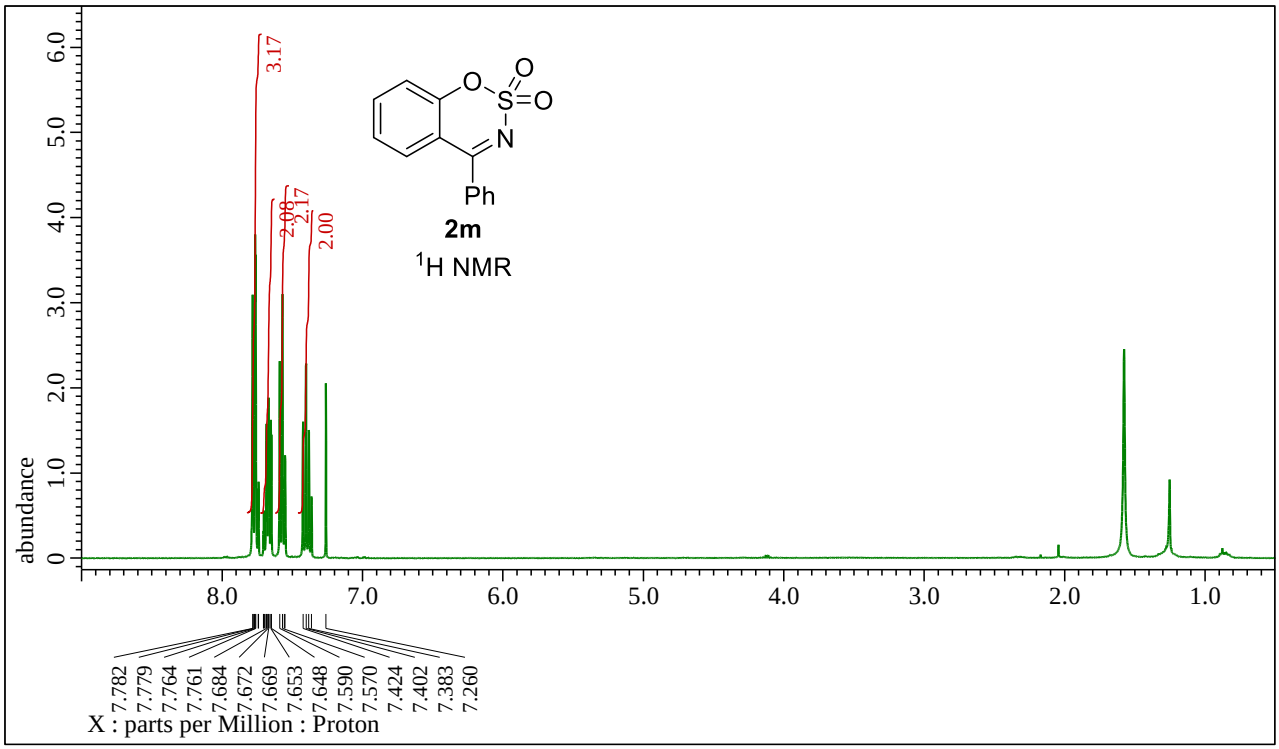
^{1}H-NMR (400 MHz, $CDCl_3$) chart of **2l**



^{13}C-NMR (100 MHz, $CDCl_3$) chart of **2l**



^{1}H-NMR (400 MHz, $CDCl_3$) chart of **2m**



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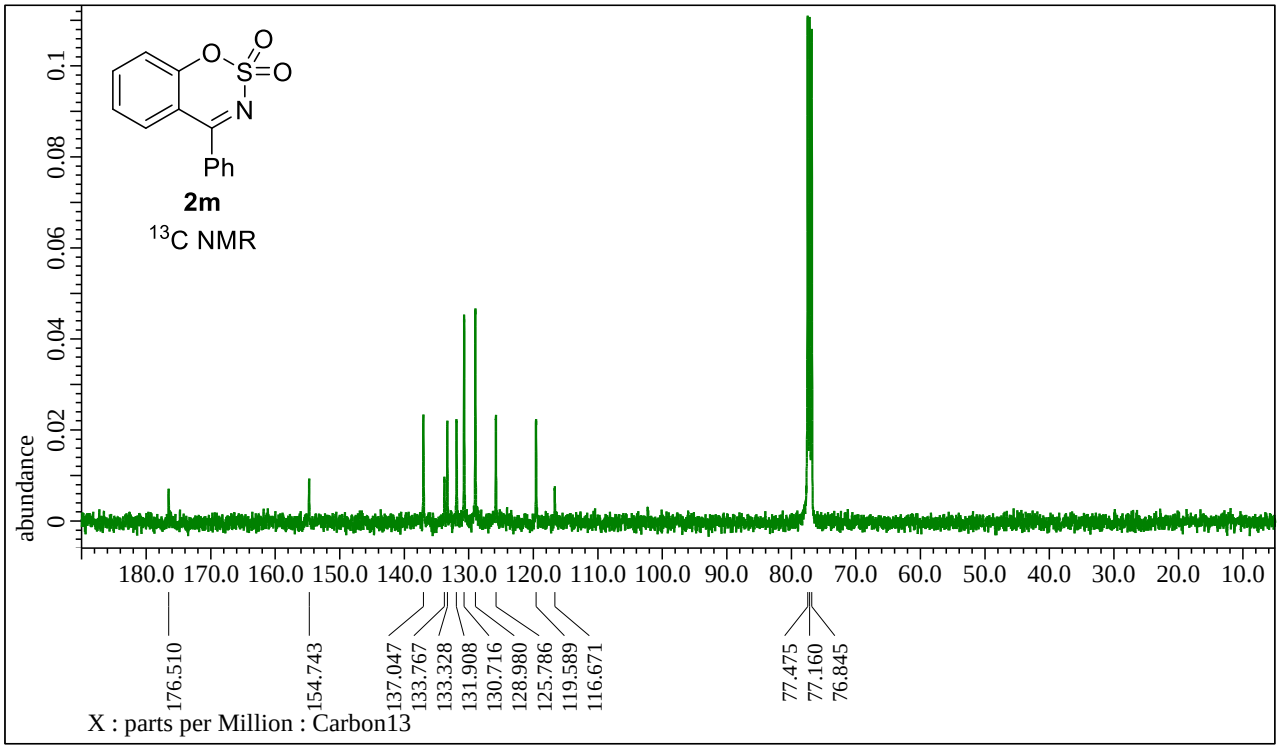

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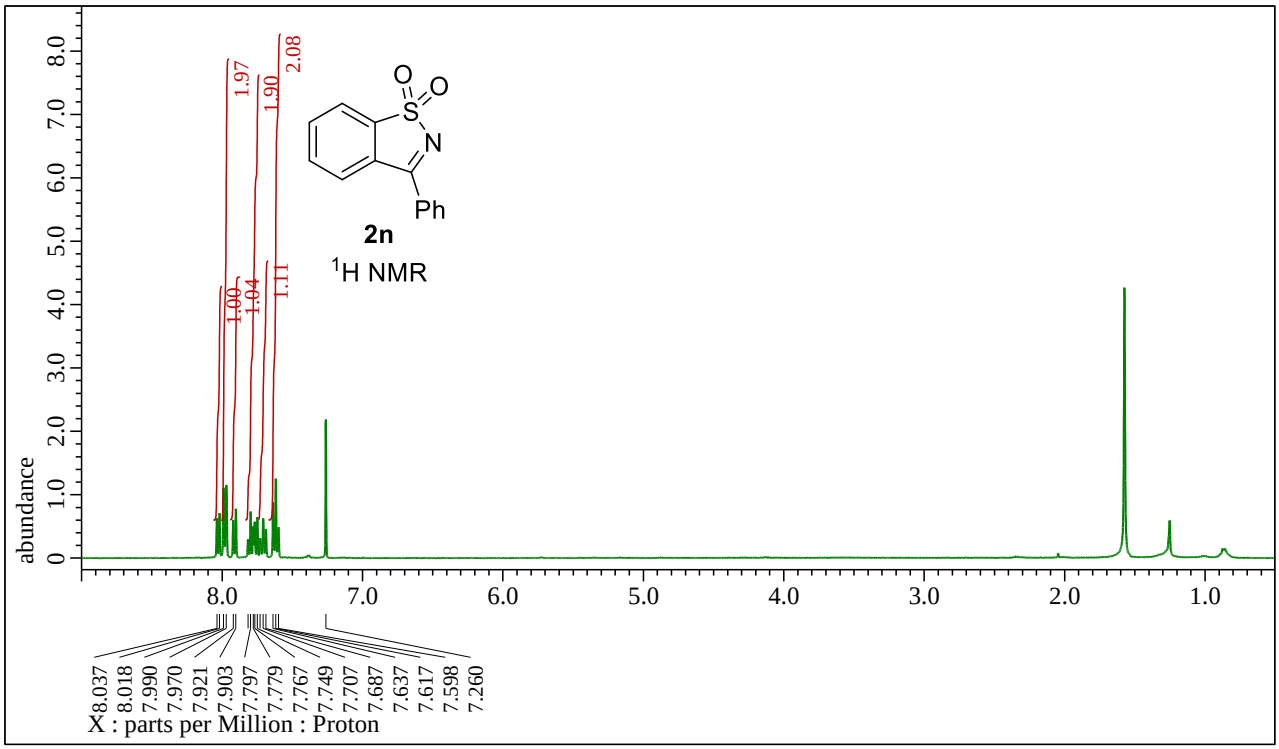

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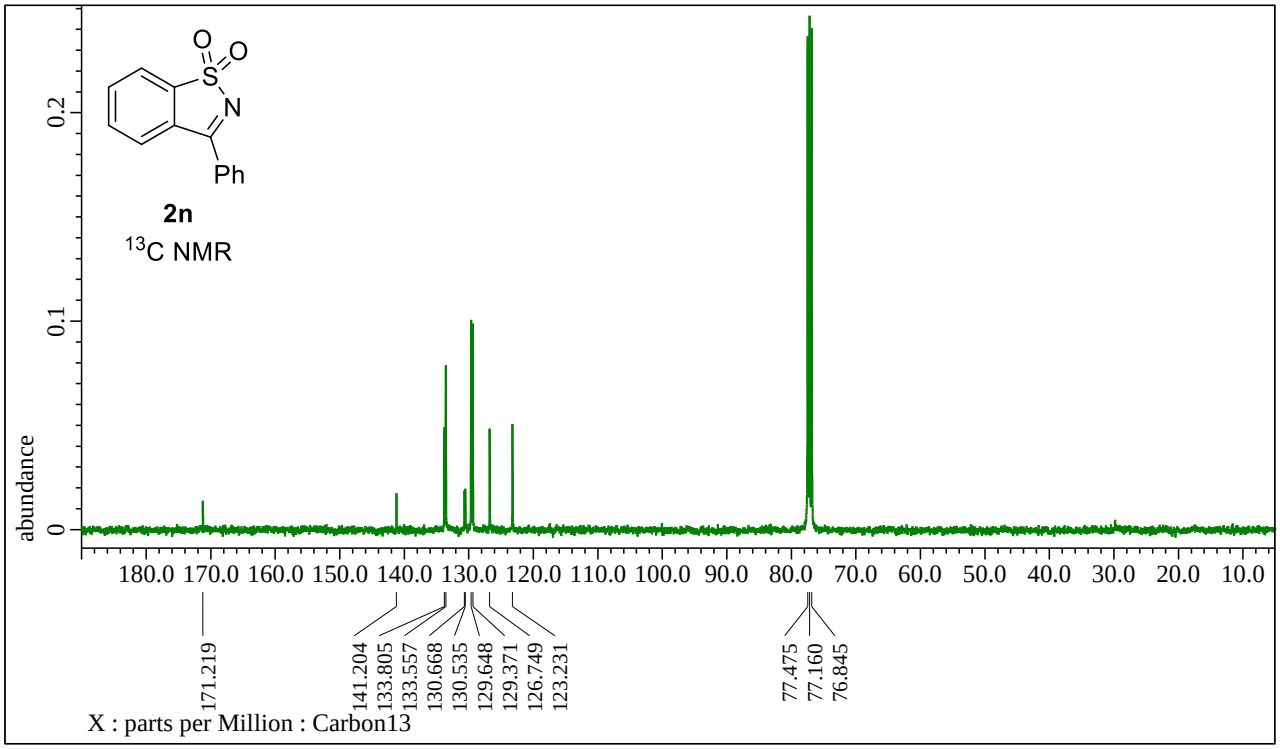

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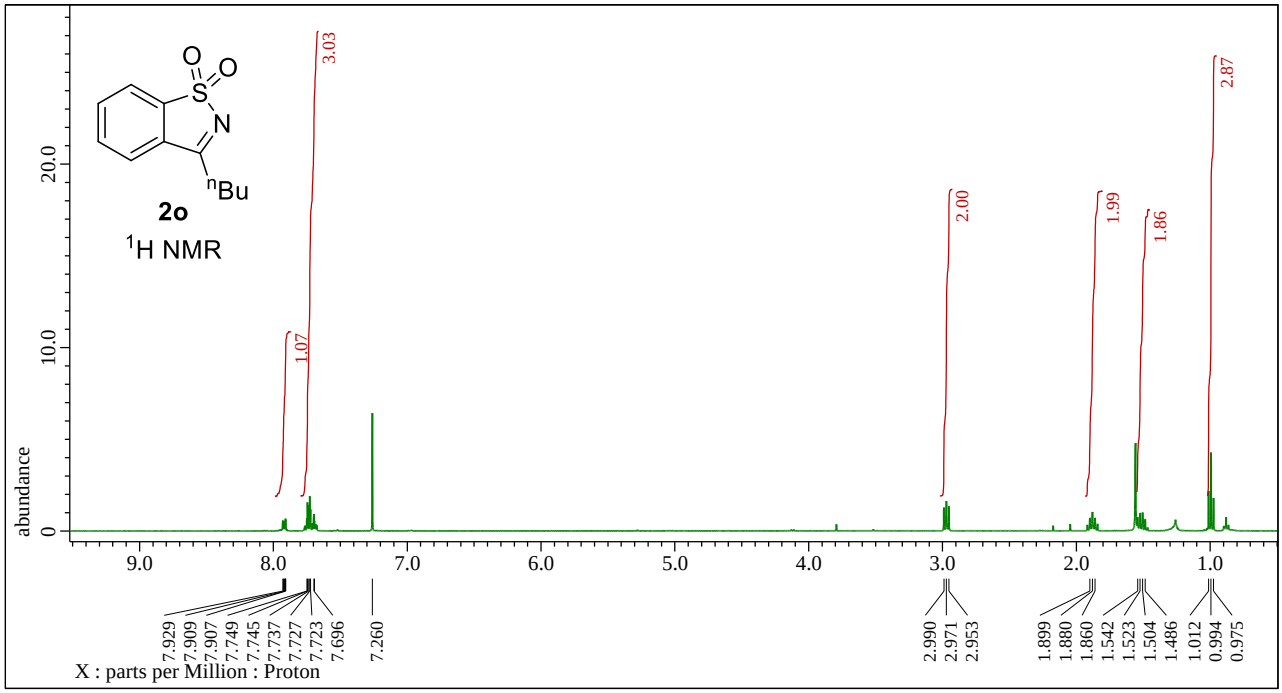

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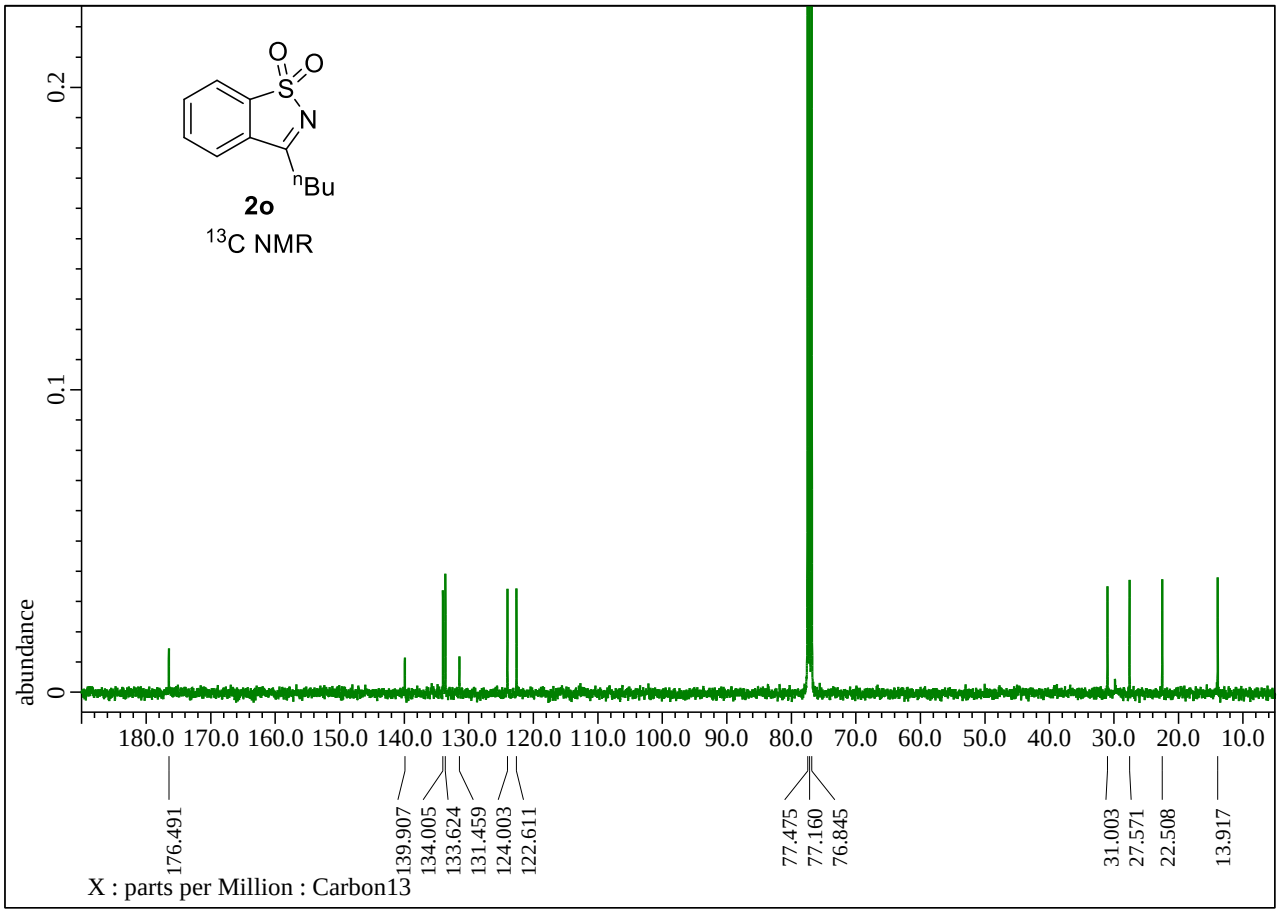

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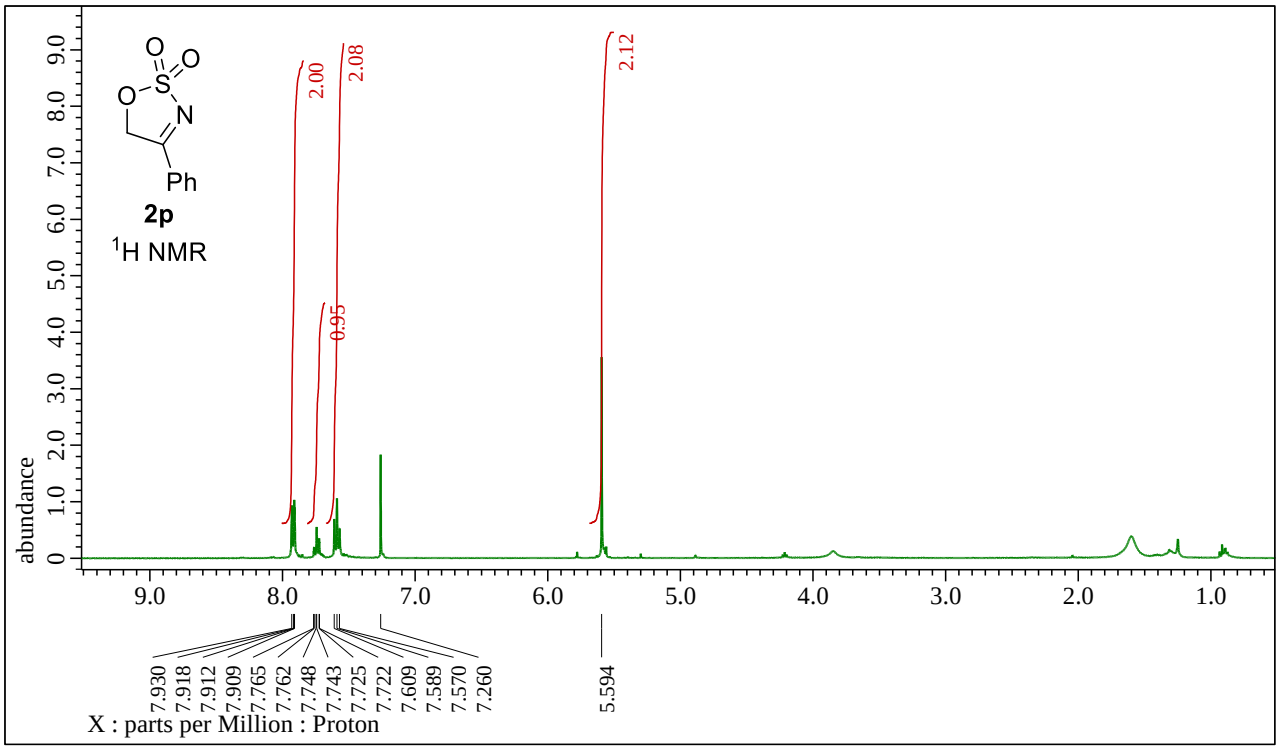

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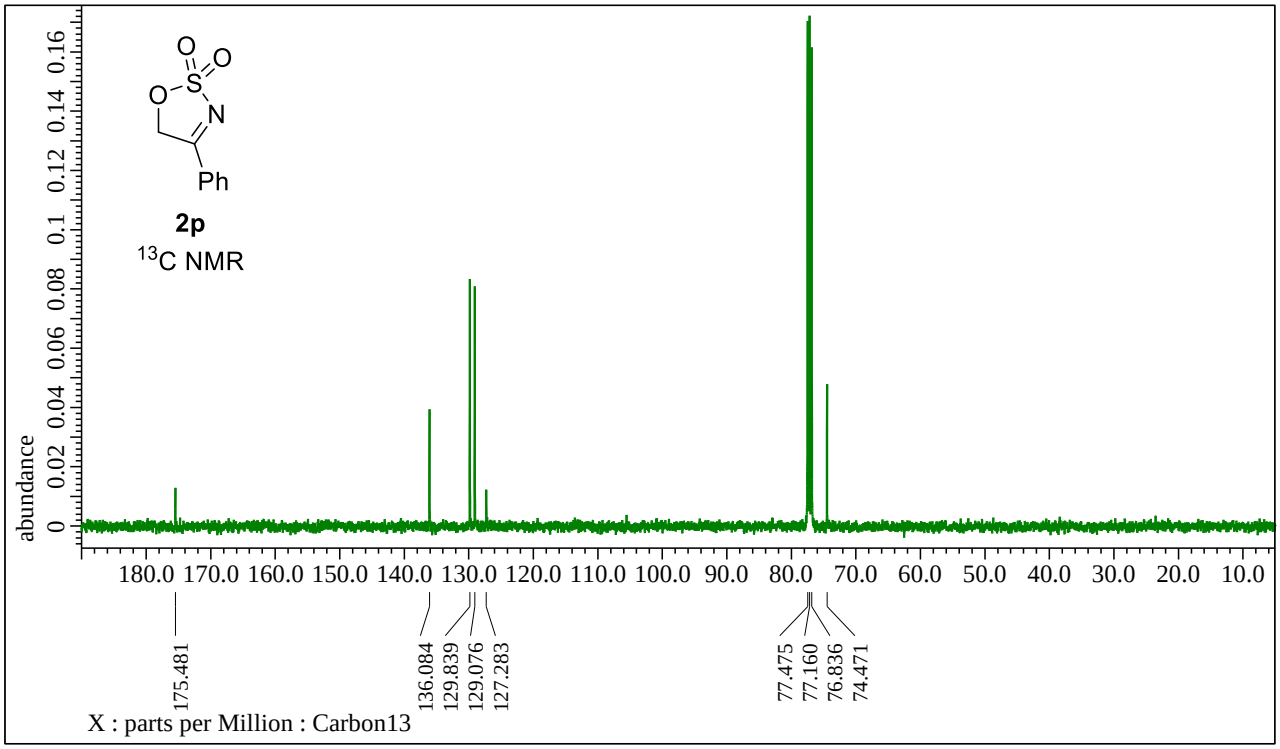
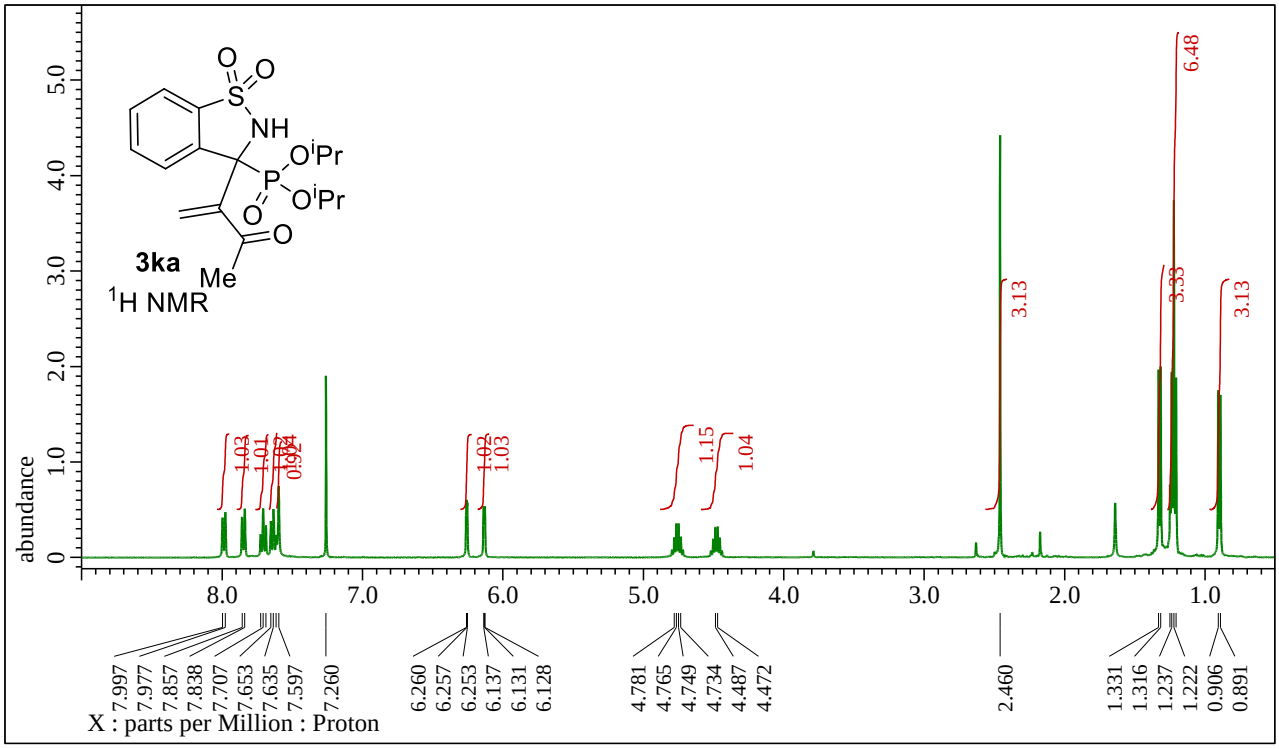
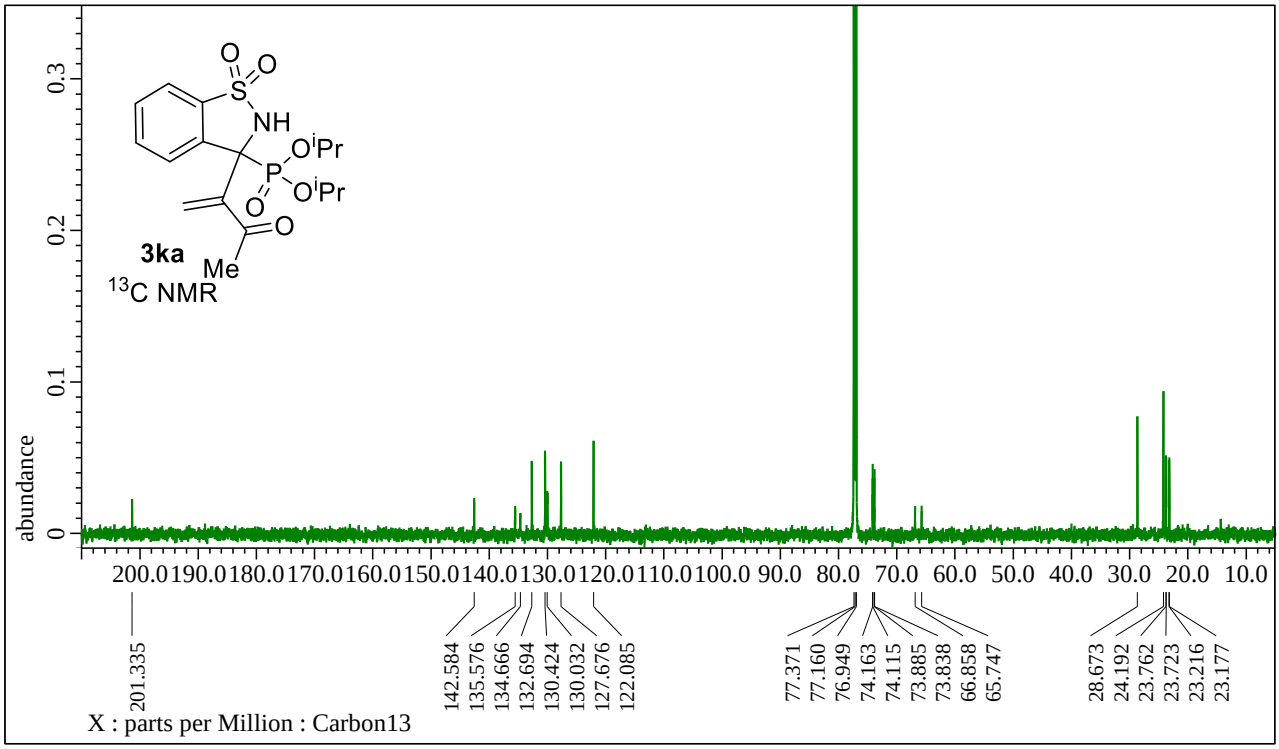


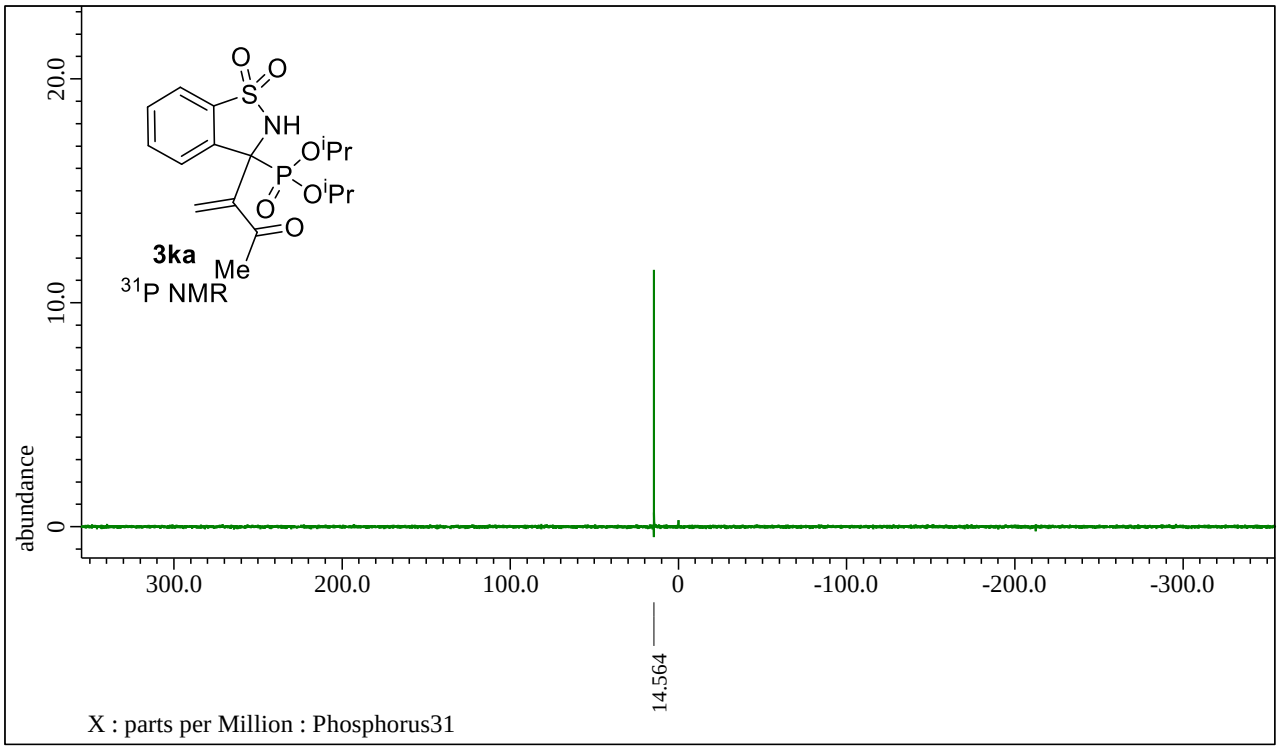
^{1}H-NMR (400 MHz, $CDCl_3$) chart of **3ka**



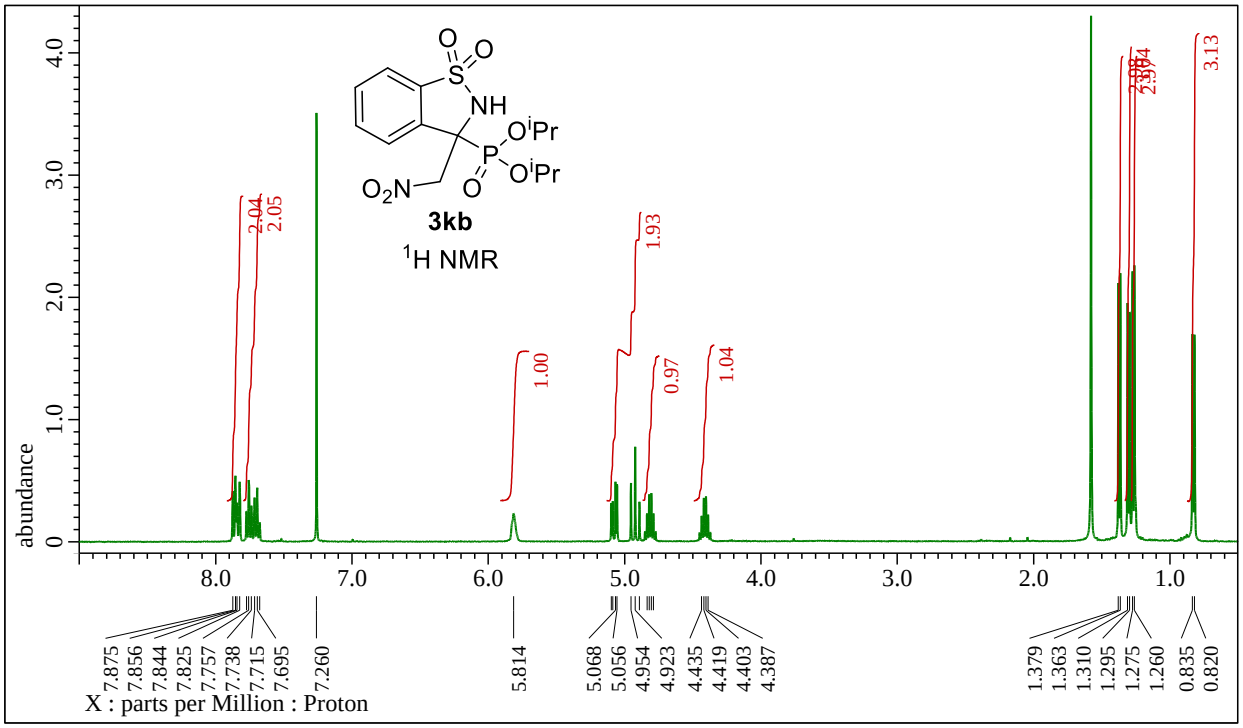
^{13}C-NMR (150 MHz, $CDCl_3$) chart of **3ka**



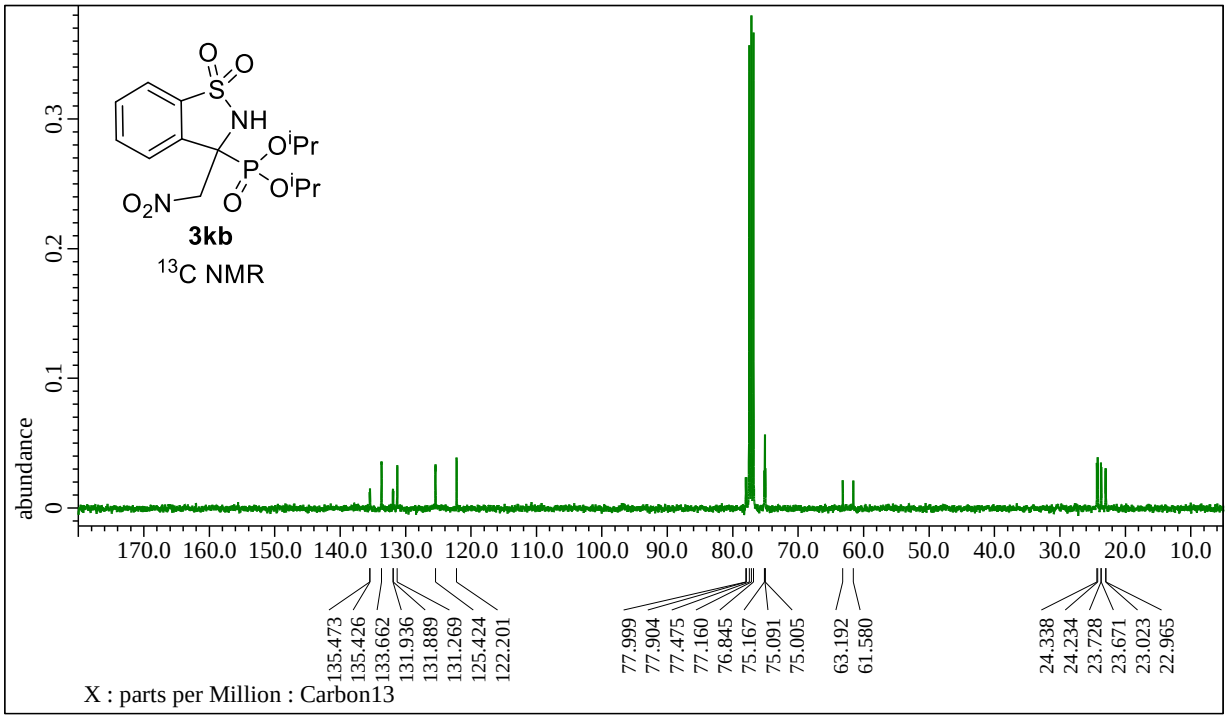
^{31}P-NMR (240 MHz, $CDCl_3$) chart of **3ka**



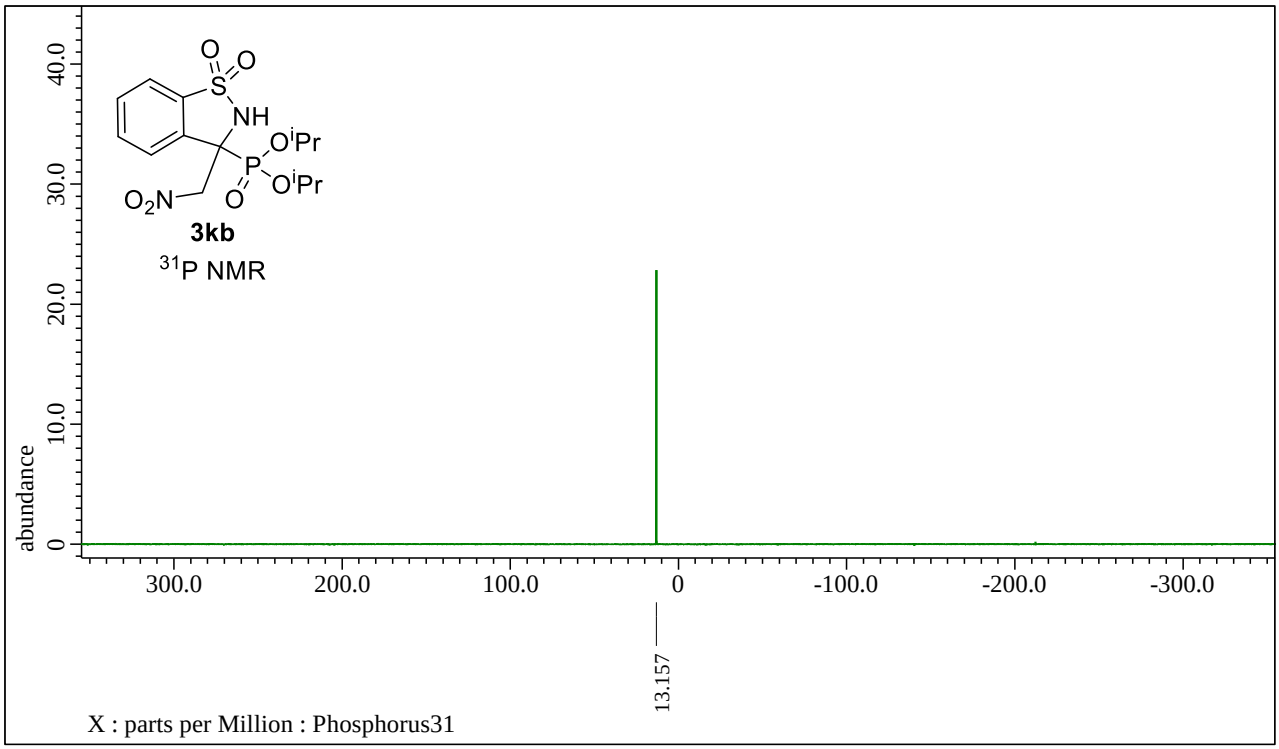
^{1}H-NMR (400 MHz, $CDCl_3$) chart of **3kb**



^{13}C-NMR (100 MHz, $CDCl_3$) chart of **3kb**

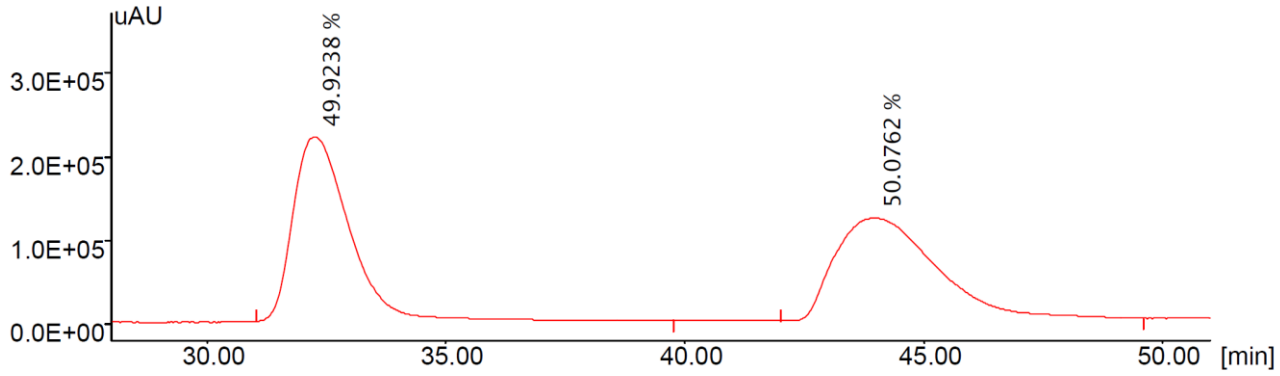


^{31}P-NMR (240 MHz, $CDCl_3$) chart of **3kb**

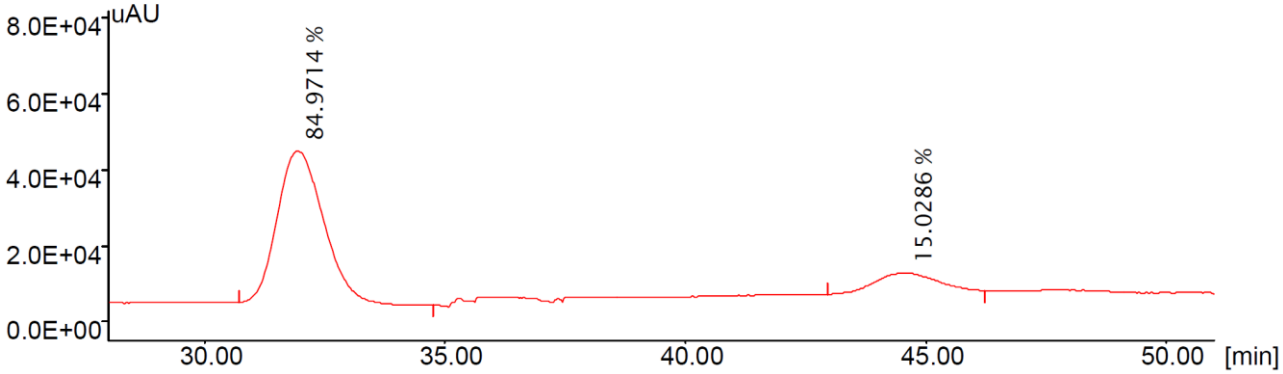


HPLC charts

***rac*-3ka**

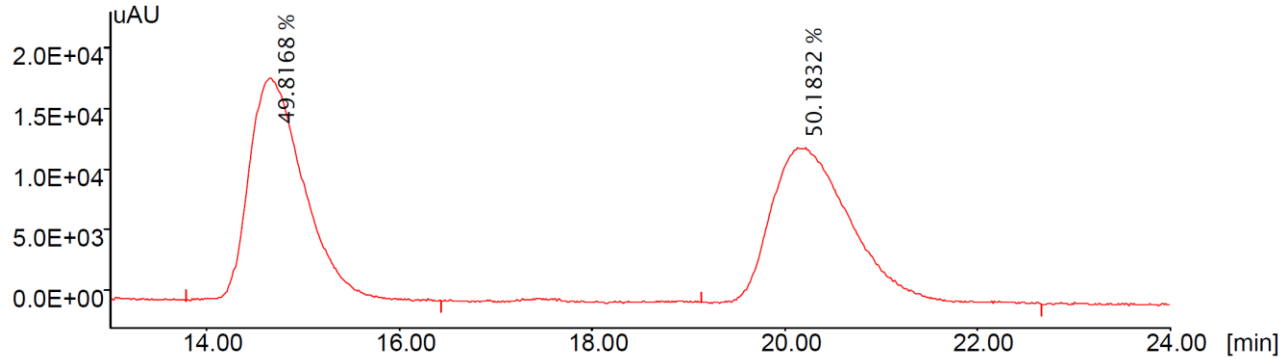


3ka (70% ee)

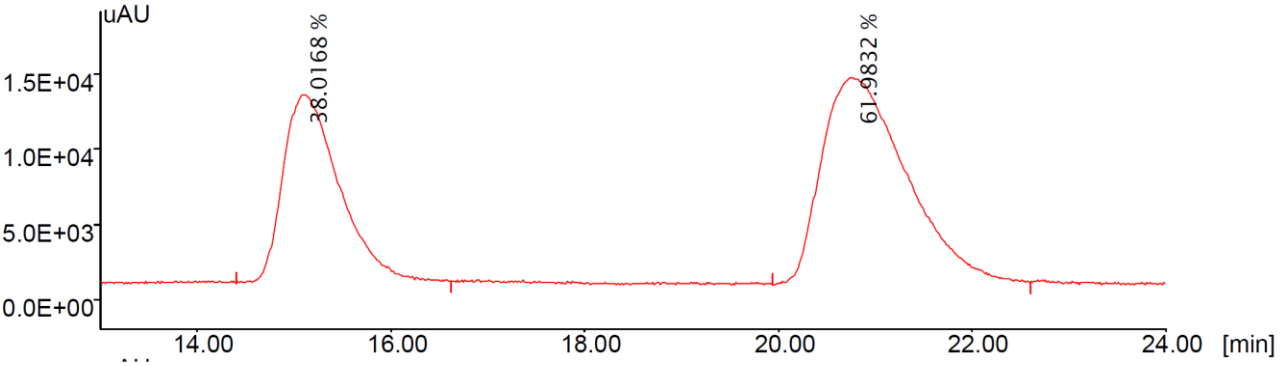


HPLC conditions: Daicel Chiralpak IE column, *n*-hexane/^{i}PrOH = 50/50, 1.0 mL/min, 224 nm, tR = 31.9 min (major isomer) and 44.6 min (minor isomer).

***rac*-3kb**



3kb (24% ee)



HPLC conditions: Daicel Chiralpak IE column, *n*-hexane/^{i}PrOH = 50/50, 1.0 mL/min, 275 nm, tR = 14.7 min (minor isomer) and 20.8 min (major isomer).