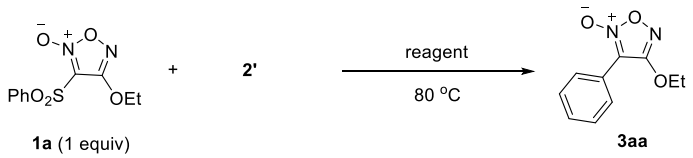
Direct arylation of furoxan using potassium aryltrifluoroborates

Table of Contents:

1. Optimization of Reaction Conditions

It is well known that arylboronic acids are commonly used aryl radical precursors. We began our screening between furoxan **1a** and phenylboronic acid (Table S1, entries 1−22). Several oxidant such as $KMnO_4$, $Mn(OAc)_3$, $Mn(acac)_3$ (acac = acetylacetonate), $Mn(OAc)_2$, di-*tert*-butyl peroxide (DTBP), $K_2S_2O_8$, etc (entries 1−9) were screened. The product **3aa** could be obtained in slightly lower yields when $Mn(OAc)_3$ and $K_2S_2O_8$ were used as oxidants (entries 2 and 6). Subsequently, further methodology was carried out for these two oxidants. For $K_2S_2O_8$, catalytic amount of different additives and large amount of reagents were tested, but had no significant improvement on the yield (entries 10−13, 15). For $Mn(OAc)_3$, different solvents were examined and revealed that CH_3CN was the suitable solvent (entries 16−19). Increasing the amount of phenylboronic acid and oxidant to 7.0 equiv increased the yield to 36% (entry 21). Although the yield was slightly improved, there is no advantage to employ expensive oxidant in large quantities. The large amount of starting furoxan remaining and oxidant consumption forced us to consider other aryl partners. Firstly, phenyl diazonium tetrafluoroborate was investigated (entries 23 and 24). However, these strategies had no beneficial effect. In addition, aryl partners with bulky hindrance was performed to attempt to reduce the radical formation rate but was ineffective for the reaction (entry 25).

Table S1. Optimization of Reaction Conditions with other aryl radical precursors[a]



1a (1 equiv) **3aa**

entry	**2'** (equiv)	reagent (equiv)	additive (equiv)	solvent	time/h	yield/%[b]
1	$PhB(OH)_2$ (2)	$KMnO_4$ (2)	−	CH_3CN	13	8
2	$PhB(OH)_2$ (2)	$Mn(OAc)_3$ (2)	−	CH_3CN	15	18
3	$PhB(OH)_2$ (2)	$Mn(acac)_3$ (2)	−	CH_3CN	18	10
4	$PhB(OH)_2$ (2)	$Mn(OAc)_2$ (2)	−	CH_3CN	18	0
5[c]	$PhB(OH)_2$ (2)	DTBP (3)	−	CH_3CN	16	trace
6	$PhB(OH)_2$ (2)	$K_2S_2O_8$ (2)	−	CH_3CN/H_2O (1/1)	15	15
7	$PhB(OH)_2$ (2)	$(NH_4)_2S_2O_8$ (2)	−	CH_3CN/H_2O (1/1)	15	trace
8	$PhB(OH)_2$ (2)	$(PyH)_2S_2O_8$ (2)	−	CH_3CN	23	0
9	$PhB(OH)_2$ (2)	$(n\text{-}Bu_4N)_2S_2O_8$ (2)	−	CH_3CN	4	trace
10	$PhB(OH)_2$ (2)	$K_2S_2O_8$ (2)	$AgNO_3$ (0.2)	CH_3CN/H_2O (1/1)	18	14
11	$PhB(OH)_2$ (2)	$K_2S_2O_8$ (2)	$Mn(OAc)_3$ (0.2)	CH_3CN/H_2O (1/1)	18	21
12	$PhB(OH)_2$ (2)	$K_2S_2O_8$ (2)	$Mn(OAc)_2$ (0.2)	CH_3CN/H_2O (1/1)	18	19
13	$PhB(OH)_2$ (2)	$K_2S_2O_8$ (2)	$Pd(OAc)_2$	CH_3CN/H_2O	20	0

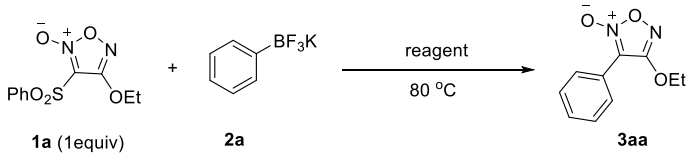
			(0.2)	(1/1)		
14	$PhB(OH)_2$ (2)	$K_2S_2O_8$ (2)	–	H_2O	18	14[d]
15	$PhB(OH)_2$ (14)	$K_2S_2O_8$ (16)	–	CH_3CN/H_2O (1/1)	18	31[d]
16	$PhB(OH)_2$ (2)	$Mn(OAc)_3$ (2)	–	toluene	18	trace
17	$PhB(OH)_2$ (2)	$Mn(OAc)_3$ (2)	–	DMF	18	0
18	$PhB(OH)_2$ (2)	$Mn(OAc)_3$ (2)	–	DMSO	18	16[d]
19	$PhB(OH)_2$ (2)	$Mn(OAc)_3$ (2)	–	DCE	18	16[d]
20[e]	$PhB(OH)_2$ (2)	$Mn(OAc)_3$ (2)	–	CH_3CN	18	31[d]
21	$PhB(OH)_2$ (7)	$Mn(OAc)_3$ (7)	–	CH_3CN	18	36
22[f]	$PhB(OH)_2$ (2)	$Mn(OAc)_3$ (2)	–	CH_3CN	4	28[d]
23[g]	PhN_2BF_4 (2)	Ascorbic acid (2)	–	DMF	24	0
24[g]	PhN_2BF_4 (2)	Pyrazole (0.2)	*t*-BuOK (2)	DMSO	24	trace
25	Phenylborate **S1** (3)	$K_2S_2O_8$ (3)	–	CH_3CN/H_2O (1/1)	22	15[d]

[a] Reaction conditions: **1a** (0.15 mmol), solvent (1.5 mL), Schlenk tube, argon atmosphere, 80 °C. [b] Isolated yield. [c] The temperature was 120 °C. [d] Determined by ^1H NMR analysis using durene as an internal standard. [e] Solvent (0.8 mL). [f] The temperature was 100 °C. [g] Room temperature.

S1

Next, we started to use aryltrifluoroborate **2a**. The main results of the condition screening using **2a** are shown in the main text and herein the additional investigation of reaction conditions with **2a** are shown (Table S2). In order to avoid the hydrolysis of aryltrifluoroborate, acetonitrile-soluble peroxydisulfates were examined, but had no improvement on the yield (entry 3). Phase transfer catalysts failed to improve the yield in our heterogeneous condition (entries 4 and 5). Following, other solvents, different concentration and different equivalent were further tested, all of which were ineffective (entries 7−13).

Table S2. Optimization of Reaction Conditions[a]



1a (1equiv) **2a** **3aa**

entry	reagent (equiv)	additive (equiv)	solvent	time/h	yield/%[b]
1	Selectfluor (2)	$AgNO_3$ (0.2)	CH_3CN/H_2O (1/1)	48	23
2	DTBP (3)	–	CH_3CN	16	trace
3	$(PyH)_2S_2O_8$ (3)	–	CH_3CN	23	0
4	$K_2S_2O_8$ (3)	PEG 400 (0.1)	CH_3CN/H_2O (1/1)	7	35
5	$K_2S_2O_8$ (3)	TBAB (0.1)	CH_3CN/H_2O (1/1)	7	42
6	$K_2S_2O_8$ (3)	$Mn(OAc)_3$ (0.2)	CH_3CN/H_2O (1/1)	4	42

7	$K_2S_2O_8$ (5)	–	CH_3CN/H_2O (1/1)	4	38
8[c]	$K_2S_2O_8$ (3)	–	CH_3CN/H_2O (1/1)	4	45
9[d]	$K_2S_2O_8$ (3)	–	CH_3CN/H_2O (1/1)	4	42
10[e]	$K_2S_2O_8$ (3)	–	CH_3CN/H_2O (1/1)	4	42
11	$K_2S_2O_8$ (3)	–	DMF	4	0
12	$K_2S_2O_8$ (3)	–	DMSO	4	trace
13	$K_2S_2O_8$ (3)	–	CH_3CN	4	0
14[f]	$K_2S_2O_8$ (3)	–	CH_3CN/H_2O (1/1)	4	45

[a] Reaction conditions: **1a** (0.15 mmol), **2a** (3 equiv), solvent (1.5 mL), Schlenk tube, argon atmosphere, 80 °C. [b] Determined by ^1H NMR analysis using durene as an internal standard. [c] 5 equiv of **2a** was used. [d] Solvent (0.8 mL). [e] Solvent (3 mL). [f] $K_2S_2O_8$ was dissolved in H_2O and its solution was added dropwise at 80 °C to solution of **1a** and **2a** over 2 h.

2. DFT-calculation

Thermodynamic properties are estimated at 298.15 K and 1 atm. unit: hartree

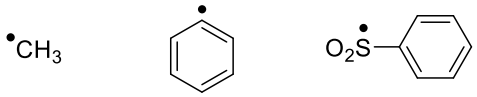
	E_{tot}	E_0	E_{298}	H_{298}	G_{298}
S1	-39.8382917567	-39.808465	-39.805359	-39.804414	-39.828291
S2	-231.561275821	-231.473660	-231.469291	-231.468347	-231.501703
S3	-780.196532967	-780.097763	-780.090146	-780.089202	-780.131488
RT	-1231.34013447	-1231.166102	-1231.151092	-1231.150147	-1231.209850
Me-TS1	-1271.17414588	-1270.967520	-1270.949582	-1270.948638	-1271.015070
Ph-TS1	-1462.90031956	-1462.638653	-1462.617844	-1462.616900	-1462.692368
Me-INT	-1271.24244415	-1271.030971	-1271.013683	-1271.012739	-1271.077409
Ph-INT*	-1462.97281777	-1462.708627	-1462.688095	-1462.687151	-1462.759891
Me-TS2	-1271.24010847	-1271.029959	-1271.012709	-1271.011765	-1271.077286
Ph-TS2*	-1462.97180570	-1462.708629	-1462.688344	-1462.687400	-1462.760129
Me-PD	-491.057959413	-490.947243	-490.938396	-490.937452	-490.981886
Ph-PD	-682.796816744	-682.632512	-682.620977	-682.620033	-682.671898

E_{tot}: The total electronic energy

E_0: Sum of electronic and zero-point Energies

E_{298}: Sum of electronic and thermal Energies

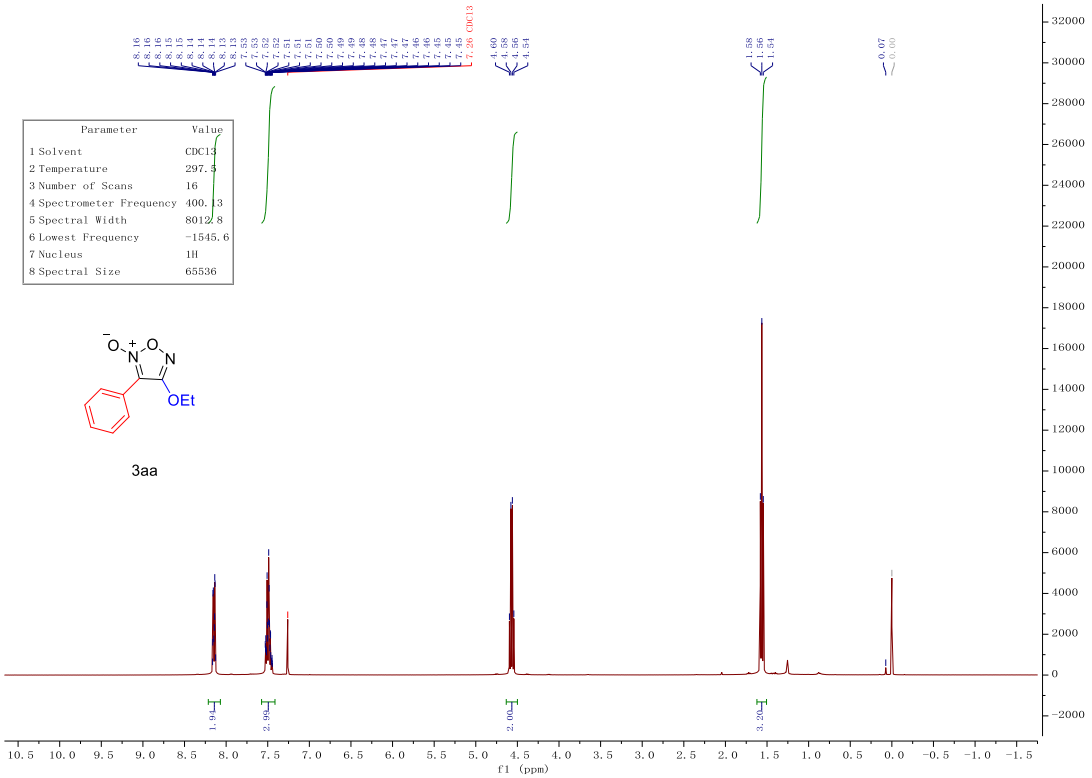
H_{298}: Sum of electronic and thermal Enthalpies
G_{298}: Sum of electronic and thermal Free Energies

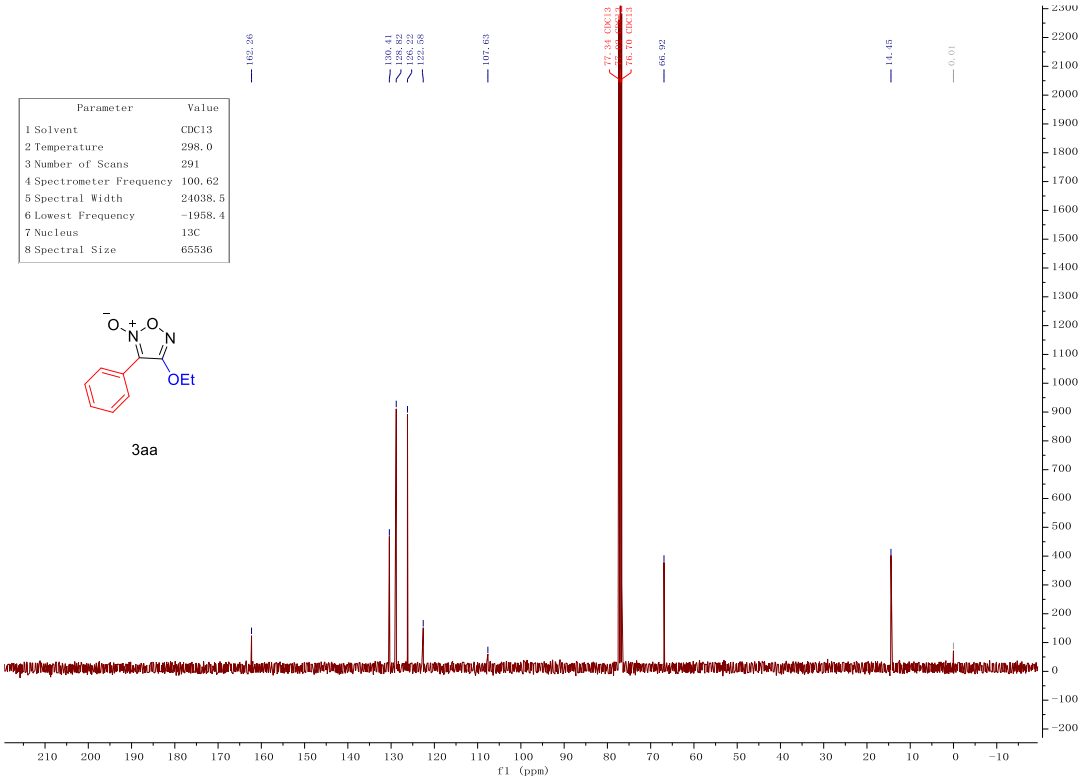


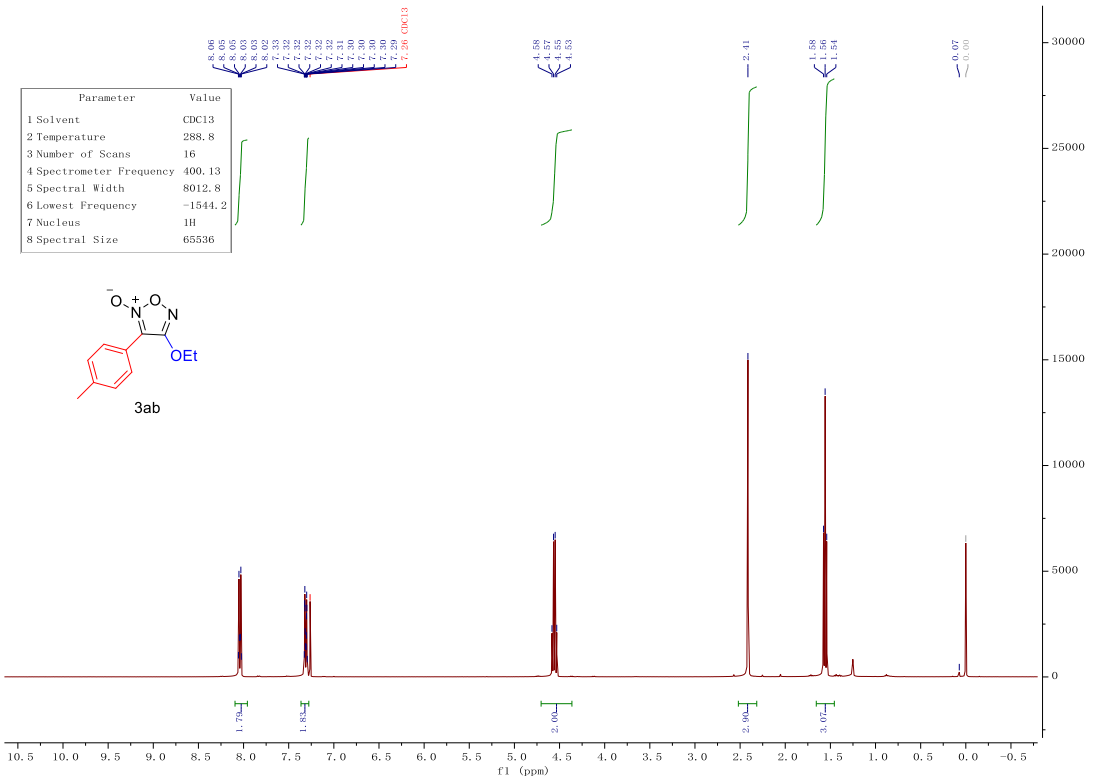
S1 **S2** **S3**

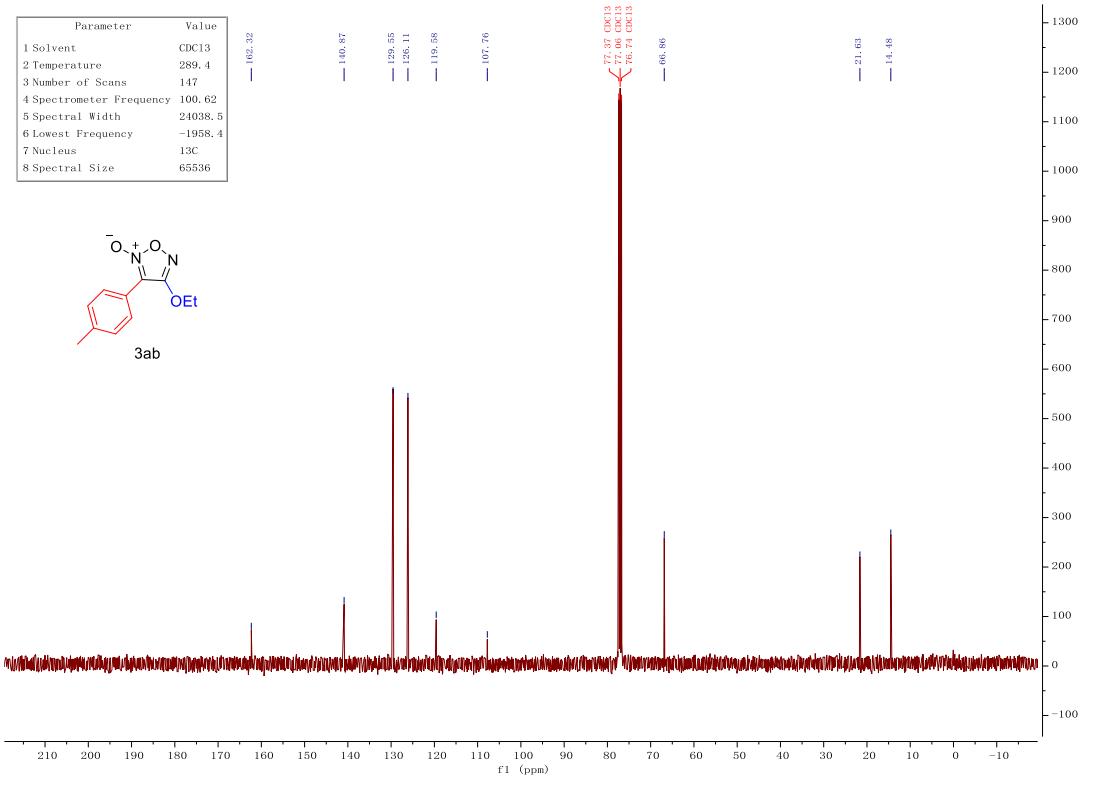
* **Ph-INT** and **Ph-TS2** are very close in energy. **Ph-INT** is lower in E_{tot} but higher in G_{298} than **Ph-TS2**, which can be ascribed to the accuracy limitation of the computational calculation. This result implies that the elimination of the $PhSO_2$ radical can be concerted with the addition of the phenyl radical rather than the stepwise addition-elimination mechanism.

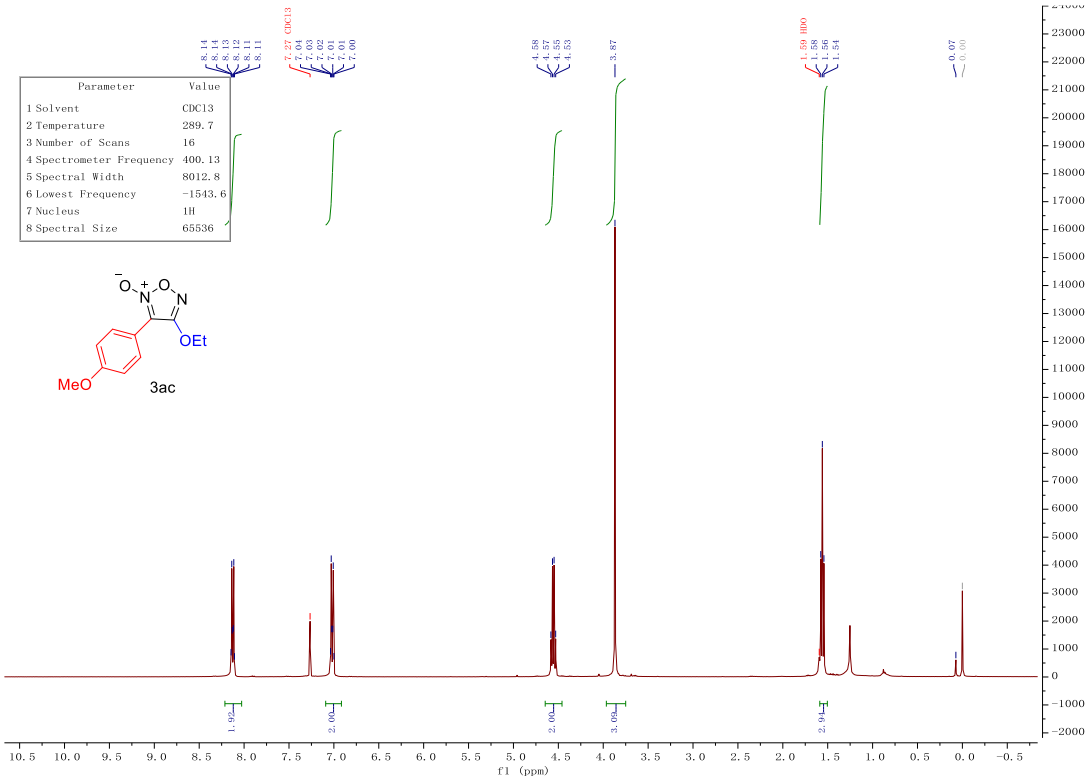
3. ^{1}H NMR and ^{13}C NMR Spectra

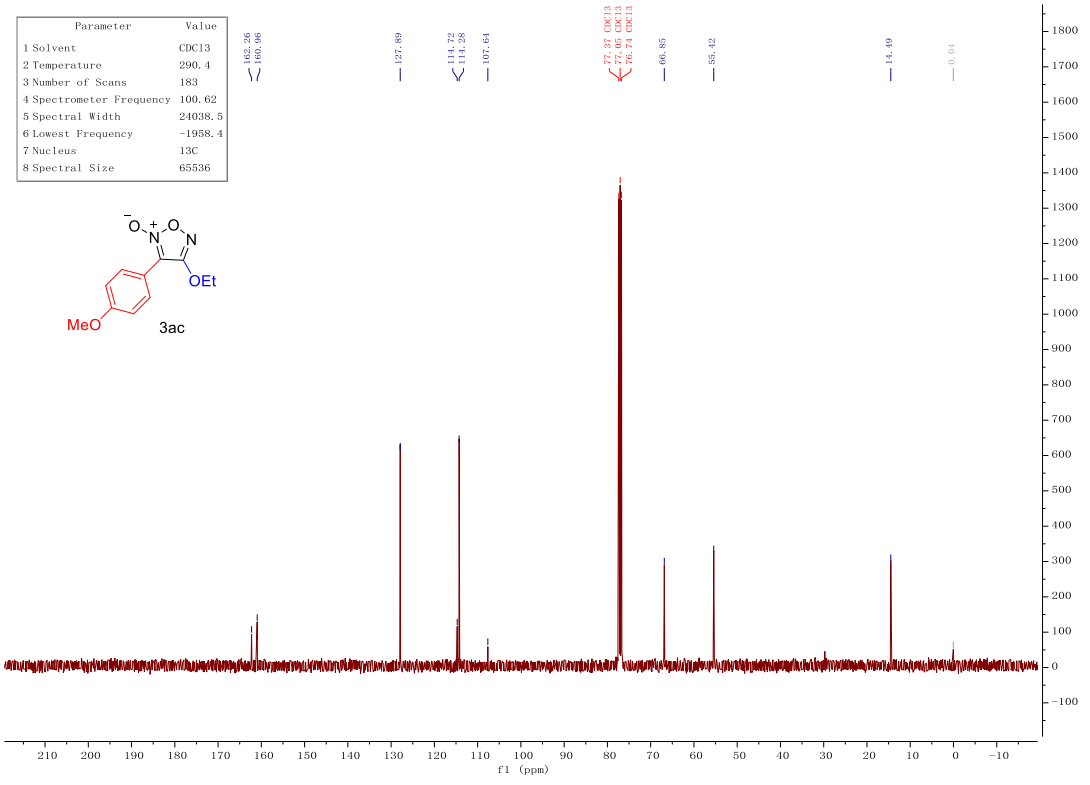


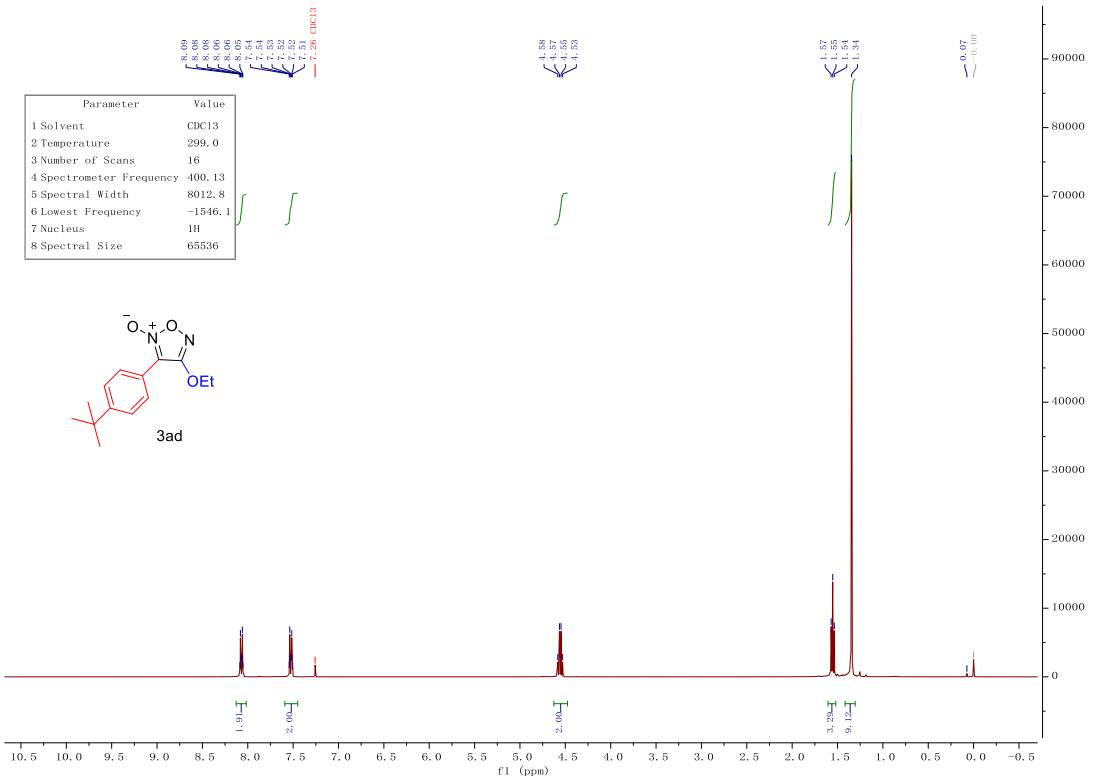


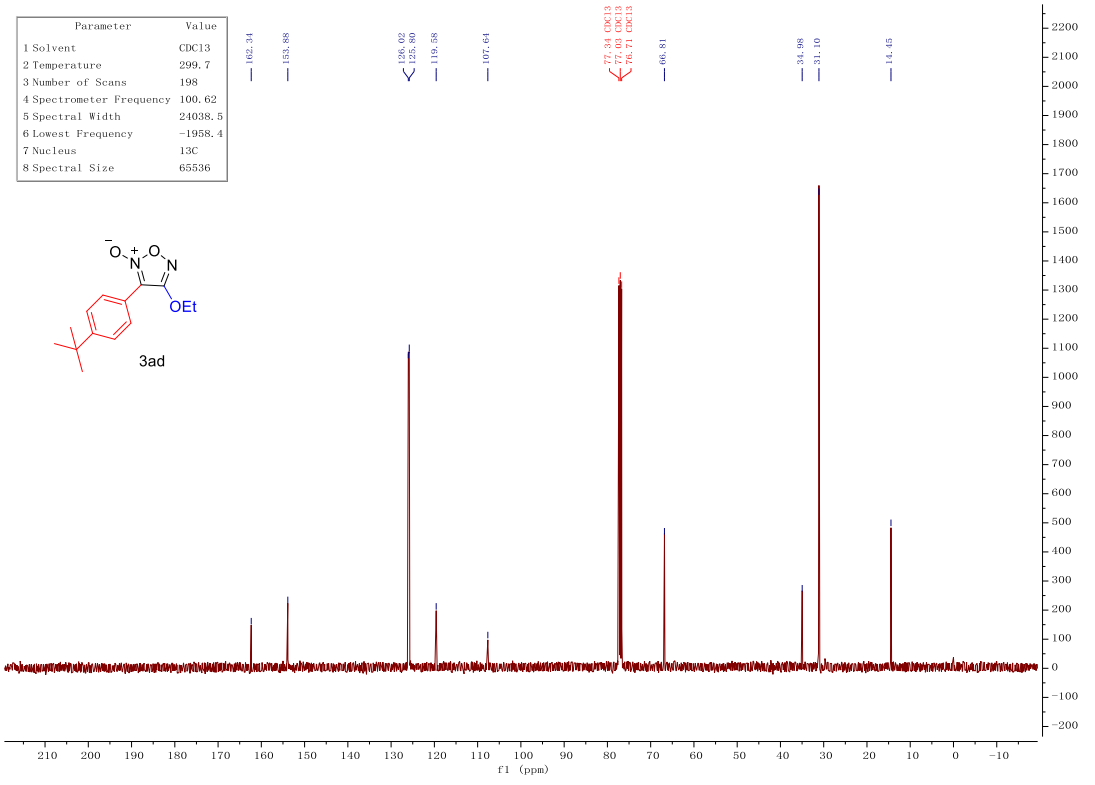

Parameter Value
1 Solvent CDCl3
2 Temperature 288.8
3 Number of Scans 16
4 Spectrometer Frequency 400.13
5 Spectral Width 8012.8
6 Lowest Frequency -1544.2
7 Nucleus 1H
8 Spectral Size 65536
OEt
3ab
f1 (ppm)

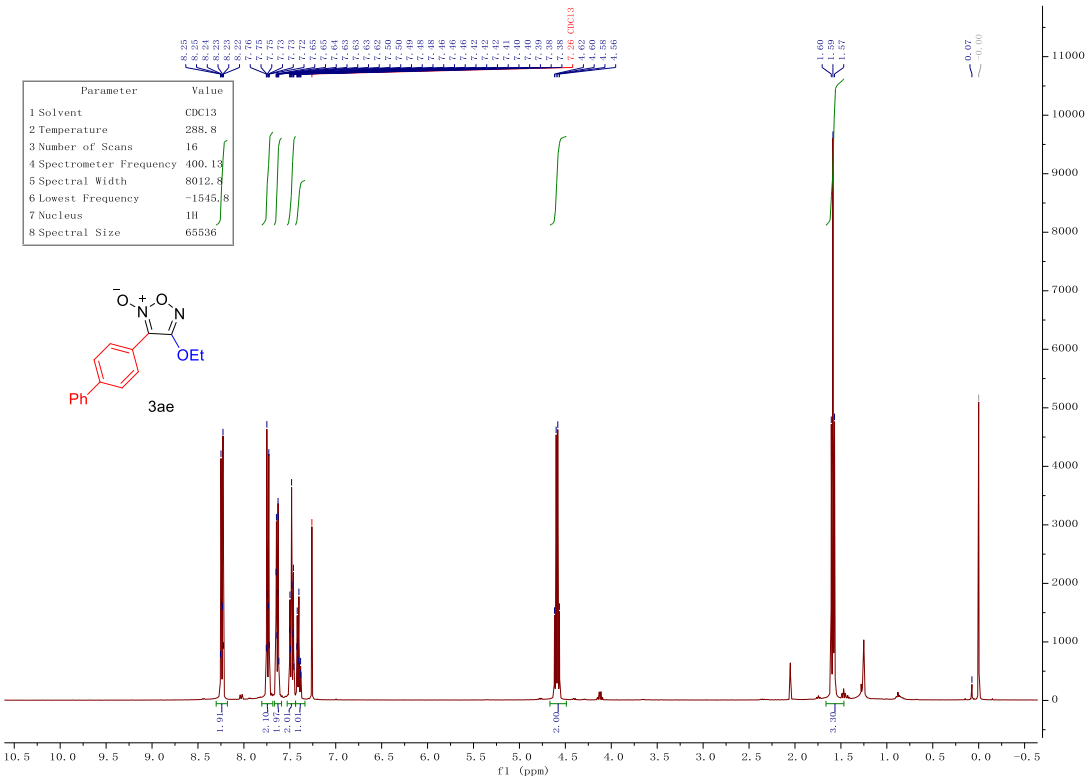

Parameter Value
1 Solvent CDCl3
2 Temperature 289.4
3 Number of Scans 147
4 Spectrometer Frequency 100.62
5 Spectral Width 24038.5
6 Lowest Frequency -1958.4
7 Nucleus 13C
8 Spectral Size 65536
OEt
3ab
f1 (ppm)

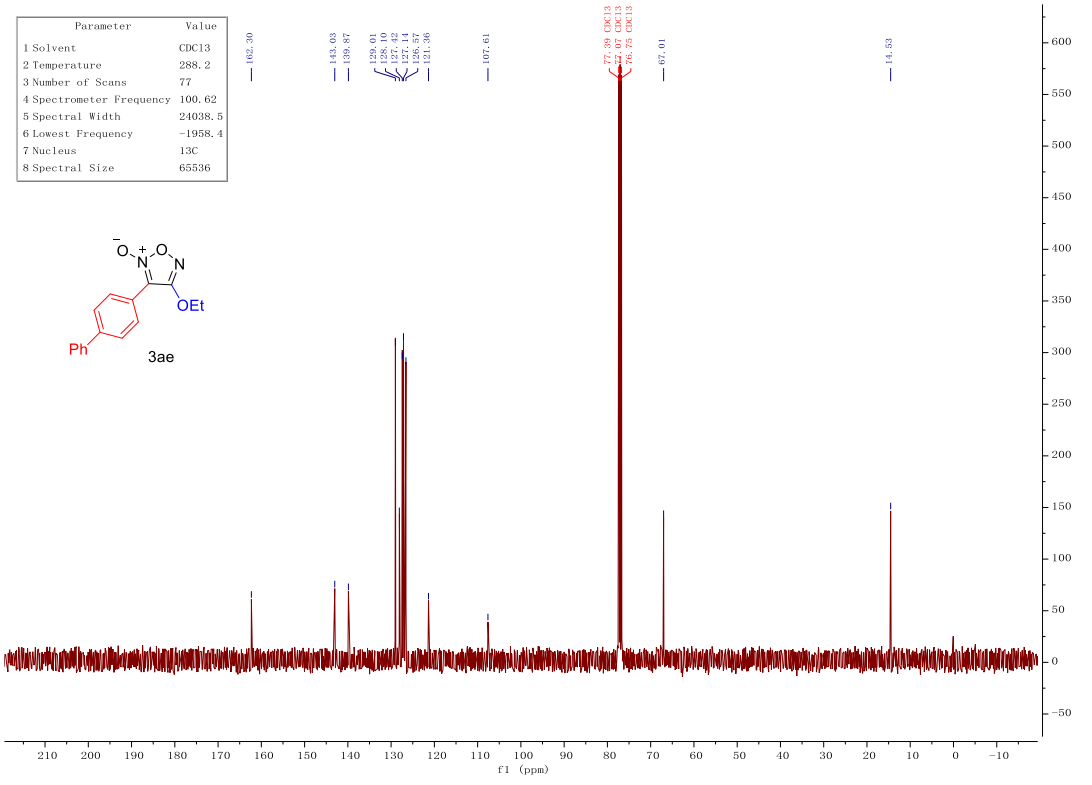

Parameter Value
1 Solvent CDCl3
2 Temperature 289.7
3 Number of Scans 16
4 Spectrometer Frequency 400.13
5 Spectral Width 8012.8
6 Lowest Frequency -1543.6
7 Nucleus 1H
8 Spectral Size 65536
OEt
MeO
3ac
f1 (ppm)

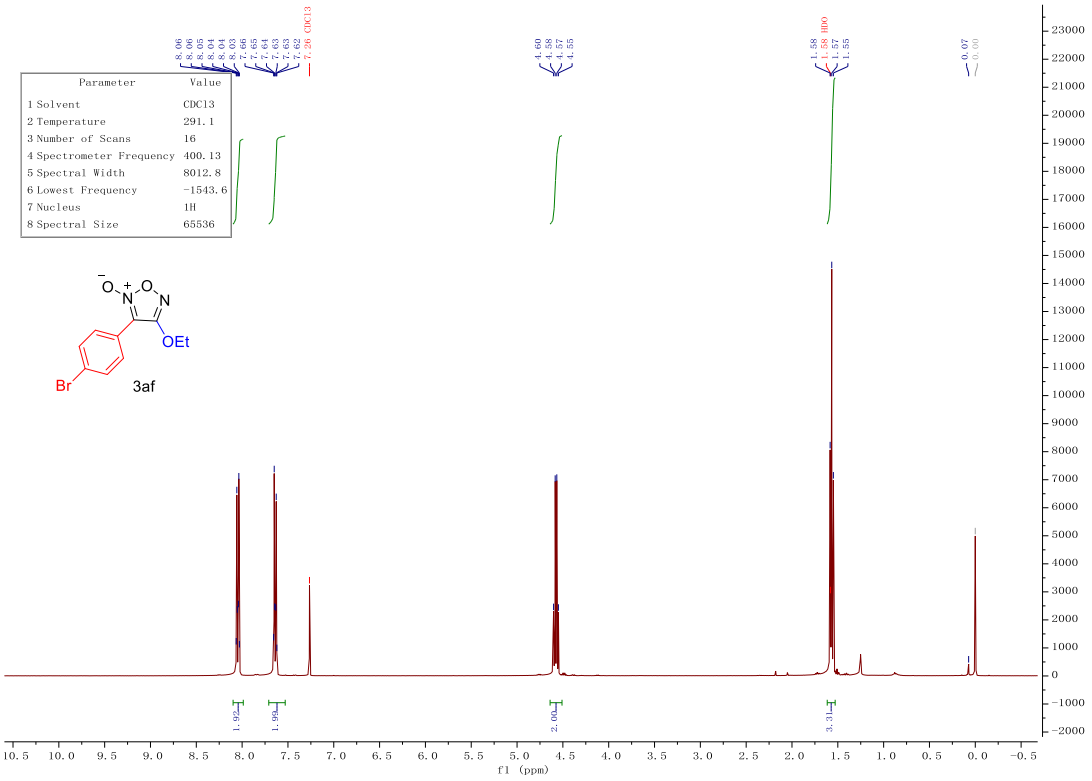

Parameter Value
1 Solvent CDCl3
2 Temperature 290.4
3 Number of Scans 183
4 Spectrometer Frequency 100.62
5 Spectral Width 24038.5
6 Lowest Frequency -1958.4
7 Nucleus 13C
8 Spectral Size 65536
OEt
MeO
3ac
f1 (ppm)

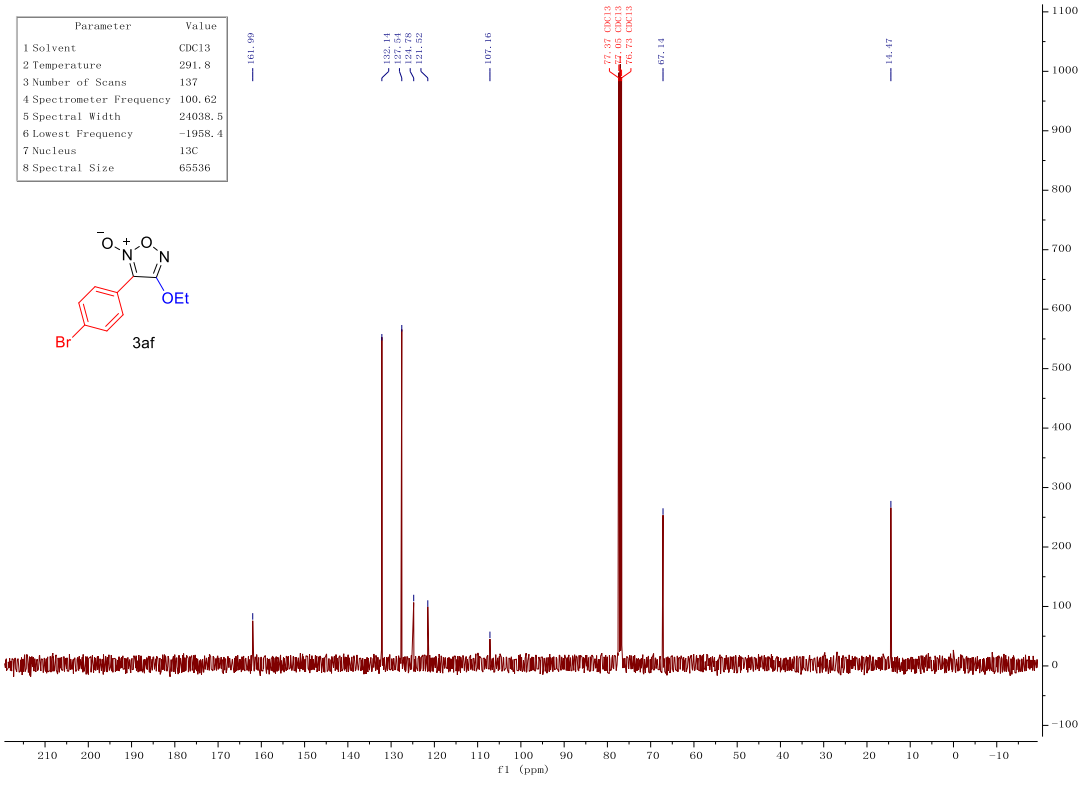

Parameter Value
1 Solvent CDCl3
2 Temperature 299.0
3 Number of Scans 16
4 Spectrometer Frequency 400.13
5 Spectral Width 8012.8
6 Lowest Frequency -1546.1
7 Nucleus 1H
8 Spectral Size 65536
OEt
3ad
f1 (ppm)

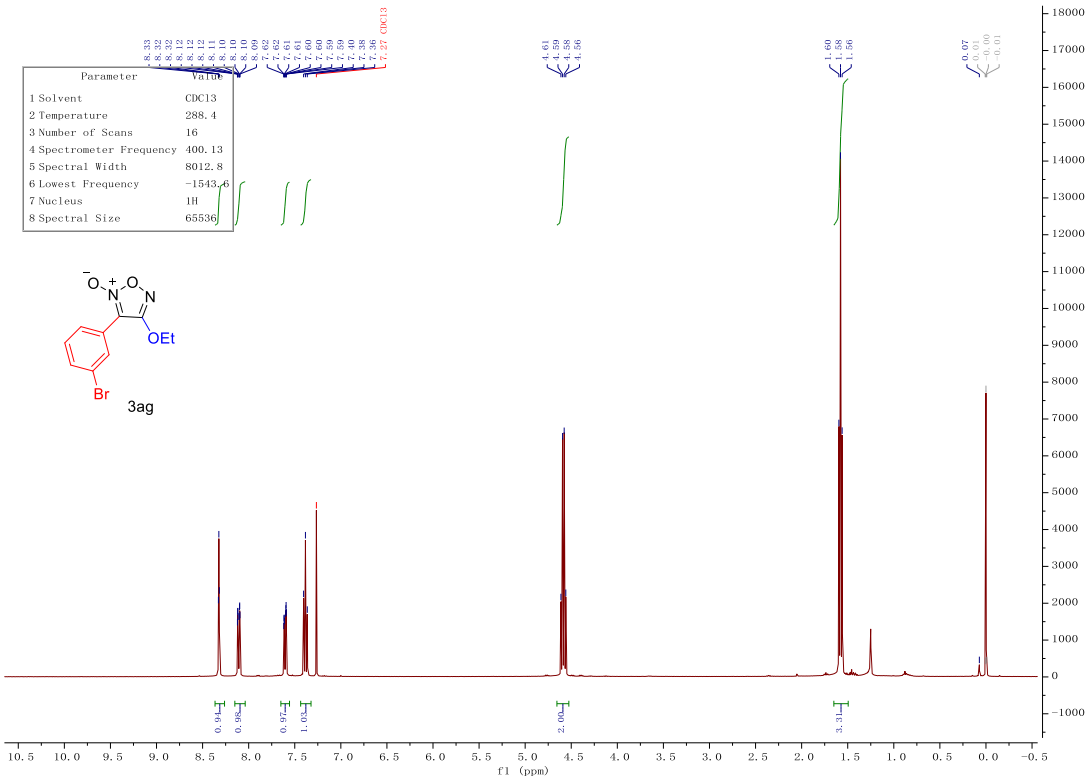

Parameter Value
1 Solvent CDCl3
2 Temperature 299.7
3 Number of Scans 198
4 Spectrometer Frequency 100.62
5 Spectral Width 24038.5
6 Lowest Frequency -1958.4
7 Nucleus 13C
8 Spectral Size 65536
OEt
3ad
f1 (ppm)

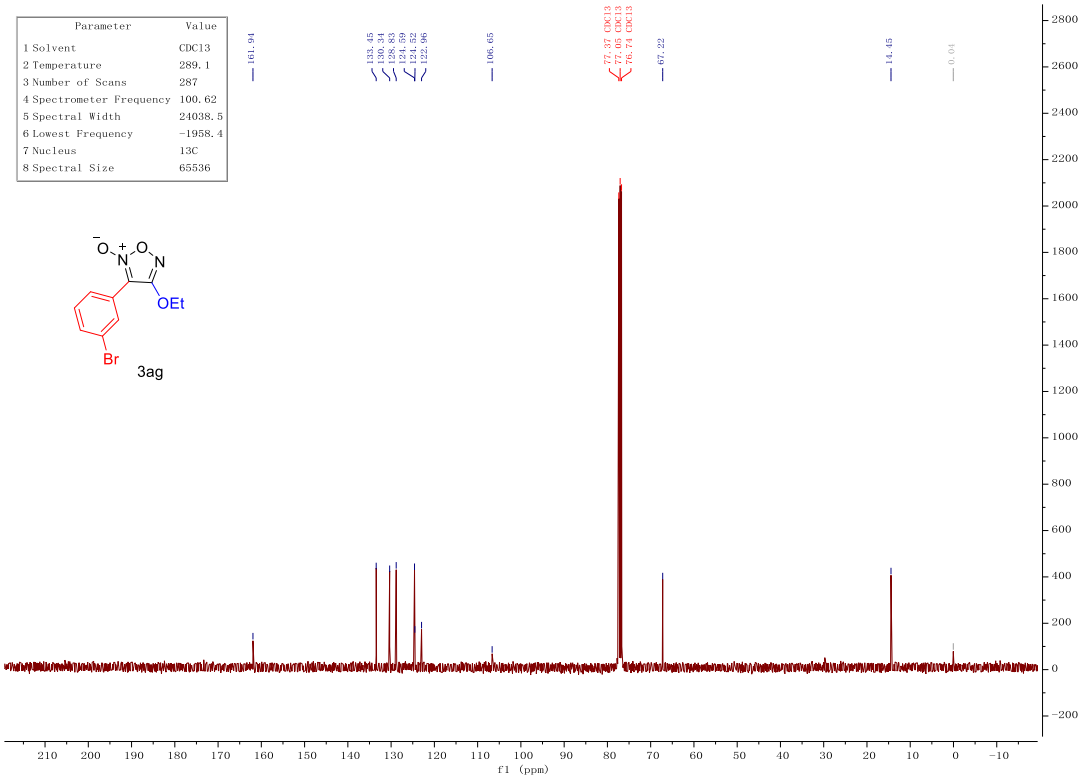

Parameter Value
1 Solvent CDCl3
2 Temperature 288.8
3 Number of Scans 16
4 Spectrometer Frequency 400.13
5 Spectral Width 8012.8
6 Lowest Frequency -1545.8
7 Nucleus 1H
8 Spectral Size 65536
OEt
Ph
3ae
f1 (ppm)

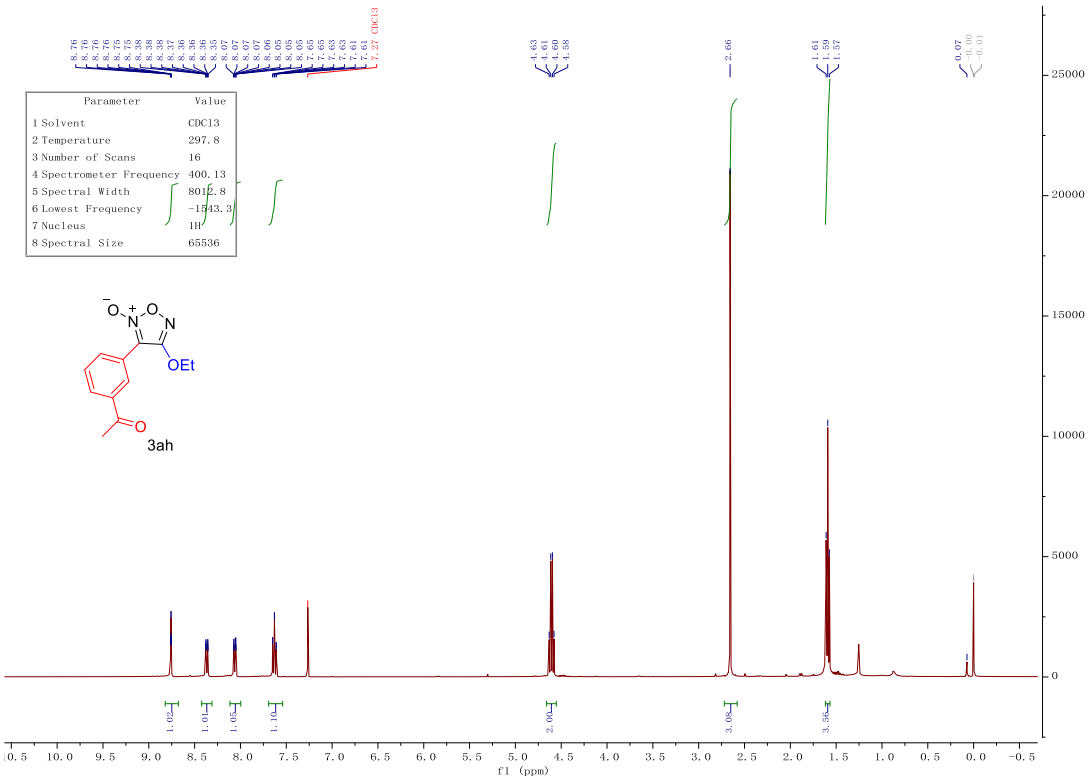

Parameter Value
1 Solvent CDCl3
2 Temperature 288.2
3 Number of Scans 77
4 Spectrometer Frequency 100.62
5 Spectral Width 24038.5
6 Lowest Frequency -1958.4
7 Nucleus 13C
8 Spectral Size 65536
OEt
Ph
3ae
f1 (ppm)

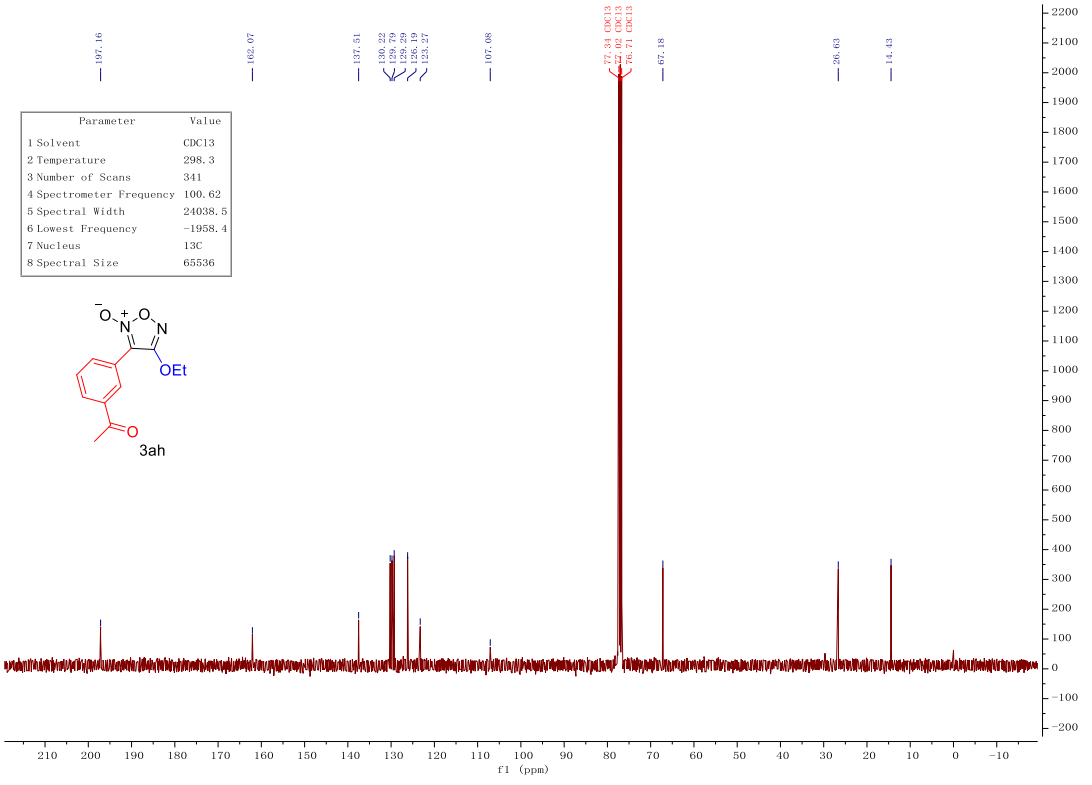

8.06
8.06
8.05
8.04
8.04
8.03
7.66
7.65
7.64
7.63
7.63
7.62
7.26 CDCl3
4.60
4.58
4.57
4.55
1.58
1.58 H2O
1.57
1.55
0.07
0.00
Parameter Value
1 Solvent CDCl3
2 Temperature 291.1
3 Number of Scans 16
4 Spectrometer Frequency 400.13
5 Spectral Width 8012.8
6 Lowest Frequency -1543.6
7 Nucleus 1H
8 Spectral Size 65536
OEt
Br
3af
1.92
1.99
2.00
3.31
f1 (ppm)

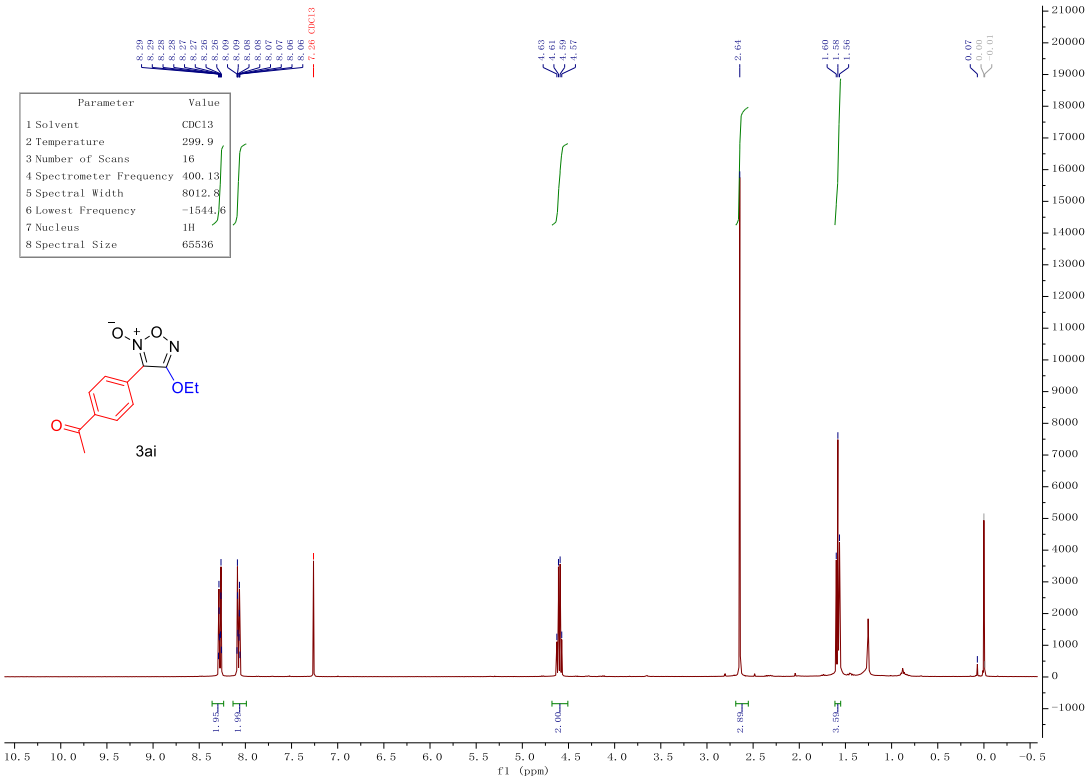

Parameter Value
1 Solvent CDCl3
2 Temperature 291.8
3 Number of Scans 137
4 Spectrometer Frequency 100.62
5 Spectral Width 24038.5
6 Lowest Frequency -1958.4
7 Nucleus 13C
8 Spectral Size 65536
161.99
132.14
127.54
124.78
121.52
107.16
77.37 CDCl3
77.05 CDCl3
76.73 CDCl3
67.14
14.47
OEt
Br
3af
f1 (ppm)

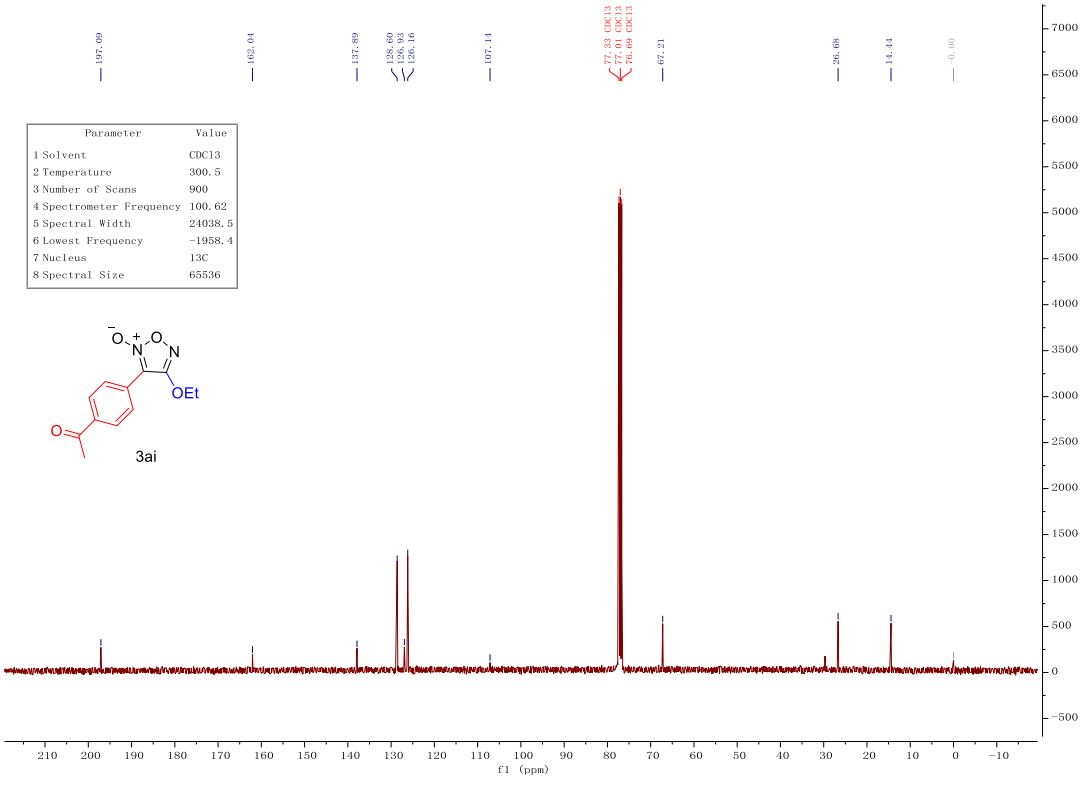

Parameter Value
1 Solvent CDCl3
2 Temperature 288.4
3 Number of Scans 16
4 Spectrometer Frequency 400.13
5 Spectral Width 8012.8
6 Lowest Frequency -1543.6
7 Nucleus 1H
8 Spectral Size 65536
OEt
Br
3ag
f1 (ppm)

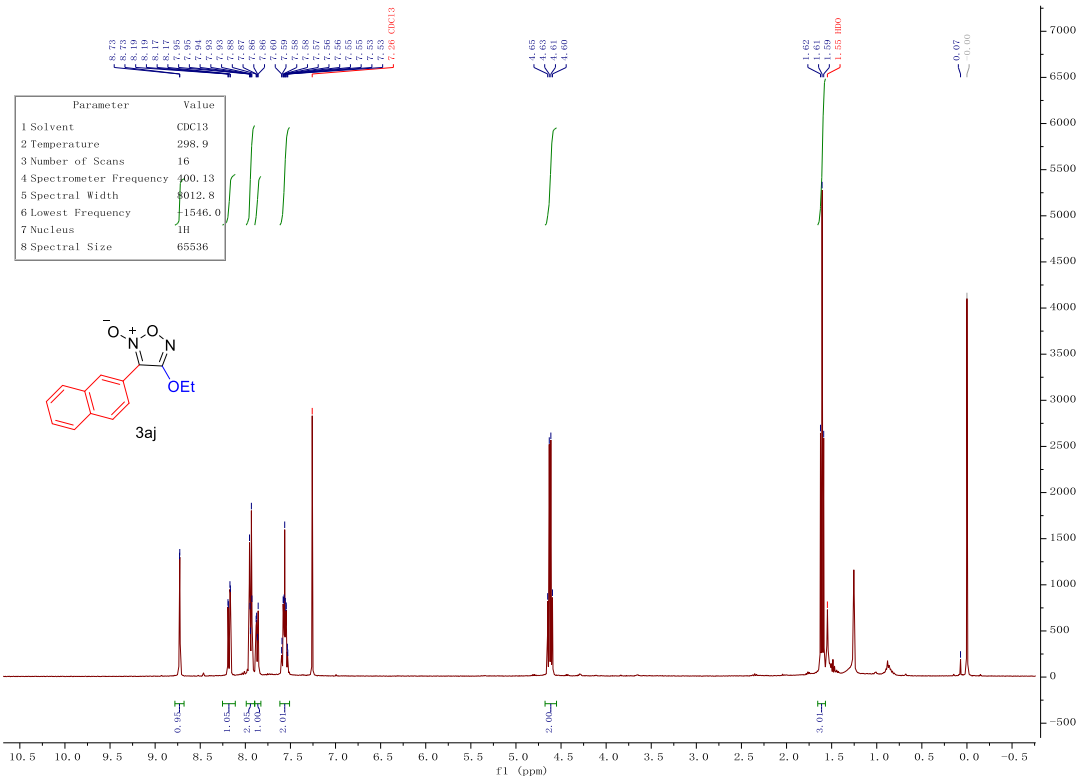

Parameter Value
1 Solvent CDCl3
2 Temperature 289.1
3 Number of Scans 287
4 Spectrometer Frequency 100.62
5 Spectral Width 24038.5
6 Lowest Frequency -1958.4
7 Nucleus 13C
8 Spectral Size 65536
OEt
Br
3ag
f1 (ppm)

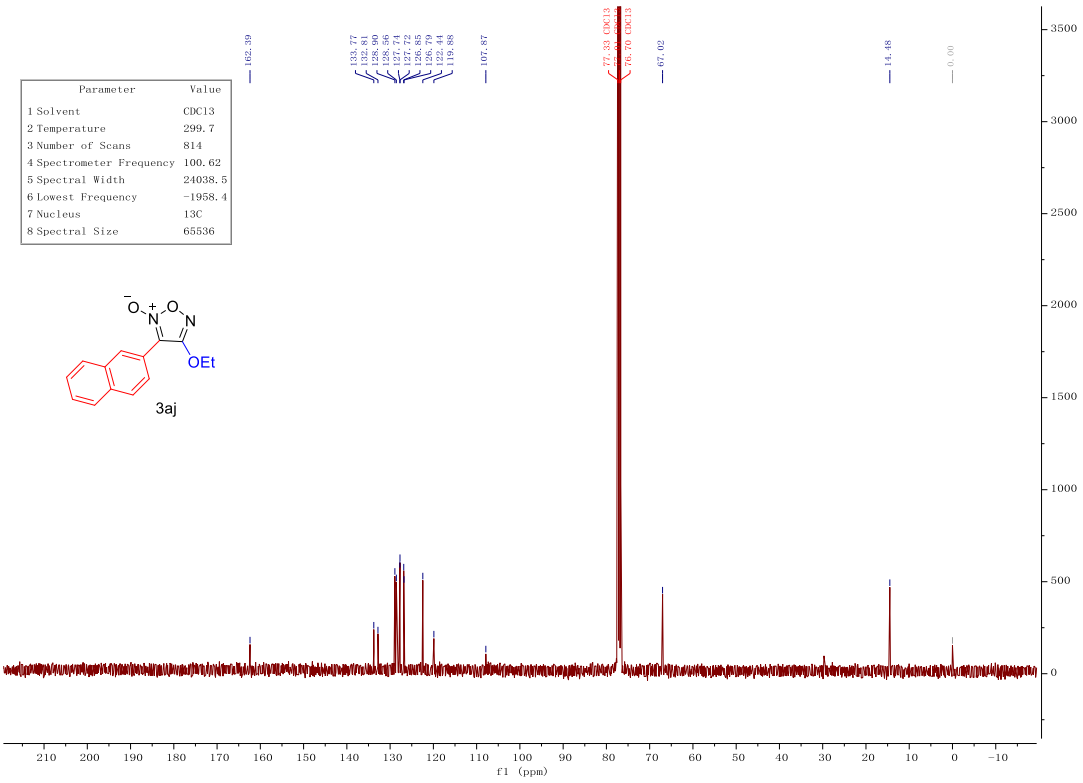

Parameter Value
1 Solvent CDCl3
2 Temperature 297.8
3 Number of Scans 16
4 Spectrometer Frequency 400.13
5 Spectral Width 8012.8
6 Lowest Frequency -1543.3
7 Nucleus 1H
8 Spectral Size 65536
OEt
O
3ah
f1 (ppm)

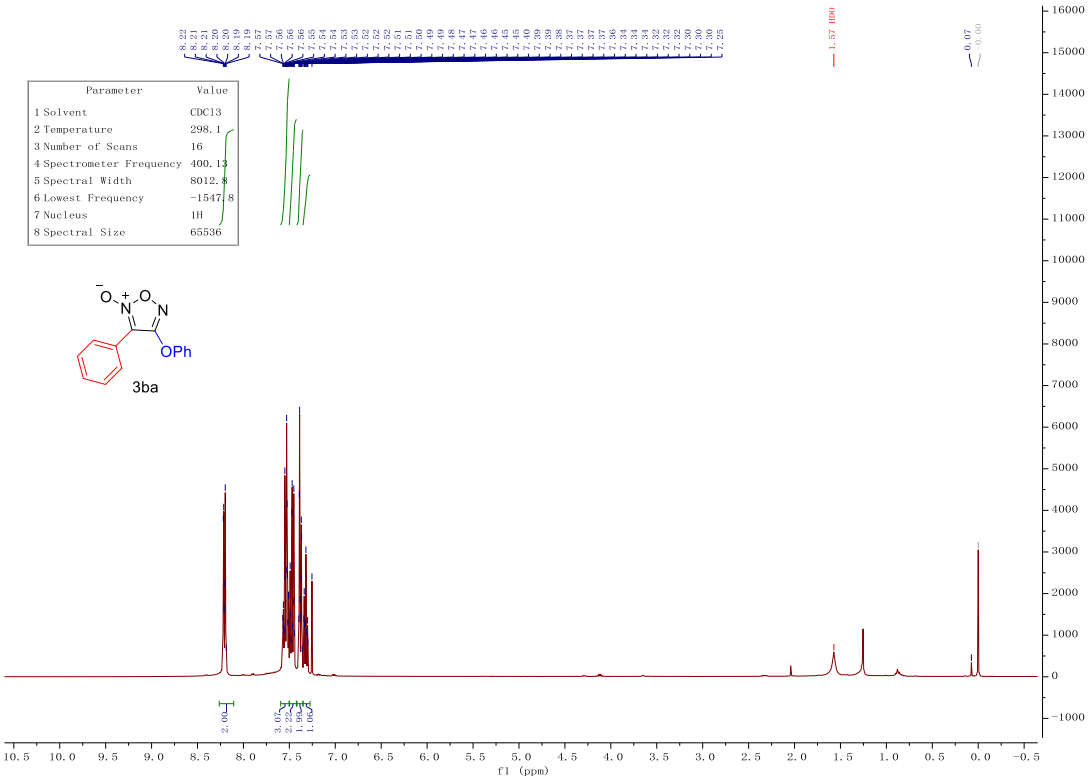

Parameter Value
1 Solvent CDCl3
2 Temperature 298.3
3 Number of Scans 341
4 Spectrometer Frequency 100.62
5 Spectral Width 24038.5
6 Lowest Frequency -1958.4
7 Nucleus 13C
8 Spectral Size 65536
OEt
O
3ah
f1 (ppm)

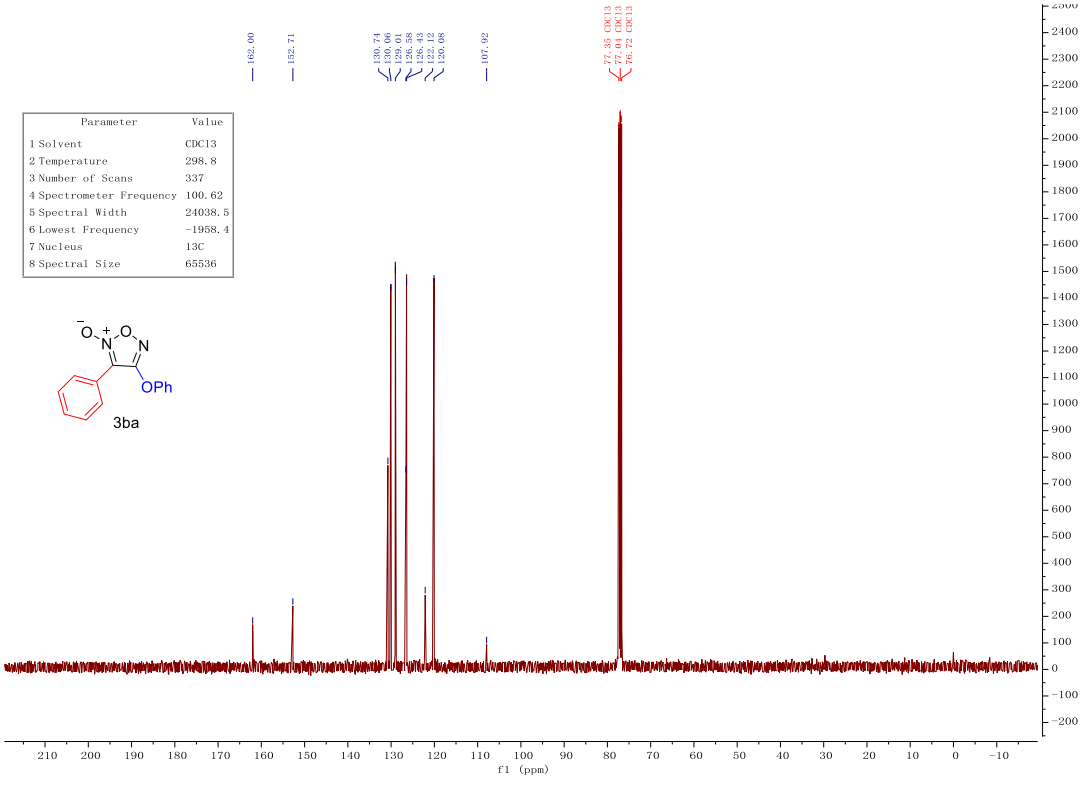

Parameter Value
1 Solvent CDCl3
2 Temperature 299.9
3 Number of Scans 16
4 Spectrometer Frequency 400.13
5 Spectral Width 8012.8
6 Lowest Frequency -1544.6
7 Nucleus 1H
8 Spectral Size 65536
OEt
O
3ai
f1 (ppm)

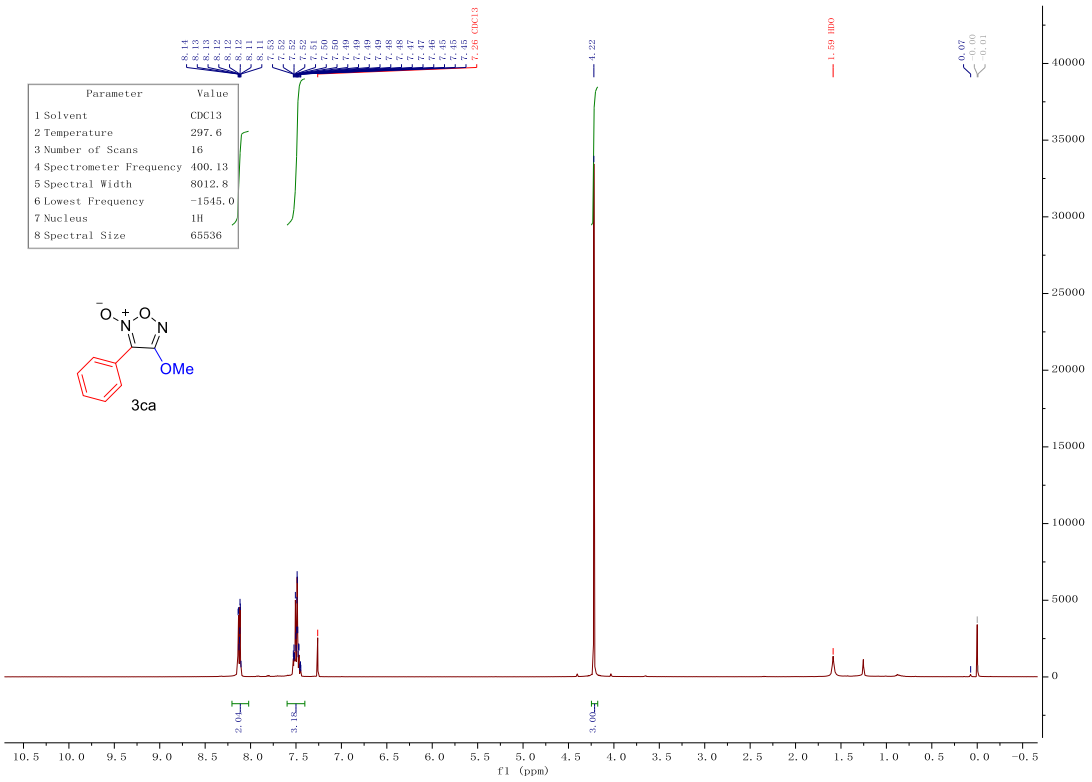

Parameter Value
1 Solvent CDCl3
2 Temperature 300.5
3 Number of Scans 900
4 Spectrometer Frequency 100.62
5 Spectral Width 24038.5
6 Lowest Frequency -1958.4
7 Nucleus 13C
8 Spectral Size 65536
OEt
O
3ai
f1 (ppm)

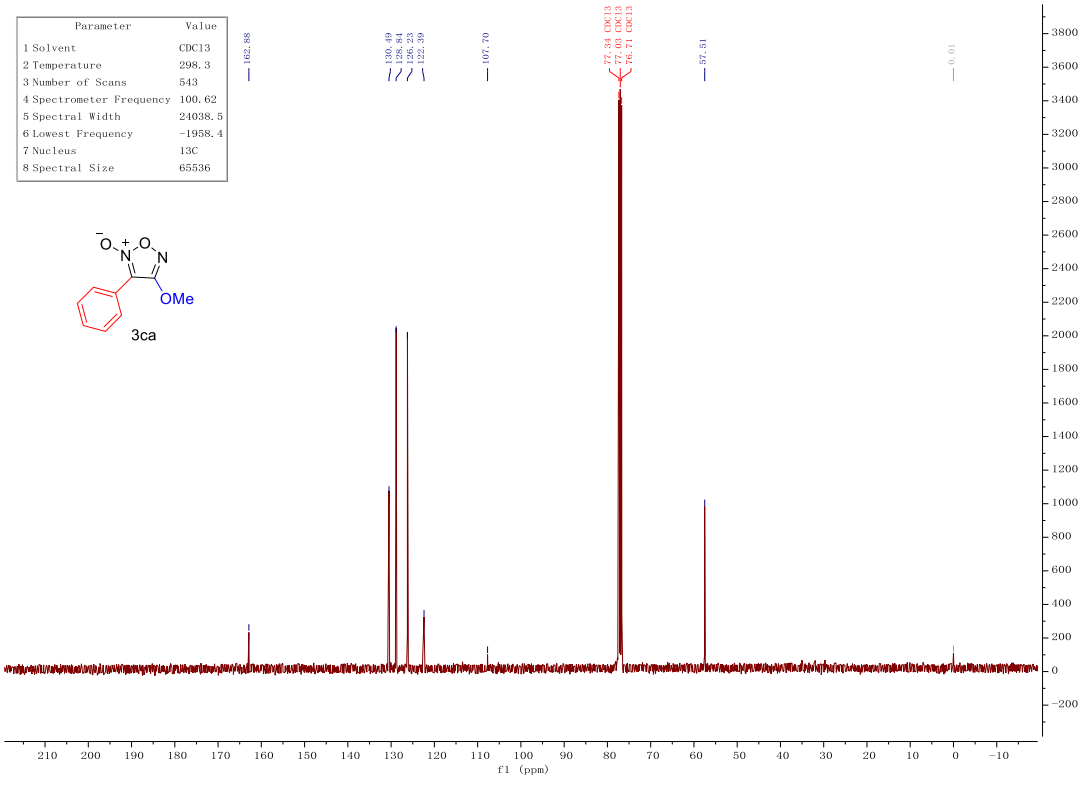

Parameter Value
1 Solvent CDCl3
2 Temperature 298.9
3 Number of Scans 16
4 Spectrometer Frequency 400.13
5 Spectral Width 8012.8
6 Lowest Frequency -1546.0
7 Nucleus 1H
8 Spectral Size 65536
OEt
3aj
f1 (ppm)

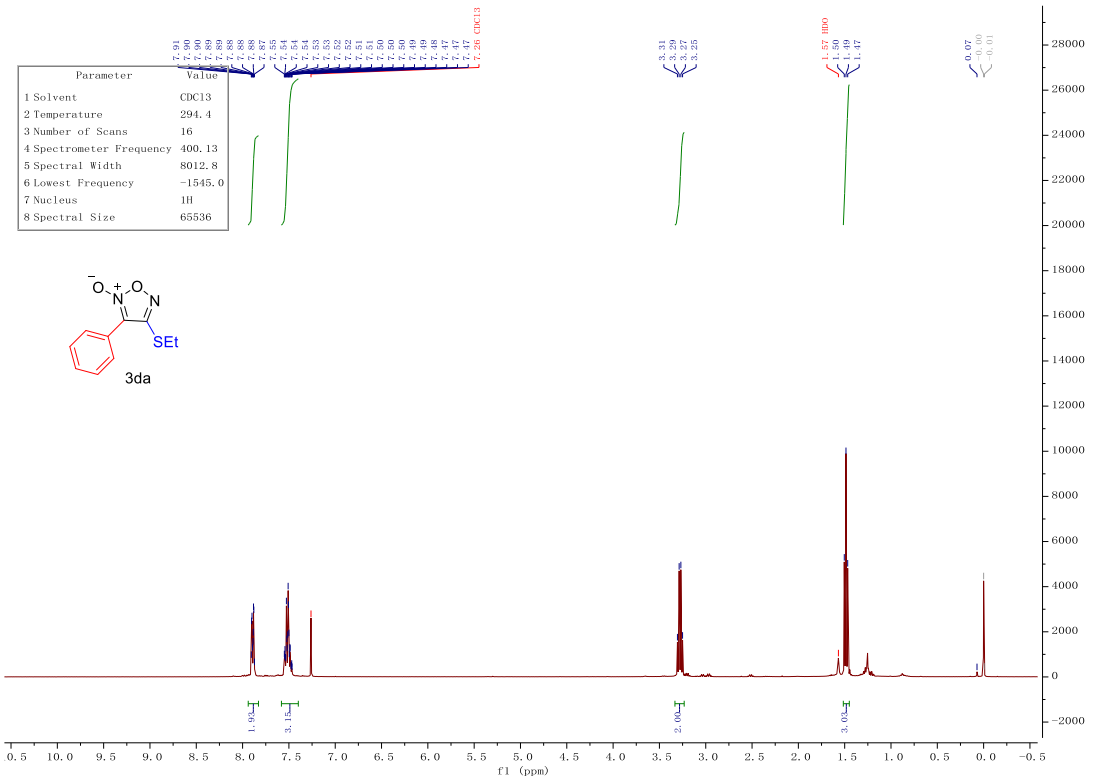

Parameter Value
1 Solvent CDCl3
2 Temperature 299.7
3 Number of Scans 814
4 Spectrometer Frequency 100.62
5 Spectral Width 24038.5
6 Lowest Frequency -1958.4
7 Nucleus 13C
8 Spectral Size 65536
OEt
3aj
f1 (ppm)

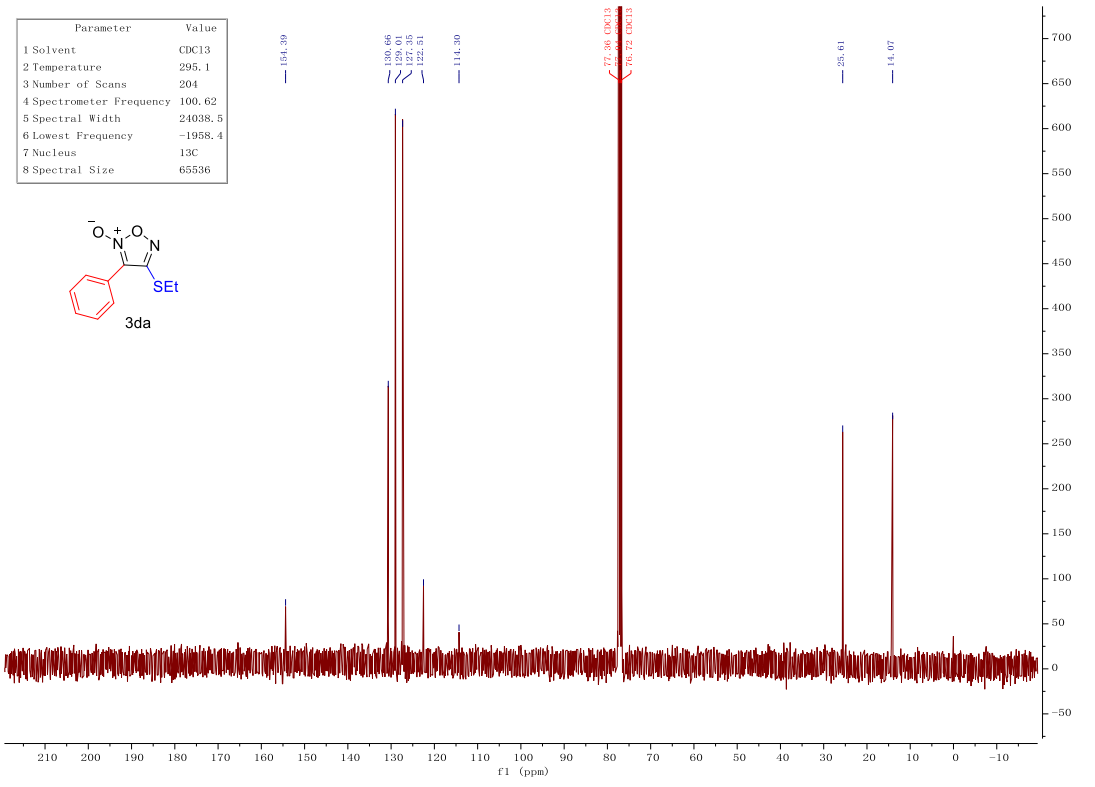

Parameter Value
1 Solvent CDCl3
2 Temperature 298.1
3 Number of Scans 16
4 Spectrometer Frequency 400.13
5 Spectral Width 8012.8
6 Lowest Frequency -1547.8
7 Nucleus 1H
8 Spectral Size 65536
OPh
3ba
f1 (ppm)


Parameter Value
1 Solvent CDCl3
2 Temperature 298.8
3 Number of Scans 337
4 Spectrometer Frequency 100.62
5 Spectral Width 24038.5
6 Lowest Frequency -1958.4
7 Nucleus 13C
8 Spectral Size 65536
OPh
3ba
f1 (ppm)


Parameter Value
1 Solvent CDCl3
2 Temperature 297.6
3 Number of Scans 16
4 Spectrometer Frequency 400.13
5 Spectral Width 8012.8
6 Lowest Frequency -1545.0
7 Nucleus 1H
8 Spectral Size 65536
OMe
3ca
f1 (ppm)


Parameter Value
1 Solvent CDCl3
2 Temperature 298.3
3 Number of Scans 543
4 Spectrometer Frequency 100.62
5 Spectral Width 24038.5
6 Lowest Frequency -1958.4
7 Nucleus 13C
8 Spectral Size 65536
OMe
3ca
f1 (ppm)


Parameter Value
1 Solvent CDCl3
2 Temperature 294.4
3 Number of Scans 16
4 Spectrometer Frequency 400.13
5 Spectral Width 8012.8
6 Lowest Frequency -1545.0
7 Nucleus 1H
8 Spectral Size 65536
SEt
3da
f1 (ppm)


Parameter Value
1 Solvent CDCl3
2 Temperature 295.1
3 Number of Scans 204
4 Spectrometer Frequency 100.62
5 Spectral Width 24038.5
6 Lowest Frequency -1958.4
7 Nucleus 13C
8 Spectral Size 65536
SEt
3da
f1 (ppm)