Radical-Radical Cross-Coupling for C-S Bond Formation

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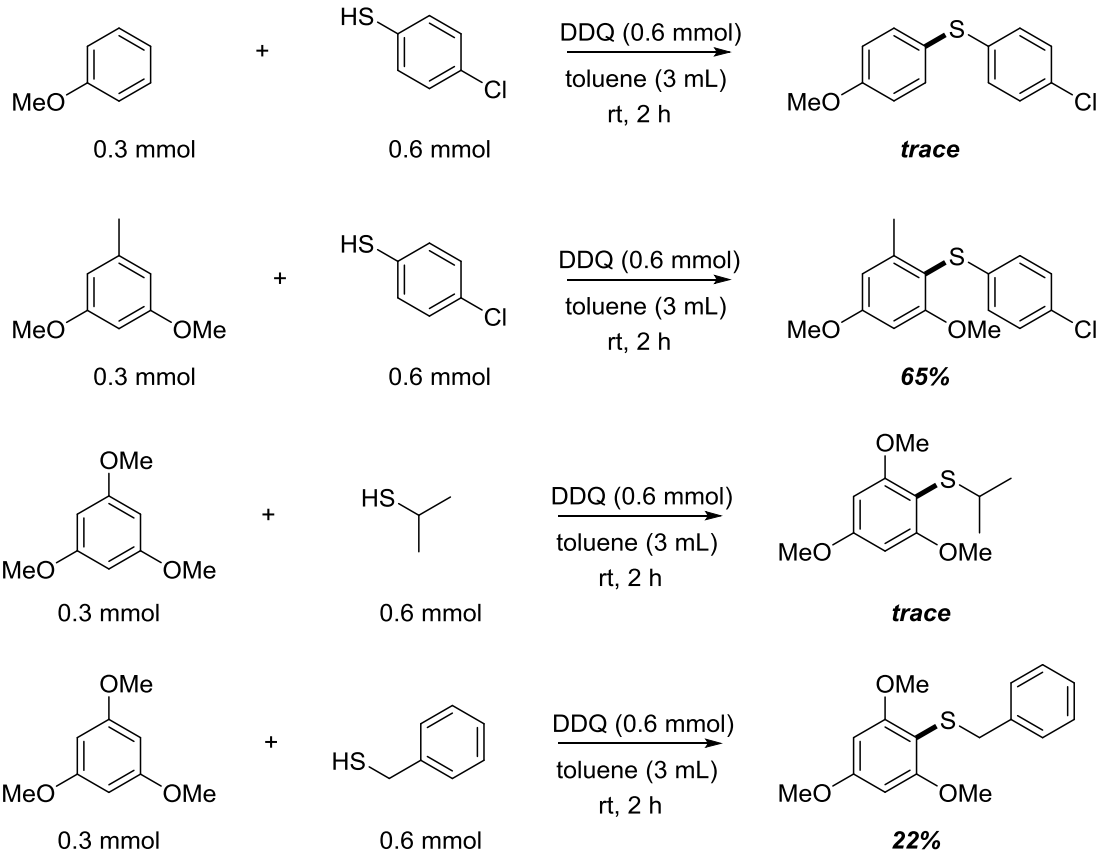
1. General Considerations

All manipulations were carried out using standard Schlenk Techniques. All glassware was oven dried at 120 ^{o}C for more than 1 hour prior to use. Toluene and CH_3CN was dried and distilled from 4Å molecular sieves under nitrogen. Unless otherwise noted, analytical grade solvents and commercially available reagents were used as received. Thin layer chromatography (TLC) employed glass 0.25 mm silica gel plates. Flash chromatography columns were packed with 200-300 mesh silica gel in petroleum (bp. 60-90 ^{o}C). Gradient flash chromatography was conducted eluting with a continuous gradient from petroleum to the indicated solvent, which are listed below as volume/volume ratios. All new compounds were characterized by ^{1}H NMR, ^{13}C NMR and HRMS. The known compounds were characterized by ^{1}H NMR, ^{13}C NMR. The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker-BioSpin spectrometers at 400 MHz (^{1}H NMR), 100 MHz (^{13}C NMR). The chemical shifts (δ) were given in part per million relative to internal tetramethylsilane (0 ppm for ^{1}H) and $CDCl_3$ (77.00 ppm for ^{13}C). High resolution mass spectra (HRMS) were measured with a Waters Micromass GCT instrument and accurate masses were reported for the molecular ion ($[M+H]^+$). GC yields were recorded with a Varian GC 3900 gas chromatography instrument with a FID detector.

2. General Procedure for Oxidative C-H/S-H cross-coupling between electron-rich arene and thiol.

In an oven dried Schlenk tube equipped with a stir-bar, electron-rich arene (0.3 mmol) and DDQ (0.6 mmol) were combined. The reaction tube was allowed to be vacuumed and purged with nitrogen for three times. Then, toluene (1 mL) was added by syringe under nitrogen. After that, 2 mL of toluene solution of thiol (0.6 mmol) was added to the mixture by constant-flow pump in 10 min. Finally, the Schlenk tube was allowed to stir at room temperature for 2 h. After completion of the reaction, the reaction mixture was quenched by water and extracted with ethyl ether (3 x 10 mL). The organic layers were combined and dried over sodium sulfate. The pure product was

obtained by flash chromatography on silica gel with petroleum ether/ethyl acetate (60/1).



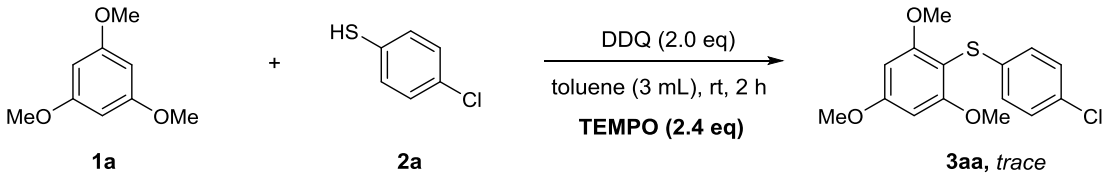
Besides the substrates in Scheme 2 of the manuscript, some other electron-rich arenes and alkylthiols were also tested for this transformation. As shown above, when anisole or 1,3-dimethoxy-5-methylbenzene was employed as the substrate to react with 4-chlorobenzenethiol, the corresponding product could be obtained in trace amount or 65% yield. Propane-2-thiol could react with 1, 3, 5-trimethoxybenzene to afford the corresponding product in trace amount, while phenylmethanethiol could give 22% yield.

3. The Procedure for Controlled Experiments.

Radical inhibition experiment

In an oven dried Schlenk tube equipped with a stir-bar, 1, 3, 5-trimethoxybenzene **1a** (0.3 mmol), DDQ (0.6 mmol) and TEMPO (0.72 mmol) were combined. The reaction

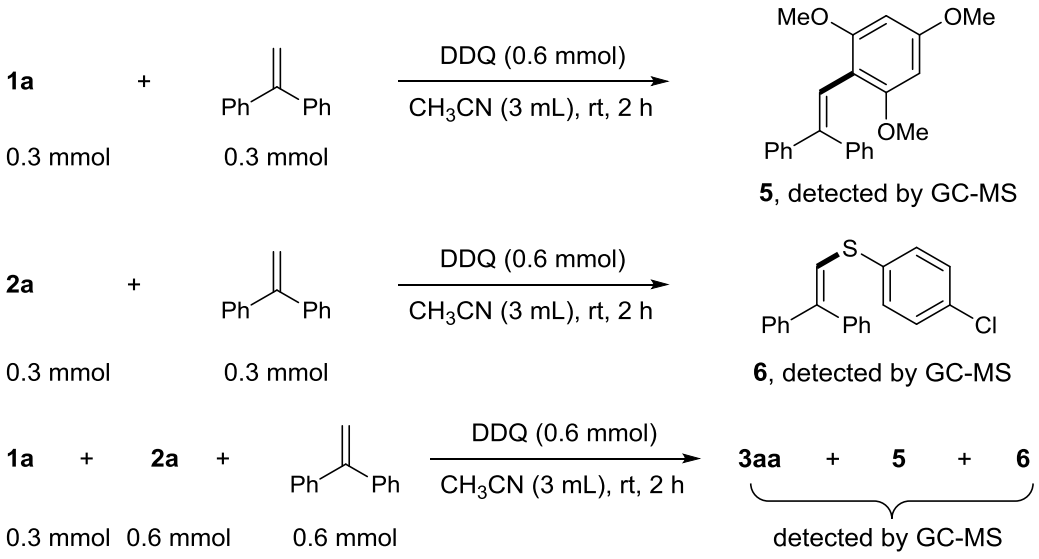
tube was allowed to be vacuumed and purged with nitrogen for three times. Then, toluene (1 mL) was added by syringe under nitrogen. After that, 2 mL of toluene solution of 4-chlorobenzenethiol **2a** (0.6 mmol) was added to the mixture by constant-flow pump in 10 min. Finally, the Schlenk tube was allowed to stir at room temperature for 2 h. After completion of the reaction, the reaction mixture was quenched by water and biphenyl was then added. GC yield was recorded with a Varian GC 2000 gas chromatography.

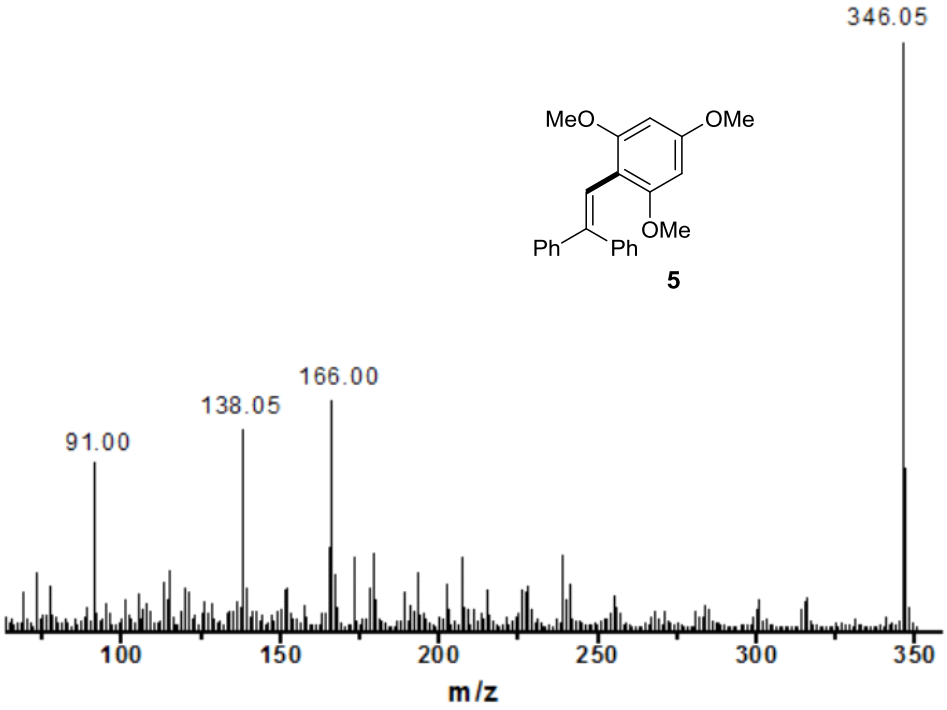


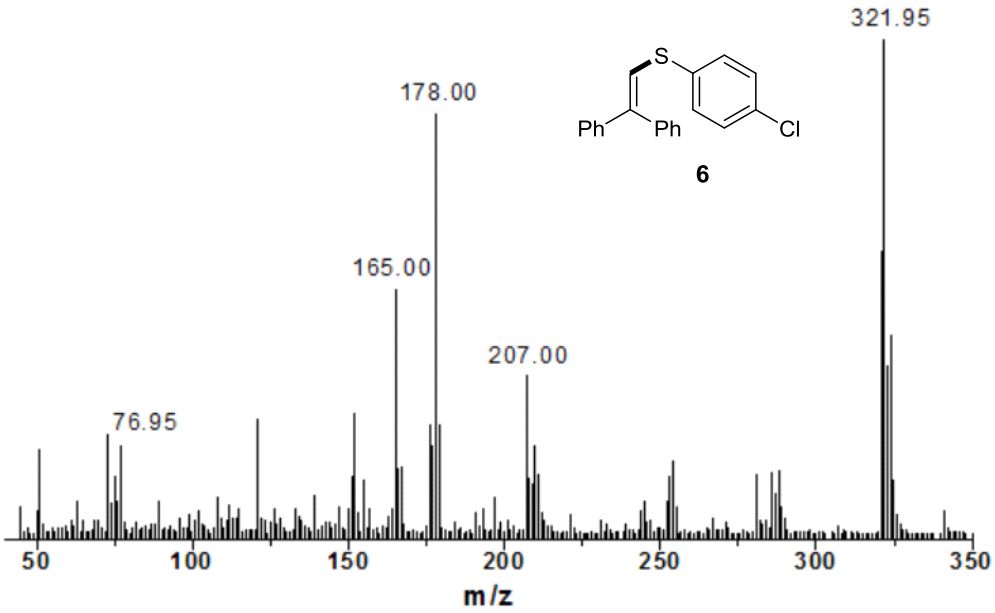
1a **2a** **3aa,** *trace*

Radical trapping experiments

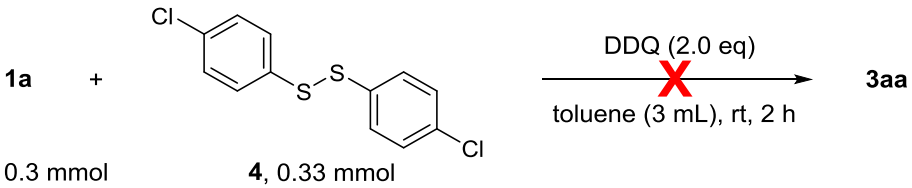
In an oven dried Schlenk tube equipped with a stir-bar, 1, 3, 5-trimethoxybenzene **1a** or 4-chlorobenzenethiol **2a** or both were combined with DDQ. The reaction tube was allowed to be vacuumed and purged with nitrogen for three times. Then, 1,1-diphenylethylene and toluene (3 mL) were added by syringe under nitrogen. Finally, the Schlenk tube was allowed to stir at room temperature for 2 h. After completion of the reaction, it was quenched by water. The reaction mixture was recorded with Shimadzu GCMS-QP2010.







Reaction of 1a and bis(4-chlorophenyl) disulfide 4 under standard conditions



In an oven dried Schlenk tube equipped with a stir-bar, 1, 3, 5-trimethoxybenzene **1a**

(0.3 mmol), DDQ (0.6 mmol) were combined. The reaction tube was allowed to be vacuumed and purged with nitrogen for three times. Then, toluene (1 mL) was added by syringe under nitrogen. After that, 2 mL of toluene solution of **4** (0.6 mmol) was added to the mixture by constant-flow pump in 10 min. Finally, the Schlenk tube was allowed to stir at room temperature for 2 h. After completion of the reaction, the reaction mixture was quenched by water and biphenyl was then added. GC yield was recorded with a Varian GC 2000 gas chromatography.

4. General Computational Calculation Details

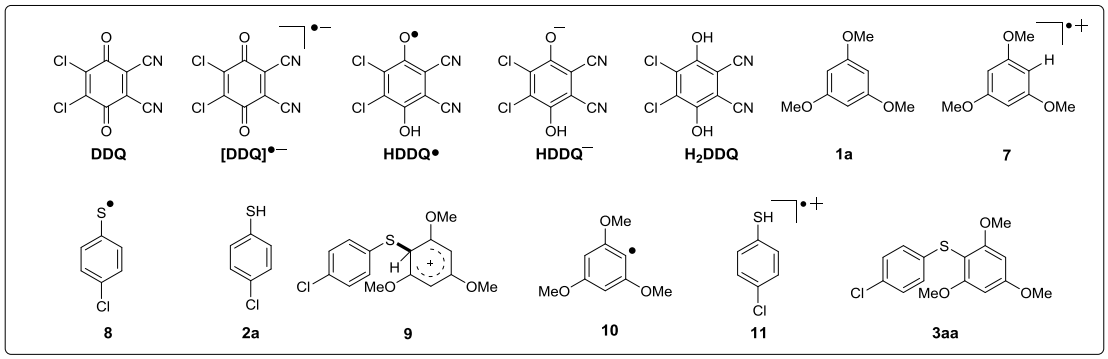
Complete Reference for Gaussian 09

Gaussian 09, Revision D.01, Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, Jr., J. A.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, N. J.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, Ö.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. Gaussian, Inc., Wallingford CT, **2013**.

Absolute Calculation Energies, Enthalpies, and Free Energies

All the DFT calculations were carried out with the GAUSSIAN 09 series of programs. DFT method B3-LYP[1] with a standard 6-31G(d) basis set was used for geometry optimizations. Harmonic frequency calculations were performed for all stationary points to confirm them as a local minima or transition structures and to

derive the thermochemical corrections for the enthalpies and free energies. M06 functional,[2] which could give more accurate energy information, is used to calculate single point energies. Solvent effects were considered by single point calculations on the gas-phase stationary points with a SMD continuum solvation model.[3] The larger basis set 6-311+G(d,p) is used in the solvation single point calculations. The energies given in this work are the M06 calculated Gibbs free energies in acetonitrile solvent.

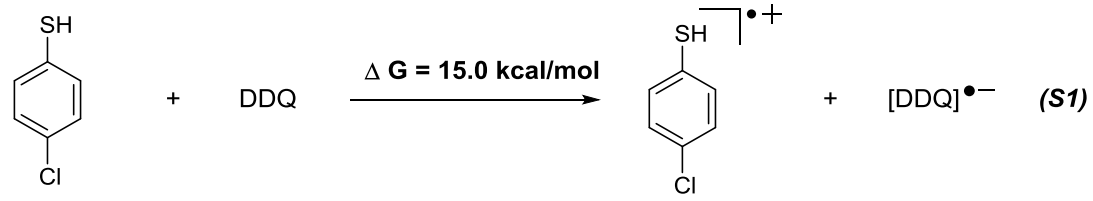


Geometry	$E_{(elec\text{-}B3LYP)}$[a]	$G_{(corr\text{-}B3LYP)}$[b]	$H_{(corr\text{-}B3LYP)}$[c]	$E_{(solv,\ M06)}$[d]	IF[e]
DDQ	-1485.075304	0.022546	0.076025	-1484.909075	-
[DDQ]•-	-1485.203033	0.021561	0.074827	-1485.101208	-
HDDQ•	-1485.683527	0.033808	0.087381	-1485.531512	-
HDDQ-	-1485.804010	0.034296	0.087283	-1485.723771	-
H_2DDQ	-1486.319839	0.047168	0.100326	-1486.176958	-
1a	-575.8080921	0.161423	0.212271	-575.611819	-
7	-575.5443935	0.160005	0.211977	-575.3995032	-
8	-1089.394768	0.048558	0.088945	-1089.274993	-
2a	-1090.017441	0.057656	0.097438	-1089.902183	-
9	-1664.998349	0.231405	0.305277	-1664.734791	-
10	-575.1159527	0.147244	0.199316	-574.9221967	-
11	-1089.727870	0.057728	0.098864	-1089.685196	-
3aa	-1664.620884	0.219641	0.292019	-1664.30877	-

[a]The electronic energy calculated by B3LYP in gas phase. [b]The thermal correction to Gibbs free energy calculated by B3LYP in gas phase. [c]The thermal correction to enthalpy calculated by B3LYP in gas phase. [d]The electronic energy calculated by M06 in acetonitrile solvent. [e]The B3LYP calculated imaginary frequencies for the transition

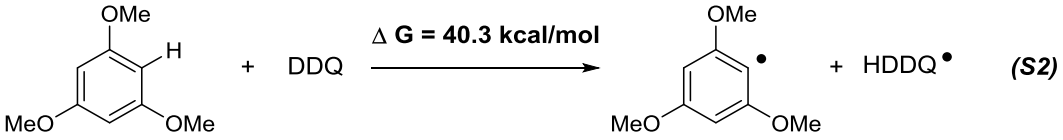
states.

The electron transfer pathway for the formation of thiyl radical:



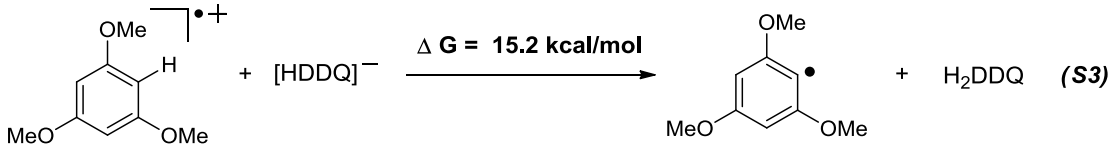
(S1)

The hydrogen atom transfer (HAT) pathway for the formation of 1,3,5-trimethoxy phenyl radical:

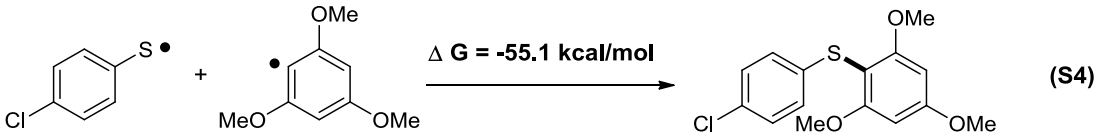


(S2)

The pathway which involves the deprotonation process before radical-radical cross-coupling:

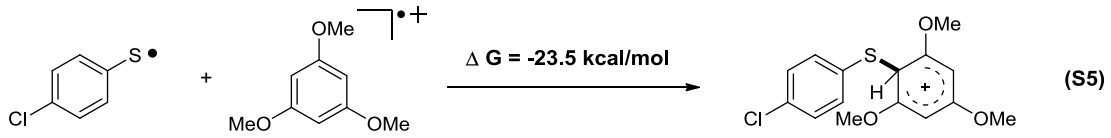


(S3)



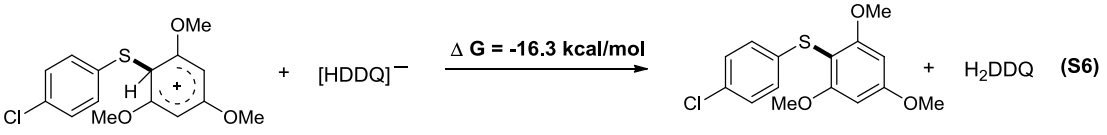
(S4)

The radical-radical cross-coupling pathway for C-S bond formation:



(S5)

The deprotonation step after radical-radical combination:



(S6)

Optimized geometries for all the compounds and transition states

DDQ

C	1.15595600	-0.67790900	0.00001900
C	-0.11973000	-1.45940500	0.00008900
C	-1.40507100	-0.67983200	0.00000600
C	-1.40507100	0.67983200	0.00000100
C	-0.11972800	1.45940500	0.00009700
C	1.15595700	0.67790900	-0.00002800
Cl	2.59372400	1.61712000	-0.00013700
Cl	2.59372100	-1.61712100	-0.00002400
C	-2.60811800	1.44714300	-0.00005400
C	-2.60812000	-1.44714000	-0.00006500
N	-3.58934300	2.07062800	-0.00011900
N	-3.58934700	-2.07062300	-0.00012300
O	-0.13826100	2.67320700	0.00032500
O	-0.13826300	-2.67321100	0.00018100

[DDQ]•-

C	1.10690600	-0.68259500	-0.00001300
C	-0.13522300	-1.48274900	-0.00002900
C	-1.36555900	-0.70084400	-0.00001600
C	-1.36555900	0.70084400	-0.00001900
C	-0.13522400	1.48274900	-0.00002800
C	1.10690500	0.68259500	-0.00001100
Cl	2.58799100	1.60678500	0.00000900
Cl	2.58799100	-1.60678500	0.00000100
C	-2.58646100	1.43792000	-0.00000800
C	-2.58646100	-1.43792000	0.00000200
N	-3.58871200	2.03277300	0.00000800
N	-3.58871200	-2.03277400	0.00001800
O	-0.12410500	2.72576800	0.00002300
O	-0.12410500	-2.72576800	0.00002200

HDDQ•

C	-1.13312100	-0.71315300	0.00032500
C	-1.09802500	0.66675700	0.00016300
C	0.15449200	1.34741300	-0.00016900
C	1.37149400	0.61540400	0.00011200
C	1.36200800	-0.78166400	0.00031200
C	0.09949800	-1.52541400	-0.00013100

O	0.07488200	-2.76243900	-0.00173600
Cl	-2.61248600	-1.57901600	0.00039300
Cl	-2.53580700	1.62918800	0.00014600
C	2.57298100	-1.52566700	0.00057600
C	2.57571000	1.38409900	-0.00037700
N	3.57470600	-2.11882100	0.00058300
N	3.48401700	2.11246200	0.00034700
O	0.13025300	2.68037800	-0.00077100
H	1.03861600	3.04145200	-0.00047700

HDDQ-

C	0.09883000	-1.57079700	-0.00025800
C	-1.10023200	-0.71346900	0.00004800
C	-1.06036700	0.67077100	-0.00002100
C	0.16990300	1.36456100	-0.00007500
C	1.35036100	0.61365200	-0.00008600
C	1.33708900	-0.81021000	-0.00008100
O	0.03818800	-2.81240500	-0.00051300
Cl	-2.52667800	1.64054800	-0.00004000
Cl	-2.62583700	-1.56086500	0.00030700
C	2.56456100	1.36394500	0.00015600
C	2.56150600	-1.52835300	-0.00008200
N	3.48569800	2.08115500	0.00021400
N	3.58041900	-2.09911500	0.00030500
O	0.15238600	2.73573100	-0.00023700
H	1.07545000	3.04389100	0.00020900

H_2DDQ

C	-0.13069200	-1.41894100	0.00008800
C	1.07649900	-0.69901500	0.00003900
C	1.07651800	0.69902800	0.00000800
C	-0.13068700	1.41894300	0.00016900
C	-1.34344700	0.70695200	0.00009800
C	-1.34345100	-0.70694400	0.00000700
O	-0.19215200	2.76472500	0.00053800
H	0.70781600	3.13549400	-0.00011200
O	-0.19214500	-2.76472100	0.00031100
H	0.70782500	-3.13548500	-0.00048800
Cl	2.56726400	1.60272000	-0.00019500
Cl	2.56726600	-1.60272300	-0.00006700
C	-2.57233900	1.43618700	0.00006200
C	-2.57233900	-1.43618000	-0.00023000

N	-3.57062700	2.03188000	-0.00044300
N	-3.57060700	-2.03190400	-0.00001000

1a

C	-0.55966000	-1.29141700	-0.00004700
C	0.82085000	-1.12283000	-0.00011200
C	1.39814800	0.16117800	-0.00003700
C	0.56196500	1.27245300	-0.00002300
C	-0.83865800	1.13035800	0.00002300
C	-1.38301200	-0.14945000	0.00002300
H	-1.03349500	-2.26424900	0.00001500
H	2.47757100	0.23721500	-0.00011400
H	-1.44410300	2.02718700	0.00017100
O	1.00462300	2.56459100	0.00010300
O	1.71876100	-2.15204300	-0.00008600
O	-2.72330500	-0.41239100	-0.00000900
C	-3.62016000	0.68546600	-0.00001900
H	-3.49336100	1.31032200	-0.89403400
H	-4.62300400	0.25367500	-0.00025000
H	-3.49363900	1.31002200	0.89423800
C	2.40385400	2.79186500	-0.00000900
H	2.88123900	2.36980100	-0.89429200
H	2.53181500	3.87620800	0.00017700
H	2.88149300	2.36944500	0.89398200
C	1.21644000	-3.47762300	0.00012400
H	0.61216200	-3.68049300	-0.89400300
H	2.09187600	-4.13012400	0.00017000
H	0.61221600	-3.68026700	0.89432700

7

C	-1.18230900	0.81705300	-0.00023800
C	-1.51648200	-0.52466700	0.00013800
C	-0.47333700	-1.49424400	0.00029400
C	0.90900100	-1.09141200	0.00006500
C	1.25292300	0.25202000	-0.00006900
C	0.19960800	1.19576300	-0.00020900
H	-1.91723600	1.61148800	-0.00033800
H	-0.71578900	-2.55161600	0.00051400
H	2.28447600	0.57217300	-0.00042200
O	1.74956800	-2.11669200	0.00005400
O	-2.74696300	-1.03800900	0.00035800
O	0.38390400	2.50169700	-0.00044000

C	1.70714300	3.08199200	0.00051400
H	2.24908600	2.78317600	-0.90093900
H	1.54214600	4.15777300	0.00118100
H	2.24828200	2.78174600	0.90198700
C	3.17069400	-1.88296800	-0.00024800
H	3.46242900	-1.33302300	0.90015600
H	3.62434200	-2.87239800	-0.00008200
H	3.46215400	-1.33345200	-0.90097300
C	-3.87454200	-0.14652800	-0.00021200
H	-3.86771400	0.47827300	-0.89982100
H	-4.75212000	-0.79089700	-0.00032300
H	-3.86831600	0.47874400	0.89907300

8

C	0.65939400	-1.22249400	0.00000800
C	-0.72723200	-1.21833100	-0.00001300
C	-1.45954100	-0.00000900	0.00003300
C	-0.72722300	1.21832500	-0.00000200
C	0.65938800	1.22248900	0.00000000
C	1.34445300	-0.00001300	0.00003800
H	1.21502000	-2.15401300	-0.00000200
H	-1.27526700	-2.15475700	-0.00002000
H	-1.27528200	2.15473800	-0.00001500
H	1.21504600	2.15398700	-0.00001500
Cl	3.09184800	0.00000700	-0.00001100
S	-3.18352300	0.00000800	-0.00000900

9

C	-2.78239100	-1.30724100	-0.19949800
C	-1.46298900	-1.02433700	-0.47792900
C	-1.96828100	1.43609700	-0.36165200
C	-3.27734900	1.13928600	-0.09439300
C	-3.67422400	-0.22485800	0.01089000
H	-3.14524200	-2.32440300	-0.17951400
H	-4.04750100	1.89267600	0.00524500
C	-0.92338200	0.36555100	-0.39104900
H	-0.18933100	0.55611600	-1.17575300
S	0.05233700	0.49505800	1.25310100
C	1.73408100	0.25878700	0.71465500
C	2.44790700	1.32336100	0.14089000
C	2.37225500	-0.97028400	0.93853600
C	3.78045800	1.15635800	-0.22361100
H	1.96144700	2.28193400	-0.01127400

C	3.71065100	-1.13813100	0.59049900
H	1.82533300	-1.78871900	1.39469200
C	4.40364400	-0.07529300	0.00507400
H	4.33969000	1.97309900	-0.66684800
H	4.21487300	-2.08163400	0.76883000
Cl	6.07522900	-0.28426100	-0.44176200
O	-0.53644900	-1.90606000	-0.80050500
O	-1.46251500	2.63910800	-0.56402200
O	-4.95457800	-0.38737700	0.27958300
C	-0.85435900	-3.31181000	-0.83743300
H	0.07075400	-3.80643700	-1.12843900
H	-1.17114700	-3.65354900	0.15241500
H	-1.63272200	-3.50411400	-1.58172200
C	-2.31502400	3.79788800	-0.46396200
H	-2.73386000	3.87044300	0.54391500
H	-1.66650300	4.64903200	-0.66414400
H	-3.11238300	3.74682200	-1.21127500
C	-5.53995800	-1.70013400	0.40895400
H	-5.05685000	-2.25389000	1.21860100
H	-6.58544900	-1.51862900	0.65218000
H	-5.46529800	-2.24406100	-0.53684900

10

C	0.33132500	-1.34285900	0.00000100
C	1.35517100	-0.39075700	-0.00010500
C	0.98207600	0.94942300	-0.00014000
C	-0.31891000	1.39684900	-0.00000700
C	-1.35280500	0.43472800	-0.00000300
C	-1.01222800	-0.91663900	0.00001100
H	0.52849700	-2.40799400	-0.00001200
H	-2.37772000	0.78463700	0.00005700
O	-0.68907500	2.70499200	-0.00018200
O	2.68787100	-0.67333700	-0.00008300
O	-1.92647700	-1.93273000	-0.00003000
C	0.37622200	3.64879800	0.00018200
H	-0.09206400	4.63494000	0.00091600
H	1.00450700	3.53448000	0.89267900
H	1.00411800	3.53563800	-0.89274100
C	-3.30281200	-1.59458900	0.00006700
H	-3.57747700	-1.01932600	-0.89420200
H	-3.84463100	-2.54251900	-0.00014500
H	-3.57738000	-1.01965800	0.89458500
C	3.07166500	-2.03959200	0.00011900

H	2.70609500	-2.56086200	-0.89428400
H	4.16327500	-2.04228500	0.00014900
H	2.70599300	-2.56062100	0.89461200

2a

C	-0.67771400	-1.20893300	-0.01271800
C	0.71746100	-1.21506300	-0.00471600
C	1.40226400	-0.00000500	0.00135000
C	0.71746500	1.21506100	-0.00467400
C	-0.67770400	1.20894100	-0.01262100
C	-1.38340800	0.00000200	-0.00655300
H	-1.22101300	-2.14849300	-0.02444700
H	1.26697200	-2.15041800	-0.00613800
H	1.26699400	2.15040600	-0.00604000
H	-1.22102000	2.14849100	-0.02421100
S	-3.18567100	0.00008400	-0.07070800
H	-3.40960100	-0.00128900	1.26347600
Cl	3.15871900	-0.00000300	0.00989900

3aa

C	2.85293400	1.02119000	0.52548200
C	1.74165000	1.10220100	-0.32276100
C	1.08282100	-0.04154900	-0.79482500
C	1.56513700	-1.30896300	-0.37067800
C	2.67011600	-1.40098100	0.47384700
C	3.31199800	-0.23592000	0.91986900
H	3.30370100	1.94295100	0.87019100
H	3.05689100	-2.35281200	0.81417200
O	1.27047000	2.36025200	-0.62508100
O	0.88961700	-2.39197900	-0.82980700
O	4.37439200	-0.44324400	1.74545900
C	1.78695400	2.93252800	-1.82796300
H	1.47928200	2.35216700	-2.70519300
H	1.36676300	3.93864100	-1.89238500
H	2.88286700	2.99482800	-1.79311200
C	1.33196500	-3.68436600	-0.44430300
H	0.65155800	-4.38588600	-0.92992100
H	2.35760900	-3.87651300	-0.78475000
H	1.27987200	-3.81977800	0.64359800
C	5.07096900	0.68918500	2.24398500
H	4.41604900	1.33032000	2.84785400
H	5.87076900	0.29434300	2.87295000
H	5.50737300	1.28290200	1.43034000

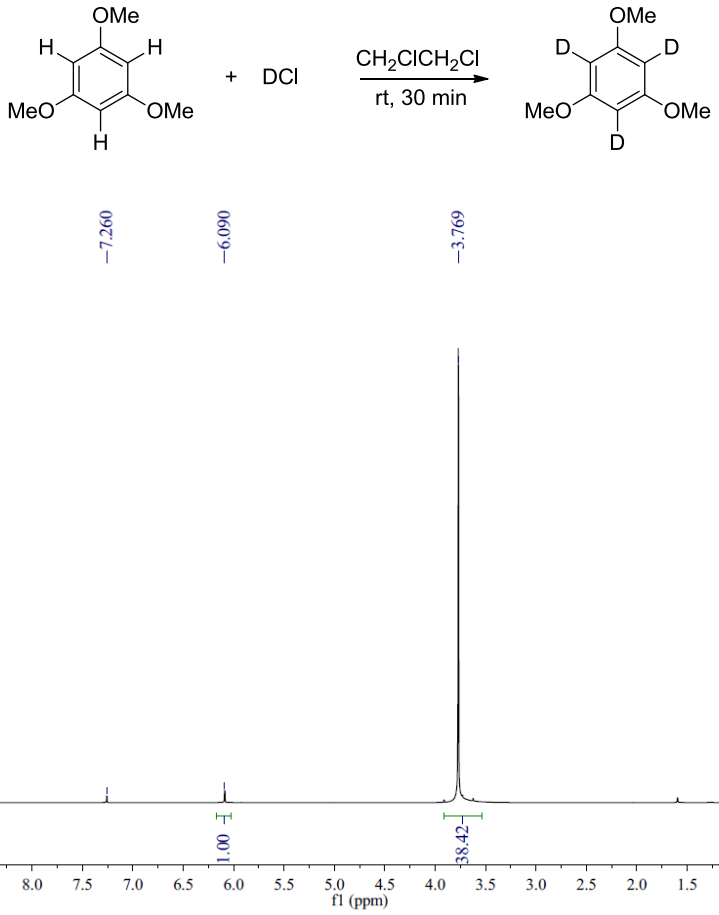
S	-0.27942300	0.07676000	-1.94581100
C	-1.71912200	0.10150000	-0.86861900
C	-2.75629300	-0.80612700	-1.11186000
C	-1.85415800	1.04477600	0.15918000
C	-3.91995000	-0.77723400	-0.34094000
H	-2.65028200	-1.54502400	-1.90026000
C	-3.00297300	1.06594800	0.94836900
H	-1.06289300	1.76677100	0.33336200
C	-4.02852800	0.15558800	0.68832100
H	-4.72481300	-1.48046200	-0.52741100
H	-3.10972600	1.79100900	1.74850900
Cl	-5.48418800	0.18773600	1.67752000

11

C	-0.67367000	-1.24221200	0.00040900
C	0.70098200	-1.23708000	0.00045900
C	1.39654700	0.00060500	0.00021500
C	0.69827500	1.23460900	0.00047000
C	-0.67633200	1.23139900	0.00051600
C	-1.38987000	-0.00769600	0.00022900
H	-1.20970600	-2.18624000	0.00063700
H	1.26052500	-2.16635700	0.00079900
H	1.25335500	2.16640000	0.00052800
H	-1.22196300	2.17035900	0.00068600
S	-3.10985200	0.08549900	-0.00049400
H	-3.36736300	-1.24114300	-0.00027300
Cl	3.10042300	0.00066200	-0.00048600

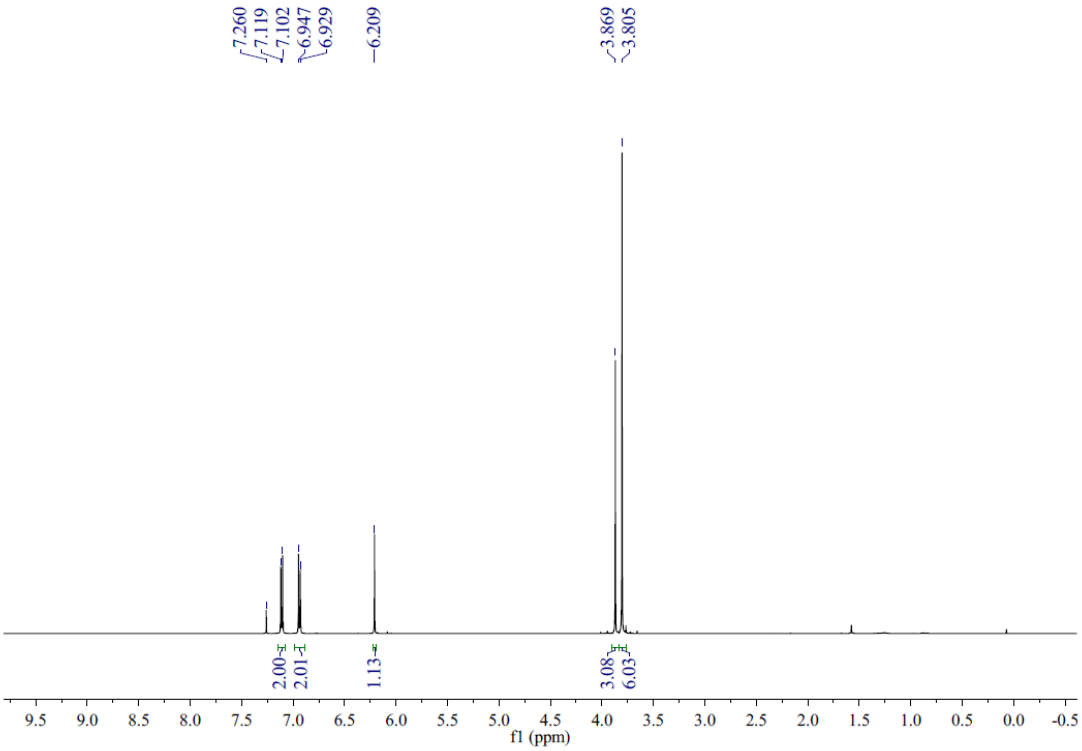
5. Kinetic Isotope Effect (KIE) experiment.

Synthesis of 1,3,5-trimethoxybenzene-d3.

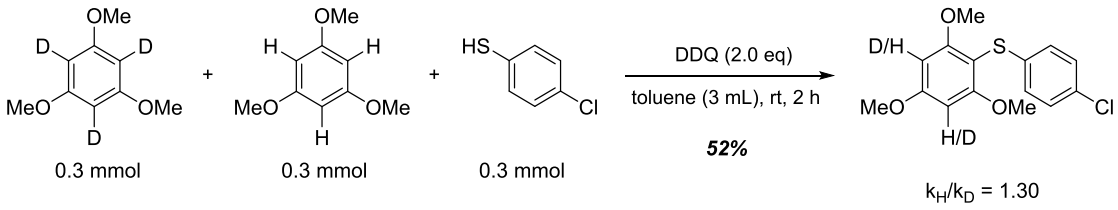


In an oven dried Schlenk tube equipped with a stir-bar, 1,3,5-trimethoxybenzene (2.0 mmol) was added. The reaction tube was allowed to be vacuumed and purged with nitrogen for three times. Then, 1,2-dichloroethane (2 mL) and deuterium chloride solution (1 mL, 35 wt. % in D_2O, 99 atom % D (Aldrich)) was added by syringe under nitrogen. Finally, the Schlenk tube was allowed to stir at room temperature for 30 min. After completion of the reaction, the reaction mixture was extracted with dichloromethane (3 x 5 mL). The organic layers were combined and dried over sodium sulfate. The desired product (92 atom % D) was obtained after removing the solvents. ^{1}H NMR spectra for the product was shown as above:

Procedure for KIE measurement.



Eq. (2)



In an oven dried Schlenk tube equipped with a stir-bar, 1,3,5-trimethoxybenzene (0.3 mmol), 1,3,5-trimethoxybenzene-d3 (0.3 mmol), and 4-chlorobenzenethiol (0.3 mmol) were combined. The reaction tube was allowed to be vacuumed and purged with nitrogen for three times. Then, toluene (3 mL) was added by syringe. After that, DDQ (0.6 mmol) was added to the mixture under nitrogen. Finally, the Schlenk tube was allowed to stir at room temperature for 2 h. After completion of the reaction, the reaction mixture was quenched by water and extracted with ethyl ether (3 x 10 mL). The organic layers were combined and dried over sodium sulfate. The pure product was obtained by flash chromatography on silica gel with petroleum ether/ethyl acetate (60/1). ^{1}H NMR spectra for the isolated product was shown as above:

6. Kinetic Studies

In an oven dried self-prepared three-necked micro reactor with a magnetic stirrer, DDQ (136.2 mg, 0.6 mmol) and 1,3,5-trimethoxybenzene (**1a**) were added. The reactor was allowed to be vacuumed and purged with nitrogen for three times. Toluene (3 mL) and 4-chlorobenzenethiol (**2a**) (86.7 mg, 0.6 mmol, in 2 mL of toluene) was added in via syringe. The mixture was allowed to stir at room temperature and monitored by React IR. After the completion of the reaction, the reaction mixture was quenched by water and diphenyl as the internal standard were added. Finally, the yield was determined by GC.

The reactions of DDQ (136.2 mg, 0.6 mmol), **2a** (86.7 mg, 0.6 mmol) and different concentrations of **1a** (0.005 M, 0.015 M, 0.03 M, 0.05 M, 0.06 M, 0.08 M, 0.12 M) give GC yields were 29%, 67%, 65%, 60%, 53%, 53% and 38%, respectively. According to the increase of IR absorption of the product vs t and its initial and final concentration, the change of concentration of the product vs t could be calculated, and then the initial rate also could be obtained. Figure S1-S2 were obtained by this method and were farther treated.

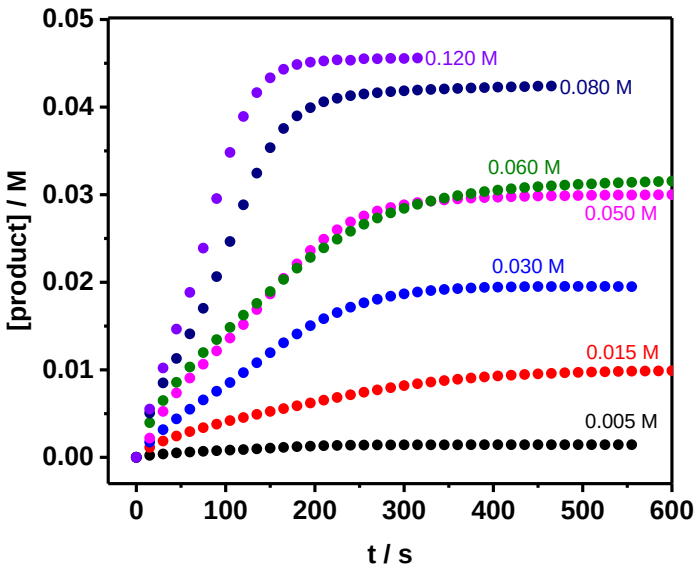


Figure S1. Kinetic profiles of the reactions with different concentrations of **1a** from 0.005 M ~ 0.12 M. DDQ (0.6 mmol, 0.12 M), **2a** (0.6 mmol, 0.12 M).

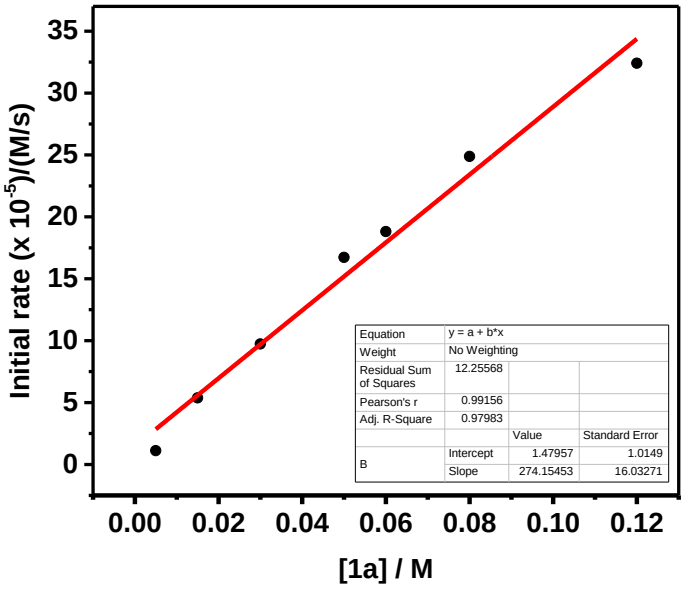
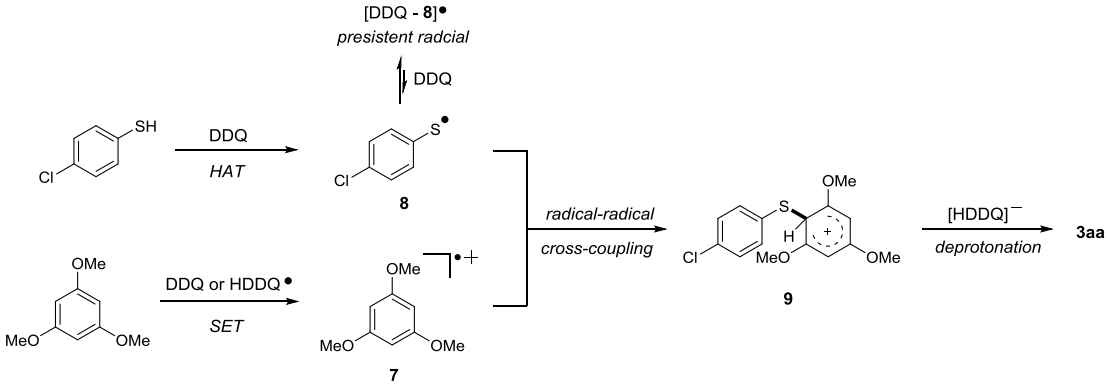


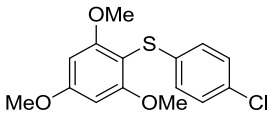
Figure S2 Kinetic plots of the reactions with different concentrations of **1a** from 0.005 M ~ 0.12 M. DDQ (0.6 mmol, 0.12 M), **2a** (0.6 mmol, 0.12 M).

7. Proposed Mechanism



Scheme S1. Proposed mechanism.

8. Analytical Data of Products.

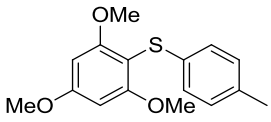


(4-Chlorophenyl)(2,4,6-trimethoxyphenyl)sulfane (3aa).[4]

Purified by column chromatography on a silica gel column using petroleum ether : ethyl acetate = 60:1 as the eluent to give the title compound as a white solid (91.4 mg, 98% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11 (d, *J* = 8.4 Hz, 2H), 6.94 (d, *J* = 8.8 Hz, 2H), 6.21 (s, 2H), 3.86 (s, 3H), 3.80 (s, 6H).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.06, 162.36, 137.29, 129.98, 128.50, 126.84, 98.03, 91.10, 56.25, 55.42.

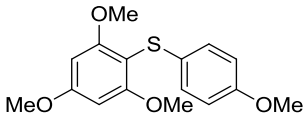


p-Tolyl(2,4,6-trimethoxyphenyl)sulfane (3ab).[4]

Purified by column chromatography on a silica gel column using petroleum ether : ethyl acetate = 60:1 as the eluent to give the title compound as a white solid (60.9 mg, 70% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.06 – 6.86 (m, 4H), 6.20 (s, 2H), 3.86 (s, 3H), 3.80 (s, 6H), 2.24 (s, 3H).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 162.70, 162.40, 134.91, 134.03, 129.22, 125.84, 99.05, 91.04, 56.23, 55.36, 20.84.

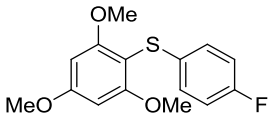


(4-Methoxyphenyl)(2,4,6-trimethoxyphenyl)sulfane (3ac).[5]

Purified by column chromatography on a silica gel column using petroleum ether : ethyl acetate = 20:1 as the eluent to give the title compound as a white solid (72.6 mg, 79% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.06 (d, *J* = 9.2 Hz, 2H), 6.73 (d, *J* = 9.2 Hz, 2H), 6.19 (s, 2H), 3.84 (s, 3H), 3.81 (s, 6H), 3.73 (s, 3H).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 162.48, 162.17, 157.38, 129.06, 128.35, 114.12, 100.22, 91.00, 56.16, 55.31, 55.17.

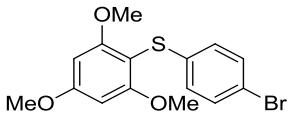


(4-Fluorophenyl)(2,4,6-trimethoxyphenyl)sulfane (3ad).[4]

Purified by column chromatography on a silica gel column using petroleum ether : ethyl acetate = 60:1 as the eluent to give the title compound as a light yellow solid (68.9 mg, 78% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.09 - 6.96 (m, 2H), 6.94 - 6.80 (m, 2H), 6.21 (d, J = 2.0 Hz, 2H), 3.86 (d, J = 2.0 Hz, 3H), 3.81 (d, J = 2.0 Hz, 6H).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 162.85, 162.26, 160.64 (d, *J* = 241 Hz), 133.47 (d, *J* = 3.1 Hz), 127.66 (d, *J* = 7.8 Hz), 115.43 (d, *J* = 22.0 Hz), 99.04, 91.06, 56.20, 55.37.

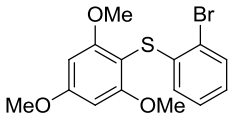


(4-Bromophenyl)(2,4,6-trimethoxyphenyl)sulfane (3ae).[4]

Purified by column chromatography on a silica gel column using petroleum ether : ethyl acetate = 60:1 as the eluent to give the title compound as a white solid (101.2 mg, 95% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.16 (m, 2H), 6.95 – 6.79 (m, 2H), 6.21 (s, 2H), 3.87 (s, 3H), 3.80 (s, 6H).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.06, 162.31, 137.99, 131.34, 127.08, 117.70, 97.77, 91.06, 56.22, 55.40.

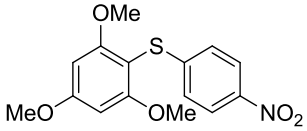


(2-Bromophenyl)(2,4,6-trimethoxyphenyl)sulfane (3af).[4]

Purified by column chromatography on a silica gel column using petroleum ether : ethyl acetate = 60:1 as the eluent to give the title compound as a white solid (93.8 mg, 88% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, *J* = 8.0 Hz, 1H), 7.02 (t, *J* = 7.6 Hz, 1H), 6.88 (t, *J* = 7.6 Hz, 1H), 6.51 (d, *J* = 8.0 Hz, 1H), 6.23 (s, 2H), 3.87 (s, 3H), 3.78 (s, 6H).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.28, 162.52, 139.67, 132.37, 127.16, 125.28, 125.10, 119.97, 97.44, 91.08, 56.21, 55.40.



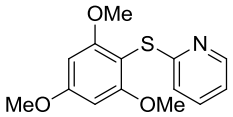
(4-Nitrophenyl)(2,4,6-trimethoxyphenyl)sulfane (3ag).[4]

Purified by column chromatography on a silica gel column using petroleum ether :

ethyl acetate = 20:1 as the eluent to give the title compound as a light yellow solid (88.7 mg, 92% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, *J* = 8.8 Hz, 2H), 7.05 (d, *J* = 8.8 Hz, 2H), 6.25 (s, 2H), 3.90 (s, 3H), 3.81 (s, 6H).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.71, 162.31, 149.39, 144.49, 124.71, 123.61, 95.77, 91.20, 56.21, 55.45.



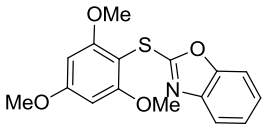
2-((2,4,6-Trimethoxyphenyl)thio)pyridine (3ah).

Purified by column chromatography on a silica gel column using petroleum ether : ethyl acetate = 60:1 as the eluent to give the title compound as a white solid (73.2 mg, 88% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (dd, *J* = 4.8, 0.9 Hz, 1H), 7.36 (td, *J* = 8.0, 1.8 Hz, 1H), 6.96-6.86 (m, 1H), 6.72 (d, *J* = 8.0 Hz, 1H), 6.23 (s, 2H), 3.88 (s, 3H), 3.80 (s, 6H).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.08, 162.22, 161.67, 149.12, 136.05, 119.22, 118.82, 97.44, 91.12, 56.18, 55.38.

HRMS (ESI) calcd for $C_{14}H_{15}NO_3S$ $[M+H]^+$: 278.0851; found: 278.0844.



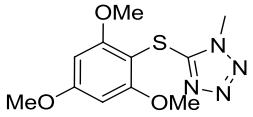
2-((2,4,6-Trimethoxyphenyl)thio)benzo[d]oxazole (3ai).

Purified by column chromatography on a silica gel column using petroleum ether : ethyl acetate = 20:1 as the eluent to give the title compound as a yellow solid (77.1 mg, 81% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 – 7.48 (m, 1H), 7.36 (d, *J* = 7.5 Hz, 1H), 7.25 – 7.11 (m, 2H), 6.22 (s, 2H), 3.86 (s, 3H), 3.81 (s, 6H).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 164.37, 163.67, 161.92, 151.72, 142.29, 123.85, 123.33, 118.51, 109.68, 93.59, 91.24, 56.21, 55.39.

HRMS (ESI) calcd for $C_{16}H_{15}NO_4S$ $[M+H]^+$: 318.0800; found: 318.0793.



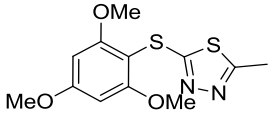
1-Methyl-5-((2,4,6-trimethoxyphenyl)thio)-1H-tetrazole (3aj).

Purified by column chromatography on a silica gel column using petroleum ether : ethyl acetate = 20:1 as the eluent to give the title compound as a white solid (46.6 mg, 55% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.18 (s, 2H), 3.97 (s, 3H), 3.88-3.74 (m, 9H).

$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 163.66, 161.53, 153.61, 92.90, 91.22, 56.13, 55.39, 33.61.

HRMS (ESI) calcd for $C_{11}H_{14}N_4O_3S$ $[M+H]^+$: 283.0865; found: 283.0858.



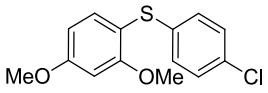
2-Methyl-5-((2,4,6-trimethoxyphenyl)thio)-1,3,4-thiadiazole (3ak).

Purified by column chromatography on a silica gel column using petroleum ether : ethyl acetate = 20:1 as the eluent to give the title compound as a white solid (70.7 mg, 79% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.19 (s, 2H), 3.88 (s, 3H), 3.84 (s, 6H), 2.60 (s, 3H).

$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 170.97, 164.41, 163.99, 161.90, 97.74, 91.04, 56.17, 55.43, 15.51.

HRMS (ESI) calcd for $C_{12}H_{14}N_2O_3S_2$ $[M+H]^+$: 299.0524; found: 299.0517.



(4-Chlorophenyl)(2,4-dimethoxyphenyl)sulfane (3al).

Purified by column chromatography on a silica gel column using petroleum ether : ethyl acetate = 60:1 as the eluent to give the title compound as a light yellow solid (59.8 mg, 71% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (d, *J* = 8.2 Hz, 1H), 7.16 (d, *J* = 8.6 Hz, 2H), 7.02 (d, *J* = 8.6 Hz, 2H), 6.57-6.46 (m, 2H), 3.83 (s, 3H), 3.79 (s, 3H).

$^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 162.13, 160.42, 137.06, 136.61, 130.99, 128.74, 128.50, 111.22, 105.34, 99.28, 55.89, 55.45.

HRMS (ESI) calcd for $C_{14}H_{13}ClO_2S$ $[M+H]^+$: 281.0403; found: 281.0318.

9. References

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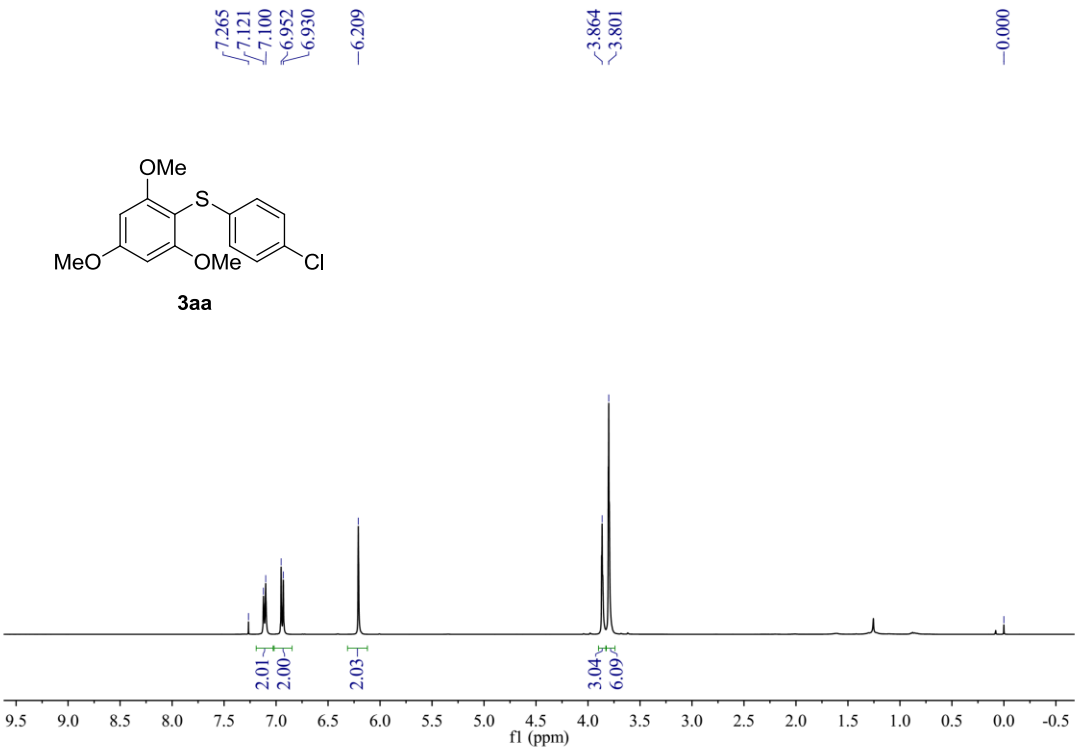
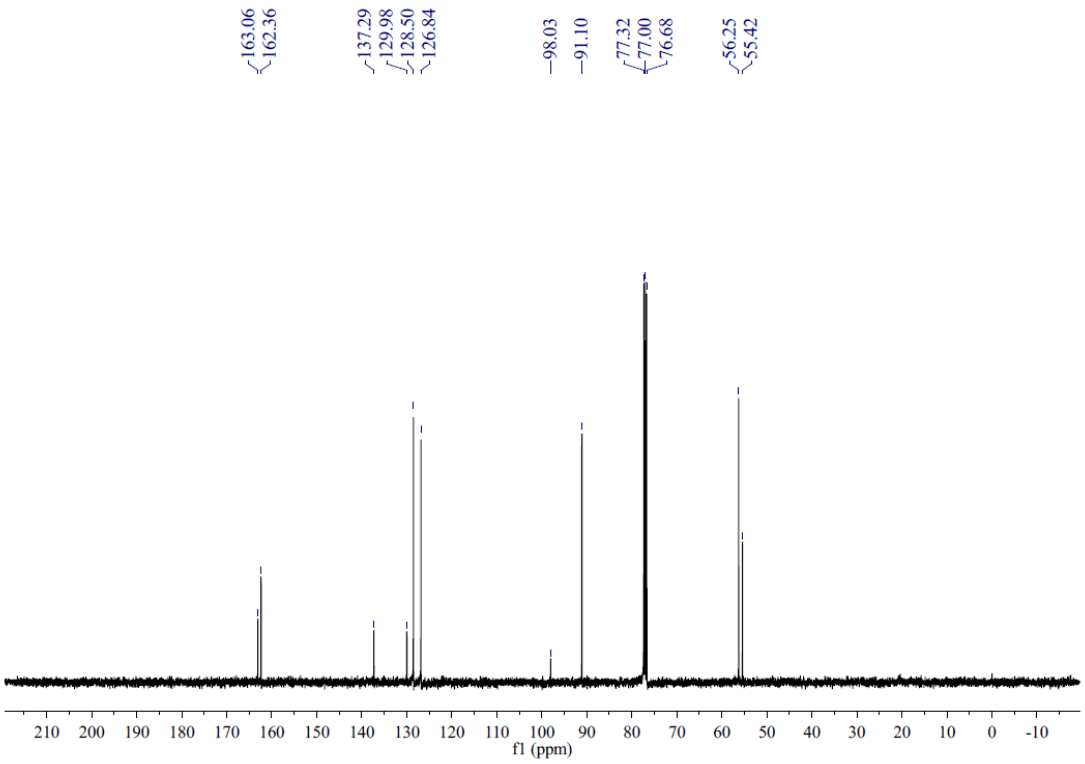


^{1}H NMR



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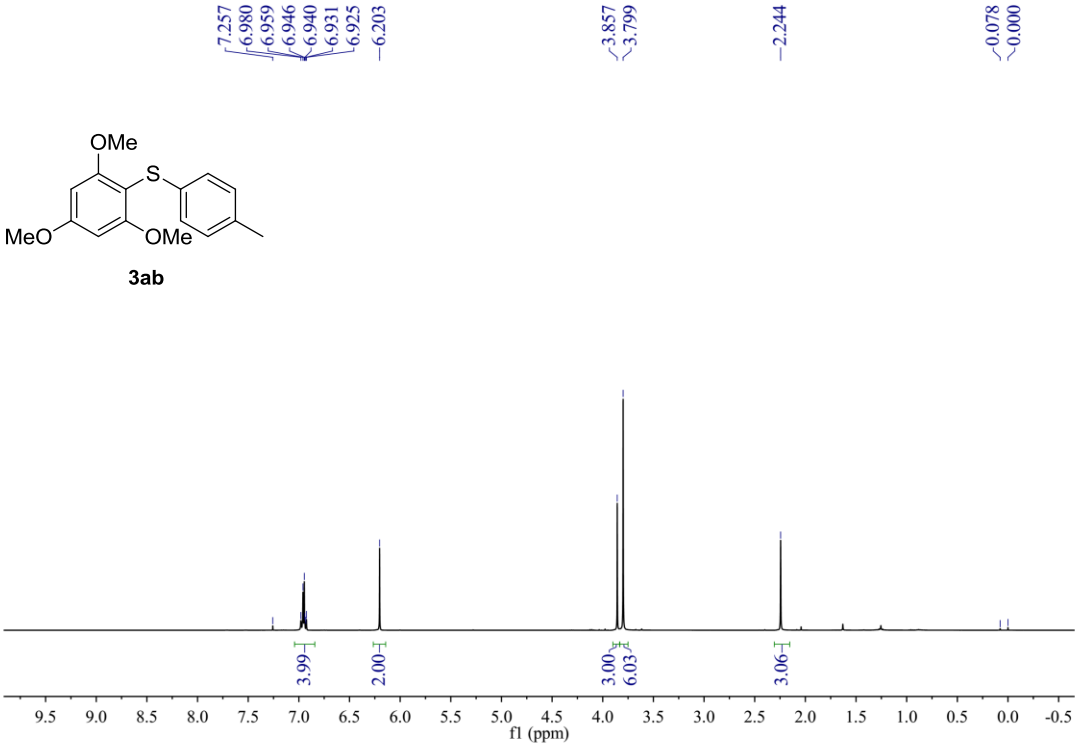

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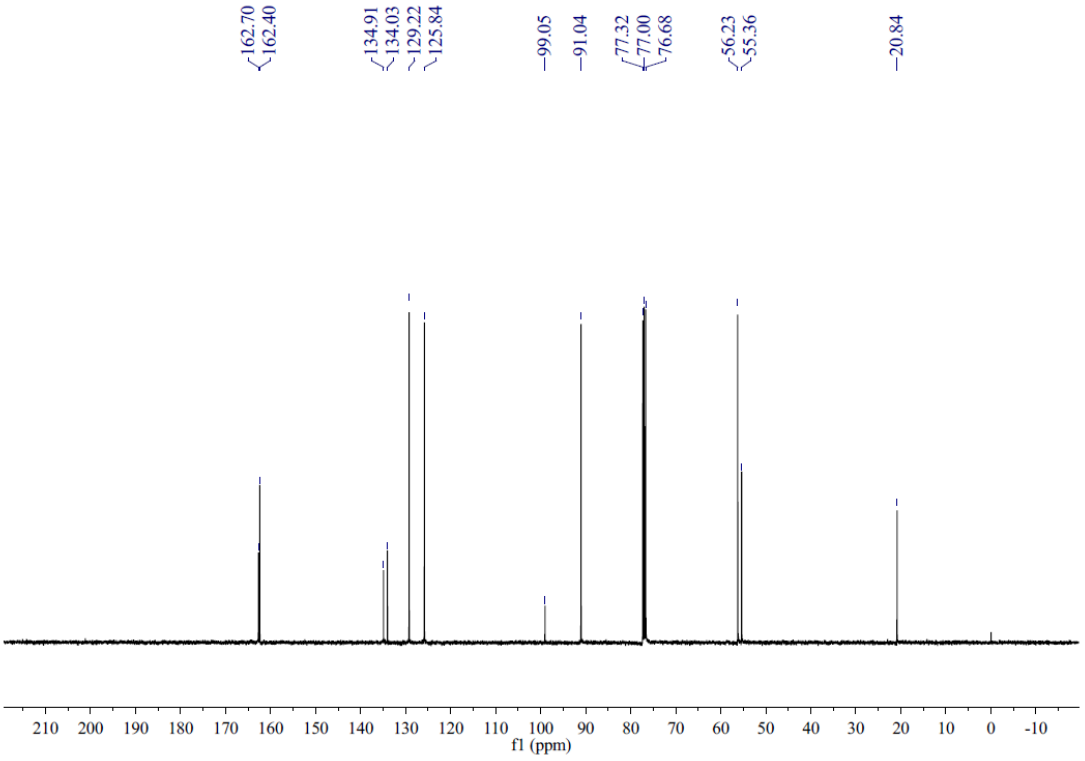

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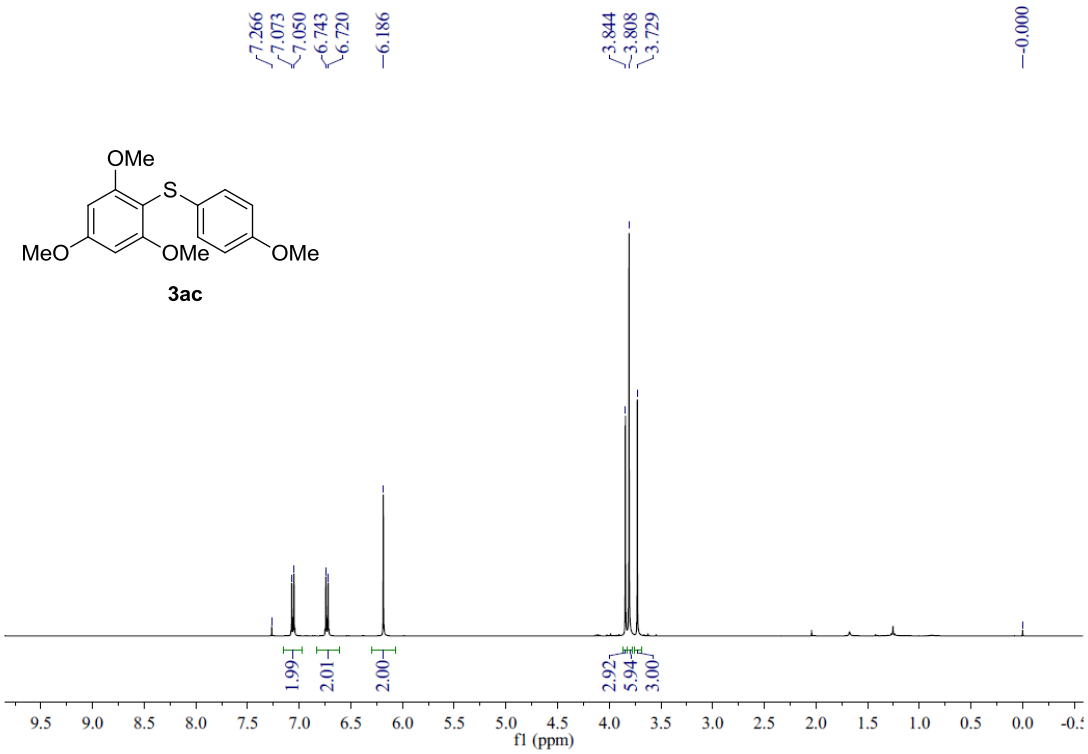

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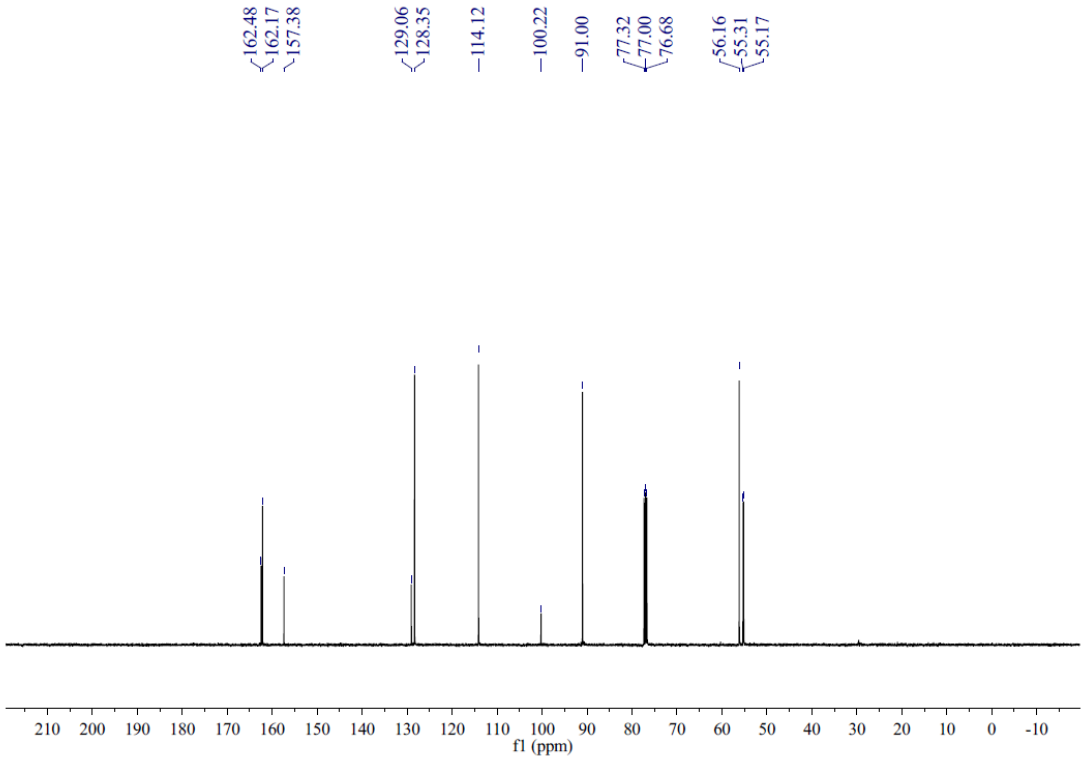

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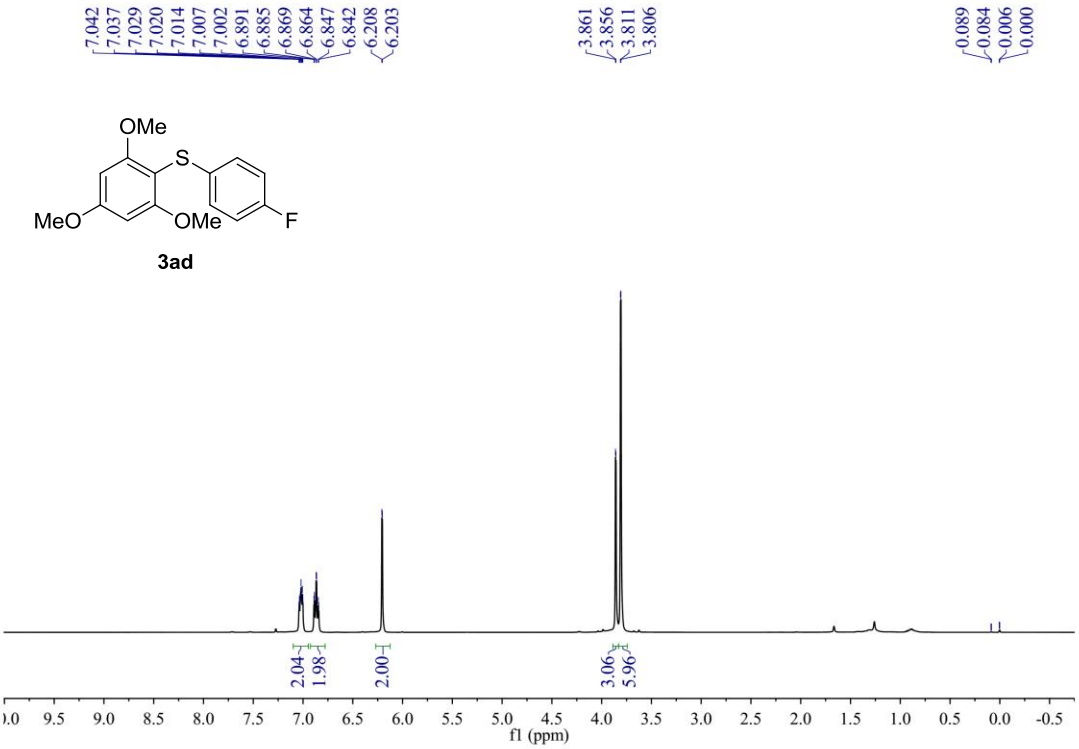

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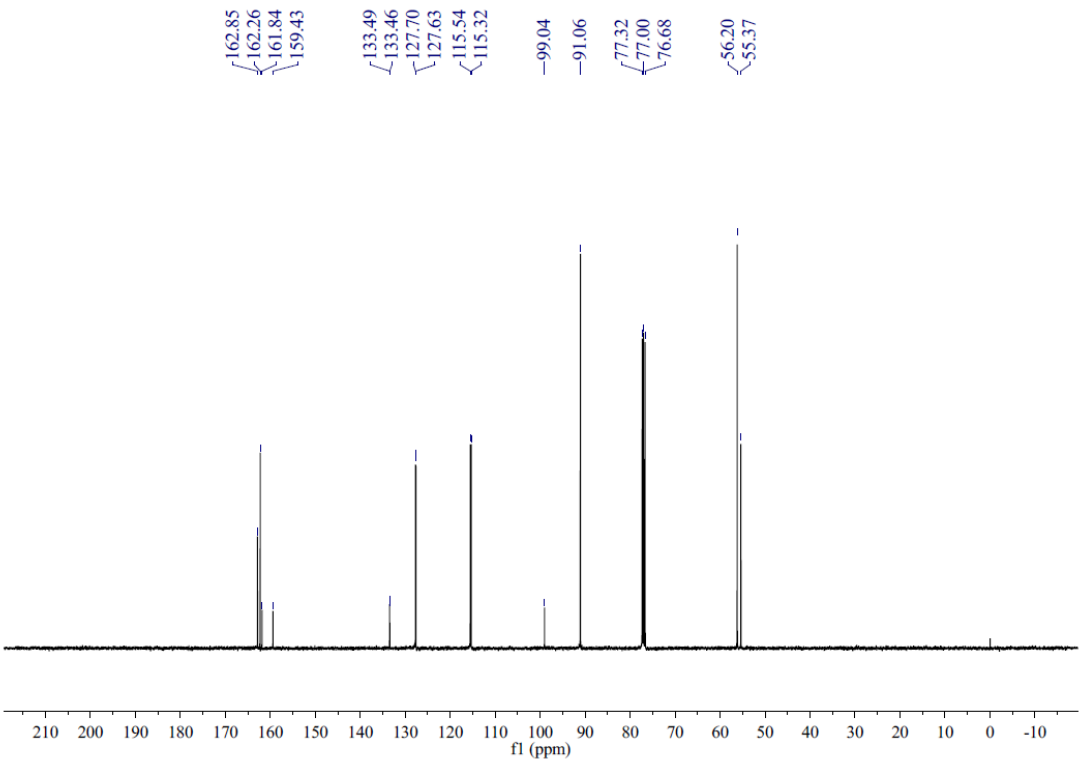

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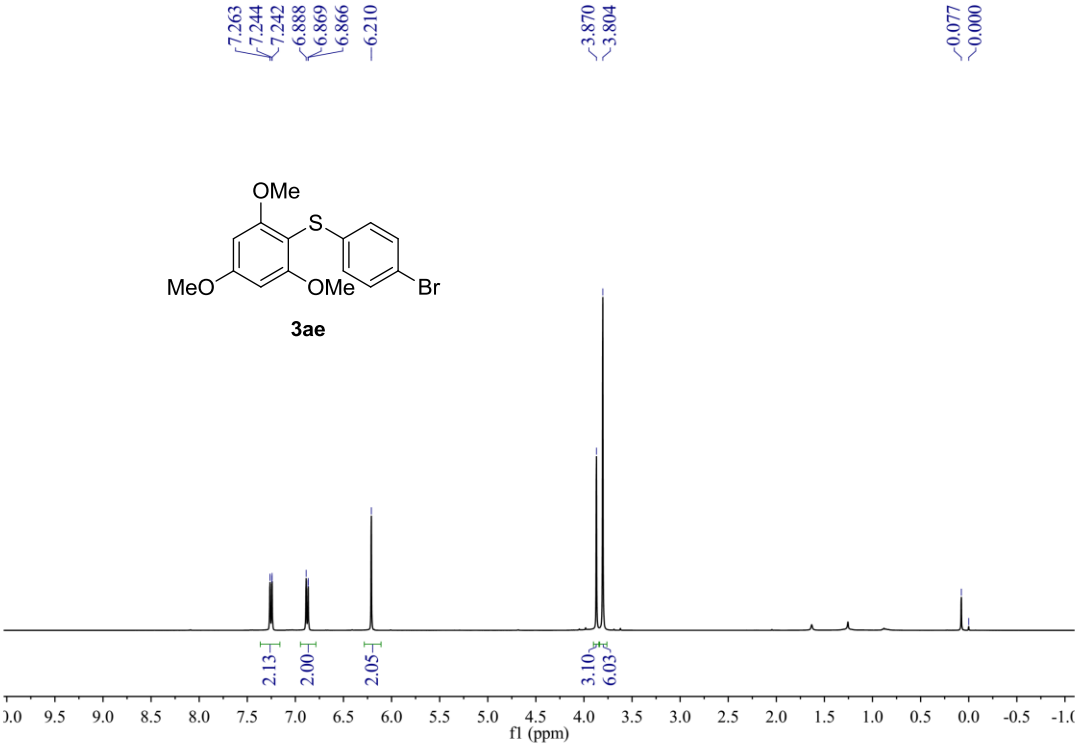

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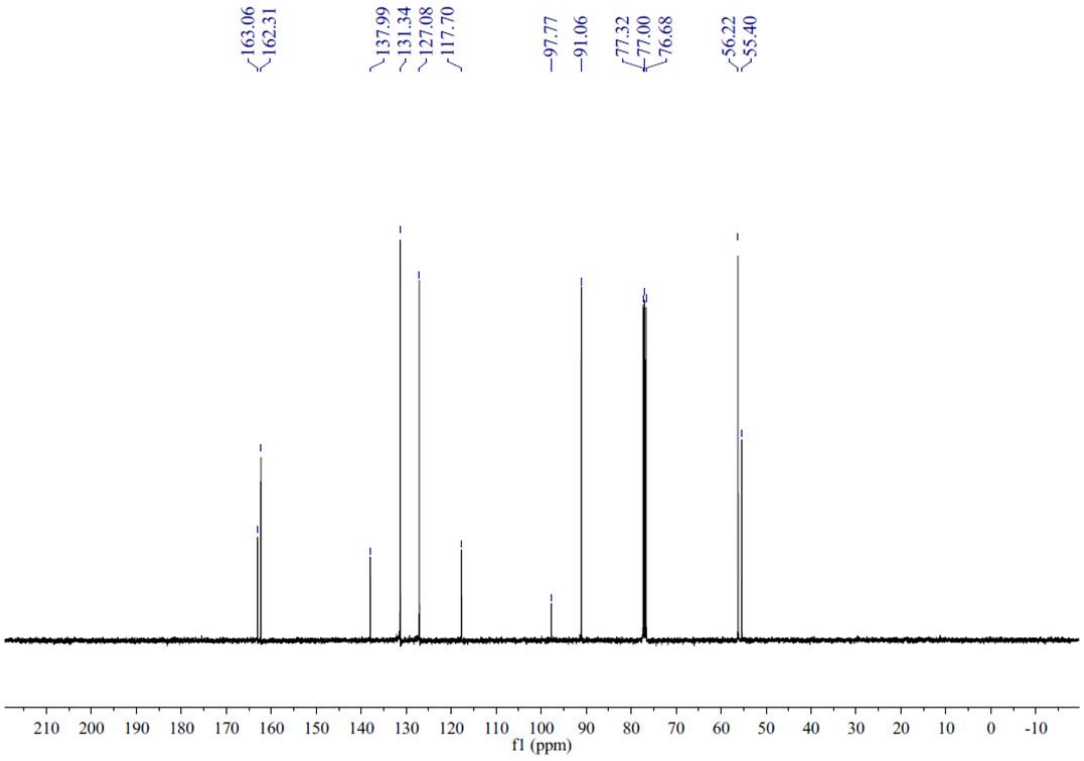

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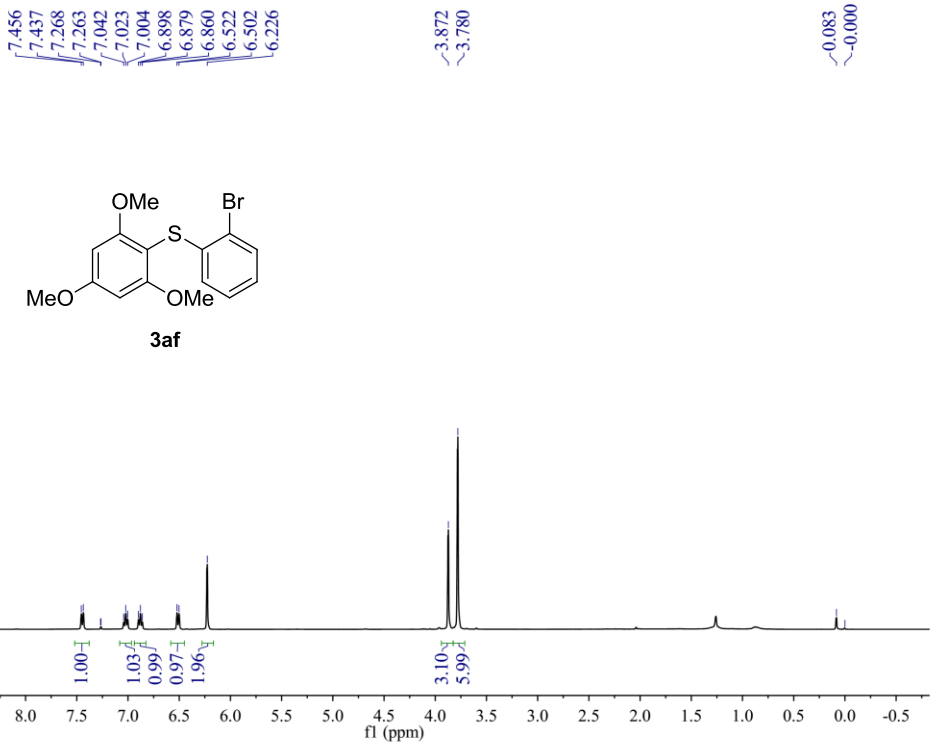

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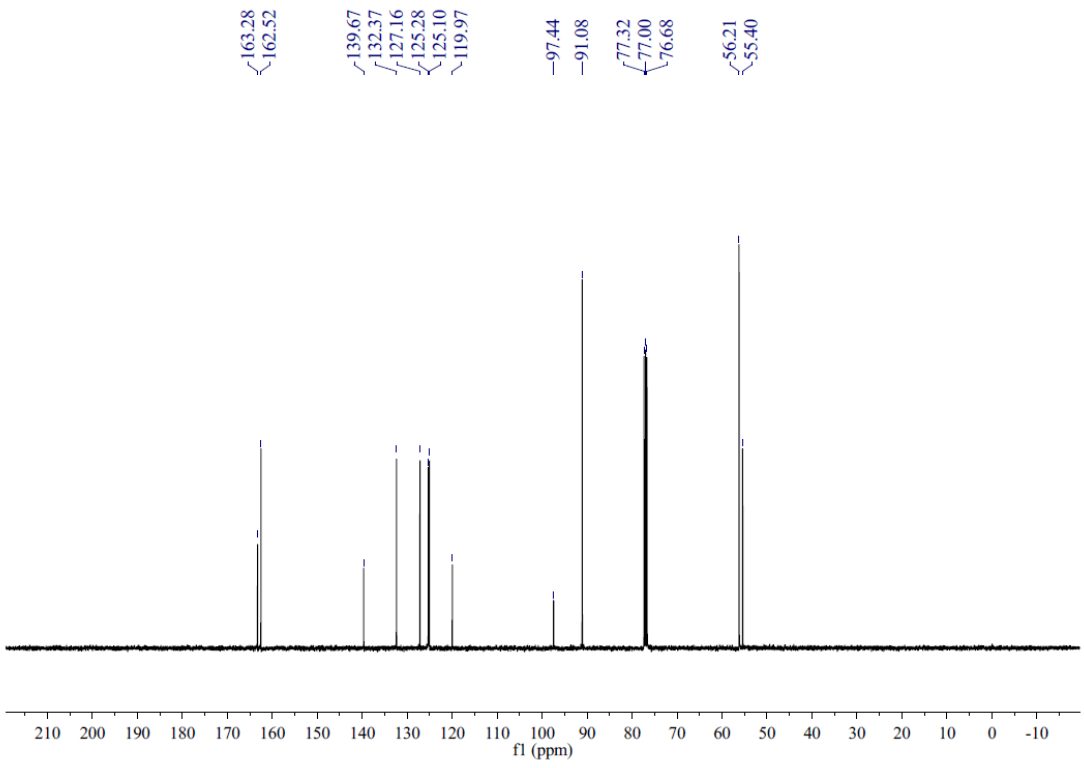

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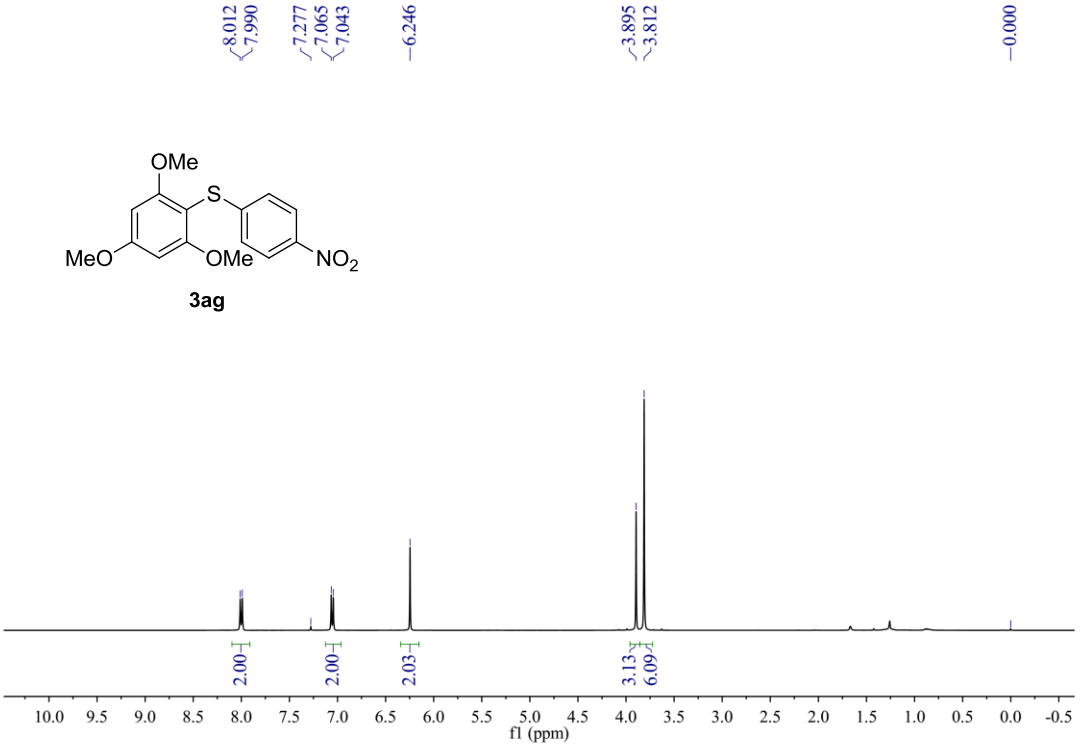

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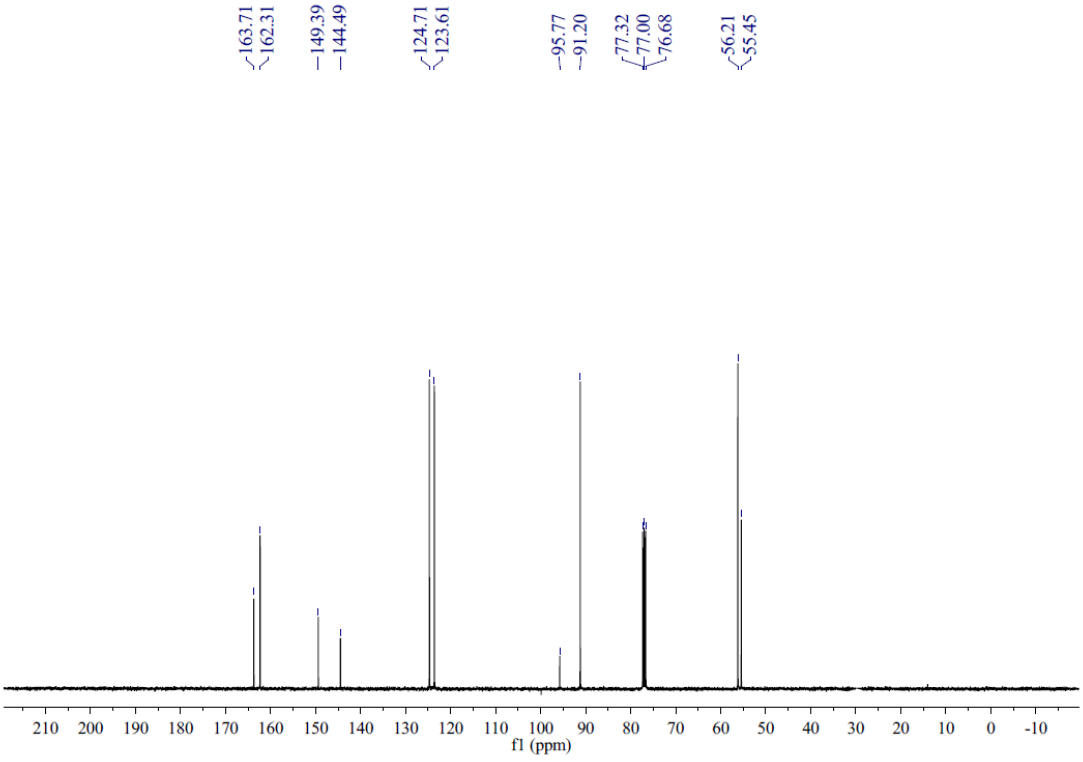

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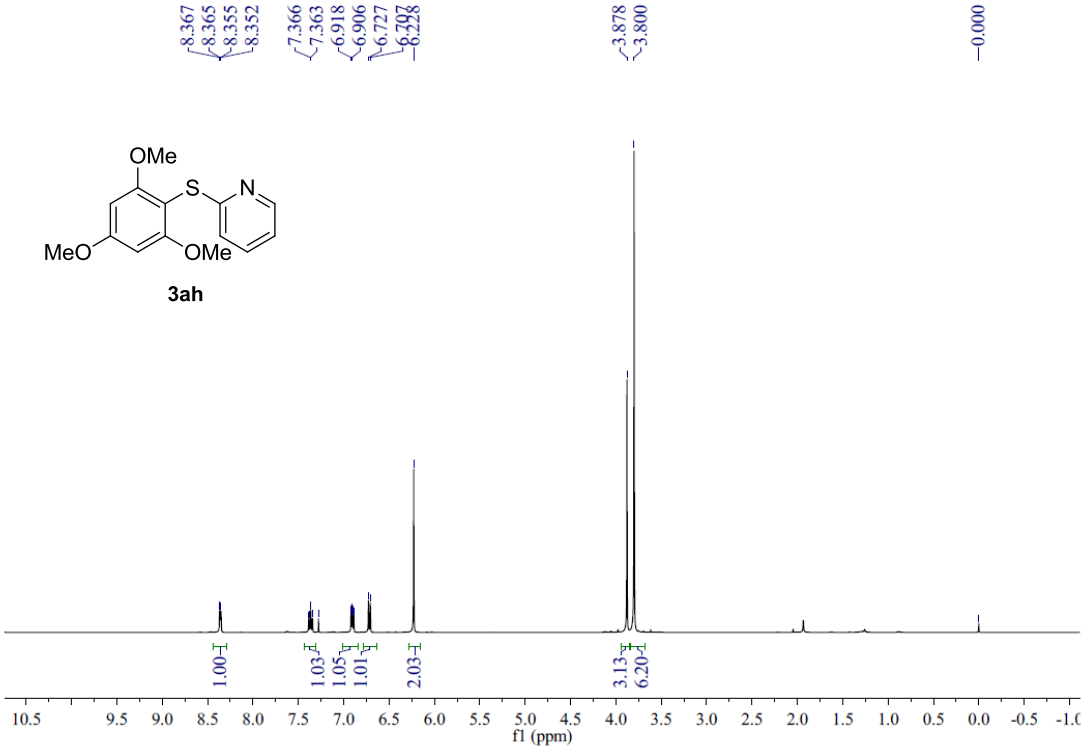

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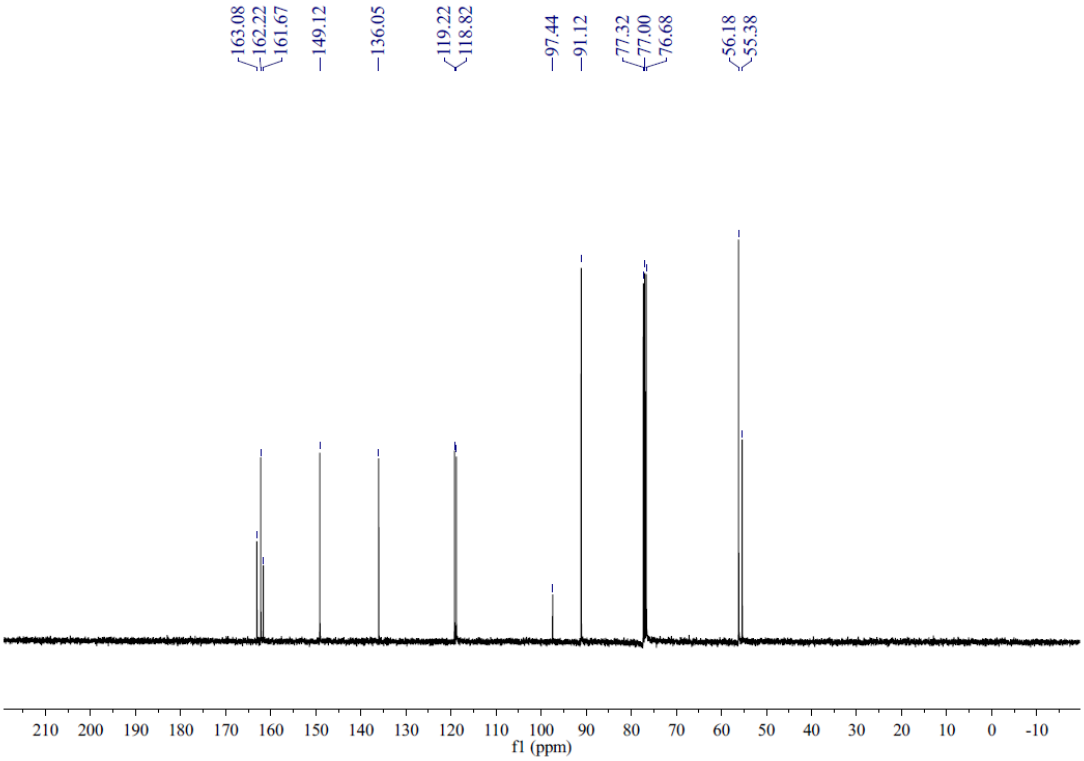

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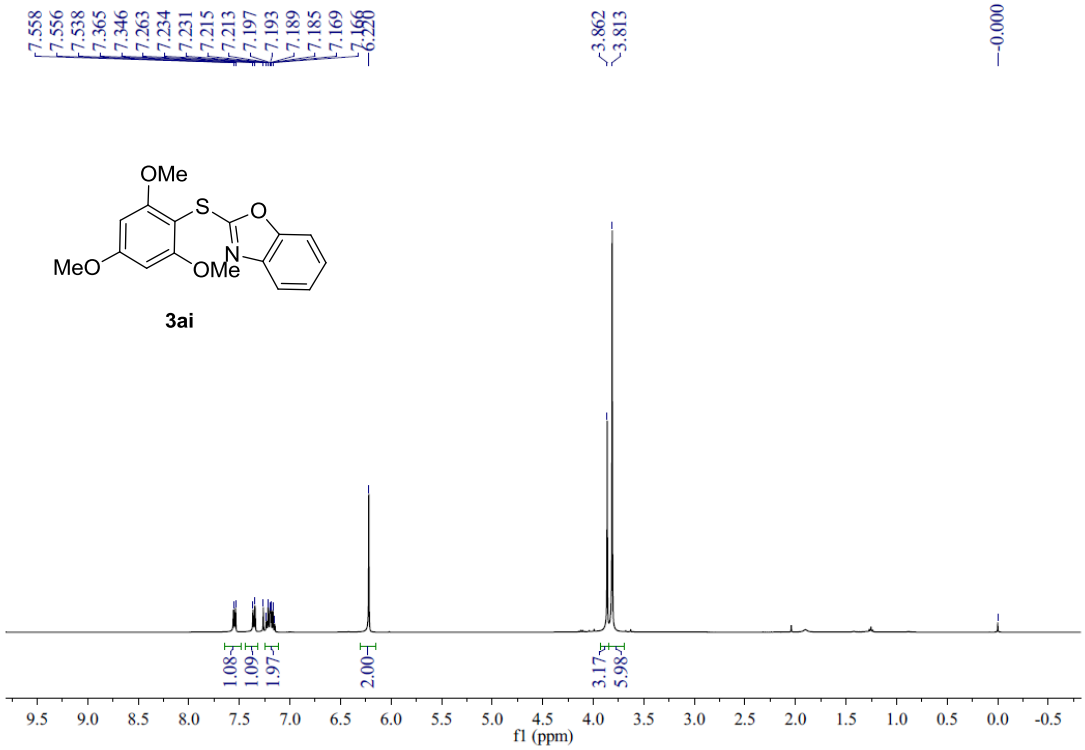

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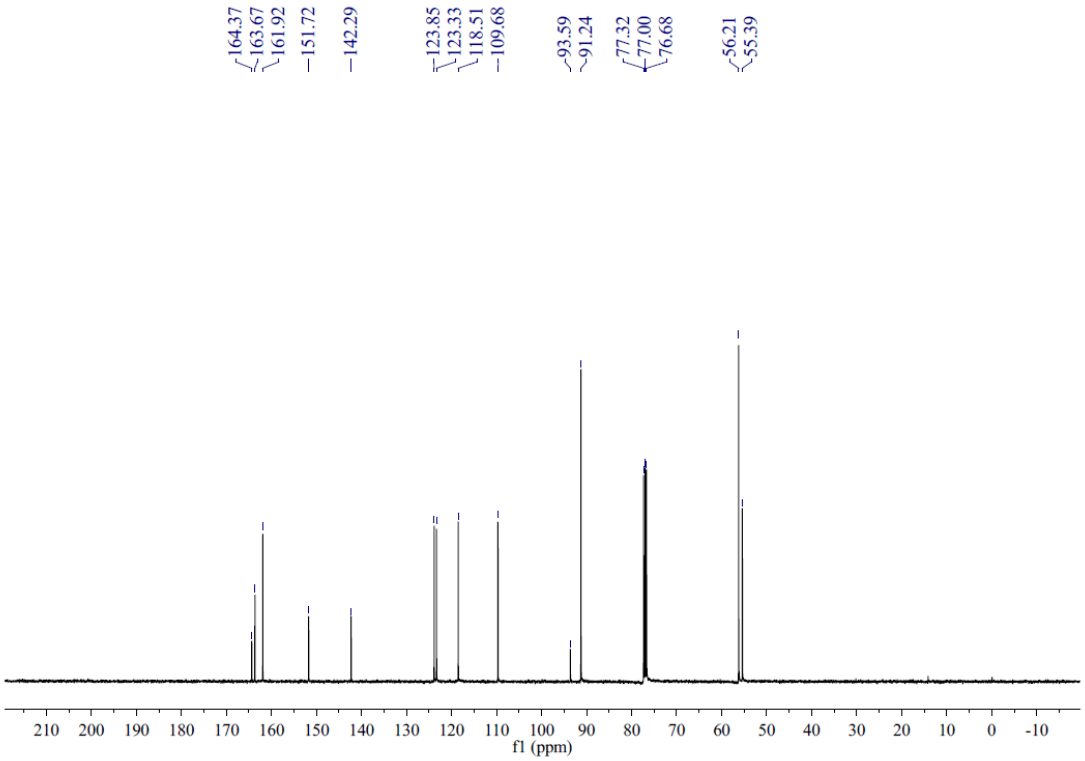

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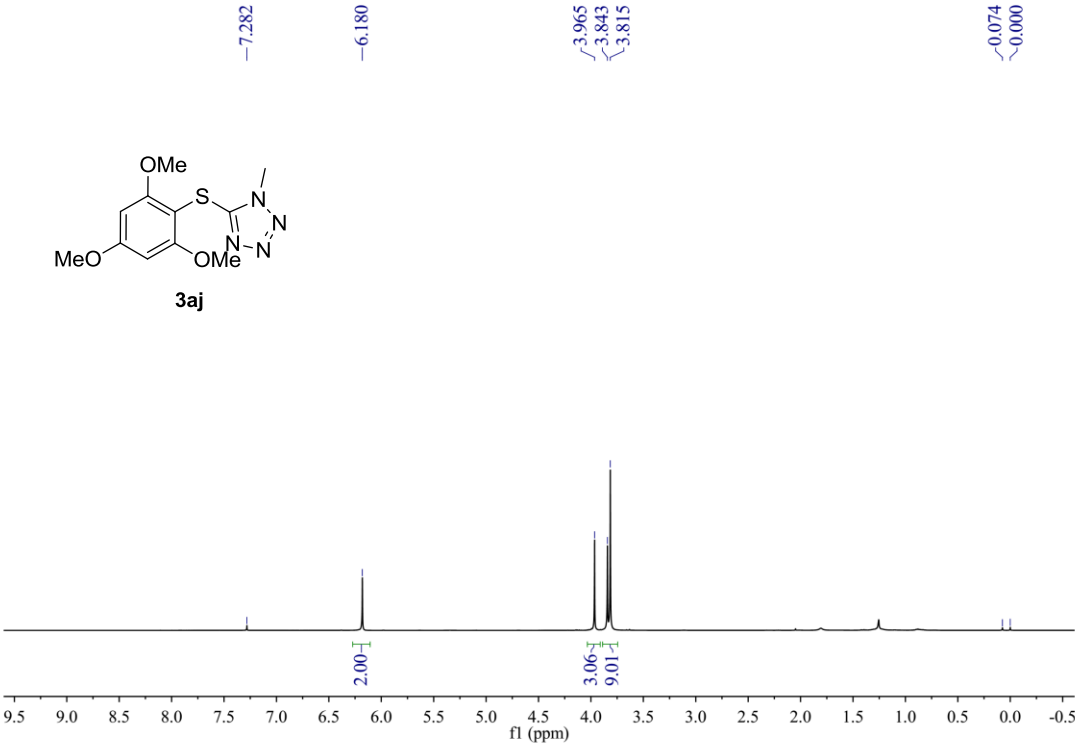
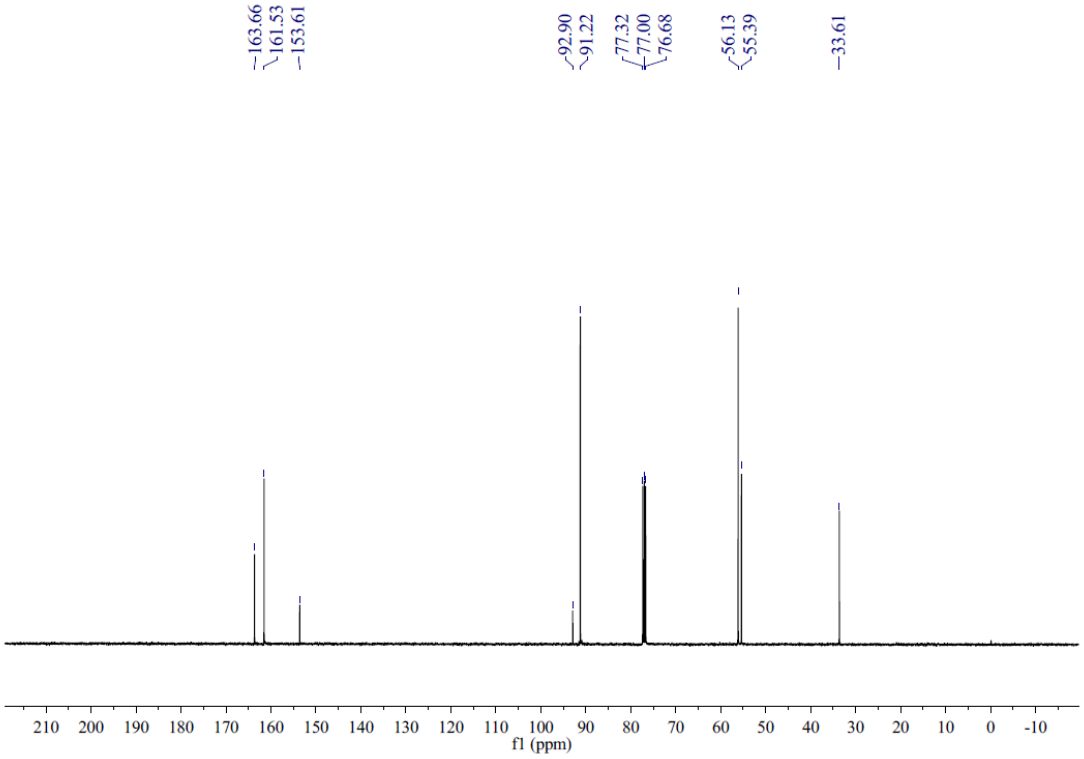


3aj

^{1}H NMR



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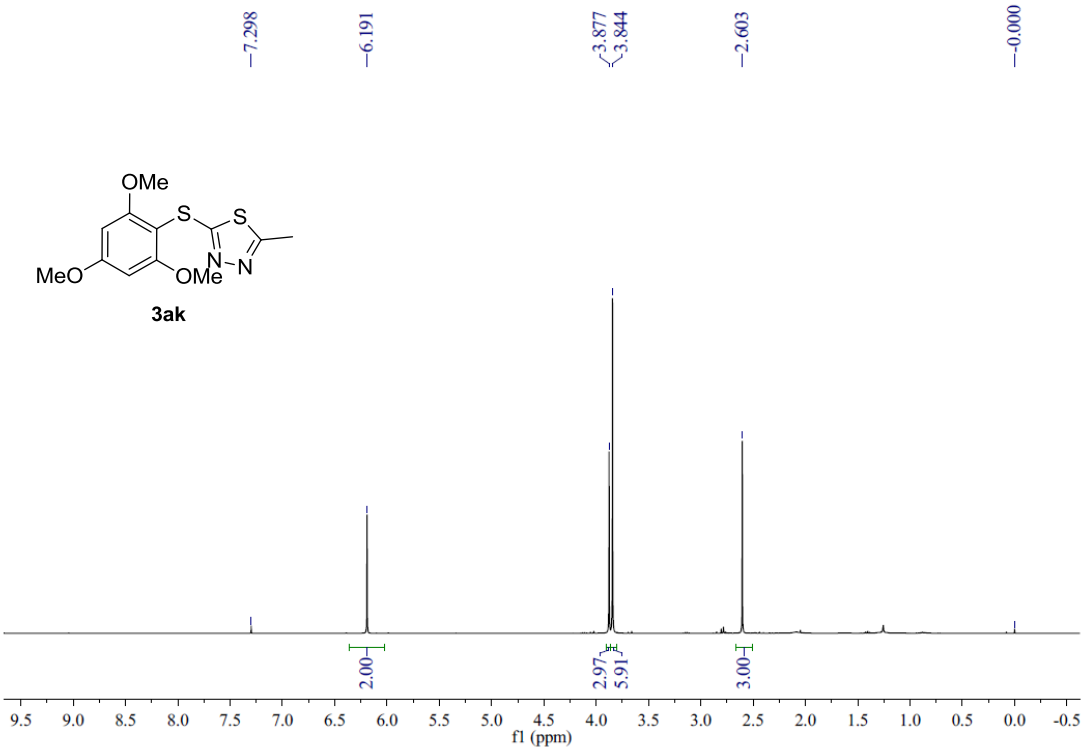

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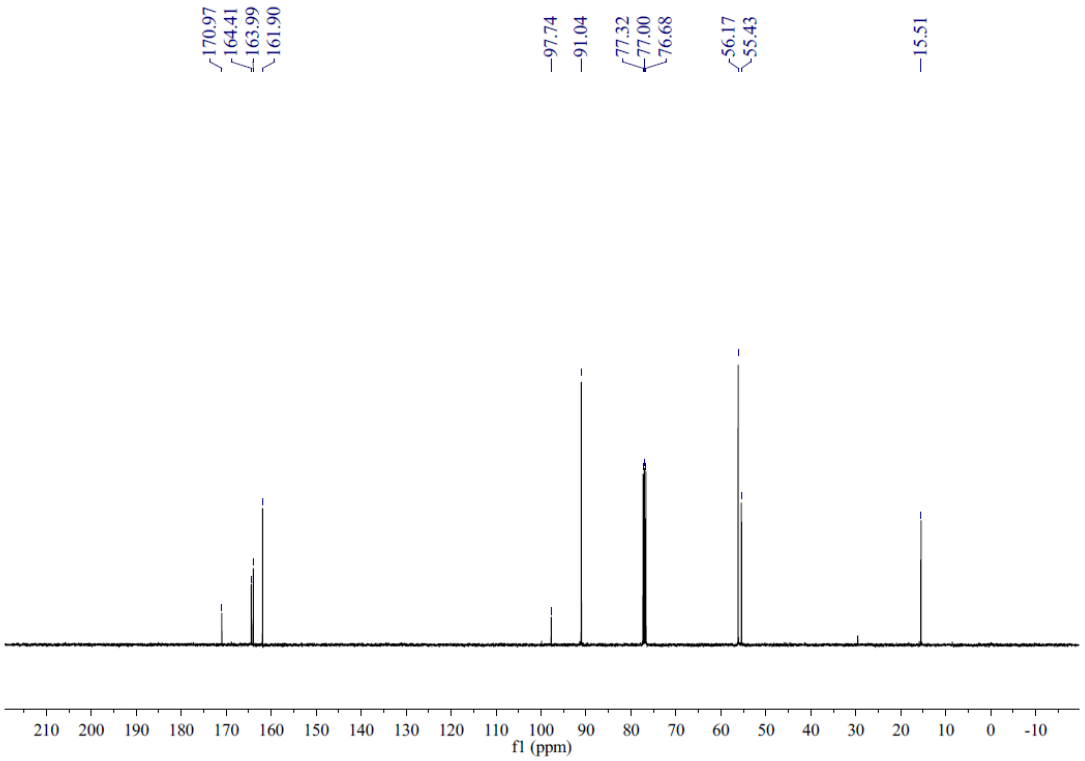

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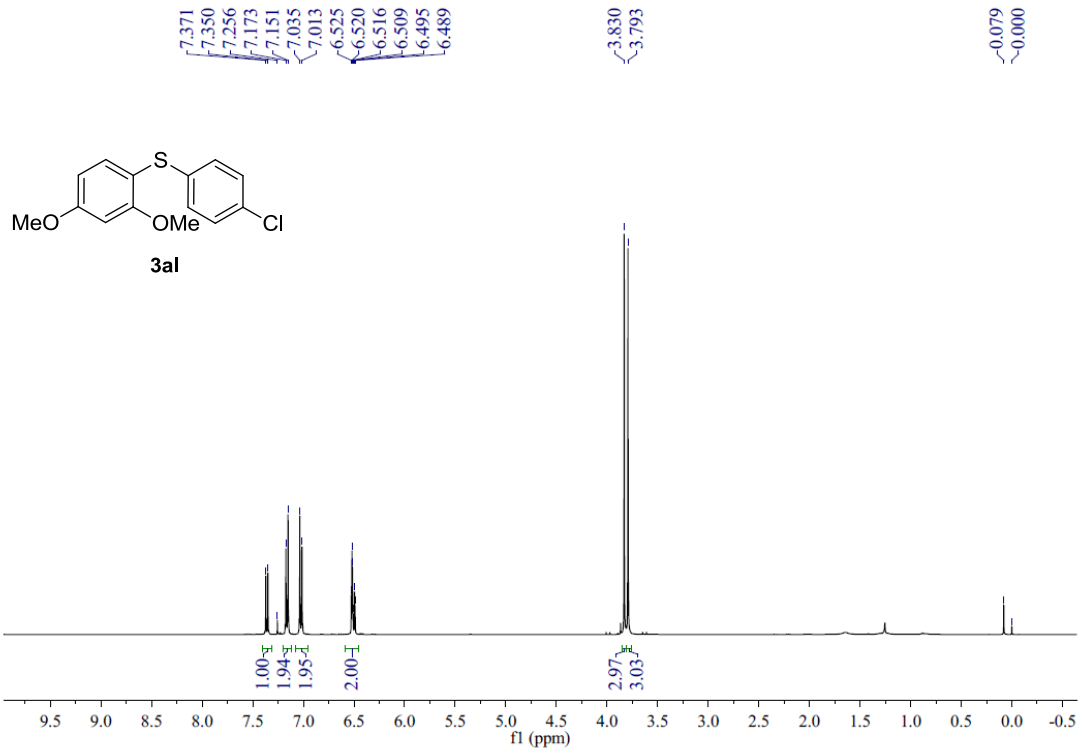

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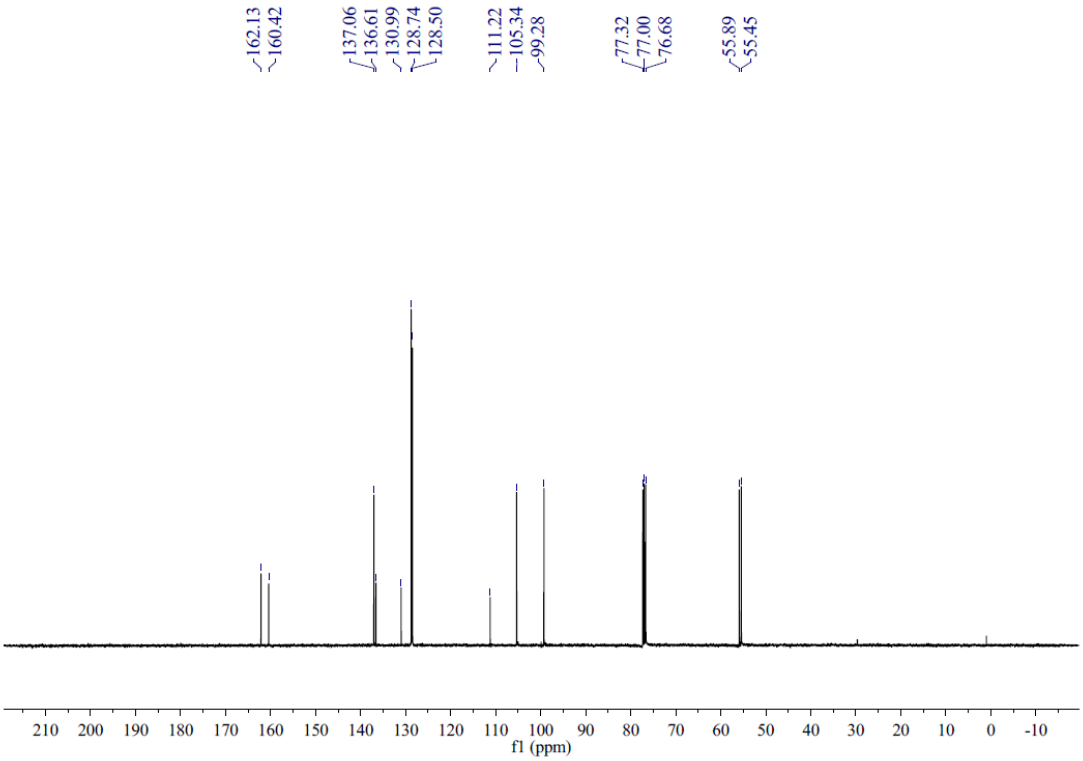

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