Electronic Supplementary Material (ESI) for ChemComm.

Supporting information

HTE and AI-Assisted Development of DHP Catalyzed Decarboxylative Selenation

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Content

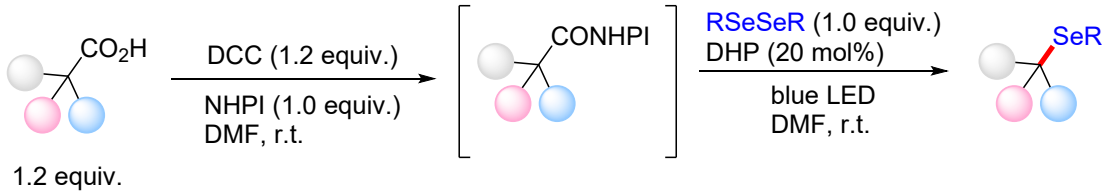
1. General Information

Materials. Reagents were purchased from commercial suppliers (Energy, Aladdin, Alfa Aesar, Sigma-Aldrich, and J&K Scientific) and used with no further purification. NADH analogues were prepared according to references.[1] Anhydrous solvents in sure-seal bottle were purchased from Energy and used with no further purification. All reactions were set up inside Vigor glovebox with constant N_2 purge (oxygen typically < 5 ppm).

Instruments. ^{1}H and ^{13}C NMR spectra were recorded at 600 MHz (^{13}C at 150 MHz) on Bruker Avance III 600 MHz spectrometer, as indicated. NMR spectra run in solutions of deuterated chloroform ($CDCl_3$) with residual chloroform as internal standard (7.26 ppm for 1H, and 77.16 ppm for ^{13}C), and chemical shifts were reported in parts per million (ppm). ^{19}F NMR spectra were recorded on a Bruker Avance III 600 MHz (^{19}F at 564 MHz) and were reported unreferenced. Abbreviations for signal multiplicity are as follow: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublet, etc. Coupling constants (J values) were calculated directly from the spectra. Reactions were analyzed using a Waters Acquity UPLC-MS. Column: Acquity UPLC BEH C18 1.7 μm 2.1 × 50 mm (Part No. 186002350), Mobile Phase A: 2.0 mL formic acid + 3998 mL Water, Mobile Phase B: 4000 mL MeCN, Weak Wash: 100 mL MeCN + 900 mL Water. The instrument was equipped with an SQ Detector 2 with electrospray ionization (ESI) source in the positive mode. Flash column chromatography was performed using silica gel of 300–400 μm. Thin layer chromatographic (TLC) analysis was performed with glass-backed silica gel plates, visualizing with UV light (254 nm). Liquid was handled with Eppendorf continuous manual dispenser.

2. General Procedure (Procedure A) of HTE

2.1 General Procedure of Reaction Setup



The procedure was illustrated as following: 1) Stocking solutions preparation: alkyl acids, 1,4-dihydropyridines analogues (DHP), dicyclohexylcarbodiimide (DCC) and *N*-Hydroxyphthalimide (NHPI) were dissolved in DMF, diselide and DHP were dissolved in reaction solvent; 2) Reaction setup: to the 96-well aluminum blocks equipped with 900 μL glass tubes were added DCC (0.003 mmol, 100μL), NHPI (0.0025 mmol, 50 μL) and alkyl acid solution (0.003 mmol, 50μL) in sequence via repetitive pipette and screwed the covers of plates in glove box; 3) The 96-well aluminum blocks were placed on orbital agitators at room temperature for 12 h; 4) After 12 hours, DMF were removed at 50 °C under reduced pressure in centrifugal concentrator embedded in glove box; 5) To 900 μL glass tubes in 96-well aluminum blocks were added diselane reagents (0.0025 mmol, 100 μL) and DHP solution (0.0005 mmol, 100 μL) via repetitive pipette in glove box, which were dissolved in reaction solvents prior to be used; 6) 96-well aluminum blocks were sealed, then the blocks were placed on the blue LED array embedded on the orbital agitators, the blocks were irradiated and agitated at room temperature for 12 h. The current for the LED array was set to 30 mA and temperature was controlled by fan; 7) Dual internal standards (1,1'-biphenyl, 4-bromo-1,1'-biphenyl) were added to the reaction mixture and the reaction was diluted with CH_3CN and DMSO if the yield data was acquired via UPLC-MS. Otherwise, the reactions were concentrated under reduced pressure and the yield was determined by ^1H NMR using 1,3,5-trimethoxybenzene as internal standard; 8) Data acquisition and processing. The yields were obtained via standard curve method when the data was acquired with UPLC-MS.

Note: Light was irradiated from the bottom of 96-well aluminum block.

Figure S1. Reaction equipment when data was collected via HTE

2.2 General Procedure of Data Analysis

2.2.1 Inlet Method of UPLC-MS

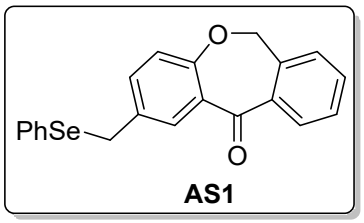
Table S1. Inlet method of UPLC-MS

Time(min)	Flow Rate (mL/min)	H_2O (%) with 0.5% formic acid	CH_3CN (%)	Curve
Initial	0.8	90	10	Initial
0.5	0.8	90	10	6
3.5	0.8	10	90	6
4	0.8	10	90	6
4.01	0.8	90	10	1
5	0.8	90	10	6

The column used in the data acquisition: BEH Phenyl column, 2.5 μm, 2.1*75 mm or BEH C18 column, 1.7 μm, 2.1*50 mm

2.2.2 Standard Curves

Standard curves were used for yield determination, selected two examples are shown below.



AS1

Table S2. Data of AS1 acquired from UPLC-MS

#	Ratio of AS1 vs IS[1]	RT of AS1 (min) [2]	UV Area of AS1[3]	UV Area of IS [3,4]	Ratio of UV Area[5]
1	1	3.05	17397.9	15499.4	1.122
2	0.8	3.05	12819.96	14574.34	0.88
3	0.6	3.05	9460.978	14512.89	0.652
4	0.4	3.05	6260.597	14615.86	0.428
5	0.2	3.05	3323.079	14918.58	0.223

[1] The ratio of AS1 and internal standard (IS) added into the sample solution

[2] BEH Phenyl column, 2.5 μm, 2.1*75 mm

[3] PDA was used as detector and UV area of the corresponding peaks were acquired at 242 nm.

[4] 1,1'-biphenyl as IS

[5] The UV area ratio of AS1 over IS

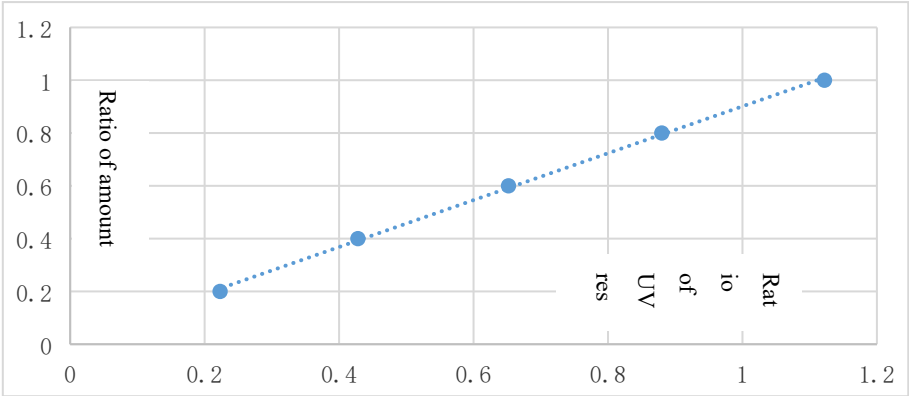


Figure S2. The standard curve of AS1

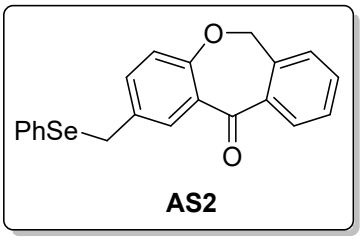


Table S3. Data of AS2 acquired from UPLC-MS

#	Ratio of AS2 vs IS[1]	RT of AS2 (min) [2]	UV Area of AS2[3]	UV Area of IS [3,4]	Ratio of UV Area[5]
1	1	3.05	17589.066	16733.621	1.051
2	0.8	3.05	13181.706	15807.08	0.834
3	0.6	3.05	9783.499	15790.92	0.62
4	0.4	3.05	6503.933	15994.239	0.407
5	0.2	3.05	3345.161	16119.778	0.208

[1] The ratio of AS1 and internal standard (IS) added into the sample solution

[2] BEH Phenyl column, 2.5 μm, 2.1*75 mm

[3] PDA was used as detector and UV area of the corresponding peaks were acquired at 245 nm.

[4] 4-bromo-1,1'-biphenyl as IS

[5] The UV area ratio of AS2 over IS

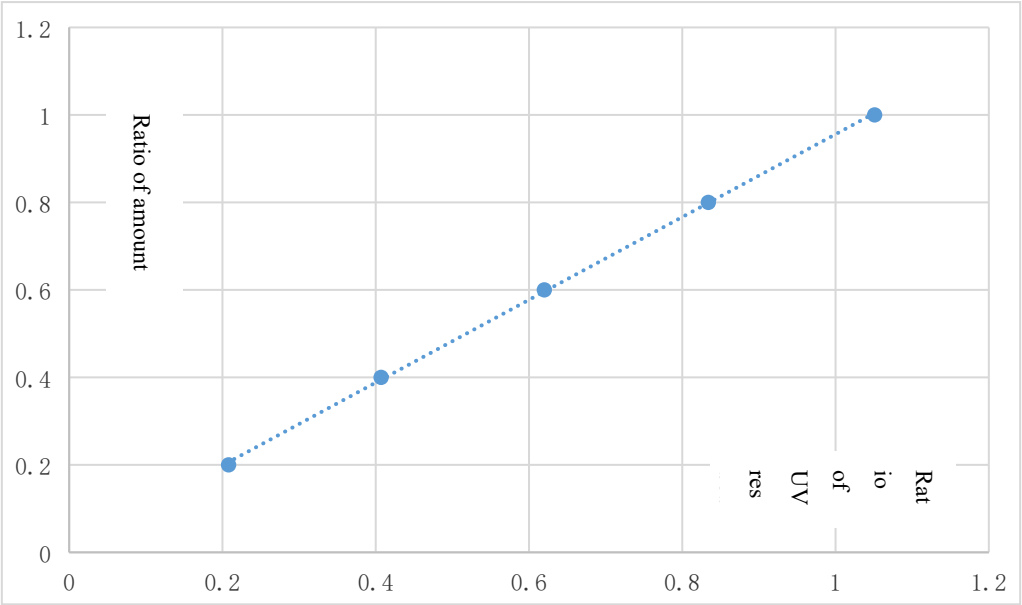
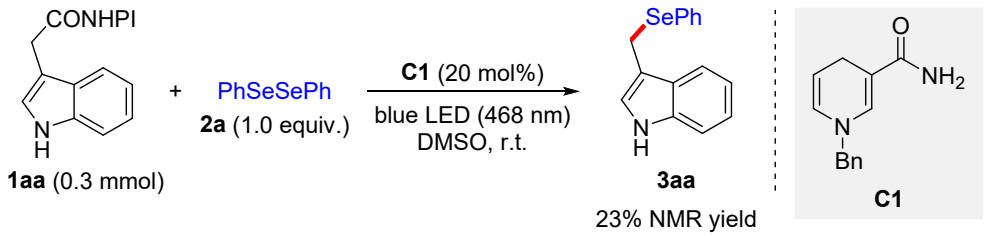


Figure S3. The standard curve of AS2

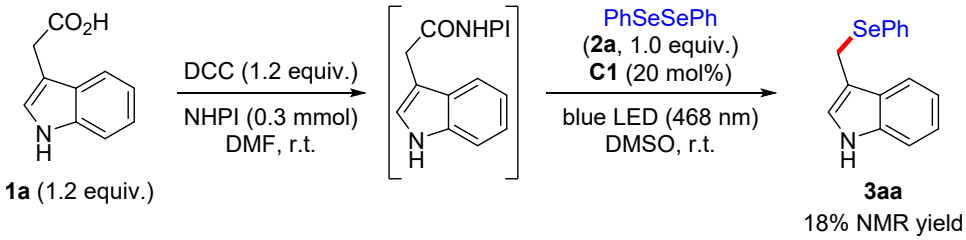
3. Reaction initial exploration and conditions Screening of selected compounds

Initial exploration

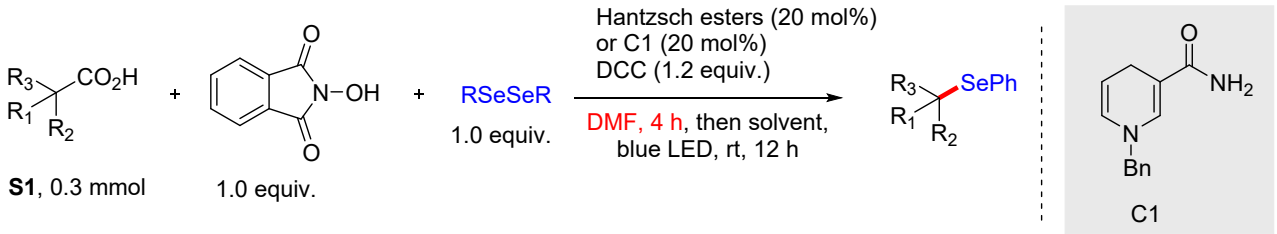
Test reaction using NHPI ester



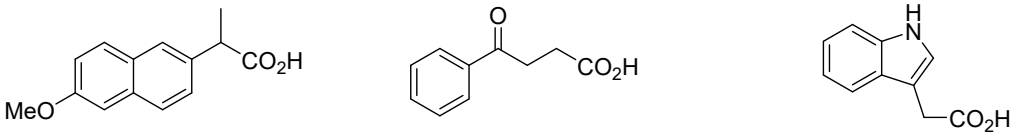
One-pot reaction using carboxylic acid



Reaction conditions screening



C1



Solvent			
DMSO	18% NMR yield	20% NMR yield	23% NMR yield
DMF	64% NMR yield	15% NMR yield	5% NMR yield
Hantzsch esters			
DMSO	4% NMR yield	25% NMR yield	18% NMR yield

Table S4. The results of reaction screening

4. Machine Learning Model

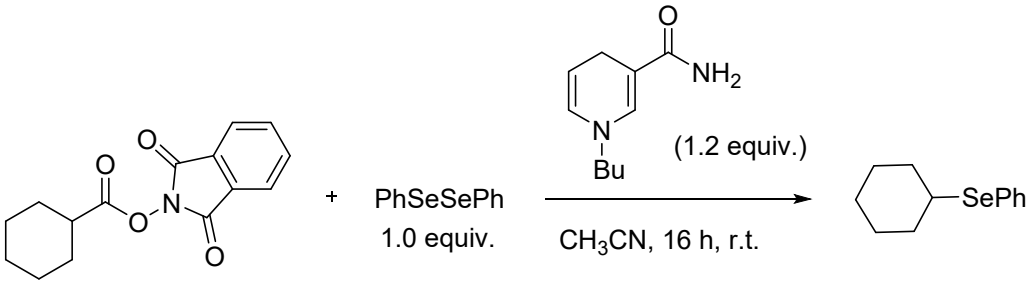
4.1. The identification of key variables

Given the expense and time needed to perform the corresponding reaction, we just studied the key variables in this study.

Our reaction was a two-step one-pot reaction, the yield of NHPI ester intermediate should be maximum when only NHPI was served as the limited reagent. In our reaction, the amount of acids and DCC (1.2 equivalent) should be enough for the complete transformation of NHPI, thus, more reagents (NHPI, DCC, acids) would have tiny effect on the generation of NHPI ester intermediate.

We also studied the effect of other variables, such as the intensity and wavelength of light, temperature, but we did not present these results in the previous manuscript. Other light source usually resulted in poor yield, though the loading of DHP catalysts was increased to 1.2 equiv. (Table S5). Intensity of light and concentration seem to have no impact on the yield (Scheme S1) Besides, we also found that high temperature was not good for the transformation, may due to the low bond dissociation energy of Se–Se bond.

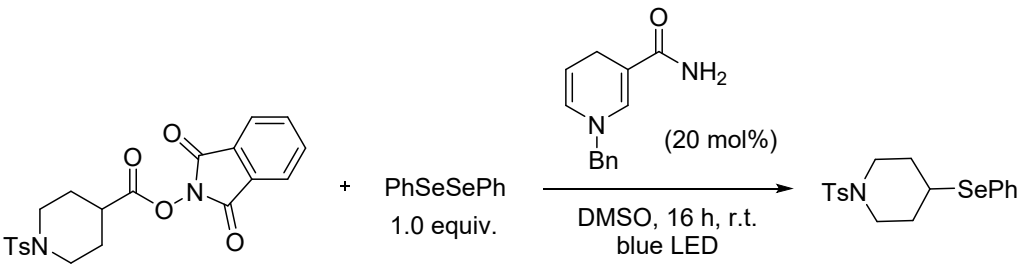
Based on these reasons, we didn't study their effect further in the HTE experiments, we just the study the effect of substates, the redox potential of DHP derivatives (Table S6) and solvents in the training and validation of model.



Entry	Light source	Conversion	NMR yield
1	Blue	>99%	99%
2	Green	33%	33%
3	White	>99%	99%
4	Yellow	12%	0%
5	Red	0%	0%

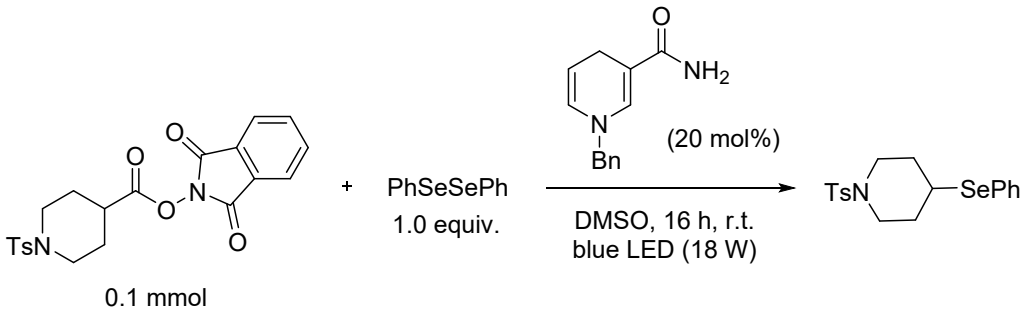
Table S5 The effect of light source

Intensity effect



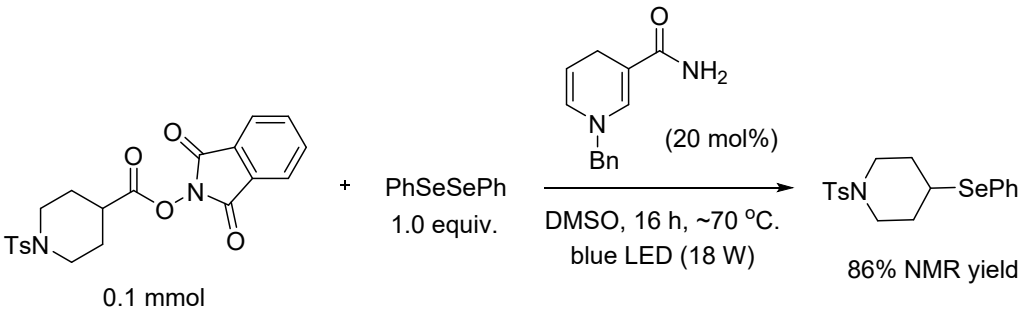
Conditions:
1) 12 W, 99% NMR yield
2) 18 W, 99% NMR yield

Concentration effect

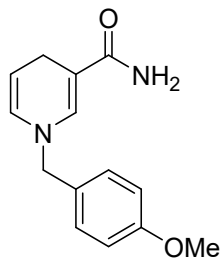


Conditions:
1) C = 0.0125 M, 99% NMR yield
2) C = 0.025 M, 99% NMR yield
3) C = 0.05 M, 97% NMR yield

Temperature effect



Scheme S1. The intensity effect of light, concentration effect and temperature effect

Entry	Catalysts	Eox (V)	References
1		0.50	*J. Am. Chem. Soc.* **1987**, *109*, 305

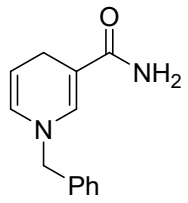
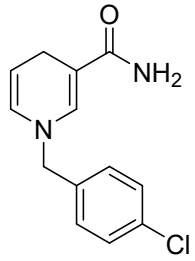
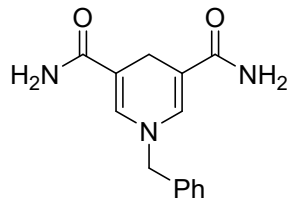
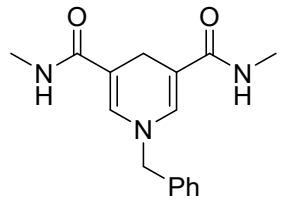
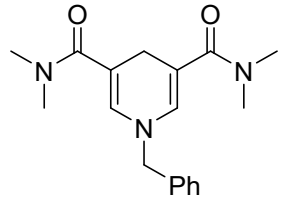
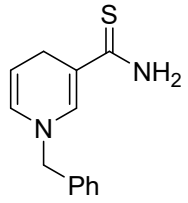
2		0.57	*J. Am. Chem. Soc.* **1987**, *109*, 305
3		0.62	*J. Am. Chem. Soc.* **1987**, *109*, 305
4		0.42	*ACS Omega* **2018**, *3*, 13598
5		0.39	*ACS Omega* **2018**, *3*, 13598
6		0.38	*J. Electroanal. Chem.* **1990**, *286*, 63
7		>0.57 (~0.7)	*Chem. Commun.* **2016**, *52*, 6471

Table S6 The oxidative potential of some representative DHP derivatives

4.2. Data Collection

The data collection procedure was also followed procedure A. All reactions were also repeated two times and reaction data with difference over 10% yield were discarded. We also omitted some reactions or discarded some data due to the availability of catalysts or the difficulties in analysis, such as lack of authentic samples or product peak overlapped by impurities. to ensure the quality of data.

4.3. Codes Availability

Our codes were executed in KNIME (the Konstanz Information Miner). All programming workflows were available in https://kni.me/w/dXii490pAXJvFMgs

4.4. Data

In our study, two datasets were used, one dataset for modelling and one dataset for external validation. The SMILES of alkyl acids, selenium compounds, DHP, solvents and products, in addition to the observed yield were included in datasets.

1. Data set A (532 reaction data) was split as 80/20, 426 reaction data were used as training set, 106 reaction data were used as test set for modeling.

2. Data set B (336 reaction data) involved 5 brand new catalysts was used as an external validation set for the model built from dataset A. We used dataset A to build model, and then used dataset B as an external validation for the model built from dataset A.

4.5. Input

MAF

We provided a representation, molecular additive fingerprints (MAF) as inputs, that show the capacity of reaction prediction in good practices. The example for MAF development in this reaction were shown in figure S4. Besides, we also employed two types of commonly used descriptor for yield prediction: RDKit descriptors and one-hot encoding.

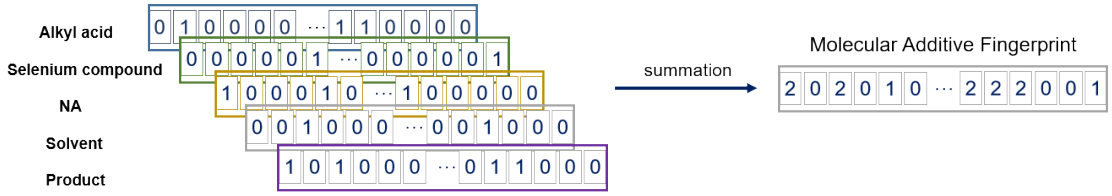


Figure S4. the example for MAF development in this reaction.

RDKit descriptors

RDKit descriptor generation was conducted in a KNIME workflow. In total, 144 descriptors were calculated for each reaction component using “RDKit Descriptors Calculation” node. The descriptors we used are as following:

SlogP, SMR, LabuteASA, TPSA, AMW, ExactMW, NumLipinskiHBA, NumLipinskiHBD, NumRotatableBonds, NumHBD, NumHBA, NumAmideBonds, NumHeteroAtoms, NumHeavyAtoms, NumAtoms, NumStereocenters, NumUnspecifiedStereocenters, NumRings, NumAromaticRings, NumSaturatedRings, NumAliphaticRings, NumAromaticHeterocycles, NumSaturatedHeterocycles, NumAliphaticHeterocycles, NumAromaticCarbocycles, NumSaturatedCarbocycles, NumAliphaticCarbocycles, FractionCSP3, Chi0v, Chi1v, Chi2v, Chi3v, Chi4v, Chi1n, Chi2n, Chi3n, Chi4n, HallKierAlpha, kappa1, kappa2, kappa3, slogp_VSA1, slogp_VSA2, slogp_VSA3, slogp_VSA4, slogp_VSA5, slogp_VSA6, slogp_VSA7, slogp_VSA8, slogp_VSA9, slogp_VSA10, slogp_VSA11, slogp_VSA12, smr_VSA1, smr_VSA2, smr_VSA3, smr_VSA4, smr_VSA5, smr_VSA6, smr_VSA7, smr_VSA8, smr_VSA9, smr_VSA10, peoe_VSA1, peoe_VSA2, peoe_VSA3, peoe_VSA4, peoe_VSA5, peoe_VSA6, peoe_VSA7, peoe_VSA8, peoe_VSA9, peoe_VSA10, peoe_VSA11, peoe_VSA12, peoe_VSA13, peoe_VSA14, MQN1, MQN2, MQN3, MQN4, MQN5, MQN6, MQN7, MQN8, MQN9, MQN10, MQN11, MQN12, MQN13, MQN14, MQN15, MQN16, MQN17, MQN18, MQN19, MQN20, MQN21, MQN22, MQN23, MQN24, MQN25, MQN26, MQN27, MQN28, MQN29, MQN30, MQN31, MQN32, MQN33, MQN34, MQN35, MQN36, MQN37, MQN38, MQN39, MQN40, MQN41, MQN42.

One-hot encoding

A one-hot encoding based on all available reaction substrates and conditions (catalysts, bases, solvents, additives) was generated. The bit value '0' or '1' corresponds to the absence or presence for specific reaction components. The creation of one-hot descriptor was done via a KNIME workflow, and an array of one-hot encodings of substrates and products was calculated in "One to Many" node.

4.6 Machine Learning Methods

Four commonly used machine learning methods were employed including gradient boosting trees (GBM), random forest regression (RF), extreme gradient boosting(XGB) and support vector regression (SVR). The metrics of squared correlation coefficient (R^2), the root mean squared error (RMSE), and the mean absolute error (MAE) were used for evaluation. The dataset for modelling was randomly split into 80% used for model training (training set, 433) and 20% used for evaluation (test set, 109). Hyper-parameters optimization was conducted using a grid search approach for our best model. A 5-fold cross validation procedure was carried out for test set evaluation. The ultimate hyper-parameters of four machine learning models were listed in Table S7~S10. The results were illustrated in Figure S5 ~ Figure S14.

Hyperparameters	**Considered values**
Tree depth	5{**5**, 10, 15, 20}
Number of models	500{300, 400, **500**}
Learning rate	0.1{0.05, **0.1**, 0.15}

Table S7**.** The hyper-parameters of GBT.

Hyperparameters	**Considered values**
Tree depth	auto
Number of models	100
Early stop	auto

Table S8. The hyper-parameters of RF.

Hyperparameters	**Considered values**
Boosting rounds	300
Booster	tree
Eta	0.1
Maximum depth	7

Table S9. The hyper-parameters of XGB.

Hyperparameters	**Considered values**
Kernel	linear
Cost	1.0

Nu	0.5
Epsilon	0.001

Table S10. The hyper-parameters of SVR.

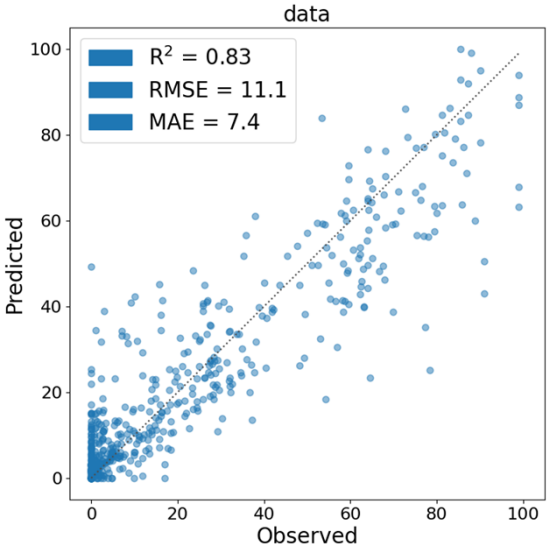


Figure S5. Regression plot for 5-fold cross-validation using XGB developed by MAF

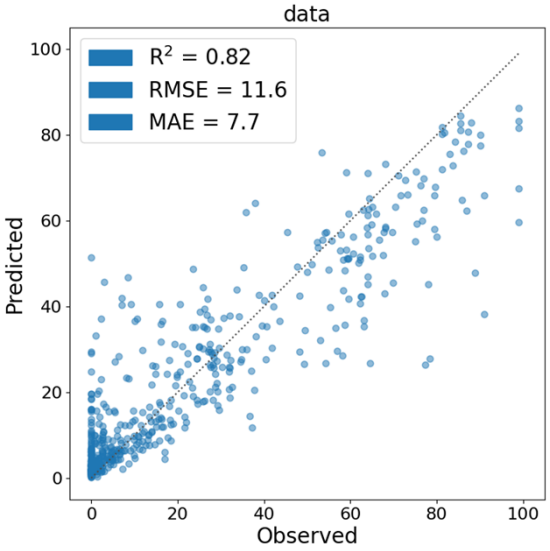


Figure S6. Regression plot for 5-fold cross-validation using RF developed by MAF

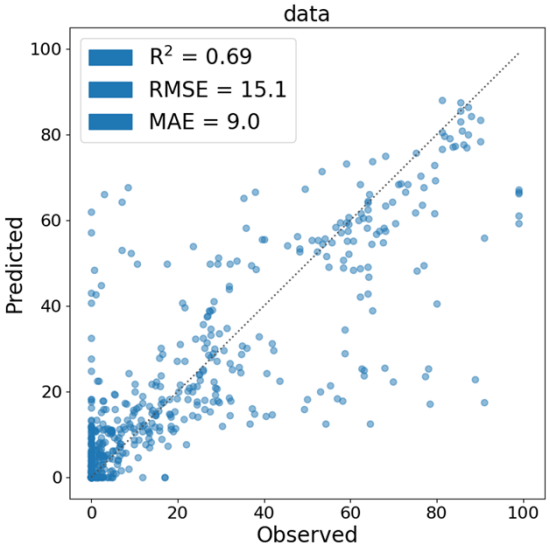


Figure S7. Regression plot for 5-fold cross-validation using SVR developed by MAF

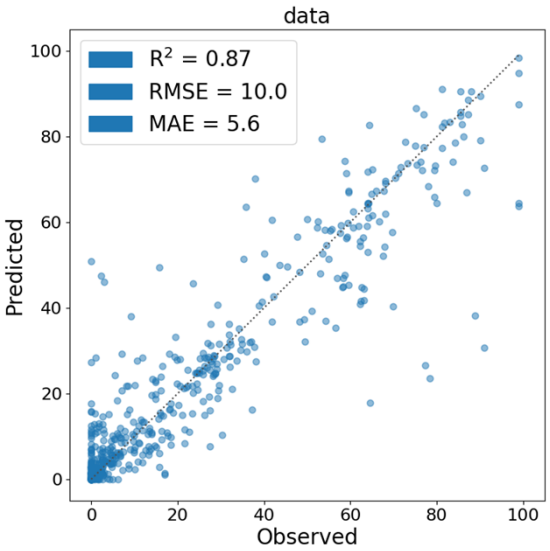


Figure S8. Regression plot for 5-fold cross-validation using GBT developed by MAF

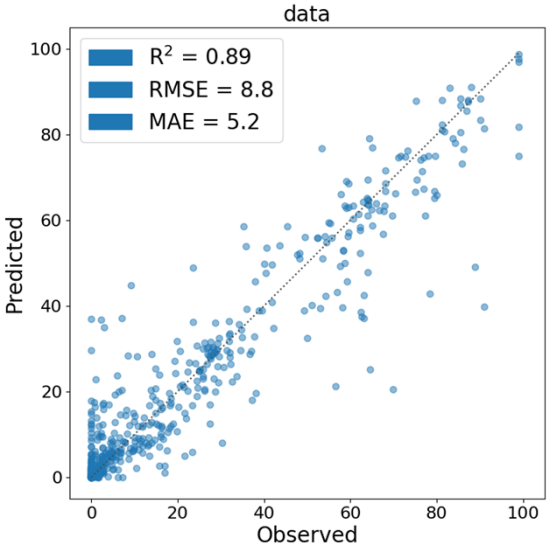


Figure S9. Regression plot for 5-fold cross-validation using GBT developed by MAF and smiles

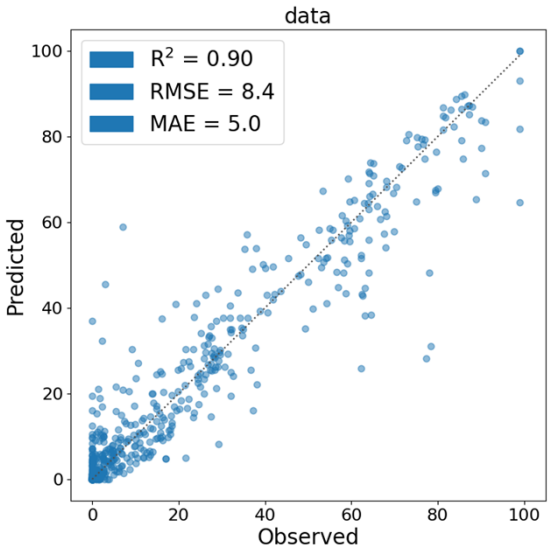


Figure S10. Regression plot for 5-fold cross-validation using GBT developed by RDKit descriptors

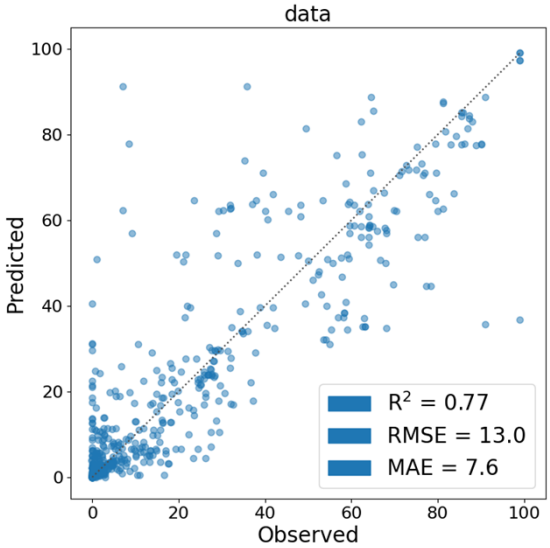


Figure S11. Regression plot for 5-fold cross-validation using GBT developed by one-hot encoding

4.7. Performance with External Set

Using our best model, the possible yields were predicted and correlated with the observed yields. The out-of-sample performance of this external datasets was shown in Figure S12~Figure S14.

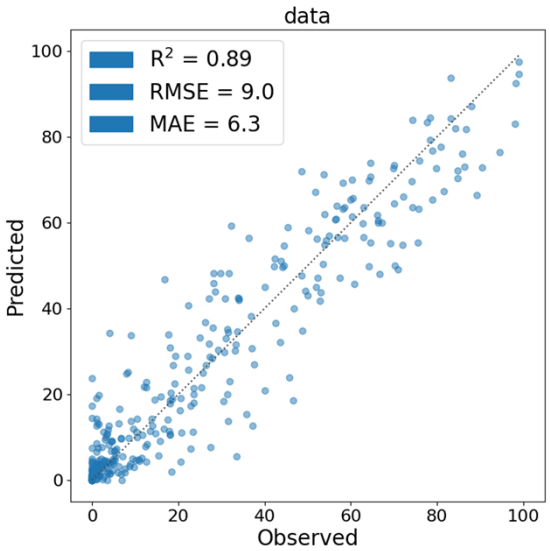


Figure S12. Regression plot for predicting external dataset using GBT developed by MAF and smiles.

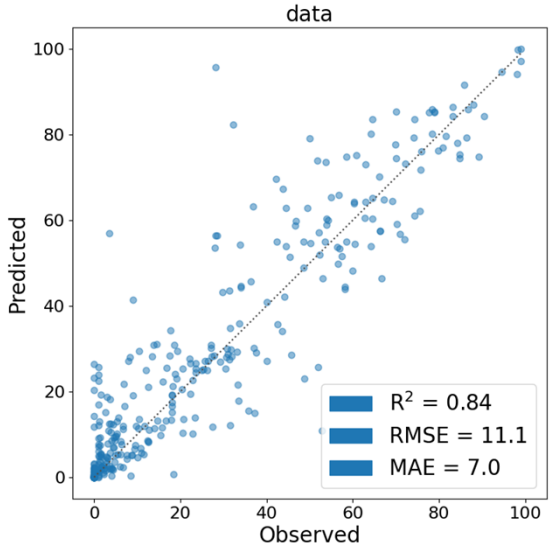


Figure S13. Regression plot for predicting external dataset using GBT developed by RDKit descriptors

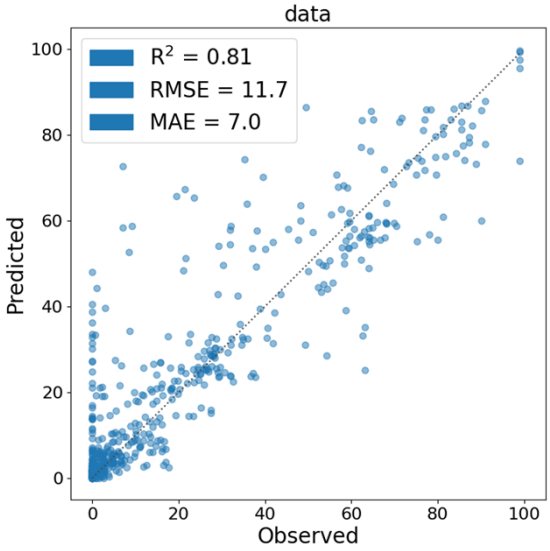


Figure S14. Regression plot for external set (data set B) to predict training set (data set A) using GBT developed by MAF and smiles.

4.8. The discussion on model interpretability

In order to gain more insight about the reaction, we also sought to use feature importance to understand the key structural features. Because GBT model could not see the corresponding feature importance, we first rebuilt the Random Forest model with python（https://github.com/PussInCode/Feature_Importance_Analysis.git）.

The metrics of 5-fold cross validation was consistent with those obtained via Knime platform (Table S11). Besides, the high metrics enable the conclusions from this model should be reliable. With these result in hand, we then obtained the feature importance of vectors (128 bits) and the results were illustrated in Figure S_1.

R^2	MAE	RMSE
0.85	0.067	0.101

Table S11 The metrics of Random Forest rebuilt with python

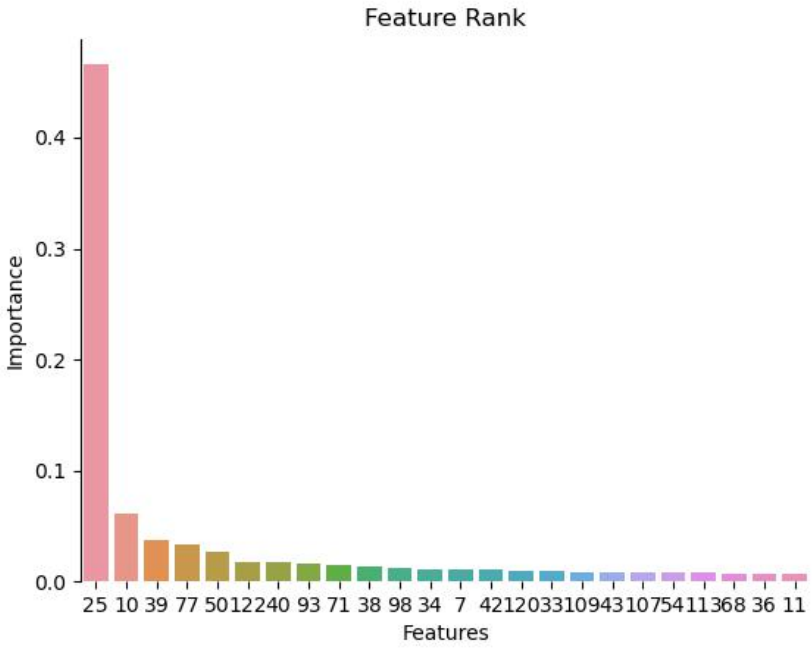


Figure S_1 The ranks of features

Based on the results of feature importance analysis, we labeled the key substructures of acids, diselanes and DHP derivatives. To our delight, the Random Forest model could recognize that the reactive site (carboxyl group), bond breaking site, and substituents of the acid were important factors (Figure S_2). Indeed, substituents of the acid could affect the stability of the corresponding alkyl radical intermediates through electronic effect.

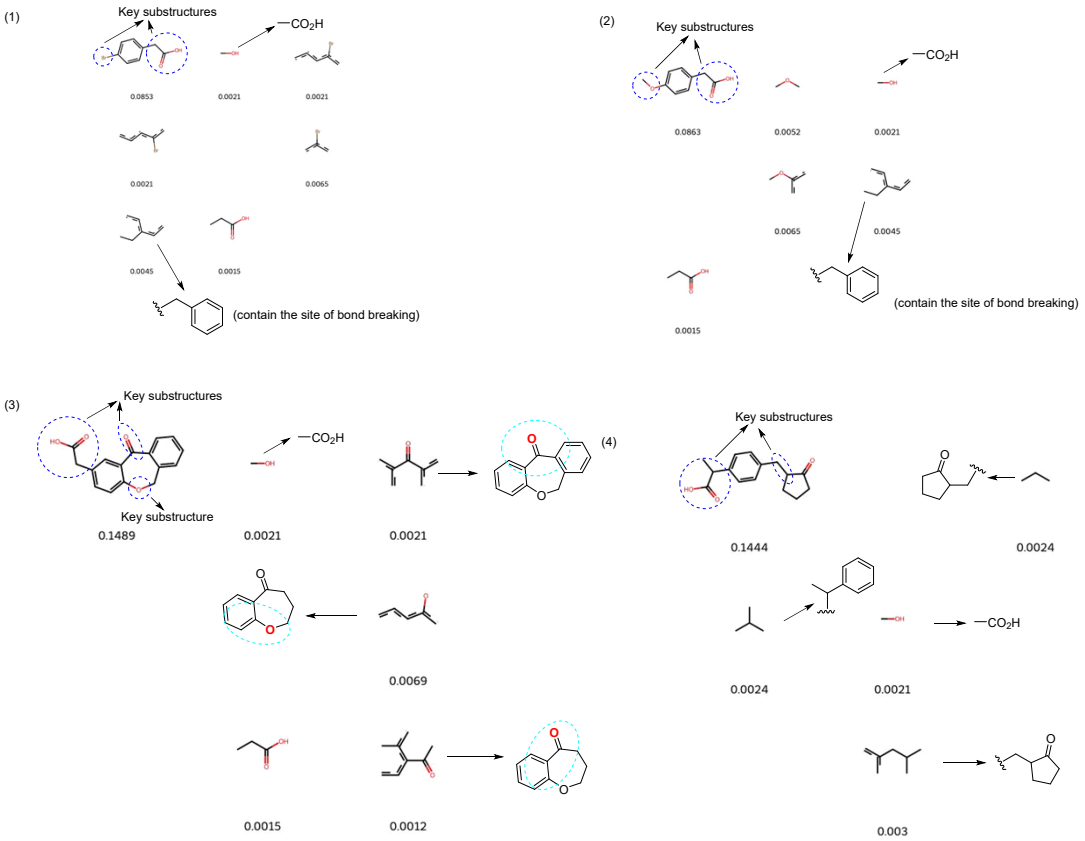


Figure S_2 Key substructures of some representative acids

Besides, the model proposed that different diselane compounds owned different key substructures (Figure S_3). The results were consistent with the BDE data of Se–Se bond. The low BDE of 1,2-diphenyldiselane (~42 kcal/mol, *Chem. Mater.* **2018**, *30*, 5704) led to the stability of resulting radical is more important for the trapping of alkyl radical intermediate. In contrast, 1,2-diethyldiselane with higher BDE (~56.41 kcal/mol, *ACS Nano* **2013**, *7*, 3616–3626) resulting in the dissociation of Se–Se bond was more important.

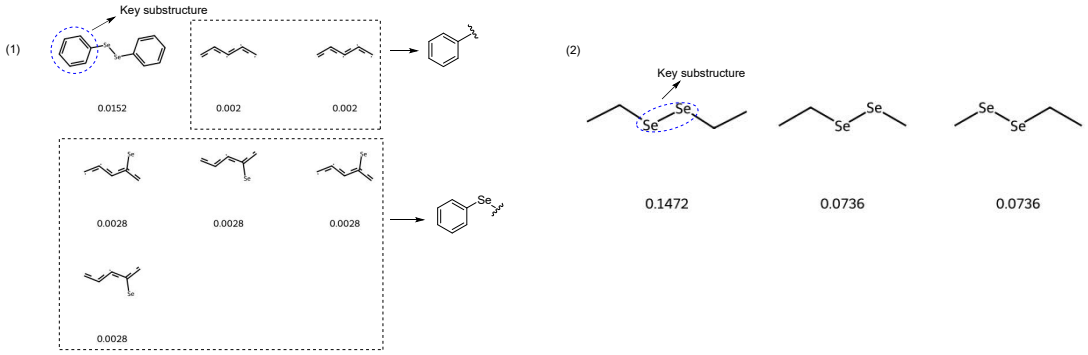


Figure S_3 Different diselanes with different key substructures

Finally, the model found that the nitrogen atom which was served as one electron donor, nitrogen substituentand the substituent at the 3-position of DHP, which may both affect the reduction potential, were important for the reaction (Figure S_4) .

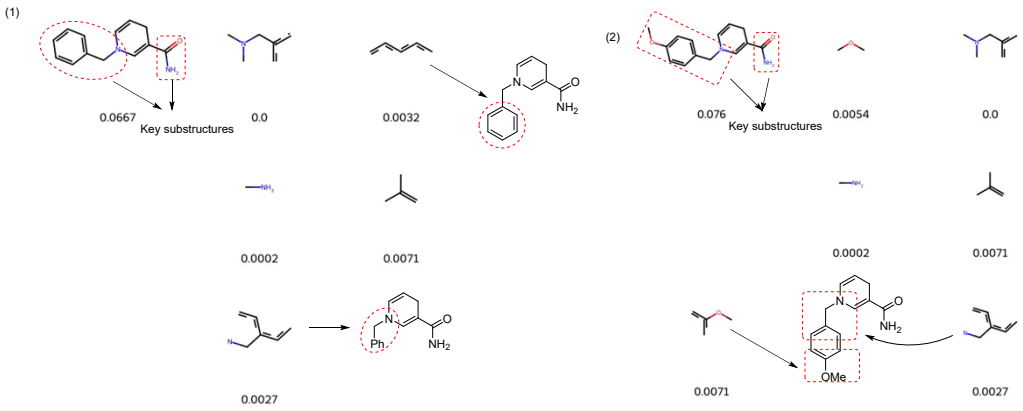
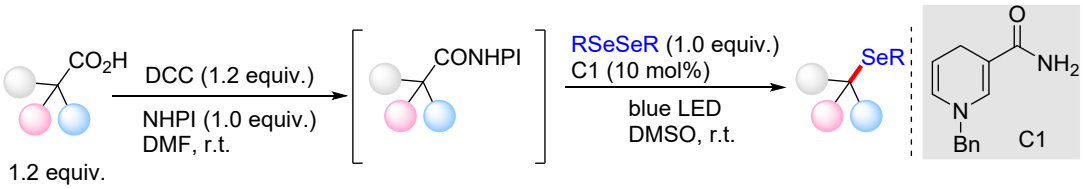


Figure S_4 Key substructures of some representative DHP derivatives

5. Batch Reaction

5.1 General Procedure (Procedure B) for One-pot Decarboxylative Selenation



In a nitrogen-filled glove box, to an oven-dried 40 mL screw-cap vial equipped with a magnetic stir bar was added carboxylic acid (0.36 mmol, 1.2 equiv), NHPI (48.9 mg, 0.3 mmol, 1.0 equiv), anhydrous DMF (12.0 mL), DCC (74.16 mg, 0.36 mmol, 1.2 equiv) was then added, and the mixture was stirred for 4 h, then the reaction was quenched with water and extracted with ethyl acetate (50 mL*3), the combined organic layer was dried over Na_2SO_4, filtered to remove Na_2SO_4 and concentrated under reduced pressure. The resulting residue was dissolved in DMSO (12 mL), then diselide (0.3 mmol, 1.0 equiv), 1-benzyl-1,4-dihydropyridine-3-carboxamide (6.4 mg, 0.03 mmol, 10 mmol%) was added. The reaction was irradiated under blue light source (15 W) at room temperature for 4 h. The reaction was quenched with water and extracted with ethyl acetate (50 mL*3), the combined organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting residue was purified by silica gel chromatography to afford the desired product.

Note: Light was irradiated from the side of caps

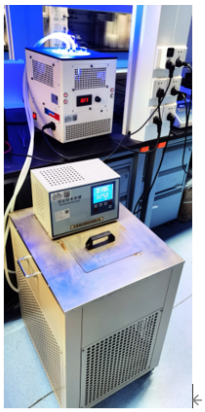
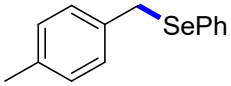


Figure S_5. Equipment used in reaction setup

5.2 Detail of Compound synthesis

5.2.1 The preparation of (4-methylbenzyl)(phenyl)selane[2]



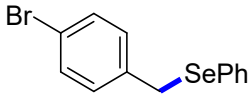
According to the general procedure B, *N*-hydroxyphthalimide (48.9 mg, 0.3 mmol, 1.0 equiv.) 2-(*p*-tolyl)acetic acid (54.1 mg, 0.36 mmol, 1.2 equiv.), diphenyldiselenide (93.6 mg, 0.3 mmol, 1.0 equiv.), and 1-benzyl-1,4-dihydropyridine-3-carboxamide (6.4 mg, 10% mmol.) were used. The crude product was purified by column chromatography on silica gel (petroleum ether/EA = 200:1) to afford final product (50.9 mg, 65%).

(4-Methylbenzyl)(phenyl)selane, colorless oil.

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.53 – 7.47 (m, 2H), 7.30 – 7.25 (m, 3H), 7.14 (d, *J* = 8.0 Hz, 2H), 7.09 (d, *J* = 8.0 Hz, 2H), 4.13 (s, 2H), 2.34 (s, 3H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 136.51, 135.43, 133.30, 130.69, 129.12, 128.94, 128.68, 127.13, 31.96, 21.09.

5.2.3 The preparation of (4-bromobenzyl)(phenyl)selane[2]



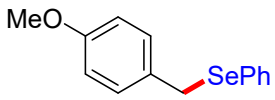
According to the general procedure, *N*-hydroxyphthalimide (48.9 mg, 0.3 mmol, 1.0 equiv.) 2-(4-bromophenyl)acetic acid (77.4 mg, 0.36 mmol, 1.2 equiv.), diphenyldiselenide (93.6 mg, 0.3 mmol, 1.0 equiv.), and 1-benzyl-1,4-dihydropyridine-3-carboxamide (6.4 mg, 10% mmol.) were used. The crude product was purified by column chromatography on silica gel (petroleum ether/EA = 200:1) to afford final product (36.2 mg, 37%).

(4-Bromobenzyl)(phenyl)selane, white solid.

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.45 – 7.41 (m, 2H), 7.38 (d, *J* = 8.4 Hz, 2H), 7.28 – 7.23 (m, 3H), 7.07 (d, *J* = 8.4 Hz, 2H), 4.02 (s, 2H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 138.00, 134.05, 131.61, 130.60, 129.87, 129.21, 127.74, 120.78, 31.64.

5.2.4 The preparation of (4-methoxybenzyl)(phenyl)selane[2]



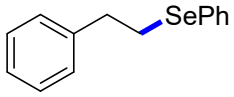
According to the general procedure, *N*-hydroxyphthalimide (48.9 mg, 0.3 mmol, 1.0 equiv.) 2-(4-methoxyphenyl)acetic acid (59.8 mg, 0.36 mmol, 1.2 equiv.), diphenyldiselenide (93.6 mg, 0.3 mmol, 1.0 equiv.), and 1-benzyl-1,4-dihydropyridine-3-carboxamide (6.4 mg, 10% mmol.) were used. The crude product was purified by column chromatography on silica gel (petroleum ether/EA = 200:1) to afford final product (35.8 mg, 43%).

(4-Methoxybenzyl)(phenyl)selane, white solid.

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.49 – 7.40 (m, 2H), 7.26 – 7.22 (m, 3H), 7.13 (d, *J* = 8.6 Hz, 2H), 6.78 (d, *J* = 8.6 Hz, 2H), 4.08 (s, 2H), 3.77 (s, 3H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 158.65, 133.60, 130.75, 130.69, 130.06, 129.09, 127.32, 113.98, 55.39, 31.86.

5.2.5 The preparation of phenethyl(phenyl)selane[3]



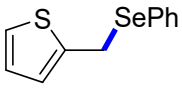
According to the general procedure, *N*-hydroxyphthalimide (48.9 mg, 0.3 mmol, 1.0 equiv.) 3-phenylpropanoic acid (54.1 mg, 0.36 mmol, 1.2 equiv.), diphenyldiselenide (93.6 mg, 0.3 mmol, 1.0 equiv.), and 1-benzyl-1,4-dihydropyridine-3-carboxamide (6.4 mg, 10% mmol.) were used. The crude product was purified by column chromatography on silica gel (petroleum ether/EA = 300:1) to afford final product (57.2 mg, 65%).

Phenethyl(phenyl)selane, colorless oil.

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.59 – 7.52 (m, 2H), 7.37 – 7.29 (m, 5H), 7.28 – 7.25 (m, 1H), 7.25 – 7.19 (m, 2H), 3.21 – 3.17 (m, 2H), 3.04 (dd, *J* = 9.1, 6.9 Hz, 2H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 140.98, 132.56, 130.17, 129.05, 128.47, 128.35, 126.82, 126.37, 36.56, 28.66.

5.2.6 The preparation of 2-((phenylselanyl)methyl)thiophene



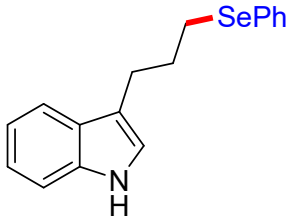
According to the general procedure, *N*-hydroxyphthalimide (48.9 mg, 0.3 mmol, 1.0 equiv.), 2-(thiophen-2-yl)acetic acid (51.2 mg, 0.36 mmol, 1.2 equiv.), diphenyldiselenide (93.6 mg, 0.3 mmol, 1.0 equiv.), and 1-benzyl-1,4-dihydropyridine-3-carboxamide (6.4 mg, 10% mmol.) were used. The crude product was purified by column chromatography on silica gel (petroleum ether/EA = 300:1) to afford final product (38.7 mg, 51%).

2-((Phenylselanyl)methyl)thiophene, colorless oil.

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.44 – 7.42 (m, 2H), 7.22 – 7.20 (m, 3H), 7.10 (dd, *J* = 5.1, 1.2 Hz, 1H), 6.80 (dd, *J* = 5.2, 3.5 Hz, 1H), 6.74 (dq, *J* = 3.5, 0.9 Hz, 1H), 4.26 (s, 2H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 141.80, 133.77, 130.15, 129.07, 127.57, 126.79, 126.21, 124.76, 25.77.

5.2.7 The preparation of 3-(3-(phenylselanyl)propyl)-1H-indole



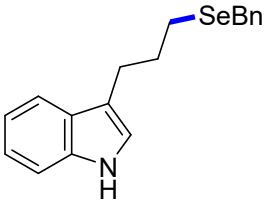
According to the general procedure, *N*-hydroxyphthalimide (48.9 mg, 0.3 mmol, 1.0 equiv.), 4-(1H-indol-3-yl)butanoic acid (73.2 mg, 0.36 mmol, 1.2 equiv.), diphenyldiselenide (93.6 mg, 0.3 mmol, 1.0 equiv.), and 1-benzyl-1,4-dihydropyridine-3-carboxamide (6.4 mg, 10% mmol.) were used. The crude product was purified by column chromatography on silica gel (petroleum ether/EA = 10:1) to afford final product (61.3 mg, 65%).

3-(3-(Phenylselanyl)propyl)-1H-indole, yellowish oil.

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.92 (s, 1H), 7.62 (d, *J* = 7.9 Hz, 1H), 7.52 (dd, *J* = 7.4, 2.1 Hz, 2H), 7.38 (d, *J* = 8.1 Hz, 1H), 7.30 – 7.26 (m, 3H), 7.24 (t, *J* = 7.6 Hz, 1H), 7.15 (t, *J* = 7.4 Hz, 1H), 6.97 (d, *J* = 2.4 Hz, 1H), 3.02 (t, *J* = 7.3 Hz, 2H), 2.94 (t, *J* = 7.3 Hz, 2H), 2.17 (p, *J* = 7.3 Hz, 2H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 136.29, 132.38, 130.45, 128.97, 127.37, 126.59, 121.92, 121.43, 119.17, 118.89, 115.41, 111.04, 30.22, 27.46, 25.01.

5.2.8 The preparation of 3-(3-(benzylselanyl)propyl)-1H-indole



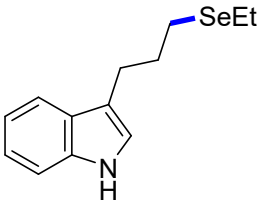
According to the general procedure, *N*-hydroxyphthalimide (48.9 mg, 0.3 mmol, 1.0 equiv.), 4-(1H-indol-3-yl)butanoic acid (73.2 mg, 0.36 mmol, 1.2 equiv.), dibenzyldiselenide (102.1 mg, 0.3 mmol, 1.0 equiv.), and 1-benzyl-1,4-dihydropyridine-3-carboxamide (6.4 mg, 10% mmol.) were used. The crude product was purified by column chromatography on silica gel (petroleum ether/EA = 20:1) to afford final product (60.1 mg, 61%).

3-(3-(Benzylselanyl)propyl)-1H-indole, yellowish oil.

^{1}H NMR (600 MHz, Chloroform-d) δ 7.97 – 7.87 (m, 1H), 7.62 (dd, *J* = 7.9, 1.0 Hz, 1H), 7.39 (dt, *J* = 8.2, 1.0 Hz, 1H), 7.30 – 7.25 (m, 4H), 7.23 (ddd, *J* = 8.3, 4.9, 1.4 Hz, 2H), 7.17 – 7.14 (m, 1H), 6.96 (t, *J* = 1.7 Hz, 1H), 3.80 (s, 2H), 2.87 (td, *J* = 7.5, 1.0 Hz, 2H), 2.59 (t, *J* = 7.4 Hz, 2H), 2.08 (q, *J* = 7.5 Hz, 2H).

^{13}C NMR (151 MHz, Chloroform-d) δ 139.72, 136.45, 128.94, 128.57, 127.56, 126.69, 122.07, 121.53, 119.32, 119.05, 115.77, 111.19, 30.66, 26.99, 25.35, 23.83.

5.2.9 The preparation of 3-(3-(ethylselanyl)propyl)-1H-indole



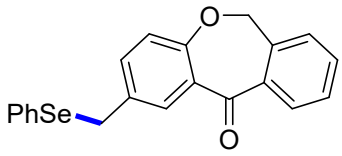
According to the general procedure, *N*-hydroxyphthalimide (48.9 mg, 0.3 mmol, 1.0 equiv.), 4-(1H-indol-3-yl)butanoic acid (73.2 mg, 0.36 mmol, 1.2 equiv.), diethyldiselenide (64.8 mg, 0.3 mmol, 1.0 equiv.), and 1-benzyl-1,4-dihydropyridine-3-carboxamide (6.4 mg, 10% mmol.) were used. The crude product was purified by column chromatography on silica gel (petroleum ether/EA = 20:1) to afford final product (53.5 mg, 67%).

3-(3-(Ethylselanyl)propyl)-1H-indole, yellowish oil.

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.91 (s, 1H), 7.64 (dt, *J* = 7.9, 1.0 Hz, 1H), 7.36 (dt, *J* = 8.1, 1.0 Hz, 1H), 7.22 (ddd, *J* = 8.2, 7.1, 1.2 Hz, 1H), 7.14 (tt, *J* = 7.8, 0.9 Hz, 1H), 6.99 (dd, *J* = 2.2, 1.0 Hz, 1H), 2.92 – 2.88 (m, 2H), 2.67 (t, *J* = 7.4 Hz, 2H), 2.60 (q, *J* = 7.5 Hz, 2H), 2.11 (p, *J* = 7.3 Hz, 2H), 1.45 – 1.39 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 136.43, 127.57, 122.03, 121.48, 119.28, 119.03, 115.84, 111.18, 30.92, 25.37, 23.30, 17.27, 15.97.

5.2.10 The preparation of 2-((phenylselanyl)methyl)dibenzo[b,e]oxepin-11(6H)-one

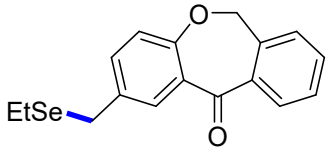


According to the general procedure, *N*-hydroxyphthalimide (48.9 mg, 0.3 mmol, 1.0 equiv.), Isoxepac (96.6 mg, 0.36 mmol, 1.2 equiv.), diphenyldiselenide (93.6 mg, 0.3 mmol, 1.0 equiv.), and 1-benzyl-1,4-dihydropyridine-3-carboxamide (6.4 mg, 10% mmol.) were used. The crude product was purified by column chromatography on silica gel (petroleum ether/EA = 20:1) to afford final product (85.3 mg, 75%).

2-((phenylselanyl)methyl)dibenzo[b,e]oxepin-11(6H)-one

^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.02 (d, *J* = 2.5 Hz, 1H), 7.90 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.58 (td, *J* = 7.4, 1.4 Hz, 1H), 7.51 – 7.46 (m, 3H), 7.39 – 7.35 (m, 2H), 7.29 – 7.24 (m, 3H), 6.97 (d, *J* = 8.4 Hz, 1H), 5.18 (s, 2H), 4.14 (s, 2H). **^{13}C NMR (151 MHz, Chloroform-*d*)** δ 190.69, 160.15, 140.43, 135.86, 135.40, 133.79, 132.68, 132.40, 131.72, 129.89, 129.38, 129.22, 129.00, 127.75, 127.45, 124.85, 120.90, 73.52, 31.23.

5.2.11 The preparation of 2-((ethylselanyl)methyl)dibenzo[b,e]oxepin-11(6H)-one



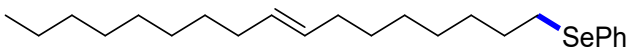
According to the general procedure, *N*-hydroxyphthalimide (48.9 mg, 0.3 mmol, 1.0 equiv.), Isoxepac (96.6 mg, 0.36 mmol, 1.2 equiv.), diethyldiselenide (64.8 mg, 0.3 mmol, 1.0 equiv.), and 1-benzyl-1,4-dihydropyridine-3-carboxamide (6.4 mg, 10% mmol.) were used. The crude product was purified by column chromatography on silica gel (petroleum ether/EA = 30:1) to afford final product (55.6 mg, 56%).

2-((ethylselanyl)methyl)dibenzo[b,e]oxepin-11(6H)-one

^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.09 (d, *J* = 2.5 Hz, 1H), 7.89 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.57 – 7.53 (m, 1H), 7.49 – 7.45 (m, 2H), 7.36 (dd, *J* = 7.5, 1.2 Hz, 1H), 7.00 (d, *J* = 8.4 Hz, 1H), 5.18 (s, 2H), 3.79 (s, 2H), 2.52 (q, *J* = 7.5 Hz, 2H), 1.38 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 190.95, 160.23, 140.56, 136.13, 135.66, 133.60, 132.87, 131.43, 129.63, 129.37, 127.91, 124.99, 121.29, 73.74, 25.77, 17.67, 15.62.

5.2.12 The preparation of (*E*)-heptadec-8-en-1-yl(phenyl)selane



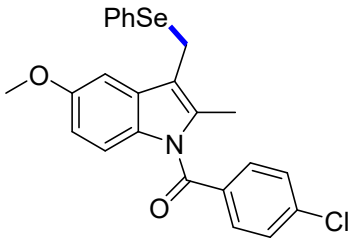
According to the general procedure, *N*-hydroxyphthalimide (48.9 mg, 0.3 mmol, 1.0 equiv.), Oleic acid (101.7 mg, 0.36 mmol, 1.2 equiv.), diphenyldiselenide (93.6 mg, 0.3 mmol, 1.0 equiv.), and 1-benzyl-1,4-dihydropyridine-3-carboxamide (6.4 mg, 10% mmol.) were used. The crude product was purified by column chromatography on silica gel (petroleum ether/EA = 500:1) to afford final product (80.3 mg, 68%).

(E)-heptadec-8-en-1-yl(phenyl)selane, colorless oil.

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.51 – 7.45 (m, 2H), 7.27 – 7.22 (m, 3H), 5.34 (dd, *J* = 4.6, 1.0 Hz, 2H), 2.93 – 2.89 (m, 2H), 2.01 (q, *J* = 6.9, 6.2 Hz, 4H), 1.70 (p, *J* = 7.5 Hz, 2H), 1.42 – 1.37 (m, 2H), 1.34 – 1.26 (m, 18H), 0.88 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 132.49, 130.84, 130.15, 129.89, 129.11, 126.71, 32.06, 30.26, 29.94, 29.92, 29.81, 29.67, 29.47, 29.27, 29.12, 28.07, 27.36, 27.30, 22.84, 14.27.

5.2.13 The preparation of (4-chlorophenyl)(5-methoxy-2-methyl-3-((phenylselanyl)methyl)-1H-indol-1-yl)methanone



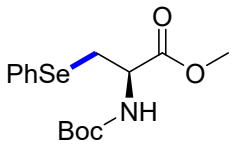
According to the general procedure, *N*-hydroxyphthalimide (48.9 mg, 0.3 mmol, 1.0 equiv.), Indometacin (128.8 mg, 0.36 mmol, 1.2 equiv.), diphenyldiselenide (93.6 mg, 0.3 mmol, 1.0 equiv.), and 1-benzyl-1,4-dihydropyridine-3-carboxamide (6.4 mg, 10% mmol.) were used. The crude product was purified by column chromatography on silica gel (petroleum ether/EA = 10:1) to afford final product (71.7 mg, 51%).

(4-Chlorophenyl)(5-methoxy-2-methyl-3-((phenylselanyl)methyl)-1H-indol-1-yl)methanone, yellowish oil.

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.62 – 7.57 (m, 2H), 7.52 – 7.45 (m, 4H), 7.35 – 7.30 (m, 1H), 7.28 – 7.24 (m, 2H), 6.99 (d, *J* = 2.5 Hz, 1H), 6.94 (d, *J* = 9.0 Hz, 1H), 6.71 (dd, *J* = 9.0, 2.5 Hz, 1H), 4.18 (s, 2H), 3.85 (s, 3H), 2.01 (s, 3H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 168.09, 155.89, 139.17, 135.32, 135.08, 133.85, 131.11, 130.91, 129.90, 129.76, 129.04, 128.85, 127.77, 116.10, 114.98, 111.79, 101.51, 55.68, 21.32, 12.93.

5.2.14 The preparation of methyl (*R*)-2-((tert-butoxycarbonyl)amino)-3-(phenylselanyl)propanoate



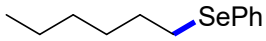
According to the general procedure, *N*-hydroxyphthalimide (48.9 mg, 0.3 mmol, 1.0 equiv.), *N*-Boc Asp(OH)Ome (89.0 mg, 0.36 mmol, 1.2 equiv.), diphenyldiselenide (93.6 mg, 0.3 mmol, 1.0 equiv.), and 1-benzyl-1,4-dihydropyridine-3-carboxamide (6.4 mg, 10% mmol.) were used. The crude product was purified by column chromatography on silica gel (petroleum ether/EA = 20:1) to afford final product (49.4 mg, 46%).

methyl (*R*)-2-((tert-butoxycarbonyl)amino)-3-(phenylselanyl)propanoate, yellowish oil.

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.46 (dd, *J* = 6.5, 3.0 Hz, 2H), 7.19 – 7.17 (m, 3H), 5.28 (d, *J* = 7.5 Hz, 1H), 4.65 – 4.53 (m, 1H), 3.41 (s, 3H), 3.25 (d, *J* = 4.9 Hz, 2H), 1.34 (s, 9H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 171.22, 155.09, 133.88, 129.27, 129.01, 127.69, 80.21, 53.39, 52.40, 30.82, 28.40.

5.2.15 The preparation of hexyl(phenyl)selane[4]



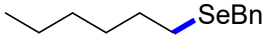
According to the general procedure, *N*-hydroxyphthalimide (48.9 mg, 0.3 mmol, 1.0 equiv.), Heptanoic acid (46.9 mg, 0.36 mmol, 1.2 equiv.), diphenyldiselenide (93.6 mg, 0.3 mmol, 1.0 equiv.), and 1-benzyl-1,4-dihydropyridine-3-carboxamide (6.4 mg, 10% mmol.) were used. The crude product was purified by column chromatography on silica gel (petroleum ether/EA = 20:1) to afford final product (40.5 mg, 56%).

Hexyl(phenyl)selane, colorless oil.

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.53 – 7.44 (m, 2H), 7.28 – 7.22 (m, 3H), 2.94 – 2.90 (m, 2H), 1.74 – 1.68 (m, 2H), 1.43 – 1.38 (m, 2H), 1.31 – 1.26 (m, 4H), 0.89 – 0.86 (m, 3H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 132.48, 130.85, 129.11, 126.71, 31.43, 30.26, 29.67, 28.10, 22.68, 14.17.

5.2.16 The preparation of benzyl(hexyl)selane



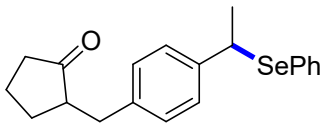
According to the general procedure, *N*-hydroxyphthalimide (48.9 mg, 0.3 mmol, 1.0 equiv.), Heptanoic acid (46.9 mg, 0.36 mmol, 1.2 equiv.), dibenzyl diselenide (102.1 mg, 0.3 mmol, 1.0 equiv.), and 1-benzyl-1,4-dihydropyridine-3-carboxamide (6.4 mg, 10% mmol.) were used. The crude product was purified by column chromatography on silica gel (petroleum ether/EA = 20:1) to afford final product (16.1 mg, 21%).

Benzyl(hexyl)selane, colorless oil.

^{1}H NMR (600 MHz, Chloroform-d) δ 7.29 (d, J = 4.7 Hz, 4H), 7.24 – 7.18 (m, 1H), 3.77 (s, 2H), 2.52 – 2.48 (m, 2H), 1.65 – 1.60 (m, 2H), 1.37 – 1.31 (m, 2H), 1.27 (dtd, J = 17.9, 11.0, 9.8, 5.1 Hz, 4H), 0.88 (t, J = 7.1 Hz, 3H).

^{13}C NMR (151 MHz, Chloroform-d) δ 139.78, 128.93, 128.57, 126.70, 31.47, 30.38, 29.77, 27.05, 24.26, 22.67, 14.17.

5.2.17 The preparation of 2-(4-(1-(phenylselanyl)ethyl)benzyl)cyclopentan-1-one



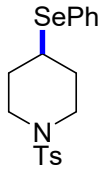
According to the general procedure, *N*-hydroxyphthalimide (48.9 mg, 0.3 mmol, 1.0 equiv.), Loxoprofen (88.7 mg, 0.36 mmol, 1.2 equiv.), diphenyldiselenide (93.6 mg, 0.3 mmol, 1.0 equiv.), and 1-benzyl-1,4-dihydropyridine-3-carboxamide (6.4 mg, 10% mmol.) were used. The crude product was purified by column chromatography on silica gel (petroleum ether/EA = 20:1) to afford final product (78.3 mg, 73%).

2-(4-(1-(phenylselanyl)ethyl)benzyl)cyclopentan-1-one, yellowish oil.

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.49 – 7.41 (m, 2H), 7.30 – 7.27 (m, 1H), 7.24 (t, *J* = 7.5 Hz, 2H), 7.18 (d, *J* = 7.9 Hz, 2H), 7.07 (d, *J* = 7.9 Hz, 2H), 4.47 (dd, *J* = 7.1, 2.0 Hz, 1H), 3.12 (dd, *J* = 14.0, 4.3 Hz, 1H), 2.53 (dd, *J* = 14.0, 9.4 Hz, 1H), 2.36 (ddd, *J* = 19.7, 8.2, 2.6 Hz, 2H), 2.17 – 2.05 (m, 2H), 1.97 (ddd, *J* = 8.8, 4.4, 2.2 Hz, 1H), 1.76 (d, *J* = 7.1 Hz, 3H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 141.32, 141.30, 138.60, 135.41, 129.87, 128.78, 128.72, 127.72, 127.24, 50.91, 42.17, 42.14, 38.20, 35.14, 29.06, 29.04, 22.12, 22.10, 20.52.

5.2.18 The preparation of 4-(phenylselanyl)-1-tosylpiperidine



According to the general procedure, *N*-hydroxyphthalimide (48.9 mg, 0.3 mmol, 1.0 equiv.), 1-tosylpiperidine-4-carboxylic acid (102.0 mg, 0.36 mmol, 1.2 equiv.), diphenyldiselenide (93.6 mg, 0.3 mmol, 1.0 equiv.), and 1-benzyl-1,4-dihydropyridine-3-carboxamide (6.4 mg, 10% mmol.) were used. The crude product was purified by column chromatography on silica gel (petroleum ether/EA = 5:1) to afford final product (106.5 mg, 89%).

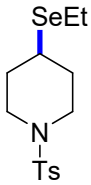
4-(phenylselanyl)-1-tosylpiperidine, white solid.

^{1}H NMR (600 MHz, Chloroform-d) δ 7.63 (d, *J* = 8.3 Hz, 2H), 7.52 (d, *J* = 8.3 Hz, 2H), 7.32 (m, 3H), 7.29 – 7.26 (m, 2H), 3.57 (dt, *J* = 10.2, 4.1 Hz, 2H), 3.09 (tt, *J* = 10.4, 3.9 Hz, 1H), 2.54 (ddd, *J* = 12.5, 10.5, 3.0 Hz, 2H), 2.45 (s, 3H), 2.06 (dd, *J* = 13.6, 3.9 Hz, 2H), 1.83 (dtd, *J* = 14.0, 10.3, 3.9 Hz, 2H).

^{13}C NMR (101 MHz, CDCl3) δ (ppm) = 170.9, 162.1, 138.2, 134.7, 134.6, 132.2, 129.0, 123.9, 123.9, 49.7, 46.5, 42.6, 40.7, 29.6.

HRMS (ESI): $[M+H]^+$ calcd for $C_{18}H_{22}NO_2SSe^+$ 396.0531, found 396.0529.

5.2.19 The preparation of 4-(ethylselanyl)-1-tosylpiperidine



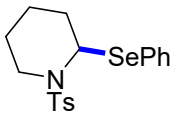
According to the general procedure, *N*-hydroxyphthalimide (48.9 mg, 0.3 mmol, 1.0 equiv.), 1-tosylpiperidine-4-carboxylic acid (102.0 mg, 0.36 mmol, 1.2 equiv.), diethyldiselenide (64.8 mg, 0.3 mmol, 1.0 equiv.), and 1-benzyl-1,4-dihydropyridine-3-carboxamide (6.4 mg, 10% mmol.) were used. The crude product was purified by column chromatography on silica gel (petroleum ether/EA = 50:1) to afford final product (49 mg, 47%).

4-(Ethylselanyl)-1-tosylpiperidine, yellowish oil.

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.68 – 7.59 (m, 2H), 7.38 – 7.29 (m, 2H), 3.59 – 3.42 (m, 2H), 2.87 – 2.76 (m, 1H), 2.61 – 2.52 (m, 4H), 2.43 (s, 3H), 2.10 – 2.02 (m, 2H), 1.81 (dtd, *J* = 13.7, 10.0, 3.8 Hz, 2H), 1.35 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 143.68, 133.30, 129.80, 127.81, 46.35, 33.79, 32.87, 21.68, 16.39, 16.05.

5.2.20 The preparation of 2-(phenylselanyl)-1-tosylpiperidine



According to the general procedure, *N*-hydroxyphthalimide (48.9 mg, 0.3 mmol, 1.0 equiv.), 1-tosylpiperidine-2-carboxylic acid (102.0 mg, 0.36 mmol, 1.2 equiv.), diphenyldiselenide (93.6 mg, 0.3 mmol, 1.0 equiv.), and 1-benzyl-

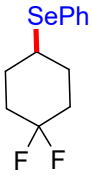
1,4-dihydropyridine-3-carboxamide (6.4 mg, 10% mmol.) were used. The crude product was purified by column chromatography on silica gel (petroleum ether/EA = 5:1) to afford final product (61.5 mg, 52%).

2-(Phenylselanyl)-1-tosylpiperidine, white solid.

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.59 (d, *J* = 8.4 Hz, 2H), 7.56 – 7.51 (m, 2H), 7.30 – 7.25 (m, 3H), 7.20 (d, *J* = 8.3 Hz, 2H), 5.93 – 5.89 (m, 1H), 3.73 – 3.68 (m, 1H), 3.09 – 3.03 (m, 1H), 2.39 (s, 3H), 1.91 (dtd, *J* = 13.6, 10.2, 9.7, 6.4 Hz, 2H), 1.83 – 1.76 (m, 1H), 1.65 (td, *J* = 12.3, 11.5, 6.2 Hz, 2H), 1.49 – 1.41 (m, 1H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 143.52, 136.56, 135.34, 129.60, 129.28, 129.02, 128.02, 127.89, 61.55, 42.59, 32.86, 24.95, 21.70, 20.07.

5.2.21 The preparation of (4,4-difluorocyclohexyl)(phenyl)selane



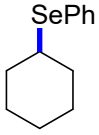
According to the general procedure, *N*-hydroxyphthalimide (48.9 mg, 0.3 mmol, 1.0 equiv.), 4,4-difluorocyclohexane-1-carboxylic acid (59.0 mg, 0.36 mmol, 1.2 equiv.), diphenyldiselenide (93.6 mg, 0.3 mmol, 1.0 equiv.), and 1-benzyl-1,4-dihydropyridine-3-carboxamide (6.4 mg, 10% mmol.) were used. The crude product was purified by column chromatography on silica gel (petroleum ether/EA = 500:1) to afford final product (47.6 mg, 56%).

(4,4-difluorocyclohexyl)(phenyl)selane, colorless oil.

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.65 – 7.57 (m, 2H), 7.35 – 7.30 (m, 3H), 3.35 (tt, *J* = 9.1, 6.3, 5.0 Hz, 1H), 2.22 – 2.13 (m, 2H), 2.13 – 2.05 (m, 2H), 1.84 (tdd, *J* = 16.2, 13.8, 7.1 Hz, 4H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 135.06, 129.09, 128.41, 127.84, 122.64 (t, *J* = 241.1 Hz), 39.52, 33.21 (t, *J* = 24.0 Hz), 29.60 (t, *J* = 4.9 Hz).

5.2.22 The preparation of cyclohexyl(phenyl)selane



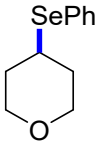
According to the general procedure, *N*-hydroxyphthalimide (48.9 mg, 0.3 mmol, 1.0 equiv.), cyclohexanecarboxylic acid (46.1 mg, 0.36 mmol, 1.2 equiv.), diphenyldiselenide (93.6 mg, 0.3 mmol, 1.0 equiv.), and 1-benzyl-1,4-dihydropyridine-3-carboxamide (6.4 mg, 10% mmol.) were used. The crude product was purified by column chromatography on silica gel (petroleum ether/EA = 500:1) to afford final product (40.9 mg, 57%).

Cyclohexyl(phenyl)selane, colorless oil.

^{1}H NMR (600 MHz, Chloroform-d) δ 7.58 – 7.50 (m, 2H), 7.27 – 7.24 (m, 3H), 3.25 (tt, J = 10.8, 3.7 Hz, 1H), 2.04 – 2.00 (m, 2H), 1.74 (dq, J = 12.8, 4.0 Hz, 2H), 1.63 – 1.58 (m, 1H), 1.54 – 1.47 (m, 2H), 1.34 – 1.25 (m, 3H).

^{13}C NMR (151 MHz, Chloroform-d) δ 134.83, 131.63, 128.97, 127.33, 43.38, 34.36, 27.00, 25.88.

5.2.23 The preparation of 4-(phenylselanyl)tetrahydro-2H-pyran



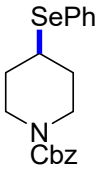
According to the general procedure, *N*-hydroxyphthalimide (48.9 mg, 0.3 mmol, 1.0 equiv.), tetrahydro-2H-pyran-4-carboxylic acid (46.8 mg, 0.36 mmol, 1.2 equiv.), diphenyldiselenide (93.6 mg, 0.3 mmol, 1.0 equiv.), and 1-benzyl-1,4-dihydropyridine-3-carboxamide (6.4 mg, 10% mmol.) were used. The crude product was purified by column chromatography on silica gel (petroleum ether/EA = 500:1) to afford final product (61.5 mg, 55%).

4-(Phenylselanyl)tetrahydro-2H-pyran, colorless oil.

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.57 (dd, *J* = 7.7, 2.0 Hz, 2H), 7.32 – 7.24 (m, 3H), 3.93 (dt, *J* = 11.8, 3.9 Hz, 2H), 3.42 (td, *J* = 11.0, 2.5 Hz, 2H), 3.38 (ddd, *J* = 10.8, 6.8, 4.0 Hz, 1H), 1.94 (dd, *J* = 13.4, 3.8 Hz, 2H), 1.80 (dtd, *J* = 14.8, 10.7, 4.2 Hz, 2H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 135.24, 128.96, 127.97, 127.71, 68.00, 38.70, 33.96.

5.2.24 The preparation of benzyl 4-(phenylselanyl)piperidine-1-carboxylate



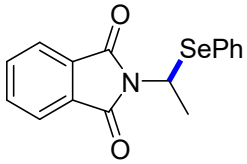
According to the general procedure, *N*-hydroxyphthalimide (48.9 mg, 0.3 mmol, 1.0 equiv.), 1-((benzyloxy)carbonyl)piperidine-4-carboxylic acid (94.8 mg, 0.36 mmol, 1.2 equiv.), diphenyldiselenide (93.6 mg, 0.3 mmol, 1.0 equiv.), and 1-benzyl-1,4-dihydropyridine-3-carboxamide (6.4 mg, 10% mmol.) were used. The crude product was purified by column chromatography on silica gel (petroleum ether/EA = 10:1) to afford final product (94.3 mg, 84%).

Benzyl 4-(phenylselanyl)piperidine-1-carboxylate, yellowish oil.

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.60 – 7.53 (m, 2H), 7.39 – 7.26 (m, 8H), 5.11 (s, 2H), 3.99 (s, 2H), 3.33 (ddd, *J* = 10.3, 6.4, 3.8 Hz, 1H), 3.02 (t, *J* = 11.5 Hz, 2H), 1.98 (d, *J* = 14.0 Hz, 2H), 1.67 (d, *J* = 11.6 Hz, 2H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 155.07, 136.68, 135.25, 129.00, 128.42, 127.92, 127.90, 127.81, 127.78, 67.04, 44.11, 39.66.

5.2.25 The preparation of 2-(1-(phenylselanyl)ethyl)isoindoline-1,3-dione



According to the general procedure, *N*-hydroxyphthalimide (48.9 mg, 0.3 mmol, 1.0 equiv.), PHT-ALA-OH (78.9 mg, 0.36 mmol, 1.2 equiv.), diphenyldiselenide (93.6 mg, 0.3 mmol, 1.0 equiv.), and 1-benzyl-1,4-dihydropyridine-3-carboxamide (6.4 mg, 10% mmol.) were used. The crude product was purified by column chromatography on silica

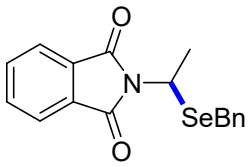
gel (petroleum ether/EA = 10:1) to afford final product (70.3 mg, 71%).

2-(1-(Phenylselanyl)ethyl)isoindoline-1,3-dione, yellowish oil.

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.79 (dt, *J* = 4.9, 2.5 Hz, 2H), 7.70 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.56 (dt, *J* = 7.0, 1.3 Hz, 2H), 7.29 – 7.23 (m, 1H), 7.22 – 7.16 (m, 2H), 5.82 (q, *J* = 7.2 Hz, 1H), 2.01 (dd, *J* = 7.3, 1.8 Hz, 3H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 166.80, 135.41, 134.01, 131.60, 128.97, 128.64, 128.22, 123.20, 46.54, 21.13.

5.2.26 The preparation of 2-(1-(benzylselanyl)ethyl)isoindoline-1,3-dione



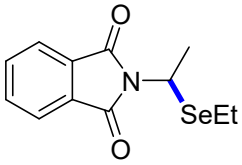
According to the general procedure, *N*-hydroxyphthalimide (48.9 mg, 0.3 mmol, 1.0 equiv.), PHT-ALA-OH (78.9 mg, 0.36 mmol, 1.2 equiv.), dibenzyl diselenide (102.1 mg, 0.3 mmol, 1.0 equiv.), and 1-benzyl-1,4-dihydropyridine-3-carboxamide (6.4 mg, 10% mmol.) were used. The crude product was purified by column chromatography on silica gel (petroleum ether/EA = 20:1) to afford final product (82.6 mg, 80%).

2-(1-(benzylselanyl)ethyl)isoindoline-1,3-dione, yellowish oil.

^{1}H NMR (600 MHz, Chloroform-d) δ 7.80 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.71 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.36 – 7.30 (m, 2H), 7.18 (dd, *J* = 8.7, 6.8 Hz, 2H), 7.07 (t, *J* = 7.4 Hz, 1H), 5.67 (q, *J* = 7.3 Hz, 1H), 4.01 – 3.92 (m, 2H), 1.88 (d, *J* = 7.3 Hz, 3H).

^{13}C NMR (151 MHz, Chloroform-d) δ 167.17, 138.51, 133.95, 131.78, 128.75, 128.39, 126.56, 123.21, 42.53, 28.67, 21.37.

5.2.27 The preparation of 2-(1-(ethylselanyl)ethyl)isoindoline-1,3-dione



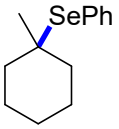
According to the general procedure, *N*-hydroxyphthalimide (48.9 mg, 0.3 mmol, 1.0 equiv.), PHT-ALA-OH (78.9 mg, 0.36 mmol, 1.2 equiv.), diethyldiselenide (64.8 mg, 0.3 mmol, 1.0 equiv.), and 1-benzyl-1,4-dihydropyridine-3-carboxamide (6.4 mg, 10% mmol.) were used. The crude product was purified by column chromatography on silica gel (petroleum ether/EA = 20:1) to afford final product (60.1 mg, 71%).

2-(1-(ethylselanyl)ethyl)isoindoline-1,3-dione, yellowish oil.

^{1}H NMR (600 MHz, Chloroform-d) δ 7.83 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.71 (dd, *J* = 5.4, 3.0 Hz, 2H), 5.62 (q, *J* = 7.4 Hz, 1H), 2.70 (ddq, *J* = 54.0, 12.0, 7.5 Hz, 2H), 1.93 (d, *J* = 7.3 Hz, 3H), 1.40 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (151 MHz, Chloroform-d) δ 167.41, 134.24, 131.97, 123.47, 41.76, 21.61, 18.85, 15.95.

5.2.28 The preparation of (1-methylcyclohexyl)(phenyl)selane



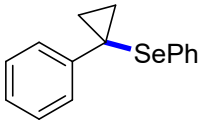
According to the general procedure, *N*-hydroxyphthalimide (48.9 mg, 0.3 mmol, 1.0 equiv.), 1-methylcyclohexane-1-carboxylic acid (51.2 mg, 0.36 mmol, 1.2 equiv.), diphenyldiselenide (93.6 mg, 0.3 mmol, 1.0 equiv.), and 1-benzyl-1,4-dihydropyridine-3-carboxamide (6.4 mg, 10% mmol.) were used. The crude product was purified by column chromatography on silica gel (petroleum ether/EA = 200:1) to afford final product (69.1 mg, 91%).

(1-methylcyclohexyl)(phenyl)selane, colorless oil.

^{1}H NMR (600 MHz, Chloroform-d) δ 7.64 (dt, J = 8.2, 1.0 Hz, 2H), 7.40 – 7.35 (m, 1H), 7.32 – 7.29 (m, 2H), 1.78 (tdd, J = 16.5, 15.3, 9.8, 3.5 Hz, 4H), 1.54 (ddt, J = 13.6, 10.2, 5.5 Hz, 3H), 1.47 (ddd, J = 12.9, 9.4, 3.5 Hz, 2H), 1.39 (s, 3H), 1.38 – 1.31 (m, 1H).

^{13}C NMR (151 MHz, Chloroform-d) δ 138.55, 128.66, 128.47, 127.74, 50.00, 39.38, 26.02, 23.38.

5.2.29 The preparation of phenyl(1-phenylcyclopropyl)selane



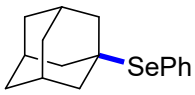
According to the general procedure, *N*-hydroxyphthalimide (48.9 mg, 0.3 mmol, 1.0 equiv.), 1-phenylcyclopropane-1-carboxylic acid (58.4 mg, 0.36 mmol, 1.2 equiv.), diphenyldiselenide (93.6 mg, 0.3 mmol, 1.0 equiv.), and 1-benzyl-1,4-dihydropyridine-3-carboxamide (6.4 mg, 10% mmol.) were used. The crude product was purified by column chromatography on silica gel (petroleum ether/EA = 200:1) to afford final product (45.1 mg, 55%).

Phenyl(1-phenylcyclopropyl)selane, colorless oil.

^{1}H NMR (600 MHz, Chloroform-d) δ 7.43 – 7.38 (m, 2H), 7.28 – 7.19 (m, 7H), 7.17 – 7.12 (m, 1H), 1.43 – 1.41 (m, 2H), 1.35 – 1.33 (m, 2H).

^{13}C NMR (151 MHz, Chloroform-d) δ 145.10, 133.95, 130.59, 128.90, 128.87, 128.17, 127.53, 126.61, 25.80, 16.67.

5.2.30 The preparation of ((3s,5s,7s)-adamantan-1-yl)(phenyl)selane



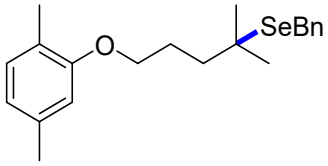
According to the general procedure, *N*-Hydroxyphthalimide (48.9 mg, 0.3 mmol, 1.0 equiv.), 1-Adamantanecarboxylic acid (64.9 mg, 0.36 mmol, 1.2 equiv.), diphenyldiselenide (93.6 mg, 0.3 mmol, 1.0 equiv.), and 1-benzyl-1,4-dihydropyridine-3-carboxamide (6.4 mg, 10% mmol.) were used. The crude product was purified by column chromatography on silica gel (petroleum ether/EA = 20:1) to afford final product (18.3 mg, 21%).

((3s,5s,7s)-adamantan-1-yl)(phenyl)selane, colorless oil.

^{1}H NMR (600 MHz, Chloroform-d) δ 7.64 – 7.56 (m, 2H), 7.41 – 7.33 (m, 1H), 7.33 – 7.27 (m, 2H), 2.00 – 1.92 (m, 9H), 1.69 – 1.61 (m, 6H).

^{13}C NMR (151 MHz, Chloroform-d) δ 138.50, 128.59, 128.45, 126.47, 47.12, 44.78, 36.31, 30.84.

5.2.31 The preparation of benzyl(5-(2,5-dimethylphenoxy)-2-methylpentan-2-yl)selane



According to the general procedure, *N*-hydroxyphthalimide (48.9 mg, 0.3 mmol, 1.0 equiv.), Gemfibrozil (90.1 mg, 0.36 mmol, 1.2 equiv.), dibenzyl diselenide (102.1 mg, 0.3 mmol, 1.0 equiv.), and 1-benzyl-1,4-dihydropyridine-3-carboxamide (6.4 mg, 10% mmol.) were used. The crude product was purified by column chromatography on silica gel (petroleum ether/EA = 20:1) to afford final product (74.3 mg, 66%).

Benzyl(5-(2,5-dimethylphenoxy)-2-methylpentan-2-yl)selane,

^{1}H NMR (600 MHz, Chloroform-d) δ 7.32 (dd, J = 8.0, 1.4 Hz, 2H), 7.28 – 7.24 (m, 2H), 7.22 – 7.13 (m, 1H), 7.00 (d, J = 7.4 Hz, 1H), 6.66 (d, J = 7.5 Hz, 1H), 6.63 – 6.57 (m, 1H), 3.91 (t, J = 6.2 Hz, 2H), 3.81 (s, 2H), 2.31 (s, 3H), 2.18 (s, 3H), 1.98 – 1.90 (m, 2H), 1.78 – 1.72 (m, 2H), 1.48 (s, 6H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 157.10, 139.31, 136.61, 130.44, 129.14, 128.61, 126.65, 123.67, 120.81, 112.06, 67.94, 44.50, 40.26, 30.30, 26.15, 25.71, 21.57, 16.01.

6. Mechanistic study

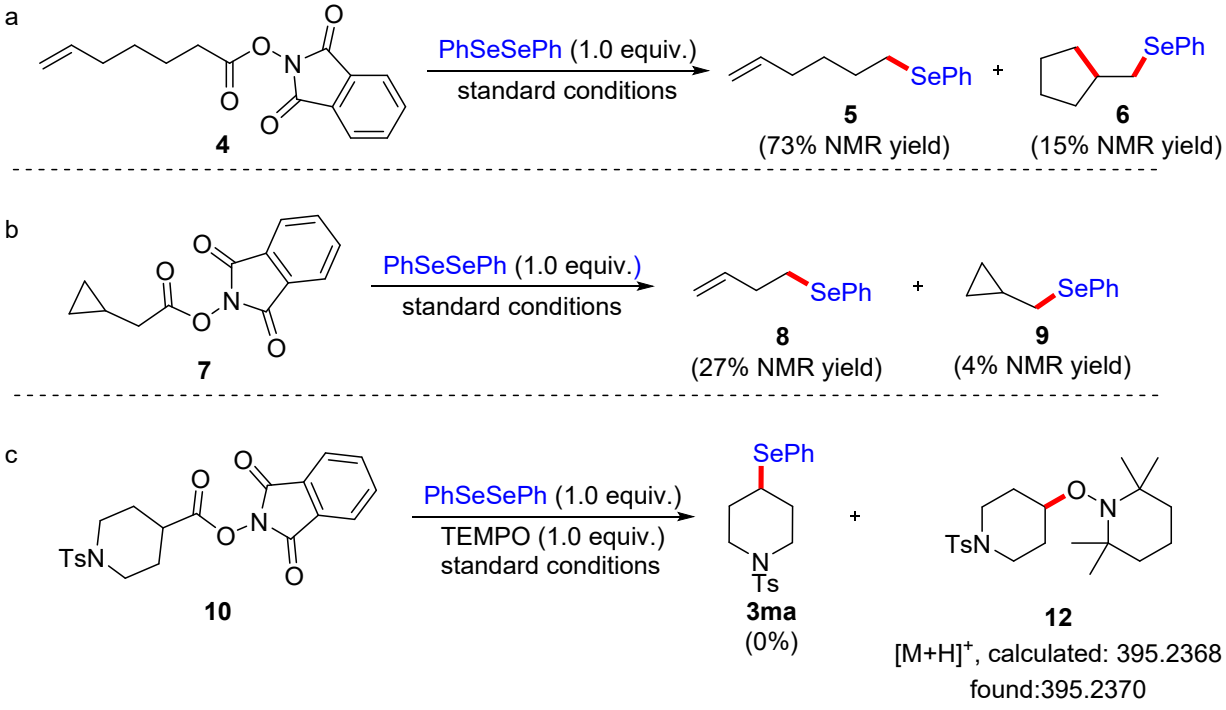


Figure S15. Radical control experiments

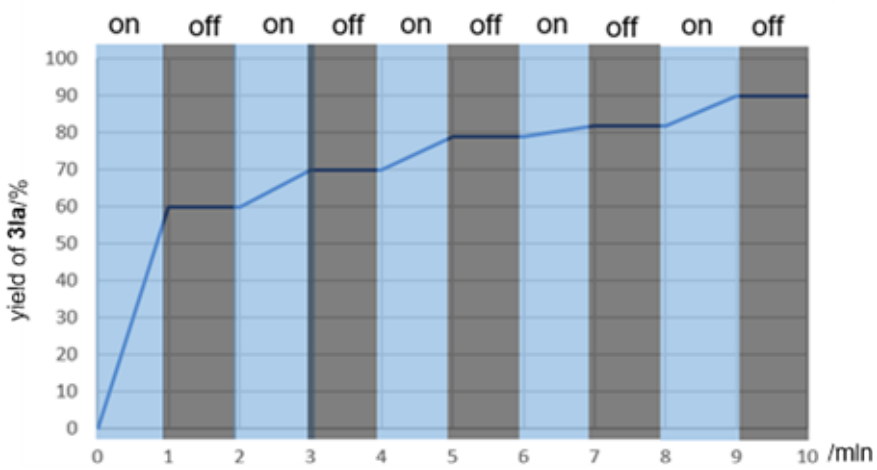
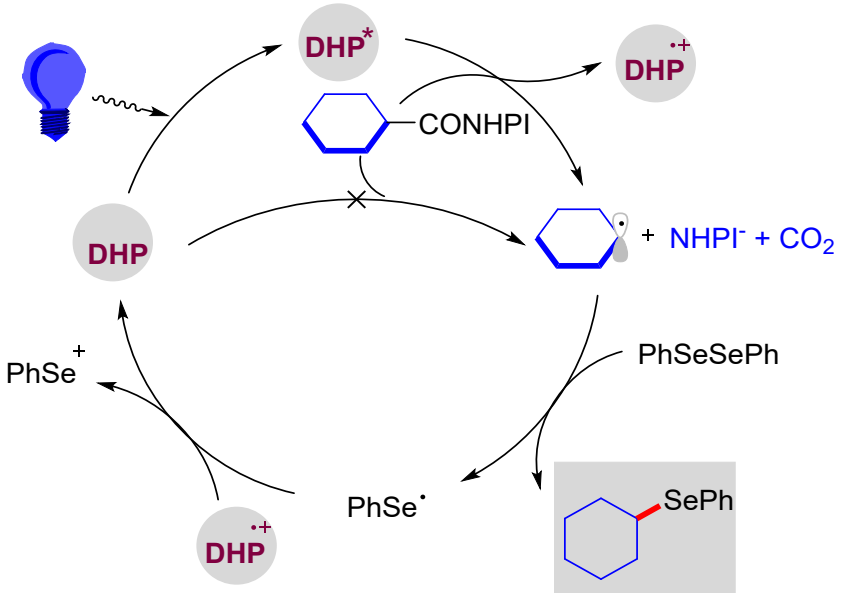


Figure S16. Turn on/off experiments.



NHPI = *N*-Hydroxyphthalimide, DHP = 1,4-dihydropyridines analogue

Figure S17. Proposed mechanism.

7. References

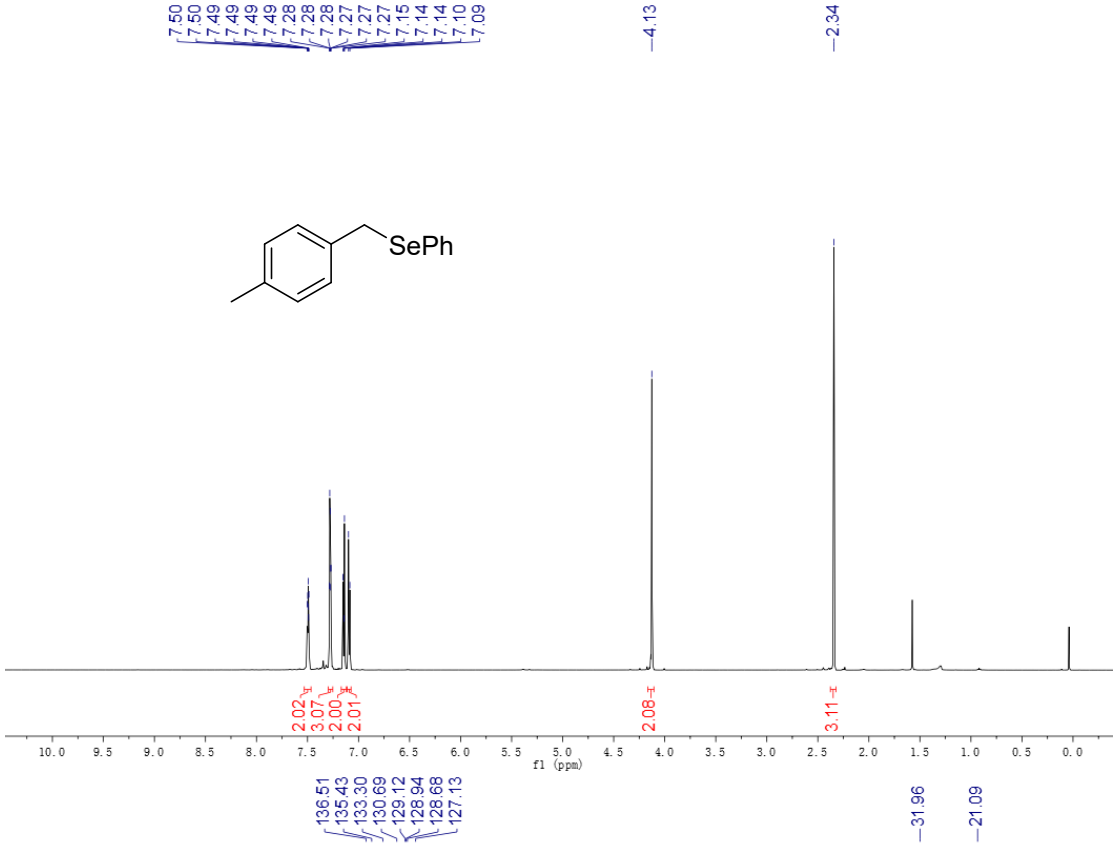
1) a) Paul, C. E.; Gargiulo, S.; Opperman, D. J.; Lavandera, I.; Gotor-Fernández, V.; Gotor, V.; Taglieber, An.; W. Arends, I. C. E.; Hollmann, F. *Org. Lett.* **2013**, *15*, 180–183; b) Zhao, H.; Li, Y.; Zhu, X.-Qi. *ACS Omega* **2018**, *3*, 13598−13608; c) Valente, A. M. S.; Meade, S.; Carafa, V.; Tardugno, M.; Nebbioso, A.; Galmozzi, A.; Mitro, N.; Fabiani, E. D.; Altucci, L.; Kazantsev, A. *J. Med. Chem.* **2009**, *52*, 5496–5504; d) Zhang, L.; Yuan, J.; Xu, Y.; Zhang, Y.-H. P.; Qian, X. *Chem. Commun.* **2016**, *52*, 6471–6474.

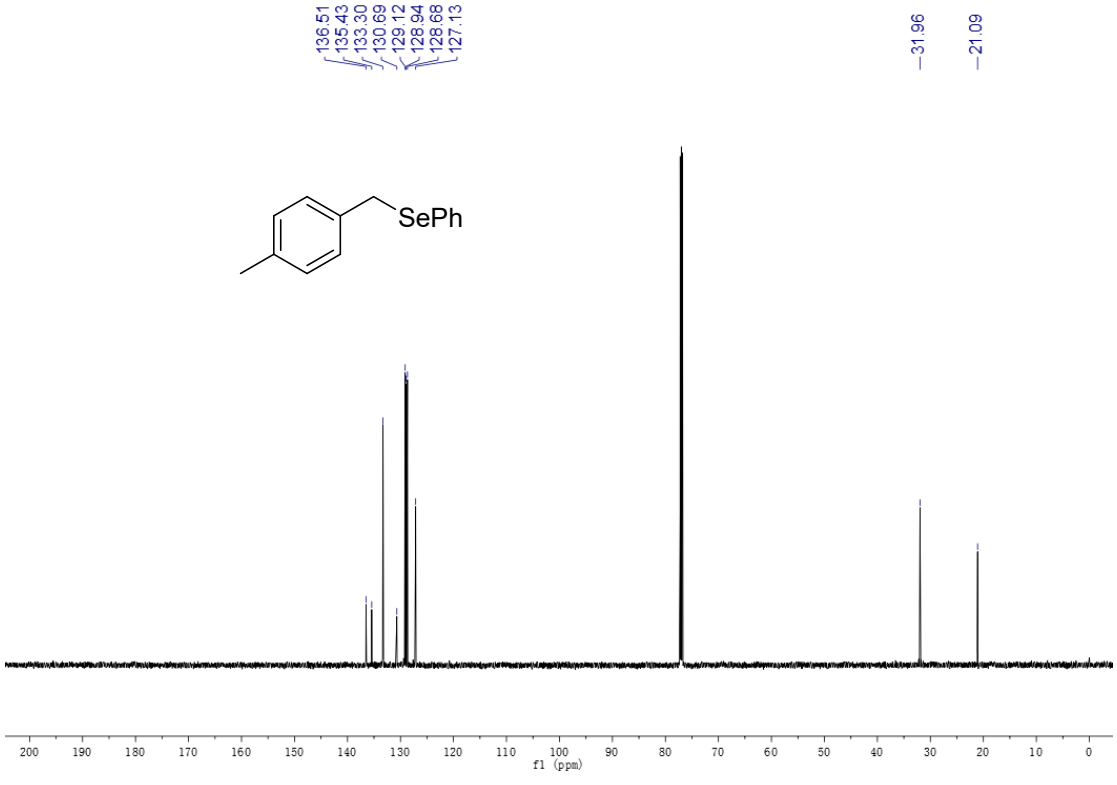
2) Li, F.; Wang, D.; Chen, H.; He, Z.; Zhou, L.; Zeng, Q. *Chem. Commun.* **2020**, *56*, 13029-13032.

3) Banerjee, S.; Adak, L.; Ranu, B. C. *Tetrahedron Lett*. **2012**, *53*, 2149-2152.

4) Verma, A.; Jana, S.; Prasad, C. D.; Yadav, A.; Kumar, S. *Chem. Commun.* **2016**, *52*, 4179-4182.

8. NMR Spectrum



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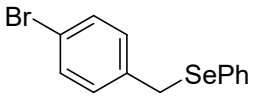
4.02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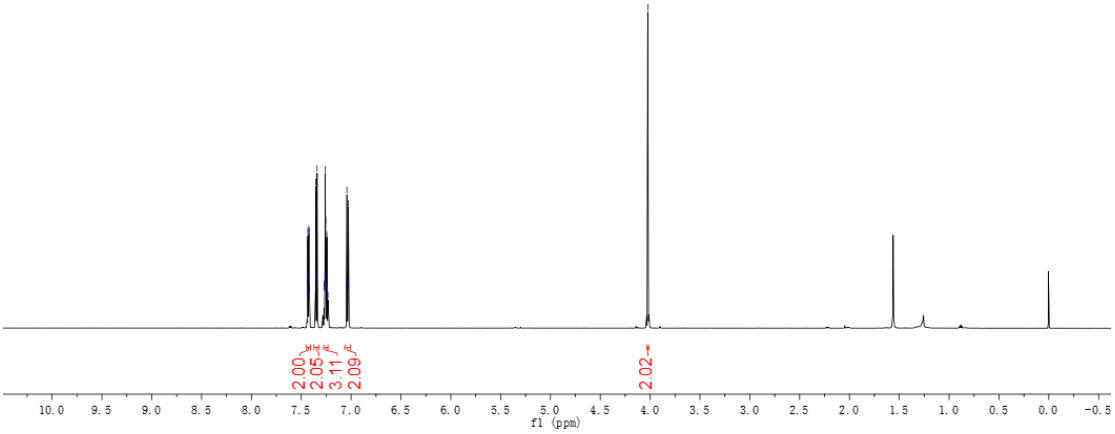
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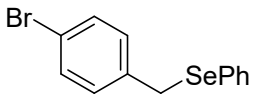
31.63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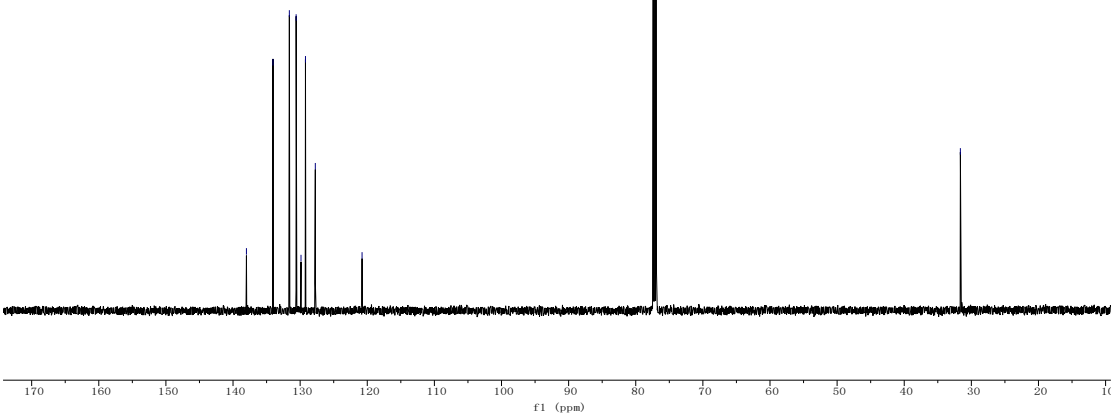
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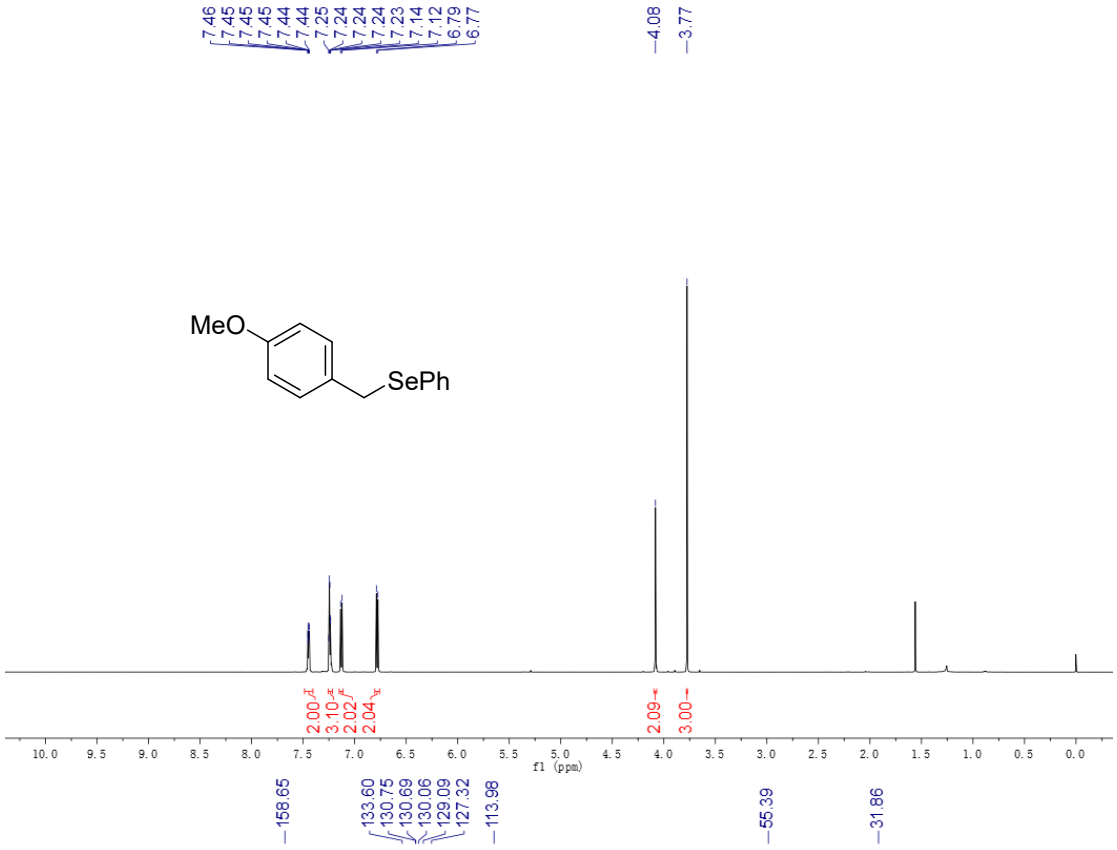
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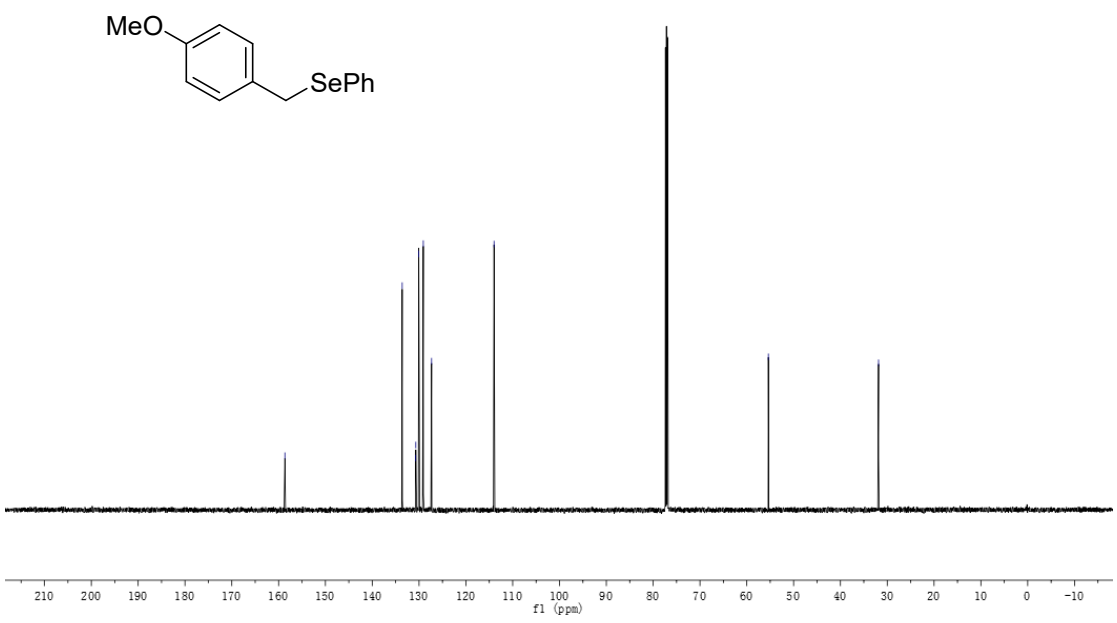
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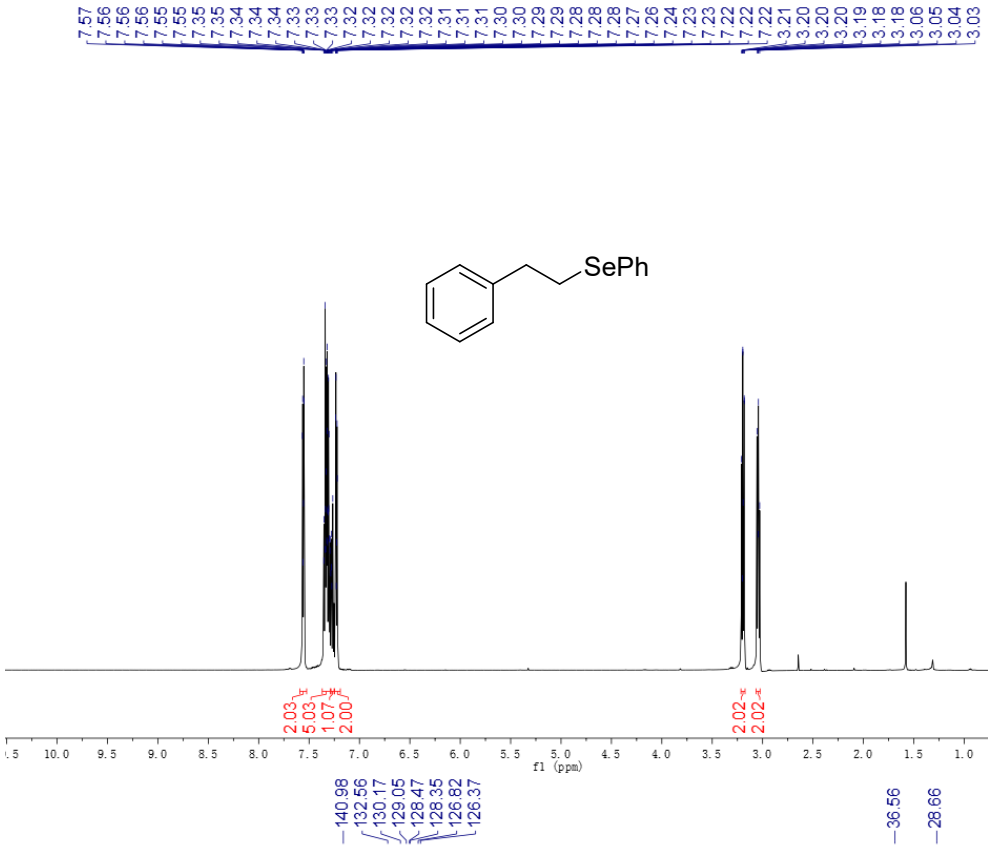
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f1 (ppm)
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f1 (ppm)


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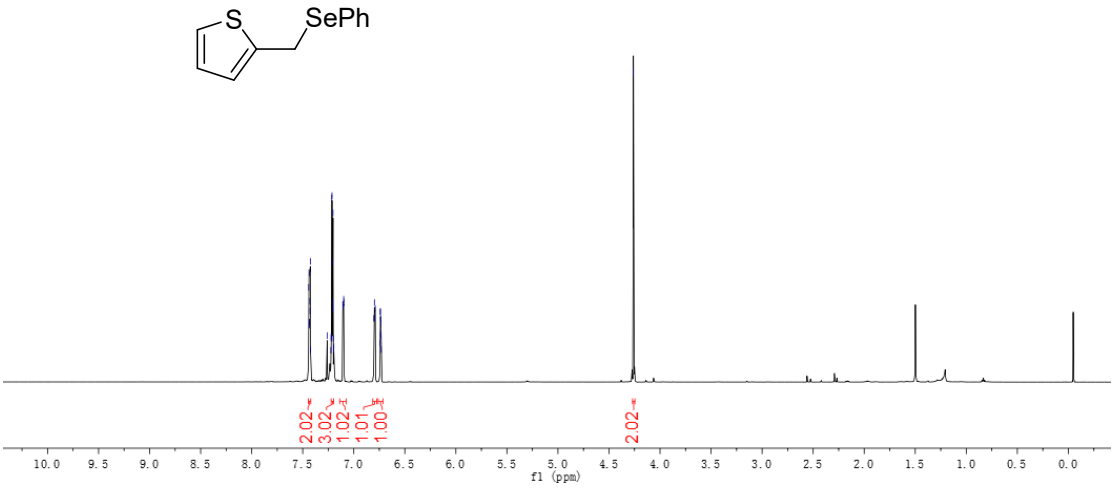
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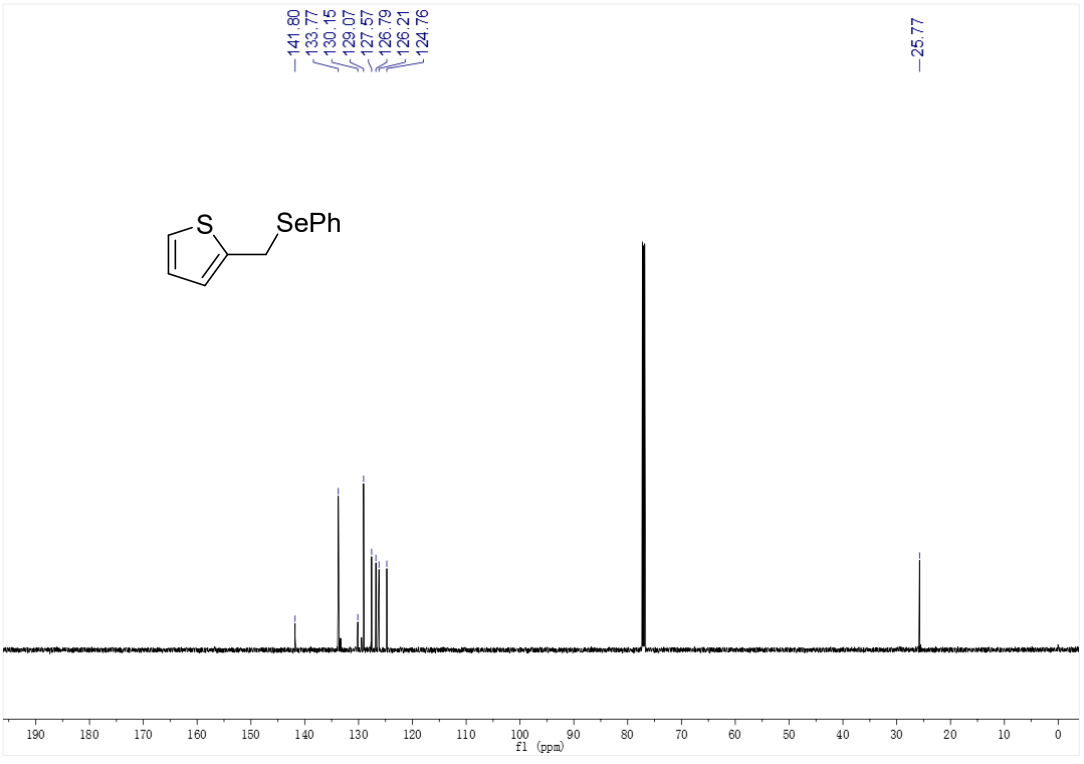
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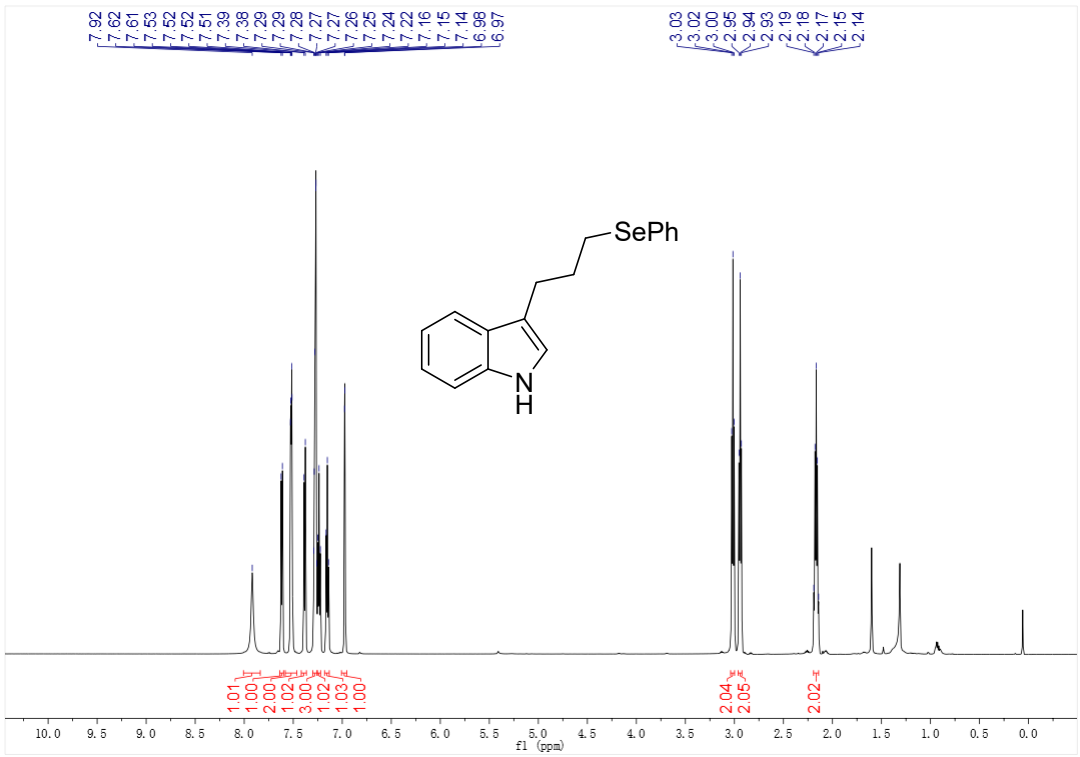
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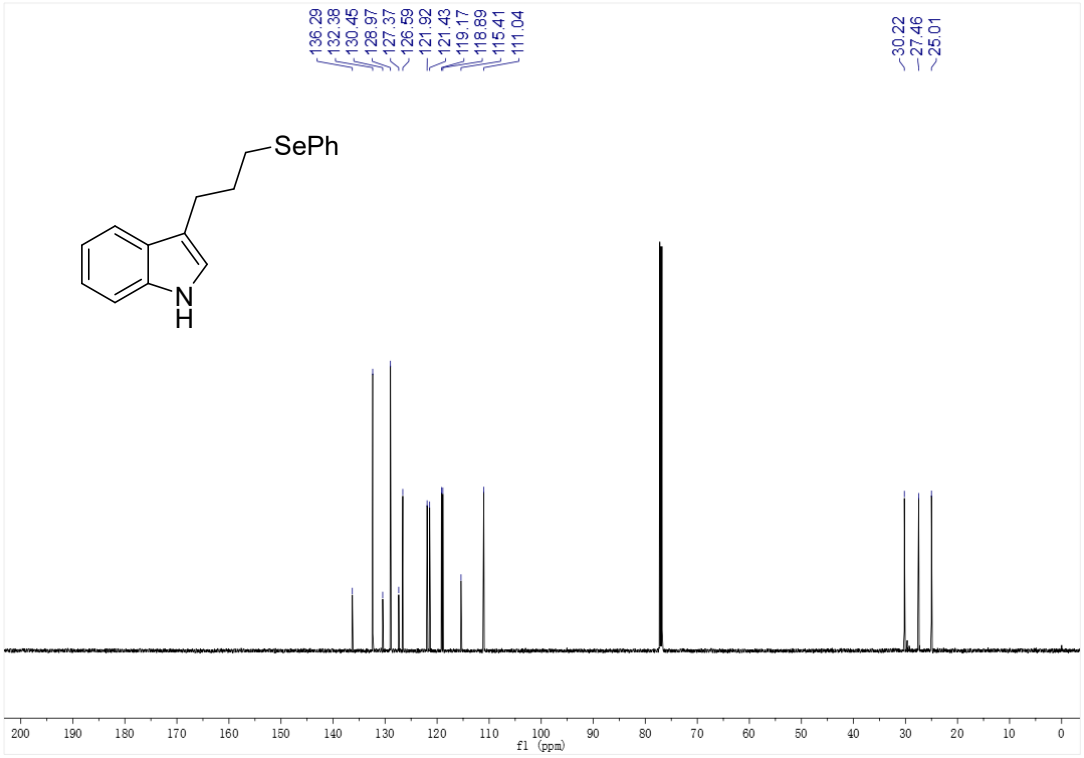
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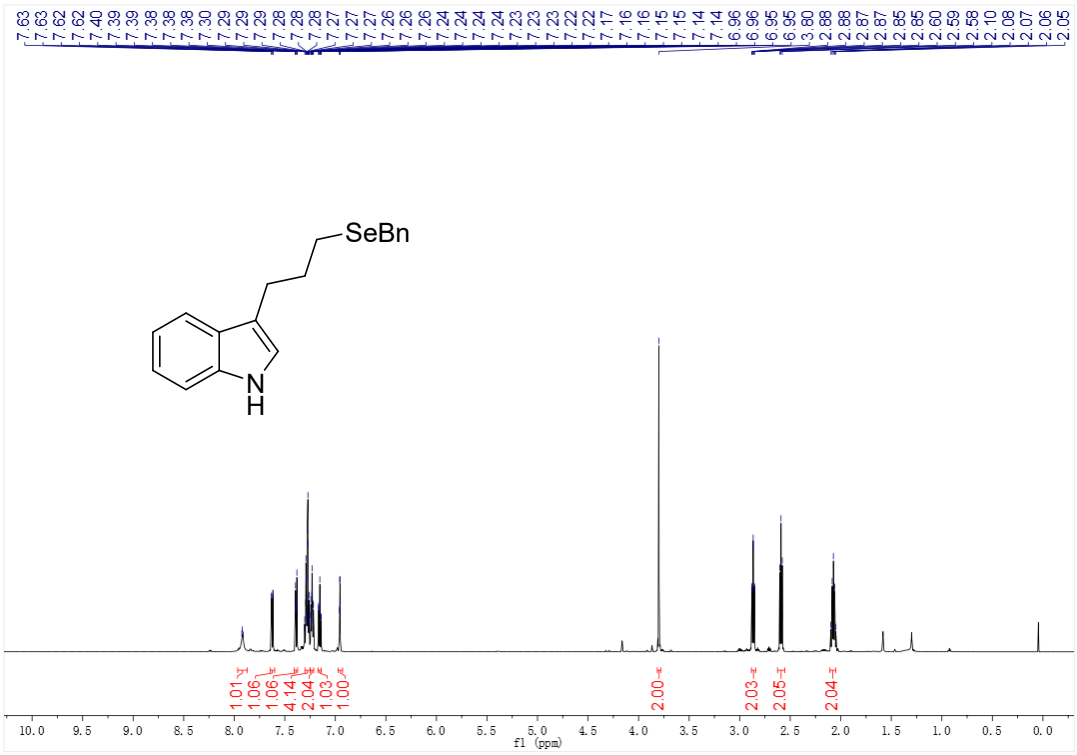
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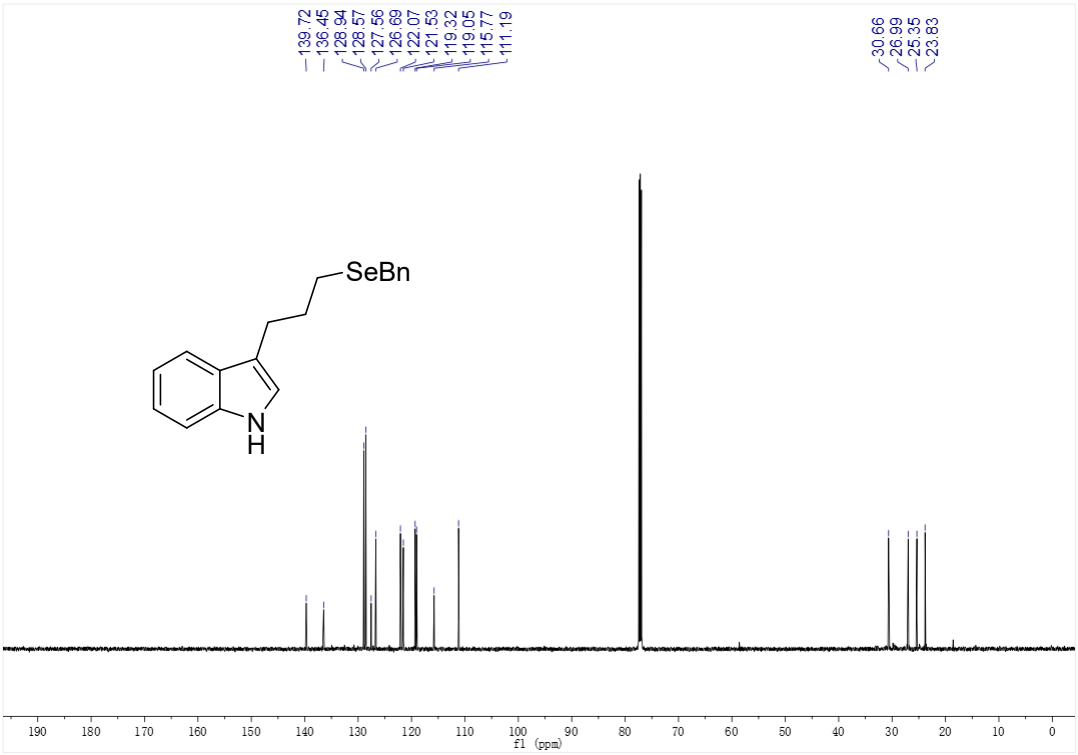
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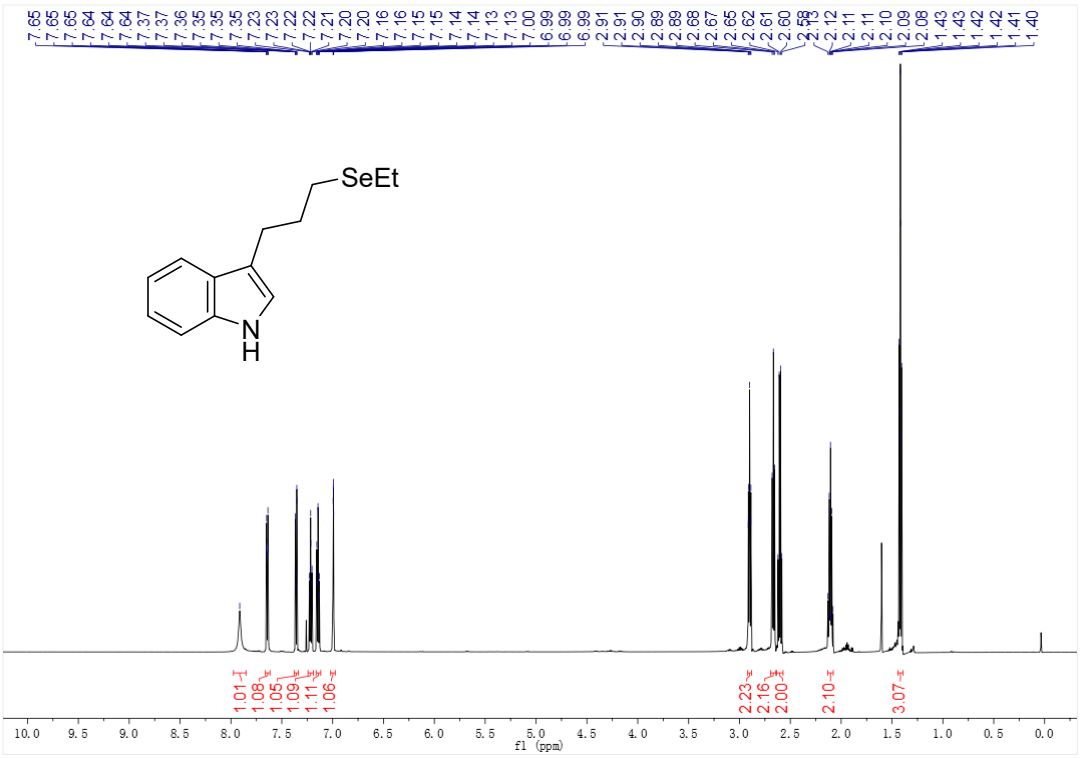
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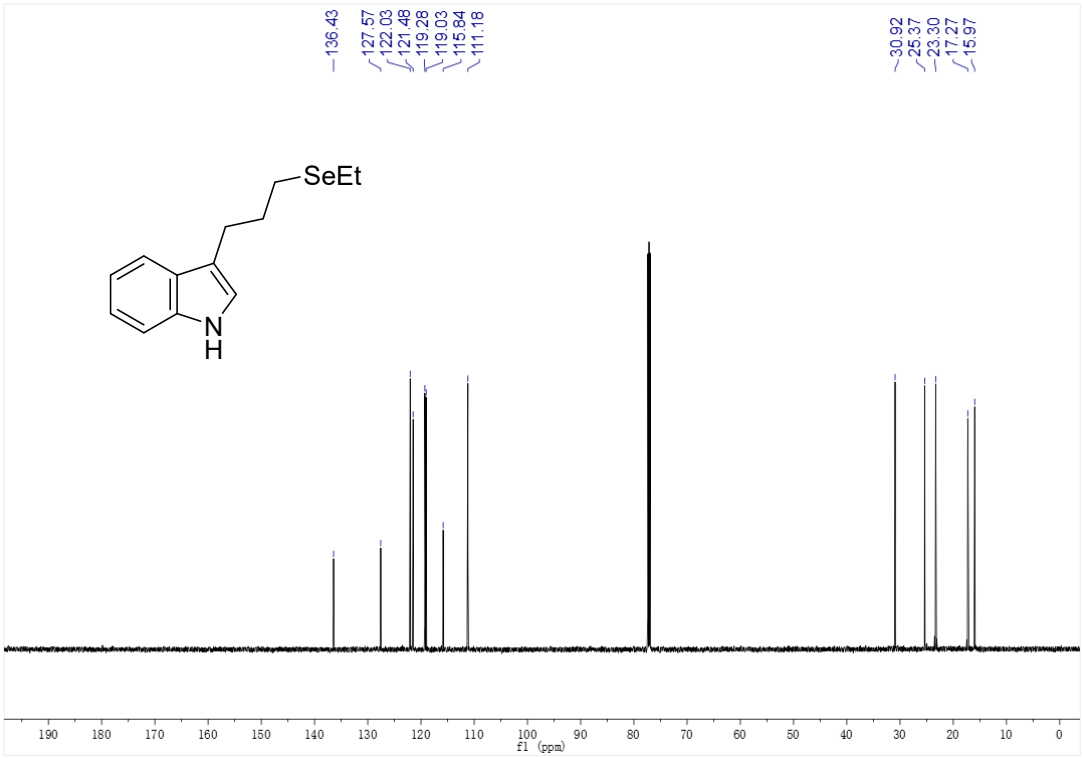
1.01 1.08 1.05 1.09 1.11 1.06
2.23 2.16 2.00 2.10 3.07
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


136.43 127.57 122.03 121.48 119.28 119.03 115.84 111.18
30.92 25.37 23.30 17.27 15.97
SeEt
N
H
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


8.03
8.02
7.90
7.90
7.89
7.89
7.59
7.59
7.58
7.58
7.56
7.56
7.51
7.51
7.50
7.49
7.48
7.48
7.48
7.48
7.47
7.47
7.47
7.38
7.38
7.37
7.37
7.36
7.35
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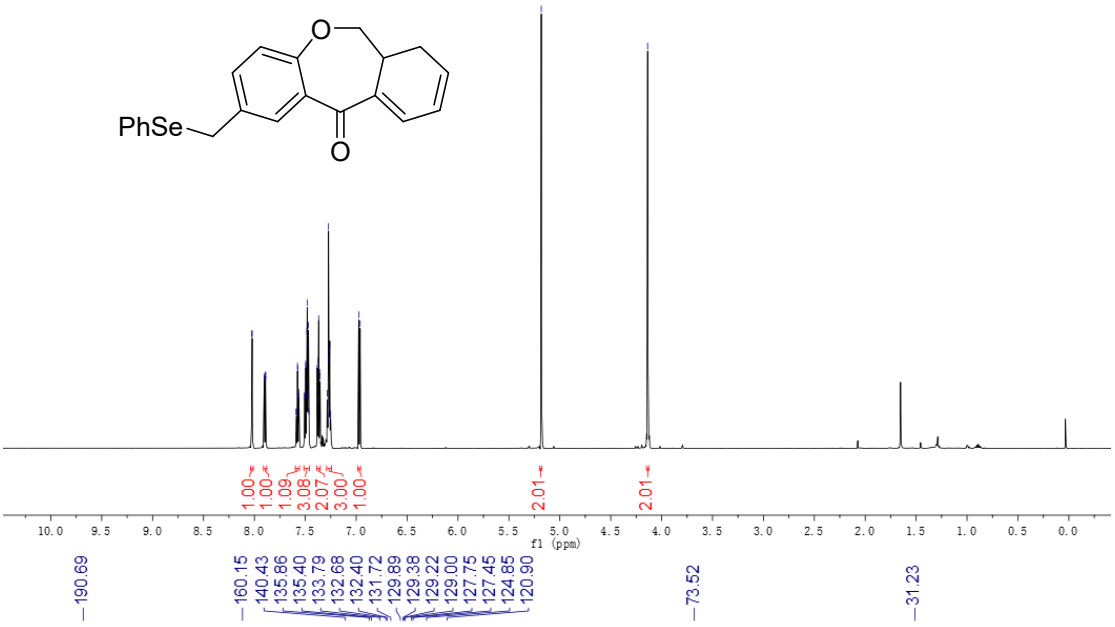
7.25
6.98
5.18
4.14


O
PhSe
O
1.00
1.00
1.09
3.08
2.07
3.00
1.00
2.01
2.01
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

190.69
160.15
140.43
135.86
135.40
133.79
132.68
132.40
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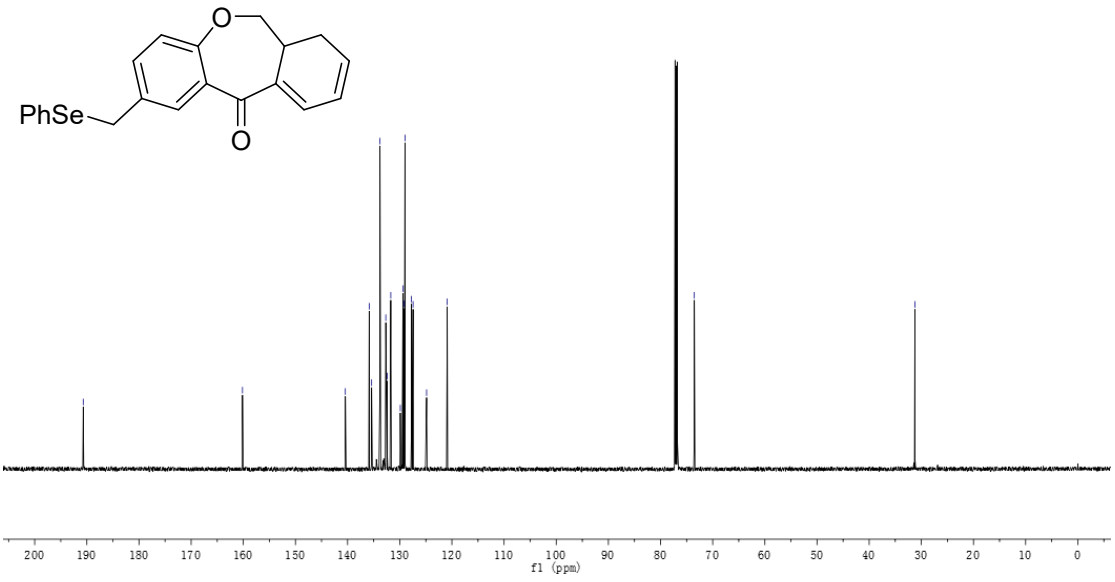
129.89
129.38
129.22
129.00
127.75
127.45
124.85
120.90
73.52
31.23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PhSe
O
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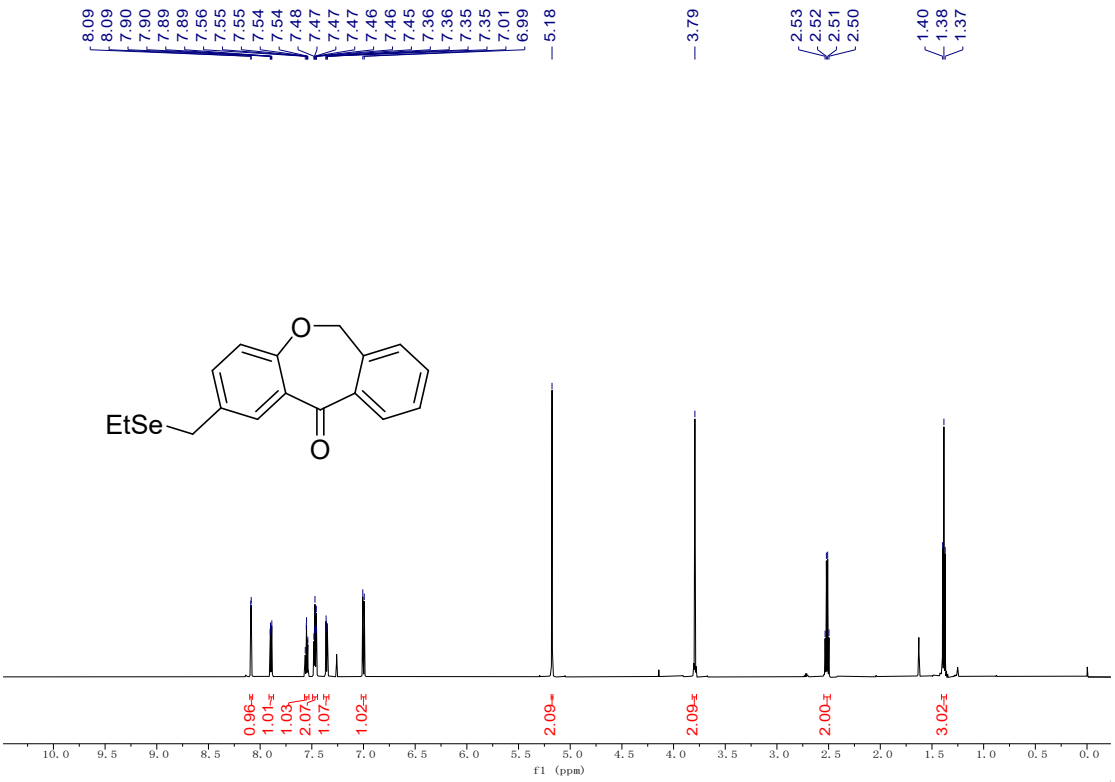
f1 (ppm)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7.90
7.90
7.89
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7.55
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7.48
7.47
7.47
7.47
7.46
7.46
7.45
7.36
7.35
7.35
7.01
6.99
5.18
3.79
2.53
2.52
2.51
2.50
1.40
1.38
1.37
EtSe
O
O
0.96
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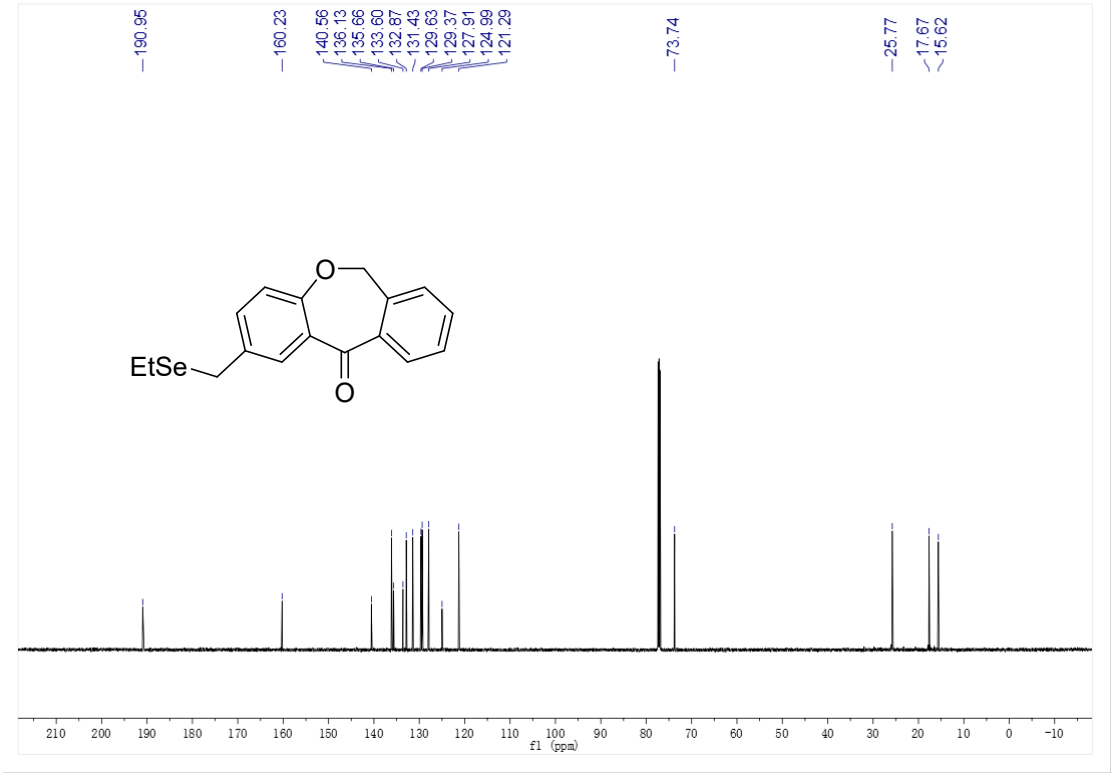
1.03
2.07
1.07
1.02
2.09
2.09
2.00
3.02
f1 (ppm)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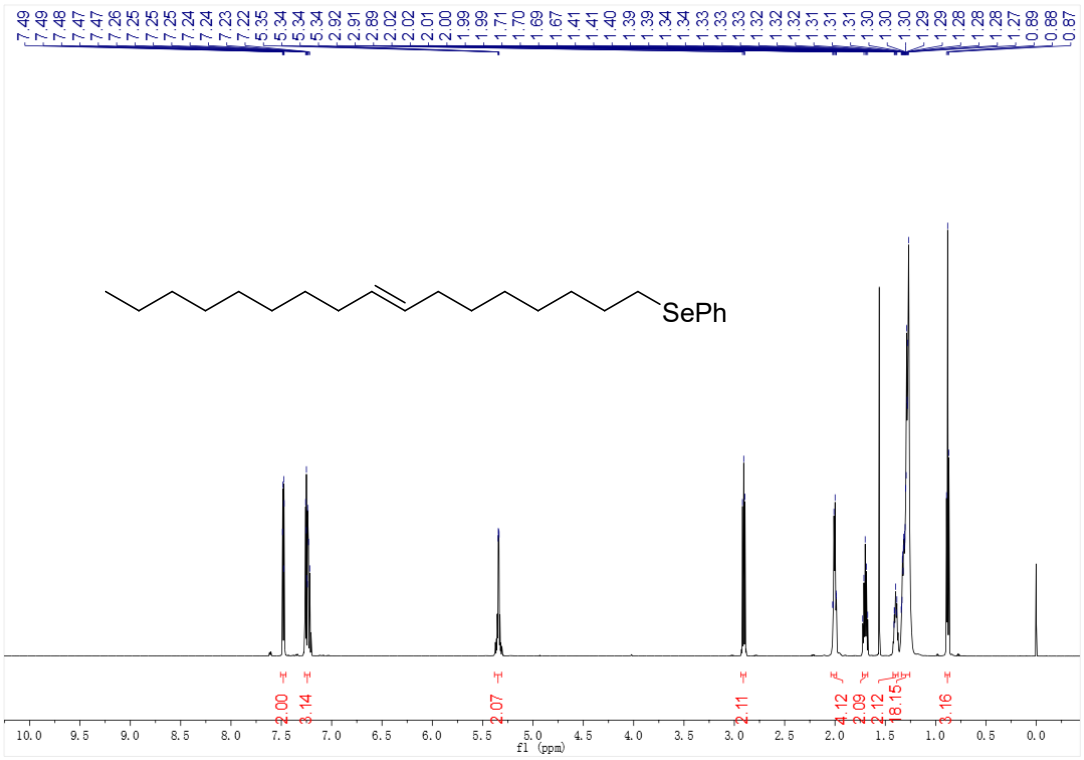
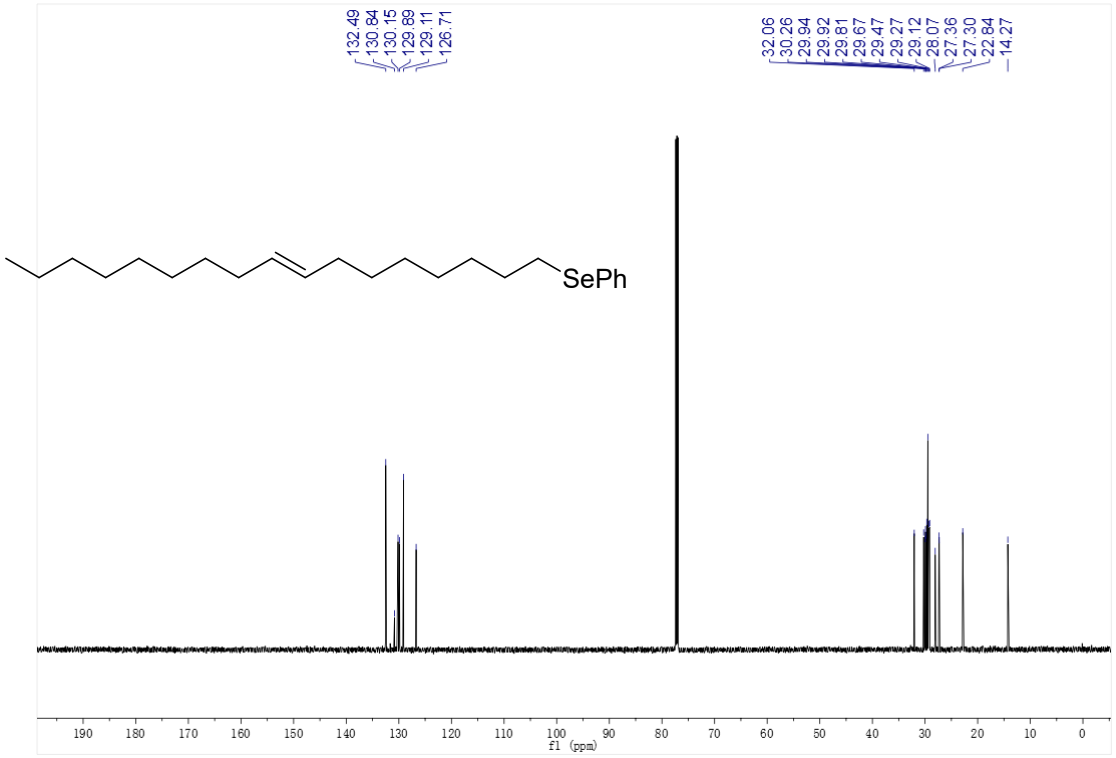
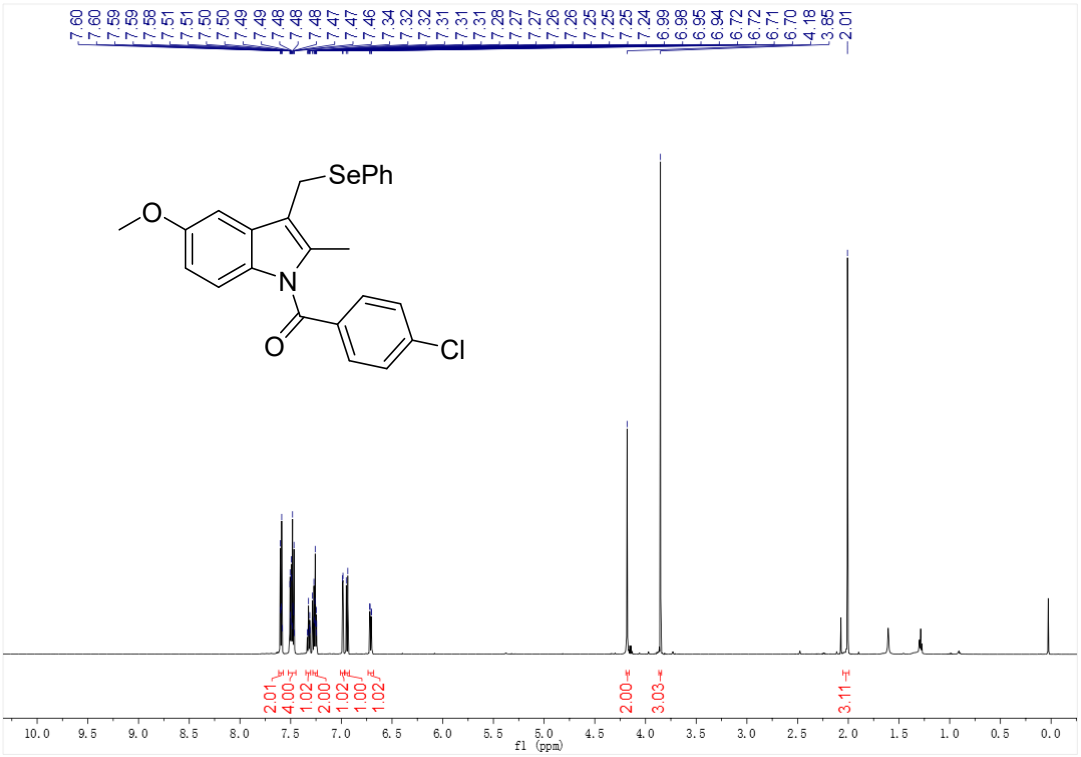
135.66
133.60
132.87
131.43
129.63
129.37
127.91
124.99
121.29
73.74
25.77
17.67
15.62
EtSe
O
O
f1 (ppm)


SePh
f1 (ppm)


SePh
f1 (ppm)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7.47
7.46
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7.32
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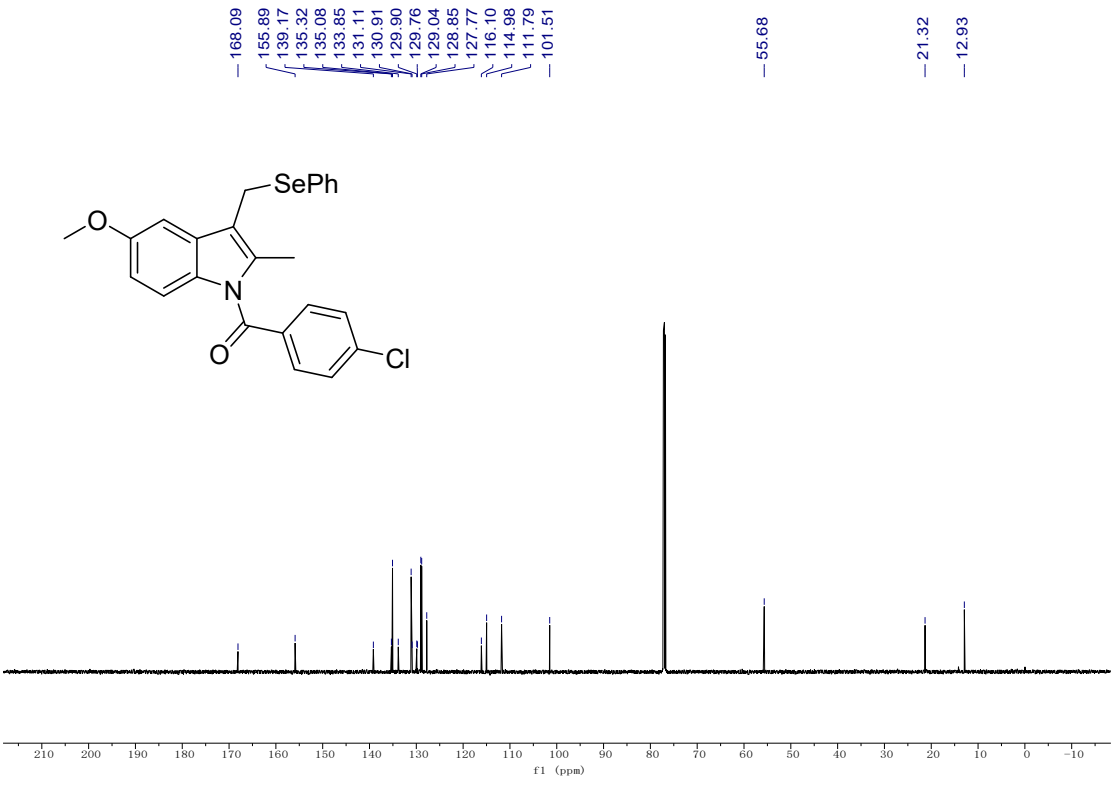
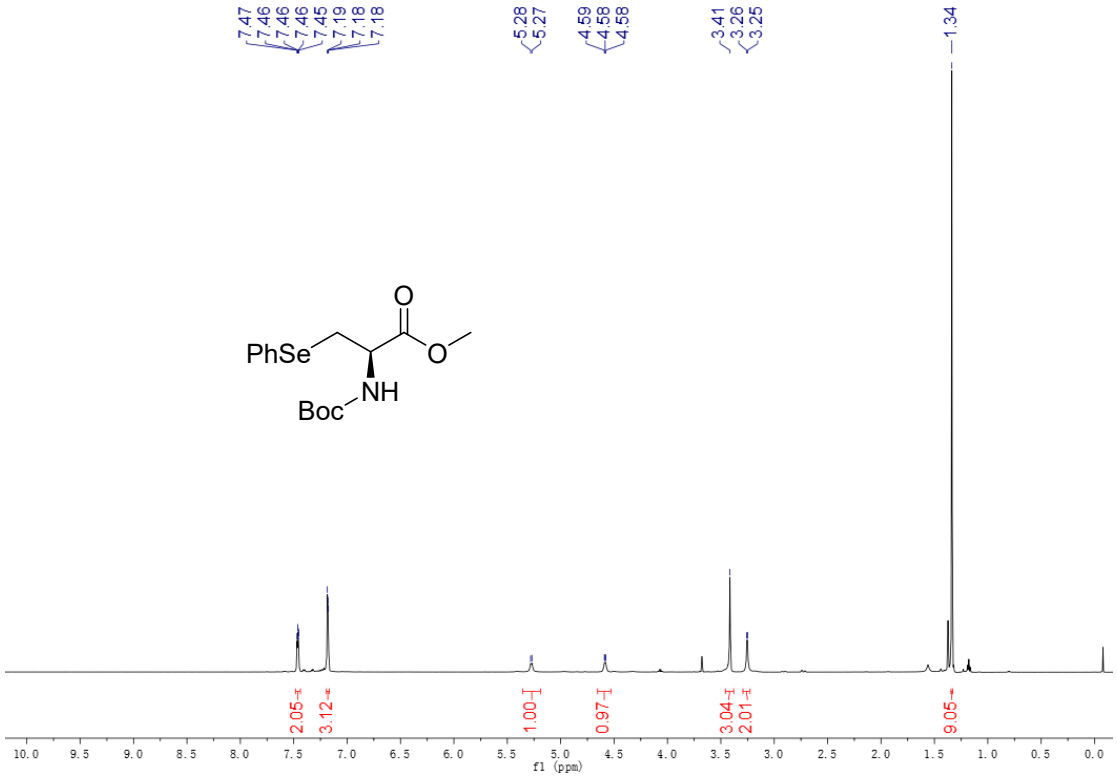
7.31
7.28
7.27
7.27
7.26
7.26
7.25
7.25
7.25
7.24
6.99
6.98
6.95
6.94
6.72
6.72
6.71
6.70
4.18
3.85
2.01
SePh
O
N
O
Cl
2.01
4.00
1.02
2.00
1.02
1.00
1.02
2.00
3.03
3.11
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


168.09
155.89
139.17
135.32
135.08
133.85
131.11
130.91
129.90
129.76
129.04
128.85
127.77
116.10
114.98
111.79
101.51
55.68
21.32
12.93
SePh
O
N
O
Cl
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)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7.46
7.46
7.45
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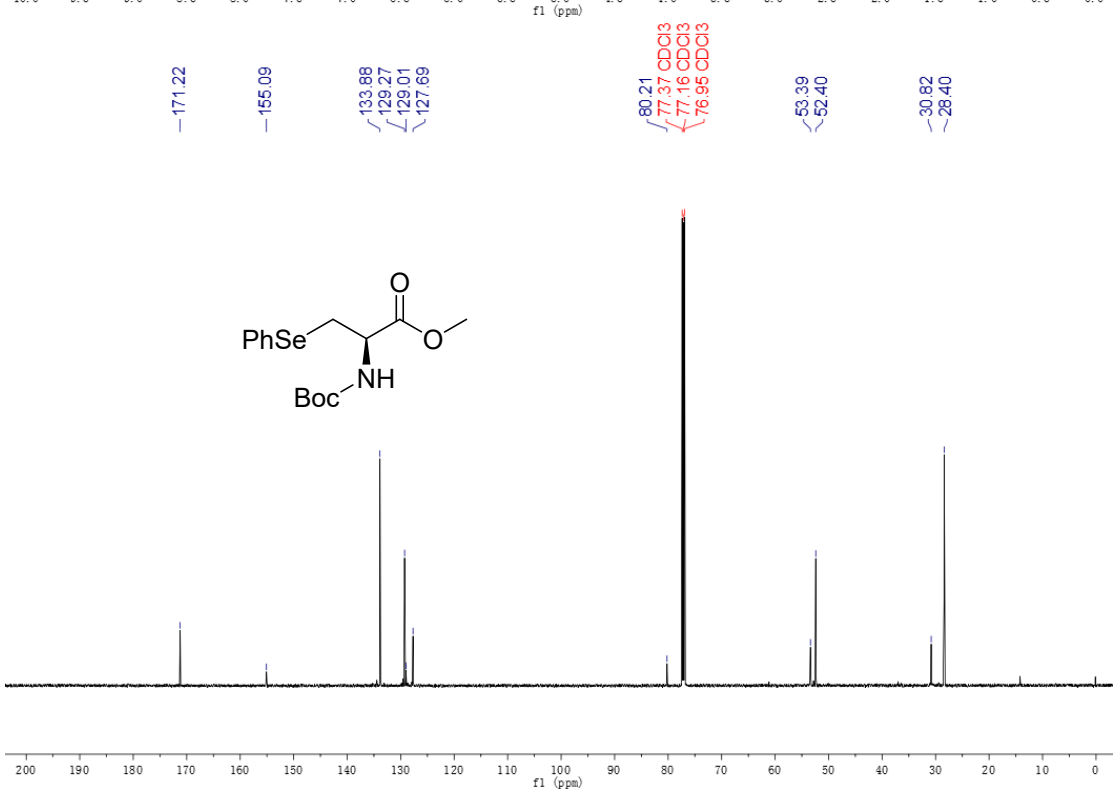
7.18
7.18
5.28
5.27
4.59
4.58
4.58
3.41
3.26
3.25
1.34
PhSe
O
O
NH
Boc
2.05
3.12
1.00
0.97
3.04
2.01
9.05
f1 (ppm)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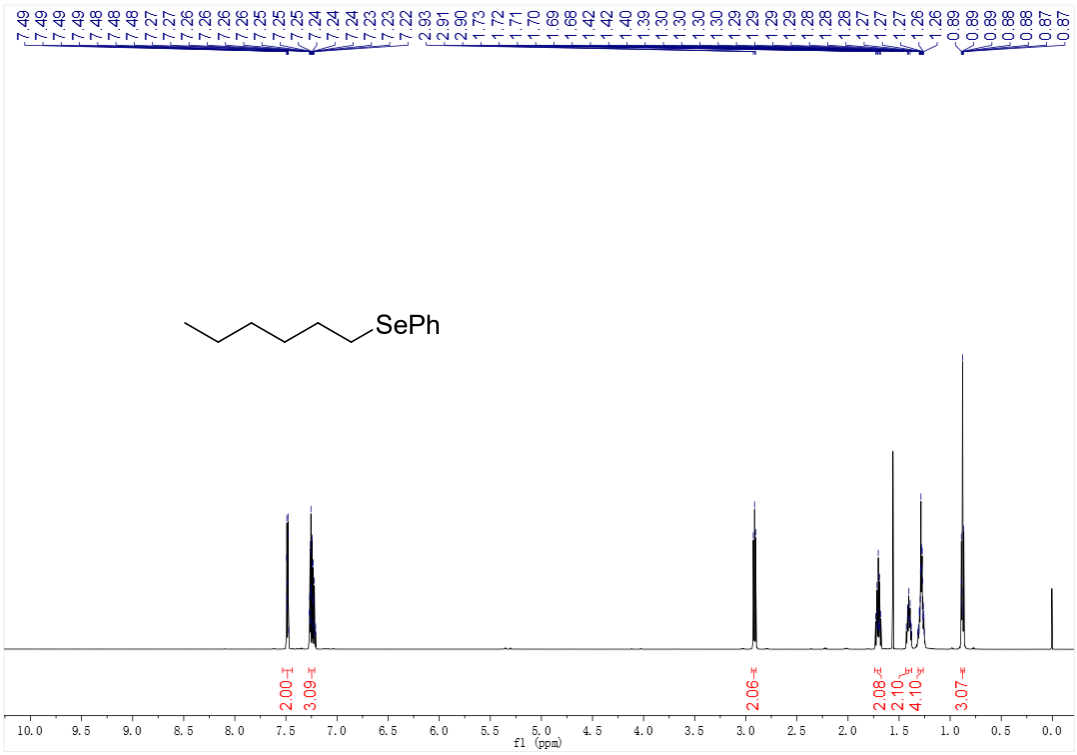
133.88
129.27
129.01
127.69
80.21
77.37 CDCl3
77.16 CDCl3
76.95 CDCl3
53.39
52.40
30.82
28.40
PhSe
O
O
NH
Boc
f1 (ppm)


SePh
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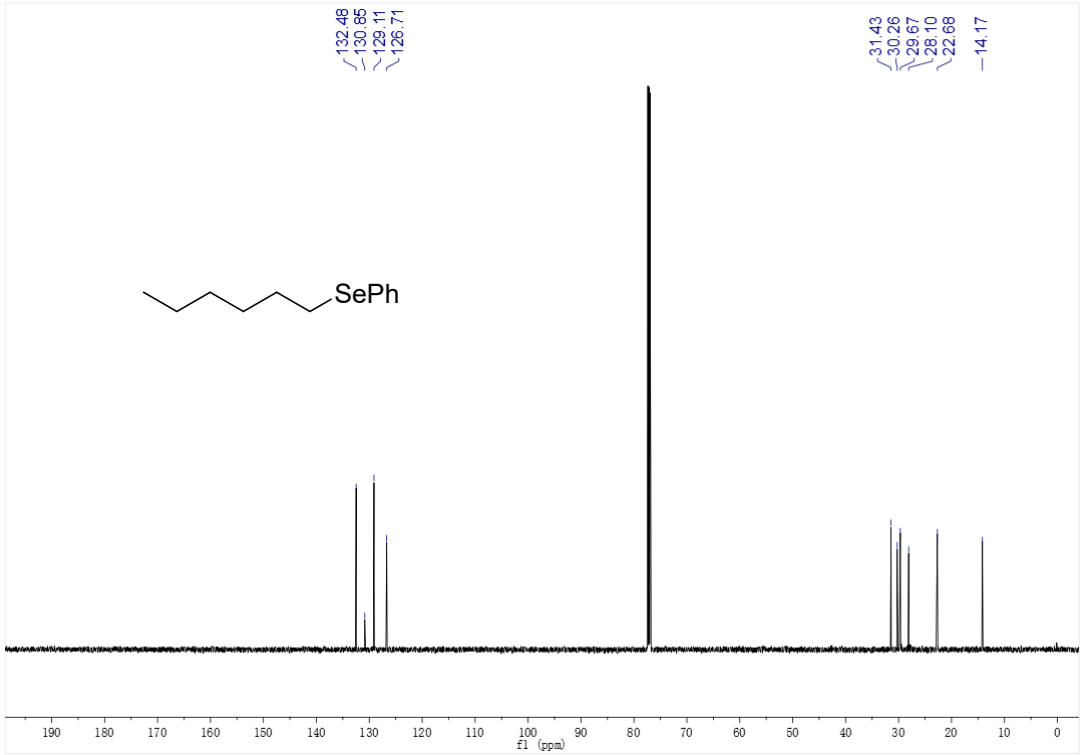
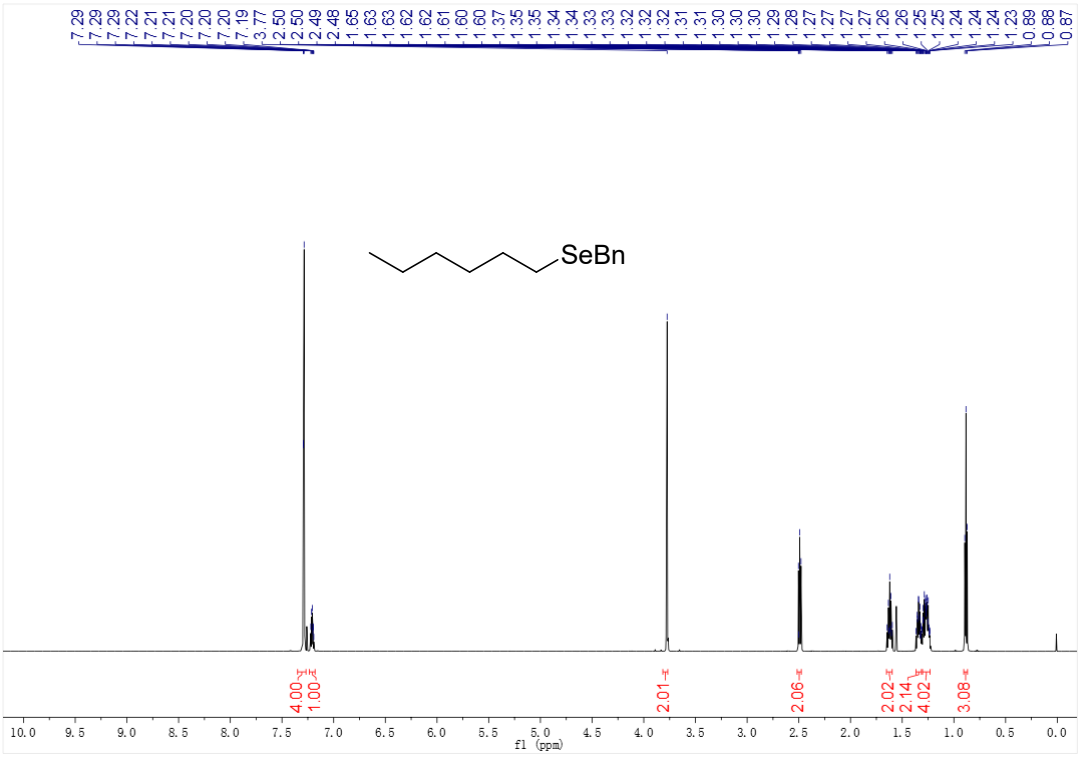
3.09
2.06
2.08
2.10
4.10
3.07
f1 (ppm)


SePh
f1 (ppm)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3.77
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2.48
1.65
1.63
1.63
1.62
1.62
1.61
1.60
1.60
1.37
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1.34
1.33
1.33
1.32
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1.30
1.29
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1.27
1.27
1.27
1.27
1.26
1.26
1.25
1.25
1.24
1.24
1.24
1.23
0.89
0.88
0.87
SeBn
4.00
1.00
2.01
2.06
2.02
2.14
4.02
3.08
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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4.5
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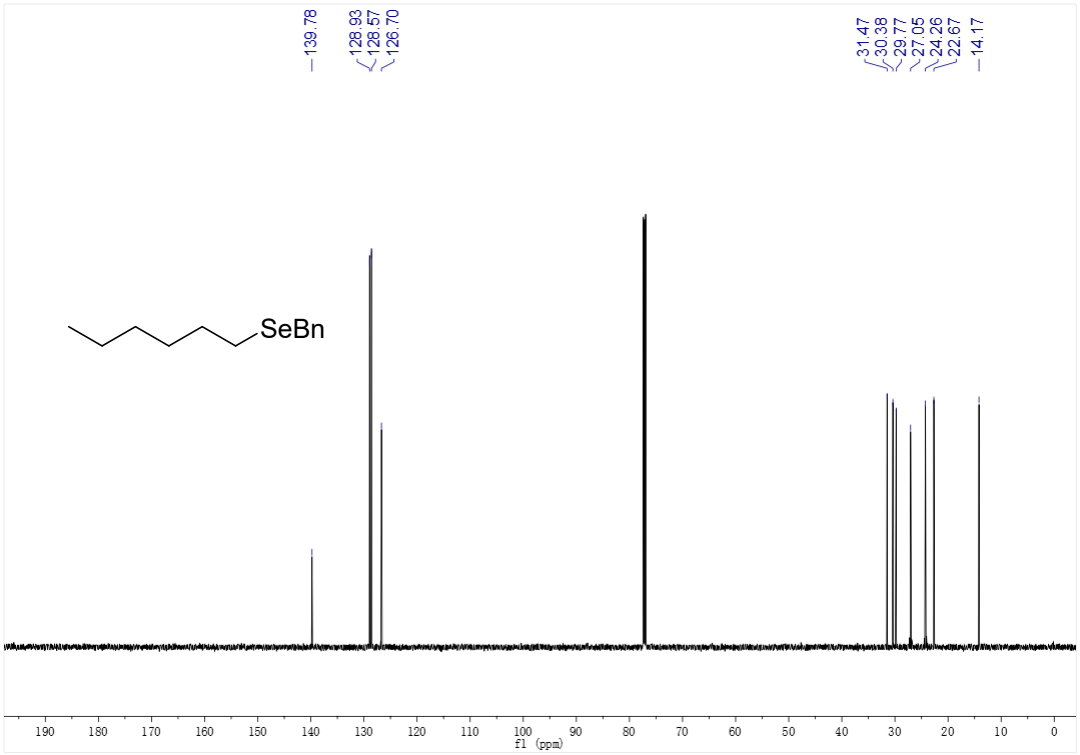
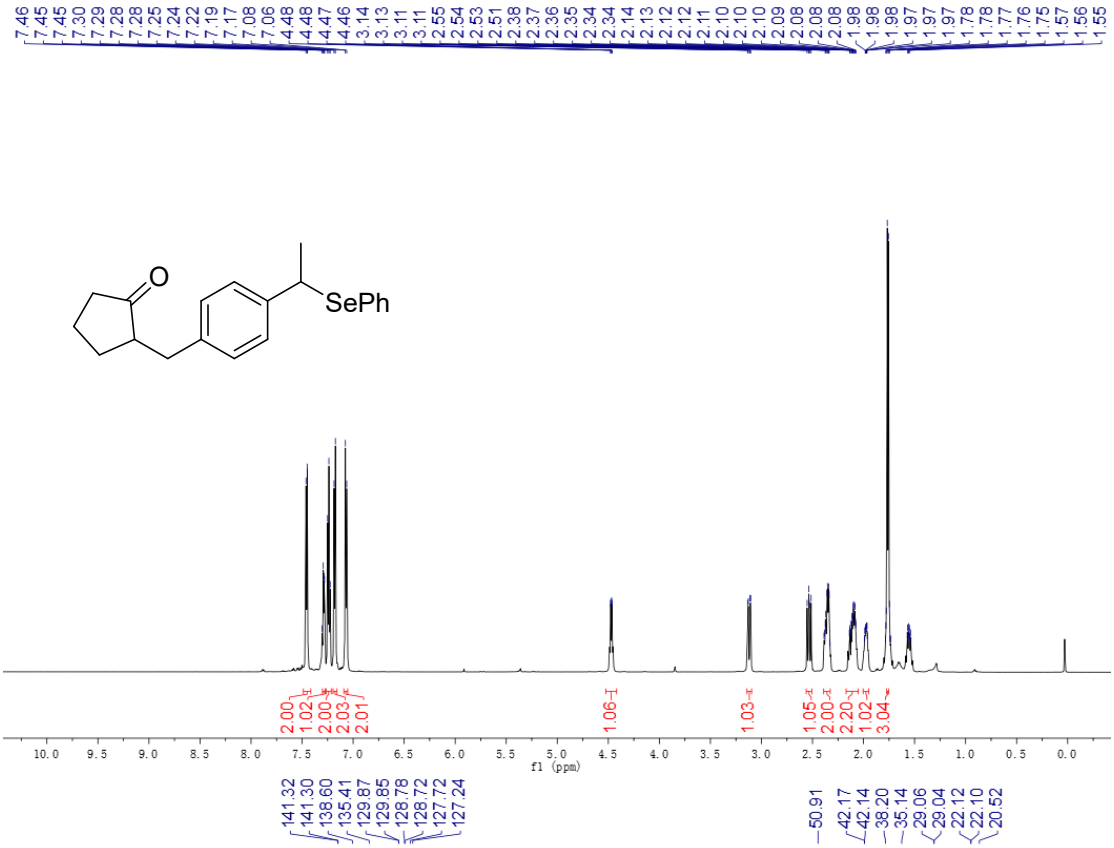
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


139.78
128.93
128.57
126.70
31.47
30.38
29.77
27.05
24.26
22.67
14.17
SeBn
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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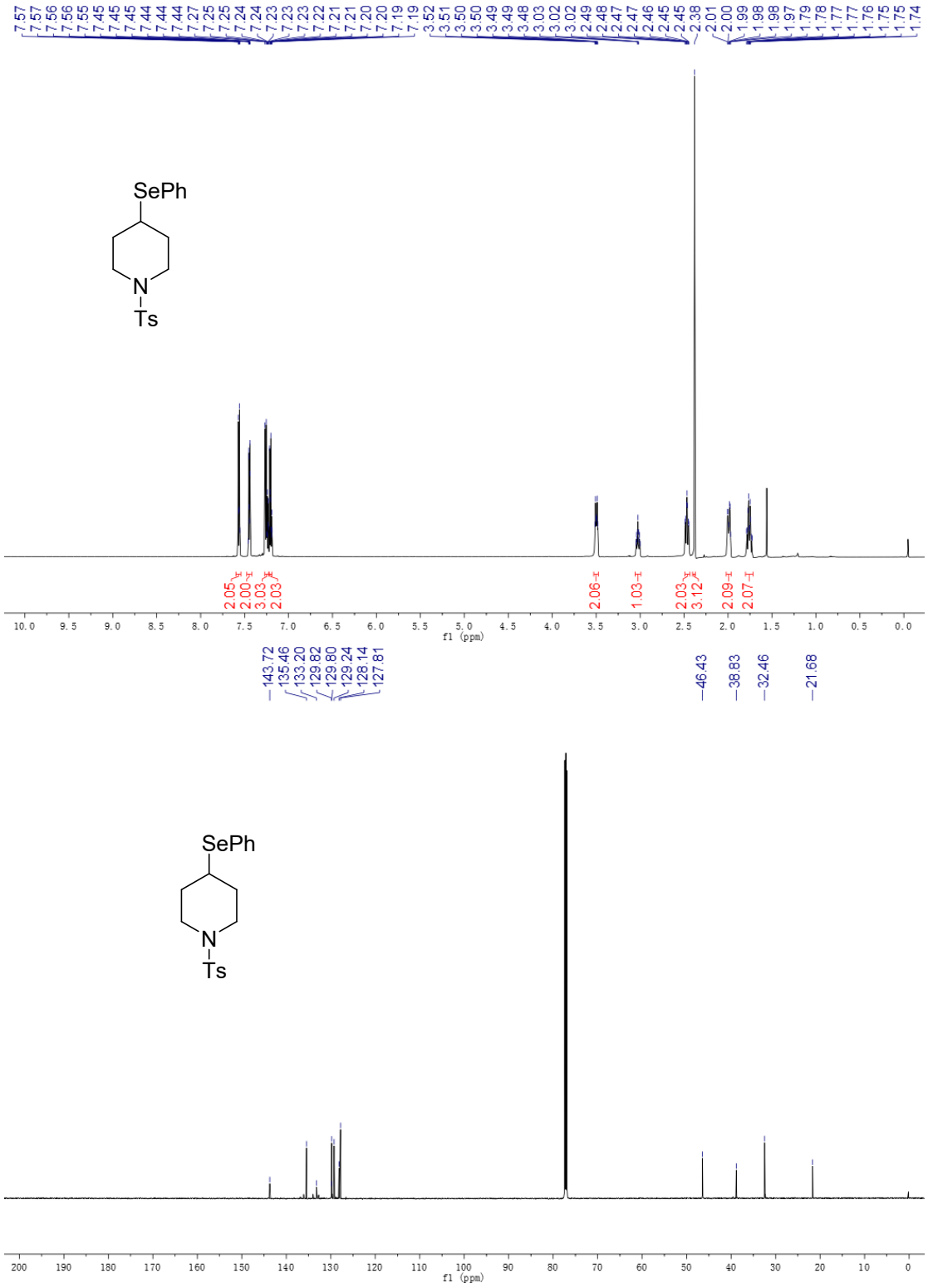
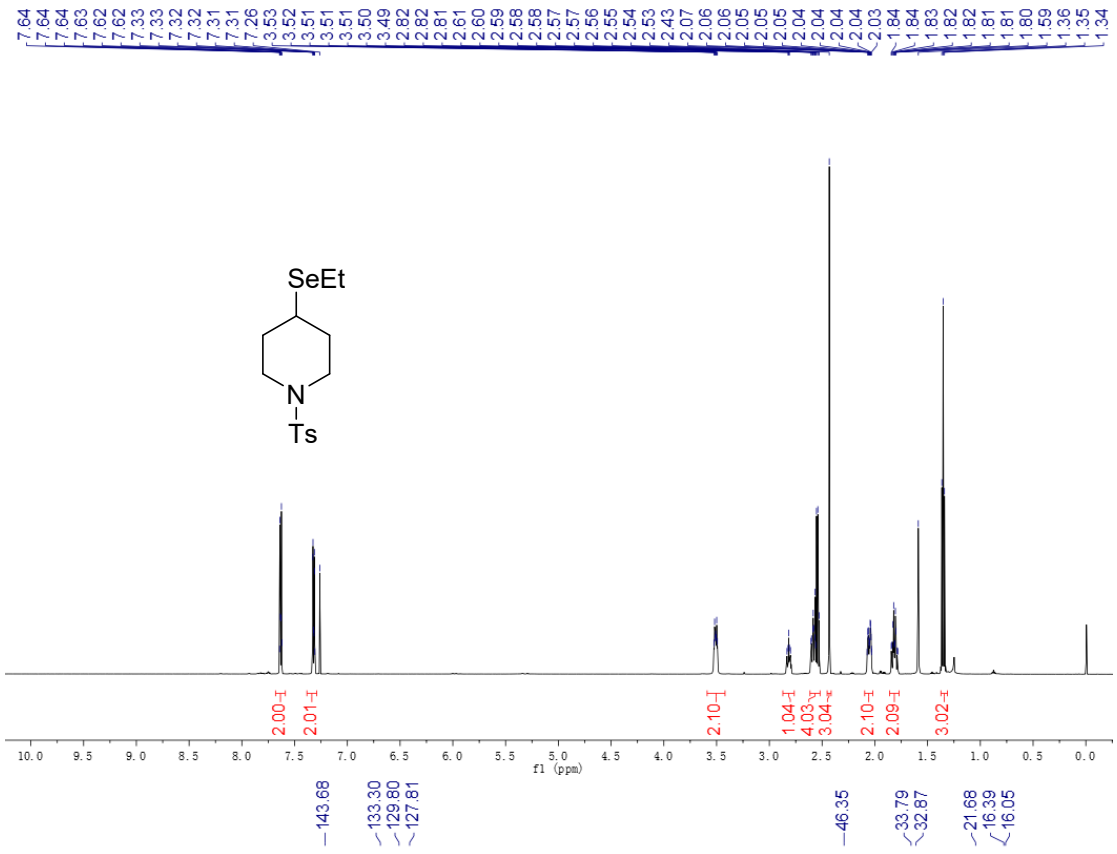
O
SePh
2.00 1.02 2.00 2.03 2.01 1.06 1.03 1.05 2.00 2.20 1.02 3.04
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)
141.32 141.30 138.60 135.41 129.87 129.85 128.78 128.72 127.72 127.24 50.91 42.17 42.14 38.20 35.14 29.06 29.04 22.12 22.10 20.52
O
SePh
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


SePh
N
Ts
f1 (ppm)
SePh
N
Ts
f1 (ppm)


SeEt
N
Ts
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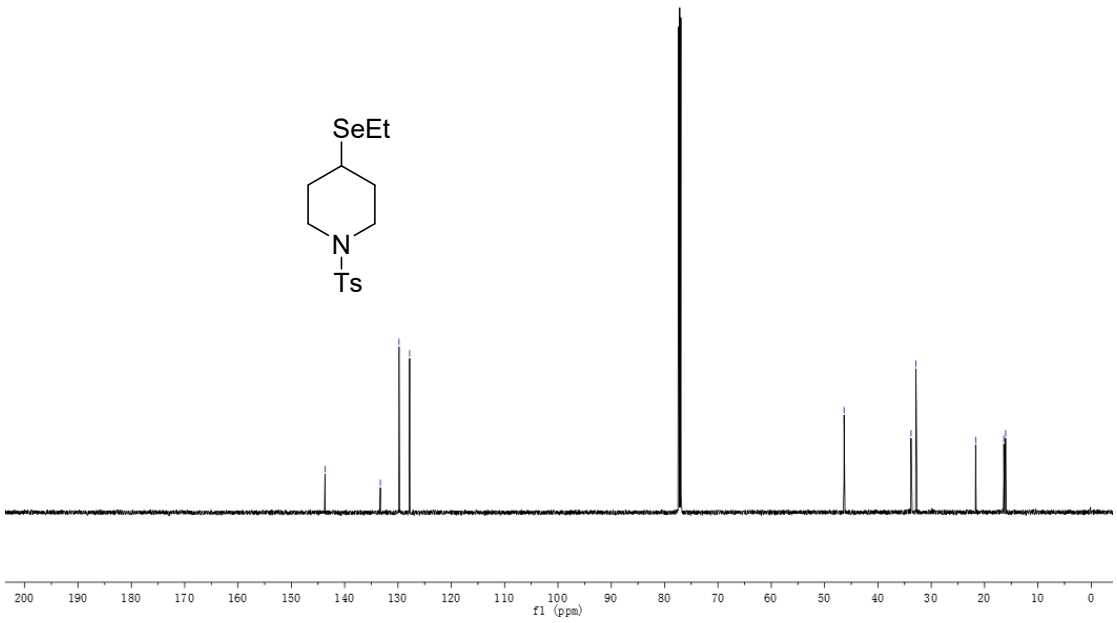
2.00 2.01 2.10 1.04 4.03 3.04 2.10 2.09 3.02
f1 (ppm)


SeEt
N
Ts
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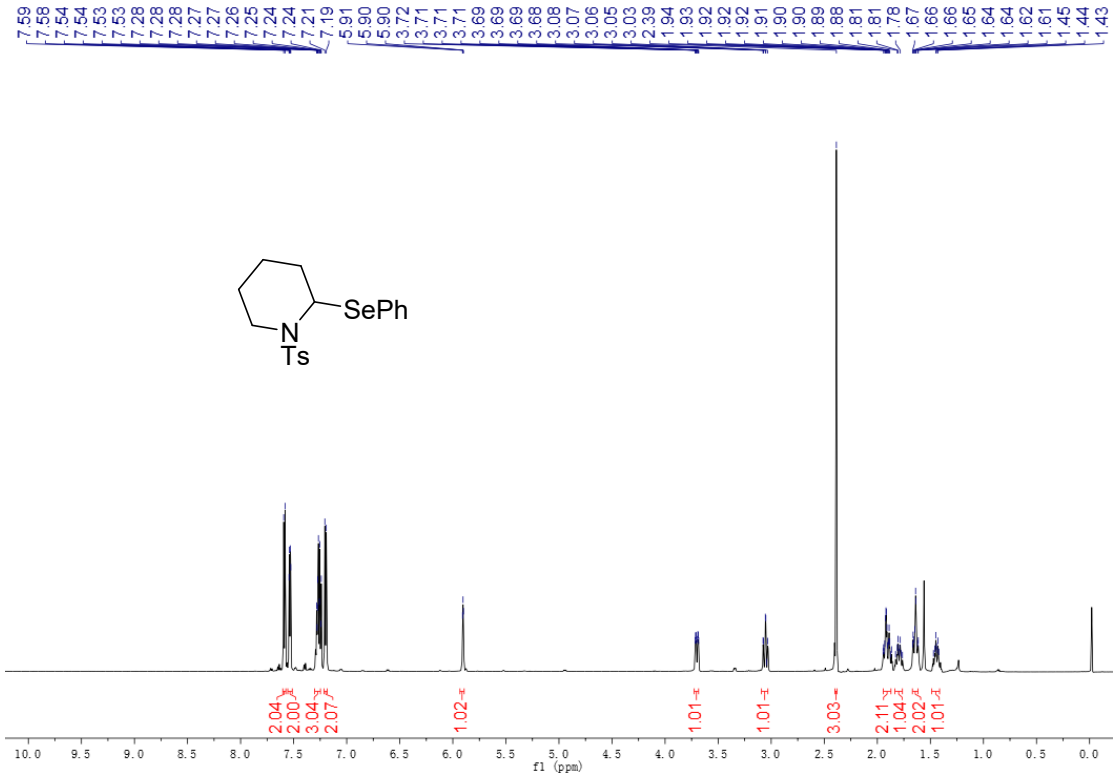
f1 (ppm)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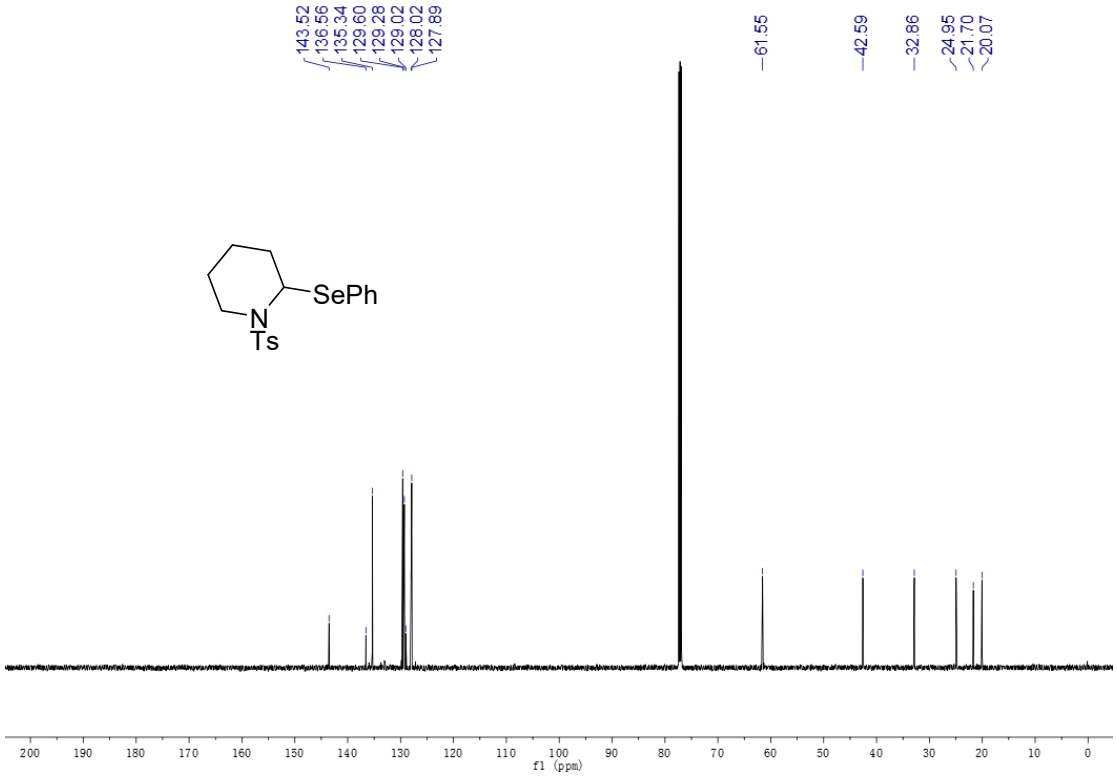
N
Ts
f1 (ppm)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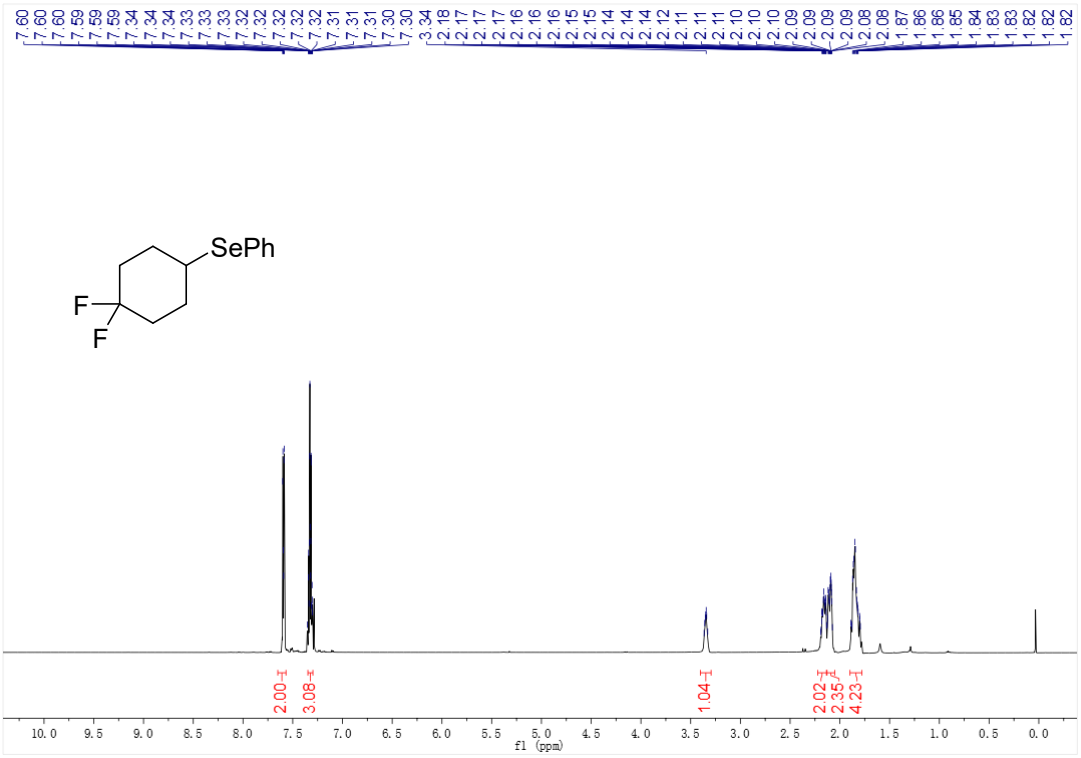
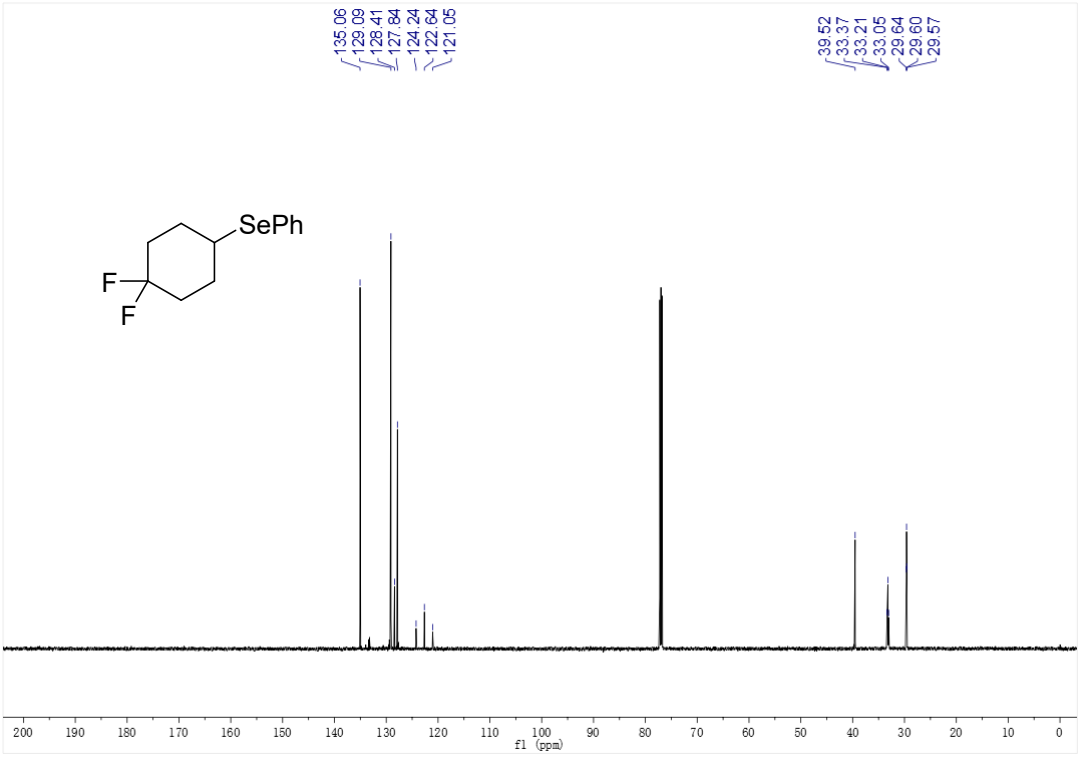
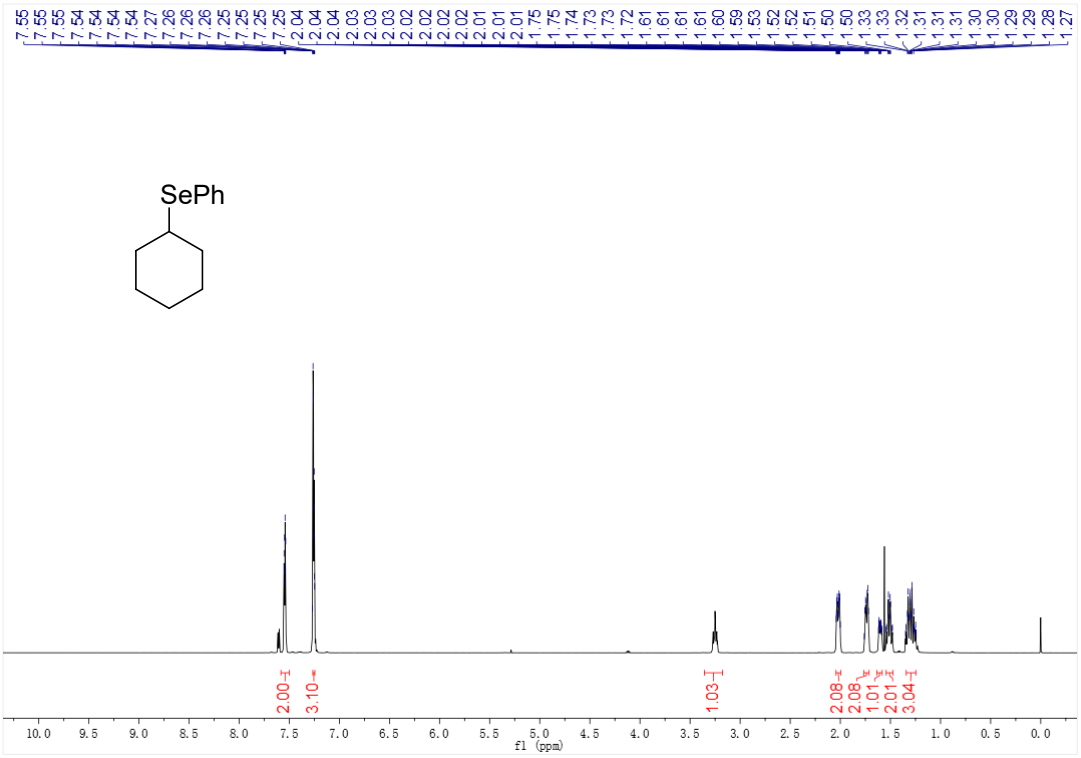
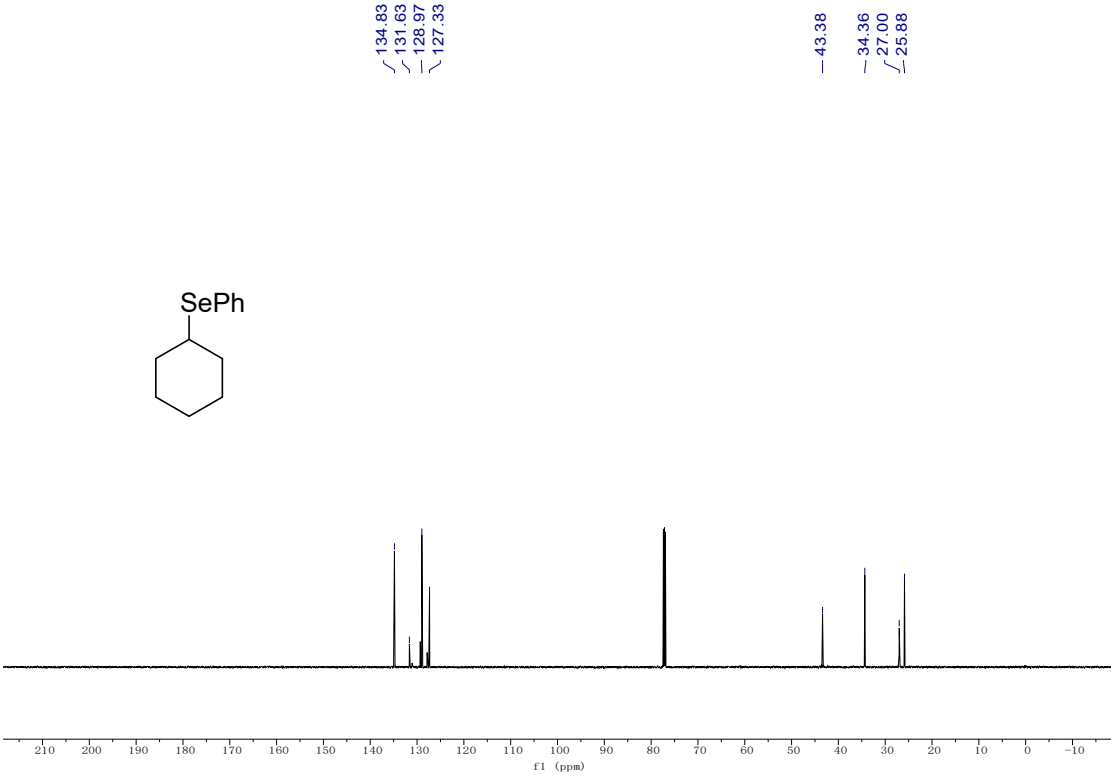
N
Ts
f1 (ppm)


SePh
F
F
2.00
3.08
1.04
2.02
2.35
4.23
f1 (ppm)


SePh
F
F
f1 (ppm)


SePh
7.55 7.55 7.55 7.54 7.54 7.54 7.54 7.27 7.26 7.26 7.25 7.25 7.25 7.25 2.04 2.04 2.04 2.03 2.03 2.03 2.02 2.02 2.02 2.02 2.01 2.01 2.01 1.75 1.75 1.74 1.73 1.73 1.72 1.61 1.61 1.61 1.61 1.60 1.59 1.53 1.52 1.52 1.51 1.50 1.50 1.33 1.32 1.31 1.31 1.30 1.30 1.29 1.29 1.28 1.27
2.00 3.10 1.03 2.08 2.08 1.01 2.01 3.04
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


SePh
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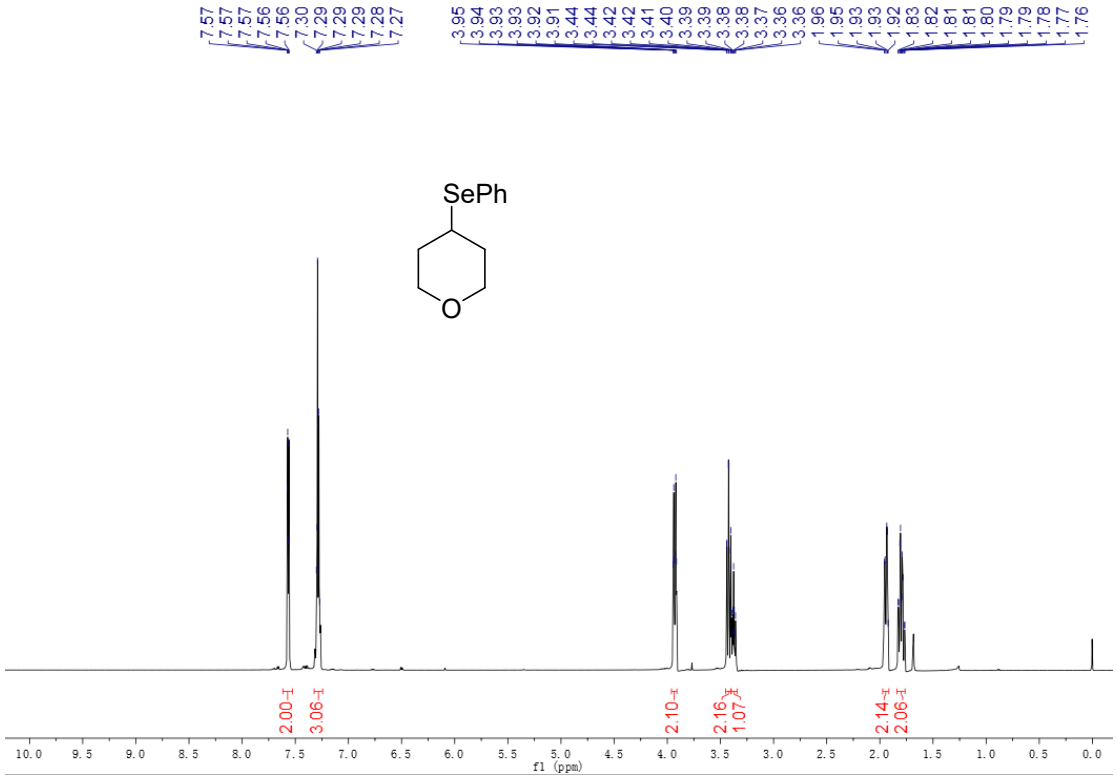
27.00
25.88
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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3.92
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1.93
1.93
1.92
1.83
1.82
1.81
1.81
1.80
1.79
1.79
1.78
1.77
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SePh
O
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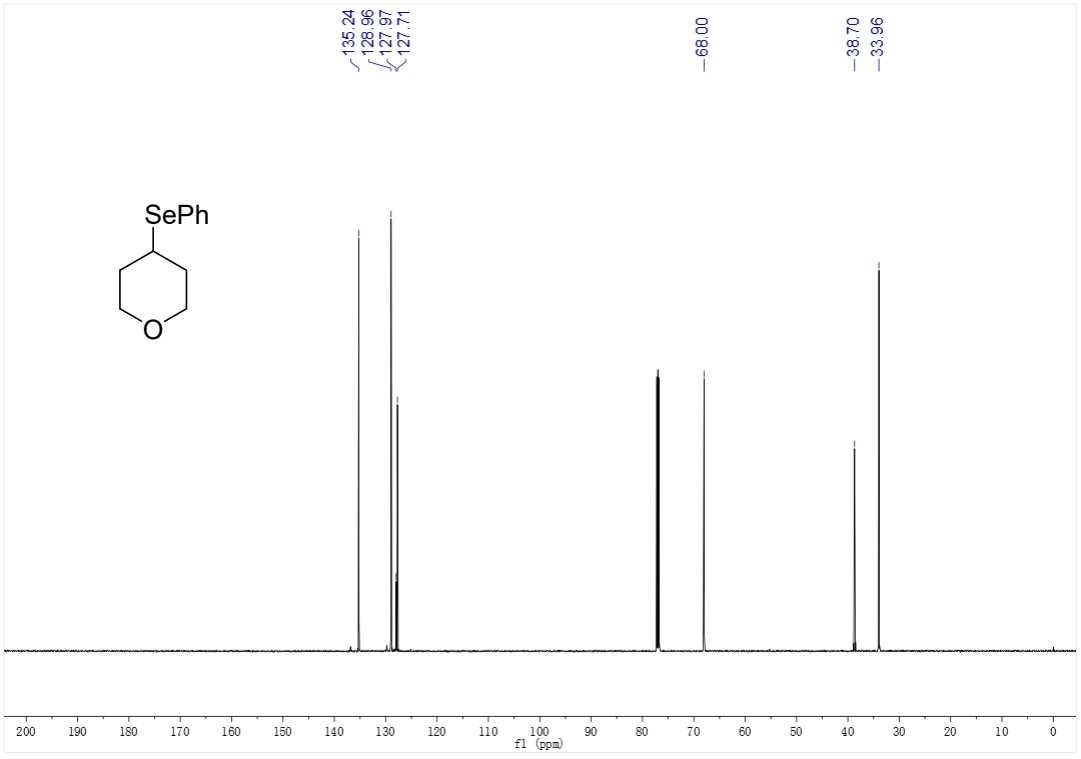
3.06
2.10
2.16
1.07
2.14
2.06
f1 (ppm)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128.96
127.97
127.71
68.00
38.70
33.96
SePh
O
f1 (ppm)


7.57
7.56
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7.55
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7.55
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7.26
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3.04
3.02
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2.00
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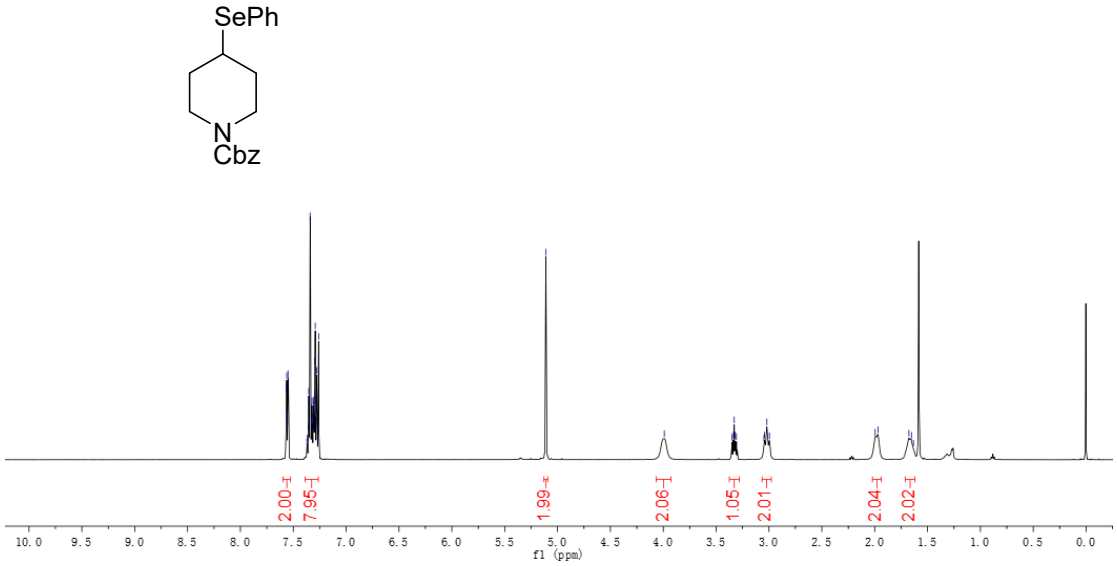
1.65
1.63


SePh
N
Cbz
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1.99
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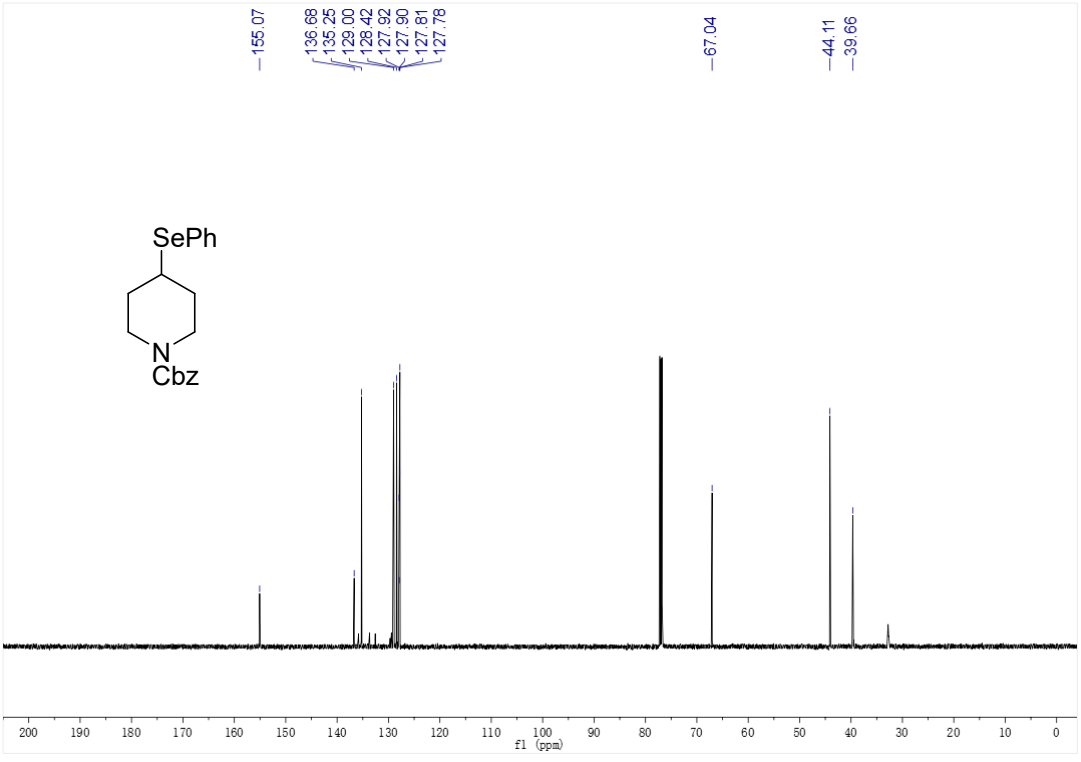
1.05
2.01
2.04
2.02
f1 (ppm)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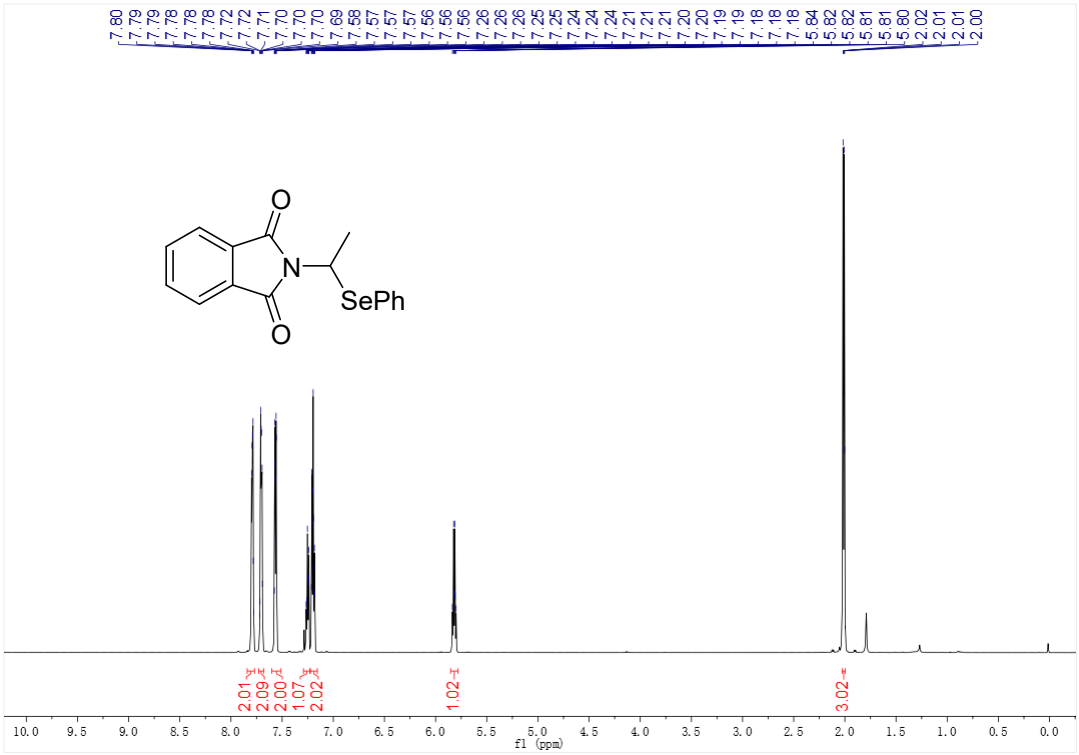
127.90
127.81
127.78
67.04
44.11
39.66
SePh
N
Cbz
f1 (ppm)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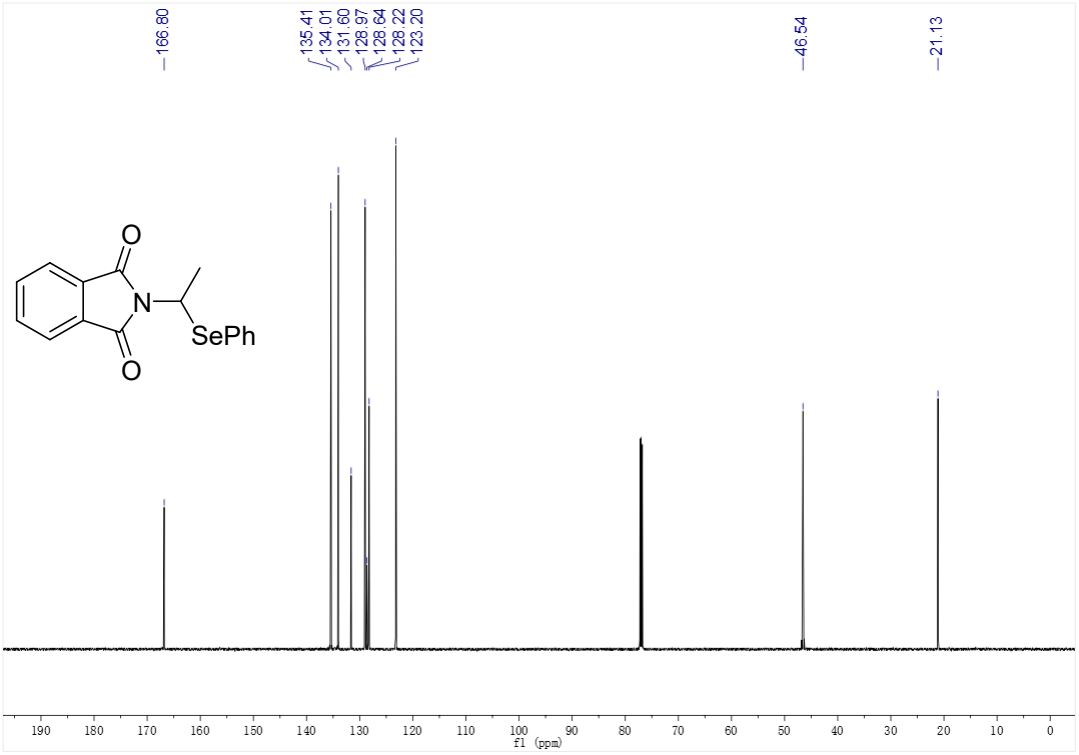
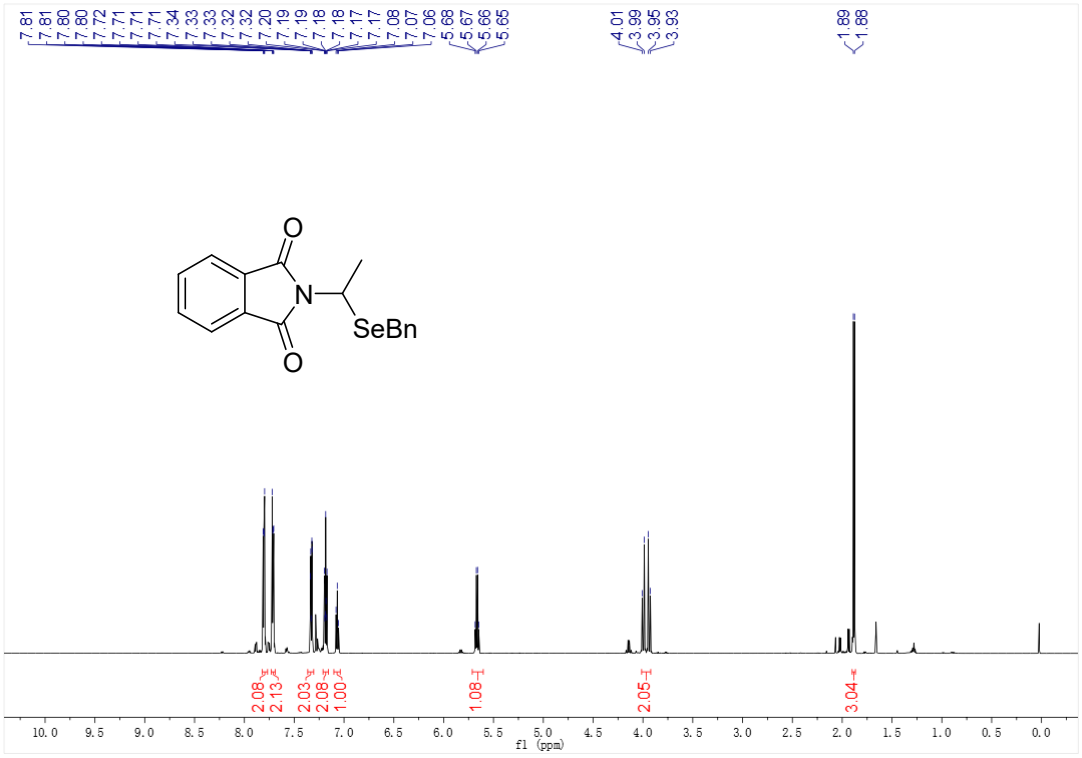
O
N
SePh
O
2.01 2.09 2.00 1.07 2.02
1.02
3.02
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


166.80
135.41
134.01
131.60
128.97
128.64
128.22
123.20
46.54
21.13
O
N
SePh
O
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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7.81
7.80
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7.71
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7.33
7.32
7.32
7.20
7.19
7.19
7.18
7.18
7.17
7.17
7.08
7.07
7.06
5.68
5.67
5.66
5.65
4.01
3.99
3.95
3.93
1.89
1.88
O
N
SeBn
O
2.08
2.13
2.03
2.08
1.00
1.08
2.05
3.04
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
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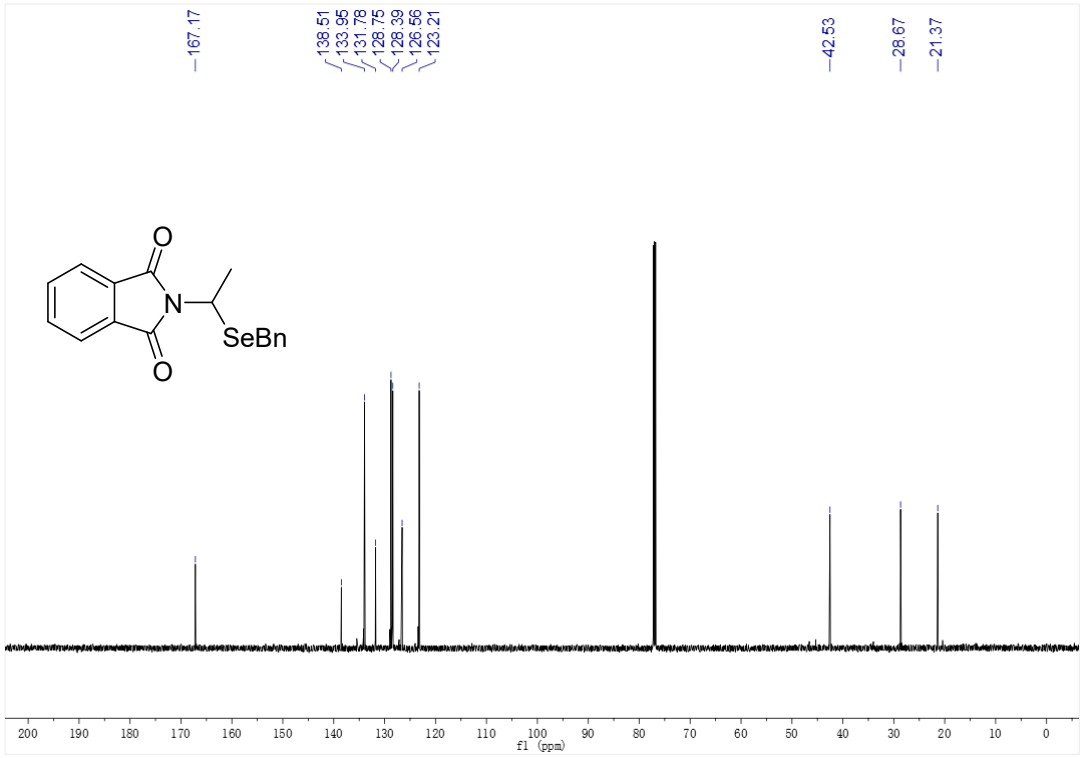
0.0
f1 (ppm)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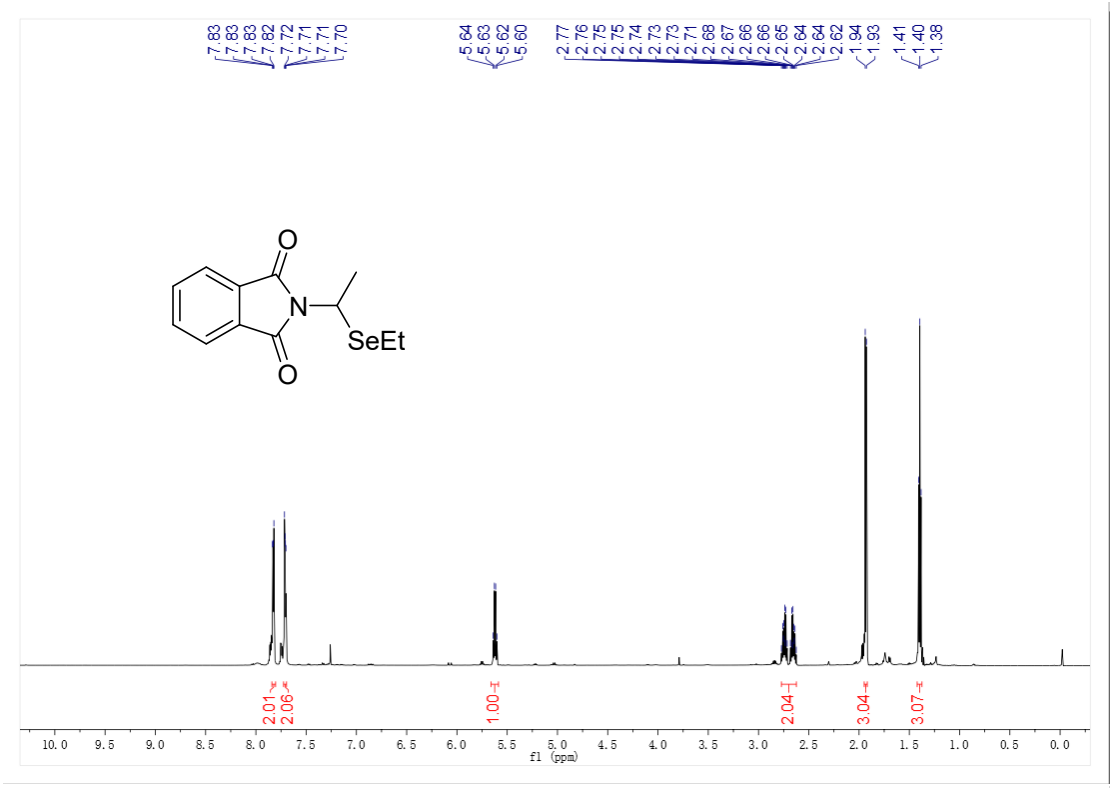
138.51
133.95
131.78
128.75
128.39
126.56
123.21
42.53
28.67
21.37
O
N
SeBn
O
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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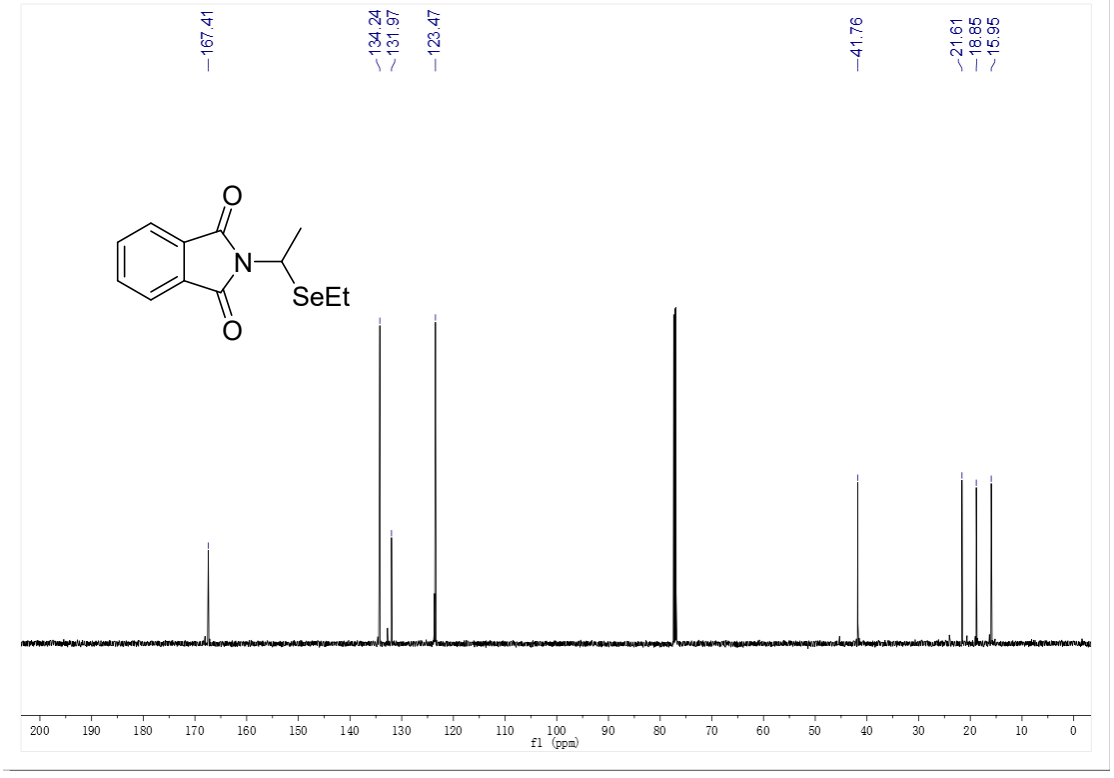
7.82
7.72
7.71
7.71
7.70
5.64
5.63
5.62
5.60
2.77
2.76
2.75
2.75
2.74
2.73
2.71
2.68
2.67
2.66
2.66
2.65
2.64
2.64
2.62
1.94
1.93
1.41
1.40
1.38
O
N
SeEt
O
2.01
2.06
1.00
2.04
3.04
3.07
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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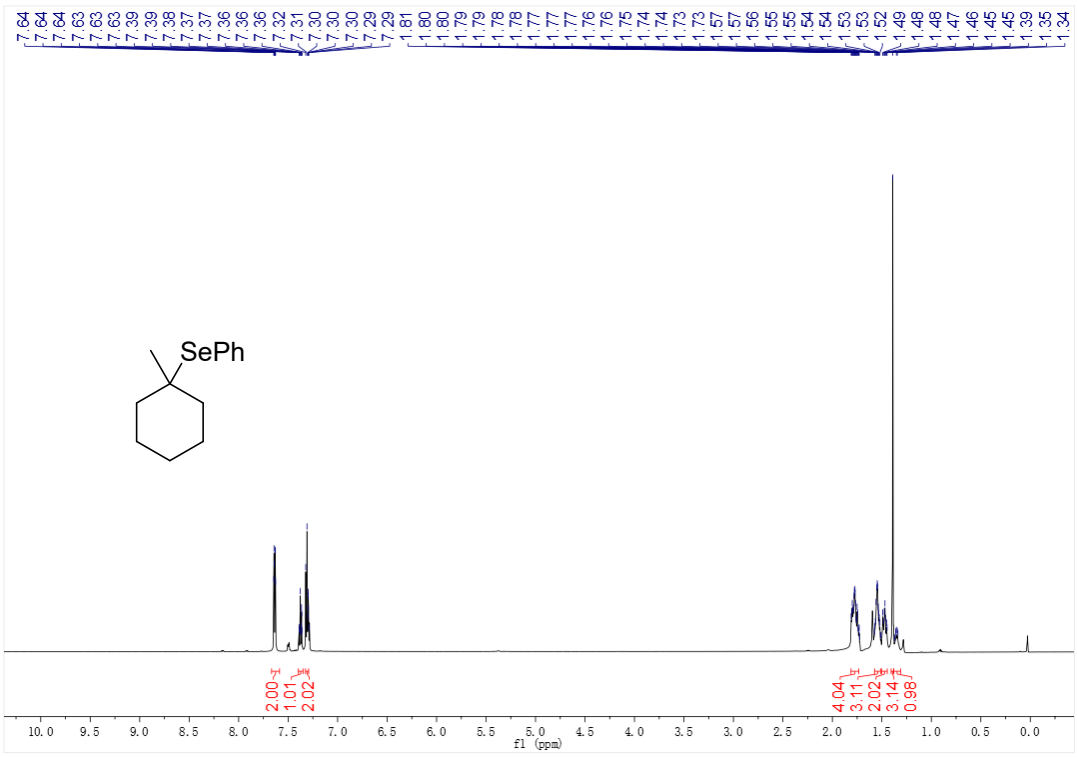
131.97
123.47
41.76
21.61
18.85
15.95
O
N
SeEt
O
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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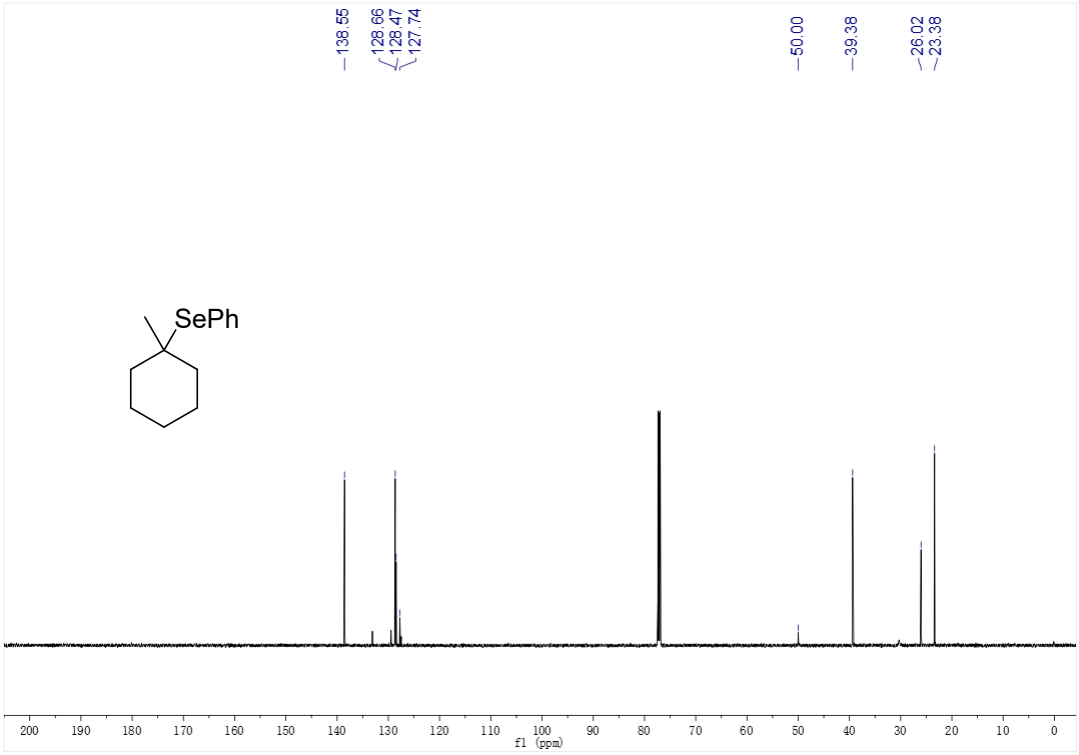
1.74
1.74
1.73
1.73
1.57
1.57
1.56
1.55
1.55
1.54
1.54
1.53
1.53
1.52
1.49
1.48
1.48
1.47
1.46
1.45
1.45
1.39
1.35
1.34
SePh
2.00
1.01
2.02
4.04
3.11
2.02
3.14
0.98
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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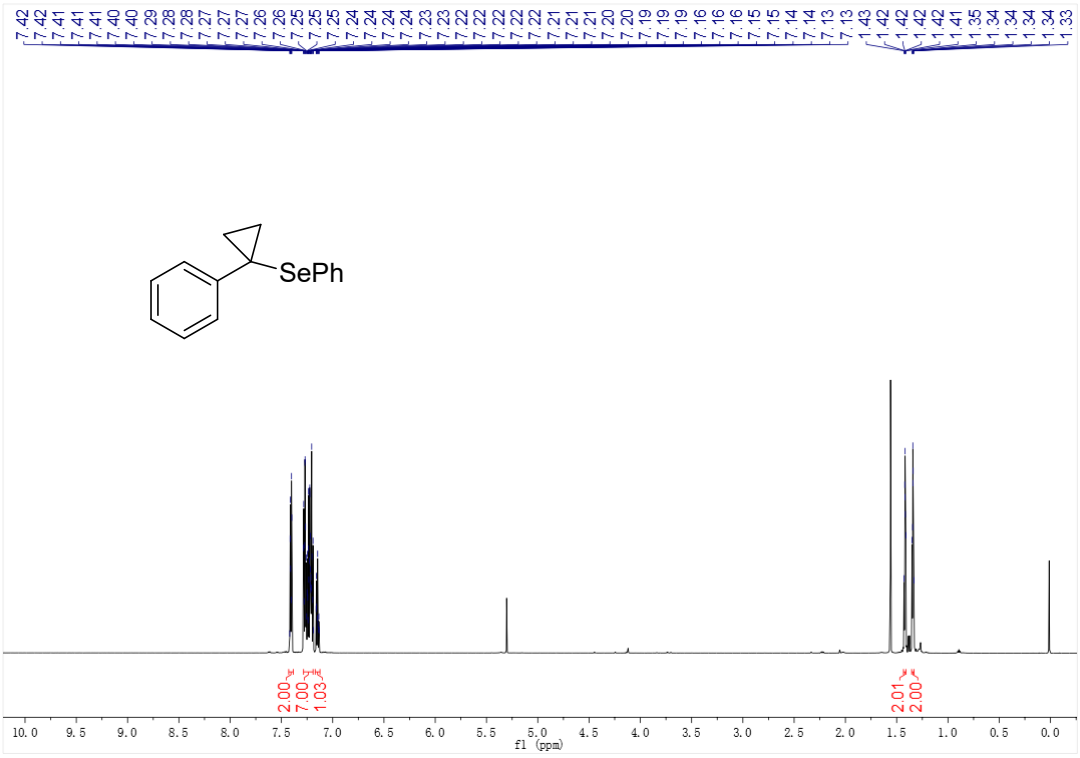
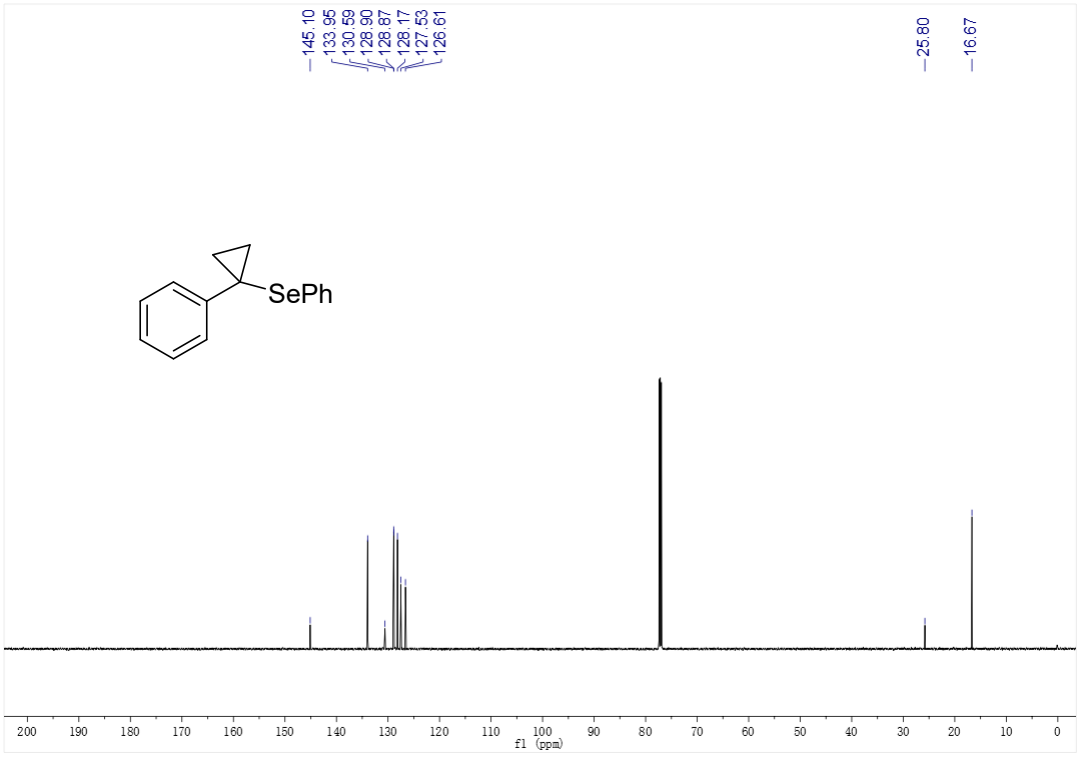
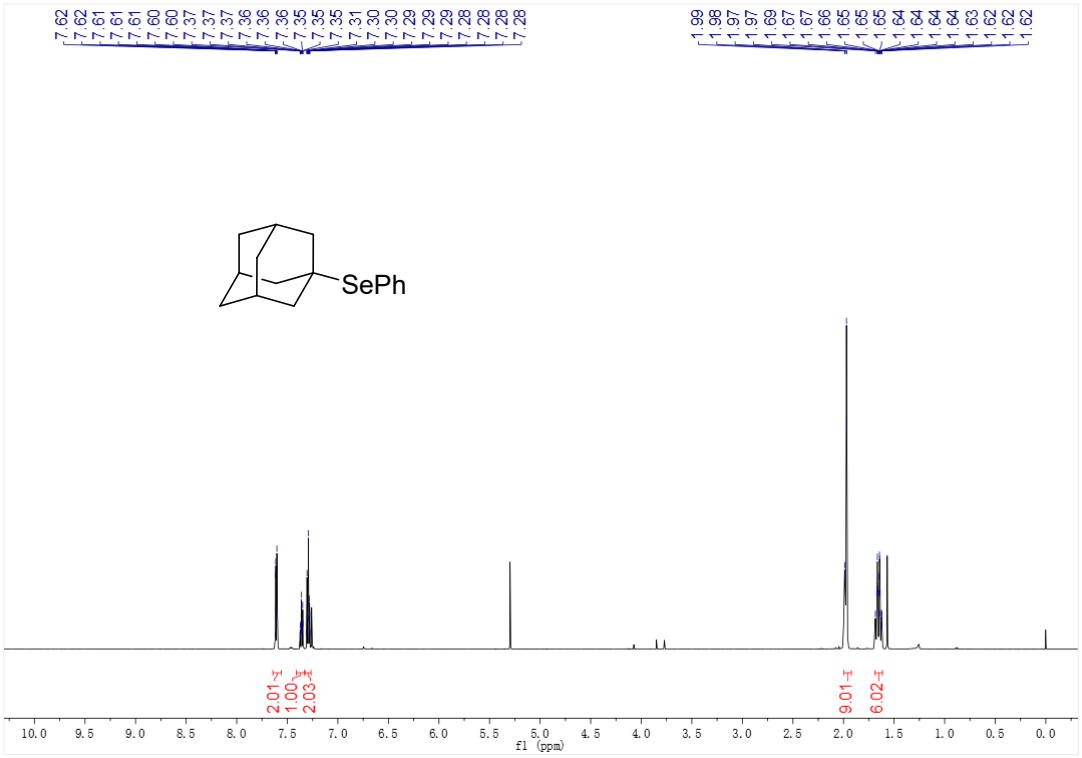
127.74
50.00
39.38
26.02
23.38
SePh
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


SePh
f1 (ppm)


SePh
f1 (ppm)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7.37
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1.97
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1.67
1.66
1.65
1.65
1.65
1.64
1.64
1.64
1.64
1.63
1.62
1.62
1.62
SePh
2.01
1.00
2.03
9.01
6.02
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
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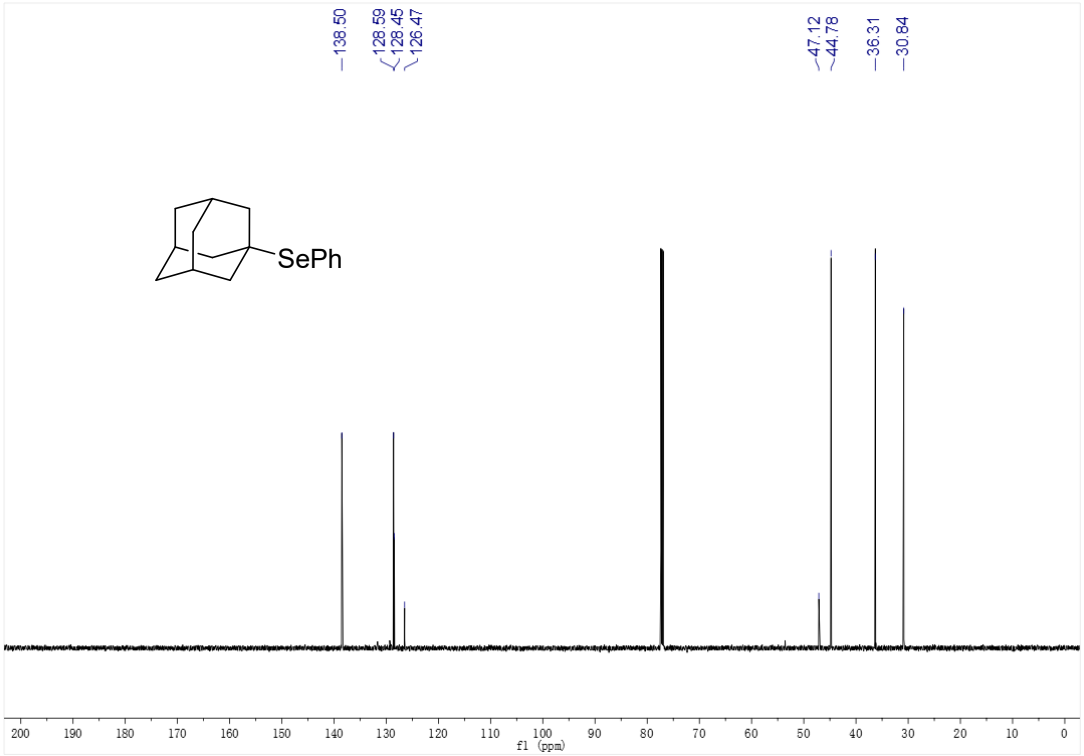
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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SePh
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180
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150
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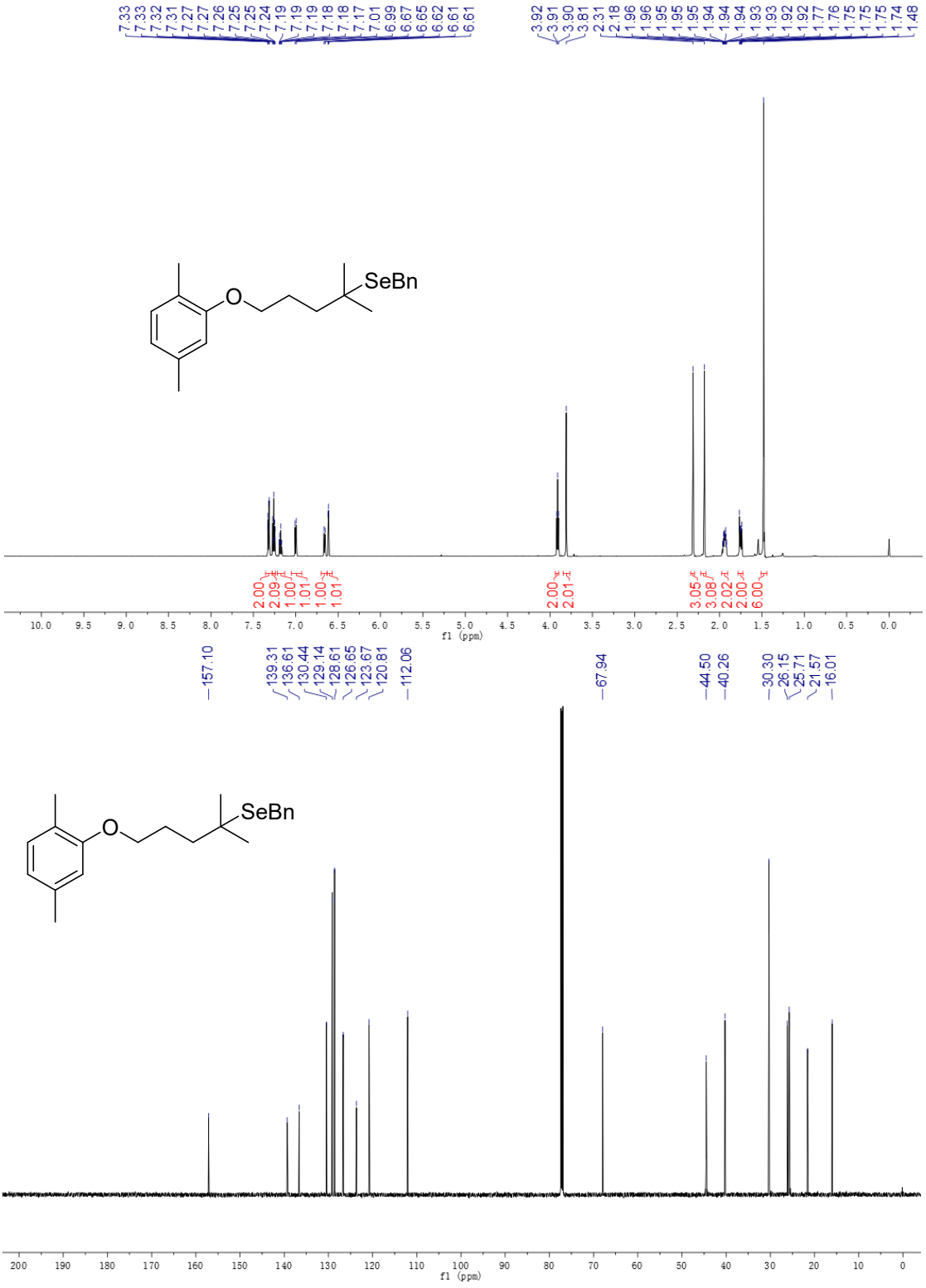
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.27
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7.25
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7.24
7.19
7.19
7.19
7.18
7.18
7.17
7.01
6.99
6.67
6.65
6.62
6.61
6.61
3.92
3.91
3.90
3.81
2.31
2.18
1.96
1.96
1.95
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1.94
1.94
1.93
1.93
1.92
1.92
1.77
1.76
1.75
1.75
1.75
1.74
1.48
SeBn
O
2.00
2.09
1.00
1.01
1.00
1.01
2.00
2.01
3.05
3.08
2.02
2.00
6.00
f1 (ppm)
157.10
139.31
136.61
130.44
129.14
128.61
126.65
123.67
120.81
112.06
67.94
44.50
40.26
30.30
26.15
25.71
21.57
16.01
SeBn
O
f1 (ppm)