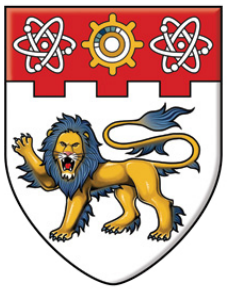
PART I: DEHYDRO OF THIOESTERS PART II: INDIUM CATALYZED CYCLIZATION.
ZHANG QIUCHI 2018



NANYANG TECHNOLOGICAL UNIVERSITY

PART I: DEHYDROGENATION OF CARBONYL COMPOUNDS *VIA* SELENIUM REAGENTS ELIMINATION.

PART II: INDIUM CATALYZED CYCLIZATION REACTION OF ACRYLATE.

ZHANG QIUCHI

SCHOOL OF PHYSICAL ANDMATHEMATICAL SCIENCES

2019

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ZHANG QIUCHI

School of Physical and Mathematical Sciences

A thesis submitted to the Nanyang Technological University
in partial fulfillment of the requirement for the degree of
Doctor of Philosophy

2019

Statement of Originality

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Authorship Attribution Statement

This thesis contains material from 1 paper published in the following peer-reviewed journal where I was the first and/or corresponding author.

Each chapter in Part II is published as Zhang, Q. -C.; Zhang, W. -W.; Shen, L.; Shen, Z. -L.; Loh, T. P., In(III)-TMSBr-Catalyzed Cascade Reaction of Diarylalkynes with Acrylates for the Synthesis of Aryldihydronaphthalene Derivatives. *Molecules* **2018**, *23*, 979.

The contributions of the co-authors are as follows:

- Prof Loh Teck-Peng provided the initial project direction and edited the manuscript drafts.
- Prof Loh Teck-Peng and Zhang Wenwei conceived and designed the experiments
- I and Shen Liang performed the experiments as well as mechanism study.
- Shen Liang and Shen Zhiliang wrote this paper.
- Zhang Wenwei and Shen Liang analyzed the data.

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ACKNOWLEDGEMENTS

Firstly, I would like to thank my supervisor Prof. Li Tianhu and co-supervisor Prof. Loh Teck Peng for their kind guidance and support.

I would also like to thank all my lab mates for their support and helpful input, in particular to Dr. Zhao Kai, Dr. Hu Xuhong, Dr. Shen Zhiliang, Dr. Sreekumar Pnkajakshan, Dr. Jakson Koh Peng Fei, Zhang Yonghui, Cheng Jun Kee and Wu Liuhai. Special thanks to Dr. Sheng Liang for the cooperation on Part II of this thesis, and Dr. Manikantha Maraswami and Jeffrey Goh's help on the technical correction of this dissertation.

Next, I would like to thank all technical and administrative staff in CBC, especially to to Ms. Chen Xiaoping, Ms. Florence Ng Pei Fan and Ms. Celine Hum Wei Mei for all administrative assistance rendered. Special mention goes to Ms. Goh Ee Ling and Ms. Zhu Wen Wei for their assistance in NMR and HRMS.

Finally, I would also like to give my deepest appreciatiation to my parents for their continuous support throughout the course of my Ph.D. studies

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LIST OF ABBREVIATIONS

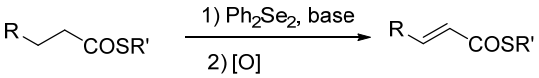
δ	chemical shift
°C	degree centigrade
Ac	acetyl
acac	acetylacetonate
aq	aqueous
Ar	aryl
Bn	benzyl
brs	broad singlet
d	doublet
dd	doublet of doublets
ddd	doublet of doublets of doublets
ddt	doublet of doublets of triplets
dq	doublet of quartets
dt	doublet of triplets
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DCE	1,2-dichloroethane
DCM	dichloromethane
DIPEA	diisopropylethylamine
DMA	*N*,*N*-dimethylacetamide
DMF	*N*,*N*-dimethylformamide
DMI	1,3-Dimethyl-2-imidazolidinone
DMP	Dess-Martin periodate
DMPU	*N*,*N*′-Dimethylpropyleneurea
DMSO	dimethylsulfoxide
2D NMR	two-dimensional nuclear magnetic resonance spectroscopy
ESI	electrospray ionization
Et	ethyl

h	hour
HMPA	hexamethylphosphoramide
HRMS	high resolution mass spectrometry
hv	photoirradiation
Hz	Hertz
Hex	n-hexyl
^{i}Pr	isopropyl
J	coupling constant
KPht	potassium phthalimide
*m*CPBA	*meta*-chloroperbenzoic acid
m	multiplet
Me	methyl
min	minute
NBS	*N*-Bromosuccinimide
NCS	*N*-chlorosuccinimide
NMP	*N*-methylpyrrolidone
NMR	nuclear magnetic resonance
NOESY	Nuclear Overhauser Enhancement spectroscopy
OTf	triflate
Ph	phenyl
PivOH	pivalic acid
p-TsOH	*p*-toluenesulfonic acid
py	pyridine
q	quartet
qd	quartet of doublets
qt	quartet of triplets
r.t.	room temperature
s	singlet
t	triplet
td	triplet of doublets

tt	triplet of triplets
tfacac	trifluoroacetylacetonate
THF	tetrahydrofuran
TLC	thin layer chromatography
TMS	trimethylsilyl
TMSX	trimethylsilyl halide

Summary

In the first part of this thesis, the elimination of thioesters in the presence of a selenium reagent is discussed.



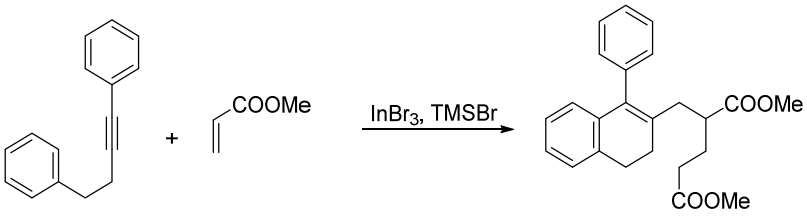
In chapter I, a brief review of the synthesis of α,β-unsaturated carbonyl compounds by dehydrogenation and the application of selenium reagents is summarized.

In chapter II, the reaction conditions of the elimination reaction of thioesters and the substrate scope of the reaction is presented.

In chapter III, the experimental procedure and the spectral data of the products are listed.

In the final chapter, some unsuccessful substrates are listed. In addition, the results of elimination reactions with esters under modified conditions is shown.

In the second part of this dissertation, the In(III)-TMSBr-catalyzed aryldihydronaphthalene derivatives synthesis is discussed.



In chapter I, an introduction of the application of the combination of indium salts and trimethylsilane halide is briefly summarized.

In chapter II, the condition of the aryldihydronaphthalene derivative synthesis reaction and the substrate scope of the reaction is outlined.

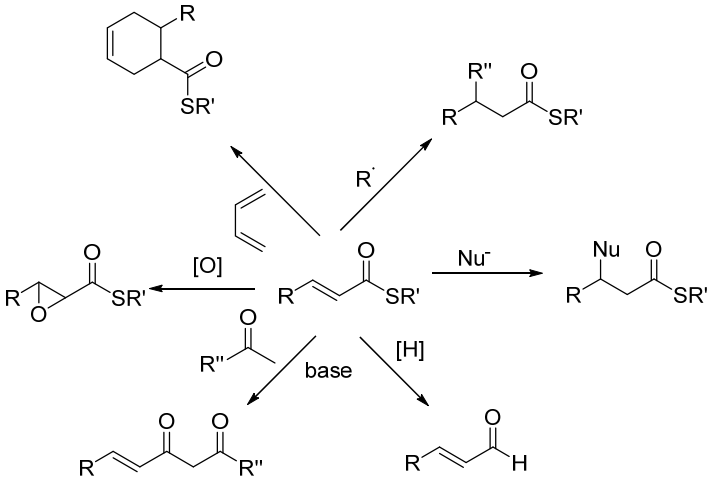
In chapter III, the experimental procedures and the spectral data of the products are listed.

Part I: α,β-dehydrogenation of carbonyl compounds *via* selenium reagents elimination

Chapter I: Introduction

The *α,β*-unsaturated carbonyl compounds are an important class of compounds; they are also crucial intermediates for the synthesis of pharmaceuticals and other bioactive molecules.[1,2] They could be attacked by a nucleophilic reagent, such as undergoing a Michael addition reaction by behaving as the Michael acceptor. In addition, these substrates could also participate in a Diels-Alder reaction to afford the corresponding adduct.

The *α,β*-unsaturated thioesters, with similar properties as their ester analogues, also have some unique properties of their own. For example, they are more reactive in the case of a Michael addition with Grignard reagents and normally only undergo 1,4 addition.[3] In addition, they can be easily reduced to form an aldehyde.[4]



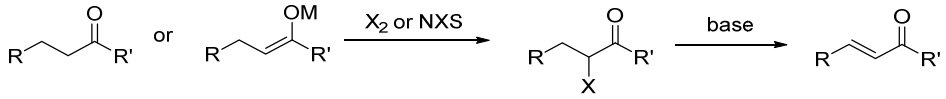
Scheme 1: Some applications of the *α,β*-unsaturated thioesters.

One method to synthesize *α,β*-unsaturated carbonyl compounds is by elimination reaction from saturated carbonyl compounds. There are only a few isolated examples that are reported for the dehydrogenation of thioesters. Methods for the dehydrogenation of their analogues, esters, are relatively more well-known. Below is a brief summary on the different dehydrogenation methods reported till date.

1. Methods for dehydrogenation of carbonyl compounds

1.1 Halogenation-dehydrohalogenation reactions

One of the most straightforward methods is the halogenation-dehydrohalogenation reaction. The first step is halogenation of the *α* hydrogen, either by direct halogenation or by converting it to an enolate before halogenation. The second step to afford the corresponding α,β-carbonyl compound is promoted by a base.



Scheme 2: The halogenation-dehydrohalogenation reactions.

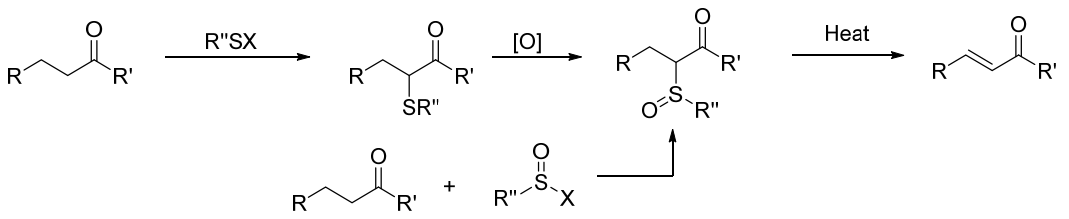
Bromine is most commonly used as the halogenating atom in the first step of the reaction; and it is introduced by reagents such as NBS[6], Br_2[7] or $CuBr_2$[8]. The direct halogenation normally requires a high temperature and the selectivity is usually poor[9]. An alternative method, by converting the carbonyl compound to its enolate form, could give the reaction a better selectivity and under milder conditions[10]. Alternatively, converting the carbonyl compounds to stable enolate derivatives, such as silyl enol ethers[11] or enol acetates[12], before using it for the halogenation reactions has also been reported.

For the second step, a base is typically used to promote the reaction[13]. Both organic and inorganic bases are used. Common organic bases used are 1,5-diazabicyclononene (DBN), 1,8-diazabicycloundec-7-ene (DBU), 1,4-diazabicyclo[2.2.2]octane (DABCO), Et_3N and KO^{t}Bu, while common inorganic bases that are utilized include NaOH, KOH

and KNH_2.

This method has been developed in the dehydrogenation of different carbonyl compounds, including aldehydes, ketones[10], esters[14], lactones[15] and amides[16]. In addition, a similar method of using $BrCCl_3$ and DBU has also been developed, which provides good yields for synthesizing heterocyclic compounds[17].

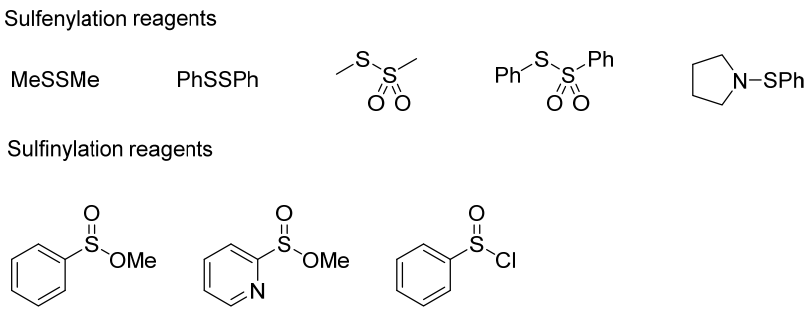
1.2 Organosulfur reagents



Scheme 3: The oxidation-elimination of organosulfur compounds.

Organosulfur reagents introduced in elimination reaction was originally discovered and developed by B. M. Trost and several other groups in the 1970s.[18] The organosulfur intermediates of the carbonyl compounds are normally formed by converting the carbonyl compound to an enolate or enol ether before reacting with organosulfur reagents. Dimethyl disulfide and diphenyl disulfide are commonly used as the organosulfur reagents due to their stability and availability commercially. Peroxides, periodates or ozone are usually used in the oxidation of the sulfur-containing intermediate in the second step.

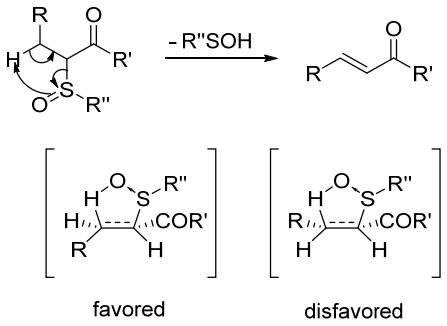
Alternatively, sulfinylation reagents are used for the reaction to form the sulfoxide intermediate in one step[19]. This method could avoid undesired oxidation of the substrate, especially if the substrate is vulnerable to oxidation.



Scheme 4: Some commonly used organosulfur reagents.

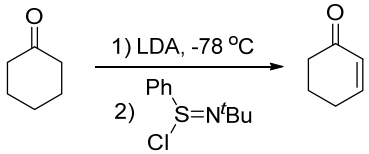
The elimination of the sulfoxide intermediate normally requires a high temperature (about 120 ^{o}C), and it is eliminated *via* a stereospecific 5-membered concerted

transition-state[20], which means it affords a (*E*)/(*Z*) stereoselectivity of the products for some of the substrates. As shown below, if the newly formed double bond is 1,2-disubstituted, the (*E*)-isomer is predominantly formed, as the transition state for the (*Z*) isomer is disfavored; on the other hand, if the newly formed double bond is tri- or tetrasubstituted, the (*E*)/(*Z*) stereochemistry would be poor, as both transition states have a similar energy.



Scheme 5: Mechanism of the elimination of the sulfoxide intermediate.

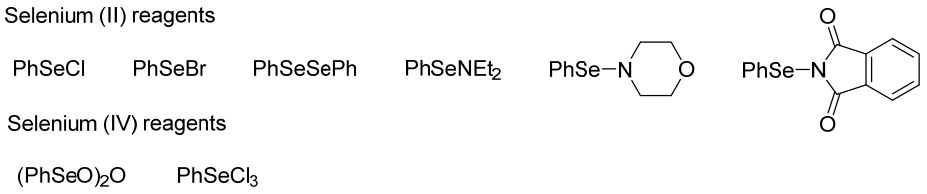
Another similar method is using the reagent *N*-*tert*-butyl phenylsulfinimidoyl chloride[21] as the sulfur reagent, which is similar to the sulfinylation reagents mentioned above. This intermediate could eliminate at a low temperature, which allows this reaction to be done as a two-step one-pot reaction.



Scheme 6: Reaction with the reagent *N*-*tert*-butyl phenylsulfinimidoyl chloride.

1.3 Organoselenium reagents

Similar to organosulfur reagents, organoselenium reagents, mainly developed by the groups of Reich[22] and Sharpless[23], can also provide the elimination needed. The main advantage of organoselenium reagents is that they can eliminate at low temperatures (depending on the conditions, elimination often can proceed smoothly and in a facile manner at room temperature), thus it is widely employed as a reagent for the elimination reaction compared to organosulfur reagents.[24]



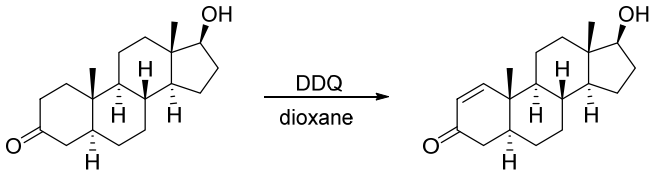
Scheme 7: Some commonly used organoselenium reagents.

The approach and mechanism are similar to their organosulfur analogues, it can be acheived by a selenium (II) reagent and followed by oxidation, and it could also be directly obtained by a selenium (IV) reagent; the mechanism is also *via* a 5-membered concerted transition-state and gives a similar (*E*)/(*Z*) selectivity as the sulfoxide intermediate.

Further discussions with regards to this approach is shown in **section 2** of this chapter.

1.4 Dichlorodicyanoquinone (DDQ)

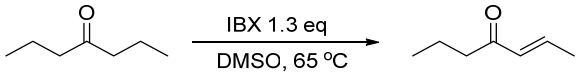
Among most of quinone derivatives, DDQ presents a high reactivity to the α hydrogen of carbonyl compounds.[25] Mechanistic study suggests that it starts with a slow hydride transfer from the starting material to the DDQ, and followed by a fast deprotonation.[26] The main application of DDQ is the dehydrogenation of 3-ketosteroid derivatives[27], which is generally bio-active. For dehydrogenation of simple ketones and esters, it could be achieved by transforming it to silyl enol ethers[28] before introducing DDQ.



Scheme 8: The use of DDQ as a dehydrogenation reagent.

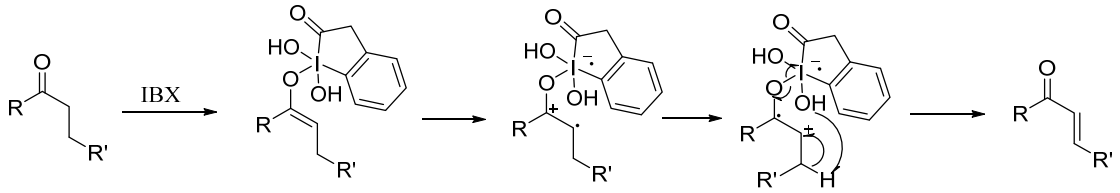
1.5 Hypervalent iodine reagents

2-Iodoxybenzoic acid (IBX) was firstly reported in 1893[29], and has been widely used as an oxidant for the oxidation of alcohols.[30] In 2000, it was discovered to be suitable for the *α*,*β*-dehydrogenation of aldehyde and ketones by Nicolaou's group[31].



Scheme 9: The first use of IBX as a dehydrogenation reagent.

IBX can be easily synthesized by the oxidation of 2-iodobenzoic acid with potassium bromate[32] or oxone.[33] The mechanism of the of the reaction with IBX is via a single electron transfer (SET) mechanism[34]. As the 1-hydroxy-3*H*-1,2-benziodaoxol-3-one (IBA) is formed as a byproduct by the reaction of IBX with DMSO, excess amount of IBX is needed. In addition, because the SET reaction requires the formation of the enolate, the weakly acidic compounds such as esters, amides, lactones, lactams and thioesters are generally not reactive.



Scheme 10: The SET mechanism of IBX as a dehydrogenation reagent.

As the IBX can also oxidize the alcohol, it can also be applied to convert the alcohols to *α*,*β*-unsaturated aldehydes or ketones. DMSO is important to the reaction because it is one of the few solvents capable of dissolving the oxidant. Fluorobenzene or THF is occasionally used as a co-solvent to increase the solubility of the starting material. In addition, DMSO can also act as a ligand to IBX and stabilize the intermediate. *N*-methylmorpholine-*N*-oxide (NMO) or 4-methoxypyridine-*N*-oxide (MPO) is also sometimes used as the ligand.[35]

Other modified IBX, such as 5-trimethylamino-2-iodoxybenzoic acid[36] and tetrafluoro-2-iodoxybenzoic acid[37] are also reported. They can overcome some of IBX's limitations, but they usually require multiple steps to synthesize. Alternatively, using a catalytic amount of 2-iodobenzoic acid or sodium 2-iodobenzenesulfonate with oxone is

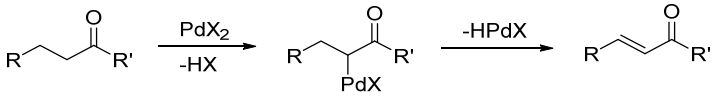
reported[38].

Another use of IBX is the dehydrogenation of silyl enol ethers and esters[39], the ketones can be converted to silyl enol ether by TMSOTf/NEt_3, then IBX (with NMO as ligand) is used for the reaction. Alternatively, using LDA or LiHMDS and subsequently adding TMSCl is also possible for synthesizing the silyl enol ethers.

Another similar method is by utilizing HIO_3 or I_2O_5 dissolved in DMSO as an alternative method IBX[40]. It shows a similar scope as the IBX, but gives a better result for five-membered cyclic ketones.

1.6 Transition metal reagents or catalysts

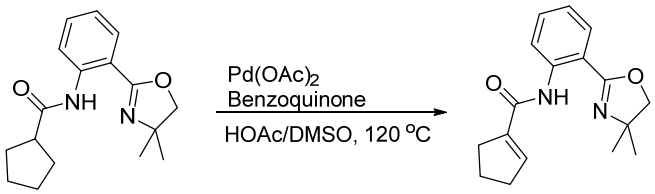
Palladium is one of the most widely exploited transition metal as the catalyst for the dehydrogenation of aldehyde and ketones. It has been investigated in the early 1970s[41]. These reactions are believed to be a two-step reaction, the first step is a "C–H activation", the palladium insert through an α hydrogen cleavage, form a palladium-enolate intermediate. The second step is a β-hydride elimination to form the double bond[42].



Scheme 11: Mechanism of the palladium mediated dehydrogenation reactions.

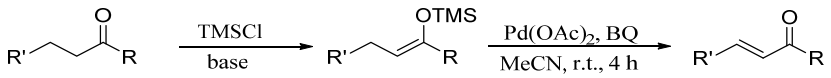
Palladium catalysts that are widely used include $PdCl_2$[43], $PdCl_2(PhCN)_2$[44], $Pd(PPh_3)_2Cl_2$[45], $Pd(OAc)_2$[46] and $Pd(TFA)_2$[47]. The reaction could be conducted with either a stoichiometric amount of palladium reagent or a catalytic amount of palladium reagent combined with another oxidant.

Although palladium catalyst is normally unreactive to esters and amides due to the lack of activity of the α hydrogen, it is reported that a directing group[48] could make it possible for amides to participate in the reaction:



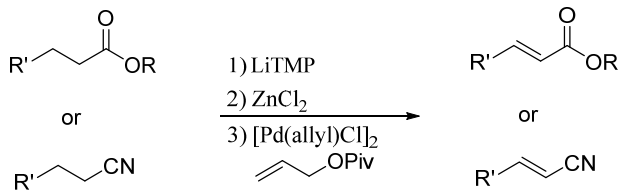
Scheme 12: The dehydrogenation of amides using a directing group.

Another method for the palladium catalyst approach is to convert the carbonyl compounds to silyl enol ethers before dehydrogenation with the palladium reagents, which is known as the Saegusa-Ito reaction[49].



Scheme 13: The Saegusa-Ito reaction.

A similar approach is by utilizing the enolate zinc salt[50] instead of the silyl enol ether, which proved to be useful for esters and nitriles:



Scheme 14: the enolate zinc salt approach for the palladium catalyst dehydrogenation.

Other transition metals, such as Cu, Ni and Mn are also reported as efficient catalyst or reagent for dehydrogenation reactions.[51]

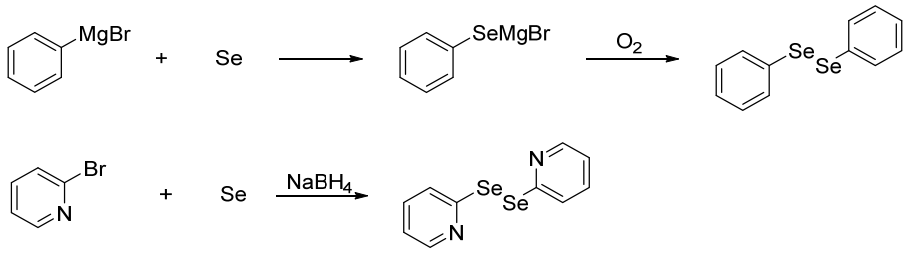
2. Detailed discussion of organoselenium reagents

Since this work mainly focuses on the organoselenium reagent mediated dehydrogenation reaction, a further review about this approach is outlined below.

2.1 Reagents for introducing the seleno-group

2.1.1. Electrophilic selenium reagents

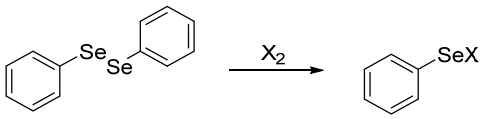
Diselenide, such as diphenyl diselenide[52] and bis(2-pyridyl) diselenide[53], are the commonly used selenium reagents. They are relatively easy to prepare and stable on storage. They are also commonly used precursor for other selenium reagents. Diphenyl diselenide can be prepared by reacting selenium powder with the Grignard reagent phenylmagnesium bromide, and subsequently oxidized by oxygen[52]. Bis(2-pyridyl) diselenide could be synthesized by reacting selenium powder with sodium borohydride, then reflux with 2-bromopyridine[53]. Other diselenide reagents can also be synthesized by these two methods.



Scheme 15: Synthesis of diselenium reagents.

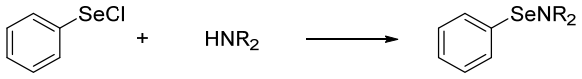
Selenenyl halides, such as benzeneselenenyl chloride/bromide[52] or 2-pyridineselenenyl

chloride/bromide[53], are strong electrophilic selenium reagents and are widely used. Both chloride and bromide reagents are relatively stable for storage, albeit that both are slightly sensitive to moisture. They could be prepared by stoichiometric reaction of chlorine or bromine with diselenide.



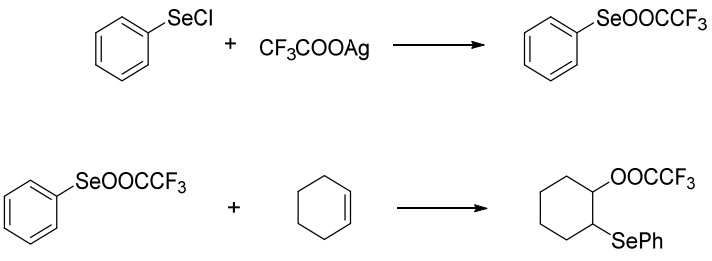
Scheme 16: Synthesis of selenenyl halide reagents.

Selenenamides, such as *N*,*N*-diethylbenzeneselenenamide[54] and *N*-(phenylseleno)phthalimide[55], are also reported to be efficient for introducing a seleno-group, they could react smoothly with certain dicarbonyl compounds even without a base. They could be prepared by reacting selenenyl chloride with dialkyamines.



Scheme 17: Synthesis of selenenamide reagents.

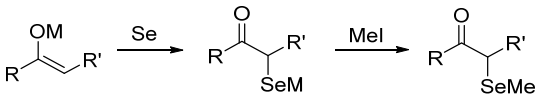
Benzeneselenenyl trifluoroacetate[56] is also reported as a selenium reagent. It could be synthesized by treating benzeneselenenyl chloride/bromide with silver trifluoroacetate. Unlike the reagents mentioned above, it is mainly used on addition reactions with olefins, and both selenium and trifluoroacetate are added across the double bond.



Scheme 18: Synthesis and uses of benzeneselenenyl trifluoroacetate.

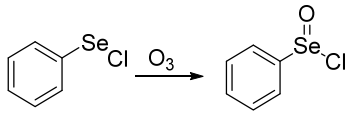
Elemental selenium is also occasionally reported as a selenium reagent[57], it could react

with an enolate, followed by alkylation with an alkyl halide to afford the seleno product.



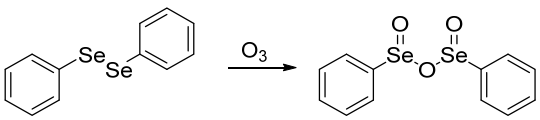
Scheme 19: Using elemental selenium as the reagent.

Benzeneseleninyl chloride[22b,58], which could be prepared by oxidizing benzeneselenenyl chloride with ozone, provide an advantage of direct synthesis of the selenoxide product, and it could be useful when the substrate is sensitive to oxidation. However, it is also quite moisture sensitive and must be handled under inert atmosphere.



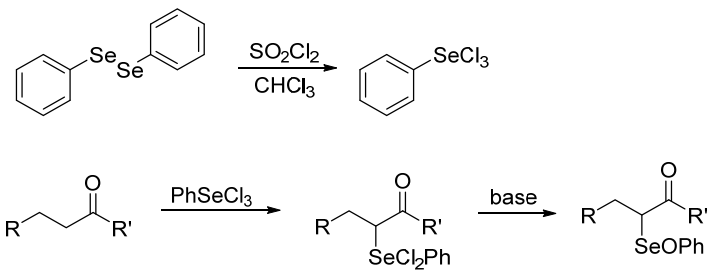
Scheme 20: Synthesis of benzeneseleninyl chloride.

Benzeneseleninic anhydride[59], which can be prepared by oxidizing diphenyl diselenium with ozone, also provides a similar advantage to that of benzeneseleninyl chloride. Compared to benzeneseleninyl chloride, it is not as moisture sensitive and can be handled under air. As a result, it is widely used on dehydrogenation on a variety of carbonyl compounds[58,60].



Scheme 21: Synthesis of benzeneseleninic anhydride.

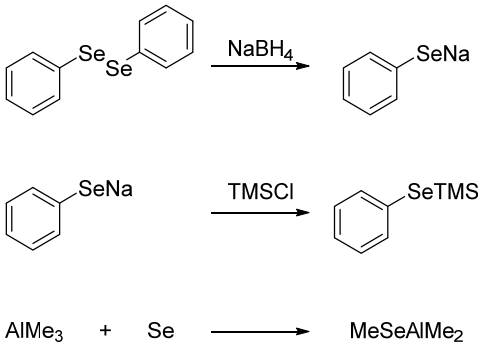
Phenylselenium trichloride[61] is another selenium (IV) reagent, it can be prepared by treating diphenyl diselenium with sulfuryl chloride in chloroform. It is sensitive to moisture and must be stored at low temperatures. Reaction of phenylselenium trichloride gives a dichloroselenium product, it could be isolated by filtration and then hydrolysis to the selenoxide intermediate with a base, which could then easily eliminate.



Scheme 22: Synthesis of phenylselenium trichloride and general reaction scope of it.

2.1.2. Nucleophilic selenium reagents

Sodium benzeneselenolate[23a,62] is one of the widely used nucleophilic selenium reagent. It is prepared by reducing diphenyl diselenium with sodium borohydride. Other nucleophilic selenium reagents like trimethylsilyl phenyl selenide[63] and dimethylaluminum methyl selenide[64] are also reported, but their applications are relatively more limited.



Scheme 23: Synthesis of some nucleophilic selenium reagents.

2.2 Methods of introducing the seleno-group

2.2.1 Electrophilic selenenylation

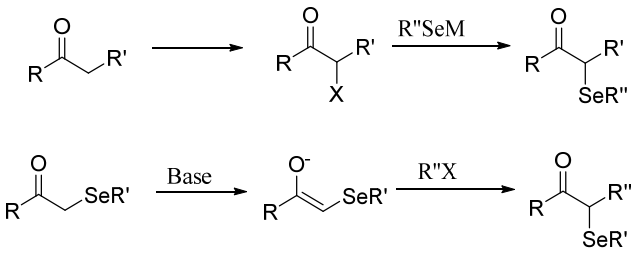
Electrophilic selenenylation is one of the most straightforward methods for selenenylation of carbonyl compounds. There are normally three methods for selenenylation: direct selenenylation, selenenylation of enolates and selenenylation of silyl enol ethers.

Direct selenenylation is the simplest method, it is often carried out with a selenenamide, and reacts mainly with ketones and aldehydes, catalyzed by a weak base or acid[23a]. Selenenylation of enolates is the most commonly used method for α selenenylation of carbonyl compounds, and it is usually carried out as a one-pot reaction. Firstly, the carbonyl compound is converted to an enolate by a strong base, usually LDA, then, the enolate solution is reacted with one of the electrophilic selenium reagent mentioned above. Benzeneselenenyl chloride and bromide are the most commonly used reagents. Diphenyl diselenide is also used occasionally.

Selenenylation of silyl enol ethers involves the conversion of the enolate to silyl enol ether by TMSCl or other silyl reagents, then followed by the selenenylation step. Compared to the methods above, despite introducing one more step, it often provides a higher yield and a product of higher purity[63].

2.2.2 Nucleophilic selenenylation

Nucleophilic selenenylation is less straightforward compared to the electrophilic method. It is normally done by substitution of an α-halo or α-sulfonyloxy carbonyl compound[64], or alternatively, by alkylation of an already-existing α-seleno carbonyl compound[65].



Scheme 24: Nucleophilic selenenylation procedure.

2.3 Oxidation of the seleno-group

Many oxidation reagents can be used to transform the selenide to selenoxide. Depending on the substrate, different oxidants and conditions are applied.

Hydrogen peroxide is the most commonly used oxidant, it is usually done in DCM (may also contain an equivalent amount of pyridine) or THF (with a trace amount of acetic acid) at 0 ^{o}C or room temperature. Two equivalents of hydrogen peroxide is required for this reaction, but the oxidant is usually added in excess because the selenium by-product can both react with it to form a Se (VI) compound and catalytically decomposes H_2O_2 present in the reaction mixture.

Ozone is another oxidant commonly used for this reaction, it is normally carried out at -78 ^{o}C. It can oxidize the selenide to selenoxide with no formation of other by-products, This is hence crucial for certain substrates that are sensitive to acids or bases[66]. Also, since the selenoxide does not eliminate at this low temperature, it is also possible to get the selenoxide as the product.

meta-Chloroperoxybenzoic acid is also commonly used for oxidation, a solution of DCM or THF is usually used, the reaction temperature is normally carried out at -78 ^{o}C or -40 ^{o}C.

Sodium metaperiodate is also used when the product is sensitive to other oxidants, for example, the product with an amine group group[67] or electro-rich double bond[68]. As sodium metaperiodate is not soluble in most organic solvents, it is normally done in aqueous methanol, THF, ethyl acetate, or glyme at room temperature.

Other oxidants, like *tert*-butyl hydroperoxide[69], oxaziridines[70], chloramine-T[71], chromium trioxide/pyridine[72], NBS[73] and NCS[74] are also reported, but are less commonly used.

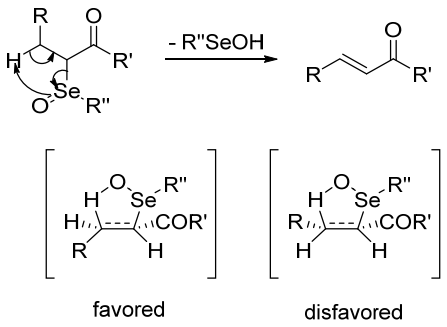
2.4 Reaction rate, mechanism and selectivity of the selenoxide elimination

2.4.1 Elimination rate of selenoxide

The elimination reaction of selenoxide is relatively fast at room temperature. Simple alkyl selenoxides eliminate with a half-life from a few minutes to hours, and carbonyl selenoxides eliminate much faster, and with a half-life about a few minutes even at -50 ^{o}C[75]. However, if the elimination process forms a strained double bond or the steric effect prohibits the elimination, the selenoxide could be stable at room temperature, one such example is 1-phenylselenino-1-cyanocyclopropane[74]. In addition, the electronic effect also affects the elimination rate, electron-withdrawing groups increase the rates, while electron-donating groups decrease it[75].

2.4.2 Mechanism and selectivity of selenoxide elimination

The elimination process proceeds via a syn elimination[76], with a five membered ring transition state, similar to the mechanism of the sulfoxide elimination mentioned in previous section.



Scheme 25: Mechanism of selenoxide elimination.

Similar to the sulfoxide examples, the elimination mainly gives the (*E*) isomer as the major product and for the single-chain carbonyl compounds, normally only (*E*) products are observed[77].

The regio-selectivity of the elimination follows the trends as below:

1. Elimination toward the less substituted carbon is favored.

2. Elimination to form conjugated double bonds is favored.

3. Elimination toward oxygen and nitrogen substituent is disfavored.

4. Elimination to form endocyclic olefins is usually favored over exocyclic in 5- and 6-membered rings, unless there is no *syn* hydrogen.

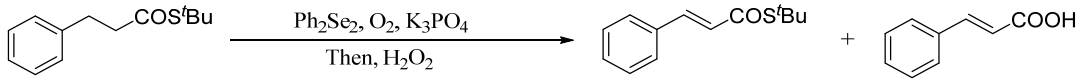
Chapter II: Results and discussion

Inspired by the selenization of ketones with diphenyl diselenide, a base and oxygen[78], and considering that the α hydrogen of the thioesters is more acidic than esters[79], *S*-(*tert*-butyl) 3-phenylpropanethioate (**1a**) was chosen as the model substrate for the optimization reaction.

1. Optimizing the reaction conditions

Firstly, different solvents were screened, following the reported reaction conditions.

Table 1: The result of different solvents.[a]



1a **a** **b**

entry	solvent	yield (a%)[b]	yield (b%)[b]
1	DCE	-	-
2	dioxane	-	-
3	toluene	-	-
4	DMF	13	5
5	NMP	5	trace
6	MeCN	-	-
7	^{t}BuOH	-	-
8	py	4	-
9	**DMSO**	**24**	**4**
10	**DMA**	**29**	**-**
11	HMPA	15	-
12	DMI	trace	-
13	**DMPU**	**31**	**-**

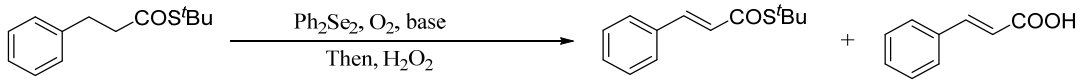
[a] all reactions were performed with **1a** (0.2 mmol), diphenyl diselenide (0.1 mmol) and K_3PO_4 (0.2 mmol) with 1 mL of solvent at 80 ^{o}C under a balloon of O_2 for 12 h, then the second step is 0.3 mL of 30% H_2O_2 for 1h. [b] NMR yields.

From the table, only DMSO and some other polar aprotic solvents like DMF, DMA and DMPU afforded the desired product. No reaction was observed in low polar solvents or protic solvents. Among them, DMSO (**entry 9**), DMA (**entry 10**) and DMPU (**entry 13**) afforded the best results. As DMSO is more abundant and cheaper than DMA and DMPU, DMSO was chosen as the optimized solvent for subsequent screening of the

conditions.

A variety of bases were subsequently screened (**Table 2**).

Table 2: The result of different bases.[a]



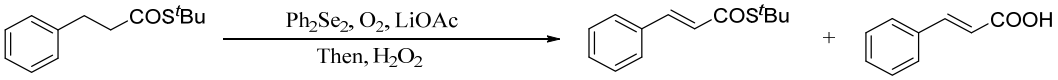
1a **a** **b**

entry	base	yield (a%)[b]	yield (b%)[b]
1	NaOAc	19	7
2	NaOH	6	17
3	KOAc	44	10
4	DIPEA	-	-
5	DBU	5	26
6	PhCOOK	5	trace
7	$Na_2C_2O_4$	-	-
8	K_2HPO_4	-	-
9	**CsOAc**	**63**	**10**
10	**LiOAc**	**69**	**trace**
11	K_2CO_3	8	-
12	CsOPiv	47	20
13	Cs_2CO_3	-	trace
14	NH_4OAc	trace	-
15	NBu_4OAc	26	17
16	CsF	trace	12
17	RbOAc[c]	63	10
18	LiO^tBu	trace	-
19	EMIMOAc[d,e]	66	-
20	EMIMOAc[d]	-	trace
21	LiOH	30	trace
22	$Mg(OAc)_2$[c]	trace	-
23	$Ca(OAc)_2$[c]	20	-
24	$Ba(OAc)_2$[c]	trace	-
25	Li_2CO_3	22	
26	LiF	-	-
27	LiOPiv[c]	65	-
28	$LiBO_2$[c]	50	-
29	Li_3PO_4[c]	-	-
30	lithium tartrate[c]	-	-
31	**KPht**[f]	**45**	**30**

[a] all reactions were performed with **1a** (0.2 mmol), diphenyl diselenide (0.1 mmol) and base (0.2 mmol) with 1 mL of DMSO at 80 °C under a balloon of O_2 for 12 h, then the second step is 0.3 mL of 30% H_2O_2 for 1h. [b] NMR yields. [c] Synthesized by treating the acid with the hydroxide, and dried before use. [d] 1-ethyl-3-methylimidazolium acetate, an ionic liquid. [e] also sever as solvent instead of DMSO. [f] potassium phthalimide.

From the table above, the lithium and caesium salt give better yield compared to other alkali metals of the same anion, RbOAc also gives a comparable yield as caesium (**entry 17**), and KOAc gives a better yield than NaOAc. Comparing the counter anions of the various bases screened, the acetate anion provided better yields of the product while the pivalate anion afforded a similar yield. Organic base like DIPEA (**entry 4**) yielded no desired product and stronger organic base like DBU (**entry 5**) decomposes most of the substrate. Strong bases such as LiO^tBu (**entry 18**) and LiOH (**entry 21**) also failed to afford the product. Among bases screened, LiOAc (**entry 10**) and KPht (**entry 31**) gave the best results. Hence, these bases were screened further.

Table 3: The result of LiOAc as base in different conditions.[a]



1a **a** **b**

entry	temperature	yield (a%)[b]	yield (b%)[b]
1[c]	80 °C	49	trace
2[d]	80 °C	56	-
3[e]	80 °C	58	-
4	60 °C	34	-
5	100 °C	55	9
6	120 °C	9	18

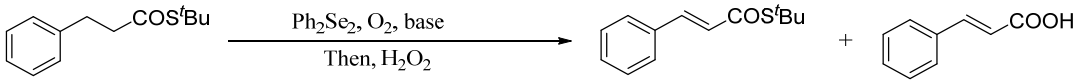
[a] unless otherwise stated, all reactions were performed with **1a** (0.2 mmol), diphenyl diselenide (0.1 mmol) and LiOAc (0.2 mmol) with 1 mL of DMSO at indicated temperature under a balloon of O_2 for 12 h, then the second step is 0.3 mL of 30% H_2O_2 for 1h. [b] NMR yields. [c] under air. [d] 2 equiv. of base. e 0.5 equiv. of base

In **Table 3** above, the reaction proceeded smoothly under air albeit that a lower yield was obtained (**entry 1**). In addition, it is observed that addition (**entry 2**) or reducing (**entry 3**) the amount of base reduces the yield. Furthermore, any change in temperature from optimum reduces the yield.

Considering potassium phthalimide giving an unusually high yield, other similar bases

were hence synthesized and screened on this reaction.

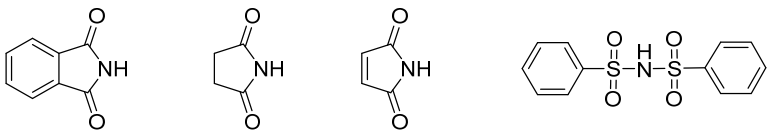
Table 4: The result of different phthalimide-like bases.[a]



1a **a** **b**

entry	Base	Yield (a%)[b]	Yield (b%)[b]
1	lithium phthalimide	36	29
2	lithium succinimide	50	trace
3	lithium maleimide	45	trace
4	lithium dibenzenesulfonimide	25	-
5	caesium phthalimide	61	-
6	rubidium phthalimide	75	-

[a] all reactions were performed with **1a** (0.2 mmol), diphenyl diselenide (0.1 mmol) and base (0.2 mmol) with 1 mL of DMSO at 80 ºC under a balloon of O_2 for 12 h, then the second step is 0.3 mL of 30% H_2O_2 for 1h. [b] NMR yields.

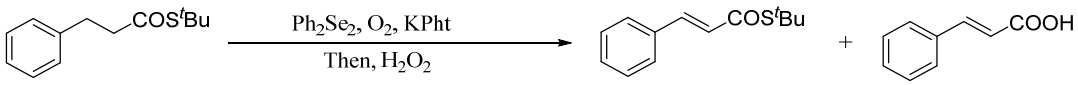


phthalimide succinimide maleimide dibenzenesulfonimide

Scheme 26: Structure of different base.

However, the bases screened in **Table 4** did not show any improvements to the yield of the desired product as compared to potassium phthalimide. In addition, in contrast to the acetate-containing bases, the potassium salt provides the best yield compared to other alkali metals. Since the other salts are not commercially available, potassium phthalimide was chosen as the optimized base and and further optimization screening was proceeded.

Table 5: The result of potassium phthalimide under different conditions.[a,e]



1a **a** **b**

entry	temperature	Solvent	Yield (a+b%)[b]
1	100 ºC	DMSO	29
2	60 ºC	DMSO	90
3	40 ºC	DMSO	92

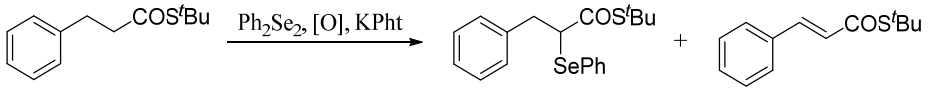
4[c]	r.t.	DMSO	85
5	40 °C	DMA	39
6	40 °C	DMF	45
7	40 °C	DMPU	48
8	40 °C	DMSO[d]	88

[a] unless otherwise stated, all reactions were performed with **1a** (0.2 mmol), diphenyl diselenide (0.1 mmol) and base (0.2 mmol) with 1 mL of indicated solvent at the indicated temperature under a balloon of O_2 for 24 h, then the second step is 0.3 mL of 30% H_2O_2 for 1h. [b] NMR yields. [c] react for 4 d. [d] extra dry. [e] In addition, methanol, DCM, THF, toluene and acetonitrile were also screens as solvent in these conditions, but none of them afforded any yield.

This table shows that potassium phthalimide greatly promoted the reaction and the reaction proceeded smoothly even at room temperature (**entry 4**). It is found that the reaction gave the best yield of the product when the reaction was carried out at 40 °C. Other analogues of DMSO solvent gave lower yields than DMSO (**entry 5 – 7**), and dry DMSO (**entry 8**) did not make much difference in this reaction.

Considering that there is still about 10% of unreacted stating material, which is difficult to separate from both the product and the selenium intermediate, additional oxidant (or additive) was tested for this reaction, as moisture and oxygen do not affect the reaction, it was conducted in open air.

Table 6: The result of using different oxidants.[a]



1a **1a-i** **4a**

entry	oxidant	1a%	1a-i%	4a%
1	-	25	75	-
2	$PhIO_2$	5	95	trace
3	PhIO	12	84	4
4	$PhI(OAc)_2$.	100	-	-
5	IBX	100	-	-
6	DMP[b]	100	-	-
7	$NaIO_4$	5	82	13
8	**KIO_4**	**3**	**85**	**12**
9	KIO_3	9	91	trace

10	$KBrO_3$	14	80	6
11	$KClO_4$	17	83	trace
12	$KClO_3$	22	78	-
13	$NaClO_2$	53	47	-
14	KNO_3	17	83	-
15	KNO_2	21	79	-
16	Oxone	100	-	-
17	$K_2S_2O_8$	66	25	9
18	$Na_2CO_3{\cdot}H_2O_2$	14	86	-
19	$NaBO_3{\cdot}4H_2O$	4	96	-
20	DDQ[c]	100	-	-
21	$urea{\cdot}H_2O_2$	77	23	-
22	SeO_2	100	-	-
23	KIO_4[c]	5	63	32
24	$NaBO_3{\cdot}4H_2O$[c]	16	79	5
25	KIO_4[d]	4	89	7
26	KIO_4[e]	2	98	trace

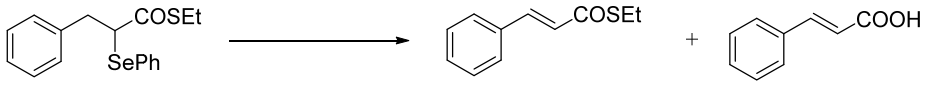
[a] unless otherwise stated, all reactions were performed with **1a** (0.2 mmol), diphenyl diselenide (0.1 mmol), potassium phthalimide (0.2 mmol) and 0.2 mmol of indicated oxidant with 1 mL of DMSO at 40 ^oC under air for 24 h, then after DMSO removed, the crude product was examined by ^1H NMR to get the ratio of the three substance. [b] Dess-Martin periodate [c] 2 equivalent. [d] under N_2. [e] 0.55 equivalent of diphenyl diselenide used.

As observed in **Table 8**, potassium periodate (**entry 8**) gave the best overall conversion, other oxidants such as iodoxybenzene (**entry 2**) and sodium perborate (**entry 19**) also provided good results. On the contrary, some oxidant shows a negative effect on the reaction, such as IBX (**entry 4**), oxone (**entry 16**), DDQ (**entry 20**) and selenium dioxide (**entry 22**); these oxidants seemingly halted the progress of the reaction. Increasing the amount of oxidant (**entry 23**) does not increase the overall conversion, however, it does increase the amount of the final product. Reaction under nitrogen (**entry 25**) has insignificant impact on the reaction; this thus implies that potassium periodate could behave as the sole oxidant. Finally, increasing the amount of the diselenide also does not increase the overall conversion, possibly because the yield is already high enough.

Despite the fact that periodates are widely used as oxidants (**section 2.3** in **Chapter I**). they do not appear to function effectively in this reaction. This could be due to the fact that they do not work well in DMSO in the absence of water.. As a result, hydrogen peroxide is still used as oxidant in the second step.

However, despite hydrogen peroxide providing good yields to the *tert*-butyl thioesters, when it is changed to a less hindered ethyl thioester (**1b**), some product were decomposed to form cinnamic acid. As a result, a further test on different conditions for the oxidant step were performed on the selenium substituted ethyl thioester.

Table 7: Different oxidant step conditions on the intermediate of ethyl thioester.[a]



a **b** **c**

entry	Oxidant	temp.	dilution solvent	time	a	b	c
1	H_2O_2 (30%, 0.1 mL)	r.t.	-	15 min	1	66	33
2	***m*CPBA (1.2 equiv.)**	**-40 °C**	**DCM**	**3 h**	**0**	**95**	**5**
3	*m*CPBA (1.2 equiv.)	-78 °C	DCM	3 h	5	95	-
4	^{t}BuOOH (70%, 0.1 mL)	r.t.	-	3 h	100	-	-
5	$NaIO_4$	60 °C	MeOH	2 h	17	33	50
6	$(PhCOO)_2$ (1.2 equiv.)	r.t.	-	2 h	60	30	10
7	H_2O_2 (30%, 0.1 mL)	r.t.	DCM/H_2O	3 h	50	50	-
8	NCS (1.2 equiv.)	0 °C	MeOH	1 h	55	35	15

[a] unless otherwise stated, the first step was in standard conditions (except using the ethyl thioester), the reaction were performed with the oxidant at the indicated temperature and time, the mixture may also be dilute with 2 mL of the indicated solvent, then after a standard water washing and extraction work up, the crude product were examined by ^{1}H NMR to get the ratio of the three substance (unreacted starting material were ignored).

Considering that the intermediate **a** is difficult to separate from the product, and cinnamic acid could be easily separated, the results obtained based on **entry 2** is chosen as the optimized conditions for the second step of less hindered thioesters.

It is also worth mentioning that for the hindered thioesters, although directly addition

of H_2O_2 in the mixture gave a good yield, a trace amount of unreacted intermediate and a small amount of cinnamic acid can still be observed in the ^1H NMR. Hence the condition was changed to dilute with 2 mL of THF at 0 ^oC before adding H_2O_2. As a result, no unreacted intermediate and less decomposed product can be observed.

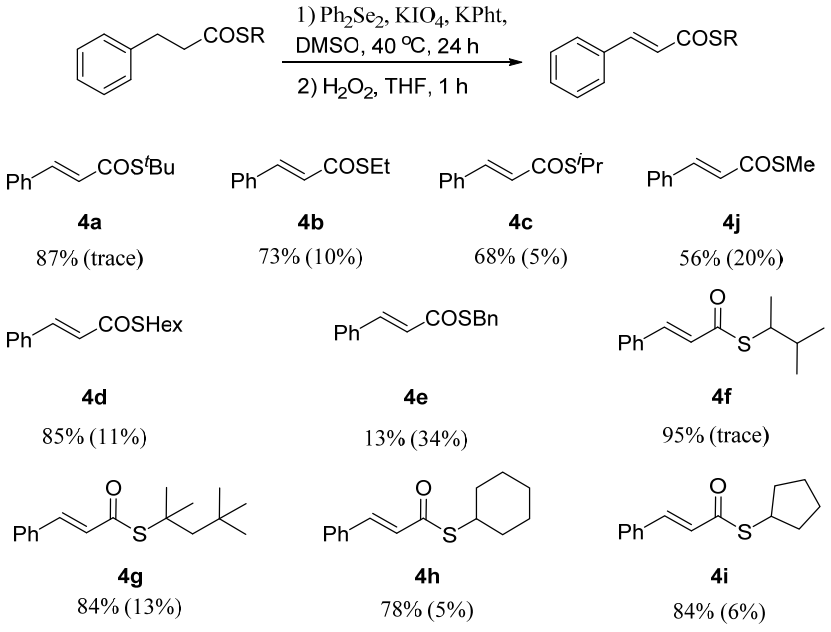
In conclusion, the optimized condition for the reaction is determined to be 0.5 equiv. of diphenyl diselenide, 1 equiv. of potassium phthalimide and 1 equiv. of potassium periodate in 1 mL of DMSO at 40 ^oC for 24 h.

The second step is to dilute with THF before treating with H_2O_2 at 0 ^oC for 1 h or 1.2 equiv. of *m*CPBA at -40 ^oC for less hindered thioesters.

2. Substrate scope under optimized conditions

With the optimized condition in hand, different substrates were tested with this conditions to examine the substrate scope of this reactions. In addition, the intermediates were not separated and the reaction was done in a two-step one-pot manner. Finally, as it is difficult to separate the unreacted starting material with the product through column chromatography, the yields were calculated from the weight of separate mixture of starting material and product and their ratio obtained from ^{1}H NMR. The product was then further purified by preparative TLC plate for NMR and HRMS analysis.

Table 8: Substrate scope of the thioester of variety of thiols with hydrocinnamic acid.[a,b,c]



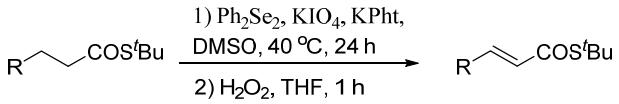
[a] unless otherwise stated, all reactions were performed with the thioester (0.2 mmol), diphenyl diselenide (0.1 mmol), potassium phthalimide (0.2 mmol) and potassium periodate (0.2 mmol) with 1 mL of DMSO at 40 °C under air for 24 h, the second step is dilute with 2 mL of THF and react with 0.3 mL of 30% H_2O_2 for 1 h. [b] The second step for **4b**, **4i** and **4j** is dilute with 2 mL of DCM and react with *m*CPBA at -40 °C for 3 h. [c] isolated yield, the number in parentheses is the amount of unreacted stating material.

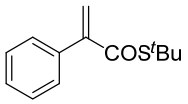
Other thioesters, except methyl (**4j**) and benzyl (**4e**) thioester, provided excellent yields

of the desired product. In addition, more hindered thioesters generally give higher yield and lower unreacted starting material, though if the thioesters become bulkier than a *tert*-butyl group (**4g**), the unreacted starting material would increase. The benzyl thioester gave a poor yield of the product, possibly due to the weak stability of its intermediate.

Subsequently, thioesters formed from different aromatic and aliphatic were tested.

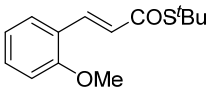
Table 9: Substrate scope of the thioester of variety of aromatic acids[a,b].





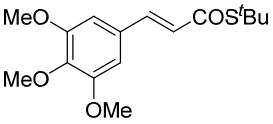
5a

77% (trace)



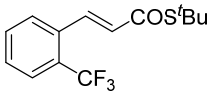
5b

71% (24%)



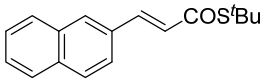
5c

81% (trace)



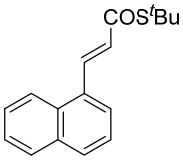
5d

70% (trace)



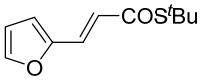
5e

70% (8%)



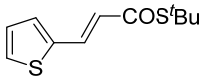
5f

74% (trace)



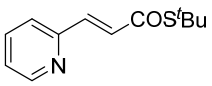
5g

88% (trace)



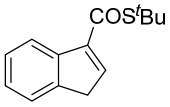
5h

85% (trace)



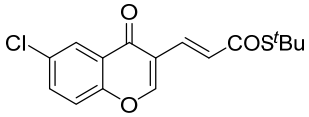
5i

90% (trace)



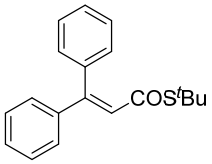
5j

56% (7%)



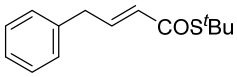
5k

79% (16%)



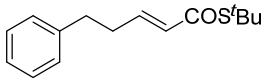
5l

95% (trace)



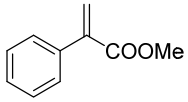
5q

52% (29%)



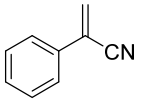
5r

39% (55%)



5s

45% (5%), at 60 °C



5t

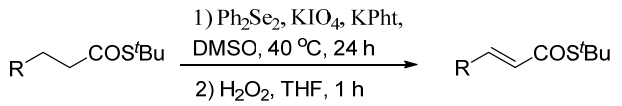
14% (34%), at 60 °C

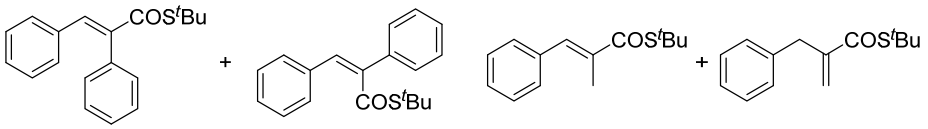
[a] unless otherwise stated, all reactions were performed the same conditions as **table 7**. [b] isolated yield, the number in parentheses is the amount of unreacted stating material.

Other aromatic groups, such as naphthalenyl (**5e**, **5f**), furanyl (**5g**), thiophenyl (**5h**) and pyridineyl (**5i**) all gave a similar yields. Substrate **5k** indicates this reaction has a good functional group tolerance of ketone without α hydrogens. Electron-donating (**5b**, **5c**) or electron-withdrawing (**5d**) groups on the phenyl ring have insignificant effect on the

reaction. Substrates with α hydrogens adjacent to the phenyl ring also reacts, but gives a lower yield, for **5a**, the reason could be that the product is relatively unstable (it could be observed that the solution of **5a** in $CDCl_3$ turned yellow after a storage for a few days) and can possibly be decomposed by H_2O_2. Steric effects could possibly affect the overall yield for product **5j**. If the formation of the double bond is not conjugated with the phenyl ring (**5q**, **5r**), the conversion rate and yield drops. Finally, although this condition is observed to have no reaction on normal esters and nitriles (for example, methyl hydrocinnamate does not react even at 80 °C), esters with more acidic α hydrogen (**5s**) does give a moderate yield at a higher temperature, while active nitriles (**5t**), albeit at a lower yield.

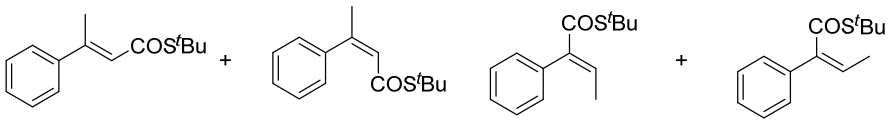
Table 10: Substrate scope of the thioester of variety of aromatic acid with a selectivity.[a,b]





5ma **5mb** **5na** **5nb**

24% + 16% (48%) 28% + 21% (26%)[c], at 60 °C



5oa **5ob** **5pa** **5pb**

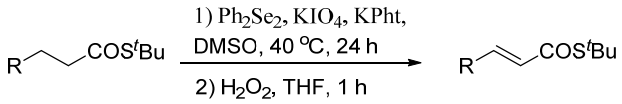
24% + 24% (35%) 16% + 28% (31%)

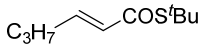
[a] unless otherwise stated, all reactions were performed the same conditions as **table 7**. [b] isolated yield, the number in parentheses is the amount of unreacted stating material. [c] no (*Z*) isomer of 5na observed form ^{1}H NMR.

As seen in **section 2.4.2** in **chapter I** (page 32), most substrates give almost exclusively (*E*) product (as no (*Z*) product was observed in the ^{1}H NMR), for the product with

trisubstituted double bond, a mixture of (*E*)/(*Z*) isomers was observed in the product. As **Table 9** indicates, trisubstituted substrates gave a lower conversion rate and overall yield, possibly due to steric effects. Surprisingly, for **5na** and **5nb**, no (*Z*) isomer of **5na** was observed in the ^{1}H NMR. This could be due to the (Z) isomer forming is disfavored in the elimination step or the (*Z*) isomer is not stable enough for the work-up. In addition, for **5na** and **5nb**, it gives a near 1:1 ratio of two isomers, which are formed by different regioselectivity, possibly due to the conflict of **rule 1** and **rule 2** discussed in **2.4.2** in **chapter I**.

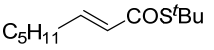
Table 11: Substrate scope of the thioester of variety of aliphatic acid.[a,b]





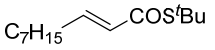
6a

14% (31%) at 40 °C
57% (13%) at 60 °C



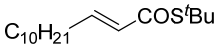
6b

14% (81%) at 40 °C
35% (41%) at 60 °C



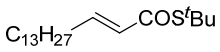
6c

trace at 40 °C
60% (23%) at 60 °C



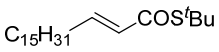
6d

trace at 40 °C
45% (35%) at 60 °C



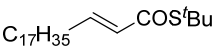
6e

28% (72%) at 60 °C
68% (28%) at 80 °C



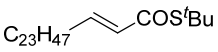
6f

15% (85%) at 60 °C
63% (37%) at 80 °C



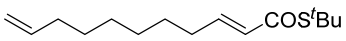
6g

13% (87%) at 80 °C
56% (37%) at 100 °C



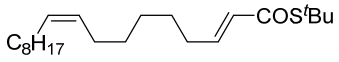
6h

27% (37%) at 100 °C, 3 d



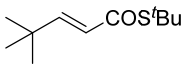
6i

18% (57%) at 40 °C
45% (12%) at 60 °C



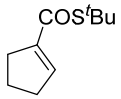
6j

42% (58%) at 60 °C



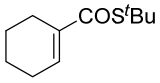
6k

59% (trace) at 60 °C



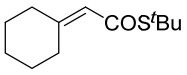
6l

60% (21%) at 60 °C



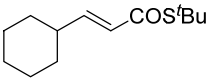
6m

54% (18%) at 60 °C



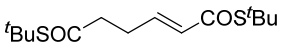
6n

33% (14%) at 60 °C



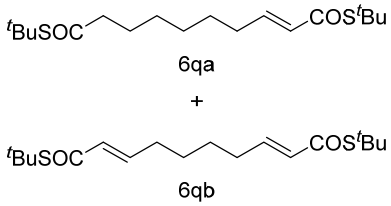
6o

33% (40%) at 40 °C



6p

40% (55%), at 40 °C



28% + 14% (57%), at 40 °C

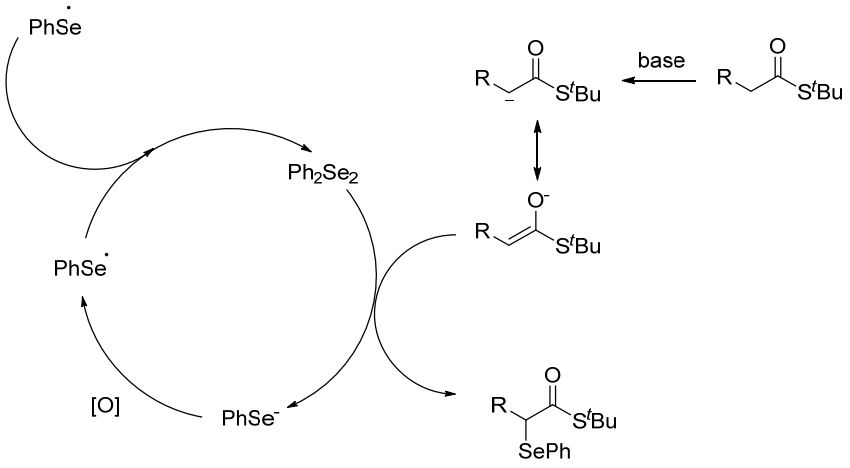
[a] unless otherwise stated, all reactions were performed the same conditions as **table 7**. [b] isolated yield, the number in parentheses is the amount of unreacted stating material.

For the thioesters of aliphatic acids, the reaction become less favored. For the thioesters of the straight chain natural fatty acids (**6a** to **6h**), the conversion rate and yield decrease as the chain length increases, and an increase in reaction temperature is required. This could possibly due to the longer chain makes the α hydrogen more difficult to be attacked as well as decreases the substrate solubility in DMSO. Chain with a double

bond (**6i**, **6j**) increases the yield compared to the saturated chain of similar length, this could possibly due to the double bond increases the solubility of substrates in DMSO. Branched chain (**6k** to **6o**) gives a better yield compared to the straight chain of similar size, this could also possibly due to its solubility in the solvent. For the substrates with two reaction sites (**6p**, **6qa**, **6qb**), disubstitution is difficult, for **6p**, no double substituted product is observed, this could possibly due to the two sites being too close in proximity.

3. Mechanistic study

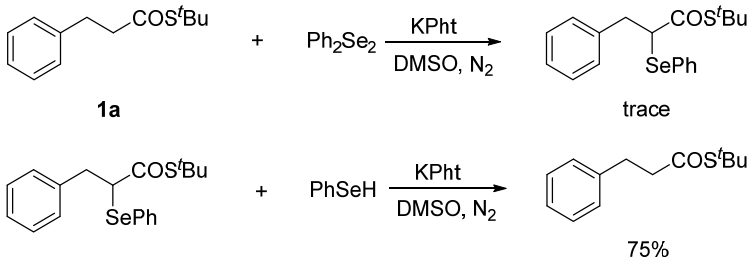
The mechanism of the first step of this reaction appears to be the same as the substitution of ketones[78b]. The first step is the thioester forming an enolate in the presence of the base, then, the enolate could react with diphenyl diselenide to form the selenium-substituted product. The selenium anion formed as the by-product can then be oxidized back to diphenyl diselenide by the oxidant.



Scheme 27: A plausible reaction mechanism.

The substitution step of the diphenyl diselenide is reversible, and enolate form is favored over the selenium-substituted product, so an oxidant is needed to remove the benzeneselenolate ion.

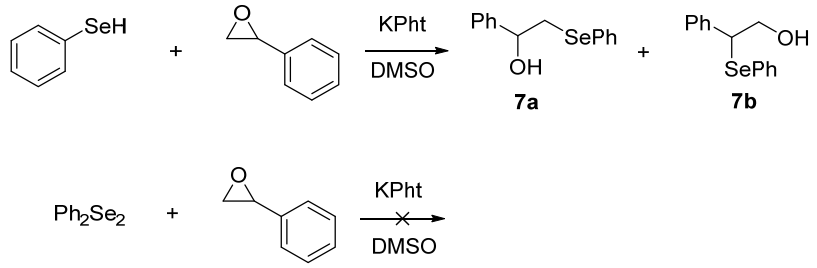
Two control reactions are done as shown below:



Scheme 28: Two control reactions.

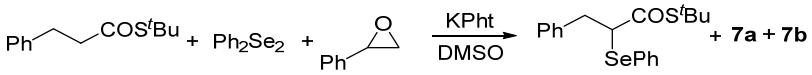
If thioester **1a**, diphenyl diselenide and potassium phthalimide were reacted in degassed DMSO at 40 °C for 24 h, only a trace amount of the selenium-substituted product could be observed; on the other hand, if the selenium-substituted product, benzeneselenol and potassium phthalimide were reacted in degassed DMSO at 40 °C for 24 h, the thioester **1a** could be observed in about 75% yield. These two reaction indicates that the first step is reversible and an oxidant is needed.

Next, the intermediate, benzeneselenolate ion, is possible to be trapped with an epoxide such as styrene oxide. In addition, styrene oxide does not react with diphenyl diselenide under these conditions.



Scheme 29: Trapping the benzeneselenolate ion with styrene oxide.

With these results in hand, next experiment was to use the styrene oxide as an oxidant in this reaction. When react the thioester **1a**, diphenyl diselenide (1 equiv. instead of normally 0.5 equiv.), potassium phthalimide and styrene oxide, the selenium-substituted product could be observed in about 66% yield, as well as **7a** and **7b**. This reaction indicates that the intermediate benzeneselenolate ion was generated.



Scheme 30: Styrene oxide promoted reaction.

The benzeneselenolate ion could be oxidized to the selenium radical, which quickly dimerize back to diphenyl diselenide. The selenium radical is not very reactive towards

alkene and difficult to trap[80]. As a result, trials of adding TEMPO or styrene both show little effect on the yield in this reaction.

The mechanism of the second step should be the same as discussed in **chapter I**.

4. Conclusion

In conclusion, a new method for dehydrogenation of thioesters by introducing a selenium group and have it oxidized and followed by eliminate in a one-pot two-step manner was discovered. The dehydrogenation of thioesters could undergo in mild conditions with a weak base, in open air and at low temperature. Compared to similar reactions reported in other literature, to our best knowledge, this is the first method which systematically describes the dehydrogenation reaction of thioesters instead of other carbonyl compounds. In addition, it shows an advantage over traditional methods discussed in **Chapter I** by reacting under milder conditions. While most of methods involving an enolate intermediate that requires a strong base like LDA, an inert atmosphere and very low temperature. Comparing to other methods like metal catalyst, they either only works on ketones or aldehydes or require a specific structure.

Chapter III: Experimental sections

1. General Information

Unless otherwise noted, all reagents and solvents were purchased from the commercial sources and used as received.

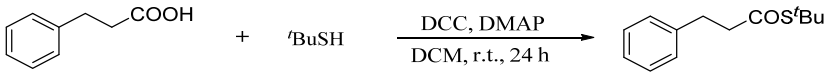
Thin layer chromatography (TLC) was used to monitor the reaction on Merck 60 F254 precoated silica gel plate (0.2 mm thickness). TLC spots were visualized by UV-light irradiation on Spectroline Model ENF-24061/F 254 nm.

Flash column chromatography was performed using Merck silica gel 60 with analytical grade solvents as eluents.

^{1}H NMR, ^{13}C NMR and 2D NMR spectra were recorded using BrukerAvance 400 MHz spectrometers. Corresponding chemical shifts are reported in ppm downfield relative to TMS and were referenced to the signal of chloroform-d (δ = 7.26, singlet, for ^{1}H NMR and δ = 77.36, triplet, for ^{13}C NMR). Multiplicities were given as: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublets, td = triplet of doublets, dt = doublet of triplets, tt = triplet of triplets, dq = doublet of quartets and so on. Values of coupling constant are reported as *J* in Hz.

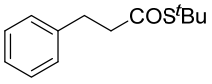
2. Experimental Sections

2.1 General Procedure for the starting material[81]



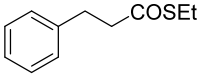
Scheme 31: General procedure for the stating material.

A dry round bottom flask with a magnetic stir bar was charged with phenylpropionic acid (1 equiv., 10 mmol, 1.5 g), 4-Dimethylaminopyridine (DMAP, 0.1 equiv., 1 mmol, 0.12 g) and dichloromethane (40 mL) under N_2 atmosphere. *N*,*N*'-dicyclohexylcarbodiimide (DCC, 1.1 equiv., 11 mmol, 2.2 mL, pre-melt in a 50 ^oC oven) was then added, followed by 2-methyl-2-propanethiol (1 equiv., 10 mmol, 1.1 mL). The resulting mixture was stirred at room temperature for 24 h. It was then filtered, the solvent of filtrate was removed under reduced pressure and the residue was purified by flash column chromatography on silica gel to afford the desired product.



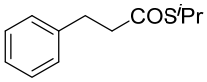
1a Colorless Oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.30 – 7.26 (m, 2H), 7.22 – 7.17 (m, 3H), 2.95 (t, *J* = 7.9 Hz, 2H), 2.75 (t, *J* = 7.8 Hz, 2H), 1.46 (s, 9H).



1b Colorless Oil.

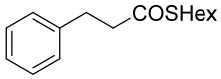
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.30 – 7.26 (m, 2H), 7.21 – 7.19 (m, 3H), 4.12 (q, *J* = 7.1 Hz, 2H), 2.95 (t, *J* = 7.8 Hz, 2H), 2.62 (t, *J* = 7.8 Hz, 2H), 1.23 (t, *J* = 7.2 Hz, 3H).



1c Colorless Oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.30 – 7.26 (m, 2H), 7.22 –

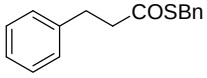
7.17 (m, 3H), 3.73 – 3.63 (m, 1H), 2.96 (t, *J* = 7.6 Hz, 2H), 2.75 (t, *J* = 7.8 Hz, 2H), 1.29 (d, *J* =6.9 Hz, 6H).



1d

Colorless Oil.

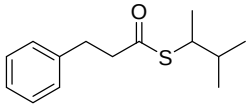
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.31 – 7.26 (m, 2H), 7.22 – 7.18 (m, 3H), 2.98 (t, *J* = 7.9 Hz, 2H), 2.89 – 2.83 (m, 4H), 1.36 – 1.25 (m, 6H), 0.88 (t, *J* =6.8 Hz, 3H).



1e

Colorless Oil.

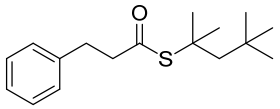
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.31 – 7.16 (m, 10H), 4.13 (s, 2H), 3.00 (t, *J* = 7.6 Hz, 2H), 2.75 (t, *J* = 7.5 Hz, 2H).



1f

Colorless Oil.

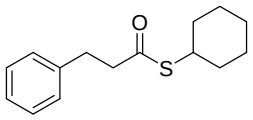
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.30 – 7.26 (m, 2H), 7.21 – 7.18 (m, 3H), 3.61 – 3.54 (m, 1H), 2.97 (t, *J* = 7.8 Hz, 2H), 2.84 (t, *J* = 7.6 Hz, 2H), 1.88 – 1.80 (d, *J* = 7.1 Hz, 3H), 0.93 – 0.90 (m, 6H).



1g

Colorless Oil.

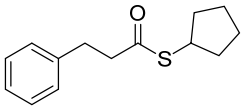
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.30 – 7.26 (m, 2H), 7.21 – 7.17 (m, 3H), 2.94 (t, *J* = 7.8 Hz, 2H), 2.74 (t, *J* = 7.8 Hz, 2H), 1.81 (s, 2H), 1.54 (s, 6H), 1.00 (s, 9H).



1h

Colorless Oil.

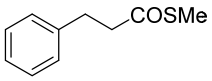
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.30 – 7.26 (m, 2H), 7.22 – 7.18 (m, 3H), 3.56 – 3.50 (m, 1H), 2.96 (t, *J* = 7.8 Hz, 2H), 2.82 (t, *J* = 7.8 Hz, 2H), 1.92 – 1.87 (m, 2H), 1.73 – 1.66 (m, 2H), 1.61 – 1.54 (m, 1H), 1.48 – 1.34 (m, 4H), 1.32 – 1.24 (m, 1H).



1i

Colorless Oil.

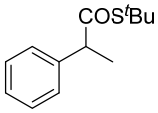
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.30 – 7.26 (m, 2H), 7.22 – 7.17 (m, 3H), 3.76 – 3.69 (m, 1H), 2.97 (t, *J* = 7.8 Hz, 2H), 2.82 (t, *J* = 7.8 Hz, 2H), 2.13 – 2.04 (m, 2H), 1.73 – 1.58 (m, 4H), 1.56 – 1.46 (m, 2H).



1j

Yellowish Oil.

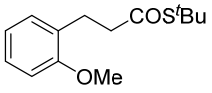
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.31 – 7.27 (m, 2H), 7.23 – 7.18 (m, 3H), 2.99 (t, *J* = 7.9 Hz, 2H), 2.88 (t, *J* = 7.8 Hz, 2H), 2.30 (s, 3H).



2a

Colorless Oil.

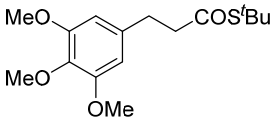
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.34 – 7.27 (m, 5H), 3.76 – 3.80 (q, *J* = 7.1 Hz, 1H), 1.48 (d, *J* = 7.1 Hz, 3H), 1.42 (s, 9H).



2b

Colorless Oil.

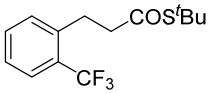
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.19 (td, J_1 = 7.8 Hz, J_2 = 1.8 Hz, 1H), 7.11 (dd, J_1 = 7.4 Hz, J_2 = 1.8 Hz, 1H), 6.88 – 6.82 (m, 2H), 3.82 (s, 3H), 2.93 (t, *J* = 7.8 Hz, 2H), 2.73 (t, *J* = 7.8 Hz, 2H), 1.45 (s, 9H).



2c

Colorless Oil.

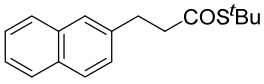
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 6.39 (s, 2H), 3.84 (s, 6H), 3.82 (s, 3H), 2.89 (t, *J* = 7.6 Hz, 2H), 2.73 (t, *J* = 7.6 Hz, 2H), 1.46 (s, 9H).



2d

Colorless Oil.

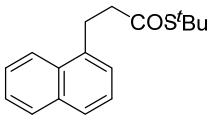
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.64 (d, *J* = 7.7 Hz, 1H), 7.48 (t, *J* = 7.5 Hz, 1H), 7.35 – 7.28 (m, 2H), 3.14 (t, *J* = 7.8 Hz, 2H), 2.77 (t, *J* = 7.8 Hz, 2H), 1.49 (s, 9H).



2e

Colorless Oil.

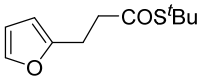
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.81 – 7.76 (m, 3H), 7.70 – 7.62 (m, 1H), 7.48 – 7.41 (m, 2H), 7.33 – 7.30 (m, 1H), 3.11 (t, *J* = 7.8 Hz, 2H), 2.84 (t, *J* = 7.8 Hz, 2H), 1.45 (s, 9H).



2f

Colorless Oil.

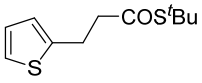
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.02 (d, *J* = 8.3 Hz, 1H), 7.85 (d, *J* = 7.7 Hz, 1H), 7.73 (d, *J* = 8.1 Hz, 1H), 7.55 – 7.46 (m, 2H), 7.39 (t, *J* = 7.6 Hz, 1H), 7.33 (d, *J* = 6.8 Hz, 1H), 3.41 (t, *J* = 8.0 Hz, 2H), 2.88 (t, *J* = 8.0 Hz, 2H), 1.48 (s, 9H).



2g

Colorless Oil.

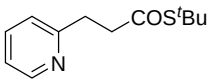
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.31 – 7.29 (m, 1H), 6.27 – 6.26 (m, 1H), 6.01 – 6.00 (m, 1H), 2.96 (t, *J* = 7.8 Hz, 2H), 2.78 (t, *J* = 7.8 Hz, 2H), 1.46 (s, 9H).



2h

Colorless Oil.

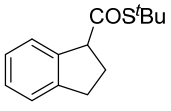
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.13 – 7.11 (m, 1H), 6.92 – 6.89 (m, 1H), 6.81 – 6.80 (m, 1H), 3.16 (t, *J* = 7.8 Hz, 2H), 2.82 (t, *J* = 7.8 Hz, 2H), 1.46 (s, 9H).



2i

Colorless Oil.

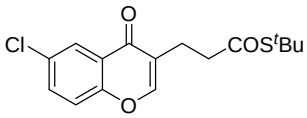
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.52 (d, *J* = 4.4 Hz, 1H), 7.58 (td, J_1 = 7.7 Hz, J_2 = 1.8 Hz, 1H), 7.15 (d, *J* = 7.8 Hz, 1H), 7.13 – 7.09 (m, 1H), 3.10 (t, *J* = 7.8 Hz, 2H), 2.94 (t, *J* = 7.8 Hz, 2H), 1.44 (s, 9H).



2j

Yellow Oil.

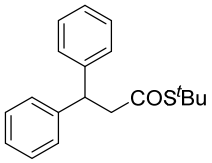
^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) 7.37 (d, *J* = 6.9 Hz, 1H), 7.24 – 7.16 (m, 3H), 4.15 – 4.11 (m, 1H), 3.15 – 3.07 (m, 1H), 2.94 – 2.87 (m, 1H), 2.46 – 2.37 (m, 1H), 2.36 – 2.28 (m, 1H), 1.47 (s, 9H).



2k

White solid.

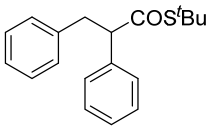
^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) 8.18 (d, *J* = 2.5 Hz, 1H), 7.83 (s, 1H), 7.58 (dd, J_1 = 8.8 Hz, J_2 = 2.6 Hz, 1H), 7.39 (d, *J* = 8.9 Hz, 1H), 2.82 – 2.75 (m, 4H), 1.43 (s, 9H).



2l

White solid.

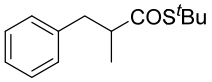
^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) 7.29 – 7.25 (m, 4H), 7.22 – 7.16 (m, 6H), 4.59 (t, *J* = 7.8 Hz, 1H), 3.17 (d, *J* = 7.8 Hz, 2H), 1.35 (s, 9H).



2m

Colorless Oil.

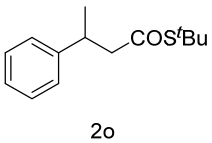
^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) 7.44 – 7.15 (m, 8H), 6.84 – 6.82 (m, 2H), 4.11 (dd, J_1 = 9.4 Hz, J_2 = 6.3 Hz, 1H), 3.51 (dd, J_1 = 13.8 Hz, J_2 = 9.4 Hz, 1H), 3.14 (dd, J_1 = 13.7 Hz, J_2 = 6.3 Hz, 1H), 1.54 (s, 9H).



2n

Colorless Oil.

^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) 7.29 – 7.25 (m, 2H), 7.21 – 7.19 (m, 1H), 7.16 – 7.14 (m, 2H), 3.03 (dd, J_1 = 13.4 Hz, J_2 = 6.7 Hz, 1H), 2.83 – 2.74 (m, 1H), 2.60 (dd, J_1 = 13.4 Hz, J_2 = 7.9 Hz, 1H), 1.42 (s, 9H), 1.12 (d, *J* = 6.8 Hz, 3H).

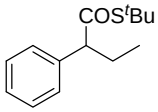


2o

Colorless Oil.

^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) 7.31 – 7.26 (m, 2H), 7.21 –

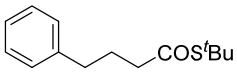
7.17 (m, 3H), 3.35 – 3.26 (m, 1H), 2.72 (dd, J_1 = 14.4 Hz, J_2 = 6.4 Hz, 1H), 2.64 (dd, J_1 = 14.5 Hz, J_2 = 8.5 Hz, 1H), 1.42 (s, 9H), 1.29 (d, J = 6.9 Hz, 3H).



2p

Colorless Oil.

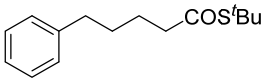
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.34 – 7.23 (m, 5H), 3.54 (t, J = 7.6 Hz, 1H), 2.18 – 2.07 (m, 1H), 1.83 – 1.72 (m, 1H), 1.41 (s, 9H), 0.89 (d, J = 7.4 Hz, 3H).



2q

Colorless Oil.

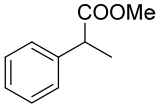
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.30– 7.26 (m, 2H), 7.21 – 7.16 (m, 3H), 2.64 (t, J = 7.6 Hz, 2H), 2.47 (t, J = 7.5 Hz, 2H), 1.99 – 1.92 (m, 2H), 1.46 (s, 9H).



2r

Colorless Oil.

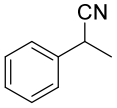
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.29– 7.25 (m, 2H), 7.19 – 7.16 (m, 3H), 2.62 (t, J = 7.1 Hz, 2H), 2.47 (t, J = 7.0 Hz, 2H), 1.71 – 1.61 (m, 4H), 1.45 (s, 9H).



2s

Colorless Oil.

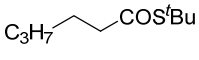
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.34 – 7.24 (m, 5H), 3.72 (q, J = 7.2 Hz, 1H), 3.66 (s, 3H), 1.50 (d, J = 7.2 Hz, 3H).



2t

Colorless Oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.41 – 7.30 (m, 5H), 3.89 (q, J = 7.3 Hz, 1H), 1.64 (d, J = 7.3 Hz, 3H).

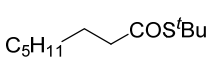


3a

Colorless Oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.44 (t, J = 7.5 Hz, 2H), 1.66

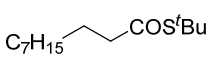
– 1.59 (m, 2H), 1.45 (s, 9H), 1.34 – 1.26 (m, 4H), 0.89 (t, *J* = 7.0 Hz, 3H).



3b

Colorless Oil.

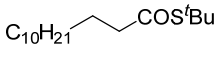
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.43 (t, *J* = 7.5 Hz, 2H), 1.64 – 1.60 (m, 2H), 1.45 (s, 9H), 1.30 – 1.26 (m, 8H), 0.88 (t, *J* = 6.6 Hz, 3H).



3c

Colorless Oil.

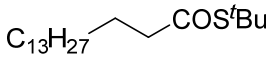
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.43 (t, *J* = 7.5 Hz, 2H), 1.65 – 1.58 (m, 2H), 1.45 (s, 9H), 1.32 – 1.20 (m, 12H), 0.88 (t, *J* = 6.8 Hz, 3H).



3d

Colorless Oil.

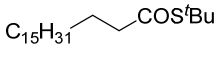
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.43 (t, *J* = 7.5 Hz, 2H), 1.65 – 1.58 (m, 2H), 1.46 (s, 9H), 1.35 – 1.21 (m, 18H), 0.88 (t, *J* = 6.6 Hz, 3H).



3e

Colorless Oil.

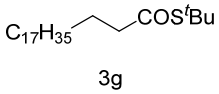
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.43 (t, *J* = 7.5 Hz, 2H), 1.65 – 1.58 (m, 2H), 1.46 (s, 9H), 1.31 – 1.25 (m, 24H), 0.88 (t, *J* = 6.8 Hz, 3H).



3f

White solid.

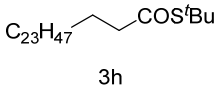
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.43 (t, *J* = 7.5 Hz, 2H), 1.65 – 1.58 (m, 2H), 1.45 (s, 9H), 1.33 – 1.21 (m, 28H), 0.88 (t, *J* = 6.8 Hz, 3H).



3g

White solid.

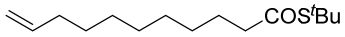
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.43 (t, *J* = 7.5 Hz, 2H), 1.63 – 1.58 (m, 2H), 1.45 (s, 9H), 1.32 – 1.21 (m, 32H), 0.88 (t, *J* = 6.8 Hz, 3H).



3h

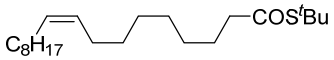
White solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.43 (t, *J* = 7.5 Hz, 2H), 1.63 – 1.59 (m, 2H), 1.45 (s, 9H), 1.32 – 1.23 (m, 44H), 0.88 (t, *J* = 6.8 Hz, 3H).



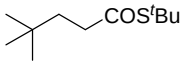
3i Colorless Oil.

^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) 5.81 (ddt, J_1 = 16.9 Hz, J_2 = 10.1 Hz, J_3 = 6.7 Hz, 1H), 4.99 (dq, J_1 = 17.2 Hz, J_2 = 1.8 Hz, 1H), 4.92 m, 1H), 2.43 (t, J = 7.5 Hz, 2H), 2.06 – 2.01 (m, 2H), 1.65 – 1.58 (m, 2H), 1.46 (s, 9H), 1.39 – 1.35 (m, 44H), 1.31 – 1.25 (m, 3H).



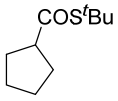
3j Colorless Oil.

^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) 5.39 – 5.30 (m, 2H), 2.43 (t, J = 7.5 Hz, 2H), 2.03 – 1.98 (m, 4H), 1.65 – 1.60 (m, 2H), 1.45 (s, 9H), 1.36 – 1.25 (m, 20H), 0.88 (t, J = 6.7 Hz, 3H).



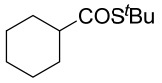
3k Colorless solid.

^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) 2.44 – 2.40 (m, 2H), 1.56 – 1.52 (m, 2H), 1.45 (s, 9H), 0.88 (s, 9H).



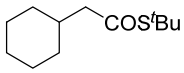
3l Colorless Oil.

^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) 2.92 – 2.84 (m, 1H), 1.87 – 1.75 (m, 4H), 1.73 – 1.65 (m, 2H), 1.61 – 1.53 (m, 2H), 1.46 (s, 9H).



3m Colorless Oil.

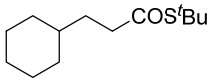
^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) 2.37 (tt, J_1 = 11.5 Hz, J_2 = 3.5 Hz, 1H), 1.90 – 1.86 (m, 2H), 1.80 – 1.74 (m, 2H), 1.66 – 1.61 (m, 1H), 1.45 (s, 9H), 1.44 – 1.38 (m, 2H), 1.31 – 1.16 (m, 3H).



3n Colorless Oil.

^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) 2.30 (d, J = 7.9 Hz, 2H), 1.86 – 1.76 (m, 1H), 1.74 – 1.60 (m, 5H), 1.45 (s, 9H), 1.31 – 1.08 (m, 3H), 0.99 – 0.89 (m,

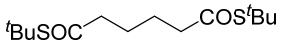
2H).



3o

Colorless Oil.

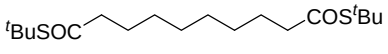
^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) 2.45 (t, *J* = 7.9 Hz, 2H), 1.71 – 1.61 (m, 5H), 1.55 – 1.47 (m, 2H), 1.45 (s, 9H), 1.29 – 1.11 (m, 4H), 0.92 – 0.83 (m, 2H).



3p

White solid.

^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) 2.47 – 2.43 (m, 4H), 1.67 – 1.63 (m, 4H), 1.45 (s, 18H).



3q

White solid.

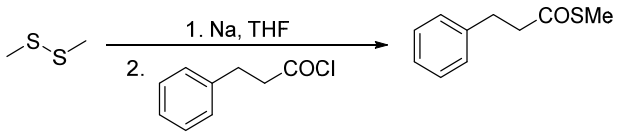
^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) 2.43 (t, *J* = 7.5 Hz, 4H), 1.83 – 1.59 (m, 4H), 1.45 (s, 18H), 1.31 – 1.27 (m, 4H).

2.1.1 Synthesis for some individual starting materials

3p and **3q** was synthesized using the same method, except 0.5 equiv. of the acid (adipic acid and dodecanedioic acid respectively) was added instead of 1 equiv..

3h was synthesized using a similar method, except 4-pyrrolidinopyridine was added as catalyst instead of DMAP.

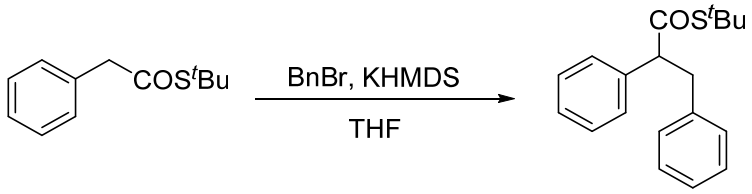
1j was synthesized by the following method:



Scheme 32: Synthesis for **1j**.

A dry round bottom flask with a magnetic stir bar was charged with sodium metal (2 equiv., 10 mmol, 0.46 g) and 30 mL of dry THF under N_2, dimethyl disulfide (1 equiv., 5 mmol, 0.44 mL) was added in one portion, the mixture was stirred vigorously for 48 h and a grey suspension was formed. The suspension was cooled to 0 ^oC, a solution of 3-phenylpropanoyl chloride (2 equiv., 10 mmol, 1.48 mL) in 10 mL of dry THF was added *via* syringe pump in 1 h, the mixture was stirred at room temperature for 24 h. It was then quenched by slowly add water in an ice bath, the mixture was then extracted with ether (3 x 30 mL), the organic layer was dried over sodium sulfate, the ether was then removed under vacuum and the residue was purified by flash column chromatography on silica gel (eluent: hexane/ethyl acetate 98:2) to afford the desired product.

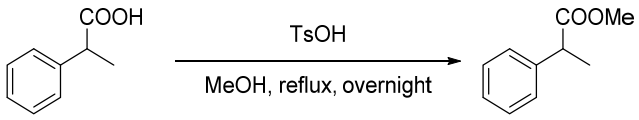
2m was synthesized by the following step[82]:



Scheme 33: Synthesis for **2m**.

A dry reaction tube was charged with potassium bis(trimethylsilyl)amide (1.2 equiv., 1.2 mmol, 0.24 g) and 2 mL of dry THF under N_2. The mixture was cooled to -78 ^oC and *S*-(*tert*-butyl) 2-phenylethanethioate (synthesized form phenylacetic acid and *tert*-butyl thiol using the standard method, 1 equiv., 1 mmol, 0.208 g) was added dropwise. The mixture was stirred at that temperature for 1 h and benzyl bromide (1 equiv., 1 mmol, 0.12 mL) was added dropwise. The mixture was stirred at that temperature for 30 min, then at room temperature for 2 h. It was quenched with saturated NH_4Cl solution, it was then extracted with ether (3 x 10 mL). The combined organic layer was then washed with brine and dried over Na_2SO_4, after the organic solvent was removed under vacuum, the residue was purified by flash column chromatography on silica gel (eluent: hexane/ethyl acetate 98:2) to afford the desired product.

2s was synthesized by the following method:

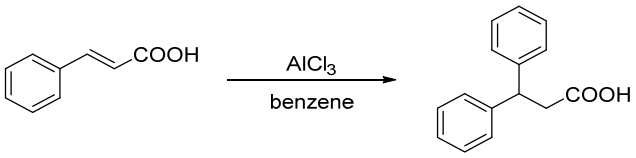


Scheme 34: Synthesis for **2s**.

A dry round bottom flask with a magnetic stir bar was charged with 2-phenylpropionic acid (1 equiv., 10 mmol, 1.5 g), a catalyst amount of *p*-toluenesulfonic acid monohydrate and methanol (40 mL) under N_2 atmosphere. The solution was heated under reflux overnight, the excess methanol was removed under vacuum and the residue

was purified by flash column chromatography on silica gel (eluent: hexane/ethyl acetate 98:2).

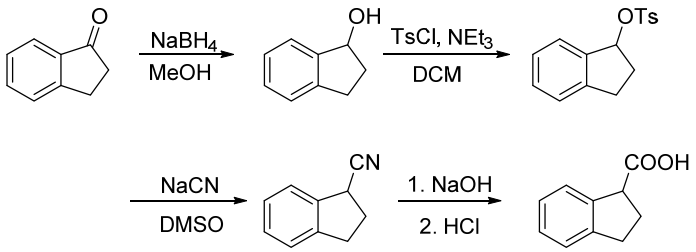
The acid part of **2l** was synthesized by the following method[83]:



Scheme 35: Synthesis for the acid part of **2l**.

A dry reaction tube with cinnamic acid (1 equiv., 5 mmol, 0.74 g) in 5 mL of benzene under N_2 was added aluminum chloride (2.2 equiv., 11 mmol, 1.46 g) at 0 °C. The mixture was stirred at room temperature for 1 h and then quenched by 2 M HCl. It was extracted with ether (3 x 10 mL). The combined organic layer was then washed with brine and dried over Na_2SO_4, after the organic solvent was removed under vacuum, the residue was used for the next step without further purification.

The acid part of **2j** was synthesized by the following method[84,85,86]:



Scheme 36: Synthesis route for the acid part of **2j**.

A dry round bottom flask with a magnetic stir bar was charged with sodium borohydride (2 equiv., 20 mmol, 0.76 g) and 20 mL of dry methanol at 0 °C, 1-indanone (1 equiv., 10 mmol, 1.32 g) was added in portions. The mixture was then stirred at room temperature for 2 h before quenched by water. It was extracted with ether (3 x 10 mL). The combined organic layer was then washed with brine and dried over Na_2SO_4, after

the organic solvent was removed under vacuum, the residue was used for the next step without further purification.

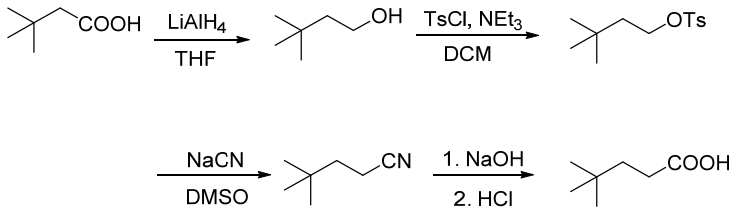
A dry round bottom flask with a magnetic stir bar charged with the crude 1-indanol (1 equiv.), triethylamine (2 equiv., 20 mmol. 2.8 mL) and 30 mL of DCM under N_2 was cooled to 0 ^oC. *p*-Toluenesulfonyl chloride (1 equiv., 10 mmol, 1.9 g) was added in small portions. The mixture was then stirred overnight and quenched with saturated NH_4Cl solution, it was extracted with DCM (3 x 20 mL). The combined organic layer was then washed with brine and dried over Na_2SO_4, after the organic solvent was removed under vacuum, the residue was used for the next step without further purification.

A dry round bottom flask with a magnetic stir bar was charged with the crude intermediate (1 equiv.) and 40 mL of DMSO under N_2. Sodium cyanide (1.2 equiv., 12 mmol, 0.59 g) was added in one portion. It was stirred at 60 ^oC for 24 h. After the reaction was completed, the mixture was allowed to cool to room temperature and 40 mL of water was added. It was then extracted with ethyl acetate (3 x 30 mL) and the combined organic layer was then washed with brine and dried over Na_2SO_4. After the organic solvent was removed under vacuum, the residue was used for the next step without further purification.

To a round bottom flask with the crude intermediate was added 40 mL of 1 M NaOH solution in 1:1 MeOH/H_2O, the mixture was heated under reflux for 24 h. After the reaction was completed, the mixture was allowed to cool to room temperature, the methanol was removed under vacuum and then the aqueous phase was washed with 30

mL of ether. Then, it was acidified by HCl, extracted with ether (3 x 30 mL) and the combined organic layer was then washed with brine and dried over Na_2SO_4, after the organic solvent was removed under vacuum, the residue was used for the next step without further purification.

The acid part of **3k** was synthesized by the following method[87]:

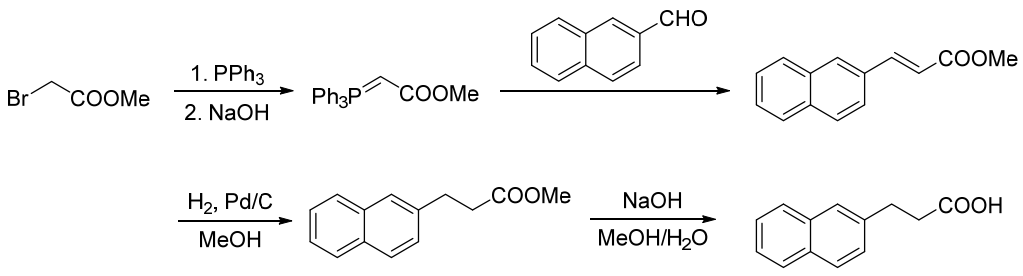


Scheme 37: Synthesis route for the acid part of **3k**.

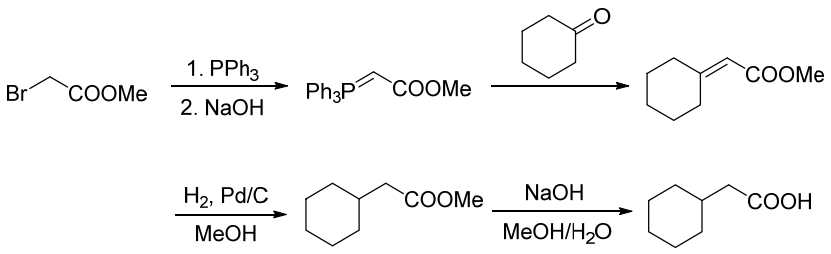
To a suspension of lithium aluminum hydride (2.2 equiv., 22 mmol, 0.84 g) in 30 mL of dry THF under N_2 at 0 ºC was added 3,3-dimethylbutyric acid (1 equiv., 10 mmol, 1.27 mL) dropwise, after the addition was completed, it was stirred at room temperature for 24 h. Sodium sulfate decahydrate was added in small portions until the mixture become white, it was then filtered through a pad of celite, the filtrate was extracted with ether (3 x 30 mL) and the combined organic layer was then washed with brine and dried over Na_2SO_4, after the organic solvent was removed under vacuum, the residue was used for the next step without further purification.

The following step is the same as described in the procedure of **2j**.

The acid part of **2e** and **3n** was synthesized by the following method[88]:



Scheme 38: Synthesis route for the acid part of **2e**.



Scheme 39: Synthesis route for the acid part of **3n**.

To a solution of triphenylphosphine (1 equiv., 10 mmol, 2.62 g) in 30 mL of ethyl acetate was added methyl bromoacetate (1 equiv., 10 mmol, 0.95 mL), the mixture was stirred at room temperature overnight, a white precipitate was formed, it was collected by filtration and washed twice with a small amount of ethyl acetate.

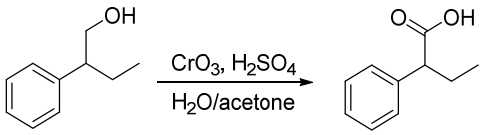
The solid was dissolved in 20 mL of DCM, followed by addition of 20 mL of 1 M NaOH solution, the mixture was stirred for at room temperature for 1 h, after that, it was extracted with DCM (3 x 30 mL) and the combined organic layer was then washed with brine and dried over Na_2SO_4, after the organic solvent was removed under vacuum, the residue was used for the next step without further purification.

To a solution of the phosphorus ylide (1 equiv., 10 mmol, 3.34 g) in 30 mL DCM was added the aldehyde or ketone (1 equiv., 10 mmol), the mixture was stirred at room temperature overnight, it was then filtered and the solvent of the filtrate was removed under vacuum, the residue was flushed through a short pad of silica gel to remove the triphenylphosphine oxide and used for the next step without further purification.

To a solution of the ester in 30 mL methanol was added palladium on carbon (10% Pd, 1% mol), it was stirred at room temperature for 24 h under H_2, after which, it was filtered and 30 mL of 2 M NaOH was added. The mixture was stirred for an additional

24 h, the methanol was removed under vacuum and then the aqueous phase was washed with 30 mL of ether. Then, it was acidified by HCl, extracted with ether (3 x 30 mL) and the combined organic layer was then washed with brine and dried over Na_2SO_4, after the organic solvent was removed under vacuum, the residue was used for the next step without further purification.

The acid part of **2p** was synthesized by the following method[89]:

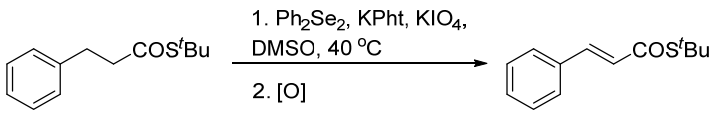


Scheme 40: Synthesis route for the acid part of **2p**.

To a solution of chromium trioxide (1.2 equiv., 12 mmol, 1.2 g) in 20 mL of 6 M sulfuric acid was added a solution of 2-phenyl-1-butanol (1.0 equiv., 10 mmol, 1.56 mL) in 10 mL of acetone at 0 ^oC. It was stirred at room temperature and monitored by TLC. After the reaction was complete, it was dilute with water and extracted with ether (3 x 40 mL), the combined organic layer was then washed with brine and dried over Na_2SO_4, after the organic solvent was removed under vacuum, the residue was used for the next step without further purification.

2t was commercially available and used as received.

2.2 General procedure for the reaction



Scheme 41: General procedure for the reaction.

A reaction tube with a stir bar was charged with diphenyl diselenide (0.5 equiv., 0.1 mmol, 31.2 mg), potassium phthalimide (1 equiv., 0.2 mmol, 38.0 mg), potassium periodate (1 equiv., 0.2 mmol, 46.0 mg) and 1 mL of DMSO, followed by addition of the thioester (1 equiv., 0.2 mmol). The mixture was stirred at 40 °C for 24 h and used for the second step without purification.

Procedure A: The resulting mixture from the first step was dilute with 2 mL of THF and cooled to 0 °C on ice bath. 0.3 mL of 30% H_2O_2 solution was added dropwise, it was then stirred at this temperature for 1 h and quenched by diluting with brine. The mixture was extracted twice with ethyl acetate, the combined organic layer was dried over Na_2SO_4 and purified by flash column chromatography on silica gel (eluent: hexane/ethyl acetate 98:2) to afford the crude product with a trace amount of starting material as impurity. The crude product was further purified by productive TLC plate to afford the pure product for analysis.

For each substrate, unless otherwise stated, the **procedure A** was used for the second step.

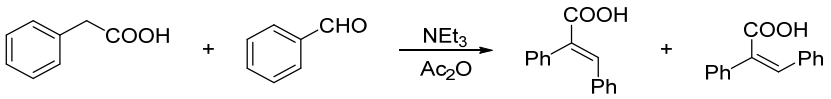
Procedure B: The resulting mixture from the first step was dilute with 1 mL of DCM and cooled to -40 °C in a low temperature reactor. A solution of *meta*-chloroperoxybenzoic acid (1.2 equiv., 0.24 mmol, 60% purity, 70 mg) in 1 mL of DCM was added dropwise. The resulting mixture was stirred at this temperature for 3 h. The

residue was then directly purified by flash column chromatography on silica gel (eluent: hexane/ethyl acetate 98:2) to afford the crude product with a trace amount of starting material as impurity. The crude product was further purified by productive TLC plate to afford the pure product for analysis.

Substrate **1b**, **1e** and **1j** was done using this procedure.

For substrate **5ma** and **5mb** as well as **5na** and **5nb**, as it fails to separate them, a sample of them are synthesized as reference, they are synthesized using the standard method for the starting material as described above.

For **5ma** and **5mb**, the acid part was synthesized using method showing below[90]:

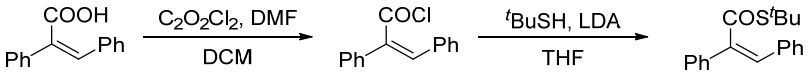


Scheme 42: Synthesis for the acid part of **5ma** and **5mb**.

A seal tube with a stir bar under N_2 was charged with phenylacetic acid (1 equiv., 20 mmol, 2.72 g), benzaldehyde (1 equiv., 20 mmol, 2.08 mL), triethylamine (1 equiv., 20 mmol, 2.82 mL) and acetic anhydride (2 equiv., 40 mmol, 3.78 mL). The mixture was stirred at 150 ^{o}C for 5 h, after cooling to room temperature, it was poured to 30 mL of 2 M HCl, the mixture was stirred for 30 min to help the precipitate form, it was then collect by filtration, washed with cold water and then dissolved in 100 mL of 0.2 M NaOH solution, the solution was washed twice with 20 mL of benzene. It was then acidified to pH = 5 by acetic acid to afford a precipitate, the precipitate was collected by filtration, washed with cold water and dried to afford the (*E*) isomer as one of the product. The filtrated was further acidified by concentrated HCl to form another precipitate, it was then collected by filtration, washed with cold water and dried to

afford the (*Z*) isomer.

In addition, for **5mb**, using standard method would result a mixture of **5ma** and **5mb** and transfer the acid to acetyl chloride and react with the thiol in the presence of triethylamine showed no reaction, it was synthesized using the following method:



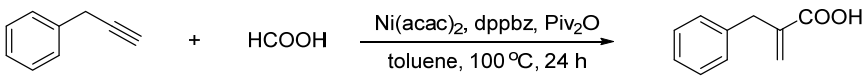
Scheme 43: Synthesis of **5mb**.

To a solution of (*Z*)-2,3-diphenylacrylic acid (1 equiv., 1 mmol, 224.3 mg) in 1 mL of DCM was added oxalyl chloride (1.1 equiv., 1.1 mmol, 0.095 mL), followed by 1 drop of DMF. The mixture was stirred under N_2 for 2 h and directly used for the next step without further purification.

To a solution of *tert*-butyl thiol (1 equiv., 1 mmol, 0.113 mL) was added LDA (1.1 equiv., 1.1 mmol, 2 M in THF, 0.55 mL) dropwise at -78 ^oC under N_2. The mixture was stirred at this temperature for 1 h, then a solution of (*Z*)-2,3-diphenylacryloyl chloride prepared from method above was added to this mixture *via* a syringe pump in 1 h. After the addition the mixture was then stirred at room temperature for 3 h, it was quenched with saturated NH_4Cl solution, it was then extracted with ether (3 x 10 mL). The combined organic layer was then washed with brine and dried over Na_2SO_4, after the organic solvent was removed under vacuum, the residue was purified by flash column chromatography on silica gel (eluent: hexane/ethyl acetate 98:2) to afford the desired product.

For **5na**, the acid part, (*E*)-*α*-methylcinnamic acid, is commercially available (no (*Z)* isomer observed in the ^1H NMR); for **5nb**, the acid part, 2-benzylacrylic acid, was

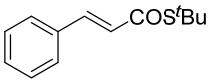
synthesized by the following method[91]:



Scheme 44: Synthesis for the acid part of **5nb**.

A reaction tube with a stir bar was charged with nickel(II) acetylacetonate ($Ni(acac)_2$, 5 mol%, 0.05 mmol, 12.9 mg) and 1,2-bis(diphenylphosphino)benzene (dppbz, 7 mol%, 7 mmol, 31.3 mg) under N_2. 2 mL of toluene was added, followed by 3-phenylpropyne (1 equiv., 1 mmol, 125 μL), formic acid (2 equiv., 2 mmol, 76 μL) and pivalic anhydride (Piv_2O, 0.2 equiv., 0.2 mmol, 41 μL). The mixture was stirred at 100 °C for 24 h, after it was cooled to room temperature, it was poured to 30 mL of 1 M NaOH solution, it was wash twice with 20 mL of ether, acidified by HCl, then extracted with ether (3 x 20 mL), the combined organic layer was then washed with brine and dried over Na_2SO_4, after the organic solvent was removed under vacuum, the residue was used for the next step without further purification.

2.3 Product characterization and spectral data



4a

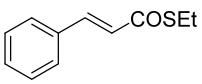
***S*-(*tert*-butyl) (*E*)-3-phenylprop-2-enethioate (4a)**

87% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.54 (d, *J* = 15.8 Hz, 1H) 7.53 – 7.51 (m, 2H), 7.38 – 7.37 (m, 3H), 6.62 (d, *J* = 15.8 Hz, 1H), 1.55 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 191.0, 139.6, 134.7, 130.6, 129.2, 128.6, 126.2, 48.6, 30.3.

HRMS (ESI, m/z): calcd for $C_{13}H_{17}OS^+$ $[M+H]^+$ 221.1000, found: 221.0998.



4b

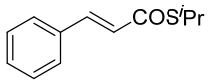
***S*-ethyl (*E*)-3-phenylprop-2-enethioate (4b)**

73% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.61 (d, *J* = 15.8 Hz, 1H), 7.55 – 7.53 (m, 2H), 7.40 – 7.38 (m, 3H), 6.71 (d, *J* = 15.8 Hz, 1H), 3.02 (q, *J* = 7.4 Hz, 2H), 1.32 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 190.3, 140.6, 134.5, 130.8, 129.3, 128.7, 125.5, 23.7, 15.2.

HRMS (ESI, m/z): calcd for $C_{11}H_{13}OS^+$ $[M+H]^+$ 193.0687, found: 193.0693.



4c

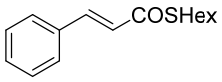
***S*-isopropyl (*E*)-3-phenylprop-2-enethioate (4c)**

68% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.59 (d, *J* = 15.8 Hz, 1H), 7.54 – 7.52 (m, 2H), 7.40 – 7.38 (m, 3H), 6.67 (d, *J* = 15.8 Hz, 1H), 3.85 – 3.75 (m, 1H), 1.38 (d, *J* = 7.4 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 190.3, 140.4, 134.6, 130.8, 129.3, 128.7, 125.7, 25.1, 23.5.

HRMS (ESI, m/z): calcd for $C_{12}H_{15}OS^+$ $[M+H]^+$ 207.0844, found: 207.0836.



4d

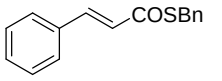
***S*-hexyl (*E*)-3-phenylprop-2-enethioate (4d)**

85% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.61 (d, *J* = 15.8 Hz, 1H), 7.55 – 7.53 (m, 2H), 7.40 – 7.37 (m, 3H), 6.71 (d, *J* = 15.8 Hz, 1H), 3.01 (t, *J* = 7.3 Hz, 2H), 1.67 – 1.60 (m, 2H), 1.45 – 1.38 (m, 2H), 1.35 – 1.28 (m, 4H), 0.90 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 190.3, 140.5, 134.6, 130.8, 129.3, 128.7, 125.6, 31.7, 29.9, 29.4, 28.9, 22.9, 14.4.

HRMS (ESI, m/z): calcd for $C_{15}H_{21}OS^+$ $[M+H]^+$ 249.1313, found: 249.1318.



4e

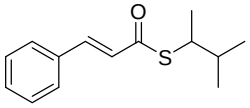
***S*-benzyl (*E*)-3-phenylprop-2-enethioate (4e)**

13% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.64 (d, *J* = 15.8 Hz, 1H), 7.55 – 7.52 (m, 2H), 7.41 – 7.29 (m, 7H), 7.27 – 7.23 (m, 1H), 6.72 (d, *J* = 15.8 Hz, 1H), 4.27 (s, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 189.5, 141.3, 137.9, 134.4, 131.0, 129.3, 129.2, 129.0, 128.8, 127.7, 125.0, 33.6.

HRMS (ESI, m/z): calcd for $C_{16}H_{15}OS^+$ $[M+H]^+$ 255.0844, found: 255.0842.



4f

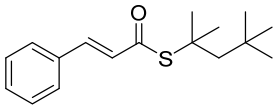
***S*-(3-methylbutan-2-yl) (*E*)-3-phenylprop-2-enethioate (4f)**

95% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.59 (d, *J* = 15.8 Hz, 1H), 7.55 – 7.53 (m, 2H), 7.40 – 7.38 (m, 3H), 6.70 (d, *J* = 15.8 Hz, 1H), 3.77 – 3.71 (m, 1H), 1.99 – 1.89 (d, *J* = 7.1 Hz, 3H), 1.33 (d, *J* = 7.1 Hz, 3H), 0.99 (dd, J_1 = 6.8 Hz, J_2 = 2.8 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 190.2, 140.2, 134.7, 130.7, 129.3, 128.7, 125.9, 46.0, 33.5, 19.9, 19.8, 18.7.

HRMS (ESI, m/z): calcd for $C_{14}H_{19}OS^+$ $[M+H]^+$ 235.1157, found: 235.1162.



4g

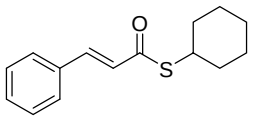
***S*-(2,4,4-trimethylpentan-2-yl) (*E*)-3-phenylprop-2-enethioate (4g)**

84% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.53 (d, *J* = 15.9 Hz, 1H), 7.54 – 7.51 (m, 2H), 7.39 – 7.36 (m, 3H), 6.62 (d, *J* = 15.8 Hz, 1H), 1.92 (s, 2H), 1.64 (s, 3H), 1.05 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 190.9, 139.4, 134.7, 130.6, 129.2, 128.6, 126.3, 54.0, 53.7, 33.1, 32.0, 30.1.

HRMS (ESI, m/z): calcd for $C_{17}H_{25}OS^+$ $[M+H]^+$ 277.1626, found: 277.1620.



4h

***S*-cyclohexyl (*E*)-3-phenylprop-2-enethioate (4h)**

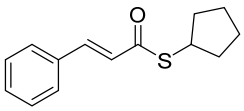
78% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.58 (d, *J* = 15.8 Hz, 1H), 7.54 – 7.52 (m, 2H), 7.39 – 7.37 (m, 3H), 6.67 (d, *J* = 15.8 Hz, 1H), 3.71 – 3.64 (m, 1H), 2.02 – 1.96 (m,

2H), 1.79 – 1.70 (m, 2H), 1.64 – 1.58 (m, 1H), 1.53 – 1.42 (m, 4H), 1.36 – 1.26 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 190.0, 140.3, 134.6, 130.7, 129.3, 128.7, 125.8, 42.7, 33.5, 26.3, 26.0.

HRMS (ESI, m/z): calcd for $C_{15}H_{19}OS^+$ $[M+H]^+$ 247.1157, found: 247.1159.



4i

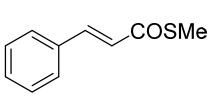
S-cyclopentyl (*E*)-3-phenylprop-2-enethioate (4i)

84% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.58 (d, *J* = 15.9 Hz, 1H), 7.54 – 7.52 (m, 2H), 7.39 – 7.37 (m, 3H), 6.68 (d, *J* = 15.8 Hz, 1H), 3.91 – 3.84 (m, 1H), 2.20 – 2.12 (m, 2H), 1.77 – 1.56 (m, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 190.9, 140.3, 134.6, 130.7, 129.3, 128.7, 125.6, 42.8, 33.7, 25.2.

HRMS (ESI, m/z): calcd for $C_{14}H_{17}OS^+$ $[M+H]^+$ 233.1000, found: 233.0999.



4j

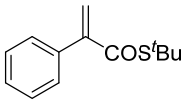
S-methyl (*E*)-3-phenylprop-2-enethioate (4j)

56% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.62 (d, *J* = 15.8 Hz, 1H), 7.56 – 7.54 (m, 2H), 7.40 – 7.39 (m, 3H), 6.74 (d, *J* = 15.8 Hz, 1H), 2.43 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 190.6, 140.6, 134.5, 130.9, 129.3, 128.7, 125.2, 12.0.

HRMS (ESI, m/z): calcd for $C_{10}H_{11}OS^+$ $[M+H]^+$ 179.0531, found: 179.0540.



5a

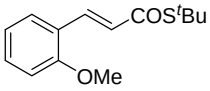
***S*-(*tert*-butyl) 2-phenylprop-2-enethioate (5a)**

77% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.40 – 7.34 (m, 5H), 6.09 (s, 1H), 5.72 (s, 1H), 1.53 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 195.0, 149.6, 136.7, 128.8, 128.6, 128.5, 122.0, 48.7, 30.1.

HRMS (ESI, m/z): calcd for $C_{13}H_{17}OS^+$ $[M+H]^+$ 221.1000, found: 221.0993.



5b

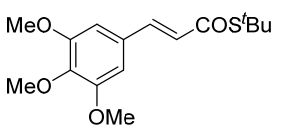
***S*-(*tert*-butyl) (*E*)-3-(2-methoxyphenyl)prop-2-enethioate (5b)**

71% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.86 (d, J = 15.9 Hz, 1H), 7.49 (dd, J_1 = 7.7 Hz, J_2 = 1.7 Hz, 1H), 7.34 (td, J_1 = 7.9 Hz, J_2 = 1.7 Hz, 1H), 6.95 (t, J = 7.5 Hz, 1H), 6.90 (d, J = 8.3 Hz, 1H), 6.72 (d, J = 15.9 Hz, 1H), 3.88 (s, 3H), 1.54 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 191.5, 159.0, 135.2, 131.8, 129.3, 129.9, 123.7, 121.1, 111.5, 55.8, 48.4, 30.3.

HRMS (ESI, m/z): calcd for $C_{14}H_{19}O_2S^+$ $[M+H]^+$ 251.1106, found: 251.1105.



5c

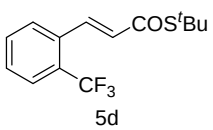
***S*-(*tert*-butyl) (*E*)-3-(3,4,5-trimethoxyphenyl)prop-2-enethioate (5c)**

81% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.45 (d, J = 15.7 Hz, 1H), 6.73 (s, 2H), 6.52 (d, J = 15.7 Hz, 1H), 3.88 (s, 6H), 3.87 (s, 3H), 1.54 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$): 190.4, 153.4, 140.2, 139.4, 129.8, 125.2, 105.4, 61.0, 56.2, 56.1, 48.3, 30.0.

HRMS (ESI, m/z): calcd for $C_{16}H_{23}O_4S^+$ $[M+H]^+$ 311.1317, found: 311.1313.



5d

S-(*tert*-butyl) (*E*)-3-(2-trifluoromethylphenyl)prop-2-enethioate (5d)

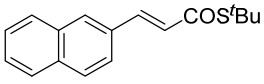
70% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.91 (dq, J_1 = 15.7 Hz, J_2 = 2.2 Hz, 1H), 7.71 – 7.68 (m, 2H), 7.55 (t, J = 7.6 Hz, 1H), 7.47 (t, J = 7.6 Hz, 1H), 6.57 (d, J = 15.6 Hz, 1H), 1.55 (s, 9H).

^{19}F NMR (375 MHz, $CDCl_3$): δ (ppm) -58.94.

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 190.4, 135.1 (q, J = 2.2 Hz), 133.7 (q, J = 1.6 Hz), 132.4, 130.1, 129.9, 129.6 (q, J = 30.2 Hz), 128.1, 126.6 (q, J = 5.6 Hz), 124.3 (q, J = 272.2 Hz), 49.0, 30.2.

HRMS (ESI, m/z): calcd for $C_{14}H_{16}OSF_3^+$ $[M+H]^+$ 289.0874, found: 289.0872.



5e

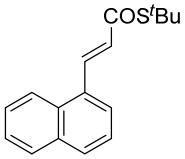
S-(*tert*-butyl) (*E*)-3-(naphthalen-2-yl)prop-2-enethioate (5e)

70% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.93 (s, 1H), 7.86 – 7.81 (m, 3H), 7.70 (d, J = 15.8 Hz, 1H), 7.64 (dd, J_1 = 8.6 Hz, J_2 = 1.8 Hz, 1H), 7.53 – 7.48 (m, 2H), 6.74 (d, J = 15.8 Hz, 1H), 1.57 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 190.9, 139.7, 134.6, 133.7, 132.2, 130.6, 129.0, 128.9, 128.1, 127.6, 127.0, 126.4, 123.9, 48.7, 30.3.

HRMS (ESI, m/z): calcd for $C_{17}H_{19}OS^+$ $[M+H]^+$ 271.1157, found: 271.1168.



5f

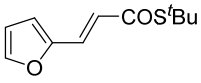
***S*-(*tert*-butyl) (*E*)-3-(naphthalen-1-yl)prop-2-enethioate (5f)**

74% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.39 (d, *J* = 15.6 Hz, 1H), 8.20 (d, *J* = 8.2 Hz, 1H), 7.88 (t, *J* = 7.2 Hz, 2H), 7.74 (d, *J* = 7.2 Hz, 1H), 7.60 – 7.51 (m, 2H), 7.47 (t, *J* = 7.7 Hz, 1H), 6.72 (d, *J* = 15.6 Hz, 1H), 1.59 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 190.9, 136.5, 134.0, 132.0, 130.9, 129.1, 128.8, 127.2, 126.6, 125.8, 125.3, 123.7, 48.7, 30.3.

HRMS (ESI, m/z): calcd for $C_{17}H_{19}OS^+$ $[M+H]^+$ 271.1157, found: 271.1157.



5g

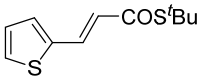
***S*-(*tert*-butyl) (*E*)-3-(furan-2-yl)prop-2-enethioate (5g)**

88% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.47 (d, *J* = 1.8 Hz, 1H), 7.28 (d, *J* = 15.3 Hz, 1H), 6.62 (d, *J* = 3.4 Hz, 1H), 6.52 (d, *J* = 15.5 Hz, 1H), 6.46 (dd, J_1 = 3.4 Hz, J_2 = 1.8 Hz, 1H), 1.53 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 190.6, 151.3, 145.1, 125.9, 123.8, 115.8, 112.8, 48.6, 30.3.

HRMS (ESI, m/z): calcd for $C_{11}H_{15}O_2S^+$ $[M+H]^+$ 211.0793, found: 211.0794.



5h

***S*-(*tert*-butyl) (*E*)-3-(thiophen-2-yl)prop-2-enethioate (5h)**

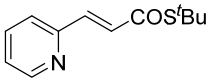
85% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.64 (d, *J* = 15.5 Hz, 1H), 7.36 (d, *J* = 5.1 Hz,

1H), 7.25 (d, J = 3.4 Hz, 1H), 7.04 (dd, J_1 = 5.0 Hz, J_2 = 3.6 Hz, 1H), 6.42 (d, J = 15.4 Hz, 1H), 1.53 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 190.4, 139.9, 132.1, 131.8, 128.8, 128.5, 125.1, 48.6, 30.3.

HRMS (ESI, m/z): calcd for $C_{11}H_{15}OS_2^+$ $[M+H]^+$ 227.0564, found: 227.0556.



5i

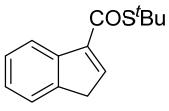
***S*-(*tert*-butyl) (*E*)-3-(pyridin-2-yl)prop-2-enethioate (5i)**

90% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.63 (ddd, J_1 = 4.7 Hz, J_2 = 1.8 Hz, J_3 = 0.9 Hz, 1H), 7.69 (td, J_1 = 7.7 Hz, J_2 = 1.8 Hz, 1H), 7.50 (d, J = 15.4 Hz, 1H), 7.40 (dt, J_1 = 7.8 Hz, J_2 = 1.0 Hz, 1H), 7.25 (ddd, J_1 = 7.6 Hz, J_2 = 4.8 Hz, J_3 = 1.1 Hz, 1H), 7.11 (d, J = 15.4 Hz, 2H), 1.54 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 191.1, 153.3, 150.5, 137.9, 137.1, 129.9, 125.1, 124.5, 48.7, 30.2.

HRMS (ESI, m/z): calcd for $C_{12}H_{16}NOS^+$ $[M+H]^+$ 222.0953, found: 222.0951.



5j

***S*-(*tert*-butyl) 1*H*-indene-3-carbothioate (5j)**

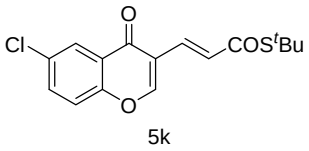
56% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.02 (dt, J_1 = 7.7 Hz, J_2 = 1.0 Hz, 1H), 7.46 (dt, J_1 = 7.4 Hz, J_2 = 1.0 Hz, 1H), 7.36 (t, J = 2.2 Hz, 1H), 7.33 (t, J = 7.2 Hz, 1H), 7.25 (td, J_1 = 7.7 Hz, J_2 = 1.1 Hz, 1H), 3.51 (d, J = 2.0 Hz, 2H), 1.59 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 189.9, 144.2, 143.5, 141.8, 140.8, 127.0, 126.1,

124.1, 122.9, 48.5, 38.8, 30.4.

HRMS (ESI, m/z): calcd for $C_{14}H_{17}OS^+$ $[M+H]^+$ 223.1000, found: 223.0999.



5k

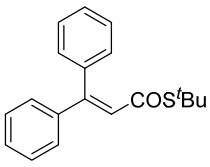
***S*-(*tert*-butyl) (*E*)-3-(6-chloro-4-oxo-4*H*-chromen-3-yl)prop-2-enethioate (5k)**

79% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.22 (d, J = 2.5 Hz, 1H), 8.10 (s, 1H), 7.63 (dd, J_1 = 8.9 Hz, J_2 = 2.6 Hz, 1H), 7.53 (d, J = 15.5 Hz, 1H), 7.44 (d, J = 8.9 Hz, 1H), 7.20 (d, J = 15.6 Hz, 1H), 1.53 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 191.6, 175.0, 158.1, 154.2, 134.6, 132.3, 130.4, 129.5, 126.1, 125.4, 120.2, 119.6, 48.6, 30.2.

HRMS (ESI, m/z): calcd for $C_{16}H_{16}O_3SCl^+$ $[M+H]^+$ 323.0509, found: 323.0495.



5l

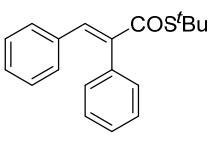
***S*-(*tert*-butyl) 3,3-diphenylprop-2-enethioate (5l)**

95% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.37 – 7.22 (m, 10H), 6.48 (s, 1H), 1.43 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 190.6, 152.2, 141.4, 139.1, 129.9, 129.7, 128.9, 128.7, 128.7, 128.3, 125.3, 48.6, 30.1.

HRMS (ESI, m/z): calcd for $C_{19}H_{21}OS^+$ $[M+H]^+$ 297.1313, found: 297.1320.



5ma

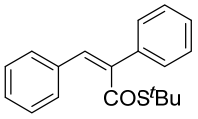
***S*-(*tert*-butyl) (*E*)-2,3-diphenylprop-2-enethioate (5ma)**

24% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.62 (s, 1H), 7.40 – 7.37 (m, 3H), 7.27 – 7.23 (m, 2H), 7.20 – 7.10 (m, 3H), 7.01 – 6.99 (m, 2H), 1.49 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 194.4, 140.6, 130.9, 135.8, 124.8, 131.2, 130.8, 129.3, 129.1, 128.7, 128.5, 48.5, 30.1.

HRMS (ESI, m/z): calcd for $C_{18}H_{21}OS^+$ $[M+H]^+$ 285.1313, found: 285.1322.



5mb

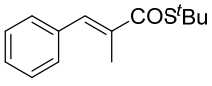
***S*-(*tert*-butyl) (*Z*)-2,3-diphenylprop-2-enethioate (5mb)**

16% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.53- 7.46 (m, 4H), 7.41 – 7.30 (m, 6H), 6.93 (s, 1H), 1.50 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 198.4, 141.8, 137.4, 135.7, 131.2, 130.9, 129.9, 129.9, 129.1, 128.7, 128.6, 126.6, 49.2, 29.8.

HRMS (ESI, m/z): calcd for $C_{18}H_{21}OS^+$ $[M+H]^+$ 285.1313, found: 285.1299.



5na

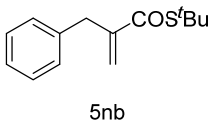
***S*-(*tert*-butyl) (*E*)-2-methyl-3-phenylprop-2-enethioate (5na)**

28% yield (at 60 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.59 (q, J = 1.5 Hz, 1H), 7.40 – 7.35 (m, 4H), 7.33 – 7.28 (m, 1H), 2.11 (d, J = 1.5 Hz, 3H), 1.54 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 195.7, 137.6, 136.5, 136.0, 130.0, 128.7, 128.6, 48.0, 30.2, 14.3.

HRMS (ESI, m/z): calcd for $C_{14}H_{19}OS^+$ $[M+H]^+$ 235.1157, found: 235.1163.



5nb

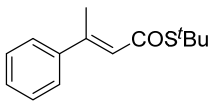
***S*-(*tert*-butyl) 2-benzylprop-2-enethioate (5nb)**

21% yield (at 60 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.32 – 7.27 (m, 2H), 7.23 – 7.16 (m, 3H), 6.10 (t, *J* = 0.9 Hz, 1H), 5.33 (t, *J* = 1.5 Hz, 1H), 3.62 (s, 3H), 1.48 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 194.7, 149.1, 138.7, 129.5, 128.8, 126.7, 123.2, 48.1, 37.9, 30.2.

HRMS (ESI, m/z): calcd for $C_{14}H_{19}OS^+$ $[M+H]^+$ 235.1157, found: 235.1156.



5oa

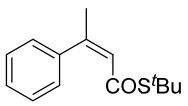
***S*-(*tert*-butyl) (*E*)-3-phenylbut-2-enethioate (5oa)**

24% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.47 – 7.45 (m, 2H), 7.38 – 7.36 (m, 3H), 6.32 (s, 1H), 2.54 (s, 3H), 1.53 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 191.0, 151.3, 142.1, 129.1, 128.6, 126.5, 124.4, 48.1, 29.9, 18.6.

HRMS (ESI, m/z): calcd for $C_{14}H_{19}OS^+$ $[M+H]^+$ 235.1157, found: 235.1158.



5ob

***S*-(*tert*-butyl) (*Z*)-3-phenylbut-2-enethioate (5ob)**

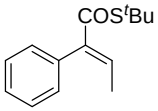
24% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.36 – 7.30 (m, 3H), 7.25 – 7.23 (m, 2H), 6.08 (q, *J* = 1.4 Hz, 1H), 2.13 (d, *J* = 1.5 Hz, 3H), 1.40 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 190.7, 150.6, 140.8, 128.4, 128.3, 127.6, 125.6,

48.3, 30.1, 27.0.

HRMS (ESI, m/z): calcd for $C_{14}H_{19}OS^+$ $[M+H]^+$ 235.1157, found: 235.1157.



5pa

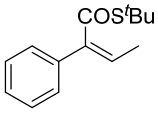
***S*-(*tert*-butyl) (*E*)-2-phenylbut-2-enethioate (5pa)**

16 % yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.40 – 7.34 (m, 3H), 7.20 – 7.18 (m, 2H), 6.96 (q, *J* = 7.0 Hz, 1H), 1.66 (d, *J* = 7.1 Hz, 3H), 1.46 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 193.8, 143.5, 135.7, 125.2, 130.6, 128.5, 128.2, 48.3, 30.2, 15.5.

HRMS (ESI, m/z): calcd for $C_{14}H_{19}OS^+$ $[M+H]^+$ 235.1157, found: 235.1166.



5pb

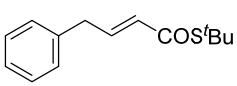
***S*-(*tert*-butyl) (*Z*)-2-phenylbut-2-enethioate (5pb)**

28 % yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.38 – 7.09 (m, 5H), 6.03 (q, *J* = 7.2 Hz, 1H), 1.96 (d, *J* = 7.1 Hz, 3H), 1.53 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 196.9, 143.0, 137.5, 128.9, 128.8, 128.1, 127.0, 49.2, 30.2, 15.8.

HRMS (ESI, m/z): calcd for $C_{14}H_{19}OS^+$ $[M+H]^+$ 235.1157, found: 235.1154.



5q

***S*-(*tert*-butyl) (*E*)-4-phenylbut-2-enethioate (5q)**

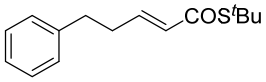
52% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.33– 7.29 (m, 2H), 7.26 – 7.21 (m, 1H), 7.18

– 7.15 (m, 1H), 6.94 (dt, J_1 = 15.4 Hz, J_2 = 6.8 Hz, 1H), 5.99 (dt, J_1 = 15.4 Hz, J_2 = 1.6 Hz, 1H), 3.48 (dd, J_1 = 6.7 Hz, J_2 = 1.7 Hz, 2H), 1.49 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 191.0, 142.4, 138.0, 130.6, 129.2, 129.0, 127.0, 48.3, 38.6, 30.2.

HRMS (ESI, m/z): calcd for $C_{14}H_{19}OS^+$ $[M+H]^+$ 235.1157, found: 235.1153.



5r

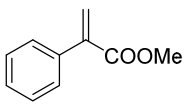
***S*-(*tert*-butyl) (*E*)-5-phenylpent-2-enethioate (5r)**

39% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.31– 7.27 (m, 2H), 7.22 – 7.17 (m, 3H), 6.84 (dt, J_1 = 15.5 Hz, J_2 = 6.9 Hz, 1H), 6.04 (dt, J_1 = 15.5 Hz, J_2 = 1.5 Hz, 1H), 2.76 (t, J = 7.8 Hz, 2H), 2.52 – 2.46 (m, 2H), 1.50 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 191.1, 143.2, 141.1, 130.1, 128.8, 128.7, 126.5, 48.3, 34.7, 34.1, 30.3.

HRMS (ESI, m/z): calcd for $C_{14}H_{19}OS^+$ $[M+H]^+$ 249.1313, found: 249.1321.



5s

Methyl 2-phenylacrylate (5s)

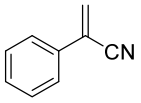
45% yield (at 60 ^{o}C).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.42 – 7.30 (m, 5H), 6.37 (s, 1H), 5.90 (s, 1H), 3.83 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 167.6, 141.7, 137.1, 128.6, 128.5, 128.4, 127.2,

52.5.

HRMS (ESI, m/z): calcd for $C_{10}H_{21}O_2^+$ $[M+H]^+$ 173.1542, found: 173.1550.



5t

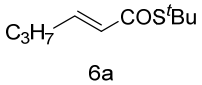
2-Phenylacrylonitrile (5t)

14% yield (at 60 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.62 – 7.59 (m, 2H), 7.43 – 7.41 (m, 3H), 6.34 (s, 1H), 6.11 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 132.7, 130.2, 129.4, 128.3, 126.1, 123.4, 118.0.

HRMS (ESI, m/z): calcd for $C_9H_8N^+$ $[M+H]^+$ 130.0657, found: 130.0658.



6a

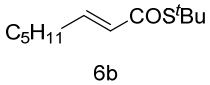
***S*-(*tert*-butyl) (*E*)-hex-2-enethioate (6a)**

57% yield (at 60 °C, 14% yield at 40 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 6.81 (dt, J_1 = 15.5 Hz, J_2 = 7.0 Hz, 1H), 6.04 (dt, J_1 = 15.5 Hz, J_2 = 1.5 Hz, 1H), 2.14 (qd*, J_1 = 7.3 Hz, J_2 = 1.6 Hz, 2H), 1.51 – 1.43 (m, 2H), 1.50 (s, 9H), 0.93 (t, J = 7.4 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 191.3, 144.4, 129.8, 48.2, 34.4, 30.3, 21.7, 14.0.

HRMS (ESI, m/z): calcd for $C_{10}H_{19}OS^+$ $[M+H]^+$ 187.1157, found: 187.1156.



6b

***S*-(*tert*-butyl) (*E*)-oct-2-enethioate (6b)**

35% yield (at 60 °C, 14% yield at 40 °C).

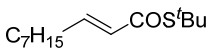
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 6.81 (dt, J_1 = 15.5 Hz, J_2 = 6.9 Hz, 1H), 6.01 (dt, J_1 = 15.5 Hz, J_2 = 1.5 Hz, 1H), 2.14 (qd, J_1 = 7.1 Hz, J_2 = 1.6 Hz, 2H), 1.50 (s, 9H),

* It is likely that the three hydrogen nearby have a similar J value, which gives a q peak rather than dt or td peak. The same is true for other product with similar structure. (**6a** – **6j**)

1.46 – 1.41 (m, 2H), 1.33 – 1.25 (m, 4H), 0.89 (t, J = 7.0 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 191.3, 144.7, 129.6, 48.1, 32.4, 31.7, 30.3, 28.1, 22.8, 14.3.

HRMS (ESI, m/z): calcd for $C_{12}H_{23}OS^+$ $[M+H]^+$ 215.1470, found: 215.1469.



6c

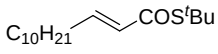
***S*-(*tert*-butyl) (*E*)-dec-2-enethioate (6c)**

60% yield (at 60 ºC).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 6.83 (dt, J_1 = 15.5 Hz, J_2 = 7.0 Hz, 1H), 6.04 (dt, J_1 = 15.4 Hz, J_2 = 1.6 Hz, 1H), 2.14 (qd, J_1 = 7.6 Hz, J_2 = 1.6 Hz, 2H), 1.52 (s, 9H), 1.48 – 1.42 (m, 2H), 1.36 – 1.26 (m, 8H), 0.90 (t, J = 7.4 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 191.3, 144.7, 129.6, 48.1, 32.4, 32.1, 30.3, 29.5, 29.4, 28.4, 23.0, 14.4.

HRMS (ESI, m/z): calcd for $C_{14}H_{27}OS^+$ $[M+H]^+$ 243.1783, found: 243.1778.



6d

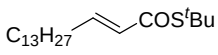
***S*-(*tert*-butyl) (*E*)-tridec-2-enethioate (6d)**

45% yield (at 60 ºC).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 6.81 (dt, J_1 = 15.4 Hz, J_2 = 7.0 Hz, 1H), 6.00 (dt, J_1 = 15.5 Hz, J_2 = 1.6 Hz, 1H), 2.14 (qd, J_1 = 7.6 Hz, J_2 = 1.6 Hz, 2H), 1.49 (s, 9H), 1.45 – 1.37 (m, 2H), 1.33 – 1.24 (m, 14H), 0.90 (t, J = 7.4 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 191.3, 144.7, 129.6, 48.1, 32.4, 32.2, 30.3, 29.9, 29.8, 29.7, 29.6, 29.5, 28.4, 23.0, 14.5.

HRMS (ESI, m/z): calcd for $C_{17}H_{33}OS^+$ $[M+H]^+$ 285.2252, found: 285.2262.



6e

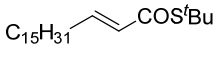
***S*-(*tert*-butyl) (*E*)-hexadec-2-enethioate (6e)**

68% yield (at 80 ºC, 28% yield at 60 ºC).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 6.81 (dt, J_1 = 15.4 Hz, J_2 = 7.0 Hz, 1H), 6.00 (dt, J_1 = 15.5 Hz, J_2 = 1.5 Hz, 1H), 2.15 (qd, J_1 = 7.5 Hz, J_2 = 1.6 Hz, 2H), 1.49 (s, 9H), 1.47 – 1.40 (m, 2H), 1.33 – 1.21 (m, 20H), 0.88 (t, J = 6.7 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 191.3, 144.7, 129.6, 48.2, 32.4, 42.3, 30.3, 30.0, 30.0, 30.0, 29.9, 29.7, 29.7, 29.5, 28.4, 23.0, 14.5.

HRMS (ESI, m/z): calcd for $C_{20}H_{39}OS^+$ $[M+H]^+$ 327.2722, found: 327.2737.



6f

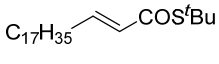
***S*-(*tert*-butyl) (*E*)-octadec-2-enethioate (6e)**

63% yield (at 80 °C, 15% yield at 60 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 6.81 (dt, J_1 = 15.5 Hz, J_2 = 7.0 Hz, 1H), 6.00 (dt, J_1 = 15.5 Hz, J_2 = 1.5 Hz, 1H), 2.15 (qd, J_1 = 7.5 Hz, J_2 = 1.6 Hz, 2H), 1.49 (s, 9H), 1.47 – 1.40 (m, 2H), 1.33 – 1.23 (m, 24H), 0.88 (t, J = 6.8 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 191.3, 144.7, 129.6, 48.1, 32.4, 32.3, 30.3, 30.1, 30.0, 30.0, 30.0, 30.0, 29.9, 29.7, 29.5, 28.4, 23.0, 14.5.

HRMS (ESI, m/z): calcd for $C_{22}H_{43}OS^+$ $[M+H]^+$ 355.3035, found: 355.3045.



6g

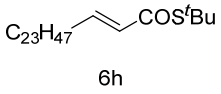
***S*-(*tert*-butyl) (*E*)-icos-2-enethioate (6g)**

56% yield (at 100 °C, 13% yield at 80 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 6.81 (dt, J_1 = 15.4 Hz, J_2 = 7.0 Hz, 1H), 6.00 (dt, J_1 = 15.5 Hz, J_2 = 1.5 Hz, 1H), 2.15 (qd, J_1 = 7.5 Hz, J_2 = 1.6 Hz, 2H), 1.49 (s, 9H), 1.47 – 1.40 (m, 2H), 1.33 – 1.19 (m, 28H), 0.88 (t, J = 6.7 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 191.3, 144.7, 129.6, 48.1, 32.4, 32.3, 30.3, 30.1, 30.0, 30.0, 30.0, 29.9, 29.7, 29.7, 29.5, 28.4, 23.0, 14.5.

HRMS (ESI, m/z): calcd for $C_{24}H_{47}OS^+$ $[M+H]^+$ 383.3348, found: 383.3352.



6h

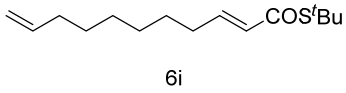
***S*-(*tert*-butyl) (*E*)-hexacos-2-enethioate (6h)**

27% yield (at 100 °C, 3 d).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 6.81 (dt, J_1 = 15.5 Hz, J_2 = 7.0 Hz, 1H), 6.00 (dt, J_1 = 15.4 Hz, J_2 = 1.5 Hz, 1H), 2.15 (qd, J_1 = 7.1 Hz, J_2 = 1.6 Hz, 2H), 1.50 (s, 9H), 1.47 – 1.40 (m, 2H), 1.33 – 1.20 (m, 40H), 0.88 (t, J = 6.8 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 191.3, 144.7, 129.6, 48.1, 32.4, 32.3, 30.3, 30.1, 30.0, 30.0, 29.9, 29.7, 29.7, 29.5, 28.4, 23.1, 14.5.

HRMS (ESI, m/z): calcd for $C_{30}H_{59}OS^+$ $[M+H]^+$ 467.4287, found: 467.4288.



6i

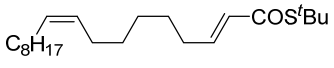
***S*-(*tert*-butyl) (*E*)-undeca-2,10-dienethioate (6i)**

45% yield (at 60 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 6.81 (dt, J_1 = 15.5, J_2 = 7.0 Hz, 1H), 6.00 (dt, J_1 = 15.5, J_2 = 1.5 Hz, 1H), 5.80 (ddt, J_1 = 17.0, J_2 = 10.2, J_3 = 6.7 Hz, 1H), 4.99 (dq, J_1 = 17.2, J_2 = 1.8 Hz, 1H), 4.93 (ddt, J_1 = 10.2, J_2 = 2.2, J_3 = 1.2 Hz, 1H), 2.15 (qd, J_1 = 7.1, J_2 = 1.6 Hz, 2H), 2.04 (qt, J_1 = 6.7, J_2 = 1.5 Hz, 2H), 1.50 (s, 9H), 1.45 – 1.25 (m, 8H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 191.3, 144.6, 139.4, 129.7, 114.6, 48.2, 34.1, 32.4, 30.3, 29.3, 29.2, 29.1, 28.3.

HRMS (ESI, m/z): calcd for $C_{15}H_{27}OS^+$ $[M+H]^+$ 255.1783, found: 255.1793.



6j

***S*-(*tert*-butyl) (2*E*,9*Z*)-octadeca-2,9-dienethioate (6j)**

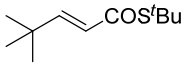
42% yield (at 60 °C).

^{1}H NMR (400 MHz, $CDCl_3$): 6.81 (dt, J_1 = 15.4 Hz, J_2 = 7.0 Hz, 1H), 6.00 (dt, J_1 = 15.6 Hz, J_2 = 1.5 Hz, 1H), 5.40 – 5.30 (m, 2H), 2.15 (qd, J_1 = 7.1 Hz, J_2 = 1.5 Hz, 2H),

2.04 – 1.98 (m, 4H), 1.50 (s, 9H), 1.47 – 1.41 (m, 2H), 1.35 – 1.26 (m, 16H), 0.88 (t, *J* = 6.6 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 191.3, 144.6, 130.6, 129.8, 129.7, 48.2, 32.4, 32.3, 30.3, 30.2, 29.9, 29.8, 29.7, 29.7, 29.2, 28.3, 27.6, 27.4, 23.0, 14.5.

HRMS (ESI, m/z): calcd for $C_{22}H_{41}OS^+$ $[M+H]^+$ 353.2878, found: 353.2881.



6k

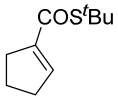
***S*-(*tert*-butyl) (*E*)-4,4-dimethylpent-2-enethioate (6k)**

59% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 6.81 (d, *J* = 15.7 Hz, 1H), 5.92 (d, *J* = 15.7 Hz, 1H), 1.50 (s, 9H), 1.07 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 191.8, 154.1, 125.1, 48.2, 34.0, 30.3, 29.0.

HRMS (ESI, m/z): calcd for $C_{11}H_{21}OS^+$ $[M+H]^+$ 201.1313, found: 201.1306.



6l

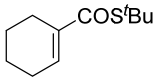
***S*-(*tert*-butyl) cyclopent-1-ene-1-carbothioate (6l)**

61% yield (at 60 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 6.74 – 6.72 (m, 1H), 2.61 – 2.55 (m, 2H), 2.51 – 2.46 (m, 2H), 1.97 – 1.90 (m, 2H), 1.50 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 190.6, 145.3, 141.2, 48.0, 33.7, 31.5, 30.4, 23.3.

HRMS (ESI, m/z): calcd for $C_{10}H_{17}OS^+$ $[M+H]^+$ 185.1000, found: 185.0991.



6m

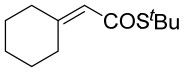
***S*-(*tert*-butyl) cyclohex-1-ene-1-carbothioate (6m)**

54% yield (at 60 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 6.93 – 6.90 (m, 1H), 1.90 – 1.86 (m, 2H), 2.28 – 2.24 (m, 2H), 2.21 – 2.16 (m, 1H), 1.67 – 1.57 (m, 4H), 1.49 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 194.5, 139.7, 137.6, 47.5, 30.4, 26.1, 24.3, 22.4, 21.9.

HRMS (ESI, m/z): calcd for $C_{11}H_{19}OS^+$ $[M+H]^+$ 199.1157, found: 199.1156.



6n

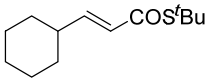
***S*-(*tert*-butyl) 2-cyclohexylideneethanethioate (6n)**

31% yield (at 60 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 5.81 (s, 1H), 2.77 (t, J = 5.6 Hz, 2H), 2.12 (t, J = 5.9 Hz, 2H), 1.70 – 1.58 (m, 6H), 1.49 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 191.5, 180.1, 121.1, 48.0, 38.0, 30.8, 30.3, 30.2, 28.2, 26.5.

HRMS (ESI, m/z): calcd for $C_{12}H_{21}OS^+$ $[M+H]^+$ 213.1313, found: 213.1306.



6o

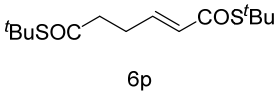
***S*-(*tert*-butyl) (*E*)-3-cyclohexylprop-2-enethioate (6o)**

33% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 6.76 (dd, J_1 = 15.6 Hz, J_2 = 6.8 Hz, 1H), 5.96 (dd, J_1 = 15.6 Hz, J_2 = 1.4 Hz, 1H), 2.14 – 2.04 (m, 1H), 1.77 – 1.72 (m, 4H), 1.50 (s, 9H), 1.33 – 1.08 (m, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 191.6, 149.4, 127.3, 48.2, 40.6, 32.1, 30.3, 26.3, 26.1.

HRMS (ESI, m/z): calcd for $C_{13}H_{23}OS^+$ $[M+H]^+$ 227.1470, found: 227.1466.



6p

***S*,*S*-di-*tert*-butyl (*E*)-hex-2-enebis(thioate) (6p)**

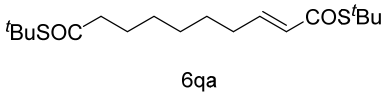
40% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 6.75 (dt, J_1 = 15.5 Hz, J_2 = 6.7 Hz, 1H), 6.75 (dq, J_1 = 15.4 Hz, J_2 = 1.4 Hz, 1H), 2.59 (t, J_1 = 7.4 Hz, 2H), 2.52 – 2.44 (m, 2H), 1.49

(s, 9H), 1.46 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 199.0, 190.9, 141.4, 130.5, 48.6, 48.4, 42.7, 30.2, 30.1, 27.9.

HRMS (ESI, m/z): calcd for $C_{14}H_{25}O_2S_2^+$ $[M+H]^+$ 289.1296, found: 289.1297.



6qa

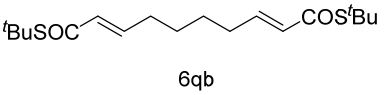
S,S-di-*tert*-butyl (*E*)-dec-2-enebis(thioate) (6qa)

28% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 6.79 (dt, J_1 = 15.4 Hz, J_2 = 8.4 Hz, 1H), 6.00 (dt, J_1 = 15.5 Hz, J_2 = 1.5 Hz, 1H), 2.43 (t, J_1 = 7.5 Hz, 2H), 2.18 – 2.12 (m, 2H), 1.66 – 1.58 (m, 2H), 1.49 (s, 9H), 1.45 (s, 9H), 1.35 – 1.28 (m, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 200.8, 191.2, 144.4, 129.8, 48.2, 48.1, 32.3, 30.3, 30.2, 29.1, 29.0, 25.8.

HRMS (ESI, m/z): calcd for $C_{18}H_{33}O_2S_2^+$ $[M+H]^+$ 345.1922, found: 345.1929.



6qb

S,S-di-*tert*-butyl (2*E*,8*E*)-deca-2,8-dienebis(thioate) (6qb)

14% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 6.78 (dt, J_1 = 15.4 Hz, J_2 = 7.0 Hz, 2H), 6.01 (dt, J_1 = 15.6 Hz, J_2 = 1.6 Hz, 2H), 2.20 – 2.15 (m, 4H), 1.68 – 1.60 (m, 4H), 1.50 (s, 18H).

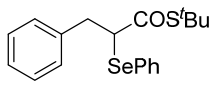
^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 191.2, 143.8, 130.0, 48.3, 32.1, 30.3, 27.9.

HRMS (ESI, m/z): calcd for $C_{18}H_{31}O_2S_2^+$ $[M+H]^+$ 343.1765, found: 343.1780.

2.4 Spectral data of the intermediate

It is also possible to separate the selenium substituted intermediate by directly purify the resulting mixture of the first step by flash column chromatography on silica gel. The crude intermediate obtained normally contains a small amount of the final product as well as a trace amount of staring material. It could be further purified by productive TLC plate for analysis.

One intermediate (**1a-1**) was isolated for characterize.



1a-i

S-(*tert*-butyl) 3-phenyl-2-(phenylselanyl)propanethioate (1a-i)

Light yellow oil.

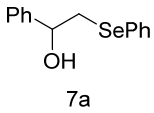
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.58 – 7.55 (m, 2H), 7.35 – 7.19 (m, 6H), 7.18 – 7.13 (m, 2H), 3.88 (dd, J_1 = 9.1 Hz, J_2 = 6.4 Hz, 1H), 3.29 (dd, J_1 = 14.0 Hz, J_2 = 9.1 Hz, 1H), 3.02 (dd, J_1 = 14.0 Hz, J_2 = 6.4 Hz, 1H), 1.37 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 198.4, 138.7, 136.4, 129.5, 129.4, 129.0, 128.7, 128.2, 127.0, 54.0, 38.8, 38.7, 30.0.

HRMS (ESI, m/z): calcd for $C_{19}H_{23}O_2SSe^+$ $[M+H]^+$ 379.0635, found: 379.0653.

3. Mechanistic study reactions and relative spectral data

A reaction tube with a stir bar under N_2 was charged with potassium phthalimide (1 equiv., 0.2 mmol, 38.0 mg), benzeneselenol (1 equiv., 0.2 mmol, 21.2 μL) or diphenyl diselenide (0.5 equiv., 0.1 mmol, 31.2 mg) and 1 mL of degassed DMSO. The mixture was stirred at 40 °C for 24 h and purified by flash column chromatography on silica gel.



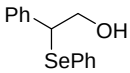
7a

1-phenyl-2-(phenylselanyl)ethan-1-ol (7a)

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.57 – 7.52 (m, 2H), 7.35 – 7.25 (m, 8H), 4.75 (ddd, J_1 = 9.3 Hz, J_2 = 3.1 Hz, J_3 = 2.7 Hz, 1H), 3.31 (dd, J_1 = 12.8 Hz, J_2 = 3.7 Hz, 1H), 3.13 (dd, J_1 = 12.8 Hz, J_2 = 9.4 Hz, 1H), 2.78 (d, J = 2.7 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 142.8, 133.5, 129.6, 129.5, 128.9, 128.3, 127.8, 126.1, 75.6, 38.8.

HRMS (ESI, m/z): calcd for $C_{14}H_{15}OSe^+$ $[M+H]^+$ 279.0288, found: 279.0276.



7b

2-phenyl-2-(phenylselanyl)ethan-1-ol (7b)

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.48 – 7.46 (m, 2H), 7.32 – 7.22 (m, 8H), 4.40 (t, J = 7.1 Hz, 1H), 4.05 – 4.00 (m, 1H), 3.97 – 3.91 (m, 1H), 1.96 (t, J = 6.1 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 135.8, 131.9, 129.5, 129.4, 129.1, 128.6, 128.4, 128.0, 65.4, 51.4.

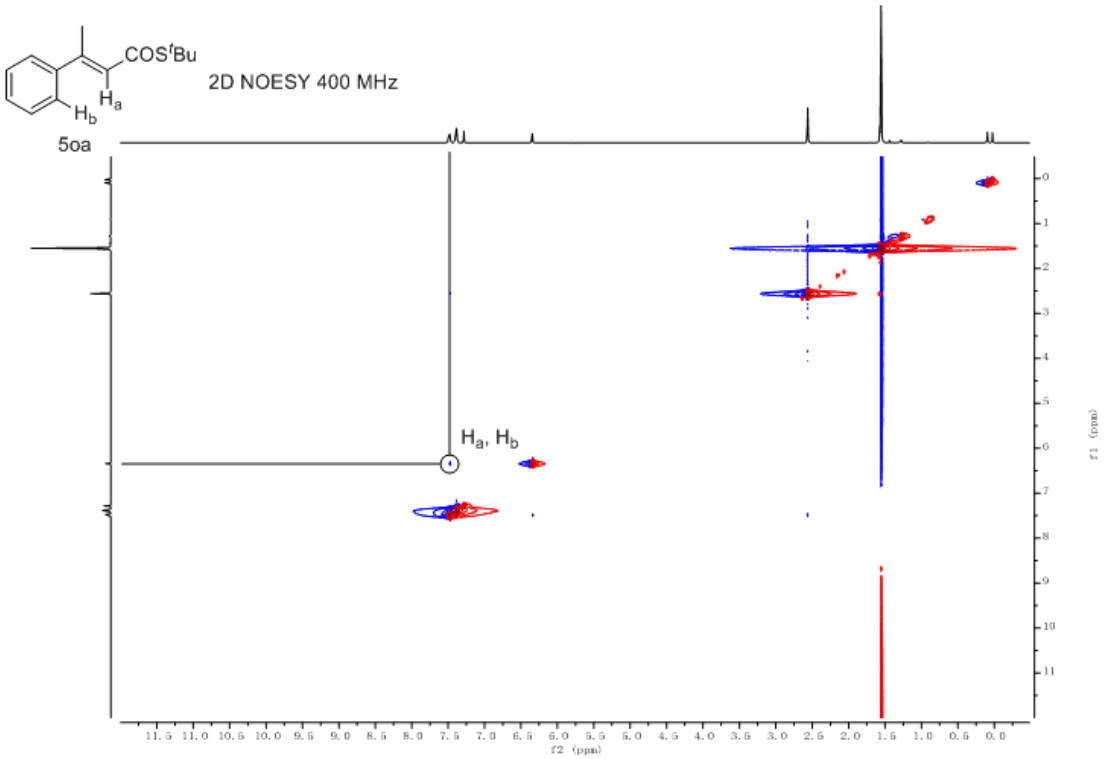
HRMS (ESI, m/z): calcd for $C_{14}H_{15}OSe^+$ $[M+H]^+$ 279.0288, found: 279.0296.

4. (*E*)/(*Z*) isomer structure determination

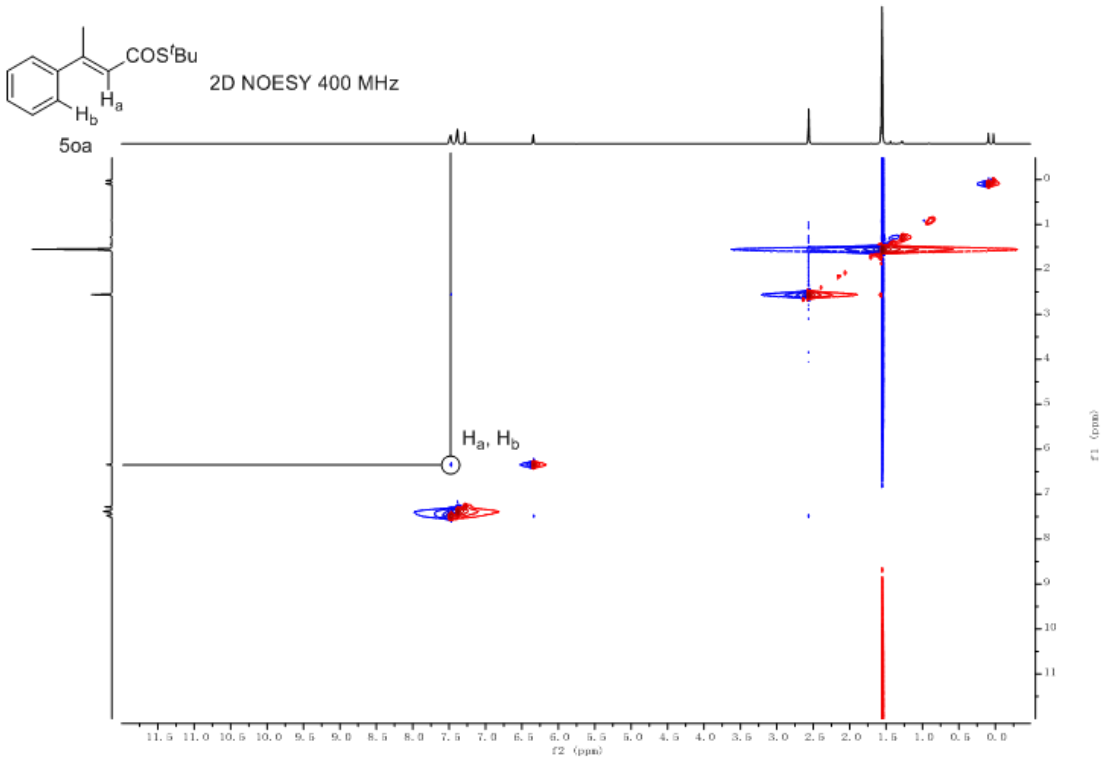
For substrate with (*E*)/(*Z*) isomers (**5ma**, **5mb**, **5na**, **5oa**, **5ob**, **5pa** and **5pb**), the (*E*)/(*Z*) configuration of the double bond was determined by the following method:

The acid part of **5ma**, **5mb** and **5na** have been obtained, and their configurations are known, and another sample of them were synthesized from the acid part, thus their configurations can be determined.

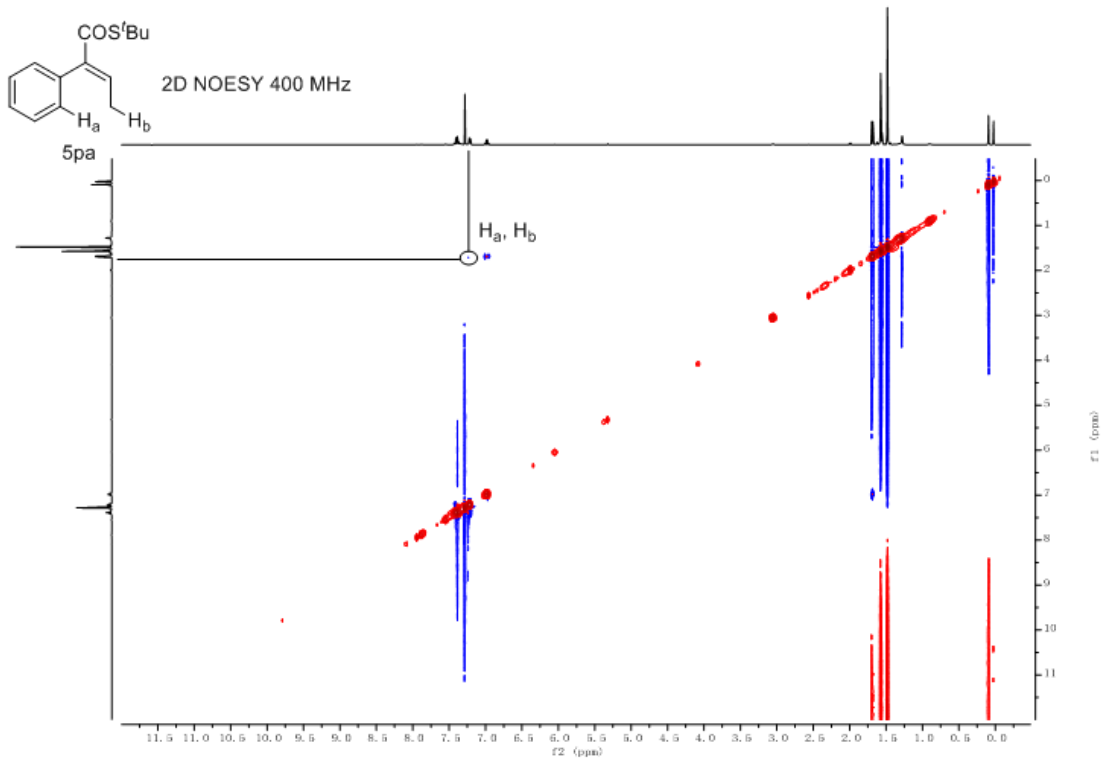
For **5oa**, **5ob**, **5pa** and **5pb**, a 2D NOESY for each of them was performed to determine their configurations:



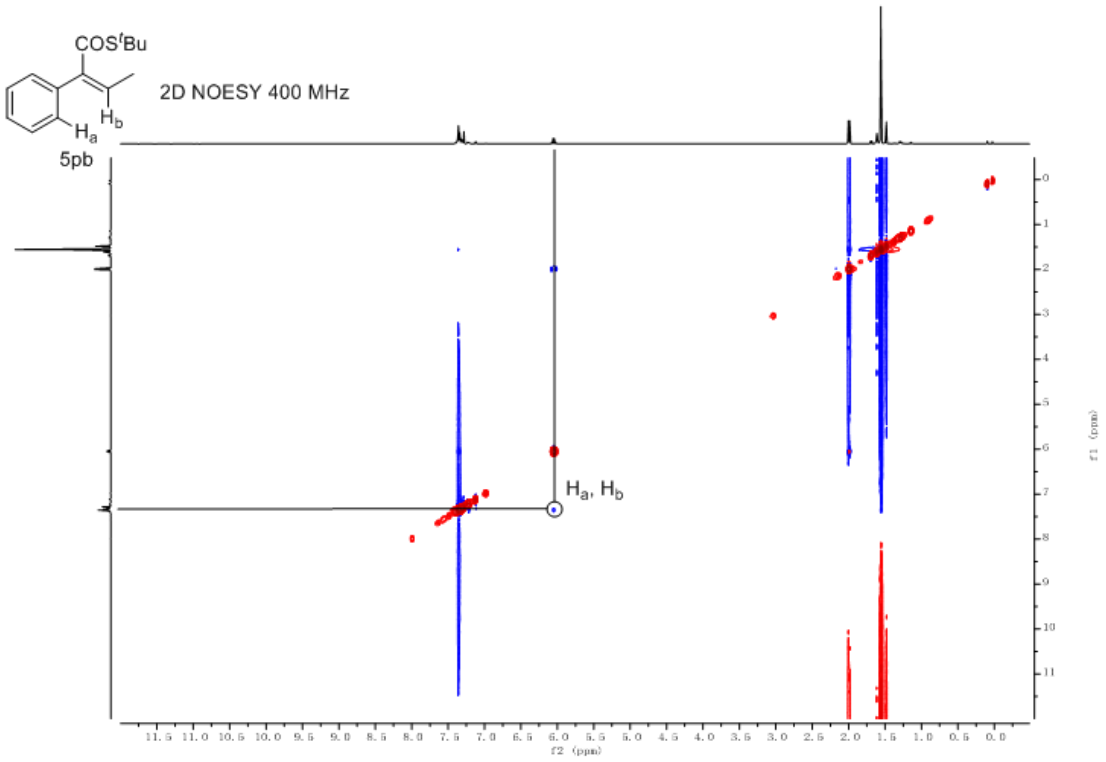
Scheme 45: 2D NOESY of **5oa**.



Scheme 46: 2D NOESY of **5ob**.



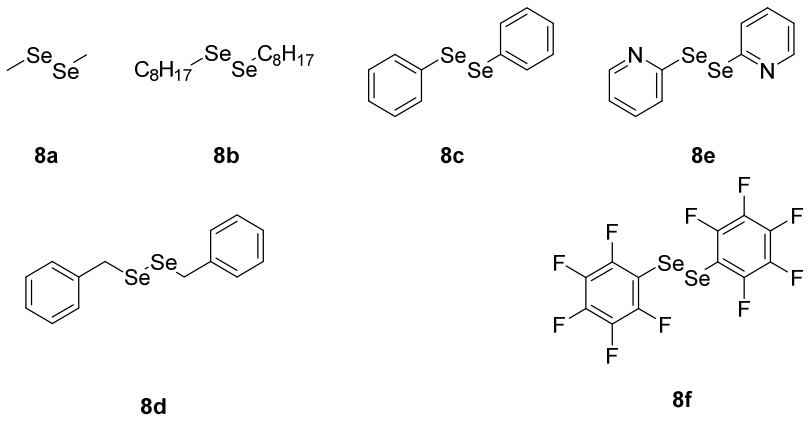
Scheme 47: 2D NOESY of **5pa**.



Scheme 48: 2D NOESY of **5pb**.

Chapter IV: Appendix

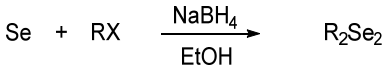
1. Study on other selenium reagent



Scheme 49: Different diselenides.

Diphenyl diselenide (**8c**) and dibenzyl diselenide (**8d**) are commercially available and used as received.

8a and **8b** were synthesized by the following method[92]:



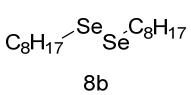
Scheme 50: Synthesis of **8a** and **8b**.

A round bottom flask with a stir bar was charged selenium powder (0.5 equiv., 5 mmol, 0.4 g) and 15 mL of ethanol was added sodium borohydride (1.5 equiv., 15 mmol, 0.567 g) in portions under N_2, after no bubble initiated, another portion of selenium (0.5 equiv., 5 mmol, 0.4 g) was added. The mixture was heated under reflux for 30 min, after cooling to room temperature, iodomethane (1.1 equiv., 11 mmol, 0.69 mL) or 1-bromooctane (1.0 equiv., 10 mmol, 1.74 mL) was added. The mixture was stirred overnight, it was then filtered, after the solvent of the filtrate removed under vacuum, the residue was purified by flash column chromatography on silica gel.


8a

Yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.57 (s, 6H).

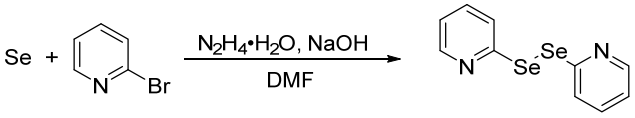


8b

Orange Oil.

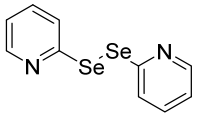
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.91 (t, *J* = 7.4 Hz, 4H), 1.76 – 1.69 (m, 4H), 1.42 – 1.35 (m, 4H), 1.34 – 1.26 (m, 16H), 0.88 (t, *J* = 6.8 Hz, 6H).

8e was synthesized by the following method[93]:



Scheme 51: Synthesis of **8e**.

To a mixture of selenium powder (1 equiv., 12.5 mmol, 1.0 g) and sodium hydroxide (1.5 equiv., 19 mmol, 0.75 g) in 50 mL of DMF under N_2 was added hydrazine hydrate (1 equiv., 12.5 mmol, 0.5 mL). It was stirred at room temperature for 2 h, then heated under reflux for 4 h. After cooling to room temperature, it was dilute with water, extract with ether (3 x 30 mL). The combined organic layer was washed with brine, dried over Na_2SO_4 and after the solvent removed under vacuum, it was purified by flash column chromatography on silica gel.

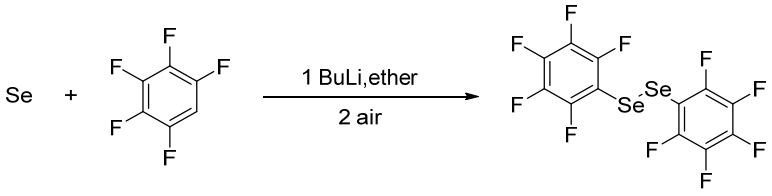


8e

Brown oil.

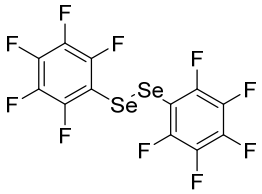
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.50 – 8.42 (m, 2H), 7.80 (dt, J_1 = 8.1 Hz, J_2 = 0.9 Hz, 2H), 7.54 (td, J_1 = 7.7 Hz, J_2 = 1.9 Hz, 2H), 7.08 (ddd, J_1 = 7.4 Hz, J_2 = 4.8 Hz, J_3 = 1.1 Hz, 2H).

8f was synthesized by the following method[94]:



Scheme 52: Synthesis of **8f**.

A solution of pentafluorobenzene (1 equiv., 10 mmol, 1.11 mL) in 40 mL of dry ether was added butyl lithium (1 equiv., 10 mmol, 1.6 M in hexane, 6.25 mL) *via* syringe pump in 1 h at -78 ^{o}C under N_2, it was then stirred at this temperature for an addition hour and selenium powder (1 equiv., 10 mmol, 0.8 g) was added in one portion. It was then slowly warmed to room temperature and stirred at this temperature for 4 h. The reaction was then quenched with NH_4Cl and extracted with ether (3 x 20 mL), the combined organic layer was dried over Na_2SO_4 and then stirred under air for 24 h. After the solvent removed under vacuum, it was purified by flash column chromatography on silica gel.



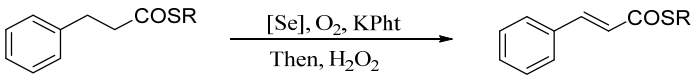
8f

Brown oil.

^{19}F NMR (375 MHz, $CDCl_3$): δ (ppm) -125.0 (m), -148.6 (m), -159.2 (m).

The diselenides mentioned above as well as a few other selenium reagent were screened for the reaction. All diselenides are added in 0.5 equiv., and other reagents are added in 1 equiv..

Table 12: results of using different selenium reagents.[a]



entry	R	[Se]	Yield%[b]
1	Et	8a	47
2	Et	8b	24
3	Et	8c	43
4	Et	8d	34
5	Et	8e	23
6	^{t}Bu	8f	-
7	^{t}Bu	PhSeH	76
8	^{t}Bu	PhSeCl	-

9	^{t}Bu	PhSeBr	-
10[c]	^{t}Bu	Ph_2S_2[d]	trace
11[c]	^{t}Bu	PhSH	trace

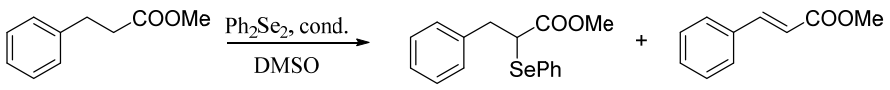
[a] unless otherwise stated, all reactions were performed with the thioester (0.2 mmol), diselenide (0.1 mmol) and potassium phthalimide (0.2 mmol) with 1 mL of DMSO at the indicated temperature under a balloon of O_2 for 24 h, then the second step is 0.3 mL of 30% H_2O_2 for 1h for *tert*-butyl thioester or *m*CPBA at -40 ^{o}C for 3 h for ethyl thioester. [b] NMR yields. [c] no oxidising step. [d] 0.5 equiv.

Other diselenide reagents, except for **8f**, afforded a variety of yields, and **8a** even afforded a slightly higher yield for the ethyl thioester compared to diphenyl diselenide. However, as they are not readily available as diphenyl diselenide, some of them are difficult to purify (**8b** and **8f**) or unstable on storage (**8e**) and they did not show overwhelming advantage over diphenyl diselenide, diphenyl diselenide was still chosen as the selenium reagent for this reaction. For other selenium reagents, benzeneselenol gives a similar yield, very likely because it can be easily oxidized to diphenyl diselenide; benzeneselenenyl chloride and bromide (**entry 8**, **9**) failed to afford any yield, likely because they react with the base instead of the thioester. The sulfur analogue (**entry 10**, **11**) of the selenium reagents also failed to give the sulfide product, likely because it is less reactive.

2. Modification towards dehydrogenation reactions of esters

As esters have less acidic α hydrogen, simple esters does not react in these conditions. However, with a stronger base, it seems possible to have some esters react. Methyl hydrocinnamate (**10a**) were used as the model substrate for the reactions.

Table 13: results of using different conditions of dehydrogenation of methyl hydrocinnamate.[a]



a b c

entry	base	temperature	oxidant	a%	b%	c%
1	KO^{t}Bu	60 °C	KIO_4	43	43	14
2	KO^{t}Bu	60 °C	$PhIO_2$	81	17	2
3	KO^{t}Bu	60 °C	$NaBO_3{\cdot}4H_2O$	76	22	2
4	NaO^{t}Bu	60 °C	$NaIO_4$	27	70	3
5	KO^{t}Bu	40 °C	KIO_4	32	39	29
6	KO^{t}Bu	80 °C	KIO_4	44	28	28
7	KO^{t}Bu	r.t.	KIO_4	25	75	trace
8	KO^{t}Bu	100 °C	KIO_4	49	15	36
9	KOH	60 °C	KIO_4	100	trace	-
10	LiO^{t}Bu	60 °C	Li_5IO_6	100	trace	-
11	NaOMe	r.t.	$NaIO_4$	100	-	-
12	NaOMe	60 °C	$NaIO_4$	100	-	-
13[b]	KO^{t}Bu	60 °C	KIO_4	75	25	-
14	NaOEt	r.t.	$NaIO_4$	100	-	-
15	NaO^{t}Bu	r.t.	$NaIO_4$	100	-	-
16	NaO^{t}Bu	40 °C	$NaIO_4$	25	75	-
17[c]	KO^{t}Bu	r.t.	KIO_4	13	87	-
18[d]	KO^{t}Bu	r.t.	KIO_4	20	80	trace
19[e]	KO^{t}Bu	r.t.	KIO_4		decomposed	
20	DBU	r.t.	KIO_4		decomposed	

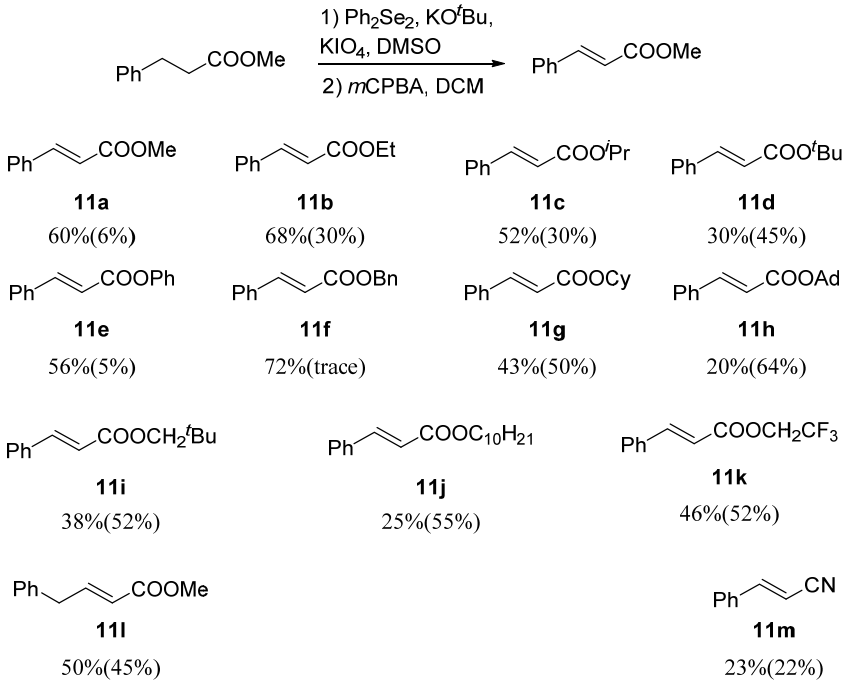
[a] unless otherwise stated, all reactions were performed with the 9s (0.2 mmol), diphenyl diselenide (0.1 mmol) and base (0.2 mmol) with 1 mL of extra dry DMSO at the indicated temperature under N_2 for 24 h, then after DMSO removed, the crude product was examined by ^{1}H NMR to get the ratio of the three substance. [b] under O_2 [c] 0.6 equiv. of diphenyl diselenide [d] 1.2 equiv. of KO^{t}Bu [e] 2 equiv. of KO^{t}Bu

Potassium *tert*-butoxide with potassium periodate gave a good yield even at room

temperature (**entry 8**), slightly increase the amount of base or diselenide (**entry 17**, **18**) also slightly increased the yield. But too much base (**entry 19**) decomposed the starting material. Sodium *tert*-butoxide with sodium periodate also gave a good yield at higher temperature, but afforded no result at room temperature. Other strong bases did not give any yield and organic strong base DBU (**entry 20**) decomposed it.

For the second step, directly adding H_2O_2 does not result any product, probably the product is not stable with H_2O_2 in the presence of KO^{t}Bu. However using **procedure B** described in **Chapter III** above (dilute with DCM at – 40 ^{o}C, then add *m*CPBA) could give the desired product without much decomposing. Alternatively, using a standard aqueous workup for the mixture, dissolve the crude intermediate in THF and react it with H_2O_2 at 0 ^{o}C can also give the desired product in a similar yield. Considering using *m*CPBA can reduce the work-up procedure and both procedure give a similar yield, other substrate was all using *m*CPBA for the second step.

Table 14. Substrate scope of dehydrogenation of esters[a,b]



[a] Unless otherwise stated, all reactions were performed with the thioester (0.2 mmol), diphenyl diselenide (0.1 mmol), potassium *tert*-butoxide (0.2 mmol) and potassium periodate (0.2 mmol) with 1 mL of DMSO at r.t. under N_2 for 72 h, the second step is dilute with 2 mL of DCM and react with *m*CPBA at -40 ^oC for 3 h. [b] isolated yield, the number in parentheses is the amount of unreacted stating material.

As summarized in **Table 14**, in general, esters afforded the product in low to moderate yields. In contrast to their thioester analogues, more hindered esters (**11d**, **11h** and **11i**) gave a lower yield, presumably, hindered esters are less likely to be attacked by the base or selenium reagent. Finally, as the acidity of the α hydrogen of nitriles is similar to that of esters, they could also undergo this reaction under the same conditions (**11m**), albeit in lower yields.

It is also noteworthy to highlight that aliphatic esters react rather sluggishly under this conditions. Less reactive amides such as **9u** still appear unreactive using this condition while thioesters such as **9o** decomposed under the similar conditions.

2.1 Experimental sections

2.1.1 Synthesis of starting material

10h was synthesized using the generally method for thioesters. (cinnamic acid and 1-adamantanol)

10a, **10b**, **10c** and **10l** was synthesized using similar method as **2s**.

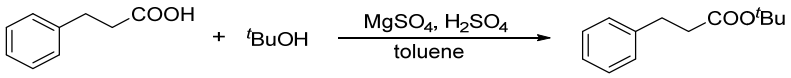
10f and **10g** was also synthesized using similar method as **2s** except 5 mL of alcohol was used as solvent, the mixture was heated to 100 ^{o}C and the mixture was directly purified by flash column chromatography on silica gel.

For **10e**, **10i**, **10j**, and **10k**, they were synthesized using the method below:

Scheme 57: Synthesis of **10e**.

A dry round bottom flask with a magnetic stir bar was charged with phenol (1 equiv., 10 mmol, 0.94 g), triethylamine (1 equiv., 10 mmol, 1.4 mL) and 30 mL of DCM. The mixture was cooled to 0 ^{o}C on an ice bath and a solution of hydrocinnamoyl chloride (1 equiv., 10 mmol, 1.5 mL) in 10 mL of DCM was added dropwise through an addition funnel. The mixture was then stirred at room temperature overnight, quenched with saturated NH_4Cl solution. The mixture was then extracted with ether (3 x 30 mL), the organic layer was dried over sodium sulfate, the ether was then removed under vacuum and the residue was purified by flash column chromatography on silica gel (eluent: hexane/ethyl acetate 98:2) to afford the desired product.

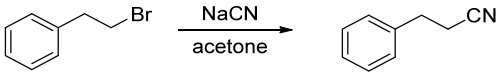
10d was synthesized using the following method[98]:



Scheme 58: Synthesis of **10d**.

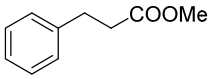
To a dry round button flask with a stir bar under nitrogen was added 40 mL of dry toluene. Anhydrous magnesium sulfate (4 equiv., 40 mmol, 4.8 g) was then added, followed by concentrated sulfuric acid (1 equiv., 10 mmol, 0.55 mL). The mixture was stirred at room temperature for 15 min, and then 3-phenylpropionic acid (1 equiv., 10 mmol, 1.5 g) and *tert*-butyl alcohol (5 equiv., 50 mmol, 4.8 mL.) were added. It was then stirred for 24 h at room temperature, then 50 mL of water and 50 mL ethyl acetate were added, the organic layer was then washed by 50 mL of brine, dried over sodium sulfate, concentrated and purified by flash column chromatography using hexane/ethyl acetate (20/1).

10m was synthesized by the following method:



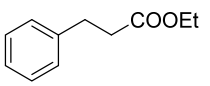
Scheme 59: Synthesis of **10m**.

To a solution of 2-bromo-1-phenylethane (1 equiv., 10 mmol, 1.37 mL) in 30 mL acetone was added sodium cyanide (1.2 equiv., 12 mmol, 0.59 g), the mixture was heated under reflux for 24 h. After completion, it was filtered, dried under vacuum and purified by flash column chromatography on silica gel (eluent: hexane/ethyl acetate 98:2).



10a Colorless Oil.

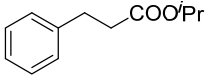
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.31 – 7.26 (m, 2H), 7.22 – 7.18 (m, 3H), 3.67 (s, 3H), 2.95 (t, *J* = 7.9 Hz, 2H), 2.63 (t, *J* = 7.8 Hz, 2H).



10b Colorless Oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.31 – 7.26 (m, 2H), 7.22 –

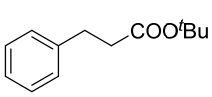
7.18 (m, 3H), 4.13 (q, *J* = 7.2 Hz, 2H), 2.95 (t, *J* = 7.9 Hz, 2H), 2.62 (t, *J* = 7.8 Hz, 2H), 1.23 (t, *J* = 7.2 Hz, 3H).



10c

Colorless Oil.

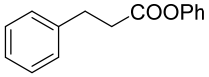
^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) 7.30 – 7.25 (m, 2H), 7.21 – 7.18 (m, 3H), 5.00 (m, 1H), 2.94 (t, *J* = 7.8 Hz, 2H), 2.59 (t, *J* = 7.8 Hz, 2H), 1.20 (d, *J* = 6.3 Hz, 6H).



10d

Colorless Oil.

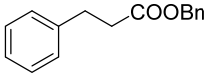
^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) 7.29 – 7.25 (m, 2H), 7.22 – 7.17 (m, 3H), 2.91 (t, *J* = 7.8 Hz, 2H), 2.54 (t, *J* = 7.8 Hz, 2H), 1.42 (s, 9H).



10e

Colorless Oil.

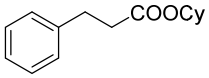
^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) 7.38 – 7.19 (m, 8H), 7.02 – 7.00 (m, 2H), 3.08 (t, *J* = 7.7 Hz, 2H), 2.89 (t, *J* = 7.7 Hz, 2H).



10f

Colorless Oil.

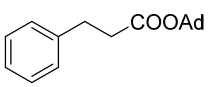
^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) 7.37 – 7.26 (m, 8H), 7.22 – 7.18 (m, 2H), 5.11 (s, 2H), 2.97 (t, *J* = 7.6 Hz, 2H), 2.69 (t, *J* = 7.6 Hz, 2H).



10g

Colorless Oil.

^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) 7.29 – 7.24 (m, 2H), 7.21 – 7.16 (m, 3H), 4.79 – 4.72 (m, 1H), 2.94 (t, *J* = 7.9 Hz, 2H), 2.60 (t, *J* = 7.8 Hz, 2H), 1.83 – 1.75 (m, 2H), 1.72 – 1.65 (m, 2H), 1.55 – 1.49 (m, 1H), 1.42 – 1.20 (m, 5H).

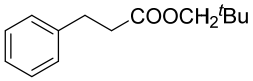


10h

Colorless Oil.

^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) 7.29 – 7.24 (m, 2H), 7.20 –

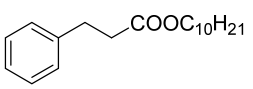
7.16 (m, 3H), 2.90 (t, *J* = 7.8 Hz, 2H), 2.53 (t, *J* = 7.8 Hz, 2H), 2.14 (t, *J* = 3.1 Hz, 3H), 2.07 (d, *J* = 3.1 Hz, 6H), 1.65 – 1.64 (m, 6H).



10i

Colorless Oil.

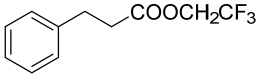
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.29 – 7.24 (m, 2H), 7.21 – 7.16 (m, 3H), 3.76 (s, 2H), 2.96 (t, *J* = 7.8 Hz, 2H), 2.65 (t, *J* = 7.8 Hz, 2H), 0.90 (s, 9H).



10j

Colorless Oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.30 – 7.24 (m, 2H), 7.21 – 7.18 (m, 3H), 4.06 (t, *J* = 6.7 Hz, 2H), 2.95 (t, *J* = 7.8 Hz, 2H), 2.62 (t, *J* = 7.8 Hz, 2H), 1.62 – 1.57 (m, 2H), 1.32 – 1.26 (m, 14H), 0.88 (t, *J* = 6.7 Hz, 3H).

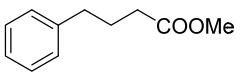


10k

Colorless Oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.32 – 7.28 (m, 2H), 7.24 – 7.19 (m, 3H), 4.45 (t, *J* = 8.5 Hz, 2H), 2.99 (t, *J* = 7.8 Hz, 2H), 2.75 (t, *J* = 7.8 Hz, 2H).

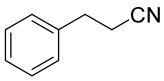
^{19}F NMR (375 MHz, $CDCl_3$): δ (ppm) -77.80 (t, *J* = 8.4 Hz)



10l

Colorless Oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.30 – 7.26 (m, 2H), 7.21 – 7.17 (m, 3H), 3.66 (s, 3H), 2.65 (t, *J* = 7.6 Hz, 2H), 2.33 (t, *J* = 7.5 Hz, 2H), 2.00 – 1.92 (m, 2H).

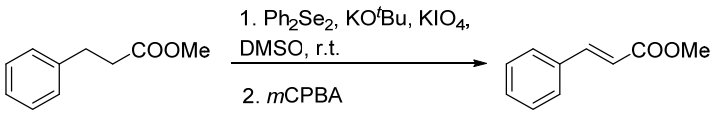


10m

Colorless Oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.34 – 7.29 (m, 2H), 7.27 – 7.19 (m, 3H), 2.90 (t, *J* = 7.4 Hz, 2H), 2.56 (t, *J* = 7.4 Hz, 2H).

2.1.2 General procedure for dehydrogenation of esters



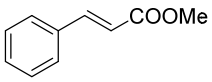
Scheme 60: Dehydrogenation reaction of **10a.**

A reaction tube with a stir bar under N_2 was charged with diphenyl diselenide (0.5 equiv., 0.1 mmol, 31.2 mg), potassium *tert*-butoxide (1.1 equiv., 0.22 mmol, 24.6 mg), potassium periodate (1 equiv., 0.2 mmol, 46.0 mg) and 1 mL of dry DMSO, followed by addition of the ester (1 equiv., 0.2 mmol). The mixture was stirred at room temperature for 72 h.

The resulting mixture from the first step was dilute with 1 mL of DCM and cooled to -40 ^oC in a low temperature reactor. A solution of *meta*-chloroperoxybenzoic acid (1.2 equiv., 0.24 mmol, 60% purity, 70 mg) in 1 mL of DCM was added dropwise. The resulting mixture was stirred at this temperature for 3 h. The residue was directly purified by flash column chromatography on silica gel (eluent: hexane/ethyl acetate 98:2) to afford the crude product with a trace amount of starting material as impurity. The crude product was further purified by productive TLC plate to afford the pure product for analysis.

For **10b**, **10g**, **10h**, **10i**, **10j** and **10l**, as we failed to separate the product with the starting material, a sample of them was synthesized (for **11b** – **11j**, they were synthesized by similar procedure of **10e**, for **11l**, it was synthesized using the first two steps of synthesizing the acid part of **2e**) as a reference. By comparing the ^1H NMR and ^{13}C NMR of the reference, stating material and the mixture, it could prove that the NMR obtained from the mixture is the mixture of the product and starting material.

2.1.3 Characterizing of the product of the esters



11a

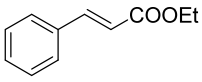
Methyl cinnamate (11a)

60% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.73 (d, *J* = 16.0 Hz, 1H), 7.57 – 7.55 (m, 2H), 7.43 – 7.41 (m, 3H), 6.48 (d, *J* = 16.0 Hz, 1H), 2.84 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 167.8, 145.2, 134.8, 130.6, 129.2, 128.4, 118.2, 52.0.

HRMS (ESI, m/z): calcd for $C_{10}H_{11}O_2^+$ $[M+H]^+$ 163.0759, found: 163.0767.



11b

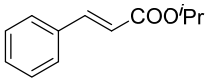
Ethyl cinnamate (11b)

68% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.69 (d, *J* = 16.0 Hz, 1H), 7.54 – 7.51 (m, 2H), 7.40 – 7.36 (m, 3H), 6.44 (d, *J* = 16.0 Hz, 1H), 4.27 (q, *J* = 7.1 Hz, 2H), 1.34 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 167.3, 144.9, 134.8, 130.5, 129.2, 128.4, 118.6, 16.8, 14.7.

HRMS (ESI, m/z): calcd for $C_{11}H_{13}O_2^+$ $[M+H]^+$ 177.0916, found: 177.0915.



11c

Isopropyl cinnamate (11c)

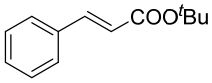
52% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.67 (d, *J* = 16.0 Hz, 1H), 7.54 – 7.51 (m, 2H),

7.40 – 7.37 (m, 3H), 6.42 (d, *J* = 16.0 Hz, 1H), 5.17 – 5.11 (m, 1H), 1.32 (d, *J* = 6.2 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 166.9, 144.7, 134.9, 130.5, 129.2, 128.4, 119.2, 68.2, 22.3.

HRMS (ESI, m/z): calcd for $C_{12}H_{15}O_2^+$ $[M+H]^+$ 191.1072, found: 191.1063.



11d

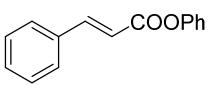
***tert*-Butyl cinnamate (11d)**

30% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.59 (d, *J* = 16.0 Hz, 1H), 7.52 – 7.50 (m, 2H), 7.38 – 7.36 (m, 3H), 6.37 (d, *J* = 16.0 Hz, 1H), 1.54 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 166.7, 143.9, 135.0, 130.3, 129.2, 128.3, 120.6, 80.9, 28.6.

HRMS (ESI, m/z): calcd for $C_{13}H_{17}O_2^+$ $[M+H]^+$ 205.1229, found: 205.1226.



11e

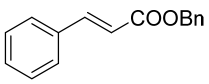
Phenyl cinnamate (11e)

56% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.88 (d, *J* = 16.0 Hz, 1H), 7.61 – 7.58 (m, 2H), 7.45 – 7.39 (m, 4H), 7.19 – 7.16 (m, 2H), 6.64 (d, *J* = 16.0 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 165.7, 151.2, 146.9, 134.5, 131.0, 129.8, 129.3, 128.7, 126.1, 122.0, 117.7.

HRMS (ESI, m/z): calcd for $C_{15}H_{13}O_2^+$ $[M+H]^+$ 225.0916, found: 225.0918.



11f

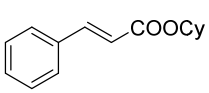
Benzyl cinnamate (11f)

72% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.73 (d, *J* = 16.0 Hz, 1H), 7.54 – 7.51 (m, 2H), 7.39 – 7.34 (m, 8H), 6.49 (d, *J* = 16.0 Hz, 1H), 5.26 (s, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 167.1, 145.5, 136.4, 134.7, 130.7, 129.2, 128.9, 128.6, 128.6, 128.4, 118.2, 66.7.

HRMS (ESI, m/z): calcd for $C_{16}H_{15}O_2^+$ $[M+H]^+$ 239.1072, found: 239.1076.



11g

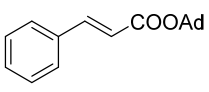
Cyclohexyl cinnamate (11g)

43% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.70 (d, *J* = 16.0 Hz, 1H), 7.57 – 7.54 (m, 2H), 7.42 – 7.39 (m, 3H), 6.46 (d, *J* = 16.0 Hz, 1H), 4.96 – 4.89 (m, 1H), 1.98 – 1.93 (m, 2H), 1.84 – 1.76 (m, 2H), 1.64 – 1.27 (m, 7H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 166.8, 144.6, 134.9, 130.4, 129.2, 128.4, 119.2, 73.1, 32.1, 25.8, 24.2.

HRMS (ESI, m/z): calcd for $C_{15}H_{19}O_2^+$ $[M+H]^+$ 231.1385, found: 231.1380.



11h

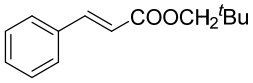
1-Adamantanyl cinnamate (11h)

20% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.57 (d, *J* = 16.0 Hz, 1H), 7.52 – 7.50 (m, 2H), 7.38 – 7.35 (m, 3H), 6.36 (d, *J* = 16.0 Hz, 1H), 2.20 (s, 9H), 1.74 – 1.66 (m, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 166.3, 143.8, 135.0, 130.2, 129.1, 128.3, 120.7, 80.9, 41.8, 36.6, 31.2.

HRMS (ESI, m/z): calcd for $C_{19}H_{23}O_2^+$ $[M+H]^+$ 283.1698, found: 283.1688.



11i

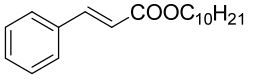
Neopentyl cinnamate (11i)

38% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.69 (d, *J* = 16.0 Hz, 1H), 7.56 – 7.53 (m, 2H), 7.40 – 7.38 (m, 3H), 6.47 (d, *J* = 16.0 Hz, 1H), 3.92 (s, 2H), 1.00 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 167.5, 144.9, 134.8, 130.6, 129.2, 128.4, 118.7, 74.2, 31.8, 26.9.

HRMS (ESI, m/z): calcd for $C_{14}H_{19}O_2^+$ $[M+H]^+$ 219.1385, found: 219.1390.



11j

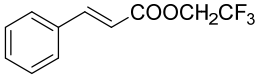
Decyl cinnamate (11j)

25% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.68 (d, *J* = 16.0 Hz, 1H), 7.54 – 7.51 (m, 2H), 7.40 – 7.37 (m, 3H), 6.44 (d, *J* = 16.0 Hz, 1H), 4.20 (t, *J* = 6.7 Hz, 2H), 1.74 – 1.67 (m, 2H), 1.42 – 1.23 (m, 14H), 0.88 (t, *J* = 6.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 167.4, 144.9, 134.8, 130.5, 129.2, 128.4, 118.7, 85.1, 32.3, 29.9, 29.7, 29.6, 29.1, 26.3, 23.0, 14.5.

HRMS (ESI, m/z): calcd for $C_{19}H_{29}O_2^+$ $[M+H]^+$ 289.2168, found: 289.2163.



11k

2,2,2-Trifluoroethyl cinnamate (11k)

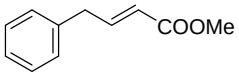
46% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.79 (d, *J* = 16.0 Hz, 1H), 7.57 – 7.54 (m, 2H), 7.42 – 7.40 (m, 3H), 6.49 (d, *J* = 16.0 Hz, 1H), 4.59 (q, *J* = 8.5 Hz, 2H).

^{19}F NMR (375 MHz, $CDCl_3$): δ (ppm) -73.7 (q, *J* = 8.5 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 165.5, 147.5, 134.2, 131.2, 129.3, 128.6, 121.2 (q, *J* = 275.4 Hz), 116.2, 60.7 (q, *J* = 36.4 Hz).

HRMS (ESI, m/z): calcd for $C_{11}H_{10}O_2F_3^+$ $[M+H]^+$ 231.0633, found: 231.0642.



11l

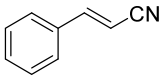
Methyl (*E*)-4-phenylbut-2-enoate (11l)

50% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.34– 7.29 (m, 2H), 7.26 – 7.21 (m, 1H), 7.18 – 7.15 (m, 2H), 7.11 (dt, J_1 = 15.6 Hz, J_2 = 6.8 Hz, 1H), 5.82 (dt, J_1 = 15.5 Hz, J_2 = 1.7 Hz, 1H), 3.72 (s, 3H), 3.48 (dd, J_1 = 6.7 Hz, J_2 = 1.6 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 167.2, 147.9, 138.0, 129.1, 129.0, 127.0, 122.3, 51.8, 38.8.

HRMS (ESI, m/z): calcd for $C_{11}H_{13}O_2^+$ $[M+H]^+$ 177.0916, found: 177.0915.



11m

Cinnamonitrile (11m)

23% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.46 – 7.37 (m, 6H), 6.87 (d, *J* = 16.6 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 150.8, 133.8, 131.5, 129.4, 127.6, 118.4, 96.6.

HRMS (ESI, m/z): calcd for $C_9H_8N^+$ $[M+H]^+$ 130.0657, found: 130.0658.

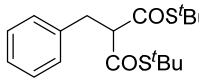
2.2 Conclusion

In conclusion, a modified method for dehydrogenation of esters was found, by replacing the base with a stronger KO^{t}Bu, it is possible for the esters to dehydrogenate to afford the desired product in a moderate yields. However, there are still a few problems (as seen in the section shown below). Firstly, the condition is not entirely optimal since an inert environment and the usage of a strong base is still required for the reaction. Secondly, esters of aliphatic acids afforded poor yields; increasing the temperature of the reaction also did not improve the yields of the desired product. Lastly, less reactive amides appear to be unreactive under the reaction conditions.

3. Unsuccessful substrates

9a – **9u** were unsuccessful substrates in the conditions for the dehydrogenation of thioesters; **12a** – **12f**, as well as **9o** and **9u**, were unsuccessful substrates in the conditions for the dehydrogenation of esters

Unless otherwise stated, thioesters were synthesized using the same method as **1a** (using react with the acid and thiol in the presence of DCC and DMAP), **12a** – **12d** were synthesized using similar method of **2s** (reflux of the acid in methanol with a catalytic amount of TsOH), **12e** and **12f** was synthesized using similar method of **10a** (using the acetyl chloride).

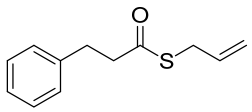


9a

White solid.

^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) 7.28 – 7.08 (m, 5H), 3.85 (t, J = 7.8 Hz, 1H), 3.18 (d, J = 7.6 Hz, 2H), 1.42 (s, 18H).

4a was obtain as the major product and a trace amount of **1a** was also observed, further study found that **9a** was decomposed during the first step and **1a-i** was obtain as the major product for the first step. It was likely that the enolate intermediate decomposed in the process.



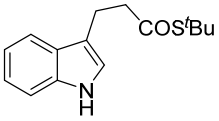
9b

Colorless oil.

^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) 7.31 – 7.27 (m, 2H), 7.23 – 7.17 (m, 3H), 5.79 (ddt, J_1 = 16.9 Hz, J_2 = 9.9 Hz, J_3 = 7.0 Hz, 1H), 5.23 (dq, J_1 = 16.9 Hz, J_2 = 1.4 Hz, 1H), 5.10 (dq, J_1 = 10.0, J_2 = 1.1 Hz, 1H), 3.54 (dt, J_1 = 6.9 Hz, J_2 = 1.1 Hz, 2H), 3.03 – 2.93 (m, 2H), 2.92 – 2.83 (m, 2H).

About 20% yield from NMR, unable to purify, mainly contains unreacted staring

material, also contains some unknown impurities. Likely not stable enough for the reaction.

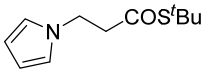


9c

Yellow oil.

^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) 7.84 (brs, 1H), 7.60 (d, J = 7.8 Hz, 1H), 7.36 (d, J = 8.1 Hz, 1H), 7.20 (td, J_1 = 7.5, J_2 = 1.2 Hz, 1H), 7.12 (td, J_1 = 7.5, J_2 = 1.1 Hz, 1H), 7.00 (d, J = 2.4 Hz, 1H), 3.11 (t, J = 7.7 Hz, 2H), 2.85 (t, J = 7.8 Hz, 2H), 1.47 (s, 9H).

About 60% yield from NMR, unable to purify, contains some unknown impurities. Likely not stable enough for the reaction.

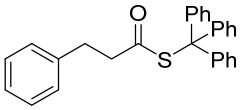


9d

Colorless oil.

^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) 6.63 (t, J = 2.1 Hz, 2H), 6.13 (t, J = 2.1 Hz, 2H), 4.19 (t, J = 6.9 Hz, 2H), 2.89 (t, J = 6.9 Hz, 2H), 1.45 (s, 9H).

Possibly contains the product from NMR, too messy to purify.

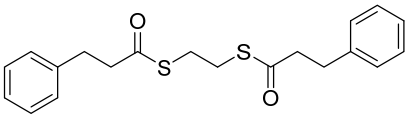


9e

White Solid.

^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) 7.30 – 7.21 (m, 12H), 7.20 – 7.12 (m, 8H), 2.91 – 2.87 (m, 2H), 2.83 – 2.79 (m, 2H).

Possibly contains the product from NMR, too messy to purify.

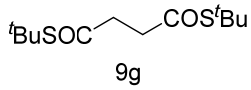


9f

White Solid.

^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) 7.31 – 7.27 (m, 4H), 7.23 – 7.17 (m, 6H), 3.04 (s, 4H), 3.00 – 2.96 (m, 4H), 2.89 – 2.85 (m, 4H).

Possibly contains the product from NMR, too messy to purify.

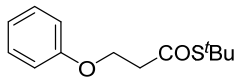


9g

White solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.77 (s, 4H), 1.45 (s, 18H).

Too messy, likely decomposed.

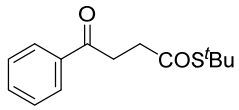


9h

Colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.30 – 7.25 (m, 2H), 6.97 – 6.89 (m, 3H), 4.24 (t, *J* = 6.5 Hz, 2H), 2.93 (t, *J* = 6.5 Hz, 2H), 1.48 (s, 9H).

Too messy, possibly because the product is not stable.

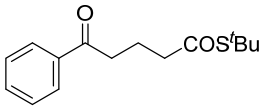


9i

Yellowish solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.99 – 7.96 (m, 2H), 7.59 – 7.55 (m, 1H), 7.49 – 7.44 (m, 2H), 3.31 (t, *J* = 6.8 Hz, 2H), 2.95 (t, *J* = 6.8 Hz, 2H), 1.47 (s, 9H).

Too messy to purify, likely decomposed.

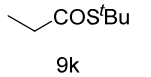


9j

Brown oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.97 – 7.94 (m, 2H), 7.61 – 7.52 (m, 1H), 7.48 – 7.44 (m, 2H), 3.03 (t, *J* = 7.2 Hz, 2H), 2.58 (t, *J* = 7.2 Hz, 2H), 2.08 (m, 2H), 1.46 (s, 9H).

Too messy to purify, ‘ikely decomposed.

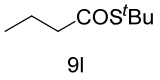


9k

Colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.47 (q, *J* = 7.5 Hz, 2H), 1.46 (s, 9H), 1.13 (t, *J* = 7.5 Hz, 3H).

Too volatile to separate.

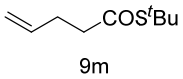


9l

Colorless oil.

^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) 2.42 (t, *J* = 7.4 Hz, 2H), 1.70 – 1.61 (m, 2H), 1.46 (s, 9H), 0.94 (t, *J* = 7.4 Hz, 3H).

Too volatile to separate.

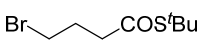


9m

Colorless oil.

^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) 5.80 (ddt, J_1 = 16.8 Hz, J_2 = 10.0 Hz, J_3 = 6.5 Hz, 1H), 5.05 (d, *J* = 17.2 Hz, 1H), 5.00 (d, *J* = 10.2 Hz, 1H), 2.54 (dd, J_1 = 8.6 Hz, J_2 = 6.4 Hz, 2H), 2.37 (q, *J* = 7.2 Hz, 2H), 1.46 (s, 9H).

Too volatile to separate.

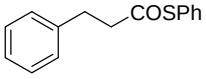


9n

Colorless Oil.

^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) 3.43 (t, *J* = 6.6 Hz, 2H), 2.64 (t, *J* = 7.2 Hz, 2H), 2.17 (m, 2H), 1.46 (s, 9H).

Too messy. Possibly react with the base.



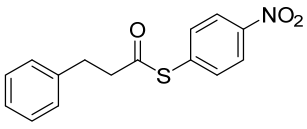
9o

White solid.

^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) 7.42 – 7.38 (m, 5H), 7.33 – 7.27 (m, 2H), 7.24 – 7.20 (m, 3H), 3.05 – 2.95 (m, 4H).

No reaction, likely that it is not active enough for this reaction.

Decomposed when using the conditions for dehydrogenation of esters.

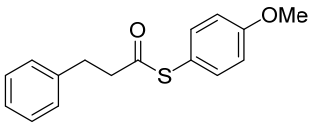


9p

Light yellow solid.

^{1}H NMR (400 MHz, CDCl$_3$): δ (ppm) 8.26 – 8.23 (m, 2H), 7.58 – 7.56 (m, 2H), 7.34 – 7.30 (m, 2H), 7.26 – 7.20 (m, 3H), 3.06 – 3.01 (m, 4H).

Decomposed.

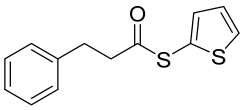


9q

Light yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.32 – 7.28 (m, 4H), 7.24 – 7.20 (m, 3H), 6.95 – 6.92 (m, 2H), 3.83 (s, 3H), 3.03 – 2.99 (m, 2H), 2.96 – 2.92 (m, 2H).

No reaction, likely that it is not active enough for this reaction.

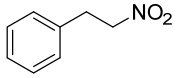


9r

Yellowish oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.55 (dd, J_1 = 5.2 Hz, J_2 = 1.4 Hz, 1H), 7.33 – 7.28 (m, 2H), 7.25 – 7.19 (m, 3H), 7.14 – 7.10 (m, 2H), 3.04 – 3.00 (m, 2H), 2.98 – 2.93 (m, 2H).

Too messy, likely decomposed.

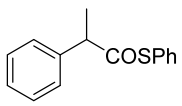


9s

Light yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.41 – 7.27 (m, 3H), 7.24 – 7.19 (m, 2H), 4.62 (td, J_1 = 7.4 Hz, J_2 = 0.9 Hz, 2H), 3.33 (t, J = 7.4 Hz, 2H).

No reaction.

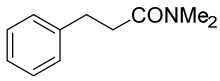


9t

Colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.39 – 7.29 (m, 10H), 4.00 (q, J = 7.1 Hz, 1H), 1.58 (d, J = 7.1 Hz, 3H).

Likely decomposed, possibly some 2-phenyl acrylic acid as product.

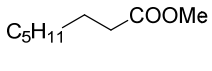


9u

Light yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.31 – 7.27 (m, 2H), 7.24 – 7.18 (m, 2H), 2.97 (t, *J* = 7.5 Hz, 2H), 2.95 (s, 3H), 2.93 (s, 3H), 2.54 (t, *J* = 7.5 Hz, 2H).

No reaction in either conditions.

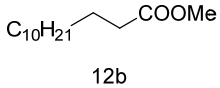


12a

Colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 3.67 (s, 3H), 2.30 (t, *J* = 7.5 Hz, 2H), 1.66 – 1.56 (m, 2H), 1.32 – 1.26 (m, 8H), 0.88 (t, *J* = 6.7 Hz, 3H).

Less than 10% yield, unable to separate. No reaction at 60 °C.

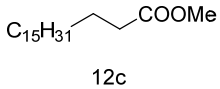


12b

Colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 3.67 (s, 3H), 2.30 (t, *J* = 7.6 Hz, 2H), 1.65 – 1.58 (m, 2H), 1.30 – 1.26 (m, 18H), 0.88 (t, *J* = 6.8 Hz, 3H).

Less than 10% yield, unable to separate. No reaction at 60 °C.

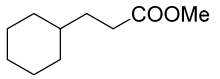


12c

Colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 3.67 (s, 3H), 2.30 (t, *J* = 7.6 Hz, 2H), 1.65 – 1.58 (m, 2H), 1.30 – 1.26 (m, 28H), 0.88 (t, *J* = 6.8 Hz, 3H).

No reaction at r.t. or 60 °C.

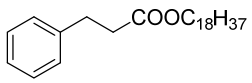


12d

Colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 3.66 (s, 3H), 2.32 (t, *J* = 7.9 Hz, 2H), 1.73 – 1.65 (m, 5H), 1.53 – 1.50 (m, 2H), 1.27 – 1.11 (m, 4H), 0.93 – 0.84 (m, 2H).

Less than 10% yield, unable to separate. No reaction at 60 °C.

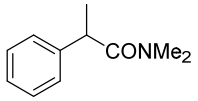


12e

Colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.28 – 7.27 (m, 3H) 7.21 – 7.18 (m, 2H), 4.06 (t, *J* = 6.7 Hz, 2H), 2.95 (t, *J* = 7.8 Hz, 2H), 2.62 (t, *J* = 7.8 Hz, 2H), 1.60 – 1.54 (m, 2H), 1.31 – 1.26 (m, 30H), 0.88 (t, *J* = 6.8 Hz, 3H).

No reaction at r.t. or 60 °C.



12f

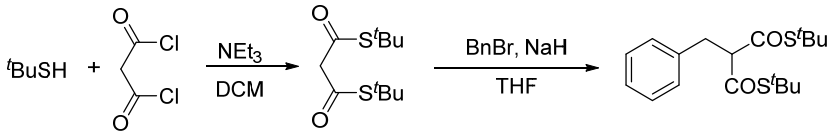
Colorless crystal.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.33 – 7.20 (m, 5H), 3.88 (q, *J* = 6.9 Hz, 1H), 2.95 (s, 3H), 2.89 (s, 3H), 1.44 (d, *J* = 6.9 Hz, 3H).

No reaction.

3.1 Synthesis for some individual substrates

9a was synthesized by the following method:



Scheme 53: Synthesis route of **9a**.

A dry round bottom flask with a magnetic stir bar was charged with 2-Methyl-2-propanethiol (2 equiv., 10 mmol, 1.1 mL), triethylamine (5 equiv., 25 mmol, 3.5 mL) and 30 mL of DCM, it was cooled to 0 °C. A solution of malonyl chloride (1 equiv., 5 mmol, 0.49 mL) in 10 mL of DCM was added dropwise *via* an addition funnel. After the addition was complete, the mixture was stirred at room temperature overnight. It was then washed with saturated NH_4Cl solution, followed by brine. The organic layer was the dried over Na_2SO_4, after the organic solvent was removed under vacuum, the residue was purified by flash column chromatography on silica gel (eluent: hexane/ethyl acetate 4:1) to afford the intermediate *S,S*-di-tert-butyl propanebis(thioate).

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 3.60 (s, 2H), 1.48 (s, 18H).

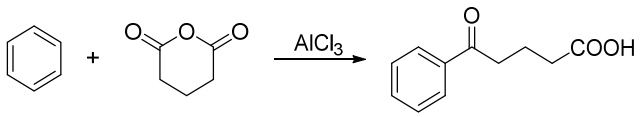
The second step is using a similar method from the literature.[95]

A dry round bottom flask with a magnetic stir bar was charged with sodium hydride (1.2 equiv, 60% dispersion in mineral oil, 6 mmol, 0.24 g) and 20 mL of THF. The intermediate *S,S*-di-tert-butyl propanebis(thioate) (1 equiv., 5 mmol, 1.24 g) in 5 mL of THF was added dropwise at 0 °C. After stirred for 15 min, benzyl bromide (1 equiv., 5 mmol, 0.6 mL) was added. The mixture was then heat to 60 °C and stirred overnight. It

was then quenched with water and extracted with ether (3 x 20 mL). The combined organic layer was then washed with brine and dried over Na_2SO_4, after the organic solvent was removed under vacuum, the residue was purified by flash column chromatography on silica gel (eluent: hexane/ethyl acetate 4:1) to afford the product **9a**.

9f and **9g** was synthesized using the standard method for the thioesters except using 0.5 equiv. of the thiol and acid respectively.

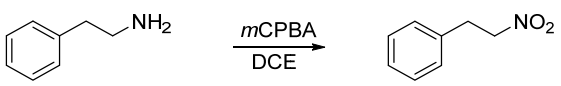
The acid part of **9j** was synthesized using the following method[96]:



Scheme 54: Synthesis the acid part of **9j**.

To a solution of glutaric anhydride (1.0 equiv., 5 mmol, 0.57 g) in 5 mL of dry benzene at 0 ^oC was added aluminum chloride (2.2 equiv., 11 mmol, 1.47 g) in one potion. The mixture was stirred at 0 ^oC for 1 h, and then at room temperature for 2 h. It was quenched by slowly addition of water at 0 ^oC, it was then filtered and extracted with ether (3 x 20 mL). The combined organic layer was dried over Na_2SO_4, after the solvent removed under vacuum, the crude product was used for the next step without further purification.

9s was synthesized using the following method[97]:

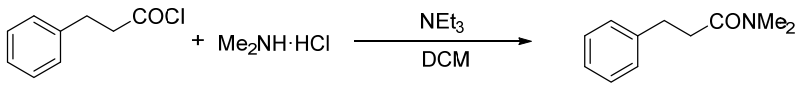


Scheme 55: Synthesis of **9s**.

A dry round bottom flask was charged *meta*-chloroperoxybenzoic acid (4 equiv., 20

mmol, 60% purity, 5.8 g) and 20 mL of 1,2-dichloroethane, the solution was heated to reflux and a solution of 2-phenylethylamine (1 equiv., 5 mmol, 0.63 mL) in 5 mL of 1,2-dichloroethane was added dropwise. The mixture was continued to reflux for 3 h. After it was cooled to room temperature, it was filtered, washed with 1 M NaOH solution and brine, dried over Na_2SO_4 and the solvent was removed under vacuum. The residue was then purified by flash column chromatography on silica gel (eluent: hexane/ethyl acetate 9:1).

9u was synthesized using the following method:



Scheme 56: Synthesis of **9u**.

To a dry round button flask with a stir bar and a dropping funnel under nitrogen was charged with dimethylamine hydrochloride (1 equiv., 10 mmol, 0.82 g), triethylamine (5 equiv., 50 mmol, 7 mL), and 30 mL of DCM. Then, the mixture was cooled to 0 ^oC by ice bath, and the 3-phenylpropanoyl chloride (1 equiv., 10 mmol, 1.48 mL) in 20 mL of dichloromethane was added dropwise through the dropping funnel. It was allowed to warm to room temperature and stirred overnight. And it was filtered, the filtrate was concentrated and purified by flash column chromatography using hexane/ethyl acetate (7/3).

Part II: Indium catalyzed cyclization reaction of acrylate

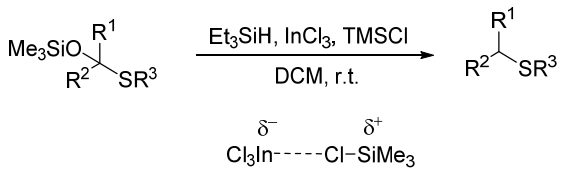
Chapter I: Introduction

1. Development of combining indium salt and silane halide as catalyst

Indium and its compounds have been found widely applied in organic synthesis for a couple of decades[99]. One of the most interesting properties of indium salts and organoindium reagents is that they are relatively air and moisture stable, which implies that the solvent does not need to be dried or degassed, and the reaction can be conducted without the need for an inert atmosphere. In addition, indium can be used as catalyst in a variety of reactions, such as aldol reactions[100], Diels-Alder reaction[101], Prins cyclization[102], ene reactions[103], Friedel-Crafts reactions[104] etc..

However, reaction with indium reagents is still much less developed compared to similar aluminum or boron reagents. This could be due to weaker acidity of indium salts as Lewis acid. One way to overcome this problem is to combine it with a silane derivative, such as trimethylsilyl chloride and bromide.

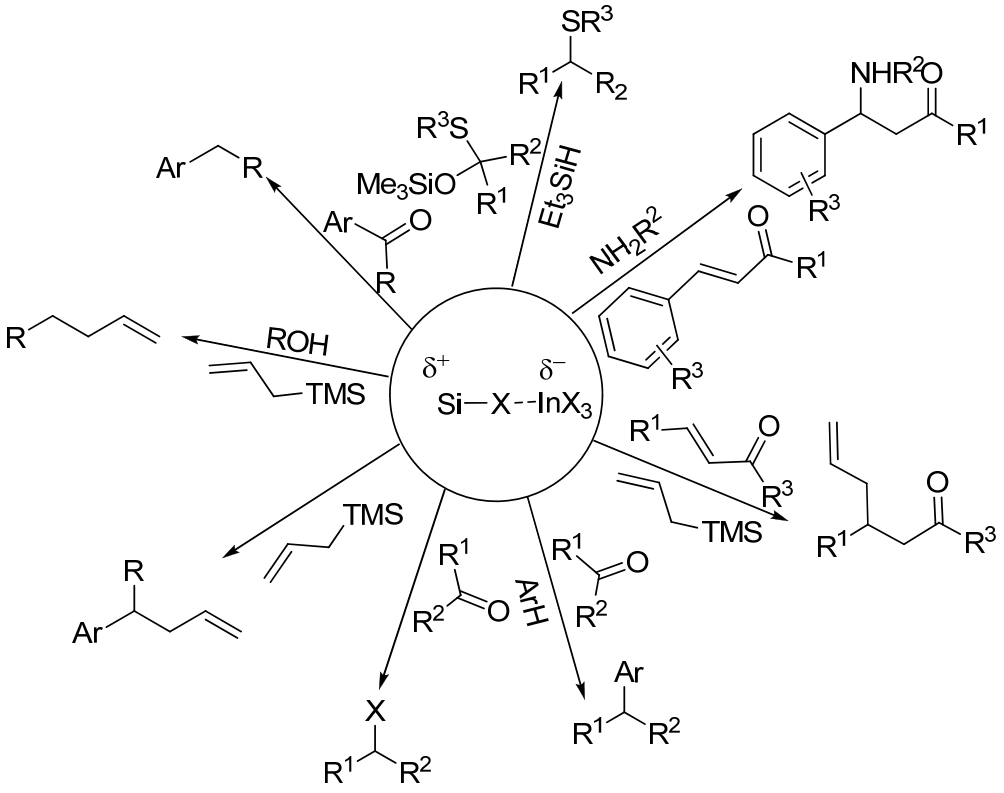
The combination of indium and trimethylsilyl halide was first reported in 1990[105] by using $InCl_3$ and TMSCl in *O*-trimethylsilyl monothioacetal reaction. In this reaction, stronger Lewis acid such as BF_3OEt_2 or $TiCl_4$ failed to yield any product, using trimethylsilyl halide alone or using other transition metal salt such as $SnCl_2$ also gave no reactions. A cationic specie was assumed to be the active intermediate to catalyze this reaction.



Scheme 1: First reported combination of indium and trimethylsilyl halide reaction, and hypothesized

active specie.

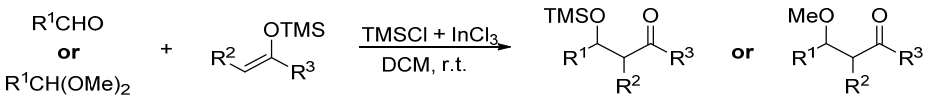
Over the years, this system has been reported on reactions such as aza-Michael addition[106], Hosomi-Sakurai reaction[107], reductive Friedel-Crafts alkylation[108], deoxygenative halogenations[109], deoxygenative allylation[110], reductive deoxygenation[111], alkylation of alcohols[112] etc..



Scheme 2: A brief summary about the catalyst system of combination of indium and trimethylsilyl halide.

Some examples are mentioned below:

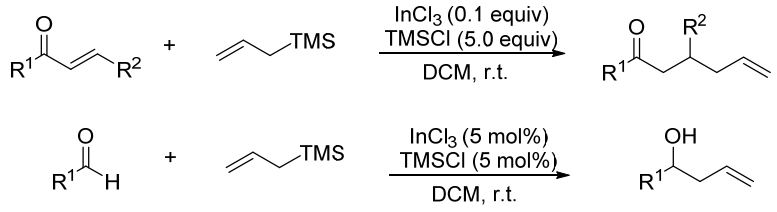
In 1991, the same group also reported an aldol reaction using the same system[113]. In this reaction, aldehydes or dimethyl acetals react with silyl enol ethers to afford aldol adducts with catalytic amount of TMSCl and $InCl_3$.



Scheme 3: Indium-trimethylsilyl halide catalyzed aldol reaction.

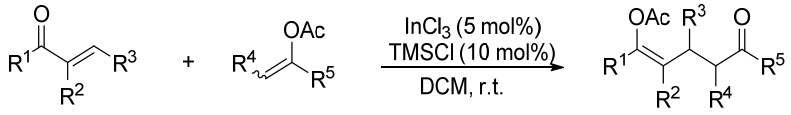
In 2001, the addition of allyltrimethylsilane to conjugated enones using catalytic

amount of $InCl_3$ and TMSCl to yield δ,ε-enones was reported[107a,b]. At the same year, a similar reaction of addition with aldehydes was also reported by another group[107c,d].



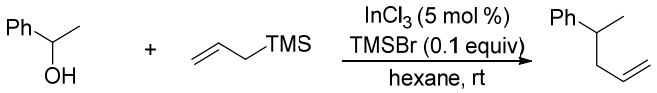
Scheme 4: Indium-trimethylsilyl halide catalyzed Sakurai-Hosomi reaction.

Another interesting report for the application of this system is the Mukaiyama-Michael reaction[114]. In this report, α,β-unsaturated carbonyl compounds react with enol acetates in the presence of $InCl_3$ and TMSCl.



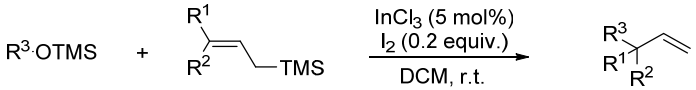
Scheme 5: Indium-trimethylsilyl halide catalyzed Mukaiyama-Michael reaction.

Besides TMSCl, TMSBr is also reported to be effective in this system, one related report is a hydroxyl group activation reaction[112].

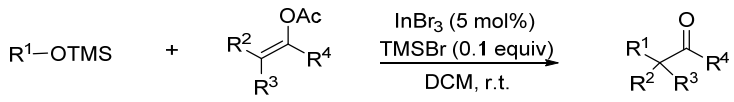


Scheme 6: Indium-trimethylsilyl bromide catalyzed hydroxyl group activation reaction.

The next application of the catalytic system is the activation of silyl ether group. In 2007, Baba and co-workers[115] demonstrated a cross coupling reaction of alkyl trimethylsilyl ethers and allylsilanes catalyzed by $InCl_3$ and TMSI, the TMSI is generated *in situ* from $InCl_3$ and I_2. In 2010, the same group reported a similar reaction of enol acetates[116] with indium tribromide and TMSBr as catalyst.

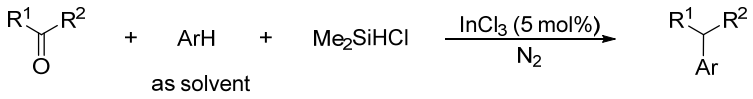


Scheme 7: Indium-trimethylsilyl iodide catalyzed silyl ether group reaction.

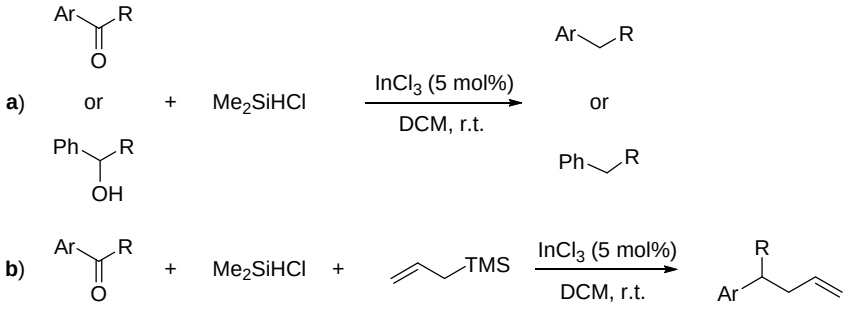


Scheme 8: Indium-trimethylsilyl bromide catalyzed enol acetate reaction.

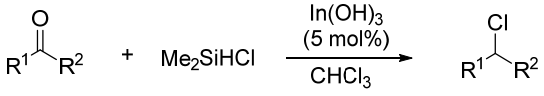
In 1998, $InCl_3$-catalyzed reductive Friedel-Crafts alkylation with chlorodimethylsilane (Me_2SiHCl) acts as both the reductant to carbonyl substrates and the hydrosilylation precedes the alkylation of aromatics has been firstly reported by Baba's group[108]. Then, a similar deoxygenation of ketones and alcohols[110,111a] was reported by the same group next year. In 2002, this group reported another similar deoxy-halogenation reaction with $In(OH)_3$ as catalyst (along with chlorodimethylsilane)[109]. In 2007, another reaction with this indium-chlorodimethylsilane system was reported by this group[117] and in the next year, a similar reaction using esters instead of acids was reported[118]



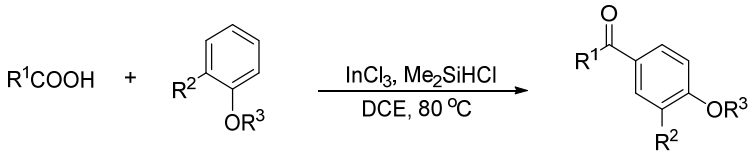
Scheme 9: Indium-chlorodimethylsilane catalyzed reductive Friedel-Crafts alkylation reaction.



Scheme 10: Indium-chlorodimethylsilane catalyzed deoxygenation of ketones and alcohols as well as deoxygenation-allylation reaction.

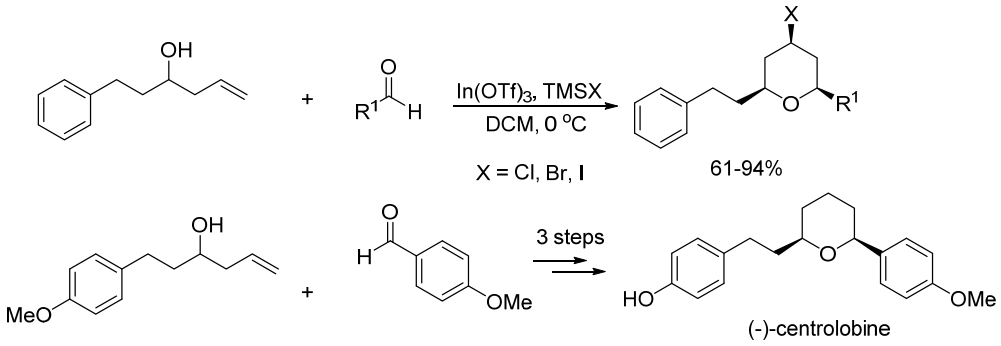


Scheme 11: Indium-chlorodimethylsilane catalyzed deoxy-halogenation reaction.

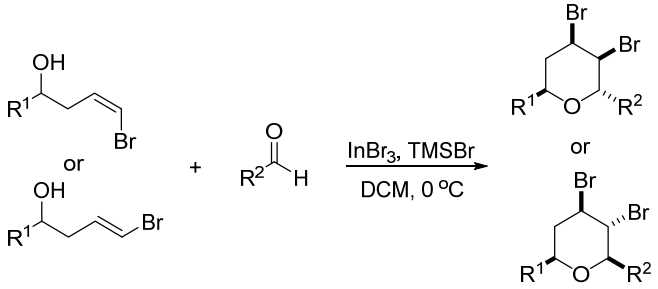


Scheme 12: Indium-chlorodimethylsilane catalyzed Friedel-Crafts acylation of aromatic ethers.

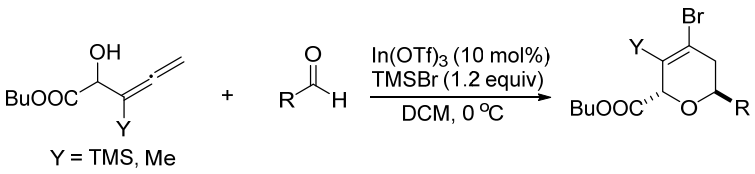
Finally, our group also reported several indium approaches to synthesize the tetrahydropyran ring, the first example[119] is in 2005, with $In(OTf)_3$ and trimethylsilane halide as catalyst, which becomes a key step in the synthesis of (-)-centrolobine. In the following year, another system with $InBr_3$ and TMSBr was proved[120] to be an effective method for the synthesis of 4,5-dibromotetrahydropyrans in a stereospecific manner. In 2009, the combination of $In(OTf)_3$ and TMSBr was proved to be useful for the synthesis of 2,6-transdihydropyrans from allenic alcohols and aldehydes[121]. Recently, an indium-trimethylsilyl bromide catalyzed [2+2]-cycloaddition and dearomatizing cascade reaction[122] was reported.



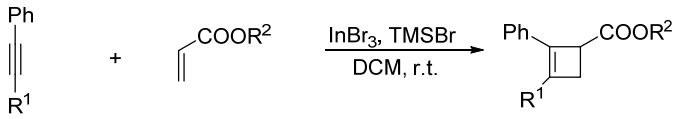
Scheme 13: Indium-trimethylsilane halide catalyzed approach to 4-halide tetrahydropyran ring.



Scheme 14: Indium-trimethylsilane bromide catalyzed approach to 3,4-dibromotetrahydropyran ring.



Scheme 15: Indium-trimethylsilane bromide synthesis of 2,6-transdihydropyrans.



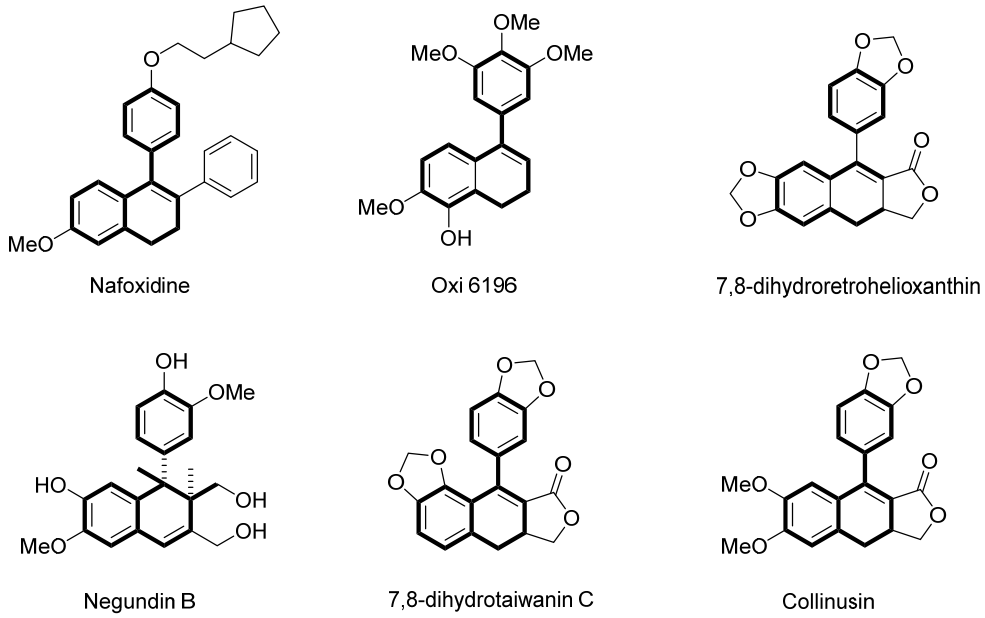
Scheme 16: Indium-trimethylsilyl bromide catalyst [2 + 2]-cycloaddition reaction.

Scheme 17: Indium-trimethylsilyl bromide catalyst dearomatizing cascade reaction.

Chapter II: Results of catalyzed aryldihydronaphthalene derivatives synthesis

1. A brief introduction about aryldihydronaphthalene derivatives

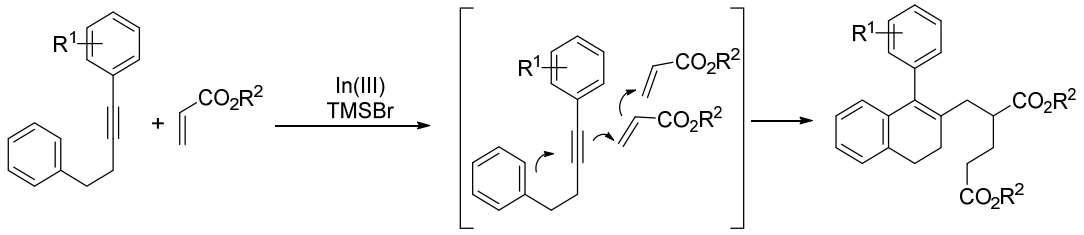
Aryldihydronaphthalene derivatives are important structure in synthesis as they are present in abundance in natural products and bioactive compounds[123]. In addition, they also have applications as fluorescent ligands in biochemistry studies or building blocks towards the synthesis of several biologically-active cyclic molecules[124].



Scheme 18: Some natural products or bioactive compounds with aryldihydronaphthalene structures.

As a result, many synthetic methodologies have been developed for these compounds. Prominently, the intramolecular hydroarylation of 4-phenyl-1-butyne or its derivatives is one of the most versatile protocols for the construction of aryldihydronaphthalene derivatives[125]. Since the pioneering studies by Fujiwara *et al.*[126], numerous catalytic methods have been developed in this field in which a series of transition metals, Lewis and Brønsted acids have been found effective for catalyzing the hydroarylation[127]. More recently, Corey[127g] and Pérez Sestelo and Martínez[127u,v] have independently reported the formation of six-membered oxa- and carbocycles by an In(III)-catalyzed

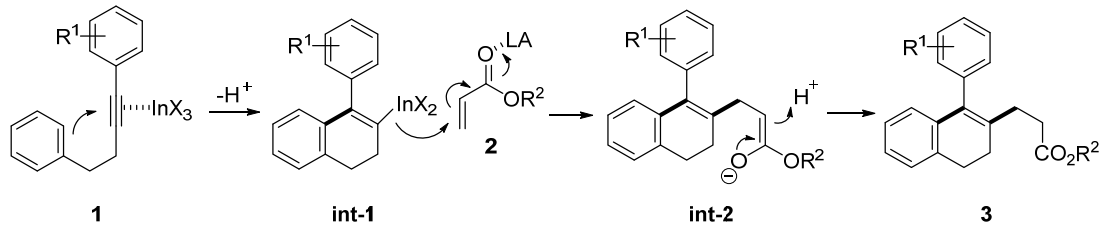
hydroarylation of acetylenic substrates. Herein an example of the In(III)-TMSBr-catalysed cascade reaction of diarylalkynes with acrylates to access a series of dihydronaphthalene derivatives in a one-pot manner was explored.



Scheme 19: In(III)-TMSBr-catalysed cascade reaction of diarylalkynes with acrylates for the synthesis of dihydronaphthalene derivatives.

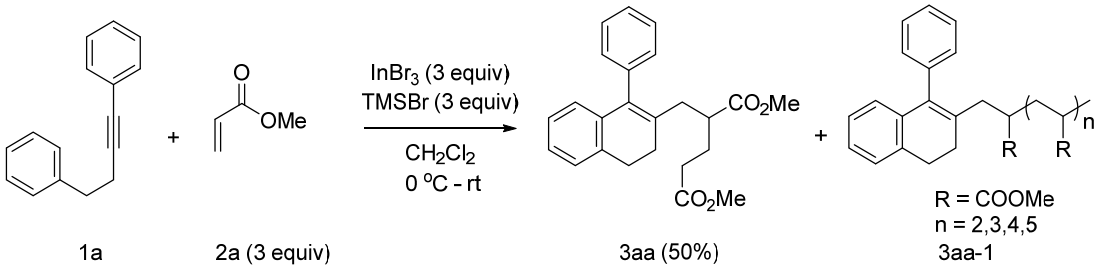
2. Preliminary results

Inspired by previously reported method by our group[122], a cascade reaction between diarylalkyne **1** and acrylate **2** to prepare aryldihydronaphthalene derivatives with combined Lewis acid of $InBr_3$ and TMSBr was envisaged. Initially, an intramolecular Friedel-Crafts type arylation reaction might proceed, to give alkenyl indium species int-**1** which will then undergo nucleophilic attack on the activated acrylate **2** to give the dihydronaphthalene enolate **int-2**. A further enolate protonation will give the final 1,2-dihydronaphthalene derivative **3**.



Scheme 20: Proposed In(III)-TMSBr-catalysed cascade reaction of diarylalkynes with acrylates.

In order to test our hypothesis, the model reaction involving but-1-yne-1,4-diyldibenzene (**1a**) and methyl acrylate (**2a**) was carried out to explore the proposed cascade reaction. In the presence of $InBr_3$ and TMSBr, an 1,2-dihydronaphthalene derivative 3aa with two propionate motifs was obtained in moderate yield with trace amounts of intractable mixture of 1,2-dihydronaphthalene derivatives containing more propionate motifs (**Scheme 21**). Interestingly, no 1,2-dihydronaphthalene derivative with a single propionate motif in original proposal could be obtained.

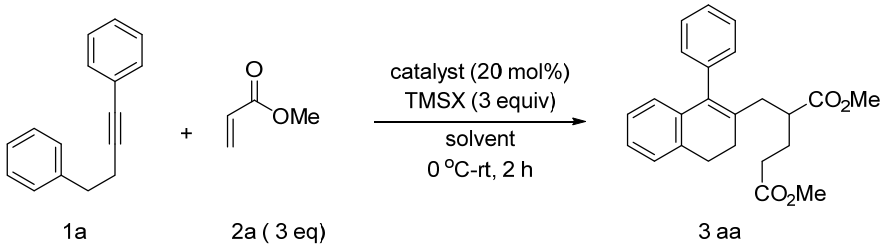


Scheme 21: Initial results of In(III)-TMSBr-catalysed cascade reaction of but-1-yne-1,4-diyldibenzene (**1a**) with methyl acrylates (**2a**).

3. Optimization conditions

The reaction conditions were subsequently optimized by using but-1-yne-1,4-diyldibenzene (**1a**) and methyl acrylate (**2a**) as model substrates. The results are summarized in **Table 1**. At the outset, it was found that both In(III) catalyst and TMSBr were indispensable for the efficient progress of this reaction (**entries 2**, **3**). Among the different indium catalysts studied (**entries 1** and **4** – **8**), $In(tfacac)_3$ was found to exhibit the best catalytic activity to afford the desired product 3aa in 61% yield (**entry 7**). Other common Lewis acid catalysts like $AlBr_3$ and $ZnCl_2$ (**entry 9**, **10**) were also tested, which mostly resulted in no product formation. In addition, this reaction was found to proceed only in chlorinated solvents, such as DCM or 1,2-dichloroethane (DCE), with the latter giving a higher yield of 70% (**entry 7** and **entry 11**). In comparison, when TMSBr was replaced by TMSCl, the product yield eroded significantly to less than 5% (**entry 12**). An attempt to decrease the amount of TMSBr or $In(tfacac)_3$ led to lower yields (**entry 13**, **14**). Finally, reducing the stoichiometry of methyl acrylate (**2a**) to only one equivalent resulted in a significantly decreased yield of **3aa**, and 1,2-dihydronaphthalene derivative with a single propionate motif remained absent (**entry 15**).

Table 1: In(III)-TMSBr-catalyzed cascade reaction of diarylalkyne 1a with methyl acrylate (2a)[a].



entry	Catalyst	Solvent	TMSX	Yield (%) [b]
1	$InBr_3$	DCM	TMSBr	50
2	$InBr_3$	DCM	-	0
3	-	DCM	TMSBr	0 [c]
4	$InCl_3$	DCM	TMSBr	14
5	InI_3	DCM	TMSBr	47
6	$In(OTf)_3$	DCM	TMSBr	37
7	$In(tfacac)_3$	DCM	TMSBr	61
8	$In(acac)_3$	DCM	TMSBr	0
9	$AlBr_3$	DCM	TMSBr	0
10	$ZnCl_2$	DCM	TMSBr	0
11	**$In(tfacac)_3$**	**DCE**	**TMSBr**	**70**
12	$In(tfacac)_3$	DCE	TMSCl	<5
13	$In(tfacac)_3$	DCE	TMSBr	60 [c]
14	$In(tfacac)_3$	DCE	TMSBr	57 [d]
15	$In(tfacac)_3$	DCE	TMSBr	33 [e]

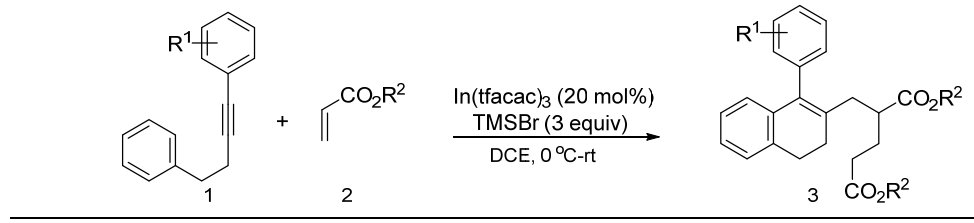
[a] Unless otherwise noted, all reactions were performed with **1a** (0.4 mmol), **2a** (1.2 mmol), catalyst (20 mol%), TMSX (3 equiv.), 0 °C-rt, 2 h, N_2. [b] Isolated yields. [c] 2.0 equiv. of TMSBr was added. [d] 10 mol% of $In(tfacac)_3$ was added. [e] 1.0 equiv. of **2a** was added.

4. Substrate scope

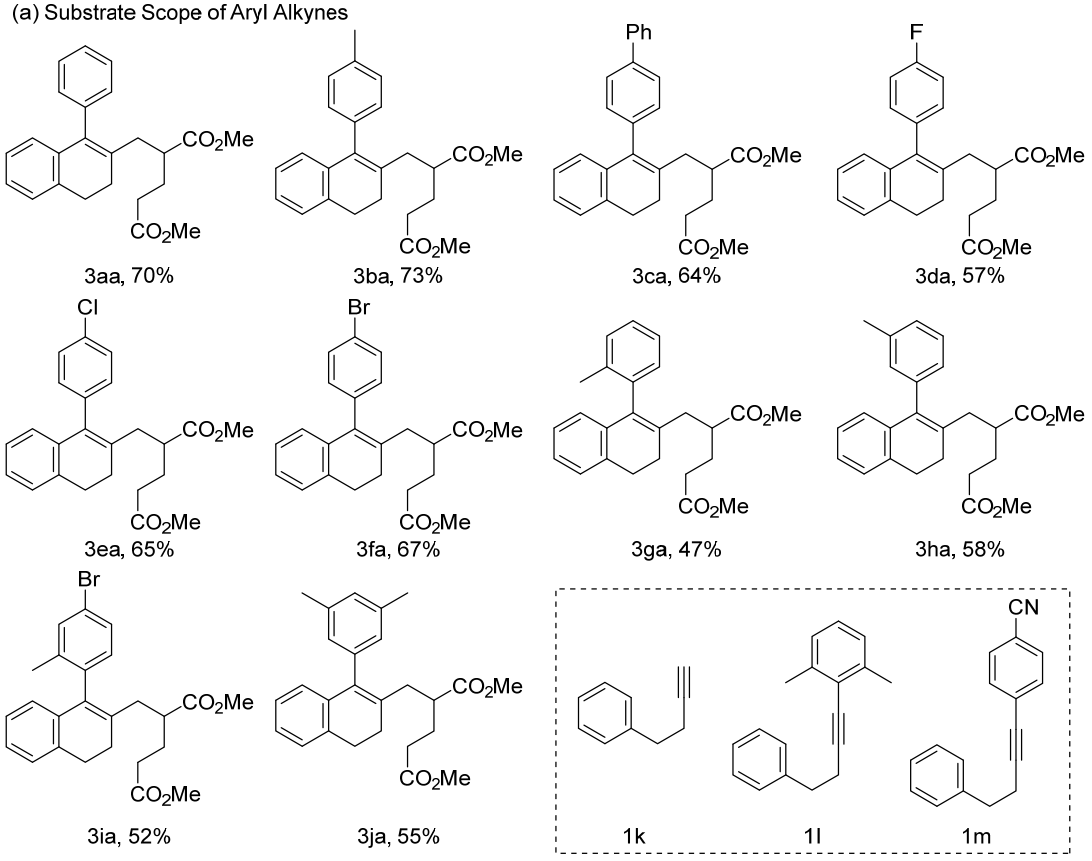
With the optimized reaction conditions in hand (**Table 1**, **entry 11**), the generality of diarylalkyne substrate scope of this reaction with respect to methyl acrylate (**2a**) was investigated, and the results are listed in **Table 2a**. Various substituted but-1-yne-1,4-diyldibenzene derivatives on the phenyl ring were well suited for this protocol, producing the corresponding product **3** in 47% to 73% yields (**3aa-ja**). As expected, substrates with *ortho*-substituent on phenyl ring gave respective products in lower yields than those with *meta*- or *para*-substituents (**3ga** vs. **3ba** and **3ha**, **3fa** vs. **3ia**) and no cyclization product could be detected when **1l** was used under the same conditions. In addition, the incompatibility of 4-phenyl-1-butyne (**1k**) with the current transformation emphasized the importance of the phenyl ring moiety for this reaction. Finally, a substrate with a strong aryl electron-withdrawing substituent (e.g., **1m**) was also unsuitable for this reaction.

With but-1-yne-1,4-diyldibenzene (**1a**) as the standard coupling partner, the scope of acrylate 2 in the present protocol was examined (**Table 2b**). In addition to methyl acrylate (**3a**), acrylates bearing longer *O*-alkyl chains also reacted smoothly to give 1,2-dihydronaphthalene products 3ab-3ad, albeit in relatively low yields (37–60%). Aside from the alkyl chain, reactions of acrylates tethering the chloroethyl group proceeded well to give 3ae in moderate yield (50%). However, the use of other olefinic substrates, such as ethyl methacrylate (**2g**), ethyl but-2-enoate (**2h**), and but-3-en-2-one (**2i**), could not provide any desired product.

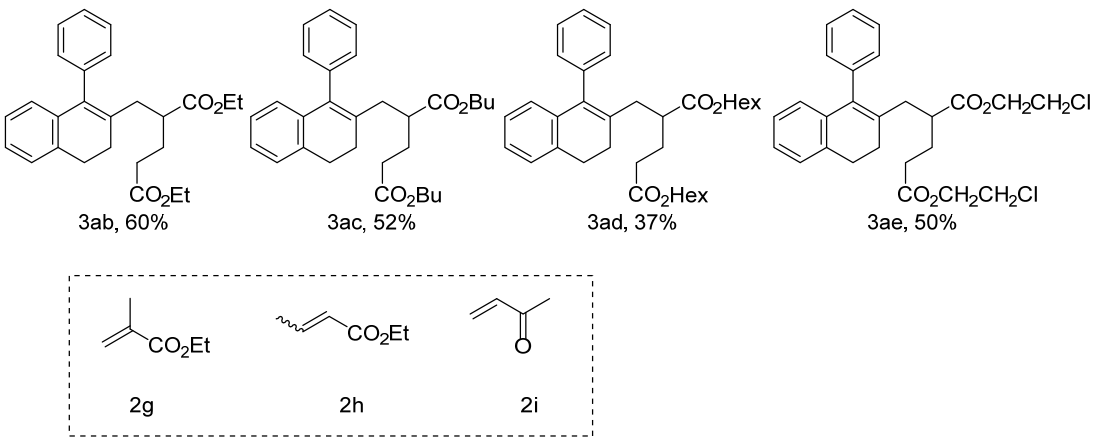
Table 2: Substrate scope for the In(III)-TMSBr-catalysed cascade reaction of diarylalkyne with acrylates[a,b].



(a) Substrate Scope of Aryl Alkynes



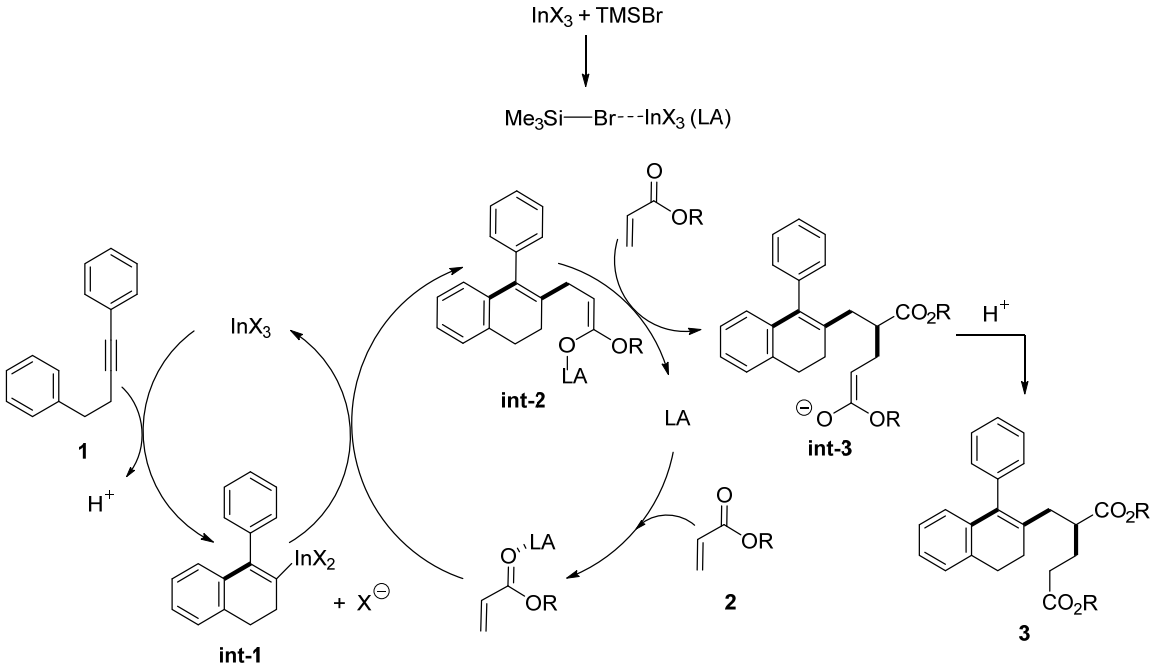
(b) Substrate Scope of Acrylates



[a] Unless otherwise noted, all reactions were performed with **1** (0.4 mmol), **2** (1.2 mmol), In(tfacac)$_3$ (20 mol%), TMSBr (3 equiv.), 0 °C-rt, N_2. [b] Isolated yields.

5. Mechanistic discussion

On the basis of above experimental results and precedent literature reports[107c,112b,122,127u,v] , a plausible reaction pathway for this In(tfacac)$_3$-TMSBr-catalyzed cascade reaction of diarylalkynes with acrylates was proposed in **Scheme 22**: In(tfacac)$_3$ and TMSBr would first form a combined Lewis acid complex (LA) with heightened acidity than either of them solely; second, an intramolecular Friedel-Crafts type arylation reaction takes place to generate an alkenyl indium species **int-1**; this is followed by a nucleophilic attack of **int-1** onto activated acrylate **2**, giving rise to **int-2**, which subsequently attacks another molecule of acrylate to give **int-3**; finally, the **int-3** is quenched by the proton generated from the first step to furnish the final product **3**.



Scheme 22: Plausible reaction mechanism of the In(tfacac)3-TMSBr-catalysed cascade reaction of diarylalkynes with acrylates.

In conclusion, an efficient method to assemble aryldihydronaphthalene derivatives *via* the cascade reaction of diarylalkynes with acrylates employing the catalysis of a combined Lewis acid system formed from In(III) salt and TMSBr was described. Both indium(III) and TMSBr are indispensable for the efficient progress of the reaction. In most cases, the reaction proceeded smoothly to afford the corresponding aryldihydronaphthalene derivatives in moderate to good yields. With reference to current experimental observations and literature reports, a possible mechanistic pathway for this reaction is also provided.

Chapter III: Experimental sections

1. General Information

Unless otherwise noted, all reagents and solvents were purchased from the commercial sources and used as received. The TMSBr and $InBr_3$ used was purchased from Sigma-Aldrich.

Thin layer chromatography (TLC) was used to monitor the reaction on Merck 60 F254 precoated silica gel plate (0.2 mm thickness). TLC spots were visualized by UV-light irradiation on Spectroline Model ENF-24061/F 254 nm. Other visualization method was staining with a basic solution ofpotassium permanganate or acidic solution of ceric molybdate, followed by heating.

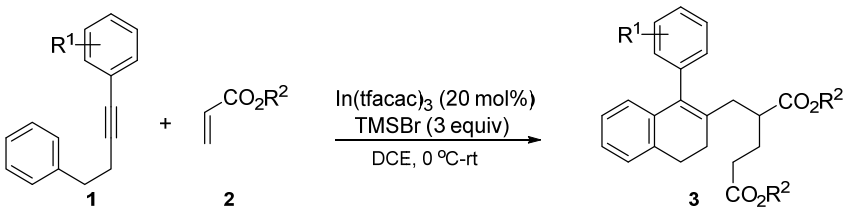
Flash column chromatography was performed using Merck silica gel 60 with analytical grade solvents as eluents.

^{1}H NMR, ^{13}C NMR and 2D NMR spectra were recorded using BrukerAvance 400 MHz spectrometers. Corresponding chemical shifts are reported in ppm downfield relative to TMS and were referenced to the signal of chloroform-d (δ = 7.26, singlet). Multiplicities were given as: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, brs = broad singlet, dd=doublet of doublets, td= triplet of doublets. Values of coupling constant are reported as *J* in Hz.

HRMS spectra were recorded on a Waters Q–TofPermier Spectrometer.

2. Experimental Sections

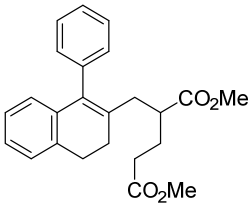
2.1 General procedure



Scheme 23: General procedure of In(III)-TMSBr-catalyzed cascade reaction.

A dry reaction tube was charged with aryl alkyne **1** (0.4 mmol), acrylate **2** (1.2 mmol), indium (III) trifluoroacetylacetonate ($In(tfacac)_3$, 20 mol%, 0.08 mmol, 45.9 mg) and DCE (2 mL) under N_2 atmosphere at 0 ^oC. Bromotrimethylsilane (TMSBr, 3 equiv, 1.2 mmol, 183.6 mg) was added and the reaction mixture was stirred at room temperature for 2 h. Upon completion of the reaction as indicated by TLC analysis, the residue was directly purified by flash column chromatography on silica gel (eluent: hexane/ethyl acetate 10:1) to afford the desired product **3**.

2.2 Product Characterization and Spectral Data



3aa

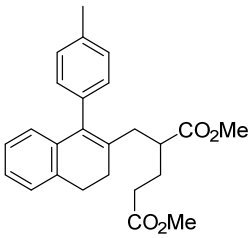
Dimethyl 2-((1-phenyl-3,4-dihydronaphthalen-2-yl)methyl) pentanedioate (3aa)

Colorless oil, 106.2 mg, 0.281 mmol, 70% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.45 - 7.41 (m, 2H), 7.38 - 7.34 (m, 1H), 7.18 - 7.10 (m, 4H), 7.05 -7.02 (m, 1H), 6.58 (d, *J* = 7.5 Hz, 1H), 3.67 (s, 3H), 3.65 (s, 3H), 2.91 (t, *J* = 7.7 Hz, 2H), 2.66 - 2.61 (m, 1H), 2.44 - 2.31 (m, 4H), 2.22 - 2.18 (m, 2H), 1.79 - 1.76 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 175.4, 173.3, 139.2, 136.7, 136.3, 135.2, 134.3, 130.2, 128.4, 127.0, 126.9, 126.4, 126.2, 125.8, 51.6, 51.5, 43.5, 37.0, 31.6, 28.4, 27.4, 26.7.

HRMS (ESI, m/z): calcd for $C_{24}H_{27}O_4^+$ $[M+H]^+$ 379.1909, found: 379.1895.



3ba

Dimethyl 2-((1-(*p*-tolyl)-3,4-dihydronaphthalen-2-yl)methyl) pentanedioate (3ba)

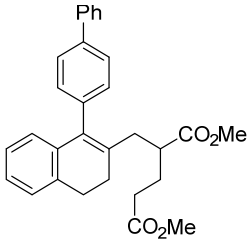
Colorless oil, 114.5 mg, 0.292 mmol, 73% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.24 - 7.22 (m, 2H), 7.17 - 7.12 (m, 1H), 7.11 - 7.08 (m, 1H), 7.05 - 7.01 (m, 3H), 6.60 (d, *J* = 7.0 Hz, 1H), 3.67 (s, 3H), 3.65 (s, 3H), 2.89 (t, *J* = 7.8 Hz, 2H), 2.66 -2.62 (m, 1H), 2.44 (s, 3H), 2.43 - 2.35 (m, 4H), 2.22 - 2.18 (m, 2H), 1.79 - 1.74 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 175.5, 173.3, 136.8, 136.4, 136.2, 136.0, 135.2, 134.2, 130.1, 129.1, 127.0, 126.3, 126.2, 125.9, 51.6, 51.5, 43.4, 37.0, 31.6, 28.4, 27.4,

26.6, 21.2.

HRMS (ESI, m/z): calcd for $C_{25}H_{29}O_4^+$ $[M+H]^+$ 393.2066, found: 393.2063.



3ca

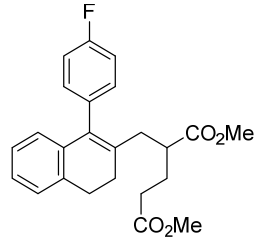
Dimethyl 2-((1-([1,1'-biphenyl]-4-yl)-3,4-dihydronaphthalen-2-yl) methyl) pentanedioate (3ca)

Colorless oil, 116.3 mg, 0.256 mmol, 64% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.71 - 7.66 (m, 4H), 7.51 - 7.47 (m, 2H), 7.44 - 7.37 (m, 2H), 7, 23 (br, 2H), 7.15 - 7.11 (m, 1H), 7.08 - 7.04 (m, 1H), 6.67 (d, J = 7.6 Hz, 1H), 3.66 (s. 3H). 3.65 (s, 3H), 2.94 - 2.90 (m, 2H), 2.70 - 2.66 (m, 1H), 2.50 - 2.41 (m, 4H), 2.25 - 2.19 (m, 2H), 1.83 - 1.77 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 175.5, 173.3, 140.9, 139.6, 138.2, 136.7, 135.9, 135.2, 134.5, 130.7, 130.7, 128.8, 127.3, 127.1, 127.1, 126.4, 126.2, 125.9, 51.7, 51.6, 43.5, 37.0, 31.6, 28.4, 27.4, 26.6.

HRMS (ESI, m/z): calcd for $C_{30}H_{31}O_4^+$ $[M+H]^+$ 455.2222, found: 455.2210.



3da

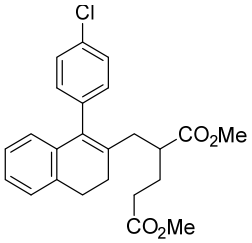
Dimethyl 2-((1-(4-fluorophenyl)-3,4-dihydronaphthalen-2-yl) methyl) pentanedioate (3da)

Colorless oil, 90.3 mg, 0.228 mmol, 57% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.18 - 7.16 (m, 1H), 7.14 - 7.10 (m, 5H), 7.07 - 7.03 (m, 1H), 6.56 - 6.54 (d, J = 7.5 Hz, 1H), 3.68 (s, 3H), 3.65 (s, 3H), 2.90 (t, J = 7.9 Hz, 2H), 2.66 - 2.61 (m, 1H), 2.44 - 2.29 (m, 4H), 2.24 - 2.19 (m, 2H), 1.80 - 1.73 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 175.3, 173.3, 161.9 (d, J = 243.7 Hz), 136.5, 135.3, 135.2, 134.9 (d, J = 4.0 Hz), 134.8, 131.8 (d, J = 7.8 Hz), 127.1, 126.5, 126.2, 125.7, 115.3 (d, J = 21.1 Hz), 51.7, 51.6, 43.4, 37.0, 31.5, 28.3, 27.4, 26.7.

HRMS (ESI, m/z): calcd for $C_{24}H_{26}O_4F^+$ $[M+H]^+$ 397.1815, found: 397.1810.



3ea

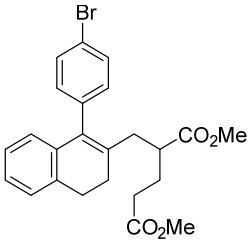
Dimethyl 2-((1-(4-chlorophenyl)-3,4-dihydronaphthalen-2-yl) methyl)pentanedioate (3ea)

Colorless oil, 107.1 mg, 0.260mmol, 65% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.61 - 7.59 (m, 2H), 7.22 - 7.14 (m, 3H), 7.10 - 7.06 (m, 2H), 6.58 (d, *J* = 7.6 Hz, 1H), 3.72 (s, 3H), 3.69 (s, 3H), 2.93 (t, *J* = 7.8 Hz, 2H), 2.71 - 2.67 (m, 1H), 2.48 - 2.41 (m, 4H), 2.37 - 2.32 (m, 2H), 1.83 - 1.77 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 175.3, 173.2, 138.1, 136.2, 135.2, 135.1, 134.8, 132.0, 131.6, 127.1, 126.6, 126.3, 125.7, 121.0, 51.7, 51.6, 43.3, 37.0, 31.5, 28.3, 27.3, 26.7.

HRMS (ESI, m/z): calcd for $C_{24}H_{26}O_4Cl^+$ $[M+H]^+$ 425.1520, found: 425.1508.



3fa

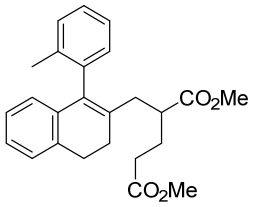
Dimethyl 2-((1-(4-bromophenyl)-3,4-dihydronaphthalen-2-yl) methyl)pentanedioate (3fa)

Colorless oil, 122.2 mg, 0.268 mmol, 67% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.41 - 7.39 (m, 2H), 7.17 - 7.02 (m, 5H), 6.54 (d, *J* = 7.6 Hz, 1H), 3.67 (s, 3H), 3.65 (s, 3H), 2.89 (t, *J* = 7.9 Hz, 2H), 2.68 - 2.61 (m, 1H), 2.43 - 2.26 (m, 4H), 2.24 - 2.19 (m, 2H), 1.79 - 1.75 (m, 2H).

^{3}C NMR (100 MHz, $CDCl_3$): δ (ppm) 175.3, 173.2, 137.6, 136.3, 135.1, 134.9, 132.9, 131.7, 128.7, 128.7, 127.1, 126.6, 126.3, 125.7, 51.7, 51.6, 43.3, 37.0, 31.5, 28.3, 27.3, 26.7.

HRMS (ESI, m/z): calcd for $C_{24}H_{26}O_4Br^+$ $[M+H]^+$ 469.1014, found: 469.1020.



3ga

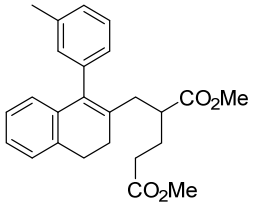
Dimethyl 2-((1-(*o*-tolyl)-3,4-dihydronaphthalen-2-yl)methyl) pentanedioate (3ga)

Colorless oil, 73.7 mg, 0.188 mmol, 47% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.28 - 7.22 (m, 3H), 7.18 - 7.17 (m, 1H), 7.12 - 7.08 (m, 2H), 7.03 - 7.00 (m, 1H), 6.49 (d, J = 7.4 Hz, 1H), 3.66 (s, 3H), 3.65 (s, 3H), 2.92 - 2.90 (m, 2H), 2.64 - 2.61 (m, 1H), 2.46 - 2.29 (m, 4H), 2.19 - 2.15 (m, 2H), 2.05 (s, 3H), 1.79 - 1.72 (m, 2H).

^{13}C NMR(100 MHz, $CDCl_3$): δ (ppm) 175.7, 173.3, 138.3, 136.8, 135.8, 135.4, 135.1, 134.2, 130.6, 130.4, 130.1, 127.3, 127.0, 126.4, 125.8, 125.1, 51.6, 51.5, 43.3, 36.8, 31.5, 28.4, 27.1, 26.5, 19.3.

HRMS (ESI, m/z): calcd for $C_{25}H_{29}O_4^+$ $[M+H]^+$ 393.2066, found: 393.2063.



3ha

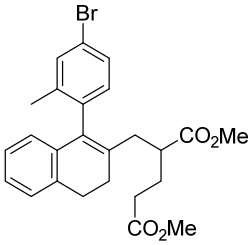
Dimethyl 2-((1-(*m*-tolyl)-3,4-dihydronaphthalen-2-yl)methyl) pentanedioate (3ha)

Colorless oil, 90.9 mg, 0.232 mmol, 58% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm)7.32 - 7.30 (m, 1H), 7.17 - 7.15 (m, 2H), 7.12 - 7.08 (m, 1H), 7.05 - 7.01 (m, 1H), 6.97 - 6.93 (m, 2H), 6.59 (d, J = 7.5 Hz, 1H), 3.66 (s, 3H), 3,65 (s, 3H), 2.91 - 2.87 (m, 2H), 2.65 - 2.62 (m, 1H), 2.43 - 2.34 (m, 4H), 2.39 (s, 3H), 2.22 - 2.17 (m, 2H), 1.79 - 1.76 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 175.6, 173.3, 139.0, 136.7, 136.3, 135.1, 134.1, 130.8, 128.2, 127.6×2, 127.2, 127.0, 126.3, 126.2, 125.9, 51.6, 51.5, 43.4, 36.9, 31.6, 28.4, 27.3, 26.6, 21.5.

HRMS (ESI, m/z): calcd for $C_{25}H_{29}O_4^+$ $[M+H]^+$ 393.2066, found: 393.2065.



3ia

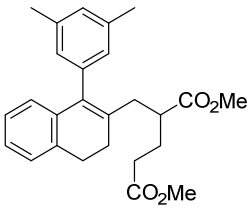
Dimethyl 2-((1-(4-bromo-2-methylphenyl)-3,4-dihydronaphthalen -2-yl) methyl)pentanedioate (3ia)

Colorless oil, 97.8 mg, 0.208 mmol, 52% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.44 (s, 1H), 7.38 (d, J = 8.1 Hz, 1H), 7.17 (d, J = 7.1 Hz, 1H), 7.13 - 7. 10 (m, 1H), 7.04 - 7.00 (m, 1H), 6.97 (d, J = 8.1 Hz, 1H), 6.45 (d, J = 7.4 Hz, 1H), 3.67 (s, 3H), 3.66 (s, 3H), 2.92 - 2.88 (m, 2H), 2.64 - 2.62 (m, 1H), 2.46 - 2.34 (m, 4H), 2.22 - 2.11 (m, 2H), 2.03 (s, 3H), 1.80 - 1.70 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 175.5, 173.2, 139.4, 137.3, 135.3, 135.1, 134.8, 134.3, 133.0, 132.1, 129.0, 127.2, 126.6, 126.4, 124.9, 121.1, 51.7, 51.6, 43.2, 36.9, 31.5, 28.3×2, 27.0, 26.5.

HRMS (ESI, m/z): calcd for $C_{25}H_{28}O_4Br^+$ $[M+H]^+$ 471.1171, found: 471.1169.



3ja

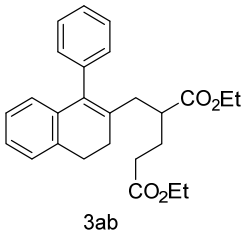
Dimethyl 2-((1-(3,5-dimethylphenyl)-3,4-dihydronaphthalen -2-yl)methyl) pentanedioate (3ja)

Colorless oil, 89.4 mg, 0.220 mmol, 55% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.17 - 7.15 (m, 1H), 7. 12 - 7.08 (m, 1H), 7.06 - 7.02 (m, 1H), 6.98 (s, 1H), 6.78 (s, 1H), 6.73 (s, 1H), 6.62 (d, J = 7.5 Hz, 1H), 3.67 (s, 3H), 3.66 (s, 3H), 2.91 - 2.86 (m, 2H), 2.66 - 2.61 (m, 1H), 2.44 - 2.37 (m, 4H), 2.35 (s, 6H), 2.24 - 2.14 (m, 2H), 1.81 - 1.75 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 175.7, 173.3, 139.0, 137.7, 136.8, 136.4, 135.1, 133.9, 128.4, 127.9, 126.9, 126.2, 126.1, 125.9, 51.6, 51.5, 43.5, 37.0, 31.6, 28.4, 27.3, 26.6, 21.3.

HRMS (ESI, m/z): calcd for $C_{26}H_{31}O_4^+$ $[M+H]^+$ 407.2222, found: 407.2224.



3ab

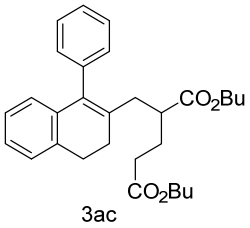
Diethyl 2-((1-phenyl-3,4-dihydronaphthalen-2-yl) methyl) pentanedioate (3ab).

Colorless oil, 97.5 mg, 0.240 mmol, 60% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.44 - 7.40 (m, 2H), 7.37 - 7.33 (m 1H), 7.18 - 7.16 (m, 3H), 7.12 - 7.09 (m, 1H), 7.05 - 7.01 (m, 1H), 6.58 (d, *J* = 7.6 Hz, 1H), 4.17 - 4.08 (m, 4H), 2.90 (t, *J* = 8.3 Hz, 2H), 2.65 - 2.58 (m, 1H), 2.43 - 2.30 (m, 4H), 2.21 - 2.14 (m, 2H), 1.79 - 1.74 (m, 2H), 1.29 - 1.27 (m, 6H);

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 175.1, 172.9, 139.2, 136.7, 136.2, 135.2, 134.5, 130.3, 128.4, 127.0, 126.8, 126.3, 126.2, 125.8, 60.4, 60.3, 43.5, 37.0, 31.8, 28.4, 27.4, 26.8, 14.2.

HRMS (ESI, m/z): calcd for $C_{26}H_{31}O_4^+$ $[M+H]^+$ 407.2222, found: 407.2202.



3ac

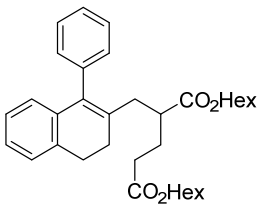
Dibutyl 2-((1-phenyl-3,4-dihydronaphthalen-2-yl) methyl) pentanedioate (**3ac**).

Colorless oil, 96.2 mg, 0.208 mmol, 52% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.44 - 7.40 (m, 2H), 7.37 - 7.33 (m, 1H), 7.17 - 7.09 (m, 4H), 7.05 - 7.01 (m, 1H), 6.58 (d, *J* = 7.0 Hz, 1H), 4.07 - 4.03 (m, 4H), 2.91 (t, *J* = 8.1 Hz, 2H), 2.66 - 2.57 (m, 1H), 2.47 - 2.30 (m, 4H), 2.21 - 2.12 (m, 2H), 1.81 - 1.73 (m, 2H), 1.65 - 1.54 (m, 4H), 1.42 - 1.29 (m, 4H), 0.97 - 0.89 (m, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 175.1, 173.0, 139.2, 136.7, 136.2, 135.1, 134.4, 130.3, 128.4, 127.0, 126.8, 126.3, 126.2, 125.8, 64.4, 64.3, 43.5, 37.0, 31.9, 30.7, 30.6, 28.4, 27.4,26.8, 19.1 × 2, 13.7, 13.6.

HRMS (ESI, m/z): calcd for $C_{30}H_{39}O_4^+$ $[M+H]^+$ 463.2848, found: 463.2844.



3ad

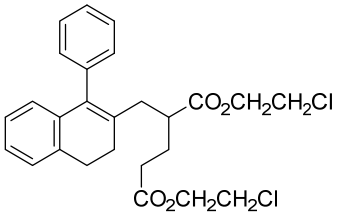
Dihexyl 2-((1-phenyl-3,4-dihydronaphthalen-2-yl) methyl) pentanedioate (**3ad**).

Colorless oil, 66.1 mg, 0.148 mmol, 37% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.44 - 7.40 (m, 2H), 7.37 - 7.35 (m, 1H), 7.17 - 7.16 (m, 3H), 7.12 - 7.08 (m, 1H), 7.05 - 7.01 (m, 1H), 6.57 (d, *J* = 7.5 Hz, 1H), 4.09 - 4.02 (m, 4H), 2.92 - 2.88 (m, 2H), 2.64 - 2.62 (m, 1H), 2.45 - 2.32 (m, 4H), 2.22 - 2.16 (m, 2H), 1.79 - 1.71 (m, 2H), 1.65 - 1.56 (m, 6H), 1.32 - 1.28 (m, 10H), 0.93 - 0.87 (m, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 175.1, 173.0, 139.2, 136.7, 136.2, 135.1, 134.4, 130.3, 128.4, 127.0, 126.8, 126.3, 126.2, 125.8, 64.7, 64.6, 43.5, 37.0, 31.8, 31.4, 31.3, 28.6, 28.5, 28.4, 27.4, 26.7, 25.6 × 2, 22.5, 22.4, 14.0 ×2 .

HRMS (ESI, m/z): calcd for $C_{34}H_{43}O_4^+$ $[M+H]^+$ 515.1361, found: 515.1351.



3ae

Bis(2-chloroethyl) 2-((1-phenyl-3,4-dihydronaphthalen-2-yl) methyl)pentanedioate (**3ae**).

Colorless oil, 89.2 mg, 0.200 mmol, 50.0% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.45 - 7.43 (m, 2H), 7.38 - 7.36 (m, 1H), 7.18 - 7.10 (m, 4H), 7.06 - 7.02 (m, 1H), 6.58 (d, *J* = 7.6 Hz, 1H), 4.35 - 4.29 (m, 4H), 3.70 - 3.63 (m, 4H), 2.94 -2.89 (m, 2H), 2.73 - 2.67 (m, 1H), 2.50 - 2.33 (m, 4H), 2.31 - 2.26 (m, 2H), 1.84 - 1.79 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) : δ (ppm) 174.6, 172.4, 139.1, 136.6, 136.4, 135.1, 134.0, 130.2, 128.4, 127.0, 126.9, 126.4, 126.2, 125.9, 64.0, 63.9, 43.2, 41.5, 41.4, 36.9, 31.5, 28.4, 27.4, 26.4.

HRMS (ESI, m/z): calcd for $C_{26}H_{29}O_4Cl_2^+$ $[M+H]^+$ 475.1443, found: 475.1434.

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List of Publications.

Zhang, Q. -C.; Zhang, W. -W.; Shen, L.; Shen, Z. -L.; Loh, T. P., In(III)-TMSBr-Catalyzed Cascade Reaction of Diarylalkynes with Acrylates for the Synthesis of Aryldihydronaphthalene Derivatives. *Molecules* **2018**, *23*, 979.