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# Nouvelle application de la chimie radicalaire des xanthates

Zeng Xianzhu

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# New application of the radical chemistry of xanthates

Thèse de doctorat de l'Institut Polytechnique de Paris  
préparée à École Polytechnique

École doctorale n°626 École Doctorale de l'Institut Polytechnique de  
Paris (ED IP Paris)  
Spécialité de doctorat: Chimie

Thèse présentée et soutenue à Palaiseau, le 19 Septembre 2022, par

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## List of Abbreviations

Abbreviations	Chemical Name
Ac	acetyl
Ac <sub>2</sub> O	acetic anhydride
AIBN	2,2'-azo-bis-isobutyronitrile
Ar	aryl
Bn	benzyl
Boc	<i>tert</i> -butoxycarbonyl
cm <sup>-1</sup>	wavenumber (s)
<sup>13</sup> C NMR	carbon nuclear magnetic resonance
°C	degree Celsius
d	day (s); doublet
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DCE	1,2-dichloroethane
DCM	dichloromethane
DLP	dilauroyl peroxide
DMSO	dimethylsulfoxide
DMAP	4-dimethylaminopyridine
DMF	<i>N,N</i> -dimethylformamide
dr	diastereomeric ratio
EI <sup>+</sup>	electronic ionisation (positive ion mode)
equiv	equivalent (s)
Et	ethyl
EWG	electron-withdrawing group
EDG	electron donating group
g	gram (s)
h	hours

$^1\text{H}$ NMR	proton nuclear magnetic resonance
HPLC	high pressure liquid chromatography
HRMS	high resolution mass spectrometry
h $\nu$	irradiation with light
Hz	hertz
IR	infrared spectroscopy
<i>J</i>	coupling constant in Hz (NMR)
LDA	lithium diisopropylamide
M	molarity (mol / L); molecular formula (HRMS)
Me	methyl
MHz	megahertz
mg	milligram (s)
mL	milliliter (s)
min	minutes
Ms	mesyl
mol	mole (s)
MS	mass spectrometry
Mp	melting point
NBS	<i>N</i> -bromosuccinimide
NMR	nuclear magnetic resonance
NPhth	phthalimide
NR	no reaction
Nu	nucleophile
pH	hydrogen ion concentration in aqueous solution
Ph	phenyl
ppm	parts per million
py	pyridine

<i>i</i> -Pr	isopropyl
rt	room temperature
<i>t</i> -Bu	<i>tert</i> -butyl
TBS	<i>tert</i> -butyldimethylsilyl
TFA	trifluoroacetic acid
THF	tetrahydrofuran
TLC	thin layer chromatography
TMS	trimethylsilyl
Xa	<i>O</i> -ethyl xanthate

## Avant-Propos

Mes projets de recherche doctorale sont principalement liés à la chimie radicalaire des xanthates et à leurs applications en synthèse. Ils sont réalisés sous la supervision du Prof. Samir Z. Zard au Laboratoire de Synthèse Organique de l'Ecole Polytechnique. Ce manuscrit est composé de trois chapitres et d'une section expérimentale.

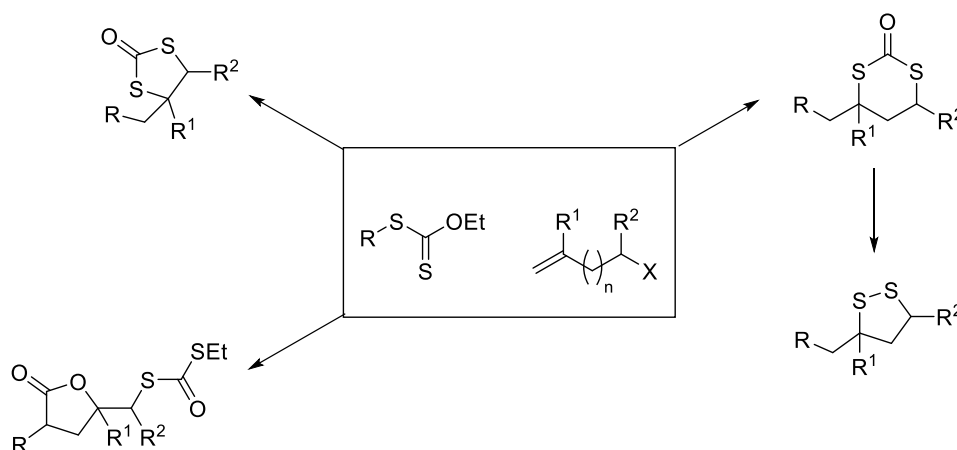
Dans le chapitre 1, la chimie radicalaire des xanthates est utilisée comme un outil puissant pour la création de liaisons carbone-carbone. La découverte, le concept général et le mécanisme de la chimie radicalaire des xanthates ont été brièvement décrits. Ce chapitre présente différentes approches pour la préparation des xanthates primaires, secondaires et tertiaires. Les xanthates sont principalement préparés par des méthodes ioniques et radicalaires. Les xanthates se sont avérés très utiles pour les additions radicalaires intramoléculaires et intermoléculaires et la cyclisation radicalaire. Dans le cas des xanthates primaires et secondaires, il est généralement nécessaire d'avoir un groupe fonctionnel supplémentaire pour augmenter la stabilité du radical. Les cétones jouent un rôle central dans la synthèse organique et la richesse de leur chimie est fréquemment exploitée dans la planification synthétique. Cependant, certaines réactions de base peuvent être problématiques. L'alkylation des énolates est l'un des piliers de la chimie des cétones. Elle souffre d'une concurrence telle que l'alkylation multiple, l'auto-condensation, la condensation aldolique et les éliminations. La chimie du xanthate peut résoudre ces difficultés par l'addition d'un radical-cétonyle à un alcène inactif pour donner le produit alkylé après élimination réductrice du xanthate. Une variété de dérivés d'acides aminés protégés peut être synthétisée sur la base de l'addition-transfert radicalaire dérivative de xanthates sur des alcènes. En général, la partie acide aminé masquée peut être placée sur l'alcène ou le partenaire xanthate ou sur les deux. Nous avons brièvement résumé la synthèse totale de produits naturels et de cibles particulières impliquant une séquence d'addition-fragmentation ou d'addition-cyclisation radicalaire médiée par les xanthates comme étape clé. Cette

méthode présente une variété d'avantages tels que des réactifs bon marché et facilement disponibles, des conditions de réaction douces, une procédure expérimentale simple et la compatibilité avec une large gamme de groupes fonctionnels.

Dans le chapitre 2: (±)-Eptazocine est largement utilisée pour la gestion des douleurs liées au cancer et des douleurs postopératoires. Shiotani, qui vient du Japon, a été le premier à synthétiser (±)-eptazocine dont la structure contient un centre de carbone quaternaire benzylique. Nous avons décrit une variété de stratégies antérieures, telles que la réaction de Heck, une réaction enzymatique, la cyclisation aza-prins et la cascade de Heck Catellani/redox-relay, pour synthétiser (±)-eptazocine. Ces stratégies souffrent de certaines limitations telles que des réactifs coûteux, des conditions de réaction difficiles, des procédures de synthèse complexes et des rendements médiocres. Les xanthates peuvent servir de médiateur pour une séquence d'addition-fragmentation ou d'addition-cyclisation radicalaire en tant qu'étape clé qui peut être utilisée pour la synthèse de produits naturels ou de cibles particulières. Trois voies différentes vers la (±)-eptazocine impliquant la séquence d'addition-cyclisation radicalaire comme étape clé ont été développées. Les méthodes de synthèse que nous avons développées présentent certains avantages : (a) les conditions de réaction sont douces et la procédure expérimentale est simple et sûre ; (b) aucun métal de transition n'est impliqué dans la réaction ; (c) le réactif et la plupart des matières premières sont bon marché et la réaction est facile à mettre à l'échelle. Bien que la (±)-eptazocine n'ait pas pu être synthétisée avec succès, son squelette central de centre de carbone quaternaire benzylique a été construit. Les principaux défis de la synthèse totale de la (±)-eptazocine sont la réaction de décarboxylation et la réaction de Mannich.

Dans le chapitre 3, nous avons décrit une variété de méthodes précédentes pour synthétiser des 1,3-dithiane-2-ones et des 1,3-dithiolan-2-ones. Ces méthodes souffrent de certaines limitations telles que la nécessité d'utiliser des réactifs toxiques, des conditions de réaction difficiles, des substrats limités et des rendements faibles.

Nous avons développé trois voies d'accès pratiques, convergentes et peu coûteuses aux 1,3-dithiane-2-ones, basées sur l'addition radicalaire de xanthates à des oléfines portant un groupe partant ou fonctionnel convenablement situé. En outre, un mécanisme de réaction plausible a été proposé. Ceux-ci peuvent être facilement convertis en 1,2-dithiolanes par hydrolyse médiée par une base et une oxydation médiée par  $MnO_2$ . Nous avons développé une voie convergente vers les 1,3-dithiolan-2-ones basée sur l'addition radicalaire des xanthates aux acétates allyliques. Une réaction inhabituelle a eu lieu conduisant à la formation inattendue de lactones et un mécanisme de réaction plausible a été proposé. Les méthodes que nous avons développées présentent certains avantages : (a) les voies de synthèse sont très courtes ; les matières premières et les réactifs sont bon marché ; (b) une grande variété de groupes fonctionnels différents peut être tolérée et les conditions de réaction sont douces ; (c) cette méthode est économique en atomes puisque les deux atomes de soufre des xanthates se retrouvent dans les produits. Les 1,3-dithiols et 1,2-dithiols dérivés des 1,3-dithiane-2-ones et 1,3-dithiolan-2-ones correspondants ont de nombreuses applications.



Dans la section expérimentale (au chapitre 4), les 98 produits des chapitres 2 et 3 ont été préparés par les méthodes générales correspondantes et caractérisés par  $^1H$  NMR,  $^{13}C$  NMR, IR, HRMS et par point de fusion pour les produits solides.

En résumé, le processus de transfert de xanthate peut apparaître comme l'un des outils



synthétiques les plus puissants pour synthétiser les 1,3-dithiane-2-ones, le précurseur de la (±)-eptazocine, 1,3-dithiolan-2-ones à partir d'oléfines. Cette méthode sans métal se caractérise par des réactifs bon marché et facilement disponibles, une procédure expérimentale simple et sûre, des conditions de réaction douces, une bonne tolérance aux groupes fonctionnels et un bon champ d'application du substrat.

## General Introduction

My PhD research projects are mainly related to the radical chemistry of xanthates and their applications in synthesis. They are accomplished under the supervision of Prof. Samir Z. Zard in the Laboratoire de Synthèse Organique in Ecole Polytechnique. This manuscript consists of three chapters and an experimental section.

In chapter 1, the radical chemistry of xanthates is used as a powerful tool for the creation of carbon-carbon bonds. The discovery, general concept and mechanism of the radical chemistry of xanthates were briefly introduced. This chapter presented various approaches for the preparation of primary, secondary and tertiary xanthates.

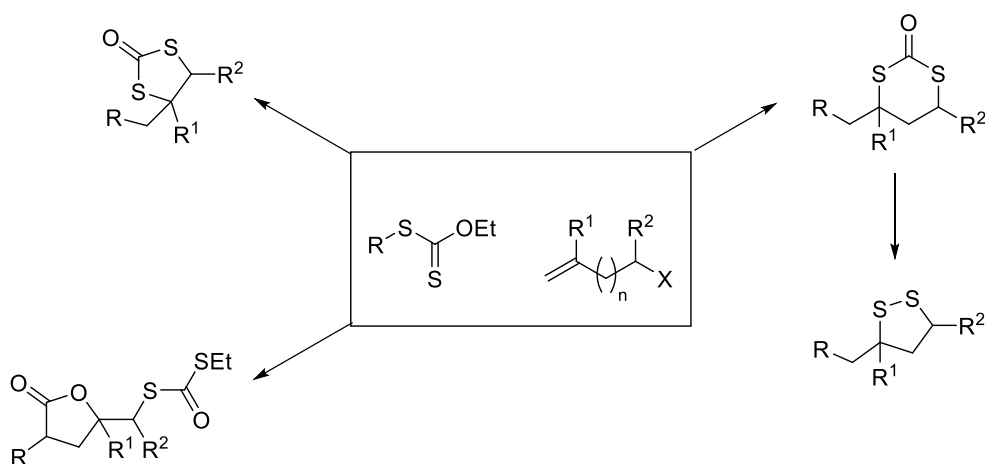
Xanthates are mainly prepared by ionic and radical methods. Xanthates have proved to be widely useful for intramolecular, intermolecular radical additions and radical cyclization. In the case of primary and secondary xanthates, it is usually necessary to have an extra functional group to increase the stability of the radical. Ketones play a central role in organic synthesis and their rich chemistry is frequently exploited in synthetic planning. However, some basic reactions can be problematic. The alkylation of enolates is one of the backbones of ketones chemistry. It suffers from competing such as multiple alkylations, self-condensations, aldol condensations and eliminations. Xanthate chemistry can solve these difficulties by the addition of a  $\alpha$ -ketonyl radical to an inactive alkene to afford the alkylated product after reductive removal of the xanthate. A variety of protected amino acid derivatives can be synthesized based on the degenerative radical addition-transfer of xanthates onto alkenes. In general, the masked amino acid moiety can be placed on the alkene or the xanthate partner or on both. We briefly summarized the total synthesis of natural products and particular targets involving xanthates mediated radical addition-fragmentation or addition-cyclization sequence as the key step. This method features a variety of advantages such as cheap and readily available reagents, mild reaction conditions, a simple experimental procedure and compatibility with a wide range of functional

groups.

In chapter 2: (±)-Eptazocine is widely used for the management of cancer-related and postoperative pain. Shiotani, who come from Japan, first synthesized (±)-eptazocine which contains a benzylic quaternary carbon center in structure. We described a variety of previous strategies, such as Heck reaction, an enzymatic reaction, aza-prins cyclization and Catellani/redox-relay Heck cascade, to synthesize (±)-eptazocine. These strategies suffer from some limitations such as expensive reagents, harsh reaction conditions, complex synthetic procedures and poor yields. Xanthates can mediate radical addition-fragmentation or addition-cyclization sequence as the key step, which can be utilized in synthesis of natural products or particular targets. Three different routes to (±)-eptazocine involving the radical addition-cyclization sequence as the key step were developed. The synthetic methods we developed have some advantages: (a) the reaction conditions are mild and the experimental procedure is simple and safe; (b) no transition metals are involved in the reaction; (c) the reagent and most of starting materials are cheap and the reaction are easy to scale up. Although (±)-eptazocine could not be successfully synthesized, its core skeleton of benzylic quaternary carbon center has been constructed. The major challenges of achieving total synthesis of (±)-eptazocine are decarboxylation reaction and Mannich reaction.

In chapter 3, we described a variety of previous methods to synthesize 1,3-dithiane-2-ones and 1,3-dithiolan-2-ones. These methods suffer from some limitations such as necessity of using toxic reagents, harsh reaction conditions, narrow substrates scope and poor yields. We developed three practical, convergent, and cheap routes to 1,3-dithiane-2-ones based on the radical addition of xanthates to olefins bearing a suitably located leaving or functional group. In addition, its plausible reaction mechanism was proposed. These can be readily converted into 1,2-dithiolanes by base mediated hydrolysis and MnO<sub>2</sub> mediated oxidation. We

developed a convergent route to 1,3-dithiolan-2-ones based on the radical addition of xanthates to allylic acetates. An unusual reaction took place leading to the unexpected formation of lactones and its plausible reaction mechanism was proposed. These methods we developed have some advantages: (a) the synthetic routes are very short; starting materials and reagents are cheap; (b) a broad variety of different functional groups can be tolerated and the reaction conditions are mild; (c) it is atom economical since both sulfur atoms of the xanthates end up in the products. The 1,3-dithiols and 1,2-dithiols derived from the corresponding 1,3-dithiane-2-ones and 1,3-dithiolan-2-ones have numerous applications.



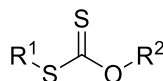
In the experimental section (in chapter 4), the 98 products in chapter 2 and 3 were prepared by the corresponding general methods and characterized by  $^1H$  NMR,  $^{13}C$  NMR, IR, HRMS and melting point for the solid products.

In summary, the xanthate transfer process can emerge as one of the most powerful synthetic tools to synthesize the 1,3-dithiane-2-ones, the precursor of ( $\pm$ )-eptazocine, 1,3-dithiolan-2-ones starting with olefins. This metal-free method features cheap and readily available reagents, a simple and safe experimental procedure, mild reaction conditions, good functional group tolerance and good substrate scope.

# Chapter 1. The Radical Chemistry of Xanthates

## 1.1 Introduction

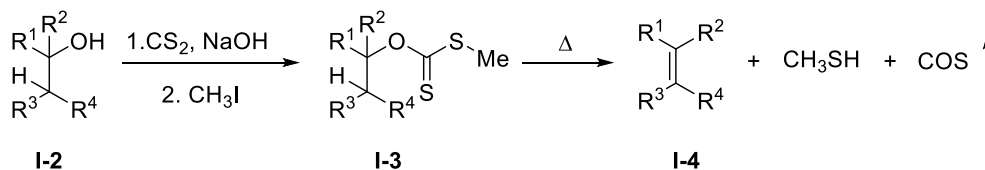
The more systematic and less evocative names of xanthates are dithiocarbonates or carbonodithioates. Xanthates have been known for almost two centuries, and they have common structural features as shown in **Scheme 1-1**. In 1822, Zeise and co-workers first reported the xanthate salt, but their chemistry remained largely unexplored compared to other functional groups.<sup>1</sup> Organic chemists paid little attention to the chemistry of xanthates for a long time, until recently when it was found to be important in radical reactions.



I-1

**Scheme 1-1.** Structure of the xanthate

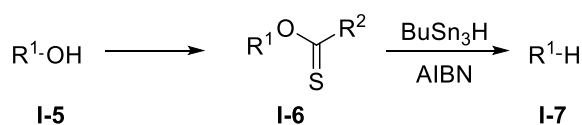
Xanthates were initially used in the Chugaev elimination<sup>2</sup>, which readily produces alkenes and thiols upon heating as shown in **Scheme 1-2**. In 1965, Okawara and co-workers reported that *S*-benzyl xanthate can be used as photosensitizer for the polymerization of vinyl monomers.<sup>3</sup> In 1975, Barton and co-workers reported the Barton-McCombie radical deoxygenation reaction, which facilitated the development of the radical chemistry of xanthates, especially for the modification of carbohydrates and radical sources from alcohols.<sup>4</sup> Over 35 years ago, Zard and coworkers deduced from a mechanistic study of the Barton-McCombie reaction that the carbon-sulfur bond of xanthates can be easily cleaved.<sup>5</sup> This resulted in the development of degenerative reversible transfer of xanthates, which has proved to be a powerful tool for the construction of carbon-carbon bonds.<sup>6</sup>



**Scheme 1-2.** Chugaev elimination

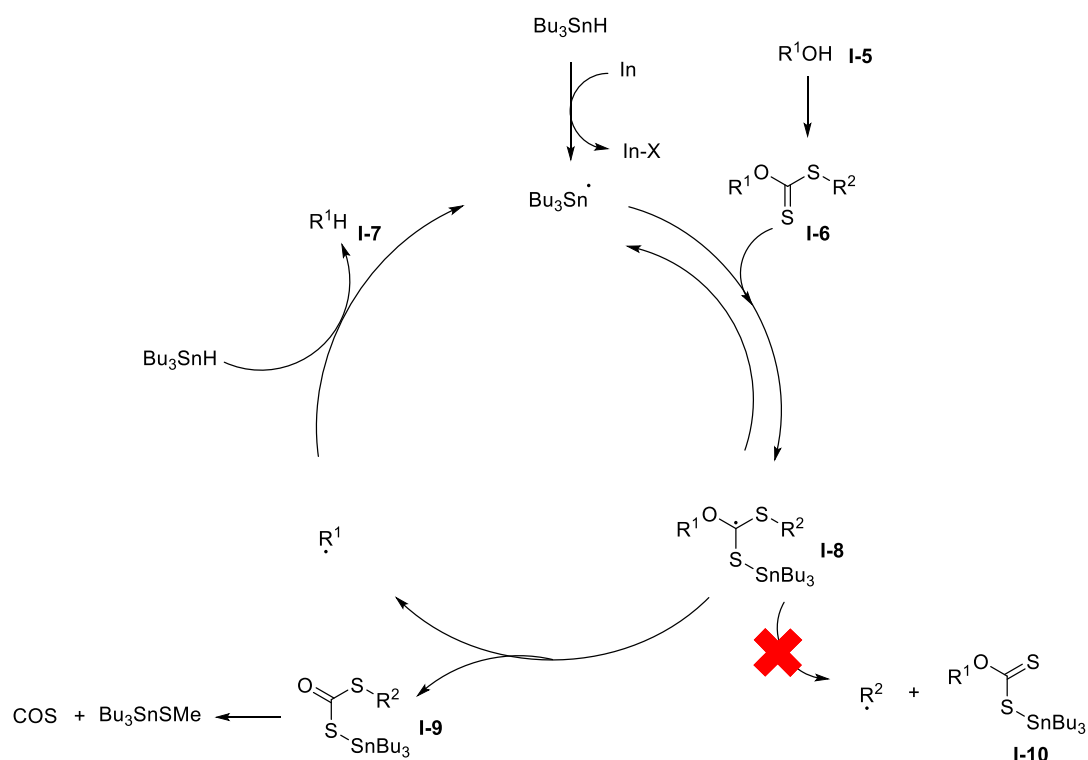
## 1.2 The Barton-McCombie deoxygenation

In 1975, Barton and co-workers first reported that xanthates derived from secondary alcohols could be deoxygenated with tributylstannane in the presence of AIBN to give the corresponding hydrocarbons in high yields via a remarkably powerful radical chain process (**Scheme 1-3**).<sup>4</sup> This method is widely used, especially in the field of carbohydrates and aminoglycosides.



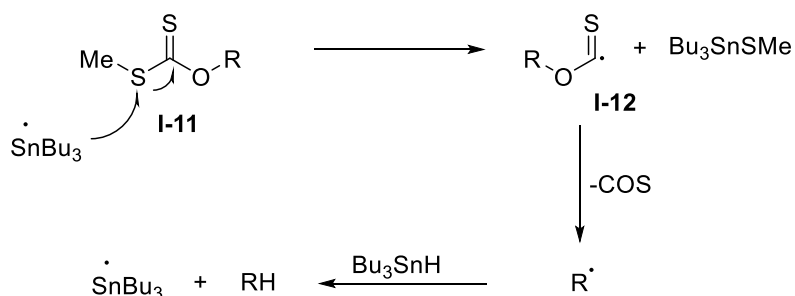
**Scheme 1-3.** Barton-McCombie deoxygenation

A reasonable mechanism of Barton-McCombie deoxygenation is shown in **Scheme 1-4**. First, a  $\text{Bu}_3\text{Sn}$  radical is generated in the presence of the initiator, which is followed by the addition of the tin radical on the thiocarbonyl group of the xanthate in a reversible way to form the intermediate **I-8**. It undergoes  $\beta$ -scission of the carbon-oxygen bond to form new alkyl radical  $\text{R}^1$ . The resulting alkyl radical  $\text{R}^1$  easily abstracts a hydrogen atom from the tributyltin hydride to furnish the desired alkane **I-7** and regenerates a new tributylstannyl radical, which propagates the radical chain. The limiting step in this process is the  $\beta$ -scission of the carbon-oxygen bond. The co-product **I-9** is unstable and releases carbon oxysulfide. The deoxygenation of primary alcohols usually requires higher reaction temperatures. Xanthates derived from tertiary alcohols easily undergo Chugaev elimination to give alkenes.



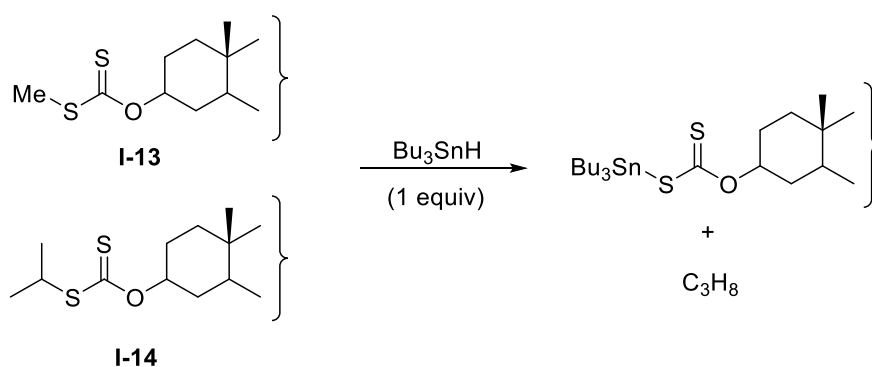
**Scheme 1-4.** The mechanism of Barton-McCombie deoxygenation

About a decade later, Barker and Beckwith questioned the mechanism of the Barton-McCombie deoxygenation and proposed another possible pathway, involving the  $S_H2$  attack of the stannyl radical on the sulfide sulfur atom basing their reasoning on a series of ESR experiments (**Scheme 1-5**).<sup>7</sup> They observed an ESR signal of an alkoxythiocarbonyl radical **I-12** when a mixture of a xanthate and hexabutylstannane was irradiated with UV light.



**Scheme 1-5.** The Beckwith-Barker mechanism

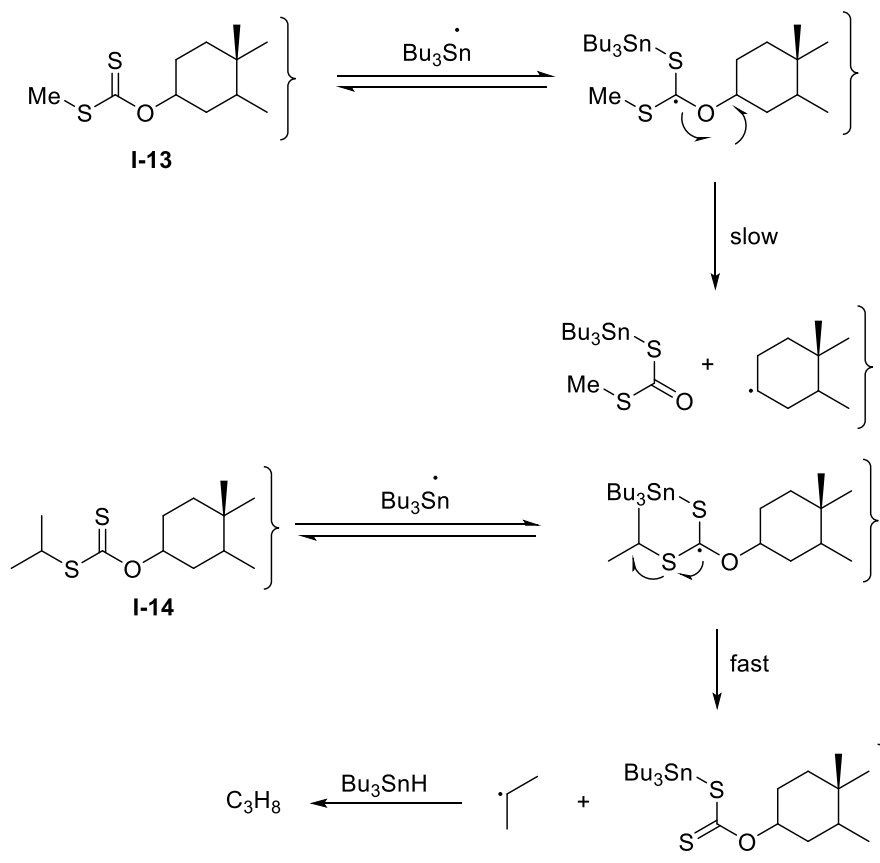
To gain further insight into these two possible mechanisms, a competition experiment was designed by the Barton group.<sup>8</sup> A equimolar mixture of *S*-methyl- and *S*-2-propyl xanthates **I-13** and **I-14** was treated with one equivalent of tributylstannane, as shown in **Scheme 1-6**. If it proceeds by an  $S_H2$  attack of the stannyl radical on the sulfide sulfur atom, then steric hindrance should slow down the reaction rate of the *S*-2-propyl xanthate. If the thiocarbonyl group is the reaction center, then no significant difference in the reaction rates will be observed. It was unexpected that the result of the experiment was neither of the two possibilities. It turned out that the *S*-2-propyl xanthate reacted much faster than that of *S*-methyl xanthate, and the products were a cholestanyl xanthate and propane.



**Scheme 1-6.** The key competition experiment

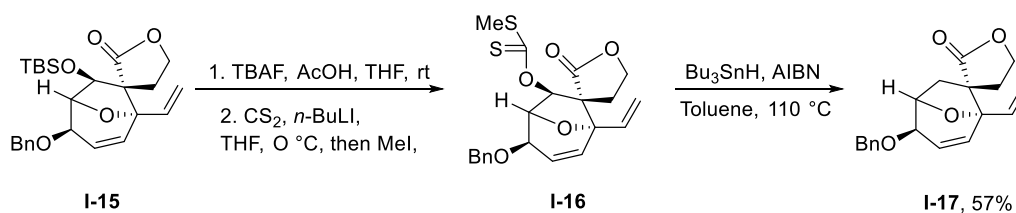
According to the results of this experiment, a mechanism was proposed, as shown in **Scheme 1-7**. Two conclusions could be drawn from the competition experiment. One is that the addition of the tin radical to the thiocarbonyl group of the xanthate is fast and reversible and the other one is that the rate-determining step is the  $\beta$ -scission of the carbon-oxygen or the carbon-sulfur bond. The reversible radical addition is not limited to stannyl radical but also other carbon radicals can be used instead.





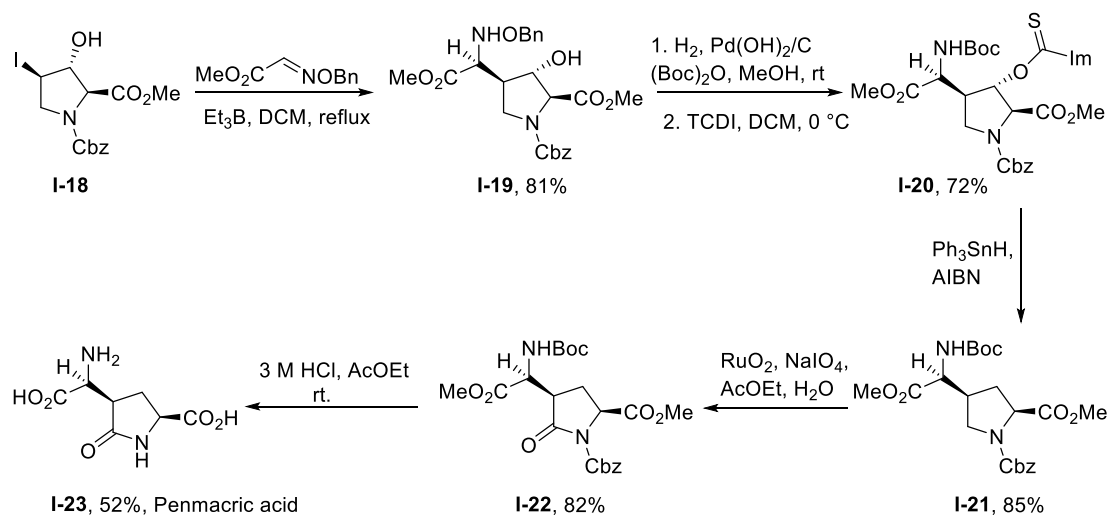
**Scheme 1-7.** Mechanistic rationale for the competition experiment.

The Barton-McCombie reaction is widely used for deoxygenation, since it is mild and tolerates many functional groups. The Barton-McCombie reaction is often used in the total synthesis of natural products. For example, in 2011, Nishikawa and co-workers successfully synthesized the polygalolide A starting from D-glucal using the Barton-McCombie reaction as the key step. The protected hydroxyl group was transformed into the corresponding xanthate and then treated with tributyltin hydride in the presence of AIBN to accomplish the desired deoxygenation (as shown in **Scheme 1-8**).<sup>9</sup>



**Scheme 1-8.** The key step in total synthesis of the polygalolide A

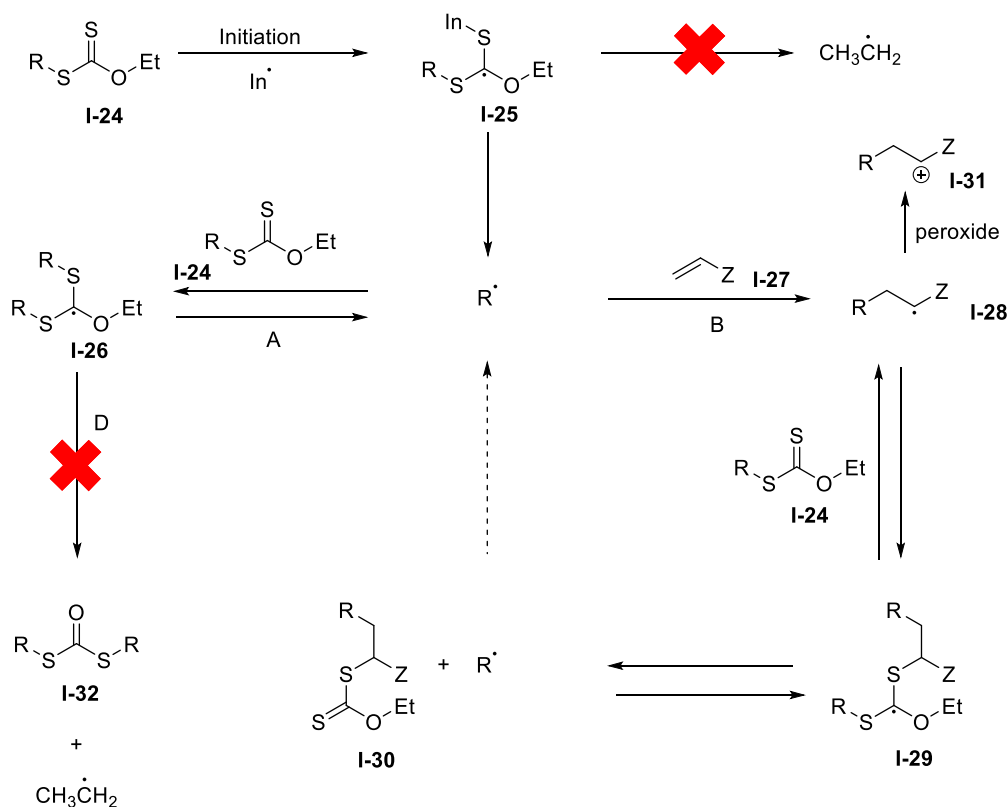
Takeaki and coworkers reported the total synthesis of penmacric acid and its stereoisomer starting from *trans*-4-hydroxy-L-proline using the Barton-McCombie reaction to efficiently remove the hydroxyl group.<sup>10</sup>



**Scheme 1-9.** Hydroxyl group reduction in the total synthesis of penmacric acid.

### 1.3 The degenerative xanthate transfer process

Following the study of the Barton-McCombie reaction mechanism, a new radical chemistry of xanthates based on the cleavage of the carbon–sulfur bond was developed. The group attached to the oxygen of the xanthate is generally a primary alkyl group to prevent cleavage of the C–O bond. The simplified mechanism for the xanthate transfer process is shown in **Scheme 1-10**. It illustrates the addition of a xanthate **I-24** to an alkene **I-27**.



**Scheme 1-10.** The simplified mechanism for the xanthate transfer process

In the initiation process, the radical  $\text{In}$  readily adds to the thiocarbonyl group of the starting xanthate **I-24** to generate radical intermediate **I-25**, which in turn produces a small amount of the radical  $\text{R}$ . This radical has the choice of either reacting with the starting xanthate **I-24** (path A) **or** reacting with the olefin **I-27** (path B). The reaction of radical  $\text{R}$  with the starting xanthate **I-24** is degenerate (path A). The effective lifetime of radical  $\text{R}$  is increased in the medium since it is reversibly stored as radical **I-26**, which acts as a convenient reservoir for the radical  $\text{R}$ . The active radical  $\text{R}$  can readily add to un-activated olefin **I-27** to give the adduct radical **I-28** (path B), which is in turn reversibly captured by the thiocarbonyl group of the starting xanthate **I-24** to generate intermediate **I-29**. The latter then undergoes fragmentation to generate another xanthate **I-30** and a new radical  $\text{R}$ , which propagates the chain. In this process, a new carbon-carbon and a new carbon-sulfur bond are constructed.

In this degenerative transfer of xanthates, the  $\beta$ -scission of the carbon-oxygen bond of the intermediate radical **I-26** is unlikely because it would lead to a thermodynamically

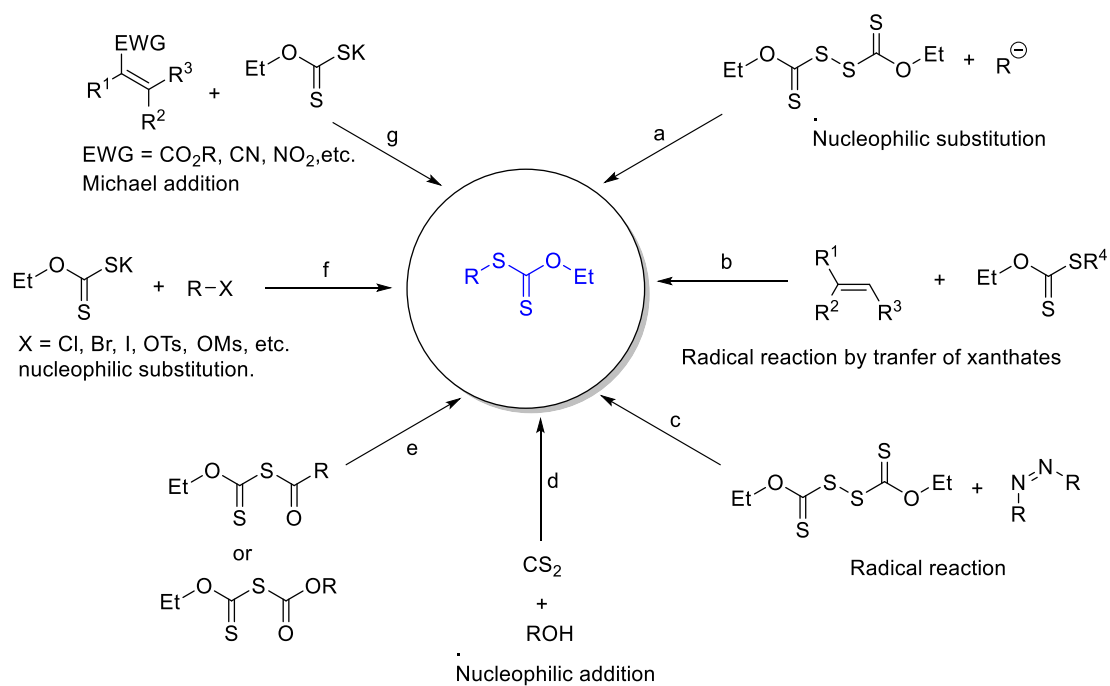
less stable ethyl radical and requires rupture of a strong bond. In path A, radical R is not consumed, so no competition occurs between path A and B. The relative stabilities of the radical R and adduct radical **I-28** play an important role in allowing control of the process and avoiding the formation of unwanted oligomers.

There are many advantages in this chemistry of degenerative transfer of xanthates.

- a. The reagent: potassium *O*-ethyl xanthate and the common initiator DLP (dilauroyl peroxide), are cheap, readily available, easy to handle, safe and stable to air.
- b. No toxic transition metals are involved in the reaction system.
- c. The radical additions can be carried out under high concentration, typically 1 to 4 M. and even neat, without solvent in some cases.
- d. A variety of solvents (benzene, cyclohexane, dichloroethane, toluene, chlorobenzene and so on) can be used, including the environmentally friendly water. Ethyl acetate is often the most convenient.
- e. The reaction conditions are mild and the experimental procedure is usually simple
- f. It is easy to scale up.
- g. Because all of the starting materials used in the reaction process are converted into the final product, the reactions are highly atom economical.
- h. Various functional groups can be tolerated and a wide diversity of structures can be assembled.
- i. The product, being also a xanthate, can be used as a starting point for another radical sequence or modification using the rich chemistry of sulfur.

## 1.4 Preparation of xanthates

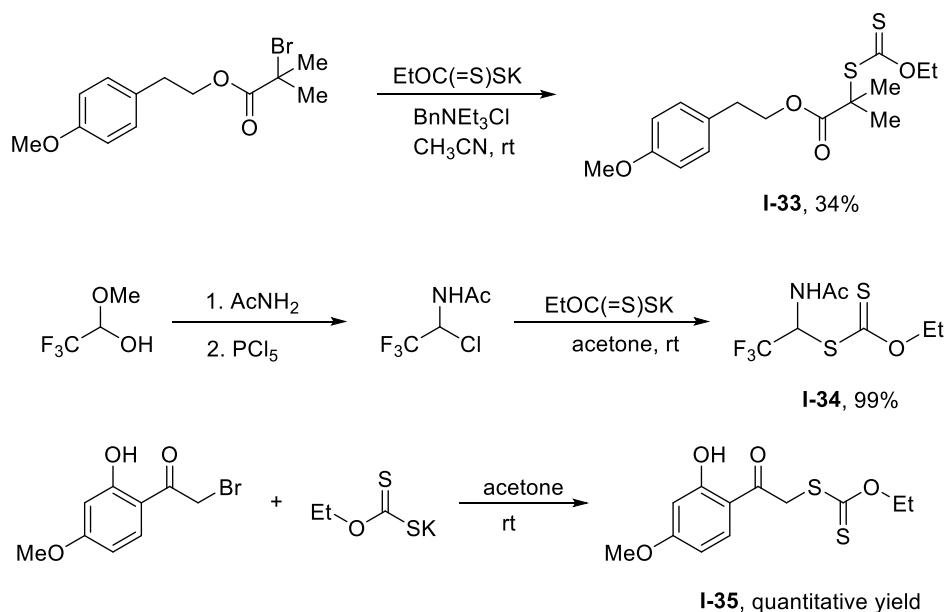
There are numerous methods for preparing xanthates with different functional groups. We introduce common methods for synthesizing xanthates such as ionic methods and radical methods. Some methods of synthesizing xanthates are summarized in **Scheme 1-11**.



**Scheme 1-11.** Some methods for preparing xanthates

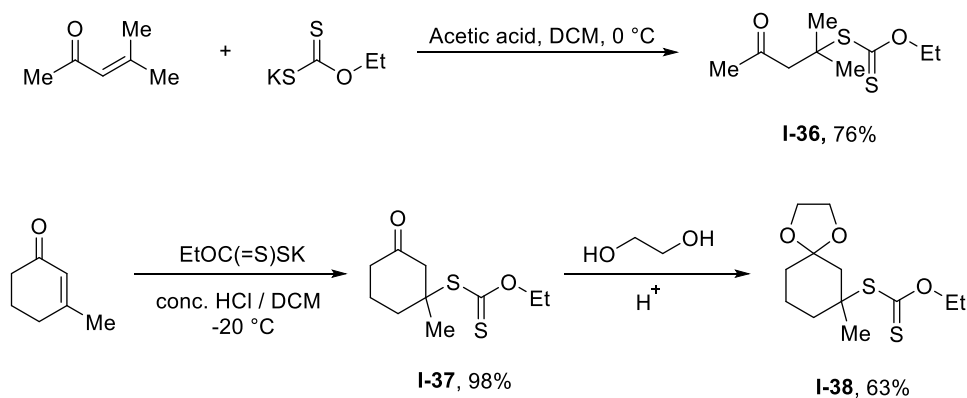
### 1.4.1 Xanthates prepared by ionic methods

Direct nucleophilic substitution is the most common method of preparation xanthates, which is suitable for the preparation of primary, secondary or tertiary xanthates (**Scheme 1-12**). However, only a handful of simple tertiary xanthates are prepared by direct nucleophilic substitution. For example, the tertiary xanthate **I-33** was prepared by standard nucleophilic substitution.<sup>11</sup> Its modest yield reflects the difficulty of the process. The secondary xanthate **I-34** was obtained in excellent yield from the commercially available 2,2,2-trifluoro-1-methoxyethan-1-ol as starting material<sup>12</sup>; the primary xanthate **I-35** was prepared in quantitative yield from the cheap 2-bromo-1-(2-hydroxy-4-methoxyphenyl)ethan-1-one.<sup>13</sup>



**Scheme 1-12.** Synthesis of primary, secondary and tertiary xanthates by direct substitution of a halide

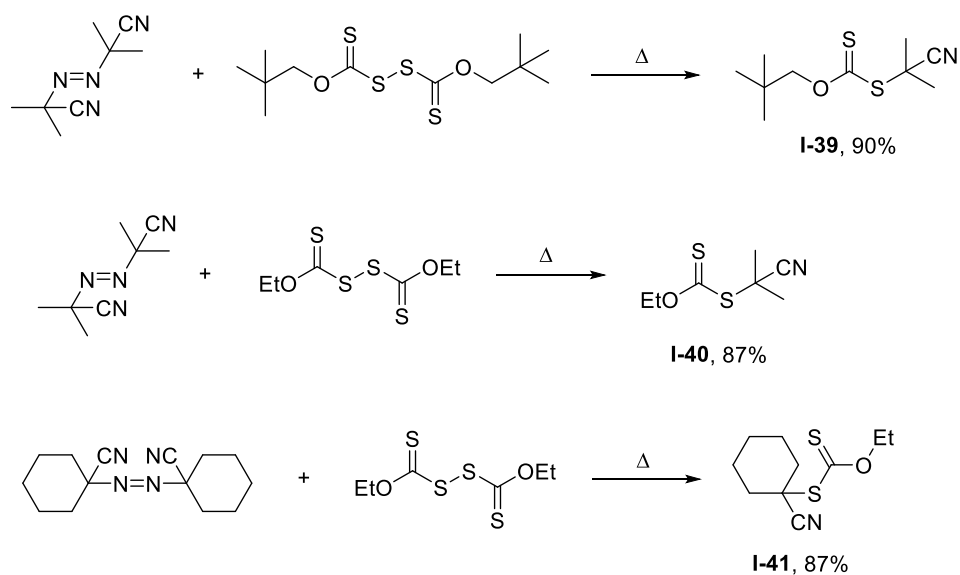
Tertiary xanthates can be prepared by Michael addition of xanthate salts to electrophilic alkenes in the presence of acid, as shown in **Scheme 1-13**. Xanthate **I-36** was prepared in good yield by the reaction of mesityl oxide with potassium *O*-ethyl xanthate in acetic acid.<sup>14</sup> As the Michael addition is reversible, it must be performed under acidic medium to prevent retro-Michael reaction. Xanthate **I-37** was obtained in excellent yield from 3-methylcyclohex-2-en-1-one. It is sensitive to the retro-Michael process and is best converted into an acetal to avoid elimination.<sup>14</sup>



**Scheme 1-13.** Synthesis of tertiary xanthates by Michael addition

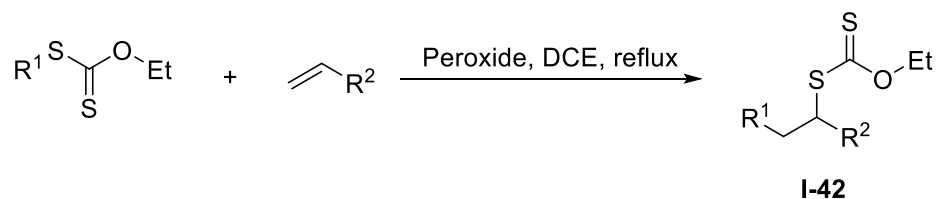
## 1.4.2 Xanthates prepared by radical methods

Radical processes constitute effective routes for the preparation of functional tertiary xanthates. For example, various tertiary *S*-alkyl dithiocarbonyl derivatives could be obtained easily in good yield by thermal decomposition of diazo compounds with bis-dithiocarbonate (**Scheme 1-14**).<sup>15</sup> This method is highly atom economical and can be extended to a variety of diazo precursors with more complex structures.



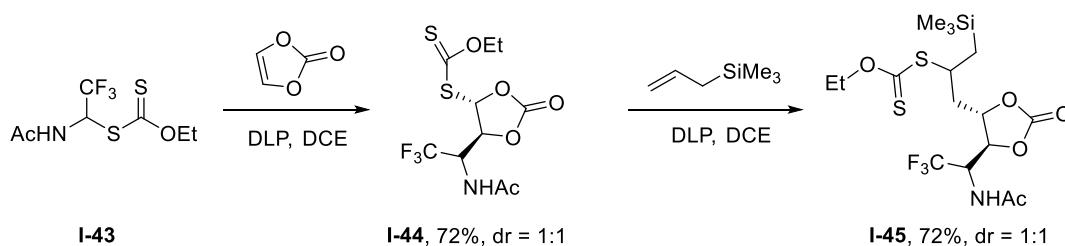
**Scheme 1-14.** Tertiary xanthates by thermal decomposition of diazo compounds

Complex xanthates decorated by numerous functional groups are prepared by radical addition of xanthates to inactive alkenes, as shown in **Scheme 1-15**. The resulting xanthate can be used as a starting point for another radical sequence or it can be modified using rich chemistry of sulfur.



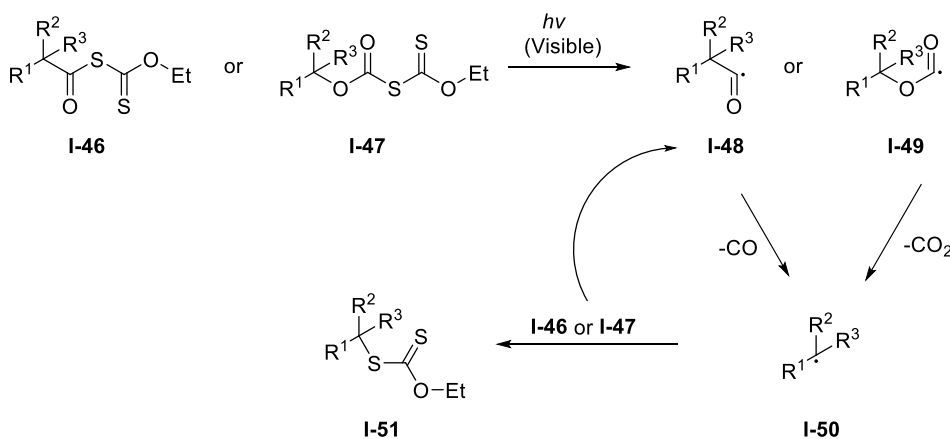
**Scheme 1-15.** Xanthates prepared by a radical addition.

For example, the readily available xanthate **I-43** efficiently adds to vinylidene carbonate to furnish xanthate **I-44**, which can then be implicated in a second addition to allyl trimethylsilane to give the densely functionalized xanthate **I-45**, as shown in **Scheme 1-16**.<sup>12</sup>



**Scheme 1-16.** Densely functionalized xanthates prepared by a radical addition

Sometimes the route to tertiary xanthates relies on the generation of acyl or alkoxy-carbonyl radical from tertiary *S*-acyl or *S*-alkoxy-carbonyl-xanthates. These radicals undergo loss of CO and CO<sub>2</sub> respectively to afford alkyl radicals, which then transfer a xanthate group gives tertiary xanthates (**Scheme 1-17**).

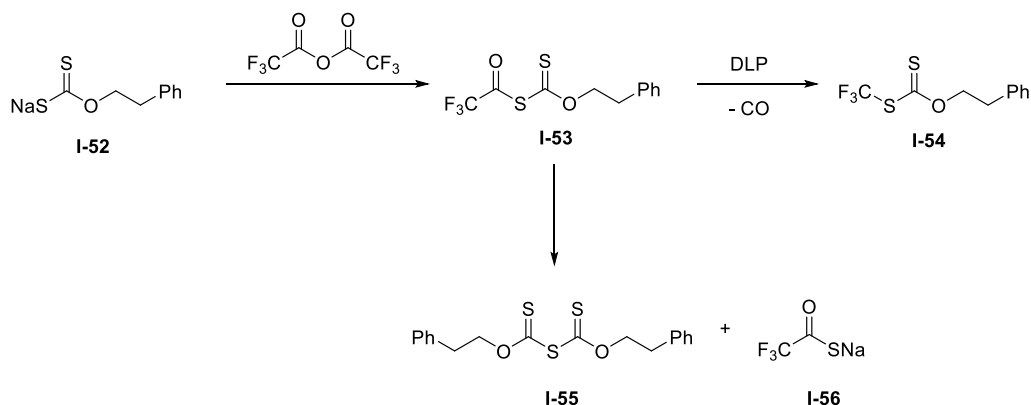


**Scheme 1-17.** Tertiary xanthates by radical decarbonylation and decarboxylation.

For example, trifluoromethyl xanthates were prepared in moderate yield by decarbonylation of *S*-trifluoroacetyl xanthate in the presence of DLP triggering the radical chain reaction, as shown in **Scheme 1-18**.<sup>16</sup> The reason *O*-phenethyl xanthate is used rather than the simpler *O*-ethyl xanthate is to avoid handling a potentially

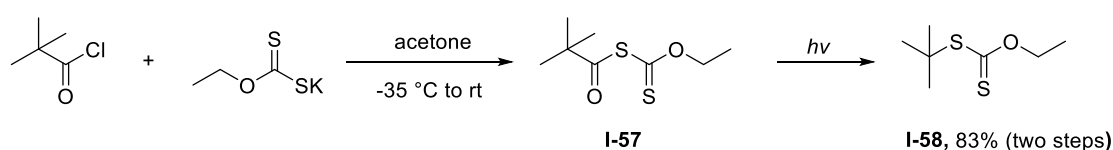


volatile and perhaps malodorous substance. The xanthate salt is used as the limiting reagent because the *S*-acyl xanthate **I-53** can be completely decomposed by an ionic chain reaction to give xanthic anhydride **I-55** and sodium thiofluoroacetate **I-56**. This method proved to be useful and effective because the *S*-trifluoroacetyl xanthate could not be obtained by nucleophilic substitution.



**Scheme 1-18.** Xanthates by radical decarbonylation

The *S*-*tert*-butyl-*O*-ethyl-xanthate could be also prepared on large scale by reaction of pivaloyl chloride with potassium *O*-ethyl-xanthate followed by irradiation with a tungsten filament lamp, as shown in **Scheme 1-19**.<sup>17</sup>



**Scheme 1-19.** Tertiary xanthates by radical decarbonylation

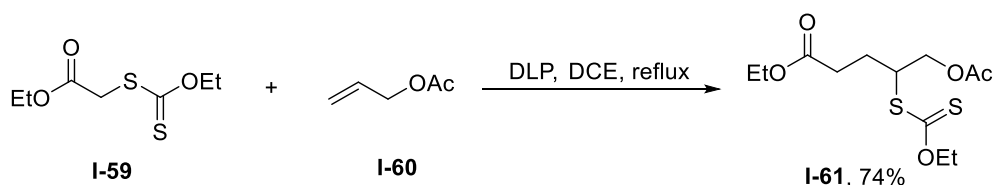
## 1.5 Application of xanthates

Since xanthates have special chemical properties, they can undergo various chemical reactions such as intermolecular additions, ring-closure on internal alkenes, ring-closure on aromatic derivatives, fragmentation reactions and transformation of xanthates into other functional groups.

### 1.5.1 Intermolecular additions

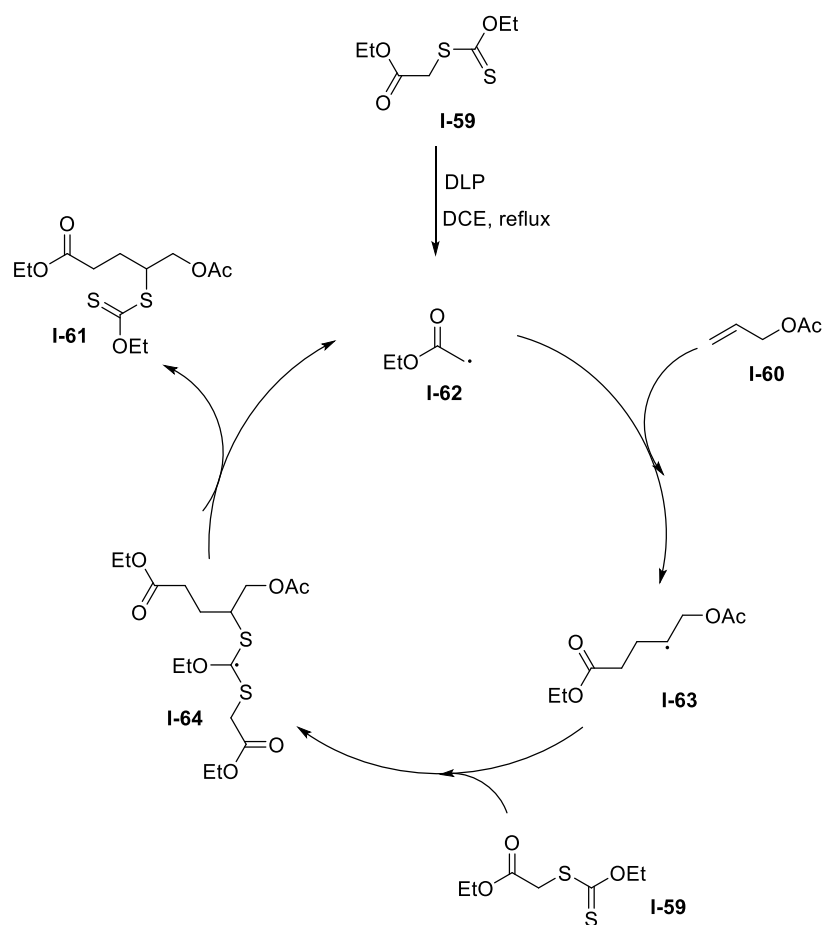
Xanthates activated by initiators provide primary, secondary or tertiary radicals, which react efficiently with various unactivated olefins to furnish the corresponding adducts. In the case of primary and secondary xanthates, it is usually necessary to have an extra functional group to increase the stability of the radical. Xanthates bearing various functional groups such as ketones, esters, nitriles, boronates and so on, can participate in intermolecular radical additions to construct new carbon-carbon bonds.

For example, xanthate **I-59** can generate a primary radical, which is added efficiently to the un-activated alkene **I-60** to give the corresponding adduct **I-61** in good yield, as shown in **Scheme 1-20**.<sup>18</sup>



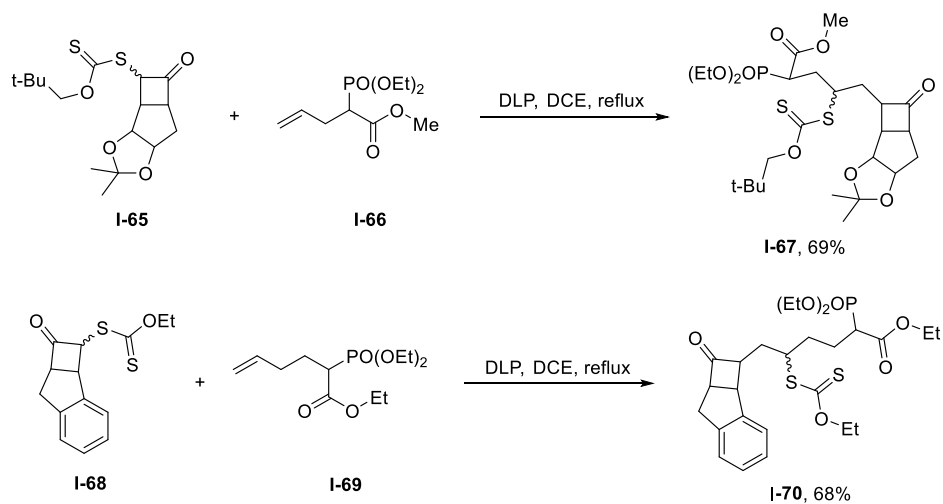
**Scheme 1-20.** Addition of primary radicals to an alkene

The starting xanthate **I-59** generates radical **I-62** in the presence of DLP. Radical **I-62** then adds to an un-activated olefin to generate the adduct radical **I-63**. Since the adduct radical **I-63** is less stable than the radical **I-62** derived from the starting xanthate **I-59**, no oligomers are formed. The intermediate radical **I-64** undergoes fragmentation to give an adduct **I-61** and returns to the starting radical **I-62**. The relative stabilities of the starting and adduct radicals plays a crucial role in the xanthate addition process. The mechanism of primary radical to olefins is shown in **Scheme 1-21**.



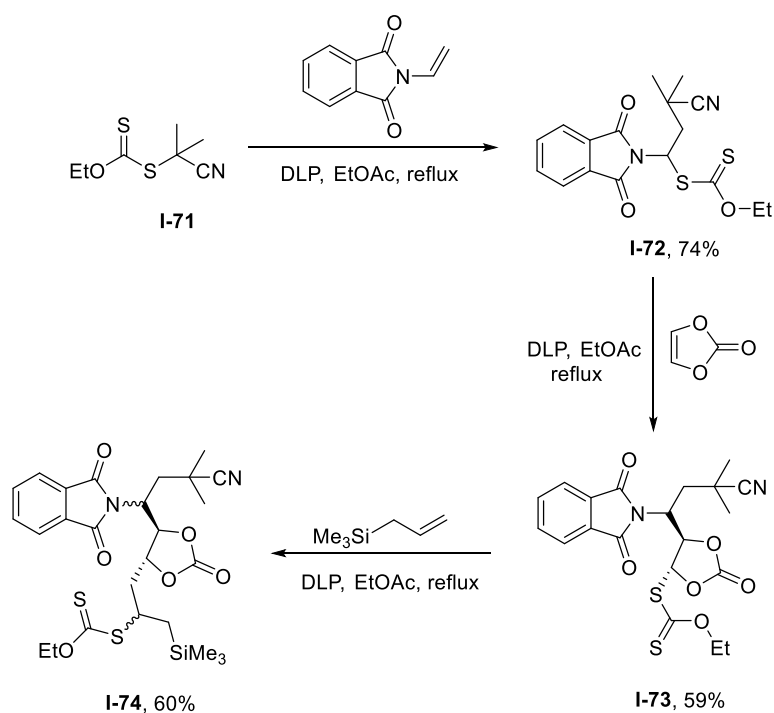
**Scheme 1-21.** The mechanism of addition of primary radicals to olefins

$\alpha$ -Xanthyl cyclobutanones undergo intermolecular secondary radical additions to olefins with a variety of functional groups to give the corresponding adducts (**Scheme 1-22**).<sup>19</sup>



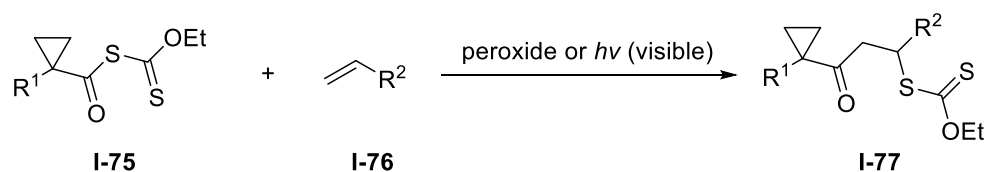
**Scheme 1-22.** Addition of secondary radicals to alkenes

Compounds with complex structures can be obtained by sequential addition of hindered tertiary xanthates to three different olefins using the same experimental conditions, as shown in **Scheme 1-23**.<sup>20</sup> Since the relative stereochemistry is not controlled, there is no diastereoselectivity in this process.



**Scheme 1-23.** Sequential addition of tertiary radicals to three different alkenes

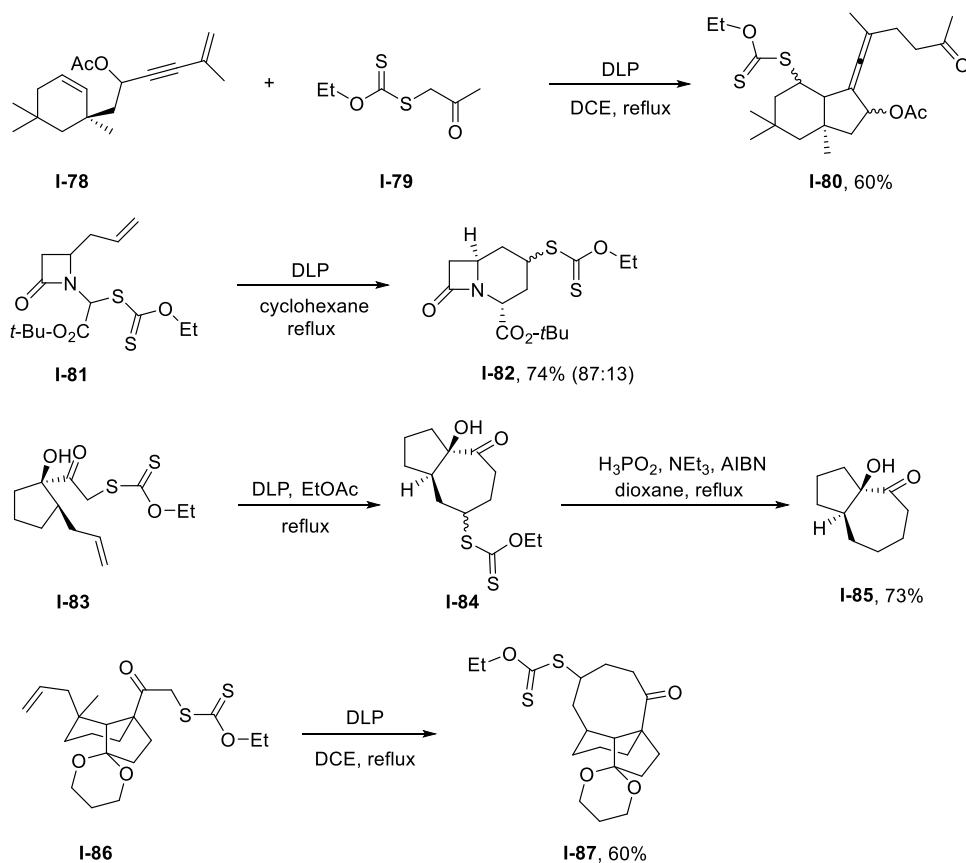
The special cyclopropylacetyl radicals derived from *S*-cyclopropylacetyl xanthates **I-75** undergo intermolecular additions to various olefins under initiation with peroxide or irradiation with visible light without loss of CO or ring opening, to give the corresponding adduct **I-77** (**Scheme 1-24**).<sup>21</sup> This approach provides a simple and flexible route to cyclopropyl ketones.



**Scheme 1-24.** Addition of special cyclopropylacetyl radicals to alkenes

## 1.5.2 Ring-closure onto internal alkenes

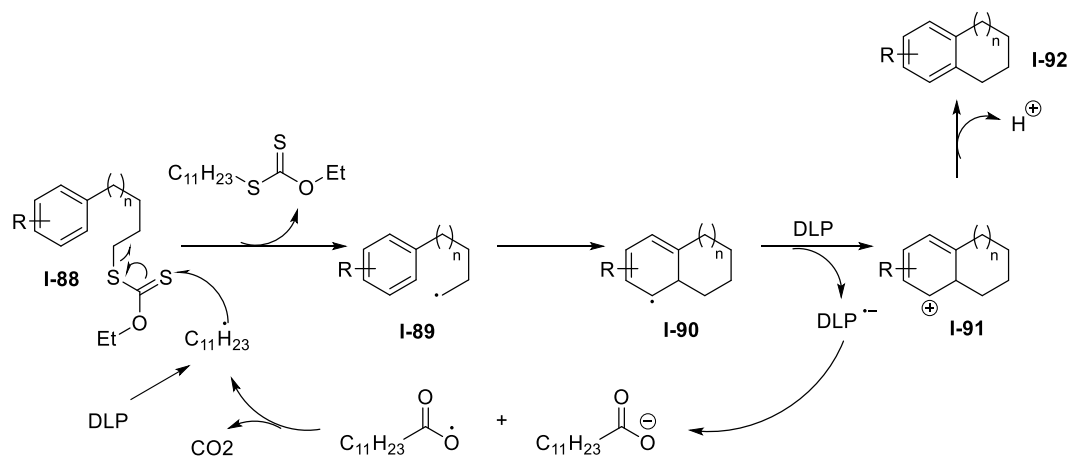
The degenerative xanthate transfer process is used as a useful tool for radical cyclization. If the molecule contains both xanthate groups and alkenyl groups in the proper position, it can undergo intramolecular radical addition-cyclization to give five, six, seven, or eight-membered ring compounds. For example, enynes **I-78** undergoes radical sequence of addition/cyclization with  $\alpha$ -xanthyl ketone **I-79** in the presence of a small amount of DLP in refluxing DCE to furnish *cis*-fused bicyclic adduct **I-80** as mixture of diastereoisomers.<sup>22</sup> Xanthate **I-81** undergoes intramolecular radical addition using a small amount of DLP to afford bicyclic  $\beta$ -lactam in good yield as 87:13 mixture of diastereoisomers.<sup>23</sup> Xanthate **I-83** was treated with a substoichiometric amount of DLP in refluxing ethyl acetate to give perhydroazulenone **I-84**, which was not purified. But reduced with hypophosphite to afford ketone **I-85** in 73% overall yield.<sup>24</sup> Xanthate **I-86** underwent an *8-endo-trig* cyclization in the presence of a small amount of DLP to afford tricyclic compound **I-87** in 60% yield.<sup>25</sup> Then some representative examples of ring-closure onto internal alkenes are shown in **Scheme 1-25**.



**Scheme 1-25.** Examples of ring-closure on internal alkenes

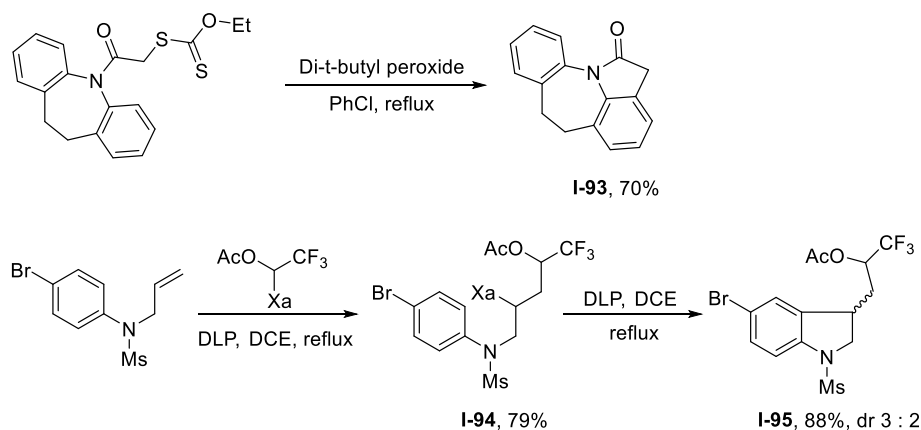
### 1.5.3 Ring-closure on aromatic derivatives

The intramolecular addition of xanthates to aromatic rings gives structures not containing xanthate groups. The mechanism of these ring-closures is shown in **Scheme 1-26**. Radical **I-89** derived from xanthate **I-88** reacts with the aromatic ring to generate cyclohexadienyl radical **I-90**, which is too stable to propagate the radical chain, but can be easily oxidized by DLP into the corresponding cation **I-91**. Loss of a proton finally produces the desired bicyclic structure **I-92**.



**Scheme 1-26.** The mechanism of ring-closure to aromatic rings

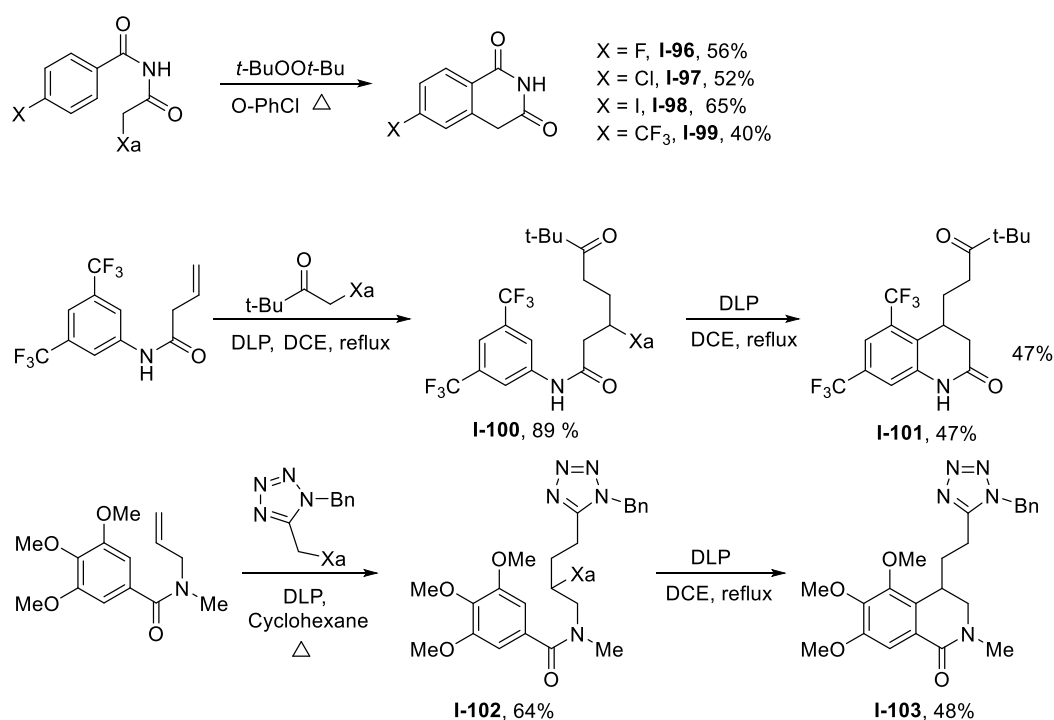
Indolones can be prepared in good yield by a direct radical ring closure to the aromatic ring.<sup>26</sup> Indoline can be obtained in excellent yield by an intermolecular radical addition of a xanthate to a protected *N*-allylaniline, followed by radical ring closure to the aromatic ring (**Scheme 1-27**).<sup>27</sup> Electron-donating and withdrawing groups on the aromatic rings are tolerated. The cyclization step to the aromatic ring requires the use of a stoichiometric amount of peroxide. Because it acts as both a initiator and a stoichiometric oxidant.



**Scheme 1-27.** Synthesis of indolones and indoline.

Various six-membered rings fused with aromatic rings can be prepared by a similar approach, as shown by the examples in **Scheme 1-28**. A noteworthy feature is that the cyclization takes place despite the absence of a substituent on the nitrogen.

Homophthalimides can be obtained by direct radical ring-closure to the aromatic ring.<sup>28</sup> The radical cyclization step is not significantly affected by the nature of the substituents on the aromatic ring. Dihydroquinolone **I-101** can be prepared in acceptable yield by an intermolecular addition to *N*-(3,5-bis(trifluoromethyl)phenyl)but-3-enamide followed by radical ring-closure to the aromatic ring.<sup>29</sup> This example is particularly interesting since aromatic rings with two trifluoromethyl groups are difficult partners when employing Friedel-Crafts and related electrophilic substitutions. The isomeric dihydroquinolones can also be obtained by the same strategy as illustrated by example **I-103**, where the biologically important tetrazole ring is introduced via the xanthate.<sup>30</sup>

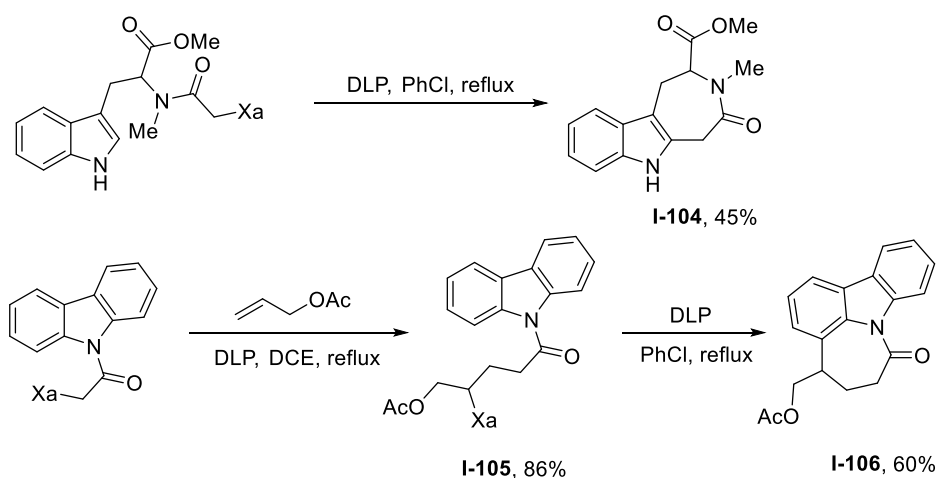


**Scheme 1-28.** Six membered ring-closure to aromatic rings.

The radical ring closure to an aromatic ring can even form a seven-membered ring, as demonstrated by the synthesis of benzazepinones, which can be prepared by radical ring-closure to the aromatic ring as the key step (**Scheme 1-29**).<sup>31</sup> This is a new route to synthesize aromatic compounds with complex structures containing an adjoining

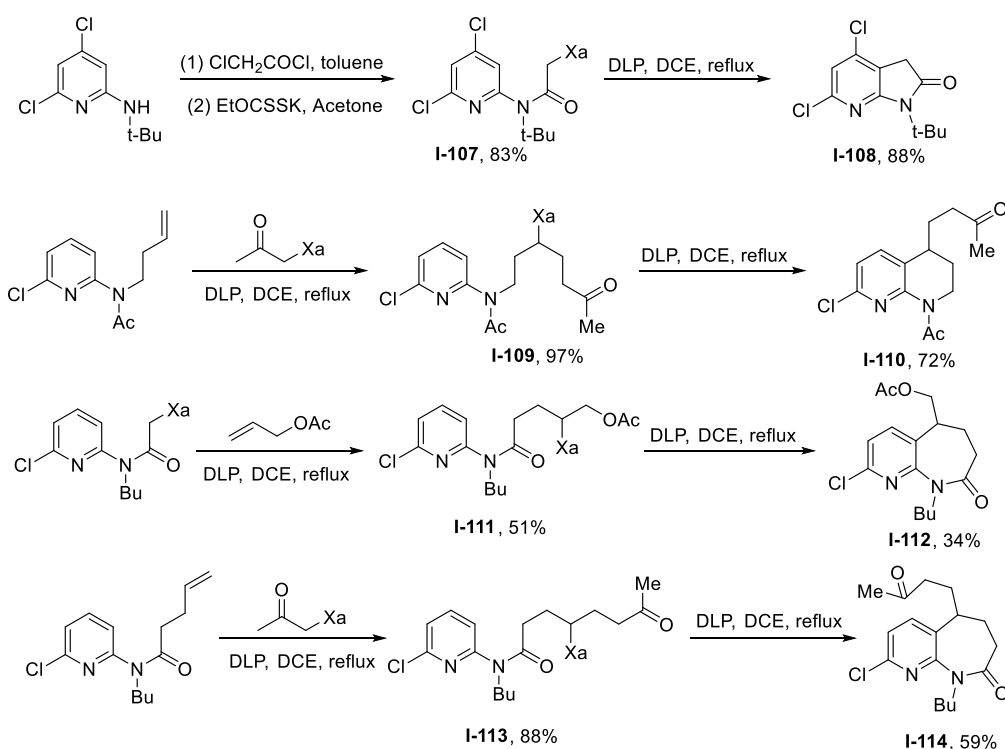


seven-membered rings.



**Scheme 1-29.** Examples of xanthates-mediated annelation of seven-membered rings.

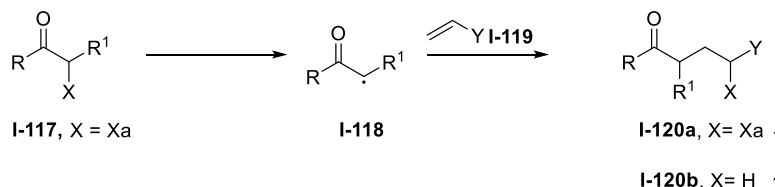
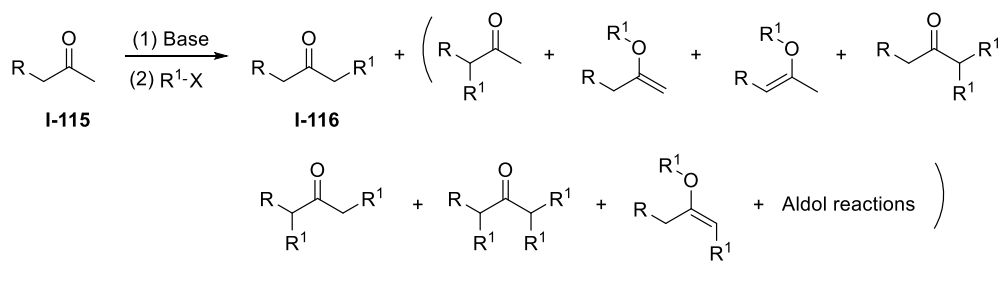
Bicyclic pyridine derivatives are heteroaromatic of significant medicinal importance. Compared to benzene analogues, such pyridine derivatives are not generally readily available. However, they can be prepared starting from various 2,6-dichloropyridines by the xanthate mediated intermolecular/cyclization sequence. Since the nitrogen in the pyridine ring is more electronegative as compared with the benzene ring, electrophilic aromatic substitution is difficult to accomplish. Some examples such as azaoxindoles, azaindoles and pyridoazepinones are presented in **Scheme 1-30**.<sup>32</sup> Five, six and sometimes even seven-membered rings can thus be easily assembled.



**Scheme 1-30.** Examples of ring closures to pyridines.

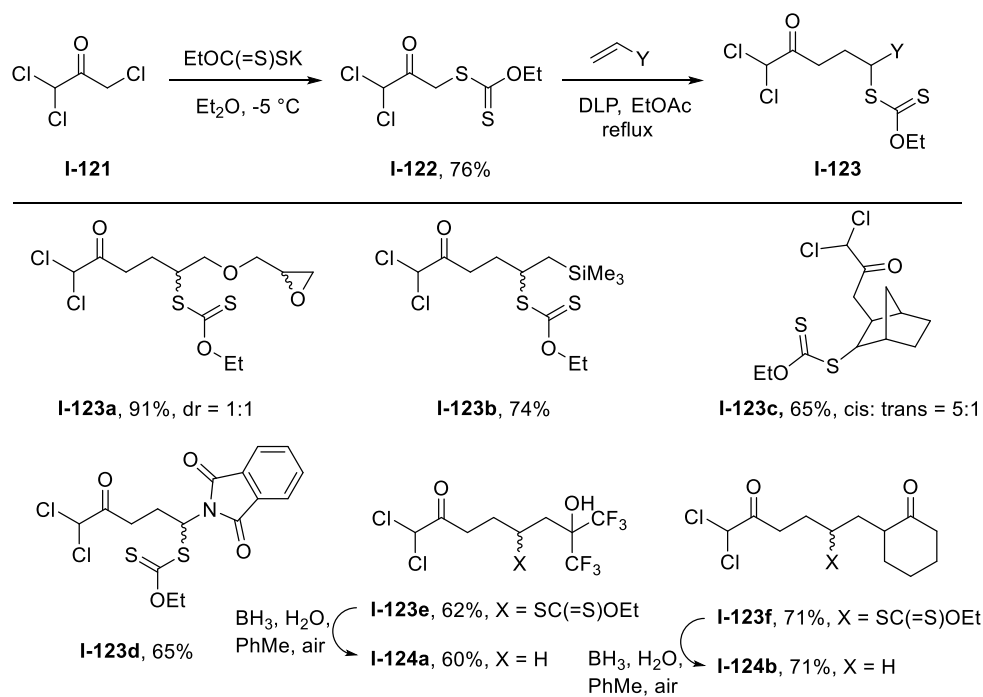
### 1.5.4 Xanthates route to ketones

Ketones play a central role in organic synthesis and their rich chemistry is frequently exploited in synthetic planning. The alkylation of enolates is one of the backbones of ketone chemistry. However, some basic reactions can be problematic. The alkylation of enolates suffers from competing, for example multiple alkylations, self-condensations, aldol condensations and competing eliminations. Xanthates chemistry can solve these difficulties by the addition of a  $\alpha$ -ketonyl radical **I-118** to an alkene **I-119** to afford the alkylated product after reductive removal of the xanthate (**Scheme 1-31**).



**Scheme 1-31.** Side products in the alkylation of ketones

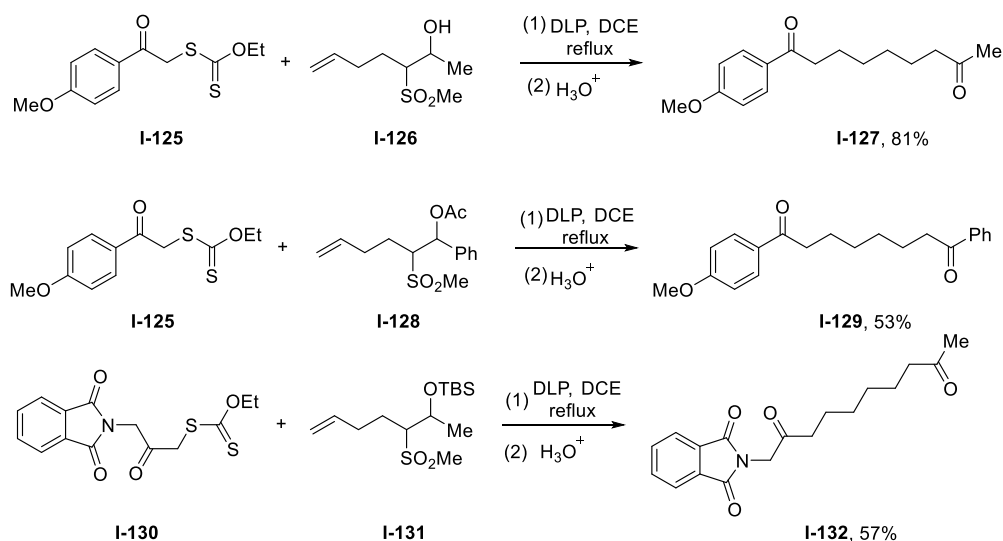
Examples of xanthate addition-transfer for the indirect regioselective monoalkylation of the base-sensitive dichloroacetone are presented in **Scheme 1-32**.<sup>33</sup> The radical addition of xanthate **I-122** to various olefins proceeded smoothly in the presence of DLP to furnish the corresponding dichloromethyl ketone **I-123**. A variety of useful functional groups in the olefins such as epoxides, trimethylsilane, ketones and alcohols can be tolerated. The xanthate groups in adducts can be removed using the triethylborane/water combination, as reported by Wood.<sup>34</sup>



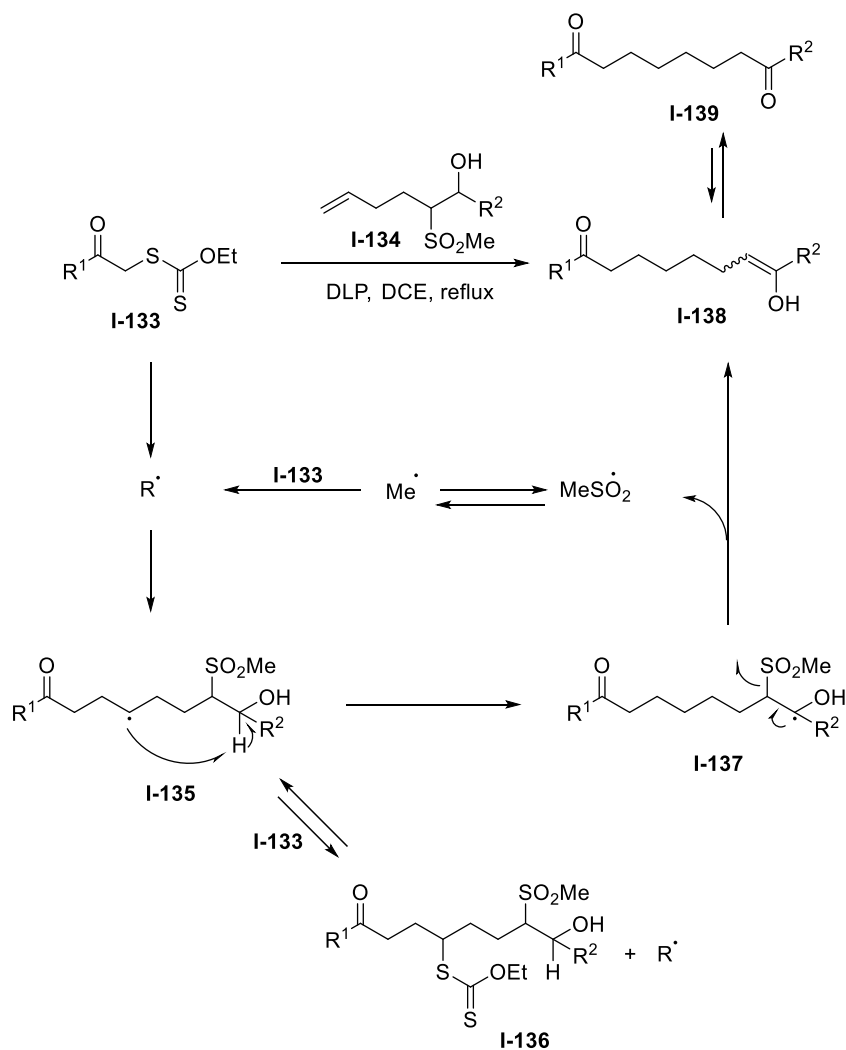
**Scheme 1-32.** Synthesis of dichloromethyl ketones.

1,8-Diketones were obtained in good yield by radical addition of  $\alpha$ -ketonyl xanthates

with alkenes possessing suitably located, free or protected alcohol in a vicinal position to a sulfone. The addition is followed by an intramolecular hydrogen abstraction to give the 1,8-diketone either directly or after hydrolysis in the case of protected precursors (**Scheme 1-33**).<sup>35</sup>

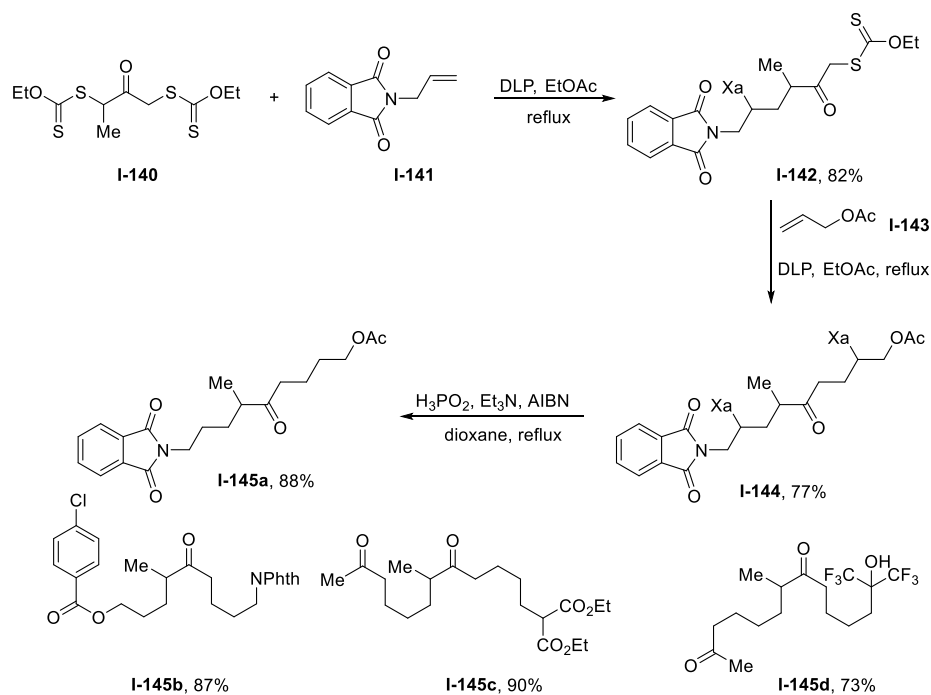


The mechanism for this transformation is presented in **Scheme 1-34**. First, DLP initiated the radical addition of xanthate **I-133** to alkene **I-134** affords the adduct **I-136**, which is in equilibrium with radical **I-135** via a reversible radical addition-fragmentation sequence. Radical **I-135** undergoes an intramolecular 1,5-hydrogen atom transfer forming radical **I-137**.  $\beta$ -Elimination of a methylsulfonyl radical rapidly occurs to furnish adduct **I-138**, which undergoes tautomerization into the corresponding 1,8-diketone **I-139**. It is worth noting that the methylsulfonyl radical can collapse into a molecule of  $\text{SO}_2$  and a methyl radical that is able to propagate the radical chain.



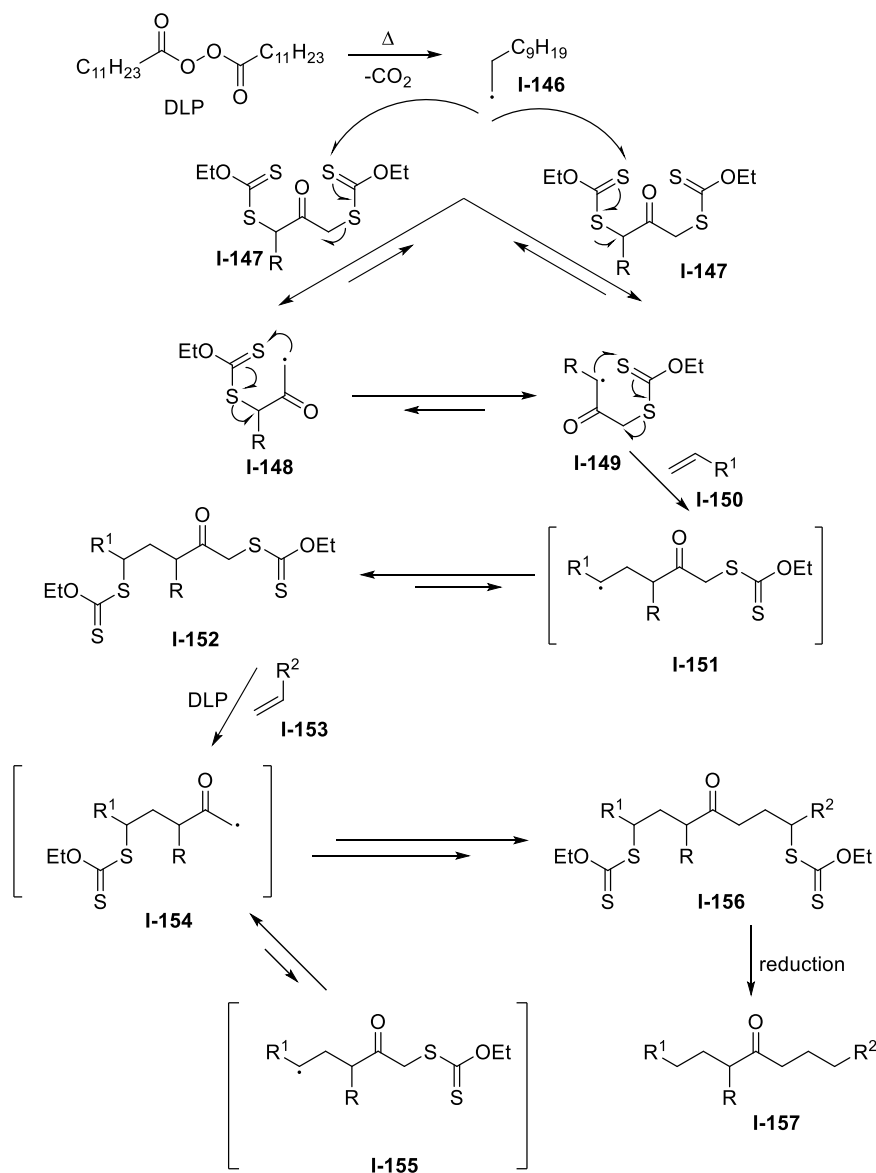
**Scheme 1-34.** The mechanism of intramolecular hydrogen abstraction

In 2016, our group developed a new method for the non-symmetrical dialkylation of ketones through radical addition of dioxanthates to un-activated olefins followed by reduction using the Barton's method, as shown in **Scheme 1-35**.<sup>36</sup> In the first addition step, the olefin partner is used as the limiting reagent to avoid the second radical addition resulting in unwanted side products. In the second radical addition step, the resulting xanthate is employed as the limiting reagent.



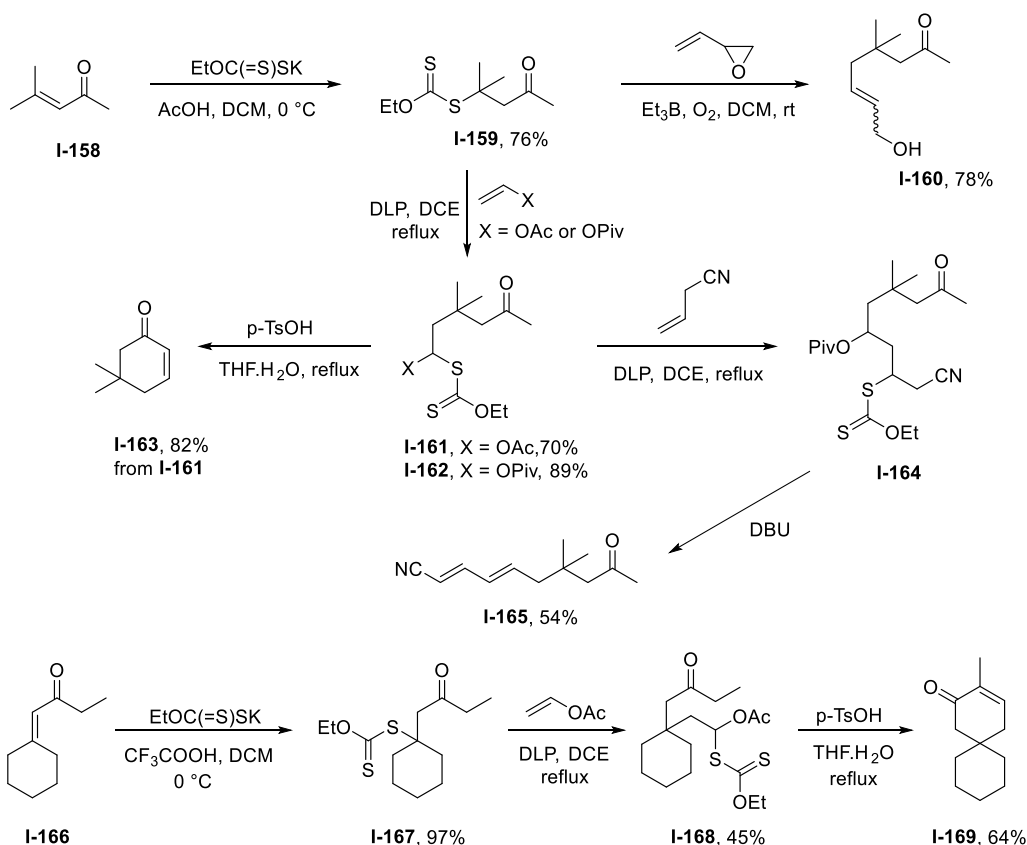
**Scheme 1-35.** The distal dialkylation of butanone

The mechanism of formation of the unsymmetrical dialkylation of ketones is presented in **Scheme 1-36**. The undecyl radical **I-146** generated by thermolysis of dilauroyl peroxide (DLP) can attack both xanthate groups in the unsymmetrical dixanthate **I-147** with approximately equal probability to generate radicals **I-148** and **I-149**. Radical **I-148** and **I-149** are themselves in a state of rapid equilibrium via exchange of the xanthate. However, radical **I-149** is more stable than radical **I-148** as it has substituents R to stabilize the radical. When using olefin **I-150** as the limiting reagent, adduct **I-152** with two xanthate groups is obtained as the major product, because the addition of radical **I-149** is greatly favored over the addition of radical **I-148**. The resulting adduct **I-152** is then exposed to excess of olefin **I-153** to selectively give adduct **I-156**, since radical **I-154** is more stable than radical **I-155**. Finally, the non-symmetrical dialkylation of ketone **I-157** is obtained from adduct **I-156** by reductive removal of two xanthate groups using Barton's method or other reduction procedures.



**Scheme 1-36.** The mechanism of unsymmetrical dialkylation of ketones

Xanthates **I-158** and **I-167** can be easily prepared by Michael addition under acidic conditions. The radical generated at the  $\beta$  position of a ketone from the tertiary xanthate, can smoothly react with various olefins to give the corresponding adducts, which are easily converted into allylic alcohols **I-160**, cyclohexenones **I-163** and dienes **I-165** containing a newly created quaternary center via second radical addition and elimination of both the xanthate and the pivalate group.<sup>14, 37</sup>



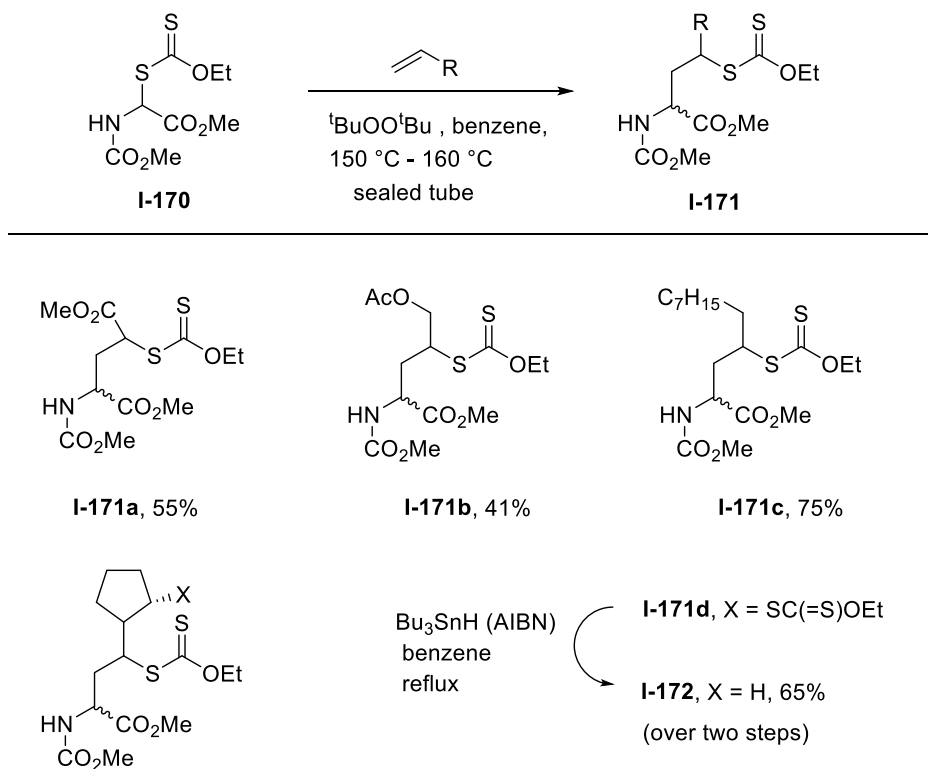
**Scheme 1-37.** Reactions at the  $\beta$ -position of ketones.

### 1.5.5 The xanthate route to amino acids

A variety of protected amino acids and proline derivatives can be synthesized based on the degenerative radical addition-transfer of xanthates onto alkenes. In general, the masked amino acid moiety can be placed on the alkene or the xanthate partner or on both.

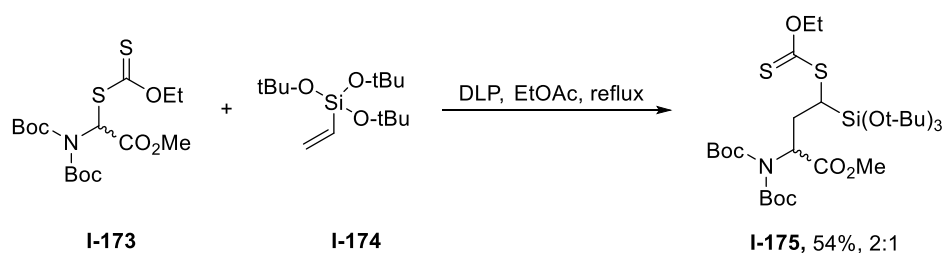
In 1994, Hiemstra and co-workers applied the addition of a protected  $\alpha$ -amino acid motif bearing xanthates to various alkenes to synthesize protected  $\alpha$ -amino acid derivatives, as shown in **Scheme 1-38**.<sup>38</sup> The xanthate group on  $\alpha$ -amino acid derivatives can be reductively removed with  $\text{Bu}_3\text{SnH/AIBN}$  in refluxing benzene to afford sulfur-free products.



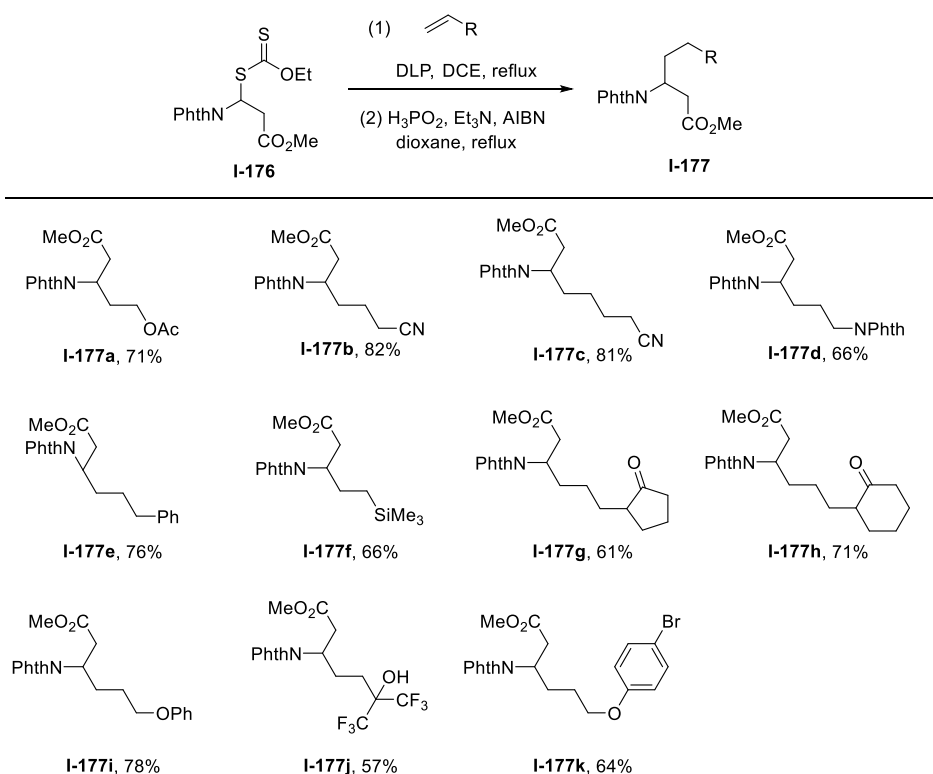


**Scheme 1-38.** Formation of protected  $\alpha$ -amino acids

In 2014, our group reported the preparation of a protected  $\alpha$ -amino acid derivative under mild reaction conditions as part of a study on the synthesis of trialkoxysilane (**Scheme 1-39**).<sup>39</sup> Xanthate **I-173** is more reactive than xanthate **I-170** because of two Boc groups on the nitrogen.



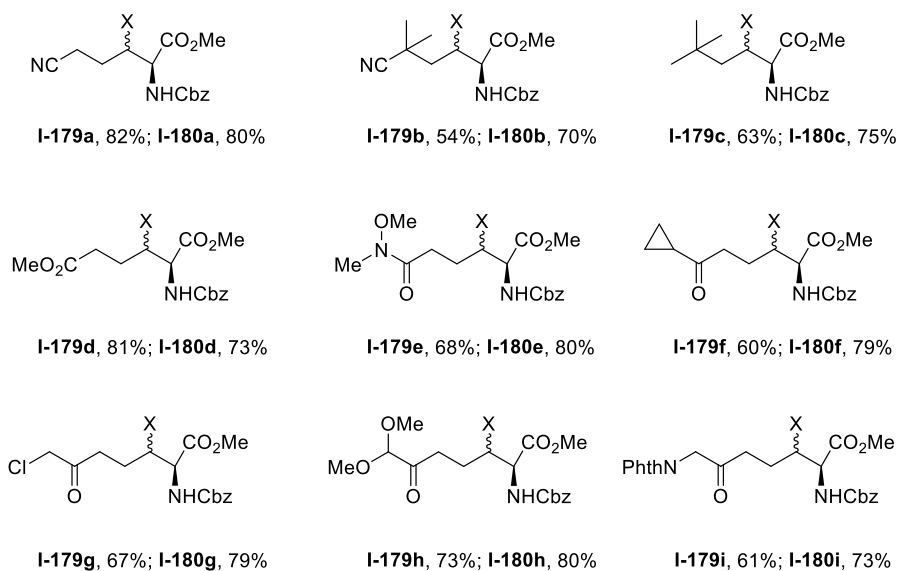
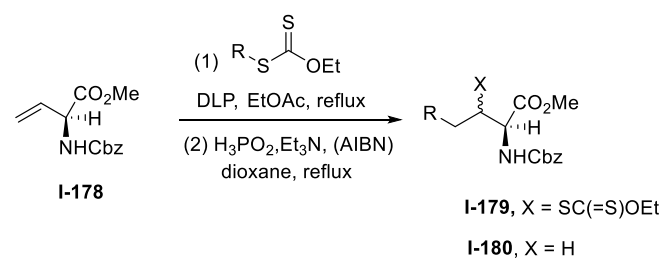
**Scheme 1-39.** Synthesis of protected  $\alpha$ -amino acids



**Scheme 1-40.** Synthesis of protected  $\beta$ -amino acids.

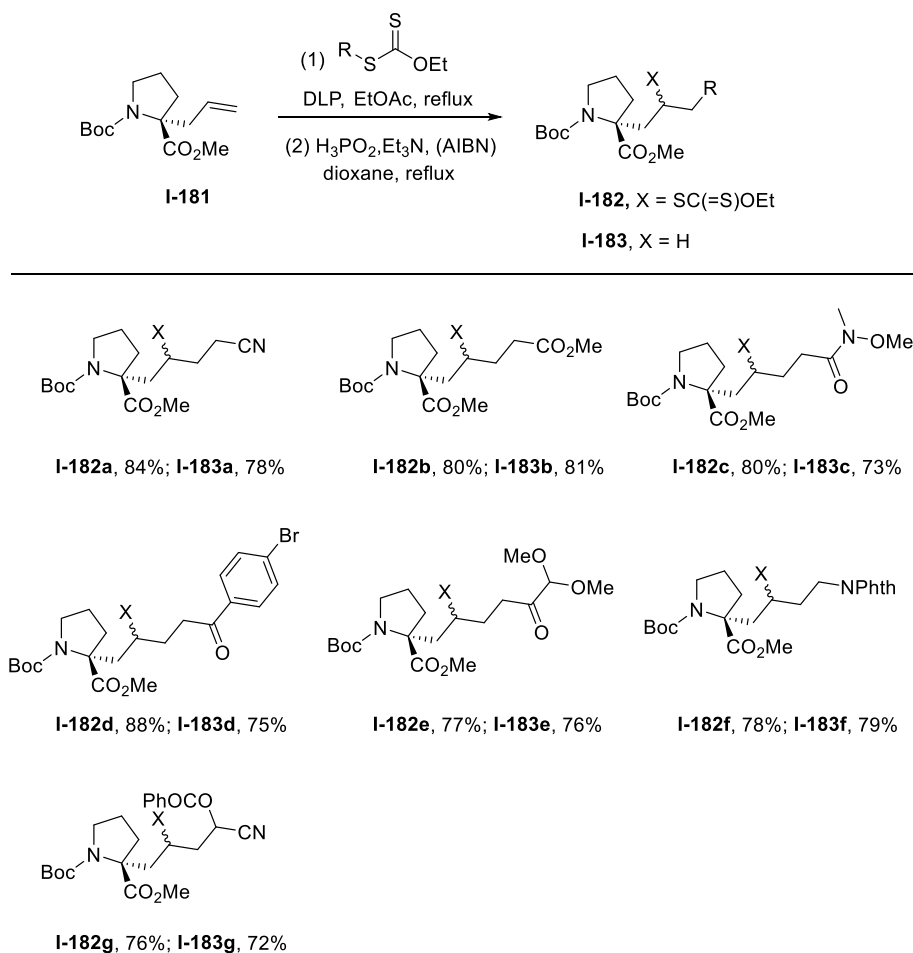
$\beta$ -Amino acids are useful building blocks for constructing stable peptidomimetics and synthetic targets, because such motifs can be found in many biologically active substances.<sup>40</sup> Such protected  $\beta$ -amino acids can be obtained by the addition of xanthate **I-176** to a variety of olefins, as shown in **Scheme 1-40**.<sup>41</sup> For  $\beta$ -amino acids **I-177g** and **I-177h**, cyclization of the deprotected amine with the ketone would result in bicyclic  $\beta$ -amino acid derivatives.

It is a powerful strategy to place the amino acid motif not only on the xanthate but also on the alkene. Some examples of placing the amino acid motif on the alkene are given below. The addition of various xanthates to protected vinyl glycine affords non-racemic  $\alpha$ -amino acids, as shown in **Scheme 1-41**.<sup>42</sup> Functional groups such as tertiary butyl (**I-180c**), polar nitrile (**I-180a**, **I-180b**), ester (**I-180d**), and Weinreb amide (**I-180e**) are readily introduced. No racemization takes place during the radical addition and reductive dethylation steps.



**Scheme 1-41.** Radical additions to protected vinyl glycine

Xanthates can also react with Boc-protected allyl proline to give rise to the corresponding adduct **I-182a-g**, which can be cleanly desulfurized into proline derivatives **I-183a-g**, as shown in **Scheme 1-42**.<sup>42</sup>



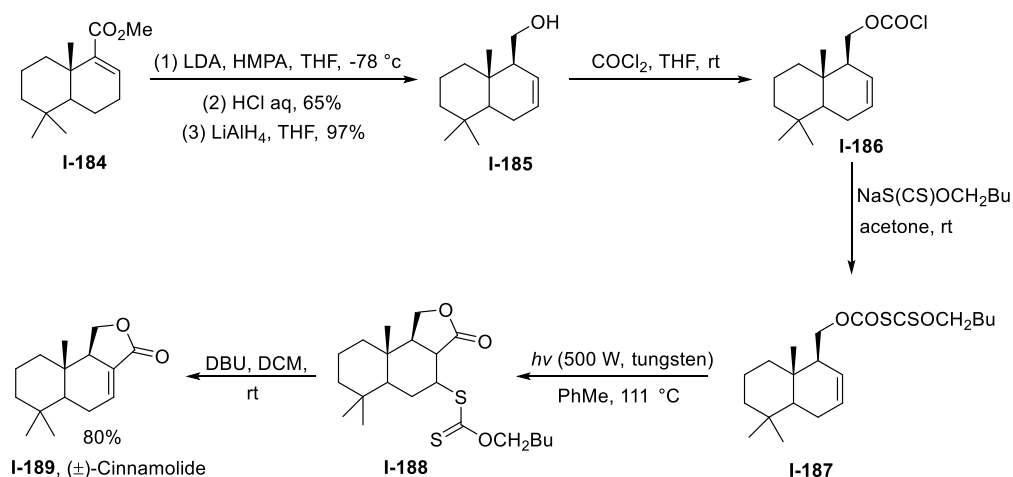
**Scheme 1-42.** Synthesis of Boc-protected proline derivatives

### 1.5.6 Application of xanthates in total synthesis

The xanthate mediated radical addition-fragmentation or addition-cyclization can be applied for synthesis natural products or a particular target. Radical chemistry is one of numerous synthetic strategies for constructing core structures. Compared to ionic or organometallic reactions, radical methods have some advantages: mild and neutral reaction conditions, lower sensitivity to steric hindrance, lower sensitivity to solvent effects, less tendency to rearrangement and  $\beta$ -eliminations. Some representative examples to illustrate the application of xanthates in total synthesis are presented below.

The first example is the total synthesis of ( $\pm$ )-cinnamolide and ( $\pm$ )-methylenolactocin. Both were accomplished using a radical cyclization as the key step involving an alkoxy carbonyl radical.<sup>43</sup> **Scheme 1-43** shows the total synthesis of ( $\pm$ )-cinnamolide.

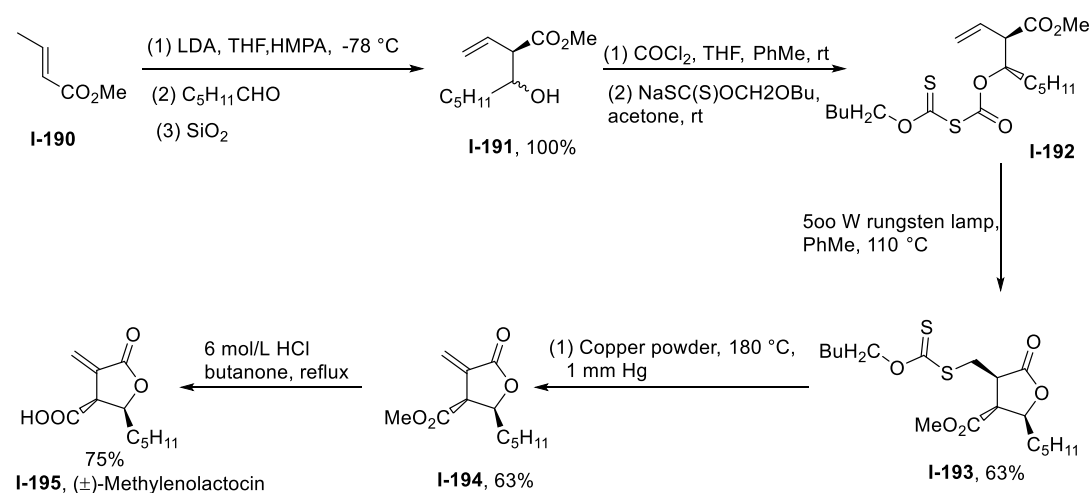
The synthesis started with unsaturated ester **I-184**, undergoing isomerisation and reduction to give the corresponding homoallylic alcohol **I-185**. The latter reacted smoothly with phosgene at room temperature to give the chloroformate **I-186**. The key *S*-alkoxycarbonyl xanthate **I-187** was obtained by nucleophilic substitution of chloroformate **I-186** with sodium *O*-neopen-tyl xanthate. A rearrangement took place under irradiation with visible light to afford the xanthate derivative **I-188** as a single diastereoisomer. Finally, treatment with a strong organic base, such as DBU induced elimination of the xanthate group and afforded ( $\pm$ )-cinnamolide **I-189** in 80% isolated yield.



**Scheme 1-43.** Total synthesis of ( $\pm$ )-cinnamolide

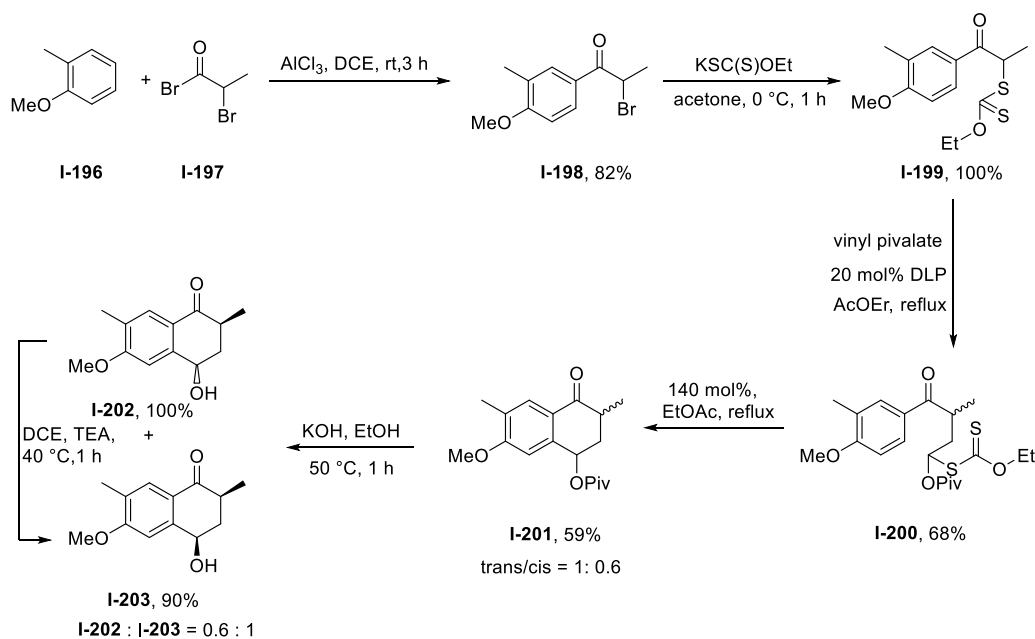
( $\pm$ )-Methylenolactocin was synthesized in few steps using a radical cyclization as the key step, as shown in **Scheme 1-44**.<sup>43</sup> Methylenolactocin, isolated from the culture filtrate of penicillium, belongs to the  $\alpha$ -methylene- $\beta$ -butyrolactone antibiotics family.<sup>44</sup> First, the addition of methyl crotonate anion to hexanal gave **I-191** as 1:1 diastereoisomeric mixture in quantitative yield which could be separated by chromatography. Then the treatment with phosgene at room temperature followed by nucleophilic substitution gave the corresponding *S*-alkoxycarbonyl xanthate **I-192**, which was irradiated with 500 W tungsten of lamp to afford the crystalline cyclic xanthate derivative **I-193**. The elimination of the xanthate moiety in lactone **I-193**

took place in the presence of copper powder and 1 mm Hg pressure at high temperature to furnish the unsaturated lactone **I-194** in 63% isolated yield. Last step was the acidic hydrolysis of unsaturated lactone **I-194** to finally afford ( $\pm$ )-methylenolactocin **I-195** in 75% isolated yield.



**Scheme 1-44.** Total synthesis of ( $\pm$ )-methylenolactocin

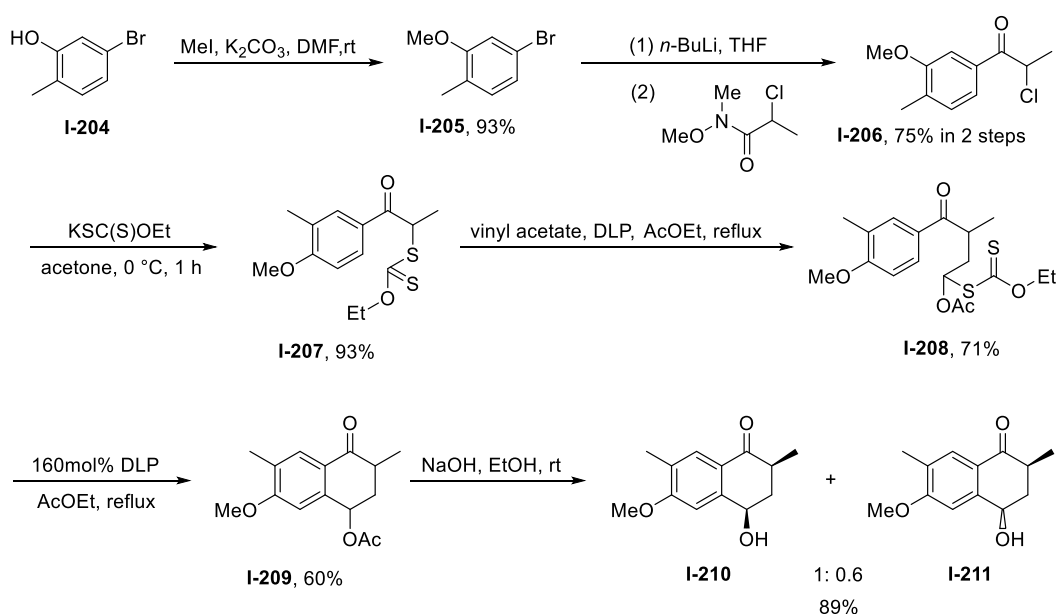
Flossonol, isolated from *pararistolochia flos-avi*, exhibits significant cytotoxicity against PS cell in culture.<sup>45</sup> Guignard has reported the total synthesis of the purported structure of flossonol in only five steps using a radical addition and cyclization strategy as the key step, as shown in **Scheme 1-45**.<sup>46</sup>



**Scheme 1-45.** Total synthesis of (±)-flossonol

First, bromoketone **I-198** was obtained as single regioisomer by the Friedel-Crafts reaction of 1-methoxy-2-methylbenzene **I-196** with 2-bromopropanoyl bromide **I-197** using aluminum chloride as a catalyst in DCE. Then nucleophilic substitution of the bromide **I-198** with potassium *O*-ethyl xanthate in acetone at 0 °C gave the key xanthate **I-199** in quantitative yield. The radical addition of **I-199** with vinyl pivalate in refluxing ethyl acetate produced **I-200** in 68% yield, which was cyclized in the presence of a stoichiometric amount of DLP to afford **I-201**. By using sterically hindered vinyl pivalate instead of vinyl acetate, it was possible to avoid cyclization to the adjacent position of the methyl group. Saponification of the ester **I-201** with potassium hydroxide as base in ethanol gave **I-202** and **I-203** as a 0.6:1 mixture of two epimers. It is worth noting that **I-202** was treated with trimethylamine in dichloromethane to give **I-202/I-203** with the same 0.6:1 isomeric ratio as before. And the possible structure for flossonol was prepared by Guignard in only seven steps as shown in **Scheme 1-46**.<sup>46</sup> 5-Bromo-2-methylphenol **I-204** was methylated with MeI in the presence of K<sub>2</sub>CO<sub>3</sub> and DMF to give intermediate **I-205** in 93% isolated yield. Lithium-halogen exchange on compound **I-205** with *n*-BuLi followed by the addition of Weinreb amide produced chloroketone **I-206** in 75% isolated yield. Then

nucleophilic substitution of **I-206** by potassium *O*-ethyl xanthate in cold acetone afforded the desired xanthate **I-207** in 93% yield. Both intermolecular addition and intramolecular cyclization proceeded smoothly to afford xanthate **I-208** and intermediate **I-209** in 71% and 60% isolated yield, respectively. Final saponification of **I-209** under mild conditions yielded a mixture of two epimers, which were isolated by column chromatography to obtain **I-210** and **I-211** in an 89% combined yield.

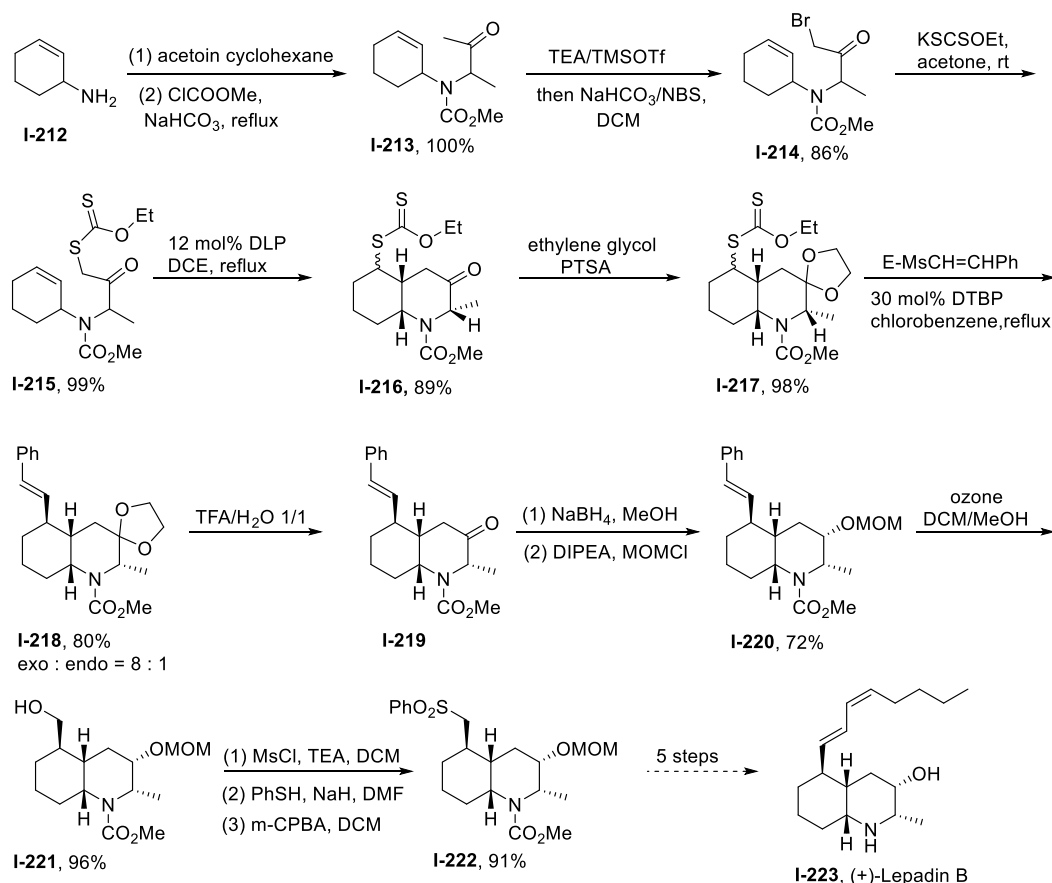


**Scheme 1-46.** Other possible structure for flossonol

(±)-Lepadine B possesses significant *in vitro* cytotoxicity against human cancer cell lines.<sup>47</sup> In 1995, Andersen and co-workers first isolated the lepadine B from *Clavelina lepadiformis*.<sup>47</sup> In 2002, our group disclosed a formal synthesis of lepadine B using cyclohexenylamine as starting material (**Scheme 1-47**).<sup>48</sup> First, the condensation of cyclohex-2-enylamine **I-212** with acetoin and protection of the nitrogen with methylchloroformate afforded intermediate **I-213** in quantitative yield. *In situ* formation of the trimethylsilyl enol ether in DCM at 0 °C followed by treatment with *N*-bromosuccinimide gave  $\alpha$ -bromo ketone **I-214** in 86% isolated yield. The xanthate derivative **I-215** was obtained in excellent yield by nucleophilic substitution with potassium *O*-ethyldithiocarbonate. Treatment of xanthate **I-215** with 12 mol% of



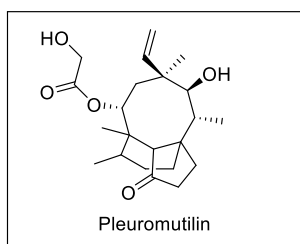
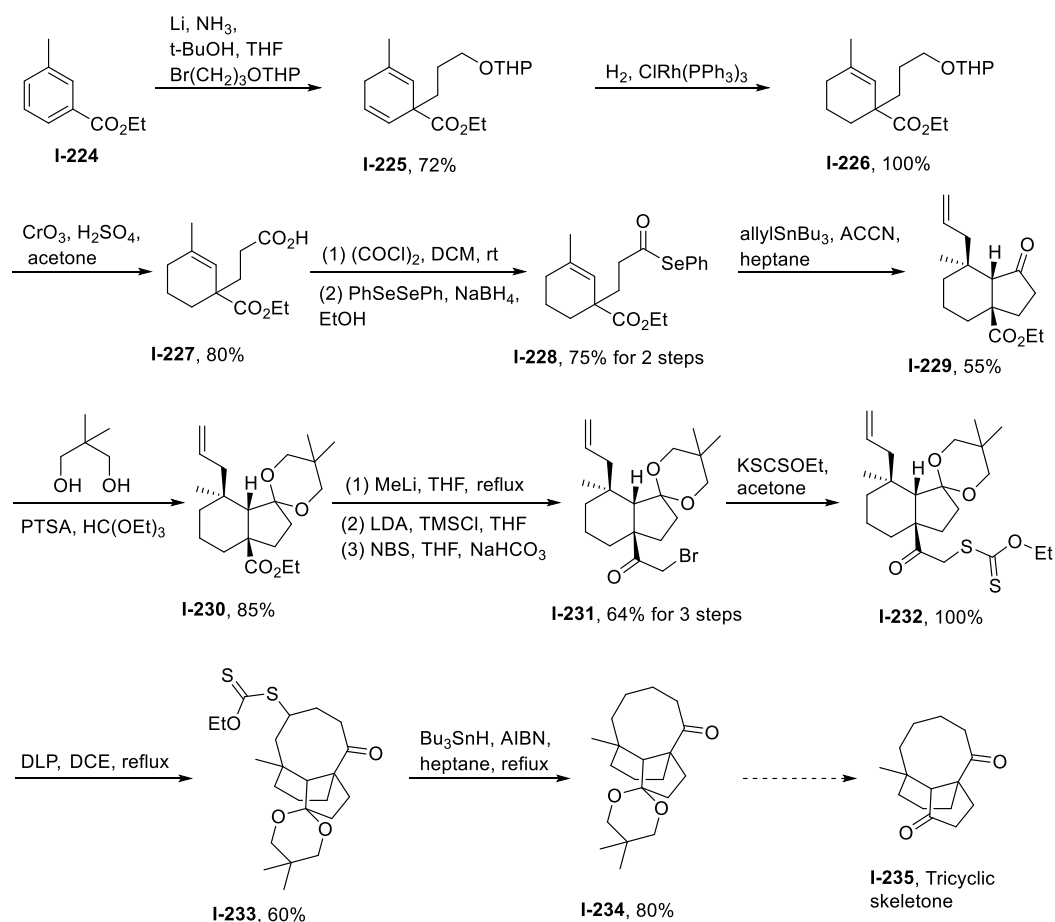
dilauroyl peroxide in refluxing 1,2-dichloroethane afforded bicyclic derivative **I-216** with the correct *cis*-ring fusion in 89% yield. Masking of ketone in **I-216** with ethylene glycol in the presence of *p*-toluene sulfonic acid yielded the cyclic ketal **I-217** in 98% yield. The radical vinylation of the cyclic ketal **I-217** with ethyl styryl sulfone in the presence of *tert*-butyl peroxide in refluxing chlorobenzene afforded styryl bicycle **I-218** with  $\beta$ -epimer dominating 8:1 in 80% yield. Removal of the acetal group in **I-218** with aqueous 50% trifluoroacetic acid gave crude ketone **I-219**, which was reduced with NaBH<sub>4</sub> in methanol and protected with chloromethoxy-methane to give MOM ether **I-220** in overall 72% yield for three steps. Ozonolysis of the styryl double bond in **I-220** in the mixture of DCM/MeOH at -78 °C followed by reduction with NaBH<sub>4</sub> gave **I-221** in 96% yield for two steps. This compound was converted into **I-222** in excellent yield for three steps via mesylation, displacement with sodium phenylthiolate and oxidation with *meta*-chloroperbenzoic acid. The sulfone **I-222** has previously been converted into lepadin B in a five steps sequence.<sup>49</sup>



**Scheme 1-47.** Formal synthesis of the ( $\pm$ )-lepadin B

Pleuromutilin, isolated from various basido-mycete microorganisms, is used as antimicrobial.<sup>50</sup> In 2003, our group reported a concise synthesis of the tricyclic skeleton of pleuromutilin based on an *8-endo-trig* radical cyclization of a xanthate precursor, as shown in **Scheme 1-48**.<sup>25, 51</sup> In this study, the core skeleton of the pleuromutilin was constructed based on the Barton decarboxylation and the xanthate chemistry. Cyclohexadiene **I-225** was obtained by the alkylative Birch reduction of ethyl *m*-toluate using THP-protected-3-bromo propanol as the alkylating reagent. The disubstituted double bond in cyclohexadiene **I-225** was selectively reduced with Wilkinson's catalyst to afford **I-226** in quantitative yield. The carboxylic acid **I-227** was obtained in high yield by the deprotection of the alcohol in **I-226** and its oxidation with Jones reagent. The acyl phenylselenide **I-228** was obtained via the acid chloride through a standard procedure, which was followed by treatment with allyltributyltin and a small amount of ACCN in refluxing heptane to afford

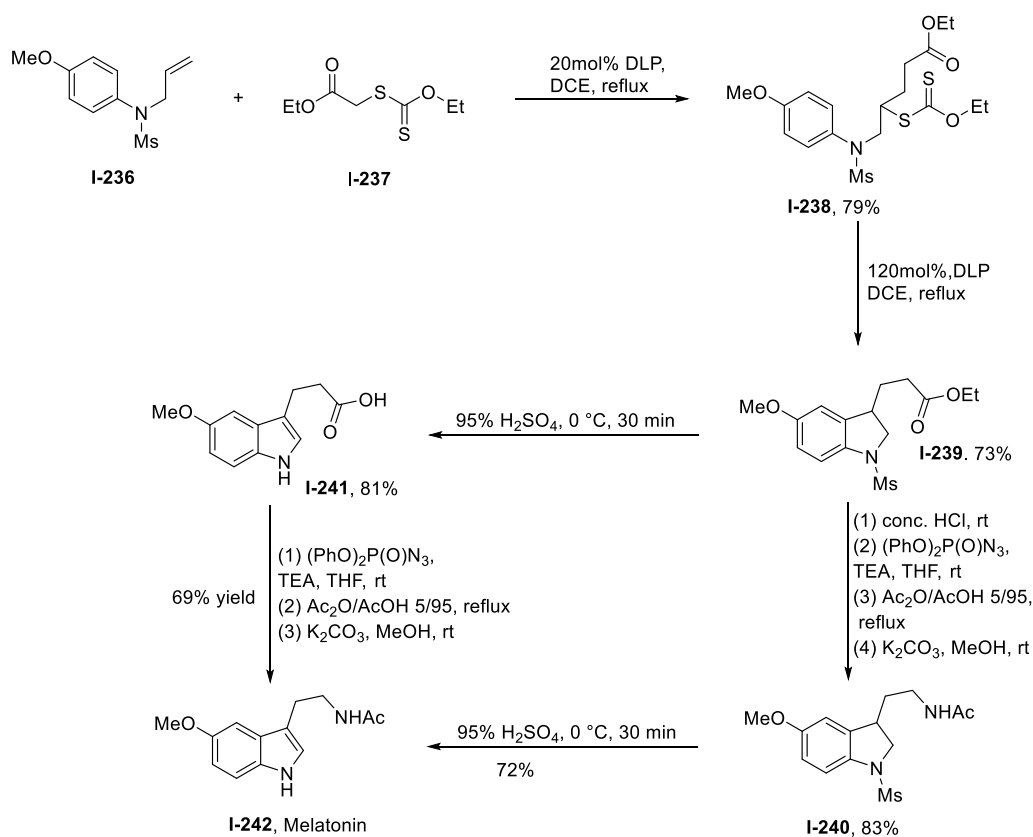
hydrindanone **I-229** in moderate yield. The ketone group in **I-229** was protected via a standard condition to give ketal **I-230**. The bromide **I-231** was prepared easily in good yield for three steps. Nucleophilic substitution of bromide **I-231** with potassium *O*-ethyl xanthate proceeded smoothly to afford the desired xanthate **I-232** in quantitative yield. The xanthate **I-232** underwent an *8-endo-ring* cyclization as the key step by exposure to a small amount of lauroyl peroxide in refluxing DCE to give compound **I-233** in 60% isolated yield. The xanthate function in **I-233** was reductively removed by exposure to  $\text{Bu}_3\text{SnH}$  to give rise to intermediate **I-234**, which embodies the tricyclic skeleton of pleuromutilin.



**Scheme 1-48.** Synthesis of the tricyclic skeleton of pleuromutilin

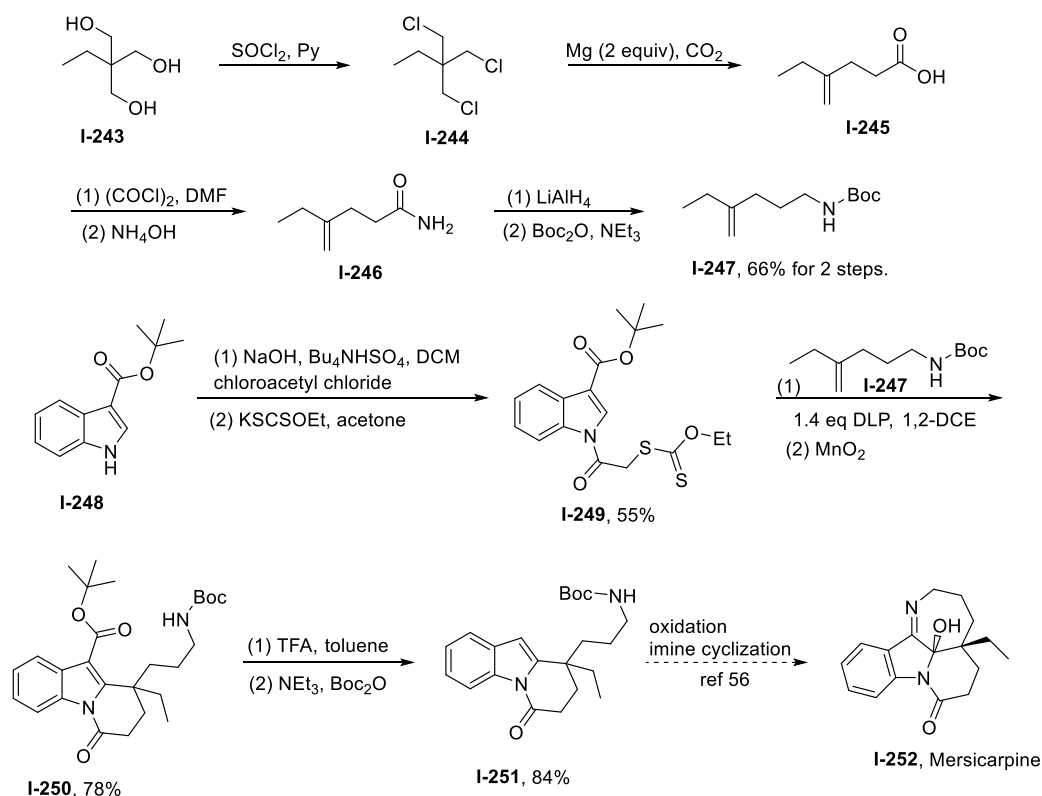
Melatonin is a hormone secreted by the pineal gland, which is used for the regulation of sleep and temperature rhythms in mammals.<sup>52</sup> In 2002, our group reported the synthesis of melatonin by a radical addition-cyclization sequence, as shown in **Scheme 1-49**.<sup>27</sup> First, the intermolecular radical addition of xanthate **I-237** to mesyl protected *N*-allylaniline **I-236** gave the corresponding adduct **I-238** in good yield. Indoline **I-239** was obtained in good yield by a stoichiometric amount of DLP induced radical ring closure to the aromatic ring.

Two different routes were used to converting indoline **I-239** into melatonin **I-242**. The first route involved hydrolysis of the ester group with concentrated HCl and Curtius degradation followed by removed of the mesyl group with 95% cold sulfuric acid to afford melatonin **I-242** in good yield. The second route involved removal of the ester and mesyl group and a Curtius rearrangement mediated by diphenylphosphoryl azide to obtain melatonin in good yield. The first route is slightly better than the second one in terms of overall yield.



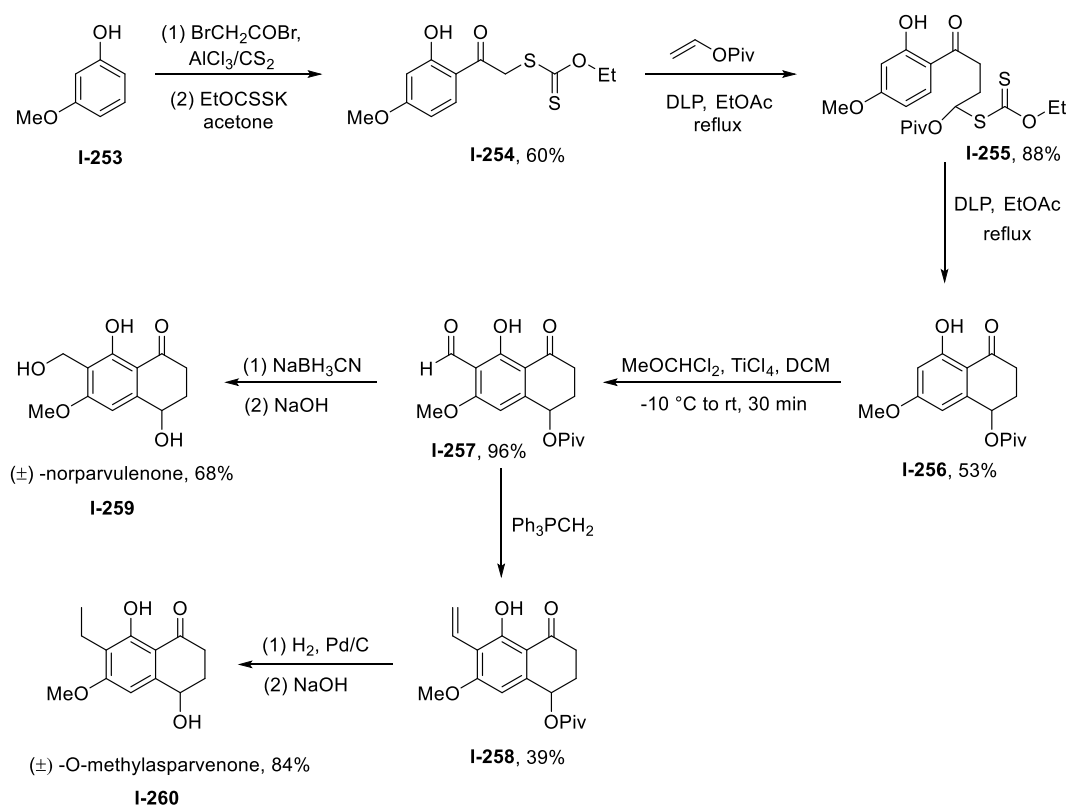
**Scheme 1-49.** Synthesis of melatonin

Mersicarpine, first isolated by Kam and co-workers in 2004 from the kopsia species of plants, is part of a class of indole alkaloids containing a typical quaternary center.<sup>53</sup> In 2009, our group reported the formal synthesis of mersicarpine using an intermolecular radical addition-cyclization cascade.<sup>54</sup> First, olefin **I-247** was prepared by a traditional method of synthesis according to the procedure reported by Magnus and co-workers.<sup>55</sup> Xanthate **I-249** was prepared by acylation of *tert*-butyl-1H-indole-3-carboxylate with chloroacetyl chloride followed by displacement of the chloride with potassium *O*-ethyl xanthate in cold acetone at room temperature. Lactam **I-250** was obtained in good yield by peroxide (DLP) induced radical addition-cyclization. The *t*-butylcarboxylate on C3 of the indole ring plays an important role in the cyclization step. In its absence, the cyclization proved to be inefficient. Deprotection of the Boc-group and decarboxylation proceeded smoothly in the presence of the trifluoroacetic acid and re-protection of the amine with Boc anhydride afforded compound **I-251**, which had been converted into mersicarpine by the group of Kerr.<sup>56</sup> The formal synthesis route to the (±)-mersicarpine is shown in **Scheme 1-50**.



**Scheme 1-50.** Formal synthesis of (±)-mersicarpine

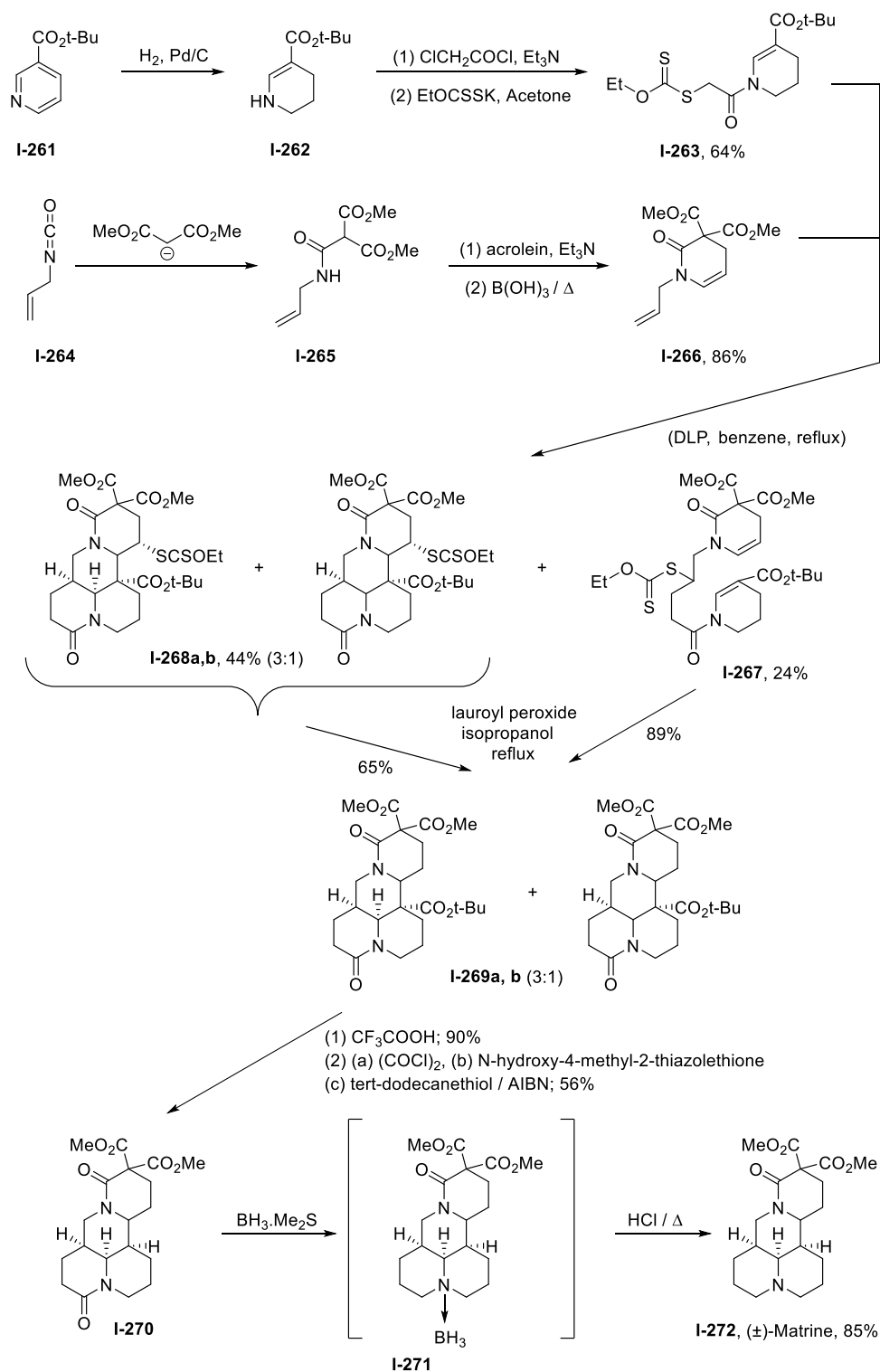
In 2003, our group reported a short total synthesis of (±)-norparvulenone and (±)-*O*-methylasparvenone starting from commercially available *m*-methoxyphenol (**Scheme 1-51**).<sup>13</sup> (±)-Norparvulenone, isolated from *Microsphaeropsis*, possess *in vitro* anti-flu virus biological activity and (±) *O*-methylasparvenone can be used against depression and obsessive-compulsive disorders.<sup>13</sup> Xanthate **I-254** was prepared by a Friedel–Crafts acylation of *m*-methoxyphenol followed by nucleophilic substitution. Tetralone **I-256** was obtained in good yield by xanthate-mediated radical addition-cyclization sequence. The next step for the preparation of the important intermediate **I-257** was the introduction of a formyl substituent by a modified Friedel–Crafts reaction. (±)-Norparvulenone was obtained in good yield by selective reduction of aldehyde **I-257** followed by saponification of the pivalate group. (±)-*O*-methylasparvenone was prepared by Wittig reaction of aldehyde **I-257** followed by reduction of the vinyl group.



**Scheme 1-51.** Total synthesis of (±)-norparvulenone and (±)-O-methylasparvenone

In 1998, our group reported the total synthesis of (±)-matrine, the main alkaloid found in *sophora flavescens* ait, involving several radical processes and a cascade reaction mediated by a xanthate group, as shown in **Scheme 1-52**.<sup>57</sup> The xanthate component **I-263** was prepared readily by catalytic hydrogenation, chloro-acetylation and nucleophilic substitution, starting with *tert*-butyl nicotinate. Amide **I-265** was obtained by addition of the anion of dimethylmalonate to allyl isocyanate. Cyclic enamide **I-266** was prepared in good overall yield in one pot reaction by the Michael addition of amide **I-265** with acrolein followed by heating with boric acid in toluene. The radical addition of **I-263** with cyclic enamide **I-266** in the presence of a small amount of DLP afforded three major compounds, the two tricyclic derivatives **I-268ab** and the bicyclic intermediate **I-267**. It is not necessary to isolate these major compounds because they were converted into the reduced mixture **I-269ab** in the presence of a stoichiometric amount of lauroyl peroxide in refluxing isopropanol. To obtain (±)-matrine, the butyl ester in **I-269ab** was selectively cleaved with TFA and the free acid was reductively decarboxylated using the Barton method. Finally, the

regioselective reduction of the least hindered lactam **I-270** with borane afforded the important intermediate **I-271**, which was treated with hot hydrochloric acid to give the target ( $\pm$ )-matrine **I-272** in 85% yield.



**Scheme 1-52.** Total synthesis of ( $\pm$ )-matrine



## 1.6 Conclusion

The radical chemistry of xanthates represents one of the most powerful tools for the creation of carbon-carbon bonds. The discovery, general concept and mechanism of the radical chemistry of xanthates were briefly introduced. This chapter presented a variety of approaches for the preparation of primary, secondary and tertiary xanthates. Xanthates are mainly prepared by the ionic and radical methods. Xanthates have proved to be widely useful for intramolecular, intermolecular radical additions and radical cyclization. A variety of protected amino acid derivatives can be synthesized based on the degenerative radical addition-transfer of xanthates onto alkenes. The total synthesis of natural products and particular targets were summarized involving xanthates mediated radical addition-fragmentation or addition-cyclization sequence as the key step. This method features a variety of advantages such as cheap and readily available reagents, mild reaction conditions, simple experimental procedures, and compatibility with a wide range of functional groups.

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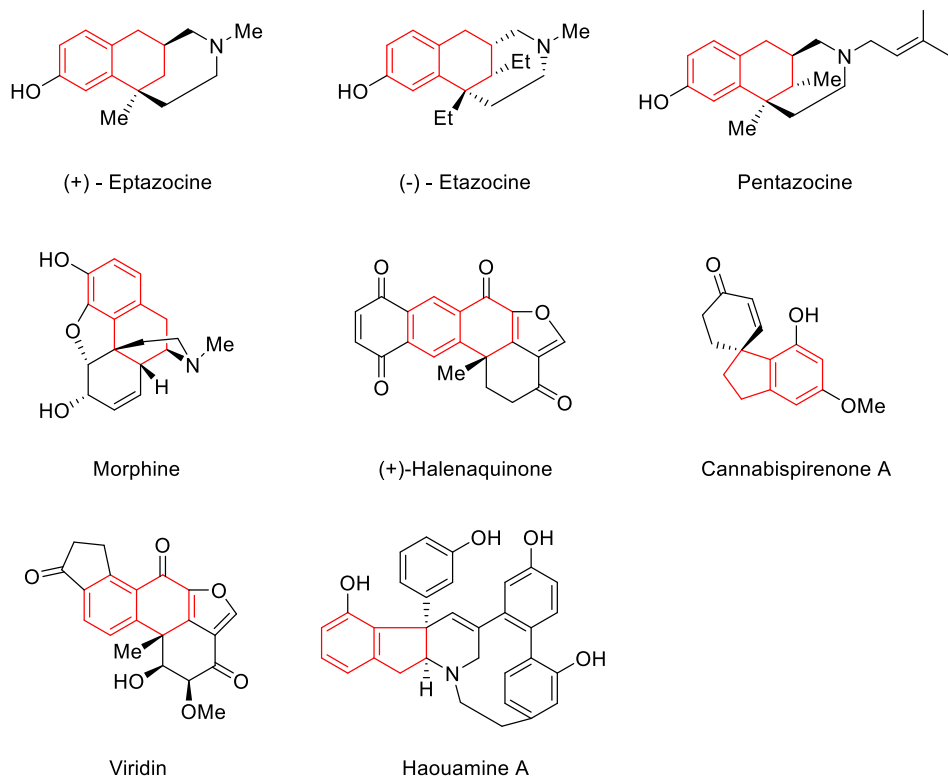
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## Chapter 2 Total Synthesis of ( $\pm$ )-Eptazocine

### 2.1 Introduction

Eptazocine was first synthesized by Shiotani in Japan in 1976 and introduced to the market in 1987, as a narcotic antagonist analgesic.<sup>1</sup> Eptazocine is widely used for the management of cancer-related and postoperative pain because it has only limited ability to induce respiratory depression, physical dependence, or tolerance.<sup>2</sup> The structure of eptazocine contains a benzylic quaternary carbon center, which attracted the attention of organic chemists. The efficient construction of this benzylic quaternary carbon centers remains a synthetic challenge. Benzylic quaternary carbon centers can be found in various bioactive natural products and pharmaceuticals such as pentazocine,<sup>3</sup> (-)-etazocine,<sup>4</sup> morphine,<sup>5</sup> (+)-halenaquinone,<sup>6</sup> furanosteroid viridian,<sup>7</sup> cannabispirenone A,<sup>8</sup> haouamine A<sup>9</sup> (**Scheme 2-1**).

As mentioned in chapter 1, xanthates can mediate radical addition - fragmentation or addition – cyclization, which can be utilized in the synthesis of natural products or particular targets. In this chapter, we will describe some general routes for synthesizing ( $\pm$ )-eptazocine, which will involve radical reaction mediated by a xanthate in order to construct benzylic quaternary carbon center.



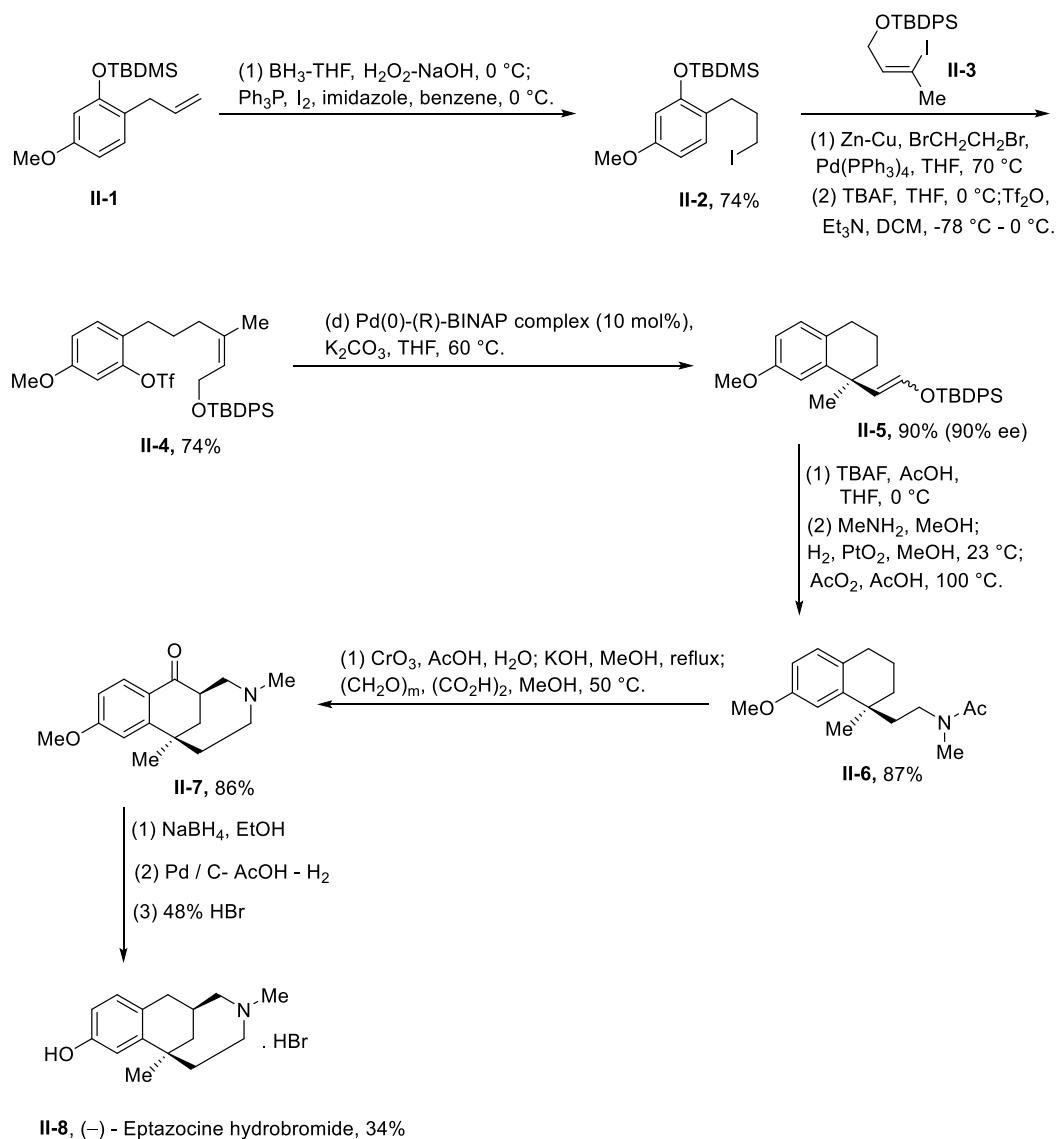
**Scheme 2-1.** Bioactive natural products and pharmaceuticals containing benzylic quaternary carbon centers

## 2.2 Previous total synthesis of ( $\pm$ )-eptazocine

In 1993, Shibasaki and co-workers first applied an asymmetric intramolecular Heck reaction for the catalytic asymmetric synthesis of (-)-eptazocine.<sup>10</sup> The trisubstituted benzene derivative **II-1** was obtained in three steps from the commercially available 3-methoxyphenol.<sup>11</sup> Product **II-2** was synthesized in 74% yield via hydroboration – oxidation and iodination. Cross-coupling of compound **II-2** with iodide **II-3** followed by deprotection of TBDMS ether and trifluoromethanesulfonylation gave the intermediate **II-4** in 74% yield in two steps. The cyclized product **II-5** was obtained in excellent yield by coupling reaction using Pd as catalyst and  $K_2CO_3$  as base in THF. Treatment of cyclized product **II-5** with TBAF-AcOH in THF afforded the corresponding aldehyde, which was followed by exposure to methylamine, hydrogen-PtO<sub>2</sub> and acetic anhydride to give acetamide **II-6** in 87% overall yield. Acetate **II-6** underwent oxidation to afford the corresponding ketone, which was



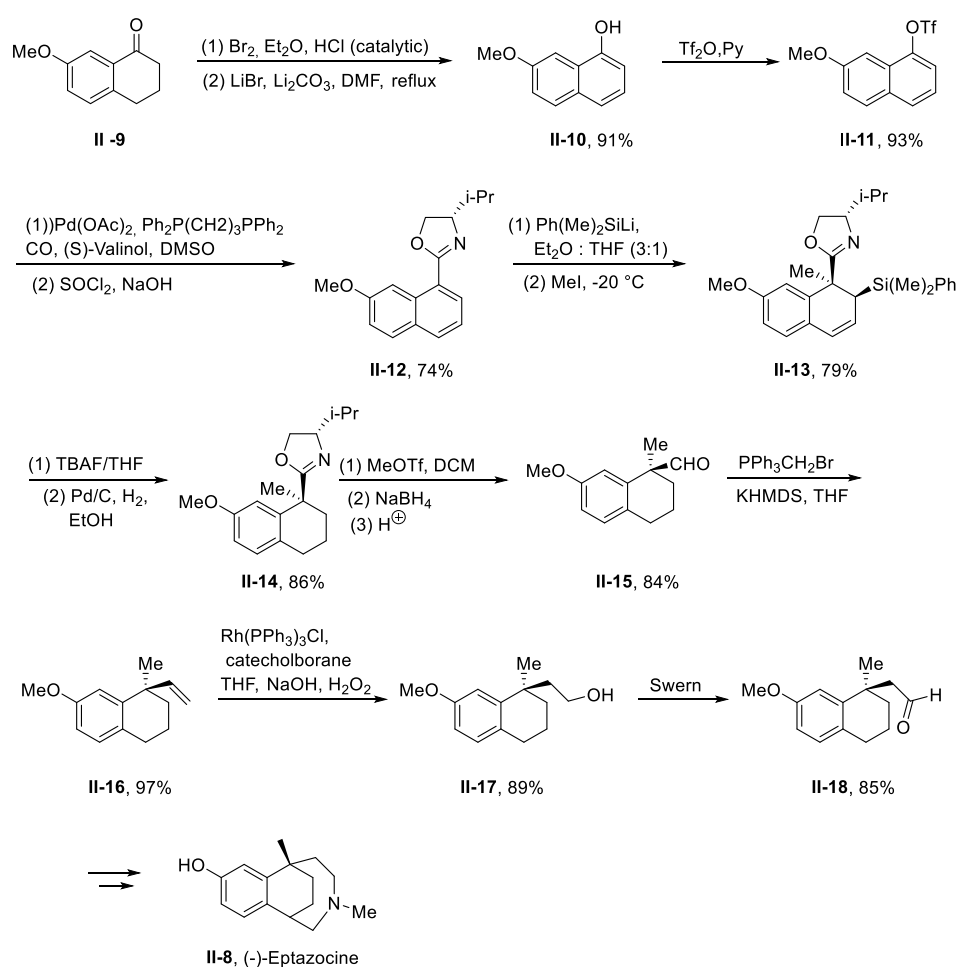
treated with KOH and paraformaldehyde to furnish tricyclic **II-7** in 86% overall yield. Finally, (-)-eptazocine **II-8** was obtained in 34% overall yield by reduction, dehydration-hydrogenation and demethylation.



**Scheme 2-2.** Catalytic asymmetric synthesis of (-)-eptazocine

In 1995, Meyers and co-workers reported the asymmetric synthesis of the key intermediates involving an asymmetric addition to naphthalene derivatives leading to (-)-eptazocine, as shown in **Scheme 2-3**.<sup>12</sup> Naphthol **II-10** was obtained in 91% yield by a bromination-dehydrobromination sequence from commercially available tetralone **II-9**. Triflate formation proceeded smoothly to give compound **II-11**, which

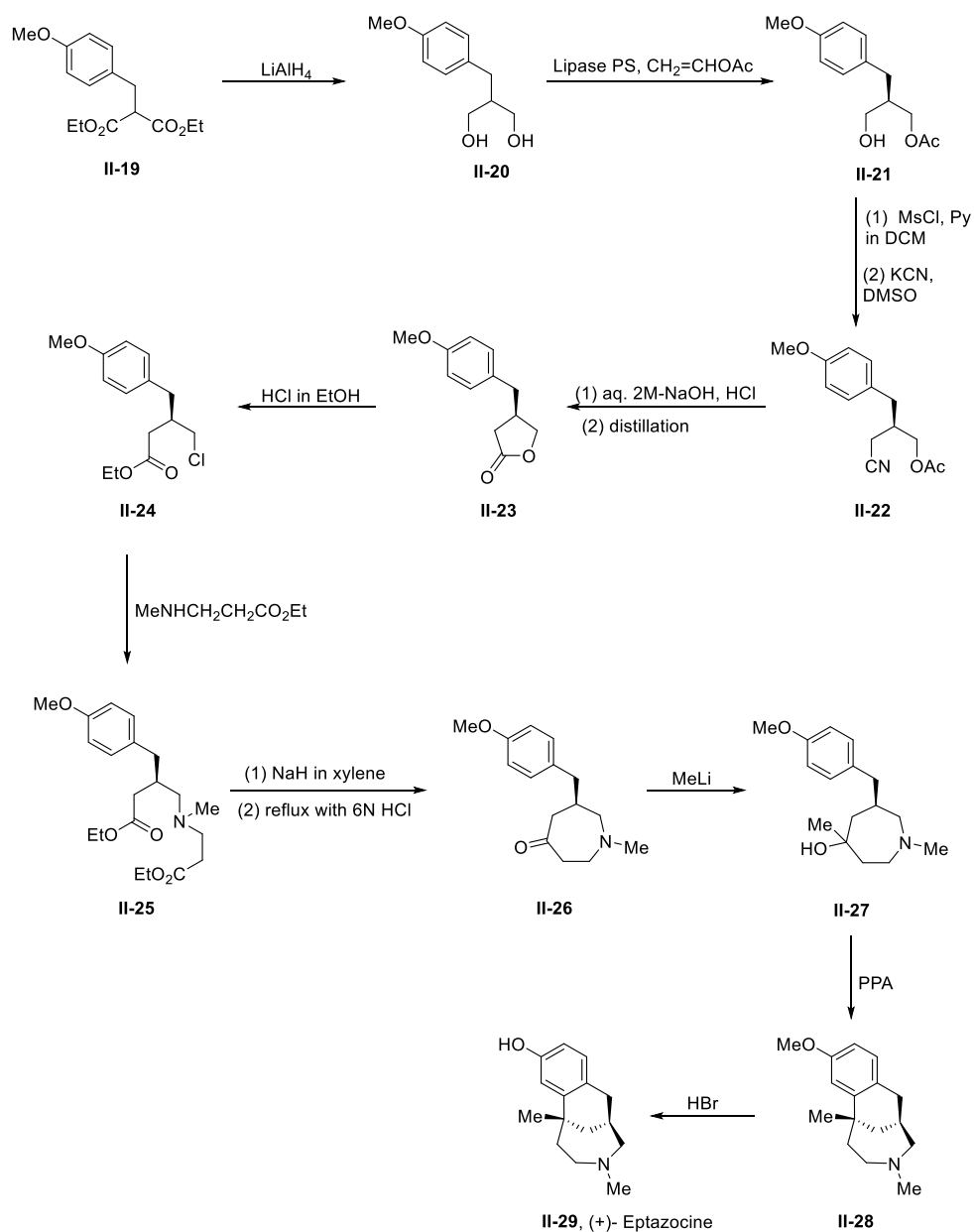
was treated with carbon monoxide and valinol using palladium acetate as catalyst to afford an unstable hydroxyl amide which was converted immediately into oxazoline **II-12** in 74% yield by treatment with thionyl chloride followed by work up with a NaOH solution. Trans-addition product **II-13** was obtained as the major diastereomer in 79% isolated yield by reaction of oxazoline **II-12** with lithiodimethylphenylsilane followed by electrophilic quench with iodomethane. Desilylation with TBAF was followed by reduction of the double bond to afford tetralin derivative **II-14** in 86% yield over two steps, which was then converted into aldehyde **II-15** in excellent yield under reductive hydrolytic conditions. The key intermediate **II-18** in the Shibasaki synthesis of (-)-eptazocine was obtained easily by Wittig condensation, hydroboration and Swern oxidation.



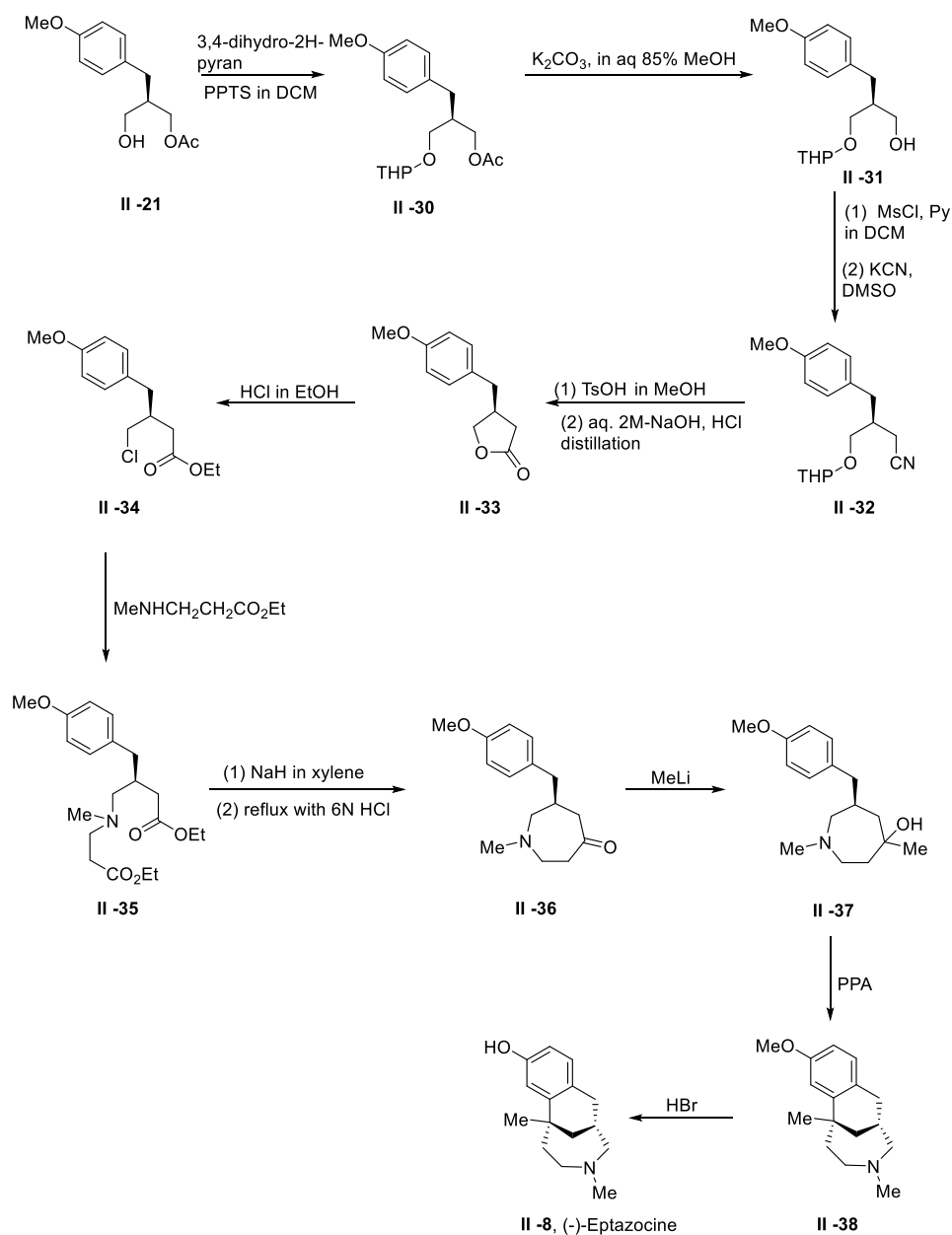
**Scheme 2-3.** Synthesis of a key intermediate.

In 1996, Nakamoto and co-workers reported the asymmetric synthesis of (+) and

(-)-eptazocine via an enzymatic reaction as a key step, as shown in **Schemes 2-4** and **2-5**.<sup>13</sup> 2-(*p*-Methoxybenzyl)-1,3-propanediol **II-20** was obtained by treatment of commercially available **II-19** with LiAlH<sub>4</sub>. The optically pure monoacetate **II-21** was obtained by treatment of 2-(*p*-methoxybenzyl)-1,3-propanediol **II-20** with lipase PS in a mixture of diisopropyl ether and water in the presence of vinyl acetate as the acetyl donor. The hydroxyl group in **II-21** was mesylated and treated with KCN in DMSO to afford cyanoacetate **II-22**. Hydrolysis with NaOH solution followed by acidification and vacuum distillation produced lactone **II-23**, a key intermediate. Lactone **II-23** was treated with HCl in anhydrous ethanol to afford compound **II-24**, which was refluxed with ethyl 3-methyl-aminopropionate in chlorobenzene using K<sub>2</sub>CO<sub>3</sub> as base to give diester **II-25** in good yield. Dieckmann cyclization of diester **II-25** with NaH as base in xylene followed by refluxing with 6N HCl afforded ketone **II-26**. Treatment of this compound with methyllithium furnished the corresponding alcohol **II-27**, which was cyclized with polyphosphoric acid to produce tricyclic compound **II-28**. The last step is demethylation using HBr to give (+)-eptazocine.



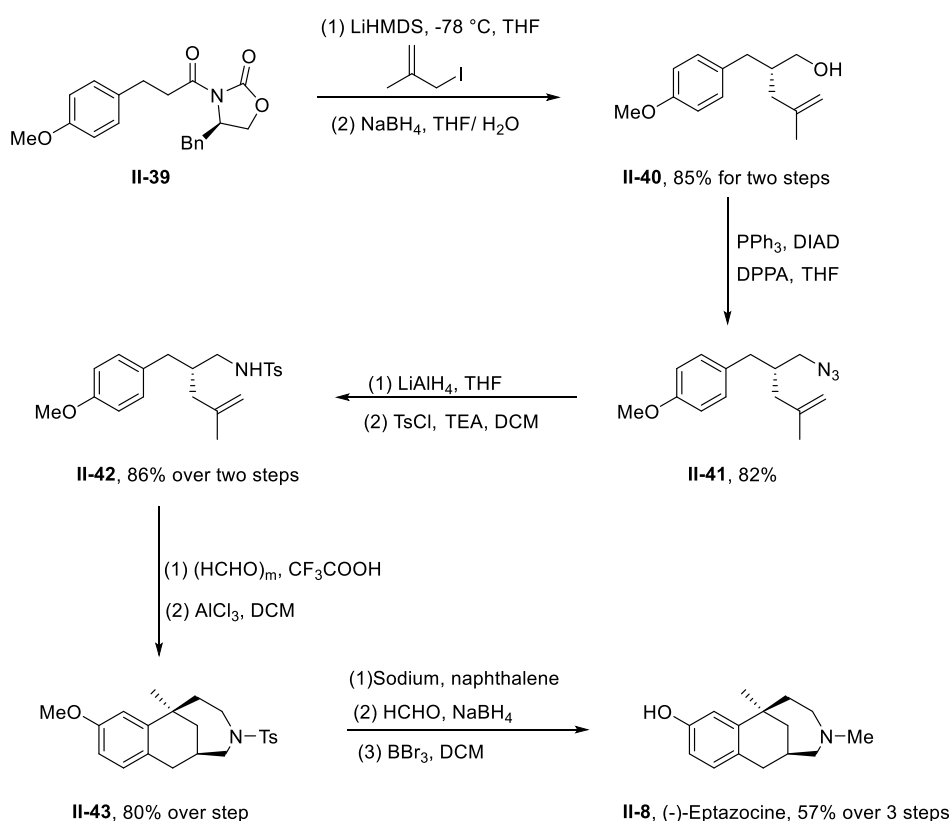
**Scheme 2-4.** Total synthesis (+)-eptazocine



**Scheme 2-5.** Total synthesis (-)-eptazocine

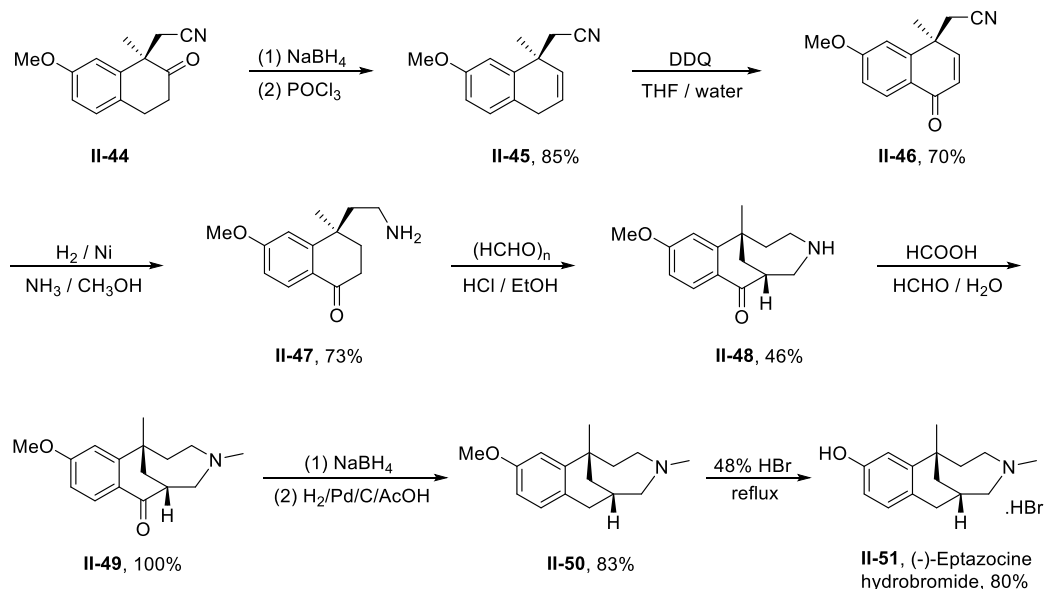
For the synthesis of (-)-eptazocine, a cyano group had to be introduced in place of the acetate in compound **II-21**. The hydroxyl group was first protected as the THP derivative **II-30** and the acetoxy group selectively hydrolyzed with  $\text{K}_2\text{CO}_3$  in aqueous MeOH to give alcohol **II-31** without racemization. Mesylation followed by treatment with KCN in DMSO afforded nitrile **II-32** in good yield. Deprotection of the THP group with TsOH in MeOH followed by hydrolysis of the cyano group with NaOH solution and acidification gave lactone **II-33**, an important intermediate in the synthesis of (-)-eptazocine, as shown in **Scheme 2-5**.

In 2012, She and co-workers reported the asymmetric synthesis of (-)-eptazocine by an aza-prins cyclization and intramolecular Friedel-Crafts reaction as a key step, as shown in **Scheme 2-6**.<sup>14</sup> Evans alkylation of oxazolidinone **II-39** with methallyl iodide and cleavage of the chiral auxiliary gave alcohol **II-40** as the only isomer in 85% isolated yield for two steps. Alcohol **II-40** was easily converted into the corresponding azide **II-41** in 82% isolated yield under Mitsunobu reaction conditions. Reduction of the azide group with LiAlH<sub>4</sub> followed by protection of the amine with TsCl afforded the intermediate **II-42** in 86% isolated yield for two steps. Tricyclic compound **II-43** was obtained in 80% yield for two steps by treatment of tosylamide **II-42** with formaldehyde and TFA in CH<sub>2</sub>Cl<sub>2</sub> at room temperature followed by reaction of the resulting product with AlCl<sub>3</sub> in CH<sub>2</sub>Cl<sub>2</sub>. The last step is deprotection of the tosyl group, N-methylation with formaldehyde/sodium borohydride, and demethylation with BBr<sub>3</sub> to give the desired (-)-eptazocine in 57% yield over three steps.



**Scheme 2-6.** Total synthesis of (-)-eptazocine by an aza-prins cyclization

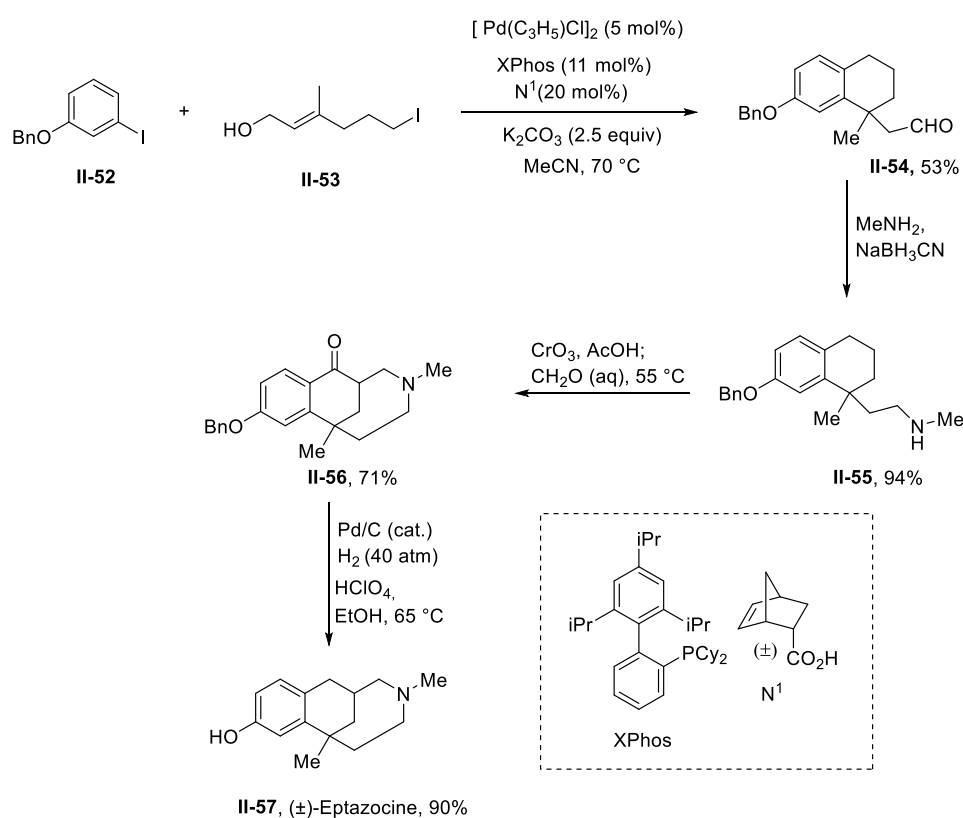
In 2018, Zhou and co-workers reported a novel and practical asymmetric synthesis of eptazocine hydrobromide as shown in **Scheme 2-7**.<sup>15</sup> Dihydronaphthalene **II-45** was obtained in 85% yield from tetralone **II-44** by reduction with NaBH<sub>4</sub> in methanol followed by dehydration with POCl<sub>3</sub> at reflux. Dihydronaphthalene **II-45** was next converted into ketone **II-46** in good yield by oxidation with DDQ in THF/water. Primary amine **II-47**, obtained in 73% yield by hydrogenation of ketone **II-46** in the presence of Raney–Ni as catalyst in NH<sub>3</sub>/CH<sub>3</sub>OH, was treated with paraformaldehyde in HCl/MeOH at reflux to give tricyclic amine **II-48** in 46% yield. Reductive methylation under Eschweiler–Clarke reaction conditions (formic acid/formaldehyde/reflux) afforded the corresponding *N*-methyl derivative **II-49** in quantitative yield. Reduction of the ketone with NaBH<sub>4</sub> in methanol followed by hydrogenation with H<sub>2</sub>/Pd/C in acetic acid furnished compound **II-50** in 83% overall yield. Finally, demethylation with 48% aqueous HBr solution provided (-)-eptazocine hydrobromide in 80% yield.



**Scheme 2-7.** Total synthesis of (-)-eptazocine hydrobromide

In 2018, Zhou and co-workers reported a general method for total synthesis of ( $\pm$ )-eptazocine with 32% overall yield in four steps (**Scheme 2-8**).<sup>16</sup> The desired aldehyde **II-54** could be obtained in moderate yields from the readily available iodo

benzene **II-52** and olefin **II-53** using  $[\text{Pd}(\text{C}_3\text{H}_5)\text{Cl}]_2$  and 5-norbornene-2-carboxylic acid as cooperative catalyst, XPhos as ligand,  $\text{K}_2\text{CO}_3$  as base in MeCN. A facile reductive amination of aldehyde **II-54** gave the corresponding secondary amine **II-55** in 94% yield. The key tricyclic intermediate **II-56** was synthesized by a cascade reaction involving C-H bond oxidation and a Mannich reaction. Finally, it underwent the reduction of the ketone group and debenzoylation using Pd/C in acidic medium under 40 atm  $\text{H}_2$  at 65 °C to furnish the racemic ( $\pm$ )-eptazocine in 90% yield.



**Scheme 2-8.** A 4-step total synthesis ( $\pm$ )-eptazocine

These methods suffer from some limitations such as expensive reagents, harsh reaction conditions, complex synthetic procedures and poor yields. We described three short, practical and convergent synthetic routes to ( $\pm$ )-eptazocine involving a radical cascade reaction of xanthates as the key step. The synthesis methods we developed have several advantages: (1) the reaction conditions are mild and the experimental produce is simple and safe; (2) no transition metals or toxic metals are involved in the reaction; (3) the reagent and most of starting materials are cheap and

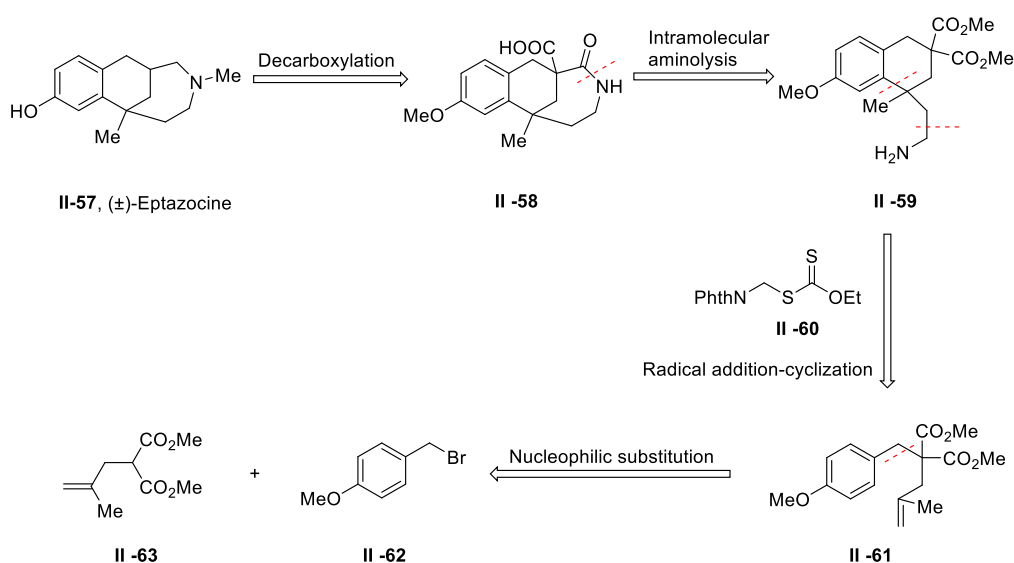


the reactions are easy to scale up.

## 2.3 The first synthetic route to ( $\pm$ )-eptazocine based on the xanthate mediated radical reaction.

### 2.3.1 Retrosynthesis

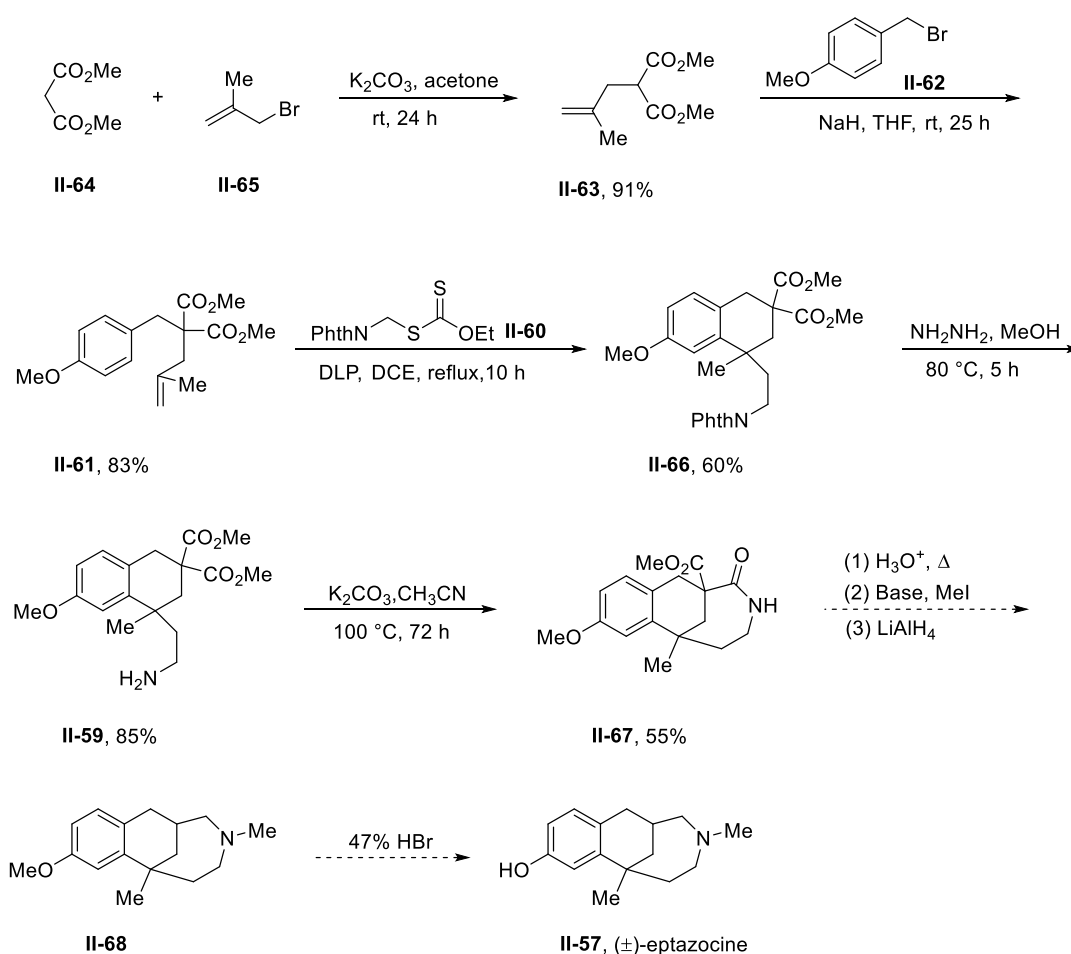
( $\pm$ )-Eptazocine could be obtained by decarboxylation of **II-58** under heating. However, this decarboxylation reaction requires harsh reaction conditions such as high temperature. The tricyclic **II-58** would be formed by intramolecular aminolysis from **II-59**. The intermediate **II-59** might be generated from xanthate **II-61** and olefin **II-60** through radical addition–cyclization. The olefin **II-60** might be introduced by nucleophilic substitution from easily available **II-63** and **II-62**.



**Scheme 2-9.** Retrosynthesis of ( $\pm$ )-eptazocine in the first synthetic route.

The first approach is shown in **Scheme 2-10**. Dimethyl allylmalonate **II-63** was synthesized in excellent yield from commercially available dimethyl malonate **II-64** and further alkylated with 1-(bromomethyl)-4-methoxybenzene **II-62** in the presence

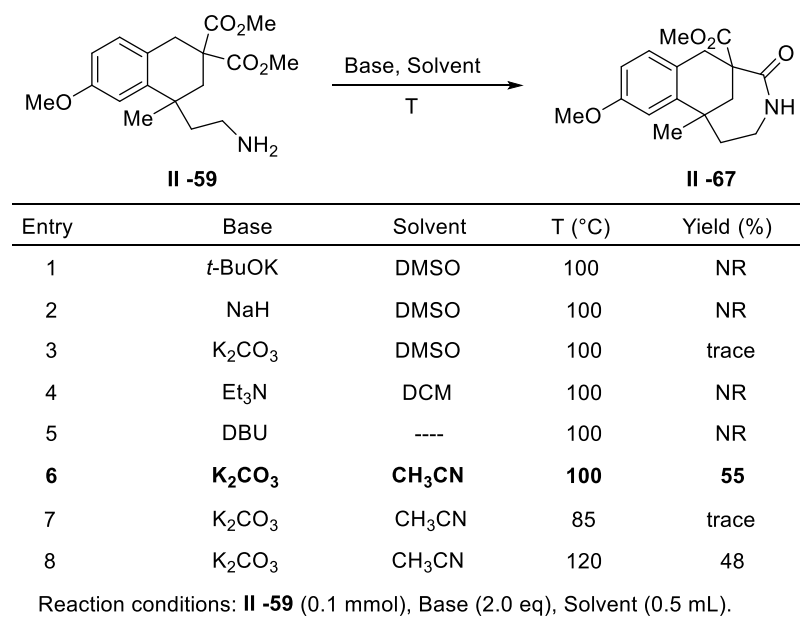
of NaH in THF at room temperature to give compound **II-61** in good yield. This compound was then reacted with xanthate **II-60** in refluxing dichloroethane using dilauroyl peroxide (DLP) as a radical initiator. The radical addition-cyclization afforded bicyclic product **II-66** in 60% yield. This *N*-alkylated phthalimide was then converted into the corresponding primary alkyl amine **II-59** in good yield by hydrazinolysis. The formation of seven membered ring lactam **II-67** was achieved by intramolecular aminolysis of one of the ester groups using potassium carbonate as base at 100 °C in acetonitrile. To complete the synthesis, lactam **II-67** must be methylated, the remaining ester group hydrolyzed and decarboxylated, and the lactam reduced into known amine **II-68** with LiAlH<sub>4</sub>. Finally, demethylation with 48% aqueous HBr solution should provide the target (±)-eptazocine.



**Scheme 2-10.** The first planned approach to (±)-eptazocine using xanthate chemistry

Surprisingly, the formation of lactam **II-67** was not as straightforward as anticipated,

as indicated by the experiments summarized in **Scheme 2-11**.  $K_2CO_3$  as base in  $CH_3CN$  at 100 °C proved to be the best conditions, even if the yield of the desired product remained moderate (55%). Other bases such as *t*-BuOK, NaH,  $Et_3N$ , and DBU resulted in no reaction at all. Solvent screening revealed that  $CH_3CN$  is the best solvent and 100 °C is the most suitable reaction temperature.



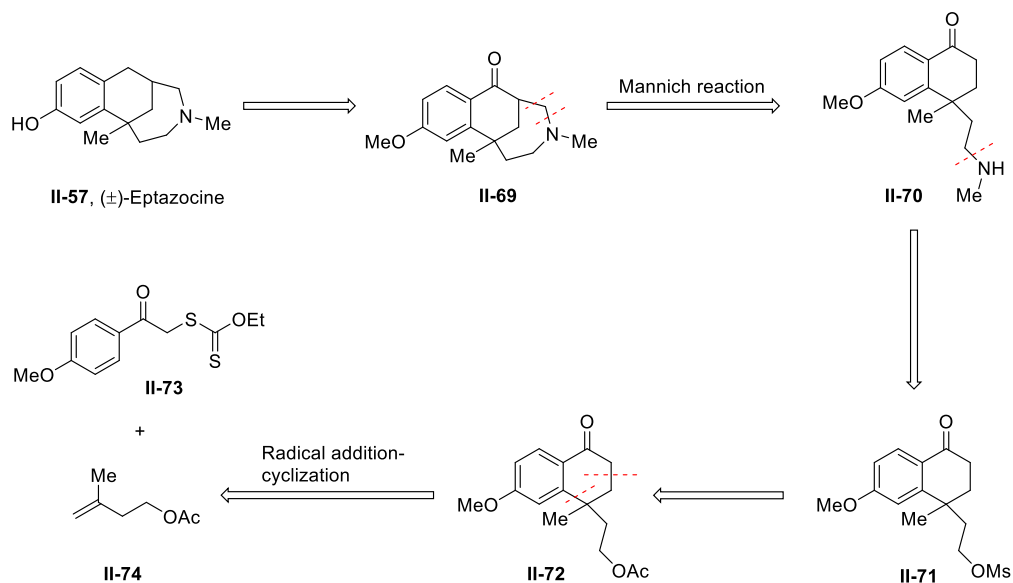
**Scheme 2-11.** Optimization of the key step

## 2.4 The second route to (±)-eptazocine based on the xanthate mediated radical reaction.

### 2.4.1 Retrosynthesis

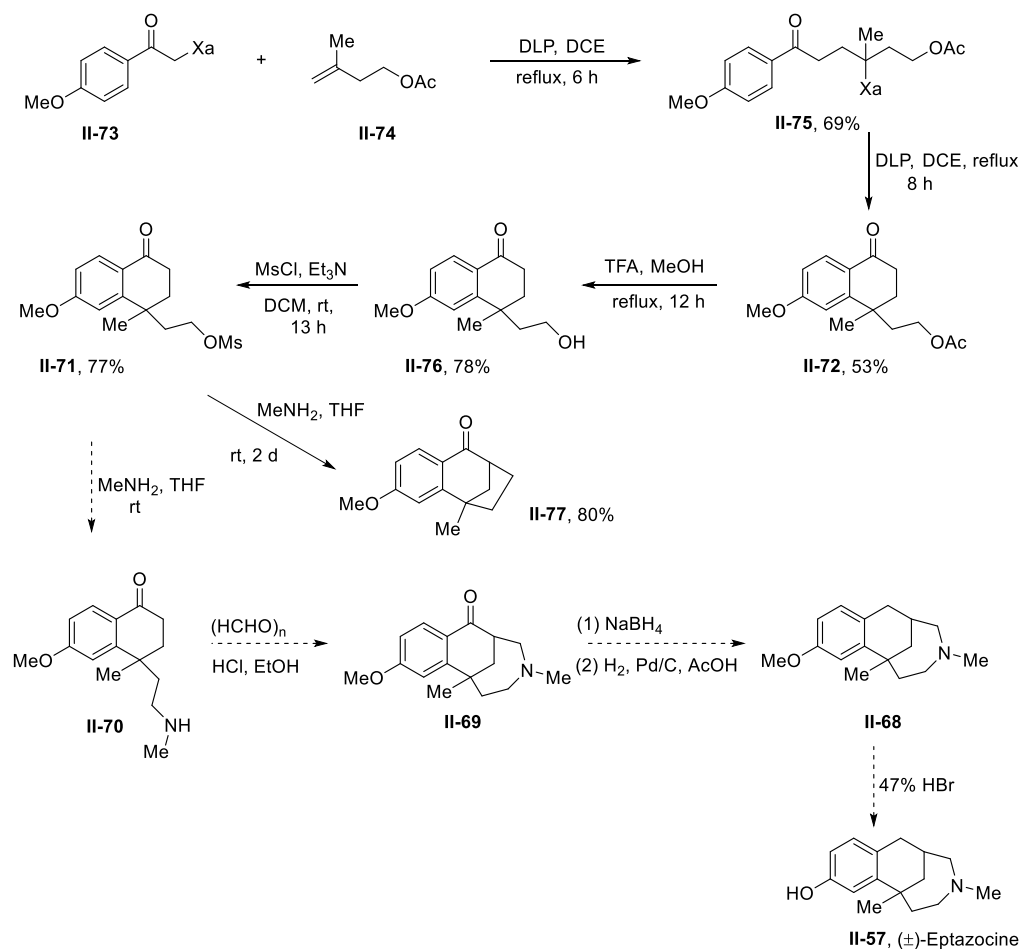
(±)-Eptazocine could be obtained by reduction from the corresponding ketone **II-69**. The tricyclic **II-69** can be formed by Mannich reaction from the corresponding secondary amine **II-70**, where this reaction is the key step. The intermediate **II-70** would be generated by *N*-Methylation from the mesylate **II-71**, which would be obtained by de-esterification and sulphonation from the key intermediate **II-72**. The key intermediate **II-72** would be obtained by radical addition-cyclization between the

xanthate **II-73** and the olefin **II-74**.



**Scheme 2-12.** Retrosynthesis of (±)-eptazocine in the second synthetic route

The second synthetic route to eptazocine is presented in **Scheme 2-13**. The radical addition of the xanthate **II-73** to olefin **II-74** using dilauroyl peroxide (DLP) as the radical initiator in refluxing 1,2-dichloroethane afforded adduct **II-75** in 69% isolated yield. Exposure of this adduct to a stoichiometric amounts of peroxide in refluxing 1,2-dichloroethane promoted ring closure into tetralone **II-72** in 53% isolated yield. The acetyl group was next removed with TFA at reflux to give alcohol **II-76** in 78% yield and mesylation with methanesulfonyl chloride and Et<sub>3</sub>N at room temperature afforded mesylate **II-71** in 77% yield. Unfortunately, this compound could not be converted into methylamine **II-70** under a variety of conditions. Even under mild basic conditions, mesylate **II-71** underwent intramolecular substitution with the enolate of the ketone to give tricyclic tetralone **II-77**.

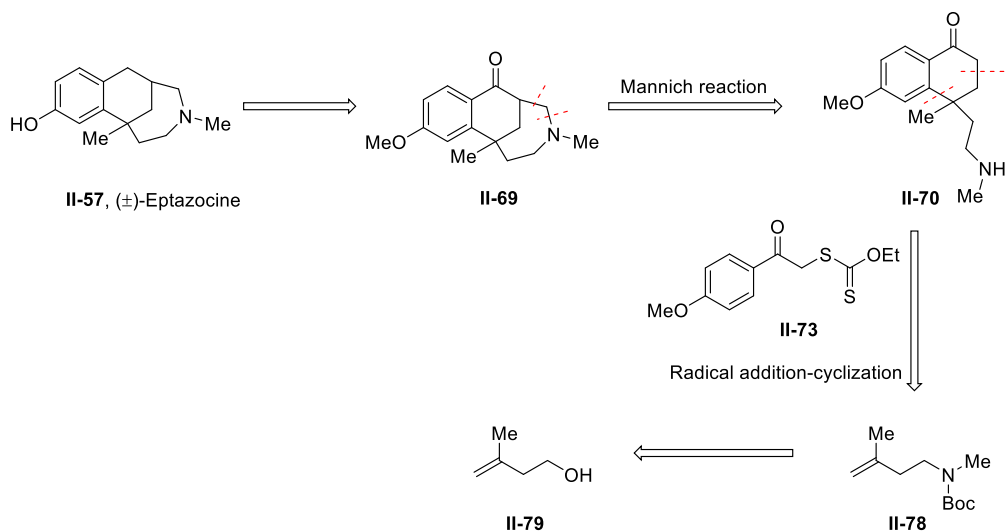


**Scheme 2-13.** The second route for synthesis of ( $\pm$ )-eptazocine using xanthate chemistry

## 2.5 The third route to ( $\pm$ )-eptazocine based on the xanthate mediated radical reaction.

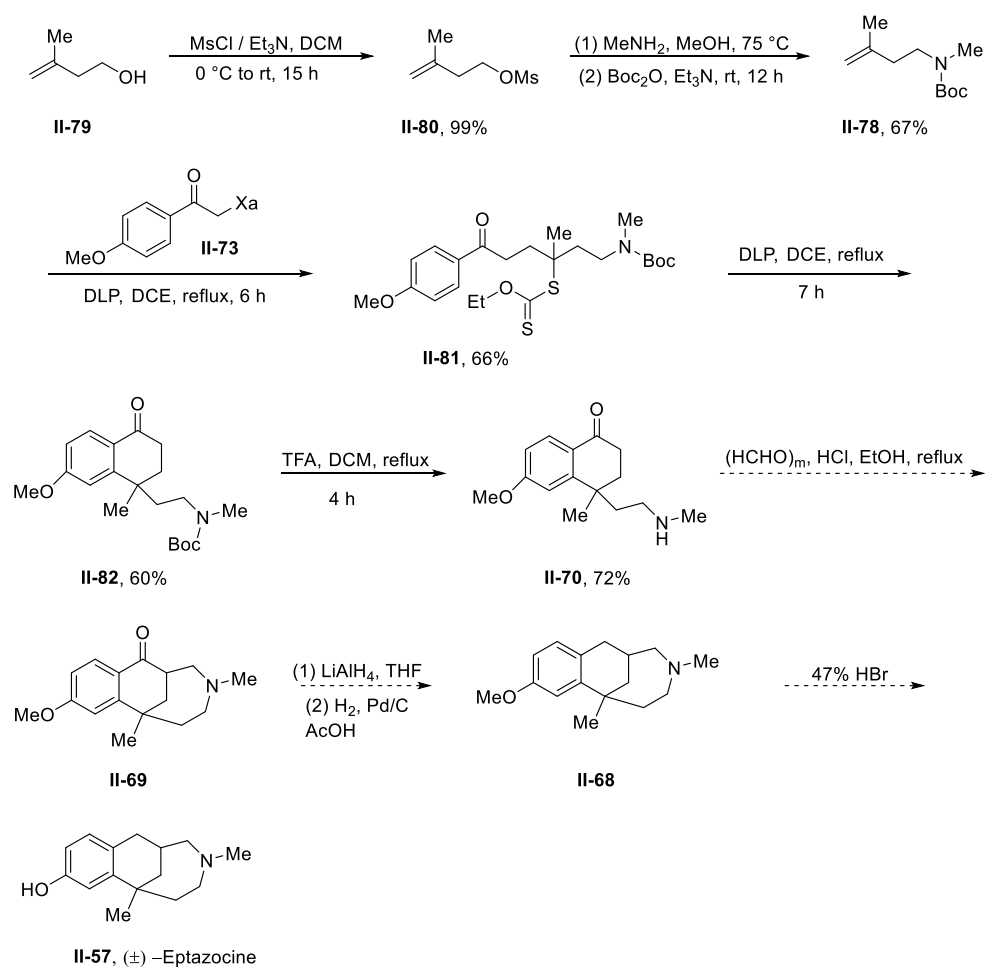
### 2.5.1 Retrosynthesis

The target ( $\pm$ )-eptazocine could in principle be achieved by reduction from intermediate **II-69**, which would be generated through a Mannich reaction from intermediate **II-70**. The intermolecular radical addition of the xanthate **II-73** with the olefin **II-78** would afford the corresponding adduct, which would further undergo intramolecular radical cyclization to give the key intermediate **II-70**. Olefin **II-78** could be obtained from the commercially available alcohol **II-79**.

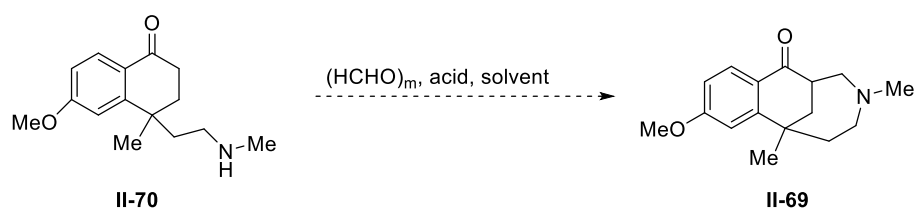


**Scheme 2-14.** Retrosynthesis of (±)-eptazocine in the third synthetic route

The third synthetic route of (±)-eptazocine is shown in **Scheme 2-15**. Mesylate **II-80** was obtained in 99% yield by reaction of commercially available 3-methyl-3-butenol **II-79** with MsCl and Et<sub>3</sub>N. The protected alcohol reacted with methylamine in methanol at 75 °C and protection with Boc<sub>2</sub>O using Et<sub>3</sub>N as base afforded olefin **II-78** in 67% yield for the two steps. Addition of xanthate **II-73**, prepared in excellent yield by reaction of 2-bromo-1-(4-methoxyphenyl)ethan-1-one with commercially available potassium *O*-ethyl carbonodithioate, to olefin **II-78**, mediated by a small amount of the DLP, provided the corresponding adduct **II-81** in 66% isolated yield. This adduct cyclized smoothly by the action of stoichiometric amounts of DLP in refluxing DCE to furnish tetralone **II-82** in 60% yield. The Boc group was readily removed in the presence of TFA to give the corresponding amine **II-70** in 72% yield. The key Mannich cyclization has surprisingly not succeeded so far, as shown by the experiments summarized in **Scheme 2-16**. Nevertheless, the synthesis of (±)-eptazocine is almost complete. More effort will be invested in overcoming the Mannich cyclization step, which is in fact preceded on these structures (see for example the conversion of **II-47** into **II-48** in **Scheme 2-7**). Furthermore, both the radical addition step leading to **II-81** and cyclization into tetralone **II-82** will be further improved and telescoped so that they can be done in the same flask.



**Scheme 2-15.** The third route for synthesis of ( $\pm$ )-eptazocine using xanthate chemistry



entry	solvent	acid	temperature	yield
1	EtOH	HCl	reflux	NR
2	MeOH	HCl	reflux	NR
3	<i>n</i> -PrOH	HCl	reflux	NR
4	EtOH	CH <sub>3</sub> COOH	reflux	NR
5	EtOH	CF <sub>3</sub> COOH	reflux	NR

Reaction conditions: the reaction was performed with **II-70** (1 equiv) and paraformaldehyde (6 equiv).

**Scheme 2-16.** Conditions used for the Mannich cyclization

## 2.6 Conclusion and perspective

In this chapter, we described a brief overview of various strategies to synthesize ( $\pm$ )-eptazocine molecule. These previous strategies suffer from some limitations such as expensive reagents, harsh reaction conditions, complex synthetic procedures and poor yields. Xanthates can mediate radical addition-fragmentation or addition-cyclization sequence as the key step, which can be utilized in synthesis of natural products or particular targets. Three different routes to ( $\pm$ )-eptazocine molecule were developed involving the radical addition-cyclization sequence as the key step. The synthetic methods we developed have some advantages: (a) the reaction conditions are mild and the experimental procedure is simple and safe; (b) no transition metals are involved in the reaction; (c) the reagent and most of starting materials are cheap and the reaction are easy to scale up. Although ( $\pm$ )-eptazocine could not be successfully synthesized, its core skeleton of benzylic quaternary carbon center has been constructed. The major challenges of achieving total synthesis of ( $\pm$ )-eptazocine are decarboxylation reaction and Mannich reaction. Further work is needed to overcome these challenges to finish total synthesis of ( $\pm$ )-eptazocine.

## 2.7 References

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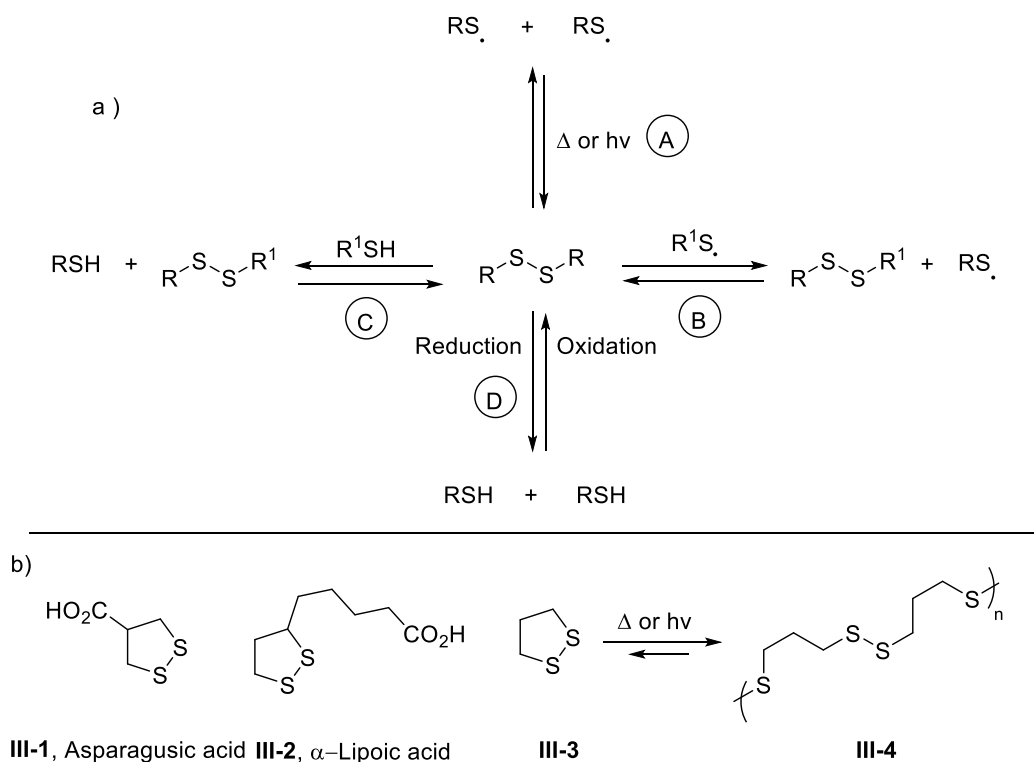
## Chapter 3 Modular Routes to 1,3-Dithiane-2-ones,

### 1,3-Dithiolan-2-ones and 1,2-Dithiolanes

#### 3.1 Introduction

The sulfur-sulfur bond in disulfides is thermodynamically stable. But it is kinetically unstable because it can be reversibly cleaved by the action of thiol radicals or by nucleophilic displacement with a thiol or a thiolate (Scheme 3-1a).<sup>1</sup> The disulfide exchange can occur in redox environment. Because of the high chemical reactivity of thiols, they are chosen as a chemical entity for chemo-selective modification reactions and used in polymeric and polypeptide chemistry.<sup>2</sup>

The cyclic disulfides such as 1,2-dithiolanes are present in asparagusic acid **III-1** and  $\alpha$ -lipoic acid **III-2**. Asparagusic acid **III-1**, isolated from asparagus, is widely used for the treatment of angiopathy and against the cyclooxygenases.<sup>3</sup>  $\alpha$ -Lipoic acid **III-2**, found in animal tissues, spinach, broccoli, peas, brussels sprouts and potatoes, is a natural product which is widely used for the treatment of nerve-related symptoms of diabetes, including burning pain, and numbness in the legs and arms.<sup>4</sup> Interestingly, in the fairly flat 5-membered disulfide bonds, the lone pairs on adjacent sulfur atoms are eclipsed, whereas in homologous 6-membered disulfide bonds, they are staggered. The eclipsed disposition can increase the electronic repulsion and weaken the disulfide bond. Because of this ring strain in 1,2-dithiolanes **III-3**, they are in equilibrium with the open chain polymers **III-4** under mild thermal or photochemical conditions, with the latter being favored.<sup>5</sup> These observations have encouraged numerous studies. However, most of the work has focused on commercially available lipoic and asparagusic acids and simple derivatives. The broaden preparation of disulfides and their 1,3-dithiol precursors has in fact been rarely pursued.

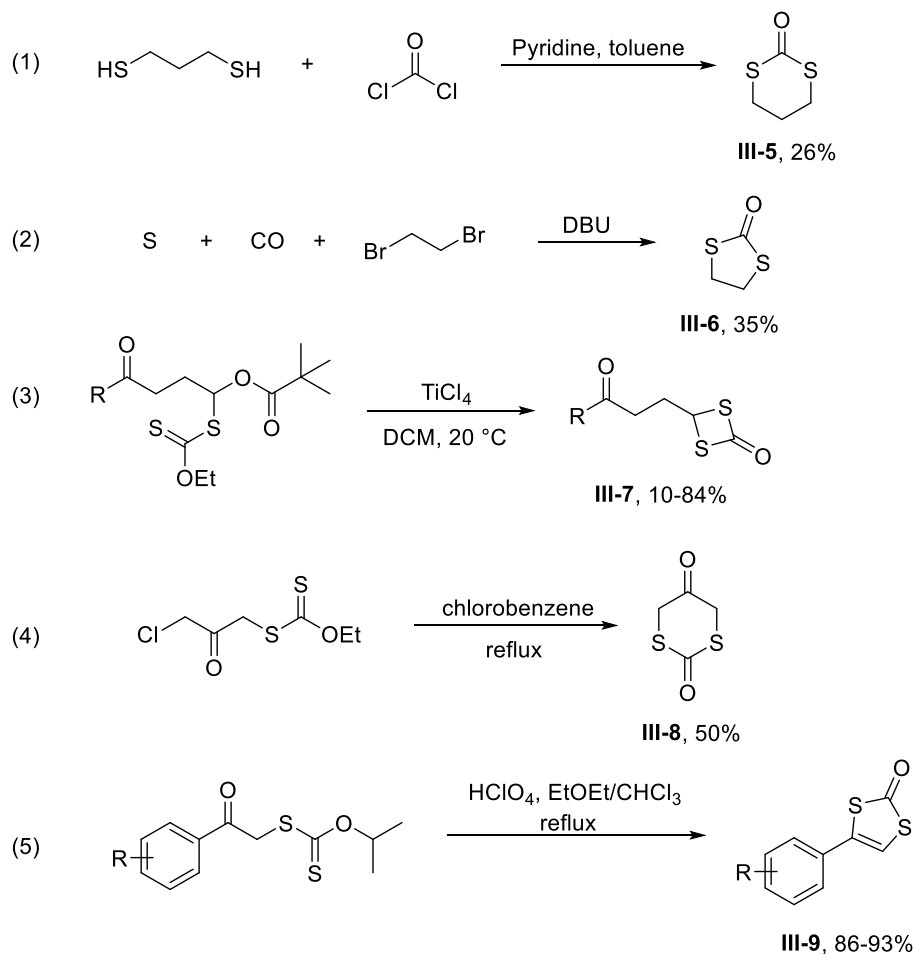


**Scheme 3-1.** Some aspects of disulfide chemistry

## 3.2 Synthetic routes to 1,3-dithiane-2-ones and 1,3-dithiolan-2-ones

It is surprising to us that the synthesis of 1,3-dithiane-2-ones and 1,3-dithiolan-2-ones have been very rarely reported in the open literature. In 1987, Patin and co-workers reported the synthesis of the 1,3-dithiane-2-ones **III-5** by the reaction between dithiols and phosgene under alkaline conditions (**Scheme 3-2, eq 1**).<sup>6</sup> In 1990, Mizuno and co-workers reported a facile synthesis of the 1,3-Dithiolan-2-ones **III-6** from sulfur, carbon monoxide and alkyl halides (**Scheme 3-2, eq 2**).<sup>7</sup> In 2003, our group reported that Lewis acid titanium tetrachloride catalyzed ring closure to synthesize the 1,3-dithid-2-ones **III-7** (**Scheme 3-2, eq 3**).<sup>8</sup> In 2006, a new method for preparing 1,3-dithiane-2-one **III-8** by heating mono-xanthate alone in refluxing chlorobenzene was uncovered (**Scheme 3-2, eq 4**).<sup>9</sup> In 2010, Pintus and co-workers reported that strong acid catalyzed intramolecular substitution-elimination to afford unsaturated 1,3-dithiane-2-ones **III-9** in excellent yield (**Scheme 3-2, eq 5**).<sup>10</sup> These methods

suffered from some limitations such as necessity of using toxic reagents, harsh reaction conditions, narrow substrates scope and poor yields. Recently, we have developed some new methods to synthesize the 1,3-dithiane-2-ones and 1,3-dithiolan-2-ones based on the radical addition of xanthates to various olefins bearing a suitably located leaving or functional group.

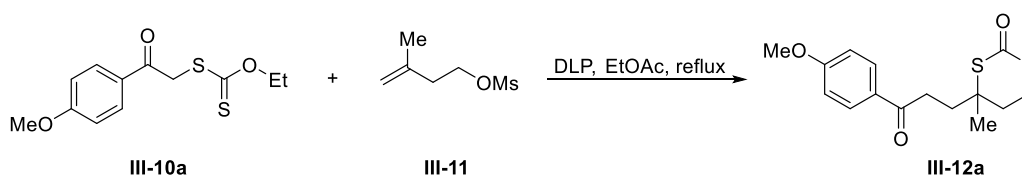


**Scheme 3-2.** Some synthetic strategies for 1,3-dithiane-2-ones and 1,3-dithiolan-2-ones

### 3.3 Synthesis of 1,3-dithiane-2-ones

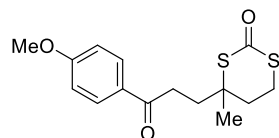
1,3-Dithiane-2-ones were synthesized by the intermolecular radical addition of a xanthate to olefins bearing a suitably located leaving group. Cheap, readily available

xanthate **III-10a** was chosen as a model substrate to test our synthetic approach. To our delight, the corresponding 1,3-Dithiane-2-ones **III-12a** was formed in 79% yield upon heating of xanthate **III-10a** and 3-methylbut-3-en-1-yl methanesulfonate **III-11** with DLP in refluxing ethyl acetate, as shown in **Scheme 3-3**. It is worth pointing out that the cyclization was completed by heating the reaction mixture without isolation of intermediates.

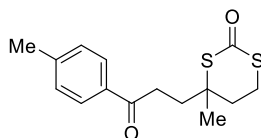


**Scheme 3-3.** Model reaction for the synthesis of 1,3-dithiane-2-ones

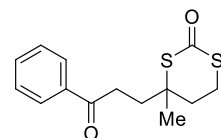
After optimization of reaction conditions, the substrate scope of xanthates was examined as shown in **Scheme 3-4**. A broad range of xanthates reacted smoothly to furnish the corresponding 1,3-dithiane-2-ones in medium to good yield. Both electron-donating and electron-withdrawing group on the phenyl ring of phenacyl-type xanthates were compatible with the system (**III-12a-h**). Heterocyclic groups such as furan and thiophene were also tolerated (**III-12i-j**). Xanthates bearing a naphthalene ring, as well as aliphatic xanthates are valid substrates for synthesizing the corresponding 1,3-dithiane-2-ones (**III-12k-12m**). The last example, obtained as a 1:1 mixture of *meso*- and *dl*-diastereoisomers, illustrates the possibility of forming bis (1,3-dithiane-2-ones) through a double radical addition.



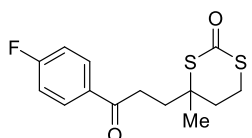
**III-12a**, 11 h, 79%



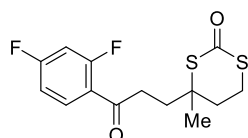
**III-12b**, 14 h, 70%



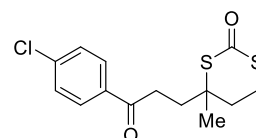
**III-12c**, 11 h, 62%



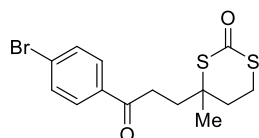
**III-12d**, 10 h, 80%



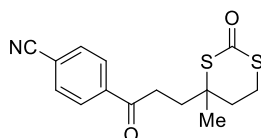
**III-12e**, 12 h, 83%



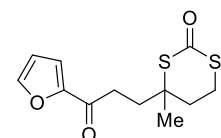
**III-12f**, 10 h, 60%



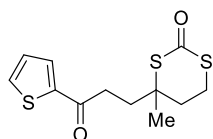
**III-12g**, 13 h, 61%



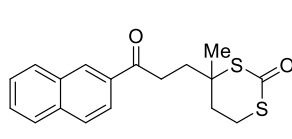
**III-12h**, 10 h, 66%



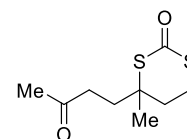
**III-12i**, 13 h, 55%



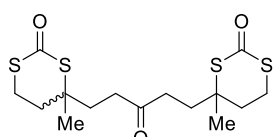
**III-12j**, 12 h, 61%



**III-12k**, 14 h, 50%



**III-12l**, 10 h, 70%

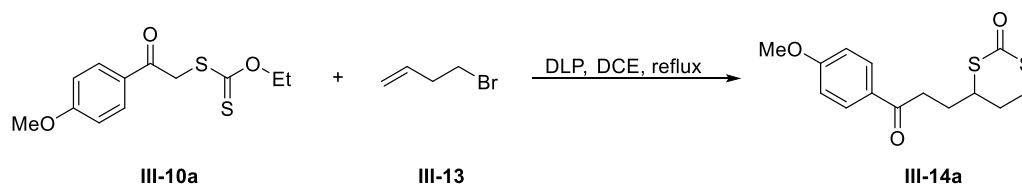


**III-12m**, 13 h, 36%, dr = 1:1

Reaction conditions: the reactions were carried out with **III-10** (3 mmol), **III-11** (6 mmol) and DLP (1.8 to 2.4 mmol) in ethyl acetate (3 mL) at reflux.

#### Scheme 3-4. Substrate scope for the synthesis of 1,3-dithiane-2-ones

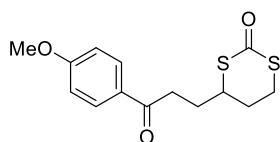
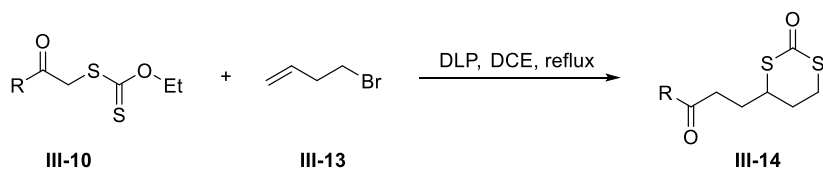
After the success in the synthesis of 1,3-dithiane-2-ones from homoallylic mesylate **III-11**, we examined the possibility of obtaining such derivatives by using a homoallylic bromide such as 4-bromobut-1-ene **III-13**. We were again pleased to find that the desired product, 1,3-dithiane-2-one **III-14a**, was obtained in good yield (70%) under the same reaction conditions, as shown in **Scheme 3-5**.



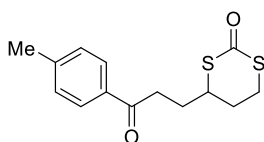
**Scheme 3-5.** First example of a 1,3-dithiane-2-one starting with 3-butenyl bromide.

The substrate scope with respect to xanthates was investigated, as shown in **Scheme 3-5**. Moderate to good yields were observed for xanthates with either electron-donating groups such as *p*-OMe and *p*-Me substituents (**III-14a-b**) or with electron-withdrawing groups such as chlorine and iodine substituents (**III-14d-e**) on the phenyl ring. A variety of aliphatic xanthates afforded the corresponding 1,3-dithiane-2-ones, also in moderate to good yields (**III-14f-i**).  $\alpha$ -Ketonyl xanthates containing furan, thiophene, and naphthalene rings are tolerated, giving the corresponding products in moderate yields (**III-14j**, **III-14k** and **III-14l**). Moreover, xanthates **III-10m** and **III-10n** bearing a lactone and a thiolactone proved well suitable in this reaction system, furnishing 1,3-dithietan-2-ones **III-14m** and **III-14n** in 75% and 57% yields, respectively. As with mesylate **III-11**, bis-(1,3-dithietan-2-one) **III-14o** was obtained by a double radical addition, but the yield of 67% was pleasingly much higher than that of **III-12l** (35%, **Scheme 3-4**).

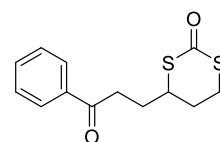




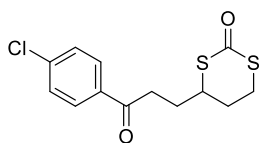
**III-14a**, 21 h, 70%



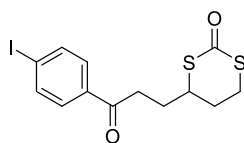
**III-14b**, 14 h, 69%



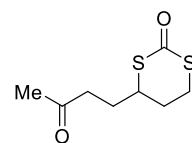
**III-14c**, 16 h, 50%



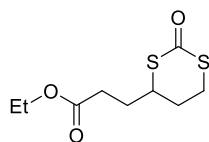
**III-14d**, 19 h, 72%



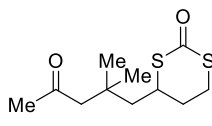
**III-14e**, 14 h, 59%



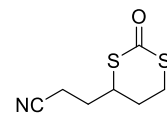
**III-14f**, 20 h, 58%



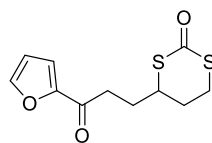
**III-14g**, 20 h, 64%



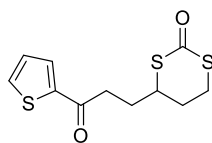
**III-14h**, 19 h, 47%



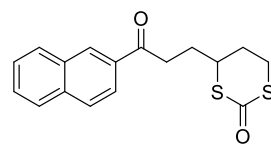
**III-14i**, 20 h, 56%



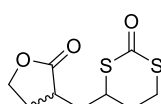
**III-14j**, 20 h, 45%



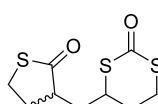
**III-14k**, 18 h, 72%



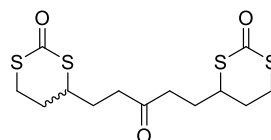
**III-14l**, 20 h, 50%



**III-14m**, 16 h, 75%, dr = 3:2



**III-14n**, 16 h, 57%, dr = 2:1



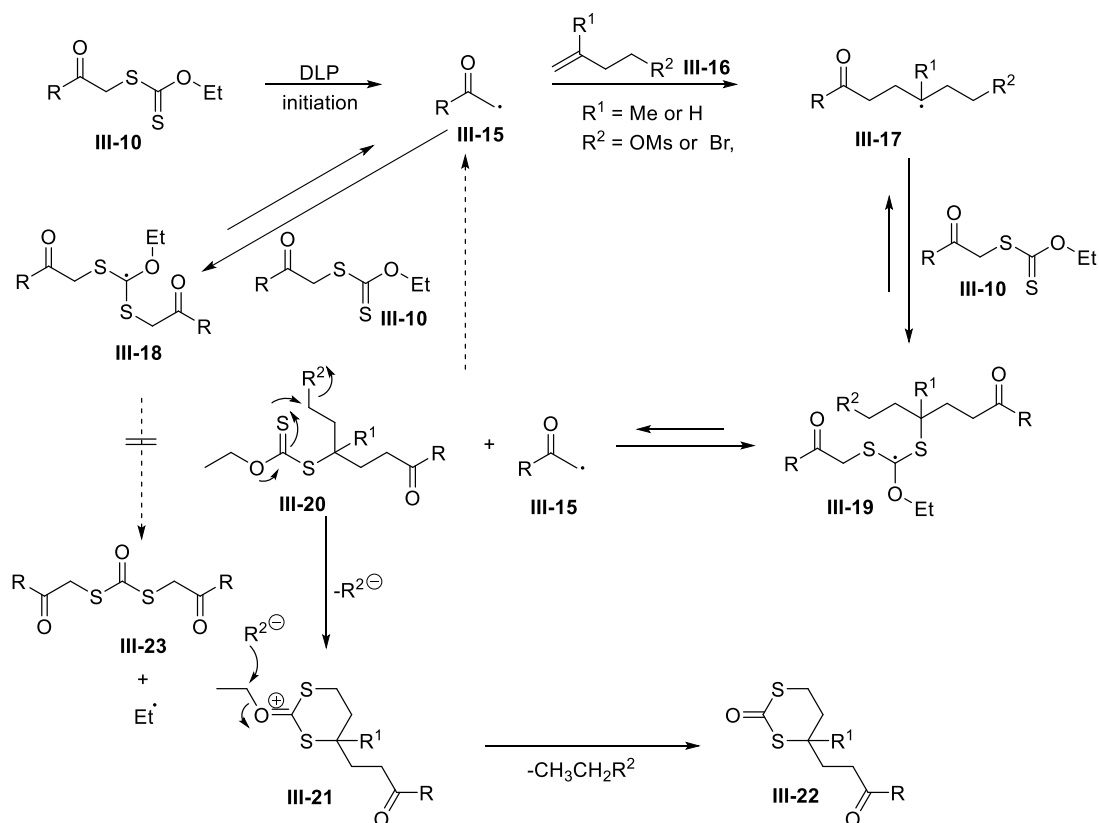
**III-14o**, 17 h, 67%, dr = 1:1

Reaction conditions: the reactions were carried out with **III-10** (3 mmol), **III-13** (6 mmol), and DLP (0.75 mmol to 2.1 mmol) in DCE (3 mL) at reflux..

**Scheme 3-6.** Examples of 1,3-dithiane-2-ones starting with 3-butenyl bromide.

On the basis of our experimental results, a plausible reaction mechanism is proposed in **Scheme 3-7**. Radical **III-15** is generated by the action of the DLP initiator from easily available xanthate **III-10**. The highly radicophilic C=S double bond of the xanthate reversibly captures radical **III-15** to give tertiary radical **III-18**, which is stabilized by three heteroatoms. Thus radical **III-15** is stored in a relatively non-active form and continuously regenerated. Therefore its effective lifetime in the medium is considerably increased, allowing it to react with even un-activated olefins, such as

**III-16**, to give a new adduct radical **III-17**. Further addition to the C=S of the starting xanthate **III-10** leads to product **III-20** via intermediate **III-19**, another stabilized and dormant radical that also acts as a reversible reservoir for the active radicals **III-15** and **III-17**. The collapse of intermediate **III-19** into product **III-20** also releases radical **III-15** which propagates the chain process. In the present case, the alkene partner **III-16** is a homoallylic mesylate or bromide and, at the level of adduct **III-20**, a spontaneous displacement of leaving group R<sup>2</sup> by the sulfur of the xanthate thiocarbonyl occurs under the reaction conditions to give the observed 1,3-dithiane-2-ones **III-22**. It is worth noting that the product **III-23** is not formed as the ethyl radical is more unstable than that radical **III-15**.

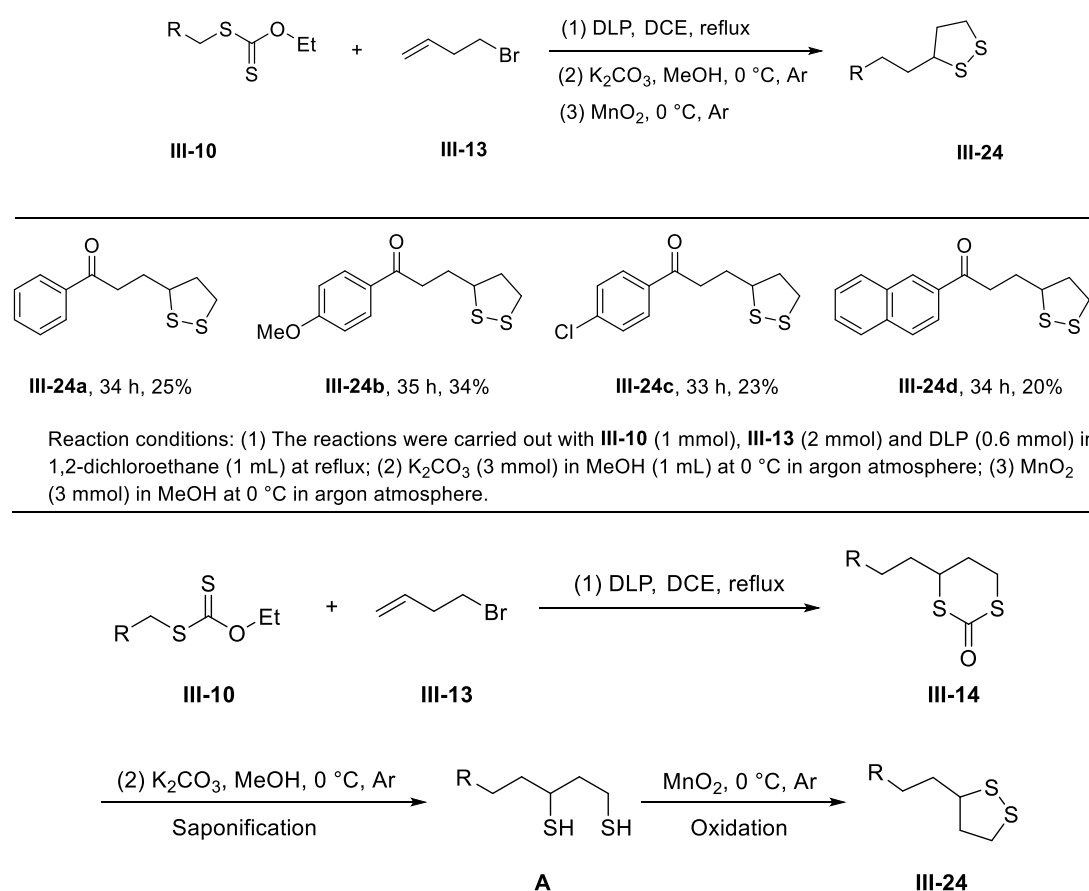


**Scheme 3-7.** The mechanism of 1,3-dithiane-2-one formation

### 3.4 Synthesis of 1,2-dithiolanes

1,3-Dithiane-2-ones are rare structures. A search of the REAXYS data base returned only 17 entries. However, they are immediate precursors of 1,2-dithiolanes, which are

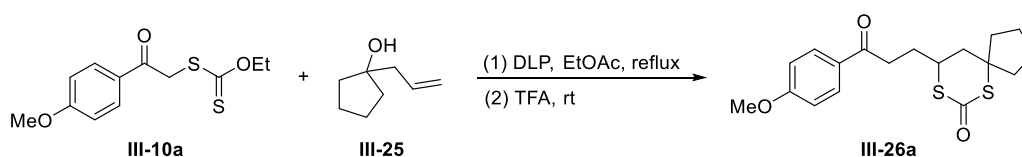
much more widespread in the chemical literature and they are presented in a few natural products such as lipoic acid, charatoxin and neyeistoxin; furthermore 1,2-dithiolanes cannot be regarded as cyclic dithioacetals or ketals and they are not widely distributed in nature. In any case, a few natural products containing 1,2-dithiolanes moieties, and especially the important lipoic acid, have been discussed in the introductory section. The one-pot synthesis of 1,2-dithiolanes **III-24a-d** without isolation of the intermediate 1,3-dithiane-2-ones is presented in **Scheme 3-8**. The overall yield of 1,2-dithiolanes **III-24a-d** is modest, possibly because the polydisulfide polymer was obtained by the competing reaction. The one pot synthesis of 1,2-dithiolanes contains intermolecular radical addition of xanthate **III-10** with olefin **III-13**, saponification and oxidation of the 1,3-dithiol (Scheme 3-8).



**Scheme 3-8.** One-pot synthesis of 1,2-dithiolanes

### 3.5 A second route to 1,3-dithian-2-ones

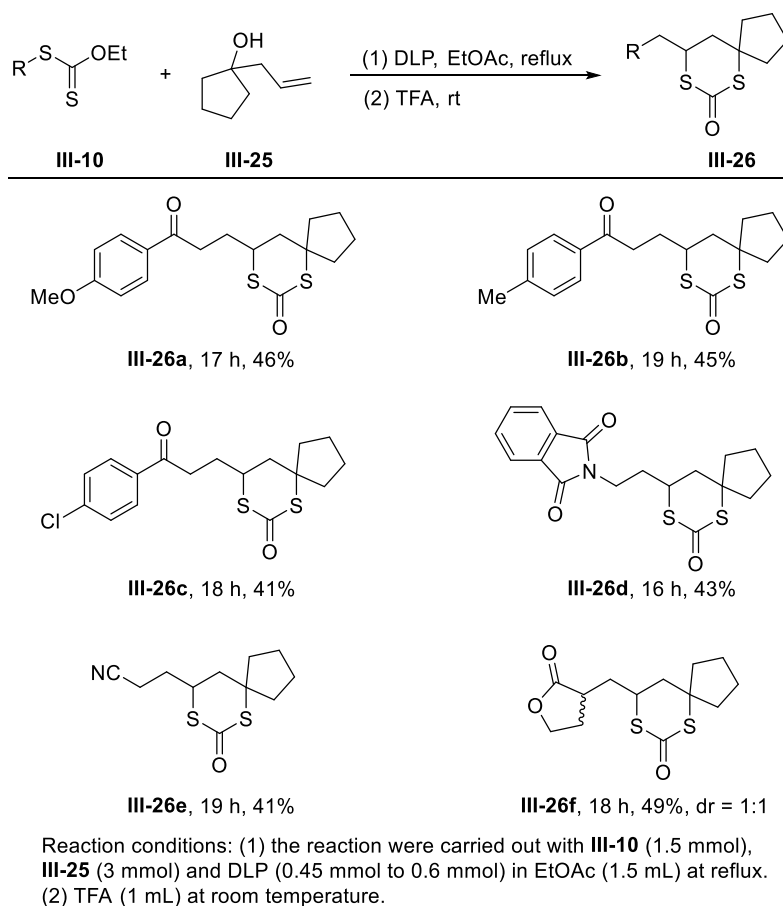
Encouraged by the previous result, we were surprised to find that heating 1.0 equivalent of xanthate **III-10** with 2.0 equivalents of olefins **III-25** in refluxing ethyl acetate gave the corresponding adduct, which followed by was treated with TFA to afford 1,3-dithiane-2-ones **8a** in 46% yield over two steps (**Scheme 3-9**). This is also a one pot process that does not require the isolation of the intermediate radical adducts.



**Scheme 3-9.** Model reaction in the second route for the synthesis of 1,3-dithiane-2-ones

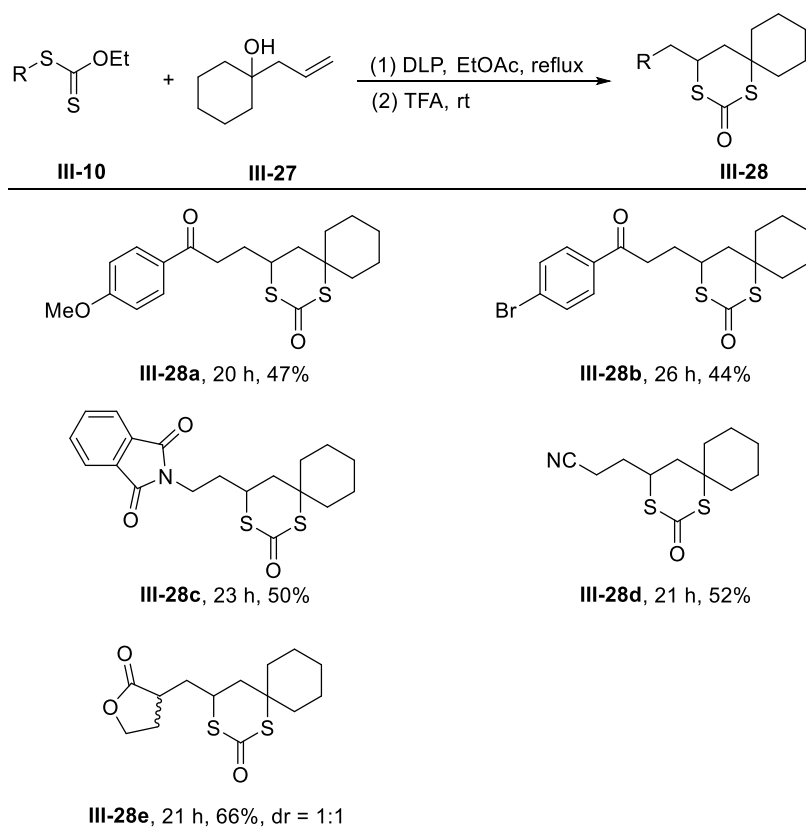
If this method proved to be general, it would offer a new and practical method for synthesizing 1,3-dithiane-2-ones derivatives.

This inspiring result encouraged us to explore the scope of xanthate substrates (**Scheme 3-10**). Xanthates with either electron-donating groups such as *p*-OMe and *p*-Me substituents (**III-26a**, **III-26b**) or with electron-withdrawing groups such as chlorine substituents (**III-26c**) on the phenyl ring can react with olefin **III-25** to afford the corresponding 1,3-dithiane-2-ones derivatives in moderate yield in two steps. Aliphatic xanthate afforded the corresponding 1,3-Dithiane-2-ones, also in moderate yield (**III-26e**). Happily, addition of *S*-phthalimidomethyl xanthates to 1-allylcyclopentan-1-ol **III-25** followed by the treatment with TFA afforded 1,3-dithiane-2-ones **III-26d** in moderate yield. In the same manner, a lactone bearing xanthate can participate in this reaction system in order to provide the corresponding 1,3-dithiane-2-ones **III-26f**.



**Scheme 3-10.** Substrate scope for the synthesis of 1,3-dithiane-2-ones starting with 1-allylcyclopentan-1-ol.

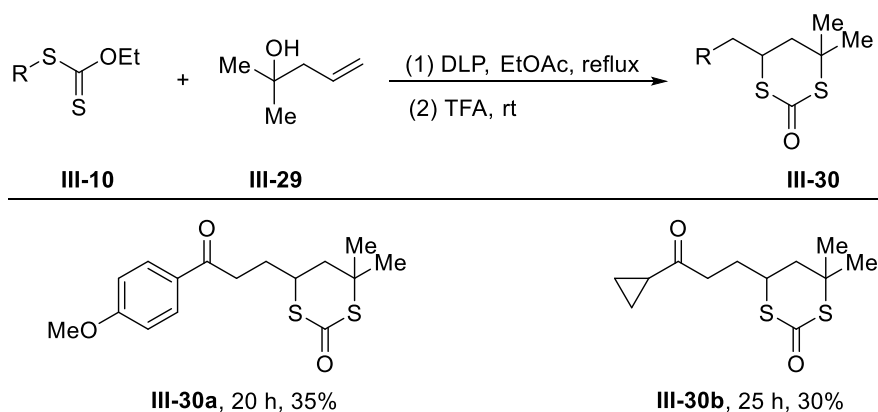
Another interesting extension of the scope of this reaction is the introduction of the 1,3-dithiane-2-ones derivatives, accomplished by using 1-allylcyclohexan-1-ol **III-27** as a starting material. In the same manner, various 1,3-dithiane-2-ones derivatives **III-28a-e** were obtained as shown by the results collected in **scheme 3-11**. Xanthates bearing various functional groups added to 1-allylcyclohexan-1-ol **III-27** to afford the corresponding adducts, which were treated with TFA to afford the corresponding 1,3-dithiane-2-ones derivatives **III-28a-e**.



Reaction conditions: (1) the reaction were carried out with **III-10** (1.5 mmol), **III-27** (3 mmol) and DLP (0.45 mmol to 0.6 mmol) in EtOAc (1.5 mL) at reflux. (2) TFA (1 mL) at room temperature.

**Scheme 3-11.** Substrate scope for the synthesis of 1,3-dithiane-2-ones starting with 1-allylcyclohexan-1-ol.

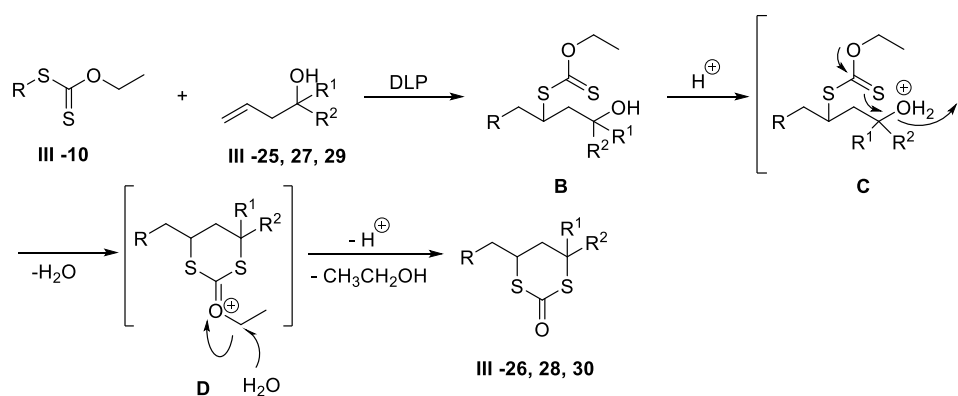
Encouraged by the success of the preliminary experiments presented in **Scheme 3-10** and **Scheme 3-11**, we developed a complementary route to 1,3-dithiane-2-ones derivatives, as shown in **Scheme 3-12**. It involves radical addition of xanthate **III-10** to tertiary homoallylic alcohols **III-29** followed by the treatment of resulting adducts with TFA. The yields of 1,3-dithian-2-ones derivatives **III-30a-b** are moderate.



Reaction conditions: (1) the reaction were carried out with **III-10** (1.5 mmol), **III-29** (3 mmol) and DLP (0.45 mmol to 0.6 mmol) in EtOAc (1.5 mL) at reflux. (2) TFA (1 mL) at room temperature.

**Scheme 3-12.** Examples of 1,3-dithiane-2-ones starting with 2-methylpent-4-en-2-ol.

A plausible reaction mechanism of the second route to 1,3-dithiane-2-ones is proposed in **Scheme 3-13**. First, adduct **B** is formed by intermolecular radical addition of xanthate **III-10** to allyl alcohol derivatives **III-25** or **III-27** or **III-29**. Then it undergoes protonation to form intermediate **C**, which loses a molecule of water to form intermediate **D**. Finally, 1,3-dithiane-2-one **III-26** or **III-28** or **III-30** can be obtained by losing a proton and molecule of ethanol from intermediate **D**.

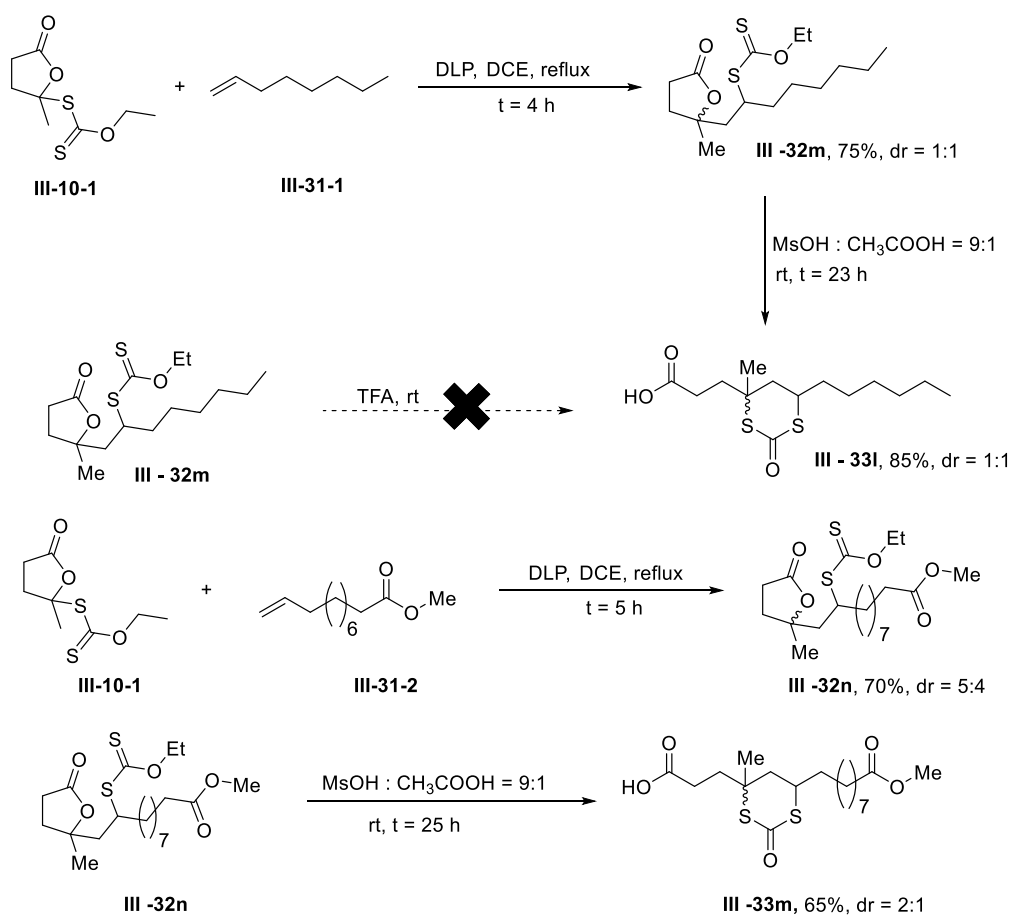


**Scheme 3-13.** The mechanism of formation of 1,3-dithiane-2-ones in the second route

### 3.6 A third route to 1,3-dithiane-2-ones and unexpected route to 1,3-dithiolan-2-ones

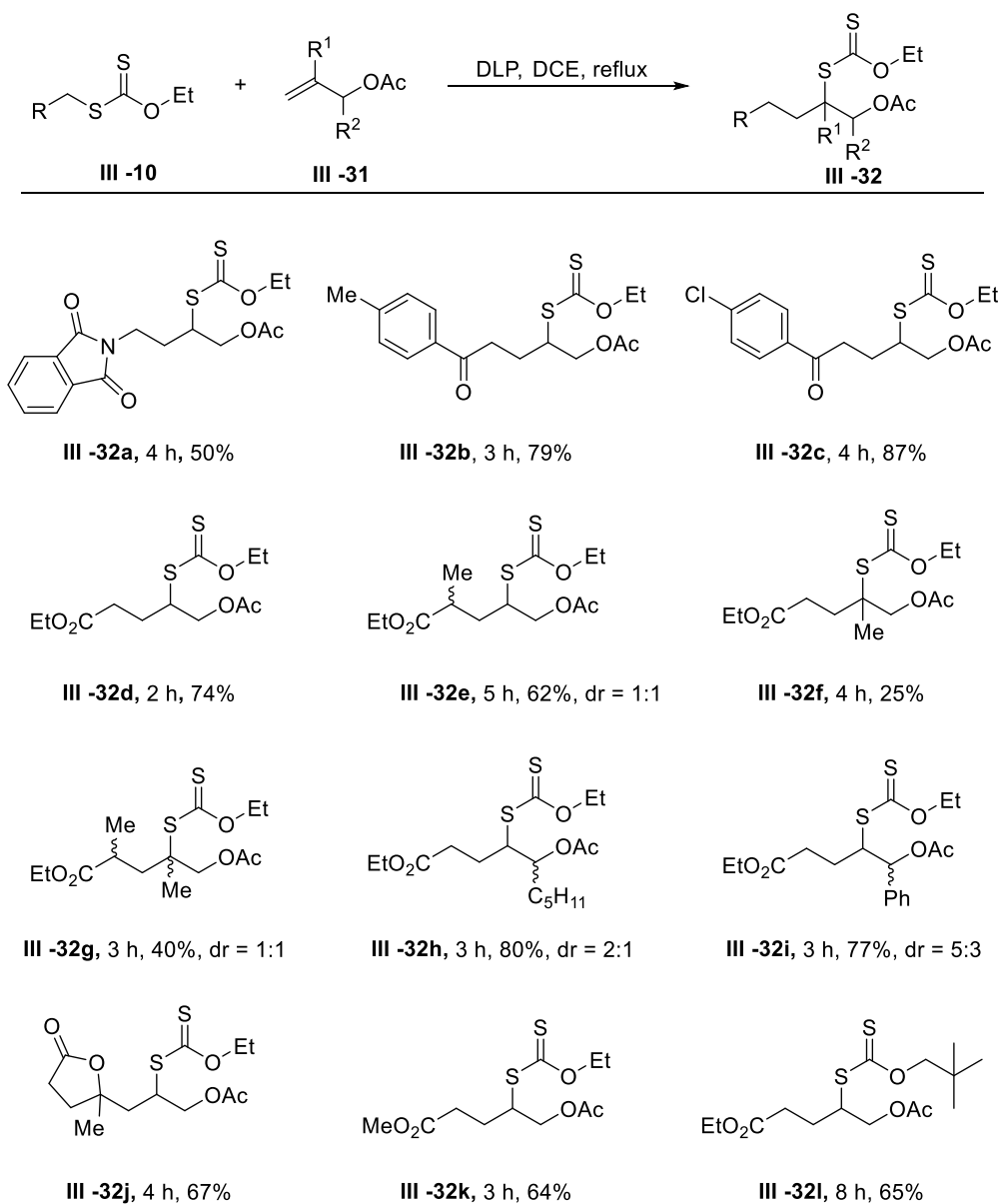
We developed a third route to 1,3-dithiane-2-ones **III-33** possessing a tertiary center starting from the easily available xanthate **III-10-1** and olefins **III-31-1-2**, whereby all the components constructed the sulfur heterocycle are present in the starting xanthate and the olefins are only used to add additional functional groups. This strategy is illustrated by two examples in **Scheme 3-14**. The radical addition reaction of the xanthate **III-10-1** with olefins **III-31-1-2** took place smoothly under the standard conditions to furnish the corresponding adducts **III-32m** and **III-32n**, which was exposed to a 9:1 mixture of methanesulfonic acid (MsOH) and acetic acid at room temperature leading to the formation of the corresponding 1,3-dithiane-2-ones **III-33l** and **III-33m** in a good yield. TFA proved to be too weak to induce the formation of 1,3-dithiane-2-ones **III-33l** and **III-33m**, so the good reaction conditions included a 9:1 mixture of MsOH and acetic acid as catalyst.





**Scheme 3-14.** The third route to 1,3-dithiane-2-ones

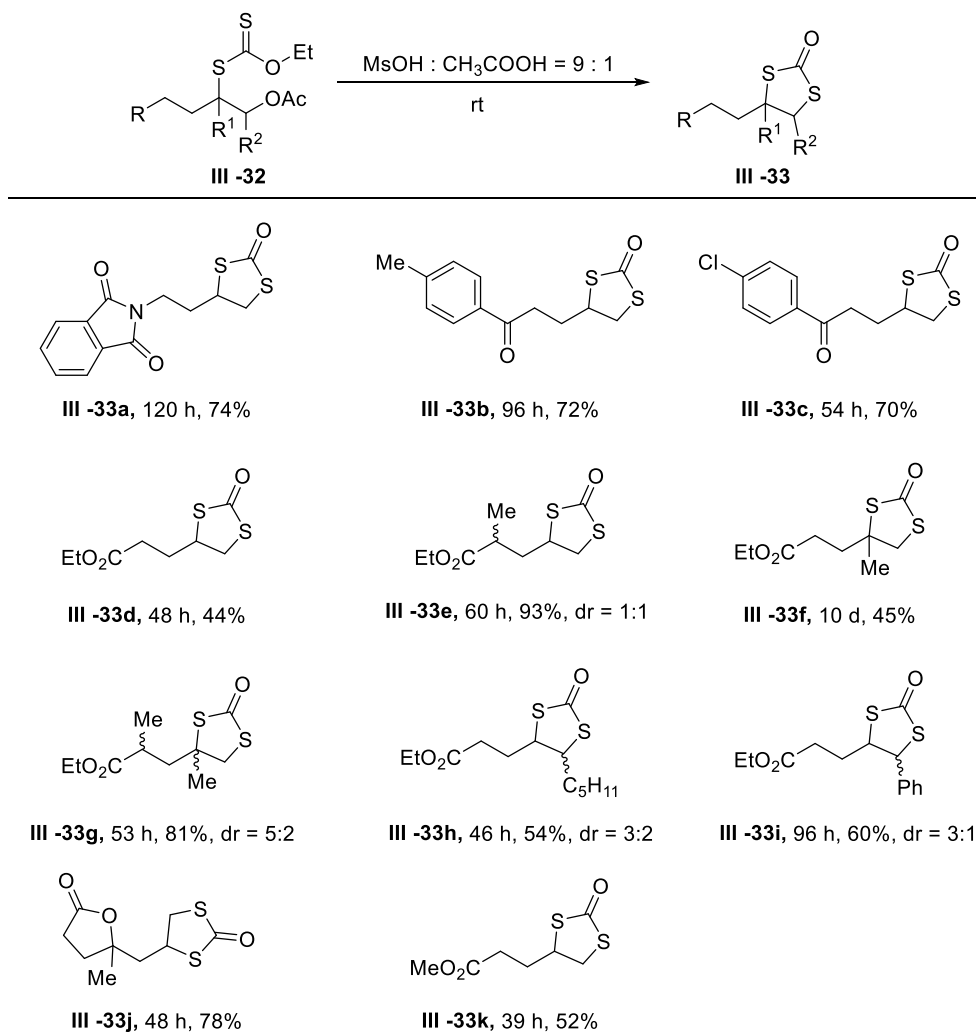
In order to further exemplify this strategy, we also prepared some additional adducts **III-32a-1** in moderate to good yield by the DLP mediated radical addition of xanthates **III-10** to allyl acetate **III-31**, as shown in **Scheme 3-15**.



Reaction conditions: (1) the reaction were carried out with **III-10** (1 eq), **III-31** (2 eq) and DLP (0.2 eq to 0.5 eq) in DCE (x mL) at reflux.

### Scheme 3-15. Substrate scope of the adducts

The reaction conditions, using a 9:1 mixture of MsOH and acetic acid as catalysts without solvent at room temperature were applied to a large variety of adducts and proved to be quite general with yields ranging from 44% - 93% depending on the substrate. Aromatic substituents **III-32b-c**, esters **III-32d -k** were tolerated (**Scheme 3-16**). It should be noted that the displacement of primary acetate is obviously faster than the opening of the tertiary lactone under stronger acidic media (**III-33j**).



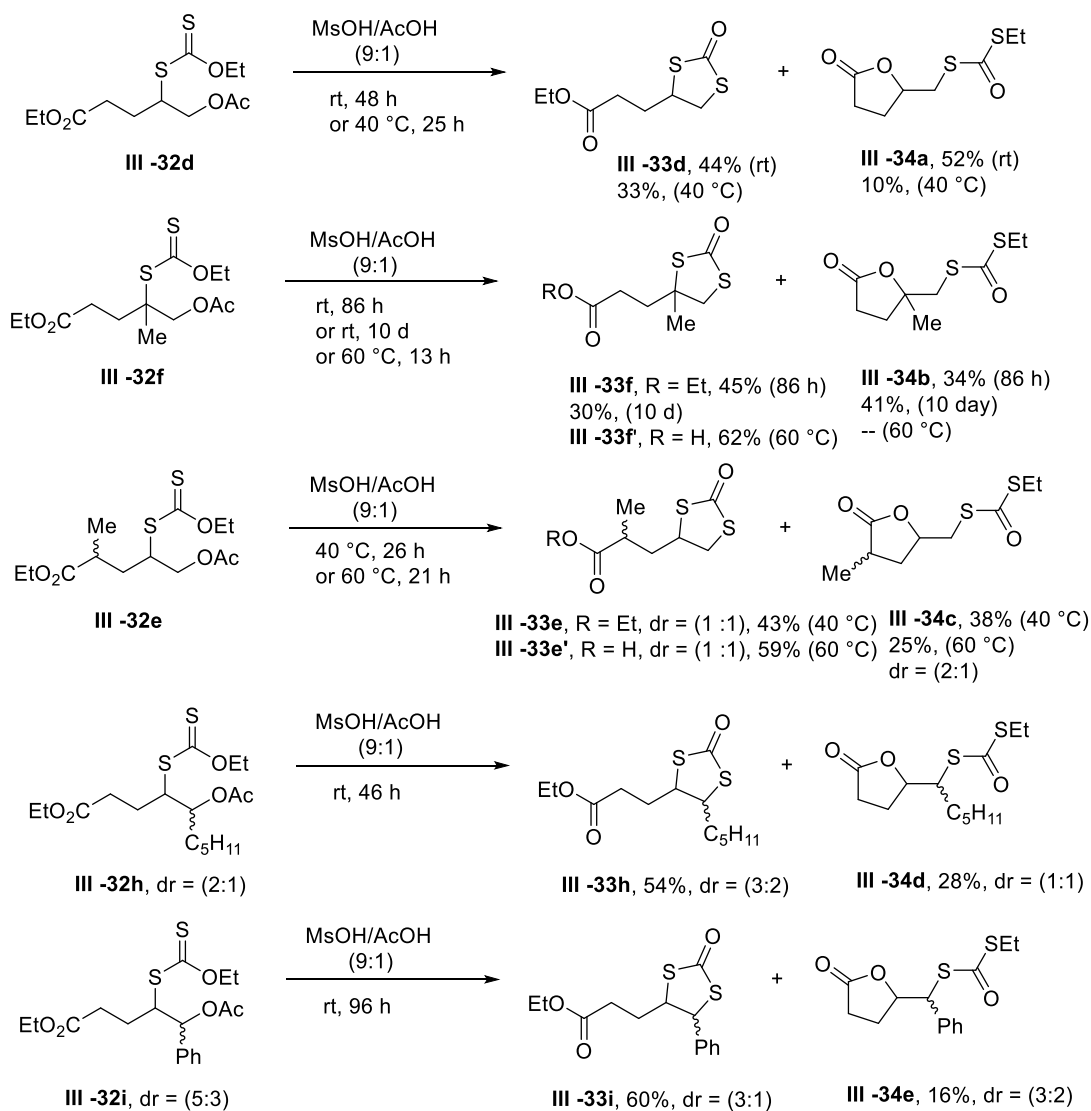
Reaction conditions: (1) the reaction were carried out with **III-32** (x mmol) in x mL of MsOH : CH<sub>3</sub>COOH = 9 : 1 at room temperature.

**Scheme 3-16.** A unexpected route to 1,3-dithiolan-2-ones

### 3.7 Unexpected synthesis of lactones

A new method for preparing lactones was found when we examined the synthesis of adduct **III-32d**. Under the same conditions, the reaction gave lactone **III-34a** along with the expected 1,3-dithiolan-2-one **III-33d** in excellent combined yield. When the reaction temperature was raised to 40°C, the yield of both products decreased significantly. When we examined the methallyl acetate adduct **III-32f**, signs of the cause of this decline appeared. After 86 hours of reaction at room temperature, adduct

**III-32f** was converted into **III-33f** and **III-34b** in 45% and 34% yield, respectively. When reaction time was prolonged to 10 days at room temperature, the yield of the former dropped to 30% and the latter increased slightly to 41%. It is surprising that when the temperature was raised to 60 °C, only the carboxylic acid was obtained in 62% yield. The slow hydrolysis of the ester group caused the decrease in yield treated with adduct **III-32d** when the temperature was raised to 40°C. When a similar method was applied to the branched ester **III-32e** and only 1,3-dithiolan-2-ones **III-33e** was obtained in excellent yield at room temperature. At 40 °C, the corresponding lactone **III-34c** was obtained in only 38% yield, while the yield of the corresponding 1,3-dithiolan-2-ones **III-33e** decreased to 43%. At 60 °C, the carboxylic acid was obtained in 59% yield, while the yield of the corresponding lactone **III-34c** was 25%. The steric hindrance of the  $\alpha$ -methyl group had impact on the hydrolysis of the ester group and it allowed the formation of lactone **III-34c** at higher temperature. Finally, this method was extended to the adducts **III-32h** and **III-32i** derived from the radical addition of the ester xanthate to two substituted allyl acetate. The corresponding lactones **III-34d** and **III-34e** were produced in low yields, while the respective 1,3-dithiolan-2-one **III-33h** and **III-33i** were formed in moderate yield.

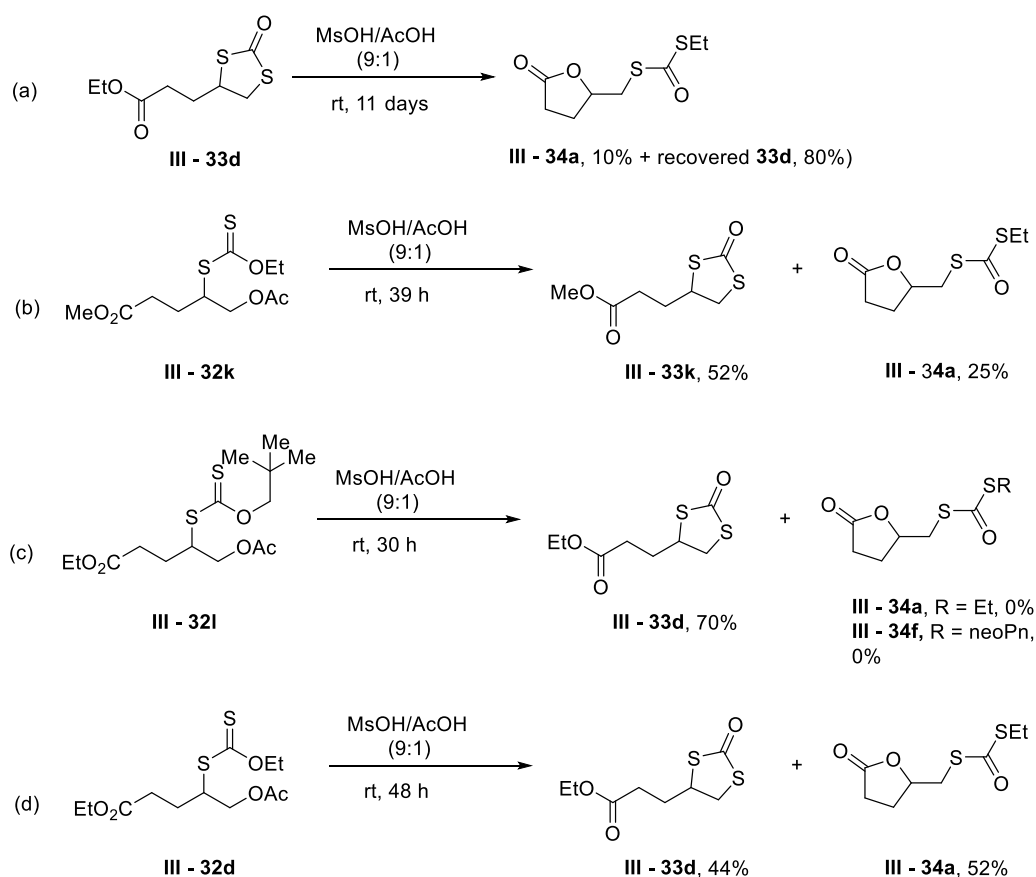


**Scheme 3-17.** The unexpected synthesis of lactones

### 3.8. Further experiments and mechanistic hypothesis

Our initial mechanistic hypothesis was that lactones **III-34a-e** were formed from the transformation of the respective 1,3-dithiolan-2-one **III-32d-f**, **32h** and **32i** and the ethyl group on the dithiolanone came from the ethyl carboxylate. In order to prove the mechanistic hypothesis, we performed some control experiments under the same reaction conditions (**Scheme 3-18**). First, the 1,3-dithiolan-2-one **III-33d** was treated with mixture acid (MsOH : CH<sub>3</sub>COOH = 9 : 1) for 11 days at room temperature. The corresponding lactom **III-34a** was indeed obtained; but the yield was low, only 10%,

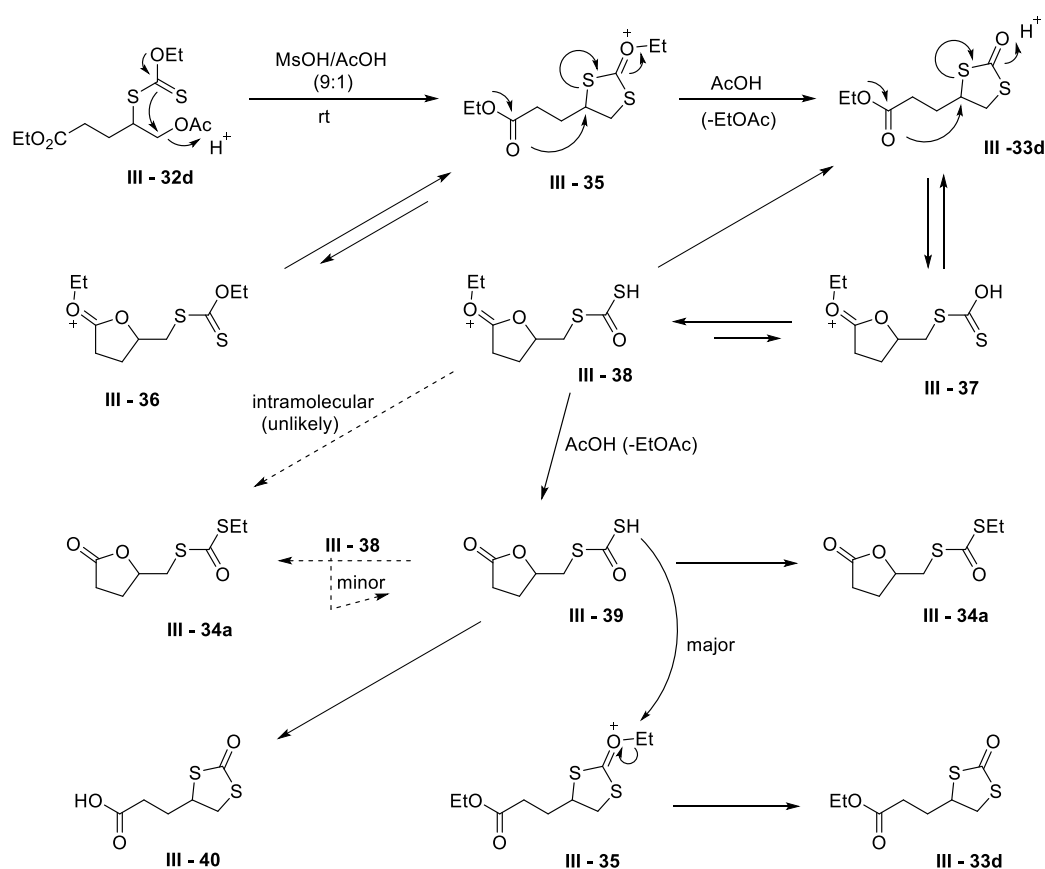
while the starting material was mostly recovered (the rate of recovery is 80%). If the reaction operated completely via this pathway, the corresponding lactone **III-34a** would be the major product. In the second control experiment, the adduct **III-32k** was treated with the same mixture acid to afford the corresponding 1,3-dithiolan-2-one **III-33k** and lactone **III-34a** with ethyl group on the side chain, therefore this ethyl group must come from the xanthate and not from the carboxylate. In the third control experiment, the ethyl group on the xanthate **III-32d** was replaced by the sterically hindered neopentyl group. In this case, the reaction produced only 1,3-dithiolan-2-one **III-33d**; neither the ethyl nor neopentyl lactam **III-34a** nor **III-34f** were obtained.



**Scheme 3-18.** Some examples of control experiments

Based on above control experiments, a plausible reaction mechanism is proposed in **Scheme 3-19**. Acid catalyzed intramolecular nucleophilic substitution of adduct **III-32d** to give the intermediate **III-35**, which can undergo a reversible ring opening

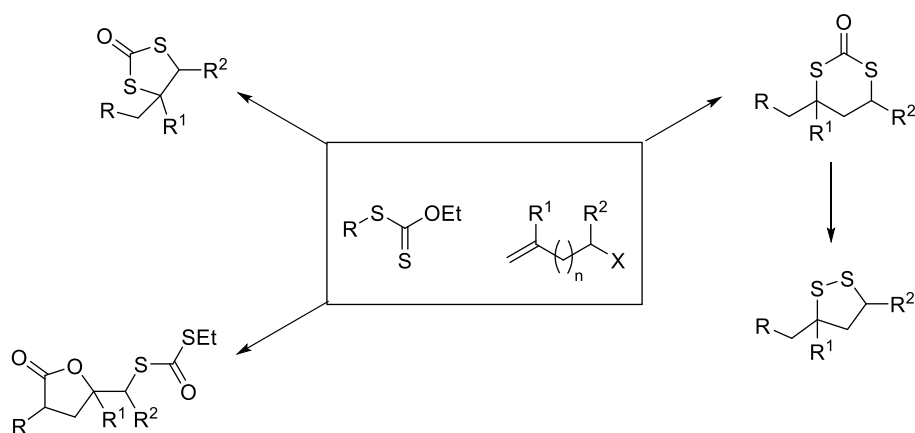
to afford the compound **III-36**. The equilibrium favors the intermediate **III-35**, where the positive charge is stabilized by the lone pairs of two sulfur atoms. The acid cleaved the intermediate **III-35** to give the 1,3-dithiolan-2-one **III-33d**, which contains the ester group. The protonation can induce a reversible ring opening of 1,3-dithiolan-2-one **III-33d** to afford intermediate **III-38**, which was cleaved slowly by acetic acid to give the lactone **III-39**. The intermolecular reaction of lactone **III-39** with intermediate **III-35** provides the final lactone **III-34a** and 1,3-dithiolan-2-one **III-33d**. The alkylation of the lactone **III-39** by intermediate **III-38** is also possible but it is a minor pathway, possibly because the concentration of intermediate **III-38** is lower than that of the intermediate **III-35**. This could explain why the transformation of 1,3-dithiolan-2-one **III-33d** into the lactone **III-34a** is slow. It is worth noting that the ethyl group comes from the ester and not from the xanthate by this minor path. Finally, the acid can induce ring opening of lactone **III-39** at higher temperature to furnish the free acid **III-40**.



**Scheme 3-19.** The mechanism of formation of lactones and 1,3-dithiolan-2-ones.

### 3.9. Conclusion and perspective

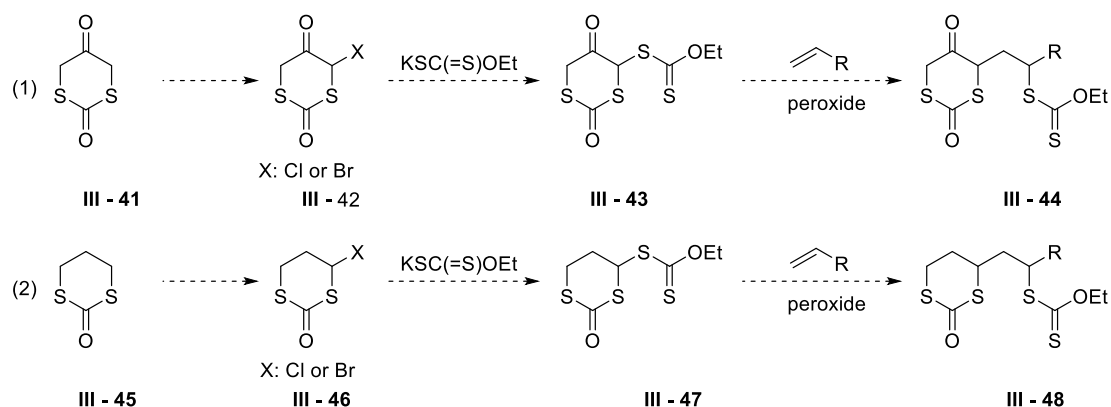
In summary, three practical, convergent, and cheap routes to 1,3-dithiane-2-ones were developed based on the radical addition of xanthates to various olefins bearing a suitably located leaving or functional group. 1,2-Dithiolanes were obtained in one pot procedure. We have also described a convergent route to 1,3-dithiolan-2-ones, where the corresponding adducts were exposed to a 9:1 mixture of MsOH and acetic acid at room temperature. Adducts bearing xanthates were obtained by the radical addition of easily available xanthates and allyl acetates. An unusual reaction took place leading to the unexpected formation of lactones and a plausible reaction mechanism was proposed. These methods we developed have some advantages: (a) synthetic routes are very short; use inexpensive starting materials and reagents; (b) a broad variety of functional groups can be tolerated and the reaction conditions are mild and neutral; (c) it is atom economical since both sulfur atoms of xanthates end up in the products; (d) these 1,3-dithianones are a protected form of 1,3-dithiols that are easily oxidized into the corresponding 1,2-dithiolanes. The 1,3-dithiols and 1,2-dithiols derived from the corresponding 1,3-dithiane-2-ones and 1,3-dithiolan-2-ones have a variety of applications. For example, the 1,2-dithiolanes related to lipoic acid have been used to make adhesive polymers.<sup>11</sup>



**Scheme 3-20.** Synthesis of 1,3-dithiane-2-ones, 1,3-dithiolan-2-ones, 1,2-dithiolanes and lactones



The possible extension of this work will focus on the synthesis of several important organosulfur compounds based on xanthates radical chemistry, as shown in **Scheme 3-21**. Organosulfur derivatives will be obtained by the radical addition of the corresponding xanthates **III-43** or **III-47** to various olefins.



**Scheme 3-21.** Access to organosulfur compounds.

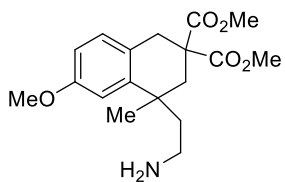
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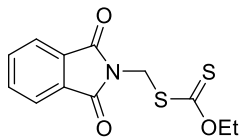
- 4348-4367; (c) Endo, K.; Yamanaka, T., Copolymerization of Lipoic Acid with 1,2-Dithiane and Characterization of the Copolymer as an Interlocked Cyclic Polymer. *Macromolecules* **2006**, *39*, 4038-4043; (d) Endo, K.; Shiroi, T.; Murata, N.; Kojima, G.; Yamanaka, T., Synthesis and Characterization of Poly(1,2-dithiane). *Macromolecules* **2004**, *37*, 3143-3150.
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11. Pavlinec, J.; Kleinova, A.; Angermann, J.; Lamparth, I.; Moszner, N., Monomers for Adhesive Polymers 12 Synthesis and Free-Radical Homo- and Copolymerization of 2-Ethoxycarbonylallyl-5-(1,2-dithiolane-3-yl)-pentanoate. *Macromol. Mater. Eng.* **2013**, *298*, 1220-1231.

## **Chapter 4 Experiment Part**

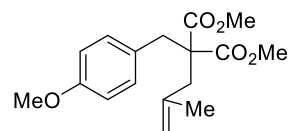
## 4.1 Molecules of chapter 2



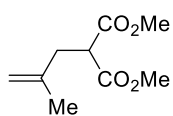
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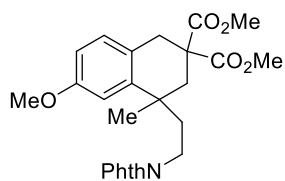
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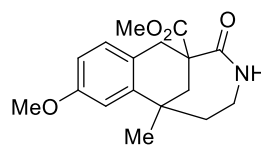
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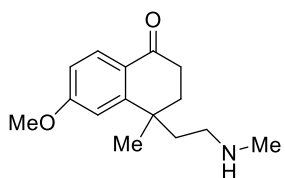
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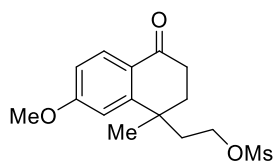
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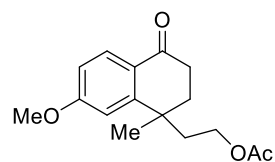
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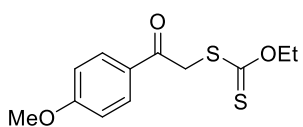
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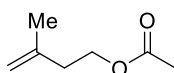
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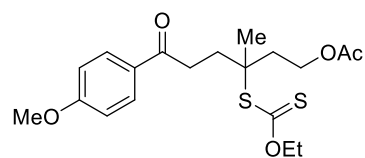
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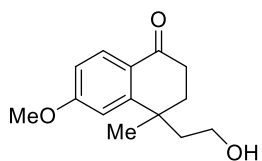
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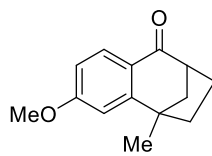
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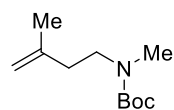
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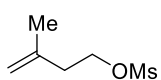
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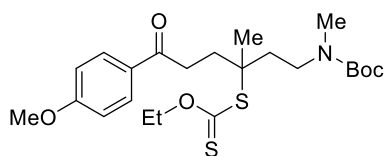
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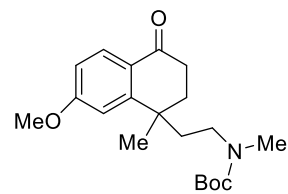
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II-80

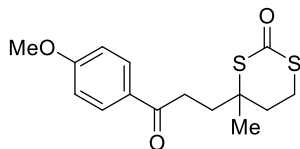


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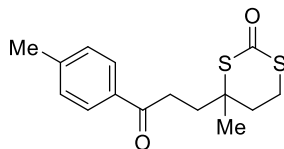


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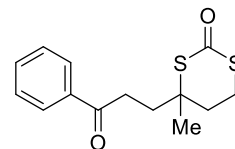
## 4.2 Molecules of chapter 3



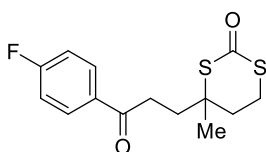
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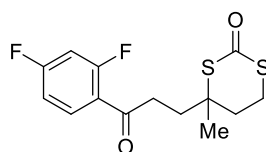
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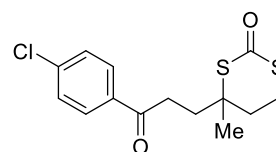
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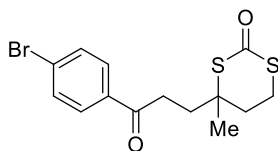
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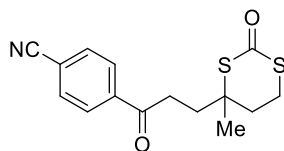
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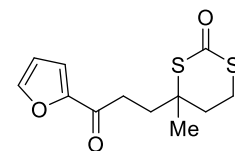
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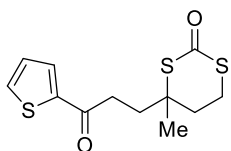
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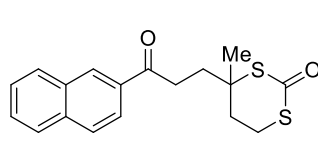
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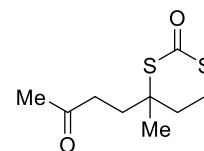
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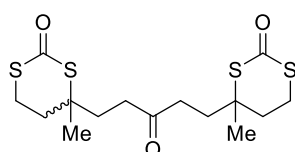
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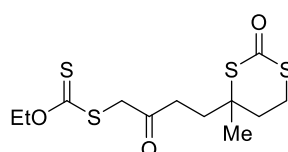
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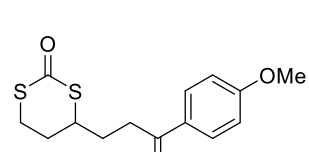
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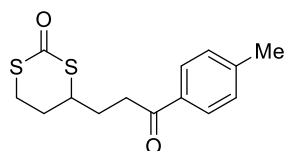
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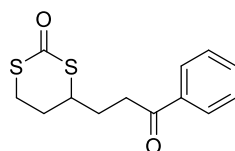
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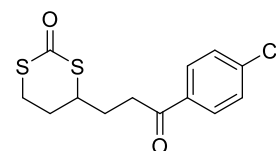
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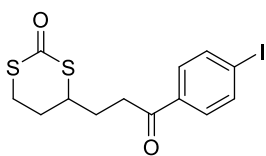
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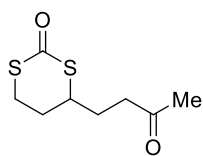
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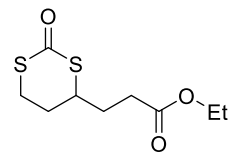
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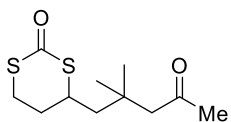
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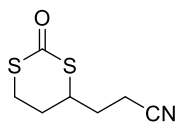
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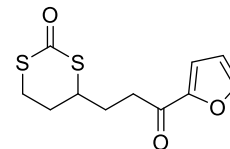
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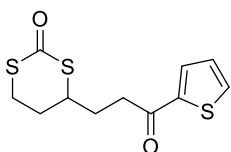
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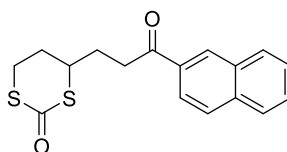
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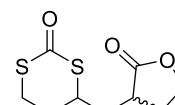
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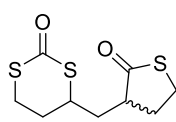
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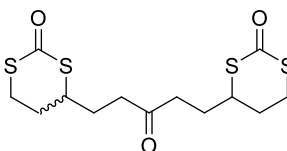
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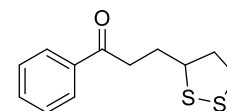
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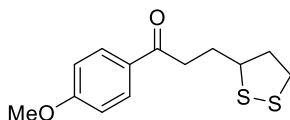
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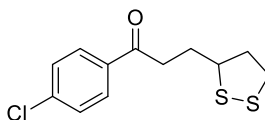
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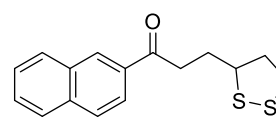
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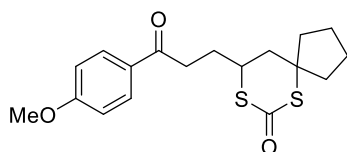
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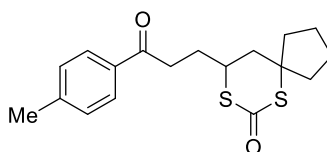
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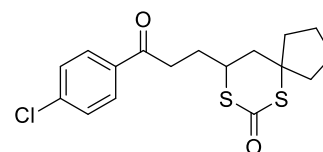
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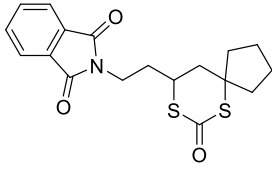
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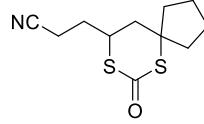
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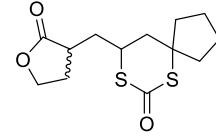
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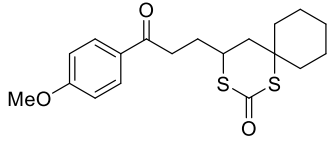
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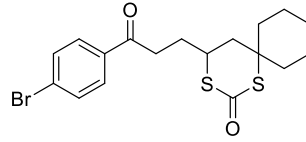
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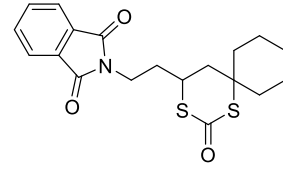
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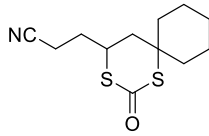
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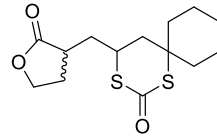
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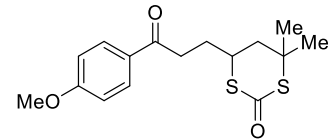
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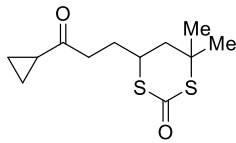
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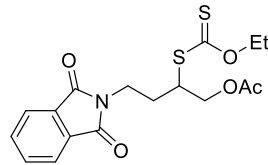
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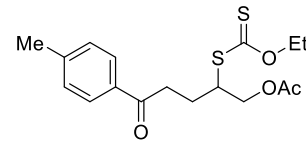
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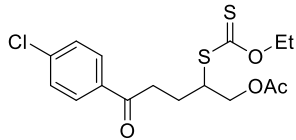
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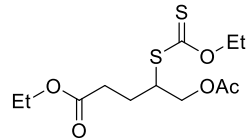
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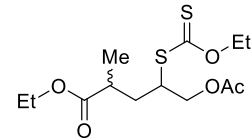
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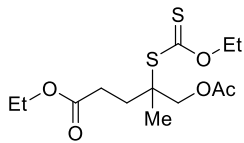
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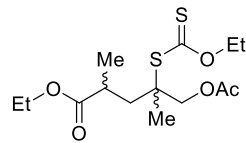
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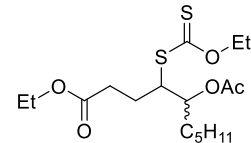
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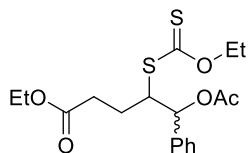
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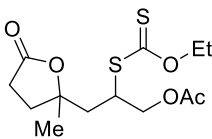
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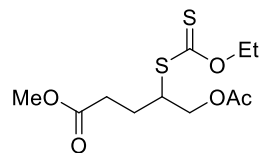
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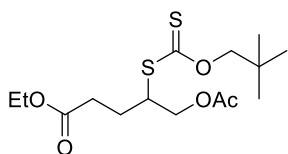
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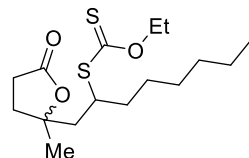
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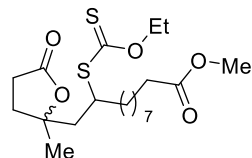
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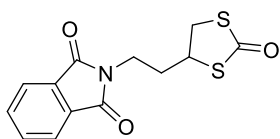
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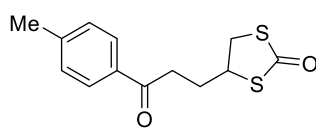
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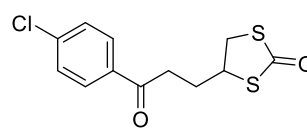
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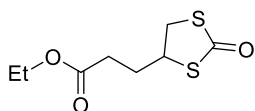
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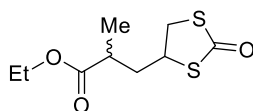
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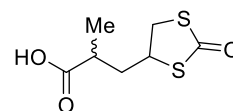
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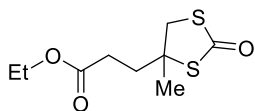
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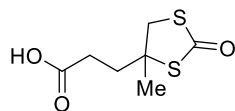
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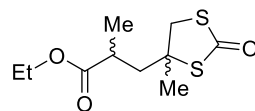
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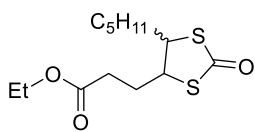
III -33f



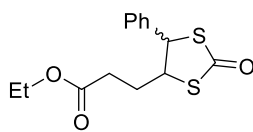
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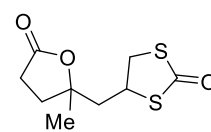
III -33g



III -33h

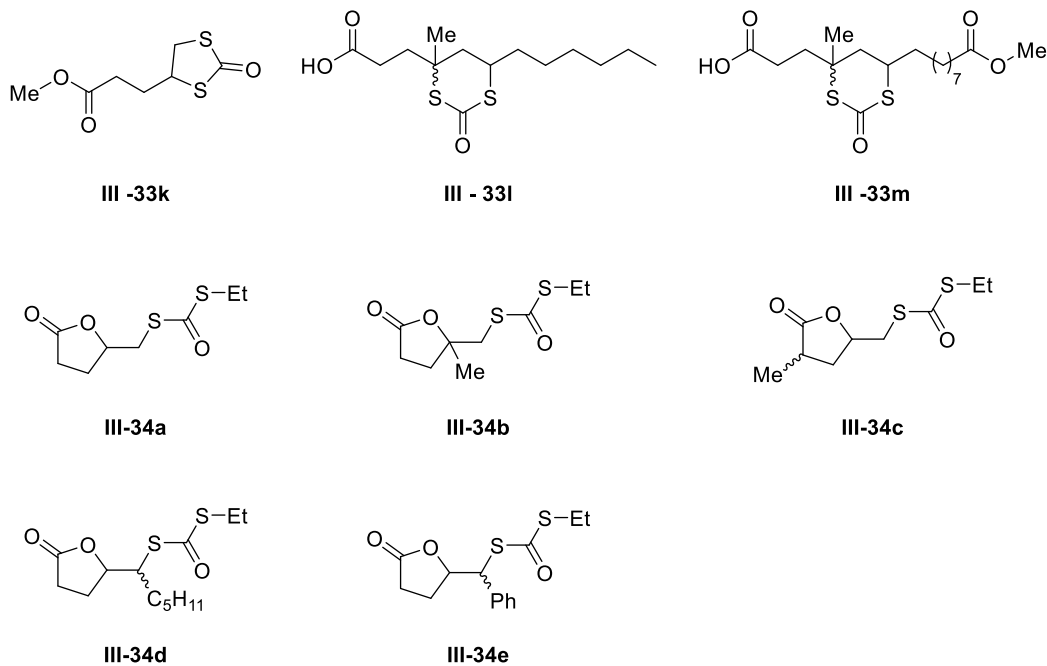


III -33i



III -33j





### 4.3 General experimental methods

Reactions sensitive to air and/or moisture were carried out under nitrogen atmosphere. For the reactions that require heating, an oil bath or a DrySyn heating block was used as the heat source.

Flash column chromatography was carried out on silica gel 60 (40-63  $\mu\text{m}$ ). Thin layer chromatography (TLC) was performed on alumina plates precoated with silica gel (Merck silica gel, 60 F<sub>254</sub>). Products spots were visualized by exposure to the UV light ( $\lambda_{\text{max}} = 254 \text{ nm}$ ) and/or by staining with vanillin in acidic ethanol solution and/or basic aqueous  $\text{KMnO}_4$ , followed by heating. Preparative TLC was performed on glass plates coated with silica gel (Merck PLC silica gel, 60 F<sub>254</sub>). Petroleum ether refers to the fraction of petroleum boiling between 40  $^{\circ}\text{C}$  and 60  $^{\circ}\text{C}$ .

Nuclear magnetic resonance spectra were recorded at ambient temperature on a Bruker Avance DPX 400 instrument. Proton magnetic resonance spectra ( $^1\text{H}$  NMR) were recorded at 400 MHz and coupling constants ( $J$ ) are reported to  $\pm 0.5 \text{ Hz}$ . The following abbreviations were utilized to describe peak patterns when appropriate: br = broad, s = singlet, d = doublet, t = triplet, q = quartet and m = multiplet. Carbon

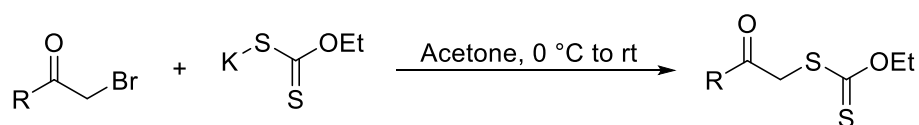
magnetic resonance spectra ( $^{13}\text{C}$  NMR) were recorded at 100 MHz. Chemical shifts (H, C) are quoted in parts per million (ppm) and are referenced to the residual solvent peak ( $\text{CDCl}_3$ :  $\delta\text{H} = 7.26$  and  $\delta\text{C} = 77.16$ ; DMSO:  $\delta\text{H} = 2.50$  and  $\delta\text{C} = 39.2$ ; acetone:  $\delta\text{H} = 2.05$  and  $\delta\text{C} = 29.4$ ).

High resolution mass spectrometry experiments were performed on a tims-TOF mass spectrometer (Bruker, France). Electrospray source has been used in positive mode. The quoted masses are accurate to  $\pm 5$  ppm. Infrared spectra were recorded on a Perkin-Elmer Spectrum Two apparatus. Absorption maxima ( $\nu_{\text{max}}$ ) are reported in wavenumbers ( $\text{cm}^{-1}$ ). Melting points were recorded in degrees Celsius ( $^{\circ}\text{C}$ ), using a Stuart SMP40 Automatic Melting Point apparatus.

## 4.4 Experimental procedures and spectroscopic data

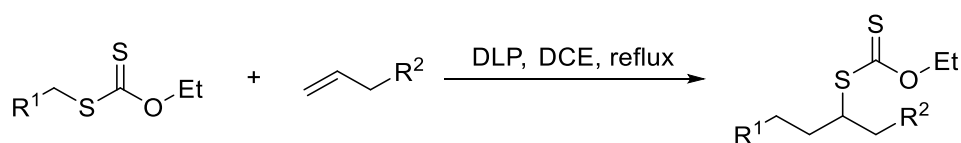
### 4.4.1 Chapter 2 general procedures

#### General procedure A1 synthesis of xanthates



The  $\alpha$ -halogenated ketone (30 mmol, 1.0 equiv) was dissolved in acetone (40 mL) and the solution cooled in an ice-water bath. Potassium *O*-ethyl carbonodithioate (33 mmol, 1.1 equiv) was then added portion-wise under stirring. The reaction mixture was further stirred for a few hours at room temperature. After consumption of all the starting material, the acetone was evaporated and the reaction mixture was diluted with water (150 mL) and extracted with  $\text{Et}_2\text{O}$  ( $3 \times 150$  mL). The combined organic phases were dried over  $\text{Na}_2\text{SO}_4$  and filtered, and the crude product purified by recrystallization from DCM/petroleum ether or by column chromatography to provide the corresponding xanthate.

### General procedure B1 for the radical addition



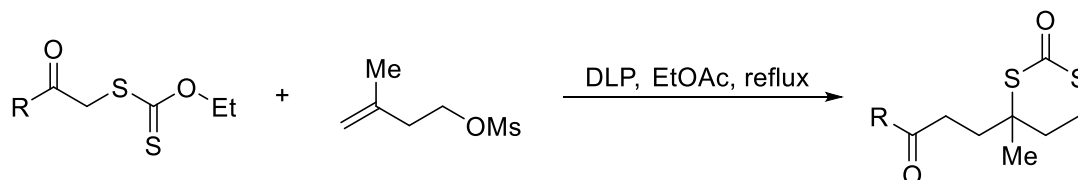
A solution of the xanthate (1 eq.) and olefin (2 eq.) in DCE or EtOAc (1.0 M of xanthate) was refluxed for 15-20 minutes under N<sub>2</sub>. DLP (0.05 eq.) was then added to the refluxing solution, followed by additional portions (0.05 eq.) every 60 min until the starting xanthate was completely consumed (analysis by TLC). The reaction mixture was then cooled to room temperature, concentrated under reduced pressure and purified by flash column chromatography on silica gel to give the desired compound.

### General procedure C1 for the radical cyclization

A solution of the corresponding adduct (1 eq.) in DCE or EtOAc (0.1 M of xanthate) was refluxed for 15-20 minutes under N<sub>2</sub>. DLP (0.1 eq.) was then added to the refluxing solution, followed by additional portions (0.1 eq.) every 60 min until the starting adduct was completely consumed (analysis by TLC). The reaction mixture was then cooled to room temperature, concentrated under reduced pressure and purified by flash column chromatography on silica gel to give the desired product.

## 4.4.2 Chapter 3 general procedures

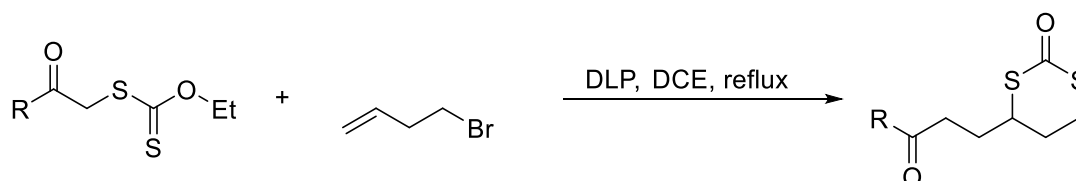
### General procedure A (intermolecular radical addition of a xanthate to olefins bearing a mesylate leaving group)



A solution of the xanthate (1 eq.) and olefin (2 eq.) in EtOAc (1.0 M in xanthate) was refluxed for 15-20 minutes under N<sub>2</sub>. Dilauroyl peroxide (DLP) (0.05 eq.) was then added to the refluxing solution, followed by additional portions (0.05 eq.) every 60 min until the starting xanthate was completely consumed (analysis by TLC). The

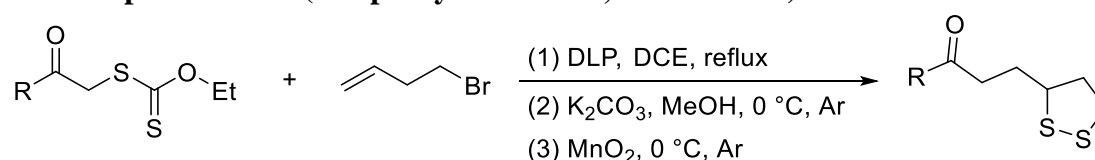
reaction mixture was then cooled to room temperature, concentrated under reduced pressure and purified by flash column chromatography on silica gel to give the desired product.

**General procedure B (intermolecular radical addition of a xanthate to 4-bromobut-1-ene)**



A solution of the xanthate (1 eq.) and 4-bromobut-1-ene (2 eq.) in 1,2-dichloroethane (DCE) (1.0 M in xanthate) was refluxed for 15-20 minutes under N<sub>2</sub>. DLP (0.05 eq.) was then added to the refluxing solution, followed by additional portions (0.05 eq.) every 60 min until the starting xanthate was completely consumed (analysis by TLC). Refluxing was continued for a few hours without addition of DLP. The reaction mixture was then cooled to room temperature, concentrated under reduced pressure and purified by flash column chromatography on silica gel to give the desired product.

**General procedure C (one pot synthesis of 1,2-dithiolanes)**



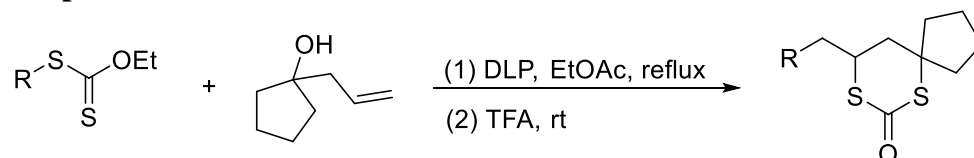
(1) A solution of the xanthate (1 eq.) and 4-bromobut-1-ene (2 eq.) in DCE (1.0 M of xanthate) was refluxed for 15-20 minutes under N<sub>2</sub>. DLP (0.05 eq.) was then added to the refluxing solution, followed by additional portions (0.05 eq.) every 60 min until the starting xanthate was completely consumed (analysis by TLC). Refluxing was continued for a few hours without addition of DLP. The reaction mixture was then cooled to room temperature and concentrated under reduced pressure.

(2) Potassium carbonate (3 equiv.) was added slowly to the crude mixture in methanol (1.0 M) at 0 °C under an argon atmosphere and the resulting solution stirred for 2 hours at the same temperature.

(3) MnO<sub>2</sub> (4 equiv.) were added to the reaction mixture and the stirring continued at 0 °C

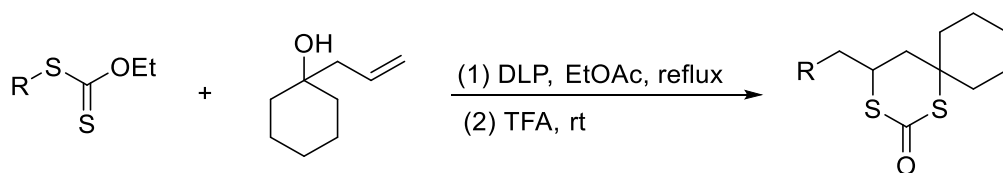
under an argon atmosphere for 12 hours. The reaction was monitored by TLC. The crude mixture was filtered to remove the MnO<sub>2</sub> and concentrated in vacuum and the residue purified by column chromatography on silica gel to give the desired product.

#### General procedure D



A solution of the xanthate (1 eq.) and the olefin (2 eq.) in EtOAc (1.0 M in xanthate) was refluxed for 15-20 minutes under N<sub>2</sub>. DLP (0.1 eq.) was then added to the refluxing solution, followed by additional portions (0.1 eq.) every 60 min until the starting xanthate was completely consumed (analysis by TLC). The reaction mixture was then cooled to room temperature and concentrated under reduced pressure. TFA (1.0 M) was added to the residue in a 10 mL round-bottomed flask. The resulting solution was stirred at room temperature for a few hours. The solvent and TFA were then evaporated and the crude residue purified by column chromatography on silica gel to give the desired product.

#### General procedure E

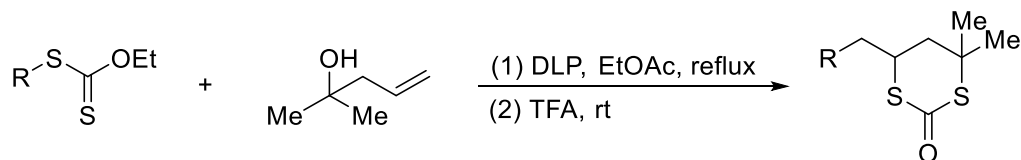


A solution of the xanthate (1 eq.) and olefin (2 eq.) in EtOAc (1.0 M of xanthate) was refluxed for 15-20 minutes under N<sub>2</sub>. DLP (0.1 eq.) was then added to the refluxing solution, followed by additional portions (0.1 eq.) every 60 min until the starting xanthate was completely consumed (analysis by TLC). The reaction mixture was then cooled to room temperature and concentrated under reduced pressure.

TFA (1.0 M) was added to the reaction mixture in a 10 mL round-bottomed flask and the resulting solution was stirred at room temperature for a few hours. The solvent and TFA were then evaporated and the crude residue purified by column

chromatography on silica gel to give the desired product.

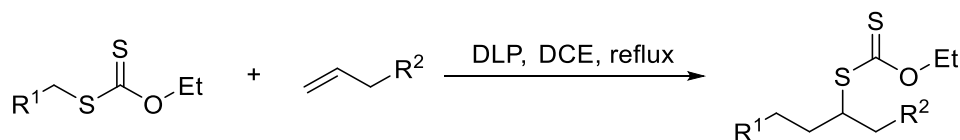
### General procedure F



A solution of the xanthate (1 eq.) and olefin (2 eq.) in EtOAc (1.0 M in xanthate) was refluxed for 15-20 min under N<sub>2</sub>. DLP (0.1 eq.) was then added to the refluxing solution, followed by additional portions (0.1 eq.) every 60 min until the starting xanthate was completely consumed (analysis by TLC). The reaction mixture was then cooled to room temperature and concentrated under reduced pressure.

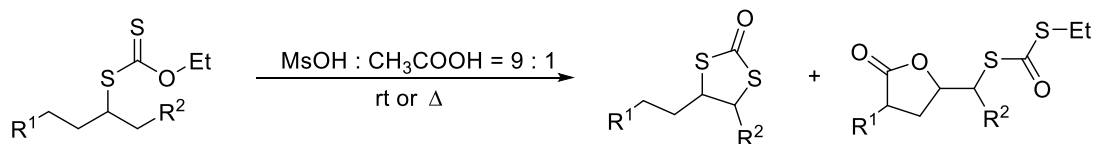
TFA (1.0 M) was added to the reaction mixture in a 10 mL round-bottomed flask and the resulting solution was stirred at room temperature for a few hours. The solvent and TFA were then evaporated and the crude residue purified by column chromatography on silica gel to give the desired product.

### General procedure G



A solution of the xanthate (1 eq.) and olefin (2 eq.) in DCE (1.0 M of xanthate) was refluxed for 15-20 minutes under N<sub>2</sub>. DLP (0.1 eq.) was then added to the refluxing solution, followed by additional portions (0.1 eq.) every 60 min until the starting xanthate was completely consumed (analysis by TLC). Then continue to keep heating under reflux was continued for a few hours without addition of DLP. The reaction mixture was then cooled to room temperature, concentrated under reduced pressure and purified by flash column chromatography on silica gel to give the desired compound.

### General procedure H

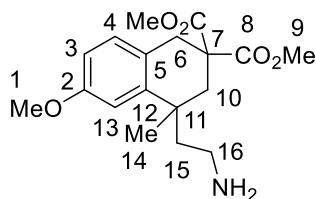


To a 10 mL oven dried round-bottomed flask equipped with a magnetic stirring bar was added the adduct (1 eq.) followed by methanesulfonic acid : acetic acid (9:1 ) (0.3 to 1.0 mL). The mixture was stirred for a few hours at room temperature or at the stated temperature and the progress was monitored by TLC. The reaction mixture was poured into water (5 mL) and extracted with DCM (3×5 mL). The organic phases were dried over Na<sub>2</sub>SO<sub>4</sub> and filtered. The crude residue after evaporation of the solvent was purified by column chromatography on silica gel (petroleum ether/ethyl acetate) to give the desired product.

## 4.5 Spectroscopic data

### 4.5.1 Chapter 2 spectroscopic data

#### Dimethyl-4-(2-aminoethyl)-6-methoxy-4-methyl-3,4-dihydronaphthalene-2,2(1H)-dicarboxylate (**II-59**)



Chemical Formula: C<sub>18</sub>H<sub>25</sub>NO<sub>5</sub>  
Exact Mass: 335.1733

To a 10 mL oven-dried round-bottomed flask equipped with a magnetic stir bar was added **II-66** (603 mg, 1.3 mmol), NH<sub>2</sub>NH<sub>2</sub>·H<sub>2</sub>O (84 mg, 1.686 mmol) in 5 ml of methanol. The reaction mixture was stirred at 80 °C for 5 hours. Then reaction mixture was cooled to room temperature and was concentrated in vacuum. The residue was further purified by column chromatography on Al<sub>2</sub>O<sub>3</sub> (methanol/acetone =1:1) to give **II-59** (369 mg, 85%) as a colorless oil.

<sup>1</sup>H NMR (δ, ppm)(400 MHz, CDCl<sub>3</sub>) δ 7.03 (d, *J* = 8.4 Hz, 1H, H<sub>4</sub>), 6.77 (d, *J* = 2.4

Hz, 1H, H<sub>13</sub>), 6.69 (dd,  $J = 8.4, 2.4$  Hz, 1H, H<sub>3</sub>), 3.76 (s, 3H, H<sub>1</sub>), 3.73 (s, 3H, H<sub>9</sub>), 3.64 (s, 3H, H<sub>9</sub>), 3.30 (d,  $J = 15.4$  Hz, 1H, H<sub>6</sub>), 2.96 (d,  $J = 15.8$  Hz, 1H, H<sub>6</sub>), 2.83 (dd,  $J = 18.8, 10.0$  Hz, 1H, H<sub>16</sub>), 2.70 (dd,  $J = 18.8, 10.0$  Hz, 1H, H<sub>16</sub>), 2.28 (dd,  $J = 33.8, 14.2$  Hz, 2H, H<sub>10</sub>), 1.99 (t,  $J = 8.2$  Hz, 2H, H<sub>15</sub>), 1.24 (d,  $J = 11.2$  Hz, 5H, H<sub>14</sub>, NH<sub>2</sub>).

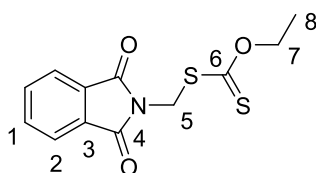
<sup>13</sup>C NMR ( $\delta$ , ppm)(100 MHz, CDCl<sub>3</sub>)  $\delta$  172.3 (C<sub>8</sub>), 171.7 (C<sub>8</sub>), 158.6 (C<sub>Ar</sub>), 142.0 (C<sub>Ar</sub>) 129.9 (C<sub>Ar</sub>), 125.3 (C<sub>Ar</sub>), 112.4 (C<sub>Ar</sub>), 111.2 (C<sub>Ar</sub>), 55.3 (C<sub>1</sub>), 53.0 (C<sub>9</sub>), 52.6(C<sub>9</sub>), 52.5 (C<sub>7</sub>), 43.1 (C<sub>10</sub>), 39.4 (C<sub>6</sub>), 36.8 (C<sub>16</sub>), 36.3 (C<sub>15</sub>), 34.5 (C<sub>11</sub>), 30.7 (C<sub>14</sub>).

IR ( $\nu$ , cm<sup>-1</sup>, CDCl<sub>3</sub>) 2952, 2214, 1730, 1610, 1500, 1433, 1223, 1040, 910, 814, 728.

HRMS (EI<sup>+</sup>)  $m/z$ : [M + Na]<sup>+</sup> calculated for C<sub>18</sub>H<sub>25</sub>NNaO<sub>5</sub>: 358.1625, found: 358.1637.

R<sub>f</sub> = 0.45 (EtOAc / PE = 1/2).

### S-((1,3-dioxoisindolin-2-yl)methyl)-O-ethyl-carbonodithioate (**II-60**)<sup>1</sup>



Chemical Formula: C<sub>12</sub>H<sub>11</sub>NO<sub>3</sub>S<sub>2</sub>  
Exact Mass: 281.0180

According to the general procedure A1, the reaction was carried out with 2-(bromomethyl)isindoline-1,3-dione (7.17 g, 30 mmol) and potassium *O*-ethyl carbonodithioate (5.28 g, 33 mmol) in acetone (30 mL), and needed 5 h for the reaction to go to completion. Recrystallization from ethanol gave product **II-60** (6.74 g, 80%) as a white solid.

<sup>1</sup>H NMR ( $\delta$ , ppm)(400 MHz, CDCl<sub>3</sub>)  $\delta$  7.89 – 7.81 (m, 2H, H<sub>2</sub>), 7.77 – 7.70 (m, 2H, H<sub>1</sub>), 5.32 (s, 2H, H<sub>5</sub>), 4.67 (q,  $J = 7.0, 0.8$  Hz, 2H, H<sub>7</sub>), 1.45 (td,  $J = 7.0, 0.8$  Hz, 3H, H<sub>8</sub>).

<sup>13</sup>C NMR ( $\delta$ , ppm)(100 MHz, CDCl<sub>3</sub>)  $\delta$  210.2 (C<sub>6</sub>), 166.7 (C<sub>4</sub>), 134.5 (C<sub>3</sub>), 131.9 (C<sub>1</sub>), 123.7 (C<sub>2</sub>), 70.6 (C<sub>7</sub>), 41.3 (C<sub>5</sub>), 13.8 (C<sub>8</sub>).

IR ( $\nu$ , cm<sup>-1</sup>, CDCl<sub>3</sub>) 2983, 1777, 1716, 1407, 1377, 1281, 1223, 1111, 1080, 1041, 913,

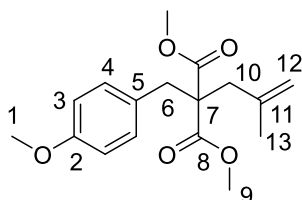


722.

**HRMS** (EI<sup>+</sup>) m/z: [M + H]<sup>+</sup> calculated for C<sub>12</sub>H<sub>12</sub>NO<sub>3</sub>S<sub>2</sub>: 282.0253, found: 282.0257.

**R<sub>f</sub>** = 0.45 (EtOAc / PE = 1/4).

**Dimethyl -2-(4-methoxybenzyl)-2-(2-methylallyl)malonate (II-61)**



Chemical Formula: C<sub>17</sub>H<sub>22</sub>O<sub>5</sub>  
Exact Mass: 306.1467

To a solution of **II-63** (1.66 g, 8.92 mmol) in THF (20 mL) was added slowly sodium hydride (642 mg, 26.76 mmol) at 0 °C. After the solution was stirred for 1 hour in the ice bath, a solution of **II-62** (1.96 g, 9.81 mmol) in THF (10 ml) was added dropwise. The mixture was stirred at room temperature 24 hours. The reaction was quenched by addition of water (10 mL) and most of the solvent was removed under reduced pressure. Organic compounds were extracted with DCM (3×40 mL) and dried over Na<sub>2</sub>SO<sub>4</sub>. The crude product was further purified by column chromatography on silica gel (petroleum ether/ethyl acetate =100:3) to give product **II-61** (2.26 g, 83%) as a colorless oil.

**<sup>1</sup>H NMR** (δ, ppm)(400 MHz, CDCl<sub>3</sub>) δ 7.07 – 6.98 (m, 2H, H<sub>4</sub>), 6.81 – 6.74 (m, 2H, H<sub>3</sub>), 5.03 – 4.62 (m, 2H, H<sub>12</sub>), 3.76 (s, 3H, H<sub>1</sub>), 3.67 (s, 6H, H<sub>9</sub>), 3.24 (s, 2H, H<sub>6</sub>), 2.64 (s, 2H, H<sub>10</sub>), 1.71 (d, J = 0.6Hz, 3H, H<sub>13</sub>).

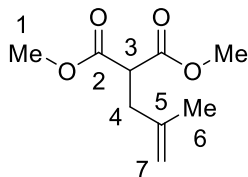
**<sup>13</sup>C NMR** (δ, ppm)(100 MHz, CDCl<sub>3</sub>) δ 171.6 (C<sub>8</sub>), 158.5 (C<sub>2</sub>), 141.0 (C<sub>11</sub>), 131 (C<sub>5</sub>), 128.1 (C<sub>4</sub>), 115.0 (C<sub>3</sub>), 113.6 (C<sub>12</sub>), 58.7 (C<sub>1</sub>), 55.1 (C<sub>9</sub>), 52.3 (C<sub>7</sub>), 40.3 (C<sub>6</sub>), 38.1(C<sub>10</sub>), 23.6 (C<sub>13</sub>).

**IR** (ν, cm<sup>-1</sup>, CDCl<sub>3</sub>) 2951, 1730, 1611, 1512, 1439, 1300, 1244, 1173, 1071, 899, 841, 747.

**HRMS** (EI<sup>+</sup>) m/z: [M + H]<sup>+</sup> calculated for C<sub>17</sub>H<sub>23</sub>O<sub>5</sub>: 307.1540, found: 307.1551.

**R<sub>f</sub>** = 0.45 (EtOAc / PE = 1/6).

## Diethyl-2-(2-methylallyl)-malonate (**II-63**)<sup>2</sup>



Chemical Formula: C<sub>9</sub>H<sub>14</sub>O<sub>4</sub>  
Exact Mass: 186.0892

Dimethyl malonate **II-64** (1.98 g, 15 mmol) and 3-bromo-2-methylprop-1-ene **II-65** (1.35 g, 10 mmol) were added to a solution of K<sub>2</sub>CO<sub>3</sub> (4.14 g, 30 mmol) in acetone (30 mL) and the mixture was stirred for 24 hours at room temperature. The reaction mixture was quenched by addition of saturated aqueous ammonium chloride solution (50 mL) and extracted with DCM (3 × 50 mL). The combined organic layers were dried Na<sub>2</sub>SO<sub>4</sub> and the solvent was removed under reduced pressure. The crude product was further purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 100:5) to give product **II-63** (1.69 g, 91%) as a colorless oil.

<sup>1</sup>H NMR (δ, ppm)(400 MHz, CDCl<sub>3</sub>) δ 4.83 – 4.68 (m, 2H, H<sub>7</sub>), 3.73 (s, 6H, H<sub>1</sub>), 3.62 (t, J = 7.8 Hz, 1H, H<sub>3</sub>), 2.67 – 2.56 (m, 2H, H<sub>4</sub>), 1.78 – 1.66 (m, 3H, H<sub>6</sub>).

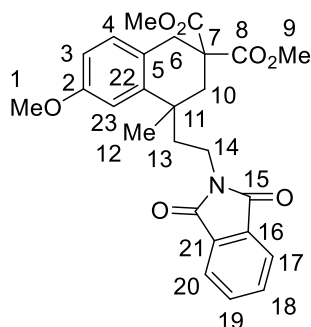
<sup>13</sup>C NMR (δ, ppm)(100 MHz, CDCl<sub>3</sub>) δ 169.4 (C<sub>2</sub>), 141.5 (C<sub>5</sub>), 112.3 (C<sub>7</sub>), 52.5 (C<sub>1</sub>), 50.2 (C<sub>4</sub>), 36.5 (C<sub>3</sub>), 22.2 (C<sub>6</sub>).

IR (ν, cm<sup>-1</sup>, CDCl<sub>3</sub>) 2955, 1736, 1651, 1436, 1339, 1226, 1149, 1048, 896, 694.

HRMS (EI<sup>+</sup>) m/z: [M + H]<sup>+</sup> calculated for C<sub>9</sub>H<sub>15</sub>O<sub>4</sub>: 187.0965, found: 187.0960.

R<sub>f</sub> = 0.42 (EtOAc / PE = 1/6).

## Dimethyl-4-(2-(1,3-dioxoisindolin-2-yl)ethyl)-6-methoxy-4-methyl-3,4-dihydro-1H-naphthalene-2,2-dicarboxylate (**II-66**)



Chemical Formula: C<sub>26</sub>H<sub>27</sub>NO<sub>7</sub>  
Exact Mass: 465.1788

According to the general procedure B1, the reaction was carried out with xanthate **II-60** (3.08 g, 10.96 mmol) and olefin **II-61** (1.679 g, 5.48 mmol) in 1,2-dichloroethane (7 mL), and needed 10 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (100:1 to 3:1) to afford product **II-66** (1.53 g, 60%) as a colorless oil.

<sup>1</sup>H NMR (δ, ppm)(400 MHz, CDCl<sub>3</sub>) δ 7.70 (dt, *J* = 6.6, 3.4 Hz, 3H, CH<sub>Ar</sub>), 7.67 – 7.61 (m, 2H, CH<sub>Ar</sub>), 6.90 (d, *J* = 8.4 Hz, 1H, CH<sub>Ar</sub>), 6.73 (d, *J* = 2.6 Hz, 1H, CH<sub>Ar</sub>), 6.41 (dd, *J* = 8.4, 2.6 Hz, 1H, CH<sub>Ar</sub>), 3.78 (s, 3H, H<sub>1</sub>), 3.77 – 3.72 (m, 2H, H<sub>6</sub>), 3.69 (s, 3H, H<sub>9</sub>), 3.64 (s, 3H, H<sub>9</sub>), 3.31 (dd, *J* = 15.8, 1.4 Hz, 1H, H<sub>14</sub>), 3.02 (d, *J* = 15.6 Hz, 1H, H<sub>14</sub>), 2.66 (d, *J* = 14.2 Hz, 1H, H<sub>10</sub>), 2.27 (ddd, *J* = 15.2, 10.4, 5.0 Hz, 2H, H<sub>13</sub>), 1.92 – 1.85 (m, 1H, H<sub>10</sub>), 1.23 (s, 3H, H<sub>12</sub>).

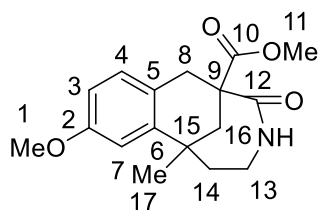
<sup>13</sup>C NMR (δ, ppm)(100 MHz, CDCl<sub>3</sub>) δ 172.2 (C<sub>8</sub>), 171.9 (C<sub>15</sub>), 168.0 (C<sub>Ar</sub>), 158.1 (C<sub>Ar</sub>), 141.6 (C<sub>Ar</sub>), 133.6 (C<sub>Ar</sub>), 132.0 (C<sub>Ar</sub>), 129.9 (C<sub>Ar</sub>), 125.4 (C<sub>Ar</sub>), 122.8 (C<sub>Ar</sub>), 112.2 (C<sub>Ar</sub>), 110.8 (C<sub>Ar</sub>), 54.9 (C<sub>1</sub>), 52.9(C<sub>9</sub>), 52.6 (C<sub>9</sub>), 52.4 (C<sub>7</sub>), 40.7(C<sub>13</sub>), 38.6 (C<sub>10</sub>), 36.3(C<sub>6</sub>), 34.4(C<sub>14</sub>), 34.1 (C<sub>11</sub>), 31.6 (C<sub>12</sub>).

IR (ν, cm<sup>-1</sup>, CDCl<sub>3</sub>) 2952, 1733, 1706, 1611, 1502, 1398, 1272, 1227, 1084, 749, 718.

HRMS (EI<sup>+</sup>) m/z: [M + H]<sup>+</sup>calculated for C<sub>26</sub>H<sub>28</sub>NO<sub>7</sub>: 466.1860, found: 466.1876.

R<sub>f</sub> = 0.30 (EtOAc / PE = 1/4).

**Methyl-10-methoxy-1-methyl-5-oxo-1,2,3,4,5,7-hexahydro-6H-1,6-methanobenzo [e]azonine-6-carboxylate (II-67)**



Chemical Formula: C<sub>17</sub>H<sub>21</sub>NO<sub>4</sub>

Exact Mass: 303.1471

A solution of the **II-59** (100 mg, 0.298 mmol) and K<sub>2</sub>CO<sub>3</sub> (165 mg, 1.19 mmol) in CH<sub>3</sub>CN (1 mL) in 10 mL round-bottomed flask with a magnetic stir bar was stirred at 100 °C for 72 hours and the reaction was monitored by TLC plate and HPLC-MS. The crude mixture was concentrated in vacuum and was purified by column chromatography on silica gel (petroleum ether/ethyl acetate =2:1 to ethyl acetate) to give product **II-67** (50 mg, 55%) as a colorless oil.

<sup>1</sup>H NMR (δ, ppm)(400 MHz, CDCl<sub>3</sub>) δ 7.08 (d, *J* = 8.4 Hz, 1H, NH), 6.81 (d, *J* = 2.6 Hz, 1H, H<sub>Ar</sub>), 6.74 (dd, *J* = 8.4, 2.6 Hz, 1H, H<sub>Ar</sub>), 6.18 (s, 1H, H<sub>Ar</sub>), 3.79 (s, 3H, H<sub>1</sub>), 3.78 (s, 3H, H<sub>11</sub>), 3.67 – 3.56 (m, 1H, H<sub>13</sub>), 3.24 (d, *J* = 18.0 Hz, 1H, H<sub>13</sub>), 3.05 – 2.94 (m, 1H, H<sub>8</sub>), 2.83 – 2.70 (m, 1H, H<sub>8</sub>), 2.47 (dd, *J* = 14.2, 1.4 Hz, 1H, H<sub>16</sub>), 1.88 (d, *J* = 14.2 Hz, 1H, H<sub>16</sub>), 1.82 (dd, *J* = 7.2, 4.2 Hz, 2H, H<sub>14</sub>), 1.44 (s, 3H, H<sub>17</sub>).

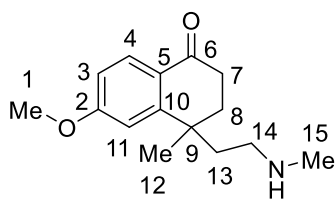
<sup>13</sup>C NMR (δ, ppm)(100 MHz, CDCl<sub>3</sub>) δ 177.8 (C<sub>10</sub>), 173.4 (C<sub>12</sub>), 158.5 (C<sub>Ar</sub>), 142.6 (C<sub>Ar</sub>), 129.8 (C<sub>Ar</sub>), 126.4 (C<sub>Ar</sub>), 111.9 (C<sub>Ar</sub>), 111.0 (C<sub>Ar</sub>), 55.3 (C<sub>1</sub>), 53.9 (C<sub>11</sub>), 52.7 (C<sub>16</sub>), 44.2 (C<sub>8</sub>), 39.6 (C<sub>13</sub>), 39.4 (C<sub>9</sub>), 37.3 (C<sub>14</sub>), 33.8 (C<sub>15</sub>), 30.9 (C<sub>17</sub>).

IR (ν, cm<sup>-1</sup>, CDCl<sub>3</sub>) 3272, 2937, 1735, 1646, 1611, 1497, 1361, 1264, 1217, 1053, 911, 810, 730.

HRMS (EI<sup>+</sup>) *m/z*: [M + H]<sup>+</sup> calculated for C<sub>17</sub>H<sub>22</sub>NO<sub>4</sub>: 304.1543, found: 304.1557.

R<sub>f</sub> = 0.60 (EtOAc / PE = 1/2).

**6-methoxy-4-methyl-4-(2-(methylamino)ethyl)-3,4-dihydronaphthalen-1(2H)-one (II-70)**



Chemical Formula: C<sub>15</sub>H<sub>21</sub>NO<sub>2</sub>  
Exact Mass: 247.1572

To a 10 mL oven-dried round-bottomed flask equipped with a magnetic stir bar was added **II-82** (242 mg, 0.697 mmol), TFA (1 mL) in 2 ml of DCM. The reaction mixture was stirred at reflux for 4 hours. Then reaction mixture was cooled to room temperature and was concentrated in vacuum. The residue was further purified by column chromatography on Al<sub>2</sub>O<sub>3</sub> (methanol/DCM = 1:10 to 1:1) to give **II-70** (124 mg, 72%) as a brown oil.

<sup>1</sup>H NMR (δ, ppm)(400 MHz, CDCl<sub>3</sub>) δ 8.03 – 7.96 (m, 1H, H<sub>4</sub>), 6.82 – 6.76 (m, 2H, H<sub>11</sub>, H<sub>3</sub>), 3.84 (s, 3H, H<sub>1</sub>), 2.71 – 2.60 (m, 2H, H<sub>14</sub>), 2.59 – 2.49 (m, 2H, H<sub>7</sub>), 2.37 (s, 3H, H<sub>15</sub>), 2.12 – 2.02 (m, 1H, H<sub>8</sub>), 1.98 – 1.84 (m, 3H, H<sub>13</sub>, NH), 1.82 – 1.70 (m, 1H, H<sub>8</sub>), 1.35 (s, 3H, H<sub>12</sub>).

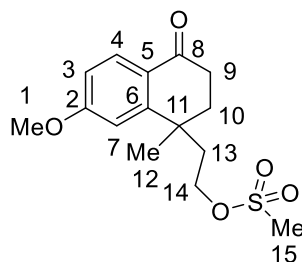
<sup>13</sup>C NMR (δ, ppm)(100 MHz, CDCl<sub>3</sub>) δ 197.0 (C<sub>6</sub>), 163.9 (C<sub>2</sub>), 153.5 (C<sub>10</sub>), 130.3 (C<sub>5</sub>), 125.3 (C<sub>4</sub>), 111.9 (C<sub>3</sub>), 111.3 (C<sub>11</sub>), 55.5 (C<sub>1</sub>), 47.9 (C<sub>14</sub>), 41.2 (C<sub>7</sub>), 36.6 (C<sub>13</sub>), 36.4 (C<sub>15</sub>), 34.5 (C<sub>8</sub>), 34.3 (C<sub>9</sub>), 27.7 (C<sub>12</sub>).

IR (ν, cm<sup>-1</sup>, CDCl<sub>3</sub>) 2927, 2843, 2795, 1671, 1594, 1486, 1457, 1329, 1233, 1172, 1032, 828, 729.

HRMS (EI<sup>+</sup>) m/z: [M + H]<sup>+</sup>calculated for C<sub>15</sub>H<sub>22</sub>NO<sub>2</sub>: 248.1645, found: 248.1647.

R<sub>f</sub> = 0.25 (EtOAc / PE = 1/1).

### 2-(7-methoxy-1-methyl-4-oxo-1,2,3,4-tetrahydronaphthalen-1-yl)ethyl methanesulfonate (**II-71**)



Chemical Formula: C<sub>15</sub>H<sub>20</sub>O<sub>5</sub>S  
Exact Mass: 312.1031

A solution of acetyl chloride (23 mg, 0.2 mmol) in DCM (1 mL) was added dropwise to a mixture of **II-76** (23 mg, 0.1 mmol) and Et<sub>3</sub>N (20 mg, 0.2 mmol) in DCM (1 mL) at 0 °C. Following addition, the reaction mixture was allowed to warm to room temperature for overnight. The reaction mixture was then diluted with ether (3 mL) and quenched with 1 M aqueous HCl (3 mL). The aqueous layer was extracted with ether (3×5 mL), dried over MgSO<sub>4</sub>, filtered and the solvent was evaporated. The crude mixture was concentrated in vacuum and was purified by column chromatography on silica gel (petroleum ether/ethyl acetate =100:5 to 1:1) to give product **II-77** (24 mg, 77%) as a colorless oil.

<sup>1</sup>H NMR (δ, ppm)(400 MHz, CDCl<sub>3</sub>) δ 8.05 (d, *J* = 8.6 Hz, 1H, H<sub>4</sub>), 6.96 – 6.74 (m, 2H, H<sub>7</sub>, H<sub>3</sub>), 4.31-4.20 (m, 2H, H<sub>14</sub>), 3.88 (s, 3H, H<sub>1</sub>), 2.96 (s, 3H, H<sub>15</sub>), 2.69 (t, *J* = 6.8 Hz, 2H, H<sub>13</sub>), 2.34 – 1.93 (m, 4H, H<sub>9</sub>, H<sub>10</sub>), 1.44 (s, 3H, H<sub>12</sub>).

<sup>13</sup>C NMR (δ, ppm)(100 MHz, CDCl<sub>3</sub>) δ 196.2 (C<sub>8</sub>), 164.1 (C<sub>2</sub>), 151.8 (C<sub>6</sub>), 130.6 (C<sub>5</sub>), 125.2 (C<sub>4</sub>), 112.4 (C<sub>3</sub>), 111.1 (C<sub>7</sub>), 66.5 (C<sub>14</sub>), 55.5 (C<sub>1</sub>), 39.7 (C<sub>9</sub>), 37.5 (C<sub>15</sub>), 36.3 (C<sub>13</sub>), 34.4 (C<sub>10</sub>), 34.2 (C<sub>11</sub>), 27.7 (C<sub>12</sub>).

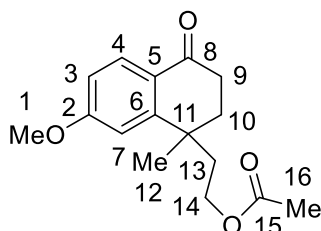
IR (ν, cm<sup>-1</sup>, CDCl<sub>3</sub>) 2960, 2933, 1671, 1595, 1488, 1462, 1349, 1332, 1256, 1236, 1171, 1058, 1015, 973, 952, 833, 802.14.

HRMS (EI<sup>+</sup>) *m/z*: [M + H]<sup>+</sup> calculated for C<sub>15</sub>H<sub>21</sub>O<sub>5</sub>S: 313.1104, found: 313.1098.

R<sub>f</sub> = 0.40 (EtOAc / PE = 1/1).

## 2-(7-methoxy-1-methyl-4-oxo-1,2,3,4-tetrahydronaphthalen-1-yl)ethylacetate

(**II-72**)



Chemical Formula: C<sub>16</sub>H<sub>20</sub>O<sub>4</sub>  
Exact Mass: 276.1362

According to the general procedure C1, the reaction was carried out with adduct **II-74** (155 mg, 0.39 mmol) in 1,2-dichloroethane (4 mL), and needed 8 h for the reaction to

go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (10:1 to 1:1) to afford product **II-75** (56 mg, 53%) as a colorless oil.

**<sup>1</sup>H NMR** ( $\delta$ , ppm)(400 MHz, CDCl<sub>3</sub>)  $\delta$  8.10 – 7.98 (m, 1H, H<sub>4</sub>), 6.89 – 6.79 (m, 2H, H<sub>7</sub>, H<sub>3</sub>), 4.17-4.05 (m, 2H, H<sub>14</sub>), 3.87 (s, 3H, H<sub>1</sub>), 2.76 – 2.63 (m, 2H, H<sub>13</sub>), 2.20 – 2.08 (m, 2H, H<sub>9</sub>), 2.07 – 1.88 (m, 5H, H<sub>16</sub>, H<sub>10</sub>), 1.41 (s, 3H, H<sub>12</sub>).

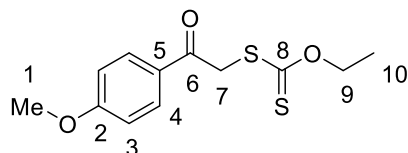
**<sup>13</sup>C NMR** ( $\delta$ , ppm)(100 MHz, CDCl<sub>3</sub>)  $\delta$  196.6 (C<sub>8</sub>), 171.0 (C<sub>15</sub>), 164.0 (C<sub>2</sub>), 152.7 (C<sub>6</sub>), 130.4 (C<sub>5</sub>), 125.2 (C<sub>4</sub>), 112.1 (C<sub>3</sub>), 111.1 (C<sub>7</sub>), 61.3 (C<sub>14</sub>), 55.4 (C<sub>1</sub>), 39.2 (C<sub>9</sub>), 36.2 (C<sub>13</sub>), 34.4 (C<sub>10</sub>), 34.2 (C<sub>11</sub>), 27.6 (C<sub>12</sub>), 21.0 (C<sub>16</sub>).

**IR** ( $\nu$ , cm<sup>-1</sup>, CDCl<sub>3</sub>) 2963, 2929, 1735, 1675, 1596, 1487, 1461, 1366, 1275, 1259, 1234, 1055, 1033, 764, 749.

**HRMS** (EI<sup>+</sup>) m/z: [M + H]<sup>+</sup> calculated for C<sub>16</sub>H<sub>21</sub>O<sub>4</sub>: 277.1434, found: 277.1435.

**R<sub>f</sub>** = 0.33 (EtOAc / PE = 1/3).

### ***O*-ethyl-*S*-(2-(4-methoxyphenyl)-2-oxoethyl)-carbonodithioate (**II-73**)<sup>3</sup>**



Chemical Formula: C<sub>12</sub>H<sub>14</sub>O<sub>3</sub>S<sub>2</sub>  
Exact Mass: 270.0384

According to the general procedure A1, the reaction was carried out with 2-bromo-1-(4-methoxyphenyl)-ethan-1-one (6.84 g, 30 mmol) and potassium *O*-ethyl carbonodithioate (5.28 g, 33 mmol) in acetone (30 mL), and needed 7 h for the reaction to go to completion. Recrystallization from ethanol gave product **II-71** (6.89 g, 85%) as a white solid.

**<sup>1</sup>H NMR** ( $\delta$ , ppm)(400 MHz, CDCl<sub>3</sub>)  $\delta$  8.00 – 7.93 (m, 2H, H<sub>4</sub>), 6.99 – 6.90 (m, 2H, H<sub>3</sub>), 4.64 – 4.56 (m, 4H, H<sub>9</sub>, H<sub>7</sub>), 3.86 (s, 3H, H<sub>1</sub>), 1.36 (t,  $J$  = 7.0 Hz, 3H, H<sub>10</sub>).

**<sup>13</sup>C NMR** ( $\delta$ , ppm)(100 MHz, CDCl<sub>3</sub>) 213.4 (C<sub>8</sub>), 190.8 (C<sub>6</sub>), 164.0 (C<sub>2</sub>), 130.8 (C<sub>4</sub>), 128.8 (C<sub>5</sub>), 114.0 (C<sub>3</sub>), 70.6 (C<sub>9</sub>), 55.6 (C<sub>1</sub>), 43.4 (C<sub>7</sub>), 13.8 (C<sub>10</sub>).

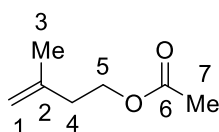
**IR** ( $\nu$ , cm<sup>-1</sup>, CDCl<sub>3</sub>) 2998, 2835, 1667, 1597, 1506, 1416, 1308, 1212, 1171, 1051,

987, 814, 732.

**HRMS** (EI<sup>+</sup>) m/z: [M + Na]<sup>+</sup>calculated for C<sub>12</sub>H<sub>14</sub>NaO<sub>3</sub>S<sub>2</sub>: 293.0277, found: 293.0276.

**R<sub>f</sub>** = 0.50 (EtOAc / PE = 1/4).

### 3-methylbut-3-en-1-yl-acetate (**II-74**)<sup>4</sup>



Chemical Formula: C<sub>7</sub>H<sub>12</sub>O<sub>2</sub>

Exact Mass: 128.0837

A solution of acetyl chloride (2.04 g, 26 mmol) in DCM (10 mL) was added dropwise to a mixture of alcohol **II-73** (1.72 g, 20 mmol) and Et<sub>3</sub>N (3.03 g, 30 mmol) in DCM (10 mL) at 0 °C. Following addition, the reaction mixture was allowed to warm to room temperature for overnight. The reaction mixture was then diluted with ether (50 mL) and quenched with 1 M aqueous HCl (50 mL). The aqueous layer was extracted with ether (3 × 50 mL), dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and the solvent was evaporated. The crude mixture was concentrated in vacuum and was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 100:5 to 3:1) to give product **II-72** (1.90 g, 74%) as a colorless oil.

**<sup>1</sup>H NMR** (δ, ppm)(400 MHz, CDCl<sub>3</sub>) δ 4.84 – 4.68 (m, 2H, H<sub>1</sub>), 4.18 (t, J = 6.8 Hz, 2H, H<sub>5</sub>), 2.34 (t, J = 6.8 Hz, 2H, H<sub>4</sub>), 2.04 (s, 3H, H<sub>7</sub>), 1.76 (s, 3H, H<sub>3</sub>).

**<sup>13</sup>C NMR** (δ, ppm)(100 MHz, CDCl<sub>3</sub>) δ 171.0 (C<sub>6</sub>), 141.6 (C<sub>2</sub>), 112.2 (C<sub>1</sub>), 62.6 (C<sub>5</sub>), 36.6 (C<sub>4</sub>), 22.4 (C<sub>7</sub>), 20.9 (C<sub>3</sub>).

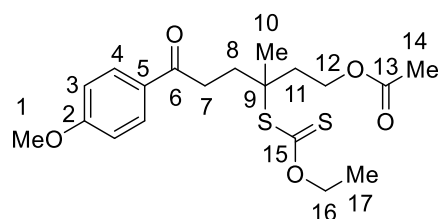
**IR** (ν, cm<sup>-1</sup>, CDCl<sub>3</sub>) 2959, 2925, 2854, 2039, 2010, 1768, 1735, 1652, 1454, 1230, 1116, 1036, 891, 808.

**HRMS** (EI<sup>+</sup>) m/z: [M + H]<sup>+</sup>calculated for C<sub>7</sub>H<sub>13</sub>O<sub>2</sub>: 129.0910, found: 129.0905.

**R<sub>f</sub>** = 0.80 (EtOAc / PE = 1/10).

### 3-((ethoxycarbonothioyl)thio)-6-(4-methoxyphenyl)-3-methyl-6-oxohexyl-acetate



**(II-75)**

Chemical Formula: C<sub>19</sub>H<sub>26</sub>O<sub>5</sub>S<sub>2</sub>  
Exact Mass: 398.1222

According to the general procedure B1, the reaction was carried out with xanthate **II-71** (540 mg, 2 mmol) and olefin **II-72** (512 mg, 4 mmol) in 1,2-dichloroethane (2 mL), and needed 6 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (100:10 to 100:13) to afford product **II-74** (544 mg, 69%) as a colorless oil.

<sup>1</sup>H NMR (δ, ppm)(400 MHz, CDCl<sub>3</sub>) δ 8.08 – 7.79 (m, 2H, H<sub>4</sub>), 7.07 – 6.82 (m, 2H, H<sub>3</sub>), 4.66 (q, *J* = 6.8 Hz, 2H, H<sub>16</sub>), 4.25 (t, *J* = 7.0 Hz, 2H, H<sub>12</sub>), 3.87 (s, 3H, H<sub>1</sub>), 3.13-3.05 (m, 2H, H<sub>7</sub>), 2.45 – 2.32 (m, 2H, H<sub>11</sub>), 2.23 – 2.08 (m, 2H, H<sub>8</sub>), 2.04 (s, 3H, H<sub>14</sub>), 1.44 (dd, *J* = 8.4, 5.8 Hz, 6H, H<sub>10</sub>, H<sub>17</sub>).

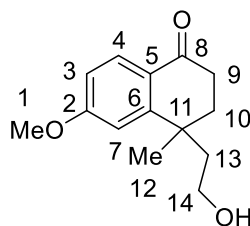
<sup>13</sup>C NMR (δ, ppm)(100 MHz, CDCl<sub>3</sub>) δ 212.4 (C<sub>15</sub>), 197.6 (C<sub>6</sub>), 170.9 (C<sub>13</sub>), 163.6 (C<sub>2</sub>), 130.3 (C<sub>5</sub>), 129.7 (C<sub>4</sub>), 113.8 (C<sub>3</sub>), 69.8 (C<sub>16</sub>), 61.1 (C<sub>12</sub>), 56.7 (C<sub>1</sub>), 55.5 (C<sub>11</sub>), 38.3 (C<sub>8</sub>), 34.2 (C<sub>9</sub>), 33.5 (C<sub>7</sub>), 24.9 (C<sub>14</sub>), 21.0 (C<sub>10</sub>), 13.7 (C<sub>17</sub>).

IR (ν, cm<sup>-1</sup>, CDCl<sub>3</sub>) 1735, 1674, 1598, 1510, 1459, 1365, 1257, 1222, 1169, 1111, 1032, 984, 909, 810, 749.

HRMS (EI<sup>+</sup>) *m/z*: [M + Na]<sup>+</sup>calculated for C<sub>19</sub>H<sub>26</sub>NaO<sub>5</sub>S<sub>2</sub>: 421.1114, found: 421.1116.

R<sub>f</sub> = 0.40 (EtOAc / PE = 1/3).

**4-(2-hydroxyethyl)-6-methoxy-4-methyl-3,4-dihydronaphthalen-1(2H)-one****(II-76)**



Chemical Formula: C<sub>14</sub>H<sub>18</sub>O<sub>3</sub>  
Exact Mass: 234.1256

**II-75** (92 mg, 0.333 mmol), TFA (1 mL), methanol (1 mL) were added in 10 mL round-bottomed flask with a magnetic stir bar. The resulting solution was stirred at reflux for overnight. The crude mixture was concentrated in vacuum and was purified by column chromatography on silica gel (petroleum ether/ethyl acetate =10:1 to 1:1) to give product **II-76** (61 mg, 78%) as a colorless oil.

<sup>1</sup>H NMR (δ, ppm)(400 MHz, CDCl<sub>3</sub>) δ 8.08 – 7.96 (m, 1H, H<sub>4</sub>), 6.83 (dd, *J* = 10.6, 2.4 Hz, 2H, H<sub>7</sub>, H<sub>3</sub>), 3.86 (s, 3H, H<sub>1</sub>), 3.73 – 3.66 (m, 2H, H<sub>14</sub>), 2.77 – 2.58 (m, 2H, H<sub>9</sub>), 2.18 – 1.86 (m, 5H, H<sub>10</sub>, H<sub>13</sub>, OH), 1.41 (s, 3H, H<sub>12</sub>).

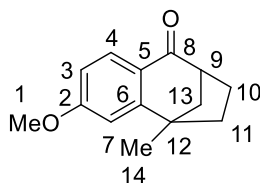
<sup>13</sup>C NMR (δ, ppm)(100 MHz, CDCl<sub>3</sub>) δ 197.1 (C<sub>8</sub>), 163.9 (C<sub>2</sub>), 153.4 (C<sub>6</sub>), 130.3 (C<sub>5</sub>), 125.2 (C<sub>4</sub>), 111.8 (C<sub>3</sub>), 111.3 (C<sub>7</sub>), 59.5 (C<sub>14</sub>), 55.4 (C<sub>1</sub>), 43.5 (C<sub>9</sub>), 36.3 (C<sub>13</sub>), 34.5 (C<sub>10</sub>), 31.2 (C<sub>11</sub>), 27.7 (C<sub>12</sub>).

IR (ν, cm<sup>-1</sup>, CDCl<sub>3</sub>) 3404, 2934, 2868, 1667, 1594, 1461, 1416, 1348, 1307, 1237, 1138, 1056, 1016, 856, 787.

HRMS (EI<sup>+</sup>) *m/z*: [M + H]<sup>+</sup> calculated for C<sub>14</sub>H<sub>19</sub>O<sub>3</sub>: 235.1329, found: 235.1322.

R<sub>f</sub> = 0.37 (EtOAc / PE = 1/1).

### 3-methoxy-5-methyl-5,6,7,8-tetrahydro-9H-5,8-methanobenzo[7]annulen-9-one (**II-77**)



Chemical Formula: C<sub>14</sub>H<sub>16</sub>O<sub>2</sub>  
Exact Mass: 216.1150

**II-77** (36 mg, 0.12 mmol) was added in 5 mL of pressurized vessel with 0.5 mL of

THF and then add a solution of methylamine in water (93 mg, 1.2 mmol) with MW of 40%. Leave the resulting solution at room temperature for 2 days. The reaction was monitored by TLC plate and HPLC-MS. The crude mixture was concentrated in vacuum and was purified by column chromatography on silica gel (petroleum ether/ethyl acetate =20: 1 to 10:1) to give product **II-78** (22 mg, 80%) as a colorless oil.

**<sup>1</sup>H NMR** ( $\delta$ , ppm)(400 MHz, CDCl<sub>3</sub>)  $\delta$  8.00 (d,  $J$  = 8.6 Hz, 1H, H<sub>4</sub>), 6.90 – 6.73 (m, 2H, H<sub>3</sub>, H<sub>7</sub>), 3.87 (s, 3H, H<sub>1</sub>), 3.09 (dd,  $J$  = 7.6, 4.8 Hz, 1H, H<sub>9</sub>), 2.28 (d,  $J$  = 13.2 Hz, 1H, H<sub>13</sub>), 2.06 (d,  $J$  = 11.6 Hz, 1H, H<sub>13</sub>), 1.94 – 1.80 (m, 1H, H<sub>11</sub>), 1.79 – 1.59 (m, 3H, H<sub>11</sub>, H<sub>10</sub>), 1.58 (s, 3H, H<sub>14</sub>).

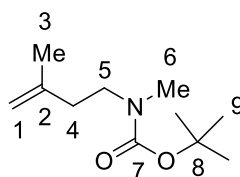
**<sup>13</sup>C NMR** ( $\delta$ , ppm)(100 MHz, CDCl<sub>3</sub>)  $\delta$  200.9 (C<sub>8</sub>), 163.9 (C<sub>2</sub>), 155.5 (C<sub>6</sub>), 130.0 (C<sub>5</sub>), 123.8 (C<sub>4</sub>), 111.5 (C<sub>3</sub>), 109.1 (C<sub>7</sub>), 55.4 (C<sub>1</sub>), 50.7 (C<sub>9</sub>), 46.8 (C<sub>12</sub>), 44.7 (C<sub>13</sub>), 39.2 (C<sub>11</sub>), 26.7 (C<sub>10</sub>), 23.3 (C<sub>14</sub>).

**IR** ( $\nu$ , cm<sup>-1</sup>, CDCl<sub>3</sub>) 2946, 1677, 1594, 1568, 1486, 1335, 1235, 1121, 1048, 946, 893, 800

**HRMS** (EI<sup>+</sup>)  $m/z$ : [M + H]<sup>+</sup>calculated for C<sub>14</sub>H<sub>17</sub>O<sub>2</sub>: 217.1223, found: 217.1218.

**R<sub>f</sub>** = 0.55 (EtOAc / PE = 1/4).

### ***Tert*-butyl-methyl(3-methylbut-3-en-1-yl)-carbamate (**II-78**)<sup>5</sup>**



Chemical Formula: C<sub>11</sub>H<sub>21</sub>NO<sub>2</sub>  
Exact Mass: 199.1572

To a solution of crude **II-80** (1.64 g, 10 mmol) was added a solution of methylamine in water (1.16 g, 15 mmol) with MW of 40%, then added 5 mL of methanol. The reaction mixture was heated to 75 °C in a pressurized vessel for 2 hours then cooled to room temperature. Then *di*-tert-butyl dicarbonate (2.18 g, 10 mmol) and Et<sub>3</sub>N (1.52 g, 15 mmol) were added to reaction mixture, the resulting solution was stirred at room

temperature for 10 hours. The crude mixture was concentrated in vacuum and was purified by column chromatography on silica gel (petroleum ether/ethyl acetate =100:0 to 10:1) to give product **II-79** (1.321 g, 67%) as a colorless oil.

$^1\text{H NMR}$  ( $\delta$ , ppm)(400 MHz,  $\text{CDCl}_3$ )  $\delta$  4.65 (d,  $J = 22.6$  Hz, 2H,  $\text{H}_1$ ), 3.23 (t,  $J = 6.8$  Hz, 2H,  $\text{H}_5$ ), 2.76 (s, 3H,  $\text{H}_6$ ), 2.13 (t,  $J = 6.8$  Hz, 2H,  $\text{H}_4$ ), 1.68 (s, 3H,  $\text{H}_3$ ), 1.38 (s, 9H,  $\text{H}_9$ ).

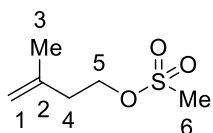
$^{13}\text{C NMR}$  ( $\delta$ , ppm)(100 MHz,  $\text{CDCl}_3$ )  $\delta$  155.5 ( $\text{C}_7$ ), 142.6 ( $\text{C}_2$ ), 112.0 ( $\text{C}_1$ ), 79.0 ( $\text{C}_8$ ), 47.5 ( $\text{C}_5$ ), 36.1 ( $\text{C}_6$ ), 33.9 ( $\text{C}_4$ ), 28.3 ( $\text{C}_9$ ), 22.2 ( $\text{C}_3$ ).

**IR** ( $\nu$ ,  $\text{cm}^{-1}$ ,  $\text{CDCl}_3$ ) 2973, 2930, 1693, 1650, 1453, 1423, 1392, 1365, 1167, 1136, 1050, 884, 772.

**HRMS** ( $\text{EI}^+$ )  $m/z$ :  $[\text{M} + \text{Na}]^+$  calculated for  $\text{C}_{11}\text{H}_{21}\text{NNaO}_2$ : 222.1464, found: 222.1459.

$R_f = 0.60$  (EtOAc / PE = 1/10).

### 3-methylbut-3-en-1-yl-methanesulfonate (**II-80**)<sup>6</sup>



Chemical Formula:  $\text{C}_6\text{H}_{12}\text{O}_3\text{S}$   
Exact Mass: 164.0507

To a solution of the alcohol **II-73** (1.72 g, 20 mmol) and  $\text{NEt}_3$  (3.03 g, 30 mmol) in DCM (20 mL) at 0 °C was added methanesulfonyl chloride (2.75 g, 24 mmol) over 1 hour. The reaction mixture was allowed to room temperature over 2 hours and stirred at room temperature for an additional 13 hours. Water (20 mL) was added and the mixture was extracted with DCM (3  $\times$  20 mL). The organic phase dried over  $\text{MgSO}_4$  and concentrated to afford crude product **II-80** (3.24 g, 99%) as a light yellow oil.

$^1\text{H NMR}$  ( $\delta$ , ppm)(400 MHz,  $\text{CDCl}_3$ )  $\delta$  4.93 – 4.70 (m, 2H,  $\text{H}_1$ ), 4.32 (t,  $J = 6.8$  Hz, 2H,  $\text{H}_5$ ), 3.01 (s, 3H,  $\text{H}_6$ ), 2.46 (t,  $J = 6.8$  Hz, 2H,  $\text{H}_4$ ), 1.78 (s, 3H,  $\text{H}_3$ ).

$^{13}\text{C NMR}$  ( $\delta$ , ppm)(100 MHz,  $\text{CDCl}_3$ )  $\delta$  140.2 ( $\text{C}_2$ ), 113.3 ( $\text{C}_1$ ), 68.0 ( $\text{C}_5$ ), 37.4 ( $\text{C}_4$ ),

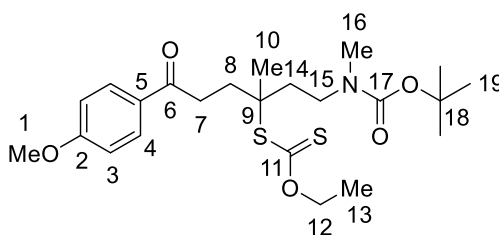
37.0 (C<sub>6</sub>), 22.4 (C<sub>3</sub>).

**IR** ( $\nu$ , cm<sup>-1</sup>, CDCl<sub>3</sub>) 2941, 1651, 1450, 1334, 1169, 951, 897, 803.

**HRMS** (EI<sup>+</sup>) m/z: [M + Na]<sup>+</sup> calculated for C<sub>6</sub>H<sub>12</sub>NaO<sub>3</sub>S: 187.0399, found: 187.0399.

R<sub>f</sub> = 0.45 (EtOAc / PE = 1/3).

**Tert-butyl-(3-((ethoxycarbonothioyl)-thio)-6-(4-methoxyphenyl)-3-methyl-6-oxohexyl)(methyl)carbamate (II-81)**



Chemical Formula: C<sub>23</sub>H<sub>35</sub>NO<sub>5</sub>S<sub>2</sub>  
Exact Mass: 469.1957

According to the general procedure B1, the reaction was carried out with xanthate **II-71** (540 mg, 2 mmol) and olefin **II-79** (797 mg, 4 mmol) in 1,2-dichloroethane (2 mL), and needed 6 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (100:10 to 100:15) to afford product **II-81** (619 mg, 66%) as a colorless oil.

**<sup>1</sup>H NMR** ( $\delta$ , ppm)(400 MHz, CDCl<sub>3</sub>)  $\delta$  7.96 (d,  $J$  = 8.8 Hz, 2H, H<sub>4</sub>), 7.01 – 6.77 (m, 2H, H<sub>3</sub>), 4.66 (q,  $J$  = 7.0 Hz, 2H, H<sub>12</sub>), 3.87 (s, 3H, H<sub>1</sub>), 3.52 – 3.20 (m, 2H, H<sub>7</sub>), 3.19 – 2.95 (m, 2H, H<sub>15</sub>), 2.84 (s, 3H, H<sub>16</sub>), 2.42 – 2.28 (m, 1H, H<sub>14</sub>), 2.17 (ddd,  $J$  = 13.6, 11.0, 5.2 Hz, 2H, H<sub>8</sub>), 2.05 – 1.89 (m, 1H, H<sub>14</sub>), 1.49 – 1.38 (m, 14H, H<sub>9</sub>, H<sub>10</sub>, H<sub>13</sub>).

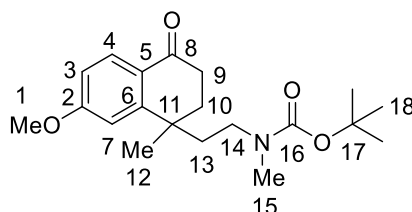
**<sup>13</sup>C NMR** ( $\delta$ , ppm)(100 MHz, CDCl<sub>3</sub>)  $\delta$  212.6 (C<sub>11</sub>), 197.8 (C<sub>6</sub>), 163.6 (C<sub>Ar</sub>), 155.5 (C<sub>17</sub>), 130.4 (C<sub>Ar</sub>), 129.8 (C<sub>Ar</sub>), 113.8 (C<sub>Ar</sub>), 69.7 (C<sub>18</sub>), 55.8 (C<sub>12</sub>), 55.5 (C<sub>1</sub>), 33.5 (C<sub>15</sub>), 31.9 (C<sub>14</sub>), 29.6 (C<sub>16</sub>), 29.5 (C<sub>8</sub>), 28.5 (C<sub>9</sub>), 24.7 (C<sub>7</sub>), 24.2 (C<sub>19</sub>), 22.7 (C<sub>10</sub>), 13.7 (C<sub>13</sub>).

**IR** ( $\nu$ , cm<sup>-1</sup>, CDCl<sub>3</sub>) 2971, 2929, 1681, 1599, 1480, 1455, 1392, 1364, 1255, 1216, 1160, 1035, 985, 837, 774.

**HRMS** (EI<sup>+</sup>) m/z: [M + H]<sup>+</sup> calculated for C<sub>23</sub>H<sub>36</sub>NO<sub>5</sub>S<sub>2</sub>: 470.2029, found: 470.2011.

R<sub>f</sub> = 0.42 (EtOAc / PE = 1/3).

***Tert*-butyl-(2-(7-methoxy-1-methyl-4-oxo-1,2,3,4-tetrahydronaphthalen-1-yl)ethyl)(methyl)carbamate (**II-82**)**



Chemical Formula: C<sub>20</sub>H<sub>29</sub>NO<sub>4</sub>  
Exact Mass: 347.2097

According to the general procedure C1, the reaction was carried out with the adduct **II-81** (3.3 g, 7.03 mmol) in 1,2-dichloroethane (15 mL), and needed 7 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (10:1 to 5:1) to afford product **II-82** (1.44 g, 60%) as a colorless oil.

<sup>1</sup>H NMR (δ, ppm)(400 MHz, CDCl<sub>3</sub>) δ 8.16 – 7.90 (m, 1H, H<sub>Ar</sub>), 7.02 – 6.64 (m, 2H, H<sub>Ar</sub>), 3.88(s, 3H, H<sub>1</sub>), 3.35 – 3.03 (m, 2H, H<sub>14</sub>), 2.91 – 2.56 (m, 4H, H<sub>15</sub>, H<sub>9</sub>), 2.21 – 1.66 (m, 4H, H<sub>9</sub>, H<sub>13</sub>), 1.42 (d, *J* = 11.2 Hz, 10H, H<sub>18</sub>, H<sub>10</sub>), 1.26 (s, 3H, H<sub>12</sub>), 0.92 – 0.83 (m, 1H, H<sub>10</sub>).

<sup>13</sup>C NMR (δ, ppm)(100 MHz, CDCl<sub>3</sub>) δ 196.5 (C<sub>8</sub>), 163.9 (C<sub>2</sub>), 155.5 (C<sub>16</sub>), 130.4 (C<sub>Ar</sub>), 125.2 (C<sub>Ar</sub>), 111.2 (C<sub>Ar</sub>), 55.4 (C<sub>1</sub>), 36.1 (C<sub>14</sub>), 34.4 (C<sub>13</sub>), 29.6 (C<sub>11</sub>), 28.5 (C<sub>15</sub>), 27.2 (C<sub>9</sub>), 22.7 (C<sub>10</sub>), 14.1 (C<sub>12</sub>).

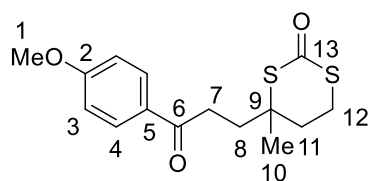
IR (ν, cm<sup>-1</sup>, CDCl<sub>3</sub>) 2965, 2927, 1681, 1596, 1393, 1365, 1233, 1161, 1056, 1037, 880, 832, 772, 731.

HRMS (EI<sup>+</sup>) *m/z*: [M + Na]<sup>+</sup>calculated for C<sub>20</sub>H<sub>29</sub>NNaO<sub>4</sub>: 370.1989, found: 370.1989.

R<sub>f</sub> = 0.30 (EtOAc / PE = 1/3).

#### 4.5.2 Chapter 3 spectroscopic data

#### 4-(3-(4-methoxyphenyl)-3-oxopropyl)-4-methyl-1,3-dithian-2-one (III-12a)



Chemical Formula: C<sub>15</sub>H<sub>18</sub>O<sub>3</sub>S<sub>2</sub>

Exact Mass: 310.0697

According to the general procedure A, the reaction was carried out with *O*-ethyl *S*-(2-(4-methoxyphenyl)-2-oxoethyl)-carbonodithioate (810 mg, 3 mmol) and 3-methylbut-3-en-1-yl-methanesulfonate (984 mg, 6 mmol) in EtOAc (3 mL), and needed 11 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (10:1 to 1:1) to afford product **III-12a** (735 mg, 79%) as a light yellow oil.

<sup>1</sup>H NMR (δ, ppm)(400 MHz, CDCl<sub>3</sub>) δ 7.95 (d, *J* = 8.8 Hz, 2H, H<sub>4</sub>), 7.10 – 6.82 (m, 2H, H<sub>3</sub>), 3.87 (s, 3H, H<sub>1</sub>), 3.47 – 3.29 (m, 2H, H<sub>12</sub>), 3.24 – 2.98 (m, 2H, H<sub>7</sub>), 2.27-2.20 (m, 3H, H<sub>8</sub>, H<sub>8</sub>, H<sub>11</sub>), 2.14 – 2.00 (m, 1H, H<sub>11</sub>), 1.53 (s, 3H, H<sub>10</sub>).

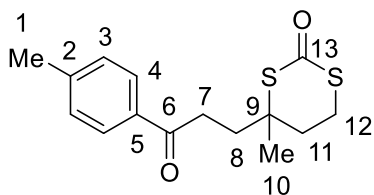
<sup>13</sup>C NMR (δ, ppm)(100 MHz, CDCl<sub>3</sub>) δ 197.2 (C<sub>6</sub>), 189.3 (C<sub>13</sub>), 163.7 (C<sub>2</sub>), 130.4 (C<sub>5</sub>), 129.5 (2C<sub>4</sub>), 113.9 (2C<sub>3</sub>), 55.6 (C<sub>1</sub>), 52.8 (C<sub>9</sub>), 36.7 (C<sub>7</sub>), 35.0 (C<sub>8</sub>), 32.8 (C<sub>12</sub>), 28.6 (C<sub>11</sub>), 28.2 (C<sub>10</sub>).

IR (ν, cm<sup>-1</sup>, CDCl<sub>3</sub>) 2932, 2839, 1672, 1594, 1574, 1510, 1419, 1308, 1258, 1222, 1170, 1027, 930, 889.

HRMS (EI<sup>+</sup>) *m/z*: [M + H]<sup>+</sup> calculated for C<sub>15</sub>H<sub>19</sub>O<sub>3</sub>S<sub>2</sub>: 311.0770, found: 311.0770.

R<sub>f</sub> = 0.25 (EtOAc / PE = 1/4).

#### 4-methyl-4-(3-oxo-3-(*p*-tolyl)propyl)-1,3-dithian-2-one (III-12b)



Chemical Formula: C<sub>15</sub>H<sub>18</sub>O<sub>2</sub>S<sub>2</sub>

Exact Mass: 294.0748

According to the general procedure A, the reaction was carried out with *O*-ethyl *S*-(2-oxo-2-(*p*-tolyl)ethyl)-carbonodithioate (762 mg, 3 mmol) and 3-methylbut-3-en-1-yl-methanesulfonate (984 mg, 6 mmol) in EtOAc (3 mL), and needed 14 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (20:1 to 10:1) to afford product **III-12b** (617 mg, 70%) as a light yellow solid.

**<sup>1</sup>H NMR** ( $\delta$ , ppm)(400 MHz, CDCl<sub>3</sub>)  $\delta$  7.86 (d,  $J$  = 8.0 Hz, 2H, H<sub>4</sub>), 7.27 (d,  $J$  = 8.0 Hz, 2H, H<sub>3</sub>), 3.48 – 3.30 (m, 2H, H<sub>12</sub>), 3.21-3.05 (m, 2H, H<sub>7</sub>), 2.42 (s, 3H, H<sub>1</sub>), 2.34 – 2.15 (m, 3H, H<sub>8</sub>, H<sub>8</sub>, H<sub>11</sub>), 2.13 – 2.01 (m, 1H, H<sub>11</sub>), 1.53 (s, 3H, H<sub>10</sub>).

**<sup>13</sup>C NMR** ( $\delta$ , ppm)(100 MHz, CDCl<sub>3</sub>)  $\delta$  198.3 (C<sub>6</sub>), 189.2 (C<sub>13</sub>), 144.3 (C<sub>2</sub>), 134.0 (C<sub>5</sub>), 129.4 (C<sub>4</sub>), 128.2 (C<sub>3</sub>), 52.7 (C<sub>9</sub>), 36.6 (C<sub>7</sub>), 35.0 (C<sub>8</sub>), 33.1 (C<sub>12</sub>), 28.6 (C<sub>11</sub>), 28.2 (C<sub>10</sub>), 21.7 (C<sub>1</sub>).

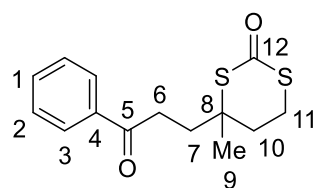
**IR** ( $\nu$ , cm<sup>-1</sup>, CDCl<sub>3</sub>) 2935, 1678, 1600, 1444, 1380, 1367, 1295, 1224, 1181, 1034, 931, 890, 819, 778.

**HRMS** (EI<sup>+</sup>)  $m/z$ : [M + H]<sup>+</sup> calculated for C<sub>15</sub>H<sub>19</sub>O<sub>2</sub>S<sub>2</sub>: 295.0821, found: 295.0827.

**Mp**: 80-82 °C.

**R<sub>f</sub>** = 0.25 (EtOAc / PE = 1/4).

#### 4-methyl-4-(3-oxo-3-phenylpropyl)-1,3-dithian-2-one (III-12c)



Chemical Formula: C<sub>14</sub>H<sub>16</sub>O<sub>2</sub>S<sub>2</sub>  
Exact Mass: 280.0592

According to the general procedure A, the reaction was carried out with *O*-ethyl *S*-(2-oxo-2-phenylethyl)-carbonodithioate (720 mg, 3 mmol) and 3-methylbut-3-en-1-yl-methanesulfonate (984 mg, 6 mmol) in EtOAc (3 mL), and needed 11 h for the reaction to go to completion. It was purified by column



chromatography on silica gel using petroleum ether/ethyl acetate (20:1 to 10:1) to afford product **III-12c** (521 mg, 62%) as a colorless oil.

$^1\text{H NMR}$  ( $\delta$ , ppm)(400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.97 (dt,  $J = 8.4, 1.6$  Hz, 2H,  $\text{H}_3$ ), 7.62 – 7.54 (m, 1H,  $\text{H}_1$ ), 7.52 – 7.44 (m, 2H,  $\text{H}_2$ ), 3.45 – 3.32 (m, 2H,  $\text{H}_{11}$ ), 3.27-3.08 (m, 2H,  $\text{H}_6$ ), 2.35 – 2.15 (m, 3H,  $\text{H}_7, \text{H}_7, \text{H}_{10}$ ), 2.12-2.04 (m, 1H,  $\text{H}_{10}$ ), 1.53 (s, 3H,  $\text{H}_9$ ).

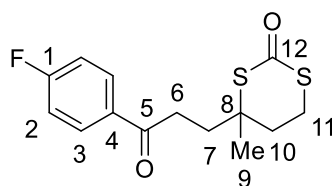
$^{13}\text{C NMR}$  ( $\delta$ , ppm)(100 MHz,  $\text{CDCl}_3$ )  $\delta$  198.7 ( $\text{C}_5$ ), 189.2 ( $\text{C}_{12}$ ), 136.5 ( $\text{C}_4$ ), 133.5 ( $\text{C}_3$ ), 128.8 ( $\text{C}_2$ ), 128.1 ( $\text{C}_1$ ), 52.7 ( $\text{C}_8$ ), 36.5 ( $\text{C}_6$ ), 35.0 ( $\text{C}_7$ ), 33.2 ( $\text{C}_{11}$ ), 28.6 ( $\text{C}_{10}$ ), 28.2 ( $\text{C}_9$ ).

$\text{IR}$  ( $\nu$ ,  $\text{cm}^{-1}$ ,  $\text{CDCl}_3$ ) 3060, 2935, 1682, 1598, 1447, 1318, 1216, 929, 890, 742, 690.

$\text{HRMS}$  ( $\text{EI}^+$ )  $m/z$ :  $[\text{M} + \text{H}]^+$  calculated for  $\text{C}_{14}\text{H}_{17}\text{O}_2\text{S}_2$ : 281.0664, found: 281.0656.

$R_f = 0.30$  (EtOAc / PE = 1/4).

#### 4-(3-(3-fluorophenyl)-3-oxopropyl)-4-methyl-1,3-dithian-2-one (**III-12d**)



Chemical Formula:  $\text{C}_{14}\text{H}_{15}\text{FO}_2\text{S}_2$   
Exact Mass: 298.0497

According to the general procedure A, the reaction was carried out with *O*-ethyl *S*-(2-(4-fluorophenyl)-2-oxoethyl)-carbonodithioate (774 mg, 3 mmol) and 3-methylbut-3-en-1-yl-methanesulfonate (984 mg, 6 mmol) in EtOAc (3 mL), and needed 10 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (20:1 to 100:15) to afford product **III-12d** (715 mg, 80%) as a white solid.

$^1\text{H NMR}$  ( $\delta$ , ppm)(400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.05 – 7.97 (m, 2H,  $\text{H}_3$ ), 7.19 – 7.11 (m, 2H,  $\text{H}_2$ ), 3.49 – 3.33 (m, 2H,  $\text{H}_{11}$ ), 3.25-3.06 (m, 2H,  $\text{H}_6$ ), 2.35 – 2.18 (m, 3H,  $\text{H}_7, \text{H}_7, \text{H}_{10}$ ), 2.11-2.03 (m, 1H,  $\text{H}_{10}$ ), 1.54 (s, 3H,  $\text{H}_9$ ).

$^{13}\text{C NMR}$  ( $\delta$ , ppm)(100 MHz,  $\text{CDCl}_3$ )  $\delta$  197.0 ( $\text{C}_5$ ), 189.1 ( $\text{C}_{12}$ ), 165.9 ( $\text{C}_1$ )(d,  $J_{\text{C-F}} = 255.0$  Hz), 132.9 ( $\text{C}_4$ )(d,  $J_{\text{C-F}} = 3.0$  Hz), 130.7 ( $\text{C}_3$ )(d,  $J_{\text{C-F}} = 9.0$  Hz), 115.9 ( $\text{C}_2$ )(d,  $J_{\text{C-F}}$

= 21.6 Hz), 52.6 (C<sub>8</sub>), 36.5 (C<sub>6</sub>), 35.1 (C<sub>7</sub>), 33.1 (C<sub>11</sub>), 28.7 (C<sub>10</sub>), 28.2 (C<sub>9</sub>).

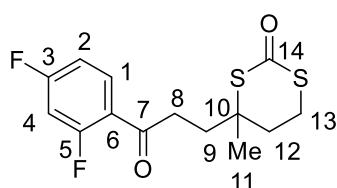
**IR** ( $\nu$ , cm<sup>-1</sup>, CDCl<sub>3</sub>) 3074, 2933, 1682, 1593, 1505, 1409, 1381, 1297, 1220, 1156, 989, 930, 889, 841, 730.

**HRMS** (EI<sup>+</sup>)  $m/z$ : [M + H]<sup>+</sup> calculated for C<sub>14</sub>H<sub>16</sub>FO<sub>2</sub>S<sub>2</sub>: 299.0570, found: 299.0562.

**Mp**: 105-106 °C.

**R<sub>f</sub>** = 0.20 (EtOAc / PE = 1/4).

#### 4-(3-(2,4-difluorophenyl)-3-oxopropyl)-4-methyl-1,3-dithian-2-one (III-12e)



Chemical Formula: C<sub>14</sub>H<sub>14</sub>F<sub>2</sub>O<sub>2</sub>S<sub>2</sub>  
Exact Mass: 316.0403

According to the general procedure A, the reaction was carried out with *S*-(2-(2,4-difluorophenyl)-2-oxoethyl)-*O*-ethyl-carbonodithioate (828 mg, 3 mmol) and 3-methylbut-3-en-1-yl methanesulfonate (984 mg, 6 mmol) in EtOAc (3 mL), and needed 12 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (20:1 to 10:1) to afford product **III-12e** (787 mg, 83%) as a light yellow oil.

**<sup>1</sup>H NMR** ( $\delta$ , ppm)(400 MHz, CDCl<sub>3</sub>)  $\delta$  7.93 (d,  $J$  = 6.8 Hz, 1H, H<sub>1</sub>), 6.94 (d,  $J$  = 32.8 Hz, 2H, H<sub>2</sub>, H<sub>4</sub>), 3.40 (s, 2H, H<sub>13</sub>), 3.08 (d,  $J$  = 42.0 Hz, 2H, H<sub>8</sub>), 2.24 (s, 3H, H<sub>9</sub>, H<sub>9</sub>, H<sub>12</sub>), 2.08 (s, 1H, H<sub>12</sub>), 1.53 (s, 3H, H<sub>11</sub>).

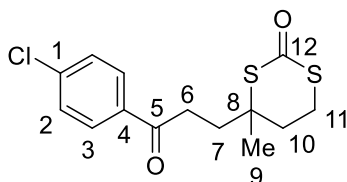
**<sup>13</sup>C NMR** ( $\delta$ , ppm)(100 MHz, CDCl<sub>3</sub>)  $\delta$  195.4 (C<sub>7</sub>)(d,  $J_{C-F}$  = 4.6 Hz), 189.1 (C<sub>14</sub>), 166.0 (C<sub>5</sub>)(dd,  $J_{C-F}$  = 257.4, 12.2 Hz), 162.8 (C<sub>3</sub>)(dd,  $J_{C-F}$  = 257.0, 12.2 Hz), 132.7 (C<sub>1</sub>)(dd,  $J_{C-F}$  = 10.6, 4.2 Hz), 121.8 (C<sub>6</sub>)(dd,  $J_{C-F}$  = 13.2, 3.6 Hz), 112.4 (C<sub>2</sub>)(dd,  $J_{C-F}$  = 21.2, 3.2 Hz), 104.9 (C<sub>4</sub>)(dd,  $J_{C-F}$  = 27.6, 25.2 Hz), 52.5 (C<sub>10</sub>), 38.1 (C<sub>8</sub>)(d,  $J_{C-F}$  = 8.0 Hz), 36.3 (C<sub>9</sub>)(d,  $J_{C-F}$  = 2.0 Hz), 35.0 (C<sub>13</sub>), 28.5 (C<sub>12</sub>), 28.3 (C<sub>11</sub>).

**IR** ( $\nu$ , cm<sup>-1</sup>, CDCl<sub>3</sub>) 2934, 1684, 1597, 1495, 1426, 1299, 1266, 1233, 1195, 1140, 1099, 1081, 969, 933, 887, 852, 783, 731.

**HRMS** (EI<sup>+</sup>) m/z: [M + H]<sup>+</sup> calculated for C<sub>14</sub>H<sub>15</sub>F<sub>2</sub>O<sub>2</sub>S<sub>2</sub>: 317.0476, found: 317.0473.

**R<sub>f</sub>** = 0.30 (EtOAc / PE = 1/4).

#### 4-(3-(4-chlorophenyl)-3-oxopropyl)-4-methyl-1,3-dithian-2-one (III-12f)



Chemical Formula: C<sub>14</sub>H<sub>15</sub>ClO<sub>2</sub>S<sub>2</sub>

Exact Mass: 314.0202

According to the general procedure A, the reaction was carried out with S-(2-(4-chlorophenyl)-2-oxoethyl) O-ethyl carbonodithioate (821 mg, 3 mmol) and 3-methylbut-3-en-1-yl methanesulfonate (984 mg, 6 mmol) in EtOAc (3 mL), and needed 10 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (10:1 to 5:1) to afford product **III-12f** (565 mg, 60%) as a white solid.

**<sup>1</sup>H NMR** (δ, ppm)(400 MHz, CDCl<sub>3</sub>) δ 7.91 (d, *J* = 8.4 Hz, 2H, H<sub>3</sub>), 7.45 (d, *J* = 8.4 Hz, 2H, H<sub>2</sub>), 3.50 – 3.30 (m, 2H, H<sub>11</sub>), 3.27 – 3.01 (m, 2H, H<sub>6</sub>), 2.35 – 2.14 (m, 3H, H<sub>7</sub>, H<sub>7</sub>, H<sub>10</sub>), 2.16 – 1.98 (m, 1H, H<sub>10</sub>), 1.53 (s, 3H, H<sub>9</sub>).

**<sup>13</sup>C NMR** (δ, ppm)(100 MHz, CDCl<sub>3</sub>) δ 197.4 (C<sub>5</sub>), 189.0 (C<sub>12</sub>), 139.8 (C<sub>4</sub>), 134.8 (C<sub>1</sub>), 129.5 (C<sub>3</sub>), 129.0 (C<sub>2</sub>), 52.6 (C<sub>8</sub>), 36.4 (C<sub>6</sub>), 35.1 (C<sub>7</sub>), 33.2 (C<sub>11</sub>), 28.6 (C<sub>10</sub>), 28.2 (C<sub>9</sub>).

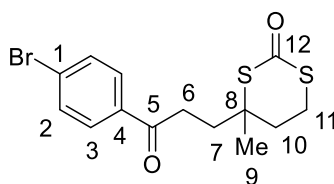
**IR** (ν, cm<sup>-1</sup>, CDCl<sub>3</sub>) 2967, 1682, 1585, 1444, 1399, 1282, 1212, 1088, 1010, 920, 889, 840, 765, 749.

**HRMS** (EI<sup>+</sup>) m/z: [M + H]<sup>+</sup> calculated for C<sub>14</sub>H<sub>16</sub>ClO<sub>2</sub>S<sub>2</sub>: 315.0275, found: 315.0275.

**Mp**: 101-102 °C.

**R<sub>f</sub>** = 0.25 (EtOAc / PE = 1/4).

#### 4-(3-(4-bromophenyl)-3-oxopropyl)-4-methyl-1,3-dithian-2-one (III-12g)



Chemical Formula: C<sub>14</sub>H<sub>15</sub>BrO<sub>2</sub>S<sub>2</sub>

Exact Mass: 357.9697

According to the general procedure A, the reaction was carried out with *S*-(2-(4-bromophenyl)-2-oxoethyl)-*O*-ethyl-carbonodithioate (953 mg, 3 mmol) and 3-methylbut-3-en-1-yl-methanesulfonate (984 mg, 6 mmol) in EtOAc (3 mL), and needed 13 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (10:1 to 5:1) to afford product **III-12g** (655 mg, 61%) as a light yellow solid.

<sup>1</sup>H NMR (δ, ppm)(400 MHz, CDCl<sub>3</sub>) δ 7.83 (d, *J* = 8.0 Hz, 2H, H<sub>3</sub>), 7.62 (d, *J* = 7.4 Hz, 2H, H<sub>2</sub>), 3.47 – 3.31 (m, 2H, H<sub>11</sub>), 3.26 – 2.99 (m, 2H, H<sub>6</sub>), 2.36 – 2.13 (m, 3H, H<sub>7</sub>, H<sub>7</sub>, H<sub>10</sub>), 2.13 – 1.99 (m, 1H, H<sub>10</sub>), 1.53 (s, 3H, H<sub>9</sub>).

<sup>13</sup>C NMR (δ, ppm)(100 MHz, CDCl<sub>3</sub>) δ 197.6 (C<sub>5</sub>), 189.0 (C<sub>12</sub>), 135.2 (C<sub>4</sub>), 132.1 (C<sub>2</sub>), 129.6 (C<sub>3</sub>), 128.6 (C<sub>1</sub>), 52.6 (C<sub>8</sub>), 36.4 (C<sub>6</sub>), 35.1 (C<sub>7</sub>), 33.2 (C<sub>11</sub>), 28.7 (C<sub>10</sub>), 28.2 (C<sub>9</sub>).

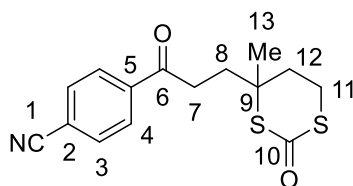
IR (ν, cm<sup>-1</sup>, CDCl<sub>3</sub>) 3076, 2934, 1684, 1598, 1584, 1483, 1396, 1296, 1212, 1070, 934, 890.

HRMS (EI<sup>+</sup>) *m/z*: [M + H]<sup>+</sup> calculated for C<sub>14</sub>H<sub>16</sub>BrO<sub>2</sub>S<sub>2</sub>: 358.9770, found: 358.9772.

Mp: 40-42 °C.

R<sub>f</sub> = 0.40 (EtOAc / PE = 1/4).

#### . 4-(3-(4-methyl-2-oxo-1,3-dithian-4-yl)propanoyl)benzonitrile (III-12h)



Chemical Formula: C<sub>15</sub>H<sub>15</sub>NO<sub>2</sub>S<sub>2</sub>

Exact Mass: 305.0544

According to the general procedure A, the reaction was carried out with

*S*-(2-(4-cyanophenyl)-2-oxoethyl)-*O*-ethyl-carbonodithioate (795 mg, 3 mmol) and 3-methylbut-3-en-1-yl-methanesulfonate (984 mg, 6 mmol) in EtOAc (3 mL), and needed 10 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (10:1 to 3:1) to afford product **III-12** (604 mg, 66%) as a light yellow oil.

<sup>1</sup>H NMR (δ, ppm)(400 MHz, CDCl<sub>3</sub>) δ 8.07 (d, *J* = 8.6 Hz, 2H, H<sub>3</sub>), 7.80 (d, *J* = 8.6 Hz, 2H, H<sub>4</sub>), 3.50 – 3.33 (m, 2H, H<sub>11</sub>), 3.28 – 3.11 (m, 2H, H<sub>7</sub>), 2.38 – 2.17 (m, 3H, H<sub>8</sub>, H<sub>8</sub>, H<sub>12</sub>), 2.15 – 2.00 (m, 1H, H<sub>12</sub>), 1.54 (s, 3H, H<sub>13</sub>).

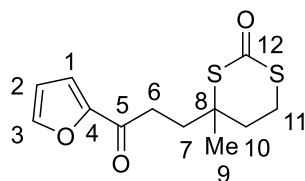
<sup>13</sup>C NMR (δ, ppm)(100 MHz, CDCl<sub>3</sub>) δ 197.3 (C<sub>6</sub>), 188.8 (C<sub>10</sub>), 139.4 (C<sub>5</sub>), 132.7 (C<sub>3</sub>), 128.5 (C<sub>4</sub>), 117.9 (C<sub>1</sub>), 116.6 (C<sub>2</sub>), 52.5 (C<sub>9</sub>), 36.2 (C<sub>7</sub>), 35.1 (C<sub>8</sub>), 33.6 (C<sub>11</sub>), 28.7 (C<sub>12</sub>), 28.2 (C<sub>13</sub>).

IR (ν, cm<sup>-1</sup>, CDCl<sub>3</sub>) 2929, 2230, 1690, 1598, 1403, 1293, 1212, 1174, 991, 933, 891, 848, 733.

HRMS (EI<sup>+</sup>) *m/z*: [M + H]<sup>+</sup> calculated for C<sub>15</sub>H<sub>16</sub>NO<sub>2</sub>S<sub>2</sub>: 306.0617, found: 306.0614.

R<sub>f</sub> = 0.35 (EtOAc / PE = 1/2).

#### 4-(3-(furan-2-yl)-3-oxopropyl)-4-methyl-1,3-dithian-2-one (**III-12i**)



Chemical Formula: C<sub>12</sub>H<sub>14</sub>O<sub>3</sub>S<sub>2</sub>  
Exact Mass: 270.0384

According to the general procedure A, the reaction was carried out with *O*-ethyl *S*-(2-(furan-2-yl)-2-oxoethyl)-carbonodithioate (690 mg, 3 mmol) and 3-methylbut-3-en-1-yl-methanesulfonate (984 mg, 6 mmol) in EtOAc (3 mL), and needed 13 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (20:1 to 5:1) to afford product **III-12i** (446 mg, 55%) as a light yellow oil.

<sup>1</sup>H NMR (δ, ppm)(400 MHz, CDCl<sub>3</sub>) δ 7.61 (d, *J* = 1.0 Hz, 1H, H<sub>3</sub>), 7.24 (d, *J* = 3.4

Hz, 1H, H<sub>1</sub>), 6.61 – 6.52 (m, 1H, H<sub>2</sub>), 3.40 (t, *J* = 5.4 Hz, 2H, H<sub>6</sub>), 3.16 – 2.89 (m, 2H, H<sub>11</sub>), 2.31 – 2.15 (m, 3H, H<sub>7</sub>, H<sub>7</sub>, H<sub>10</sub>), 2.13 – 2.02 (m, 1H, H<sub>10</sub>), 1.52 (s, 3H, H<sub>9</sub>).

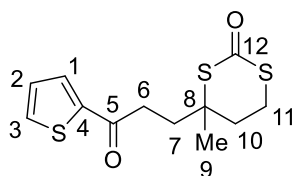
<sup>13</sup>C NMR (δ, ppm)(100 MHz, CDCl<sub>3</sub>) δ 189.1 (C<sub>12</sub>), 187.7 (C<sub>5</sub>), 152.3 (C<sub>4</sub>), 146.6 (C<sub>3</sub>), 117.4 (C<sub>1</sub>), 112.5 (C<sub>2</sub>), 52.7 (C<sub>8</sub>), 36.2 (C<sub>6</sub>), 34.8 (C<sub>7</sub>), 33.1 (C<sub>11</sub>), 28.5 (C<sub>10</sub>), 28.2 (C<sub>9</sub>).

IR (ν, cm<sup>-1</sup>, CDCl<sub>3</sub>) 3131, 2931, 1670, 1595, 1567, 1466, 1394, 1384, 1299, 1237, 1159, 1018, 914, 884, 765, 729.

HRMS (EI<sup>+</sup>) *m/z*: [M + H]<sup>+</sup> calculated for C<sub>12</sub>H<sub>15</sub>O<sub>3</sub>S<sub>2</sub>: 271.0457, found: 271.0451.

R<sub>f</sub> = 0.30 (EtOAc / PE = 1/2).

#### 4-methyl-4-(3-oxo-3-(thiophen-2-yl)-propyl)-1,3-dithian-2-one (III-12j)



Chemical Formula: C<sub>12</sub>H<sub>14</sub>O<sub>2</sub>S<sub>3</sub>  
Exact Mass: 286.0156

According to the general procedure A, the reaction was carried out with *O*-ethyl *S*-(2-oxo-2-(thiophen-2-yl)ethyl)-carbonodithioate (738 mg, 3 mmol) and 3-methylbut-3-en-1-yl-methanesulfonate (984 mg, 6 mmol) in EtOAc (3 mL), and needed 12 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (20:1 to 8:1) to afford product **III-12j** (523 mg, 61%) as a white solid.

<sup>1</sup>H NMR (δ, ppm)(400 MHz, CDCl<sub>3</sub>) δ 7.83 – 7.58 (m, 2H, H<sub>1</sub>, H<sub>3</sub>), 7.16 (s, 1H, H<sub>2</sub>), 3.40 (s, 2H, H<sub>11</sub>), 3.24 – 2.95 (m, 2H, H<sub>6</sub>), 2.37 – 2.00 (m, 4H, H<sub>7</sub>, H<sub>10</sub>), 1.53 (s, 3H, H<sub>9</sub>).

<sup>13</sup>C NMR (δ, ppm)(100 MHz, CDCl<sub>3</sub>) δ 191.6 (C<sub>5</sub>), 189.2 (C<sub>12</sub>), 143.6 (C<sub>4</sub>), 134.1 (C<sub>1</sub>), 132.3 (C<sub>3</sub>), 128.4 (C<sub>2</sub>), 52.7 (C<sub>8</sub>), 36.6 (C<sub>6</sub>), 34.9 (C<sub>7</sub>), 33.9 (C<sub>11</sub>), 28.6 (C<sub>10</sub>), 28.3 (C<sub>9</sub>).

IR (ν, cm<sup>-1</sup>, CDCl<sub>3</sub>) 3092, 2966, 2921, 1657, 1594, 1516, 1412, 1352, 1292, 1232,

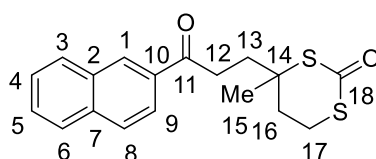
1062, 914, 888, 857, 724.

**HRMS** (EI<sup>+</sup>) m/z: [M + H]<sup>+</sup> calculated for C<sub>12</sub>H<sub>15</sub>O<sub>2</sub>S<sub>3</sub>: 287.0229, found: 287.0237.

**Mp**: 102-103 °C.

**R<sub>f</sub>** = 0.25 (EtOAc / PE = 1/4).

**4-methyl-4-(3-(naphthalen-2-yl)-3-oxopropyl)-1,3-dithian-2-one (III-12k)**



Chemical Formula: C<sub>18</sub>H<sub>18</sub>O<sub>2</sub>S<sub>2</sub>  
Exact Mass: 330.0748

According to the general procedure A, the reaction was carried out with *O*-ethyl *S*-(2-(naphthalen-2-yl)-2-oxoethyl)-carbonodithioate (870 mg, 3 mmol) and 3-methylbut-3-en-1-yl-methanesulfonate (984 mg, 6 mmol) in EtOAc (3 mL), and needed 14 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (20:1 to 8:1) to afford product **III-12k** (495 mg, 50%) as a white solid.

**<sup>1</sup>H NMR** (δ, ppm)(400 MHz, CDCl<sub>3</sub>) δ 8.47 (s, 1H, H<sub>1</sub>), 7.99 (dd, *J* = 14.2, 8.0 Hz, 2H, H<sub>3</sub>, H<sub>8</sub>), 7.93 – 7.78 (m, 2H, H<sub>6</sub>, H<sub>9</sub>), 7.59 (dd, *J* = 16.8, 8.4 Hz, 2H, H<sub>4</sub>, H<sub>5</sub>), 3.47 – 3.12 (m, 4H, H<sub>17</sub>, H<sub>12</sub>), 2.40 – 2.02 (m, 4H, H<sub>13</sub>, H<sub>16</sub>), 1.55 (s, 3H, H<sub>15</sub>).

**<sup>13</sup>C NMR**(δ, ppm)(100 MHz, CDCl<sub>3</sub>) δ 198.6 (C<sub>11</sub>), 189.1 (C<sub>18</sub>), 135.7 (C<sub>10</sub>), 133.8 (C<sub>2</sub>), 132.5 (C<sub>1</sub>), 129.9 (C<sub>7</sub>), 129.7 (C<sub>3</sub>), 128.7 (C<sub>6</sub>), 128.6 (C<sub>8</sub>), 127.8 (C<sub>4</sub>), 127.0 (C<sub>5</sub>), 123.7 (C<sub>9</sub>), 52.8 (C<sub>14</sub>), 36.7 (C<sub>12</sub>), 35.1 (C<sub>13</sub>), 33.3 (C<sub>17</sub>), 28.7 (C<sub>16</sub>), 28.3 (C<sub>15</sub>).

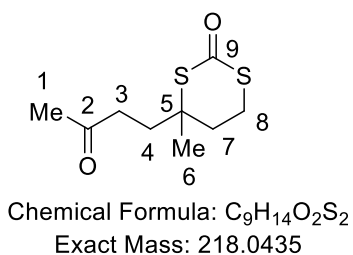
**IR** (ν, cm<sup>-1</sup>, CDCl<sub>3</sub>) 3057, 2965, 1676, 1596, 1468, 1369, 1293, 1181, 1123, 940, 890, 863, 823, 734.

**HRMS** (EI<sup>+</sup>) m/z: [M + H]<sup>+</sup> calculated for C<sub>18</sub>H<sub>19</sub>O<sub>2</sub>S<sub>2</sub>: 331.0821, found: 331.0815.

**Mp** 108-109 °C.

**R<sub>f</sub>** = 0.40 (EtOAc / PE = 1/4).

#### 4-methyl-4-(3-oxobutyl)-1,3-dithian-2-one (III-12l)



According to the general procedure A, the reaction was carried out with *O*-ethyl *S*-(2-oxopropyl)-carbonodithioate (534 mg, 3 mmol) and 3-methylbut-3-en-1-yl methanesulfonate (984 mg, 6 mmol) in EtOAc (3 mL), and needed 10 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (10:1 to 3:1) to afford product **III-12l** (458 mg, 70%) as a colorless oil.

<sup>1</sup>H NMR ( $\delta$ , ppm)(400 MHz, CDCl<sub>3</sub>)  $\delta$  3.45 – 3.26 (m, 2H, H<sub>8</sub>), 2.75 – 2.51 (m, 2H, H<sub>3</sub>), 2.20 (s, 3H, H<sub>1</sub>), 2.19 – 2.14 (m, 2H, H<sub>4</sub>), 2.14 – 2.06 (m, 1H, H<sub>7</sub>), 1.93-1.86 (m, 1H, H<sub>7</sub>), 1.46 (s, 3H, H<sub>6</sub>).

<sup>13</sup>C NMR ( $\delta$ , ppm)(100 MHz, CDCl<sub>3</sub>)  $\delta$  207.0 (C<sub>2</sub>), 189.1 (C<sub>9</sub>), 52.4 (C<sub>5</sub>), 38.1 (C<sub>3</sub>), 35.9 (C<sub>1</sub>), 35.0 (C<sub>4</sub>), 30.2 (C<sub>8</sub>), 28.5 (C<sub>7</sub>), 28.1 (C<sub>6</sub>).

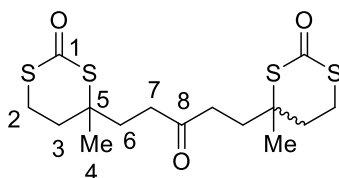
IR ( $\nu$ , cm<sup>-1</sup>, CDCl<sub>3</sub>) 2932, 1712, 1599, 1431, 1358, 1293, 1171, 935, 911, 887.

HRMS (EI<sup>+</sup>) *m/z*: [M + Na]<sup>+</sup> calculated for C<sub>9</sub>H<sub>14</sub>O<sub>2</sub>NaS<sub>2</sub>: 241.0327, found: 241.0332.

R<sub>f</sub> = 0.45 (EtOAc / PE = 1/2).

#### 4,4'-(3-oxopentane-1,5-diyl)bis(4-methyl-1,3-dithian-2-one) (III-12m)





Chemical Formula: C<sub>15</sub>H<sub>22</sub>O<sub>3</sub>S<sub>4</sub>  
Exact Mass: 378.0452

According to the general procedure A, the reaction was carried out with *O,O'*-diethyl *S,S'*-(2-oxopropane-1,3-diyl)-bis(carbonodithioate) (894 mg, 3 mmol) and 3-methylbut-3-en-1-yl-methanesulfonate (984 mg, 6 mmol) in EtOAc (3 mL), and needed 13 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (10:1 to 2:1) to afford product **III-12m** (408 mg, 36%) as a light yellow oil.

<sup>1</sup>H NMR (δ, ppm)(400 MHz, CDCl<sub>3</sub>) δ 3.44 – 3.26 (m, 4H, H<sub>2</sub>), 2.75 – 2.53 (m, 4H, H<sub>7</sub>), 2.22 – 2.05 (m, 6H, H<sub>6</sub>, H<sub>3</sub>), 1.95 – 1.87 (m, 2H, H<sub>3</sub>), 1.47 (s, 6H, H<sub>4</sub>).

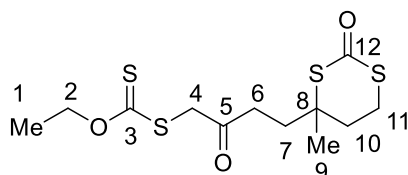
<sup>13</sup>C NMR (δ, ppm)(100 MHz, CDCl<sub>3</sub>) δ 209.0 (C<sub>8</sub>), 207.5 (C<sub>8</sub>), 189.1 (C<sub>1</sub>), 189.0 (C<sub>1</sub>), 52.5 (C<sub>5</sub>), 52.4 (C<sub>5</sub>), 52.4 (C<sub>5</sub>), 40.4 (C<sub>7</sub>), 37.5 (C<sub>6</sub>), 37.5 (C<sub>6</sub>), 37.4 (C<sub>6</sub>), 37.2 (C<sub>6</sub>), 35.9 (C<sub>2</sub>), 35.9 (C<sub>2</sub>), 35.9 (C<sub>2</sub>), 35.8 (C<sub>2</sub>), 35.0 (C<sub>2</sub>), 35.0 (C<sub>2</sub>), 34.9 (C<sub>2</sub>), 30.2 (C<sub>3</sub>), 29.0 (C<sub>3</sub>), 28.6 (C<sub>3</sub>), 28.5 (C<sub>3</sub>), 28.5 (C<sub>3</sub>), 28.2 (C<sub>3</sub>), 19.1 (C<sub>4</sub>).

IR (ν, cm<sup>-1</sup>, CDCl<sub>3</sub>) 2930, 1711, 1594, 1436, 1350, 1297, 1172, 917, 887, 729.

HRMS (EI<sup>+</sup>) m/z: [M + H]<sup>+</sup> calculated for C<sub>15</sub>H<sub>23</sub>O<sub>3</sub>S<sub>4</sub>: 379.0525, found: 379.0526.

R<sub>f</sub> = 0.20 (EtOAc / PE = 1/1).

***O*-ethyl-*S*-(4-(4-methyl-2-oxo-1,3-dithian-4-yl)-2-oxobutyl)-carbonodithioate  
(III-12n)**



Chemical Formula: C<sub>12</sub>H<sub>18</sub>O<sub>3</sub>S<sub>4</sub>  
Exact Mass: 338.0139

According to the general procedure A, the reaction was carried out with *O,O'*-diethyl *S,S'*-(2-oxopropane-1,3-diyl)bis(carbonodithioate) (894 mg, 3 mmol) and 3-methylbut-3-en-1-yl-methanesulfonate (984 mg, 6 mmol) in EtOAc (3 mL), and needed 13 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (10:1 to 2:1) to afford product **III-12n** (355 mg, 35%) as a light yellow oil.

<sup>1</sup>H NMR ( $\delta$ , ppm)(400 MHz, CDCl<sub>3</sub>)  $\delta$  4.64 (q, *J* = 7.0 Hz, 2H, H<sub>2</sub>), 4.03 (s, 2H, H<sub>4</sub>), 3.46 – 3.30 (m, 2H, H<sub>11</sub>), 2.93 – 2.70 (m, 2H, H<sub>6</sub>), 2.25 – 2.10 (m, 3H, H<sub>7</sub>, H<sub>7</sub>, H<sub>10</sub>), 1.99-1.92 (m, 1H, H<sub>10</sub>), 1.48 (s, 3H, H<sub>1</sub>), 1.43 (t, *J* = 7.0 Hz, 3H, H<sub>9</sub>).

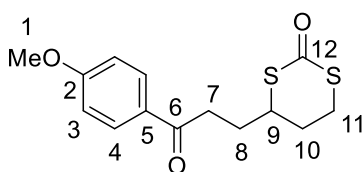
<sup>13</sup>C NMR ( $\delta$ , ppm)(100 MHz, CDCl<sub>3</sub>)  $\delta$  213.3 (C<sub>3</sub>), 202.0 (C<sub>5</sub>), 189.1 (C<sub>12</sub>), 71.1 (C<sub>2</sub>), 52.5 (C<sub>8</sub>), 45.4 (C<sub>6</sub>), 36.7 (C<sub>4</sub>), 35.9 (C<sub>7</sub>), 34.8 (C<sub>11</sub>), 28.5 (C<sub>10</sub>), 28.2 (C<sub>9</sub>), 13.8 (C<sub>1</sub>).

IR ( $\nu$ , cm<sup>-1</sup>, CDCl<sub>3</sub>) 2931, 1719, 1596, 1441, 1362, 1292, 1218, 1111, 1041, 932, 888, 728.

HRMS (EI<sup>+</sup>) *m/z*: [M + H]<sup>+</sup> calculated for C<sub>12</sub>H<sub>19</sub>O<sub>3</sub>S<sub>4</sub>: 339.0212, found: 339.0213.

R<sub>f</sub> = 0.40 (EtOAc / PE = 1/1).

#### 4-(3-(4-methoxyphenyl)-3-oxopropyl)-1,3-dithian-2-one (**III-14a**)



Chemical Formula: C<sub>14</sub>H<sub>16</sub>O<sub>3</sub>S<sub>2</sub>

Exact Mass: 296.0541

According to the general procedure B, the reaction was carried out with *O*-ethyl *S*-(2-(4-methoxyphenyl)-2-oxoethyl)-carbonodithioate (810 mg, 3 mmol) and 4-bromobut-1-ene (803 mg, 6 mmol) in DCE (3 mL), and needed 21 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (10:1 to 5:1) to afford product **III-14a** (622 mg, 70%) as a light yellow oil.

<sup>1</sup>H NMR ( $\delta$ , ppm)(400 MHz, CDCl<sub>3</sub>)  $\delta$  7.98 – 7.88 (m, 2H, H<sub>4</sub>), 6.98 – 6.90 (m, 2H,

H<sub>3</sub>), 3.87 (s, 3H, H<sub>1</sub>), 3.75-3.68 (m, 1H, H<sub>9</sub>), 3.37 – 3.23 (m, 2H, H<sub>11</sub>), 3.17 – 3.00 (m, 2H, H<sub>7</sub>), 2.57 – 2.46 (m, 1H, H<sub>8</sub>), 2.31 – 2.18 (m, 1H, H<sub>8</sub>), 2.13-2.01 (m, 2H, H<sub>10</sub>).

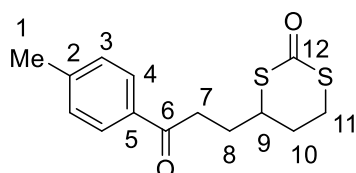
<sup>13</sup>C NMR (δ, ppm)(100 MHz, CDCl<sub>3</sub>) δ 197.0 (C<sub>6</sub>), 189.8 (C<sub>12</sub>), 163.7 (C<sub>2</sub>), 130.3 (C<sub>5</sub>), 129.5 (C<sub>4</sub>), 113.9 (C<sub>3</sub>), 55.6 (C<sub>1</sub>), 46.9 (C<sub>9</sub>), 34.3 (C<sub>7</sub>), 30.4 (C<sub>10</sub>), 30.1 (C<sub>11</sub>), 29.2 (C<sub>8</sub>).

IR (ν, cm<sup>-1</sup>, CDCl<sub>3</sub>) 2924, 2839, 1671, 1594, 1574, 1509, 1418, 1365, 1310, 1252, 1168, 1025, 900, 835, 729.

HRMS (EI<sup>+</sup>) m/z: [M + H]<sup>+</sup> calculated for C<sub>14</sub>H<sub>17</sub>O<sub>3</sub>S<sub>2</sub>: 297.0614, found: 297.0615.

R<sub>f</sub> = 0.30 (EtOAc / PE = 1/4).

#### 4-(3-oxo-3-(p-tolyl)propyl)-1,3-dithian-2-one (III-14b)



Chemical Formula: C<sub>14</sub>H<sub>16</sub>O<sub>2</sub>S<sub>2</sub>  
Exact Mass: 280.0592

According to the general procedure B, the reaction was carried out with *O*-ethyl *S*-(2-oxo-2-(p-tolyl)ethyl)-carbonodithioate (762 mg, 3 mmol) and 4-bromobut-1-ene (803 mg, 6 mmol) in DCE (3 mL), and needed 14 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (20:1 to 10:1) to afford product **III-14b** (580 mg, 69%) as a light yellow oil.

<sup>1</sup>H NMR (δ, ppm)(400 MHz, CDCl<sub>3</sub>) δ 7.90 – 7.80 (m, 2H, H<sub>4</sub>), 7.27-7.25 (m, 2H, H<sub>3</sub>), 3.77 – 3.65 (m, 1H, H<sub>9</sub>), 3.36 – 3.24 (m, 2H, H<sub>11</sub>), 3.19 – 3.04 (m, 2H, H<sub>7</sub>), 2.57 – 2.46 (m, 1H, H<sub>8</sub>), 2.41 (s, 3H, H<sub>1</sub>), 2.28-2.19 (m, 1H, H<sub>8</sub>), 2.14 – 1.98 (m, 2H, H<sub>10</sub>).

<sup>13</sup>C NMR (δ, ppm)(100 MHz, CDCl<sub>3</sub>) δ 198.1 (C<sub>6</sub>), 189.8 (C<sub>12</sub>), 144.3 (C<sub>2</sub>), 134.0 (C<sub>5</sub>), 129.4 (C<sub>4</sub>), 128.1 (C<sub>3</sub>), 46.8 (C<sub>9</sub>), 34.6 (C<sub>7</sub>), 30.4 (C<sub>10</sub>), 30.0 (C<sub>11</sub>), 29.2 (C<sub>8</sub>), 21.7 (C<sub>1</sub>).

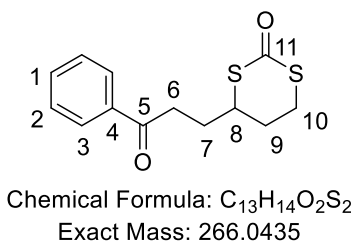
IR (ν, cm<sup>-1</sup>, CDCl<sub>3</sub>) 3039, 2921, 1676, 1598, 1431, 1407, 1366, 1206, 1179, 977, 932,

900, 813, 780, 730.

**HRMS** (EI<sup>+</sup>) m/z: [M + H]<sup>+</sup>calculated for C<sub>14</sub>H<sub>17</sub>O<sub>2</sub>S<sub>2</sub>: 281.0664, found:281.0667.

**R<sub>f</sub>** = 0.30 (EtOAc / PE = 1/4).

#### 4-(3-oxo-3-phenylpropyl)-1,3-dithian-2-one (III-14c)



According to the general procedure B, the reaction was carried out with *O*-ethyl *S*-(2-oxo-2-phenylethyl)-carbonodithioate (720 mg, 3 mmol) and 4-bromobut-1-ene (803 mg, 6 mmol) in DCE (3 mL), and needed 16 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (20:1 to 6:1) to afford product **III-14c** (399 mg, 50%) as a light yellow oil.

**<sup>1</sup>H NMR** (δ, ppm)(400 MHz, CDCl<sub>3</sub>) δ 7.99 – 7.92 (m, 2H, H<sub>3</sub>), 7.59 (t, *J* = 7.4 Hz, 1H, H<sub>1</sub>), 7.48 (t, *J* = 7.6 Hz, 2H, H<sub>2</sub>), 3.76-3.69 (m, 1H, H<sub>8</sub>), 3.38 – 3.25 (m, 2H, H<sub>10</sub>), 3.24 – 3.08 (m, 2H, H<sub>6</sub>), 2.56-2.49 (m, 1H, H<sub>7</sub>), 2.35 – 2.20 (m, 1H, H<sub>7</sub>), 2.18 – 1.98 (m, 2H, H<sub>9</sub>).

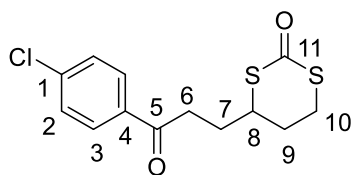
**<sup>13</sup>C NMR** (δ, ppm)(100 MHz, CDCl<sub>3</sub>) δ 198.5 (C<sub>5</sub>), 189.7 (C<sub>11</sub>), 136.4 (C<sub>4</sub>), 133.5 (C<sub>3</sub>), 128.8 (C<sub>2</sub>), 128.0 (C<sub>1</sub>), 46.8 (C<sub>8</sub>), 34.7 (C<sub>6</sub>), 30.5 (C<sub>9</sub>), 29.9 (C<sub>10</sub>), 29.3 (C<sub>7</sub>).

**IR** (ν, cm<sup>-1</sup>, CDCl<sub>3</sub>) 3060, 2923, 2853, 1681, 1599, 1447, 1367, 1305, 1270, 1214, 1000, 938, 901, 781, 743, 690.

**HRMS** (EI<sup>+</sup>) m/z: [M + H]<sup>+</sup>calculated for C<sub>13</sub>H<sub>15</sub>O<sub>2</sub>S<sub>2</sub>: 267.0508, found: 267.0516.

**R<sub>f</sub>** = 0.30 (EtOAc / PE = 1/4).

#### 4-(3-(4-chlorophenyl)-3-oxopropyl)-1,3-dithian-2-one (III-14d)



Chemical Formula: C<sub>13</sub>H<sub>13</sub>ClO<sub>2</sub>S<sub>2</sub>

Exact Mass: 300.0045

According to the general procedure B, the reaction was carried out with *S*-(2-(4-chlorophenyl)-2-oxoethyl)-*O*-ethyl-carbonodithioate (822 mg, 3 mmol) and 4-bromobut-1-ene (803 mg, 6 mmol) in DCE (3 mL), and needed 19 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (10:1 to 5:1) to afford product **III-14d** (648 mg, 72%) as a light yellow solid.

**<sup>1</sup>H NMR** ( $\delta$ , ppm)(400 MHz, CDCl<sub>3</sub>)  $\delta$  7.89 (d,  $J$  = 8.2 Hz, 2H, H<sub>3</sub>), 7.45 (d,  $J$  = 8.2 Hz, 2H, H<sub>2</sub>), 3.71 (dd,  $J$  = 8.9, 4.3 Hz, 1H, H<sub>8</sub>), 3.31 (t,  $J$  = 5.6 Hz, 2H, H<sub>10</sub>), 3.10 (d,  $J$  = 18.0 Hz, 2H, H<sub>6</sub>), 2.53 (dd,  $J$  = 9.6, 4.6 Hz, 1H, H<sub>7</sub>), 2.27 (dd,  $J$  = 13.4, 6.4 Hz, 1H, H<sub>7</sub>), 2.20 – 1.95 (m, 2H, H<sub>9</sub>).

**<sup>13</sup>C NMR** ( $\delta$ , ppm)(100 MHz, CDCl<sub>3</sub>)  $\delta$  197.2 (C<sub>5</sub>), 189.5 (C<sub>11</sub>), 139.9 (C<sub>4</sub>), 134.8 (C<sub>1</sub>), 129.5 (C<sub>3</sub>), 129.1 (C<sub>2</sub>), 46.7 (C<sub>8</sub>), 34.7 (C<sub>6</sub>), 30.4 (C<sub>9</sub>), 29.8 (C<sub>10</sub>), 29.3 (C<sub>7</sub>).

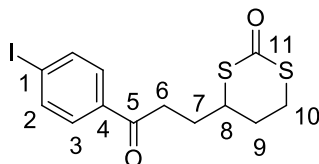
**IR** ( $\nu$ , cm<sup>-1</sup>, CDCl<sub>3</sub>) 2923, 1681, 1593, 1486, 1431, 1398, 1367, 1309, 1275, 1211, 1175, 1090, 1011, 985, 936, 901, 834, 731.

**HRMS** (EI<sup>+</sup>)  $m/z$ : [M + Na]<sup>+</sup>calculated for C<sub>13</sub>H<sub>13</sub>ClNaO<sub>2</sub>S<sub>3</sub>: 322.9938, found: 322.9944.

**Mp** 87-88 °C.

**R<sub>f</sub>** = 0.25 (EtOAc / PE = 1/4).

#### 4-(3-(4-iodophenyl)-3-oxopropyl)-1,3-dithian-2-one (**III-14e**)



Chemical Formula:  $C_{13}H_{13}IO_2S_2$

Exact Mass: 391.9402

According to the general procedure B, the reaction was carried out with *O*-ethyl *S*-(2-(4-iodophenyl)-2-oxoethyl)-carbonodithioate (1098 mg, 3 mmol) and 4-bromobut-1-ene (803 mg, 6 mmol) in DCE (3 mL), and needed 14 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (20:1 to 10:1) to afford product **III-14e** (694 mg, 59%) as a light yellow solid.

$^1\text{H NMR}$  ( $\delta$ , ppm)(400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.84 (d,  $J = 8.0$  Hz, 2H,  $\text{H}_3$ ), 7.66 (d,  $J = 8.0$  Hz, 2H,  $\text{H}_2$ ), 3.71 (s, 1H,  $\text{H}_8$ ), 3.31 (t,  $J = 5.6$  Hz, 2H,  $\text{H}_{10}$ ), 3.09 (d,  $J = 18.2$  Hz, 2H,  $\text{H}_6$ ), 2.52 (d,  $J = 10.6$  Hz, 1H,  $\text{H}_7$ ), 2.26 (dd,  $J = 12.6, 6.0$  Hz, 1H,  $\text{H}_7$ ), 2.10 (dd,  $J = 13.8, 6.4$  Hz, 2H,  $\text{H}_9$ ).

$^{13}\text{C NMR}$  ( $\delta$ , ppm)(100 MHz,  $\text{CDCl}_3$ )  $\delta$  197.7 ( $\text{C}_5$ ), 189.6 ( $\text{C}_{11}$ ), 138.1 ( $\text{C}_4$ ), 135.7 ( $\text{C}_1$ ), 129.4 ( $\text{C}_3$ ), 101.6 ( $\text{C}_2$ ), 46.7 ( $\text{C}_8$ ), 34.7 ( $\text{C}_6$ ), 30.5 ( $\text{C}_9$ ), 29.8 ( $\text{C}_{10}$ ), 29.3 ( $\text{C}_7$ ).

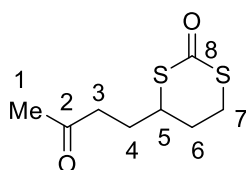
**IR** ( $\nu$ ,  $\text{cm}^{-1}$ ,  $\text{CDCl}_3$ ) 2923, 1682, 1600, 1579, 1562, 1392, 1212, 1180, 1053, 1004, 901, 806.

**HRMS** ( $\text{EI}^+$ )  $m/z$ :  $[\text{M} + \text{H}]^+$  calculated for  $\text{C}_{13}\text{H}_{14}\text{IO}_2\text{S}_3$ : 392.9474, found: 392.9476.

**Mp** 102-104 °C.

**R<sub>f</sub>** = 0.32 (EtOAc / PE = 1/4).

#### 4-(3-oxobutyl)-1,3-dithian-2-one (**III-14f**)



Chemical Formula:  $\text{C}_8\text{H}_{12}\text{O}_2\text{S}_2$

Exact Mass: 204.0279

According to the general procedure B, the reaction was carried out with *O*-ethyl *S*-(2-oxopropyl)-carbonodithioate (534 mg, 3 mmol) and 4-bromobut-1-ene (803 mg, 6 mmol) in DCE (3 mL), and needed 20 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (10:1 to 5:1) to afford product **III-14f** (355 mg, 58%) as a light yellow oil.

<sup>1</sup>H NMR (δ, ppm)(400 MHz, CDCl<sub>3</sub>) δ 3.66-3.59 (m, 1H, H<sub>5</sub>), 3.38 – 3.23 (m, 2H, H<sub>7</sub>), 2.71 – 2.54 (m, 2H, H<sub>3</sub>), 2.53 – 2.41 (m, 1H, H<sub>4</sub>), 2.18 (s, 3H, H<sub>1</sub>), 2.13 – 1.88 (m, 3H, H<sub>4</sub>, H<sub>6</sub>, H<sub>6</sub>).

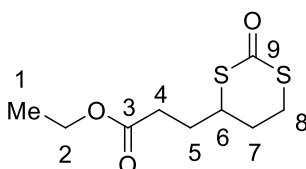
<sup>13</sup>C NMR (δ, ppm)(100 MHz, CDCl<sub>3</sub>) δ 207.0 (C<sub>2</sub>), 189.7 (C<sub>8</sub>), 46.6 (C<sub>5</sub>), 39.6 (C<sub>3</sub>), 30.4 (C<sub>6</sub>), 30.1 (C<sub>7</sub>), 29.3 (C<sub>4</sub>), 29.2 (C<sub>1</sub>).

IR (ν, cm<sup>-1</sup>, CDCl<sub>3</sub>) 2925, 1711, 1599, 1427, 1363, 1298, 1164, 934, 901.

HRMS (EI<sup>+</sup>) m/z: [M + H]<sup>+</sup>calculated for C<sub>8</sub>H<sub>13</sub>O<sub>2</sub>S<sub>2</sub>: 205.0351, found: 205.0354.

R<sub>f</sub> = 0.20 (EtOAc / PE = 1/4).

### Ethyl-3-(2-oxo-1,3-dithian-4-yl)propanoate (**III-14g**)



Chemical Formula: C<sub>9</sub>H<sub>14</sub>O<sub>3</sub>S<sub>2</sub>  
Exact Mass: 234.0384

According to the general procedure B, the reaction was carried out with ethyl 2-((ethoxycarbonothioyl)thio)acetate (624 mg, 3 mmol) and 4-bromobut-1-ene (803 mg, 6 mmol) in DCE (3 mL), and needed 20 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (20:1 to 6:1) to afford product **III-14g** (449 mg, 64%) as a light yellow oil.

<sup>1</sup>H NMR (δ, ppm)(400 MHz, CDCl<sub>3</sub>) δ 4.15 (q, *J* = 7.0 Hz, 2H, H<sub>2</sub>), 3.61 (d, *J* = 46.4 Hz, 1H, H<sub>6</sub>), 3.31 (s, 2H, H<sub>8</sub>), 2.45 (dd, *J* = 23.2, 6.6 Hz, 3H, H<sub>4</sub>, H<sub>4</sub>, H<sub>5</sub>), 2.19 – 1.84 (m, 3H, H<sub>5</sub>, H<sub>7</sub>, H<sub>7</sub>), 1.27 (t, *J* = 7.0 Hz, 3H, H<sub>1</sub>).

<sup>13</sup>C NMR (δ, ppm)(100 MHz, CDCl<sub>3</sub>) δ 189.6 (C<sub>9</sub>), 172.3 (C<sub>3</sub>), 60.8 (C<sub>2</sub>), 46.5 (C<sub>6</sub>),

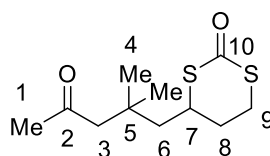
30.8 (C<sub>7</sub>), 30.8 (C<sub>4</sub>), 30.4 (C<sub>8</sub>), 28.9 (C<sub>5</sub>), 14.2 (C<sub>1</sub>).

**IR** ( $\nu$ , cm<sup>-1</sup>, CDCl<sub>3</sub>) 2938, 1726, 1602, 1433, 1375, 1303, 1175, 1026, 937, 899, 790.

**HRMS** (EI<sup>+</sup>) [M + Na]<sup>+</sup> calculated for C<sub>9</sub>H<sub>14</sub>NaO<sub>3</sub>S<sub>2</sub>: 257.0277, found: 257.0270.

**R<sub>f</sub>** = 0.50 (EtOAc / PE = 1/5).

#### 4-(2,2-dimethyl-4-oxopentyl)-1,3-dithian-2-one (III-14h)



Chemical Formula: C<sub>11</sub>H<sub>18</sub>O<sub>2</sub>S<sub>2</sub>  
Exact Mass: 246.0748

According to the general procedure B, the reaction was carried out with *O*-ethyl *S*-(2-methyl-4-oxopentan-2-yl)-carbonodithioate (660 mg, 3 mmol) and 4-bromobut-1-ene (803 mg, 6 mmol) in DCE (3 mL), and needed 19 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (20:1 to 10:1) to afford product **III-14h** (347 mg, 47%) as a light yellow oil.

**<sup>1</sup>H NMR** ( $\delta$ , ppm)(400 MHz, CDCl<sub>3</sub>)  $\delta$  3.60 (s, 1H, H<sub>7</sub>), 3.28 (s, 2H, H<sub>9</sub>), 2.59 – 2.29 (m, 3H, H<sub>3</sub>, H<sub>3</sub>, H<sub>8</sub>), 2.14 (s, 3H, H<sub>1</sub>), 2.04-1.82 (m, 3H, H<sub>8</sub>, H<sub>6</sub>, H<sub>6</sub>), 1.06 (s, 6H, H<sub>4</sub>).

**<sup>13</sup>C NMR** ( $\delta$ , ppm)(100 MHz, CDCl<sub>3</sub>)  $\delta$  208.1 (C<sub>2</sub>), 190.4 (C<sub>10</sub>), 53.5 (C<sub>3</sub>), 47.5 (C<sub>6</sub>), 43.6 (C<sub>7</sub>), 33.6 (C<sub>8</sub>), 32.5 (C<sub>5</sub>), 31.2 (C<sub>1</sub>), 30.4 (C<sub>9</sub>), 28.1 (C<sub>4</sub>).

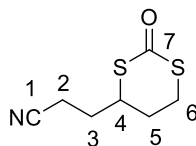
**IR** ( $\nu$ , cm<sup>-1</sup>, CDCl<sub>3</sub>) 2931, 1707, 1600, 1470, 1429, 1386, 1360, 1155, 942, 904, 727.

**HRMS** (EI<sup>+</sup>) *m/z*: [M + Na]<sup>+</sup> calculated for C<sub>11</sub>H<sub>18</sub>NaO<sub>2</sub>S<sub>2</sub>: 269.0640, found: 269.0639.

**R<sub>f</sub>** = 0.25 (EtOAc / PE = 1/4).

#### 3-(2-oxo-1,3-dithian-4-yl)-propanenitrile (III-14i)





Chemical Formula: C<sub>7</sub>H<sub>9</sub>NOS<sub>2</sub>

Exact Mass: 187.0126

According to the general procedure B, the reaction was carried out with *S*-(cyanomethyl) *O*-ethyl-carbonodithioate (483 mg, 3 mmol) and 4-bromobut-1-ene (803 mg, 6 mmol) in DCE (3 mL), and needed 20 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (10:1 to 3:1) to afford product **III-14i** (314 mg, 56%) as a light brown oil.

<sup>1</sup>H NMR (δ, ppm)(400 MHz, CDCl<sub>3</sub>) δ 3.75 (s, 1H, H<sub>4</sub>), 3.33 (s, 2H, H<sub>6</sub>), 2.69 – 2.39 (m, 3H, H<sub>2</sub>, H<sub>2</sub>, H<sub>3</sub>), 2.26 – 1.92 (m, 3H, H<sub>3</sub>, H<sub>5</sub>, H<sub>5</sub>).

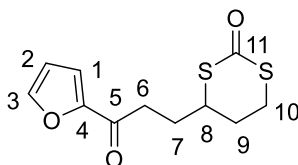
<sup>13</sup>C NMR (δ, ppm)(100 MHz, CDCl<sub>3</sub>) δ 188.7 (C<sub>7</sub>), 118.5 (C<sub>1</sub>), 45.7 (C<sub>4</sub>), 31.5 (C<sub>5</sub>), 30.3 (C<sub>6</sub>), 28.6 (C<sub>3</sub>), 14.8 (C<sub>2</sub>).

IR (ν, cm<sup>-1</sup>, CDCl<sub>3</sub>) 2926, 2853, 2246, 1713, 1599, 1430, 1154, 940, 927, 901, 836, 727.

HRMS (EI<sup>+</sup>) m/z: [M + Na]<sup>+</sup>calculated for C<sub>7</sub>H<sub>9</sub>NaNOS<sub>2</sub>: 210.0018, found: 210.0014.

R<sub>f</sub> = 0.32 (EtOAc / PE = 1/1).

#### 4-(3-(furan-2-yl)-3-oxopropyl)-1,3-dithian-2-one (III-14j)



Chemical Formula: C<sub>11</sub>H<sub>12</sub>O<sub>3</sub>S<sub>2</sub>

Exact Mass: 256.0228

According to the general procedure B, the reaction was carried out with *O*-ethyl *S*-(2-(furan-2-yl)-2-oxoethyl)-carbonodithioate (690 mg, 3 mmol) and 4-bromobut-1-ene (803 mg, 6 mmol) in DCE (3 mL), and needed 20 h for the reaction to go to completion. It was purified by column chromatography on silica gel using

petroleum ether/ethyl acetate (6:1 to 1:1) to afford product **III-14j** (346 mg, 45%) as a white solid.

**<sup>1</sup>H NMR** ( $\delta$ , ppm)(400 MHz, CDCl<sub>3</sub>)  $\delta$  7.61 (s, 1H, H<sub>3</sub>), 7.23 (d,  $J$  = 3.4 Hz, 1H, H<sub>1</sub>), 6.56 (d,  $J$  = 1.6 Hz, 1H, H<sub>2</sub>), 3.78 – 3.62 (m, 1H, H<sub>8</sub>), 3.31 (t,  $J$  = 5.4 Hz, 2H, H<sub>6</sub>), 3.02 (t,  $J$  = 8.0 Hz, 2H, H<sub>7</sub>), 2.54-2.51 (m, 1H, H<sub>10</sub>), 2.28-2.20 (m, 1H, H<sub>10</sub>), 2.14-2.01 (m, 2H, H<sub>9</sub>).

**<sup>13</sup>C NMR** ( $\delta$ , ppm)(100 MHz, CDCl<sub>3</sub>)  $\delta$  189.6 (C<sub>11</sub>), 187.5 (C<sub>5</sub>), 152.3 (C<sub>4</sub>), 146.7 (C<sub>3</sub>), 117.5 (C<sub>1</sub>), 112.5 (C<sub>2</sub>), 46.7 (C<sub>8</sub>), 34.6 (C<sub>6</sub>), 30.4 (C<sub>9</sub>), 29.7 (C<sub>10</sub>), 29.2 (C<sub>7</sub>).

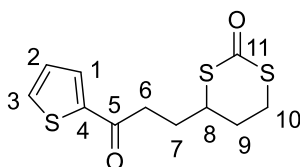
**IR** ( $\nu$ , cm<sup>-1</sup>, CDCl<sub>3</sub>) 2923, 1670, 1598, 1567, 1466, 1433, 1395, 1282, 1160, 1083, 1020, 939, 900, 882, 767.

**HRMS** (EI<sup>+</sup>)  $m/z$ : [M + Na]<sup>+</sup> calculated for C<sub>11</sub>H<sub>12</sub>NaO<sub>3</sub>S<sub>2</sub>: 279.0120, found: 279.0116

**Mp**: 81 – 82 °C.

**R<sub>f</sub>** = 0.20 (EtOAc / PE = 1/3).

#### 4-(3-oxo-3-(thiophen-2-yl)propyl)-1,3-dithian-2-one (**III-14k**)



Chemical Formula: C<sub>11</sub>H<sub>12</sub>O<sub>2</sub>S<sub>3</sub>  
Exact Mass: 271.9999

According to the general procedure B, the reaction was carried out with *O*-ethyl *S*-(2-oxo-2-(thiophen-2-yl)ethyl)-carbonodithioate (738 mg, 3 mmol) and 4-bromobut-1-ene (803 mg, 6 mmol) in DCE (3 mL), and needed 18 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (6:1 to 1:1) to afford product **III-14k** (588 mg, 72%) as a light yellow solid.

**<sup>1</sup>H NMR** ( $\delta$ , ppm)(400 MHz, CDCl<sub>3</sub>)  $\delta$  7.74 (d,  $J$  = 2.6 Hz, 1H, H<sub>1</sub>), 7.67 (d,  $J$  = 4.6 Hz, 1H, H<sub>3</sub>), 7.15 (s, 1H, H<sub>2</sub>), 3.72 (s, 1H, H<sub>8</sub>), 3.31 (s, 2H, H<sub>10</sub>), 3.10 (t,  $J$  = 6.6 Hz,

2H, H<sub>6</sub>), 2.52 (d,  $J = 11.0$  Hz, 1H, H<sub>7</sub>), 2.37 – 2.19 (m, 1H, H<sub>7</sub>), 2.17-2.04 (m, 2H, H<sub>9</sub>).

<sup>13</sup>C NMR ( $\delta$ , ppm)(100 MHz, CDCl<sub>3</sub>)  $\delta$  191.4 (C<sub>5</sub>), 189.6 (C<sub>11</sub>), 143.7 (C<sub>4</sub>), 134.1 (C<sub>1</sub>), 132.3 (C<sub>3</sub>), 128.4 (C<sub>2</sub>), 46.7 (C<sub>8</sub>), 35.4 (C<sub>6</sub>), 30.5 (C<sub>9</sub>), 30.1 (C<sub>10</sub>), 29.2 (C<sub>7</sub>).

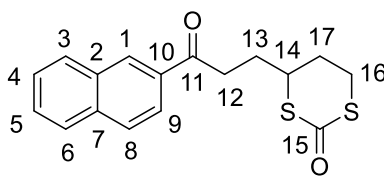
IR ( $\nu$ , cm<sup>-1</sup>, CDCl<sub>3</sub>) 3093, 2922, 1655, 1594, 1516, 1412, 1368, 1353, 1305, 1274, 1236, 1218, 1055, 935, 901, 854, 726.

HRMS (EI<sup>+</sup>)  $m/z$ : [M + H]<sup>+</sup> calculated for C<sub>11</sub>H<sub>13</sub>O<sub>2</sub>S<sub>3</sub>: 273.0072, found: 273.0066.

Mp 83-84 °C.

R<sub>f</sub> = 0.20 (EtOAc / PE = 1/3).

#### 4-(3-(naphthalen-2-yl)-3-oxopropyl)-1,3-dithian-2-one (III-14I)



Chemical Formula: C<sub>17</sub>H<sub>16</sub>O<sub>2</sub>S<sub>2</sub>  
Exact Mass: 316.0592

According to the general procedure B, the reaction was carried out with *O*-ethyl *S*-(2-(naphthalen-2-yl)-2-oxoethyl)-carbonodithioate (870 mg, 3 mmol) and 4-bromobut-1-ene (803 mg, 6 mmol) in DCE (3 mL), and needed 20 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (10:1 to 3:1) to afford product **III-14I** (474 mg, 50%) as a light yellow solid.

<sup>1</sup>H NMR ( $\delta$ , ppm)(400 MHz, CDCl<sub>3</sub>)  $\delta$  8.45 (s, 1H, H<sub>1</sub>), 7.93 (dd,  $J = 34.0, 10.2$  Hz, 4H, H<sub>3</sub>, H<sub>8</sub>, H<sub>6</sub>, H<sub>9</sub>), 7.74 – 7.41 (m, 2H, H<sub>4</sub>, H<sub>5</sub>), 3.73 (s, 1H, H<sub>14</sub>), 3.29 (s, 4H, H<sub>16</sub>, H<sub>12</sub>), 2.51 (s, 1H, H<sub>13</sub>), 2.29 (s, 1H, H<sub>13</sub>), 2.11 (d,  $J = 29.4$  Hz, 2H, H<sub>17</sub>).

<sup>13</sup>C NMR ( $\delta$ , ppm)(100 MHz, CDCl<sub>3</sub>)  $\delta$  198.4 (C<sub>11</sub>), 189.7 (C<sub>15</sub>), 135.7 (C<sub>10</sub>), 133.8 (C<sub>2</sub>), 132.5 (C<sub>1</sub>), 129.9 (C<sub>7</sub>), 129.7 (C<sub>3</sub>), 128.7 (C<sub>6</sub>), 128.6 (C<sub>8</sub>), 127.8 (C<sub>4</sub>), 127.0 (C<sub>5</sub>), 123.6 (C<sub>9</sub>), 46.9 (C<sub>14</sub>), 34.8 (C<sub>12</sub>), 30.5 (C<sub>17</sub>), 30.0 (C<sub>16</sub>), 29.3 (C<sub>13</sub>).

IR ( $\nu$ , cm<sup>-1</sup>, CDCl<sub>3</sub>) 3057, 2924, 1677, 1600, 1468, 1433, 1369, 1278, 1213, 1182,

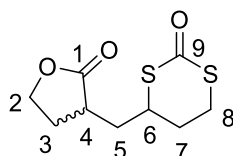
1123, 939, 904, 864, 823, 750.

**HRMS** (EI<sup>+</sup>) m/z: [M + H]<sup>+</sup> calculated for C<sub>17</sub>H<sub>17</sub>O<sub>2</sub>S<sub>3</sub>: 317.0664, found: 317.0656.

**Mp** 108-110 °C.

**R<sub>f</sub>** = 0.30 (EtOAc / PE = 1/4).

### 3-((2-oxo-1,3-dithian-4-yl)methyl)dihydrofuran-2(3H)-one (**III-14m**)



Chemical Formula: C<sub>9</sub>H<sub>12</sub>O<sub>3</sub>S<sub>2</sub>  
Exact Mass: 232.0228

According to the general procedure B, the reaction was carried out with *O*-ethyl *S*-(2-oxotetrahydrofuran-3-yl)-carbonodithioate (616 mg, 3 mmol) and 4-bromobut-1-ene (803 mg, 6 mmol) in DCE (3 mL), and needed 16 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (20:1 to 10:8) to afford product **III-14m** (522 mg, 75%) as a light yellow oil.

**<sup>1</sup>H NMR** (δ, ppm)(400 MHz, CDCl<sub>3</sub>) δ 4.39 (d, *J* = 7.8 Hz, 1H, H<sub>2</sub>), 4.23 (s, 1H, H<sub>2</sub>), 3.89 (d, *J* = 100.6 Hz, 1H, H<sub>6</sub>), 3.34 (s, 2H, H<sub>8</sub>), 2.77 (s, 1H, H<sub>5</sub>), 2.52 (s, 2H, H<sub>5</sub>, H<sub>4</sub>), 2.41 – 2.18 (m, 1H, H<sub>3</sub>), 2.15 – 1.77 (m, 3H, H<sub>7</sub>, H<sub>3</sub>, H<sub>7</sub>).

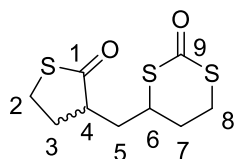
**<sup>13</sup>C NMR** (δ, ppm)(100 MHz, CDCl<sub>3</sub>) δ 189.2 (C<sub>9</sub>), 178.4 (C<sub>1</sub>), 178.2 (C<sub>1</sub>), 66.6 (C<sub>2</sub>), 45.3 (C<sub>6</sub>), 45.0 (C<sub>6</sub>), 37.2 (C<sub>4</sub>), 36.7 (C<sub>4</sub>), 36.6 (C<sub>5</sub>), 36.5 (C<sub>5</sub>), 30.4 (C<sub>7</sub>), 30.2 (C<sub>7</sub>), 30.0 (C<sub>8</sub>), 29.3 (C<sub>8</sub>), 29.2 (C<sub>3</sub>), 29.1 (C<sub>3</sub>).

**IR** (ν, cm<sup>-1</sup>, CDCl<sub>3</sub>) 2920, 1762, 1600, 1436, 1376, 1211, 1185, 1156, 1021, 937, 903, 708.

**HRMS** (EI<sup>+</sup>) m/z: [M + Na]<sup>+</sup> calculated for C<sub>9</sub>H<sub>12</sub>NaO<sub>3</sub>S<sub>2</sub>: 255.0120, found: 255.0115.

**R<sub>f</sub>** = 0.40 (EtOAc / PE = 1/1).

### 4-((2-oxotetrahydrothiophen-3-yl)methyl)-1,3-dithian-2-one (**III-14n**)



Chemical Formula: C<sub>9</sub>H<sub>12</sub>O<sub>2</sub>S<sub>3</sub>

Exact Mass: 247.9999

According to the general procedure B, the reaction was carried out with *O*-ethyl *S*-(2-oxotetrahydrothiophen-3-yl)-carbonodithioate (666 mg, 3 mmol) and 4-bromobut-1-ene (803 mg, 6 mmol) in DCE (3 mL), and needed 17 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (10:1 to 3:1) to afford product **III-14n** (424 mg, 57%) as a light yellow oil.

<sup>1</sup>H NMR (δ, ppm)(400 MHz, CDCl<sub>3</sub>) δ 3.82 (d, *J* = 88.2 Hz, 1H, H<sub>6</sub>), 3.31 (s, 4H, H<sub>2</sub>, H<sub>2</sub>, H<sub>8</sub>, H<sub>8</sub>), 2.62 (d, *J* = 49.4 Hz, 3H, H<sub>5</sub>, H<sub>5</sub>, H<sub>4</sub>), 2.30 (s, 1H, H<sub>3</sub>), 2.14 – 1.62 (m, 3H, H<sub>7</sub>, H<sub>7</sub>, H<sub>3</sub>).

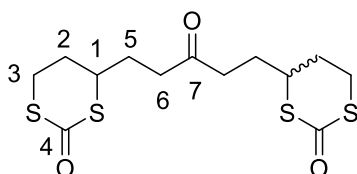
<sup>13</sup>C NMR (δ, ppm)(100 MHz, CDCl<sub>3</sub>) δ 209.5 (C<sub>1</sub>), 209.0 (C<sub>1</sub>), 189.3 (C<sub>9</sub>), 48.6 (C<sub>6</sub>), 48.5 (C<sub>6</sub>), 45.3 (C<sub>4</sub>), 45.2 (C<sub>4</sub>), 36.7 (C<sub>5</sub>), 36.1 (C<sub>5</sub>), 33.0 (C<sub>7</sub>), 32.0 (C<sub>7</sub>), 30.4 (C<sub>2</sub>), 30.3 (C<sub>2</sub>), 30.2 (C<sub>8</sub>), 30.2 (C<sub>8</sub>), 29.4 (C<sub>3</sub>), 29.3 (C<sub>3</sub>).

IR (ν, cm<sup>-1</sup>, CDCl<sub>3</sub>) 2929, 2857, 1686, 1598, 1435, 1281, 1037, 949, 898, 877, 854, 731.

HRMS (EI<sup>+</sup>) *m/z*: [M + Na]<sup>+</sup> calculated for C<sub>9</sub>H<sub>12</sub>NaO<sub>2</sub>S<sub>3</sub>: 270.9892, found: 270.9887.

R<sub>f</sub> = 0.30 (EtOAc / PE = 1/10).

#### 4,4'-(3-oxopentane-1,5-diyl)bis(1,3-dithian-2-one) (**III-14o**)



Chemical Formula: C<sub>13</sub>H<sub>18</sub>O<sub>3</sub>S<sub>4</sub>

Exact Mass: 350.0139

According to the general procedure B, the reaction was carried out with *O,O'*-diethyl *S,S'*-(2-oxopropane-1,3-diyl)bis(carbonodithioate) (894 mg, 3 mmol) and 4-bromobut-1-ene (803 mg, 6 mmol) in DCE (3 mL), and needed 18 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (10:1 to 1:1) to afford product **III-14o** (703 mg, 67%) as a brown oil.

<sup>1</sup>H NMR (δ, ppm)(400 MHz, CDCl<sub>3</sub>) δ 3.62 (s, 2H, H<sub>1</sub>), 3.40 – 3.16 (m, 4H, H<sub>3</sub>), 2.62 (s, 4H, H<sub>6</sub>), 2.47 (d, *J* = 10.8 Hz, 2H, H<sub>5</sub>), 2.19 – 1.82 (m, 6H, H<sub>5</sub>, H<sub>2</sub>).

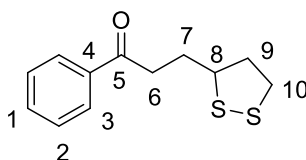
<sup>13</sup>C NMR (δ, ppm)(100 MHz, CDCl<sub>3</sub>) δ 207.5 (C<sub>7</sub>), 189.6 (C<sub>4</sub>), 46.6 (C<sub>1</sub>), 39.0 (C<sub>6</sub>), 30.4 (C<sub>2</sub>), 29.3 (C<sub>3</sub>), 29.2 (C<sub>5</sub>)

IR (ν, cm<sup>-1</sup>, CDCl<sub>3</sub>) 2922, 1710, 1593, 1428, 1374, 1289, 1095, 935, 898, 729.

HRMS (EI<sup>+</sup>) *m/z*: [M + H]<sup>+</sup> calculated for C<sub>13</sub>H<sub>19</sub>O<sub>3</sub>S<sub>4</sub>: 351.0212, found: 351.0205.

R<sub>f</sub> = 0.15 (EtOAc / PE = 1/10).

### 3-(1,2-dithiolan-3-yl)-1-phenylpropan-1-one (**III-24a**)



Chemical Formula: C<sub>12</sub>H<sub>14</sub>OS<sub>2</sub>  
Exact Mass: 238.0486

According to the general procedure C, the reaction was carried out with *O*-ethyl *S*-(2-oxo-2-phenylethyl)-carbonodithioate (240 mg, 1 mmol) and 4-bromobut-1-ene (268 mg, 2 mmol) in DCE (1 mL), and needed 34 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (100:1 to 100:3) to afford product **III-24a** (60 mg, 25%) as a light yellow oil.

<sup>1</sup>H NMR (δ, ppm)(400 MHz, CDCl<sub>3</sub>) δ 8.00 – 7.94 (m, 2H, H<sub>3</sub>), 7.60 – 7.51 (m, 1H, H<sub>1</sub>), 7.50 – 7.42 (m, 2H, H<sub>2</sub>), 3.80 – 3.64 (m, 1H, H<sub>8</sub>), 3.29 – 3.04 (m, 4H, H<sub>10</sub>, H<sub>10</sub>, H<sub>6</sub>, H<sub>6</sub>), 2.59 – 2.43 (m, 1H, H<sub>9</sub>), 2.23 – 2.15 (m, 1H, H<sub>9</sub>), 2.12 – 1.89 (m, 2H, H<sub>7</sub>).

<sup>13</sup>C NMR (δ, ppm)(100 MHz, CDCl<sub>3</sub>) δ 199.1 (C<sub>5</sub>), 136.7 (C<sub>4</sub>), 133.2 (C<sub>3</sub>), 128.7 (C<sub>2</sub>),

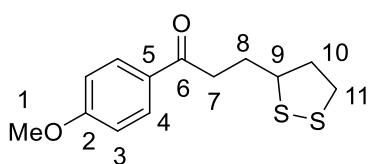
128.1 (C<sub>1</sub>), 55.9 (C<sub>8</sub>), 40.4 (C<sub>9</sub>), 38.5 (C<sub>10</sub>), 37.7 (C<sub>6</sub>), 28.9 (C<sub>7</sub>).

**IR** ( $\nu$ , cm<sup>-1</sup>, CDCl<sub>3</sub>) 2923, 1680, 1596, 1580, 1447, 1364, 1207, 981, 745, 689.

**HRMS** (EI<sup>+</sup>)  $m/z$ : [M + H]<sup>+</sup> calculated for C<sub>12</sub>H<sub>15</sub>OS<sub>2</sub>: 239.0559, found: 239.0558.

**R<sub>f</sub>** = 0.50 (EtOAc / PE = 1/4).

### 3-(1,2-dithiolan-3-yl)-1-(4-methoxyphenyl)propan-1-one (III-24b)



Chemical Formula: C<sub>13</sub>H<sub>16</sub>O<sub>2</sub>S<sub>2</sub>  
Exact Mass: 268.0592

According to the general procedure C, the reaction was carried out with *O*-ethyl *S*-(2-(4-methoxyphenyl)-2-oxoethyl)-carbonodithioate (270 mg, 1 mmol) and 4-bromobut-1-ene (268 mg, 2 mmol) in DCE (1 mL), and needed 35 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (100:1 to 100:3) to afford product **III-24b** (91 mg, 34%) as a light yellow oil.

**<sup>1</sup>H NMR** ( $\delta$ , ppm)(400 MHz, CDCl<sub>3</sub>)  $\delta$  7.96 (d,  $J$  = 9.0 Hz, 2H, H<sub>4</sub>), 6.94 (d,  $J$  = 9.0 Hz, 2H, H<sub>3</sub>), 3.87 (s, 3H, H<sub>1</sub>), 3.78 – 3.65 (m, 1H, H<sub>9</sub>), 3.31 – 2.96 (m, 4H, H<sub>11</sub>, H<sub>7</sub>), 2.59 – 2.42 (m, 1H, H<sub>10</sub>), 2.22 – 2.14 (m, 1H, H<sub>8</sub>), 2.11 – 1.88 (m, 2H, H<sub>8</sub>, H<sub>10</sub>).

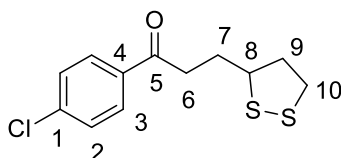
**<sup>13</sup>C NMR** ( $\delta$ , ppm)(100 MHz, CDCl<sub>3</sub>)  $\delta$  197.7 (C<sub>6</sub>), 163.6 (C<sub>2</sub>), 130.4 (C<sub>5</sub>), 129.8 (C<sub>4</sub>), 113.8 (C<sub>3</sub>), 56.0 (C<sub>1</sub>), 55.5 (C<sub>9</sub>), 40.4 (C<sub>10</sub>), 38.5 (C<sub>11</sub>), 37.3 (C<sub>7</sub>), 29.1 (C<sub>8</sub>).

**IR** ( $\nu$ , cm<sup>-1</sup>, CDCl<sub>3</sub>) 2927, 2838, 1710, 1672, 1598, 1575, 1509, 1457, 1418, 1365, 1311, 1254, 1210, 1169, 1111, 1028, 983, 835.

**HRMS** (EI<sup>+</sup>)  $m/z$ : [M + H]<sup>+</sup> calculated for C<sub>13</sub>H<sub>17</sub>O<sub>2</sub>S<sub>2</sub>: 269.0664, found: .269.0665.

**R<sub>f</sub>** = 0.50 (EtOAc / PE = 1/4).

### 1-(4-chlorophenyl)-3-(1,2-dithiolan-3-yl)propan-1-one (III-24c)



Chemical Formula: C<sub>12</sub>H<sub>13</sub>ClOS<sub>2</sub>

Exact Mass: 272.0096

According to the general procedure C, the reaction was carried out with *S*-(2-(4-chlorophenyl)-2-oxoethyl)-*O*-ethyl-carbonodithioate (274 mg, 1 mmol) and 4-bromobut-1-ene (268 mg, 2 mmol) in DCE (1 mL), and needed 33 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (100:1 to 100:3) to afford product **III-24c** (63 mg, 23%) as a light yellow oil.

<sup>1</sup>H NMR (δ, ppm)(400 MHz, CDCl<sub>3</sub>) δ 7.96 – 7.88 (m, 2H, H<sub>3</sub>), 7.49 – 7.41 (m, 2H, H<sub>2</sub>), 3.78 – 3.63 (m, 1H, H<sub>8</sub>), 3.27 – 3.04 (m, 4H, H<sub>10</sub>, H<sub>6</sub>), 2.58 – 2.44 (m, 1H, H<sub>9</sub>), 2.24 – 2.10 (m, 1H, H<sub>7</sub>), 2.10 – 1.95 (m, 2H, H<sub>7</sub>, H<sub>9</sub>).

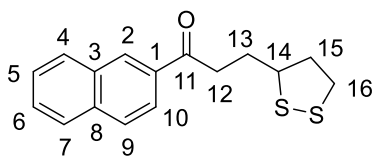
<sup>13</sup>C NMR (δ, ppm)(100 MHz, CDCl<sub>3</sub>) δ 197.9 (C<sub>5</sub>), 139.7 (C<sub>4</sub>), 135.0 (C<sub>1</sub>), 129.5 (C<sub>3</sub>), 129.0 (C<sub>2</sub>), 55.8 (C<sub>8</sub>), 40.4 (C<sub>9</sub>), 38.5 (C<sub>10</sub>), 37.6 (C<sub>6</sub>), 28.8 (C<sub>7</sub>).

IR (ν, cm<sup>-1</sup>, CDCl<sub>3</sub>) 2924, 1732, 1682, 1588, 1570, 1487, 1438, 1399, 1365, 1262, 1204, 1175, 1091, 1012, 984, 838, 817.

HRMS (EI<sup>+</sup>) m/z: [M + H]<sup>+</sup>calculated for C<sub>12</sub>H<sub>14</sub>ClOS<sub>2</sub>: 273.0169, found: 273.0165.

R<sub>f</sub> = 0.50 (EtOAc / PE = 1/4).

### 3-(1,2-dithiolan-3-yl)-1-(naphthalen-2-yl)propan-1-one (III-24d)



Chemical Formula: C<sub>16</sub>H<sub>16</sub>OS<sub>2</sub>

Exact Mass: 288.0643

According to the general procedure C, the reaction was carried out with *O*-ethyl *S*-(2-(naphthalen-2-yl)-2-oxoethyl)-carbonodithioate (290 mg, 1 mmol) and 4-bromobut-1-ene (268 mg, 2 mmol) in DCE (1 mL), and needed 34 h for the reaction to go to completion. It was purified by column chromatography on silica gel using



petroleum ether/ethyl acetate (100:1 to 100:3) to afford product **III-24d** (58 mg, 20%) as a light yellow oil.

$^1\text{H NMR}$  ( $\delta$ , ppm)(400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.49 (s, 1H, H<sub>2</sub>), 8.03 (dd,  $J$  = 8.6, 1.4 Hz, 1H, H<sub>4</sub>), 7.97 (d,  $J$  = 7.8 Hz, 1H, H<sub>9</sub>), 7.89 (t,  $J$  = 8.3 Hz, 2H, H<sub>7</sub>, H<sub>10</sub>), 7.58 (ddd,  $J$  = 17.4, 11.4, 6.8 Hz, 2H, H<sub>5</sub>, H<sub>6</sub>), 3.90 – 3.65 (m, 1H, H<sub>14</sub>), 3.38 – 3.11 (m, 4H, H<sub>16</sub>, H<sub>12</sub>), 2.62 – 2.44 (m, 1H, H<sub>15</sub>), 2.32 – 2.17 (m, 1H, H<sub>13</sub>), 2.16 – 2.01 (m, 2H, H<sub>13</sub>, H<sub>15</sub>).

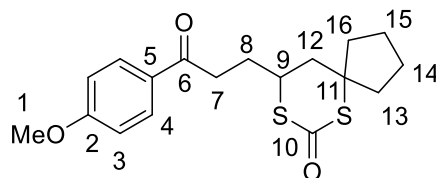
$^{13}\text{C NMR}$  ( $\delta$ , ppm)(100 MHz,  $\text{CDCl}_3$ )  $\delta$  199.1 (C<sub>11</sub>), 135.6 (C<sub>1</sub>), 134.0 (C<sub>3</sub>), 132.5 (C<sub>2</sub>), 129.8 (C<sub>8</sub>), 129.6 (C<sub>4</sub>), 128.5 (C<sub>7</sub>), 128.5 (C<sub>9</sub>), 127.8 (C<sub>6</sub>), 126.8 (C<sub>5</sub>), 123.8 (C<sub>10</sub>), 56.0 (C<sub>14</sub>), 40.4 (C<sub>16</sub>), 38.5 (C<sub>15</sub>), 37.8 (C<sub>12</sub>), 29.1 (C<sub>13</sub>).

**IR** ( $\nu$ ,  $\text{cm}^{-1}$ ,  $\text{CDCl}_3$ ) 3056, 2922, 2852, 1676, 1626, 1468, 1436, 1366, 1273, 1182, 1122, 985, 862, 748.

**HRMS** (EI<sup>+</sup>)  $m/z$ : [M + H]<sup>+</sup> calculated for C<sub>16</sub>H<sub>17</sub>OS<sub>2</sub>: 289.0715, found: 289.0714.

**R<sub>f</sub>** = 0.50 (EtOAc / PE = 1/4).

### 9-(3-(4-methoxyphenyl)-3-oxopropyl)-6,8-dithiaspiro[4.5]decan-7-one (**III-26a**)



Chemical Formula: C<sub>18</sub>H<sub>22</sub>O<sub>3</sub>S<sub>2</sub>

Exact Mass: 350.1010

According to the general procedure D, the reaction was carried out with *O*-ethyl *S*-(2-(4-methoxyphenyl)-2-oxoethyl)-carbonodithioate (405 mg, 1.5 mmol) and 1-allylcyclopentan-1-ol (330 mg, 3 mmol) in EtOAc (1.5 mL), and needed 17 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (20:1 to 10:1) to afford product **III-26a** (242 mg, 46%) as a light yellow oil.

$^1\text{H NMR}$  ( $\delta$ , ppm)(400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.94 (d,  $J$  = 9.0 Hz, 2H, H<sub>4</sub>), 6.94 (d,  $J$  = 9.0 Hz, 2H, H<sub>3</sub>), 3.88 (s, 3H, H<sub>1</sub>), 3.87 – 3.80 (m, 1H, H<sub>9</sub>), 3.09 (t,  $J$  = 7.2 Hz, 2H, H<sub>7</sub>),

2.33 – 2.19 (m, 2H, H<sub>8</sub>), 2.18 – 1.98 (m, 3H, H<sub>16</sub>, H<sub>12</sub>, H<sub>13</sub>), 1.95 – 1.65 (m, 7H, H<sub>15</sub>, H<sub>14</sub>, H<sub>12</sub>, H<sub>13</sub>, H<sub>14</sub>, H<sub>15</sub>, H<sub>16</sub>).

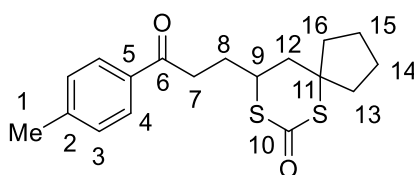
<sup>13</sup>C NMR (δ, ppm)(100 MHz, CDCl<sub>3</sub>) δ 197.0 (C<sub>6</sub>), 190.4 (C<sub>10</sub>), 163.7 (C<sub>2</sub>), 130.3 (C<sub>5</sub>), 129.6 (C<sub>4</sub>), 113.9 (C<sub>3</sub>), 59.1 (C<sub>1</sub>), 55.5 (C<sub>11</sub>), 44.0 (C<sub>9</sub>), 42.4 (C<sub>7</sub>), 42.0 (C<sub>8</sub>), 40.9 (C<sub>12</sub>), 33.9 (C<sub>13</sub>), 30.6 (C<sub>16</sub>), 23.8 (C<sub>14</sub>), 23.5 (C<sub>15</sub>).

IR (ν, cm<sup>-1</sup>, CDCl<sub>3</sub>) 2952, 1673, 1594, 1575, 1509, 1418, 1309, 1255, 1211, 1168, 1028, 913, 837, 786.

HRMS (EI<sup>+</sup>) m/z: [M + H]<sup>+</sup> calculated for C<sub>18</sub>H<sub>23</sub>O<sub>3</sub>S<sub>2</sub>: 351.1083, found: .351.1072.

R<sub>f</sub> = 0.70 (EtOAc / PE = 1/4).

### 9-(3-oxo-3-(p-tolyl)propyl)-6,8-dithiaspiro[4.5]decan-7-one (III-26b)



Chemical Formula: C<sub>18</sub>H<sub>22</sub>O<sub>2</sub>S<sub>2</sub>  
Exact Mass: 334.1061

According to the general procedure D, the reaction was carried out with *O*-ethyl *S*-(2-oxo-2-(*p*-tolyl)ethyl)-carbonodithioate (381 mg, 1.5 mmol) and 1-allylcyclopentan-1-ol (330 mg, 3 mmol) in EtOAc (1.5 mL), and needed 19 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (20:1 to 10:1) to afford product **III-26b** (225 mg, 45%) as a light yellow oil.

<sup>1</sup>H NMR (δ, ppm)(400 MHz, CDCl<sub>3</sub>) δ 7.86 (d, *J* = 8.2 Hz, 2H, H<sub>4</sub>), 7.32 – 7.23 (m, 2H, H<sub>3</sub>), 3.88– 3.80 (m, 1H, H<sub>9</sub>), 3.12 (t, *J* = 7.2 Hz, 2H, H<sub>7</sub>), 2.42 (s, 3H, H<sub>1</sub>), 2.36 – 1.99 (m, 5H, H<sub>8</sub>, H<sub>8</sub>, H<sub>16</sub>, H<sub>12</sub>, H<sub>13</sub>), 1.98 – 1.64 (m, 7H, H<sub>15</sub>, H<sub>14</sub>, H<sub>12</sub>, H<sub>13</sub>, H<sub>14</sub>, H<sub>15</sub>, H<sub>16</sub>).

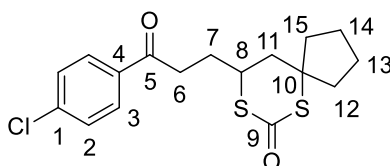
<sup>13</sup>C NMR (δ, ppm)(100 MHz, CDCl<sub>3</sub>) δ 198.1 (C<sub>6</sub>), 190.3 (C<sub>10</sub>), 144.3 (C<sub>2</sub>), 134.0 (C<sub>5</sub>), 129.4 (C<sub>4</sub>), 128.2 (C<sub>3</sub>), 59.1 (C<sub>11</sub>), 44.0 (C<sub>9</sub>), 42.4 (C<sub>7</sub>), 42.0 (C<sub>8</sub>), 40.9 (C<sub>12</sub>), 34.2 (C<sub>13</sub>), 30.5 (C<sub>16</sub>), 23.8 (C<sub>14</sub>), 23.5 (C<sub>15</sub>), 21.7 (C<sub>1</sub>).

**IR** ( $\nu$ ,  $\text{cm}^{-1}$ ,  $\text{CDCl}_3$ ) 2950, 2871, 1679, 1601, 1446, 1408, 1368, 1231, 1204, 1120, 968, 914, 809, 731.

**HRMS** ( $\text{EI}^+$ )  $m/z$ :  $[\text{M} + \text{H}]^+$  calculated for  $\text{C}_{18}\text{H}_{23}\text{O}_2\text{S}_2$ : 335.1134, found: 335.1133.

$R_f = 0.70$  (EtOAc / PE = 1/4).

**9-(3-(4-chlorophenyl)-3-oxopropyl)-6,8-dithiaspiro[4.5]decan-7-one (III-26c)**



Chemical Formula:  $\text{C}_{17}\text{H}_{19}\text{ClO}_2\text{S}_2$   
Exact Mass: 354.0515

According to the general procedure D, the reaction was carried out with *S*-(2-(4-chlorophenyl)-2-oxoethyl)-*O*-ethyl-carbonodithioate (411 mg, 1.5 mmol) and 1-allylcyclopentan-1-ol (330 mg, 3 mmol) in EtOAc (1.5 mL), and needed 18 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (20:1 to 10:1) to afford product **III-26c** (218 mg, 41%) as a light yellow solid.

$^1\text{H NMR}$  ( $\delta$ , ppm)(400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.95 – 7.84 (m, 2H,  $\text{H}_3$ ), 7.49 – 7.41 (m, 2H,  $\text{H}_2$ ), 3.88 – 3.81 (m, 1H,  $\text{H}_8$ ), 3.12 (t,  $J = 7.2$  Hz, 2H,  $\text{H}_6$ ), 2.33 – 2.19 (m, 2H,  $\text{H}_7$ ), 2.19 – 2.02 (m, 3H,  $\text{H}_{15}$ ,  $\text{H}_{11}$ ,  $\text{H}_{12}$ ), 1.96 – 1.65 (m, 7H,  $\text{H}_{14}$ ,  $\text{H}_{13}$ ,  $\text{H}_{11}$ ,  $\text{H}_{12}$ ,  $\text{H}_{13}$ ,  $\text{H}_{14}$ ,  $\text{H}_{15}$ ).

$^{13}\text{C NMR}$  ( $\delta$ , ppm)(100 MHz,  $\text{CDCl}_3$ )  $\delta$  197.2 ( $\text{C}_5$ ), 190.1 ( $\text{C}_9$ ), 139.9 ( $\text{C}_4$ ), 134.8 ( $\text{C}_1$ ), 129.5 ( $\text{C}_3$ ), 129.1 ( $\text{C}_2$ ), 59.1 ( $\text{C}_{10}$ ), 43.9 ( $\text{C}_8$ ), 42.4 ( $\text{C}_6$ ), 42.0 ( $\text{C}_7$ ), 40.9 ( $\text{C}_{11}$ ), 34.3 ( $\text{C}_{12}$ ), 30.3 ( $\text{C}_{15}$ ), 23.8 ( $\text{C}_{13}$ ), 23.5 ( $\text{C}_{14}$ ).

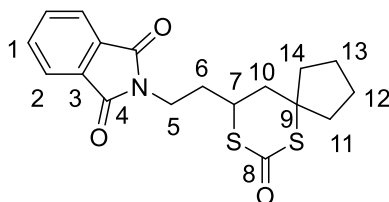
**IR** ( $\nu$ ,  $\text{cm}^{-1}$ ,  $\text{CDCl}_3$ ) 2952, 1683, 1589, 1487, 1399, 1369, 1205, 1091, 1012, 915, 837.

**HRMS** ( $\text{EI}^+$ )  $m/z$ :  $[\text{M} + \text{H}]^+$  calculated for  $\text{C}_{17}\text{H}_{20}\text{ClO}_2\text{S}_2$ : 355.0588, found: 355.0579.

**Mp**: 94-95 °C.

$R_f = 0.40$  (EtOAc / PE = 1/4).

## 2-(2-(7-oxo-6,8-dithiaspiro[4.5]decan-9-yl)ethyl)isoindoline-1,3-dione (III-26d)



Chemical Formula: C<sub>18</sub>H<sub>19</sub>NO<sub>3</sub>S<sub>2</sub>  
Exact Mass: 361.0806

According to the general procedure D, the reaction was carried out with *S*-((1,3-dioxoisoindolin-2-yl)methyl)-*O*-ethyl-carbonodithioate (421 mg, 1.5 mmol) and 1-allylcyclopentan-1-ol (330 mg, 3 mmol) in EtOAc (1.5 mL), and needed 16 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (10:1 to 4:1) to afford product **III-26d** (233 mg, 43%) as a colorless oil.

<sup>1</sup>H NMR (δ, ppm)(400 MHz, CDCl<sub>3</sub>) δ 7.90 – 7.82 (m, 2H, H<sub>2</sub>), 7.79 – 7.70 (m, 2H, H<sub>1</sub>), 3.90 – 3.77 (m, 2H, H<sub>7</sub>, H<sub>5</sub>), 3.75 – 3.68(m, 1H, H<sub>5</sub>), 2.42 (dd, J = 14.2, 3.4 Hz, 1H, H<sub>10</sub>), 2.16 – 2.00 (m, 4H, H<sub>6</sub>, H<sub>6</sub>, H<sub>10</sub>, H<sub>11</sub>), 1.97 – 1.89 (m, 2H, H<sub>13</sub>, H<sub>12</sub>), 1.89 – 1.70 (m, 5H, H<sub>10</sub>, H<sub>11</sub>, H<sub>12</sub>, H<sub>14</sub>, H<sub>13</sub>).

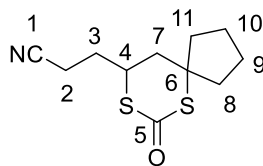
<sup>13</sup>C NMR (δ, ppm)(100 MHz, CDCl<sub>3</sub>) δ 190.0 (C<sub>8</sub>), 168.2 (C<sub>4</sub>), 134.3 (C<sub>3</sub>), 131.9 (C<sub>1</sub>), 123.4 (C<sub>2</sub>), 59.1 (C<sub>9</sub>), 42.0 (C<sub>5</sub>), 41.8 (C<sub>7</sub>), 41.4 (C<sub>6</sub>), 40.6 (C<sub>10</sub>), 35.2 (C<sub>11</sub>), 34.7 (C<sub>14</sub>), 23.8 (C<sub>12</sub>), 23.4 (C<sub>13</sub>).

IR (ν, cm<sup>-1</sup>, CDCl<sub>3</sub>) 2948, 2872, 1770, 1704, 1598, 1434, 1395, 1365, 1147, 1072, 912, 716.

HRMS (EI<sup>+</sup>) m/z: [M + H]<sup>+</sup> calculated for C<sub>18</sub>H<sub>20</sub>NO<sub>3</sub>S<sub>2</sub>: 362.0879, found: 362.0867.

R<sub>f</sub> = 0.20 (EtOAc / PE = 1/4).

## 3-(7-oxo-6,8-dithiaspiro[4.5]decan-9-yl)propanenitrile (III-26e)



Chemical Formula: C<sub>11</sub>H<sub>15</sub>NOS<sub>2</sub>

Exact Mass: 241.0595

According to the general procedure D, the reaction was carried out with *S*-(cyanomethyl)-*O*-ethyl-carbonodithioate (242 mg, 1.5 mmol) and 1-allylcyclopentan-1-ol (330 mg, 3 mmol) in EtOAc (1.5 mL), and needed 19 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (20:1 to 10:1) to afford product **III-26e** (148 mg, 41%) as a light yellow oil.

<sup>1</sup>H NMR (δ, ppm)(400 MHz, CDCl<sub>3</sub>) δ 3.89-3.82 (m, 1H, H<sub>4</sub>), 2.55 (td, *J* = 7.3, 1.4 Hz, 2H, H<sub>2</sub>), 2.24 (dd, *J* = 14.2, 3.8 Hz, 1H, H<sub>3</sub>), 2.21 – 2.00 (m, 4H, H<sub>3</sub>, H<sub>7</sub>, H<sub>11</sub>, H<sub>8</sub>), 1.97 – 1.69 (m, 7H, H<sub>10</sub>, H<sub>9</sub>, H<sub>7</sub>, H<sub>8</sub>, H<sub>9</sub>, H<sub>10</sub>, H<sub>11</sub>).

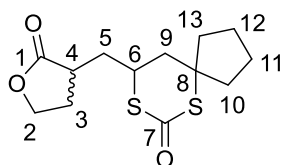
<sup>13</sup>C NMR (δ, ppm)(100 MHz, CDCl<sub>3</sub>) δ 189.0 (C<sub>5</sub>), 118.3 (C<sub>1</sub>), 59.0 (C<sub>6</sub>), 42.9 (C<sub>4</sub>), 41.9 (C<sub>7</sub>), 41.5 (C<sub>8</sub>), 40.7 (C<sub>11</sub>), 31.9 (C<sub>3</sub>), 23.8 (C<sub>9</sub>), 23.4 (C<sub>10</sub>), 14.3 (C<sub>2</sub>).

IR (ν, cm<sup>-1</sup>, CDCl<sub>3</sub>) 2953, 2872, 2247, 1596, 1445, 1425, 1172, 1011, 964, 913, 730.

HRMS (EI<sup>+</sup>) *m/z*: [M + Na]<sup>+</sup>calculated for C<sub>11</sub>H<sub>15</sub>NNaOS<sub>2</sub>: 264.0487, found: 264.0480.

R<sub>f</sub> = 0.30 (EtOAc / PE = 1/4).

### 3-((7-oxo-6,8-dithiaspiro[4.5]decan-9-yl)methyl)dihydrofuran-2(3H)-one (III-26f)



Chemical Formula: C<sub>13</sub>H<sub>18</sub>O<sub>3</sub>S<sub>2</sub>

Exact Mass: 286.0697

According to the general procedure D, the reaction was carried out with *O*-ethyl *S*-(2-oxotetrahydrofuran-3-yl)-carbonodithioate (309 mg, 1.5 mmol) and

1-allylcyclopentan-1-ol (330 mg, 3 mmol) in EtOAc (1.5 mL), and needed 18 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (20:1 to 10:1) to afford product **III-26f** (210 mg, 49%) as a light yellow oil.

$^1\text{H NMR}$  ( $\delta$ , ppm)(400 MHz,  $\text{CDCl}_3$ )  $\delta$  4.37 – 4.31 (m, 2H,  $\text{H}_2$ ), 4.25 – 4.15 (m, 2H,  $\text{H}_2$ ), 4.09 – 3.99 (m, 1H,  $\text{H}_6$ ), 3.94 – 3.84 (m, 1H,  $\text{H}_6$ ), 2.78 – 2.62 (m, 2H,  $\text{H}_5$ ), 2.54 – 2.44 (m, 2H,  $\text{H}_5$ ), 2.33 – 2.19 (m, 4H,  $\text{H}_3$ ,  $\text{H}_3$ ), 2.18 – 1.94 (m, 6H,  $\text{H}_4$ ,  $\text{H}_4$ ,  $\text{H}_9$ ,  $\text{H}_9$ ), 1.94 – 1.65 (m, 16H,  $\text{H}_{10}$ ,  $\text{H}_{10}$ ,  $\text{H}_{11}$ ,  $\text{H}_{11}$ ,  $\text{H}_{12}$ ,  $\text{H}_{12}$ ,  $\text{H}_{13}$ ,  $\text{H}_{13}$ ).

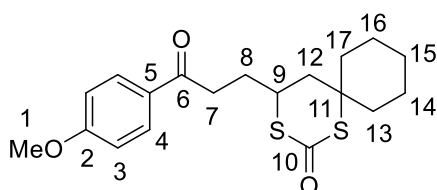
$^{13}\text{C NMR}$  ( $\delta$ , ppm)(100 MHz,  $\text{CDCl}_3$ )  $\delta$  189.9 ( $\text{C}_7$ ), 189.8 ( $\text{C}_7$ ), 178.3 ( $\text{C}_1$ ), 178.2 ( $\text{C}_1$ ), 66.6 ( $\text{C}_2$ ), 66.5 ( $\text{C}_2$ ), 59.2 ( $\text{C}_8$ ), 59.1 ( $\text{C}_8$ ), 42.9 ( $\text{C}_6$ ), 42.5 ( $\text{C}_6$ ), 42.2 ( $\text{C}_4$ ), 42.1 ( $\text{C}_4$ ), 42.1 ( $\text{C}_5$ ), 40.9 ( $\text{C}_3$ ), 40.9 ( $\text{C}_3$ ), 37.9 ( $\text{C}_9$ ), 37.0 ( $\text{C}_9$ ), 36.7 ( $\text{C}_{10}$ ), 36.3 ( $\text{C}_{10}$ ), 30.1 ( $\text{C}_{13}$ ), 29.3 ( $\text{C}_{11}$ ), 23.9 ( $\text{C}_{12}$ ), 23.5 ( $\text{C}_{12}$ ).

$\text{IR}$  ( $\nu$ ,  $\text{cm}^{-1}$ ,  $\text{CDCl}_3$ ) 2951, 2873, 1761, 1598, 1450, 1376, 1207, 1186, 1156, 1022, 982, 912, 728.

$\text{HRMS}$  ( $\text{EI}^+$ )  $m/z$ :  $[\text{M} + \text{Na}]^+$  calculated for  $\text{C}_{13}\text{H}_{18}\text{NaO}_3\text{S}_2$ : 309.0590, found: 309.0581.

$R_f = 0.35$  (EtOAc / PE = 1/2).

#### 4-(3-(4-methoxyphenyl)-3-oxopropyl)-1,3-dithiaspiro[5.5]undecan-2-one (**III-28a**)



Chemical Formula:  $\text{C}_{19}\text{H}_{24}\text{O}_3\text{S}_2$   
Exact Mass: 364.1167

According to the general procedure E, the reaction was carried out with *O*-ethyl *S*-(2-(4-methoxyphenyl)-2-oxoethyl)-carbonodithioate (405 mg, 1.5 mmol) and 1-allylcyclohexan-1-ol (420 mg, 3 mmol) in EtOAc (1.5 mL), and needed 20 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (20:1 to 10:1) to afford product **III-28a** (257 mg,

47%) as a light yellow oil.

<sup>1</sup>H NMR (δ, ppm)(400 MHz, CDCl<sub>3</sub>) δ 7.94 (d, *J* = 8.8 Hz, 2H, H<sub>4</sub>), 6.95 (d, *J* = 8.8 Hz, 2H, H<sub>3</sub>), 3.88 (s, 3H, H<sub>1</sub>), 3.87 – 3.80 (m, 1H, H<sub>9</sub>), 3.09 (t, *J* = 7.2 Hz, 2H, H<sub>7</sub>), 2.37 – 2.17 (m, 2H, H<sub>8</sub>), 2.01 (ddt, *J* = 32.6, 20.4, 10.4 Hz, 4H, H<sub>17</sub>, H<sub>12</sub>, H<sub>17</sub>, H<sub>13</sub>), 1.78 – 1.49 (m, 7H, H<sub>13</sub>, H<sub>12</sub>, H<sub>14</sub>, H<sub>16</sub>, H<sub>16</sub>, H<sub>14</sub>, H<sub>15</sub>), 1.33 (s, 1H, H<sub>15</sub>).

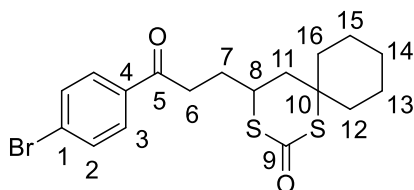
<sup>13</sup>C NMR (δ, ppm)(100 MHz, CDCl<sub>3</sub>) δ 197.0 (C<sub>6</sub>), 189.7 (C<sub>10</sub>), 163.7 (C<sub>2</sub>), 130.3 (C<sub>5</sub>), 129.6 (C<sub>4</sub>), 113.9 (C<sub>3</sub>), 55.5 (C<sub>1</sub>), 53.4 (C<sub>11</sub>), 43.3 (C<sub>9</sub>), 41.7 (C<sub>7</sub>), 40.5 (C<sub>13</sub>), 37.5 (C<sub>17</sub>), 33.9 (C<sub>8</sub>), 30.6 (C<sub>12</sub>), 25.4 (C<sub>15</sub>), 21.9 (C<sub>14</sub>), 21.5 (C<sub>16</sub>).

IR (ν, cm<sup>-1</sup>, CDCl<sub>3</sub>) 2927, 2855, 1673, 1596, 1576, 1510, 1445, 1418, 1367, 1311, 1255, 1212, 1169, 1111, 1028, 983, 915, 837, 735.

HRMS (EI<sup>+</sup>) *m/z*: [M + H]<sup>+</sup> calculated for C<sub>19</sub>H<sub>25</sub>O<sub>3</sub>S<sub>2</sub>: 365.1240, found: 365.1236.

R<sub>f</sub> = 0.25 (EtOAc / PE = 1/5).

#### 4-(3-(4-bromophenyl)-3-oxopropyl)-1,3-dithiaspiro[5.5]undecan-2-one (III-28b)



Chemical Formula: C<sub>18</sub>H<sub>21</sub>BrO<sub>2</sub>S<sub>2</sub>  
Exact Mass: 412.0166

According to the general procedure E, the reaction was carried out with *S*-(2-(4-bromophenyl)-2-oxoethyl)-*O*-ethyl-carbonodithioate (477 mg, 1.5 mmol) and 1-allylcyclohexan-1-ol (420 mg, 3 mmol) in EtOAc (1.5 mL), and needed 26 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (100:3 to 10:1) to afford product **III-28b** (272 mg, 44%) as a light yellow solid.

<sup>1</sup>H NMR (δ, ppm)(400 MHz, CDCl<sub>3</sub>) δ 7.87 – 7.77 (m, 2H, H<sub>3</sub>), 7.67 – 7.58 (m, 2H, H<sub>2</sub>), 3.88 – 3.81 (m, 3.3 Hz, 1H, H<sub>8</sub>), 3.11 (t, *J* = 7.2 Hz, 2H, H<sub>6</sub>), 2.36 – 2.17 (m, 2H, H<sub>7</sub>), 2.15 – 1.84 (m, 4H, H<sub>16</sub>, H<sub>11</sub>, H<sub>16</sub>, H<sub>12</sub>), 1.78 – 1.49 (m, 7H, H<sub>12</sub>, H<sub>11</sub>, H<sub>13</sub>, H<sub>15</sub>,

H<sub>15</sub>, H<sub>13</sub>, H<sub>14</sub>), 1.40 – 1.27 (m, 1H, H<sub>14</sub>).

<sup>13</sup>C NMR (δ, ppm)(100 MHz, CDCl<sub>3</sub>) δ 197.4 (C<sub>5</sub>), 189.5 (C<sub>9</sub>), 135.2 (C<sub>4</sub>), 132.1 (C<sub>2</sub>), 129.6 (C<sub>3</sub>), 128.7 (C<sub>1</sub>), 53.4 (C<sub>10</sub>), 43.3 (C<sub>8</sub>), 41.6 (C<sub>6</sub>), 40.5 (C<sub>12</sub>), 37.5 (C<sub>16</sub>), 34.3 (C<sub>7</sub>), 30.3 (C<sub>11</sub>), 25.4 (C<sub>14</sub>), 21.9 (C<sub>13</sub>), 21.4 (C<sub>15</sub>).

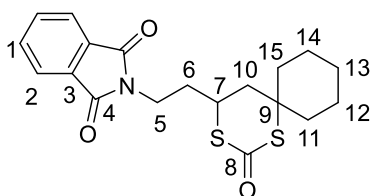
IR (ν, cm<sup>-1</sup>, CDCl<sub>3</sub>) 2928, 2856, 1685, 1599, 1585, 1445, 1397, 1206, 1070, 1009, 984, 916.

HRMS (EI<sup>+</sup>) m/z: [M + H]<sup>+</sup> calculated for C<sub>18</sub>H<sub>22</sub>BrO<sub>2</sub>S<sub>2</sub>: 413.0239, found: 413.0227.

Mp: 133 – 135 °C.

R<sub>f</sub> = 0.25 (EtOAc / PE = 1/5).

### 2-(2-(2-oxo-1,3-dithiaspiro[5.5]undecan-4-yl)ethyl)isoindoline-1,3-dione (III-28c)



Chemical Formula: C<sub>19</sub>H<sub>21</sub>NO<sub>3</sub>S<sub>2</sub>  
Exact Mass: 375.0963

According to the general procedure E, the reaction was carried out with *S*-((1,3-dioxoisoindolin-2-yl)methyl)-*O*-ethyl-carbonodithioate (421 mg, 1.5 mmol) and 1-allylcyclohexan-1-ol (420 mg, 3 mmol) in EtOAc (1.5 mL), and needed 23 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (10:1 to 2:1) to afford product **III-28c** (281 mg, 50%) as a light yellow oil.

<sup>1</sup>H NMR (δ, ppm)(400 MHz, CDCl<sub>3</sub>) δ 7.87-7.84 (m, 2H, H<sub>2</sub>), 7.80 – 7.68 (m, 2H, H<sub>1</sub>), 3.90 – 3.78 (m, 2H, H<sub>5</sub>), 3.77– 3.70 (m, 1H, H<sub>7</sub>), 2.44 (dd, *J*= 14.4, 3.2 Hz, 1H, H<sub>10</sub>), 2.18 – 1.88 (m, 5H, H<sub>15</sub>, H<sub>6</sub>, H<sub>6</sub>, H<sub>15</sub>, H<sub>11</sub>), 1.78 – 1.47 (m, 7H, H<sub>10</sub>, H<sub>11</sub>, H<sub>12</sub>, H<sub>14</sub>, H<sub>14</sub>, H<sub>12</sub>, H<sub>13</sub>), 1.41 – 1.26 (m, 1H, H<sub>13</sub>).

<sup>13</sup>C NMR (δ, ppm)(100 MHz, CDCl<sub>3</sub>) δ 189.3 (C<sub>8</sub>), 168.1 (C<sub>4</sub>), 134.2 (C<sub>3</sub>), 131.9 (C<sub>1</sub>), 123.4 (C<sub>2</sub>), 53.4 (C<sub>9</sub>), 42.7 (C<sub>5</sub>), 40.5 (C<sub>7</sub>), 39.6 (C<sub>11</sub>), 37.2 (C<sub>15</sub>), 35.2 (C<sub>6</sub>), 34.8 (C<sub>10</sub>), 25.3 (C<sub>13</sub>), 21.9 (C<sub>12</sub>), 21.4 (C<sub>14</sub>).

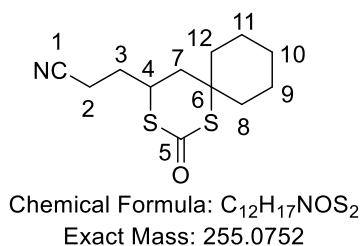
IR (ν, cm<sup>-1</sup>, CDCl<sub>3</sub>) 2929, 2857, 1771, 1711, 1605, 1466, 1440, 1397, 1369, 918, 720.



**HRMS** (EI<sup>+</sup>) m/z: [M + H]<sup>+</sup> calculated for C<sub>19</sub>H<sub>22</sub>NO<sub>3</sub>S<sub>2</sub>: 376.1036, found: 376.1034.

**R<sub>f</sub>** = 0.40 (EtOAc / PE = 1/4).

### 3-(2-oxo-1,3-dithiaspiro[5.5]undecan-4-yl)propanenitrile (**III-28d**)



According to the general procedure E, the reaction was carried out with *S*-(cyanomethyl)-*O*-ethyl-carbonodithioate (242 mg, 1.5 mmol) and 1-allylcyclohexan-1-ol (420 mg, 3 mmol) in EtOAc (1.5 mL), and needed 21 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (20:1 to 5:1) to afford product **III-28d** (199 mg, 52%) as a colorless oil.

**<sup>1</sup>H NMR** (δ, ppm)(400 MHz, CDCl<sub>3</sub>) δ 3.93 – 3.79 (m, 1H, H<sub>4</sub>), 2.64 – 2.46 (m, 2H, H<sub>2</sub>), 2.36 – 2.21 (m, 1H, H<sub>3</sub>), 2.17 – 1.87 (m, 5H, H<sub>3</sub>, H<sub>7</sub>, H<sub>12</sub>, H<sub>12</sub>, H<sub>8</sub>), 1.79 – 1.51 (m, 7H, H<sub>7</sub>, H<sub>8</sub>, H<sub>9</sub>, H<sub>11</sub>, H<sub>11</sub>, H<sub>9</sub>, H<sub>10</sub>), 1.40 – 1.26 (m, 1H, H<sub>10</sub>).

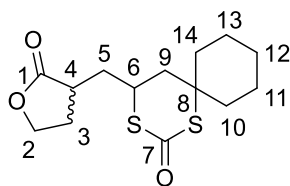
**<sup>13</sup>C NMR** (δ, ppm)(100 MHz, CDCl<sub>3</sub>) δ 188.4 (C<sub>5</sub>), 118.3 (C<sub>1</sub>), 53.4 (C<sub>6</sub>), 42.4 (C<sub>4</sub>), 40.8 (C<sub>8</sub>), 40.4 (C<sub>12</sub>), 37.3 (C<sub>3</sub>), 31.8 (C<sub>7</sub>), 25.3 (C<sub>10</sub>), 21.9 (C<sub>9</sub>), 21.4 (C<sub>11</sub>), 14.2 (C<sub>2</sub>).

**IR** (ν, cm<sup>-1</sup>, CDCl<sub>3</sub>) 2928, 2857, 2247, 1598, 1442, 1367, 1255, 941, 914, 852.

**HRMS** (EI<sup>+</sup>) m/z: [M + H]<sup>+</sup> calculated for C<sub>12</sub>H<sub>18</sub>NOS<sub>2</sub>: 256.0824, found: 256.0821.

**R<sub>f</sub>** = 0.50 (EtOAc / PE = 1/5).

### 3-((2-oxo-1,3-dithiaspiro[5.5]undecan-4-yl)methyl)dihydrofuran-2(3H)-one (**III-28e**)



Chemical Formula: C<sub>14</sub>H<sub>20</sub>O<sub>3</sub>S<sub>2</sub>

Exact Mass: 300.0854

According to the general procedure E, the reaction was carried out with *O*-ethyl *S*-(2-oxotetrahydrofuran-3-yl)-carbonodithioate (309 mg, 1.5 mmol) and 1-allylcyclohexan-1-ol (420 mg, 3 mmol) in EtOAc (1.5 mL), and needed 21 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (10:1 to 3:1) to afford product **III-28e** (297 mg, 66%) as a white solid.

**<sup>1</sup>H NMR** ( $\delta$ , ppm)(400 MHz, CDCl<sub>3</sub>)  $\delta$  4.43 – 4.36 (m, 2H, H<sub>2</sub>), 4.25 – 4.20 (m, 2H, H<sub>2</sub>), 4.14 – 4.02 (m, 1H, H<sub>6</sub>), 3.98 – 3.88 (m, 1H, H<sub>6</sub>), 2.82 – 2.61 (m, 2H, H<sub>5</sub>), 2.57 – 2.46 (m, 2H, H<sub>5</sub>), 2.36 – 2.23 (m, 4H, H<sub>4</sub>, H<sub>3</sub>), 2.14 – 1.78 (m, 10H, H<sub>3</sub>, H<sub>9</sub>, H<sub>14</sub>, H<sub>10</sub>), 1.78 – 1.49 (m, 14H, H<sub>10</sub>, H<sub>11</sub>, H<sub>13</sub>, H<sub>2</sub>), 1.36 – 1.28 (m, 2H, H<sub>12</sub>).

**<sup>13</sup>C NMR** ( $\delta$ , ppm)(100 MHz, CDCl<sub>3</sub>)  $\delta$  189.2 (C<sub>7</sub>), 189.1 (C<sub>7</sub>), 178.3 (C<sub>1</sub>), 178.1 (C<sub>1</sub>), 66.5 (C<sub>2</sub>), 66.5 (C<sub>2</sub>), 53.5 (C<sub>8</sub>), 53.3 (C<sub>8</sub>), 43.4 (C<sub>6</sub>), 43.0 (C<sub>6</sub>), 40.7 (C<sub>4</sub>), 40.5 (C<sub>4</sub>), 40.4 (C<sub>5</sub>), 39.9 (C<sub>5</sub>), 37.8 (C<sub>10</sub>), 37.5 (C<sub>10</sub>), 37.5 (C<sub>14</sub>), 36.9 (C<sub>14</sub>), 36.6 (C<sub>3</sub>), 36.2 (C<sub>3</sub>), 30.0 (C<sub>9</sub>), 29.3 (C<sub>9</sub>), 25.3 (C<sub>12</sub>), 21.9 (C<sub>11</sub>), 21.4 (C<sub>13</sub>), 21.4 (C<sub>13</sub>).

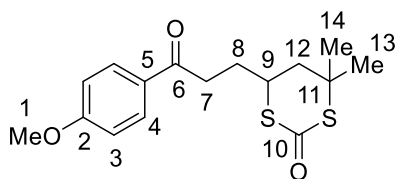
**IR** ( $\nu$ , cm<sup>-1</sup>, CDCl<sub>3</sub>) 2926, 2856, 1762, 1597, 1445, 1375, 1256, 1206, 1154, 1107, 1021, 915, 853, 730.

**HRMS** (EI<sup>+</sup>) *m/z*: [M + H]<sup>+</sup> calculated for C<sub>14</sub>H<sub>21</sub>O<sub>3</sub>S<sub>2</sub>: 301.0927, found: 301.0918.

**Mp**: 136 – 137 °C.

**R<sub>f</sub>** = 0.30 (EtOAc / PE = 1/5).

**6-(3-(4-methoxyphenyl)-3-oxopropyl)-4,4-dimethyl-1,3-dithian-2-one (III-30a)**



Chemical Formula: C<sub>16</sub>H<sub>20</sub>O<sub>3</sub>S<sub>2</sub>  
Exact Mass: 324.0854

According to the general procedure F, the reaction was carried out with *O*-ethyl *S*-(2-(4-methoxyphenyl)-2-oxoethyl)-carbonodithioate (405 mg, 1.5 mmol) and 2-methylpent-4-en-2-ol (300 mg, 3 mmol) in EtOAc (1.5 mL), and needed 20 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (100:3 to 10:1) to afford product **III-30a** (170 mg, 35%) as a light yellow oil.

<sup>1</sup>H NMR (δ, ppm)(400 MHz, CDCl<sub>3</sub>) δ 7.97 – 7.90 (m, 2H, H<sub>4</sub>), 6.98 – 6.90 (m, 2H, H<sub>3</sub>), 3.88 (s, 3H, H<sub>1</sub>), 3.87 – 3.80 (m, 1H, H<sub>9</sub>), 3.10 (t, *J* = 7.2 Hz, 2H, H<sub>7</sub>), 2.33 – 2.17 (m, 2H, H<sub>8</sub>), 2.15 – 1.88 (m, 2H, H<sub>12</sub>), 1.54 (s, 3H, H<sub>14</sub>), 1.47 (s, 3H, H<sub>13</sub>).

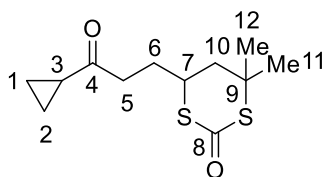
<sup>13</sup>C NMR (δ, ppm)(100 MHz, CDCl<sub>3</sub>) δ 196.9 (C<sub>6</sub>), 190.1 (C<sub>10</sub>), 163.8 (C<sub>2</sub>), 130.3 (C<sub>5</sub>), 129.5 (C<sub>4</sub>), 113.9 (C<sub>3</sub>), 55.5 (C<sub>1</sub>), 48.7 (C<sub>11</sub>), 44.0 (C<sub>9</sub>), 43.4 (C<sub>7</sub>), 33.9 (C<sub>8</sub>), 31.7 (C<sub>12</sub>), 30.5 (C<sub>14</sub>), 29.9 (C<sub>13</sub>).

IR (ν, cm<sup>-1</sup>, CDCl<sub>3</sub>) 2964, 2927, 1673, 1595, 1574, 1510, 1418, 1368, 1311, 1255, 1210, 1168, 1027, 982, 912, 834, 731.

HRMS (EI<sup>+</sup>) *m/z*: [M + Na]<sup>+</sup>calculated for C<sub>16</sub>H<sub>20</sub>NaO<sub>3</sub>S<sub>2</sub>: 347.0746, found: 347.0749.

R<sub>f</sub> = 0.40 (EtOAc / PE = 1/5).

### 6-(3-cyclopropyl-3-oxopropyl)-4,4-dimethyl-1,3-dithian-2-one (III-30b)



Chemical Formula: C<sub>12</sub>H<sub>18</sub>O<sub>2</sub>S<sub>2</sub>  
Exact Mass: 258.0748

According to the general procedure F, the reaction was carried out with *S*-(2-cyclopropyl-2-oxoethyl)-*O*-ethyl-carbonodithioate (306 mg, 1.5 mmol) and 2-methylpent-4-en-2-ol (300 mg, 3 mmol) in EtOAc (1.5 mL), and needed 25 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (100:3 to 10:1) to afford product **III-30b** (116 mg, 30%) as a light yellow oil.

<sup>1</sup>H NMR ( $\delta$ , ppm)(400 MHz, CDCl<sub>3</sub>)  $\delta$  3.79 – 3.72 (m, 1H, H<sub>7</sub>), 2.75 (t,  $J$  = 7.4 Hz, 2H, H<sub>5</sub>), 2.22 – 2.01 (m, 2H, H<sub>6</sub>), 2.03 – 1.84 (m, 3H, H<sub>10</sub>, H<sub>3</sub>), 1.52 (s, 3H, H<sub>12</sub>), 1.46 (s, 3H, H<sub>11</sub>), 1.08 – 0.98 (m, 2H, H<sub>2</sub>, H<sub>1</sub>), 0.97 – 0.86 (m, 2H, H<sub>2</sub>, H<sub>1</sub>).

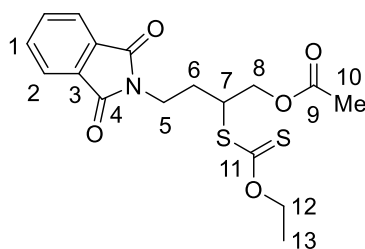
<sup>13</sup>C NMR ( $\delta$ , ppm)(100 MHz, CDCl<sub>3</sub>)  $\delta$  209.1 (C<sub>4</sub>), 190.1 (C<sub>8</sub>), 48.7 (C<sub>9</sub>), 43.9 (C<sub>7</sub>), 43.1 (C<sub>5</sub>), 39.0 (C<sub>6</sub>), 31.7 (C<sub>10</sub>), 29.9 (C<sub>11</sub>), 29.9 (C<sub>12</sub>), 20.7 (C<sub>3</sub>), 11.1 (C<sub>2</sub>), 11.1 (C<sub>1</sub>).

IR ( $\nu$ , cm<sup>-1</sup>, CDCl<sub>3</sub>) 3007, 2965, 2925, 1777, 1694, 1599, 1444, 1388, 1370, 1082, 1015, 910, 818.

HRMS (EI<sup>+</sup>)  $m/z$ : [M + H]<sup>+</sup> calculated for C<sub>12</sub>H<sub>19</sub>O<sub>2</sub>S<sub>2</sub>: 259.0821, found: 259.0819.

R<sub>f</sub> = 0.30 (EtOAc / PE = 1/5).

#### 4-(1,3-dioxoisindolin-2-yl)-2-((ethoxycarbonothioyl)thio)butyl acetate (**III-32a**)<sup>7</sup>



Chemical Formula: C<sub>17</sub>H<sub>19</sub>NO<sub>5</sub>S<sub>2</sub>

Exact Mass: 381.0705

According to the general procedure G, the reaction was carried out with *S*-((1,3-dioxoisindolin-2-yl)methyl)-*O*-ethyl-carbonodithioate (2.81 g, 10 mmol) and allyl acetate (2.0 g, 20 mmol) in DCE (10 mL), and needed 4 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (100:1 to 10:1) to afford product **III-32a** (1.91 g, 50%) as a light yellow oil.

**<sup>1</sup>H NMR** ( $\delta$ , ppm)(400 MHz, CDCl<sub>3</sub>)  $\delta$  7.82 – 7.77 (m, 2H, H<sub>1</sub>), 7.74 – 7.64 (m, 2H, H<sub>2</sub>), 4.64 – 4.50 (m, 2H, H<sub>8</sub>), 4.42 – 4.32 (m, 1H, H<sub>12</sub>), 4.24 (ddd,  $J = 11.4, 5.8, 1.4$  Hz, 1H, H<sub>12</sub>), 4.00 – 3.63 (m, 3H, H<sub>7</sub>, H<sub>5</sub>), 2.20 – 2.08 (m, 1H, H<sub>6</sub>), 2.08 – 1.92 (m, 4H, H<sub>10</sub>, H<sub>6</sub>), 1.35 (td,  $J = 7.0, 1.4$  Hz, 3H, H<sub>13</sub>).

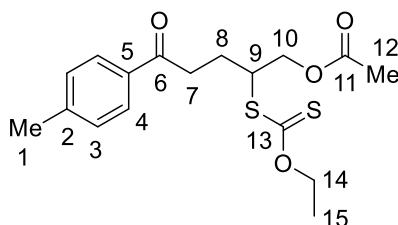
**<sup>13</sup>C NMR** ( $\delta$ , ppm)(100 MHz, CDCl<sub>3</sub>)  $\delta$  212.7 (C<sub>11</sub>), 170.7 (C<sub>9</sub>), 168.3 (C<sub>4</sub>), 134.1 (C<sub>3</sub>), 132.1 (C<sub>1</sub>), 123.4 (C<sub>2</sub>), 70.4 (C<sub>12</sub>), 65.2 (C<sub>8</sub>), 47.0 (C<sub>5</sub>), 35.7 (C<sub>7</sub>), 29.9 (C<sub>6</sub>), 20.9 (C<sub>10</sub>), 13.8 (C<sub>13</sub>).

**IR** ( $\nu$ , cm<sup>-1</sup>, CDCl<sub>3</sub>) 2940, 1772, 1741, 1706, 1614, 1467, 1436, 1395, 1364, 1217, 1111, 1045, 868, 793, 719.

**HRMS** (EI<sup>+</sup>)  $m/z$ : [M + Na]<sup>+</sup> calculated for C<sub>17</sub>H<sub>19</sub>NNaO<sub>5</sub>S<sub>2</sub>: 404.0597, found: 404.0585.

**R<sub>f</sub>** = 0.60 (EtOAc / PE = 1/5).

### 2-((ethoxycarbonothioyl)thio)-5-oxo-5-(p-tolyl)pentyl acetate (**III-32b**)



Chemical Formula: C<sub>17</sub>H<sub>22</sub>O<sub>4</sub>S<sub>2</sub>  
Exact Mass: 354.0960

According to the general procedure G, the reaction was carried out with *O*-ethyl *S*-(2-oxo-2-(*p*-tolyl)-ethyl)-carbonodithioate (2.54 g, 10 mmol) and allyl acetate (2.0 g, 20 mmol) in DCE (10 mL), and needed 3 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (100:1 to 20:1) to afford product **III-32b** (2.8 g, 79%) as a colorless oil.

**<sup>1</sup>H NMR** ( $\delta$ , ppm)(400 MHz, CDCl<sub>3</sub>)  $\delta$  7.92 – 7.74 (m, 2H, H<sub>4</sub>), 7.39 – 7.13 (m, 2H, H<sub>3</sub>), 4.75 – 4.49 (m, 2H, H<sub>10</sub>), 4.42 – 4.21 (m, 2H, H<sub>14</sub>), 4.17 – 3.96 (m, 1H, H<sub>9</sub>), 3.24 – 3.06 (m, 2H, H<sub>7</sub>), 2.41 (s, 3H, H<sub>1</sub>), 2.37 – 2.21 (m, 1H, H<sub>8</sub>), 2.07 (s, 3H, H<sub>12</sub>), 2.06 – 1.97 (m, 1H, H<sub>8</sub>), 1.40 (t,  $J = 7.0$  Hz, 3H, H<sub>15</sub>).

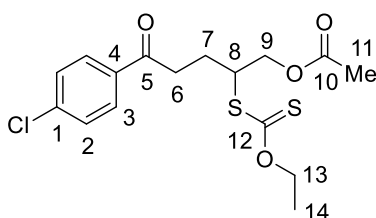
<sup>13</sup>C NMR ( $\delta$ , ppm)(100 MHz, CDCl<sub>3</sub>)  $\delta$  212.8 (C<sub>13</sub>), 198.3 (C<sub>6</sub>), 170.7 (C<sub>11</sub>), 144.0 (C<sub>2</sub>), 134.2 (C<sub>5</sub>), 129.3 (C<sub>3</sub>), 128.1 (C<sub>4</sub>), 70.3 (C<sub>14</sub>), 65.8 (C<sub>10</sub>), 49.0 (C<sub>9</sub>), 35.5 (C<sub>7</sub>), 25.1 (C<sub>8</sub>), 21.6 (C<sub>1</sub>), 20.8 (C<sub>12</sub>), 13.7 (C<sub>15</sub>).

IR ( $\nu$ , cm<sup>-1</sup>, CDCl<sub>3</sub>) 2936, 1741, 1681, 1606, 1573, 1444, 1408, 1380, 1363, 1216, 1180, 1110, 1043, 980, 807, 789.

HRMS (EI<sup>+</sup>)  $m/z$ : [M + Na]<sup>+</sup>calculated for C<sub>17</sub>H<sub>22</sub>NaO<sub>4</sub>S<sub>2</sub>: 377.0852, found: 377.0849.

R<sub>f</sub> = 0.80 (EtOAc / PE = 1/5).

### 5-(4-chlorophenyl)-2-((ethoxycarbonothioyl)thio)-5-oxopentyl acetate (**III-32c**)



Chemical Formula: C<sub>16</sub>H<sub>19</sub>ClO<sub>4</sub>S<sub>2</sub>  
Exact Mass: 374.0413

According to the general procedure G, the reaction was carried out with *S*-(2-(4-chlorophenyl)-2-oxoethyl)-*O*-ethyl-carbonodithioate (2.74 g, 10 mmol) and allyl acetate (2.0 g, 20 mmol) in DCE (10 mL), and needed 4 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (100:1 to 20:1) to afford product **III-32c** (3.25 g, 87%) as a light yellow oil.

<sup>1</sup>H NMR ( $\delta$ , ppm)(400 MHz, CDCl<sub>3</sub>)  $\delta$  7.89 – 7.84 (m, 2H, H<sub>3</sub>), 7.45 – 7.38 (m, 2H, H<sub>2</sub>), 4.60 (qd,  $J$  = 7.0, 2.4 Hz, 2H, H<sub>9</sub>), 4.38 – 4.21 (m, 2H, H<sub>13</sub>), 4.05 (ddt,  $J$  = 9.6, 6.2, 4.8 Hz, 1H, H<sub>8</sub>), 3.21 – 3.04 (m, 2H, H<sub>6</sub>), 2.35 – 2.23 (m, 1H, H<sub>7</sub>), 2.06 (s, 3H, H<sub>11</sub>), 2.04 – 1.95 (m, 1H, H<sub>7</sub>), 1.39 (t,  $J$  = 7.0 Hz, 3H, H<sub>14</sub>).

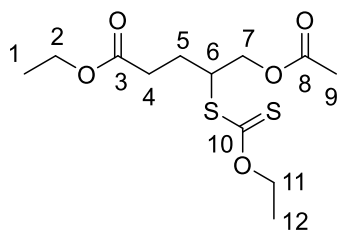
<sup>13</sup>C NMR ( $\delta$ , ppm)(100 MHz, CDCl<sub>3</sub>)  $\delta$  212.9 (C<sub>13</sub>), 197.5 (C<sub>5</sub>), 170.7 (C<sub>10</sub>), 139.7 (C<sub>4</sub>), 135.0 (C<sub>1</sub>), 129.5 (C<sub>3</sub>), 129.0 (C<sub>2</sub>), 70.5 (C<sub>13</sub>), 65.8 (C<sub>9</sub>), 49.1 (C<sub>8</sub>), 35.7 (C<sub>6</sub>), 25.0 (C<sub>7</sub>), 20.9 (C<sub>11</sub>), 13.8 (C<sub>14</sub>).

**IR** ( $\nu$ ,  $\text{cm}^{-1}$ ,  $\text{CDCl}_3$ ) 2929, 1739, 1683, 1588, 1571, 1487, 1443, 1363, 1211, 1176, 1147, 1110, 1090, 1041, 1012, 984, 838, 813, 795.

**HRMS** ( $\text{EI}^+$ )  $m/z$ :  $[\text{M} + \text{Na}]^+$  calculated for  $\text{C}_{16}\text{H}_{19}\text{ClNaO}_4\text{S}_2$ : 397.0305, found: 397.0298.

$R_f = 0.70$  (EtOAc / PE = 1/5).

**Ethyl-5-acetoxy-4-((ethoxycarbonothioyl)thio)pentanoate (III-32d)<sup>8</sup>**



Chemical Formula:  $\text{C}_{12}\text{H}_{20}\text{O}_5\text{S}_2$   
Exact Mass: 308.0752

According to the general procedure G, the reaction was carried out with ethyl 2-((ethoxycarbonothioyl)thio)-acetate (1.89 g, 9 mmol) and allyl acetate (1.84 g, 18 mmol) in DCE (9 mL), and needed 2 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (20:1 to 10:1) to afford product **III-32d** (2.05 g, 74%) as a colorless oil.

**$^1\text{H}$  NMR** ( $\delta$ , ppm)(400 MHz,  $\text{CDCl}_3$ )  $\delta$  4.62 (q,  $J = 7.0$  Hz, 2H,  $\text{H}_7$ ), 4.31 – 4.17 (m, 2H,  $\text{H}_2$ ), 4.11 (q,  $J = 7.0$  Hz, 2H,  $\text{H}_{11}$ ), 4.03 – 3.93 (m, 1H,  $\text{H}_6$ ), 2.55 – 2.37 (m, 2H,  $\text{H}_4$ ), 2.23 – 1.99 (m, 4H,  $\text{H}_5$ ,  $\text{H}_9$ ), 1.96 – 1.82 (m, 1H,  $\text{H}_5$ ), 1.40 (t,  $J = 7.0$  Hz, 3H,  $\text{H}_{12}$ ), 1.23 (t,  $J = 7.0$  Hz, 3H,  $\text{H}_1$ ).

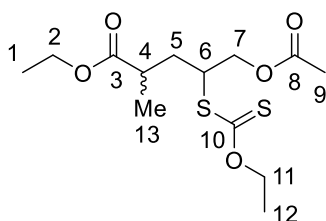
**$^{13}\text{C}$  NMR** ( $\delta$ , ppm)(100 MHz,  $\text{CDCl}_3$ )  $\delta$  212.8 ( $\text{C}_{10}$ ), 172.6 ( $\text{C}_3$ ), 170.7 ( $\text{C}_8$ ), 70.4 ( $\text{C}_{11}$ ), 65.6 ( $\text{C}_7$ ), 60.7 ( $\text{C}_2$ ), 48.9 ( $\text{C}_6$ ), 31.6 ( $\text{C}_4$ ), 26.1 ( $\text{C}_5$ ), 20.8 ( $\text{C}_9$ ), 14.3 ( $\text{C}_{12}$ ), 13.8 ( $\text{C}_1$ ).

**IR** ( $\nu$ ,  $\text{cm}^{-1}$ ,  $\text{CDCl}_3$ ) 2968, 1734, 1447, 1373, 1215, 1152, 1110, 1039, 855, 805.

**HRMS** ( $\text{EI}^+$ )  $m/z$ :  $[\text{M} + \text{Na}]^+$  calculated for  $\text{C}_{12}\text{H}_{20}\text{NaO}_5\text{S}_2$ : 331.0644, found: 331.0653.

$R_f = 0.80$  (EtOAc / PE = 1/5).

### Ethyl-5-acetoxy-4-((ethoxycarbonothioyl)thio)-2-methylpentanoate (III-32e)



Chemical Formula: C<sub>13</sub>H<sub>22</sub>O<sub>5</sub>S<sub>2</sub>  
Exact Mass: 322.0909

According to the general procedure G, the reaction was carried out with ethyl 2-((ethoxycarbonothioyl)thio)-propanoate (1.75 g, 7.9 mmol) and allyl acetate (1.58 g, 15.8 mmol) in DCE (8 mL), and needed 5 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (100:1 to 20:1) to afford product **III-32e** (1.57 g, 62%) as a colorless oil.

<sup>1</sup>H NMR (δ, ppm)(400 MHz, CDCl<sub>3</sub>) δ 4.65 – 4.56 (m, 2H, H<sub>7</sub>), 4.31 – 4.17 (m, 2H, H<sub>11</sub>), 4.16 – 4.07 (m, 2H, H<sub>2</sub>), 4.06 – 3.95 (m, 1H, H<sub>6</sub>), 2.73 – 2.54 (m, 1H, H<sub>4</sub>), 2.23 – 1.98 (m, 4H, H<sub>9</sub>, H<sub>5</sub>), 1.86 – 1.54 (m, 1H, H<sub>5</sub>), 1.40 (td, *J* = 7.0, 2.4 Hz, 3H, H<sub>12</sub>), 1.24 (td, *J* = 7.0, 3.4 Hz, 3H, H<sub>1</sub>), 1.18 (dd, *J* = 7.0, 4.4 Hz, 3H, H<sub>13</sub>).

<sup>13</sup>C NMR (δ, ppm)(100 MHz, CDCl<sub>3</sub>) δ 212.9 (C<sub>10</sub>), 212.9 (C<sub>10</sub>), 175.8 (C<sub>3</sub>), 175.8 (C<sub>3</sub>), 170.8 (C<sub>8</sub>), 170.7 (C<sub>8</sub>), 70.4 (C<sub>11</sub>), 70.3 (C<sub>11</sub>), 66.0 (C<sub>7</sub>), 65.8 (C<sub>7</sub>), 60.7 (C<sub>2</sub>), 48.0 (C<sub>6</sub>), 47.4 (C<sub>6</sub>), 37.2 (C<sub>4</sub>), 37.1 (C<sub>4</sub>), 34.6 (C<sub>5</sub>), 34.1 (C<sub>5</sub>), 20.9 (C<sub>9</sub>), 18.1 (C<sub>9</sub>), 17.0 (C<sub>13</sub>), 14.3 (C<sub>12</sub>), 14.3 (C<sub>12</sub>), 13.8 (C<sub>1</sub>).

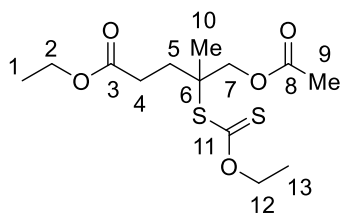
IR (ν, cm<sup>-1</sup>, CDCl<sub>3</sub>) 2979, 1730, 1461, 1379, 1227, 1210, 1110, 1038, 854, 732.

HRMS (EI<sup>+</sup>) *m/z*: [M + Na]<sup>+</sup>calculated for C<sub>13</sub>H<sub>22</sub>NaO<sub>5</sub>S<sub>2</sub>: 345.0801, found: 345.0795.

R<sub>f</sub> = 0.50 (EtOAc / PE = 1/5).

### Ethyl-5-acetoxy-4-((ethoxycarbonothioyl)thio)-4-methylpentanoate (III-32f)





Chemical Formula: C<sub>13</sub>H<sub>22</sub>O<sub>5</sub>S<sub>2</sub>  
Exact Mass: 322.0909

According to the general procedure G, the reaction was carried out with ethyl 2-((ethoxycarbonothioyl)thio)-acetate (3.33 g, 16 mmol) and 2-methylallyl acetate (3.60 g, 32 mmol) in DCE (16 mL), and needed 4 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (100:1 to 100:7) to afford product **III-32f** (1.29 g, 25%) as a colorless oil.

<sup>1</sup>H NMR (δ, ppm)(400 MHz, CDCl<sub>3</sub>) δ 4.65 (qd, *J* = 7.0, 2.4 Hz, 2H, H<sub>7</sub>), 4.37 (q, *J* = 7.0 Hz, 2H, H<sub>2</sub>), 4.11 (q, *J* = 7.2 Hz, 2H, H<sub>12</sub>), 2.54 – 2.22 (m, 3H, H<sub>4</sub>, H<sub>5</sub>), 2.12 – 1.95 (m, 4H, H<sub>5</sub>, H<sub>9</sub>), 1.45 (t, *J* = 7.0 Hz, 3H, H<sub>13</sub>), 1.35 (s, 3H, H<sub>1</sub>), 1.24 (t, *J* = 7.0 Hz, 3H, H<sub>10</sub>).

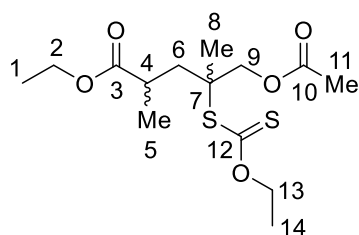
<sup>13</sup>C NMR (δ, ppm)(100 MHz, CDCl<sub>3</sub>) δ 211.6 (C<sub>11</sub>), 172.9 (C<sub>3</sub>), 170.6 (C<sub>8</sub>), 70.1 (C<sub>12</sub>), 68.6 (C<sub>7</sub>), 60.8 (C<sub>2</sub>), 56.2 (C<sub>6</sub>), 31.6 (C<sub>5</sub>), 29.6 (C<sub>4</sub>), 22.1 (C<sub>10</sub>), 20.9 (C<sub>9</sub>), 14.3 (C<sub>1</sub>), 13.7 (C<sub>13</sub>)

IR (ν, cm<sup>-1</sup>, CDCl<sub>3</sub>) 2980, 2934, 1732, 1446, 1373, 1292, 1219, 1183, 1113, 1035, 854.

HRMS (EI<sup>+</sup>) *m/z*: [M + Na]<sup>+</sup>calculated for C<sub>13</sub>H<sub>22</sub>NaO<sub>5</sub>S<sub>2</sub>: 345.0801, found: 345.0797.

R<sub>f</sub> = 0.60 (EtOAc / PE = 1/5).

**Ethyl-5-acetoxy-4-((ethoxycarbonothioyl)thio)-2,4-dimethylpentanoate (III-32g)**



Chemical Formula: C<sub>14</sub>H<sub>24</sub>O<sub>5</sub>S<sub>2</sub>  
Exact Mass: 336.1065

According to the general procedure G, the reaction was carried out with ethyl 2-((ethoxycarbonothioyl)thio)-propanoate (8.88 g, 40 mmol) and 2-methylallyl acetate (2.282 g, 20 mmol) in DCE (20 mL), and needed 3 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (100:1 to 20:1) to afford product **III-32g** (2.69 g, 40%) as a light yellow oil.

<sup>1</sup>H NMR (δ, ppm)(400 MHz, CDCl<sub>3</sub>) δ 4.68 – 4.56 (m, 2H, H<sub>9</sub>), 4.40 – 4.26 (m, 2H, H<sub>13</sub>), 4.16 – 4.04 (m, 2H, H<sub>2</sub>), 2.78 – 2.31 (m, 2H, H<sub>4</sub>, H<sub>6</sub>), 2.07 (d, *J* = 2.2 Hz, 3H, H<sub>11</sub>), 1.93 – 1.59 (m, 1H, H<sub>6</sub>), 1.46 (td, *J* = 7.0, 4.6 Hz, 3H, H<sub>14</sub>), 1.33 (d, *J* = 26.2 Hz, 3H, H<sub>1</sub>), 1.24 (td, *J* = 7.0, 2.8 Hz, 3H, H<sub>5</sub>), 1.19 – 1.16 (m, 3H, H<sub>8</sub>).

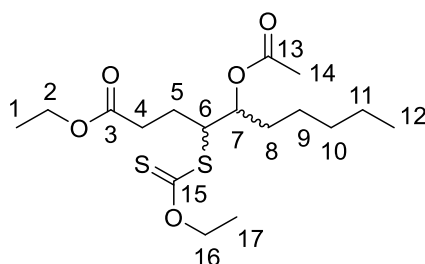
<sup>13</sup>C NMR (δ, ppm)(100 MHz, CDCl<sub>3</sub>) δ 211.9 (C<sub>12</sub>), 211.8 (C<sub>12</sub>), 176.8 (C<sub>3</sub>), 176.5 (C<sub>3</sub>), 170.6 (C<sub>10</sub>), 170.6 (C<sub>10</sub>), 70.1 (C<sub>13</sub>), 70.0 (C<sub>13</sub>), 68.7 (C<sub>9</sub>), 68.5 (C<sub>9</sub>), 60.9 (C<sub>2</sub>), 60.8 (C<sub>2</sub>), 57.1 (C<sub>7</sub>), 56.4 (C<sub>7</sub>), 40.3 (C<sub>4</sub>), 39.8 (C<sub>4</sub>), 35.9 (C<sub>6</sub>), 35.9 (C<sub>6</sub>), 22.5 (C<sub>8</sub>), 21.7 (C<sub>8</sub>), 20.9 (C<sub>11</sub>), 20.9 (C<sub>11</sub>), 20.3 (C<sub>5</sub>), 20.2 (C<sub>5</sub>), 14.2 (C<sub>14</sub>), 13.8 (C<sub>14</sub>), 13.7 (C<sub>1</sub>).

IR (ν, cm<sup>-1</sup>, CDCl<sub>3</sub>) 2977, 2936, 1730, 1461, 1373, 1219, 1179, 1113, 1035, 1002, 912, 855, 763.

HRMS (EI<sup>+</sup>) *m/z*: [M + Na]<sup>+</sup>calculated for C<sub>14</sub>H<sub>24</sub>NaO<sub>5</sub>S<sub>2</sub>: 359.0957, found: 359.0961.

R<sub>f</sub> = 0.50 (EtOAc / PE = 1/5).

### Ethyl-5-acetoxy-4-((ethoxycarbonothioyl)thio)decanoate (**III-32h**)



Chemical Formula: C<sub>17</sub>H<sub>30</sub>O<sub>5</sub>S<sub>2</sub>  
Exact Mass: 378.1535

According to the general procedure G, the reaction was carried out with ethyl 2-((ethoxycarbonothioyl)thio)-acetate (1.04 g, 5 mmol) and oct-1-en-3-yl acetate (1.70 g, 10 mmol) in DCE (5 mL), and needed 3 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (100:1 to 20:1) to afford product **III-32h** (1.51 g, 80%) as a colorless oil.

<sup>1</sup>H NMR (δ, ppm)(400 MHz, CDCl<sub>3</sub>) δ 5.17 (ddd, *J* = 7.8, 5.6, 2.8 Hz, 1H, H<sub>7</sub>), 4.66 (qd, *J* = 7.0, 0.8 Hz, 2H, H<sub>2</sub>), 4.24 – 3.98 (m, 3H, H<sub>16</sub>, H<sub>6</sub>), 2.58 – 2.37 (m, 2H, H<sub>4</sub>), 2.07 (s, 3H, H<sub>14</sub>), 1.93 – 1.80 (m, 1H, H<sub>5</sub>), 1.72 – 1.60 (m, 2H, H<sub>8</sub>), 1.43 (t, *J* = 7.0 Hz, 3H, H<sub>1</sub>), 1.34 – 1.20 (m, 10H, H<sub>5</sub>, H<sub>17</sub>, H<sub>9</sub>, H<sub>10</sub>, H<sub>11</sub>), 0.94 – 0.79 (m, 3H, H<sub>12</sub>).

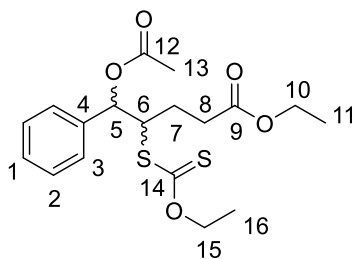
<sup>13</sup>C NMR (δ, ppm)(100 MHz, CDCl<sub>3</sub>) δ 213.9 (C<sub>15</sub>), 213.8 (C<sub>15</sub>), 173.4 (C<sub>3</sub>), 172.9 (C<sub>3</sub>), 172.8 (C<sub>13</sub>), 170.9 (C<sub>13</sub>), 170.6 (C<sub>7</sub>), 170.4 (C<sub>7</sub>), 75.4 (C<sub>2</sub>), 75.1 (C<sub>2</sub>), 73.8 (C<sub>16</sub>), 70.5 (C<sub>16</sub>), 70.4 (C<sub>6</sub>), 60.6 (C<sub>6</sub>), 60.6 (C<sub>4</sub>), 60.4 (C<sub>4</sub>), 53.8 (C<sub>14</sub>), 53.8 (C<sub>14</sub>), 34.1, 34.0, 33.5, 31.9, 31.7, 31.7, 31.6, 31.6, 31.6, 31.6, 31.4, 27.4, 25.3, 25.3, 25.0, 24.4, 22.6, 22.6, 22.5, 21.3, 21.1, 21.0, 20.8, 14.3, 14.3, 14.1, 14.1, 14.0, 13.8.

IR (ν, cm<sup>-1</sup>, CDCl<sub>3</sub>) 2955, 2931, 2860, 1733, 1446, 1371, 1292, 1225, 1211, 1156, 1110, 1044, 1019, 853.

HRMS (EI<sup>+</sup>) *m/z*: [M + Na]<sup>+</sup>calculated for C<sub>17</sub>H<sub>30</sub>NaO<sub>5</sub>S<sub>2</sub>: 401.1427, found: 401.1412.

R<sub>f</sub> = 0.50 (EtOAc / PE = 1/10).

**Ethyl-5-acetoxy-4-((ethoxycarbonothioyl)thio)-5-phenylpentanoate (III-32i)**



Chemical Formula: C<sub>18</sub>H<sub>24</sub>O<sub>5</sub>S<sub>2</sub>  
Exact Mass: 384.1065

According to the general procedure G, the reaction was carried out with ethyl 2-((ethoxycarbonothioyl)thio)-acetate (2.08 g, 10 mmol) and 1-phenylallyl acetate (3.52 g, 20 mmol) in DCE (10 mL), and needed 3 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (100:1 to 100:7) to afford product **III-32i** (2.96 g, 77%) as a light yellow oil.

<sup>1</sup>H NMR (δ, ppm)(400 MHz, CDCl<sub>3</sub>) δ 7.38 – 7.26 (m, 5H, H<sub>2</sub>, H<sub>1</sub>, H<sub>3</sub>), 6.19 – 5.95 (m, 1H, H<sub>5</sub>), 4.72 – 4.44 (m, 2H, H<sub>10</sub>), 4.33 – 4.00 (m, 3H, H<sub>15</sub>, H<sub>6</sub>), 2.58 – 2.25 (m, 2H, H<sub>8</sub>), 2.19 – 2.01 (m, 4H, H<sub>7</sub>, H<sub>13</sub>), 1.92 – 1.70 (m, 1H, H<sub>7</sub>), 1.40 (dt, *J* = 27.2, 7.0 Hz, 3H, H<sub>16</sub>), 1.21 (dt, *J* = 17.6, 7.0 Hz, 3H, H<sub>11</sub>).

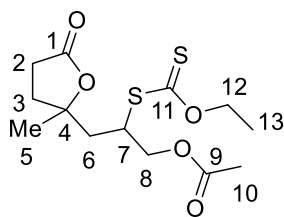
<sup>13</sup>C NMR (δ, ppm)(100 MHz, CDCl<sub>3</sub>) δ 213.6 (C<sub>14</sub>), 213.0 (C<sub>14</sub>), 172.7 (C<sub>9</sub>), 172.7 (C<sub>9</sub>), 169.8 (C<sub>12</sub>), 169.7 (C<sub>12</sub>), 137.6 (C<sub>4</sub>), 137.6 (C<sub>4</sub>), 128.6 (C<sub>2</sub>), 128.5 (C<sub>2</sub>), 128.4 (C<sub>1</sub>), 128.2 (C<sub>1</sub>), 127.1 (C<sub>3</sub>), 126.2 (C<sub>3</sub>), 76.6 (C<sub>5</sub>), 76.4 (C<sub>5</sub>), 70.5 (C<sub>15</sub>), 70.4 (C<sub>15</sub>), 60.7 (C<sub>10</sub>), 60.6 (C<sub>10</sub>), 55.5 (C<sub>6</sub>), 55.1 (C<sub>6</sub>), 31.8 (C<sub>8</sub>), 31.6 (C<sub>8</sub>), 26.4 (C<sub>7</sub>), 23.0 (C<sub>7</sub>), 21.1 (C<sub>13</sub>), 21.0 (C<sub>13</sub>), 14.3 (C<sub>16</sub>), 14.3 (C<sub>16</sub>), 13.9 (C<sub>11</sub>), 13.8 (C<sub>11</sub>).

IR (ν, cm<sup>-1</sup>, CDCl<sub>3</sub>) 2981, 2935, 1731, 1451, 1372, 1290, 1213, 1150, 1111, 1043, 951, 854.

HRMS (EI<sup>+</sup>) *m/z*: [M + Na]<sup>+</sup>calculated for C<sub>18</sub>H<sub>24</sub>NaO<sub>5</sub>S<sub>2</sub>: 407.0957, found: 407.0958.

R<sub>f</sub> = 0.45 (EtOAc / PE = 1/10).

**2-((ethoxycarbonothioyl)-thio)-3-(2-methyl-5-oxotetrahydrofuran-2-yl)-propyl acetate (III-32j)<sup>9</sup>**



Chemical Formula: C<sub>13</sub>H<sub>20</sub>O<sub>5</sub>S<sub>2</sub>  
Exact Mass: 320.0752

According to the general procedure G, the reaction was carried out with *O*-ethyl *S*-(2-methyl-5-oxotetrahydrofuran-2-yl)-carbonodithioate (1.1 g, 5.0 mmol) and allyl acetate (1.98 g, 10 mmol) in DCE (5 mL), and needed 4 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (20:1 to 6:1) to afford product **III-32j** (1.07 g, 67%) as a colorless oil.

<sup>1</sup>H NMR (δ, ppm)(400 MHz, CDCl<sub>3</sub>) δ 4.63 (q, *J* = 7.0 Hz, 2H, H<sub>8</sub>), 4.37 – 3.97 (m, 3H, H<sub>12</sub>, H<sub>7</sub>), 2.74 – 2.46 (m, 2H, H<sub>2</sub>), 2.37 – 1.92 (m, 7H, H<sub>3</sub>, H<sub>10</sub>, H<sub>6</sub>), 1.55 – 1.33 (m, 6H, H<sub>5</sub>, H<sub>13</sub>).

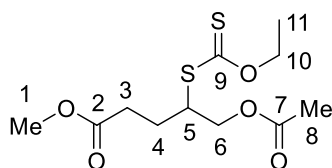
<sup>13</sup>C NMR (δ, ppm)(100 MHz, CDCl<sub>3</sub>) δ 212.6 (C<sub>11</sub>), 176.1 (C<sub>1</sub>), 176.0 (C<sub>1</sub>), 170.6 (C<sub>9</sub>), 170.6 (C<sub>9</sub>), 85.6 (C<sub>4</sub>), 85.3 (C<sub>4</sub>), 70.6 (C<sub>12</sub>), 70.5 (C<sub>12</sub>), 66.2 (C<sub>8</sub>), 65.7 (C<sub>8</sub>), 45.4 (C<sub>7</sub>), 44.9 (C<sub>7</sub>), 41.5 (C<sub>3</sub>), 40.9 (C<sub>3</sub>), 34.5 (C<sub>6</sub>), 32.7 (C<sub>6</sub>), 29.0 (C<sub>2</sub>), 28.8 (C<sub>2</sub>), 26.7 (C<sub>5</sub>), 25.1 (C<sub>5</sub>), 20.9 (C<sub>10</sub>), 20.8 (C<sub>10</sub>), 13.8 (C<sub>13</sub>).

IR (ν, cm<sup>-1</sup>, CDCl<sub>3</sub>) 2962, 1767, 1738, 1450, 1383, 1364, 1217, 1147, 1109, 1040, 938, 853, 801.

HRMS (EI<sup>+</sup>) *m/z*: [M + H]<sup>+</sup> calculated for C<sub>13</sub>H<sub>21</sub>O<sub>5</sub>S<sub>2</sub>: 321.0825, found: 321.0821.

R<sub>f</sub> = 0.50 (EtOAc / PE = 1/2).

### Methyl-5-acetoxy-4-((ethoxycarbonothioyl)thio)-pentanoate (**III-32k**)



Chemical Formula: C<sub>11</sub>H<sub>18</sub>O<sub>5</sub>S<sub>2</sub>  
Exact Mass: 294.0596

According to the general procedure G, the reaction was carried out with methyl 2-((ethoxycarbonothioyl)thio)-acetate (1.94 g, 10 mmol) and allyl acetate ( 2.0 g, 20 mmol) in DCE (10 mL), and needed 3 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (100:1 to 100:7) to afford product **III-32k** (1.88 g, 64%) as a light yellow oil.

$^1\text{H NMR}$  ( $\delta$ , ppm)(400 MHz,  $\text{CDCl}_3$ )  $\delta$  4.62 (q,  $J = 7.0$  Hz, 2H,  $\text{H}_{10}$ ), 4.32 – 4.16 (m, 2H,  $\text{H}_6$ ), 3.98 (ddt,  $J = 9.8, 6.2, 4.8$  Hz, 1H,  $\text{H}_5$ ), 3.66 (s, 3H,  $\text{H}_1$ ), 2.57 – 2.39 (m, 2H,  $\text{H}_3$ ), 2.22 – 2.09 (m, 1H,  $\text{H}_4$ ), 2.05 (s, 3H,  $\text{H}_8$ ), 1.97 – 1.84 (m, 1H,  $\text{H}_4$ ), 1.40 (t,  $J = 7.0$  Hz, 3H,  $\text{H}_{11}$ ).

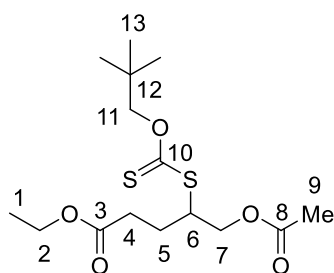
$^{13}\text{C NMR}$  ( $\delta$ , ppm)(100 MHz,  $\text{CDCl}_3$ )  $\delta$ . 212.8 ( $\text{C}_9$ ), 173.1 ( $\text{C}_2$ ), 170.7 ( $\text{C}_7$ ), 70.4 ( $\text{C}_{10}$ ), 65.6 ( $\text{C}_6$ ), 51.9 ( $\text{C}_1$ ), 48.8 ( $\text{C}_5$ ), 31.3 ( $\text{C}_3$ ), 26.1 ( $\text{C}_4$ ), 20.9 ( $\text{C}_8$ ), 13.8 ( $\text{C}_{11}$ )

$\text{IR}$  ( $\nu$ ,  $\text{cm}^{-1}$ ,  $\text{CDCl}_3$ ) 2952, 1735, 1437, 1380, 1364, 1210, 1110, 1043, 847.

$\text{HRMS}$  ( $\text{EI}^+$ )  $m/z$ :  $[\text{M} + \text{Na}]^+$  calculated for  $\text{C}_{11}\text{H}_{18}\text{NaO}_5\text{S}_2$ : 317.0488, found: 317.0488.

$R_f = 0.35$  (EtOAc / PE = 1/8).

### Ethyl-5-acetoxy-4-(((neopentyloxy)carbonothioyl)thio)pentanoate (**III-32l**)



Chemical Formula:  $\text{C}_{15}\text{H}_{26}\text{O}_5\text{S}_2$   
Exact Mass: 350.1222

According to the general procedure G, the reaction was carried out with ethyl 2-(((neopentyloxy)carbonothioyl)thio)-acetate (1.96 g, 7.838 mmol) and allyl acetate (1.57 g, 15.68 mmol) in DCE (8 mL), and needed 8 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (100:1 to 20:1) to afford product **III-32l** (1.78 g, 65%) as a light yellow oil.

**<sup>1</sup>H NMR** ( $\delta$ , ppm)(400 MHz, CDCl<sub>3</sub>)  $\delta$  4.34 – 4.21 (m, 4H, H<sub>7</sub>, H<sub>11</sub>), 4.14 (q,  $J$  = 7.0 Hz, 2H, H<sub>2</sub>), 4.08 – 4.00 (m, 1H, H<sub>6</sub>), 2.59 – 2.42 (m, 2H, H<sub>4</sub>), 2.25 – 2.12 (m, 1H, H<sub>5</sub>), 2.08 (s, 3H, H<sub>9</sub>), 2.00 – 1.85 (m, 1H, H<sub>5</sub>), 1.26 (t,  $J$  = 7.0 Hz, 3H, H<sub>1</sub>), 1.01 (s, 9H, H<sub>13</sub>).

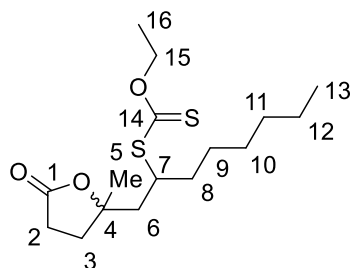
**<sup>13</sup>C NMR** ( $\delta$ , ppm)(100 MHz, CDCl<sub>3</sub>)  $\delta$  213.1 (C<sub>10</sub>), 172.6 (C<sub>3</sub>), 170.7 (C<sub>8</sub>), 83.7 (C<sub>11</sub>), 65.7 (C<sub>7</sub>), 60.7 (C<sub>2</sub>), 48.7 (C<sub>6</sub>), 31.9 (C<sub>4</sub>), 31.6 (C<sub>12</sub>), 26.6 (C<sub>5</sub>), 26.1 (C<sub>13</sub>), 20.9 (C<sub>9</sub>), 14.3 (C<sub>1</sub>).

**IR** ( $\nu$ , cm<sup>-1</sup>, CDCl<sub>3</sub>) 2959, 1733, 1465, 1366, 1273, 1224, 1213, 1183, 1063, 1025, 950, 932, 906, 856.

**HRMS** (EI<sup>+</sup>)  $m/z$ : [M + Na]<sup>+</sup> calculated for C<sub>15</sub>H<sub>26</sub>NaO<sub>5</sub>S<sub>2</sub>: 373.1114, found: 373.1113.

**R<sub>f</sub>** = 0.30 (EtOAc / PE = 1/8).

***O*-ethyl-*S*-(1-(2-methyl-5-oxotetrahydrofuran-2-yl)-octan-2-yl)-carbonodithioate  
(III-32m)**



Chemical Formula: C<sub>16</sub>H<sub>28</sub>O<sub>3</sub>S<sub>2</sub>  
Exact Mass: 332.1480

According to the general procedure G, the reaction was carried out with *O*-ethyl *S*-(2-methyl-5-oxotetrahydrofuran-2-yl)-carbonodithioate (1.1 g, 5 mmol) and oct-1-ene (1.12 g, 10 mmol) in DCE (5 mL), and needed 4 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (100:1 to 100:7) to afford product **III-32m** (1.25 g, 75%) as a colorless oil.

**<sup>1</sup>H NMR** ( $\delta$ , ppm)(400 MHz, CDCl<sub>3</sub>)  $\delta$  4.62 (q,  $J$  = 7.0 Hz, 2H, H<sub>15</sub>), 3.92 – 3.67 (m, 1H, H<sub>7</sub>), 2.69 – 2.24 (m, 2H, H<sub>2</sub>), 2.17 – 1.59 (m, 6H, H<sub>3</sub>, H<sub>5</sub>, H<sub>6</sub>), 1.51 – 1.17 (m, 14H, H<sub>6</sub>, H<sub>8</sub>, H<sub>9</sub>, H<sub>10</sub>, H<sub>11</sub>, H<sub>12</sub>, H<sub>16</sub>), 0.85 (t,  $J$  = 7.0 Hz, 3H, H<sub>13</sub>).

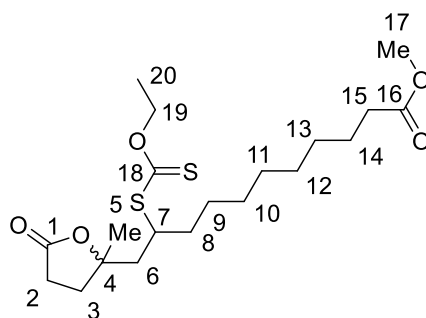
<sup>13</sup>C NMR ( $\delta$ , ppm)(100 MHz, CDCl<sub>3</sub>)  $\delta$  214.3 (C<sub>14</sub>), 214.2 (C<sub>14</sub>), 176.4 (C<sub>1</sub>), 176.4 (C<sub>1</sub>), 86.3 (C<sub>4</sub>), 86.0 (C<sub>4</sub>), 70.0 (C<sub>15</sub>), 70.0 (C<sub>15</sub>), 47.5 (C<sub>7</sub>), 46.8 (C<sub>7</sub>), 45.2 (C<sub>2</sub>), 44.4 (C<sub>2</sub>), 36.1 (C<sub>3</sub>), 34.9 (C<sub>6</sub>), 34.8 (C<sub>6</sub>), 32.5 (C<sub>5</sub>), 31.8 (C<sub>8</sub>), 31.7 (C<sub>8</sub>), 29.2 (C<sub>9</sub>), 29.1 (C<sub>9</sub>), 29.1 (C<sub>10</sub>), 28.8 (C<sub>10</sub>), 27.2 (C<sub>11</sub>), 26.8 (C<sub>11</sub>), 24.9 (C<sub>12</sub>), 22.6 (C<sub>12</sub>), 14.1 (C<sub>16</sub>), 13.9 (C<sub>13</sub>).

IR ( $\nu$ , cm<sup>-1</sup>, CDCl<sub>3</sub>) 2954, 2925, 2855, 1771, 1456, 1422, 1383, 1363, 1290, 1211, 1145, 1110, 1046, 1003, 941, 801, 726.

HRMS (EI<sup>+</sup>) m/z: [M + H]<sup>+</sup> calculated for C<sub>16</sub>H<sub>29</sub>O<sub>3</sub>S<sub>2</sub>: 333.1553, found: 333.1554.

R<sub>f</sub> = 0.60 (EtOAc / PE = 1/4).

**Methyl-10-((ethoxycarbonothioyl)-thio)-11-(2-methyl-5-oxotetrahydrofuran-2-yl)undecanoate (III-32n)<sup>9</sup>**



Chemical Formula: C<sub>20</sub>H<sub>34</sub>O<sub>5</sub>S<sub>2</sub>  
Exact Mass: 418.1848

According to the general procedure G, the reaction was carried out with *O*-ethyl *S*-(2-methyl-5-oxotetrahydrofuran-2-yl)-carbonodithioate (1.1 g, 5 mmol) and methyl undec-10-enoate (1.98 g, 10 mmol) in DCE (5 mL), and needed 5 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (10:1 to 5:1) to afford product **III-32n** (1.46 g, 70%) as a light yellow oil.

<sup>1</sup>H NMR ( $\delta$ , ppm)(400 MHz, CDCl<sub>3</sub>)  $\delta$  4.66 – 4.55 (m, 2H, H<sub>19</sub>), 3.91 – 3.71 (m, 1H, H<sub>7</sub>), 3.63 (s, 3H, H<sub>17</sub>), 2.72 – 2.46 (m, 2H, H<sub>2</sub>), 2.41 – 2.23 (m, 2H, H<sub>15</sub>), 2.18 – 1.53 (m, 7H, H<sub>3</sub>, H<sub>6</sub>, H<sub>14</sub>, H<sub>8</sub>), 1.50 – 1.17 (m, 17H, H<sub>8</sub>, H<sub>5</sub>, H<sub>12</sub>, H<sub>20</sub>, H<sub>13</sub>, H<sub>9</sub>, H<sub>10</sub>, H<sub>11</sub>).

<sup>13</sup>C NMR ( $\delta$ , ppm)(100 MHz, CDCl<sub>3</sub>)  $\delta$  214.2 (C<sub>18</sub>), 214.1 (C<sub>18</sub>), 176.9 (C<sub>16</sub>), 176.4



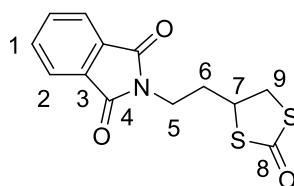
(C<sub>16</sub>), 176.4 (C<sub>1</sub>), 174.4 (C<sub>1</sub>), 88.7 (C<sub>19</sub>), 87.0 (C<sub>19</sub>), 86.3 (C<sub>7</sub>), 86.0 (C<sub>7</sub>), 70.0 (C<sub>17</sub>), 70.0 (C<sub>17</sub>), 51.5 (C<sub>4</sub>), 47.5 (C<sub>4</sub>), 46.8 (C<sub>2</sub>), 45.2 (C<sub>2</sub>), 44.4 (C<sub>15</sub>), 41.0 (C<sub>15</sub>), 36.0 (C<sub>3</sub>), 34.8 (C<sub>3</sub>), 34.8 (C<sub>6</sub>), 34.1 (C<sub>6</sub>), 33.0, 32.5, 29.9, 29.8, 29.5, 29.4, 29.4, 29.3, 29.3, 29.3, 29.3, 29.2, 29.2, 29.1, 28.7, 27.2, 26.7, 25.7, 25.0, 25.0, 24.9, 23.9, 21.2, 13.9.

**IR** ( $\nu$ , cm<sup>-1</sup>, CDCl<sub>3</sub>) 2926, 2854, 1770, 1735, 1447, 1383, 1362, 1211, 1171, 1110, 1047, 1004, 940, 772.

**HRMS** (EI<sup>+</sup>) m/z: [M + H]<sup>+</sup> calculated for C<sub>20</sub>H<sub>35</sub>O<sub>5</sub>S<sub>2</sub>: 419.1920, found: 419.1912.

**R<sub>f</sub>** = 0.40 (EtOAc / PE = 1/4).

### 2-(2-(2-oxo-1,3-dithiolan-4-yl)ethyl)isoindoline-1,3-dione (**III-33a**)



Chemical Formula: C<sub>13</sub>H<sub>11</sub>NO<sub>3</sub>S<sub>2</sub>  
Exact Mass: 293.0180

According to the general procedure H, the reaction was carried out with adduct **III-32a** (598 mg, 1.569 mmol) in methanesulfonic acid : acetic acid (9:1; 1.0 mL), and needed 120 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (10:1 to 5:1) to afford product **III-33a** (340 mg, 74%) as a white solid.

**<sup>1</sup>H NMR** ( $\delta$ , ppm)(400 MHz, CDCl<sub>3</sub>)  $\delta$  7.86 – 7.80 (m, 2H, H<sub>1</sub>), 7.77 – 7.69 (m, 2H, H<sub>2</sub>), 4.04 (dtd,  $J$  = 8.2, 6.4, 5.2 Hz, 1H, H<sub>7</sub>), 3.93 – 3.75 (m, 3H, H<sub>5</sub>, H<sub>9</sub>), 3.47 (dd,  $J$  = 12.0, 6.4 Hz, 1H, H<sub>9</sub>), 2.42 – 2.16 (m, 2H, H<sub>6</sub>).

**<sup>13</sup>C NMR** ( $\delta$ , ppm)(100 MHz, CDCl<sub>3</sub>)  $\delta$  197.1 (C<sub>8</sub>), 168.3 (C<sub>4</sub>), 134.4 (C<sub>3</sub>), 131.9 (C<sub>1</sub>), 123.6 (C<sub>2</sub>), 50.2 (C<sub>5</sub>), 40.9 (C<sub>7</sub>), 35.9 (C<sub>9</sub>), 33.7 (C<sub>6</sub>).

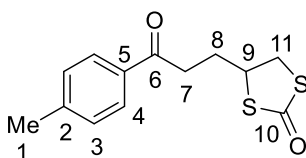
**IR** ( $\nu$ , cm<sup>-1</sup>, CDCl<sub>3</sub>) 2937, 1770, 1704, 1644, 1467, 1434, 1395, 1360, 1332, 1301, 1188, 1108, 1028, 922, 872, 852, 718.

**HRMS** (EI<sup>+</sup>) m/z: [M + H]<sup>+</sup> calculated for C<sub>13</sub>H<sub>12</sub>NO<sub>3</sub>S<sub>2</sub>: 294.0253, found: 294.0244.

**MP:** 136-138 °C.

**R<sub>f</sub>** = 0.50 (EtOAc / PE = 1/5).

**4-(3-oxo-3-(p-tolyl)-propyl)-1,3-dithiolan-2-one (III-33b)**



Chemical Formula: C<sub>13</sub>H<sub>14</sub>O<sub>2</sub>S<sub>2</sub>  
Exact Mass: 266.0435

According to the general procedure H, the reaction was carried out with adduct **III-32b** (1110 mg, 3.13 mmol) in methanesulfonic acid : acetic acid (9:1; 1.0 mL), and needed 96 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (100:1 to 100:7) to afford product **III-33b** (599 mg, 72%) as a colorless oil.

**<sup>1</sup>H NMR** (δ, ppm)(400 MHz, CDCl<sub>3</sub>) δ 7.85 – 7.81 (m, 2H, H<sub>4</sub>), 7.30 – 7.22 (m, 2H, H<sub>3</sub>), 4.30 – 4.16 (m, 1H, H<sub>9</sub>), 3.81 (dd, *J* = 11.8, 5.2 Hz, 1H, H<sub>11</sub>), 3.48 (dd, *J* = 11.8, 6.6 Hz, 1H, H<sub>11</sub>), 3.25 – 3.02 (m, 2H, H<sub>7</sub>), 2.41 (s, 3H, H<sub>1</sub>), 2.39 – 2.23 (m, 2H, H<sub>8</sub>).

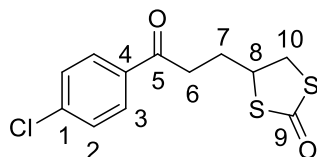
**<sup>13</sup>C NMR** (δ, ppm)(100 MHz, CDCl<sub>3</sub>) δ 197.9 (C<sub>6</sub>), 197.2 (C<sub>10</sub>), 144.5 (C<sub>2</sub>), 134.0 (C<sub>5</sub>), 129.5 (C<sub>3</sub>), 128.2 (C<sub>4</sub>), 52.5 (C<sub>9</sub>), 41.5 (C<sub>11</sub>), 36.1 (C<sub>7</sub>), 28.9 (C<sub>8</sub>), 21.8 (C<sub>1</sub>).

**IR** (ν, cm<sup>-1</sup>, CDCl<sub>3</sub>) 2920, 1726, 1676, 1640, 1605, 1572, 1428, 1407, 1368, 1330, 1289, 1230, 1205, 1180, 1120, 1002, 972, 857, 826, 777.

**HRMS** (EI<sup>+</sup>) *m/z*: [M + H]<sup>+</sup> calculated for C<sub>13</sub>H<sub>15</sub>O<sub>2</sub>S<sub>2</sub>: 267.0508, found: 267.0501.

**R<sub>f</sub>** = 0.70 (EtOAc / PE = 1/5).

**4-(3-(4-chlorophenyl)-3-oxopropyl)-1,3-dithiolan-2-one (III-33c)**



Chemical Formula: C<sub>12</sub>H<sub>11</sub>ClO<sub>2</sub>S<sub>2</sub>

Exact Mass: 285.9889

According to the general procedure H, the reaction was carried out with adduct **III-32c** (748 mg, 2.0 mmol) in methanesulfonic acid : acetic acid (9:1; 1.0 mL), and needed 54 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (100:1 to 100:6) to afford product **III-33c** (400 mg, 70%) as a white solid.

<sup>1</sup>H NMR (δ, ppm)(400 MHz, CDCl<sub>3</sub>) δ 7.89 – 7.85 (m, 2H, H<sub>3</sub>), 7.46 – 7.40 (m, 2H, H<sub>2</sub>), 4.34 – 4.17 (m, 1H, H<sub>8</sub>), 3.82 (dd, *J* = 11.8, 5.2 Hz, 1H, H<sub>10</sub>), 3.47 (dd, *J* = 11.8, 6.6 Hz, 1H, H<sub>10</sub>), 3.20 – 2.95 (m, 2H, H<sub>6</sub>), 2.44 – 2.22 (m, 2H, H<sub>7</sub>).

<sup>13</sup>C NMR (δ, ppm)(100 MHz, CDCl<sub>3</sub>) δ 197.1 (C<sub>5</sub>), 197.0 (C<sub>9</sub>), 140.0 (C<sub>4</sub>), 134.7 (C<sub>1</sub>), 129.5 (C<sub>3</sub>), 129.1 (C<sub>2</sub>), 52.3 (C<sub>8</sub>), 41.5 (C<sub>10</sub>), 36.2 (C<sub>6</sub>), 28.7 (C<sub>7</sub>).

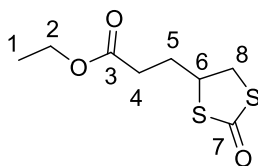
IR (ν, cm<sup>-1</sup>, CDCl<sub>3</sub>) 2926, 1681, 1639, 1587, 1570, 1487, 1428, 1399, 1368, 1283, 1225, 1203, 1176, 1090, 1012, 975, 856, 836, 807, 796.

HRMS (EI<sup>+</sup>) *m/z*: [M + Na]<sup>+</sup>calculated for C<sub>12</sub>H<sub>11</sub>ClNaO<sub>2</sub>S<sub>2</sub>: 308.9781, found: 308.9780.

Mp 68-70 °C.

R<sub>f</sub> = 0.60 (EtOAc / PE = 1/5).

### Ethyl-3-(2-oxo-1,3-dithiolan-4-yl)propanoate (**III-33d**)



Chemical Formula: C<sub>8</sub>H<sub>12</sub>O<sub>3</sub>S<sub>2</sub>

Exact Mass: 220.0228

According to the general procedure H, the reaction was carried out with adduct

**III-32d** (520 mg, 1.687 mmol) in methanesulfonic acid : acetic acid (9:1; 1.0 mL), and needed 48 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (20:1 to 4:1) to afford product **III-33d** (162 mg, 44%) as a colorless oil.

$^1\text{H NMR}$  ( $\delta$ , ppm)(400 MHz,  $\text{CDCl}_3$ )  $\delta$  4.20 – 4.08 (m, 3H,  $\text{H}_6$ ,  $\text{H}_2$ ), 3.78 (dd,  $J = 11.8$ , 5.2 Hz, 1H,  $\text{H}_8$ ), 3.42 (dd,  $J = 11.8$ , 6.6 Hz, 1H,  $\text{H}_8$ ), 2.57 – 2.35 (m, 2H,  $\text{H}_5$ ), 2.28 – 2.14 (m, 2H,  $\text{H}_4$ ), 1.25 (td,  $J = 7.0$ , 0.6 Hz, 3H,  $\text{H}_1$ ).

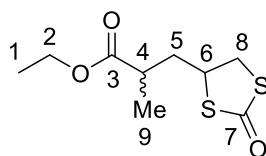
$^{13}\text{C NMR}$  ( $\delta$ , ppm)(100 MHz,  $\text{CDCl}_3$ )  $\delta$  197.0 ( $\text{C}_7$ ), 172.2 ( $\text{C}_3$ ), 61.0 ( $\text{C}_2$ ), 52.1 ( $\text{C}_6$ ), 41.2 ( $\text{C}_8$ ), 32.2 ( $\text{C}_4$ ), 29.7 ( $\text{C}_5$ ), 14.3 ( $\text{C}_1$ ).

$\text{IR}$  ( $\nu$ ,  $\text{cm}^{-1}$ ,  $\text{CDCl}_3$ ) 2981, 2933, 1726, 1645, 1435, 1375, 1182, 1096, 1028, 924, 861, 723.

$\text{HRMS}$  ( $\text{EI}^+$ )  $m/z$ :  $[\text{M} + \text{Na}]^+$  calculated for  $\text{C}_8\text{H}_{12}\text{NaO}_3\text{S}_2$ : 243.0120, found: 243.0116.

$R_f = 0.50$  (EtOAc / PE = 1/5).

### Ethyl-2-methyl-3-(2-oxo-1,3-dithiolan-4-yl)propanoate (**III-33e**)



Chemical Formula:  $\text{C}_9\text{H}_{14}\text{O}_3\text{S}_2$   
Exact Mass: 234.0384

According to the general procedure H, the reaction was carried out with adduct **III-32e** (1017 mg, 3.157 mmol) in methanesulfonic acid : acetic acid (9:1; 1.0 mL), and needed 60 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (20:1 to 10:1) to afford product **III-33e** (686 mg, 93%) as a colorless oil.

$^1\text{H NMR}$  ( $\delta$ , ppm)(400 MHz,  $\text{CDCl}_3$ )  $\delta$  4.16 – 4.04 (m, 3H,  $\text{H}_6$ ,  $\text{H}_2$ ), 3.75 (ddd,  $J = 11.8$ , 5.2, 3.8 Hz, 1H,  $\text{H}_8$ ), 3.39 (ddd,  $J = 13.0$ , 11.8, 7.0 Hz, 1H,  $\text{H}_8$ ), 2.61 – 2.46 (m, 1H,  $\text{H}_4$ ), 2.35 – 2.14 (m, 1H,  $\text{H}_5$ ), 2.06 – 1.88 (m, 1H,  $\text{H}_5$ ), 1.29 – 1.15 (m, 6H,  $\text{H}_1$ ,  $\text{H}_9$ ).

$^{13}\text{C NMR}$  ( $\delta$ , ppm)(100 MHz,  $\text{CDCl}_3$ )  $\delta$  197.2 ( $\text{C}_7$ ), 197.0 ( $\text{C}_7$ ), 175.4 ( $\text{C}_3$ ), 175.1 ( $\text{C}_3$ ),

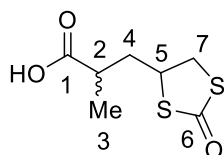
60.9 (C<sub>2</sub>), 60.9 (C<sub>2</sub>), 51.4 (C<sub>6</sub>), 50.7 (C<sub>6</sub>), 41.6 (C<sub>8</sub>), 41.0 (C<sub>8</sub>), 38.6 (C<sub>4</sub>), 38.4 (C<sub>4</sub>), 37.9 (C<sub>5</sub>), 37.8 (C<sub>5</sub>), 18.2 (C<sub>9</sub>), 17.0 (C<sub>9</sub>), 14.3 (C<sub>1</sub>).

**IR** ( $\nu$ , cm<sup>-1</sup>, CDCl<sub>3</sub>) 2977, 2936, 1723, 1644, 1462, 1431, 1378, 1259, 1178, 1126, 1096, 1061, 1022, 934, 859, 840, 752.

**HRMS** (EI<sup>+</sup>)  $m/z$ : [M + Na]<sup>+</sup> calculated for C<sub>9</sub>H<sub>14</sub>NaO<sub>3</sub>S<sub>2</sub>: 257.0277, found: 257.0280.

**R<sub>f</sub>** = 0.40 (EtOAc / PE = 1/4).

### 2-methyl-3-(2-oxo-1,3-dithiolan-4-yl)propanoic acid (**III-33e'**)



Chemical Formula: C<sub>7</sub>H<sub>10</sub>O<sub>3</sub>S<sub>2</sub>  
Exact Mass: 206.0071

According to the general procedure H, the reaction was carried out with adduct **III-32e'** (739 mg, 2.29 mmol) in methanesulfonic acid : acetic acid (9:1; 1.0 mL), and needed 21 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (20:1 to 10:1) to afford product **III-33e'** (278 mg, 59%) as a colorless oil.

**<sup>1</sup>H NMR** ( $\delta$ , ppm)(400 MHz, CDCl<sub>3</sub>)  $\delta$  4.35 – 4.06 (m, 1H, H<sub>5</sub>), 3.79 (dt,  $J$  = 11.8, 5.0 Hz, 1H, H<sub>7</sub>), 3.42 (ddd,  $J$  = 12.8, 11.8, 6.8 Hz, 1H, H<sub>7</sub>), 2.70 – 2.54 (m, 1H, H<sub>2</sub>), 2.40 – 2.15 (m, 1H, H<sub>4</sub>), 2.08 – 1.92 (m, 1H, H<sub>4</sub>), 1.27 (t,  $J$  = 6.8 Hz, 3H, H<sub>3</sub>).

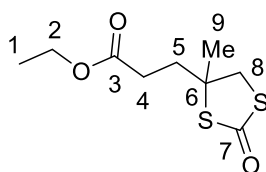
**<sup>13</sup>C NMR** ( $\delta$ , ppm)(100 MHz, CDCl<sub>3</sub>)  $\delta$  197.2 (C<sub>6</sub>), 197.0 (C<sub>6</sub>), 181.8 (C<sub>1</sub>), 181.6 (C<sub>1</sub>), 51.2 (C<sub>5</sub>), 50.4 (C<sub>5</sub>), 41.6 (C<sub>7</sub>), 41.0 (C<sub>7</sub>), 38.4 (C<sub>2</sub>), 38.3 (C<sub>2</sub>), 37.8 (C<sub>4</sub>), 37.5 (C<sub>4</sub>), 18.0 (C<sub>3</sub>), 16.8 (C<sub>3</sub>).

**IR** ( $\nu$ , cm<sup>-1</sup>, CDCl<sub>3</sub>) 2974, 2934, 1699, 1640, 1462, 1429, 1277, 1238, 1176, 1124, 917, 875, 847.

**HRMS** (EI<sup>+</sup>)  $m/z$ : [M + Na]<sup>+</sup> calculated for C<sub>7</sub>H<sub>10</sub>NaO<sub>3</sub>S<sub>2</sub>: 228.9964, found: 228.9971.

**R<sub>f</sub>** = 0.50 (EtOAc / PE = 1/2).

### Ethyl-3-(4-methyl-2-oxo-1,3-dithiolan-4-yl)propanoate (III-33f)



Chemical Formula: C<sub>9</sub>H<sub>14</sub>O<sub>3</sub>S<sub>2</sub>  
Exact Mass: 234.0384

According to the general procedure H, the reaction was carried out with adduct **III-32f** (1.2 g, 3.725 mmol) in methanesulfonic acid : acetic acid (9:1; 1.0 mL), and needed 10 days for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (20:1 to 10:1) to afford product **III-33f** (262 mg, 30%) as a colorless oil.

<sup>1</sup>H NMR ( $\delta$ , ppm)(400 MHz, CDCl<sub>3</sub>)  $\delta$  4.16 – 4.08 (m, 2H, H<sub>2</sub>), 3.53 – 3.41 (m, 2H, H<sub>8</sub>), 2.53 – 2.34 (m, 3H, H<sub>5</sub>, H<sub>4</sub>), 2.20 – 2.00 (m, 1H, H<sub>4</sub>), 1.65 (s, 3H, H<sub>9</sub>), 1.29 – 1.21 (m, 3H, H<sub>1</sub>).

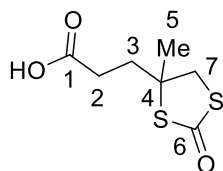
<sup>13</sup>C NMR ( $\delta$ , ppm)(100 MHz, CDCl<sub>3</sub>)  $\delta$  196.4 (C<sub>7</sub>), 172.4 (C<sub>3</sub>), 61.4 (C<sub>2</sub>), 60.9 (C<sub>6</sub>), 47.2 (C<sub>8</sub>), 35.8 (C<sub>5</sub>), 30.9 (C<sub>4</sub>), 26.3 (C<sub>9</sub>), 14.2 (C<sub>1</sub>).

IR ( $\nu$ , cm<sup>-1</sup>, CDCl<sub>3</sub>) 2978, 2929, 1727, 1644, 1445, 1425, 1378, 1296, 1232, 1181, 1146, 1021, 915, 861, 785.

HRMS (EI<sup>+</sup>) m/z: [M + Na]<sup>+</sup> calculated for C<sub>9</sub>H<sub>14</sub>NaO<sub>3</sub>S<sub>2</sub>: 257.0277, found: 257.0282.

R<sub>f</sub> = 0.50 (EtOAc / PE = 1/5).

### 3-(4-methyl-2-oxo-1,3-dithiolan-4-yl)propanoic acid (III-33f')



Chemical Formula: C<sub>7</sub>H<sub>10</sub>O<sub>3</sub>S<sub>2</sub>  
Exact Mass: 206.0071

According to the general procedure H, the reaction was carried out with adduct

**III-32f'** (422 mg, 1.31 mmol) in methanesulfonic acid : acetic acid (9:1; 1.0 mL), and needed 13 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (20:1 to 5:1) to afford product **III-33f'** (168 mg, 62%) as a colorless oil.

<sup>1</sup>H NMR ( $\delta$ , ppm)(400 MHz, CDCl<sub>3</sub>)  $\delta$  3.51 (d,  $J$  = 0.8 Hz, 2H, H<sub>7</sub>), 2.61 – 2.40 (m, 3H, H<sub>2</sub>, H<sub>3</sub>), 2.16 (ddd,  $J$  = 14.0, 8.6, 7.2 Hz, 1H, H<sub>3</sub>), 1.68 (s, 3H, H<sub>5</sub>).

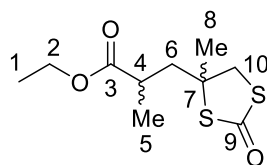
<sup>13</sup>C NMR ( $\delta$ , ppm)(100 MHz, CDCl<sub>3</sub>)  $\delta$  196.3 (C<sub>6</sub>), 178.5 (C<sub>1</sub>), 61.3 (C<sub>4</sub>), 47.3 (C<sub>7</sub>), 35.5 (C<sub>3</sub>), 30.7 (C<sub>2</sub>), 26.3 (C<sub>5</sub>).

IR ( $\nu$ , cm<sup>-1</sup>, CDCl<sub>3</sub>) 2970, 2927, 1706, 1643, 1446, 1424, 1382, 1296, 1220, 1144, 865, 836, 773.

HRMS (EI<sup>+</sup>)  $m/z$ : [M + Na]<sup>+</sup> calculated for C<sub>7</sub>H<sub>10</sub>NaO<sub>3</sub>S<sub>2</sub>: 228.9964, found: 228.9971.

R<sub>f</sub> = 0.40 (EtOAc / PE = 1/2).

### Ethyl-2-methyl-3-(4-methyl-2-oxo-1,3-dithiolan-4-yl)propanoate (**III-33g**)



Chemical Formula: C<sub>10</sub>H<sub>16</sub>O<sub>3</sub>S<sub>2</sub>  
Exact Mass: 248.0541

According to the general procedure H, the reaction was carried out with adduct **III-32g** (1050 mg, 3.124 mmol) in methanesulfonic acid : acetic acid (9:1; 1.0 mL), and needed 53 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (100:1 to 100:4) to afford product **III-33g** (627 mg, 81%) as a colorless oil.

<sup>1</sup>H NMR ( $\delta$ , ppm)(400 MHz, CDCl<sub>3</sub>)  $\delta$  4.16 – 4.09 (m, 2H, H<sub>2</sub>), 3.52 (dd,  $J$  = 12.0, 3.4 Hz, 1H, H<sub>10</sub>), 3.39 (dd,  $J$  = 12.0, 3.6 Hz, 1H, H<sub>10</sub>), 2.71 – 2.41 (m, 2H, H<sub>6</sub>), 2.11 – 1.76 (m, 1H, H<sub>4</sub>), 1.64 (d,  $J$  = 22.2 Hz, 3H, H<sub>8</sub>), 1.29 – 1.16 (m, 6H, H<sub>1</sub>, H<sub>5</sub>).

<sup>13</sup>C NMR ( $\delta$ , ppm)(100 MHz, CDCl<sub>3</sub>)  $\delta$  196.7 (C<sub>9</sub>), 176.4 (C<sub>3</sub>), 176.0 (C<sub>3</sub>), 61.9 (C<sub>2</sub>), 61.4 (C<sub>2</sub>), 61.0 (C<sub>7</sub>), 61.0 (C<sub>7</sub>), 47.7 (C<sub>10</sub>), 47.2 (C<sub>10</sub>), 44.5 (C<sub>4</sub>), 44.4 (C<sub>4</sub>), 37.6 (C<sub>6</sub>),

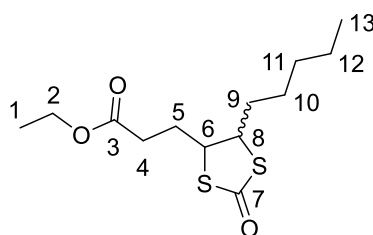
37.1 (C<sub>6</sub>), 26.8 (C<sub>8</sub>), 26.1 (C<sub>8</sub>), 19.9 (C<sub>5</sub>), 14.2 (C<sub>1</sub>), 14.2 (C<sub>1</sub>).

**IR** ( $\nu$ , cm<sup>-1</sup>, CDCl<sub>3</sub>) 2976, 2932, 1725, 1646, 1455, 1379, 1262, 1179, 1157, 1078, 1022, 896, 851, 752.

**HRMS** (EI<sup>+</sup>)  $m/z$ : [M + H]<sup>+</sup> calculated for C<sub>10</sub>H<sub>17</sub>O<sub>3</sub>S<sub>2</sub>: 249.0614, found: 249.0618.

**R<sub>f</sub>** = 0.40 (EtOAc / PE = 1/5).

### Ethyl-3-(2-oxo-5-pentyl-1,3-dithiolan-4-yl)propanoate (**III-33h**)



Chemical Formula: C<sub>13</sub>H<sub>22</sub>O<sub>3</sub>S<sub>2</sub>  
Exact Mass: 290.1010

According to the general procedure H, the reaction was carried out with adduct **III-32h** (1030 mg, 2.72 mmol) in methanesulfonic acid : acetic acid (9:1; 1.0 mL), and needed 46 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (20:1 to 10:1) to afford product **III-33h** (426 mg, 54%) as a colorless oil.

**<sup>1</sup>H NMR** ( $\delta$ , ppm) (400 MHz, CDCl<sub>3</sub>)  $\delta$  4.21 – 3.60 (m, 4H, H<sub>6</sub>, H<sub>8</sub>, H<sub>2</sub>), 2.62 – 1.71 (m, 6H, H<sub>4</sub>, H<sub>5</sub>, H<sub>9</sub>), 1.48 – 1.27 (m, 6H, H<sub>10</sub>, H<sub>11</sub>, H<sub>12</sub>), 1.25 (t, J = 7.0 Hz, 3H, H<sub>1</sub>), 0.93 – 0.82 (m, 3H, H<sub>13</sub>).

**<sup>13</sup>C NMR** ( $\delta$ , ppm)(100 MHz, CDCl<sub>3</sub>)  $\delta$  196.5 (C<sub>7</sub>), 196.4 (C<sub>7</sub>), 172.5 (C<sub>3</sub>), 172.4 (C<sub>3</sub>), 60.9 (C<sub>6</sub>), 58.0 (C<sub>6</sub>), 57.6 (C<sub>8</sub>), 56.7(C<sub>8</sub>), 55.5 (C<sub>2</sub>), 35.5 (C<sub>2</sub>), 32.0 (C<sub>4</sub>), 31.9 (C<sub>4</sub>), 31.5 (C<sub>5</sub>), 31.4 (C<sub>5</sub>), 30.6 (C<sub>9</sub>), 30.2 (C<sub>9</sub>), 27.8 (C<sub>10</sub>), 27.7 (C<sub>10</sub>), 24.6 (C<sub>11</sub>), 22.5 (C<sub>11</sub>), 22.5 (C<sub>12</sub>), 14.3 (C<sub>1</sub>), 14.0 (C<sub>13</sub>)

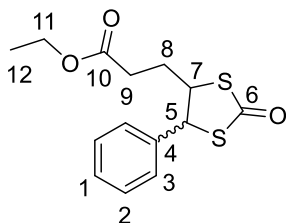
**IR** ( $\nu$ , cm<sup>-1</sup>, CDCl<sub>3</sub>) 2956, 2929, 2857, 1729, 1649, 1464, 1375, 1254, 1179, 1159, 1034, 864.

**HRMS** (EI<sup>+</sup>)  $m/z$ : [M + Na]<sup>+</sup> calculated for C<sub>13</sub>H<sub>22</sub>NaO<sub>3</sub>S<sub>2</sub>: 313.0903, found: 313.0902.



$R_f = 0.50$  (EtOAc / PE = 1/4).

**Ethyl-3-(2-oxo-5-phenyl-1,3-dithiolan-4-yl)propanoate (III-33i)**



Chemical Formula:  $C_{14}H_{16}O_3S_2$   
Exact Mass: 296.0541

According to the general procedure H, the reaction was carried out with adduct **III-32i** (1003 mg, 2.611 mmol) in methanesulfonic acid : acetic acid (9:1; 1.0 mL), and needed 96 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (100:7 to 5:1) to afford product **III-33i** (464 mg, 60%) as a colorless oil.

$^1\text{H NMR}$  ( $\delta$ , ppm)(400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.51 – 7.32 (m, 5H,  $\text{H}_2, \text{H}_3, \text{H}_1$ ), 5.51 – 4.80 (m, 1H,  $\text{H}_5$ ), 4.38 – 4.22 (m, 1H,  $\text{H}_7$ ), 4.15 – 4.01 (m, 2H,  $\text{H}_{11}$ ), 2.49 – 1.79 (m, 4H,  $\text{H}_9, \text{H}_8$ ), 1.22 (td,  $J = 7.1, 4.7$  Hz, 3H,  $\text{H}_{12}$ ).

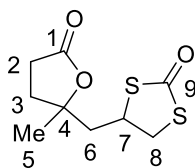
$^{13}\text{C NMR}$  ( $\delta$ , ppm)(100 MHz,  $\text{CDCl}_3$ )  $\delta$  194.6 ( $\text{C}_6$ ), 172.2 ( $\text{C}_{10}$ ), 171.9 ( $\text{C}_{10}$ ), 135.4 ( $\text{C}_4$ ), 134.6 ( $\text{C}_4$ ), 129.3 ( $\text{C}_2$ ), 129.2 ( $\text{C}_2$ ), 129.1 ( $\text{C}_3$ ), 129.0 ( $\text{C}_3$ ), 128.5 ( $\text{C}_1$ ), 128.1 ( $\text{C}_1$ ), 61.5 ( $\text{C}_{11}$ ), 60.9 ( $\text{C}_{11}$ ), 60.8 ( $\text{C}_5$ ), 60.2 ( $\text{C}_5$ ), 58.9 ( $\text{C}_7$ ), 56.6 ( $\text{C}_7$ ), 32.8 ( $\text{C}_9$ ), 32.0 ( $\text{C}_9$ ), 28.6 ( $\text{C}_8$ ), 25.8 ( $\text{C}_8$ ), 14.2 ( $\text{C}_{12}$ ).

$\text{IR}$  ( $\nu$ ,  $\text{cm}^{-1}$ ,  $\text{CDCl}_3$ ) 1726, 1644, 1493, 1452, 1375, 1256, 1179, 1155, 1028, 874, 752.

$\text{HRMS}$  ( $\text{EI}^+$ )  $m/z$ :  $[\text{M} + \text{H}]^+$  calculated for  $\text{C}_{14}\text{H}_{17}\text{O}_3\text{S}_2$ : 297.0614, found: 297.0621.

$R_f = 0.50$  (EtOAc / PE = 1/4).

**5-methyl-5-((2-oxo-1,3-dithiolan-4-yl)methyl)dihydrofuran-2(3H)-one (III-33j)**



Chemical Formula: C<sub>9</sub>H<sub>12</sub>O<sub>3</sub>S<sub>2</sub>

Exact Mass: 232.0228

According to the general procedure H, the reaction was carried out with adduct **III-32j** (284 mg, 0.887 mmol) in methanesulfonic acid : acetic acid (9:1; 0.5 mL), and needed 48 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (10:1 to 2:1) to afford product **III-33j** (160 mg, 78%) as a light yellow oil.

<sup>1</sup>H NMR (δ, ppm)(400 MHz, CDCl<sub>3</sub>) δ 4.28 (d, *J* = 7.2 Hz, 1H, H<sub>7</sub>), 3.84 – 3.46 (m, 2H, H<sub>8</sub>), 2.73 – 2.51 (m, 2H, H<sub>6</sub>), 2.40 – 2.00 (m, 4H, H<sub>2</sub>, H<sub>3</sub>), 1.45 (s, 3H, H<sub>5</sub>).

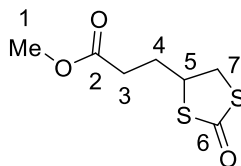
<sup>13</sup>C NMR (δ, ppm)(100 MHz, CDCl<sub>3</sub>) δ 197.0 (C<sub>9</sub>), 175.7 (C<sub>1</sub>), 84.9 (C<sub>4</sub>), 48.5 (C<sub>7</sub>), 45.5 (C<sub>8</sub>), 42.1 (C<sub>3</sub>), 34.6 (C<sub>6</sub>), 28.5 (C<sub>2</sub>), 25.0 (C<sub>5</sub>).

IR (ν, cm<sup>-1</sup>, CDCl<sub>3</sub>) 2975, 2934, 1763, 1641, 1456, 1385, 1256, 1183, 1084, 937, 875, 850.

HRMS (EI<sup>+</sup>) *m/z*: [M + H]<sup>+</sup> calculated for C<sub>9</sub>H<sub>13</sub>O<sub>3</sub>S<sub>2</sub>: 233.0301, found: 233.0304.

R<sub>f</sub> = 0.30 (EtOAc / PE = 1/2).

### Methyl-3-(2-oxo-1,3-dithiolan-4-yl)propanoate (**III-33k**)



Chemical Formula: C<sub>7</sub>H<sub>10</sub>O<sub>3</sub>S<sub>2</sub>

Exact Mass: 206.0071

According to the general procedure H, the reaction was carried out with adduct **III-32k** (1097 mg, 3.73 mmol) in methanesulfonic acid : acetic acid (9:1; 1.0 mL), and needed 39 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (100:1 to 100:7) to

afford product **III-33k** (400 mg, 52%) as a colorless oil.

$^1\text{H NMR}$  ( $\delta$ , ppm)(400 MHz,  $\text{CDCl}_3$ )  $\delta$  4.20 – 4.09 (m, 1H,  $\text{H}_5$ ), 3.78 (dd,  $J = 11.8, 5.2$  Hz, 1H,  $\text{H}_7$ ), 3.68 (s, 3H,  $\text{H}_1$ ), 3.42 (dd,  $J = 11.8, 6.6$  Hz, 1H,  $\text{H}_7$ ), 2.56 – 2.38 (m, 2H,  $\text{H}_3$ ), 2.27 – 2.13 (m, 2H,  $\text{H}_4$ ).

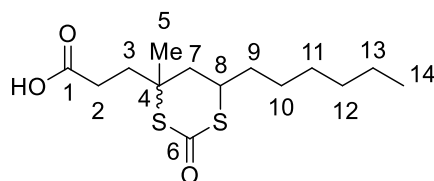
$^{13}\text{C NMR}$  ( $\delta$ , ppm)(100 MHz,  $\text{CDCl}_3$ )  $\delta$  196.9 ( $\text{C}_6$ ), 172.6 ( $\text{C}_2$ ), 52.0 ( $\text{C}_1$ ), 52.0 ( $\text{C}_5$ ), 41.1 ( $\text{C}_7$ ), 31.9 ( $\text{C}_3$ ), 29.7 ( $\text{C}_4$ ).

**IR** ( $\nu$ ,  $\text{cm}^{-1}$ ,  $\text{CDCl}_3$ ) 2950, 1728, 1640, 1434, 1368, 1331, 1260, 1197, 1170, 1009, 983, 860, 723.

**HRMS** ( $\text{EI}^+$ )  $m/z$ :  $[\text{M} + \text{Na}]^+$  calculated for  $\text{C}_7\text{H}_{10}\text{NaO}_3\text{S}_2$ : 228.9964, found: 228.9960.

$R_f = 0.45$  (EtOAc / PE = 1/5).

### 3-(6-hexyl-4-methyl-2-oxo-1,3-dithian-4-yl)propanoic acid (**III-33l**)



Chemical Formula:  $\text{C}_{14}\text{H}_{24}\text{O}_3\text{S}_2$   
Exact Mass: 304.1167

According to the general procedure H, the reaction was carried out with adduct **III-32x** (106 mg, 0.319 mmol) in methanesulfonic acid : acetic acid (9:1; 1.0 mL), and needed 23 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (5:1 to 2:1) to afford product **III-33l** (82 mg, 85%) as a colorless oil.

$^1\text{H NMR}$  ( $\delta$ , ppm)(400 MHz,  $\text{CDCl}_3$ )  $\delta$  3.76 – 3.59 (m, 1H,  $\text{H}_8$ ), 2.65 – 2.20 (m, 3H,  $\text{H}_2$ ,  $\text{H}_3$ ), 2.15 – 1.81 (m, 3H,  $\text{H}_3$ ,  $\text{H}_9$ ), 1.77 – 1.59 (m, 2H,  $\text{H}_{13}$ ), 1.53 (s, 2H,  $\text{H}_7$ ), 1.47 – 1.23 (m, 9H,  $\text{H}_{10}$ ,  $\text{H}_{11}$ ,  $\text{H}_{12}$ ,  $\text{H}_5$ ), 0.94 – 0.76 (m, 3H,  $\text{H}_{14}$ ).

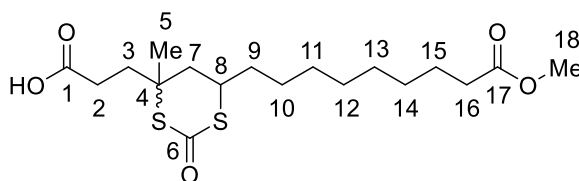
$^{13}\text{C NMR}$  ( $\delta$ , ppm)(100 MHz,  $\text{CDCl}_3$ )  $\delta$  190.2 ( $\text{C}_6$ ), 190.0 ( $\text{C}_6$ ), 178.8 ( $\text{C}_1$ ), 178.7 ( $\text{C}_1$ ), 51.9 ( $\text{C}_4$ ), 51.1 ( $\text{C}_4$ ), 43.4 ( $\text{C}_8$ ), 43.3 ( $\text{C}_8$ ), 43.2 ( $\text{C}_3$ ), 42.2 ( $\text{C}_3$ ), 38.5 ( $\text{C}_{12}$ ), 36.5 ( $\text{C}_9$ ), 36.1 ( $\text{C}_9$ ), 35.9 ( $\text{C}_2$ ), 31.6 ( $\text{C}_{11}$ ), 29.4 ( $\text{C}_{11}$ ), 29.1 ( $\text{C}_7$ ), 29.0 ( $\text{C}_7$ ), 28.9 ( $\text{C}_5$ ), 28.8 ( $\text{C}_5$ ), 28.1 ( $\text{C}_{10}$ ), 26.2 ( $\text{C}_{10}$ ), 26.2 ( $\text{C}_{13}$ ), 22.6 ( $\text{C}_{13}$ ), 14.1 ( $\text{C}_{14}$ ).

**IR** ( $\nu$ ,  $\text{cm}^{-1}$ ,  $\text{CDCl}_3$ ) 2925, 2855, 1707, 1603, 1450, 1416, 1382, 1295, 1222, 1163, 1091, 911, 773, 729.

**HRMS** ( $\text{EI}^+$ )  $m/z$ :  $[\text{M} + \text{H}]^+$  calculated for  $\text{C}_{14}\text{H}_{25}\text{O}_3\text{S}_2$ : 305.1240, found: 305.1239.

$R_f = 0.20$  (EtOAc / PE = 1/2).

**3-(6-(9-methoxy-9-oxononyl)-4-methyl-2-oxo-1,3-dithian-4-yl)-propanoic acid (III-33m)**



Chemical Formula:  $\text{C}_{18}\text{H}_{30}\text{O}_5\text{S}_2$

Exact Mass: 390.1535

According to the general procedure H, the reaction was carried out with adduct **III-32y** (473 mg, 1.131 mmol) in methanesulfonic acid : acetic acid (9:1; 0.5 mL), and needed 25 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (6:1 to 3:1) to afford product **III-33m** (287 mg, 65%) as a colorless oil.

$^1\text{H NMR}$  ( $\delta$ , ppm)(400 MHz,  $\text{CDCl}_3$ )  $\delta$  3.66 (s, 3H,  $\text{H}_{18}$ ), 2.65 – 2.20 (m, 5H,  $\text{H}_8$ ,  $\text{H}_2$ ,  $\text{H}_3$ ), 2.14 – 1.79 (m, 3H,  $\text{H}_{16}$ ,  $\text{H}_7$ ), 1.73 – 1.20 (m, 18H,  $\text{H}_7$ ,  $\text{H}_{15}$ ,  $\text{H}_9$ ,  $\text{H}_{14}$ ,  $\text{H}_{13}$ ,  $\text{H}_{12}$ ,  $\text{H}_{11}$ ,  $\text{H}_{10}$ ,  $\text{H}_5$ ).

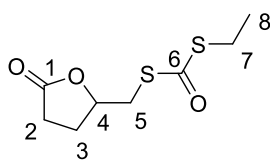
$^{13}\text{C NMR}$  ( $\delta$ , ppm)(100 MHz,  $\text{CDCl}_3$ )  $\delta$  190.1 ( $\text{C}_6$ ), 190.0 ( $\text{C}_6$ ), 178.2 ( $\text{C}_1$ ), 178.1 ( $\text{C}_1$ ), 174.6 ( $\text{C}_{17}$ ), 174.5 ( $\text{C}_{17}$ ), 51.8 ( $\text{C}_4$ ), 51.6 ( $\text{C}_4$ ), 51.1 ( $\text{C}_{18}$ ), 43.4 ( $\text{C}_8$ ), 43.2 ( $\text{C}_8$ ), 43.2 ( $\text{C}_{16}$ ), 42.2 ( $\text{C}_{16}$ ), 38.5 ( $\text{C}_3$ ), 36.5 ( $\text{C}_9$ ), 36.0 ( $\text{C}_9$ ), 36.0 ( $\text{C}_2$ ), 34.2 ( $\text{C}_2$ ), 29.3, 29.3, 29.2, 29.1, 29.1, 28.9, 28.8, 28.1, 26.2, 26.2, 25.0.

**IR** ( $\nu$ ,  $\text{cm}^{-1}$ ,  $\text{CDCl}_3$ ) 2926, 2854, 1767, 1734, 1610, 1444, 1355, 1249, 1196, 1169, 1006, 936, 916, 869.

**HRMS** ( $\text{EI}^+$ )  $m/z$ :  $[\text{M} + \text{H}]^+$  calculated for  $\text{C}_{18}\text{H}_{31}\text{O}_5\text{S}_2$ : 391.1607, found: 391.1605.

$R_f = 0.25$  (EtOAc / PE = 1/2).

**S-ethyl-S-((5-oxotetrahydrofuran-2-yl)-methyl)-carbonodithioate (III-34a)**



Chemical Formula: C<sub>8</sub>H<sub>12</sub>O<sub>3</sub>S<sub>2</sub>  
Exact Mass: 220.0228

According to the general procedure H, the reaction was carried out with adduct **III-32d** (520 mg, 1.687 mmol) in methanesulfonic acid : acetic acid (9:1; 1.0 mL), and needed 48 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (20:1 to 4:1) to afford product **III-34a** (194 mg, 52%) as a colorless oil.

<sup>1</sup>H NMR (δ, ppm)(400 MHz, CDCl<sub>3</sub>) δ 4.65 (tt, *J* = 7.0, 5.8 Hz, 1H, H<sub>4</sub>), 3.29 (dd, *J* = 5.6, 2.0 Hz, 2H, H<sub>5</sub>), 3.00 (q, *J* = 7.4 Hz, 2H, H<sub>7</sub>), 2.68 – 2.44 (m, 2H, H<sub>2</sub>, H<sub>3</sub>), 2.36 (dddd, *J* = 12.6, 8.8, 6.8, 5.6 Hz, 1H, H<sub>2</sub>), 2.03 – 1.85 (m, 1H, H<sub>3</sub>), 1.29 (td, *J* = 7.4, 0.4 Hz, 3H, H<sub>8</sub>).

<sup>13</sup>C NMR (δ, ppm)(100 MHz, CDCl<sub>3</sub>) δ 188.9 (C<sub>6</sub>), 176.3 (C<sub>1</sub>), 78.5 (C<sub>4</sub>), 33.9 (C<sub>5</sub>), 28.6 (C<sub>2</sub>), 26.6 (C<sub>3</sub>), 25.6 (C<sub>7</sub>), 15.0 (C<sub>8</sub>).

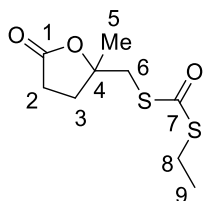
IR (ν, cm<sup>-1</sup>, CDCl<sub>3</sub>) 2972, 2932, 1773, 1643, 1454, 1416, 1374, 1341, 1266, 1169, 1139, 1026, 988, 916, 866, 744.

HRMS (EI<sup>+</sup>) *m/z*: [M + Na]<sup>+</sup> calculated for C<sub>8</sub>H<sub>12</sub>NaO<sub>3</sub>S<sub>2</sub>: 243.0120, found: 243.0117.

R<sub>f</sub> = 0.40 (EtOAc / PE = 1/2).

### S-ethyl-S-((2-methyl-5-oxotetrahydrofuran-2-yl)-methyl)-carbonodithioate

#### (III-34b)



Chemical Formula: C<sub>9</sub>H<sub>14</sub>O<sub>3</sub>S<sub>2</sub>  
Exact Mass: 234.0384

According to the general procedure H, the reaction was carried out with adduct

**III-32f** (1.2 g, 3.725 mmol) in methanesulfonic acid : acetic acid (9:1; 1.0 mL), and needed 10 days for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (20:1 to 10:1) to afford product **III-34b** (357 mg, 41%) as a colorless oil.

$^1\text{H NMR}$  ( $\delta$ , ppm)(400 MHz,  $\text{CDCl}_3$ )  $\delta$  3.30 (s, 2H,  $\text{H}_6$ ), 3.00 (qt,  $J = 7.4, 0.6$  Hz, 2H,  $\text{H}_8$ ), 2.71 – 2.52 (m, 2H,  $\text{H}_2$ ), 2.21 – 2.08 (m, 1H,  $\text{H}_3$ ), 2.08 – 1.93 (m, 1H,  $\text{H}_3$ ), 1.44 (s, 3H,  $\text{H}_5$ ), 1.29 (tt,  $J = 7.4, 0.6$  Hz, 3H,  $\text{H}_9$ ).

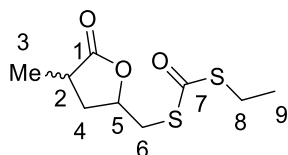
$^{13}\text{C NMR}$  ( $\delta$ , ppm)(100 MHz,  $\text{CDCl}_3$ )  $\delta$  189.0 ( $\text{C}_7$ ), 175.9 ( $\text{C}_1$ ), 85.2 ( $\text{C}_4$ ), 38.9 ( $\text{C}_6$ ), 31.8 ( $\text{C}_3$ ), 29.2 ( $\text{C}_2$ ), 25.9 ( $\text{C}_5$ ), 25.7 ( $\text{C}_8$ ), 15.0 ( $\text{C}_9$ ).

$\text{IR}$  ( $\nu$ ,  $\text{cm}^{-1}$ ,  $\text{CDCl}_3$ ) 2974, 2932, 1772, 1732, 1644, 1452, 1379, 1234, 1169, 1132, 1074, 1036, 943, 865, 776.

$\text{HRMS}$  ( $\text{EI}^+$ )  $m/z$ :  $[\text{M} + \text{H}]^+$  calculated for  $\text{C}_9\text{H}_{15}\text{O}_3\text{S}_2$ : 235.0457, found: 235.0452.

$R_f = 0.50$  (EtOAc / PE = 1/2).

**S-ethyl-S-((4-methyl-5-oxotetrahydrofuran-2-yl)-methyl)-carbonodithioate**  
(**III-34c**)



Chemical Formula:  $\text{C}_9\text{H}_{14}\text{O}_3\text{S}_2$   
Exact Mass: 234.0384

According to the general procedure H, the reaction was carried out with adduct **III-32e** (878 mg, 2.726 mmol) in methanesulfonic acid : acetic acid (9:1; 1.0 mL), and needed 26 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (20:1 to 10:1) to afford product **III-34c** (243 mg, 38%) as a colorless oil.

$^1\text{H NMR}$  ( $\delta$ , ppm)(400 MHz,  $\text{CDCl}_3$ )  $\delta$  4.69 – 4.44 (m, 1H,  $\text{H}_5$ ), 3.35 – 3.16 (m, 2H,  $\text{H}_6$ ), 3.00 (qd,  $J = 7.4, 1.2$  Hz, 2H,  $\text{H}_8$ ), 2.82 – 2.46 (m, 1H,  $\text{H}_2$ ), 2.37 – 1.94 (m, 1H,  $\text{H}_4$ ), 1.62 – 1.36 (m, 1H,  $\text{H}_4$ ), 1.32 – 1.23 (m, 6H,  $\text{H}_3, \text{H}_9$ ).

$^{13}\text{C NMR}$  ( $\delta$ , ppm)(100 MHz,  $\text{CDCl}_3$ )  $\delta$  188.9 ( $\text{C}_7$ ), 188.9 ( $\text{C}_7$ ), 179.2 ( $\text{C}_1$ ), 178.6 ( $\text{C}_1$ ),

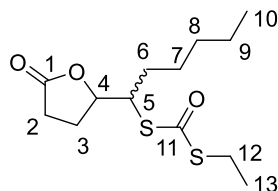
76.4 (C<sub>5</sub>), 76.2 (C<sub>5</sub>), 36.0 (C<sub>6</sub>), 35.9 (C<sub>6</sub>), 34.2 (C<sub>2</sub>), 33.9 (C<sub>2</sub>), 33.9 (C<sub>4</sub>), 33.8 (C<sub>4</sub>), 25.6 (C<sub>8</sub>), 25.6 (C<sub>8</sub>), 16.0 (C<sub>3</sub>), 15.1 (C<sub>3</sub>), 15.0 (C<sub>9</sub>).

**IR** ( $\nu$ , cm<sup>-1</sup>, CDCl<sub>3</sub>) 2972, 2932, 2876, 1770, 1643, 1453, 1346, 1180, 1158, 1046, 1013, 927, 867.

**HRMS** (EI<sup>+</sup>)  $m/z$ : [M + Na]<sup>+</sup> calculated for C<sub>9</sub>H<sub>14</sub>NaO<sub>3</sub>S<sub>2</sub>: 257.0277, found: 257.0278.

**R<sub>f</sub>** = 0.30 (EtOAc / PE = 1/2).

### **S-ethyl-S-(1-(5-oxotetrahydrofuran-2-yl)-hexyl)-carbonodithioate (III-34d)**



Chemical Formula: C<sub>13</sub>H<sub>22</sub>O<sub>3</sub>S<sub>2</sub>  
Exact Mass: 290.1010

According to the general procedure H, the reaction was carried out with adduct **III-32h** (1030 mg, 2.72 mmol) in methanesulfonic acid : acetic acid (9:1; 1.0 mL), and needed 46 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (20:1 to 10:1) to afford product **III-34d** (221 mg, 28%) as a colorless oil.

**<sup>1</sup>H NMR** ( $\delta$ , ppm)(400 MHz, CDCl<sub>3</sub>)  $\delta$  4.72 (td,  $J$  = 7.4, 2.8 Hz, 1H, H<sub>4</sub>), 3.84 (ddd,  $J$  = 9.8, 5.2, 2.8 Hz, 1H, H<sub>5</sub>), 3.08 – 2.86 (m, 2H, H<sub>12</sub>), 2.63 – 2.44 (m, 2H, H<sub>2</sub>), 2.29 (dddd,  $J$  = 13.2, 9.6, 7.4, 5.0 Hz, 1H, H<sub>3</sub>), 2.01 (dddd,  $J$  = 13.2, 10.2, 8.8, 7.4 Hz, 1H, H<sub>3</sub>), 1.81 – 1.58 (m, 2H, H<sub>6</sub>), 1.56 – 1.19 (m, 9H, H<sub>7</sub>, H<sub>8</sub>, H<sub>9</sub>, H<sub>13</sub>), 0.90 – 0.82 (m, 3H, H<sub>10</sub>).

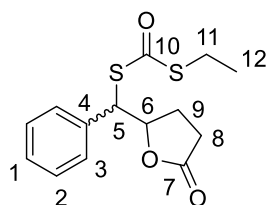
**<sup>13</sup>C NMR** ( $\delta$ , ppm)(100 MHz, CDCl<sub>3</sub>)  $\delta$  189.3 (C<sub>11</sub>), 188.6 (C<sub>11</sub>), 176.6 (C<sub>1</sub>), 176.5 (C<sub>1</sub>), 81.6 (C<sub>4</sub>), 81.4 (C<sub>4</sub>), 49.5 (C<sub>5</sub>), 49.2 (C<sub>5</sub>), 32.0 (C<sub>12</sub>), 31.4 (C<sub>12</sub>), 31.4 (C<sub>2</sub>), 30.7 (C<sub>2</sub>), 28.6 (C<sub>3</sub>), 26.7 (C<sub>6</sub>), 26.2 (C<sub>6</sub>), 25.8 (C<sub>7</sub>), 25.6 (C<sub>7</sub>), 25.6 (C<sub>8</sub>), 25.1 (C<sub>8</sub>), 22.5 (C<sub>9</sub>), 14.9 (C<sub>13</sub>), 14.0 (C<sub>10</sub>).

**IR** ( $\nu$ , cm<sup>-1</sup>, CDCl<sub>3</sub>) 2955, 2929, 2858, 1775, 1736, 1642, 1455, 1264, 1175, 1147, 1055, 1021, 912, 859.

**HRMS** (EI<sup>+</sup>) m/z: [M + Na]<sup>+</sup>calculated for C<sub>13</sub>H<sub>22</sub>NaO<sub>3</sub>S<sub>2</sub>: 313.0903, found: 313.0903.

**R<sub>f</sub>** = 0.20 (EtOAc / PE = 1/4).

**S-ethyl-S-((5-oxotetrahydrofuran-2-yl)(phenyl)-methyl)-carbonodithioate**  
**(III-34e)**



Chemical Formula: C<sub>14</sub>H<sub>16</sub>O<sub>3</sub>S<sub>2</sub>  
Exact Mass: 296.0541

According to the general procedure H, the reaction was carried out with adduct **III-32i** (1003 mg, 2.611 mmol) in methanesulfonic acid : acetic acid (9:1; 1.0 mL), and needed 96 h for the reaction to go to completion. It was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (100:7 to 5:1) to afford product **III-34e** (124 mg, 16%) as a colorless oil.

**<sup>1</sup>H NMR** ( $\delta$ , ppm) (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.35 – 7.27 (m, 5H, H<sub>3</sub>, H<sub>2</sub>, H<sub>1</sub>), 4.98 – 4.86 (m, 2H, H<sub>6</sub>, H<sub>5</sub>), 3.11 – 2.89 (m, 2H, H<sub>11</sub>), 2.53 – 1.93 (m, 4H, H<sub>8</sub>, H<sub>9</sub>), 1.29 (td, *J* = 7.4, 1.0 Hz, 3H, H<sub>12</sub>).

**<sup>13</sup>C NMR** ( $\delta$ , ppm)(100 MHz, CDCl<sub>3</sub>)  $\delta$  188.2 (C<sub>10</sub>), 176.4 (C<sub>7</sub>), 176.3 (C<sub>7</sub>), 137.7 (C<sub>4</sub>), 136.0 (C<sub>4</sub>), 129.1 (C<sub>2</sub>), 129.0 (C<sub>2</sub>), 129.0 (C<sub>1</sub>), 128.8 (C<sub>1</sub>), 128.6 (C<sub>3</sub>), 128.4 (C<sub>3</sub>), 81.8 (C<sub>6</sub>), 81.5 (C<sub>6</sub>), 52.5 (C<sub>5</sub>), 52.2 (C<sub>5</sub>), 28.3 (C<sub>8</sub>), 25.8 (C<sub>9</sub>), 25.8 (C<sub>9</sub>), 25.7 (C<sub>11</sub>), 15.0 (C<sub>12</sub>), 14.9 (C<sub>12</sub>).

**IR** ( $\nu$ , cm<sup>-1</sup>, CDCl<sub>3</sub>) 2937, 1776, 1643, 1347, 1171, 1058, 1007, 971, 916, 862, 812.

**HRMS** (EI<sup>+</sup>) m/z: [M + H]<sup>+</sup>calculated for C<sub>14</sub>H<sub>17</sub>O<sub>3</sub>S<sub>2</sub>: 297.0614, found: 297.0621.

**R<sub>f</sub>** = 0.20 (EtOAc / PE = 1/4).



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**Titre :** Nouvelle application de la chimie radicalaire des xanthates

**Mots clés :** xanthates, eptazocine, 1,3-dithiane-2-ones, 1,3-dithiolan-2-ones, 1,2-dithiolanes.

**Résumé :** Dans cette thèse, nous nous concentrons sur la nouvelle application de la chimie radicalaire des xanthates pour la synthèse de produits naturels et de composés organo-soufrés. La chimie radicalaire des xanthates est utilisée comme un outil puissant pour la création de liaisons carbone-carbone. Trois voies différentes vers la (±)-eptazocine ont été développées en utilisant la séquence d'addition radicalaire-cyclisation comme étape clé. Bien que la (±)-eptazocine n'ait pas pu être synthétisée avec succès, son squelette central de centre de carbone quaternaire benzylique a été construit. Trois voies pratiques et convergentes vers les 1,3-dithianes-2-ones ont été développées sur la base de l'addition radicalaire de xanthates à diverses oléfines portant un groupe partant convenablement situé.

Les 1,2-dithiolanes peuvent être obtenus par une procédure en un seul pot. Une voie convergente vers les 1,3-dithiolan-2-ones a été développée sur la base de l'addition radicalaire de xanthates à des acétates allyliques. Une réaction inhabituelle a eu lieu, conduisant à la formation inattendue de lactones, et son mécanisme de réaction plausible a été proposé. Cette méthode se caractérise par des réactifs bon marché et facilement disponibles, des procédures expérimentales simples et sûres, des conditions de réaction douces, une bonne tolérance des groupes fonctionnels, une bonne portée du substrat et une économie atomique.

**Title :** New application of the radical chemistry of xanthates

**Keywords :** xanthates, eptazocine, 1,3-dithiane-2-ones, 1,3-dithiolan-2-ones, 1,2-dithiolanes.

**Abstract :** In this thesis, we focus on the new application of the radical chemistry of xanthates for the synthesis of natural products and organosulfur compounds. The radical chemistry of xanthates is used as a powerful tool for the creation of carbon-carbon bonds. Three different routes to (±)-eptazocine were developed involving the radical addition-cyclization sequence as the key step. Although (±)-eptazocine could not be successfully synthesized, its core skeleton of benzylic quaternary carbon center has been constructed. Three practical and convergent routes to 1,3-dithiane-2-ones were developed based on the radical addition of xanthates to various olefins bearing a suitably located leaving group.

1,2-Dithiolanes can be obtained in a one pot procedure. A convergent route to 1,3-dithiolan-2-ones was developed based on the radical addition of xanthates to allylic acetates. An unusual reaction took place leading to the unexpected formation of lactones and its plausible reaction mechanism was proposed. This method features cheap and readily available reagents, simple and safe experimental procedures, mild reaction conditions, good tolerance of functional groups, good substrate scope and atomic economy.