Enantioselective Photoelectrocyclization of Tropolone Derivative in Solid State

By

Letian Wang

B.Sc., Xiamen University, P.R. China, 1994
M.Sc., Graduate School of Chinese Academia of Science, 1997

A THESIS SUBMITTED IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTER OF SCIENCE

In

THE FACULTY OF GRADUATE STUDIES
(DEPARTMENT OF CHEMISTRY)

We accept this thesis as conforming to the required standard

THE UNIVERSITY OF BRITISH COLUMBIA

DECEMBER 1999

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Department of Chemistry
The University of British Columbia
Vancouver, Canada

Date Feb 11, 2000

DE-6 (2/88)
ABSTRACT

Acid 27 and its esters (29 and 21) were prepared, and studies of their photochemical reactivity were investigated in solution. The acid reacts with optical pure amines to form salts whose photoelectrocyclization reactions were studied in solid state. The chiral amines serve as an ionic chiral auxiliary to induce asymmetric synthesis of 32 which could give satisfied enantiomeric excess (up to 79%).

The effort has been tried to stop the reaction at the first step that gives only cyclization product. But both compound 29 and 21 gave photorearrangement product 32 and 31.

Some other tropolone derivatives with phenyl group also have been synthesized and their photochemical reactions were studied in solution phase.

The highlight of the project was to apply the ionic chiral auxiliary method, which was successfully in asymmetric induction in di-π-methane rearrangement reaction and Norrish/Yang type II reaction, to photoelectrocyclization reaction.
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ACKNOWLEDGEMENT

I would like to thank my research supervisor Dr. John R. Scheffer for his valuable guidance and encouragement on my study throughout the years at UBC. I am grateful for his diligence in reading and correcting this thesis and I appreciate his understanding patience in helping me finishing my M.Sc. thesis. His dedication and expertise in the field of organic photochemistry have been a source of inspiration to me.

I would also like to thank past and present member of the Scheffer photochemistry group. It is a pleasure time to work with this fabulous group member. Special thanks goes to Matt Netherton, who has incredible insight in organic chemistry, for his advice and showing me some know-how about instrument. I am also grateful to Katja Rademacher and Ting Kang for their help on instrument. I also like to extend my gratitude to Eugene Cheung, who helps me look at my crystals. Finally, I would like to thank Carl Scott and rest of our group members for their encouragement. It is fortunate for me to work with this wonderful group.

This work would not be done without the help of other members of chemistry department of UBC. I would express my appreciation for all the help from Marietta Austria and Liane Darge of NMR laboratory, Mr. Peter Borda o
Elemental Analysis laboratory, the staff of MS laboratory, the group of X-ray crystallography group under the supervision of Dr. James Trotter and the Chemistry departmental staff in various aspects.

I would express my deepest gratitude to my wife for her fully supporting me to do my work and I also grateful to my parents for their encouragement. Thank you, all my friends, who contribute much to my memorable life here in Vancouver.
Dedicated to my family

with love and thanks
INTRODUCTION

Chapter 1 Introduction

1.1 General Introduction

My research work is focused mainly on a new approach to asymmetric synthesis in the crystalline state called the ionic chiral auxiliary method that has been developed in the Scheffer photochemistry group in recent years. Scheffer and coworkers have successfully applied the solid state ionic auxiliary method to studies of the di-\(\pi\)-methane rearrangement\(^1,2,3\) and the Norrish/Yang type II photocyclization reaction\(^4,17\). This method shows great potential in asymmetric induction strategies. Chiral products can be generated from achiral precursors in the chiral environment provided by an ionic chiral auxiliary.

The goal of my research is to extend this methodology to the photoelectrocyclization reaction. The first part of this thesis is an introduction to the ionic chiral auxiliary method in solid state photochemistry. The second part is a brief review of the photoelectrocyclization reaction, and the final part describes my investigation of the photoelectrocyclization reaction using the solid state ionic chiral auxiliary approach.
The study of solid state photochemistry has a long history. As early as 1834, Hermann Trommsdorff reported the curious observation that crystals of santonin turn yellow and shatter on exposure to sunlight. The occurrence of photoreactions in the crystalline state was recognized and widely reported by the end of the last century. At that time photochemistry was a modest facet of the exciting and rapidly expanding science of organic chemistry. Most investigations in this area focused on reactions in solution phase.

One possible reason why more photochemical reactions have been studied in solution than the solid state stems from the difficulty of determining the structure of crystals. The nature of the intermolecular and lattice forces operative in solid compounds was not well-understood. This was an obstacle to studying the detailed mechanism of reactions in the solid state. With the development of solid-state $^{13}$C NMR techniques and X-ray crystallography, which can pinpoint the exact structure under study, these impediments are rapidly being removed. It has now become possible to investigate in depth the correlation between reactivity and structure in the solid state. Well-organized crystals provide media for the performance of reactions with increased stereo-, regio-, and enantioselectivity. A chiral molecule can be transformed by reaction into optically active product under the influence of the chiral lattice. The field of organic photochemistry in the solid state is one of the faster-developing and more intriguing areas in chemistry in recent years.
However, this new subject is still in its infancy relative to the study of photochemistry in solution. The reasons for this are the followings: it is still not possible to predict the packing arrangement of organic molecules in crystals. The factors that control crystal packing are not yet fully understood, and knowledge of the interactions between molecules in the solid state is still relatively limited. Much of the description of solid-state chemical reactions is, to some extent, at the stage of "show and tell". In addition, organic crystals with sufficient quality for X-ray analysis are often difficult to obtain, sometimes even impossible.

Another impediment to studying photochemistry in the solid state is that bimolecular reactions that are relatively easy to carry out in solution phase become problematic in the solid state. The geometric and distance requirements for bimolecular reactions are hard to meet in the crystalline state due to the limited mutual solid state solubility of structurally different compounds. Two molecules can not freely approach close enough to react in the organic solid.

Scheffer and coworkers have developed a new approach to asymmetric synthesis called the solid state ionic auxiliary concept to overcome some of the obstacles described above. In this approach the chromophore under investigation is linked to an ionic auxiliary by simple salt formation and these salts are then irradiated in the solid state. The Scheffer photochemistry research group has carried out extensive research on these systems. Since 1990, many papers have been published on this topic. The most common systems are salts formed from carboxylic acids and amines. The acid and amine are held together ionically by means of acid-base chemistry. The carboxylic
acids, which contain the substrate under investigation, are treated with amines that can perturb the reactivity of the substrate. The resulting crystals are then irradiated in the solid state. For asymmetric synthesis studies an optically pure ammonium ion serves as an ionic chiral handle to provide an asymmetric environment which can induce an asymmetric reaction in the crystalline state. Of course, the opposite approach, involving an optically active acid auxiliary and amine-tethered substrate has also been studied\textsuperscript{15,16,17}. Quenchers or sensitizers can also be introduced into two-component salts by using the ionic auxiliary method\textsuperscript{18}. The ionic auxiliary method can also be extended to the study of heavy atom effects in solid state photoreactions\textsuperscript{19}.

The solid-state ionic auxiliary approach has shown great utility and promises to become one of the most general methods for asymmetric synthesis in organic photochemistry\textsuperscript{20}. This new approach to asymmetric synthesis in the crystalline state is the main focus of my research work.

1.1 Asymmetric Synthesis

Chirality is common from molecules to human beings\textsuperscript{21}. Optically active materials have great importance for medical science and the pharmaceutical industry\textsuperscript{22,26} since, in general, only one of the enantiomers is biologically active or possesses pharmacological relevance. All biological receptors are chiral, and as such can distinguish between the two enantiomers of a substrate or ligand. The (+) and (-) enantiomers can have very different biological activities and often have different odors or tastes\textsuperscript{23,24}. More than one-half of marketed drugs are
The need to produce enantiomerically pure compounds for use as drug candidates is increasing. In recent years, enantioselective production of chiral compounds has continued to grow at a rapid pace. There are many ways to obtain an enantiomerically pure compound. One option is to resolve it from the racemic mixture, but this can be time-consuming and labor-intensive. Another choice is to find a plant or bacterium to produce it, but this organism/enzyme approach is restricted to the production of only one enantiomer by a given route and finding the proper plant or bacterium can be a tedious work. Another way to obtain pure enantiomers is by asymmetric synthesis.

Asymmetric synthesis is defined as a reaction in which an achiral unit in a molecule is converted into a chiral unit by a reactant in such a manner that the stereoisomeric products are formed in unequal amounts. The reactants can include chemical reagents, catalysts, solvents, circularly polarized light and substrates. The following sections will briefly describe each of these asymmetric synthesis approaches by using selected examples.

### 1.1.1 Chemical Reagents

Generation of a new chiral center in an achiral molecule can be accomplished with a chiral reagent, though it is rare that 100% selectivity is observed. A simple example of this approach is the alkylation of cycloalkanones provided in Figure 1.
Figure 1 Example of asymmetric synthesis using chiral reagent

The ketone reacts with the chiral auxiliary reagent and is then treated with base to give the chelated lithium enolate. This enolate has a rigid conformation and the chiral reagent provides a strong facial bias, so that formation of one of the two alkylated diastereoisomers is preferred. Removal of the chiral auxiliary unit gives mainly one enantiomer. This is represents one of most common approaches to asymmetric synthesis.

1.1.2 Catalysts

A catalyst can be used for asymmetric synthesis. Figure 2 shows an example of the reduction of a ketone in the presence of an optically pure organometallic catalyst. The chiral catalyst generates a nonracemic complex with the prochiral substrate. Using this intermediate as the reducing agent results in transition states which had previously been enantiomeric becoming diastereoisomeric and therefore of different energies. The hydrogen transfers to
the substrate to give the modified substrate product. Finally the modified substrate decomplexes from the catalyst to give the product. The removed catalyst remains and another catalytic cycle can start. The transition states leading to the possible stereoisomers can be diastereomeric. In this particular case the enantiomeric excess of the product is 95% in favour of the (R)-alcohol.

![Chemical structure](image1)

**Figure 2** Example of asymmetric synthesis using catalyst

The major advantage of this approach is that only a catalytic amount of chiral mediator is needed. The expense of the catalyst is relatively small as so little is required. This is very economical and practical. A major drawback is that there are relatively few such catalysts presently available.
1.1.3 Solvent

The reactant will be solvated if the reaction takes place in solution. Consequently, the use of chiral, non-racemic solvents can lead to asymmetric induction because the solvent is likely to be involved in the transition states. Figure 3 shows an example of this type of asymmetric synthesis. The optically pure diamine solvent preferentially solvates a reaction intermediate of tin (II) enolate before reaction with the aldehyde. The product has a 75 per cent enantiomeric excess.

![Chiral Solvent](image)

**Figure 3 Example of asymmetric synthesis using chiral solvent**

This approach to asymmetric synthesis is currently of little general use, as the stereoselectivity is often low and unpredictable. Furthermore, there are few optically pure compounds available in sufficient quantity and with good properties to serve as useful solvents.

1.1.4 Circularly Polarized Light

Circularly polarized light can be used to initiate photochemical reactions in which a chiral product rich in one enantiomer is formed. Figure 4 shows that
irradiation of racemic E-cyclooctene converts the mixture progressively into the achiral Z isomer\textsuperscript{32}.

![Chemical Reaction Scheme]

Figure 4 Example of asymmetric synthesis using circularly polarized light

With a circularly polarized light source (I-CPL), the (R)-enantiomer reacts faster than its mirror image, and (S)-E-cyclooctene accumulates in solution. However, such experiments have not proved effective and universal. The levels of optical enhancement in the above experiment are small (less than 1% e.e.).

1.1.5 Active Substrate

A new chiral center can be generated in the crystalline state. An achiral compound, but whose crystals are chiral, can be converted by ultraviolet light into an optically enriched product\textsuperscript{33}. Molecules in crystals are arranged in a rigid periodic three dimensional pattern. The packing of the reactants, as well as the separation distances and orientation of the functional groups, can greatly affect the products of reaction. So the crystalline lattice can serve as a chiral medium for asymmetric induction. The Scheffer photochemistry research group has done
a lot of work in investigating on this type of reaction. Figure 5 gives an example of an absolute asymmetric photochemical rearrangement in the solid state. Diabenzobarrelene 1 can crystallize in the chiral space group $P2_12_12_1$, and the di-$\pi$-methane rearrangement of an enantiomorphously pure single crystal of this compound gives photoproduct 2 with e.e. $> 95\%$.

**Figure 5** Example of asymmetric synthesis using active substrate

Photolysis of 1 in solution or in its crystal with achiral space group Pbca gave racemic product. This demonstrates that crystal chirality can induce optical activity in the chiral product through a stereospecific photorearrangement in the solid state. The results of such enantioselective solid-state photoreactions provide not only a reasonable explanation for the prebiotic origin of optical activity on earth, but also suggest a promising method of asymmetric synthesis. The Scheffer photochemistry group has carried out extensive research on developing a more general approach of asymmetric synthesis by using the power of chiral crystals. This is the ionic auxiliary approach described below.
1.2 Ionic Auxiliary Concept

In 1853, Louis Pasteur discovered the resolution of racemic tartaric acid by treatment with an optically active amine followed by fractional crystallization\(^{34}\). This is the origin of the idea of the ionic chiral auxiliary method, which is an alternative dynamic approach to achieving nonracemic products. The principle of the solid state ionic chiral auxiliary is illustrated in Figure 6.

In this approach, carboxylic acids and amines can be modified through organic synthesis to serve the desired function. Suppose the substrate is an achiral, photoreactive acid and the auxiliary is an optically pure amine. The acid and amine are tethered by salt formation and the resulting chiral crystal is irradiated by ultraviolet light. Such photoreactions proceed through ionic transition states that are diastereomerically related. If the difference in activation energy of the transition states is sufficiently large, a single desired photoproduct enantiomer can be obtained through a kinetically controlled process (Figure 6)\(^{17}\) after the removal of the amine auxiliary. Thus an enantiomeric excess is achieved through the photoreaction in the crystalline state. This approach works well in the solid state, as the reaction medium is chiral, which is due to the fact that optically active materials are required to crystallize in chiral space groups\(^9\). The opposite approach, in which the salts are formed from amine substrate and optically active carboxylic acid auxiliary, is equally valid. One of the limitations of the solid-state ionic chiral auxiliary approach is that the reactant candidates must bear acidic or basic functional groups which allow salt formation.
The ionic auxiliary method differs significantly from the covalent chiral auxiliary method, which is a popular approach in asymmetric synthesis in
solution. The substrates involved in these two methods are illustrated in Figure 7.

Figure 7 Auxiliary methods of asymmetric synthesis

Covalent auxiliaries are tethered to the substrate through covalent bonds, while ionic auxiliaries are linked to the substrate through ionic bonds. Cram's Rule$^{35}$ (see Figure 8) provides a good example of the covalent auxiliary method in asymmetric synthesis.

Figure 8 Cram's Rule
An aldehyde or ketone that has an adjacent stereocenter can be thought of as possessing a covalent chiral auxiliary that can direct a nucleophilic addition from the less hindered side. In some cases, the oxygen atom can chelate the metal ion of the nucleophile. This chelation can result in a conformationally rigid intermediate, which translates into a large energy difference in the transition state. The high conformational rigidity can lead to high diastereoselectivity and predictability. Examples of stereochemical control that involve more remote chiral centers are relatively rare.

The following are some of the characteristic features and advantages of the solid-state ionic auxiliary method: the chiral auxiliary is not necessarily located close to the site of reaction, while in the covalent auxiliary method (most of them in solution phase) the chiral auxiliary unit must be close enough to influence the reaction center in order to achieve a predominance of one stereoisomer (enantiomer or diastereomer) over the other. The chiral crystalline environment is responsible for asymmetric induction.

Owing to the ionic character, salts formed between carboxylic acids and organic amines tend to have high melting points and strong crystal lattice forces. Such materials are more robust than purely molecular crystals and have a greater ability to sustain the lattice motif and survive photolysis to higher conversions without loss of topochemical control, which is necessary for this type of reaction to be synthetically useful. With this high thermal stability, a wide range of reaction temperatures can also be chosen. Easy removal of ionic auxiliary after photochemical reaction is another advantage of this method.
1.3 Application of The Ionic Chiral Auxiliary Method in Solid State Photochemistry

The Scheffer research group has applied this method to many systems, which shows it to be a general and useful technique for acquiring optically pure compounds. Here are some representative examples that show the application of the method.

1.3.1 Application in the Norrish/Yang Type II Reaction

Asymmetric synthesis through the Norrish/Yang type II reaction is fully studied using this method. The Norrish/Yang type II reaction (shown in Figure 9) involves intramolecular abstraction of a $\gamma$-hydrogen atom followed by cyclization to give an alcohol. Abstractions of $\beta$- and $\delta$-hydrogens are usually observed only when the $\gamma$-hydrogen is absent.

![Norrish/Yang type II reaction](image)

**Figure 9** Norrish/Yang type II reaction
Two examples of the application of the solid-state ionic chiral auxiliary approach to asymmetric induction in the well-known Yang type II photocyclization reaction are provided. The first is shown in Figure 10. *cis*-4-tert-butyl-1-methylcyclohexyl phenyl carboxylic acid 4 is treated with optically pure (S)-(-)-α-methyl benzylamine 3 and forms a crystalline salt with a chiral space group. Since the auxiliary 3 is optically active, such salts are required to crystallize in chiral space groups, and this provides the asymmetric medium in which the photoreaction is carried out. The salt 5 gave, upon irradiation in the crystalline state and diazomethane workup, 96.9% enantiomeric excess of the Yang cyclization photoproduct 6. A series of closely related compounds has also been studied and similar results are obtained.
Figure 10  Example of asymmetric induction in Yang type II photocyclization reaction through solid state ionic chiral auxiliary method
Another example is shown in Figure 11. The achiral 14-membered ring aminoketone 8, which forms a chiral salt 9 with the optically active phosphonic acid, (R)-(−)-2-hydroxy-5,5-dimethyl-4-phenyl-1,3,2-dioxaphosphorinane-2-oxide 7, undergoes efficient Norrish/Yang type II reaction in the solid state to give the chiral cis-cyclobutanol 10, with enantiomeric excesses of 98% in favour of the (−)-enantiomer at 21% conversion, as well as the achiral cleavage product 12 (Figure 11\textsuperscript{17}). Salts formed from a number of enantiomerically pure carboxylic, sulfonic, and phosphoric acids have been irradiated in the solid state. The enantiomeric excesses obtained for cis-cyclobutanol 10 range from 98% to 44%. In the crystalline state molecular motions are severely restricted. Analysis of the X-ray structure of reactants shows that the distance between the oxygen atom and hydrogen atom in the crystalline state governs the hydrogen abstraction. The conformational rigidity of the molecule in the chiral crystalline state is of critical importance for controlling the course of asymmetric induction.
Figure 11 Another example of asymmetric induction in Yang type II photocyclization reaction
Other unimolecular Norrish type II photoreactions have been investigated for the purpose of studying asymmetric synthesis in the solid state and give the similar results\textsuperscript{38}.

\subsection*{1.3.2 Application to the Di-\pi-methane Rearrangement Reaction}

The di-\pi-methane (or Zimmerman) rearrangement is one of the most general and thoroughly studied organic photoreactions\textsuperscript{39,40}. The reaction is the photochemical conversion of 1,4-dienes to vinyl cyclopropanes via a radical mechanism (Figure 12).

This photochemical reaction take place in compounds that possess two \(\pi\)-bonds separated by a \(sp^3\) hybridized carbon atom\textsuperscript{41}. Upon irradiation, the compounds can be converted into products that have a vinylcyclopropane moiety. The three-step mechanism involves an initial 2,4-bond formation to give a 1,4-cyclopropylidicarbinyl biradical. The biradical then undergoes rearrangement to give a 1,3-biradical which subsequently closes to yield the final photoproduct. Replacement of one of the vinyl groups by an aromatic ring gives a similar rearrangement, shown in Figure 13.
Figure 12 Di-π-methane rearrangement reaction

Figure 13 Di-π-methane rearrangement reaction in aromatic compound

An example of a solid state ionic chiral auxiliary-induced asymmetric induction in a di-π-methane rearrangement reaction is shown in Figure 14. The salts are formed from anti-9-carboxybenzonorbornadiene 13 with a series of
optically active amines such as L-valine 4-benzoylphenyl ester 14. Enantiomeric excesses are generally high. A 91% enantiomeric excess of (-)-16 obtained at quantitative conversion (-20 °C) of salts in this case.

The examples described above demonstrate the power of the crystal lattice in directing unimolecular chemical reactions. Crystal lattice control of organic photochemical reactivity described above is an innovative, exciting and
rapidly emerging area of organic chemistry. This solid state ionic auxiliary method promises to become a powerful and useful tool in asymmetric synthesis.

2. The Photoelectrocyclization Reaction

The goal of my work is to test the solid state ionic chiral auxiliary method on a photoelectrocyclization reaction. The following is a brief introduction to photoelectrocyclization reactions.

2.1 Introduction to Photoelectrocyclization Reactions

An electrocyclic reaction is an intramolecular reaction in which a $\pi$ bond in the reactant is lost so that a cyclic compound with a new sigma bond can be formed. The cyclic product has one fewer double bond than the reactant. The molecular rearrangement involves the formation of a sigma bond between the termini of a fully conjugated linear pi-electron system (or a linear fragment of a pi-electron system) and a decrease by one in the number of pi bonds, or the reverse of that process. An example is shown in Figure 15.

![Figure 15 Photoelectrocyclization reaction](image-url)
When a polyene undergoes an electrocyclic ring closure to form a cycloalkene, the terminal carbons of the polyene chain must rotate approximately 90° to convert the p orbitals into the sp\(^3\) orbitals forming the new σ bond. The stereochemistry of such a process is termed "conrotatory" if the substituents at the interacting termini of the conjugated system both rotate in the same sense or "disrotatory" if one terminus rotates in a clockwise and the other in a counterclockwise sense (shown in Figure 16).

![Figure 16 Conrotatory and disrotatory](image)

Concerted electrocyclization reactions are governed by selection rules which are now commonly known as the Woodward-Hoffmann rules\(^{42}\). Conjugated polyenes can undergo electrocyclization reactions on irradiation with ultraviolet light as well as on heating. Photochemical electrocyclization of systems of 4n π
electrons should be disrotatory, and the reaction of systems containing $4n+2$ pi electrons should be conrotatory.

Orbital correlation diagrams are used to analyze the electrocyclization reaction. Figure 17 shows the symmetry properties of cyclobutene and butadiene. Concerted photochemical conversion of butadiene to cyclobutene by a conrotatory process would require raising an electron to the high-energy $\sigma^*$ orbital of cyclobutene (shown in Figure 18). In contrast, the disrotatory reaction would yield the lowest-energy excited state of cyclobutene. The product would be formed by disrotatory reaction.
Symmetry

<table>
<thead>
<tr>
<th>Orbitals</th>
<th>$\sigma$</th>
<th>$\pi$</th>
<th>$\pi^*$</th>
<th>$\sigma^*$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respect to plane</td>
<td>S</td>
<td>S</td>
<td>A</td>
<td>A</td>
</tr>
<tr>
<td>Respect to $C_2$ axis</td>
<td>S</td>
<td>A</td>
<td>S</td>
<td>A</td>
</tr>
</tbody>
</table>

**Figure 17** Symmetry properties of cyclobutene and butadiene orbitals

**Figure 18** Correlation diagram for cyclobutene and butadiene molecular orbitals
Both the conrotatory process and the disrotatory process can be analyzed by comparing the symmetry classification of the reactant and product orbitals. If the excited state orbitals are involved in the correlation diagram, the transformation would happen in the excited state which is a photoelectrocyclization reaction.

2.2 The Photoelectrocyclization Reaction in Organized Media

During the past decade, many elegant and efficient chiral induction strategies, most of them in solution, have been developed for a variety of thermal reactions\textsuperscript{43,44}. However, there are relatively few examples of asymmetric induction in photochemical electrocyclization reactions\textsuperscript{45,46}.

A successful example of an enantioselective photoelectrocyclization in the solid state was reported by Toda and co-workers\textsuperscript{47}. Upon excitation, α-tropolone alkyl ethers, complexed with optically pure host diol 18, undergo intramolecular cyclization to afford the corresponding bicyclic products by disrotatory ring closure as illustrated in Figure 19. Irradiation in solution results in a racemic mixture as the result of an equal probability of “in” and “out” rotation as illustrated in Figure 19. Depending on the direction of disrotation, two optical isomers may be formed.
In solution:

\[
\text{17: } R = \text{Me} \quad \xrightarrow{hv} \quad \text{a: } (1S, 5R)(-), \quad \text{b: } (1R, 5S)(+), \quad 20 \quad \text{Racemic}
\]

Figure 19 Toda's work

Although racemic products are obtained in solution, irradiation of crystalline inclusion complexes of \(\alpha\)-tropolone alkyl ethers with 1,6-bis(2-chlorophenyl)-1,6-diphenylhexa-2,4-diyne-1,6-diol 18 gave cyclic products of 100% optical purity. The X-ray structure of the 1:1 \(\alpha\)-tropolone ethyl ether complex with diol 18 shows that the guest molecule is held by hydrogen bonds to one host molecules as illustrated in Figure 20. On the basis of the crystal
packing, Kaftory reasoned that the enantiomeric control results from the chiral environment provided by the host and from the differences in short contacts that develop between the alkoxy group of the guest and the aryl group of the host during the two directions of rotation\textsuperscript{48}.

\begin{center}
\includegraphics[width=0.5\textwidth]{figure.png}
\end{center}

Figure 20 Asymmetric induction via Host-guest molecule

Recently V. Ramamurthy and his co-workers have reported the enantioselective photoelectrocyclization of tropolone methyl ether in chirally modified zeolites\textsuperscript{49} (10 - 50\% e.e.). The bicyclic photoisomer 20 is obtained by irradiating $\alpha$-tropolone methyl ether using UV light (Figure 21). An approach to
control the mode of cyclization is to adsorb the compound on a surface, since under these conditions, it is possible that the surface could interfere with one of the two modes of disrotation. Even then racemic products would be expected because the reactant should not show any preference for adsorption from either enantiotopic face. On the other hand, when the surface is chiral, preferential adsorption from one of the two enantiotopic faces is likely, and under such conditions, one might anticipate enantioselectivity in the formation of product. The medium is a zeolite with incorporation of various optically active amines and alcohols in the supercages. The relatively low e.e. obtained suggests that not all molecules are present in their idealized arrangement.

Figure 21 Enantioselective photoelectrocyclization of tropolone methyl ether in zeolite
These examples show that asymmetric introduction in photoelectrocyclization reactions is possible in a solid chiral medium.
RESULTS AND DISCUSSION

Chapter 2 Results and Discussion

2.1 Preparation and Identification of Acids

2.1.1 Synthesis and Identification of Troplone Esters 21 and 23

Synthesis of Compound 21

The starting materials are tropolone and alkyl halides. Tropolone is one of a family of \( \alpha \)-hydroxyl ketones that can undergo a tautomeric hydrogen shift. The activation energy for hydrogen transfer between the two degenerate forms of tropolone in solution is low, no restrictions being imposed on the reaction by the surrounding solvent molecules\(^{50}\). The tautomeric proton transfer (as illustrated in Figure 22) in solution is so fast that carbon-13 NMR spectra always exhibit averaged signals due to the two tautomeric forms.

![Tautomeric proton transfer of tropolone](image)

Figure 22 Tautomeric proton transfer of tropolone
The structure of tropolone can be thought to have $C_2$ symmetry. Instead of showing seven peaks, the $^{13}C$ spectrum shows four carbon peaks. After alkylation, the seven carbons of the tropolone ring show different chemical shifts in the $^{13}C$ spectrum.

Compound 21 was synthesized according to the procedure reported by Bass\textsuperscript{51} (shown in Figure 23) in which the alkyl halide $R-X$ was added to the tropolone anion prepared \textit{in situ} by treatment of tropolone with potassium carbonate.

![Figure 23 Synthesis of compound 21](image)

Modifications were made to the original procedure. Originally, a solution of alkyl halide, tropolone and potassium carbonate were mixed together and then heated to 80 °C. However, we found that this method led to a low yield of ester. The yield can be improved by mixing tropolone and potassium carbonate first and then adding the alkyl halide and keeping reaction at room temperature overnight. Optimization of this procedure eventually led to an 81% yield of compound 21. The water in the solvent can significantly affect the yield of the ester. The reaction, which takes place in anhydrous acetonitrile, can give a yield
more than twice that in non-dried solution (38%). The solvent can also affect the yield. Table 1 shows the yields in different solvents after 18 h at room temperature.

Table 1 Yield of compound 21 in different solvents

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetonitrile</td>
<td>81</td>
</tr>
<tr>
<td>Tetrahydrofuran</td>
<td>60</td>
</tr>
<tr>
<td>Methanol</td>
<td>21</td>
</tr>
</tbody>
</table>

NMR Analysis of Compound 21

$^1$H and $^{13}$C NMR spectra of 21 were obtained. In order to solve the structure, $^1$H-$^{13}$C correlation spectra (HMQC) and $^1$H-$^1$H correlation spectroscopy (COSY) were required. The NMR data for compound 21 are presented in Tables 2 and 3.
### Table 2  $^1$H NMR data for compound 21

<table>
<thead>
<tr>
<th>$^1$H NMR (500 MHz), δ ppm (# H, multiplicity)</th>
<th>Assignment</th>
<th>COSY Correlation (400 MHz)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6.94 (1, t)</td>
<td>H-3</td>
<td>H-4, H-2</td>
</tr>
<tr>
<td>6.85 (1, d)</td>
<td>H-2</td>
<td>H-3</td>
</tr>
<tr>
<td>6.75 (1, t)</td>
<td>H-5</td>
<td>H-6, H-4</td>
</tr>
<tr>
<td>6.62 (1, t)</td>
<td>H-4</td>
<td>H-3, H-5</td>
</tr>
<tr>
<td>6.55 (1, d)</td>
<td>H-6</td>
<td>H-5 H-8*</td>
</tr>
<tr>
<td>4.55 (2, s)</td>
<td>H-8</td>
<td>H-6*, H-10*</td>
</tr>
<tr>
<td>3.93 (2, q)</td>
<td>H-10</td>
<td>H-11, H-8*</td>
</tr>
<tr>
<td>0.96 (3, t)</td>
<td>H-11</td>
<td>H-10,</td>
</tr>
</tbody>
</table>

* very weak
Table 3 $^{13}$C NMR data for compound 21 and correlation to the $^1$H NMR spectrum

<table>
<thead>
<tr>
<th>Assignment</th>
<th>$^{13}$C NMR, δ ppm (APT phase from 75 MHz)</th>
<th>HMQC correlation to $^1$H NMR (500 MHz), δ ppm</th>
</tr>
</thead>
<tbody>
<tr>
<td>C-1</td>
<td>180.25 (+)</td>
<td></td>
</tr>
<tr>
<td>C-2</td>
<td>137.90 (-)</td>
<td>6.85 (H-2)</td>
</tr>
<tr>
<td>C-3</td>
<td>136.35 (-)</td>
<td>6.94 (H-3)</td>
</tr>
<tr>
<td>C-4</td>
<td>129.31 (-)</td>
<td>6.62 (H-4)</td>
</tr>
<tr>
<td>C-5</td>
<td>132.13 (-)</td>
<td>6.75 (H-5)</td>
</tr>
<tr>
<td>C-6</td>
<td>116.34 (-)</td>
<td>6.55 (H-6)</td>
</tr>
<tr>
<td>C-7</td>
<td>163.37 (+)</td>
<td></td>
</tr>
<tr>
<td>C-8</td>
<td>65.70 (+)</td>
<td>4.55 (H-8)</td>
</tr>
<tr>
<td>C-9</td>
<td>167.59 (+)</td>
<td></td>
</tr>
<tr>
<td>C-10</td>
<td>61.36 (+)</td>
<td>3.93 (H-10)</td>
</tr>
<tr>
<td>C-11</td>
<td>13.91 (-)</td>
<td>0.96 (H-11)</td>
</tr>
</tbody>
</table>
Synthesis of Compound 23

Compound 23 is a new compound. The method (shown in Figure 24) of synthesis of 23 is copied from the Bass approach. The yield of product after flash chromatography was 85%. The product was recrystallized from a methanol and ethyl acetate mixture to afford white needles, m.p. 145.5 - 146.2 °C.

Figure 24 Synthesis of compound 23
2.1.2 Synthesis of the Acids from the Corresponding Ester

The key to synthesizing the corresponding acids 27 and 28 lies in using the proper base to hydrolyze the esters. The synthetic pathways are outlined in Figure 25.

Some common bases were chosen for the hydrolysis of tropolone ester 21. The trial conditions are listed in Table 4. Unfortunately, the expected acids were not obtained. Instead the tropolone lithium, potassium and sodium salts were formed (Figure 26).

Figure 25 Synthesis of acids 27 and 28
**Table 4** Conditions for Hydrolysis of Tropolone Ester 21

<table>
<thead>
<tr>
<th>Base</th>
<th>Concentration (M) *</th>
</tr>
</thead>
<tbody>
<tr>
<td>LiOH</td>
<td>2.0, 1.0, 0.5</td>
</tr>
<tr>
<td>NaOH</td>
<td>2.0, 1.0, 0.5</td>
</tr>
<tr>
<td>KOH</td>
<td>1.5, 1.0, 0.4</td>
</tr>
</tbody>
</table>

* The concentration of base refers to an aqueous solution. This solution was mixed with methanol (1:2 v/v) and then used to react with the ester. All the reactions were conducted at room temperature for 2 h.

Figure 26 Tropolone lithium, potassium and sodium salts

The reaction temperature was decreased to 0°C, but the final products were the same - tropolone salts. All these tropolone metal salts are bright yellow fine powder. The lithium salt was recrystallized from methanol. Large cubic crystals suitable for X-ray analysis were readily obtained.
There are two possible ways (path A and path B, shown in Figure 28) to break the O-C bond. Path A can be thought as an addition and elimination process, while path B can be thought as a nucleophilic substitution reaction. Because the goal of the project was to study the photoelectrocyclization reaction in solid state, the mechanism of the reaction (shown in Figure 28) was not further investigated. In order to determine whether the reaction goes in path A or path B, isotope $^{18}$O could be used. The strategy can be described in Figure 27.

![Figure 27 Strategy of determination of mechanism by deuterium agent](image)
Figure 28 Two Possible ways to break O-C bond
The negative charge on the oxygen of the tropolone anion can be stabilized not only by the metal cation, but can also be delocalized by the \( \pi \) system in the tropolone ring. These salts have high thermal stability with melting points > 300°C. The hydrolysis of compound 21 using different concentrations of alkaline solution gave the same products the corresponding tropolone salts. The tropolone salts were formed faster in the concentrated base solution than in dilute base solution.

Since alkali metal bases did not work for the hydrolysis of the ester, we switched to the weaker alkaline earth hydroxides. Barium hydroxide octahydrate, \( \text{Ba(OH)}_2\cdot8\text{H}_2\text{O} \), was chosen as a candidate. No special preference was made in selecting this base other than it was readily available for study. Fortunately, barium hydroxide worked well for the hydrolysis of the ester, giving a 59% yield of the corresponding acid after workup with HCl. \( \text{Ba(OH)}_2\cdot8\text{H}_2\text{O} \) was ground to a fine powder before use. The solubility of \( \text{Ba(OH)}_2\cdot8\text{H}_2\text{O} \) in methanol is poor. No extra water was needed to add. When the ester was mixed with methanol and \( \text{Ba(OH)}_2\cdot8\text{H}_2\text{O} \), a viscous gel-like solution was formed immediately. The solution was stirred vigorously for 2 h. The yield of acid was affected by the time of hydrolysis. Table 5 shows the yields of acid with different reaction times.
Table 5 Yields of acid from compound 3 with different times of hydrolysis

<table>
<thead>
<tr>
<th>Time of Hydrolysis</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5</td>
<td>47</td>
</tr>
<tr>
<td>1</td>
<td>51</td>
</tr>
<tr>
<td>2</td>
<td>59</td>
</tr>
<tr>
<td>3</td>
<td>35</td>
</tr>
<tr>
<td>3.5</td>
<td>28</td>
</tr>
</tbody>
</table>
**Synthesis of Methyl Ester 29 from Acid 27**

A common way of methyl esterification from the corresponding acid is using methanol under acid catalysis. Methyl ester 29 was prepared from the acid by sulfuric acid-catalyzed Fischer esterification in refluxing methanol, as shown in Figure 29, but the yield was only 7%.

![Figure 29 Synthesis of compound 29 by acid-catalyzed esterification](image)

Acid 27 was dissolved in methanol in the presence of sulfuric acid. After 30 min, the reaction mixture was tested by TLC (ethyl acetate - hexane 1:3). The TLC pattern showed that there was some brown material left at the origin on the plate. When the developing agent was changed to pure acetyl acetate, the brown spot did not move from the origin. Above the brown spot, strong tailing was observed, which was the same pattern and r.f. value of tropolone. The methyl ester 29 was obtained after separation using flash column (acetyl acetate: hexane = 1:2). The final yield of methyl ester 29 from the acid was an unsatisfactory 7%. The low yield and TLC analysis indicated that the major part of the ester had decomposed.
The methyl ester 29 was synthesized in better yield by using diazomethane which can give a 97% yield as shown in Figure 30. This is a common way of transforming carboxylic acids to the corresponding methyl esters in our laboratory. A diethyl ether solution of diazomethane is usually prepared immediately before use. Diazald, mixed with ethanol and sodium hydroxide, is used for generation of diazomethane. The structure of esterification product 29 was confirmed by NMR data. The transformation of carboxylic acid by treatment with diazomethane is also an alternative way to prove the existence of carboxylic acid of starting materials. So the reaction shown in Figure 30 can also be a proof for the acid structure of reactant 27.

Figure 30 Methyl esterification
NMR Analysis of Acids 27 and 28

The NMR assignments for compounds 21, 27 and 28 are given in Table 6. The structures are shown in Figure 31. The NMR data of Compound 21 was listed as reference for the acids.

Figure 31 Structures of compound 21, 27 and 28
<table>
<thead>
<tr>
<th></th>
<th>C₁</th>
<th>C₂</th>
<th>C₃</th>
<th>C₄</th>
<th>C₅</th>
<th>C₆</th>
<th>C₇</th>
<th>C₈</th>
<th>C₉</th>
<th>C₁₀</th>
<th>C₁₁</th>
<th>C₁₂</th>
<th>C₁₃</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Compounds</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>21</td>
<td>180.25</td>
<td>137.90</td>
<td>136.35</td>
<td>129.31</td>
<td>132.13</td>
<td>116.34</td>
<td>163.37</td>
<td>65.70</td>
<td>167.59</td>
<td>61.36</td>
<td>13.91</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>27</td>
<td>179.30</td>
<td>140.02</td>
<td>138.02</td>
<td>131.07</td>
<td>135.3</td>
<td>117.91</td>
<td>165.21</td>
<td>66.3</td>
<td>171.06</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>28</td>
<td>179.30</td>
<td>136.75</td>
<td>136.59</td>
<td>128.25</td>
<td>133.09</td>
<td>114.58</td>
<td>163.75</td>
<td>69.44</td>
<td>140.92</td>
<td>127.57</td>
<td>129.52</td>
<td>130.38</td>
<td>167.06</td>
</tr>
</tbody>
</table>
2.2 Photochemical Studies of Compound 21

2.2.1 Initial Investigation

The photochemical reaction of ester 21 was first investigated in solution (Figure 32), because the products could be obtained in relatively large amounts, which facilitated their structure elucidation.

![Figure 32](image-url)
The mechanism of photolysis of tropolone methyl ether was first brought by Chapman\textsuperscript{52} (shown in Figure 33). We think the mechanism of formation of the second photoproduct was similar with the photolysis of tropolone methyl ether.

The ester 21 was dissolved in anhydrous acetonitrile forming a 0.33 M solution and degassed for one hour under nitrogen gas. The sample vial was irradiated at room temperature\textsuperscript{*} through Pyrex with a medium pressure mercury lamp. The progress of the photoreaction was followed by GC and TLC analysis by taking aliquots during and after irradiation. The GC analysis showed that at the beginning of reaction a small peak was formed, called the first photoproduct, whose structure is probably 30. This peak decreased after further photolysis, and another peak, called the second photoproduct 31, grew in. The formation and disappearance of 30 is shown in Figure 34. The yield of the first photoproduct 30 was low, no more than 9%. Flash column and Chromatron chromatography were used to try to separate the first photoproduct, but a pure sample could not be

\footnote{Without good ventilation, the temperature in the photo box increases to 40-45 °C after more than two hours irradiation.}
obtained. Actually, a pure fraction, which showed one peak on GC, had been obtained just after flash column, but it began to convert to second product 31 just after it came out of the flash column. After 3 min, 30% of this fraction converted to second product 31. So only the mixture was left. The difficulty of separation of first photoproduct 30 may be that it is easy to convert to second product 31 in the presence of the room light and the yield is small.

![Graph showing the yield of Compound 13 over time of photolysis](image)

**Figure 34** The formation of first photoproduct 30 from compound 21

The second photoproduct 31 was successfully separated in pure form. After 40 h, the major product is the second photoproduct 31. The results of its yield and conversion are displayed in Table 7. The variation in yield of 31 with photolysis time is plotted in Figure 35.

The values of conversion and yield are reported from the GC analysis. We assume that all the components of the reaction mixture are shown on GC. The definitions of yield and conversion are the following:
Yield = % of Photoproduct Peak
Conversion = 100% - % Starting Materials

Table 7 Results of irradiation of ester 21 in solution

<table>
<thead>
<tr>
<th>Irradiation Time (hour)</th>
<th>% Conversion</th>
<th>% Yield of second photoproduct</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.0</td>
<td>10.2</td>
<td>3.5</td>
</tr>
<tr>
<td>4.0</td>
<td>17.4</td>
<td>7.7</td>
</tr>
<tr>
<td>8.2</td>
<td>42.7</td>
<td>26.7</td>
</tr>
<tr>
<td>14.0</td>
<td>62.2</td>
<td>40.9</td>
</tr>
<tr>
<td>19.0</td>
<td>80.4</td>
<td>57.9</td>
</tr>
<tr>
<td>28.0</td>
<td>91.2</td>
<td>71.7</td>
</tr>
<tr>
<td>35.5</td>
<td>95.5</td>
<td>83.2</td>
</tr>
<tr>
<td>44.5</td>
<td>96.9</td>
<td>93.3</td>
</tr>
</tbody>
</table>
As shown, irradiation of 21 for over 45 h in CH$_3$CN gave one major photoproduct at high conversion (> 90%). The first photoproduct completely converted to the second photoproduct 31.

The reason that the conversion of 31 is low at the beginning of the photolysis is due to formation of the first photoproduct 30. The first photoproduct continues to absorb light and convert to the second photoproduct 31, which accumulates. After 40 h, the second photoproduct 31 is obtained in over 90% yield at over 95% conversion.

The photoreaction was carried out in different solvents (Table 8). As shown, the reaction in CH$_3$CN is faster than the reactions in CH$_3$OH and benzene. The GC results agreed with the experimental observation that the color...
of the reaction solution in CH$_3$CN changed faster from yellowish brown to reddish brown than in the other solvents.

**Table 8** Comparison of yields of reaction in different solvents after 4 h of irradiation

<table>
<thead>
<tr>
<th>Solvent</th>
<th>% Yield of Second Photoproduct 31</th>
</tr>
</thead>
<tbody>
<tr>
<td>CH$_3$CN</td>
<td>7.7</td>
</tr>
<tr>
<td>CH$_3$OH</td>
<td>2.7</td>
</tr>
<tr>
<td>C$_6$H$_6$</td>
<td>1.9</td>
</tr>
</tbody>
</table>

Compound 29 went the similar photo-reaction (shown in Figure 36). After 30 h photolysis in acetonitrile solution, 29 gave the second photoproduct 32 with 65% yield. Rf value of TLC for Compound 32 was smaller than that of Compound 31, which indicated that 32 is more polar than 31.

![Diagram of compounds 29 and 32](image)

**Figure 36** Formation of second photoproduct 32 in solution

$^1$H and $^{13}$C NMR spectra of the second photoproducts were obtained. In order to solve the structure, 2D NMR spectra were needed; $^1$H-$^{13}$C correlation
(HMQC) and COSY were obtained. The NMR data for the methylester 32 are shown in Table 9 and 10, and the NMR data for ethylester 31 are shown in Table 11 and 12.
Table 9 $^1$H NMR data for 32

<table>
<thead>
<tr>
<th>$^1$H NMR (500 MHz), $\delta$ ppm (# H, multiplicity)</th>
<th>Assignment</th>
<th>COSY Correlation (400 MHz)</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.64 (1, dd)</td>
<td>H-3</td>
<td>5.98 (H-2), 3.58 (H-4)</td>
</tr>
<tr>
<td>5.98 (1, d)</td>
<td>H-2</td>
<td>7.64 (H-3)</td>
</tr>
<tr>
<td>5.05 (1, d)</td>
<td>H-5</td>
<td>3.58 (H-4)</td>
</tr>
<tr>
<td>4.41 (2, dd)</td>
<td>H-8</td>
<td>3.74 (H-10)*</td>
</tr>
<tr>
<td>3.74 (3, s)</td>
<td>H-10</td>
<td>4.41 (H-8)*</td>
</tr>
<tr>
<td>3.66 (1, d)</td>
<td>H-7</td>
<td>3.58 (H-4)</td>
</tr>
<tr>
<td>3.58 (1, m)</td>
<td>H-4</td>
<td>3.66 (H-7), 5.05 (H-5), 7.64 (H-3)</td>
</tr>
</tbody>
</table>

* very weak
Table 10 $^{13}$C NMR data for 32

<table>
<thead>
<tr>
<th>Assignment</th>
<th>$^{13}$C NMR, $\delta$ ppm (APT phase from 75 MHz)</th>
<th>HMQC correlation to $^1$H NMR (500 MHz), $\delta$ ppm</th>
</tr>
</thead>
<tbody>
<tr>
<td>C-1</td>
<td>204.22 (+)</td>
<td></td>
</tr>
<tr>
<td>C-2</td>
<td>133.39 (-)</td>
<td>5.98(H-2)</td>
</tr>
<tr>
<td>C-3</td>
<td>164.42 (-)</td>
<td>7.64(H-3)</td>
</tr>
<tr>
<td>C-4</td>
<td>40.65 (-)</td>
<td>3.58(H-4)</td>
</tr>
<tr>
<td>C-5</td>
<td>103.29 (-)</td>
<td>5.05(H-5)</td>
</tr>
<tr>
<td>C-6</td>
<td>153.52 (+)</td>
<td></td>
</tr>
<tr>
<td>C-7</td>
<td>54.24 (-)</td>
<td>3.66(H-7)</td>
</tr>
<tr>
<td>C-8</td>
<td>65.84 (+)</td>
<td>4.41(H-8)</td>
</tr>
<tr>
<td>C-9</td>
<td>168.41 (+)</td>
<td></td>
</tr>
<tr>
<td>C-10</td>
<td>52.25 (-)</td>
<td>3.74(H-10)</td>
</tr>
</tbody>
</table>
Table 11 $^1$H NMR data for 31

<table>
<thead>
<tr>
<th>$^1$H NMR (500 MHz), δ ppm (# H, multiplicity)</th>
<th>Assignment</th>
<th>COSY Correlation (400 MHz)</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.64 (1, dd)</td>
<td>H-3</td>
<td>5.96 (H-2), 3.56 (H-4)</td>
</tr>
<tr>
<td>5.96 (1, dd)</td>
<td>H-2</td>
<td>7.64 (H-3)</td>
</tr>
<tr>
<td>5.03 (1, d)</td>
<td>H-5</td>
<td>3.56 (H-4)</td>
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<tr>
<td>4.38 (2, dd)</td>
<td>H-8</td>
<td>4.19 (H-10)*</td>
</tr>
<tr>
<td>4.19 (3, q)</td>
<td>H-10</td>
<td>1.24 (H-11), 4.38(H-8)*</td>
</tr>
<tr>
<td>3.64 (1, d)</td>
<td>H-7</td>
<td>3.56 (H-4)</td>
</tr>
<tr>
<td>3.56 (1, m)</td>
<td>H-4</td>
<td>3.64 (H-7), 5.03 (H-5), 7.64 (H-3)</td>
</tr>
<tr>
<td>1.24 (3, t)</td>
<td>H-11</td>
<td>4.19 (H-10)</td>
</tr>
</tbody>
</table>

*very weak
### Table 12 $^{13}$C NMR data for 31

<table>
<thead>
<tr>
<th>Assignment</th>
<th>$^{13}$C NMR, δ ppm (APT phase from 75 MHz)</th>
<th>HMQC Correlation to $^1$H NMR (500 MHz), δ ppm</th>
</tr>
</thead>
<tbody>
<tr>
<td>C-1</td>
<td>204.17(+)</td>
<td></td>
</tr>
<tr>
<td>C-2</td>
<td>133.29(-)</td>
<td>5.96(H-2)</td>
</tr>
<tr>
<td>C-3</td>
<td>164.42(-)</td>
<td>7.64(H-3)</td>
</tr>
<tr>
<td>C-4</td>
<td>40.61(-)</td>
<td>3.56(H-4)</td>
</tr>
<tr>
<td>C-5</td>
<td>103.14(-)</td>
<td>5.03(H-5)</td>
</tr>
<tr>
<td>C-6</td>
<td>153.51(+)</td>
<td></td>
</tr>
<tr>
<td>C-7</td>
<td>54.19(-)</td>
<td>3.64(H-7)</td>
</tr>
<tr>
<td>C-8</td>
<td>65.89(+)</td>
<td>4.38(H-8)</td>
</tr>
<tr>
<td>C-9</td>
<td>167.90(+)</td>
<td></td>
</tr>
<tr>
<td>C-10</td>
<td>61.33(+)</td>
<td>4.19(H-10)</td>
</tr>
<tr>
<td>C-11</td>
<td>14.03(-)</td>
<td>1.24(H-11)</td>
</tr>
</tbody>
</table>
Attempt to Stop the Photoreaction after the First Step

Because the goal of this project is to study the enantioselectivity of photoelectrocyclization reaction in solid state, the ideal photoproduct is the first photoproduct, 30 which is ring closure product, not the second photoproduct, 31 which is a product via ring closure followed by a rearrangement reaction. We therefore attempted to stop the photoreaction after the first step.

The wavelength filter has been adopted. In order to avoid formation the second photoproduct, the wavelength range, in which first photoproduct does not absorb but the starting material does, should be chosen. Due to the unavailable of first photoproduct, we just try different wavelength filters. They were Uranium glass filter, which absorbs wavelengths less than 350 nm, and the potassium chromate solution filter, which absorbs below 400 nm. But none made the photoreaction stop at the first step. The sample under the filter still gave the second photoproduct 32. The expected first photoproduct was not obtained.

The next trial was to use catalytic hydrogenation to saturate one or both double bonds of photoproduct and try to prevent the formation of the second photoproduct. Hydrogen gas was introduced during the irradiation as shown in Scheme 1. Mass spectrum of reaction mixture showed neither photoproduct 34 nor 35 was obtained. No further investigation was done to study the products of this reaction.
Scheme 1 Attempt to stop the photoreaction at the first step
2.2.2 Photochemical Studies on Ester 23

Compound 23 was irradiated in CH$_3$CN solution through a Pyrex glass filter for 30 min. The solution changed from colorless to yellow-brown. After 2.5 h of irradiation, one main photoproduct was formed in 14.8% according to GC analysis. Several other products were formed, but their GC peaks were less 5% each. More side products were generated upon longer irradiation. The main photoproduct was separated by flash column chromatography with diethyl ether and hexane (1:3). There were substantial amounts of red-brown material left on the silica gel column, which could only be eluted with ethyl acetate-methanol. The reaction is shown in Figure 37.

![Figure 37 Photoreaction of Compound 23](image)

An interesting feature of the separated photoproduct was the chemical shift value for one hydrogen at downfield in the $^1$H NMR spectrum shown in Figure 38. The proton with the chemical shift of 16.8 ppm is probably either from an aldehyde or from a hydroxyl group, which could be from a carboxylic acid. A deuterium exchange was performed by adding three drops of D$_2$O and shaking the NMR sample tube violently for about 3 min. The $^1$H NMR spectrum after deuterium exchange is shown in Figure 39.
The proton ($\delta=16.8$) disappeared after D$_2$O exchange, so this proton could not be an aldehyde hydrogen. The photoproduct was eluded out by diethyl ether.
and hexane mixture (1:3). So the polarity of the compound is not high at all. And the photoproduct did not react with diazomethane which can test the existence of carboxyl group. Therefore, the proton with the chemical shift of 16.8 ppm could not from the carboxylic group. It might be proton from the hydroxyl group (-OH). The question of this assignment is that whether it is possible for the proton of hydroxyl group going that downfield.

Figure 40 Hydrogen bond between carbonyl group and hydroxyl group

The NMR database showed that the proton from the hydroxyl group of structure (shown in Figure 40) could have a chemical shift range from 8.8 ppm up to 17.2 ppm. The hydrogen bonding may contribute the low chemical shift of the proton. So it is possible that the proton from hydroxyl group has a chemical shift with 16.8 ppm. The $^1$H-NMR of tropolone is also studied. The chemical shift of proton of tropolone, which is concentration dependable, is from 8.3 ~ 9.3 ppm (shown in Figure 41). The more concentrated sample, the more chemical shift of the sample moves toward the downfield. And the peak of proton of hydroxyl group became sharper with more concentrated sample. Therefore, the proton of photoproduct with 16.8 ppm could be assigned to the proton of hydroxyl group.
Concentration of Tropolone

7 mg / 6ml

17 mg / 6 ml

25 mg / 6 ml

50 mg / 6 ml

80 mg / 6 ml

180 mg / 6 ml

Solvent: CDCl₃

Figure 41 Chemical shift of proton of hydroxyl group of tropolone
The $^1$H-NMR spectra shown in Figure 38 and Figure 39 were obtained through very concentrated sample (~ 80 mg / 6 ml ) which was the same sample for $^{13}$C-NMR. So the peak of proton of hydroxyl group is very sharp (shown in Figure 38).

Comparing the $^1$H NMR spectrum of the starting ester 5 with that of the photoproduct from 8.2 ppm to 0 ppm shows the two spectra to be similar (see Figure 43). This indicates that the structure of the photoproduct may be similar to that of the starting material.

The HMBC NMR spectrum shows that the methylene group of the photoproduct has a strong correlation to the carbons of the tropolone ring as well as to the carbons of the benzene ring. If the methylene group was still connected to oxygen, as in the photoproduct, there should be a weak because of the oxygen atom separating the methylene group from the tropolone ring. Structure 36 was ruled out for the structure of photoproduct. There were two reasons. One was that the $^{13}$C-NMR spectrum of 36 would show eleven peaks due to the tautomeric hydrogen transfer (shown in Figure 42), while the photoproduct showed fourteen carbon peaks. The other was that the hydroxyl group stay far from the carbonyl group. So less hydrogen bonding interaction

![Figure 42 Tautomeric hydrogen transfer](image)

65
Figure 43 Comparing $^1$H spectra of starting material and photoprocess
between carbonyl group and hydroxyl group might not lead the chemical shift of proton of hydroxyl group going to that downfield (16.8 ppm).

The assignment of structure to photoprodut 37 is shown in Table 13, 14 and 15. The tautomeric proton transfer of 37 is shown in Figure 44. So the NMR signal of photoprodut is probably the average of these two following structures.

37

Figure 44 Tautomeric proton transfer of 37
### Table 13 Assignment of structure of photoproduct 37: $^1$H and COSY NMR

<table>
<thead>
<tr>
<th>$^1$H NMR (500 MHz), $\delta$ ppm (# H, multiplicity)</th>
<th>Assignment</th>
<th>COSY Correlation (400 MHz)</th>
</tr>
</thead>
<tbody>
<tr>
<td>8.09 (2, d)</td>
<td>H-11</td>
<td>7.65 (H-10)</td>
</tr>
<tr>
<td>7.66 (2, d)</td>
<td>H-10</td>
<td>8.09 (H-11)</td>
</tr>
<tr>
<td>6.40 (1, d)</td>
<td>H-2</td>
<td>6.21 (H-3)</td>
</tr>
<tr>
<td>6.26 (1, dd)</td>
<td>H-4</td>
<td>5.61 (H-5), 6.21(H-3)</td>
</tr>
<tr>
<td>6.20 (1, dd)</td>
<td>H-3</td>
<td>6.43 (H-2), 6.27(H-4)</td>
</tr>
<tr>
<td>5.61 (1, td)</td>
<td>H-5</td>
<td>6.27 (H-4), 2.99(H-8)</td>
</tr>
<tr>
<td>3.93 (3, s)</td>
<td>H-14</td>
<td></td>
</tr>
<tr>
<td>2.98 (2, d)</td>
<td>H-8</td>
<td>5.61 (H-5)</td>
</tr>
</tbody>
</table>
Table 14 Assignment of structure of photoproduct 37: $^{13}$C and HMQC NMR

<table>
<thead>
<tr>
<th>Assignment</th>
<th>$^{13}$C NMR, $\delta$ ppm (APT phase from 75 MHz)</th>
<th>HMQC Correlation to $^1$H NMR (500 MHz), $\delta$ ppm</th>
</tr>
</thead>
<tbody>
<tr>
<td>C-1</td>
<td>189.66 (+)</td>
<td></td>
</tr>
<tr>
<td>C-2</td>
<td>127.47 (-)</td>
<td>6.43 (H-2)</td>
</tr>
<tr>
<td>C-3</td>
<td>124.67 (-)</td>
<td>6.21 (H-3)</td>
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<tr>
<td>C-4</td>
<td>129.01 (-)</td>
<td>6.27 (H-4)</td>
</tr>
<tr>
<td>C-5</td>
<td>120.09 (-)</td>
<td>5.61 (H-5)</td>
</tr>
<tr>
<td>C-6</td>
<td>132.15 (+)</td>
<td></td>
</tr>
<tr>
<td>C-7</td>
<td>186.36 (+)</td>
<td></td>
</tr>
<tr>
<td>C-8</td>
<td>40.00 (+)</td>
<td>2.99 (H-8)</td>
</tr>
<tr>
<td>C-9</td>
<td>140.09 (+)</td>
<td></td>
</tr>
<tr>
<td>C-10, C-11</td>
<td>129.09 (-)</td>
<td>7.65 (H-10 / H-11)</td>
</tr>
<tr>
<td>C-11, C-10</td>
<td>129.28 (-)</td>
<td>8.09 (H-11 / H-10)</td>
</tr>
<tr>
<td>C-12</td>
<td>129.00 (+)</td>
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</tr>
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<td>C-13</td>
<td>166.30 (+)</td>
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</tr>
<tr>
<td>C-14</td>
<td>52.43 (+)</td>
<td>3.93 (H-14)</td>
</tr>
</tbody>
</table>
Table 15 Assignment of structure of photoproduct 37: $^1$H and HMBC NMR

<table>
<thead>
<tr>
<th>$^1$H NMR (500 MHz)</th>
<th>Assignment</th>
<th>HMBC Correlation ($^{13}$C 125 MHz)</th>
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<tr>
<td>16.86 (OH)</td>
<td>OH</td>
<td>C-8</td>
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<td>7.66 (2, d)</td>
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<td>C-11</td>
</tr>
<tr>
<td>6.40 (1, d)</td>
<td>H-2</td>
<td>C-3</td>
</tr>
<tr>
<td>6.26 (1, dd)</td>
<td>H-4</td>
<td>C-5, C-3</td>
</tr>
<tr>
<td>6.20 (1, dd)</td>
<td>H-3</td>
<td>C-2, C-4</td>
</tr>
<tr>
<td>5.61 (1, td)</td>
<td>H-5</td>
<td>C-4, C-8</td>
</tr>
<tr>
<td>3.93 (3, s)</td>
<td>H-14</td>
<td></td>
</tr>
<tr>
<td>2.98 (2, d)</td>
<td>H-8</td>
<td>C-5</td>
</tr>
</tbody>
</table>

37
2.2.3 Photochemical Study on Compound 38

Compound 37 can be thought as aryl migrate photoproduct (Figure 37). In order to study whether it is a general trend for the aryl tropolone ether to have a migrate photoproduct, Compound 38 is chosen for the model study. Compound 38 was synthesized according to the procedure reported by Bass\textsuperscript{51}. Benzyl bromide was added to the tropolone anion prepared \textit{in situ} by treatment of tropolone with potassium carbonate (Figure 45). The white product was purified by flash chromatography in 81\% yield, m.p. 82.0 – 83.5 °C (literature 82.5-84.5°C).

\begin{center}
\includegraphics[width=0.5\textwidth]{figure45.png}
\end{center}

\textbf{Figure 45} Synthesis of compound 38

Compound 38 was irradiated in CH$_3$CN solution through a Pyrex filter for 5 min. The color of the solution changed from colorless to pale brown. GC analysis showed there were three main products. Flash column and Chromatatron
chromatography were used to separate them, but only one pure compound was obtained (yield 15%). Another two compounds always came as a mixture. We also try the method, which was provided by Dr. V. Ramamurthy lab. They could separate the ring closure photoproduct of \( \text{38} \), which came from zeolite, with column chromatography (Isopropanol: Hexane = 1:99). Unfortunately the fraction came out the flash column or Chromatatron using that method still showed two peaks on GC and \(^1\text{H}-\text{NMR}\) also showed that it was a mixture. So only one pure product was obtained after photolysis of compound \( \text{38} \) in acetonitrile.

The proton NMR spectra of starting material \( \text{38} \) and photoproduct are shown in Figure 46. The top spectrum is of starting material and the bottom one is of the photoproduct. The pattern of peaks of \(^1\text{H}-\text{NMR}\) of photoproduct is not much changed comparing with that of starting material. The photoproduct has two types of hydrogen. One is hydrogen connected to \( \text{sp}^2 \) carbon (\( \delta = 7.03 \sim 7.42 \text{ ppm} \)) and the other is hydrogen connected to \( \text{sp}^3 \) carbon (\( \delta = 5.84 \text{ ppm} \)). There is another peak (\( \delta = 2.5 \text{ ppm} \sim 3.0 \text{ ppm, broad} \)) which may be assigned to hydroxyl group.

In order to determine the nature of the hydrogen that is connected to \( \text{sp}^3\)-C, HMBC NMR spectra (Figure 47) are obtained. The top figure is the HMBC spectrum of starting material \( \text{38} \). It shows that the methylene group is separated from the tropolone ring by the an oxygen atom (\( \text{sp}^2 \text{ C-O-CH}_2\)). There is no correlation between the hydrogens of the methylene group and the \( \text{sp}^2 \) carbons of the tropolone ring. The hydrogens (-CH\(_2\)-) only correlate with the \( \text{sp}^2 \) carbons of the adjacent benzene ring.
Figure 46 Comparison of $^1$H-NMR spectra of Starting Material (top) and Photoprodut (bottom)
Figure 47  HMBC Spectra of starting material (top) and photoproduct (bottom)
The bottom figure in Figure 47 is the HMBC spectrum of photoproduct. The spectrum shows that the unique CH of the photoproduct has a strong correlation with the sp² carbons of the tropolone ring as well as with the sp² carbons of the benzene ring. So the CH group is likely directly connected to sp² carbons.

\[
\begin{align*}
39 & \quad \text{O} \quad \text{Ph} \\
40 & \quad \text{O} \quad \text{OH} \\
41 & \quad \text{HO} \quad \text{S} \\
42 & \quad \text{O} \quad \text{OH}
\end{align*}
\]

The mass spectrum shows there is no molecular weight change after the photoreaction. The APT $^{13}$C-NMR of the photoproduct shows that the phase for C-8 of the photoproduct is negative, which means that C-8 is either CH or CH$_3$. So the photoproduct cannot be the phenyl migration product 40 in which C-8 is CH$_2$. The IR spectrum shows that the photoproduct has a strong C=O absorption at 1718 cm$^{-1}$. Therefore structure 41 cannot be the structure of photoproduct. For structure 42, the chemical shift of hydrogen connected to the sp²-C in the 8-member ring is not likely from 7.03 ppm to 7.42 ppm due to the absence of aromaticity* of the 8-member ring. So the structure of photoproduct is not likely 42. The favorable structure for photoproduct is 39, which can fit all NMR data (shown in Table 16)

* Strictly speaking, tropolone is not aromatic.
Table 16 Assignment of structure to photoproduct 39

<table>
<thead>
<tr>
<th>Assignment</th>
<th>$^{13}$C NMR (125 MHz), δ ppm (APT phase from 75 MHz)</th>
<th>HMQC Correlation to $^1$H NMR (500 MHz), δ ppm</th>
</tr>
</thead>
<tbody>
<tr>
<td>C-1</td>
<td>187.59 (+)</td>
<td></td>
</tr>
<tr>
<td>C-2, C-3, C-4, C-5, C-6</td>
<td>141.83 (-)</td>
<td>7.05</td>
</tr>
<tr>
<td>C-3, C-2, C-4, C-5, C-6</td>
<td>136.22 (-)</td>
<td>7.14</td>
</tr>
<tr>
<td>C-4, C-2, C-3, C-5, C-6</td>
<td>135.19 (-)</td>
<td>7.36</td>
</tr>
<tr>
<td>C-5, C-2, C-3, C-5, C-6</td>
<td>134.36 (-)</td>
<td>7.03, 7.05</td>
</tr>
<tr>
<td>C-6, C-2, C-3, C-4, C-5</td>
<td>134.18 (-)</td>
<td>7.05, 7.03</td>
</tr>
<tr>
<td>C-7</td>
<td>154.15 (+)</td>
<td></td>
</tr>
<tr>
<td>C-8</td>
<td>75.94 (-)</td>
<td>5.84</td>
</tr>
<tr>
<td>C-9</td>
<td>141.55 (+)</td>
<td></td>
</tr>
<tr>
<td>C-10, C-11</td>
<td>128.36 (-)</td>
<td>7.33</td>
</tr>
<tr>
<td>C-11, C-10</td>
<td>126.60 (-)</td>
<td>7.42</td>
</tr>
<tr>
<td>C-12</td>
<td>127.65 (-)</td>
<td>7.26</td>
</tr>
</tbody>
</table>
The possible mechanism of formation of photoproduct 39 is shown in Figure 48. At first step, \( \gamma \)-hydrogen is abstracted and biradicals are formed. The radical in tropolone ring and benzyl radicals can be stabilized by the resonance structures. Then three-member ring intermediate is probably formed. Finally the ring opening gives the photoproduct 39.

**Figure 48** Possible mechanism of formation of photoproduct 39
Although the NMR data fit the structure of 39 well and the mechanism of forming 39 is reasonable, the IR data of photoproduct is not normal for structure 39. The carbonyl groups of tropolone and tropone have strong absorption at 1618 and 1638 cm\(^{-1}\) respectively. The photoproduct has a strong absorption at 1718 cm\(^{-1}\) which is normally carbonyl group of ester (\(-\text{COOR}\)-). This peak may due to the impurity such as residue solvent. The difference of absorption of carbonyl group between the structure 39 and tropolone is not negligible. But structure 39 is still the most plausible structure for the photoproduct among the structures that have been discussed.
2.3 Study of Photoelectrocyclization Reaction in Chiral Salts

2.3.1 Preparation of Chiral Salts

The goal of my work was to investigate the enantioselectivity of photoelectrocyclization using the chiral ionic auxiliary approach. No special preferences were made in selecting amines other than that they were optically pure, formed solids with acids and were readily available.

The salts were prepared from tropolone carboxylic acid 27 and optically pure amines as shown in Table 17. Since the aim of this thesis was to test asymmetric induction with the use of ionic chiral auxiliaries in a photoelectrocyclization reaction achiral amines were not used. All the reactions of salt formation were carried out at room temperature. The yield of recrystallized salt and crystal morphology are described in Table 18.

All of the salts were shown to be simple 1:1 complexes. The characterization of the newly formed salts was performed mainly by $^1$H-NMR analysis. The NH protons from the salt $(\text{R}_1\text{-NH}_3^+ \cdot \text{OOC-R}_2)$ are shifted downfield about 0.5 ppm due to the positive charge on the adjacent nitrogen atom, compared with the protons from the corresponding amine (R$_1$-NH$_2$). Secondly, the mass spectra of the salts, which showed (M+1)$^+$ peaks in each case, indicated the formation of salts. Thirdly, salt formation also resulted in a characteristic change in the IR spectrum. The OH stretching band at ca. 3500-2500 cm$^{-1}$ of the carboxylic acid was replaced with multiple combination bands.
for ammonium in the 3200-2200 cm\(^{-1}\) region. Finally, the melting points of the salts were different from those of their precursors.

**Table 17 Salts and their corresponding chiral amine**

<table>
<thead>
<tr>
<th>Salts Number</th>
<th>Name of Corresponding Amines (which form the salts)</th>
<th>Structure of salts</th>
</tr>
</thead>
</table>
| 44           | (R)-(+)\(\alpha\) Methylbenzylamine 45  
              or (R)-(−)\(\alpha\)-phenethylamine | ![Structure](image1) |
| 46           | (S)-(−)\(\alpha\) Methylbenzylamine 47  
              or (S)-(−)\(\alpha\)-phenethylamine | ![Structure](image2) |
| 48           | (R)-(+)\(\beta\)-Methylphenethylamine 49  
              or (R)-(+)\(\alpha\)-phenethylamine | ![Structure](image3) |
<p>| 50           | (S)-(−)1-(1-Naphthyl)ethylamine 51 | <img src="image4" alt="Structure" /> |
| 52           | (R)-(+)(\alpha),4-Dimethylbenzylamine 53 | <img src="image5" alt="Structure" /> |
| 54           | (−)-cis-myrtanylamine 55 | <img src="image6" alt="Structure" /> |</p>
<table>
<thead>
<tr>
<th>Salts Number</th>
<th>Name of Corresponding Amines (which form the salts)</th>
<th>Structure of salts</th>
</tr>
</thead>
<tbody>
<tr>
<td>56</td>
<td>(R)-(+)‐Bornylamine 57</td>
<td><img src="image" alt="Structure" /></td>
</tr>
<tr>
<td>58</td>
<td>(R,2S)-(+)‐cis‐1‐Amino‐2‐indanol 59</td>
<td><img src="image" alt="Structure" /></td>
</tr>
<tr>
<td>60</td>
<td>L‐prolinamide 61</td>
<td><img src="image" alt="Structure" /></td>
</tr>
<tr>
<td>62</td>
<td>(1R,2R)(-)‐1,2, diamino cyclohexane 63</td>
<td><img src="image" alt="Structure" /></td>
</tr>
</tbody>
</table>
Table 18 Yield and crystal morphology of chiral salts

<table>
<thead>
<tr>
<th>Salts #</th>
<th>Yield of Recrystallized Salt (solvent)</th>
<th>Crystal morphology</th>
</tr>
</thead>
<tbody>
<tr>
<td>44</td>
<td>76 (acetonitrile)</td>
<td>white powder</td>
</tr>
<tr>
<td>46</td>
<td>74 (acetonitrile)</td>
<td>white powder</td>
</tr>
<tr>
<td>48</td>
<td>27 (ethyl acetate)</td>
<td>Yellow flakes</td>
</tr>
<tr>
<td>50</td>
<td>45 (acetonitrile)</td>
<td>Off-white flakes</td>
</tr>
<tr>
<td>52</td>
<td>80 (acetonitrile)</td>
<td>White powder</td>
</tr>
<tr>
<td>54</td>
<td>71 (acetonitrile)</td>
<td>White powder</td>
</tr>
<tr>
<td>56</td>
<td>65 (acetonitrile)</td>
<td>White powder</td>
</tr>
<tr>
<td>58</td>
<td>33 (methanol)</td>
<td>White powder</td>
</tr>
<tr>
<td>60</td>
<td>55 (acetonitrile)</td>
<td>Off-white powder</td>
</tr>
<tr>
<td>62</td>
<td>61 (acetonitrile)</td>
<td>Off-white powder</td>
</tr>
</tbody>
</table>

2.3.2 Irradiation of Chiral Salts

2.3.2.1 Irradiation of Acid 27

It was relatively easy to start the study of the photoelectrocyclization reaction with the acid 27, because the acid has no auxiliary "handle" – chiral amine. The scheme is shown in Figure 49. It was also convenient to find the proper conditions on chiral HPLC to determine the enantiomeric excess.

The photoproduct can be converted to ester 32, which was already characterized, by treatment with diazomethane after photolysis. The ester was then separated by chromatography, and the enantiomeric excess (e.e.) could be
determined. The results of photolysis of compound 27 both in methanol solution and in solid state are shown in Table 19. As expected, irradiation in the solution phase did not lead to any enantiomeric excess in the product formed.

Figure 49 Irradiation of acid 32

At the beginning of the photolysis, the yield of the second photoproduct was low because of the formation of the first photoproduct. The yield increased as the irradiation time increased. But the yield declined after two hours because of side-product formation. There was no e.e. observed via chiral HPLC, as expected. In solution, there is no chiral media to induce the asymmetric procedure. There are two ways to rotate the p orbital on the tropolone ring when photocyclization reaction happens. The chance of flipping above the ring and the chance of flipping below the ring are the same. So after rearrangement, the two enantiomers are equal-amount (e.e.=0, shown in Table 19). The mechanism, shown in , of formation of photoproduct is similar to the one that was bought up by Chapman who studied tropolone methyl ether (R = OCH₃). This procedure can be thought as a double photorearrangement. When starting material is irradiated, there are two possible ways (Path A and Path B) to rotate p orbitals in
tropolone ring. Path A and Path B would lead to two enantiomers (32-B and 32-A).

![Chemical structure diagram]

R= CH$_3$COOH
OCH$_3$

**Figure 50** Mechanism of formation of photoproduct – a double photorearrangement procedure

The two enantiomers of photoproduct 27 can be separated by HPLC with CHIRALPAK® AS column using isopropanol and hexane (5:95, v/v). The
chromatographic result obtained for separation of the racemic photoproduct 27 is shown in Figure 51.

The result of photolysis of acid 27 in the solid state was similar to that in solution. There was no obviously e.e. (shown in Table 19) and GC analysis showed more peaks for the reaction in the solid state, which means more side products, than for the reaction in solution.

Table 19 Photolysis of compound 27

<table>
<thead>
<tr>
<th>Name</th>
<th>Time of Photolysis (min)</th>
<th>Conversion (%)</th>
<th>Yield (%)</th>
<th>e.e. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Photolysis in MeOH</td>
<td>5</td>
<td>9</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>13</td>
<td>14</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>25</td>
<td>13</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>60</td>
<td>51</td>
<td>13</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>120</td>
<td>77</td>
<td>9</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>240</td>
<td>91</td>
<td>9</td>
<td>0</td>
</tr>
<tr>
<td>Compound 27 in Solid State</td>
<td>5</td>
<td>7</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>10</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>21</td>
<td>11</td>
<td>0</td>
</tr>
</tbody>
</table>
**Figure 51** Chromatogram of racemic sample of photoproduct 27

HPLC conditions: CHIRALPAK AS* column (25cm x 0.46 cm) at room temperature  
Solvent (95:5 hexane/2-propanol), 2ml/minute  
Detector (250nm),  
Retention time (First Peak, 31.7mins; Second Peak, 39.5mins)

In methanol solution, irradiation of the chiral salts gave racemic ester photoproduct 27, after diazomethane workup. The crystal lattice arrangement, which serves as the chiral medium in a solid state photochemical reaction, does not exist in solution, and there is no chiral environment to generate the asymmetric induction in the liquid phase. The conversion in solution is relatively

- This column is packed with silica-gel coated by Amylose tris(S)-α-methylbenzyl carbamate.

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higher than that for each salt in the solid state, so the reaction in methanol goes faster than in the solid state.

2.3.2.2 Irradiation of Chiral Salts in the Solid State

The salts used for photoreaction were recrystallized. The solid state reaction was carried out using two quartz plates between which the sample was sandwiched. After 30 min degassing, the sample was placed in the RayNet photochemical reactor equipped with six UV lamps (RPR-3500, λ>350nm). The photoreaction took place at room temperature. During the reaction, no melting of samples was observed, and the color of sample changed from white to pale brown. After reaction, the sample was dissolved in methanol and treated with diazomethane. Then the sample solution was prefiltered and subjected to separation on the Chromatatron. Finally, the separated methyl ester product was run on HPLC with the chiral column for the e.e. measurement. Optical purity is defined as:

\[ \text{e.e.\%} = \frac{[R]-[S]}{[R]+[S]} \times 100\% \]

The results of the solid state salt irradiations are given in Table 20. As shown, some optically active amines tested gave poor results; others worked well. Salt 44 gave an 81% e.e. at 23% conversion. It was general that enantiomeric excesses tended to decrease on increasing conversion. When a crystal was irradiated, the lattice arrangement tended to break down. The defects were more on the surface than in the crystal. So the photoreaction did not occur evenly through out the whole crystal.
Table 20 Asymmetric Induction in the Solid State Photochemistry of Salts of Acid 27

( at room temperature, $\lambda > 350$ nm )

<table>
<thead>
<tr>
<th>Salts</th>
<th>Optically active amine</th>
<th>Irradiation time (min)</th>
<th>Conversion (%)</th>
<th>e.e.%</th>
</tr>
</thead>
<tbody>
<tr>
<td>44</td>
<td>(R)-(+)-$\alpha$ Methyl benzylamine</td>
<td>5</td>
<td>7</td>
<td>79#1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>30</td>
<td>23</td>
<td>73</td>
</tr>
<tr>
<td></td>
<td></td>
<td>150</td>
<td>55</td>
<td>71</td>
</tr>
<tr>
<td></td>
<td></td>
<td>210</td>
<td>77</td>
<td>56</td>
</tr>
<tr>
<td>46</td>
<td>(S)-(+)-$\alpha$ Methyl benzylamine</td>
<td>5</td>
<td>11</td>
<td>77#2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>30</td>
<td>24</td>
<td>76</td>
</tr>
<tr>
<td></td>
<td></td>
<td>150</td>
<td>56</td>
<td>69</td>
</tr>
<tr>
<td></td>
<td></td>
<td>200</td>
<td>81</td>
<td>53</td>
</tr>
<tr>
<td>48</td>
<td>(R)-(+)-$\beta$-Methylphenethylamine</td>
<td>5</td>
<td>7</td>
<td>17#2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>20</td>
<td>23</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td></td>
<td>90</td>
<td>59</td>
<td>9</td>
</tr>
<tr>
<td>50</td>
<td>(S)-(+)-(1-Naphthyl) ethyl-amine</td>
<td>5</td>
<td>39</td>
<td>57#1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>30</td>
<td>56</td>
<td>45</td>
</tr>
<tr>
<td></td>
<td></td>
<td>120</td>
<td>83</td>
<td>30</td>
</tr>
<tr>
<td>52</td>
<td>(R)-(+)-$\alpha,4$-Dimethylbenzylamine</td>
<td>5</td>
<td>15</td>
<td>33#1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>30</td>
<td>54</td>
<td>26</td>
</tr>
<tr>
<td></td>
<td></td>
<td>120</td>
<td>85</td>
<td>19</td>
</tr>
</tbody>
</table>

Conversions were determined by GC.

Enantiomeric excesses (e.e.) were determined by HPLC.

#1 means on chiral HPLC the major peak was the first peak ($t_r=30$ min)

#2 means on chiral HPLC the major peak was the second peak ($t_r=40$ min)
Table 20 Asymmetric Induction in the Solid State Photochemistry of Salts of Acid 27 (continued)

<table>
<thead>
<tr>
<th># of Salts</th>
<th>Optically active amine</th>
<th>Irradiation time (min)</th>
<th>Conversion (%)</th>
<th>e.e.%</th>
</tr>
</thead>
<tbody>
<tr>
<td>54</td>
<td>(-)-cis-myrtanylamine</td>
<td>8</td>
<td>13</td>
<td>37#2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>30</td>
<td>35</td>
<td>21</td>
</tr>
<tr>
<td></td>
<td></td>
<td>120</td>
<td>89</td>
<td>17</td>
</tr>
<tr>
<td>56</td>
<td>(R)-(+)‐Bornylamine</td>
<td>8</td>
<td>11</td>
<td>75#2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>20</td>
<td>30</td>
<td>72</td>
</tr>
<tr>
<td></td>
<td></td>
<td>90</td>
<td>81</td>
<td>63</td>
</tr>
<tr>
<td>58</td>
<td>(R,2S)-(+)‐cis-1-Amino-2-indanol</td>
<td>1</td>
<td>7</td>
<td>73#1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3</td>
<td>45</td>
<td>70</td>
</tr>
<tr>
<td></td>
<td></td>
<td>20</td>
<td>81</td>
<td>63</td>
</tr>
<tr>
<td></td>
<td></td>
<td>30</td>
<td>95</td>
<td>60</td>
</tr>
<tr>
<td>60</td>
<td>L‐prolinamide</td>
<td>5</td>
<td>17</td>
<td>7#1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>30</td>
<td>38</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>60</td>
<td>56</td>
<td>3</td>
</tr>
<tr>
<td>62</td>
<td>(1R,2R)-(−)-1,2, diamino cyclohexane</td>
<td>5</td>
<td>15</td>
<td>10#1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>20</td>
<td>33</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td></td>
<td>30</td>
<td>65</td>
<td>5</td>
</tr>
</tbody>
</table>

Conversions were determined by GC.
Enantiomeric excesses (e.e.) were determined by HPLC.

#1 means on chiral HPLC the major peak was the first peak (t_r=30 min)

#2 means on chiral HPLC the major peak was the second peak (t_r=40 min)
The mechanism of photorearrangement in solid state is shown in Figure 52. This procedure can be thought as a double rearrangement. A photocyclization is first taken place, followed by the migration of carbonyl group and ring opening procedure which lead to the product. In solid state, the skeleton of the molecule was restricted by the lattice of crystals. The group of molecule can not move freely the same way as in solution. In solution there is absent of lattice restrain. The reactions via Path A and via Path B (shown in Figure 50) are the same chance. So there is no e.e. observed for the photoproduct 32 in solution. In solid state, the chances of reactions that go in Path A and Path B are different due to the present of chiral media which lead to a enantiomeric excess of photoproduct (P-A and P-B).

It is the chiral crystals that contribute to the high enantioselectivity of the double photorearrangement for the salts. The chiral crystal lattices can be thought as a "director" in solid-state photoreaction. The orientation of lattice in crystal could affect the direction of rearrangement, which can result in different enantiomers. It is not surprising that the lattice break-down tends to lead to racemic product. There is no crystal lattice in solution, and therefore no asymmetric influence during the irradiation process. It is easy to rationalize that no e.e. was obtained in solution phase.
Figure 52 Mechanism of photorearrangement in solid state

Assumed that each photo rearrangement has the same enantioselectivity in the double rearrangement procedure, in order to achieve the final e.e. each step should have high enantioselectivity, theoretically square root of the number
of final e.e. For example, Salt 46 obtained 77% of final e.e. and therefore each step of photo rearrangement got 87% of e.e. (87% × 87% = 77%). For salts 44, 46, 56 and 58, the enantioselectivities of photoreaction in solid state are high and so does the each step of the double rearrangement.

The solid-state samples were prepared for photolysis by crushing the crystals between two quartz plates. Attempts were made to spread the samples as evenly as possible, but it was very difficult to keep a perfectly even thickness, although this is the ideal. Upon irradiation, the thinner part of the sample reacts faster than the thicker part of the sample. For example, the color from the edge of the sample is a little darker than that from the center. Thus, the conversion value obtained is an average of the percent conversions for the different regions. The enantiomeric excess also reflects an averaged value.

Attempts were made to grow large, single crystals of these salts. Unfortunately, large crystals could not be obtained and the quality was not good enough for X-ray analysis, which is a great tool to explain the enantioselectivities obtained from experiments. Therefore we could not establish the correlation of crystal structure with reaction enantioselectivity. But the ionic chiral auxiliary method did achieve asymmetric induction in the photoelectrocyclization reaction.
2.3.2.3 Photolysis of Chiral Salts at Low Temperature

It is important to prevent the crystal lattice from melting, which can reduce the enantioselectivity of the photoreaction. Therefore the photoreaction of salts 44 and 52 were investigated at −78°C to determine whether lowering the temperature can improve the enantiomeric excess. The results are shown in Table 21. The sample was dipped into a container filled with dry ice and ethanol. The reaction at −78 °C went slower compared with the one at room temperature.

Table 21 Photolysis of chiral salts 44 and 52 at low temperature

<table>
<thead>
<tr>
<th>Salts</th>
<th>Optically active amine</th>
<th>Irradiation time (min)</th>
<th>Conversion (%)</th>
<th>Temperature (°C)</th>
<th>e.e.%</th>
</tr>
</thead>
<tbody>
<tr>
<td>44</td>
<td>(R)-(+)−α Methyl benzylamine</td>
<td>10</td>
<td>9</td>
<td>RT</td>
<td>79¹</td>
</tr>
<tr>
<td></td>
<td></td>
<td>30</td>
<td>23</td>
<td>RT</td>
<td>73</td>
</tr>
<tr>
<td></td>
<td></td>
<td>10</td>
<td>6</td>
<td>-78</td>
<td>80</td>
</tr>
<tr>
<td></td>
<td></td>
<td>30</td>
<td>17</td>
<td>-78</td>
<td>78</td>
</tr>
<tr>
<td>52</td>
<td>(R)-(+)−α,4- Dimethylbenzylamine</td>
<td>5</td>
<td>15</td>
<td>RT</td>
<td>33¹</td>
</tr>
<tr>
<td></td>
<td></td>
<td>30</td>
<td>54</td>
<td>RT</td>
<td>26</td>
</tr>
<tr>
<td></td>
<td></td>
<td>120</td>
<td>85</td>
<td>RT</td>
<td>19</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5</td>
<td>10</td>
<td>-78</td>
<td>37</td>
</tr>
<tr>
<td></td>
<td></td>
<td>30</td>
<td>33</td>
<td>-78</td>
<td>29</td>
</tr>
<tr>
<td></td>
<td></td>
<td>120</td>
<td>54</td>
<td>-78</td>
<td>17</td>
</tr>
</tbody>
</table>

Enantiomeric excesses are slightly higher, although not dramatically, at low temperature. The lower conversion is probably due to the slower reaction and the lower intensity of UV light. The intensity of the UV light is relatively lower because of the glass container and the heavy condensation on the outside wall.
of the container. Salt 44 gives satisfactory results in photoproduct enantiomeric excess at low conversions and temperatures.

Most of the irradiations of chiral salts were carried out at room temperature because of the no big difference in e.e. and inconvenient of manipulation of reaction at low temperature.
Chapter 3 Experimental

3.1 General Procedures

Melting Points (MP)

Melting points were determined on a Fisher-Johns melting point apparatus and were not corrected.

Elemental Analysis (Anal.)

Elemental analyses were carried out by Mr. Peter Borda, Department of Chemistry, University of British Columbia.

Infrared Spectra (IR)

Infrared spectra were recorded on a Perkin-Elmer 1710 Fourier transform spectrometer. The position of the absorption maxima ($\nu_{\text{max}}$) are reported in cm$^{-1}$. Solid samples were prepared by grinding the compound with anhydrous potassium bromide in a mortar and pestle, and pelleted in an evacuated die (Perkin Elmer 186-0002) with a laboratory press (Carver, model B) at 17,000 psi. Liquid samples were run neat as thin films between two sodium chloride plates.

Mass Spectra (MS)

Low and high resolution electron ionization (EI) mass spectra were obtained on a KRATOS MS50 instrument. Liquid secondary ion mass spectra (LSIMS) were determined on a KRATOS Concept IIHQ hybrid mass spectrometer. Fast
atom bombardment (FAB) mass spectra were obtained on an AEI MS-9 mass spectrometer with xenon bombardment of an alcohol matrix (as indicated in parentheses) of the sample. Mass to charge ratios (m/e) are reported with relative intensities in parentheses (only for EI). Molecular ions are designed as M\(^+\) (for EI) and M\(^+\)+1 (for FAB).

**Ultraviolet and Visible Spectra (UV)**

Ultraviolet spectra were recorded on a Perkin-Elmer Lambda-4B UV/Vis spectrometer. Wavelengths for each absorption maximum (\(\lambda_{\text{max}}\)) are reported in nanometers (nm), and extinction coefficient (\(\epsilon\) (M\(^-1\)cm\(^-1\))) are given in parentheses. Spectral grade solvents available from BDH or Fisher were used without further purification.

**Nuclear Magnetic Resonance Spectra (NMR)**

**Proton Nuclear Magnetic Resonance (\(^1\)H NMR) Spectra**

The spectrometers used to record \(^1\)H NMR were: Bruker AC-200 (200 MHz), Varian XL-300 (300 MHz), Bruker WH-400 (400 MHz) and Bruker AMX 500 (500 MHz). Signal positions are given as chemical shifts (\(\delta\)) in parts per million (ppm) using tetramethylsilane (TMS) as an internal reference standard. The chemical shifts are reported, followed by the multiplicity of the signals, number of protons, coupling constants (\(J\)) in Hz and the molecular assignment. The multiplicities are abbreviated as follows: s = singlet, d = doublet, dd = doublet of doublets, dt = doublet of triplets, t = triplet, q = quartet, m = multiplet,
br = broad. In some cases, HMQC (Heteronuclear Multiple Quantum Coherence, $^1$H-$^{13}$C correlation) and HMBC (Heteronuclear Multiple-Bond Connectivities, $^1$H-$^{13}$C long range correlation) experiments were carried out on the Bruker AMX 500 spectrometer, and COSY (Correlated Spectroscopy) experiments on the Bruker WH-400 instrument in order to verify structures.

**Carbon Nuclear Magnetic Resonance ($^{13}$C NMR) Spectra**

The spectrometers used to record $^{13}$C NMR spectra were: Bruker AC-200 at 50 MHz, Varian XL-300 at 75 MHz, Bruker AM-400 at 100 MHz and Bruker AMX 500 at 125 MHz. All spectra were run under broad band proton decoupling. Signal positions are given as chemical shifts ($\delta$) in parts per million (ppm) using tetramethylsilane (TMS) as an internal reference standard. Assignments were supported by APT (Attached Proton Test) spectra. For APT, positive (+) signifies C or CH$_2$ while negative (-) signifies CH or CH$_3$.

**Crystallographic Analysis (X-RAY)**

The crystal structures were determined using single-crystal X-ray analysis, on a Rigaku AFC6S 4-circle diffractometer, and drawn with a locally modified version of the ORTEP* (Oak Ridge Thermal Ellipsoid Plot) program at the 50% probability level. The determinations were carried out by Eugene Cheung under the supervision of Professor James Trotter in the Chemistry Department of the University of British Columbia.

* The Oak Ridge Thermal Ellipsoid Plot (ORTEP) program is a computer program, written in Fortran, for drawing crystal structure illustrations. Ball-and-stick type illustrations of a quality suitable for publication are produced with either spheres or thermal-motion probability ellipsoids, derived from anisotropic temperature factor parameters, on the atomic sites.
Gas Chromatography (GC)

Gas chromatographic analyses were run on a Hewlett-Packard 5890A gas chromatograph, using a 30 m × 0.25 mm fused silica capillary column with a column head pressure (carrier gas: helium) of 14 psi. The injector temperature was kept at 250 °C unless otherwise specified. The signal from a flame ionization detector was integrated by a Hewlett-Packard 3392A integrator.

High Pressure Liquid Chromatography (HPLC)

High pressure liquid chromatography was performed on a Waters 600E system controller connected to a tunable absorbance UV detector (Waters 486). The chiral column Chiralcel AS, 250 mm × 4.6 mm, Chiral Technologies Inc., was used to determine enantiomeric excesses (optical purities).

Silica Gel Chromatography

Thin layer chromatography (TLC) was performed on commercial pre-coated silica gel plates (E. Merck, 60, 230-400 mesh) with an aluminum backing and fluorescent indicator (F254). Flash column chromatography was carried out by using 230-400 mesh size silica gel slurry packed and eluting with the appropriate solvent combination.

Differential Scanning Calorimetry (DSC)

DSC was performed on a TA instrument Thermal Analyst 2000 thermal analyzer equipped with a DSC 910S differential scanning calorimeter. Data analyses were
done on an IBM PS/1 personal computer connected to the above instrument running DSC Calibration Data Analysis Program Version 5.0.

**Solvents and Reagents**

All solvents and reagents were used as supplied by Fisher Scientific, unless specified. Further purification was not carried out unless otherwise noted. The deuterated solvents are from Cambridge Isotope Laboratories. Unless otherwise specified, reagents were used as supplied by the Aldrich Chemical Company.
3.2 Experimental Details

Preparation of Ester 21

\[
\begin{align*}
&\text{O} \\
&\text{O} \\
&\text{OCH}_2\text{CH}_3
\end{align*}
\]

Tropolone ester 21 was originally synthesized according to the procedure reported by R.J. Bass\textsuperscript{51}. Modifications were made to improve the yield. To a dried 250 ml round-bottom flask was added tropolone (6.12 g, 50 mmol), potassium carbonate (20.75 g, 150 mmol), and 150 ml of anhydrous acetonitrile (CH\textsubscript{3}CN). The mixture was vigorously stirred for 30 min at 40°C until a fine yellow precipitate formed. Then, ethyl bromoacetate (27.7 ml, 250 mmol) was carefully added to the reaction mixture. After stirring for 45 h at room temperature, the reaction solution turned reddish brown. A clear solution was obtained after suction filtration. The solvent was removed by the rotatory evaporation. The residue was dissolved in methylene chloride and washed three times with 15 ml of 0.2 M sodium bicarbonate, and the organic layer was dried with anhydrous magnesium sulphate, and the solvent removed \textit{in vacuo}. The residue was viscous dark brown oil, which was purified by flash chromatography (hexane/EtOAc, 3:1). Upon removal of solvent, a clear reddish brown oil was obtained (8.42 g, 81%).
Anal. Calculated for C_{11}H_{12}O_{4}: C, 63.44; H, 5.81; O, 31.75. Found C, 63.67; H, 5.65.

LRMS m/e (relative intensity): 208 (M^+, 7), 179 (6), 163 (7), 135 (100), 105 (43), 77 (31).

HRMS: Calculated mass for C_{11}H_{12}O_{4}: 208.0733. Found: 208.0733.

IR (KBr) ν_{max} : 1752 (C=O), 1596 (7-membered ring C=O), 1181 (C-O) cm^{-1}.

UV (methanol) λ_{max} : 320 (7959), 230 (15507), 227 (15528), 226 (15483), 222 (15078) nm.

^1H NMR (400 MHz, CDCl₃): δ 7.15-7.14 (m, 2H, aromatic H), 6.95 (t, 1H, J=9.8 Hz, aromatic H), 6.86-6.81 (m, 1H, aromatic), 6.72 (d, 2H, J=9.7 Hz, H₆), 4.76 (S, 2H, OCH₂CO₂Et), 4.17 (q, 2H, J=7.1 Hz, OCH₂CH₃), 1.20 (t, 3H, J=7.1 Hz, OCH₂CH₃).

^13C NMR (75 MHz, CDCl₃): δ 180.3 (+), 167.6 (+), 163.4 (+), 137.9 (-), 136.4 (-), 132.1 (-), 129.3 (-), 116.3 (-), 65.7 (+), 61.4 (+), 13.9 (-).
Preparation of Compound 24

To a 50 ml flask was added compound 21 (1.04 g, 5 mmol) and 10 ml of methanol. To this mixture was added 5 ml of an aqueous solution of lithium hydroxide (1M). The mixture was left stirring at room temperature for 3 h. Acetone (15 ml) was added to the reaction mixture. The solvent was removed by rotatory evaporation. After standing in the vacuum overnight, a yellow powder was collected (0.58g, yield 70.8%). The product was recrystallized from methanol, and the yellow cubic crystals obtained were suitable good for X-ray analysis.

**MP:** > 300 °C

**Anal.** Calculated for C$_7$H$_5$O$_2$Li·2H$_2$O: C, 51.20; H, 5.53. Found C, 50.96; H, 5.54.

**LRMS** m/e (relative intensity): 129 (M+1, 7), 128 (M$^+$, 4), 115(68), 109 (30), 99 (9), 93 (11), 91 (100), 90 (12), 73 (31), 61(17), 57 (32).

**HRMS:** Calculated mass for C$_7$H$_5$O$_2$Li: 128.0450. Found: 128.0449.

**IR (KBr) $v_{max}$:** 3252.0 (=C-H), 1651.0 (C=O), 1598.0 (C=C), 1511.0 (C=C), 1424.0 (C=C), 1363 (C-O), 1226.0 (C-O) cm$^{-1}$. 

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UV (methanol) $\lambda_{\text{max}}$: 311 (6234), 230 (11081) nm.

$^1$H NMR (400 MHz, CD$_3$OD): $\delta$ 7.23 (t, 2H, J=10.3 Hz, CH), 7.03 (d, 1H, J= 16.2 Hz, CH), 6.69 (t, 2H, 9.29Hz, CH).

$^{13}$C NMR (75 MHz, CD$_3$OD): $\delta$ 184.1 (+), 138.2 (-), 125.2 (-), 123.3 (-).
Preparation of Compound 25

To a 25 ml flask was added compound 21 (0.52 g, 2.5 mmol) and 5 ml of methanol. To this mixture was added 3 ml of an aqueous solution of sodium hydroxide (1M). The mixture was left stirring at room temperature for 3 h. Acetone (8 ml) was added to the reaction mixture. The solvent was removed by rotatory evaporation. After standing in the vacuum overnight, a yellow powder was collected (0.34g, yield 75.9%).

**MP:** > 300 °C

**Anal.** Calculated C<sub>7</sub>H<sub>5</sub>O<sub>2</sub>Na·2H<sub>2</sub>O: C, 46.67; H, 5.04. Found C, 46.07; H, 5.09.

**LRMS** m/e (relative intensity): 145 (M+1, 2), 144 (M<sup>+</sup>, 3), 113 (14), 109 (18), 91 (100), 90 (8), 73 (20), 61 (11), 57 (22).

**HRMS:** Calculated mass for C<sub>7</sub>H<sub>5</sub>O<sub>2</sub>Na: 144.0188. Found: 144.0187.

**IR** (KBr) ν<sub>max</sub>: 3305, 1661.0 (C=O), 1630.0 (C=C), 1605.0 (C=C), 1447.0 (C=C), 1242 (C-O), 1223.0 (C-O) cm<sup>-1</sup>.

**UV** (methanol) λ<sub>max</sub>: 311 (6134), 230 (11005) nm.
$^1$H NMR (400 MHz, CD$_3$OD): $\delta$ 7.22 (t, 2H, J=10.3 Hz, CH), 7.02 (d, 1H, J= 16.2 Hz, CH), 6.68 (m, 2H, CH).

$^{13}$C NMR (75 MHz, CD$_3$OD): $\delta$ 183.7 (+), 137.2 (-), 125.5 (-), 121.7 (-).
Preparation of Compound 26

To a 25 ml flask was added compound 21 (0.52 g, 2.5 mmol) and 5 ml of methanol. To this mixture was added 3 ml of an aqueous solution of potassium hydroxide (1M). The mixture was left stirring at room temperature for 3 h. Acetone (8 ml) was added to the reaction mixture. The solvent was removed by rotatory evaporation. After standing in the vacuum overnight, a yellow powder was collected (0.38g, yield 76.9%).

**MP:** > 300 °C

**Anal.** Calculated for C\textsubscript{7}H\textsubscript{5}O\textsubscript{2}K 2H\textsubscript{2}O: C, 42.84; H, 4.62. Found C, 42.51; H, 4.70.

**LRMS** m/e (relative intensity): 161 (M+1, 2), 153 (26), 131 (100), 91 (36), 90 (6), 86 (8), 73 (9), 61(7), 57 (13).

**HRMS:** Calculated mass for C\textsubscript{7}H\textsubscript{5}O\textsubscript{2}K: 159.9927. Found: 159.9921.

**IR (KBr) \nu_{\text{max}}:** 3500, 1657 (C=O), 1606, 1441 (C=C), 1243 (C-O) cm\textsuperscript{-1}.

**UV (methanol) \lambda_{\text{max}}:** 311 (6217), 230 (11281) nm.

**\textsuperscript{1}H NMR** (400 MHz, CD\textsubscript{3}OD): δ 7.24 (t, 2H, J=10.3 Hz, CH), 7.04 (d, 1H, J= 16.2 Hz, CH), 6.71 (m, 2H, CH).

**\textsuperscript{13}C NMR** (75 MHz, DMSO): δ 183.0 (+), 134.6(-), 121.5(-), 115.7(-).
Preparation of Compound 27

To a 100ml flask was added barium hydroxide octahydrate (1.10 g) and compound 21 (6.00 g, 28.8 mmol) in methanol (40ml). The reaction mixture became a cloudy viscous slurry after stirring for 3 min at room temperature. The mixture continued to be stirred for 2 h. Then, HCl (2N) was added to neutralize the base, and the reaction mixture turned clear. The reaction solution was concentrated by rotatory evaporation to remove most of the solvent (5ml viscous liquid left), and 20 ml of methylene chloride added to the residue. White solid was formed. The solid was filtered and washed with three 5ml portions of diethyl ether. The product was dried under vacuum for 24 h. Grayish white solid was obtained (3.23g, yield, 59.3%). The solid was purified by recrystallization from methanol and acetonitrile. Off-white solid (2.96g) was obtained after recrystallization.

**MP:** 144-147 °C

**Anal.** Calculated for C\textsubscript{9}H\textsubscript{8}O\textsubscript{4}: C, 60.00; H, 4.48; O, 35.52. Found C, 59.75; H, 4.50.
LRMS m/e (relative intensity): 181 (M+1, 5), 180 (M⁺, 36), 136 (10), 135 (100), 123 (26.), 106 (13), 105 (44), 77 (14).


IR (KBr) νmax: 3187 (O-H), 1735 (acid C=O), 1595 (7-membered ring C=O), 1474 (C=C), 1269 (C-O), 1207 (C-O) cm⁻¹.

UV (methanol) λmax: 320 (9056), 236 (14372), 234 (14607), 229 (14981), 226 (15084) nm.

¹H NMR (400 MHz, CD₃OD): δ 7.38-7.33 (m, 1H, CH), 7.18-6.99 (m, 4H, CH), 4.86 (s, 2H, O-CH₂-C=O).

¹³C NMR (75 MHz, CD₃OD): δ 179.3 (+), 171.1 (+), 165.2 (+), 140.0 (-), 138.0 (-), 135.3 (-), 131.1 (-), 117.9 (-), 66.3 (+).
Preparation of Compound 33

To a dried flask was added compound 21 (135 mg, 0.65 mmol) and 80 ml of acetonitrile. The reaction mixture was degassed under N₂ for 30 min. Then the mixture was irradiated for 2.5 h (Pyrex, λ>290 nm). The color of the solution was changed from light orange to reddish brown. The solvent was removed by rotatory evaporation, and the residue was oil. The crude reaction mixture was purified by flash column (hexane/diethyl ether, 7:3), affording 93 mg of compound 33 (oil, yield 69%).

**Anal.** Calculated for C₁₁H₁₂O₄: C, 63.44; H, 5.81; O, 31.75. Found C, 63.71; H, 5.61.

**LRMS** m/e (relative intensity): 208 (M⁺, 3), 179 (3), 135 (100), 121 (25), 107 (14), 106 (24), 105 (35), 93 (20), 78 (12), 77 (31), 73 (8), 45 (6).

**HRMS:** Calculated mass for C₁₁H₁₂O₄: 208.0733. Found: 208.0732.

**IR (thin film) **ν\text{max} : 1759 (ester C=O), 1698 (5-member ring C=O), 1631 (C=C), 1212(C-O)cm⁻¹.

**UV (methanol) **λ\text{max} : 302 (2156), 223 (10151) nm.
$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.64 (dd, 1H, J=5.8 & 2.4 Hz, H$_3$), 5.96 (dd, 1H, J=5.7 & 0.6 Hz, H$_2$), 5.03 (d, 1H, J=0.9 Hz, H$_5$), 4.38 (dd, 2H, J=8.0 & 4.9 Hz, H$_8$), 4.19 (qd, 2H, J=7.1 & 1.7 Hz, OCH$_2$CH$_3$), 3.64 (dd, 1H, J=2.6 & 0.6 Hz, H$_7$), 3.57-3.56 (td, 1H, J=2.6 & 0.9 Hz, H$_4$), 1.24 (t, 3H, J=7.1, OCH$_2$CH$_3$).

$^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 204.2 (+), 167.9 (+), 164.4 (-), 153.5 (+), 133.3 (-), 103.1 (-), 65.9 (+), 61.3 (+), 54.2 (-), 40.6 (-), 14.0 (-).
Preparation of Compound 38

The approach to synthesizing Compound 38 is the same method reported by R.J. Bass. Modifications were made to improve the yield. To a dried 100 ml round-bottom flask was added tropolone (0.61 g, 5.0 mmol), potassium carbonate (2.07 g, 15.0 mmol), and 50 ml of anhydrous acetonitrile (CH₃CN). The mixture was vigorously stirred for 30 min at 40°C until a yellow fine precipitate formed. Then, benzyl bromide (2.57 g, 15.0 mmol) was carefully added. After stirring for 40 h at room temperature, the reaction mixture turned white. A clear solution was obtained after suction filtration. The solvent was removed by rotatory evaporation until 10 ml of liquid remained. The reaction mixture was cooled by a NaCl salt and ice bath. A white solid was formed and filtered off. After standing under the vacuum overnight, a white powder was collected (0.86 g, yield 81%). The product was recrystallized from methylene chloride.

MP: 82.0 – 83.5 °C (lit. 82.5-84.0 °C)
**Anal.** Calculated for C_{14}H_{12}O_{2}: C, 79.23; H, 5.70; O, 15.08. Found C, 78.94; H, 5.67.

**LRMS** 
*m/e* (relative intensity): 213 (M+1, 12), 212 (M^+, 67), 106 (23), 91 (100), 65 (13).

**HRMS** Calculation for C_{14}H_{12}O_{2}: 212.0837. Found: 212.0835.

**IR** (KBr) \(\nu_{\text{max}}\): 1575 (C=O), 1494 (C=C), 1177 (C-O) cm\(^{-1}\).

**UV** (methanol) \(\lambda_{\text{max}}\): 319 (3939), 234 (11040) nm.

**\(^1\)H NMR** (400 MHz, CDCl\(_3\)): \(\delta\) 7.42-7.15 (m, 8H, aromatic H), 6.83-6.75 (m, 2H, 7-membered ring CH), 6.94 (t, 1H, J=9.9 Hz, 7-membered ring CH), 5.24 (s, 2H, CH\(_2\)).

**\(^{13}\)C NMR** (75 MHz, CDCl\(_3\)): \(\delta\) 180.6 (C\(_1\)), 164.3 (C\(_7\)), 137.3 (C\(_2\)), 136.3 (C\(_3\)), 135.2 (C\(_9\)), 132.5 (C\(_5\)), 128.7 (C\(_4/C\(_{11}\)\)), 128.1 (C\(_{11}/C\(_4\)\)), 128.0 (C\(_{10}\)), 127.0 (C\(_{12}\)), 114.6 (C\(_6\)), 70.8 (C\(_8\)).
Preparation of Compound 39

![Chemical Structure of 39](image)

To a dried flask was added compound 38 (330 mg, 1.56 mmol) and 80 ml of benzene. The reaction mixture was degassed under N\textsubscript{2} for 30 min. Then the mixture was irradiated for 2.5 h (Pyrex, \(\lambda > 290\) nm). The color of the solution changed from colorless to pale brown. The solvent was removed by rotatory evaporation, and the residue was an oil. The crude reaction mixture was purified by flash chromatography (hexane/EtOAc 3:1), affording 45 mg of compound 39 (pale brown oil, yield 10.6%) and 183 mg of starting material.

**Anal.** Calculated for C\textsubscript{14}H\textsubscript{12}O\textsubscript{2}: C, 79.23; H, 5.70; O, 15.08. Found C, 78.97; H, 5.71.

**LRMS** \(m/e\) (relative intensity): 213 (M\textsuperscript{+} 1, 16), 212 (M\textsuperscript{+}, 100), 211 (10), 183 (10), 166 (14), 165 (54), 135 (5), 107 (9), 106 (9), 105 (53), 77 (28).

**HRMS** Calculation for C\textsubscript{14}H\textsubscript{12}O\textsubscript{2}: 212.0837. Found: 212.0839.

**IR** (KBr) \(\nu_{\text{max}}\): 3500-3300(OH), 1718 (C=O), 1628, 1455 (C=C), 1175, 1107(C-O) cm\(^{-1}\).
$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.42-7.30 (m, 5H, C$_6$H$_5$ CH), 7.27-6.98 (m, 5H, CH), 5.48 (s, 1H, CH), 2.6-3.0 (broad, 1H, OH).

$^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 187.6 (+), 154.2 (+), 141.8 (-), 141.6 (+), 136.2 (-), 135.2 (-), 134.4 (-), 134.2 (-), 128.4 (-), 126.6 (-), 127.7 (-), 76.0 (-).
Preparation of Compound 23

The approach to synthesizing Compound 23 is the same method reported by R.J. Bass. Modifications were made to improve the yield. To a dried 250 ml flask equipped with a stirrer and condenser, was added tropolone (0.90 g, 7.3 mmol), potassium carbonate (3.03 g, 22.0 mmol) and 80 ml of acetonitrile. The mixture was vigorously stirred for 30 min at 40°C until yellow fine precipitate formed. Then, methyl 4-(bromomethyl)-benzoate (5.0 g, 21.8 mmol) was carefully added. After stirring for 36 h at room temperature, the reaction mixture turned white. A clear solution was obtained after suction filtration. The solvent was removed by rotatory evaporation until 15ml of liquid remained. The reaction mixture was cooled by NaCl salt and ice mixture. White solid was formed, and filtered off. After standing under the vacuum overnight, a white powder was collected (1.54 g, yield 81%). The product was recrystallized from methylene chloride, and white needles were obtained.
MP: 145.5 - 146.2 °C

Anal. Calculated for C_{16}H_{14}O_{4}: C, 71.10; H, 5.22; O, 23.68. Found C, 71.39; H, 5.36.

LRMS m/e (relative intensity): 271 (M+1, 5), 270 (M^+, 27), 239 (4), 150 (10), 149 (100), 121 (16), 118 (6), 107 (3), 106 (26), 105 (8), 90 (8), 89 (4), 78 (2), 77 (3), 65 (4).

HRMS Calculation for C_{16}H_{14}O_{4}: 270.0892. Found: 270.0892.

IR (KBr) ν_max: 2947 (C-H), 1714 (C=O), 1631(C=O), 1582, 1496, 1472, 1439, 1315, 1285, 1230 (C=C), 1200, 1117, 1079, 1024 (C-O) cm^{-1}.

UV (methanol) λ_max: 319 (8611), 230 (26625), 227 (26139), 204 (150625)nm.

^1H NMR (400 MHz, CD_{3}OD): δ 8.02 (d, 2H, J= 8.3 Hz, benzene CH), 7.49 (d, 2H, J=8.3 Hz, benzene CH), 7.24-7.16 (m, 2H, 7-membered ring CH), 6.94 (t, 1H, J=10.5 Hz, 7-membered ring CH), 6.85-6.80 (m, 1H, 7-membered ring CH), 6.72 (d, 1H, J= 9.8 Hz, 7-membered ring CH), 5.28 (s, 2H, O-CH_{2}), 3.89 (s, 3H, OCH_{3}).

^13C NMR (75 MHz, CD_{3}OD): δ 180.5 (+), 166.6 (+), 164.0 (+), 140.4 (+), 137.5 (-), 136.4 (-), 132.3 (-), 129.98 (-), 129.97 (+), 128.6 (-), 126.7 (-), 114.9 (-), 70.1 (+), 52.1 (-).
To a 50 ml flask equipped with a stirrer and condenser, was added compound 28 (1.35 g, 5.0 mmol) and 20 ml of methanol. Then, 10 ml of an aqueous solution of lithium hydroxide (1M) was slowly added to the flask at room temperature. The reaction mixture became cloudy. The temperature was raised to 60 °C with continued stirring. The reaction solution became clear and colorless after stirring for 4 h. Then, HCl (2N) was added to neutralize the solution to PH6.5-6. White solid was formed, and filtered off. After standing under vacuum overnight, a white powder was collected (0.97 g, yield 76%). The product was recrystallized from methylene chloride and ethyl acetate, and white needle crystals were obtained.

**MP:** 182.3 – 184.1 °C
Anal. Calculated for C_{15}H_{12}O_{4}: C, 70.31; H, 4.72; O, 24.97. Found C, 70.03; H, 4.69.

LRMS m/e (relative intensity): 257 (M+1, 6), 256 (M^+, 28), 239 (4), 136 (8), 135 (100), 121 (15), 118 (6), 107 (4), 106 (22), 105 (9), 90 (7), 89 (4), 78 (3), 77 (3).

HRMS Calculation for C_{15}H_{12}O_{4}: 256.0736. Found: 256.0741.

IR (KBr) ν_{max}: 3300-2800 (broad, -OH), 1703 (HO-C=O), 1617 (C=O), 1592, 1542, 1489, 1476, 1464 (C=C), 1288, 1235, 1201, 1111, 1082 (C-O) cm^{-1}.

UV (methanol) ν_{max}: 319 (8410), 230 (26487), 227 (25897), 204 (147112) nm

^{1}H NMR (400 MHz, CD_{3}OD): δ 12.95 (broad, 1H, COOH), 7.97 (d, 2H, J= 8.2 Hz, benzene 2CH), 7.57 (d, 2H, J= 8.2 Hz, benzene 2CH), 7.32 (ddd, 1H, J=16.7, 8.55 & 0.78 Hz, 7-membered ring CH), 7.15 (t, 1H, J=10.1 Hz, 7-membered ring CH), 7.06 (m, 2H, 7-membered ring CH), 6.95 (t, 1H, J= 8.5 Hz, 7-membered ring CH), 5.27 (s, 2H, CH_2), 3.31 (s, 3H, OCH_3).

^{13}C NMR (75 MHz, DMSO): δ 179.3 (+), 167.1 (+), 163.8 (+), 140.9 (+) 136.8 (-), 136.6 (-), 133.1 (-), 130.4 (+), 129.5 (-), 128.3 (-), 127.6 (-), 114.6 (-), 69.4 (+).
Preparation of Compound 37

To a dried flask was added compound 23 (137 mg, 0.51 mmol) and 100 ml of acetonitrile. The reaction mixture was degassed under N₂ for 30 min. Then the mixture was irradiated for 30 min (Pyrex, λ>290 nm). The color of the solution was changed from colorless to pale brown. The solvent was removed by rotatory evaporation, and the residue was an oil. The crude reaction mixture was purified by flash chromatography (hexane/diethyl ether, 2:1), affording 41 mg of compound 37 (oil, yield 29%).


LRMS m/e (relative intensity): 271 (M+1, 8), 270 (M⁺, 45), 269 (11), 255 (31), 239 (14), 211 (25), 181 (14), 165 (13), 164 (12), 163 (100), 155 (7), 135 (34), 134 (13), 120 (8), 119 (6), 107 (9), 105 (26), 104 (11), 103 (12), 77 (24).

HRMS Calculation for C₁₆H₁₄O₄: 270.0892. Found: 270.0887.
IR (KBr) $\nu_{\text{max}}$: 3300-3280 (-OH), 1728 (C=O), 1625 (C=O), 1592, 1542, 1489, 1476, 1464 (C=C), 1288, 1235, 1201, 1111, 1082 (C-O) cm$^{-1}$.

$^1$H NMR (400 MHz, CDCl$_3$): 8.09 (d, 2H, J=8.4 Hz, benzene CH), 7.65 (d, 2H, J=8.4 Hz, benzene CH), 6.43 (d, 1H, J=11.3 Hz, 7-membered ring CH), 6.27 (1H, m, 7-membered ring CH), 6.20 (m, 1H, 7-membered ring CH), 5.61 (m, 1H, 7-membered ring CH), 3.93 (s, 3H, OCH$_3$), 2.99 (d, 2H, J=6.8 Hz, -CH$_2$-).

$^{13}$C NMR (75 MHz, CDCl$_3$): 189.7 (C$_1$), 127.5 (C$_2$), 124.7 (C$_3$), 129.0 (C$_4$), 120.1 (C$_5$), 132.2 (C$_6$), 186.4 (C$_7$), 40.0 (C$_8$), 140.1 (C$_9$), 129.1 (C$_{10}$/C$_{11}$), 129.3 (C$_{11}$/C$_{12}$), 129.0 (C$_{12}$), 166.3 (C$_{13}$), 52.4 (C$_{14}$).
Preparation of Compound 29

![Chemical Structure](image)

Compound 27 (91 mg, 0.48 mmol) was dissolved in 3 ml of methanol. Diazomethane (diethyl ether solution) was slowly added until there was no bubble coming from the reaction mixture. The reaction mixture was stirred for about 2 h. Then diazomethane solution was added again (1 ml) and stirring continued for another 2 h. The solvent was removed by rotatory evaporation. The residual oil was purified by Chromatatron (hexane/EtOAc, 1:1), affording 89 mg of compound 29 (dark yellow oil, yield, 96%).

**Anal.** Calculated for C$_{10}$H$_{10}$O$_{4}$: C, 61.84; H, 5.19. Found C, 61.73; H, 5.23.

**LRMS** $m/e$ (relative intensity): 195 (M+1, 3), 194 (M$^+$, 24), 179 (6), 163 (10), 136 (6), 135 (100), 107 (6), 106 (17), 105 (36), 79 (4), 78 (10), 77 (23), 65 (5), 51 (6).

**HRMS** Calculation for C$_{10}$H$_{10}$O$_{4}$: 194.0579. Found: 194.0577.

**IR** (KBr) $\nu_{max}$: 2953 (C-H), 1757 (C=O), 1627 (C=O), 1596, 1496, 1473, 1438 (C=C), 1176 (C-O), 1094, 1033 cm$^{-1}$.

**UV** (methanol) $\lambda_{max}$: 319 (7914), 229 (1514), 227 (15501), 226 (15124), 222 (14821) nm.
$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.24-7.14 (m, 2H, 7-membered ring CH), 6.97 (t, 1H, J= 9.8 Hz, 7-membered ring CH), 6.86 (m, 1H, 7-membered ring CH), 6.75 (d, 1H, J=9.8 Hz, 7-membered ring CH), 4.80 (s, 2H, O-CH$_2$), 3.73 (s, 3H, OCH$_3$).

$^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 180.4 (+), 168.2 (+), 163.4 (+), 138.1 (-), 136.5 (-), 132.2 (-), 129.5 (-), 116.7 (-), 65.7 (+), 52.3 (-).
Preparation of Compound 32

![Compound 32](image)

To a dried flask was added compound 29 (126 mg, 0.65 mmol) and 80 ml of acetonitrile. The reaction mixture was degassed under N₂ for 30 min. Then the mixture was irradiated for 30 h (Pyrex, λ>290 nm). The color of the solution changed from pale orange to pale reddish-brown. The solvent was removed by rotatory evaporation, and the residue was an oil. The crude reaction mixture was purified by Chromatatron (hexane/diethyl ether 3:1), affording 82 mg of compound 32 (oil, yield 65%).


**LRMS** m/e (relative intensity): 194 (M⁺, 4), 179 (3), 166 (2), 135 (100), 121 (23), 107 (15), 106 (24), 105 (36), 93(23), 78(14), 77 (36).

**HRMS** Calculation for C₁₀H₁₀O₄: 194.0580. Found: 194.0579.

**IR** (thin film) νmax: 1762 (ester C=O), 1698 (5-member ring C=O), 1631, 1220 (C-O) cm⁻¹.

**UV** (methanol) λmax: 302 (2123), 223 (10253) nm.
$^1$H NMR (400 MHz, CDCl$_3$): δ 7.64 (dd, 1H, J=5.9 and 2.3 Hz, H$_3$), 5.98 (dd, 1H, J=5.9 and 0.7 Hz, H$_2$), 5.05 (d, 1H, J=1.0 Hz, H$_5$), 4.41 (dd, 2H, J=8.0 & 6.0 Hz, H$_8$), 3.74 (s, 3H, OCH$_3$), 3.66 (d, 1H, J=2.3, H$_7$), 3.58 (m, 1H, H$_4$).

$^{13}$C NMR (75 MHz, CDCl$_3$): δ 204.2 (C$_1$), 168.4 (C$_9$), 164.4 (C$_3$), 153.5 (C$_6$), 133.4 (C$_2$), 103.3 (C$_5$), 65.8 (C$_8$), 54.2 (C$_7$), 52.3 (C$_{10}$), 40.7 (C$_4$).
Preparation of Compound 44

To a 25 ml flask was added acid 27 (0.11g, 0.58 mmol) and 15 ml of THF. Then, (R)-(+)-α-methylbenzylamine (75 mg, 0.62 mmol) in THF (3 ml) was added dropwise to the solution. White solid formed after stirring at room temperature for 3.5 h. The solid was filtered out and washed twice with 5 ml portions of diethyl ether. After standing under vacuum overnight, salt 44 was collected as a white powder (0.14 g, 80%). The salt was recrystallized from acetonitrile for photolysis.

**MP:** 109.8 – 112.0 °C

**Anal.** Calculated for C$_{17}$H$_{19}$O$_4$N$_1$: C, 67.74 ; H, 6.36 ; N, 4.65 . Found C, 67.13 ; H, 6.21 ; N, 4.62 .

**LRMS +LSIMS** (matrix: thioglycerol): 302 (M+1, 54), 181 (98), 122 (82), 105 (100), 91 (32).

**HLRMS** Calculated for C$_{17}$H$_{19}$O$_4$N$_1$: 302.1392. Found: 302.1394.

**IR** (KBr) $\nu_{max}$: 2974 (C-H), 1620 (C=O), 1553 (C=O), 1474, 1407 (C=C), 1283 (C-O), 1198 (C-O), 774, 705 cm$^{-1}$.
**UV** (methanol) $\lambda_{\text{max}}$: 402 (496), 320 (10401), 229 (22386), 214 (19703), 210 (20181) nm.

$^1$H NMR (400 MHz, CD$_3$OD): $\delta$ 7.49-7.24 (m, 7H, CH), 7.09-7.00 (m, 3H, 7-membered ring CH), 4.82 (broad, 3H, NH$_3$), 4.51 (s, 2H, O-CH$_2$-C=O), 4.43 (t, 1H, J=6.9 Hz, CH-NH$_3$), 1.62 (d, 3 H, J=6.9 Hz, CH$_3$).

$^{13}$C NMR (75 MHz, CD$_3$OD): $\delta$ 182.4 (+), 173.9 (+), 165.7 (+), 140.1 (+), 139.7 (-), 137.5 (-), 135.5 (-), 130.5 (-), 130.1 (-), 129.8 (-), 127.8 (-), 117.4 (-), 69.2 (-), 52.0 (-), 20.8 (-).
Preparation of Compound 46

To a 25 ml flask was added acid 27 (75g, 0.42 mmol) and 11 ml of THF. Then, (S)-(−)-α-methylbenzylamine (61 mg, 0.50 mmol) in THF (2 ml) was added dropwise to the solution. White solid formed after stirring at 60 °C for 2.5 h. The mixture was left overnight. The solid was filtered off and washed twice with 3 ml portions of diethyl ether. After standing under vacuum overnight, salt 46 was obtained as a fine white fine powder (97 mg, 77%). The salt was recrystallized from acetonitrile for photolysis.

MP: 109.0 – 112.5 °C

Anal. Calculated for C_{17}H_{19}O_{4}N_{1}: C, 67.74 ; H, 6.36 ; N, 4.65 . Found C, 67.91; H, 6.34; N, 4.62.

LRMS +LSIMS (matrix: thioglycerol): 302 (M+1, 75), 181 (100), 122 (80), 105 (76), 91 (28).

HRMS: Exact mass calculated for C_{17}H_{19}O_{4}N_{1}: 302.1392. Found: 302.1391.
**IR (KBr)** ν\(_{\text{max}}\): 2948, 1622 (C=O), 1552 (C=O), 1475, 1406 (C=C), 1283 (C-O), 1196 (C-O), 773, 703 cm\(^{-1}\).

**UV (methanol)** λ\(_{\text{max}}\): 402 (491), 320 (10398), 229 (22301), 214 (19689), 210 (20175) nm.

**\(^1\)H NMR** (400 MHz, CD\(_3\)OD): δ 7.49-7.24 (m, 7H, aromatic CH), 7.10-7.00 (m, 3H, 7-membered ring CH), 4.84 (broad, 3H, NH\(_3\)), 4.50 (s, 2H, O-CH\(_2\)-C=O), 4.43 (t, 1H, J=6.8 Hz, CH-NH\(_3\)), 1.62 (d, 3H, J=6.8 Hz, CH\(_3\)).

**\(^13\)C NMR** (75 MHz, CD\(_3\)OD): δ 182.4 (+), 173.9 (+), 165.7 (+), 140.0 (+), 139.7 (-), 137.4 (-), 135.5 (-), 130.5 (-), 130.1 (-), 129.9 (-), 127.8 (-), 117.3 (-), 69.2 (+), 52.1 (-), 20.8 (-).
Preparation of Compound 50

To a 25 ml flask was added acid 27 (91 mg, 0.51 mmol) and 10 ml of THF. Then, (S)-(−)-1-(1-Naphthyl) ethylamine (110 mg, 0.63 mmol) in THF (2 ml) was added dropwise to the solution under nitrogen. White solid formed after stirring at room temperature for 30 min. The solid was filtered and washed twice with 2 ml of diethyl ether. After standing under vacuum overnight, off-white flakes of salt 50 were collected (0.29 g, 83%). The salt was recrystallized from acetonitrile for photolysis.

**MP:** 105.0 – 106.2 °C

**Anal.** Calculated for C$_{21}$H$_{21}$O$_4$N$_1$: C, 71.76; H, 6.03; N, 3.99; O, 18.22. Found C, 71.84; H, 5.89; N, 4.14.

HRMS: Exact mass calculated for C_{21}H_{21}O_{4}N_{1}: 352.1549. Found: 352.1547

IR (KBr) \nu_{\text{max}} : 2907, 1610 (C=O), 1558 (C=O), 1475, 1408 (C=C), 1190 (C-O) \text{ cm}^{-1}.

UV (methanol) \lambda_{\text{max}} : 403 (283), 319 (7869), 292 (8011), 281 (8276), 270 (6750), 223 (29527) \text{ nm}.

^1H NMR (400 MHz, CD_{3}OD): \delta 8.08 (d, 1H, J=8.4 Hz, naphthyl ring CH), 7.86 (dd, 1H, J=8.3 & 6.4 Hz, naphthyl ring CH), 7.70 (d, 1H, J=6.6 Hz, naphthyl ring CH), 7.57-7.46 (m, 4H, naphthyl ring CH), 7.40 (dd, 1H, J=8.5 & 1.2 Hz, 7-membered ring CH), 7.25-7.14 (m, 2H, 7-membered ring CH), 7.03 (dd, 1H, J=8.5 & 10.6 Hz, 7-membered ring CH), 6.92 (d, 1H, J=10.1 Hz, 7-membered ring CH), 5.36 (t, 1H, J=6.7 Hz, CH-NH_{3}), 4.85 (broad, 3H, NH_{3}), 4.38 (s, 2H, O-CH_{2}-C=O), 1.75 (d, 3 H, J=6.8 Hz, CH_{3}).

^13C NMR (75 MHz, CD_{3}OD): \delta 182.3 (+), 174.0 (+), 165.5 (+), 139.6 (-), 137.4 (-), 136.0 (+), 135.5 (-), 135.3 (+), 131.5 (+), 130.5 (-), 130.3 (-), 130.1 (-), 128.0 (-), 127.2 (-), 126.5 (-), 124.0 (-), 123.3 (-), 117.3 (-), 69.1 (+), 47.1 (-), 21.0 (-)
Preparation of Compound 52

To a 25 ml flask was added acid 27 (78 mg, 0.43 mmol) and 10 ml of THF. Then, (R)-(+-α,4-dimethyl benzylamine (77 mg, 0.57 mmol) in THF (1ml) was added dropwise to the solution under nitrogen. White precipitate was formed after stirring at room temperature for 30 min. Stirring was continued for 2.5 h. The solid was filtered and washed twice with 2 ml of diethyl ether. After standing under vacuum overnight, salt 52 was obtained as a white powder (0.24 g, 75%). The salt was recrystallized from acetonitrile for photolysis.

MP: 128.0 – 130.2 °C

Anal. Calculated for C_{18}H_{21}N_{1}O_{4}: C, 68.54; H, 6.72; N, 4.44; O, 20.30. Found C, 68.74; H, 6.65; N, 4.64.
LRMS + LSIMS (matrix: thioglycerol): 317(M+2, 12), 316(M+1, 51), 271(3), 182(6), 181 (55), 137 (6), 136 (47), 135 (6), 120 (15), 119 (100), 118 (5), 105 (4), 91 (9), 77 (3), 73 (3).

HRMS: Exact mass calculated for C_{18}H_{21}N_{4}O_{4}: 316.1549 Found: 316.1545

IR (KBr) ν_{max}: 3369, 2930 (C-H), 1630 (C=O), 1597 (C=O), 1560, 1493 (C=C), 1475 (C=C), 1266, 1195 (C-O), 1089 (C-O) cm^{-1}.

UV (methanol) λ_{max}: 320 (9278), 236 (15477), 235 (15347), 229 (18754), 227 (17489) nm.

^1{}H NMR (400 MHz, CD_{3}OD): δ 7.46 (dd, 1H, J= 8.9 & 11.3 Hz, 7-membered ring CH), 7.32-7.23 (m, 3H, 7-membered ring CH), 7.17 (d, 2H, J=7.5, benzene CH), 7.07 (t, 1H, J=9.3 Hz, 7-membered ring CH), 7.00 (d, 2H, J=10.1, benzene CH), 4.84 (broad, 3H, NH_{3}), 4.47 (s, 2H, O-CH_{2}-C=O), 4.38 (q, 1H, J=6.8 Hz, CH-NH_{3}), 2.29 (s, 3H, ph-CH_{3}), 1.60 (d, 3H, J=6.8 Hz, 3HN-CH-CH_{3}).

^1{}C NMR (75 MHz, CD_{3}OD): δ 182.4 (+), 173.9 (+), 165.7 (+), 139.9 (-), 139.7 (-), 137.5 (+), 137.0 (-), 135.5 (+), 130.59 (+), 130.55 (-), 130.51 (-), 130.47 (-), 127.8 (-), 117.3 (-), 69.2 (+), 51.8 (-), 21.1 (-), 20.7(-).
Preparation of Compound 54

To a 25 ml flask was added acid 27 (86 mg, 0.48 mmol) and 15 ml of THF. Then, (-)-cis-myrtanylamine (160 mg, 104 mmol) in THF (1 ml) was added dropwise to the solution. White precipitate was formed immediately. The suspension continued to be stirred for 2 h. The solid was filtered and washed twice with 5 ml of diethyl ether. After standing under vacuum overnight, salt 54 was obtained as a white powder (0.30 g, 91%). The salt was recrystallized from acetonitrile for photolysis.

MP: 165.0 – 168.7 °C

Anal. Calculated for C_{19}H_{27}O_{4}N_{1}: C, 68.44; H, 8.16; N, 4.20; O, 19.19. Found C, 68.42; H, 8.25; N, 4.15.

LRMS +LSIMS (matrix: thioglycerol): 335 (12), 334 (50), 181 (69), 155 (12), 154 (100), 137(4), 135 (7), 95 (11), 93 (6), 91 (5), 81 (35).
HRMS: Exact mass calculated for C_{19}H_{27}O_{4}N_{1}: 334.2018 Found: 334.2015

IR (KBr) $v_{\text{max}}$: 3445, 1623 (C=O), 1588(C=O), 1490(C=C), 1411(C=C), 1187(C=O), 1081 (C-O) cm$^{-1}$.

UV (methanol) $\lambda_{\text{max}}$: 319 (8745), 235 (14142), 234 (14025), 228 (14793), 226 (14854) nm.

$^1$H NMR (400 MHz, CD$_3$OD): $\delta$ 7.47 (dd, 1H, J= 8.1 & 0.9 Hz, 7-membered ring CH), 7.33-7.25 (m, 2H, 7-membered ring CH), 7.10-7.05 (m, 2H, 7-membered ring CH), 4.85 (broad, 3H, NH$_3$), 4.57 (s, 2H, O-CH$_2$-C=O), 2.93 (dd, 2H, J=7.8 & 3.1 Hz, CH$_2$-NH$_3$), 2.44-2.35 (m, 2H, CH$_2$), 2.08-1.98 (m, 2H, CH$_2$), 1.95-1.90 (m, 2H, CH$_2$), 1.88-1.50 (m, 1H, CH), 1.60-1.50 (m, 1H, CH), 1.21 (s, 3H, CH$_3$), 1.01 (s, 3H, CH$_3$), 0.96 (d, 1H, J=9.8 Hz, CH).

$^{13}$C NMR (75 MHz, CD$_3$OD): $\delta$ 182.5(+), 173.9(+), 165.9(+), 139.6(-), 137.4(-), 135.5(-), 130.4(-), 117.3(-), 69.3(+), 46.1(+), 44.6(-), 42.4(-), 40.9(-), 39.6(+), 33.7(+), 28.1(-), 26.7(+), 23.4(-), 20.5(+).
Preparation of Compound 56

To a 25 ml flask was added acid 27 (114 mg, 0.63 mmol) and 14 ml of THF. Then, (R)-(+)-bornylamine (100mg, 0.65 mmol) in THF (1.4 ml) was added dropwise to the solution under nitrogen. White solid was formed after stirring at room temperature for 2 min. The suspension continued to be stirred for 2.5 h. The solid was filtered and washed twice with 3 ml of diethyl ether. After standing under vacuum overnight, salt 56 was obtained as a white powder (0.17 g, 83%). The salt was recrystallized from acetonitrile for photolysis.

**MP:** 159.5 – 161.0 °C

**Anal.** Calculated for C$_{19}$H$_{27}$NiO$_4$: C, 68.44; H, 8.16 ; N, 4.20. Found C, 68.35; H, 8.11; N, 4.16.

**LRMS +LSIMS** (matrix: thioglycerol): 335 (M+2, 12), 334 (M+1, 53), 182 (5), 181 (43), 155 (12), 154 (100), 152 (4), 137 (32), 122 (3), 107 (3), 95 (8), 93 (7), 91 (4), 82 (5), 81 (39), 79 (3), 77 (4).

IR (KBr) $v_{\text{max}}$: 3013 (=C-H), 1607 (C=O), 1539(C=O), 1475, 1414(C=C), 1274, 1237, 1192, 1086, 1004 (C-O) cm$^{-1}$.

UV (methanol) $\lambda_{\text{max}}$: 319 (11031), 235 (15321), 234 (14895), 228 (15231), 226 (16145) nm.

$^1\text{H}$ NMR (400 MHz, CD$_3$OD): $\delta$ 7.48 (dd, 1H, J= 8.7 & 1.3 Hz, 7-membered ring $\text{CH}=\text{C}$), 7.33-7.26 (m, 2H, 7-membered ring $\text{CH}$), 7.11-7.06 (m, 2H, 7-membered ring $\text{CH}$), 4.84 (broad, 3H, $\text{NH}_3$), 4.57 (s, 2H, O-$\text{CH}_2$-C=O), 3.71(t, 1H, J=6.6 Hz, $\text{CH}$$-$NH$_3$), 2.35-2.26 (m, 1H, bridge $\text{CH}$), 1.87-1.76 (m, 2H, CH$_2$), 1.72-1.59 (m, 2H,CH$_2$), 1.50 (t, 1H, J= 13.1 Hz, CH$_2$-$\text{CH}$-$\text{NH}_3$), 1.35 (t, 1H, J= 10.5 Hz, CH$_2$-$\text{CH}$-$\text{NH}_3$), 1.21 (s, 3H, CH$_3$), 0.93 (s, 3H, CH$_3$), 0.92 (s, 3H, CH$_3$).

$^{13}\text{C}$ NMR (75 MHz, CD$_3$OD): $\delta$ 182.4 (+), 173.9 (+), 165.7 (+), 139.8 (-), 137.5 (-), 135.5 (-), 130.5 (-), 117.4 (-), 69.3 (+), 57.7 (-), 50.1 (+), 45.9 (-), 35.4 (+), 28.5 (+), 28.1 (+), 26.5 (+), 19.9 (-), 18.8 (-), 13.5 (-).
Preparation of Compound 58

To a 25 ml flask was added acid 27 (120 mg, 0.67 mmol) and 12 ml of THF. Then, (1R, 2S)-(+)-cis-1-amine-2-indanol (140 mg, 0.78 mmol) in THF (2 ml) was added dropwise to the solution. White solid formed after stirring for 30 min at room temperature. The suspension continued to be stirred for 2 h. The solid was filtered and washed twice with 2 ml of diethyl ether. After standing under vacuum overnight, salt 58 was obtained as a white powder (0.20 g, 91%). The salt was recrystallized from methanol for photolysis.

**MP:** 178.4 – 180.0 °C

**Anal.** Calculated for C\textsubscript{18}H\textsubscript{19}O\textsubscript{5}N: C, 65.64; H, 5.81; N, 4.25. Found C, 65.49; H, 5.71, 4.18.

**LRMS +LSIMS** (matrix: thioglycerol): 330 (M+1, 8), 299 (4), 214 (4), 182 (7), 181(59), 151 (12), 150(100), 147 (5), 135 (8), 134 (9), 133 (81), 105 (8), 107 (7), 91(18), 73 (16).

**HRMS:** Calculated for C\textsubscript{18}H\textsubscript{20}O\textsubscript{5}N\textsubscript{1}(M+1): 330.1342. Found: 330.1337.
IR (KBr) νmax: 3094 (=C-H), 1601, 1564 (C=O), 1482, 1443, 1413 (C=C), 1289, 1202, 1092, 1010 (C-O) cm⁻¹.

UV (methanol) λmax : 403 (512), 321 (11447), 230 (24125), 215 (21450), 210 (21501) nm.

¹H NMR (400 MHz, CD₃OD): δ 7.46 (d, 1H, J=7.1 Hz, 7-membered ring CH), 7.26 (m, 4H, benzene ring CH), 7.13 (t, 1H, J=10.1 Hz, 7-membered ring CH), 7.03 (d, 1H, J=12.0 Hz, 7-membered ring CH), 6.89 (dd, 1H, J=10.6 & 8.3 Hz, 7-membered ring CH), 6.77 (d, 1H, J= 10.1 Hz, 7-membered ring CH), 4.55 (m,1H, CH-OH), 4.43 (d, 1H, J= 5.6 Hz, CH-NH₃), 4.41 (s, 2H, O-CH2-C=O), 3.08 (dd, 1H, J=16.2 & 6.0 Hz, 5-member ring CH₂), 2.89 (dd, 1H, J=16.2 & 3.6 Hz, 5-member ring CH₂).

¹³C NMR (75 MHz, DMSO): δ 179.5 (+), 170.1 (+), 164.6 (+), 141.4, (+), 138.5 (+), 136.7 (-), 136.1 (-), 133.5 (-), 128.6 (-), 127.4 (-), 126.6 (-), 125.2 (-), 125.0 (-), 114.1 (-), 70.5 (-), 67.8 (+), 56.6 (-), 41.3 (+).
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