CHAPTER 2

N-Heterocyclic Carbene Catalyzed Reaction of Enals with Nitroalkenes via Homoenolate: Stereoselective Synthesis of δ-Nitro Esters

2.1. Introduction

Carbon-carbon bond forming reactions constitute a challenging area in organic chemistry; hence, the discovery of new, efficient synthetic methods for the construction of C-C bond remains a topic of great interest. From the literature, it is evident that most of the carbon-carbon bond forming reactions proceed via the intermediacy of enol/enolate or enamine. The versatile reactive intermediate enolate anion is generated by the removal of alpha proton of carbonyl compounds, often with the aid of alkali metal reagents. As we have already discussed in the introductory chapter (Chapter 1), it is possible to facilitate the reaction of an electrophile at the β-position of a carbonyl group by the intermediacy of homoenolate. The introduction of NHC for the generation of homoenolate from enals made it possible to explore the synthetic utility of this uniquely reactive intermediate. Since the subject matter of this chapter is the N-heterocyclic carbene catalyzed conjugate addition of homoenolate to nitroalkenes, a brief overview of Michael additions to nitroalkenes is presented first.

2.1.1. Michael Addition to Nitroalkenes

Conjugate addition of nucleophiles to electron deficient alkenes, generally called Michael addition, is an important tool for the creation of carbon-carbon and carbon-heteroatom bonds. These reactions proceed under very mild reaction conditions and tolerate various functional groups. Nitroalkenes are powerful Michael acceptors, due to the presence of a strong electron withdrawing nitro group. Because of the ease of conversion of nitro group to various functional groups, nitro compounds have been used extensively in organic synthesis.

Oxygen, sulfur, nitrogen and phosphorous anions are good heteroatom-centered nucleophiles for the Michael addition to nitroalkenes. Use of such nucleophiles renders a useful method for the introduction of two heteroatoms at vicinal positions. The addition
of thiols and alcohols has frequently found use in organic synthesis because of the stability of the addition product. For example, the reaction of thiols with nitroalkenes readily proceeds in the presence of catalytic amount of base to give β-nitro sulphides in quantitative yields. The stereoselectivity of this type of reactions is low and the diastereomers are formed in 1:1 ratio (Scheme 2.1).

Scheme 2.1

β-nitrosulphides are useful intermediates for the preparation of various heterocycles containing sulphur atoms. Clark and co-workers reported the synthetic application of conjugate addition of thiols to nitroalkenes in a stereospecific total synthesis of biotin 6 (Scheme 2.2).3

Scheme 2.2

Kamimura et al. reported a very simple method for the stereo-control of the Michael addition of thiols, selenols and alcohols. The Michael addition of thiols to nitroalkenes followed by protonation at -78 °C gives anti β-nitrosulphides. This process was then extended to anti β-nitro selenides and anti β-nitro ethers (Scheme 2.3).4

Scheme 2.3

The Michael addition of alkoxide to nitroalkenes generally gives a complex mixture of products due to the polymerization of nitroalkenes.5 The effect of alkoxides
has been examined carefully and it was found that potassium and sodium alkoxides give pure β-nitroethers in excellent yields (Scheme 2.4).\(^6\)

![Scheme 2.4](image)

The Michael addition of oxygen nucleophiles to nitroalkenes and subsequent cyclization or cycloaddition of adducts provides an important method for the preparation of oxygen-heterocycles. For example, various substituted 3-nitro-2\(H\)-chromenes have synthesized by the reaction of salicylaldehydes with nitroalkenes (Scheme 2.5).\(^7\)

![Scheme 2.5](image)

Tandem Michael addition of oxygen nucleophiles has received much attention for the construction of octahydro benzo[b] furans. Treatment of 1-nitro-1-cyclohexene with methyl 4-hydroxy-2-butyrate in the presence of potassium tert-butoxide gave 3α-nitrooctahydrobenzo[b]furan in excellent yield through a tandem conjugate addition initiated by the oxygen nucleophile (Scheme 2.6).\(^8\)

![Scheme 2.6](image)

A Convenient method for the preparation of 1,2-diamine from the corresponding nitroalkene was accomplished by Imagawa, by successive reactions of Michael addition of ethoxyamine to nitroalkene and reduction with hydrogen (Scheme 2.7). This preparative method is applicable to various nitroalkenes in one-pot procedure.\(^9\)

![Scheme 2.7](image)
Conjugate addition of chiral nitrogen nucleophiles to nitro alkenes provides access to chiral compounds having nitrogen functionalities at vicinal positions (Scheme 2.8).\(^9\)

![Scheme 2.8](image)

Amino alcohols like (s)–prolinols react with nitroalkenes very rapidly with very high facial selectivity. Rapid and stereoselective reduction of nitro group is essential for the conversion of products to 1,2-diamine derivatives with retention of configuration. \(\text{SmI}_2\) is utilized in the stereoselective reduction of the thermally unstable 2-amino nitroalkenes to give a range of useful 1,2-diamines (Scheme 2.9).\(^10\)

![Scheme 2.9](image)

In 2006, Won et al. reported a cinchona alkaloid promoted Michael addition of \(N\)-heterocycles to nitro alkenes, with moderate to high enantioselectivities (Scheme 2.10).\(^11\)

![Scheme 2.10](image)

Substituted pyrazoles are important synthetic targets in the pharmaceutical industry because numerous biologically active compounds possess the pyrazole motif. A regio and stereoselective synthesis of 1,3,5-tri- and 1,3,4,5-tetra substituted pyrazoles by the reaction of \(N\)-aryl hydrazones and nitroalkens has been reported. The reaction mechanism involves a stepwise cycloaddition pathway (Scheme 2.11).\(^12\)

![Scheme 2.11](image)
2.1.2. Michael Addition of Carbon Centered Nucleophiles

Classically, the reaction of nitroalkenes with carbon centered nucleophiles has been limited to reactions carried out under mild basic condition using relatively acidic reaction partners such as malonate derivatives and 1,3-diketones.\textsuperscript{13} For example, the reaction of acetylacetone or ethyl acetate with nitrostyrene proceeds in the presence of triethylamine at room temperature to give adduct in high yield. Yoshikoshi and co-workers have found that the potassium fluoride catalyzed addition of 1,3-diketones to nitroalkenes leads to the formation of furans or Michal adducts and their Nef products (Scheme 2.12).\textsuperscript{14}

![Scheme 2.12](image)

Michael addition of nitroalkanes to nitroalkenes is catalyzed by triethylamine to give 1,3-dinitrocompounds. In some cases intramolecular displacement of nitro group take place to give cyclic nitronates (Scheme 2.13).\textsuperscript{15}

![Scheme 2.13](image)

Seebach and co-workers have developed the Michael type addition of lithium enolates to nitroalkenes (Scheme 2.14).\textsuperscript{16}

![Scheme 2.14](image)

Pyroglutamic acid is a useful starting material for the synthesis of several natural products, such as pyrrolidine alkaloids, kainoids and other unnatural amino acids.
Interesting chemoselective Michael addition of pyroglutamate anions to indole-derived nitroalkenes was reported by Braña et al.\textsuperscript{17} By choosing appropriate amide protecting groups, the reaction can be carried out either at C2 or C4 position (Scheme 2.15).

\begin{center}
\begin{tikzpicture}
\node at (0,0) {1. LiHMDS/THF -78 °C};
\node at (2.5,0) {2.};
\node at (0.25,-1) {49 PG \text{CO}_2\text{Me}};
\node at (2.5,-1) {50 Boc NO\text{Boc} MeO};
\node at (3.5,0) {52, 55\%};
\node at (3.5,-1) {51, 59\%};
\node at (0.5,-3.5) {O NO\text{Boc} \text{Boc} \text{MeO}};
\node at (2,-3.5) {49 PG = Bn};
\node at (3,-3.5) {49 PG = Boc};
\end{tikzpicture}
\end{center}

\textbf{Scheme 2.15}

Valentine and co-workers have extensively studied the reaction of enamines with nitroalkenes.\textsuperscript{18} The reaction of morpholino-cyclohexene with nitropropenes proceed under mild conditions to give \( \gamma \)-nitroketones (Scheme 2.16).\textsuperscript{19} The morpholine-enamine of monoprotected butane-2,3-dione reacts with cyclic and acyclic conjugated nitroalkenes in a Michael-type reaction to yield nitro-substituted \( \alpha \)-diketones, after acidic hydrolysis of the mononitroalkylated enamine adducts. Cyclopentanone, hexahydro-1\textit{H}-pentalen-2-one and octahydro-2\textit{H}-inden-2-one derivatives are readily obtained by base-catalyzed intramolecular nitroaldol reaction of the acyclic hydrolysis products.\textsuperscript{20}

\begin{center}
\begin{tikzpicture}
\node at (0,0) {53};
\node at (2.5,0) {54 \text{MeNO}};
\node at (4.5,0) {55, 85\%};
\node at (7,0) {56, 80\%};
\node at (0.5,-3.5) {57 \text{NO}};
\node at (2,-3.5) {58 \text{MeNO} t-Bu};
\node at (4,0) {10% HCl};
\node at (0.5,-3.5) {57 \text{NO}};
\node at (2,-3.5) {58 \text{MeNO} t-Bu};
\end{tikzpicture}
\end{center}

\textbf{Scheme 2.16}

The reaction of enamine 57 with 2-nitro-2-propen-1-yl pivaloates gives 4-nitro cyclohexenone 59 via route that can be regarded as formal [3+3] carbocyclization.\textsuperscript{21} With proper substitution of reactants, up to five stereogenic centers can be installed in this reaction (Scheme 2.17).

\begin{center}
\begin{tikzpicture}
\node at (0,0) {57 \text{NO}};
\node at (2.5,0) {58 \text{MeNO} t-Bu};
\node at (4.5,0) {59, 58\% (de >95\%)};
\node at (0,-3.5) {57 \text{NO}};
\node at (2.5,-3.5) {58 \text{MeNO} t-Bu};
\node at (0,-3.5) {57 \text{NO}};
\node at (2.5,-3.5) {58 \text{MeNO} t-Bu};
\end{tikzpicture}
\end{center}

\textbf{Scheme 2.17}
A binaphthyl-derived amine thiourea catalyzed Michael addition reaction of diketones to nitroalkenes with high enantioselectivity was developed by Wang and co-workers. Because of high catalytic activity, utilization of the catalyst in an amount as low as 1 mol % is sufficient for the process (Scheme 2.18).  

![Scheme 2.18](image)

Optically active 2-indolyl-1-nitro derivatives in good yield and enantioselectivity can be synthesized by a novel catalytic enantioselective Friedel–Crafts alkylation of indoles with nitroalkenes using a simple thiourea organocatalyst (Scheme 2.19). The high synthetic versatility of the products render this new approach highly appealing for the synthesis of optically active target compounds such as tryptamines and 1,2,3,4-tetrahydro-β-carbolines.

![Scheme 2.19](image)

Highly enantio- and diastereoselective Michael addition reactions of ketones and aldehydes with nitroalkenes in water has been achieved by the reusable fluororous (S)-pyrrolidine sulfonamide organocatalyst (Scheme 2.20). The catalyst is conveniently recovered from the reaction mixture by fluororous solid-phase extraction and can be subsequently reused (up to six cycles) without significant loss of catalytic activity and stereoselectivity.

![Scheme 2.20](image)

Enders and co-workers reported a chemo-, diastereo- and enantioselective three-component domino reaction of nitroalkene and aldehydes. This proline derived
organocatalytic reaction afforded tetra-substituted cyclohexene carbaldehydes in moderate yield. The four stereogenic centers are generated in three consecutive carbon–carbon bond formations with high diastereo- and complete enantiocontrol (Scheme 2.21).

![Scheme 2.21](image)

Prolinol silyl ether catalyzed highly enantioselective Michael reaction of acetaldehyde with nitroalkenes was reported by List et al (Scheme 2.22).

![Scheme 2.22](image)

Recently, Namboothiri et al. reported a novel reaction of curcuminoids with nitroalkenes (Scheme 2.23). Highly functionalized cyclohexanones possessing three contiguous chiral centers with complete diastereoselectivity have been synthesized through an inter–intramolecular double Michael reaction involving curcumin and nitroalkene under extremely simple experimental conditions (K₂CO₃ in aqueous THF). Under identical conditions, curcuminoids react with α-bromonitroalkenes to afford dihydrofurans through an intermolecular Michael addition-intramolecular nucleophilic substitution (O-alkylation), which is analogous to an ‘interrupted’ Feist–Benary reaction. Later the authors have reported the asymmetric version of this reaction by a combination of a dihydrocinchonine-thiourea organocatalyst and K₂CO₃.

![Scheme 2.23](image)

2.2. Background to the Present Work

In the context of our recent discovery of synthetic routes for cyclopentanones and related organic compounds by the reaction of homoenolates with chalcones in methanol
(see Chapter 1), it was of interest to investigate the prospect of homoenolate addition to nitroalkenes. Evidently, the nitroalkenes are unique Michael acceptors endowed with the powerful electron-withdrawing group (EWG), which is amenable to a variety of synthetic transformations. A successful Michael addition of homoenolate to β-nitroalkene as envisioned above would provide access to functionalized five-carbon synthons potentially useful in the synthesis of δ-amino acid derivatives and related compounds of therapeutic value. The results of our work constituting the novel synthesis of δ-nitro esters are presented in the following sections.

2.3. Results and Discussion

Against the above backdrop, in a pilot experiment, cinnamaldehyde 69 and 2,5-dimethoxy-β-nitrostyrene 79 were exposed to imidazolin-2-ylidene, generated from catalytic amount of imidazolium chloride, by potassium carbonate in THF–methanol. The reaction mixture was processed after 24 h and the crude product on purification by chromatography afforded a crystalline solid 80 as the major product (Scheme 2.24).

![Scheme 2.24](image)

The structure of the product was assigned on the basis of spectroscopic data. $^1$H NMR spectrum showed two sets of methoxy proton signals at $\delta$ 3.75 and $\delta$ 3.57 respectively. The methylene protons appeared as doublet of doublets. The benzylic protons were found to resonate as multiplets. The ester group displayed $^{13}$C resonance signal at $\delta$ 172 and it was supported by the carbonyl absorption at 1730 cm$^{-1}$ in the IR spectrum. The nitro group showed its characteristic absorption 1552 cm$^{-1}$. The mass spectrum obtained was in good agreement with the proposed structure.
The final confirmation of the structure and relative stereochemistry of 80 was obtained from single crystal X-ray analysis.
Figure 2.3. Single crystal X-ray structure of 80. CCDC number: 743837.

In view of the success of the reaction, it was obligatory to assess the usefulness of other commonly available NHC catalysts in this reaction. A number of experiments were conducted, and the results are summarized in Table 1.

**Table 2.1. Catalyst Screening**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Condition</th>
<th>Yield(%)&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>C1</td>
<td>THF:MeOH(9:1), 70 °C, 24 h</td>
<td>56</td>
</tr>
<tr>
<td>2</td>
<td>C2</td>
<td>THF:MeOH(9:1), 70 °C, 24 h</td>
<td>70</td>
</tr>
<tr>
<td>3</td>
<td>C3</td>
<td>THF:MeOH(9:1), 70 °C, 24 h</td>
<td>20</td>
</tr>
<tr>
<td>4</td>
<td>C4</td>
<td>THF:MeOH(9:1), 70 °C, 36 h</td>
<td>-</td>
</tr>
</tbody>
</table>

<sup>a</sup> isolated yield

Among the four catalysts investigated, imidazolinium catalyst C2 gave the best result. The benzimidazolium catalyst C3 gave low yield of the product, while the triazolium catalyst, C4, was completely ineffective. Although it is not possible to rationalize the superior performance of C2 vis-à-vis other catalysts, it is noteworthy that
C2 is the most nucleophilic one in this group.

With a view to optimize the yield of the product, we studied the influence of different bases in generating the NHC catalyst and the results are shown in Table 2. Interestingly the best results were obtained with potassium carbonate in THF/MeOH (9:1).

**Table 2.2. Condition optimization**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Base</th>
<th>Condition</th>
<th>Yield(^a) %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>DBU</td>
<td>THF:MeOH (9:1), 70 °C, 24 h</td>
<td>-</td>
</tr>
<tr>
<td>2.</td>
<td>K₂CO₃</td>
<td>THF:MeOH (9:1), 70 °C, 24 h</td>
<td>70</td>
</tr>
<tr>
<td>3.</td>
<td>CsCO₃</td>
<td>THF:MeOH (9:1), 70 °C, 24 h</td>
<td>34</td>
</tr>
<tr>
<td>4.</td>
<td>Na₂CO₃</td>
<td>THF:MeOH (9:1), 70 °C, 24 h</td>
<td>37</td>
</tr>
<tr>
<td>5.</td>
<td>BaCO₃</td>
<td>THF:MeOH (9:1), 70 °C, 24 h</td>
<td>-</td>
</tr>
<tr>
<td>6.</td>
<td>Li₂CO₃</td>
<td>THF:MeOH (9:1), 70 °C, 24 h</td>
<td>-</td>
</tr>
<tr>
<td>7.</td>
<td>K₂CO₃</td>
<td>THF:MeOH (7:2), 70 °C, 24 h</td>
<td>56</td>
</tr>
<tr>
<td>8.</td>
<td>K₂CO₃</td>
<td>THF:MeOH (1:1), 70 °C, 24 h</td>
<td>34</td>
</tr>
<tr>
<td>9.</td>
<td>K₂CO₃</td>
<td>THF:MeOH (1:1), rt, Ar, 24 h</td>
<td>-</td>
</tr>
<tr>
<td>10.</td>
<td>K₂CO₃</td>
<td>THF, 70 °C, 24 h</td>
<td>-</td>
</tr>
<tr>
<td>11.</td>
<td>K₂CO₃</td>
<td>MeOH, 70 °C, 24 h</td>
<td>-</td>
</tr>
<tr>
<td>12.</td>
<td>K₂CO₃</td>
<td>PhMe:MeOH (7:2), 70 °C, 24 h</td>
<td>15</td>
</tr>
</tbody>
</table>

\(^{a}\)isolated yield

After having reasonably established the optimum parameters, the reaction was extended to a number of nitroalkenes and the results are summarized in Scheme 2.25. Inevitable polymerization of nitroalkenes may be the reason for a substantial decrease in the product formation. In our studies, useful yields of products were obtained only with aryl substituted enals and β- nitrostyrenes.
**2.4. Mechanism**

Mechanistically the reaction may be viewed as involving the initial formation of homoenolate by the reaction of NHC with the enal followed by its Michael addition to β-nitrostyrene. The stereoselectivity observed in the product formation may be attributed to the trans-selective Michael addition (Scheme 2.26).
Scheme 2.26. Proposed mechanism

2.5. Conclusion

In conclusion, the first report on the efficient, NHC catalyzed stereoselective Michael addition of enals to β-nitrostyrenes via the intermediacy homoenolate is developed. The saturated imidazolinium chloride is used as a catalyst for the first time to generate homoenolate from enals. It is reasonable to assume that since the products are doubly functionalized five carbon synthons; this reaction will find application in organic synthesis, especially in the synthesis of biologically active piperidinone and δ-amino acid derivatives.

2.6. Experimental Details

NMR spectra were recorded at 500 (1H) or 300 (1H) and 126 (13C) or 75 (13C) MHz respectively on Brucker Avance DPX - 500 or 300 MHz NMR spectrometer. Chemical shifts (δ) are reported relative to TMS (1H) and CDCl$_3$ (13C) as the internal standards. Coupling constant (J) is reported in Hertz (Hz). Mass spectra were recorded under EI/HRMS or FAB using JEOL JMS 600H mass spectrometer. IR spectra were recorded on Brucker Alpha-T or E FT-IR spectrophotometer; absorbencies are reported in cm$^{-1}$. Commercially available enals were purchased from Aldrich Chemical Co. and others were synthesized by Wittig reaction between (triphosphoranylidene)acetaldehyde and the corresponding aldehydes. The nitrostyrenes were easily prepared by the condensation of corresponding aldehydes with nitromethane (Henry reaction). The carbene precursor 1,3-dimesityl-imidazolinium chloride was also prepared according to known literature procedure. Commercial grade solvents were distilled prior to use. All reactions were carried out in oven-dried glassware. Progress of reactions was monitored...
by Thin Layer Chromatography. Gravity column chromatography was performed using
60-120/100-200 mesh silica gel, and mixtures of petroleum ether-ethyl acetate were used
for elution. Melting points were recorded on a Büchi melting point apparatus and are
uncorrected.

2.6.1. General Experimental Procedure

_Synthesis of methyl 4-(2, 5-dimethoxyphenyl)-5-nitro-3-phenylpentanoate 80_: 

\[ \text{K}_2 \text{CO}_3 \ (13.8 \text{ mg}, 20 \text{ mol } \% \) was added to a solution of 1,3-dimesityl imidazolinium 
chloride C2 (26 mg, 15 mol %), cinnamaldehyde (132 mg, 1 mmol) and 2,5-dimethoxy-β-
nitrostyrene (104.5 mg, 0.5 mmol) in 9:1 dry THF: methanol, this solution was stirred for
24 h at 70 °C under reflux condition. After the completion of the reaction, the reaction 
mixture was acidified by 1:1 HCl. After the removal of the solvent, the residue was 
extracted with ethyl acetate and organic layer was dried with anhydrous Na₂SO₄. The 
concentrated residue was subjected to column chromatography on a silica gel (100-200 
mesh) column using 93:7 hexane: ethyl acetate solvent mixture to afford 80 (50% yield).

2.6.2. Characterization Data of Compounds

**Methyl-4-(2,5-dimethoxyphenyl)-5-nitro-3-phenylpentanoate **(80)

Following the general procedure, the reaction of 2, 5-dimethoxy-β-nitrostyrene 
(104.5 mg, 0.5 mmol), cinnamaldehyde (132 mg, 2 mmol), 1,3-dimesityl 
imidazolinium chloride (26 mg, 15 mol %) and K₂CO₃ (13.8 mg, 20 mol %) in 9:1 
THF:MeOH solvent mixture afforded methyl 4-(2,5-dimethoxyphenyl)-5-nitro-3-
phenylpentanoate in 50% (93 mg) yield as white crystalline solid.

**Chemical Formula:** C₂₀H₂₃NO₆

\[ \text{mp } 112-114 \text{ °C}. \]

**IR (film)** ν_{max} 1730, 1552, 1377, 1265, 1046 cm⁻¹.

**¹H NMR (500 MHz, CDCl₃)** δ = 7.22-7.15 (m, 3H) 6.95-6.93 (m, 2H) 6.73 (d, J = 9 Hz, 1H) 6.66-6.68 (m, 1H) 6.05
(d, J = 3 Hz, 1H) 4.68 (dd, J =13 Hz, 7 Hz, 1H) 4.63 (dd, J =13 Hz, 8.5 Hz, 1H) 4.277-4.319 (m, 1H) 3.746 (s, 3H) 3.64-
3.69 (m, 1H) 3.57(s, 3H) 3.57(s, 3H) 2.76(dd, J = 16 Hz, 7 Hz, 1H) 2.60 (dd, J = 16.5 Hz, 8.5 Hz, 1H). ¹³C NMR (126
MHz, CDCl₃) δ = 171.9, 152.9, 151.5, 139.4, 128.5, 128.0,
Methyl-4-(furan-2-yl)-5-nitro-3-phenylpentanoate (81)

Following the general procedure, the reaction of 2-(2-nitrovinyl)furan (69.5 mg, 0.5 mmol), cinnamaldehyde (132 mg, 1 mmol), 1,3-dimesityl imidazolinium chloride (26 mg, 15 mol %) and K$_2$CO$_3$ (13.8 mg, 20 mol %) in 9:1 THF:MeOH solvent mixture afforded methyl 4-(furan-2-yl)-5-nitro-3-phenylpentanoate in 70% (106 mg) yield as yellow viscous liquid.

**Chemical Formula:** C$_{16}$H$_{17}$NO$_5$

**IR (film) v$_{\text{max}}$** 1738, 1557, 1377, 1261, 1013 cm$^{-1}$.

$^1$H NMR (500 MHz, CDCl$_3$) $\delta = 7.33-7.3$ (m, 1H) 7.24-7.25 (m, 3H) 6.87-6.89 (m, 2H) 6.29-6.30 (m, 1H) 5.99 (d, $J = 3.5$ Hz, 1H) 4.56(dd, $J = 13.5$ Hz, 7 Hz, 1H) 4.51 (dd, $J = 13$ Hz, 8.5 Hz, 1H) 4.07-4.11 (m, 1H) 3.63 (s, 3H) 3.53-3.58 (m, 1H) 2.87 (dd, $J = 16$ Hz, 7.5 Hz, 1H) 2.72 (dd, $J = 16$ Hz, 8Hz, 1H). $^{13}$C (126 MHz, CDCl$_3$) $\delta = 171.6$, 150.0, 142.1, 138.4, 128.3, 128.2, 127.5, 110.4, 108.6, 75.7, 51.7, 43.3, 41.5, 37.4.

**HRMS-EI** Calculated for C$_{16}$H$_{17}$NO$_5$: 303.1107, Found: 303.1128.

Methyl-5-nitro-3-phenyl-4-p-tolylpentanoate (82)

Following the general procedure, the reaction of 1-methyl-4-(2-nitrovinyl)benzene (81.5 mg, 0.5 mmol), cinnamaldehyde (132 mg, 1 mmol), 1,3-dimesityl imidazolinium chloride (26 mg, 15 mol %) and K$_2$CO$_3$ (13.8 mg, 20 mol %) in 9:1 THF:MeOH solvent mixture afforded methyl 5-nitro-3-phenyl-4-p-tolylpentanoate in 70% (114.5 mg) yield as white solid.

**Chemical Formula:** C$_{19}$H$_{21}$NO$_4$

mp 79-81 °C.

**IR (film) v$_{\text{max}}$** 1732, 1557, 1379, 1263, 1021 cm$^{-1}$.

$^1$H NMR (500 MHz, CDCl$_3$) $\delta = 7.19-7.21$ (m, 3H) 7.00 (d, $J = 8$ Hz, 2H) 6.83-6.85 (m, 2H) 6.68 (d, $J = 8$ Hz, 2H) 4.67 (dd, $J = 13$ Hz, 7 Hz, 1H) 4.51 (dd, $J = 13$ Hz, 8.5 Hz, 1H) 3.83-3.85 (m, 1H) 3.60 (s, 3H) 3.52-3.54 (m, 1H) 2.72 (dd, $J$
Methyl-5-nitro-3-phenyl-4-(thiophen-2-yl)pentanoate (83)

Following the general procedure, the reaction of 2-(2-nitrovinyl)thiophene (77.6 mg, 0.5 mmol), cinnamaldehyde (132 mg, 1 mmol), 1,3-dimesityl imidazolium chloride (26 mg, 15 mol %) and K₂CO₃ (13.8 mg, 20 mol %) in 9:1 THF:MeOH solvent mixture afforded methyl 5-nitro-3-phenyl-4-(thiophen-2-yl)pentanoate in 63% (100.5 mg) yield as white solid.

Chemical Formula: C₁₆H₁₇NO₄S

m.p. 61–63 °C.

IR (film) ν_max 1736, 1556, 1379, 1258, 1018 cm⁻¹.

¹H NMR (500 MHz, CDCl₃) δ = 7.25-7.27 (m, 3H) 7.18-7.19 (m, 1H) 6.94-9.96 (m, 2H) 6.89-6.91 (m, 1H) 6.55-6.56 (m, 1H) 4.68 (dd, J = 13 Hz, 7 Hz, 1H) 4.51 (dd, J = 13 Hz, 8.5 Hz, 1H) 4.25-4.27 (m, 1H) 3.64 (s, 3H) 3.57-3.59 (m, 1H) 2.85 (dd, J = 16 Hz, 7.5 Hz, 1H) 2.72 (dd, J = 16 Hz, 7.5 Hz, 1H).

¹³C NMR (125 MHz, CDCl₃) δ = 171.6, 138.1, 137.9, 128.7, 128.3, 127.6, 126.7, 126.7, 124.8, 78.2, 51.8, 44.1, 43.1, 37.4.

HRMS-EI Calculated for C₁₆H₁₇NO₄S: 319.0878, Found: 319.0868.

Methyl-4-(4-methoxyphenyl)-5-nitro-3-phenylpentanoate (84)

Following the general procedure, the reaction of 1-methoxy-4-(2-nitrovinyl)benzene (89.5 mg, 0.5 mmol), cinnamaldehyde (132 mg, 1 mmol), 1,3-dimesityl imidazolium chloride (26 mg, 15 mol %) and K₂CO₃ (13.8 mg, 20 mol %) in 9:1 THF:MeOH solvent mixture afforded methyl 4-(4-methoxyphenyl)-5-nitro-3-phenylpentanoate in 63% (108 mg) yield as white solid.

Chemical Formula: C₁₉H₂₁NO₅

m.p. 67-69 °C.

IR (film) ν_max 1732, 1556, 1379, 1252, 1032 cm⁻¹.

¹H NMR (500 MHz, CDCl₃) δ = 7.22-7.23 (m, 3H) 6.84-
nitrovinyl)benzene (83.6 mg, 0.5 mmol), cinnamaldehyde (132 mg, 1 mmol), 1,3-dimesitylimidazolinium chloride (26 mg, 15 mol %) and K$_2$CO$_3$ (13.8 mg, 20 mol %) in 9:1 THF:MeOH solvent mixture afforded methyl 4-(4-fluorophenyl)-5-nitro-3-phenylpentanoate in 60% (104.6 mg) yield as yellow viscous liquid.

**Methyl-4-(4-fluorophenyl)-5-nitro-3-phenylpentanoate (85)**

Following the general procedure, the reaction of 1-fluoro-4-(2-nitrovinyl)benzene (83.6 mg, 0.5 mmol), cinnamaldehyde (132 mg, 1 mmol), 1,3-dimesitylimidazolinium chloride (26 mg, 15 mol %) and K$_2$CO$_3$ (13.8 mg, 20 mol %) in 9:1 THF:MeOH solvent mixture afforded methyl 4-(4-fluorophenyl)-5-nitro-3-phenylpentanoate in 63% (104 mg) yield as yellow viscous liquid.

**Chemical Formula:** C$_{19}$H$_{21}$NO$_5$

**IR (film)** $\nu_{\text{max}}$ 1738, 1556, 1379, 1251, 1033 cm$^{-1}$.

$^1$H NMR (500 MHz, CDCl$_3$) $\delta =$ 7.19-7.213 (m, 3H) 6.87-6.91 (m, 2H) 6.76-6.82 (m, 4H) 4.71 (dd, $J =$ 13 Hz, 7 Hz, 1H) 4.53 (dd, $J =$ 13 Hz, 9 Hz, 1H) 3.85-3.89 (m, 1H) 3.62 (s, 3H) 3.51-3.52 (m, 1H) 2.72 (dd, $J =$ 15.5 Hz, 7.5 Hz, 1H) 2.61 (dd, $J =$ 15.5 Hz, 7.5 Hz, 1H).

$^{13}$C NMR (126 MHz, CDCl$_3$) $\delta =$ 171.9, 152.9, 151.5, 139.4, 128.5, 128.0, 127.1, 125.5, 115.6, 113.3, 111.6, 77.9, 55.7, 55.4, 51.6, 43.0, 41.9, 37.0. **HRMS-EI** Calculated for C$_{19}$H$_{21}$NO$_5$: 343.1420, Found: 343.1405.

**Methyl-3-(4-methoxyphenyl)-5-nitro-4-phenylpentanoate (86)**

Following the general procedure, the reaction of (2-nitrovinyl)benzene (74.6 mg, 0.5 mmol), 4-methoxycinnamaldehyde (162 mg, 1 mmol), 1,3-dimesitylimidazolinium chloride (26 mg, 15 mol %) and K$_2$CO$_3$ (13.8 mg, 20 mol %) in 9:1 THF:MeOH solvent mixture afforded methyl 3-(4-methoxyphenyl)-5-nitro-4-phenylpentanoate in 60% (104.6 mg) yield as yellow viscous liquid.

**Chemical Formula:** C$_{18}$H$_{18}$FNO$_4$

**IR (film)** $\nu_{\text{max}}$ 1732, 1556, 1379, 1251, 1033 cm$^{-1}$.
Methyl-4-(naphthalen-1-yl)-5-nitro-3-phenylpentanoate (87)

Following the general procedure, the reaction of 1-(2-nitrovinyl)naphthalene (99.6 mg, 0.5 mmol), cinnamaldehyde (132 mg, 1 mmol), 1,3-dimesityl imidazolinium chloride (26 mg, 15 mol %) and K₂CO₃ (13.8 mg, 20 mol %) in 9:1 THF:MeOH solvent mixture afforded methyl 4-(naphthalen-1-yl)-5-nitro-3-phenylpentanoate in 60% (109 mg) yield as brown viscous liquid.

**Chemical Formula:** C₂₂H₂₁NO₄

**IR (film) νmax** 1732, 1553, 1377, 1259, 1017 cm⁻¹.

**¹H NMR (500 MHz, CDCl₃)** δ = 7.20-7.21 (m, 3H) 6.79 - 6.81 (m, 2H) 6.72 (m, 4H) 4.6 (dd, J = 13 Hz, 7.5 Hz, 1H) 4.53 (dd, J = 12.5 Hz, 8.5 Hz, 1H) 3.32-3.86 (m, 1H) 3.75 (s, 3H) 3.60 (s, 3H) 3.48-3.52 (m, 1H) 2.69 (dd, J = 15.5 Hz, 7 Hz, 1H) 2.55 (dd, J = 15.5 Hz, 8 Hz, 1H). **¹³C NMR (126 MHz, CDCl₃)** δ = 171.8, 158.7, 135.6, 130.1, 129.8, 129.0, 128.2, 127.79, 113.5, 77.8, 55.0, 51.7, 47.7, 43.0, 37.8.

**HRMS-EI** Calculated for C₁₉H₂₁NO₅: 343.1420, Found: 343.1425.

Methyl 3-(2-methoxyphenyl)-5-nitro-4-p-tolylpentanoate (88)

Following the general procedure, the reaction of 1-methyl-4-(2-nitrovinyl)benzene (81.5 mg, 0.5 mmol), 2-methoxycinnamaldehyde (162 mg, 1 mmol), 1,3-dimesityl imidazolinium chloride (26 mg, 15 mol %) and K₂CO₃ (13.8 mg, 20 mol %) in 9:1 THF:MeOH solvent mixture afforded methyl 3-(2-methoxyphenyl)-5-nitro-4-p-tolylpentanoate in 57% (101.8 mg) yield as yellow viscous liquid.

**Chemical Formula:** C₂₂H₂₁NO₄

**IR (film) νmax** 1732, 1553, 1377, 1259, 1017 cm⁻¹.

**¹H NMR (500 MHz, CDCl₃)** δ = 8.1 (d, J = 10 Hz, 1H) 7.81(d, J = 10 Hz, 1H) 7.71 (d, J = 10 Hz, 1H) 7.56-7.53 (m, 1H) 7.48-7.45 (m, 1H) 7.37-7.38 (m, 1H) 7.16-7.20 (m, 3H) 6.995 (d, J = 5 Hz, 2H) 6.83-6.85 (m, 1H) 4.94 (bs, 1H) 4.80-4.73 (m, 2H) 3.84-3.81 (m, 1H) 3.49 (s, 3H) 2.69-2.66 (m, 1H) 2.63-2.60 (m, 1H). **¹³C NMR (126 MHz, CDCl₃)** δ = 171.9, 140.4, 134.0, 132.6, 129.2, 128.4, 128.3, 127.9, 127.4, 126.6, 125.8, 124.6, 122.6, 77.5, 51.6, 44.1, 39.0, 36.5.

**HRMS-EI** Calculated for C₂₂H₂₁NO₄: 363.1471, Found: 363.1472.
Chemical Formula: C_{20}H_{23}NO_{5}

IR (film) ν_{max} 1732, 1557, 1379, 1244, 1026 cm\(^{-1}\).

\(^1\)H NMR (500 MHz, CDCl\(_3\)) δ = 7.19-7.21 (m, 1H) 7.02 (d, J = 7.5 Hz, 2H) 6.87 (d, J = 7.5 Hz, 1H) 6.74-6.79 (m, 3H) 6.50-6.651 (m, 1H) 4.72 (dd, J = 13.5 Hz, 6.5 Hz, 1H) 4.51 (dd, J = 13.5 Hz, 9.5 Hz, 1H) 4.10 (m, 1H) 3.95 (m, 1H) 3.86 (s, 3H) 3.63 (s, 3H) 2.69 (dd, J = 16 Hz, 8 Hz, 1H) 2.54 (dd, J = 15.5 Hz, 7.5 Hz, 1H) 2.31 (s, 3H). \(^{13}\)C NMR (126 MHz, CDCl\(_3\)) δ = 172.2, 157.0, 137.0, 133.1, 129.7, 129.4, 128.2, 127.1, 120.1, 110.4, 77.3, 55.2, 51.6, 46.3, 36.8, 36.5, 21.0. HRMS-EI Calculated for C_{20}H_{23}NO_{5}: 357.1576. Found: 357.1524.

Methyl-3-(4-methoxyphenyl)-5-nitro-4-p-tolypentanoate (89)

Following the general procedure, the reaction of 1-methyl-4-(2-nitrovinyl)benzene (81.5 mg, 0.5 mmol), 4-methoxycinnamaldehyde (162 mg, 1 mmol), 1,3-dimesityl imidazolinium chloride (26 mg, 15 mol %) and K\(_2\)CO\(_3\) (13.8 mg, 20 mol %) in 9:1 THF:MeOH solvent mixture afforded methyl 3-(4-methoxyphenyl)-5-nitro-4-p-tolypentanoate in 53% (94.6 mg) yield as yellow viscous liquid.

Chemical Formula: C_{20}H_{23}NO_{5}

IR (film) ν_{max} 1737,1603,1556,1378,1251,1033 cm\(^{-1}\).

\(^1\)H NMR (500 MHz, CDCl\(_3\)) δ = 7.03 (d, J = 8 Hz, 2H) 6.78-6.74 (m, 4H) 6.71 (d, J = 8 Hz, 2H) 4.68 (dd, J = 13 Hz, 7.5 Hz, 1H) 4.52 (dd, J = 12.5 Hz, 8.5 Hz, 1H) 3.80-3.84 (m, 1H) 3.79 (s, 3H) 3.62 (s, 3H) 3.52-3.48 (m, 1H) 2.71 (dd, J = 15.5 Hz, 7 Hz, 1H) 2.56 (dd, J = 16 Hz, 8 Hz, 1H) 2.32 (s, 3H). \(^{13}\)C NMR (126 MHz, CDCl\(_3\)) δ = 171.9, 158.7, 137.3, 132.4, 130.2, 130.2, 129.9, 128.9, 114.5, 113.4, 77.9, 55.0, 51.7, 47.3, 43.0, 37.8, 21.0. HRMS-EI Calculated for C_{20}H_{23}NO_{5}: 357.1576. Found: 357.1581.

Methyl-3-(4-methoxyphenyl)-4-(naphthalen-1-yl)-5-nitropentanoate (90)

Following the general procedure, the reaction of 1-(2-nitrovinyl)naphthalene (99.6 mg, 0.5 mmol), 4-methoxycinnamaldehyde (162 mg, 1 mmol), 1,3-dimesityl imidazolinium chloride (26 mg, 15 mol %) and K\(_2\)CO\(_3\) (13.8 mg, 20 mol %) in 9:1
THF:MeOH solvent mixture afforded methyl 3-(4-methoxyphenyl)-4-(naphthalen-1-yl)-5-nitropentanoate in 47% (92.3 mg) yield as yellow viscous liquid.

**Chemical Formula:** $C_{23}H_{23}NO_5$

**IR** (film) $\nu_{\text{max}}$ 1732, 1553, 1377, 1252, 1032 cm$^{-1}$.

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ = 8.20 (d, $J$ = 8.5 Hz, 1H) 7.86 (d, $J$ = 7.5 Hz, 1H) 7.75 (d, $J$ = 8.5 Hz, 1H) 7.57-7.6 (m, 1H) 7.49-7.54 (m, 1H) 7.30-7.33 (m, 1H) 7.31 (t, $J$ = 8.5 Hz, 1H) 6.93 (d, $J$ = 7 Hz, 2H) 6.84 (d, $J$ = 7 Hz, 1H) 6.77 (d, $J$ = 7 Hz, 2H) 4.95 (m, 1H) 4.72-4.78 (m, 1H) 3.79-3.84 (m, 1H) 3.77 (s, 3H) 3.53 (s, 3H) 2.65-2.70 (m, 1H) 2.54-2.59 (m, 1H).

$^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ = 171.9, 158.7, 134.0, 132.6, 132.1, 131.0, 129.5, 129.2, 128.9, 128.4, 126.5, 125.7, 124.5, 122.6, 114.5, 113.7, 77.6, 55.0, 51.6, 43.2, 36.8.

**HRMS-EI** Calculated for $C_{23}H_{23}NO_5$: 393.1576, Found: 393.1560.

**Methyl-4-(4-chlorophenyl)-3-(4-methoxyphenyl)-5-nitropentanoate (91)**

Following the general procedure, the reaction of 1-chloro-4-(2-nitrovinyl)benzene (91.5 mg, 0.5 mmol), 4-methoxycinnamaldehyde (162 mg, 1 mmol), 1,3-dimesitylimidazolinium chloride (26 mg, 15 mol %) and $K_2CO_3$ (13.8 mg, 20 mol %) in 9:1 THF:MeOH solvent mixture afforded methyl 4-(4-chlorophenyl)-3-(4-methoxyphenyl)-5-nitropentanoate in 40% (75.4 mg) yield as yellow viscous liquid.

**Chemical Formula:** $C_{19}H_{20}ClNO_5$

**IR** (film) $\nu_{\text{max}}$ 1732, 1556, 1378, 1251, 1033 cm$^{-1}$.

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ = 7.16 (d, $J$ = 8.5 Hz, 1H) 7.12 (d, $J$ = 8.5 Hz, 2H) 6.67-6.69 (m, 5H) 4.62 (dd, $J$ = 13 Hz, 7 Hz, 1H) 4.43 (dd, $J$ = 13 Hz, 9 Hz, 1H) 3.75-3.78 (m, 1H) 3.70 (s, 3H) 3.55 (s, 3H) 3.40-3.42 (m, 1H) 2.6 (dd, $J$ = 16 Hz, 8 Hz, 1H) 2.48 (dd, $J$ = 15.5 Hz, 7.5 Hz, 1H).

$^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ = 171.6, 159.1, 158.8, 134.1, 133.8, 130.2, 129.8, 129.7, 129.4, 128.4, 114.6, 113.6, 77.9, 55.0, 51.8, 47.1, 43.0, 37.8. **HRMS-EI** Calculated for $C_{19}H_{20}ClNO_5$: 377.1030, Found: 377.1020.
2.7. References


