CHAPTER 3

PALLADIUM CATALYZED SYNTHESIS OF LACTONES AND LACTAMS
This chapter is divided into two sections.

Section 1. Palladium catalyzed reaction of α-bromoacrylic acids with 1, 3-dienes.

INTRODUCTION AND BACKGROUND

The palladium catalyzed C-C and C-X single bond formation is a challenging area in synthetic organic chemistry. The activation of bifunctional molecule for the reaction with alkynes and dienes in the presence of palladium catalyst to form complex organic molecules is a recent development in palladium chemistry. Such type of innovative reactions catalyzed by palladium complexes are described below in details.

The palladium-catalyzed arylannulation of 1, 3-dienes with functionally substituted aryl halides proceeds under mild conditions to yield a wide variety of functionally substituted carbocycles with good stereo and regio selectivity (scheme-1).

Scheme-1

Aryl halides bearing heteroatom- or potential carbanion-containing functionality in ortho position, have been shown to react with 1, 2-dienes in the presence of a palladium catalyst and a carbonate base to afford five and six membered hetero- and carbo cycles in high yield (scheme-2).
Monocyclic and bicyclic 6-membered ring heterocycles and carbocycles were synthesized by the palladium-catalyzed annulation of 1, 4-dienes with aryl halides bearing ortho-heteroatom and carbanion-stabilizing groups (Scheme-3). The mechanism involves aryl palladium complex formation, addition to the diene, palladium migration and intramolecular π-allyl palladium displacement.

Synthesis of 3-Hydroxyalkylbenzo[b]furans via the palladium-catalyzed heteroannulation of silyl-protected alkynols with 2-iodophenol is shown in scheme-4.
A simple, convenient and regioselective route to synthesis of tri- and tetra-substituted pyrones by the palladium catalyzed reactions of vinylic iodides; bromides or triflates bearing ester functionality with internal alkynes is shown in scheme-5.\(^5\)

**Scheme-5**

\[
\begin{align*}
\text{R}_1 & = \text{Me, Ph, Et} \\
\text{R}_2 & = \text{H, Ph, Me} \\
\text{R}_3 & = \text{Me, Ph} \\
\text{R}_4 & = \text{Ph, Me}
\end{align*}
\]

Ortho-substituted phenols have been reported to react with various allylic alcohols in the presence of palladium catalysts to give heterocyclic compounds in very good yield (scheme-6).\(^6\)

**Scheme-6**

Larock et al. developed a methodology involving the palladium-catalyzed reaction of bifunctional molecule bearing halogen and a carbon nucleophile with vinyl cyclopropanes to form five membered carbocyclic rings as shown in scheme-7.\(^7\)

**Scheme-7**
A highly convergent route to the synthesis of benzofurans by the palladium mediated reaction of o-iodophenol with terminal acetylenes and copper iodide as co-catalyst for this reaction (scheme-8).  

Scheme-8

\[
\begin{align*}
\text{Pd(OAc)}_2, (\text{PPh}_3)_2 \\
\text{Piperidine, Cul, 80%}
\end{align*}
\]

Larock et al. developed a methodology towards the synthesis of bicyclic compounds by activating bifunctional molecule bearing a halogen and carbon nucleophile for the reaction with 1, 4-cyclohexadiene (scheme-9).  

Scheme-9

\[
\begin{align*}
Pd(OAc)_2, & \text{ Bu}_4\text{NCl} \\
\text{AcONa, DMF} & \text{ 5 days, 64%}
\end{align*}
\]

The palladium catalyzed reaction of o-iodophenol with allenes gave the substituted benzofuran derivatives having exocyclic double bond (scheme-10).  

Scheme-10

\[
\begin{align*}
Pd(OAc)_2, & \text{ PPh}_3 \\
\text{K}_2\text{CO}_3, 100 \degree \text{C} & 71\%
\end{align*}
\]

Larock et al. exploited the palladium-mediated activation of bifunctional molecules with dienes and alkynes. The last example is the reaction of o-iodobenzaldehyde with internal alkyne
in presence of palladium acetate and tetrabutylammonium chloride to give the substituted indenones in very good yield (scheme-11).\textsuperscript{11}

**Scheme-11**

![Chemical reaction diagram]

**OBJECTIVE**

The objective of the study was to develop an efficient synthetic methodology towards synthesis of biologically important butyrolactone by palladium catalyzed reaction of bifunctional molecule such as \( \alpha \)-bromoacrylic acids with 1, 3 dienes. The reaction involves the formation of \( \pi \)-allylpalladium complex as intermediate and the subsequent nucleophilic attack of the carboxylic oxygen on \( \pi \)-allylpalladium to form the expected lactone.
PRESENT WORK

Our present study involves the activation of olefinic bifunctional molecule bearing halogen and an oxygen nucleophile to react with 1,3-diene in the presence of palladium catalysts to form a new class of γ-butyrolactones. This reaction goes through π-allylpalladium intermediates followed by attack of the nucleophile on the π-allylpalladium complex to form cyclised product. To study the palladium catalyzed reactions of bifunctional molecules, different α-bromoacrylic acids were synthesized based on the literature methods. The α-bromocinnamic acid and 3-furyl-2-bromo-2-propenoic acid were synthesized from the corresponding acrylic esters, methylcinnamate and 3-furyl-2-propenoic acid-methyl ester by bromination, dehydrobromination and followed by hydrolysis as shown in scheme-12.\(^{12}\)

Scheme-12

\[
\begin{align*}
R = \text{Ph, Fuvl} \\
\text{(Z) α-Bromocrotonic acid was synthesized from crotonic acid by bromination and dehydrobromination using excess of pyridine based on the literature method (scheme-13).}^{13}
\end{align*}
\]

Scheme-13

Initially the reaction of α-bromocinnamic acid with 1, 3-cyclohexadiene was carried out in the presence of PdCl\(_2\)(PPh\(_3\))\(_2\) as catalyst. Copper iodide was used as co-catalyst in this reaction
and potassium carbonate as base and N-methylpyrrolidinone as solvent at 90-100 °C. The expected cyclised product was obtained in 30% yield (scheme-14).

Scheme-14

Later, a detailed study on the reactions of various α-bromoacrylic acids with 1,3 dienes was carried out with PdCl₂(PPh₃)₂ as catalyst (10 mol %) and ZnCl₂ was found to be the more effective co-catalyst than copper iodide for this reaction. Potassium carbonate was used as a base and the reaction was carried out at 90-100 °C. The butyrolactones were obtained in 22 to 74 % yield (scheme-15) and the results are tabulated in table-4.

Scheme-15
Table 4. Reactions of α-bromoacrylic acids with 1,3-dienes

<table>
<thead>
<tr>
<th>S.NO</th>
<th>α-Bromosacid</th>
<th>1,3-Diene</th>
<th>Time (h)</th>
<th>Product</th>
<th>Yield, %</th>
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RESULTS AND DISCUSSION

The α-bromoacrylic acids were prepared from the corresponding acrylic esters by bromination, dehydrobromination followed by hydrolysis. The IR, $^1$H NMR, $^{13}$C NMR and Mass spectral data confirmed the structure of bromoacrylic acids. A mixture of E and Z α-bromocinnamic acids were synthesized from methylcinnamate. The IR spectrum of the mixture of products showed a broad peak at 3400 cm$^{-1}$ and a sharp peak at 1680 cm$^{-1}$ indicating the presence of O-H and C=O groups respectively. The $^1$H NMR spectrum of the product gave a broad singlet at δ 9.5 corresponding to COOH group and two sharp singlets, at δ 8.45 (calculated chemical shift: δ 8.33) and 7.60 (calculated chemical shift: δ 7.40) confirmed the presence of olefinic protons of Z and E isomers respectively. The ratio of the isomer was determined based on the integration of olefinic protons. The stereochemistry of α-bromocinnamic acid was confirmed by the literature evidence. The mass spectrum of the product showed molecular ion peak at m/z 226 further evidence for confirming the structure of α-bromocinnamic acid.

In a similar manner the structure of α-bromocrotonic acid was also deduced. The IR spectrum gave a broad peak at 3300 cm$^{-1}$ (O-H) and a sharp peak at 1678 cm$^{-1}$ (C=O). The $^1$H NMR spectrum displayed a broad singlet at δ 9.4 for O-H proton and a quartet at δ 7.5 corresponding to olefinic proton. The mass spectrum of the product showed a molecular ion peak at m/z 166. The above data confirmed the structure of α-bromocrotonic acid. The stereochemistry of the double bond was determined by comparing the chemical shifts with the calculated chemical shift value (δ 7.42) based on empirical rules.

The structure of the product (34) obtained from the palladium catalyzed reaction of a mixture of (E/Z) α-bromocinnamic acid with 1, 3-cyclohexadiene was confirmed by IR, $^1$H
NMR, $^{13}$C NMR and mass spectral data. The reaction goes through the formation of $\pi$-allylpalladium intermediate and the attack of oxygen nucleophile on the $\pi$-allylpalladium complexes to form $\alpha$, $\beta$-unsaturated lactone (Figure-1).

Figure-1

The IR spectrum of the product showed a sharp peak at 1745 cm$^{-1}$ and 1640 cm$^{-1}$ indicating the presence of C=O and C=C groups of lactone respectively. The $^1$H NMR of the product showed two multiplets, one at $\delta$ 4.8 - 4.7 and another at $\delta$ 3.6 - 3.45 corresponding to the presence of ring junction protons of the product as shown below in figure-2. The olefinic proton of $E$ (34a) and $Z$ (34b) isomers was confirmed by comparing the observed chemical shift value with theoretical values. In the case of $E$-isomer, olefinic proton appeared at $\delta$ 7.6 (theoretical: $\delta$ 7.5) and the proton of $Z$-isomer showed a doublet at $\delta$ 6.9 (theoretical: $\delta$ 6.86) with allylic coupling.
The stereochemistry of the ring junction protons was determined by the coupling constants values obtained from the homonuclear proton decoupling experiments. The $^1$H NMR, $^{13}$C NMR spectra and spectra of decoupling experiments of the product are shown on page 112, 113 (34a) and 114, 115 (34b). The irradiation of the proton at $\delta$ 6.15 - 6.00 gave a clean doublet at $\delta$ 4.75 with coupling constant, $J = 6.0$ Hz, which determined the cis -stereochemistry of the ring junction. The stereochemistry of double bond was also determined by the calculation of chemical shifts for olefinic proton of both E and Z isomer based on the literature and by 2D NOESY experiments as shown on page 116.

The connectivity between the olefinic proton and methylenic protons of cyclohexyl ring was observed as shown in figure-3.
The $^{13}$C NMR spectrum revealed all required carbon signals of the product. The two signals appeared at $\delta$ 171.34 and 168.13 corresponding to carbonyl carbon of E (34a) and Z (34b) isomer of lactone. The mass spectrum of the product showed a molecular ion peak appeared at m/z 226. The structure of the product, 3-(1-phenyl-methylidene)-2,3,3a,4,5,7a-hexahydro(b)furano-2-one (34) was confirmed based on the above spectroscopic data.

The product (35) of the palladium catalyzed reaction between (E/Z) o-bromocinnamic and 2-methyl 1, 3-pentadiene showed a prominent peak at 1748 cm$^{-1}$ and a sharp peak at 1646 cm$^{-1}$ in infrared spectrum indicating the presence of C=O and C=C of butyro lactone respectively. The $^{1}$H NMR spectrum displayed a multiplet at $\delta$ 3.3 - 2.8 corresponding to allylic methylene protons of the lactone ring of the product as shown below (figure-4). The comparison of $^{1}$H NMR spectra of lactone (35) with (34), showed absence of one of the ring junction proton at $\delta$ 4.9 - 4.7 indicating the formation of quaternary center adjacent to oxygen atom of the product and the mode of insertion of 1, 3-diene between palladium and vinyl carbon in the reaction mechanism. The ratio of isomers was determined based on the integration of protons of E and Z.

Figure-4

In addition, the mass spectrum of the product showed a molecular ion peak at m/z 228 corresponding to the expected 5-methyl-3-(1-phenylmethylidene)-5-((E)-1-propenyl)tetrahydro-2-furanone (35).

The IR spectrum of product formed from the palladium catalyzed reaction of a mixture of (E/Z) o-bromocinnamic with 2, 3 dimethyl-1, 3-butadiene displayed two strong absorption bands
at 1754 cm\(^{-1}\) and 1658 cm\(^{-1}\) for C=O and C=C groups of lactone. The \(^1\)H NMR spectrum of the product showed two singlets, one at \(\delta\) 1.8 and another one at \(\delta\) 1.5 due to the presence of allylmethyl and quaternary methyl protons. Two singlets appeared at \(\delta\) 5.1 and \(\delta\) 4.9, which was assigned to terminal olefinic protons of the product (36). The ratio of the \(E\) and \(Z\) isomer calculated based on the integration of protons in \(^1\)H NMR spectrum.

The product obtained from the reaction of \((E/Z)\) \(\alpha\)-bromocinnamic acid with isoprene showed a prominent peak at 1753 cm\(^{-1}\) and 1655 cm\(^{-1}\) in infrared spectrum indicating the stretching frequency of C=O and C=C groups of lactone (37). The \(^1\)H NMR spectrum of the product (37) is shown on page 117 displayed a singlet at \(\delta\) 1.8 confirming the presence of allylic methyl proton. The two multiplets, at \(\delta\) 5.0 and 3.1 - 2.9 due to the presence of ring junction protons of butyrolactone (37), as shown below (Figure-4).

**Figure-4**

The IR spectrum of butyrolactone obtained from the reaction of \((Z)\)-\(\alpha\)-bromocrotonic acid with 2, 3-dimethyl-1, 3-butadiene showed prominent peaks at 1755 cm\(^{-1}\) (C=O) and 1681 cm\(^{-1}\) (C=C). The \(^1\)H NMR spectrum of the product (shown in page ) displayed a multiplet at \(\delta\) 2.65-2.50 indicating the presence of methylenic protons of cyclised product with coupling of allylic and geminal proton and there were two singlets at \(\delta\) 5.1 and 4.9 corresponding to terminal olefinic protons. At \(\delta\) 1.9-1.75 two doublets were overlapped with an integration of 6 protons showing the presence of two allylic methyl protons of the cyclised product. The \(^{13}\)C NMR
(spectrum is shown in page 118) revealed all the carbon signals. The carbonyl carbon of lactone appeared at δ 170. The mass spectrum of the product showed a molecular ion peak at m/z 166. The above spectroscopic data proved the structure of expected butyrolactone (38).

The product formed from the reaction of (Z)-α-bromocrotonic acid and 2-methyl 1, 3-pentadiene showed a sharp peak at 1753 cm\(^{-1}\) in the infrared spectrum indicating the presence of C=O group of lactone. The \(^1\)H NMR spectrum displayed a multiplet at δ 6.8 - 6.7 confirming the presence of olefinic proton of α, β- unsaturated system of lactone and a multiplet appeared at 5.85 - 5.60 could be assigned to other olefinic proton adjacent to methyl group. A doublet with \(J = 13.5\) Hz at δ 5.5 showed the presence of other olefinic proton. The methylenic proton of lactone was identified by a multiplet at δ 2.85 - 2.60. One of the allylic methyl appeared as a doublet with coupling constant, \(J = 8.0\) Hz at δ 1.9 and the other at δ 1.7. The \(^{13}\)C NMR spectrum of the product revealed signals for all carbons of the product. The carbonyl carbon signal appeared at δ 170.92 and methylenic carbon at δ 32.36 in DEPT spectrum. The mass spectra showed a molecular ion peak at m/z 166. All the above spectroscopic data confirmed the structure of expected product 3-((E)-ethylidene)-5-methyl-5((E)-propenyl)tetrahydro-2-furanone (39). The \(^1\)H NMR and \(^{13}\)C NMR spectra shown on page 119.

The IR spectrum of the product obtained from the reaction of α-bromocrotonic acid with 1, 3-cyclohexadiene showed two strong absorption bands at 1750 cm\(^{-1}\) and 1701 cm\(^{-1}\) for C=O and C=C bonds respectively. The \(^1\)H NMR spectrum (on page 120) displayed a quartet at δ 6.8 with \(J = 7.0\) Hz which corresponding to olefinic proton on β-carbon. Two olefinic protons of the cyclohexene ring appeared as multiplets at δ 6.3 - 6.1 and δ 6.15 - 5.95. One of the ring junction proton which is adjacent to oxygen atom appeared as a multiplet at δ 4.75 -4.65. The other ring junction proton appeared at δ 3.22 - 3.0 as a multiplet with allylic and vicinal coupling. A multiplet at δ 2.15 - 2.05 is assigned for allylic methylenic protons (2H) and one methylenic
proton. A doublet appeared at $\delta$ 2.0 with coupling constant $J = 9.0$ Hz confirming the allylic methyl protons. The mass spectrum displayed a molecular ion peak at $m/z$ 166. All the data mentioned above confirmed the structure of the expected product 3-((E)-ethylidene)-2,3,3a,4,5,7a-hexahydrobenzo(b)furan-2-one (40).

The reaction of 3-furyl-2-bromo-2-propenoic acid (33) with isoprene gave the expected product in low yield and the product was characterized by the usual spectroscopic methods. The IR spectrum showed sharp peaks at 1747 cm$^{-1}$ and 1643 cm$^{-1}$ corresponding to the carbonyl and C=C of $\alpha$, $\beta$-unsaturated system respectively. The $^1$H NMR spectrum (shown on page 121) displayed a doublet at $\delta$ 7.85 indicating the presence of aromatic proton and a singlet at $\delta$ 7.5 assigned to the olefinic proton of the $\alpha$, $\beta$-unsaturated system. The other two protons of furan ring appeared at $\delta$ 6.85 and 6.5. The terminal olefinic proton of the isoprene system appeared as two singlets, one at $\delta$ 5.1 and another at $\delta$ 4.9. A multiplet at $\delta$ 4.85 - 4.75 was due to the proton which is adjacent to the oxygen atom and two diastereotopic methylenic protons of the lactone ring gave two multiplets at $\delta$ 3.2 - 3.1 and 2.95 - 2.85. A singlet at 1.8 confirmed the presence of allylic methyl protons. The mass spectrum of the product showed a molecular ion peak at $m/z$ 204. These data confirmed the structure of the expected product 3-(1-(2-furyl)-(E)-methylidene)-5-isopropenyl tetrahydro-2-furanone (41).

The product obtained from the reaction of 3-furyl-2-bromo-2-propenoic acid (33) with 1,3-cyclohexadiene showed prominent peaks at 1740 cm$^{-1}$ and 1652 cm$^{-1}$. The ratio of isomers (E/Z) was determined based on the $^1$H NMR spectrum. The proton NMR spectra of both the isomers are shown on page 122 (42a) and 123 (42b). A molecular ion peak appeared at $m/z$ 216 supported the formation of the expected lactone 3-(1-(2-furyl)-methylidene)-2, 3, 3a, 4, 5, 7a-hexahydrobenzo(b)furan-2-one (42). The palladium-catalyzed reaction of $\alpha$-bromocinnamic acid (28) with phenyl propiolate was unsuccessful.
CONCLUSION

We have developed novel palladium catalyzed methodology towards the synthesis of a new class of $\alpha$, $\beta$-unsaturated butyrolactone from simple precursors such as $\alpha$-bromoacrylic acids and 1, 3-dienes in good yield.
EXPERIMENTAL

Preparation of α-Bromomethylcinnamate (27)

A 100 mL RB flask equipped with magnetic stirring bar was charged with methyl cinnamate (3.24 g, 20 mmol) and dichloromethane (30 mL). To the stirred solution, bromine (3.2 g, 20 mmol) was added slowly at 0 °C for 10 min. After addition of bromine, the reaction mixture was allowed to stir for 30 min. To this reaction mixture, triethylamine (2.02 g, 20 mmol) was added slowly at 0 °C and the reaction mixture was allowed to stir for 12 h. The reaction mixture was neutralised with dil HCl (10% by volume) and the product extracted with dichloromethane (3×10 mL). The combined organic layer was dried over anhydrous sodium sulphate and concentrated under reduced pressure to give the crude product (Z:E, 0.6:0.4) which was purified by silica gel column chromatography using a mixture of petroleum ether-ethyl acetate (9:1).

Yield : 4.3 g (89%)

Mol. F : C_{19}H_{18}BrO_2

IR (Neat) : 2932, 1705, 1610, 1040, 860, 755 cm⁻¹

¹H NMR (200 MHz, CDCl₃) : 8 8.3 (s, 0.6H), 7.9 - 7.8 (m, 2H), 7.5 - 7.3 (m, 3.4H), 3.9 (s, 1.8H), 3.8 (s, 1.2H)

Mass (m/z) : 241 (M⁺, 35), 226 (14), 210 (40), 161 (100), 77 (60).

Preparation of α-bromocinnamic acid (28)

A 250 mL RB flask equipped with magnetic stirring bar was charged with α-bromomethylcinnamate (2.4 g, 10 mmol) and 25 mL of THF. To the stirred solution, lithium hydroxide (1N, 1.15 g in 50 mL of water) was added slowly at 0 °C and the reaction mixture was allowed to stir for 12 h. The reaction mixture was neutralised with dil HCl and the product
extracted with ethyl acetate (3×15 mL). The combined organic layer was dried over anhydrous sodium sulphate and concentrated under reduced pressure to give α-bromocinnamic acid in 92% yield (1:3:1, Z: E). The crude product was purified by column chromatography using 100-200 mesh silica gel and petroleum ether-ethyl acetate mixture (8:2).

Yield : 2.1g (92%)

Mol. F : C_{9}H_{7}BrO_{2}

M. P : 95 °C

IR (Nujol) : 2860, 1680, 1450, 1390, 930, 810, 780 cm^{-1}

{^1}H NMR (200 MHz, CDCl_{3}) : δ 9.0 (bs, 1H), 8.4 (s, 1H), 7.95 - 7.7 (m, 2H), 7.6 (s, 1H), 7.50 - 7.35 (m, 8H)

{^{13}}C NMR (50 MHz, CDCl_{3}) : δ 169.59, 169.34, 143.84, 143.53, 134.78, 133.60, 131.15, 130.94, 129.61, 128.81, 111.75, 110.94

Mass (m/z) : 226 (M^+, 31), 147 (100), 129 (38), 118 (7), 102 (42), 77 (26).

Synthesis of (Z)- α-bromocrotonic acid (29)

A 30 mL solution of crotonic acid (4.3 g, 50 mmol) in dichloromethane was charged into 100 mL RB flask equipped with magnetic stirring bar. To the stirred solution, bromine (8 g, 50 mmol) was added slowly at 0 °C for 15 min and the reaction mixture was continued to stir for 1h. Concentration of dichloromethane under reduced pressure gave white solid, dibromocrotonic acid in 100% yield. Dibromocrotonic acid (5 g, 20 mmol) and pyridine (10 mL) were charged into 100 mL RB flask equipped with magnetic stirring bar and the reaction was allowed to stir at 90 °C for 2h. The reaction mixture was neutralized with dil. HCl (10% by volume) and the product extracted with ethyl acetate (3×10 mL). The combined ethyl acetate layer was dried
over anhydrous sodium sulphate, concentrated under reduced pressure to give α-bromocrotonic acid.

Yield : 1.0 g (30%)
Mol.F : C₄H₅BrO₂
M. P : 97 °C
IR (CHCl₃) : 3300, 2995, 1678, 1600, 1410, 1260, 1220, 770 cm⁻¹

¹H NMR (300 MHz, CDCl₃) : δ 9.4 (bs, 1H), 7.55 - 7.5 (q, J = 7.5 Hz, 1H), 2.0 (d, J = 7.5 Hz, 3H)
¹³C NMR (75 MHz, CDCl₃) : δ 167.49, 144.20, 117.12, 18.17.

Synthesis of 3-furyl-2-propenoic acid (30)

A 100 mL RB flask equipped with magnetic stirring bar was charged with freshly distilled furfural (6.88 g, 70 mmol) and pyridine (7.5 g, 94 mmol). The reaction mixture was allowed to heat at 100 °C for 3 h. The reaction mixture was neutralized with dil. HCl (10% by volume) and the light brown color solid obtained was filtered, washed with water and dried over desiccator for 12 h to give the pure product.

Yield : 4.3 g (56%)
Mol.F : C₇H₆O₃
M. P : 148 - 150 °C
IR (Nujol) : 3390, 1680, 1605, 1056, 960, 863 cm⁻¹

¹H NMR (200 MHz, CDCl₃) : δ 10.50 (bs, 1H), 7.55 - 7.45 (m, 2 H), 6.75 (d, J = 7.0 Hz, 1H)
6.50 (d, J = 7.0 Hz, 1H), 6.25 (d, J = 12.9 Hz, 1H)

¹³C NMR (50 MHz, CDCl₃) : δ 168.11, 151.01, 146.16, 131.42, 116.79, 115.91, 113.23.
Mass (m/z) : 138 (M⁺, 100), 121 (31), 110 (23), 92 (27), 82 (16)
A mixture of 3-furyl-2-propenoic acid (3.72 g, 30 mmol) and dry methanol (25 mL) was charged into 25 mL RB flask equipped with magnetic stirring bar. To the stirred solution, freshly distilled thionyl chloride (3 mL) was added slowly at 0 °C for 25 min. The excess of thionyl chloride was removed by distillation and the product obtained was purified by column chromatography using 60-120-mesh silica gel and petroleum ether -ethyl acetate mixture (9:1).

**Yield**
- 3.13 g (76%)

**Mol. F**
- C₉H₇O₂

**IR (Neat)**
- 2995, 2950, 1698, 1660, 1430, 840, 750 cm⁻¹

**¹H NMR (200 MHz, CDCl₃)**
- δ 7.45 (d, J = 14.6 Hz, 1H), 6.6 (d, J = 7.0 Hz, 1H), 6.45 (s, 1H), 6.3 (d, J = 14.7 Hz, 1H), 3.8 (s, 3H)

**¹²C NMR (50 MHz, CDCl₃)**
- δ 164.08, 149.56, 144.45, 129.28, 115.38, 114.50, 112.51, 53.00.


A solution of 3-furyl-2-propenoic acid-methyl ester (2.72 g, 20 mmol) in dichloromethane (25 mL) was charged into 25 mL RB flask equipped with magnetic stirring bar. Bromine (3.2 g, 20 mmol) was added to the stirred solution at 0 °C and allowed to stir for 30 min. To this stirring solution, triethylamine (4.04 g, 40 mmol) was added dropwise at 0 °C and continued to stir at RT for 12 h. The reaction mixture was neutralised with dil.HCl and the product extracted with dichloromethane (3 × 10 mL). The combined organic layer was dried over anhydrous sodium sulphate, concentrated under reduced pressure to get the pure product.

**Yield**
- 3.6 g (85%)

**Mol. F**
- C₉H₇BrO₂
Synthesis of 3-furyl-2-bromo-2-propenoic acid (33)

Yield : 2.0 g (90%)

Mol. F : C₇H₇BrO₃

M. P : 140 °C

IR (Nujol) : 2920, 1670, 1595, 1460, 1340, 1030, 790 cm⁻¹

¹H NMR (200 MHz, CDCl₃) : δ 7.6 - 7.2 (m, 3H), 7.1 (bs, 1H), 6.5 (d, J = 7.0 Hz, 1H)

General procedure for the Pd catalyzed reaction of α-bromoacrylic acid with 1,3-dienes.

A 25 mL RB flask equipped with magnetic stirring bar, reflux condenser and argon balloon was charged with α-bromoacrylic acid (1 mmol), 1,3 diene (2 mmol), PdCl₂(PPh₃)₂ (0.07g, 0.1 mmol), potassium carbonate (0.275 g, 2 mmol), zinc chloride (0.067 g, 0.5 mmol) and degassed N-methylpyrrolidone (4 mL). The reaction mixture was flushed with argon thrice and allowed to stir at 90 °C for 2-48 h. The reaction mixture was neutralised with dil. HCl and the product extracted with ethyl acetate (3 × 5 mL). The combined organic layer was dried over anhydrous sodium sulphate and concentrated under reduced pressure to give the crude product. The crude product on silica gel column chromatographic purification using a mixture of petroleum ether and ethyl acetate (8:2) gave the corresponding lactones in moderate to good yields.
3- (1-Phenylmethylidene)-2,3,3a,4,5,7a-hexahydro(b)furan-2-one (34)

(E : Z, 3.3 : 1)

E-isomer (34a)

Mol. F : C₁₅H₁₄O₂

IR (Neat) : 3000, 1745, 1640, 1440, 1230, 1180, 1000 cm⁻¹

¹H NMR (200 MHz, CDCl₃) : δ 7.6 - 7.3 (m, 6H), 6.45 - 6.35 (m, 1H), 6.15 - 6.0 (m, 1H), 4.8 - 4.7 (m, 1H), 3.6 - 3.45 (m, 1H), 2.3 - 2.0 (m, 3H), 1.55 - 1.35 (m, 1H).

¹³C NMR (75 MHz, CDCl₃) : δ 171.34, 136.00, 134.37, 134.06, 130.89, 129.56, 129.51, 128.80, 122.79, 37.87, 23.43, 22.42.

Z-isomer (34b)

¹H NMR (200 MHz, CDCl₃) : δ 7.95 - 7.85 (m, 2H), 7.45 - 7.30 (m, 3H), 6.90 (d, J = 6.0 Hz, 1H), 6.25 - 6.15 (m, 1H), 5.95 - 5.85 (m, 1H), 4.95 - 4.85 (m, 1H), 3.25 - 3.15 (m, 1H), 2.25 - 1.75 (m, 4H).

¹³C NMR (75 MHz, CDCl₃) : δ 168.13, 138.44, 133.22, 130.20, 129.01, 128.70, 127.66, 123.48, 72.27, 40.96, 24.38, 21.64.

Mass (m/z) : 226 (M⁺, 62), 208 (27), 181 (30), 165 (42), 141 (50), 115 (87), 104 (38), 91 (86), 77 (38).
Scheme 1 is heterocyclic system? 

Can it give tautomeric form? 

Time... A & H very similar? 

Printed article with C4 & N nucleus - not successful. 

Nuclear for N, basal? Organometallic 

Imidazoline... is it known, not? 

Hle 16c (C-29)?
what are they or how do you measure them?

No. 1, 2, 3 in lead?

in table... number on 15, 16,

pull aside... do it known... not 24. 18 or 17?

why ca amny? reference to products... known compounds?

Zodi cm.?? How do you see this?

number... on products... confusing?

not just observe 57... but no number.
5-Methyl-3-(1-phenylmethylidene)-5-((E)-1-propenyl)tetrahydro-2-furanone (E&Z, 2:1) (35)

\[
\text{Mol. F} : \quad \text{C}_{13}\text{H}_{16}\text{O}_2 \\
\text{IR (Neat)} : \quad 2921, 1748, 1646, 1604, 1495, 1451, 1217, 1178, 1109 \text{ cm}^{-1} \\
\text{\textsuperscript{1}H NMR (200 MHz, CDCl}_3) : \quad \delta 7.8 - 7.7 (m, 4H), 7.6 - 7.3 (m, 3H), 6.9 - 6.8 (m, 2H), 5.85 - 5.55 (m, 1H), 5.35 - 5.15 (m, 2H), 3.3 - 2.8 (m, 2H), 1.8 (d, } J = 5.4 \text{ Hz, 3H}), 1.6 (s, 3H), 1.5 (s, 3H) \\
\text{\textsuperscript{13}C NMR (50.35 MHz, CDCl}_3) : \quad \delta 168.70, 168.19, 139.97, 139.46, 139.01, 136.77, 133.89, 133.84, 130.77, 130.05, 129.89, 129.49, 129.02, 128.21, 125.96, 125.56, 125.41, 123.42, 82.63, 81.86, 74.14, 44.50, 38.93, 27.47, 26.92, 25.88, 18.53, 17.76. \\
\text{Mass (m/z)} : \quad 228 (\text{M}^+, 7), 213 (2), 200 (2), 187 (3), 173 (7), 144 (45), 121 (10), 116 (100), 105 (23), 91 (13), 77 (16). \\
\]

5-Isopropenyl-5-methyl-3-(1-phenylmethylidene)tetrahydro-2-furanone (E&Z, 4 : 1) (36)

\[
\text{Mol. F} : \quad \text{C}_{13}\text{H}_{16}\text{O}_2 \\
\text{IR (Neat)} : \quad 2978, 1754, 1658, 1445, 1377, 1317 \text{ cm}^{-1} 
\]
$^1$H NMR (200 MHz, CDCl$_3$) : $\delta$ 7.8 (d, J = 8.1 Hz, 0.8H), 7.6 - 7.3 (m, 4H), 6.9 (s, 0.2H) 5.1 (s, 1H), 4.9 (s, 1H), 3.2 - 2.8 (m, 2H), 1.8 (s, 3H), 1.5 (s, 3H).

$^{13}$C NMR (50.35 MHz, CDCl$_3$) : $\delta$ 171.47, 146.47, 139.60, 136.85, 134.68, 130.71, 130.01, 129.90, 129.45, 128.98, 128.14, 125.64, 125.46, 111.00, 84.73, 83.71, 43.09, 39.67, 26.87, 26.33, 18.65.

Mass (m/z) : 228 (M$^+$, 1), 184 (36), 169 (10), 157 (8), 151 (23), 144 (100), 129 (23).

5-Isopropenyl-3-(1-phenyl-(E)-methylidene)tetrahydro-2-furanone (37)

Mol. F : C$_{14}$H$_{14}$O$_2$

IR (CHCl$_3$) : 2923, 2853, 1753, 1655, 1449, 1043, 906 cm$^{-1}$

$^1$H NMR (300 MHz, CDCl$_3$) : $\delta$ 7.6 - 7.3 (m, 6H), 5.1 (s, 1H), 5.0 (m, 1H), 4.9 (s, 1H), 3.45 - 3.35 (m, 1H), 3.1 - 2.9 (m, 1H), 1.8 (s, 3H).

$^{13}$C NMR (75 MHz, CDCl$_3$) : $\delta$ 142.10, 136.12, 129.46, 129.34, 128.39, 124.58, 123.66, 113.26, 112.37, 79.11, 32.26, 16.33

Mass (m/z) : 214 (M$^+$, 12), 186 (5), 170 (7), 144 (44), 115 (100), 91 (7), 77 (7)
3-((E)-Ethylidene)-5-isoprpenyl-5-methyltetrahydro-2-furanone (38)

![Chemical Structure]

**Mol. F** : C₁₀H₁₄O₂  
**IR (Neat)** : 2978, 2926, 1755, 1681, 1443, 1378, 1023, 987, 713 cm⁻¹  
**¹H NMR (200 MHz, CDCl₃)** : δ 6.85 - 6.75 (m, 1H), 5.1 (s, 1H), 4.9 (s, 1H), 2.58 - 2.65 (m, 2H), 1.9 - 1.75 (m, 6H), 1.4 (s, 3H)  
**¹³C NMR (50 MHz, CDCl₃)** : δ 170, 147, 136, 128, 111, 84, 38, 25, 18, 15.  
**Mass (m/z)** : 166 (M⁺, 4), 151 (30), 125 (23), 105 (7), 91 (16), 82 (100).

3-((E)-Ethylidene)-5-methyl-5-((E)-propenyl)tetrahydro-2-furanone (39)

![Chemical Structure]

**Mol. F** : C₁₀H₁₄O₂  
**IR (Neat)** : 2972, 2919, 2850, 1754, 1680, 1379, 1133, 973, 716 cm⁻¹  
**¹H NMR (200 MHz, CDCl₃)** : δ 6.85 - 6.65 (m, 1H), 5.6 - 5.20 (m, 2H), 3.1 - 2.95 (m, 1H), 2.65 - 2.45 (m, 1H), 1.8 - 1.6 (m, 9H).  
**¹³C NMR (50 MHz, CDCl₃)** : δ 170.92, 139.40, 135.19, 127.79, 123.87, 74.36, 32.36, 25.75, 18.42, 15.73.  
**Mass (m/z)** : 166 (M⁺, 4), 151 (20), 123 (13), 111(8), 107 (13), 95 (25), 91 (30), 82 (100), 69 (18).
3-((E)-Ethylidene)-2,3,3a,4,5,7a-hexahydrobenzo(b)furan-2-one (40)

Mol. F : C_{10}H_{12}O_{2}
IR (Neat) : 3056, 2928, 1750, 1701, 1590, 996, 925 cm^{-1}
^1H NMR (200 MHz, CDCl_{3}) : δ 6.8 (q, J = 7.0 Hz, 1H), 6.3 - 6.1 (m, 1H), 6.15-5.95 (m, 1H), 4.75 - 4.65 (m, 1H), 3.2 - 3.0 (m, 1H), 2.15-2.05 (m, 3H), 2.0 (d, J = 7.0 Hz, 3H), 1.5 - 1.35 (m, 1H)
Mass (m/z) : 166 (M^+, 11), 136 (48), 122 (48), 105 (27), 91 (39), 79 (26).

3-(1-(2-Furyl)-(E)-methylidene)-5-isopropenyltetrahydro-2-furanone (41)

Mol. F : C_{12}H_{12}O_{3}
IR (Neat) : 2924, 2854, 1747, 1643, 1473, 1091, 904, 758 cm^{-1}.
^1H NMR (300 MHz, CDCl_{3}) : δ 7.85 (d, J = 8.1 Hz), 7.5 (s, 1H), 6.85 (s, 1H), 6.5 (d, J = 8.0 Hz, 1H), 5.1 (s, 1H), 4.9 (s, 1H), 4.85 (s, 1H), 3.2 - 3.1 (m, 1H), 2.95 - 2.85 (m, 1H), 1.8 (s, 3H).
Mass (m/z) : 204 (M^+, 2), 160 (2), 149 (5), 134 (20), 106 (100), 91(8),78 (9), 57 (6).
$E:Z, 1:3:1$

**Mol. F** : C$_{13}$H$_{12}$O$_3$

**IR (CHCl$_3$)** : 3019, 2923, 1740, 1652, 1492, 1177, 1019 cm$^{-1}$

**$E$-isomer**

$^1$H NMR (300 MHz, CDCl$_3$) : δ 7.55 (s, 1H), 7.25 (s, 1H), 6.75-6.65 (d, $J = 4$ Hz, 1H), 6.5 (d, $J = 4$ Hz, 1H), 6.20-6.10 (m, 1H), 6.05 - 5.95 (m, 1H), 4.8 - 4.7 (m, 1H), 3.55 -3.45 (m, 1H), 2.15 - 1.95 (m, 3H), 1.45 - 1.25 (m, 1H).

**$Z$-isomer** : δ 7.9-7.8 (d, $J = 4$ Hz, 1H), 7.5 (s, 1H), 6.8 (s, 1H), 6.5 (m, 1H), 6.15-6.05 (m, 1H), 5.95-5.85 (m, 1H), 4.9-4.8 (m, 1H) 3.25-3.25 (m, 1H), 2.15-1.75 (m, 4H).

**Mass (m/z)** : 216 (M$^+$, 52), 170 (24), 159 (37), 128 (49), 115 (57), 91 (100).
Section 2. Palladium catalyzed reaction of α-bromoacrylic amides with 1, 3-dienes.

INTRODUCTION AND BACKGROUND

Palladium mediated reactions of bifunctional molecule bearing halogen and soft nucleophile with alkynes and dienes to construct five and six membered carbocycles and heterocycles are very attractive reactions in synthetic organic chemistry. This kind of palladium-catalyzed reactions of bifunctional molecule bearing nitrogen nucleophile are discussed below.

The palladium-catalyzed reaction of o-iodoaniline with 1, 3-diene using triethylamine as a base gave cyclised product reported by Connor et al. as shown in scheme-16.\(^\text{16}\)

Scheme-16

\[
\begin{align*}
\text{I} & \quad + \quad \text{H} \\
\text{N} & \quad \text{Pd(OAc)}_2, \text{PPh}_3, \quad \text{B}_{3}\text{N}, \quad 70\% \quad \rightarrow \\
\text{N} & \quad \text{H}
\end{align*}
\]

Kundu and co-workers reported the palladium catalyzed highly regio-and stereo-selective synthesis of (Z)-3-aryl(alkyl)ideneisoindolin-1-ones by annulation of alkynes with ortho-iodobenzamide (scheme-17).\(^\text{17}\)

Scheme-17

\[
\begin{align*}
\text{I} \quad \text{NHR}_1 & \quad + \quad \text{CR}_2 \quad \text{Pd catalyst} \quad \text{Cul, Et}_3\text{N}, \text{DMF} \\
\text{N} \quad \text{C} & \quad \text{H} \quad \text{R}_2 \\
\text{NHR}_1 & \quad \text{H}
\end{align*}
\]
The palladium-catalyzed coupling of 2-iodoaniline and the corresponding N-methyl,N-acetyl and tosyl derivatives with a wide variety of internal alkynes provides 2, 3-disubstituted indoles in good yield as shown in scheme-18.\textsuperscript{18}

Scheme-18

\[
\text{R}_1 + \text{R}_2 \equiv \text{R}_3 \xrightarrow{\text{Pd(0)}} \text{NHR}_1 \xrightarrow{\text{K}_2\text{CO}_3, \text{LiCl}} \xrightarrow{100^\circ\text{C}, 20-40\text{~h}} \text{N} \xrightarrow{\text{R}_1} \text{R}_2 \xrightarrow{\text{R}_3}
\]

Larock \textit{et al.} developed an efficient palladium catalyzed synthesis of isoquinolines, tetrahydroisoquinolines, pyridines from \textit{ortho}-functionally substituted imines with internal alkynes in moderate to good yield (scheme-19).\textsuperscript{19}

Scheme-19

\[
\text{N} \xrightarrow{\text{Bu}} + \text{R}_1 \equiv \text{R}_2 \xrightarrow{\text{Pd(OAc)}_2, \text{PPh}_3} \xrightarrow{\text{Na}_2\text{CO}_3, \text{DMF}, 100^\circ\text{C}} \xrightarrow{65-96\%} \text{N} \xrightarrow{\text{R}_1} \text{R}_2
\]
OBJECTIVE

Our aim was to study the palladium-catalyzed activation of bifunctional vinyl halides, α-bromoacrylic amides with 1, 3-dienes and alkynes to form α, β-unsaturated butyrolactams. The reaction involves the formation of oxidative addition complexes with vinyl halide and then the insertion of 1, 3 dienes between the carbon-palladium bond leading to π-allylpalladium complexes and the heteroatom nucleophile attack on the π-allylpalladium complexes, which leads the expected lactams.

PRESENT WORK

Our present study involves the synthesis of various α-bromoacrylic amides and palladium catalyzed reaction of α-bromoacrylic amides with 1, 3- dienes to form a new and novel class of butyrolactams. α-Bromoacrylic amides were synthesized from the corresponding α-bromoacrylic acids by treating with SOCl₂ and then the reaction of acid chloride with substituted anilines in the presence of triethylamine at room temperature (scheme-20).

Scheme-20

\[
\begin{align*}
\text{R} & \quad \text{SOCl}_2, \text{RT, 2 h} \\
\text{R} & \quad \text{Br} \\
\text{Br} & \quad \text{Br} \\
\text{R} & \quad \text{NH}_2 \\
\text{R} & \quad \text{Br} \\
\text{R} & \quad \text{Ph, Me} \\
\text{R}_1 & \quad \text{NO}_2, \text{OCH}_3
\end{align*}
\]

Initial study was on the reaction of 1N-(4-methoxyphenyl)-2-bromo-3-phenyl-(E)-2-propenamide with 1, 3 cyclohexadiene catalyzed by PdCl₂(PPh₃)₂ and co-catalyst, zinc chloride to yield the expected butyrolactam, 1-(4-methoxyphenyl)-3-(1-phenyl-(E)-methylidene)-2,3,3a, 4,5,7a-hexahydro-1H-2-indolone as shown in scheme-21.
Similar reactions of various α-bromoacrylic amides with different 1, 3-dienes and alkynes were carried out in the presence of PdCl$_2$(PPh$_3$)$_2$ and zinc chloride at 90-100 °C under argon atmosphere to yield the corresponding substituted butyrolactams in good yield (scheme-22 & 23). The results of reactions of α-bromoacrylic amides with 1, 3 dienes are tabulated in table-5.

**Scheme-22**

\[
\text{R} = \text{Ph, Me} \quad \text{R}_1 = \text{NO}_2, \text{OCH}_3
\]

1, 3 dienes : \( \text{C}_2\text{H}_4 \), \( \text{C}_2\text{H}_4\text{Br} \), \( \text{C}_2\text{H}_4\text{Br} \), \( \text{C}_2\text{H}_4\text{Ph} \), \( \text{C}_2\text{H}_4\text{Me} \)

**Scheme-23**

\[
\text{R}_1 = \text{COOMe, H} \quad \text{R} = \text{Ph, C}_4\text{H}_{13}
\]
Table 5. Palladium catalyzed reaction of α-bromoacrylic amides with 1, 3-Dienes

<table>
<thead>
<tr>
<th>S.No</th>
<th>αBromoacrylicamide</th>
<th>1, 3-Diene</th>
<th>Product</th>
<th>Time(h)</th>
<th>Yield(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>CONHPh-4-OMe</td>
<td></td>
<td>N-Ph-4-OMe</td>
<td>24</td>
<td>53</td>
</tr>
<tr>
<td>2.</td>
<td>CONHPh-4-NO₂</td>
<td></td>
<td>N-Ph-4-NO₂</td>
<td>6</td>
<td>51</td>
</tr>
<tr>
<td>3.</td>
<td>CONHPh-4-OMe</td>
<td></td>
<td>N-Ph-4-OMe</td>
<td>10</td>
<td>70</td>
</tr>
<tr>
<td>4.</td>
<td>CONHPh-4-OMe</td>
<td></td>
<td>N-Ph-4-OMe</td>
<td>4</td>
<td>45</td>
</tr>
<tr>
<td>5.</td>
<td>CONHPh-4-OMe</td>
<td></td>
<td>N-Ph-4-OMe</td>
<td>6</td>
<td>26</td>
</tr>
<tr>
<td>6.</td>
<td>CONHPh-4-OMe</td>
<td></td>
<td>N-Ph-4-OMe</td>
<td>6</td>
<td>20</td>
</tr>
<tr>
<td>7.</td>
<td>CONHPh-4-OMe</td>
<td></td>
<td>N-Ph-4-OMe</td>
<td>4</td>
<td>60</td>
</tr>
<tr>
<td>8.</td>
<td>CONHPh-4-OMe</td>
<td></td>
<td>N-Ph-4-OMe</td>
<td>6</td>
<td>55</td>
</tr>
<tr>
<td>9.</td>
<td>CONHCy</td>
<td></td>
<td>N-Cy</td>
<td>24</td>
<td>30</td>
</tr>
</tbody>
</table>
RESULTS AND DISCUSSION

The reactions of α-bromoacrylic amides with 1, 3-dienes in the presence of palladium catalyst afforded the expected products which were characterized by IR, NMR and Mass spectroscopic studies. The reaction involves the oxidative addition of vinyl halide to palladium and the insertion of 1, 3-dienes in between the carbon-palladium bond, which led to the formation of π-allylpalladium intermediate and then attack by nitrogen nucleophile leads to expected α, β-unsaturated lactams (figure-1).

Figure-1

The precursors, α-bromoacrylic amides required for the palladium-catalyzed reaction with 1, 3-dienes were synthesized from corresponding α-bromoacrylic acids. Also, the 1, 3-dienes were prepared according to the literature methods. Both isomers, 1N-(4-methoxyphenyl)-2-bromo-3-phenyl-(Z)-2-propenamide (43) and 1N-(4-methoxyphenyl)-2-bromo-3-phenyl-(E)-2-propenamide (44) were prepared and characterized by the usual spectroscopic methods. The IR spectrum showed a broad peak at 3300 cm⁻¹ and a sharp peak at 1651 cm⁻¹ indicating the presence of N-H and C=O groups of amide. The ¹H NMR spectrum displayed a broad singlet at δ 8.5 corresponding to proton on nitrogen and another singlet at δ 8.4 due to the presence of olefinic proton of Z isomer (compared with calculated chemical shift for
olefinic proton of the Z-isomer, i.e. δ 8.2. The olefinic proton of E-isomer overlapping with aromatic protons (theoretical chemical shift δ 7.36) and a singlet at δ 3.79 confirmed the presence of methoxy proton. There was a multiplet at δ 7.5 - 7.3 corresponding to the aromatic protons. The mass spectrum showed a M+1 peak at m/z 333. These above data confirmed the structure of 1N-(4-methoxyphenyl)-2-bromo-3-phenyl-2-propenamide. In the literature, the NOE technique has been demonstrated to differentiate the olefinic protons of Z and E isomer of similar compounds.\(^\text{20}\) Irradiation of the amide proton signal of Z isomer resulted in large negative enhancement of 34% for the olefinic proton of Z isomer but no enhancement was observed for the E isomer. The proton NMR and NOE irradiation spectra of both the isomers are shown on page 124, 125. The structure of the product obtained from α-bromocrotonic acid and p-anisidine was also characterized by IR, \(^1\)H NMR, \(^{13}\)C NMR and Mass spectral analysis. The IR spectrum showed a broad peak corresponding to N-H stretching frequency at 3330 cm\(^{-1}\) and another sharp peak at 1650 cm\(^{-1}\) indicating the presence of C=O group of the product. The \(^1\)H NMR spectrum displayed a broad singlet at δ 8.5 for amide proton. A quartet and doublet overlapping which corresponding to the olefinic and aromatic protons at δ 7.50 - 7.40 is also observed. The methoxy proton of the product appeared at δ 3.80 and allylic methyl protons appeared as a doublet at δ 1.9 with coupling constant of J = 4.0 Hz. The mass spectrum of the product showed a molecular ion peak at m/z 271. The above spectroscopic data confirmed the structure of 1N-(4-methoxyphenyl)-2-bromo-(Z)-2-butenamide (45). Similarly, the structure of 1N-(4-nitrophenyl)-2-bromo-3-phenyl-2-propenamide was confirmed based on spectroscopic data.

The palladium-catalyzed reaction of α-bromoacrylic amides with 1, 3-dienes and alkynes to form a new class of butyrolactams was carried out. All the products obtained from the reaction of α-bromoacrylic amide with 1, 3-diene and alkynes were characterized by IR, NMR and mass spectra. IR spectrum of the product obtained from 1N-(4-methoxyphenyl)-2-bromo-3-phenyl-
(Z)-2-propenamide (43) with 1, 3-cyclohexadiene showed a sharp peak at 1681 cm\(^{-1}\) and another peak at 1645 cm\(^{-1}\) indicating the presence of C=O and C=C groups respectively. The \(^1\)H NMR spectrum showed a doublet at \(\delta\) 7.6 with the allylic coupling of \(J = 4.0\) Hz which confirmed the presence of olefinic proton of the product and that was compared with the calculated chemical shift values based on empirical rule. A multiplet at \(\delta\) 7.55 - 7.40 due to aromatic proton and the olefinic protons of cyclohexene ring appeared as multiplets, one at \(\delta\) 6.15 - 6.05 and another at \(\delta\) 5.85 - 5.70. One of the ring junction proton which is adjacent to nitrogen atom appeared as a multiplet at \(\delta\) 4.60 - 4.50 and another multiplet appeared at \(\delta\) 3.65 - 3.55 confirmed the other ring junction proton of the product. The chemical shift assignment product is shown in Figure-2. The \(^1\)H NMR and \(^13\)C NMR spectra of the product 49 shown on page 126.

**Figure -2.**

![Chemical structure](image)

The stereochemistry of the ring junction protons was determined based on coupling constant value obtained from the homonuclear proton decoupling experiment. The irradiation of proton signal at \(\delta\) 5.85 - 5.75 gave a clean doublet at \(\delta\) 4.5 with coupling constant \(J = 6.0\) Hz (Figure-3).

**Figure-3**
The proton decoupling NMR spectra and 2D COSY spectrum are shown on page 127 and 128. The stereochemistry of the double bond was confirmed by comparison with calculated chemical shift value for olefinic proton based on empirical rules and 2D NOE experiment. The 2D COSY spectrum is shown on page-.. The $^1$ C NMR spectrum revealed all the carbon signals corresponding to the structure of the product. A carbonyl carbon signal appeared at δ 168.65 and a signal at δ 158.19 corresponding to the β-carbon of unsaturated lactam (figure-3). Two methylenic carbon signals appeared at δ 24.45 and 23.93 which was confirmed by DEPT spectrum.

**Figure-4**

The mass spectrum gave a molecular ion peak at $m/z$ 331 corresponding to the molecular weight of expected product. The above spectroscopic data confirmed the structure of product 1-(4-methoxyphenyl)-3-(1-phenyl-(E)-methylidene)-2,3,3a,4,5,7a hexahydro-1H-2-indolone (49).
The IR spectrum of product obtained from the palladium catalyzed reaction of \( 1\text{N}-(4\text{-methoxyphenyl})-2\text{-bromo-3-phenyl-(Z)-2-propenamide (43)} \) with isoprene showed a sharp peak at 1681 cm\(^{-1} \) confirming the presence of carbonyl group of unsaturated system. The \(^1\text{H NMR} \) spectrum displayed a doublet merged with a multiplet at \( \delta 7.6 - 7.4 \) and indicating the presence of olefinic proton (with allylic coupling of \( J = 4.0 \text{ Hz} \)) of \( \alpha, \beta \)-unsaturated system and multiplet corresponding to aromatic protons. A doublet appeared at \( \delta 6.9 \) with \( J = 8.0 \text{ Hz} \) which assigned for aromatic protons of \( A_2B_2 \) pattern. The terminal olefinic protons appeared as two singlets, one at \( \delta 5.05 \) and another at \( \delta 4.90 \). One multiplet appeared at \( \delta 4.85-4.75 \) indicating the presence one of the lactam ring protons adjacent to nitrogen atom of the product. The presence of two methylenic protons of the lactam was confirmed by the appearance of two separable multiplets, one at \( \delta 3.55-3.25 \) and another at \( \delta 2.95-2.65 \) with allylic, vicinal and geminal coupling. The allylic methyl proton appeared at \( \delta 1.6 \) as a singlet. The mass spectrum showed a molecular ion peak at \( m/z \) 319. The above spectral data confirmed the structure of the expected product, \( 5\text{-isopropenyl}-(4\text{-methoxyphenyl})-3-(1\text{-phenyl-(Z)-methylidene})\text{tetrahydro-1H-2-pyrrolone (50)} \).

The \(^1\text{H NMR} \) spectra is shown on page 129. Similarly, the structure of product obtained from the reaction of 43 with ethyl-(\( Z \)-2,4-pentadienoate was also confirmed. The IR spectrum showed a sharp peak at 1687 cm\(^{-1} \) due to the presence of carbonyl group of the product. The \(^1\text{H NMR} \) spectrum (page no. 130) showed a multiplet between \( \delta 7.6 - 7.3 \) for aromatic and olefinic proton of \( \alpha, \beta \)-unsaturated system and doublet at 6.9 with \( J = 8.0 \text{ Hz} \) corresponding to \( A_2B_2 \) type aromatic protons. A multiplet appeared at 6.85 - 6.80 was assigned to olefinic proton on \( \beta \) carbon to the ester group (figure-4). A doublet at \( \delta 5.8 \) with \( J = 13.0 \text{ Hz} \) confirmed the presence of other olefinic proton of the unsaturated ester group. A multiplet appeared at \( \delta 4.90 - 4.75 \) indicating the ring junction proton which is adjacent to nitrogen atom and a quartet at \( \delta 4.2 \) with \( J = 8.0 \text{ Hz} \) assigned to \( \text{OCH}_2 \) of the ester group. A singlet at \( \delta 3.81 \) was attributed to methoxy protons. Two
multiplets appeared, one at $\delta$ 3.65-3.40 and another at $\delta$ 3.10 - 2.90 confirming the presence of methyleneic protons of lactam ring with geminal, vicinal and allylic coupling. A triplet at $\delta$ 1.25 confirmed the presence of methyl proton (figure-4).

Figure-4

The $^{13}$C NMR spectrum (page no. 130) showed two signals at $\delta$ 167.83 and 165.23 due to carbonyl carbons of lactam and ester respectively. Two methyleneic carbon signals appeared at $\delta$ 60.43 and 31.43, which was reliably confirmed by DEPT experiment. The mass spectrum showed a molecular ion peak at $m/z$ 377. The above spectroscopic data confirmed the structure of ethyl-3-((1-(4-methoxyphenyl)-5-oxo-4-(1-phenyl-(E)-methylidene)tetrahydro-1H-2-pyrrolyl)-(E)-2-propenoate(51). The stereochemistry also confirmed by 2D NOESY and COSY experiments (page no. 131 and 132).

The product obtained from the reaction of 45 with ethyl-(2E)-2,4-pentadienoate was characterized as follows. The IR spectrum showed two sharp peaks at 1704 cm$^{-1}$ and 1674 cm$^{-1}$ due to the presence of carbonyl groups of unsaturated ester and lactam respectively. The $^1$H NMR spectrum showed two doublets at $\delta$ 7.4 and 6.9 indicating the aromatic protons of $A_2B_2$ type. The proton on $\beta$-carbon of $\alpha$, $\beta$-unsaturated ester appeared as a doublet of doublet at $\delta$ 6.85-6.75 with the coupling constant, $J = 4.0$ Hz, 12.5 Hz. The olefinic proton of unsaturated lactam showed a multiplet at $\delta$ 6.7 - 6.6 due to the vicinal coupling with CH$_3$ and allylic coupling
with methylenic proton of lactam ring. The proton on α-carbon of unsaturated ester appeared as a doublet with $J = 12.5$ Hz indicating the trans-stereochemistry of olefinic protons. A multiplet at $\delta 4.85 - 4.75$ due to proton of lactam ring, which is adjacent to nitrogen atom, which was strong evidence for the formation of lactam. A quartet at $\delta 4.2$ and a singlet at $\delta 3.74$ are due to the presence of OCH$_2$ and OCH$_3$ protons respectively. Two distinct multiplets appeared, one at $\delta 3.15 - 3.0$ and another at $\delta 2.60 - 2.50$ for CH$_2$ proton of lactam ring indicating that these protons have vicinal coupling, geminal coupling and allylic coupling. A doublet at $\delta 1.83$ with $J = 4.0$ Hz and a triplet at $\delta 1.27$ with $J = 5.0$ Hz is attributed to allylic CH$_3$ and CH$_2$ groups. The important chemical shift values and the corresponding protons are given in figure-5.

**Figure-5**

![Chemical structure](image)

The $^1$C NMR spectrum showed two signals at $\delta 165.45$ and 165.72 due to the presence of carbonyl carbons of lactam and ester, respectively while the other two signals appeared at $\delta 159.77$ and 159.69 were assigned to the β-carbons of unsaturated lactam and ester respectively. The $^1$H NMR spectrum is shown on page 133. The mass spectrum showed a molecular ion peak at $m/z$ 315 which confirming the expected product. The above spectroscopic data proved the structure of product (52). Similarly the structure of product, ethyl-2-ethyl-3-[4-((E)-ethylidene)-
1-(4-methoxyphenyl)-5-oxo-tetrahydro-1H-2-pyrrolyl-(E)-2-propenoate (53) obtained from the palladium catalyzed reaction of 45 with ethyl-2-ethyl-(2E)-2,4-pentadienoate was deduced from the spectroscopic data such as IR, $^1$H NMR, $^{13}$C NMR and Mass. The proton and $^{13}$C NMR spectra are shown on page no. 134.

A mixture of (E/Z, 8:2) lactam (54) obtained from the reaction of mixture of 48 (Z/E, 9:1) was also characterized. The IR spectrum gave a sharp peak at 1693 cm$^{-1}$ corresponding to carbonyl stretching frequency. The $^1$H NMR spectrum showed two doublets between $\delta$ 8.80 - 8.70 for $A_2B_2$ type of aromatic proton and aromatic protons appeared as a multiplet between $\delta$ 7.8 - 7.3. The olefinic proton of the cyclohexene ring of lactam appeared as multiplets at $\delta$ 6.25 - 5.85. There were two multiplets at $\delta$ 4.85 - 4.70 and 4.75 - 4.65 could be assigned to ring junction proton which is adjacent to nitrogen atom with the integration of 0.2 H and 0.8 H respectively, which determined the ratio of the isomers. The $^{13}$C NMR spectrum revealed all the required carbon signals of both the isomers. The mass spectrum gave a molecular ion peak at $m/z$ 346. These above data helped us to prove the structure of the product (54). One of the isomer separated from the mixture by column chromatography.

The IR spectrum of the product from the reaction of 47 with ethyl-1, 3-pentadienoic acid ester showed sharp peaks at 1682 and 1705 cm$^{-1}$ indicating the carbonyl stretching frequency of both lactam and ester groups. The $^1$H NMR spectrum (page no. 135) showed all important protons as multiplets at $\delta$ 4.55 - 4.45, 3.40 - 3.25 and 2.65 - 2.45 supporting the formation of expected lactam product. The presence of cyclohexyl ring protons was confirmed by the appearance of multiplet at $\delta$ 2.0 - 1.2. The $^{13}$C NMR spectrum (page no. 135) was clearly indicating the presence of two carbonyl carbons by showing two signals at $\delta$ 168.74 and $\delta$ 165.51. The mass spectrum of the product gave a molecular ion peak at $m/z$ 353, which is the
further evidence for the formation of expected lactam product. All these data confirmed the structure of required lactam (56).

The IR spectrum of the product obtained from the reaction of amide (43) with 1-phenyl-1, 3-butadiene showed sharp peaks at 1683 cm\(^{-1}\) and 1605 cm\(^{-1}\) indicating the presence of C=O and C=C bonds respectively. In the \(^1\)H NMR spectrum of the product, a multiplet appeared at \(\delta\) 7.65 - 7.25 confirming the presence of aromatic protons (13H). A doublet at \(\delta\) 6.85 with coupling constant, \(J = 8.0\) Hz was attributed to aromatic protons of \(A_2B_2\) pattern. A doublet of doublet appeared at \(\delta\) 6.65 (\(J = 4.0\) Hz, \(J = 12.5\) Hz) could be assigned to olefinic protons of the product. A doublet at 6.10 assigned for other olefinic proton. The most important proton which appeared as a multiplet at \(\delta\) 4.90 - 4.80, 3.65 - 3.50 and 3.15 - 2.95 confirmed the formation of expected cyclised product \(1-(4\text{-methoxyphenyl})-5-[2\text{-phenyl-}(E)-1\text{-ethenyl}]-3-[1\text{-phenyl-(E)-methylidene}]\text{-tetrahydro-1H-2-pyrrolone} (55)\). The product obtained from the reaction of \(1N-(4\text{-methoxyphenyl})-2\text{-bromo-3-phenyl-}(Z)-2\text{-propenamide} (43)\) with phenyl propiolate in the presence of palladium catalyst was characterized by the usual spectroscopic method. The IR spectrum gave a strong absorption band at 1705 cm\(^{-1}\) and the \(^1\)H NMR spectrum showed a multiplet at \(\delta\) 7.75 - 7.25 was assigned to aromatic protons (13H) and two singlets at 3.84 and 3.72 with an integration of 3 protons of each indicating the presence of two methoxy groups. The mass spectrum displayed a molecular ion peak at \(m/z\) 411. The above data confirmed the structure of the expected product (57). Similarly the structure of the product (58) obtained from the reaction of amide (45) with 1, 3-cyclohexadiene was also confirmed.
CONCLUSION

A new and novel methodology was developed towards the synthesis of \( \alpha, \beta \)-unsaturated butyrolactams by the palladium catalyzed reactions of \( \alpha \)-bromoacrylic amides with 1, 3 dienes and alkynes.

EXPERIMENTAL

General procedure for synthesis of bromoacrylic amides

A 25 mL round-bottomed flask equipped with a calcium chloride guard tube was charged with \( \alpha \)-bromoacrylic acid (10 mmol) and freshly distilled thionyl chloride (1.62 g, 12 mmol). The reaction mixture was allowed to stand for 2 h at room temperature. The excess of thionyl chloride was removed by distillation and the pure acid chloride obtained was stored under argon atmosphere.

A mixture of dry triethylamine (10 mmol) and substituted anilines (10 mmol) in dry dichloromethane (25 mL) was charged into a two necked round bottomed flask equipped with a magnetic stirring bar and argon balloon. To the stirring solution, the freshly prepared acid chloride was added slowly at 0 °C for 10 min. and the reaction was allowed to stir for 1 h at RT. The reaction mixture was neutralized with dil. HCl and the product extracted with dichloromethane (3 \( \times \) 10 mL). The combined organic layer was dried over anhydrous sodium sulphate and concentrated under reduced pressure to give the crude product. Silica gel column chromatographic purification of the crude product using a mixture of petroleum ether and ethyl acetate (9:1) gave the product in high yield.

\( \alpha \)-bromoacrylic amides

\( 1H-(4\text{-}methoxyphenyl)\text{-}2\text{-}bromo-3\text{-}phenyl\text{-}(Z)\text{-}2\text{-}propenamide \) (43)

Mol. F : \( C_{16}H_{14}BrNO_2 \)
M. P : 107 - 108 °C

IR (Nujol) : 3294, 2925, 2854, 1651, 1608, 1460, 1446, 1309, 1033, 825, 690 cm⁻¹.

¹H NMR (200 MHz, CDCl₃) : δ 8.5 (bs, 1H), 8.4 (s, 1H), 7.8 - 7.6 (m, 2H), 7.5 (d, J = 8.0 Hz, 2H), 7.5 - 7.3 (m, 2H), 6.9 (d, J = 8.0 Hz, 2H), 3.79 (s, 3H).

³C NMR (50.32 MHz, CDCl₃) : δ 160.14, 156.87, 138.05, 133.97, 131.02, 130.15, 129.74, 128.34, 122.17, 114.12, 55.34.

Mass (m/z) : 333 (M+1, 83), 271(11), 252 (100), 211(58), 181(28), 122 (33), 102 (45).

¹N-(4-methoxyphenyl)-2-bromo-3-phenyl-(E)-2-propenamide (44)

Mol. F : C₁₆H₁₄BrNO₂

M. P : 137 - 138 °C

IR (Nujol) : 3263, 2923, 1650, 1616, 1184, 1024, 918, 825, 694 cm⁻¹.

¹H NMR (200 MHz, CDCl₃) : δ 7.45 - 7.2 (m, 8H), 6.85 (d, J = 7.8 Hz, 2H), 3.78 (s, 3H).

³C NMR (50.32 MHz, CDCl₃) : δ 162.60, 157.08, 136.65, 134.48, 130.29, 128.89, 128.41, 122.20, 116.50, 114.30, 55.60..

Mass (m/z) : 333 (M+1, 83), 271(11), 252 (100), 211(58), 181 (28), 122 (33), 102 (45).

¹N-(4-methoxyphenyl)-2-bromo-(Z)-2-butenamide (45)

Yield : 1.25 g (92%)

Mol. F : C₁₁H₁₂BrNO₂
M. P : 59 - 60 °C

IR (Nujol) : 3330, 2954, 1650, 1596, 1029, 831, 732 cm⁻¹

¹H NMR (200 MHz, CDCl₃) : δ 8.5 (bs, 1H), 7.5 (m, 1H), 7.45 (d, J = 8.0 Hz, 2H), 6.8 (d, J = 8.0 Hz, 2H), 3.8 (s, 3H), 1.9 (d, J = 2.0 Hz, 3H).

¹³C NMR (50.32 MHz, CDCl₃) : δ 159.58, 156.90, 137.93, 130.47, 122.16, 119.37, 114.19, 55.45, 17.77.

Mass (m/z) : 271 (M⁺, 43), 270 (6), 269 (47), 190 (25), 162 (12), 147 (65), 108 (49), 80 (16).

1-N-cyclohexyl-2-bromo-(Z)-2-butenamide (46)

Yield : 0.925 g (74%)

Mol. F : C₁₀H₁₄BrNO

IR (Nujol) : 3417, 2931, 1658, 1620, 760 cm⁻¹

¹H NMR (200 MHz, CDCl₃) : δ 7.4 (q, J = 6.0 Hz, 1H), 6.5 (bs, 1H), 3.8 - 3.6 (m, 1H), 1.95 (d, J = 6.0 Hz, 3H), 1.8 - 1.2 (m, 10 H).

¹³C NMR (50.32 MHz, CDCl₃) : δ 160.34, 136.30, 119.54, 48.78, 32.42, 25.22, 24.34, 17.10

Mass (m/z) : 247 (M⁺, 17), 245 (18), 204 (11), 166 (100), 147 (58), 121 (23), 98 (31).

1-N-cyclohexyl-2-bromo-3-phenyl-(Z)-2-propenamide (47)

Yield : 1.31 g (85%)

M. P : 109 - 111 °C

Mol. F : C₁₃H₁₉BrNO

IR (Nujol) : 3309, 2920, 2854, 1645, 1616, 1020, 757 cm⁻¹.

¹H NMR (200 MHz, CDCl₃) : δ 8.31 (s, 1H), 7.8 - 7.7 (m, 2H), 7.5 - 7.35 (m, 3H), 6.74 (bs, 1H), 4.0 - 3.8 (m, 1H), 2.1 - 1.9 (m, 2H), 1.8 - 1.5 (m,
13C NMR (50.32 MHz, CDCl3): δ 161.62, 144.53, 130.11, 129.77, 128.61, 115.92, 49.72, 33.00, 25.79, 25.00.

Mass (m/z): 308 (M^+, 4), 210 (12), 183 (12), 145 (13), 131 (19), 116 (4), 91 (5), 76 (10).

1N-(4-nitrophenyl)-2-bromo-3-phenyl-2-propenamide (48)

Yield: 1.25 g (82%)

Mol. F: C12H11BrN2O3

M. P: 127 - 128 °C

IR (Nujol): 3330, 1683, 1598, 852 cm⁻¹

1H NMR (200 MHz, CDCl3): δ 8.9 (bs, 1H), 8.5 (s, 0.9 H), 8.30 (d, J = 8.0 Hz, 2H), 7.8 - 7.70 (m, 4H), 7.55 - 7.35 (m, 3.1H)

Mass (m/z): 346 (M^+, 2), 267 (34), 221 (10), 183 (23), 102 (100), 91 (8).

General procedure for the palladium-catalyzed reactions of α-bromoacrylic amides with 1,3-dienes.

A 25 mL RB flask equipped with a magnetic stirring bar, reflux condenser and argon balloon was charged with α-bromoacrylic amide (1 mmol), 1,3-diene (2 mmol), PdCl₂(PPh₃)₂ (0.07g, 0.1 mmol), sodium carbonate (0.275 g, 2 mmol), zinc chloride (0.067 g, 0.5 mmol) and degassed N-methylpyrrolidone (4 mL). The reaction mixture was flushed with argon thrice and allowed to stir at 90 °C for 2-48 h. The reaction mixture was neutralized with dil. HCl and the product was extracted with ethyl acetate (3 × 5 mL). The combined organic layer was dried over anhydrous sodium sulphate and concentrated under reduced pressure to give crude product. The
crude product on silica gel column chromatographic purification using a mixture of petroleum ether and ethyl acetate gave the corresponding butyrolactams in moderate to good yield.

1-(4-methoxyphenyl)-3-(1-phenyl-(E)-methylidene)-2,3,3a,4,5,7a-hexahydro-1H-2-indolone (49)

\[
\begin{align*}
\text{Mol. F} & : \text{C}_{22}\text{H}_{21}\text{O}_{2}\text{N} \\
\text{M. P} & : 135 - 137 \, ^\circ\text{C} \\
\text{IR (Nujol)} & : 3018, 2935, 1681, 1645, 1608, 1290, 1247, 1033, 692 \, \text{cm}^{-1} \\
^1\text{H NMR (200 MHz, CDCl}_3\text{)} & : \delta 7.6 \, (d, J = 4.0 \, \text{Hz}, 1\text{H}), 7.55 - 7.4 \, (m, 5\text{H}), 7.3 \, (d, J = 8.0 \, \text{Hz}, 2\text{H}), 6.95 \, (d, J = 8.0 \, \text{Hz}, 2\text{H}), 6.15 - 6.05 \, (m, 1\text{H}), 5.85 - 5.7 \, (m, 1\text{H}), 4.6 - 4.5 \, (m, 1\text{H}), 3.8 \, (s, 3\text{H}), 3.65 - 3.50 \, (m, 1\text{H}), 2.25 - 2.0 \, (m, 3\text{H}), 1.6 - 1.45 \, (m, 1\text{H}). \\
^{13}\text{C NMR (50.32 MHz, CDCl}_3\text{)} & : \delta 168.65, 158.19, 136.52, 135.60, 133.25, 130.00, 129.77, 129.13, 126.63, 123.27, 114.64, 55.76, 54.77, 36.51, 24.45, 23.93. \\
\text{Mass (m/z)} & : 331 (M^+, 100), 302 (15), 212 (18), 179 (12), 165 (22), 134 (19), 115 (37), 91 (24), 77 (54)
\end{align*}
\]
5-isopropenyl-1-(4-methoxyphenyl)-3-(1-phenyl-(E)-methylene)tetrahydro-1H-2-pyrrolone (50)

\[
\text{Mol. F : C}_{21}\text{H}_{21}\text{O}_{2}\text{N}
\]

\[
\text{M. P : 183 - 184 °C}
\]

\[
\text{IR (CHCl}_3) : 3016, 2839, 1704, 1512, 1180, 831, 761 \text{ cm}^{-1}.
\]

\[
\text{H NMR (200 MHz, CDCl}_3) : \delta 7.65 - 7.4 (m, 8H), 6.9 (d, J = 8.0 \text{ Hz}, 2H), 5.05 (s, 1H), 4.9 (s, 1H), 4.85 - 4.75 (m, 1H), 3.82 (s, 3H), 3.55 - 3.25 (m, 1H), 2.95 - 2.65 (m, 1H), 1.65 (s, 3H).
\]

\[
\text{C NMR (75 MHz, CDCl}_3) : \delta 168.83, 157.56, 144.51, 136.09, 131.51, 130.07, 129.10, 124.15, 114.81, 114.36, 63.11, 55.76, 31.62, 16.75.
\]

\[
\text{Mass (m/z) : 319 (79), 304 (23), 278 (66), 174 (12), 160 (24), 128 (48), 115 (100), 91 (21), 77 (14).}
\]

\[
\text{Analysis : Calculated : C (78.98), H (6.60), N (4.37) Found : C (78.01), H (6.43), N (4.10)}
\]

Ethyl3-[(1-(4-methoxyphenyl)-5-oxo-4-(1-phenyl-(E)-methylene)tetrahydro-1H-2-pyrrolyl)-(E)-2-propenoate (51)
**Mol. F**: $C_{23}H_{23}NO_4$

**M. P**: 147-148 °C

**IR (Nujol)**: 3018, 1716, 1687, 1652, 1512, 1035, 757 cm$^{-1}$

$^1$H NMR (200 MHz, CDCl$_3$): 6 7.6 - 7.3 (m, 8H), 6.92 (d, $J = 8.0$ Hz, 2H), 6.9 - 6.8 (m, 1H), 5.8 (d, $J = 13.0$ Hz, 1H), 4.9 - 4.75 (m, 1H), 4.2 (q, $J = 7.5$ Hz, 2H), 3.81 (s, 3H), 3.65-3.40 (m, 1H), 3.1 - 2.9 (m, 1H), 1.25 (t, $J = 7.5$ Hz, 3H).

$^{13}$C NMR (50.32 MHz, CDCl$_3$): 6 167.83, 165.23, 157.05, 146.25, 135.08, 131.84, 130.59, 129.43, 128.94, 128.52, 123.08, 113.99, 60.43, 57.59, 55.12, 53.99, 53.34, 51.43, 13.86.

**Mass (m/z)**: 377 (M$^+$, 100), 348 (29), 304 (51), 204 (20), 160 (25), 116 (100).

**Analysis**

**Calculated**: C (73.19), H (6.14), N (3.71)

**Found**: C (72.60), H (6.32), N (3.22)

**Ethyl-3-[4-[(E)-ethylidenel-1-(4-methoxyphenyl)-5-oxotetrahydro-1H-2-pyrrolyl]-(E)-2-propenoate (52)**

![Chemical Structure]

**Mol. F**: $C_{18}H_{21}O_4N$

**IR (Nujol)**: 3016, 2839, 1704, 1674, 1369, 1180, 975, 761 cm$^{-1}$

$^1$H NMR (200 MHz, CDCl$_3$): 6 7.4 (d, $J = 8.0$ Hz, 2H), 6.9 (d, $J = 8.0$ Hz, 2H), 6.85 - 6.75 (dd, $J_1 = 4.0$ Hz, $J_2 = 12.5$ Hz, 1H), 6.75 - 6.65 (m, 1H), 5.8
(d, $J = 12.5$ Hz, 1H), 4.75 - 4.65 (m, 1H), 4.1 (q, $J = 7.5$ Hz, 2H), 3.78 (s, 3H), 3.15 - 3.05 (m, 1H), 2.65 - 2.50 (m, 1H), 1.6 (d, $J = 4.0$ Hz, 3H), 1.25 (t, $J = 7.5$ Hz, 3H).

$^{13}$C NMR (50.35 MHz, CDCl$_3$) : δ 167.45, 165.72, 159.77, 159.69, 150.32, 131.40, 130.10, 129.77, 123.89, 121.54, 114.11, 60.56, 55.38, 54.57, 29.28, 14.69, 14.17.

Mass (m/z) : 315 (M', 100), 286 (41), 270 (17), 242 (83), 134 (26), 106 (25), 91(12).

Ethyl-2-ethyl-3-[4-[(E)-ethylidene]-1-(4-methoxyphenyl)-5-oxotetrahydro-1H-2-pyrrolyl]- (E)-2-propenoate (53)

\[
\begin{align*}
\text{NMR (200 MHz, CDCl}_3) & : \delta 7.3 \text{ (d, } J = 8.0 \text{ Hz, 2H)}, 6.8 \text{ (d, } J = 8.0 \text{ Hz, 2H)}, 6.7 - 6.6 \text{ (m, 1H)}, 6.5 \text{ (d, } J = 4.0 \text{ Hz, 1H)}, 5.0 - 4.9 \text{ (m, 1H)}, 4.2 \text{ (q, } J = 7.0 \text{ Hz, 2H)}, 3.77 \text{ (s, 3H)}, 2.3 \text{ (q, } J = 7.5 \text{ Hz, 2H)}, 1.75 \text{ (d, } J = 4.0 \text{ Hz, 3H)}, 1.3 \text{ (t, } J = 7.0 \text{ Hz, 3H)}, 1.0 \text{ (t, } J = 7.5 \text{ Hz, 3H}).
\end{align*}
\]

$^{13}$C NMR (50.35 MHz, CDCl$_3$) : δ 166.99, 166.48, 157.25, 140.42, 135.86, 130.90, 129.35, 124.50, 121.50, 113.88, 60.43, 55.03, 54.88, 29.34, 20.11, 14.30, 3.79, 13.64.
Mass (m/z) : 343 (M⁺, 49), 328 (9), 314 (28), 254 (15), 173 (18), 134 (49), 108 (37).

Analysis : Calculated : C (69.96), H (7.33), N (4.07)
           Found : C (69.90), H (7.06), N (4.14)

1-(4-nitrophenyl)-3-[1-phenyl-(E)-methylidene]-2,3,3a,4,5,7a-hexahydro-1H-2-indolone (54)

E/Z (8:2)

Mol. F : C₂₁H₁ₘN₂O₃

M. P : 102 - 113 °C

IR (Nujol) : 3018, 2929, 1693, 852 cm⁻¹

¹H NMR (200 MHz, CDCl₃) : 8 8.80 - 8.75 (m, 2H), 7.8 - 7.30 (m, 7.8H), 6.25 - 5.885 (m, 2H), 4.85 - 4.75 (m, .2H), 4.75 - 4.65 (m, 0.8H), 3.75 - 3.60 (m, 0.8H), 3.45 - 3.30 (m, 0.2H), 2.2 - 2.0 (m, 3H), 1.65 - 1.45 (m, 1H).

¹³C NMR (75 MHz, CDCl₃) : 8 168.96, 168.26, 145.31, 143.78, 139.66, 135.05, 134.66, 134.14, 132.73, 130.92, 130.01, 129.01, 128.52, 127.97, 126.08, 124.43, 123.24, 121.62, 119.70, 119.20, 55.15, 53.26, 35.62, 23.41, 23.50.

Analysis : Calculated : C (72.62), H (5.21), N (8.06)
           Found : C (72.32), H (5.22), N(8.01)
1-(4-methoxyphenyl)-5-[2-phenyl-(E)-1-ethenyl]-3-[1-phenyl-(E)-methylidene]-tetrahydro-
1H-2-pyrrole (55)

\[
\text{Mol. F} : \text{C}_{26}\text{H}_{24}\text{NO}_2 \\
\text{IR (Nujol)} : 2925, 1683, 1603, 1170, 970, 862 \text{ cm}^{-1} \\
\text{\textsuperscript{1}H NMR (200 MHz, CDCl}_3) : \delta 7.65 - 7.25 \text{ (m, 13 H), } 6.85 \text{ (d, } J = 8.0 \text{ Hz, 2H), } 6.65 \text{ (dd, } J_1 = 4.0 \text{ Hz, } J_2 = 13 \text{ Hz, 1H), } 6.10 \text{ (d, } J = 4.0 \text{ Hz, 1H), } 4.9 \text{ (m, 1H), } 3.78 \text{ (s, 3H), } 3.65 - 3.50 \text{ (m, 1H), } 3.15 - 2.95 \text{ (m, 1H).} \\
\text{Mass (m/z)} : 381 (M^+, 25), 350 (35), 304 (23), 277 (40), 105 (100), 77 (63)
\]

Ethyl, 3-{1-cyclohexyl-5-oxo-4-[1-phenyl-(E)-methylidene]tetrahydro-1H-2-pyrrolyl-(E)-2-
propenoate (56)

\[
\text{Mol. F} : \text{C}_{22}\text{H}_{27}\text{NO}_3 \\
\text{M. P} : 153 - 154 \text{ °C} \\
\text{IR (Nujol)} : 3016, 2921, 1712, 1868, 1041, 763 \text{ cm}^{-1} \\
\text{\textsuperscript{1}H NMR (200 MHz, CDCl}_3) : \delta 7.60 - 7.30 \text{ (m, 5H), } 6.90 - 6.80 \text{ (dd, } J_1 = 4.0 \text{ Hz, } J_2 = 12.5 \text{ Hz, 1H), } 4.5 - 4.4 \text{ (m, 1H), } 4.2 \text{ (q, } J = 1.0 \text{ Hz, 2H), } 4.0 - 3.8 \text{ (m, 1H), } 3.45 - 3.25 \text{ (m, 1H), 2.85 - 2.60}
\]
1.1 (m, 1H), 2.0 - 1.20 (m, 10H).

$^{13}$C NMR (50.35 MHz, CDCl$_3$): $\delta$ 168.74, 165.51, 148.78, 135.54, 135.38, 130.53, 129.55, 129.34, 128.52, 121.99, 60.61, 55.61, 52.35, 48.49, 32.87, 32.35, 31.71, 29.61, 25.67, 25.24, 24.72, 14.01.

Mass (m/z): 353 (M$^+$, 75), 324 (15), 280 (61), 270 (37), 224 (46), 198 (64), 183 (100), 105 (84), 77 (14).

**Analysis**

<table>
<thead>
<tr>
<th>Calculated</th>
<th>Found</th>
</tr>
</thead>
<tbody>
<tr>
<td>C (74.77), H (7.69), N (3.96)</td>
<td>C (74.14), H (7.40), N (4.01)</td>
</tr>
</tbody>
</table>

*Methyl-1-(4-methoxyphenyl)-2-oxo-4-phenyl-3-[1-phenyl-(E)-methylidene-2, 3-dihydro-1H-5-pyrrolecarboxylate (57)*

\[
\begin{align*}
\text{Mol. F} & : C_{25}H_{21}NO_4 \\
\text{IR (CHCl$_3$)} & : 1616, 1596, 1514, 1492, 1249, 1031, 932 \text{ cm}^{-1}.
\end{align*}
\]

$^1$H NMR (CDCl$_3$, 200 MHz): $\delta$ 8.14 (d, $J = 8.0$ Hz, 2H), 7.75 - 7.25 (m, 13H), 3.74 (s, 3H), 3.18 (s, 3H).

Mass (m/z): 411 (M$^+$, 100), 352 (9), 325 (18), 210 (58), 105 (18), 77 (12).
3-[(E)-ethylidene]-1-(4-methoxyphenyl)-2, 3, 3a, 4, 5, 7a-hexahydro-1H-indolone (58)

Mol. F : C_{17}H_{19}NO_4
IR (CHCl_3) : 2923, 1683, 1603, 1430, 1047, 932 cm$^{-1}$
$^1$H NMR (200 MHz, CDCl$_3$) : 8 7.4 (d, $J=8.0$ Hz, 2H), 6.9 (d, $J=8.0$ Hz, 2H), 6.8 - 6.7 (m, 1H), 6.0 - 5.9 (m, 1H), 5.7 - 5.6 (m, 1H), 4.6 - 4.5 (m, 1H), 3.78 (s, 3H), 3.3 - 3.2 (m, 1H), 2.1 - 1.9 (m, 3H), 1.76 (d, $J=4.0$ Hz, 3H), 1.6 - 1.5 (m, 1H).
Mass (m/z) : 271 (M$^+$, 23), 240 (50), 164 (43), 139 (27), 105 (100), 76 (60)
References


Spectra
1H NMR and 13C NMR Spectra of 34a
Proton Decoupling Spectra of

![Chemical Structures]

(irradiation proton)
1H NMR and 13C NMR Spectra of 34b
Decoupling Spectra of 34b
2D NOESY Spectrum of 34b
$^1$H NMR Spectrum of
$^{1}H$ NMR and $^{13}C$ NMR Spectra of 38
$^{1}H$ NMR and $^{13}C$ NMR Spectra of
$^{1}H$ NMR Spectrum of
H NMR and NOE irradiation spectra of 43

![Graphical representation of H NMR spectra]

Current Lab Parameters

- **Chemical Shifts**
  - H2: 8.5 ppm
  - H2: 8.5 ppm

- **Integration**
  - H2: 8.5 ppm
  - H2: 8.5 ppm

- **Coupling Constants**
  - J1: 8.5 Hz
  - J2: 8.5 Hz

**Experimental Details**

- **Solvent:** DMSO-d6
- **Temperature:** 25°C

**Note:**

- All values are given in ppm.
- The spectra were obtained using a Varian Spectrometer.

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**Figure Legends**

- **Figure 1:** H NMR spectrum of 43.
- **Figure 2:** NOE irradiation spectrum of 43.
1H NMR and NOE irradiation spectra of

DM 2
$^1$H NMR and $^{13}$C NMR Spectra of 49
Decoupling Spectra of 49
2D COSY Spectrum of 49
1H NMR and 13C NMR Spectra of

\[ \text{Compound Structure} \]
$^{1}H$ NMR and $^{13}C$ NMR Spectra of 51
1H NMR and 13C NMR Spectra of 53
$^1$H NMR and $^{13}$C NMR spectra of 56