Chapter 2

Conversion of Cyclobutenediones to New
Functionalized Organic Compounds
2.1 Introduction

2.1 Reactions of carbonyl compounds catalyzed by L-proline and secondary amines

In recent years, organocatalysis has been widely used in organic synthesis.\textsuperscript{1,2} Organocatalysis offers many advantages for synthetic organic chemistry. In contrast to many metal catalysts, most organocatalysts are stable to air and water, easily handled experimentally, relatively nontoxic and readily separated from the crude reaction mixture.

Among various organic catalysts, L-proline and secondary amines have been widely used.\textsuperscript{3} As discussed in chapter 1, methods have been developed for cyclobutenedione synthesis using iron carbonyls and alkynes. We became interested to examine the reactivity pattern of cyclobutenediones in the presence of L-proline and pyrrolidine reagents. Organocatalysts with secondary amine functionality are useful in either enamine catalysis through forming catalytic quantities of an active enamine nucleophile or iminium catalysis by forming catalytic quantities of an activated iminium electrophile. A brief review on L-proline and secondary amines catalyzed organic transformations will be helpful for the discussion.
2.1.1 L-Proline catalyzed aldol reactions

2.1.1.1 L-Proline catalyzed intramolecular aldol reactions

One of the extensively studied organocatalyzed reaction is the aldol condensation of aldehydes and ketones. The aldol reaction is among the most commonly applied C-C bond forming reactions. The versatility of this reaction stems from its utility in constructing chiral building blocks via the stereoselective formation of C-C bonds for the synthesis of structurally complex molecules, namely natural products or non-natural drug molecules. For example, in the presence of L-proline 1 the triketones 2 and 3 undergo intramolecular aldol reaction to furnish the corresponding aldols 4 and 5 in good yields with high enantioselectivity (Scheme 1).

Scheme 1

It was reported that the acyclic 4-substituted 2,6-heptandiones 6, achiral heptanedials 8, hexanedral 10, dicarbonyl compounds 12 undergo intramolecular aldol reaction in the
presence of L-proline catalyst to provide the corresponding cyclohexenone derivative 7, anti-aldols 9, 5-enolexo aldols 11 and 2,3-dihydrobenzofuranols 13 (Chart 1).\textsuperscript{7-11}

**Chart 1**

\[
\begin{align*}
\text{DMF/5 d} & \quad \text{O} \quad \text{O} \\
\text{Ph} & \quad \text{Ph} \\
\text{<30\% yield} & \quad 47\% \text{ ee}
\end{align*}
\]

\[
\begin{align*}
\text{CH}_2\text{Cl}_2/\text{rt} & \quad \text{OH} \\
\text{95\% yield} & \quad 10: 1 \text{ dr} \\
& \quad 99\% \text{ ee}
\end{align*}
\]

\[
\begin{align*}
\text{CH}_3\text{CN/rt/7 h} & \quad \text{OHC} \\
\text{79\% ee} & \quad \text{37\% ee}
\end{align*}
\]

\[
\begin{align*}
\text{DMF/rt} & \quad \text{O} \quad \text{O} \\
\text{74-96\% yield} & \quad 73- 99 \% \text{ dr} \\
& \quad 76- 87\% \text{ ee}
\end{align*}
\]
2.1.1.2 L-Proline catalyzed intermolecular aldol reactions

In the presence of a catalytic amounts of L-proline (typically 20-30 mol %) in DMSO, acetone undergoes aldol reaction with aromatic and α-branched aldehydes, to provide the corresponding aldols 16 in good yields and enantioselectivities (Scheme 2).\(^{12}\)

**Scheme 2**

\[
\text{CH}_3\text{C} = \text{O} + \text{H}_2\text{C} = \text{O} \rightarrow \text{CH}_3\text{C} = \text{CH}_2 \rightarrow \text{CH}_3\text{C} = \text{CH}_2 - \text{OH}
\]

Unmodified ketones undergo aldol reaction with 4-oxoazetidine-2-carbaldehydes 17 in the presence of catalytic amount of L-proline or D-proline, to give the corresponding γ-amino-α-hydroxy ketones 19 with good yields and diastereoselectivities (Scheme 3).\(^{22}\)

**Scheme 3**

Several other intermolecular asymmetric transformations have been reported (Chart 2).\(^{13-17, 20}\)
Chart 2

\[
\begin{align*}
& \text{Chart 2} \\
& \text{1} + \text{20} \rightarrow \text{21} \\
& \text{DMSO/rt} \\
& & 79\% \text{ yield} \\
& & 96\% \text{ ee, }>20:1\text{dr} \\
& \text{22} \\
& \text{O} \text{COOEt} \\
& \text{O} \\
& \text{O} \\
& \text{+ COOEtOHO} \\
& \text{neat/-30 °C/rt} \\
& & 65\% \text{ yield} \\
& & 87\% \text{ ee} \\
& \text{24} \\
& \text{O} \text{POEt}_2 \\
& \text{O} \\
& \text{O} \\
& \text{+ PO} \\
& \text{3} \\
& \text{Et} \\
& \text{2} \\
& \text{OHO} \\
& \text{O} \\
& \text{O} \\
& \text{O} \\
& \text{DMSO/rt} \\
& & 60\% \text{ yield} \\
& & 99\% \text{ ee} \\
& \text{27} \\
& \text{O} \text{OH} \\
& \text{O} \\
& \text{O} \\
& \text{+HO} \\
& \text{Bn} \\
& \text{2} \\
& \text{N} \\
& \text{Me} \\
& \text{Bn} \\
& \text{2} \\
& \text{N} \\
& \text{29} \\
& \text{DMF/2 °C/3-6 d} \\
& & 88\% \text{ yield} \\
& & 30:1\%\text{de} \\
& \text{27} \\
& \text{O} \text{OH} \\
& \text{O} \\
& \text{O} \\
& \text{+ COOEt} \\
& \text{R} \\
& \text{3} \\
& \text{31-97\% yield} \\
& 1.5:1-98: 2\% \text{dr} \\
& 25-97\% \text{ee} \\
& \text{32} \\
& \text{OH} \\
& \text{COOH} \\
& \text{20} \\
& \text{21} \\
& \text{22} \\
& \text{24} \\
& \text{27} \\
& \text{29} \\
& \text{30} \\
& \text{31} \\
& \text{32} \\
& \text{33} \\
& \text{34} \\
& \text{35}
\end{align*}
\]
2.1.1.3 L-Proline catalyzed self aldol reactions

In the presence of catalytic amount of L-proline, acetaldehyde 36 undergoes enantioselective self-aldolization reaction to provide the 5-hydroxy-(2E)-hexenal 37, an aldol trimer of acetaldehyde, with up to 90% ee in low yield (Scheme 4).\(^{19}\)

**Scheme 4**

\[
\text{H}_2\text{C} = \text{CHOH} \quad \text{(10\% yield, 90\% ee)}
\]

The 2,2-dimethyl-1,3-dioxan-5-one (DHA) 30 and α-oxaldehyde 39 undergo self-aldolization to afford the corresponding aldol adduct 38 and 40 in better yields under L-proline catalysis (Scheme 5).\(^{18,21}\)

**Scheme 5**

\[
\text{DMF/2 °C/6d}
\]

\[
\text{CH}_2\text{Cl}_2/0 °C
\]

\[
\text{H}_2\text{C} = \text{CHOH} \quad \text{(73\% yield, 98\% ee, 4:1 dr)}
\]

\[
\text{H}_2\text{C} = \text{CHOH} \quad \text{(57\% yield, 94\% ee)}
\]
2.1.2 L-Proline and secondary amine catalyzed Michael reactions

The C-C bond formation by conjugate addition of nucleophiles to the β-position of α,β-unsaturated carbonyl compounds (Michael reaction) are frequently used in organic synthesis. In the case of carbonyl compounds, in organocatalytic Michael addition reactions, the donors are activated via formation of enamine or enol intermediates and the acceptors are activated via formation of iminium ion intermediates. Among different Michael acceptors, nitroalkenes, alkylidene malonate and vinyl ketones are the most commonly used because of their high reactivity and the possible further conversion of the product to other useful functionalities.

The unactivated symmetric ketones react with nitroolefins to furnish the γ-nitro ketones in high yields and good diastereoselectivities but only with low enantioselectivities (Scheme 6).

Scheme 6

It has been reported that acetone undergoes proline catalyzed Michael addition reaction with aromatic alkylidene malonate and cyclohexenone in DMSO solvent. The corresponding Michael adducts were formed respectively in 90% (14% ee) and 15% (20% ee) yields (Scheme 7).
Introduction

Scheme 7

Simple aldehydes 31 undergo Michael addition reaction with vinyl ketones 48 in the presence of (S)-2-[bis(3,5-dimethylphenyl) methyl]pyrrolidine catalyst 49 to give the 5-keto aldehydes 50 in good yields and good enantioselectivity (Scheme 8).\textsuperscript{26}

Scheme 8

α,β-Unsaturated aldehydes 51 undergo self-condensation to give the trisubstituted cyclohexadienes 52 in good yields and moderate enantioselectivity under proline catalysis (Scheme 9).\textsuperscript{27}
Scheme 9

\[
\begin{align*}
\text{R} & \quad \text{EtOH/rt/16-24 h} \\
51 & \quad \text{L-Proline (1.5 equiv.)} \\
\text{R= alkenyl, aryl} \\
52 & \quad \text{47- 89% yield} \\
& \quad \text{40- 62% ee}
\end{align*}
\]

2.1.3 L-Proline catalyzed Mannich reaction

Aliphatic 31 and aromatic aldehydes 53 and amines 54 and N-PMP-protected α-imino glyoxylates 56 undergo Mannich reactions to afford the β-amino carbonyl compounds 55 and 57 in the presence of L-proline catalyst (Scheme 10). 28, 29

Scheme 10

2.1.4 Other organocatalytic transformations

It has been reported that L-proline is also useful as a catalyst for α-amination of aldehydes. Simple aldehydes 31 and a mixture of acetone and aldehydes undergo reaction
with azodicarboxylates 58 to give the corresponding α-hydrazino aldehydes 59 and β-amino alcohols 60 (Scheme 11). 30, 31

Scheme 11

Cyclohexanone 20 reacts with nitrosobenzene 61 in the presence of L-proline in DMF solvent to give the α-aminoxylated ketone 62 with good yields and enatioselectivity (Scheme 12). 32

Scheme 12

In the presence of catalytic quantities of pyrrolidine 64 (5 mol%) and acetic acid, α, α-dialkylaldehydes 63 undergo aldol reaction with aryl aldehydes (Scheme 13). 33 The
corresponding quaternary carbon containing aldol products 65 were obtained in good yields. It was observed that L-proline is a poor catalyst for this reaction.\textsuperscript{33}

Scheme 13

\[
\begin{align*}
\text{H_3C} & \quad \text{R'} \quad \text{H} \\
\text{CHO} & \quad \text{Ar} \quad \text{CHO} \quad \text{Ar} \\
63 & \quad 53 \\
\end{align*}
\]

The 1,3-indandione 67 reacts with aromatic aldehydes and \( \alpha,\beta \)-unsaturated ketones 66 in the presence of pyrrolidine 64 to give the corresponding spiro compounds 68 in excellent yields with syn-selectivity (Scheme 14).\textsuperscript{34}

Scheme 14

In the presence of catalytic amounts of piperidine 69 and 4Å molecular sieves, aliphatic aldehydes 70 reacts with nitro alkanes 71 to give the (E)- or (Z)-nitro alkenes (72 or 73) in good yields.\textsuperscript{35} Simply by changing reaction conditions (solvent and temperature), it is possible to control the stereochemical outcome of the reaction (Scheme 15).\textsuperscript{35}

Scheme 15
Acyclic α,β-unsaturated ketones 74 undergo oxa-Diels–Alder reaction with aldehydes in the presence of 30 mol % pyrrolidine 64 and AcOH to give the substituted tetrahydropyran-4-ones 75 in good yields with >95% diastereoselectivity (Scheme 16).\(^{36}\)

**Scheme 16**

\[
\begin{align*}
\text{R} & \quad \text{Ar} \\
\text{74} & \quad \text{75} \\
+ \quad + \\
\text{53} & \quad \text{Pyrrolidine (30 mol %)} \\
\text{AcOH (30 mol %)} & \quad \text{CH}_2\text{Cl}_2/\text{rt} \\
\end{align*}
\]

In the presence catalytic quantity of piperidine 69, cyclohexyl isocyanide 76 react with various aldehydes and 1,3-dicarbonyl compounds 77 to give the 5-hydroxy-2H-pyrrol-2-one 78 derivatives in moderate to good yields (Scheme 17).\(^{37}\)

**Scheme 17**

\[
\begin{align*}
\text{Cy-NC} & \quad \text{ArCHO} \\
76 & \quad 53 \\
+ & \quad + \\
\text{R}^2 & \quad \text{Piperidine} \\
\text{toluene/rt} & \quad \text{77} \\
\end{align*}
\]

Polyhydroquinoline derivatives 80 were obtained in good yields from aldehyde, dimedone 79, acetoacetate ester or acetylacetone 77 and ammonium acetate in the presence of L-proline 1 catalyst (Scheme 18).\(^{38}\)

**Scheme 18**

\[
\begin{align*}
\text{79} & \quad \text{ArCHO} \\
+ & \quad + \\
\text{R}^2 & \quad \text{L-Proline} \\
\text{10 mol %} & \quad \text{NH}_4\text{OAc/rt} \\
\end{align*}
\]
2-Aminoacetophenone 81 reacts with aryl aldehyde in the presence of 30 mol % of L-proline to give the substituted 2-aryl-2,3-dihydroquinolin-4(1H)-ones 82 in good yields. The efficiency of the catalyst was established using a variety of electron-deficient to electron-rich aryl aldehyde substrates (Scheme 19).39

Scheme 19

In the presence of L-proline 1, o-phenylenediamines 83 and aryl aldehydes 53 undergo condensation in chloroform solvent at ambient temperature to give the 2-aryl-1-arylmethyl-benzimidazoles 84 in moderate to excellent yields via the corresponding iminium ion intermediate (Scheme 20).40

Scheme 20

5-Amino-1-phenyl-3-methylpyrazole 85 and aldehydes 15 undergo reaction with tetronic acid 86 in the presence of catalytic amount of L-proline to give the 3-methyl-1-phenyl-4-substituted-4,8-dihydrofuro[30,40:5,6]pyrido[2,3-c]pyrazole derivatives 87 in ethanol and the products were obtained in moderate to good yields (Scheme 21).41
Cyclic and acyclic ketones participate in Diels–Alder reaction with 1,2,4,5-tetrazines 88 in the presence of catalytic amount of L-proline, to give the corresponding adducts 90 in high yields. The transformation was explained via formation of an enamine intermediate (Scheme 22).  

Scheme 22

Tertiary aromatic amines 91, formaldehyde 92 and 2-naphthols 93 undergo Mannich type reactions in the presence of 20 mol % of L-proline to produce the corresponding diarylmethane derivatives 94 in moderate to good yields (Scheme 23).  

Scheme 23

Aldehydes undergo aldol condensation reaction with 1,3-dicarbonyl compounds 95 in the presence of catalytic amount of L-proline to give the corresponding conjugated
enones 96 and dienones 98. In these reactions, only one isomer was obtained with most of the 1,3-dicarbonyl compounds and aldehydes (Scheme 24).44

**Scheme 24**

\[
\begin{align*}
\text{RCHO} + \text{(95)} & \rightarrow \text{(96)} \\
\text{L-Proline (10 mol%)} & \\
\text{60-90%}
\end{align*}
\]

\[
\begin{align*}
\text{R} + \text{(95)} & \rightarrow \text{(98)} \\
\text{L-Proline (10 mol%)} & \\
\text{72-93%}
\end{align*}
\]

In the presence of catalytic quantities of L-proline and triethylamine (TEA), various ketones and a wide range of aldehydes undergo aldol condensation to produce the corresponding (E)-α,β-unsaturated ketones 100 in excellent yields (Scheme 25).45

**Scheme 25**

\[
\begin{align*}
\text{ArCHO} + \text{(99)} & \rightarrow \text{(100)} \\
\text{L-Proline (15 mol%)} & \text{TEA (30 mol%)} \\
\text{60-98%}
\end{align*}
\]

In the presence of 15 mol % of L-proline, aryl aldehydes 53, aryl methyl ketone 101 and NH₄OAc undergo condensation reaction to give the symmetrically substituted pyridine derivatives 102. When this reaction was carried out in the presence of indan-1,3-dione 68, highly substituted pyridine derivatives 103 were obtained (Scheme 26).47
**Scheme 26**

\[
\begin{align*}
\text{H}_2\text{ArO} + \text{R-COCH}_3 + \text{NH}_4\text{OAC} & \xrightarrow{\text{L-Proline (15 mol %)}} \text{Ar}_1\text{R}_2\text{N} \\
53 + 101 & \rightarrow 102 \\
& \text{EtOH/rt/3-4 h} \\
\text{82-93%}
\end{align*}
\]

\[
\begin{align*}
\text{O} + \text{H}_2\text{ArO} + \text{R-COCH}_3 + \text{NH}_4\text{OAC} & \xrightarrow{\text{L-Proline (15 mol %)}} \text{Ar}_1\text{R}_2\text{N} \\
68 + 53 + 101 & \rightarrow 103 \\
& \text{EtOH/rt/2-4 h} \\
& \text{83-92 %}
\end{align*}
\]

2,4,5-Trisubstituted imidazoles 105 were obtained in the three component cyclocondensation of 1,2-dicarbonyl compound 104, aldehyde 15 and ammonium acetate in the presence of 15 mol % of L-proline in methanol solvent. In this process, the products were obtained in high yields and purified by non-chromatographic methods. When the above reaction was carried out in the presence of primary amine 106, the N-substituted imidazole derivatives 107 were obtained in good yields (Scheme 27).\(^{46}\)

**Scheme 27**

\[
\begin{align*}
\text{O} + \text{R-CHO} + \text{NH}_4\text{OAc} & \xrightarrow{\text{L-Proline (15 mol %)}} \text{Ar}_1\text{R}_2\text{N} \\
104 + 15 + 106 & \rightarrow 105 \\
& \text{MeOH/60 °C} \\
& \text{42-90%}
\end{align*}
\]

\[
\begin{align*}
\text{O} + \text{R-CHO} + \text{NH}_4\text{OAc} + \text{R}_1\text{NH}_2 & \xrightarrow{\text{L-Proline (15 mol %)}} \text{Ar}_1\text{R}_2\text{N} \\
104 + 15 + 106 & \rightarrow 107 \\
& \text{MeOH/60 °C} \\
& \text{76-86%}
\end{align*}
\]

The results of our studies using the readily accessible cyclobutenedione derivatives in organocatalytic transformations are presented in the next section.
2.2 Results and Discussion

2.2.1 Stereoselective synthesis of alkenyl cyclobutenediones

As outlined in chapter 1, cyclobutenediones and its derivatives are important synthons, useful in the synthesis of compounds for medicinal chemistry and material science applications.\textsuperscript{48,49} A large number of cyclobutenedione derivatives and related compounds have been prepared in order to synthesize novel bioactive agents with improved pharmacological properties.\textsuperscript{50,51} As discussed in chapter 1, we have developed several methods to access cyclobutenediones using iron carbonyl reagents and alkynes. In continuation of these efforts, we have explored the development of new organic transformations using cyclobutenediones in the presence of organic catalysts.

As discussed in the introductory section, various aldehydes and ketones undergo aldol reaction in the presence of amine catalysts. However, there has been no report on organo catalytic aldol reaction involving cyclobutenediones. Therefore, we have examined aldol condensation reaction of cyclobutenediones with aromatic aldehyde catalyzed by pyrrolidine.

Initially, the aldol condensation reaction of 3-methyl-4-phenylcyclobutenedione 108 and benzaldehyde in MeOH solvent was investigated. We have observed that catalytic amount of pyrrolidine 64 (20 mol \%) catalyzes the reaction to give the desired condensation product in 88\% yield at 25 °C (Table 1, entry 1).
Scheme 28

The reaction was carried out in various solvents like CH$_3$OH, C$_2$H$_5$OH, DMSO, CH$_2$Cl$_2$, CHCl$_3$ and THF. In all the cases, the products were obtained in comparable yields (Table 1, entries 1-6). To optimize the catalyst loading, the conversion was carried out using 10 mol %, 20 mol %, and 30 mol % of pyrrolidine. The results are summarized in Table 1. A 20 mol % loading of pyrrolidine was sufficient to push the reaction forward. Use of higher amount of catalyst did not lead to significant change in the product yield. We have also examined the transformation using other organic catalysts like piperidine 69, morpholine 111 and l-proline 1. In all the cases, the products were obtained in similar yields (Table 1, entries 1, 9, 10 and 11). However, in the case of pyrrolidine (20 mol %), the products were obtained in good yields in shorter reaction time in methanol. The results are summarized in Table 1.
Table 1. Stereoselective olefination on 3-methyl-4-phenyl-cyclobutene-1,2-dione 108 using various organic catalysts in different solvents.\(^a\)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Solvent</th>
<th>mol (%)</th>
<th>Time</th>
<th>yield(^b)(%)</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>Pyrrolidine(64)</td>
<td>MeOH</td>
<td>20</td>
<td>1h</td>
<td>88</td>
</tr>
<tr>
<td>2</td>
<td>Pyrrolidine</td>
<td>EtOH</td>
<td>20</td>
<td>1h</td>
<td>86</td>
</tr>
<tr>
<td>3</td>
<td>Pyrrolidine</td>
<td>DMSO</td>
<td>20</td>
<td>1h</td>
<td>82</td>
</tr>
<tr>
<td>4</td>
<td>Pyrrolidine</td>
<td>THF</td>
<td>20</td>
<td>1.5h</td>
<td>85</td>
</tr>
<tr>
<td>5</td>
<td>Pyrrolidine</td>
<td>CH(_2)Cl(_2)</td>
<td>20</td>
<td>1.5h</td>
<td>83</td>
</tr>
<tr>
<td>6</td>
<td>Pyrrolidine</td>
<td>CHCl(_3)</td>
<td>20</td>
<td>1.5h</td>
<td>85</td>
</tr>
<tr>
<td>7</td>
<td>Pyrrolidine</td>
<td>MeOH</td>
<td>10</td>
<td>2h</td>
<td>80</td>
</tr>
<tr>
<td>8</td>
<td>Pyrrolidine</td>
<td>MeOH</td>
<td>30</td>
<td>1h</td>
<td>88</td>
</tr>
<tr>
<td>9</td>
<td>Piperdine(69)</td>
<td>MeOH</td>
<td>20</td>
<td>1h</td>
<td>80</td>
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<td>10</td>
<td>Morpholine(111)</td>
<td>MeOH</td>
<td>20</td>
<td>1h</td>
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</tr>
<tr>
<td>11</td>
<td>L-Proline(1)</td>
<td>MeOH</td>
<td>20</td>
<td>8h</td>
<td>78</td>
</tr>
</tbody>
</table>

\(^a\) All the reactions were carried out using cyclobutenedione 108 (0.5 mmol) aldehyde 53 (1.5 mmol), 3 equiv.) and catalyst at 25 °C. \(^b\) Yields reported are for the isolated products and based on the amount of cyclobutenedione (108) used.
After establishing the optimal reaction conditions required, the generality of this condensation reaction was examined. A number of alkenyl substituted cyclobutenediones derivatives were synthesized in good yields (Table 2). A variety of functional groups such as alkoxy, halide and amine are tolerated in this transformation. The results are summarized in Table 2. The substituted benzaldehyde derivatives having electron donating and withdrawing groups afforded the products in good yields (Table 2, entries 9 and 10). The structures of the condensation products 112 and 122 were confirmed by single crystal x-ray analysis.

Figure 1. ORTEP diagrams of compounds 112 and 122
### Table 2. X-ray data collection and structure refinement for 112

<table>
<thead>
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<th>Property</th>
<th>Value</th>
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<tbody>
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<td>Empirical formula</td>
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</tr>
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<td>Fw</td>
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<td>Temp., wavelength</td>
<td>298(2), 0.71073 Å</td>
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<td>Cryst. syst., space group</td>
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<td>Unit cell dimensions</td>
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<td></td>
<td>$b=8.1161(17)$ Å, $\beta=90^\circ$</td>
</tr>
<tr>
<td></td>
<td>$c=23.806(5)$ Å, $\gamma=90^\circ$</td>
</tr>
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<td>Z, calcd. density</td>
<td>8, 1.263 mg/m$^3$</td>
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<td>Abs. coeff.</td>
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<td>$F(000)$</td>
<td>1088</td>
</tr>
<tr>
<td>Cryst. size</td>
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</tr>
<tr>
<td>$\theta$ range for data collection</td>
<td>1.71 to 25.94°</td>
</tr>
<tr>
<td>Limiting indices</td>
<td>$-17 \leq h \leq 13$, $-9 \leq k \leq 9$, $-29 \leq l \leq 28$</td>
</tr>
<tr>
<td>Reflns. collected, unique</td>
<td>14223, 2660 [R(int)=0.0507]</td>
</tr>
<tr>
<td>Refinement method</td>
<td>full-matrix least-square on $F^2$</td>
</tr>
<tr>
<td>Data/restraints/params</td>
<td>2660/0/181</td>
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<tr>
<td>Goodness-of-fit on $F^2$</td>
<td>1.017</td>
</tr>
<tr>
<td>Final $R$ indices[I&gt; 2σ (I)]</td>
<td>$R_1=0.0531$, $wR_2=0.1023$</td>
</tr>
<tr>
<td>$R$ indices (all data)</td>
<td>$R_1=0.0992$, $wR_2=0.1191$</td>
</tr>
<tr>
<td>Largest diff. peak and hole</td>
<td>0.121, -0.095 e. Å$^3$</td>
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</table>
### Table 3. X-ray data collection and structure refinement for 122

<table>
<thead>
<tr>
<th>Description</th>
<th>Value</th>
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<tr>
<td>Empirical formula</td>
<td>C$<em>{19}$H$</em>{14}$O$_{2}$</td>
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<tr>
<td>Fw</td>
<td>274.30</td>
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<tr>
<td>Temp., wavelength</td>
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</tr>
<tr>
<td>Cryst. syst., space group</td>
<td>monoclinic, P-21/c</td>
</tr>
<tr>
<td>Unit cell dimensions</td>
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</tr>
<tr>
<td></td>
<td>b=14.943(3) Å, β=93.491° (3)</td>
</tr>
<tr>
<td></td>
<td>c=7.2161(12) Å, γ=90°</td>
</tr>
<tr>
<td>Volume</td>
<td>1386.0(4) Å$^3$</td>
</tr>
<tr>
<td>Z, calcd. density</td>
<td>4, 1.315 mg/m$^3$</td>
</tr>
<tr>
<td>Abs. coeff.</td>
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<tr>
<td>$F(000)$</td>
<td>576</td>
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<tr>
<td>Cryst. size</td>
<td>0.40×0.12×0.08 mm</td>
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<td>$\theta$ range for data collection</td>
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<tr>
<td>Limiting indices</td>
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</tr>
<tr>
<td>Reflns. collected, unique</td>
<td>12898, 2448[R(int)=0.0726]</td>
</tr>
<tr>
<td>Refinement method</td>
<td>full-matrix least-square on F$^2$</td>
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<tr>
<td>Data/restraints/params</td>
<td>2448/0/191</td>
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<tr>
<td>Goodness-of-fit on F$^2$</td>
<td>1.210</td>
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<td>Final $R$ indices [I&gt; 2σ (I)]</td>
<td>$R_1$=0.0785, wR$_2$=0.1635</td>
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<tr>
<td>$R$ indices (all data)</td>
<td>$R_1$=0.0955, wR$_2$=0.1715</td>
</tr>
<tr>
<td>Largest diff. peak and hole</td>
<td>0.321, -0.331 e. Å$^{-3}$</td>
</tr>
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</table>
Table 4. Stereoselective synthesis of alkenyl cyclobutenediones using pyrrolidine catalysts in methanol solvent

\[
\text{R}^\text{Ph} \quad \text{O} \quad \text{O} + \text{Ar-CHO} \xrightarrow{\text{Pyrrolidine (20 mol %)}} \text{MeOH/25 °C/1 h} \quad \text{Ar}^\text{Ph} \quad \text{R}^\text{H} \quad \text{H} \quad \text{Ph} \quad \text{O} \quad \text{O}
\]

\[
\text{R} = \text{H}, \text{CH}_3, n-\text{C}_3\text{H}_7
\]

<table>
<thead>
<tr>
<th>Entry</th>
<th>R</th>
<th>Ar-CHO</th>
<th>Product</th>
<th>yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>H</td>
<td>+</td>
<td>112</td>
<td>88</td>
</tr>
<tr>
<td>2</td>
<td>H</td>
<td>Cl-+</td>
<td>113</td>
<td>85</td>
</tr>
<tr>
<td>3</td>
<td>H</td>
<td>Br-+</td>
<td>114</td>
<td>82</td>
</tr>
<tr>
<td>4</td>
<td>H</td>
<td>Me-+</td>
<td>115</td>
<td>83</td>
</tr>
<tr>
<td>5</td>
<td>H</td>
<td>Et-+</td>
<td>116</td>
<td>85</td>
</tr>
</tbody>
</table>

\(^a\)
(Table 4 continued…)

<table>
<thead>
<tr>
<th>Entry</th>
<th>R</th>
<th>Ar-CHO</th>
<th>Product(^b)</th>
<th>yield(^c) %</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>H</td>
<td><img src="117" alt="Image" /></td>
<td><img src="117" alt="Image" /></td>
<td>78</td>
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<td>7</td>
<td>H</td>
<td><img src="118" alt="Image" /></td>
<td><img src="118" alt="Image" /></td>
<td>82</td>
</tr>
<tr>
<td>8</td>
<td>H</td>
<td><img src="119" alt="Image" /></td>
<td><img src="119" alt="Image" /></td>
<td>80</td>
</tr>
<tr>
<td>9</td>
<td>H</td>
<td><img src="120" alt="Image" /></td>
<td><img src="120" alt="Image" /></td>
<td>90</td>
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<td>10</td>
<td>H</td>
<td><img src="121" alt="Image" /></td>
<td><img src="121" alt="Image" /></td>
<td>91</td>
</tr>
<tr>
<td>11</td>
<td>CH(_3)</td>
<td><img src="109" alt="Image" /></td>
<td><img src="109" alt="Image" /></td>
<td>85</td>
</tr>
<tr>
<td>12</td>
<td>n-C(_3)H(_7)</td>
<td><img src="110" alt="Image" /></td>
<td><img src="110" alt="Image" /></td>
<td>80</td>
</tr>
</tbody>
</table>

\(^a\) All the reactions were carried out using cyclobutenedione (0.5 mmol) aldehyde (1.5 mmol, 3 equiv.) and pyrrolidine (20 mmol %) in MeOH (2.5 mL) at 25 °C for 1 h. \(^b\) The products were identified by spectral
data (IR, $^1$H-NMR, $^{13}$C-NMR and Mass). Yields reported are for the isolated products and based on the amount of cyclobutenedione used.

This transformation is also successful with dialkyl cyclobutenedione 124. In these experiments, highly conjugated dialkenyl substituted cyclobutenediones are obtained in excellent yields. Initially, we have carried out this reaction using 3,4-diethylcyclobutenedione 124 (0.5 mmol) and benzaldehyde (2 mmol) with 20 mol % of pyrrolidine. The corresponding 3,4-distyrylcyclobutene-1,2-dione 125 was obtained in 85% yield (Scheme 29).

Scheme 29

![Scheme 29](image)

The structure of 3,4-bis((E)-1-phenylprop-1-en-2-yl)cyclobutene-1,2-dione 125 was also confirmed by single crystal x-ray analysis.

![Figure 2](image)

**Figure 2.** ORTEP diagram of compound 125.
Table 5. X-ray data collection and structure refinement for 125

<table>
<thead>
<tr>
<th>Empirical formula</th>
<th>C_{22}H_{18}O_{2}</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fw</td>
<td>314.36</td>
</tr>
<tr>
<td>Temp., wavelength</td>
<td>100(2), 0.71073 Å</td>
</tr>
<tr>
<td>Cryst. syst., space group</td>
<td>orthorhombic, pbca</td>
</tr>
<tr>
<td>Unit cell dimensions</td>
<td>a = 12.851(4) Å, α = 90°</td>
</tr>
<tr>
<td></td>
<td>b = 13.648(5) Å, β = 90°</td>
</tr>
<tr>
<td></td>
<td>c = 18.969(6) Å, γ = 90°</td>
</tr>
<tr>
<td>Volume</td>
<td>3327.0(19) Å³</td>
</tr>
<tr>
<td>Z, calcd. density</td>
<td>8, 1.255 mg/m³</td>
</tr>
<tr>
<td>Abs. coeff.</td>
<td>0.079 mm⁻¹</td>
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<tr>
<td>F(000)</td>
<td>1328</td>
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<tr>
<td>Cryst. size</td>
<td>0.42×0.34×0.24 mm</td>
</tr>
<tr>
<td>θ range for data collection</td>
<td>2.15 to 26.01°</td>
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<tr>
<td>Limiting indices</td>
<td>-15 ≤ h ≤ 15, -16 ≤ k ≤ 16, -23 ≤ l ≤ 23</td>
</tr>
<tr>
<td>Reflns. collected, unique</td>
<td>32135, 3251 [R(int)=0.0610]</td>
</tr>
<tr>
<td>Refinement method</td>
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<tr>
<td>Data/restraints/params</td>
<td>3251/0/219</td>
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<tr>
<td>Goodness-of-fit on F²</td>
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<tr>
<td>Final R indices[I &gt; 2σ (I)]</td>
<td>R₁ = 0.0614, wR₂ = 0.1391</td>
</tr>
<tr>
<td>R indices (all data)</td>
<td>R₁ = 0.0691, wR₂ = 0.1441</td>
</tr>
<tr>
<td>Largest diff. peak and hole</td>
<td>0.232, -0.218 e. Å⁻³</td>
</tr>
</tbody>
</table>
We have also carried out this reaction with various aldehydes. The corresponding substituted 3,4-distyrylcyclobutene-1,2-diones were obtained in good yields (Scheme 29). The results are summarized in Table 6.

Table 6. Synthesis of 3,4-distyrylcyclobut-3-ene-1,2-diones using pyrrolidine catalyst

<table>
<thead>
<tr>
<th>Entry</th>
<th>ArCHO</th>
<th>Product</th>
<th>yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>124</td>
<td>![Product Image 1]</td>
<td>85</td>
</tr>
<tr>
<td>2</td>
<td>125</td>
<td>![Product Image 2]</td>
<td>82</td>
</tr>
<tr>
<td>3</td>
<td>126</td>
<td>![Product Image 3]</td>
<td>75</td>
</tr>
<tr>
<td>4</td>
<td>127</td>
<td>![Product Image 4]</td>
<td>70</td>
</tr>
</tbody>
</table>

*a* All the reactions were carried out using cyclobutenedione 124 (0.5 mmol) aldehyde (2 mmol, 4 equiv.) and pyrrolidine (20 mmol %) in MeOH (3 mL) at 25 °C for 1.5 h. *b* The products were identified by spectral data (IR, ¹H-NMR, ¹³C-NMR and Mass). *c* Yields reported are for the isolated products and based on the amount of cyclobutenedione (124) used.
The $\gamma$-olefination of cyclobutenediones (Scheme 28 and 29) can be explained by considering a tentative mechanism outlined in Scheme 30. The reaction of the dienolate intermediate 129 with the iminium ion derived from aldehyde to give the product (112-123) via the intermediate 130 may be considered (path A, Scheme 30). However, the alternative mechanism as outlined in Path B involving the reaction of the intermediate 133 to give the product (112-123) via the intermediate 134 cannot be also ruled out (Scheme 30).

Scheme 30

The stereoselectivity of the present transformation is excellent and only one isomer was obtained in all cases. This observation may be rationalized considering the transition
states 130 or 130A and 134 or 134A (Scheme 31). Thus, the intermediates 130 and 134 are favored over the intermediates 130A and 134A, leading to compounds 112-123 as the only products (Scheme 31). It is of interest to note that such condensation reactions of aldehydes with certain 1,3-dicarbonyl compounds gave only one geometrical isomer (Scheme 24).

Scheme 31

The mild and efficient methods for the preparation of highly conjugated mono- and di-alkenyl substituted cyclobutenediones using aldehydes and cyclobutenediones under amine catalysis have good synthetic potential. The mildness of the reaction conditions allows rapid and easy preparation of functionalized cyclobutenediones in high yields under very benign reaction conditions.
The derivates of alkenyl substituted cyclobutenediones are of interest in medicinal chemistry and some of these cyclobutenedione derivatives have also proven application as organic optical materials. Accordingly, the method described here has considerable potential for the synthesis of bioactive molecules and donor-acceptor cyclobutenedione derivates for material science applications. Previously, such cyclobutenedione derivatives were prepared using palladium reagents and through methods employing strong Lewis or bronsted acids (Scheme 32).

Scheme 32

These reported methods suffer from harsh reaction conditions, long reaction times, expensive reagents and lower yields compared to the organocatalytic methods described here.
2.2.2 New Cyclobutenediones via Michael Reaction

The Michael addition is one of the most useful carbon-carbon bond-forming reactions widely used in organic synthesis.\textsuperscript{23,55} Direct Michael-type conjugate addition reactions are amongst the most simple, efficient and atom-economical process in organic synthesis. Generally, these reactions are carried out using stoichiometric amounts of inorganic bases such as sodium ethoxide, potassium tert-butoxide, potassium hydroxide, sodium metal, LDA, sodium hydride or \textit{n}-butyllithium.\textsuperscript{56} Strong basic conditions can, however, lead to side reactions. Recently, excellent enantioselective Michael reactions have been developed using transition metal catalysts and these procedures are also not free from disadvantages.\textsuperscript{57} Organocatalysis has been recognized as having special features such as being environmentally benign and having atom economy and convenient synthetic operation. As discussed in the introductory section, several Michael addition reactions were reported using L-proline catalyst. However, to the best of our knowledge, there has been no report on organocatalytic Michael addition reaction involving cyclobutenediones. We have examined L-proline catalyzed Michael addition reaction of cyclobutenedione derivatives.

Initially, we have carried the reaction of acetone and diphenylcyclobutenedione \textsuperscript{139} in the presence of L-proline (30 mol \%) catalyst in DMSO solvent at room temperature. The corresponding 1,4-addition product \textsuperscript{140} that exists in enol form was isolated. Unfortunately, compound \textsuperscript{140} was obtained as recemic mixture, presumably, because of
formation of 1:1 ratio two enantiomers (Scheme 33). Also, recemization due to rearrangements of the corresponding enols 141 cannot be ruled out (Scheme 33).

**Scheme 33**

Conjugate addition is one of the most important bond forming strategies available to synthetic organic chemists. This is mainly due to the broad spectrum of donors and acceptors that can be employed in this reaction. Therefore, we have further examined the reactivity of substituted cyclobutenediones with acetone in the presence of L-proline (30 mol %). Surprisingly, in the case of silyl substituted cyclobutenedione, the Michael addition takes place with concomitant desilylation. Interestingly, the Michael addition products obtained exists in an enol form (Scheme 34).

**Scheme 34**
This product 148 was also characterized by single crystal X-ray analysis. It exists in enol form and there is a strong intramolecular hydrogen bonding interactions (-O-H…..O distance 1.852 Å).

We have also examined this reaction using DMF solvent in place of DMSO. In this case, the corresponding desilylated cyclobutenedione derivative was obtained only in 45% yield. Runs using other catalysts like pyrrolidine, piperidine in the place of L-proline gave only unidentifiable mixture of products. We have also carried out this reaction using 20 mol % L-proline, but 30 mol % of L-proline gave better results. After establishing the optimal reaction conditions, the reaction was carried out using different silyl substituted cyclobutenediones. The corresponding enolic cyclobutenedione derivatives were obtained in moderate to good yields (Table 8). In the case of chloro substituted cyclobutenediones (entries 4 and 6) the reaction was completed in 5 min. after adding the cyclobutenedione to the reaction mixture.

Figure 3. ORTEP diagram of compound 148
### Table 7. X-ray data collection and structure refinement for 148

<table>
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<tr>
<th>Metric</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Empirical formula</strong></td>
<td>(\text{C}<em>{13}\text{H}</em>{10}\text{O}_3)</td>
</tr>
<tr>
<td><strong>Fw</strong></td>
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</tr>
<tr>
<td><strong>Temp., wavelength</strong></td>
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</tr>
<tr>
<td><strong>Cryst. syst., space group</strong></td>
<td>orthorhombic, Pna2(1)</td>
</tr>
<tr>
<td><strong>Unit cell dimensions</strong></td>
<td>(a= 8.4940(9) \text{ Å}, \alpha=90°)</td>
</tr>
<tr>
<td></td>
<td>(b= 21.048(2) \text{ Å}, \beta= 90°)</td>
</tr>
<tr>
<td></td>
<td>(c= 5.9259(6) \text{ Å}, \gamma= 90°)</td>
</tr>
<tr>
<td><strong>Volume</strong></td>
<td>1059.43(19) Å</td>
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<td><strong>Z, calcd. density</strong></td>
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<td><strong>Abs. coeff.</strong></td>
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<td><strong>F(000)</strong></td>
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<td><strong>Cryst. size</strong></td>
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<td>1.94 to 25.95°</td>
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<tr>
<td><strong>Limiting indices</strong></td>
<td>(-10\leq h\leq 10, -25\leq k\leq 25, -5\leq l\leq 7)</td>
</tr>
<tr>
<td><strong>Reflns. collected, unique</strong></td>
<td>5664, 1720 [R(int)=0.0276]</td>
</tr>
<tr>
<td><strong>Refinement method</strong></td>
<td>full-matrix least-square on (\text{F}^2)</td>
</tr>
<tr>
<td><strong>Data/restraints/params</strong></td>
<td>1720/1/147</td>
</tr>
<tr>
<td><strong>Goodness-of-fit on (\text{F}^2)</strong></td>
<td>1.060</td>
</tr>
<tr>
<td><strong>Final (R) indices[(I\geq 2\sigma(I))]</strong></td>
<td>(R_1=0.0423, \text{wR}_2=0.0955)</td>
</tr>
<tr>
<td><strong>(R) indices (all data)</strong></td>
<td>(R_1=0.0569, \text{wR}_2=0.1018)</td>
</tr>
<tr>
<td><strong>Largest diff. peak and hole</strong></td>
<td>0.133, -0.159 e. Å(^{-3})</td>
</tr>
</tbody>
</table>
**Table 8.** Reaction of acetone with cyclobutenediones in the presence of L-proline

![Reaction Scheme]

$\text{Me}_3\text{Si} \quad \text{Ar} \quad \overset{\text{L-Proline}}{\text{DMSO/25°C/5 min}} \quad \text{Acetone} \quad \text{H}_3\text{C} \quad \text{OH} \quad \text{H}^- \quad \text{Ar} \quad \text{O} \quad \text{H}_3\text{C} \quad \text{OH} \quad \text{H}^- \quad \text{Ar} \quad \text{O}$

<table>
<thead>
<tr>
<th>Entry</th>
<th>Dione</th>
<th>Product$^b$</th>
<th>Yield$^c$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="image" alt="Cyclobutenedione 142" /></td>
<td><img src="image" alt="Product 148" /></td>
<td>75</td>
</tr>
<tr>
<td>2</td>
<td><img src="image" alt="Cyclobutenedione 143" /></td>
<td><img src="image" alt="Product 149" /></td>
<td>60</td>
</tr>
<tr>
<td>3</td>
<td><img src="image" alt="Cyclobutenedione 144" /></td>
<td><img src="image" alt="Product 150" /></td>
<td>65</td>
</tr>
<tr>
<td>4</td>
<td><img src="image" alt="Cyclobutenedione 145" /></td>
<td><img src="image" alt="Product 151" /></td>
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<tr>
<td>5</td>
<td><img src="image" alt="Cyclobutenedione 146" /></td>
<td><img src="image" alt="Product 152" /></td>
<td>58</td>
</tr>
<tr>
<td>6</td>
<td><img src="image" alt="Cyclobutenedione 147" /></td>
<td><img src="image" alt="Product 153" /></td>
<td>55</td>
</tr>
</tbody>
</table>

$^a$ All the reactions were carried out using cyclobutenedione (0.5 mmol), acetone (0.3 mL) and L-Proline (30 mmol%) in DMSO (4 mL) at 25 °C. $^b$ The products were identified by spectral data (IR, $^1$H-NMR, $^{13}$C-NMR and Mass). $^c$ Yields reported are for the isolated products and based on the amount of cyclobutenedione used.
The 1,4-addition of acetone to silylcyclobutenedione in the presence L-proline can be explained by considering a tentative mechanism outlined in Scheme 35.

**Scheme 35**

The use of enamines in Michael addition reactions is well established. Accordingly, the enamine generated from acetone and L-proline is expected to react with cyclobutenedione at the silyl substituted carbon to give the intermediate species 154a. This on further rearrangement could give the intermediate 154b, which could undergo desilylation followed by hydrolysis to give the enolic substituted cyclobutenedione derivatives (Scheme 35). This enol form may be more stable due to extended conjugation and intramolecular hydrogen bonding.
Chapter 2  Conversion of Cyclobutenediones to...

The new cyclobutenedione derivatives obtained via organocatalytic Michael reaction described above have considerable potential for further synthetic exploitations in view of their multifunctional character.

2.2.3 Conversion of silyl substituted cyclobutenediones to alkyl substituted cyclobutenediones by using Grignard reagent

Previously, it was reported that alkynyl magnesium reagents react with diphenylcyclobutenedione 139 to give various addition products (Eq. 1). Also, addition of alkynyl magnesium compounds to cyclobutanedione 159 yields 1,4-diketones after MnO₂ oxidation (Eq. 2).

![Chemical structures](image)

We became interested in the reaction of alkyl magnesium reagents with 3-phenyl-4-trimethylsilylcyclobutenedione 142 to compare the reactivity pattern with the above mentioned reactions. Initially, we have carried out this reaction at room temperature and obtained unidentifiable mixture of products. Fortunately, when the reaction was carried out
at -40 °C, new desilylated cyclobutenedione derivatives 109, 110, 162-164 were obtained in moderate yields (Scheme 36).

**Scheme 36**

\[
\text{Me}_3\text{Si} + \text{R}\text{MgBr} \rightarrow \text{THF/15 min./-40 °C} \rightarrow \text{Ph} \quad \text{Yield up to 51%}
\]

**Table 9.** Synthesis of phenyl alkyl substituted cyclobutenediones by using Grignard reagent

<table>
<thead>
<tr>
<th>Entry</th>
<th>Alkyne</th>
<th>Product</th>
<th>yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>C\textsubscript{2}H\textsubscript{5}MgBr</td>
<td><img src="image" alt="Product 109" /></td>
<td>45</td>
</tr>
<tr>
<td>2</td>
<td>n-C\textsubscript{3}H\textsubscript{7}MgBr</td>
<td><img src="image" alt="Product 162" /></td>
<td>46</td>
</tr>
<tr>
<td>3</td>
<td>n-C\textsubscript{4}H\textsubscript{9}MgBr</td>
<td><img src="image" alt="Product 163" /></td>
<td>51</td>
</tr>
<tr>
<td>4</td>
<td>n-C\textsubscript{3}H\textsubscript{11}MgBr</td>
<td><img src="image" alt="Product 164" /></td>
<td>40</td>
</tr>
<tr>
<td>5</td>
<td>n-C\textsubscript{6}H\textsubscript{13}MgBr</td>
<td><img src="image" alt="Product 165" /></td>
<td>42</td>
</tr>
</tbody>
</table>

\(^a\) All the reactions were carried out using cyclobutenedione 142 (1 mmol) Grignard reagent (1 mmol) in THF (15 mL) at -40 °C. \(^b\) The products were identified by spectral data (IR, \(^1\)H-NMR, \(^13\)C-NMR and Mass). \(^c\) Yields reported are for the isolated products and based on the amount of cyclobutenedione (142) used.
The formation of alkyl phenyl cyclobutenediones from 3-phenyl-4-(trimethylsilyl) cyclobutenedione and Grignard reagent can be explained by considering the mechanism outlined in Scheme 37. The Grignard reagent could undergo reaction at the carbonyl carbon followed by rearrangement and desilylation to give the new cyclobutenediones via the intermediates 165 and 166 (Scheme 37). The aromaticity of the cyclobutenedione moiety would be driving force for such a transformation.

**Scheme 37**

![Scheme 37 Diagram]

However, the intermediacy of the unstable antiaromatic dioxycyclobutadiene 167 cannot be ruled out as it would be expected to react with molecular oxygen to give the aromatic cyclobutenedione along with oxygenated trimethylsilyl magnesium bromide (Scheme 37).
2.3 Conclusions

3-Alkyl-4-phenylcyclobutenediones undergo stereoselective aldol condensation reaction with various aldehydes to provide the alkenyl substituted cyclobutenediones in 78-91% yields under ambient reaction conditions. The 3,4-diethylcyclobutenediones undergoes double aldol condensation reaction with various aldehydes under similar reaction conditions to give the dialkenyl substituted cyclobutenedione derivatives in 70-85% yields.

Diphenylcyclobutenedione undergoes Michael addition with acetone in the presence of L-proline catalyst to provide the corresponding 1,4-addition product in 75% yield. The 3-aryl-4-trimethylsilylcyclobutenediones also undergo 1,4-addition reaction to provide the corresponding aryl alkyl substituted cyclobutenediones in 52-75% yields with concomitant desilylation.

Several new functionalized, highly conjugated cyclobutenedione derivatives are accessed through transformations described here. These methods have good potential for further synthetic exploitations, since the products are important class of multifunctional organic synths.
2.4 Experimental Section

2.4.1 General information:

The general information given in the section 1.4 is also applicable to the experiments described in this section. The cyclobutenediones were prepared by following a reported procedure.\textsuperscript{59}

2.4.2 Preparation of (\textit{E})-3-phenyl-4-styrylcyclobut-3-ene-1,2-dione 112

To a mixture of 3-methyl-4-phenyl-cyclobutene-1,2-dione 108 (0.086 g, 0.5 mmol) and benzaldehyde (0.15 mL, 1.5 mmol) in 2.5 mL of MeOH catalytic amount of pyrrolidine (8.2 µL, 20 mol %) was added. The reaction mixture was stirred for 1 h at room temperature. It was treated with 5mL of saturated ammonium chloride solution and extracted with ethyl acetate (3x10 mL). The combined organic layer was dried over anhydrous Na\textsubscript{2}SO\textsubscript{4} and concentrated under reduced pressure. The residue was subjected to column chromatography (silica gel, hexane-EtOAc). Ethyl acetate (3%) in hexane eluted the (\textit{E})-3-phenyl-4-styrylcyclobut-3-ene-1,2-dione 112.

Yield : 0.114 g (88%)

\textbf{mp} : 148-150 °C (Lit.\textsuperscript{54} mp 160 °C)

\textbf{IR (KBr)} : 1759 cm\textsuperscript{-1}
1H NMR : (400 MHz) $\delta = 8.30$ (d, $J = 14.8$ Hz, 1H), 8.09-8.07 (m, 2H), 7.68-7.45 (m, 9H) ppm (Spectrum No. 25)

13C NMR : (100 MHz) $\delta = 196.7, 195.9, 184.2, 183.4, 146.1, 134.9, 133.2, 131.4, 129.4, 129.2, 129.0, 128.7, 128.4, 115.2$ ppm (Spectrum No. 26)

MS (EI) : $m/z$ 261 (M+1).

Analysis : for C$_{18}$H$_{12}$O$_2$

Calculated: C, 83.06%; H, 4.65%

Found: C, 83.25%; H, 4.59%

The above procedure was followed for the condensation of other aldehydes with 3-alkyl-4-phenyl-cyclobutene-1,2-dione.

Yield : 0.125 g (85%)

mp : 171-173 °C (Lit. 54 mp 185 °C)

IR (KBr) : 1759 cm$^{-1}$

1H NMR : (400 MHz) $\delta = 8.25$ (d, $J = 15.6$ Hz, 1H), 8.09-8.06 (m, 2H), 7.62-7.56 (m, 5H), 7.48 (d, $J = 15.6$ Hz, 1H), 7.43-7.41 (m, 2H) ppm
$^{13}$C NMR: (100 MHz) $\delta = 196.6, 195.8, 183.8, 183.7, 144.4, 137.4, 133.4, 129.8, 129.5, 128.9, 128.4, 115.7$ ppm

MS (EI): $m/z$ 295 (M+1)

Analysis: for C$_{18}$H$_{11}$ClO$_2$

Calculated: C, 73.35%; H, 3.76%

Found: C, 73.51%; H, 3.71%

Yield: 0.138 g (82%)

mp: 166-168 °C

IR (KBr): 1747 cm$^{-1}$

$^1$H NMR: (400 MHz) $\delta = 8.26$ (d, $J = 15.6$ Hz, 1H), 8.10-8.08 (m, 2H), 7.62-7.54 (m, 7H), 7.51 (d, $J = 15.6$ Hz, 1H) ppm (Spectrum No. 27)

$^{13}$C NMR: (100 MHz) $\delta = 196.5, 195.8, 183.85, 183.81, 144.5, 133.8, 133.3, 132.5, 129.9, 129.5, 128.9, 128.4, 125.8, 115.7$ ppm (Spectrum No. 28)

MS (EI): $m/z$ 339 (M+2)

Analysis: for C$_{18}$H$_{11}$BrO$_2$
Calculated: C, 63.74%; H, 3.27%

Found: C, 63.85%; H, 3.21%

Yield : 0.114 g (83%)
mp : 156-158 °C (Lit. mp 163 °C)
IR (KBr) : 2914, 1751, 1736 cm⁻¹

¹H NMR : (400 MHz) δ = 8.33 (d, J = 15.6 Hz, 1H), 8.12-8.10 (m, 2H), 7.61-7.60 (m, 5H), 7.50 (d, J = 15.6 Hz, 1H), 7.29-7.27 (m, 2H), 2.44 (s, 3H) ppm (Spectrum No. 29)

¹³C NMR : (100 MHz) δ = 196.8, 195.8, 184.4, 182.8, 146.3, 142.2, 133.0, 132.2, 129.9, 129.4, 129.1, 128.8, 128.3, 114.2, 21.6 ppm (Spectrum No. 30)

MS (EI) : m/z 275 (M+1)

Analysis : for C₁₉H₁₄O₂

Calculated: C, 83.19%; H, 5.14%

Found: C, 83.31%; H, 5.08%
Yield : 0.122 g (85%)

mp : 118-120 °C

IR (KBr) : 2966, 2926, 1751 cm⁻¹

¹H NMR : (400 MHz) δ = 8.32 (d, J = 15.6 Hz, 1 H), 8.10-8.08 (m, 2H), 7.63-7.57 (m, 5H), 7.48 (d, J = 15.6 Hz, 1H), 7.30-7.28 (m, 2H), 2.70 (q, J = 7.6 Hz, 2H), 1.27 (t, J = 7.6 Hz, 3H) ppm

¹³C NMR : (100 MHz) δ = 196.8, 195.8, 184.4, 182.8, 148.5, 146.4, 133.0, 132.5, 129.4, 129.1, 128.9, 128.7, 128.3, 114.3, 28.9, 15.1 ppm

MS (EI) : m/z 289 (M+1)

Analysis : for C₂₀H₁₆O₂

Calculated: C, 83.31%; H, 5.59%

Found: C, 83.45%; H, 5.51%
**Experimental Section**

Yield : 0.118 g (78%)

mp : 126-128 °C

IR (KBr) : 2959, 2926, 1766 cm\(^{-1}\)

\(^1\)H NMR : (400 MHz) \(\delta = 8.32\) (d, \(J = 15.6\) Hz, 1H), 8.10-8.08 (m, 2H), 7.63-7.57 (m, 5H), 7.48 (d, \(J = 15.6\) Hz, 1H), 7.33-7.31 (m, 2H), 3.01-2.91 (m, 1H), 1.28 (d, \(J = 6.8\) Hz, 6H) ppm

\(^13\)C NMR : (100 MHz) \(\delta = 196.8, 195.8, 184.4, 182.9, 153.1, 146.4, 133.0, 132.6, 129.4, 129.2, 128.9, 128.3, 127.3, 114.4, 34.2, 23.6\) ppm

MS (EI) : \(m/z\) 303 (M+1)

Analysis : for C\(_{21}\)H\(_{18}\)O\(_2\)

Calculated: C, 83.42%; H, 6.00%

Found: C, 83.35%; H, 6.12%
Yield : 0.119 g (82%)
mp : 140-142 °C (Lit.\(^{54}\) mp 156 °C)
IR (KBr) : 2978, 1763, 1751 cm\(^{-1}\)
\(^1\)H NMR : (400 MHz) \(\delta = 8.31 (d, J = 15.6 \text{ Hz}, 1\text{H}), 8.09-8.08 (m, 2\text{H}), 7.67-7.57 (m, 5\text{H}), 7.39 (d, J = 15.6 \text{ Hz}, 1\text{H}), 6.97 (d, J = 8.4 \text{ Hz}, 2\text{H}), 3.87 (s, 3\text{H}) \text{ ppm}\)
\(^{13}\)C NMR : (100 MHz) \(\delta = 197.1, 195.7, 184.5, 182.1, 162.5, 146.2, 132.8, 130.8, 129.4, 129.3, 128.2, 127.7, 114.7, 113.0, 55.5 \text{ ppm}\)
MS (EI) : \(m/z 291 (M+1)\)
Analysis : for C\(_{19}\)H\(_{14}\)O\(_3\)
Calculated: C, 78.61%; H, 4.86%
Found: C, 78.45%; H, 4.92%

Yield : 0.122 g (80%)
mp : 136-138 °C
IR (KBr) : 2978, 2924, 1763, 1743 cm\(^{-1}\)
**Experimental Section**

\(^1H\) NMR : \((400\ MHz)\ \delta = 8.28\ (d,\ J = 15.6\ Hz,\ 1H),\ 8.08-8.06\ (m,\ 2H),\ 7.64-7.55\ (m,\ 5H),\ 7.36\ (d,\ J = 15.6\ Hz,\ 1H),\ 6.94\ (d,\ J = 8.4\ Hz,\ 2H),\ 4.08\ (q,\ J = 7.2\ Hz,\ 2H),\ 1.44\ (t,\ J = 7.2\ Hz,\ 3H) \text{ ppm (Spectrum No. 31)}\)

\(^{13}C\) NMR : \((100\ MHz)\ \delta = 197.1,\ 195.7,\ 184.5,\ 182.0,\ 161.9,\ 146.3,\ 132.8,\ 130.8,\ 129.4,\ 129.3,\ 128.2,\ 127.5,\ 115.2,\ 112.8,\ 63.8,\ 14.7 \text{ ppm (Spectrum No. 32)}\)

MS (EI) : \(m/z\ 303\ (M^-1)\)

Analysis : for C\(_{20}\)H\(_{16}\)O\(_3\)

Calculated: C, 78.93%; H, 5.30%

Found: C, 78.81%; H; 5.41%

Yield : 0.136 g (90%)

mp : 215-217 °C (Lit.\(^{54}\) mp 227 °C)

IR (KBr) : 1755, 1728 cm\(^{-1}\)
$^1$H NMR : (400 MHz) $\delta = 8.28$ (d, $J = 15.6$ Hz, 1H), 8.08-8.06 (m, 2H), 7.58-7.54 (m, 5H), 7.22 (d, $J = 15.6$ Hz, 1H), 6.67 (d, $J = 9.2$ Hz, 2H), 3.06 (s, 6H) ppm (Spectrum No. 33)

$^{13}$C NMR : (100 MHz) $\delta = 197.7$, 195.3, 184.5, 179.5, 152.6, 147.5, 132.2, 131.2, 129.8, 129.2, 127.9, 122.7, 111.9, 109.8, 40.0 ppm (Spectrum No. 34)

MS (EI) : m/z 304 (M+1)

Analysis : for C$_{20}$H$_{17}$NO$_2$

Calculated: C, 79.19%; H, 5.65%; N, 4.62

Found: C, 79.10%; H, 5.61%; N, 4.75

Yield : 0.149 g (91%)

mp : 140-142 °C

IR (KBr) : 1768, 1747 cm$^{-1}$

$^1$H NMR : (400 MHz) $\delta = 8.30$ (d, $J = 15.6$ Hz, 1H), 8.09 (d, $J = 8$ Hz, 2H), 7.79 (d, $J = 8$ Hz, 2H), 7.70 (d, $J = 8$ Hz, 2H), 7.62-7.58 (m, 4H) ppm
**Experimental Section**

$^{13}$C NMR: (100 MHz) $\delta = 196.3, 195.8, 184.6, 183.4, 143.6, 138.2, 133.6, 132.3$ (q, $J = 32$ Hz), 129.6, 128.8, 128.7, 128.6, 126.1 (q, $J = 4$ Hz), 123.7 (q, $J = 271$ Hz), 117.4 ppm

MS (EI): $m/z$ 329 (M+1)

Analysis: for C$_{19}$H$_{11}$F$_3$O$_2$

Calculated: C, 69.51%; H, 3.38%

Found: C, 69.38%; H, 3.45%

![Chemical reaction](image)

Yield: 0.117 g (85 %)

mp: 96-98 °C

IR (KBr): 2968, 1765 cm$^{-1}$

$^1$H NMR: (400 MHz) $\delta = 8.02$ (s, 1H), 7.89-7.86 (m, 2H), 7.56-7.36 (m, 8H), 2.31 (s, 3H) ppm (Spectrum No. 35)

$^{13}$C NMR: (100 MHz) $\delta = 196.1, 195.7, 190.2, 186.2, 141.6, 135.3, 132.3,$ 130.3, 129.3, 128.9, 128.8, 128.6, 128.0, 127.1, 16.9 ppm (Spectrum. No. 36)

MS (EI): $m/z$ 275 (M+1)
**Analysis** : for C\(_{19}\)H\(_{14}\)O\(_2\)

Calculated: C, 83.19%; H, 5.14%

Found: C, 83.31%; H, 5.08%

Yield : 0.121 g (80 %)

mp : semi solid

IR (KBr) : 2962, 2934, 1786, 1768 cm\(^{-1}\)

\(^1\)H NMR : (400 MHz) \(\delta = 7.96-7.93 \text{ (m, 2H), 7.76 \text{ (s, 1H), 7.58-7.38 \text{ (m, 8H), 2.81 \text{ (t, } J = 7.6 \text{ Hz, 2H), 1.47-1.37 \text{ (m, 2H), 0.81 \text{ (t, } J = 7.2 \text{ Hz, 3H)}}}\)}

\(^{13}\)C NMR : (100 MHz) \(\delta = 196.5, 196.0, 191.5, 186.9, 139.2, 135.1, 133.0, 132.6, 129.7, 129.0, 128.7, 128.4, 128.3, 30.4, 22.1, 13.6 \text{ ppm}\)

MS (EI) : \(m/z\) 303 (M\(^+\))

**Analysis** : for C\(_{21}\)H\(_{18}\)O\(_2\)

Calculated: C 83.42%; H, 6.00%

Found: C, 83.31%; H, 5.92%
2.4.3 Preparation of 3,4-bis((E)-1-phenylprop-1-en-2-yl)cyclobutene-1,2-dione 125

To a mixture of 3,4-diethylcyclobutenedione 124 (0.069 g, 0.5 mmol) in 3 mL of MeOH solvent and catalytic amount of pyrrolidine (8.2 µL, 20 mol %), benzaldehyde (0.2 mL, 2 mmol) was added. And the reaction mixture was stirred for 1.5 h at room temperature. The reaction mixture was treated with 5 mL of saturated ammonium chloride solution and extracted with ethyl acetate (3×10 mL). The combined organic layer was dried over anhydrous Na$_2$SO$_4$ and concentrated under reduced pressure. The residue was subjected to column chromatography (silica gel, hexane-EtOAc). Ethyl acetate (3%) in hexane eluted the 3,4-bis((E)-1-phenylprop-1-en-2-yl)cyclobutene-1,2-dione 125.

![Chemical Reaction Image]

**Yield**: 0.133 g (85 %)

**mp**: 118-120 °C

**IR (KBr)**: 1743 cm$^{-1}$

**$^1$H NMR**: (400 MHz) $\delta$ = 7.74 (s, 2H), 7.54-7.39 (m, 10H), 2.37 (s, 6H) ppm

*(Spectrum No. 37)*
\[^{13}\text{C NMR}\] : (100 MHz) \(\delta = 196.1, 189.7, 140.7, 135.6, 130.3, 129.2, 128.7, 127.2, 17.4\) ppm \textbf{(Spectrum No. 38)}

\[\text{MS (EI)}\] : \(m/z\) 315 (M+1)

\[\text{Analysis}\] : for \(\text{C}_{22}\text{H}_{18}\text{O}_{2}\)

Calculated: C, 84.05%; H, 5.77%

Found: C, 84.18%; H, 5.71%

The above procedure was followed for the reaction of other aldehydes with 3,4-diethylcyclobutenedione 124.

![Chemical Reaction Diagram]

\[\text{Yield}\] : 0.140 g (82 %)

\[\text{mp}\] : 156-158 °C

\[\text{IR (KBr)}\] : 2922, 1745 cm\(^{-1}\)

\[^{1}\text{H NMR}\] : (400 MHz) \(\delta = 7.74\) (s, 2H), 7.46 (d, \(J = 8\) Hz, 4H), 7.27 (d, \(J = 8\) Hz, 4H), 2.42 (s, 6H), 2.38 (s, 6H) ppm

\[^{13}\text{C NMR}\] : (100 MHz) \(\delta = 196.2, 189.3, 140.8, 139.6, 132.8, 130.4, 129.4, 126.3, 21.5, 17.6\) ppm

\[\text{MS (EI)}\] : \(m/z\) 343 (M+1)

\[\text{Analysis}\] : for \(\text{C}_{24}\text{H}_{22}\text{O}_{2}\)
Calculated: C, 84.18%; H, 6.48%

Found: C, 84.05%; H, 6.55%

Yield : 0.140 g (75 %)

mp : 164-166 °C

IR (KBr) : 2961, 1739 cm⁻¹

¹H NMR : (400 MHz) δ = 7.72 (s, 2H), 7.52 (d, J = 8.8 Hz, 4H), 6.96 (d, J = 8.8 Hz, 4H), 3.86 (s, 6H), 2.36 (s, 6H) ppm (Spectrum No. 39)

¹³C NMR : (100 MHz) δ = 196.2, 188.9, 160.4, 140.5, 132.3, 128.5, 125.0, 114.2, 55.4, 17.8 ppm (Spectrum No. 40)

MS (EI) : m/z 373 (M-1)

Analysis : for C₂₄H₂₂O₄

Calculated: C, 76.99%; H, 5.92%

Found: C, 76.88%; H, 5.97%
Yield : 0.140 g (70%)

mp : 156-158 °C

IR (KBr) : 2922, 1743 cm⁻¹

¹H NMR : (400 MHz) δ = 7.74 (s, 2H), 7.51 (d, J = 8 Hz, 4H), 6.72 (d, J = 8 Hz, 4H), 3.05 (s, 12H), 2.37 (s, 6H) ppm

¹³C NMR : (100 MHz) δ = 196.4, 187.5, 150.7, 141.3, 132.6, 124.0, 122.7, 111.7, 40.1, 18.2 ppm

MS (EI) : m/z 401 (M+1)

Analysis : for C₂₆H₂₈N₂O₂

Calculated: C, 77.97%; H, 7.05%; N, 6.99%

Found: C, 77.91%; H, 7.15%; N, 6.85%

3.4.4 Reaction of acetone with the diphenylcyclobutenedione 139 in the presence of L-proline catalyst

To a solution of L-proline (0.017 g, 30 mol %) in DMSO (1.5 mL), acetone (0.5 mL) was added at 25 °C and stirred for 15 min. Diphenylcyclobutenedione (0.117 g, 0.5 mmol) in DMSO (1.5 mL) was added dropwise and the contents were stirred for 5 h. The reaction mixture was treated with 5 mL of saturated NH₄Cl solution and extracted with ethyl acetate (3x10 mL). The combined organic extract was washed with brine solution and dried over anhydrous Na₂SO₄. The solvent was removed and the residue was subjected to column chromatography (silica gel, hexane-EtOAc). Ethyl acetate (20%) in hexane eluted the 2-hydroxy-4-(2-oxopropyl)-3,4-diphenylcyclobuten-2-one 140.
Yield : 0.109 g (75%)

mp : 148-150 °C

IR (KBr) : 3449, 1753, 1712 cm\(^{-1}\)

\(^1\)H NMR : (400 MHz) \(\delta = 9.34 (s, 1H), 7.71-7.24 (m, 10H), 3.45 (s, 2H), 2.1 (s, 3H) \) ppm

\(^{13}\)C NMR : (100 MHz) \(\delta = 206.6, 188.9, 147.9, 144.2, 139.4, 130.9, 130.0, 129.2, 128.9, 128.7, 127.5, 126.5, 62.9, 45.4, 31.5 \) ppm

MS (EI) : \(m/z\) 293 (M+1)

2.4.5 Reaction of acetone with 3-phenyl-4-(trimethylsilyl)-cyclobutene-1,2-dione 142 in the presence of L-proline catalyst

To a solution of L-proline (0.017 g, 30 mol %) in DMSO (2 mL), acetone (0.3 mL) was added and stirred for 15 min. at 25 °C. 3-Phenyl-4-(trimethylsilyl)-cyclobut-3-ene-1,2-dione (0.115 g, 0.5 mmol) in DMSO (2 mL) was added dropwise. The contents were stirred for 15 min. The reaction mixture was treated with 5 mL of saturated NH\(_4\)Cl solution and extracted with ethyl acetate (3x10 mL). The combined organic extract was washed with brine solution and dried over anhydrous Na\(_2\)SO\(_4\). The solvent was removed and the
residue was subjected to column chromatography (silica gel, hexane-EtOAc). Ethyl acetate (20%) in hexane eluted the (Z)-3-(2-hydroxyprop-1-enyl)-4-phenylcyclobutene-1,2-dione 148.

![Chemical structure](image)

Yield : 0.080 g (75%)

mp : 152-154 °C

IR (KBr) : 3449, 1753, 1712 cm⁻¹

¹H NMR : (400 MHz) δ = 11.45 (s, 1H), 8.03-8.01 (m, 2H), 7.57-7.52 (m, 3H), 5.84 (s, 1H), 2.23 (s, 3H) ppm (Spectrum No. 41)

¹³C NMR : (100 MHz) δ = 202.9, 188.6, 182.4, 178.5, 176.9, 133.0, 129.4, 129.3, 128.3, 92.9, 23.3 ppm (Spectrum No. 42)

MS (EI) : m/z 213 (M-1)

Analysis : for C₁₃H₁₀O₃

Calculated: C, 72.89%; H, 4.71%

Found: C, 72.95%; H, 4.66%

The above procedure was followed for the reaction of acetone with other cyclobutenediones.
Yield : 0.068 g (60%)

mp : 148-150 °C

IR (KBr) : 3437, 1761, 1707 cm⁻¹

¹H NMR : (400 MHz) δ = 11.46 (s, 1H), 7.93 (d, J = 7.2 Hz, 2H), 7.34 (d, J = 7.2 Hz, 2H), 5.81 (s, 1H), 2.45 (s, 3H), 2.22 (s, 3H) ppm (Spectrum No. 43)

¹³C NMR : (100 MHz) δ = 202.5, 188.8, 181.8, 178.6, 176.3, 144.3, 130.1, 128.3, 126.8, 92.9, 23.2, 22.0 ppm (Spectrum No. 44)

MS (EI) : m/z 229 (M+1)

Analysis : for C₁₄H₁₂O₃

Calculated: C, 73.67%; H, 5.30%

Found: C, 73.55%; H, 5.38 %
Yield : 0.079 g (65%)

mp : 150-152 °C

IR (KBr) : 3472, 1766, 1699 cm⁻¹

¹H NMR : (400 MHz) δ = 11.49 (s, 1H), 8.02 (d, J = 8.8 Hz, 2H), 7.03 (d, J = 8.8 Hz, 2H), 5.78 (s, 1H), 3.90 (s, 3H), 2.21 (s, 3H) ppm

¹³C NMR : (100 MHz) δ = 201.9, 188.9, 180.7, 175.8, 163.5, 130.6, 122.4, 114.9, 92.8, 55.6, 23.2 ppm

MS (EI) : m/z 245 (M+1)

Analysis : for C₁₄H₁₂O₄

Calculated: C, 68.85%; H, 4.95%

Found: C, 68.71%; H, 4.86%

Yield : 0.064 g (52%)

mp : 134-136 °C

IR (KBr) : 3491, 1761, 1712 cm⁻¹

¹H NMR : (400 MHz) δ = 11.47 (s, 1H), 7.96 (d, J = 8.8 Hz, 2H), 7.52 (d, J = 8.8 Hz, 2H), 5.80 (s, 1H), 2.24 (s, 3H) ppm
**Experimental Section**

\[ ^{13}\text{C} \text{NMR} \quad (100 \text{ MHz}) \delta = 202.6, 188.2, 182.3, 177.5, 176.7, 139.2, 129.8, 129.4, 127.7, 92.9, 23.3 \text{ ppm} \]

**MS (EI)** : \( m/z \) 249 (M+1)

**Analysis** : for C\(_{13}\)H\(_9\)ClO\(_3\)

Calculated: C, 62.79%; H, 3.65%

Found: C, 62.59%; H, 3.71%

Yield : 0.066 g (58%)

mp : 132-134 °C

IR (KBr) : 3540, 1747, 1712 cm\(^{-1}\)

\[ ^{1}\text{H} \text{NMR} \quad (400 \text{ MHz}) \delta = 11.46 \text{ (s, 1H)}, 7.81 \text{ (s, 1H)}, 7.80-7.78 \text{ (m, 1H)}, 7.45-7.37 \text{ (m, 2H)}, 5.84 \text{ (s, 1H)}, 2.44 \text{ (s, 3H)}, 2.23 \text{ (s, 3H)} \text{ ppm} \]

\[ ^{13}\text{C} \text{NMR} \quad (100 \text{ MHz}) \delta = 202.9, 188.7, 182.4, 178.8, 176.7, 139.2, 133.9, 129.3, 129.2, 128.8, 125.4, 92.9, 23.3, 21.4 \text{ ppm} \]

**MS (EI)** : \( m/z \) 229 (M+1)

**Analysis** : for C\(_{14}\)H\(_{12}\)O\(_3\)

Calculated: C 73.67%; H, 5.30%

Found: C, 73.75%; H, 5.22%
Yield : 0.068 g (55%)

IR (KBr) : 3443, 1745, 1714 cm\(^{-1}\)

\(^1\)H NMR : (400 MHz) \(\delta = 11.46\) (s, 1H), 7.96 (s, 1H), 7.93-7.91 (m, 1H), 7.57-7.49 (m, 2H), 5.84 (s, 1H), 2.28 (s, 3H) ppm

\(^13\)C NMR : (100 MHz) \(\delta = 202.9, 188.0, 182.7, 177.9, 176.4, 135.4, 132.6, 130.7, 130.6, 127.7, 126.2, 92.9, 23.4\) ppm

MS (EI) : \(m/z 247\) (M-1)

Analysis : for C\(_{13}\)H\(_9\)ClO\(_3\)

Calculated: C, 62.79%; H, 3.65%

Found: C, 62.85%; H, 3.61%

2.4.6 Preparation of 3-ethyl-4-phenylcyclobut-3-ene-1,2-dione 110

Magnesium turnings (1mmol, 0.024 g) were treated with bromoethane (1 mmol, 0.07 mL) in THF (5 mL) for 1 h at 25 °C. The ethyl magnesium bromide prepared in this way was added slowly to the solution of 3-phenyl-4-(trimethylsilyl)-cyclobutene-1,2-dione (0.230 g, 1 mmol) in THF (10 mL) at −40 °C. The contents were stirred for 15 min at the same temperature. The reaction mixture was brought to room temperature and quenched
with saturated NH₄Cl solution (5 mL) and extracted with diethyl ether (3x10 mL). The combined organic extract was washed with brine solution and dried over anhydrous Na₂SO₄. The solvent was removed and the residue was subjected to column chromatography (silica gel, hexane-EtOAc). Ethyl acetate (3%) in hexane eluted the 3-ethyl-4-phenylcyclobutenedione 110.

![Diagram of reaction](attachment:reaction_diagram.png)

**Yield**: 0.083 g (45%)

The IR, ¹H NMR and ¹³C NMR data show 1:1 correspondence with the data of the compound previously obtained in the reaction of ethyl phenyl acetylene with the Fe(CO)₅/NaH/MeI reagent system (Chapter 1).

The above procedure was followed for the addition of other Grignard reagents to 3-phenyl-4-(trimethylsilyl) cyclobutenedione 142.

![Diagram of reaction](attachment:reaction_diagram2.png)

**Yield**: 0.092 g (46%)

The IR, ¹H NMR and ¹³C NMR data show 1:1 correspondence with the data of the compound previously obtained in the reaction of 1-phenyl-1-pentyn with the Fe(CO)₅/t-BuOK reagent system (Chapter 1).
Yield : 0.109 g (51%)

The IR, $^1$H NMR and $^{13}$C NMR data show 1:1 correspondence with the data of the compound previously obtained in the reaction of 1-phenyl-1-hexyne with the Fe(CO)$_5$/t-BuOK reagent system (Chapter 1)

Yield : 0.091 g (40%)

IR (KBr) : 1751 cm$^{-1}$

$^1$H NMR : (400 MHz) $\delta$ = 8.02-8.00 (m, 2H), 7.59-7.56 (m, 3H), 3.05 (t, $J$ = 7.6 Hz, 2H), 1.89-1.82 (m, 2H), 1.46-1.36 (m, 4H), 0.91 (t, $J$ = 7.2 Hz, 3H). ppm

$^{13}$C NMR : (100 MHz) $\delta$ = 198.5, 198.1, 197.4, 190.6, 133.5, 129.5, 128.5, 32.0, 27.7, 25.7, 22.3, 13.9. ppm

MS (EI) : $m/z$ 227(M-1)
Yield : 0.101 g (42%)

IR (KBr) : 1766 cm$^{-1}$

$^1$H NMR : (400 MHz) $\delta$ = 8.03-8.01 (m, 2H), 7.59-7.57 (m, 3H), 3.05 (t, $J$ = 7.6 Hz, 2H), 1.89-1.81 (m, 2H), 1.45-1.32 (m, 6H), 0.89 (t, $J$ = 6.8 Hz, 3H). ppm

$^{13}$C NMR : (100 MHz) $\delta$ = 198.5, 198.1, 197.4, 190.5, 133.4, 129.4, 128.5, 31.4, 29.6, 27.8, 26.0, 22.4, 14.0. ppm

MS (EI) : m/z 243 (M+1)

Analysis : for C$_{16}$H$_{18}$O$_2$

Calculated: C, 79.31%; H, 7.49%

Found: C, 79.15%; H, 7.41%
2.5 References


References


