Ring Expansion of Carbocyclic \( \beta \)-Keto-ester with Acetylenic Esters

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Diaryl-2-cyclohexen-1-one, Bicyclooctadienone, Ring Expansion Reaction, Cyclooctadienone

The \( \beta \)-keto-ester \( 1 \mathbf{b} \) and \( 7 \) reacted with dimethyl acetylenedicarboxylate (DMAD) to give the cyclooctadienone derivatives \( (2 \mathbf{a} \text{ and } 3 \mathbf{b}) \), the acid hydrolysis of which afforded the anhydride \( 4 \).

Also \( 1 \mathbf{a}, \mathbf{b} \) reacted with ethyl propiolate and gave substituted cyclooctadienone \( (6 \mathbf{a}, \mathbf{b}) \). Michael reaction of \( 11 \) with DMAD gave adduct \( 12 \) which underwent cyclization via photo-cycloaddition \((2+2)\) to give the photo-product \( 14 \).

Introduction

It was reported recently [1–3] that the Michael adducts from dimethyl acetylenedicarboxylate (DMAD) and 4-carboethoxy-1-benzazepin-5-one or 2-carboethoxy-6-methoxytetralone-1 undergo ring expansion simultaneously to give 1-benzoazininone and benzocyclooctenone derivatives respectively. In a previous paper [4] we described the successful application of a novel ring expansion involving reaction of the sodio derivative of 2-cyclohexen-1-one-6-carboxylate with DMAD. Here we report more of other novel derivatives of the above \( \beta \)-keto-ester.

Results and Discussion

The reaction of the sodium salts of ethyl 3-phenyl- or (3-styryl)-5-phenyl-2-cyclohexen-1-one-6-carboxylate \( (1 \mathbf{a}, \mathbf{b}) \) [5] with DMAD gave a mixture of two isomeric compounds, which were identified as dimethyl ethyl 1-oxo-3,5-diphenyl-2,6- (or 2,7)-cyclooctadiene-6,7,8-tricarboxylate \( (2 \mathbf{a}, 3 \mathbf{a}) \) [4] and dimethyl ethyl 1-oxo-3-styryl-5-phenyl-2,6- (or 2,7)-cyclooctadiene-6,7,8-tricarboxylate \( (2 \mathbf{b}, 3 \mathbf{b}) \), as a tautomeric mixture which was found difficult to separate in adequate amounts for further investigation.

However, it was shown from the NMR spectrum of \( 2 \mathbf{b}, 3 \mathbf{b} \) mixture to contain 80% of \( 2 \mathbf{b} \) and 20% of \( 3 \mathbf{b} \). In particular, compound \( 2 \mathbf{b} \) showed a singlet at \( \delta \) 12.6 for the enolic proton, whereas, for \( 3 \mathbf{b} \) the enolic proton appeared at 12.3. These enolic protons disappear when shaken with \( \text{D}_2\text{O} \) which confirms that this compound is almost found in its enolic form.

The products showed the chemical properties expected for \( \beta \)-keto-esters; thus acid hydrolysis of both using acetic acid-hydrochloric acid mixture gave only the keto-anhydride derivative \( (4) \) in good yield. This was esterified with 10% sulphuric acid in ethanol to give diethyl 1-oxo-3,5-diphenyl-2,6-cyclooctadiene-6,7-dicarboxylate \( (5) \).

Formulation of structure \( 4 \) and \( 5 \) was based on elemental and spectral analysis. The IR spectrum of \( 4 \) showed bands at 1820 and 1780 cm\(^{-1}\) attributable to the anhydride. The IR spectrum of \( 5 \) showed band at 1710 cm\(^{-1}\) characteristic for the carbonyl group of the ester. The NMR spectrum of \( 5 \) showed a quartet at \( \delta \) 4 and 3.9 for 2 CH\(_2\)O, and a triplet at 1.2 and 1.1 for 2 CH\(_3\).

On the other hand, enlargement of the ring of the sodio derivatives of \( 1 \mathbf{a}, \mathbf{b} \) has been affected by ethyl propiolate to give diethyl 1-oxo-3-phenyl- (or

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3-styryl)-5-phenyl-2,6-cyclooctadiene-6,8-dicarboxylate (6a, b).

The structure of 6a, b was assigned from their analytical and spectral data. The NMR spectrum showed a singlet at $\delta$ 12.7 for 1H at C8, singlets at 6.4 for 1H at C6 and at 6 for 1H at C7.

Michael reaction of ethyl 2-oxo-4,8-diphenylbicyclo[4.2.0]octane-1,5-diene-3-carboxylate (7) [6] with DMAP was performed with the expectation that a dimethyl ethyl 2-oxo-6,10-diphenylbicyclo[6.2.0]decan-1,4,7-triene-3,4,5-tricarboxylate (8) will be formed, via ring expansion.

The NMR spectrum of 8 displayed a singlet at $\delta$ 12.7 for the proton at C3, two singlets at 3.7 and 3.4 for the two methyl groups of methyl esters, a quartet at 3.8 for the methylene group of the ethyl ester, and a triplet at 0.9 for the methyl group of the ethyl ester.

A part of our study was directed toward the use of 3-styryl-5-phenyl-2-cyclohexenone (11) [5] instead of the $\beta$-keto-ester 1, and we found that 11 with DMAP afforded only the adduct 12 and no dimethyl $\beta$-oxo-3-styryl-5-phenyl-2,6-cyclooctadiene-7,8-dicarboxylate (13) was formed.

It was reported [7, 8] that isopiperitenone (9) undergoes photocyclization to give the predicted product (10).

Irradiation of the adduct (12) with ultraviolet light gave dimethyl 6-oxo-2-styryl-4-phenyl-tricyclo[3.3.0.0^2_7]octane-1,8-dicarboxylate (14) [(2+2) photo-cycloaddition].

The NMR spectrum of 12 showed two singlets at $\delta$ 3.4 and 3.6 for the two CH$_3$ esters, and a singlet at 4.3 for the protons of the maleic ester side chain. Whereas, the main characteristic feature of the NMR of the product 14 is the presence of multiplet at $\delta$ 2.9–3.8 for 10 protons (2 OCH$_3$, 1H at C-4, 1H at C-5, 1H at C-7, and 1H at C-8).

**Experimental**

All melting points (°C) are uncorrected and were taken in a Fischer electric melting point apparatus. IR spectra were performed on a Unicam SP2000 infrared spectrophotometer using KBr. NMR spectra were obtained in CDCl$_3$ solution with a Varian model EM 360 A.

**General procedure for the preparation of cyclooctadienone derivatives from cyclohexenones**

To sodium hydride (50% dispersion in oil; 0.4 g; 0.02 mol) in dry toluene (30 ml) under nitrogen, $\beta$-keto-ester (1a, b and 7) (0.01 mol) was added with stirring over 0.5 h. The white paste so obtained was stirred at room temperature for 1 h, and then cooled to 0–5°C. While stirring dimethyl acetylenedicarboxylate (DMAD) or ethyl propiolate (0.016 mol) was added during 1 h, keeping the temperature of the reaction mixture below 10°C. After 5 h at this temperature the reaction was shown by TLC to be complete. The reaction mixture was cooled before adding acetic acid (6 ml) followed by hydrochloric acid (2 M; 10 ml), and the aqueous layer separated and washed with toluene (3×10 ml). The organic phase was washed with water (10 ml), dried and evaporated under reduced pressure to give dark red gum which crystallized from ethanol to afford colourless crystals in 60–70% yield.

(a) Dimethyl ethyl $\beta$-oxo-5-phenyl-3-styryl-2,6-(and 2,7)-cyclooctadiene-7,8-dicarboxylate (2b and 3b) was obtained in 70% yield from 1b (3.46 g; 0.01 mol) and DMAD (2.34 g; 0.016 mol), m.p. 175°C.

Analysis for C$_{21}$H$_{23}$O$_7$ (488.543) Calcd C 71.30 H 5.77, Found C 71.19 H 5.98.

IR: 1710 (esters), 1650 (CO) and 1600 cm$^{-1}$ (C=C). The NMR spectrum showed that this product contains compound 2b (80%) and the tautomer 3b (20%).

Tautomer 2b: NMR: $\delta$ 0.9 (t, 3H, OCH$_2$CH$_3$), 3.25 (m, 2H, 4-H$_2$), 3.7 (s, 3H, CO$_2$CH$_3$ at C-7), 3.85 (s, 3H, CO$_2$CH$_3$ at C-8), 4.0 (q, 2H, OCH$_2$CH$_3$), 4.85 (m, 1H, 5-H), 6.1 (s, 1H, 2-H), 6.5 (s, 1H, CH=CH), 6.8–7.1 (m, 10H, aromatic and 1H, CH=CH) and 12.6 (s, 1H, 8-H).

Tautomer 3b: NMR: $\delta$ 1.1 (t, 3H, OCH$_2$CH$_3$), 4.05 (q, 2H, OCH$_2$), 6.4 (s, 1H, 2-H), 12.3 (s, 1H, 6-H), the remaining signals at 3b are the same as 2b.

(b) Diethyl $\beta$-oxo-3,5-diphenyl-2,6-cyclooctadiene-6,8-dicarboxylate (6a) and diethyl $\beta$-oxo-3-styryl-2,6-cyclooctadiene-6,8-dicarboxylate (6b) were...
Table I. Elemental analyses of 6a, b.

<table>
<thead>
<tr>
<th>Compound</th>
<th>M.p. [°C]</th>
<th>Formula (mol.wt.)</th>
<th>Carbon [%] Caled Found</th>
<th>Hydrogen [%] Caled Found</th>
</tr>
</thead>
<tbody>
<tr>
<td>6a</td>
<td>60</td>
<td>C₂₉H₂₅O₅ (418.494)</td>
<td>74.62 74.65</td>
<td>6.26 6.27</td>
</tr>
<tr>
<td>6b</td>
<td>158</td>
<td>C₂₉H₂₅O₅ (444.532)</td>
<td>75.65 75.63</td>
<td>6.35 6.13</td>
</tr>
</tbody>
</table>

obtained in 60 and 65% yield from 1a or 1b (3.2 g, or 3.46 g: 0.01 mol) and ethyl propiolate (1.6 g, 0.016 mol). The results of the elemental analysis are given in Table I.

NMR (6a): δ 1.1 (t, 3H, OCH₃ at C-6), 1.2 (t, 3H, OCH₂CH₃ at C-8), 1.7 (m, 2H, 4-H₂), 2 (s, 1H, 2-H), 3 (m, 1H, 5-H), 4.1 (q, 2H, OCH₂), 6 (s, 1H, 7-H), 6.4 (s, 2H, aromatic) and 6.7 (s, 1H, 2-H) and 7.2 (m, 10H, aromatic) and 12.7 (s, 1H, 3-H).

(a) Diethyl methyl 2-oxo-6,10-diphenyl-bicyclo[6.2.0]decane-l,4,7-triene-3,4,5-tricarboxylate (8) was prepared in 70% yield via the reaction of 7 (3.46 g, 0.01 mol) with DMAD (2.34 g, 0.016 mol), m.p. 180 °C.

Analysis for C₂₆H₂₄O₅ (416.478)
Caled C 74.98 H 5.80.
Found C 74.71 H 6.18.

IR: 1710 (ester), and 1600 cm⁻¹ (C=C).
NMR: δ 1.1 (t, 3H, OCH₂CH₃), 1.2 (t, 3H, OCH₂CH₃), 2.8 (m, 1H, 5-H), 3 (s, 2H, 4-H₂), 3.8 (m, 4H, 8-H and OCH₂), 4 (q, 2H, OCH₂), 5.8 (s, 1H, 1H, 2-H) and 6.9–7.1 (s, 10H, aromatic).

3-Styryl-5-phenyl-6-(1',2'-dimethoxycarbonyl-ethylenyl)-2-cyclohexenone (12)

This compound was synthesized in the same manner as above for the preparation of cyclooctadienones, from 11 (2.74 g, 0.01 mol) and DMAD (2.34 g, 0.016 mol) in 70% yield (ethanol), m.p. 203 °C.

Analysis for C₃₂H₂₈O₅ (416.478)
Caled C 74.98 H 5.80.
Found C 74.59 H 6.04.

IR: 1710 (ester), and 1600 cm⁻¹ (C=C).
NMR: δ 2.8 (s, 1H, 5-H), 3.1 (s, 2H, 4-H₂), 3.4 (s, 3H, OCH₃), 3.6 (s, 3H, OCH₃), 4.3 (s, 1H, COCH=CCO), 5.8 (s, 1H, CH=CH), 6.4 (s, 1H, CH=CH), 6.7–7.1 (s, 11H, aromatic and CH=CH) and 12.4 (s, 1H, 6-H).

3,5-Diphenyl-2,6-cyclooctadiene-1-one-6,7-dicarboxylic acid anhydride (4)

Compound (2a and 3a) (6.93 g, 0.015 mol) glacial acetic acid (120 ml), water (18 ml) and hydrochloric acid (18 ml) were refluxed for 72 h, after which evaporation under reduced pressure gave dark red gum which crystallized from toluene to give pale yellow crystals in 65% yield, m.p. 80 °C.

Analysis for C₂₆H₂₄O₅ (344.370)
Caled C 76.73 H 4.68.
Found C 77.01 H 4.55.

IR: 1820 and 1780 (anhydride), 1690 (CO), and 1610 cm⁻¹ (C=C).
NMR: δ 1.1 (s, 1H, 8-H), 2 (s, 2H, 4-H₂), 2.6 (m, 1H, 5-H), 6.2 (s, 1H, 2-H), 6.8–7.2 (m, 10H, aromatic) and 8.1 (s, 1H, enolic OH).

Diethyl-1-oxo-3,5-diphenyl-2,6-cyclooctadiene-6,7-dicarboxylate (5)

A solution of 4 (3.44 g, 0.01 mol) in ethanol (20 ml) and concentrated sulphuric acid (2 ml) was refluxed for 3 h. The reaction mixture was evaporated under reduced pressure gave dark red gum which crystallized with ethanol to give pale yellow crystals in 55% yield, m.p. 90 °C.

Analysis for C₂₂H₁₆O₄ (418.494)
Found C 74.45 H 6.35.

IR: 1710 (ester), and 1600 cm⁻¹ (C=C).
NMR: δ 1.1 (t, 3H, OCH₂CH₃), 1.2 (t, 3H, OCH₂CH₃), 2.8 (m, 1H, 5-H), 3 (s, 2H, 4-H₂), 3.8 (m, 4H, 8-H and OCH₂), 4 (q, 2H, OCH₂), 5.8 (s, 1H, 1H, 2-H) and 6.9–7.1 (s, 10H, aromatic).

3-Styryl-5-phenyl-6-(1',2'-dimethoxycarbonyl-ethylenyl)-2-cyclohexenone (12)

This compound was synthesized in the same manner as above for the preparation of cyclooctadienones, from 11 (2.74 g, 0.01 mol) and DMAD (2.34 g, 0.016 mol) in 70% yield (ethanol), m.p. 203 °C.

Analysis for C₃₂H₂₈O₅ (416.478)
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Found C 74.59 H 6.04.

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NMR: δ 2.8 (s, 1H, 5-H), 3.1 (s, 2H, 4-H₂), 3.4 (s, 3H, OCH₃), 3.6 (s, 3H, OCH₃), 4.3 (s, 1H, COCH=CCO), 5.8 (s, 1H, CH=CH), 6.4 (s, 1H, CH=CH), 6.7–7.1 (s, 11H, aromatic and CH=CH) and 12.4 (s, 1H, 6-H).

Dimethyl-2-styryl-4-phenyl-tricyclo[3.3.0.0²⁷]octan-6-one-1,8-dicarboxylate (14)

A solution of 12 (3.92 g, 0.01 mol) in benzene (500 ml) was irradiated with a 500 W Hg lamp at 20–25 °C in a quartz vessel for 80 h. By this time the reaction was shown by TLC to be complete. The solvent was removed under reduced pressure to give pale yellow crystals in 60% yield, m.p. 212 °C.

Analysis for C₃₄H₃₄O₆ (516.576)
Caled C 74.98 H 5.80.
Found C 74.71 H 6.18.

IR: 1710 (ester), and 1600 cm⁻¹ (C=C).
NMR: δ 2 (broad, 2H, 3-H₂), 2.9–3.8 (m, 10H, 2 OCH₃, 4-H₂, 5-H, 7-H and 8-H), 6.7 (s, 1H, CH=CH) and 6.8–7.1 (s, 11H, aromatic and CH=CH).