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[8+2] Cycloaddition Reactions of 2H-Cyclohepta[b]furan-2-one with Acyclic 1,3-Dienes: A Facile Route to Novel Bicyclo [5.3.0] ring Systems.[#]

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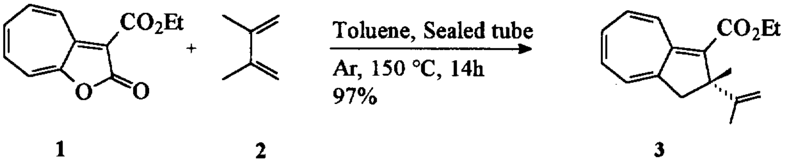
Abstract: Novel [8+2] cycloaddition reactions of 3-ethoxy carbonyl 2H-cyclohepta[b]furan-2-one with acyclic 1,3-dienes are described. The potential application of this process in the synthesis of modified colchicinoids incorporating bicyclo [5.3.0] ring systems has also been studied.

The cycloaddition reactions of troponoid systems have received considerable attention.[1] In addition to the common [6+4] addition mode, some of these systems are known to undergo [8+2] cycloaddition yielding azulene derivatives.[2] In the context of our interest in the cycloaddition reactions of fulvenoids,[3] we have been exploring the chemistry of 3-ethoxy carbonyl 2H-cyclohepta[b]furan-2-one **1**.[4] Most of the previous studies on this system have involved mainly its [8+2] addition with electron rich dienophiles and [4+2] addition with electron deficient dienophiles.[5,6] We have now examined the reactivity of **1** with dienes and our preliminary results are presented in this communication.

The reaction of **1** with a variety of acyclic 1,3-dienes was found to proceed exclusively in an [8+2] addition mode, resulting in novel substituted [5.3.0]ring systems. The reaction of **1** with 2,3-dimethylbutadiene **2** is illustrative (Scheme 1).[7]



Scheme 1

The product **3** was chromatographically purified. The IR spectrum of **3** showed only one carbonyl absorption at 1686 cm^{-1}, indicating that the reaction proceeded in an [8+2] pathway followed by

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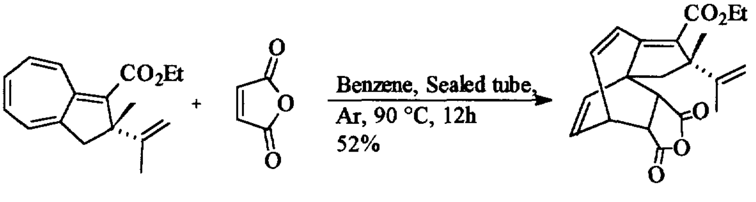
[#] *This paper is dedicated with respect and affection to Professor R. H. Sahasrabudhey* decarboxylation. The structure was further confirmed by the ^{1}H NMR spectrum, which showed the characteristic doublet at δ 7.47 (J=12.29 Hz) corresponding to the olefinic proton at C-8 position. The ^{13}C NMR showed only one carbonyl at δ 166.54.[8] Conclusive evidence for the regio and stereochemistry of **3** was derived from single crystal X-ray analysis of **5** obtained by the [4+2] cycloaddition of **3** with maleic anhydride (Scheme 2).[9]

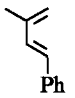
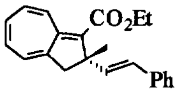
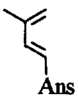
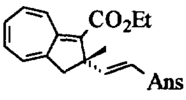
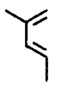
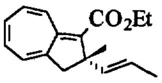
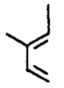
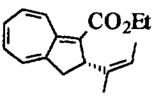


3 **4** **5**

Scheme 2

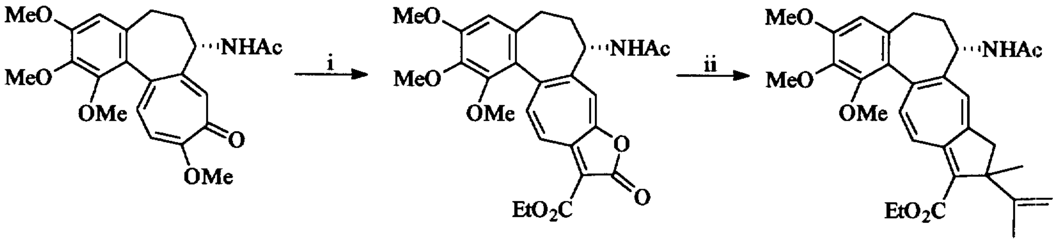
The [8+2] cycloaddition of **1** with acyclic 1,3 dienes leading to dihydroazulenes appears to be a general reaction . The results obtained with various dienes are summarised in Table 1.

Table 1. Cycloaddition reactions of **1** with acyclic 1,3- dienes

Entry	Diene	Product*	Yield (%)^a
1^{i}			71
2^{i}			51
3^{ii}			86
4^{ii}			90

Reaction conditions (i) Toluene, Sealed tube, Ar, 130 °C, 14h. (ii) Xylene, Sealed tube, Ar, 150 °C, 5h.
(a) Yield based on unreacted **1**. * Regio and stereochemical assignment is based on analogy with **3**.

The versatility of the process described herein was attested by its application to the furanone **8** derived from the antimitotic agent colchicine (Scheme 3).



7 8 9

i) Na, $H_2C(COOEt)_2$, dry ether/benzene, RT, 14h, 60%. ii) Dimethyl butadiene, Xylene, Sealed tube, Ar, 190 °C, 36h, 74%.

Scheme 3

The tetracyclic compounds **8** and **9** were characterized by spectral analysis. The IR spectrum of **8** showed the characteristic broad carbonyl absorptions at 1777 cm^{-1} and 1681 cm^{-1} corresponding to the lactone and ester carbonyl groups respectively. The [8+2] adduct **9** showed the absorption at 1680 cm^{-1} in the IR spectrum, ^1H and ^{13}C NMR were also in accordance with the proposed structure.

In order to explain the observed reactivity we have carried out some MNDO and AM1 calculations using MOPAC program.[10] It was clear from the calculations that HOMO(1)-LUMO(diene) interaction controls the [8+2] additions. The observed regiochemistry was also in agreement with the calculated orbital coefficient values.

In conclusion, we have observed a facile [8+2] addition of 2H-cyclohepta[b]furan-2-one systems with acyclic 1,3-dienes which is potentially applicable to the synthesis of modified colchicinoids incorporating bicyclo [5.3.0] ring system. Further work is in progress.

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7. Typical experimental procedure: A solution of 3-ethoxycarbonyl-2H-cyclohepta[b]- furan-2-one (0.218 g, 1 mmol) and 2,3-dimethylbutadiene (0.410 g, 5 mmol) in dry toluene (0.5 mL) was sealed under argon in a Schlenk glass tube and heated at 150 °C for 14 h. The reaction mixture was subjected to chromatography on a silica gel column (1% ethyl acetate-hexane) to afford 3 (0.175 g, 97%) as a blood red viscous liquid. The unreacted furanone (0.064 g) was recovered using 30% ethyl acetate-hexane as the eluent.
8. Spectral data for 3; IR(KBr) 2972, 1686, 1540, 1449, 1400, 1260, 1156, 1053, 882, 784 cm^{-1}. ^1H NMR($CDCl_3$) δ ppm. 7.47 (d, J=12.29 Hz, 1H), 6.00 (m, 4H), 4.72 (d, 2H), 4.12 (q, 2H), 2.53 (dd, 2H), 1.710 (s, 3H), 1.38 (s, 3H), 1.22 (t, 3H). ^{13}C NMR ($CDCl_3$) δ ppm. 166.54, 156.32, 153.20, 151.12, 133.05, 132.97, 130.92, 129.919, 129.914, 124.55, 108.70, 59.47, 51.14, 48.27, 25.66,20.63, 14.39. HRMS : $C_{17}H_{20}O_2$: 256.14633; Found: 256.14628.
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