

## Intramolecular Diels–Alder Reaction of 1-Ethoxycarbonyl-4-alkenylcyclopentadienes

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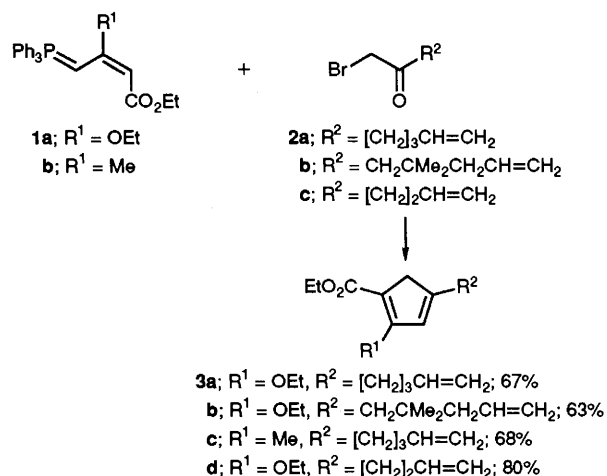
4-(But-3-enyl)- and 4-(pent-4-enyl)-1-ethoxycarbonyl-2-ethoxycyclopentadiene, prepared from allylidetriphenylphosphorane and  $\alpha$ -haloketones, underwent a regioselective intramolecular Diels–Alder reaction to give two types of the functionalized tricyclic products depending on the linking carbon-chain length.

The intramolecular Diels–Alder reaction using cyclopentadienes as the diene is a powerful tool for the construction of naturally occurring cyclopentanoids.<sup>1</sup> It is well documented that the thermal reaction of alkenylcyclopentadienes provides several types of tricyclic [2 + 4] cycloaddition products, depending on the linking carbon-chain length between the cyclopentadiene and the dienophile, by rapid 1,5-sigmatropic migration.<sup>1,2</sup> However, there are few precedents for the intramolecular Diels–Alder reaction of di- or tri-substituted cyclopentadienes owing to the general inaccessibility of the regioselective construction method and rapid 1,5-sigmatropic migration<sup>3</sup> in these cyclopentadienes. Recently, we reported the regioselective formation of substituted cyclopentadienes

from allylidetriphenylphosphorane and  $\alpha$ -haloketones.<sup>4</sup> This led us to investigate the intramolecular Diels–Alder reaction of trisubstituted cyclopentadienes **3** linked by a two or three carbon chain to an alkene. We now report preliminary results on the regio- and stereo-chemical outcome of the thermal reactions of compounds **3**.

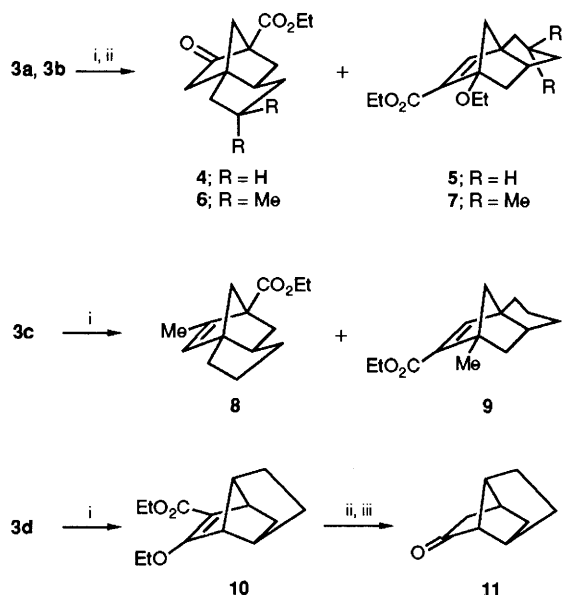
The cyclopentadienes **3a–d** were prepared in good yields according to the reported method<sup>4</sup> (Scheme 1). 3-Ethoxyallylidetriphenylphosphorane **1a** reacted with 1 equiv. of the  $\alpha$ -bromoketones **2a–c** in dichloromethane in the presence of  $\text{Cs}_2\text{CO}_3$  at 30 °C to give good yields of **3a**, **3b** and **3d**. The reaction of **1b** with **2a** was conducted in a two-phase system of  $\text{CH}_2\text{Cl}_2$ –aqueous  $\text{NaHCO}_3$  at room temperature. These cyclopentadienes were unchanged upon heating in boiling benzene for 6 h.

The cyclopentadienes **3a–c**, having a three-carbon link, underwent intramolecular Diels–Alder reactions at 140 °C (Scheme 2). The regioselectivity depended on the substituents and the reaction temperature. When a benzene solution of compound **3a** was heated at 140 °C for 6 h in an autoclave and then treated with aqueous acid, two products **4** and **5** were obtained in a ratio of 88:12<sup>†</sup> in 56% total yield, with 42% recovery of **3a**. The minor product **5** may arise from **12a** by 1,5-sigmatropic migration (Scheme 3). However, **12a** was not detected in the recovered cyclopentadiene. This implies that **12a**, in very low equilibrium concentration at 140 °C, undergoes an intramolecular Diels–Alder reaction more easily than **3a**. Prolonged heating at 140 °C for 48 h gave **4** and **5** in 92% yield (**4**:**5** = 86:14) but heating at 180 °C for 6 h reduced the



Scheme 1

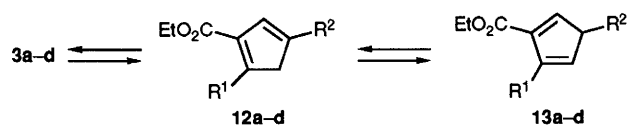
<sup>†</sup> The ratios of the isomers were determined by GLC (3 m DC-550 silicone column, 180 °C).



**Scheme 2** Reagents and conditions: i, heat in benzene ( $0.01 \text{ mol dm}^{-3}$ ) in an autoclave; for the conditions see text; ii, aq.  $2 \text{ mol dm}^{-3}$  HCl,  $\text{CHCl}_3$ , room temp.; iii, NaCl,  $\text{Me}_2\text{SO}$ ,  $\text{H}_2\text{O}$ ,  $140^\circ\text{C}$ , 8 h

selectivity (**4**:**5** = 78:22, 95% yield). Previous examples demonstrate exclusive formation of the *exo*-adduct from cyclopentadienes having a three-carbon link.<sup>1,5</sup> We also confirmed the *exo*-orientation of the linking carbon chain in the main product **4** by an X-ray crystallographic study of the carboxylic acid derived from **4**. An improved regioselectivity was obtained with **3b** having a geminal dimethyl group in the side chain, which gave, on heating in benzene at  $140^\circ\text{C}$  for 6 h, followed by acid hydrolysis, **6** and **7** in a ratio of 96:4 in 95% total yield. The high yield and high regioselectivity can be explained on the basis of acceleration of cyclization by the geminal dimethyl group of the side chain.<sup>6</sup> On the other hand, the 3-methylcyclopentadiene **3c** showed poor selectivity giving **8** and **9** in a 64:36 ratio and 82% total yield under the same conditions ( $140^\circ\text{C}$ , 6 h).

When the two-carbon linked cyclopentadiene **3d** was heated at  $200^\circ\text{C}$  for 24 h in benzene, a single Diels–Alder reaction product **10** was obtained in 76% yield. The structure of **10** was proved by conversion to the known tricyclic ketone **11**, brexan-5-one,<sup>7</sup> by acid treatment followed by decarboxylation



**Scheme 3**

(91% total yield). The Diels–Alder precursor of **10** must be **13d** and the high regioselectivity may be attributable to the directing effect of both the ethoxy and the ethoxycarbonyl groups.<sup>8</sup>

In conclusion, we have demonstrated that readily available ethoxycyclopentadienes with two- or three-carbon linked dienophiles underwent an inverse electron demand, intramolecular, Diels–Alder reaction in a highly regio- and stereo-selective manner. Further elaboration of the keto ester **6** towards the synthesis of natural cyclopentanoids is currently underway in our laboratories.

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