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MOLECULAR STRUCTURES OF ENDO[4+2]π AND EXO[6+4]π CYCLOADDUCTS VIA CYCLOADDITION REACTION OF N-ETHOXYCARBONYLAZEPINE WITH 2,5-DIMETHOXYCARBONYL-3,4-DIPHENYLCYCLOPENTADIENONE

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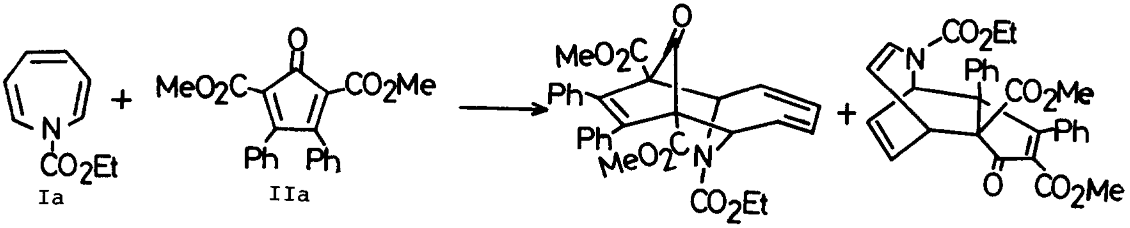
Summary The cycloaddition reaction of N-ethoxycarbonyl-1H-azepine with 2,5-dimethoxycarbonyl-3,4-diphenylcyclopentadienone gave anti-endo [4+2]π and exo [6+4]π cycloadducts These structures were fully identified by X-ray crystallographic techniques Mechanism for their cycloaddition reactions are also discussed

Chemistry of seven-membered ring unsaturated compounds has attracted much attentions because of their interesting features in cycloaddition reaction and much efforts have been made to establish their capability for cycloaddition. However, there is only one report concerning the isolation of [6+4]π cycloadduct from 1H-azepine and diene such as tetracyclone in very low yield.1), 2)

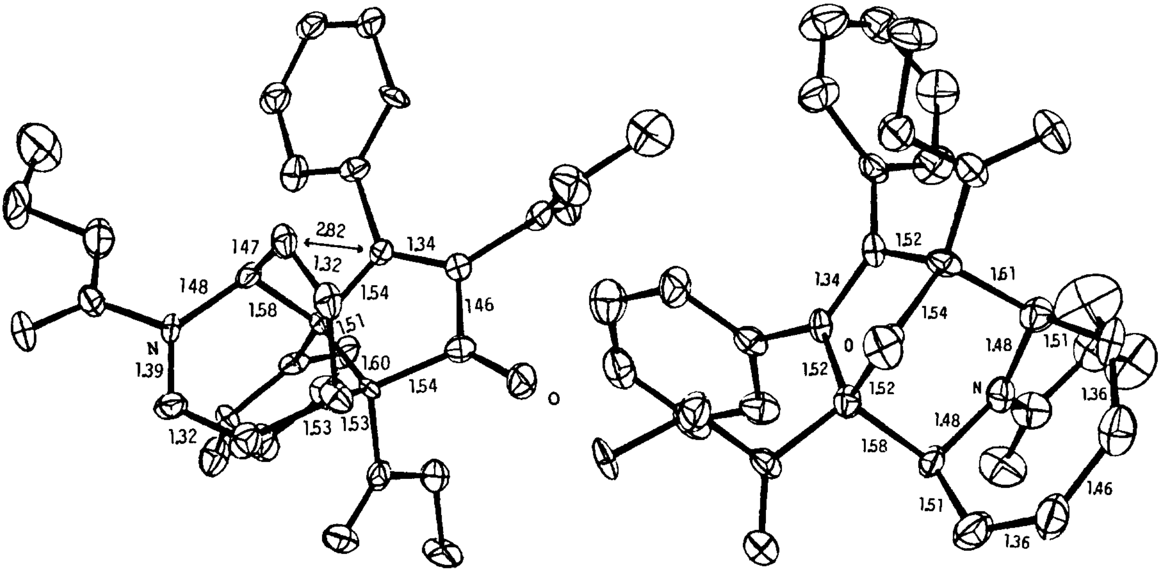
Related to this mode of cycloaddition, we now wish to report the result of cycloaddition of N-ethoxycarbonylazepine (Ia) and 2,5-dimethoxycarbonyl-3,4-diphenylcyclopentadienone(IIa)3) involving the isolation and characterization of novel [6+4]π cycloadduct.

Heating a mixture of Ia and IIa in benzene at 80° for 6 hr resulted in the formation of two crystalline products, IIIa, mp 206-208°, yield 17% and IVa, mp 155-157°, yield 81%, assigned the formula, $C_{30}H_{27}NO_7$ which are responsible for the corresponding 1:1 adduct.



Ia IIa
exo[6+4] IIIa anti-endo[4+2] IVa

The IR spectra of IIIa showed a characteristic carbonyl band at 1770 cm^{-1} suggesting the presence of a bridged carbonyl group. On the other hand, IVa exhibited IR bands at 1740 (ester carbonyl) and 1700 (urethane carbonyl) cm^{-1}, and no absorption due to strained carbonyl. The PMR spectrum of IIIa exhibited complex absorption bands owing to the nature of the adduct which would due to nonequivalence resulting from the partial double-bond character of the N-C bond and to smaller separation of the bands of azepine moiety (6H, 5.6-6.5 ppm).



anti-endo[4+2]π adduct (IVa) exo[6+4]π adduct (IIIa)

Fig. 1. ORTEP drawing of IIIa and IVa

By contrast, the ^{13}CMR spectrum (14.59, 52.38, 58.01, 58.18, 62.34 and 70.55 ppm) of IIIa suggested a symmetrical structure. In the case of IVa, the PMR and ^{13}CMR spectra were difficult to analyze precisely because of the large number of overlapping of resonances. In order to elucidate the complete stereostructure of these adducts, the crystal structure analyses were carried out.

Unit cell dimensions were obtained from least-squares refinement of the 2θ angles of 15 reflections measured on a Syntex P$\bar{1}$ automated diffractometer (Mo, λ=0.71069 Å). In the case of IIIa, crystals are monoclinic, space group $P2_1/c$ which is judged from systematic absence of reflections and there are four molecules in the unit cell of dimensions a=16.447 (6), b=9.993 (4), c=16.331 (6) Å, β=100.53 (3)°. In the case of IVa, crystals are triclinic and the space group was established as P$\bar{1}$ because the unit cell contains two molecules. The unit cell parameters are a=11.069 (13), b=11.961 (13), c=10.579 (9) Å, α=91.06 (8), β= 100.06 (9), γ=68.71 (8)°. Intensity data of them were collected using θ-2θ scan technique to maximum value of 2θ=50°, for IIIa, 3940 independent reflections were collected, of which 1956 were considered to be observed. For IVa, 3970 reflections were treated as observed ($I>2.5\delta(I)$). For both cases, structures were solved by the direct method using the MULTAN series of programs,$^{4)}$ E-maps computed with the normalized structure factors with value of E>1.6 revealed the entire structures except hydrogen atoms. Refinements were carried out by the block-diagonal least-squares method using BDLS-60 program.$^{5)}$ Final R values for IIIa and IVa were 0.083 and 0.076 for the observed reflections respectively. The molecular structures of IIIa and IVa drawn by the ORTEP program$^{6)}$ are shown in Fig. 1. It has thus been firmly established that the reaction of Ia and IIa leads to exo[6+4]π and anti-endo[4+2]π cycloadducts. In addition to the recent results of our studies[7)] with these informations in hand, the reaction pathway outlined in Chart 1 is presented, which involves all of the thermally allowed cycloadducts from cyclopentadienone and 1H-azepine by either direct or indirect pathway.

With respect to the regiochemistry of the cycloaddition, two [4+2]π regioisomers (IVa and IV'a) may be derived from the independent pathway and the interconversion of these isomers can not be allowed in the thermal conditions.

When Ia and IIa were dissolved in $CDCl_3$ at 40°, the NMR monitoring of the ensuing reaction by analyzing the NMR spectra of the O-Me groups of IIa at δ 3.64, IIIa at δ 3.51 and 3.59, IVa at δ 2.88 and Va at δ 3.62 revealed initial formation of Va.[8)] As illustrated by Fig. 2, the concentration of Va increased rapidly until a maximum was reached (2.0 hours) and then decreased gradually with the increase of IVa. From the consumption of Va and the behavior of the other compositions (IIa and IIIa), it is obvious that Va is converted to IVa. These data suggest that anti endo [4+2]π cycloadduct (IVa) is the result of a Cope rearrangement[9)] of the alternative [4+2]π cycloadduct (Va) in which IIa acts as the diene. While exo [6+4]π cycloadduct(IIIa) forms directly, the transition state for the formation of IIIa might be similar to that of Va as shown in Fig. 3.

Thus, the predominant formation of Va may be mainly attributed to influence of the steric interactions and the secondary orbital interactions in the transition state (Fig. 3).

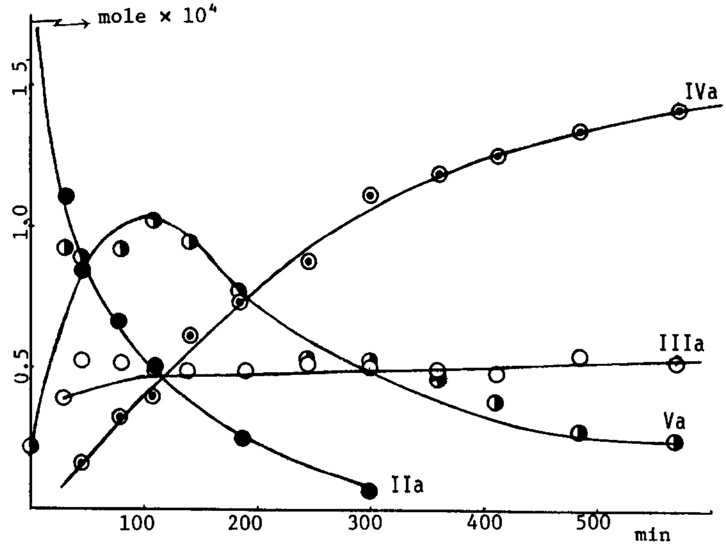


Fig. 2. Rate of reaction of N-ethoxycarbonylazepine(Ia) with 2,5-dimethoxycarbonyl-3,4-diphenylcyclopentadienone(IIa) in $CDCl_3$ at 43°.

The X-ray analysis of an interesting cage compound from photochemical conversion of the anti-endo [4+2]π cycloadduct will be presented in the near future.

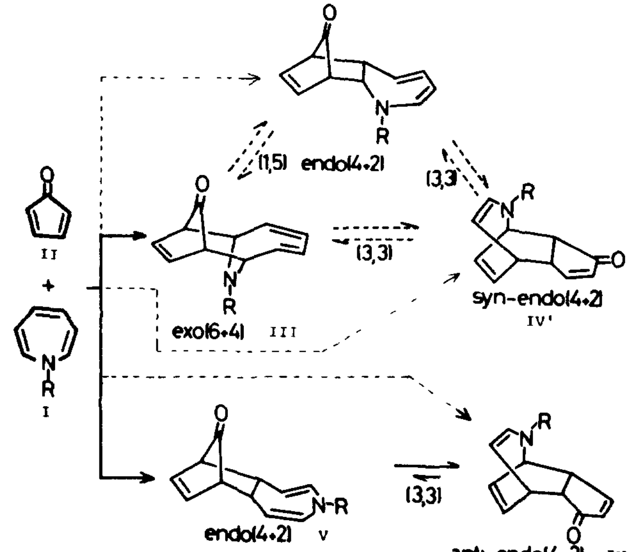
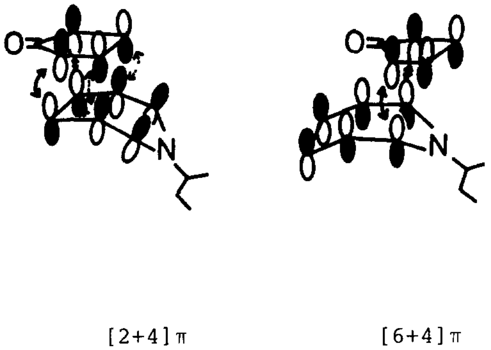


Chart 1. Reaction Pathway



[2+4]π [6+4]π

Fig. 3 Transition States

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