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Effect of $>C=O\cdots H-Ar$ interaction on *endo/exo* selectivity in the Diels–Alder reaction of phenyl-substituted cyclopentadienones

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Abstract

The cycloaddition of 2,5-bis(methoxycarbonyl)-3,4-diphenylcyclopentadienone with *S*-allyl *S*-methyl dithiocarbonate gave the *endo* cycloadduct whereas phencyclone gave a mixture of the *endo* and *exo* cycloadducts. The X-ray analysis of the cycloadduct of phencyclone and *S*-allyl *S*-methyl dithiocarbonate indicated the presence of a short contact of $Ar-H\cdots O=C<$ type. A possible role of the interaction in determining the *endo/exo* selectivity was discussed based on the X-ray crystallographic data and the transition structures from the MO calculation data. © 2000 Elsevier Science Ltd. All rights reserved.

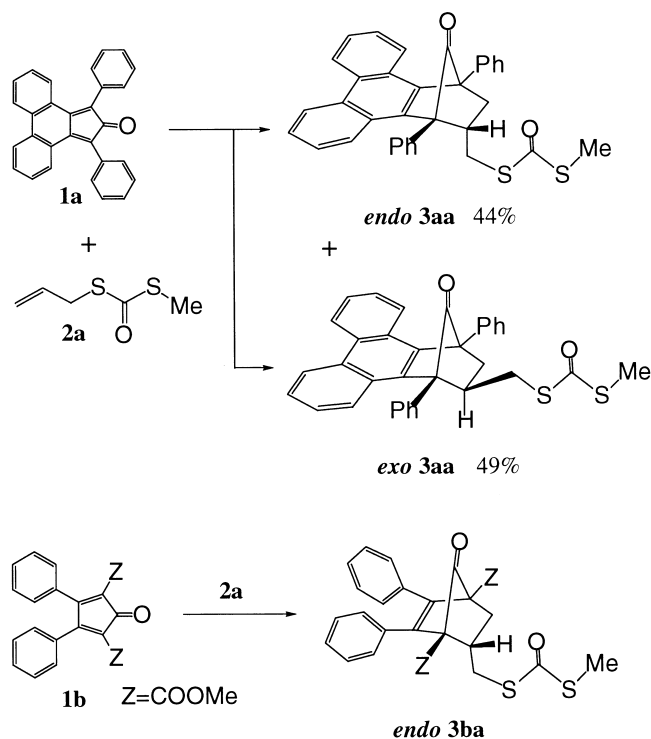
Keywords: cyclopentadienone; *S*-allyl *S*-methyl dithiocarbonate; cycloaddition; *endo/exo* selectivity; $CH\cdots O$ hydrogen bond; X-ray analysis.

During the course of our study on the pericyclic reaction of phenyl-substituted cyclopentadienones,^{1,2} we observed an incomprehensible *endo/exo* selectivity which could not be explained in terms of the secondary orbital interaction³ alone. This paper deals with a role of $>C=O\cdots H-C_6H_4-$ interaction in determining the *endo/exo* selectivity of the cycloaddition reaction of the cyclopentadienones with olefins having a nonconjugated carbonyl group.

Phencyclone (**1a**) was allowed to react with *S*-allyl *S*-methyl dithiocarbonate⁴ (**2a**) in benzene at 60° for 6 h to give the [4+2] π cycloadducts (**3aa**) (Scheme 1). The ¹H NMR spectrum showed a mixture of the *endo* and the *exo* cycloadducts. The products were separated by chromatography on silica gel to give the *endo* **3aa** (44%, mp 253–255°C) and *exo* **3aa** (49% mp 257–259°C).

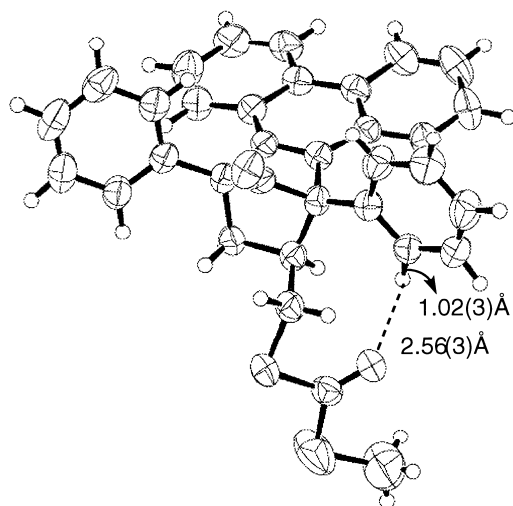
In contrast, the cycloaddition of **1a** with 2,5-bis(methoxycarbonyl)-3,4-diphenylcyclopentadienone (**1b**) gave only the *endo* cycloadduct in spite of the serious steric interference between the substituents of the addends, indicating that another factor must be taken into consideration for the explanation of the observed *endo/exo* selectivity.

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Scheme 1.

In concerted cycloadditions, the transition-state (TS) geometries are assumed to be reflected in the corresponding cycloadducts. We performed the single crystal X-ray analysis⁵ of *exo* 3aa. As shown in Fig. 1, there exists an intramolecular $>C=O \cdots H-C_6H_4-$ type hydrogen bond⁷ between the dithiolcarbonate oxygen atom and the 2-hydrogen atom of the phenyl substituent. The

Figure 1. ORTEP drawing of molecular structure of *exo* 3aa

AM1 structure optimization⁸ reproduced the observed conformation of **3aa**. The calculated $>C=O\cdots H-C_6H_4-$ distance is 2.489 Å, slightly shorter than the observed one [2.56(3) Å]. The PM3 distance (2.921 Å) differs significantly from the X-ray value. The AM1 TS calculation suggested the contribution of intermolecular $>C=O\cdots H-C_6H_4-$ interaction to the stabilization of the TS. As shown in Fig. 2, both *endo* TS and the *exo* TS structures also have a similar hydrogen bond. The energy difference between the *endo* TS and *exo* TS is 0.4 kcal/mol, supporting the observed *endo/exo* selectivity.

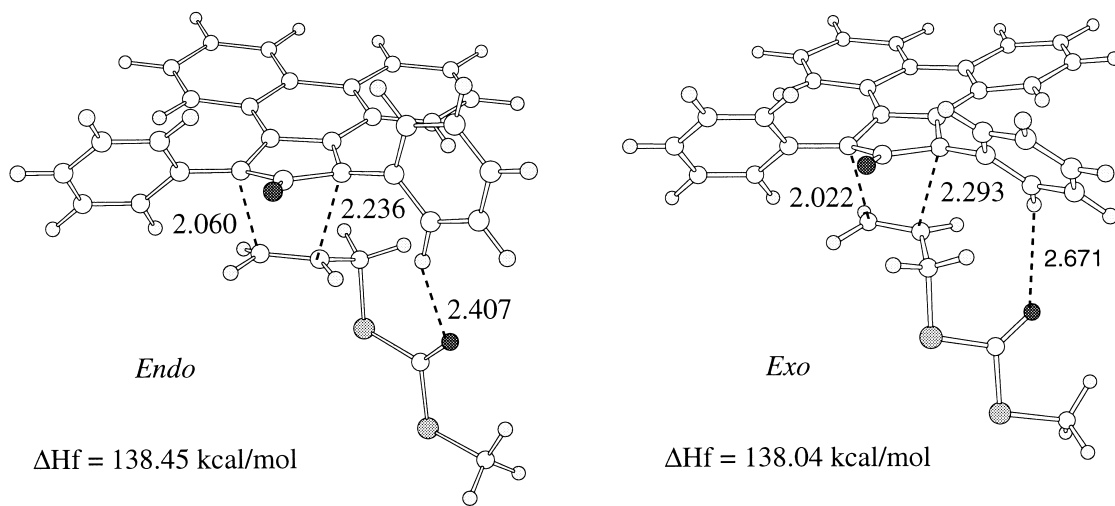


Figure 2. *endo* and *exo* TS structures for cycloaddition of **1a** with **2a**

Fig. 3 shows the *endo* and *exo* transition structures for the reaction of **2a** with **1b** which has phenyl substituents at the 3,4-positions of the cyclopentadienone moiety. The AM1-calculated conformations of the cyclopentadienone moiety in both the TS structures are similar to the X-ray geometry of the cycloadduct of **1b** and cyclooctatetraene.⁹

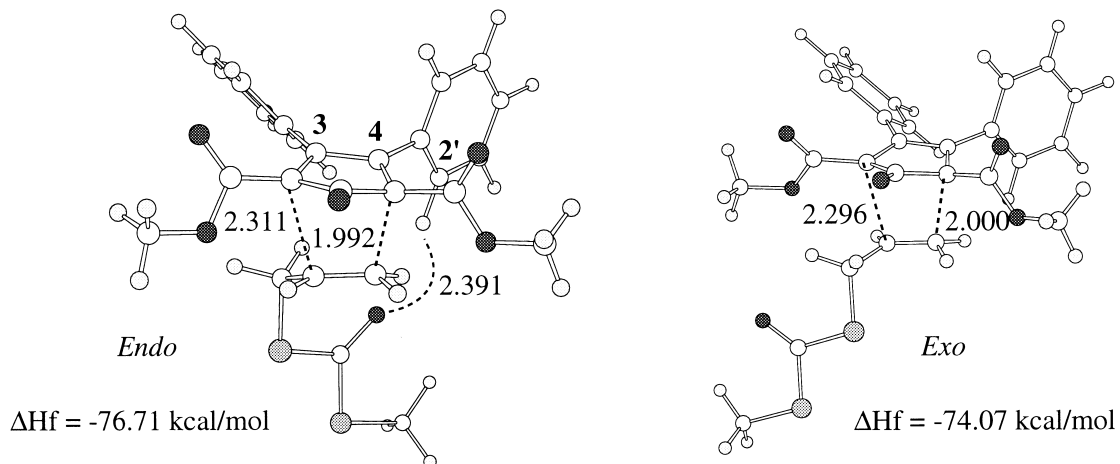


Figure 3. *endo* and *exo* TS structures for cycloaddition of **1b** with **2a**

In the *endo* TS, the $>C=O\cdots H-C_6H_4-$ interaction is found between the dithiolcarbonate oxygen of **2a** and the 2'-hydrogen of the 4-phenyl group of **1b** (see Fig. 3). The *endo* TS is ca. 2 kcal/mol more stable than the *exo* TS.

To confirm the interaction of this type, we performed the cycloaddition of several unsaturated compounds with **1b** (Fig. 4). With simple alkenes, some mixtures of the *endo/exo* adducts were obtained. The only products obtained from allylic dithiolcarbonates⁴ (**2a–c**) are the *endo* cycloadducts. The main product from the cycloaddition with allyl acetate is the *endo* cycloadduct (*endo:exo* = 3.8:1). In contrast, the cycloaddition of **2a–c** with **1a** gave some mixtures of *endo* and *exo* cycloadducts.

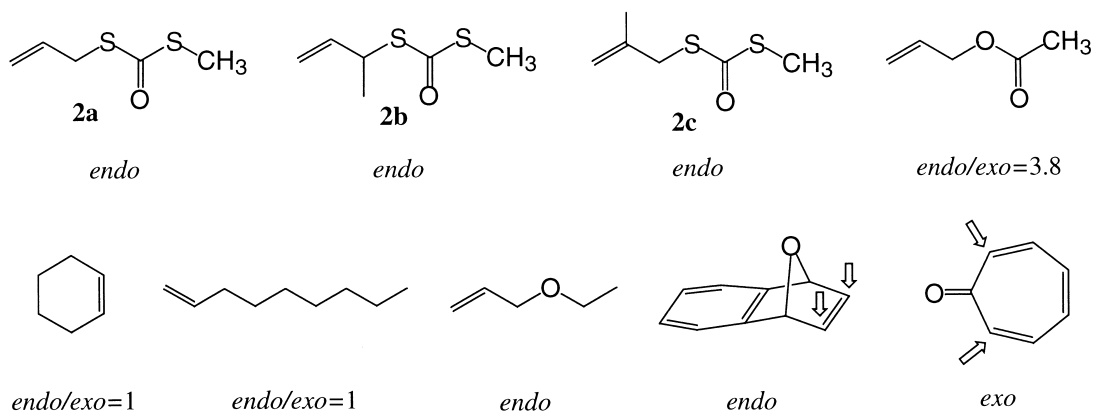


Figure 4. *endo/exo* Selectivity for cycloaddition of **1b** with various dienophiles

Recently, Scheiner et al. made a theoretical study of fundamental properties of the $CH\cdots O$ interaction, indicating that the $CH\cdots O$ interaction can be categorized as a true H-bond and the interaction energy of CH_4 with $O=CH_2$ is about 0.3 kcal/mol, whereas those of $FH_2CH\cdots O=CH_2$ and $F_2HCH\cdots O=CH_2$ are 1.2 and 2.1 kcal/mol, respectively.^{7a} The density functional theory

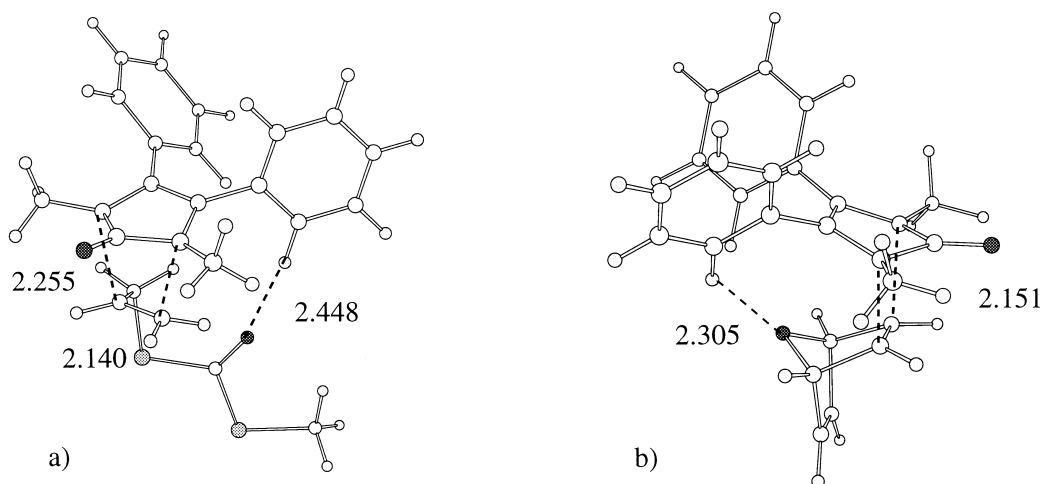


Figure 5. (a) 3-21G* TS structure for cycloaddition of **1c** with **2a**. (b) AM1 TS structure for cycloaddition of **1c** with epoxybenzene

(DFT) calculation (B3LYP/6-31+G**) for Ph-H...O=C(SH)₂ interaction by us indicated that the interaction energy for Ph-H...O=C(SH)₂ is 0.75 kcal/mol and the -H...O= distance is 2.588 Å.^{7e} The AM1 calculation gave 0.73 kcal/mol with 2.389 Å.

Based on these results and discussion, at least in phenyl-substituted cyclopentadienones, we can consider that the >C=O...H-C₆H₄- interaction plays an important role in determining the *endo/exo* selectivity for the cycloaddition. The ab initio TS calculation at 3-21G* level¹⁰ predicted a similar structural feature (see Fig. 5a).

A similar argument may be applied to the cycloaddition behavior of epoxynaphthalene.^{1c} The TS for a model reaction of 2,5-dimethyl-3,4-diphenylcyclopentadienone (**1c**) with epoxybenzene has a short contact between the dithiolcarbonate oxygen and the 2-hydrogens of the diphenyl groups (Fig. 5b). The formation of the *endo* cycloadduct from allyl ethyl ether supports this assumption. In the reaction of tropone,^{1a,b} the formation of the *exo* [6+4] π cycloadduct may be stabilized by the >C=O...H-C₆H₄- interaction.

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