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Letter

Transition structures and exo/endo stereoselectivities of concerted [6 + 4] cycloadditions with density functional theory

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Abstract. Density functional theory transition structures were located for three concerted [6 + 4] cycloaddition reactions involving *cis*-hexatriene and butadiene, cyclopentadiene and cycloheptatriene, and cyclopentadiene and tropone. Geometries, energies, and entropies were computed at the Becke3LYP/6-31G* level. The activation energy of the concerted [6 + 4] cycloaddition of hexatriene and butadiene is 33.3 kcal/mol, about 8 kcal/mol above the activation energy of the butadiene plus ethylene [4 + 2] cycloaddition. The endo concerted [6 + 4] transition state is 1.1 kcal/mol higher than the exo. The [6 + 4] reaction of cyclopentadiene and cycloheptatriene has a barrier of 25.9 kcal/mol, while the cyclopentadiene–tropone barrier drops to 20.7 kcal/mol.

Key words: Secondary orbital interactions – B3LYP – Diels–Alder reaction

1 Introduction

At a time when no cycloadditions involving ten electrons were known, Woodward and Hoffmann predicted that the all-suprafacial [6 + 4] cycloaddition could occur by a concerted mechanism [1]. They also predicted that the reaction would give the exo stereochemistry preferentially [2], in contrast to the endo preference known for the Diels–Alder cycloaddition. Shortly thereafter, Cookson et al. [3] and Ito and coworkers [4] reported that cyclopentadiene and tropone react at 80°C to give the exo [6 + 4] adduct stereospecifically. Houk and Woodward [5, 6] reported several [6 + 4] cycloadditions of cyclopentadienones with tropone and cycloheptatriene, in competition with [4 + 2] and [8 + 2] processes (see Fig. 1). Since then, related [6 + 4] cycloadditions have been discovered [7, 8] and both Garst and coworkers [9] and Rigby and coworkers [10] have elaborated this reaction for the synthesis of ten-membered rings and derivatives. Pressure effects on the [6 + 4] cycloaddition of tropone and cyclopentadiene indicate that the reaction has a concerted mechanism [11].

We have undertaken a theoretical study of the three [6 + 4] cycloadditions shown in Fig. 2, and describe here the transition structures of the concerted exo and endo cycloaddition pathways obtained from density functional calculations. These are compared to similar work on the [4 + 2] cycloadditions [12].

2 Computational methodology

Calculations were carried out with Gaussian 94 [13]. Geometries for all structures were fully optimized with analytical energy gradients using the Becke3LYP functional and the 6-31G* basis set. Vibrational frequencies were calculated for all reactants, products, and transition structures. The frequencies were used to compute the zero-point vibrational energies and entropies.

3 Results and discussion

3.1 Thermochemistries and geometries

The energetics for the three reactions studied here are shown in Table 1. The reaction of **1** and **2** is more exothermic than the reaction of **4** and **5** by about 4 kcal/mol. The reaction of **5** and **7** is exothermic by only 4 kcal/mol. The B3LYP/6-31G* optimized geometries of reactants, transition structures, and products of reactions are shown in Figs. 3–5, and the forming bond lengths, along with computed activation energies, are given in Table 2.

3.2 Activation energies

The concerted exo transition state for hexatriene and butadiene is 1.1 kcal/mol lower than the endo transition state (Table 2). The [6 + 4] activation barrier

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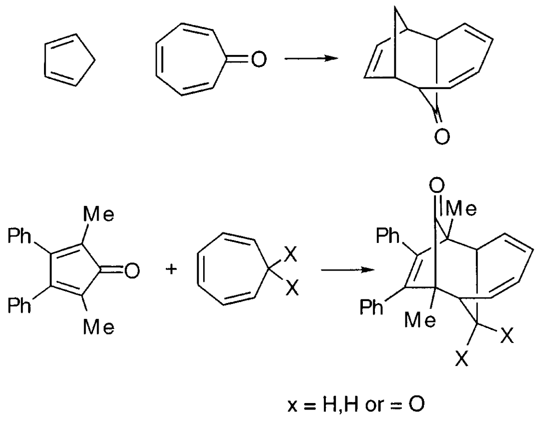

Fig. 1. The [6 + 4] cycloadditions first discovered after the Woodward–Hoffmann prediction

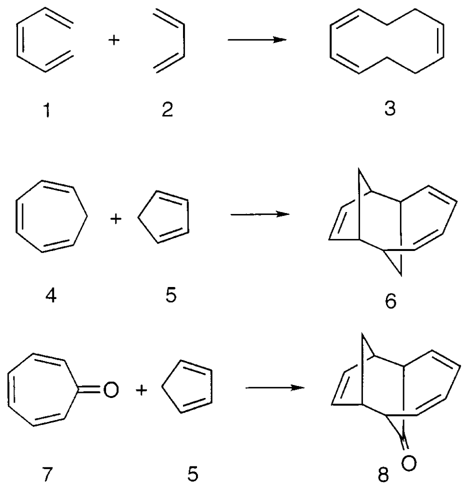

Fig. 2. The three reactions investigated computationally in this work

Table 1. Energies of reaction of [6 + 4] cycloadditions. Calculated RB3LYP/6-31G* total energies and zero-point energies (*ZPE*) (in atomic units) of hexatriene, butadiene, cyclopentadiene, cycloheptatriene and tropone are −233.39552 (0.11942), −155.99213 (0.08540), −194.10100 (0.09283), −271.50959 (0.12839), and −345.53739 (0.11062), respectively

Reaction	$-\Delta E_{\mathrm{rxn}}$ (kcal/mol)	
	B3LYP/6-31G*	E + ZPE
cis-Hexatriene (**1**) + butadiene (**2**)	22.4	16.2
Cycloheptatriene (**4**) + cyclopentadiene (**5**)	18.5	12.8
Cyclopentadiene (**5**) and tropone (**7**)	8.7	4.2

(33.3 kcal/mol) is nearly 8 kcal/mol above that for the butadiene–ethylene Diels–Alder barrier of 24.8 kcal/mol calculated at this level [12].

Table 2. Becke3LYP/6-31G* calculated concerted activation barriers (kcal/mol) including ZPE and C—C forming bond lengths (Å) for [6 + 4] cycloaddition reactions

Reaction	E_{a}	C—C	
		R_1 (Å)	R_2 (Å)
Hexatriene (**1**) + butadiene (**2**)			
exo – (**9**)	33.3	2.266	2.267
endo – (**10**)	34.5	2.261	2.262
Cycloheptatriene (**4**) + cyclopentadiene (**5**)			
exo – (**11**)	25.9	2.268	2.268
Cyclopentadiene (**5**) + tropone (**7**)			
exo – (**12**)	20.7	1.913	2.787

The forming bond lengths are 2.27 and 2.26 Å in the exo and endo transition states, respectively. The exo transition state, **9**, is shown in Fig. 3. The bond lengths are similar to the forming bond lengths in the ethylene and butadiene Diels–Alder reaction (2.27 Å) [12] and are typical of concerted pericyclic reactions [14]. Previous work on the C_s transition structures of the [6 + 4] cycloaddition of *cis*-hexatriene and butadiene at the RHF/3-21G level predicted an early exo transition state and found the endo approach not to be a true transition structure [14]. By contrast, the density functional theory wave functions yield both the exo and endo forms as transition structures.

Table 2 and Fig. 4 give details for the reaction of cyclopentadiene and cycloheptatriene. For this reaction, a second-order saddle point, **11**, was formed for the concerted exo reaction. A large imaginary frequency corresponds to the reaction coordinate. The vibration which converts this C_s exo stationary point to an asynchronous transition state is a very small imaginary value (14i cm^{-1}), indicative of a very flat potential surface for this asynchronous motion. We did not search for this transition state. The endo transition state could not be found. The exo barrier resembles that found for the [4 + 2] cycloaddition: 25.9 kcal/mol for the [6 + 4] cycloaddition of **4** and **5**. This barrier is 7 kcal/mol lower than the barrier for the reaction of **1** and **2**. The forming bond length is 2.27 Å.

The activation energy for the exo transition state of tropone and cyclopentadiene is lower than the cycloheptatriene–cyclopentadiene barrier by 5 kcal/mol. It is now an asynchronous transition state, as shown in Fig. 5. No stable endo transition state for the reaction of **5** and **7** was found. For highly reactive species, asynchronous and synchronous reactions are nearly the same in energy, and sometimes the asynchronous becomes favored compared to the synchronous [15]. Here, in the [6 + 4] reaction of **5** and **7**, the asynchronicity is pronounced: one forming bond length is 1.9 Å, and the other is 2.8 Å.

The exo preferences found here are in good accord with the Woodward–Hoffmann prediction and with the available experimental data. In the case of the parent reaction, the 1-kcal/mol preference probably reflects the small repulsive influence of secondary orbital interactions. With cyclopentadiene, the endo reactions become

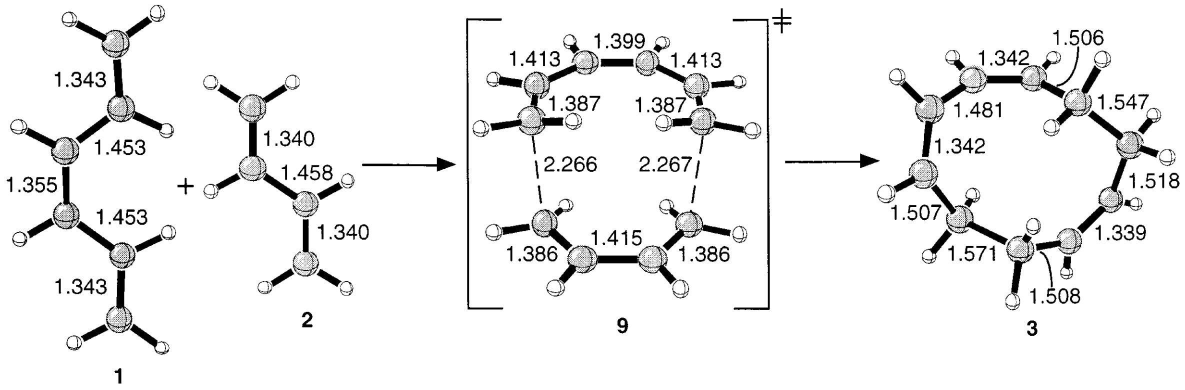

Fig. 3. Bond lengths of stationary points in the [6 + 4] cycloaddition of *cis*-1,3,5-hexatriene and butadiene

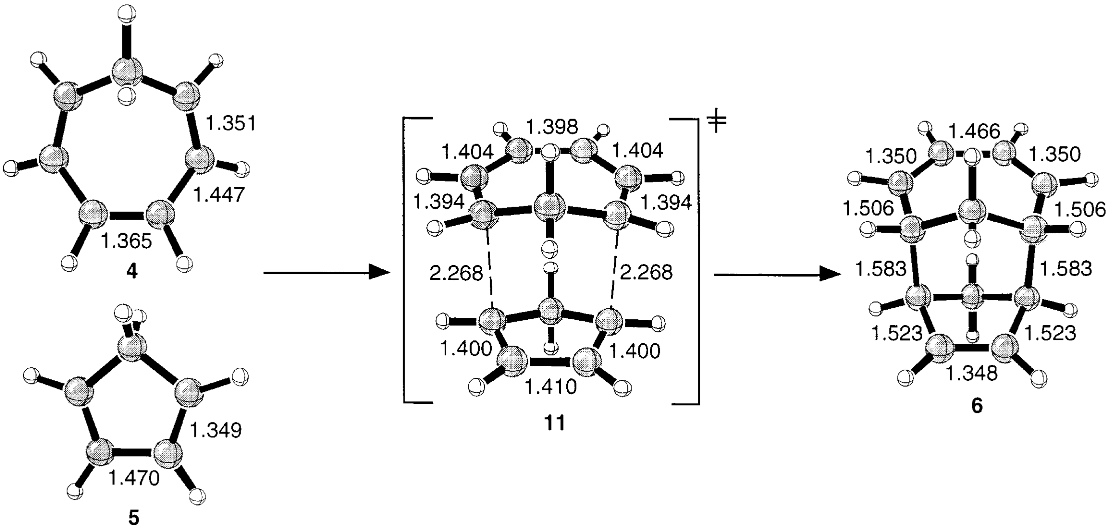

Fig. 4. Bond lengths of stationary points in the [6 + 4] cycloaddition of cycloheptatriene and cyclopentadiene

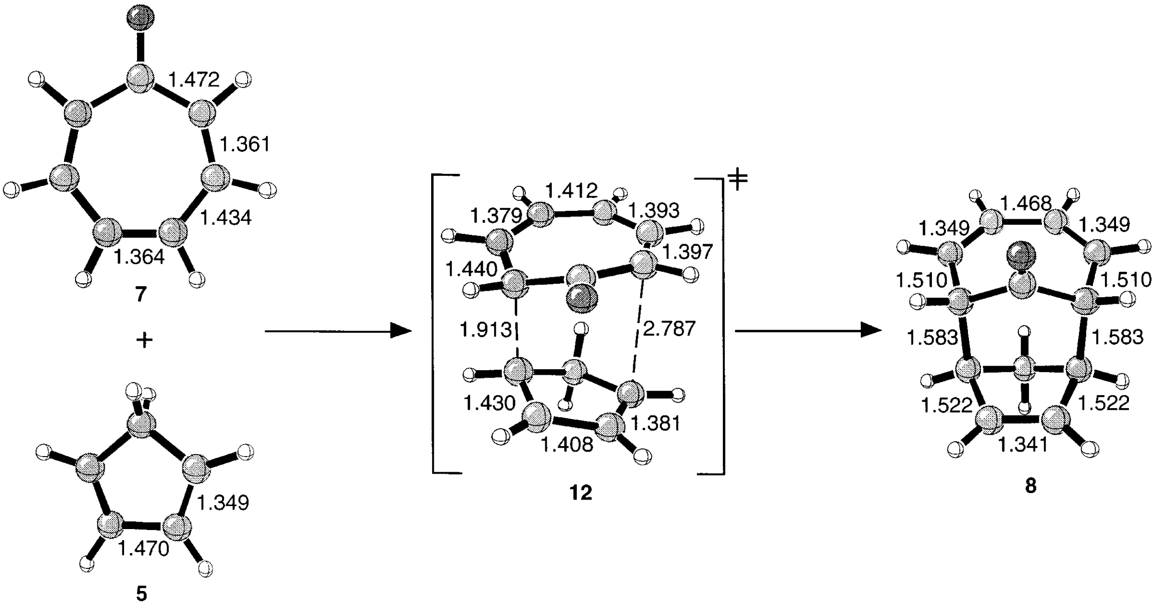

Fig. 5. Bond lengths of stationary points in the [6 + 4] cycloaddition of tropone and cyclopentadiene

highly disfavored due to the severe steric repulsions involving the methylene of cyclopentadiene and the methylene of cycloheptatriene in the endo transition state.

The surprisingly high barrier of the parent reaction is likely to be due to the relatively poor overlap of the diene and triene termini in the transition state. The interaction only occurs at the expense of the transannular repulsion of the "inner" hydrogens on the triene and the diene. Conversion of the transoid polyenes to the all-cis arrangements causes an increase in activation energy of 13 kcal/mol. The activation energy of the cyclic dienes is quite low because the polyenes are already fixed in cisoid conformations. The increase in electrophilicity of the triene by conversion of cycloheptatriene to tropone further lowers the activation barrier, but the strained product can readily revert to reactants. The aromaticity of tropone also influences the energy of reaction.

These ten π-electron systems might have relatively low energies of concert. Potentially competing stepwise mechanisms and the competition among various symmetry-allowed concerted processes – known as periselectivity [8] – are the subjects of ongoing investigations.

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