

# Gas-phase Diels–Alder cycloaddition reaction in the presence of methanol and water vapor

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**epoc** ABSTRACT: Hydrogen bonding effects of protic solvents, apart from bulk properties, on the reaction rate of the cycloaddition of cyclopentadiene and vinyl acetate in the presence of water and methanol in the gas phase were investigated. The results showed that methanol increases the reaction rate in the gas phase more than the water. This is attributed to the stronger hydrogen bonding effect of methanol in this phase. *Ab initio* and semi-empirical calculations show that methanol stabilizes the transition state of the reaction more than water. This arises from two different origins, distribution of charge and geometry of the hydrogen bond. Copyright © 2002 John Wiley & Sons, Ltd. Additional material for this paper is available from the epoc website at <http://www.wiley.com/epoc>

KEYWORDS: cycloaddition reaction; hydrogen bonding; solvent effect; theoretical study; gas phase kinetics

## INTRODUCTION

Interest in the role of solvents in organic reactions has increased over the last few years. A considerable influence of solvents on chemical processes (reaction rate, selectivity, etc.) has been well established in the last decade.<sup>1–5</sup> Studies have revealed that a number of organic reactions proceed more rapidly in aqueous solutions than in organic solvents.<sup>6–11</sup> The use of water as a solvent has obvious environmental and economic advantages over other solvents.

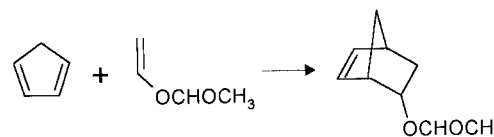
Diels–Alder (DA) cycloaddition reactions have become a benchmark for theoretical and experimental studies of solvent effects.<sup>2–5,12</sup> In previous studies, it has been reported that the acceleration of DA reactions in water is mainly a result of a combination of hydrophobic interactions and hydrogen bonding.<sup>13</sup> For experimental investigation of the influence of hydrogen bonding on DA reactions, Otto *et al.* compared the DA reaction of cyclopentadiene (CPD) and methyl vinyl ketone with the reaction of the corresponding sulfone in some protic and aprotic solvents.<sup>14</sup> Blake *et al.* calculated extent of hydrogen bonding to the dienophile and also its effect on the stability of the transition state (TS) in the DA reaction using *ab initio* calculations. As in previous calculations, they noted that hydrogen bonding is particularly sensitive to small charge variations, and consequently the largest solvent effects will be found in hydrogen bond donor solvents.<sup>2</sup>

No experimental work has been reported on hydrogen bonding effects of protic solvents on DA reactions separately from their bulk properties. For this purpose, we have carried out DA reactions of cyclopentadiene and vinyl acetate in the gas phase as a model reaction in the presence of water and methanol vapor (Scheme 1). Theoretical calculations were also carried out to achieve a better understanding of this effect, especially to compare the hydrogen bonding abilities of methanol and water in the stabilization of the TS of this DA reaction.

## RESULTS AND DISCUSSION

The experimental results of the kinetic study of the reaction are given in Table 1. The reaction rate was obtained in the presence of methanol, water, a mixture of methanol and water vapor and without any solvent vapor. For the three vapor phases, the reaction rates were higher than that in the absence of any solvent vapor.

Since the reaction was carried out in the presence of a saturated vapor of solvents, it may be mistakenly concluded that this increase could arise from the pressure effect of the solvent vapor. We selected the reaction



Scheme 1

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**Table 1.** Pseudo-first-order rate constants of the reaction in the gas phase at 296.1 K

Conditions	$K_{\text{obs}}$ ( $\text{s}^{-1}$ )
Without any solvent vapor	$2.70 \times 10^{-4}$
In presence of water vapor	$4.60 \times 10^{-4}$
In presence of methanol vapor	$7.92 \times 10^{-4}$
In presence of both water and methanol vapor	$3.47 \times 10^{-4}$

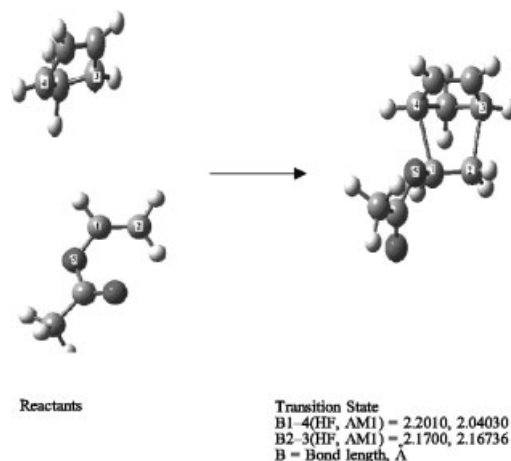
conditions to be pseudo-first order, and first-order reactions are independent of pressure.<sup>15</sup> Furthermore, when we compare the vapor pressure of water (20.9 mmHg at 296.1 K) with that of a vapor mixture of water and methanol (19.1 mmHg at 296.1 K) (for a 2:1 volume ratio of liquid phase of water and methanol, obtained using the Ramsay–Yang method),<sup>16</sup> we see they are nearly the same. Hence we expect that the reaction rate will not change on going from water vapor to a mixture vapor of water and methanol unless there is a difference in chemical origin. Consequently, pressure cannot explain the variation of the reaction rate.

A common feature of methanol and water is that both are protic solvents and could have hydrogen bond interactions with the hydrogen bond sites on other molecules. The dienophile of this reaction (vinyl acetate) has an oxygen atom bonded to the vinyl group. Hence this oxygen could have a short-length interaction with a protic solvent molecule through hydrogen bond formation. Therefore, the existence of hydrogen bond interactions can increase the reaction rate in the presence of water, methanol or their vapor mixture.

The difference between the reaction rates in the vapor phase of methanol and water is due to the difference in the hydrogen bond donor ability of the solvents in the gas phase. If the strength of hydrogen bonding is a key factor in increasing of the reaction rate, from the kinetic results obtained (Table 1) it seems that methanol is a stronger hydrogen bond donor than water in the gas phase. This may be expected from the greater acidity of alcohols than water in the gas phase.

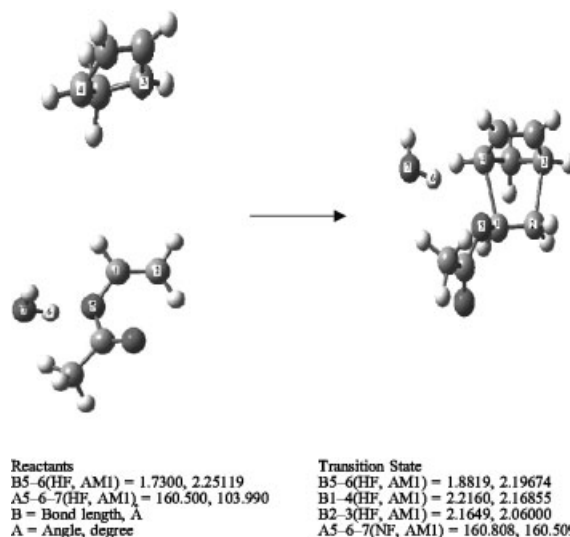
To investigate the effect of hydrogen bonding on the activation energy of this reaction theoretically, we carried out *ab initio* and AM1 calculations using Gaussian 98.<sup>17</sup> For this purpose we considered complexes of the TS and dienophile (vinyl acetate) with a solvent molecule near the hydrogen bond site. Since the ether-type COC oxygen of vinyl acetate was closer to the reaction center than the carbonyl oxygen, it was considered as a hydrogen bond acceptor site.

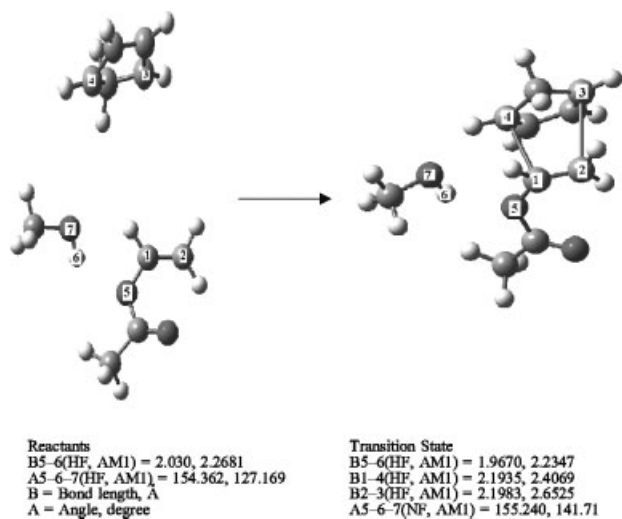
The synchronous transit-guided quasi-Newton (STQN) method implemented by Schlegel *et al.*<sup>18</sup> was used to locate the TS. This method was performed with the QST2 and QST3 options. The location of the TS was done using QST3, which requires three molecule specifications: the reactants, the product(s) and an initial structure for the transition state. In all calculations, identical conformers

**Figure 1.** Structural specification of the reaction in the absence of solvent molecules according to AM1 and HF calculations

were considered for the CPD and VAC. Full geometry optimization was performed at the semi-empirical and HF/3–21G levels, and the other single-point calculations were carried out on the HF/3–21G optimized structures. Some structural information is given for the reaction in the gas phase without any solvent vapor and for reaction in the presence of water and methanol molecules in Figs 1–3.

It is well known that the energy of the hydrogen bond depends on the  $Y \cdots H$  distance and the  $X-H \cdots Y$  angle (where X is a hydrogen bond donor and Y is a hydrogen bond accepting atom). Based on the  $Y \cdots H$  distance, all hydrogen bonds can be divided into strong, medium and weak. An alternative approach to an analysis of the hydrogen bond energy is provided by the electron density distribution.<sup>19</sup> It has been demonstrated that the value of

**Figure 2.** Structural specification of the reaction in the presence of water molecules according to AM1 and HF calculations



**Figure 3.** Structural specification of the reaction in the presence of methanol molecules according to AM1 and HF calculations

the electron density in the bond critical point correlates with the bond energy.<sup>20</sup> Therefore, a comparison of the H-bond strength may also be carried out based on the charges of atoms contributing to the hydrogen bond.

According to AM1 calculations, the activation energy of the reaction is lower in the presence of methanol (Table 2), but the water molecule geometrically is somewhat better partitioned than methanol within the hydrogen bonds of the TS (Figs 2 and 3). Mulliken charges can help us to compare atomic charges of the hydrogen bonding atoms in complexes of the dienophile and the TS with solvent molecules. The calculated atomic charges are presented in Tables 3 and 4. As atomic charges calculated using AM1 show, going from vinyl acetate to the TS of the reaction in the presence of water is accompanied by more charge separation on atoms contributing to the hydrogen bonding. In contrast, the methanol molecule better distributes charges on the TS to the rest of the complex. Therefore, according to the AM1 calculation, better distribution of charges is a reason why the methanol molecule stabilizes the TS of the reaction and decreases the activation energy more than the water molecule (Table 2).

**Table 2.** Calculated energy of the reactant and TS of the reaction with and without the solvent molecule

Conditions		Energy (hartree)					
		AM1	HF/3-21G	HF/6-31G	HF/6-31G*	HF/6-31++G*	B3LYP/6-31++G*
Pure gas phase	Reactant	-0.04733	-494.6986	-497.2557	-497.4668	-497.4814	-500.5870
	TS	0.00155	-494.6449	-497.1845	-497.3949	-497.4072	-500.5450
	TS-reactant	0.04888	0.0537	0.0712	0.0719	0.0742	0.0420
In presence of water	Reactant	-0.14176	-570.2994	-573.2415	-573.4718	-573.4918	-577.0079
	TS	-0.09829	-570.2492	-573.1770	-573.4073	-573.4241	-576.9713
	TS-reactant	0.04347	0.0502	0.0645	0.0645	0.0677	0.0366
In presence of methanol	Reactant	-0.14173	-609.1111	-612.2485	-612.5024	-612.5215	-616.3148
	TS	-0.11987	-609.0654	-612.1867	-612.4407	-612.4564	-616.2816
	TS-reactant	0.02186	0.0457	0.0618	0.0617	0.0651	0.0332

**Table 3.** Calculated Mulliken charges of the dienophile and TS of the reaction in the presence of water molecules (Fig. 2)

	Mulliken charge					
	AM1	HF/3-21G	HF/6-31G	HF/6-31G*	HF/6-31++G*	B3LYP/6-31++G*
<b>Dienophile</b>						
O-5	-0.32459	-0.77013	-0.83818	-0.70966	-0.59289	-0.44477
H-6	0.23199	0.42925	0.48984	0.50772	0.66691	0.59655
O-7	-0.46192	-0.77215	-0.86186	-0.92584	-1.11621	-1.05007
<b>Transition state</b>						
O-5	-0.30837	-0.75423	-0.82023	-0.69902	-0.47724	-0.32328
H-6	0.24294	0.42413	0.48594	0.50534	0.63554	0.60073
O-7	-0.47036	-0.77692	-0.86622	-0.92982	-1.11756	-1.05954
$\Delta$ (charge) <sup>a</sup>						
O-5	0.01622	0.01591	0.01795	0.01064	0.11565	0.12148
H-6	0.01094	-0.00512	-0.00391	-0.00237	-0.03137	0.00419
O-7	-0.00844	-0.00476	-0.00436	-0.00398	-0.00135	-0.00946

<sup>a</sup>  $\Delta$ (charge) = charge on TS – charge on dienophile.

**Table 4.** Calculated Mulliken charges of the dienophile and TS of the reaction in the presence of methanol molecules (Fig. 3)

	Mulliken charge					
	AM1	HF/3-21G	HF/6-31G	HF/6-31G*	HF/6-31++G*	B3LYP/6-31++G*
<b>Dienophile</b>						
O-5	-0.30793	-0.75465	-0.80399	-0.68583	-0.54079	-0.40576
H-6	0.24857	0.40091	0.45480	0.48155	0.59692	0.55989
O-7	-0.39165	-0.70171	-0.78321	-0.78331	-0.78398	-0.68037
<b>Transition state</b>						
O-5	-0.30758	-0.73126	-0.78594	-0.67877	-0.43693	-0.27245
H-6	0.25152	0.42107	0.47834	0.50363	0.58609	0.61520
O-7	-0.39584	-0.71498	-0.79819	-0.79679	-0.77448	-0.68756
$\Delta(\text{charge})^a$						
O-5	0.00035	0.02339	0.01805	0.00705	0.10386	0.13331
H-6	0.00295	0.02016	0.02354	0.02208	-0.00883	0.05531
O-7	-0.00419	-0.01327	-0.01498	-0.01349	0.00950	-0.00719

<sup>a</sup>  $\Delta(\text{charge}) = \text{charge on TS} - \text{charge on dienophile}$ .

In spite of the AM1 results presented above, HF and DFT calculations show that distribution of charges on the TS occurs better in the presence of water molecules (Tables 3 and 4). For example, the hydrogen atom is more positive in the presence of methanol molecules. On the other hand, hydrogen bond formation in the presence of methanol has a better geometric condition. Bond lengths and angles derived from these calculations support this argument. Methanol has a shorter hydrogen bond length in TS than in the dienophile, whereas water has a greater hydrogen bond length (Figs 2 and 3). From the change in hydrogen bond length of water with TS relative to dienophile, it would be expected that water would increase the activation energy of the reaction. However, since water decreases the negative charge on O-5 and positive charge on H-6 (key atoms in the hydrogen bond), the net result is that water also decreases the activation energy of the reaction. The net contribution of the charge distribution and the geometry can be summarized in the energetics of the reaction (Table 2). Therefore, according to HF calculations, geometric specification is the reason why methanol has a stronger hydrogen bond interaction with the TS relative to reactants than water.

In summary, hydrogen bond donor solvents such as methanol and water could affect the rate of DA reactions through short-length interactions. According to experimental and theoretical results obtained in this study, in the gas phase methanol increases the rate of this reaction more than water. Also, it can be concluded that, since the hydrogen bond donor ability of water is higher than that of methanol in the liquid phase,<sup>21</sup> hydrogen bond cooperativity could exist in liquid-phase water which induces dramatic effects on the solute properties through hydrogen bond interactions.

## EXPERIMENTAL

**Materials.** Cyclopentadiene (CPD) was prepared from its

dimer immediately before use. Methanol and vinyl acetate (VAC) was distilled before use and water was redistilled in a quartz distillation unit.

**Kinetic measurements.** The reaction was studied pseudo-first order with respect to CPD. The concentration of VAC was selected to be at least 10 times that of CPD. The quantitative analysis of CPD was done by gas chromatography with a Porapack-Q column and flame ionization detection. Since the concentration of VAC was nearly constant (for the pseudo-first-order conditions of the kinetic study), it was also considered as an internal standard in chromatographic analysis.

The reaction was carried out in a two-necked flask, one neck being used to connect the flask to a vacuum system with a controller valve and the other having a septum inlet for injection of reactants and solvents into the vessel. For each measurement, the system was evacuated to near 1 mmHg, then the system was saturated with the required solvents and finally the reactants were injected separately into the vessel. The second inlet was also used for sampling of the reaction mixture with a gas syringe at different times to measure the concentration of CPD.

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