# Dependence of *endo* and *exo* selectivities on the water contents available in salt solutions for the reaction of cyclopentadiene with methyl acrylate

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ABSTRACT: The effect of the water contents present in different salt solutions on the endo selectivities has been investigated for the Diels-Alder reaction of cyclopentadiene with methyl acrylate. For aqueous LiCl and CaCl₂, endo product increases with an increase in the moles of water and then remains almost invariant at higher water content. On the contrary, a regular decrease in endo product is noted in aqueous guanidinium chloride and LiClO₄ solution reaching a tapering at higher water content. The results show that the available surface area can provide an effective method to alter the endo/exo ratios of a Diels-Alder reaction. Copyright © 2000 John Wiley & Sons, Ltd.

KEYWORDS: Diels-Alder reactions; salt effect; stereoselectivities; water content; hydrophobic effects

## INTRODUCTION

The origins of the accelerations shown by Diels–Alder reactions in water and other hydrogen bonding media is a matter of continuing interest to both the synthetic and mechanistic communities in organic chemistry. Rideout, Breslow and co-workers:[1] were the first to report impressive rate enhancements of Diels–Alder reactions in water medium. Later, the schools of Breslow[1b–e] and Grieco[2] revealed the unusual effects of water and aqueous and non-aqueous salt solutions. The issue of how water, organic solvents and their mixtures can influence the kinetic progress of Diels–Alder reactions is a subject of intense investigation by several research groups.[3] The results of these investigations have been interpreted in terms of polarizability, Brownstein and Kosower solvophobicity parameters, enforced hydrophobic interactions, etc.

Intrigued by the unusual role of water and its salt solutions, in recent years we have set out to quantify the origin of the forces responsible for both the rate acceleration and retardation in aqueous and non-aqueous media. In this regard, we had proposed correlations of the reaction rates with the internal pressure of salt solutions,[4] in addition to those of pure solvents[5] (some authors have doubted the role of internal pressure in enhancing the reaction rates; for example, see Ref. 6), for several Diels–Alder reactions. Most recently, we examined the concentration dependence of the *endo* and *exo* products for the reaction of cyclopentadiene with methyl acrylate in several rate-promoting and-retarding salt solutions.[7] In general, the spectacular variations in the reaction rates of Diels–Alder reactions have been attributed to hydrogen bonding, solvent polarity, Lewis acid catalysis, hydrophobic hydration, aggregation, etc. The studies of the concentration dependence on the rates and stereoselectivity ratios from Breslow and co-workers[1] and this laboratory[7] have shown that these kinetic profiles vary significantly with the ionic concentrations in water before reaching a maximum or minimum depending upon the nature of the ion involved. Aqueous salt solutions of LiCl, NaCl, NaBr, etc., promote the reaction rates of Diels–Alder reactions whereas those of guanidinium chloride (GnCl) and LiClO₄ act in the opposite manner. These studies at fixed concentrations of diene and dienophile have been conducted at different salt concentrations. Since a diene such as cyclopentadiene is very poorly soluble in water, its reaction with a dienophile is expected to depend on the available interface at which reaction is expected to occur. One of the parameters that can be effective in the kinetics of such a reaction is the volume or amount or moles of water available for the reaction at fixed amounts of diene with dienophile. In this paper we report the *endo* and *exo* selectivities for the model reaction of cyclopentadiene with methyl acrylate in varying amounts of aqueous salt solutions of definite compositions. The aqueous salt solutions selected for this study were LiCl (1 M), CaCl₂ (1 M), GnCl (1 and 2 M) and LiClO₄ (1 M). As far as we know, this is the first report of

**Table 1.** The *endo* product for the reaction of cyclopentadiene and methyl acrylate as a function of number of moles of water, $n_w$, available in different aqueous salt solutions

| $n_w$ | *endo* (%) | $n_w$ | *endo* (%) | $n_w$ | *endo* (%) | $n_w$ | *endo* (%) |
|---|---|---|---|---|---|---|---|
| *LiCl (1 M)* | | *CaCl$_2$ 1 (M)* | | 1.43 | 57 | 0.29 | 64 |
| 0.21 | 67 | 0.21 | 66 | | | 0.41 | 62 |
| 0.23 | 68 | 0.25 | 67 | *GnCl (2 M)* | | 0.47 | 61 |
| 0.35 | 71 | 0.43 | 68 | 0.21 | 66 | 0.59 | 59 |
| 0.45 | 77 | 0.61 | 71 | 0.33 | 63 | 0.78 | 57 |
| 0.59 | 79 | 0.79 | 73 | 0.37 | 60 | | |
| 0.71 | 83 | 0.95 | 73 | 0.44 | 60 | *Pure water* | |
| 0.78 | 86 | 1.14 | 74 | 0.62 | 56 | 0.21 | 66 |
| 0.91 | 89 | *GnCl (1 M)* | | 0.84 | 56 | 0.40 | 67 |
| 0.98 | 87 | 0.21 | 66 | 1.01 | 53 | 0.58 | 68 |
| 1.11 | 89 | 0.38 | 64 | 1.31 | 54 | 0.69 | 68 |
| 1.34 | 91 | 0.47 | 62 | 1.51 | 53 | 0.96 | 70 |
| 1.47 | 90 | 0.53 | 61 | 1.52 | 53 | 1.34 | 70 |
| 1.60 | 87 | 0.63 | 61 | | | | |
| 1.62 | 88 | 0.68 | 59 | *LiClO$_4$ (1 M)* | | *Neat reaction* | |
| 1.64 | 89 | 0.96 | 58 | 0.21 | 66 | 0 | 62[a] |

[a] Reaction time about 9 h.

the dependence of water present in salt solutions on the *endo* and *exo* products of the above reaction. Although the *endo* and *exo* products have been examined in water and its mixtures in alcohols by others,[3c,d] their results do not throw any light on how the water molecules present in varying amounts of the salt solutions can have fine control over the stereoisomers.

## EXPERIMENTAL

Cyclopentadiene freshly cracked from its dimer and methyl acrylate from Merck were used in the reaction. Salt solutions were prepared by dissolving analytical-reagent grade salts in deionized water. In a typical run, 0.3 ml (3.63 mmol) of cyclopentadiene was dissolved in 2 ml of the salt solution. Then, 0.3 ml (3.33 mmol) of methyl acrylate was dissolved in different volumes of the salt solution, thereby changing the number of moles of water. The solution containing cyclopentadiene was added to the solution containing methyl acrylate. The moles of water, $n_w$ ($n_w$ = weight of water in g/molecular weight of water in $g\,mol^{-1}$) in each experiment were calculated from the densities of the salt solutions. The concentration scale based on $mol\,l^{-1}$ is not preferred here, as cyclopentadiene has very low solubility in water. The *endo* products were reproducible to $\pm1\%$ (calculated based on triplicate data) including the reactions in pure water. If the number of moles of cyclopentadiene, methyl acrylate and solvent were doubled, the values of *endo* selectivity were again reproducible to $\pm1\%$ based on at least four reactions. The reaction mixture was stirred magnetically at 30 °C for about 5 h. The *endo* and *exo* stereoselectivities were determined using NMR as described elsewhere.[8]

## RESULTS AND DISCUSSION

The results obtained are listed in Table 1 in the form of *endo* products with corresponding moles of water, $n_w$, present in different salt solutions. For the purpose of illustration, in Fig. 1 are plotted the *endo* (%) products as a function of $n_w$ in pure water and its solutions of LiCl, CaCl$_2$, GnCl and LiClO$_4$.

Figure 1 reveals some interesting trends in the variation of *endo* product with the water content present in a salt solution. First, let us comment on the *endo* selectivities obtained in water alone as a controlled reaction for which a marginal increase in *endo* selectivity from 66 to 70 is recorded against a substantial change in $n_w$ from 0.21 to 1.34. It should be noted that 0.21 mol of water was required for carrying out the reaction smoothly in 5 h. A reaction time of 9 h was otherwise required in
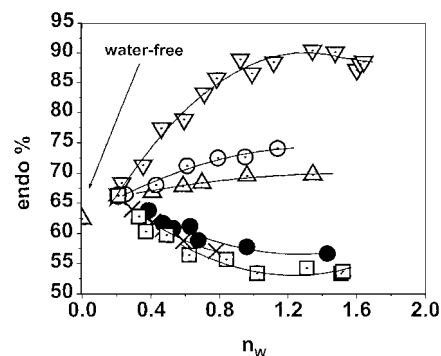


**Figure 1.** Plots of *endo* product (%) versus number of moles of water, $n_w$, in aqueous salt solutions for the reaction of cyclopentadiene with methyl acrylate: ($\triangledown$) 1 M LiCl; ($\bigcirc$) 1 M CaCl$_2$; ($\triangle$) water; ($\bullet$) 1 M GnCl; ($\times$) 1 M LiClO$_4$; ($\square$) 2 M GnCl.

the absence of water. In order to compare the results, consistency was obtained by applying an identical reaction time in all the experiments. In LiCl solution, a remarkable enhancement of the *endo* product is observed up to $n_w \approx 1$. No noticeable change in the *endo* product occurs thereafter. In other words, the *endo* vs $n_w$ curve tapers from $n_w \approx 1$ onwards. In a similar fashion, an increase in $n_w$ for the reaction in CaCl$_2$ leads to higher *endo* selectivity compared with that in water alone. The increase in *endo* product in the case of CaCl$_2$, however, is less than that in LiCl. The rate enhancement in aqueous Diels–Alder reactions can be attributed to the hydrophobicity in addition to other parameters mentioned earlier. Salts such as LiCl, NaCl and CaCl$_2$ enhance the hydrophobic effects, thereby causing the rate acceleration. With this in mind, it seems that the hydrophobic effects increase with increase in $n_w$, yielding a maximum in *endo* selectivity.

The reaction in aqueous GnCl and LiClO$_4$ resulted in a decrease in the *endo* selectivity compared with that in water alone. For 1 M GnCl solution, a decrease of ca 9% in the *endo* product is noted, and in 2 M GnCl the decrease is ca 13%. Use of 1 M LiClO$_4$ lowers the *endo* selectivity by ca 9% again. In short, the *endo* product decreases with increase in water content. As in the case of LiCl and CaCl$_2$, the *endo* product vs $n_w$ curves for both the GnCl and LiClO$_4$ solutions become flat at $n_w \geq 1$.

Analysis of the above experimental data suggests that for a definite amount of cyclopentadiene and methyl acrylate, the hydrophobic effects can be maximized or minimized at $n_w \approx 1$ depending on the rate-promoting or -retarding salt, respectively. In view of very low solubility of cyclopentadiene in water, the reaction takes place in two phases. If this reaction occurs at interface, the rate should then depend on the surface area available for completing the reaction. By enhancing $n_w$, we increased the surface area available for the reaction. Hence it is clear that appreciable changes in the *endo* selectivity can be achieved by increasing or decreasing $n_w$ or the available reaction area for the reactants to realize the reaction in the salt solutions. The plots of *endo* product versus $n_w$ for different ions are important findings of this study. This study in salt solutions is presented for the first time with a view to developing a powerful strategy for fine control of the *endo* and *exo* products of Diels–Alder reactions. The forces responsible for realizing such a reaction may involve interfacial phenomena, hydrophobic interactions, etc., which we are currently investigating. We are collecting experimental

kinetic data on a number of dienophiles with cyclopentadiene to understand the influence of varying interfacial areas on the *endo* selectivity. An interfacial model in this regard is planned shortly.

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