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A Diels–Alder reaction catalyzed by eutectic complexes autogenously formed from solid state phenols and quinones

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Abstract—A Diels–Alder reaction starting from a stoichiometric solid mixture of dimethylanthracene (DMA) and *p*-benzoquinone (BQ) was efficiently catalyzed by adding a small amount of phenol derivatives via autogenous formation of eutectic complexes. The main mechanisms for the formation of eutectic complex with hydrogen bonds were the interposition of the charge transfer from a phenol to a quinone under the influence of steric hindrance by alkyl groups introduced into phenols.

1. Introduction

Solid-state organic syntheses[1,2] and organo-catalytic systems[3,4] are recently gathering interest not only from the green-chemical viewpoints, but also from the idea of utilizing specific reaction fields, for example, via host–guest inclusion complexes. One of the major obstacles for a solid state reaction is the restricted number of reaction fronts, that is only at the inter-particulate contact points between dissimilar reactant species.

In a solid state host–guest complex, however, a large number of molecules are tied up in a specific crystal field. We have been interested in recent solid state syntheses in the context of designing catalytic systems based upon unusual properties imparted to a solid state. One of the simplest examples of solid state host–guest complexes with hydrogen bonds is a charge transfer complex (CTC) between hydroquinone (electron donor) and benzoquinone (electron acceptor).[5,6] Phenols,[7,8] naphthols[9,10] or 1-1′-bi-2-naphthol (BINOL)[11–13] can serve as an electron donor. In the case of BINOL, aromatic compounds such as benzene and anthracene are incorporated into the crystalline network of CTC between BQ and BINOL. This kind of composite crystal is formed directly in a solid state process.[11]

We previously demonstrated the acceleration of the solid state Diels–Alder reaction between dimethylanthracene (DMA) and *p*-benzoquinone (BQ) incorporated in the CTC between BQ and BINOL.[14] Utilization of the host guest field in a heterogeneous solid state reaction increases the reaction rates by (a) a catalytic effect due to strong hydrogen bonds rich in the CTC crystal, and (b) the formation of homogeneous reaction fields with efficient juxtaposition of both diene and dienophile of a Diels–Alder reaction in the CTC crystal fields. However, one of the important requirements for these reaction systems, that is incorporation of diene into CTC, is not always facile, particularly when we deal with a diene compound with large functional groups[13].

On the other hand, some organic reactions starting from a solid state take place rapidly via formation of eutectic phase.[15] In a reaction system between thiocarbonyldiimidazole and some crystalline alcohols, for instance,[16,17] autogenous fusion takes place through the formation of hydrogen-bonded complex between hydroxy groups of alcohols and imidazole, formed as intermediates of the reaction, as we have recently reported.[18]

From these findings, we will be able to significantly increase the overall rate of the Diels–Alder reaction, provided that we succeed in the preparation of the eutectic complex between BQ and phenols by starting from a solid state system. We are presenting below some preliminary results with these respects (Scheme 1).

Keywords: Diels–Alder reaction; Catalysis of charge transfer complexes; Benzoquinone; Anthracene; Autogenous fusion; Eutectic complexes.

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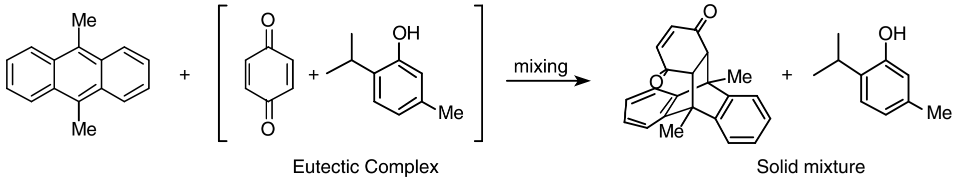

Scheme 1. Catalytic Diels–Alder reaction with eutectic system.

2. Results and discussion

Table 1 summarizes the state and color of the resulted complexes with *p*-benzoquinone (BQ), methyl-*p*-benzoquinone (MeBQ), and *tert*-butyl-*p*-benzoquinone (TBBQ) used as a quinone, and cresol (CR), thymol (TM) or 3-*tert*-butylphenol (TBP) as a phenol. When we use MeBQ or TBBQ as a quinone, all the combinations led to autogenous fusion with simultaneous color change into either dark red or light orange.

When we use BQ as a quinone, mixtures with CR or TBP in the stoichiometric proportion turned their color into red to indicate the formation of CTCs, but remained in a solid state without autogenous fusion. On the other hand, combination of the BQ and TM at the molar ratio 1:2 resulted in an autogenous fusion to change into a red eutectic complex.

We then compared the systems BQ–TBP, which gave solid complex, and BQ–TM, which gave eutectic complex, to examine the difference in the molecular interaction by virtue of IR spectroscopy. According to the literature on the properties of CTC,[19] hydrogen bond formation leads to a red shift of C=O stretching band, while π-charge transfer interaction causes a red shift of the out-of-plane C–H deformation band.

As shown in Table 2, C=O stretching band of BQ ($1658\,cm^{-1}$ in $CHCl_3$) was red shifted in the combinations BQ–TBP ($\Delta\lambda = -15\,cm^{-1}$ in a solid state) and BQ–TM ($\Delta\lambda = -5\,cm^{-1}$ in a eutectic state), respectively. From these results, we recognize that hydrogen bonds are also formed in the eutectic complex. In contrast, C–H out of plane bending band of BQ ($883\,cm^{-1}$ in $CHCl_3$), red shifted in BQ–TBP ($\Delta\lambda = -7\,cm^{-1}$ solid state) system, but not in BQ–TM ($\Delta\lambda = -1\,cm^{-1}$ eutectic state) system. This indicates that the C-T interaction through π-electron systems is almost faded in a eutectic complex, presumably due to the steric hindrance of the molecules.

Table 1. State, ratio, and color of the complexes between various quinones and phenols

Quinone	Phenol	Molar ratio quinone:phenol	State	Color
BQ	CR	1:1	Solid	Red
BQ	TM	1:2	Liquid	Red
BQ	TBP	1:1	Solid	Red
MeBQ	CR	1:1	Liquid	Red
MeBQ	TM	1:1	Liquid	Red
MeBQ	TBP	1:1	Liquid	Red
TBBQ	CR	1:1	Liquid	Orange
TBBQ	TM	1:1	Liquid	Orange
TBBQ	TBP	1:1	Liquid	Orange

Table 2. IR shifts of BQ C=O and C–H bands in CTCs

Complex	Condition	γ C–H (cm^{-1})		ν C=O (cm^{-1})	
		Peaks	Shifts	Peaks	Shifts
BQ	$CHCl_3$ solution	883	—	1658	—
BQ + TBP	Solid complex	876	−7	1643	−15
BQ + TM	Eutectic complex	882	−1	1653	−5
BQ + TM	$CHCl_3$ solution	883	0	1658	0

Decreasing intensity of the C-T bands in UV–vis spectrum also demonstrates the weakness of C-T interactions in eutectic complexes (see Supporting information). This agrees with our primary hypothesis that, the introduction of the bulky functional groups to the donor or acceptor molecules hinders charge transfer and, hence, destabilizes the crystalline state of CTC. In addition, the observed peaks of chloroform solution of BQ–TM eutectic mixture were completely identical with those of BQ in a chloroform solution. These observations confirm that the present eutectic complexes are dissociated in a solution.

We further examined a Diels–Alder reaction in a eutectic complex medium. As a model reaction, we have chosen the reaction system between 9,10-dimethylanthracene (DMA) and *p*-benzoquinone. In the course of the reaction, viscosity of the reaction mixture increased, and the mixture completely solidified after 30 min to complete the reaction, as shown in Figure 1.

Table 3 and Figure 2 summarize the yield of the Diels–Alder reactions with TM, in both a eutectic suspension and a solution. Addition of a stoichiometric amount of TM (Table 3 entry 3) showed a 95% yield in 30 min. Table 4 summarizes differences in the yields of Diels–Alder reactions with various additives. In the case of additives, giving solid state complexes, the yield was only modulate. This clearly demonstrates that the reaction in a eutectic medium is much faster than those in a solid state complex. In addition, the reaction carried out in a solution gave moderate yields (Table 3 entries 4 and 5). These results are explained by the absence of the hydrogen bonds in a solution. Catalytic activities of the additives in the hydrogen-bond-mediated Diels–Alder reactions are generally classified by their acidity denoted in pK_a values (shown in the footnote of Table 4). Even the differences were quite small, all the solution phase reactions examined in this study (Table 4 entries 6–9) are predominated by pK_a, but not under the present solvent free conditions.

Pyrene acts as an electron donor to form the 1:1 CTC with BQ without any hydrogen bonds.[19] Catalytic effects through hydrogen bond are, therefore, automatically

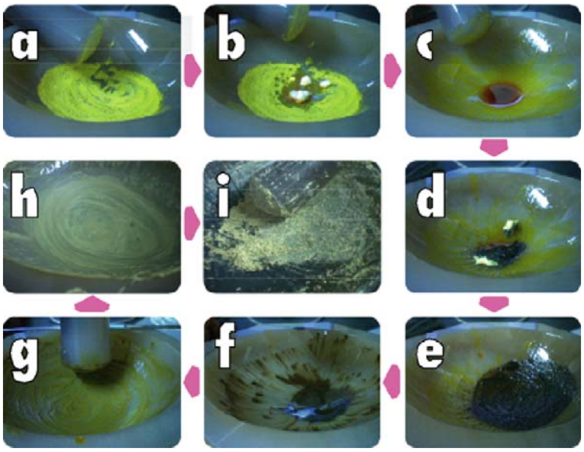

Figure 1. Time resolved observation of a reaction course of eutectic Diels–Alder reaction. Crystalline powders of TM (2 mmol), BQ (1 mmol), and DMA (1 mmol) were mixed in an agate mortar and pestle in an ambient condition: (a) quinone powder, (b) TM added, (c) autogenous fusion, (d) DMA added (0 min), (e) 1 min, (f) 5 min, (g) 10 min, (h) 20 min, and (i) reaction completed with solidification (30 min).

Table 3. Diels–Alder reaction with addition of TM

Entry	Additives	Amount (mol %)	Condition	Time (h)	Yield[a] (%)
1	None	—	Solid[b]	5	26
2	Thymol	10	Solid[b]	2	95
3	Thymol	200	Eutectic[c]	0.5	95
4	None	—	Solution[d]	1	9
5	Thymol	200	Solution[d]	1	17

[a] Yield determined by ^{1}H NMR (chloroform-*d* solution).

[b] Solid state reactions were carried out under milling with Pulverisette (Fritsch).

[c] Eutectic reaction was carried out in a state of suspension under mixing in an a gate mortar with an automatic piston stirrer.

[d] Solution reactions were carried out in 15 mM solution of chloroform. See experimental section for detail.

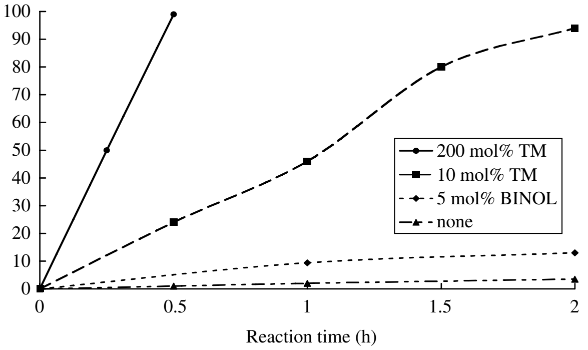

Figure 2. Diels–Alder reaction with eutectic complex.

Table 4. Diels–Alder reaction with various additives

Entry	Additives	Condition	Time (h)	Yield (%)
1	None	Solid state	1	1
2	None	Solution	1	9
3	BINOL	Solid state	1	18
4	BINOL	Solution	1	22
5	2-Naphthol	Solid state	1	9
6	2-Naphthol	Solution	1	18
7	Thymol	Eutectic	0.5	**95**
8	Thymol	Solution	1	17
9	Pyrene	Solid state	1	3

pK_a of the additives, BINOL: 8.28, 2-naphthol: 9.57, thymol: 10.59. Yields were determined by ^{1}H NMR ($CDCl_3$ solution). Additives (200 mol %) was used in entries 1–8. Additive (100 mol %) was used in entry 9. See Experimental section for reaction details.

absent with pyrene, even if destruction of the BQ crystal was enhanced by the formation of the complex. We actually observed the catalytic effect of pyrene only in a slight extent, as shown in Table 4 (entry 5). We therefore confirm the significant role of hydrogen bonds in the present solvent free reactions. We cannot overemphasize, however that increased molecular mobility via autogenous fusion plays a more important role under the solvent free reactions.

Addition of a catalytic amount (10 mol %) of TM to the same reaction system was examined (Table 3, entry 2). The amount of the eutectic phase was very minute under this condition, so that the reaction mixture could be handled like a solid state reaction, to use a ball mill. The reaction was also fast with a catalytic amount of TM to give 95% yield by milling for 2 h.

In summary, we demonstrated benefits of utilizing autogenously formed eutectic complexes in the solid state Diels–Alder reaction. By this procedure, notorious bottleneck of solid state reactions, that is, sluggishness of the reaction, is significantly eliminated. We also emphasize that simultaneous hydrogen bonding during the complex formation process furnishes additional merits of the present organic catalyses in solvent-free Diels–Alder reactions.

3. Experimental

3.1. Materials

All the starting materials were used as purchased from Aldrich, Kanto Kagaku, or Tokyo Kasei Kogyo, without particular pretreatment.

3.2. Formation of eutectics

An equimolar mixture (typically 1 mmol, each) of crystalline powders of phenol derivatives and BQ, were mixed in an agate mortar with a pestle in ambient atmosphere at 298 K.

3.3. Diels–Alder reaction with eutectic complex

Crystalline powders of thymol (2 mmol) and BQ (1 mmol) were mixed in an agate mortar with an automatic pestle in an ambient condition. The powder mixtures were turned to red liquid, immediately after mixing. Crystalline powders of DMA (1 mmol) were added to the mixture while mixing continuously. During the reaction, DMA was not dissolved in this liquid complex. After mixing for 30 min, the reaction mixture solidified to complete the Diels–Alder reaction. The powder mixtures were dissolved into deuterated chloroform and subjected to ^1H NMR spectroscopy at 300 MHz (Varian Mercury-300) to determine the yield.

3.4. Diels–Alder reaction with catalytic amount of TM

An equimolar mixture (typically 1 mmol, each) of crystalline powders, DMA and BQ, with catalytic amount (10 mol %) of thymol were mechanically milled in a closed agate mortar with a single vibrating agate ball (Fritsch, Pulverisette 0) in nitrogen atmosphere at 298 K. Amplitude and frequency of the ball vibration were chosen to be 2 mm and 50 Hz, respectively. Infrared spectroscopy was carried out by a conventional KBr disk method for solid state samples (IR, FTS-175, BIO RAD), and React IR were used for eutectic and solution samples (ReactIR 4000 S.T. Japan Inc.), respectively.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2006.04.030.

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