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Acceleration of solid state Diels–Alder reactions by incorporating the reactants into crystalline charge transfer complexes

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Abstract—Diels–Alder reactions in a solid state between anthracene (AN) derivatives and *p*-benzoquinone (BQ) under mechanical stressing are accelerated by adding a catalytic amount of 2-naphthol (NP) or (*rac*)-1,1′-bis-2-naphthol (BN). Their catalytic effects are based on the formation of the charge transfer complex with strong hydrogen bonds. BN is capable of incorporating BQ together with its reaction partner, AN derivatives, simultaneously. The resulted molecular complex with BN provides crystallographically ordered homogenic reaction fields, resulting in the higher rates of the present solid state Diels–Alder reaction.

1. Introduction

Solid-state organic syntheses gather increasing interests due to their environmentally benign character and higher yields in a relatively shorter period.[1,2] Toda and his school have made an enormous achievement in this field.[3–6] In order to avoid notorious sluggishness of a solid-state reaction, various efforts were paid, among others, by giving mechanical stressing,[7,8] UV irradiation[9,10] or ultrasonication.[11–13]

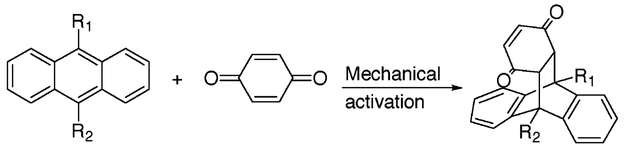
A metal-free organo-catalyst is an alternative candidate to expedite organic syntheses.[14,15] Some Diels–Alder reactions are known as excellent examples of the systems to demonstrate the effects of organo-catalytic reaction through the activation of dienophile with strong hydrogen-bond donor additives like bisphenols or ureas.[16]

p-Benzoquinone (BQ) is one of the most common dienophiles for a Diels–Alder reaction. BQ is also well known as an electron acceptor to form a charge transfer complex (CTC). Mixing BQ with a number of electron donors containing hydroxyl groups results in the crystalline CTCs stabilized with hydrogen bonds.[17–22] Cheung et al. recently demonstrated the formation of the crystalline CTC from a 2:2:1 mixture of (*rac*)-1,1′-bis-2-naphthol (BN), BQ and anthracene (AN).[23–26] In these cases, AN molecules are incorporated into the crystalline network of CTC between BQ and BN, that is, both diene and dienophile are incorporated and face vertically within a same crystalline domain.

We reasonably anticipate that the rapid CTC formation between BQ and BN accelerates a solid-state Diels–Alder reaction due to the following aspects: (1) strong interaction by hydrogen bonding in a solid state and (2) formation of the specific crystal networks, serving as a local reaction field for the solid-state Diels–Alder reaction (Scheme 1).

2. Results and discussion

Table 1 summarizes the yield of the Diels–Alder reaction determined by ^{1}H NMR. Under the present condition in a vibration mill (entries 1–5), only those AN derivatives with electron donating functional groups gave rise to Diels–Alder adducts. The reaction yield



Scheme 1. Solid-state Diels–Alder reaction between anthracene derivatives and *p*-benzoquinone.

Keywords: Solid-state Diels–Alder reaction; Catalysis of charge transfer complexes; Benzoquinone; Anthracene; BINOL; 2-Naphthol.

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Table 1. Yields of Diels–Alder reaction under various conditions

Entry	R_1	R_2	Condition	Time (h)	Yield (%)[c]
1	Br	Br	Agate 2 mm amp[a]	5	0
2	CH_2Cl	CH_2Cl	Agate 2 mm amp[a]	5	0
3	H	H	Agate 2 mm amp[a]	5	0
4	Me	H	Agate 2 mm amp[a]	5	8
5	Me	Me	Agate 2 mm amp[a]	5	26
6	Me	Me	Mixing[b]	48	Trace
7	Me	Me	Chloroform solution	5	40

[a] Reactions were carried out under milling with Pulverisette 0 at 298 K.
[b] Mixing two powdered compounds in a rotary evaporator.
[c] Yield determined by ^{1}H NMR (chloroform-*d* solution).

was, however, relatively low as compared to the conventional solution reaction (entry 7). When we simply mix the preliminarily milled starting powders of DMAN and BQ in a rotary evaporator, only a trace of the reaction was observed even after 48 h (entry 6). Constant and continuous creation of new contact points between dissimilar reactant species is, therefore, indispensable for a solid-state reaction. We now try to overcome this kind of intrinsic problem of the reaction via a solid state route by using additives to expect their unique catalytic effects.

Our first trial was to add the stoichiometric amount of 2-naphthol (NP) or BN to the reaction system, DMAN+BQ, which exhibited highest reactivity among those we examined. Immediately after we milled a 1:1:1 mixture of NP–BQ–DMAN or 2:2:1 mixture of BN–BQ–DMAN, we observed rapid colour change from green to red, suggesting the formation of CTC.

CTC crystals comprising BQ and NP or BQ and BN are stabilized by hydrogen bonds between the carbonyl of BQ and OH of NP[20] or BN.[23–26] Kubinyi and Varasanyi investigated the infrared spectra of a series of complexes between phenol derivatives and BQ.[27] They observed red shifts of the C=O stretching band (1650 cm^{-1}) due to hydrogen bonds formation, and out-of-plane C–H deformation band (892 cm^{-1}) due to π-charge transfer interaction, respectively, in CTC in a solid state. We also observe the spectrum changes during CTC formation in the system of BQ–NP and BQ–BN that does not contain diene in the mixture, as shown in Table 2. When we observed C=O stretching band of BQ as a measure of the hydrogen bonding effect, the peak shift was −20 cm^{-1} with NP and −10 cm^{-1} with BN, respectively. As for the C–H deformation of BQ, the peak shifts were −18 cm^{-1} and −19 cm^{-1} with NP and BN, respectively. This implies that the catalytic effect expected from the viewpoints of hydrogen bond formation of NP is stronger than that of BN.

Table 2. IR peak shifts due to CTC formation

Complex	γC–H $\delta\lambda$ (cm^{-1}) (892 cm^{-1})	νC=O $\delta\lambda$ (cm^{-1}) (1650 cm^{-1})
BQ+NP	−18	−20
BQ+BN	−19	−10

Crystallographic changes during CTC formation were observed by X-ray diffractometry on the stoichiometric CTC mixtures of NP:BQ:DMAN at 1:1:1 and BN:BQ:DMAN at 2:2:1, respectively. In the case of NP–BQ–DMAN system, peaks assigned to DMAN remained unchanged after 1 h milling, and all the other peaks appeared were assigned to CTC between NP and BQ, as shown in Figure 1. This suggests the rapid formation of CTC with an entirely new crystalline phase of NP–BQ without incorporating DMAN. The XRD profiles of the BN–BQ–DMAN system are shown in Figure 2. They exhibit completely different profiles from

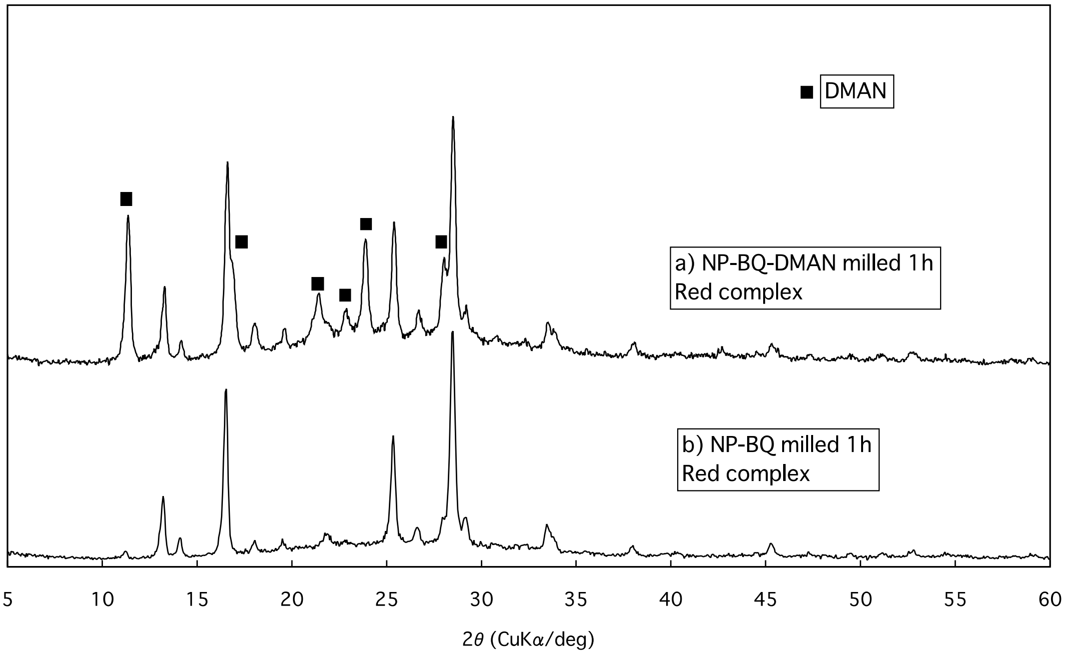

Figure 1. XRD profiles of (a) NP–BQ–DMAN (1:1:1) (top) and (b) NP–BQ (1:1) (bottom) both after milling for 1 h.

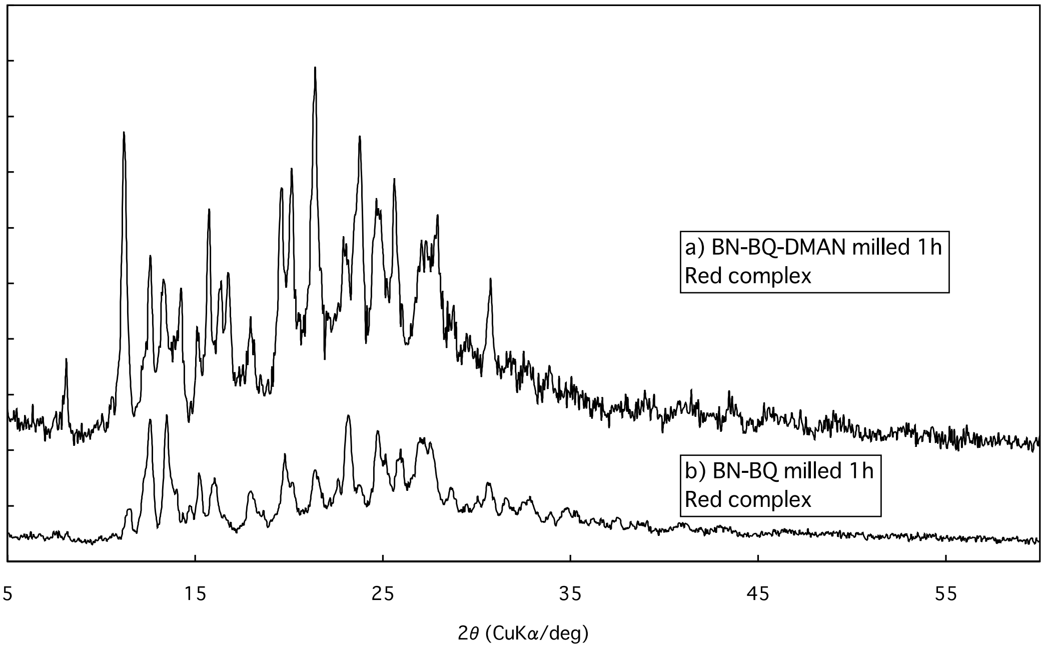

Figure 2. XRD profiles of (a) BN–BQ–DMAN (2:2:1) (top) and (b) BN–BQ (1:1) (bottom) both after milling for 1 h.

those of the BN–BQ CTC crystal. This suggests that the incorporation of diene occurred even when AN was replaced by DMAN.

A Diels–Alder reaction in CTC was carried out with NP:BQ:DMAN at 4:2:1 and BN:BQ:DMAN at 2:2:1, respectively, to give an equivalent amount of dienophile and catalyst OH groups. In both cases, yields rose to above 99% with 5 h milling, as compared to 26% without additives. We also carried out the same reaction in chloroform at the molar ratio, NP:BQ:DMAN at 2:1:1. The yield was 56% after 5 h at 298 K, as compared to 40% without additives. It is noteworthy that the catalytic effects of the additives in the solution are much less significant compared to those in a solid state.

The effects of the additives in a catalytic amount were investigated by adding 10 mol % NP or 5 mol % BN to the reaction system, DMAN+BQ. The quantity of the two additives was chosen to give an equivalent amount of OH groups. As shown in Figure 3, the yield after 5 h milling increases from 26% to 75% or 85% with NP or BN, respectively. A closer look on the kinetic curves in Figure 3 further reveals that with BN, no eventual incubation time exists like in the case of the solution reaction. In contrast, addition of 10 mol % of 2-adamantanol, an alcohol without aromatic ring and

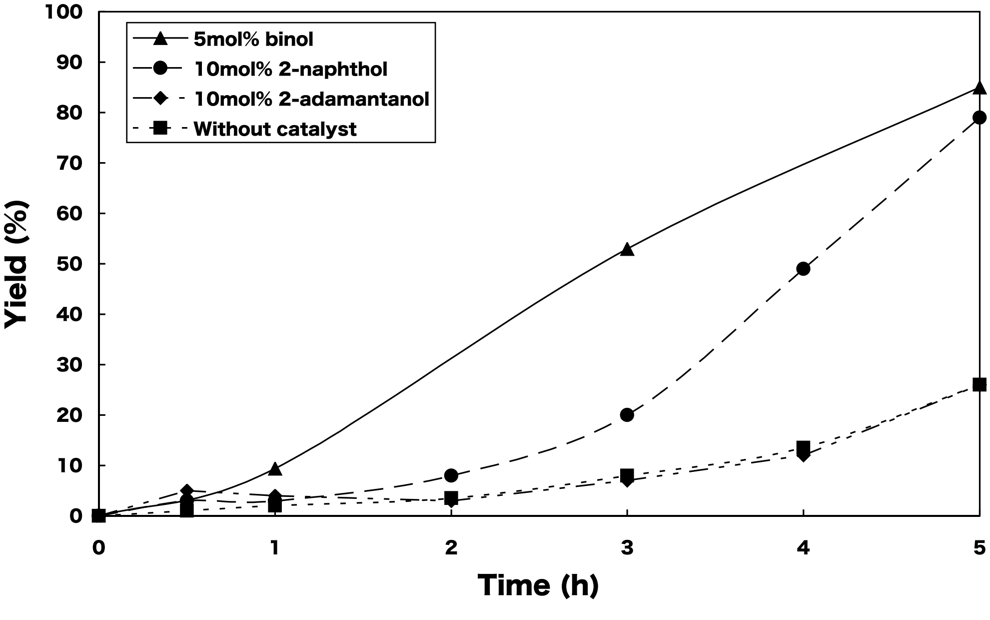

Figure 3. Effect of alcohols on the rate of Diels–Alder reaction. All the reactions were carried out under milling with Pulverisette 0 at 298 K.

incapable of forming CTC with BQ, does not exhibit any catalytic effects or colour change. Therefore, the formation of CTC crystal is essential to this catalytic system for the activation of a dienophile in a solid state.

In summary, the observed acceleration of the solid-state Diels–Alder reaction by NP or BN is attributed to the strong hydrogen bonds in CTCs in a solid state. Efficient juxtaposition of both diene and dienophile in the CTC crystal fields plays an additional important role in the BQ–BQ–DMAN catalytic system.

3. Experimental section

All the starting materials were used as purchased from Aldrich, Kanto Kagaku or Tokyo Kasei Kogyo, without particular pretreatment. An equimolar mixture (typically 1 mmol, each) of crystalline powders, AN derivatives and BQ, was mechanically stressed in a closed agate mortar with a single vibrating ball (Fritsch, Pulverisette 0) in nitrogen atmosphere at 298 K.[28] The amplitude and frequency of the ball vibration were chosen to be 2 mm and 50 Hz, respectively.

The powder mixtures just after milling were dissolved into deuterated chloroform and subjected to ^{1}H NMR spectroscopy.[29] This was performed at 300 MHz by a spectrometer (Varian Mercury-300). The infrared spectroscopy of the powdered samples was carried out with a conventional KBr disk method (IR, FTS-175, BIO RAD). Crystalline states were analyzed by X-ray diffractometry (XRD, RINT 2200, Rigaku) with Cu Kα beam.

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28. The bulk temperature during stressing did not exceed 313 K, as we observed no trace of melting by milling menthol (mp 313 K) under the same condition for 5 h. We, therefore, exclude the participation of a liquid phase in the present reaction under mechanical stressing.
29. Since it took less than 5 min for NMR measurement, we are convinced that the value of the yield determined by conventional NMR in solution does not significantly skew the results of solid state reaction.