Promotion of organic reactions by interfacial hydrogen bonds on hydroxyl group rich nano-solids†

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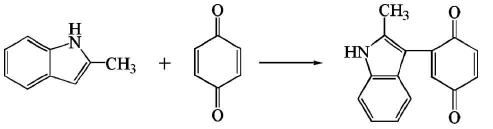
Surface hydroxyl group rich nano-structured solids dramatically increase the rate of several organic reactions; such effect is attributed to the formation of interfacial hydrogen bonds between the surface hydroxyl groups and the reactants; this catalytic effect is versatile and applicable for a broad range of reaction conditions.

Promotion of some organic reactions by hydrogen-bond donors have attracted considerable attentions.[1] One fascinating example is the acceleration of Diels–Alder reaction rate by the hydrogen bond donors, which was reported by Kelly *et al*.[2] The catalytic effect is due to the presence of biphenylenediol, an organic hydrogen bond donor. Other examples of catalytic effect of hydrogen bond donors include asymmetric catalysis by chiral hydrogen bond donors[3] and organo-catalysis mediated by thiourea derivatives[4] in homogenous systems. It is proposed that the essence of hydrogen bond catalysis is both energetic and conformational: the hydrogen bond catalyzes the Diels–Alder reaction by lowering the LUMO energy of the carbonyl-containing dienophiles and stabilizing the charged transition state of the reaction; while in asymmetric catalysis, hydrogen bonds may help the reactants to retain preferred conformations for asymmetric reactions. However, such catalytic effect by hydrogen bond donors has not yet been fully exploited using heterogeneous hydrogen bond donors. Using inorganic solids to catalyze organic reactions may not only expand our understanding of interfacial chemistry, but also benefit the environment due to certain advantages of a heterogeneous system.

In previous studies, we synthesized several nano-structured metal oxide nano-particles, including iron oxide,[5] titanium oxide[6] and cerium oxide.[7] These materials have large surface areas and abundant surface hydroxyl groups. When a nano-solid particle is immersed in a solution, its external surface is exposed to the molecules in the solution. The surface hydroxyl groups can then form interfacial hydrogen bonds with organic molecules in the solution, the same way as the hydrogen bonds can form in homogeneous solutions. Inspired by the catalytic effect of hydrogen bonds in homogeneous system, we speculated that similar catalytic effect by interfacial hydrogen bonds will also promote the organic reactions.

In this communication, we will demonstrate that some organic reactions can be catalyzed by the interfacial hydrogen bonds between the reactants and surface hydroxyl groups on nano-iron hydroxide and other hydroxyl group rich solids. The function of these nano-solids is as hydrogen bond donors to provide hydroxyl groups for forming hydrogen bonds with reactants, as illustrated in Scheme 1. In several organic reactions, we observed a dramatic increase of reaction rate due to the presence of these nano-solids. Nano-solid catalysts are versatile and applicable to a broader range of reaction conditions than homogeneous systems.

Iron hydroxide nano-particles with large surface area and abundant surface hydroxyl groups can catalyze the coupling reaction between *p*-benzoquinone and 2-methylindole (reaction (1)) at room temperature and dramatically increase the reaction rate (See ESI† for experimental details). Soon after iron hydroxide nano-particles and a reaction mixture consisting of THF, reactants **1** and **2** were mixed and stirred, a characteristic violet colour appeared, indicating the formation of product **3**.

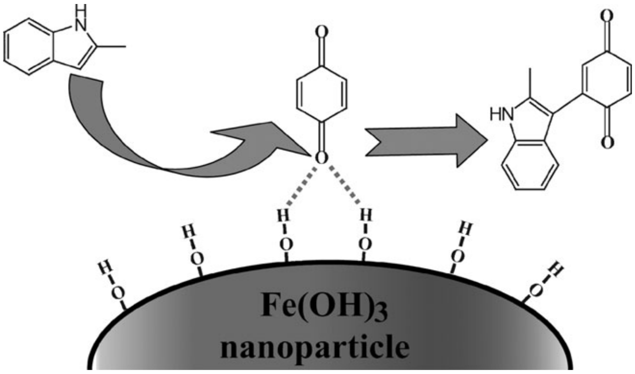


(1)

1 **2** **3**

After 24 h of reaction, a 72% yield for product **3** was achieved. No by-product was detected by GC. In sharp contrast, when no iron hydroxide nanoparticles was used, no product was detected (Table 1), suggesting very low reaction rate for reaction (1) by itself.

As a control experiment, water was added to the reaction mixture, forming a homogeneous solution. The presence of water also helped, and the yield was 5% after 24 h and 21% after 120 h.



Scheme 1 Reaction promoted by hydrogen bonds between the reactant and hydrogens on hydroxyl rich nano-particles.

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Table 1 Yields of product **3** in reaction (1) using different nano-solids

Added reagent	t/h	Surface area/m^2 g^{-1}	Conversion (%)	Yield (%)
$Fe(OH)_3$	24	214	72	72
$Fe(OH)_3$	24	15	12	12
α-Fe_2O_3	24	30	0	ND[a]
—	24	N/A	0	ND
Water	24	N/A	5	5
Water	120	N/A	21	21

[a] Not detected.

Note that the amount of water used was 10 times the amount of iron hydroxide used. In two other control experiments, we measured the reaction yields using iron hydroxide with low surface area and hydroxyl group free α-iron oxide. While 72% of product **3** yield was achieved using iron hydroxide nano-particles with high surface area of 214 m^2 g^{-1}, only a 12% yield was obtained using iron hydroxide particles with low surface area. Interestingly, hydroxyl group free α-iron oxide showed no reactivity, and no product was detected from the same reaction.

TEM images of the iron hydroxide nano-particles (see ESI†) shows that the average diameter of these nano-particles is about 10 nm. There are abundant free hydroxyl groups on the surface of iron hydroxide nano-particles.[8] The hydroxyl groups can insert into the liquid at the liquid–solid interface, form interfacial hydrogen bonds with the reactant molecules and intermediate species, as depicted in Scheme 1, and catalyze the reaction through lowering the energy states of key reaction components. The number of surface hydroxyl groups on an iron hydroxide sample is proportional to its surface area. (Thus, there are less hydroxyl groups on the surface of micron sized iron hydroxide particles.) Table 1 indicates that the yield of the reaction is roughly proportional to the surface area and the amount of surface hydroxyl groups of iron hydroxides. Such dependence on the amount of surface hydroxyl groups suggests that the presence of hydroxyl groups is the crucial factor for promoting the reaction.

Fig. 1 showed that the yield of product **3** increases almost linearly with reaction time. The linear increase of the product yield suggests a zero-order reaction. Reactants **1** and **2** were added at a 1 : 2 mole ratio, so during the reaction, both reactants were consumed substantially and their concentrations were decreasing. However, the reaction rate did not change much with the reaction time, indicating a zero-order reaction kinetic and a constant reaction rate. This agrees well with the interfacial hydrogen bond promotion mechanism shown in Scheme 1, where the reaction rate is determined by the number of *p*-benzoquinone molecules that form hydrogen bonds with the hydroxyl groups. In this study, since the amount of surface hydroxyl groups on iron hydroxide is constant, therefore the reaction rate is also constant.

The above results establish that the reaction rate for reaction (1) is increased dramatically when hydroxyl group rich iron hydroxide nano-particles are added to the reaction. Reaction (1) can be catalyzed by Brønsted or Lewis acids.[9] In order to check whether nano-iron hydroxides' ability to promote reaction is *via* solid acid catalysis or interfacial hydrogen bond catalysis, we studied the H/D exchange during reaction (1). $Fe(OD)_3$ was prepared to repeat the same experiments for reaction (1). The rationale behind this H/D exchange experiment is that if iron hydroxide is a solid acid catalyst, the hydroxyl group on its surface will be involved in the C–H bond activation step; and H/D exchange is expected to form deuterated product **3**. However, GC-MS analyses of product **3** showed no H/D exchange (see ESI†). Exactly the same molecular ion mass patterns were observed for product **3** from four different experiments, indicating that deuterium atoms are not incorporated into product **3** when $Fe(OD)_3$ is used.

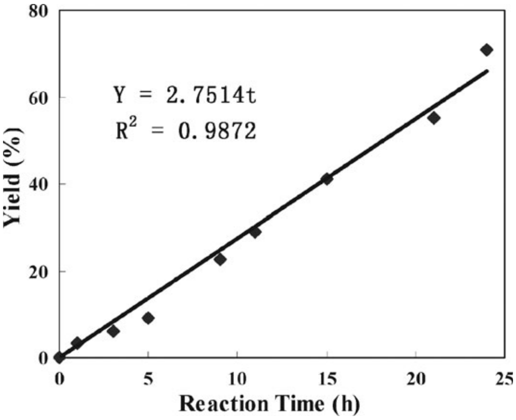


Fig. 1 Time dependant yield of product **3** in reaction (1) promoted by iron hydroxide nano-particles.

Similar results were obtained when D_2O is added in control experiments (Table 2). The lack of H/D exchange on surface hydroxyl groups suggested that the main function of iron hydroxide nanoparticles is to provide hydroxyl groups to form hydrogen bonds with reactant **2**, as illustrated in Scheme 1, and the reaction is promoted by the interfacial hydrogen bonds between hydroxyl groups and reactant **2**.

The above results also suggest that besides iron hydroxide; other solids with enough free surface hydroxyl groups should also promote reaction (1). In other sets of experiments, various solids were added to a 2-methylindole–*p*-benzoquinone–THF mixture to study their catalytic activities. These solids are chosen as pairs, one with sufficient amount of surface hydroxyl groups, and the other without enough hydroxyl groups. Differences in the reaction rate are expected from each pair. Table 3 shows the details of these materials and their performances in reaction (1). γ-Al_2O_3 is a well studied material as it is a frequently used industrial catalyst supporter. There are many hydroxyl groups on the surface of γ-Al_2O_3.[10] γ-Al_2O_3 with surface area of 240 m^2 g^{-1} has a larger amount of surface hydroxyl groups and leads to a higher product **3** yield of 56%, while a low surface area γ-Al_2O_3 only resulted in a 5% yield. For zinc oxide and zinc hydroxide, hydroxyl group rich zinc hydroxide results in a 27% yield; while on zinc oxide, which has no surface hydroxyl groups, no product is produced. These results further confirm that hydroxyl rich solids can catalyze certain organic reactions through interfacial hydrogen bonds.

Table 2 H/D exchange results for reaction (1)

Added reagent	t/h	Deuterium content in product **3** (atom%)
$Fe(OD)_3$	24	0[a]
D_2O	24	0[a]

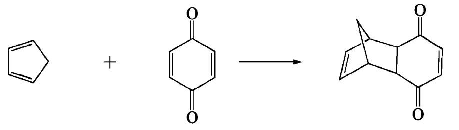
[a] Based on the identical mass ion peaks in mass spectrometry.

Table 3 Yields of product **3** in reaction (1) using various solids

Solid	t/h	Surface area/$m^2\ g^{-1}$	Conversion (%)	Yield (%)
γ-Al_2O_3	24	240	56	56
γ-Al_2O_3	24	2.0	5	5
ZnO	24	14	0	ND[a]
$Zn(OH)_2$	24	43	27	27

[a] Not detected.

The ability of hydroxyl rich nano-particles to promote organic reactions is not limited to reaction (1). We also carried out a Diels–Alder reaction between *p*-benzoquinone and cyclopentadiene (reaction (2)) using iron hydroxide nano-particles. After 24 h of reaction at room temperature, the yield of product **5** reached 84%, while no product was detected under control experiments without solid particles. So the catalytic effect of interfacial hydrogen bonds may be a general effect.



(2)

4 **2** **5**

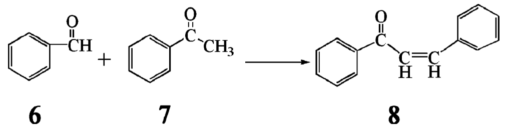
Such interfacial hydrogen bond catalysis again shows the crucial, yet not fully explored roles of hydrogen bond in chemical reactions and even biological systems.[11] Besides the hydrogen bond catalysis in homogeneous solution[1–4] mentioned above and for the heterogeneous system reported here, in a so-called on-water reaction, the hydrogen bonds between water and organic molecules at the water/oil interface also catalyze some organic reactions.[12] Wang and co-workers[13] studied reaction (1) in an on-water reaction. The result from our work is compared with reaction results from other catalytic systems, even though there are fundamental differences among them. For example, in Wang *et al.*'s on-water reaction study, the yield for product **3** was 82% using water after 10 h. Apparently the rate increases from nano-iron hydroxide promotion is slightly less than that from water.

A heterogeneous catalytic system has many advantages. For example, in a homogeneous system, the hydrogen-bond donor molecules must be soluble with reactants, and separating the organic hydrogen bond donor and the product is difficult. However, for heterogeneous systems with solid particles, such difficulty is avoided. A simple centrifugation or filtration will separate the solid and liquid. If combined with magnetic nano-solids, catalyst recovery may become even easier. In addition, reaction temperature may be limited in on-water reactions. So far water promoted reactions must be carried out below 100 °C. With solid particles, the reaction can be carried out at a broader temperature range. This will enable us to study reactions that can not be promoted by water.

As a preliminary example, an aldol condensation reaction (reaction (3)) is studied using *p*-xylene as solvent. As shown in Table 4, a control experiment without solid at 120 °C produces no product **8** at all. Adding water does not help either, partly because water does not stay as liquid at 100 °C, and no stable hydrogen bonds are formed. However, when iron hydroxide is added, a 36% yield is obtained at 20 °C in 8 h; and 90% yield is achieved at 120 °C in 3 h. Another hydroxyl group rich solid, γ-Al_2O_3 gives 92% yield. Reaction (3) usually requires acid or base to initiate the reaction. γ-Al_2O_3 is a Lewis acid, which may help to catalyze the reaction. However, as mentioned earlier for reaction (1), iron hydroxide is not known to show significant basicity or acidity. Its ability to promote reaction (3) is very likely due to catalysis effect of interfacial hydrogen bonds.

Table 4 Yields of product **8** in reaction (3) under various conditions

Added reagent	T/°C	t/h	Conversion (%)	Yield (%)
—	120	24	0	0
H_2O	100	24	Trace	Trace
$Fe(OH)_3$	20	8	40	36
$Fe(OH)_3$	120	3	98	90
γ-Al_2O_3	120	3	99	92



(3)

6 **7** **8**

In summary, dramatic reaction rate increases were observed at the presence of hydroxyl rich nano-solids. The extent of rate increase is determined by the amount of surface hydroxyl groups. Solids with more hydroxyl groups lead to higher yields, while hydroxyl group free solids do not promote the reaction at all. H/D exchange results established that interfacial hydrogen bonds between surface hydroxyl groups and reactant molecules are responsible for such catalytic effect. Future work will focus on exploiting the interfacial hydrogen bond catalysis by nano-iron hydroxide for more organic reactions.

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