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Hydroxyl Group Rich C_{60} Fullerenol: An Excellent Hydrogen Bond Catalyst with Superb Activity, Selectivity, and Stability

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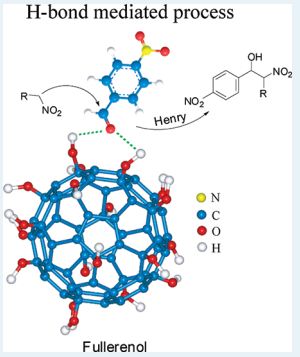
Supporting Information

ABSTRACT: Fullerenol is a superb hydrogen bond catalyst with high catalytic activity, selectivity, and stability in several organic reactions. It exhibits favorable features from both homogeneous and heterogeneous catalysis.

KEYWORDS: Fullerenol, hydrogen bond catalysis, heterogeneous catalysis, Henry reaction, Aldol reaction



Fullerene molecules (C_{60} in this study) have remarkable features for catalysis. They are molecules with well-defined structures and nanoparticles with their large molecular sizes (0.71 nm for C_{60}). More importantly, fullerene cages have superb ability to accommodate electrons,[1−3] and the ability to hold and release electrons is the essence of catalysis. However, the lack of active sites on the fullerene cages prevents the direct use of fullerene in catalysis. There are only a few studies using fullerenes as a component in composite catalysts.[4,5]

Fullerenes can be functionalized with hydroxyl groups and become fullerenols.[6,7] With these hydroxyl groups, we envisioned that fullerenols might be used as hydrogen bond catalysts. Hydrogen bond catalysis requires the catalysts to provide hydroxyl groups for hydrogen bonding with reactants, and consequently the hydrogen bond enhances the reaction rate. Several organic molecules with hydroxyl groups have been reported as useful homogeneous hydrogen bond catalysts.[8−11] Solid particles with abundant surface hydroxyl groups can also function as hydrogen bond catalysts.[12,13] For example, the Aldol reaction could be catalyzed by the hydroxyl groups on the $Fe(OH)_3$ shell of the Fe_3O_4@$Fe(OH)_3$ core−shell composite microspheres.[14]

Since hydroxyl groups are directly attached to the fullerene cages, C_{60} fullerenol will benefit from the strong electron affinity of the C_{60} cage as hydrogen bond catalyst. In this report, we will show that C_{60} fullerenol is indeed an outstanding catalyst for several organic reactions, including Henry reactions, Aldol reactions, Michael addition reaction, and Friedel−Crafts reaction, showing desirable features for both homogeneous catalysis and heterogeneous catalysis. In Henry reactions, high activity, 100% product selectivity, and superb stability are observed.

C_{60} fullerenol was prepared according to a reported method (See Supporting Information).[15] FTIR absorption spectrum, synchrotron radiation based X-ray absorption near-edge spectroscopy (XANES) and X-ray photoelectron spectroscopy (XPS) analysis (Supporting Information, Figures S1, S2, and S3) indicated the presence of abundant hydroxyl groups. On the basis of the XANES and XPS data, the average molecular formula of the fullerenol sample was determined to be $Na_2C_{60}O_4(OH)_{15}$. For control experiments, $Fe(OH)_3$ catalyst was also prepared (Supporting Information, Figure S4).

The catalytic activity of the C_{60} fullerenol was tested in Henry reaction, which is an important method for carbon−carbon bond formation in organic synthesis. In Henry reactions, the resulting nitro alcohol (nitroaldol) products are precursors for various nitrogen and oxygen-containing derivatives, including nitro alkenes, amino alcohols, and amino acids and so forth.[16] Many homogeneous catalysts, including metallic Lewis acids,[17−20] tetraalkylammonium,[21] Cinchona derivatives,[22−24] thiourea-guanidine bifunctional catalyst,[25] and heterogeneous catalysts, such as nanocrystalline MgO,[26] have been developed to catalyze Henry reactions.

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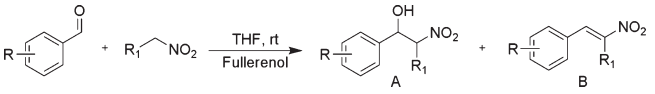
Table 1. Henry Reactions Catalyzed by C_{60} Fullerenol and $Fe(OH)_3$ at Room Temperature



				yields[b] (A, %/B, %)	
entry[a]	R	R_1	time (h)	Fullerenol	$Fe(OH)_3$
1	4-NO_2	C_2H_5	10	94/0	43/11
2	4-NO_2	CH_3	10	96/0	45/10
3	4-NO_2	H	10	97/0	48/14
4	4-CN	H	6	98/0	54/17
5	4-CF_3	H	10	89/0	20/46
6	3-CF_3	H	10	93/0	10/0
7	3,4,5-$(F)_3$	H	10	97/0	53/6
8	4-Br	H	10	90/0	30/50
9	4-Cl	H	24	72/0	21/44
10	4-F	H	24	55/0	15/26
11	4-CH_3	H	24	32/0	5/43
12	4-OCH_3	H	24	28/0	0/39
13	H	H	24	43/0	14/3

[a] Reaction conditions: 0.2 mmol of aromatic aldehyde, 1 mmol of nitroalkane, 0.1 mmol of toluene (internal standard), 30 mg of C_{60} fullerenol or $Fe(OH)_3$ catalyst, 2 mL THF, room temperature. [b] Calculated by HPLC results.

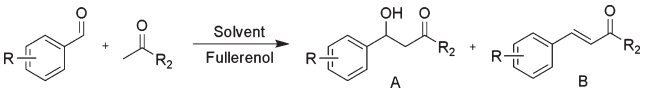
We chose nitromethane, nitroethane, and nitropropane to react with aromatic aldehydes using C_{60} fullerenol catalyst at room temperature. All three nitroalkanes showed similar reactivity. As shown in Table 1, most Henry reactions involving aromatic aldehydes substituted with electron-withdrawing groups (NO_2, CN, CF_3) resulted in excellent yields, while 4-methylbenzaldehyde and 4-methoxybenzaldehyde, which had electron-donating groups resulted in lower yields (Table 1, entry 11 and 12). The reactivity difference was likely because electron withdrawing groups would decrease the electron density on the C atom at the carbonyl group, making the C atom a better target for the nucleophiles, while electron donating groups had the opposite effect.

Note that the products in all reactions in Table 1, catalyzed by C_{60} fullerenol, were 100% nitro alcohol products (product A, determined by NMR and HPLC, Supporting Information). No dehydration product (product B) was observed.

For comparison, the same amount of $Fe(OH)_3$ was used under the same reaction conditions, and the results were listed beside the fullerenol results in Table 1. In sharp contrast, Henry reactions catalyzed by $Fe(OH)_3$ produced both nitro alcohol and dehydrated nitro alkene products with various product distributions.

Aldol reaction is another important C−C bond formation route in organic synthesis for many pharmaceutical intermediates or natural products.[27] Again the C_{60} fullerenol catalyst showed excellent catalytic ability for Aldol reactions. As listed in Table 2, the results of Aldol reactions between aromatic aldehydes and methyl ketones were similar to these of Henry reactions. The reactions involving aromatic aldehydes substituted with a stronger electron-withdrawing group resulted in higher yields. The selectivity for β−hydroxyl ketone products was 100%, indicating again that no dehydration occurred.

Table 2. Aldol Reactions Catalyzed by C_{60} Fullerenol at Room Temperature



entry[a]	R	R_2	solvent	time (h)	yield[b] (A, %/B, %)
1	4-NO_2	CH_3	acetone	12	90/0
2	4-CN	CH_3	acetone	12	85/0
3	4-Br	CH_3	acetone	48	24/0
4	3-Cl	CH_3	acetone	48	3/0
5	4-NO_2	C_6H_5	DMF	12	88/0
6	4-CN	C_6H_5	DMF	12	99/0
7	4-Br	C_6H_5	DMF	12	55/0
8	4-Cl	C_6H_5	DMF	12	45/0
9	4-CF_3	C_6H_5	DMF	12	80/0
10	3,4,5-$(F)_3$	C_6H_5	DMF	12	46/0

[a] Reaction conditions: 0.2 mmol of aromatic aldehyde, 1 mmol of ketone, 0.1 mmol of toluene (internal standard), 30 mg of C_{60} fullerenol, 5 mL acetone, 50 °C or 5 mL DMF, 110 °C. [b] Calculated by HPLC results.

It is a very desirable feature for C_{60} fullerenol catalyst that only hydroxyl group containing products were produced in both Henry reactions and Aldol reactions. The hydroxyl groups on the products were usually desirable functional groups, and product purification became much easier when there was only one product. Dehydration products in Henry reactions and related condensation reactions were usually due to the acidity or basicity of the catalysts. When conventional acid or base catalysts were used, dehydration was inevitable.[28] And in our control experiments, dehydration was also observed on H_2SO_4 and NaOH catalysts (Supporting Information, Table S1). In our previous studies on Aldol reactions and this study on Henry reactions, dehydration reactions occurred when $Fe(OH)_3$ was used.[14] However, the hydroxyl groups on C_{60} fullerenol catalyst lead to 100% product selectivity.

The C_{60} fullerenol was also active for catalyzing Michael addition reactions as well as Friedel−Crafts reactions. As listed in Supporting Information (Tables S2 and S3), in Michael addition reactions, an excellent yield of 94% was obtained from the reaction between chalcone and nitromethane, and all Friedel−Crafts reactions resulted in good yields.

The C_{60} fullerenol catalyst was a heterogeneous catalyst in these reactions. With its hydrophilicity induced by the abundant hydroxyl groups, the C_{60} fullerenol molecules were insoluble in organic solvent. Thus the separation of the catalyst from the reaction mixture was quite easy via centrifugation. At the same time, C_{60} fullerenol catalyst exhibits superb stability that was observed only on molecular catalyst in homogeneous system.

In a preliminary stability test, the Henry reaction between nitromethane and 4-nitrobenzaldehyde was repeated 10 times using recycled C_{60} fullerenol catalyst. All 10 runs had constant yields of about 96% (Supporting Information, Figure S5), showing no sign of catalyst deactivation.

The C_{60} fullerenol catalyst was then put through a series of time-consuming experiments to test the limit of its stability. Excessive amount of reaction solution (10 times of that used in Table 1) was used in each run, while the amount of the C_{60}

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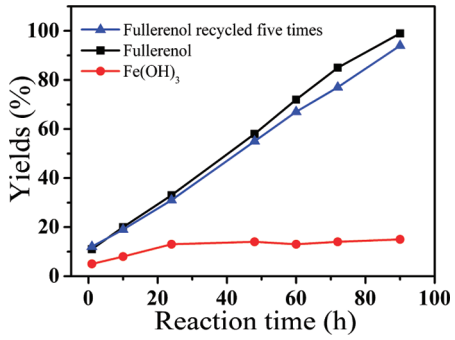


Figure 1. Time dependent yields of Henry reaction between nitromethane and 4-nitrobenzenealdehyde catalyzed by C_{60} fullerenol and $Fe(OH)_3$ catalysts. Reaction conditions: $Fe(OH)_3$ or C_{60} fullerenol catalyst (30 mg), nitromethane (10 mmol), 4-nitrobenzenealdehyde (2 mmol), and toluene (1 mmol, as internal standard compound) in THF (20 mL) solution at room temperature.

fullerenol was kept the same at 30 mg. The rationale behind this design was that by using excessive amount of reaction substrate, the reaction rate would be a constant. The product's yield would increase steadily if the catalyst was active, and become flat if the catalyst was deactivated. HPLC samples were taken periodically to monitor the reaction yields.

The C_{60} fullerenol catalyst showed impressive stability. During the first run, the product yield increased linearly along the reaction time as shown in Figure 1. Because of the large amount of reactant used in this experiment, the reaction processed slowly and needed nearly 100 h to complete. Such long-time run was repeated five times by recycling the catalyst. The time dependent yields of the product were almost the same in all five runs (the results from the first and fifth run were shown in Figure 1), indicating that the catalytic activity of the C_{60} fullerenol did not decrease after 450 h of total run time.

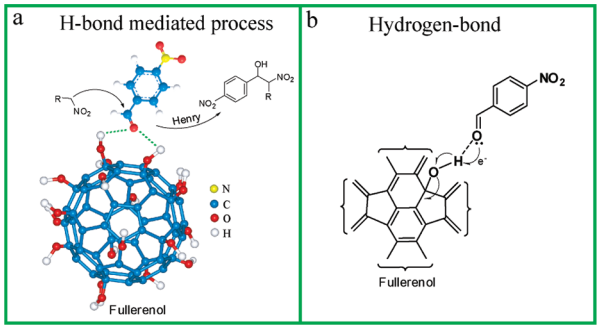
Linear increase of the product yield in Figure 1 indicated that the reaction was a zero order reaction. This was consistent with hydrogen bond catalysis, and the reaction rate was determined by the amount of activated reactants, that is, the amount of the catalyst active sites.

In sharp contrast, when $Fe(OH)_3$ catalyst was used for Henry reraction under the same testing condition, the reaction proceeded slowly at the beginning. The reaction was nearly stopped after 24 h of reaction, and the product yield reached a plateau at 13%, indicating total deactivation of the $Fe(OH)_3$ catalyst. $Fe(OH)_3$, which contained various pores and large surface area to accommodate the active sites, was more likely to induced coke deposition on its surface that led to the deactivation.

The above stability test results suggest that heterogeneous C_{60} fullerenol catalyst behaves like a homogeneous molecular catalyst, which has lasting catalytic activity. However, normal homogeneous molecular catalysts are hard to recycle; yet the C_{60} fullerenol catalyst can be easily recycled as a heterogeneous catalyst. In this regard, the C_{60} fullerenol catalyst has the desirable features from both heterogeneous and homogeneous catalysts, that is, easy catalyst recycling and long catalyst life.

The Henry reactions, Aldol reactions, Michael addition, and Friedel–Crafts reaction showed essentially no conversion using pure C_{60} fullerene as catalyst. Since the only difference between C_{60} fullerene and C_{60} fullerenol is largely the surface hydroxyl groups (and small amounts of other oxygenate species and sodium cations), these species must be the source of the observed catalytic activity.

Scheme 1. Mechanism Illustration of (a) Henry Reaction Catalyzed by C_{60} Fullerenol via an H-Bond Mediated Process and (b) the Allylic Hydroxyl Groups Enhanced Hydrogen Bond between C_{60} Fullerenol Molecule and 4-Nitrobenzenealdehyde Molecule



A hydrogen bond intermediated process was proposed to be the key of the superb ability of C_{60} fullerenol catalysts. The strong electron affinity of the C_{60} cage makes the surface hydroxyl group a better hydrogen bond donor.

For Henry reactions, the surface hydroxyl groups of C_{60} fullerenol may form hydrogen bonds with aromatic aldehydes to activate the carbonyl group of aromatic aldehydes (Scheme 1a). The hydrogen bond between aromatic aldehydes and the C_{60} fullerenol can be strengthened because of the electron affinity of C_{60} cage and the allylic feature of the hydroxyl group (Scheme 1b). The allylic structure of the hydroxyl group could promote the electron transfer from hydrogen to the fullerene cage, leading to a more electron depleted H atom and enhance the hydrogen bond strength. The strengthened hydrogen bonding could further activate the C atom at carbonyl group, thus accelerating the reactions.

It will be very interesting if there is some experimental evidence that a hydrogen bond forms. However, it is hard to get such a result with the fullerenol sample in this work because of its poor solubility in an organic solvent and its mixture feature. We are trying to study such a catalytic mechanism with other fullerenol samples.

DFT calculation was carried out to calculate hydrogen bond energy and hydrogen bond length between benzaldehyde and C_{60} fullerenol (or methanol for comparison). As listed in Supporting Information, Table S5 and Figure S6, the hydrogen bond between C_{60} fullerenol and benzaldehyde was stronger than that between methanol and benzaldehyde with higher bond energy and shorter bond length, confirming that the strong electron affinity of the C_{60} cage and allylic feature of the hydroxyl group were indeed contributing to the outstanding ability of C_{60} fullerenol catalyst. In a control experiment, 30 mg of methanol was used to catalyze the Henry reaction between benzaldehyde and nitromethane under the same conditions, and no reaction product was detected.

Other oxygenate species on the C_{60} fullerenol, especially the sodium associated oxygenate species, may also play important roles for the outstanding catalytic ability of the catalyst. They may help to activate the nitroalkane.[26] In this case, the C_{60} fullerenol may be considered as a bifunctional catalyst. An investigation is underway to explore the role of other oxygenate species and sodium cations.

There are several advantages of using C_{60} fullerenol as a hydrogen bond catalyst to catalyze condensation type reactions

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via hydrogen bonding to the carbonyl group. First, the C_{60} fullerenol catalyst has excellent catalytic activity. And also, as a heterogeneous catalyst, C_{60} fullerenol can be recycled easily via centrifugation. More importantly, compared to conventional Lewis acid catalyst (anhydrous and oxygen-free environment is needed),[29] C_{60} fullerenol catalyst has milder reaction conditions. It exhibits superb activity in atmosphere. Thus, the C_{60} fullerenol catalyst can be regard as an important advance.

In conclusion, we found a superb catalytic ability of C_{60} fullerenol for Henry reactions, Aldol reactions, Michael addition reactions, and Friedel−Crafts reactions as a hydrogen bond catalyst. It showed excellent catalytic activity and stability, and was easy to be recycled. In Henry reactions, C_{60} fullerenol showed high catalytic activity at room temperature, remarkable stability with no deactivation after 450 h of run, and 100% selectivity for nitro alcohol product.

■ ASSOCIATED CONTENT

Supporting Information. Preparation and characterization results of fullerenol and $Fe(OH)_3$, general reaction procedure for Henry reaction, Aldol reaction, Michael addition reaction, and Friedel−Crafts reaction, reaction results and recycling results of fullerenol, and the results of DFT calculations. This material is available free of charge via the Internet at http://pubs.acs.org.

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