Efficient heterogeneous catalysts for the cyclopropanation of olefins

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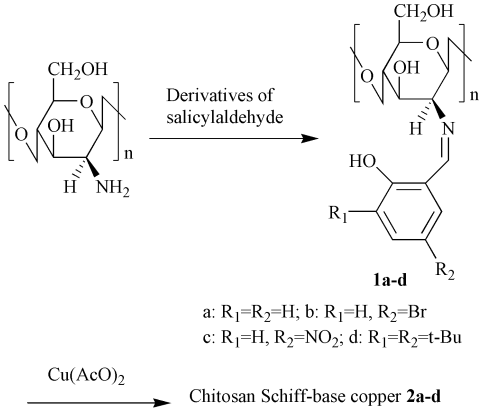
Solid chitosan-Schiff base copper(II) catalysts catalyze cyclopropanation of styrene with ethyl diazoacetate. High conversion in cyclopropanation is achieved and the catalysts can be reused without loss of cyclopropanation activity.

The development of new methods for the efficient and selective preparation of cyclopropanes is of great interest in organic chemistry owing to the frequent existence of this kind of structure in biologically active compounds.[1] In this respect, a good number of metal complexes bearing chiral ligands are able to promote the transfer of carbene from diazo compounds to alkenes with high enantioselectivities through metal-carbene complexes.[2] But the chiral complexes cannot be recovered, thus preventing their applications on a large scale. Heterogeneous catalysts are widely used in industry due to the well-known advantage of easier product-catalyst separation. Furthermore, in some cases, heterogeneous catalysts can be recovered with only minor changes in activity and selectivity, so that they are suitable for use in continuous flow reactions. The development of heterogeneous catalysts for the olefin cyclopropanation reaction is a field of growing interest. The main strategies consist in the anchoring of the ligands to the support by electrostatic interactions and subsequent metal addition to those already-fixed ligands.[3]

Chitosan is a natural optically active polymer. It can be easily obtained from chitin, which is widely distributed in living organisms. Because chitosan has excellent properties such as biocompatibility, biodegradability, non-toxicity, and adsorption, *etc*., it finds use in a variety of functional materials.[4] In this work, we used salicylaldehyde derivatives to modify chitosan and obtain chitosan-Schiff base polymer supports. Copper ion is absorbed by the supports and chitosan-Schiff base copper(II) catalysts are obtained (Scheme 1). The catalysts show high catalytic activity in cyclopropanation of styrene. They can be used without any loss of cyclopropanation activity for at least five successive runs. In addition, the catalysts show low enantioselectivity (23.4% ee).



Scheme 1 Procedure for synthesis of the chitosan-Schiff base copper(II) catalysts **2a–d**.

Results and discussion

The chiral polymer supports and catalysts were characterized by various techniques. The IR spectral data (Table 1) show that for chitosan-Schiff base supports the asymmetric stretching vibrations $\nu_{C=N}$ are in the range of 1632–1644 cm^{-1}. The C=N stretching vibrations in chitosan-Schiff base copper catalysts were different because the backbones were influenced by the copper ion. In order to confirm the structure of the chitosan-Schiff base copper catalysts, XPS data were measured (Table 2), which show that the binding energy of N_{1s} and O_{1s} in chitosan-Schiff base copper catalyst **2a** is higher than that in chitosan-Schiff base support **1a**, and the $Cu_{2p3/2}$ binding energies of chitosan-Schiff base copper catalyst **1a** and Cu $(OAc)_2$ are different. These results suggest that coordination bonds are formed between the nitrogen, oxygen and copper. The $Cu_{2p3/2}$ binding energies in $Cu(OAc)_2$ and the catalyst **3** in which the copper ion is directly absorbed onto the chitosan are similar. Furthermore, the catalyst **3** had no catalytic activity in the cyclopropanation of styrene.

Catalytic cyclopropanation was carried out in the presence of 5 mol% of chitosan-Schiff base copper catalysts. At first, we studied the effect of temperature and solvents on the reaction activity for cyclopropanation of styrene using chitosan-Schiff base copper(II) complex **2a** as the catalyst. As shown in Table 3, a higher yield was obtained at a higher temperature. However, better enantiomeric excesses were obtained at 60 °C. At this temperature, the nature of the solvent has a profound influence on the yield, which decreases from 91.5 to 41.5% as the solvent is varied from 1,2-dichloroethane to ethyl acetate, to acetonile to toluene. The enantioselectivity decreases in a similar fashion. In addition, the molar ratio of styrene and ethyl diazoacetate is very important for this reaction. When the molar ratio of styrene and ethyl diazoacetate was about 17/1, the reaction results were fairly good in this reaction system. As this ratio was decreased, the yield and enantioselectivity declined gradually. As the ratio was reduced to 2/1, the yield reached only 45.3%. In conclusion, the preferable reaction conditions are 60 °C with 1,2-dichloroethane as the reaction solvent, and the molar ratio of styrene and ethyl diazoacetate being about 17/1.

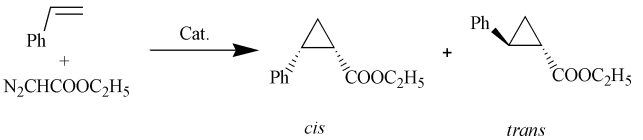
Table 1 IR data of chitosan-Schiff base and catalysts

	$\nu_{C=N}/cm^{-1}$			
Compound	**a**	**b**	**c**	**d**
Chitosan-Schiff base supports **1**	1632.55	1632.47	1643.39	1634.86
Chitosan-Schiff base copper catalysts **2**	1630.99	1630.75	1642.17	1618.32

Table 2 XPS data for chitosan-Schiff base **1a** and chitosan-Schiff base copper catalyst **2a**

	Binding energy/eV			
Compound	C_{1s}	N_{1s}	O_{1s}	$Cu_{2p3/2}$
$Cu(OAc)_2$	—	—	—	931.8
Chitosan	285.20 283.62	398.16	531.62	—
Chitosan copper catalyst **3**	285.00 283.25	398.34	531.26	931.91
Chitosan-Schiff base support **1a**	286.40 284.78	399.07	533.01	—
Chitosan-Schiff base copper catalyst **2a**	286.28 284.64	399.33	532.70	934.39

Table 3 Influence of temperature and solvents on the reaction results using catalyst **2a**[a]



cis *trans*

Entry	T/K	Solvent	Yield[b] (%)	*cis* : *trans*	ee of *cis* (%)	ee of *trans* (%)
1[c]	293	$ClCH_2$–CH_2Cl	14.9	38.4 : 61.6	1.9	4.2
2[c]	313	$ClCH_2$–CH_2Cl	62.1	35.9 : 64.1	9.4	5.8
3[c]	333	$ClCH_2$–CH_2Cl	91.5	33.3 : 66.7	17.1	10.2
4[c]	353	$ClCH_2$–CH_2Cl	92.7	32.4 : 67.6	12.1	9.3
5[c]	333	CH_3CN	58.5	36.7 : 63.3	15.3	9.5
6[c]	333	EtOAc	84.5	37.0 : 63.0	17.0	10.5
7[c]	333	Toluene	41.5	41.7 : 58.3	14.3	6.0
8[d]	333	$ClCH_2$–CH_2Cl	45.3	32.1 : 67.9	8.0	4.4
9[e]	333	$ClCH_2$–CH_2Cl	64.1	34.4 : 65.6	15.6	7.5
10[f]	333	$ClCH_2$–CH_2Cl	79.4	34.8 : 65.2	16.7	8.8

[a] Reaction time of 3 h and using 1 mmol of ethyl diazoacetate. [b] GC yield based on the amount of substrate consumed. [c] Using 17 ml of styrene. [d] Using 2 mmol of styrene. [e] Using 4 mmol of styrene. [f] Using 8 mmol of styrene.

We also investigated the catalytic activity of the different chitosan-Schiff base copper(II) catalysts. As shown in Table 4, all the catalysts **2a**–**2d** showed high catalytic activity. **2c**, bearing the nitro substitute, is the best catalyst of those tested for the cyclopropanation of styrene; up to 23.4% ee has been obtained (Table 4, entry 3). For comparison, the chitosan-copper(II) catalyst **3**, in which copper(II) ion is directly absorbed onto the chitosan, shows no catalytic activity. Generally, trifluoromethanesulfonate copper(II) is an effective precursor for cyclopropanation reactions, so the catalyst **4** was synthesized using chitosan-Schiff base **1a** and $Cu(OTf)_2$. Contrary to our expectations, the reaction result was not good with **4** as the catalyst. When the chitosan-Schiff base **1a** and $Cu(OTf)_2$ (**5**) were used directly as the catalyst, a high conversion and low enantioselectivity in cyclopropanation were obtained (Table 4, entry 7).

Since chitosan-Schiff base copper(II) catalysts are insoluble in most solvents, the catalysts can be easily recovered after reaction, by filtration of the reaction mixture. The catalyst can then be reused for further reactions. The above procedure was repeated for five times and the results obtained are shown in Table 5; we see that the catalyst still retains a high catalytic activity during the fifth cycle.

In conclusion, we have developed a new, practical solid catalysts that show high catalytic activity in the cyclopropanation of olefins. Furthermore, the catalyst can be reused while retaining its high catalytic activity. A more detailed study of this new class of catalysts is underway.

Experimental

Chitosan was obtained from Zhejiang Xianju Chitin Co. Ltd. (viscometric average molecular weight is about 247000, degree of deacetylation $\geqslant$91.3). IR spectra were recorded in KBr disks on a Bruker IFS 120HR FTIR spectrometer. X-Ray photoelectron spectroscopy (XPS) measurements were carried out on a VG ESCALAB 210 photoelectron spectrometer (VG

Table 4 Influence of different Schiff base copper(II) catalysts on the reaction results[a]

Entry	Catalyst	Yield[b] (%)	*cis* : *trans*	ee of *cis* (%)	ee of *trans* (%)
1	**2a**	91.5	33.3 : 66.7	17.1	10.2
2	**2b**	90.1	34.5 : 65.5	19.7	10.0
3	**2c**	89.5	38.0 : 62.0	23.4	13.7
4	**2d**	90.5	33.7 : 66.3	19.6	9.9
5	**3**	0	—	—	—
6	**4**	19.4	36.7 : 63.3	3.5	1.7
7	**5**[c]	90.6	42.9 : 57.1	1.8	0.7

[a] Reaction time of 3 h at 60 °C. [b] GC yield based on the amount of substrate consumed. [c] Chitosan-Schiff base **1a** and $CuO(Tf)_2$.

Table 5 Cyclopropanation of styrene with chitosan-Schiff base copper(II) catalyst **2c** recycling[a]

Entry	Recycle no.	Yield[b] (%)	*cis* : *trans*	ee of *cis* (%)	ee of *trans* (%)
1	Fresh	89.5	36.2 : 63.8	23.4	13.7
2	1	89.6	38.0 : 62.0	23.4	12.2
3	2	89.0	38.6 : 61.4	21.5	10.6
4	3	91.3	38.6 : 61.4	21.6	11.5
5	4	87.8	38.5 : 61.5	21.9	12.4

[a] Reaction time of 3 h at 60 °C. [b] GC yield based on the amount of substrate consumed.

Scientific Co.). Atomic absorption results were obtained on a WFX-10 atomic absorption apectrophotometer. The reaction products of cyclopropanation were analyzed by a GC-MS (HP 6890/5973) system. The yield, the ratio of *cis* and *trans* isomers and ee values were determined on a HP5890 II GC with a SE-54 capillary column and HP6890GC with a CP-Chirasil-Dex CB capillary column (25 m × 0.25 mm, 0.25 μm i.d.). The conditions were as follow: injector temperature of 250 °C, detector temperature of 250 °C, column temperature of 130 °C, column flow 1.0 ml min^{-1}, split ratio 50 : 1.

Syntheses

General procedure for the synthesis of chitosan-Schiff base supports 1a–d. Chitosan (1.9 g) and 30 mmol of salicylaldehyde derivatives were refluxed in 30 mL of methanol and 3 mL of acetic acid for 10 h. After the completion of the reaction, chitosan-Schiff base supports were collected by filtration, washed with ethanol and then acetone and dried under vacuum.

General procedure for the synthesis of chitosan-Schiff base copper(II) catalysts 2a–d. Chitosan-Schiff bases (1 g) and 8 mmol of $Cu(OAc)_2 \cdot H_2O$ were refluxed in 20 mL of ethanol for 10 h. After the reaction, chitosan-Schiff base copper(II) catalysts were collected by filtration, washed with water and ethanol, then dried under vacuum. The copper contents of the catalysts were determined by atomic absorption spectroscopy: **2a** (1.18 mmol g^{-1}), **2b** (1.06 mmol g^{-1}), **2c** (0.65 mmol g^{-1}), **2d** (1.18 mmol g^{-1}).

Synthesis of chitosan-copper(II) catalyst 3. Chitosan (1 g) and 8 mmol of $Cu(OAc)_2 \cdot H_2O$ were refluxed in 20 mL of ethanol for 10 h. After the reaction, chitosan-copper(II) catalyst **3** was collected by filtration, washed with water and ethanol, then dried under vacuum. The copper content of the catalyst was determined by atomic absorption spectroscopy: **3** (0.44 mmol g^{-1}).

Synthesis of chitosan-copper(II) catalyst 4. Chitosan-Schiff base **1a** (1 g) and 0.8 mmol of $Cu(OTf)_2$ were refluxed in 10 mL of ethanol for 10 h. After the reaction, chitosan-copper(II) catalyst **4** was collected by filtration, washed with methanol and dried under vacuum. The copper content of the catalyst was determined by atomic absorption spectroscopy: **4** (0.63 mmol g^{-1}).

Catalytic studies

General procedure for cyclopropanation of styrene. Under an argon atmosphere, a few drops of a solution of 1 mmol of ethyl diazoacetate in 4.0 ml of 1,2-dichloroethane was added to a mixture of 5 mol % catalyst, 2.0 ml of styrene and 2.0 ml of 1,2-dichloroethane at 80 °C to initiate the reaction. After the mixture was cooled to 60 °C, the rest of the ethyl diazoacetate solution was added over 1 h by a syringe pump and the mixture was stirred for another 2 h after the addition was complete. When the reaction was completed, the mixture was filtrated. The catalyst was recovered for further reactions. The products were identified by GC-MS.

Procedure for cyclopropanation of styrene using 5 as catalyst. Under an argon atmosphere, 30 mg of chitosan-Schiff base **1a** and 18.1 mg of $Cu(OTf)_2$ were added to 4 ml of 1,2-dichloroethane and the mixture was stirred for 2 h at 60 °C. Then 2 ml of styrene and a few drops of a solution of 1 mmol of ethyl diazoacetate in 4.0 ml of 1,2-dichloroethane were added at 80 °C to initiate the reaction. After the mixture was cooled to 60 °C, the rest of the ethyl diazoacetate solution was added over 1 h by a syringe pump and the mixture was stirred for another 2 h after the addition was complete. When the reaction was completed, the mixture was filtrated. The products were identified by GC-MS.

GC analysis: ethyl 2-phenylcyclopropane-1-carboxylate [*cis*: 17.8(major) and 19.2(minor) min; *trans*: 20.2(minor) and 20.9(major) min].

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