

Hydrolyzed octadecyltrichlorosilane functionalized with amino acids as heterogeneous enantioselective catalysts

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Abstract Heterogeneous asymmetric catalysts using amino acids as chiral promoter were synthesized by attachment of amino acids such as L-glutamic acid and L-phenylalanine onto the hydrophilic part of hydrolyzed octadecyltrichlorosilane (OTS). The catalysts exhibited 12–18% enantiomeric excess (ee) for the asymmetric hydration of epoxycyclohexene to yield (1R,2R)-*trans*-1,2-cyclohexanediol and (1S,2S)-*trans*-1,2-cyclohexanediol.

Keywords Heterogeneous asymmetric catalysts · Amino acid as chiral promoter · Asymmetric hydration of epoxycyclohexene

Introduction

The control of enantioselectivity by heterogeneous asymmetric catalysis remains a big challenge today. The main drive has been to find new, exciting routes to chiral molecules while achieving high enantiomer selectivity. To date, there have been numerous approaches to the design of heterogeneous asymmetric catalysts [1–7]. In this paper, a new strategy to obtain active catalysts in the enantioselective hydration of epoxycyclohexene is proposed. The research strategy is based on the ideas that the enantioselective reactions could be induced by chiral amino acids and the use of heterogeneous catalysis for synthetic purposes will overcome practical separation problems. In order to realize these ideas, a chiral amino acid needs to be attached to the hydrophilic part of hydrolyzed OTS. Amino acids such as L-glutamic acid and L-phenylalanine have been chosen because of their water-soluble properties; hence

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they can be easily removed by treatment with water. It is expected that the attachment of the amino acid would result in a chiral solid catalyst with bimodal hydrophobic-hydrophilic character (see Fig. 1). In addition, as OTS has three chloro functional groups, it can be expected to have a high tendency to polymerize.

Experimental

Two types of heterogeneous asymmetric catalyst were prepared using two kinds of amino acids as a chiral promoter i.e. L-glutamic acid and L-phenylalanine. The amino acids are attached onto the hydrophilic part of hydrolyzed OTS during sol-gel synthesis. 10 mmol of OTS was added into 20 mmol of L-glutamic acid. Ten mL of toluene was added into the mixture which was then stirred at ambient temperature under open atmosphere in order to hydrolyze the OTS. The resulting solids were then washed thoroughly using boiling distilled water to remove free L-glutamic acid which is not attached to hydrolyzed OTS and finally dried in an oven at 50 °C. The as-prepared catalyst was denoted as hydrolyzed OTS-Glu. A similar procedure was also carried out to prepare L-Phenylalanine attached to hydrolyzed OTS (denoted as hydrolyzed OTS-PheAla).

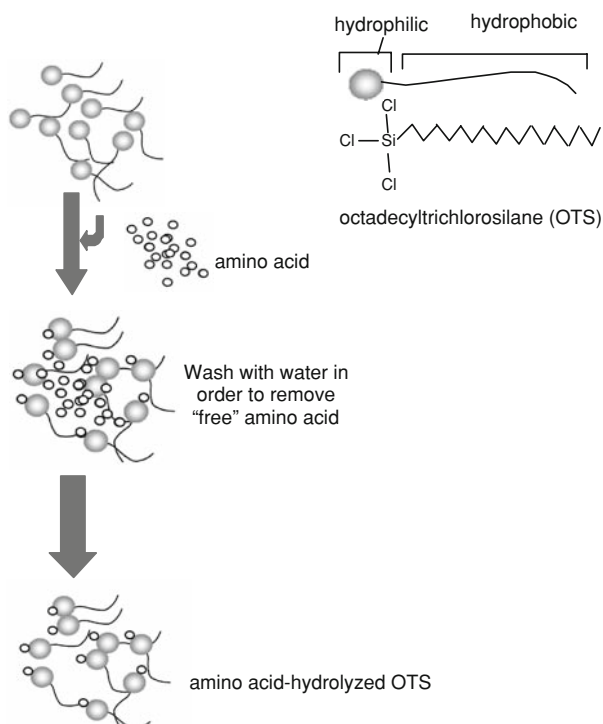


Fig. 1 Attachment of a chiral amino acid onto the hydrophilic part of hydrolyzed OTS

The structural information about the chemically modified material is obtained by means of solid-state MAS NMR spectroscopy. The MAS NMR experiments were performed using Bruker Avance 400 MHz 9.4T spectrometer. The ^{29}Si MAS NMR spectra were recorded at 79.44 MHz using 4 μs radio frequency pulses, a recycle delay of 9 s and spinning rate of 7.0 kHz using a 4 mm zirconia sample rotor. The ^{13}C MAS NMR spectra were collected by a cross polarization (CP) MAS method at 100.62 MHz with a 3,000 μs ^{13}C pulse, 5 s recycle delay and spinning rate of 7.0 kHz using a 4 mm zirconia sample rotor. Both ^{29}Si and ^{13}C NMR chemical shifts were referred to external TMS at 0 ppm.

The catalytic performance of the synthesized heterogeneous asymmetric catalyst was tested using the hydration of epoxycyclohexene as a model reaction. The hydration of epoxycyclohexene to cyclohexanediol, in principle, yields three stereoisomers: the *cis*-1,2-cyclohexanediol and a pair of enantiomers, namely (1*S*,2*S*)-*trans*-1,2-cyclohexanediol and (1*R*,2*R*)-*trans*-1,2-cyclohexanediol. The hydrolysis of epoxycyclohexene to 1,2-cyclohexanediol was performed as follows. The catalyst particles (50 mg) were placed in a glass tube and then 10 μmol of 0.1 M H_2SO_4 was added to the catalysts. Then 50 mmol of epoxycyclohexene (Merck, >99%) was added to the solid catalyst wetted with H_2SO_4 and reacted for 24 h at room temperature under stirring condition. The products of the reaction were analyzed by Agilent Model 7890 N gas chromatography using ChiralDEX B-DM capillary column containing 2,3-di-*o*-methyl-6-*t*-butyl silyl derivative of (α -cyclodextrin. 1 μl of the sample was injected into the GC inlet with the split ratio 100:1. The oven conditions were as follows: initial temperature 50 $^\circ\text{C}$, ramp at 4.3 $^\circ\text{C min}^{-1}$ to reach 120 $^\circ\text{C}$, hold for 9 min, and finally ramp at 5 $^\circ\text{C min}^{-1}$ to reach 160 $^\circ\text{C}$ with a constant flow of 1.7 mL min^{-1} . Authentic samples i.e. *cis*-1,2-cyclohexanediol (Aldrich, >99%) (1*S*,2*S*)-*trans*-1,2-cyclohexanediol (Fluka, >99%) and (1*R*,2*R*)-*trans*-1,2-cyclohexanediol (Fluka, >99%) were used to determine the products.

Results and discussion

Figures 2 and 3 show the ^{13}C CP/MAS NMR spectra of hydrolyzed OTS-Glu and hydrolyzed OTS-PheAla. The NMR spectrum of hydrolyzed OTS-Glu shows two major signals at 177.0 and 174.1 ppm which provide strong evidence for the prevalence of $-\text{COOH}$ group of L-glutamic acid. The strong signal at 29.1 ppm corresponds to C3 in the alkylsilyl group of hydrolyzed OTS. It is clearly observed that the peaks of C1 and C5 of $-\text{COOH}$ groups of L-glutamic acid attached to hydrolyzed OTS are shifted towards a higher magnetic field in comparison to those of pure L-glutamic acid (Fig. 2). The shifting of the C2 peak toward a lower magnetic field of $-\text{COOH}$ was observed for hydrolyzed OTS-PheAla (Fig. 3). The shifting of the ^{13}C NMR signals can be explained by the interaction of the free electron pairs of the oxygen atoms of carboxyl functional group of the amino acids with hydrolyzed OTS.

Figure 4 shows the ^{29}Si MAS NMR spectra of hydrolyzed OTS and hydrolyzed OTS-Glu. The intense peak at -110 ppm is from $\text{Si}(\text{OSi})_3$ in hydrolyzed OTS. In Fig. 4, it is observed that the three additional peaks from -50 to -80 ppm

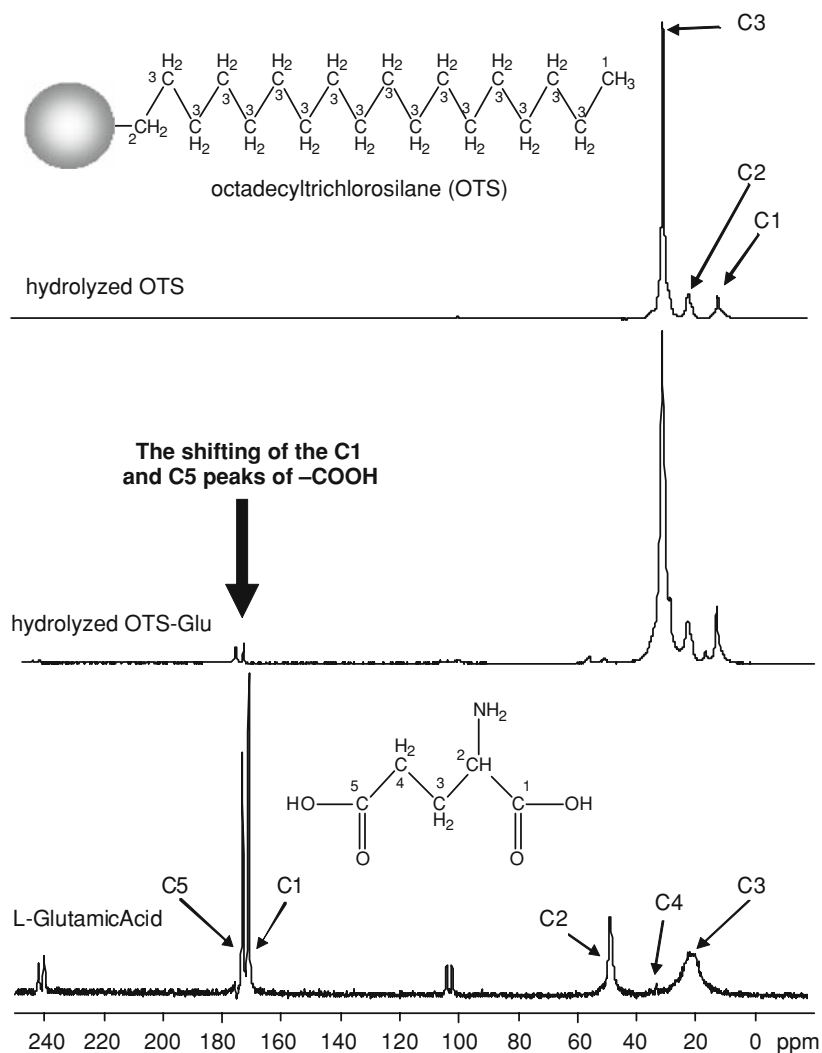


Fig. 2 ^{13}C CP/MAS NMR spectra of hydrolyzed OTS, L-glutamic acid and hydrolyzed OTS-Glu

correspond to three different environments of the siloxane groups in the hydrolyzed OTS-Glu [8, 9]: (i) isolated groups that are not bound to any neighbouring siloxanes (ii) terminal groups that are only bound to one neighbouring siloxane, and (iii) cross-linked groups that are bound to two neighbouring siloxane. However, the peak at -110 ppm from $-\text{Si}(\text{OSi}-)_3$ is not observed in hydrolyzed OTS-PheAla. Based on the above results, it is suggested that the presence of amino acid during sol-gel synthesis of the hydrolyzed OTS-Glu inhibits the formation of $\text{Si}(\text{OSi}-)_3$ bonding in the sample. This result suggested that the amino acid was attached by cross-linked $-(\text{OH})\text{Si}(\text{R})-\text{O}-(\text{OH})\text{Si}(\text{R})-$ of the hydrolyzed OTS.

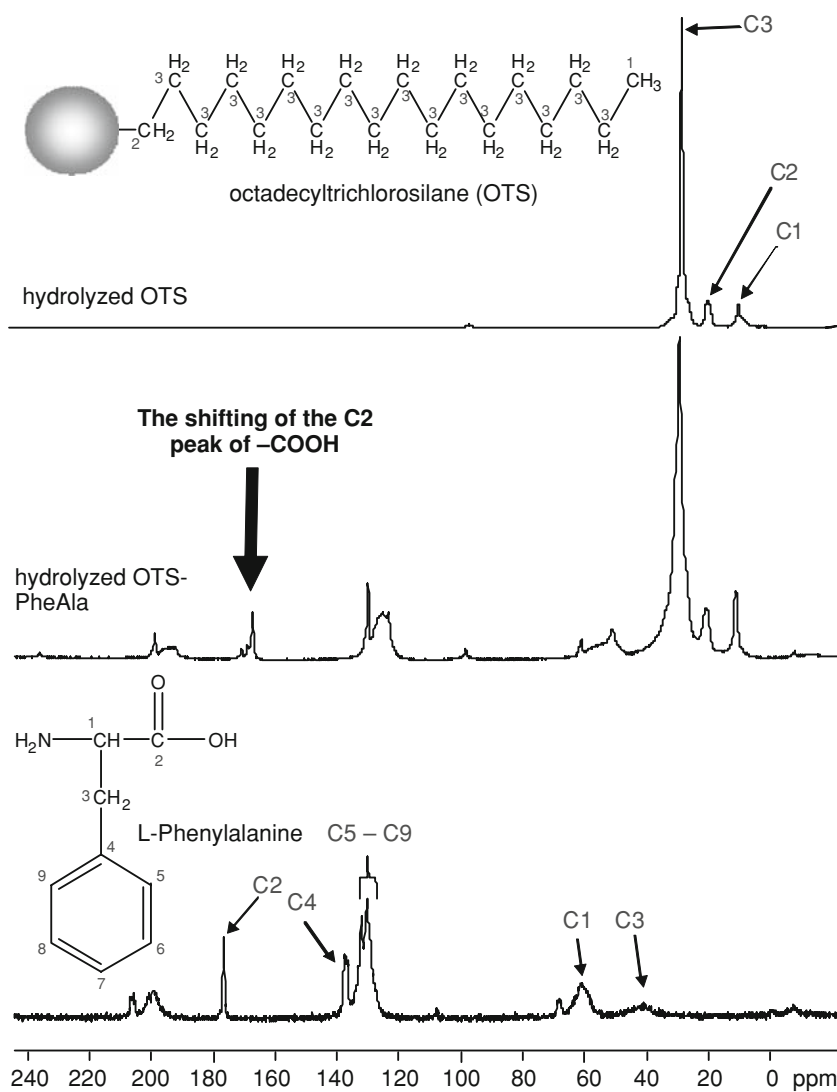


Fig. 3 ^{13}C CP/MAS NMR spectra of hydrolyzed OTS, L-phenylalanine and hydrolyzed OTS-PheAla

The prepared catalysts were tested for the asymmetric hydration of epoxycyclohexene. All the catalysts are active for this reaction (Fig. 5). (1R,2R)-*Trans*-1,2-cyclohexanediol (1S,2S)-*trans*-1,2-cyclohexanediol and *cis*-1,2-cyclohexanediol were the products detected. The catalysts show promising enantioselectivity with 12–18% ee (S) for R and S of *trans*-1,2-cyclohexanediol. Considering that the amino acids are the integral part of the catalysts, the lower enantioselectivity of hydrolyzed OTS-PheAla compared to that of hydrolyzed OTS-Glu may be due to the different structure of the amino acid in the two samples since their concentrations are almost

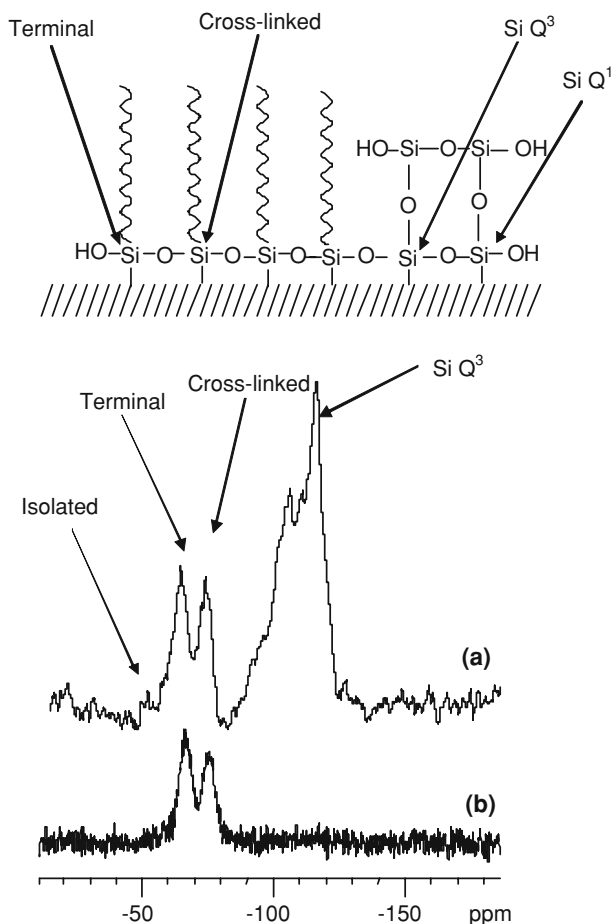


Fig. 4 ^{29}Si NMR of (a) hydrolyzed OTS and (b) hydrolyzed OTS-Glu

the same (*ca.* 50%). It may be suggested that the enhanced catalytic activity of the hydrolyzed OTS-amino acids is mainly caused by the specific adsorption and physical properties of the catalysts with the amino acid as a chiral promoter. The alternative explanation for the different enantioselectivity of the two tested amino acids is that L-glutamic acid contains an additional carboxyl group available for hydrogen bonding which can definitely contribute to the larger enantioselectivity in the non-covalent catalysis.

During the reaction under stirring, an abrupt visual homogenization was observed suggesting the formation of an emulsion in the presence of the solid particles. One considers that a catalyst which possesses both hydrophobic and hydrophilic components exhibits amphiphilic character. The flexibility of the hydrophobic octadecyl groups therefore allows the formation of micellar aggregates in the system containing immiscible organic and aqueous phases. A schematic representation of

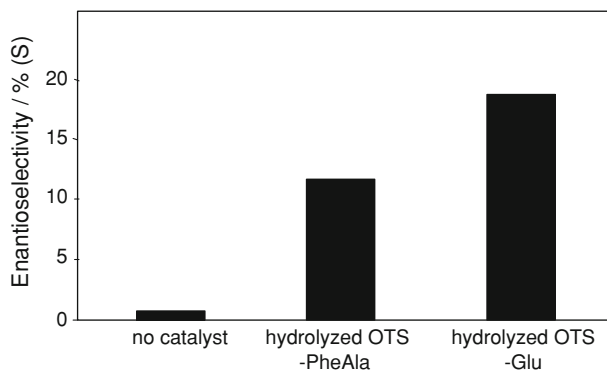


Fig. 5 Enantioselectivity of catalysts for *R* and *S* *trans*-1,2-cyclohexanediol in the asymmetric hydration of epoxycyclohexene

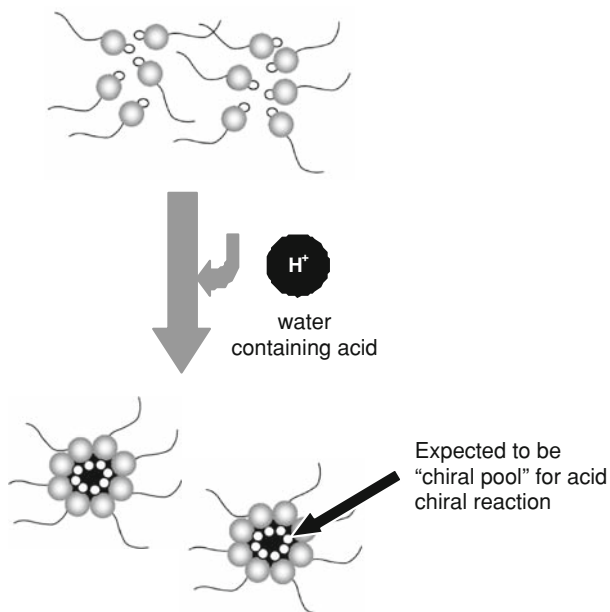


Fig. 6 Amphiphilic chiral solid catalyst as heterogeneous micellar catalyst in enantioselective hydration of epoxycyclohexene

heterogeneous micellar catalysis is depicted in Fig. 6. As shown in Fig. 6, it is expected that the hydrophilic microdomains in micellar aggregates will act as “chiral pool” for acid chiral reaction. The enantioselectivity, albeit not yet high enough, demonstrates the possibility for synthesizing a new kind of chiral solid catalysts for potential applications in asymmetric reactions.

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