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Novel synthesis of bifunctional catalysts with different microenvironments†

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Acid-base bifunctional activity governed by $-NH_2$ group's microenvironment is evident from two different catalysts scrutinized by interchanging the location of $-SO_3H/NH_2$ groups on periodic mesoporous ethylenesilica. The hydrophobic local environment plays a significant role in one-pot deacetalization/ nitroaldol condensation.

In modern catalysis, designing catalysts with spatially isolated multiple active sites to accomplish multi-step reaction cascades mimicking biological systems remains a major challenge. In heterogeneous catalytic systems, the intrinsic bifunctional activity of mesoporous catalysts often depends on the relative separation between the acidic- and basic-sites as demonstrated by several research groups.^{1–7} An elegant work describing an acidic framework (–SO₃H in the hydrophobic part) and –NH₂ protruding the channels (SiO₂– in the hydrophilic part) of periodic mesoporous benzenesilica was reported by Thiel *et al.*⁸ Similarly, what would be the effect when the positions of these acid/base functionalities were reversed on the same silica support?

To implement the idea above, periodic mesoporous ethylenesilica⁹ (PMES) containing bridging -C=C- was used as a silica support. Scheme 1 depicts catalyst preparation methods by **path A** and **path B**, both of which involve a combination of co-condensation and novel post-synthetic modification. Initial co-condensation of bis(triethoxysilyl)ethylene (BTSE) with 3-aminopropyl triethoxysilane using Pluronic P_{123} ($M_n = 5800$) leads to hybrid PMES-NH2 (path A). Post-synthetic addition of NaHSO₃ across -C=C- of PMES-NH₂ results in bifunctional catalyst PMES-NH₂-SO₃H-A. In path B, the positions of -NH₂/SO₃H groups are reversed and using hybrid PMES-SH obtained by co-condensation of BTSE and 3-mercaptopropyl trimethoxysilane, the -NH₂ group was grafted across -C=Cthrough epoxidation followed by amination. The important salient features of the present method compared to earlier reports¹⁻⁷ are that (i) attachment of $-NH_2/SO_3H$ groups without any organic spacer, (ii) no protection/deprotection steps, and (iii) amenable for interchangeability of functional groups between hydrophobic and hydrophilic parts.



Scheme 1 Strategies for preparation of bifunctional catalysts.

Prior to modification, the structural ordering and physical characteristics were evaluated using X-ray diffraction (XRD), transmission electron microscope (TEM) and N₂ sorption analyses. Both **PMES–NH₂** and **PMES–SH** after surfactant extraction exhibit a hexagonal *P6mm* symmetry (Fig. S1 and S2, ESI†). The N₂ adsorption/desorption isotherms (Fig. S3, **path** A, ESI†) are found to be of Type IV in nature and exhibited a hysteresis loop characteristic of ordered mesoporous materials with very high surface area and pore volume (Table S4, ESI†).

The addition of NaHSO₃ across -C=-C- of **PMES–NH₂** in an O₂ atmosphere^{10,11} under standardized reaction conditions (Table S5, ESI†) was confirmed by ¹³C–CP MAS NMR and Raman spectroscopies. The presence of a strong signal at 147 ppm (Fig. 1, **path A**) corresponds to -C=-C- linked to silicon; whereas the propyl spacer shows resonance signals at 16.2, 25.5, and 35.0 ppm corresponding to different carbon environments.^{9,12} The peaks marked by asterisks correspond to spinning side bands. A band of peaks at about 55–70 ppm is assigned to ether groups of the EO–PO–EO surfactant residue. The appearance of a new resonance signal at 45 ppm for the bisulfite treated **PMES–NH₂** confirms that –SO₃H was successfully grafted across the hydrophobic -C==C- bond. A similar observation was also made for introduction of –SO₃H in **PMES** itself by our group (unpublished results).

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The ²⁹Si MAS NMR spectrum of **PMES–NH₂–SO₃H–A** (Fig. 1, **path A**) exhibits three signals at -83.5, -74.0, and -63.0 ppm. They can be assigned as ³T and ²T for silicon attached with ethylene (83.5 and -74.0 ppm) and aminopropyl (-74.0 and -63.0 ppm), respectively.¹² The broad signal centered at -74.0 ppm is the mixture of ³'T and ²T for Si connected with aminopropyl and ethylene moieties, respectively. The immobilization of $-SO_3H$ was further confirmed by the appearance of the $-SO_3$ stretching vibrational band at 1038 cm⁻¹ in Raman spectra.¹³ Furthermore, the reduction in the pore-size of **PMES–NH₂–SO₃H–A** is very small (~ 0.4 nm) as seen from pore-size distribution curves (Fig. S3, **path A**, ESI†). The amount of sulfonic acid estimated by potentiometric acid–base titration was found to be 1.14 mmol g⁻¹; whereas the elemental analysis showed 1.29 mmol g⁻¹ of amino groups.

As **path B** involves a new functionalization strategy, the epoxidation has been thoroughly investigated with respect to various oxidants, pH, and temperature (Tables S6 and S7, ESI†). Since the \equiv Si-C=C-Si \equiv moiety is an electron deficient olefin (due to conjugation with Si), the epoxidation was performed under mild basic conditions (pH 8.5) using anhydrous *tert*-butyl hydroperoxide.^{14,15} The formation of epoxide was clearly seen from FTIR spectra (Fig. S8, ESI†). The epoxy-product was subsequently treated with ammonia to get the required bifunctional catalyst and characterized by Raman spectroscopy. **PMES–SH** exhibits two strong bands at 1560 and 1300 cm⁻¹ (Fig. 2, spectrum A) which can be ascribed to -C=C- and -C-H stretching vibrations, respectively.⁹ The weak band at 646 cm⁻¹ is attributed to S–C stretching vibrations.¹⁶ After oxidation with TBHP, new bands at 1211 and 1032 cm⁻¹

C=0

Chemic

100

 \equiv Si-C-C(NH₂)-Si-C₃H₆SO₃H

SO₂H NH₂

shift (PPM

Path A

250

250

¹CH₂-²CH₂-³CH₂-NH₂

200

Path B

PMES-SH

200

Path B

 \equiv Si-C-C(SO₃H)-Si-C₃H₆NH₂

SO₂H

Fig. 1 ¹³C MAS NMR (top two) and ²⁹Si MAS NMR (bottom) spectra. The asterisk symbol indicates the spinning side bands.

Chemical shift (PPM)

corresponding to the epoxide-ring and SO₃ stretching vibrations (spectrum B), respectively, were observed.^{13,17} After NH₃ treatment, the band at 1211 cm⁻¹ vanished due to amination of epoxide (spectrum C). Although N–H stretching vibration was swamped in the –C–H stretching region, weak bands at 1226 and 906 cm⁻¹ originating from –N–H in plane bending and deformation modes were clearly observed.^{18,19} In addition, the minor band at 1226 cm⁻¹ is not due to the unreacted epoxide moiety but indeed due to the N–H group as confirmed by our parallel study (unpublished results).

The ¹³C NMR of **PMES–SH** exhibited characteristic signals of -C=-C- along with signals at 14.7, 26.9, and 28.0 ppm originating from mercaptopropyl groups (Fig. 1, **path B**). After oxidation and amination, new peaks at 38 and 50.5 ppm attributed to $-NH_2$ and $-SO_3H$ groups, respectively, appeared. The ²⁹Si MAS NMR spectrum (Fig. 1, **path B**) also exhibited three signals at -82.8, -73.6, and -64.5 ppm ascribed to ³T and ²T for silicon attached with ethylene (82.8 and -73.6 ppm) and mercaptopropyl (-73.6 and -64.5 ppm), respectively. The amount of $-SO_3H$ and $-NH_2$ were found to be 1.19 and 1.35 mmol g⁻¹, respectively.

The cooperative catalytic activities in a one-pot reaction sequence comprising acid-catalyzed deacetalization of dimethyl acetal 1 to yield the respective aldehyde 2 followed by basecatalyzed nitroaldol (Henry) reaction to obtain 3 are shown in Scheme 2 and Table 1. The PMES-SO₃H-NH₂-A ("A" refers to "path A") converts 1 (entry 1) to the corresponding aldol product 3 in almost quantitative yields and illustrates the efficiency of the catalysts. In contrast, the final aldol adduct 3 obtained over PMES-SO₃H-NH₂-B ("B" refers to "path B") was 76.9% with an appreciable amount of unreacted benzaldehyde under similar experimental conditions. To gain further insight, the reaction was performed over various dimethylacetals. Entries 3-5 exhibit reactivity of various acetals over PMES-SO₃H-NH₂-A and the observed selectivity for the desired nitroolefin 3 is again always higher than 98%; whereas PMES-SO₃H-NH₂-B invariably led to lower selectivity of 3 (entries 6-8) and the sole side-product was aldehydes formed from acid-catalyzed deprotection of dimethylacetals. It is noteworthy to mention that, in spite of similar acid/base contents of PMES-SO₃H-NH₂-A (SO₃H and NH₂ = 1.14and 1.29 mmol g^{-1} , respectively) and PMES-SO₃H-NH₂-B (SO₃H and NH₂ = 1.19 and 1.36 mmol g^{-1} , respectively), they exhibit rather different catalytic behavior under identical reaction conditions. Furthermore, after prolonged reaction



Fig. 2 Raman spectra of **path B**: (A) PMES–SH, (B) PMES–SO₃Na–epoxide, and (C) PMES–NH₂–SO₃H.

Scheme 2 One-pot deacetalization-nitroaldol condensation.

 Table 1
 Activity of bifunctional catalysts^a

Entry	R	Catalysts	Conv. 1 [%]	2 [%]	3 [%]
1	Н	Α	100	1.7	98.3
2	Н	В	100	23.1	76.9
3	NO_2	Α	100	1.9	98.1
4	OCH ₃	Α	100	1.0	99.0
5	CH ₃	Α	100	2.0	98.0
6	NO_2	В	100	21.0	79.0
7	OCH ₃	В	100	19.5	80.5
8	CH ₃	В	100	21.4	78.6
9^b	Н	В	100	10.7	89.3
10^{c}	Н	В	100	3.4	96.6
11	Н	$\mathbf{A} + \mathbf{P}\mathbf{A}$	Trace	Trace	Trace
12	Н	A + PTS	100	100	Trace
13	Н	PMES-NH ₂	Trace	Trace	Trace
14	Н	PMES-SO ₃ H	100	100	Trace

^{*a*} Reaction conditions: aldehyde dimethyl acetal (2 mmol), CH₃NO₂ (5 mL), **PMES-SO₃H-NH₂-A** (22 mg, 0.025 mmol SO₃H, 0.028 mmol), temperature 90 °C, reaction time 24 h. ^{*b*} Reaction was carried out for 48 h. ^{*c*} Reaction time 65 h. PA = propylamine. PTS = *p*-toluene sulfonic acid. The mass balance obtained by an internal standard method (chlorobenzene standard) was in the range of 99 \pm 2% for all the experiments.

times of 48 h and 65 h, the selectivity of **3** is increased from 76.9% to 89.3% and then to 96.6%, respectively. As expected, no desired aldol product **3** was obtained when either of the homogeneous analogues of sulfonic acid or amine (entries 11 and 12) were used with **PMES–SO₃H–NH₂–A**, as these functionalities apparently neutralize each other. In the absence of $-SO_3H$ (entry 13), the starting material remains unchanged even after 24 h; whereas the presence of $-SO_3H$ (entry 14) leads to quantitative deprotection of dimethylacetal to the respective aldehydes.

The conversion of 1 to 2 is always quantitative for both catalysts A and B; however, they differ catalytically in aminecatalyzed transformation of 2 to 3. In order to understand the variable cooperative catalytic behavior of these microstructurally different PMES-SO₃H-NH₂-A and PMES-SO₃H-NH₂-B materials, we have compared the kinetics of -NH2 (PMES-NH2) groups in SiO₂- hydrophilic (path A) and -C=C- hydrophobic environments, where the latter was obtained by following epoxidation/amination over PMES in a separate experiment for comparison. The nitroaldol condensation with benzaldehyde was performed over these two amine-functionalized materials in the absence of -SO₃H under identical reaction conditions. For both the catalysts, the turn-over-frequency (TOF) for desired aldol product 3 decreased with increasing reaction time due to decreased concentration of starting materials. However, -NH2 in the hydrophobic environment exhibited relatively lower TOF than that located in the hydrophilic environment (Fig. S9, ESI⁺). Interestingly, these -NH2 functionalized materials exhibit higher activity than the MCM-41 based catalysts⁷ possibly due to

regular ordering of catalytic sites coupled with high hydrophobicity. Therefore, the observed difference between these bifunctional catalysts may be originated from the activities of -NH₂ groups situated at different microenvironments rather than diffusion limitation. Unlike PMES-SO₃H-NH₂-A, the -NH2 groups in PMES-SO3H-NH2-B are conjugated with two electropositive silicon atoms (Si-C-C(NH2)-Si) and as a result the basic strength could be relatively lower due to hyperconjugation. Furthermore, the presence of benzaldehyde in the reaction medium and lower rate of amine-catalyzed nitroaldol condensation of PMES-NH₂ in the hydrophobic environments corroborate our speculation that strength of the amine moiety could play a crucial role in quantitative one-pot deacetalization and nitroaldol condensation. Both the catalysts were recycled four times successively (Table S10, ESI⁺) suggesting the high stability of these bifunctional catalysts. The N/S contents by elemental analysis of spent catalysts were nearly unchanged confirming the stability of different organic tethering.

In conclusion, we have demonstrated novel methods for preparation of efficient and stable bifunctional catalysts without any protection/deprotection steps. The present method enables us to attach $-SO_3H/NH_2$ without an organic spacer. The amine groups located in the hydrophobic environment exhibited lower activity due to decreased basicity compared with that of the hydrophilic SiO₂ network.

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