## A novel route for the synthesis of piperazine from N-(2,3-dihydroxypropyl)ethylenediamine over composite photocatalysts

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## Semiconductor loaded zeolite composite catalysts (5 wt% $TiO_2/H\beta$ ) have been used to photocatalytically synthesize piperazine from *N*-(2,3-dihydroxypropyl)ethylenediamine with yields up to 59.0 mol%.

The synthesis of piperazine and its derivatives has received growing interest because of their potent applications in the drugs, perfumery and pharmaceutical industries. Although several methods<sup>1-3</sup> are reported for their synthesis, the importance of these molecules has provided the impetus to develop more convenient and environmentally friendly procedures. Selective production of these compounds comprises cyclization, dehydronitrogenation and dehydration reactions. A great variety of chemical transformations in the presence of CdS or TiO<sub>2</sub> have been reported in earlier reviews.<sup>4,5</sup> Despite several semiconductor mediated reactions reported, the examples of inter and intramolecular cyclizations are rather limited.6-8 Semiconductor loaded zeolites have recently drawn increased attention as potential composite photocatalysts due to their unique pore structure and adsorption properties. Reports on semiconductor loaded zeolites for organic sythesis are scarce.9 The present work demonstrates a new photocatalytic route with the combined advantages of semiconductor and zeolite catalysts for the synthesis of piperazine at room temperature.

The photocatalysts were prepared as described elsewhere<sup>10</sup> and characterized by BET, XRD, NH3 TPD and elemental analysis (EDX and AAS). The results of AAS and EDX analysis showed good agreement for the known and observed amounts (wt%) of semiconductor loading on zeolites.<sup>11</sup> N-(2,3-Dihydroxypropyl)ethylenediamine (NPEDA) was prepared as reported by Surrey et al.12 The respective catalysts (100 mg) were suspended with 0.268 g of NPEDA (2 mmol) in 20 ml of acetonitrile solvent. The suspension was magnetically stirred and irradiated under a constant stream of molecular O2 (20 ml  $h^{-1}$ ) at room temp., using a 250 W high pressure mercury lamp in a cylindrical round bottomed quartz photoreactor of 200 ml capacity ( $\emptyset = 2 \text{ cm}, L = 20 \text{ cm}$ ) and equipped with a refluxing condensor at the top. The reaction mixture was centrifuged after irradiation (12 h) to separate the catalyst. Thin layer chromatorgraphy (TLC) was performed in a CH<sub>3</sub>OH : CHCl<sub>3</sub> (10 : 90) solvent system to detect the product spots. Further purification was done by column chromatography and the product was characterized by <sup>1</sup>H NMR, melting point, electron impact mass spectroscopy (EI-MS), GC-MS and C,H,N analysis.

The progress of the reaction was monitored by TLC and yields reported were estimated on the basis of isolated yields. The reaction conditions were optimized by several trials to get the maximum yield. Parallel experiments were also carried out using bare  $TiO_2$ , CdS, ZnO and different semiconductor loaded zeolites to compare the photocatalytic activity. The results are summarized in Table 1.

Table 1 shows the representative results of the photocatalytic reaction of non-aqueous NPEDA solution by various types of semiconductor loaded zeolite catalysts. On the other hand, bare semiconductor powder (TiO<sub>2</sub>, CdS, ZnO) photocatalyzed reaction did not yield piperazine. The reaction, in this case,

predominantly progressed to total oxidation of NPEDA. It has been experimentally proved (Table 2) that the reaction is *photocatalytic* since this reaction proceeds only in the copresence of oxygen, irradiation and a photocatalyst. As clearly seen in Table 1, the formation of piperazine depended on the nature of the zeolite support. In this study, one of the best photcatalysts for the production of piperazine was found to be 5 wt% TiO<sub>2</sub>/H $\beta$ . A change in the physical properties of the semiconductor loaded zeolite catalysts was not observed and XRD analysis (results not shown) confirms that no loss of crystallinity occurs after the modification and subsequent

 Table 1 Photocatalytic intramolecular cyclization of NPEDA achieved by semiconductor/zeolite composite catalysts

Catalyst	Surface area <sup>a/</sup> m <sup>2</sup> g <sup>-1</sup>	Acidity <sup>b/</sup> mmol g <sup>-1</sup>	Isolated product III <sup>c</sup> (mol%)
TiO <sub>2</sub> (2%)/HZSM5 (30) <sup>d</sup>	350	0.37	35.2
TiO <sub>2</sub> (5%)/HZSM5 (30)	320	0.32	38.6
TiO <sub>2</sub> (2%)/HY (4.4)	400	0.25	39.4
TiO <sub>2</sub> (5%)/HY (4.4)	341	0.20	40.5
$TiO_2(2\%)/H\beta$ (30)	495	0.43	46.1
TiO <sub>2</sub> (5%)/Hβ (30)	485	0.47	59.0
ZnO(2%)/HZSM5 (30)	326	0.13	17.9
ZnO(5%)/HZSM5 (30)	320	0.15	22.1
ZnO(2%)/HY (4.4)	336	0.18	25.3
ZnO(5%)/HY (4.4)	300	0.21	27.4
ZnO(2%)/Hβ (30)	490	0.41	29.6
ZnO(5%)/Hβ (30)	483	0.40	30.4
CdS(2%)/HZSM5 (30)	356	0.45	31.9
CdS(5%)/HZSM5 (30)	349	0.49	33.0
CdS(2%)/HY (4.4)	409	0.31	37.1
CdS(5%)/HY (4.4)	389	0.36	38.2
CdS(2%)/Hβ (30)	468	0.33	41.8
CdS(5%)/Hβ (30)	459	0.37	52.7
TiO <sub>2</sub>	50	_	
ZnO	30		
CdS	_		

 $^a$  BET surface area measured with liquid  $N_2$  at 77 K.  $^b$  TPD of  $NH_3$  measured on Autochem 2910 (Micromeritics, USA).  $^c$  Irradiation (12 h; 250 W HP mercury lamp).  $^d$  SiO\_2/Al\_2O\_3 ratios of zeolites are shown in parentheses ().

Table 2 Control experiments for the photocatalytic synthesis of piperazine

Conditions	Irradiation time/h	Isolated product III (mol%)
Semiconductor/zeolite, light, O <sub>2</sub>	12	59.0
Semiconductor/zeolite, dark, O <sub>2</sub>	12	0
Light, O <sub>2</sub>	12	0
Zeolite, light, O <sub>2</sub>	12	0
Semiconductor, light, O <sub>2</sub>	12	0
Semiconductor, light	12	0

reaction. It is seen that moderate hydrophobicity and acid site strength of the composite catalyst favours the present intramolecular cyclization reaction. Also the structure of H $\beta$  zeolite may help to attain the maximum yield of piperazine, as it is known that H $\beta$  is a combination of both HZSM-5 (channel pore system, high Si/Al ratio) and Y (12-ring pore system) zeolites.<sup>13</sup> After the illumination, the reaction mixture is waxy in nature. This made it difficult to estimate exactly the % NPEDA conversion, product selectivity and yield. Therefore, in Table 1 we report only the amount of isolated piperazine in mol%. Thus we find that the highest possible recoverable yield is 59%. However, the nature of by-products has been established by GC (Poropak Q column, He carrier gas) and GC-MS techniques. The major by-product is  $CO_2$  and the minor product is 1,2-dihydropiperazinecarbinol (traces).

Table 2 shows the control experiments performed to confirm the intramolecular cyclization of NPEDA which requires light, semiconductor/zeolite and oxygen for the formation of piperazine. In the semiconductor, light and O<sub>2</sub> (without zeolite) system, the reaction leads to the total mineralization of NPEDA to  $CO_2$ . The degree of total oxidation is strongly influenced by the %  $TiO_2$  in the zeolite. For higher loading of  $TiO_2$  (10%), the evolution of CO<sub>2</sub> was higher, leading to a lower selectivity of piperazine. In the absence of  $O_2$ , no  $CO_2$  was observed. The catalyst showed consistent activity for at least 3 cycles (tried only up to 3 cycles) of reuse after an activation step at 200 °C for 2-3 h.

Scheme 1 shows a plausible reaction mechanism. As the reaction requires the presence of a photocatalyst, it can be deduced that oxidation and/or reduction processes are involved. The secondary alcohol position of NPEDA may be oxidized first by a positive hole (h<sup>+</sup>), which is generated as a result of photoexcitation of the valence-band electron into the conduction band of the semiconducting material, to form a ketone<sup>10</sup> with the simultaneous liberation of hydrogen. The ketone, by losing a water molecule, forms a cyclic Schiff base (CSB) intermediate I which is initially stabilized by the zeolite, but ultimately losing a proton as reported by Beaune et al.9 We attempted to synthesize the CSB to show the intermediacy for the formation of **III** but failed due to its instability under its synthetic conditions. However, the formation of CSB was observed by GC-MS (m/z M<sup>-</sup> 113) analysis. It is acknowledged that zeolite catalysts can stabilize the reactive intermediates in several photochemical reactions.<sup>14,15</sup> Intermediate I upon



further loss of hydrogen forms aldehyde II, which undergoes further oxidation to the corresponding acid. It is likely that the intermediate aldehyde and acid are formed, but not observed as free compounds, since under our experimental conditions these intermediates are most likely to be transformed photocatalytically to III. Subsequent decarboxylation leads to the desired product III piperazine.<sup>16</sup> The other by-products are 1,2-dihydropiperazinecarbinol and CO<sub>2</sub>.

The intermediate compounds mentioned in the proposed scheme are likely to be formed in-situ and their separation seems to be difficult. CSB (cyclic Schiff base) was the only intermediate observed by GC-MS analysis, under our experimental conditions. All liquid samples were analyzed using a flame ionization detector equipped with a 10% SE 30 column. Since the catalyst is a zeolite, which is able to act as a substrate to which the reactant can adsorb as well as exchange protons with, it is most likely that the intermediate compounds are formed on the catalyst and are impossible to isolate.

In conclusion, we have succeeded in synthesizing piperazine photocatalytically with a maximum yield of 59.0 mol% through the intramolecular cyclization of NPEDA over a semiconductor loaded zeolite. This is the first report, to the best of our knowledge, on the synthesis of piperazine by photocatalysis. Photocatalysis, in our opinion, is a technique which can make valuable contributions to the chemistry of the future because of its potential as an environmentally friendly organic synthetic route which may avoid the formation of waste products and residues. The present process is better than the conventional synthesis starting from pyrazine or ethylenediamine. Pyrazine is an expensive starting material compared to glycidol and ethylenediamine (EDA). NPEDA is prepared easily from the latter two compounds. For synthesis of piperazine from pyrazine, a large amount of Ni containing catalyst is also required.<sup>17</sup> Alternately, from EDA, piperazine is prepared at 350 °C by using a pentasil zeolite catalyst with 50% yield.<sup>3</sup> Our new route reduces some of the difficult reaction conditions like high temperatures and the use of corrosive chemicals and catalysts. Further it avoids the formation of by-products which are difficult to remove and tedious purification procedures.

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- 16 Compound **III**: <sup>1</sup>H NMR (D<sub>2</sub>O): δ 2.79, (s, 8H); Found: C, 55.70; H, 11.72; N, 32.52%. Calcd for C4H10N2: C, 55.81; H, 11.62; N, 32.55; MS (EI): m/z 86 [M<sup>+</sup>]; m.p. = 108–110 °C.
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