A novel one step photocatalytic synthesis of dihydropyrazine from ethylenediamine and propylene glycol†

K. V. Subba Rao,[a] B. Srinivas,[a] A. R. Prasad[b] and M. Subrahmanyam*[a]

[a] *Catalysis and Physical Chemistry Division, Indian Institute of Chemical Technology, Hyderabad-500 007, India. E-mail: subrahmanyam@iict.ap.nic.in*

[b] *Organic Chemistry Division-I, Indian Institute of Chemical Technology, Hyderabad-500 007, India*

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Dihydropyrazine (DHP), the intermediate for pyrazine, is synthesized from ethylenediamine and propylene glycol; it is assumed that the reaction proceeds by photooxidation of propylene glycol and cyclization with ethylenediamine to give dihydromethylpyrazine, which by subsequent oxidative demethylation *via* the corresponding acid, forms dihydropyrazine; molecular oxygen, light and TiO_2/zeolite promote the reaction.

In the last few years heterogeneous photocatalysis applied to synthetic chemistry has become an exciting and rapidly growing area of research. For a multistep synthesis illuminated semiconductors offer unique features. Many studies[1a–f] have reported photocatalytic organic reactions using mild experimental conditions. To date they are mostly in the categories of oxidations and oxidative cleavage, reduction, geometric and valence isomerization, substitution, condensation and polymerization. The discovery of the photo-Kolbe reaction by Kraeutler and Bard[2] using Pt/TiO_2 as a photocatalyst for the conversion of acetic acid to methane and CO_2 has attracted much attention. However, in spite of several titanium dioxide mediated reactions, examples of inducing intermolecular C–C bonding are rather limited in the literature. A recent report demonstrated that platinized TiO_2 is a successful photocatalyst in the selective *N*-cyclization of *N*ε-carbamyl-L-lysine into virtually optically pure L-pipecolinic acid.[3] Also Nishimoto *et al.*[4] showed photocatalytic intermolecular conversion of primary diamines to cyclic secondary amines in an aqueous suspension of Pt/TiO_2. In contrast to thermal processes by homogeneous and heterogeneous catalysts, these reactions proceed at ambient temperature. Furthermore, study of the photochemistry of organic molecules adsorbed on solid surfaces such as zeolites and microporous solids to conduct phototransformations has been explored.[5a–g] Combining the photocatalytic activity of TiO_2 with the utility of zeolites for photoinduced organic synthesis[9a,b]/degradation[6] has, so far, been little exploited.

Thermal catalytic processes are available for the synthesis of pyrazine and its derivatives.[7a–e] The present photocatalytic synthesis of dihydropyrazine by the cyclization of ethylenediamine and propylene glycol using TiO_2/zeolite, to the best of our knowledge, has not been reported.

In the present work zeolites HY, HZSM-5, Hβ and HM were used to support TiO_2 (Degussa P25) or ZnO (Fluka). The SiO_2/Al_2O_3 ratios of the above zeolites are 4.4, 30, 20 and 30, respectively. The preparation method for the catalysts consisted of mechanical mixing of TiO_2 or ZnO and zeolites using a low-boiling organic solvent (ethanol), evaporation of the solvent, drying at 110 °C and finally calcination at 400 °C for 6 h. Prior to the evaluation, the catalysts were activated at 300 °C for 4 h. The photocatalytic reaction was carried out in a batch type cylindrical quartz reactor of 200 ml capacity with a refluxing condensor at the top of the reactor. The slurry, which was composed of an equimolar ratio (1 : 1) of ethylenediamine and propylene glycol (either of the reactants in excess did not provide any better yields) and 100 mg of photocatalyst along with 20 ml of acetonitrile solvent.‡ A provision for bubbling molecular oxygen at a rate of 20 ml h^{-1} was also provided to the reactor. The reactants were stirred magnetically with simultaneous irradiation§ from a 250 W high pressure mercury lamp (Philips India) for 15 h at ambient temperature. Parallel experiments were also carried out for the synthesis of DHP using ZnO[8] and ZnO supported zeolite but lower yields were observed compared to TiO_2/zeolite catalysts. All the experimental results are shown in Table 1.

Table 1 Results obtained after 15 h of irradiation (250 W high pressure mercury lamp) over different TiO_2/zeolite combinations for the cyclization of ethylenediamine and propylene glycol[a]

Entry	Catalyst	Surface area[b]/m^2 g^{-1}	Acidity[c]/ mmol g^{-1}	Yield of DHP[d] (%)
1	2wt% TiO_2/HZSM-5	350	0.37	13.0
2	2wt% TiO_2/HY	400	0.25	13.6
3	2wt% TiO_2/Hβ	406	0.20	20.4
4	2wt% TiO_2/HM	391	0.12	2.03
5	2wt% ZnO/HZSM-5	326	0.13	8.12
6	2wt% ZnO/HY	336	0.18	8.06
7	TiO_2	50	—	—
8	ZnO	30	—	—

[a] All reactions were performed with an equimolar ratio (1 : 1) of ethylenediamine and propylene glycol in 20 ml of acetonitrile using 100 mg of catalyst under oxygen bubbling at room temperature. [b] Measured by the BET technique with liquid N_2 at 77 K. [c] Measured by STPD of NH_3. [d] Yields were calculated based on the recovery of propylene glycol.

At the end of the reaction, 20 ml of demineralized water was added to the reaction mixture which was centrifuged, which allowed recovery of the adsorbed substrates and products on the surface of the solid catalyst. The supernatant liquid was analyzed with a Chemito 3865 Gas Chromatography unit using a 6 ft, 10% SE-30 packed column. The products were further identified by ^1H NMR and mass spectrometry.

Further experiments were carried out to confirm whether the reaction is photocatalytic or non-photocatalytic and it was observed that no product was formed in the absence of molecular oxygen + irradiation + TiO_2/zeolite catalyst. Zeolite alone without TiO_2 did not yield any product. Irradiation in the presence of photocatalyst when carried out using conventional liquid acids such as HCl and solid acids such as silica gel did not yield the product.

Zeolite acidity seems to influence the reaction mechanism; the oxidation is dependent on the acidity of the reaction mixture[9a] and ethylenediamine is adsorbed preferentially relative to propylene glycol in the internal surface area of the zeolite pores. The preferential adsorption of ethylenediamine leads propylene glycol to undergo oxidation to the diketone (step 1, Scheme 1) at the oxidizing site of TiO_2. The diketone formed undergoes cyclization with ethylenediamine to give dihydromethylpyrazine (DHMP) with loss of 2 mol of water. The methyl group of dihydromethylpyrazine is oxidatively demethylated leading to dihydropyrazine (DHP) as shown in

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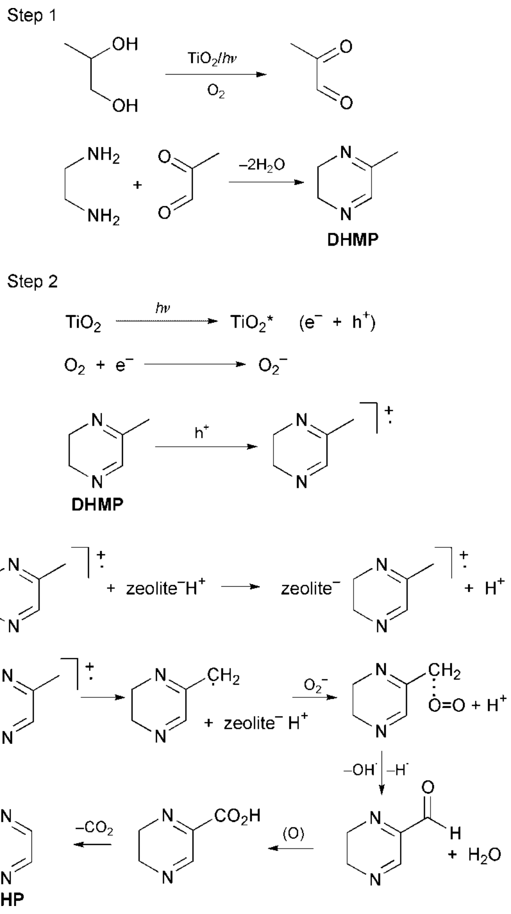

Scheme 1 Proposed reaction mechanism for the formation of DHP.

step 2 of Scheme 1. Photoexcitation of the semiconductor in step 2 would produce an electron and a hole. Oxygen serves as an electron acceptor for the conduction band electron and the dihydromethyl pyrazine supplies an electron to the photogenerated hole at the surface of the TiO_2 particle forming an adsorbed radical cation. The zeolite may assist the stability of the radical cation through proton transfer as observed by Beaune *et al.*[9b] Thus, the proposed mechanism of step 2 is enhanced by more acidic zeolites. Here, dihydropyrazine carbaldehyde undergoes further oxidation to the corresponding acid which in turn forms the dihydropyrazine after decarboxylation. The obtained dihydropyrazine was subjected to dehydrogenation[10] using a conventional method which yielded the pyrazine thereby confirming the product formation (DHP).

The reaction was then attempted with ethylene glycol instead of propylene glycol, but no cyclic product was observed. This shows that the electron donating substituent, *i.e.* the methyl group of propylene glycol, may favour the oxidation mechanism.[9c] In aerated solutions, the photogenerated electron can be trapped by adsorbed oxygen to form superoxide or other negatively charged adsorbed oxygen species.[11]

Hydrogen peroxide [eqn. (1)] thus formed by sequential

$$\begin{array}{lcl} O_2 + e^- & \longrightarrow & O_2^{\cdot -} \\ O_2^{\cdot -} + H^+ & \longrightarrow & HOO^{\cdot} \\ 2HOO^{\cdot} & \longrightarrow & H_2O_2 + O_2 \\ H_2O_2 + O_2^{\cdot -} & \longrightarrow & OH^{\cdot} + OH^- + O_2 \end{array} \qquad (1)$$

electron and proton transfer readily decomposes on illuminated TiO_2 to hydroxy radicals and oxygen. Since the recombination is inhibited by adsorbed oxygen, it is reasonable to expect that the rate of photocatalytic oxidation should be high as oxygen is continuously bubbled in a steady state. Thus the selectivity for the primary alcohol site of propylene glycol is higher in pure oxygen than in air. The secondary alcohol site is oxidized to a greater extent by the adjacent electron donating group *i.e.* methyl at the TiO_2 center. No photodegradation of compounds (formation of CO_2) was observed for lower wt% values of TiO_2 on the zeolite. The evaluation of TiO_2/zeolite catalysts in the cyclization of ethylenediamine and propylene glycol show that 2wt% TiO_2 is optimal since higher loadings lead to total oxidation.

As seen from Table 1, 2 wt% TiO_2/HZSM-5 and 2wt% TiO_2/HY show more or less the same activity and yield of dihydropyrazine. The hydrophobicity and acid site strength of zeolites influences the activity of these zeolite systems in the order Hβ > HZSM-5 = HY. This order illustrates that the cyclization is favoured by a combination of moderate hydrophobicity and acidity. However, 2wt% TiO_2/Hβ is found to be more active, leading to a high yield of dihydropyrazine which may be possibly explained by the structure of Hβ which is a combination of both HZSM-5 (channel pore system, high Si/Al ratio) and Y (12-ring pore system) zeolites.[12]

Dihydropyrazine was obtained with a yield of 20.4% over 2wt% TiO_2/Hβ during the cyclization of ethylenediamine and propylene glycol by photocatalysis *via* the proposed reaction scheme under irradiation in the presence of molecular oxygen.

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Notes and references

‡ MeCN is the most stable among tested solvents under photocatalytic conditions.[13]

§ Irradiation with low pressure mercury lamps was not efficient.

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