A Novel One Step Photocatalytic Synthesis of 2-Methyl Quinoxaline from *o*-Phenylenediamine and Propyleneglycol over TiO_2/zeolite Mediated System

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Molecular oxygen, Light, TiO_2/zeolite composite promoted 2-methyl quinoxaline (2-MQ) and quinoxaline (Q) synthesis from *o*-phenylenediamine and propyleneglycol. The oxidation of propyleneglycol and its further cyclization with *o*-phenylenediamine formed 2-MQ and subsequent oxidative demethylation of 2-MQ *via* the corresponding acid, formed quinoxaline (Q).

Quinoxaline and its derivatives have been the subject of much research due to their importance in various applications and they are wide spread for their biochemical significance.[1] For example, 2-methyl quinoxaline N, N′-dioxides substituted in the 3-position with amide, amidino, hydrazinocarbonyl and ester groups are potent bacteriocides.[2] The classical synthesis of qunioxaline and its derivatives involve the facile condensation of an aromatic *o*-diamine and α-dicarbonyl compound.[2] It is also reported that irradiation of quinoxaline in acidified methanol furnishes 2-methyl quinoxaline.[3a] Further it is reported[3b] that substitution of quinoxaline takes place at C-2 position when it is irradiated in ether, methanol, or ethanol.

Numerous reports have been published relating to TiO_2 mediated organic synthesis reactions, however, examples of intermolecular C-C bonding are rather limited.[4a–d] Ohtani, *et al.* have described the application of photocatalytic cyclizations as a practical route to synthesize heterocyclic compounds.[5a–c] Furthermore, the study of photochemsitry of organic molecules adsorbed on zeolite surfaces to conduct phototransformations have also been explored.[6a–d] The combined strengths of both photocatalytically active TiO_2 and the versatile zeolite for photoinduced organic synthesis is not much explored.[7a–b] As part of our continued effort towards synthesis of N-heterocyclization reactions using TiO_2/zeolite composite system,[8a–c] herein we report for the first time the novel intermolecular photocatalytic cyclization of *o*-phenylenediamine and propyleneglycol resulting in the formation of 2-methyl quinoxaline and quinoxaline compounds.

The TiO_2 or ZnO/zeolite powders were prepared by mechanical mixing of TiO_2 (P25, 80% anatase and 20% rutile, with a surface area of 50 m^2/g from Degussa Corporation) or ZnO (Fluka) with zeolites HY-4.4 (Conteka, Sweden), Hβ-20 (NCL, India), Hβ-30 (SÜD CHEMIE AG, Germany) and HZSM5-30 (PQ Corporation, USA) HZSM5-90 (SÜD CHEMIE AG, Germany) using a low boiling solvent (CH_3COCH_3), drying the catalyst to evaporate the solvent at 110 °C and finally calcining the samples at 400 °C for 6 h. All the catalysts were activated at 200 °C for 2 h before use. The respective catalysts (130 mg) were suspended in propyleneglycol (0.3 ml) *o*-phenylenediamine (432 mg) of 1 : 2 molar ratio in acetonitrile (20 ml) solvent. The stirred suspension was irradiated under a constant stream of molecular oxygen bubbles (60 ml h^{-1}) at room temperature using a 250 W high pressure mercury lamp (Phillips, India) in a cylindrical round bottomed quartz photoreactor of 200 ml capacity (Ø = 2 cm, L = 20 cm) equipped with a refluxing condenser at the top. The reaction mixture was filtered after the irradiation (10 h) to remove the catalyst. Thin Layer Chromatography (TLC) was performed to detect the product spots in CH_3OH : $CHCl_3$ (10 : 90) solvent system, isolated by column chromatography and confirmed with ^{1}H-NMR and EI-MS. The progress of the reaction was monitored by TLC and yields observed were estimated on the basis of isolated products. Parallel experiments were also carried out using ZnO,[9] which is known to exhibit good semiconducting properties along with ZnO/zeolite composite to compare with TiO_2 and TiO_2/zeolite composite. All the results obtained are shown in Table 1.

Table 1. Cyclization of *o*-phenylenediamine and propyleneglycol over TiO_2/zeolite composite photocatalytic systems

Catalyst	Surface Area[a] /m^2 g^{-1}	Acidity[b] /mmol g^{-1}	Yield of 2-MQ[c] /%	Yield of Q[c] /%
2 wt%TiO_2-HZSM-5(30)	350	0.37	11.6	4.7
5 wt%TiO_2-HZSM-5(30)	320	0.32	12.5	5.0
2 wt%TiO_2-HZSM-5(90)	340	0.44	13.6	4.5
5 wt%TiO_2-HZSM-5(90)	326	0.40	14.5	5.6
2 wt%TiO_2-HY(4.4)	400	0.25	10.5	4.8
5 wt%TiO_2-HY(4.4)	341	0.20	11.5	5.0
2 wt%TiO_2-Hβ(20)	406	0.26	13.8	6.9
5 wt%TiO_2-Hβ(20)	400	0.24	15.6	7.5
2 wt%TiO_2-Hβ(30)	495	0.43	18.5	7.5
5 wt%TiO_2-Hβ(30)	485	0.47	22.5	12.6
2 wt%ZnO-HZSM-5(30)	326	0.13	8.5	4.0
2 wt%ZnO-HY(4.4)	336	0.18	4.6	3.0
5 wt%TiO_2/Hβ(30)[d]	—	—	3.6	2.4

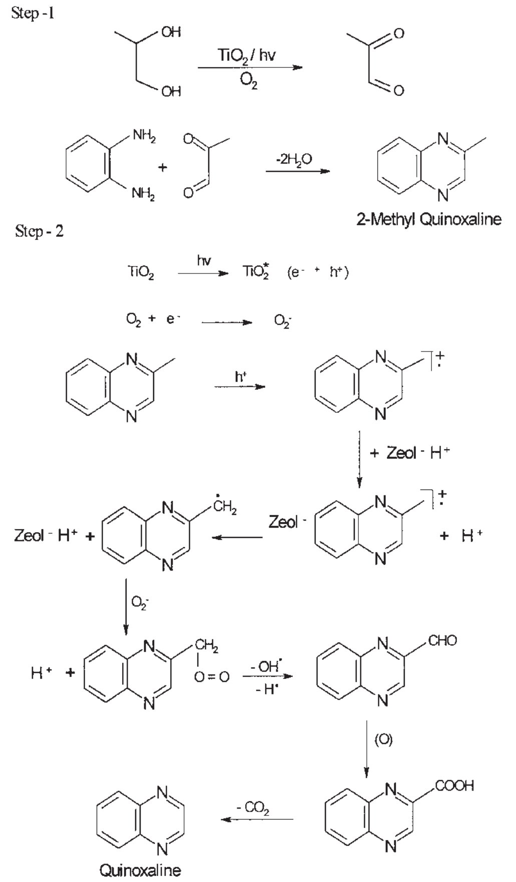
[a]BET technique measured with liquid N_2 at 77 K. [b]TPD of NH_3 measured on AutoChem 2910 (Micromeritics, USA). [c]Isolated yields after column chromatography. [d]Mechanically ground TiO_2 and zeolite (uncalcined). Numbers in parentheses are SiO_2/Al_2O_3 ratios of zeolites.

Further experiments were carried out in the presence of light, O_2 and TiO_2/zeolite catalyst to confirm whether the reaction was photocatalytic or non-photocatalytic. The data of control experiments given in Table 2 proves very much that the synthesis reactions are photocatalytic and also they occur especially in the presence of zeolite only. Irradiation in the presence of conventional liquid acid HCl, and solid acid silica gel also did not yield any product of our interest.

Table 2. Photocatalytic synthesis of 2-methyl quinoxaline and quinoxaline control experiments using *o*-phenylenediamine and propyleneglycol

Conditions	Irradiation Period /h	2-MQ /%	Q /%
TiO_2/zeolite, Light, O_2	10	22.5	12.6
TiO_2/zeolite, Dark, O_2	>10	0	0
Light, O_2	>10	0	0
Zeolite, Light, O_2	>10	0	0
TiO_2/or ZnO, Light, O_2	>10	0	0

It is already established that alcohols can be easily oxidized on semiconductor surface to its corresponding aldehyde or ketone.[10a–d] Also known that zeolite acidity influences the reaction mechanism and the oxidation depends on the acidity of the reaction mixture.[7a] Moreover, *o*-phenylenediamine is adsorbed preferentially than propyleneglycol in the internal surface area of the zeolite pores. The preferential adsorption of *o*-phenylenediamine is making propyleneglycol to undergo oxidation to keto-aldehyde (Step-1) at the oxidizing site of TiO_2. The keto-aldehyde formed undergoes cyclization with *o*-phenylenediamine to give 2-methyl quinoxaline by loss of 2 mol of water. The methyl group of 2-methyl quinoxaline is oxidatively demethylated giving to quinoxaline as is shown in Step 2 of Scheme 1. Photoexcitation of semiconductor in Step 2 would produce an electron and a hole. Oxygen serves as an electron acceptor for the conduction band electron and the 2-methyl quinoxaline supplies an electron to the photogenerated hole at the surface of TiO_2 particle forming an adsorbed radical cation. Zeolite catalysts are known to stabilize reactive intermediates in several photochemical reactions.[11a–b] Thus, zeolite may assist the stability of the radical cation through proton transfer as is observed by Beaune, *et al.*[7b] and also from our earlier report.[8a] The formation of quinoxaline may be enhanced by using more acidic zeolites as is evidenced in the proposed mechanism (Step 2). The quinoxaline-2-carbaldehyde (found in traces) formed undergoes further oxidation to the corresponding acid (found in traces), which inturn forms the quinoxaline in view of decarboxylation.



Scheme 1. Proposed reaction mechanism for the formation of 2-methyl quinoxaline and quinoxaline.

The electron donating substituent i.e, methyl group of propyleneglycol, also may favour the oxidation mechanism.[12] In aerated solutions, the photogenerated electron can be trapped by adsorbed oxygen to form superoxide or other negatively charged adsorbed oxygen species.[13]

Hydrogen peroxide (eq 1) thus formed by

$$\left.\begin{array}{lcl} O_2 + e^- & \longrightarrow & O_2^{\cdot -} \\ O_2^{\cdot -} + H^+ & \longrightarrow & HOO^- \\ 2HOO^- & \longrightarrow & H_2O_2 + O_2 \\ H_2O_2 + O_2^{\cdot -} & \longrightarrow & OH^{\cdot} + OH^- + O_2 \end{array}\right] \longrightarrow \text{eq 1}$$

sequential 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. The selectivity for primary alcohol site of propyleneglycol is more in pure oxygen than with air. The secondary alcohol site is preferentially oxidized by the adjacent electron donating group i.e., methyl at TiO_2 center. Pore size of the zeolite did not affect the formation of bulky molecules in the present work.

The evaluation of TiO_2/zeolite catalysts for the cyclization of *o*-phenylenediamine and propyleneglycol show that 5 wt% $TiO_2/H\beta(30)$ has shown high yields. The hydrophobicity and acid site strength of zeolites may be the influencing factor for the activity of these zeolite systems in the order $H\beta > HZSM\text{-}5 > HY$. This trend illustrates that the cyclization is preferred by a combination of moderate hydrophobicity and acidity. However, 5 wt% $TiO_2/H\beta(30)$ is found to have more activity forming high yield of 2-methyl quinoxaline. Incorporation of TiO_2 in the zeolites may be altering the acidic site strength of the individual zeolites. Furthermore, the same acid strength values were obtained in the reproducibility experiments of TPD. This may be possibly explained as the structure of $H\beta$ is a combination of both HZSM-5 (channel pore system, high Si/Al ratio) and Y (12-ring pore system) zeolites.[8a]

In conclusion, the formation of 2-methyl quinoxaline (22.5%) and quinoxaline (12.6%) during the cyclization of *o*-phenylenediamine and propyleneglycol at ambient temperature is reported over 5 wt% $TiO_2/H\beta(30)$ photocatalyst for the first time.

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