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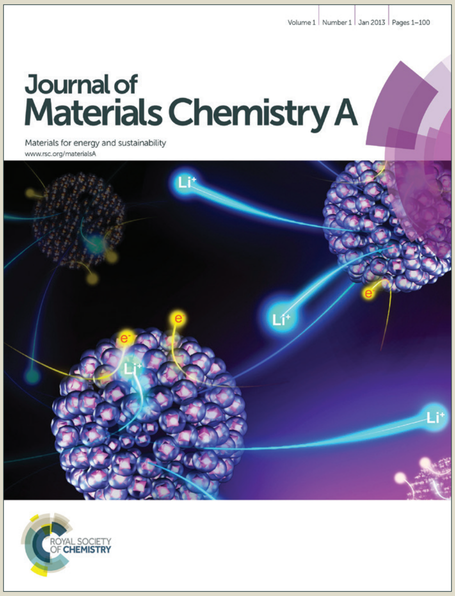

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TiO_2 immobilized Ru(II) polyazine complex: a visible-light active photoredox catalyst for oxidative cyanation of tertiary amines.

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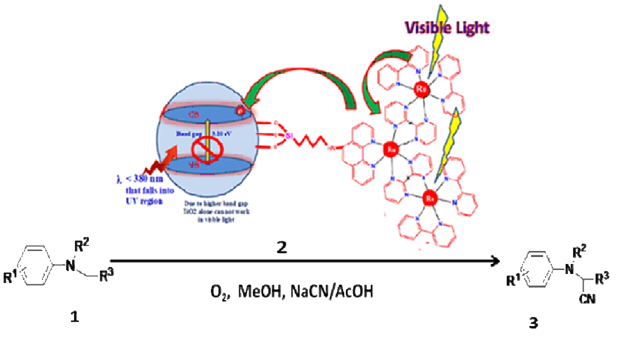
Chemically functionalized nanocrystalline TiO_2 grafted ruthenium (II) polyazine complex was found to be an efficient visible light photoredox catalyst for the oxidative cyanation of tertiary amines to the corresponding α-aminonitriles in high to excellent yields using molecular oxygen as oxidant and sodium cyanide in acetic acid as a cyanide source. The developed photoredox catalyst could be easily recovered by simple filtration and reused for several runs with consistent catalytic activity.

The use of visible light sensitization as a means to initiate organic reactions is an attractive tool as the visible light is ubiquitous, renewable and clean source of energy.[1] Furthermore, lack of visible light absorbance by organic compounds hinders the possibilities of side reactions often associated with photochemical reactions conducted with high energy UV light. Among these, the use of photoredox catalysts in particular Ru(II)polypyridine complexes for organic transformations are of notable importance due to their ease of synthesis, stability at room temperature, and excellent photoredox properties.[2] However, similar to the homogeneous catalysis, these complexes also suffer from the drawbacks of tedious recovery and non-recycling ability of the catalyst. One of the elegant approaches for making these catalysts recyclable is to fix the homogeneous metal complexes to solid matrix. In the recent decades, modification of titanium dioxide via immobilization or functionalization with metal complexes has become an appealing approach as these immobilized metal complexes can harvest visible light and inject photogenerated electrons into the conduction band of the titania.[3]

α-Aminonitriles are highly useful and versatile intermediates for a wide range of natural products and nitrogen containing bioactive compounds such as alkaloids.[4] Also these compounds show dual reactivity as the nucleophilic addition provides an easy access to various compounds such as α-amino aldehydes, ketones and β-amino alcohols. On the other hand, these compounds can be easily hydrogenated to useful compounds 1,2-diamines.[5] The most common method for their synthesis also known as Strecker reaction is well documented in the literature, albeit consisting of multistep synthesis.[6] An alternative and more convenient approach for the preparation of these structural motifs is the catalytic oxidative cyanation of sp^3 C-H bonds adjacent to the nitrogen atoms in tertiary amines. In this context, a number of metal catalysts including Ru, Fe, V etc. in the presence of stoichiometric oxidants such as *m*-chloroperbenzoic acid, *tert*-butyl hydroperoxide, O_2, H_2O_2 has been reported.[7] However, scanty reports are known on the use of photoredox catalysts for this transformation. In this regard, Rueping et al reported $[Ir(ppy)_2bpy]PF_6$ as a visible light photoredox catalyst for aerobic oxidative cyanation of tertiary amines.[8] However difficult recovery and non-recyclability of the catalyst makes this method of limited synthetic utility.

In continuation to our recent research programme on photo catalysis, we herein report an efficient, heterogeneous, easily recoverable and recyclable visible light active TiO_2 immobilized ruthenium polyazine photoredox catalyst for the oxidative cyanation of tertiary amines using molecular oxygen as oxidant and NaCN in acetic acid as a cyanide source (Scheme 1).



Scheme 1: Visible light active photoredox catalyst for the oxidative cyanation of tertiary amines

Synthesis and characterization of the catalyst **2**

During the present investigation, nanocrystalline TiO2 was prepared by following the literature procedure.[9] Hydroxyl groups placed on TiO_2 were targeted for grafting of ruthenium polyazine complex by using 3-chloropropyltrimethoxysilane (CPTS) as a coupler. The strategy opted for the synthesis of TiO_2 immobilized ruthenium-polyazine photocatalyst is shown in Scheme 2.

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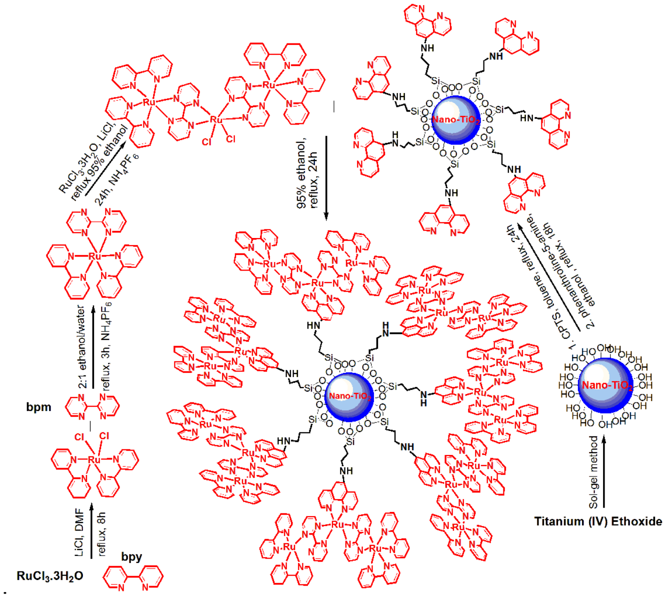

Scheme 2: Synthesis of nanocrystalline TiO_2 immobilized ruthenium polyazine complex **2**

The successful synthesis of nanocrystalline TiO_2 and TiO_2 grafted ruthenium polyazine complex **2** were confirmed by various techniques including XRD, SEM, TEM, ICP-AES, CHNS, UV-Vis, NMR, ^{13}C NMR and FTIR spectroscopy. Characterization data of the catalyst are given in the supporting information. The values of BET surface area and BJH pore volume of **2** as determined by nitrogen adsorption were found to be 26.50 $m^2\ g^{-1}$ and 0.0622 $cm^3\ g^{-1}$, respectively (Supporting Fig S3).

The crystallinity of the as-synthesized TiO_2 and TiO_2-Ru(II) polyazine photocatalyst **2** was examined by XRD[10] analysis (Fig. 1). As shown in Fig 1a, the well resolved peaks and their intensity revealed the good crystallinity of the TiO_2 mainly in anatase phase and the rutile form was present only in a small quantity. The peaks at 2θ values of 24.86, 37.41, 47.68, 54.23, 54.51, 63.33, 69.48, and 73.69 were identified by comparison with literature data and confirmed the successful synthesis of TiO_2 nanoparticles with anatase structure. The as synthesized TiO_2 was combined with phenanthroline-5-amine ligands followed by its reaction with ruthenium pyridyl complex (Scheme 2). The XRD pattern of the TiO_2 immobilized ruthenium polyazine complex **2** is shown in Fig 1b. For the comparison purpose we also prepared homogeneous ruthenium polyazine complex by combining the ruthenium pyridyl complex with phenanthroline-5-amine ligand. The XRD pattern of the homogeneous ruthenium complex is shown in Fig. 1c. As shown, the XRD pattern of TiO_2 immobilized ruthenium photocatalyst (Fig 1b) exhibits combination of peaks originated from TiO_2 (Fig. 1a) and ruthenium polyazine complex (Fig. 1c). Importantly, no impurity peaks appeared in the diffractogram of the synthesized photocatalyst **2** except for those of anatase TiO_2 and ruthenium polyazine complex. Furthermore appearance of ruthenium polyazine complex peaks in the XRD pattern of **2** confirmed the successful attachment of ruthenium complex to TiO_2. Furthermore, deposition of Ru(II)-polyazine onto the TiO_2 did not affect the morphology of the TiO_2 support (Fig 1b).

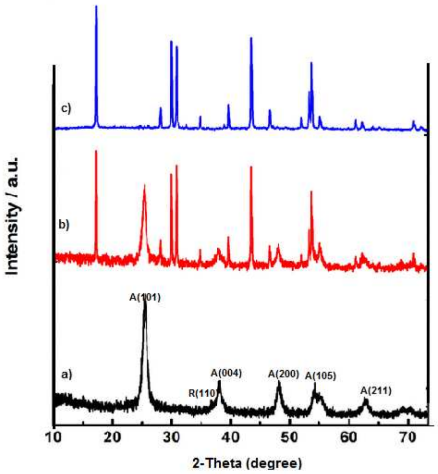

Fig. 1: XRD pattern of a) TiO_2; b) TiO_2 grafted Ru-polyazine photocatalyst **2;** c) Ru-polyazine complex

The size and morphology of the samples were analyzed by SEM and TEM measurements. The SEM image of the TiO_2 and photocatalyst **1** are given in supporting information.

TEM image (Fig. 2) revealed that the product consisted of the homogeneous distribution of ruthenium over TiO_2 support and showed the particle size 10-20 nm. The black particles visible in TEM image (Fig. 2a) are might be attributed to the presence of ruthenium, which is further confirmed by EDX. Furthermore, selected area electron diffraction (SAED) analysis was carried out to identify the crystalline phases of TiO_2 (Fig. 2b)

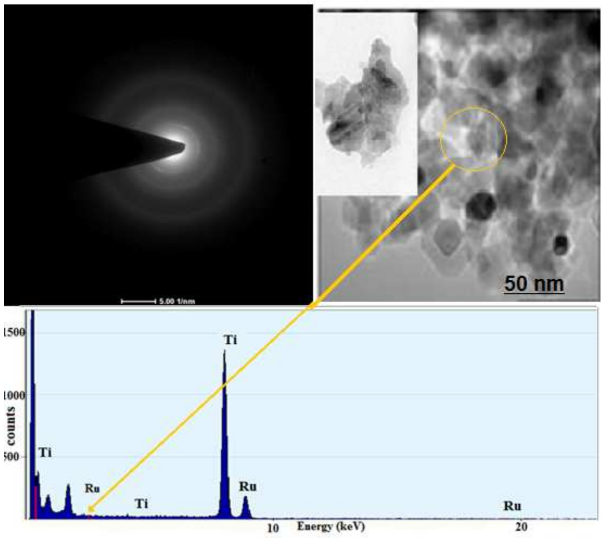

Fig. 2: a) TEM image of TiO_2-grafted photocatalyst **2;** b) SEAD image; c) EDX

The catalytic efficiency of the as synthesized photocatalyst **2** was examined for the oxidative cyanation of tertiary amines **1** to α-aminonitriles **3** with molecular oxygen in the presence of NaCN and acetic acid using methanol as solvent under visible irradiation, using a household white LED (20 W) at room temperature (Scheme 1). We initiated our studies by selecting the photochemical oxidation of *N,N*-dimethyl aniline in order to optimize the reaction conditions (Table 1). To our delight, we could isolate the desired α-aminonitrile in very high yield (96%)

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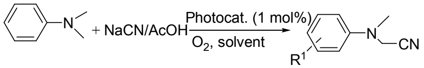
in 4h using only 1 mol% of the TiO_2-grafted ruthenium photocatalyst **2** (Table 1, entry 2). In a controlled blank experiment, there was no reaction occurred in the absence of photocatalyst (Table 1, entry 1). Similarly, there was no reaction observed by using nanocrystalline TiO_2 as a catalyst (Table 1, entry 3), proving that the ruthenium-polyazine was truly required for this transformation. When the reaction was performed by using homogeneous ruthenium(II) polyazine complex as catalyst (1 mol%) under described experimental conditions. The reaction did occur but afforded poor yield of the desired product, indicating the promoting effect of TiO_2 on the photocatalytic activity of the catalyst (Table 1, entry 4). However, the reaction of *N,N*-dimethyl aniline with TiO_2 immobilized photocatalyst **2** in the dark was found to be very slow and afforded poor yield of the desired product (Table 1, entry 5). Furthermore, the use of air in place of molecular oxygen afforded desired product in comparatively lower yield (Table 1, entry 6). Acetic acid was found to be crucial in this transformation and no reaction was taken place in its absence (Table 1, entry 7). The role of acetic acid can be attributed to the liberation of HCN in the presence of AcOH. Hence, acetic acid acts as a co-catalyst in this transformation. To evaluate the effect of solvent, photochemical oxidative cyanation of *N,N*-dimethylaniline was studied in various solvents such as dichloroethane, acetonitrile, toluene, methanol and ethanol. The results of these experiments are summarized in Table 1 (entries 8-11). Among the various solvents studied polar and protic solvents such as methanol and ethanol were found to be best reaction media for this transformation.

Table 1: Results of the optimization experiments[a]

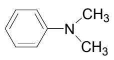
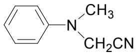
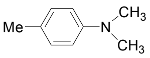
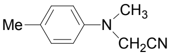
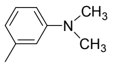
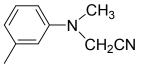
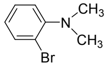
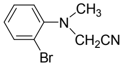
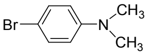
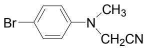
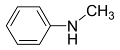
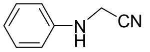
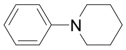
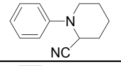
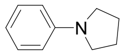
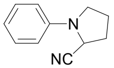
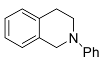
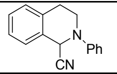
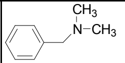
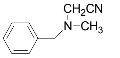
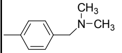
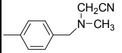


Entry	Catalyst (1 mol %)	Solvent	Yield (%)[b]	TOF (h^{-1})
1	-	MeOH	-	-
2	**2**	MeOH	96	24
3	TiO_2	MeOH	-	-
4	Ru(II)polyazine	MeOH	90	22.5
5	**2**	MeOH	40[c]	10
6	**2**	MeOH	92[d]	23
7	**2**	MeOH	20[e]	5
8	**2**	$ClCH_2CH_2Cl$	trace	-
9	**2**	Toluene	25	6.3
10	**2**	CH_3CN	40	10
11	**2**	EtOH	92	23

[a]Reaction conditions: substarte (1 mmol), photocatalyst (1 mol%), NaCN (1.2 mmol), solvent (4 ml) in the presence of molecular oxygen; reaction time 4h; [b]Isolated yield; [c]Reaction was performed in dark; [d]by using air in place of oxygen; [e]In the absence of acetic acid.

To further investigate the substrate scope, the oxidative cyanation of a variety of aromatic and cyclic tertiary amines was studied under similar experimental conditions. The results of these experiments are presented in Table 2. The conversion and selectivity of the product was confirmed by GCMS and identity was confirmed by comparing the physical and spectral data with those of authentic samples. Among the various substrates, aromatic substrates having electron donating groups (Table 2, entries 2-3) were found to be more reactive as compared to the substrates bearing electron withdrawing groups (Table 2, entries 4-5). Cyclic amines such as *N*-phenyl piperidine, *N*-phenylpyrrolidine and *N*-phenyltetrahydro-isoquinoline yielded corresponding α-aminonitrile in high yields (Table 2, entries 7-9). Under the described experimental conditions, aliphatic tertiary amine such as *tert*-butyl amine did not produce any product (Table 2, entry 10). However, the reaction of tertiary amines containing benzyl group was found to be slow and provided corresponding amino nitriles in moderate yields (Table 2, entries 11-12).

Table 2: TiO_2-immobilized ruthenium polyazine complex **2**-catalyzed oxidative cyanation of tertiary amines[a]

Entry	Reactant **1**	Product **3**	Time (h)	Yield (%)[b]	TOF (h^{-1})
1			4	96	24
2			4	91	23
3			3.5	84	24
4			5	75	15
5			4	85	21.2
6			4	90	22.5
7			4.5	88	19.5
8			4.5	89	20
9			5	92	18.4
10	(*n*-Bu)$_3$N	-	48	-	-
11			30	48[d]	1.6
12			24	55	2.3

[a]Reaction conditions: Substrate **1** (1 mmol), catalyst **2** (1 mol %),NaCN (1.2 mmol), AcOH (1 ml), MeOH (4 mL) in the presence of O_2 at room temperature. [b]isolated yield

Further, we tested the recycling of the photocatalyst by selecting the photochemical oxidation of the *N,N*-dimethylaniline as representative example. After completion of the reaction, the photocatalyst was easily separated by filtration, washed with acetone, dried and reused for subsequent experiments (for eight runs). The results of the recycling experiments are depicted in Fig. 3. In all cases, the yield of the desired product was found to be almost similar, establishing the efficient recycling of the catalyst. Furthermore, the selected filtrate samples were subjected to ICP-AES analysis to check the leaching of the metal/ ligand. No metal/ligand was observed during this course, proving that the reaction was truly heterogeneous in nature and no leaching had occurred during the photochemical reaction.

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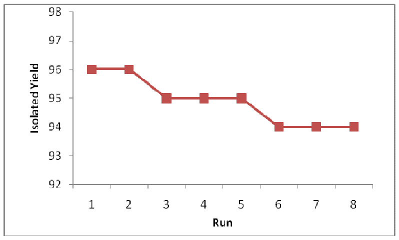
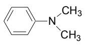
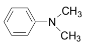
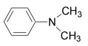
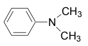
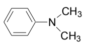
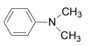
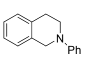
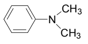
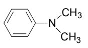


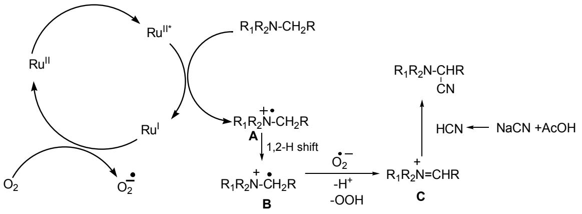
Fig. 3: Results of recycling experiments

A comparison of the catalytic performance of the developed photocatalyst with the previously reported heterogeneous catalysts is shown in Table 3. In comparison to the previously known catalysts (Table 3), the present photocatalyst has the following significant advantages; a) the use of visible light, b) the use of molecular oxygen as a terminal oxidant, c) the use of lower catalyst concentration (1 mol%), d) higher product yields, e) mild experimental conditions, f) the reusability of the TiO_2 grafted ruthenium photocatalyst.

Table 3: Comparison of various heterogeneous catalysts for oxidative cyanation of tertiary amines

Substrate	Catalyst	CN source/ oxidant	Time/ h	Yield (%)	Ref
	Ru/C (2 mol%)	Ethyl cyano-Formate/ TBHP	6.0	95	11
	$Fe_{0.64}H_{0.36}PMo_{12}O_{40}$/ Nb_2O_5 (50 mg)	Ethyl cyano-formate/ TBHP	7.0	96	12
	$RuCl_4^-$ on Starch (2 mol%)	$NaCN/H_2O_2$	2.0	82	7j
	Polymer supported Fe(II)Pc (2 mol%)	$NaCN/H_2O_2$	2.5	95	7f
	Iron@graphene oxide (2 mol%)	NaCN/(*t*BuO)$_2$	2.5	90	7k
	Iron oligopyridine / SBA-15 (5 mol %)	NaCN/ O_2	12	71	13
	TiO_2 (1 eq.) (11 W fluorescent)	KCN/ O_2	20	95	14
	MnO_2-based catalyst (2g)	TMSCN/ O_2	2	90	15
	TiO_2 supported ruthenium (II)polyazine (1mol%)	NaCN/ O_2	4.0	96	-

Although the exact mechanism of the reaction is not known at this stage, the possible mechanistic pathway of the reaction is shown in Scheme 3. In analogy to the existing reports, two important steps can be assumed for the photocatalytic oxidative cyanation of the tertiary amine. The first step of the reaction may involve the single electron transfer from tertiary amine for reductive quenching of the excited triplet state of the complex (*[Ru(bpy)$_2$]$^{2+}$ to generate intermediate [Ru(bpy)$_2$]$^{+}$ and a radical cation of tertiary amine. The formation of transient species [Ru(bpy)$_2$]$^{+}$ under visible light in the presence of a donor is well documented in the literature. The photoredox catalyst was regenerated by its reoxidation with molecular oxygen to give superoxide radical anion ($O_2^{\cdot-}$). The second step of the reaction probably involves the abstraction of hydrogen atom ($H^{\bullet}$) from the amine cation radical **B** by the superoxide anion (O^{2-}) to give iminium ion intermediate **C** as shown in Scheme 3. The iminium ion intermediate **C** subsequently reacts with hydrogen cyanide that is insitu generated from NaCN and acetic acid to yield corresponding α-amino nitrile.



Scheme 3: Possible mechanism of the photocatalytic oxidative cyanation

In summary, we have developed for the first time an efficient, recyclable and heterogeneous aerobic photocatalytic oxidative cyanation of the tertiary amines to valuable compounds α-aminonitriles in high yields with molecular oxygen in presence of NaCN in acetic acid under visible irradiation, using a household white LED (20 W). It is anticipated that the developed visible light photoredox catalyst can be further explored to develop a number of environmentally benign and cost effective methodologies for organic transformations.

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Notes and references

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General experimental procedure: A 25 mL round bottomed flask equipped with a magnetic stirrer bar was charged with tertiary amine (1 mmol), NaCN (1.2 mmol), MeOH (2 mL), catalyst (1 mol %) and AcOH (1 mL). The stirring was continued at room temperature under oxygen atmosphere under visible irradiation, using a household white LED (20 W). The progress of the reaction was monitored by TLC (SiO_2). After completion of the reaction, the catalyst was recovered by precipitation with diethyl ether followed by filtration. The obtained organic layer was washed with water, dried over anhydrous Na_2SO_4 and concentrated under vacuum to give crude product, which was purified by flash chromatography to afford pure α-aminonitrile. The conversion of tertiary amines into corresponding α-aminonitriles and their selectivity was determined by GC-MS (EI quadrupol mass analyzer, EM detector) and the identity of the selected products was established by comparing their spectral data with authentic samples.

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TiO_2 immobilized Ru(II) polyazine complex: a visible-light active photoredox catalyst for oxidative cyanation of tertiary amines

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