

# N-doped Yellow TiO<sub>2</sub> hollow sphere mediated visible light driven efficient esterification of alcohol and N-Hydroxyimides to active esters

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**Abstract:** Herein we report a simple synthetic protocol for N-doped yellow TiO<sub>2</sub> (N-TiO<sub>2</sub>) hollow sphere as an efficient visible light active photocatalyst using aqueous titanium peroxocarbonate complex (TPCC) solution as precursor and NH<sub>4</sub>OH. In the developed strategy, the ammonium ion of TPCC and NH<sub>4</sub>OH act as nitrogen source and structure directing agent. The synthesized N-TiO<sub>2</sub> hollow sphere is capable of synthesizing active esters of N-hydroxyimide and alcohol through simultaneous selective oxidation of alcohol to aldehyde followed by cross-dehydrogenative coupling (CDC) under the ambient condition on irradiation of visible light. It is possible to develop a novel and cost-effective one-pot strategy for the synthesis of important esters and amides in gram scale using the developed strategy. The catalytic activity of N-TiO<sub>2</sub> hollow sphere is much superior to that of other reported N-TiO<sub>2</sub> as well as TiO<sub>2</sub> with varying morphology.

#### Introduction

Esterification of N-hydroxyimide (NHI) to corresponding active ester is one of the most important organic transformations not only for its importance as intermediate for amides and esters but also their use in C-H amination, C-S, C-C & C-N coupling, alkynylation.<sup>1</sup> Cross- dehydrogenative coupling (CDC) reaction of aldehyde and NHI have been developed as a straightforward alternative of traditional coupling with acid.[1-3] But due to easy availability, stability, and cost-effectivity, starting with alcohol instead of the corresponding aldehyde is more convenient and highly demanding. Unfortunately, such strategy has been scarcely explored in literature, with only a few examples using hyper-valent iodine(III), iodide and iron salt as homogeneous catalysts.<sup>[4]</sup> These reported homogeneous catalysts not only generate hazardous waste, required energy to control the reaction temperature but also needs additional product purification step to remove the possible contaminations from catalysts. Towards sustainable development, energy efficient hazardous waste free reactions at ambient condition are highly

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desirable. Being one of the prime sustainable energy resources on earth, conversion of solar energy to chemical energy, visible reactions (photo-catalysis) liaht-driven usina reusable heterogeneous photocatalyst, have been stimulated in recent years.<sup>[5-6]</sup> Essentially, the esterification of NHI from alcohol is basically a two steps reaction, selective oxidation of alcohol to aldehyde followed by CDC reaction. However, the photo-induced transformation of such tandem reaction is challenging and to the best of our knowledge, there is no report on such visible light induced tandem reactions. Thus, it is highly desirable to develop a visible light active catalyst, preferably heterogeneous, for such tandem reaction.

In this concern, Titanium oxide (TiO<sub>2</sub>) is the most popular heterogeneous photocatalyst, owing to the low cost, abundance, chemical- & photo- stability, and nontoxicity.<sup>[7]</sup> However, its wide band-gap (3.2 eV, anatase), non-effectivity in visible light, and severe recombination of photo-generated e<sup>-</sup>/h<sup>+</sup> pair restrict it's widespread photocatalytic application.<sup>[7]</sup> Doping of anionic nitrogen in TiO<sub>2</sub> structure (N-TiO<sub>2</sub>) is an effective and successful strategy to improve its visible light efficiency, due to its comparable size to that of oxygen as well as small ionization energy and metastable defect complex.<sup>[8-12]</sup> N-doping not only modifies the band structure to facilitate the visible light absorption but also reduce the recombination rate of photo-generated e/h+ pair and improve the photocatalytic activity. The catalytic activity of TiO<sub>2</sub> is also highly dependent on morphology and surface structure. Thus, N-TiO<sub>2</sub> with varying morphology have been reported.<sup>[8-12]</sup> Recent years, 3D TiO<sub>2</sub> porous hollow structures have received exceptional attention for the photocatalytic application not only for its enhanced surface area from inner hollow architecture but also for the generation of micro-reactor environment.<sup>[13-14]</sup> In addition. Gao et al.<sup>[14]</sup> reported that the TiO<sub>2</sub> hollow sphere showed reduced recombination comparison to that of a corresponding solid sphere, owing to that of improved light scattering behavior. There are plenty of literature reports on bare TiO<sub>2</sub> hollow structures, but the synthesis of N-TiO<sub>2</sub> hollow structure is scarcely reported, which are complicated and utilize hazardous chemicals. Xiang and his group synthesized N-TiO<sub>2</sub> hollow spheres through the solvothermal treatment of TiCN in the presence of hazardous HF.<sup>[15]</sup> Cho et al. <sup>[16]</sup> and Li et al. <sup>[17]</sup> reported the synthesis of N-TiO<sub>2</sub> hollow spheres by the templateassisted method using SiO<sub>2</sub> and melamine formaldehyde microspheres as a templet. Thus, it is essential to develop a simple single step protocol for the synthesis of N-TiO2 hollow spheres.

Further, the utilization of N-TiO $_2$  is limited to degrade pollutants and water splitting. The reports on visible light induced

organic transformations are very limited to some simple straight forward reactions, and the development of visible light-induced multi-step tandem organic transformation is highly demanding. Herein, we report the synthesis of visible light active N-TiO<sub>2</sub> hollow sphere under hydrothermal condition using an aqueous titanium peroxo-carbonate complex (TPCC) solution.<sup>[18]</sup> We have

also developed a simple visible light mediated photocatalytic protocol of such cascade reaction, i.e., esterification of NHI with alcohol, at ambient condition using the synthesis N-TiO<sub>2</sub> hollow sphere as a reusable heterogeneous catalyst and 40W CFL lamp as visible light source, for the first time.

#### **Results and Discussion**

#### Catalyst characterization

The N-TiO<sub>2</sub> hollow spheres were synthesized by hydrothermal treatment of freshly prepared TPCC in the presence of the varying amount of ammonium hydroxide (NH<sub>4</sub>OH) solution followed by calcination. In the developed strategy, both the ammonium carbonate of precursor TPCC and NH<sub>4</sub>OH act as a nitrogen source, and the NH<sub>4</sub>OH also helped in the formation of the hollow interior, through decreasing the rate of hydrothermal reactor and formation of the gaseous internal cavity. Hereafter, the TiO<sub>2</sub> synthesized without or with 10 - 50 ml NH<sub>4</sub>OH with respect to TPCC solution from 3 ml titanium isopropoxide will be termed as "N-TiO<sub>2</sub>-0" and "N-TiO<sub>2</sub>-X", respectively, where X= 10, 20, 30, 40, 50, the amount of NH<sub>4</sub>OH used.

**XRD pattern analysis.** The phase and purity of the synthesized materials were investigated by powder X-ray diffraction (XRD) analysis and Figure 1 represent the respective XRD patterns of as-synthesized and calcined materials. XRD pattern of as- synthesized materials showed the presence of distinct diffraction peaks at 9.3, 24.6, 28.5, 34.1, 38.9, 48.4 20





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angle, recognized as (200), (110), (310), (301), (501) and (020) planes of orthorhombic layered di-titanate (H2Ti2O5·H2O; JCPDS 47-0124).<sup>[18]</sup> The diffraction at  $2\theta = 9.3$  for (200) is nothing but the interlayer distance. However, after calcination all the respective diffraction peaks for layered di-titanate disappeared and a new set of peaks ascribed to (101), (004), (200), (105), and (211) planes of anatase TiO<sub>2</sub> (JCPDS 21-1272) was identified. All the synthesized calcined samples showed identical pattern and absence of any peak for layered di-titanate or peak other than anatase TiO<sub>2</sub> confirm the complete phase transformation on heating and formation of phase pure anatase TiO<sub>2</sub>. The corresponding crystallite size of the synthesized TiO<sub>2</sub> was calculated by Scherrer equation using the line broadening of XRD peaks. More interestingly, it was observed that crystallite size was decreased with the increase in the amount of ammonium hydroxide in the precursor solution, i.e., degree of nitrogen doping, which most probably due to the surface strain originating from the substitution of 'N' having higher atomic radius with O ( $O^{2-} = 140$ Å and  $N^{3-} = 171$  Å) and in agreement of previous reports.<sup>[9]</sup> For further confirmation, we did the strain calculation using Williamson-Hall equation and observed that strain was increased with enhancement of amount of added NH<sub>4</sub>OH in precursor solution (Figure S1 and Table S1).<sup>[19]</sup> This implies that with enhance of NH<sub>4</sub>OH the degree of N doping was increased and for which the corresponding crystal strain was increased, which is the prime origin of the gradual reduction of crystallite size. Thus the XRD results evidenced that the degree of nitrogen doping has a significant effect on the crystallite size of TiO<sub>2</sub>. Digital photograph evidenced that the synthesized N-TiO2-30 is quite bright yellow in colour (inset Figure 1).



Figure 2. Raman spectra of the synthesized N-TiO<sub>2</sub>-x samples.

**Raman spectra analysis.** Raman spectroscopy was performed for the detailed investigation of microstructural and surface stoichiometric information of  $TiO_2$ . Figure 2 represents the Raman spectra of the N-TiO<sub>2</sub> synthesized with varying amount of ammonium hydroxide in the precursor solution, i.e., 'N' doping. In

# **FULL PAPER**

the Raman spectra of all the synthesized N-TiO<sub>2</sub> evidenced the presence of Raman bands at around 144, 197, 397, 520, and 640 cm<sup>-1</sup> can be ascribed to the Eg, Eg, B1g, A1g/B1g, and Eg phonon modes of anatase TiO<sub>2</sub>, respectively.<sup>[9]</sup> Detailed investigation evidenced that with the enhancement of the extent of nitrogen doping the highly intense lowest frequency peak at 151 cm<sup>-1</sup> gradually blue shifted (toward the higher wavenumber region), with enhanced peak intensity and the corresponding peak widths. The observed phenomenal change in lower frequency peak at 151 cm<sup>-1</sup> is due to the reasonable unite cell strain due to the incorporation of nitrogen with larger size and N (dopant) induced particle size reduction. Thus Raman results evidenced the gradual enhancement of the extent of N doping with the enhancement of the amount of ammonium hydroxide in the precursor solution. The Raman spectroscopic results are quite consistent with the XRD results with respect to that of phase purity and peak broadening, i.e., reduction of crystallite size.



Figure 3. SEM and TEM images of synthesized a) N-TiO<sub>2</sub>-0, b-f) N-TiO<sub>2</sub>-30.

SEM and TEM analysis. Shape and morphology of the synthesized N-TiO<sub>2</sub> materials were evaluated using electron microscopic study. Figure 3 a & b represents the representative SEM image of the N-TiO2-0 and N-TiO2-30. SEM image evidenced that the morphology of N-TiO2-0 is nothing but the flower-like assembly of 2D sheets. However, on the introduction of ammonium hydroxide in the precursor solution the generation of the hollow spherical structure was started. With the enhancement of the amount of ammonium hydroxide, the size dispersion of hollow structure becomes narrower. Although N-TiO<sub>2</sub>-30 showed quite uniform hollow spherical structure in the range of 1-1.3 µm, some smaller hollow spheres also observed. Whereas, N-TiO<sub>2</sub>-50 showed almost uniform hollow spherical structure. Inner hollow core in the broken sphere, as marked by the dotted white circle in inset Figure 3b, evidenced the formation of the hollow sphere. Figure 3c-f represents the TEM and HR-TEM images of corresponding N-TiO<sub>2</sub>-30 hollow spheres. TEM image evidenced the formation 2D sheet assembled spheres. In the corresponding magnified image, the contrast difference between the inner and outer part confirmed the presence of void interior geometry and formation of hollow structure (Figure 3d). The respective magnified image further confirmed that the spheres are made of sheets and the sheets are very thin (Figure 3e). Corresponding HR-TEM image revealed the presence of distinct crystal planes with an inter-planar distance of 0.35 nm, ascribed to the (101) plane of anatase  $TiO_2$  and confirm the formation of crystalline anatase  $TiO_2$  and support the XRD result (Figure 3f). For further confirmation for the presence of hollow interior, the synthesized spheres were sectioned through microtomy and taken the TEM image. The TEM image of corresponding sectioned spheres confirmed the presence of hollow interior in the synthesized sphere (Figure S2).

XPS analysis. Ti 2p spectra in the range of 450-468 eV evidenced the presence of two peaks at 464.8 and 459.1 eV, can be assigned to Ti2p1/2 and Ti2p3/2, respectively. These data agree well with previously reported XPS data for N-doped TiO<sub>2</sub> and confirm the presence of Ti<sup>4+</sup> in pure anatase TiO<sub>2</sub>. All the synthesized samples almost identical spectral pattern (Figure S3). The respective O1s spectra of the samples showed the presence of two peaks at 529.8 eV and 531.7eV (Figure S3). The peak located at 529.8 eV corresponds to lattice oxygen of TiO<sub>2</sub>, whereas the peak at 531.7eV is for remnant surface hydroxyl group. Although all the samples showed almost identical pattern. from the area of corresponding fitted peak it was identified that the N-TiO<sub>2</sub>-30 and N-TiO<sub>2</sub>-50 content approximately 2-2.5% less surface hydroxyl group, which is most probably due to the N doping in the crystal structure. The fitted convoluted N1s spectra in the range of 398-402 eV displayed mainly two peaks at binding energies of 398.08 and 399.11 eV, which are ascribed to substitutional N in the form of O-Ti-N bonding and oxidized Ti-O-N species, <sup>[9, 11]</sup> respectively. In addition to these peaks, N-TiO<sub>2</sub>-50 evidence the presence of one additional low intense peak at 401.3 eV, ascribed to the surface adsorbed oxidized species of nitrogen, essentially adsorbed NOx (Figure 4, Figure S3). The detailed study of the corresponding area of the fitted spectra evidenced that with the enhancement of the amount of NH4OH in the precursor solution, in turn the extent of doped nitrogen, the amount of substitutional 'N' is increased till N-TiO<sub>2</sub>-30 and in N-TiO<sub>2</sub>-50 the excess nitrogen is present in the form of surface adsorbed oxidized nitrogen species. The observation also support the calculated crystal strain, where the difference in the strain values for N-TiO<sub>2</sub>-30 and N-TiO<sub>2</sub>-50 are quite low. Survey XPS spectrum of N-TiO<sub>2</sub>-30 evidenced the presence of at around 5% 'N' in TiO<sub>2</sub>,



Figure 4. XPS N1s spectra of the synthesized N-TiO<sub>2</sub> hollow spheres.

whereas it is approximately 1% in N-TiO<sub>2</sub>-0. The probable origin of 'N' in N-TiO<sub>2</sub>-0 is the ammonium carbonate present in TPCC solution.

Textural and microstructural analysis. Figure **S**4 represents the nitrogen adsorption-desorption isotherms and pore size distribution curve of the synthesized N-TiO<sub>2</sub> hollow sphere. The pattern of the nitrogen sorption isotherms of all the samples are almost identical, typically correspond to type IV indicating the microstructure of synthesized N-TiO<sub>2</sub> hollow spheres is mesoporous in nature. The pore size distribution analysis using the BJH method from desorption part of the isotherms of N-TiO<sub>2</sub> hollow sphere indicates the presence of a quite narrow pore size distribution. Here it is essential to mention that the BET surface area of N-TiO<sub>2</sub>-0 is 109 m<sup>2</sup>g<sup>-1</sup> and it was increased gradually with the incorporation of NH<sub>4</sub>OH in the precursor solution which is most probably due to the formation of hollow interior structures. The maximum surface area of 155 m<sup>2</sup>g<sup>-1</sup> was obtained in N-TiO<sub>2</sub>-30. Further enhancement of NH<sub>4</sub>OH the surface area is decreased. The pore size of the samples N-TiO<sub>2</sub>-0 to N-TiO<sub>2</sub>-20 is at around 12 nm, whereas it is 7 nm for N-TiO<sub>2</sub>-30 to N-TiO<sub>2</sub>-50.



Figure 5. UV-Vis absorption and PL spectra of synthesized N-TiO<sub>2</sub>-30, N-TiO<sub>2</sub>-0 and bulk TiO2 (P25).

**DRS and PL analysis**. Figure 5 and Figure S5 represents the UV–Visible diffuse reflectance spectra (DRS) of all the synthesized N-TiO<sub>2</sub> samples along with commercial TiO<sub>2</sub>, P25. A reasonable improvement of the light absorption in the visible region of N-TiO<sub>2</sub> samples compared to that of P25 is observed. Visible light absorption efficiency is increased gradually with the enhancement of doped 'N' in TiO<sub>2</sub>. Corresponding Tauc. plots (inset Figure S5) obtained from the UV-Vis spectra of the synthesized N-TiO<sub>2</sub> samples also evidenced the gradual reduction of band gap with the enhancement of doped N in TiO<sub>2</sub> structure, which is most probably due to the formation of new energy state by doped 'N', closer to that of valence band (VB) of TiO<sub>2</sub>. The nitrogen doping not only increases the visible light absorption, *in-turn* generation of enhanced photo-generated e'/h<sup>+</sup> pair, but also reduce the extent of recombination rate of e'/h<sup>+</sup> pair.

as evidenced by the massive reduction of respective PL peak intensity (inset Figure 5).

#### Catalytic application:

The prime goal of the present work was not only the synthesis of visible light active N-TiO<sub>2</sub> hollow sphere, but also the use of this material as a heterogeneous catalyst for the development of a suitable visible light-induced photocatalytic protocol for the synthesis of active esters of NHI, starting from corresponding alcohol under ambient condition, which has yet to be explored. For optimization of reaction condition, the reaction of 4-chloro benzyl alcohol (1a) and N-hydroxyphthalimide (NHPI) (2a) was chosen as a model reaction and Table 1 & S2 represent the corresponding optimization results. Inspiring from our previous experience for selective oxidation of alcohol to aldehyde, initial reactions were performed using CH<sub>3</sub>CN and benzotrifluoride (BTF) as solvents.<sup>[6]</sup> N-TiO<sub>2</sub>-30 resulted in only 20% ester with a large amount of unreacted alcohol in CH<sub>3</sub>CN solvent under O<sub>2</sub> as sole oxidant (entry 1, Table 1). Whereas, in BTF no ester was identified and mostly corresponding aldehyde was identified (entry 2, Table 1). To understand the origin of the inferior yield, we have performed simple alcohol oxidation and CDC reaction of aldehyde and NHPI to the corresponding ester, separately using BTF and CH<sub>3</sub>CN as the solvent, keeping all



Reaction condition: Unless otherwise specified, all the optimization reactions were carried out with 4-chlorobenz alcohol **1a** (0.4 mmol, 2.0 equiv) and *N*-hydroxyphthalimide **2a** (0.2 mmol, 1.0 equiv), TBHP in dacane, 2 ml solvent, catalyst N-TiO2-30 15 mg, under the irradiation of light from 40W CFL lamp, O<sub>2</sub> baloon, and ambient condition. <sup>[a]</sup> TBHP (70%) in water.

# **FULL PAPER**

other parameters identical (Table S3). It was observed that the rate of alcohol oxidation in CH<sub>3</sub>CN is very slow to that of BTF and ended with 55% and 99% yield of aldehyde in 6 h, respectively. Whereas, for the 2<sup>nd</sup> step of the overall tandem reaction, i.e., CDC reaction, BTF is not a suitable solvent and no desired ester was identified. Whereas, 95% yield of ester was identified in CH<sub>3</sub>CN solvent after 12 h reaction. From the results, it was predicted that due to unavailability of sufficient aldehyde, originating from the slow rate of alcohol oxidation in CH<sub>3</sub>CN solvent, the progress of 2<sup>nd</sup> step, i.e., CDC reaction, was slow and ended with low yield. Generally, the excess aldehyde is required for efficient CDC reaction.<sup>[1-3]</sup> For the enhancement of alcohol oxidation rate different co-oxidant was used. TBHP was found to be the suitable co-oxidant (entry 3-6, Table 1). It was observed that the reaction in CH<sub>3</sub>CN solvent, with 2 equivalent of TBHP in decane and 15 mg of catalyst for 0.4 mmol of 1a (4-chloro benzyl alcohol) and 0.2 mmol of NHPI (2a) provided the best result in 18h (92%, isolated vield). The reaction was repeated in optimized reaction condition with other synthesized N-TiO<sub>2</sub> hollow spheres with varying 'N' doping and it was

Table 2. Scope of the visible-light-induced a reaction of alcohol with NHPI (2a) through visible light induced catalyzed by N-TiO<sub>2</sub>-30.



Alcohol 0.4 mmol; NHPI 0.2 mmol, TBHP 0.8 mmol,  $CH_3CN$  2ml, under  $O_2$  baloon

observed that N-TiO<sub>2</sub>-30 showed much superior activity to that of other synthesized N-TiO<sub>2</sub> samples. No product was identified in N-TiO<sub>2</sub>-0 most probably due to the extreme recombination (entry 17, Table S2). N-TiO<sub>2</sub>-20 showed 40 % yield, originating to that of improved recombination and it was not optimized (entry 18, Table S2). Although N-TiO<sub>2</sub>-50 contain more N, it showed only 35% yield (entry 19, Table S2) most probably due to the low surface area and oxidized nitrogen species may also interface in the progress of the reaction. Reaction has also been performed using N-TiO<sub>2</sub> as well as pure TiO<sub>2</sub> with varying morphology synthesized by literature reported methods (entry 17-32, Table S2). It was observed that the yield of the desired ester for the developed N-TiO<sub>2</sub>-30 hollow sphere is superior. The yield is much superior to that of N-TiO<sub>2</sub> hollow spheres synthesized by literature reported methods.<sup>[16-17]</sup> The catalyst is reusable for at least 4 times without a reasonable reduction of the respective yield (Figure S6).

Next, we extended the substrate scope with various alcohols (aromatic and aliphatic), containing several functional groups. For most of the substrates, the reaction proceeded smoothly with moderate to excellent yield, but some cases it required longer reaction as mentioned in Table 2. Aromatic alcohols, having electron donating or withdrawing group, gave good to excellent vield (up to 92%, 3a-h). However, heteroaromatic and aliphatic alcohols resulted in moderate yield (20-46%, 3i-o). It is noteworthy that cinnamyl alcohol also participated in this reaction with 30% yield (3k). Next, we examined N-hydroxysuccinimide (NHSI, 2b) as substrate instead of NHPI (2a), to our delight the reaction proceeds smoothly with a moderate to good yield (Table 3). The reduction of yield in NHSI to that of NHPT might be due to the high bond dissociation energy of N-OH bond during the generation of the reactive N-O' radical in NHSI (2b) compare to NHPI (2a).<sup>[3]</sup> Upscaling is another issue to demonstrate the utility of the strategy and respective gram scale reaction of 4-chloro benzyl alcohol (1a) and NHPI (2b) resulted in 85 % isolated yield of ester (3a, Table 2).

**Table 3.** Scope of the visible-light-induced a reaction of alcohol with NHPI (2a) through visible light induced catalyzed by N-TiO<sub>2</sub>-30.





The importance of the developed strategy is the synthesis of a wide variety of amides and esters in one-pot with an excellent yield by the simple addition of respective amine or alcohol to the reaction mixture after 18h, i.e., completion of NHPI. A wide range of amides, both primary and secondary, and esters was

## **FULL PAPER**

synthesized with excellent yield in one pot (Scheme 1). Inspiring from the results, we have conducted gram scale synthesis for the important drug "Moclobemide" through the one-pot approach and obtained 80% isolated yield (Scheme 2). From this reaction mixture, we have also recovered the 95% of NHPI, which could be reused for the next reaction. It is noteworthy that the addition



Scheme 1. One pot synthesis of various amides and esters.



Scheme 2. Gram-scale synthesis of moclobemide in one pot.

of amine in the initial stage and use of the catalytic amount of NHPI resulted in a lower yield, although the NHPI remain intact after reaction.

From the above-mentioned results and supporting reactions, a possible reaction mechanism is proposed and presented in Scheme 3. The reactions pass through a radical mechanism. In a representative control reaction of 1a and 2a in the presence of 2,2,6,6- tetramethyl-1-piperidine-1-oxyl (TEMPO) no product was obtained, we have identified the TEMPO trapped radical in mass spectroscopy (Figure S7) and it indicates that reaction may proceed through redical mechanism (Scheme S1). In the proposed visible light-induced reaction, initially photo-excited e-/h<sup>+</sup> pairs is generated in the band structure if N-TiO<sub>2</sub> by the absorption of visible light. Alcohol (1) transformed to the aldehyde (8) by photo-generated e<sup>-</sup>/h<sup>+</sup> pair and in this step TBHP facilitate the electron transfer process through the formation of tert-butoxyl and tert-butylperoxyl radicals. Here the role of TBHP is to accelerate the rate of selective oxidation of alcohol to aldehyde and in a control reaction, the yield of the ester is guite low (65%) in absence of oxygen and even with 4 eq of TBHP (Scheme S2). Simultaneously, NHI (2) transformed into its oxidized radical cation (9) by adsorbing the hole from VB, which



Scheme 3. Proposed reaction mechanism.

from active *N*-oxylimide radical (10) by deprotonation. Then the active *N*-oxylimide radical (10) reacts with aldehyde (8) and form hemiacetal radical (12), which on oxidation resulted in the desired active ester (3). The 2<sup>nd</sup> step, i.e., redical based CDC coupling, is well studied by Tan *et al.* <sup>[1a]</sup> and Dinda *et al.* <sup>[3]</sup>, and our proposed mechanism is in the line of both of the studied work. N-TiO<sub>2</sub>-30 hollow spheres showed much superior activity to that of synthesized other N-TiO<sub>2</sub> hollow spheres as well as reported N-TiO<sub>2</sub> with varying morphology not only due to the enhanced surface area, micro- reactor environment and reduced recombination for light scattering originating from inner hollow structure, but also optimized N doping which enhance the maximum visible light absorption efficiency and reduce recombination.

#### Conclusions

In conclusion, we have demonstrated a novel and efficient protocol for the synthesis of N-TiO<sub>2</sub> hollow sphere with superior visible light absorption efficiency and reduced recombination rate of photo-generated e<sup>-</sup>/h<sup>+</sup> pair. The synthesized N-TiO<sub>2</sub> hollow sphere showed excellent photocatalytic activity for esterification of N-hydroxyimide (NHI) and alcohol through simultaneous selective oxidation of alcohol to aldehyde followed by crossdehydrogenative coupling (CDC) and the catalytic activity is much superior to that of reported N-TiO<sub>2</sub> with varying morphology. The developed strategy also offers a straightforward, energy efficient and atom-efficient process for the one-pot transformation of alcohol to desired amides or esters in gram scale and should be attractive to synthetic chemists. The applicability of the method further showcased by the gram scale synthesis of moclobemide, a drug mainly used for the treatment of depression and social anxiety. The catalyst is reused for 4 times without significant loss of reactivity. The synthesized N-TiO<sub>2</sub> hollow sphere will be useful for the development of a wide range of radical reactions.

### **Experimental Section**

**Generalized synthesis of N-TiO<sub>2</sub> hollow spheres.** In a typical synthetic procedure, to a 30 ml TPCC solution <sup>[18]</sup> (obtained from 0.01 mole, 3ml, titanium isopropoxide), 0-50 ml of 30% NH<sub>4</sub>OH solution was added under constant stirring and final volume of the solution was made up to 90 ml by adding deionized water. Then, 33 ml of this clear solution mixture was transferred to a 50 ml Teflon lined stainless steel autoclave, sealed properly and transferred to a pre-heated electric oven at 120 °C for 18 h. The resultant precipitate was filtered, washed with de-ionized water followed by ethanol and dried in ambient conditions overnight. Finally the dried materials were calcined at 400°C for 2 h.

**Characterizations**. Powder X-ray diffraction patterns were recorded using a Miniflex-II (FD 41521) powder diffractometer (Rigaku, Japan). Morphological determines were performed using JEOL JSM 7100F scanning electron microscope (SEM) and a JEOL JEM 2100 transmission electron microscope (TEM). UV-Vis diffuse reflectance spectra (DRS) were collected on a Shimadzu UV-2550 spectrophotometer. Raman spectra were recorded using a Raman spectrometer (NICOLET ALMECA XR) with a 532 nm laser beam. ESCALAB 250 XPS System with a monochromatic Al K $\alpha$  (150 W) source was used to record the X-ray photoelectron spectra (XPS). PL recorded on a Horiba Jobin spectrophotometer. For sectioning the hollow sphere through microtomy on LEICA EM UC6, the synthesized hollow spheres were embedded in spurr resin and polymerized by heating at 80 °C for 12 h in air oven.

General synthetic procedure for the synthesis of N-hydroxyimide esters from N-hydroxyimide (NHI) and alcohol under visible light. In a typical procedure, 0.2 mmol NHI, 0.4 mmol alcohol, 2 mL acetonitrile (solvent) and 0.8 mmol TBHP were taken in a 15 mL reaction tube. The reaction tube was sealed by a septum and filled with oxygen ballon and then, transferred to a photocatalytic reaction chamber. The reaction mixture was irradiated by 40W CFL lamp under constant stirring from 18-24h. After completion of the reaction, the catalyst was separated by filtration, and the organic layer was diluted with ethyl acetate and washed with water. The organic part was dried over  $Na_2SO_4$  and evaporated under reduced pressure. The crude product was purified by column chromatography by using an eluent mixture of EtOAC: Hexane.

#### General procedure for one pot the synthesis of amide and ester:

After 18h reaction of NHI and alcohol under visible light, the light was switch-off, 3.0 equivalent amine or alcohol was added in the reaction mixture and stirring was continued for another 2h. After completion of the reaction, the reaction mixture was poured into H<sub>2</sub>O (20 ml) and extracted with ethyl acetate (3×20 ml). The combined organic layer was washed with brine (30 ml) and dried over Na<sub>2</sub>SO<sub>4</sub>. The solvent was removed under reduced pressure, and the crude reaction mixture was purified by flash column chromatography using hexane /ethyl acetate as an eluent to isolate the desired product. The NHI was also recovered for re-use.

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**Keywords:** Nitrogen-doped TiO<sub>2</sub> • hollow spheres • active ester • N-hydroxyimide • photocatalysis

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## **Table of Contents**

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A simple synthetic protocol for yellow N-TiO<sub>2</sub> hollow sphere, capable of visible light induced photocatalytic esterification of Nhydroxyimide and alcohol to corresponding active ester through simultaneous selective oxidation of alcohol to aldehyde followed by CDC reaction, is developed.



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#### Page No. – Page No.

N-doped Yellow TiO<sub>2</sub> hollow sphere mediated visible light driven efficient esterification of alcohol and N-Hydroxyimides to active esters