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catalyst to one-pot solvent-free synthesis of propargylamines† Digambar B. Bankar,^{ab} Ranjit R. Hawaldar,^a Sudhir S. Arbuj, [®] Mansur H. Moulavi,^a

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ZnCl₂ loaded TiO₂ nanomaterial: an efficient green

One-pot green synthesis of propargylamines using ZnCl₂ loaded TiO₂ nanomaterial under solvent-free conditions has been effectively accomplished. The aromatic aldehydes, amines, and phenylacetylene were reacted at 100 °C in the presence of the resultant catalyst to form propargylamines. The nanocrystalline TiO₂ was initially synthesized by a sol-gel method from titanium(w) isopropoxide (TTIP) and further subjected to ZnCl₂ loading by a wet impregnation method. X-ray diffraction (XRD) patterns revealed the formation of crystalline anatase phase TiO₂. Field emission scanning electron microscopy (FESEM) showed the formation of agglomerated spheroid shaped particles having a size in the range of 25-45 nm. Transmission electron microscopy (TEM) validates cubical faceted and nanospheroid-like morphological features with clear faceted edges for the pure TiO₂ sample. Surface loading of ZnCl₂ on spheroid TiO₂ nanoparticles is evident in the case of the ZnCl₂ loaded TiO₂ sample. X-ray photoelectron spectroscopy (XPS) confirmed the presence of Ti⁴⁺ and Zn²⁺ species in the ZnCl₂ loaded TiO₂ catalyst. Energy-dispersive X-ray (EDS) spectroscopy also confirmed the existence of Ti, O, Zn and Cl elements in the nanostructured catalyst. 15% ZnCl₂ loaded TiO₂ afforded the highest 97% yield for 3-(1-morpholino-3-phenylprop-2-ynyl)phenol, 2-(1-morpholino-3-phenylprop-2-ynyl)phenol and 4-(1,3-diphenylprop-2ynyl)morpholine under solvent-free and aerobic conditions. The proposed nanostructure-based heterogeneous catalytic reaction protocol is sustainable, environment-friendly and offers economic viability in terms of recyclability of the catalyst.

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1. Introduction

Organic reactions involving three or more components are becoming increasingly important day by day since they allow many starting materials to be combined easily in one-pot forming a single compound.¹ One-pot, multi-component carbon-carbon and carbon-nitrogen bond forming reactions were successfully accomplished for producing molecular complexity.² Three-component coupling of aldehyde, amine, and alkyne is one of the most extensively used methods for the preparation of several propargylamines through C-H bond activation.³ Propargylamine derivatives play a significant role in synthetic organic chemistry by acting as a versatile intermediate for the synthesis of many biologically active heterocyclic compounds such as 2-aminoimidazoles,⁴ pyrrolidines,⁵ pyrroles,⁶ phenanthrolines,⁷ oxazolidinones,⁸ aminoindolizines,⁹ *etc.* Moreover, they are the important structural ingredients of therapeutic drug molecules and also of natural products.¹⁰ For example, rasagiline containing Azilect as a moiety of propargylamine has been used for the symptomatic therapy in early Parkinson's disease.^{11–13} Also, propargylamines are essential intermediates for the preparation of PF960IN as a biologically active drug molecule.¹⁴

The literature survey reveals that the synthesis of propargylamines *via* classical routes involves the addition of alkynylmetal reagents to the imines^{15,16} in the separate step. However, the addition of moisture sensitive Grignard or Li acetylides reagent is tedious. Through direct amination of propargylic electrophiles like propargyl halides, triflates and phosphates,¹⁷ the formation of propargylamine derivatives also has been achieved.

In the last few decades, enormous progress has been made for the C-H bond activation of terminal alkynes. A variety of

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homogeneous transition metallic systems such as Cu(1) salts,¹⁸ Ag(1) salts,¹⁹ ZnMe₂,²⁰ Fe(m) salts,²¹ Cu(1) salts,²² Zr complex,²³ Ni(π) salts,²⁴ InCl₃,²⁵ Ir complex²⁶ and AgOAc²⁷ were used for the C-H bond activation of terminal alkynes. Researchers also used Cu-Ru bimetallic system,²⁸ InBr₃,²⁹ Co(π)³⁰ and Au(π) salen complexes³¹ as a homogeneous catalytic system for the activation of C-H bond of the terminal alkynes. However, some of these catalytic systems have certain limitations due to the use of expensive and excess amount of catalyst, toxic solvents, and the requirement of inert atmospheric conditions.

Diverse heterogeneous catalysts such as layered double hydroxide-supported gold (LDH-AuCl₄) catalyst,³² polystyrenesupported NHC-Ag(I) catalyst,³³ Fe₃O₄ nanoparticles,³⁴ Ag nanoparticles/Ni metal-organic framework,35 copper(1) anchored onto MCM-41 silica,³⁶ Fe₃O₄(a)SBA-15 (ref. 37) etc. were used for the synthesis of propargylamines. Nanoscale metal oxides such as ZnO³⁸ and In₂O₃ (ref. 39) were also used for the synthesis of propargylamines. Further, copper ferrite nanoparticles,40 Ni-Y zeolites,41 nanosize Co3O4,42 Cu nanoparticles on TiO2,43 Au nanoparticles supported on ionic liquid,44 Au nanoparticles supported on polyacrylamide,45 Zn(II)/HAP/Fe₃O₄,⁴⁶ Zn(L-proline)₂,⁴⁷ etc. were used as heterogeneous catalysts for the three component synthesis of propargylamines. Besides, a super paramagnetic MCM-41 with dendrites copper complex⁴⁸ was utilized as a recyclable catalyst for the propargylamine synthesis. Nonetheless, there are disadvantages to some of such catalytic systems viz. requirement of high catalyst amount, use of inert gas, use of solvent, longer reaction time, etc. Hence, there is a need to find a simple and efficient method for the synthesis of propargylamines.

In the context of heterogeneous catalysis, nanocrystalline materials can play significant role due to their large surface to volume ratio, easy separation and desirable physico-chemical characteristics.⁴⁹ Specifically, nanocrystalline TiO₂ is one of the most important materials extending widespread applications in pigments, catalytic systems, inorganic membranes, gas sensors, support ceramics,⁵⁰ etc. Also, non-toxic nature and low cost of TiO₂ nano-particulate system made it a better catalyst. The TiO₂ supported with transition metals brings the advantage of heterogeneous catalysis in the propargylamine synthesis. Fe doped TiO₂ nanoparticles are used as a heterogeneous catalyst for the activation of C-H bond of terminal alkynes under microwave irradiation.⁵¹ Recently, Ag/TiO₂ and Pt/TiO₂ nanocatalyst have been applied as active recyclable catalysts for the synthesis of propargylamines under microwave irradiation at 140 °C.52

Effective use of zinc salts⁵³ for the propargylamine synthesis motivated us to perform one-pot synthesis of propargylamine using ZnCl₂ loaded TiO₂ nanomaterial.

In this report, we have demonstrated a synthetic strategy in which inexpensive and commercially available $ZnCl_2$ is loaded by wet impregnation technique on sol–gel generated TiO_2 nanoparticles. The as-synthesized nanocrystalline $ZnCl_2$ loaded TiO_2 has been used as an efficient and green heterogeneous catalyst for the synthesis of propargylamines under solvent-free and aerobic conditions.

2. Experimental

2.1. General

All the chemicals were AR grade and purchased from a local dealer. The chemicals were used as received without further purification. The progress of reaction was monitored by thin layer chromatography (TLC) technique. The crystal structure of the synthesized catalyst was detected by XRD using a Rigaku MiniFlex-600 diffractometer (Cu K α radiation, $\lambda = 1.5406$ Å). The surface morphology and particle size were examined using field emission scanning electron microscope (Hitachi S-4800). Elemental compositions were determined by energy-dispersive X-ray spectroscopy (EDS) analysis. For fine-scale nanostructural evaluation, field emission transmission electron microscopic (FETEM) images of the typical sample were obtained using the JEOL JEM-2200 FS instrument. The same instrument was also used for obtaining the Energy Dispersive Spectroscopy (EDS) and allied elemental mapping information using scanning transmission electron microscopy (STEM) in bright field mode. For the confirmation of chemical composition, X-ray photoelectron spectroscopic (XPS) scans were recorded using Al Ka (Monochromatic) anode with 6 mA beam current and 12 kV X-ray source. The as-synthesized propargylamine derivatives were spectrally characterized by Nuclear Magnetic Resonance (NMR) spectroscopy and High-Resolution Mass Spectrometry (HRMS) techniques. ¹H and ¹³C NMR spectra were recorded using CDCl₃ and DMSO-d₆ solvents on 500 and 125 MHz Bruker NMR spectrometer, respectively. The HRMS was taken in methanol solvent using high-resolution mass spectrometer (Bruker Germany, Model: Impact HD, UHR Impact II ESI-Q-TOF). All yields refer to the isolated products after purification by column chromatography with ethyl acetate and *n*-hexane as an eluent.

2.2. Synthesis of TiO₂ nanoparticles

Synthesis of TiO₂ nanoparticles was performed by sol-gel method using titanium(w) isopropoxide as a titanium precursor. Initially, 80 ml of glacial acetic acid was added dropwise to a 40 ml of titanium(w) isopropoxide (TTIP) in a 500 ml round bottom flask immersed in an ice bath with constant stirring. Later, 100 ml isopropyl alcohol was gradually added with vigorous stirring for a period of 30 min at room temperature. In the resulting solution, 10 g polyvinyl alcohol (PVA) in 50 ml isopropyl alcohol was added, stirred for 10 min and subsequently, 10 ml of 1 M HCl was added and the resultant solution was subjected to constant stirring at room temperature for 4 h. For natural gel formation, the obtained mixture was transferred into 500 ml beaker and kept for 5 days. Finally, the gel was dried at 110 °C for 12 h, transferred into a mortar, powdered with pestle and further calcined in a muffle furnace at 400 °C for 4 h.

2.3. Synthesis of $ZnCl_2$ loaded TiO_2 nanomaterial ($ZnCl_2$ -TiO₂ catalyst)

Loading of 15 wt% $ZnCl_2$ over TiO_2 nanoparticles was performed by wet impregnation technique. A mixture of $ZnCl_2$ (0.3

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g) and TiO₂ nanoparticles (2.0 g) was grinded for 10 min and subsequently transferred into the 250 ml round bottom flask containing 50 ml ethanol. Further, it was stirred at room temperature for 1 h and then refluxed for 4 h with persistent stirring. The excess ethanol was concentrated under vacuum distillation and obtained solid material was dried at 200 °C for 6 h. The same procedure was repeated for the loading of 5 wt%, 10 wt% and 20 wt% ZnCl₂ over TiO₂ nanoparticles.

2.4. General procedure for the synthesis of propargylamine derivatives

In a typical procedure, aromatic aldehyde (1 mmol), secondary amine (1.2 mmol) and phenylacetylene (1.5 mmol) were taken in a clean and oven-dried round bottom flask. The nanocrystalline ZnCl₂-TiO₂ catalyst (0.2 mmol) was added into the round bottom flask and the resulting reaction mixture was placed in pre-heated oil bath at 100 °C and stirred at the same temperature for 6 h. Progress of the reaction was checked by thin layer chromatography (TLC). After cooling, ethyl acetate was added to the reaction mass and stirred at room temperature for 15 min. Ethyl acetate layer was separated by filtration and again remaining reaction residue was washed with ethyl acetate. Combined ethyl acetate washings were mixed with water. The organic layer was separated by extraction, dried over anhydrous Na2SO4 and filtered. The organic solvent was concentrated under reduced pressure and obtained crude residue was purified by column chromatography to yield the propargylamine derivative. The pure organic desired compounds were characterized by ¹H NMR, ¹³C NMR, and HRMS spectral techniques (please see ESI[†]).

3. Results and discussion

3.1. Catalyst characterization

3.1.1. XRD analysis. Fig. 1 depicts the XRD patterns of pure TiO₂ and ZnCl₂-TiO₂ nanostructures. The characteristic peaks with 2θ values at 25.26°, 37.70°, 48.07°, 53.86°, 55.00°, 62.68°, 68.76°, 70.26° and 75.06° can be indexed as (101), (004), (200), (105), (211), (204), (116), (220) and (215) planes corresponding to anatase polymorph of TiO_2 (Fig. 1a). The angular positions and relative intensities of all the diffraction peaks are in close concurrence with the JCPDS card no. 21-1272 for anatase phase of TiO2. The XRD peak patterns corresponding to 5%, 10%, 15% and 20% ZnCl₂ loaded TiO₂ samples also exhibit formation of anatase phase of TiO₂ (Fig. 1b-e). Furthermore, no additional peaks other than those matching with the crystalline anatase TiO₂ were found in the XRD, indicating the phase purity of the synthesized materials. It has been observed that 2θ values are slightly shifted to higher values for ZnCl₂ loaded TiO₂ samples in comparison to pure TiO₂ implying successful loading of $ZnCl_2$ over TiO₂ surface as shown in inset of Fig. 1 for (101) plane. The 2θ values of (101) plane for pure TiO₂, 5% and 10% ZnCl₂-TiO₂ samples are almost the same (around 25.26°, 25.28° and 25.26°, respectively). For higher loading i.e. 15% and 20% $ZnCl_2$ -TiO₂, the 2 θ values of (101) plane are observed to be around 25.42° and 25.44°, respectively. The XRD peaks due to



Fig. 1 XRD patterns of (a) pure TiO₂, (b) 5% ZnCl₂-TiO₂, (c) 10% ZnCl₂-TiO₂, (d) 15% ZnCl₂-TiO₂ and (e) 20% ZnCl₂-TiO₂. Inset is enlarged view of (101) plane.

zinc species could not be observed, as expected, due to low concentration and highly uniform dispersion of Zn species over the nanocrystalline TiO₂.⁵⁴

The crystallite size of all as-synthesized samples was calculated by Scherrer's equation using broadening of (101) anatase peak of TiO₂. The crystallite size of unloaded TiO₂ is 16 nm, whereas 5%, 10%, 15% and 20% ZnCl₂ loaded TiO₂ showed crystallite size values of 16, 15, 13 and 14 nm respectively. It may be, however, noted that there is no prominent change in the overall crystallite size of all the samples under investigation. The miniscule decrease in crystallite size of ZnCl₂–TiO₂ in comparison to pure TiO₂ as well as the marginal shift in 2 θ value of (101) plane with increasing loading percentage of ZnCl₂ on TiO₂ nanoparticles can be ascribed to the effective surface coating of ZnCl₂ over TiO₂ and/or might be due to partial incorporation of Zn species in the crystalline lattice of TiO₂.

3.1.2. FESEM analysis. The surface morphology of the pure TiO_2 and $15\% ZnCl_2$ - TiO_2 was investigated by FESEM analysis and images are shown in the Fig. 2. Pure TiO_2 sample displays the formation of homogeneously distributed spheroidal shaped particles having size in the range of 15–30 nm (Fig. 2a and b). In case of $15\% ZnCl_2$ - TiO_2 sample (Fig. 2c and d), almost same morphology is observed with increased particle size (25–45 nm) as compared to pure TiO_2 due to agglomeration of particles and surface coating/loading of TiO_2 nanoparticles by $ZnCl_2$.

3.1.3. FETEM analysis. Fig. 3 displays FETEM images corresponding to pure TiO_2 and 15% ZnCl₂ loaded TiO_2 nanomaterials. Low and intermediate magnification FETEM images (Fig. 3a and b) show cubical faceted and spheroid-like morphological features with clear faceted edges for pure TiO_2 sample. Occasionally, nanorods like features are also seen. Surface coating/loading of spheroid particles of TiO_2 by ZnCl₂ is visible in case of ZnCl₂ loaded TiO_2 sample when compared



Fig. 2 FESEM images of (a and b) Pure TiO_2 and (c and d) 15% $\text{ZnCl}_2-\text{TiO}_2.$

with pure TiO₂ sample. The average particle size for TiO₂ and ZnCl₂-TiO₂ was found to be in the range of 15-35 nm. The lattice fringes with inter-planar spacing (d) of 0.365 nm (Fig. 3c) and 0.369 nm (Fig. 3g), respectively, for pure and ZnCl₂-TiO₂ samples corresponding to (101) plane of anatase TiO₂ are seen.⁵⁵ The lattice fringes corresponding to (105), (103), (004), (200), etc. planes are also noticed in case of both the samples which is an indication of polycrystalline nature of the samples. The selected area electron diffraction (SAED) patterns as shown in Fig. 3(d and h) evince nanocrystalline behaviour of the samples showing presence of ring like patterns, however, such rings are not continuous but are dominated by the regular bright spots.⁵⁶ SAED patterns confirm anatase phase TiO₂ in case of both the samples when compared with XRD diffractograms and allied database (Fig. 1). The overall FETEM study revealed formation of nanoscale spheroids exhibiting nanocrystalline nature.

3.1.4. FETEM-STEM-EDS analysis of \text{ZnCl}_2-TiO₂ catalyst. The energy dispersive X-ray spectroscopy (EDS) analysis was used for the confirmation and quantification of presence of elements in the given sample in STEM mode. In our investigation, weight by weight amount of ZnCl_2 and TiO_2 were used in the wet impregnation method. For TEM-EDS elemental composition analysis, we considered 15% ZnCl_2 -TiO₂ sample and the relevant spectrum with quantitative data (in tabular form) is reproduced in Fig. 4.

The EDS spectrum discloses that the 15% ZnCl₂–TiO₂ catalyst contains 33.36 wt% of oxygen, 6.08 wt% of chlorine, 43.29 wt% of titanium and 17.27 wt% of Zn, even though the XRD pattern did not show any Zn peaks. Thus, EDS spectrum revealed that the sample is composed of Ti, O, Zn, and Cl which is in good agreement with results obtained by XPS (Fig. 6).

The EDS-elemental mapping images of 15% ZnCl₂-TiO₂ sample in scanning transmission electron microscopy (STEM) mode are shown in Fig. 5.

The elemental mapping images due to Ti and O (Fig. 5b and c, respectively) overlap well with corresponding electron image (Fig. 5a). The intensity of the colours assigned to Ti and O is also



Fig. 3 TEM images: (a and b) pure TiO₂, (e and f) 15% ZnCl₂-TiO₂. HRTEM images: (c) TiO₂, (g) 15% ZnCl₂-TiO₂. (d and h) are the corresponding SAED patterns of TiO₂ and 15% ZnCl₂-TiO₂.

very high. The elemental mapping images for Zn and Cl (Fig. 5d and e, respectively) also overlap with the corresponding electron image, however, the intensity of the colours ascribable to these



Fig. 4 TEM-EDS spectrum exhibiting quantitative elemental composition data for nanostructured 15% ZnCl₂-TiO₂.



Fig. 5 FETEM-STEM-EDS elemental mapping images of 15% ZnCl₂-TiO₂ catalyst: (a) Electron image (b) Ti, (c) O, (d) Zn and (e) Cl.

two elements is low which is quite obvious as ZnCl_2 is used only for the purpose of surface loading. FETEM images correspond well with FESEM images and endorse the surface loading of ZnCl₂ over TiO₂ nanoparticles.

3.1.5. XPS analysis. XPS scans of the nanostructured ZnCl_2 -TiO₂ were acquired to determine the elemental composition and the electronic state of the Ti, O, Zn and Cl elements. Fig. 6 shows the high resolution XPS scans corresponding to 15% ZnCl_2 -TiO₂ sample. The binding energies were corrected with respect to the peak for adventitious C 1s at 284.8 eV. High resolution scans of core level Ti 2p, Zn 2p and Cl 2p exhibit symmetrical single peaks, while core level O 1s exhibits asymmetry due to ensemble of two peaks as noticed in its deconvolution spectrum.

The Ti binding energy peaks observed at 458.72 and 464.35 eV are related to Ti $2p_{3/2}$ and Ti $2p_{1/2}$, in close resemblance with that of Ti⁴⁺ in TiO₂.⁵⁷ The two O 1s peaks (inset of



Fig. 6 High resolution XPS scans of the respective elements corresponding to 15% ZnCl₂-TiO₂ sample. The inset of (b) displays deconvoluted spectrum.

Fig. 6b) can be assigned to lattice oxygen (O–Ti) at 529.80 eV and surface-bound hydroxyl group (Ti–OH) at 531.78 eV. The binding energy peaks at 1022.20 eV and 1045.20 eV can be associated with Zn $2p_{3/2}$ and Zn $2p_{1/2}$ energy states, respectively (Fig. 6c). The peak at 1022.20 eV could be assigned to Zn²⁺ species in ZnO (1021.9 eV),⁵⁸ ZnCl₂ (1022.5 eV)⁵⁹ or Zn(OH)₂ (1022.6).⁶⁰ Subsequently, we studied the chloride XPS peak (Fig. 6d) to detect the presence of Zn²⁺ species among the ZnO, ZnCl₂ or Zn(OH)₂. The binding energy at 199.59 eV signifies the Cl $2p_{3/2}$ energy state of metal chloride. It apparently confirms the presence of ZnCl₂ (ref. 61) confined to surface in the ZnCl₂–TiO₂ catalyst (since XPS is surface sensitive technique).

The overall appearance of peaks in XPS scans demonstrates the successful loading of $ZnCl_2$ on the surface of TiO_2 nanoparticles.

3.2. Catalytic activity of ZnCl₂ loaded TiO₂ nanomaterial

After successful synthesis and characterization of $\text{ZnCl}_2-\text{TiO}_2$ catalysts, it is employed as heterogeneous catalyst in multicomponent synthesis of propargylamine. To optimize the reaction conditions, several parameters such as catalyst, temperature and time were studied and corresponding results are summarized in Table 1. To achieve sustainable green chemistry approach, prior reaction was set under solvent-free and aerobic conditions. In the initial optimizations, 3-hydrox-ybenzaldehyde, morpholine, and phenylacetylene were used as substrates for the model reaction (Scheme 1).

When the reaction was performed at 30 °C in the presence of commercial ZnCl_2 , no product formation was observed even after 6 h (Table 1, entry 1). However, when the reaction was carried out at 70 °C, low yield of product was obtained in 6 h (Table 1, entry 2). In addition, an increase in yield (76%) was observed as the temperature was raised to 100 °C (Table 1, entry 3). This indicates that the temperature plays an important role in this reaction. The lower yield using commercial ZnCl₂ can be due to its hygroscopic

Table 1Optimization of catalyst, temperature and time for modelreactionbetween3-hydroxybenzaldehyde,morpholinephenylacetylene^a

Entry	Catalvet	Temp (°C)	Time (h)	Vield ^b (%)
Entry	Catalyst	Temp. (C)	Time (II)	Tield (70)
1	$ZnCl_2$	30 °C	6.0	_
2	$ZnCl_2$	70 °C	6.0	53
3	$ZnCl_2$	100 °C	6.0	76
4	Pure TiO ₂	100 °C	6.0	38
5	5% ZnCl ₂ -TiO ₂	100 °C	6.0	76
6	10% ZnCl ₂ -TiO ₂	100 °C	3.0	57
7	10% ZnCl ₂ -TiO ₂	100 °C	6.0	86
8	15% ZnCl ₂ -TiO ₂	30 °C	6.0	_
9	15% ZnCl ₂ -TiO ₂	70 °C	6.0	74
10	15% ZnCl ₂ -TiO ₂	100 °C	3.0	68
11	15% ZnCl ₂ -TiO ₂	100 °C	6.0	97
12	20% ZnCl ₂ -TiO ₂	100 °C	6.0	97

^{*a*} Reaction conditions: 3-hydroxybenzaldehyde (1 mmol), morpholine (1.2 mmol), phenylacetylene (1.5 mmol), catalyst (0.2 mmol), temp., time, solvent-free condition. ^{*b*} Isolated yield.



nature. We also performed the reaction using pure TiO_2 , but observed only 38% yield (Table 1, entry 4).

Subsequently, the catalytic activities of 5%, 10%, 15% and 20% ZnCl₂ loaded TiO₂ nanoparticles (nanocrystalline ZnCl₂-TiO₂ catalysts) were examined. For 5% and 10% ZnCl₂ supported TiO₂ catalysts, yields of 76% and 86%, respectively, were obtained (Table 1, entries 5 and 7). This means that as the loading of ZnCl₂ on TiO₂ increases, an increase in product yield is observed under a constant mmol of catalyst (0.2 mmol). Therefore, we studied the reaction with 15% ZnCl₂ loaded TiO₂. No product formation was detected at 30 °C using 15% ZnCl₂ loaded TiO₂ catalyst (Table 1, entry 8), 74% yield obtained at 70 °C in 6 h (Table 1, entry 9), 68% yield obtained at 100 °C in 3 h (Table 1, entry 10). However, when the reaction was performed at 100 °C for 6 h, 97% yield of the desired product was observed (Table 1, entry 11). 15% ZnCl₂ loading over TiO₂ was necessary as the optimum amount of ZnCl₂ loading and increasing the loading of ZnCl₂ (20%) did not improve the yield (Table 1, entry 12).

It is clearly noticed that the nanostructured ZnCl_2 -TiO₂ system exhibits excellent catalytic activity after loading ZnCl_2 over TiO₂ nanoparticles. The excellent catalytic activity of the nanostructured ZnCl_2 -TiO₂ can be attributed to the greater degree of crystallinity at nanoscale.

It is very interesting to see the effect of solvents on catalytic activity of 15% ZnCl₂-TiO₂ catalyst. Therefore, we investigated the role of various solvents such as toluene, CH₃CN, DMF, THF, and H₂O.

From Table 2, is very clear that catalyst exhibits poor activity in polar solvents (CH_3CN , DMF, H_2O and THF). Non-polar solvent (toluene) shows good catalytic activity, while under solvent-free conditions, catalyst shows excellent catalytic activity. The reason for lowering the yield of propargylamine and hence catalytic activity lies in solvation of reactants and

Table 2	e 2 Solvent study for model reaction ^a		
Entry	Solvent	$\operatorname{Yield}^{b}(\%)$	
1	Toluene	76	
2	CH_3CN	68	
3	DMF	40	
4	H ₂ O	36	
5	Solvent-free	97	
6	THF	44	

^{*a*} Reaction conditions: 3-hydroxybenzaldehyde (1 mmol), morpholine (1.2 mmol), phenylacetylene (1.5 mmol), ZnCl₂–TiO₂ (0.2 mmol), 100 °C, 6.0 h, solvent. ^{*b*} Isolated yield.

catalyst. In solvent, reactants are dispersed so it delays the contact with the catalyst. Under solvent-free conditions, reactants and catalyst can quickly come in intimate contact with each other which, in turn, can accelerate the reaction on the surface of the catalyst. Thus, best results could be observed for 15% ZnCl₂ loaded TiO₂ nanoparticle catalyst with 97% yield under solvent-free conditions.

After optimization of the reaction parameters, we have extended the scope of reaction to the different aromatic aldehydes, cyclic secondary amines (pyrrolidine and morpholine), and phenylacetylene using 15% ZnCl₂-TiO₂ (Scheme 2 and Table 3, entries 1–12).

The results in Table 3 indicate that the aromatic aldehydes with electron-donating and halogen substituents showed high reactivity and produced the corresponding propargylamines in better yields. Aryl aldehydes with a hydroxyl group at meta or ortho positions (Table 3, entries 1, 4 and 5), afforded excellent yields as compared to aldehydes having methoxy group at para position (Table 3, entries 2 and 3). The reactivity of 2-chloro and 4-chlorobenzaldehydes (Table 3, entries 9-11) was found to be slightly more than 4-flourobenzaldehyde (Table 3, entry 8) and 4-bromobenzaldehyde (Table 3, entry 12). Benzaldehyde afforded the coupling products in excellent yield (Table 3, entries 6 and 7). We observed slightly higher yields of the products using morpholine as compared to pyrrolidine. Thus, 15% ZnCl₂-TiO₂ catalyst worked as an efficient catalyst for the synthesis of propargylamines under solventfree conditions. It may be noted that, the as-synthesized propargylamines are all chiral compounds and spectral data of all products confirmed that they are single compounds and not mixture of isomers.

The reusability of the $ZnCl_2$ -TiO₂ catalyst was also examined for the reaction between 3-hydroxybenzaldehyde, morpholine, and phenylacetylene under the optimized reaction conditions (Table 3, entry 1). After the first run, the solid catalyst was separated from the reaction mixture by filtration, washed with the ethyl acetate and dried at 120 °C for 4 h. The dried catalyst was then subjected to the next run of the reaction under optimized conditions and afforded 94% yield. Similar procedure was followed for next runs. The relevant results are presented in Table 4. As can be seen, the catalyst could be recycled for five successive runs without significant loss of catalytic activity.

The recycled ZnCl_2 -TiO₂ catalyst was further characterized by XRD which confirms retention of anatase phase of TiO₂ (Fig. S1, ESI[†]). It is, thus, noted that the crystal structure of the



Scheme 2 General reaction for propargylamine synthesis.

Table 3Propargylamine synthesis by three-component coupling of
aromatic aldehyde, secondary amines and phenylacetylene catalysed
by $ZnCl_2-TiO_2 NPs^a$



Table 3 (Contd.)



 a Reaction conditions: aromatic aldehyde (1 mmol), amine (1.2 mmol), phenylacetylene (1.5 mmol), ZnCl₂–TiO₂ (0.2 mmol), 100 °C, 6.0 h, solvent-free condition. b Isolated yield.

recovered catalyst has not changed. The sharp peaks signify that the nature of recovered catalyst is crystalline.

The transition metals are generally used to activate the C-H bond of terminal alkynes in carbon-carbon coupling reactions. The transition metal supported on solid support such as TiO₂ nanoparticles might bring the advantage of heterogeneous catalysis in C-C bond forming reactions.⁵¹ In the proposed reaction, the ZnCl₂ loaded TiO₂ nanomaterial (ZnCl₂-TiO₂) can also lead to activation of C-H bond of terminal alkyne. A tentative mechanism for the one-pot propargylamine synthesis under solvent-free condition using ZnCl₂ loaded TiO₂ nanomaterial is pictorially demonstrated in Scheme 3. The reaction initially involves activation of C-H bond of phenylacetylene (3) by ZnCl₂ from the nanostructured ZnCl₂-TiO₂ catalyst. The generated phenylacetylide-ZnCl₂-TiO₂ intermediate (a) is then reacted with iminium ion (b) (which is produced *in situ* from aldehyde 1 and amine 2) in order to offer the desired product of propargylamine 4. Here, ZnCl₂ in the ZnCl₂-TiO₂ nanomaterial is the main species to activate the C-H bond of terminal alkynes and anatase TiO₂ provides solid support for ZnCl₂. Due to their synergistic effect, nanostructured ZnCl₂-TiO₂ can work as an efficient heterogeneous catalyst for the synthesis of propargylamines.

Table 4 Recyclability study of ZnCl₂-TiO₂^a

Run	$\mathrm{Yield}^{b}\left(\%\right)$
1	97
2	94
3	90
4	88
5	84

^{*a*} Reaction conditions: 3-hydroxybenzaldehyde (1 mmol), morpholine (1.2 mmol), phenylacetylene (1.5 mmol), recycled ZnCl₂-TiO₂ catalyst, 100 °C, 6.0 h, solvent-free. ^{*b*} Isolated yield.



Scheme 3 A tentative mechanism for the synthesis of propargylamine catalysed by $ZnCl_2-TiO_2$ nanoparticles (NPs).

4. Conclusion

We have reported a simple and efficient route for the synthesis of propargylamine using small amount of nanocrystalline $ZnCl_2$ -TiO₂ as a heterogeneous catalyst. The role of catalyst is significantly observed for alkyne C-H bond activation. The reported technique is solvent-free and required mild reaction conditions. The synthesized 15% $ZnCl_2$ loaded TiO₂ nanomaterial was found to be an excellent catalyst for the synthesis of diverse propargylamine derivatives. We believe that our present protocol is eco-friendly for green approach and can become an alternative to conventional homogeneous catalysis for the synthesis of propargylamine.

Conflicts of interest

There are no conflicts to declare.

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