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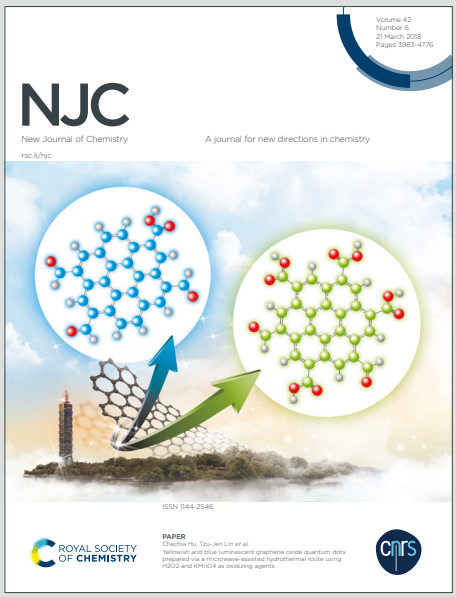

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DOI: 10.1039/D0NJ01674H

ARTICLE

Ru–g-C_3N_4 as highly active heterogeneous catalyst for transfer hydrogenation of α–keto amide into β–aminol or α–hydroxyl amide

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

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This work reports a sustainable route for the catalytic transfer hydrogenation (CTH) of α–keto amide into β–aminol *via* an efficient heterogeneous catalyst wherein ruthenium incorporated on active graphite sheet of carbon nitride support (Ru-g-C_3N_4). Different other metal like Ni and Pd also has been screened with same support but none of them shows efficient activity. Although partial hydrogenation of ketone to alcohol also have been observed based on optimization of reaction parameter using all the above catalyst. Catalyst has been characterized using field emission gun scanning electron microscopy (FEG-SEM), X-Ray diffraction (XRD), X-Ray Photoelectron Spectroscopy (XPS), Infra-Red (IR) Spectroscopy and Thermogravimetric analysis (TGA). Furthermore, catalyst has been recycled and it is further characterized which doesn't show any significant changes in its reactivity for CTH process. Ru-g-C_3N_4 as a recyclable heterogenous catalyst has been used first time for CTH of α–keto amide into β–aminol making the process sustainable because of economical and environmentally benign isopropyl alcohol as a solvent system. Proposed catalytic system shows wide range of substrate scope for α-hydroxyamide and β–aminol derivatives which are confirmed from ^{1}H & ^{13}C-NMR.

Introduction

β–aminol and α–hydroxyl amide, are very important moieties which are used in pharma industry, as it has reactive centre and versatile intermediates for the synthesis of natural originated biological active compounds.[1] β–aminol shows high activity as β-blockers, chiral axillaries and also act as insecticidal agents. [2] Similarly α–hydroxyl amide behaves as ligands and shows several biological activities like anticonvulsant action, antimycobacterial and in antibacterial drugs.[3] Synthesis of both the products can be achieved by chemo-selective reduction or hydrogenation of α–keto amide, but complete reduction or hydrogenation of ketone as well as amide in α–keto amide is quite difficult. Govindsamy and co-workers reported the selective reduction of α–keto amide into α–hydroxyl amide using Pd metals in presence of silane as reducing agent, dissolved in THF solvent[4a]. Same group also reported the use of K_3PO_4 as catalyst in silane dissolved in 1,4-dioxane solvent[4b] even with Cs_2CO_3 as catalyst in presence of silane as reducing agent in presence of solvent 2-MeTHF[4c] for the synthesis of α–hydroxyl amide. However, all these systems involve hazardous, non-recyclable inorganic bases and catalyst, along with use of silane, all the mentioned protocol limits with work-up issue. Recently Wu and co-workers showed some interesting results for the synthesis of α–hydroxyl amide by the use of NaOH, DMF (dimethyl formamide) in H_2O under argon pressure at 120 ^oC.[4d] However they are unable to prepare β–aminol by the same protocol. Selective hydrogenation or reduction of α–keto amide into α–hydroxyl amide has been reported by our group by both reduction using NS-Ceria (Nano Sphere) catalyst and by the use of UiO-66 catalyst wherein catalytic transfer hydrogenation process has been achieved.[5] Govindsamy and co-workers showed progress in β–aminol synthesis from α–keto amide by the use of Ni metal with KO^{t}Bu base[6a] or TBAF (Tetrabutylammonium fluoride)[6b] as catalyst in silane as reducing agent dissolved in THF (Tetrahydrofuran) solvent. However, protocol demands base additives or the use of fluorinated hydro-silylation which limits it scope. The reduction of secondary amides is quite difficult [7] and therefore apart from less expensive, non-toxic metal based supported catalyst which can be recycled, are current requirement for industrial and academic research. Encouraged by our lab work in the field of transfer hydrogenation reaction,[8] herein we report the use of Ru-g-C_3N_4 as a heterogeneous catalyst for complete transfer hydrogenation of α–keto amide into β–aminol for the first time. The advantage of the catalyst is that it can be modulated to show selective partial transfer hydrogenation into α–hydroxyl amide in presence of inexpensive and eco-friendly solvent IPA (isopropyl alcohol) which also acts as supporting hydrogen source or for complete transfer hydrogenation of α–keto amide wherein addition of FA:TEA (5:4) [Formic acid: Tri-ethylamine; F/T] as hydrogen donor along with above solvent IPA used, for synthesis of desired compound β–aminol, within a short period of time at 80

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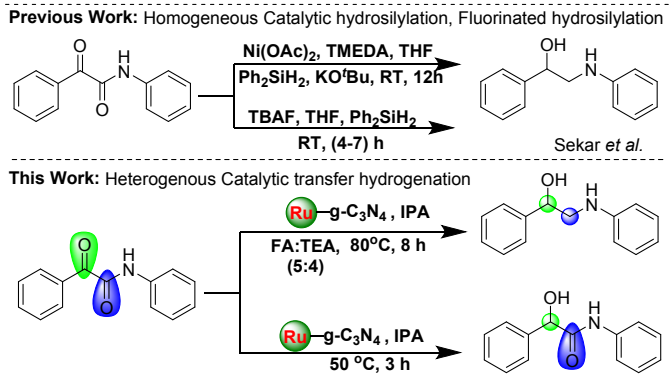
†Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/x0xx00000x

°C. Although as per literature transfer hydrogenation of carbonyl require very high temperature or presence of base or long duration however these problems can be overcome using Ru-g-C_3N_4 as heterogeneous catalyst. Now in the mentioned catalyst, graphitic-C_3N_4 is chemically inert in nature both in acidic and basic condition, and it is photo-catalytically highly active for organic transformations [9] because of its visible light storage energy along with band gap of ~ 2.7 eV which shows its semiconductor properties with absorption wavelength at 460 nm. [10] Typically g-C_3N_4 is primarily used as support for catalytic hydrogenation and oxidation reaction. Many groups started doping of different metal like Pd, Pt, Cu, Ni, etc. on the surface g-C_3N_4 to enhances their catalytic activity. [11] Pt metal initially used which enormously boost hydrogen evolution from g-C_3N_4. [12a] Similarly Ge *et. al.* reported Ag catalyst which increases hydrogen evolution by twelve times over g-C_3N_4 due to the synergic effect of Ag metal with g-C_3N_4. [12b] Similarly Mo also evolve hydrogen eleven times higher than g-C_3N_4 because of matching energy. [12c] However Yu et. al. reported hydrogen evolution with 0.5 mol% Ni metal [12d] as $Ni(OH)_2$ at a rate of 7.6 µmol/h which can be equal to hydrogen evolved with 1.0 wt% Pt-g-C_3N_4. [12e] Based on the previous work on the use of Ru-metal for hydrogenation of carbonyl group, [5c, 8] Ru, Pd and Ni metal doped on the g-C_3N_4 were prepared for catalytic transfer hydrogenation of α–ketoamide. From the above data even, addition of metal enhances activity of catalyst which boost the hydrogen production. Catalytic screening study shows that metal doped C_3N_4 shows the higher rate of hydrogen evolution than undoped C_3N_4. In same context we focused to establish a network on the catalytic performance of Ru-g-C_3N_4 for the parallel synthesis of β–aminol and α–hydroxyl amide at different conditions based on thermal activity of catalyst. Herein we report Ru-g-C_3N_4 as thermally most stable and active catalyst as compared to Ni and Pd supported on g-C_3N_4 for complete transfer hydrogenation of α–ketoamide into β–aminol and partial transfer hydrogenation into α–hydroxyl amide in presence of economical and environmentally benign isopropyl alcohol as a solvent.



Scheme 1: Catalytic Transfer Hydrogenation of α–keto amide into β–aminol & α–hydroxyl amide

Results and discussion

Graphitic support C_3N_4 is prepared by known procedure reported somewhere else.[13] Different metals like Ru, Cu, Ni and Pd are doped into it to study their effect for transfer hydrogenation. Heterogenous Ru-g-C_3N_4 catalyst was synthesized by ultrasonic deposition method. In this method 500 mg of yellow g-C_3N_4 (synthesized by pyrolytic method) dispersed in 60 ml of H_2O which is then ultrasonicated for 2 h after which, 12 mg of $RuCl_3$ is further added, followed by ultrasonication for another 30 min. Then 10 ml of $NaBH_4$ solution was added with continuous stirring which result into grey-blue product which was then filtered and washed several times with water and ethanol. After washing it was dried at 60°C. The weight of Ru-g-C_3N_4 obtained was 480 mg considering the handling loss (†See ESI). Prepared Ru-g-C_3N_4 was well characterized by various characterization techniques.

a) Powder X-Ray Diffraction

Typical X-Ray Diffraction (XRD) pattern of a) g-C_3N_4 and b) Ru-g-C_3N_4 observed in Fig. 1 which clearly indicates peak (2θ value) at 13.38° and 27.18°. These peaks are well recorded and are in proper pattern as per reported procedure [14a] which corresponds to (100) and (002) diffraction planes of graphitic g-C_3N_4 materials, respectively. In both the XRD-pattern, (002) plane which corresponds to 2θ value 27.18° is more intense as compare to other reflection. This peak corresponds to stacking of conjugated aromatic system. [14] The absence of peak related to Ru is due to lower loading of Ru with uniform distribution of

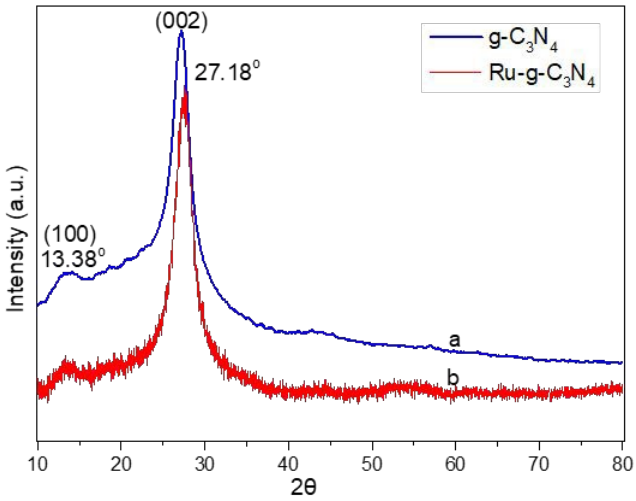


Figure 1: XRD pattern of a) g-C_3N_4 and b) Ru-g-C_3N_4

the surface of C_3N_4. Similarly, for Pd-g-C_3N_4 and for Ni-g-C_3N_4 material, XRD pattern has been recorded (†Fig. S4 in ESI) which resembles g-C_3N_4 indicating retention of conjugated aromatic system.

b) FEG-SEM and Elemental Mapping using EDX

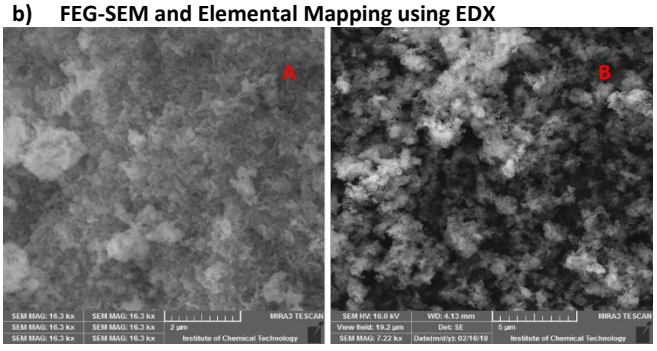


Figure 2: SEM images of catalyst A) and B) Ru-g-C_3N_4

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Synthesized ruthenium loaded g-C_3N_4 materials i.e.; Ru-g-C_3N_4 are characterized by FEG-SEM analysis. Visualization of SEM analysis shows sheet like aggregation morphology of C_3N_4 with aggregation of sheets of g-C_3N_4 at several places as visualized in (†Fig. S1 in ESI) whereas Fig. 2 and †Fig S1 (D, E, F) clearly represent images for Ru-g-C_3N_4 material, shows smaller unit of agglomeration of g-C_3N_4 where several very small Ru-NP's dispersed on the surface of g-C_3N_4. Enlarge portion of figure shows a uniform distribution of Ru nanoparticle over the surface of g-C_3N_4 layer. Moreover, elemental mapping (Fig. 3)

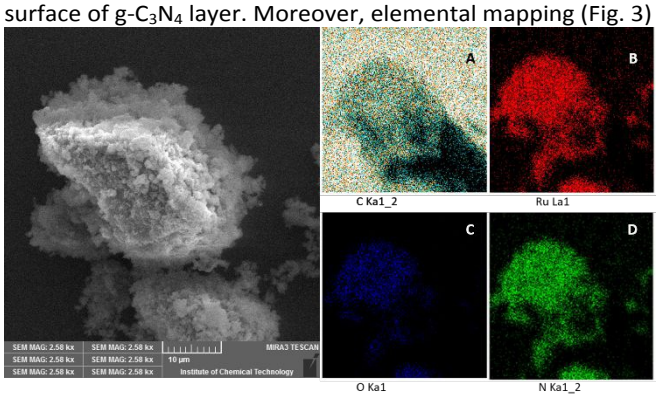

Figure 3: Elemental mapping of catalyst Ru-g-C_3N_4: A) Carbon B) Ruthenium C) Oxygen and D) Nitrogen

Using Energy-Dispersive X-ray spectroscopy (EDX) (†Fig. S3 in ESI) also confirms uniform loading of ruthenium metal on g-C_3N_4 materials by showing uniform distribution of carbon, nitrogen and ruthenium nanoparticle in the material.

c) X-Ray Photoelectron Spectroscopy

Furthermore, to determine the electronic state of the Ru element in Ru-g-C_3N_4 material, XPS spectroscopy technique has been employed (†Fig. S2 in ESI). XPS analysis was done with a PHI 5500 multi-technique system using a standard Al X- ray

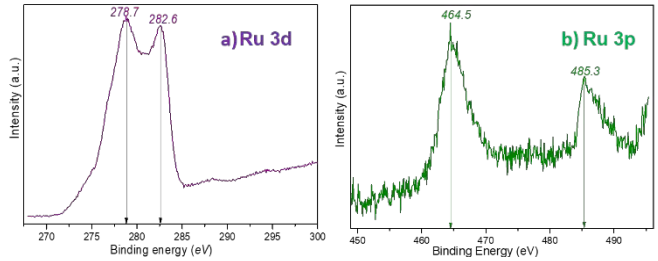

Figure 4: XPS spectra: a) Ru 3d region of Ru-g-C_3N_4; b) Ru 3p region of Ru-g-C_3N_4

source. XPS analysis makes easy way to determine the chemical environment and formal oxidation state of all elements like incorporation of ruthenium metal over g-C_3N_4 material has been studied. From †Fig S2, it is easily visible that C 1s spectrum shows two characteristic peak components at 284.8 eV (represent C-C) and 287.9 eV (represent N=C–N). [9d] In Fig. 4, Ru 3d spectra peak observed at 278.7 eV and 282.6 eV represents metallic Ru phase, which is overlapping with the characteristic peak of C 1s spectrum (as observed in †Fig. S2 full scan of Ru-g-C_3N_4 catalyst). Apart from this, peak at 398.9 eV indicates presence of sp^2 hybridized nitrogen (C=N–C) present in pyridine-N species which is observed in N 1s spectrum respectively. Along with that one major peak also observed at 464.5 eV in Ru 3p XPS spectra with another peak observed at 485.3 eV. [15a] (Fig. 4) These peaks correspond to ruthenium oxide species which can also be confirmed by peak observed for O 1s spectrum at 531.9 eV. (†Fig. S2) [15b]

d) AT-IR Spectroscopy and TGA of Catalyst

Characterization of synthesized material g-C_3N_4 and Ru-g-C_3N_4 has also been done by AT-IR spectroscopy to affirm the functional groups. As visualized in Fig. 5A, broad bands at around 3165 cm^{-1} indicates presence of N–H stretching vibrations. Some intense band are also observed at around 1610 cm^{-1} which confirm the presence of C=N stretching vibration, whereas absorption at 1240 cm^{-1} confirm presence of C–N stretching vibrations. Apart from it, in addition sharp band also observed at 810 cm^{-1} which reflects characteristic breathing mode of triazine units which is related to s-triazine ring absorption band vibration. Intense band at 1560 cm^{-1} and 1409 cm^{-1} are also observed which signifies typical stretching vibration modes of triazine derived repeating units. Fig. 5A clearly reflects parallel bands for both synthesized material g-C_3N_4 and Ru-g-C_3N_4 which indicates preservation of all modes of vibration after doping of ruthenium metal on g-C_3N_4 without changing its molecular structure. Apart from it AT-IR for Ni-g-C_3N_4 and Pd-g-C_3N_4 has also been recorded which shows same peak in comparison to Ru-g-C_3N_4 material as observed in †Fig. S6. This confirm presence of all functional group stretching characteristic vibration in characterized catalyst. In fact, mostly all the metal loaded peak shows similarity to g-C_3N_4. However little shifting for characteristic peak of triazine units has been observed around (790-820) cm^{-1} which may be because of different metal loaded into it. After understanding comparative AT-IR spectra for the synthesized catalyst, stability of prepared heterogenous catalyst with g-C_3N_4 support has been checked. The stability of synthesized materials was measured by using TGA technique. Samples were heated from room temperature to 900 °C at a rate of 10 °C min^{-1} under nitrogen atmosphere, and the TGA curves are shown in Fig. 5B which shows the fluctuation for Ru-g-C_3N_4. From graph it is cleared that catalyst decomposition starts at 348 °C and it completely ends near to 435 °C with residual weight fraction of ~ 5.65% which may be because of formation of oxides of ruthenium metal. Similarly, other catalyst like Ni-g-C_3N_4 and Pd-g-C_3N_4 has been prepared and are characterized. It makes clear that Ru-g-C_3N_4 starts decomposition at lower temperature than other metal on the

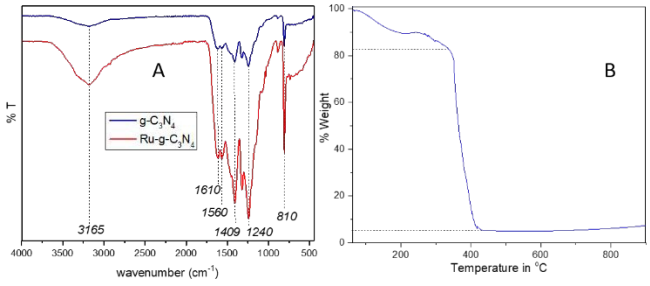

Figure 5: A) AT-IR spectra of g-C_3N_4 and Ru-g-C_3N_4; b) TGA Graph of catalyst Ru-g-C_3N_4

same support. Ni on g-C_3N_4 shows decomposition at 398 °C and ends at 525 °C apart from it Pd on g-C_3N_4 shows decomposition at 496 °C and ends at 640 °C. However, when TGA for plain g-C_3N_4 has been processed, it shows decomposition at 525 °C and

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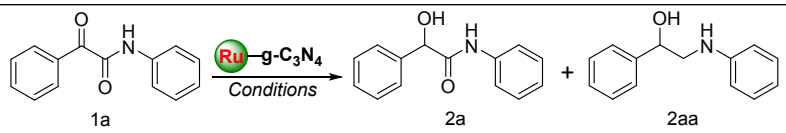
Table 1: Optimisation of Ru-catalysed transfer hydrogenation of α-ketoamide into β-aminol and α-hydroxyl amide



Entry No.	Catalyst	Catalyst loading	Hydrogen source	Solvent	Time in h	Temp in °C	Yield[d] in %		Conv in %
							2a	2aa	
1	g-C_3N_4	20 mg	FA: TEA[a] (5:2)	IPA	24	80	-	-	-
2	Ru-g-C_3N_4	50 mg	FA: TEA[a] (5:2)	IPA	24	80	-	86	100
3	Ni-g-C_3N_4	50 mg	FA: TEA[a] (5:2)	IPA	24	80	55	35	100
4	Pd-g-C_3N_4	50 mg	FA: TEA[a] (5:2)	IPA	24	80	65	20	100
5	$RuCl_3$	40 mg	FA: TEA[a] (5:2)	IPA	24	80	30	-	40
6	Cu $(OAc)_2$	36 mg	FA: TEA[a] (5:2)	IPA	24	80	57	-	80
7	-	-	FA: TEA[a] (5:2)	IPA	24	80	-	-	20
8	Ru-g-C_3N_4	50 mg	FA: TEA[a] (5:2)	DCM	24	50	55	18	100
9	Ru-g-C_3N_4	50 mg	FA: TEA[a] (5:2)	EtOH	24	80	25	-	30
10	Ru-g-C_3N_4	50 mg	FA: TEA[a] (5:2)	MeOH	24	80	45	-	80
11	Ru-g-C_3N_4	50 mg	IPA		24	80	97	-	100
12	Ru-g-C_3N_4	50 mg	HCOONa[a]	IPA	24	80	59	-	75
13	Ru-g-C_3N_4	50 mg	$NaBH_4$[b]	MeOH	24	80	82	-	95
14	Ru-g-C_3N_4	50 mg	IPA: H_2O (1:1)		24	80	63	-	90
15	Ru-g-C_3N_4	50 mg	FA: TEA[a] (5:4)	IPA	24	80	-	98	100
16	Ru-g-C_3N_4	40 mg	FA: TEA[a] (5:4)	IPA	24	80	-	98	100
17	Ru-g-C_3N_4	30 mg	FA: TEA[a] (5:4)	IPA	24	80	-	98	100
18	Ru-g-C_3N_4	20 mg	FA: TEA[a] (5:4)	IPA	24	80	-	82	100
19	Ru-g-C_3N_4	30 mg	FA: TEA[a] (5:4)	IPA	12	80	-	97	100
20	Ru-g-C_3N_4	30 mg	FA: TEA[a] (5:4)	IPA	8	80	-	97	100
21	Ru-g-C_3N_4	30 mg	FA: TEA[a] (5:4)	IPA	6	80	20	68	100
22	Ru-g-C_3N_4	30 mg	FA: TEA[a] (5:4)	IPA	8	60	11	62	100
23	Ru-g-C_3N_4	30 mg	FA: TEA[a] (5:4)	IPA	8	RT	56	15	100
24	Ru-g-C_3N_4	30 mg	FA: TEA[a] (5:4)	IPA	8	100	-	98	100
25	Ru-g-C_3N_4	30 mg	IPA		5	80	98	-	100
26	Ru-g-C_3N_4	30 mg	IPA		3	80	98	-	100
27	Ru-g-C_3N_4	30 mg	IPA		3	50	97	-	100
28	Ru-g-C_3N_4	30 mg	IPA (10 ml)		8	80	97	-	100
29	Ru-g-C_3N_4	30 mg	FA: TEA[c] (5:4)	DCM	8	50	25	54	90

Conditions: 1 mmol of compound 1a dissolved in 5 ml solvent, along with mentioned catalyst. [a] 0.2 ml of FA: TEA (5:2) / (5:4) in IPA solvent; [b] 1 mmol of $NaBH_4$ in 5 ml of MeOH solvent and [c] 1 ml of FA: TEA (5:4) taken in 5 ml of DCM solvent; [d] Isolated yield based on GC-MS analysis.

ends at 685 °C reflecting that when metal loaded on g-C_3N_4 it enhances its reactivity. (†Fig. S7)

With all characterized data in hand, catalyst has been used for application process in synthetic chemistry. Based on the literature study of catalyst for the use in hydrogenation process, we tried to implement the same process on our previous model substrate 2-oxo-*N*-2-diphenylacetamide to understand catalyst effect as compare to other catalyst used so far. Our initial step commenced with the use of series of same family of heterogenous catalyst g-C_3N_4, with different metal loading such as Ru, Ni and Pd. From the Table 1 it is quite clear that Ru metal shows better activity for hydrogenation over other metal for conversion of α-ketoamide into β-aminol, whereas Ni shows predominantly synthesis of 55% of α-hydroxyl amide along with 35% of β-aminol similarly, Pd shows 65% of α-hydroxyl amide and 20% of β-aminol respectively (Table 1, Entry 1-4). However, $RuCl_3$ and $Cu(OAc)_2$ shows only formation of α-hydroxyl amide about 30% and 57% yield (Table 1, Entry 5-6). Although absence of catalyst doesn't favour progress of reaction which confirms the importance of catalyst for hydrogenation process. (Table 1 entry 7) From these data it can be predicted that Ru in (+3) oxidation state can't satisfy for complete hydrogenation rather only allow CTH of α-ketoamide into α-hydroxyl amide to some extent whereas when it is loaded in (0) oxidation state on g-C_3N_4 support, it can show complete hydrogenation reaction into β-aminol. It indicates Ru in 0 oxidation state shows better activity for hydrogenation as compared to Ru in its +3-oxidation state. Henceforth solvent study was screened where DCM solvent shows 55% yield of α-hydroxyl amide along with 18% of β-aminol (Table 1 entry 8) whereas increasing the polarity of solvent to EtOH and MeOH doesn't favour β-aminol synthesis but it shows only formation of α-hydroxyl amide (Table 1 entry 9-10). After that, hydrogen source has been screened out and it has been observed that solvent IPA alone which can show dual role both

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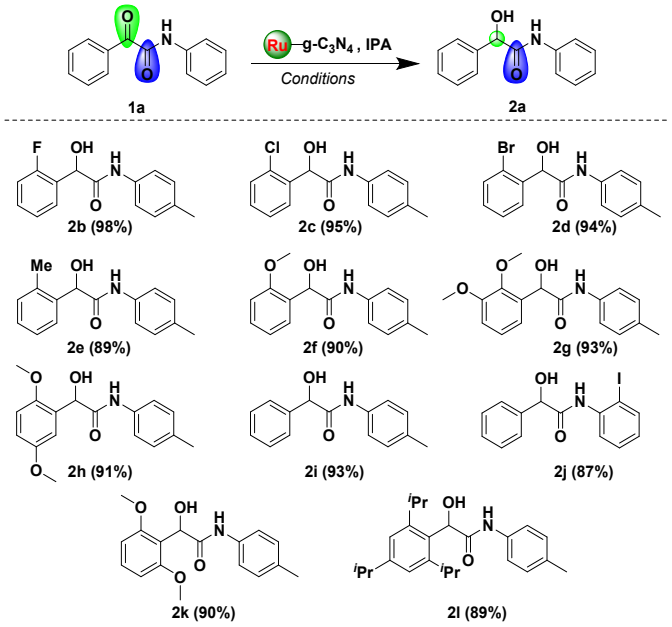
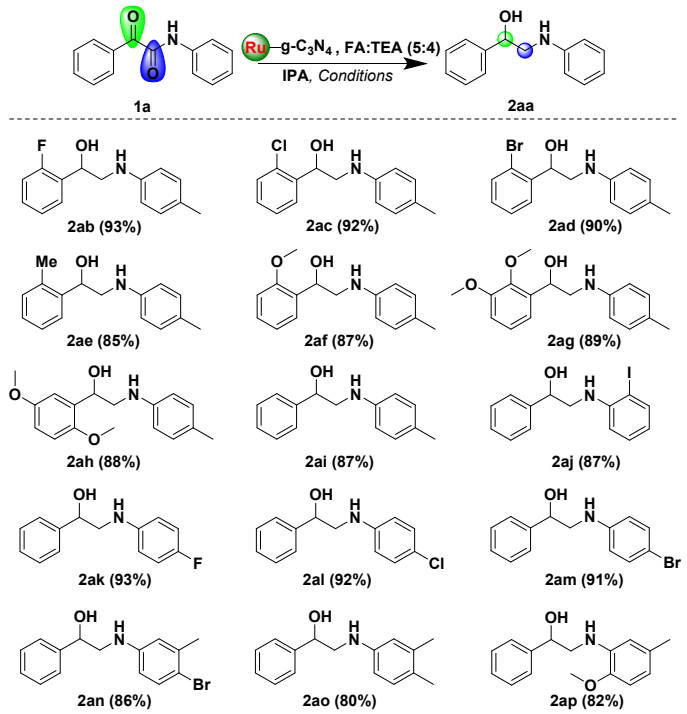
as solvent and hydrogen source deliver 97% yield of α-hydroxyl amide (Table 1 entry 11) whereas using HCOONa decreased the yield of α-hydroxyl amide to 59% (Table 1 entry 12). Nonetheless, using $NaBH_4$ in MeOH solvent increased the yield to 82% (Table 1 entry 13). Further to make the process more sustainable IPA: H_2O were used in ration of (1:1) however 63% yield of α-hydroxyl amide was observed (Table 1 entry 14). Further FA: TEA in ration of (5:4) were used which shows surprisingly dominancy for the desired product β-aminol as compare to other the hydrogen source. Comparing with FA: TEA in ratio of (5:2) (which shows 86% yield of β-aminol) (Table 1 entry 2), (5:4) ratio of FA: TEA, increased the yield to 98% (Table 1 entry 15) which may be because with lower F/T molar ratio from 2.5 to 1.25 increases pH of the medium which initiates complete CTH of α-keto amide, this confirms that CTH is pH dependent. With product in hand catalyst loading is screened which shows 30 mg is sufficient for complete transfer hydrogenation reaction for the synthesis of desired product. Yield remain same by increasing the catalyst loading to 40 mg whereas decreasing catalyst loading to 20 mg reduced the yield to 82% (Table 1, Entry 16-18). Furthermore, time scale and temperature has been optimized where 8 h and 80 °C shows excellent yield of β-aminol. Yield remain same by decreasing the time from 24 h to 8 h but further decrease to 6h decreases the yield of desired β-aminol whereas simultaneously also shows presence of α-hydroxyl amide, which reflects that α-hydroxyl amide may be intermediate during the synthesis of β-aminol (Table 1, Entry 19-21). During temperature scale study it seems that lower temperature more prone to α-hydroxyl amide as compared to β-aminol. From Table 1 entry (22-24) it is clear that reducing the temperature to 60 °C further decreases the yield of β-aminol to 62% which further decreased to 35% when temperature reduced to RT (29 °C). However same temperature increases the yield of α-hydroxyl amide to 56% and when temperature increased to 100 °C it shows 98% of β-aminol but no α-hydroxyl amide. From observed data it can be confirmed that at higher temperature and at moderate basic condition β-aminol is favoured and lower temperature favours α-hydroxyl amide synthesis. Henceforth encouraged with result observed in entry 11, synthesis of α-hydroxyl amide also has been screened, where solvent IPA shows dual role (also as hydrogen source) producing 97% yield of above said product. Further optimisation study shows that lowering temperature to 50 °C doesn't affect the yield significantly, nearly similar results obtained while decreasing the time to 3 h from 5 h (Table 1, Entry 25-27). To understand the effect of IPA in hydrogenation process it is even increased to 10 ml so that it may yield β-aminol but it favours only α-hydroxyl amide (Table 1, Entry 28). Further entry 8 insist us to optimise DCM as solvent so it has been used in presence of hydrogen donor FA: TEA (5:4) in excess amount but it shows decrease in yield of β-aminol to 54% (Table 1 entry 29). Thus, from entry (8-11), 25,29 clearly indicates IPA and FA: TEA (5:4) tandemly work for synthesis of β-aminol. Hence entry 20 reports selectivity, for β-aminol synthesis when azeotropic mixture FA:TEA ratio of 1.25 used along with IPA which behaves like supportive hydrogen donor and solvent both, at 80 °C whereas entry 27 reports selective synthesis of α-hydroxyl amide when only IPA used both as hydrogen donor as well as solvent at 50 °C (†see ESI, Fig. 9). Both the condition requires Ru-g-C_3N_4 as a heterogenous catalyst.

Table 2: Substrate scope of 1a for partial transfer hydrogenation of α-ketoamide into α-hydroxyl amide



Conditions: 1 mmol of substrate compound (1a) and its derivatives dissolved in 5 ml IPA solvent, along with 30 mg of mentioned catalyst. Isolated yield based on GC-MS analysis.

Table 3: Substrate scope of 1a for complete transfer hydrogenation of α-ketoamide into β-aminol



Conditions: 1 mmol of substrate compound (1a) and its derivatives in presence of 0.2 ml of FA: TEA (5:4) dissolved in 5 ml IPA solvent, along with 30 mg of mentioned catalyst. Isolated yield based on GC-MS analysis.

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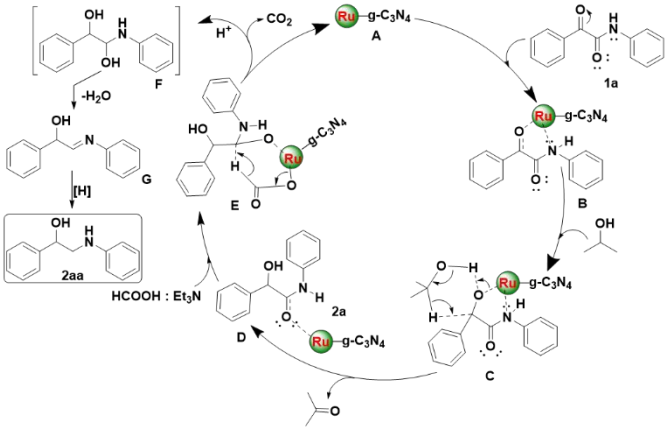
DOI: 10.1039/D0NJ01674H

With optimization table in hand, substrate scope also has been studied for the derivative synthesis of α–hydroxyl amide and β–aminol. Initiation for substrate study done from purification of α-hydroxyl amide and its derivatives where both electron withdrawing and electron donating tendency has been measured for CTH reaction. According to the observation from the Table 2 it is quite clear that with respect to model substrate electron withdrawing group shows better yield as compare to electron donating group. When at *ortho* position, -F (2b) group present on aromatic part of ketone, 98% yield is obtained which remains nearly same by substitution with -Cl (95%) or -Br (94%), whereas when *ortho* position is occupied by electron donating group like -Me yield reduced to 89% or by -OMe (90%). However, when 2nd and 3rd position (*ortho* and *meta* position) are occupied by -OMe then yield remains 93% which even remains same when 2nd and 5th position is occupied by same moiety. However small loss in yield to 90% is observed when -OMe substituted at both ortho position i.e.; 2nd and 6th position. Apart from that isopropyl group at di-ortho (2nd and 6th position) and para i.e.; 4th position also has been studied which shows 89% yield (2l). It clearly reflects electron donating group showing (+I effect) promotes transfer hydrogenation process but lesser than (-I effect) as it deactivates carbonyl carbon of ketone from electrophilic nature. After that substituted aromatic part of amide is studied, keeping -Me group (2i) at *para* position without any substitution on aromatic of ketone it shows 93% yield whereas when *ortho* position is substituted with -I group (2j) then it shows 87% yield.

To further explore wide substrate applicability of this protocol β-aminol synthesis has been studied. In this derivative study, initially when *ortho* position of aromatic part of ketone substituted with -F it shows 93% yield. Reaction progress when α-keto amide along with 5 ml of IPA and 30 mg of catalyst is heated at 80 °C and after 3 h FA: TEA (5:4) is added into it, so it can be concluded that reaction progress for β-aminol *via* synthesis of α-hydroxyl amide. Thus, it can also be predicted that α-keto amide converted to 97% of 2aa *via* 98% of 2a. Similarly, 93% of 2ab product is obtained *via* 98% of 2b and 92% of 2ac product obtained *via* 95% 2c. After that 90% of 2ad is obtained when -Br group is present at *ortho* position. However, with EDG like -Me and -OMe group when present at *ortho* position shows slightly lower yield like 2ae produced in 85% yield *via* 89% of 2e whereas 87% yield of 2af is produced. When -OMe group are present at 2nd and 3rd position it shows same yield of 89% as observed in 2ag from table 3 similarly yield remain same when -OMe group present at 2nd and 5th position. Now to understand the effect of substitution for β-aminol synthesis EWG like -F (2ak), -Cl (2al), -Br(2am), -I (2aj) are substituted on the aromatic part of amide, which shows good yield of about 90% like for 2aj 87%, 2ak 93% and >90% for both 2al and 2am. In these cases, it can be understood that EWG showing (-I effect) favours transfer hydrogenation which employed β-aminol synthesis in larger amount, where all the 2j (α-hydroxyl amide) converted into 2aj (β-aminol). In the case of 2an -Br at *para* position and -Me at *meta* position shows dual effect (-I effect of -Br and +I effect of Me) for its yield of about 86% however when -Me is present at both *meta* and *para* position it shows 80% yield which increase to 87% when -Me present solely at *para* position in 2ai. After this -OMe at *ortho* position and -Me at *meta* position shows its dual effect in 2ap for its yield to 85% respectively. Here, it can be clear that (+I effect) shows favours in β-aminol synthesis in lesser yield as compare to EWG which shows (-I effect).



Scheme 2: Possible Mechanism for complete and partial CTH of α–keto amide

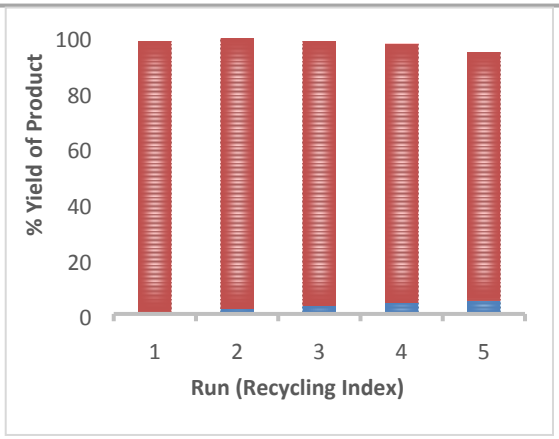


Figure 6: Recycling study of Ru-g-C_3N_4 catalyst under the optimised condition for complete transfer hydrogenation of α-ketoamide into β-aminol

Based on the results obtained from control experiment (†see ESI) and previous report in literature, plausible reaction mechanism for selective synthesis of β-aminol has been proposed in Scheme 2. Initially Ru-catalyst (A), catalysed transfer hydrogenation of ketone part of α-ketoamide (1a), leads to the formation of penta-co-ordinated intermediate [B] where Ru binds with carbonyl oxygen of ketonic part and nitrogen of amide substrate (1a), which finally leads to the generation of 6 membered intermediate (C) with IPA. Finally, it converts into α-hydroxyl amide (2a) which on prolonged exposure in front of excess Ru–catalyst (A) leads to the formation of complex (2a) where [Ru] binds with carbonyl oxygen of amide because of the presence of high electron density, further FA: TEA (5:4) generates $HCOO^-$ where electron rich oxygen binds with catalyst ultimately generates 6 membered intermediate (D) which finally produces hemi-aminol intermediate (E). Intermediate (E) may undergo direct dehydration into compound (F) [16] [may be because hydrogen of nitrogen is more acidic, as it also leads to the formation of

stable conjugated product F] which finally produces targeted β–aminol (2aa).

Further, catalyst was recycled five times for the same complete CTH reaction and 4th recycled catalyst has been characterized which shows retention of metal loaded on it. (†Fig. S5 in ESI) XRD pattern, FEG-SEM images and EDX spectra confirms no change in morphology, retention of metal on the g-C_3N_4. Although at the same time, reactivity for the catalyst also has been observed which shows not much reduction in the yield of product. (Fig. 6)

Conclusions

In conclusion remarks efficient, sustainable and easy handy protocol has been achieved where catalytic transfer hydrogenation process can be modulated either for partial selective or for complete hydrogenation reaction of α–keto amide. Heterogeneous Ru-g-C_3N_4 catalyst has been developed and has been comparatively studied with different metal like Ni and Pd on same support. Protocol involves activity and reactivity of Ru catalyst for CTH process in eco-friendly solvent like IPA and F/T ratio about 1.25 for desired compound β-aminol. Catalyst has been recycled and it is further characterized where no effect observed in its reactivity neither any reasonable loss has been observed after reaction. Different derivatives of α-hydroxyl amide and β-aminol has been synthesized and has been characterized with NMR spectroscopy. Based on literature study, possible mechanism has been drawn for the CTH of α–keto amide.

Conflicts of interest

"There are no conflicts to declare".

Acknowledgements

Author AAM is thankful to the Department of Science and Technology (DST-INSPIRE), New Delhi, India, for providing Senior Research Fellowship (SRF).

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DOI: 10.1039/D0NJ01674H

Graphical Abstract

Ru–g-C_3N_4 as highly active heterogeneous catalyst for transfer hydrogenation of α–keto amide into β–aminol or α–hydroxyl amide

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