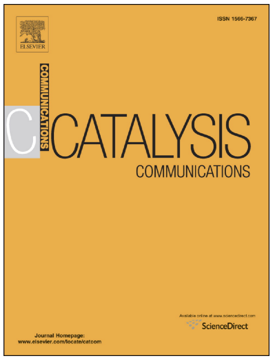


Borrowing hydrogen activity of NH2-MIL-125 for N-alkylation of amines with alcohols under solvent and base free condition

Nisha B. Patel, Naresh Vala, Atindra Shukla, Subhadip Neogi, Manish Kumar Mishra

PII: S1566-7367(20)30161-8

DOI: https://doi.org/10.1016/j.catcom.2020.106085

Reference: CATCOM 106085

To appear in: *Catalysis Communications*

Received date: 1 March 2020

Revised date: 26 May 2020

Accepted date: 9 June 2020

Please cite this article as: N.B. Patel, N. Vala, A. Shukla, et al., Borrowing hydrogen activity of NH2-MIL-125 for N-alkylation of amines with alcohols under solvent and base free condition, *Catalysis Communications* (2019), https://doi.org/10.1016/j.catcom.2020.106085

Borrowing hydrogen activity of NH_2-MIL-125 for N-alkylation of amines with alcohols under solvent and base free condition

Nisha B. Patel,[a] Naresh Vala,[b] Atindra Shukla,[b] Subhadip Neogi,[c] Manish Kumar Mishra[a,*]

[a]*Department of Chemistry, Sardar Patel University,*

Vallabh Vidyanagar- 388 120, Gujarat, India.

[b]*Shah-Schulman Center for Surface Science and Nanotechnology,*

Dharmsinh Desai University, College Road, Nadiad – 387 001, Gujarat, India.

[c]*Department of Inorganic Materials and Catalysis, Central Salt and Marine Chemicals Research Institute*

(CSMCRI), Council of Scientific and Industrial Research (CSIR), GB Marg, Bhavnagar 364002, Gujarat, India.

E-mail: manishorgch@gmail.com; Tel: +91 2692 226856

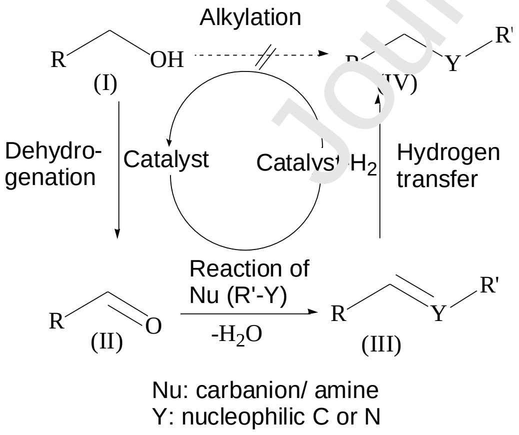
Abstract

The NH_2-MIL-125 showed excellent activity in solvent and base free N-alkylation of amines with alcohols *via* borrowing hydrogen mechanism. The Ti–O clusters of NH_2-MIL-125 provide acidic-basic active sites for the catalysis of reaction. The NH_2-MIL-125 was found to be stable and reusable in the reaction.

Keywords: Borrowing hydrogen methodology; metal-organic frameworks; NH_2-MIL-125; N-alkylation of amines; alcohols.

1. Introduction

Borrowing hydrogen methodology is an atom efficient and greener approach for the synthesis of chemicals using alcohols as inexpensive and green alkylating reagent [**1**]. This methodology involves the activation of an alcohol (**I**) by removal of hydrogen (H_2; dehydrogenation) to a carbonyl (**II**) for the reaction with a nucleophile (Nu; carbanions/ amines) to an unsaturated product (**III**), followed by hydrogenation using H_2 generated in dehydrogenation step to finally saturated product (**IV**) (**Scheme 1**) [**2**]. The borrowing hydrogen method has been adapted to use alcohols as an alkylating agent in alkylation of carbonyls (α-C alkylation) [**3-7**] and amines (N-alkylation) [**5-11**] under greener route. The noble metals in the form of homogeneous as well as heterogeneous catalysts have shown excellent activity in the borrowing hydrogen reactions (see Table S1 & S2). The bases/ additives and solvents are used with most of these reported catalysts, which detriment the eco-friendly nature of the process. The borrowing hydrogen methodology is still in need of suitable heterogeneous catalytic system involving less precious metal, and no base/ additive and solvent for its viable application.



Scheme 1. Activation of an alcohol for C-/ N-alkylation *via* borrowing hydrogen mechanism.

Metal-organic frameworks (MOFs) possess attractive features such as high surface area, high porosity, and tunable textural and functional characteristics [**12**], which make them very suitable for their exploration as catalysts and support materials in the area of heterogeneous catalysis. There has been significant progress on exploration of MOFs in heterogeneous catalysis [**13**]. The NH_2-functionalized MIL-125 (NH_2-MIL-125) is one of the stable MOFs [**14**], which has been much investigated for the development of efficient visible light active photocatalysts [**13**]. We were interested to study the activity of NH_2-MIL-125 for borrowing hydrogen catalysis under thermal condition, because of its excellent stability and basicity due to $–NH_2$ functionality [**15**], which can trigger the alcohols for dehydrogenation through deprotonation [**16**]. We found that NH_2-MIL-125 exhibited excellent borrowing hydrogen activity giving good conversion of alcohols in N-alkylation of amines. The Ti–O clusters of NH_2-MIL-125 provide active sites (Ti– and O– as Lewis acidic and basic sites, respectively) for the catalysis of borrowing hydrogen reaction. The study opens up a new area of catalytic application for NH_2-MIL-125 and other MOFs, and provides a solvent and base free catalytic route for borrowing hydrogen reactions.

2. Experimental

2.1. Synthesis of NH_2-MIL-125 and MIL-125

NH_2-MIL-125 and MIL-125 materials were prepared by a solvothermal route, which is a slightly modified method reported by H. Yamashita [**17**]. For the synthesis of NH_2-MIL-125, a solution of titanium tetra *iso*-propoxide (3.5 mmol) and 2-aminoterephthalic acid (7 mmol) in a 50 mL mixture of DMF and methanol (1:1; v/v) was prepared by stirring at room temperature (30°C). The solution was transferred to a 150 mL Teflon-lined autoclave and heated at 150°C for 48 h in an oil bath. The solution was cooled to room temperature. A solid mass was obtained after filtration, which was washed with DMF (N,N-dimethylformamide; 50 mL) and then with methanol (50 mL). The solid mass was activated under vacuum at 150°C for 15 h. MIL-125 was also synthesized by solvothermal reaction of titanium tetra *iso*-propoxide (9 mmol) with terephthalic acid (15 mmol) in a 50 mL mixture of DMF and methanol (9:1; v/v) as described above for NH_2-MIL-125. The characteristics of the synthesized NH_2-MIL-125 and MIL-125 are given in electronic supplementary information (**ESI**).

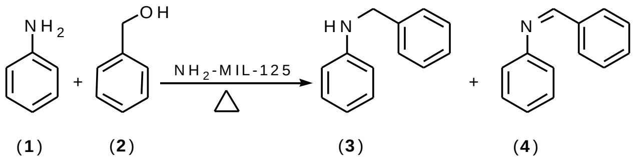
2.2. General procedure for N-alkylation of amines with alcohols

A mixture of amine and alcohol in required molar ratio along with the catalyst were taken in a 50 mL round bottom flask equipped with a water cooled condenser. The mixture was heated at desired temperature under stirring for required period of time. After the completion of reaction, the reaction mixture was cooled and diluted with methanol (2 mL). The diluted reaction mixture was centrifuged to separate the catalyst from the liquid phase and the reaction mixture was analyzed by gas chromatography to calculate the conversion of alcohol and selectivity of products (see ESI).

3. Results and discussion

Initially, the catalytic activity of NH_2-MIL-125 was assessed for N-alkylation of aniline (**1**) with benzyl alcohol (**2**), as a model reaction, using their equimolar amount (10 mmol) and 10 wt.% of catalyst at 100°C to 180°C for 15 h (**Table 1**). The reaction at 160°C gave highest conversion of **2** (97%) into 95% N-alkylated product (**3**) showing 160°C to be optimum temperature for borrowing hydrogen activity of NH_2-MIL-125. At lower (140°C) and higher (180°C) temperatures, the imine product (**4**) was in significant amount. The increase in molar amount of either **1** or **2** decreased the conversion of alcohol as well as selectivity of **3** (**Table 1**). This is an advantage with NH_2-MIL-125 that substantially high conversion of alcohol is achieved with equimolar amount of alcohol; many heterogeneous catalysts require higher molar quantity of alcohol to give a high conversion to N-alkylated product (Table S2). The results (**Table 1**) show excellent activity of NH_2-MIL-125 for borrowing hydrogen reaction giving highest conversion of alcohol and selective formation of N-alkylated product in equimolar reaction of an amine and an alcohol at catalytic amount (10 wt.%). The kinetics of the reaction (equimolar reaction of **1** and **2** using 10 wt.% catalyst at 160°C; **Table 1**) depicts that 15 h reaction gives highest conversion of **2** (97%) with highest selectivity of **3** (95%). Generally, longer reaction time (24-72 h) is required with most of heterogeneous catalysts to achieve highest yield (Table S2). The longer reaction with NH_2-MIL-125 reduces the selectivity of **3** (**Table 1**) due to its conversion (dehydrogenation) into **4**. The oxidative dehydrogenation of a secondary amine (**3**) into imine (**4**) has been reported over Au/TiO_2 catalyst [**18**]. The formation of significant amount of **4** in some of the reactions (**Table 1**) is a clear evidence of the borrowing hydrogen mechanism, which involves the formation of imine intermediate followed by hydrogenation with hydrogen generated during dehydrogenation of alcohol [**2**]. The direct nucleophilic substitution of alcoholic –OH of benzyl alcohol by $–NH_2$ of aniline is another possible mechanism for the formation of N-alkylated product [**19**,**20**]. The dehydrogenative activity of NH_2-MIL-125 was evaluated for dehydrogenation of **2** at 160°C in absence of **1**; 79% conversion of **2** into 95% benzaldehyde (along with 5% dibenzyl ether) was obtained. The formation of significant amount of imine intermediate (**4**) in the reactions and dehydrogenative activity of NH_2-MIL-125 (in dehydrogenation of **3** to **4** and **2** to benzaldehyde) reveal the occurrence of N-alkylation reaction *via* borrowing hydrogen mechanism.

Table 1. Optimization of reaction parameters (temperature, catalyst amount, molar ratio of reactants and reaction time) for NH_2-MIL-125 catalyzed N-alkylation of **1** with **2**.

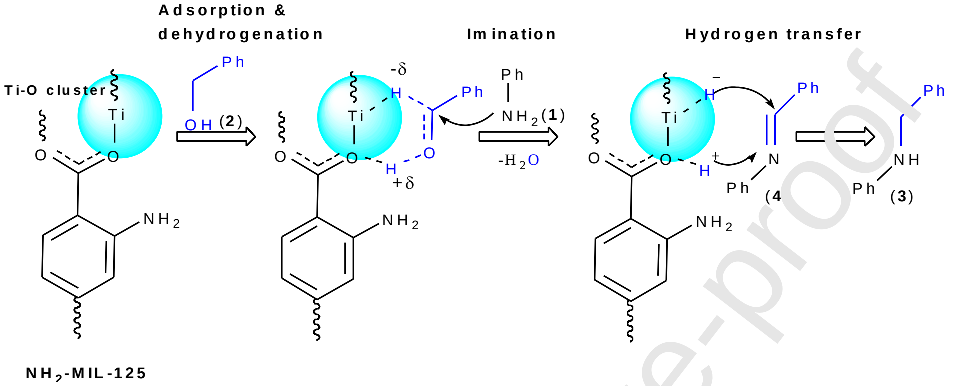


Reaction parameter	Conv. (%) of 2	Select. (%) of 3	Select. (%) of 4
Temperature (°C)^a			
100	0		
120	0		
140	20	75	25
160	97	95	5
180	92	72	27
Catalyst amount (wt.%)^b			
10	97	95	5
5	60	99	1
2.5	30	99	1
Molar ratio of 1 and 2^c			
1:1	97	95	5
1:2	21	42	58
2:1	22	8	68
Reaction time (h)^d			
1	25	99	1
2	30	99	1
3	50	99	1
6	75	99	1
9	84	99	1
12	90	99	1
15	97	95	5
18	97	87	13
24	98	10	90
48	98	1	99

[a] 10 mmol **1**, 10 mmol **2**, 10 wt.% NH_2-MIL-125, 15 h.
[b] 10 mmol **1**, 10 mmol **2**, 160°C, 15 h.
[c] 10 wt.% NH_2-MIL-125, 160°C, 15 h.
[d] 10 mmol **1**, 10 mmol **2**, 10 wt.% NH_2-MIL-125, 160°C.

The dehydrogenation of an alcohol can occur over acidic and basic sites located in vicinity [**21**]. The defect metal sites (Ti–) and O–atoms of Ti–O clusters of NH_2-MIL-125 may provide vicinal Lewis acidic and Lewis basic sites, respectively [**15**] to catalyze dehydrogenation-hydrogen transfer (*i.e.*, borrowing hydrogen) reaction. The direct involvement of $-NH_2$ group of NH_2-MIL-125 as basic site in catalysis of borrowing hydrogen can also be anticipated. However, the substantial conversion of **2** (65%) into **3** (83%) with MIL-125 in the reaction (equimolar reaction of **1** and **2** using 10 wt.% catalyst at 160°C for 15 h) reveals that Ti– and O–atoms of metal cluster are possibly catalytic sites. In a Ti–O cluster of NH_2-MIL-125, Ti–atom is coordinated with six O–atoms, which can act as basic sites: three O–atoms provided by carboxylates, one O–atom of bridging hydroxo group, and two bridging O–atoms joining two Ti– atoms [**22**]. The titania (prepared by a sol-gel method [**23**]; **ESI**), in which Ti–atom has only bridging hydroxo and bridging O–atoms but no carboxylates' O–atom, gave 29% conversion of **2** into **4** (100%) in the equimolar reaction of **1** and **2** [10 mmol **1**, 10 mmol **2**, 10 wt.% catalyst, 160°C, 15 h], without formation of **3**. This indicates that the carboxylates' O–atoms are active basic sites for borrowing hydrogen activity.

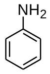
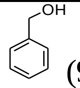
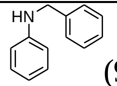
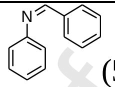
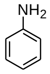
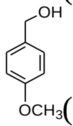
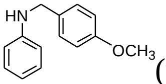
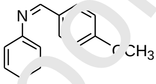
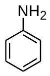
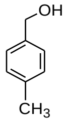
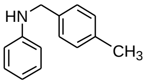
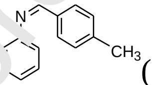
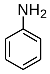
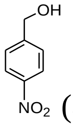
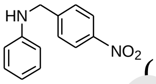
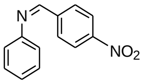
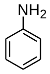
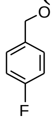
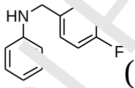
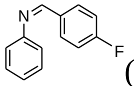
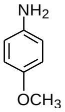
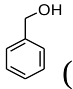
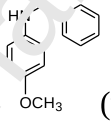
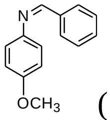
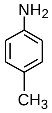
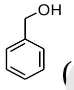
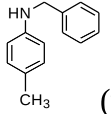
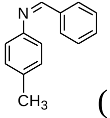
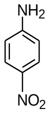
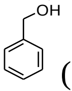
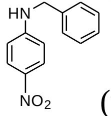
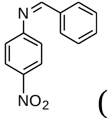
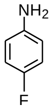
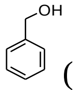
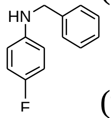
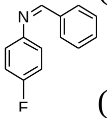
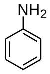
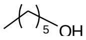
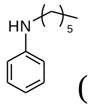
The Ti– and carboxylates' O–atoms of a Ti–O cluster can dehydrogenate **2** to a carbonyl intermediate (benzaldehyde) by abstracting hydroxyl hydrogen of **2** as proton and a benzylic hydrogen, respectively (**Scheme 2**). However, we did not observed benzaldehyde in reaction mixture by GC analysis, probably due to its adsorption over the sites and prompt nucleophilic reaction of **1** converting into **4**. The hydride and proton abstracted by Ti– and carboxylates' O–atoms, respectively, are transferred to **4** to produce **3** (**Scheme 2**). The mesomeric (+M) effect of $-NH_2$ can enhance electron density at carboxylates' O–atoms in NH_2-MIL-125 making them more basic than carboxylates' O–atoms in MIL-125 and therefore, NH_2-MIL-125 showed higher catalytic activity. The addition of an organobase, 1,5,7-Triazabicyclo[4.4.0]dec-5-ene (TBD; 20%), in a reaction with MIL-125 increased the conversion (65% to 85%) but greatly decreased the selectivity of N-alkylated product (11%). This result indicates that use of additional base facilitates the dehydrogenation reaction by helping in deprotonation and giving benzaldehyde and its conversion into imine, however, the protons abstracted by TBD molecules are not transferred to imine for reduction giving poor selectivity of N-alkylated product. This result shows that the metal- and basic- sites should be in vicinity for effective hydrogen transfer, which is possible in NH_2-MIL-125 or in MIL-125.



Scheme 2. Plausible mechanism of N-alkylation of **1** with **2** *via* borrowing hydrogen reaction over NH_2-MIL-125.

Numerous expensive metal based homogeneous and heterogeneous catalysts have been studied for N-alkylation of **1** with **2** (Table S1 & S2). These catalysts perform well in the presence of excess amount of bases/ additives and solvent. NH_2-MIL-125 is an inexpensive catalyst, which exhibits similar activity (conversion/ yield) under bases/ additives and solvent free condition. The catalytic efficiency of NH_2-MIL-125 was also evaluated for N-alkylation of different aromatic amines with alcohols under similar reaction condition as optimized above (**Table 2**). The NH_2-MIL-125 showed activity with all types of substrates. However, the nature of substituents present in substrates affects the reaction (conversion and selectivity of N-alkylated product). The presence of electron withdrawing groups (e.g., -NO_2 and –F; Entry 4, 5, 8 & 9; **Table 2**) in amines/ alcohols slowed down the reaction giving less conversion of alcohol.

Table 2. Conversion and selectivity in NH_2-MIL-125 catalyzed N-alkylation reactions of amines with alcohols.[a]

Entry	**Amine**	**Alcohol (Conv.; %)**	**N-alkylated product (Select.; %)**	**Imine product (Select.; %)**
1		 (97)	 (95)	 (5)
2		 (97)	 (97, 94[b])	 (3)
3		 (81)	 (92)	 (8)
4		 (5, 28[c])	 (10, 49[c])	 (90, 51[c])
5		 (28)	 (99)	 (1)
6		 (86)	 (99)	 (1)
7		 (59)	 (99)	 (1)
8		 (20, 40[c])	 (99)	 (1)
9		 (27)	 (99)	 (1)
10		 (25)	 (100)	

[a] 10 mmol amine, 10 mmol alcohol, 10 wt.% NH_2-MIL-125, 160°C, 15 h.
[b] Isolated yield.
[c] Reaction time: 24 h.

An electron withdrawing group in alcohol may reduce electron density on oxygen of –OH group through a long range inductive effect [**24**], which may adversely affect alcohol-acidic site interaction through oxygen of –OH group thus slowing down adsorption and dehydrogenation and giving less conversion of alcohol. The less selectivity of N-alkylated products with nitro derivative of alcohol (Entry 4; **Table 2**) shows reduced hydrogen transfer, probably due to much slow adsorption and dehydrogenation processes. The presence of an electron withdrawing group in aromatic amines (Entry 8 and 9; **Table 2**) may reduce their nucleophilicity (electron density at N) slowing down the imination step or formation of corresponding imine product and lowering the conversion of alcohol. The longer reaction time increased the conversion of alcohol as well as selectivity of N-alkylated products (Entry 4 and 8; **Table 2**). NH_2-MIL-125 also exhibited activity in N-alkylation with an aliphatic alcohol, *n*-hexanol (Entry 10; **Table 2**). The boiling point of *n*-hexanol (157°C) is close to the reaction temperature (160°C). During the reaction, *n*-hexanol will be mostly in vapor phase, which will minimize its contact with catalyst and aniline present in liquid phase. Therefore, the conversion of *n*-hexanol was less (25%). The conversion of alcohols having low boiling points can be improved by carrying out reactions in a sealed/ pressurized vessel [**10**].

The spent NH_2-MIL-125 was separated by filtration, washed with methanol (5 mL) and dried at 100°C for 6 h, and then was used in subsequent three reaction cycles under similar reaction condition. The spent catalyst was found to be reusable without significant loss in catalytic activity (98% conversion and 97% selectivity of **3** after third cycle). Furthermore, the characteristics of spent catalyst (measured by XRD, FTIR and BET surface area analysis; **ESI**) were observed to be similar to the fresh catalyst.

Conclusion

The NH_2-MIL-125 was found to be an excellent catalyst for borrowing hydrogen reactions, which was demonstrated for N-alkylation of amines with alcohols. The Ti– and carboxylates' O–atoms of Ti–O clusters are active sites for the catalysis of reaction. The NH_2-MIL-125 was found to be stable in the reaction showing reusability. This report suggests to study the catalytic activity of different MOFs, especially NH_2-functionalized MOFs, for borrowing hydrogen reactions.

Acknowledgement

The authors are thankful to Department of Science and Technology (DST), New Delhi, India for providing financial support (File No.: EMR/2016/000896), to the Vice-chancellor, D.D. University for providing analytical support, and to Department of Chemistry, S.P. University for support under CPEPA and CAS programs.

References

[1] A. Corma, J. Navas, M.J. Sabater, Advances in one-pot synthesis through borrowing hydrogen catalysis, Chem. Rev. 118 (2018) 1410–1459.

[2] A.J.A. Watson, J.M.J. Williams, The give and take of alcohol activation, Science 329 (2010) 635–636.

[3] A. Charvieux, J.B. Giorgi, N. Duguet, E. Métay, Solvent-free direct α-alkylation of ketones by alcohols catalyzed by nickel supported on silica–alumina, Green Chem. 20 (2018) 4210–4216.

[4] F. Huang, Z. Liu, Z. Yu, C-Alkylation of Ketones and Related Compounds by Alcohols: Transition-Metal-Catalyzed Dehydrogenation, Angew. Chem. Int. Ed. 55 (2016) 862–875.

[5] T. Irrgang, R. Kempe, 3d-Metal Catalyzed N- and C-Alkylation Reactions via Borrowing Hydrogen or Hydrogen Autotransfer, Chem. Rev. 119 (2019) 2524-2549.

[6] B.G. Reed-Berendt, K. Polidano, L.C. Morrill, Recent advances in homogeneous borrowing hydrogen catalysis using earth-abundant first row transition metals, Org. Biomol. Chem. 17 (2019) 1595–1607.

[7] M. Dixit, M. Mishra, P.A. Joshi, D.O. Shah, Clean borrowing hydrogen methodology using hydrotalcite supported copper catalyst, Catal. Commun. 33 (2013) 80–83.

[8] C. Risi, M. Calamante, E. Cini, V. Faltoni, E. Petricci, F. Rosatia, M. Taddei, In water alkylation of amines with alcohols through a borrowing hydrogen process catalysed by ruthenium nanoparticles, Green Chem. 22 (2020) 327–331.

[9] A.K. Bains, A. Kundu, S. Yadav, D. Adhikari, Borrowing Hydrogen-Mediated N-Alkylation Reactions by a Well-Defined Homogeneous Nickel Catalyst, ACS Catal. 9 (2019) 9051–9059.

[10] X. Liu, P. Hermange, J. Ruiz, D. Astruc, Pd/C as an efficient and reusable catalyst for the selective N-alkylation of amines with alcohols, ChemCatChem 8 (2016) 1043–1045.

[11] H. Yang, X. Cui, X. Dai, Y. Deng, F. Shi, Carbon-catalysed reductive hydrogen atom transfer reactions, Nat. Commun. 6 (2015) 6478-6488.

[12] H. Furukawa, K.E. Cordova, M. O'Keeffe, O.M. Yaghi, The chemistry and applications of metal-organic frameworks, Science 341 (2013) 974–986.

[13] A. Dhakshinamoorthy, Z. Li, H. Garcia, Catalysis and photocatalysis by metal organic frameworks, Chem. Soc. Rev. 47 (2018) 8134–8172.

[14] S. Yuan, L. Feng, K. Wang, J. Pang, M. Bosch, C. Lollar, Y. Sun, J. Qin, X. Yang, P. Zhang, Q. Wang, L. Zou, Y. Zhang, L. Zhang, Y. Fang, J. Li, H.-C. Zhou, Stable metal–organic frameworks: design, synthesis, and applications, Adv. Mater. 30 (2018) 1704303.

[15] S.-N. Kim, J. Kim, H.-Y. Kim, H.-Y. Cho, W.-S. Ahn, Adsorption/catalytic properties of MIL-125 and NH_2-MIL-125, Catal. Today 204 (2013) 85–93.

[16] X. Wang, D.Z. Wang, Aerobic oxidation of secondary benzylic alcohols and direct oxidative amidation of aryl aldehydes promoted by sodium hydride, Tetrahedron 67 (2011) 3406–3411.

[17] M. Martis, K. Mori, K. Fujiwara, W.-S. Ahn, H. Yamashita, Amine-functionalized MIL-125 with imbedded palladium nanoparticles as an efficient catalyst for dehydrogenation of formic acid at ambient temperature, J. Phys. Chem. C 117 (2013) 22805−22810.

[18] A. Grirrane, A. Corma, H. Garcia, Highly active and selective gold catalysts for the aerobic oxidative condensation of benzylamines to imines and one-pot, two-step synthesis of secondary benzylamines, J. Catal. 264 (2009) 138–144.

[19] M.M. Reddy, M.A. Kumar, P. Swamy, M. Naresh, K. Srujana, L.Satyanarayana, A. Venugopala, N. Narender,N-alkylation of amines with alcohols over nanosized zeolite beta, Green Chem. 15 (2013) 3474–3483.

[20] K.N. Tayade, M. Mishra, Munusamy K., R.S. Somani, Solvent free acid catalysed direct N-alkylation of amines with alcohols using Al grafted MCM-41, J. Mol. Catal. A: Chem. 390 (2014) 91–96.

[21] V.K. Díez, C.R. Apesteguía, J.I. Di Cosimo, Effect of the chemical composition on the catalytic performance of Mg_yAlO_x catalysts for alcohol elimination reactions, J. Catal. 215 (2003) 220–233.

[22] D. Sun, W. Liu, Y. Fu, Z. Fang, F. Sun, X. Fu, Y. Zhang, Z. Li, Noble metals can have different effects on photocatalysis over metal-organic frameworks (MOFs): a case Study on M/NH_2-MIL-125(Ti) (M=Pt and Au), Chem. Eur. J. 20 (2014) 4780–4788.

[23] V.G. Gandhi, M.K. Mishra, M.S. Rao, A. Kumar, P.A. Joshi, D.O. Shah, Comparative study on nano-crystalline titanium dioxide catalyzed photocatalytic degradation of aromatic carboxylic acids in aqueous medium, J. Ind. Eng. Chem. 17 (2011) 331–339.

[24] R. Tandon, T.A. Nigst, H. Zipse, Inductive Effects through alkyl groups-How long is long enough?, Eur. J. Org. Chem. 24 (2013) 5423–5430.

CRediT author statement

Nisha B. Patel: investigation,

Naresh Vala: validation,

Atindra Shukla: resources,

Subhadip Neogi: resources,

Manish Kumar Mishra: Conceptualization, methodology, supervision, writing, reviewing, and editing.

Declaration of interests

√ **The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.**

× The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Not applicable

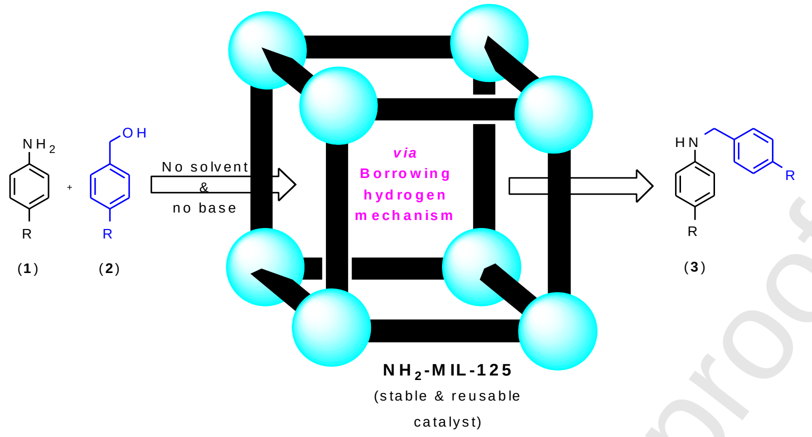
Ref.: Manuscript (CATCOM-D-20-00169) titled "Borrowing hydrogen activity of NH_2-MIL-125 for N-alkylation of amines with alcohols under solvent and base free condition".

Authors: Nisha B. Patel, Naresh Vala, Atindra Shukla, Subhadip Neogi, Manish Kumar Mishra

Dr. Manish Kumar Mishra Date: 25/05/2020

Department of Chemistry, Sardar Patel University

Vallabh Vidyanagar-388 120, Gujarat, India


NH2
OH
R
R
(1)
(2)
No solvent
&
no base
via
Borrowing
hydrogen
mechanism
NH2-MIL-125
(stable & reusable
catalyst)
HN
R
R
(3)

Research highlights

- Excellent borrowing hydrogen activity of NH_2-MIL-125.
- Solvent and base free N-alkylation of amines with alcohols using NH_2-MIL-125.
- Catalysis of reaction by Ti–O clusters of NH_2-MIL-125.
- Stability and reusability of NH_2-MIL-125 in the reaction.