JCRS

Journal of Chemical Reactivity and Synthesis 2023: 13(3) 240-254

Research Article

Employment of the magnetic nano-catalyst Fe_3O_4@SiO_2@CS@ $PO(OH)_2$/Cu(II) for the amination of alcohols

Farzaneh Ebrahimzadeh*

Department of Chemistry, Marvdasht Branch, Islamic Azad University, Marvdasht, Iran.

Department of Applied Researches, Chemical, Petroleum & Polymer Engineering, Research Center, Shiraz Branch, Islamic Azad University, Shiraz, Iran

ARTICLE INFO:

Received:
5 August 2023

Accepted:
18 October 2023

Available online:
20 October 2023

✉: F. Ebrahimzadeh
polychemfar@miau.ac.ir

ABSTRACT

In this research study, the Fe_3O_4@SiO_2@CS@ $PO(OH)_2$/Cu(II) core-shell nanoparticle serves as a highly effective magnetic catalyst. Benzylamine and ammonia were employed as the amination agents. The optimization process studied various factors, including the presence and kind of a base, reaction temperature, time of reaction, type of transition metal, and amount of catalyst to identify the most favorable parameters. The optimal conditions were observed when using 0.35 mmol of catalyst liganded to Cu(II) under reflux conditions for a duration of 5-24 h corresponding to the substrate in the presence of K_2CO_3. The results of the study revealed that electron-donating groups have a positive impact on the reaction rate, whereas electron-withdrawing groups, such as nitro, negatively influence the overall yield. It offers exceptional practicality in organic chemistry and industrial applications, primarily due to the ease of separating the catalyst using an external magnetic field, its stability, and its ability to be reused multiple times.

Keywords: Amination; Magnetic nanocatalyst; Core-shell nanoparticle; Catalyst optimization; Alcohol.

1. Introduction

Nitrogen-containing compounds, particularly amines, and their derivatives play a crucial role as versatile foundational units for diverse organic molecules and act as precursors to a range of biologically active compounds [1-3]. Synthetic organic chemists are fascinated by the formation of carbon–nitrogen bonds due to their broad applicability [4]. The progress in this field significantly contributes to generating a diverse range of organic molecules and bioactive compounds. In response to the growing demand for these compounds, various synthetic methods have been established, encompassing the Buchwald-Hartwig reaction [5], Ullmann reaction [6], Hofmann alkylation [7], hydrogen transfer processes [8], hydroamination [9], amination or hydroamination of alkenes and alkynes [10], amine production through the reduction of carbonyl compounds [11], and reduction of nitriles and nitro compounds [12]. However, these techniques present unique challenges, including the requirement for aryl/alkyl halide activation, the use of hazardous reagents, and dependence on potent reducing agents, all contributing to unfavorable environmental consequences. The development of efficient and practical catalytic systems for alcohol amination represents a significant leap towards more sustainable and environmentally conscious synthetic processes [13]. The process involves the transfer of hydrogen from alcohol to amine via the oxidation of alcohol to aldehyde, followed by amine formation and the reduction of imine.

Numerous transition-metal-based catalysts for the amination of alcohols have been investigated in the context of this oxidation/imination/reduction sequence [14]. Most of these catalysts are homogeneous, based on ruthenium [15-18], rhodium [19], platinum [20, 21], and iridium [22-24]. Despite the effectiveness of reported homogeneous catalysts in facilitating this reaction, they pose significant drawbacks, notably being more expensive and nonrecoverable. Exploring heterogeneous catalysts in the synthesis of specialty chemicals has emerged as a significant research focus. This interest stems from the potential benefits of these materials, including simplified recovery and reusability, along with the possibility of using inexpensive transition metals [25].

The findings clearly demonstrate that the incorporation of transition metals, such as Cu [26, 27], Fe [27, 28], Co [29], plays an essential role in facilitating the conversion of alcohols into amines .Within this category of catalysts, combinations of Cu-based metal precursors and ligands have emerged as potent catalytic systems, offering cost-effectiveness and selectivity, particularly in the production of primary amines using ammonia as the nitrogen source. Noteworthy catalysts employed in recent iterations of this reaction include copper-aluminum hydrotalcite NCM@EDTA/Cu(II) [26], $Cu(OH)_x/TiO_2$ [30, 31], CuAl-HT/K_2CO_3 [32], NiCu/Al_2O_3 [33], CuO-NiO/γ-Al_2O_3 [34], $Cu(OH)_x/Al_2O_3$ [35], Cu-Fe [36], Co/γ-Al_2O_3 [37], Ni/AlSiO, Ni/LaO and Ni /LaAlSiO [38], MgO/Hap [39] and iron-based heterogeneous catalysts [40].

The phosphate group exhibits remarkable ligand compatibility with transition metals, particularly displaying rapid and intriguing binding when in association with these metals. Recognizing the impact of these intermediary metals, the Fe_3O_4@SiO_2@CS@$POCl_{2-X}$ nanocomposite emerges as an advanced catalyst featuring a distinctive multilayered core-shell structure. Developed by our research group, this composite comprises layers beginning with an initial coating of iron oxide nanoparticles supported on silica, followed by chitosan, and ultimately, NCP@ $POCl_{2-X}$ [41]. Its primary application lies in the conversion of alcohols into alkyl halides. Notably, NCP@ $POCl_{2-X}$ readily transforms into $PO(OH)_2$ in the presence of trace amounts of water.

For simplicity, we will refer to this catalyst as NCP@$PO(OH)_2$, representing Fe_3O_4@SiO_2@CS@$PO(OH)_2$. This catalyst holds significance due to its ease of separation from the solution with a magnet and its stability in the reaction environment, attributed to the attached functional groups facilitating fast and stable ligand binding to transition metals. The synthesis of this catalyst is straightforward, and it has not been previously utilized in organic syntheses. In our research, we found it to be a practical and cost-effective tool for synthesizing amines. We employ it to convert alcohols, using NCP@$POCl_{2-X}$, Cu(II) solution, and a base as catalysts. Utilizing a catalyst in alcohol amination offers advantages such as recyclability, easy separation with a magnet, a simple synthesis process, and excellent selectivity. These qualities make it an attractive option for both researchers and industries.

2. Experimental

2.1. Catalyst Preparation: NCP@$PO(OH)_2$/Cu(II)

All material purchased from Merck company. The catalyst preparation method for NCP@ $POCl_{2-x}$ as previously reported [42], can be summarized as follows: Chitosan (2.5 g) is initially converted into a gel form using a 2% acetic acid solution and then sonicated for 3h. Simultaneously, in another container, Fe_3O_4@SiO_2 (2 g) [42] is mixed with CTAB salt (2.5 g) in deionized water. Then, the prepared chitosan gel is added to the above solution, and glutaraldehyde (30 µl) is introduced as a cross-linking agent for chitosan. Subsequently, @$POCl_{2-X}$ monohydrate (0.87 g) is added to the container contents, and the mixture is stirred for 5h. Following this, NCP@$POCl_{2-X}$ is separated and, after washing with water, it is dried under vacuum conditions for 24h at 50°C. In continuation, 1.0 M copper nitrate solution (20 mL) is added to 1g of NCP@$PO(OH)_2$ and left to equilibrate at room temperature for 24h. Finally, under the influence of an external magnetic field, the nanoparticles of NCP@$PO(OH)_2$ /Cu(II) are separated. After washing with water, they are dried at 50°C.

2.2. Alkylation of Benzyl Amine with Ammonia or Benzyl Alcohol Derivatives Using NCP@$PO(OH)_2$/Cu(II) Catalyst

In alkylation method, NCP@PO$(OH)_2$/Cu(II) (0.93 g, 0.35 mmol), the relevant benzyl alcohol (1 mmol) or ammonia (1 mmol), and benzylamine (3 mmol) are mixed together in the presence of 10 ml of acetonitrile as a solvent in a round-bottom flask. The mixture is heated and refluxed under argon gas conditions at 80°C for 3 to 24h . the time related to substrate. Conversion and product yield are examined via Thin-layer chromatography (TLC), and the final purification is conducted. The NMR spectrum is compared to a standard sample. All the products are known compounds, and the NMR spectrum characteristics of the products listed in Table 2 are provided:

1. Dibenzylamine: Table 2, entry 1. ^{1}H NMR ($CDCl_3$) δ(ppm) = 6.12 (m, 10H), 3.69 (s, 4H).

2. *N*-Benzyl-N-(4-methoxybenzyl)amine: Table 2, entry 3.^{1}H NMR ($CDCl_3$) δ(ppm) = 7.62-7.15 (m, 9H), 3.87 (s, 4H), 3.77 (s, 3H), 1.76 (s, 1H).

3. *N*-Benzyl-N-(4-nitrophenyl)amine: Table 2, entry 4. ^{1}H NMR ($CDCl_3$) δ(ppm) = 8.16 (d, 2H), 7.41-7.17 (m, 5H), 6.65 (d, 2H), 4.78 (s, 1H), 4.66 (s, 1H).

4. *N*-Benzylheptan-1-amine: Table 2, entry 5.^{1}H NMR ($CDCl_3$) δ(ppm) = 7.52-6.17 (m, 5H), 3.49 (d, 2H), 2.81 (s1, H), 1.58 (m, 2H), 1.36 (m, 2H), 0.90 (m, 3H).

3. Results and discussion

The phosphoric functional group has taken our interest in the field of chemistry, prompting us to conduct a more detailed examination of the recently reported NCP@$POCl_{2-x}$. FESEM of the catalyst represented in Figure 1. It shows that the presence of the phosphate group leads to an increase in the size of nanoparticles in comparison to the core-shell catalyst, which involves the Fe_3O_4@SiO_2@Chitosan layer, exhibiting an average size of 190 nm. In contrast, the NCP@$POCl_{2-x}$ configuration reveals nanoparticles with a larger average size, measuring 236 nm. This size variation could potentially influence the catalytic properties and overall performance of the NCP@$POCl_{2-x}$ catalyst, and further exploration is warranted to understand its implications in chemical processes.

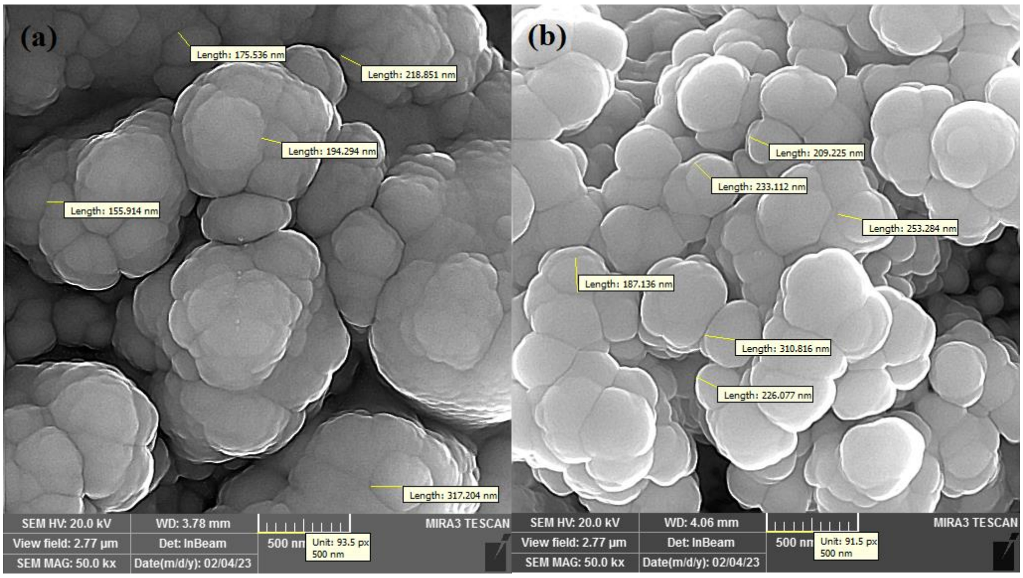
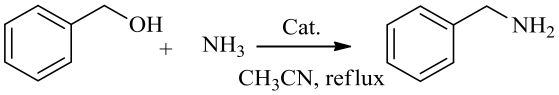


Fig. 1. FESEM image of (a) NCP (b)NCP@$POCl_{2-x}$

To improve the synthesis of the second type of amines, our initial investigations focused on examining the amination of benzyl alcohol with ammonia. We initiated this reaction using the NCP@$POCl_{2-x}$ catalyst. Various parameters were accurately studied, including the choice of base, the type of transition metal, the reaction duration, temperature, and the quantity of catalyst used.

The experiments were conducted using K_2CO_3 as the base at a temperature of 80°C. Optimization results revealed that the inclusion of a reducing agent, such as $NaBH_4$, in the reaction completion and reduction step significantly improved the reaction yield (Table 1, entry 4). However, in the absence of a reducing agent, the reaction still proceeded but required an extended duration and the major product is the oxidation product. The presence of another transition metal (Co(II)) was also studied, and the results indicated that the reaction could proceed with the catalyst serving as a ligand for Co(II), but a higher conversion yield was obtained in the presence of Cu(II) (Table 1, entries 4-7). In the presence of Co(II), some benzyl aldehyde is produced as a byproduct because the conversion of Co(II) to Co(I) occurs more slowly than Cu(II) to Cu(I). Therefore, our focus remains on NCP@PO(OH)$_2$/Cu(II). The optimal result was achieved using 0.35 mmol of NCP@PO(OH)$_2$/Cu(II) catalyst per 1 mmol of benzyl alcohol at 80 °C, under reflux conditions for 7 h, resulting in a 90% conversion (Table 1, entry 9). We recognize that a significant portion of @POCl$_{2-x}$ transforms into @PO(OH)$_2$ in the presence of water. Due to this observation, entries 4 to 8 in Table 1 prompted us to rename the catalyst as @PO(OH)$_2$.

Table 1. Optimization of alcohol (1 mmol) to amine conversion in the presence of NCP@PO(OH)$_2$/Cu(II) catalyst.



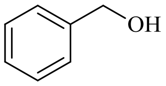
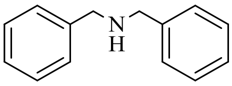
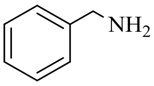
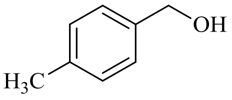
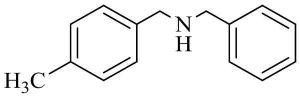
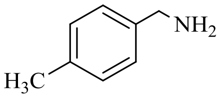
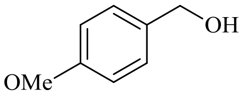
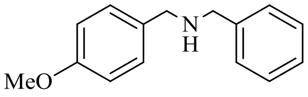
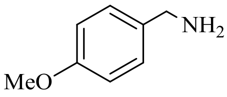
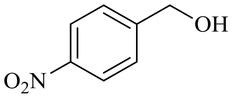
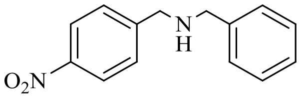
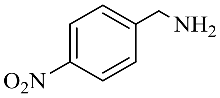
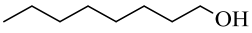
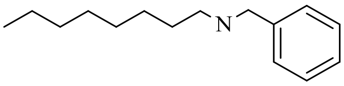
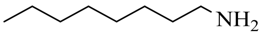
Entry	Amount of Catalyst (mmol)	Catalyst (type)	Base/ reducing agent	Time(h)	Yield of benzyl amin (%)	Yield of benzaldehyde as a by-product (%)
1	0.4	NCP@ POCl$_{2-x}$	-	24	-	0
2	1	NCP@ POCl$_{2-x}$ /Cu(II)	-	24	-	65
3	1	NCP@ PO(OH)$_2$/Cu(II)	K_2CO_3	5	90	10
4	1	NCP@@PO(OH)$_2$/Cu(II)	K_2CO_3/$NaBH_4$	3	100	0
5	1	NCP@PO(OH)$_2$/Co(II)	K_2CO_3/$NaBH_4$	24	93	0
6	1	NCP@PO(OH)$_2$/Cu(II)+Co(II)	K_2CO_3/$NaBH_4$	24	87	0
7	1	NCP@PO(OH)$_2$/ Co(II)	K_2CO_3	24	85	15
8	0.5	NCP@PO(OH)$_2$/Cu(II)	K_2CO_3	5	100	0
9	0.35	NCP@PO(OH)$_2$/Cu(II)	K_2CO_3	7	90	0

Titration studies, employing a standard Mg^{2+} solution with the Eriochrome Black T (EBT) indicator, indicated that each gram of the NCP@$POCl_{2-x}$ catalyst contains approximately 4.0 mmol of phosphate group. Consequently, the optimized 3.5 mmol catalyst base on phosphate functional group approximately is 0.87 g. The addition of copper ions results in the coordination of phosphate ligands with copper ions, forming complexes.

We explored reactions involving benzyl alcohol derivatives with various functional groups, encompassing both electron-withdrawing groups like nitro and electron-donating groups like methoxy in the presence of ammonia or benzyl alcohol. The findings indicated that the presence of electron-donating groups in the benzyl ring enhanced the reaction rate, whereas the inclusion of electron-withdrawing groups, such as nitro, diminished the reaction rate and necessitated a longer reaction time. Furthermore, the overall yield decreased in cases with electron-withdrawing groups (Table 2, entries 3,4). The results also clearly showed that in the presence of ammonia, the reaction was carried out with a higher yield compared to benzyl amine.

In the case of aliphatic alcohols, there was a notable decrease in the conversion rate and overall yield, with aliphatic alcohols generally exhibiting lower yields compared to benzyl alcohols (Table 2, entry 5). This can be attributed to the increased complexity associated with generating carbonyl intermediates from aliphatic alcohols. The results of these investigations are summarized in Table 2.

Table 2. Conversion of various alcohols in terms of structure in the reaction with ammonia or benzylamine in the presence of the NCP@@POCl$_{2-X}$ /Cu(II) catalyst.

Entry	substrate	Amin	Product	Time(h)	Yield (%)
1		Benzyl amin		10	89
		Ammonia		7	90
2		Benzyl amin		8	92
		Ammonia		5	93
3		Benzyl amin		8	89
		Ammonia		5	90
4		Benzyl amin		24	70
		Ammonia		24	76
5		Benzyl amin		24	65
		Ammonia		24	60

While this method requires relatively high reaction temperatures and additional amounts of amines, the use of the cost-effective and heterogeneous catalyst NCP@PO(OH)$_2$/Cu(II), instead of expensive and non-recyclable homogeneous catalysts, offers the advantage of easy separation in the presence of an external magnetic field. It demonstrates the versatility of the process in converting various aliphatic and benzylic alcohols containing both electron-donating and electron-withdrawing groups into amines. The presence of ammonia slightly accelerates the reaction time with almost equal conversion yield.

The reaction mechanism involves the conversion of alcohol into a carbonyl compound, followed by the formation of an imine between the amine and the newly generated carbonyl, which is then subsequently reduced.

The phosphate groups in the catalyst exhibit a remarkable ability to fast form a complex with Cu(II) ions, creating the catalytic ensemble NCP@ $PO(OH)_2$/Cu(II). This cooperative interaction facilitates the conversion of Cu(II) to Cu(I) and vice versa, occurring seamlessly within the framework of the NCP@ $PO(OH)_2$ catalyst (Figure 2). During research into the role of a base in alcohol amination, reactions shown without a base resulted in no observable product formation. This observation suggests that the oxidation step likely proceeds through alkoxide formation, involving the dissociation of a proton from the alcohol in the presence of a base and its coordination with the copper center in NCP@ $PO(OH)_2$/Cu(II).

The amino groups linked to chitosan in the catalyst play a crucial role in enhancing reaction kinetics and facilitating the elimination of hydrogen from the alkoxy intermediate. This process ultimately aids in the in-situ preparation of aldehyde and subsequent imine formation. This enhancement enables the reaction under mild alkaline conditions. Subsequently, copper alkoxy intermediates undergo conversion to amine products, revealing a dynamic process involving the reversible transformation of Cu(I) to Cu(II), facilitated by the catalyst's structure. The $PO(OH)_2$ ligand, along with the hydroxyl and amino groups linked to chitosan in the nanostructured catalyst, establishes an environment favorable for the easy variety of the oxidation state of the Cu ion. Essentially, the presence of $PO(OH)_2$

simplifies the conditions required to revert Cu(I) to its Cu(II) oxidation state. The reaction mechanism is depicted in Figure 2.

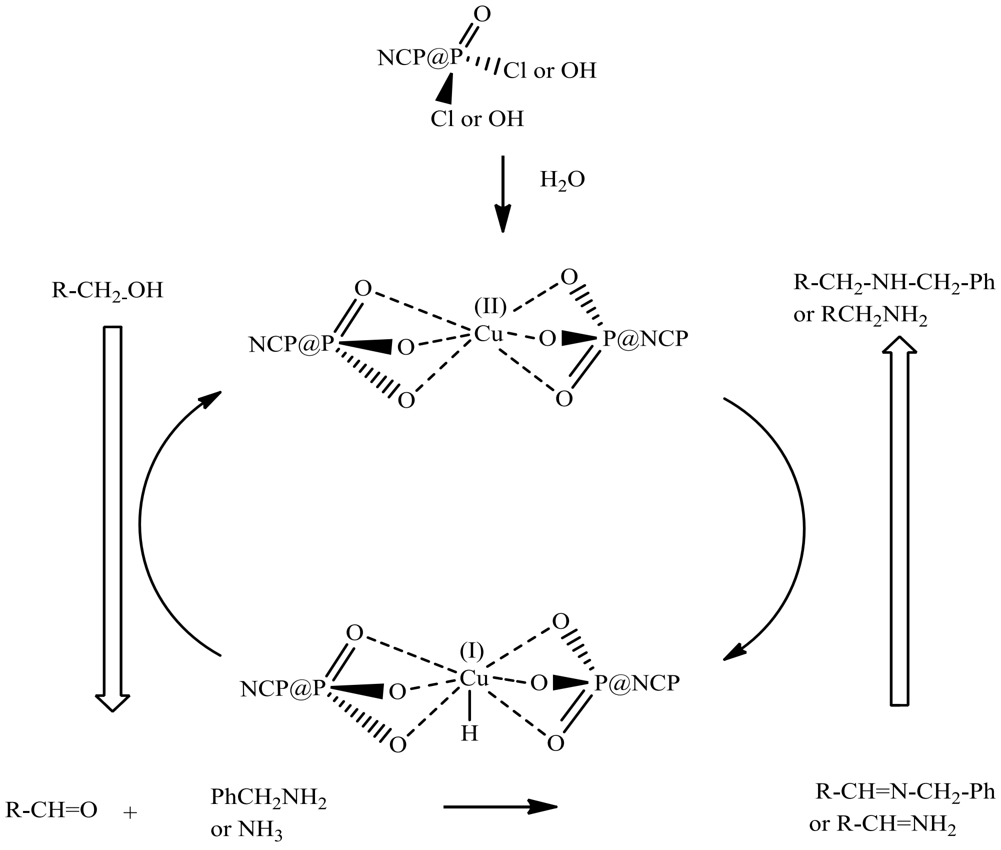
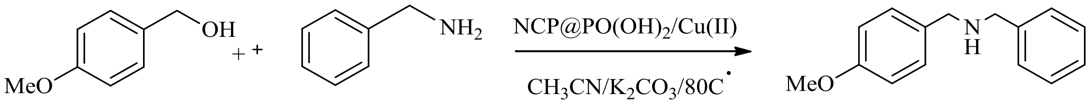


Fig. 2. Proposed Mechanism for the Reaction of Alcohols with Amines in the Presence of the NCP@ $PO(OH)_2$ /Cu(II) Catalyst.

The NCP@P $PO(OH)_2$/Cu(II) catalyst can be easily separated from the reaction mixture with the aid of an external magnetic field. After recovery, the catalyst underwent washing with acetone, ethanol, and water sequentially, followed by drying at 65 ˚C. This recovered catalyst was then employed in subsequent cycles to assess its reusability and effectiveness, as detailed in Table 3.

Table 3. Catalyst recovery in the reaction of methoxybenzyl alcohol and benzyl amine



Entry	Recovery Steps	Yield (%)
1	first	89
2	Second	85
3	third	80
4	forth	65

In conclusion, the NCP@PO$(OH)_2$/Cu(II) catalyst demonstrates its efficacy in the amination of benzyl alcohols, yielding a high conversion rate under optimal conditions. This catalytic system shows considerable potential in organic chemistry, presenting advantages like facile catalyst separation through an external magnetic field, stability in the reaction environment, and straightforward recyclability.

References:

[1] D. Erdag, O. Merhan, B. Yildiz, *Biogenic amines* 8 (2018) 1-14.

[2] V. Froidevaux, C. Negrell. S, Caillol. J.-P, Pascault, B, Boutevin, *Chemical Reviews* 116 (2016) 14181-14224.

[3] A. K. Kar, A. Chauhan, R. Srivastava, *Sustainable Energy & Fuels* 7 (2023) 1855-1869.

[4] Kantak, A. A. ; Carbon-nitrogen bond formation via tandem carbon-hydrogen (CH) and nitrogen-hydrogen (NH) bond functionalization, University of Rhode Island 2014.

[5] C. J. Lu, Q. Xu, J. Feng, R. R. Liu, *Angewandte Chemie International Edition* 62 (2023) e202216863.

[6] H. Lin, D. Sun, *Organic preparations and procedures international* 45 (2013) 341-394.

[7] C. M. Pearson. J. W. Fyfe, T. N. Snaddon, *Angewandte Chemie International Edition* 58 (2019) 10521-10527.

[8] A. Corma, J. Navas, M. J. Sabater, *Chemical reviews* 118 (2018) 1410-1459.

[9] J. M. Alonso, M. P. Muñoz, *Organic letters* 21 (2019) 7639-7644.

[10] J. Escorihuela, A. Lledós, G. Ujaque, *Chemical Reviews* 123 (2023) 9139-9203.

[11] C. Xie, J. Song, M. Hua, Y. Hu, X. Huang, H. Wu, G. Yang, B. Han, *ACS Catalysis* 10 (2020) 7763-7772.

[12] B. Zeynizadeh, F. Mohammad Aminzadeh, H. Mousavi, *Research on Chemical Intermediates* 45 (2019) 3329-3357.

[13] A. Baiker, J. Kijenski, *Catalysis Reviews Science and Engineering* 27 (1985) 653-697.

[14] R. B. Wilson, R. M. Laine, *Journal of the American Chemical Society* 107 (1985) 361-369.

[15] X. Ye. P. N. Plessow, M. K. Brinks, M. Schelwies, T. Schaub, F. Rominger, R. Paciello, M. Limbach, P. Hofmann, *Journal of the American Chemical Society* 136 (2014) 5923-5929,.

[16] E. Balaraman, D. Srimani, Y. Diskin-Posner, D. Milstein, *Catalysis Letters* 145 (2015) 139-144.

[17] X.-P. Fu, P. Han, Y.-Z. Wang, S. Wang, N. Yan, *Journal of Catalysis* 399 (2021) 121-131.

[18] H. Zou, J. Chen, *Applied Catalysis B: Environmental* 309 (2022) 121262-121265.

[19] S. A. Runikhina, M. A. Arsenov, V. B. Kharitonov, E. R. Sovdagarova, O. Chusova, Y. V. Nelyubina, G. L. Denisov, D. L. Usanov, D. Chusov, D. A. Loginov, *Journal of Organometallic Chemistry* 867 (2018) 106-112.

[20] J. J. Wilson, S. J. Lippard, *Chemical reviews* 114 (2014) 4470-4495.

[21] T. Ohshima, Y. Miyamoto, J. Ipposhi, Y. Nakahara, M. Utsunomiya, K. Mashima, *Journal of the American Chemical Society* 131 (2009) 14317-14328.

[22] F. Li, C. Sun, H. Shan, X. Zou, J. Xie, *ChemCatChem* 5 (2013) 1543-1552.

[23] S. Michlik, T. Hille, R. Kempe, *Advanced Synthesis & Catalysis* 354 (2012) 847-862.

[24] C. M. Galvin, R. M. Waymouth, *Journal of the American Chemical Society* 142 (2020) 19368-19378.

[25] H. Huang, Y. Wei, Y. Cheng, S. Xiao, M. Chen, Z. Wei, *Catalysts* 13 (2023) 1350-1355.

[26] F. Ebrahimzadeh, *International Research Journal of Modernization in Engineering Technology and Science* 5 (2023) 2640-2646,.

[27] T. Irrgang, R. Kempe, *Chemical reviews* 119 (2018) 2524-2549.

[28] T. Yan, B. L. Feringa, K. Barta, *Nature Communications* 5 (2014) 5602-5607.

[29] Z. Wei, H. Liu, K. Zhou, H. Shu, Y. Liu, *Reaction Kinetics, Mechanisms and Catalysis* 127 (2019) 931-943.

[30] J. He, K. Yamaguchi, N. Mizuno, *Chemistry letters* 39 (2010) 1182-1183.

[31] K. Yamaguchi, N. Mizuno, *Journal of the Japan Petroleum Institute* 57 (2014) 251-260.

[32] P. R. Likhar, R. Arundhathi, M. L. Kantam, P. S. Prathima, Wiley Online Library2009.

[33] X. Wang, J. Hu, C. Xu, Y. Chen, L. Dai, *Molecular Catalysis* 547 (2023) 113359-113362,.

[34] J.-M. Huang, L.-F. Xu, C. Qian, X.-Z. Chen, *Chemical Papers* 66 (2012) 304-307.

[35] C. Luo, C. Qian, H. Luo, L. Feng, Y. Chen, X. Chen, *Asia□Pacific Journal of Chemical Engineering* 9 (2014) 272-279.

[36] G. Gogoi, M. J. Baruah, S. Biswas, N. Hoque, S. Lee, Y.-B. Park, L. Saikia, K. K. Bania, *Molecular Catalysis* 528 (2022) 112458-112462.

[37] J. H. Cho, J. H. Park, T.-S. Chang, G. Seo, C.-H. Shin, *Applied Catalysis A: General* 417-418 (2012) 313-319.

[38] S. Li, M. Wen, H. Chen, Z. Ni, J. Xu, J. Shen, *Journal of Catalysis* 350 (2017) 141-148.

[39] N. Kerru, L. Gummidi, S. Maddila, S. B. Jonnalagadda, *Inorganic Chemistry Communications* 123 (2021) 108321-108325.

[40] D. Sahu, A. R. Silva, P. Das, *RSC advances* 5 (2015) 78553-78560.

[41] F. Ebrahimzadeh, A. Jamalain, S. Zaree, *Phosphorus, Sulfur, and Silicon and the Related Elements* (2023), 10.1080/10426507.2023.2279614, *in press*.

[42] H. Ding, Y. Zhang, S. Wang, J. Xu, S. Xu, G. Li, *Chemistry of Materials* 24 (2012) 4572-4580.