

# Cost-Effective Iron Metal Catalyst for the Synthesis of Primary Carbonates from Alcohols and Urea

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## ABSTRACT

A simple cheap iron metal precursor iron (II) per chlorate  $[\text{Fe}(\text{ClO}_4)_2 \cdot x\text{H}_2\text{O}]$  is used in this work as efficient catalyst for the synthesis of primary carbamates. Carboamylation of alcohols in presence of inexpensive and non toxic carbonyl source urea allow us to produce the desired product under mild reaction conditions. Without use of phosgene and its derivatives which are usually employ to prepare the mentioned product, make the catalytic protocol eco-friendly and pleasing. Here the developed catalytic protocol is atom economical direct process to obtain valuable fine chemicals N-unsubstituted carbamates or primary carbamates from easily available urea and alcohols.

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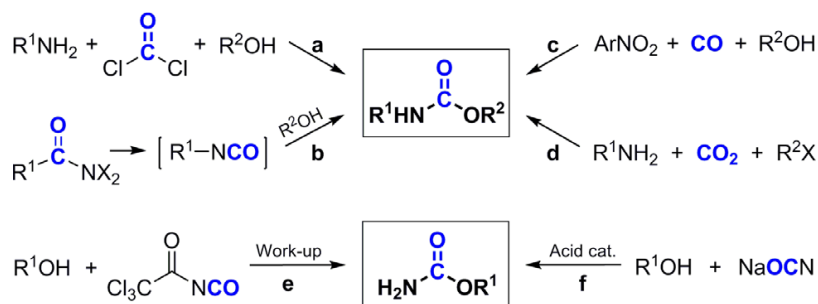
## INTRODUCTION

Now a day's efficient, cheap and sustainable methodologies development for the production of valuable chemicals and superior building blocks is gaining extraordinary attentions towards the researchers (Patel, A. D. Meesters, K. den Uil, H. de Jong, E. Blok, K. Patel, M. K. 2012). The focus of classical synthesis of organic compounds mainly relied high yield process whereas recent protocols stipulate perfections of waste prevention, toxicity, and sustainability (P. Anastas, N. Eghbali, 2010). The replacements of hazardous reagents by more readily available environmentally benign resources make those methodologies greener. Again, it is vastly preferred to amplify the atom efficiency and develop step-economy for a given transformation to diminish the quantity of residues. For this purpose the use of catalytic protocols are advantageous contrasts to stoichiometric reactions for scheming the yield selectivity and reactivity of substrates (Delidovich I. and Palkovits, R. 2016).

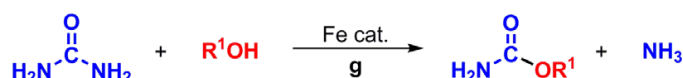
Recently due to low toxicity and high abundance nature of iron metal, the Fe-containing catalysts are gaining particular interest to develop efficient catalytic process. Moreover a numbers of iron metal salts readily accessible and cheap as a result a variety of catalysis processes are already established where Fe is utilized as catalyst (Bauer, I. and Knçlker, H.-J. 2015). In this purpose, here we represent an iron catalyzed transformation of production of primary carbamates. The said product is an important type of organic compound which are frequently found in agro chemicals (as herbicides, antiviral agents, bactericides, and pesticides) (Ocampo, J.A. Barea, J.M. 1985), several medicines (like albendazole, flupirtine, retigabine, physostigmine etc.) (Wickenden, A.D. Yu, W. Zou, A. Jegla, T. Wagoner, P.K. 2000), cosmetics, polymer, biologically active compounds and organic fine chemicals (Kreye, O. Mutlu, H. Meier M. A. R. 2013). Moreover carbamates can protect amino groups of various amino acids as a consequence the compound is utilized in peptide synthesis chemistry (Jacquemard, U. Bénèteau, V. Lefoix, M. Routier, S. Mérour, J.-Y. Coudert, G. 2004).

Till date various reaction processes are published for the synthesis of carbamates. Among them most widely used conventional methods involves the utilization of highly toxic phosgene and its derivatives (Scheme 1a). Substitute catalytic methodologies have been flourished, like rearrangement reactions (Lossen, Hoffmann, Curtius,) via isocyanate intermediates (Hamon, F. Prie, G. Lecornue, F. Papot, S. 2009) nitroaromatics reductive carbonylation (Gadge, S. T. Bhanage, B. M. 2014), or amines carboxylation with carbon dioxide in presence of alcohols electrophilic agents (Scheme 1b-d) (Watile, R. A. Bhanage, B. M. 2014). But all these methods can't smoothly applied for the production of primary carbamates. A conventional methods are established to synthesis of primary carbamates by the reaction of alcohols with cyanate salt or organic isocyanates (Scheme 1e-f) (Sardarian, A. R. Inaloo, I. D. 2015). Such protocol suffers from the drawbacks of the requirement of selective acid catalyst or manufacture of carbamoylation agent's using lethal precursors. In this perspective, an eco-friendly alternative route is developed thereafter where catalytic reaction of alcohols in presence of urea is employed for the preparation of primary carbamates (Scheme 1g). Very few number of research articles are published following the above route regarding the said compound synthesis in presence of  $\text{BF}_3$ ,  $\text{PbO}$ , polyphosphoric acid, or Pd catalyst (Qin, F. Li, Q. Wang, J. Feng, Y. Kang, M. Zhu, Y. Wang, X. 2008).

**Conventional syntheses of N-substituted and primary carbamates**



**This work: Iron-catalyzed reaction of urea with alcohols**



Scheme 1 Traditional Methodologies for the Preparation of Primary and N-Substituted Carbamates. Iron Catalyzed Reaction of Alcohols With urea.

**MATERIALS AND REAGENTS**

All reagent grade chemicals are commercially obtainable and brought those from commercial resource. The reagents were used as received. Aldrich chemical company, USA supplied the metal precursor  $\text{Fe}(\text{ClO}_4)_2 \cdot x\text{H}_2\text{O}$  and utilized devoid of further purification.

*Caution!* Although no problem was encountered during the laboratory work, it should be always remembered that metal perchlorate salts are potentially explosive so small quantity of material should be synthesized with carefully handle.

**Physical Measurement**

Bruker AMX- 400 instrument was used for  $^1\text{H}$  NMR spectra of the products in presence of TMS (tetramethylsilane) as internal standard.

**RESULTS AND DISCUSSION**

**Primary carbonates synthesis from urea and alcohols in presence of iron perchlorate as catalyst**

Catalytic process for primary carbamates synthesis was carried out using carbonylation reaction of alcohols with environmentally benign carbonyl source urea (Scheme 2).

**Scheme 2: Catalytic Primary Carbamates Synthesis**

At first we performed the reaction by using propyl alcohol (8 mmol) as model substrate and urea (6 mmol) in presence of iron perchlorate (0.01 mmol) under MeCN (acetonitrile) solvent medium at  $90^\circ\text{C}$ . As per our expectation we got 68% of propyl carbamate product (Table 1, entry 1) after 6h of reaction. When the same reaction is carried out in absence of any catalyst, only trace amount of desired product was obtained (Table 1, entry 2). Thus the result indicates that without any catalyst the reaction will not proceed smoothly. Then the reaction was carried out under different solvent medium in presence of the iron catalyst (Table 1, entries 3-11). All most all solvent gave us nearly moderate quantity yield of desired product except water and n-butyl ether. Absent of any solvent produced only traces of the product (Table 1, entry 12). Among the all solvents, 1,4-dioxane was the suitable one for the reaction as the product yield was obtained (75%) from the reaction under that solvent (Table 1, entry 10).

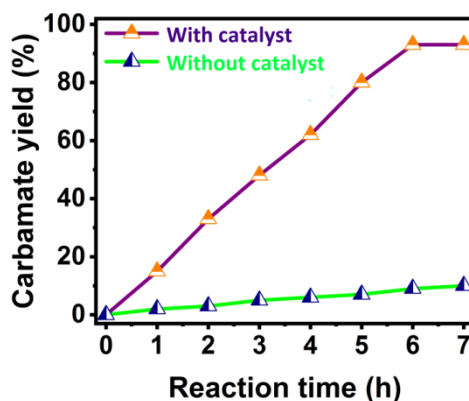
After selection of solvent, the temperature optimization for the reaction was checked. Lowering the reaction temperature ( $80^\circ\text{C}$ ), yielded lower amount of desired product (Table 1, entry 13) due to the less amount of substrate crossed the activation energy barrier upon decreasing temperature. Now enhancement of reaction temperature gave us better quantity product yield (Table 1, entries 14, 15). From the table it is clear that the optimum temperature of the catalytic reaction is  $110^\circ\text{C}$  as further increased of reaction temperature (i.e.  $120^\circ\text{C}$ ) did not enhanced much product yield percentage (Table 1, entry 16).

Finally kinetics of the catalytic reaction was observed, figure 1 described the kinetics plot of the reaction under optimized reaction conditions (i.e. propyl alcohol (6 mmol), urea (4 mmol), Fe (ClO<sub>4</sub>)<sub>2</sub>.xH<sub>2</sub>O (0.01 mmol), 1,4-dioxane (8 ml), 110°C).

**Table 1: Control Reactions for Optimization of Catalytic Process**

Entry	Solvent	Temperature (°C)	% yield of propyl carbamate <sup>b</sup>
1	MeCN	90	68
2	MeCN	90	Trace amount
3	DCM (Dichloromethane)	90	50
4	CHCl <sub>3</sub> (Chloroform)	90	48
5	Toluene	90	45
6	Benzene	90	57
7	DMF	90	54
8	DMSO	90	60
9	Water	90	23
10	1,4-Dioxane	90	75
11	n-Bu <sub>2</sub> O	90	31
12	No solvent	90	Trace amount
13	1,4-Dioxane	80	61
14	1,4-Dioxane	100	84
15	1,4-Dioxane	110	92
16	1,4-Dioxane	120	93

<sup>a</sup>Reaction conditions: alcohol (8 mmol), urea (6mmol), Fe(ClO<sub>4</sub>)<sub>2</sub>.xH<sub>2</sub>O (0.01 mmol), 6h; <sup>b</sup>isolated yield.



**Figure 1: kinetics of the catalytic reaction [reaction conditions: propyl alcohol (8 mmol), urea (6 mmol), Fe (ClO<sub>4</sub>)<sub>2</sub>.xH<sub>2</sub>O (0.01 mmol), 1, 4-dioxane (8 ml), 110°C].**

After receiving the optimizing reaction condition we performed the substrate tolerance for the reaction by varying the alcohol substrate. Like propyl alcohol butyl alcohol as well as isopropyl alcohol produced high percentage of respective primary carbamates product after 6h of reaction (Table 2).

**Table 3: Substrate Tolerance of the Catalytic Reaction**

Entry	Alcohol	Products	Time (h)	Yield (%) <sup>b</sup>
1			6	92
2			6	94
3			6	88

<sup>a</sup>Reaction conditions: propyl alcohol (8 mmol), urea (6 mmol), Fe(ClO<sub>4</sub>)<sub>2</sub>.xH<sub>2</sub>O (0.01 mmol), 1,4-dioxane (8 ml), 110°C, 6h; <sup>b</sup>isolated yield.

### Experimental Section

Urea (6 mmol) and aliphatic alcohol (8 mmol) and Fe(ClO<sub>4</sub>)<sub>2</sub>.xH<sub>2</sub>O (0.01 mmol) were purged in a 20 ml round bottom flask under 8 ml 1,4-dioxane medium. The mixture was stirring at 110°C temperature for 6h. Then the reaction was quenched and the mixture was filtered. To the filtrate work up was done using CH<sub>3</sub>COOEt (ethyl acetate) and brine solution for multiple times. The organic layer was separated and dried by dry sodium sulphate. After purification of organic layer was concentrated by rota-evaporator and obtained sample was characterized by <sup>1</sup>H NMR spectroscopy.

<sup>1</sup>H NMR spectra of obtained primary carbamate products

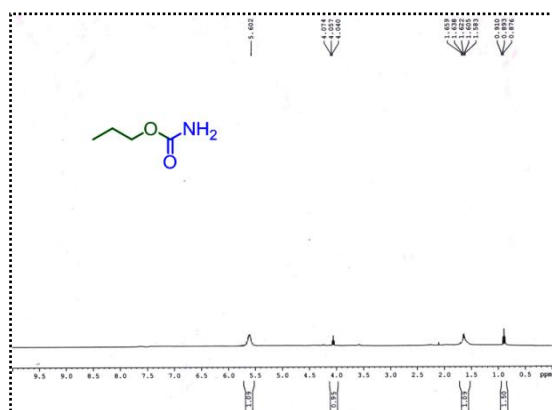


Figure 2: <sup>1</sup>H NMR Spectra of Propyl Carbonate

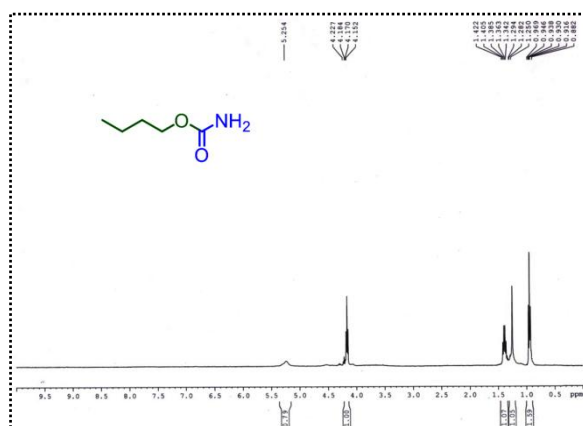


Figure 3: <sup>1</sup>H NMR spectra of Butyl carbonate

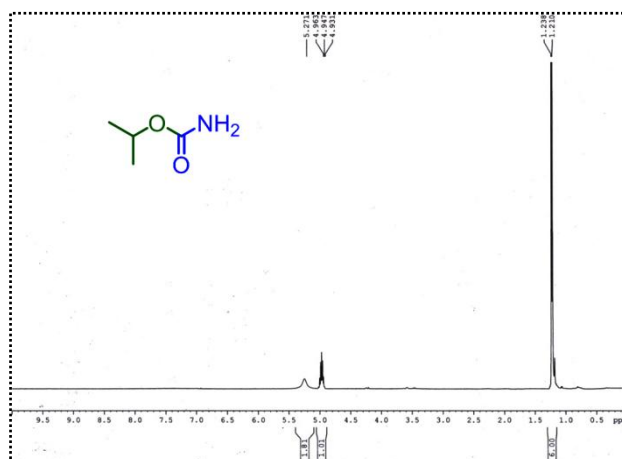


Figure 4: <sup>1</sup>H NMR Spectra of Isopropyl Carbonate

## CONCLUSION

A methodology has developed here for iron perchlorate catalyzed reaction of easily available nucleophile (like alcohol) and urea. An uncomplicated nucleophilic substitution permits us to produce primary carbamates from cheap urea and alcohols. Application of inexpensive, safe, abundant, less toxic  $\text{Fe}(\text{ClO}_4)_2 \cdot x\text{H}_2\text{O}$  as catalyst, high selectivity desired primary carbamates yield is obtained without formation of bi-products like oligo-, polymers or acyclic carbonates. In view of build up this protocol, other important Lewis acids be useful for near future implementations.

## REFERENCES

- [1]. Patel, A. D. Meesters, K. den Uil, H. de Jong, E. Blok, K. and Patel, M. K. 2012. Sustainability assessment of novel chemical processes at early stage: application to biobased processes. *Energy & Environmental Science*, 5, 8430-8444.
- [2]. Anastas, P. and Eghbali, N. 2010. *Green Chemistry: Principles and Practice*. Chemical Society Reviews, 39, 301-312.
- [3]. Delidovich, I. and Palkovits, R. 2016. Catalytic *versus* stoichiometric reagents as a key concept for Green Chemistry. *Green Chemistry*, 18, 590– 593.
- [4]. Bauer, I. and Knölker, H.-J. 2015. Iron Catalysis in Organic Synthesis. *Chemical Reviews*, 115, 3170– 3387.
- [5]. Ocampo, J.A. and Barea, J.M. 1985. Effect of carbamate herbicides on VA mycorrhizal infection and plant growth, *Plant Soil*, 85, 375–383.
- [6]. Wickeder, A.D. Yu, W. Zou, A. Jegla, T. Wagoner, P.K. 2000. Retigabine, A Novel Anti-Convulsant, Enhances Activation of KCNQ2/Q3 Potassium Channels, *Molecular pharmacology*, 58, 591– 600.
- [7]. Kreye, O. Mutlu, H. Meier, M.A.R. 2013. Sustainable routes to polyurethane precursors, *Green Chemistry*, 15, 1431–1455.
- [8]. Jacquemard, U. Bénétteau, V. Lefoix, M. Routier, S. Mérour, J.-Y. Coudert, G. 2004. Mild and selective deprotection of carbamates with  $\text{Bu}_4\text{NF}$ , *Tetrahedron*. 60, 10039–10047.
- [9]. F. Hamon, G. Prie, F. Lecornue, Papot, S. 2009. Cyanuric chloride: an efficient reagent for the Lossen rearrangement *Tetrahedron Letter*. 50, 6800-6802.
- [10]. Gadge, S. T. and Bhanage, B. M. 2014. Recent developments in palladium catalysed carbonylation reactions. *RSC Advances*. 4, 10367-10389.
- [11]. Wailed, R. A. and Bhanage, B. M. 2014. Ruthenium catalyzed regioselective coupling of terminal alkynes, amine and carbon dioxide leading to anti-Markovnikov adducts. *RSC Advances*. 4, 23022– 23026.
- [12]. Sardinian, A. R. Inaloo, I. D. 2015. 4-Dodecylbenzenesulfonic acid (DBSA) promoted solvent-free diversity-oriented synthesis of primary carbamates, *S*-thiocarbamates and ureas. *RSC Advances*. 5, 76626-76641.
- [13]. Qin, F. Li, Q. Wang, J. Feng, Y. Kang, M. Zhu, Y. Wang, X. 2008. One Pot Synthesis of Methyl *N*-Phenyl Carbamate from Aniline, Urea and Methanol. *Catalysis Letter*. 126, 419-425.