International Journal of Advance and Innovative Research
Volume 6, Issue 1 (XVI): January - March, 2019
ISSN 2394 - 7780

SYNTHESIS OF CARBONATES FROM CHLOROMETHYL CHLOROFORMATES AND ITS SOME APPLICATIONS

Navnath D. Gunjal, Somnath S. Gholap, Sunil S. Bhagat
Department of Chemistry, R. B. Attal Arts, Science and Commerce College, Georai, Dist-Beed
Department of Chemistry, Padmashri Vikhe Patil College, Pravaranagar Tal-Rahata, Dist-Ahmednagar

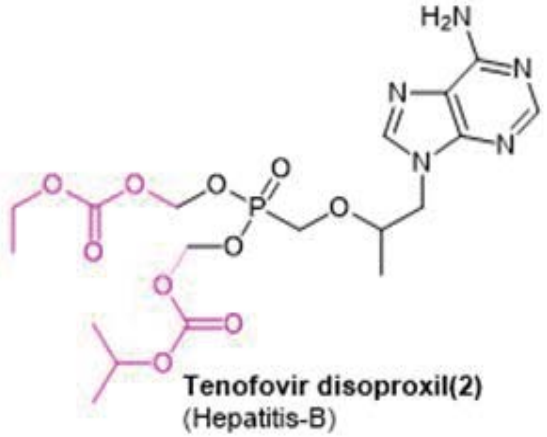
ABSTRACT
We are developed an efficient, simple and scalable process of various carbonates from chloromethyl chloroformates. This novel methodology procedure offers a very effective and environmentally suitable procedure for carbonates preparation. This conversion offers corresponding carbonates in good to excellent yields. Alkyl carbonates are important role in organic chemistry as well as a biodegradable chemical intermediates because its moderate toxicity.

Keywords: Chloromethyl chloroformate, alcohols, carbonates, 4-dimethylaminopyridine and dimethylformamide

INTRODUCTION
The carbonates are very important role in organic compounds and intermediates due to their unique properties physicochemical as well as versatility chemicals. Organic carbonates are widely used in industrial level as synthesis of plastics, many more pharmaceuticals, herbicides, agrochemicals, additives and as well as lubricants due to its environmentally safe and it easily biodegradability for human health due to their moderate toxicity1. Carbonates are used for the extraction of metals like bismuth, iron, lead, cadmium, gold from acidic solution as salts as well as complexes form2. Many carbonates an excellent polar additives are used for skin cleaners, lipstick, hair conditioners and also in other aromatic products3. The many typical methods of carbonates are using toxic gases like phosgene used, this are used in excess pyridine in anhydrous solvent at different temperatures4. Some methods for carbonate formation using carbon dioxide with alcohol through hemicarbonic acids is also decomposes and unstable to alcohol, it isolated as inorganic salts solids and it high melting inorganic salts5. In direct phosgenation reaction of hydroxyl compounds requires higher temperatures and gets a lower quality as well as yield obtained, also forms a unwanted impurities6. The formation of carbonates from using alcohols and carbon monoxide through metal compounds in particular as mercury, palladium and copper they not get the selective product formation7. Carbonates formation using quaternary ammonium salts, this requires high temperature and yield not satisfactory for scaleble8. Some symmetrical carbonates synthesis of alkyl halides at nucleophilic substitution reactions using TEAC, this results side reactions of alcohol formation so decrease the yield of carbonates9. In the above reported methods have disadvantages are very toxic reagents, unsuitability reaction conditions and it not a biodegradable. It has a unsatisfactory yields, unsuitable for commercial scale up, has no reusability and a limited scope for industrial level. Therefore in last year we are developed new methods for industrial usable and easily commercially produced this products.

The carbonate compounds as a Baloxavir marboxil(1) is an antiviral medication for treatment of influenza A and influenza B10, Tenofovir disoproxil(2), is a medication used to treat chronic hepatitis B and to prevent and treat HIV/AIDS11, Clopidogrel prodrug(3), is an antiplatelet medication that is used to reduce the risk of heart disease and stroke in those at high risk12, Imatinib prodrug(4), is a medication used to treat cancer, specifically, it is used for chronic myelogenous leukemia (CML) and acute lymphocytic leukemia13 Figure-1.

Baloxavir marboxil(1)
(Antiviral)



Tenofovir disoproxil(2)
(Hepatitis-B)

ISSN 2394 - 7780

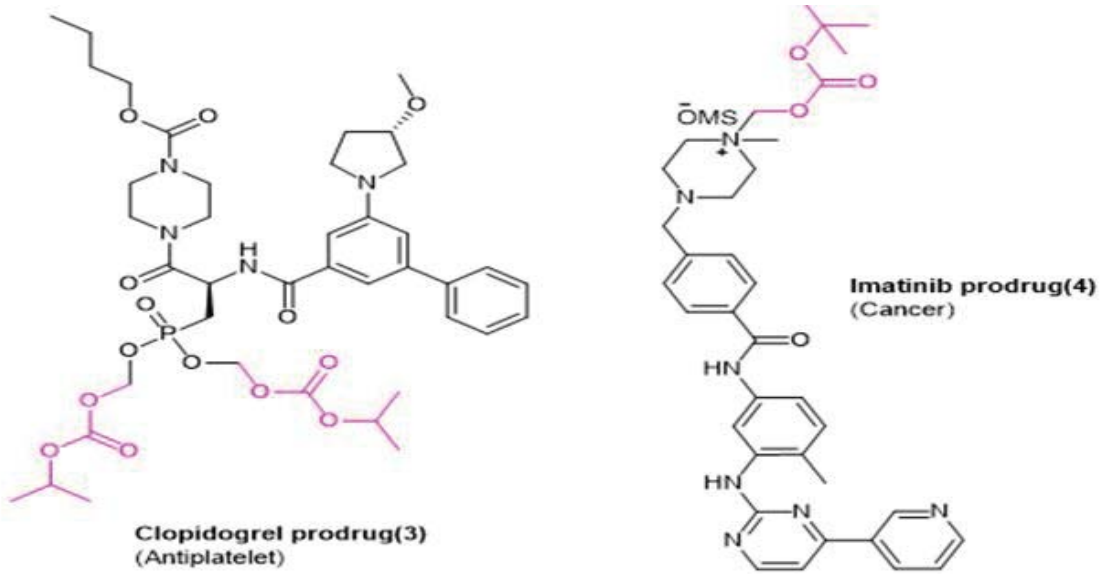


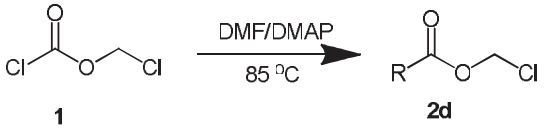
Figure-1: Some biologically active carbonate compounds

In coming days, the carbonate chemistry development is very needful due to its various and wide application in active ingredients, therefore development of carbonate is very numerous and well efforts for development. The chloroformate to carbonate synthesis, many more methods available using pyridine, phosgene intermediates, toxic metals but various drawbacks of this methods like silver carbonate, alkyl halides14, using palladium metals15, antimony trioxide and aluminium trioxide have required higher temperature16, activating agent required such as crown ethers, polyamines17. Considering these reported methods has several drawbacks and several disadvantages for using it drastic condition, hazardous reagents and chemicals, using expensive catalysts, limited scope and environmentally hazardous effluent. So, therefore still need to develop economically valuable and industrial suitable method for carbonate synthesis from chloroformates.

In this development, the chloromethyl chloroformate is synthesis using methyl formate, this process is chlorine gas purged at heating condition to get monochloro derivative of chloroformate it distilled under reduced pressure to get chloromethyl chloroformate23. In this conversion of carbonates synthesis the dimethylformamide and dimethylamino pyridine is easily available in reagent grade. In this method development of protocols easily availability of solvent has much a low toxicity and used in a variety of products24.It has used as a various chemical synthesis as well as a daily routine in pharmaceutical industry, agrochemical and lubricating coating division for various surfaces in aqueous and non-aqueous environments25 .It has been used to for catalytic amount in various synthesis, is a active role in transformation of reaction as good rates26. Therefore in this way, we shows here the one-pot green protocol , catalyst free, yield efficient synthesis of nitriles from aldehydes using polyethylene glycol-200 as a green solvents (Scheme-1).

In conclusion, we have developed a practical, easily scalable, cost efficient with the scope and limitations of catalyst for transformation of chloroformate to carbonates mediated by dimethylamino pyridine and dimethylformamide. Initially we have chosen tert-butanol as a model compound for the desired carbonate formations from chloromethyl chloroformate. We have reacted chloromethyl chloroformate 1 (1.00 mmol) with tert-butanol (5 ml) using dimethylamino pyridine (0.15 mmol) and dimethylformamide(1 ml) as a catalytic solvent and it optimize as a different temperatures for reaction conditions to product forms tert-butyl chloromethyl carbonate 2d(Table 1)

Table-1: Reaction condition optimization.



1 2d

Sr. No	Temperature (^{0}C)	Time(h)	Yield 2d^b(%)
1	RT	24	-
2	50	24	42
3	85	9	89

ISSN 2394 - 7780

4	85	24	-[c]
5	85	24	23[d]
6	85	24	20[e]
7	100	9	86
8	120	9	89

[a]Reactions are performed using the chloromethyl chloroformate

1 (1.00 mmol), Dimethylamino pyridine (0.15 mmol),

Dimethylformamide(1 ml) in tert-butanol (5 ml).

[b] Product isolated yields shows.

[c] Reaction preformed without dimethylamino pyridine.

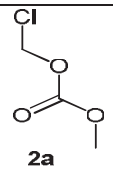
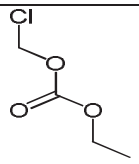
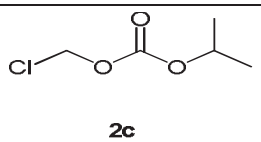
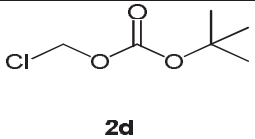
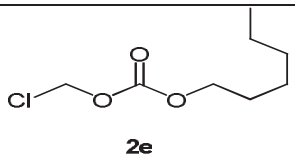
[d] Reaction performed without dimethylformamide.

[e] Reaction performed in dimethylamino pyridine and without dimethylformamide.

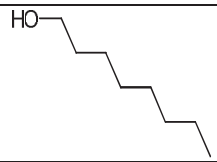
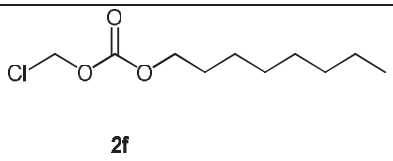
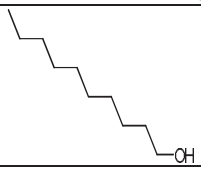
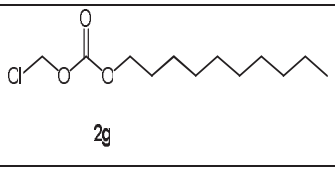
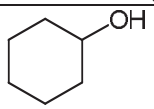
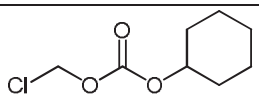
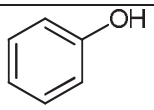
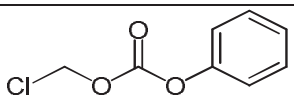
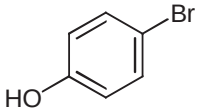
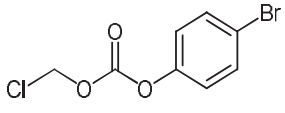
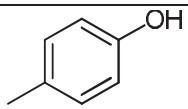
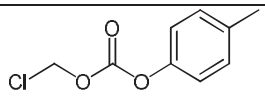
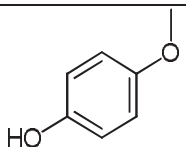
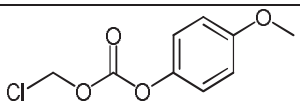
Table-2: Comparison of yield of 2d with other methods reported in literature

Entry	Catalytic System	Yield (%)	Lit.
1.	Dichloromethane/Pyridine	76	18
2.	Manganese salt with palladium	65	19
3.	Diethyl ether/Pyridine/10	56	20
4.	Pyridine/-10 °C	59	21
5.	$Hg(oAc)_2$/180-200 °C	82	22
6.	Antimony trioxide and aluminum trioxide/195-200 °C	73	16
7.	Present method	89	--

Table-2: Synthesis of Carbonates from chloromethyl chloroformates using various alcohols

Entry	Alcohol	Product(2)	Time (h)	Yield (%)	Boiling Point (^{0}C)/Torr		Ref
					Found	Reported	
1	—OH	 2a	12.5	86	137-139	139-140	27
2	HO—	 2b	11	85	133.6-134	135.1	28
3	HO	 2c	14	83	148.5	147.63	28
4	HO	 2d	9	89	156-157.6	160	29
5	HO	 2e	16	89	147.6	145.6-146.1	28

ISSN 2394 - 7780

6		 **2f**	16	85	163.1-164.8	165	29
7		 **2g**	17	82	165.3	160.5	29
8		 **2h**	14	65	123.1	128.2-128.7	29
9		 **2i**	20	70	166	-	29
10		 **2j**	19	67	136.6	-	30
11		 **2k**	15	88	173-174.6	174.3-175.1	30
12		 **2l**	15	86	186.5	-	30

[a]Reactions are performed using the chloromethyl chloroformate 1 (1.00 mmol), Dimethylamino pyridine (0.15 mmol), dimethylformamide(1ml) in alcohols (5 ml).

[b]Product isolated yields shows.

At room temperature product 2d was not formed, chloromethyl chloroformate unreacted as such as shown on Table 1.The reaction was further probed by increasing the temperature at 85°C, the reaction was proceeds smoothly and tert-butyl chloromethyl carbonate 2d was obtained 89 % yield (Table 1,Sr.No.3). Therefore it is observed that the good yield of carbonate was obtained in presence of dimethylamino pyridine and dimethylformamide at 850C (Table 1,Sr.No.3). There is more improvement on reaction time and reaction temperature, but product yield not significant improve as per our expectations (Table 1, Sr.No.7 and Sr.No.8), so 850C was chosen the reaction temperature. When we performed reaction without dimethylamino pyridine no product was formed (Table 1,Sr.No.4). We performed reaction without dimethylformamide, the very less product was formed (Table 1,Sr. No.5). It is also important to mention that when the reaction was performed using dimethylamino pyridine and out dimethylformamide, the 2d product was formed very less (Table 1,Sr.No.6). In an developed reaction condition, chloromethyl chloroformate 1(1.00 mmol), dimethylamino pyridine (0.15 mmol) and dimethylformamide (1 ml) was added in tert-butanol (4 ml) and stir at 850C for 9 h to obtained tert-butyl chloromethyl carbonate 2d in 89 % yield (Table 1,Sr.No.3).

We have optimized that the one-pot transformation of chloromethyl chloroformate to corresponding carbonate using alcohol was maintained to the same extent with structurally diverse alcohols (Table 2). The carbonate formation reaction was almost complete in less than nine hours for all substrates tested by TLC, boiling point were recorded using open capillary and is uncorrected. Carbonates were isolated in good to excellent yields as described in Table 2. The interaction of chloromethyl chloroformate in to dimethylamino pyridine and

ISSN 2394 - 7780

dimethylformamide to forms C-N- insitu weak bond. Then the C-N- bond easily cleavage through alcohol nucleophilic substitution addition to forms our desired carbonate. Then subsequent expulsion of carbonate to regenerates dimethylamino pyridine and is acting as a catalyst. These reaction process is mechanistically related to oxidation of chloroformate to carbonates. After the reaction condition optimization, a study regarding the reuse of dimethylamino pyridine was not performed due to after reaction completion the reaction mass quenched in water and extracted to dichloromethane. The dimethylamino pyridine was soluble in water and its isolation is shows31 from water.

In day to day life environment pollution is a serious concern to reduced effluent to reduce the pollution, has been an increasing interests to the design of degradable catalyst reactions, a absence of hazardous solvents, low cost, recyclable and environmentally friendly solvents due to reduced effluent to reduce pollution. In mostly all the chemical and pharmaceutical industries observed that the catalysts and hazardous solvents are not always eco-friendly or biodegradable. In this way our development method is superior and promoting environment friendly method due to our method effluent is biodegradable and it minimizes COD and BOD. The dimethylamino pyridine and dimethylformamide has a different combination of chemical and physical properties such as a polarity, no flammability, high boiling point, low toxicity and it easily availability so it promoted to use as good solvent in organic solvents. Therefore we developed here the efficient, one-pot synthesis of carbonates from chloromethyl chloroformate using alcohol as a solvent. The main aspect of dimethylamino pyridine and dimethylformamide in this reaction was established by the fact that in the absence of dimethylamino pyridine and dimethylformamide the formation of carbonates from chloroformates does not takes place. Therefore it conclude that the dimethylamino pyridine and dimethylformamide is an essential component for reaction. In addition optimization, we have performed reaction using tertiary nitrogen base like triethyl amine to gives the less conversion obtained, therefore the role of dimethylamino pyridine and dimethylformamide in this transformation is required.

In conclusion, we have developed here a practical and cost efficient one-pot protocol for the transformation of chloromethyl chloroformate to corresponding carbonates by using corresponding alcohols in presence of dimethylamino pyridine and dimethylformamide as catalyst. These method advantages are wide scope of transformations, it can readily applied to big scale processes at plant level with excellent yield, cost efficient, selectivity, biodegradable effluent for environment secure, and convenient process for preparation of desired product.

ACKNOWLEDGMENTS
The authors are thankful to the DST, New Delhi for financial support and we thanks to Atul Ltd for providing chemicals.

REFERENCES
1. Frevel L. K.; Gilpin J. A, Mich M.; (The Dow Chemical Co.) U.S. Pat. 3,642,868, 1972; Chem. Abstr. 1972, 77, 62818.
2. Masakatsu N.; Yoshuki T.; (Mitsui Toatsu Chemicals) Jap. Pat. 05,77,553, 1993; Chem. Abstr. 1993, 119, 59853.
3. Houben Weyl.; Methoden der Organischen Chemie ; Georg Thieme Verlag: Stuttgart, 1983; Vol. E4, p 64.
4. Chemische Fabrik von Heyden.; Ger. Pat. 109,933, 1900 Friedl, 1901, 5.
5. Houben Weyl.; Methoden der Organischen Chemie; Georg Thieme Verlag: Stuttgart, 1983; Vol. E4, p 64.
6. Nguyen, M. T.; Ha, T. K. J.; Am. Chem. Soc. 1984, 106, 599.
7. Romano U.; Tesei, R.; Massi, M. M.; Rebora, P.; Ind. Eng. Chem. Prod. Res. Dev. 1980, 19, 396; Romano, U. S. Chim.Ind. 1993, 75.
8. (a)Rokicki, G.; Kuran, W. Monatsh. Chem soc.. 1984, 115, 205. (b) Rokicki, G.; Kuran, W. Bull. Chem. Soc. Jpn. 1984, 57, 1662.
9. Mucciante, V.; Rossi, L.; Feroci, M.; Sotgiu, G. Synth. Commun. 2002, 32, 1205.
10. Hayden F.G, et al.; Engl J Med 2018; 379:913–23.
11. Wei, Kaiju et al.; Faming Zhuanli Shenqing, 102399149, 04 Apr 2012.
12. Caroff, Eva et al.; Journal of Medicinal Chemistry, 58(23), 9133-9153; 2015.
13. Yang FC, Ingram DA, Chen S, Zhu Y, Yuan J, Li X, Yang X, Knowles S; Cell. 135 (3): 437–48.

ISSN 2394 - 7780

14. Beilstein Handbuch der Organischen Chemie; Springer-Verlag:Berlin, 1921; Vol. III, pp 3, 5.
15. Hallgren, J. E.; Lucas, G. M.; Matthews, R. O. J. Organomet. Chem. 1981, 204, 135.
16. Ball, P.; Fullmann, H.; Heitz, W. Angew. Chem., Int. Ed. Engl.1980, 19 (9), 718.
17. Rokicki, G.; Pawlicki, J.; Kuran, W. Polymer J. 1982, 14 (11), 839.
18. Chemische Fabrik von Heyden .;Ger. Pat. 116,386 1900 Friedl, 1904, 6, 1160.
19. Romano, U.; Tesei, R.; Massi, M. M.; Rebora, P. Ind. Eng.Chem. Prod. Res. Dev. 1980, 19, 396
20. Arimilli, Murty N. et al.; PCT Int. Appl., 9804569, 05 Feb 1998.
21. Thomas, Joshua D. and Sloan, Kenneth B.;Tetrahedron Letters, 48(1), 109-112; 2007.
22. Pews, R. G. J. Chem. Soc., Chem. Commun. 1974, 4, 119.
23. J. prakt. Chem., 1887, 36, 213-305; Bull. soc. chim., 1920, 27, 97; Rev. prod, chim., 1922, 25, 685.
24. Sheftel, Victor O. (2000), CRC. pp. 1114–1116.
25. Taft, R. W.; Abraham, M. H.; Doherty, R. M.; Kamlet, M. J. (1985). Nature. 313 (6001): 384–386.
26. Hofle, G.; Steglich, W.; Vorbruggen, H. (1978). "4-Dialkylaminopyridines as Highly Active Acylation Catalysts". Angew. Chem. Int. Ed. Engl. 17(8): 569–583
27. H. Buysch, N. Schon, and G. Jeromin .;U.S. Pat. 6,175,017.; Jan. 16, 2001.
28. Naesens L1, Bischofberger N, Augustijns P, Annaert P, Van den Mooter G, Arimilli MN, Kim CU, De Clercq E.Antimicrob Agents Chemother. 1998 Jul; 42(7): 1568–1573
29. R. Grigg and V. Savic, Chem. Comm. 2381 (2000).
30. Avid A. Evans, Felix Urpi, Todd C. Somers, J. Stephen Clark, and Mark T. Bilodeau.; J. Am. Chem. Soc., 1990, 112 (22), pp 8215–8216.
31. Zhihui Liu, Qiaoqiao Ma, Yuxiu Liu, and Qingmin Wang.; Org. Lett., 2014, 16 (1), pp 236–239.
32. General procedure for synthesis of carbonates from chloromethyl chloroformate: To a single neck round bottom flask chloromethyl chloroformate (1.00 mmol), dimethylamino pyridine (0.15 mmol) and dimethylformamide (1 ml) in respective alcohols (5 ml). The reaction mixture was heated at respective alcohol boiling point to stir at for the time indicated in Table-2. After the completion of reaction was confirmed by TLC (10 % ethyl acetate in hexane) at TLC indicator, then reaction mixture was cooled to room temperature and diluted with water (5 ml). Product (2a to 2l) was extracted in dichloromethane (3 × 3 ml), solvent dried with magnesium sulphate and solvent evaporated under reduced pressure to give the crude residue. The crude residue material was distilled under column packing with respective carbonate boiling point under vacuum. Compounds were characterized and comparison with melting point, 1H NMR, 13C NMR, mass spectra with literatures.