Journal of CO_2 Utilization 24 (2018) 361–368

Contents lists available at ScienceDirect

Journal of CO_2 Utilization

journal homepage: www.elsevier.com/locate/jcou

Review Article

Three component coupling of amines, alkyl halides and carbon dioxide: An environmentally benign access to carbamate esters (urethanes)

Esmail Vessally[a], Robab Mohammadi[a], Akram Hosseinian[b], Ladan Edjlali[c], Mirzaagha Babazadeh[c,*]

[a] Department of Chemistry, Payame Noor University, Tehran, Iran
[b] Department of Engineering Science, College of Engineering, University of Tehran, P.O. Box 11365-4563, Tehran, Iran
[c] Department of Chemistry, Tabriz Branch, Islamic Azad University, Tabriz, Iran

ARTICLE INFO

Keywords:
Carbon dioxide
Carbamate esters
Three-component reactions
Carboxylative coupling
Cs_2CO_3

ABSTRACT

Carbamate esters represent an important class of compounds showing a wide range of interesting biological properties. Such compounds exhibit anti-cancer, anti-HIV, anticonvulsant, antiretroviral, anti-nociceptive, anti-inflammatory, anti-Alzheimer, and antibiotic properties. Moreover, these compounds have many applications in the area of synthetic organic chemistry. Consequently, considerable efforts have devoted to the development of efficient and practical synthetic routes to these useful compounds. However, common preparations leading to these target compounds are limited by requiring toxic reagents such as phosgene, its derivatives, or isocyanates. Synthesis of titled compounds employing CO_2 as a clean and safe carbonyl reagent in place of toxic phosgene or isocyanates has attracted considerable attention in recent years. In this mini-review we will highlight the most important developments on the synthesis of carbamate esters through the carboxylative coupling of amines with alkyl halides and CO_2 by hoping that it will stimulate researchers to develop new and improved methods for the synthesis of these biologically and synthetically important compounds with sustainable chemistry and Green Chemistry perspectives.

1. Introduction

Carbamate esters (urethanes) play a major role in drug discovery and development. These compounds are fundamental structural elements of many approved human therapeutic agents [1]. For example (Fig. 1), Ritonavir **1** with brand name of Norvir is a synthetic carbamate antiretroviral medication marketed worldwide for the treatment of HIV/AIDS [2]. Irinotecan **2** with trade name Camptosar is an anti-neoplastic enzyme inhibitor used to treat colorectal cancer and small cell lung cancer. This drug works by blocking topoisomerase I enzyme which cells need it to divide and grow [3]. Physostigmine **3** (Eserine) is carbamate-containing natural product isolated from the Calabar bean. This alkaloid is one of the oldest drugs and was successfully used for the treatment of certain types of glaucoma in 1864 [4]. Neostigmine **4**, sold under the brand name Prostigmin among others, is a cholinesterase inhibitor used in the treatment of myasthenia gravis and to reverse the effects of muscle relaxants such as gallamine and tubocurarine [5]. It is noted that this drug is on the world health organization's list of essential medicines. Newer drug albendazole **5** (Albenza) is a promising anti-parasitic drug that used to treat certain infections of tapeworms or other parasites [6]. Therefore, considerable efforts have devoted in the recent past for the development of efficient and practical synthetic routes to carbamate esters. Although a number of different methodologies have been proposed for the synthesis of these target compounds [7], they limited by requiring highly toxic phosgene or isocyanate derivatives. Therefore, the development of safe methods for the efficient synthesis of titled compounds is highly desirable.

The conversion of carbon dioxide (CO_2) into value-added chemicals has received more and more attention in recent years, not only because CO_2 is the chief greenhouse gas responsible for global warming and ocean acidification, but also because it has been regarded as an abundant, inexpensive, safe, nontoxic, nonflammable, and renewable C1 feedstock [8–18]. In this context, the synthesis of organic carbamates employing CO_2 as a clean and safe carbonyl reagent in place of toxic phosgene or isocyanates has attracted considerable attention in recent years [19]. Without the slightest doubt, access to organic compounds by multicomponent routes is particularly attractive in terms of synthetic efficiency, and also from the environmental point of view [20]. One of the most important methodologies for the preparation of acyclic organic carbamates from CO_2 involves the three-component reaction of

* Corresponding author.
E-mail address: babazadeh@iaut.ac.ir (M. Babazadeh).

https://doi.org/10.1016/j.jcou.2018.01.015
Received 13 October 2017; Received in revised form 15 December 2017; Accepted 22 January 2018

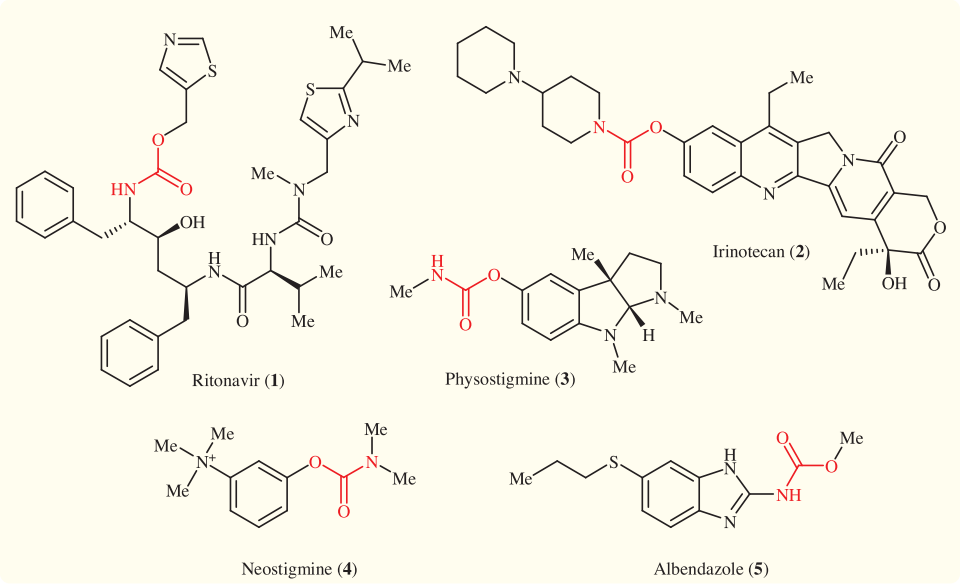


Fig. 1. Selected examples of drugs containing a urethane moiety.

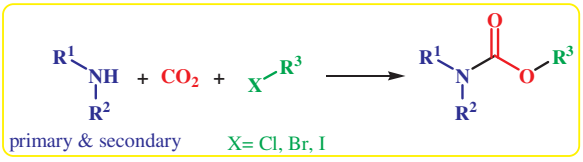
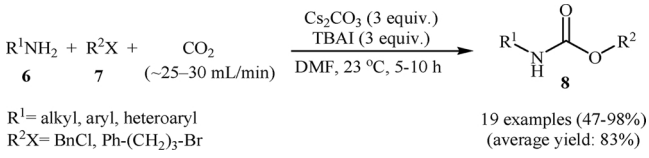


Fig. 2. Carboxylative coupling of amines with alkyl halides and CO_2.

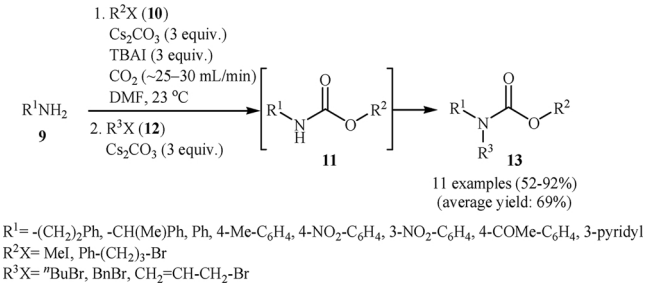
amines, alkyl halides and carbon dioxide (Fig. 2). Since a number of developments in this interesting field have occurred from 1984 to present, a comprehensive review on this chemistry seems to be timely. As a part of our continual review papers on the chemical conversion of CO_2 or propargyl derivatives into valuable organic compound [21], in this mini-review we will highlight the most important advances on the synthesis of carbamate esters through the carboxylative coupling of amines with alkyl halides and CO_2 by hoping that it will stimulate researchers to develop new and improved methods for the synthesis of these biologically and synthetically important compounds with sustainable chemistry and Green Chemistry perspectives.

2. Base-promoted couplings

The base-promoted three-component reaction of amines with alkyl halides and carbon dioxide is a well-known synthetic route to acyclic carbamates and has been the subject of a number of papers [22–25]. One of the earliest general reports on this chemistry appeared in 1994, when aliphatic amines, alkyl halides, and CO_2 underwent carboxylative coupling in the presence of Cs_2CO_3 as a base in DMF. The corresponding carbamates were obtained in moderate to excellent yields. It is noted that K_2CO_3 was also found to promote the reaction; however, in lower yields [26]. Seven years later, the group of Jung showed that the treatment of various aliphatic, aromatic and heteroaromatic amines **6** with alkyl halides **7** in the presence of Cs_2CO_3 as a base, tetrabutylammonium iodide (TBAI) as an additive, and DMF as a solvent under carbon dioxide atmosphere can produce the corresponding carbamates **8** in moderate to excellent yields (Scheme 1). This optimized protocol displayed wide functional group tolerance and was further utilized to the synthesis of amino acid-based carbamates with excellent yields [27]. Subsequently, the same authors extended their methodology to the synthesis of *N*-alkyl carbamates **13** through a one-pot, two-step reaction sequence starting from the three-component coupling of primary amines **9**, alkyl halides **10**, and CO_2 using the



Scheme 1. Synthesis of carbamate esters **8** *via* three-component reaction of amines **6** with alkyl halides **7** and carbon dioxide in the presence of Cs_2CO_3/TBAI combination as catalytic system.



Scheme 2. Jung's synthesis of carbamate esters **13**.

aforementioned catalytic system, followed by *N*-alkylation of the *in situ* generated carbamates **11** with different alkyl halides **12** in the presence of Cs_2CO_3 as a base (Scheme 2). Beside good yields, operational simplicity, and broad substrate scope can be considered as the advantages of this interesting four-component coupling process [28]. In their subsequent studies, they reinvestigated the same three-component reaction by using benzyl chloride and good results were observed [29].

Inspired by these works, Fox et al. synthesized successfully a series of biologically and synthetically important carbazates **16** *via* reaction of corresponding hydrazines **14** with alkyl halides **15** under the CO_2 atmosphere at room temperature. The reaction tolerates both aryl and alkyl hydrazines and gave corresponding products in moderate to high yields (Scheme 3). The authors also showed the application of this novel procedure for the high yielding syntheses of dithiocarbazate derivatives by replacing CO_2 with CS_2 [30].

In 2009, Hooker et al. were able to demonstrate that 1,8-diazabicyclo(5.4.0)undec-7-ene (DBU) can efficiently catalyze the carboxylative coupling of amines with alkyl halides and CO_2. Thus, a variety of radio-labeled carbamates **19** were synthesized by treatment of