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Research Note

$Al(HSO_4)_3$ Mediated for the Preparation of Primary Carbamates under Solvent-Free Conditions

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$Al(HSO_4)_3$ as an acidic salt, i.e. a mild, convenient and efficient reagent, was applied for the conversion of compounds containing a hydroxyl group to primary carbamates, at room temperature, with high yield and purity and without any epimerization, under solvent-free conditions.

INTRODUCTION

Carbamates (urethanes) are used in agriculture [1-5], pharmacology [1,2,6] and the chemical industry [1,3,7]. The carbamate group (-$OCONH_2$) constitutes a typical feature of certain classes of natural products, e.g. bleomycins, mitomycins and discodermolide [8]. In addition to these, among the various amine-protecting groups, carbamates are commonly used, due to their chemical stability towards acids, bases and hydrogenation [9]. These materials are most commonly prepared from amines and alcohols by carbonylation, using phosgene in organic solvents, which are also toxic and flammable [1-3]. These procedures, though efficient, pose environmental and operational concerns, since highly harmful and corrosive reagents are used. A safer and eco-friendly alternative was conceived by the use of non-toxic carbon dioxide [10]. However, these methods cannot produce N-unsubstituted (primary) carbamates. The synthesis of N-unsubstituted carbamates 1 from alcohols has also been accomplished by several-pot reaction methods, such as trichloroacetyl isocyanate [11,12], chloroformates (starting from toxic phosgene) [13], chlorosulfonyl isocyanate [14] and cyanogen chloride [15].

The synthesis of N-unsubstituted carbamates from alcohols, via the reaction of sodium cyanate with trifluoroacetic acid in special organic solvents like benzene, methylene chloride and tetrachloride carbon, was reported by Loev et al. without any spectral data of IR and NMR [16]. The mentioned solvents are both toxic and not eco-friendly and, also trifluoroacetic acid is expensive. From the standpoint of 'green chemistry', a significant effort has been made to find an alternative to organic solvents. An effective substitute for them was a solvent–free reaction (industrially important, due to reduced pollution, being non-expensive and easy to use in process and handling) [17-22].

In association with the synthesis of primary carbamates from phenols and alcohols in solvent–free situations, a method has been recently reported for converting compounds containing the hydroxyl group into primary carbamates, at room temperature and in a lack of solvent, using trichloroacetic acid and spectra data, such as IR, NMR and their dynamic NMR [23,24]. Furthermore, a solvent-free method for preparing them, using silica supported perchloric acid as the profit reagent, was reported [25]. Because of the corrosive and toxical properties of trichloroacetic acid, the authors are interested in utilizing methods for their synthesis using solid acids, due to their industrial importance in replacing conventional acid/base catalysts [20-22,26-29]. Solid acids have many advantages, such as simplicity of handling, decreasing reactor and plant corrosion problems and environmentally safe disposal. Also, wastes and by-products can be minimized or avoided by developing cleaner synthesis routes. On the other hand, any reduction in the amount of sulfuric acid needed and/or any simplification in handling procedures is required for risk reduction, economic advantage and environmental protection.

The use of solid acid salt catalysts, such as $Al(HSO_4)_3$, for synthesizing organic intermediates and fine chemicals is gaining increasing awareness and is

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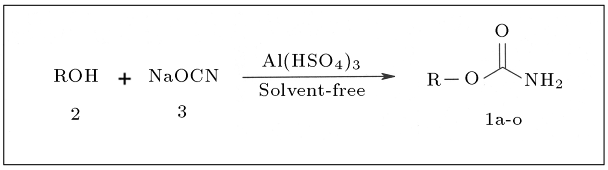
a field of intense research activity [30]. This salt is a stable and non-hygroscopic solid material; insoluble in most organic solvents.

In addition, during the recent decade, an increase in the uses of modern technology has expedited the striving towards an elimination of the requirements in organic synthesis associated with the chromatographic separation of mixtures, especially impurities [31].

In this paper, a simple and efficient solvent-free methodology was performed to prepare primary carbamates 1 at high yield and purity from compounds 2, sodium cyanate and $Al(HSO_4)_3$ (shown in Schemes 1 and 2). However, to the best of the authors knowledge, there has been no report on the use of $Al(HSO_4)_3$ for primary carbamate synthesis.

$$AlCl_3 + 3H_2SO_4 \xrightarrow{-3HCl} Al(HSO_4)_3$$

Scheme 1. Synthesis of $Al(HSO_4)_3$.



Scheme 2. Synthesis of primary carbamates.

RESULTS AND DISCUSSION

$Al(HSO_4)_3$ was prepared from $AlCl_3$ and H_2SO_4, according to [30] and shown in Scheme 1.

As shown in Table 1 and Scheme 2, getting pure primary carbamates 1a-o is possible by the reaction of alcohol or phenol 2 with sodium cyanate 3 at room temperature (or 55-65°C) and in the presence of $Al(HSO_4)_3$, which obtains a high yield product at the appropriate time.

As summarized in Table 1, there are many structural different substrates that can be used for obtaining pure primary carbamates under this cleaned synthetic direction. Also, it is a useful procedure for producing other types of carbamate, using primary, secondary, tertiary, allylic and benzylic alcohols and phenols. Indeed, it is necessary to mention that, in association with (-)-menthol, corresponding (-)-menthyl carbamate is obtained without epimerization by this process. Furthermore, the product was found to be pure enough that, in the majority of cases, purification after work up was not really necessary. In aromatic compounds, promoting the yield and purity of products would be possible at 55-65°C for 1h. However, using electron-withdrawing substitutes on phenols such as CN, COOR and CHO, did not cause any reaction to take place under the experimental situations described in this paper. This is because the mentioned functional groups decrease the nucleophlicity of the phenol oxygen in making an effective attack, in order to give the active a cid intermediates [23,25]. This is perhaps the reason

Table 1. Preparation of primary carbamates 1a-o^a.

Entry	Compound	R	Time (min)	% Yield	Mp°C	Mp(lit, ref.)°C
1	1a	(-)-Menthyl	40	82	166-168	156-157 [34]
2	1b	CH_3CH_2	40	73	46-48	48-50 [35]
3	1c	$CH_3CH_2CH_2$	40	81	58-59	60 [35]
4	1d	$CH_3CH_2CH_2CH_2$	40	77	53-55	54 [35]
5	1e	C_6H_{11}	40	80	108-110	108-110 [23]
6	1f	$(CH_3)_3C$	40	74	106-108	107-108 [16]
7	1g	$PhCH_2$	40	78	87-89	91 [35]
8	1h	$(CH_3)_2CHOCH_2CH_2$	40	81	57-59	53 [36]
9	1i	$H_2C{=}CHCH_2$	40	79	19-21	19-21 [23]
10	1j	$C_6H_5^b$	60	79	141-143	145-148 [16]
11	1k	$4\text{-}CH_3C_6H_4^b$	60	83	134-136	134-136 [23]
12	1l	$4\text{-}BrC_6H_4^b$	60	58	139-142	139-142 [23]
13	1m	$2\text{-}C(CH_3)_3\text{-}4\text{-}CH_3C_6H_4^b$	60	75	143-144	143-144 [23]
14	1n	α-naphthyl^b	60	70	178-180	175-177 [32]
15	1o	β-naphthyl^b	60	79	157-158	156-157 [33]

a: See [23, 25, 32, 33] for carbamates 1a-m, 1n and 1o, respectively.

b: Heated at 55-65°C for 1h.

for the lowering yield of compound 11 (58%). So, moieties such as *O*-isopropyl (1h, entry 8) under the reaction conditions are stable, which often undergo cleavage in strongly acidic media. Also, based on the recently reported findings [23,24], it must be noted that maintaining the reaction of α- and β-naphthol in a trichloroacetic acid media was not completely possible. Furthermore, considerable amounts of starting material remained, even after lengthy reaction times at high temperatures. The benefits of this method, compared with the recently reported method [23,24], are considerable, in terms of shortening reaction times from 12 to 1h and in removing the trichloroacetic acid (see Table 1).

Identification of the products was achieved by comparison of their IR spectra and physical properties with those of authentic samples [23,25,32-36]. Moreover, ^{1}H-NMR (500 MHz) and ^{13}C-NMR (125 MHz) spectra play an important role in their characterization, which shows that the signals belong to carbonyl carbons of aliphatic or aromatic carbamate in the range of δ 146-157 ppm.

CONCLUSION

In this paper, the development of a highly efficient method for the synthesis of primary carbamates by the reaction of substrates containing a hydroxyl group and sodium cyanate, in the presence of an efficient reagent of $Al(HSO_4)_3$, has been considered. The different parameters in making the reaction, such as solventless conditions, mildness of conversion, simplicity of experimental procedure, clear reaction profile, high yield and purity and short reaction time, are the most important profitable aspects of the method. Finally, it should be mentioned that the purification and separation processes (C.C) are not necessary to the method.

EXPERIMENTAL

General

^{1}H-NMR and ^{13}C-NMR spectra were recorded by BRUKER AVANCE DRX500 (500 MHz). The IR spectra were obtained on a SHIMADZU-470. Using a Heraeuse CHN-O-Rapid analyzer, elemental analysis was performed in the Malek-Ashtar University of Technology, Tehran, Iran. Melting points were recorded by Electro thermal 9100 and were uncorrected. The Thin Layer Chromatography (TLC) was carried out using plastic sheets precoated with silica gel 60 F. All starting materials, such as alcohols, phenols, NaOCN and solvents, were purchased from Fluka, Merck and Aldrich chemical companies and were purified with the proper purification techniques before using, if necessary [37,38]. The products 1 were identified through comparison of their spectral data, IR, ^{1}H-NMR, ^{13}C-NMR, TLC and the physical properties with those of authentic samples [23,25,32-36]. $Al(HSO_4)_3$ was prepared from $AlCl_3$ and H_2SO_4, according to the literature in [30].

General Procedure

In a typical procedure, alcohol or phenol (1.0 mmol) was added to a mixture of sodium cyanate (2 mmol) and $Al(HSO_4)_3$ (0.64 g, 2 mmol), and the mixture was pulverized in a mortar (or the mixture was stirred by a magnet in a test tube) at room temperature (or 55-65C°C) for an appropriate time (Table 1). The reaction was monitored in TLC. After completion of the reaction, $CHCl_3$ was added and the mixture was filtered for separating the reagent. The solvent ($CHCl_3$) evaporated to give the product. Pure products were obtained at high yields, as summarized in Table 1. In cases of α- and β-naphthol (entries 14 and 15), after removing $CHCl_3$, petroleum ether and, then ethyl acetate were added. The obtained solid was pure α- or β-naphthyl carbamate 1n and 1o.

Naphthalen-1-yl Carbamate 1n

Reaction afforded white crystals 1n, 70% yield, mp = 178-180 °C. [32] IR (KBr, cm^{-1}): 3430 (m), 3343 (vw), 3275 (w), 3200 (w), 3055 (vw), 2920 (vw), 1698 (vs), 1603 (s), 1360 (vs), 1254 (s), 1222 (s), 1150 (m), 1082 (s), 1041 (m), 1010 (m), 958 (m), 801 (s), 773 (vs), 582 (m), 553 (w). ^{1}H-NMR (500 MHz, $CDCl_3$), δ ppm; 6.10 (br, d, 2H), 7.20 (d, J = 7.5 Hz, 1H), 7.35-7.45 (m, 3H), 7.63 (d, J = 8.2 Hz, 1H), 7.78 (dd, J = 9.3 Hz, J = 2.1 Hz, 1H), 7.92 (dd, J = 8.8 Hz, J = 2.1 Hz, 1H). ^{13}C-NMR (125 MHz, $CDCl_3$), δ ppm; 117.7, 120.8, 124.8, 124.9, 125.6, 125.7, 126.9, 127.3, 134.0, 146.2, 154.7. Analysis Calcd. For $C_{11}H_9NO_2$: C, 70.59; H, 4.81; N, 7.49; Found; C, 70.80; H, 4.71; N, 7.60%.

Naphthalen-2-yl Carbamate 1o

Reaction afforded white crystals 1o, 79% yield, mp = 157-158 °C. [33] IR (KBr, cm^{-1}): 3405 (m), 3038 (w), 3270 (w), 3197 (vw), 3055 (vw), 1697 (vs), 1610 (w), 1506 (w), 1388 (s), 1355 (s), 1239 (s), 1206 (s), 1155 (m), 987 (s), 895 (m), 858 (m), 821 (m), 775 (m), 758 (w), 734 (m), 543 (w), 474 (m). ^{1}H-NMR (500 MHz, $CDCl_3$), δ ppm; 6.25 (br, s, 2H), 7.20 (dd, J = 8.7 Hz, J = 2.1 Hz, 1H), 7.34-7.41 (m, 2H), 7.49 (d, J = 2.1 Hz, 1H), 7.71 (d, J = 8.0 Hz, 1H), 7.75 (d, J = 8.7 Hz, 2H). ^{13}C-NMR (125 MHz, $CDCl_3$), δ ppm; 117.9, 121.2, 124.8, 125.8, 126.9, 127.1, 128.5, 130.5, 133.1, 148.3, 154.9, Analysis Calcd. For $C_{11}H_9NO_2$: C, 70.59; H, 4.81; N, 7.49; Found; C, 71.20; H, 4.65; N, 7.54%.

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