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One-pot preparation of dialkylcarbamoyl azides from tertiary amines using triphosgene and sodium azide

V. K. Gumaste and A. R. A. S. Deshmukh*

Division of Organic Chemistry (Synthesis), National Chemical Laboratory, Pune 411 008, India

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Abstract—A simple one-pot method for the preparation of dialkylcarbamoyl azides from tertiary amines using triphosgene and sodium azide is described.

Over the last few years triphosgene [bis(trichloromethyl)-carbonate] has emerged as a versatile synthetic reagent for the synthesis of large variety of organic compounds.[1] This white crystalline compound has replaced its gaseous congener, phosgene, in terms of its reactivity and safe handling. As a part of our continuous efforts in the application of triphosgene for organic synthesis,[2] we wish to report a simple one-pot method for the preparation of dialkylcarbamoyl azides from tertiary amines and sodium azide using triphosgene.

Carbamoyl azides are an important class of organic compounds having wide applications in organic synthesis.[3] Some of these azides are used as intermediates for the synthesis of various heterocyclic[4] and medicinally important compounds.[5] Carbamoyl azides are generally prepared from the corresponding carbamoyl chlorides and sodium azide,[6] by addition of hydrazoic acids to isocyanates,[7] and by nitrosation of semicarbazides.[8] They can also be prepared from carboxaldehydes[9] and carboxylic acids.[10]

In our recent communication, we showed the application of triphosgene for the preparation of various allyl azides[2e] from allyl alcohols and sodium azide in the presence of triethylamine. Formation of a trace amount of diethylcarbamoyl azide was observed during this reaction. We further investigated this reaction, and thus triphosgene was reacted with triethylamine in the presence of sodium azide.[11] To a cooled solution of triphosgene in dry acetone or acetonitrile was added triethylamine slowly at 0 °C. The reaction mixture was stirred at this temperature for 1 h and then at room temperature for 3 h. The mixture was cooled to 0 °C, sodium azide was added in one portion and the resulting mixture then stirred at this temperature for 1 h. After warming to room temperature, stirring was continued overnight. The reaction mixture was diluted with water and extractive work-up with dichloromethane followed by purification on silica gel column gave diethylcarbamoyl azide as a colorless oil in 73% yield [**CAUTION**: The use of a fume-hood and safety shield is recommended as azides are potentially explosive].

We believe that the diethylcarbamoyl azide is formed via dealkylation of triethylamine salt to give diethylcarbamoyl chloride or *N*,*N*-diethyl trichloromethyl carbamate with the loss of ethyl chloride followed by reaction with sodium azide (Scheme 1). There are several literature precedents for dealkylation of tertiary amines with phosgene[12] and triphosgene.[13]

The generality of this reaction was established by preparing various carbamoyl azides from tertiary amines in good yields (Table 1). *n*-Butyl chloride was detected by GLC along with dibutylcarbamoyl azide in the crude reaction product of tributylamine with triphosgene and sodium azide (Table 1, entry 3). This clearly indicates the loss of the alkyl group as alkyl halide. An isopropyl group was lost when diisopropylethylamine was reacted with triphosgene and sodium azide, and *N*-*i*-propyl-*N*-ethylcarbamoyl azide was

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Keywords: Carbamoyl azides; Sodium azide; Triphosgene; Tertiary amines.

* Corresponding author. Fax: +91-20-2589-3153/3355; e-mail: arasd@dalton.ncl.res.in

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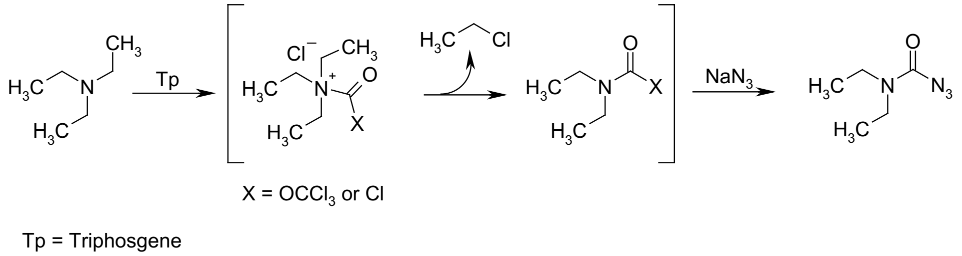
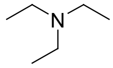
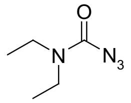
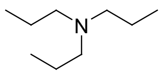
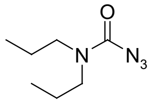
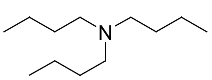
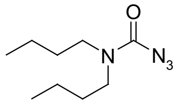
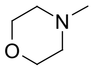
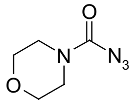
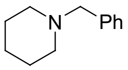
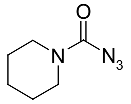
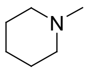
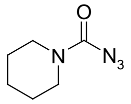
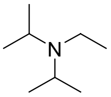
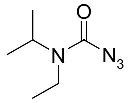
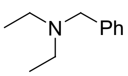
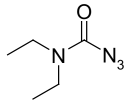


Scheme 1.

Table 1. Preparation of carbamoyl azides using triphosgene and sodium azide

Entry	Substrate	Product	Yield[a,b]
1			73
2			71
3			74
4			66
5			63
6			60
7			53
8			54

[a] Isolated yields.

[b] All the compounds were characterized by IR, NMR and Mass spectral data.

obtained in moderate yield (Table 1, entry 7). In the case of *N*-methylmorpholine and *N*-methylpiperidine (Table 1, entries 4 and 6), loss of the methyl group was observed and the corresponding products were morphol-inocarbamoyl azide and piperidinocarbamoyl azide, respectively. The benzyl group was preferentially lost as benzyl chloride in the cases of *N*-benzylpiperidine and *N*,*N*-diethylbenzylamine to give the corresponding carbamoyl azides (Table 1, entries 5 and 8).

In summary, we have shown that triphosgene can be used for the one-pot preparation of dialkylcarbamoyl azides from tertiary amines using sodium azide.

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11. Typical experimental procedure for the preparation of diethylcarbamoyl azide: To a stirred solution of triphosgene (0.74 g, 2.5 mmol) in acetone (20 mL) was added slowly triethylamine (0.750 g, 7.5 mmol) at 0 °C in 10 min. The reaction mixture was stirred for 1 h at this temperature and then at room temperature for 3 h. It was then cooled to 0 °C and sodium azide (0.65 g, 10 mmol) was added in one portion. The mixture was stirred at this temperature for 1 h and slowly warmed to room temperature then stirred for a further 18 h. Water (10 mL) was added and the mixture extracted with dichloromethane (3 × 20 mL). The organic layer was washed with 5% aq

HCl (10mL), water (10mL) and brine (10mL) and dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure at room temperature to give an oil, which was purified by silica gel column chromatography to afford diethylcarbamoyl azide as a colorless oil (0.74g, 73%) [**CAUTION**: The use of a fume-hood and safety shield is recommended, as azides are potentially explosive]. IR ($CHCl_3$): 2154, 1689, 1473, 1421, 1141, 908, 732cm^{-1}; ^1H NMR ($CDCl_3$, 200MHz): δ 1.09–1.25 (m, 6H), 3.24 (q, $J = 7.1$ Hz, 2H), 3.35 (q, $J = 7.1$ Hz, 2H); MS (EI) m/z 142 (M^+, 15), 127 (33), 113 (15), 100 (15), 85 (8), 71 (100).

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