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# Transesterification of Alkyl Carbamate to Aryl Carbamate : Effect of varying the Alkyl Group.#

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*Abstract: Phosphorus oxychloride mediated transesterification of four alkyl N-methylcarbamates to several aryl N-methylcarbamates has been studied. Best yields are obtained from benzyl N-methylcarbamate.*

## Introduction

The usual acid or base catalysed transesterification is an equilibrium process and therefore does not lend itself to the synthesis of aryl carbamates from alkyl carbamates. We had earlier devised a novel strategy to overcome this obstacle[1]. The method consisted of reacting the alkyl carbamate with $POCl_3$; this resulted in alkyl - oxygen cleavage with elimination of alkyl chloride. The reactive intermediate thus generated was attacked by the appropriate substituted phenol, resulting in the formation of an aryl carbamate (Scheme). The substrate in all our earlier experiments was a methyl carbamate.

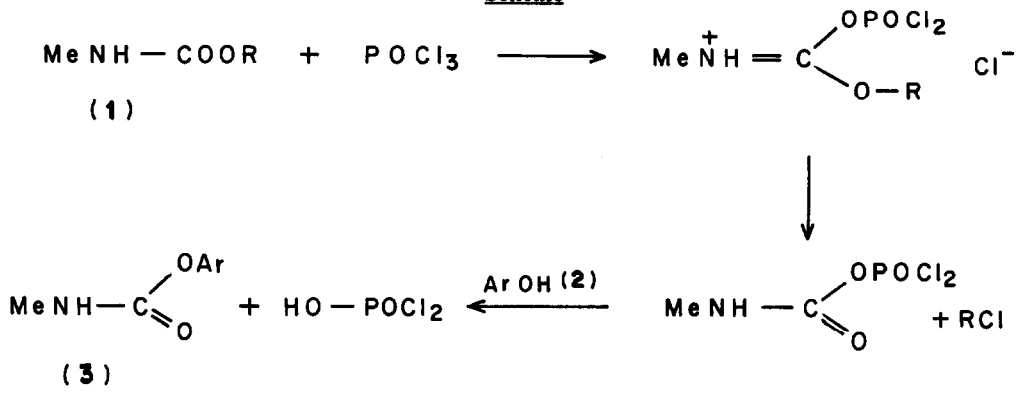
It was logical to expect that the nature of the alkyl group would affect the ease of cleavage of the C-O bond, and hence the yield of the desired aryl carbamate. In this paper, we report our results on such a study, comparing the yields of various aryl carbamates from four different alkyl carbamates.

## Results and Discussion

The substrates were the methyl (**1a**), isopropyl (**1b**), allyl (**1c**) and benzyl (**1d**) esters of N-methylcarbamic acid. Three general procedures were used for the synthesis of these alkyl esters - (i) the Hofmann rearrangement[2] of N-chloroacetamide in the appropriate alcohol; (ii) reaction of methyl N-methylthiolcarbamate[3] with the alcohol in presence of the alkoxide, and (iii) transesterification of the methyl ester to the higher alkyl ester[4].

The alkyl esters (**1a to d**) were treated with $POCl_3$ and the substituted phenols (**2a to h**) under standard conditions. The aryl carbamates (**3a to h**) were isolated and characterized. The yields are given in **Table 1**.

**Scheme**




(1)
**a** : R = $-CH_3$
**b** : R = $-CH(CH_3)_2$
**c** : R = $-CH_2-CH=CH_2$
**d** : R = $-CH_2Ph$

Ar (2 and 3)
**a** : Phenyl
**b** : 4-methylphenyl
**c** : 2-methylphenyl
**d** : 4-chlorophenyl
**e** : 2-chlorophenyl
**f** : 2,6-dichlorophenyl
**g** : 4-nitrophenyl
**h** : 4-methoxyphenyl

**Table 1**

**Yields of aryl N-methylcarbamates (3) from alkyl N-methylcarbamates (1)**

| Product (3) | | Yield % of product (3) Starting alkyl carbamate (1) | | | |
|---|---|---|---|---|---|
| **No.** | **m.p.°C(Lit.m.p.°C)** | **1a** | **1b** | **1c** | **1d** |
| 3a | 85 (85-6)[5] | 55 | 57 | 60 | 73 |
| 3b | 94 (95-6)[5] | 50 | 55 | 60 | 78 |
| 3c | 100 (101-2)[5] | 25 | 50 | 30 | 46 |
| 3d | 118 (115-6)[5] | 45 | 60 | 54 | 65 |
| 3e | 100 (90-1)[5] | 33 | 50 | 45 | 55 |
| 3f | 101-2 | 28 | 35 | 35 | 40 |
| 3g | 164 (160-2)[5] | 42 | 60 | 65 | 85 |
| 3h | 73-4 | 40 | 53 | 50 | 60 |

It is immediately obvious that benzyl carbamate gives the best results in the transesterification to aryl carbamates, followed by allyl carbamate and isopropyl carbamate. Methyl carbamate, which we had used in our earlier study[1] generally gives the poorest yield.

As regards the phenol moiety, two points of interest emerge from this study. The first, of course, is the effect of an ortho-substituent; the increased steric demand consequent on this results in a decreased yield of the product. The second, rather unexpected result, is the very good yield obtained from 4-nitrophenol. Perhaps this is due to suppression of side reactions, as for example, direct reaction with $POCl_3$ to form the ester.

## Experimental

***General*** : Freshly distilled phosphorus oxychloride was used in all the experiments. Melting points were determined on micro melting point apparatus (Yanaco) and are uncorrected. $^1H$ NMR spectra were recorded either on a WH90 FT NMR spectrometer (Bruker) or on a FT 80A NMR spectrometer (Varian) using tetramethylsilane as internal standard. The values are expressed in ppm downfield from the signal for internal $Me_4Si$. Elemental analysis were performed at the organic chemistry division NCL. IR spectra were recorded on a 599B double beam IR spectrometer. For TLC, plates coated with silica gel were run in a mixture of 5 to 20% ethyl acetate and n-hexane and spots were developed in an iodine chamber. For column chromatographic purification under gravity, column grade silica gel (60-120 mesh) activated at 100°C for 1 hr was employed.

**General procedure for the preparation of alkyl N-methylcarbamates from methyl N-methylthiolcarbamate.**

To sodium (0.23g, 0.01 m) dissolved in the alcohol (20 ml) was added methyl N-methylthiolcarbamate (4.2g, 0.04 m) and the reaction mixture was refluxed for 10-12 hrs. The progress of the reaction was followed by TLC. After completion of the reaction the alcohol was distilled out and the residue was chromatographed over a silica gel column. (eluent : pet ether : ethyl acetate 95:5) to give the alkyl N-methylcarbamate.

**Methyl N-methylcarbamate (1a):** IR : 3300$cm^{-1}$ (NH), 1700$cm^{-1}$ (C=O); $^1H$ NMR($CDCl_3$): 2.8 (d, J=5Hz, 3H, NH.$CH_3$); 3.6 (s, 3H, O-$CH_3$)

**Isopropyl N-methylcarbamate (1b):** IR : 3350$cm^{-1}$ (NH), 1710$cm^{-1}$ (C=O), $^1H$ NMR ($CDCl_3$): 1.12 (d, J=6Hz 6H,2$CH_3$), 2.78 (d,J=5Hz, 3H, N-$CH_3$), 3.93 (septet, J=6Hz, 1H, >C-H )

**Allyl N-methylcarbamate (1c):** IR : 3350$cm^{-1}$ (NH) 1710$cm^{-1}$ (C=O); $^1H$ NMR ($CDCl_3$) : 2.7 (d,J=5Hz, 3H, N-$CH_3$), 4.5 (d,J=6Hz, 2H, O-$CH_2$); 5.2 (m, 2H, C=$CH_2$), 5.9 (m, 1H, CH)

**Benzyl N-methylcarbamate (1d):** IR : 3350$cm^{-1}$ (NH) 1710$cm^{-1}$ (C=O); $^1H$ NMR, 2.74 (d, J=6Hz, 3H, N-$CH_3$), 5.12 (s, 2H, $CH_2$ ph),7.88 (s, 5H, aromatic)

**Preparation of allyl N-methylcarbamate 1c from 1a by transesterification**

Sodium (0.23g, 0.01m) was dissolved in 25 ml of allyl alcohol; methyl N-methylcarbamate (4.45g, 0.05 m) was then added. The reaction mixture was refluxed for 20 hrs. After this the solvent was removed under vacuum, the residue treated with water, neutralized with dil. HCl and extracted with dichloromethane. The organic layer was separated, dried over sodium sulfate and the solvent removed. Distillation of the residue gave pure allyl N-methylcarbamate in 68% yield (3.9 g).

**General procedure for the transesterification of alkyl N-methylcarbamates 1a-d to aryl N-methylcarbamates 3a-h**

Phosphorus oxychloride (3.08g, 0.02m) was added to a stirred mixture of alkyl N-methylcarbamate (0.02m) and the phenol (0.01m). The reaction mixture was stirred for 10-12 hrs at 60°C. After cooling, the contents were poured on ice-water slowly, neutralized with $Na_2CO_3$ and extracted with ethyl acetate. The organic extract was washed with brine and dried over anhydrous sodium sulfate. Evaporation of the solvent gave a residue which was purified by column chromatography (eluent : pet. ether : ethyl acetate 85:15) to give pure aryl N-methylcarbamates.

**Phenyl N-methylcarbamate (3a)**[5]: $^1$H NMR ($CDCl_3$) : 3.1 (d, J=5Hz, 3H, N-$CH_3$), 5.20 (b, 1H, NH); 7.2 (m, 5H, aromatic)

**4-Methylphenyl N-methylcarbamate (3b)**[5]: $^1$H NMR ($CDCl_3$): 2.33 (s, 3H, Ar-$CH_3$), 2.88 (d, J=5Hz, 3H, N-$CH_3$); 5.11 (b, 1H, N-H), 7.06 (m, 4H, aromatic)

**2-Methylphenyl N-methylcarbamate (3c)**[5]: $^1$H NMR ($CDCl_3$): 2.24 (s, 3H, Ar-$CH_3$), 2.88 (d, J=5Hz, 3H, N-$CH_3$); 5.04 (b, 1H, N-H), 7.2(m, 4H aromatic)

**4-Chlorophenyl N-methylcarbamate (3d)**[5]: $^1$H NMR ($CDCl_3$): 2.8 (d, J=5Hz, 3H, N-$CH_3$), 5.0 (b, 1H, N-H), 7.28 (m, 4H, aromatic)

**2-Chlorophenyl N-methylcarbamate (3e)**[5]: $^1$H NMR ($CDCl_3$): 2.92 (d, J = 5Hz, 3H, N-$CH_3$), 5.12 (b, 1H, N-H); 7.36 (m, 4H, aromatic)

**2,6-Dichlorophenyl N-methylcarbamate (3f)**: $^1$H NMR ($CDCl_3$): 2.9 (d, J=6Hz, 3H, N-$CH_3$), 5.2 (b, 1H, N-H); 7.38 (m, 3H, aromatic). Anal. cal. for $C_8H_7Cl_2NO_2$ (220.04): C 43.66, H 3.20, N 6.36 Found C 43.52, H 3.08, N 6.25.

**4-Nitrophenyl N-methylcarbamate (3g)**[5]: $^1$H NMR ($CDCl_3$): 2.89, (d,J=6Hz, 3H, N-$CH_3$); 5.08 (b, 1H, N-H); 7.3 (d, J=9Hz, 2H, aromatic), 8.2 (d, J=9Hz, 2H, aromatic)

**4-Methoxyphenyl N-methylcarbamate (3h)**: $^1$H, NMR ($CDCl_3$) : 2.82 (d, J=5Hz, 3H, N-$CH_3$); 3.7 (s, 3H, O-$CH_3$); 5.0 (b, 1H, N-H); 6.88 (m, 4H, aromatic). Anal. cal. for $C_9H_{11}NO_3$ (181.18): C 59.66, H 6.11, N 7.73 Found C 59.60, H 6.09, N 7.64.

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