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Novel synthetic method for *N*-allylcarbamates from allyl ethers using chlorosulfonyl isocyanate

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Abstract

Various allyl ethers were converted into the corresponding *N*-allylcarbamates using chlorosulfonyl isocyanate (CSI) via the stable allylic carbocation rather than β-lactam through [2+2] cycloaddition. The reaction of cinnamyl methyl ether with CSI afforded only methyl *N*-cinnamylcarbamate at 0°C, but at 20°C, it produced a mixture of methyl *N*-cinnamylcarbamate and methyl *N*-(1-phenylprop-2-enyl)carbamate in a 2.7:1 ratio.

Keywords: chlorosulfonyl isocyanate; allyl ether; *N*-allylcarbamate.

To date, chlorosulfonyl isocyanate (CSI) has been used in the [2+2] cycloaddition reactions of various substituted alkenes, especially enol ethers, to synthesize the β-lactam moiety of carbapenem antibiotics and β-amino acids.[1–7] Recently, chiral enol ethers have been used as the precursors of chiral β-lactam compounds and chiral β-amino acids.[8,9] As part of a program aimed at producing various amino acids which can be used as a versatile building block, benzyl allyl ether was reacted with CSI to obtain a β-lactam with a benzyloxy methyl moiety, which can be readily converted to the acid moiety. However, rather than obtaining the β-lactam, we unexpectedly obtained the corresponding carbamate.[10] Specifically, instead of obtaining the expected β-lactam products arising from formal [2+2] annulation, the corresponding *N*-allylcarbamates were obtained as sole products (Scheme 1). Early examples of *N*-allylcarbamate formation using CSI were reported by several groups, in which the reactions of unsaturated oxiranes or acetal moieties in sugars with CSI were studied.[11,12] Similar results of the conversion of tertiary or allyl alcohols to the corresponding amines using CSI were also reported.[13,14]

However, no further systematic studies on these reactions have been performed. Therefore, we investigated this novel reaction by varying solvents and temperatures to optimize the yield; the results are summarized in Table 1.

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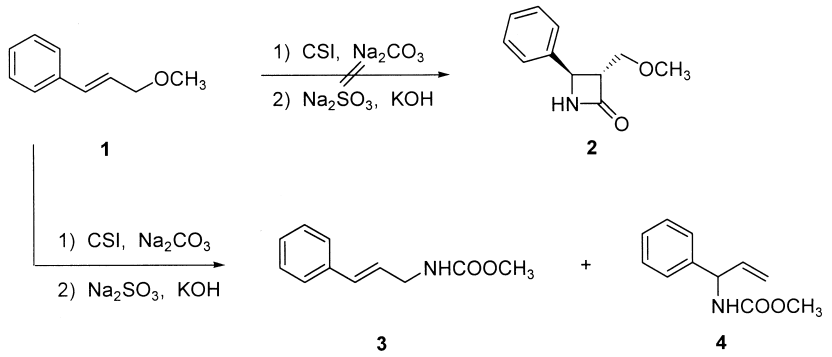


Scheme 1.

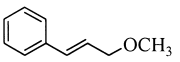
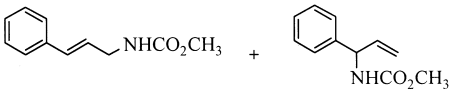
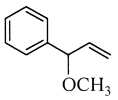
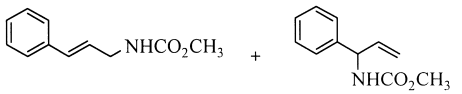
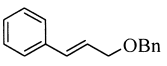
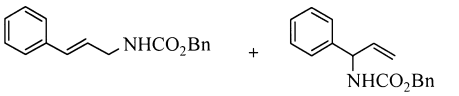
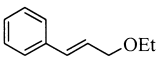
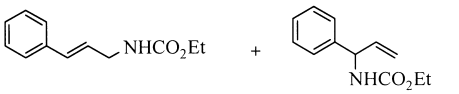
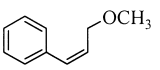
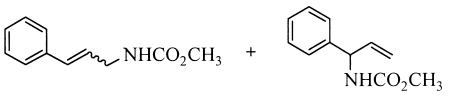
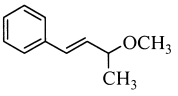
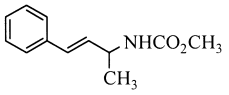
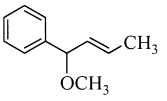
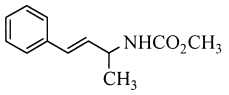
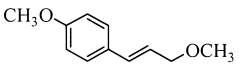
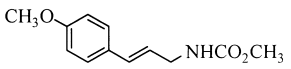
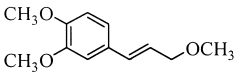
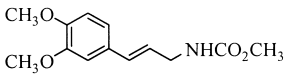
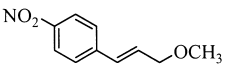
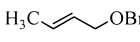
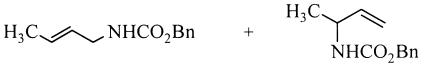
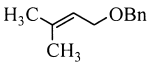
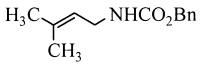
Table 1
Results of the reactions of cinnamyl methyl ether (**1**) and CSI conducted with different solvents and temperatures

Solvent	Temperature (°C)	Yields (%)	Ratio (3) : (4)
Toluene	-78	66.2	5.0 : 1
	-40	68.2	4.7 : 1
	0	78.4	4.4 : 1
	20	78.2	2.8 : 1
	40	75.3	2.8 : 1
	60	74.0	2.8 : 1
CH_2Cl_2	0	72.3	only (3)
	20	87.5	2.7 : 1
$CHCl_3$	0	80.4	6.0 : 1
	20	88.6	3.0 : 1
CCl_4	0	58.0	only (3)
Et_2O	0	58.1	4.6 : 1
n-Hexane	0	62.2	only (3)
CH_3CN	20	No Reaction	

From these results, the best condition was determined to involve methylene chloride at 20°C. Therefore, various allyl ethers were reacted with CSI under these conditions; the results are shown in Table 2.

The formation of *N*-allylcarbamates can be rationalized in terms of the abstraction of the alkoxy moiety by CSI to give the $ClSO_2$–N^-–CO_2CH_3 species and the stable allylic carbocation. Nitrogen species may attack C(1) by avoiding steric hindrance of the phenyl ring or the dimethyl moiety (entries 1–9 and 12). In the case of entry 11, a 1:1 mixture of the terminal and internal carbamate was obtained due to the reduced steric hindrance.

Table 2
Conversions of allyl ethers to the corresponding *N*-allylcarbamates with CSI[a]

Entry	Allyl ethers	N-Allylcarbamates	Yield(%)[b] (ratio)
1			87.5 2.7 : 1
2			87.3 2.6 : 1
3			89.8 8.4 : 1
4			83.5 7.0 : 1
5			86.9 2.8 : 1 cis:trans = 4:1
6			77.9
7			75.0
8			62.1
9			23.6
10		No Reaction	--
11			72.3 (1 : 1)[c]
12			82.4

[a]All the reactions are carried out at 20°C except entry 8, 9 and 12 (-78°C).

[b]Isolated yield of pure material.

[c]Isomer ratio determined by ^{1}H NMR spectrum of the mixture after column chromatography.

A typical preparatory procedure is as follows: To a solution of Na_2CO_3 (2.25 equiv.) in anhydrous methylene chloride (7 mL) was added CSI (1.5 equiv.) and a solution of cinnamyl methyl ether (350 mg, 2.36 mmol) in methylene chloride (3 mL) at 20°C. The reaction mixture was stirred for 0.5 h at 20°C, quenched with H_2O, then extracted with ethyl acetate (10 mL). The organic layer

was added to a solution of Na_2SO_3 (25%) and KOH (10%) and the reaction mixture was stirred overnight at 20°C. It was then extracted with ethyl acetate, and after the usual work-up, column chromatography afforded **3** (288 mg, 63.8%) and **4** (107 mg, 23.7%).

Compound **3**: ^{1}H NMR (500 MHz, $CDCl_3$): 3.70 (s, 3H), 3.96–3.98 (t, 2H, $J = 5$ Hz), 4.89–4.97 (br, 1H), 6.17–6.22 (m, 1H), 6.50–6.53 (d, 1H, $J = 15.5$ Hz), 7.22–7.37 (m, 5H). Compound **4**: ^{1}H NMR (500 MHz, $CDCl_3$): 3.69 (s, 3H), 5.00–5.10 (br, 1H), 5.22–5.26 (m, 2H), 5.30–5.38 (br, 1H), 5.97–6.04 (m, 1H), 7.26–7.36 (m, 5H).

In conclusion, CSI was found to react with allyl ethers at room temperature in methylene chloride to give the corresponding *N*-allylcarbamates via the stable allylic carbocation. We are actively pursuing further applications of this interesting reaction, including a more refined definition of its reaction mechanism with an eye toward regioselectivity due to preference between cationic stability and steric hindrance.

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