A Simple One-Pot Method for the Preparation of Allyl Azides from Allyl Alcohols Using Triphosgene: Synthesis of *N*1-Cinnamyl Azetidin-2-ones

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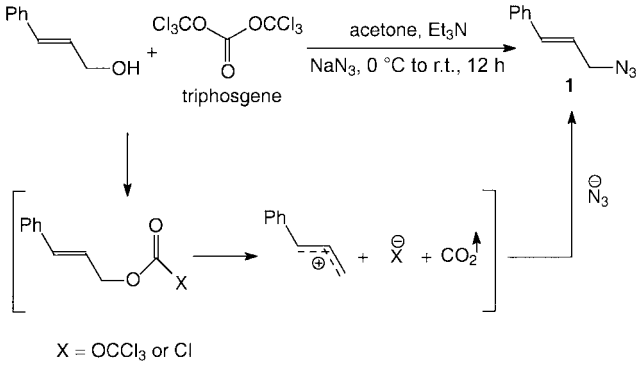
Dedicated to Dr. S. Rajappa on the occasion of his 70th birthday.

Abstract: A simple and efficient one-pot method for the preparation of allyl azides from allyl alcohols using triphosgene and sodium azide is described. An application of cinnamyl azide for the synthesis of various *N*1-cinnamyl azetidin-2-ones is also described.

Key words: allyl azides, allyl alcohols, azetidin-2-ones, triphosgene

Recently we have shown the versatility of triphosgene [bis(trichloromethyl)carbonate][1] as an acid activator in the construction of β-lactam ring via ketene-imine cycloaddition using Staudinger reaction.[2] We have also used this reagent for the preparation of various azidoformates[3] and acyl azides[4]. In this communication we wish to report a simple and efficient one-pot method for the preparation of allyl azides directly from allyl alcohols using triphosgene and sodium azide. Although, allyl azides are important synthetic intermediates[5] and a source for synthetically useful allyl amines,[6] there are very few methods available for their preparation from allyl acetates,[8] allyl halides[9] and allysilanes.[10] There are also some reports on one-pot conversion of allyl alcohols to allyl azides.[7]

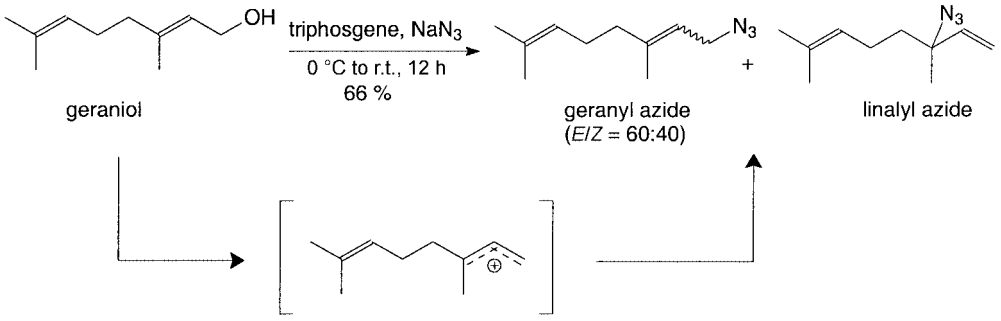
In a recent communication we have shown that the reaction of triphosgene with the aliphatic alcohols in the presence of sodium azide and triethylamine gives azidoformates in excellent yields.[3] However, under similar reaction conditions, when triphosgene was added slowly to a mixture of cinnamyl alcohol, triethylamine and sodium azide in acetone at 0 °C, cinnamyl azide (**1**) was obtained as a major product (80%) while the expected cinnamyl azidoformate was found to be a minor product (20% by GLC and ^{1}H NMR).[11]



Scheme 1

Cinnamyl azide (**1**) could be obtained in excellent isolated yield (80%) and very high purity (>98%, GLC) by a little modification in the experimental procedure. Accordingly a solution of cinnamyl alcohol and triethylamine in acetone was added to a stirred solution of triphosgene in acetone at 0 °C followed by the addition of sodium azide in one portion. The reaction mixture was stirred at room temperature for 12 hours and the usual work-up gave excellent yield of cinnamyl azide of high purity.[12]

The formation of **1** could be through the allyl carbocation generated from trichloromethyl allyl carbonate or allyl chloroformate with the evolution of carbon dioxide followed by nucleophilic addition of azide ion (Scheme 1).



Scheme 2

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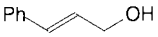
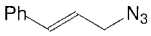
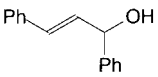
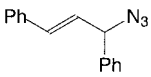
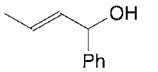
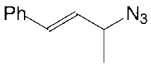
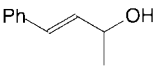
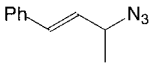
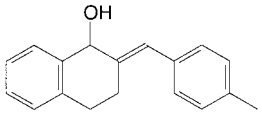
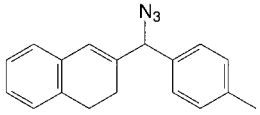
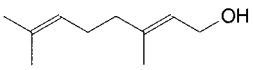
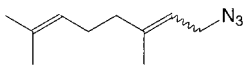
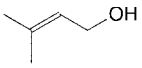
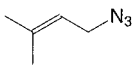
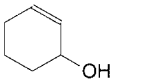
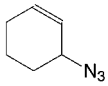
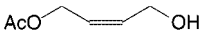
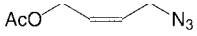
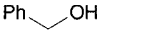
Table 1 Preparation of Allyl Azides Using Triphosgene and Sodium Azide

Entry	Substrate	Product	Yield (%)[a]
1			80
2			90
3			66
4			60
5			91
6			66[b]
7			50[c]
8			46
8			63
10			64

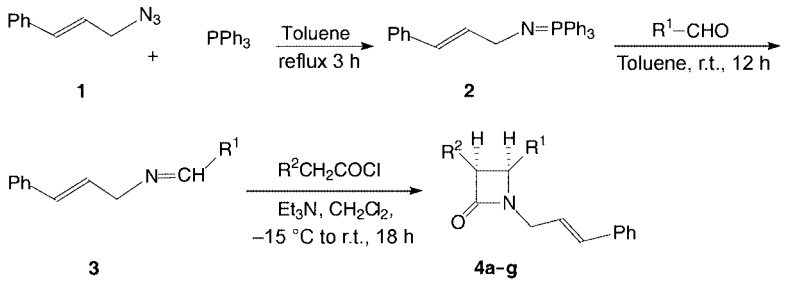
[a] Isolated yields.
[b] Mixture of geranyl azide (66%, *E*/*Z*, 60:40) and linalyl azide (10%).
[c] Mixture of primary azide and tertiary azide (75:25).

This is evident from the fact that the reaction of geraniol with triphosgene in the presence of sodium azide under similar reaction conditions gave *E*/*Z* mixture (60:40) of geranyl azides (66%) along with small amount of linalyl azide (10%), which was confirmed from the ^{1}H NMR spectrum of the reaction product (Scheme 2).

Attempts to separate linalyl azide and geranyl azide from the mixture were unsuccessful. Prenol also gave inseparable mixture of primary and tertiary allyl azides (75:25) in low isolated yield (50%).

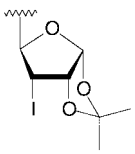
Several allyl azides were prepared by this method in good to moderate yields (Table 1).[13] 1-Phenyl-3-methyl prop-2-en-1-ol and 3-phenyl-1-methyl prop-2-en-1-ol gave same, 3-phenyl-1-methyl prop-2-en-1-azide, product through a common stable carbocation (Table 1, entries 3 and 4). Benzyl alcohol also gave benzyl azide in very good yield when reacted with triphosgene and sodium azide (Table 1, entry 10). The low yields of azides in case of lower allyl alcohols may be due to low reactivity of alcohols and the volatile nature of the allyl azides formed. In fact we could not isolate allyl azides from lower allyl alcohols such crotyl, allyl and methallyl alcohols.[14]

After developing an efficient method for allyl azides we were interested in their application for synthetic utility. As a part of our on going research program on the synthesis of polycyclic β-lactams[15] via radical cyclization reaction we were in need of *N*1-allyl substituted β-lactams. We have successfully utilized allyl azides for the synthesis of *N*1-allyl-β-lactam substrates (Scheme 3) required for intramolecular radical cyclization study.



Scheme 3

Table 2 Synthesis of *N*-Cinnamyl Azetidin-2-ones (**4a**–**g**)

Entry	Compound	R^1	R^2	Yield (%)[a,b]	Mp (°C)
1	**4a**	Ph	OCH_2Ph	74	140–141
2	**4b**	Ph	OPh	84	160–161
3	**4c**	Ph	OMe	84	90–92
4	**4d**	2-BrPh	OCH_2Ph	72	120–122
5	**4e**		OCH_2Ph	76	142–143[c]
6	**4f**	4-MeOPh	OMe	61	122–123
7	**4g**	4-MeOPh	OCH_2Ph	78	120–121

[a] Isolated yields.
[b] All the compounds gave satisfactory elemental analyses and spectral data.
[c] Mp of one of the diastereomers isolated from (1:1) diastereomeric mixture.

The iminophosphorane **2**, obtained from cinnamyl azide and triphenylphosphine, was treated with aldehyde to get aza-Wittig product **3**, which was found to be unstable and used as such without purification. The cycloaddition reaction of imine **3** with ketene, generated from acid chloride and triethylamine, gave *cis*-*N*-cinnamyl-β-lactams (**4a**–**g**) in good yields (Table 2).[16] The chiral iodoaldehyde derived from D-glucose[17] was also used for the preparation of *N*-cinnamyl imine **3e**, which on further reaction with ketene gave 1:1 diastereomeric mixture of *cis*-β-lactams **4e** in very good yield (Table 2, entry 5). Both the diastereomers could be separated by careful column chromatography. Further work on the application of other allyl azides for the synthesis of *N*-allyl azetidin-2-ones is in progress.

In summary, we have demonstrated a one-pot method for the preparation of allyl azides from allyl alcohols using triphosgene and sodium azide and shown the utility of cinnamyl azide for the synthesis of *N*-cinnamyl-β-lactams.

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(11) Spectral data for cinnamyl azidoformate: colorless oil. IR ($CHCl_3$): 2175, 2135, 1730, 1500, 1448, 1236, 966 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 4.88 (d, *J* = 6.0 Hz, 2 H), 6.25–6.35 (m, 1 H), 6.73 (d, *J* = 16.0 Hz, 1 H), 7.20–7.45 (m, 5 H).

(12) Cinnamyl azide (**1**) and other allyl azides were found to be stable at r.t. but for safety reason they were stored in the refrigerator. [**CAUTION**: We did not observe any untoward incidence while working with allyl azides. However, the use of hood and safety shield is recommended, as azides are known for their explosive property].

(13) **Typical Experimental Procedure for the Preparation of Cinnamyl Azide (1):** To a stirred solution of triphosgene (1.48 g, 5 mmol) in acetone (20 mL) was added a solution of cinnamyl alcohol (1.34 g, 10 mmol) and Et_3N (1.51 g, 15

mmol) at 0 °C. The reaction mixture was stirred for 20 min and then at r.t. for 3 h. It was cooled to 0 °C and sodium azide (1.30 g, 20 mmol) was added in one portion. It was stirred at this temperature for 1 h and kept at r.t. for 12 h. To the reaction mixture H_2O (20 mL) was added and extracted with Et_2O (3 × 20 mL). The organic layer was washed with brine (20 mL) and dried over anhyd Na_2SO_4. The solvent was removed under reduced pressure at r.t. to get pure cinnamyl azide(**1**) as yellow oil (1.28 g, 80%). [**CAUTION**: We did not observe any untoward incidence while working with allyl azides. However, the use of hood and safety shield is recommended, as azides are known for their explosive property.] IR ($CHCl_3$): 2100, 1492, 1448, 1350, 1236, 968 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 3.96 (d, *J* = 6.0 Hz, 2 H), 6.15–6.35 (m, 1 H), 6.67 (d, *J* = 17.0 Hz, 1 H), 7.10–7.55 (m, 5 H). MS: *m/z* (%) = 159 (15) [M^+], 130 (57), 117 (100), 104 (74).

(14) In these cases, *N*,*N*-dimethyl carbamoyl azide was obtained as a by-product, which was arising from the reaction of Et_3N, triphosgene and sodium azide with the loss of ethyl group. This reaction will be studied in detail and results will be communicated in future.

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(16) **Typical Experimental Procedure for the Preparation of *N*-Cinnamyl Azetidin-2-one (4a):** To a solution of cinnamyl azide (0.318 g, 2 mmol) in toluene (20 mL) was added triphenylphosphine (0.524 g, 2 mmol) and the reaction mixture was refluxed for 6 h. The reaction mixture was cooled to 0 °C and benzaldehyde (0.212 g, 2 mmol) was added to the reaction mixture. It was stirred at r.t. for 12 h. Solvent was removed under reduced pressure and the residue containing imine **3a** and triphenylphosphine oxide was dissolved in dry CH_2Cl_2 (20 mL) and directly used for the next reaction without isolation of the imine **3a** since it was found to be unstable.
To the above solution of imine in CH_2Cl_2, Et_3N (0.91 g, 9 mmol) was added and the solution was cooled to –15 °C. A solution of benzyloxyacetyl chloride in CH_2Cl_2 (10 mL) was added slowly with stirring in about 30 min and the reaction mixture was allowed to warm up to r.t. and stirred for 18 h. It was washed with H_2O (20 mL), sat. $NaHCO_3$ solution (20 mL), brine (10 mL) and dried over anhyd Na_2SO_4. Solvent was removed under reduced pressure and the crude product was purified by column chromatography to get white solid β-lactam **4a** in 74% yield. White solid, mp 140–141 °C. IR ($CHCl_3$): 1751 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 3.60 (dd, *J* = 7.8 and 15.1 Hz, 1 H), 4.18 (d, *J* = 11.2 Hz, 1 H), 4.25 (d, *J* = 11.2 Hz, 1 H), 4.34–4.41 (m, 1 H), 4.79 (d, *J* = 4.4 Hz, 1 H), 4.92 (d, *J* = 4.4 Hz, 1 H), 5.96–6.11 (m, 1 H), 6.39 (d, *J* = 15.6 Hz, 1 H). 6.94–7.40 (m, 15 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 42.1, 61.6, 72.1, 83.6, 122.1, 126.3, 127.7, 127.8, 128.0, 128.1, 128.3, 128.4, 128.5, 134.2, 136.1, 136.3, 166.7. MS: *m*/*z* = 369 (M^+). Anal. Calcd for $C_{25}H_{23}NO_2$: C, 81.27; H, 6.27; N, 3.79. Found: C, 81.44; H, 6.33; N, 3.67.

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