



Simple and facile method for the preparation of vinyl azides

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ABSTRACT

A synthetic utility of [bis(trifluoroacetoxy)iodo]benzene on α,β -unsaturated carboxylic acid is described. This is the first example of preparation of vinyl azide using α,β -unsaturated carboxylic acids directly by using hypervalent iodine reagent. The advantage of this protocol is characterized with non-toxicity of starting material and shorter reaction times to obtain good preparative yields. The method is also useful for the preparation of acyl azides.

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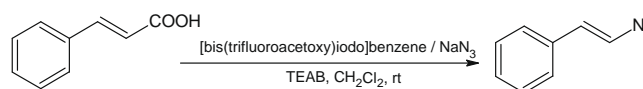
Vinyl azides have found wide applications in organic transformations such as conversions to azirine,¹ indole,² triazole,³ and many other cyclic compounds.⁴ Although vinyl azides have shown increasing importance in many aspects, synthetic studies toward these compounds are rare. There are only a few methods reported for the preparation of vinyl azides. A commonly used preparation method is the elimination of β -iodo azides,⁵ which is based on the addition of iodine azide to olefins. However this procedure was characterized by unfavorable decomposition of iodine azide in some cases. In substitution reaction, vinyl halide reacted with sodium azide in presence of CuI and L-proline.⁶ Apart from these inconvenient syntheses there is only one method reported which involves the indirect conversion of α,β -unsaturated carboxylic acids to vinyl azides. In this method, first α,β -unsaturated carboxylic acids reacted with sodium azide in acetonitrile overnight in presence of cerium ammonium nitrate. The elimination of formed nitrate intermediate then affords vinyl azide using sodium acetate.⁷ Despite the above mentioned examples, the study of novel efficient synthesis of vinyl azides is still valuable in the field of organic chemistry.

Hypervalent iodine reagents have found widespread applications in organic synthesis because of their selectivity and simplicity in use.⁸ Our group has been working extensively on the development of novel methodologies under mild reaction conditions using various hypervalent iodine reagents.⁹ [bis(trifluoroacetoxy)iodo]benzene is commercially available as colorless crystalline solid. It is fairly stable and can be kept without refrigeration for long period of time, with protection from light. It is used

for the synthesis of N-arylated and N-alkylated heterocyclic-fused aromatic compounds,¹⁰ synthesis of pyrrolidinone and lactone skeletons,¹¹ oxidative deprotection of dithiane containing alkaloids,¹² direct α -hydroxylation of ketones,¹³ and other reactions.¹⁴

During the course of our previous unpublished studies, we found that treatment of α,β -unsaturated carboxylic acids with NaN₃ and tetraethylammonium bromide (TEAB) in dichloromethane gave vinyl azides. Initially, we carried out the reaction with cinnamic acid as a model to explore the suitable reaction conditions with sodium azide and TEAB in dichloromethane at room temperature (Scheme 1; Table 1, entry 1). In this case, the reaction afforded the corresponding 3-phenylprop-2-enyl azide as a major product in absence of TEAB instead of desired vinyl azide (Scheme 2; Table 1, entry 11). We have also found that chloroform and dichloromethane are the best solvents. As we are working on hypervalent iodine system, to explore the possibility of other trivalent iodine reagents for conversion of α,β -unsaturated carboxylic acids to vinyl azide, we carried out the reaction with cinnamic acid under similar as well as different reaction conditions with hypervalent iodine reagents such as IBX and 4,4'-bis-(dichloroiodo)-biphenyl instead of [bis(trifluoroacetoxy)iodo]benzene, no formation of vinyl azide was observed even after 48 h.

In order to explore the reaction scope, a variety of α,β -unsaturated carboxylic acids, prepared by standard reported procedures,



Scheme 1. Cinnamic acid converted into vinyl azide using [bis(trifluoroacetoxy)iodo]benzene and sodium azide and TEAB.

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Table 1
Carboxylic acid reaction with [bis(trifluoroacetoxy)iodo]benzene and sodium azide

Entry	Substrate ^b	Product	Time (min)	Yield ^c (%)
1 ^a			30	80
2			30	84
3			35	80
4			120	75
5			30	87
6			35	88
7			180	70
8			180	70
9		—	24 h	NR ^d
10		—	24 h	NR ^d
11 ^e			30	86
12			30	88

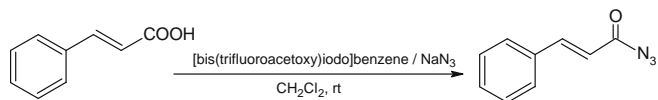
^a Reaction conditions (entries 1–10): substrate (1.0 equiv), [bis(trifluoroacetoxy)iodo]benzene (1.2 equiv), TEAB (1.2 equiv), anhyd CH₂Cl₂, rt, and sodium azide (1.2 equiv).

^b Starting compounds were prepared by standard reported procedures.

^c Isolated yields after column chromatography and structures were confirmed by comparison of the IR and ¹H NMR spectra with those of authentic materials.

^d No reaction.

^e Reaction conditions (entries 11 and 12): substrate (1.0 equiv), [bis(trifluoroacetoxy)iodo]benzene (1.2 equiv), sodium azide (1.2 equiv), anhyd CH₂Cl₂, rt.



Scheme 2. Cinnamic acid converted into acyl azide using [bis(trifluoroacetoxy)iodo]benzene and sodium azide.

were converted to corresponding vinyl azides in moderate to good yields and the results are summarized in Table 1.¹⁵ It was found that either electron-rich or electron-deficient α,β -unsaturated carboxylic acids were suitable for this reaction, giving desired vinyl azide in moderate to good yields in short reaction times (Table 1, entries 2–4). It was noted that a variety of functional groups tolerated these reaction conditions (Table 1, entries 3–7). This feature would allow the use of the present method in the synthesis of wide range of vinyl azides. A lower reaction rate was observed with aliphatic α,β -unsaturated carboxylic acids (Table 1, entries 7 and 8).

Further investigations indicated that in the absence of double bond reaction does not take place (Table 1, entries 9 and 10). In the absence of TEAB under similar reaction conditions cinnamic acid and *p*-methyl cinnamic acid readily converted into corresponding acyl azides (Table 1, entries 11 and 12) without affecting the double bond.

In conclusion, a new reaction system using trivalent iodine reagents, [bis(trifluoroacetoxy)iodo]benzene, in combination with TEAB and sodium azide has been developed, which is capable of converting various α,β -unsaturated carboxylic acids into corresponding vinyl azides, at room temperature. The method developed is mild and gives moderate to good yields of vinyl azides and acyl azides for both aliphatic and aromatic substrates.

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15. *General procedure:* To a stirred solution of [bis(trifluoroacetoxy)iodo]benzene (1.2 equiv) in anhyd CH_2Cl_2 (15 mL) was added TEAB (1.2 equiv) in one portion. The resultant reaction mixture was stirred for 5 min followed by addition of α,β -unsaturated carboxylic acid (1.0 equiv). After completion of addition, sodium azide (1.2 equiv) was added and the mixture was stirred at room temperature until the starting material was completely consumed (TLC). The reaction mixture was diluted with CH_2Cl_2 and washed successively with 10% sodium bisulfate solution (2×20 mL), 10% sodium bicarbonate (2×15 mL), and water (2×20 mL). The organic layer was dried over anhydrous sodium sulfate and concentrated under reduced pressure to give crude product. Pure product was obtained after silica gel column chromatography (10% EtOAc-hexane). [Acyl azides were prepared using similar procedure without the addition of TEAB].