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A Simple Access to Trichloroacetimidates

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Abstract : O - Trichloroacetimidates can be prepared, under mild conditions in high yield and high purity, by reacting the substrate with trichloroacetonitrile in dichloromethane and 50% aqueous potassium hydroxide mixture containing a catalytic amount of tetra-n-butylammonium hydrogen sulfate.

Synthesis of trichloroacetimidates has gained considerable importance in recent years due to their various uses like : 1) introduction of nitrogen functionality in the molecules via their allylic / allenic rearrangements[1].
2) in the synthesis of glycosides and oligosaccharides[2].
3) stereocontrolled cyclofunctionalisations of double bonds through heterocyclic intermediates[3].
4) benzylation of a hydroxyl group by benzyltrichloroacetimidates[4] .
5) synthesis of aryl nitriles by the dehydration of their aldoximes *via* their trichloroacetimidates[5].

Reaction : $R\text{-}CH_2\text{-}OH \longrightarrow R\text{-}CH_2\text{-}O\text{-}C(=NH)\text{-}CCl_3$

There exists a number of methods in the literature for the preparation of the imidic esters according to the above reaction, viz sodium hydride in diethyl ether[1], sodium hydride in tetrahydrofuran[1,2], potassium carbonate in dichloromethane[2], 1,8-diazabicyclo[5.4.0]undec-7-ene in dichloromethane[6], metallic sodium in tetrahydrofuran[7], sodium methoxide in methanol , sodium n - butylate in butanol, sodium n-octylate in octanol, potassium tetrabenzyloxy aluminate in ethanol, lithium isopropylate in isopropanol[8] and more recently cesium carbonate in dichloromethane[9]. These methods however all need an inert atmosphere and anhydrous conditions. Furthermore the trichloroacetimidates so obtained have to be purified before they are utilised for further reactions . This is usually done by subjecting the crude sample to column chromatography and / or distillation. However it has been observed [1,7] (especially in case of allylic trichloroacetimidates) that part of the substrate undergoes allylic rearrangement and in some cases chromatographic purification leads to decomposition. Hence it is imperative that one obtains pure product after the reaction.

Herein we describe a mild, convenient and simple alternative method for the preparation of the trichloroacetimidates in high yields.This procedure does not need an inert atmosphere, nor does it require dry solvent. The products so obtained are essentially pure and need no further purification either by column chromatography or distillation and can be directly used for further reactions[10].We report, when the substrates (1-9 in the Table) in dichloromethane were treated with trichloroacetonitrile in presence of 50% aqueous potassium hydroxide, containing a catalytic amount of tetrabutylammonium hydrogen sulfate, at -15 to 25°C,

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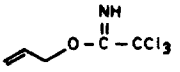
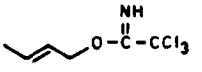
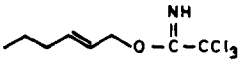
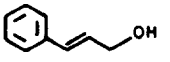
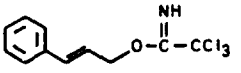
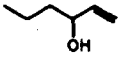
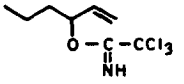
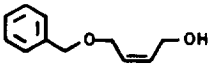
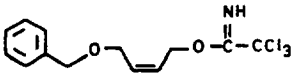
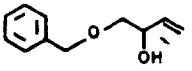
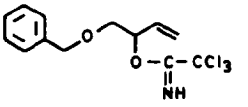
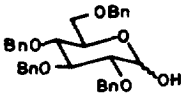
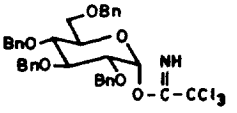
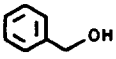
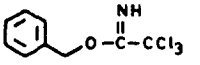
Dedicated to Dr. A . V. Rama Rao on the occasion of his 60th birthday

reacted cleanly to give the corresponding imidates in high yields (see Table). The products were obtained by simply filtering the organic layer through a pad of celite or activated charcoal or silica gel and evaporating the solvent under reduced pressure (see general procedure).

Table

Entry	SUBSTRATE[a]	PRODUCT[b]	YIELD[c] (%)	REF.
1			80	1c
2			93	1c
3			95	1c
4			93	1c
5			93	1c
6			97	11
7			92	11
8			96	2c,d
9			97	4

a. all reactions were carried out on 1.0 gm scale.

b. the structure of the compounds were confirmed by ^{1}H -NMR spectrum comparison with those reported in literature.

c. yields quoted are isolated yields of pure product.

As it can be seen from the Table primary and secondary allylic alcohols readily react to give the allylic imidates in high yields. Similarly, benzyl alcohol reacts cleanly to give the benzyl trichloroacetimidate in high yield and purity. The case of 2,3,4,6 tetra -O- benzyl -**D**- glucofuranose is of particular interest because it represents the class of O - glycosyl imidates which are of particular interest in stereospecific glycosylation and hence in the synthesis of polysaccharides [2a-d]. When 2,3,4,6 tetra -O- benzyl -**D**-glucofuranose was reacted with trichloroacetonitrile under the above mentioned conditions it reacted cleanly to furnish only one product, namely the α anomer[2d] as seen from the ^{1}H NMR spectrum of the product after isolation[2e]. We have not studied the kinetics of this reaction. Further work is under progress to apply this methodology to other sugar substrates.

In conclusion, this method provides a mild, convenient and simple alternative method for the preparation of trichloroacetimidates of a diverse range of substrates. This method is amenable for large scale reactions.

General Procedure : To the alcohol (1.0 g) in dichloromethane (10 mL) was added 50 % aqueous potassium hydroxide (10 mL) and tetra-n-butylammonium hydrogen sulphate (catalytic amount,15 mg) and the resulting mixture stirred vigorously at -15 to -10°C. After 5 minutes, trichloroacetonitrile (1.2 eq.) was added dropwise. The resulting mixture was further stirred at the same temperature for 0.5h and then allowed to warm to room temperature (25°C) in the next 0.5 h. The organic layer was separated, and the aqueous layer further extracted with dichloromethane (2 x 10 mL). The combined extracts were dried (anhydrous sodium sulfate) and concentrated under reduced pressure to 1/3 volume, then filtered through a celite pad (2 cms thick). Alternatively, a pad of activated charcoal or silica gel can also be used. The pad was further washed with dichloromethane (20 mL). Concentration of the combined filtrates under reduced pressure gave the product.

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