A Regioselective Introduction of Functional Groups to the Double Bonds of Allylic and Homoallylic Alcohols *via* the Corresponding Trichloroacetimidates

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A new regioselective iodoamination reaction starting from allylic and homoallylic alcohols is described; the iodoaminoalcohols are obtained as the salts (**2**) and (**4**) *via* the corresponding 1,3-oxazolines (**1**) and dihydro-1,3-oxazines (**3**).

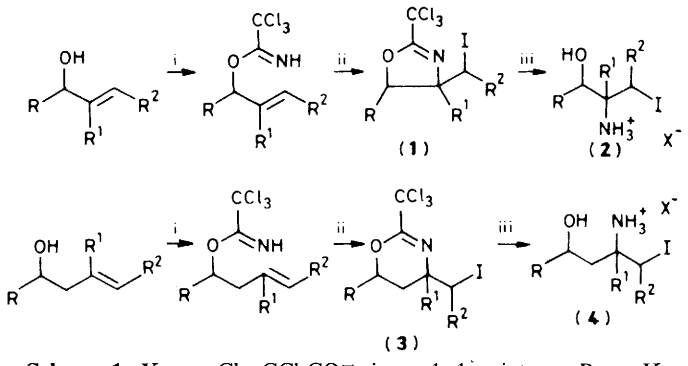
As part of a programme aimed at the total synthesis of sugar antibiotics, a new method for the stereocontrolled introduction of functional groups to the double bonds of allylic and homoallylic alcohols *via* cyclic iodocarbonates was developed recently in our laboratory.[1] The iodocarbonates are useful intermediates in the synthesis of epoxyalcohols and triols.[2]

We now report a new synthesis of 1,3-oxazolines (**1a—d**) and dihydro-1,3-oxazines (**3a—c**) *via* the introduction of functional groups to the double bond in the α or β position with respect to the trichloroacetimidate group.[3] The reaction was performed by adding I_2 in tetrahydrofuran (THF) to a solution of allylic or homoallylic trichloroacetimidates in the presence of pyridine.

The reaction showed a total regioselection; the allylic alcohols gave (**1a—d**), while the homoallylic alcohols afforded (**3a—c**), exclusively (Scheme 1). As shown by the results given in Table 1, this procedure is very efficient.

In order to investigate the stereoselection of ring closure, the diastereomeric ratios for (**1b**), (**1c**), (**1d**), (**3b**), and (**3c**) were determined by v.p.c. analysis and are reported in Table 1.

Since the rings of 1,3-oxazolines and dihydro-1,3-oxazines are cleaved easily upon acidic treatment, they are useful intermediates in organic synthesis.[4] We have found that the salts (**2**) and (**4**) or the trichloroacetamides (**6**) were obtained



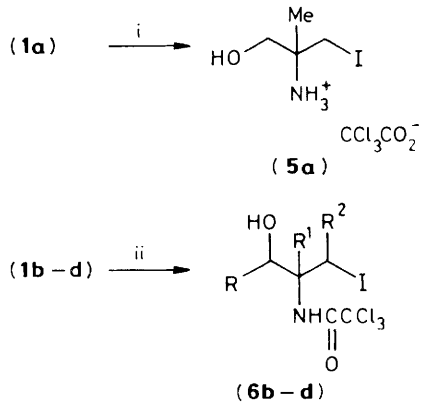
Scheme 1. X^- = Cl^-:$CCl_3CO_2^-$ in a 1:1 mixture. R = H, alkyl; R^1 = H, alkyl; R^2 = H, alkyl. *Reagents:* i, NaH catalyst, THF, CCl_3CN; ii, pyridine, I_2–THF; iii, 2 M HCl in MeOH.

selectively, with an appropriate choice of the ring cleavage conditions. Hydrolysis of the 5-unsubstituted 1,3-oxazolines (**1a**) or the 6-unsubstituted dihydro-1,3-oxazines (**3a, b**), performed in aqueous methanol at room temperature for 30 min in the presence of 1 equiv. of HCl, afforded a 1:1 mixture of trichloroacetates and hydrochlorides of the corresponding iodoaminoalcohols (**2a**) and (**4a, b**) in quantitative yield.

Table 1

Substrate	Product yield, %[a]	Diastereomeric ratio[b] (1)	Product yield, % (2)
$RCH(OH)C(R^1):CH(R^2)$			
a $R = R^2 = H$; $R^1 = Me$	85	—	95
b $R = CHMe_2$; $R^1 = R^2 = H$	70	95:5	96
c $R = C_5H_{11}$; $R^1 = R^2 = H$	60	75:25	95
d $R,R^2 = -[CH_2]_3-$; $R^1 = H$	55	99:1	94
$RCH(OH)CH_2C(R^1):CH(R^2)$		(3)	(4)
a $R = R^2 = H$; $R^1 = Me$	90	-	96
b $R = R^1 = H$; $R^2 = Et$	80	93:7	94
c $R = Me$; $R^1 = R^2 = H$	65	80:20	95

[a] Yields refer to pure isolated products. All new compounds gave satisfactory analytical and spectral data. [b] Determined by v.p.c



Scheme 2. i, MeOH, H_2O; ii, HCl, MeOH.

On the other hand, under the same reaction conditions the 5-alkyl-1,3-oxazolines (**1b—d**) gave the trichloroacetamides (**6b—d**) (Scheme 2). A longer reaction time was required to hydrolyse (**1b—d**) to the corresponding salts (**2b—d**).

In order to apply this method to the synthesis of natural molecules containing acid-sensitive groups, we also investigated the hydrolysis of (**1a—d**) in a neutral medium.[5] The reaction was carried out in aqueous methanol at 40 °C for 10 h. As reported above, the oxazoline (**1a**) gave (**5a**, $X^- = CCl_3CO_2^-$), while (**1b—d**) yielded the trichloroacetamides (**6b—d**).

The good yields obtained in the two steps of the reaction, the ease of the method, and the total regioselection provide an attractive synthetic route for the introduction of functional groups to carbon–carbon double bonds.

In a typical experimental procedure, a solution of 2-methylpropenol (2.16 g; 30 mmol) in dry THF (20 ml) was added to a suspension of NaH [120 mg of a 60% dispersion in mineral oil (Aldrich); 3 mmol] in dry THF (20 ml) at 0 °C. After 1 h the solution was dropped into trichloroacetonitrile (4.32 g; 30 mmol) in dry THF (30 ml) and the temperature was maintained at 0 °C for 2 h. Pyridine (2.4 g; 30 mmol) and then iodine (16.26 g; 64 mmol) in THF (40 ml) were added dropwise and the mixture was stirred for 12 h. After dilution with ethyl acetate, the organic layer was washed with aqueous $Na_2S_2O_8$, dried, and evaporated *in vacuo*. Silica gel chromatography of the residue (cyclohexane:ethyl acetate 9:1 as eluant) gave (**1a**) in 85% yield (8.7 g) as a solid (white crystals) [m.p. 163—165 °C (decomp.); i.r. (nujol): ν 1680 (C=N) cm^{-1}; ^1H n.m.r. ($CDCl_3$): δ 1.6 (s, 3 H, CH_3), 3.4 (s, 2 H, CH_2I), and 4.35 (ABq, 2 H, CH_2O; *J* 10 Hz)]. The compound (**1a**) (6.82 g; 20 mmol) in methanol (30 ml) was treated with 2 M HCl (10 ml) at room temperature for 30 min. The solution was evaporated and the salt (**2a**, $X^- = Cl^-:CCl_3CO_2^-$ in a 1:1 mixture) was obtained after crystallization of the residue from acetone (95% yield) [i.r. (nujol): ν 3260 (OH,NH), 2000 (NH_3^+), and 1600 (NH) cm^{-1}; ^1H n.m.r. (CD_3OD): δ 1.45 (s, 3 H, CH_3), 3.55 (s, 2 H, CH_2I), 3.75 (s, 2 H, CH_2OH), and 4.8 (br. s, 4 H, OH, NH_3^+)].

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