Mild Generation of Alkylidenecarbenes from α-Mesyloxynitriles of Sugars. Application to the Synthesis of Branched-chain Sugars

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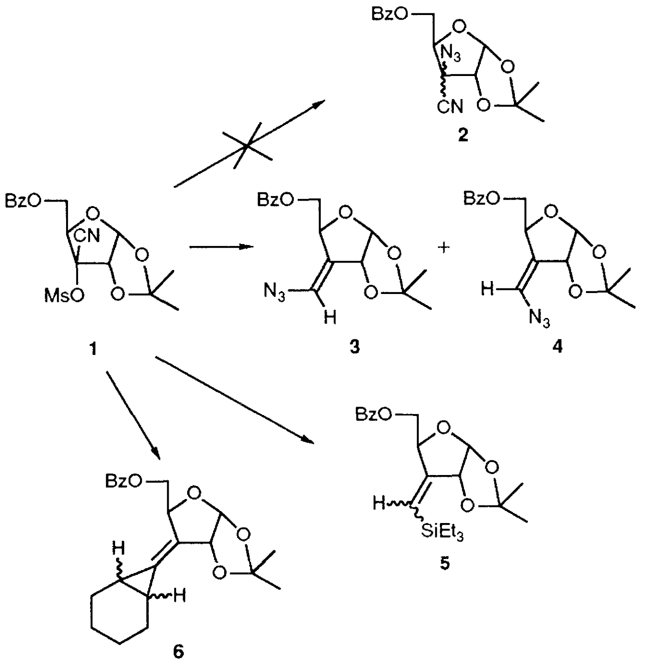
Treatment of *O*-mesylcyanohydrins of furanos-3-ulose with sodium azide affords vinylazidoderivatives; the intermediary of an alkylidenecarbene is proposed, and reactions to trap such an intermediate are described.

α-Mesyloxynitriles of carbohydrates are useful chiral synthons for naturally occurring branched-chain sugars,[1,2] and are easily obtained by reaction of uloses with sodium cyanide followed by mesylation of the corresponding cyanohydrin.

As part of our programme on the synthesis of highly functionalized branched-chain sugars, we tried to transform the α-mesyloxynitrile **1** into the corresponding α-azidonitrile **2** by nucleophilic displacement of the methanesulfonate group with an azide ion. Here, we report the unexpected behaviour of the α-mesyloxynitrile **1** which on treatment with sodium azide afforded the vinylazides **3** and **4**, and propose a mechanism for this reaction through an alkylidenecarbene



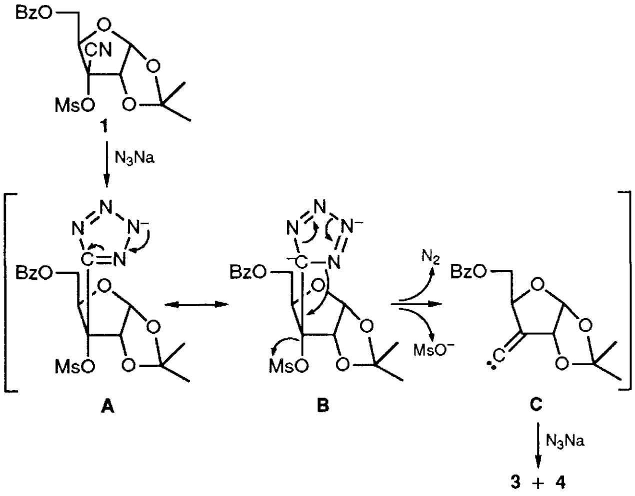
Scheme 1

intermediate. These reactive intermediates, that have not been studied so far, in carbohydrate chemistry, and offer new possibilities of functionalisation in *C*-branched carbohydrates.

Reaction of the α-mesyloxynitrile[3] **1** with an excess of sodium azide in dichloromethane, at room temperature and in the presence of tetrabutylammonium hydrogensulfate, afforded a mixture (2:3) of the vinylazides **3** and **4** in 30% yield.† Although the mixture of *E* and *Z* vinylazido derivatives **3** and **4** could not be separated by chromatography, the stereochemistry of the double bond of the minor and major isomers was established as *E* and *Z*, respectively, by NOE (nuclear Overhauser effect) difference experiments upon irradiation of the vinylic protons of both isomers.‡

The expected α-azidonitrile **2** was not detected. This seems to indicate a poor leaving-group character for the 3-*O*-mesyl group of **1**. This behaviour has also been found in a variety of crowded sulfonyloxy groups of carbohydrates.[4] Thus, we have recently described that α-mesyloxynitriles of furanos- and pyranos-uloses, on treatment with base, undergo an aldol-type cyclocondensation instead of leading to the expected elimination reaction.[5] Besides this, Czernecki *et al.* have reported the unusual formation of an acetylenic sugar on treatment of a secondary mesyloxynitrile of hexopyranoses with sodium azide.[6]

In Scheme 2 we propose a possible mechanism for the formation of the vinylazides **3** and **4**. Initial attack of the azide ion to the cyano group of **1** would lead to a tetrazolate **A**, which by charge readjustment and loss of N_2 and MsO^- would generate an alkylidenecarbene or carbenoid intermediate **C**. Subsequent reaction of **C** with the nucleophile present in the media (azide ion) would afford the vinylazides **3** and **4**. On the other hand, intermediary of an alkylidenecarbene has been proposed to be involved in the obtention of vinylazides by reaction of *N*-nitrosooxazolidones with NaN_3 under phase-transfer conditions.[7]



Scheme 2

Alkylidenecarbenes are known to insert into Si–H bonds to give vinylsilanes.[8] The preferred intermolecular reaction of alkylidenecarbenes is addition to alkenes. Such addition is commonly used to establish their intermediary in a particular reaction.[8] In order to demonstrate the participation of the alkylidenecarbene intermediate **C** in the mechanism proposed in Scheme 2, reactions to trap such an intermediate were carried out. Thus, reaction of α-mesyloxynitrile **1** with sodium azide in the presence of triethylsilane afforded the vinylsilanes **5** (58% yield),† resulting from the insertion of intermediate **C** into the Si–H bond of triethylsilane. Furthermore, treatment of **1** with NaN_3 in CH_2Cl_2 : cyclohexene (1 : 4) afforded a mixture (1 : 1) of the two possible adducts **6**† (35% yield) derived from addition of the intermediate **C** to the double bond of cyclohexene.

It can be concluded that an alkylidenecarbene or carbenoid intermediate is involved in the reaction of **1** with sodium azide. An alkylidenecarbene may also be involved in the formation of the acetylenic moiety described by Czernecki, through an intramolecular hydrogen migration, which is highly favoured in *H*-substituted alkylidenecarbenes. To the best of our knowledge, this is the first time that the intermediary of an alkylidenecarbene has been demonstrated in the chemistry of carbohydrates. The α-mesyloxynitriles of sugars, used as precursors of the alkylidenecarbene, are easily available from the corresponding uloses, and have not, so far, been employed to generate alkylidenecarbenes.

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† *Selected spectroscopic data*: **3** and **4** IR (film) ν/cm^{-1}: (N_3) 2100, (CO) 1715, (C=C–N) 1670; ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.05–5.18 (m, H-2 **3**, H-4 **4**), 5.18 (m, H-4 **3**), 5.22 (dd, H-2 **4**), 6.47 (t, H-1′ **4**), 6.64 (dd, H-1′ **3**). **5**: IR (film) ν/cm^{-1}: (C–H alkyl) 2930, 2870, (CO) 1720; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.58 [m, $(CH_3C\mathit{H}_2)_3Si$], 0.86 [m, $(C\mathit{H}_3CH_2)_3Si$], 4.83 (m, H-2*E*), 4.92–4.98 (m, H-4*E*, H-2*Z*), 5.04 (m, H-4*Z*), 5.68 (t, H-1′*E*), 6.02 (t, H-1′*Z*). **6**: IR (film) ν/cm^{-1}: (C–H alkyl) 2900, 2850, (C=C) methylencyclopropanic) 1760. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.36–1.59 (m, C_6H_{10}, Me_2C), 5.11 (dd, H-2), 5.15 (m, H-4).

‡ NOE observed upon irradiation of the vinylic proton (H-1′): **3**: H-2 (0.6%); **4**: H-4 (0.5%) and H-5a (3.4%).

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