Acetonation of methyl glycosides possessing a *cis*-diol system in the presence of tin(II) chloride—pyridine complex

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A tin(II) chloride—pyridine complex appears to be the catalyst with special steric requirements in condensation of sugars with acetone. From the saccharides studied, only the methyl glycosides having *cis*-diol groupings were effectively acetonated.

Isopropylidene derivatives of the aldoses and aldosides are important in syntheses, in structural and conformational studies and, in addition, they may serve as model substances for various investigations [1—3]. The compounds are generally prepared by the condensation of acetone with suitable hydroxylic substrates in the presence of a catalyst and the nature of the final product is usually thermodynamically controlled. As the catalyst plays an important role in these acetalations, various compounds [1] have been used for this purpose. Recently, much effort has been devoted to a search for such catalysts that would act more selectively than those already described. Thus, *Chittenden* reported [4] an improved synthesis of 1,2:5,6-di-*O*-isopropylidene-D-mannitol, where tin(II) chloride was used as the catalyst. In the acetalation reaction, however, the role of the latter could not be clarified with certainty and further investigations showed [5] that no catalyst was required. In connection with our studies [6—11] on reactions catalyzed by tin(II) chloride, we also examined the effect of this compound on acetonations of variously disposed hydroxyl groups of selected sugars and of their methyl glycosides. The primary purpose of this work is to report on a further application of tin(II) chloride and/or its adducts in carbohydrate chemistry and simultaneously, to present an alternative and rather selective method for the preparation of some isopropylidene derivatives.

When L-rhamnose, L-fucose, D-mannose, D-galactose, D-glucose, and D-xylose were treated with acetone in the presence of various amounts of tin(II) chloride, no noticeable acetalation could be observed even at elevated temperatures after a longer period of time. On the other hand, their methyl glycosides having *cis*-diol groups were converted to the corresponding isopropylidene acetals in moderate yields. Addition of pyridine to the reaction mixture promoted acetalation. The best conversions were achieved when tin(II) chloride and pyridine were added in equimolar proportions. This fact indicated forma-

tion and subsequent involvement of tin(II) chloride—pyridine complex in the promoted catalysis of the condensation reaction. In the following studies, the adduct tin(II) chloride—pyridine, $SnCl_2$ C_5H_5N, was prepared [12] and its influence on the reaction was investigated. As in the preceding case, acetalation took place with methyl glycosides possessing *cis*-diol groupings and though in both cases the products were identical, the latter approach gave higher yields by 10—15%. Again, reducing sugars were not condensed effectively under these conditions. Increasing amounts of the tin(II) chloride—pyridine complex added to the reaction mixture had apparently only a little influence on the reaction course as no substantial difference in the yields and isomer distribution of the isopropylidene acetals was found. On the other hand, elevated temperatures and longer reaction times increased the yields of desired products, which were evidently thermodynamically controlled. Heating at 110°C for 30 h in the case of methyl 6-deoxyhexopyranosides and for 60 h with methyl hexopyranosides gave optimal conversions.

The both, methyl α-L-rhamnopyranoside and methyl α-L-fucopyranoside gave on acetalation the corresponding 2,3- and 3,4-*O*-isopropylidene derivatives in ≈84% and ≈89% yields, respectively. With methyl α-L-fucopyranoside, a trace amount of 1,2:3,4-di-*O*-isopropylidene acetal could also be detected (GLC—mass spectrometry) in the reaction mixture. Methyl α-D-galactopyranoside afforded exclusively the 3,4-*O*-isopropylidene derivative in ≈79% yield while methyl α-D-mannopyranoside yielded the respective 2,3-*O*-isopropylidene and 2,3:4,6-di-*O*-isopropylidene acetals (≈72% and ≈5.8%, respectively) together with a small amount (≈1.5%) of 1,2:5,6-di-*O*-isopropylidene-D-mannofuranose. This compound was probably formed as the result of slight fission of C-1 acetal moiety and subsequent isopropylidenation.

The role of the tin(II) chloride—pyridine complex in the reaction could be elucidated only partially thus far. The compound has a limited solubility in acetone and a prerequisite for its catalytic effect is the presence of both *cis*-diol grouping and C-1 acetal moiety in a sugar molecule. The latter condition is a new aspect in the acetalation of saccharides and has not been described thus far. The results presented differ from those reported [1] for acetonations in the presence of Lewis acids, where the free sugars with or without *cis*-diol groupings may be condensed effectively with acetone, too. Moreover, the tin(II) chloride—pyridine complex has apparently a little tendency to promote formation of the 4,6-acetals, which was observed, for example, with zinc(II) chloride [13].

In conclusion, the preliminary results reported indicate distinct steric and substitution requirements for the sugars acetonated in the presence of tin(II) chloride—pyridine adduct. The potential of the method might be exemplified, *e.g.* in the selective isopropylidenation of monosaccharide mixtures and predetermined sugar units in oligosaccharides. Therefore, further investigations

are in progress to elucidate in detail the mechanism of catalysis and related structural and stereochemical problems.

Experimental

All solvents used were purified and dried. Anhydrous tin(II) chloride and the adduct tin(II) chloride—pyridine, $SnCl_2$ C_5H_5N, were prepared as described elsewhere [7, 12]. TLC was performed on Silufol plates (Kavalier, Votice) with *A* (chloroform—methanol, $\varphi_r = 19:1$) and *B* (chloroform—acetone, $\varphi_r = 5:2$) solvents. Saccharides were detected by charring after spraying the plates with 20% aqueous solution of ammonium sulfate. Dry-column chromatography was carried out on Silikagel L (40—100 μm; Lachema, Brno) in the same solvent systems. Solutions were concentrated below 50°C under diminished pressure.

GLC was performed with a Hewlett—Packard Model 5711 A chromatograph using a column (300 cm × 0.32 cm) of 4% of XE-60 on 0.147—0.175 mm Chromosorb W (AW-DMCS), in a programmed temperature range of 140°C (4 min) to 200°C, the rate of temperature increase being 2°C min^{-1} GLC—mass spectrometry was conducted with a JMS-D 100 (Jeol) spectrometer, using a column (100 cm × 0.4 cm) packed with 0.147—0.175 mm Chromosorb W (AW-DMCS) coated with 4% of XE-60. The inlet helium pressure was 101.3 kPa, temperature programmed from 120°C (4 min) to 200°C increasing at the rate of 2°C min^{-1}, and the spectra were recorded at the ionizing energy 23 eV

A typical isopropylidenation procedure is as follows. A mixture of methyl glycoside (1 g) and tin(II) chloride—pyridine complex ($SnCl_2$ C_5H_5N; 10—50 mg) in dry acetone (40 cm^3) is stirred occasionally, and heated at 110°C in a sealed tube for 30 h in the case of methyl 6-deoxyhexopyranosides and for 60 h with methyl hexopyranosides. The solution is cooled, concentrated to a low volume and the isopropylidene acetal is isolated by chromatography on a column of silica gel using solvents *A* or *B*.

The identities and purities of the isopropylidene derivatives were proved by GLC—mass spectrometry. Their mass spectra did not differ importantly from those reported [2, 14] and need not be discussed. Yields of the individual isopropylidene acetals were determined by GLC in the sample aliquots withdrawn from the reaction mixtures and were comparable with those obtained after the separation of products on silica gel.

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