*Carbohydrate Research*, 184 (1988) c5–c8
Elsevier Science Publishers B.V., Amsterdam – Printed in The Netherlands



**Preliminary communication**

# Pyruvic acetal formation from a pyruvyl thioacetal, catalyzed by methyl triflate, dimethyl(methylthio)sulfonium triflate, or nitroso tetrafluoroborate

ANDRÁS LIPTÁK AND LAJOS SZABÓ
*Institute of Biochemistry, Lajos Kossuth University, P.O. Box 55, H-4010 Debrecen (Hungary)*
(Received August 17th, 1988; accepted for publication, September 5th, 1988)

Pyruvic acid, as a cyclic acetal generator, is quite widespread among carbohydrate-containing, natural products. Many polysaccharides contain 4,6-acetals[1], and 1,4-dioxolane-type acetals formed either from *cis*-axial–equatorial[2,3] or *trans*-diequatorial[4] hydroxyl groups are also known. Recently, some pyruvic acetal-containing lipo-oligosaccharides have been isolated from the antigens of the MAIS serocomplex[5] and *Mycobacterium smegmatis*[6].

Earlier syntheses[7,8] of pyruvic acetals involving 1-acetoxy-2-propanone afforded only very low yields, and thus were unsatisfactory for preparative purposes. Since neither the direct condensation of pyruvic esters[9], nor the acetal-exchange reaction between 2,2-dialkoxypropanoic esters[9,10] and diols, resulted in the desired pyruvic acetals, the application of some indirect routes was necessary. Using the procedure of Yoshimura *et al.*[11,12], namely, the reaction of trialkylsilylated diols with aldonolactones to give cyclospiro-orthoesters, trialkylsilylated diols were treated with pyruvic esters in the presence of trimethylsilyl triflate, to yield both isomers of the pyruvated hexopyranosides[9,13] or disaccharides.

We now report on the pyruvic acetal formation reaction between diols and methyl pyruvate diphenyl dithioacetal, activated by methyl triflate (MT)[14], dimethyl(methylthio)sulfonium trifluoromethanesulfonate (DMTST)[15], or nitroso tetrafluoroborate ($NOBF_4$)[16]. These reagents were recently introduced to activate 1-thioglycosides for the preparation of glycosides and, mainly, of complex oligosaccharides[17].

It is known that the oxo compounds can be regenerated from their thioacetals by alkylation. The alkylations were achieved by different methods, such as with methyl iodide in acetone[18], with methyl fluorosulfonate ("magic methyl") in sulfur dioxide[18], benzene[19], or dichloromethane[20], or with triethyloxonium tetrafluoroborate[21]. Transformation of dithioacetals with $NOBF_4$ to afford the corresponding carbonyl compounds[22] has also been reported. Thioacetals were interchanged to give acetals by using methyl fluorosulfonate[20,23].

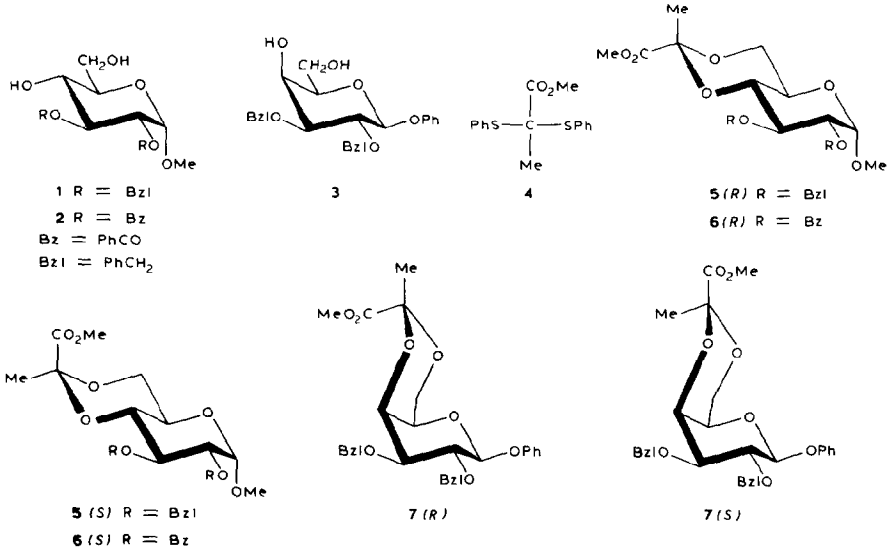
TABLE I

PHYSICAL AND $^{13}C$-N.M.R.-SPECTRAL DATA FOR THE PYRUVIC ACETALS **5–7**

| *Diol* | *Product* | *Activator* | | | | | | *M.p.* (°C) | $[\alpha]_D$ (degrees)[d] | $R_F$[e] | | *C-4* | *C-6* | *$CH_3$–* | *C–* | *$CO_2$–* | *$CH_3$* |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | *MT* | | *DMTST* | | *$NOBF_4$* | | | | *Value* | *Solvent* | | | | | | |
| | | *A*[a] | *B*[b] | *A*[a] | *B*[b] | *A*[a] | *C*[c] | | | | | | | | | | |
| **1** | **5**(*R*) | 36 | 6 | 26 | 2 | trace | 40 | 104–106 | −7.8 | 0.50 | [a] | 74.7 | 63.2 | 17.8 | 97.8 | 168.8 | 52.7 |
| **1** | **5**(*S*) | 34 | 6 | 39 | 2 | 90 | 40 | 104–106 | +43.4 | 0.70 | [a] | 78.3 | 65.6 | 25.5 | 99.0 | 170.3 | 52.5 |
| **2** | **6**(*R*) | 28 | 6 | 22 | 2 | 5 | 40 | syrup | +88.3 | 0.17 | [b] | 71.7 | 63.2 | 18.1 | 98.2 | 168.4 | 52.6 |
| **2** | **6**(*S*) | 36 | 6 | 48 | 2 | 85 | 40 | syrup | +124.4 | 0.23 | [b] | 75.3 | 65.4 | 25.1 | 99.3 | 169.9 | 52.4 |
| **3** | **7**(*R*) | 35 | 6 | 27 | 2 | 35 | 60 | solid | −33.1 | 0.61 | [c] | 68.8 | 65.5 | 25.9 | 98.1 | 168.3 | |
| **3** | **7**(*S*) | 32 | 6 | 30 | 2 | 28 | 60 | solid | −7.7 | 0.68 | [c] | 67.5 | 64.9 | 23.0 | 97.3 | 169.9 | |

[a]A = yield (%). [b]B = reaction time (h). [c]C = reaction time (min). [d]Recorded in chloroform. [e]T.l.c. solvents: a, 3:2 hexane–ethyl acetate; b, 13:7 hexane–ethyl acetate; c, 93:7 dichloromethane–ethyl acetate.

To prepare 4,6-*O*-[(1-carboxymethyl)ethylidene]hexopyranosides, compounds **1**, **2**, and **3** were used as diols, and methyl pyruvate diphenyl dithioacetal (**4**) was the acetalation reagent. Typically, a mixture of 1 mmol of a diol and 1.2 mmol of thioacetal **4** in dichloromethane (10 mL), was stirred for 10 min at −20° under dry argon, followed by the addition of MT (6.6 mmol), DMTST (8.8 mmol), or $NOBF_4$ (2.4 mmol), the course of the reaction being monitored by t.l.c. After disappearance of the starting diols, the mixture was diluted with dichloromethane (50 mL), and treated with an excess of saturated $NaHCO_3$ solution. The products were isolated by extractive workup, and the diastereoisomers were separated by column chromatography. The conditions of the reactions and the physical data for the products are given in Table I. On the basis of the isomeric ratio determined by t.l.c., it is suggested that the thermodynamic products are the (*S*)-isomers.




Determination of the configuration of the acetalic carbon atoms was based on the values of the chemical shift of the methyl groups, using regularities earlier observed[7–9].

Mechanistically, these reactions are presumed to proceed *via* different intermediates, such as $-S^+(CH_3)Ph$ (MT), $-S^+(SCH_3)Ph$ (DMTST), or $-S^+(NO)Ph$ ($NOBF_4$), to generate carbonium cations, which are then attacked by the nucleophile, to give hemithioacetals, and, finally, acetals.

The present methodology might contribute to the synthesis of otherwise difficultly available acetals of complex natural products.

REFERENCES


1 S. HIRASE, *Bull. Chem. Soc. Jpn.*, 30 (1957) 68–79.
2 Y. M. CHOY AND G. G. S. DUTTON, *Can. J. Chem.*, 52 (1974) 684–687.
3 G. G. S. DUTTON AND D. N. KARUNARATNE, *Carbohydr. Res.*, 134 (1984) 103–114.
4 P. A. J. GORIN, M. MAZUREK, H. S. DUARTE, AND J. H. DUARTE, *Carbohydr. Res.*, 92 (1981) c1–c4.
5 P. BRENNAN, G. O. ASPINALL, AND J. E. NAM SHIN, *J. Biol. Chem.*, 256 (1981) 6817–6811.
6 S. SAADAT AND C. E. BALLOU, *J. Biol. Chem.*, 258 (1983) 1813–1818.
7 P. A. J. GORIN AND T. ISHIKAWA, *Can. J. Chem.*, 45 (1967) 521–532.
8 P. J. GAREGG, B. LINDBERG, AND I. KVARNSTRÖM, *Carbohydr. Res.*, 77 (1979) 71–78.
9 A. LIPTÁK AND L. SZABÓ, *J. Carbohydr. Chem.*, in press.
10 I. E. VALESHEK, M. K. SHAKHOVA, V. A. MINAEV, AND G. I. SAMOKHVALOV, *Zhur. Obshch. Khim.*, 44 (1974) 1161–1164.
11 J. YOSHIMURA, S. HORITO, AND H. HASHIMOTO, *Chem. Lett.*, (1981) 375–376.
12 S. HORITO, K. ASANO, K. UMEMURA, H. HASHIMOTO, AND J. YOSHIMURA, *Carbohydr. Res.*, 121 (1983) 175–185.
13 H. HASHIMOTO, K. HIRUMA, AND J. TAMURA, *Carbohydr. Res.*, 177 (1988) c9–c12.
14 H. LÖNN, *Carbohydr. Res.*, 139 (1985) 105–113; 115–121.
15 P. FÜGEDI AND P. J. GAREGG, *Carbohydr. Res.*, 149 (1986) c9–c12.
16 V. POZSGAY AND H. J. JENNINGS, *J. Org. Chem.*, 52 (1987) 4635–4637.
17 P. FÜGEDI, P. J. GAREGG, H. LÖNN, AND T. NORBERG, *Glycoconjugate J.*, 4 (1987) 97–108.
18 M. FÉTIZON AND M. JURION, *J. Chem. Soc., Chem. Commun.*, (1972) 382–383.
19 T. L. HO AND C. M. WONG, *Synthesis*, (1972) 561.
20 E. J. COREY AND T. HASE, *Tetahedron Lett.*, (1975) 3267–3268.
21 T. IOSHI, K. KAMEMOTO, AND Y. BAN, *Tetrahedron Lett.*, (1972) 1085–1088.
22 G. A. OLÁH, S. C. NARANG, G. F. SALEM, AND B. G. GUPTA, *Synthesis*, (1979) 273–274.
23 R. M. MUNAVU AND H. SZMANT, *Tetrahedron Lett.*, (1975) 4543–4546.