Tetrahedron Letters, Vol.31, No.43, pp 6167-6170, 1990
Printed in Great Britain

0040-4039/90 $3.00 + .00
Pergamon Press plc

HALOENAMINES -II. A RAPID AND EFFICIENT SYNTHESIS OF CARBOHYDRATE 1,2-ORTHOESTERS

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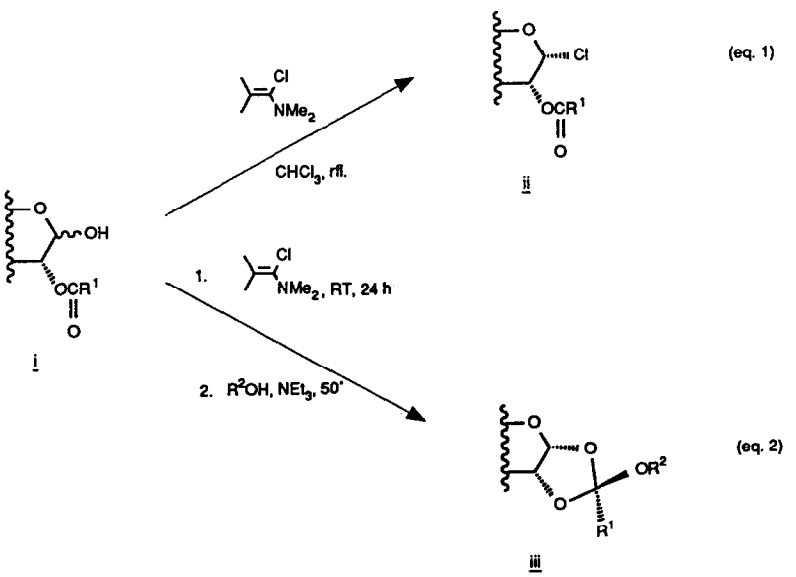
Summary: *Carbohydrate exo 1,2-orthoesters are obtained in good to excellent yields by treating furanose and pyranose hemiacetals first with 1.1 eq. 1-chloro-2,N,N-trimethyl-propenylamine and then with the appropriate alcohols in the presence of NEt_3.*

Carbohydrate 1,2-orthoesters have long been known [1] and used for the synthesis of 1,2-trans glycosides [2] as well as for selective protection of carbohydrates [3].

There are at present several methods in the literature for their preparation from the corresponding 1,2-trans glycosyl halides [4] or the more stable 1,2-cis glycosyl halides [5].

While preparatively useful in many respects, many of these methods are, nevertheless, time consuming and laborious, require heavy metal catalysts and/or hindered pyridines as proton acceptors, and lead invariably to exo/endo mixtures of carbohydrate 1,2-orthoesters.

We recently reported the use of 1-chloro-2,N,N-trimethyl-propenylamine [6] for the high-yield preparation of glycosyl halides under neutral conditions [7] (eq. 1).



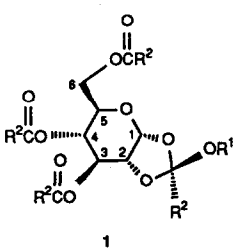
(eq. 1)

(eq. 2)

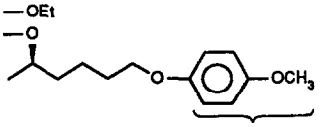
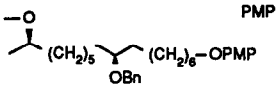
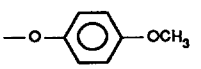
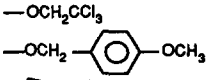
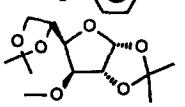
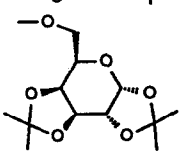
Whereas the glycosyl chlorides of 2,3,4,6-tetra-O-benzyl-D-glycopyranoses are easily formed at room temperature, the preparation of glycosyl halides ii of 2-acylated mono- and disaccharides needs elevated temperature [eq. 1].

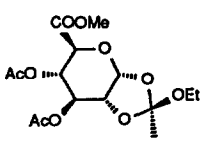
However, if the acylated hemiacetal i is treated at room temperature with 1-chloro-2,N,N-trimethyl-propenylamine followed by addition of an alcohol R^2OH and NEt_3 [8] exo 1,2-orthoesters iii are formed in excellent yields (eq. 2). Under these conditions the glycosyl chlorides are formed only in traces except in the case of 2,3,4,6-tetra-O-acetyl-mannopyranoside, where the corresponding mannosyl chloride (cf. 4 in the table) is obtained in 45% yield. Our results are summarized in the table.

Table: exo 1,2-orthoester [9]

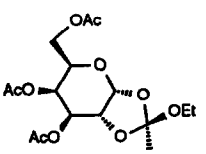


1

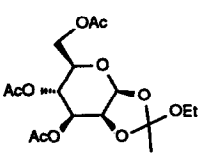
	—OR^1	R^2	Yield [10]
1a	—OEt	Me	90%
1b	—OEt	tBu	72%
1c		Me	80%
1d		Me	77%
1e		Me	89%
1f	—OEt	Ph	87%
1g	—SPh	Me	88%
1h	—$O(CH_2)_3NPhth$	Me	81%
1i	—OCH_2CCl_3	Me	84%
1k		Me	83%
1l		Me	92%
1m		Me	96%



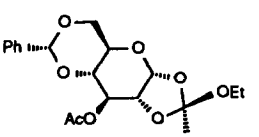
2, 75%



3, 89%

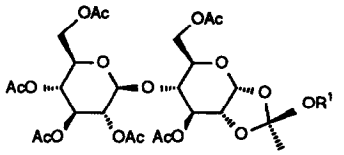


4, 42% (exo/endo)

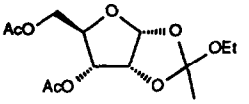


5, 85%

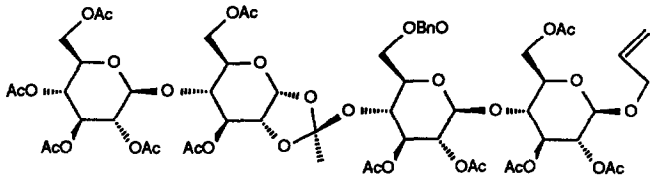
Table continued



6a ($R^1 = CH_2CCl_3$) 73%
6b ($R^1 = CH_2CHCH_2$) 88%



7, 78% (exo/endo = 86:14)



8, 68%

As the stereospecific transformation of orthoesters into 1,2-trans glycosides is well established [2] the development of this efficient synthetic procedure for orthoesters of complex aglycons [e.g. 8] makes the synthesis of complex glycosides possible.
A direct conversion of hemiacetals into glycosides via orthoester intermediate is under current investigation.

In a typical experiment a solution of 2,3,4,6-tetra-O-acetyl-D-glucopyranose in dry chloroform was treated with 1.1 equivalents of 1-chloro-2,N,N-trimethyl-propenylamine at room temperature. After being stirred for 12 hours 1.1 equivalents of each the appropriate alcohol and NEt_3 were added and the reaction mixture was stirred at 50°. After 6 hours tlc-analysis indicated completion of the reaction. Evaparation of the reaction mixture and flash chromatography [9] of the residue yielded the exo 1,2-orthoesters 1-8.

Acknowledgement: The authors are indebted to Mrs. S. Osswald for the measurement of the proton spectra.

References and notes

[1] E. Fischer, M. Bergmann, A. Rabe, Ber. Dtsch. Chem. Ges. 53, 2362 (1920); E. Pacsu, Adv. Carbohydrate Chem. 1, 77 (1945).

[2] N.K. Kochetkov, A.J. Khorlin, A.F. Bochkov, Tetrahedron 23, 693 (1967); N.K. Kochetkov, A.F. Bockkov. T.A. Solovaskaya, V.J. Snyatkova, Carbohydr. Res. 16, 17 (1971); A.F. Bochkov, Y.V. Voznyi, Carbohyd. Res. 32, 1 (1974).

[3] P.A.J. Gorin, Carbohydr. Res. 101, 12 (1982); M. Trumtel, A. Veyrière, P.Sinay, Tetrahedron Lett. 30, 2529 (1989).

[4] R.U. Lemieux, C. Brice, Can. J. Chem. 33, 109 (1955); R.U. Lemieux, J.D.T. Cipera, Can. J. Chem. 34, 906 (1956).

[5] B. Helferich, A. Doppstadt, A. Gottschlich, Naturwissenschaften 40, 441(1953); B. Helferich, K. Weis, Ber. Dtsch. Chem. Ges. 89, 314 (1956); M. Schulz, H. Steinmaus, Z. Naturforsch., B 19, 263 (1964); M. Mazurek, A.S. Perlin, Can. J. Chem. 43, 1918 (1965); R.U. Lemieux, A.R. Morgan, ibid. 43, 2199 (1965); G. Wulff, W. Krüger, Carbohyd. Res. 19, 139 (1971); S.E. Zurabyan, M.M. Tikhomirov, V.A. Nesmeyanow, A.Y. Khorlin, ibid. 26, 117 (1973); S. Hanessian, J. Banoub, ibid. 44, C14 (1975); T. Ogawa, M. Matsui, ibid. 51, C13 (1976); J. Banoub, D.R. Bundle, Can. J. Chem. 57, 2091 (1979); B.M. Dahlin, P.J. Garegg, R. Johansson, B. Samuelson, U. Örn, Acta Chem. Scand., Ser. B 35, 669 (1981); D.S.K. Tsui, P.A.J. Gorin, Carbohyd. Res. 144, 137 (1985); J. Banoub, P. Boullanger, M. Potier, G. Descotes. Tetrahedron Lett. 27, 4145 (1986).

[6] A. Devos. J. Remion, A.-M. Frisque-Hesbain, A. Colens, L. Ghosez. J. Chem. Soc., Chem. Commun. 1979, 1180.

[7] B. Ernst, T. Winkler, Tetrahedron Lett. 30, 3081 (1989).

[8] The use of sym. collidine, 2,6-lutidine or 2,4-lutidine instead of NEt_3 was not influencing the yields.

[9] ^{1}H-NMR (300 MHz, $CDCl_3$) data for the anomeric proton H-C(1) and the orthoester-methyl group are given below:
1a: 5.72 (d, J = 5.5), 1.73 (s); 1b: 5.78 (d, J = 5.7); 1c: 5.73 (d, J = 5), 1.75 (s); 1d: 5.69 (d, J = 5.3), 1.77 (s); 1e: 5.65 (d, J = 5.3), 1.72 (s); 1f: 6.05 (d, J = 5.2); 1g: 5.78 (d, J = 5.4), 1.83 (s); 1h: 5.73 (d, J = 5.0), 1.68 (s); 1i: 5.81 (d, J = 5.2), 1.80 (s); 1k: 5.68 (d, J = 5.2), 1.80 (s); 1l: 5.81 (d, J = 5), 1.81 (s); 1m: 5.73 (d, J = 5.2), 1.73 (s); 2: 5.86 (d, J = 4.6), 1.75 (s); 3: 5.80 (d, J = 4.8), 1.68 (s); 4: 5.48 (d, J = 2.6), 1.76 (s); 5: 5.75 (d, J = 5.1; 1.74 (s); 6a: 5.74 (d, J = 5.3), 1.80 (s); 6b: 5.67 (d, J = 5.0), 1.73 (s); 7: 5.94 (d, J = 4.0), 1.70 (s); 8: 5.62 (d, J = 5.2), 1.66 (s).

[10] Isolated yields after chromatography; to avoid decomposition of the orthoester on silica gel 1% NEt_3 was added to the eluant.

(Received in Germany 20 July 1990)