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STANNOUS TRIFLATE MEDIATED GLYCOSIDATIONS. A STEREOSELECTIVE SYNTHESIS OF β-D-GLUCOSIDES.

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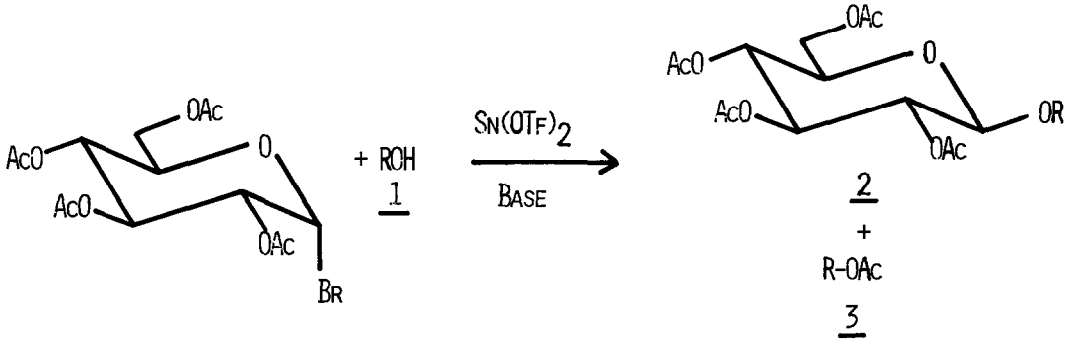
Abstract : Various 1,2 trans, β-D-linked disaccharides with glucose as non-reducing unit have been prepared with complete stereoselectivity from acetobromoglucose and suitably protected sugar derivatives using stannous triflate as promoter.

Many procedures have been reported for the synthesis of oligosaccharides. Most of them required the preparation of two polyfunctional partners : the hydroxyl component prepared by selective blocking of a sugar unit, and the glycosyl component which must be activated for the coupling step. The first partner is generally available without excessive difficulties through "blocking-deblocking" strategies, now well established in the litterature, whereas the choice of the second one may be a matter of great concern because each oligosaccharide synthesis, despite the great deal of work in this area, remains an independant problem.[1]

Since the pioneering work of Kœnigs-Knorr[2], several methods of coupling has been published giving in some case very good results. Oligosaccharides have been obtained generally as a mixture from halogenoses, orthoesters[3], and imidates[4], in the presence of acidic catalysts and/or precious or heavy metal salts. Stereoselective, general, efficient methods using easily available glycosylating agents are of interest, because the separation of mixtures is generally difficult and only one pure anomer is needed for biological evaluation. Silver triflate, introduced in the field by HANESSIAN and BANOUB for the synthesis of 1,2-trans glycosides from halogenoses[5], is now widely used as a promoter.

In the disaccharide synthesis described in this letter, the model glycosylating agent is the common, crystalline acetobromoglucose, and stannous triflate is used as promoter.[6]

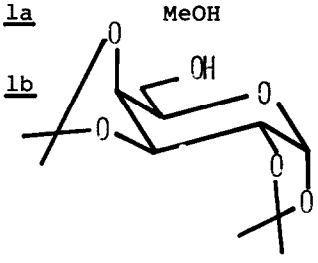
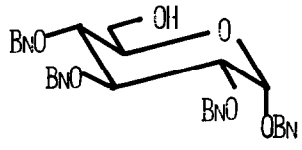
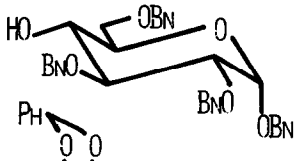
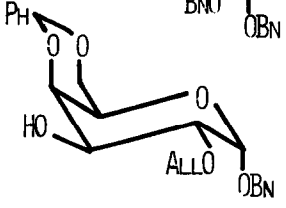


Stannous triflate is a stable white powder which was prepared as described by Mukaiyama[7], it may be stored without special precaution over a long period of time without loss of activity. Until now, it has been only used to generate divalent tin enolate[7] ; this work represents the second example of its use in organic synthesis.

The scope of the reaction was studied by varying the hydroxyl component, the solvent and the base. In each case, equimolecular proportion[8] of halogenose, alcohol, stannous triflate and base were used (in the presence of 4 Å molecular sieves to ensure strict anhydrous conditions). The reaction was totally inhibited by using two or three equivalents of base, however in the above conditions, a large variety of usual blocking groups, even acid sensitive ones like acetals, could be used. After the mixing of the reagents at room temperature, nothing seems to happen on t.l.c. examination for the next 2-6 hours. Then the reaction begins and is terminated in 30 min..
The results are summarized in table 1.

No evidence was found for the formation of α-D-anomers, either by t.l.c. or preparative H.P.L.C.. Yields seem fairly insensitive to the choice of solvents and bases, but depend upon the nature of the alcoholic partners, contrary to what is observed in the silver triflate reactions. This may be an indication for a different mecanism of action. In the case of primary alcohols, part of the reactant is wasted by transesterification. Secondary alcohols gave fairly good yields with no trace of acetate, and in view of the cheapness of the promoter, these new syntheses appear definitively interesting for high scale preparations.

table I.

entry	alcohols	solvent	base	yield[a],% 2	3
1	1a MeOH	CH_2Cl_2	collidine	33	unknown
2	1b 	CH_2Cl_2	collidine	30	14
3		CH_2Cl_2	diisopropyl-ethylamine	37	16
4		CH_2Cl_2	1,1,3,3-tetra-methyl urea	40	23
5		Toluene	collidine	38	21
6		Toluene	diisopropyl-ethylamine	35	17
7		Ether	collidine	25	14
8	1c	CH_2Cl_2	collidine	39	31
9a	1d 	CH_2Cl_2	collidine	57	0
9b				65[b](71)[c]	0
10a	1e 	CH_2Cl_2	1,1,3,3-tetra-methyl urea	52	0
10b				62[b](77)[c]	0

[a] Yields for compounds which look pure on chromatographic and spectroscopic (400 Mhz ^{1}H N.M.R.) examination, after isolation by preparative H.P.L.C.. They are not optimized.

[b] Two equivalents of acetobromoglucose and base and one and half equivalent of stannous triflate were used.

[c] Yields in brackets based on starting material recovery.

Typical experimental procedure

A solution of alcohol 1 (1 mmole) and the base (1 mmole) in CH_2Cl_2 (5 ml) is added without delay to a stirred suspension of acetobromoglucose (1 mmole), stannous triflate (1 mmole) and 4Å molecular sieves in CH_2Cl_2 (5 ml) at room temperature. The reaction procceds after a period varying from 2 to 6 hours and is complete within 30 min. when the halogenose has completly disappeared (t.l.c.). The mixture is poured onto a stirred mixture of a 5% aqueous $NaHCO_3$ solution with CH_2Cl_2. The organic phase is washed with water and dried. Evaporation of volatiles left a residue from which the pure β-D-glucoside was separated by preparative silica gel H.P.L.C..

Acknowledgments

We thank professor Serge DAVID for his interest and the CNRS for financial support.

Notes and references

1 H. PAULSEN, "Advances in selective chemical syntheses of complex oligosaccharides", Angew. Chem., 1982, 21(3), 155.

2 W. KOENIGS and E. KNORR, Ber., 1901, 34, 957.

3 N.K. KOCHETKOV and A.F. BOCHKOV, Recent developments in the chemistry of natural products, Vol 4, Akademia Kiado, Budapest, 1972, 77-191.

4 J.R. POUGNY, M.A.M NASSR, N. NAULET and P. SINAŸ, Nouv. J. Chim., 1978, 2(4), 389.

5 S. HANESSIAN and J. BANOUB, Carbohydr. Res., 1977, 53, C13.

6 It must be noted that stannous chloride is ineffective in this coupling reaction.

7 T. MUKAIYAMA, N. IWASAWA, R.W. STEVENS and T. HAGA, Tetrahedron, 1984, 40(8), 1381.

8 As indicated in table 1 (entry 9b and 10b), yields were slightly improved by adding a one more equivalent of halogenose and base and half more equivalent of stannous triflate.

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