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DIRECT GLUCOSIDATION OF TETRA-O-BENZYL-α-D-GLUCOSE BY DICHLOROSILANE - SILVER SULFONATE SYSTEM

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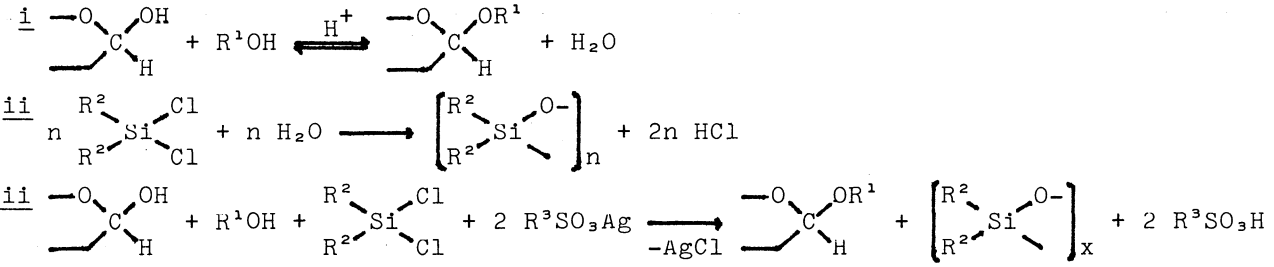
A system of dichlorodiphenylsilane - silver sulfonate has been found to be of use for the direct glucosidation of 2,3,4,6-tetra-O-benzyl-α-D-glucopyranose. Efficient synthesis of trehaloses with the system is described.

Many efforts[1] have been made for a development of a chemical method to form an O-glycoside linkage, which is a dominant pattern of the linkage of various saccharides in Nature[2]. We now wish to report a new direct glucosidation of 2,3,4,6-tetra-O-benzyl-α-D-glucopyranose[3] (I) by use of a system of diphenyldichlorosilane (DPCS) and silver sulfonate.

It is long known[4] that a reducing hydroxyl group of sugar has the intrinsic property to establish an equilibrium (i) between the alcohol, water and the O-glycoside in the presence of the acid. The effective dehydration from the reaction system is a key to a favorable O-glycoside formation (acid reversion method). The basis of the system for the glycosidation presented here is the well-known property of the dichlorosilane[5] to form polysiloxane (silicone) with a consumption of water to liberate hydrogen chloride (ii). To incorporate this dehydrating system into i, it is further planned to remove the chloride anion by use of silver sulfonate. It is well known that the sulfonate anion has less nucleophilicity toward the anomeric center[6]. Overall reaction for the glycosidation was thus obtained by combination of the above-mentioned materials to give the equation (iii).



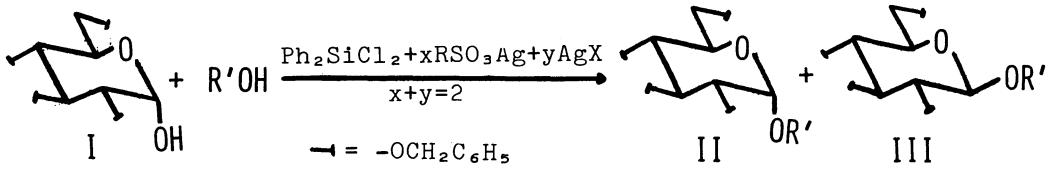
The reaction was conducted as follows: DPCS (1.0 eq.) was added to a mixture of I (0.3 mmole), methanol (1.0 eq.) and silver sulfonate (2.0 eq.) in an appropriate solvent (1 ~ 2 ml), followed by stirring at the specified conditions[7,8]. Results are summarized in TABLE I[9]. Silver trifluoromethanesulfonate (Ag-O-Tf) was used as a promoter to accelerate the reaction greatly[10]. No significant accumulation of intermediates was observed on tlc during the course of reaction. In

ratio of the promoter spurred the reaction greatly. In each case, occurrence of small quantity of V was observed on tlc at the end of reaction. V was converted into VI and VII by action of methanesulfonic acid (2.0 eq.) in dichloromethane at 0° in the yield of 73% ($\alpha/\beta \simeq 1/3.6$) even after 4 hr. Fast liberation of I was again observed at the initial course of the reaction. As no significant accumulation of V was observed, the following scheme is proposed for the reaction.

$$\text{TBG-OH} + 0.5\ \text{Cl-SiPh}_2\text{-Cl} + \text{AgO-Ms} \xrightarrow[-\text{AgCl}]{} \text{TBG-O-SiPh}_2\text{-O-TBG}$$

$$\text{TBG-OH} + \text{Ms-O-SiPh}_2\text{-O-Ms} \xrightarrow{H^+} \text{TBG-O-TBG} + [\text{-SiPh}_2\text{-O-}]_x \xleftarrow{H^+}$$

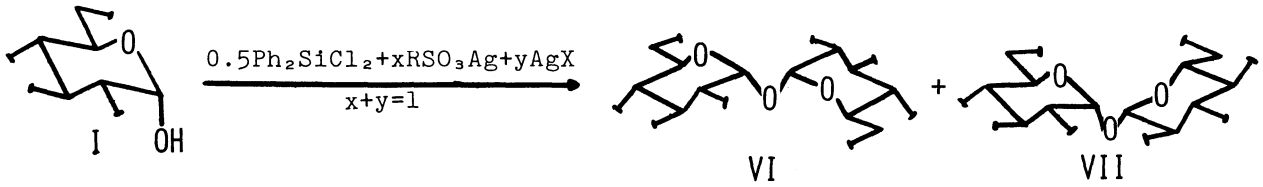
TABLE 1 GLUCOSIDATION OF TETRABENZYLGLUCOSE BY Ph_2SiCl_2 - RSO_3Ag SYSTEM



Run	R	R'OH	x	X	y	Solv.	Temp.	Dur.	I	II[1]	III[2]
1	$-CH_3$	Methanol	2.0	---	---	CH_2Cl_2	0°C	3.0hr	17%	20%	34%
2	$-C_6H_4CH_3$(p)	Methanol	2.0	---	---	$(CH_2Cl)_2$	0	5.0	-[3]	23	48
3	$-C_6H_4CH_3$(p)	Methanol	1.9	OTf[4]	0.1	$(CH_2Cl)_2$	0	2.0	9	29	49
4	$-C_6H_4CH_3$(p)	Methanol	1.0	OTf[4]	1.0	CH_3CN	-20	3.0	~0	18	43
5	$-C_6H_4CH_3$(p)	Cyclohexanol	1.0	OTf[4]	1.0	CH_3CN	-20	5.0	17	5	48
6	$-C_6H_4CH_3$(p)	MTBG-OH	2.0	---	---	$(CH_2Cl)_2$	0	4.0	-[3]	12	40
7	$-C_6H_4CH_3$(p)	MTBG-OH	1.9	OTf[4]	0.1	$(CH_2Cl)_2$	0	3.0	18	9	47

[1]IIa, $[\alpha]_D^{20}$+21°(c 2.0, $CHCl_3$), IIb, $[\alpha]_D^{20}$+29°(c 2.3, $CHCl_3$), IIc, $[\alpha]_D^{20}$+53°(c 1.4, $CHCl_3$); Pmr spectra measured in $CDCl_3$ at 60 MHz were consistent with the structures. [2]Identified with the compounds reported in ref. 3. [3]Not determined. [4]OTf = $-SO_3CF_3$.

TABLE 2 SYNTHESIS OF TREHALOSES BY Ph_2SiCl_2 - RSO_3Ag SYSTEM

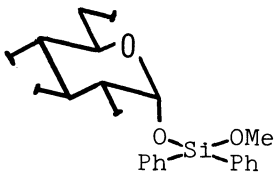


Run	R	x	X	y	Solv.	Temp.	Dur.	I	VI	VII
8	$-CH_3$	1.0	---	---	CH_2Cl_2	0°C	6.5hr	15%	23%	45%
9	$-C_6H_4CH_3$(p)	1.0	---	---	$(CH_2Cl)_2$	0	6.0	71	7	3
10	$-C_6H_4CH_3$(p)	0.9	OTf	0.1	$(CH_2Cl)_2$	0	5.0	12	28	45
11	$-C_6H_4CH_3$(p)	0.5	OTf	0.5	CH_2Cl_2	-20	1.5	11	21	52
12	$-CF_3$	1.0	---	---	CH_2Cl_2	-20	0.25	16	26	44
13	$-C_6H_4CH_3$(p)	0.9	ClO_4	0.1	$(CH_2Cl)_2$	0	3.0	13	38	44

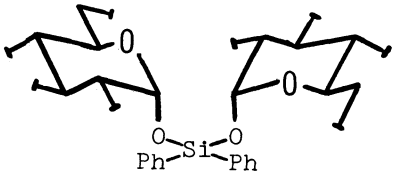
VI, $[\alpha]_D^{20}$+84°(c 1.0, $CHCl_3$), VII, mp 100~101°C, $[\alpha]_D^{20}$+52.1°(c 1.0, $CHCl_3$), Found, C, 76.67, H, 8.81%.

The authors are grateful to Toray Silicone Co. for the gift of silanes.

each case, however, there were four faint spots[11], IV, V, VI, and VII besides those of the glucosides, IIa and IIIa, and unchanged I, at the end of reaction. VI and VII (ca. 10%, altogether) were identified as O-benzylates of α,α- and α,β-trehalose, respectively (see below). IV was identified as the glucosyloxymethoxysilane, whereas V was found to be the diglucosyloxysilane[12,13]. When IV reacted with

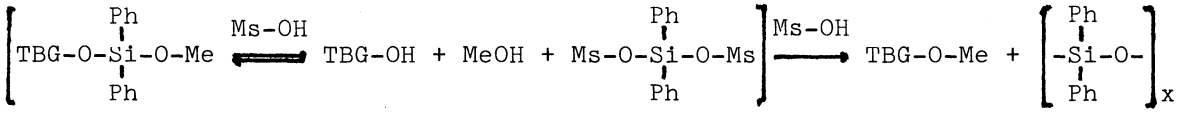


IV

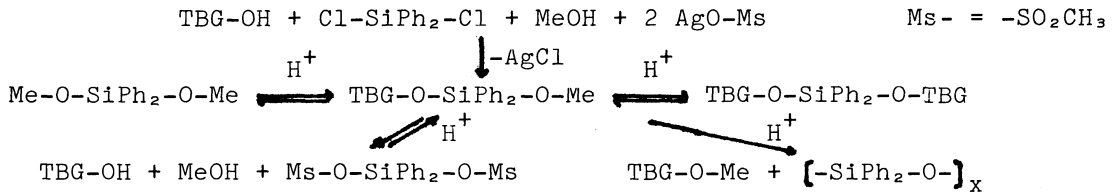


V

methanesulfonic acid (2.0 eq.) in dichloromethane at 0° for 3 hr, the glucosides were afforded in 78% yield (α/β ≃ 1/2.3). The observed fast liberation of I at the beginning of the reaction, followed by slow consumption of I was interpreted as the equilibrium (iv) between IV, I, methanol and dimethanesulfonyloxydiphenylsilane[14] with the slow glycosidation step[15]. The filtrate obtained under anhydrous condi-

iv 

tions with quantitative recovery of silver chloride after the reaction of DPCS and silver methanesulfonate (2.0 eq.) in dichloromethane at 0° for 2 hr was applied to an equimolar mixture of I and methanol to give less amount of glucosides (32%, α/β ≃ 1/1). This result appears to indicate that silver sulfonate is used as the generator of the sulfonyloxysilane[14] and the scavenger of hydrogen chloride liberated by the direct reaction of the chlorosilane and the alcohol. Glc of the reaction mixture of run 1 showed that the dichlorosilane was exhausted within 1 hr and the quantity of dimethoxydiphenylsilane maximized up to ca. 6% at 45 min[16]. The transalkylation between I and dimethoxydiphenylsilane (0.5 eq.) in the presence of methanesulfonic acid (1.0 eq.) was quite slow in dichloromethane at 0° (45%, after 16 hr)[17]. After all, the scheme for the glycosidation with dichlorosilane and silver sulfonate is presented as follows[15].



It can well be expected that the stronger acid such as trifluoromethanesulfonic acid or perchloric acid may promote the irreversible step in iv. This is the case as seen in TABLE 1[18,19].

Cyclohexanol gave glucosides (IIb and IIIb). I was coupled with methyl 2,3,4-tri-O-benzyl-α-D-glucopyranoside (MTBG-OH) by the method to give O-benzylates of methyl α-isomaltoside and α-gentiobioside (IIc and IIIc) in reasonable yields.

In the absence of alcohol for the aglyconic moiety, I was self-condensed to give benzylates of α,α- and α,β-trehalose[20] in good yields as shown in TABLE 2. Silver p-toluenesulfonate was not efficient as the methanesulfonate. Increase of the

References and Notes

1) G.Wulff and G.Röhle, Angew. Chem., 86, 173 (1974).
2) 'RODD'S Chemistry of Carbon Compounds', 2nd ed., Elsevier, 1967, Vol.I_F, Ch.24.
3) S.Koto, Y.Hamada, and S.Zen, Chem. Lett., 587 (1975).
4) 'THE CARBOHYDRATES Chemistry and Biochemistry', 2nd ed. Academic Press, 1972, Vol.IA, Ch.9.
5) F.S.Kipping, J. Chem. Soc., 101, 2108, 2125 (1912).
6) R.Eby and C.Schuerch, Carbohydrate Res., 34, 79 (1974).
7) The use of dimethyldichlorosilane afforded no good results. Triphenyl- and trimethylchlorosilane were of no effect. Silver nitrate and sulfate were useless.
8) Toluene was good for the reaction, whereas acetonitrile afforded somewhat reduced yields. 1,2-Dimethoxyethane and N,N-dimethylformamide gave very poor results.
9) After neutralization by an excess of sodium bicarbonate, the products were isolated by the chromatography over silica gel.
10) Too much use of promoter, however, brought forth the self-condensation seriously.
11) Approximate Rf values (benzene/2-butanone=40/1, charred by H_2SO_4) were, IV, 0.75, V, 0.67, IIIa, 0.55, IIa, 0.45, VI, 0.40, VII, 0.30, and I, <0.1.
12) V was easily obtained (81%) by the reaction of I with DPCS (0.5 eq.) and pyridine (1.0 eq.) in dichloromethane. When pyridine was added to the reaction system prior to the addition of methanol in the case of run 2, VI($[\alpha]_D^{20}$+47°(c 0.9,$CHCl_3$), 29%) and V($[\alpha]_D^{20}$+64°(c 1.0, $CHCl_3$), 35%) were isolated from the reaction misture. Pmr spectra measured in $CDCl_3$ at 100 MHz were consistent with the structures.
13) S.A.Baker and M.R.Harnden, J. Chem. Soc., (C), 644 (1968) and refs. cited there.
14) M. Schmidt and H.Schmidbaur, Angew. Chem., 70, 469 (1958), Chem. Ber., 95, 47 (1962).
15) TBG- denotes 2,3,4,6-tetra-O-benzyl-α-D-glucopyranosyl residue.
16) Low yield of dimethoxydiphenylsilane was substantiated by another observation[9] of an equilibrium: MTBG-OH + 0.5DPCS + Ag-OMs $\xrightarrow[-AgCl]{}$ $Ph_2Si(-O\text{-MTBG})_2$ (30%) $\xrightleftharpoons[Ms\text{-}OH]{}$ MTBG-OH (70%)
Cf. M.Momonoi and O.Yamaguchi, Nippon Kagaku Zasshi, 78, 1602 (1957).
17) A.M.Sprung, J. Org. Chem., 23, 58 (1958).
18) Reaction of trifluoromethanesulfonic acid with IV took place the intermolecular reaction to give trehaloses : 2 IV ⟶ trehaloses + Me-O[-$SiPh_2$-O]$_2$-Me.
This may show why the excessive promoter gave significant amount of trehaloses[10].
19) A mixture of I, methanol, (1.0 eq.) and DPCS (1.0 eq.) was stirred with methanesulfonic acid (2.0 eq.) in dichloromethane at 0° for 3 hr to give IIa and IIIa in the yield of 42% (α/β ≃ 1/1.5). Evolution of hydrogen chloride was observed. Simple acid reversion of I and methanol (1.0 eq.) with use of methanesulfonic acid (2.0 eq.) in dichloromethane at 0° for 3 hr gave the glucosides in the yield of 25%.
20) G.J.F.Chittenden, Carbohydrate Res., 9, 323 (1969) and refs. cited therein. F. Micheel and E.-D.Pick, Tetrahedron Lett., 1695 (1969). The structures of VI and VII were confirmed by the derivation into the known octa-O-acetates.

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