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ORGANOMETALLICS IN ORGANIC SYNTHESIS. APPLICATIONS OF A NEW DIORGANOZINC REACTION TO THE SYNTHESIS OF *C*-GLYCOSYL COMPOUNDS WITH EVIDENCE FOR AN OXONIUM-ION MECHANISM*

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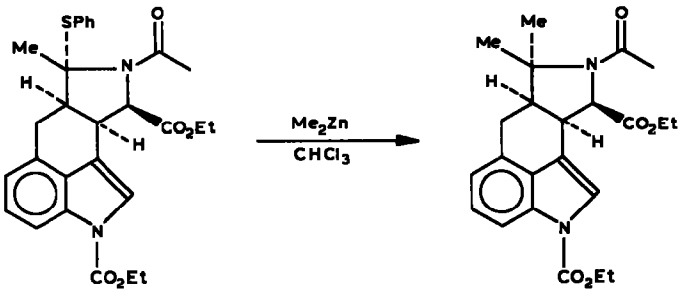
ABSTRACT

The mechanistic and stereochemical features of a new organozinc-based substitution process [heteroatom-C-(R^1,R^2)-SPh + R^3_2Zn → heteroatom-C-(R^1,R^2,R^3)], first discovered during a total synthesis of the alkaloid mycotoxin α-cyclopiazonic acid, are described. Phenyl thioglycosides were valuable substrates in studying the nature of this reaction process. Since these sulfur compounds are converted into *C*-glycosyl compounds with some degree of stereoselectivity, the organozinc chemistry does provide a new entry to these biologically active substances.

INTRODUCTION

During our investigations into the synthesis of the unique mycotoxin, α-cyclopiazonic acid, the need arose to replace a phenylthio group in **1** by a methyl group[1] in **2**. After numerous unsuccessful attempts with a wide variety of methylmetals, we finally discovered that dimethylzinc in chloroform effected this conversion in



1 2

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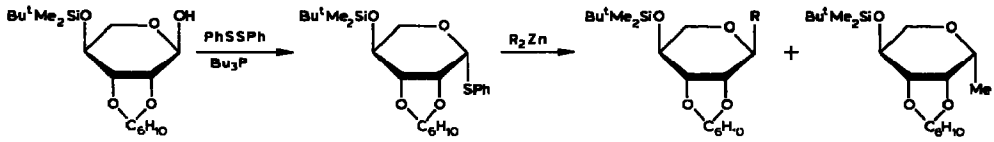
good yield. Even though a large excess of the diorganozinc reagent was employed, no products derived from a reaction at the carbonyl sites were observed, a consequence of the relatively weak nucleophilicity of organozinc reagents[2].

In order to further probe both the synthetic and mechanistic aspects of this new reaction, we have extended the zinc chemistry to several different phenyl thioglycosides. Our purpose in choosing carbohydrates as substrates was twofold: (a) these substrates were expected to provide valuable stereochemical information on the course of the zinc reaction; and (b) if the yields and stereoselectivity observed in this reaction were good, then a valuable new entry into an important class of natural product substances, the *C*-glycosyl compounds, would be at hand. Much intensive effort has been expended in devising new entries into the *C*-glycosyl compounds[3] over the past few years, primarily because of the significant biological activity exhibited by these special carbohydrate structures.



3 4 5 R = Me 6 R = All 7

RESULTS AND DISCUSSION

To begin our study of the aforementioned zinc reaction with carbohydrates as substrates, we examined first the reactions of phenyl 4-*O*-*tert*-butyldimethylsilyl-2,3-*O*-cyclohexylidene-1-thio-β-L-lyxopyranoside (**4**), a compound readily prepared by an oxidation–reduction condensation reaction[5] between the protected L-lyxose derivative[6] **3**, diphenyl sulfide, and tributylphosphine. The structure of **4** has been independently confirmed by a single-crystal X-ray analysis. The replacement of the anomeric hydroxyl group of **3** by the phenylthio group with apparent inversion of configuration was suggestive of an S$_N$2-type mechanism. When a chloroform solution of **4** was subsequently treated with excess dimethylzinc, prepared from methyl iodide and a zinc–copper couple[7], in a Kimax tube for 12 h at 75°, a single, less polar product was obtained. To this product was assigned the structure **5**, based upon a detailed n.m.r. analysis *(vide infra)*.

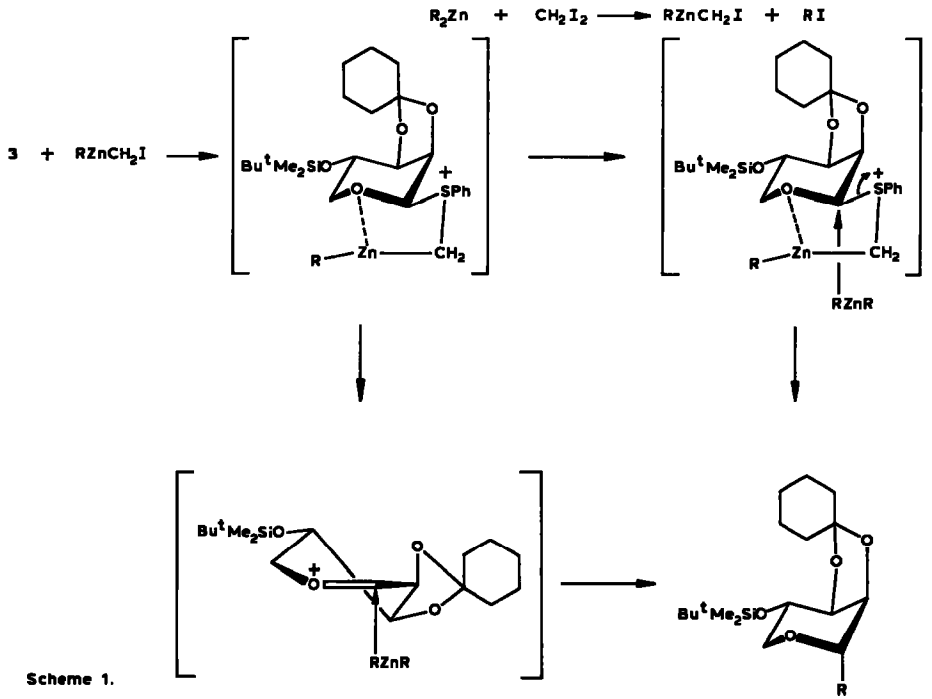
Interestingly, when the reaction just mentioned was carried out in toluene, benzene, or hexanes, in the absence of chloroform, no glycosylmethane was formed. Additionally, when a toluene solution of **4** was treated with five equivalents of diiodomethane and ten equivalents of commercially available diethylzinc for 2 h at 65°, a glycosylethane compound was obtained in a yield of 78%. Likewise, by substituting carbon tetrachloride for diiodomethane, the glycosylethane compound was again obtained, but under a milder set of reaction conditions (2 h at 35°).

Early on in our studies, we felt that the zinc reagent might be reacting with the phenyl thioglycoside through a ligand-type exchange process in which the

thiophilic zinc center might sufficiently tug on the sulfur atom to form an oxonium-ion intermediate. However, our findings regarding the necessity of the halocarbon additives does logically suggest that the dialkylzinc is performing a dual role. First, it reacts with diiodomethane or carbon tetrachloride (by a free radical pathway) to deliver a carbenoid[2,8]; subsequently, this zinc carbenoid interacts with the sulfur substituent to generate a sulfonium ion intermediate[9]. The formation of this intermediate may be additionally favored through complexation of the zinc atom with the ether oxygen atoms of the carbohydrate nucleus. Complexation of the zinc atom of the Simmons–Smith reagent with a hydroxyl group has, of course, been invoked previously to rationalize the *syn*-directing effect of an alcohol in cyclopropanation reactions[10].

Once the activated organozinc–sulfur complex has formed, it reacts with the excess diorganozinc reagent present in solution either by a direct displacement mechanism, or (better) it breaks down to a cyclic oxonium ion which then undergoes attack *via* the kinetically-preferred, axial-addition mode[11]. Thus, conformational energetics and the kinetic anomeric effect act synergistically to control the configuration resulting from the addition in the latter case (see Scheme 1).

As listed in Table I, the dimethyl-, diethyl-, and dipropyl-zinc reagents provided, within the limits of ^{1}H-n.m.r. and l.c. analysis, only the *C*-α-L-glycosyl compounds. The assignment of structure to these compounds was based on detailed spin–spin decoupling experiments carried out on the desilylated products. The anomeric proton of these α-L anomers exhibited a coupling constant of *J* 8.2–9.2



Scheme 1.

TABLE I

REACTIONS OF DIORGANOZINC REAGENTS WITH THE PHENYL THIOGLYCOSIDE **4**

Reagent R_2Zn (R)	*C-Glycosyl compounds (%)*[a]		*Yield (%)*
	α	*β*	
CH_3	>94	<6	72
CH_3CH_2	>94	<6	78
$CH_3CH_2CH_2$	>94	<6	76
$CH_3(CH_2)_2CH_2$	93	7	75
$C_2H_5CH(CH_3)$	64	36	72
$(CH_3)_2CH$	82	18	73
CH_2=CH–CH_2	60	40	35[b]

[a]A standard set of reaction conditions was adopted which consisted of treating **4** with the diorganozinc reagent (15 equiv.) and diiodomethane (8 equiv.) in toluene for 2 h at 40°. [b]The low yield in this case probably stems from our difficulty in preparing the pure diallylzinc reagent.

Hz with the neighboring pyran-ring proton[11]. The anomeric proton in the desilylated β-L anomers exhibited a coupling constant of J 1.9–2.4 Hz. The chemical shift of the C-5 axial-methylene proton was also found to differ considerably for the desilylated products of **5** and **7** (δ 3.58–3.75 and 3.03–3.34, respectively). Further proof of structure for the glycosylpropane compound was obtained by comparing it with an authentic sample generated by hydrogenating the previously known[12] α-L-glycosylpropene. With dibutylzinc, a 93:7 mixture of the α- and β-L anomers was obtained. The secondary alkylzinc reagents, prepared by reaction of the appropriate organolithium or Grignard reagent with freshly fused zinc chloride in ether, followed by distillation[2,13], proved somewhat less selective in their reactions with **4**. While the α-L anomer still preponderated, more of the β-L anomer was detected (Table I).

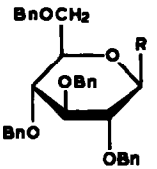
In order to test the applicability of this organozinc reaction to other carbohydrate substrates, as well as to further confirm our suspicions that this reaction was proceeding through an oxonium ion intermediate, we have examined the reaction of the additional phenyl thioglycosides listed in Table II. The phenylthio substituted derivatives of β- and α-D-glucose (**8** and **10**) provided us with an excellent opportunity to examine the effect of the configuration of the starting compound on that of the product. If an oxonium ion intermediate was being formed in the course of the organozinc-mediated reactions, then **10** and **8** would give rise to nearly identical product ratios. Indeed, as tabulated in Table II, the product ratios observed for the reactions of **10** and **8** with Me_2Zn–CH_2I_2 were quite similar. As should be noted, the major isomer is that arising from an axial-addition mode. On treating **8** with diethylzinc or diphenylzinc in the presence of diiodomethane, α- to β-ratio of anomers in the products was again found to be ~3:1. Thus, the nature of the diorganozinc reagent does not dramatically influence the product distribution. The lower level of stereoselectivity observed with this D-glucose derivative, as

TABLE II

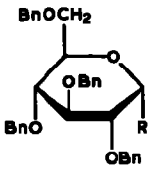
REACTIONS OF OTHER PHENYL THIOGLYCOSIDES WITH DIORGANOZINC REAGENTS

Starting phenyl thioglycoside	*Organozinc reagent*	*Reaction conditions*[a]		*Product*	*Ratio of α to β anomer*	*Yield (%)*
		Temp (°)	*Time (h)*			
8[b]	Me_2Zn	45	3.5	**29**	76:24	67
8[b]	Me_2Zn	5	72	**29**	77:23	76
8[b]	Et_2Zn	50	3	**30**	72:28	67
8[b]	Ph_2Zn	50	2	**28**	75:25	48
9[c]	Me_2Zn	90	12	**29**	67:33	24
9[c]	Me_2Zn	50	4		α-chloride[e]	44
10[c]	Me_2Zn	50	3	**29**	69:31	60
11[c]	Me_2Zn	50	4	**29**	73:27	55
12, 13[b]	Me_2Zn	40	3	**31**	84:16[d]	80
12, 13[b]	Ph_2Zn	50	1	**32**	81:19	40
14[b]	Me_2Zn	48	20	**15, 16**	37:63	91
21[f]	Et_2Zn	25	2	**33**	75:25	68

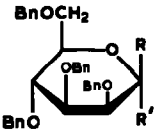
[a]These reactions were all carried out by use of 15 equiv. of the diorganozinc reagent and 8 equiv. of diiodomethane in toluene as solvent. [b]Ref. 5. [c]Ref. 14. [d]Product ratio assigned after debenzylation and conversion to the tetraacetates. [e]See text. [f]Ref. 15.



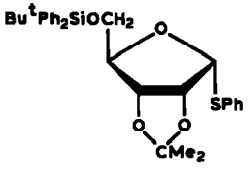
8 R = SPh
9 R = SBu



10 R = SPh
11 R = SBu



12 R = SPh, R' = H
13 R = H, R' = SPh



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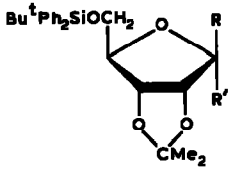


15 R = Me, R' = H
16 R = H, R' = Me

compared to that observed for the L-lyxose derivative, presumably reflects the ability of the 1,3-dioxolane ring in the latter to significantly shield the pyran ring from attack in the equatorial direction (*i.e.*, the concave-face attack is hindered).

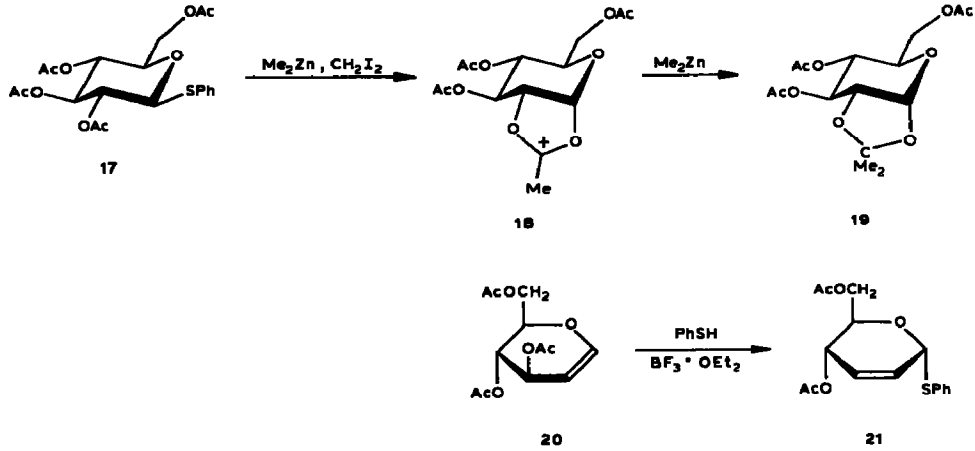
Interestingly, the butylthio derivatives **9** and **11** of D-glucose differed considerably in their reactivity towards Me_2Zn–CH_2I_2. Whereas the α anomer **11**

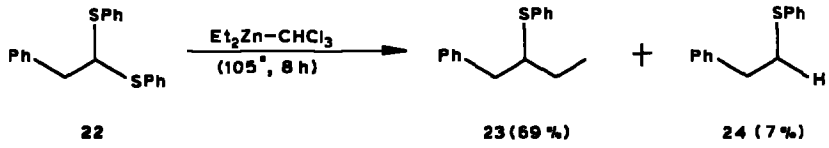
reacted within 4 h at 50° to provide a 73:27 mixture of α- and β-D-glucosylmethane, the β anomer **9** required heating for 12 h at 90° in order to generate even small amounts of the desired products. On treating **9** with Me_2Zn–CH_2I_2 for 4 h at 50°, followed by a workup with hydrochloric acid, only the corresponding glucosyl chloride could be isolated. Apparently, the sluggish character of **9** in the zinc reaction reflects both the poorer-leaving group ability of a butylsulfonium relative to a phenylsulfonium ion-group, as well as the inability of the lone pairs on the pyran-ring oxygen atom to participate in the cleavage process[11].

On treatment of a 1:1 mixture of the D-mannose-derived phenyl thioglycosides **12** and **13** with either dimethylzinc or diphenylzinc, the products of axial attack again preponderated. The presence of the β-axial benzyloxy group at C-2 may be responsible for the slight enhancement in axial selectivity relative to the D-glucose examples.

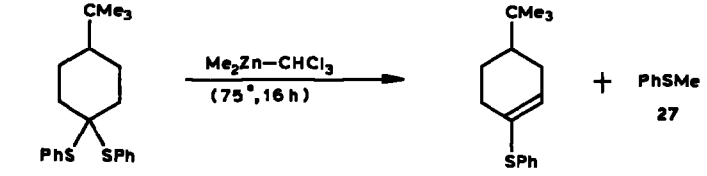
When the phenylthio derivative of α-D-ribose **14** was subjected to Me_2Zn–CH_2I_2, a mixture of furanosylmethanes was formed in excellent yield. To the major product was assigned a β-D configuration (**15**) based upon an examination of the chemical shift and coupling data of **15** and **16** vis-à-vis that reported for related compounds[16].

On exposing the *O*-acetylated derivative **17** of D-glucose to the standard reaction conditions, it was interesting to find that none of the expected glucosylmethane was formed. Instead, the 1,2-*O*-isopropylidene derivative of D-glucose **19** was isolated in 51% yield. This compound, whose structure was made apparent by ^{1}H-n.m.r. analysis, presumably resulted from attack of the C-2 acetate group on the anomeric center backside to the departing sulfur group. The resulting acyloxonium ion **18** then suffered attack by the dimethylzinc leading to the *O*-isopropylidene derivative. Not unexpectedly, the α anomer of **17** gave rise to a complex mixture of products. The zinc reaction was also applied to the phenylthio derivative **21** prepared from 3,4,6-tri-*O*-acetyl-1,5-anhydro-2-deoxy-D-*arabino*-hex-1-enitol (**20**)

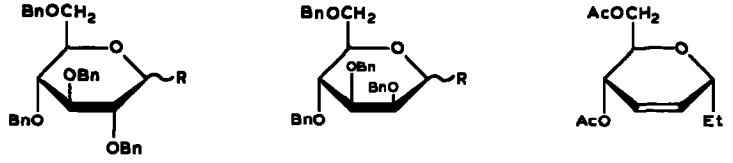




22 23 (69 %) 24 (7 %)



25 26 (43 %)



28 R = C_6H_5
29 R = Me
30 R = Et

31 R = Me
32 R = Ph

33

by Ferrier rearrangement[15]. In this case, the new alkyl group entered into the position α to the pyran-ring oxygen atom, and by literature comparisons the major anomer was found to have the α-D configuration[4] (**33**).

While we have attempted to extend the foregoing chemistry to another type of α-heteroatom containing sulfur system, the thioacetals rather complicated mixtures of products were found to be formed when these materials were exposed to diorganozinc reagents in the presence of various halocarbons. The bis(phenylthio)acetal **22** of phenylacetaldehyde reacted, for example, with diethylzinc in the presence of chloroform as solvent to give rise to the expected substitution product **23**, in which one of the phenylthio groups was replaced by an ethyl group. Additionally, some of the product of reduction **24** was isolated as well. In other cases, elimination of one of the thio groups to afford a vinyl sulfide was also observed, *e.g.*, **25** to give **26** and **27**. A recent report by Rodriguez and Nickon describes the use of similar methodology for the conversion of dithioacetals into vinyl sulfides[17].

In summary, the phenyl thioglycosides, when treated with diorganozinc reagents in the presence of halocarbon additives, lead to reasonable yields of *C*-glycosyl compounds. The resulting configuration does appear to be consistent with an axial attack on an oxonium-ion intermediate. The organozinc procedure thus offers a further addition to the rapidly growing number of new methods available for *C*-glycosyl construction[3,4].

TABLE III

^{1}H-N.M.R., I.R., M.S., AND H.R.M.S. DATA FOR THE *C*-GLYCOSIDE COMPOUNDS

Compound	*^{1}H-N.m.r.*[a]	*I.r.*	*M.s.*	*H.r.m.s.* (Anal.)
(4-*O*-*tert*-Butyldimethylsilyl-2,3-*O*-cyclohexylidene-L-lyxopyranosyl)-methane, α anomer (5)	3.97 (m, 1 H), 3.90 (m, 1 H), 3.71 (dd, 1 H, *J* 8.49, 5.05 Hz), 3.59 (m, 2 H), 3.27 (dt, 1 H, *J* 6.1, 2.02 Hz), 1.25–1.60 (m, 10 H), 1.15 (d, 3 H, *J* 6.1 Hz), 0.83 (s, 9 H), and 0.03 (s, 6 H)	2960, 2860, 1510, 1420, 1360 1250, 1190, 1090, 1040, 1010, 930, and 840[b]	342 (M^+), 299, and 285	Calc. for $C_{18}H_{34}O_4Si$: 342.2226. Found: 342.2226.
-ethane, α anomer	4.03 (m, 1 H), 3.96 (m, 1 H), 3.80 (dd, 1 H, *J* 8.2, 5.1 Hz), 3.67 (m, 2 H), 3.15 (dt, 1 H, *J* 8.29, 4.04 Hz), 1.6 (m, 12 H), 0.98 (t, 3 H, *J* 6.94 Hz), 0.88 (s, 9 H), and 0.09 (s, 6 H)	2950, 1600, 1460, 1360,1250, 1090, 1050, 890, and 840[b]	356 (M^+), 327 ($M^+ - Et$)	Calc. for $C_{19}H_{36}O_9Si$: 356.2383. Found: 356.2384.
(2,3-*O*-Cyclohexylidene-L-lyxopyranosyl)-propane α anomer	4.21 (m, 1 H), 3.97 (m, 1 H), 3.85 (m, 3 H), 3.19 (dt, 1 H, *J* 8.46, 3.56 Hz) 2.44 (d, 1 H, *J* 8.46 Hz), 1.60 (m, 14 H), and 0.93 (t, 3 H, *J* 6.99 Hz)	3580, 2950, 2850, 1520, 1460, 1370, 1200, 1160, 1110, 1080, 1035, 970, 920, and 830[b]	256 (M^+), 213 ($M^+ - Pr$)	Calc. for $C_{14}H_{24}O_4$: 256.1675. Found: 256.1674.

-butane, α anomer	4.21 (br s, 1 H), 3.97 (br d, 1 H, *J* 6.27 Hz), 3.85 (m, 3 H), 3.17 (dt, *J* 8.49, 3.44 Hz), 2.15 (d, 1 H, *J* 8.29 Hz), 1.7 (m, 10 H), 1.35 (m, 6 H), and 0.9 (t, 3 H, *J* 7.1 Hz)	3550, 3400, 2900, 2850, 1450, 1440, 1390, 1355, 1315, 1260, 1235, 1190, 1150 1100, 1060, 1040, 980, 905, and 880[b]	270 (M^+)	Calc. for $C_{21}H_{40}O_4Si$: 384.2696. Found: 384.2697. (for the mixture of silyl ethers)
-butane, β anomer	4.04 (dd, 1 H, *J* 5.46, 2.22 Hz), 3.9 (m, 2 H), 3.8 (m, 1 H), 3.55 (dt, 1 H, *J* 5.86, 2.02 Hz), 3.07 (t, 1 H, *J* 10.81 Hz), 2.0 (d, 1 H, *J* 3.64 Hz), 1.77 (m, 10 H), 1.35 (m, 6 H), and 0.9 (t, 3 H, *J* 7.1 Hz)	3600, 3430, 2950 2850, 1450 1430, 1360, 1260, 1235, 1190, 1150, 1100, 1085, 1055, 1030, 930, and 900[b]	270 (M^+)	
-1-methylpropane, α anomer	4.23 (m, 1 H), 4.06 (dd, 1 H, *J* 9.1, 5.25 Hz), 3.95 (m, 1 H), 3.75 (m, 2 H), 3.14 (dd, 0.5 H, *J* 9.3, 3.4 Hz), 3.07 (dd, 0.5 H, *J* 9.3, 5.25 Hz), 2.1 (m, 1 H), 1.6 (m, 10 H), and 1.3–0.9 (m, 9 H)	3600, 3420, 2920, 2850, 1450, 975, and 930[b]	270 (M^+) 237	Calc. for $C_{21}H_{40}O_4Si$: 384.2696. Found: 384.2692. (for the mixture of silyl ethers)

Table III (continued)

Compound	*^{1}H-N.m.r.*	*I.r.*[b]	*M.s.*	*H.r.m.s.* (Anal.)
-1-methylpropane, β anomer	4.17 (m, 1 H), 3.9 (m, 2 H), 3.8 (m, 2 H), 3.1 (dd, 1 H, *J* 8.9, 2.22), 3.03 (dt, 1 H, *J* 11.2, 2.02 Hz), 1.6 (m, 10 H), and 1.2–0.9 (m, 9 H)	3400, 2950, 2850, 1455, 1370, 1350, 1185, 1160, 1115, 1085, 1060, and 935[b]	270 (M^+) 237	
-1-methylethane, α anomer	4.23 (br d, 1 H, *J* 6.49 Hz), 4.03 (dd, 1 H, *J* 8.95, 5.25 Hz), 3.95 (br d, 1 H, *J* 6.67 Hz), 3.72 (m, 2 H), 3.00 (dd, 1 H, *J* 9.09, 5.25 Hz), 2.10 (d, 1 H, *J* 8.49 Hz), 1.83 (m, 1 H), 1.6 (m, 10 H), 1.0 (d, 3 H, *J* 6.87 Hz), and 0.95 (d, 3 H, *J* 6.67 Hz)	3630, 3480, 2950, 2870, 1450, 1430, 1370, 1350, 1315, 1260, 1190 1155, 1090, 1060, 1035, 970, 905, and 850[b]	256 (M^+), and 213 ($M^+ - iPr$)	Calc. for $C_{20}H_{38}O_4Si$: 370.2540. Found: 370.2539. (for the mixture of silyl ethers)
-1-methylethane, β anomer	4.17 (dd, 1 H, *J* 5.25, 2.36 Hz), 3.9 (m, 2 H), 3.78 (m, 1 H), 3.11 (dd, 1 H, *J* 9.4, 2.2 Hz), 3.03 (t, 1 H, *J* 11.11 Hz), 2.11 (d, 1 H, *J* 3.64 Hz), 2.05 (m, 2 H), 1.55 (m, 10 H), 1.05 (d, 3 H, *J* 6.67 Hz), and 0.97 (d, 3 H, *J* 6.67 Hz)	3600, 3400, 2930, 2890, 1450, 1360, 1345, 1315, 1260, 1240, 1190, 1156, 1105, 1085, 1065, 1015, 980, 960, 930, and 880[b]	256 (M^+) 213 ($M^+ - iPr$)	

(2,3,4,6-Tetra-*O*-benzyl-D-glucopyranosyl)-methane, α anomer (**29**)	7.41–7.09 (m, 20 H), 5.00–4.41 (m, 8 H), 4.27 (quintet, 1 H, *J* 6.6 Hz), 3.86–3.51 (m, 6 H), and 1.29 (d, 3 H, *J* 6.6 Hz)	3040, 2930, and 1050[c]	447 ($M^+ - C_6H_5CH_2$)	Calc. for $C_{28}H_{31}O_5$: 447.2172. Found: 447.2171.
β anomer (**29**)	7.42–7.08 (m, 20 H), 4.88 (s, 2 H), 4.86–4.49 (m, 6 H), 3.85–3.65 (m, 4 H), 3.48–3.46 (m, 2 H), 3.20 (t, 2 H, *J* 10.5 Hz), and 1.22 (d, 3 H, *J* 6.6 Hz)	3040, 2940, and 1050[c]	447 ($M^+ - C_6H_5CH_2$)	Calc. for $C_{28}H_{31}O_5$: 447.2172. Found: 447.2171.
-ethane, α anomer (**30**)	7.40–7.06 (m, 20 H), 5.70–4.42 (m, 8 H), 3.97–3.87 (m, 1 H), 3.83–3.49 (m, 6 H), 1.71 (quintet, 2 H, *J* 7.4 Hz), and 1.14 (t, 3 H, *J* 7.4 Hz)	3040, 2930, and 1050[c]	461 ($M^+ - C_6H_5CH_2$)	Calc. for $C_{29}H_{33}O_5$: 461.2328. Found: 461.2327.
-ethane, β anomer (**30**)	7.41–7.05 (m, 20 H), 4.96–4.42 (m, 6 H), 4.90 (s, 2 H), 3.83–3.51 (m, 4 H), 3.45–3.12 (m, 3 H), 1.97–1.85 (m, 2 H), and 1.00 (t, 3 H, *J* 7.4 Hz)	3040, 2930, and 1050[c]	461 ($M^+ - C_6H_5CH_2$)	Calc. for $C_{29}H_{33}O_5$: 461.2328. Found: 461.2328.
-benzene. α,β anomers (**28**)	7.80–7.00 (m, 25 H), 5.24 (d, 1 H, *J* 4.6 Hz), 5.01–4.41 (m, 8 H), and 4.19–3.44 (m, 6 H)	3070, 3040, and 1045[c]	509 ($M^+ - C_6H_5CH_2$)	Calc. for $C_{33}H_{33}O_5$: 509.2329. Found: 509.2327.

Table III (continued)

Compound	*^{1}H-N.m.r.*	*I.r.*[b]	*M.s.*	*H.r.m.s.* (Anal.)
(2,3,4,6-Tetra-*O*-benzyl-D-mannopyranosyl)-methane, α,β anomers (31)	7.42–7.05 (m, 20 H), 4.86–3.43 (m, 7 H), and 1.21 (d, 3 H, *J* 6.3 Hz)	3040, 2940, 1450, and 1090[c]	447 ($M^+ - C_6H_5CH_2$)	Calc. for $C_{28}H_{31}O_5$: 447.2172. Found: 447.2171.
-benzene, α anomer (32)	7.43–7.11 (m, 25 H), 5.03 (d, 1 H, *J* 4.9 Hz), 4.75–4.45 (m, 8 H), 4.08 (dd, 1 H, *J* 4.9, 3.1 Hz), 4.00–3.85 (m, 4 H), and 3.70 (dd, 1 H, *J* 6.6, 3.3 Hz)	3050, 2940, and 1090[c]	509 ($M^+ - C_6H_5CH_2$)	Calc. for $C_{33}H_{33}O_4$: 509.2329. Found: 509.2331.
β anomer (32)	7.10–7.50 (m, 25 H), 4.94–4.35 (m, 9 H), and 4.26–3.55 (m, 6 H)	3040, 2950, and 1100[c]	509 ($M^+ - C_6H_5CH_2$)	
16	7.68–7.32 (m, 10 H), 4.84 (d, 1 H, 6.0 Hz), 4.60 (dd, 1 H, *J* 5.4, 5.1 Hz), 4.22 (dq, 1 H, *J* 7.0, 4.0 Hz), 4.09 (t, 1 H, *J* 5.0 Hz), 3.74 (dd, 1 H, 11.0, 5.0 Hz), 3.66 (dd, 1 H, 11.0, 5.0 Hz), 1.49 (s, 3 H), 1.34 (s, 3 H), 1.28 (d, 3 H, *J* 6.1 Hz), and 1.03 (s, 9 H)	2950 and 1100[c]	369 ($M^+ - Bu^t$)	Calc. for $C_{21}H_{25}O_4Si$: 369.1522. Found: 369.1524.
15	7.75–7.33 (m, 10 H), 4.73 (dd, 1 H, *J* 6.4, 3.8 Hz), 4.25 (t, 1 H, *J* 6.1 Hz), 4.05–3.95 (m, 2 H), 3.77 (d, 1 H, *J* 3.9 Hz), 1.53 (s, 3 H), 1.33 (s, 3 H), 1.31 (d, 3 H, *J* 6.5 Hz), and 1.06 (s, 9 H)	2950, 1110, and 1060[c]	369 ($M^+ - Bu^t$)	Calc. for $C_{21}H_{25}O_4Si$: 369.1522. Found: 369.1522.

(4,6-Di-*O*-acetyl-2,3-dideoxy-D-*erythro*-hex-2-enopyranosyl)ethane, α anomer (33)	5.81 (d, 1 H, *J* 10.3 Hz), 5.72 (d, 1 H) 1 H, *J* 10.3 Hz), 5.25 (d, 1 H, *J* 8.8 Hz), 4.28–4.09 (m, 6 H), 3.71 (ddd, 1 H, *J* 8.8, 5.8, 2.6 Hz), 2.10 (s, 3 H), 2.08 (s, 3 H), 1.60 (qd, 2 H, *J* 7.4, 2.5 Hz), and 0.93 (t, 3 H, *J* 7.4 Hz)	2950, 1736, 1455, 1210, and 1080[c]	213 ($M^+ - C_2H_5$)	Calc. for $C_{10}H_{13}O_5$: 213.0763. Found: 213.0763.
β anomer	5.92 (ddd, 10.5, 2.4 1.5 Hz), 5.78 (dt, 10.5, 2.4 Hz), 5.17–5.09 (m, 1 H), 4.22 (dd, 1 H, 11.8, 6.5 Hz), 4.18–4.08 (m, 2 H), 3.92 (td, 1 H, *J* 6.5, 3.5 Hz), 2.10 (s, 3 H), 2.09 (s, 3 H), 1.78–1.49 (m, 2 H), and 1.00 (t, 3 H, *J* 7.4 Hz)	2950, 1736, 1450, 1220, and 1090[c]	213 ($M^+ - C_2H_5$)	Calc. for $C_{10}H_{13}O_5$: 213.0763. Found: 213.0758.
19	5.60 (d, 1 H, *J* 5.0 Hz), 5.19 (t, 1 H), *J* 3.3 Hz, 4.90 (dd, 1 H, *J* 9.6, 2.8 Hz), 4.22 (dd, 1H, *J* 12.0, 4.8 Hz), 4.19 (dd, 1 H, *J* 12.0, 3.0 Hz), 4.11 (ddd, 1 H, *J* 9.6, 4.8, 3.0 Hz), 2.11 (s, 3 H), 2.10 (s, 3 H), 2.09 (s, 3 H), 1.61 (s, 3 H), and 1.35 (s, 3 H)	2990, 1740, 1215, 1020[c]	331 ($M^+ - CH_3$)	Calc. for $C_{14}H_{19}O_9$: 331.1029. Found: 331.1037.

[a]For a solution in (^{2}H)chloroform. [b]For a solution in chloroform. [c]For a film.

EXPERIMENTAL

General methods. — Melting points were recorded with a Thomas–Hoover melting point apparatus and are uncorrected. Optical rotations were determined with a Perkin–Elmer 241 polarimeter. I.r. spectra were recorded with a Perkin–Elmer 247 grating infrared spectrometer using the polystyrene absorption at 1601 cm^{-1} as a reference. ^{1}H-N.m.r. spectra were recorded with a Varian EM-390 (90 MHz) or a Bruker WH-300 (300 MHz) instrument using tetramethylsilane as an internal standard (δ 0.00). Low-resolution mass spectra were recorded with a LKB 9000 A GC-mass spectrometer and high-resolution mass spectra with a Varian MAT CH-5DF mass spectrometer. T.l.c. was performed on Merck precoated Silica gel 60 F 254 glass plates, layer thickness 0.25 mm, with fluorescent indicator. The spots were detected by staining with a solution of $(NH_4)_6MO_7O_{24} \cdot 4\ H_2O$ (16 g) and $Ce(SO_4) \cdot n\ H_2O$ (1 g) in 10% H_2SO_4 (500 mL). Liquid chromatography was performed on a Waters Associates instrument using a μ-Porasil column. Column chromatography was performed on silica gel (70–230 mesh) from EM Reagents. All reactions were carried out under an inert atmosphere of Ar or N_2.

General procedure. — An oven-dried, resealable tube was purged with a slow stream of N_2, and then charged with the thioglycoside as a solution in benzene or toluene (~50mM) and diiodomethane (8 equiv.). The zinc reagent (~15-fold excess) was added dropwise, and the tube was sealed and heated at 40–50° for several hours. The tube was cooled in an ice-bath, and the reaction was quenched by the dropwise addition of methanol until effervescence ceased. A 5% solution of HCl was added dropwise, and the resulting mixture was extracted with dichloromethane. The organic layer was washed with aqueous $NaHCO_3$ solution, dried ($MgSO_4$), concentrated, and chromatographed. The spectral data of the *C*-glycosyl compounds obtained are reported in Table III.

[*5-O-(*tert*-Butyldiphenylsilyl)-2,3-O-isopropylidene-β-*D*-* (**15**) *and -α-*D*-ribofuranosyl]methane* (**16**). — According to the general procedure, phenyl 5-*O*-(*tert*-butyldiphenylsilyl)-2,3-*O*-isopropylidene-1-thio-α-D-ribofuranoside (**14**) (28 mg, 54 μmol) was treated with diiodomethane (52 μL, 0.54 mmol) and dimethylzinc (51 mg) in benzene (1 mL) for 20 h at 48°. After workup, the crude mixture of **15** and **16** was chromatographed on silica gel with 5% ethyl acetate–hexane as eluent to give 13.2 mg of the less polar isomer **15**, and 7.7 mg of the more polar isomer **16** (91% yield, ratio α:β 37:63).

Anal. (mixture of **15** and **16**) Calc. for $C_{25}H_{34}OSi$: C, 70.38; H, 8.03. Found: C, 70.30; H, 7.89.

(2,3,4,6-Tetra-O-benzyl-α,β-D-glucopyranosyl)benzene (**28**). — According to the general procedure, phenyl 2,3,4,6-tetra-*O*-benzyl-1-thio-β-D-glucopyranoside (**8**) (22 mg, 35 μmol) was treated with diiodomethane (22 μL, 8 equiv.) and diphenylzinc (77 mg, 10 equiv.) in benzene (0.7 mL) for 2 h at 50°. After quenching the reaction, the crude mixture was chromatographed on silica gel with 20% ethyl acetate–hexane as eluent to give a mixture (10 mg) of the α- and β-D-gluco-

pyranosylbenzenes **28** (48%). Integration of the ^{1}H-n.m.r. signals of the mixture showed that the α to β ratio of anomers was 3 to 1. The assignment of the α-D configuration to the major anomer was confirmed by conversion into the corresponding tetraacetate and comparison with an authentic sample prepared as described earlier[18]. The presence of the minor β-D anomer was confirmed by comparison of its ^{1}H-n.m.r. spectrum with the spectrum of an authentic sample prepared from 2,3,4,6-tetra-*O*-acetyl-β-D-(glucopyranosyl)benzene[18] by acetate cleavage and benzylation.

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