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Reaction of organocuprate reagents with protected 1,2-anhydro sugars. Stereocontrolled synthesis of 2-deoxy-*C*-glycosyl compounds †

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ABSTRACT

The reaction of protected 1,2-anhydro-α-D-gluco- and β-D-manno-pyranoses with alkyl and phenyl organocuprates afforded the corresponding *C*-glycosyl compounds in acceptable to high yield. Complete stereocontrol was obtained, leading respectively to the β-D or the α-D anomer. With the perbenzylated *manno* derivative, deoxygenation at C-2 was achieved in high yield, affording 2-deoxy-α-D-*C*-glycosyl compounds.

INTRODUCTION

The formation of C–C bonds at the anomeric center of sugars has attracted considerable attention in recent years because various types of *C*-glycosyl compounds having interesting biological properties are found in nature (for reviews see ref 1). In view of the occurrence of carbohydrate-like subunits in the structures of many natural products, *C*-glycosyl compounds are also used as chiral building blocks in natural product synthesis[2].

Although *C*-glycosyl compounds were recently prepared by addition of glycosyl radicals to alkenes[3], and by polarity inversion at the anomeric centre[4], most synthetic methods involve the introduction of carbon nucleophiles at the anomeric position of suitably activated sugar derivatives (for examples see ref 5). These methods generally afford a mixture of α and β anomers, especially when applied to 2-deoxy-glycosyl derivatives, as neighbouring-group participation is not possible in this case.

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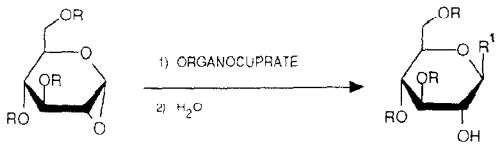


We have already reported the formation of *C*-glycosyl compounds by reaction of several organometallic reagents with a variety of sugar derivatives[6,7]. In this paper, the reaction of organocuprates with diversely protected 1,2-anhydro sugars is reported.

Opening of an oxirane ring by an organocuprate is known to proceed anti to the oxygen atom[8]. Consequently a high stereocontrol was expected in this reaction. The reaction would afford a *C*-glycosyl compound in which the C-2 hydroxyl group would be differentiated from the other ones, thus allowing further transformations. We had in mind Barton's deoxygenation[9], and thus an opportunity for a stereocontrolled synthesis of 2-deoxy-*C*-glycosyl compounds.

The opening of oxiranes with organocuprates has been well documented in carbohydrate chemistry for the preparation of branched-chain sugars[10,11]. However, to the best of our knowledge, no attempts were made with 1,2-anhydro sugars.

RESULTS AND DISCUSSION

Due to the relative inertness of organocuprate reagents[8a] towards the ester function, the readily available 3,4,6-tri-*O*-acetyl-1,2-anhydro-α-D-glucopyranose[12] **1** (Brigl's anhydride) was chosen as a model compound to evaluate the synthetic utility and the stereochemical outcome of the title reaction.

Several combinations of reagents were evaluated in diethyl ether, which is the preferred solvent for reaction of dialkyl cuprates[13] and dialkyl cyanocuprates[14]. Selected results are reported in Table I.

Although cyanocuprates gave satisfactory yields in the conjugate addition to 4,6-di-*O*-acetyl-1,5-anhydro-2-deoxy-D-*erythro* and D-*threo*-hex-1-eno-3-ulose[7], their reaction with **1** was rather slow and polar compounds were detected by TLC. They could be polymers formed by competitive reaction of the alkoxide, resulting from the addition reaction, with the starting material.

The β-*C*-glycosyl compounds **2** and **3** were isolated in low yield after acetylation (Table I, Entries 1 and 6). 2,3,6-Tri-*O*-acetyl-1,5-anhydro-2-deoxy-D-*arabino*-hex-1-enitol (tri-*O*-acetyl-D-glucal, **4**) was also formed by competitive elimination. Addition of boron trifluoride etherate, which is known to increase the rate of the reaction[15], did not improve the yield but only traces of **4** were detected in this case (Table I, Entry 3).

TABLE I

Products formed by the reaction of organocuprate reagents with the 1,2-anhydro sugar **1**

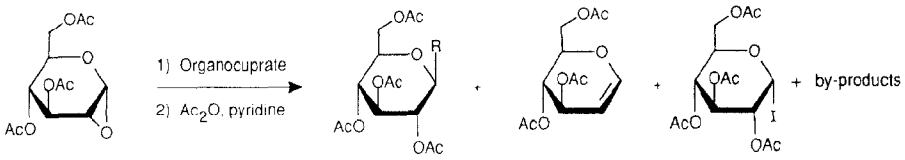
Entry	Organocuprate reagent (equiv)	Ac_2O or BF_3–Et_2O [a]	Conditions	Yields of products [b,c] (%)					
				2	**3**	**4**	**5**	**6**	
1	$Me_2CuCNLi_2$ (2.2)		−50 → 0°C and 1 h at 0°C	25		10			[d]
2	$Me_2CuCNLi_2$ (2.2)	Ac_2O 2 equiv aft.	−17 → 0°C and 1 h at 0°C	20		11			[d]
3	$Me_2CuCNLi_2$ (2.2)	BF_3–Et_2O 1 equiv aft.	10 min at −20°C and 2.5 h at 0°C	23		[e]			[d]
4	Me_2CuLi (2.2)		1 h at −20°C −20 → 0°C and 2 h at 0°C	65.5		12	17		
5	Me_2CuLi (2.7)	Ac_2O 2 equiv tog.	1 h at −20°C and 2 h at 0°C	15		10		28	
6	$Ph_2CuCNLi_2$ (2)		−50 → −20°C and 1 h at 0°C		27				[d]
7	Ph_2CuLi (2.2)		−20 → 0°C and 2 h at 0°C		23	18	38		

[a] Ac_2O or BF_3–Et_2O was added after (aft.) or together with (tog.) the anhydro sugar. [b] Acetylation with Ac_2O–pyridine before work-up except Entries 2 and 5. [c] Yield of isolated product after flash chromatography. [d] Presence of unidentified polar compounds. [e] Only traces.

With lithium dimethylcuprate (Table I, Entry 4), compound **2** was obtained in acceptable yield along with tri-*O*-acetyl-D-glucal (**4**) and 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl iodide (**5**) formed by competitive reaction of iodide ion (copper iodide was used to prepare the organocuprate). Acetylation of the crude mixture was necessary for the isolation of the *C*-glycosyl compounds because, contrary to previous claims concerning the inertness of organocuprates towards the ester function[8a], partial deacetylation of the starting material was observed under these conditions[7,16]. In an attempt to try to minimize undesired side reactions, we decided to trap the resulting alkoxide by adding **1** to the organocuprate reagent together with an electrophile (Ac_2O, Table I, Entry 5). This approach gave good results for us[7] and for others[17] in the conjugate addition to enones. Under these conditions, a compound bearing an iodine atom at C-2 in the *manno* configuration (**6**) was the major product (see Experimental section for the structure determination).

Whatever the reagent was, lower yields were obtained in the transfer of a phenyl group to the anomeric carbon atom (Table I, Entries 6 and 7).

The β configuration of the resulting *C*-glycosyl compounds **2** and **3** was confirmed by a large coupling constant between H-1 and H-2 (9.6 and 9.8 Hz) and the $^4C_1$(D) conformation by the large coupling constants between H-2, H-3, H-4, and H-5 (9–9.7 Hz). The absence of α anomer and of compound bearing a methyl or phenyl group at C-2 was confirmed by GLC analysis of the crude mixture.



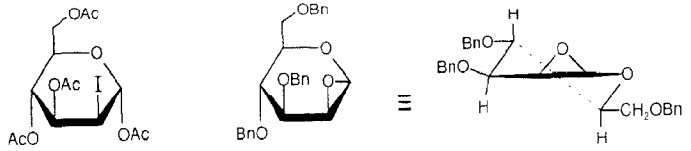
1

2 R = Me

3 R = Ph

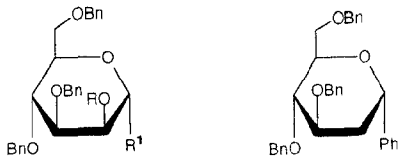
4

5



6

7



8 R = Ac, R^1 = Me

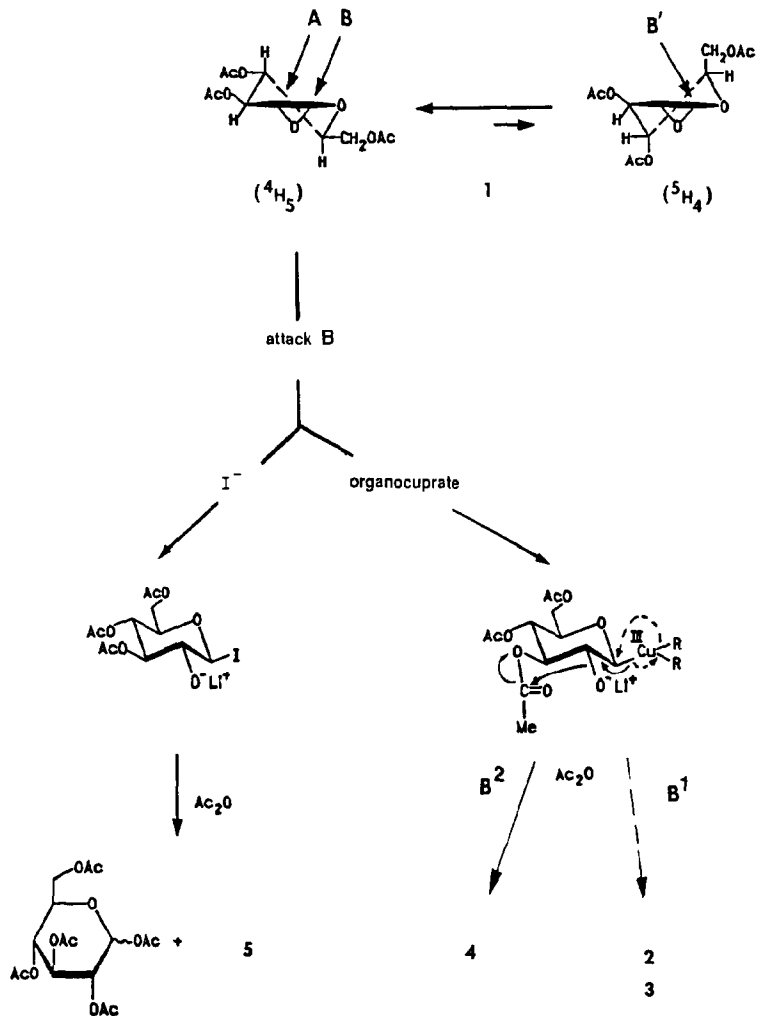
9 R = H, R^1 = Ph

10 R = Ac, R^1 = Ph

11

Since it was pointed out by Mills[18] that opening of rigid carbohydrate epoxides by nucleophiles obey the Fürst and Plattner[19] diaxial rule for steroid epoxides, many violations involving diequatorial opening have been observed. Relevant to our work, Yoshimura[11] observed that the opening of branched 2,3-epoxides, conformationally blocked by a 4,6-*O*-benzylidene group, by bulky organocuprate reagents always occurred at the less hindered side regardless of the orientation. Competitive diequatorial anti-Fürst–Plattner opening of several 4,6-*O*-benzylidene-2,3-anhydro glycopyranosides by hydride ion was also reported by Baer[20]. For monocyclic sugar epoxides, a conformational equilibrium is possible and the rationalization is more difficult.

The two possibilities for the opening of compound **1** are indicated on Scheme 2. Attack A corresponds to *trans*-diaxial opening according to the Fürst–Plattner rule. In no case, was a compound resulting from reaction of the organocuprate reagent at C-2 isolated, but, when acetic anhydride was present, compound **6** bearing an iodine atom in the *manno* configuration at C-2 was formed in an



appreciable amount. This amount was increased when an excess of CuI was present.

Attack B corresponds to a *trans*-diequatorial opening of **1** in the ground-state $^4H_5$ conformation. In agreement with the Fürst–Plattner rule, a *trans*-diaxal opening on a $^5H_4$ conformation could also be envisaged (attack B′). But, in this case, the 5-(acetoxymethyl) group is axially oriented and would hinder the axial approach of the bulky organocuprate reagent. Our results show that the regioselectivity of the ring opening is not strongly influenced by stereoelectronic effects, but rather assisted by the electron-donating effect of the ring oxygen atom. After the oxirane ring opening by the organocuprate reagent, the resulting copper(III) derivative can then collapse (route B^1) to the *C*-glycosyl compound and organocop-

per RCu or afford (route B^2) tri-*O*-acetyl-D-glucal by elimination after transesterification of the alkoxide group at C-2. Tri-*O*-acetyl-D-glucal (**4**) could also be formed by reduction of the iodide **5** by the organocuprate reagent[8]. Actually, it was verified that **4** was the major product when 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide was treated with organocuprate reagents[6c].

Competitive ring opening, according to attack B, by I^- accounts for by-product **5** which could be partially transformed into D-glucose pentaacetate during acetylation.

In spite of these side reactions, the β-alkyl *C*-glycosyl compound (**2** or **3**) was isolated as the sole anomer in acceptable yield (Table I, Entry 4). The yield was lower for aryl organocuprate because of the lower reactivity of this kind of reagent[14].

With the *manno* epoxide **7**, more stable benzyl ethers were employed as the protecting group. In the $^4H_5$(D) ground-state conformation of this compound[21], both effects (stereoelectronic and assistance of the ring oxygen atom) are in favour of a *trans*-diaxial opening at C-1. Consequently the reaction was clean, no by-product was formed and the yield was near-quantitative even without acetylation of the resulting product (90% with Me_2CuLi and 70% with Ph_2CuLi). The reaction was stereospecific and only the α anomer was formed and isolated. The configurations at C-1 and C-2 were confirmed by ^1H and ^{13}C NMR and comparison with previous results[22]. For both compounds, $J_{1,2}$ and $J_{2,3}$ were in the range (2.7–4.1 Hz) compatible with an axial–equatorial relationship.

In this case, the differenciation of the C-2 hydroxyl in the resulting *C*-glycosyl compound was possible. The deoxygenation of this position according to Barton's method[9,23] is exemplified with compound **9**. The 2-deoxy *C*-glycosyl compound **11** was isolated in good yield (84%) and its configuration was confirmed by ^1H NMR spectroscopy (H-1, δ 5.12; $J_{1,2ax}$ 4.7 and $J_{1,2eq}$ 3.7 Hz). It has been verified that hydrogenolysis of the benzyl groups could be carried out without cleavage of the pyranoside ring.

Since the outcome of the reaction is controlled only by the stereochemistry of the oxirane ring, this new method of C–C bond formation at the anomeric carbon could be applied to the synthesis of other *C*-glycosyl compounds.

The transformation into 2-deoxy derivatives is also general and compatible with a variety of protecting groups[23]. The examples illustrated here are of particular interest because they lead to compounds containing a 2-deoxy-*arabino*-hexopyranosyl moiety, a substructure present in many natural compounds[24].

EXPERIMENTAL

General methods.—Melting points were determined on a Thomas–Hoover apparatus and are uncorrected. Optical rotations were measured on a Perkin–Elmer 141 polarimeter. IR spectra (film or KBr disk) were recorded on a Unicam SP3-300 spectrophotometer. NMR spectra were recorded on Bruker AM-250 or AM-200 SY spectrometers in $CDCl_3$ solutions, with Me_4Si as internal standard.

Mass spectra were determined on a Kratos MS 30 instrument (electron impact) operating at 70 eV or on a R10-10B Nermag apparatus (chemical ionisation, NH_3). GLC was performed with a Girdel 75 FD instrument fitted with a 1 m column of 3% phenyldiethanolamine succinate (PDEAS) on Chromosorb WAW DMCS. TLC was performed on Silica Gel 60F-254 with detection by UV, and by spraying with 3 M H_2SO_4 and heating. The following solvent systems were used; solvent *A* (2:1 Et_2O–ligroin) and solvent *B* (9:1 $CHCl_3$–MeOH). Merck Silica Gel 60 (230–400 mesh) was used for flash chromatography. Elemental analyses were performed by the "Service de Microanalyse" of the Université Pierre et Marie Curie. Oxolane and Et_2O were distilled from benzophenone–sodium immediately before use. Methyl- and phenyl-lithium solutions were purchased from Aldrich and Fluka and standardized[25] before use. Copper(I) salts (CuI and CuCN) from Prolabo were used without purification. The CuBr–Me_2S complex was prepared according to ref 26. Commercial BF_3–Et_2O was distilled[27] from CaH_2 at 46°C/10 mm.

Me_2CuLi was prepared under Ar at −20°C by addition of MeLi (1.6 M, 1.25 mL, 3 mmol) to a suspension of CuI (190 mg, 1 mmol) in anhyd Et_2O (2 mL). After 10 min at −20°C, the complete formation of the organocuprate was verified by a negative Gilman test[28] with Michler's ketone. Ph_2CuLi Was prepared similarly at −50°C with CuI or CuBr–Me_2S. To prepare lithium dimethyl- or diphenyl-cyanocuprates, the organolithium derivative (2 mmol) was added under Ar, at −20°C (for MeLi) or at −50°C (for PhLi) to a suspension of copper(I) cyanide (100 mg, 1.1 mmol) in anhyd Et_2O.

Typical procedure for the reaction of organocuprate reagents with 3,4,6-tri-O-acetyl-α-D-glucopyranose (**1**).—To an etheral solution of Me_2CuLi (2.2 mmol) at −20°C, under Ar, **1** (288 mg, 1 mmol) dissolved in anhyd Et_2O (10 mL) was slowly added with a syringe. The colorless solution immediately became a bright-yellow slurry. The mixture was maintained, with good stirring, at −20°C for 1 h. The temperature was then allowed to rise to 0°C (~ 0.5 h). The course of the reaction was followed by TLC (solvents *A* and *B*). After 1 h at 0°C, the starting material had disappeared and Ac_2O (380 μL, 4 mmol) was added. The reaction was stirred overnight at room temperature. After completion of the reaction, as indicated by TLC (solvent *A*), a satd NH_4Cl solution (1 mL) was added and the product extracted with Et_2O (3 × 10 mL). The combined ether solution was washed with a satd NH_4Cl solution (2 × 5 mL) and water (5 mL), dried ($MgSO_4$), and evaporated. The crude residue was analyzed by GLC. Flash chromatography of the resulting syrup with mixtures of Et_2O–ligroin of increasing polarity afforded successively the following compounds:

The 3,4,6-tri-*O*-acetyl-1,5-anhydro-2-deoxy-D-arabino-hex-1-enitol (**4**) 32 mg (12%); R_f 0.51 (solvent *A*).

2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosylmethane (**2**), 227 mg (65.5%); R_f 0.39 (solvent *A*); mp 80–81°C (EtO_2–hexane); $[\alpha]_D^{20}$ + 0.8° (*c* 1.09, $CHCl_3$); lit.[29] mp 81–82°C; $[\alpha]_D^{20}$ + 1° ($CHCl_3$); t_R (column PDEAS 3%, 0.60 m) 7.9 min at 107°C; IR ν_{max} (neat) 1750 cm^{-1} (ester); ^1H NMR ($CDCl_3$): δ 1.24 (d, 3 H, $J_{1,Me}$ 6.2 Hz, Me),

2.00, 2.03, 2.05, 2.09 (4s, 4 OAc), 3.56 (dq, 1 H, $J_{1,2}$ 9.6 Hz, H-1), 3.66 (ddd, 1 H, $J_{4,5}$ 9, $J_{5,6a}$ 2.4, $J_{5,6b}$ 4.8 Hz, H-5), 4.1 (dd, 1 H, $J_{6a,6b}$ 12.3 Hz, H-6a), 4.2 (dd, 1 H, H-6b), 4.84 (dd, 1 H, $J_{2,3}$ 9 Hz, H-2) 5.1 (dd, 1 H, $J_{4,3}$ 9 Hz, H-4), 5.2 (dd, 1 H, H-3). Anal. Calcd for $C_{15}H_{22}O_9$ (346.32): C, 52.02; H, 6.40. Found: C, 51.67; H, 6.48.

Further elution gave **5** as an oil 78 mg (18–20%); R_f 0.30 (solvent *A*); CIMS (NH_3), *m/z* 476 (9, $[M + 18]^+$) which was shown to contain D-glucose pentaacetate, *m/z* 408 (100, $[M + 18]^+$).

In another assay carried out with Ph_2CuLi, the relative proportions of **5** and D-glucose pentaacetate were 43–57%, respectively (^1H NMR, 200 MHz, $CDCl_3$).

When Ac_2O (2 equiv) was added together with the anhydro sugar **1** (Table 1, Entry 5), flash chromatography of the crude mixture afforded **6** in addition to **4** and **2**.

1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-iodo-α-D-mannopyranose (**6**) as an oil, 128 mg (28%); R_f 0.34 (solvent *A*); $[\alpha]_D^{20}$ + 17° (*c* 0.9, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 2.04, 2.09, 2.10, 2.15 (4s, 4 OAc), ~4.10 and ~4.13 (ddd and dd, 2 H, $J_{5,6a}$ 2.4 Hz, H-5,6a), 4.18 (dd, 1 H, $J_{5,6b}$ 4.5, $J_{6,6b}$ 12.4 Hz, H-6b), 4.50 (dd, 1 H, $J_{2,3}$ 4.4 Hz, H-2), 4.54 (br dd, 1 H, $J_{3,4}$ 9.3 Hz, H-3), 5.42 (dd, 1 H, $J_{4,5}$ 9.8 Hz, H-4), 6.35 (br d, 1 H, $J_{1,2}$ 1.6 Hz, H-1); ^{13}C NMR (60 MHz, $CDCl_3$, Me_4Si) δ 20.53, 20.63, 20.74, 20.81 (4 OAc), 27.14 (C-2), 61.90 (C-6), 68.69, 67.17, 71.50 (C-3–5), 94.77 (C-1), 168.06, 169.21, 169.80, 170.55 (4 OAc); EIMS, *m/z* 399 ($M^+ - 59$); CIMS (NH_3), *m/z* 476 (100, $[M + 18]^+$).

*Reaction of lithium diphenylcuprate with 1,2-anhydro-3,4,6-tri-*O*-acetyl-α-*D*-glucopyranose* (**1**).—The general procedure described above was employed. After work-up, flash-chromatography afforded 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosylbenzene (**3**); 94 mg (23%); R_f 0.36 (solvent *A*); mp 156–158°C (from 2-propanol); $[\alpha]_D^{20}$ – 20.4° (*c* 0.94, $CHCl_3$); lit.[30] mp 155–156°C; $[\alpha]_D^{20}$ 18.6° (*c* 2.01, $CHCl_3$); GLC at 155°C, t_R 15.4 min; ^1H and ^{13}C NMR spectra were found to be identical with the data in ref. 22. Anal. Calcd for $C_{20}H_{24}O_9$ (408.41): C, 58.82; H, 5.92. Found: C, 58.53; H, 5.90.

*Reaction of lithium dimethylcuprate with 1,2-anhydro-3,4,6-tri-*O*-benzyl-β-*D*-mannopyranose* (**7**).—The procedure described above was employed with **7** (ref 31). After 1 h at −20°C, the crude mixture was acetylated and worked-up. Compound **8** was isolated by flash chromatography with mixtures of Et_2O–ligroin of increasing polarity to yield 2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosylmethane (**8**), 440 mg (90%) as a colorless oil; R_f 0.49 (solvent *A*); $[\alpha]_D^{20}$ + 3.5° (*c* 1.27, $CHCl_3$); IR ν_{max} (neat) 1735 (ester); ^1H NMR (200 MHz, $CDCl_3$): δ 1.23 (d, 3 H, J_{1,CH_3} 7.1 Hz, CH_3), 2.13 (s, 3 H, $OCOCH_3$), 3.64–3.94 (m, 5 H, H-3, 4, 5, 6a, 6b), 4.19 (dq, 1 H, $J_{1,2}$ 2.7 Hz, H-1), 4.44–4.84 (3 AB syst., 6 H, J_{AB} 10.8, 11.2, 12.2 Hz, 3 OCH_2Ph), 5.24 (dd, 1 H, $J_{2,3}$ 2.7 Hz, H-2), 7.22–7.40 (m, 15 H, 3 Ph); CIMS (NH_3), *m/z* 508 (76, $[M + 18]^+$, 491 (5, $[MH]^+$). Anal. Calcd for $C_{30}H_{34}O_6$ (490.587): c, 73.45; H, 6.99. Found: C, 73.25; H, 7.12.

*Reaction of lithium diphenylcuprate with 1,2-anhydro-3,4,6-tri-*O*-benzyl-β-*D*-man-*

nopyranose (**7**).—Addition of **7** (0.5 mmol) to Ph_2CuLi (1.1 mmol) at −78°C in anhyd Et_2O followed by reaction (1 h at −78°C, then −78°C → 0°C, and 0.75 h at 0°C) afforded, after work-up and purification by flash chromatography, (3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl) benzene (**9**): 178 mg (70%); R_f 0.26 (solvent *A*); mp 71–72°C (from ligroin); $[\alpha]_D^{20}$ + 65.8° (*c* 0.88, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$): δ 2.60 (s, 1 H, OH), 3.7–3.8 (m, 3 H, H-5, 6a, 6b), 3.72 (m, 1 H, $J_{3,4}$ 7 Hz, H-3), 3.94 (dd, 1 H, $J_{4,5}$ 7 Hz, H-4), 4.40 (dd, 1 H, $J_{2,3}$ 3 Hz, H-2), 4.50–4.75 (3 AB syst., 6 H, 3 OCH_2Ph), 4.97 (d, 1 H, $J_{1,2}$ 4.1 Hz, H-1), 7.16–7.37 (m, 20 H, 4 Ph); CIMS (NH_3), *m/z* 528 (94, $[M + 18]^+$), 511 (4, $[M + 1]^+$). Anal. Calcd for $C_{33}H_{34}O_4$ (510.624): C, 77.62; H, 6.71. Found: C, 77.95; H, 6.69.

Acetylation of **9** in the usual manner (Ac_2O, pyridine, room temperature) afforded (2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl) benzene (**10**) as an oil; R_f 0.56 (solvent *A*); IR ν_{max} (neat) 1740 cm^{-1} (ester); ^1H NMR (200 MHz, $CDCl_3$) 2.14 (s, 3 H, OAc_3), 3.58–3.75 (m, 3 H, H-5, 6a, 6b), 3.69 (m, 1 H, $J_{3,4}$ 8.8 Hz, H-3), 3.92 (dd, 1 H, $J_{4,5}$ 8.8 Hz, H-4), 4.39–4.77 (3 AB syst., 6 H, 3 OCH_2Ph), 5.04 (d, 1 H, $J_{1,2}$ 3 Hz, H-1) 5.88 (dd, 1 H, $J_{2,3}$ 3 Hz, H-2), 7.15–7.35 (m, 20 H, 4 Ph); CIMS, *m/z* 570 (100, $[M + 18]^+$), 553 (6, $[MH]^+$).

*(3,4,6-Tri-*O*-benzyl-2-deoxy-α-D-arabinopyranosyl) benzene* (**11**).—Following the procedure described by Robins et al.[23] **9** (102 mg, 0.2 mmol) was treated with phenoxythiocarbonyl chloride (40 μL, 0.22 mmol) in MeCN (3 mL) with 4-dimethylaminopyridine (51 mg, 0.42 mmol). The solution was stirred at room temperature for 24 h. After work-up, the resulting *O*-phenoxythiocarbonyl derivative was sufficiently pure to be used directly in the reduction step. The crude residue was dissolved in toluene (5 mL) and 13 mg (0.08 mmol) of azobisisobutyronitrile and nBu_3SnH (600 μL, 2 mmol) were added. The solution was degassed with Ar for 15 min and then heated at 100°C for 1 h. The solvent was evaporated and flash chromatography of the residue with mixtures of Et_2O and hexane of increasing polarity afforded **11** as an oil, 83 mg (84%); R_f 0.61 (solvent *A*); $[\alpha]_D^{20}$ + 84° (*c* 1.39, $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$): δ 2.05 (ddd, 1 H, $J_{2eq,2ax}$ 13.7, $J_{2ax,3}$ 9.5, $J_{1,2ax}$ 4.7 Hz, H-2*ax*), 2.58 (ddd, 1 H, $J_{2eq,2ax}$ 13.7, $J_{2eq,1} = J_{2eq,3} = 3.7$ Hz, H-2eq), 3.56–3.81 (m, 5 H, H-3, 4, 5, 6a, 6b), 4.49–4.82 (3 AB syst., 6 H, 3 OCH_2Ph), 5.12 (dd, 1 H, $J_{1,2ax}$ 4.7, $J_{1,2eq}$ 3.7 Hz, H-1), 7.13–7.4 (m, 20 H, 4 Ph); CIMS, *m/z* 512 (100, $[M + 18]^+$), 495 (6, $[MH]^+$). Anal. Calcd for $C_{33}H_{34}O_4$ (494.63): C, 80.13; H, 6.93. Found: C, 79.97; H, 6.83.

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