A New Approach to Carbohydrate Functionalized Aromatic Compounds

Henning Müller and Carsten Tschierske*

Institute of Organic Chemistry, Martin-Luther-University Halle-Wittenberg, Weinbergweg 16, D-06120 Halle/Saale, Germany

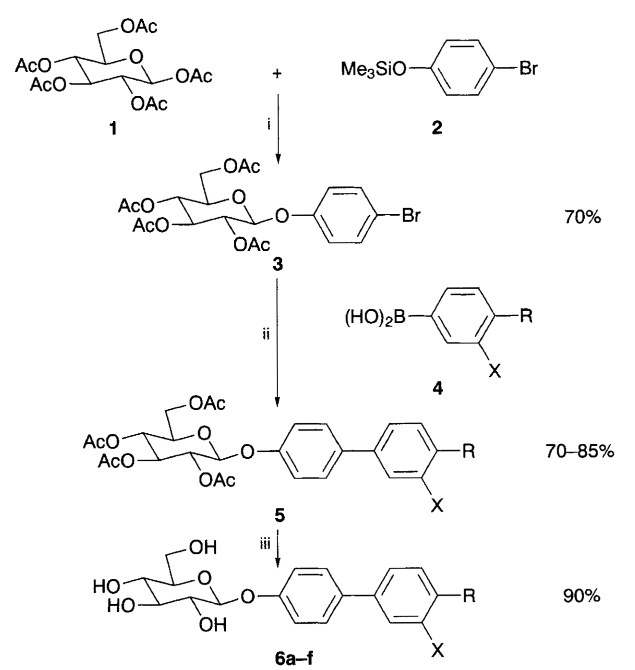
Liquid crystalline aryl-β-*O*-D-glucosides are synthesized by palladium-catalysed cross-coupling of 4-bromophenyl-β-*O*-D-tetraacetylglucoside with boronic acids.

Amphiphilic carbohydrate derivatives are known to form ordered macrostructures such as micelles and liquid crystalline phases.[1] Furthermore, these compounds are interesting because of their potential application as nonionic detergents for the solubilization of integral membrane proteins.[2] In recent studies, we found that the stability of the liquid crystalline phases of amphiphilic carbohydrate derivatives increases by the introduction of rigid structural units such as a *trans*-1,4-disubstituted cyclohexane- or a 1,4-disubstituted benzene ring into the hydrophobic chain.[3] The question arises if the further elongation of the calamitic unit increases their ability for self-organization.

Attempts to synthesize the desired compounds **6** by Koenigs–Knorr glycosylation procedures failed owing to the poor solubility of the 4′-substituted 4-hydroxybiphenyl derivatives.[4] Also the $BF_3·OEt_2$ catalysed glycosylation of α-D-glucose pentaacetate with the corresponding 4-trimethylsilyloxybiphenyl derivatives gave only low yields.[5,6] However, we have succeeded in developing an efficient method for the preparation of substituted aryl-β-*O*-D-glucosides *via* the synthetic route shown in Scheme 1.

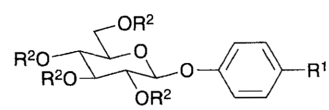
Glycosylation of **2** with α-D-glucose pentaacetate, catalysed by boron trifluoride etherate, leads to **3** in good yield. The so obtained 4-bromophenyl-β-*O*-D-tetraacetylglucoside, readily purified by recrystallization from methanol, can be used as a carbohydrate precursor in cross-coupling reactions with different phenyl boronic acids and vinyl boronic acids (*e.g. cf.* **5g**).[7,8] In a typical procedure bromophenyl-β-*O*-D-tetraacetylglucoside **3** (2.52 g, 5 mmol) and tetrakis(triphenylphosphine)-palladium(0) (0.35 g, 0.3 mmol) in 1,2-dimethoxyethane (40 ml) were stirred for 10 min at 20 °C, the boronic acid (6 mmol) was added, immediately followed by 30 ml of a 1 mol dm^{-3} sodium hydrogen carbonate solution. The reaction mixture was refluxed with vigorous stirring under nitrogen for approximately 4 h. The cross-coupling products **5** were isolated using column chromatography (silical gel 60 and $CHCl_3$ as eluent) and deprotected using standard procedures (1 mmol dm^{-3} NaOMe in MeOH) to give the glucosides **6**.

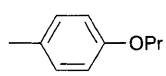
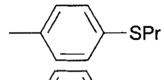
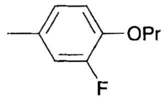
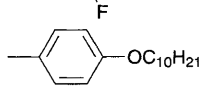
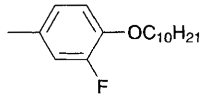
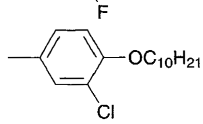
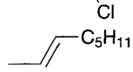
The transition temperatures of the synthesized compounds are listed in Table 1. The tetraacetates **5** are crystalline solids without any mesophase. In contrast, the glucosides **6** are enantiotropic liquid crystals with very high clearing temperatures. The mesophase observed for all compounds described is a smectic A phase. It seems that the formation of large intermolecular hydrogen-bonding networks between the hydroxy groups is the main basis of the liquid crystallinity of this class of compounds. However, if one compares the β-*O*-D-*n*-dodecylglucoside[1] (cr 80 S_A 142 is) with the biphenyl derivatives **6**, an additional mesophase stabilizing effect of the rigid biphenyl unit is clearly visible. The transition from the liquid crystalline state to the isotropic liquid is accompanied by substantial decomposition. Therefore, no detailed conclusions about the influence of lateral substituents (*cf.* **6c, 6e** and **6f**) on the mesophase stability could be drawn.



Scheme 1 *Reagents and conditions*: i, $BF_3·OEt_2$, CH_2Cl_2, 16 h; ii, $Pd(PPh_3)_4$, $NaHCO_3$, glyme; iii, NaOMe in MeOH

Table 1 Transition temperatures of the compounds **3**, **5** and **6** as determined by polarizing microscopy†



Compound (R^2 = Ac)	R^1	Mp°/C	Compound (R^2 = H)	Transition temp./°C
3	—Br	124		
5a		160	**6a**	cr 200 S_A 224 is (decomp.)
5b		147	**6b**	cr 165 S_A 195 is (decomp.)
5c		140	**6c**	cr 177 S_A 204 is (decomp.)
5d		140	**6d**	cr 165 S_A 255 is (decomp.)
5e		120	**6e**	cr 138 S_A 248 is (decomp.)
5f		126	**6f**	cr 134 S_A 252 is (decomp.)
5g		126	**6g**	cr 140 S_A 196 is (decomp.)

The research was kindly supported by the DFG and the Fond der Chemischen Industrie.

Received, 1st December 1994; Com. 4/07342H

Footnote

† Correct ^{1}H, ^{13}C NMR spectra and MS were obtained. The β-configuration of the glucosides was concluded from their ^{1}H and ^{13}C NMR spectra, *e.g.* **5f**: ^{1}H NMR [500 MHz, $(CD_3)_2SO$] δ 4.78, d, *J* 7.2 Hz, 1H, C-1H; ^{13}C NMR [125.7 MHz, $(CD_3)_2SO$] δ 100.49, C-1.

References

1 G. A. Jeffry, *Acc. Chem. Res.*, 1986, **19**, 168.
2 A. Schleiche, R. Franke, K. P. Hofmann, H. Finkelmann and W. Welte, *Biochemistry*, 1987, 5098.
3 C. Tschierske, A. Lunow and H. Zaschke, *Liquid Crystals*, 1990, **8**, 885.
4 W. Koenigs and E. Knorr, *Chem. Ber.*, 1901, **34**, 957.
5 V. Nair and J. P. Joseph, *Heterocycles*, 1987, **25**, 337.
6 L. F. Tietze, R. Fischer and H. J. Guder, *Tetrahedron Lett.*, 1982, **23**, 4661.
7 N. Miyaura and A. Suzuki, *J. Chem. Soc., Chem. Commun.*, 1979, 866.
8 S. Gronowitz and D. Peters, *Heterocycles*, 1990, **30**, 650.