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Liquid-crystal properties of octyl 6′-*O*-alkylmelibiosides

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Abstract

6-*O*-α-D-Galactopyranosyl-D-glucopyranose (melibiose) derivatives with alkyl groups at the terminal 1-*O* and 6′-*O* positions have been synthesized. They show thermotropic and lyotropic liquid-crystal properties. The *d*-spacings of the strong inner X-ray diffraction rings correspond to ~ 0.9 times the extended length of the molecule. The molecules are therefore either extended in monomolecular layers or U-shaped in bimolecular layers.

Keywords: Liquid-crystal properties; Octyl 6′-*O*-alkylmelibiosides

1. Introduction

Amphiphilic carbohydrates form thermotropic and lyotropic liquid crystals if the molecules have an appropriate shape and there is a requisite balance between the hydrophilic and hydrophobic moieties [1]. Alkylated derivatives of melibiose synthesized for the preparation of new biocatalysts [2] provided some interesting compounds for study. Of particular interest are those in which a central carbohydrate moiety is flanked by *n*-alkyl groups at either terminus, as in compounds 2–5. The following molecules were synthesized and examined for their thermotropic and lyotropic properties.

* Corresponding author for liquid-crystal properties.
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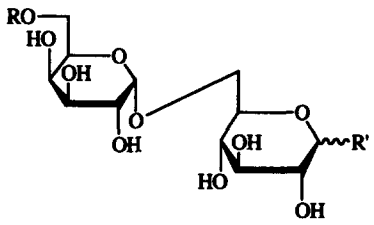


1:	**R = H**	**R' = β-OC$_8$H$_{17}$**
2:	**R = C$_5$H$_{11}$**	**R' = β-OC$_8$H$_{17}$**
3:	**R = C$_8$H$_{17}$**	**R' = β-OC$_8$H$_{17}$**
4:	**R = C$_{10}$H$_{21}$**	**R' = β-OC$_8$H$_{17}$**
5:	**R = C$_{16}$H$_{33}$**	**R' = β-OC$_8$H$_{17}$**

2. Results and discussion

The thermotropic liquid-crystal properties of the compounds **1** to **5** are summarized in Table 1. No mesogenic properties were observed for compound **1**. The DSC of compound **2** showed a single sharp peak at 142°C, however with optical microscopy a brief liquid-crystal phase was observed immediately prior to the appearance of the isotropic liquid phase at 142°C. Compounds **3–5** showed typical carbohydrate mesogenic properties, with one or more crystal-to-crystal transitions preceding that to the liquid crystal, with the isotropic transition 10 to 50°C higher [1]. As the alkyl chains became longer, the transitions became increasingly sluggish both at the clearing and melting points.

The X-ray diffraction patterns showed intense inner rings at *d*-spacings between 25 to 35 Å, with one or more weaker broad rings at 4.5 to 4.9 Å, see Table 1.

Table 1
Thermotropic properties of some alkylated melibiose compounds

Compound	cry-cry	cry-lc	lc-iso	L_{calc} [a]	d_{obs} [b]	
1	—	—	149	—	—	
2	—	141	142	26	25.7	$4.5_s4.6_m4.9_w$
3	102	120–127	138	30	30.2	$4.5_s4.7_m$
4	93 97	126	140	32	31.5	$4.9_w4.7_m4.5_s$
5	~ 45 ~ 80	117	140–150	40	34.0	4.4

[a] L_{calc}, the calculated lengths of the fully extended molecules, were extrapolated from data provided by the crystal structure analysis of melibiose hydrate ref. [3] and of *n*-octyl-α-glucopyranoside hydrate ref. [4].
[b] d_{obs} are values at the maximum intensity of the inner rings, which have a width of ~ 10 Å. For the short spacings, it is ~ 0.1 Å. The ratio of mean intensities of inner to strongest outer ring is ~ 10:1.

A diffraction pattern with an intense inner ring and weaker outer rings around 4.0 to 4.5 Å is characteristic of the smectic mesophases. In the smectic A_d phase of the alkyl glycosides the *d*-spacing of the inner ring is ~1.5 times the extended length of a molecule corresponding to interdigitated bimolecular layers [5]. In compounds **2** to **4** the spacing of the inner diffraction rings correspond to the estimated extended length of the single molecules. Compound **5**, with the longest chain, is different with the observed long spacing only 0.85 the estimated extended length, and only one diffuse short spacing. The mean increment in *d*-spacings per increase of chain length is from 1.5 Å per CH_2 for C_5–C_8 (compounds **2** to **3**) to 0.6 Å per CH_2 for C_{10}–C_{16} (compounds **4** to **5**), which suggests kinking in the longest chain. This suggests that layers are composed of extended single molecules with the disaccharide moiety as the core. Hydrogen bonding between the free hydroxyl groups of the disaccharide cores will then result in the layering that distinguishes smectic from nematic mesophases. An alternate model is an amphiphilic U-shaped molecule, with a bend at the inter-residue linkage bonds, so that a bimolecular layer can be formed. However, the increment of 1.5 Å per CH_2 group suggests an extended conformation, at least for compounds **2** and **3**.

All compounds except **1** and **2** had lyotropic properties which were investigated by microscopic observation in contact with water from 25 to 80°C. Compound **2** dissolved in water at 65°C, with no evidence of a mesophase. Compounds **3, 4**, and **5** formed lamellar mesophases on heating below 65°C. All formed myelin structures similar to those observed with other polyhydroxy amphiphilic molecules [6] The amphiphilic U-shaped model is necessary to account for the lyotropic properties of compounds **3,4**, and **5**, since a hydrophilic, i.e. carbohydrate, interface with the water molecules is necessary.

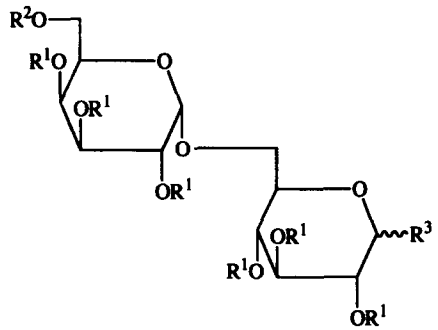
3. Experimental

Physical measurements.—For their liquid-crystal properties, the compounds were examined by calorimetry, optical microscopy, and X-ray diffraction. The differential scanning calorimetry (DSC) was done on a Mettler TA-4000 system with a heating rate of 2 K min^{-1}. The optical microscopy was with a Leitz-Wetzlar Laborlux 12 Pol polarized-light microscope with a Leitz 350 heated stage and a West 2050 temperature controller. The X-ray diffraction spectra, an example of which is shown in Fig. 1, were recorded on a Siemens X100 area detector with a Rigaku rotating anode X-ray generator (CuKα; 40 kV, 60 ma, focussed beam 0.25 mm). The exposure time was 60 s with a sample-to-detector distance of 9 cm. The specimens were heated to the liquid-crystal phase prior to recording the diffraction patterns at room temperature.

General synthetic methods.—The syntheses used the following general procedures. Melting points were determined with a Mettler FP 61 apparatus and are uncorrected. ^1H NMR spectra were recorded at 200 or 300 MHz, ^{13}C NMR spectra at 50 MHz, the chemical shifts (δ, in ppm) are relative to internal Me_4Si. TLC was performed on silica gel 60F-254 (Merck) and visualized with UV light or by charring with sulfuric acid. The eluents used in TLC for the determination of the R_f values are the same, unless

otherwise stated, as those indicated in each case for column chromatography purification.

Octyl β-melibioside **1** was prepared from melibiose by the reaction sequence **6–8** [7], **9**, **1**. Molecules **2–5** were synthesized from **1** by selective tritylation of the primary alcohol function (Ph_3CCl–pyridine [8], benzylation of the remaining hydroxyl groups (BnBr-KOH-Me_2SO) [9], detritylation (Me_3SiCl-NaI-CH_3CN) [10], alkylation (RBr-NaH-DMF) [11] and hydrogenolysis (10% Pd/C, THF-MeOH) of the benzyl protecting groups (sequence: **1**, **10–13**, **2–5**). The products **1–5** were characterized by ^1H and ^{13}C NMR spectroscopy and by elemental analysis.



	R^1	R^2	R^3
6:	H	H	OH
7:	Ac	Ac	OAc
8:	Ac	Ac	α-Br
9:	Ac	Ac	β-*O*-octyl
10:	H	trityl	β-*O*-octyl
11:	Bn	trityl	β-*O*-octyl
12:	Bn	H	β-*O*-octyl
13:	Bn	alkyl	β-*O*-octyl

Octyl 2,3,4,6-tetra-O-*acetyl-α*-D-*galactopyranosyl-(1 → 6)-2,3,4-tri*-O-*acetyl-β*-D-*glucopyranoside* (**9**).—To a solution of 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl)-(*1 → 6*)-2,3,4-tri-*O*-acetyl-α-D-glucopyranosyl bromide **8** [1] (700 mg, 1 mmol) and *n*-octanol (195 mg, 1.5 mmol) in CH_2Cl_2 (5 mL) at 20°C, under Ar was added $Hg(CN)_2$ (305 mg, 1.2 mmol). The mixture was stirred for 24 h, then the solvent was evaporated and the residue chromatographed (1:1 pentane–EtOAc) to give the alkyl glycoside **9** (560 mg, 75%), R_f 0.72; $[\alpha]^{25}_{589}$ + 66.2°, $[\alpha]^{25}_{546}$ + 78.1° (*c* 0.65, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 0.87 (t, 6.8 Hz, CH_3), 1.88–2.15 (7 s, CH_3CO), 4.48 (d, 7.8 Hz, H-1), 5.16 (d, 3.5 Hz, H-1′); ^{13}C NMR (CD_3OD): δ 14.5 (CH_3), 20.7 (CH_3CO), 21.3–32.9 (C octyl), 62.7–74.4 (C cycle), 97.5 (C-1), 101.5 (C-1), 170.8–171.8 (CO). Anal. Calcd for $C_{34}H_{52}O_{18}$: C, 54.54; H, 7.00. Found: C, 54.60; H, 7.07.

Octyl α-D-galactopyranosyl-(1 → 6)-β-D-glucopyranoside (**1**).—Compound **9** (1 g, 1.34 mmol) in MeOH (10 ml) was deacetylated by addition of NaOMe (10 mg). After 2 h at room temperature, MeOH was evaporated off and the product purified by chromatography (1:1 CH_2Cl_2–MeOH). Compound **1** was obtained (585 mg, 96%), R_f 0.75; mp 148°C; $[\alpha]_{546}^{25}$ + 46.7°, $[\alpha]_{546}^{25}$ + 55.3° (*c* 0.67, MeOH; ^{1}H NMR (CD_3OD): δ 0.9 (t, 7 Hz, CH_3), 1.3–1.7 (octyl), 4.29 (d, 8 Hz, H-1), 4.38 (large s, H-1); ^{13}C NMR (CD_3OD): δ 14.4 (CH_3), 23.7–32.9 (C octyl), 62.7–78.0 (C cycle), 100.1 (C-1), 104.6 (C-1). Anal. Calcd for $C_{20}H_{38}O_{11}$: C, 50.83; H, 8.53. Found: C, 50.77; H, 8.43.

Octyl 6-O-trityl-α-D-galactopyranosyl-(1 → 6)-β-D-glucopyranoside (**10**).—The title compound was prepared by applying the tritylation method of Adachi and Suami [8]. The product was chromatographed on silica gel (9:1 CH_2Cl_2–MeOH) to give **10** (65%). R_f 0.26; $[\alpha]_{589}^{25}$ + 20.4°, $[\alpha]_{546}^{25}$ + 24.4° (*c* 0.73, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 0.85 (t, 7 Hz, CH_3), 1.2–1.8 (octyl), 7.1–7.4 (Ar); ^{13}C NMR ($CDCl_3$): δ 14.1 (CH_3), 22.7–31.8 (C octyl), 62.7–77.1 (C cycle), 86.8 (CAr_3), 99.1 (C-1), 102.9 (C-1), 126.5–144.0 (Ar). Anal. Calcd for $C_{39}H_{52}O_{11}$: C, 67.21; H, 7.52. Found: C, 66.95; H, 7.53.

Octyl 2,3,4-tri-O-benzyl-6-O-trityl-α-D-galactopyranosyl-(1 → 6)-2,3,4-tri-O-benzyl-β-D-glucopyranoside (**11**).—To a solution of **10** (700 mg, 1 mmol) in Me_2SO was added crushed KOH (680 mg, 12 mmol). The mixture was stirred at 20°C during the dropwise addition of benzyl bromide (2.05 g, 12 mmol), then stirring was maintained for 48 h at room temperature. Diethyl ether was added and the ether solution decanted, washed with water, dried and evaporated. The benzylated compound **11** (930 mg, 75%) was obtained by chromatography on silica gel (9:1 pentane–EtOAc); R_f 0.40; ^{1}H NMR ($CDCl_3$): δ 0.88 (t, 7Hz, CH_3), 1.25–1.62 (octyl), 4.3 (d, 7.8 Hz, H-1), 5.11 (d, 3.4 Hz, H-1), 7.1–7.4 (Ar), ^{13}C NMR ($CDCl_3$): δ 14.2 (CH_3), 22.6–31.8 (C octyl), 63.1–78.3 (C cycle), 78.6–84.6 (CH_2Ar), 86.8 (CAr_3), 97.4 (C-1), 103.5 (C-1), 126.9–144.0 (Ar). Anal. Calcd for $C_{81}H_{88}O_{11}$: C, 78.61; H, 7.17. Found: C, 78.90; H, 7.28.

Octyl 2,3,4-tri-O-benzyl-α-D-galactopyranosyl-(1 → 6)-2,3,4-tri-O-benzyl-β-D-glucopyranoside (**12**).—A solution of **11** (1.25 g, 1 mmol) in dry MeCN (15 mL) was maintained under Ar at 0°C, NaI (450 mg, 3 mmol) and then chlorotrimethylsilane (0.38 ml, 3 mmol) was added. The mixture was stirred for 2 h at 0°C before addition of diethyl ether. The ether solution was washed with water, then with a $Na_2S_2O_3$ solution, dried and evaporated. Purification by chromatography (95:5 CH_2Cl_2–MeOH) gave compound **12** (970 mg, 97%). R_f 0.67 (7:3 pentane etone); mp 93°C; ^{1}H NMR ($CDCl_3$): δ 0.79 (t, 6.7 Hz, CH_3), 1.18–1.64 (octyl), 4.28 (d, 7.8 Hz, H-1), 5.03 (d, 3.4 Hz, H-1), 7.13–7.4 (Ar); ^{13}C NMR ($CDCl_3$): δ 14.3 (CH_3), 22.7–31.8 (C octyl), 62.5 –84.6 (C cycle and CH_2Ar), 97.9 (C-1), 103.6 (C-1′), 127.5–138.8 (Ar). Anal. Calcd for $C_{62}H_{74}O_{11}$: C, 74.82; H, 7.49. Found: C, 74.86; H, 7.45.

General procedures for the O-alkylation of the octyl hexa-O-benzyl-β-D-melibioside **12** *and debenzylation of products* **13**.—To a solution of **12** (298 mg, 0.3 mmol) in *N,N*-dimethylformamide (6 mL) stirred under an Ar atmosphere, NaH (60% in oil) was added (24 mg, 0.6 mmol). After 1 h at room temperature, the alkyl bromide (0.6 mmol) was slowly added and the mixture was stirred for 24 h. Then the reaction was poured onto ice and extracted with diethyl ether. The organic layer was washed with water, dried (Na_2SO_4) and evaporated to give the 6-*O*-alkylated product as a syrup which was

purified on a silica gel column eluated with pentane–EtOAc. The different alkylated compounds **13** (0.2 mmol) were dissolved in 1:4 oxolane–MeOH (20 ml), and 10% Pd–C (20 mg) was added. Hydrogenolysis was effected in a Parr apparatus under H_2 (0.3 MPa) for 16 h. The solution was then filtered, evaporated, and the residue was purified by chromatography to give compounds **2** to **5** in quantitative yields.

Octyl 6-O-pentyl-α-D-galactopyranosyl-(1 → 6)-β-D-glucopyranoside (**2**).—The alkylation of **12** with 1-bromopentane gave the octyl 6′-O-pentylmelibioside (83%); R_f 0.53 (9:1 pentane–EtOAc); ^{1}H NMR ($CDCl_3$): δ 0.78 and 0.80 (t, 6 H, CH_3), 1.11–1.52 (18 H), 3.14–4.00 (16 H), 4.27 (d, *J* 7.8 Hz, H-1), 4.48–4.90 (12 H, CH_2Ar), 5.02 (d, *J* 3.3 Hz, H-1′); 7.12–7.35 (30 H, Ar); ^{13}C NMR ($CDCl_3$): δ 14.0–31.8 (C pentyl and C octyl), 65.5 78.2 (C cycle), 82.3 84.5 (C benzyl), 97.8 (C-1β), 103.4 (C-1′), 127.2 138.8 (C arom). Then hydrogenolysis gave **2**: R_f 0.62 (7:3 EtOAc–MeOH; m,p 142°C; $[\alpha]^{25}_{578}$ + 40.8°, $[\alpha]^{25}_{546}$ + 45.5°(*c* 0.87, MeOH; ^{1}H NMR (CD_3OD): δ 0.91 and 0.92 (t, 6 H, CH_3), 1.32–1.51 (18 H), 4.2 (d, *J* 7.7 Hz, H-1), 5.03 (large s, H-1); ^{13}C NMR (CD_3OD): δ 14.4–33.0 (C octyl and C pentyl), 67.5–78.1 (C cycle), 100.0 (C-1β), 104.5 (C-1). Anal. Calcd for $C_{25}H_{48}O_{11}$: C, 57.23; H, 9.22. Found: C, 56.9; H, 9.12.

Octyl 6-O-octyl-α-D-galactopyranosyl-(1 → 6)-β-D-glucopyranoside (**3**).—The alkylation of **12** with 1-bromooctane gave the octyl 6′-*O*-octylmelibioside (95%); R_f 0.59 (9:1 pentane–EtOAc); ^{1}H NMR ($CDCl_3$): δ 0.78 (t, 6 H, CH_3), 1.17–1.73 (24 H), 3.15 –4.00 (16 H), 4.27 (d, *J* 7.8 Hz, H-1), 4.47–5.01 (12 H, CH_2Ar), 5.03 (d, *J* 3.3 Hz, H-1); 7.08–7.34 (30 H, Ar); ^{13}C NMR ($CDCl_3$): δ 14.1–31.6 (C octyl), 66.0–78.2 (C cycle), 82.3–84.5 (C benzyl), 97.8 (C_1 β), 103.3 (C-1), 127.2 –138.7 (C arom). Then hydrogenolysis gave **3**. R_f 0.53 (8:2 EtOAc–MeOH); mp 120 –138°C; $[\alpha]^{25}_{578}$ + 32.4°, $[\alpha]^{25}_{546}$ + 35.7° (*c* 0.92, MeOH); ^{1}H NMR (CD_3OD): δ 0.91 (t, 6 H, CH_3), 1.32 to 1.51 (24 H), 4.28 (d, *J* 7.7 Hz, H-1), 4.76 (large s, H-1). ^{13}C NMR (CD_3OD): δ 14.5–33.0 (C octyl), 67.5–78.1 (C cycle), 100.1 (C-1), 104.5 (C-1). Anal. Calcd for $C_{28}H_{54}O_{11}$: C, 59.34; H, 9.60. Found: C, 59.6; H, 9.53.

Octyl 6-O-decyl-α-D-galactopyranosyl-(1 → 6)-β-D-glucopyranoside (**4**).—The alkylation of **12** with 1-bromodecane gave the octyl 6′-*O*-decylmelibioside (86%); R_f 0.65 (9:1 pentane–EtOAc); ^{1}H NMR ($CDCl_3$): δ 0.78 (t, 6 H, CH_3), 1.17–1.53 (28 H), 3.21 –3.96 (16 H), 4.28 (d, *J* 7.7 Hz, H-1), 4.50–4.91 (12 H, CH_2Ar), 5.03 (d, *J* 2.8 Hz, H-1′); 7.12–7.35 (30 H, Ar). ^{13}C NMR ($CDCl_3$): δ 13.9–31.7 (C octyl and C decyl), 65.9–78.1 (C cycle), 82.2 –84.4 (C benzyl), 97.7 (C-1), 103.3 (C-1), 127.1–138.7 (C arom). Hydrogenolysis of the product gave **4**. R_f 0.53 (8:2 CH_2Cl_2–MeOH); mp 126 –140°C; $[\alpha]^{25}_{578}$ + 40.0°, $[\alpha]^{25}_{546}$ + 45.1° (*c* 0.96, MeOH); ^{1}H NMR (CD_3OD): δ 0.90 (t, 6H, CH_3), 1.30–1.59 (28 H), 4.28 (d, *J* 7.7 Hz, H-1), 4.89 (large s, H-1). ^{13}C NMR (CD_3OD): δ 14.4–33.1 (C octyl and C decyl), 67.6–78.1 (C cycle), 100.1 (C-1), 104.5 (C-1′). Anal. Calcd for $C_{30}H_{58}O_{11}$: C, 60.58; H, 9.83. Found: C, 60.12; H, 9.53.

Octyl 6-O-hexadecyl-α-D-galactopyranosyl-(1 → 6)-β-D-glucopyranoside (**5**).—The alkylation of **12** with 1-bromohexadecane gave the octyl 6′-*O*-hexadecylmelibioside (91%); R_f 0.43 (95:5 pentane–EtOAc); ^{1}H NMR ($CDCl_3$): δ 0.78 and 0.79 (t, 6 H, CH_3), 1.15–1.50 (40 H), 3.19–3.96 (16 H), 4.28 (d, *J* 7.7 Hz, H-1), 4.48–4.91 (12 H, CH_2Ar), 5.02 (d, *J* 3.4 Hz, H-1); 7.09–7.35 (30 H, Ar). ^{13}C NMR ($CDCl_3$): δ 14.0 –31.6 (C octyl and C hexadecyl), 66.0–78.1 (C cycle), 82.3–84.5 (C benzyl), 97.8 (C-1), 103.3 (C-1′), 127.4–138.7 (C arom). Hydrogenolysis gave **5**. R_f 0.43 (85:15

CH_2Cl_2 MeOH); mp 117–140°C; $[\alpha]_{578}^{25}$ + 32.9°, $[\alpha]_{546}^{25}$ + 37.0° (*c* 0.98, MeOH); ^1H NMR (CD_3OD): δ 0.90 (t, 6 H, CH_3), 1.28–1.59 (40 H), 4.27 (d, *J* 7.7 Hz, H-1), 4.88 (large s, H-1′); ^{13}C NMR (CD_3OD): δ 14.5–33.1 (C octyl and C hexadecyl), 100.1 (C-1β), 104.5 (C-1′). Anal. Calcd for $C_{36}H_{70}O_{11}$: C, 63.68; H, 10.39. Found: C, 63.78; H, 10.23.

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References

[1] G.A. Jeffrey and L.M. Wingert, *Liq. Crystals*, 12 (1992) 179–202.
[2] D. Cabaret and M. Wakselman, *Carbohydr. Res.*, 189 (1989) 341–348.
[3] M.E. Gress, G.A. Jeffrey, and D.C. Rohrer, *Acta Crystallogr., Sect. B*, 34 (1978) 508–512.
[4] G.A. Jeffrey, Y. Yeon, and J. Abola, *Carbohydr. Res.*, 169 (1987) 1–11.
[5] H.A. Van Doren and L.M. Wingert, *Molec. Crystals Liq. Crystals*, 198 (1991) 381–391.
[6] H.A. Van Doren and L.M. Wingert, *Liq. Crystals*, 9 (1991) 41–45.
[7] P.A. Levene and E. Jorpes, *J. Biol. Chem.*, 86 (1930) 403–415; A. Jeanes, C.A. Wilham, and G.E. Hilbert, *J. Am. Chem. Soc.*, 75 (1953) 3667–3673.
[8] R. Adachi and T. Suami, *Bull. Chem. Soc. Jpn.*, 50 (1977) 1901–1902.
[9] J. Defaye, H. Driguez, B. Henrissat, J. Gelas, and E. Ba-Guilloux, *Carbohydr. Res.*, 63 (1978) 41–49.
[10] A. Klemer, M. Bieber, and H. Wilbers, *Justus Liebigs Ann. Chem.*, (1983) 1416–1421.
[11] J.S. Brimacombe, *Methods Carbohydr. Chem.*, 6 (1972) 376–378.