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AN APPROACH TO THE REGIOSELECTIVE INTRODUCTION OF FUNCTIONAL GROUPS ON α-(1→4) LINKED CYCLO*MANNO*HEXAOSE: ALKYLATION AT O-2

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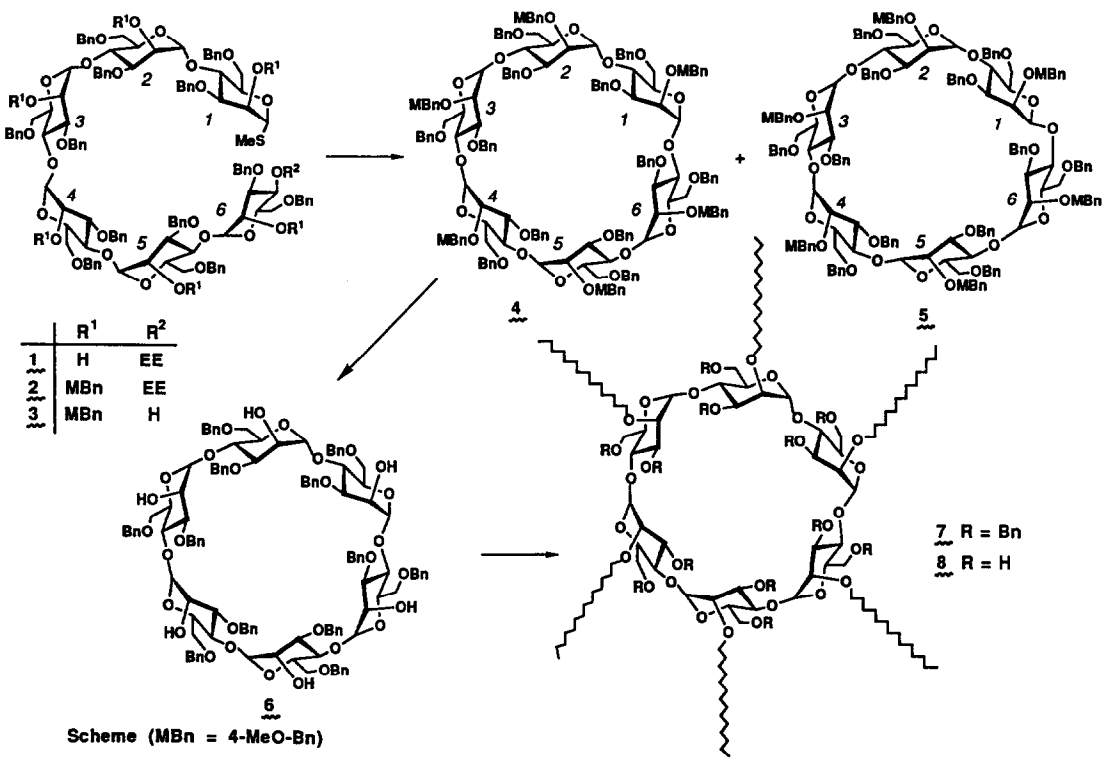
Abstract: Stereo- and regiocontrolled synthesis of a *manno* isomer of α-cyclodextrin with O-2 tetradecyl group was achieved in an unambiguous manner.

In view of the experimental difficulties[1] in the regioselective introduction of functional groups in cyclodextrin molecules, unambiguous total syntheses of regioselectively modified cyclooligoses may be envisioned as the alternative approach. As part of our project[2] on the cycloglycosylation of oligosaccharide derivatives, we now describe a facile, unambiguous, regio- and stereoselective synthesis of 2-O-tetradecyl derivative **8** of the *manno* isomer of α-cyclodextrin.



	R^1	R^2
1	H	EE
2	MBn	EE
3	MBn	H

Scheme (MBn = 4-MeO-Bn)

A versatile precursor **6** for the introduction of various substituents on C-2 hydroxy group was synthesized in a straightforward manner. As the starting material was chosen

mannohexaosyl methyl thioglycoside **1** which was obtainable from 1,2,3,4,6-penta-O-acetyl-α-D-mannopyranose in a highly stereocontrolled manner in 19 steps[3] in 5.2% overall yield. Conversion of **1** into **3**[4] was achieved in two steps via **2** (*1* 4-MeOBnCl[5], NaH, DMF, *2* Amberlyst 15 (H^+) in 1:1 CH_2Cl_2-MeOH, overall 92%). PhSeOTf[6] And powdered molecular sieves 4A promoted cycloglycosylation of **3** in $(CH_2Cl)_2$ afforded a 74% yield of the desired α-(1→4) linked product **4** along with a 3% yield of β-(1→4) linked product **5**. Highly α-D selective (α:β=25:1) cycloglycosylation of **3** into **4** was in good agreement with our previous observation[3] in the transformation of 2-O-benzyl analogue of **3**. Treatment of **4** with $(NH_4)_2Ce(NO_3)_6$[7] in 9:1 MeCN-H_2O afforded a 72% yield of the key intermediate **6** which was smoothly converted into the target **8** via **7** in two steps (*1* $C_{14}H_{29}Br$, NaH in DMF, *2* 20% $Pd(OH)_2$-C in 7:5:0.4 EtOH-EtOAc-H_2O, overall 66%).

In summary, 2-O-tetradecyl cyclomannohexaose **8** was synthesized in an unambiguous manner starting from **1** in 6 steps (overall 32%). The key intermediate **6** should be regarded as a versatile intermediate for the regioselective introduction of functional groups at O-2 of α-(1→4) linked cyclomannohexaose.

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Reference and Notes

1 J. F. Stoddart, *Ann. Reports on the Progress of Chemistry B (Royal Soc. Chem.)*, **85** 353 (1988).

2 T. Ogawa and Y. Takahashi, *Carbohydr. Res.*, **138** C5 (1985), Y. Takahashi and T. Ogawa, *ibid.*, **164** 227 (1987).

3 M. Mori, Y. Ito, and T. Ogawa, *Tetrahedron Lett.*, **30** 1273 (1989); *idem.*, *Carbohydr. Res.*, **192** 131 (1989).

4 Physical data for key compounds are described below. Values of $[\alpha]_D$ and $\delta_{H,C}$ were measured for $CHCl_3$ and $CDCl_3$ solution, respectively, at 23±3°, unless noted otherwise. All compounds descirbed with $[\alpha]_D$ value afforded correct data for combustion analysis. **2**: δ_H 3.746 (6H), 3.707, 3.698, 3.690, 3.684 (5s, 6 x OMe). **3**: $[\alpha]_D$ -6.0° (c 0.3); δ_H 5.315 (2H), 5.290, 5.280 (2H) and 5.266 (4s, 6 x H-1), 3.750, 3.709, 3.699 (6H), 3.692 and 3.687 (5s, 6 x OMe), 2.170 (s, SMe). **4**: $[\alpha]_D$ -16.2° (c 0.6); R_F 0.48 in 5:1 PhMe-EtOAc; δ_H 5.032 (d, 1.8 Hz, H-1), 3.694 (s, OMe); δ_C 100.9 ($^1J_{CH}$ 165 Hz, C-1), 55.2 (OMe). **5**: R_F 0.56 in 5:1 PhMe-EtOAc; δ_H 5.613, 5.067 (2H), 5.056 and 5.029 (5s, 5 x H-1), 3.721, 3.702, 3.697, 3.688 and 3.682 (6H, 5s, 6 x OMe). A signal for H-1*I* seems to be overlapped with other signals around δ 4.5. This compound was recovered after attempted acetylation. **6**: $[\alpha]_D$ +7.5° (c 0.1); δ_H 4.999 (d, 2.5 Hz, H-1). **7**: $[\alpha]_D$ -5.7° (c 0.7); δ_H 4.984 (d, 1.8 Hz, H-1), 0.879 (t, 7.0 Hz, CH_2CH_3). **8**: $[\alpha]_D$ +10.0° (c 0.1); δ_H (10:1 $CDCl_3$-CD_3OD) 4.962 (d, 2.7 Hz, H-1), 3.946 (dd, 3.1 and 7.3 Hz, H-3), 0.881 (t, 7.0 Hz, CH_2CH_3); FAB-MS (positive) m/z 2173 $(M+Na)^+$.

5 Y. Oikawa, T. Yoshioka, and O. Yonemitsu, *Tetrahedron Lett.*, **23** 885 (1982).

6 Y. Ito and T. Ogawa, *Tetrahedron Lett.*, **29** 1061 (1988).

7 R. Johansson and B. Samuelsson, J. Chem. Soc., Chem. Commun., 201 (1984).

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