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## Synthesis of Novel Chiral Macrocyclic Ligands bearing Methyl 4,6-*O*-Benzylidene-α-D-mannopyranoside

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*O*-Alkylation of methyl 4,6-*O*-benzylidene- $\alpha$ -D-mannopyranoside with t-butyl bromoacetate under phase-transfer conditions, followed by reduction and tosylation leads to an intermediate which was used in the formation of the two diaza-crown ethers (**3a**) and (**3b**) *via* condensation with 1,8-diamino-3,6-dioxaoctane in the presence of KF-Al<sub>2</sub>O<sub>3</sub> and *N*,*N*-bisethoxycarbonyl-1,8-diamino-3,6-dioxaoctane in Me<sub>2</sub>SO-NaH-KBr, respectively.

Chiral macrocyclic hosts have been of considerable interest for some time.<sup>1</sup> Incorporation of carbohydrate units into achiral macrocyclic rings afforded chiral hosts exhibiting complexing abilities with primary alkyl ammonium cations<sup>2</sup> and chiral recognition with racemic salts.<sup>3</sup> Replacement of two oxygen atoms by two tertiary amine functions leads to increased stabilities for the complexes with ammonium cations in comparison with all-oxygen-crown compounds<sup>4</sup> as a result of stronger hydrogen bond formation involving the nitrogen atoms in the host molecules. We now report a convenient synthesis of two chiral macrocyclic ligands containing both secondary and tertiary amine functions.

The heteromacrocyclic ligand (3a) was obtained as follows. O-Alkylation of (1a) with t-butyl bromoacetate under phasetransfer conditions<sup>5</sup> proceeded smoothly at room temperature (0.6 equiv. of  $Bun_4N^+HSO_4^-$ ,  $C_6H_6-50\%$  aqueous NaOH, 4



equiv. of BrCH<sub>2</sub>CO<sub>2</sub>Bu<sup>t</sup>, 0.5 h) to give (1b) (colourless oil) in 95% yield.<sup>†</sup> Reduction of (1b) with LiAlH<sub>4</sub> in boiling ether afforded 90% of (1c)<sup>6</sup> (viscous oil). Tosylation of (1c) (tosyl chloride, Et<sub>3</sub>N, CHCl<sub>3</sub>, 0 °C) provided (1d) in 85% yield, m.p. 127–128 °C. Condensation of the bistosylate (1d) (0.01 M) with the diamine (2a) (0.01 M) in the presence of KF on alumina<sup>7</sup> (2.5 equiv., 70 ml of tetrahydrofuran–aceto-nitrile, 1:1, reflux, 20 h) led to compound (3a) (oil) in 35% yield (after column chromatography on silica gel, 2% Et<sub>3</sub>N in MeOH): <sup>1</sup>H n.m.r. (100 MHz, CDCl<sub>3</sub>, Me<sub>4</sub>Si)  $\delta$  7.47 (m, 5H, Ph), 5.72 (s, 1H, PhCH), 4.90 (s, 1H, MeOCH), 4.40–3.50 (m, 18H, 6 × OCH<sub>2</sub> and 6H from sugar unit), 3.47 (s, 3H, OMe), 2.87 (m, 8H, 4 × NCH<sub>2</sub>), and 2.0 (br. 2 s, NH).

† Satisfactory analyses and spectral data were obtained for all new compounds.

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Condensation of the bistosylate (1d) with the bisurethane (2b) (dimethyl sulphoxide, NaH, KBr, room temperature, 48 h) gave 60% of (3b) (after column chromatography on silica gel, ethyl acetate) which was reduced with LiAlH<sub>4</sub> in boiling tetrahydrofuran for 2 h to give (3c) (colourless oil) in 90% yield: <sup>1</sup>H n.m.r. (100 MHz, CDCl<sub>3</sub>, Me<sub>4</sub>Si)  $\delta$  7.45 (m, 5H, Ph), 5.68 (s, 1H, PhCH), 4.80 (s, 1H, MeOCH), 4.40–3.50 (m, 18H, 6 × OCH<sub>2</sub> and 6H from sugar unit), 3.45 (s, 3H, OMe), 2.75 (m, 8H, 4 × NCH<sub>2</sub>), and 2.40 and 2.32 (2 × s, 2 × NMe).

Beneficial features of these syntheses are the following: (i) the preparation of (1c) avoids ozonolysis of the 2,3-diallyl derivative of (1a);<sup>6</sup> (ii) the use of KF on alumina is the first example of its application to diaza-crown formation, and in addition it avoids high-dilution conditions. Finally, this approach provides a simple and convenient synthesis of novel chiral diaza-crown ethers of potential interest in host-guest chemistry.

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