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High-pressure Approach to the Synthesis of Novel Chiral Cryptands Derived from Methyl 4,6-*O*-Benzylidene-α-D-manno-, -α-D-galacto- and -α-D-gluco-pyranoside

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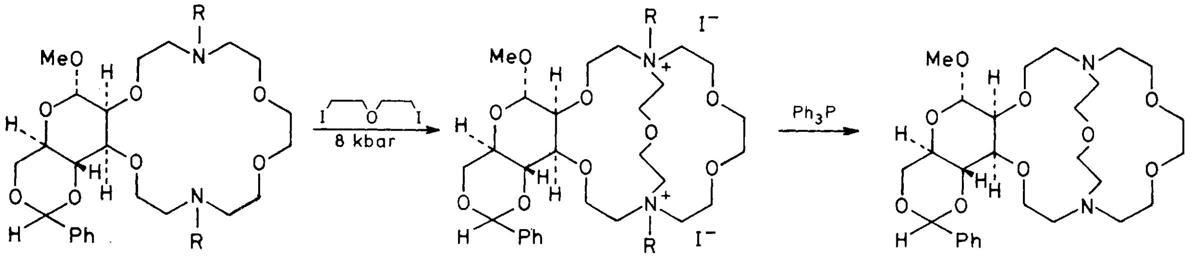
Diaza crown ethers derived from sugars react under high pressure with bis-(2-iodoethyl) ether to give the quaternary salts in quantitative yield and their subsequent demethylation with triphenylphosphine affords chiral cryptands in high yield.



(1), R = Me (2), R = Me (3)

A number of methods for the formation of cryptands has recently been reviewed.[1] In principal, high dilution techniques[2] provided the most useful method, although a quaternization–demethylation procedure[3] and a template synthesis[4] have been reported. However, the high dilution and quaternization–demethylation approaches required the reduction of bisamides and quaternary salts, respectively. In addition, the quaternization reaction proceeded under normal conditions in only *ca.* 40% yield.[3] Another limitation is the use of powerful reducing agents, so only compounds having no reducible groups could be used. We now report a greatly improved quaternization–demethylation method which, we believe, should be of general applicability.

It is well known that the volume of activation for quaternization reactions is more negative than $-40\ cm^3/mol$, and thus such reactions should be significantly accelerated by high pressure.[5] We found that quaternization of diaza crown ethers with bis-(2-iodoethyl) ether proceeded quantitatively under high pressure.

In a typical experiment† chiral diaza crown ethers derived from methyl 4,6-*O*-benzylidene-α-D-mannopyranoside (**1**)[7] reacted smoothly with one equivalent of bis-(2-iodoethyl) ether[8] (8 kbar,‡ 25 °C, acetone as solvent, 20 h, [reagents] 0.04 M) in a stereocontrolled manner to give in quantitative yield a single product (**2**) as a white solid. Demethylation followed by treatment with triphenylphosphine[9] (boiling dimethylformamide, 2 h) afforded the chiral cryptand (**3**) as an oil in 87% yield.§

The cryptand (**3**) was also obtained by an alternative method¶ from (**1**; R = H)[7] which reacted with diglycolic acid dichloride[10] under high-dilution conditions (toluene, Et_3N, 25 °C) to give the bisamide in 65% yield (after chromatography on alumina, 2% MeOH in CH_2Cl_2). The bisamide was reduced with $LiAlH_4$ (30 °C, 5 days) to afford the cryptand (**3**) in 15% yield.

Two other diaza crowns incorporating methyl 4,6-*O*-benzylidene-α-D-gluco- and -α-D-galacto-pyranoside residues [prepared analogously to (**1**)[7]] were quantitatively converted into their quaternary salts [bis-(2-iodoethyl)ether, acetone, 8 kbar, 25 °C, 20 h], and subsequent demethylation with triphenylphosphine furnished the α-D-galacto- and α-D-gluco-cryptands in 79 and 82% overall yield, respectively.

These syntheses have several important advantages: (i) quaternization proceeds quantitatively under high-pressure conditions; (ii) single products are obtained; (iii) demethylation takes place in high yield without the need for reducing agent, thus making this method particularly attractive for the syntheses of more elaborate cryptands.

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References

1 G. W. Gokel and S. H. Korzeniowski, 'Macrocyclic Polyether Syntheses,' Springer Verlag, Berlin, 1982.
2 B. Dietrich, J.-M. Lehn, and J. P. Sauvage, *Tetrahedron Lett.*, 1969, 2885.
3 G. R. Newkome, V. K. Majestic, and F. R. Fronczek, *Tetrahedron Lett.*, 1981, 3039.
4 S. Kulstad and L. A. Malmsten, *Tetrahedron Lett.*, 1980, 643.
5 T. Asano and W. J. LeNoble, *Chem. Rev.*, 1978, **78**, 407.
6 J. Jurczak, *Bull. Chem. Soc. Jpn.*, 1979, **52**, 3438.
7 M. Pietraszkiewicz and J. Jurczak, *J. Chem. Soc., Chem. Commun.*, 1983, 132.
8 S. Kulstad and L. A. Malmsten, *Acta Chem. Scand., Ser. B*, 1979, **33**, 469.
9 Tse-Lok Ho, *Synth. Commun.*, 1973, **3**, 99.
10 R. Anschütz and F. Biernaux, *Liebigs Ann. Chem.*, 1890, **273**, 64.

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† For the high-pressure experiments we used the piston–cylinder type apparatus described earlier.[6]

‡ 1 bar = 10^5 Pa.

§ Satisfactory analyses and spectral data were obtained for all new compounds: ^1H n.m.r. (200 MHz, $CDCl_3$): (**3**), δ 7.42 (m, 5H, Ph), 5.59 (s, 1H, C*H*-Ph), 4.79 (s, 1H, C*H*-OMe), 4.28—3.38 (m, 22H, sugar unit and 8 × OCH_2), 3.39 (s, 3H, OMe), and 2.82—2.66 (m, 12H, 6 × NCH_2).

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