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Modification of D-Glucose-Based 18-Crown-6 Ethers by Phosphorylation and Phosphinylation

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ABSTRACT: *The primary hydroxy groups of head-tail and head-head bis(sugar)-based crown ethers (***1** *and* **3***, respectively) were acylated by* $(EtO)_2P(O)Cl$ *and* $Ph_2P(O)Cl$ *in a selective manner. Cation binding ability of the bis-phosphorylated and phosphinylated macrocycles (***2** *and* **4***) was evaluated by the picrate extraction method. Introduction of the P-moieties led to increase of the extraction ability without significant selectivity.* © 2000 John Wiley & Sons, Inc. Heteroatom Chem 11:267–270, 2000

INTRODUCTION

It is well known that the complex forming ability of macrocycles can be modified by introduction of a side chain to the ring. A number of phosphorylated crown ethers along with derivatives with exocyclic P-function(s) on the anellated ring have been described [1–3]. Our earlier research was focused on the synthesis of different azacrown ethers, including sugar-anellated azacrowns with phosphorus containing side-chains [4–6]. These lariat-ethers were found to display a significant increase in the complex forming ability and in the selectivity toward the different cations. The sugar-based macrocycles are potential catalysts in enantioselective syntheses [6]. In this article, we disclose our results on the synthesis, spectral characterization, and cation-binding ability of *bis*(glucose)-based crown ethers containing exocyclic P-functions on the sugar moiety.

RESULTS AND DISCUSSION

Reaction of head-tail type *bis* (D-glucose)-based crown **1** [7] with diethylphosphoryl chloride and with diphenylphosphinyl chloride in pyridine at room temperature furnished products **2a** and **2b**, respectively (Scheme 1). A similar acylation of head-head type sugar-anellated crown **3** [8] with the aforementioned reagents led to products **4a** and **4b** (Scheme 2). As it could be expected, the introduction of the P-functions was completely selective; only the primary hydroxy groups were involved in the acylation. Products **2a,b** and **4a,b** did not survive column chromatography, but their solutions could be filtered fast through a thin silica layer to afford the modified

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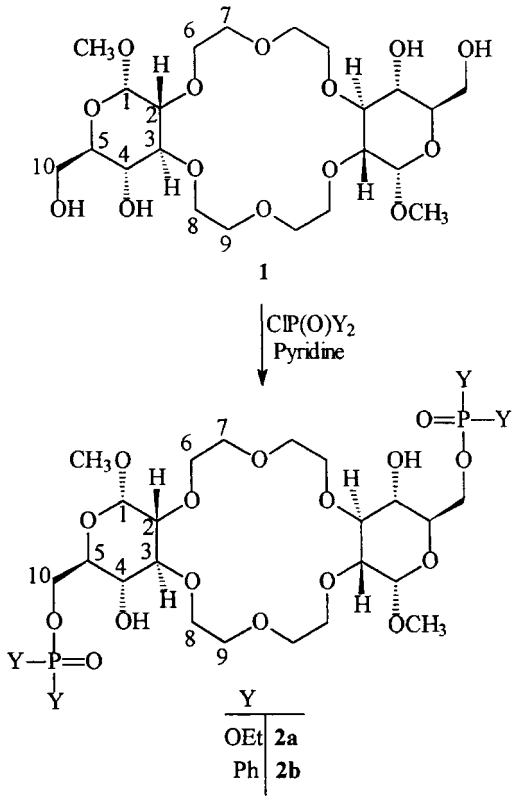
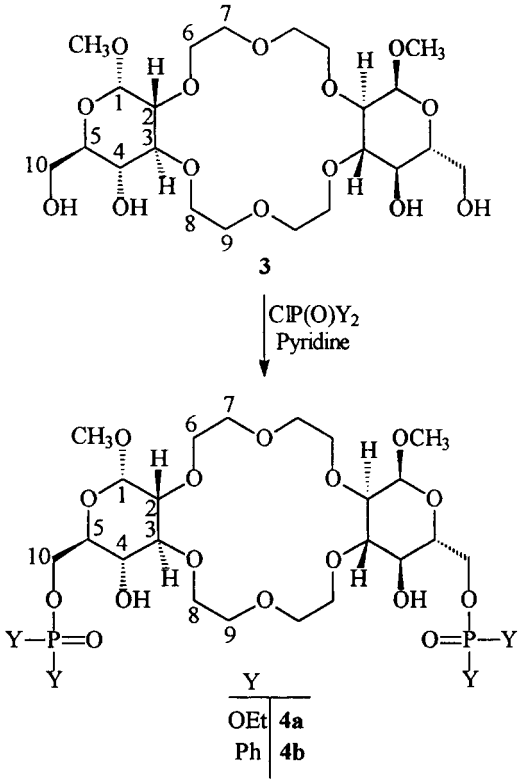


SCHEME 1



SCHEME 2

crown ethers in an 81–85% yield, in a purity of 93 to 96%. Compounds **2a,b** and **4a,b** were characterized by ^{31}P, ^{13}C, and ^{1}H NMR, as well as by fast atom bombardment (FAB) mass spectroscopy. The ^{13}C NMR spectral data are collected in Table 1. The assignments were confirmed by spectra obtained by the Attached Proton Test technique. The signals of the carbon atoms of both the glucose and the polyether rings, as well as those of the P-moieties, appeared in the expected region. The FAB measurements confirmed the molecular weights in all instances, but the [M + H] peaks were of low intensity. The P-functionalized macrocycles (**2** and **4**) were found to undergo intensive deacylation under the circumstances of FAB mass spectroscopy. Due to this instability, the elemental composition could be confirmed by HR-FAB mass spectroscopy only in one case (**2b**).

We wished to study the effect of the phosphorus-containing substituents on the complexing ability of the macrocycles. The cation binding ability of the bisphosphorylated (**2a,4a**) and phosphinylated (**2b,4b**) glucose-based crown ethers was characterized by the extracting ability (EA) of picrate salts (lithium, sodium, potassium, and ammonium picrate) from water into dichloromethane by the method of Kimura et al. [9]. Although these values may not accurately reflect the complexation ability in homogeneous solution, they still can be regarded as good indicators of the cation binding ability. A higher value indicates a better phase-transfer capability of the crown compounds. The experimental data are shown in Table 2. The error of the determination of picrates was ± 3%. As a comparison, the properties of unsubstituted crown ethers (**1, 3**) and the parent macrocycles bearing side arms with other heteroatoms (**5, 6**) were also included [10]. As can be seen, introduction of the $P(O)(OEt)_2$ (**2a, 4a**) and $P(O)Ph_2$ (**2b, 4b**) functions resulted in a significant increase in the extracting ability (65–88%) for all of the cations examined, as compared to the unsubstituted crown ethers **1** and **3** (EA = 4–14%), or to the compounds having tosyl groups (**5**, EA = 7–21%) and acetyl groups (**6**, EA = 6–15%). A probable explanation is that, on the one hand, the phosphoryl groups may increase the lipophilicity. On the other hand, the complex froming ability of compounds **2** and **4** may be increased due to secondary interactions between the P-moiety and the guest ion. No significant difference seemed to exist between the complex forming ability of the "head-foot" and "head-head" isomers (**2a, 2b,** and **4a, 4b,** respec-

TABLE 1 ^{13}C NMR Spectroscopic Data of Compounds **2a,b** and **4a,b** in $CDCl_3$ Solution

	$\delta_C(J_{PC})$														
Compound	C_1	C_2	C_3	C_4	C_5	C_6	C_7	C_8	C_9	C_{10}	$C_{1'}$	$C_{2'}$	$C_{3'}$	$C_{4'}$	*OMe*
2a	97.3	80.6	81.4	71.6	69.4	72.5	71.2	70.2	70.1	60.9	62.7 (5.8)	16.0 (7.1)	—	—	54.8
2b	97.6	80.6	81.6	72.0	69.7	72.5	71.1	70.4	70.2	61.0	135.5 (138.8)	128.2 (13.8)	131.1	131.2	54.9
4a	97.5	80.1	81.5	71.7	69.5	72.2	70.7	70.5	70.4	60.8	62.6 (5.7)	16.1 (7.1)	—	—	54.8
4b	97.7	80.3	81.6	71.8	69.7	72.4	70.9	70.7	70.5	61.1	135.4 (137.0)	128.2 (13.1)	131.1 (10.4)	131.2	54.9

tively). The phosphinic derivatives (**2a, 4a**) were found to form somewhat stronger complexes (73–88%) with the cations examined than the phosphates (**2b, 4b,** 65–82%). Although the extracting ability of the new macrocycles was significantly improved, none of the compounds showed significant selectivity toward the cations. The crown ethers with a diphenylphosphine oxide moiety (**2b, 4b**) form the strongest complexes with ammonium ion (82% and 79%, respectively). The compounds with $P(O)(OEt)_2$ substituents (**2a, 4a**) revealed the highest EA values for potassium and sodium ions; otherwise, the $K^+ \sim Na^+ > NH_4^+ > Li^+$ order was followed.

EXPERIMENTAL

The ^{31}P, ^{13}C, and ^1H NMR spectra were obtained on a Bruker DRX-500 instrument at 202.4, 125.7, and 500 MHz, respectively. The FAB measurements were performed on a ZAB-2SEQ spectrometer.

The starting macrocycles (**1** and **3**) were prepared as described earlier [7,8].

General Procedure for the Diacylation of bis(Methyl-α-D-glucopyranoside)-18-crown-6 **1** *and* **3**

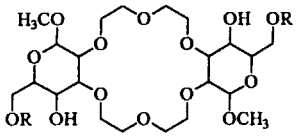
To 0.20 g (0.38 mmol) of macrocycle **1** or **3** in 15 mL of dry pyridine was added dropwise 0.11 mL (0.78 mmol) of $(EtO)_2P(O)Cl$ or 0.15 mL (0.78 mmol) of $Ph_2P(O)Cl$, and the mixture was stirred at room temperature for 24 hours. The solvent was evaporated and the so obtained residue was extracted with 40 mL of chloroform. The semicrystalline material obtained after concentration in vacuo was filtered through a 5 mm silica gel layer using 3% methanol in chloroform eluant to give the products (**2a,b** and **4a,b**) as syrups after careful evaporation.

Product **2a**: Yield, 81%; ^{31}P NMR ($CDCl_3$) δ −0.34; ^{13}C NMR, Table 1; ^1H NMR ($CDCl_3$) δ 1.34 (t, J = 7.0, 12H, OCH_2CH_3), 3.41 (s, 6H, OCH_3), 4.05–4.18 (m, OCH_2CH_3, overlapped by C(10)H, total intensity 10H), 4.83 (bs, 2H, C(1)H); FAB, 801 (M + H).

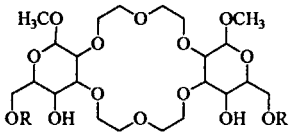
Product **2b**: Yield, 85%; ^{31}P NMR ($CDCl_3$) δ 24.3; ^{13}C NMR, Table 1; ^1H NMR ($CDCl_3$) δ 3.39 (s, 6H, OCH_3), 4.13–4.19 (m, 2H, C(10)H), 4.80 (d, J = 3.2, 2H, C(1)H), 7.33–7.78 (m, 20H, Ar); FAB, 929 (M + H); HR-FAB, M^+_{found} = 929.3095, $C_{46}H_{59}O_{16}P_2$ requires 929.3278.

Product **4a**: Yield, 84%; ^{31}P NMR ($CDCl_3$) δ −0.49; ^{13}C NMR, Table 1; ^1H NMR ($CDCl_3$) δ 1.32 (t, J = 7.0, 12H, OCH_2CH_3), 3.39 (s, 6H, OCH_3), 4.0–4.12 (m, OCH_2CH_3 overlapped by C(10)H, total intensity 10H), 4.78 (d, J = 3.2, 2H, C(1)H); FAB, 801 (M + H).

TABLE 2 Extraction of Alkali Metal and Ammonium Picrates[a]



1, 2a, 2b, 5, 6



3, 4a, 4b

		Extractability (%)[b]			
Comp.	*R*	+	Na^+	K^+	NH_4^+
1[c]	H	7	4	7	13
3[c]	H	6	5	6	14
2a	$P(O)(OEt)_2$	73	88	88	79
2b	$P(O)Ph_2$	69	70	72	82
4a	$P(O)(OEt)_2$	73	85	88	80
4b	$P(O)Ph_2$	72	65	71	79
5[c]	$SO_2PhCH_3(p)$	7	2	15	21
6[c]	$COCH_3$	6	12	15	14

[a]Temperature 20°C; aqueous phase (5 mL); [picrate] = 5×10^{-3} M; organic phase (CH_2Cl_2, 5 mL); [crown ether] = 1×10^{-2} M.
[b]Defined as percentage of picrate extracted into the organic phase, determined by UV spectroscopy [9].
[c]See Ref. [10].

Product **4b**: Yield, 82%; ^{31}P NMR ($CDCl_3$) δ 26.3; ^{13}C NMR, Table 1; ^{1}H NMR ($CDCl_3$) δ 3.41 (s, 6H, OCH_3), 4.15–4.22 (m, 2H, C(10)H), 4.80 (d, J = 3.1, 2H, C(1)H), 7.35–7.80 (m, 20H, Ar); FAB, 929 (M + H).

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