Chemistry of Heterocyclic Compounds, Vol. 41, No. 8, 2005

ACYLATION OF DIBENZO-18-CROWN-6 WITH ALKALI-METAL ACETATES IN POLYPHOSPHORIC ACID

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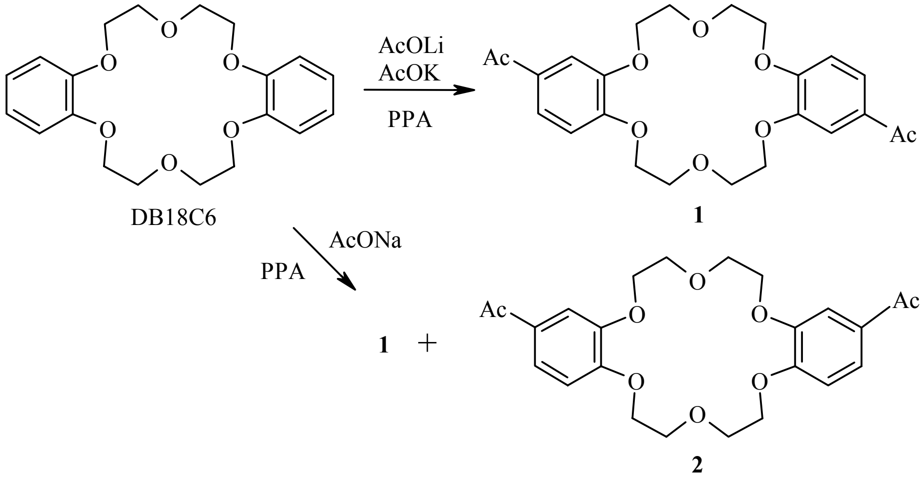
The acylation of dibenzo-18-crown-6 by lithium, sodium, and potassium acetates in polyphosphoric acid was studied. Complexes of dibenzo-18-crown-6 with the acetates were obtained. A new method is proposed for the production of mono- and diacetyldibenzo-18-crown-6 by the reaction of dibenzo-18-crown-6 complexes with metal acetates in polyphosphoric acid.

Keywords: metal acetates, dibenzo-18-crown-6, polyphosphoric acid, acylation, complex formation.

Earlier during study of the electrophilic substitution of dibenzo-18-crown-6 (DB18C6) with acetic acid and metal nitrates and sulfates in polyphosphoric acid it was found that the substituent entering one of the benzene rings affects the distribution of electron density in the second ring [1-3]. This effect was confirmed by nonidentical splitting of the signals for the carbon atoms of the ring in the ^{13}C NMR spectra [1, 4]. Such an effect results in the preferential formation of the 4',4''-disubstituted isomer, i.e., the indicated substituent probably promotes regioselectivity in the process. This was increased by the use of metal nitrates as electrophilic agents during the nitration of the dibenzo-18-crown-6, indicating active participation of the metal cations in the reaction.

In the present work we acylated dibenzo-18-crown-6 with Li, Na, and K acetates by heating in polyphosphoric acid in order to study the effect of the nature of the cation on the acylation process.



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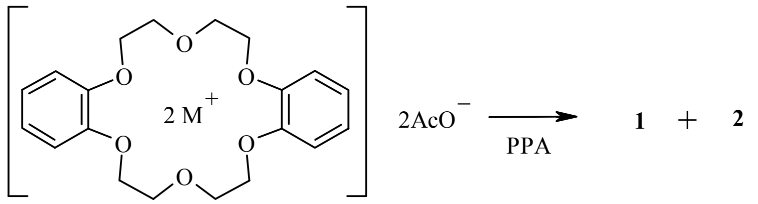
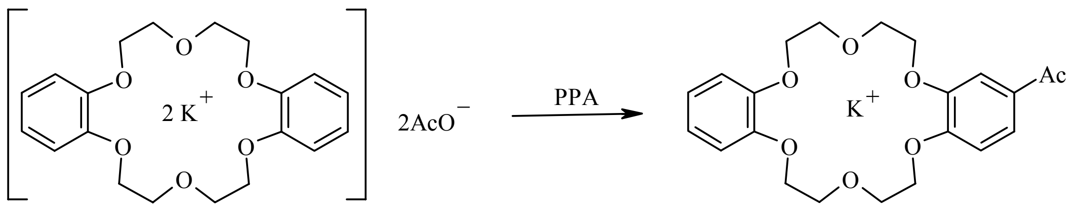
It was found that the length of the process and the composition of the reaction products, according to data from TLC, depend on the cation. Thus, diacetyl-DB18C6 is formed after 2 h during acylation with lithium acetate. This product melts at 196-200°C, indicating that it is mainly the 4',4"-isomer **1** (mp of isomer **1** 197-199°C, mp of 4',5"-isomer **2** 213-215°C [5]). It should be noted that the formation of the mono- and disubstituted products was only observed in the reaction mixture after the first 30 min. Acylation with sodium acetate under analogous conditions was complete in 7 h, and the formation of the mono- and disubstituted products was not observed in the first hour. Long heating led to the formation first of mono- and then of diacetyl-DB18C6. The reaction product melted at 192-201°C, indicating the formation of a mixture of isomers **1** and **2**. The formation of reaction products was also not observed in the first hour during the acylation with potassium acetate. After 8 h a product melting at 195-199°C was isolated, indicating the preferential formation of the 4',4"-isomer **1**.

Thus, the results show that the acylating agents have different reactivity depending on the cation employed, and lithium acetate is the most active in the reaction. Acylation with lithium and potassium acetates gives a product mostly containing the 4',4"-isomer **1**, whereas acylation with sodium acetate leads to a mixture of isomers **1** and **2** with a wider melting range. The structure of these isomers was established earlier [5]. The long duration of the process and its high selectivity in the case of potassium acetate can be explained by the formation of a more coplanar complex of the macrocycle with the potassium due to the closer conformity of the radius of the cation to the size of the macrocycle.

To confirm the effect of complexation and the nature of the cation on the selective direction of acylation the complexes of DB18C6 with sodium, lithium, and potassium acetate (K-1, K-2, and K-3) were prepared. In the case of lithium and sodium a twofold molar excess of the acylating agent was used since the formation of the complex was not observed with the reagents in an equimolar ratio. Potassium acetate forms a complex when the reagents are in an equimolar ratio. The obtained complexes were colorless amorphous substances soluble in alcohol and acetone and decomposed in water and on aluminum oxide, as shown by the identical R_f value of 0.74 corresponding to the initial DB18C6. When they are heated at 68-72°C in polyphosphoric acid, the acylation products **1** and **2** are formed.



K-1, M = Li; **K-2,** M = Na



K-3 **3**

The reaction of the complex with lithium acetate and polyphosphoric acid goes to completion in 2 h, and a mixture of isomers **1** and **2** melting at 198-203°C is formed (yield 65%). The complex with sodium acetate reacts two times more slowly, forming the products **1** and **2**, melting at 195-204°C, after 4 h (yield 62%). The disubstituted derivatives are formed in accordance with the composition of the complex, whereas the equimolar complex with potassium acetate in polyphosphoric acid forms 4'-acetyl-DB18C6 (**3**) with a yield of 33% after 4 h. The spectral data of compound **3** and *R_f* coincide with those obtained earlier during the acylation of DB18C6 with acetic acid [6]. As seen from the presented data, the activity of the complexes coincides with the activity of lithium, sodium, and potassium acetates themselves.

The heating of the crown ether complex with a metal acetate in polyphosphoric acid described above provides a new method for the introduction of an acetyl substituent into DB18C6.

EXPERIMENTAL

The reaction and the composition of the products were monitored by TLC on Silufol UV-254 plates with 2:2:1 hexane–chloroform–acetone as eluant and iodine vapor as developer. The products were purified by filtration of their solutions in chloroform through a small layer of aluminum oxide (II Brockman activity). The ^{1}H NMR spectra were obtained on a Tesla BS-567 spectrometer (100 MHz) with HMDS as internal standard (δ 0.05 ppm) and deuterochloroform as solvent.

Acylation of DB18C6 with Li, Na, and K Acetates. To a solution of DB18C6 (0.36 g, 1.0 mmol) in polyphosphoric acid (8 g) at 68-72°C we added lithium, sodium, or potassium acetate (2.5 mmol). The mixture was kept at the same temperature until the original DB18C6 had disappeared (R_f 0.74). The composition of the reaction mixture was monitored at 30 min intervals by TLC. At the end of the reaction 10 ml of water was added, and the precipitate was filtered off, washed to pH 7 with water, dried, and dissolved in chloroform. The solution was passed through a layer of aluminum oxide (product–Al_2O_3 ratio 1:10) and evaporated. The residue was boiled with acetone (5 ml) for 15 min, and the precipitate was filtered off and dried. In the reaction with AcOLi after 2 h we obtained 0.38 g (86%) of product **1**; mp 196-200°C, R_f 0.2; with AcONa after 7 h we obtained 0.34 g (78%) of a mixture of isomers **1** and **2**, mp 192-201°C, R_f 0.2; with AcOK after 8 h we obtained 0.35 g (80%) of product **1**, mp 195-199°C, R_f 0.2.

Complexes of DB18C6 with Li, Na, and K Acetates (K-1, K-2, K-3 Respectively). A mixture of DB18C6 (1 mmol) and lithium or sodium acetate (2 mmol) in 2-propanol (2 ml) was boiled for 5 h. After cooling the solvent was poured off, the remaining solvent was removed on a rotary evaporator, and the residue was dried. The respective complex **K-1** (mp 205-210°C) or **K-2** (mp 312-315°C) was obtained. The complex **K-3** (mp 240-245°C, decomp.) was obtained by the described method but with 1 mmol of potassium acetate. Elemental analysis of the compounds did not give accurate results owing to the ease of capture of solvent molecules or the formation of stable solvates.

Production of the Diacetates 1 and 2 from the Complexes K-1 and K-2. A solution of the complex **K-1** (0.38 g) or the complex **K-2** (0.4 g) in polyphosphoric acid (8 g) was kept at 68-72°C for 2 or 4 h respectively. A 10-ml portion of water was then added to the reaction mixture, and the obtained emulsion was extracted with 5-ml portions of chloroform until it had been completely extracted as monitored by TLC. The extract was evaporated, and the residue was boiled with acetone (7 ml). The residue insoluble in acetone was filtered while hot and dried. From the complex **K-1** 0.27 g (62%) of a mixture of isomers **1** and **2** was obtained; mp 198-203°C. From the complex **K-2** 0.28 g (65%) of a mixture of isomers **1** and **2** was obtained; mp 195-204°C.

Production of the Acetate 3 from the Complex K-3. An amorphous solid was obtained after 5 h from the complex **K-3** (0.36 g) and polyphosphoric acid (8 g). It was dissolved in 10 ml of chloroform and chromatographed on a column of aluminum oxide (diameter 1 cm, height 30 cm) in the 2:2:1 hexane–chloroform–acetone system. We obtained 0.1 g (33%) of 4'-acetyl-DB18C6 **3**; mp 145-147°C, R_f 0.43. ^{1}H NMR spectrum, δ, ppm: 7.48 (1H, d, H-5'); 7.43 (1H, s, H-3'); 6.76 (1H, d, H-6'); 6.81 (4H, s, H-3", 4", 5", 6"); 4.00-4.20 (8H, m, α-CH_2O); 3.80-4.00 (8H, m, β-CH_2O); 2.45 (3H, s, $COCH_3$).

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