Chemistry of Heterocyclic Compounds, Vol. 45, No. 3, 2009

SULFONATION OF 4'-ACETYL-, 4'-(*tert*-BUTYL)-DIBENZO-18-CROWN-6 AND (DIBENZO-18-CROWN-6)-4'-SULFONIC ACID WITH POTASSIUM SULFATE IN POLYPHOSPHORIC ACID

A. D. Grebenyuk[1] and A. K. Tashmukhamedova[1]*

The sulfonation of monosubstituted derivatives of dibenzo-18-crown-6 with potassium sulfate in polyphosphoric acid has been carried out. Sulfonic acids with various functional groups in the second nucleus of dibenzo-18-crown-6 have been obtained. A qualitative comparison of the reactivity of the substrates gave information on the transfer of the electronic influence of a substituent through the macrocycles. The displacement of electron density in the benzene nuclei of the substrates and the products of sulfonation was assessed from the value of the displacement of the proton signals in the ^1H NMR spectra.

Keywords: 4'-acetyl-, 4'-(*tert*-butyl)dibenzo-18-crown-6, 4'-acetyl-4"(5")-dibenzo-18-crown-6-sulfonic acid, 4'-(*tert*-butyl)-4"(5")-dibenzo-18-crown-6-sulfonic acid, (dibenzo-18-crown-6)-4',4"(5")-disulfonic acid, (dibenzo-18-crown-6)-4'-sulfonic acid, PPA (polyphosphoric acid), potassium sulfate, sulfonation.

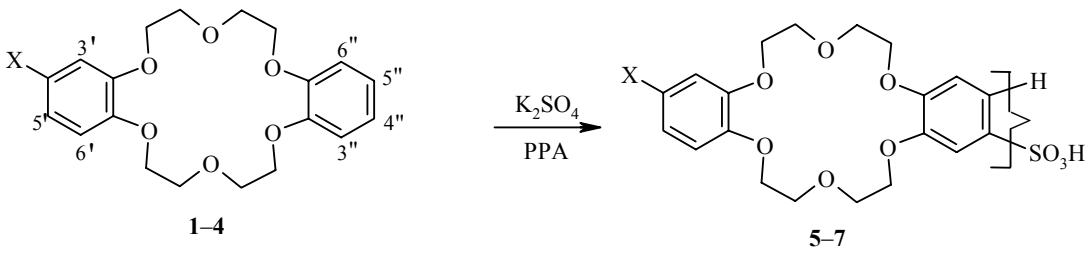
Derivatives of dibenzo-18-crown-6 (DB18C6) in which substitution is only in one benzene nucleus, are of considerable interest as substrates for carrying out electrophilic substitution reactions. These reactions open a route to disubstituted compounds with mixed functions which, as is evident from literature data [1], relate to few studied substances. At the same time the presence of two benzene nuclei with different functional groups makes these derivatives extremely promising substances for subsequent directed modification as a result of conversions of the functional groups. Study of electrophilic substitution of the hydrogen atoms of the unsubstituted benzene nucleus in monosubstituted derivatives of DB18C6 is also of considerable theoretical interest, since comparison of the reactivity of substrates with substituents of different electronic effect enables clarification of the influence of a substituent from the substituted nucleus on the unsubstituted through the macrocycle, which was called by us a "transannular transfer" [2].

An investigation was carried out previously of nitration reactions of ethyl-, nitro-, and acetyl-DB18C6 with nitrates of certain alkali metals in PPA. It was demonstrated that the nitration reaction proceeds regioselectively and depends on the nature of the substituent and the metal cation [3].

* To whom correspondence should be addressed, e-mail: tas-ainisa@yandex.ru.

[1]M. Ulugbek National University of Uzbekistan, Tashkent 700174, Uzbekistan.

Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 3, pp. 370-375, March, 2009. Original article submitted March 28, 2003; revision submitted April 23, 2008.



1–4 **5–7**

1 X = H; **2**, **5** X = MeCO; **3**, **6** X = *t*-Bu, **4**, **7** X = SO_3H

We have investigated the sulfonation of 4'-acetyl-DB18C6, 4'(*tert*-butyl)-DB18C6, and DB18C6-4'-sulfonic acid with potassium sulfate in PPA.

The sulfonation reaction was carried out by the method developed by us in [4]. Under the conditions of sulfonating DB18C6, which is accompanied by a strong evolution of heat and was complete after 2 h, reaction with 4'-acetyl-DB18C6 was weakly exothermic and was not complete after 13 h. Consequently to obtain a 71% yield of 4'-acetyl-DB18C6-4"(5")-sulfonic acid the reaction mixture at a molar substrate–reactant ratio of 1:2 and a weight ratio of substrate–PPA of 1:20 was stirred for 2 h at room temperature and 4 h at 75-80°C.

The structure of the sulfonation product as 4'-acetyl-DB18C6-4"(5")-sulfonic acid was demonstrated by the ^{1}H NMR spectrum (Table 1, compound **5**). The aromatic protons of the benzene ring with the acetyl group are displayed as three groups of signals: a doublet of doublets at 7.59 ppm, which corresponds to the proton at position 5', a singlet at 7.39 ppm, characteristic of the proton at position 3', and a doublet of doublets at 6.89 ppm, which corresponds to the protons at positions 6', 6". The aromatic protons of the benzene ring with a sulfonyl group are also displayed by three groups of signals displaced towards high field. At 7.13 ppm a singlet is displayed for the proton at position 3", at 7.04 a doublet for the proton at position 4"(5"). The protons of the macrocycle are represented by two multiplets at 4.00-4.20 (8H, m, α-OCH_2) and 3.80-3.90 ppm (8H, m, β-OCH_2). The acetyl group gives a singlet of methyl protons at 2.50 ppm.

Comparison of the obtained spectrum of 4'-acetyl-DB18C6-4"(5")-sulfonic acid with the spectra of 4'-acetyl-DB18C6 and DB18C6-4'-sulfonic acid (Table 1, compounds **5, 2, 4**) showed that the protons in position 5' are displaced towards low field. The special feature of the spectrum of 4'-acetyl-DB18C6-4"(5")-sulfonic acid is the change in the order of display of the signals of the proton series with the sulfonic acid group: the signal of the proton in position 3" (s, 7.13 ppm) is displaced to lower field in comparison with the signal of the proton in position 4"(5") (d, 7.04 ppm), while in the monosulfonic acid, as usual, the doublet of the H-5' proton is displayed at 7.18 ppm and the singlet of the H-3' proton is at 7.14 ppm. This is evidently linked with the fact that the "transannular transfer" of the effect of two groups of the same type (CH_3CO and SO_3H) in 4'-acetyl-DB18C6-4"(5")-sulfonic acid is toned down, but to a different degree depending on the mutual disposition of the groups.

In 4'-acetyl-DB18C6 the signals of the protons of the unsubstituted nucleus are displaced compared with the protons of DB18C6 by 0.03 ppm towards low field (Table 1, compounds **1, 2**). The sulfonation of 4'-acetyl-DB18C6 is reflected in the position of the proton signals of the sulfonated nucleus (for position 3" 7.13-6.81 = +0.32, for position 4"(5") 7.04-6.81 = +0.23 ppm), which are displaced towards lower field compared with the protons of the unsubstituted nucleus of 4'-acetyl-DB18C6. The introduction of a sulfonyl group is also reflected in the position of the H-5' proton 7.59-7.48 = +0.11 ppm) and the H-6' proton (6.89-6.76 = +0.13 ppm) of the acetylated nucleus, which have undergone displacement towards low field. This may only be the result of the transmission of the withdrawing influence of the sulfonyl group through the macrocycle.

Sulfonation of 4'-(*tert*-butyl)-DB18C6 was carried out on heating (65-70°C) and at room temperature for 2-2.5 h. In the first case the obtained product, according to ^{1}H NMR spectral data, was DB18C6-4',4"(5")-disulfonic acid. Yield was 80%. This indicates dealkylation. At room temperature under sulfonation conditions

of DB18C6 at a molar ratio of substrate–reactant of 1:2 and a weight ratio of substrate–PPA of 1:20 the reaction took place with self-heating and was complete after 2 h. The product was obtained in 70% yield and, according to ^{1}H NMR spectral data, corresponded to the expected 4'-(*tert*-butyl)-DB18C6-4"(5")-sulfonic acid (Table 1, compound **6**).

TABLE 1. ^{1}H NMR Spectra of Compounds **1-7**

Compound	Substance name	Chemical shifts, δ, ppm (*J*, Hz)*			
		ArH	α-OCH_2, β-OCH_2	$COCH_3$	$C(CH_3)_3$
1	DB18C6	6.78 (8H, s)	4.00-4.24 (8H, m, α-) 3.88-4.00 (8H, m, β-)		
2	4'-Acetyl-DB18C6	7.48 (1H, br. s, H-5'); 7.43 (1H, s, H-3'); 6.81 (4H, s, H-3",4",5",6"); 6.76 (1H, br. s, H-6')	4.00-4.20 (8H, m, α-) 3.80-4.00 (8H, m, β-)	2.47 (3H, s)	
3	4'-(*tert*-Butyl)-DB18C6	6.60-6.80 (3H, m, H-3',5',6'); 6.72 (4H, s, H-3",4",5",6")	3.86-4.10 (16H, m, α-, β-)		1.22 (9H, s)
4	DB18C6-4'-sulfonic acid	7.18 (1H, d, *J* = 6.0, H-5'); 7.14 (1H, s, H-3'); 6.92 (4H, s, H-3",4",5",6"); 6.85 (1H, d, *J* = 6.0, H-6')	3.96-4.39 (8H, m, α-); 3.68-3.96 (8H, m, β-)		
5	4'-Acetyl-DB18C6-4"(5")- sulfonic acid	7.59 (1H, dd, J_1 = 8.4, J_2 = 1.7, H-5'); 7.39 (1H, s, H-3'); 7.13 (1H, s, H-3"); 7.04 (1H, d, *J* = 8.6, H-4"(5")); 6.89 (2H, dd, J_1 = 8.2, J_2 = 2.0, H-6',6")	4.00-4.20 (8H, m, α-); 3.80-3.90 (8H, m, β-)	2.50 (3H, s)	
6	4'-(*tert*-Butyl)-DB18C6-4"(5")-sulfonic acid	7.10-7.20 (2H, m, H-5',5"); 6.88-6.96 (4H, m, H-3',3",6',6")	3.96-4.20 (8H, m, α-); 3.80-3.96 (8H, m, β-)		1.24 (9H, s)
7	DB18C6-4',4"(5")-disulfonic acid	7.49 (2H, d, J_1 = 8.6, H-5',5"(4')); 7.40 (2H, s, H-3',3"(6")); 7.08 (2H, dd, J_1= 8.0, J_2 = 2.0, H-6',6"(3"))	4.02-4.40 (8H, m, α-); 3.70-4.02 (8H, m, β-)		

* The ^{1}H NMR spectra were taken in $CDCl_3$ (compounds **1-3**) and DMSO-d_6 (compounds **4-7**).

Investigation of the sulfonation of DB18C6-4'-sulfonic acid with potassium sulfate in PPA showed its special features. The monosulfonic acid was obtained by us previously in [4]. At a molar ratio of substrate–reactant of 1:1.25 and a weight ratio of substrate–PPA of 1:20 the reaction proceeds with self-heating at approximately the same rate as the disulfonation [4]. After 2 h the monosulfonic acid is quantitatively converted into the disulfonic acid. The absence of a passivating influence of the sulfonyl group on the unsubstituted nucleus may be explained by the fact that in PPA, the ionizing solvent-catalyst, the monosulfonic acid dissociates while dissolving. Evidently its anion enters into the sulfonation reaction, and must display a donor

effect. The introduction into DB18C6-4'-sulfonic acid of a second sulfonyl group is regularly reflected in the spectrum of DB18C6-4',4"(5")-disulfonic acid (Table 1, compounds **4, 7**), by the displacement of the signals of the protons in positions 5,5"(4"), 3',3"(6"), and 6',6"(3") towards low field by 0.31, 0.26, and 0.23 ppm respectively.

If the ^{1}H NMR spectra of 4'-acetyl-DB18C6 and DB18C6-4'-sulfonic acid are compared with the spectrum of unsubstituted DB18C6 (Table 1, compounds **2, 4**, and **1**), it is seen that the introduction of withdrawing substituents displaces the signals of the protons in positions 5' and 3' towards low field. This is seen from the difference in the values of the signals of the protons in positions 5' and 3' in 4'-acetyl-DB18C6 and DB18C6 itself (0.70 and 0.65 ppm respectively). In DB18C6-4'-sulfonic acid the corresponding differences are 0.40 for H-5' and 0.36 ppm for H-3'.

It is interesting that not only are the protons of the substituted nucleus displaced but also the protons of the unsubstituted nucleus. The signals of the protons of the unsubstituted benzene nucleus in DB18C6 do not retain their positions on introducing CH_3CO, SO_3H, or a *tert*-butyl group into the other nucleus. The observed displacement of the signal of the 4 protons of the unsubstituted benzene nucleus (Table 1, compounds **1-4**) (CH_3CO 0.03, *tert*-C_4H_9 -0.06, SO_3H 0.14 ppm) in comparison with the signals of DB18C6 itself may be explained by transfer of the effect of the substituent through the macrocycle.

EXPERIMENTAL

The ^{1}H NMR spectra of compounds **1-4** and **6** were taken on a Tesla BS 567A instrument (100 MHz) and of compounds **5** and **7** on a Unity-400+ (400 MHz) instrument. Internal standard was HMDS. Aluminum oxide of "for chromatography" type was used for TLC. Solvent system was hexane–chloroform–acetone, 5:3:1. Analyses were carried out on a Carlo Erba EA-1108 analyzer.

Dibenzo-18-crown-6 (1) was used from the commercial manufacture of the Novosibirsk Institute of Organic Chemistry, Siberian Branch of the Academy of Sciences of the USSR. Mp 163-164°C. Starting materials were obtained by methods developed in [4-6]. The ^{1}H NMR spectra of initial and final compounds are given in Table 1.

4'-Acetyl-DB18C6 (2). $C_{22}H_{26}O_7$. Mp 165-169°C (lit. mp 164-168°C [5]).

4'-(*tert*-Butyl)-DB18C6 (3). $C_{24}H_{32}O_6$. Mp 130-134°C (lit. mp 133-134°C [6]).

4'-DB18C6-sulfonic Acid (4). $C_{20}H_{24}O_9S$. Mp 192-198°C (lit. mp 192-198°C [4]).

DB18C6-4',4"(5")-disulfonic Acid (7). $C_{20}H_{24}O_{12}S_2$, was obtained from DB18C6-4'-sulfonic acid (0.16 g, 0.36 mmol), potassium sulfate (0.08 g, 0.45 mmol), and PPA (3.20 g) by the method described previously [4]. Mp 248-252°C agrees with that obtained previously. Yield was 0.16 g (86%).

4'-Acetyl-DB18C6-4"(5")-sulfonic Acid (5). 4'-Acetyl-DB18C6 (0.06 g, 0.15 mmol) was added with stirring to PPA (1.20 g) and after several minutes K_2SO_4 (0.05 g, 0.30 mmol) was added. The mixture was stirred for 2 h at room temperature and for 4 h at 75-80°C (glycerol bath). The raspberry complex was decomposed with water (5 ml), the solution was partially neutralized with sodium carbonate to pH 6, and the solution evaporated in an evaporating dish on a water bath until the appearance of an oil, which was extracted with hot ethyl alcohol. Crystalline product precipitated from the alcoholic solution and had mp 218-223°C. Yield was 0.07 g (71%). Found, %: S 6.00. $C_{22}H_{26}O_{10}S$. Calculated, %: S 6.60.

4'-(*tert*-Butyl)-DB18C6-4"(5")-sulfonic Acid (6). 4'-(*tert*-Butyl)-DB18C6 (0.18 g, 0.43 mmol) and potassium sulfate (0.15 g, 0.86 mmol) were added with vigorous stirring to PPA (3.00 g). The mixture was stirred for 1 h. Self-heating of the mixture to 40°C was observed. The mixture was stirred for 1 h further and decomposed with ice. The copious white precipitate was filtered off by suction and washed with water. After air-drying, product (0.16 g) was obtained which contained traces of the initial 4'-(*tert*-butyl)-DB18C6. To remove this the product was boiled three times with heptane. Mp 175-185°C. Yield 0.15 g (70%). Found, %: S 5.88. $C_{24}H_{32}O_9S$. Calculated, %: S 6.40.

REFERENCES

1. J. S. Bradshaw and P. E. Stott, *Tetrahedron*, **36**, 461 (1980).
2. A. K. Tashmukhamedova, and I. A. Stempnevskaya, *J. Incl. Phen. Mol. Recogn. Chem.*, **30**, No. 2, 91 (1998).
3. S. A. Andreev, A. D. Grebenyuk, and A. K. Tashmukhamedova, *J. Incl. Phen. Macrocycl. Chem.*, **49**, No. 1-2, 145 (2004).
4. A. D. Grebenyuk, L. V. Zotova, and A. K. Tashmukhamedova, *Khim. Geterotsikl. Soedin.*, 894 (2001). [*Chem. Heterocycl. Comp.*, **37**, 822 (2001)].
5. A. K. Tashmukhamedova, I. A. Stempnevskaya, I. Yu. Morozova, and E. G. Sirotenko, *Khim. Geterotsikl. Soedin.*, 470 (1989). [*Chem. Heterocycl. Comp.*, **25**, 389 (1989)].
6. A. K. Tashmukhamedova, N. Zh. Saifullina, and I. A. Stempnevskaya, *Bioorg. Khim.*, **6**, 1099 (1980).