

SULFONATION OF BENZOCROWN ETHERS BY POTASSIUM SULFATE IN POLYPHOSPHORIC ACID

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A new method is developed for the sulfonation of benzocrown ethers with potassium sulfate in polyphosphoric acid. The reaction takes place spontaneously and gives high yields of the sulfonic acids.

Keywords: benzocrown ethers, polyphosphoric acid, potassium sulfate, sulfonation.

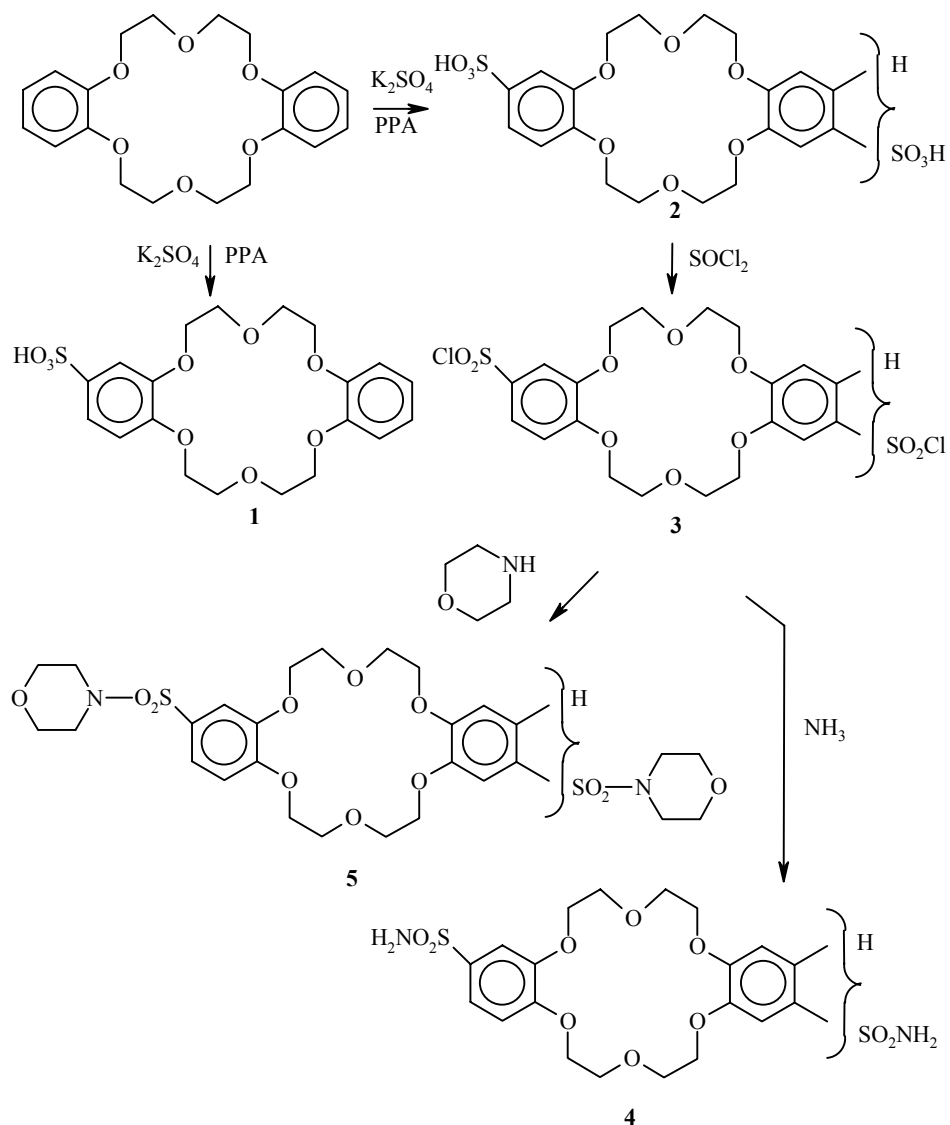
The sulfonation of benzocrown ethers has been investigated little. The sulfonation of dibenzo-18-crown-6 (DB18C6) was first carried out by Pedersen by the action of sulfuric acid in a mixture of chloroform, glacial acetic acid, and acetic anhydride [1]. Dibenzo-18-crown-6-disulfonic acid was obtained in the form of the hydrate. The sulfonation of benzo-15-crown-5 (B15C5) with concentrated sulfuric acid gave sodium benzo-15-crown-5-sulfonate [2]. The sulfochlorination of benzocrown ethers has been described [3].

While continuing an investigation into the electrophilic reactions of benzocrown ethers in polyphosphoric acid [4] and using the anions of various salts as sources of the electrophilic reagents, we realized the sulfonation of benzocrown ethers with potassium sulfate in polyphosphoric acid by the method in [5] and developed a new method for the production of the sulfonic acids of benzocrown ethers. This reaction of benzocrown ethers differs from the similar reaction of simple aromatic compounds. Under the conditions in [5] with a BCE-K₂SO₄ molar ratio of 2:1 at 130°C in reaction with dibenzo-18-crown-6 resinification occurred, while at 100-115°C 4'-dibenzo-18-crown-6-sulfonic acid (**1**) was obtained instead of the sulfone. It was shown that the reaction also takes place with an equimolar ratio of the reagents and not only with heating but also at room temperature. All the investigated benzocrown ethers react quantitatively with an excess of potassium sulfate; the reaction is accompanied by the release of heat. The sulfo group enters at position 4" of the mono-benzocrown ether and at positions 4',4" or 4',5" of the dibenzocrown ether. The structure of the obtained sulfonic acids was proved by chemical and spectral methods.

The relative reactivity of the benzocrown ethers was estimated by means of the time required for the disappearance of the initial benzocrown ether from the reaction mixture by TLC. B15C5 proved twice as active as B12C4, while DB18C6 was 1.5 times more active than DB24C8. Thus, in spite of the structural similarity of the investigated compounds, their benzene rings exhibit different reactivity, depending on the size of the macrocycle.

The products from the sulfonation of DB18C6 are the 4'-sulfonic acid **1** and the 4',4"(5")-disulfonic acid **2**. The monosulfonic acid **1**, which is poorly soluble in water, separated from the solution after dilution of the reaction mixture with water. After purification by recrystallization from ethanol it did not give a qualitative reaction for potassium and melted at 192-198°C.

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The disulfonic acid **2** was a white crystalline substance, readily soluble in water; after treatment with ethanol that had been acidified with hydrochloric acid it melted at 248-252°C. Such treatment of the sulfonation product with acidified ethanol was necessary to precipitate the sodium and potassium cations, which were entrapped by the product from the reagent and the soda used for partial neutralization of the acidic solution. The aqueous solution of the disulfonic acid **2** gave an acid reaction and actively released CO₂ from carbonates. The disulfonyl chloride **3** obtained from it was converted into the diamide **4** and the dimorpholide **5**. The product from the sulfonation of DB24C8 (**6**) was also a white crystalline substance, which after treatment with acidified alcohol melted at 197-203°C. Its aqueous solution gave an acid reaction and released CO₂ from carbonates.

The product from the sulfonation of B15C5 before and after treatment with acidified alcohol did not release CO₂ from an aqueous solution of sodium carbonate, and its aqueous solution had pH 5-6. During slow crystallization from ethanol well-formed crystals separated (mp 253-356°C), and analysis showed that the obtained substance was the monohydrate of sodium 4'-benzo-15-crown-5-sulfonate (**7**). Two molecules of this salt in the crystal are mutually coordinated in such a way that the polyether part of each molecule serves as ligand for the sodium cation of the other molecule. The sodium ions are located at the center of the macrocycle and are coordinated by all the oxygen atoms in the macrocycle of one sulfonic acid molecule and by the oxygen

TABLE 1. Characteristics of the Synthesized Compounds

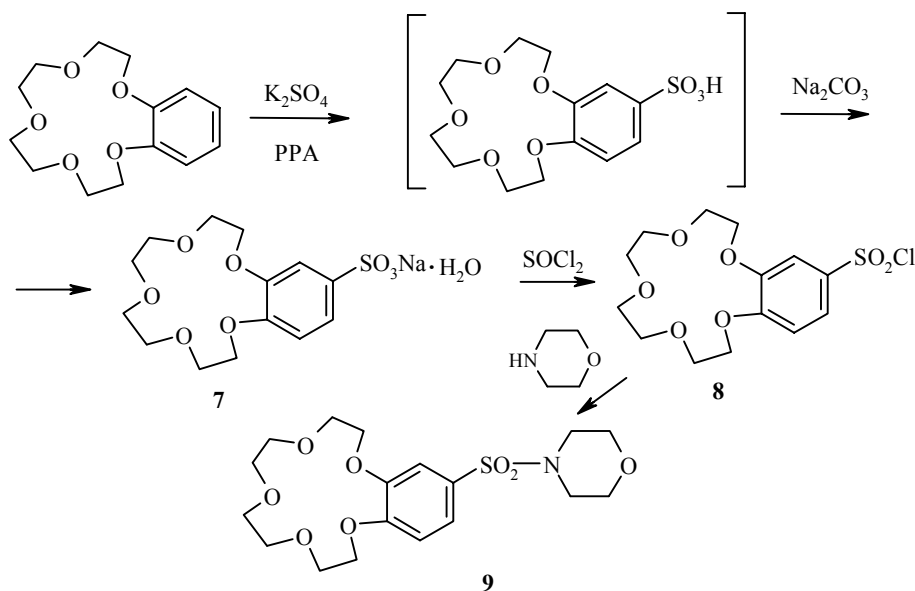
Compound	Empirical formula	$\frac{\text{Found S, \%}}{\text{Calculated S, \%}}$	mp, °C	$^1\text{H NMR spectrum, } \delta, \text{ ppm, SSCC, } J \text{ (Hz)}$	Ref.	Yield, %
1	C ₂₀ H ₂₄ O ₉ S	$\frac{6.9}{7.3}$	192-198	7.18 (1H, d, $J = 6$, ArH(5')); 7.13 (1H, d, $J = 2$, ArH(3')); 6.92 (4H, s, ArH(3'',4'', 5'',6'')); 6.87 (1H, d, $J = 6$, ArH(6')); 3.96-4.39 (8H, m, α -OCH ₂); 3.68-3.96 (8H, m, β -OCH ₂)*		87
2	C ₂₀ H ₂₄ O ₁₂ S ₂ ·2H ₂ O		248-252	7.49 (2H, d, $J = 8.6$, ArH(5',5''(4''))); 7.40 (2H, s, ArH(3',3''(6''))); 7.08 (2H, dd, $^1J = 8$, $^2J = 2$, ArH(6',6''(3''))); 4.02-4.40 (8H, m, α -OCH ₂); 3.70-4.02 (8H, m, β -OCH ₂)* ²	[1]	100
3	C ₂₀ H ₂₂ Cl ₂ O ₁₀ S ₂		155-160		[3]	37
4	C ₂₀ H ₂₆ N ₂ O ₁₀ S ₂		242-250		[3]	25
5	C ₂₈ H ₃₈ N ₂ O ₁₂ S ₂		112-114			40
6	C ₂₄ H ₃₂ O ₁₄ S ₂ ·2H ₂ O	$\frac{9.2}{9.9}$	197-203	7.50 (2H, d, $J = 7.5$, ArH(5', 5''(4''))); 7.46 (2H, s, ArH(3',3''(6''))); 7.10 (2H, d, $J = 7.5$, ArH(6',6''(3''))); 4.10-4.45 (8H, m, α -OCH ₂); 3.87-4.10 (8H, m, β -OCH ₂); 3.85 (8H, s, α -OCH ₂)* ²		80
7	C ₁₄ H ₁₉ O ₈ SNa·H ₂ O		253-256	7.54 (1H, dd, $^1J = 8$, $^2J = 2$, ArH(5')); 7.45 (1H, s, ArH(3')); 7.14 (1H, d, $J = 8$, ArH(6')); 4.10-4.38 (4H, m, α -OCH ₂); 3.86-4.00 (4H, m, β -OCH ₂); 3.76 (8H, s, γ - and δ -OCH ₂)* ²	[2, 6]	91
8	C ₁₄ H ₁₉ ClO ₇ S		72-77		[2]	25
9	C ₁₈ H ₂₇ NO ₈ S		134-136	7.27 (1H, dd, $^1J = 8$, $^2J = 2$, ArH(5')); 7.13 (1H, d, $J = 2$, ArH(3')); 6.88 (1H, d, $J = 7$, ArH(6')); 3.99-4.20 (4H, m, α -OCH ₂); 3.76-3.99 (4H, m, β -OCH ₂); 3.69 (8H, s, γ - and δ -OCH ₂); 2.80-2.98 (8H, m, CH ₂)* ³		30
10	C ₁₂ H ₁₅ O ₇ Na·H ₂ O	$\frac{8.6}{9.3}$	271-272	7.6 (1H, s, ArH(3')); 7.55 (1H, dd, $^1J = 7.5$, $^2J = 2.5$, ArH(5')); 7.28 (1H, d, $J = 7.5$, ArH(6')); 4.27-4.45 (4H, m, α -OCH ₂); 3.82-4.00 (4H, m, β -OCH ₂); 3.77 (4H, s, γ -OCH ₂)* ²		76

* The spectrum was recorded in DMSO-d₆.

*² In D₂O.

*³ In CDCl₃.

atom of the SO_3^- group in the other molecule. This product is not identical with the salt described in [2], the melting point of which is $>280^\circ\text{C}$. The sulfonyl chloride **8** obtained from the acid **7** was then converted into the morpholide **9**:



The product from the sulfonation of B12C4 before and after treatment with acidified alcohol gave a neutral reaction in aqueous solution, did not release CO_2 from carbonates, and melted at $271\text{--}272^\circ\text{C}$.

According to elemental analysis, it was the monohydrate of sodium 4'-benzo-12-crown-4-sulfonate (**10**).

EXPERIMENTAL

The ^1H NMR spectra were recorded on a Tesla BS-567 instrument with HMDS as internal standard. The analyses were conducted on a Carlo-Erba EA-1108 analyzer. Aluminum oxide of "chromatographic" grade was used for TLC.

General Procedure for the Sulfonation of Benzocrown Ethers with Potassium Sulfate in Polyphosphoric Acid. A mixture of the benzocrown ether and potassium sulfate was rubbed and added to polyphosphoric acid with vigorous stirring. The following reagent ratios BCE: K_2SO_4 (mole) and BCE:PPA (weight) were used: For the production of compound **1**, 1:1 and 1:10; for the production of compounds **2** and **6**, 1:4 and 1:20; for the production of the sulfonic acids **7** and **10**, 1:2 and 1:10.

The reaction mixture grew warm to $40\text{--}50^\circ\text{C}$, and the reaction was complete in 1.5–4 h. The reaction was monitored by TLC (2:1 hexane–acetone). The end of the reaction was determined by the disappearance of the initial benzocrown ether. The reaction mixture was diluted with water. The precipitated sulfonic acid **1**, poorly soluble in water, was filtered off, washed with water, and recrystallized from ethanol. In the case of the formation of the products **2**, **6**, **7**, **10** readily soluble in water the reaction mixture was partly neutralized with crystalline sodium carbonate to pH 2–3. An oil separated, and it was dissolved by heating in alcohol. The precipitated inorganic salts were filtered off. Well-formed crystals giving a positive reaction for sodium cation separated from the alcohol solutions on cooling. The reaction product was therefore recrystallized from alcohol acidified with hydrochloric acid. The sodium chloride poorly soluble in hot alcohol was filtered off. This treatment was repeated several times. The characteristics of the obtained compounds are given in Table 1.

4'-Dibenzo-18-crown-6-sulfonic Acid (1). Yield 87%; mp 192-198°C. ¹H NMR spectrum (DMSO-d₆), δ, *J* (Hz): 7.18 (1H, d, *J* = 6, ArH(5')); 7.13 (1H, d, *J* = 2, ArH(3')); 6.92 (4H, s, ArH(3'',4'',5'',6'')); 6.87 (1H, d, *J* = 6, ArH(6')); 3.96-4.39 (8H, m, α-OCH₂); 3.68-3.96 (8H, m, β-OCH₂).

4',4''(5'')-Dibenzo-18-crown-6-disulfonic Acid (2). Yield 100%; mp 248-252°C. ¹H NMR spectrum (D₂O), δ, ppm: 7.49 (2H, d, *J* = 8.6, ArH(5',5''(4''))); 7.40 (2H, s, ArH(3',3''(6''))); 7.08 (2H, dd, ¹*J* = 8, ²*J* = 2, ArH(6',6''(3''))); 4.02-4.40 (8H, m, α-OCH₂); 3.70-4.02 (8H, m, β-OCH₂).

4',4''(5'')-Dibenzo-24-crown-8-disulfonic Acid (6). Yield 80%; mp 197-203°C. ¹H NMR spectrum (D₂O), δ, ppm, *J* (Hz): 7.50 (2H, d, *J* = 7.5, ArH(5',5''(4''))); 7.46 (2H, s, ArH(3',3''(6''))); 7.10 (2H, d, *J* = 7.5, ArH(6',6''(3''))); 4.10-4.45 (8H, m, α-OCH₂); 3.87-4.10 (8H, m, β-OCH₂); 3.85 (8H, s, γ-OCH₂).

Sodium 4'-Benzo-15-crown-5-sulfonate (7). Yield 91%; mp 253-256°C. ¹H NMR spectrum (D₂O), δ, ppm, *J* (Hz): 7.54 (1H, dd, ¹*J* = 8, ²*J* = 2, ArH(5')); 7.45 (1H, s, ArH(3')); 7.14 (1H, d, *J* = 8, ArH(6')); 4.10-4.38 (4H, m, α-OCH₂); 3.86-4.00 (4H, m, β-OCH₂); 3.76 (8H, s, γ- and δ-OCH₂).

Sodium 4'-Benzo-12-crown-4-sulfonate (10). Yield 76%; mp 271-272°C. ¹H NMR spectrum (D₂O), δ, ppm, *J* (Hz): 7.6 (1H, s, ArH(3')); 7.55 (1H, dd, ¹*J* = 7.5, ²*J* = 2.5, ArH(5')); 7.28 (1H, d, *J* = 7.5, ArH(6')); 4.27-4.45 (4H, m, α-OCH₂); 3.82-4.00 (4H, m, β-OCH₂); 3.77 (4H, s, γ-OCH₂).

4',4''(5'')-Dibenzo-18-crown-6-disulfonyl Chloride (3). The compound was obtained by the method in [2]. Yield 37%; mp 155-160°C (Lit. mp 158-163°C [3]).

4',4''(5'')-Dibenzo-18-crown-6-disulfonamide (4). The compound was obtained by the method in [3]. Yield 25%; mp 242-250°C (Lit. mp 250°C [3]).

4',4''(5'')-Dibenzo-18-crown-6-disulfomorpholide (5). The compound was obtained by the method in [3]. Yield 40%; mp 112-114°C.

4'-Benzo-15-crown-5-sulfonyl Chloride (8). The compound was obtained similarly to compound 3. Yield 25%; mp 72-77°C (Lit. mp 78-82°C [2]).

4'-Benzo-15-crown-5-sulfomorpholide (9). The compound was obtained similarly to compound 5. Yield 30%; mp 134-136°C. ¹H NMR spectrum (CDCl₃), δ, ppm, *J* (Hz): 7.27 (1H, dd, ¹*J* = 8, ²*J* = 2, ArH(5')); 7.13 (1H, d, *J* = 2.11, ArH(3')); 6.88 (1H, d, *J* = 7, ArH(6')); 3.99-4.20 (4H, m, α-OCH₂); 3.76-3.99 (4H, m, β-OCH₂); 3.69 (8H, s, γ- and δ-OCH₂); 2.80 (8H, m, CH₂).

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