drying, were purified by reprecipitation from dioxane solutions in ether. The preparations obtained were carefully dried in vacuum over P_2O_5.

The PMR spectra were taken on a JNM-4H-100/100 MHz instrument at 22-24°C, c 10-12% by weight, internal standard HMDS, τ scale, solvent deuterochloroform.

SUMMARY

On the basis of an analysis of the PMR spectra of the lignins of *Cystoseira* of different ages, their chemical nonidentity has been confirmed and it has been established that they have different degrees of substitution of the C_3 side chain and different degrees of condensation through aromatic nuclei. The most highly condensed is the dioxane lignin of young specimens of *Cystoseira* (aged up to 1 year) and the least condensed the MWL of *Cystoseira* more than 3 years old.

LITERATURE CITED

1. I. V. Dovgan', in: Investigations in the Field of Wood Chemistry. Abstracts of Lectures [in Russian], Riga (1981), p. 36.
2. I. V. Dovran' and E. I. Medvedeva, Khim. Prir. Soedin., 85 (1983) [in this issue].
3. C. H. Ludwig, B. J. Nist, and J. L. McCarthy, J. Am. Chem. Soc., 86, 1186, 1196 (1964).
4. A. G. Zhuravlev, Yu. V. Gladkov, I. V. Sen'ko, and V. M. Reznikov, in: The Chemistry and Use of Lignin [in Russian], Riga (1974), p. 149.
5. N. A. Veksler, K. L. Seitanidi, L. S. Smirnova, Kh. A. Abduazimov, and M. R. Yagudaev, Khim. Prir. Soedin., 388 (1979).
6. C. Simionescu and A. Cernatescu, Celulozǎ şi Hîrtie, 21, No. 6, 308 (1972).
7. L. S. Smirnova, K. L. Seitanidi, Kh. A. Abduazimov, and M. G. Yagudaev, Khim. Prir. Soedin., 116 (1980).
8. E. P. Swan, Pulp Paper Mag. Can., 67, No. 10, 456 (1966).

NEW CARBOXYL-CONTAINING DERIVATIVES OF DIBENZO-18-CROWN-6

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New derivatives of dibenzo-18-crown-6 with carboxy groups in the side chain have been obtained by acylation with dibasic acids in the presence of polyphosphoric acid. Both 4',4"- and 4',5"-dicarboxydibenzo-18-crown-6's have been obtained by the oxidation of the corresponding diacetyl derivatives and have been separated into the isomers. The 4',4"- and 4',5"-diformyldibenzo-18-crown-6's have been obtained by the reaction of dibenzo-18-crown-6 with hexamethylenetetramine in polyphosphoric acid.

The present communication is a continuation of our papers [1-6] on the synthesis of functional analogs of natural ionophores belonging to the class of macrocyclic polyethers (crown compounds), which have proved to be useful tools in the study of the cationic permeability of biological and artificial membranes. Investigations on biological membranes [7, 8] showed that dibenzo-18-crown-6 derivatives are ionophores for univalent cations, especially for K^+, and only some of their acyl derivatives possessed ionophoric activity with respect to the Ca^{2+} ion. We assumed that this effect is connected with the participation in complex-formation of the oxygens of the carbonyl groups in addition to the oxygens of the macrocycle itself. A neutral Ca^{2+} ionophore described in the literature [9] contains, in addition to the ether oxygen, amide and ester groups the oxygens of which also, apparently, participate in complex formation.

The introduction of carboxy groups into acyl derivatives of the benzo-crowns makes it possible to obtain a new series of compounds from which it is easy to pass to esters and

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amides. An attempt to introduce a carboxy group into the molecule of dibenzo-18-crown-6 by acylation with succinic anhydride in the presence of aluminum chloride has been described in the literature, but the product isolated proved to have a complicated composition because of the formation of a complex of the crown ether with the aluminum chloride [10].

We have previously shown the possibility of acylating dibenzo-18-crown-6 with monocarboxylic acids in the presence of polyphosphoric acid (PPA) [1-3]. In the present communication we describe the acylation of dibenzo-18-crown-6 (I) with dibasic acids, likewise in the presence of PPA. As acylating agents we have used dibasic acids containing 2-10 carbon atoms in the molecule.

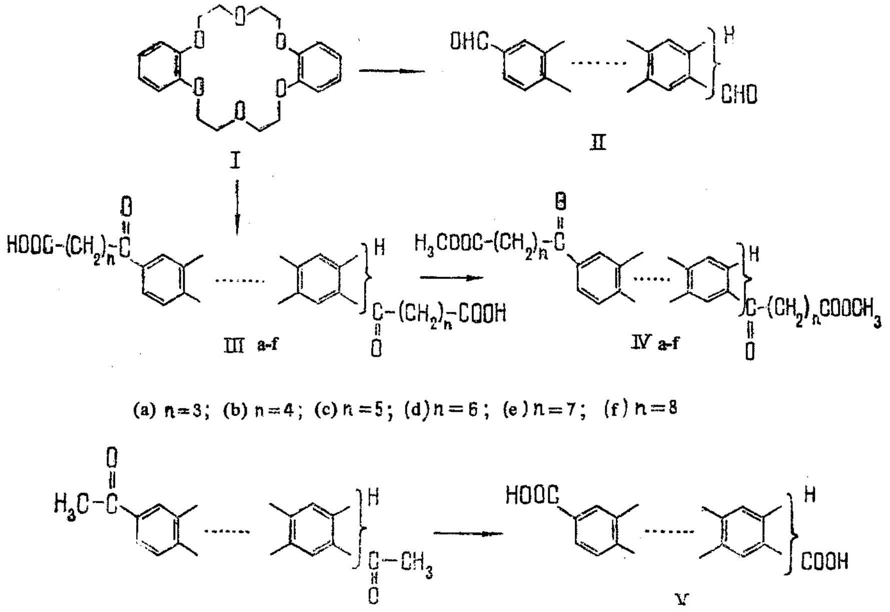
The reactions with oxalic, malonic, and succinic acids did not lead to the desired products. With oxalic acid, decarboxylation took place with the formation of diformyldibenzo-18-crown-6. This compound was not isolated but was shown to be identical (according to TLC) with the dialdehyde (II) obtained by the formylation of (I) with hexamethylenetetramine in PPA by a method used for the synthesis of aromatic aldehydes [11]. The ease of performing the reaction and isolating the product makes this method advantageous in comparison with the preparation of the diformyl derivative by the Vilsmeier reaction [12].

The reactions with malonic and succinic acids are apparently accompanied by the polycondensation of the acylated products, which leads to compounds of high molecular weight. According to mass spectra, this is a mixture of several oligomers containing only a small amount of the desired products (M^+ 532 and M^+ 560, respectively).

Beginning from glutaric acid, acylation took place smoothly and with good yields (∿ 70%) (compounds (IIIa-f)). Such results were obtained at a ratio of crown ether to acylating agent of 1 : 4 (molar) and of crown ether to PPA of 1 : 20 (by weight) at 85°C in a few minutes. When using a ratio of crown ether to PPA of 1 : 10 a longer time was necessary to perform the reaction (4-5 h).

The reaction products were identified by spectral characteristics (IR, PMR, and mass spectra) and by their conversion into methyl esters (IVa-f) [13]. It was found that the acylation products consisted of mixtures of structural isomers (4',4"- and 4',5"-) which were not separated.

The IR spectra of (III) and (IV) showed absorption bands at 1750-1710 cm^{-1} and a broadened band in the 1280-1260 cm^{-1} region caused by the O—H deformation vibrations and the stretching vibrations of C—O groups. The PMR spectra of (IV) contained, in addition to the other signals characteristic for (III), the singlet of an OCH_3 group in the 3.5-3.6 ppm region.



(a) n=3; (b) n=4; (c) n=5; (d) n=6; (e) n=7; (f) n=8

The 4',4"- and 4',5"-dicarboxydibenzo-18-crown-6's (V) were obtained by oxidizing the diacetyl derivative by analogy with [14]. As a result, a mixture of structural isomers was obtained which were separated by extraction and crystallization.

EXPERIMENTAL

The PMR spectra of compounds (IIIa-c) were obtained in CF_3COOH solution on a XL-100 spectrometer with a working frequency of 100 MHz, and the PMR spectra of (IIId-f) in $CDCl_3$ solution on a XL-200 spectrometer with a working frequency of 200 MHz; hexamethyldisiloxane was used as the internal standard, and the chemical shifts are given in the δ scale (abbreviations: s — singlet; d — doublet; t — triplet; m — multiplet). IR spectra were measured with KBr on a UR-20 spectrophotometer (GDR). Molecular weights were determined mass-spectrometrically on a MAT-311 instrument (Varian) at an energy of the ionizing electrons of 70 eV and are given for the peaks of the main isotopes (^{12}C, ^{1}H, and ^{16}O). Alumina (activity grade II) was used for thin-layer and column chromatography. Melting points were determined by the usual method in a sulfuric acid block.

4',4"- and 4',5"-Diformyldibenzo-18-crown-6's (II). To a solution of 0.72 g of (I) in 7.2 g of PPA at 150°C was rapidly added 0.56 g of hexamethylenetetramine ground to a powder. The reaction mixture was kept at this temperature for 15 min, and it was then cooled and decomposed with water. The black resinous product was extracted with chloroform, the solvent was distilled off, and the residue was chromatographed in a column using chloroform—hexane—acetone (5 : 4 : 1) as eluent. Yield 0.25 g (30%), mp 203-210°C (ac). According to the literature [12]: mp 205-207°C. Mol. wt.: found, 416, calculated for $C_{22}H_{24}O_6$, 416.4. IR spectrum (ν, cm^{-1}): 1690 (C=O), 880, 820 (1,2,4-substituted benzene). PMR spectrum (δ, ppm): 3.8-4.3 (16 H, m, 8 OCH_2), 9.72 (2 H, 2, 2 CHO).

4',4"- and 4',5"-Dicarboxybutyryldibenzo-18-crown-6's (IIIa). To a solution of 0.45 g of (I) in 10.8 g of PPA to 85°C was added 0.8 g of glutaric acid, and the mixture was heated with stirring for 5 min and was decomposed with water. The precipitate that had deposited was washed with water and then with aqueous ethanol (1 : 1). mp 141-157°C (ac.). Yield 0.63 g (71%). Molecular weight: found, 588; calculated for $C_{30}H_{36}O_{12}$, 588.6. IR spectrum (ν, cm^{-1}): 1680 (C=O), 1730-1715 (—COOH), 890, 810 (1,2-4-substituted benzene). PMR spectrum, (δ, ppm): 7.41 (2 H, d), 7.26 (2 H, s), 6.64 (2 H, d) — ArH; 3.45-4.25 (16 H, m, 8 OCH_2); 2.78 (4 H, t, 2 $COCH_2$); 2.2 (4 H, t, 2 CH_2COOH); 1.5-1.95 (4 H, m, 2 CH_2). The dimethyl ester (IVa), mp 122-138°C; mol. wt.: 616; calculated for $C_{32}H_{40}O_{12}$, 616.7. IR spectrum (ν, cm^{-1}): 1680 (C=O), 1740 (—COO$^-$), 890, 810, (1,2,4-substituted benzene). PMR spectrum (δ, ppm): 7.4 (2 H, d), 7.26 (2 H, d), 6.74 (2 H, d) — ArH; 3.54-4.22 (16 H, m, 8 OCH_2); 3.4 (6 H, 2 OCH_3); 2.78 (4 H, t, 2 $COCH_2$); 2.2 (4 H, t, 2 CH_2COOR); 1.45-2.00 (4 H, m, 2 CH_2).

Compounds (IIIb-f) were obtained similarly, and their IR and PMR spectra were similar to those of (IIIa).

4',4"- and 4'5"-Di-δ-carboxyvaleryldibenzo-18-crown-6's (IIIb). On being heated for 7 minutes, 0.54 g of (I), 10.8 g of PPA, and 0.88 g of adipic acid yielded 0.64 g (65%) of (IIIb). mp 110-121°C (abs. alc.). Dimethyl ester (IVb), mp 93-105°C. Molecular weight: found, 644; calculated for $C_{34}H_{44}O_{12}$, 644.7.

4',4" and 4',5"-Di-ω-carboxyhexanoyldibenzo-18-crown-6's (IIIc). On being heated for 10 min, 0.54 g of (I), 10.8 g of PPA, and 0.96 g of pimelic acid yielded 0.7 g (73%) of (IIIc). mp 135-150°C (ac.). Dimethyl ester (IVc), mp 103-115°C. Molecular weight: found, 672; calculated for $C_{36}H_{48}O_{12}$, 672.8.

4',4"- and 4',5"-ω-Carboxyheptanoyldibenzo-18-crown-6's (IIId). On being heated for 15 min, 0.54 g of (I), 10.8 g PPA, and 1.04 g of suberic acid yielded 0.7 g (69%) of (IIId). mp 130-146°C (ac.). Dimethyl ester (IVd), mp 109-121°C. Molecular weight: found, 700; calculated for $C_{38}H_{52}O_{12}$, 700.9.

4',4"- and 4',5"-Di-ω-carboxyoctanoyldibenzo-18-crown-6's (IIIe). On heating for 15 min, 0.54 g of (I), 10.8 g of PPA and 1.14 g of azelaic acid gave 0.72 g (68%) of (IIIe). mp 128-142°C (ac.). Dimethyl ester (IVe), mp 113-125°C. Molecular weight: found, 728; calculated for $C_{40}H_{56}O_{12}$, 728.9.

4',4"- and 4',5"-Di-ω-carboxynonanoyldibenzo-18-crown-6's (IIIf). On being heated for 20 min, 0.54 g of (I), 10.8 g of PPA, and 1.2 g of sebacic acid yielded 0.84 g (74%) of (IIIf). mp 114-125°C (ac.). Dimethyl ester (IVf), mp 100-112°C. Molecular weight: found, 756; calculated for $C_{42}H_{60}O_{12}$, 757.0.

Oxidation of 4',4"- and 4',5"-Diacetyldibenzo-18-crown-6's (V). At 0°C, 0.93 ml of bromine was added to a solution of 2.4 g of caustic soda in 12 ml of water. Then 1.3 g of diacetyldibenzo-18-crown-6 in dioxane was added. The reaction mixture was heated at 80°C with stirring for 4 h. The aqueous layer was treated with saturated sodium bisulfite solution and was then left for 12 h and was evaporated to dryness. The dry residue was acidified with concentrated hydrochloric acid and the crystals that deposited were washed with ice water. The yield of a mixture of 4',4"- and 4',5"-dicarboxydibenzo-18-crown-6's was quantitative. mp 295-308°C. The mixture was separated into isomers. The low-melting isomer isolated by extraction with benzene melted at 293-295°C. The high-melting isomer was isolated by recrystallizing the residue from acetic acid; mp 307-308°C. According to the literature [12]: mp 301-303°C. Molecular weight found, 448; calculated for $C_{22}H_{24}O_{10}$, 448.4. IR spectrum (ν, cm^{-1}): 1690 (C=O); 1710 (—COOH). PMR spectrum (δ, ppm): 7.82 (2 H, d), 7.74 (2 H, s), 7.28 (2 H, d) — ArH; 4.1-4.6 (16 H, m, 8 OCH_2).

SUMMARY

1. By the acylation of dibenzo-18-crown-6 with dibasic acids having the general formula $HOOC-(CH_2)_n-COOH$, where n = 3-8, in the presence of polyphosphoric acid, new derivatives of it with carboxy groups in the side chain have been obtained.

2. A mixture of the structural isomers 4',4"- and 4',5"-dicarboxydibenzo-18-crown-6's has been obtained by the oxidation of 4',4"- and 4',5"-diacetyldibenzo-18-crown-6's. The isomers have been separated.

3. The reaction of dibenzo-18-crown-6 with hexamethylenetetramine in polyphosphoric acid has yielded 4',4"- and 4',5"-diformyldibenzo-18-crown-6's.

LITERATURE CITED

1. A. K. Tashmukhamedova and B. A. Tashmukhamedov, Abstracts of the IInd American Symposium on Macromolecular Crown Compounds, August 14-16 (1978), Provo, Utah (1978).
2. A. K. Tashmukhamedova, R. A. Abdullaeva, I. A. Stempnevskaya, N. Zh. Saifullina, and M. T. Adylbekov, Bioorg. Khim., 4, 806 (1978).
3. A. K. Tashmukhamedova, N. Zh. Saifullina, I. A. Stempnevskaya, and R. A. Abdullaeva, Bioorg. Khim., 4, 1232 (1978).
4. A. K. Tashmukhamedova, N. Zh. Saifullina, I. A. Stempnevskaya, and B. A. Tashmukhamedov, Abstracts of Lectures at the Ist European Symposium on Organic Chemistry, August 20-23 (1979), Cologne, GFR (1979).
5. A. K. Tashmukhamedova and N. Zh. Saifullina, Bioorg. Khim., 6, 281 (1980).
6. A. K. Tashmukhamedova, N. Zh. Saifullina, and I. A. Stempnevskaya, Bioorg. Khim., 6, 1099 (1980).
7. B. A. Tashmukhamedov, S. I. Gagelgans, A. V. Shkinev, U. Z. Mirkhodjaev, M. V. Zamaraeva, and A. K. Tashmukhamedova, Frontiers of Bioorganic Chemistry and Molecular Biology. An International Symposium, Moscow—Tashkent (1978), IUPAC/Pergamon Press, Oxford (1978), pp. 439-444.
8. B. A. Tashmukhamedov, I. A. Gagel'gans, A. V. Shkinev, M. V. Zamaraeva, P. B. Usmanov, S. R. Farzalieva, and A. K. Tashmukhamedova, Bioorg. Khim., 5, 429 (1979).
9. E. Carafoli, Biochim. Biophys. Acta, 470, 437 (1977).
10. W. W. Parish, P. E. Stott, C. W. McCausland, and J. S. Bradshaw, J. Org. Chem., 43, 4577 (1978).
11. D. A. Denton and H. Suschitzky, J. Chem. Soc., 4741 (1963).
12. N. G. Luk'yanenko, A. V. Bogatskii, V. N. Pastushok, E. Yu. Kulygina, L. R. Berdnikova, and M. U. Mamina, Khim. Geterotsikl. Soedin., No. 5, 599 (1981).
13. A. N. Kost, General Practical Handbook on Organic Chemistry [in Russian], Moscow (1965), p. 533.
14. A. N. Kost, General Practical Handbook on Organic Chemistry [in Russian], Moscow (1965), p. 357.