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# Inclusion Compound of β-Cyclodextrin with Binuclear *guests* Containing Residues of Some Pharmocologically Important Aromatic Monocarboxylic Acids

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**Abstract**—Stable monomeric and dimeric inclusion compounds of β-cyclodextrin with binuclear *guests* containing the residues of some pharmacologically important aromatic monocarboxylic acids were obtained.

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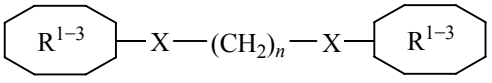
β-Cyclodextrin and some its derivatives find a wide application in pharmacology for the encapsulation of various drugs [1, 2]. Such encapsulation (formation of inclusion compounds of *guest–host* type) usually protects the drug from the biodegradation, enhances its solubility in water, and in some cases promotes effective and selective delivery of a drug to the right place. Meanwhile, the inclusion compounds themselves often are labile substances, and there is no common recommendations for their synthesis. Previously, we suggested the pathways for the synthesis of the cyclodextrin inclusion compounds with some pharmacologically important aromatic monocarboxylic acids, wihich are enough stable under normal conditions. In particular, was studied the influence of cavity size, nature of solvent and conditions of isolation on the formation and stoichiometry of the inclusion complexes [3]. In this regard, we note that the vast majority of the published works on cyclodextrin complexes were aimed mainly at the studying the structure by different physico-chemical methods of *labile* inclusion complexes in a solution, in equilibrium with the parent compound. In some studies were obtained crystalline inclusion complexes of cyclodextrins with the aim of studying the structure and composition of their crystals by X-ray diffraction (XRD). However, as a rule, such complexes in a crystal are, by the XRD data, rather complex molecular structures including in their compositions various amounts of solvents, therefore at the isolation and storage they are labile, and may have only limited practical application.

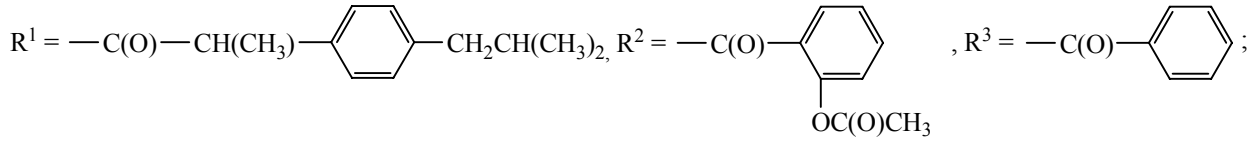
An important aspect of the problem of the cyclodextrins application as exipients lies in the fact that the features of the pharmacological action of inclusion complexes of cyclodextrins with medicinal substances of different nature require permanent search for new and more effective pharmacological forms based on cyclodextrins [2]. To date, the major pathway of insertion a necessary substance in the body is the intravenous administration of a drug (in emergency practice, at acute inflammatory processes, etc.). It is known that complex compounds with cyclodextrins reduce the half-life of the drug, causing a negative impact on renal and hepatic distribution, but without changing the overall pharmacokinetic parameters of the action of a material [4]. In addition, at intravenous

administration, a complex with cyclodextrins rapidly excreted from the body without showing its pharmacological effect, and have a toxic effect on the renal group (especially in chronic patients at a long-term administration). These side effects may be eliminated by incorporating nanosized cyclodextrin complexes into liposomes [5, 6]. This will significantly increase the capture of the complex by the organism that optimizes the overall pharmacological effect. After the integration of liposomes and their further migration into the tissues of the organism, the preparations (substances, compounds) are metabolized at a rate that depends on the stability of the complexes [6, 7]. Interesting the fact that, in turn, stability of the liposomes containing a complex compound with cyclodextrin significantly increases [8].

Another aspect of the problem lies in the fact that β-cyclodextrins are the useful carriers for water-soluble drugs, which being administered orally are metabolized in the body in the gastrointestinal tract. At such application the maximum peak of the content of such substance in the blood plasma is inhibited, while the level of its content remains stable over a long period, and the net effect is positive [9]. Thus, at present it is known that the cyclodextrin nanospheres show a significant bioadhesive effect on the mucosal of the gastrointestinal tract. As a consequence, a sufficiently large amount of injected substance can be absorbed already in the upper gastrointestinal tract, thereby increasing the rate of occurrence of the expected pharmacological effect [9]. Using the nano-scale cyclodextrin complexes will increase the bioavailability of lipophilic drugs at the oral and intravenous administration, improve the drug solubility and adsorption. Even at high doses, the effects of such compounds of cyclodextrin on the kidneys is reversible and is similar to that of the conventionally used drugs. The increase in the effectiveness of the drug associated with increased solubility will lead to a decrease in therapeutic doses, which may decrease the overall toxicity of the remedy [10].

With this in mind, we considered a possibility of obtaining stable, that is, appropriate for isolation and stable during prolonged storage, inclusion compounds of β-cyclodextrin with *guests* containing two nuclei, that is, two residues of the covalently bound pharmacologically important acids: 1-(4-isobutylphenyl)propionic acid (**I**) (medicine preparation "Ibuprofen"), acetylsalicylic acid (**II**) (medicinal drug "Aspirin") and benzoic acid (**III**), for further pharmacological tests. Were varied length (*n*) of the connecting chain, and its nature: the acids **I–III** diamides (**IV–VI, VIII–X, XII–XIV**) and diesters (**VII, XI, XV–XVII**). We assumed that the implementation of the nano-sized inclusion compounds of β-cyclodextrin with the bunuclear *guests* can substantially improve the pharmacodynamics of the complexes in biological tests. Compounds **IV–XVII** were obtained by us along the general procedure by the reaction of two molar equivalents of an acid **I–III** chloride with the corresponding dialkylamine ($R^{1–3}$ = H, X = NH) or diol ($R^{1–3}$ = H, X = O) in pyridine (see Experimental).

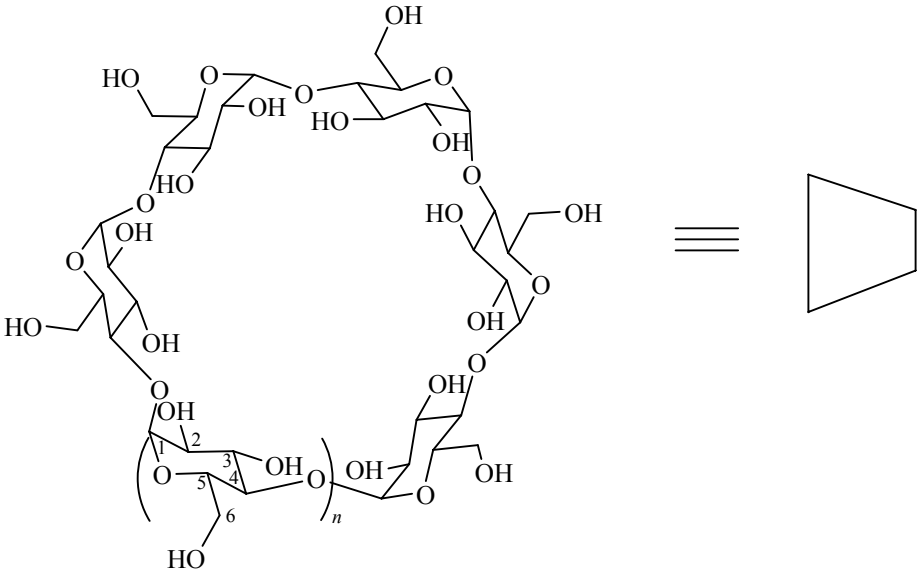


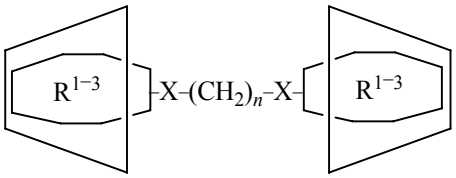

**I**, $R^1$–OH; **II**, $R^2$–OH; **III**, $R^3$–OH; **IV**, *n* = 3, X = NH, $R^1$; **V**, *n* = 4, X = NH, $R^1$; **VI**, *n* = 5, X = NH, $R^1$; **VII**, *n* = 2, X = O, $R^1$; **VIII**, *n* = 3, X = NH, $R^2$; **IX**, *n* = 4, X = NH, $R^2$; **X**, *n* = 5, X = NH, $R^1$; **XI**, *n* = 2, X = O, $R^2$; **XII**, *n* = 3, X = NH, $R^3$; **XIII**, *n* = 4, X = NH, $R^3$; **XIV**, *n* = 5, X = NH, $R^3$; **XV**, *n* = 2, X = O, $R^3$; **XVI**, *n* = 3, X = O, $R^3$; **XVII**, $C_6H_5C(O)OCH_2C·(CH_3)_2CH_2O(O)CC_6H_5$.

We investigated the formation of inclusion compounds with all binuclear *guests* **IV–XVII** by co-precipitation of each expected complex from a hot (70°C) aqueous solution containing two molar equivalent of cyclodextrin, at slow cooling to 20°C. Since all the *guests*, in contrast to cyclodextrin, are soluble in acetone, the precipitate was washed with acetone and dried in a vacuum. Individuality of the complexes to be

formed was checked by TLC, and their stoichiometric com-position was determined using $^1$H NMR spectroscopy, by comparing integratl intensities of the proton signals of cyclodextrin in the range of 3.22–5.79 ppm and the signals of the protons of the included *guest* (see Experimental).

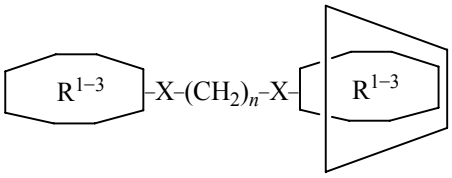


β-Cyclodextrin ($n$ = 2)



**A**

**XVIII–XXII**



**B**

**XXIII–XXV**

It turned out that under these conditions of the synthesis and isolation, β-cyclodextrin forms stable dimeric complexes of type A with *guests* **IV, V, X, XIII,** and **XV** (inclusion compounds **XVIII–XXII**), whereas with the *guests* **VII, IX, XVI,** and **XVII** it forms stable monomeric complexes of type **B** (inclusion compounds **XXIII–XXVI**), and with *guests* **VI, VIII, XI, XII,** and **XIV** the stable inclusion compounds were not formed. It is important that the complexes **XVIII–XXVI** were isolated in good yields (47–61%), and at rather rigid conditions of drying in a vacuum (1 mm Hg, 50°C, 4 h) that indicate in favor of high stability of the isolated complexes. Surprisingly that structurally very similar compounds such as **IV, V, VII** and **VI; IX, X** and **VIII, IX; XIII, XV–XVII** and **XII, XIV**, differ by their ability to form stable complexes or to form the complexes of different stoichiometric compositions. While the compounds **IV, V, X, XIII,** and **XV** form dimeric complexes of the type **A**, the compounds **VII, IX, XVI,** and **XVII** form monomeric complexes of type **B**. Obviously, this reflects a complexity and difficulty to forecast the com-petitive non-covalent interaction in the *host–guest*–solvent equilibrium system, as noted in the literature (see, e.g., [11]).

## EXPERIMENTAL

$^1$H NMR spectra were recorded on a JNM-ECX400 at 400 MHz with external TMS. For TLC were used aluminum plates with fixed layer of silica gel (Silufol UV-254), eluent chloroform–methanol 7:1 (A), benzene–chloroform 1:1 (B), benzene–acetonitrile 2:1 (C), 6% ammonia–ethanol–butanol 5:5:4 (D), aceto-nitrile–water–25% ammonia, 6:3:2 (E), acetonitrile–water–25% ammonia 7:3:2 (F), acetonitrile–water–25% ammonia, 6:6:2 (G), 6% ammonia–ethanol–butanol 5:5:2 (H), 6% ammonia–ethanol–butanol 5:5: 5 (I). We

used β-cyclodextrin from Sigma, subjected to removing water.

***N,N'*-Bis[1-(4-isobutylphenyl)propionyl]-1,3-propylenediamine (IV)**. To a solution of 1.50 g of acid chloride **I** dissolved in 10 ml of pyridine was added dropwise with stirring 0.25 g of 1,3-diaminopropane in 5 ml of pyridine. After 12 h the resulting precipitate of pyridine hydrochloride was filtered off and the filtrate was evaporated to dryness in a vacuum. The residue was dissolved in 5 ml of acetone, poured with stirring into 50 ml of water, the precipitate formed was filtered off, dried in a vacuum, recrystalized from 10 ml of diethyl ether. Yield 1.27 g (84%), mp 110–111°C, $R_f$ 0.75 (A). $^1$H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 0.87 d [12H, CH(C$\underline{H}_3$)$_2$, $^3J_{HH}$ 8.0], 1.39–1.43 m (2H, NCH$_2$C$\underline{H}_2$), 1.48 d (6H, CHC$\underline{H}_3$, $^3J_{HH}$ 8.0), 1.78–1.91 m [2H, C$\underline{H}$(CH$_3$)$_2$], 2.43 d (4H, C$\underline{H}_2$C$_6$H$_4$, $^3J_{HH}$ 7.3), 2.95–3.19 m (4H, NCH$_2$), 3.51 q (2H, C$\underline{H}$C$_6$H$_4$, $^3J_{HH}$ 7.3), 5.97–6.08 br.s (2H, NH), 7.09 d (4H, C$_6\underline{H}_{ortho}$CH$_2$, $^3J_{HH}$ 7.8), 7.17 q (4H, C$_6\underline{H}_{meta}$CH$_2$, $^3J_{HH}$ 7.8). Found, %: C 77.65, H 9.13. $C_{29}H_{42}N_2O_2$. Calculated, %: C 77.29, H 9.39.

***N,N'*-Bis[1-(4-isobutylphenyl)propionyl]-1,4-butylenediamine (V)**. The synthesis was performed analogously from 3.00 g of acid chloride **I** in 10 ml of pyridine and 0.60 g 1,4-diaminobutane in 5 ml of pyridine. Yield 2.64 g (84%), mp 165–167°C, $R_f$ 0.43 (B). $^1$H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 0.88 d [12H, CH(C$\underline{H}_3$)$_2$, $^3J_{HH}$ 6.4], 1.28–1.37 m (4H, NCH$_2$C$\underline{H}_2$), 1.48 d (6H, CHC$\underline{H}_3$, $^3J_{HH}$ 9.3), 1.77–1.89 m [2H, C$\underline{H}$(CH$_3$)$_2$], 2.44 d (4H, C$\underline{H}_2$C$_6$H$_4$, $^3J_{HH}$ 7.3), 3.07–3.17 m (4H, NCH$_2$), 3.49 q (2H, C$\underline{H}$C$_6$H$_4$, $^3J_{HH}$ 7.3), 5.43–5.52 br.s (2H, NH), 7.09 d (4H, C$_6\underline{H}_{ortho}$CH$_2$, $^3J_{HH}$ 7.8), 7.16 d (4H, C$_6\underline{H}_{meta}$CH$_2$, $^3J_{HH}$ 7.8). Found, %: C 77.02, H 9.70. $C_{30}H_{44}N_2O_2$. Calculated, %: C 77.54, H 9.54.

***N,N'*-Bis[1-(4-isobutylphenyl)propionyl]-1,5-pentylenediamine (VI)**. The synthesis was performed analogously to the preparation of compound **IV** from 1.50 g of acid chloride **I** in 10 ml of pyridine and 0.34 g of 1,5-diaminopentane in 5 ml of pyridine. Yield 1.36 g (85%), mp 92–93°C, $R_f$ 0.71 (C). $^1$H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 0.88 d [12H, CH(C$\underline{H}_3$)$_2$, $^3J_{HH}$ 6.4], 1.08–1.17 m (2H, NCH$_2$CH$_2$C$\underline{H}_2$), 1.31–1.40 m (4H, NCH$_2$C$\underline{H}_2$), 1.49 d (6H, CHC$\underline{H}_3$, $^3J_{HH}$ 7.4), 1.77–1.89 m [2H, C$\underline{H}$(CH$_3$)$_2$], 2.44 d (4H, C$\underline{H}_2$C$_6$H$_4$, $^3J_{HH}$ 7.0), 3.05–3.17 m (4H, NCH$_2$), 3.50 q (2H, C$\underline{H}$C$_6$H$_4$, $^3J_{HH}$ 7.3), 5.35–5.44 br.s (2H, NH), 7.09 d (4H, C$_6\underline{H}_{ortho}$CH$_2$, $^3J_{HH}$ 7.8), 7.17 d (4H, C$_6\underline{H}_{meta}$CH$_2$, $^3J_{HH}$ 7.8). Found, %: C 77.31, H 9.83. $C_{31}H_{46}N_2O_2$. Calculated, %: C 77.78, H 9.69.

***O,O'*-Bis[1-(4-isobutylphenyl)propionyl]-1,2-ethylendiol (VII)**. The synthesis was performed analogously to the preparation of compound **IV** from 2.94 g of acid chloride **I** in 10 ml of pyridine and 0.41 g of ethylene glycol in 5 ml of pyridine. Yield 2.30 g (80%), oily liquid, $R_f$ 0.70 (A). $^1$H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 0.91 d [12H, CH(C$\underline{H}_3$)$_2$, $^3J_{HH}$ 6.4], 1.47 d (6H, CHC$\underline{H}_3$, $^3J_{HH}$ 7.4), 1.81–1.93 m [2H, C$\underline{H}$(CH$_3$)$_2$], 2.46 d (4H, C$\underline{H}_2$C$_6$H$_4$, $^3J_{HH}$ 7.8), 3.67 q (2H, C$\underline{H}$C$_6$H$_4$, $^3J_{HH}$ 7.3), 4.18–4.32 m (4H, CH$_2$O), 7.10 d (4H, C$_6\underline{H}_{ortho}$CH$_2$, $^3J_{HH}$ 7.8), 7.20 d (4H, C$_6\underline{H}_{meta}$CH$_2$, $^3J_{HH}$ 7.8). Found, %: 76.83, H 8.64. $C_{28}N_{38}O_4$. Calculated, %: C 76.68, H 8.73.

***N,N'*-Bis(acetylsalicyl)-1,3-propylenediamine (VIII)**. The synthesis was performed analogously to the preparation of compound **IV** from 91 g of acid chloride **II** in 10 ml of pyridine and 0.36 g of 1,3-diaminopropane in 5 ml of pyridine. Yield 1.52 g (79%), mp 123–125°C, $R_f$ 0.65 (A). $^1$H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.75–1.82 m (2H, NCH$_2$CH$_2$), 2.33 s [6H, C(O)CH$_3$], 3.47–3.53 m (4H, NCH$_2$), 6.89–6.97 m (2H , NH), 7.09 d [2H, C$_6$H$_{ortho}$C(O), $^3J_{HH}$ 7.8], 7.28 t [2H, C$_6$H$_{para}$C(O), $^3J_{HH}$ 7.3], 7.45 t [2H, C$_6$H$_{meta}$C(O), $^3J_{HH}$ 7.8], 7.73 d [2H, C$_6$H$_{ortho}$OC(O), $^3J_{HH}$ 7.8]. Found, %: C 63.99, H 4.86. $C_{21}H_{22}N_2O_6$. Calculated, %: C 63.63, H 5.09.

***N,N'*-Bis(acetylsalicyl)-1,4-butylenediamine (IX)**. The synthesis was performed analogously to the preparation of compound **IV** from 1.91 g of acid chloride **II** in 10 ml of pyridine and 0.42 g of 1,4-diaminobutane in 5 ml of pyridine. Yield 1.55 g (78%), mp 139–141°C, $R_f$ 0.64 (B). $^1$H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.63–1.70 m (4H, NCH$_2$C$\underline{H}_2$), 2.28 s [6H, C(O)CH$_3$], 3.41–3.50 m (4H, NCH$_2$), 6.37–6.46 br.s (2H, NH), 7.08 d [2H, C$_6$H$_{ortho}$C(O), $^3J_{HH}$ 7.8], 7.27 t [2H, C$_6$H$_{para}$C(O), $^3J_{HH}$ 7.4], 7.45 t [2H, C$_6$H$_{meta}$C(O), $^3J_{HH}$ 7.4], 7.68 d [2H, C$_6$H$_{ortho}$OC(O), $^3J_{HH}$ 7.4]. Found, %: C 64.47, H 5.62. $C_{22}H_{24}N_2O_6$. Calculated, %: C 64.07, H 5.87.

***N,N'*-Bis(acetylsalicyl)-1,5-pentylenediamine (X).** The synthesis was performed analogously to the preparation of compound **IV** from 1.91 g of acid chloride **II** in 10 ml of pyridine and 0.49 g of 1,5–diaminopentane in 5 ml of pyridine. Yield 1.70 g (83%), mp 104–105°C, $R_f$ 0.87 (C). $^1$H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.41–1.50 m (2H, NCH$_2$CH$_2$C$\underline{H}_2$), 1.58–1.69 m (4H, NCH$_2$C$\underline{H}_2$), 2.30 s

[6H, C(O)$CH_3$], 3.38 –3.46 m (4H, $NCH_2$), 6.27–6.35 br.s (2H, NH), 7.07 d [2H, $C_6H_{ortho}C(O)$, $^3J_{HH}$ 7.4], 7.25 t [2H, $C_6H_{para}C(O)$, $^3J_{HH}$ 7.3], 7.44 t [ 2H, $C_6H_{meta}C(O)$, $^3J_{HH}$ 7.4], 7.65 d [2H, $C_6H_{ortho}OC$ (O), $^3J_{HH}$ 7.4]. Found, %: C 64.97, H 5.92. $C_{23}H_{26}N_2O_6$. Calculated, %: C 64.78, H 6.15.

***O,O'*-Bis(acetylsalicyl)-1,2-ethylenediol (XI)**. The synthesis was performed analogously to the preparation of compound **IV** from 1.91 g of acid chloride **II** in 10 ml of pyridine and 0.30 g of ethylene glycol in 5 ml of pyridine. Yield 1.43 g (77%), mp 68–69°C (published: mp 67–69°C [12]), $R_f$ 0.72 (A). $^1$H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 2.30 s [6H, C(O)$CH_3$], 4.51–4.60 br.s (4H, $CH_2$), 7.10 d [2H, $C_6H_{ortho}C(O)$, $^3J_{HH}$ 7.8], 7.31 t [2H, $C_6H_{para}C(O)$, $^3J_{HH}$ 7.8], 7.54 t [2H, $C_6H_{meta}C(O)$, $^3J_{HH}$ 7.3], 8.03 d [2H, $C_6H_{ortho}OC(O)$, $^3J_{HH}$ 7.8].

***N,N'*-Dibenzoyl-1,3-propylenediamine (XII)**. The synthesis was performed analogously to the preparation of compound **IV** from 1.83 g of acid chloride **III** in 10 ml of pyridine and 0.48 g of 1,3-diaminopropane in the 5 ml of pyridine. Yield 1.52 g (83%), mp 139–141°C (published: mp 140°C [13]), $R_f$ 0.63 (A). $^1$H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.78–1.87 m (2H, $NCH_2C\underline{H}_2$), 3.53–3.61 m (4H, $NCH_2$), 7.13–7.21 br.s (2H, NH), 7.45 t [4H, $C_6H_{meta}C(O)$, $^3J_{HH}$ 7.8], 7.49 t [4H, $C_6H_{para}C(O)$, $^3J_{HH}$ 7.8], 7.86 d [ 2H, $C_6H_{ortho}C(O)$, $^3J_{HH}$ 7.8].

***N,N'*-Dibenzoyl -1,4-butylenediamine (XIII)**. The synthesis was performed analogously to the preparation of compound **IV** from 1.59 g of acid chloride **III** in 10 ml of pyridine and 0.50 g 1,4-diaminobutane in 5 ml of pyridine. Yield 1.38 g (82%), mp 175–177°C (published: mp 175–177°C [14]), $R_f$ 0.70 (A). $^1$H NMR spectrum (DMSO-$d_6$), δ, ppm (*J*, Hz): 1.49–1.57 br.s (4H, $NCH_2C\underline{H}_2$), 3.23–3.30 m (4H, $NCH_2$), 7.41 t [4H, $C_6H_{meta}C(O)$, $^3J_{HH}$ 7.8], 7.46 t [4H, $C_6H_{para}C(O)$, $^3J_{HH}$ 7.8], 7.86 d [2H, $C_6H_{ortho}C(O)$, $^3J_{HH}$ 7.8], 8.45 br.s (2H, NH).

***N,N'*-Dibenzoyl-1,5-pentylenediamine (XIV)**. The synthesis was performed analogously to the preparation of compound **IV** from 1.83 g of acid chloride **III** in 10 ml of pyridine and 0.66 g of 1,5-diaminopentane in 5 ml of pyridine. Yield 1.53 g (76%), mp 134–136°C (published: mp 135°C [15]), $R_f$ 0.68 (A). $^1$H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.41–1.52 m (2H, $NCH_2CH_2C\underline{H}_2$), 1.63–1.72 m (4H, $NCH_2C\underline{H}_2$), 3.43–3.51 m (4H, $NCH_2$), 6.40–6.51 br.s (2H, NH), 7.37 t [4H, $C_6H_{meta}C(O)$, $^3J_{HH}$ 7.8], 7.46 t [4H, $C_6H_{para}C$ (O), $^3J_{HH}$ 7.8], 7.74 d [ 2H, $C_6H_{ortho}C(O)$, $^3J_{HH}$ 7.8].

***O,O'*-Dibenzoyl-1,2-ethylenediol (XV)**. The synthesis was performed analogously to the preparation of compound **IV** from 3.66 g of acid chloride **III** in 10 ml of pyridine and 0.81 g of ethylene glycol in 5 ml of pyridine. Yield 2.92 g (83%), mp 70–72°C (published: mp 73°C [16]), $R_f$ 0.60 (B). $^1$H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 4.64–4.70 m (4H, $CH_2O$), 7.43 t [4H, $C_6H_{meta}C(O)$, $^3J_{HH}$ 7.8], 7.55 t [4H, $C_6H_{para}C(O)$, $^3J_{HH}$ 7.4], 8.05 d [2H, $C_6H_{ortho}C(O)$, $^3J_{HH}$ 7.3].

***O,O'*-Dibenzoyl-1,3-propylendiol (XVI)**. The synthesis was performed analogously to the preparation of compound **IV** from 1.83 g of acid chloride **III** in 10 ml of pyridine and 0.50 g of 1,3-propanediol in 5 ml of pyridine. Yield 1.59 g (86%), mp 52–53°C (published: mp 52°C [17]), $R_f$ 0.49 (B). $^1$H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 2.24–2.33 m (2H, $CH_2C\underline{H}_2CH_2$), 4.51 t (4H, $CH_2O$, $^3J_{HH}$ 6.0), 7.42 t [4H, $C_6H_{meta}C(O)$, $^3J_{HH}$ 7.8], 7.54 t [4H, $C_6H_{para}C(O)$, $^3J_{HH}$ 7.8], 8.03 d [2H, $C_6H_{ortho}C(O)$, $^3J_{HH}$ 7.8].

***O,O'*-Dibenzoyl-2,2-dimethyl-1,3-propylendiol (XVII)**. The synthesis was performed analogously to the preparation of compound **IV** from 1.83 g of acid chloride **III** in 10 ml of pyridine and 0.68 g 2,2-dimethyl-1,3-propanediol in 5 ml of pyridine. Yield 1.65 g (81%), mp 53–55°C (published: mp 52–54°C [18]), $R_f$ 0.44 (B). $^1$H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.66 s (6H, $CH_3$), 4.25 s (4H, $CH_2$), 7.42 t [4H, $C_6H_{meta}C(O)$, $^3J_{HH}$ 7.8], 7.54 t [4H, $C_6H_{para}C(O)$, $^3J_{HH}$ 7.4], 8.03 d [2H, $C_6H_{ortho}C(O)$, $^3J_{HH}$ 7.3].

**Inclusion compound of β-cyclodextrin with *N,N'*-bis[1-(4-isobutylphenyl)propionyl]-1,3-propylenediamine (XVIII)**. To a solution of 0.20 g of β-cyclodextrin in 4 ml of water at 70°C was added at stirring 0.040 g of diamide **IV,** and the mixture was stirred at 70°C for 1 h. The reaction mixture was allowed to cool to room temperature, the precipitate formed after 20 h was filtered, washed with acetone (3×3 ml) and dried in vacuum (1 mm Hg) for 4 h at 50°C. Yield 0.13 g (54%), mp 238–240°C (decomp.), $R_f$ 0.61 (D). $^1$H NMR spectrum (DMSO-$d_6$), δ, ppm (*J*, Hz): β-cyclodextrin, 3.23–3.57 m (84H, $C^2H$–$C^5H$, $C^6H_2$), 4.45–4.53 m (14H, $C^6OH$), 4.74–4.83 br.s (14H, $C^1H$), 5.59–5.73 m (28H, $C^2OH$, $C^3OH$); diamide **IV,** 0.83 d [12H, $CH(C\underline{H}_3)_2$, $^3J_{HH}$ 6.4], 1.40–1.45 m ($NCH_2C\underline{H}_2$), 1.48 d (6H, $CHC\underline{H}_3$, $^3J_{HH}$ 6.9), 1.76–1.88 m [2H, $C\underline{H}(CH_3)_2$], 2.43 d (4H, $C\underline{H}_2C_6H_4$, $^3J_{HH}$ 7.0), 2.96–3.17

m (4H, $NCH_2$), 3.59 q (2H, $C\underline{H}C_6H_4$, $^3J_{HH}$ 7.2), 7.08 d (4H, $C_6\underline{H}_{ortho}CH_2$, $^3J_{HH}$ 7.4), 7.16 d (4H, $C_6\underline{H}_{meta}CH_2$, $^3J_{HH}$ 7.6), 8.15 br.s (2H, NH). Found, %: C 50.26, H 6.64. $C_{113}H_{182}N_2O_{72}$. Calculated, %: C 49.89, H 6.74.

**Inclusion compound of β-cyclodextrin with *N,N*'-bis[1-(4-isobutylphenyl)propionyl]-1,4-butylenediamine (XIX)**. Obtained similarly to the synthesis of the inclusion compound **XVIII** from 0.20 g of β-cyclodextrin and 0.041 g of diamide **V**. Yield 0.11 g (47%), mp 289–291°C (decomp.), $R_f$ 0.58 (E). $^1$H NMR spectrum (DMSO-$d_6$), δ, ppm (*J*, Hz): β-cyclodextrin, 3.28–3.68 m (84H, $C^2H$–$C^5H$, $C^6H_2$), 4.41–4.50 m (14H, $C^6OH$), 4.75–4.82 br.s (14H, $C^1H$), 5.63–5.71 br.s (14H, $C^3OH$), 5.74–5.79 br.s (14H, $C^2OH$); diamide **V**: 0.80 d [12H, $CH(C\underline{H}_3)_2$, $^3J_{HH}$ 6.4], 1.21–1.32 m (10H, $CHC\underline{H}_3$, $NCH_2$), 1.69–1.82 m [2H, $C\underline{H}(CH_3)_2$], 2.35 d (4H, $C\underline{H}_2C_6H_4$, $^3J_{HH}$ 7.3), 3.18–3.26 m (4H, $NCH_2$), 7.01 d (4H, $C_6\underline{H}_{ortho}CH_2$, $^3J_{HH}$ 7.4), 7.14 d (4H, $C_6\underline{H}_{meta}CH_2$, $^3J_{HH}$ 7.6), 7.82–7.88 br.s (2H, NH). Found, %: C 50.41, H 6.69. $C_{114}H_{184}N_2O_{72}$. Calculated, %: C 50.07, H 6.78.

**Inclusion compound of β-cyclodextrin with *N,N*'-bis(acetylsalicyl)-1,5-pentylenediamine (XX)**. Obtained similarly to the synthesis of the inclusion compound **XVIII** from 0.20 g of β-cyclodextrin and 0.038 g of diamide **X**. Yield 0.15 g (61%), mp 243–246°C (decomp.), $R_f$ 0.73 (F). $^1$H NMR spectrum (DMSO-$d_6$), δ, ppm (*J*, Hz): β-cyclodextrin, 3.25–3.72 m (84H, $C^2H$–$C^5H$, $C^6H_2$), 4.07–4.16 m (14H, $C^6OH$), 4.78–4.87 br.s (14H, $C^1H$), 5.35–5.46 br.s (14H, $C^2OH$, $C^3OH$); diamide **X**, 1.30–1.40 m (2H, $NCH_2CH_2C\underline{H}_2$), 1.45–1.57 m (4H, $NCH_2C\underline{H}_2$), 2.18 s [6H, $C(O)CH_3$], 3.15–3.23 m (4H, $NCH_2$), 7.12 d [2H, $C_6H_{ortho}C(O)$, $^3J_{HH}$ 7.8], 7.27 t [2H, $C_6H_{para}C(O)$, $^3J_{HH}$ 7.3], 7.44 t [2H, $C_6H_{meta}C(O)$, $^3J_{HH}$ 7.8], 7.62 d [2H, $C_6H_{ortho}OC(O)$, $^3J_{HH}$ 7.8], 7.78–7.85 br.s (2H, NH). Found, %: C 48.17, H 6.16. $C_{107}H_{166}N_2O_{76}$. Calculated, %: C 47.66, H 6.21.

**Inclusion compound of β-cyclodextrin with *N,N*'-dibenzoyl-1,4-butylenediamine (XXI)**. Obtained similarly to the synthesis of the inclusion compound **XVIII** from 0.20 g of β-cyclodextrin and 0.026 g of diamide **XIII.** Yield 0.13 g (57%), mp 279–282°C (decomp.), $R_f$ 0.47 (G). $^1$H NMR spectrum (DMSO-$d_6$), δ, ppm (*J*, Hz): β-cyclodextrin, 3.26–3.71 m (84H, $C^2H$–$C^5H$, $C^6H_2$), 4.06–4.15 m (14H, $C^6OH$), 4.76–4.84 br.s (14H, $C^1H$), 5.45–5.54 br.s (14H, $C^2OH$, $C^3OH$); diamide **XIII**, 1.55–1.62 m (4H, $NCH_2C\underline{H}_2$), 3.55–3.62 br.s (4H, $NCH_2$), 7.40 t [4H, $C_6H_{meta}C(O)$, $^3J_{HH}$ 7.6], 7.45 t [4H, $C_6H_{para}C(O)$, $^3J_{HH}$ 7.9], 7.80 d [2H, $C_6H_{ortho}C(O)$, $^3J_{HH}$ 7.7], 8.13–8.21 br.s (2H, NH). Found, %: C 48.29, H 6.17. $C_{102}H_{160}N_2O_{72}$. Calculated, %: C 47.74, H 6.28.

**Inclusion compound of β-cyclodextrin with *O,O*'-dibenzoyl-1,2-ethylendiol (XXII)**. Obtained similarly to the synthesis of the inclusion compound **XVIII** from 0.20 g of β-cyclodextrin and 0.024 g of diester **XV**. Yield 0.13 g (58%), mp 250–252°C (decomp.), $R_f$ 0.75 (H). $^1$H NMR spectrum (DMSO-$d_6$), δ, ppm (*J*, Hz): β-cyclodextrin, 3.22–3.68 m (84H, $C^2H$–$C^5H$, $C^6H_2$), 4.37–4.43 m (14H, $C^6OH$), 4.76–4.84 br.s (14H, $C^1H$), 5.60–5.72 br.s (14H, $C^2OH$, $C^3OH$); diester **XV**, 4.55–4.62 br.s (4H, $CH_2O$), 7.49 t [4H, $C_6H_{meta}C(O)$, $^3J_{HH}$ 7.8], 7.62 t [4H, $C_6H_{para}C(O)$, $^3J_{HH}$ 7.8], 7.93 d [2H, $C_6H_{ortho}C(O)$, $^3J_{HH}$ 7.7]. Found, %: C 47.74, H 5.98. $C_{100}H_{154}N_2O_{74}$. Calculated, %: C 47.28, H 6.11.

**Inclusion compound of β-cyclodextrin with *O,O*'-bis[1-(4-isobutylphenyl)propionyl]-1,2-ethylendiol (XXIII)**. Obtained similarly to the synthesis of the inclusion compound **XVIII** from 0.20 g of β-cyclodextrin and 0.039 g of diester **VII**. Yield 0.071 g (51%), mp 259–261°C (decomp.), $R_f$ 0.56 (E). $^1$H NMR spectrum (DMSO-$d_6$), δ, ppm (*J*, Hz): β-cyclodextrin, 3.23–3.75 m (42H, $C^2H$–$C^5H$, $C^6H_2$), 4.03–4.12 m (7H, $C^6OH$), 4.75–4.88 br.s (7H, $C^1H$), 5.42–5.57 br.s (7H, $C^2OH$, $C^3OH$); diester **VII**, 0.83 d [12H, $CH(C\underline{H}_3)_2$, $^3J_{HH}$ 6.7], 1.42 d (6H, $CHC\underline{H}_3$, $^3J_{HH}$ 6.8), 1.75–1.87 m [2H, $C\underline{H}(CH_3)_2$], 2.41 d (4H, $C\underline{H}_2C_6H_4$), 3.63–3.72 m (2H, $C\underline{H}C_6H_4$), 7.04 d ( 4H, $C_6\underline{H}_{ortho}CH_2$, $^3J_{HH}$ 7.8), 7.13 d (4H, $C_6\underline{H}_{meta}CH_2$, $^3J_{HH}$ 7.7). Found, %: C 52.88, H 7.04. $C_{70}H_{108}O_{39}$. Calculated, %: C 53.43, H 6.92.

**Inclusion compound of β-cyclodextrin with *N,N*'-bis(acetylsalicyl)-1,4-butylenediamine (XXIV)**. Obtained similarly to the synthesis of the inclusion compound **XVIII** from 0.20 g of β-cyclodextrin and 0.036 g of diamide **IX**. Yield 0.07 g (49%), mp 275–277°C (decomp.), $R_f$ 0.66 (E). $^1$H NMR spectrum (DMSO-$d_6$), δ, ppm (*J*, Hz): β-cyclodextrin, 3.25–3.71 m (42H, $C^2H$–$C^5H$, $C^6H_2$), 4.11–4.19 m (7H, $C^6OH$), 4.75–4.84 br.s (7H, $C^1H$), 5.38–5.49 br.s (7H, $C^2OH$, $C^3OH$); diamide **IX**, 1.50–1.60 m (4H, $NCH_2C\underline{H}_2$), 2.16 br.s [6H, $C(O)CH_3$], 3.16–3.22 m (4H, $NCH_2$), 7.11 d [2H, $C_6H_{ortho}C(O)$, $^3J_{HH}$ 7.6], 7.26 t [2H, $C_6H_{para}C(O)$, $^3J_{HH}$ 7.7], 7.45 t [2H, $C_6H_{meta}C(O)$, $^3J_{HH}$ 7.4], 7.62 d [2H, $C_6H_{ortho}OC(O)$, $^3J_{HH}$ 7.6], 7.92–7.01 br.s (2H, NH). Found, %: C 50.18, H 5.97. $C_{64}H_{94}N_2O_{41}$. Calculated, %: C 49.68, H 6.12.

**Inclusion compound of β-cyclodextrin with *O,O'*-dibenzoyl-1,3-propylendiol (XXV)**. Obtained similarly to the synthesis of the inclusion compound **XVIII** from 0.20 g of β-cyclodextrin and 0.025 g of diester **XVI**. Yield 0.07 g (55%), mp 254–256°C (decomp.), $R_f$ 0.68 (I). $^1$H NMR spectrum (DMSO-$d_6$), δ, ppm (*J*, Hz): β-cyclodextrin: 3.25–3.73 m (42H, $C^2H$–$C^5H$, $C^6H_2$), 4.06–4.15 m (7H, $C^6OH$), 4.78–4.86 br.s (7H, $C^1H$), 5.42–5.57 br.s (7H, $C^2OH$, $C^3OH$); diester **XVI**, 2.12–2.21 m (2H, $CH_2C\underline{H_2}CH_2$), 4.39–4.47 m (4H, $CH_2O$), 7.45 t [4H, $C_6H_{meta}C(O)$, $^3J_{HH}$ 7.9], 7.59 t [4H, $C_6H_{para}C$ (O), $^3J_{HH}$ 7.4], 7.92 d [2H, $C_6H_{ortho}C(O)$, $^3J_{HH}$ 7.6]. Found, %: C 49.43, H 6.25. $C_{59}H_{86}NO_{39}$. Calculated, %: C 49.93, H 6.11.

**Inclusion compound β-cyclodextrin with *O,O'*-dibenzoyl-2,2-dimethyl-1,3-propylendiol (XXVI).** Obtained similarly to the synthesis of the inclusion compound **XVIII** from 0.20 g of β-cyclodextrin and 0.028 g of diester **XVII**. Yield 0.06 g (47%), mp 272–274°C (decomp.), $R_f$ 0.46 (D). $^1$H NMR spectrum (DMSO-$d_6$), δ, ppm (*J*, Hz): β-cyclodextrin, 3.25–3.71 m (42H, $C^2H$–$C^5H$, $C^6H_2$), 4.02–4.12 m (7H, $C^6OH$), 4.76–4.85 br.s (7H, $C^1H$), 5.43–5.59 br.s (7H, $C^2OH$, $C^3OH$); diester **XVII**, 1.10 s (6H, $CH_3$), 4.19 s (4H, $CH_2O$), 7.47 t [4H, $C_6H_{meta}C(O)$ , $^3J_{HH}$ 7.8], 7.59 t [4H, $C_6H_{para}C(O)$, $^3J_{HH}$ 7.8], 7.94 d [2H, $C_6H_{ortho}C(O)$, $^3J_{HH}$ 7.8]. Found, %: C 50.93, H 6.18. $C_{61}H_{90}O_{39}$. Calculated, %: C 50.62, H 6.27.

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