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Synthesis of Monocationic β-Cyclodextrin Derivatives

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Abstract—Reactions of 6-bromo- and 6-iodo-6-deoxy-β-cyclodextrin with organic amines of diverse nature afforded a series of monocationic derivatives with aminium groups located in the cyclodextrin scaffold on the side of the primary hydroxy groups. The structure and composition of the obtained cationic β-cyclodextrin derivatives were confirmed by ^{1}H and ^{13}C NMR data.

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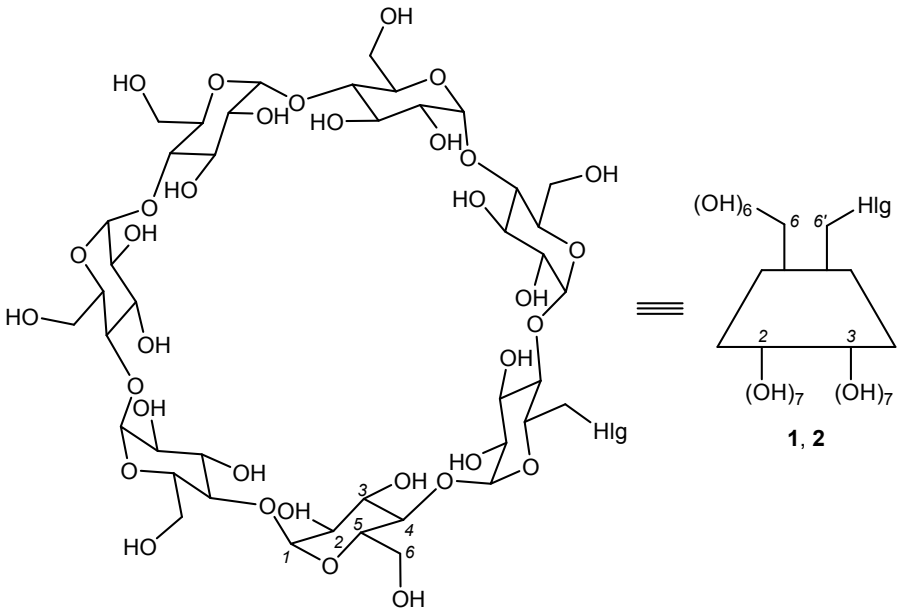
Cationic cyclodextrin derivatives owing to the positive charge on the cyclodextrin matrix are capable of incorporation in biologic membranes and of penetration through biologic barriers [1–4]. They are potential objects of pharmacological studies as drug carriers and also as carriers for the DNA delivery (vectorization) in the gene therapy [3–7].

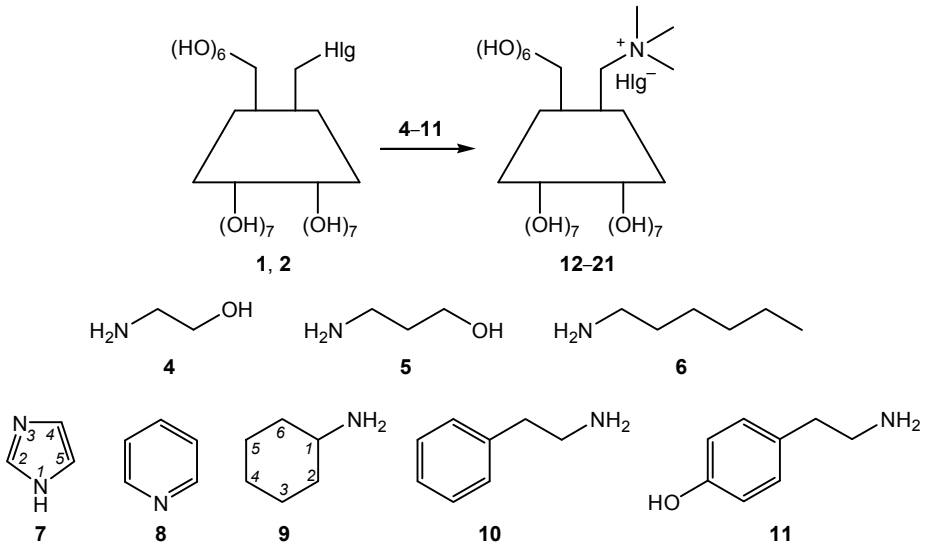
The preparation of cationic derivatives commonly utilizes 6-azido-6-deoxy cyclodextrin derivatives that are converted into amines by treating with triphenylphosphine in aqueous ammonia [8, 9]. However this method possesses a limitation since it is suitable only for the preparation of aminium cyclodextrin derivatives from primary amines.

Scheme 1.



Hlg = Br (**1**), I (**2**).

Scheme 3.

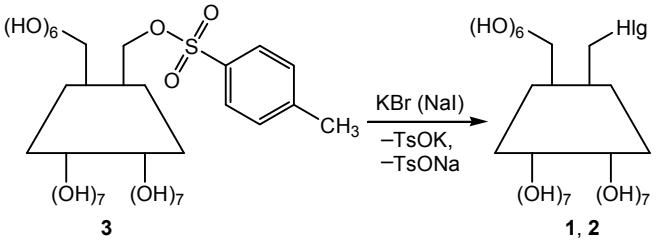


Hlg = I (**12**, **13**, **15**, **16**, **18–21**), Br (**14**, **17**).

For the preparation of cationic cyclodextrin derivatives possessing charged fragments on the side of the primary hydroxy groups we carried out the alkylation of amines both with per(6-bromo)per(6-deoxy)cyclodextrin derivatives [10] and with derivatives with lower content of bromine atoms [11, 12].[1] In the latter case the experimental difficulty consists in the determination of the number and location of the bromodeoxy groups in the position *6* of the cyclodextrin (Scheme 1).

We considered the possibility of the synthesis of monocationic derivatives from β-cyclodextrin monohalo derivatives and the corresponding amine. The synthesis of halo derivatives **1** and **2** was performed by procedure [13] from β-cyclodextrin monotosylate **3** [14] (Scheme 2).[2]

Scheme 2.



[1] In [11, 12] the average amount of introduced bromine atoms was mentioned. At the introduction of 2 to 5 bromine atoms difficultly separable position isomers can form.

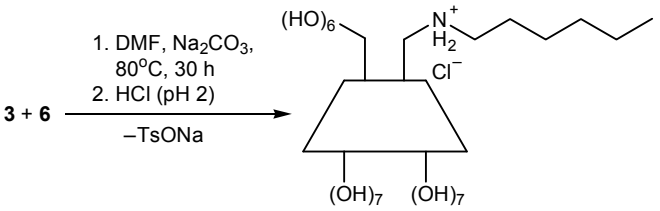
[2] From the numerous methods of monotosylate **3** preparation [15] we chose the procedure from [14] as the most reliable and efficient.

Monohalo derivatives **1** and **2** were obtained in 85 and 79% yields respectively. The structure and regiodirection of the substitution in cyclodextrins **1–3** is confirmed by the ^{1}H and ^{13}C NMR data. All ^{13}C NMR spectra of compounds **1–3** contain signals of unsubstituted C^{6} atoms at δ 60.4 ppm. The spectra of halo-substituted compounds **1** and **2** are characterized by the appearance in the upfield region of minor signals from $C^{6'}$ nuclei attached to Hlg at δ 31.5 and 15.3 ppm respectively, and in the spectrum of monotosylate **3** the corresponding signal is located at δ 69.7 ppm. No additional signals from C^{2} and C^{3} nuclei were observed in the spectrum of compound **3** showing that only the hydroxy group at the atom $C^{6'}$ underwent the substitution. The position of the signals of the hydroxyl protons was refined using their significant shift (by 0.3–0.7 ppm) at registering the sample solution at a higher temperature (80°C). The validity of signals assignments in the ^{1}H and ^{13}C NMR spectra was additionally confirmed by the analysis of 2D NMR spectra HOMOCOR {^{1}H–^{1}H} and HETCOR {^{1}H–^{13}C}.

The content of the halogen introduced in the β-cyclodextrin molecule was confirmed by argentometric titration [16]. The weight portion (~0.04 g) of compounds **1** and **2** was mineralized by Schöniger method followed by titration with 0.01 N silver nitrate solution.

Halo derivatives **1** and **2** were brought in reaction with amines **4–11** to obtain monocationic aminium β-cyclodextrin derivatives **12–21** (Scheme 3).

Scheme 4.



The synthesis was carried out in DMF at 120–130°C for 40 h (the reaction with pyridine **8** was performed at 80°C) to obtain in high yields compounds **12–21** with the positive charge on the side of the primary hydroxy groups of the cyclodextrin scaffold. With some primary amines the preparation of aminium salts is possible. For instance, at the direct treatment of tosylate **3** with hexylamine **6** followed by acidification (HCl, pH 2) compound **22** was obtained yet in this case a thorough purification from p-toluenesulfonic acid was required, since the latter was fairly strongly retained in the cyclodextrin cavity (Scheme 4).

The structure of compounds **12–22** was confirmed by ^{1}H NMR data, and the regiodirection of the substitution of the primary hydroxy groups was revealed from the ^{13}C NMR data. To be able to integrate the carbon signals in the ^{13}C NMR spectra of compounds **12–22** the registration was performed at a large delay between the pulses (8 s). The ^{13}C NMR spectra of compounds **12–22** contain the signals of nuclei of unsubstituted C^6 atoms at δ 60.4 ppm and characteristic minor upfield signals of $C^{6'}$ nuclei bearing the N^+ substituent at δ 42.9–54.6 ppm. The validity of the signals assignment was confirmed by the analysis of 2D NMR spectra of homo- (HOMOCOR {^{1}H–^{1}H}) and heteronuclear (HETCOR {^{1}H–^{13}C}) correlations, registering in the DEPT mode, and registering of spectra at 20 and 80°C to make a reliable assignment of the hydroxyl protons signals.

The obtained monocationic β-cyclodextrin derivatives are potential carriers (by the formation of inclusion compounds and conjugates) for diverse pharmaceuticals.

EXPERIMENTAL

^{1}H and ^{13}C NMR spectra were registered on a spectrometer JEOLECX-400 at operating frequencies 399.78 and 100.53 MHz respectively. Chemical shifts of ^{1}H and ^{13}C are reported with respect to $SiMe_4$ signal. Elemental analysis was carried out on an instrument Flash EA 1112HT. TLC was performed on aluminum plates equipped with a fixed layer of silica gel (Silufol UV-254), eluent butanol–ethanol–water, 5 : 4 : 3. β-Cyclodextrin of Wacker Co (USA) was used.

Mono(6-bromo-6-deoxy)-β-cyclodextrin (1). To a solution of 1.00 g (0.78 mmol) of β-cyclodextrin tosylate **3** in 10 mL of DMF and 5 mL of water was added 0.19 g (1.56 mmol) of potassium bromide and the mixture was stirred for 24 h at 50–55°C. The reaction mixture was concentrated in a vacuum to obtain a syrup-like mass, 3 mL of water was added, the mixture was stirred, the separated precipitate was filtered off, washed with water (2 × 2 mL) and 5 mL of acetone, and dried in a vacuum. Yield 0.79 g (85%), mp 230–232°C (decomp.), R_f 0.68. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 3.19–3.76 m (42H, $H^{2–5}$, C^6H_2), 4.46 br.s (6H, C^6OH), 4.78 s (7H, C^1H), 5.75 br.s (14H, C^2OH, C^3OH). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 31.5 ($C^{6'}$), 60.4 (C^6), 72.5 (C^5), 72.9 (C^2), 73.6 (C^3), 82.0 (C^4), 102.4 (C^1). Found, %: C 41.98; H 5.85; Br 6.70. $C_{42}H_{69}BrO_{34}$. Calculated, %: C 42.11; H 5.81; Br 6.67.

Mono(6-iodo-6-deoxy)-β-cyclodextrin (2). To a solution of 1.08 g (0.84 mmol) of tosylate **3** in 200 mL of water was added at stirring 4.32 g (28.82 mmol) of sodium iodide, and the mixture was stirred for 1 h at heating on a boiling water bath. The reaction mixture was concentrated in a vacuum to a volume of 10 mL, 5 mL of acetone was added, the mixture was stirred, the separated precipitate was filtered off, washed with acetone (2 × 2 mL), and dried in a vacuum. Yield 0.82 g (79%), mp 231–233°C (decomp.), R_f 0.69. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 3.19–3.76 m (42H, $H^{2–5}$, C^6H_2), 4.46 br.s (6H, C^6OH), 4.78 s (7H, C^1H), 5.75 br.s (14H, C^2OH, C^3OH). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 15.3 ($C^{6'}$), 60.4 (C^6), 72.5 (C^5), 72.9 (C^2), 73.6 (C^3), 82.0 (C^4), 102.4 (C^1). Found, %: C 40.65; H 5.53; I 10.10. $C_{42}H_{69}IO_{34}$. Calculated, %: C 40.52; H 5.59; I 10.19.

Mono[6-*O*-(4-methylbenzenesulfonyl)]-β-cyclodextrin (3) [13]. Yield 6.12 g (70%), mp 162–164°C (decomp.) (160–162°C [14]), R_f 0.77. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 2.39 m (3H, CH_3), 3.15–3.40 m (14H, C^2H, C^4H), 3.40–3.75 m (25H, C^3H, C^5H, C^6H_2), 4.16 m (1H, $C^{5'}H$), 4.33 m (2H, $C^{6'}H_2$), 4.46 br.s (6H, C^6OH), 4.74 m (1H, $C^{1'}H$), 4.79 m (6H, C^1H), 5.75 br.s (14H, C^2OH, C^3OH), 7.39 (2H, H^m),

7.71 (2H, H^{o}). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 21.2 (CH_3), 60.4 (C^{6}), 68.9 ($C^{6'}$), 69.7 ($C^{5'}$), 72.5 (C^{5}), 72.9 (C^{2}), 73.6 (C^{3}), 81.5 (C^{4}), 102.4 (C^{1}), 127.6 (C^{o}), 130.0 (C^{m}), 132.8 (C^{p}), 144.8 ($C^{i}SO_2$). Found, %: C 45.77; H 5.87. $C_{49}H_{76}O_{37}S$. Calculated, %: C 45.65; H 5.94.

Mono[6-(2-hydroxyethan-1-aminium)-6-deoxy]-β-cyclodextrin iodide (12). To a solution of 1.00 g (0.80 mmol) of β-cyclodextrin iodo derivative **2** in 15 mL of DMF was added at stirring 0.49 g (8.00 mmol) of 2-aminoethanol **4**. The solution was stirred for 40 h at 120–130°C. The reaction mixture was diluted with 25 mL of acetone, the mixture was stirred, the separated precipitate was filtered off, washed successively with chloroform (2 × 5 mL), ethanol (2 × 5 mL), acetone (2 × 5 mL), ethyl ether (2 × 5 mL), and dried in a vacuum (1 mm Hg) for 4 h at 80°C. Yield 0.89 g (85%), mp 183–185°C (decomp.), R_f 0.71. ^1H NMR spectrum (DMSO-d_6), δ, ppm: 3.09 m (2H, C<u>H</u>$_2N^+H_2$), 3.13–3.82 m (44H, H^{2-5}, $C^{6}H_2$, C<u>H</u>$_2$OH), 4.46 br.s (7H, C^{6}OH, CH_2O<u>H</u>), 4.78 s (7H, C^{1}H), 5.75 br.s (16H, C^{2}OH, C^{3}OH, N^+H_2). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 40.7 ($CH_2N^+H_2$), 47.0 ($C^{6'}$), 60.2 (CH_2OH), 60.4 (C^{6}), 72.5 (C^{5}), 72.9 (C^{2}), 73.6 (C^{3}), 82.0 (C^{4}), 102.4 (C^{1}). Found, %: C 40.37; H 5.83; N 1.01. $C_{44}H_{76}INO_{35}$. Calculated, %: C 40.47; H 5.87; N 1.07.

Compounds **13–21** were prepared similarly.

Mono[6-(3-hydroxypropan-1-aminium)-6-deoxy]-β-cyclodextrin iodide (13) was obtained from 1.00 g (0.80 mmol) of β-cyclodextrin iodo derivative **2** and 0.60 g (8.00 mmol) of 3-aminopropan-1-ol **5**. Yield 0.88 g (83%), mp 178–180°C (decomp.), R_f 0.73. ^1H NMR spectrum (DMSO-d_6), δ, ppm: 1.50 m (2H, C<u>H</u>$_2$CH$_2$OH), 3.07 m (2H, C<u>H</u>$_2N^+H_2$), 3.14–3.73 m (44H, H^{2-5}, $C^{6}H_2$, C<u>H</u>$_2$OH), 4.45 br.s (7H, C^{6}OH, CH_2O<u>H</u>), 4.78 s (7H, C^{1}H), 5.73 br.s (16H, C^{2}OH, C^{3}OH, N^+H_2). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 32.8 (<u>C</u>H$_2$CH$_2$OH), 34.9 ($CH_2N^+H_2$), 47.3 ($C^{6'}$), 58.8 (CH_2OH), 60.4 (C^{6}), 72.5 (C^{5}), 72.9 (C^{2}), 73.6 (C^{3}), 82.0 (C^{4}), 102.4 (C^{1}). Found, %: C 41.06; H 6.01; N 1.02. $C_{45}H_{78}INO_{35}$. Calculated, %: C 40.95; H 5.96; N 1.06.

Mono[6-(hexan-1-aminium)-6-deoxy]-β-cyclodextrin bromide (14) was obtained from 1.00 g (0.83 mmol) of β-cyclodextrin bromo derivative **1** and 0.84 g (8.30 mmol) of hexan-1-amine **6**. Yield 0.92 g (85%), mp 249–251°C (decomp.), R_f 0.74. ^1H NMR spectrum (DMSO-d_6), δ, ppm: 0.81 t (3H, CH_3), 1.20 m [6H, (C<u>H</u>$_2$)$_3$CH$_3$], 1.33 m (2H, NCH$_2$C<u>H</u>$_2$), 2.46 t (2H, NCH$_2$), 3.31–3.69 m (42H, H^{2-5}, $C^{6}H_2$), 4.44 br.s (6H, C^{6}OH), 4.79 s (7H, C^{1}H), 5.70 br.s (16H, C^{2}OH, C^{3}OH, N^+H_2). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 14.5 (CH_3), 22.6 (<u>C</u>H$_2$CH$_3$), 26.5 [<u>C</u>H$_2$(CH$_2$)$_2$CH$_3$], 30.0 (<u>C</u>H$_2$CH$_2$N), 31.8 (<u>C</u>H$_2$CH$_2$CH$_3$), 49.9 (CH_2N), 54.6 ($C^{6'}$), 60.4 (C^{6}), 70.1 ($C^{5'}$), 72.6 (C^{5}), 72.9 (C^{2}), 73.6 (C^{3}), 82.0 (C^{4}), 83.7 ($C^{4'}$), 102.5 (C^{1}). Found, %: C 44.44; H 6.46; N 1.16. $C_{48}H_{84}BrNO_{34}$. Calculated, %: C 44.38; H 6.52; N 1.08.

Mono[6-(hexan-1-aminium)-6-deoxy]-β-cyclodextrin iodide (15) was obtained from 1.00 g (0.80 mmol) of β-cyclodextrin iodo derivative **2** and 0.16 g (8.00 mmol) of hexan-1-amine **6**. Yield 0.93 g (86%), mp 250–252°C (decomp.), R_f 0.74. ^1H NMR spectrum (DMSO-d_6), δ, ppm: 0.81 t (3H, CH_3), 1.20 m [6H, (C<u>H</u>$_2$)$_3$CH$_3$], 1.33 m (2H, NCH$_2$C<u>H</u>$_2$), 2.50 t (2H, NCH_2), 3.31–3.69 m (42H, H^{2-5}, $C^{6}H_2$), 4.44 br.s (6H, C^{6}OH), 4.79 s (7H, C^{1}H), 5.70 br.s (16H, C^{2}OH, C^{3}OH, N^+H_2). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 14.5 (CH_3), 22.6 (<u>C</u>H$_2$CH$_3$), 26.5 [<u>C</u>H$_2$(CH$_2$)$_2$CH$_3$], 30.0 (<u>C</u>H$_2$CH$_2$N), 31.8 (<u>C</u>H$_2$CH$_2$CH$_3$), 49.9 (CH_2N), 54.6 ($C^{6'}$), 60.4 (C^{6}), 70.1 ($C^{5'}$), 72.6 (C^{5}), 72.9 (C^{2}), 73.6 (C^{3}), 82.0 (C^{4}), 83.7 ($C^{4'}$), 102.5 (C^{1}). Found, %: C 42.68; H 6.41; N 0.88. $C_{48}H_{84}INO_{34}$. Calculated, %: C 42.83; H 6.29; N 1.04.

Mono[6-deoxy-6-(imidazol-1-ium)]-β-cyclodextrin iodide (16) was obtained from 1.00 g (0.80 mmol) of iodo derivative **2** and 0.54 g (8.00 mmol) of imidazole **7**. Yield 0.74 g (70%), mp 258–260°C (decomp.), R_f 0.75. ^1H NMR spectrum (DMSO-d_6), δ, ppm: 3.15–3.79 m (42H, H^{2-5}, $C^{6}H_2$), 4.40 br.s (6H, C^{6}OH), 4.79 s (7H, C^{1}H), 5.67 br.s (15H, C^{2}OH, C^{3}OH, NH^+), 6.98 s (2H, H^{4}, H^{5})[3], 7.62 d (1H, H^{2}). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 50.5 ($C^{6'}$), 60.4 (C^{6}), 72.6 (C^{5}), 72.9 (C^{2}), 73.6 (C^{3}), 82.1 (C^{4}), 102.5 (C^{1}), 122.2 (C^{4}, C^{5}), 135.6 (C^{2}). Found, %: C 41.28; H 5.51; N 2.04. $C_{45}H_{73}IN_2O_{34}$. Calculated, %: C 41.17; H 5.60; N 2.13.

Mono[6-deoxy-6-(pyridin-1-ium)]-β-cyclodextrin bromide (17) was obtained from 1.00 g (0.83 mmol) of bromo derivative **1** and 0.66 g (8.30 mmol) of pyridine at 80°C within 40 h. Yield 0.82 g (79%), mp 268–270°C (decomp.), R_f 0.77. ^1H NMR spectrum (DMSO-d_6), δ, ppm: 3.31–3.69 m (40H, H^{2-5}, $C^{6}H_2$), 4.44 br.s (6H, C^{6}OH), 4.79 s (7H, C^{1}H), 5.26 m (2H,

[3] In the spectra of compounds **16** and **19** the protons and carbon atoms of cationic substituents are printed bold in accordance with their numeration in amines **7** and **9** on the scheme.

$C^{6'}H_2$), 5.70 br.s (14H, C^2OH, C^3OH), 8.08 t (2H, H^{β}), 8.59 t (1H, H^{γ}), 8.98 d (2H, H^{α}). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 53.9 ($C^{6'}$), 60.4 (C^6), 72.6 (C^5), 72.9 (C^2), 73.6 (C^3), 82.0 (C^4), 102.5 (C^1), 128.4 (C^{β}), 141.8 (C^{α}), 146.7 (C^{γ}). Found, %: C 44.32; H 5.79; N 1.18. $C_{47}H_{74}BrNO_{34}$. Calculated, %: C 44.21; H 5.84; N 1.10.

Mono[6-deoxy-6-(pyridin-1-ium)]-β-cyclodextrin iodide (18) was obtained similarly to compound **17** from 1.00 g (0.80 mmol) of iodo derivative **2** and 0.63 g (8.00 mmol) of pyridine. Yield 0.83 g (78%), mp 268–270°C (decomp.), R_f 0.77. ^1H NMR spectrum (DMSO-d_6), δ, ppm: 3.29–3.68 m (40H, H^{2-5}, C^6H_2), 4.43 br.s (6H, C^6OH), 4.79 s (7H, C^1H), 5.26 m (2H, $C^{6'}H_2$), 5.69 br.s (14H, C^2OH, C^3OH), 8.08 t (2H, H^{β}), 8.59 t (1H, H^{γ}), 8.98 d (2H, H^{α}). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 53.9 ($C^{6'}$), 60.4 (C^6), 72.6 (C^5), 72.9 (C^2), 73.6 (C^3), 82.0 (C^4), 102.5 (C^1), 128.4 (C^{β}), 141.8 (C^{α}), 146.7 (C^{γ}). Found, %: C 42.49; H 5.55; N 0.91. $C_{47}H_{74}INO_{34}$. Calculated, %: C 42.64; H 5.63; N 1.06.

Mono[6-deoxy-6-(cyclohexylaminium)]-β-cyclodextrin iodide (19) was obtained from 1.00 g (0.80 mmol) of iodo derivative **2** and 0.79 g (8.0 mmol) of cyclohexylamine **10**. Yield 0.79 g (73%), mp 248–250°C (decomp.), R_f 0.74. ^1H NMR spectrum (DMSO-d_6), δ, ppm: 0.98–1.27 m (6H, H^{3-5}), 1.54–1.79 m (4H, C^2H_2, C^6H_2), 3.03–3.72 m (43H, H^{2-5}, C^6H_2, C^1H), 4.45 br.s (6H, C^6OH), 4.78 s (7H, C^1H), 5.63 br.s (16H, C^2OH, C^3OH, N^+H_2). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 24.9 (C^3, C^5), 25.1 (C^4), 32.8 (C^2, C^6), 46.6 ($C^{6'}$), 60.4 (C^6), 60.7 (C^1), 72.6 (C^5), 72.9 (C^2), 73.6 (C^3), 82.0 (C^4), 102.5 (C^1). Found, %: C 42.76; H 6.07; N 0.96. $C_{48}H_{82}INO_{34}$. Calculated, %: C 42.89; H 6.15; N 1.04.

Mono[6-deoxy-6-(2-phenylethan-1-aminium)]-β-cyclodextrin iodide (20) was obtained from 1.00 g (0.80 mmol) of iodo derivative **2** and 0.97 g (8.00 mmol) of 2-phenylethan-1-amine **11**. Yield 0.84 g (76%), mp 174–176°C (decomp.), R_f 0.76. ^1H NMR spectrum (DMSO-d_6), δ, ppm: 3.17–3.78 m (46H, H^{2-5}, C^6H_2, CH_2CH_2Ph), 4.44 br.s (6H, C^6OH), 4.79 s (7H, C^1H), 5.57 br.s (16H, C^2OH, C^3OH, N^+H_2), 7.05–7.31 m (5H, Ph). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 35.5 (CH_2Ph), 39.6 ($CH_2N^+H_2$), 42.9 ($C^{6'}$), 60.4 (C^6), 72.6 (C^5), 72.9 (C^2), 73.6 (C^3), 82.1 (C^4), 102.5 (C^1), 126.7 (C^p), 128.9 (C^o), 129.1 (C^m), 139.8 (C^iCH_2). Found, %: C 43.85; H 6.01; N 0.95. $C_{50}H_{80}INO_{34}$. Calculated, %: C 43.96; H 5.90; N 1.03.

Mono-{6-[2-(4-hydroxyphenyl)ethan-1-aminium]-6-deoxy}-β-cyclodextrin iodide (21) was obtained from 1.00 g (0.80 mmol) iodo derivative **2** and 1.10 g (8.00 mmol) of 4-(2-aminoethyl)phenol **12**. Yield 0.85 g (77%), mp 173–175°C (decomp.), R_f 0.73. ^1H NMR spectrum (DMSO-d_6), δ, ppm: 2.54 t (2H, CH_2Ph), 3.03–3.75 m (44H, H^{2-5}, C^6H_2, $CH_2N^+H_2$), 4.51 br.s (6H, C^6OH), 4.79 s (7H, C^1H), 5.92 br.s (16H, C^2OH, C^3OH, N^+H_2), 6.62 d (2H, H^m), 6.93 d (2H, H^o), 9.06 s (1H, OH). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 34.7 (CH_2Ph), 39.6 ($CH_2N^+H_2$), 43.5 ($C^{6'}$), 60.4 (C^6), 72.5 (C^5), 72.9 (C^2), 73.6 (C^3), 82.0 (C^4), 102.4 (C^1), 115.7 (C^m), 129.5 (C^iCH_2), 130.0 (C^o), 156.5 (C^p). Found, % C 43.53; H 5.76; N 0.95. $C_{50}H_{80}INO_{35}$. Calculated, %: C 43.45; H 5.83; N 1.01.

Mono[6-(hexan-1-aminium)-6-deoxy]-β-cyclodextrin chloride (22). To a solution of 0.50 g (0.39 mmol) of monotosylate **3** in 20 mL of DMF was added at stirring 0.034 g of sodium hydrogen carbonate, 0.04 g (0.39 mmol) of hexan-1-amine **6**, and the reaction mixture was stirred for 28 h at 70°C. The solution was concentrated to a volume of 2 mL, filtered, diluted with 10 mL of acetone, the separated precipitate was filtered off, washed successively with chloroform (2 × 5 mL), ethanol (2 × 5 mL), acetone (2 × 5 mL), ethyl ether (2 × 5 mL), and dried in a vacuum (1 mm Hg) for 4 h at 80°C. Yield 0.38 g (82%), mp 248–250°C (decomp.), R_f 0.74. ^1H NMR spectrum (DMSO-d_6), δ, ppm: 0.84 t (3H, CH_3), 1.18–1.29 m [6H, $(CH_2)_3CH_3$], 1.34 m (2H, NCH_2CH_2), 3.01 t (2H, NCH_2), 3.29–3.72 m (42H, H^{2-5}, C^6H_2), 4.11 br.s (6H, C^6OH), 4.81 s (7H, C^1H), 5.37 br.s (15H, C^2OH, C^3OH, NH). ^1H (D_2O), δ, ppm: 0.78 t (3H, CH_3), 1.13–1.23 m [6H, $(CH_2)_3CH_3$], 1.34 m (2H, NCH_2CH_2), 2.97 t (2H, NCH_2), 3.45–3.79 m (42H, H^{2-5}, C^6H_2), 4.88 br.c (7H, C^1H). ^1H NMR spectrum (D_2O, pH 2), δ, ppm: 0.76 t (3H, CH_3), 1.11–1.18 m [6H, $(CH_2)_3CH_3$], 1.51 m (2H, NCH_2CH_2), 2.93 t (2H, NCH_2), 3.15–3.82 m (42H, H^{2-5}, C^6H_2), 4.87 br.s (7H, C^1H). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 14.5 (CH_3), 22.6 (CH_2CH_3), 27.0 [$CH_2(CH_2)_2CH_3$], 31.8 (CH_2CH_2N), 49.9 (CH_2N), 54.6 ($C^{6'}$), 60.4 (C^6), 72.5 (C^5), 72.9 (C^2), 73.6 (C^3), 82.0 (C^4), 102.4 (C^1). ^{13}C NMR spectrum (D_2O), δ, ppm: 13.4 (CH_3), 20.5 (CH_2CH_3), 25.5 [$CH_2(CH_2)_2CH_3$], 30.5 (CH_2CH_2N), 47.2 (CH_2N), 54.6 ($C^{6'}$), 60.1 (C^6), 70.7 (C^5), 72.0 (C^2), 73.2 (C^3), 81.1 (C^4), 101.9 (C^1). ^{13}C NMR spectrum (D_2O, pH 2), δ, ppm: 13.2 (CH_3), 20.6 (CH_2CH_3), 25.0 [CH_2·$(CH_2)_2CH_3$], 30.2 (CH_2CH_2N), 46.2 (CH_2N), 54.6 ($C^{6'}$), 60.2 (C^6), 71.9 (C^5), 72.2 (C^2), 73.2 (C^3), 81.1 (C^4), 101.9

(C^1). Found, %: C 46.07; H 6.71; N 1.06. $C_{48}H_{84}Cl \cdot NO_{34}$. Calculated, %: C 45.95; H 6.75; N 1.12.

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