Cationic β-cyclodextrin derivatives containing 2-(4-isobutylphenyl)- and 2-(3-benzoylphenyl)propionic acid residues*

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Cationic β-cyclodextrin derivatives containing residues of pharmacologically important acids linked by spacers of different lengths were obtained by treatment of mono-6-iodo-6-deoxy- and mono-6-tosyl-β-cyclodextrin with nucleophilic agents with terminal mono- and dimethylamino groups.

Key words: β-cyclodextrin, cationic derivatives, regiodirected functionalization, ^{1}H and ^{13}C NMR spectroscopy.

One of the most important problems of medicinal chemistry is the low solubility and bioavailability of pharmaceutical compounds.[1] Cyclodextrins, natural and readily available cyclic oligosaccharides, have long firmly occupied their niche in medicine, food technology, analytical chemistry, and biotechnology.[2] Among the plethora of β-cyclodextrin compounds, its cationic derivatives carrying a positive charge on the cyclodextrin matrix have found wide application in pharmacology due to their increased water solubility and other practically important properties. Such alkylammonium ("charged") amphiphilic cyclodextrins can be embedded and penetrate biological barriers and also serve as carriers for the delivery ("vectorization") of DNA in gene therapy.[3] Such amphiphilic cationic cyclodextrins as heptakis-[2-(ω-aminooligoethylene glycol)-6-deoxy-6-hexylthio]-β-cyclodextrin and heptakis-[2-(ω-aminooligoethylene glycol)-6-deoxy-6-hexadecylthio]-β-cyclodextrin were assessed for plasmid DNA condensation and cell transfection.[4] These derivatives can self-organize into cationic vesicles or nanoparticles and, unlike their amphiphilic non-aminated analogs, form lipoplexes with DNA, which efficiently transfect COS-7 cells.

The cationic derivatives most often are synthesized by the addition of various quaternary ammonium, phosphonium, and sulfonium salts[5] or by treatment of cyclodextrin 6-azido-6-deoxy derivatives with triphenylphosphine in aqueous ammonia to obtain amino derivatives.[6,7] However, this method has limitations since it is applicable only for the production of primary alkylammonium derivatives of cyclodextrins.

In addition, it is known that for the cyclodextrin-based structures, the efficiency of drug delivery in biological systems can be enhanced by the regulation of the spacer length linking cyclodextrin and the drug residue *via* better incorporation into the lipid matrix (the so-called "membrane anchor"), which causes its smaller structural changes.[8,9]

Earlier, we investigated the synthesis of β-cyclodextrin cationic compounds based on its per-, oligo-, and monohalodeoxy[10] and tosyl[11,12] derivatives. But, in contrast to the traditional alkylation of amines with alkyl halides, the hydrophobic cyclodextrin cavity has a specific (supramolecular) effect on the course of alkylation, which requires an individual approach to the synthesis of cationic β-cyclodextrin derivatives. Below are the structural formulas of monoiododeoxy (**1**) and monotosyl β-cyclodextrin (**2**).

The purpose of the present work is the synthesis of monoiododeoxy (**1**) and monotosyl (**2**) β-cyclodextrin-based cationic derivatives containing residues of some pharmacologically important acids, namely, 2-(4-isobutylphenyl)propionic acid (HO—Y) (an active ingredient of Ibuprofen) and 2-(3-benzoylphenyl)propionic acid (HO—Z) (an active ingredient of Ketoprofen). Note that the drug moieties are linked to the cationic fragment by the above-mentioned spacers, among which we selected the residues of 2-(dimethylamino)ethanol (**3**), 3-(di-

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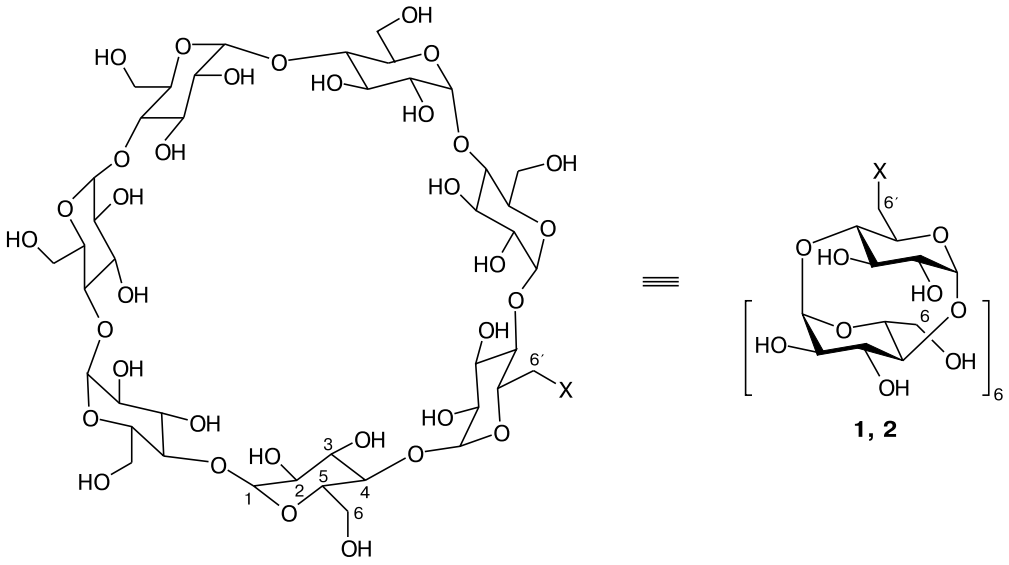


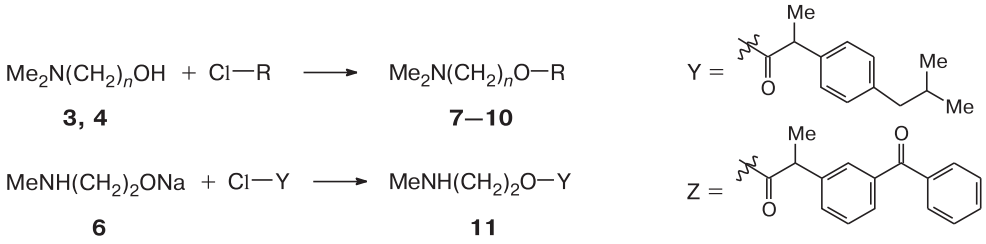
X = I (**1**), Ts (**2**)

methylamino)propan-1-ol (**4**), and 2-(methylamino)-ethanol (**5**). Earlier, we have shown the principal possibility of obtaining such cationic derivatives.[10] The advantage of the proposed approach is the absence of the necessity of protection of secondary hydroxyls and subsequent removal of protective groups, so that the "wide" part of the cyclodextrin framework remains free to accept various guests, including those with other biological action, which broadens the pharmacological possibilities of such structures. The starting mono derivatives **1** and **2** were obtained according to the improved by us procedure.[13] Nucleophilic agents **7**—**11** to be alkylated with halogen **1** and tosyl **2** derivatives were obtained by treatment of the corresponding dimethylaminoalcohol **3** or **4** or sodium methylaminoethoxide **6** with the corresponding acyl chloride Cl—Y(Z) (Scheme 1).

Dimethylaminoalkyl ethers **7**—**10** were alkylated with iodo derivative **1** in DMF solution at 100—110 °C for 30 h, while the substitution of tosyl derivative **2** with ether **11** having an *N*-methyl group was carried out at 80 °C for 6 h (Scheme 2). The corresponding cationic β-cyclodextrin derivatives **12**—**16** containing the residues of the mentioned pharmacologically important acids linked with spacers of different lengths (n = 2, 3) were isolated in 32—52% yields (see Experimental).

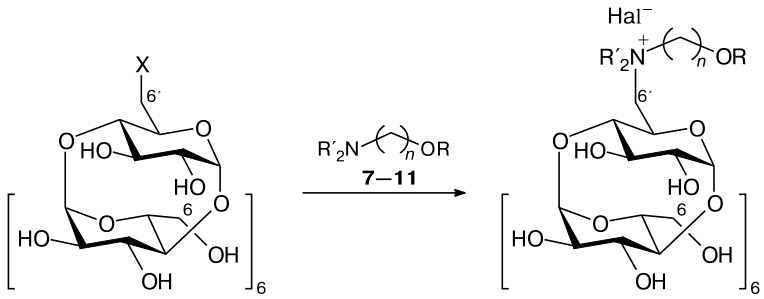
The structure and purity of compounds **7**—**16** were confirmed by NMR spectroscopy, TLC, and elemental analysis. Additionally, to integrate the signals of carbon nuclei, ^{13}C NMR spectra of compounds **7**—**16** were recorded with a long delay between pulses (8 s). The ^{13}C NMR spectra of compounds **12**—**16** exhibit signals for unsubstituted C(6) atoms at δ_C 57.5—64.5 and characteristic weak signals for C(6′) carbon atoms bearing an N substituent at δ_C 57.5—64.5 (see Experimental). The correctness of the signal assignment was further confirmed by the analysis of 2D NMR spectra of homo- (HOMOCOR {^{1}H—^{1}H}) and heteronuclear (HETCOR {^{1}H—^{13}C}) correlations, recording the DEPT spectrum of the solution, and also recording the spectrum of the solution at 20 and 80 °C for reliable assignment of signals for hydroxyl protons.

Scheme 1



R = Y (**7**, **8**), Z (**9**, **10**)
n = 2 (**3**, **7**, **9**), 3 (**4**, **8**, **10**)

Scheme 2



1, 2 **12—16**

X = I (**1**), Ts (**2**)

Compound	R′	*n*	R	Hal
7, **12**	Me	2	Y	I
8, **13**	Me	3	Y	I
9, **14**	Me	2	Z	I
10, **15**	Me	3	Z	I
11, **16**	H, Me	2	Y	—

In conclusion, we investigated new possibilities for the synthesis of cationic β-cyclodextrin derivatives containing covalently bonded residues of specified pharmacologically important acids, which are of interest to biomedical research in different directions.

Experimental

^{1}H and ^{13}C NMR spectra were recorded on a JEOL ECX-400 spectrometer (399.78 and 100.53 MHz, respectively) in DMSO-d_6, with ^{1}H and ^{13}C chemical shifts being reported relative to $SiMe_4$. Elemental analysis was performed on a FlashEA 1112HT analyzer. Thin-layer chromatography was carried out aluminum plates precoated with silica gel (Silufol UV-254), eluents: benzene—dioxane, 3 : 1 (A), *n*-butanol—ethanol—water, 5 : 4 : 3 (B). β-Cyclodextrin was purchased from Wacker (USA).

2-(Dimethylamino)ethyl (*RS*)-2-(4-isobutylphenyl)propionate (7). 2-(Dimethylamino)ethanol (**3**) (1.98 g, 22.25 mmol) in benzene (25 mL) was added dropwise to a solution of (*RS*)-2-(4-isobutylphenyl)propionyl chloride (5.00 g, 22.25 mmol) in benzene (10 mL) with stirring. After stirring at 20 °C for 3 h, benzene (30 mL) was added and the stirring was continued for 24 h at 20 °C. Then, saturated aqueous $NaHCO_3$ (10 mL) was added to the reaction mixture with stirring, the benzene layer was separated, dried with $CaCl_2$, the solvent was evaporated, the residue was evacuated (1 Torr) at 60 °C for 5 h. The yield was 5.18 g (84%), m.p. 80—82 °C, R_f = 0.45 (A). ^{1}H NMR, δ: 0.81 (d, 6 H, $CH(C\underline{H}_3)_2$, J = 6.4 Hz); 1.31 (d, 3 H, $CHC\underline{H}_3$, J = 7.0 Hz); 1.75 (m, 1 H, $C\underline{H}Me_2$); 2.09 (s, 6 H, NMe_2); 2.36 (d, 2 H, $CHC\underline{H}_2$, J = 7.3 Hz); 3.33 (t, 2 H, NCH_2); 3.72 (q, 1 H, CHC(O), J = 7.1 Hz); 4.07 (t, 2 H, CH_2O, J = 5.6 Hz); 7.04 (d, 2 H, *m*-H, J = 7.8 Hz), 7.14 (d, 2 H, *o*-H, J = 8.0 Hz). ^{13}C NMR, δ: 19.2 ($CH\underline{C}H_3$), 22.7 ($CH(\underline{C}H_3)_2$), 30.1 ($\underline{C}HMe_2$), 40.0 ($\underline{C}HC(O)$), 44.6 ($CH\underline{C}H_2$), 45.3 (NMe_2), 57.2 (NCH_2), 62.2 (OCH_2), 127.6 (*m*-C), 129.4 (*o*-C), 138.5 (*ipso*-C), 140.3 (*p*-C), 174.3 (C=O). Found (%): C, 74.02; H, 9.56; N, 5.23. $C_{17}H_{27}NO_2$. Calculated (%): C, 73.61; H, 9.81; N, 5.05.

Compounds **8—10** were obtained similarly.

3-(Dimethylamino)propyl (*RS*)-2-(4-isobutylphenyl)propionate (8) was obtained from (*RS*)-2-(4-isobutylphenyl)propionyl chloride (5.00 g, 22.25 mmol) and 3-(dimethylamino)-propan-1-ol (**4**) (2.90 g, 22.25 mmol). The yield was 5.51 g (85%), m.p. 110—112 °C, R_f = 0.40 (A). ^{1}H NMR, δ: 0.80 (d, 6 H, $CH(C\underline{H}_3)_2$, J = 6.5 Hz); 1.31 (d, 3 H, $CHC\underline{H}_3$, J = 7.1 Hz); 1.62 (m, 2 H, $NCH_2C\underline{H}_2$); 1.75 (m, 1 H, $C\underline{H}Me_2$); 2.10 (s, 6 H, NMe_2); 2.20 (t, 2 H, NCH_2); 2.37 (d, 2 H, $CHC\underline{H}_2$, J = 7.3 Hz); 3.72 (q, 1 H, CHC(O), J = 7.1 Hz); 4.07 (t, 2 H, CH_2O, J = 5.7 Hz); 7.04 (d, 2 H, *m*-H, J = 7.9 Hz); 7.14 (d, 2 H, *o*-H, J = 7.9 Hz). ^{13}C NMR, δ: 19.1 ($CH\underline{C}H_3$), 22.7 ($CH(\underline{C}H_3)_2$), 25.9 ($NCH_2\underline{C}H_2$), 30.2 ($\underline{C}HMe_2$), 40.0 ($\underline{C}HC(O)$), 44.7 ($CH\underline{C}H_2$), 46.3 (NMe_2), 55.3 (NCH_2), 62.7 (OCH_2), 127.6 (*m*-C), 129.3 (*o*-C), 138.5 (*ipso*-C), 140.3 (*p*-C), 174.4 (C=O). Found (%): C, 74.53; H, 6.86; N, 5.01. $C_{18}H_{29}NO_2$. Calculated (%): C, 74.18; H, 7.03; N, 4.81.

2-(Dimethylamino)ethyl (*RS*)-2-(3-benzoylphenyl)propionate (9) was obtained from (*RS*)-2-(3-benzoylphenyl)propionyl chloride (5.00 g, 18.33 mmol) and 2-(dimethylamino)ethanol (**3**) (1.63 g, 18.33 mmol). The yield was 5.93 g (82%), m.p. 100—102 °C (decomp.), R_f = 0.45 (A). ^{1}H NMR, δ: 1.35 (d, 3 H, $CHC\underline{H}_3$, J = 7.0 Hz); 2.10 (s, 6 H, NMe_2); 3.33 (t, 2 H, NCH_2); 3.77 (m, 1 H, $C\underline{H}CH_3$); 4.08 (t, 2 H, CH_2O, J = 5.6 Hz); 7.53—7.68 (m, 9 H, Ar). ^{13}C NMR, δ: 19.0 ($CH\underline{C}H_3$), 45.0 ($C\underline{H}Me$), 45.3 (NMe_2), 57.2 (NCH_2), 62.2 (OCH_2), 128.8—133.3 (Ar), 175.6 ($CH\underline{C}$=O), 195.9 (Ph$\underline{C}$=O). Found (%): C, 74.02; H, 7.06; N, 4.21. $C_{20}H_{23}NO_3$. Calculated (%): C, 73.82; H, 7.12; N, 4.30.

3-(Dimethylamino)propyl (*RS*)-2-(3-benzoylphenyl)propionate (10) was obtained from (*RS*)-2-(3-benzoylphenyl)propionyl chloride (5.00 g, 18.33 mmol) and 3-(dimethylamino)propan-1-ol **4** (2.39 g, 18.33 mmol). The yield was 6.27 g (83%), m.p. 123—125 °C, R_f = 40 (A). ^{1}H NMR, δ: 1.35 (d, 3 H, $CHC\underline{H}_3$, J = 7.0 Hz); 1.62 (m, $NCH_2C\underline{H}_2$); 2.10 (s, 6 H, NMe_2); 2.20 (t, 2 H, NCH_2); 3.77 (m, 1 H, $C\underline{H}Me$); 4.06 (t, 2 H, CH_2O, J = 5.6 Hz); 7.53—7.68 (m, 9 H, Ar). ^{13}C NMR, δ: 19.0 ($CH\underline{C}H_3$), 25.9 ($NCH_2\underline{C}H_2$), 45.0 ($C\underline{H}Me$), 46.3 (NMe_2), 55.3 (NCH_2), 62.6 (OCH_2), 128.8—133.3 (Ar), 175.6 ($CH\underline{C}$=O), 195.9 (Ph$\underline{C}$=O).

Found (%): C, 74.18; H, 7.49; N, 4.18. $C_{21}H_{25}NO_3$. Calculated (%): C, 74.31; H, 7.42; N, 4.13.

2-(Methylamino)ethyl (*RS*)-2-(4-isobutylphenyl)propionate (11). Sodium hydride (1.07 g, 44.50 mmol) was added to a solution of 2-(methylamino)ethanol **6** (1.67 g, 22.25 mmol) in DMF (30 mL) with stirring. The solution was stirred at 20 °C for 1 h, methanol (30 mL) was added and the stirring was continued for 1 h at 20 °C. A precipitate formed was filtered off, (*RS*)-2-(4-isobutylphenyl)propionyl chloride (5.00 g, 22.25 mmol) in benzene (30 mL) was added dropwise to the filtrate. After 24 h, a precipitate was filtered off, the filtrate was concentrated to 2 mL and diluted with diethyl ether (10 mL). An oil formed was dissolved in benzene (5 mL), the solvent was evaporated, the residue was evacuated (1 Torr) at 60 °C for 5 h. The yield was 1.64 g (28%), m.p. 78—80 °C (decomp.), R_f = 0.40 (A). ^{1}H NMR, δ: 0.81 (d, 6 H, CH(C<u>H</u>$_3$)$_2$, J = 6.9 Hz); 1.27 (d, 3 H, CHC<u>H</u>$_3$, J = 6.5 Hz); 1.75 (m, 1 H, C<u>H</u>Me$_2$); 2.36 (d, 2 H, CHC<u>H</u>$_2$, J = 7.3 Hz); 2.73 (m, 2 H, NCH$_2$); 3.49 (m, 3 H, NMe); 3.72 (q, 1 H, CHC(O), J = 7.1 Hz); 3.97 (m, 2 H, CH$_2$O); 7.02 (d, 2 H, *m*-H, J = 7.8 Hz); 7.14 (d, 2 H, *o*-H, J = 8.0 Hz). ^{13}C NMR, δ: 19.6 (CH<u>C</u>H$_3$), 22.7 (CH(<u>C</u>H$_3$)$_2$), 30.1 (<u>C</u>HMe$_2$), 33.7 (NMe), 40.0 (<u>C</u>HC(O)), 44.5 (CH<u>C</u>H$_2$), 52.2 (NCH$_2$), 58.1 (OCH$_2$), 127.7 (*m*-C), 129.2 (*o*-C), 129.6 (*ipso*-C), 138.8 (*p*-C), 175.4 (C=O). Found (%): C, 73.12; H, 9.50; N, 5.29. $C_{16}H_{25}NO_2$. Calculated (%): C, 72.97; H, 9.57; N, 5.32.

6-[(2-{2-[4-(Isobutyl)phenyl]propionyloxy}ethyl)(dimethyl)-ammonio]-6-deoxy-β-cyclodextrin iodide (12). Ether **7** (1.11 g, 4.00 mmol) was added to a solution of β-cyclodextrin iodo derivative **1** (1.00 g, 0.80 mmol), obtained by the improved procedure,[13] in DMF (30 mL) with stirring. The solution was stirred for 30 h at 100—110 °C, concentrated to 5 mL, and filtered, followed by the addition of acetone (30 mL). A precipitate formed was collected by filtration, washed with acetone (2×5 mL), and dried *in vacuo* (1 Torr) at 80 °C for 4 h. The yield was 0.63 g (52%), m.p. 260—262 °C (with decomp.), R_f = 0.75 (B). ^{1}H NMR, δ: 0.81 (d, 6 H, CH(C<u>H</u>$_3$)$_2$, J = 6.4 Hz); 1.31 (d, 3 H, CHC<u>H</u>$_3$, J = 7.0 Hz); 1.75 (m, 1 H, C<u>H</u>Me$_2$); 2.10 (s, 6 H, NMe$_2$); 2.35 (d, 2 H, CHC<u>H</u>$_2$, J = 7.3 Hz); 3.23—3.61 (m, 44 H, C(2)H—C(5)H, C(6)H$_2$, NCH$_2$); 3.85 (m, 1 H, CHC(O)); 4.07 (m, 2 H, CH$_2$O); 4.47 (br.s, 6 H, C(6)OH); 4.79 (br.s, 7 H, C(1)H); 5.71 (br.s, 14 H, C(2)OH, C(3)OH); 7.05 (d, 2 H, *m*-H, J = 7.8 Hz); 7.13 (d, 2 H, *o*-H, J = 8.0 Hz). ^{13}C NMR, δ: 19.1 (CH<u>C</u>H$_3$), 22.7 (CH(<u>C</u>H$_3$)$_2$), 30.1 (<u>C</u>HMe$_2$), 40.0 (<u>C</u>HC(O)), 44.6 (CH<u>C</u>H$_2$), 45.3 (NMe$_2$), 57.3 (NCH$_2$), 60.4 (C(6)), 62.4 (OCH$_2$), 64.5 (C(6′)), 72.5—73.6 (C(5), C(2), C(3)), 82.0 (C(4)), 102.5 (C(1)), 127.6 (*m*-C), 129.6 (*o*-C), 138.3 (*ipso*-C), 140.3 (*p*-C), 174.4 (C=O). Found (%): C, 46.73; H, 6.31; N, 0.95. $C_{59}H_{96}INO_{36}$. Calculated (%): C, 46.55; H, 6.36; N, 0.92.

Compounds **13—15** were obtained similarly.

6-[(3-{2-[4-(Isobutyl)phenyl]propionyloxy}propyl)(dimethyl)-ammonio]-6-deoxy-β-cyclodextrin iodide (13) was obtained from β-cyclodextrin iodo derivative **1** (1.00 g, 0.80 mmol) and ether **8** (1.17 g, 4.00 mmol). The yield was 0.60 g (49%), m.p. 265—267 °C (with decomp.), R_f = 0.71 (B). ^{1}H NMR, δ: 0.79 (d, 6 H, CH(C<u>H</u>$_3$)$_2$, J = 6.4 Hz); 1.31 (d, 3 H, CHC<u>H</u>$_3$, J = 7.0 Hz); 1.62 (m, 2 H, NCH$_2$C<u>H</u>$_2$); 1.75 (m, 1 H, C<u>H</u>Me$_2$); 2.15 (br.s, 6 H, NMe$_2$); 2.20 (t, 2 H, NCH$_2$); 2.46 (d, 2 H, CHC<u>H</u>$_2$, J = 7.3 Hz); 3.21—3.69 (m, 43 H, C(2)H—C(5)H, C(6)H$_2$, CHC(O)); 3.99 (m, 2 H, CH$_2$O); 4.47 (br.s, 6 H, C(6)OH); 4.79 (br.s, 7 H, C(1)H); 5.70 (br.s, 14 H, C(2)OH, C(3)OH); 7.05 (d, 2 H, *m*-H, J = 7.8 Hz); 7.13 (d, 2 H, *o*-H, J = 8.0 Hz). ^{13}C NMR, δ: 18.9 (CH<u>C</u>H$_3$), 22.7 (CH(<u>C</u>H$_3$)$_2$), 26.0 (NCH$_2$<u>C</u>H$_2$), 30.1 (<u>C</u>HMe$_2$), 40.0 (<u>C</u>HC(O)), 44.3—45.1 (NMe$_2$, CH<u>C</u>H$_2$), 55.4 (NCH$_2$), 60.4 (C(6)), 62.7 (OCH$_2$), 64.5 (C(6′)), 72.5—73.6 (C(5), C(2), C(3)), 82.0 (C(4)), 102.5 (C(1)), 127.6 (*m*-C), 129.6 (*o*-C), 138.5 (*ipso*-C), 140.3 (*p*C), 174.4 (C=O). Found (%): C, 47.04; H, 6.39; N, 0.89. $C_{60}H_{98}INO_{36}$. Calculated (%): C, 46.91; H, 6.43; N, 0.91.

6-[{2-[2-(3-(Benzoylphenyl)propionyloxy]ethyl}(dimethyl)-ammonio]-6-deoxy-β-cyclodextrin iodide (14) was obtained from β-cyclodextrin iodo derivative **1** (1.00 g, 0.80 mmol) and ether **9** (1.30 g, 4.00 mmol). The yield was 0.59 g (47%), m.p. 246—248 °C (with decomp.), R_f = 0.45 (A). ^{1}H NMR, δ: 1.35 (d, 3 H, CHC<u>H</u>$_3$, J = 7.0 Hz); 2.10 (s, 6 H, NMe$_2$); 3.23—3.61 (m, 44 H, C(2)H—C(5)H, C(6)H$_2$, NCH$_2$); 3.79 (m, 1 H, C<u>H</u>Me); 4.08 (t, 2 H, CH$_2$O, J = 5.6 Hz); 4.47 (br.s, 6 H, C(6)OH); 4.79 (br.s, 7 H, C(1)H); 5.71 (br.s, 14 H, C(2)OH, C(3)OH); 7.53—7.68 (m, 9 H, Ar). ^{13}C NMR, δ: 19.0 (CH<u>C</u>H$_3$), 45.0 (C<u>H</u>Me), 45.3 (NMe$_2$), 57.2 (NCH$_2$), 60.4 (C(6)), 62.2 (OCH$_2$), 64.5 (C(6′)), 72.5—73.6 (C(5), C(2), C(3)), 82.0 (C(4)), 102.5 (C(1)), 128.8—133.3 (Ar), 175.6 (CH<u>C</u>=O), 195.9 (Ph<u>C</u>=O). Found (%): C, 47.53; H, 5.85; N, 0.92. $C_{62}H_{92}INO_{37}$. Calculated (%): C, 47.42; H, 5.91; N, 0.89.

6-[{3-[2-(3-(Benzoylphenyl)propionyloxy]propyl}(dimethyl)-ammonio]-6-deoxy-β-cyclodextrin iodide (15) was obtained from β-cyclodextrin iodo derivative **1** (1.00 g, 0.80 mmol) and ether **10** (1.36 g, 4.00 mmol). The yield was 0.57 g (45%), m.p. 251—253 °C (with decomp.), R_f = 0.40 (A). ^{1}H NMR, δ: 1.35 (d, 3 H, CHC<u>H</u>$_3$, J = 7.0 Hz); 1.62 (m, NCH$_2$C<u>H</u>$_2$); 2.15 (br.s, 6 H, NMe$_2$); 2.20 (t, 2 H, NCH$_2$); 2.46 (d, 2 H, CHC<u>H</u>$_2$, J = 7.3 Hz); 3.21—3.69 (m, 43 H, C(2)H—C(5)H, C(6)H$_2$, CHC(O)); 3.99 (m, 2 H, CH$_2$O); 4.47 (br.s, 6 H, C(6)OH); 4.79 (br.s, 7 H, C(1)H); 5.70 (br.s, 14 H, C(2)OH, C(3)OH); 7.53—7.68 (m, 9 H, Ar). ^{13}C NMR, δ: 18.9 (CH<u>C</u>H$_3$), 26.0 (NCH$_2$<u>C</u>H$_2$), 45.0 (C<u>H</u>Me), 46.3 (NMe$_2$), 55.4 (NCH$_2$), 60.4 (C(6)), 62.6 (OCH$_2$), 64.5 (C(6′)), 72.5—73.6 (C(5), C(2), C(3)), 82.0 (C(4)), 102.5 (C(1)), 128.8—133.3 (Ar), 175.6 (CH<u>C</u>=O), 195.9 (Ph<u>C</u>=O). Found (%): C, 47.93; H, 5.93; N, 0.92. $C_{63}H_{94}INO_{37}$. Calculated (%): C, 47.76; H, 5.98; N, 0.88.

6-[(2-{2-[4-(Isobutyl)phenyl]propionyloxy}ethyl)(methyl)-ammonio]-6-deoxy-β-cyclodextrin iodide (16). Sodium carbonate (0.067 g) and ether **11** (0.21 g, 0.80 mmol) in DMF (10 mL) were added to a solution of β-cyclodextrin monotosyl derivative **2** (1.00 g, 0.80 mmol) in DMF (20 mL) with stirring. The solution was stirred at 80 °C for 6 h, concentrated 5 mL, and filtered, followed by the addition of acetone (30 mL). A precipitate formed was collected by filtration, washed with acetone (2×5 mL) and diethyl ether (2×5 mL), and dried *in vacuo* (1 Torr) for 4 h at 80 °C. The yield was 0.35 g (32%), m.p. 297—299 °C (with decomp.), R_f = 0.58 (B). ^{1}H NMR, δ: 0.79 (d, 6 H, CH(C<u>H</u>$_3$)$_2$, J = 7.0 Hz); 1.25 (d, 3 H, CHC<u>H</u>$_3$, J = 7.3 Hz); 1.74 (m, 1 H, C<u>H</u>Me$_2$); 2.33 (s, 3 H, NMe); 2.39 (d, 2 H, CHC<u>H</u>$_2$, J = 7.3 Hz); 2.46 (br.s, 2 H, NCH$_2$); 2.78 (m, 2 H, CH$_2$O); 3.21—3.33 (m, 14 H, C(2)H, C(4)H); 3.42 (m, 1 H, CHC(O)); 3.47—3.65 (m, 28 H, C(3)H, C(5)H, C(6)H$_2$); 3.98 (br.s, 20 H, C(2)OH, C(3)OH, C(6)OH); 4.78 (br.s, 7 H, C(1)H); 7.00 (d, 2 H, *m*-H, J = 7.5 Hz); 7.12 (d, 2 H, *o*-H, J = 7.6 Hz). ^{13}C NMR, δ: 19.8 (CH<u>C</u>H$_3$), 22.7 (CH(<u>C</u>H$_3$)$_2$), 30.2 (<u>C</u>HMe$_2$), 33.5 (NMe), 40.0 (<u>C</u>HC(O)), 44.8 (CH<u>C</u>H$_2$), 46.7 (OCH$_2$), 51.6 (NCH$_2$), 57.5 (C(6′)), 60.4 (C(6)), 72.5—73.6 (C(5), C(2), C(3)), 82.0 (C(4)), 102.5 (C(1)), 127.7 (*m*-C), 129.6 (*o*-C), 139.3 (*ipso*-C), 140.9 (*p*-C), 177.8 (C=O). Found (%): C, 50.63; H, 6.84; N, 0.99. $C_{58}H_{93}INO_{36}$. Calculated (%): C, 50.47; H, 6.79; N, 1.01.

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