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NMR Study of Supramolecular Inclusion Complexes of 7-[2-(Morpholin-4-yl)ethyl]-3-(2-ethoxyethyl)-3,7-diazabicyclo[3.3.1]nonane with Cyclodextrins

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Abstract—Structures of 7-[2-(morpholin-4-yl)ethyl]-3-(2-ethoxyethyl)-3,7-diazabicyclo[3.3.1]nonane and its inclusion complexes with α-, β-, and γ-cyclodextrins have been studied by ^{1}H, ^{13}C, COSY, and HMQC NMR spectroscopy. The complexes are formed via entering of one morpholine fragment of the substrate into the inner sphere of a receptor molecule.

Keywords: 7-(2-morpholinoethyl)-3-(2-ethoxyethyl)-3,7-diazabicyclo[3.3.1]nonane, α-, β-, and γ-cyclodextrin, inclusion complex, NMR spectroscopy

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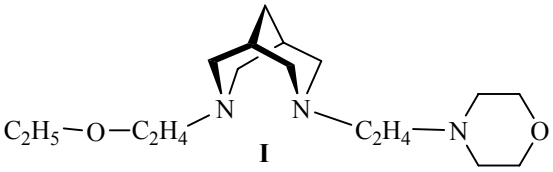
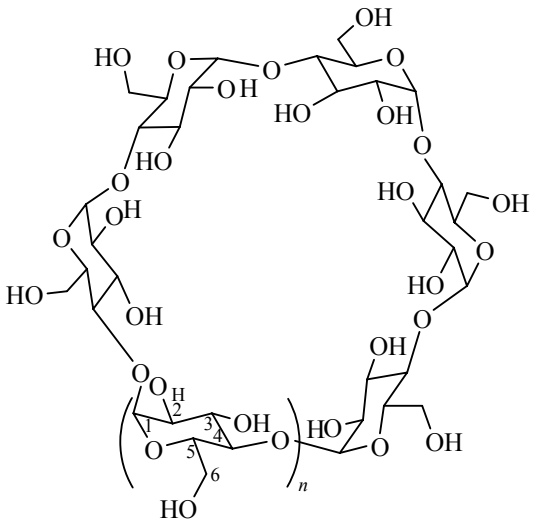
NMR spectroscopy has been recognized among the most informative methods to investigate structure and intermolecular interactions in inclusion complexes [1]. Therefore, we have applied this method to study new drug formulations of pharmaceutically active 7-[2-(morpholin-4-yl)ethyl]-3-(2-ethoxyethyl)-3,7-diazabicyclo[3.3.1]nonane **I** with cyclodextrins.

Compound **I** possesses a wide range of biological activity due to the presence of two piperidine rings in the structure; in particular, it displays a local anesthetic effect [2].

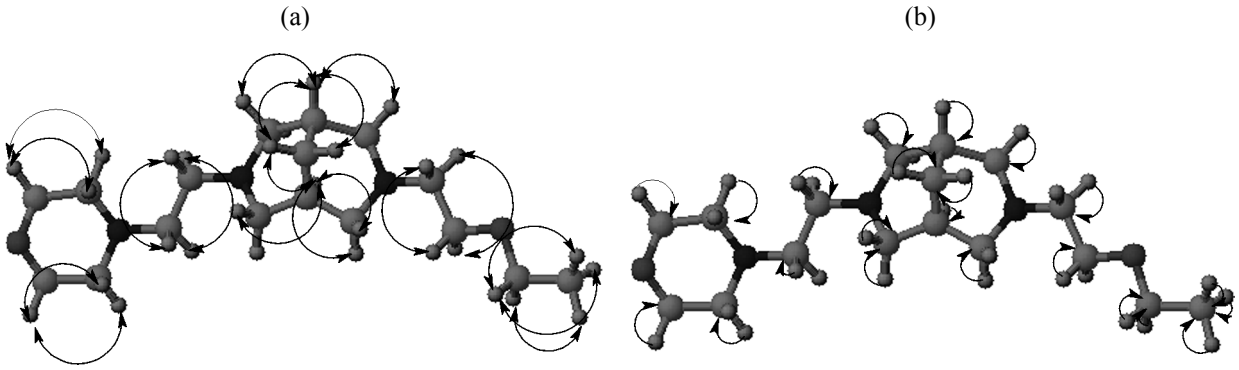


I

Inclusion of active component **I** into the cavity of a *host* molecule can increase the substance solubility, improve its bioavailability and physicochemical stability, and protect it from biodegradation by preventing the interaction with the package [3]. Among the recognized drug-encapsulating (cucurbiturils, crown ethers, calixarenes, and others), cyclodextrins [4] are distinguished by a number of advantageous properties. Cyclodextrins are accessible compounds produced from renewable source (starch), the most widespread types of them being α-, β-, and γ-cyclodextrins containing 6, 7, and 8 glucopyranose units, respectively. Cyclodextrins are capable of hydrophobic binding of a *guest* molecule in their cavity in aqueous medium.



n = 1 (α), 2 (β), 3 (γ).



Scheme of the correlations in the spectra (a) COSY and (b) HMQC of compound **I**.

NMR study of supramolecular inclusion complexes **II–IV** formed by α-, β-, and γ-cyclodextrins, respectively, is based on comparison the ^{1}H and ^{13}C chemical shifts of the substrate **I** and the receptors (α-, β-, and γ-cyclodextrins) in the free and complex states. For instance, the change of chemical shift of the inner or outer protons upon the complex formation concludes about formation of the inner or outer complexes, respectively. Similarly, changes of the substrate atoms chemical shifts define the position of the complex forming site [5, 6].

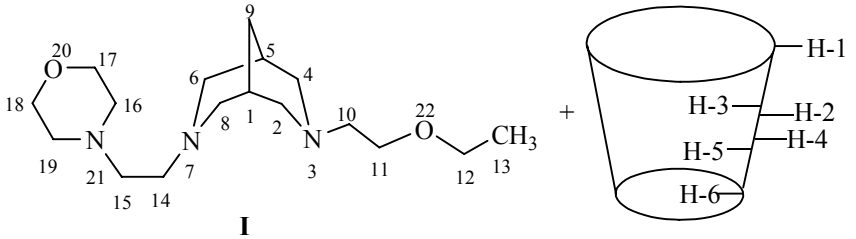
^{1}H NMR spectrum of compound **I** contained a triplet signal of the methyl group of ethoxyethyl substituent (H^{13}) in the strong-field region at 1.03–1.07 ppm. Methylene groups of the ethoxyethyl fragment resonated in weaker field at 3.38 (H^{12}), 3.40 (H^{11}), and 2.30 (H^{10}) ppm. Protons of symmetrically located CH_2 groups of morpholine ring (H^{17} and H^{18}; H^{16} and H^{19}) resonated as triplet signals at 3.50 and 2.40 ppm, respectively. The signals at 2.30–2.36 ppm were assigned to protons of the ethylene bridge (H^{14} and H^{15}).

The axial protons ($H^{2a,4a}$ and $H^{6a,8a}$) signals were observed at 2.17–2.18 and 2.60–2.63 ppm as doublets of doublets (^{2}J 10.8 and ^{3}J 3.9 Hz). The signals of equatorial protons ($H^{2e,4e}$ and $H^{6e,8e}$) were doublets of doublets as well (δ 2.20–2.21 and 2.63–2.66 ppm,

Table 1. Changes of ^{1}H and ^{13}C chemical shifts of compound **I** upon complex formation with c α- (δ_1), β- (δ_2), and γ-cyclodextrin (δ_3)

Atom	CH_x	$\Delta\delta_1$, ppm		$\Delta\delta_2$, ppm		$\Delta\delta_3$, ppm	
		^{1}H	^{13}C	^{1}H	^{13}C	^{1}H	^{13}C
1, 5	CH	0.08	–0.34	0.04	–0.23	0.06	–0.19
2*a*,4*a*	CH_2	0.03	–0.09	0.04	–0.02	0.02	–0.08
2*e*, 2*e*		0.04		0.03		0.03	
6*a*, 8*a*	CH_2	0.14	–0.09	0.00	–0.02	0.02	–0.17
6*e*, 8*e*		0.13		0.02		0.01	
9	CH_2	0.08	–0.02	0.02	–0.18	0.06	0.22
10	CH_2	0.02	–0.01	0.05	0.01	0.05	0.91
11	CH_2O	–0.04	0.08	–0.02	0.02	0.01	0.12
12	CH_2O	–0.04	–0.03	0.00	0.02	0.02	0.07
13	CH_3	0.01	–0.01	0.00	0.01	0.00	0.03
14	CH_2	0.05	0.01	0.02	1.04	0.02	–1.07
15	CH_2	0.05	0.00	0.05	0.03	0.05	0.00
16	CH_2	–0.01	–0.22	–0.01	–0.13	–0.01	–0.30
17	CH_2O	–0.08	–0.08	–0.09	–0.08	–0.10	–0.19
18	CH_2O	–0.08	–0.08	–0.09	–0.08	–0.10	–0.19
19	CH_2	–0.01	–0.22	–0.01	–0.13	–0.01	–0.30

Scheme 1.



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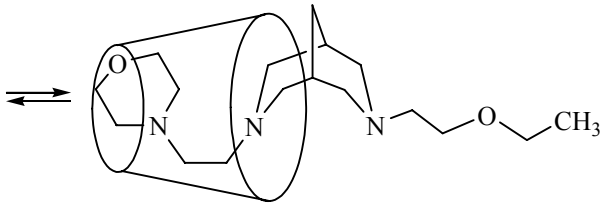

II–IV

^2J 10.8 and ^3J 1.8 Hz). Resonance of the protons at $C^{1,5}$ atoms was observed in stronger field at 1.81 ppm.

Structure of compound **I** was further confirmed by data of two-dimensional NMR spectroscopy: COSY ^1H–^1H and HMQC ^1H–^{13}C (see figure).

Formation of supramolecular inclusion complexes was confirmed by change of the proton chemical shifts Δδ in compound **I** (Table 1). In particular, majority of the proton signals of the *guest* molecule were shifted upfield in the complexes spectra. Significant difference of the chemical shifts was observed in the cases of H^{14}, H^{15}, H^{17}, and H^{18} signals, located near more electronegative oxygen and nitrogen atoms. The signals shift indicated entering of the substrate morpholine fragment into the inner sphere of cyclodextrin. Practically all proton signals of compound **I** were marginally shifted in the complexes spectra, thus indicating the non-valence interactions with the outer-sphere protons of cyclodextrin and/or of the solvent molecules.

Analysis of the ^1H NMR signals of α-, β-, and γ-cyclodextrins revealed the shift of majority of the receptor signals upon the complex formation (Table 2). The chemical shift changes were the most prominent in the cases of H^3 and H^5 atoms oriented towards the inner part of the cyclodextrin cone, evidencing about formation of the inner inclusion complexes [5, 6]. The signals shift Δδ of the H^3 and H^5 atoms ranged from –0.3 to 0.04 ppm in the cases of six- and eight-unit α- and γ-cyclodextrins. In the case of β-cyclodextrin, the chemical shifts revealed a jump by up to 0.13 ppm. The difference in the receptors spectral properties accompanying the complex formation should be assigned primarily to the different complementarity complex-forming components resulting in the different interactions strength.

Marginally changed chemical shifts of the outer-sphere protons of the macrocyclic cavity indicated the surface interactions which were the most significant in the case of β-cyclodextrin complex.

Table 2. ^1H NMR chemical shifts of α-, β-, and γ-cyclodextrin in a free state (δ_0) and in complexes **II–IV** (δ)

Atom	α-Cyclodextrin			β-Cyclodextrin			γ-Cyclodextrin		
	δ_0, ppm	δ, ppm	$\Delta\delta^a$, ppm	δ_0, ppm	δ, ppm	$\Delta\delta^a$, ppm	δ_0, ppm	δ, ppm	$\Delta\delta^a$, ppm
H^1	4.76	4.75	–0.01	4.77	4.78	0.01	4.83	4.83	0
H^2	3.22	3.23	0.01	3.27	3.28	0.01	3.30	3.32	0.02
H^3	3.37	3.34	–0.03	3.45	3.58	0.13	3.37	3.41	0.04
H^4	3.24	3.25	0.01	3.30	3.31	0.01	3.32	3.32	0
H^5	3.34	3.32	–0.02	3.45	3.58	0.13	3.37	3.41	0.04
H^6	3.60	3.60	0	3.57	3.60	0.03	3.58	3.57	–0.01

[a] $\Delta\delta = \delta - \delta_0$.

Comparison of ^{1}H signals integral intensities of the receptors and compound **I** in the free and encapsulated forms revealed that the 1 : 1 inclusion complexes of compound **I** with cyclodextrins **II–IV** were formed (Scheme 1).

EXPERIMENTAL

α-, β-, and γ-cyclodextrins were used (Fluka, 99%). ^{1}H and ^{13}C NMR spectra were recorded using a JNN-ECA 400 Jeol instrument (400 and 100 MHz, respectively) in DMSO-d_6. Chemical shifts were referenced to the residual proton signals or carbon atoms of the solvent.

7-[2-(Morpholin-4-yl)ethyl]-3-(2-ethoxyethyl)-3,7-diazobicyclo[3.3.1]nonane (I). 8.42 g of KOH was added at 60°C to a mixture of 4.0 g (0.0123 mol) of 7-[2-(morpholin-4-yl)ethyl]-3-(2-ethoxyethyl)-3,7-diazobicyclo[3.3.1]nonan-9-one and 2.04 g (0.0637 mol) of hydrazine hydrate (95%) in 36.4 mL of triethylene glycol. The reaction mixture was stirred at 150°C during 4 h. Water and excess of hydrazine were distilled off at 190–200°C. After cooling to room temperature, 60 mL of distilled water was added to the mixture, and the reaction products were extracted with diethyl ether. The combined extracts were dried over $MgSO_4$. The solvent was distilled off. Yield 2.97 g (77.5%), pale yellow oil. ^{1}H NMR spectrum, δ, ppm: 1.05 t (3H, CH_3, ^3J 7.1 Hz), 1.36 br.t (2H, $CHC\underline{H}_2CH_{pip}$, ^3J 3.2 Hz), 1.81 br.s (2H, $C\underline{H}CH_2C\underline{H}_{pip}$), 2.18 d.d (2H, $C\underline{H}_2^{ax}NC\underline{H}_2^{ax}$, ^2J 10.8, ^3J 3.9 Hz), 2.28 d.d (2H, $C\underline{H}_2^{eq}NC\underline{H}_2^{eq}$, ^2J 10.8, ^3J 1.8 Hz), 2.30 d.d (2H, $NC\underline{H}_2CH_2O$, ^2J 4.41, ^3J 3.66 Hz), 2.32 t (2H, $NC\underline{H}_2CH_2N$, ^3J 5.0 Hz), 2.34 t (2H, $NCH_2C\underline{H}_2N_{morph}$, ^3J 3.3 Hz), 2.40 br.t (4H, $C\underline{H}_2NC\underline{H}_{2morph}$, ^3J 4.1 Hz), 2.63 d.d (4H, $C\underline{H}_2^{ax}NC\underline{H}_2^{ax}$, ^2J 10.8, ^3J 3.9 Hz), 2.66 d.d (4H, $C\underline{H}_2^{eq}NC\underline{H}_2^{eq}$, ^2J 10.8, ^3J 1.8 Hz), 3.36 q (2H, $OC\underline{H}_2CH_3$, ^3J 6.9 Hz), 3.38 t (2H, $CH_2C\underline{H}_2O$, ^3J 6.4 Hz), 3.50 t (4H, $C\underline{H}_2OC\underline{H}_{2morph}$, ^3J 4.6 Hz). ^{13}C NMR spectrum, δ_C, ppm: 15.73 (CH_3), 29.27 ($\underline{C}HCH_2\underline{C}H$), 30.15 ($CH\underline{C}H_2CH$), 54.36 ($\underline{C}H_2N\underline{C}H_{2morph}$), 55.70 ($N_{pip}CH_2\underline{C}H_2N_{morph}$), 56.88 ($N_{pip}\underline{C}H_2CH_2N_{morph}$), 58.11 ($\underline{C}H_2N\underline{C}H_{2pip}$), 58.20 ($\underline{C}H_2N\underline{C}H_{2pip}$), 58.31 ($N_{pip}\underline{C}H_2CH_2O$), 65.94 ($N_{pip}CH_2\underline{C}H_2O$), 66.85 ($C\underline{H}_2OC\underline{H}_{2morph}$), 68.30 ($OC\underline{H}_2CH_3$). Found, %: C 65.55; H 10.55. $C_{17}H_{33}N_3O_2$. alculated, %: C 65.59; H 10.61.

Inclusion complex of 7-[2-(morpholin-4-yl)ethyl]-3-(2-ethoxyethyl)-3,7-diazobicyclo[3.3.1]nonane I with α-cyclodextrin (II). Hot solutions of 0.1 g (3.2 mmol) of compound **I** in 3 mL of ethanol and of 0.31 g of α-cyclodextrin in 5 mL of distilled water were mixed. The mixture was put into a desiccator to evaporate ethanol and water at 50–55°C. Yield 0.32 g, amorphous pale brown powder; charring at $T > 240$°C. ^{1}H NMR spectrum, δ, ppm: 1.06 t (3H, CH_3, ^3J 7.1 Hz), 1.44 br.t (2H, $CHC\underline{H}_2CH_{pip}$, ^3J 3.2 Hz), 1.89 br. s (2H, $C\underline{H}CH_2C\underline{H}_{pip}$), 2.21 d.d (2H, $C\underline{H}_2^{ax}NC\underline{H}_2^{ax}$, ^2J 10.8, ^3J 3.9 Hz), 2.32 d.d (2H, $C\underline{H}_2^{eq}NC\underline{H}_2^{eq}$, ^2J 10.8, ^3J 1.8 Hz), 2.32 d.d (2H, $NC\underline{H}_2CH_2O$, ^2J 4.41, ^3J 3.66 Hz), 2.37 t (2H, $N_{pip}C\underline{H}_2CH_2N_{morph}$, ^3J 5.0 Hz), 2.39 t (2H, $N_{pip}CH_2C\underline{H}_2N_{morph}$, ^3J 3.3 Hz), 2.39 br.t (4H, $C\underline{H}_2NC\underline{H}_{2morph}$, ^3J 4.1 Hz), 2.77 d.d (4H, $C\underline{H}_2^{ax}NC\underline{H}_2^{ax}$, ^2J 10.8, ^3J 3.9 Hz), 2.79 d.d (4H, $C\underline{H}_2^{eq}NC\underline{H}_{2eq}$, ^2J 10.8, ^3J 1.8 Hz), 3.23 d.d [6H, α-cyclodextrin, $(C\underline{H}OH)_6$, ^2J 10.2, ^3J 5.3 Hz], 3.25 t [6H, α-cyclodextrin, $(CHO)_6$, ^2J 10.4 Hz], 3.32 q (2H, $OC\underline{H}_2CH_3$, ^3J 6.9 Hz), 3.34 t (2H, $CH_2C\underline{H}_2O$, ^3J 6.4 Hz), 3.32 m [6H, α-cyclodextrin, $(C\underline{H}CH_2)_6$], 3.34 t {6H, α-cyclodextrin $[C\underline{H}(OH)CHO]_6$, ^2J 10.7 Hz}, 3.42 t (4H, $C\underline{H}_2OC\underline{H}_2$, ^3J 4.6 Hz) 3.60 d [12H, α-cyclodextrin, $(CH_2)_6$, ^3J 5.7 Hz], 4.75 d [6H, α-cyclodextrin, $(OC\underline{H}O)_6$, ^2J 4.8 Hz]. ^{13}C NMR spectrum, δ_C, ppm: 15.72 (CH_3), 28.93 ($\underline{C}HCH_2\underline{C}H$), 30.13 ($CH\underline{C}H_2CH$), 54.14 ($\underline{C}H_2N\underline{C}H_{2morph}$), 58.02 ($\underline{C}H_2N\underline{C}H_{2pip}$), 58.11 ($\underline{C}H_2N\underline{C}H_{2pip}$), 60.53 [α-cyclodextrin, $(CH_2)_6$], 66.02 ($N_{pip}\underline{C}H_2CH_2O$), 66.77 ($C\underline{H}_2OC\underline{H}_{2morph}$), 72.65 [α-cyclodextrin, $(\underline{C}HCH_2)_6$], 73.81 {α-cyclodextrin, $[\underline{C}H(OH)CHO]_6$}, 82.61 [α-cyclodextrin, $(CHO)_6$], 102.50 [α-cyclodextrin, $(OCHO)_6$]. Found, % C 49.59; H 7.35. $C_{53}H_{93}N_3O_{32}$. Calculated, % C 49.57; H 7.32.

Inclusion complex of 7-[2-(morpholin-4-yl)ethyl]-3-(2-ethoxyethyl)-3,7-diazobicyclo[3.3.1]nonane I with β-cyclodextrin (III) was prepared similarly from 0.137 g (0.4 mmol) of compound **I** and 0.5 g of β-cyclodextrin. Yield 0.51 g, amorphous pale brown powder; charring at $T > 240$°C. ^{1}H NMR spectrum, δ, ppm: 1.05 t (3H, CH_3, ^3J 7.1 Hz), 1.38 br.t (2H, $CHC\underline{H}_2CH_{pip}$), 1.85 br. s (2H, $C\underline{H}CH_2C\underline{H}_{pip}$), 2.22 d.d (2H, $C\underline{H}_2^{ax}NC\underline{H}_2^{ax}$, ^2J 10.8, ^3J 3.9 Hz), 2.31 d.d (2H, $C\underline{H}_2^{eq}NC\underline{H}_2^{eq}$, ^2J 10.8, ^3J 1.8 Hz), 2.35 d.d (2H, $NC\underline{H}_2CH_2O$, ^2J 4.41, ^3J 3.66 Hz), 2.34 t (2H, $N_{pip}C\underline{H}_2CH_2N_{morph}$, ^3J 5.0 Hz), 2.37 t (2H, $N_{pip}CH_2C\underline{H}_2N_{morph}$, ^3J 3.3 Hz), 2.39 br.t (4H, $C\underline{H}_2NC\underline{H}_{2morph}$, ^3J 4.1 Hz), 2.63 d.d (4H, $C\underline{H}_2^{ax}NC\underline{H}_2^{ax}$, ^2J 10.8, ^3J 3.9 Hz), 2.68 d.d (4H, $C\underline{H}_2^{eq}NC\underline{H}_2^{eq}$, ^2J 10.8, ^3J 1.8 Hz), 3.28 d.d [7H, β-cyclodextrin, $(C\underline{H}OH)_7$, ^2J 10.2 , ^3J 5.3 Hz], 3.31 t [7H, β-cyclodextrin $(CHO)_7$, ^2J 10.4 Hz], 3.36 q (2H, $OC\underline{H}_2CH_3$, ^3J 6.9 Hz), 3.36 t (2H, $CH_2C\underline{H}_2O$, ^3J 4.6 Hz), 3.58 m [7H, β-cyclo-

dextrin, (C<u>H</u>CH$_2$)$_7$], 3.58 t {7H, β-cyclodextrin [C<u>H</u>(OH)CHO]$_7$, ^2J 10.7 Hz}, 3.41 t (4H, C<u>H$_2$</u>OC<u>H$_2$</u>, ^3J 4.6 Hz), 3.60 d [14H, β-cyclodextrin, (CH$_2$)$_7$, ^3J 5.7 Hz], 4.78 d [7H, β-cyclodextrin, (OC<u>H</u>O)$_7$, ^2J 4.8 Hz]. ^{13}C NMR spectrum, δ_C, ppm: 15.74 (CH$_3$), 29.04 (<u>C</u>HCH$_2$<u>C</u>H), 29.97 (CH<u>C</u>H$_2$CH), 54.23 (<u>C</u>H$_2$N<u>C</u>H$_{2morph}$), 60.45 [β-cyclodextrin, (CH$_2$)$_7$], 65.96 (N$_{pip}$<u>C</u>H$_2$CH$_2$O), 66.77 (C<u>H$_2$</u>OC<u>H$_{2morph}$</u>), 72.57 [β-cyclodextrin, (<u>C</u>HCH$_2$)$_7$], 72.97 {β-cyclodextrin, [<u>C</u>H(OH)CHO]$_7$}, 73.58 {β-cyclodextrin, [<u>C</u>H(OH)CHO]$_7$}, 82.09 [β-cyclodextrin, (CHO)$_7$], 102.51 [β-cyclodextrin, (OCHO)$_7$]. Found, %: C 48.95; H 7.24. $C_{59}H_{103}N_3O_{37}$. Calculated, %: C 49.00; H 7.19.

Inclusion complex of 7-[2-(morpholin-4-yl)ethyl]-3-(2-ethoxyethyl)-3,7-diazobicyclo[3.3.1]nonane I with γ-cyclodextrin (IV) was prepared similarly from 0.05 g (0.16 mmol) of compound **I** and 0.2 g of γ-cyclodextrin. Yield 0.2 g, amorphous white powder; charring at T > 240°C. ^{1}H NMR spectrum, δ, ppm: 1.05 t (3H, CH$_3$, ^3J 7.1 Hz), 1.42 br.t (2H, CHC<u>H$_2$</u>CH$_{pip}$, ^3J 3.2 Hz), 1.87 br.s (2H, C<u>H</u>CH$_2$C<u>H</u>$_{pip}$), 2.20 d.d (2H, C<u>H$_2$</u>^{ax}NC<u>H$_2$</u>^{ax}, ^2J 10.8, ^3J 3.9 Hz), 2.31 d.d (2H, C<u>H$_2$</u>^{eq}NC<u>H$_2$</u>^{eq}, ^2J 10.8, ^3J 1.8 Hz), 2.35 d.d (2H, NC<u>H$_2$</u>CH$_2$O, ^2J 4.41, ^3J 3.66 Hz), 2.34 t (2H, N$_{pip}$C<u>H$_2$</u>CH$_2$N$_{morph}$, ^3J 5.0 Hz), 2.39 t (2H, N$_{pip}$CH$_2$C<u>H$_2$</u>N$_{morph}$, ^3J 3.3 Hz), 2.39 br.t (4H, C<u>H$_2$</u>NC<u>H$_{2morph}$</u>, ^3J 4.1 Hz), 2.65 d.d (4H, C<u>H$_2$</u>^{ax}NC<u>H$_2$</u>^{ax}, ^2J 10.8, ^3J 3.9 Hz), 2.67 d.d (4H, C<u>H$_2$</u>^{eq}NC<u>H$_2$</u>^{eq}, ^2J 10.8, ^3J 1.8 Hz), 3.32 d.d [8H, γ-cyclodextrin, (C<u>H</u>OH)$_8$, ^2J 10.2, ^3J 5.3 Hz], 3.32 t [8H, γ-cyclodextrin, (CHO)$_8$, ^2J 10.4 Hz], 3.38 q (2H, OC<u>H$_2$</u>CH$_3$, ^3J 6.9 Hz), 3.39 t (2H, CH$_2$C<u>H$_2$</u>O, ^3J 6.4 Hz), 3.41 m [8H, γ-cyclodextrin, (C<u>H</u>CH$_2$)$_8$], 3.41 t {8H, γ-cyclodextrin [C<u>H</u>(OH)CHO]$_8$, ^2J 10.7 Hz}, 3.40 t (4H, C<u>H$_2$</u>OC<u>H$_2$</u>, ^3J 4.6 Hz), 3.57 d [16H, γ-cyclodextrin, (CH$_2$)$_8$, ^3J 5.7 Hz], 4.83 d [8H, γ-cyclodextrin, (OC<u>H</u>O)$_8$, ^2J 4.8 Hz]. ^{13}C NMR spectrum, δ_C, ppm: 15.76 (CH$_3$), 29.08 (<u>C</u>HCH$_2$<u>C</u>H), 30.37 (CH<u>C</u>H$_2$CH), 54.06 (<u>C</u>H$_2$N<u>C</u>H$_{2morph}$), 58.03 (<u>C</u>H$_2$N<u>C</u>H$_2$), 59.22 (N<u>C</u>H$_2$CH$_2$), 60.45 [γ-cyclodextrin, (CH$_2$)$_8$], 66.06 (N$_{pip}$<u>C</u>H$_2$CH$_2$O), 66.66 (C<u>H$_2$</u>OC<u>H$_{2morph}$</u>), 72.65 [γ-cyclodextrin, (<u>C</u>HCH$_2$)$_8$], 73.09 {γ-cyclodextrin, [<u>C</u>H(OH)CHO]$_8$}, 73.41 {γ-cyclodextrin, [<u>C</u>H(OH)·CHO]$_8$}, 81.43 [γ-cyclodextrin, (CHO)$_8$], 102.21 [γ-cyclodextrin, (OCHO)$_8$]. Found, % C 48.47; H 7.04. $C_{65}H_{113}N_3O_{42}$. Calculated, % C 48.50; H 7.08.

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