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Inclusion complexes of N-sulfamoyloxazolidinones with β-cyclodextrin

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Abstract—A study of inclusion complexes of six N-sulfamoyloxazolidinone derivatives with β-cyclodextrin is described. The inclusion complexes were prepared in solution and in solid state with stoichiometry host–guest 1:1, and characterized. In solution, the complexation was carried out by spectrophotometric measurements at 25 °C. The stoichiometries and stability constants of complexes at various pHs have been determined using second-derivative spectrophotometry UV–vis. Hydrophobic properties of N-sulfamoyloxazolidinones are improved following their inclusion into β-CD.

1. Introduction

Cyclodextrins (CDs) are well-known naturally occurring cyclic oligosaccharides composed of several glucose residues linked with O-α-D-glucopyranosyl-(1 → 4) bonds. Among them, β-CD is receiving increasing attention due to its low cost and capacity to interact with a wide variety of guest molecules in aqueous media. A considerable literature was devoted to β-CD and its application, especially in the pharmacological area.[1]

β-CD is shaped like a truncated cone with a relatively hydrophobic cavity surrounded by the secondary OH in the wider rim and by the primary OH in the smaller rim. Consequently, it can accommodate many kinds of organic compounds into its cavity to form inclusion complexes in aqueous solutions.

Much interest has arisen surrounding the beneficial effect of inclusion complexes formation between β-CD and molecules of biological interests. Thus, molecular encapsulation can increase the stability, improve the solubility and bioavailability of the substance and modify the pharmacokinetics of the resulting drugs with a subsequent reduction of adverse effects.[1] Therefore as part of our ongoing investigation concerning the complexation behavior of sulfamides derivatives with β-CD, we investigated the interaction of a series of N-sulfamoyloxazolidinones with β cyclodextrin (β-CD) in aqueous solution. This work complements the recent study of inclusion complexes of 2-chloroethylnitrososulfamides (CENS) with β-cyclodextrin.[2]

N-sulfamoyloxazolidinones are attractive compounds, which combine an oxazolidinone pharmacophore and a sulfamoyl moiety.[3] They have been shown to be effective as antibacterial agent[4] and have been used as precursors in the synthesis of 2-chloroethylnitrososulfamides CENS.[5]

In the present paper, the complexation between N-sulfamoyloxazolidinones **1**–**6** (Fig. 1) and β-CD was carried out following two different procedures, in liquid phase and at the solid state. Different spectroscopic and spectrometric techniques were used to characterize inclusion complexes (second derivative spectrophotometry UV–vis, ^{1}H and ^{13}C NMR and electron spray-mass spectroscopy).

It is of particular interest to determine the extent of molecular interaction between β-CD host and

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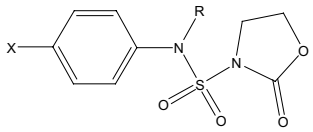

1, R = H , X= H
2, R = H , X= CH_3
3, R = H , X= OCH_3
4, R = H , X= Cl
5, R = H , X= NO_2
6, R = CH_3 , X= H

Figure 1. N-Sulfamoyloxazolidinones used in this study.

N-sulfamoyloxazolidinones molecules (guests) in a quantitative fashion. The knowledge of the stoichiometry, stability constants and octanol–water partition coefficients in solution for inclusion complexes may allow a prediction of further dissolution and bioavailability behaviors. The guests were chosen in such a way to have variations in molecular properties such as, for example, hydrophobicity, polarity and ability to form hydrogen bonds with β-CD and water. The stoichiometry and the stability constants values at various pH: 1, 3.4, 7.4, 8, 11, were performed using the second-derivative spectrophotometry.

2. Results and discussion

2.1. Characterization of solid inclusion complexes

Solid state complexes between N-sulfamoyloxazolidinones (**1**–**6**) and β-CD have been obtained, giving respectively, the complexes **C-1** to **C-6**.

In ^{1}H NMR spectra of all complexes signals for H-3 and H-5 of the β-CD moiety are shifted downfield (0.1–0.2 ppm) compared to the original chemical shifts of β-CD itself indicating that the guest compound is located close to H-3 and H-5 in the hydrophobic cavity.

The aromatic hydrogen signals of the guests protons of guests were also shifted downfield (0.2 ppm at least) when complexation with β-CD occurred. On the other hand a displacement toward the low fields was observed for the hydrogen signal of CH_2N of guests especially for **C-3**, **C-4**, and **C-5**. Also, it is important to notice that in the complexes **C-3**, **C-4**, and **C-5** besides the displacement toward the low fields of H-3 (0.2 ppm) and H-5 (0.2 ppm), a 0.45 ppm shift of the protons OH_6 (β-CD) was observed.

In the ^{13}C NMR spectra, both carbons of guests and β-CD are easily identified. The carbons C_2 and C_5 of the β-CD in complexed compounds are deshielded, respectively, by 0.5 and 0.38 ppm.

The formation of inclusion complexes of N-sulfamoyloxazolidinones with the β-CD was confirmed with the ES-MS technique, which became in the last few years a powerful tool widely used for the detection of non-covalent host–guest inclusion complexes.[6]

For the 1:1 complexes, the intensities of signals corresponding to complexes forms ($[complex+Na]^+$ or $[complex-H]^+$) are high and revealed that the inclusion complexes are stable in 'soft' ionization conditions. Spectroscopic analyses of the different complexes are reported in Ref. 7.

2.2. Detection of host–guest complexes formation in solution

Because of the poor solubility of the guests in water, the solvent system of methanol/water (10:90, v/v) has been used. This mixture was also chosen as the most suited system for the formation of inclusion complexes.

In solution the complexation of N-sulfamoyloxazolidinones with β-CD was demonstrated by spectrophotometry at UV–vis at 25 ± 0.1 °C.

2.3. Direct UV–vis spectra

The UV-vis spectrum of each of N-sulfamoyloxazolidinone studied is altered in the presence of β-CD. Following the progressive addition of β-CD on guest solutions, characteristic phenomena of the complexes formation were noticed: bathochromic shifts, reduction of the absorbance at a given wavelength and the formation of an isobestic point.

Let us examine the absorption spectra of three guests in solution containing various amounts of β-CD as shown in Figures 2–4, respectively, as the examples of the six N-sulfamoyloxazolidinones derivatives studied.

Figure 2 shows absorption spectra of guest **2** (2.5×10^{-5} mol dm^{-3}) at pH 7.4 with phosphate buffer (0.01 mol L^{-1}) containing various concentrations of β-CD.

Upon the addition of β-CD, the maximum absorption peak at 251 nm is slightly shifted to longer wavelength, accompanied by isosbestic point at 254 nm. This result probably indicates the formation of a new inclusion complex.

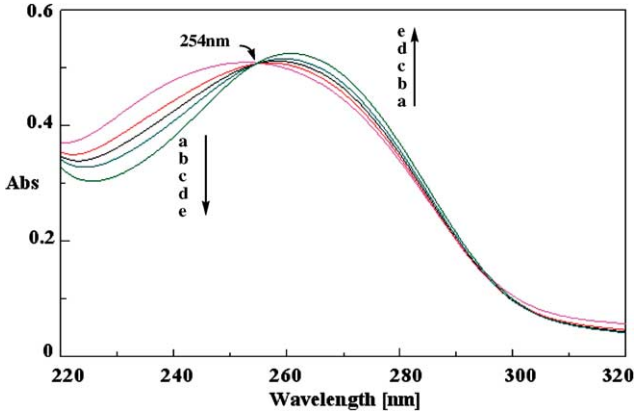

Figure 2. Absorption spectra of **2** (2.5×10^{-5} mol dm^{-3}) in phosphate buffer (pH 7.4) containing various concentrations of β-CD: (a) 0, (b) 10^{-5} M, (c) 4×10^{-5} M, (d) 10^{-4} M, (e) 5×10^{-4} M.

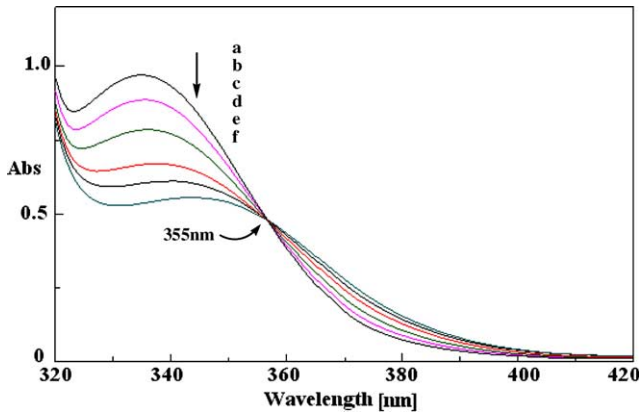

Figure 3. Absorption spectra of **5** (2.5×10^{-5} mol dm^{-3}) in phosphate buffer (pH 7.4) containing various concentrations of β-CD: (a) 0, (b) 3×10^{-5} M, (c) 6×10^{-5} M, (d) 10^{-4} M, (e) 5×10^{-4} M, (f) 8×10^{-4} M.

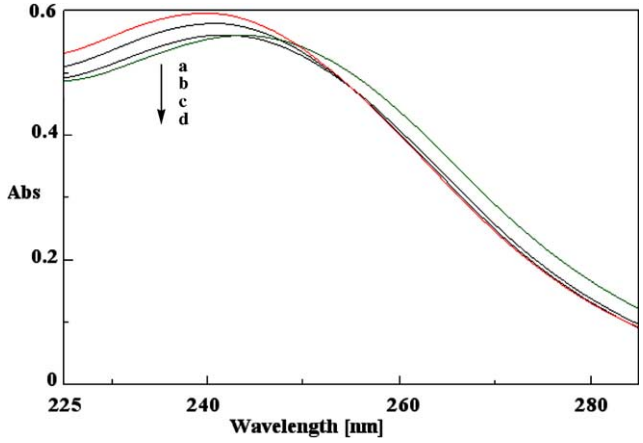

Figure 4. Absorption spectra of **6** (2.5×10^{-5} mol dm^{-3}) in phosphate buffer (pH 7.4) containing various concentrations of β-CD: (a) 0, (b) 4×10^{-5} M, (c) 6×10^{-5} M, (d) 10^{-4} M.

Figure 3 shows absorption spectra of **5** (2.5×10^{-5} mol dm^{-3}) at pH 7.4 with phosphate buffer (0.01 mol L^{-1}) containing various concentrations of β-CD. The addition of β-CD to the guest solution results in a decrease of its absorbance in UV–vis region and a significant broadening. In addition, a shift toward longer wavelength of the absorption band (340 nm) and an isobestic point at 355 nm were observed.

Figure 4 depicts absorption spectra of **6** in pH 7.4 buffer containing various concentrations of β-CD. Also, a decrease in the absorbance around 240 nm and isobestics points were observed.

2.4. Second-derivative spectra

Because of the rapid development of microcomputer technology, derivative spectrophotometry became a suitable and practical tool of great interest for increasing resolution of spectral bands, elimination of interferences originating from sample turbidity and matrix background, the enhancement of spectral details.

Derivative method emphasizes subtle spectral features of the data by presenting them in a new and visually more accessible way. Consequently, the application of such technique to the equilibra calculation studies gave successful results.[8]

The second-derivative spectra of the same compounds already measured by direct spectrophotometry are, respectively, presented in Figure 5.

The main instrumental parameters that affects the shape of derivative spectra are the wavelength speed, the wavelength increment over which the derivative is obtained

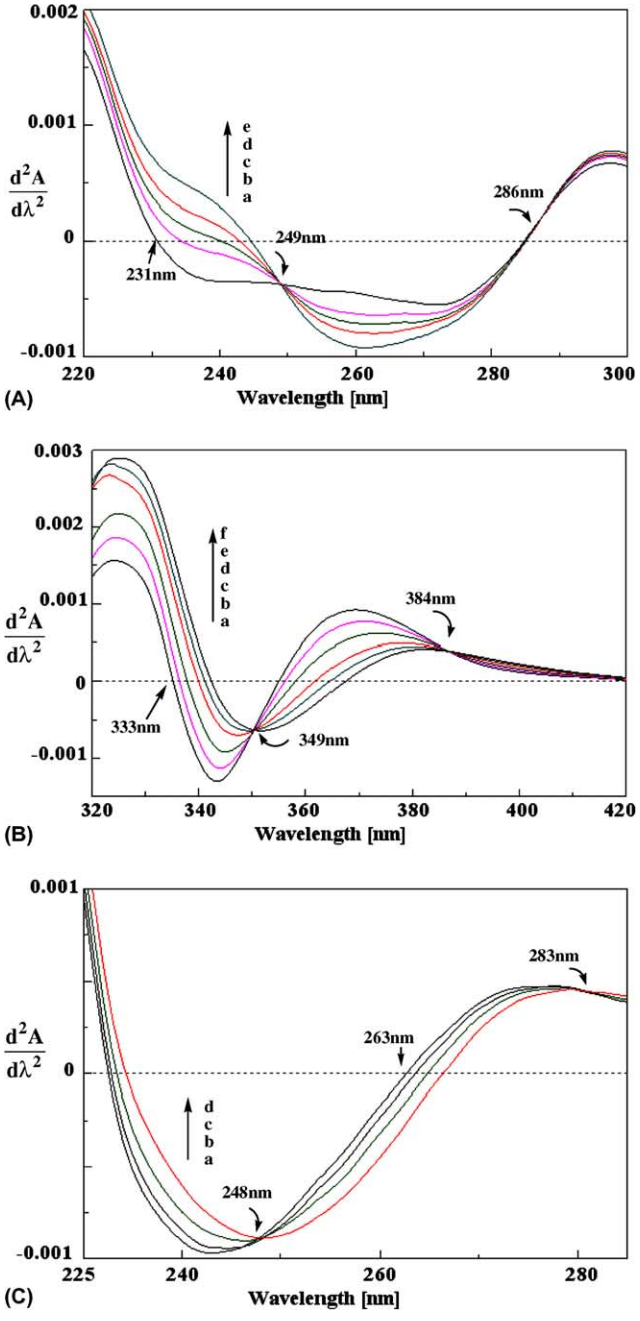

Figure 5. Second-derivative spectra A, B, and C of guests corresponding, respectively, to Figures 2–4.

($\Delta\lambda$) and the smoothing. These parameters need to be optimized to give well-resolved large peaks and a larger relatively intense signal. Generally, the noise level decreases with an increase in $\Delta\lambda$ thus decreasing the fluctuation in the derivative spectra. However if the value of $\Delta\lambda$ is too large, the spectral resolution is very poor. Therefore, the optimum value of $\Delta\lambda$ should be determined by taking into account the noise level and the resolution of the spectra. Some values of $\Delta\lambda$ were tested. $\Delta\lambda = 6$ and wavelength scanning speed = 200 nm min^{-1} were selected for second derivative method as optimal conditions to give a satisfactory signal to noise ratio.

As it can be seen in Figure 5, in each case the complexation is better visualized, the bathochromic shifts are more significant and the isobestic points are clearer. In Figure 5-C, a noteworthy difference from the original absorption spectra is that the second derivative absorption spectra isobestic points are clearly observed at 248 and 283 nm.

On the other hand it should be emphasize that in chemical equilibra calculations, the main advantage of this method compared with zero-order spectrophotometry is the accuracy of the measure of $d^2A/d\lambda^2$. This is of great interest in N-sulfamoyloxazolidinone-β-CD systems where the difference of absorbance between free and complexed forms is small and/or when the overlapping of spectra is observed.

The zero-crossing method is the approach used in this work for the determination of the stoichiometry and the stability constants of inclusion complexes.

At the zero-crossing wavelength of the spectrum of a given N-sulfamoyloxazolidinone, the amplitude (^2D) of the second-derivative spectrum is proportional to the concentration of the corresponding complex in the solution.

$$^2D = \frac{d^2A}{d\lambda^2} = \frac{d^2\varepsilon}{d\lambda^2} l\ [\text{complex}]$$

where A is the absorbance and l is the path length. The wavelengths at which the amplitudes of the complexes studied were measured (pH 7.4) are summarized in Table 1.

Table 1. Wavelengths at which the amplitudes of the complexes studied were measured

Complexes	C-1	C-2	C-3	C-4	C-5	C-6
λ, nm	230	231	227	232	333	263

It should be noted that for some compounds such as **5** (at 370 nm), the peak-to base line method could also be applied.

2.5. Determination of stoichiometry and stability constants

On the basis of the above considerations and the method of molar ratio, the stoichiometries of complexes studied were determined. Abrupt variations of the slopes in plot amplitude against molar ratios, confirmed the formation of an association between N-sulfamoyloxazolidinone and β-CD. The results indicated that molar ratio of guest: β-CD is 1:1 independently of N-sulfamoyloxazolidinone nature. In addition, taking into account the NMR results and the fact that the aromatic ring is complementary in size to cyclodextrin cavity, the most likely scheme of the reaction is represented in Figure 6.

The guest molecule is oriented in the β-CD in such position as to achieve maximum contact between the hydrophobic part of the guest molecule (aromatic ring) and the internal surface of the β-CD cavity. The hydrophilic part of the guest molecule remains, as far as possible, on the outer surface of the complex.

In order to calculate stability constants at various pH, solutions were prepared at a fixed concentration of N-sulfamoyloxazolidinone (2.5×10^{-5} M) and at a concentration of β-CD ranging from 5×10^{-5} to 4×10^{-4} M. The desired pH value was adjusted with appropriate buffer. The amplitudes ^2D of the different solutions at suitable wavelengths were processed by the method reported by Benessi-Hildebrand. The stability constants K were obtained by plotting the measured values of [Guest]/^2D versus the reciprocal of the cyclodextrin concentrations (1/[β-CD]). Experimental values of stability constants at various pHs for the different complexes are reported in Table 2.

The values of the stability constants of 1:1 guest/β-CD are influenced by medium acidity and the nature of the carrier group for the oxazolidinone moiety. For a given N-sulfamoyloxazolidinone, at pH 7.4–8.5, the stability constants are higher than those obtained at the others values of pH. Probably, in this interval the guest molecule exists in its un-protonated form with which the interaction guest/host is more powerful, than with a protonated form in the acidic media. On the other hand the lower values at pH = 11 could be attributed to a partial deprotonation of secondary hydroxyl groups of β-CD.[9]

At a fixed pH = 7.4 with a phosphate buffer, the stability constants of complexes increase in the following order:

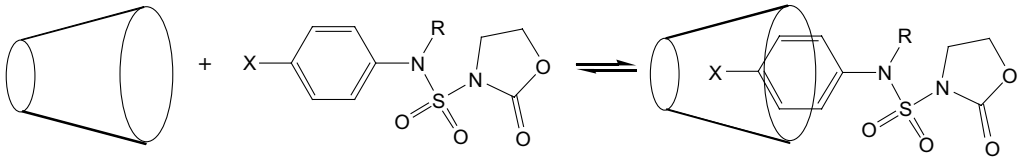

Figure 6. Inclusion of N-sulfamoyloxazolidinones inside β-CD.

Table 2. Stability constants ($1 mol^{-1}$) of 1:1 N-sulfamoyloxazolidinone/β-CD complexes at various pH values

	pH				
	1	**4.3**	**7.4**	**8.5**	**11**
C-1	608 ± 50	613 ± 40	11,000 ± 80	10,860 ± 10	9650 ± 70
C-2	2530 ± 150	1500 ± 200	27,874 ± 100	26,600 ± 150	14,647 ± 100
C-3	1356 ± 80	1163 ± 100	25,000 ± 120	27,865 ± 50	15,600 ± 80
C-4	650 ± 30	968 ± 70	16,000 ± 110	15,060 ± 50	11,923 ± 70
C-5	950 ± 25	850 ± 90	17,600 ± 60	18,650 ± 25	8800 ± 75
C-6	450 ± 35	768 ± 10	10,513 ± 50	11,400 ± 50	9500 ± 25

C-6 < C-1 < C-4 < C-5 < C-3 < C-2. This sequence seems to indicate that the increase of the hydrophobicity by substituting the aromatic ring with an alkyl group seems to be the most dominant factor for a favorable inclusion (**C-2**).

The hydrophobic properties and especially the ability of guests to form hydrogen bonds with cyclodextrin and water could explain the trend of **3**, **4**, and **5** to bind β-CD more strongly than **1** and **6**. With respect to the two first factors determining the strength of the complexation, the polarity character seems to play also a role but with a less clear influence.

From a theoretical point of view, the main driving forces that have to do with the inclusion complexation processes are Van der Waals interactions, hydrophobic interactions, hydrogen bonding and dipole–dipole and/or coulombic interactions.[10]

2.6. Measurement of octanol–water partition coefficient

The logarithm of the partition coefficient between *n*-octanol and water ($\log P$) is a leading physicochemical descriptor in many quantitative structures–activity relationship (QSAR) studies for modeling transports cross biological membranes, biochemical and pharmacokinetic processes, and toxicity of organic compounds.

Partition coefficients of N-sulfamoyloxazolidinones and their complexes were determined by the shake-flask method. For this purpose, 2.5 mL of 10^{-4} M aqueous solutions of each compound (guests or their complexes) were, respectively, mixed with the same volume of octanol at room temperature. The system was vigorously shaken under sonication until equilibrium. After centrifugation, the two phases were separated and the absorbances were measured at appropriate wavelengths.[7] The experimental results of partition coefficients measurements are shown in Table 3.

Table 3. Values of partition coefficients of N-sulfamoyloxazolidinones and their 1:1 complexes

Guest	$\log P$	Complex	$\log P$	$\Delta\log P$	K (pH = 7.4)
1	0.65	**C-1**	−0.20	0.85	11,000
2	1.12	**C-2**	0.10	1.01	27,874
3	0.77	**C-3**	−0.17	0.94	25,000
4	1.26	**C-4**	0.46	0.8	16,000
5	0.55	**C-5**	−0.35	0.9	17,600
6	0.56	**C-6**	−0.22	0.78	10,513

The hydrophobicity of N-sulfamoyloxazolidinones and their inclusion complexes decrease, respectively, in the following orders **5 > 6 > 1 > 3 > 2 > 4** and **C-5 > C-6 > C-1 > C-3 > C-2 > C-4**. The relative hydrophobicity enhancement obtained via β-cyclodextrin complexation can be expressed by the $\Delta\log P$ value defined as: $\Delta\log P = \log P$ (guest) − $\log P$ (complex).

According to the values of this quantity, it appears that following the complexation of N-sulfamoyloxazolidinones, the hydrophobicity is improved 5–10 times.

In addition, the variation of the $\Delta\log P$ values versus the inclusion complexes stability constants K at pH 7.4, showed a clear trend according to which the greater is the stability constant, the greater is the relative hydrophobicity enhancement.

3. Conclusion

The formation of solid state inclusion complexes of six N-sulfamoyloxazolidinones with β-cyclodextrin was confirmed by means of ^{1}H NMR, ^{13}C NMR, and ES-MS techniques.

In solution study, the results of spectrophotometric measurements revealed that the stability constants of 1:1 complexes are influenced by medium acidity and the nature of guest molecule. We also demonstrated that encapsulation of N-sulfamoyloxazolidinones into β-cyclodextrin improved the hydrophobic properties of the guest molecules.

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7. β-CD was recrystallized twice from water; the sulfamoyloxazolidinones were synthesized as previously described.[2] ^{1}H and ^{13}C NMR (400 MHz) spectra were recorded on a Brucker DRX-400 spectrometer using DMSO-d_6 as solvent. The complexes were dissolved in methanol (about 10^{-4} M) after stirring at room temperature, the solution were directly analyzed by ES-MS. Electron ionization mass spectra (30 and 20 eV) were recorded in positive or negative mode on a Water MicroMass ZQ. The spectrophotometric measurements were performed at 25 °C on a Jasco (Tokyo, Japan) double beam UV–vis spectrophotometer (model V530) connected to PC computer fitted with spectra analysis program and equipped with a cell compartment thermostated by a Jasco EHCT temperature controller with an accuracy of ±0.005 °C. In the derivative mode, the spectra were firstly smoothed with means-movement method (convolution width = 5 nm), then derived ($\Delta\lambda$ = 6nm).
Inclusion complexes preparation: To a stirred saturated solution of β-CD in water (2%) was added drop wise a solution of N-sulfamoyloxazolidinone (1 equiv) in methanol:water system (10:90, v/v). The mixture was stirred vigorously for 24 h at room temperature. The solution became turbid and the resulting solid was separated and dried under vacuum.
Characterization of complexes: **C-1**: ^{1}H NMR (400 MHz, DMSO-d_6) δ: 11.2 (br s, 1H, NH guest), 7.8 (s, 5H, Ar–H), 7.60 (s, 7H, OH_3 of β-CD), 5.80 (d, 7H, OH_2 of β-CD), 4.80 (d, 7H, H_1 of β-CD), 4.50 (t, 7H, OH_6 of β-CD), 4.45 (t, 2H, CH_2O of guest), 4.00 (t, 2H, CH_2N of guest), 3.70–3.50 (m, 28H, $H_{6a,b}$+H_3+H_5 of β-CD), 3.45–3.25 (m, 14H, H_4+H_2 of β-CD). ^{13}C NMR (400 MHz, DMSO-d_6) δ: 153.1 (C═O), 137.5, 128.3, 125.1, 122.0 (C–Ar), 102.3 (C_1-βCD), 81.9 (C_4-βCD), 73.4 (C_3-βCD), 72.8 (C_5-βCD), 72.4 (C_2-βCD), 63.2 (C–O–guest), 60.3 (C_6-βCD), 46.5 (C–N–guest). MS ESI^+ 30 eV *m/z*: 1399.65 $[M+Na]^+$ (15%); MS ESI^- 20 eV *m/z*: 1375.10 $[M-H]^-$ (100%). **C-2**: ^{1}H NMR (400 MHz, DMSO-d_6) δ: 11.75 (br s, 1H, NH of guest), 7.20–7.30 (m, 4H, Ar-H), 7.60 (s, 7H, OH_2 of β-CD), 5.80 (d, 7H, OH_2 of β-CD), 4.80 (d, 7H, H_1 of β-CD), 4.50 (t, 7H, OH_6 of β-CD), 4.30 (t, 2H, CH_2O of guest), 3.70–3.50 (m, 28H, $OH_{6(a,b)}$+H_3+H_5 of β-CD), 3.50–3.25 (m, 14H, H_4+H_2 of β-CD), 2.5 (t, 3H, CH_3–Ar). ^{13}C NMR (400 MHz, DMSO-d_6) δ: 153.1 (C═O), 138, 130.4, 127.0 (C–Ar), 102.4 (C_1-βCD), 82.0 (C_4-βCD), 73.5 (C_3-βCD), 72.8 (C_5-βCD), 72.5 (C_2-βCD), 63.4 (C–O of guest), 60.4 (C_6-βCD), 46.8 (C–N of guest). MS ESI^+ 30 eV *m/z*: 1413.73 $[M+Na]^+$ (50%); MS ESI^- 20 eV *m/z*: 1389.93 $[M-H]^-$ (100%). **C-3**: ^{1}H NMR (400 MHz, DMSO-d_6) δ: 11.60 (br s, 1H, NH of guest), 7.50 and 7.30 (each d, 4H, Ar-H), 5.80 (d, 7H, OH_2 of β-CD), 5.60 (s, 7H, OH_3 of β-CD), 4.80 (d, 7H, H_1 of β-CD), 4.30 (t, 2H, CH_2O of guest), 3.90 (t, 7H, OH_6 of β-CD), 3.85–3.75 (t+s, 5H, CH_2N of guest+OCH_3–Ar), 3.70–3.50 (m, 28H, $H_{6(a+b)}$+H_5+H_3), 3.45–3.20 (m, 14H, H_4+H_2 of β-CD). ^{13}C NMR (400 MHz, DMSO-d_6) δ: 153.3 (C═O), 137.4, 128.2, 127.1 (C–Ar), 102.3 (C_1-βCD), 81.7 (C_4-βCD), 73.4 (C_3-βCD), 72.9 (C_5-βCD), 72.4 (C_2-βCD), 62.3 (C–O of guest), 56.0 (O–CH_3), 46.0 (C–N of guest). MS ESI^+ 30 eV *m/z*: 1429.70 $[M+Na]^+$ (10%); MS ESI^- 20 eV *m/z*: 1405.13 $[M-H]^-$ (100%). **C-4**: ^{1}H NMR (400 MHz, DMSO-d_6) δ: 11.05 (br s, 1H, NH of guest), 7.50 (m, 4H, H-Ar), 4.90 (s, 7H, H_1 of β-CD), 4.40 (t, 2H, CH_2N of guest), 4.25–3.90 (br s, 21H, OH_2+OH_3+OH_6 of β-CD), 4.80 (t, 2H, CH_2N of guest), 4.15 (t, 2H, CH_2O of guest), 3.70–3.50 (m, 28H, H_3+$H_{6(a,b)}$+H_5 of β-CD), 3.45–3.20 (m, 14H, H_4+H_2 of β-CD). ^{13}C NMR (400 MHz, DMSO-d_6) δ: 152.1 (C═O), 135.1, 130.0, 128.9, 128.2 (C–Ar), 102.3 (C_1-βCD), 81.9 (C_4-βCD), 73.4 (C_3-βCD), 72.8 (C_5-βCD), 72.4 (C_2-βCD), 62.0 (C–O of guest), 60.3 (C_6-βCD), 45.1 (C–N of guest). MS ESI^+ 30 eV *m/z*: 1434.10 $[M+Na]^+$ (20%); MS ESI^- 20 eV *m/z*: 1409.50 $[M-H]^-$ (100%). **C-5**: ^{1}H NMR (400 MHz, DMSO-d_6) δ: 11.80 (br s, 1H, NH of guest), 8.10 and 7.70 (each m, 4H, H–Ar), 6.00–5.25 (br s, 14H, OH_2+OH_3 of β-CD), 4.95 (s, 7H, H_1 of β-CD), 4.40 (t, 2H, CH_2O of guest), 4.10 (t, 2H, CH_2N of guest), 4.00–3.50 (m, 35H, OH_6+H_3+$H_{6(a,b)}$+H_5 of β-CD), 5.45–5.10 (m, 14H, H_4+H_2 of β-CD). ^{13}C NMR (400 MHz, DMSO-d_6) δ: 149.1 (C═O), 130.5, 121.1, 108.3 (C–Ar), 102.4 (C_1-βCD), 82.0 (C_4-βCD), 73.5 (C_3-βCD), 72.8 (C_5-βCD), 72.5 (C_2-βCD), 64.6 (C–O of guest), 60.3 (C_6-βCD), 46.2 (C–N of guest). MS ESI^+ 30 eV *m/z*: 1444.60 $[M+Na]^+$ (60%); MS ESI^- 20 eV *m/z*: 1420.09 $[M-H]^-$ (100%). **C-6**: ^{1}H NMR (400 MHz, DMSO-d_6) δ: 7.60–7.10 (m, H, Ar-H), 5.80 (d, 7H, OH_2 of β-CD), 5.70 (s, 7H, OH_3 of β-CD), 4.85 (d, 7H, H_1 of β-CD), 4.55 (t, 7H, OH_6 of β-CD), 4.30 (t, 2H, CH_2O of guest), 3.90 (t, 2H, CH_2N of β-CD), 3.70 (s, 3H, NH_3), 3.65–3.45 (m, 28H, $H_{6(a,b)}$+H_3+H_5 of β-CD), 3.40–3.25 (t, 14H, H_4+H_2 of β-CD). ^{13}C NMR (400 MHz, DMSO-d_6) δ: 152.3 (C═O), 137.0, 128.2, 126.7, 121.6 (C-Ar), 102.4 (C_1-βCD), 81.9 (C_4-βCD), 73.5 (C_3-βCD), 72.8 (C_5-βCD), 72.6 (C_2-βCD), 64.1 (C–O of guest), 60.3 (C_6-βCD), 58.4 (CH_3–N), 48.1 (C–N of guest). MS ESI^+ 30 eV *m/z*: 1413.73 $[M+Na]^+$ (50%); MS ESI^- 20 eV *m/z*: 1389.13 $[M-H]^+$ (100%).
Measurements of octanol–water partition coefficients: 2.5 mL of 10^{-4} M aqueous solutions of each compound (N-sulfamoyloxazolidinone or its complex) were, respectively, mixed with the same volume of octanol at room temperature. The system was shaken vigorously until equilibrium. After centrifugation, the two phases were separated and the spectrophotometric measurements were made at the appropriate wavelength.

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