Available online at www.sciencedirect.com
SCIENCE DIRECT®
Chemical Physics Letters 407 (2005) 260–265
CHEMICAL PHYSICS LETTERS
www.elsevier.com/locate/cplett

# Photochemical intracomplex reaction between β-cyclodextrin and anthraquinone-2,6-disulfonic acid disodium salt in water solution

S.S. Petrova *, A.I. Kruppa, T.V. Leshina

*Institute of Chemical Kinetics and Combustion, Magnetic Phenomena Laboratory, Institutskaya str. 3, Novosibirsk 630090, Russia*

Received 31 January 2005; in final form 14 March 2005
Available online 13 April 2005

**Abstract**

1D and 2D $^1$H NMR studies of anthraquinone-2,6-disulfonic acid disodium salt in the β-cyclodextrin solution have identified the inclusion complex formation. The association constant of AQDS–β-CD inclusion complex was determined as 800 ± 100 $M^{-1}$. The selective intra-complex photo-oxidation of β-cyclodextrin at C6 position was detected by CIDNP method.
© 2005 Elsevier B.V. All rights reserved.

## 1. Introduction

A number of examples using cyclodextrins to alter the course of chemical (and photochemical) reactions have been reported [1,2]. The modification of the final product distribution in the photolysis of aromatic carbonyl compounds in CD media was rationalized by invoking an influence on both the ground-state conformation of the reactant and the secondary reaction steps involving the radical intermediates. Furthermore, it is possible to involve the cyclodextrin itself in the photoreaction. The intermolecular hydrogen-atom abstraction from the cyclodextrin molecule to the acceptor has been considered in several studies [2–5]. In [3] α- and β-cyclodextrins, and noncyclic carbohydrates (D-glucose, starch, dextrans) have been studied in the reaction with $SO_4^{-\bullet}$ and $^{\bullet}OH$. As compared to reactions with noncyclic carbohydrates resulting in various radicals, in reactions with cyclodextrins, a hydrogen atom is shown to separate inside the cavity. It is concluded then that $SO_4^{-\bullet}$ forms an inclusion complex with β-cyclodextrin (β-CD). In [4], a photochemical reaction between β-CD and *p*-nitroacetophenone has been studied in an inclusion complex in water solution. It is demonstrated that the inclusion complex formation is necessary for the reaction to occur and the oxidation of β-CD is selective at C3 position. In [5], the TR EPR spectroscopy method was used to study the photolysis of acetone and some other compounds included in α-, β- and γ-cyclodextrins. The various radicals of cyclodextrins, mainly the C3, C5, and C1 radicals, were observed. In one case, the C6 radical was recorded in the reaction between pyruvic acid and γ-cyclodextrin.

The present Letter studies the photointeraction between anthraquinone-2,6-disulfonic acid disodium salt (AQDS) and β-CD in water solution.

## 2. Experimental

### 2.1. Chemicals

The anthraquinone-2,6-disulfonic acid disodium salt (Reachim), β-cyclodextrin (minimum 98%, Sigma-Aldrich), $D_2O$ (99.8% isotopic purity, Aldrich) were used as received.

### 2.2. Equipment

1D and 2D $^1$H NMR spectra were recorded at room temperature on a DPX200 BRUKER NMR

* Corresponding author. Fax: +7 3832 307350.
*E-mail address:* petrova@kinetics.nsc.ru (S.S. Petrova).

0009-2614/$ - see front matter © 2005 Elsevier B.V. All rights reserved.
doi:10.1016/j.cplett.2005.03.109

spectrometer (200 MHz) $^1H$ operating frequency, ($\tau$ (90°) = 7.2 μs). The Lambda Physik EMG 101 MSC eximer laser was used as a light source (308 nm, 100 mJ at output window, 20 mJ/pulse in sample volume, with a pulse duration of 15 ns). For time resolved (TR) CIDNP experiments [6], the delay time between laser and detection pulses was varied from 0 to 100 μs. The samples in standard 5 mm Pyrex NMR tubes were irradiated directly in the probe of NMR spectrometer at 20 °C.

### 2.3. Sample preparation

Stock solutions of 10 mM β-CD and 10 mM AQDS were made up in $D_2O$. To perform the NMR shift titrations host–guest solutions were prepared by mixing a given aliquots of both components and $D_2O$ directly in the NMR tubes (5 mm, Pyrex). The AQDS concentration was constantly equal to 2 mM. The β-CD concentrations ranged between 1 and 8 mM. The pD of 2 mM AQDS solution was 2.47 (pH 2.9). For stoichiometry determination by Job's method the samples were prepared by mixing of 10 mM stock solutions of AQDS and β-CD in different ratio and constant sample volume. Both stock solutions were previously titrated to pD 2 (pH about 2.3). Both NMR shift titration and Job's method experiments were performed in 15 min after mixing.

TR CIDNP experiments were performed for mixture contained 2 mM of AQDS and 2 mM (4 mM, 8 mM) of β-CD. The samples were bubbled with argon for 10 min to remove dissolved oxygen just before photolysis.

ROESY experiments were performed for the solution of 2 mM of AQDS and 4 mM of β-CD, using a spinlock time 200 ms.

### 2.4. Molecular modeling

Geometry optimization of the inclusion complex was carried out using AM1 semi-empirical quantum-chemistry method from the HYPERCHEM 6.0 package (HYPERCUBE).

## 3. Results and discussions

In the presence of β-CD the photoexcitation of AQDS in water solution provides polarized signals in the CIDNP spectrum (Fig. 1). The chemical shifts of these lines differ from those of initial compounds, i.e., photoreaction results in a new product. The emission signal with a chemical shift of about 4.6 ppm and a splitting of about 7 Hz is observed along with the adsorption signal in the resonance region of β-CD. Since cyclodextrin is a polyatomic alcohol, either aldehydes (after carbon oxidation at position 6) or ketones (after carbon oxidation at other positions) can be the most typical

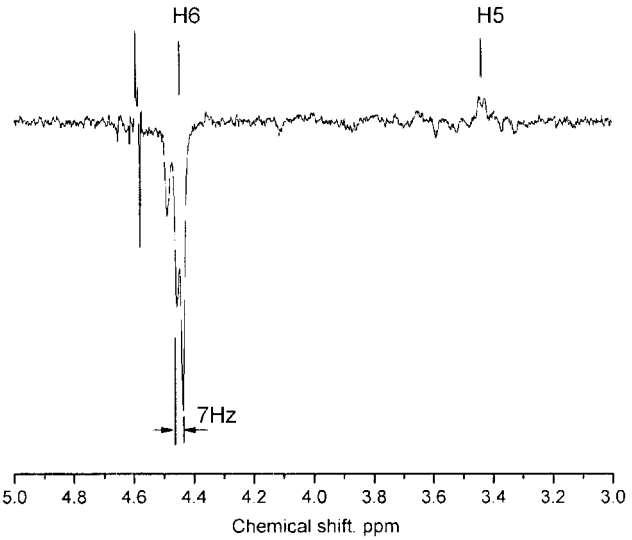
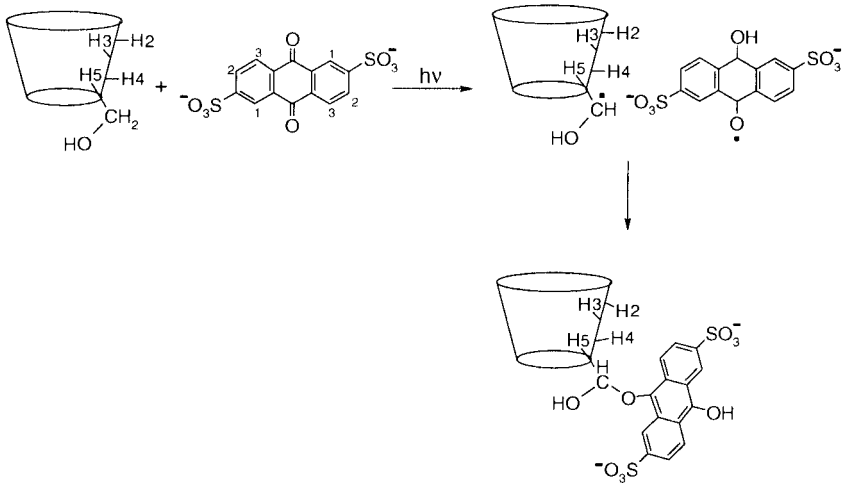



Fig. 1. $^1H$ photo-CIDNP spectrum of 2 mM AQDS and 8 mM β-CD at delay time 100 μs.

final products of its photoreaction with quinones [7]. A primary transfer of hydrogen atom from alcohol α-carbon to quinone leads to the formation of semiquinone and ketyl radicals. In anaerobic medium, the recombination of these radicals can give rise to hemiacetal which is further hydrolyzed to corresponding ketone (or aldehyde) and hydroquinone. The signal with a shift of 4.6 ppm can be most probably assigned to the acetal proton in the $R_1CH(OR_2)OH$ structure. The splitting with a spin-spin coupling constant of about 7 Hz indicates that the entire structure, which demonstrates polarization, corresponds to a $R_1R_1'CHCH(OR_2)OH$ fragment. Dihydroanthraquinone-2,6-disulfonate is also recorded as a final product which is in fair agreement with the mechanism proposed. It is also worth noting that the polarized signals fail to demonstrate any dependence on the delay time between laser and registration pulses. This allows us to claim that the polarization observed belongs to the photolysis products resulting from geminate recombination.

The chemical structure of β-CD is such that hemiacetal, which contains hydrogen at both α- and β positions, can be formed by only β-CD oxidation at the C6-position. Scheme 1 gives the general view of the mechanism proposed which includes radical of β-CD. Counter radical is protonated semiquinone radical (AQDSH$^\cdot$), because under experimental conditions (pH 2.9) only AQDSH$^\cdot$ is stable [8].

A similar formation of hemiacetal is reported in [9], where the synthesis and photochemistry of several anthraquinone-substituted β-CD are under study. In this work, anthraquinone was attached to a narrow rim of β-CD. Thus, the C6-atom is the nearest one to the anthraquinone part and the proton is expected to separate. In our case, AQDS is not bound covalently




Scheme 1.

to β-CD which is, however, observed to be selectively oxidized. The reason for such selectivity can be the inclusion complex formation between the reagents.

Downfield shifts of the AQDS protons, and upfield shifts of the β-CD protons unambiguously indicate the formation of AQDS–β-CD inclusion complex. Fig. 2 shows the $^1$H NMR spectra of both the water solution of CD and the mixed solution with concentration ratio AQDS/β-CD = 3:1 Comparing these spectra, we see that among the β-CD resonance lines most shifted are H5 (−0.18 ppm) and H6 (−0.12 ppm) whereas H2, H3, and H4 are less shifted (−0.07, −0.08, and −0.04 ppm, respectively).

Fig. 3 plots the change in the observed chemical shifts of AQDS versus β-CD concentration. This dependence

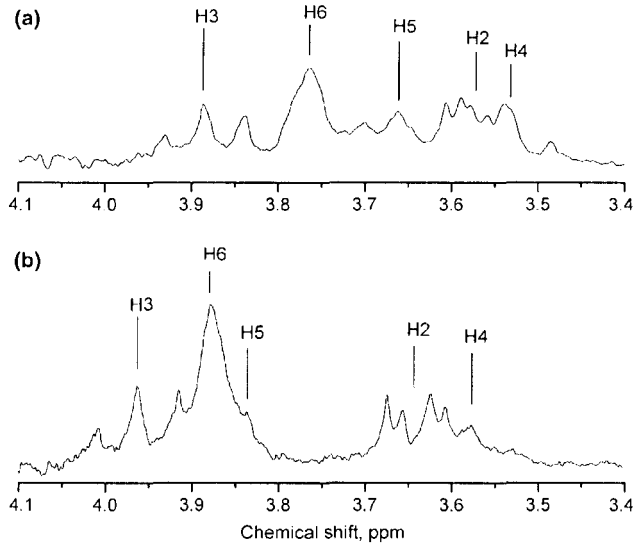



Fig. 2. Partial $^1$H NMR spectra of (a) 2 mM β-CD and (b) 2 mM β-CD and 6 mM AQDS. Only the spectral region for protons H2 to H6 of β-CD is displayed.

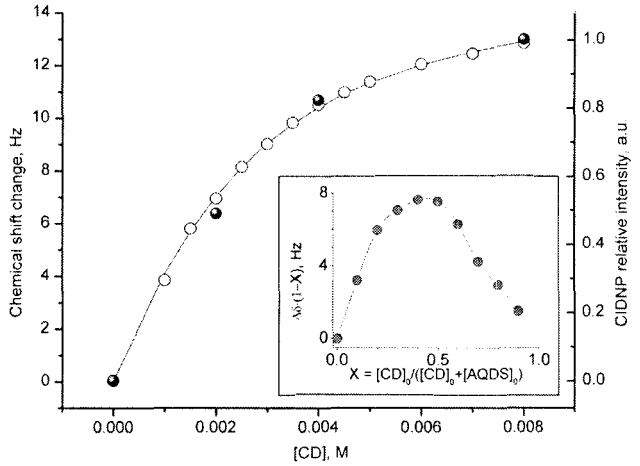



Fig. 3. Changes in the AQDS H2 and H3 central frequency (○) and in the CIDNP intensity of hemiacetal (●) as a function of the β-CD concentration. Inset shows Job's plot for AQDS–β-CD system [11].

(NMR-titration) is usually used to calculate the complex formation constant from nonlinear fitting [10]. Inset in Fig. 3 shows Job's plot for system under study. Since spectra did not demonstrate resolved lines of AQDS and complex but only exchange lines then we used modification of Job's method for complex stoichiometry estimation under fast exchange conditions [11]. As it can be seen from inset the most probable complex stoichiometry is 1:1 (mole fraction about 0.5). For the 1:1 complex stoichiometry with the same order of guest and host concentration values, the concentration of the complex obeys the following equation:

$$[\mathrm{G:CD}] = \frac{1}{2}\times\left(\frac{1}{K_f} + [\mathrm{CD}]_A + [\mathrm{G}]_T\right) - \frac{1}{2} \times \sqrt{\left[\left(\frac{1}{K_f} + [\mathrm{CD}]_A + [\mathrm{G}]_T\right)^2 - 4[\mathrm{CD}]_A[\mathrm{G}]_T\right]},$$

where G stands for guest, G:CD for complex, $T$ for total and $A$ for available amount of substance. Since only one guest is considered, the cyclodextrin concentration available to this guest is $[CD]_T$.

If guest protons of the same type m (for example, H1 of AQDS) are magnetically equivalent in homogeneously solution and have different environment in complex the observed chemical shift of guest protons $\delta^m$ under the fast exchange condition in the frame of multi site exchange model will be given by:

$$\delta^m = \frac{[G]}{[G]_T} \cdot \delta^m_G + \frac{[G:CD]}{[G]_T} \cdot \frac{1}{N} \sum_i^N \delta^m_i,$$

where $\delta^m_G$ is the chemical shift of the m-type protons of guest molecule in homogeneous solution, $\delta^m_i$ is the chemical shift of the $i$ nucleus of m-type protons of guest in complex environment and $N$ is the number of m-type protons. Since $\frac{1}{N}\sum_i^N \delta^m_i$ does not depends on complex concentration then, formally, realistic multi site exchange model can be considered as two site model with $\delta^m_{G:CD} = \frac{1}{N}\sum_i^N \delta^m_i$:

$$\delta^m = \frac{[G]}{[G]_T} \cdot \delta^m_G + \frac{[G:CD]}{[G]_T} \cdot \delta^m_{G:CD}.$$

In our case of ABX system, above expression is valid for the X (H1 of AQDS) nucleus only. For the strongly bound nuclei A and B (H2 and H3 of AQDS) the complex formation constant can be calculated from the equation for the central frequency:

$$\frac{\delta^A + \delta^B}{2} = \frac{[G]}{[G]_T} \frac{\delta^A_G + \delta^B_G}{2} + \frac{[G:CD]}{[G]_T} \frac{\delta^A_{G:CD} + \delta^B_{G:CD}}{2}.$$

The complex formation constant $K_f$ obtained by nonlinear least-squares fitting technique was $800 \pm 100\ M^{-1}$.

Fig. 3 also shows the dependence of the polarization intensity of the forming hemiacetal on the β-CD concentration. After normalization this dependence almost coincides with that of NMR-titration. The polarization observed can be given as $I = \Delta n \cdot [RP]$, where $\Delta n$ is the polarization intensity per one radical pair and [RP] is the concentration of geminate pairs. On the other hand, the curve of NMR titration indicates a change in the concentration of the AQDS–β-CD complex, i.e., the concentration of geminate pairs increases in the same manner as that of the complex with increasing β-CD concentration. Therefore, the formation of the product of selective β-CD oxidation can be unambiguously assigned to the formation of complex between reagents.

What is the structure of the AQDS–β-CD complex which leads to the selective oxidation of β-CD? As mentioned above, the greatest shifts were recorded for the H5 and H6 protons of β-CD. The most probable structures are: (i) inclusion complex, and (ii) the complex formed due to hydrogen bonds between the CO- and $SO_3$ groups of AQDS with the OH-groups at positions C6 of β-CD. Since the 1D NMR spectra fail to give the unambiguous information about the complex structure, we used the rotating frame nuclear Overhauser effect spectroscopy (ROESY) for determining the main structural complex parameters. The main advantage of the chosen variant of the 2D NMR spectroscopy is the fact that the cross-peaks occur due to the dipole–dipole interaction between nuclear spins and thus, its sensitive to the interatomic distance in the structures studied. Earlier, in the literature, there was evidence for a successful application of a given method to determine the structures of cyclodextrin inclusion complexes [10,12].

The ROESY spectrum was measured in a solution containing AQDS and β-CD in 1:2 molar ratio (Fig. 4). Taking into account the number of H6 and other type of β-CD protons, the normalized per one proton intensities of cross-peaks between the AQDS protons and H5, H3, H6 and H4 protons of β-CD are in series of decreasing intensity. This indicates that AQDS is localized near the narrow side of the β-CD cavity.

A possible location of AQDS at a given position was verified by molecular modeling and the inclusion complex geometry was optimized using the AM1 method. We started our calculations with the configuration in which AQDS is located in the β-CD cavity so that the quinoid (CO) groups of AQDS are between H3 and H5 protons of β-CD. Upon geometry optimization, the complex acquired the configuration shown in Fig. 5. The minimal distances between AQDS and β-CD protons are varied from 0.23–0.25 nm (for H5 and H3) to 0.36–0.45 nm (H6 and H4) and 0.55–0.61 nm (H1 and H2). Taking into account the sensitivity of ROESY method to distances between protons of guest and host molecules up to 0.45 nm [10] the presented model of inclusion complex is in fair agreement with the NMR data. The minimal distances between oxygen nucleus of CO group of AQDS and H6 and H5 of β-CD are 0.28 and 0.33 nm, consequently. Thus, this structure of the complex corresponds well to the selective oxidation of β-CD at C6 position. A detailed mechanism of the process is as follows:

(1) photoexcitation of the included AQDS;
(2) hydrogen atom abstraction from $CH_2$-group at the C6 position of β-CD;
(3) either the rotation of semiquinone radical of anthraquinonedisulfonate (AQDSH$^\cdot$) about the β-CD axis followed by recombination of intermediate radicals or the escape of the AQDSH$^\cdot$ radical from β-CD with the recombination of the radical pair upon re-encounters.

At present, we cannot make distinction between these two cases. In the literature there is information on both the fast rotation of included compounds along the CD

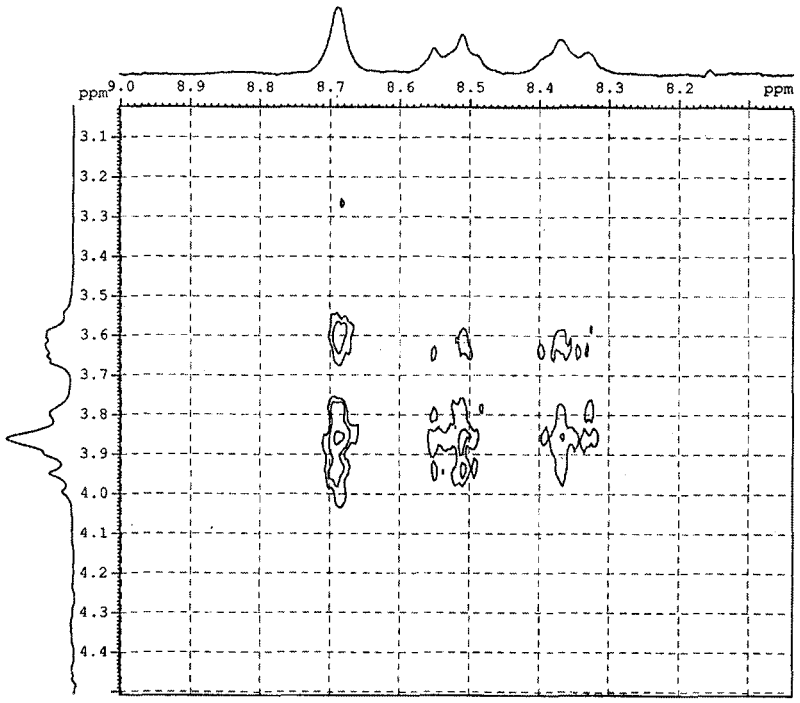



Fig. 4. Partial ROESY contour plot obtained for mixture of 4 mM β-CD and 2 mM AQDS (relaxation delay 5 s, spinlock time 200 ms).

axis [13], and the fast escape of active particles which have a charge [14].

Thus, in this Letter, the 1D, 2D NMR methods and molecular modeling have been used to demonstrate that AQDS and β-CD form the AQDS–β CD inclusion complex. The constant of complex stability was determined as 800 ± 100 $M^{-1}$ which testifies to a fairly strong binding between AQDS and β-CD. The CIDNP method shows that the main primary product of photointeraction between AQDS and β-CD is hemiacetal with semiquinone radical bound to C6 carbon of β-CD. The output of the polarized hemiacetal is in direct proportion to the shift in equilibrium: complex – starting reagents. The latter allows the conclusion that the selectivity of β-CD photo-oxidation is controlled by the inclusion complex structure.

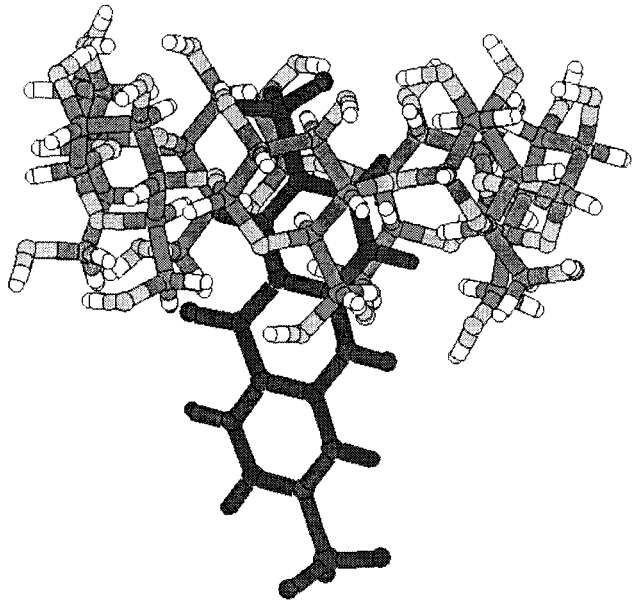


Fig. 5. The three-dimensional structure of AQDS–β-CD inclusion complex.

## Acknowledgement

The authors are grateful to the Russian Foundation for Fundamental Research (RFBR, Grant 03-03-32403) for financial support of this study.

## References

[1] T. Osa, I. Suzuki, in: J. Szejtli, T. Osa (Eds.), Comprehensive Supramolecular Chemistry, Cyclodextrins, vol. 3, Pergamon, 1996, p. 367.
[2] P. Bortolus, S. Monti, Photochemistry in cyclodextrin cavities, in: D.C. Neckers, D.H. Volman, G. von Bünau (Eds.), Advances in Photochemistry, vol. 21, 1996, p. 1, and references therein.
[3] B.C. Gilbert, J.R. Lindsay Smith, P. Taylor, S. Ward, A.C. Whitwood, J. Chem. Soc., Perkin Trans. 2 (2000) 2001.
[4] Y.L. Chow, J. Michon, P. Michon, C. Morat, A. Rassat, Tetrahedron Lett. 33 (1992) 3315.
[5] M.N. Lehmann, M.G. Bakker, J. Chem. Soc., Perkin Trans. 2 (1997) 2131.

[6] G.L. Closs, R.J. Miller, J. Am. Chem. Soc. 101 (1979) 1639; G.L. Closs, R.J. Miller, J. Am. Chem. Soc. 103 (1981) 3586.
[7] F. Wilkinson, J. Phys. Chem. 66 (1962) 2569.
[8] J. Geimer, D. Beckert, Chem. Phys. Lett. 288 (1998) 449.
[9] A.M. Aquino, C.J. Albert, K.L. Berger, C.M. Darragh, S.E. Kelley, M.V. Cossette, J. Am. Chem. Soc. 112 (1990) 5819.
[10] H.-J. Schneider, F. Hacket, V. Rüdiger, H. Ikeda, Chem. Rev 98 (1998) 1755, and references therein.
[11] K.A. Connors, Binding Constants, The Measurement of Molecular Complex Stability, Wiley–Interscience, New York, 1987, 24–28.
[12] T. Ishizu, K. Kintsu, H. Yamamoto, J. Phys. Chem. B 103 (1999) 8992.
[13] M. Okazaki, K. Kuwata, J. Phys. Chem. 88 (1984) 4181.
[14] A.E. Kaifer, Acc. Chem. Res. 32 (1999) 62.