Induced Circular Dichroism and UV−Vis Absorption Spectroscopy of Cyclodextrin Inclusion Complexes: Structural Elucidation of Supramolecular Azi-adamantane (Spiro[adamantane-2,3′-diazirine])

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Abstract: The first induced circular dichroism (ICD) analyses of diazirine@cyclodextrin inclusion complexes are reported. The stoichiometries and association constants of the guest@host complexes with α-, *β*-, and *γ*-cyclodextrin were determined. In addition, with the α-cyclodextrin complex, UV−vis spectroscopy of water−ethanol solutions showed remarkable fine structure, probably indicating that the diazirine experiences a *non*polar microenvironment. These analytical methods provide details about the architecture and nature of these supramolecular carbene precursors.

In recent years, the chemistry of reactive species entrapped within host molecules has become the object of much research activity.[1] One strategy makes use of the unique ability of the cyclodextrins to modify the physical and chemical properties of guest molecules by molecular encapsulation. We have succeeded in preparing molecular noncovalent host−guest inclusion complexes of various diazirines with cyclodextrins[2] and zeolites.[2b,3] Diazirines[4] are increasingly popular precursors for the generation of carbenes.[5] The cylodextrin hosts have been used to modify intramolecular reactions of the entrapped carbenes in order to manipulate product formation.[2] The reaction products obtained after photolysis of these supramolecular complexes in the solid state differed considerably, in some cases, from the results obtained when only physical mixtures of diazirines and host molecules were used.[2a,b,d]

It is of particular interest to obtain more detailed information about the microenvironment of the diazirine within different motion-restrictive, three-dimensional cyclodextrin inclusion complexes. This may give insight into how cyclodextrins modify the reactivities of carbenes generated in the supramolecular state. The exact stoichiometry and association constants for the formation of the inclusion complexes is of rudimentary concern. A number of spectroscopic methods have been applied for the measurement of association constants of complexes with cyclodextrin as host molecules.[6,7] The chromophore of an achiral guest may exhibit an induced circular dichroism (ICD) in the chiral environment of a cyclodextrin. The ICD has been used to determine association constants in general[8,9] and for cyclodextrins in particular,[10] even though the effects in the latter case are often very weak.[10,11] Until now, to our knowledge, an ICD of diazirines has never been observed, or used for the determination of association constants.

Because the solubility of the guest and also that of the complexes in water is generally poor, a solvent system with better solubility for all components had to be used in order to collect data for a wider range of different concentrations of the components. This is necessary for a reliable determination of association constants. A mixture of water − ethanol (30% v/v) was chosen as the system most suited for the formation of the complexes between azi-adamantane (spiro[adamantane-2,3′-diazirine]) (**1**)[2a,c,12] and α-, *β*-, and *γ*-cyclodextrin (**6-**, **7-**, **8-Cy**), respectively. For each of the three complexes, an ICD spectrum with a distinct fine structure could be observed in the absorption region of the diazirine chromophore (300−400 nm) which increased in intensity with increasing concentration of the components. While the sign of the ICD Cotton effect for **1**@-

(1) (a) *Comprehensive Supramolecular Chemistry*; Lehn, J.-M., Ed.; Pergamon: New York, 1995; Vols. 1−10. (b) Cram, D. J.; Cram, J. M. *Container Molecules and Their Guests*; Royal Society of Chemistry: Cambridge, 1994. (c) Cram, D. J. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 1009. (d) Smith, D. R. *Chem. Ind.* **1994**, 14. (e) Dowden, J.; Kilburn, J. D.; Wright, P. *Contemp. Org. Synth.* **1995**, *2*, 289.

(2) (a) Brinker, U. H.; Buchkremer, R.; Kolodziejczyk, M.; Kupfer, R.; Rosenberg, M.; Poliks, M. D.; Orlando, M.; Gross, M. L. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1344. (b) Kupfer, R.; Brinker, U. H. *Liebigs Ann.* **1995**, 1721. (c) Rosenberg, M. G.; Kam, S. M.; Brinker, U. H. *Tetrahedron Lett.* **1996**, *37*, 3235. (d) Brinker, U. H.; Rosenberg, M. G. In *Advances in Carbene Chemistry*; Brinker, U. H., Ed.; JAI: Stamford, 1998; Vol. 2, p 29.

(3) Kupfer, R.; Poliks, M. D.; Brinker, U. H. *J. Am. Chem. Soc.* **1994**, *116*, 7393.

(4) (a) *Chemistry of Diazirines*; Liu, M. T. H., Ed.; CRC: Boca Raton, 1987; Vol. 1 and 2. (b) Schmitz, E. In *Houben-Weyl, Methoden der Organischen Chemie*; Klamann, D., Ed.; Thieme Verlag: Stuttgart, 1992; Vol. E16c, p 678. (c) Kupfer, R.; Rosenberg, M. G.; Brinker, U. H. *Tetrahedron Lett*. **1996**, *37*, 6647.

(5) (a) *Advances in Carbene Chemistry*; Brinker, U. H., Ed.; JAI: Greenwich, 1994; Vol. 1; 1998; Vol. 2. (b) *Houben-Weyl, Methoden der Organischen Chemie*; Regitz, M., Ed.; Thieme Verlag: Stuttgart, 1989; Vol. E19b. (c) Jones, W. M.; Brinker, U. H. In *Pericyclic Reactions*, Vol. 1; Marchand, A. P., Lehr, R. E., Eds.; Academic: New York, 1977; p 109. (d) *Carbenes*; Jones, M., Jr.; Moss, R. A., Eds.; Wiley: New York, 1973, 1975; Vols. 1 and 2. (e) Kirmse, W. *Carbene Chemistry*, 2nd ed.; Academic: New York, 1971.

(6) (a) Connors, K. A. *Chem. Rev.* **1997**, *97*, 1325. (b) Connors, K. A. *J. Pharm. Sci.* **1995**, *84*, 843.

(7) Ivanov, P. M.; Salvatierra, D.; Jaime, C. *J. Org. Chem.* **1996**, *61*, 7012.

(8) Krois, D. *Tetrahedron* **1993**, *49*, 8855.

(9) For a detailed investigation concerning the applicability of the ICD for the determination of association constants see: Krois, D.; Lehner, H. *J. Chem. Soc., Perkin Trans. 2* **1995**, 489. Krois, D.; Lehner, H. *Monatsh. Chem.* **1995**, *126*, 349.

(10) (a) Zhdanov, Y. A.; Alekseev, Y. E.; Kompantseva, E. V.; Vergeichik, E. N. *Russ. Chem. Rev.* **1992**, *61*, 563. (b) Lightner, D. A.; Gawronski, J. K.; Gawronska, K. *J. Am. Chem. Soc.* **1985**, *107*, 2456.

(11) Easton, C. J.; Lincoln, S. F. *Chem. Soc. Rev.* **1996**, 163.

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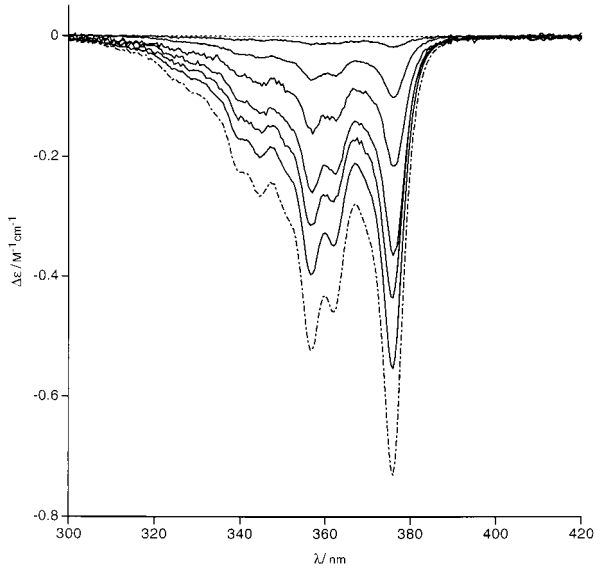


Figure 1. Induced circular dichroism (ICD) of azi-adamantane (**1**) by complex formation with α-cyclodextrin (**6-Cy**) in water with 30% v/v ethanol at 293 K. The observed concentration dependence (—) was utilized to elucidate the types of complexes formed and to determine the corresponding association constants. The spectrum for pure **1**@**2**(**6-Cy**) (—•—) was extrapolated.

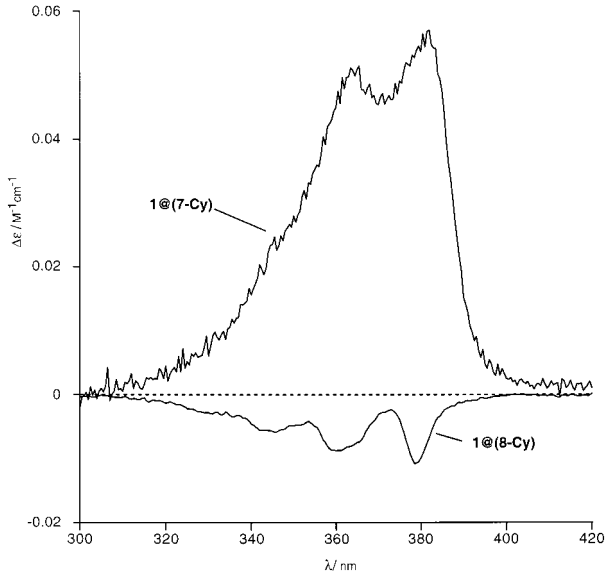


Figure 2. Circular dichroism of **1**@(**7-Cy**) and **1**@(**8-Cy**) (extrapolated) in water with 30% v/v ethanol.

(**7-Cy**) is positive, it is negative and very weak for **1**@(**8-Cy**). The data obtained for the host−guest complexes of **7-** and **8-Cy**, respectively, could easily be analyzed by a Scatchard plot[13] for a 1:1 stoichiometry (Figure 3a,b). Thus, the association constant K_1 could be determined to be 6150 M^{-1} and 2740 M^{-1}, respectively (see Table 1), even though the dichroic effects, especially in the **8-Cy** case, were quite small. During the formation of the complex of **1** with **6-Cy**, a very strong ICD spectrum (vide infra) with a negative sign of the Cotton effect was observed. Also, in this case, $|\Delta\epsilon|$ increased, without any change of fine structure, if the concentration of cyclodextrin increased. Though this suggests that only one species with a nonzero ICD was involved (see Figure 1), a Scatchard plot produced a nonlinear (convex) graph (Figure 3c). This usually signifies cooperative binding of at least two ligands.[13] Thus, the simplest model to fit the data is, at first, the formation of a 1:1 complex with essentially zero ICD within the absorption range of the diazirine chromophore. Thereafter, a 2:1 host−guest complex is formed, giving rise to the ICD observed (see Figure 1). The best fit was obtained using a $K_1 = 900$ M^{-1} and a $K_2 = 340$ M^{-1} (see Table 1 and Experimental Section). According to NMR measurements, a 2:1 host−guest complex has also been suggested for 1-bromoadamantane and **6-Cy**. Association constants, however, were not determined.[7]

In the case of **1**@(**7-Cy**), the ethanol content in the solvent mixture was varied, so that an extrapolation for the association constant in pure water could be accomplished (see Table 1). The value of 43 000 M^{-1} for K_1 is at the higher end of the range usually found for **7-Cy** complexes.[6] Comparison of the association constants of the three cyclodextrins with **1** under

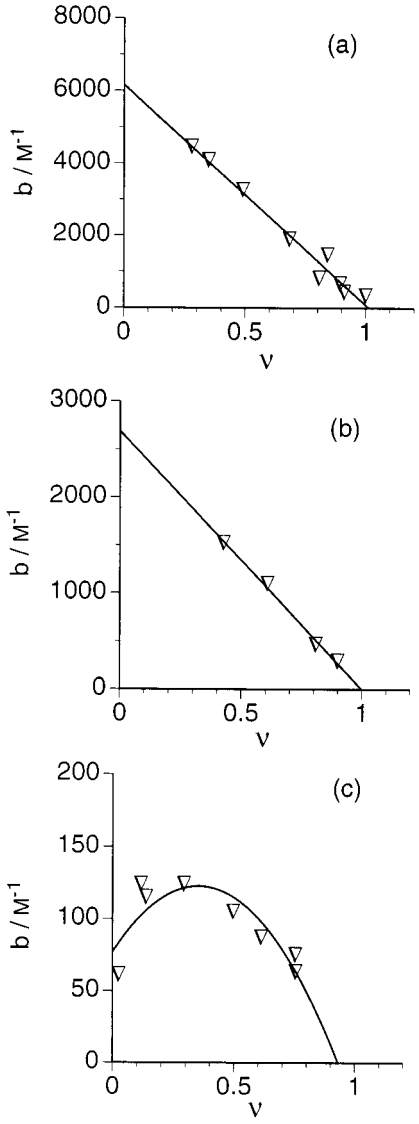


Figure 3. Scatchard plots (b vs ν; where $\nu = \Delta\epsilon/\Delta\epsilon_\infty$ and b = ν/[**Cy**]) for the complex formation of **1** with (a) **7-Cy**, (b) **8-Cy**, and (c) **6-Cy** in water with 30% v/v ethanol.

(12) (a) Isaev, S. D.; Yurchenko, A. G.; Stepanov, F. N.; Kolyada, G. G.; Novikow, S. S.; Karpenko, N. F. *Zh. Org. Khim.* **1973**, *9*, 724. (b) Bayley, H.; Knowles, J. R. *Biochemistry* **1978**, *17*, 2420. (c) Bayley, H.; Knowles, J. R. *Biochemistry* **1980**, *19*, 3883. (d) Moss, R. A.; Chang, M. J. *Tetrahedron Lett.* **1981**, *22*, 3749. (e) Modarelli, D. A.; Morgan, S.; Platz, M. S. *J. Am. Chem. Soc.* **1992**, *114*, 7034. (f) Buterbaugh, J. S.; Toscano, J. P.; Weaver, W. L.; Gord, J. R.; Hadad, C. M.; Gustavson, T. L.; Platz, M. S. *J. Am. Chem. Soc.* **1997**, *119*, 3580.

(13) Cantor, C. R.; Schimmel, P. R. *Behavior of Biological Macromolecules*, Part III; W.H. Freeman: San Francisco 1980; p 849.

Table 1. Association Constants for the Formation of Complexes of **1** with Cyclodextrins in Water−Ethanol Mixtures at 293 K Determined by the ICD Spectra Observed at Different Concentrations of Components

components	% v/v EtOH	x_{EtOH}	K_1 (M^{-1})	K_2 (M^{-1})	correlation factor for Scatchard plot	no. of points	$\Delta\epsilon_\infty$ (ca. 380 nm) (M^{-1} cm^{-1})
1 + **6-Cy**	30	0.115	900[a]	340[a]		8	−0.732
1 + **7-Cy**	30	0.115	6150 ± 300		−0.990	9	+0.057
1 + **8-Cy**	30	0.115	2740 ± 200		−0.998	4	−0.011
1 + **7-Cy**	20	0.071	15000 ± 1000		−0.999	4	+0.050
1 + **7-Cy**	15	0.052	37000 ± 2000		−0.999	4	+0.053
1 + **7-Cy**	10	0.033	40000 ± 3000		−0.992	5	+0.051
1 + **7-Cy**	0	0	43000[b]				

[a] For the confidence interval see Figure 5. [b] Extrapolated value using the association constants for the four different water−ethanol mixtures, which display a sigmoidal dependence from x_{EtOH}; confidence interval 40000−50000 M^{-1}.

similar conditions clearly reveals that **1** is accommodated best by the cavity of **7-Cy**.

The fine structures of the ICD (Figure 2) and UV−vis spectra (Figure 4b) of the diazirine chromophore for the complexes of **1** with **7-** and **8-Cy** are similar to that of the UV−vis spectra of **1** in ethanol (Figure 4b) and dioxane (not shown). This is in accord with a widely accepted belief that the polarity of the **Cy** cavity is similar to solvents such as ethanol and dioxane.[6a] In contrast with **1**@(**7-Cy**) and **1**@(**8-Cy**), the spectra for the 2:1 complex of **6-Cy** and **1** are distinctly different. Here, the UV−vis (Figure 4a) and also the ICD (Figure 1) spectrum display a detailed fine structure,[14] a phenomenon which is normally observed for diazirines only in hydrocarbon solvents.[12f] Therefore, the guest must really be situated in the hydrophobic hollow formed by two host molecules. There, the diazirine chromophore experiences a very apolar microenvironment, even in aqueous solution! Moreover, there seems to be no interaction of the lone pairs of the diazirine nitrogen atoms with the hydroxy groups of the cyclodextrin. Furthermore, on the basis of the Kirkwood−Tinoco theory of polarization developed for cyclodextrins, Harata's rule[15] predicts the following: A guest chromophore residing inside the cavity will produce a negative Cotton effect (−ICD), if the transition dipole moment of the guest chromophore is aligned perpendicular to the axis of the **Cy** cavity. For the $n_- \rightarrow \pi^*$ transition of **1**, this is in agreement with our experimental results which imply the proposed structures for **1**@**2**(**6-Cy**) (four arrangements possible, see Scheme 1). At this point, however, no decision can be made as to which of the four structures represents the isolated inclusion complex.

The above findings also parallel the solubilities of the complexes. **1**@**2**(**6-Cy**) is quite a bit more soluble in water than **7-** and **8-Cy**. For dimethyl sulfoxide (DMSO) the opposite holds true. Thus, in **1**@**2**(**6-Cy**) the main part of hydrophobic **1** should be buried in the two **6-Cy** pockets. On the other hand, the solubility of **6-Cy** itself in water is much greater than that of **7-Cy** and, therefore, also this effect may contribute to the solubilities observed for the complexes.

Although the CD induced by cyclodextrins is usually quite small,[10,11] the intensity of **1**@**2**(**6-Cy**) is surprisingly large, falling within the range for optically active diazirines.[16] This is a further indication that the diazirine moiety must experience strong interactions with the chiral skeleton of the D-glucose entities of *one* **6-Cy** molecule.[17] By contrast, the extremely weak ICD found for **1**@(**8-Cy**) can be interpreted in terms of an increased mobility of **1** within the considerably larger **8-Cy** cavity.

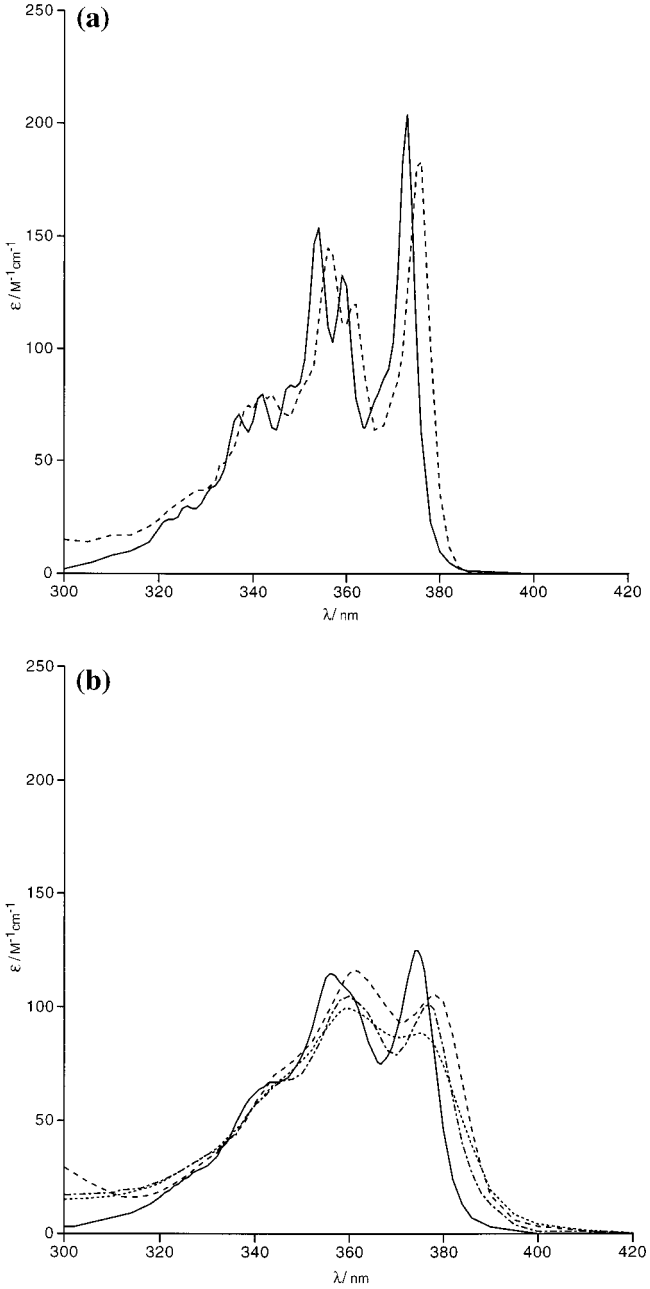


Figure 4. (a) Electronic absorption spectrum (UV−vis) of azi-adamantane (**1**) in cyclohexane (—) in comparison with the spectrum of **1**@**2**(**6-Cy**) (---) in water with 30% v/v ethanol. (b) Electronic absorption spectra (UV−vis) of azi-adamantane (**1**) in ethanol (—), of **1**@(**7-Cy**) (---), **1**@(**8-Cy**) (—·—), and of free **1** (···), the last three in water with 30% v/v ethanol.

On a preparative scale, good yields (ca. 75%) of the respective inclusion complexes could be isolated from the water−ethanol

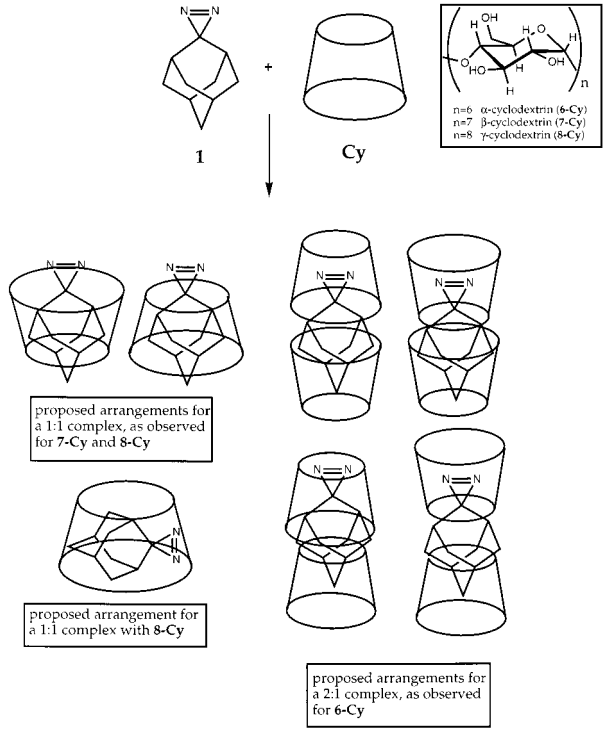
(14) The maxima in the fine structure of the UV−vis spectrum match perfectly with those of the ICD spectrum, as one would expect.

(15) (a) Harata, K. *Bioorg. Chem.* **1981**, *10*, 255. (b) Harata, K.; Uedaira, H. *Bull. Chem. Soc. Jpn.* **1975**, *48*, 375.

(16) Shustov, G. V.; Varlamov, S. V.; Rauk, A.; Kostyanovsky, R. G. *J. Am. Chem. Soc.* **1990**, *112*, 3403.

(17) This could cause a distortion of the diazirine moiety itself. Under these circumstances an agreement with Harata's rule would be coincidental.

Scheme 1



(30%) solvent system. All complexes have been characterized by mp, elemental analysis, FAB-MS, ^{1}H NMR, and UV−vis spectra. Dissolution of the complexes to record the NMR and UV spectra leads, of course, at least partially, to dissociation. Nevertheless, these methods allow the stoichiometry of the solid complexes to be determined.

In conclusion, using the ICD and UV−vis techniques outlined above, it was not only possible to determine the stoichiometry and association constants for the host−guest inclusion complexes of **1** with all three cyclodextrins but also to gain some insight into the microenvironment of the diazirine moiety. In solution, this part of the diazirine in **1**@(**7-Cy**) and **1**@(**8-Cy**) seems either to be exposed to the solvent to some extent or is placed in vicinity of the hydroxy groups of the glucose entities. In contrast, **1** experiences an apolar surrounding in **1**@**2**(**6-Cy**) in solution. These findings disagree with the widely held belief[6a] of a dioxane or ethanol-like polarity of the **Cy** cavity. In **1**@**2**(**6-Cy**) the diazirine function interacts strongly with the chiral environment of a second **6-Cy**, which leads to a very large ICD.

The results are in accord with expectations obtained from molecular modeling studies, indicating that **1** only poorly fits into the cavity of one **6-Cy** molecule.[18] Therefore, the azi moiety can be entrapped by a second **6-Cy** (see Scheme 1).

Experimental Section

UV−vis and CD spectra were recorded with a Perkin-Elmer Lambda 7 spectrometer and a CD6 circular dichrograph (I.S.A. Jobin-Yvon), respectively, in thermostated (20 ± 1 °C) quartz cuvettes (1−10 cm path length). Spectroscopic grade ethanol, cyclohexane, and dioxane were purchased from Merck (Uvasol). ^{1}H NMR spectra were obtained with a Bruker Avance DRX 250 (250 MHz) instrument at 300 K. FAB mass spectra were measured with a Finnigan MAT 900 spectrometer (Cs 35 keV, glycerol).

1 was synthesized according to the literature[12] and recrystallized from ethanol. The cyclodextrins (**6-Cy**, **7-Cy**, and **8-Cy**) were used without further purification. The purity was determined by elemental analysis and was 90% (8% H_2O, 2% cannot be accounted for), 87% (9% H_2O, 4% cannot be accounted for), and 91.5% (7% H_2O, 1.5% cannot be accounted for), respectively. The water used throughout this study was purified by a Milli-Q water system (Millipore). Ethanol, for the preparation of complexes, was spectroscopic grade (see above).

(18) Bobek, M.; Buchkremer, R.; Kupfer, R.; Rosenberg, M. G.; Brinker, U. H. Unpublished results.

Table 2. Experimental Data of the Variable Concentration ICD Measurements for the Association of **1** with **6-**, **7-**, and **8-Cy** at 293 K in Water−Ethanol Mixtures

components	% v/v EtOH	c_0 (mM)[a]	R[a]	$\Delta\epsilon$
1 + **6-Cy**	30	1.00	12.00	−0.553
		1.00	10.00	−0.552
		1.00	7.00	−0.448
		0.70	6.75	−0.364
		0.35	6.75	−0.215
		0.30	4.00	−0.101
		0.14	6.75	−0.086
		0.20	2.00	−0.018
1 + **7-Cy**	30	1.00	4.00	+0.057
		1.60	2.25	+0.052
		0.70	2.86	+0.051
		0.50	2.80	+0.046
		0.50	2.00	+0.048
		0.20	2.50	+0.039
		0.10	2.00	+0.028
		0.04	2.50	+0.020
		0.06	1.33	+0.016
1 + **8-Cy**	30	1.00	4.00	−0.0099
		0.80	3.00	−0.0089
		0.40	2.00	−0.0067
		0.28	1.43	−0.0047
1 + **7-Cy**	20	1.00	4.00	+0.050
		1.00	1.17	+0.043
		0.20	1.17	+0.032
		0.04	1.17	+0.017
1 + **7-Cy**	15	0.50	4.00	+0.0519
		0.333	3.00	+0.0505
		0.167	2.00	+0.0456
		0.054	2.00	+0.0379
1 + **7-Cy**	10	0.35	4.29	+0.0496
		0.30	2.22	+0.0487
		0.15	2.22	+0.0449
		0.050	2.22	+0.0395
		0.040	1.50	+0.0300

[a] Abbreviations as defined in Scheme 2.

Measurement of the ICD and Determination of Association Constants. For the measurement of concentration-dependent ICD spectra, stock solutions of **1** in ethanol and of the appropriate cyclodextrin in water (subsequently filtered) were mixed. Ethanol was added to give the desired ethanol content. Then the flask was filled up with water to give the final volume. The concentrations of **1** ranged from 0.04 to 2 mM. The respective cyclodextrins were always used in excess [from R (equivs) = 1.1 to R = 12] (Table 2). The preparation of solutions was done in dim light, and the solutions were measured immediately. The spectra obtained did not change within 1 h, if the solutions were kept in the dark. Only in the case of the most concentrated solutions did a faint precipitate (opaque solution) form after some time. Spectra were run in the accumulative mode (2−10 scans). It was checked, however, that no change in spectra occurred during this time. Therefore, the radiation absorbed during each scan—from 300 to 420 nm—is too weak to initiate appreciable photochemical decomposition of the diazirine. UV−vis spectra were always run parallel to the CD spectra. The $\Delta\epsilon$ values at a chosen wavelength (usually of the most bathochromic progression band at λ = ca. 380 nm) were then used for Scatchard plot analyses.[8,13] In the case of complex formation between **1** and **6-Cy** or **8-Cy**, full saturation could not be reached. The $\Delta\epsilon$ values for 100% complex ($\Delta\epsilon_\infty$) were obtained by optimization of the fit between data and association constant(s). The Scatchard plot for the association of **6-Cy** with **1** gave only convex lines, indicating that at least two association steps take place (Figure 3c). For the higher concentrations of **6-Cy**, a linear Scatchard plot could be obtained (assuming a 1:1 complex) giving K = 380 M^{-1}. In these cases, in equilibrium only **1**@(**6-Cy**) and **1**@**2**(**6-Cy**) are present

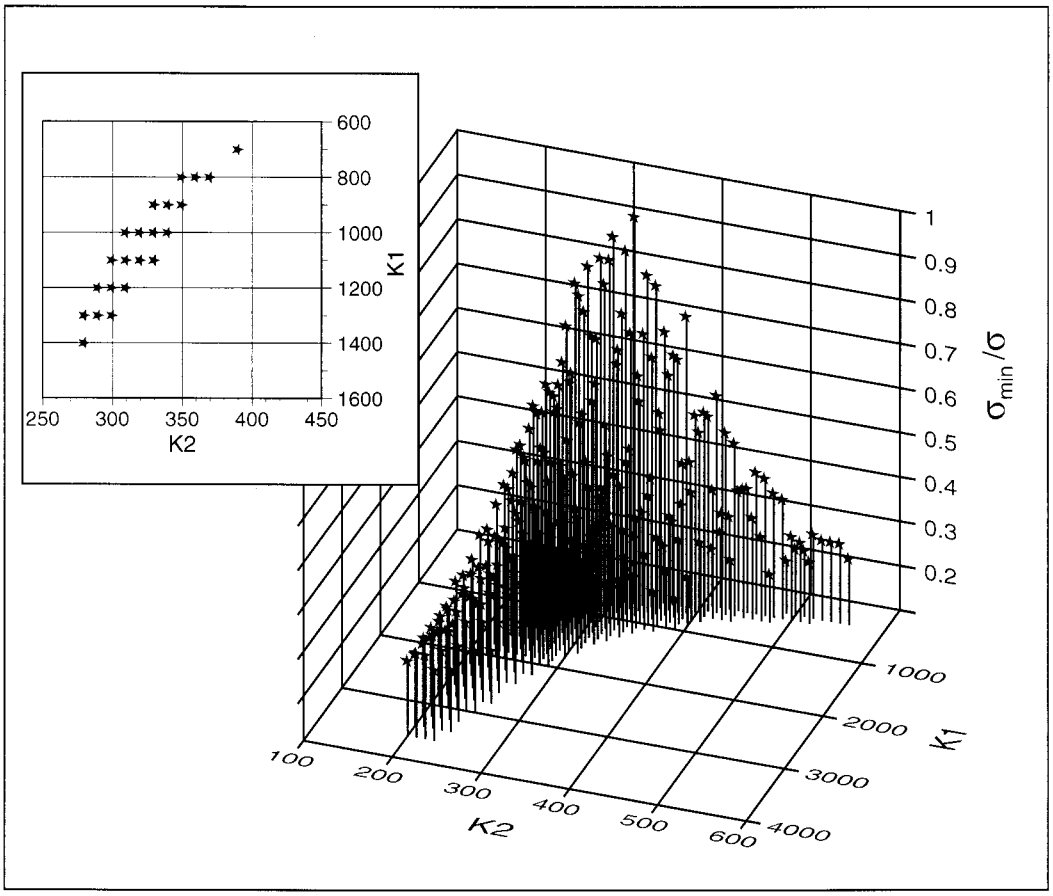
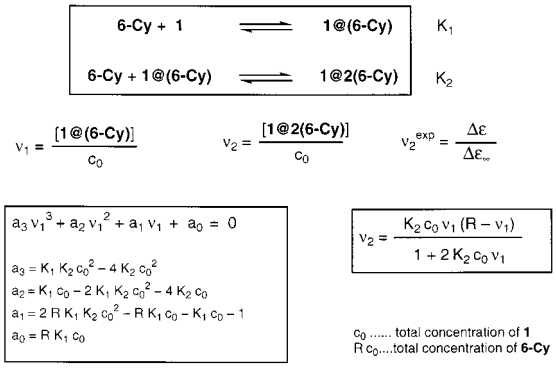


Figure 5. Agreement of the experimental data obtained for the proportion of **1@2(6-Cy)** (ν_2^{exp}) with the values calculated for different pairs of K_1/K_2 (M^{-1}). Deviations are expressed in terms of $\sigma = \Sigma(\nu_2^{exp} - \nu_2^{calcd})^2$, which reaches a minimum for the best fit ($\sigma = \sigma_{min}$) (see Experimental Section and Scheme 2). In the inset the pairs K_1/K_2 lying within a reasonable confidence level of $\sigma_{min}/\sigma \geq 0.7$ are displayed.

Scheme 2. Equilibria for the Formation of the 1:1 and 2:1 Complexes Observed for **6-Cy** with **1**. Equations for Calculation of the Proportions of **1**@(**6-Cy**) and **1**@**2**(**6-Cy**) for Selected Pairs of K_1 and K_2 and Given Values of c_0 and R



in substantial amounts. Thus, the K obtained is a fair approximation for K_2. For a determination of both equilibria, values for ν_2 (see Scheme 2) were calculated for all concentrations and chosen values of K_1 (300, 400, 500, ..., 3600 M^{-1}) and K_2 (200−650 M^{-1}, within the best fitting range in steps of 10 M^{-1}) and compared with the experimental data ν_2^{exp} by the term $\sigma = \Sigma(\nu_2^{calcd} - \nu_2^{exp})^2$. The pair K_1/K_2 (900/340) produces the smallest deviation from experimental values with $\sigma_{min} = 1.58 \times 10^{-4}$, corresponding to deviations of less than 4% for all $\Delta\epsilon$ values, with the exception of the smallest one (8% deviation), which are all well within experimental errors. The three-dimensional plot of K_1, K_2, and σ_{min}/σ allows for an estimate of the regions of K_1 and K_2 with the highest probability (Figure 5). Keeping in mind the experimental errors, pairs of K_1/K_2 with ratios $\sigma_{min}/\sigma > 0.7$ are all within a reasonable confidence level (see inset Figure 5).

Preparation of Complexes. 1@2(6-Cy). A clear solution of **6-Cy** (1000 mg, 90%, 0.925 mmol) in water (25 mL) and ethanol (9 mL) was degassed by ultrasonication for 15 min. Then it was combined with a solution of **1** (25 mg, 0.155 mmol) in ethanol (1.7 mL) under vigorous stirring. Instantly, a precipitate formed and the mixture was stirred for 2−5 h at room temperature in the dark and then kept for 20 h at 5 °C. After centrifugation at 5 °C, the supernatant was discarded and the pellet was washed once with 2−5 mL of cold water−ethanol (30% v/v). Centrifugation and drying at room temperature in vacuo (0.01 Torr) for 5 h afforded 275 mg of the complex (yield 75%, taking into account composition and content as determined by elemental analysis): mp = 295−303 °C (dec); ^{1}H NMR[19] (D_2O) δ 5.02 (d, J = 3.4 Hz, 12.6 H, **6-Cy**), 4.05−3.7 (m, 51 H, **6-Cy**), 3.63 (q, J = 7.0 Hz, 2 H, CH_3CH_2OH), 3.62−3.50 (m, 25 H, **6-Cy**), 2.45 (s br, 2 H, **1**), 2.35−2.2 (m br, 4 H, **1**), 2.10−1.93 (m br, 6 H, **1**), 1.15 (t, J = 7.0 Hz, 3 H, CH_3CH_2OH), 1.01 (s br, 2 H, **1**) ppm; UV−vis H_2O−EtOH (30%) λ 375 nm (ϵ = 102), 361 (106) (values in accord with $c = 8.5 \times 10^{-4}$ M in agreement with the content obtained by elemental analysis); MS (+FAB, glycerol containing 10% water) *m/e* 2107.5 [M^+ + 1, 2%], 1945.6 [M^+ + 1 − 162 (**1**), 3%], 1065.7 [(M^+(**6-Cy**) + 1 + 92 (glycerol), 18%], 973.6 [(M^+(**6-Cy**) + 1, 100%].

Anal. Calcd for $C_{87.6}H_{148}N_2O_{65}$ [**1**@**2.1**(**6-Cy**)·C_2H_5OH·H_2O] (2269.2): C, 46.36; H, 6.57; N, 1.23. Found: C, 44.07; H, 6.31; N, 1.19 (corresponding to a content of 96%).

1@(7-Cy). Procedure A. A clear solution of **7-Cy** (461 mg, 86.6%, 0.352 mmol) in water (52 mL) and ethanol (12 mL) was degassed by ultrasonication for 15 min. Then it was combined with a solution of

(19) The number of hydrogen atoms of the **Cy** moieties (and of ethanol molecules) corresponds to the true intregration values relative to one molecule of the guest **1**.

1 (51 mg, 0.32 mmol) in ethanol (5 mL) under vigorous stirring, forming a precipitate. After 1 h of stirring at room temperature, the mixture was kept at 5 °C for 20 h. Workup, as described for the preparation of **1**@**2**(**6-Cy**), yielded 315 mg of complex (73%, taking into account the content as determined by elemental analysis). **Procedure B.** A clear solution of **7-Cy** (461 mg, 86.6%, 0.352 mmol) in water (24 mL) was mixed at once with a solution of **1** (51 mg, 0.32 mmol) in diethyl ether (0.25 mL) under vigorous stirring and shaking. The mixture was stirred at room temperature under an argon atmosphere and protected from light for 4 days. The pellet obtained after addition of ca. 5 mL of water and centrifugation was again suspended in 10 mL of water and centrifuged and dried in vacuo (0.01 Torr) to yield 320 mg of the product (74%), identical with the product obtained by procedure A: mp = 310−314 °C (dec); ^{1}H NMR[19] (DMSO-d_6) δ 5.75−5.60 (m, 14 H, **7-Cy**), 4.84 (d, J = 3.5 Hz, 7 H, **7-Cy**), 4.44 (t, J = 5.5 Hz, 7 H, **7-Cy**), 3.75−3.5 (m, 28 H, **7-Cy**), 3.42−3.25 (m, 14 H, **7-Cy**), 2.1−1.9 (m br, 6 H, **1**), 1.85−1.73 (m br, 6 H, **1**), 0.64 (s br, 2H, **1**) ppm; UV−vis H_2O−EtOH (30%) λ 377 nm (ϵ = 97), 361 (109) (values in accord with $c = 3.9 \times 10^{-4}$ M, in agreement with the content obtained by elemental analysis); MS (+FAB) *m*/*e* 1227.5 [$M^+ + 1 - 162$ (**1**) + 92 (glycerol), 85%], 1135.7 [$M^+ + 1 - 162$ (**1**), 100%].

Anal. Calcd for $C_{52}H_{84}N_2O_{35}$ [**1**@(**7-Cy**)] (1297.18): C, 48.14; H, 6.53; N, 2.16. Found: C, 46.36; H, 6.32; N, 2.07 (corresponding to a content of 96%).

1@(8-Cy). To a clear solution of **8-Cy** (311 mg, 91.7%, 0.22 mmol) in water (11 mL) were added ethanol (2 mL) and subsequently a solution of **1** (32 mg, 0.20 mmol) in ethanol (2 mL) under vigorous stirring. Instantly, a precipitate formed and the mixture was stirred for 2 h at room temperature in the dark. Subsequently it was kept for 24 h at 5 °C. Workup as described above gave 245 mg of complex (76%, taking into account composition and content as obtained by elemental analysis): mp = 295−305 °C (dec); ^{1}H NMR[19] (DMSO-d_6) δ 5.77−5.67 (m, 16 H, **8-Cy**), 4.89 (d, J = 3.5 Hz, 8 H, **8-Cy**), 4.49 (t, J = 5.5 Hz, 8 H, **8-Cy**), 3.70−3.50 (m, 32 H, **8-Cy**), ca. 3.5 (m, 0.7 H, CH_3CH_2OH), 3.45−3.25 (m, 16 H, **8-Cy**), 2.06−1.90 (m br, 6 H, **1**), 1.85−1.74 (m br, 6 H, **1**), 1.07 (t, J = 7.0 Hz, 1 H, CH_3CH_2OH), 0.63 (s br, 2H, **1**) ppm; UV−vis H_2O−EtOH (30%) λ 376 nm (ϵ = 93), 359 (104) (values in accord with $c = 2.8 \times 10^{-4}$ M, in agreement with the content as obtained by elemental analysis); MS (+FAB) *m*/*e* 1389.7 [$M^+ + 1 - 162$ (**1**) + 92 (glycerol), 25%], 1297.7 [$M^+ + 1 -$ 162 (**1**), 100%].

Anal. Calcd for $C_{58.7}H_{104}N_2O_{44.3}$ [**1**@(**8-Cy**)·0.33C_2H_5OH·4H_2O] (1546.6): C, 45.58; H, 6.78; N, 1.81. Found: C, 43.79; H, 6.44; N, 1.70 (corresponding to a content of 96%).

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