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Zn^{II}-induced conformational control of amphiphilic cavitands in Langmuir monolayers†

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The reversible switching from the C_{4v}-symmetric *vase* to the C_{2v}-symmetric *kite* conformation of an amphiphilic resorcin[4]arene cavitand was induced by Zn^{II} ion coordination. Langmuir monolayers were obtained of both conformers with the area per molecule increasing dramatically from 120 Å^2 for the *vase* to 270 Å^2 for the *kite* form. ^{1}H NMR spectroscopy in chloroform solution supports the formation of a stoichiometric *kite*-cavitand·(Zn^{II})$_2$ complex, with the metal ions coordinating to pairs of neighbouring quinoxaline N-atoms.

Cram and co-workers showed that resorcin[4]arene cavitands with quinoxaline flaps prefer the closed *vase* conformation in apolar solvents at elevated temperature (> 318 K) whereas they adopt the open *kite* form upon cooling (< 213 K).[1] Later, Diederich and co-workers found that conformational *vase* ⟶ *kite* switching can also be reversibly induced at room temperature by protonation of the mildly basic quinoxaline N-atoms.[2] Here, we describe the discovery made during the production of Langmuir monolayers[3] of the amphiphilic cavitand **1**[4] and velcrand **2** (see ESI for characterisation†) that this switching also occurs in the presence of Zn^{II} ions. ^{1}H-NMR solution studies provide strong evidence that the ions stabilize the *kite* form by coordinating in a stoichiometric way to the quinoxaline N-atoms of the cavitand.[5]

Very different molecular area requirements were determined by X-ray crystal structure analysis for cavitand **1** and velcrand **2**.[6] For **1**, which prefers the *vase* conformation, a value of 120 Å^2 was estimated whereas for **2**, which stays exclusively in the extended *kite* conformation due to its four aromatic methyl groups,[1c] a value of 290 Å^2 was measured. Subsequently, Langmuir film studies were undertaken, by spreading solutions of **1** and **2** in CHCl$_3$ on the pure water subphase,[7] with the objective to demonstrate that this technique would allow a distinction between the two cavitand geometries (*vase* and *kite*) at the air/water interface. We hypothesized that the macrocycles would arrange themselves in monolayers in which the ester groups comprise the polar part of the molecule and the quinoxaline flaps the hydrophobic headgroup.

Fig. 2 shows the surface pressure-area (*Π*–*A*) isotherms of **1** (red curve) and **2** (blue curve) films at the air/water interface. Both cavitands form a stable monolayer with a collapse pressure of 65 mN m^{-1} and 47 mN m^{-1}, respectively. The limiting area for **1**, estimated by extrapolating the linear region of the curve to zero pressure, is approximately 125 Å^2 which is in good agreement with the predicted value. On the other hand, the extrapolation of the isotherm of velcrand **2** gives an area per molecule of 140 Å^2, about 1/2 of the value of 290 Å^2 predicted for a single-molecule monolayer. The measured limiting area value confirms that dimerisation of **2** under formation of velcraplexes,[1c,d,5] with the flat surfaces facing each other, occurs at the air/water interface, resulting in a defined double layer.

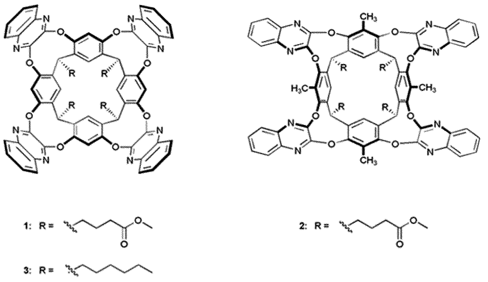

Fig. 1 Structures of the cavitands.

In another Langmuir calibration experiment, we studied the pH-promoted *vase* – *kite* switching[2] of the monolayers of **1** at the air/water interface upon addition of CF$_3$COOH (TFA) into the water subphase. Upon lowering the pH from 7 to 1, the area per molecule increased from 125 Å^2 to 225 Å^2, suggesting formation of a monolayer of **1** in the *kite* conformation (see ESI†).

The monolayers of **1** were subsequently investigated upon addition of Zn(OAc)$_2$ into the water subphase.[8] The black and blue isotherms (Fig. 3) were collected after spreading a solution of **1** in CHCl$_3$ in the absence and presence of Zn^{II} ions ([**1**]: [Zn^{II}] = 1 : 5000), respectively. The observed variation of the area per molecule (Table 1) led us to perform the experiments by spreading a solution of cavitand **1** in CHCl$_3$ and different volumes of a 7.3 mM solution of Zn(OAc)$_2$ in a mixture of CHCl$_3$/MeOH 7 : 1 on the water subphase nearly saturated by Zn(OAc)$_2$. The monolayers were allowed to equilibrate for 20 min before the compression was

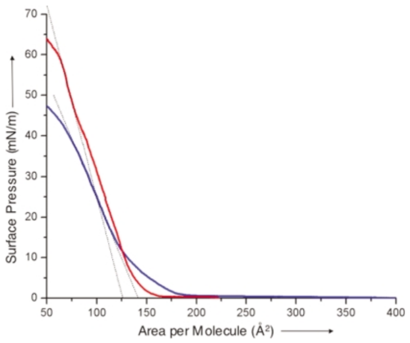

Fig. 2 Pressure–area (*Π*–*A*) isotherms of cavitand **1** (red line) and velcrand **2** (blue line) monolayers on pure water subphase.

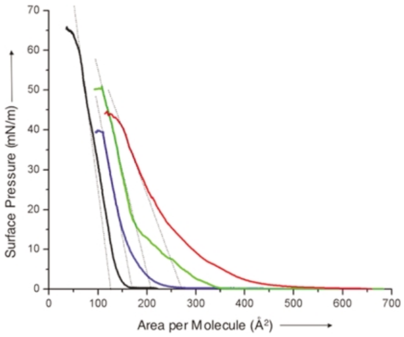

Fig. 3 Pressure–area (*Π*–*A*) isotherms of cavitand **1** (black line) on pure water subphase and (blue, green and red lines) in the presence of Zn(OAc)$_2$ in the water subphase. For experimental conditions, see Table 1.

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† Electronic supplementary information (ESI) available: characterization of **1** and **2**; protocol of Langmuir experiments performed on the water subphase at different pH; Job plot analysis. See http://www.rsc.org/suppdata/cc/b4/b405331a/

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started. The green and red isotherms were measured under these experimental conditions: the area per molecule values are now significantly larger, becoming nearly identical (red isotherm) to the theoretical value calculated for a monolayer of cavitand **1** in the *kite* conformation, which is 290 Å^2. Further increase in the concentration of $Zn(OAc)_2$ does not change the observed area per molecule.

We subsequently proceeded to obtain proof for this new metal-induced *vase* ⟶ *kite* conformational change in $CDCl_3$ by ^1H NMR spectroscopy, monitoring the resonance of the methine proton in the resorcinarene bowl.[1] These investigations were carried out with **3**[9] instead of **1**, due to the disturbing methyl ester resonances of the latter in the spectral region around 4 ppm where the triplet of the methine proton in the *kite* conformation is observed.

In the spectrum of **3** at 295 K (Fig. 4a), the methine protons appear as a triplet at 5.54 ppm, characteristic of the *vase* conformation. Addition of TFA (Fig. 4b) or lowering the temperature to 193 K (Fig. 4c) shifts the resonance upfield above 3.8 ppm, as expected for the *kite* conformer.[1] Addition of ZnI_2 and CD_3OD (2.5 eq. of CD_3OD with respect to ZnI_2 were necessary to solubilize the salt in $CDCl_3$) to a solution of **3** (c = 4.5 mM) at 295 K in $CDCl_3$ (Fig. 4d) also shifted the triplet for the methine protons above 4 ppm.‡ Complete conversion to the *kite* conformation, as indicated by a fully resolved triplet at 3.90 ppm was achieved at $[ZnI_2]$ = 0.78 M and $[CD_3OD]$ = 1.92 M, when the metal ion to cavitand ratio was 170 : 1. Upon further addition of CD_3OD (c = 3.77 M), the equilibrium is pushed back to the *vase* conformation, demonstrating the reversibility of the switching process.

Molecular models suggest that the distance between two neighbouring quinoxaline pairs in the C_{2v} symmetric *kite* form is suitable for Zn^{II} coordination ($d(N\cdots Zn^{II}) \approx 2.5$ Å). We therefore hypothesized that the coordination of two Zn^{II} ions by the two pairs of neighbouring N-atoms would provide the driving force for the observed *vase* ⟶ *kite* conversion.§ The 1 : 2 [**3** : $(Zn^{II})_2$] coordination stoichiometry was subsequently confirmed by Job plot analysis, with the maximum of the bell-shaped curve appearing at a mole fraction of **3** of 0.33 (ESI†). Zn^{II} coordination to the quinoxaline N-atoms is also apparent from the ^1H NMR spectrum of **3** (Fig. 4d) which depicts the quinoxaline resonances shifted downfield by *ca.* 0.15 ppm with respect to the corresponding resonances of the *kite* form at low temperature (Fig. 4c). A similar downfield shift of *ca*. 0.15 ppm is observed upon protonation with TFA at room temperature (Fig. 4b). The spectrum of the *kite* form complexed to two Zn^{II} ions (Fig. 4d) displays a fourfold symmetry, indicating that *kite1–kite2* interconversion described earlier[10] and ligand-metal ion exchange are fast on the NMR time scale at 295 K. Attempts to measure the kinetics of the *kite1–kite2* equilibrium in the presence of ZnI_2 failed due to poor solubility of the complex at lower temperatures.

Table 1 Experimental conditions and area per molecule values for monolayers of cavitand **1**

1 (10^{-3} mmol)	$[Zn(OAc)_2]$ (mmol)	Volume (cm^3) of $[Zn(OAc)_2]^a$	Area per molecule (Å)^2
1.6	0	0	125
1.6	8	0	169
1.6	8	0.05	210
1.6	8	0.10	270

^{a} 7.3 mM solution of $[Zn(OAc)_2]$ in $CHCl_3$/MeOH (7:1)

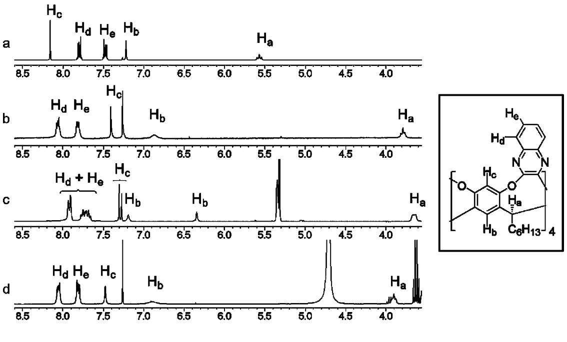

Fig. 4 ^1H NMR spectra (300 MHz) of cavitand **3**: a) $CDCl_3$, 295 K; b) $CDCl_3$, 295 K, TFA (c = 0.48 M); c) CD_2Cl_2/CD_3OD 9 : 1, 193 K; d) $CDCl_3$, 295 K, **3** (c = 4.5 mM), ZnI_2 (c = 0.78 M), CD_3OD (c = 1.92 M). The quartet at 3.62 ppm in spectrum d is due to diethyl ether, an impurity in commercial ZnI_2.

In summary, Langmuir studies on monolayers of resorcin[4]arene cavitands led to the discovery of a new, Zn^{II}-induced *vase* ⟶ *kite* switching mode and NMR investigations in solution strongly support the hypothesis, that the *kite* form is stabilized by stoichiometric coordination of two Zn^{II} ions to neighbouring quinoxaline N-atoms.

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Notes and references

‡ The ^1H NMR samples for the Zn^{II}-induced switching were prepared as follows. ZnI_2 (Acros Organics, 99.999%) was suspended in $CDCl_3$, and the appropriate amount of CD_3OD was added to dissolve the salt. This solution was filled in a 5-mm NMR tube, and cavitand **3** was added.

§ A solvent effect of CD_3OD (2.5 eq.) added for solubilising ZnI_2 is readily excluded. It is known that the *vase* conformation is predominant in polar solvents,[1a,b,2b] yet the ^1H NMR spectrum of **3** at 193 K in CD_2Cl_2 containing CD_3OD (c = 3.91 M) displays exclusively the *kite* conformation (Fig. 4c). Most probably, CD_3OD acts as a competitive ligand for the Zn^{II} ions; in fact, the equilibrium is pushed back to the *vase* conformation by further addition of the alcohol (additional 2.5 eq. with respect to ZnI_2; c_{final} = 3.77 M).

1 (*a*) J. R. Moran, S. Karbach and D. J. Cram, *J. Am. Chem. Soc.*, 1982, **104**, 5826; (*b*) J. R. Moran, J. L. Ericson, E. Dalcanale, J. A. Bryant, C. B. Knobler and D. J. Cram, *J. Am. Chem. Soc.*, 1991, **113**, 5707; (*c*) D. J. Cram, H.-J. Choi, J. A. Bryant and C. B. Knobler, *J. Am. Chem. Soc.*, 1992, **114**, 7748; (*d*) D. J. Cram and J. M. Cram, *Container Molecules and Their Guests*, Royal Society of Chemistry, Cambridge, 1994, pp. 107–130.
2 (*a*) P. J. Skinner, A. G. Cheetham, A. Beeby, V. Gramlich and F. Diederich, *Helv. Chim. Acta*, 2001, **84**, 2146; (*b*) V. A. Azov, F. Diederich, Y. Lill and B. Hecht, *Helv. Chim. Acta*, 2003, **86**, 2149.
3 F. Lagugné-Labarthet, T. Yu, W. R. Barger, D. K. Shenoy, E. Dalcanale and Y. R. Shen, *Chem. Phys. Lett.*, 2003, **381**, 322.
4 V. A. Azov, P. J. Skinner, Y. Yamakoshi, P. Seiler, V. Gramlich and F. Diederich, *Helv. Chim. Acta*, 2003, **86**, 3648.
5 For reports on $La(OTf)_3$-induced switching by different mechanisms, see: (*a*) P. Amrhein, P. L. Wash, A. Shivanyuk and J. Rebek Jr., *Org. Lett.*, 2002, **4**, 319; (*b*) P. Amrhein, A. Shivanyuk, D. W. Johnson and J. Rebek Jr., *J. Am. Chem. Soc.*, 2002, **124**, 10349.
6 (*a*) For the crystal structure of **1**, see ref. 4. A high-resolution crystal structure of **2** (P. Seiler, M. Frei and F. Diederich, unpublished results) resembles those of other velcrands previously reported at lower resolution by Cram and co-workers and will be published elsewhere.
7 (*a*) A. Ulman, *An Introduction to Ultrathin Organic Films From Langmuir-Blodgett to Self-Assembly*, Academic Press, San Diego, 1991; (*b*) G. G. Roberts, *Langmuir-Blodgett Films*, Plenum Press, New York, 1990.
8 (*a*) A. E. Martel and R. D. Hancock, *Metal Complexes in Aqueous Solutions*, Plenum Press, 1996; (*b*) F. A. Cotton, G. Wilkinson and P. L. Gaus, *Basic Inorganic Chemistry*, Wiley, New York, 1987.
9 P. Soncini, S. Bonsignore, E. Dalcanale and F. Ugozzoli, *J. Org. Chem.*, 1992, **57**, 4608.
10 V. A. Azov, B. Jaun and F. Diederich, *Helv. Chim. Acta*, 2004, **87**, 449.