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Full Papers

Molecular recognition of neutral molecules by rigid binaphthyl metalloclefts: synthesis, complexation and calculations

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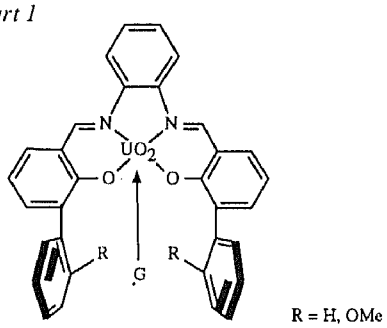
Abstract. The binaphthyl metallocleft **2** in which an electrophilic uranyl cation is immobilized was synthesized by reaction of 1,2-benzenediamine and aldehyde **5**. According to ^{1}H-NMR spectroscopy, **2** is formed as a mixture of meso and racemic diastereomers (ratio 1 : 0.85). The complexation of **2** with pyridine, (iso)quinoline, acridine, benzylamine, and 1-naphthalenemethanamine was investigated. The association constants of the complexes with aromatic amines vary from $3.5 \cdot 10^2$ to $3.6 \cdot 10^6$ M^{-1} (meso-**2**) and $1.5 \cdot 10^2$ to $1.0 \cdot 10^6$ M^{-1} (racemic-**2**). The higher stability of the complexes with meso-**2** is in agreement with the results of molecular mechanics calculations.

Introduction

In previous papers, we have demonstrated that metallomacrocycles containing an immobilized uranyl cation represent an important class of receptors for the selective complexation of neutral molecules[1]. The Lewis-acidic uranyl cation complexed in a salen* or salophene moiety prefers a pentagonal-bipyramidal coordination with the two oxygens at the apical positions and with the four coordinating sites of the salen/salophene moiety *and a neutral molecule* in the equatorial positions. Based on this concept we have recently also introduced the *metalloclefts*[2,3]. Metallocleft **1** (Chart 1) is only moderately preorganized because of the relatively low rotational barrier of the biphenyl moiety. Incorporation of a binaphthyl unit, which has a higher degree of preorganization via a larger rotational barrier, might result in the formation of diastereomers and, consequently, in the possibly chiral recognition of guest molecules. To the best of our knowledge, only a few examples are known of diastereomeric receptors for the complexation of neutral molecules[4]. *Rebek* et al.[4a,b] described Kemp's acid based dilactams, the racemic and meso form of which appeared to be selective for glycine anhydride and quinoxaline-2,3-dione, respectively. *Whitlock* et al.[4c-f] reported appropriately functionalized cyclophanes of which the meso form gave more stable complexes than the corresponding racemic diastereomers.

In the present paper, we describe metallocleft **2** having two 1,1′-binaphthyl backbones (Chart 2). In addition to the formation of two diastereomers (meso-**2** and racemic-**2**) with clefts of different geometries and sizes, this unit also has the advantage that the extended π surface may increase the complex stabilities with aromatic guests. The synthesis of the new binaphthyl metallocleft **2** and the complexation properties of the meso and racemic isomers of **2**, assessed by ^{1}H-NMR titrations and molecular mechanics calculations, will be discussed.

Chart 1



R = H, OMe

1

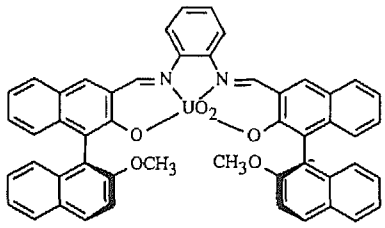
Results and discussion

Synthesis

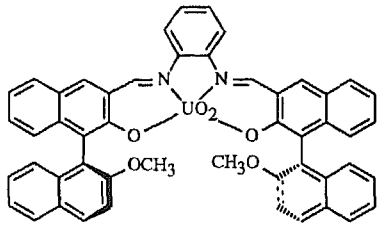
The synthesis of the metallocleft **2** is depicted in Scheme 1. Methoxymethyl ether **4** was obtained in 84% yield by reaction of ether **3** with $BrCH_2OCH_3$–NaH in Et_2O–DMF (5 : 1) at room temperature[5]. Introduction of the formyl group[6] was achieved with BuLi and DMF in THF as a solvent at room temperature to yield 78% of aldehyde **5**[7]. Reaction of aldehyde **5** with 1,2-benzenediamine in MeOH and subsequent addition of $UO_2(OAc)_2 \cdot 2H_2O$ gave metallocleft **2** as the water complex in 38% yield. The positive-ion fast-atom bombardment spectrum exhibits a

* Salen = *N,N′*-ethylenebis(salicylideneiminate)
Salophene = N,N′-phenylene(salicylideneiminate)

Chart 2



meso-2



racemic-2

(one isomer shown)

$(M + H_2O)^+$ and a $(M + H)^+$ peak, which indicate the presence of a coordinated water molecule. In the ^{1}H-NMR spectrum, two methoxy signals are present at 3.75 and 3.55 ppm (ratio of 1 : 0.85).

From X-ray analyses studies, it is known[1a-c,e] that the salophene moiety cocomplexed with a uranyl cation is not flat, but exists in the solid state in a half-open shell with the 1,2-benzenediamine moiety above or below the plane of reference. For assignment of the methoxy signals of **2**, it is important to know whether the exchange of the 1,2-benzenediamine moiety is slow or fast at room temperature on the ^{1}H-NMR time scale and whether more than one isomer can be formed. The fast exchange in the ^{1}H-NMR spectra at room temperature was shown by low-temperature experiments. In $CDCl_3$ and CD_2Cl_2 (both with 20% DMSO-d_6 as a cosolvent), coalescence of the methoxy signal at 3.55 ppm is observed at −55 and −75 °C, respectively[8]. The methoxy signals in the ^{1}H-NMR spectrum are ascribed to two different isomers, meso-**2** and racemic-**2**, and this assignment will be used throughout the present paper. Most probably, the methoxy signal at 3.55 ppm corresponds to the racemic-**2** isomer, because in this isomer the methoxy groups are in the shielding zone of the binaphthyl rings. This assignment is also in agreement with the results of the ^{1}H-NMR complexation studies (vide infra).

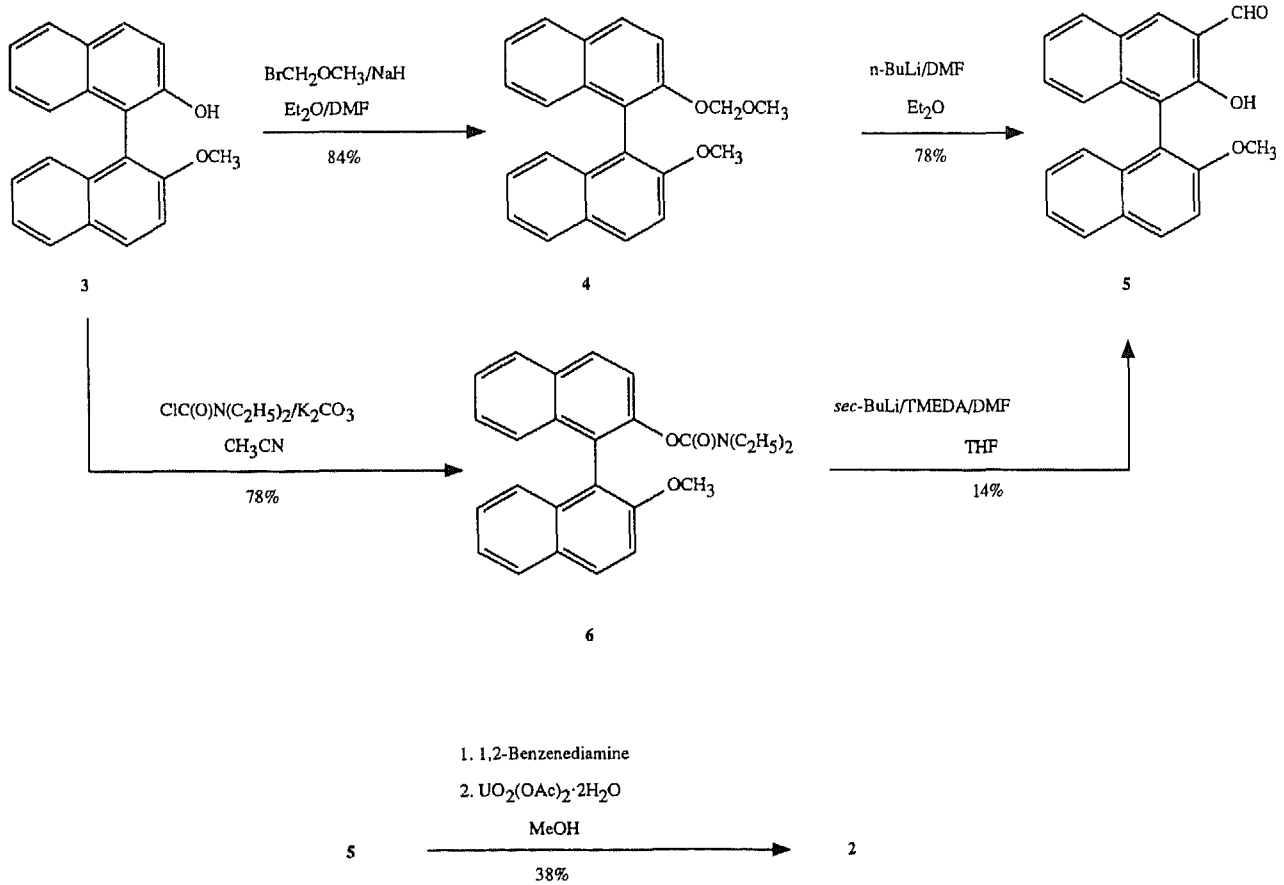
In CH_3CN, the solubility of the isomers is different; unfortunately complete separation was not possible. Chromatographic separation failed due to hydrolysis of metallocleft **2** (silica gel) to give aldehyde **5**.

Complexation

Complexation studies were performed with a mixture of meso-**2** and racemic-**2** isomers (1 : 0.85), using the methoxy signals as a probe in ^{1}H-NMR titrations and with pyridine, quinoline, isoquinoline, acridine, benzylamine, and 1-naphthalenemethanamine as guests. For evaluation of the titration data, two equilibria must be taken into account (equilibria 1 and 2), where G, H(M), and H(R) are the guest, meso and racemic diastereomer, respectively.

$$H(M) + G \rightleftharpoons H(M)\cdot G \qquad K_m = [H(M)\cdot G]/[H(M)][G] \quad (1)$$

$$H(R) + G \rightleftharpoons H(R)\cdot G \qquad K_r = [H(R)\cdot G]/[H(R)][G] \quad (2)$$



Scheme 1

Several methods are available to calculate the association constants of 1 : 1 complexes. Models for a two-ligand- and one-guest-molecule equilibrium have been used less frequently[9]. For calculation of the association constants (K_m and K_r) from the titration data, the chemical shifts of the meso-**2**, meso-**2** · guest, racemic-**2**, and racemic-**2** · guest methoxy signals were used. The chemical shifts of the complexes were determined by adding an excess of guest. A more detailed description of the method is given in the Experimental.

Upon complexation, the upfield shift of the racemic-**2** methoxy signal ($\leq \Delta\delta$ 0.35 ppm) is much larger than that of the meso-**2** methoxy signal ($\leq \Delta\delta$ 0.10 ppm)[10], because in the complexes of racemic-**2** the methoxy groups will be situated more in the shielding zone of the aromatic moiety of the guest. The calculated association constants are presented in Table I.

Several conclusions can be drawn from these results of this table:

(i) Pyridine, quinoline and isoquinoline give the most stable complexes with the meso-**2** isomer. Acridine does not fit in the cleft, which results in a low association constant of $<25\ M^{-1}$ for both isomers. The model cannot be used for the calculation of the stability constants of the 1-naphthalenemethanamine complexes, because the meso-**2** isomer exhibits slow exchange and the racemic-**2** isomer fast exchange. For the meso-**2** and racemic-**2** isomers complexes, stability constants of $3.6 \cdot 10^6$ and $1.0 \cdot 10^6\ M^{-1}$ were calculated (Experimental), respectively. The preorganization of the meso-**2** isomer for the target molecules is reflected in higher association constants.

(ii) The $\Delta\Delta G$ of -2.44 kcal · mol^{-1} (meso-**2** · isoquinoline *vs.* racemic-**2** · isoquinoline) is higher than the differences in selectivities between the previously reported meso and racemic diastereomers, a $\Delta\Delta G$ value of -1.3 kcal · mol^{-1} was published by *Whitlock*[4c-f].

(iii) In addition to the all-hydrogen-bond (*Rebek*)[4a,b] and the hydrogen-bond-stacking (*Whitlock*)[4c-f] approach, the incorporation of a Lewis-acidic metal center in the receptor is a third possibility to achieve selective recognition by diastereomers.

Cram et al.[11,12] incorporated binaphthyl moieties in crown ethers for the chiral recognition of ammonium *cations*. Currently, enantioselective recognition of *neutral molecules*, and biologically active molecules in particular, is of interest[3f,3j,4a-b,13]. Preliminary experiments with chiral guests (*R*- or *S*-methylbenzylamine) reveal that the methoxy signal of the racemic-**2** isomer (3.55 ppm) is split into two clearly separated signals of equal intensity (Figure 1). The two methoxy groups of the *enantiotopic* meso-**2** isomer (3.75 ppm) are also slightly separated upon addition of chiral guest.

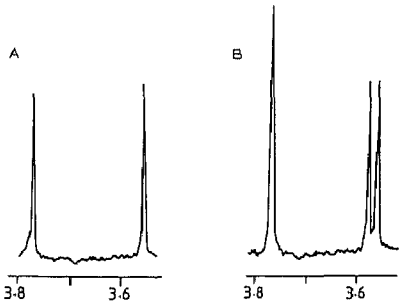


*Figure 1. Part of ^{1}H-NMR spectrum of metallocleft-**2** (A) before and (B) after addition of* R- *or* S*-benzylmethylamine.*

Calculations

Molecular-mechanics calculations were performed in order to rationalize the results of the complexation studies with achiral guests. Since the 1,2-benzenediamine moiety is positioned above and below the plane of reference (*vide supra*), the meso-$\mathbf{2}_{up}$ (methoxy groups and the 1,2-benzenediamine moiety above the plane of reference), meso-$\mathbf{2}_{down}$ (methoxy groups above and the 1,2-benzenediamine moiety below the plane of reference), and racemic-**2** isomer (Chart I) were included in the calculations. The parameters for the uranyl cation and the salophene moiety were used as described[2].

$$\Delta\Delta G = (E_{host \cdot guest1} - E_{host \cdot guest2}) - (E_{guest1} - E_{guest2}) \quad (3)$$

The relative energies of complexation (Eqn. 3) of the metalloclefts meso-$\mathbf{2}_{up}$, meso-$\mathbf{2}_{down}$ and racemic-**2** with MeOH, water, pyridine, quinoline, and isoquinoline as the guests were calculated. MeOH is included because the synthesis of the metallocleft **2** was performed in this solvent (*vide supra*), and water because it is present in the free ligand prior to complexation. The calculated complex stabilities have been compared with those of the water complexes.

From the data in Table II, it is clear that racemic-**2** · MeOH is more stable than the meso-$\mathbf{2}_{up}$ · MeOH and meso-$\mathbf{2}_{down}$ · MeOH complexes by 1.61 and 1.76 kcal · mol^{-1}, respectively. The difference is too small to expect exclusive formation of one isomer in solution. It is also evident that complexation is likely to occur between the meso-$\mathbf{2}_{up}$ isomer and pyridine, quinoline, and isoquinoline. The mini-

Table I Data of complexation experiments in $CDCl_3$ at 298 K.

Guest	$\delta_{complex}$ (ppm)[a]		K_{ass} (M^{-1})[b]		$\Delta\Delta G$ (kcal · mol^{-1})
	meso-**2**	racemic-**2**	meso-**2**	racemic-**2**	
pyridine	3.650	3.329	$1.1 \cdot 10^3$	$7.3 \cdot 10^2$	−0.27
quinoline	3.639	3.471	$3.5 \cdot 10^2$	$1.5 \cdot 10^2$	−0.50
isoquinoline	3.629	3.291	$3.1 \cdot 10^4$	$5.1 \cdot 10^2$	−2.44
acridine	3.724	3.532	<25[c]	<25[c]	–
benzylamine	3.760	3.560	[d]	[d]	–
1-naphthalenemethanamine	3.663	3.527	$3.6 \cdot 10^6$	$1.0 \cdot 10^6$	−0.76[e]

[a] Shifts refer to the methoxy signals of the host: free meso-**2**: δ_{OMe} 3.752 ppm; free racemic-**2**: δ_{OMe} 3.552 ppm. [b] Correlation coefficients of the meso-**2** and racemic-**2** complexes are 0.999 and 0.999 (pyridine), 0.955 and 0.950 (quinoline), 0.981 and 0.947 (isoquinoline), respectively. [c] Estimated values. [d] A major change in the aromatic part of the spectrum is observed; due to the small $\Delta\delta$, no association constants could be determined. [e] For procedure see Experimental.

mized structures of these complexes are depicted in Figure 2.

For the pyridine and isoquinoline complex, T-shaped stacking of both binaphthyl moieties of the cleft with the guest is calculated (Figures 2a and 2b). In the minimized structure of the quinoline complex, parallel stacking with one of the two binaphthyl moieties is observed (Figure 2c). In the isoquinoline complex parallel stacking is not possible due to the relative size and geometry of the host and guest. The same steric reasons allow quinoline to stack parallel with one binaphthyl moiety. *Rebek* demonstrated that parallel stacking for a host with an extended π system is more favorable than with a smaller aromatic ring[3a].

The experimentally determined selectivity of the meso-**2** receptor agrees best with the calculated selectivity for the meso-$\mathbf{2}_{up}$ complexes.

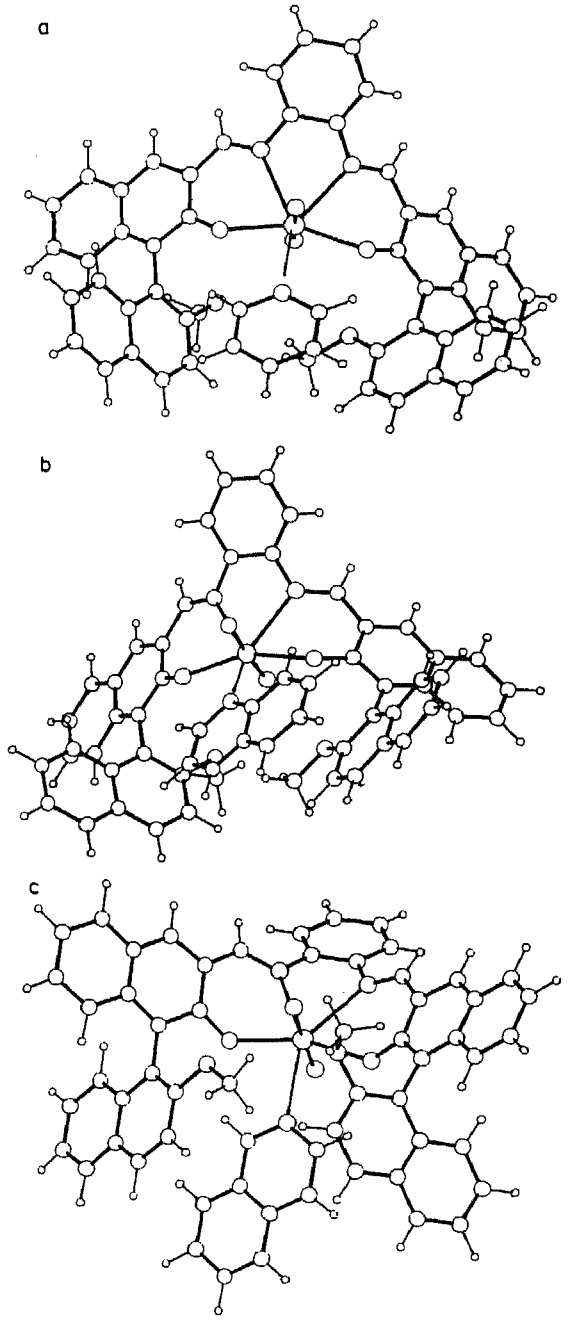


*Figure 2. View of calculated metallocleft-***2** *(a) pyridine, (b) isoquinoline, and (c) quinoline complex structures.*

Table II Calculated relative energies of complexation (kcal · mol^{-1})[a].

Guest	meso$_{up}$-**1**	meso$_{down}$-**1**	racemic-**1**
MeOH	0.20	0.35	−1.41
H_2O	0.00	−0.06	−2.21
pyridine	−3.86	5.14	0.27
quinoline	−17.17	−6.17	7.30
isoquinoline	−7.46	4.75	−2.95

[a] Energies are relative to meso-$\mathbf{1}_{up} \cdot H_2O$ complex.

Conclusions

Aldehyde **5** was synthesized by direct *ortho*-metalation of methoxymethyl ether **4**. Metallocleft **2** was obtained by reaction of aldehyde **5** and 1,2-benzenediamine to give a mixture of meso-**2** and racemic-**2** diastereomers in a 1 : 0.85 ratio. The combination of coordination to a Lewis-acidic metal center in addition to aromatic interactions can be used for selective recognition between meso and racemic isomers.

Experimental

General methods

NMR spectra were recorded on a Nicolet NT-200 WB or a Bruker AC-250 spectrometer in $CDCl_3$ with TMS as internal standard, if not stated otherwise. Mass spectra were obtained with a Finnigan MAT 90 spectrometer. Positive-Ion Fast-Atom Bombardment (FAB) mass spectra were obtained with *m*-nitrobenzyl alcohol as a matrix. IR spectra were recorded with a Nicolet 5 SCX FT spectrophotometer. Melting points were determined with a Reichert melting point apparatus and are uncorrected. Elemental analyses were carried out by a Model 1106 Carlo Erba Strumentazione Elemental Analyzer. Petroleum ether and CH_2Cl_2 were distilled before use. Petroleum ether (PE) refers to the fraction with b.p. 40–60°C. Diethyl ether was freshly distilled from $CaCl_2$ and THF from sodium/benzophenone. CH_3CN and DMF were stored over molecular sieves (4 Å). Other chemicals and solvents were of reagent grade and were used without purification. Compound **3** was synthesized according to a known procedure[14]. Column chromatography was performed with silica gel (Merck; 0.015–0.040 mm; 230–400 ASTM). All reactions were carried out in a static nitrogen atmosphere.

Care was taken when handling uranyl containing compounds because of their toxicity and radioactivity[15].

Synthetic procedures

(±)-2-Methoxy-2'-(methoxymethoxy)-[1,1'-binaphthalene] (**4**). 2'-Methoxy-[1,1'-binaphthalene]-2-ol (**3**) (2.27 g, 7.57 mmol) was added to a suspension of NaH (80% in oil, 2.50 g, 8.33 mmol; prewashed with PE), in ether (25 ml)/DMF (5 ml). After 15 min stirring at room temperature, a solution of bromomethyl methyl ether (1.13 g, 9.03 mmol) in ether (2 ml) was added. The reaction was complete after 20 min as followed from TLC (SiO_2; $CHCl_3$/PE 5 : 1), whereupon the reaction mixture was quenched with water (50 ml) and extracted with ether (3 × 100 ml). The combined organic layers were washed with 2 M NaOH (2 × 100 ml) and saturated aqueous NaCl (100 ml). Drying over $MgSO_4$ and concentration *in vacuo* yielded the crude product, which was recrystallized from CH_2Cl_2/PE. An analytical sample of **4** was prepared by recrystallization from ether; yield 84%; m.p. 131–135°C (ether). Anal. calcd. for $C_{23}H_{20}O_3$ (344.409): C 80.31, H 5.85; found: C 80.61, H 5.73%. ^{1}H-NMR: δ 7.93–7.12 (m, 12H, Ar H); 5.05 (d, *J* 6.7 Hz, 1H, CH_2); 4.98 (d, *J* 6.7 Hz, 1H, CH_2); 3.76 (s, 3H, OCH_3); 3.50 (s, 3H, CH_2OCH_3). ^{13}C NMR: δ 155.0, 152.7 (s, C-2, C'-2); 134.2, 130.1 (s, C-1, C'-1); 129.6, 129.4, 129.2, 128.1, 128.0, 126.5, 126.4, 125.6, 125.4, 124.1, 123.7, 121.5, 119.5, 117.5, 114.0 (d, Ar C); 95.2 (t, CH_2), 56.7, 55.9 (q, OCH_3), Ms (EI), *m/z* 344.147 (M^+, calcd. 344.141).

Table III Data of complexation experiments in $CDCl_3$ at 298 K according to method B.

Guest	Experimental $\delta_{complex}$ (ppm)		K_r (M^{-1}) meso-**1**	Method B[a]		
	meso-**1**	rac-**1**		K_m (M^{-1}) rac-**1**	$\delta_{complex}$ (ppm)	
					meso-**1**	rac-**1**
pyridine	3.650	3.329	1020	664	3.647	3.322
quinoline	3.639	3.471	151	557	3.573	3.511
isoquinoline	3.629	3.291	4063	1632	3.598	3.390

[a] Regression results: $1.0 \cdot 10^{-3} < R^2 < 1.0 \cdot 10^{-5}$ ppm.

(±)-Diethylcarbamic acid, 2'-methoxy-[1,1'-binaphthalene]-2-yl ester (**6**)[6]. A mixture of 2'-methoxy-[1,1'-binaphthalene]-2-ol (**3**) (1.50 g, 5.0 mmol), diethylcarbamoyl chloride (0.77 g, 5.7 mmol) and K_2CO_3 (2.08 g, 15.0 mmol) in CH_3CN (100 ml) was refluxed (for 8 h) till completion (TLC; SiO_2; CH_2Cl_2/PE 1:1). Subsequently, the solvent was evaporated and water was added (50 ml); the remaining mixture was extracted with CH_2Cl_2 (3 × 50 ml). The combined organic layers were washed with saturated aqueous NaCl (50 ml), dried over $MgSO_4$, and concentrated *in vacuo* to give **6** as a colorless sticky oil; yield 90%. ^{1}H-NMR: δ 8.0–7.2 (m, 12H, Ar H); 3.73 (s, 3H, OCH_3); 3.08–2.99 (m, 2H, CH_2); 2.72–2.61 (m, 2H, CH_2); 0.82 (t, *J* 6.9 Hz, 3H, CH_3); 0.43 (t, *J* 6.9 Hz, 3H, CH_3). ^{13}C NMR: δ 155.0, 153.5 (s, C-2, C'-2); 147.4, (s, C=O); 133.8, 133.6, 131.4, 129.0, 124.6, 118.5 (s, Ar C); 129.7, 128.6, 128.0, 127.6, 126.4, 126.1, 125.9, 125.5, 125.0, 123.6, 122.6, 113.7 (d, Ar C); 56.7 (q, OCH_3), 41.7, 41.2 (t, CH_2); 13.1, 13.0 (q, CH_3). IR (KBr): 1715 cm^{-1} (C=O). Ms (EI), *m/z* 399.191 (M^+, calcd. for $C_{26}H_{25}NO_3$ 399.183).

(±)-2-Hydroxy-2'-methoxy-[1,1'-binaphthalene]-3-carboxaldehyde (**5**). Two procedures were followed to obtain aldehyde **5**. Method A is discussed in the results and discussion section and comments on method B are given in note 6.

Method A: BuLi (1.5 ml of a 1.5 M solution in hexane, 2.33 mol) was added to a suspension of the methyl methoxymethyl diether **4** (0.66 g, 1.92 mmol) in ether (20 ml) at room temperature. After stirring for 2 h, DMF (280 µl, 4.07 mmol) was added. Within 3 min, the reaction mixture became clear yellow. Stirring was continued for 30 min, whereupon the reaction mixture was quenched with HCl containing MeOH (prepared *in situ* from NaCl and concentrated H_2SO_4) and stirred for 15 min to remove the *ortho*-directing methyl methyl ether group. Water (50 ml) was added, the pH was adjusted to pH 7 with 0.1 M NaOH, and the resulting mixture was extracted with ether (3 × 100 ml). The combined organic layers were washed with saturated aqueous NaCl, dried over $MgSO_4$ and concentrated *in vacuo* to yield the crude product. Purification was achieved by flash chromatography (SiO_2; CH_2Cl_2/PE 5:1) to afford **5** in 78% yield.

Method B: *sec*-BuLi (1.8 ml, 1.25 M in ether) was added to a solution of carbamate **6** (0.80 g, 2.06 mmol) and TMEDA* (0.26 g, 2.26 mmol) in THF (15 ml) at −90/−95 °C. After stirring for 1 h, DMF (145 µl, 2.11 mmol) was added. The reaction mixture was slowly warmed to room temperature overnight. Water (50 ml) was added, the pH was adjusted to pH 2 with 2 M HCl and the reaction mixture was extracted with CH_2Cl_2 (2 × 25 ml). The combined CH_2Cl_2 layers were washed with saturated aqueous NaCl, dried over $MgSO_4$, and concentrated *in vacuo* to yield the crude product, which was purified by flash chromatography (SiO_2; CH_2Cl_2/PE 5:1) to give pure **5** in a yield of 14%.

An analytical sample of **5** was obtained by recrystallization from ether/PE: m.p. 190–194 °C (ether/PE). Anal. calcd. for $C_{22}H_{16}O_3$ (328.367): C 80.47, H 4.91; found: C 80.28, H 4.86%. ^{1}H NMR: δ 10.43 (s, 1H, OH); 10.18 (s, 1H, CHO); 8.29–7.10 (m, 11H, Ar H); 3.80 (s, 3H, OCH_3). ^{13}C NMR: δ 196.8 (d, CHO); 155.1, 153.4 (s, C-2, C'-2); 137.8, 130.3, 130.1, 129.8, 128.2, 126.7, 125.4, 124.7, 124.2, 123.7, 113.9 (d, Ar C); 133.6, 129.3, 127.5, 122.1, 118.5, 117.3 (s, Ar C); 56.8 (q, OCH_3). IR (KBr): 1657 cm^{-1} (C=O). Ms (EI), *m/z* 328.114 (M^+, calcd. 328.110).

* TMEDA = N,N,N',N'-tetramethylethylenediamine

(±)-Dioxo-[[3,3-[1,2-phenylenebis(nitrilomethylidyne)]bis[2'-methoxy-[1,1'binaphthalene]-2-olato]](2-)-N,N',O,O']uranium · H_2O · 0.67CH_2Cl_2 (**2**). A solution of aldehyde **5** (0.23 g, 0.70 mmol) and 1,2-benzenediamine (0.039 g, 0.35 mmol) in CH_3OH (100 ml) was refluxed for 30 min. $UO_2(OAc)_2 \cdot 2H_2O$ (0.15 g, 0.35 mmol) was added and reflux was continued for 30 min. The mixture was concentrated to approximately 50 ml and stored overnight at 5 °C. The precipitate was filtered off, dissolved in a minimal amount of CH_2Cl_2 and precipitated with PE to give pure **2**: yield 38%; m.p. > 310 °C (CH_2Cl_2/PE). Anal. calcd. for $C_{50}H_{34}N_2O_6U \cdot H_2O \cdot 0.67CH_2Cl_2$ (1079.826): C 56.80, H 3.51, N 2.61; found: C 57.13, H 3.53, N 2.55%. ^{1}H NMR: δ 9.68 (s, 2H, CH=N); 9.66 (s, 2H, CH=N); 8.37–6.81 (m, 26H, Ar H); 5.30 (s, 1.34H, 0.67 CH_2Cl_2); 3.75 (s, 3H, OCH_3); 3.55 (s, 3H, OCH_3). ^{13}C NMR (DMSO-d_6): δ 167.7 (d, CH=N); 162.9 (s, C-2); 155.6, 155.3 (s, C-3, C'-3); 146.7, 146.6 (s, C''-1, C''-2); 138.1–114.5 (23 Ar C); 56.2, 56.0 (q, OCH_3). IR (KBr): 1602 (C=N); 904 (O–U–O) cm^{-1}. Ms (FAB), *m/z* 1014.4 ($(M + H_2O)^+$, calcd. 1014.3), 997.3 [$(M + H)^+$, calcd. 997.3].

Calculations

Molecular-mechanics calculations were performed with CHARMm and the graphical QUANTA interface[16]. Force-field parameters were taken from CHARMm, except the non-bonded parameters for the uranyl cation. For the uranyl cation, the non-bonded parameters were determined to reproduce the experimental hydration geometry and enthalpy[17]. The Schiff-base moiety of reported structures[1a,b,d,2] shows its invariance; therefore, this moiety was kept fixed by atom constrains (value −1, described in the CHARMm users guide) in the calculations.

With molecular mechanics, the steric minima of the complexes and of the isolated guest molecules were determined by variation of all the relevant degrees of freedom: position and orientation of the guest and rotatable bonds in the substituent to the Schiff-base moiety of the host. Minimizations were terminated at RMS < 0.0001.

^{1}H-NMR titrations

Quantitative data were obtained with a 250-MHz ^{1}H-NMR spectrometer operating at a digital resolution of 0.001 ppm. Measurements were carried out at 298 K in $CDCl_3$, with TMS as an internal standard. Host was titrated with guest, the total starting concentration of metallocleft, both meso-**2** and racemic-**2** isomer, was 0.42–0.48 mM. Higher concentrations of the cleft could not be achieved due to the limited solubility. Guest concentrations were 0.13–9.60 mM. For each titration experiment, 8–10 spectra of samples with varying host-guest ratios were recorded. The chemical shifts of the methoxy signals of both the meso-**2** and the racemic-**2** complexes, which are determined experimentally by adding a large excess of guest (20–50 equiv), are used to calculate the association constants. Varying the excesses of guest learns whether the chemical shift of the pure complex was reached.

Data evaluations were performed assuming 1:1 complexation under rapid-exchange conditions. The observed chemical shift is the weighted average of the chemical shift of the free ligand and the complex (Eqn. 4), in which δ_{obs}, δ_H, and δ_{HG} are the observed chemical shift, and the chemical shifts of the free ligand and complex, respectively.

$$\delta_{obs} = \alpha \cdot \delta_{HG} + (1 - \alpha) \cdot \delta_{H} \quad (4)$$

The mol fractions α and 1-α are defined as $\alpha = [HG]/\{[H] + [HG]\}$ and $1 - \alpha = [H]/\{[H] + [HG]\}$, respectively.
Combination of Eqns. 1, 2 and 4 gives Eqn. 5.

$$(\delta_{obs} - \delta_{H})/(\delta_{HG} - \delta_{obs}) = K \cdot [G] \quad (5)$$

There is a linear correlation between the concentration of the free guest and $(\delta_{obs} - \delta_{H})/(\delta_{HG} - \delta_{obs})$, with the association constant K as the slope. The equations above are valid for both the meso-**2** and the racemic-**2** isomers. The concentration of G is given by Eqn. 6.

$$[G] = [G_{tot}] - [H(M) \cdot G] - [H(R) \cdot G] \quad (6)$$

This equation is rearranged to an expression with known or measurable parameters (Eqn. 7).

$$[G] = [G_{tot}] - \{(\delta_{obs} - \delta_{H})/(\delta_{HG} - \delta_{H})\}_{M} \cdot [H(M)_{tot}] - \{(\delta_{obs} - \delta_{H})/(\delta_{HG} - \delta_{obs})\}_{R} \cdot [H(R)_{tot}] \quad (7)$$

Linear regression was used on Eqn. 5 to determine the value of K. The left-hand side of Eqn. 5 was calculated from the observed chemical shift values whereas the concentration of the free guest [G] (substitution of Eqn. 7) was calculated from the observed chemical shifts and the stoichiometric concentrations of guest and both host forms. Linear regression to calculate K_m and K_r was performed with LOTUS 1-2-3. The results are presented in Table I.

Procedure for calculation of association constants of 1-naphthalene-methanamine complexes. Firstly, the free ligand and the complex concentrations of the meso-**2** isomer were calculated from the integrals. Secondly, the free ligand and the complex concentrations of the racemic-**2** isomer were calculated, using the experimentally determined chemical shift of the complex (adding a large excess). The relative stability of the meso-**2** and racemic-**2** complex is determined at 3.6 with Eqn. 8.

$$K_{rel} = K_m/K_r = \{[H(M) \cdot G][H(R)]\}/\{[H(M)][H(M) \cdot G]\} \quad (8)$$

Upon addition of 2.0 or 2.3 equivalents of guest (meso-**2** or racemic-**2** isomer, respectively), greater than 95% complexation was achieved. From this observation and the relative stability of 3.6, association constants of $1.0 \cdot 10^6\ M^{-1}$ and $3.6 \cdot 10^6\ M^{-1}$ were calculated, for the meso-**2** and racemic-**2** isomer, respectively.

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