Novel Dioxadiazadecalin Podands and Their Heavy Metal Ion Complexes[‡]

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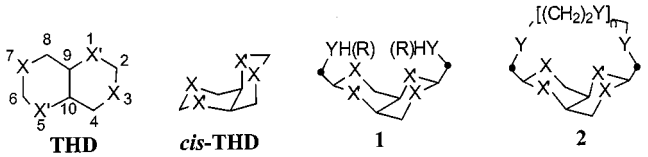
We present new approaches to podands based on the recently introduced 1,5-dioxa-3,7-diazadecalin (DODAD) core, with functionalized termini in the 2,6- and/or 3,7-positions. Two such podands (**12**, **14**) were prepared and their structures and conformations were studied by NMR. Compound **14** was also analyzed by X-ray and computational (CFF98) techniques. Both podands underwent complexation with cadmium ions, with active participation of the dioxadiazadecalin core cavity. The Cd^{2+} complexes were studied by NMR and MS techniques. Allosteric effects were observed in the complexation of **12**, whereas **14** was preorganized for complexation.

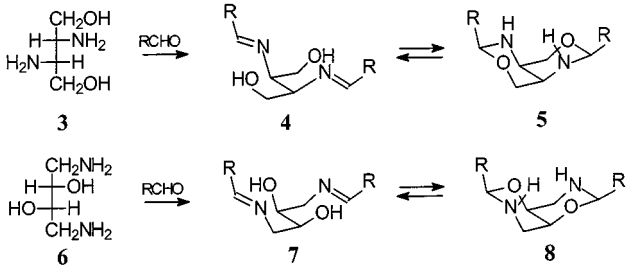
Introduction

We have been investigating 1,3,5,7-tetraheterodecalin (**THD**) diastereoisomeric systems (Scheme 1), in particular the *cis*-**THD** forms, as cores of new host compounds, on the basis of the anticipated high lone pair concentration in their cavities. In this context, we recently reported a variety of tetraoxadecalin (TOD) and tetraazadecalin (TAD) systems. Both *cis*-TOD[2] (**1a**) and *cis*-TAD[3] (**1b**) podands and the resulting macrocycles (**2**) showed good to excellent complexation capability towards earth, alkaline, and heavy metal ions.



Scheme 1. The 1,3,5,7-tetraheterodecalin (**THD**) system, its *cis*-X-inside diastereoisomer and the derived podands and macrocycles

Recently, the new systems 1,5-diaza-3,7-dioxadecalin (DADOD) (**THDc**) and 1,5-dioxa-3,7-diazadecalin (DODAD) (**THDd**) have been prepared.[4] The *cis*-THD systems, obtained from the respective *threo*-diaminobutanediols (Scheme 2), were studied in particular detail, including ring-chain tautomerism in these systems.[1b,5] To understand how the relative stability of these dioxadiazadecalin systems, relative to their diimine tautomers, were affected by the 2,6-substituents, we performed[5] an LFER (Hammett−Brown) analysis of 2,6-*para*-aryl-substituted derivatives[6] and found that, whereas *cis*-DADOD systems were more stable than their parent Schiff bases in all cases, the *cis*-DODAD systems prevailed only when they possessed electron-withdrawing substituents. Additionally, as

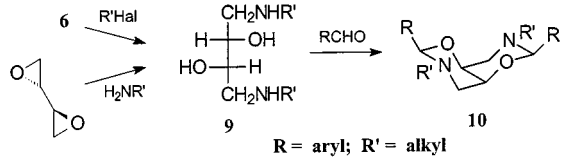


Scheme 2. Formation of the *cis*-DADOD (**5**) and *cis*-DODAD (**8**) bicyclic systems from the respective *threo*-diaminobutanediols **3**, **6** via the corresponding Schiff bases **4**, **7**

ortho-substituted 2-aryl systems are of particular interest[6] due to H-bonding (besides the usual electronic and steric effects), we investigated the *N*-salicylideneamino Schiff bases (Scheme 2), and their respective cyclic *cis*-DADOD and *cis*-DODAD tautomers, and examined this system (**4** ⥋ **5**) in detail in a parallel paper.[1b] We now turned to the *cis*-DODAD system (**7** ⥋ **8**) and, to utilize it as a complexation ligand, sought approaches to podands with substituents featuring suitably functionalized termini.

Results and Discussion

A viable technique[4b] for obtaining ring-closed products (such as **10**), avoiding Schiff base formation and ring-chain tautomerism, is to use *N*-substituted diaminobutanediols **9** (Scheme 3). These are procurable either by (R′X) alkylation of diaminobutanediols or by aminolytic regioselective ring-opening of *threo*-diepoxybutane. Both techniques are stereospecific, but the latter is more efficient, albeit not enantioselective.



Scheme 3. Preparative approaches to *N*,*N*′- and 2,6-substituted DODADs

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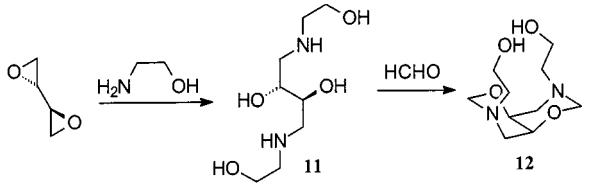
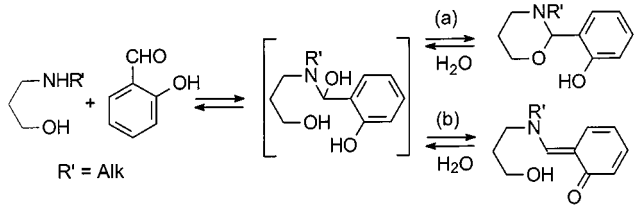
Using the above synthetic strategy, we set out to prepare two types of dioxadiazadecalin podands with either *N,N′*-dialkyl- or 2,6-diaryl-functionalized substituents, both for complexation purposes and as springboards for macrocyclic ring-closure.[1] Thus, in the former (R′ = alkyl) class, 1,4-bis(hydroxyethylamino)-2,3-butanediol (**11**) was prepared (Scheme 4) by aminolytic ring-opening of *threo*-diepoxybutane with ethanolamine, which proceeded regioselectively and smoothly in aqueous solution. On subsequent treatment of **11** with formaldehyde, the *rac*-3,7-bis(2-hydroxyethyl)-*cis*-DODAD (**12**) was readily isolated.



Scheme 4. Synthesis of 3,7-bis(2-hydroxyethyl)-*cis*-DODAD (**12**)

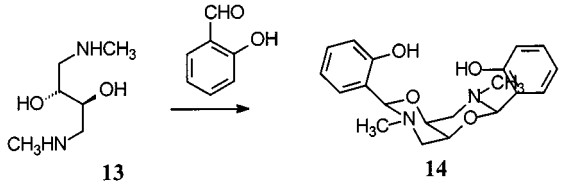
For the second (R = aryl, Scheme 2) class of functionalized podands, we used our ability to manipulate ring-chain tautomerism in such systems.[5] As pointed out earlier,[6] when secondary amines are added to aldehydes, the initially formed *N,N′*-disubstituted hemiaminals cannot lose water to give Schiff bases but do so rather in the opposite direction, if an α-hydrogen atom is present, to give an enamine. In the case of secondary 1,3-aminopropanols [Scheme 5 (a)], oxazines can be formed via a hemiaminal



Scheme 5. Tautomeric reaction pathways of 3-(alkylamino)propanol with salicylaldehyde

intermediate. Salicylaldehyde [Scheme 5 (b)], however, while devoid of α-hydrogen atoms, has the acidic phenol proton to offer for elimination of water from the intermediate hemiaminal, to form the oxo-enamine.

Hence, *rac*-1,4-bis(methylamino)-2,3-butanediol (**13**) was treated with salicylaldehyde in ethanol (Scheme 6), to give a distinctive yellow solution (of the oxo-enamine intermediate), from which *rac*-*cis*-2,6-bis(*o*-hydroxyphenyl)-3,7-dimethyl-*cis*-DODAD (**14**) precipitated as a white solid.



Scheme 6. Synthesis of *cis*-2,6-bis(*o*-hydroxyphenyl)-3,7-dimethyl-*cis*-DODAD (**14**)

The characteristic yellow color is due to the oxo-enamine tautomeric form (Scheme 5b) of **14**, related systems of which are known to exhibit an absorption band around 400 nm.[1b,7] This oxo-enamine form is therefore bound to show up in hydrolysis/dehydration processes of **14** [as illustrated in Scheme 5, (a) ⇆ (b)] and can be detected by warming any water or methanol solution of it, or upon loading a colorless chloroform solution of **14** onto a silica column or TLC plate, immediately giving a yellow ring (spot). This also enabled us to monitor the reaction depicted in Scheme 6 by using UV/Vis spectroscopy (Figure 1). It is clear that, when heated in methanolic solution, **14** is joined by its (absorbing at about 400 nm) oxo-enamine form.

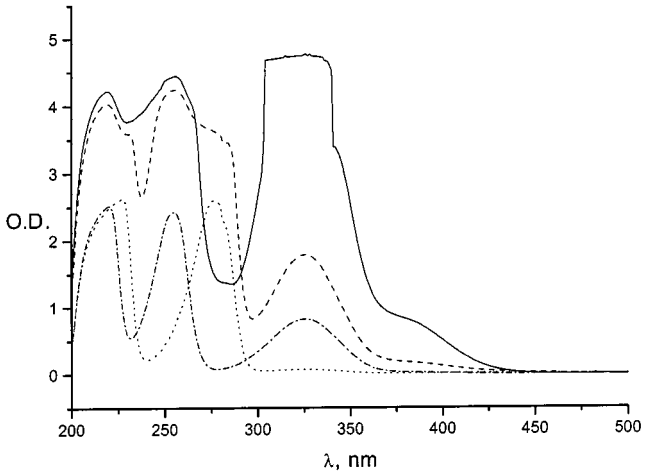


Figure 1. UV/Vis absorption spectra in methanol of: - · · · - salicylaldehyde ($2.4\cdot10^{-4}$ M) [λ (ε) = 325 nm (3300), 256 (11000), 213 (18000)]; · · · · · **14** ($6.2\cdot10^{-4}$ M); - - - - **14** at 50 °C ($1.7\cdot10^{-3}$ M); — — — reaction (Scheme 6) end product (from $1.1\cdot10^{-3}$ M aldehyde)

Turning to structure and conformation, of the two possible (O,N-inside and O,N-outside) diastereomeric forms, both **12** and **14** exist as the O,N-inside variants, as previously shown by NMR techniques for all known *cis*-DODAD and -DADOD compounds.[1,4,5] We have also shown[4] that N−H, or even N−Me, moieties in these systems occur mostly in axial conformation, due to the *anomeric effect* (allowing the equatorial lone pairs to mix into the adjacent σ^*_{C-O} orbital), apparently reinforced by intramolecular N−H···O hydrogen bonds. In solution, the orientation of the N−R′ bond can be ascertained[4,8] from the geminal coupling constant of the methylene protons at C2(6) (equatorial/axial about 7.5/10.5 Hz) or at C4(8) (equatorial/axial about 11.5/14.5 Hz).

Using this criterion in the conformational analysis of 3,7-bis(2-hydroxyethyl)-*cis*-DODAD (**12**) in solution, we could assume that it exists predominantly with ($^2J_{2(6)}$ = 10.1 Hz) *N*-axial 2-hydroxyethyl groups. The latter are also freely rotating, according to the averaged vicinal coupling constants in the CH_2-CH_2 moiety.

In contrast to **12**, 2,6-bis(*o*-hydroxyphenyl)-3,7-dimethyl-*cis*-DODAD (**14**) exists in solution, according to NMR, with its N−Me groups equatorial to an appreciable extent ($^2J_{4(8)}$ = 13.3 Hz). This is presumably due to the vicinal *gauche* equatorial *o*-phenoxy groups, which interfere sterically and oppose the anomeric effect through their internal ArOH···N hydrogen bonds (see below). An X-ray dif-

fraction analysis of **14** was carried out (Figure 2), along with computation using the CFF-98 force field.[9] The experimental and computed structural parameters are in good agreement (Table 1), except for the lack of full symmetry in the crystal. Both showed an all-equatorial arrangement, with geometrical features characteristic of the disrupted anomeric effect in this molecule.[4] The latter phenomenon is convincingly manifested in the structure (Table 1), in that, for example, C2−N3 (C6−N7) are not shortened (1.47 Å) and O1−C2 (O5−C6) are not lengthened (on the contrary: 1.417, 1.434 Å). Thus, of the two podands, **12** and **14**, with the O,N-inside cavity, only the latter has a well-preconditioned cavity for coordination, due to the high lone pair concentration in it. Both were examined, however, for their complexation capability with Cd^{2+}, as a typical heavy metal ion.

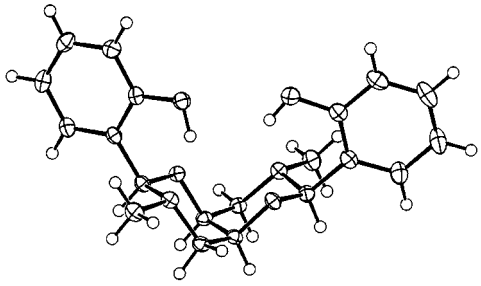


Figure 2. ORTEP drawing with 50% probability ellipsoids (for the heavy atoms) from the X-ray analysis of **14** at 110 K

Table 1. Observed (X-ray) vs. calculated (CFF-98) structural parameters of (**14**)

	X-ray	CFF-98
O1−C2 (O5−C6)[a]	1.417 (1.434)	1.435
O1−C9 (O5−C10)[a]	1.442 (1.437)	1.433
C2−N3 (C6−N7)[a]	1.476 (1.470)	1.477
N3−C4 (N7−C8)[a]	1.472 (1.475)	1.468
N3−C25 (N7−C26)[a]	1.472 (1.465)	1.462
C9−C10[a]	1.513	1.537
O1−C2−N3 (O5−C6−N7)[b]	110° (109°)	110°
N3−C2−C17−C12 (N7−C6−C24−C19)[c]	−41° (−65°)	−51°
O1−C2−N3−C25 (O5−C6−N7−C26)[c]	178° (−177°)	−175°
O11−H11···O1[d] (O18−H18···O5)	0.959, 2.788, 111° (0.886, 2.144, 131°)	0.973, 2.559, 120°
O11−H11···N3 (O18−H18···N7)	0.959, 1.796, 147° (0.886, 2.498, 126°)	0.973, 2.244, 132°

[a] Bond lengths in Å, all with e.s.d. = 0.002. − [b] Bond angles. − [c] Torsion angles. − [d] Hydrogen bonds: bond lengths[a] X−H···Y and angles XHY.

The complex of **12** with $CdBr_2$ precipitated from the methanolic reaction mixture as a colorless solid, which, according to FAB-MS, was a 1:1 complex (**15**, M = Cd). It was soluble in DMSO, but free ligand was also observed, indicating ready ligand exchange and hampering ion titration work in this solvent. The change of counteranion to perchlorate, however, had a favorable effect on the solubility and stability of the complex in methanol. Titration of **12** with cadmium perchlorate, monitored by NMR, showed progressive complex formation (Figure 3) in methanol, achieving a plateau at a 1:2 metal ion/ligand ratio. The FAB mass spectra of both (1:2 and 1:1 metal/ligand) complexes showed only an ML species: $[ML(ClO_4)]^+$ and $[ML-H]^+$ (Table 2).

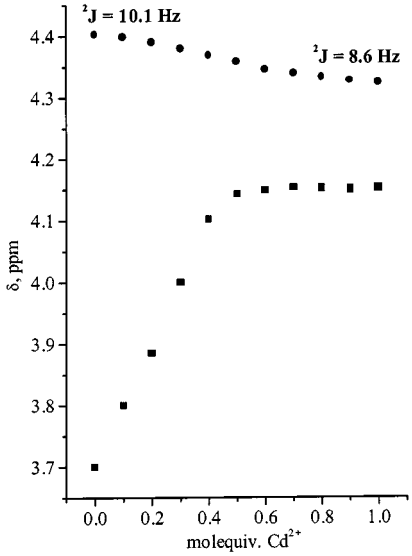
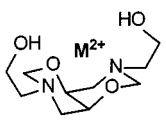


Figure 3. ^1H NMR monitoring of **12** complexation with $CdClO_4$ in [D_4]methanol: bottom curve − chemical shift of the angular protons; top curve − chemical shift and geminal coupling constant of the 2(6) axial proton

Table 2. FAB-MS data for $Cd(ClO_4)_2$ complexes of **12** and **14**

Podand (L)	M/L	*m/z* (%)[a]	Assignment[b]
12	1:1	345 (25%)	$[CdL - H]^+$
		445 (57%)	$[CdL(ClO_4)]^+$
	1:2	345 (21%)	$[CdL - H]^+$
		445 (55%)	$[CdL(ClO_4)]^+$
		up to 7%	clusters
14	1:1	467 (65%)	$[CdL - 3\ H]^+$
		679 (75%)	$[Cd_2L - 2\ H(ClO_4)]^+$
	1:2	467 (25%)	$[CdL - 3\ H]^+$
		679 (5%)	$[Cd_2L - 2\ H(ClO_4)]^+$
		up to 30%	clusters

[a] Relative to molecular peak of the free ligand. − [b] Isotope patterns were verified (vs. calculated ones) for each species.



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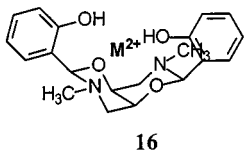

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To understand how the axial N−R′ groups in **12** allow complexation, we included a study of $^2J_{2(6)}$ of the C2 geminal protons in the above NMR spectral analysis (Figure 3, top). In the course of the ion titration, there was a reduction of $^2J_{2(6)}$ from 10.1 to 8.6 Hz, and of $^2J_{4(8)}$ from 14.3 Hz to 13 Hz. As well as this, the proton signals of the hydroxyethyl moiety were now well separated and the nuclei coupled with different vicinal coupling constants. This means that the hydroxyethyl pendant units were now no longer capable

of free rotation, in addition to being largely diequatorial (cf. **15**). This disrupts the anomeric effect, but this destabilization is compensated for by electron release, to effect metal ion complexation. That this occurs with the aid of active participation of the O,N-inside DODAD cavity is manifested in the deshielding of the angular protons (ca. 0.5 ppm downfield shift) (Table 3). This is consistent with the general behavior of such (tetraheterodecalin) systems:[2−4] The angular protons are considerably shielded, due to lone-pair delocalization into the adjacent antiperiplanar O−C and C−C bonds, and when this electron density is relocalized and drained by coordination the angular protons are deshielded accordingly.

Table 3. ^{1}H NMR chemical shifts ($\delta_{compl} - \delta_{lig}$) of **12** and **14** vs. their Cd^{2+} complexes

Compound	Solvent	$H_{2,6eq}$	$H_{2,6ax}$	$H_{9,10}$	$H_{4,8eq}$	$H_{4,8ax}$
12	CD_3OD	0.08	−0.08	0.45	0.36	−0.27
14	CD_3CN	−	0.11	0.43	0.23	0.10

The complexation products obtained from **14** were also analyzed in depth by FAB-MS (Table 2). Notably, the loss of acidic phenol protons was observed during these FAB experiments. In the NMR spectra of **14**, all protons shifted downfield during complexation, while $^2J_{4(8)}$ barely changed (from 13.3 to 13.1 Hz), implying that **16** was formed with no conformational change during complexation, as expected from the preorganization of **14** for complexation, mentioned above.

The ^{113}Cd NMR chemical shift is known[10] to be remarkably sensitive to changes in the coordination sphere around the cation, and the signal of $^{113}Cd^{2+}$ ion bound solely to oxygen atoms is shifted to higher field relative to when nitrogen atoms are also involved in the metal ion coordination. Complexation of podands **12** and **14** with Cd^{2+} was monitored by ^{113}Cd NMR over the course of addition of the podands to 0.1 M solutions of cadmium perchlorate at ambient temperature; the ^{113}Cd chemical shifts are listed in Table 4. In case of **12**, much as in the ^{1}H NMR, $[Cd\cdot(\mathbf{12})_2]^{2+}$ complex formation was observed, and at this stage the free cadmium signal practically disappeared and broad signals were observed, suggesting rapid equilibration between the cadmium-specific sites. In case of **14**, however, distinct resonances were obtained, indicating that the free cadmium ion and the complexes were in slow (almost stopped) exchange. At the start of addition of **14** to 0.1 M $CdClO_4$, a 1:1 complex was formed exclusively, with a sharp line at $\delta = 46$. Increasing the concentration of the ligand **8** to 0.2 M and above resulted in the formation of a new complex (at $\delta = 69$), via an intermediate with a very broad resonance at $\delta \approx 50$. Notably, even at a higher excess of ligand, both of these last signals are evident in the ^{113}Cd NMR spectra; that is, a slow equilibrium state between these species exists in solution. These observations were backed up by ^{1}H and ^{13}C NMR reverse titration studies (excess of **14** from the beginning). Some intermediate species were formed and then disappeared and, when an equimolar solution was reached, a well-defined axisymmetric complex was registered.

Table 4. ^{113}Cd NMR spectroscopic data of the $CdClO_4$ complexes of **12** and **14** at variable ratios (external reference: 1 M $Cd(ClO_4)_2$ aq.)

Podand	Solvent	M/L ratio 1:0	2:1	1:1	1:1.5	1:2
12	CH_3OH	−36	−37[a]	−37[a]	−37[a]	none
14	CH_3CN	23	23, 46	46	ca. 50[b]	46, 69

[a] Decreased intensity. − [b] Very broad peak.

Other (heavy and transition) metal ions were found to complex well with these podands and are being investigated in detail for structure and catalytic activity, in particular with enantiopure versions of **12** and **14**.

In conclusion, approaches to new, chiral dioxadiazadecalin ligands have been developed, and two such podands (**12** and **14**) prepared and their structures and conformations studied by NMR. Compound **14** was also analyzed by X-ray and molecular mechanics techniques. Both podands underwent complexation with Cd^{II} salts, with active participation of the dioxadiazadecalin core cavity. Allosteric effects were observed in the complexation of **12**, whereas **14** was preorganized for complexation. New types of chiral ligands have thus been introduced, readily preparable and with excellent complexation capability for heavy metal ions.

Experimental Section

Melting points were recorded with a capillary melting point apparatus and are uncorrected. − The ^{1}H and ^{13}C NMR spectra were obtained with Bruker AC 200 or ARX 500 spectrometers and referenced to TMS as internal standard. Spectra in D_2O are calibrated relative to TMS salt as internal standard. ^{113}Cadmium NMR spectra were recorded with a Bruker ARX 500 spectrometer, using a broad-band probe and ca. 2.1 mL of solutions in 10-mm tubes at 110.9 MHz (^{113}Cd transmitter frequency) and are externally referenced to 1 M aqueous $Cd(ClO_4)_2$ solution at ambient temperature. − Mass spectra (DEI-MS, DCI-MS, and FAB) were recorded with a VG Autospec 250 mass spectrometer. Elemental analyses were performed at the Hebrew University of Jerusalem. − IR spectra were measured with a Nicolet 205 FTIR instrument in potassium bromide pellets (solids), sodium chloride cells (solutions), or sodium chloride plates (neat). − UV spectra were taken with a Unikon 931 spectrophotometer.

***rac*-1,4-Bis[(2-hydroxyethyl)amino]-2,3-butanediol (11):** *threo*-1,2,3,4-Diepoxybutane (2.2 mL, 27.5 mmol) was added dropwise with good stirring to a cold (0−5 °C) solution of ethanolamine (11 mL) in water (33 mL). The reaction mixture was stirred overnight at room temperature. The excess of ethanolamine was continuously extracted with chloroform. The aqueous clear solution was concentrated and then the solvent coevaporated with benzene, to give about 10 g of a white solid product (containing traces of ethanolamine). Recrystallization from ethanol gave 4.25 g (75%) of **11** as a white solid, m.p. 114 °C. − ^{1}H NMR (200 MHz, D_2O): δ = 3.64 (m, H_2, 2 $H_{1'}$), 2.67 (m, 2 H_1, 2 $H_{2'}$); − ^{13}C NMR (50.3 MHz, D_2O): δ = 73.9 (d, C_2), 62.9 (t, $C_{1'}$), 53.3 (t, C_1), 52.6 (t, $C_{2'}$). − UV/Vis (methanol): λ (ε) = 205 nm (376). − CI MS; *m/z* (%): 209.2

(90) $[MH]^+$, 191.2 (45) $[M - OH]^+$, 148.1 (100) $[M - C_2H_6NO]^+$. − $C_8H_{20}N_2O_4$ (208.3): calcd. C 46.14, H 9.68, N 13.45; found C 46.56, H 9.51, N 13.16.

3,7-Bis(2-hydroxyethyl)-*cis*-DODAD (12): Aqueous formaldehyde (1.65 mL, 22 mmol) was added dropwise at room temperature to a solution of 1,4-bis(hydroxyethylamino)-2,3-butanediol (**11**) (2.08 g, 10 mmol) in water (30 mL). The reaction mixture was heated at 55°C for 3 h and stirred at room temperature overnight. Concentration to constant weight gave a pale oil (2.30 g, 99%), which solidified on standing. − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 4.54 (dd, ^2J = 10.5, $^4J \approx 1$, H_{2eq}), 4.27 (d, ^2J = 10.5, H_{2ax}), 3.62 (t, ^3J = 5.3, 2 $H_{1'}$), 3.49 (br. s, H_{ang}), 3.13 (t, ^3J = 5.3, 2 $H_{2'}$), 3.02 (s, $2H_4$), ca. 2.8 (br. s, OH). − ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 84.0 (t, C_2), 72.7 (d, C_9), 59.8 (t, $C_{1'}$), 55.6 (t, C_4), 54.4 (t, $C_{2'}$). − UV/Vis (methanol): λ (ε) = 275 nm (5500), 226 (4300), 199 (86234). − IR (neat): $\tilde{\nu}$ = 3358 cm^{-1} (broad), 1666 cm^{-1} (strong), 1073 cm^{-1} (strong). − DCI-MS; *m/z* (%): 233 (92) $[MH]^+$, 215 (30) $[M - OH]^+$, 116 (16) $[M/2]^+$, 88 (100) $[C_3H_6NO_2]^+$. − HR-CI MS: calcd. for $C_{10}H_{21}N_2O_4$ $[MH]^+$ 233.1501, found 233.1501.

***rac*-*cis*-2,6-Bis(*o*-hydroxyphenyl)-3,7-dimethyl-*cis*-DODAD (14):** Salicylaldehyde (3.9 mL, 37.4 mmol) was added to a solution of *rac*-1,4-bis(methylamino)-2,3-butanediol[4b] (**13**) (2.43 g, 16.4 mmol) in hot ethanol (60 mL). The solution turned yellow instantaneously and was stirred at room temperature overnight. Compound *rac*-**14** precipitated from the yellow ethanol solution as a white solid, which was isolated by filtration (5.5 g, 94%); m.p. 146 °C (MeCN). − ^{1}H NMR ([D$_3$]MeCN): δ = 7.23 (dt, ^3J = 7.9, ^4J = 1.7, H_c), 7.20 (dd, ^3J = 7.6, ^4J = 1.5, H_a), 6.83 (dt, ^3J = 7.4, ^4J = 1, H_b), 6.77 (dd, ^3J = 8, ^4J = 1, H_d), 4.73 (s, H_2), 3.83 (br. s, H_9), 3.21 (dd, ^2J = 13.3, ^3J = 1.5, H_{4eq}), 2.78 (dd, ^2J = 13.3, ^3J = 1.8, H_{4ax}), 2.10 (s, N-CH_3). − ^{13}C NMR ([D$_3$]MeCN): δ = 156.8, 122.9 (s, Ar), 130.2, 128.9, 118.9, 115.8 (d, Ar), 94.8 (d, C_2), 70.7 (d, C_9), 56.5 (t, C_4), 38.5 (q, N-CH_3). − DCI MS; *m/z* (%): 357.3 (100) $[MH]^+$, 253.3 (60), 208.2 (14), 178.2 (9), 150.2 (10), 140.2 (12), 123.2 (46), 84.0 (32). − HR DEI MS: calcd. for $C_{20}H_{24}N_2O_4$ $[M]^{+\bullet}$ 356.1736, found 356.1733.

The 12·$CdBr_2$ Complex: Treatment of 3,7-bis(2-hydroxyethyl)-*cis*-DODAD (**12**) with cadmium bromide in MeOH quantitatively gave **12·$CdBr_2$** as a white solid precipitate; m.p. 165 °C (dec.). − IR (KBr): $\tilde{\nu}$ = 3310 cm^{-1} (broad), 2934 cm^{-1} (medium), 1086 cm^{-1} (strong), 1053 cm^{-1} (strong), 1010 (strong). − FAB-MS; *m/z* (%): 424.9 (43) $[LCdBr]^+$, 233.1 (100) $[LH]^+$.

NMR Titration Procedure for the Complexation of the Podands 12 and 14 with Cd^{II} Salts: a) Portions (10 μL, 3 μmol) of the cadmium (II) salt solution (150 μmol in 0.5 mL) were added to the solution of the podand (30 μmol) in the deuterated solvent (0.5 mL) in an NMR tube, and ^{1}H NMR spectra were measured periodically (see Table 2). − b) Portions (105 μmol) of podand were added to 0.1 M solutions of the cadmium perchlorate in the solvent (2.1 mL) in an NMR tube, and ^{113}Cd NMR spectra were measured periodically (see Table 3). − Complexation of 3,7-bis(2-hydroxyethyl)-*cis*-DODAD (**12**) with $CdClO_4$ was monitored by NMR up to a constant 1:1 ratio of ligand to metal (Figure 3). − ^{1}H NMR ([D$_4$]MeOH): δ = 4.83 (d, ^2J = 8.2, H_{2eq}), 4.32 (d, ^2J = 8.6, H_{2ax}), 4.15 (s, H_9), 4.00 (dd, ^2J = 14.8, $H_{1'}$), 3.96 (dd, $H_{1''}$), 3.10 (ddd, ^2J = 13, ^3J = 4.7, $H_{2'}$), 2.71 (dd, ^2J = 13.1, ^3J = 1.5, $H_{2''}$), 3.64 (d, ^2J = 13, H_{4eq}), 2.91 (d, ^2J = 13, H_{4ax}). − FAB-MS; *m/z* (%): 445.0 (44) $[LCd(ClO_4)]^+$, 343.0 (22) $[LCd(ClO_4)]^+$, 232.1 (75) $[L]^+$. − Complexation of *rac*-*cis*-2,6-bis(*o*-hydroxyphenyl)-3,7-dimethyl-*cis*-DODAD (**14**) with cadmium perchlorate was monitored by NMR up to a constant 1:1 ratio of ligand/metal. − ^{1}H NMR ([D$_3$]MeCN): δ = 7.20 (t, ^3J = 7.4, H_c), 7.05 (d, ^3J = 7.0, H_a), 6.82 (d, ^3J = 8, ^4J = 1, H_d), 6.68 (t, ^3J = 7.3, H_b), 4.84 (br. s, H_2), 4.26 (br. s, H_9), 3.44 (d, ^2J = 13.1, H_{4eq}), 2.88 (d, ^2J = 13, H_{4ax}), 2.20 (s, N-CH_3). − ^{13}C NMR ([D$_3$]MeCN): δ = 131.4, 131 (d, Ar), 100.3 (d, C_2), 70.5 (d, C_9), 58.0 (t, C_4), 33.7 (q, N-CH_3). − FAB-MS; *m/z* (%): 678.8 (75) $[(L - 2H)Cd_2(ClO_4)]^+$, 466.9 (65) $[(L - 3H)Cd]^+$, 355.1 (100) $[L - H]^+$.

The 14·Cd^{2+} Complex: A solution of *rac*-*cis*-2,6-bis(*o*-hydroxyphenyl)-3,7-dimethyl-*cis*-DODAD (**14**) (43 mg, 0.12 mmol) in methanol (10 mL) was treated with KOH (13.2 mg, 0.25 mmol, pH = 11), after which cadmium perchlorate (50 mg, 0.12 mmol) was added. After filtration of the precipitated potassium perchlorate (35 mg, 100%), evaporation of the solvent gave the **14·Cd^{2+}** salt in quantitative yield as a colorless solid (62 mg); m.p. 170°C (dec.); − FAB-MS; *m/z* (%): 972.9 (10) $[Cd_2(L - 2H)_2K]^+$, 935.0 (30) $[Cd_2(L - 2H)_2H]^+$, 506.9 (50) $[Cd(L - 2H)K]^+$, 466.9 [Cd(L − 3 H)]$^+$, 355.1 (30) $[L - H]^+$.

X-ray Diffraction Analysis of 14: The diffraction data were collected with a Nonius KappaCCD diffractometer. Crystal data: $C_{20}H_{24}N_2O_4 \cdot 0.5CH_3CN$, molecular mass 376.94, orthorhombic, space group *Pbcn*, a = 16.459(1), b = 9.667(1), c = 23.960(1) Å, V = 3812.3(5) Å^3, Z = 8, $D_{calcd.}$ = 1.313 g/cm^3, T =110 K, $F(000)$ = 1608, μ(Mo-K_α) = 0.92 cm^{-1}, $2\theta_{max}$ = 60°, R = 0.050 for 3632 observations with $F_o > 4\sigma(F_o)$ and R = 0.072 for all 4831 unique data; at convergence, S = 1.03 and $|\Delta\rho| \leq 0.37$ e·Å^{-3}. The crystal includes somewhat disordered CH_3CN solvent molecules located in the crystal on twofold rotation axes. Crystallographic data for the structure of **14** reported in this paper have been deposited at the Cambridge Data Centre. Deposition number: CCDC-147732. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: internat. + 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

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