Cleft-Type Diamidinium Receptors for Dicarboxylate Binding in Protic Solvents

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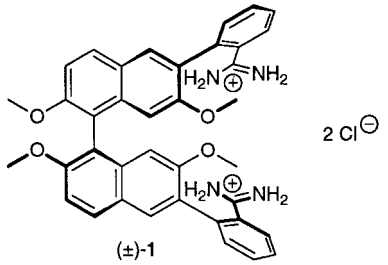
A series of potential cleft-type receptors for dicarboxylate substrates were prepared by attachment of two phenylamidinium ions to either naphthalene or 1,1′-binaphthalene scaffolds. Their synthesis (*Schemes 1–4*) involved the Pd^0-catalyzed cross-coupling of aryl nitriles to the central scaffold, followed by transformation of the nitrile into amidinium groups using the *Garigipati* reaction. The 1,1′-binaphthalene derivative (±)-**1** with phenylamidinium residues attached to the 6,6′-positions in the major groove was found to be a highly efficient receptor for dicarboxylate guests, such as glutarate and isophthalates, even in competing protic solvents such as CD_3OD (*Table 1*). The *van't Hoff* analysis of variable-temperature ^{1}H-NMR (VT-NMR) titrations (*Table 2* and *Fig. 3*) and isothermal microcalorimetry (ITC; *Table 3* and *Fig. 4*) revealed that complexation in MeOH is strongly entropically driven with an unfavorable enthalpic change, which partially compensates the entropic gain. These thermodynamic quantities are best explained by a particularly favorable solvation of the binding partners in the unbound state and the release of the MeOH molecules, which solvate the free ions into the bulk upon complexation. Receptor (±)-**1** binds flexible glutarate and rigid isophthalates with similar association strength. This lack in response to guest preorganization and reduced guest selectivity is explained with the non-directionality of the coulombic charge-charge interactions in the complexes.

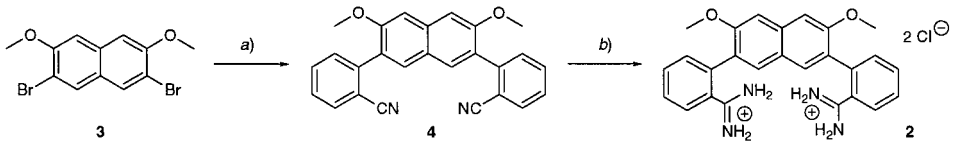
1. Introduction. – Anions play essential roles in both chemical and biological recognition processes, and, consequently, a significant interest in synthetic receptors (for reviews, see [1–3]) and receptor-based sensoric devices [4] for these substrates developed. Carboxylates have been complexed in protic solvents by a variety of macrocyclic [5–10] and cleft-type [11–15] hosts containing ammonium or guanidinium groups, with ion pairing [16] and ionic H-bonding interactions providing the main driving forces for host-guest association. We have in the past pursued the development of enantioselective cleft-type receptors which complex α,ω-dicarboxylic acids such as *N*-protected excitatory amino-acid derivatives *via* neutral H-bonds between the COOH residues of the guest and 2-(carboxamido)pyridine moieties of the host in non-competitive solvents [17]. To enhance the relevance of the artificial systems as biological mimics, we became interested in developing receptors for the complexation of dicarboxylates in protic solvents. Here, we describe the synthesis of novel naphthalene- and 1,1′-binaphthalene-derived cleft-type receptors containing phenylamidinium ions as selective carboxylate recognition sites [18][19]. The 1,1′-binaphthalene host (±)-**1** forms stable complexes with α,ω-dicarboxylates in CD_3OD, and we show by variable-temperature ^{1}H-NMR (VT-NMR) titrations and isothermal titration calorimetry (ITC) that host-guest association is largely entropy-driven.

2. Results and Discussion. – 2.1. *Synthesis.* Our first target molecule was the diamidinium salt **2**. For its synthesis (*Scheme 1*), dibromonaphthalene **3** [20] was



dilithiated and transformed into the corresponding bis(boronic acid) which was subjected to the *Suzuki* coupling [21][22] with 2-bromobenzonitrile to yield bis[benzonitrile] **4**. The low yield (4%) of the conversion **3** → **4** is due to the instability of the intermediate bis(boronic acid). Compound **4** was subsequently converted into diamidinium salt **2** in high yield, using the *Garigipati* method [23]. The reagent for this conversion, (chloro)(methyl)aluminum amide, was prepared from Me_3Al and NH_4Cl in PhMe.

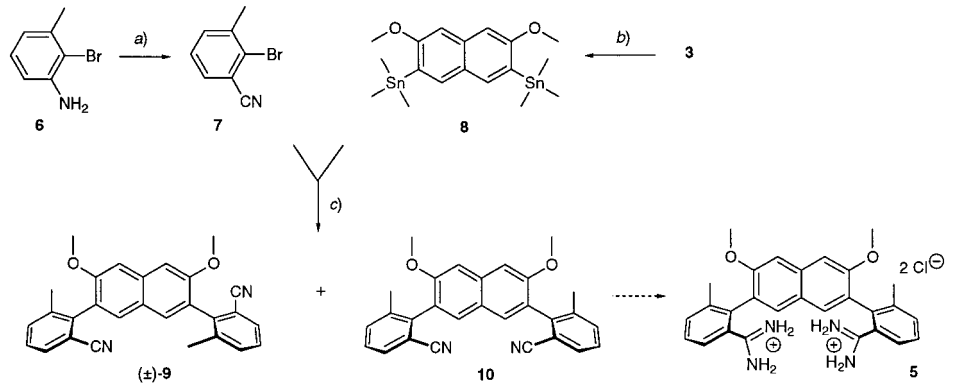
Scheme 1. *Synthesis of Diamidinium Salt* **2**



a) 1. BuLi, THF, −78°, 1 h; 2. BH_3, THF, 20°, 1 d; 3. H_2O; 4. 2-bromobenzonitrile, $[PdCl_2(PPh_3)_2]$, Na_2CO_3, PhH/EtOH/H_2O, Δ, 24 h; 4%. *b*) $MeAlNH_2Cl$, PhMe, 80°, 4 d; 98%.

In an attempt to further rigidify the receptor and to enhance its preorganization for binding, we targeted the preparation of **5**, in which the barrier for atropisomerism would be significantly enhanced. Starting from aniline **6** [24], benzonitrile **7** was obtained in high yield by a *Sandmeyer* reaction (*Scheme 2*). Distannylated **8** for the

Scheme 2. *Attempted Synthesis of Diamidinium Salt* **5**



a) 1. $NaNO_2$, H_2SO_4, 0°; 2. CuCN, NaCN, H_2O, 100°, 20 min; 83%. *b*) 1. BuLi, THF, −90°, 80 min; 2. Me_3SnCl, 20°, 2.5 h; 66%. *c*) $[Pd(PPh_3)]_4$, LiCl, DMF, 2,6-bis(1,1-dimethylethyl)-4-methylphenol (BHT), 80°, 42 h; 10% of (±)-**9** and 16% of **10**.

projected Pd^0-catalyzed cross-coupling step [22][24] to construct the C-frame of the receptor was obtained by metallation of dibromonaphthalene **3**, followed by reaction with Me_3SnCl. The subsequent coupling of **7** and **8** produced the two atropisomers (±)-**9** and **10** in modest yield. Structural identification of the two isomers was facilitated by an X-ray crystal-structure analysis for the less polar isomer (±)-**9** (*Fig. 1*). Although the two isomers were readily separated by column chromatography (SiO_2; CH_2Cl_2), atropisomerization already took place at 50°, which prevented the selective synthesis of receptor **5**. Since facile atropisomerization was also to be expected for **5**, thereby eliminating the advantage of an enhanced preorganization as compared to **2**, the synthesis of this receptor was discontinued.

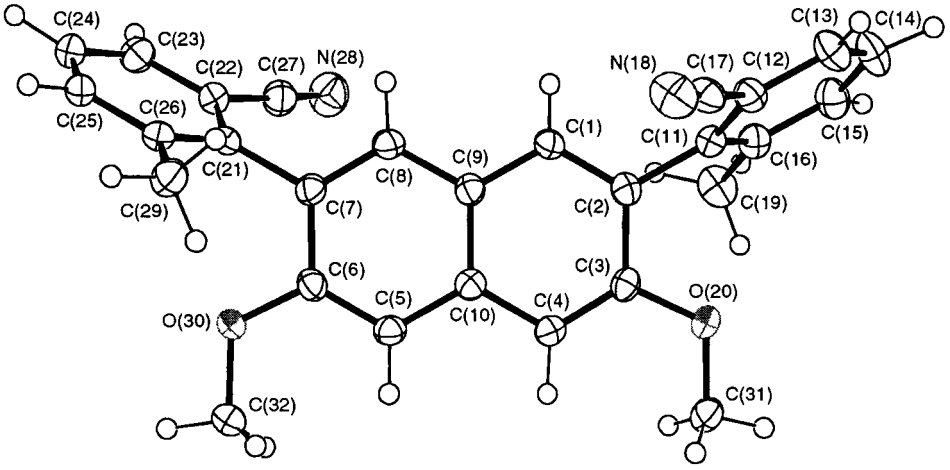


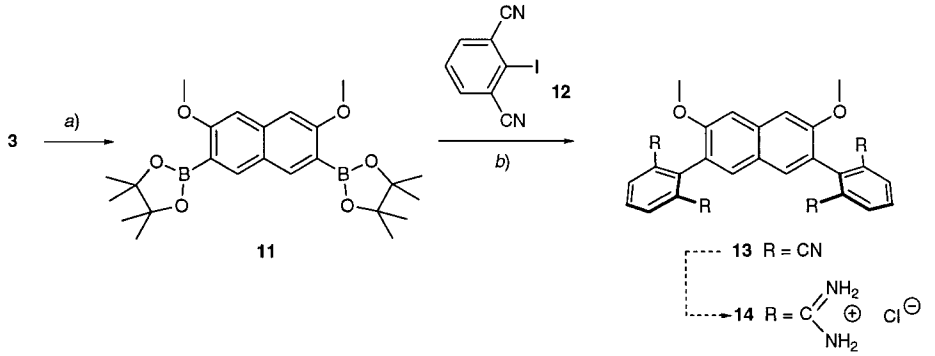
Fig. 1. *X-Ray crystal structure of (±)-***9**. Arbitrary numbering. Atomic displacement parameters obtained at 150 K are drawn at the 50% probability level. The solvent (Et_2O) included in the crystal is not shown.

In a final approach towards a more preorganized receptor, bis(pinacol borate) **11**, obtained from **3**, was coupled with 2-iodoisophthalonitrile **12** [25] to give tetracarbonitrile **13** (*Scheme 3*). However, all attempts to prepare the tetraamidinium salt **14** by the *Garigipati* reaction failed and afforded only mixtures of di- and triamidinium derivatives.

The synthesis of the 1,1′-binaphthalene-derived receptor (±)-**1** (*Scheme 4*), which was used in the subsequent molecular recognition studies (*Sect. 2.2*), started from brominated naphthalenediol **15** [20], which was alkylated to give **16**. Oxidative coupling yielded 1,1′-binaphthalene derivative (±)-**17**, which was converted into the tetramethoxy derivative (±)-**18**. *Suzuki* cross-coupling with 2-bromobenzonitrile afforded (±)-**19**, which was transformed, by the *Garigipati* reaction, to the desired receptor (±)-**1**.

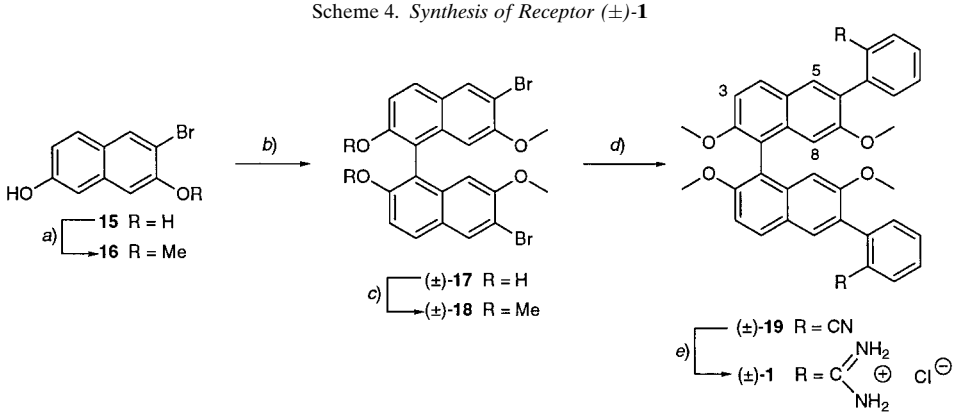
2.2. *Complexation Studies.* The ability of (±)-**1** to bind dicarboxylates **19**–**22** in solvents of different polarity ($(CD_3)_2SO$, CD_3CN, and CD_3OD) was investigated by ^{1}H-NMR binding titrations (500 MHz, 300 K) at fast host-guest exchange. Titrations in the two aprotic solvents were run at constant receptor concentration ($c = 0.1$ mM), and large complexation-induced downfield shifts $\Delta\delta$ of the resonance of binaphthalene proton H–C(8) (for numbering, see *Scheme 4*) were observed upon complexation of

Scheme 3. *Attempted Synthesis of Tetraamidinium Salt* **14**



a) 1. BuLi, THF, −100°, 1 h; 2. BH_3, THF, 20°, 1 d; 3. HCl, H_2O; 4. pinacol, NH_4Cl, PhMe, Δ, 2 h; 17%. *b*) [$PdCl_2$(dppf)] (dppf = 1,1′-bis(diphenylphosphanyl)ferrocene), Na_2CO_3, PhH/EtOH/H_2O, Δ, 2 h; 70%.

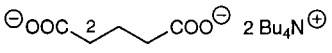
Scheme 4. *Synthesis of Receptor (±)-***1**



a) MeI, K_2CO_3, DMF, 20°, 5.5 h; 54%. *b*) $CuCl_2$, (*t*-Bu)NH_2, MeOH, Δ, 4 h; 69%. *c*) Me_2SO_4, K_2CO_3, Me_2CO, Δ, 4.5 h; 99%. *d*) 1. BuLi, THF, −78°, 50 min; 2. BH_3, THF, −78° (2 h) → 20° (14 h) → 65° (2 h); 3. HCl, H_2O; 4. 2-Bromobenzonitrile, [$PdCl_2(PPh_3)_2$], Na_2CO_3, PhH/EtOH/H_2O, Δ, 21 h; 53%. *e*) $MeAlNH_2Cl$, PhMe, 90°, 4 d; 59%.

the dicarboxylate guests. Maximum observed $\Delta\delta$ values varied from +0.26 ppm (addition of **19**) to +0.44 ppm (addition of **20**). However, the association constants for 1:1 complexation in these solvents were too large (K_a values > 10^6 1 mol^{-1}; $\Delta G < -35$ kJ mol^{-1}) to be accurately determined by ^{1}H-NMR titrations. Furthermore, higher-order association was observed in the titration with **19** in $(CD_3)_2SO$.

Addition of the more competitive solvent CD_3OD decreased the binding constants and suppressed the higher-order complexation. Nevertheless, the association constants for 1:1 host-guest complexation in CD_3CN/CD_3OD 4:1, evaluated with the nonlinear least-squares curve-fitting program *Associate V. 1.6* [26], were still at the upper limit of values, for which the use of the ^{1}H-NMR technique is meaningful and therefore not very accurate (*Table 1*).



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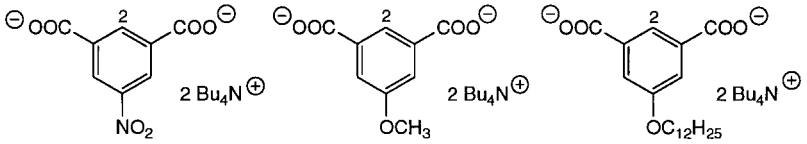


20 **21** **22**

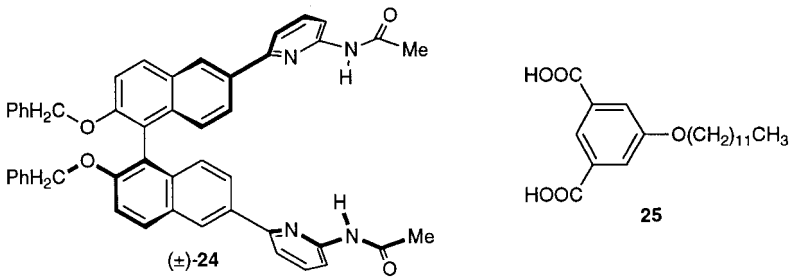
Table 1. *Association Constants* (K_a) *and Complexation Free Enthalpies* (ΔG) *from* ^{1}*H-NMR Titrations for 1 : 1 Complexes of Dicarboxylates* **19**–**22** *with Receptor* (±)-**1** ($T = 300$ K). Also shown are the maximum observed complexation-induced shifts $\Delta\delta_{max\ obs}$ (+ = downfield) and, in parentheses, the calculated shifts $\Delta\delta_{sat}$ at saturation binding of host and guest resonances monitored during the titrations.

Guest	K_a [l mol^{-1}]	ΔG [kJ mol^{-1}]	$\Delta\delta_{max\ obs}$ ($\Delta\delta_{sat}$) [ppm]
In CD_3CN/CD_3OD 4 : 1[a])			
19	140000 ± 30000	− 29.6 ± 0.5	+ 0.225 (+ 0.240)[b])
20	118000 ± 59000	− 29.1 ± 1.4	+ 0.218 (+ 0.228)[b])
In CD_3OD[c])			
19	8200 ± 2000	− 22.5 ± 0.6	− 0.119 (− 0.138)[d])
20	5100 ± 400	− 21.3 ± 0.2	− 0.092 (− 0.119)[e])
21	8300 ± 600	− 22.5 ± 0.2	− 0.123 (− 0.141)[e])
22	10000 ± 1000	− 23.0 ± 0.3	− 0.183 (− 0.205)[e])

[a]) Constant receptor concentration: 0.1 or 0.2 mM. [b]) Receptor resonance H−C(8) (for numbering, see *Scheme 4*). [c]) Constant guest concentration: 0.5 mM. [d]) Guest resonance H−C(3) (for numbering, see *Formulae* **19**–**22**). [e]) Guest resonance H−C(2).

An accurate determination of the association strength by ^{1}H-NMR titrations was possible in pure CD_3OD. In titrations at constant receptor concentration in this solvent, however, the $\Delta\delta$ values observed for receptor protons were too small (< 0.03 ppm) to be evaluated. Therefore, titrations at constant guest concentration were performed, during which selected resonances of the dicarboxylates (*Table 1*) were followed. Complexation-induced upfield shifts larger than 0.1 ppm were measured, and a satisfactory fit of the titration data to the 1:1 host-guest complex model yielded association constants in the range of $K_a = 5000$ to 10000 l mol^{-1} (*Table 1*).

Interestingly, changes in rigidity of the guest do not affect complexation strength: flexible glutarate **19** and the more rigid isophthalates bind with similar affinity. This is in sharp contrast to previous results obtained with cleft-type 1,1′-binaphthalene receptors such as (±)-**24** bearing (carboxamido)pyridine H-bonding sites at the 6,6′-positions of the major groove [27]. In the non-competitive solvent $CDCl_3$, (±)-**24** showed a large preference for complexation of 5-(dodecyloxy)isophthalic acid (**25**) ($K_a = 1.3 \times 10^5$ l mol^{-1}, $-\Delta G = 28.7$ kJ mol^{-1}, 293 K) over glutaric acid ($K_a = 2.5 \times 10^3$ l mol^{-1}, $-\Delta G = 19.1$ kJ mol^{-1}). The different response of (±)-**1** and (±)-**24** to increasing guest rigidity could largely originate from differences in host-guest binding geometries, although computer modeling shows them to be favorable in each case. On the other hand, a key contribution could also result from the differences in bonding interactions



in the various solvents. Complexation by (±)-**24** in $CDCl_3$ is driven by *neutral* H-bonding between the two (acetamido)pyridine moieties of the host and the two COOH groups of the guest (*Fig. 2*). In contrast, ion pairing and ionic H-bonding interactions between the amidinium residues of the receptor and the carboxylate groups of the guests are the major attractive interactions in the complexes formed by (±)-**1** in CD_3OD.

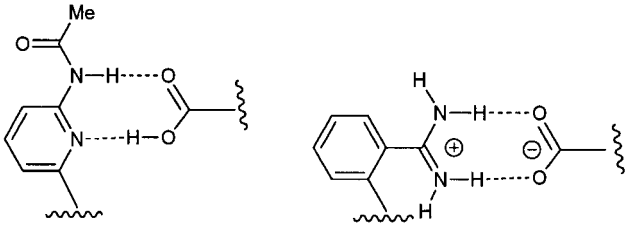


Fig. 2. *Major attractive interactions in the complex between receptor (±)-***24** *and isophthalic acid* **25** *in* $CDCl_3$ (left) *and between receptor (±)-***1** *and dicarboxylates* **19**–**22** *in* CD_3OD (right)

Attempts to investigate the complexation of dicarboxylates **19**–**22** by (±)-**1** in D_2O led to the precipitation of a solid. This precipitate was re-dissolved in $(CD_3)_2SO$, and integration of the ^{1}H-NMR resonances confirmed that it consisted of the host-guest complex with 1:1 stoichiometry in each case.

Variable-temperature ^{1}H-NMR (VT-NMR) binding titrations were executed with receptor (±)-**1** (0.125–1.25 mM) and nitroisophthalate **20** ($c = 0.5$ mM) between 275 and 306 K in CD_3OD, and the data (*Table 2*) were evaluated by a *van't Hoff* analysis (*Fig. 3*). The association constant K_a was found to increase with increasing temperature, which is characteristic for an endothermic process; correspondingly, ΔH_{300K} for the complexation process is positive and the association entropy-driven (*Table 3*).

Table 2. *Association Constants* (K_a) *and Complexation Free Enthalpies* ($-\Delta G$) *from VT-NMR Titrations for the 1:1 Complex of Nitroisophthalate* **20** *with Receptor (±)-***1** *in* CD_3OD. Also shown are the maximum observed complexation-induced upfield shifts $\Delta\delta_{max\,obs}$ and, in parentheses, the calculated shifts $\Delta\delta_{sat}$ at saturation binding of the guest resonance H–C(2) monitored during the titrations.

T [K]	K_a [l mol^{-1}]	ΔG [kJ mol^{-1}]	$\Delta\delta_{max\,obs}$ ($\Delta\delta_{sat}$) [ppm]
275	3750 ± 250	– 18.8 ± 0.2	– 0.125 (– 0.164)
283	4160 ± 150	– 19.6 ± 0.1	– 0.131 (– 0.168)
289	4450 ± 190	– 20.2 ± 0.1	– 0.134 (– 0.170)
299	4940 ± 250	– 21.1 ± 0.1	– 0.140 (– 0.174)
306	5330 ± 260	– 21.8 ± 0.1	– 0.146 (– 0.180)

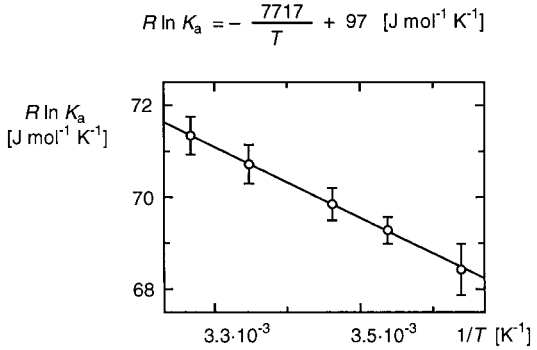


Fig. 3. *VT-NMR Data* (Table 2) *fitted to the* van't Hoff *equation*

These findings were confirmed by isothermal titration calorimetry (ITC) [28][29]. This method gives ΔH directly as a primary parameter of measurement, whereas ΔG and K_a are estimated from the titration curve fitting. The complexation entropy ΔS may then be readily calculated. Dilution of nitroisophthalate **20** in MeOH was found to be strongly exothermic (*Fig. 4*, gray line) and thermally compensating the weakly endothermic association (*Fig. 4*, black line) of **20** with receptor (±)-**1**. Subtracted integrals of each heat pulse at each titration step were analyzed using the program DIGITAM V. 3.0 [30]. The analysis revealed that the association was mildly endothermic (ΔH^0 (298 K) = 11.6 ± 0.4 kJ mol^{-1}) and that a favorable entropy change ($T\Delta S^0 = 35.0 \pm 0.8$ kJ mol^{-1}) was providing the driving force for stable host-guest association (*Table 3*). Although not identical, the thermodynamic quantities obtained by *van't Hoff* analysis of VT-NMR data and ITC were found to be in reasonable agreement. By ITC, complexation of glutarate **19** by (±)-**1** was also found to be entropically driven (*Table 3*).

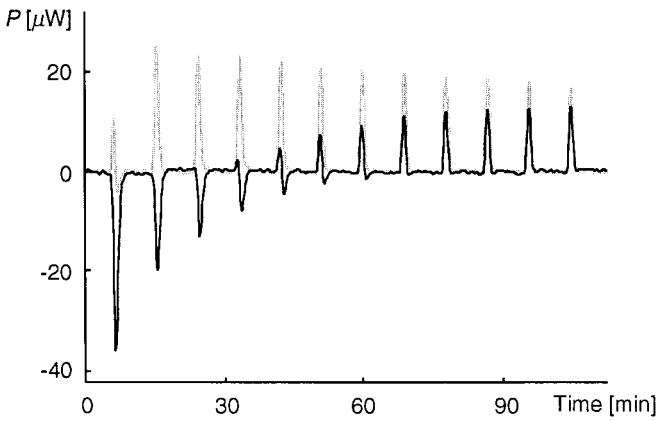


Fig. 4. *Thermogram of the calorimetric titration of receptor* (±)-**1** (c = 0.5 mM, 3 ml) *with* **20** (c = 19 mM; 15 μl additions) *in MeOH at 298 K* (bold line) *compared with dilution of* **20** *in MeOH* (gray line). Negative P values correspond to endothermic processes.

Table 3. *Thermodynamic Parameters for the Complexation between (±)-***1** *and Dicarboxylate Guests*

Guest	K_a [l mol^{-1}]	ΔG [kJ mol^{-1}]	ΔH [kJ mol^{-1}]	$T\Delta S$ [kJ mol^{-1}]
Van't Hoff analysis of VT-NMR data[a])				
20	5100 ± 600	− 21.3 ± 3.0[b])	7.7 ± 1.5	29.0 ± 1.5
ITC Data[c])				
19	6000 ± 2000	− 21.4 ± 0.8	11.3 ± 1.0	32.7 ± 1.8
20	12600 ± 2000	− 23.4 ± 0.4	11.6 ± 0.4	35.0 ± 0.8

[a]) CD_3OD, 300 K. [b]) Calculated as $\Delta H_{300} - T\Delta S_{300}$; ΔG_{300} was determined as − 21.1 ± 0.1 kJ mol^{-1} (*Table 2*). [c]) MeOH, 298 K.

The particular thermodynamic quantities can be explained by considering the solvation of the free and complexed states. In the unbound state, the ionic groups in both receptor (±)-**1** and dicarboxylate guest are strongly solvated by CD_3OD molecules. Upon complexation, these solvent molecules are largely released from the solvation shell of the ionic groups into the bulk, which provides the entropic driving force for complexation. On the other hand, the solvation of the free components presumably is more exothermic than the host-guest complexation process, which could explain the unfavorable enthalpic term. Thus, part of the entropic gain is compensated by loss in enthalpy upon complexation.

Our results are in agreement with recent ITC measurements by *Berger* and *Schmidtchen* [31]. These authors reported that the complexation of the SO_4^{2-} ion by a bis(guanidinium) receptor in CD_3OD is also strongly entropically driven, with an unfavorable enthalpic change partially compensating the entropic driving force. Their explanation for these observations was similar to that proposed above for dicarboxylate complexation by receptor (±)-**1**.

3. Conclusion. – In a series of bis(phenylamidinium) clefts, the 1,1′-binaphthalene derivative (±)-**1** was found to be a highly efficient receptor for dicarboxylate guests such as glutarate and isophthalates even in the protic solvent MeOH, which competes for the ionic H-bonding. The thermodynamic analysis by both VT-NMR and ITC showed that complexation is strongly entropy-driven, with an unfavorable enthalpic change partially compensating the entropic gain. These thermodynamic characteristics are best explained by the strong solvation of the binding partners in the unbound state and the entropically favorable release of the ion-solvating MeOH molecules into the bulk upon complexation. Similar thermodynamic data had recently been measured by ITC for SO_4^{2-} ion binding by a bis(guanidinium) receptor [31]. We conclude that associations between strongly solvated organic ions by ion pairing and ionic H-bonding in protic solvents such as MeOH or H_2O presumably are generally entropically driven, and it is hoped that more calorimetric data will become available to support this hypothesis.

Interestingly, the degree of conformational homogeneity and rigidity of the dicarboxylate substrates does not affect the binding free enthalpy, since flexible glutarate and the more rigid isophthalates form complexes of similar stability with (±)-**1** in CD_3OD. This is in strong contrast to the results obtained in the complexation of the corresponding non-dissociated carboxylic acids by the neutral H-bonding receptor (±)-

24 in the non-competitive solvent $CDCl_3$. Receptor (±)-**24** shows a large preference for binding the more rigid isophthalic acids. Although variations in binding geometry and solvent must clearly be taken into consideration, we feel that the different response to guest preorganization may be largely due to the different nature of the host-guest interactions in the complexes. Neutral H-bonding association by (±)-**24** seems to require a directionally better defined alignment of the interacting groups than the association by (±)-**1**, which involves not only ionic H-bonds but also strong, non-directional coulombic charge-charge interactions (*Fig. 2*). A higher directionality of the host-guest bonding forces should lead to a larger response of the receptor to the degree of conformational preorganization of the guest and, therefore, a higher substrate selectivity. Less directional host-guest interactions, in return, reduce the loss in entropy resulting from the association of the two binding partners, and this loss is readily compensated by the much larger entropic gain from desolvation, making the overall complexation process an entropically driven one. It is worthwhile exploring whether these conclusions are of a more general nature.

Experimental Part

General. Solvents and reagents were reagent-grade purchased from commercial suppliers and used without further purification unless otherwise stated. Compounds **3** [20], **6** [24], and **12** [25] were prepared according to the literature procedures. THF and PhMe were freshly distilled from sodium benzophenone ketyl. Evaporation *in vacuo* was conducted at H_2O aspirator pressure; drying of products were performed at 0.05 Torr if not stated otherwise. TLC: SiO_2 *60* F_{254} precoated plates from *Merck*, UV detection at 254 or 366 nm. Column chromatography (CC): SiO_2 *60* (230–400 mesh, 0.040–0.063 mm) from *Fluka*, *Merck*, or *Macherey-Nagel*. Reversed-phase chromatography (RPLC): *Lichroprep RP-16* (40–63 μm) from *Merck*. M.p.: *Büchi SMP-20*; *Büchi 510*; uncorrected. UV/VIS [λ_{max} (nm), ε (M^{-1} cm^{-1})]: *Varian Cary 5 UV/VIS/NIR*. IR Spectra [cm^{-1}]: *Perkin-Elmer 1600-FT IR*. NMR Spectra: *Bruker AMX 500* and *Varian Gemini 300* or *200* at 296 K; with solvent peak as reference. MS (*m*/*z* (%)): EI: *VG TRIBRID* spectrometer at 70 eV; FAB: *VG ZAB2-SEQ* spectrometer with 3-nitrobenzyl alcohol (NOBA) as matrix. Elemental analyses were performed by the Mikrolabor at the Laboratorium für Organische Chemie, ETH-Zürich.

^{1}H-NMR Titrations. The ammonium dicarboxylates **19**–**22** were prepared starting from commercially available dicarboxylic acids. Two equiv. of a 2M soln. of Bu_4NOH in MeOH were added to the acid in MeOH. The resulting soln. was evaporated *in vacuo*, and the solid salt was dried (0.01 Torr, 60°, 12 h). All ^{1}H-NMR titrations were performed on a 500-MHz *Bruker AMX 500* instrument. A set of 10–12 titration samples was prepared for each titration. In all samples, the concentration of one component was kept constant, whereas the concentration of the other component was varied to cover a 20–80% complexation range. The exper. data were fitted using the program *Associate V.1.6* [26].

Isothermal Titration Calorimetry (ITC). The calorimetric titrations were performed on a *TAM* microcalorimeter (*ThermoMetric*). With a computer-controlled syringe-pump (*Lund*), the guest soln. ($c = 1.9 \times 10^{-2}$ M) was added in portions (12 × 15 μl) to the host soln. ($c = 5 \times 10^{-4}$ M, 3 ml) or to the pure solvent (3 ml; for the determination of the heat of dilution) at 298 K. The thermal signal was integrated for each guest addition step, corrected for guest dilution, and evaluated as a function of guest concentration using the program *DIGITAM V. 3.0* [30] to give K_a and ΔH values.

2,2′-(3,6-Dimethoxynaphthalene-2,7-diyl)bis[benzonitrile] (**4**). To dry THF (100 ml) at −78° under Ar, BuLi (1.6M in hexane; 31.3 ml, 50.00 mmol) was added. A soln. of **3** (3.46 g, 10.00 mmol) in dry THF (30 ml) was added dropwise, and the mixture was stirred at −78° for 1 h. BH_3 (1M in THF; 100 ml, 100.0 mmol) was added rapidly, and the mixture was stirred at −78° for 2 h, then at 20° for 24 h. The solvents were removed *in vacuo*, and the residue was stirred with H_2O (200 ml) for 1 h and extracted with Et_2O (3 × 330 ml). The combined org. layers were dried ($MgSO_4$) and concentrated *in vacuo*. A mixture of the crude bis[boronic acid] (5 mmol), 2-bromobenzonitrile (1.82 g, 10.00 mmol), [$PdCl_2(PPh_3)_2$] (350 mg, 0.50 mmol), Na_2CO_3 (1.06 g, 10.00 mmol), PhH (50 ml), EtOH (12 ml), and H_2O (22 ml) was heated to reflux under Ar for 24 h. The org. phase obtained by extraction with AcOEt (3 × 150 ml) was dried ($MgSO_4$) and concentrated *in vacuo*. CC

(SiO_2; PhMe/AcOEt 95:5 → 90:10) and recrystallization (THF/Et_2O/hexane) afforded **4** (86 mg, 4.4%). White crystals. M.p. 260–261°. IR (KBr): 2224*m*, 1629*s*, 1595*w*, 1466*s*, 1407*m*. ^{1}H-NMR ($CDCl_3$, 500 MHz): 7.76 (*ddd*, *J* = 7.7, 1.3, 0.5, 2 H); 7.69 (*s*, 2 H); 7.65 (*dt*, *J* = 7.7, 1.3, 2 H); 7.54 (*ddd*, *J* = 7.7, 1.3, 0.5, 2 H); 7.45 (*dt*, *J* = 7.7, 1.3, 2 H); 7.25 (*s*, 2 H); 3.96 (*s*, 6 H). ^{13}C-NMR ($CDCl_3$, 125 MHz): 155.81; 142.26; 136.58; 132.69; 132.34; 131.03; 130.58; 127.45; 127.25; 123.45; 118.51; 113.69; 105.28; 55.56. FAB-MS: 390.3 (100, M^+). Anal. calc. for $C_{26}H_{18}N_2O_2 \cdot 0.3\ Et_2O$ (390.45 + 22.24): C 79.17, H 5.13, N 6.79; found: C 79.18, H 5.07, N 6.88.

2,2′-(3,6-Dimethoxynaphthalene-2,7-diyl)bis[benzamidinium] Dichloride (**2**). To a stirred suspension of NH_4Cl (600 mg, 11.2 mmol) in dry PhMe (3 ml) at 0° under Ar, Me_3Al (2M in PhMe; 5 ml, 10.0 mmol) was slowly added, and the mixture was stirred at 20° for 1 h. To this soln. of $MeAlNH_2Cl$ in PhMe (3.7 mmol), **4** (100 mg, 0.26 mmol) was added, and the mixture was stirred under Ar at 80° for 1 d. Additional $MeAlNH_2Cl$ (3.7 mmol) in PhMe was added, and stirring at 80° was continued for 3 d. The mixture was slowly poured into a suspension of SiO_2 (20 g) in $CHCl_3$ (50 ml). After stirring for 5 min, the SiO_2 was filtered off and washed with MeOH/H_2O 1:1. The filtrate was concentrated *in vacuo*, the residue was stirred with 5% aq. NaOH soln. (50 ml) and extracted with CH_2Cl_2 (4 × 100 ml). The combined org. layers were concentrated *in vacuo*, and the residue was dissolved in 10M ethanolic HCl (10 ml). Concentration *in vacuo* and recrystallization (MeOH/Et_2O) yielded **2** (125 mg, 98%). M.p. 271–275° (dec.). IR (KBr): 3125 (br.), 1670*s*, 1628*s*, 1480*m*, 1410*m*, 1226*m*, 1169*m*, 1031*m*, 780*m*. ^{1}H-NMR ($CDCl_3$, 500 MHz): 7.93 (*s*, 2 H); 7.79 (*dt*, *J* = 7.5, 1.0, 2 H); 7.74 (*dd*, *J* = 7.5, 1.0, 2 H); 7.64 (*dt*, *J* = 7.5, 1.0, 2 H); 7.62 (*d*, *J* = 7.5, 2 H); 7.41 (*s*, 2 H); 3.95 (*s*, 6 H). ^{13}C-NMR ($CDCl_3$, 125 MHz): 170.07; 156.87; 138.78; 137.94; 133.74; 133.24; 132.09; 131.42, 129.28; 129.06; 128.53; 125.30; 105.89; 55.67. FAB-MS: 425.1 (100, $[M - H - 2\ Cl]^+$). HR-FAB-MS: 425.1977 ($[M - H - 2\ Cl]^+$, $C_{26}H_{25}N_4O_2^+$; calc. 425.1978).

2-Bromo-3-methylbenzonitrile (**7**). A soln. of $NaNO_2$ (2.01 g, 29.16 mmol) in H_2O (11.7 ml) was slowly added at 0° to **6** (6.18 g, 27.77 mmol) in 50% aq. H_2SO_4 soln. (10 ml). The resulting viscous soln. was added at 0° under stirring to CuCN (12.44 g, 138.85 mmol) and NaCN (10.00 g, 374.90 mmol) in H_2O (83 ml). The mixture was warmed to 20° (formation of HCN!), heated to reflux for 20 min, cooled, and extracted with CH_2Cl_2 (4 × 100 ml). The combined org. layers were dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified byCC (SiO_2; CH_2Cl_2) to give **7** (4.50 g, 83%). M.p. 69–70° (hexane). IR (KBr): 2230*m*, 1571*w*, 1453*m*, 1385*m*, 1032*m*, 780*s*, 702*m*. ^{1}H-NMR ($CDCl_3$, 500 MHz): 7.43–7.48 (*m*, 2 H); 7.30 (*t*, *J* = 7.7, 1 H); 2.44 (*s*, 3 H). ^{13}C-NMR ($CDCl_3$, 125 MHz): 139.98; 134.72; 131.83; 127.46; 127.09; 117.56; 116.21; 23.27. EI-MS: 197.0/195.0 (14/15, M^+), 116.1 (100, $[M - Br]^+$), 115.1 (37), 89.1 (26). Anal. calc. for C_8H_6BrN (196.05): C 49.01, H 3.07, Br 40.76; N 7.14; found: C 48.95, H 3.05, Br 40.94, N 7.12.

3,6-Dimethoxy-2,7-bis(trimethylstannyl)naphthalene (**8**). BuLi (1.6M in hexane; 31.3 ml, 50.0 mmol) was added at −100° under Ar to **3** (3.47 g, 10.0 mmol) in dry THF (100 ml), and the soln. was stirred at this temp. for 80 min. Me_3SnCl (10.00 g, 50.00 mmol) was added at −100°, then the mixture was stirred for 2.5 h at 20°. Sat. aq. $NaHCO_3$ soln. (100 ml) was added, the org. layer was separated, and the aq. layer was extracted with Et_2O (2 × 100 ml). The combined org. layers were washed with H_2O (3 × 100 ml) and sat. aq. NaCl soln. (100 ml), dried ($MgSO_4$), and concentrated *in vacuo*. CC (SiO_2 (washed with hexane/Et_3N 95:5); hexane/Et_3N 99.5:0.5 → hexane/Et_2O/Et_3N 94.5:5:0.5) yielded **8** (3.39 g, 66%). White solid. M.p. 164–165° (hexane). IR (KBr): 2933*m*, 1724*w*, 1611*s*, 1452*m*, 1420*m*, 1392*s*, 1220*s*, 1204*m*, 1168*m*, 1048*m*, 770*s*, 532*s*, 512*m*. ^{1}H-NMR ($CDCl_3$, 500 MHz): 7.76 (*s*, 2 H); 7.00 (*s*, 2 H); 3.91 (*s*, 6 H); 0.35 (*s*, 18 H). ^{13}C-NMR ($CDCl_3$, 125 MHz): 162.28; 137.37; 136.31; 129.71; 125.51; 102.80; 55.22; −9.01. EI-MS: 514.0 (10, M^+), 499.0 (100), 468.9 (26), 438.9 (19), 406.8 (15), 242.1 (38). Anal. calc. for $C_{18}H_{28}O_2Sn_2$ (513.84): C 42.08, H 5.49; found: C 42.06, H 5.50.

*(a*RS,*a*RS*)-2,2′-(3,6-Dimethoxynaphthalene-2,7-diyl)-3,3′-dimethylbis[benzonitrile]* ((±)-**9**) *and (a*R,*a*S*)-2,2′-(3,6-Dimethoxynaphthalene-2,7-diyl)-3,3′-dimethylbis[benzonitrile]* (**10**). A mixture of **7** (392 mg, 2.00 mmol), **8** (514 mg, 1.00 mmol), LiCl (254 mg, 6.00 mmol), $[Pd(PPh_3)_4]$ (58 mg, 0.05 mmol), and BHT (11 mg, 0.05 mmol) in dry DMF (10 ml) was stirred under Ar at 80° for 42 h. H_2O (100 ml) was added, and the suspension was extracted with Et_2O (3 × 50 ml). The combined org. layers were washed with sat. aq. NaCl soln., dried ($MgSO_4$), and concentrated *in vacuo*. CC (SiO_2; CH_2Cl_2) gave (±)-**9** (43 mg, 10%) and **10** (65 mg, 16%).

Data of (±)-**9**: M.p. 218–219°. R_f (SiO_2; CH_2Cl_2) 0.47. IR (KBr): 2959*w*, 2224*m*, 1631*s*, 1467*s*, 1406*s*, 1227*s*, 1178*s*, 1035*s*, 788*s*. ^{1}H-NMR ($CDCl_3$, 500 MHz): 7.59–7.60 (*m*, 2 H); 7.54 (*s*, 2 H); 7.50–7.52 (*m*, 2 H); 7.36 (*t*, *J* = 7.7, 2 H); 7.25 (*s*, 2 H); 3.90 (*s*, 6 H); 2.18 (*s*, 6 H). ^{13}C-NMR ($CDCl_3$, 125 MHz): 155.82; 141.90; 139.04; 136.52; 134.07; 130.15; 130.11; 127.65; 126.13; 123.63; 118.71; 113.90; 105.22; 55.64; 20.25. EI-MS: 418.1 (100, M^+). HR-FAB-MS: 418.1684 (M^+, $C_{28}H_{22}N_2O_2^+$; calc. 418.1681). X-Ray Analysis: see *Fig. 1*.

Data of **10**: R_f (SiO_2; CH_2Cl_2) 0.11. ^{1}H-NMR ($CDCl_3$, 500 MHz): 7.59–7.61 (*m*, 2 H); 7.55 (*s*, 2 H); 7.50–7.52 (*m*, 2 H); 7.36 (*t*, *J* = 7.7, 2 H); 7.27 (*s*, 2 H); 3.91 (*s*, 6 H); 2.19 (*s*, 6 H). ^{13}C-NMR ($CDCl_3$, 125 MHz): 155.91; 141.63; 138.55; 136.43; 134.00; 130.27; 130.17; 127.63; 126.09; 123.50; 118.47; 114.27; 105.34; 55.70; 20.31. EI-MS: 418.1 (100, M^+).

2,2′-(3,6-Dimethoxynaphthalene-2,7-diyl)bis[isophthalonitrile] (**13**). A soln. of **3** (1.73 g, 5.0 mmol) in dry THF (30 ml) was added dropwise at −100° under Ar to BuLi (1.6M in hexane; 15.6 ml, 25.0 mmol) in dry THF (100 ml), and the mixture was stirred for 1 h at that temp. BH_3 (1M in THF, 50 ml; 50.0 mmol) was added rapidly, and the mixture was stirred at −100° for 2 h and at 20° for 24 h. After evaporation *in vacuo*, the residue was stirred with H_2O (200 ml) and 2M HCl (50 ml) for 1 h, and the mixture was extracted with AcOEt (4 × 50 ml). The combined org. layers were dried (Na_2SO_4) and concentrated *in vacuo*. Pinacol (5.91 g, 50 mmol), NH_4Cl (1 g, 18.7 mmol), and PhMe (20 ml) were added, and the mixture was heated to reflux for 2 h. The resulting yellow oil was extracted with CH_2Cl_2 (3 × 100 ml), and the combined org. layers were washed with H_2O (200 ml), dried ($MgSO_4$), and concentrated *in vacuo*. Recrystallization (hexane/Et_2O, −20°) yielded crude bis[boronate] **11** (370 mg, 17%), which was used without further purification. A degassed mixture of **12** (115 mg, 0.45 mmol), **11** (100 mg, 0.23 mmol), Na_2CO_3 (50 mg, 0.45 mmol), [$PdCl_2$(dppf)] (3 mg, 3.7 μmol), PhH (13.2 ml), EtOH (3.6 ml), and H_2O (6 ml) was heated to reflux under Ar for 2 h. After extraction with CH_2Cl_2 (3 × 70 ml), the combined org. layers were dried ($MgSO_4$) and concentrated *in vacuo*. CC (SiO_2; CH_2Cl_2) afforded **13** (70 mg, 70%). White solid. M.p. 378–379° ($CHCl_3$). IR (KBr): 3078*w*, 2956*w*, 2236*m*, 1631*s*, 1468*s*, 1230*s*, 1184*s*, 1031*s*. ^{1}H-NMR ($CDCl_3$, 500 MHz): 7.95 (*d*, *J* = 7.9, 4 H); 7.81 (*s*, 2 H); 7.57 (*t*, *J* = 7.9, 2 H); 7.31 (*s*, 2 H); 3.97 (*s*, 6 H). ^{13}C-NMR ($CDCl_3$, 125 MHz): 155.71; 145.36; 138.13; 136.48; 131.48; 128.33; 123.42; 122.98; 116.61; 115.66; 105.94; 55.72. EI-MS: 440.1 (100, M^+). HR-FAB-MS: 440.1279 (M^+, $C_{28}H_{16}N_4O_2^+$; calc. 440.1273). Anal. calc. for $C_{28}H_{16}N_4O_2 \cdot 0.06\ CHCl_3$ (440.46 + 7.16): C 75.29, H 3.62, N 12.52; found: C 75.24, H 3.58, N 12.47.

6-Bromo-7-methoxynaphthalen-2-ol (**16**). *3-Bromonphthalene-2,7-diol* (**15**; 1.00 g, 4.2 mmol) was added to a suspension of K_2CO_3 (1.16 g, 8.4 mmol) in DMF (25 ml), and the mixture was stirred at 20° under Ar for 15 min. A soln. of MeI (0.23 ml, 3.7 mmol) in DMF (2 ml) was added *via* syringe pump over 5 h, and the mixture was stirred at 20° for 30 min, filtered through a pad of *Celite*, and evaporated *in vacuo*. CC (SiO_2; CH_2Cl_2) and recrystallization (PhMe/hexane) afforded **16** (572 mg, 54%). White solid. M.p. 140–141°. UV/VIS (MeOH): 234 (60500). IR (KBr): 3476*s*, 1635*s*, 1596*m*, 1573*m*, 1503*s*, 1462*m*, 1424*m*. ^{1}H-NMR ($CDCl_3$, 200 MHz): 7.96 (*s*, 1 H); 7.59 (*d*, *J* = 8.8, 1 H); 7.04 (*d*, *J* = 2.5, 1 H); 6.99 (*s*, 1 H); 6.97 (*dd*, *J* = 8.8, 2.5, 1 H); 5.11 (*s*, 1 H); 3.98 (*s*, 3 H). ^{13}C-NMR ($(CD_3)_2CO$, 75 MHz): 157.33; 154.98; 136.64; 132.82; 129.47; 125.46; 117.74; 110.19; 109.23; 106.60; 56.49. EI-MS: 254.0/252.0 (82/81, M^+), 211.0/209.0 (77/76), 102.1 (100). Anal. calc. for $C_{11}H_9BrO_2$ (253.09): C 52.20, H 3.58, Br 31.57; found: C 52.38, H 3.54, Br 31.28.

(±)-6,6′-Dibromo-7,7′-dimethoxy-1,1′-binaphthalene-2,2′-diol ((±)-**17**). $CuCl_2$ (2.95 g, 21.9 mmol) was added to **16** (2.70 g, 10.7 mmol) in degassed MeOH (338 ml), and the mixture was stirred under Ar at 20° for 15 min. A soln. of (*t*-Bu)NH_2 (4.9 ml, 46.3 mmol) in degassed MeOH (34 ml) was added *via* syringe pump at 20° over 30 min, and the mixture was heated to reflux for 4 h. The dark soln. was cooled to 0°, and 6M HCl (60 ml) was added. The mixture was extracted with CH_2Cl_2 (5 × 200 ml), the combined org. layers were washed with H_2O (2 × 300 ml), dried ($MgSO_4$), and concentrated *in vacuo*. CC (SiO_2; CH_2Cl_2) and recrystallization (PhMe/hexane 1:1) yielded **17** (1.86 g, 69%). White crystals. M.p. 228–229°. UV/VIS (MeOH): 236 (91500). IR (KBr): 3450*s*, 2969*w*, 1611*s*, 1595*m*, 1497*s*, 1464*s*. ^{1}H-NMR ($CDCl_3$, 200 MHz): 8.10 (*s*, 2 H); 7.83 (*d*, *J* = 9.0, 2 H); 7.26 (*d*, *J* = 9.0, 2 H); 6.44 (*s*, 2 H); 5.05 (*s*, 2 H); 3.59 (*s*, 6 H). ^{13}C-NMR ($(CD_3)_2CO$, 50 MHz): 155.53; 155.12; 135.79; 133.31; 129.82; 126.10; 118.11; 114.30; 110.23; 105.09; 56.08. EI-MS: 504.1 (6, M^+), 100.0 (12), 28.0 (100). Anal. calc. for $C_{22}H_{16}Br_2O_4$ (504.17): C 52.41, H 3.20, Br 31.70; found: C 52.39, H 3.23, Br 31.42.

(±)-6,6′-Dibromo-2,2′,7,7′-tetramethoxy-1,1′-binaphthalene ((±)-**18**). Me_2SO_4 (225 μl, 2.38 mmol) was added to a suspension of **17** (400 mg, 0.79 mmol) and K_2CO_3 (440 mg, 3.18 mmol) in dry Me_2CO (5 ml) under Ar, and the mixture was heated to reflux for 4.5 h. After evaporation *in vacuo*, the residue was suspended in H_2O (7 ml), and the mixture was stirred at 20° for 30 min, then extracted with CH_2Cl_2 (4 × 25 ml). The combined org. layers were dried ($MgSO_4$) and concentrated *in vacuo*. CC (SiO_2; CH_2Cl_2) and recrystallization (PhMe/hexane) yielded (±)-**18** (432 mg, 99%). White crystals. M.p. 199–200°. UV/VIS (MeOH): 238 (92000). IR (KBr): 2935*w*, 2835*w*, 1615*s*, 1586*m*, 1495*s*, 1461*s*, 1424*m*, 1406*s*. ^{1}H-NMR ($CDCl_3$, 200 MHz): 8.06 (*s*, 2 H); 7.82 (*d*, *J* = 9.0, 2 H); 7.31 (*d*, *J* = 9.0, 2 H); 6.41 (*s*, 2 H); 3.76 (*s*, 6 H); 3.53 (*s*, 6 H). ^{13}C-NMR ($CDCl_3$, 75 MHz): 155.71; 154.17; 134.14; 132.36; 128.54; 125.40; 118.06; 112.22; 110.91; 104.08; 56.55; 55.79. EI-MS: 531.9 (100, M^+). Anal. calc. for $C_{24}H_{20}Br_2O_4$ (532.22): C 54.16, H 3.78, Br 30.02; found: C 54.03, H 3.95, Br 29.76.

(±)-2,2′-(2,2′,7,7′-Tetramethoxy-1,1′-binaphthalene-6,6′-diyl)bis[benzonitrile] ((±)-**19**). BuLi (1.6M in hexane, 10 ml, 15.95 mmol) was added to dry THF (45 ml) at −78° under Ar, followed by the dropwise addition of a soln. of (±)-**18** (1.70 g, 3.19 mmol) in dry THF (10 ml). After stirring at −78° for 50 min under Ar, BH_3 (1M in THF; 48 ml, 47.85 mmol) was added rapidly, and the mixture was stirred at −78° for 2 h, at 20° for 14 h, and at reflux for 2 h. The mixture was concentrated *in vacuo*, H_2O (200 ml) was added, and the suspension was stirred for 3 h at 20°. After addition of 2M HCl (10 ml), the mixture was extracted with Et_2O (3 × 130 ml), and the

combined org. layers were dried ($MgSO_4$) and concentrated *in vacuo* to give crude bis[boronic acid], which was used without further purification. A mixture of the crude bis[boronic acid] (3.19 mmol), 2-bromobenzonitrile (1.16 g, 6.39 mmol), [$PdCl_2(PPh_3)_2$] (225 mg, 0.32 mmol), Na_2CO_3 (677 mg, 6.39 mmol), PhH (68 ml), EtOH (20 ml), and H_2O (32 ml) was heated to reflux under Ar for 21 h, then cooled and extracted with AcOEt (2 × 150 ml). The combined org. layers were washed with sat. aq. $NaHCO_3$ soln. (2 × 100 ml) and sat. aq. NaCl soln. (2 × 100 ml), dried ($MgSO_4$), and concentrated *in vacuo*. The residue was purified by CC (SiO_2; hexane/AcOEt 4:1 → 3:2; then SiO_2; CH_2Cl_2) and recrystallization (CH_2Cl_2) to give (±)-**19** (982 mg, 53%). White solid. M.p. 245–246°. UV/VIS (MeOH): 229 (158000). IR (KBr): 2934*w*, 2226*m*, 1626*s*, 1492*s*, 1461*s*, 1409*m*. ^{1}H-NMR ($CDCl_3$, 500 MHz): 7.92 (*d*, *J* = 9.0, 2 H); 7.75 (*s*, 2 H); 7.72 (*ddd*, *J* = 7.7, 1.3, 0.6, 2 H); 7.62 (*dt*, *J* = 7.7, 1.3, 2 H); 7.53 (*ddd*, *J* = 7.7, 1.3, 0.6, 2 H); 7.41 (*dt*, *J* = 7.7, 1.3, 2 H); 7.34 (*d*, *J* = 9.0, 2 H); 6.61 (*s*, 2 H); 3.82 (*s*, 6 H); 3.50 (*s*, 6 H). ^{13}C-NMR ($CDCl_3$, 125 MHz): 156.10; 155.31; 142.52; 135.30; 132.81; 132.22; 131.18; 130.79; 129.71; 127.31; 126.72; 124.33; 118.65; 118.12; 113.55; 111.86; 103.80; 56.70; 55.33. EI-MS: 576.1 (100, M^+). Anal. calc. for $C_{38}H_{28}N_2O_4 \cdot 0.5\ H_2O$ (577.66 + 9.01): C 77.93, H 4.99, N 4.78; found: C 77.93, H 4.92, N 4.62.

(±)-2,2′-(2,2′,7,7′-Tetramethoxy-1,1′-binaphthalene-6,6′-diyl)bis[benzamidinium] Dichloride ((±)-**1**). Me_3Al (2M in PhMe; 1.2 ml, 2.4 mmol) was slowly added to a stirred suspension of NH_4Cl (134 mg, 2.5 mmol) in dry PhMe (3 ml) at 0° under Ar, and the mixture was stirred at 20° for 2.5 h. To this soln. of $MeAl(Cl)NH_2$ (2.4 mmol) in PhMe, (±)-**19** (200 mg, 347 μmol) was added, and the soln. was stirred at 90° under Ar for 2 d. Additional $MeAl(Cl)NH_2$ (2.4 mmol) in PhMe was added, and the mixture was stirred at 90° for 2 d, then cooled and slowly poured into a suspension of SiO_2 (20 g) in $CHCl_3$ (50 ml). After stirring for 5 min, the SiO_2 was filtered off, and the residue was washed with MeOH/H_2O 1:1. The filtrate was concentrated *in vacuo*, the residue was stirred with 5% aq. NaOH soln. (100 ml) and extracted with CH_2Cl_2 (3 × 100 ml). The combined org. layers were dried (Na_2SO_4) and concentrated *in vacuo*. The residue was dissolved in 10M ethanolic HCl (10 ml). Concentration *in vacuo* and MPLC (*RP16*; MeOH/H_2O 1:1) provided (±)-**1** (140 mg, 59%). M.p. 273–275° (dec.). UV/VIS (MeOH): 232 (77200). IR (KBr): 3383*s*, 3100*s*, 1672*s*, 1626*s*, 1598*w*, 1490*s*, 1463*m*, 1409*w*. ^{1}H-NMR (CD_3OD, 500 MHz): 7.97 (*d*, *J* = 8.8, 2 H); 7.88 (*s*, 2 H); 7.66–7.69 (*m*, 2 H); 7.60 (*d*, *J* = 7.4, 2 H); 7.49–7.54 (*m*, 4 H); 7.39 (*d*, *J* = 8.8, 2 H); 6.44 (*s*, 2 H); 3.73 (*s*, 6 H); 3.34 (*s*, 6 H). ^{13}C-NMR (CD_3OD, 50 MHz): 170.59; 157.98; 156.68; 139.22; 136.94; 134.24; 133.73; 132.94; 131.77; 131.78; 129.70; 129.42; 128.46; 126.56; 119.86; 113.48; 103.96; 57.30; 55.27. FAB-MS: 647.3 (41. [$M - Cl$]$^+$), 611.3 (100, [$M - H - 2\ Cl^-$]$^+$), 307.1 (25). HR-FAB-MS: 611.2654 ([$M - H - 2\ Cl^-$]$^+$, $C_{38}H_{35}N_4O_4^+$; calc. 611.2658).

*X-Ray Crystal Structure of (±)-***9** (Et_2O solvate). X-Ray crystal data for $C_{28}H_{22}N_2O_2 \cdot 0.5\ C_4H_{10}O$ (M_r = 455.21): monoclinic space group $P2_1/c$, D_c = 1.234 g cm^{-3}, Z = 4, a = 11.982(2), b = 13.610(4), c = 15.342(8) Å, β = 94.26(3)°, V = 2495(2) Å^3, CuK_α radiation, λ = 1.5184 Å, $3.70 \leq \theta \leq 67.03°$, 4747 unique reflections, T = 150 K. The structure was solved by direct methods and refined by full-matrix least-squares analysis [32]. All heavy atoms were refined anisotropically, H-atoms isotropically. The solvent molecule is disordered and was refined isotropically over two positions with H-positions based on stereochemical considerations. Final $R(F)$ = 0.0562, $wR(F^2)$ = 0.2041 for 389 parameters, 6 restraints, and 3895 reflections with $I > 3\sigma(I)$. Crystallographic data (excluding structure factors) for compound (±)-**9** have been deposited with the *Cambridge Crystallographic Data Centre* as deposition No. CCDC-137138. Copies of the data can be obtained, free of charge, on application to the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44(1223)336033; e-mail: deposit@ccdc.cam.ac.uk).

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