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Synthesis and Evaluation of a Cyclophane Receptor for Acetic Acid

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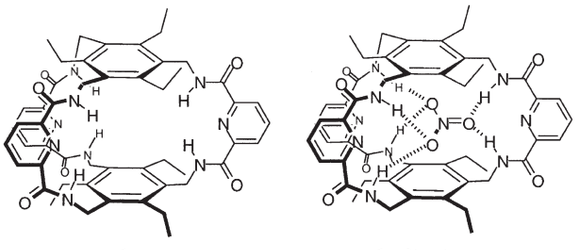
A bicyclic cyclophane (2) containing one pyridine nitrogen and four amide N–H groups oriented toward the interior of the cavity was synthesized. The binding constants of various carboxylic acids with 2 were measured by UV/Vis spectroscopy. Acetic acid bound to 2 with a K_a of 980 ± 90 M^{-1} in chloroform while branched carboxylic acids showed significantly lower binding. The data indicate that acetic acid was bound within the cavity of 2. Only one acetic acid binds to two control hosts, whereas 2 shows definitive 1:1 binding. The results suggest that selectivity in the binding of carboxylic acids can be achieved via size constraints dictated by the receptor cavity, and that the same size restrictions lead to only one carboxylic acid bound to the cyclophane. The crystal structure of 2 is reported.

INTRODUCTION

A major interest in molecular recognition is the creation of synthetic receptors for small guest molecules [1–5]. In many of these studies, the targets are inorganic or organic cations and anions where electrostatic interactions contribute to the binding affinity. Of course, the size of the guest molecule is also an important factor in the selectivity. Very few receptors for neutral organic compounds have selectivities related to the size of the organic molecules, but rather to the complimentarity of the functional group partners of both the receptor and guest [6–11]. Recently, we reported the design and synthesis of C_3-symmetric bicyclic receptor **1**, and its binding selectivity for planar anions such as nitrate and enolates in organic media [12]. In these cases, compound **1** bound the guests via multiple neutral hydrogen bonds with N–H protons directed into the interior of the cavity. We have also used this receptor to complex enolates of active methylene compounds [13]. Herein, as an application of this receptor motif, we report the design and synthesis of a new bicyclic cyclophane (**2**) and its propensity for inclusion of linear carboxylic acids [14–18]. The constraints of the cavity preclude binding of branched carboxylic acids.



1 **1·nitrate**

RESULTS AND DISCUSSION

Design Criteria

The bicyclic receptor **2** has one pyridine nitrogen and four N–H protons directed into the cavity. The pyridine nitrogen in **2** is more basic than that of pyridine due to the appendant dimethylamino group, and thereby serves as a better hydrogen bond acceptor. The amido N–H protons serve as possible hydrogen bond donors. The design is reminiscent of cyclophanes created in the Whitlock group [19,20].

A small neutral monocarboxylic acid is expected to bind in the idealized geometry shown below. When a carboxylic acid binds to **2**, the acidic proton is

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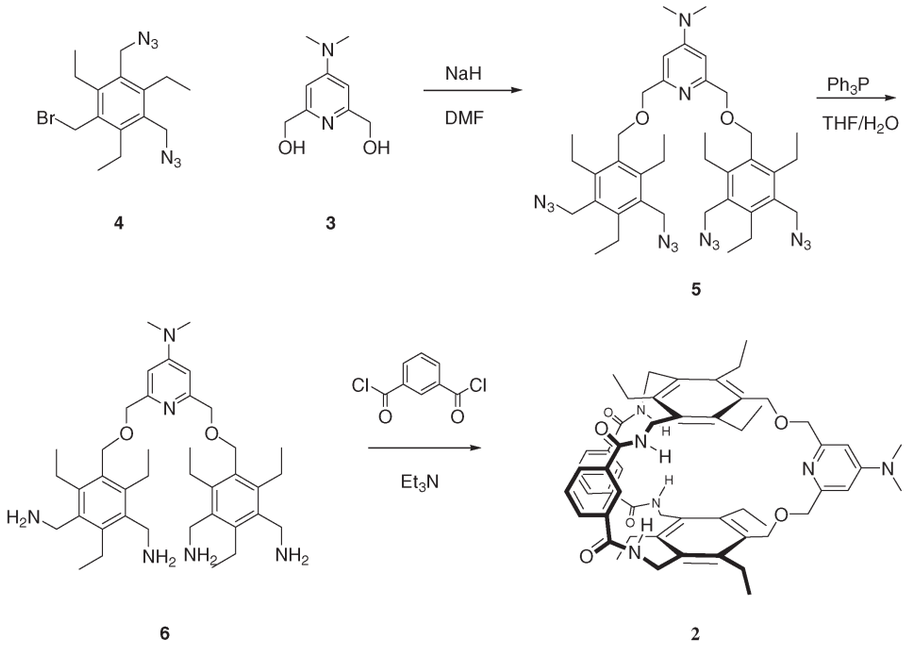
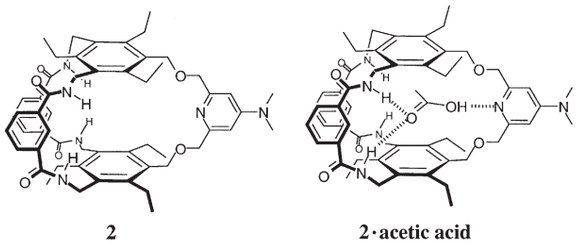


SCHEME 1 Synthesis of cyclophane **2**.

expected to interact with the pyridine nitrogen, effecting a change in the electron density of the ring system. Hence, we expected the UV/Vis absorption spectrum of **2** to change upon addition of a carboxylic acid.



Synthesis

4-Dimethylaminopyridine-2,6-dimethanol [21] (**3**) was combined with 2.2 equivalents of [3,5-bis(azidomethyl)-2,4,6-triethylphenyl]methyl bromide [22] (**4**) under Williamson ether synthesis conditions (Scheme 1). Subsequent reduction of the azido groups yielded **6**. Reaction of **6** with 2.4 equivalents of isophthaloyl chloride in the presence of triethylamine afforded the desired cyclophane (**2**) as a white solid in a 31% yield.

X-ray Crystallography

A crystal of **2** (Fig. 1a and b) was obtained by slow evaporation of a solution of **2** in acetonitrile/methanol.[†] The X-ray crystal structure of **2** confirmed the proposed orientation of the amide hydrogens into the interior of the cavity. Attempts to isolate crystals in the presence of acetic acid did not yield a X-ray quality co-crystal.

Binding Behavior of Carboxylic Acids with Receptor 2

Figure 2 shows the typical change of the absorption spectra of **2** (20 μM) in chloroform upon addition of acetic acid (0, 1.118, 2.22, 3.33 mM). The absorbance at 286 nm increased with increasing acetic acid concentration. This spectral change is proposed to be indicative of the formation of a hydrogen bond between the pyridine moiety of **2** and acetic acid.

4-Dimethylaminopyridine was used as a control host for the titration of acetic acid. Changes in the UV/Vis spectrum of 4-dimethylaminopyridine in chloroform were observed as aliquots of acetic acid were added. The resulting binding isotherm indicated that two pyridine units were bound to one acetic acid, the proposed complex of which is shown below. The N atom within one pyridine ring may be protonated in the presence of acetic acid. In water

[†]Crystallographic data for **2**. Crystals grew as plates (0.46 mm × 0.27 mm × 0.10 mm) by slow evaporation from acetonitrile and methanol, orthorhombic, $Z = 4$ in a cell of dimensions $a = 18.6720(4)$, $b = 21.2440(4)$, $c = 15.3380(3)$ Å, $V = 6084.1(2)$ Å^3, $\rho = 1.08\,\mathrm{Mg\,mm^{-3}}$, $F(000) = 2112$. A total of 13,477 reflections were measured, 7213 unique ($R_{int} = 0.0378$), Nonus Kappa CCD using graphite monochromatized Mo-Kα radiation ($\lambda = 0.71073$ Å) at −120°C. The structure was refined on F^2 to an $R_w = 0.247$, with a conventional $R = 0.0977$ (4544 reflections with $F_0 > 4[\alpha(F_0)]$), and a goodness to fit of 1.691 for 331 refined parameters. CCDC 171792.

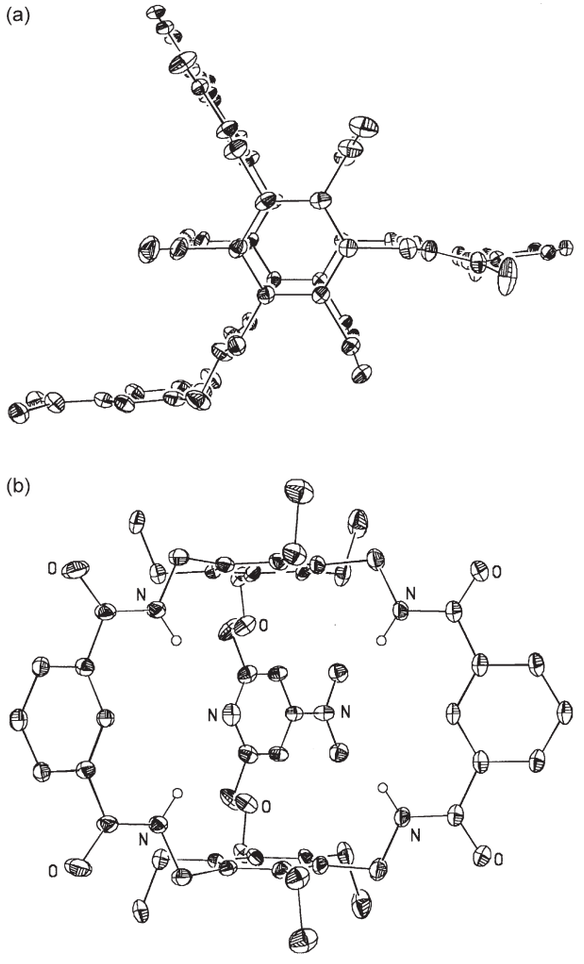


FIGURE 1 (a) Top view of **2**. The view direction is perpendicular to the crystallographic mirror plane of symmetry that bisects the cryptand. Displacement ellipsoids are scaled to the 30% probability level. Most hydrogen atoms have been removed for clarity. (b) View of **2** with only the heteroatoms labeled. Displacement ellipsoids are scaled to the 30% probability level. Most hydrogen atoms have been removed for clarity. The cryptand lies on a crystallographic mirror plane of symmetry $z = 0$. The two nitrogen atoms of the *N*,*N*-dimethylaminopyridine moiety lie on the mirror plane which also bisects two adjacent phenyl rings.

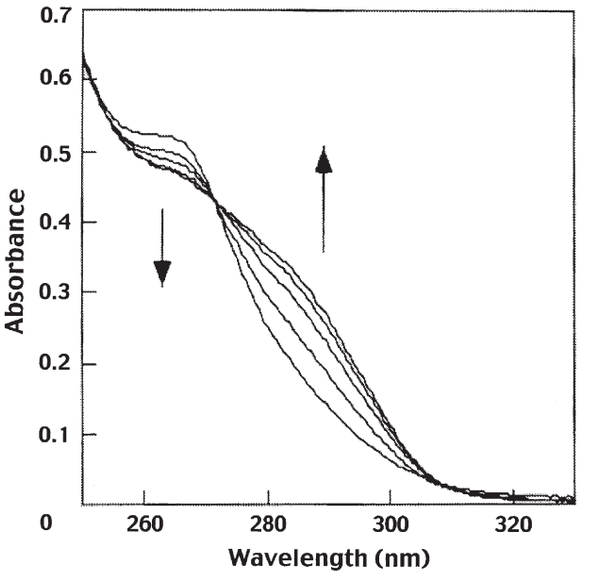
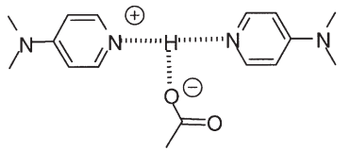


FIGURE 2 UV/Vis absorption spectra of **2** (20 μM) in chloroform upon addition of acetic acid (0, 0.368, 1.18, 2.22, 3.33 mM).



this proton transfer is expected, but in chloroform aggregation is expected. A second dimethylaminopyridine can hydrogen bond to the dimethylaminopyridinium ion. Additionally, an acetic acid dimer can serve as a hydrogen bond acceptor or simply as part of a tight ion pair. Simple carboxylic acids and phosphoric acids are known to participate in hydrogen bonding interactions and aggregation in low dielectric media [23–26]. Conversely, phosphoric acid dimers have been shown to complex with pyridine in chloroform [27,28]. It is, therefore, reasonable to attribute the observed 2:1 pyridine–acetic acid complex shown below to the greater basicity of dimethylaminopyridine relative to that of pyridine.

The changes in absorbance at 286 nm upon addition of several carboxylic acids to **2** are shown in Fig. 3. Complexation of **2** with acetic acid yields the maximum change and the largest binding affinity. These results suggest that the size of the guest affects the measured binding affinities.

Values for the maximum molar absorbance coefficient change ($\Delta\varepsilon_{max}$), and the binding constant (K_a) for the binding of **2** to each of the guests, were obtained from curve fitting analyses of binding isotherms [29]. The K_a and $\Delta\varepsilon_{max}$ values were also obtained using the Benesi–Hildebrand method [30]. The aforementioned values are summarized in Table I. Similar results were obtained from each of these methods.

Acetic acid, the smallest carboxylic acid analyzed, had the largest K_a and $\Delta\varepsilon_{max}$ values. Previous studies showed that acetate formed an inclusion complex with **1** upon binding. Therefore, in the case of cyclophane **2**, acetic acid was expected to reside within the cavity with the acidic proton interacting with the pyridine nitrogen. There are several studies of synthetic hosts for dicarboxylic acids that have binding constants in the order of $10^4\ M^{-1}$ in organic solvents [31]. Considering that our targets were monocarboxylic acids in this study, the K_a range of

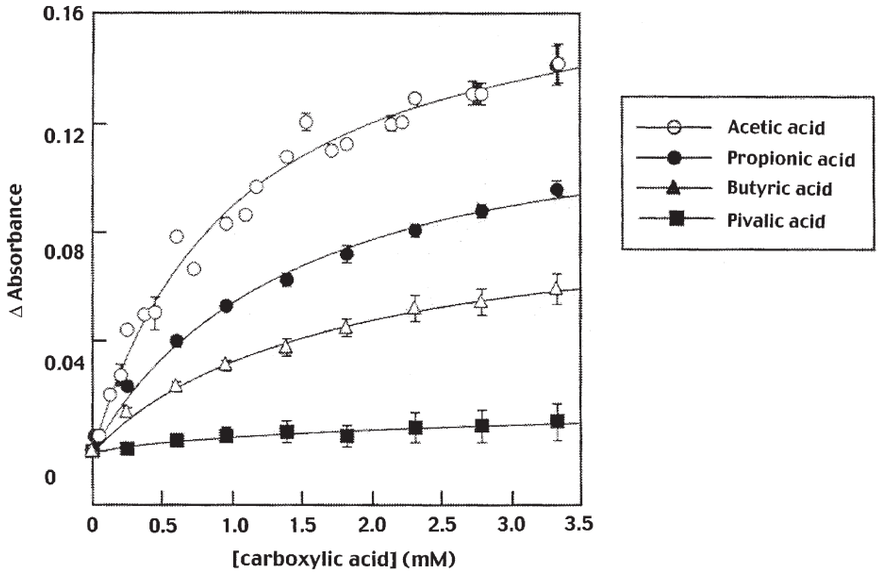


FIGURE 3 Absorption spectral changes at 286 nm of **2** (20 μM) upon addition of carboxylic acid in chloroform. (○) Acetic acid, (●) propionic acid, (▲) butyric acid and (■) pivalic acid. Error bars show standard error.

10^2–$10^3\,M^{-1}$ is reasonable. Propionic acid showed smaller K_a and $\Delta\varepsilon_{max}$ values than acetic acid. Propionic acid is larger than acetic acid, so it is expected that there will be steric restrictions to binding within the cavity of **2**. Carboxylic acids of four to six carbons showed even lower binding than propionic acid. Butyric acid and isovaleric acid, which have no branch at the α-position, have larger K_a values compared to isobutyric acid and cyclohexanecarboxylic acid, which contain a branch at the α-position. However, there is no detectable binding using pivalic acid. The measured K_a values are not coincident with pK_a values of these carboxylic acids [32]. Therefore, these results serve to reflect the differences in the molecular structures of these carboxylic acids and not their acidities.

Molecular mechanics MMFF calculations using MACSPARTAN [33] were performed on the proposed complex of **2** and acetic acid and on the proposed complex of **2** and isobutyric acid. The minimized structure of the **2**:acetic acid complex (Fig. 4) indicates that acetic acid can sit within the cavity and is positioned so as to participate in three point hydrogen bonding. These interactions include hydrogen bonding between the acidic hydrogen and the N of the dimethylaminopyridine ring and two hydrogen bonds between the amide hydrogens and the lone pairs on the carbonyl oxygen. Similar calculations with isobutyric acid within the cavity indicate that the cavity is widened and stretched, thereby introducing significant strain. Any interaction between **2** and isobutyric acid is, therefore, thought to occur from the exterior of the cavity to avoid this strain.

CONCLUSION

A bicyclic receptor **2** for monocarboxylic acids was designed and synthesized. The UV/Vis spectroscopic studies showed that **2** has a significantly

TABLE I Binding constants (K_a) and $\Delta\varepsilon_{max}$ of carboxylic acid binding to **2** in chloroform and pK_a values of carboxylic acids

Carboxylic acid	K_a/M^{-1}		$\Delta\varepsilon/10^3\,M^{-1}\,cm^{-1}$		pK_a
Acetic acid	980 ± 90*	1000†	9.0 ± 0.3*	8.7†	4.76
Propionic acid	680 ± 70	730	6.7 ± 0.3	6.4	4.88
Butyric acid	590 ± 60	640	4.4 ± 0.2	4.1	4.82
Isobutyric acid	280 ± 70	370	5.1 ± 0.8	4.2	4.86
Isovaleric acid	510 ± 70	640	3.6 ± 0.2	3.1	4.78
Pivalic acid	n.d.	n.d.	n.d.	n.d.	5.05
Cyclohexanecarboxylic acid	340 ± 70	440	5.6 ± 0.7	4.7	4.90

*Values were obtained from curve fitting analyses of binding isotherms (Fig. 2). †Values were obtained from Benesi–Hildebrand plots. n.d.=not determined due to small $\Delta\varepsilon_{max}$ or large error.

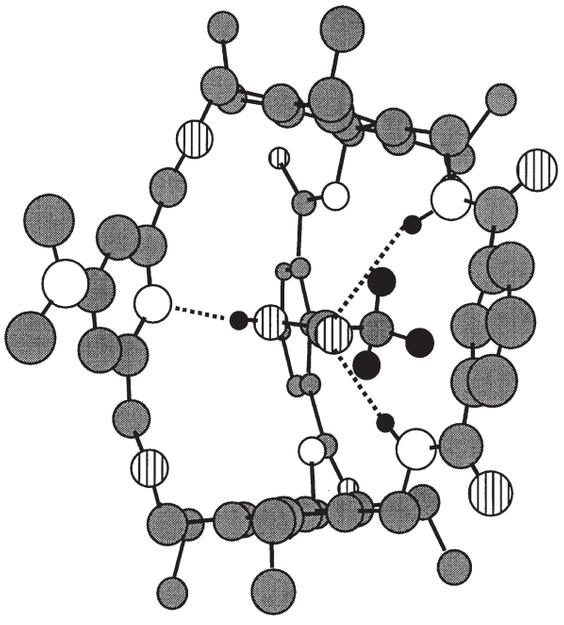


FIGURE 4 Minimized structure of **2**:acetic acid complex using molecular mechanics MMFF calculations. The hydrogens have been removed from **2** for clarity. The dashed lines indicate hydrogen-bonding of the acetic acid to the dimethylaminopyridine ring.

larger binding affinity for acetic acid as compared to the binding affinities for other larger carboxylic acids. It is postulated that acetic acid binds in the cavity of **2** and its acidic proton interacts with the pyridine nitrogen of **2**.

EXPERIMENTAL

General Considerations

The chemicals used were obtained from Aldrich, Sigma and EM Science and were used without further purification, except where noted. Tetrahydrofuran (THF) was refluxed over sodium and distilled over sodium and benzophenone. Dichloromethane, acetonitrile, pyridine, and triethylamine were refluxed over calcium hydride and distilled. Methanol was refluxed over magnesium and distilled. Flash chromatography was performed on Whatman 60 Å 230–400 mesh silica gel. ^{1}H(75 MHz) and ^{13}C (300 MHz) spectra were measured by Varian Unity Plus spectrometer. Mass spectra were recorded on a Finnigan VG analytical ZAB2-E spectrometer.

Synthesis

4-Dimethylaminopyridine-2,6-dimethanol (**3**). 4-Dimethylaminopyridine-2,6-dicarboxylate (0.881 g, 3.40 mmol) was dissolved in distilled THF (90 ml). To this, sodium borohyride (0.538 g, 14.2 mmol) was slowly added at 0°C. The reaction mixture was refluxed for 20 h under nitrogen. The mixture was a white suspension. The mixture was cooled and neutralized by HCl at 0°C. The solvent was evaporated by a rotary evaporator. The residue was suspended in dichloromethane/methanol and filtered to remove inorganic salts. The filtrate was evaporated and the residue was purified by a flash column chromatography (5–20% gradient of ammonia saturated methanol in dichloromethane). The resulting pale-yellow solid was dried *in vacuo* (0.554 g, 3.04 mmol, 89%).

^{1}H-NMR ($CDCl_3 + CD_3OD$ drop, TMS): δ 6.49 (s, 2H, Ar), 4.62(s, 4H, ArCH_2OH), 3.06(s, 6H, CH_3N) ^{13}C NMR ($CDCl_3 + CD_3OD$ drop): δ 156.67, 126.46, 102.23, 62.53, 39.52. Mass (normal mode CI+): 183 (M + H) ($C_9H_{14}N_2O_2$, calcd. 182.11).

[2,6-Bis-(3,5-bis-azidomethyl-2,4,6-triethyl-benzyloxymethyl)-pyridin-4-yl]-dimethyl amine (**5**). 4-Dimethylaminopyridine-2,6-dimethanol (0.328 g, 1.80 mmol) was dissolved in anhydrous DMF (40 ml). Sodium hydride (60% oil dispersion, 0.353 g, 8.8 mmol) was slowly added at 0°C. [3,5-Bis(azidomethyl)-2,4,6-triethylphenyl]methyl bromide (1.47 g, 4.02 mmol) in anhydrous DMF (40 ml) was added dropwise at 0°C. The reaction mixture was stirred at room temperature for 17 h under nitrogen. The mixture was slowly poured into 0.1 N aqueous HCl (300 ml) and extracted with ethyl acetate (4 × 200 ml). The organic layer was washed with brine, dried over sodium sulfate and filtered. The solvent was evaporated by rotary evaporation and a brown liquid was obtained. The product was purified by flash column chromatography (1–5% gradient of ammonia saturated methanol in dichloromethane). A brown liquid was dried *in vacuo* (0.965 g, 1.29 mmol, 71%).

^{1}H-NMR ($CDCl_3$, TMS): δ 6.64(s, 2H, Ar), 4.68 (s, 4H, ArCH_2O), 4.66(s, 4H, ArCH_2O), 4.49(s, 8H, CH_2N_3), 2.98(s, 6H, CH_3N), 2.92–2.82(m, 12H, CH_2CH_3), 1.24–1.19(m, 18H, CH_2CH_3). ^{13}C NMR ($CDCl_3 + CD_3OD$ drop): δ 145.39, 144.76, 144.35, 132.808, 129.50, 103.10, 66.81, 48.01, 39.25, 23.078, 23.01, 22.88, 16.35, 16.15, 15.80. Mass (normal mode CI+): 751 (M + H) ($C_{39}H_{54}N_{14}O_2$, calcd. 750.46).

[2,6-Bis-(3,5-bis-aminomethyl-2,4,6-triethyl-benzyloxymethyl)-pyridin-4-yl]-dimethyl amine (**6**). Compound **5** (0.948 g, 1.26 mmol) and triphenylphosphine (3.11 g, 11.9 mmol) were combined in a 250 ml round-bottomed flask. To this, THF (75 ml) and water (10 ml) were added. The reaction mixture was stirred at room temperature for 17 h under nitrogen. The solvent was removed under reduced pressure. The resulting residue was suspended in 1 N aqueous HCl (150 ml) and washed with dichloromethane (3 × 50 ml). The pH of the aqueous layer was adjusted to 11 using aqueous sodium hydroxide

and extracted with dichloromethane (4 × 70 ml). The organic layer was dried over sodium sulfate, filtered, and concentrated under reduced pressure. The resulting brown liquid was dried *in vacuo*. The residue was a pale brown solid (0.671 g, 1.04 mmol, 82%).

^{1}H-NMR ($CDCl_3$, TMS): δ 6.68(s, 2H, Ar), 4.69(s, 4H, ArCH_2O), 4.63(s, 4H, ArCH_2O), 3.88 (s, 8H, CH_2NH_2), 3.01(s, 6H, CH_3N), 2.88–2.80(m, 12H, CH_3CH_3), 1.43(s, 8H, NH_2), 1.25–1.19(m, 18H, CH_2CH_3). Mass (HRMS CI+): 647 (M + H) ($C_{39}H_{62}N_6O_2$, calcd. 646.49).

9-(Dimethylamino)-2,16,18,32,45,47-hexaethyl-5,13-dioxa-21,29,34,42,48-pentaazaheptacyclo[15.15.11.1^{3,31}.1^{7,11}.1^{15,19}.1^{23,27}.1^{26,40}]octatetraconta-l,3,(45), 7,9,11(48), 15,17,19(47),23,25,27(46),31,36,38,40(44)-pentadecane-22,28,35,41-tetrone (**2**). Compound **6** (0.671 g, 1.04 mmol) and distilled triethylamine (2 ml, 14 mmol) were dissolved in distilled dichloromethane (40 ml) in a 100 ml round-bottomed flask and stirred at room temperature for 30 min. To this, a solution of isophthaloyl chloride (0.503 g, 2.48 mmol) in distilled dichloromethane was added dropwise. The reaction mixture was stirred at room temperature for 92 h under argon. The solvent was evaporated by rotary evaporation. The residue was purified by a flash column chromatography (eluent: 1–25% gradient of ammonia saturated methanol in ethyl acetate). A white solid was isolated and dried *in vacuo* (0.292 g, 0.322 mmol, 31%).

^{1}H-NMR ($CDCl_3$, TMS): δ 8.31(d, 4H, Ar), 8.02 (s, 2H, Ar), 7.60(t, 2H, Ar), 6.90(s, 4H, NH), 6.48(s, 2H, pyridine-Ar), 4.66–4.63(s × 2, 8H, ArCH_2O), 4.55–4.50(s × 2, 8H, CH_2NH), 3.06(s, 6H, CH_3N), 2.82(q, 4H, CH_3CH_3), 2.59(q, 8H, CH_3CH_3), 1.20–1.15(m, 18H, CH_2CH_3). ^{13}C NMR ($CDCl_3$, TMS): δ 174.41, 166.12, 144.49, 132.79, 132.34, 130.64, 129.18, 122.192, 104.21, 74.13, 66.96, 49.62, 39.26, 38.88, 29.60, 23.21, 22.63, 21.77, 16.21, 16.04. Mass (HRMS CI+): 907.515 (M + H) (M + H, $C_{55}H_{57}N_6O_6$, calcd. 907.512).

UV/Vis Titrations

Propionic acid and pivalic acid were purchased from Fisher and Sigma, respectively. Other carboxylic acids were purchased from Aldrich. Spectrum grade chloroform was purchased from EM science ("Omnisolv" brand). All chemicals were used without further purification. UV/Vis spectra were recorded on a Beckman DU-640 spectrophotometer.

Experiments were done at 23°C. Aliquots of a solution of carboxylic acid (20 mM) and **2** (20 μM) in chloroform were added to a solution of **2** (20 μM) in chloroform (800 μL). With each addition, the cuvette was shaken well and incubated 5 min prior to recording the spectrum. The change of the absorbance at 286 nm was monitored as a function of carboxylic acid concentration. Portions of an acetic acid solution (1.4 mM) and *N*-dimethylaminopyridine (75 μM) in chloroform were added to a solution of *N*-dimethylaminopyridine (75 μM) in chloroform. The absorbance change at 260 nm was observed as a function of acetic acid concentration.

Acknowledgements

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References

[1] Hartley, J.H., James, T. and Ward, C.J. (2000), *J. Chem. Soc., Perkin Trans. 2*, 3155–3184.
[2] Antonisse, M.M.G. and Reinhoudt, D.N. (1998), *Chem. Commun.*, 443–448.
[3] Beer, P. and Gale, P.A. (2001), *Angew. Chem. Int. Ed.* **40**, 486–516.
[4] Schmidtchen, F.P. and Berger, M. (1997), *Chem. Rev.* **97**, 1609–1646.
[5] Schrader, T. (1999), *J. Inclusion Phenom. Macro. Chem.* **34**, 117–129.
[6] Pieters, R.J., Cuntze, J., Bonnet, M. and Diederich, F. (1997), *J. Chem. Soc., Perkin Trans. 2*, 1891–1901.
[7] Bhattarai, K., Davis, A., Perry, J. and Walter, C.J. (1997), *J. Org. Chem.* **62**, 8463–8473.
[8] Davis, A.P. and Wareham, R.S. (1998), *Angew. Chem. Int. Ed.* **37**, 2270–2273.
[9] Cloninger, M.J. and Whitlock, H.W. (1998), *J. Org. Chem.* **63**, 6153–6159.
[10] Neugebauer, R. and Knoche, W. (1998), *J. Chem. Soc., Perkin Trans. 2*, 529–534.
[11] Schlogl, J. and Krautler, B. (1999), *Synlett*, 969–971.
[12] Nikura, K., Bisson, A.P. and Anslyn, E.V. (1999), *J. Chem. Soc., Perkin Trans. 2*, 1111–1114.
[13] Snowden, T.S., Bisson, A.P. and Anslyn, E.V. (1999), *J. Am. Chem. Soc.* **121**, 6324–6325.
[14] Antonio, E., Galan, A. and Mendoza, J. (1989), *J. Am. Chem. Soc.* **111**, 4994–4995 (For other carboxylic acid synthetic receptors).
[15] Fredericks, J., Yang, J., Geib, S.J. and Hamilton, A.D. (1994), *Proc. Acad. Sci. (Chem. Sci.)* **106**, 923–935 (For other carboxylic acid synthetic receptors).
[16] Shyamaprosad, G., Ghosh, K. and Dasgupta, S. (1996), *Tetrahedron*, 12223–12232 (For other carboxylic acid synthetic receptors).
[17] Tejeda, A., Olivia, A.I., Simon, L., Grande, M., Caballero, M. and Moran, J.R. (2000), *Tetrahedron Lett.*, 4563–4566 (For other carboxylic acid synthetic receptors).
[18] Shyamaprosad, G., Ghosh, K. and Dasgupta, S. (2000), *J. Org. Chem.* **65**, 1907–1914.
[19] Whitlock, B.J. and Whitlock, H.W. (1994), *J. Am. Chem. Soc.* **116**, 2301–2311.
[20] Haeg, M.E., Whitlock, B.J. and Whitlock, H.W. (1989), *J. Am. Chem. Soc.* **111**, 692–696.
[21] Otsuka, M., Satake, H., Sugiura, Y., Murakami, S., Shibasaki, M. and Kobayashi, S. (1993), *Tetrahedron Lett.* **34**, 8297–8500.
[22] Niikura, K. and Anslyn, E.V. (1999), *J. Chem. Soc., Perkin Trans. 2*, 2769–2775.
[23] Turi, L. and Dannenburg, J. (1994), *J. Am. Chem. Soc.* **16**, 8714.
[24] Johnson, J.F. and Cole, R.H. (1951), *J. Am. Chem. Soc.* **73**, 4536–4540.
[25] Gandour, R. (1981), *Bioorg. Chem.* **10**, 169–176.
[26] Tadayoni, B.M., Huff, J. and Rebek, Jr, J. (1991), *J. Am. Chem. Soc.* **113**, 2247–2253.

[27] Denisov, G.S. and Golubev, N.S. (1981), *J. Mol. Struct.* **75**, 311–326.
[28] Chu, F., Flatt, L. and Anslyn, E.V. (1994), *J. Am. Chem. Soc.* **116**, 4194–4204.
[29] Conners, K.A. (1987) *Binding Constants, the Measurement of Molecular Complex Stability* (Wiley, New York).
[30] Benesi, H.A. and Hildebrand, J.H. (1949), *J. Am. Chem. Soc.* **71**, 2703–2707.
[31] Goswani, S. and Ghosh, K. (1997), *Tetrahedron Lett.* **38**, 4503–4506.
[32] Braude, E.A., Nachod, F.C., eds, (1995) *Determination of organic structures by physical methods* (Academic Press, Inc., New York).
[33] MacSpartan Pro/MacSpartan Plus, Version 2.0 (2000) (Wavefunction, Inc., Irvine California).