Experimental Section

The purity of materials on the solid support was assessed by cleavage at **L1** and analysis by using high-pressure liquid chromatography (HPLC) on a Hewlett Packard Series 1050 instrument. Column: Supercosil ABZ$^+$PLUS 3.3 cm × 4.6 mm, 3 μm, reverse phase. Eluent A: water, 0.1% trifluoroacetic acid; eluent B: acetonitrile 95%, water 5%, trifluoroacetic acid 0.05%; flow rate: $1\,\mathrm{mL\,min^{-1}}$; detection: UV (diode array: 215, 230, 254, 386 nm); typical method: gradient 10–95% B in A, over 7 min. Liquid chromatography mass spectra (LCMS) were recorded on a Micromass Platform by using thermospray positive and negative ionization. Column: Supercosil ABZ$^+$PLUS 3.3 cm × 4.6 mm, 3 μm, reverse phase. Eluent A: 10 mM solution of ammonium acetate in water, 0.1% formic acid; eluent B: acetonitrile 95%, water 5%, formic acid 0.05%; flow rate: $1\,\mathrm{mL\,min^{-1}}$; detection: UV (diode array: 215, 230, 254 nm); typical method: gradient 0–100% B in A, over 3.5 min, 100% B 3.5 min.

Cleavage at **L1** was carried as follows: A) Modified Rink constructs **8**–**12**. A small resin sample was incubated for 5–10 min at room temperature with a solution (10 μL) composed of 2-mercaptoethanol (21 μL), and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) (70 μL) in acetonitrile (250 μL). After filtration the filtrate was diluted to a final volume of 20 μL with acetonitrile prior to analysis. B) Modified Sasrin constructs **15**–**22**. A small resin sample was incubated for 5–10 min at room temperature with a solution (10 μL) composed of thiophenol (25 μL), and diisopropylethylamine (50 μL) in acetonitrile (250 μL). After filtration the filtrate was evaporated under a stream of nitrogen and the residue dissolved in acetonitrile (20 μL) prior to analysis. Conditions B were chosen to avoid cleavage of the ester bond in compounds **16**–**22**.

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[1] A. W. Czarnik, *Anal. Chem.* **1998**, *70*, 378A.

[2] a) H. M. Geysen, C. D. Wagner, W. M. Bodnar, C. J. Markworth, G. J. Parke, F. J. Schoenen, D. D. Wagner, D. S. Kinder, *Chem. Biol.* **1996**, *3*, 679; b) M. R. Carrasco, M. C. Fitzgerald, Y. Oda, S. B. H. Kent, *Tetrahedron Lett.* **1997**, *38*, 6331.

[3] a) S. C. McKeown, S. P. Watson, R. A. E. Carr, P. Marshall, *Tetrahedron Lett.* **1999**, *40*, 2407; b) P. J. Murray, C. Kay, J. J. Scicinski, S. C. McKeown, S. P. Watson, R. A. E. Carr, *Tetrahedron Lett.* **1999**, *40*, 5609.

[4] Dual-linker analytical constructs incorporating the dansyl and dabsyl groups have also been prepared and their properties studied as both UV chromophores and for fluorescence detection: see A. Zaramella, N. Conti, M. Dal Cin, A. Paio, P. Seneci, S. Gehanne, *Anal. Chem.* submitted.

[5] The three-carbon-chain tether was found to be the minimum length necessary to avoid fragmentation and loss of anthracene during MS analysis.

[6] C. Kay, P. J. Murray, L. Sandow, A. B. Holmes, *Tetrahedron Lett.* **1997**, *38*, 6941.

[7] Commercially available from Peakdale Fine Chemicals.

[8] J. P. Desvergne, N. Bitit, A. Castellan, M. Webb, H. Bouas-Laurent, *J. Chem. Soc. Perkin Trans. 2* **1988**, *10*, 1885.

[9] T. Fukuyama, C.-K. Jow, M. Cheung, *Tetrahedron Lett.* **1995**, *36*, 6373.

[10] ($CDCl_3$): $\delta = 7.7$ (m, 4H) for **11a**; 5.7 and 4.9 (m, 3H) for **11b**; 2.9 (s, 6H) for **11c**; 0.9 (s, 9H) for **11d**.

[11] In addition by construction of a standard curve using 9-methylanthracene and its use as an internal standard, the absolute quantification of the resin-bound products can be assessed. See Supporting Information.

[12] S. I. Klein, B. F. Molino, M. Czekaj, C. J. Gardner, V. Chu, K. Brown, R. D. Sabatino, J. S. Bostwick, C. Kasiewski, R. Bentley, V. Windisch, M. Perrone, C. T. Dunwiddie, R. J. Leadley, *J. Med. Chem.* **1998**, *41*, 2492.

[13] Careful examination of the mass spectral data of each intermediate analytical fragment indicated that no unexpected ion doublets were present, suggesting that the anthracene group was stable to all of the reaction conditions for the synthesis.

Redox-Switched Control of Binding Strength in Hydrogen-Bonded Metallocene Complexes

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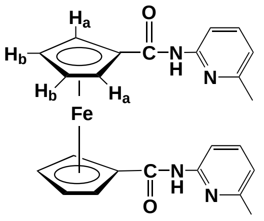
Redox-switched binding of organic molecules by either organic[1] or inorganic[2] electroactive species is attracting continued interest in the area of supramolecular electrochemistry. Those examples in which the binding interaction is through hydrogen bonds are relevant to recent studies which indicate that hydrogen bonds play an important role in tuning the redox potential of certain proteins.[3] Herein we compare the dicarboxylic acid binding properties of **1** with those of its charged cobaltocenium analogue **2**[4] and show that the strength of the hydrogen bonding interaction can be controlled by changing the oxidation state of the metal in each receptor.



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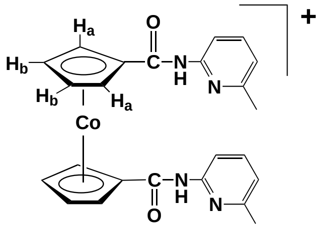

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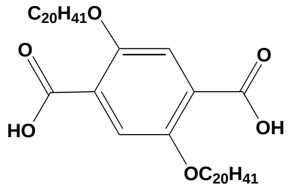

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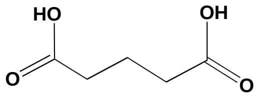

GA

As found previously with **1**[5] and with other organic[6] and inorganic[7] bis-amidopyridine receptors, **2** binds dicarboxylic acids in organic solvents. ^1H NMR studies in $CDCl_3$/[D_6]DMSO (0.5%) revealed downfield shifts in the amide and Cp proton resonances of **2** upon addition of excess glutaric acid (GA). A titration of the H_a proton resonance against molar equivalents of GA revealed a complex stoi-

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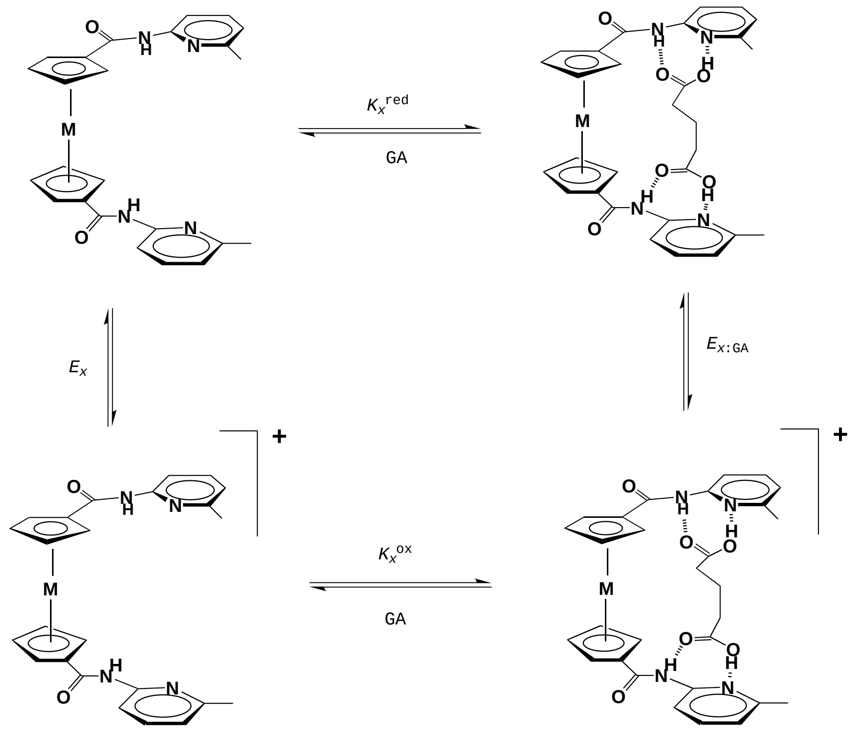
Supporting information for this article is available on the WWW under http://www.wiley-vch.de/home/angewandte/ or from the author.

chiometry of 1:1 (downfield shift in H_a protons upon complexation (ppm): **1**, +0.36; **2**, +0.19). The resulting binding constants (298 K), evaluated by EQNMR[8] for a monomeric complex, (Scheme 1) show that the interaction of GA with **2** in $CDCl_3$/[D_6]DMSO(0.5%) is approximately twenty times stronger than that with **1** ($K_2^{ox} = 98000\,\text{M}^{-1} \pm 10\%$ where $K_2^{ox} = [\mathbf{2}{:}GA]/[\mathbf{2}][GA]$; $K_1^{red} = 4600\,\text{M}^{-1} \pm 5\%$ where $K_1^{red} = [\mathbf{1}{:}GA]/[\mathbf{1}][GA]$). A ^1H NMR competition experiment was carried out to corroborate these results. Figure 1 depicts the Cp regions of **1** and **2** in $CDCl_3$/[D_6]DMSO (0.5%) (each 0.80 mM) and the effect of adding one (Figure 1b) and five molar equivalents (Figure 1c) of GA to the solution. Clearly the first addition (Figure 1b) shifts the Cp signals for **2** downfield (ca. 70% complexation), whereas those for **1** move only slightly (ca. 11% complexation). The binding constant K [Eq. (1)] evaluated from this data[9] is virtually the same as that obtained by dividing K_2^{ox} by K_1^{red}. Only upon the addition of an excess of guest (Figure 1c) does **1** bind GA to any great extent.

$$\mathbf{1}{:}GA + \mathbf{2} \overset{K}{\rightleftharpoons} \mathbf{2}{:}GA + \mathbf{1} \qquad (1)$$



Scheme 1. Square scheme showing the relationship between the binding constants and the electrode potentials for receptors **1** (M = Fe, x = 1) and **2** (M = Co, x = 2).

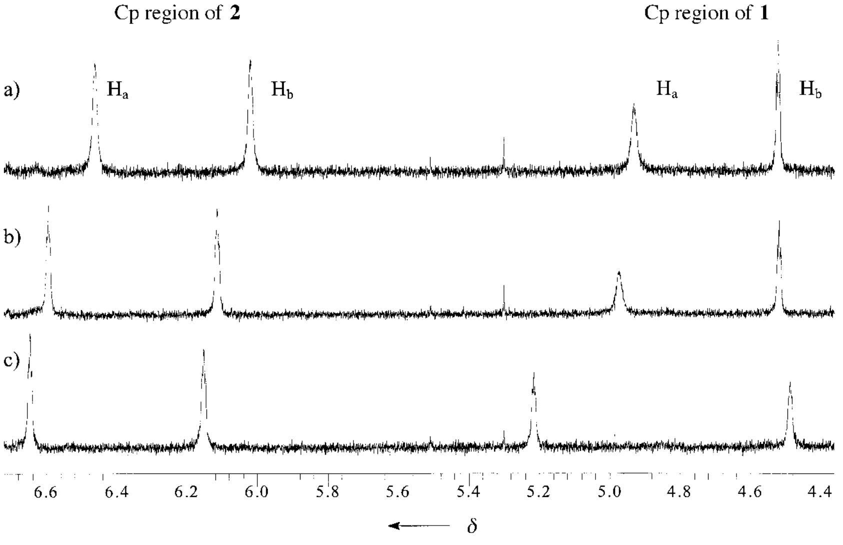


Figure 1. ^1H NMR spectra of an equimolar mixture of **1** and **2** (Cp region) in $CDCl_3$/[D_6]DMSO (0.5%) with a) no GA; b) 1 molar equivalent of GA; c) 5 molar equivalents of GA.

The X-ray structures of complexes [**1**:GA]$_2$ (Figure 2) and [**2**:GA]$_2$ (Figure 3) reveal dimeric metallocenes, formed by intermolecular bonding through two GA units. The metallocene receptors form symmetric hydrogen bonds with the carboxylic acid groups on both GA molecules, where as expected, the amide protons associate with the carbonyl moiety and the pyridyl nitrogen atoms with the alcohol group. The functional groups on each metallocene are eclipsed in [**2**:GA]$_2$ and staggered in the 1,2-positions in [**1**:GA]$_2$. Interestingly, whereas the hydrogen bonds involving the pyridyl nitrogen atoms are of a similar length in both complexes, the amide hydrogen bonds in the cobalt complex are shorter ($N{-}H \cdots O_{av}/O{-}H \cdots N_{av}$ 2.970(6)/2.662(3) and 2.897(4)/2.656(4) Å for [**1**:GA]$_2$ and [**2**:GA]$_2$, respectively). In addition, the amide N–H bond lengths within these hydrogen bonds in the cobalt complex are longer than those in the iron complex (0.945 and 0.880 Å, respectively). It is likely that both complexes are present as 2:2 dimers in the solid state due to favorable packing interactions, since there was no evidence for their formation in solution at millimolar concentrations. Solubility problems precluded vapor pressure osmometry (VPO) measurements but a 1:1 complex with **2**, expected on entropic (i.e. chelate formation) grounds and found for related complexes,[6, 7] was shown to be exclusively present under ESMS conditions (see Supporting Information). Furthermore, NMR studies revealed that the introduction of a rigid spacer group to the diacid guest (compound **3**) to preclude monomer formation due to steric hinderance and favor dimer formation resulted in only a very weak binding interaction.[10] There was no evidence for the formation of mixed metallocene complexes from the competition studies.

Cyclic voltammetry studies[11] in CH_2Cl_2 (0.5% DMSO) revealed identical negative shifts in the reversible Fe^{III}/Fe^{II} and Co^{III}/Co^{II} couples of the receptors (Scheme 1) upon the addition of excess GA (E

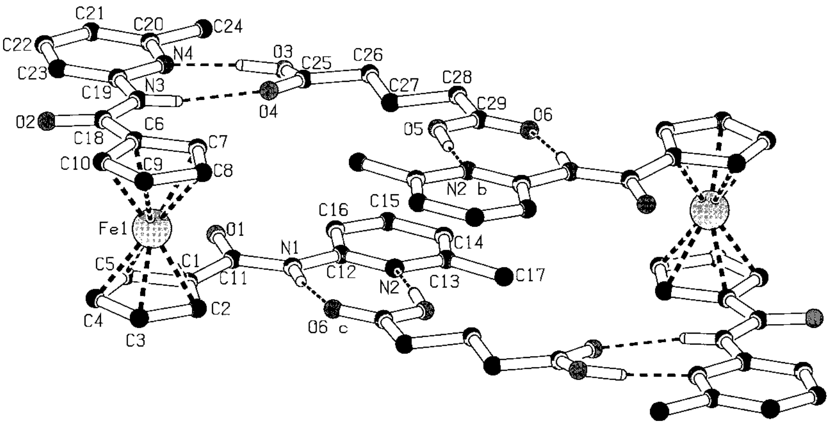


Figure 2. X-ray structure of the dimer $[\mathbf{1}{:}\mathrm{GA}]_2$. Selected bond lengths [Å] and angles [°]: C1-C11 1.478(10), C11-N1 1.373(8), N1-C12 1.402(8), C6-C18 1.505(9), C18-N3 1.350(8), N3-C19 1.402(8); C1-C11-N1 117.4(7), C11-N1-C12 126.4(6), C6-C18-N3 116.9(7), C18-N3-C19 126.1(6).

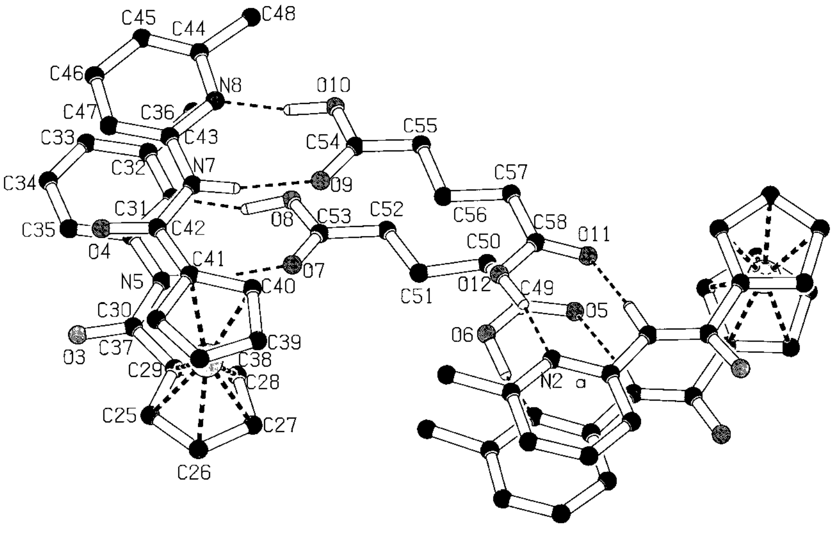


Figure 3. X-ray structure of $[\mathbf{2}{:}\mathrm{GA}]_2$ (PF_6^- counteranions omitted and only one independent molecule shown for clarity). Selected bond lengths [Å] and angles [°]: C29-C30 1.495(10), C30-N5 1.382(9), N5-C31 1.428(9), C41-C42 1.495(11), C42-N7 1.385(9), N7-C43 1.416(9); C29-C30-N5 114.5(8), C30-N5-C31 124.3(8), C41-C42-N7 115.9(8), C42-N7-C43 124.2(7).

(±10 mV) vs. Fc^+/Fc internal couple: E_1 +0.45 V, $E_{1:\mathrm{GA}}$ +0.36 V; E_2 −0.83 V; $E_{2:\mathrm{GA}}$ −0.92 V; ΔE: **1**, −90 mV; **2**, −90 mV). Since the binding constant between GA and each receptor in one redox state is known, the binding constant in the other redox state, as shown in the square scheme (Scheme 1), can be evaluated[1b] by using Equation (2) ($x = \mathbf{1}$ or **2**). Clearly the binding constants with GA are similar for

$$\frac{K_x^{\mathrm{ox}}}{K_x^{\mathrm{red}}} = \exp\left[\frac{-nF(\Delta E)}{RT}\right] \qquad (2)$$

either of these metallocene receptors in their reduced (ferrocene, $\log K_1^{\mathrm{red}} = 3.66 \pm 0.02$; cobaltocene, $\log K_2^{\mathrm{red}} = 3.45 \pm 0.2$) or oxidized forms (ferrocenium $\log K_1^{\mathrm{ox}} = 5.2 \pm 0.2$; cobaltocenium $\log K_2^{\mathrm{ox}} = 4.99\,\mathrm{M}^{-1} \pm 0.04$). Therefore, the factor responsible for this redox-switched effect must be the introduction of positive charge at the metallocene center, which, in pulling electron density away from the amide units, increases the acidity of the amide protons and makes hydrogen bonding stronger. The N−H stretching frequency for each receptor in CH_3CN (**1**: 3354 cm^{-1}; **2**: 3178 cm^{-1}) and the bond lengths from the X-ray data are consistent with this explanation. In conclusion, we have shown how the ratio of binding strengths between two hydrogen-bonded complexes can be *reversibly inverted* by switching the charge of these receptors on or off.

Experimental Section

X-ray studies: $[\mathbf{1}\mathrm{GA}]_2$; crystals from slow diffusion of diethyl ether into CH_2Cl_2, $C_{24}H_{22}N_4O_2Fe \cdot C_5H_8O_4 \cdot 0.5(CH_3CH_2OH)$, $M_r = 609.45$; crystal dimensions $0.2 \times 0.16 \times 0.12$ mm^3; monoclinic; space group $P2_1/n$; $a = 15.617(3)$, $b = 9.222(2)$, $c = 21.185(4)$ Å, $\beta = 103.43(3)°$, $Z = 4$, $V = 2967.6(10)$ Å^3, $\rho_{\mathrm{calcd}} = 1.364$ mg m^{-3}, $T = 150(2)$ K; θ range = 1.98–24.96°; 11075 measured reflections merged to 4357 unique reflections ($R_{\mathrm{int}} = 0.1123$); $R_1 = 0.055$ and 0.1455 and $wR_2 = 0.1113$ and 0.1287 for observed data ($I > 2\sigma(I)$) and for all data, respectively; $\rho_{\max}/\rho_{\min} = 0.820$ and −0.319 e Å^{-3}. $[\mathbf{2}{:}\mathrm{GA}]_2$; crystals from slow diffusion of diethyl ether into CH_2Cl_2, $C_{24}H_{22}N_4O_2Co \cdot C_5H_8O_4 \cdot PF_6$, $M_r = 734.47$; crystal dimensions $0.3 \times 0.18 \times 0.09$ mm^3; triclinic; space group $P\bar{1}$; $a = 11.575(2)$, $b = 12.682(2)$, $c = 22.171(3)$ Å, $\alpha = 72.402(12)$, $\beta = 80.474(12)$, $\gamma = 87.362(11)°$, $Z = 2$, $V = 3059.3(11)$ Å^3, $\rho_{\mathrm{calcd}} = 1.595$ mg m^{-3}, $T = 293(2)$ K; θ range = 1.78–25.05°; 11985 measured reflections merged to 7893 unique ($R_{\mathrm{int}} = 0.0796$); $R_1 = 0.0514$ and 0.1175 and $wR_2 = 0.0919$ and 0.1047 for observed data ($I > 2\sigma(I)$) and for all data, respectively; $\rho_{\max}/\rho_{\min} = 0.492$ and −0.338 e Å^{-3}. Both datasets were measured on a Nonius FAST TV area detector at the window of a Nonius FR591 rotating anode, $Mo_{K\alpha}$ radiation ($\lambda = 0.71073$ Å); absorption correction applied using the RefDelf method of DIFABS; structures solved by Patterson methods using SHELXS-86 and refined with SHELXL-93. Non-hydrogen atoms anisotropic, hydrogen atoms isotropic riding model. Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC-142347 ($[\mathbf{1}{:}\mathrm{GA}]_2$) and CCDC-142348 ($[\mathbf{2}{:}\mathrm{GA}]_2$). Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: (+44)1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

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[1] a) P. R. Ashton, V. Balzani, J. Becher, A. Credi, M. C. T. Fyfe, G. Mattersteig, S. Menzer, M. B. Nielsen, F. C. Raymo, J. F. Stoddart, M. Venturi, D. J. Williams, *J. Am. Chem. Soc.* **1999**, *121*, 3951, and references therein; b) A. Niemz, V. M. Rotello, *Acc. Chem. Res.* **1999**, *32*, 44, and references therein.

[2] a) C. M. Cardona, S. Mendoza, A. E. Kaifer, *Chem. Soc. Rev.* **2000**, *29*, 37, and references therein; b) A. N. J. Moore, D. D. M. Wayner, *Can. J. Chem.* **1999**, *77*, 681.

[3] N. Suzuki, T. Higuchi, Y. Urano, K. Kikuchi, H. Uekusa, Y. Ohashi, T. Uchida, T. Kitagawa, T. Nagano, *J. Am. Chem. Soc.* **1999**, *121*, 11571, and references therein; A. Ivancich, K. Artz, J. C. Williams, J. P. Allen, T. A. Mattioli, *Biochemistry* **1998**, *37*, 11812.

[4] The counter anion is PF_6^-. For a similar synthetic procedure, see: M. D. Rausch, J. E. Sheats, *J. Org. Chem.* **1970**, *35*, 3245.

[5] J. D. Carr, L. Lambert, D. E. Hibbs, M. B. Hursthouse, K. M. A. Malik, J. H. R. Tucker, *Chem. Commun.* **1997**, 1649.

[6] F. Garcia-Tellado, S. Goswami, S. K. Chang, S. J. Geib, A. D. Hamilton, *J. Am. Chem. Soc.* **1990**, *112*, 7393; S. P. Lustenberger, E. Martinborough, T. M. Denti, F. Diederich, *J. Chem. Soc. Perkin Trans. 2* **1998**, 747; S. Goswami, K. Ghosh, S. Dasgupta, *J. Org. Chem.* **2000**, *65*, 1907.

[7] M. S. Goodman, A. D. Hamilton, J. Weiss, *J. Am. Chem. Soc.* **1995**, *117*, 8447; I. Prévot-Halter, T. J. Smith, J. Weiss, *J. Org. Chem.* **1997**, *62*, 2186.

[8] M. J. Hynes, *J. Chem. Soc. Dalton Trans.* **1993**, 311.

[9] After the addition of one equivalent of GA, [**2**:GA]/[**2**] = (70 ± 2)/(30 ± 2) and [**1**]/[**1**:GA] = (89 ± 2)/(11 ± 2), K = [**2**:GA][**1**]/[**2**][**1**:GA] = 19 ± 5.

[10] A ^{1}H NMR study revealed that the amide and Cp protons of **1** (1 mM in CDCl$_3$/[D$_6$]DMSO (0.5 %)) underwent very small downfield shifts upon the addition of excess **3** (e.g. H$_a$, +0.08 ppm) with 50 % complexation only achieved after the addition of six molar equivalents of diacid.

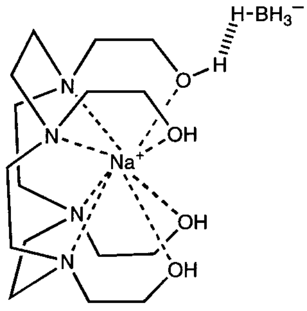
[11] For previous cyclic voltammetry studies with **1** and for experimental conditions, see reference [5].

Toward Crystalline Covalent Solids: Crystal-to-Crystal Dihydrogen to Covalent Bonding Transformation in NaBH$_4$ · THEC**

Radu Custelcean,* Mircea Vlassa, and
James E. Jackson*

The hydridic-to-protonic interaction, or dihydrogen bonding, between negatively charged hydrogen atoms of M–H (M = Al, B, Ga, Ir, Mo, Mn, Os, Re, Ru, W) bonds and conventional proton donors has been extensively studied since 1994.[1] With characteristics similar to those found in classical hydrogen bonding, this unconventional interaction can influence reactivity and stereoselectivity in solution.[2] In the solid state, dihydrogen bonds have the ability to direct crystal packing, thus finding utility in supramolecular synthesis.[3] Along this line, we have employed O–H ··· H–B hydrogen bonds in the construction of novel one-, two-, and three-dimensional extended structures with various topologies.[4] More interestingly, some of these systems can react topochemically in the solid state, releasing H$_2$ and exchanging the weak O–H ··· H–B interactions for strong B–O covalent bonds, to form ordered, extended covalent materials.[4] However, due to the cumulative shrinkage of the B–O distances during decomposition, these topochemically assembled solids have shown poor crystallinity. In 1998 we suggested two strategies to circumvent this problem: a) design of cations to form closed loops in coordination with hydride-bearing anions, in which case the lattice distortion accompanying decomposition would not be cumulative, and b) selection of globular cations large enough that their close packing determines the lattice parameters, with the hydridic anions fitting into the interstitial holes, in which bond formation via flexible arms would induce minimal change in the unit cell.[4a] We now describe a dihydrogen-bonded system that satisfies both of these geometrical criteria, leading as a result to a crystalline covalent product, in a crystal-to-crystal thermal decomposition.

N,N′,N″,N‴-tetrakis-(2-hydroxyethyl)cyclen (THEC) and NaBH$_4$ form a 1:1 complex (**1**), which precipitates as a white crystalline solid from 2-propanol.[5]



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Single crystals suitable for X-ray crystallography were obtained by slow diffusion of diethyl ether into a solution of **1** in acetonitrile. The crystal structure is depicted in Figure 1.[6] The THEC adopts a conformation with all hydroxyethyl arms oriented toward the same face of the azacrown ring, as observed in previously reported metal complexes containing this ligand.[7] The nitrogen and oxygen atoms are thus organized in a pseudo-cubic geometry, encapsulating the octacoordinated Na cation. The Na$^+$THEC units have thus the appropriate geometry for the formation of the desired closed-looped dihydrogen-bonded assembly. Indeed, these cations self-assemble into D_2-symmetrical dimers, held together by four conventional O(2)–H ··· O(1) hydrogen bonds, complemented by four orthogonal O(1)–H ··· H–B proton-hydride interactions involving the borohydride anions (Figure 1 a). There is no hydrogen bonding interconnecting the dimers, which are packed into two-dimensional layers (Figure 1 b). The layers are stacked in a parallel fashion, thus creating one-dimensional channels along the *a* axis, in which the BH$_4^-$ ions reside.

The association in closed loops, as well as the packing mode of the large globular [Na$_2$(THEC)$_2$]$^{2+}$ ions, appear to fulfill the two geometrical requirements that we predicted should favor the transfer of crystallinity from dihydrogen- to covalent-bonded networks.[4a] Solid-state decomposition of **1**, induced by heating under an inert atmosphere at 160 °C for 20 h, results in complete elimination of H$_2$, as indicated by the FT-

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