Anion-Induced Motion in a Ferrocene Diamide

Katja Heinze*[a] and Manuela Schlenker[a]

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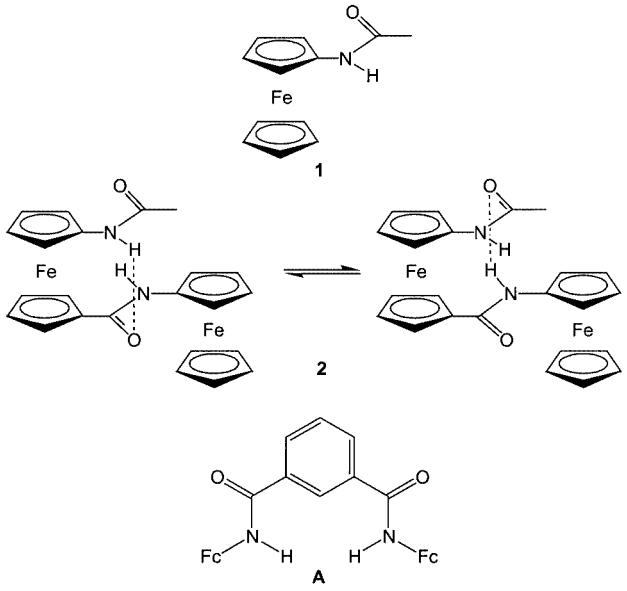
An unsymmetrical diferrocene diamide has been reacted with chloride ions. The anion splits the intramolecular hydrogen bond of the receptor and is coordinated simultaneously by both amide groups of the receptor via hydrogen bonds. Chloride coordination changes the relative angular position of the cyclopentadienyl rings and the potential of the ferrocene/ferricinium redox couple.

Introduction

Control of mechanical motions of single molecules by external stimuli has attracted great attention in relation to biological machines such as muscles and for the development of artificial molecular machines and devices. Various molecular machines have been reported, such as motors, shuttles, switches and tweezers that respond to stimuli such as protons (pH), electrons (redox processes) and light.[1−3] Here we describe an anion-driven molecular hinge where the opening of an intramolecular lock is transformed into an angular motion. Examples of such an interlocking mechanical motion are still rare;[4] most precedent machines, based on rotaxanes or catenanes, operate by individual motions of driving parts.



Scheme 1. Ferrocene amides **1**, **2** and Crabtree's receptor **A**[6] (Fc = ferrocenyl)

Results and Discussion

Recently, we prepared the unsymmetrical diferrocene diamide **2**, which possesses a dynamic intramolecular hydrogen bond in solution (Scheme 1, middle).[5] This dynamic bridge remains intact up to 55 °C, as shown by NMR and IR spectroscopy and corroborated by DFT calculations.[5] The amide protons of **2** do not undergo H/D exchange with D_2O in CH_2Cl_2, underlining this stability. Thus, the hydrogen-bond lock hinders the normally free rotation of the cyclopentadienyl rings of the disubstituted ferrocene.

Conversely, external hydrogen acceptors such as anions bind to amide groups.[7] This could, presumably, affect the internal hydrogen bond. Thus ferrocene amides **1**, which represents "one half" of **2** (Scheme 1), and **2** were treated with chloride ions in the non-coordinating solvent dichloromethane.

Addition of chloride ions as their tetra-*n*-butyl ammonium salts to the receptors **1** and **2** leads to the disappearance of the signal of the "free" NH groups (**1**: 3435 cm^{-1}; **2**: 3430 cm^{-1}) from the IR spectra (Figure 1, left) and a shift of the CO stretching signals to lower energy (Figure 1, right: **1**: 1685 → 1666 cm^{-1}; **2**: 1679/1660 → 1659 cm^{-1}) for both ferrocene amides, indicating that the chloride ions interact with the amide groups. As the strong signals of the CH vibrations of the tetra-*n*-butyl ammonium

[a] Anorganisch-Chemisches Institut der Universität Heidelberg
Im Neuenheimer Feld 270, 69120 Heidelberg, Germany
Fax: (internat.) + 49-(0)6221-545707
E-mail: katja.heinze@urz.uni-heidelberg.de

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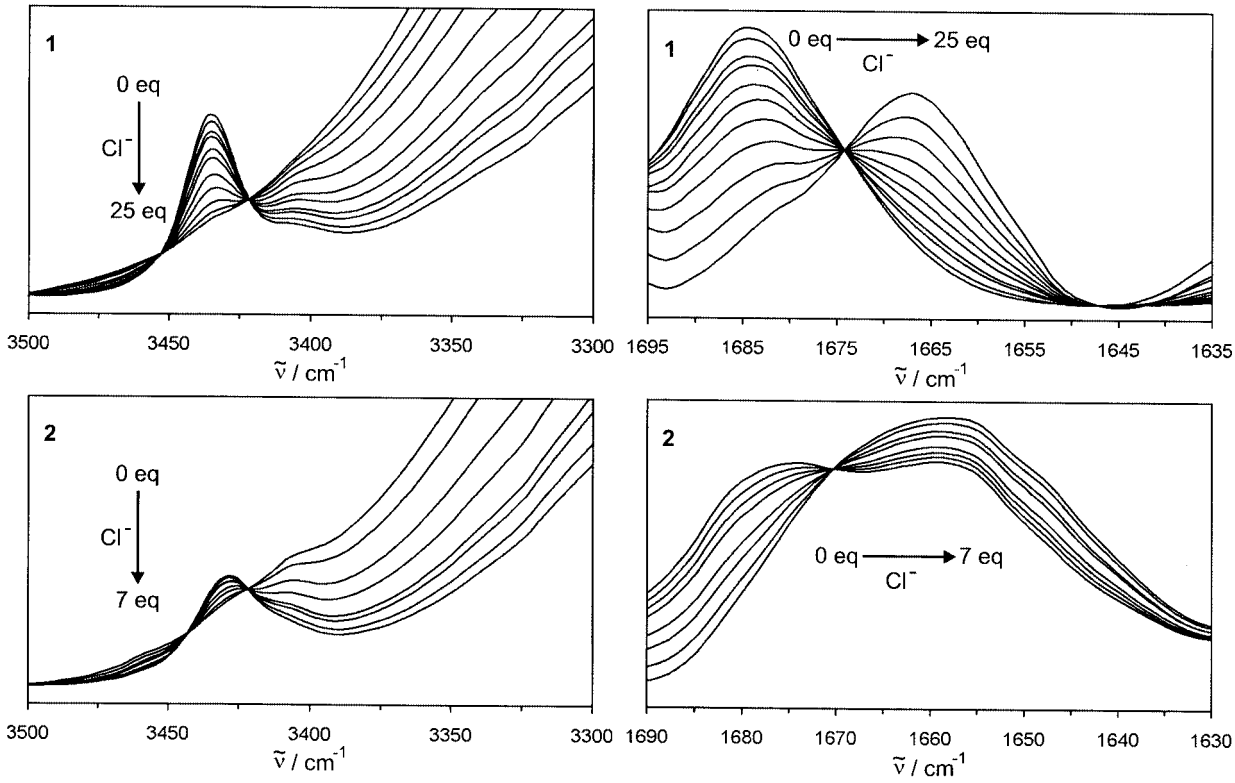


Figure 1. IR spectra of **1** (top) and **2** (bottom) during addition of $(n\text{Bu})_4\text{NCl}$ in CH_2Cl_2 at 300 K (0.0036 M)

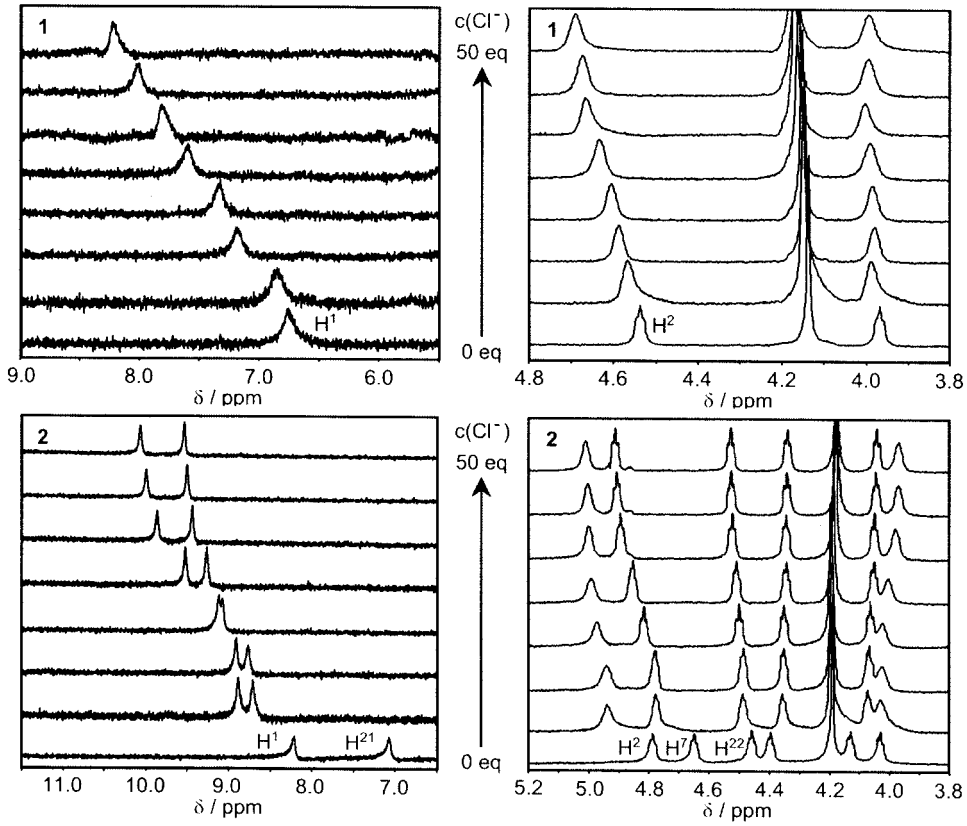


Figure 2. ^{1}H NMR spectra of **1** (top) and **2** (bottom) (NH and Cp-H region) during addition of $(n\text{Bu})_4\text{NCl}$ at 300 K (0.005 M)

cation strongly modify the baseline, integration of the NH stretching vibration signals proved unreliable. However, receptor **1** requires more chloride ions than receptor **2** to reach saturation − as seen qualitatively from the IR spectra (Figure 1).

To obtain deeper insight into the association process proton NMR spectra[8] were recorded during the addition of chloride ions (Figure 2). Several proton signals of the ferrocene amides are shifted significantly to lower field upon increasing chloride concentration. The shift is especially pronounced for signals of the amide protons H^1 and H^{21} and the neighboring cyclopentadienyl protons H^2 ("upper" cyclopentadienyl ring), H^{22} and H^7 ("middle" cyclopentadienyl rings) (see Figure 4 for atom numbering).

Saturation is reached at relative concentrations of approximately 1:50 (**1**:Cl^-) and 1:20 (**2**:Cl^-), respectively (Figure 3), which is in qualitative agreement with the IR data. Thus, diamide **2** has a much larger affinity to chloride ions than monoamide **1**. If the amide groups of **2** behaved independently the amount of anion needed to satisfy both groups of **2** should be about twice that needed for monoamide **1**, i.e. saturation would be expected at a **2**:Cl^- ratio of ca. 1:100. As this is obviously not the case the two amide groups of **2** bind chloride ions in a cooperative way.

Thorough investigation of the CIS (chemically induced shift) values of **2** revealed that the two NH groups, with their neighboring CH groups, display different affinity towards chloride ions, with H^1 and its neighboring H^2 having a stronger affinity than H^{21} and its neighboring H^{22} and H^7 (Figure 3, bottom). This finding is in contrast to observations made for the symmetrical diferrocene diamide **A** prepared by Crabtree[6] (Scheme 1, bottom) as the protons of the two amides of **A** are spectroscopically indistinguishable. The strongly shifted amide protons H^1 and H^{21} and the Cp protons H^2, H^7 and H^{22} allow us to map the sites of receptor **2** where anion coordination takes place (Figure 4). According to Figure 4, the chloride ion can approach the receptor at the "upper" amide group (H^1, H^2), at the "lower" amide group (H^{21}, H^7, H^{22}) or at both NH groups simultaneously in a different conformation of **2**. To prove that both amide groups are accessible for chemical attack, **2** has been reacted with excess sodium amide and

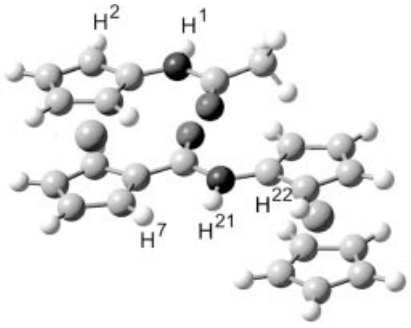


Figure 4. Protons of **2** affected by anion coordination

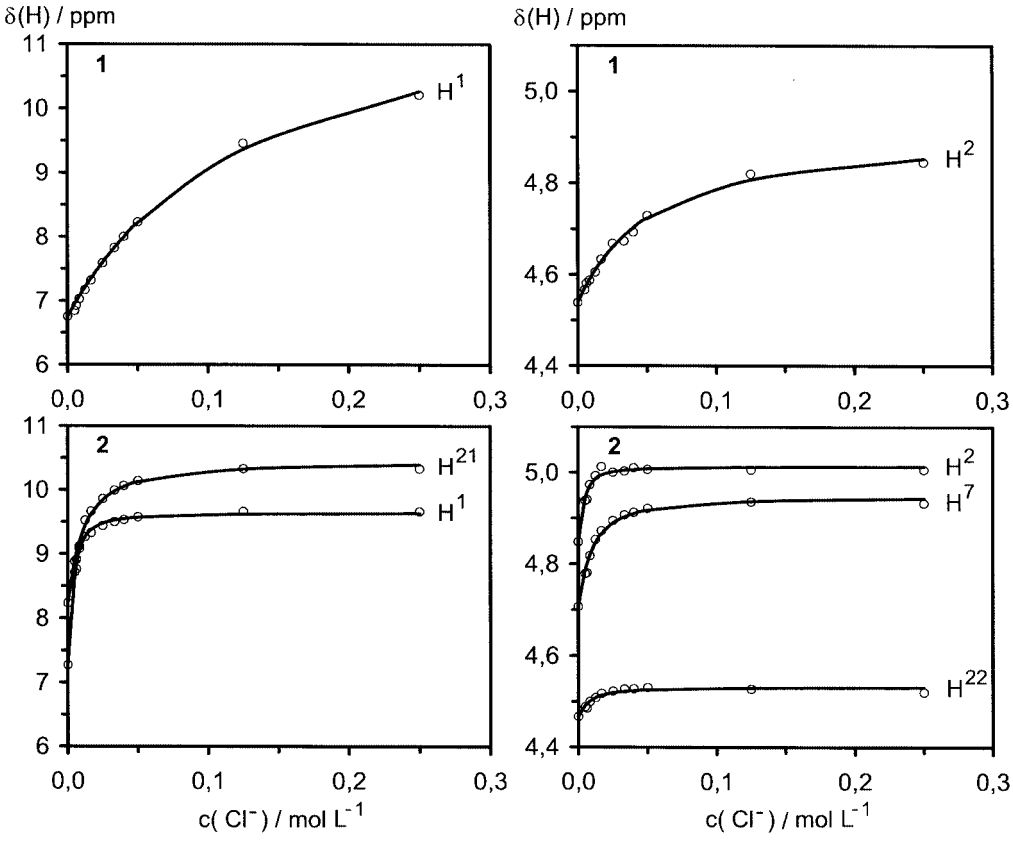


Figure 3. ^1H NMR titration plots of **1** (top) and **2** (bottom) with $(n\text{Bu})_4NCl$ in CD_2Cl_2 at 300 K (0.005 M)

quenched with D_2O. Proton NMR and IR spectra of the final product (see Supporting Information) show that **2** can be deprotonated either at H^1 or at H^{21} with equal probability.[9] Thus, sterically, H^1 and H^{21} are equally accessible.

The much stronger binding capability of **2** as compared to that of **1** is certainly due to a chelate effect, which has numerous precedents in anion recognition chemistry.[10] However, the cooperative binding of the two amide groups is much less pronounced for **2** than for the "unlocked" preorganised receptor **A** (Scheme 1, bottom).[6] Thus, we propose a stepwise mechanism of anion association to **2** (Figure 5).

According to DFT calculations (B3LYP, LanL2DZ; see Supporting Information), the chloride ion can associate to H^1 (Figure 5, structure **I**), to H^2 (Figure 5, structure **II**) or to both amide protons simultaneously (Figure 5, structure **III**).[11] This accords with the NMR spectroscopic data, which show that both amide protons interact with the chloride ion, and with the IR data, which show the disappearance of "free" NH groups upon chloride addition. All three minimum structures **I**−**III** possess two hydrogen bonds: structure **I** displays a hydrogen bond from H^1 to chloride and an intramolecular hydrogen bond from H^2 to O^1; **II** shows a hydrogen bond from H^2 to chloride and an intramolecular hydrogen bond from H^1 to O^2; and in structure **III** the chloride ion is attached to H^1 and H^2 simultaneously, which corresponds to the most stable structure. The loss of the intramolecular NH···O hydrogen bond in **III** explains the lower affinity of **2** compared to the preorganised receptor **A**.[6]

All the structures can be interconverted by hydrogen bond-making/breaking processes and concomitant relative rotation of the cyclopentadienyl rings. As the equilibria could not be frozen out down to 190 K on the NMR time scale (500 MHz), intermolecular[11] low-energy pathways should exist that easily interconvert **I**, **II** and **III** and their respective enantiomers.

For the lowest energy structure **III** the two cyclopentadienyl rings of the 1,1′-disubstituted ferrocene are rotated against each other by 95°, which is about twice the angle calculated for a light-driven ferrocene-based "molecular scissor" (49°).[4]

The native "locked" state of **2**, i.e. the intramolecular hydrogen bond, can be restored by removal of the chloride ions through the addition of excess thallium cations.[12] Angular motion of the cyclopentadienyl rings of **2** can thus be triggered by the presence or absence of chloride ions (Scheme 2, a). Thus the anion-based system presented resembles Lehn's cation-induced dynamic chemical device based on a *transoid/cisoid* rearrangement of terpyridines (Scheme 2, b).[3]

In addition to the angular motion induced by anion binding, the ferrocene moieties provide the electrochemical response expected for amide substituted ferrocenes.[10] Figure 6 shows the cyclic voltammograms of receptors **1** and **2** during the addition of chloride ions. For receptor **2**, the second oxidation becomes irreversible at higher chloride concentrations, probably due to the coordination of another anion to the charged receptor.

The anion-induced cathodic shift of the ferrocene/ferricinium oxidation wave is linear up to two equivalents of chloride ions for monoamide **1** (Figure 7). Due to the larger anion affinity of **2**, saturation is reached at 1.2 equivalents of chloride (Figure 7). As the maximum cathodic shifts $\Delta E_{1/2}$ are equal for both amidoferrocenes (30 mV within the linear range[13]), the slope of the $\Delta E_{1/2}$ vs. $[Cl^-]$ plot,

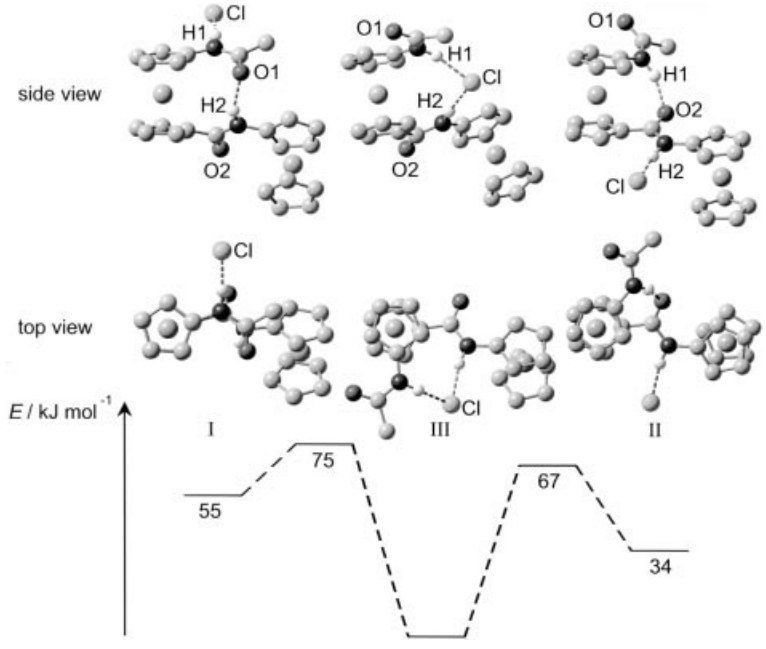
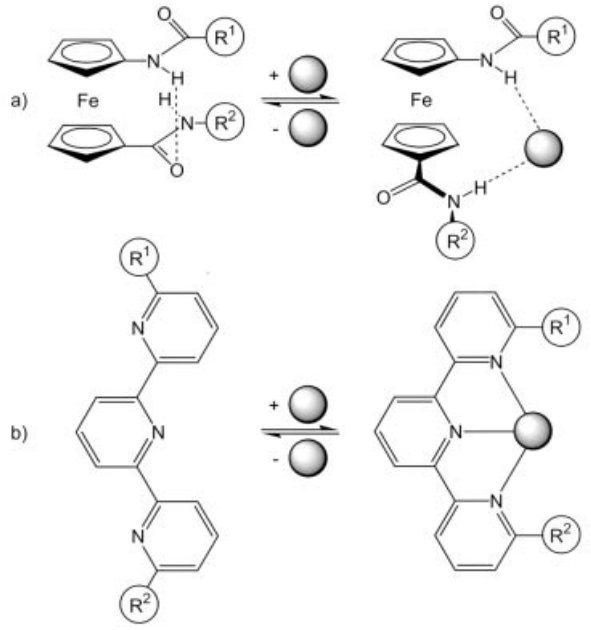


Figure 5. DFT calculated minimum structures **I**−**III** for chloride association to **2** (C−H protons not shown)



Scheme 2. (a) $R^1 = CH_3$, R^2 = ferrocenyl, grey circle: chloride anion; (b) $R^1 = R^2$ = pyrenyl, grey circle: zinc cation

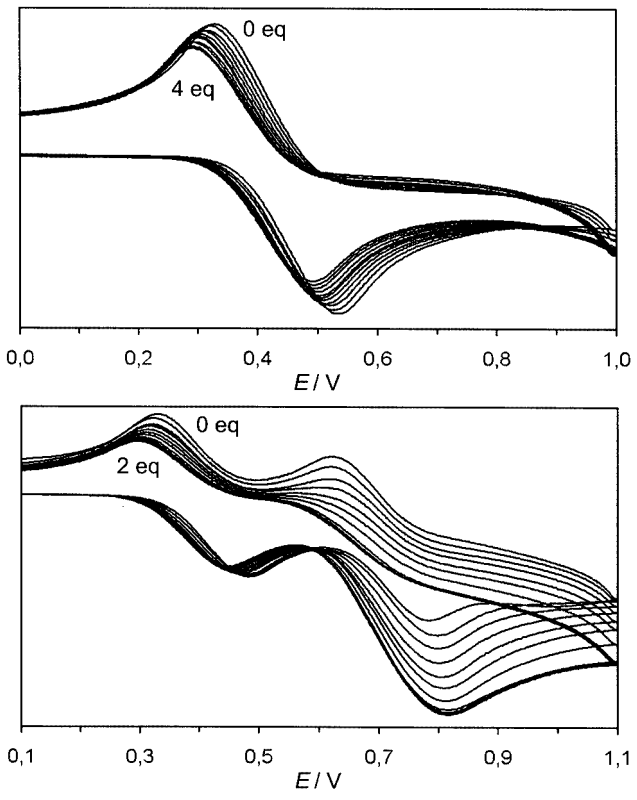


Figure 6. Cyclic voltammograms of **1** (top) and **2** (bottom) in the presence of $(n\text{Bu})_4\text{NCl}$ in 0.1 M $(n\text{Bu})_4\text{NBF}_4/CH_2Cl_2$ vs. SCE at 300 K (scan rate 200 mV s^{-1})

and thus the sensitivity as anion sensor, is enhanced for receptor **2** relative to **1** (Figure 7).

Consequently, **2** is a "dual-functional molecular machine", giving a mechanical and an electrochemical output upon a simple chemical input. Incorporation of this flexible

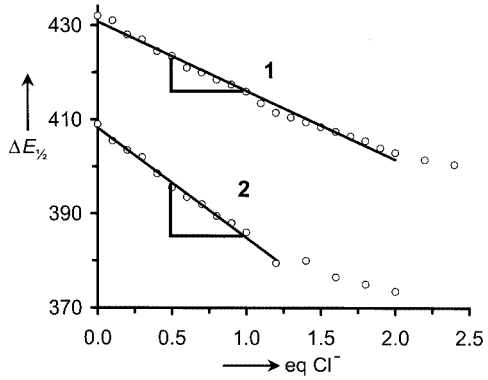


Figure 7. ΔE vs. eq Cl^- plots for receptors **1** and **2**

but controllable building block into larger arrays, e.g. in the backbone of peptides (R^1, R^2 = peptides in Scheme 2, a), or between fluorescent reporter groups may lead to novel hybrid (bio)materials with unconventional dynamics and (redox) functions.[14–16] Work in this direction is currently in progress.

Experimental Section

Compounds **1** and **2** were prepared by published procedures.[5] NMR: Bruker Avance DPX 200 at 200.15 MHz (^1H) at 303 K; chemical shifts (δ) in ppm with respect to residual solvent peaks as internal standard: CD_2Cl_2 (^1H: δ = 5.32 ppm). IR spectra were recorded on a BioRad Excalibur FTS 3000 spectrometer using CaF_2 cells in CH_2Cl_2. Cyclic voltammetry was performed using a glassy carbon electrode, a platinum electrode and a SCE electrode, 10^{-3} M in 0.1 M $n\text{Bu}_4\text{NBF}_4/CH_2Cl_2$; potentials are given relative to SCE. Computational method: density functional calculations were carried out with the Gaussian03/DFT[17] series of programs. B3LYP formulation of density functional theory was used employing the LanL2DZ basis set.[17] Harmonic vibrational frequencies and infrared intensities were calculated by numerical second derivatives using analytically calculated first derivatives. All points were characterised as minima or first-order saddle points by frequency analysis.

Acknowledgments

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[9] In the IR spectrum deuterated **2** shows an ND stretching absorption at 2451 cm^{-1} and an NH stretching absorption at 3316−3327 cm^{-1} with equal intensity. In the ^1H NMR spectrum of deuterated **2**, H^1 and H^{21} signals display only half of the original intensity. See Supporting Information.

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[11] Job Plots reveal that the receptor:chloride binding stoichiometry is 2:1 for both complexes (see Supporting Information), showing that the chloride ion is associated to two receptor molecules. This stoichiometry does not affect the dynamic behavior of the system as all calculated minimum structures (**I**−**III**) with 1:1 stoichiometry can form the corresponding 2:1 complexes. The 2:1 stoichiometry and the narrow solubility window of **1** and **2** prevented the determination of 2:1 binding constants $K^{21} = [(\mathbf{1})_2Cl^-]/[\mathbf{1}]^2[Cl^-]$ and $K^{21} = [(\mathbf{2})_2Cl^-]/[\mathbf{2}]^2[Cl^-]$, respectively. This prevented direct comparison with literature data on 1:1 binding constants of receptor/anion complexes (e.g. refs. 6 and 7). However, NMR spectroscopic data (at 0.005 M concentrations of **1** and **2**) can be fitted to 1:1 binding isotherms, giving $K^{11} = 7.8\ M^{-1}$ (**1**; based on H^1; $R^2 = 0.9976$), $K^{11} = 630\ M^{-1}$ (**2**; based on H^1; $R^2 = 0.9963$) and $K^{11} = 120\ M^{-1}$ (**2**; based on H^{21}; $R^2 = 0.9938$); which can be compared qualitatively to those measured for Fc-CO-NH-*n*Bu ($K^{11} = 4.7\ M^{-1}$ in $CDCl_3$ at 0.01 M[7l]) and for **A** ($K^{11} = 9500\ M^{-1}$ in CD_2Cl_2 at 0.001 M[6]). In addition, 2:1 complexes have been observed between Fc-CO-NH-py and the neutral guest glutaric acid: [11a] J. D. Carr, L. Lambert, D. E. Hibbs, M. B. Hursthouse, K. M. Abdul Malik, J. H. R. Tucker, *Chem. Commun.* **1997**, 1649−1650.

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