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Communication

Helix-Like Receptors for Perrhenate Recognition Forming Hydrogen Bonds with All Four Oxygen Atoms †

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† This article is dedicated to Professor Jonathan Sessler on his 65th birthday.

Abstract: Supramolecular recognition of perrhenate is a challenging task due to therelatively large size and low charge density of this anion. In this work, we design and synthesize a family of helix-like synthetic receptors that can bind perrhenate by forming hydrogen bonds with all four oxygen atoms of the anion. Among the investigated rigid helix-forming subunit derived from 1,1′-ferrocenedicarboxylic acid, 1,3-phenylenediacetic acid and 2,2′-(ethyne-1,2-diyl)dibenzoic acid, the latter one shows the best selectivity for perrhenate recognition. However, the receptor based on 1,1′-ferrocenedicarboxylic acid demonstrates selectivity to bind chloride in a 1:2 fashion. The properties of the receptors are investigated in the acetonitrile solution by using NMR, UV–Vis, and in the solid state by single crystal X-ray analysis.

Keywords: synthetic receptor; host–guest chemistry; anion binding; perrhenate recognition

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1. Introduction

Anions play a significant role in living systems. The design of artificial anion receptors is a challenge in supramolecular chemistry that has received great attention in recent years [1–6], moving from being an entirely fundamental area of supramolecular chemistry to a range of applications. Perrhenate (ReO_4^-) and pertechnetate (TcO_4^-) are considered to be the anions that are among the most "difficult to bind" due to their relatively large size and low charge density [7,8]. These anions are available from $^{99}Mo/^{99m}Tc$ and $^{188}W/^{188}Re$ generators and are widely used in nuclear medicine as a part of diagnostic imaging tools and therapeutic devices [9–11]. ^{99}Tc is mostly produced from nuclear fuel cycles, and it is considered as one of the most hazardous pollutants due to long half-life and high mobility in the environment [12–15]. These radionuclides exist in the generator as the solution containing oxoanions. Thus, it is a challenge to develop synthetic receptors that are capable of capturing these radionuclides in the form of $^{99m}TcO_4^-$ and $^{188}ReO_4^-$ for further utilization. Several approaches have been recently explored to bind or extract the anions in question: the design of synthetic receptors [16–26], fluorescent probes [27,28], and inorganic materials [29–34]. In our recent study, we have elucidated how the nature of the binding sites influence the overall binding affinity of receptors [8]. The studied receptors coordinated only two oxygen atoms of ReO_4^- or TcO_4^- [17,19,22]. One possible approach to achieve greater selectivity and affinity is to design receptors that can coordinate all four oxygen atoms of the tetrahedral anion. Such an approach haas been already implemented for recognition of sulfate and phosphate anions resulting in a highly selective binding [35–42].

Herein, we present a design of helix-like receptors that can form hydrogen bonds with all four oxygen atoms of the perrhenate anion. The design of the receptor consists of a rigid

helix-forming subunit derived from 1,1′-ferrocenedicarboxylic acid, 1,3-phenylenediacetic acid and 2,2′-(ethyne-1,2-diyl)dibenzoic acid (Figure 1). These subunits are equipped with a 2,6-pyridine dicarboxamide moiety connected through p-xylylenediamine spacers, which have been proven in our previous work [8] to generate optimal distance between NH-binding sites. Among three new synthesized receptors, the receptor with a diphenylacetylene helix-forming subunit has demonstrated the best affinity and selectivity for the perrhenate anion.

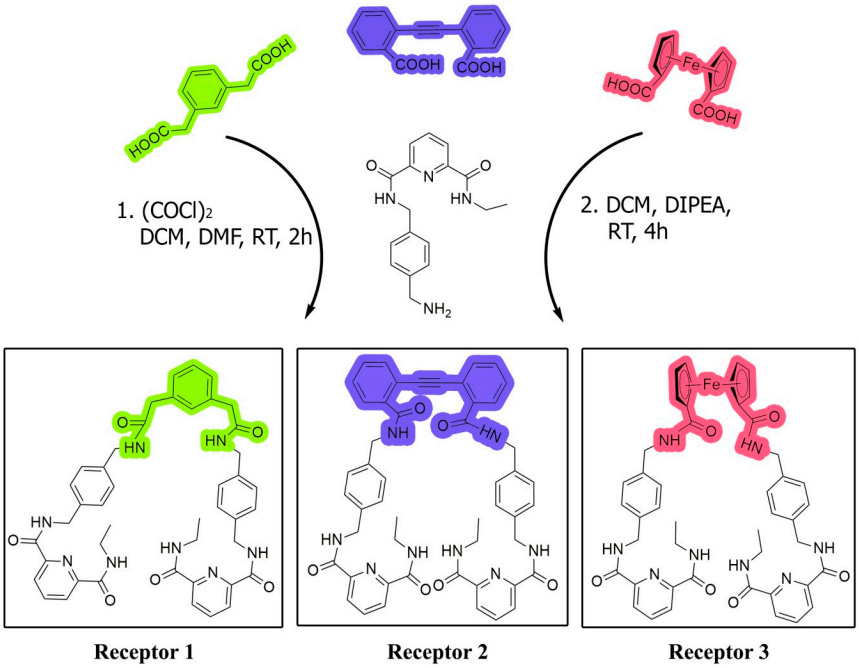

Figure 1. Synthesis of receptors with different helix-forming subunits.

2. Materials and Methods

2.1. General Information

All the solvents were dried according to standard procedures. Crude products were purified by column chromatography on silica gel 60. TLC plates were visualized by exposure to ultraviolet light and/or by exposure to acidic ethanolic solution of ninhydrin followed by heating (<1 min) with a heat gun (~250 °C). NMR Spectra were measured with an ASCEND 600 FT spectrometer (Bruker Corp., Billerica, MA, USA), 600 MHz for ^{1}H NMR and 150.9 MHz for ^{13}C NMR. The chemical shifts are reported in δ [ppm] relative to external standards (solvent residual peak). The solvent used is reported for each spectrum. Mass Spectra: Finnigan MAT TSQ 7000 ESI (Thermo Fisher Scientific Inc., Waltham, MA, USA). Absorption spectra were measured in 1 cm quartz cuvettes with Varian Cary BIO 50 UV/VIS/NIR Spectrometer (Agilent, Santa Clara, CA, USA). The starting compounds were purchased from TCI (Eschborn, Germany), Sigma-Aldrich (Darmstadt, Germany) and Acros Chemicals (Geel, Belgium).

4-(Boc-aminomethyl)benzylamine [43], 6-[(ethylamino)carbonyl]-2-pyridinecarboxylic acid [44], and 2,2′-(ethyne-1,2-diyl)dibenzoic acid [45] were prepared according to the literature procedure. 1,3-Benzenediacetic acid and 1,1′-ferrocenedicarboxylic acid are commercially available products.

2.2. Synthesis of Boc-Protected Amine 4

[(Ethylamino)carbonyl]-2-pyridinecarboxylic acid (3 g, 15.5 mmol) and oxalyl chloride (1.59 mL, 18.5 mmol) were mixed together, followed by addition of two drops of dimethylformamide (DMF) in anhydrous DCM (dichloromethane) (77.5 mL) under nitrogen atmosphere at 0 °C and stirred at room temperature for 2 h. The residue obtained after evaporation of the solvent in the presence of nitrogen atmosphere was diluted with

anhydrous DCM (15 mL) and added to a solution of 4-(boc-aminomethyl)benzylamine (3.7 g, 15.5 mmol), DIPEA (8.1 mL, 46.5 mmol) in DCM (45 mL) at 0 °C and stirred at room temperature. After 4 h, the reaction mixture was quenched by adding cold H_2O (30 mL) and diluted with CH_2Cl_2 (100 mL). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 50 mL). The combined organic layers were washed with brine (50 mL), dried over anhydrous Na_2SO_4, filtered, and the solvent was evaporated under reduced pressure to afford the crude product. The crude product was purified by column chromatography (MeOH:DCM, 5:95) yielding a white solid (5.6 g, 13.5 mmol) with 87% of yield. TLC: *Rf* = 0.4 (MeOH:CH_2Cl_2, 3:97); M.p. 127–129 °C; ^{1}H NMR (600 MHz, DMSO-d_6): δ 9.87 (t, *J* = 6.3 Hz, 1H), 9.42 (t, *J* = 6.1 Hz, 1H), 8.26 (t, *J* = 7.7, 1.4 Hz, 2H), 8.23–8.20 (m, 1H), 7.41 (t, *J* = 6.1 Hz, 1H), 7.33 (d, *J* = 8.0 Hz, 2H), 7.25 (d, *J* = 8.0 Hz, 2H), 4.64 (d, *J* = 6.3 Hz, 2H), 4.14 (d, *J* = 6.1 Hz, 2H), 3.48–3.40 (m, 2H), 1.42 (s, 9H), 1.22 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (151 MHz, DMSO): δ 163.8, 163.2, 156.2, 149.3, 149.0, 139.9, 139.3, 138.1, 127.5, 127.4, 124.7, 124.7, 78.2, 43.6, 42.4, 34.0, 28.7, 15.5. HRMS (ESI): m/z Calc. for $[M + H]^+$: $C_{22}H_{28}N_4O_4$: 413.2183, found 413.2187.

2.3. Receptor 1

To a solution of 1,3-benzenediacetic acid (0.4 g, 2.05 mmol) was added oxalyl chloride (0.43 mL, 5 mmol) and two drops of DMF in anhydrous DCM (12 mL) under nitrogen atmosphere at 0 °C and then stirred at room temperature for 2 h. After 2 h, the mixture was evaporated under reduced pressure. The Boc-amine obtained on the first step (2.06 g, 5 mmol) was diluted in DCM (10 mL) and trifluoroacetic acid (5 mL) was added at once. After the mixture was stirred at room temperature for 1 h, the solvent was evaporated in high vacuum. The residue obtained after evaporation in the presence of nitrogen atmosphere was diluted with anhydrous DCM (3 mL) and added to a solution of 1,3-benzenediacetyl dichloride, DIPEA (1.1 mL, 6 mmol) in anhydrous DCM (5 mL) at 0 °C and stirred at rt. After 4 h, the reaction mixture was quenched by adding cold H_2O (10 mL) and diluted with DCM (40 mL). Layers were separated and the aqueous layer was extracted with DCM (2 × 20 mL). The combined organic layers were washed with brine (20 mL), dried over anhydrous Na_2SO_4, filtered and the solvent was evaporated under reduced pressure. The crude product was purified by column chromatography (MeOH: DCM, 5:95, *Rf* = 0.4) to afford pure product as a white solid (0.87 g, 1.1 mmol) with 54% of yield.; M.p. 127–129 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 9.83 (t, *J* = 6.1 Hz, 2H), 9.37 (t, *J* = 6.1 Hz, 2H), 8.51 (t, *J* = 6.2 Hz, 2H), 8.23–8.15 (m, 6H), 7.28–7.10 (m, 12H), 4.57 (d, *J* = 6.3 Hz, 4H), 4.23 (d, *J* = 6.4 Hz, 4H), 3.04 (s, 2H), 1.16 (m, 7H); ^{13}C NMR (151 MHz, DMSO-d_6) δ 170.5, 163.8, 163.3, 149.3, 149.0, 139.9, 138.5, 138.3, 136.7, 130.1, 128.5, 127.8, 127.54, 124.7, 42.7, 42.4, 34.0, 15.5. HRMS (ESI): m/z Calc. for $[M + H]^+$: $C_{44}H_{47}N_8O_6$: 783.3619, found 783.3623. Anal. Calcd for $C_{44}H_{46}N_8O_6$: C, 67.50; H, 5.92; N, 14.31. Found: C, 67.10; H, 5.97; N, 14.33.

2.4. Receptor 2

To a solution of 2,2′-(ethyne-1,2-diyl)dibenzoic acid (0.53 g, 2.0 mmol) was added oxalyl chloride (0.43 mL, 5 mmol) and two drops of DMF in anhydrous DCM (10 mL) under nitrogen atmosphere at 0 °C and then stirred at rt for 2 h. The solvent was evaporated under reduced pressure. The Boc-amine obtained on the first step (2.06 g, 5 mmol) was diluted in DCM (10 mL) and trifluoroacetic acid (5 mL) was added at once. After the mixture was stirred at room temperature for 1 h, the solvent was evaporated in high vacuum. The residue obtained after evaporation was diluted with anhydrous DCM (3 mL) under nitrogen atmosphere and added to a solution of 2,2′-(ethyne-1,2-diyl)dibenzodicarbonyl chloride, DIPEA (1.1 mL, 6 mmol) in anhydrous DCM (5 mL) at 0 °C were added to the solution and the reaction mixture was stirred at room temperature. After 4 h, the reaction mixture was quenched by adding cold H_2O (20 mL) and diluted with DCM (40 mL). Layers were separated and the aqueous layer was extracted with DCM (2 × 20 mL). The combined organic layers were washed with brine (20 mL), dried over anhydrous Na_2SO_4, filtered and the solvent was evaporated under reduced pressure. The crude product was purified by

column chromatography (MeOH:DCM, 5:95, *Rf* = 0.5) to afford the pure product as a white solid (1.2 g, 1.4 mmol) with 70% of yield.; M.p. 130–135 °C with decomposition; ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.98 (t, *J* = 5.6 Hz, 2H), 8.58 (t, *J* = 5.7 Hz, 2H), 8.28-8.23 (m, 4H), 8.08 (t, *J* = 8.2 Hz, 2H), 7.86 (t, *J* = 5.6 Hz, 2H), 7.80 (d, *J* = 8.5 Hz, 2H), 7.58-7.55 (m, 2H), 7.47 (t, *J* = 7.2 Hz, 2H), 7.42 (t, *J* = 7.2 Hz, 2H), 7.13 (d, *J* = 7.2 Hz, 4H), 7.03 (d, *J* = 7.2 Hz, 4H), 4.50 (d, *J* = 6.8 Hz, 4H), 4.38 (d, *J* = 6.8 Hz, 4H), 3.36-3.31 (m, 4H), 1.12-1.09 (m, 6H); ^{13}C NMR (151 MHz, DMSO-d_6) δ 167.37, 163.81, 163.28, 149.38, 149.06, 139.96, 138.62, 138.50, 138.24, 133.37, 130.33, 129.16, 128.58, 127.81, 127.41, 124.79, 124.72, 120.21, 92.10, 42.97, 42.44, 34.07, 15.58. HRMS (ESI): m/z Calc. for $[M + H]^+$: $C_{50}H_{47}N_8O_6$: 855.3619, found 855.3625. Anal. Calcd for $C_{50}H_{46}N_8O_6$: C, 70.24; H, 5.42; N, 13.11. Found: C, 69.99; H, 5.51; N, 13.32.

2.5. Receptor 3

To a solution of 1,1′-ferrocenedicarboxylic acid (0.55 g, 2.0 mmol) was added oxalyl chloride (0.43 mL, 5 mmol) and two drops of DMF in anhydrous DCM (7.5 mL) under nitrogen atmosphere at 0 °C and then stirred at rt for 3 h. After 3h, the mixture was evaporated under reduced pressure. The Boc-amine obtained on the first step (2.06 g, 5 mmol) was diluted in DCM (10 mL) and trifluoroacetic acid (5 mL) was added at once. After the mixture was stirred at room temperature for 1h, the solvent was evaporated in high vacuum. The residue obtained after evaporation was diluted with anhydrous DCM (3 mL) in the presence of nitrogen atmosphere and added to a solution of 1,1′-ferrocene dicarbonyl chloride, DIPEA (1.1 mL, 6 mmol) in anhydrous DCM (5 mL) at 0 °C and stirred at room temperature. After 4 h, the reaction mixture was quenched by adding cold H_2O (10 mL) and diluted with DCM (40 mL). Layers were separated and the aqueous layer was extracted with DCM (2 × 20 mL). The combined organic layers were washed with brine (20 mL), dried over anhydrous Na_2SO_4, filtered and the solvent was evaporated under reduced pressure. The crude product was purified by column chromatography (MeOH:DCM, 0.1:0.9, R_f = 0.7) to afford the pure product as a brown solid (0,8 g, 0,9 mmol) with 45% of yield.; M.p. 141–145 °C with decomposition; ^{1}H NMR (600 MHz, DMSO-d_6) δ 9.83 (t, *J* = 6.1 Hz, 2H), 9.37 (t, *J* = 6.1 Hz, 2H), 8.40 (t, *J* = 6.2 Hz, 2H), 8.23–8.15 (m, 6H), 7.35–7.16 (m, 8H), 4.73 (broad s, 2H), 4.58 (broad s, 2H), 4.34 (broad s, 2H), 4.24 (broad s, 2H), 1.16–1.09 (m, 6H); ^{13}C NMR (151 MHz, DMSO-d_6) δ 168.92, 163.8, 163.2, 149.3, 149.0, 139.9, 139.1, 138.2, 127.7, 127.4, 124.7, 124.6, 78.2, 72.0, 69.9, 67.4, 65.3, 42.5, 34.0, 15.5. HRMS (ESI): m/z Calc. for $[M + H]^+$: $C_{46}H_{47}FeN_8O_6$: 863.2968, found 863.2967. Anal. Calcd for $C_{46}H_{46}N_8O_6$: C, 64.04; H, 5.37; N, 12.99. Found: C, 63.98; H, 5.51; N, 12.98.

3. Results

Design and Synthesis

As inferred from our previous studies [8], the acylation of p-xylylenediamine leads to the formation of two amide groups, which serve as hydrogen bond donor sites for the coordination of two oxygen atoms of perrhenate or pertechnetate anions. The distance between the amide groups of 7 Å is optimal to achieve binding complementarity between two oxygen atoms of the perrhenate anion and NH-binding sites. We have proposed that the introduction of a helix-forming subunit together with additional two binding sites would allow us to bind all four oxygen atoms of the perrhenate anion. Recent analysis of the literature on helical anion foldamers shows that this kind of synthetic receptors demonstrates high selectivity even in an aqueous medium [46]. Preliminary quantum chemical modeling of the receptor structures revealed that dicarboxamide derivatives of ferrocene, m-xylylene, and diphenylacetylene are promising helix-forming subunits. They are symmetrical and, in certain conformation, can reach the distance of 7 Å between two attached amide groups. Ferrocene and diphenylacetylene are the most rigid subunits. However, the latter already provides the required distance between amide groups (NH-NH distance), while in ferrocene, the cyclopentyl rings should be rotated in different directions to achieve this distance.

The synthesis of three receptors was accomplished starting with 6-(ethylcarbamoyl) pyridine-2-carboxylic acid [44], which was further attached to a mono-Boc protected p-xylylenediamine via the reaction between acid chloride and amine. The building block **4** was obtained after deprotection with trifluoroacetic acid. The target receptors **1**, **2**, and **3** were formed by amide-bond formation reaction between **4** and corresponding diacids in moderate yields (54%, 70%, and 45%, respectively, Figure 2).

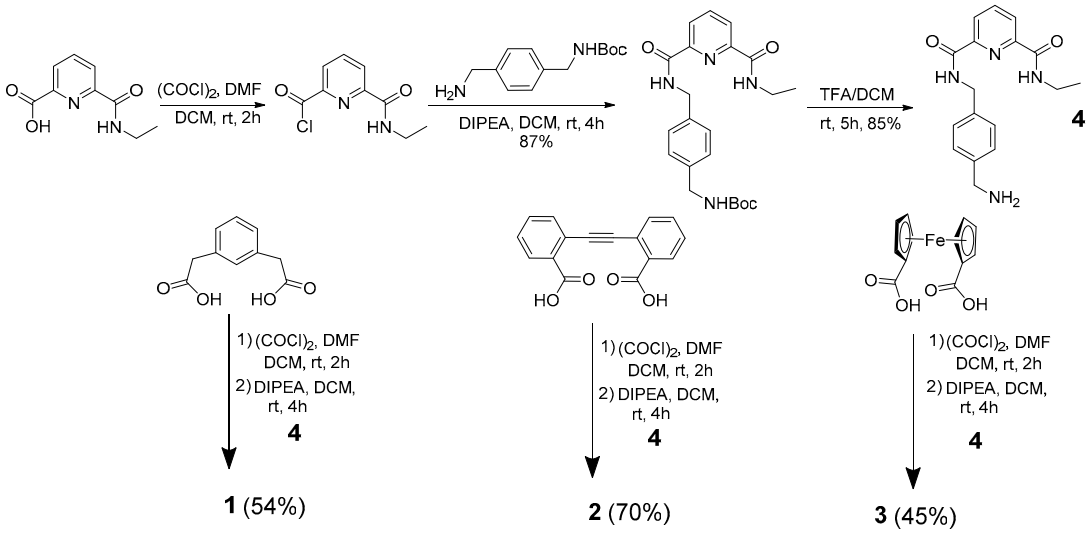

Figure 2. Synthetic route to receptors **1**, **2**, and **3**.

According to the single crystal X-ray analysis of free receptor **2**, it has a conformation with two arms looking in different directions. In the crystal structure, the molecules of **2** interact with each other though hydrogen bonds formed between the pyridine NH binding sites and the carbonyl oxygen atoms of the neighboring molecule (Figure 3). Such a network is not favorable for the interaction with anions. Therefore, we carried out the dilution experiment with the help of UV–Vis spectroscopy. The absorbance of **2** has a linear relationship along the concentrations range 10^{-6}–10^{-4} M in a CH_3CN solution containing 8% of $CHCl_3$ (see Figure S11 in the Supplementary Materials).

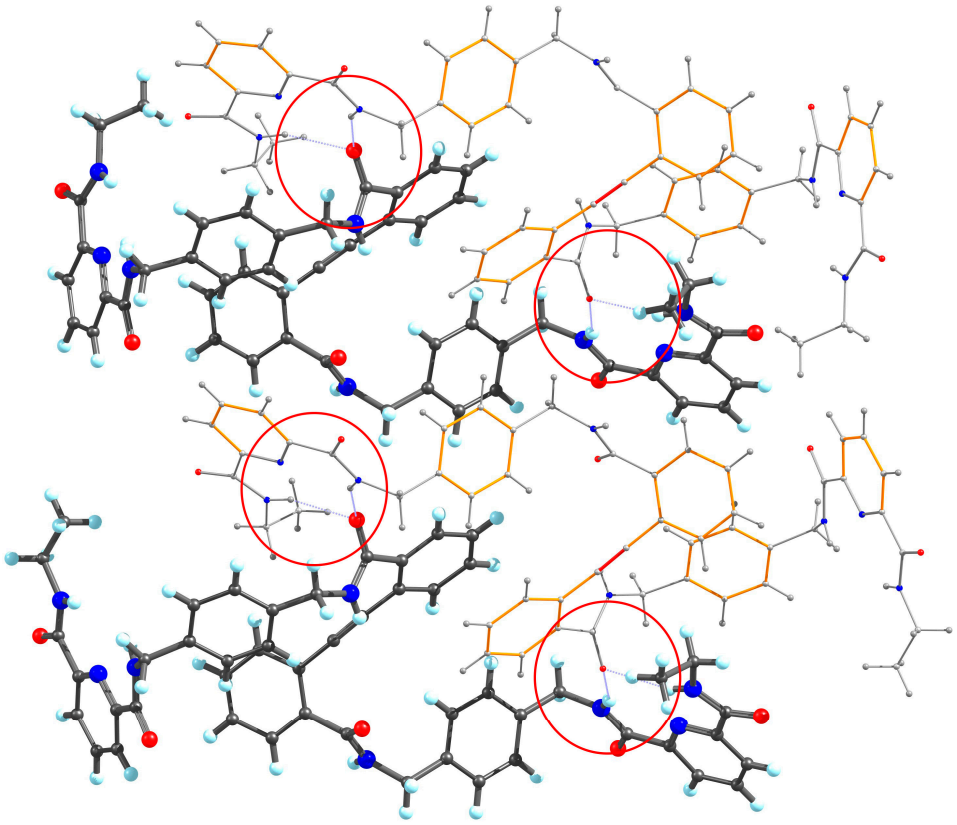

Figure 3. Molecular structure of receptor **2** according to the single crystal X-ray analysis; the hydrogen bonding interactions between molecules in the crystal lattice marked with red circles. Average distance and torsion angle of hydrogen bonds are 2.92 Å and 156°, respectively.

4. Discussion

4.1. Anion Binding Studies

NMR-titration experiments were conducted to determine the binding constants and selectivity of receptors for anions. The tested anions include halides, hydrogen sulfate as a hydrophilic anion, and perchlorate as a representative of an anion with low surface-charge density. Pertechnetate has the same geometrical parameters as those of perrhenate and thus we studied only non-radioactive perrhenate. Analysis of the NMR data reveals that all N-H binding sites participate in the interaction with the investigated anions. The anions with low charge-density ratio such as perrhenate, iodide, and perchlorate induce smaller proton shifts than those observed in titrations with chloride and sulfate. The fitting of the obtained titration curves by the HypNMR program [47] supports a major 1:1 binding stoichiometry. According to the calculated binding constants (Table 1), receptor **2** demonstrates the best affinity (8300 M^{-1}) and 10-fold selectivity for perrhenate as compared to binding constants with other anions. This fact supports our suggestion that the most rigid helix-forming subunit with an appropriate NH–NH distance has the best selectivity. Receptor **3** also binds anions with affinities of 10^3 M^{-1} but shows a preference to bind chloride. Receptor **1** showed lower selectivity than that of receptors **2** and **3**. Presumably, receptor **1** has a higher conformational freedom provided by linking CH_2 groups.

Table 1. Binding constants (log*K*) of receptors **1–3** for anions as tetrabutylammonium salts determined by ^{1}H NMR titrations in CD_3CN (8% of $CDCl_3$) at 25 °C. Experimental errors estimated to be no more than ± 5% calculated for *K* (M^{-1}) from at least two independent experiments.

Anion [a]	Receptor 1	Receptor 2	Receptor 3
Cl^-	2.57(1); 1.51(3) [a]	2.44(1); 1.20(1) [a]	3.40(1); <1 [a]
Br^-	1.99(1)	2.77(1); 1.19(8) [a]	2.87(1); <1 [a]
I^-	1.46(1)	2.94(1)	2.56(1)
HSO_4^-	1.96(1)	2.90(1)	3.27(1)
ReO_4^-	2.88(3)	3.92(1)	3.06(1)
ClO_4^-	- [b]	- [b]	- [b]

[a] 1:2 binding stoichiometry was revealed from the fitting analysis. The second binding constants as logK_{12} are given in the table. [b] no detectable shifts were observed.

According to the NMR data, chloride induces the strongest NMR shifts among other anions. The amide NH signals are shifted to lower field at almost 3 ppm units (Figure 4a). In case of chloride and bromide recognition, the 1:2 binding event was evident from the fitting analysis [48]. Such a behavior can be understood in terms of ability of the receptor to possess two possible conformations: the helix-like and the linear conformation that was observed in the crystal structure. As the receptor bears multiple binding sites, the saturation of the receptor with anions leads to facilitate binding of the second anion. In case of receptor **2**, the second binding event was too weak to determine the association constant. In contrast to chloride recognition, the perrhenate anion induces small NMR shifts in the titration experiment. The shifts of NH groups and aromatic signals are comparable (Figure 4b).

In order to confirm the selectivity of **2** towards perrhenate, we conducted a competition experiment with chloride. As the addition of perrhenate results in smaller proton shifts than the addition of chloride, we expected that after formation of chloride complex, perrhenate would shift the signals back upfield. As can be seen in Figure 4c, addition of up to 3 equivalents of chloride results in downfield shifts and broadening of amide NH signals. The following addition of only one equivalent of ReO_4^- leads to sharpening the signals, and upfield shifts with more equivalents of ReO_4^- are observed. Thus, perrhenate indeed displaces chloride from the receptor, which is reflected by NMR shifts observed in separate titration experiments. Sharpening of the proton signals might result from the more precise conformation of the receptor-perrhenate complex than that for chloride. Chloride is known to be much better solvated by water than perrhenate, such that the chemical exchange with water in the chloride complex is more pronounced. This could be another reason for the observed broad signals in the chloride complex.

UV–Vis measurements of diluted solutions of receptor **2** at concentrations 10^{-6}–10^{-4} M showed linear dependence of the absorption from concentration indicating the absence of receptor aggregation in acetonitrile solution. The binding constants obtained from UV–Vis titration experiments were in a good agreement with those measured by the NMR method: log*K*(ReO_4^-) = 4.22(4), log*K*(Cl^-) = 3.02(2), log*K*(HSO_4^-) = 3.21(4) (Figure 4d).

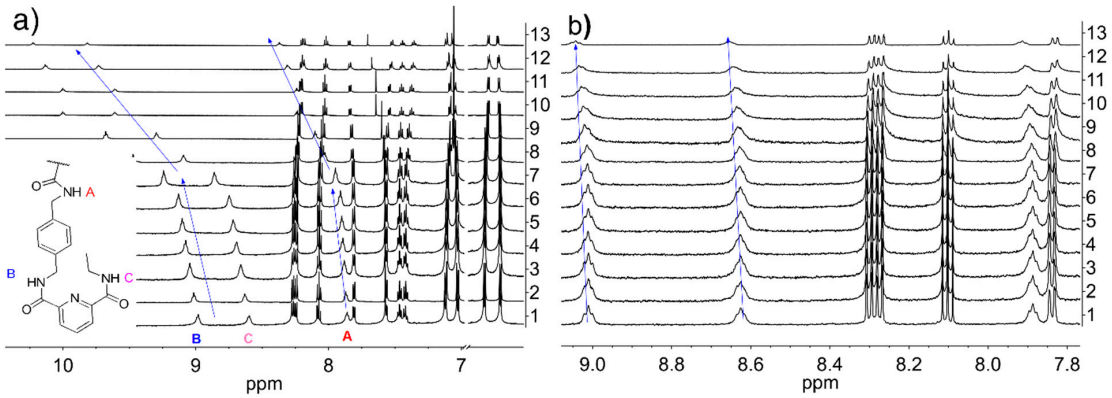

Figure 4. *Cont.*

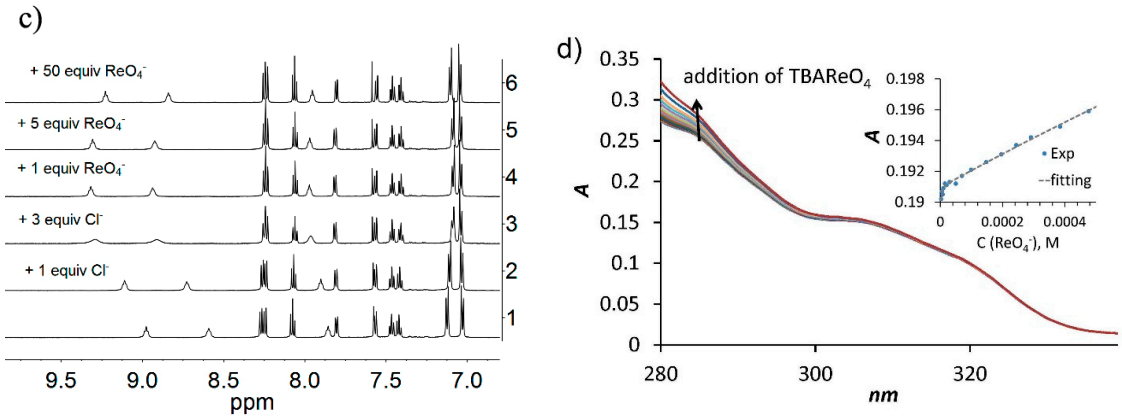

Figure 4. NMR titration of **2** (0.87 mM) with (**a**) TBACl and (**b**) $TBAReO_4$. Spectra 1–13 correspond to additions of 0.25, 0.5, 0.75, 1.0, 1.5, 2.0, 2.5, 3.0, 3.8, 4.8, 5.8, 6.7, 7.6, 8.5. and 9.3 equiv. of the anion. (**c**) Competition experiment: addition of 3 eq. of Cl^- followed by addition of $TBAReO_4$. (**d**) UV–Vis titration of receptor 2 with $TBAReO_4$. Conditions: 0.01 mM receptor in CD_3CN (8% $CHCl_3$).

The analysis of NMR titration data reveals that spherical and tetrahedral anions have different patterns of proton shifts, which suggests that, e.g., chloride and perrhenate possess different coordination modes. For example, in the titration with chloride, the aromatic signals of the xylylene spacer coalesces at 10 equivalents of the anion and change their positions with more equivalents. This fact suggests that the receptor undergoes considerable conformational changes upon saturation of the receptor with the first equivalents, in which both pyridine binding sites are involved. Binding of the second equivalents should induce further conformational rearrangements. In the final 1:2 complex, each of the pyridine binding sites could coordinate one chloride anion.

4.2. DFT Calculations

To understand possible binding modes of the receptors we conducted DFT calculations (TZ-basis, PBE functional) of receptor **2** with perrhenate and chloride anions. As can be seen in Figure 5, the perrhenate anion fits the receptor with high complementary. The anion forms six hydrogen bonds with the receptor with O-H-N angles: 170° for coordination with diphenylacetylene fragment and 155° for the hydrogen bonds with the pyridine dicarboxamide fragment. Careful investigation of the conformational space of possible binding modes of the receptor with the chloride anion yielded structure **2**·Cl^- depicted in Figure 5. The receptor forms a perfect cavity for chloride, in which both pyridine subunits participate in anion coordination providing four hydrogen bonds. We proposed that this structure could explain the ability of all receptors to coordinate chloride anions. For example, receptor **3** demonstrates the highest affinity for chloride according to the experimental findings. This fact can be explained by the shortest distance between the carbonyl groups of the ferrocene unit as compared to other receptors and thus optimal alignment of the pyridine fragments to bind chloride.

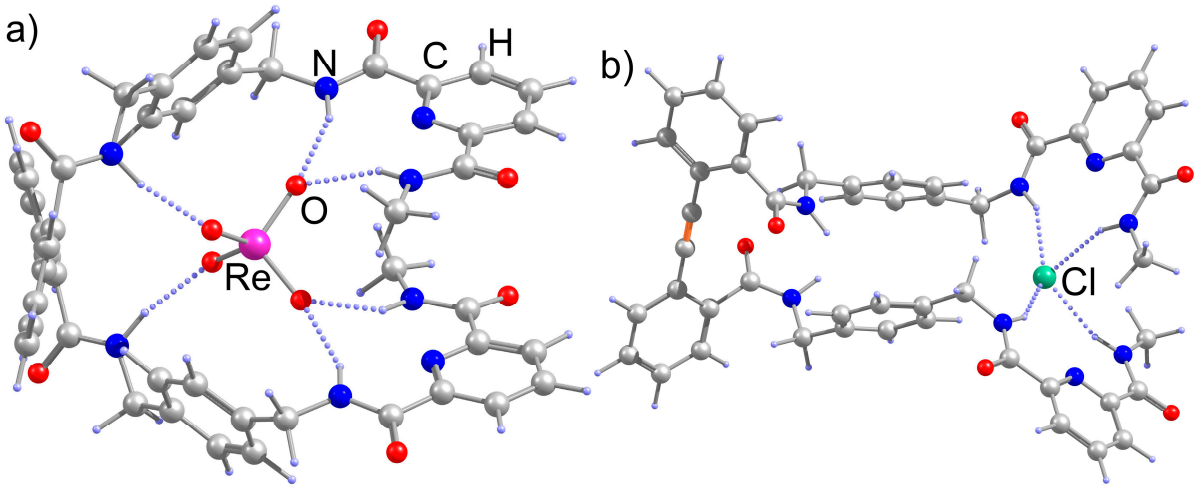

Figure 5. DFT optimized structures of receptor 2 with (**a**) perrhenate and (**b**) chloride anions, respectively.

5. Conclusions

In summary, three new helix-like receptors have been designed and synthesized to complementary bind perrhenate by hydrogen bonding interactions with all four oxygen atoms of the anion. Solution and solid-state investigations have revealed that receptors are rather flexible and combine unexpected properties. They form self-assembled structures in the solid state, which are hold by hydrogen bonding pyridine dicarboxamide–carbonyl interactions. The receptors bind anions with affinity of 10^3 M^{-1} in CH_3CN solution according to ^1H NMR and UV–Vis titrations. Receptor **2** has demonstrated the best selectivity for perrhenate, while receptor **3** appeared to be selective for chloride. This difference has been explained in terms of different distance of the NH-binding sites in the helix-forming subunit. DFT calculations have predicted the possible binding mode of the receptor with chloride anions, which involves the interaction of the anion with two pyridine dicarboxamide subunits. Competition ^1H NMR experiments have confirmed the selectivity of **2** for perrhenate against chloride in acetonitrile solution. This work has provided evidence that helix-like synthetic receptors are able to recognize perrhenate with good selectivity. However, the receptor flexibility gives rise to other possible conformations that can adopt smaller anions such as chloride. Thus, the design of new receptors with macrocyclic or rigid structures for binding perrhenate in polar solvents is currently in progress.

Supplementary Materials: The following are available online at https://www.mdpi.com/article/10.3390/chemosensors9050093/s1, Figure S1. ^1H NMR spectrum of the Boc-protected compound **4**. Figure S2. ^{13}C NMR spectrum of the Boc-protected compound **4**, Figure S3. ^1H NMR spectrum of receptor **1.** Figure S4. ^{13}C NMR spectrum of receptor **1.** Figure S5. ^1H NMR spectrum of receptor **2**. Figure S6. ^{13}C NMR spectrum of receptor **2.** Figure S7. 13C NMR spectrum of receptor **3.** Figure S8. ^{13}C NMR spectrum of receptor **3.** Figure S9. 1H-1H COSY spectrum of receptor **2.** Figure S10. ^1H-^1H ROESY spectrum of receptor **2.** Figure S11. UV-Vis spectra of receptor **2** at different concentrations together with the linear fitting analysis. Scheme S1: Synthesis of tert-butyl-4-((6-(ethylcarbamoyl)picolinamido)methyl)benzylcarbamate. Scheme S2. Synthesis of Receptor 1. Scheme S3. Synthesis of receptor **2.** Scheme S4. Synthesis of receptor **3.** Scheme S4. Synthesis of receptor **3.** Table S1. Proton shifts observed during NMR titration experiments of Receptor **1** with anions in CH_3CN (8% $CHCl_3$) together with the fitting graphics of the aromatic and NH protons, which were exported from the HypNMR program. Table S2. Proton shifts observed during NMR titration experiments of Receptor **2** with anions in CH_3CN (8% $CHCl_3$) together with the fitting graphics of the aromatic and NH protons, which were exported from the HypNMR program. Table S3. Proton shifts observed during NMR titration experiments of Receptor **3** with anions in CH_3CN (8% $CHCl_3$) together with the fitting graphics of the aromatic and NH protons, which were exported from the HypNMR program.

Author Contributions: A.R. and B.S.M. synthesized the compounds and measured the NMR, spectra. A.S.O. did dilution experiments and measured UV–Vis spectra. T.R. and H.L. have made X-ray crystal structure analysis. E.A.K. summarized the results and, together with co-authors, wrote the paper. All authors have read and agreed to the published version of the manuscript.

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