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Dual Sensing by Simple Heteroditopic Salt Receptors Containing an Anthraquinone Unit

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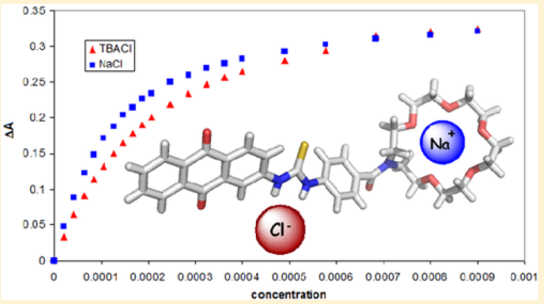
Supporting Information

ABSTRACT: We synthesized simple ion pair receptors consisting of a crown ether cation binding site and an anthraquinone-supported thiourea anion binding domain and studied their anion-, cation-, and salt-binding properties using spectroscopic, spectrophotometric, and electrochemical measurements in acetonitrile solution. Apart from carboxylate anions, which cause deprotonation, all the anions tested were found to associate with receptor **1** more strongly in the presence of sodium cations, whereas in the presence of potassium or ammonium cation the anion binding strength was greatly diminished. A homotopic anion receptor **3**, lacking a crown ether unit, was unable to bind sodium salt more strongly than tetrabutylammonium salts. Solution and solid-state X-ray measurements revealed that strong sodium coordination with the cation-binding domain is responsible for the salt-binding enhancement. Electrochemical measurements showed that the addition of anions to the receptor **1** pretreated with sodium cations resulted in greater changes in reduction potentials compared to the addition of anions to receptor **1** in the absence of Na^+.



INTRODUCTION

Anthraquinones, colored compounds that are good fluorophores, serve as the fundamental construction for many natural colors found in plants.[1] Apart from their optical properties, in nonaqueous, aprotic media, the quinone system in anthraquinone derivatives usually gives two 1 e peaks. The corresponding processes can be written as $AQ + e = AQ^{\bullet-}$ and $AQ^{\bullet-} + e = AQ^{2-}$.[2] Therefore, anthraquinones are convenient dual-signaling subunits in the construction of sensors able to recognize both anions or cations. The recognition event in such molecular receptors involves signaling by optical changes or perturbation in potential signals. Various receptors have been proposed for the recognition of anions consisting of amide, urea or thiourea and imidazole or pyrrole conjugate. Nevertheless, most of these are selective toward basic anions such as fluoride and acetate ions.[3] Furthermore, an anthraquinone moiety connected to the receptor scaffold might be useful for cation detection, producing optical/electrochemical responses toward target analytes.[4] However, ion-pair receptors that are able to simultaneously recognize cations and anions and bear anthraquinone moieties displaying the dual-sensing mode are limited.[5] Moreover, the simplest ion-pair receptors displaying significantly enhanced affinities toward anions in the presence of cations possess a crown ether unit and a urea or thiourea group linked together. The crown ether substituent is usually located in close proximity to the (thio)urea group acting as an electron-donating group, which may diminish the acidity of NH protons and as a consequence reduce the hydrogen bond interaction ability.[6]

Therefore, in this study we synthesized and tested the optical and electrochemical behavior of a simple salt receptor consisting of an anthraquinone-based anion binding site and a crown ether unit responsible for cation association. The cation binding site is linked to the receptor platform in a way that reduces the electron density on the thiourea binding site and thus enables stronger interaction with anion and ion pairs. We also discuss in this paper the role of the individual structural elements on anion and ion-pair binding.

EXPERIMENTAL SECTION

All reagents and chemicals were of reagent-grade quality and purchased commercially. ^1H and ^{13}C NMR spectra were recorded on a Bruker 300 MHz spectrometer. ^1H NMR chemical shifts δ are reported in parts per million referenced to residual solvent signal (deuterated dimethyl sulfoxide (DMSO-d_6) or $CDCl_3$). UV−vis titrations were performed in acetonitrile using a Thermo Spectronic Unicam UV500 Spectrophotometer. High-resolution mass spectra (HRMS) were measured on a Quattro LC Micromass unit using electrospray ionization (ESI) technique.

Preparation of Compound 4a. To a solution of 3-nitrobenzoyl chloride (1 g, 5.39 mmol) and 0.9 mL of triethylamine in 50 mL of dry dichloromethane, 1-aza-18-crown-6 (1.42 g, 5.40 mmol) at 0 °C (ice bath) was added. The reaction mixture was stirred for 30 min and then left at room temperature (r.t.) overnight. The organic phase was then washed twice with distilled water, 1 M HCl, and saturated $NaHCO_3$ and dried over $MgSO_4$. After evaporation of dichloromethane the residue was purified by silica gel column chromatography (5% methanol in chloroform) to give the title product as a colorless oil (2.15 g, 97% yield).

HRMS (ESI): calcd for $C_{19}H_{28}N_2O_8Na$ $[M + Na]^+$: 435.1743, found: 435.1747.

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^{1}H NMR (300 MHz, DMSO-d_6) δ 3.40−3.80 (m, 24H), 7.71−7.77 (m, 1H), 7.80−7.89 (m, 1H), 8.20−8.35 (m, 2H).

^{13}C NMR (75 MHz, DMSO-d_6) δ 45.66, 50.08, 68.71, 70.19, 70.40, 70.64, 122.25, 124.27, 130.60, 133.77, 138.92, 147.97, 169.15.

Preparation of Compound 4b. To a solution of 4-nitrobenzoyl chloride (1 g, 5.39 mmol) and 0.9 mL of triethylamine in 50 mL of dry dichloromethane, 1-aza-18-crown-6 (1.42 g, 5.40 mmol) at 0 °C (ice bath) was added. The reaction mixture was stirred for 30 min and then left at r.t. overnight. The organic phase was then washed twice with distilled water, 1 M HCl, and saturated $NaHCO_3$ and dried over $MgSO_4$. After evaporation of dichloromethane the residue was purified by silica gel column chromatography (5% methanol in chloroform) to give the title product as a colorless oil (2.10 g, 95% yield). mp 84−86 °C.

HRMS (ESI): calcd for $C_{19}H_{28}N_2O_8Na$ $[M + Na]^+$: 435.1743, found: 435.1750.

^{1}H NMR (300 MHz, DMSO-d_6) δ 3.40−3.75 (m, 24H), 7.60−7.70 (m, 2H), 8.22−8.35 (m, 2H).

^{13}C NMR (75 MHz, DMSO-d_6) δ 45.59, 49.79, 68.63, 68.82, 70.09, 70.24, 70.39, 70.61, 124.11, 128.55, 143.79, 147.93, 169.56.

Preparation of Compound 5a and 5b. To a degassed solution of **4a** or **4b** (2 g, 4.85 mmol) in 150 mL of tetrahydrofuran (THF)/MeOH (1:4), a catalytic amount of 10% Pd/C was added. The reaction mixture was kept under H_2 atmosphere (balloon pressure) at r.t. overnight. The catalyst was removed by filtration through a pad of diatomaceous earth and washed with MeOH. The filtrate was concentrated under reduced pressure to give the crude product in quantitative yield (1.85 g). The amine was used in next step without further purification.

5a: HRMS (ESI): calcd for $C_{19}H_{30}N_2O_6Na$ $[M + Na]^+$: 405.2002, found: 405.2011.

5b: HRMS (ESI): calcd for $C_{19}H_{30}N_2O_6Na$ $[M + Na]^+$: 405.2002, found: 405.2008.

Preparation of Compound 6. To a solution of 2-aminoanthraquinone (500 mg, 2.24 mmol) in dichloromethane (20 mL) 1,1′-thiocarbonyldi-2(1*H*)-pyridone (780 mg, 3.36 mmol) was added. After 30 min the reaction was completed (as monitored by thin-layer chromatography). The reaction mixture was concentrated under reduced pressure, and the residue was purified by silica gel column chromatography (20% hexane in dichloromethane) to give the title product as a yellow fluffy solid (356 mg, 60% yield). mp 208−209 °C.

HRMS (ESI): calcd for $C_{15}H_7NO_2SNa$ $[M + Na]^+$: 288.0095, found: 288.0107.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.57−7.70 (m, 1H), 7.80−7.90 (m, 2H), 8.12−8.14 (m, 1H), 8.31−8.45 (m, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 124.11, 127.23, 127.43, 129.26, 130.66, 131.44, 133.36, 134.14, 134.34, 134.57, 134.92, 137.49, 181.77, 181.99.

Preparation of Receptor 1. To the solution of amine **5a** (428 mg, 1.12 mmol) in 30 mL of dry THF, isothiocyanate **6** (300 mg, 1.13 mmol) was added. After it was stirred overnight at r.t., the reaction mixture was concentrated and purified by silica gel column chromatography (2% methanol in chloroform) to give receptor **1** as an orange solid (456 mg, 63% yield). mp 72−75 °C.

HRMS (ESI): calcd for $C_{34}H_{37}N_3O_8SNa$ $[M + Na]^+$: 670.2199, found: 670.2208.

^{1}H NMR (300 MHz, DMSO-d_6) δ 3.40−3.80 (m, 24H), 7.15−7.20 (m, 1H), 7.40−7.58 (m, 3H), 7.84−7.98 (m, 2H), 8.08−8.25 (m, 4H), 8.40−8.47 (m, 1H), 10.36 (s, 1H), 10.54 (s, 1H).

^{13}C NMR (75 MHz, DMSO-d_6) δ 45.77, 50.01, 68.75, 69.28, 70.38, 70.47, 119.40, 122.29, 123.63, 124.66, 127.16, 127.22, 127.40, 128.34, 128.61, 129.33, 133.56, 133.66, 134.11, 134.76, 135.09, 137.71, 139.39, 145.98, 170.74, 180.01, 181.90, 182.84.

Anal. Calcd for $C_{34}H_{37}N_3O_8S$: C, 63.0; H, 5.8; N, 6.5; S, 5.0%. Found: C, 62.9; H, 5.7; N, 6.3; S, 5.0%.

Receptor 2. Receptor **2** was synthesized analogously to receptor **1** with the exception that amine **5b** was used.

Yellow solid, 60% yield. mp 177−179 °C.

HRMS (ESI): calcd for $C_{34}H_{36}N_3O_8S$ $[M - H]^-$: 646.2223, found: 646.2227.

^{1}H NMR (300 MHz, DMSO-d_6) δ 3.40−3.70 (m, 24H), 7.30−7.45 (m, 2H), 7.51−7.60 (m, 2H), 7.90−7.98 (m, 2H), 8.05−8.28 (m, 4H), 8.44−8.46 (m, 1H), 10.40 (bs, 1H), 10.56 (bs, 1H).

^{13}C NMR (75 MHz, DMSO-d_6) δ 66.88, 70.20, 70.40, 70.47, 119.38, 123.37, 127.15, 127.20, 127.38, 127.74, 128.32, 128.61, 133.53, 133.58, 133.63, 134.08, 134.74, 135.08, 140.14, 145.93, 170.98, 179.73, 181.73, 181.88, 182.81.

Anal. Calcd for $C_{34}H_{37}N_3O_8S$: C, 63.0; H, 5.8; N, 6.5; S, 5.0%. Found: C, 62.9; H, 5.6; N, 6.4; S, 4.9%.

Preparation of Receptor 3. To the solution of aniline (54 mg, 0.58 mmol) in 10 mL of dry THF, isothiocyanate **6** (54 mg, 154 mmol) was added. After it was stirred overnight at r.t., the reaction mixture was concentrated and purified by silica gel column chromatography (50% hexane in dichloromethane) to give receptor **3** as a yellow solid (160 mg, 77% yield). mp 207−208 °C.

HRMS (ESI): calcd for $C_{21}H_{14}N_2O_2SNa$ $[M + H]^+$: 381.0647, found: 381.0675.

^{1}H NMR (300 MHz, DMSO-d_6) δ 7.10−7.25 (m, 1H), 7.30−7.58 (m, 4H), 7.85−8.00 (m, 2H), 8.05−8.30 (m, 4H), 8.47 (s, 1H).

^{13}C NMR (75 MHz, DMSO-d_6) δ 119.32, 124.24, 125.49, 127.14, 127.20, 127.30, 128.30, 128.49, 129.14, 133.56, 133.66, 134.07, 134.73, 135.06, 139.44, 146.12, 179.81, 181.89, 182.85.

Anal. Calcd for $C_{21}H_{14}N_2O_2S$: C, 70.4; H, 3.9; N, 7.8; S, 8.9%. Found: C, 70.2; H, 3.8; N, 7.8; S, 8.8%.

Electrochemical Measurement. The electrochemical investigations were performed in a three-electrode cell. The electrode potential was controlled by CH Instrument, model 700D potentiostat, controlled via producer's software. A platinum wire served as the counter electrode, and a Ag/Ag(I) system (0.1 M $AgNO_3$ acetonitrile solution) was used as the reference electrode. The supporting electrolyte was 0.1 M tetrabutylammonium hexafluorophosphate ($TBAPF_6$) in acetonitrile. A 3.0 mm, in diameter, glassy carbon disk electrode was used as the working electrode. Before each experiment, the electrode was polished with aluminum oxide powder of various size on a wet pad, rinsed with water, and then dried with ethanol. To minimize the electric noise, the electrochemical cell was kept in a grounded Faraday cage. More information about electrochemical measurements are in Supporting Information.

X-ray Measurement. The crystallographic data for **2**·$NaClO_4$ were deposited with the Cambridge Crystallographic Data Center as Supplementary Publication No. CCDC 1438 959. Complex of **2**·$NaClO_4$ was crystallized by slow diffusion of Et_2O into acetontrile/methanol solution. The X-ray measurement of receptor **2**·$NaClO_4$ was performed at 100(2) K on a Bruker D8 Venture Photon100 diffractometer equipped with a TRIUMPH monochromator and a Mo Kα fine focus sealed tube (λ = 0.710 73 Å). A total of 870 frames were collected with Bruker APEX2 program.[12] The frames were integrated with the Bruker SAINT software package[13] using a narrow-frame algorithm. The integration of the data using a monoclinic unit cell yielded a total of 33 913 reflections to a maximum θ angle of 25.05° (0.84 Å resolution), of which 6573 were independent (average redundancy 5.159, completeness = 99.9%, R_{int} = 4.06%, R_{sig} = 3.83%) and 4920 (74.85%) were greater than $2\sigma(F^2)$. The final cell constants of a = 8.5544(5) Å, b = 15.2860(8) Å, c = 28.4211(15) Å, β = 91.532(2)°, and volume = 3715.1(4) Å^3 are based upon the refinement of the XYZ-centroids of 9883 reflections above 20 $\sigma(I)$ with 4.938° < 2θ < 50.56°. Data were corrected for absorption effects using the multiscan method (SADABS).[14] The ratio of minimum to maximum apparent transmission was 0.909. The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.8990 and 0.9870.

The structure was solved and refined using SHELXTL Software Package[15] using the space group $P121/n1$, with Z = 4 for the formula unit, $C_{35.29}H_{40.71}ClN_{3.29}NaO_{12.80}S$. The final anisotropic full-matrix least-squares refinement on F^2 with 513 variables converged at $R1$ = 4.03%, for the observed data, and at $wR2$ = 9.37% for all data. The goodness-of-fit was 1.052. The largest peak in the final difference electron density synthesis was 0.272 e$^-$/Å^3, and the largest hole was −0.327 e$^-$/Å^3 with an RMS deviation of 0.049 e$^-$/Å^3. On the basis of

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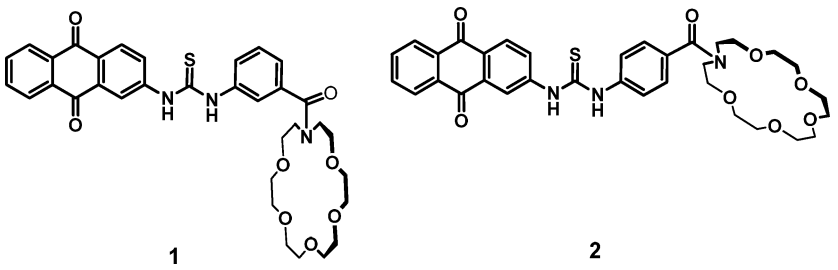


Figure 1. Structure of receptors **1** and **2**.

the final model, the calculated density was 1.441 g/cm^3 and $F(000)$, 1687 e$^-$.

The structure contains non-stoichiometric amount of solvent molecules. Na cation trapped in crown ether is coordinated from one side by methanol/acetonitrile with refined occupancy ratio equal to 0.71:0.29. This substitutional disorder is associated with a presence of less than 10% of water. Hydrogen atoms of this low-occupancy H_2O molecule were not assigned.

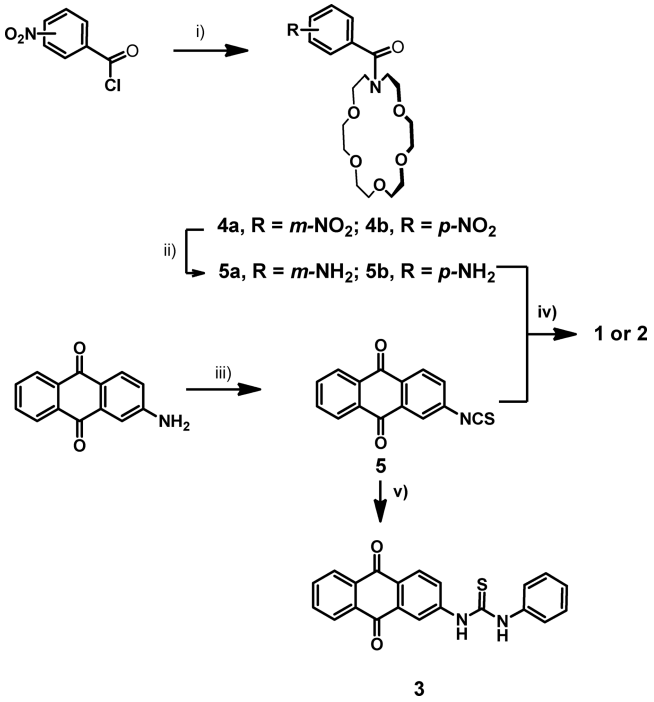
The non-hydrogen atoms, except low-occupancy water O atom, were refined anisotropically. Most of the hydrogen atoms were placed in calculated positions and refined within the riding model. The temperature factors of hydrogen atoms were not refined and were set to be equal to either 1.2 or 1.5 times larger than U_{eq} of the corresponding heavy atom. Position sand temperature factors of two hydrogen atoms in the urea fragment were refined. Position of hydroxyl H atom in the methanol was refined as well. The atomic scattering factors were taken from the International Tables.[16]

RESULTS AND DISCUTIONS

Receptor Synthesis. The new salt receptors **1** and **2** (Figure 1) as well as anion receptor **3** were prepared in a simple approach according to Scheme 1. The reaction of 3-nitrobenzoyl chloride with 1-aza-18-crown ether in the presence of triethylamine allowed a cation binding domain to be introduced in 97% yield. The nitro group in the compound **4a** was then reduced using hydrogen and palladium/carbon catalyst in quantitative yield. The obtained amine **5a** was then reacted with isothiocynate **6** to give receptor **1** in 63% yield. To avoid very toxic tiophosgene, previously reported isothiocyanate **6** was prepared in 60% yield from commercially available 2-aminoanthraquinone using 1,1′-thiocarbonyldi-2(1*H*)-pyridone.[7] The regioisomeric ion pair receptor **2** was prepared in analogous manner starting from 4-nitrobenzoyl chloride. Finally, treatment of isothiocynate **6** with aniline afforded the anion receptor **3** in 77% yield.

Ultraviolet−Visible Binding Study. A quantitative evaluation of the anion-, cation-, and salt-binding ability of **1** was investigated by the spectrophotometric titrations method in CH_3CN.[8] To rule out the possibility that self-association might be occurring in the range of concentration under investigation, dilution studies were first performed, and indeed no evidence was found of self-association for receptor **1**. Similarly, test experiments with tetrabutylammonium perchlorate ruled out the interaction of receptor **1** with these ions. Job plot experiments were performed, with the results showing a 1:1 stoichiometry complexation between **1** and the investigated ions. Then, the affinity of receptors **1** toward selected anions accompanied by the noncoordinated tetrabutylammonium cation were studied. The addition of TBA salts of various anions to 1.24×10^{-4} M solution of **1** caused bathochromic shifts in the absorption maximum of receptor (Figure 2). The association constants calculated by nonlinear regression analysis of the binding isotherms are listed in Table 1. The investigated

Scheme 1. Synthesis[a] of Receptors 1, 2, and 3



[a]Reagents and conditions: (i) Et_3N, 1-aza-18-crown-6, CH_2Cl_2, 0°C to r.t., 97% and 95% for **4a** and **4b**, respectively; (ii) H_2, Pd/C, MeOH, quantitative; (iii) 1,1′-thiocarbonyldi-2(1*H*)-pyridione, CH_2Cl_2, r.t., 60%; (iv) Et_3N, THF, r.t., 63% and 60% for **1** and **2**, respectively; (v) aniline, THF, r.t., 77%.

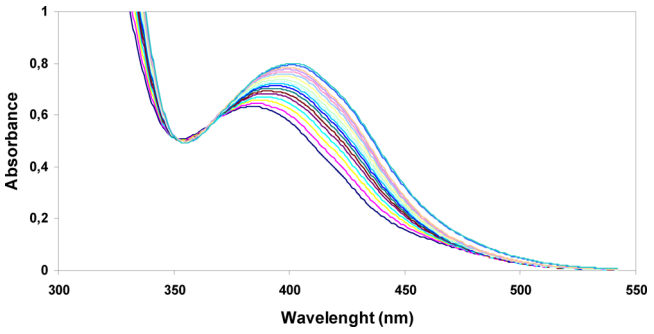


Figure 2. Representative UV−vis titration spectra of receptor **1** (upon gradual addition of tetrabutylammonium chloride). [**1**] = 1.28×10^{-4} M; optical path length 10 mm.

anions were bound to the receptor moderately, in the order $NO_3^- < Br^- < NO_2^- < Cl^-$. Moreover, upon addition of basic benzoate and acetate anions, the deprotonation of receptor **1** was observed, together with a color change of the receptor from

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Table 1. Association Constants (K_a) for Interactions between Receptors 1 and Selected Anions in the Absence or Presence of 1 equiv of Sodium Perchlorate[a]

	1	1+Na^+	cooperativity factor
Cl^-	10 000	30 900	3.09
NO_2^-	4300	5600	1.30
Br^-	630	2700	4.28
NO_3^-	230	600	2.61
$PhCOO^-$	b	b	
AcO^-	b	b	

[a]UV−vis, solvent CH_3CN, temperature 293 K, [1] = 1.28 × 10^{-4} M, anions added as TBA salts [TBAX] ≈ 6 × 10^{-3} M; M^{-1}, sodium added as $NaClO_4$, Errors <10%. [b]Deprotonation.

yellow to red. Initially we concluded that receptor **1** was deprotonated only by the more basic acetate anion because typical UV−vis spectra for benzoate titration were collected. However, analysis of the ^1H NMR spectra recorded upon gradual addition of acetate and benzoate anions indicated that receptor **1** was deprotonated in both cases. Namely, the addition of carboxylate anions resulted in the disappearance of signals assigned to thiourea protons (Supporting Information). In the presence of sodium cations, all moderately bound anions associated with receptor **1** with remarkably higher stability constants. The highest cooperativity factor, meaning the greatest enhancement in anion binding in the presence of sodium cation relative to tetrabutylammonium salt coordination, was found for halides. Bromide and chloride anions were 4.28 times and 3.09 times, respectively, more strongly associated with receptor **1** in the presence of sodium cations.

Since the addition of sodium cations into acetonitrile solution of receptor **1** caused no change in the UV−vis absorption band, the selectivity toward cations was studied using titration with chloride anions in the presence of sodium, potassium, and ammonium cations. Notably, a significant improvement in salt binding was observed only in the presence of sodium cations (K= 10 000 M^{-1} for chloride anions vs K = 30 900 M^{-1} for chloride anions in the presence of 1 equiv of Na^+). Both potassium and ammonium chlorides were associated with receptor **1** even more weakly than tetrabutylammonium chloride (K = 6900 M^{-1} for chloride anions in the presence of 1 equiv of K^+ and K = 4450 M^{-1} for chloride anions in the presence of 1 equiv of NH_4^+), which evidence the high selectivity of **1** toward sodium cations.

To establish the role of the cation binding domain in salt binding, a molecular receptor **3** lacking a crown ether binding domain and without any substituent on the phenyl ring was synthesized and tested (Scheme 1). As expected, receptor **3** was not able to bind sodium salts more strongly than its tetrabutylammonium counterparts; specifically, sodium chloride was bound to the receptor more than half as strongly than tetrabutylammonium chloride (K = 7600 M^{-1} for chloride and K = 3550 M^{-1} for chloride anions in the presence of 1 equiv of Na^+). Interestingly, receptor **3** likewise associated tetrabutylammonium chloride more weakly than receptor **1** (7600 M^{-1} vs 10 000 M^{-1}). This proves that the crown ether unit connected to receptor **1** through an amide bond acts not only as a cation binding site but also diminishes the electron density in the phenyl ring linked with the anion binding site and as a consequence reinforces anion binding. Furthermore, the 2-aminoanthraquinone-based anion receptor **3** is able to create much stronger complexes with chloride anion than its regioisomer synthesized from 1-aminoanthraquinone. In the case of the latter (contrary to the presented receptors **1**−**3**), intramolecular hydrogen bond formation between the NH of the thiourea anion binding site and the carbonyl group of the antraquinone unit highly diminishes the ability of the receptor to interact with anions (K = 7600 M^{-1} for receptor **1** vs K = 4300 M^{-1} for its regioisomer).[9]

Initially, we presumed that the salt-binding enhancement by receptor **1** is caused by the simultaneous coordination of sodium cation to the crown ether and interaction with the thiourea carbonyl group, a binding mode previously reported for amino acid-based salt receptors.[10] However, the regioisomeric reference receptor **2** possessing binding domains in para position similarly binds sodium salts more strongly than anions (K = 11 500 M^{-1} for chloride and K = 25 700 M^{-1} for chloride anions in the presence of 1 equiv of Na^+), which rules out the aforementioned binding mode of receptors (Table 2). Thus, we

Table 2. Comparison of Association Constants (K_a) for Interactions between Receptors 1, 2, and 3 and Chloride Anions in the Absence or Presence of 1 equiv of Sodium Perchlorate[a]

L	1	2	3
K_{Cl^-}	10 000	11 500	7600
$K_{[L+Na+]\cdot Cl^-}$	30 900	25 700	3550

[a]UV−vis, solvent CH_3CN, temperature 293 K, [1] = 1.28 × 10^{-4} M, [2] = 1.33 × 10^{-4} M, [3] = 1.17 × 10^{-4} M, errors <10%.

concluded that the enhancement of anion binding in the presence of sodium cations might be attributed to electrostatic interaction and cation complexation-induced increased acidity of the thiourea protons of receptors.

^1H Nuclear Magnetic Resonance Binding Study. To gain more insight into the ion-pair binding mechanism, ^1H NMR titrations were performed in acetonitrile solution for receptor **1**. The subsequent addition of sodium perchlorate to 3.2 solution of receptor **1** caused considerable chemical shifts in the ^1H NMR spectrum of the signals corresponding to crown ether −O−CH_2− as well as less pronounced variation of both thiourea protons. This indicates strong sodium coordination into the crown ether unit. Analysis of the binding isotherm so obtained revealed that the receptor coordinated to the sodium cation strongly, with the high association constant value of 19 950 M^{-1}. However, the addition of potassium or ammonium hexafluorophosphate to the solution of receptor **1** caused less pronounced changes in the ^1H NMR spectra. The stability constants for these cations are much lower than for sodium cations and were calculated to be 125 and 300 M^{-1}, respectively. Therefore, we concluded that, contrary to the other investigated cations, strong sodium cation association to the crown ether units makes this group more electron-withdrawing and reduces the electron density on the phenyl ring. Hence, this complexation is responsible for increasing the acidity of the thiourea protons and thus enhances anion binding. Indeed, upon addition of sodium cations into receptor solution, the perturbation in signals assigned to the phenyl ring connected with the crown ether unit was observed, while the anthraquinone system remained unchanged. Interestingly, a slight downfield shift of the thiourea proton attached to the anthraquinone scaffold was observed; however, the second one was shifted slightly upfield. The assignment of thiourea protons was done based on ^1H−^1H ROESY NMR.

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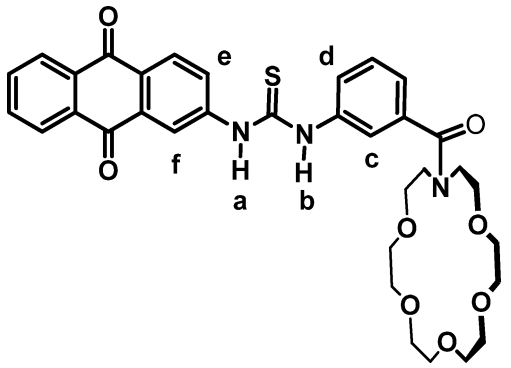
Table 3. ^{1}H NMR Shifts ($\Delta\delta$) of Selected Protons and Association Constants (K_a) for Interactions of Receptor 1 with Bromide Anions in the Absence or Presence of 1 equiv of Sodium Cations[a]

	H_a	H_b	H_c	H_d	H_e	H_f	K
1	2.69	2.27	0.40	0.21	0.33	0.45	950
1 + 1 equiv of Na^+	2.75	2.42	0.34	0.29	0.31	0.47	3710
cooperativity factor							3.90

[a] ^{1}HNMR, solvent CD_3CN, temperature 293 K, [1] = 3.03 mM, [TBABr] = 48.4 mM; M^{-1}, errors <10%.

Then ^{1}H NMR anion binding studies were performed. Upon addition of TBABr, considerable downfield shifts in both NH protons were observed (Figure 3, Table 3), indicating the formation of strong hydrogen bonds between anions and receptor **1**.



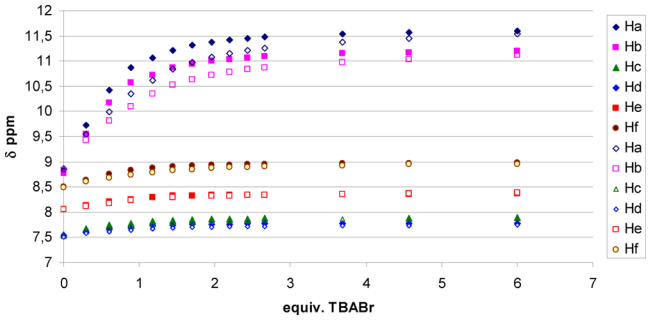


Figure 3. ^{1}H NMR titrations of receptor **1** with TBABr in the presence of 1 equiv of $NaClO_4$. Profiles based on the chemical shift (δ, ppm) of thiourea and aromatic protons. Open symbols refer to the titration in the absence of sodium cations; full symbols refer to the titration in the presence of sodium cations.

These anion-induced shifts were higher for NH connected to the anthraquinone unit and lower for NH attached to the phenyl ring, indicating the differing participation of thiourea protons in H-bond formation. Interestingly, the higher anion-induced shift was observed for the thiourea proton, which was shifted downfield upon addition of sodium cations. Similarly, all four aromatic protons neighboring the anion binding site, H_c, H_e, H_f, and H_e, which can form internal C−H···S hydrogen bonds, also underwent downfield shifts, albeit less distinctly so, in the range of $\Delta\delta$ = 0.21−0.45. Titration of **1** in the presence of 1 equiv of sodium cations with bromide anions (added as TBA salts) induced downfield shifts for all mentioned protons of receptor **1**, similar to those seen in the absence of sodium cations, although the changes were more drastic in the presence of a cation. Analyzing the anion complexation-induced shifts of all mentioned protons of receptor **1** allowed the stability constants to be determined. Thus, we found that receptor **1** associated with bromide anion moderately (K_{Br^-} = 950 M^{-1}). However, in the presence of sodium cations the association of bromide anions was greatly enhanced. Specifically, the bromide anions were 3.90 times more strongly bound to receptor **1**. The data collected from ^{1}H NMR titrations experiments are consistent with those obtained from UV−vis titration measurements.

X-ray Measurements. The strong sodium cation binding is also supported by solid-state X-ray crystallography measurements. Despite making a number of attempts to crystallize guest complexes of receptor **1**, we were unable to obtain crystals. However, slow diffusion of diethyl ether into an MeCN/MeOH solution of sodium pretreated reference receptor **2** enabled us to obtain crystals suitable for X-ray diffraction analysis. Because receptor **2** possesses the same binding domains as receptor **1**, the [**2**·$NaClO_4$] complex was used as a model for further considerations.

In the solid state the sodium cation is located in the 18-aza-6-crown ether cavity, similarly to the sodium complexes of 15-crown-5.[11] In the [**2**·$NaClO_4$] complex the sodium cation is

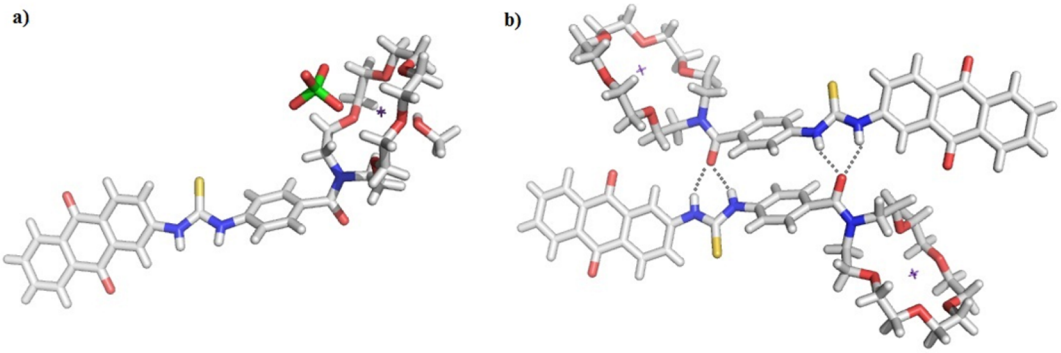


Figure 4. (a) X-ray crystal structure of [**2**·$NaClO_4$] complex. (b) Hydrogen bonding interactions in [**2**·Na^+] complex (with lattice solvents and perchlorate anion omitted for clarity).

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strongly bonded to five O atoms, with the Na−O distances ranging from 2.430 to 2.581 Å, while the nitrogen atom is involved in amide bond formation and does not participate in sodium complexation. The average Na−O distance is 2.49 Å and is rather longer than that found for the sodium complexes of 15-crown-5. This is due to two longer Na−O bonds with the oxygen atoms located close to the nitrogen atom (2.537 and 2.581 Å, respectively). The sodium cation in the [**2**·$NaClO_4$] complex is also coordinated from on site to oxygen atoms of perchlorate anion and on the opposite site is coordinated by methanol/acetonitrile with refined occupancy ratio equal to 0.71:0.29. The sodium cation lies almost in the center of the plane formed by the five O atoms of the crown ether (0.043 Å above the plane toward the perchlorate anion). Two O atoms of the crown ether lie below this plane, the other three above. Moreover in the solid state (in the absence of anions) the thiourea group interacts through two hydrogen bonds with the oxygen atom of the amide group (N−H−O distance 2.819 and 2.901 Å) forming head-to-tail dimers (Figure 4).

Electrochemical Measurements. Finally, the electrochemical properties of receptor **1** toward selected anions in the absence and presence of Na^+ were studied using cyclic voltammetry. Receptor **1** shows two consecutive one-electron reversible waves in acetonitrile solution, corresponding to two single-electron reductions to give mono- and dianion species. The cyclic voltammogram obtained for receptor **1** is presented in Figure 5 as a solid black line. Potentials corresponding to reduction peaks for receptors **1** are found to be $E_{p(I)} = -1.166$ V and $E_{p(II)} = -1.473$ V. The potentials of the two peaks depend on the addition of anions and sodium salts. However, the potential changes for the first peak are more marked, and therefore behavior of this peak was used for further analysis. Upon addition of 1, 3, or 5 equiv of anions (Cl^-, Br^-, NO_2^-, NO_3^-) the potential of the first peak shifts gradually toward more negative potentials. Typical voltammograms recorded after adding NO_2^- are presented in Figure 5A. However, upon addition of sodium cations the potential of the first peak also shifts, but this time toward positive potentials. This could support the conclusion that complexation of sodium cations into the crown ether ring decreases electron density, which is perceptible in the antraquinone reporter unit. Then, addition of anions again gradually shifts the peak potential toward more negative potential. Typical voltammograms recorded after adding 1 equiv of Na^+ and then 1, 3, or 5 equiv of NO_2^- are presented in Figure 5B. Numerical data showing changes in reduction potentials for other investigated anions are shown in Table 4.

Therefore, the changes in reduction potentials upon addition of anions to the **1** + 1 equiv of Na^+ are much greater than for the association of receptor **1** with anions in the absence of sodium cations. Furthermore, in the case of homotopic anion receptor **3** the addition of chloride anions in the presence of sodium cations resulted in smaller changes in reduction potentials relative to chloride anion association. This difference is a consequence of ion-pair formation out of the receptor, in the case of the binding event involving the homotopic receptor **3**, lacking a crown ether unit.

In the case of acetate and benzoate anions, different behavior was observed. Specifically, upon addition of 1 equiv of carboxylate anions the potential of the peak was shifted considerably, and excess of anions added resulted in no further changes in the cyclic voltammogram. This could suggest strong complexation of acetate and benzoate toward receptor **1**.

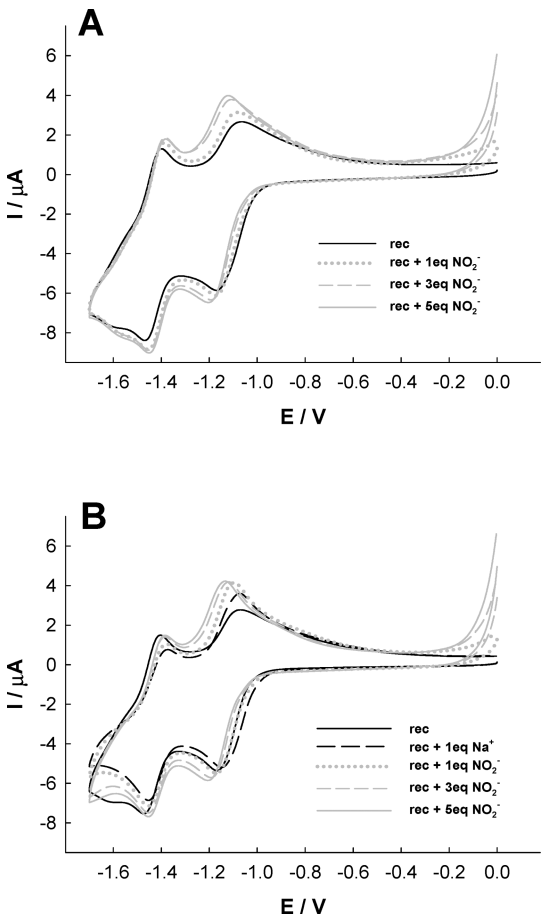

Figure 5. Cyclic voltammograms recorded for 0.5 mM solution of receptor **1** (solid black line), after adding 1, 3, and 5 equiv of $TBANO_2$ (gray lines) (A); after adding 1 equiv of $NaClO_4$ (dashed black line) and then after adding 1, 3, and 5 equiv of $TBANO_2$ (gray lines) (B) in acetonitrile. The concentration of supporting electrolyte $TBAPF_6$ was 0.1 M, and scan rate was 100 mV s^{-1}.

Table 4. Changes in Reduction Potentials (mV) of Receptors 1 and 3 after Addition of Various Amounts of Anions and Sodium Salts[a]

	Cl^-		Br^-		NO_2^-		NO_3^-	
equiv	**1**	**1** + Na^+	**1**	**1** + Na^+	**1**	**1** + Na^+	**1**	**1** + Na^+
1	20	29	2	3	5	23	*b*	*b*
3	46	58	6	14	22	44	3	6
5	62	79	11	20	34	56	7	8

	Cl^-			
equiv	**2**	**2** + Na^+	**3**	**3** + Na^+
1	20	28	16	8
3	40	45	44	36
5	51	58	65	54

[a]Anions added as TBA salts, sodium salts added as mixture of TBA salts and 1 equiv of $NaClO_4$, $\Delta E = E_{p(I)\ \text{free receptor (or + 1 equiv of Na}^+\text{)}} - E_{p(I)\ \text{anion complex}}$. [b]The reduction potentials shifts were too small to determine ΔE accurately.

However, careful analysis of the response of receptor **1** upon addition of 0.25, 0.5, and 0.75 equiv of of carboxylate anions showed that, unlike the other anions investigated, in this case there is no gradual shifting of the peak but rather a disappearance of the old one and the formation of a new

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peak. This can be attributed to the formation of a new species, namely, a deprotonated form of receptor **1**. Typical voltammograms recorded after adding AcO^- are presented in Figure 6.

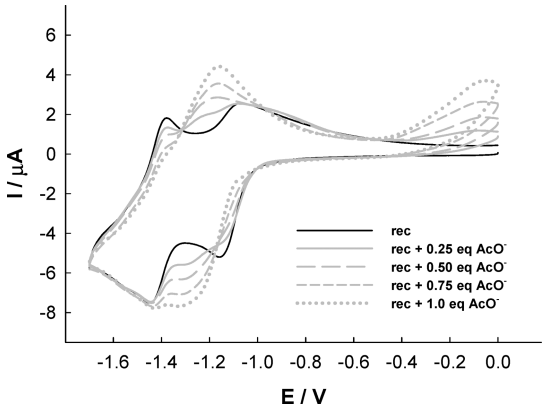

Figure 6. Cyclic voltammograms recorded for 0.5 mM solution of receptor **1** (solid black line), after adding 0.25, 0.50, 0.75, and 1 equiv of TBAAcO (gray lines) in acetonitrile. The concentration of supporting electrolyte $TBAPF_6$ was 0.1 M, and scan rate was 100 mV s^{-1}.

CONCLUSION

In conclusion, we have synthesized simple but effective salt receptors able to bind sodium salts selectively. Consisting of a thiourea anion binding domain supported with an anthraquinone-sensing unit, these receptors are able to sense anions and ion pairs optically and electrochemically. The cation binding site is linked to the receptor scaffold in such a way as to reinforce anion binding and, as a consequence, salt binding. Using titration experiments as well as X-ray measurement we have shown that strong sodium interaction with the crown ether unit is responsible for this enhancement in anion binding. The stability constants of the receptors' complexes with selected anions and salts were determined spectrophotometrically in acetonitrile solution, and all the anions tested (apart from carboxylates, which induce deprotonation of receptors) were found to associate with the salt receptors more strongly in the presence of sodium cations. A homotopic receptor structure lacking a cation binding domain showed no ability for effective ion-pair recognition. The spectroscopic investigations gained additional support from electrochemical measurements, showing that the addition of anions to the receptor **1** pretreated with sodium cations resulted in greater changes in reduction potentials as compared to the addition of anions to receptor **1** in the absence of Na^+.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.inorgchem.6b00132.

^1H and ^{13}C NMR spectra of compounds **4a**, **5a**, **6**, and receptors **1**, **2**, and **3**; $^1H-^1H$ ROESY of [**1**·Na^+]; representative UV−vis and ^1H NMR titration spectra of receptor **1**; dilution curve and Job plot of receptor **1**; UV−vis and NMR binding isotherms, cyclic voltammograms for **2** and **3**; crystal data of [**2**·$NaClO_4$] complex. (PDF)

X-ray crystallographic information on [**2**·$NaClO_4$]. (CIF)

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Notes

The authors declare no competing financial interest.

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