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Binding studies and anion-selective electrodes with neutral isophthalamide-based receptors†

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Two acyclic isophthalamide-based hosts have been synthesised and their anion binding properties have been evaluated by ^{1}H-NMR titrations. Different binding modes have been detected for the series of tested anions. The attachment of aminomethylpyrrole groups resulted in an improved binding selectivity. Additionally, the receptors have been incorporated as ionophores in plasticised polymeric membrane-based anion-selective electrodes. The potentiometric studies were in agreement with the NMR experiments and revealed a good sensing ability, considering the structural simplicity of the receptors and their interactions purely based on hydrogen bonding. These preliminary experiments have revealed an interesting selectivity towards highly hydrophilic anions such as fluoride and sulfate. Moreover, a particularly low detection limit ($9x10^{-7}$ M) has been determined for the fluoride anion.

Introduction

The topic of anion recognition has reached its maturity within the area of supramolecular chemistry.[1, 2] Throughout the last decades a vast diversity of anion receptors has been explored.[3-7] Despite the rich variety of reported binding units, there are certain building blocks which, due to their structural and chemical properties, have become authentic corner stones in the supramolecular chemistry of anions. This is the case of the easily accessible isophthalamide unit. Since Crabtree and co-workers firstly reported the employment of simple acyclic isophthalamide derivatives as neutral hosts for halide recognition,[8, 9] that building block has been extensively incorporated into acyclic,[10] macrocyclic[11, 12] and more intricate structures.[13] Additionally, the 1,3-relative arrangement of the amide groups has inspired the synthesis of related anion receptors with different aromatic and heteroaromatic spacers.[14-17] Interestingly, the easy derivatisation of the plain isophthalamide core has rendered many examples which illustrate how slight structural alterations can have a remarkable influence in the binding ability of the receptor.[18-20] In this regard, our interest in the design of pyrrole-based receptors[21-25] has led us to combine the isophthalamide fragment with pyrrole units which can contribute to expand and enhance the original binding cavity.

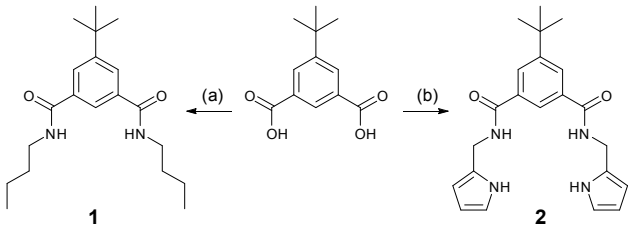
Focusing on the application of the isophthalamide motif, beyond the elemental anion recognition studies, recently, it has also been applied to a different discipline of the supramolecular chemistry of anions, playing the role of transmembrane anion transporters.[26-32] Nevertheless, it is quite surprising that among all the studies reported about isophthalamide derivatives, which demonstrate their great potential as anion receptors, these compounds have scarcely ever been studied in plasticised polymeric membrane ion-selective electrodes (ISEs).[33, 34] The incorporation of synthetic ionophores into the membrane represents a useful strategy for the improvement of selectivity in ion-selective electrodes. Additionally, the development of ionophores for anion-selective electrodes is a challenging goal to enhance their analytical application.[35,36] This becomes specially interesting when targeting hydrophilic anions in the Hofmeister series, since these species have to overcome the enthalpically unfavourable phase transfer from an aqueous solution into the electrode membrane. Thus, herein we report the synthesis and anion complexation studies of two neutral isophthalamide derivatives, as well as, the incorporation of these molecules as ionophores in anion-selective electrodes. These devices, fabricated with structurally simple isophthalamides, have rendered good results in terms of the response selectivity and sensibility towards highly hydrophilic anions such as fluoride and sulfate.

Results and Discussion

Outlined in Scheme 1 is the synthesis of receptors **1** and **2**. Treatment of 5-(*tert*-butyl)isophthalic acid with *N,N'*-Carbonyldiimidazole (CDI) in *N,N'*-Dimethylformamide (DMF), followed by addition of *n*-butylamine afforded the desired receptor **1**. Additionally, receptor **2** was synthesised by reaction of the corresponding 5-(*tert*-butyl)isophthaloyl dichloride with 2-aminomethylpyrrole in the presence of

triethylamine. Compounds **1** and **2** were fully characterised by NMR and HRMS analyses.

These isophthalamide-based hosts define an internal binding cavity whose number of available hydrogen-bond donor sites increase from three, in the case of **1**, to five, in **2**. In order to evaluate the binding affinities of receptors **1** and **2** towards a range of anionic guests, ^{1}H-NMR titration experiments were carried out with species of different geometry, namely spherical (F^-, Cl^-), angular (AcO^-, PhO^-) and tetrahedral ($H_2PO_4^-$, SO_4^{2-})[37] and DMF-d_7 was chosen as solvent to work under a competitive environment.



Scheme 1 Synthesis of receptors **1** and **2**. (a) CDI, *n*-butylamine, DMF, r.t.; (b) i) $SOCl_2$; ii) 2-aminomethylpyrrole, Et_3N, DMF, r.t.

Both receptors displayed qualitatively similar responses. In general, all the hydrogen bond donor groups, namely the amide and pyrrole NHs as well as the aromatic CH at the position 2 in the central ring, experienced a downfield shift due to the deshielding effect resulting from the interaction with the anionic guests. As expected, receptor **2** yielded more stable complexes as a consequence of the presence of the two appended pyrrole units, which supported the suitability of the designed molecule.

Table 1 Anion binding parameters for receptors **1** and **2** [a]

Host	Parameter	F^- [b]	Cl^-	AcO^-	BzO^-	$H_2PO_4^-$	SO_4^{2-}
1	K_a (M^{-1})	880 480	73	185	153	115	1040[b] 670
	Δδ (ppm)	2.13	0.71	1.55	1.51	1.23	2.28
2	K_a (M^{-1})	935 124	124	683	472	1330	[c] –
	Δδ (ppm)	2.18	0.55	1.54	1.65	1.48	1.74

[a] Determined in DMF-d_7 following the amide NH chemical shift, [Host] = $4x10^{-3}$ M, 293 K; error<10% in all cases. [b] K_{11} and K_{12}. [c] The titration isotherm could not be accurately fitted due to a too strong interaction (see ESI).

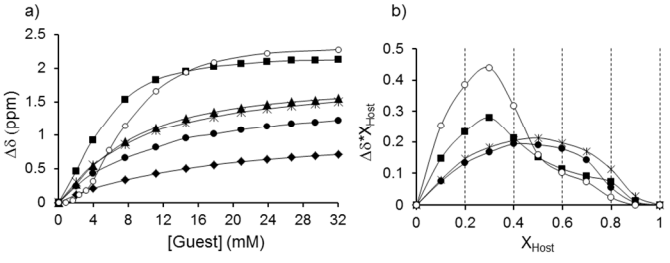


Fig. 1 a) Titration isotherms and b) Job plots of **1**. ■ F^-, ◆ Cl^-, ▲ AcO^-, ∗ $PhCOO^-$, ● $H_2PO_4^-$, ○ SO_4^{2-}, following the NH_{amide}.

Association constants were determined by non-linear fitting of the experimental binding isotherm and are summarised in Table 1.[38] Most of the titrated anions formed complexes with a 1:1 stoichiometry as it could be assessed by the method of continuous variation, Job plot (Fig. 1).[39]

Anyhow, it is worth highlighting the particular behaviour observed in the titrations with the fluoride anion (Fig. 2). Not surprisingly, the signals corresponding to the amide (and pyrrolic NHs in the case of compound **2**) shifted downfield in the course of the titration experiment. Nevertheless, the signal assigned to the CH in position 2 of the benzene ring, which initially shifted downfield, experience the opposite displacement towards lower chemical shifts when a slight excess of fluoride had been added. Simultaneously, the protons in the positions 4 and 6, which started shifting upfield, moved to higher chemical shifts. This two-phase titration curves are normally due to a change in the binding mode of the studied system.

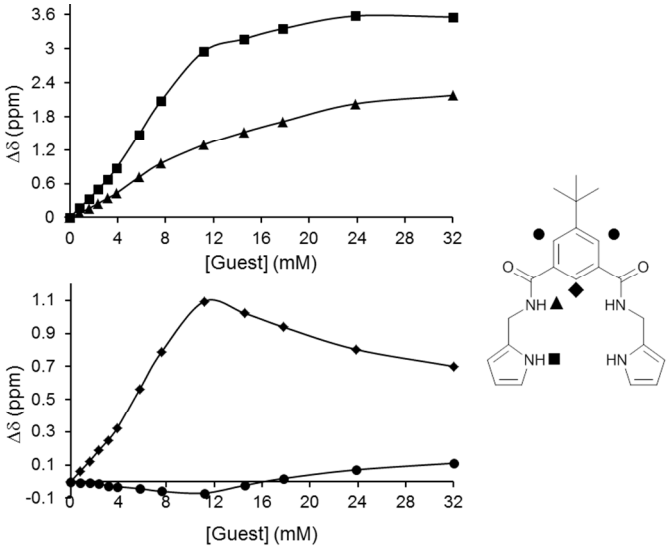


Fig. 2 TBAF titration isotherms monitoring different nuclei from **2**.

It is known that isophthalamide structures can adopt different conformations with a relative stability that follows the trend: *syn-anti* > *syn-syn* > *anti-anti*.[11, 40] In this case, the first aliquots of fluoride anion caused an induced fit effect which oriented the amide groups according to a *syn-syn* conformation, in which all hydrogen bond donor groups converged to bind the anion. The excess of fluoride anion can force the isophthalamide receptors to adopt an anti-anti conformation where two equivalents of anion would be accommodated. This conformational change perfectly correlates with the evolution of the ^{1}H-NMR signals previously described. Moreover, a maximum located at a molar fraction value of 0.3 could be detected in the Job plot (Fig. 1) which confirmed the 1:2 (H:G) stoichiometry of the final complex. A similar behaviour was also evidenced for the sulfate complexation by receptor **1**.

Concerning the cases with 1:2 (H:G) stoichiometry, in agreement with the measured binding constants (K_{11} > K_{12}) these responses correspond to a multiple equilibria system with

negative allosteric cooperativity. As a result, when the 1:1 stoichiometry prevails, the anion is bound by three and five hydrogen bonds in the receptors **1** and **2** respectively. In certain cases, the excess of anion induces a conformational change leading to 1:2 complexes where each anion is stabilised by two or three hydrogen bonds (Fig. 3). Accordingly, assuming that solvation effects are not relevant, a decrease in the enthalpy and the entropy of the system results in a thermodynamically unfavourable evolution from the 1:1 to the 1:2 complex.

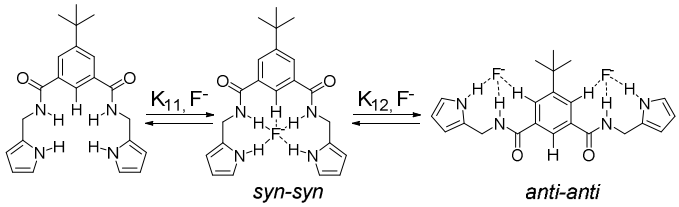


Fig. 3 Proposed binding modes for the complexation equilibria with fluoride.

Due to the interest in developing anion-selective electrodes, particularly in the case of highly hydrophilic anions such as sulfate and fluoride, the anion binding affinity displayed by **1** and **2** encouraged us to further develop a sensing device through the incorporation of the receptors into plasticised membrane electrodes. Most of the examples of molecular receptors used as ionophores in plasticised polymeric membranes for the determination of anionic analytes are based on metalorganic compounds.[41] The strong dative bond from a Lewis acid-base interaction between the metal centre and the anionic species represents the driving force which influences the ion-exchange equilibrium happening in the membrane. Thus, neutral receptors have less frequently been explored as anion ionophores in ISEs.[42-46] Nevertheless the combination of several weak interacting sites, adequately arranged in the structure of the receptor, can contribute to an enhanced binding selectivity as it happens in biological systems.

In this regard, plasticised polymeric membranes with different weight percentage compositions (Table 2) were prepared as described in the experimental section with polyvinyl chloride (PVC) as polymeric matrix, 2-nitrophenyloctyl ether (NPOE) as plasticiser, receptors **1** or **2** as ionophores and tridodecylmethylammonium chloride (TDMACl) as ionic additive.

Table 2 Optimisation of membrane composition (w/w)

Membrane	PVC	NPOE	Receptor **1**[a]	Receptor **2**[a]	TDMACl
A	33	66	1.0		
B	33	66			1.0
C	32.7	65.5	0.8 (1.4)		1.0
D	32.6	65.3	1.1 (2.0)		1.0
E	32.4	64.7	1.9 (3.3)		1.0
F	32.6	65.1		1.3 (2.0)	1.0

[a] Ionophore/TDMACl molar ratio is given in brackets.

Among the different available plasticisers,[47-49] the choice of NPOE arises from its high dielectric constant, which prevents the formation of ion-paired species in the membrane and correlates well with the previously described binding experiments performed in solution. NPOE is commonly used when working with membranes based on hydrogen-bond forming ionophores.[50, 51]

The presence of ionic additives, which promote the ion-exchange process, plays a critical role in the optimisation of the response for ionophore-based ion-selective electrodes.[52] In our case, it was observed that a membrane containing the ionophore and no cationic additive (membrane A) showed only a weak response towards all the tested anions (perchlorate, salicylate, thiocyanate, iodide, nitrate, bromide, chloride, fluoride, sulfate, acetate, dihydrogenphosphate, oxalate and hydrogen carbonate anions). On the contrary, when a cationic additive was incorporated (membrane D) a good potential response was observed, as shown in Fig. 4a and 4b for chloride and fluoride, respectively.

The influence of the ionophore-to-ionic additive molar ratio on the potentiometric response of the membranes was studied by keeping the amount of ionic additive constant in the membrane and varying the amount of receptor **1**, to cover a molar ratio range between 0 and 3.3 (membranes B-E).

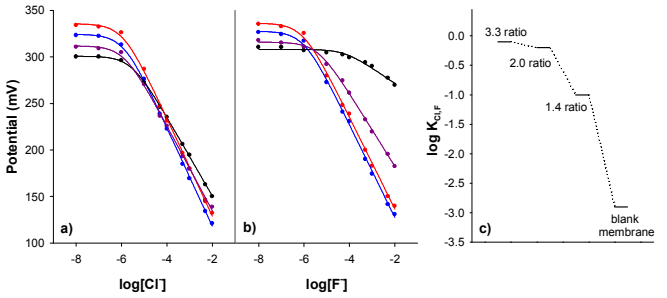


Fig. 4 Calibration graphs for different molar concentrations of (a) chloride and (b) fluoride using membranes with different ionophore-to-ionic ratios. (Membrane B: black; C: purple; D: blue; E: red). (c) Plot of the logarithmic selectivity coefficients for different ionophore-to-ionic additive molar ratio.

As can be seen in Fig. 4a and 4b, the total span of the potential response for chloride and fluoride increased with the ionophore-to-ionic additive ratio up to a molar ratio of 2.0, remaining almost constant beyond that point. This effect was more accused for fluoride than chloride and it became manifest by an increase in the selectivity coefficient $K_{Cl,F}^{pot}$ (Fig. 4c). In other words, this change in the coefficient indicated an increase in the selectivity for fluoride versus chloride. This fact was in good agreement with the complexation constant values found for receptor **1** with these anions. Taking all these results into account an ionophore/TDMACl molar ratio of 2.0 was used for further studies.

Calibration plots with membranes B, D and F were obtained for all the studied anions (Fig. 5). The blank membrane (membrane B) revealed the expected Hofmeister trend dictated by the lipophilicity of the anion. Nevertheless, the incorporation of isophthalamide receptors **1** or **2** into the electrode membrane (membranes D and F) altered this order and the magnitude of the total potential response span. A significant enhancement in

the potentiometric response was detected for the fluoride anion, in the case of ISEs containing the receptor **1** and for fluoride and sulfate anions in the case of receptor **2**.

It is worth highlighting the difficulty in potentiometrically sensing the fluoride anion with plasticised polymeric membranes due to its high hydration energy,[53] which reinforces the adequacy of the isophthalamide derivatives as neutral ionophores.

Additionally, the response of membranes containing either of two ionophores towards hydroxyl anions was also obtained by using sodium hydroxide. No potentiometric response was observed up to a concentration $5x10^{-4}$ M. From this concentration a small potential change was found (20 to 30 mV) for the maximum concentration assayed 10^{-2} M.

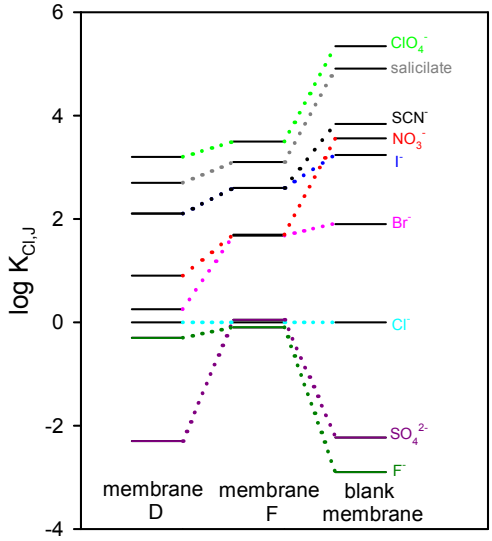


Fig. 5 Pot of the logarithmic selectivity coefficients obtained for membranes containing receptor **1** or receptor **2** (membranes D and F respectively) and for blank membrane (membrane B).

This screening of anionic species enabled the calculation of the selectivity coefficients[54] by the separate solutions method for equal concentration of primary (chloride) and interfering anion (J) (Figure 5 and Table S1 in the ESI).[55] Due to the frequent use of chloride as primary ion in the literature, we adopted this criterion for comparative purposes.

As it is observed in Figure 5, the most relevant change in the selectivity of the electrodes containing isophthalamide receptors, when compared to the blank membrane, corresponded to fluoride, whose selectivity over chloride increased about 500-fold. Regarding receptor **2** the response for sulfate and dihydrogenphosphate anions, produced an increase in the selectivity over chloride of about 200-fold and 10-fold respectively. Calibration parameters obtained for fluoride and sulfate anions are shown in Table 4.

Table 4 Potentiometric response characteristics

	Membrane D	Membrane F	
Parameter	Fluoride	Fluoride	Sulfate
Total span (mV)	200	164	220
Slope (mV/dec)[a]	-51.7±0.2	-47.3±0.1	-31.1±0.2
Linear range (M)	10^{-5} - 10^{-2}	10^{-5} - 10^{-2}	$5x10^{-5}$ - 10^{-2}
Detection limit (M)[a]	$(9.0±0.3)x10^{-7}$	$(1.7±0.2)x10^{-6}$	$(2.5±0.2)x10^{-5}$
Response time (s)[b]	<10	<11	<12

[a] Mean value ± SD (n=3). [b] Time required to reach 95% of equilibrium potential at different anion concentrations. This time was measured for all the points in the calibration plot.

Interestingly, a fast response time was obtained for both electrodes (See time trace in ESI).The electrode with receptor **1** as ionophore displayed a higher slope and a lower detection limit for fluoride than electrode with receptor **2**. Moreover, the fabricated electrodes displayed a linear response over three concentration decades. Additionally, a detection limit of $9.0x10^{-7}$ M could be determined from these preliminary studies, which is slightly lower than that commonly described for commercially available electrodes based on lanthanum fluoride membranes. Recently, several fluoride ionophores mainly based on metalorganic complexes Al and Zr have been published in the literature.[56-63] These compounds can bind fluoride by forming dative-covalent bonds with the metal centres. Despite the good selectivity claimed for these compounds as potentiometric sensors, the reported limits of detection do not reach the sensitivity achieved by the isophthalamide-based ISEs. This highlights the goodness of our results, which have been obtained with ionophores that exclusively interact through hydrogen bonds in plasticised membrane electrodes showing a highly selective profile towards fluoride, very good limit of detection and rapid response time. These characteristics point to real application opportunities, i.e. determination of fluoride in mouthwashes, toothpastes[64] and certain dietary supplements[65] and food stuffs,[66,67] but this purpose escapes from the scope of the present work.

Moreover, a significant response was obtained for the electrode with receptor **2,** which showed a near-Nernstian behaviour over 2.5 concentration decades for the very hydrophilic sulfate anion. It is worth recalling the difficulty in detecting anions with high hydration energy using ion-selective electrodes, due to the biphasic transfer of the analyte that governs the functioning of these devices. This hydrophilicity is the reason why the electrode with receptor **1** did not detect sulfate anion. The Gibbs free energies of sulfate and fluoride hydration are -1080 kJ/mol and -465 kJ/mol respectively.[68] In agreement with the previously discussed NMR experiments, receptor **1** had very similar binding constants for fluoride and sulfate. Thus, the anion hydration becomes an energy barrier for the sulfate to be sensed by the electrode. Accordingly, the hydration energy also justifies the results obtained for the electrode with receptor **2**. Although a better interaction could be qualitatively determined for sulfate over fluoride by NMR titration experiments, the higher hydration energy of sulfate makes more difficult its transfer to the plasticised membrane. Nevertheless,

the very strong interaction determined for receptor **2** with sulfate, still makes possible that this anion can be detected by the electrode. Only few examples of sulfate-selective electrodes have been reported in the literature using synthetic ionophores (either metalorganic,[69] positively charged[70] or neutral[71-76]). Regarding the electrode fabricated with receptor **2**, the wide concentration range with a Nernstian response, the low detection limit and the fast response time (Table 4) are features that support its suitability to be applied for the determination of sulfate anion.

Conclusion

The synthesis of isophthlamide based receptors with different number of hydrogen bond donor sites has been described. Anion binding experiments in DMF solution revealed a preferential complexation of fluoride, dihydrogenphosphate and sulfate with different binding modes being detected by ^{1}H-NMR. The incorporation of these isophthalamide derivatives as ionophores in ion-selective electrodes has been described. A study on potentiometric anion sensing, exclusively based on hydrogen bond interactions, has revealed a good selectivity and sensitivity towards fluoride anion, and sulfate anion in the case of receptor **2**. These results prove the adequacy of isophthalamide-based receptors to work as ionophores for the preparation of anion-selective electrodes. A detection limit lower than the commercially available fluoride ion-selective electrodes based on lanthanum fluoride membrane has been achieved.

Experimental Section

General

Reagents used as starting materials were commercially available and were used without further purification. Solvents were dried following the usual protocols. Unless stated otherwise, all reactions were carried out under nitrogen atmosphere. Column chromatography was run with silica gel 60 A CC 70-200 μm as stationary phase and using HPLC grade solvents. Melting points were measured in a Reichert instrument and are not corrected. ^{1}H-NMR and ^{13}C-NMR experiments were recorded on either a Bruker AV300 or AV 400 instrument. Chemical shifts are referred to the residual peak of the solvent and are given in ppm. *J* values are given in Hz. Mass spectrometry was recorded on HPLC-MS TOF 6220 instrument. Potentiometric measurements were recorded using a homemade high-impedance data acquisition 16-channel box connected to a PC by USB. An Orion Ag/AgCl double-junction reference electrode (Orion 90-02) containing 10^{-2} M KCl in the outer compartment was also used. Polyvinyl chloride (PVC) of high molecular weight, 2-nitrophenyl octyl ether (NPOE), tridodecylmethylammonium chloride (TDMACl) and tetrahydrofuran (THF) were purchased from Fluka. Perchlorate, salicylate, thiocyanate, iodide, nitrate, bromide, chloride, sulfate, acetate, dihydrogenphosphate, fluoride and hydrogen carbonate, solutions were prepared by dissolving the corresponding sodium salts in Milli-Q water.

Synthetic procedure

5-(*tert*-Butyl)-*N,N'*-dibutylisophthalamide, 1. Over a stirred solution of 5-(*tert*-butyl)isophthalic acid (0.4 g, 1.8 mmol) in anhydrous dimethylformamide (30 mL), under nitrogen atmosphere, *N,N'*-carbonyldiimidazole (1.17 g, 7.2 mmol) was added. The resulting mixture was stirred at room temperature for 3 hours. Next, freshly distilled *n*-butylamine (0.89 mL, 9.0 mmol) was added dropwise and the reaction mixture was then stirred at room temperature for 8 hours. The solvent was removed under reduced pressure and the residue was treated with *n*-hexane. The resulting precipitate was filtered and dried under vacuum. The isolated white solid correspond to the desired pure compound **1** (0.48 g, 80%). Mp 125-127 ºC. ^{1}H-NMR δ (300 MHz, $CDCl_3$) 0.89-0.94 (6H, m), 1.30-1.40 (13H, m), 1.5-1.6 (4H, m), 3.35-3.55 (4H, m), 6.7 (2H, br s, NH_{amide}), 7.90-8.00 (3H, m); ^{13}C-NMR δ (75 MHz, $CDCl_3$) 13.8 (2xCH_3), 20.1 (2xCH_2), 31.1 (3xCH_3), 31.6 (2xCH_2), 34.9 (C_q), 39.9 (2xCH_2), 122.3 (CH), 127.1 (2xCH), 134.6 (2xC_q), 152.4 (C_q), 167.4 (2xC=O). HRMS-(*m/z*) for $C_{20}H_{33}N_2O_2$, found 333.2538 $(M+H)^+$, calcd: 333.2537.

5-(*tert*-Butyl)-*N,N'*-(pyrrol-2-ylmethyl)-isophthalamide, 2. A solution of 5-(*tert*-butyl)isophthalic acid (0.6 g, 2.7 mmol) in $SOCl_2$ (60 mL) was refluxed for 20 hours under nitrogen atmosphere. Then, the reaction mixture was allowed to cool to room temperature and the remaining $SOCl_2$ was evaporated under reduced pressure. The resulting residue was washed three times with dry toluene and concentrated under vacuum. Following, the residue was dissolved in dry dichloromethane (20 mL) and added dropwise over a stirred solution of 2-aminomethylpyrrole (0.65 g, 6.75 mmol) and freshly distilled triethylamine (1.76 mL, 13.50 mmol) in dry dichloromethane (15 mL) under nitrogen atmosphere. The reaction mixture was stirred under these conditions for 8 h. The solvent was removed under vacuum and the residue was purified by column chromatography on silica gel eluting with ethyl acetate: dichloromethane (1:2) to isolate **2** as a white solid (0.61 g, 60%). Mp 113-116 ºC. ^{1}H-NMR δ (300 MHz, DMSO-d_6) 1.33 (9H, s), 4.42 (4H, d, J = 5.4), 5.91-5.93 (4H, m), 6.62-6.65 (2H, m), 8.01 (2H, s), 8.18 (1H, s), 8.85 (2H, t, J = 5.4, NH_{amide}), 10.57 ppm (2H, br s, $NH_{pyrrole}$); ^{13}C-NMR δ (75 MHz, DMSO-d_6) 31.0 (3xCH_3), 34.8 (C_q), 36.3 (2xCH_2), 105.9 (2xCH), 107.2 (2xCH), 117.1 (2xCH), 123.9 (CH), 126.7 (2xCH), 128.9 (2xC_q), 134.3 (2xC_q), 150.9 (C_q), 166.0 (2xC=O). HRMS-(*m/z*) for $C_{22}H_{27}N_4O_2$, found 379.2116 $(M+H)^+$, calcd: 379.2129.

Titration Experiments

A stock solution of the corresponding receptor was prepared in deuterated dimethylformamide with an estimated water content of 0.15% v/v, [Host] = $4x10^{-3}$ M. The anions, used as tetrabutylammonium salts, were then dissolved with the appropriate volume of the former solution to obtain the correct concentration of the titrant. Aliquots of the latter solution were

added to the solution which contained the receptor, without having to consider any dilution effects on the titrated species.

Membranes and Electrodes Preparation

Membranes summarised in Table 2 were prepared by dissolving appropriate amounts of the corresponding membrane components (PVC, NPOE, ionophore and ionic additive) in 3 mL of THF. This solution was poured into a Fluka glass ring (inner diameter 28 mm, height 30 mm) and allowed to settle overnight until total evaporation of THF had occurred, to obtain a thin plastic membrane. A 6-mm-diameter piece was cut out with a punch for ion-selective membranes and incorporated into a Fluka electrode body ISE containing $1x10^{-4}$ M KCl as internal filling solution. The electrodes were conditioned in water until they reached a constant potential. When not in use, electrodes were kept immersed in water.

Potentiometric measurements

Dynamic calibrations of the electrodes were made by adding, while stirring, small aliquots of the corresponding standard solution of anion, used as sodium salts, to cover the concentration range from $1x10^{-7}$ to $1x10^{-2}$ M. The electrode was conditioned in water until the original potential was recovered before each new calibration. If the base line did not fully reach that value, the water was renewed. The steady-state potentials were plotted versus logarithmic values of the corresponding concentrations. When the potentiometric response for the anion was of Nikolsky-Eisenman type, data were fitted to the equation:

$$E = E^0 + S \cdot \log(C_A + DL) \quad (1)$$

where Eº is the standard potential of the cell, S is the calibration slope, C_A is the concentration of the corresponding anion and DL is the detection limit. When the potentiometric response for the anion displayed an initial super-Nernstian behaviour, only the data in the linear range (Nernstian response) were fitted to a linear function, and the limit of detection was calculated using the extended definition given by IUPAC as the measured potential which deviates S·log2 from the extrapolated Nernstian response.[77] All potentiometric measurements were performed at room temperature in non-buffered solutions. From pH measurements of these solutions it was checked that all the anions assayed are almost entirely as the mentioned anionic form.

Logarithmic selectivity coefficients were calculated applying the separate solution method.[55] The potentials (E) obtained at the same concentration (10^{-2} M) of primary (chloride) and interfering anion (J) were substituted in equation (2):

$$\log K_{Cl,J}^{pot} = \frac{(E_J - E_{Cl})}{S_{Cl}} + (1 - \frac{z_{Cl}}{z_J}\log C_{Cl}) \quad (2)$$

where S_{Cl} is the calibration slope for chloride, z_{Cl} and z_J are the ionic charges of the anions and C_{Cl} is 10^{-2} M.

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Notes and references

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†Electronic Supplementary Information (ESI) available: ^{1}H-NMR spectra, ^{13}C-NMR spectra, titration isotherms and Job plots of **2,** fit plots for the NMR titrations. See DOI: 10.1039/b000000x/

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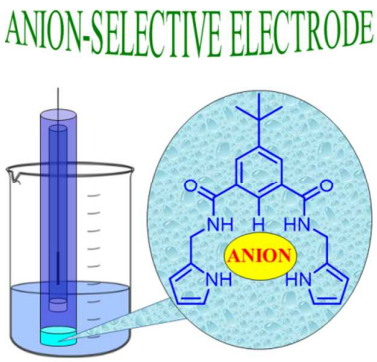

The incorporation of neutral and structurally simple isophthalamide-based receptors into plasticised polymeric membrane anion-selective electrodes has afforded devices with a good sensing ability.