Synthesis of novel uranyl salophene derivatives and evaluation as sensing molecules in chemically modified field effect transistors (CHEMFETs)

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Several anion receptors have been synthesized based on the uranyl salophene moiety. The binding selectivity of the receptors can be influenced by substituents near the uranyl binding site of the receptor, which change the electron density of the uranyl center, the lipophilicity of the binding cleft, or provide sites for hydrogen bonding. The differences in binding selectivity are reflected in the selectivity of potentiometric sensors (chemically modified field effect transistors, CHEMFETs) developed with these receptors. The use of a uranyl salophene derivative with phenyl substituents near the binding site yields acetate selective sensors with selectivity over much more lipophilic anions like Cl^- and Br^- (log $K^{Pot}_{AcO,j} = -1.2$). Lipophilic *N*-octanamido substituents near the uranyl center provide F^- selective CHEMFETs. The presence of urea moieties in the proximity of the binding site results in an even stronger F^- binding receptor which yields CHEMFETs which can detect F^- even in the presence of a 150-fold excess of the very lipophilic SCN^- anion (log $K^{Pot}_{F,SCN} = -2.2$).

Introduction

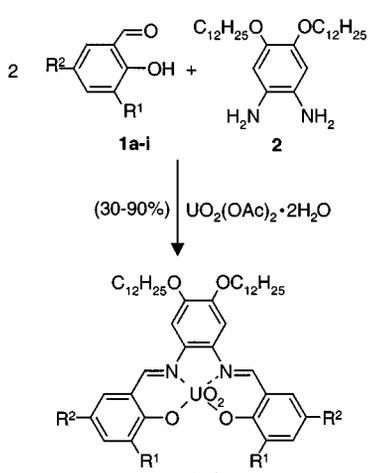
The selective detection of ions requires a chemical recognition process involving the specific interaction with a receptor molecule. Although for cations many receptors have been synthesized and used in sensing devices, the number of receptors that have been developed for selective anion binding is only limited.[1] In previous papers we have reported that *neutral* uranyl salophene derivatives show anion binding properties due to the Lewis acidic character of the uranyl center.[2,3] In order to make this class of anion receptors applicable as receptor molecules in polymeric membrane sensors like ion-selective electrodes (ISEs) and chemically modified field effect transistors (CHEMFETs), the salophene moiety has been modified with lipophilic aliphatic substituents.[4] The lipophilic uranyl salophene derivative **3a** shows a strong interaction with the $H_2PO_4^-$ anion, and this receptor could be successfully applied in CHEMFETs with selectivity towards this hydrophilic anion.[4,5] By introduction of substituents at the salophene moiety in close proximity of the anion coordination site of the uranyl center, the binding selectivity of uranyl salophene derivatives can be influenced. For example, the presence of the methoxy-substituents in uranyl salophene derivative **3b** results in sensors with an improved $H_2PO_4^-$ sensitivity.[5] When the $H_2PO_4^-$ anion is bound with one of the oxygen atoms to the uranyl center a hydrogen bond can be donated to the methoxy group and consequently the binding strength is increased. On the other hand, the presence of acetamido groups in derivative **3c** reduce the $H_2PO_4^-$ binding strength, but these hydrogen bond donating substituents induced strong binding for the F^- anion.[4,6]

This paper describes the synthesis of various new lipophilic uranyl salophene derivatives and their evaluation as sensing molecules in ISE and CHEMFET membranes. Besides the incorporation of hydrogen bond donating and accepting substituents near the uranyl binding center, substituents that affect anion binding by electronic or steric effects have also been included.

Results and discussion

Synthesis and properties of lipophilic uranyl salophene derivatives

The lipophilic uranyl salophene derivatives are easily synthesized by condensation of 1,2-dialkoxy-4,5-diaminobenzene (**2**) with salicylaldehyde **1a**–**i** in methanol and subsequent addition of uranyl acetate (Scheme 1).[4] By using salicylaldehyde



a $R^1 = R^2 = H$ **d** $R^1 = F$, $R^2 = H$
b $R^1 = OMe$, $R^2 = H$ **e** $R^1 = C_6H_5$, $R^2 = H$
c $R^1 = NHC(O)Me$, $R^2 = t$-butyl **f** $R^1 = R^2 = t$-butyl
g $R^1 = OCH_2C(O)NH(4\text{-}Me\text{-}C_6H_4)$, $R^2 = H$
h $R^1 = NHC(O)C_7H_{15}$, $R^2 = t$-butyl
i $R^1 = NHC(O)NHC_3H_7$, $R^2 = t$-butyl

Scheme 1

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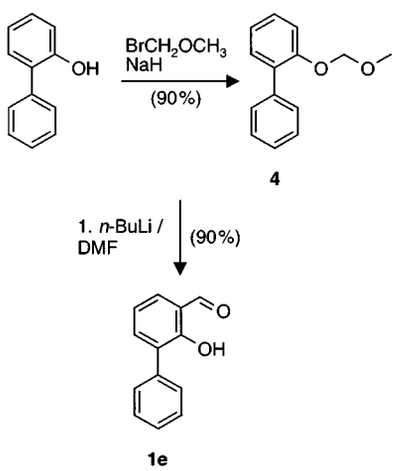
derivatives with the desired substituent at the 3-position, this substituent is introduced in the uranyl salophene receptor in close proximity to the uranyl center. For example the use of 3-fluorosalicylaldehyde (**1d**), results in the formation of derivative **3d** in 70% yield. The presence of the electron-withdrawing fluoro substituents in this compound lowers the electron density of the uranyl center resulting in a higher electrophilicity of the center. The opposite effect is obtained by the introduction of methoxy substituents as these are present in the previously synthesized methoxy-substituted derivative **3b**.

In derivative **3e** the phenyl substituents form a lipophilic cleft and a coplanar positioning of these substituents allows π–π interactions with aromatic guests.[7] The synthesis of **3e** starts with 2-hydroxy-1,1′-biphenyl-3-carbaldehyde (**1e**) which was obtained from 2-hydroxybiphenyl by first protecting the hydroxy moiety with a methoxy methyl ether group yielding **4**, followed by formylation with DMF and deprotection with HCl (Scheme 2). The aldehyde **1e** was reacted with **2** to give **3e** in

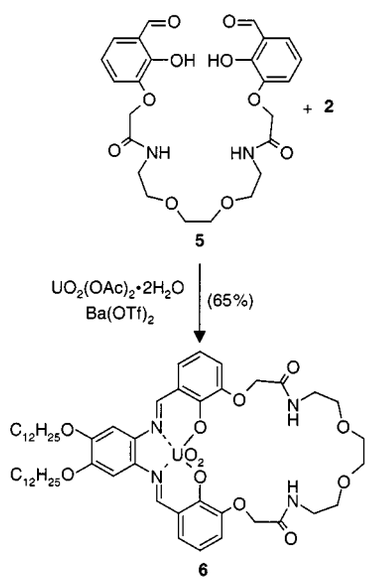


Scheme 2

69% yield. Derivative **3f** was obtained from 3,5-di-*tert*-butylsalicylaldehyde (**1f**) in 53% yield and also in this compound the binding cleft is rather apolar and small due to the presence of *tert*-butyl substituents.

In derivative **3g** the $-OCH_2CONH-$ moieties can contribute to the binding of dihydrogen phosphate anions by hydrogen donation from the amide hydrogen atoms and hydrogen bond acceptance from one ether oxygen atom. Such a binding mode was previously shown in the X-ray crystal structure of the phosphate complex of the corresponding salophene derivative lacking the dodecyl substituents.[2] The ^{1}H NMR spectrum of **3g** in DMSO-d_6 has the appearance that is normally expected for uranyl salophene derivatives, with a singlet signal of the imine hydrogen atom at 9.62 ppm. However, the spectrum of **3g** in $CDCl_3$ shows two singlets at 9.34 and 9.17 ppm, and also double signals of the amide hydrogen atoms (at 12.78 and 10.54 ppm) and the tolyl methyl hydrogen atoms (at 1.98 and 1.65 ppm) are clearly visible, similar to the signals observed for derivative **3c**.[8] This is probably due to the formation of dimers of **3g**, as is known from the X-ray crystal structure of the corresponding non-lipophilic derivative.[2] In this structure one amido oxygen atom is coordinated to the uranyl center of a second uranyl salophene molecule and *vice versa*. No change in NMR spectrum is observed upon dilution, indicating a high association constant. Alternatively, Corey–Pauling–Koltun (CPK) models show that the asymmetry in molecule **3g** can also be caused by intramolecular coordination of one of the amido carbonyl oxygens with the uranyl center. This is in contrast to derivative **3c** which can only form *inter*molecular interactions. Coordination of the carbonyl oxygen of **3g** to the uranyl center is also reflected in a shift of the C=O vibration in the IR spectrum which is present at 1608 cm^{-1} instead of 1685 cm^{-1} (as for **1g**).[9]

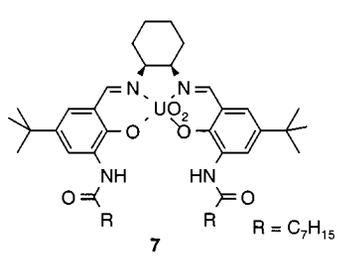
The amido substituents of uranyl salophene **6** are linked *via* a polyether bridge. This salophene derivative was obtained by cyclization of dialdehyde **5** with diamine **2** in the presence of $Ba(OTf)_2$ as a template, followed by addition of $UO_2(OAc)_2 \cdot 2H_2O$ (Scheme 3). In contrast to **3g**, the ^{1}H NMR spectra of



Scheme 3

this compound do not show any indication of the formation of dimers. The short bridge between the amido substituents reduces the flexibility of these substituents and no inter- or intramolecular interactions can be formed between the amido carbonyl and the uranyl center.

Because of the successful application of derivative **3c** in the development of F^- selective CHEMFETs, the lipophilicity of this derivative was further enhanced by introducing octanoic acid amido substituents (**3h**, **7**) instead of the acetamido moieties. Uranyl salene **7** was prepared by reaction of **1h** with *cis*-1,2-diaminocyclohexane. Although compound **7** lacks the



lipophilic dodecyloxy substituents, the octanoic acid amido substituents make this salene well soluble in for example chloroform. Like compound **3c**, derivatives **3h** and **7** also form dimers and double signals are present in the ^{1}H NMR spectra. Even the methyl hydrogen atoms of the octanoyl group of **3h**, which are located at a large distance from the coordinating carbonyl moiety, show a pair of triplets at 0.71 and 0.53 ppm.

In uranyl salophene derivative **3i** the presence of the urea moieties results in an increased number of donating hydrogen atoms in this receptor. The *N*-propylurea substituted salicylaldehyde derivative was obtained by first treatment of salicylaldehyde derivative **1c** with hydrazine (Scheme 4). In this procedure in one step the carbonyl moieties are protected and the acetyl moieties are removed by *trans*-amidation. Treatment with propyl isocyanate and HCl results in salicylaldehyde derivative **1i**.

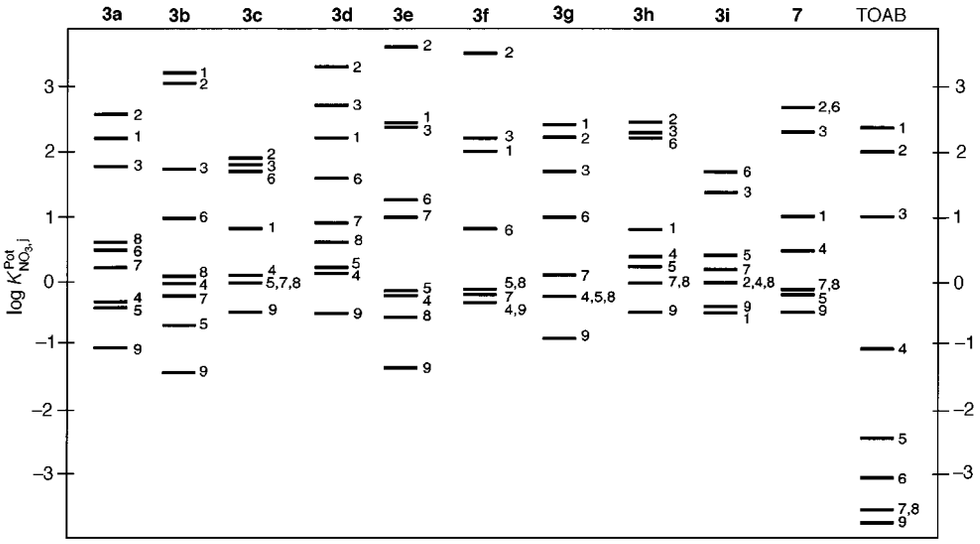
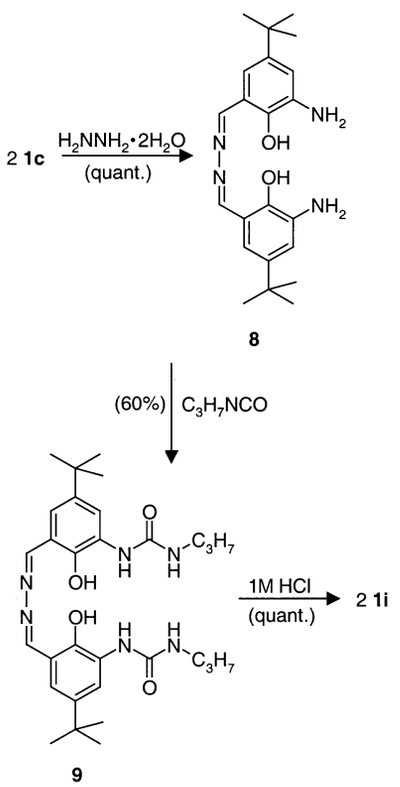


Fig. 1 SSM selectivity coefficients of ISEs with uranyl salophene derivatives **3a–i**, **6**, or **7** (1 wt% and 20 mol% TOAB in NPOE plasticized PVC membranes) or with 0.1 wt% of TOAB (Hofmeister series). 1: ClO_4^-, 2: SCN^-, 3: Sal^-, 4: Br^-, 5: Cl^-, 6: F^-, 7: AcO^-, 8: $H_2PO_4^-$, 9: SO_4^{2-}.



Scheme 4

Evaluation of the receptor properties in ion-selective membranes

The applicability of the novel lipophilic uranyl salophene derivatives in potentiometric sensor devices was first studied in ion-selective electrodes. For this purpose plasticized poly(vinyl chloride) (PVC) membranes were made containing 1 mg of the receptor, 33 mg of PVC, 66 mg of *o*-nitrophenyl *n*-octyl ether (NPOE) and 20 mol% (with respect to the receptor) of tetraoctylammonium bromide (TOAB). All compounds, with the exception of macrocycle **6**, are well soluble in the membrane at this concentration with the result that clear, homogeneous, orange membranes were formed. The sensor selectivity of the ISEs was evaluated according to the separate solution method (SSM) at pH 6 (0.01 M 2-morpholinoethanesulfonic acid (MES)) buffer and the results are depicted in Fig. 1. For comparison also the data of ISEs with salophene derivatives **3a–c** and the Hofmeister selectivity sequence obtained with ISE membranes with only TOAB are included. Several of the salophene receptors induce a different sensor selectivity. The ISEs with uranyl salophene derivatives **3c–g** all show increased selectivity towards the F^- anion and among the lipophilic anions enhanced selectivity is observed towards the small SCN^- anion with receptors **3e** and **3f**. The electron-withdrawing fluoro substituents of **3d** induce a decrease in sensor sensitivity towards NO_3^-. Consequently most SSM selectivity values are shifted to more positive values compared to receptors **3a** and **3b**. Furthermore, the apolar cleft formed by the phenyl substituents of salophene **3e** results in selectivity for AcO^- over NO_3^-, which is a remarkable result as the acetate ion is a hydrophilic anion which is close to $H_2PO_4^-$ and SO_4^{2-} in the Hofmeister series (see Fig. 1, TOAB). Remarkably, membranes with salophene **3g** do not show any preference for $H_2PO_4^-$ and an equal sensitivity is obtained as for SO_4^{2-}. This latter result was not expected on the basis of the previously determined association constants in DMSO-d_6 for salene derivatives related to **3g** (and **3b**) based on diaminocyclohexane ($K_a = 8.0 \times 10^3$ M^{-1} and 5.1×10^2 M^{-1}, respectively).[2] Dimerization of **3g**, as was observed in media like $CDCl_3$ and in the solid state, might reduce the binding properties of this receptor in the ion-selective membrane. A strong interaction between the amido oxygen atom and the uranyl center then competes with the interaction of the uranyl salophene with the $H_2PO_4^-$ anion.

Compared to the F^- binding uranyl salophene **3c,** the related but more lipophilic compounds **3h** and **7** give an even better selectivity over other hydrophilic anions and ClO_4^-, although the lipophilic SCN^- still severely interferes at equal or higher concentrations. By increasing the number of hydrogen bond donating sites, as in **3i**, even selectivity over this generally strongly interfering anion is obtained. Compared to the Hofmeister selectivities the presence of receptor **3i** in the membrane results in an increase in the F^- selectivity over SCN^- with a factor of 10^5.

The various ISEs were also investigated for selectivity towards anions that are only present in alkaline solutions, for example HPO_4^{2-} and HCO_3^-. Equal selectivity towards HPO_4^{2-}, HCO_3^-, NO_3^-, Cl^-, and F^- was observed for these sensors at pH 8, with the exception of the ISEs based on the uranyl sal(oph)enes **3h–i** and **7** which show an increased selectivity towards F^- even at this pH. Probably, at pH 8 for most sensors the interference of OH^- becomes dominant, thereby masking any other preferential binding of the receptor.[5]

Table 1 Sensor characteristics of acetate selective CHEMFETs with receptor **3e**

		log $K^{Pot}_{AcO,j}$ [slope mV decade^{-1}][a]				
Receptor	Det. limit[b]	NO_3^-	Br^-	Cl^-	$H_2PO_4^-$	SO_4^{2-}
3e	−3.5 [−56]	−0.3 [−49][c]	−1.2 [−49]	1.2 [−52]	−2.4 [−54]	−2.5 [−51]

[a] [j] = 0.1 M in 0.01 M MES, pH = 6.0. [b] log [AcO^-] in 0.01 M MES, pH = 6.0. [c] [j] = 0.01 M in 0.01 M MES, pH = 6.0.

Table 2 Sensor characteristics of F^- selecctive CHEMFETs with receptors **3h**, **3i** and **7**

		log $K^{Pot}_{F,j}$[slope mV decade^{-1}][a]				
Receptor	Det. limit[b]	SCN^-	ClO_4^-	NO_3^-	Br^-	Cl^-
3h	−3.4 [−54]	>0	−1.6 [−53]	−2.4 [−56]	−2.2 [−52]	−2.4 [−54]
7	−3.6 [−54]	>0	−1.6 [−54]	−2.5 [−55]	−2.1 [−50]	−2.5 [−54]
3i	−3.7 [−47]	−2.2 [−36]	−2.9 [−38]	−2.9 [−43]	−2.9 [−48]	−2.8 [−46]

[a] [j] = 0.1 M in 0.01 M MES, pH = 6.0. [b] log [F^-] in 0.01 M MES, pH = 6.0. [c] [NO_3^-] = 0.01 M in 0.01 M MES, pH = 6.0.

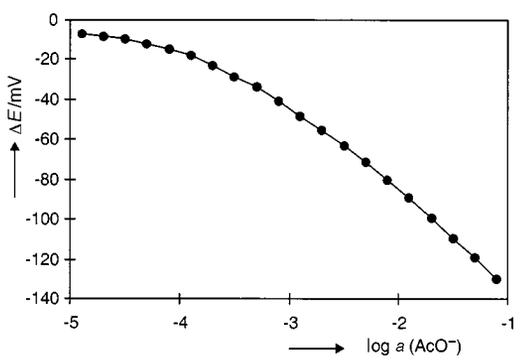


Fig. 2 Acetate response of a CHEMFET with receptor **3e** in the presence of 0.1 M NaH_2PO_4 (in 0.01 M MES, pH = 6.0).

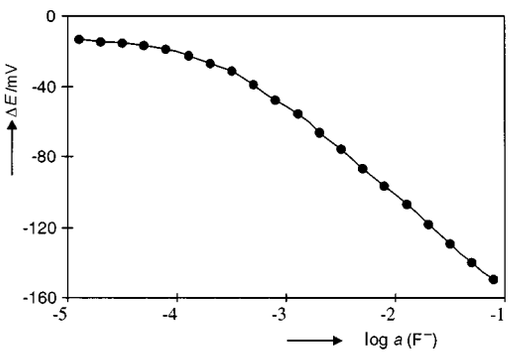


Fig. 3 Fluoride response of a CHEMFET with receptor **3h** in the presence of 0.1 M $NaNO_3$ (in 0.01 M MES, pH 6.0).

The performance of the uranyl salophene receptors in anion sensing

The SSM selectivity data obtained with ISEs show that the novel uranyl salophene derivatives **3e**, **3h**, **3i**, and **7** bind strongly to hydrophilic anions and can result in sensors with selectivities strongly deviating from the Hofmeister selectivity that is seen for TOAB (Fig. 1). Therefore these receptors were applied as the selector element in potentiometric CHEMFET microsensors. To this end membrane solutions of the same composition as used for ISEs were cast on top of the gate of the CHEMFETs and the response characteristics were evaluated.

It was found that ISEs with uranyl salophene receptor **3e** showed an increased selectivity towards acetate which can be attributed to a favorable interaction between the phenyl substituents and the acetate methyl group. The acetate anion is very hydrophilic and is located in the Hofmeister series between F^- and $H_2PO_4^-$. CHEMFETs with **3e** as anion receptor were investigated for their sensitivity and selectivity towards this anion at pH 6 (Table 1). The sensors respond to acetate at concentrations $\geq 3 \times 10^{-4}$ M with an almost Nernstian slope of −56 mV decade^{-1}. In spite of the high hydrophilicity of acetate, selectivity for acetate is obtained over more lipophilic anions like Cl^-, Br^-, and NO_3^- (log $K^{Pot}_{AcO,j} = -1.2$, −1.2, and −0.3, respectively). Also over $H_2PO_4^-$ a 250-fold selectivity is obtained (Fig. 2). Apparently, the phenyl substituents of **3e** which give a favorable interaction with the methyl group of the acetate anion, unfavorably interact with the tetrahedral $H_2PO_4^-$ anion and consequently reduce the binding strength of the $H_2PO_4^-$ anion with the uranyl center. The acetate over $H_2PO_4^-$ selectivity of sensors with **3e** is reversed compared to CHEMFETs with salophene **3a**. The latter sensors also show a much lower selectivity for acetate over bromide (log $K^{Pot}_{AcO,Br} = -0.6$ *vs.* −1.2) and over NO_3^- (log $K^{Pot}_{AcO,NO_3} > 0$ *vs.* −0.3) underlining the beneficial interaction of the acetate anion with the phenyl substituents of **3e**.

Fluoride is a strong hydrogen bond acceptor and this makes the ion very hydrophilic and difficult to extract into organic media. Selective measurement of fluoride anions with polymeric membrane sensors therefore requires the presence of extremely selective fluoride receptors in the membrane. The F^- selectivity observed for the uranyl salophene derivatives in several of the developed ISEs indicates that the uranyl center has a strong interaction with this anion and that hydrogen bond donating sites can enhance the selectivity. Previously, well functioning F^- selective CHEMFETs have been developed[4,6] based on uranyl salophene derivative **3c**. However, as already indicated by the SSM selectivity data, the increased lipophilicity of the amido binding site in **3h** improves the CHEMFET characteristics (Table 2). The F^- selectivity over NO_3^- and Cl^- is increased (log $K^{Pot}_{F,Cl} = -2.4$). As shown in Fig. 3 even in the presence of 0.1 M NO_3^- the sensors start to respond to F^- with an almost Nernstian slope of −56 mV decade^{-1} at concentrations $\geq 8 \times 10^{-4}$ M. Also in the presence of the other investigated anions the response slopes are improved compared to the less lipophilic receptor **3c**. The lipophilic *tert*-butyl substituents and the octanamido substituents improve the solubility of the uranyl salophene, and also uranyl salene derivative **7**, comprising the cyclohexane unit, is well soluble in the ion-selective membrane. This is reflected in the similar response slopes and selectivities of CHEMFETs with **3c** or **7**.

The CHEMFETs with *N*-propylurea substituted uranyl salophene derivative **3i** show an even higher F^- selectivity. The presence of 0.1 M of various anions which are more lipophilic

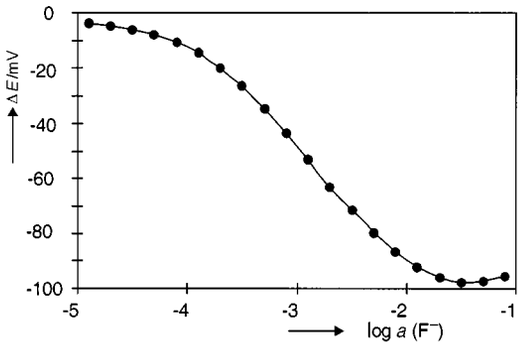


Fig. 4 Fluoride response of a CHEMFET with receptor **3i** in the presence of 0.1 M NaBr (in 0.01 M MES, pH 6.0).

than F^- has no influence on the detection limit of the sensors and F^- anions can be detected at concentrations $\geq 10^{-4}$ M (log $K^{Pot}_{Fj} = -2.9$, Table 2). Moreover, the use of this receptor results in selectivity for F^- over the lipophilic SCN^- anion (log $K^{Pot}_{F,SCN} = -2.2$). This anion is generally strongly interfering in SSM measurements with the uranyl salophene receptors as was shown in Fig. 1. The high selectivities induced by **3i** points to a strong F^- binding, and has the consequence that at high F^- concentrations coextraction takes place of F^- anions with sample cations (Donnan exclusion failure). This then results in a decrease of the response slope and eventually even in a positive *cation* response slope. In Fig. 4 it is shown that indeed the slope of the response starts to decrease at F^- concentrations above 0.05 M.

In summary, the present results illustrate that the use of the uranyl salophene moiety opens various possibilities for the development of anion receptors applicable in potentiometric sensors. The salophene moiety can be modified with substituents that change the nature of the anion binding site, *i.e.* vary the electron density of the uranyl binding center, vary the lipophilicity and aromaticity of the binding cleft, or provide in the availability of hydrogen bonding donating and accepting sites. In this paper it is shown that besides an improvement of the previously reported $H_2PO_4^-$ and F^- selective CHEMFETs, selectivity can be introduced towards organic acetate anions.

Experimental

Synthesis

NMR spectra were recorded in $CDCl_3$ on a Bruker AC 250 spectrometer. Residual solvent hydrogen atoms were used as internal standard and chemical shifts are given in ppm relative to TMS. Ion fast atom bombardment (FAB) mass spectra were obtained with *m*-nitrobenzyl alcohol as a matrix. Melting points are uncorrected. CH_2Cl_2 was distilled from $CaCl_2$ and stored over molecular sieves (4 Å). All commercially available chemicals were of reagent grade quality from Acros, Aldrich, or Merck, and were used without further purification. Bis-(dodecyloxy)derivative **2**[4] and aldehydes **1g**[2] and **5**[2] were made according to literature procedures.

CAUTION: *Care should be taken when handling uranyl-containing compounds because of their toxicity and radioactivity.*[10]

2-Methoxymethoxy-1,1′-biphenyl (4)

To a suspension of 14.2 mmol of NaH in 20 mL of dry DMF 2 g (11.8 mmol) of 2-phenylphenol was added at 55 °C. After 20 min the solution was allowed to cool to 35 °C and 1.25 mL of bromomethyl methyl ether (tech., 90%) was slowly added during 15 min. After 30 min the reaction was quenched by the addition of 1 mL of MeOH, 50 mL of toluene was added to the solution and the reaction mixture was washed with 50 mL of water. The aqueous layer was extracted with 50 mL of toluene, and the combined organic layers were washed with 5% NaOH, water, and brine. After drying over Na_2SO_4, the solvent was evaporated, yielding 2.3 g (90%) of **4** as a colorless oil. ^{1}H NMR δ 7.66 (dd, 2H, J = 8.1 Hz and 1.2 Hz, ArH), 7.56–7.33 (m, 7H, ArH), 7.25–7.20 (m, 1H, ArH), 5.21 (s, 2H, OCH_2OCH_9), 3.49 (s, 3H, OCH_2OCH_3). ^{13}C NMR δ 154.4 (s), 138.8 (s), 132.1 (s), 131.2 (d), 128.8 (d), 128.2 (d), 127.1 (d), 122.5 (d), 115.9 (d), 95.2 (t), 56.2 (q). MS-EI *m*/*z* 214.1 (M^+, calcd. for $C_{14}H_{14}O_2$ 214.1).

2-Hydroxy-1,1′-biphenyl-3-carbaldehyde (1e)

To a solution of 1.0 g of **4** in 40 mL of dry Et_2O, was added 1.1 eq *n*-BuLi (5.1 mL of a 1.6 M solution in hexane) at −78 °C. The mixture was slowly warmed to room temperature and a solution of 0.8 mL of DMF in 5 mL of Et_2O was added and after 2 h the solvent was evaporated. To remove the methoxy methyl ether group the crude product was dissolved in 50 mL of MeOH, and 6 g of NaCl and 5 g of H_2SO_4 were added to produce *in situ* HCl. After stirring for 30 min 50 mL water was added, and the solution was extracted with 50 mL Et_2O. The organic layer was washed with 0.1 M NaOH until the pH reached 7, and dried over Na_2SO_4. Evaporation of the solvent yielded 0.6 g (65%) of **1e**. ^{1}H NMR δ 10.30 (s, 1H, OH), 9.95 (s, 1H, CHO), 7.64 (m, 7H, ArH), 7.11 (t, 1H, J = 7.6 Hz, ArH).

N-(5-*tert*-Butyl-3-formyl-2-hydroxyphenyl)octanamide (1h)

To a solution of 0.50 g (3.0 mmol) of 2-amino-4-*tert*-butylphenol and 0.46 mL of Et_3N in 50 mL of $CHCl_3$ was added 0.56 mL (3.3 mmol) of octanoyl chloride at 0 °C. After stirring for 4 h 50 mL of water was added and the organic layer was washed with 0.1 M HCl. After drying over $MgSO_4$ the solvent was evaporated, yielding crude *N*-(5-*tert*-butyl-2-hydroxyphenyl)octanamide in quantitative yield. Mp: 74–75 °C. ^{1}H NMR δ 8.75 (s, 1H, OH), 7.48 (s, 1H, NH), 7.15 (dd, 1H, J = 8.5 and 2.3 Hz, ArH), 6.95 (d, 1H, J = 8.6 Hz, ArH), 6.92 (d, 1H, J = 2.3 Hz, ArH), 2.45 (t, 2H, J = 7.8 Hz, OCH_2), 1.75–1.70 (m, 2H, OCH_2CH_2), 1.45–1.26 (m, 17H, $(CH_2)_4CH_3$ and $C(CH_3)_3$), 0.88 (t, 3H, J = 6.5 Hz, CH_2CH_3). ^{13}C NMR δ 173.6 (s), 146.5 (s), 143.5 (s), 124.7 (s), 124.4 (d), 119.6 (d), 119.0 (d), 37.0 (t), 34.0 (s), 31.6 (t), 31.4 (q), 29.1 (t), 29.0 (t), 25.8 (t), 22.6 (t), 14.17 (q). MS-FAB *m*/*z* 292.2 ($[M + H]^+$, calcd. for $C_{18}H_{29}NO_2$ 292.2). Since this intermediate compound slowly decomposes, the crude product was used for further reactions. According to the procedure for the synthesis of **1c**,[4] aldehyde **1h** was prepared starting with 0.88 g (3 mmol) of *N*-(5-*tert*-butyl-2-hydroxyphenyl)octanamide. The crude product was purified using column chromatography (SiO_2, CH_2Cl_2–hexane 2:3) yielding 0.47 g (50%) of the product as an off-white solid. Mp: 83–84 °C. ^{1}H NMR δ 11.29 (s, 1H, ArOH), 9.86 (s, 1H, ArCHO), 8.79 (d, 1H, J = 2.2 Hz, ArH), 7.71 (br s, 1H, ArNH), 7.24 (d, 1H, J = 2.3 Hz, ArH), 2.42 (t, 2H, J = 7.3 Hz, $C(O)CH_2$), 1.75–1.70 (m, 2H, $C(O)CH_2CH_2$), 1.32–1.24 (m, 17H, $(CH_2)_4CH_3$ and $C(CH_3)_3$), 0.87 (t, 3H, J = 6.5 Hz, CH_2CH_3). ^{13}C NMR δ 197.0 (d), 171.7 (s), 147.9 (s), 143.4 (s), 127.1 (s), 124.6 (d), 123.3 (d), 119.1 (s), 37.9 (t), 34.5 (s), 31.7 (t), 31.2 (q), 29.2 (t), 29.0 (t), 25.4 (t), 22.6 (t), 14.1 (q). MS-EI *m*/*z* 319.1 (M^+, calcd. 319.2), 193.0 ($[M + H - C(O)C_7H_{15}]^+$). Anal. Calcd. for $C_{19}H_{29}NO_3$: C, 71.4; H, 9.2; N, 4.4. Found: C, 71.6; H, 9.3; N, 4.5%.

Bisamine intermediate 8

A solution of 0.6 g (2.9 mmol) of *N*-(5-*tert*-butyl-3-formyl-2-hydroxyphenyl)acetamide (**1c**) in 15 ml of hydrazine monohydrate was stirred for 3 days at 70 °C. Evaporation yielded the crude product which was triturated with EtOH. The product was obtained as a yellow solid in quantitative yield. Mp 222–224 °C. ^{1}H NMR δ 8.69 (s, 2H, imine NCH), 6.93 (d, 2H, J = 2.2 Hz, ArH), 6.79 (d, 2H, J = 2.2 Hz, ArH), 3.90 (br s, 4H,

NH_2), 1.32 (s, 18H, $C(CH_3)_3$). ^{13}C NMR δ 164.5 (d), 144.7 (s), 142.3 (s), 134.3 (s), 117.9 (d), 116.0 (d), 115.4 (s), 113.3 (d), 33.5 (s), 30.9 (q). MS-FAB *m*/*z* 382.2 (M^+, calcd. 382.2). Anal. Calcd. for $C_{22}H_{30}N_4O_2$: C, 69.1; H, 7.9; N, 14.7. Found: C, 69.7; H, 7.9; N, 14.7%.

Bisurea intermediate 9

To a solution of 0.18 g (0.47 mmol) of **8** in 30 ml of CH_2Cl_2 was added 0.18 ml (1.88 mmol) of propyl isocyanate. After stirring the solution overnight at room temperature water was added to destroy the excess of isocyanate, and subsequently the solvent was evaporated. The crude product was triturated with MeOH. Filtration yielded 0.14 g (54%) of the product as a yellow solid. Mp: 227–229 °C. ^1H NMR (DMSO-d_6) δ 8.66 (s, 2H, imine NCH), 8.35 (d, 2H, J = 2.6 Hz, ArH), 7.86 (s, 2H, ArNH), 6.93 (d, 2H, J = 2.6 Hz, ArH), 6.70 (br t, 2H, CH_2NH), 3.09 (q, 4H, J = 7.0 Hz, CH_2NH), 1.53–1.40 (m, 4H, $CH_2CH_2CH_3$), 1.23 (s, 18H, $C(CH_3)_3$), 0.87 (t, 6H, J = 7.3 Hz, CH_2CH_3). ^{13}C NMR δ 164.2 (d), 155.8 (s), 145.2 (s), 142.0 (s), 137.5 (s), 128.1 (d), 120.0 (d), 115.5 (s), 41.5 (t), 33.9 (s), 31.4 (q), 22.8 (t), 11.1 (q). MS-FAB *m*/*z* 553.3 ([M + H]$^+$, calcd. 554.1) Anal. Calcd. for $C_{30}H_{44}N_6O_4$·1.5MeOH: C, 62.9; H, 8.4; N, 14.0. Found: C, 62.9; H, 8.2; N, 13.9%.

***N*-(5-*tert*-Butyl-3-formyl-2-hydroxyphenyl) propyl urea (1i)**

A mixture of 0.26 g (0.47 mmol) of **9**, 0.09 g (0.52 mmol) $CuCl_2$·$2H_2O$, 1.5 mL (0.05 M) phosphate buffer, 2.5 ml H_2O, and 8 ml THF was stirred at 50 °C for 6 h. The reaction mixture was evaporated and washed with water and brine. After drying over Na_2SO_4, the solvent was evaporated. The crude product could be purified using column chromatography (SiO_2, CH_2Cl_2–EtOAc 9:1). The product was obtained as a yellow solid in quantitative yield. Mp 165–168 °C. ^1H NMR δ 11.15 (s, 1H, ArOH), 9.77 (s, 1H, ArCHO), 8.44 (d, 1H, J = 2.2 Hz, ArNH), 7.09 (d, 1H, J = 2.3 Hz, ArH), 5.26 (br t, CH_2NH), 3.17 (q, 2H, J = 6.9 Hz, $NHCH_2$), 1.57–1.42 (m, 2H, $CH_2CH_2CH_3$), 1.24 (s, 9H, $C(CH_3)_3$), 0.87 (t, 3H, J = 7.4 Hz, CH_3). ^{13}C NMR δ 197.1 (d), 155.3 (s), 147.9 (s), 143.3 (s), 128.1 (s), 124.1 (d), 122.0 (d), 119.1 (s), 42.2 (t), 34.5 (s), 31.2 (q), 23.3 (t), 11.4 (q). MS-FAB 279.2 ([M + H]$^+$ 279.2). Anal. Calcd. for $C_{15}H_{22}N_2O_3$: C, 64.7; H, 8.0; N, 10.1. Found: C, 64.6; H, 8.0; N, 9.9%.

General procedure for the synthesis of UO_2 salophenes 3d–i

A solution of 1.3 mmol of the appropriate aldehyde (3-fluorosalicylaldehyde (**1d**), **1e**, 3,5-di-*tert*-butylsalicylaldehyde (**1f**), **1g**, **1h**, or **1i**) and 0.3 g (0.65 mmol) of diamine **2** in 25 mL of methanol was refluxed for 1 h. Subsequently 0.27 g (0.65 mmol) of $UO_2(OAc)_2$·$2H_2O$ was added, and refluxing was continued for another 1 h. After the solution had cooled down, the precipitate was filtered off and washed with cold methanol to yield **3d**–**i** as an orange or red solid.

{6,6′-Difluoro-2,2′-[4,5-bis(dodecyloxy)-1,2-phenylenebis(nitrilo-κ*N*-methylene)]diphenolato-κ*O*}dioxouranium (3d). Yield 0.45 g (70%). Mp: 155–158 °C. ^1H NMR δ 9.28 (s, 2H, imine NCH), 7.60–7.29 (m, 4H, phenol ArH), 7.02 (s, 2H, phenylene diamine ArH), 6.65 (br d, 2H, phenol ArH), 4.02 (t, 4H, J = 6.3 Hz, OCH_2), 1.80–1.75 (m, 4H, OCH_2CH_2), 1.60–1.20 (m, 36H, $OCH_2CH_2(CH_2)_9$), 0.80 (t, 6H, J = 6.3 Hz, CH_3). ^{13}C NMR δ 163.5 (d), 156.5 (s), 152.6 (s), 150.4 (s), 140.1 (s), 129.8 (d), 126.3 (s), 120.6 (d), 117.2 (d), 104.7 (d), 69.9 (t), 31.9 (t), 29.8 (t), 29.7 (2 × t), 29.5 (t), 29.4 (t), 29.2 (t), 26.1 (t), 22.7 (t), 14.2 (q). MS-FAB *m*/*z* 989.9 ([M + H]$^+$, calcd. 989.5). Anal. Calcd. for $C_{44}H_{60}F_2N_2O_6U$·$1.5H_2O$: C, 52.0; H, 6.3; N, 2.8. Found: C, 51.8; H, 6.2; N, 2.9%.

{3,3′-[4,5-Bis(dodecyloxy)-1,2-phenylenebis(nitrilo-κ*N*-methylene)]bis(1,1′-biphenyl-2-olato-κ*O*)}dioxouranium (3e). Yield 0.48 g (69%). Mp: 209–210 °C. ^1H NMR δ 9.35 (s, 2H, imine NCH), 7.84 (dd, 4H, J = 7.0 and 1.4 Hz, ArH), 7.68 (dd, 2H, J = 1.7 and 7.3 Hz, ArH), 7.63 (dd, 2H, J = 7.9 and 1.6 Hz, ArH), 7.50 (t, 4H, J = 7.0 Hz, ArH), 7.39 (t, 2H, J = 7.2 Hz, ArH), 7.11 (s, 2H, phenylene diamine ArH), 6.81 (t, 2H, J = 7.5 Hz, ArH), 4.14 (t, 4H, J = 6.5 Hz, OCH_2), 1.90–1.85 (m, 4H, OCH_2CH_2), 1.60–1.20 (m, 36H, $OCH_2CH_2(CH_2)_9$), 0.88 (t, 6H, J = 6.3 Hz, CH_2CH_3). ^{13}C NMR δ 166.9 (s), 163.7 (d), 150.3 (s), 140.1 (s), 139.7 (s), 136.1 (d), 134.8 (d), 132.5 (s), 130.1 (d), 128.1 (d), 127.0 (d), 124.5 (s), 118.0 (d), 104.5 (d), 69.9 (t), 31.9 (t), 29.7 (t), 29.6 (t), 29.4 (t), 29.3 (t), 26.1 (t), 22.7 (t), 14.1 (q). MS-FAB *m*/*z* 1106.0 ([M + H]$^+$, calcd. 1105.6). Anal. Calcd. for $C_{56}H_{70}N_2O_6U$·H_2O: C, 59.9; H, 6.5; N, 2.5. Found: C, 60.0; H, 6.5; N, 2.6%.

{4,4′,6,6′-Tetra-*tert*-butyl-2,2′-[4,5-bis(dodecyloxy)-1,2-phenylenebis(nitrilo-κ*N*-methylene)]diphenolato-κ*O*}dioxouranium (3f). Yield 0.41 g (53%), recrystallized from CH_2Cl_2. Mp: 275–278 °C. ^1H NMR δ 9.36 (s, 2H, imine NCH), 7.75 (d, 2H, J = 2.4 Hz, phenol ArH), 7.47 (d, 2H, J = 2.3 Hz, phenol ArH), 7.06 (s, 2H, phenylene diamine ArH), 4.13 (t, 4H, J = 6.5 Hz, phenol ArH), 1.90–1.85 (m, 4H, OCH_2CH_2), 1.71 (s, 9H, $C(CH_3)_3$), 1.60–1.20 (m, 54H, $OCH_2CH_2(CH_2)_9$ and $C(CH_3)_3$), 0.87 (t, 6H, J = 6.3 Hz, CH_3). ^{13}C NMR δ 167.3 (d), 164.4 (s), 149.9 (s), 140.4 (s), 139.4 (s), 139.2 (s), 131.1 (d), 129.7 (d), 124.4 (s), 104.8 (d), 69.9 (t), 35.2 (s), 33.9 (s), 31.9 (t), 31.6 (q), 30.2 (q), 29.7 (t), 29.6 (t), 29.5 (t), 29.4 (t), 26.1 (t), 22.7 (t), 14.1 (q). MS-FAB *m*/*z* 1176.7 (M^+, calcd. 1176.8). Anal. Calcd. for $C_{60}H_{94}N_2O_6U$·$0.75CH_2Cl_2$: C, 58.8; H, 7.8; N, 2.3. Found: C, 58.7; H, 8.0; N, 2.4%.

{6,6′-Bis[2-(4-Methylphenylamino)-2-oxoethoxy]-2,2′-[4,5-bis(dodecyloxy)-1,2-phenylenebis(nitrilo-κ*N*-methylene)]-diphenolato-κ*O*}dioxouranium (3g). Yield 0.24 g (30%). Mp: 172–174 °C. ^1H NMR (DMSO-d_6) δ 10.63 (s, 2H, NH), 9.62 (s, 2H, imine NCH), 7.67 (d, 4H, J = 8.4 Hz, methylphenyl ArH), 7.55–7.50 (m, 6H, phenylene diamine ArH and phenol ArH), 6.95 (d, 4H, J = 8.3 Hz, methylphenyl ArH), 6.73 (t, 2H, J = 7.8 Hz, phenol ArH), 4.98 (s, 4H, $OCH_2C(O)$), 4.18 (t, 4H, J = 6.0 Hz, $OCH_2(CH_2)_{10}$), 2.19 (s, 6H, $ArCH_3$), 1.78 (m, 4H, OCH_2CH_2), 1.50–1.20 (m, 36H, $OCH_2CH_2(CH_2)_9$), 0.86 (t, 6H, J = 6.1 Hz, CH_2CH_3); ($CDCl_3$) 12.78 (s, 1H), 10.54 (s, 1H), 9.34 (s, 1H), 9.17 (s, 1H), 7.38 (br s, 2H), 7.23 (d, 4H, J = 7.0 Hz), 7.07 (s, 2H), 7.02 (d, 1H, J = 7.6 Hz), 6.83 (d, 1H, J = 7.6 Hz), 6.60–6.55 (m, 2H), 6.44 (d, 2H, J = 8.3 Hz), 5.75 (d, 2H J = 7.0 Hz), 5.55 (d, 1H, J = 15.9 Hz), 4.70 (d, 1H, J = 17.7 Hz), 4.30–4.05 (m, 6H), 1.98 (s, 3H), 1.90–1.85 (m, 4H), 1.65 (s, 3H), 1.51–1.20 (m, 36H), 0.81 (t, 6H, J = 5.5 Hz). ^{13}C NMR (DMSO-d_6) δ 167.4 (s), 164.9 (d), 160.4 (s), 149.8 (s), 149.3 (s), 139.9 (s), 135.8 (s), 132.5 (s), 129.5 (d), 129.0 (d), 125.1 (s), 122.6 (d), 119.6 (d), 116.5 (d), 105.1 (d), 71.2 (t), 68.9 (t), 31.3 (t), 29.1 (t), 29.0 (t), 28.8 (t), 28.7 (t), 25.7 (t), 22.1 (t), 20.3 (q), 13.9 (q). IR (KBr) ν 1608 (C=O, C=N), 908 (OUO) cm^{-1}. MS-FAB *m*/*z* 1301.6 ([M + Na]$^+$, calcd. 1301.6). Anal. Calcd. for $C_{62}H_{80}N_4O_{10}U$: C, 58.2; H, 6.3; N, 4.4. Found: C, 58.1; H, 6.1; N, 4.5%.

{4,4′-Di-*tert*-butyl-6,6′-bis(octanamido)-2,2′-[4,5-bis-(dodecyloxy)-1,2-phenylenebis(nitrilo-κ*N*-methylene)]diphenolato-κ*O*} dioxouranium (3h). The crude product was purified by column chromatochraphy (Al_2O_3). The impurities were removed with CH_2Cl_2–EtOAc 7:3 as eluent, after which the eluent polarity was increased to CH_2Cl_2–MeOH 95:5. Yield 0.53 g (60%). Mp: 123–126 °C. ^1H NMR (DMSO-d_6) δ 9.62 (s, 2H, imine NCH), 9.09 (s, 2H, NH), 8.75 (s, 2H, phenol ArH), 7.50 (br s, 4H, phenol ArH and phenylene diamine ArH), 4.16 (br t, 4H, OCH_2), 2.65 (br t, 2H, $NHC(O)CH_2$), 1.75–1.75 (m, 4H, OCH_2CH_2), 1.60–1.20 (m, 74H, $OCH_2CH_2(CH_2)_9$, $C(O)CH_2(CH_2)_5$ and $C(CH_3)_3$), 0.85 (br t, 6H, $(CH_2)_{11}CH_3$), 0.70 (br t, 6H, $(CH_2)_6CH_3$); ($CDCl_3$) δ 11.25, 8.86 (2 × s, 2H, NH), 9.34, 9.20 (2 × s, 2H, imine NCH), 9.00, 7.14 (2 × d, 2H,

J = 2.3 Hz, phenol ArH), 7.54, 7.26 (2 × d, 2H, J = 3.4 Hz phenol ArH), 7.05, 7.06 (2 × s, 2H phenylene diamine ArH), 4.14–4.04 (m, 4H, OCH_2), 2.50, 2.43 (2 × t, 4H, J = 7.3 Hz, $NHC(O)CH_2$), 1.85–1.80, 1.75–1.70 (m, 4H, OCH_2CH_2), 1.50–1.10 (m, 74H, $OCH_2CH_2(CH_2)_9$, $C(O)CH_2(CH_2)_5$ and $C(CH_3)_3$), 0.81 (br t, 6H, $(CH_2)_{11}CH_3$), 0.71, 0.53 (2 × t, 6H, J = 6.9 Hz, $(CH_2)_6CH_3$). ^{13}C NMR (DMSO-d_6) δ 170.9 (s), 165.3 (d), 156.5 (s), 149.2 (s), 139.8 (s), 138.4 (s), 129.4 (d), 124.8 (s), 121.9 (d), 105.0 (d), 68.9 (t), 33.7 (s), 31.4 (q), 31.3 (2 × t), 31.1 (t), 29.1 (2 × t), 28.7 (2 × t), 25.7 (t), 25.1 (t), 22.1 (t), 13.9 (2 × q). MS-FAB m/z 1347.9 ([M + H]$^+$, calcd. 1348.0). Anal. Calcd. for $C_{68}H_{108}N_4O_8U$: C, 60.6; H, 8.1; N, 4.2. Found: C, 60.9; H, 8.0; N, 4.3%.

{4,4′-Di-*tert*-butyl-6,6′-(propylaminocarbonylamino)-2,2′-[4,5-bis(dodecyloxy)-1,2-phenylenebis(nitrilo-κ*N*-methylene)]-diphenolato-κ*O*}dioxouranium (3i). The crude product was purified by column chromatography (SiO_2, CH_2Cl_2–MeOH 95 : 5). Yield 0.41 g (50%). Mp 164–167 °C. ^{1}H NMR (DMSO-d_6) δ 9.49 (s, 2H, imine NCH), 8.68 (d, 2H, J = 2.6 Hz, ArH), 8.28 (s, 2H, ArNH), 7.48 (br t, $NHCH_2$), 7.42 (s, 2H, phenylene diamine ArH), 7.27 (d, 2H, J = 2.6 Hz, ArH), 4.17 (br t, 4H, J = 6.2 Hz, OCH_2), 3.20–3.13 (m, 4H, $NHCH_2$), 1.81–1.74 (m, propyl CH_2CH_3), 1.59–1.46 (m, 4H, CH_2CH_3), 1.30 (s, 36H, $(CH_2)_9$), 1.25 (s, 18H, $C(CH_3)_3$), 0.97 (t, 6H, J = 7.3 Hz, CH_3), 0.85 (t, 6H, J = 7.0 Hz, CH_3). ^{13}C NMR δ 165.2 (s), 156.3 (d), 155.3 (s), 149.1 (s), 140.2 (s), 138.0 (s), 131.1 (s), 121.8 (d), 121.1 (d), 105.0 (t), 33.5 (s), 31.3 (t), 31.1 (t), 29.1 (t), 29.0 (t), 28.8 (t), 28.7 (t), 25.6 (t), 22.0 (t), 13.5 (q), 11.2 (q). MS-FAB m/z 1287.6 ([M + Na]$^+$, calcd. 1287.8). Anal. Calcd. for $C_{60}H_{94}N_6O_8U$·MeOH: C, 56.5; H, 7.6; N, 6.5. Found: C, 56.5; H, 7.4; N, 6.8%.

{27,28-Bis(dodecyloxy)-6,17-dioxo-6,7,8,9,11,12,15,16,17,18-decahydro-5*H*,14*H*-tribenzo[*qr*,*u*,*za*$_1$][1,7,10,16,4,13,21,24]-tetraoxatetraazoctacosin-κ^2*N*^{25,30}-3a^1,19a^1-diolato-κ*O*}-dioxouranium (6). To a refluxing solution of $Ba(OTf)_2$ (0.57 g, 1.0 mmol) in 50 mL of MeOH were added two separate solutions of bisaldehyde **5**[2] (0.24 g, 0.47 mmol) in 50 mL MeOH and **2** (0.22 g, 0.47 mmol) in 50 mL of MeOH using a perfusor in 0.5 h. After 0.5 h 0.20 g (0.47 mmol) of $UO_2(OAc)_2$·$2H_2O$ in 10 mL of MeOH was added and reflux was maintained for 0.5 h. The reaction mixture was evaporated and washed with a large amount of water. Recrystallization from CH_2Cl_2–MeOH yielded 0.29 g (65%) of **6**. Mp: 185–186 °C. ^{1}H NMR δ 9.27 (s, 2H, imine NCH), 9.20 (s, 2H, NH), 7.29 (d, 2H, phenol ArH), 7.07 (s, 2H, phenylene diamine ArH), 6.87 (d, 2H, J = 7.1 Hz, phenol ArH), 6.51 (t, 2H, J = 7.9 Hz, phenol ArH), 4.61 (s, 4H, $OCH_2C(O)$), 4.12 (t, 4H, J = 6.4 Hz, $OCH_2(CH_2)_{10}$), 3.70 (br s, 8H, CH_2OCH_2), 3.58 (br s, 4H, $NHCH_2$), 1.90–1.85 (m, 4H, OCH_2CH_2), 1.50–1.20 (m, 36H, $OCH_2CH_2(CH_2)_9$), 0.87 (t, 6H, J = 6.1 Hz, CH_2CH_3). ^{13}C NMR (DMSO-d_6) δ 163.3 (s), 160.1 (d), 150.4 (s), 149.6 (s), 140.3 (s), 124.4 (d), 117.7 (d), 104.6 (d), 77.2 (d) , 69.9 (t), 31.9 (t), 29.7 (2 × t), 29.4 (2 × t), 29.2 (t), 26.1 (t), 22.7 (t), 14.1 (q). IR (KBr) ν 1653 (C=O), 1606 (C=N), 903 (OUO) cm^{-1}. MS-FAB m/z 1213.4 ([M + H]$^+$, calcd. 1213.6). Anal. Calcd. for $C_{56}H_{84}N_4O_8U$·$2CH_2Cl_2$: C, 48.6; H, 6.0; N, 4.1. Found: C, 48.8; H, 5.9; N, 4.4%.

{4,4′-Di-*tert*-butyl-6,6′-bis(octanamido)-2,2′-[1,2-cyclohexylenebis(nitrilo-κ*N*-methylene)]diphenolato-κ*O*}dioxouranium (7). *cis*-1,2-Diaminocyclohexane (0.03 g, 0.24 mmol) was reacted with 0.15 g (0.47 mmol) of **1h**, and 0.1 g (0.24 mmol) of $UO_2(OAc)_2$·$2H_2O$ according to the general procedure for the synthesis of salophenes, yielding 0.16 g (70%) of salene **7**. Mp: 220–221 °C. ^{1}H NMR (DMSO-d_6) δ 9.87 (s, 2H, imine NCH), 9.07 (s, 2H, NH), 8.75 (d, 2H, J = 2.1 Hz, phenol ArH), 7.39 (d, 2H, J = 2.1 Hz, phenol ArH), 4.7 (br m, 2H, cyclohexyl CH), 2.63 (t, 2H, J = 7.2 Hz, $C(O)CH_2$), 2.37–2.34 (br m, 2H, cyclohexyl CH_2), 1.90–1.20 (m, 44H, cyclohexyl CH_2, $C(O)CH_2(CH_2)_5$ and $C(CH_3)_3$), 0.88 (t, 6H, J = 6.1 Hz, $(CH_2)_{11}CH_3$); ($CDCl_3$) δ 11.02 (d, 1H , J = 7.7 Hz, NH), 9.41, 9.34 (2 × s, 2H, imine NCH), 9.05, 7.14 (2 × d, 2H, J = 2.3 Hz, phenol ArH), 9.00 (s, 1H, NH), 7.26, 7.14 (2 × d, 2H, J = 3.4 Hz, phenol ArH), 4.76–4.73 (br m, 2H, cyclohexyl CH), 2.56 (m, 6H, J = 7.2 Hz, $C(O)CH_2$, cyclohexyl CH_2), 2.00–1.20 (m, 44H, cyclohexyl CH_2, $C(O)CH_2(CH_2)_5$ and $C(CH_3)_3$), 0.82, 0.68 (t, 6H, J = 6.2 Hz, $(CH_2)_{11}CH_3$); ^{13}C NMR (DMSO-d_6) δ 170.8 (s), 168.6 (d), 155.7 (s), 138.1 (s), 129.1 (s), 129.4 (d), 121.2 (s), 120.6 (d), 70.6 (d), 37.0 (t), 33.7 (s), 31.4 (q), 31.3 (t), 28.8 (t), 28.7 (t), 27.4 (t), 25.1 (t), 22.1 (t), 21.4 (t), 13.9 (q). MS-FAB m/z 985.7 ([M + H]$^+$, calcd. 985.6). Anal. Calcd. for $C_{44}H_{66}N_4O_6U$·$1.5H_2O$: C, 52.2; H, 6.9; N, 5.5. Found: C, 51.9; H, 6.8; N, 5.4%.

ISE and CHEMFET measurements

Reagents. High molecular weight (HMW) PVC was obtained from Fluka. *o*-Nitrophenyl *n*-octyl ether (NPOE) was synthesized according to a literature procedure.[11] Tetraoctylammonium bromide (TOAB) was purchased from Fluka. THF was freshly distilled from sodium–benzophenone ketyl before use. The anion sodium salts were of analytical grade (Fluka). All solutions were made with deionized doubly distilled water. The measurements were carried out in solution with 0.01 M 2-morpholinoethanesulfonic acid (MES, Fluka) adjusted to the desired pH with NaOH.

Fabrication of ISEs and measurements. The ion-selective membranes were prepared by dissolving in 0.7 mL of THF approximately 100 mg of a mixture composed of 33 wt% PVC, 66 wt% NPOE, 1 wt% receptor, and 20 mol% (with respect to the receptor) of TOAB. This solution was poured into a glass ring (id 24 mm) resting on a glass plate. After evaporation of the THF overnight, disks of 7 mm id were cut. The membrane disks were mounted in electrode bodies (Philips IS 561). As internal filling solution 0.1 M KCl was used. Membrane potentials were measured *vs*. a saturated calomel electrode (SCE), connected to the stirred sample solution *via* a salt bridge filled with 1.0 M LiOAc. The ISE response data were collected with a Zeus Mux 03 14ch multiplexer. After changing the sample the ISEs were conditioned for 5 min before measuring the membrane potential. The potentiometric selectivity coefficients ($K_{i,j}^{Pot}$) were determined by the separate solution method (SSM)[12] with 0.1 M sodium salt solutions, 0.01 M MES, pH = 6.0. The response towards pH changes was obtained by the addition of small volumes of 1.0 M or 0.01 M NaOH solution to 40 mL of an 0.1 M Na_2SO_4 solution pH 4.5, under an argon atmosphere.

Fabrication of CHEMFETs and measurements. CHEMFETs were prepared from ISFETs with dimensions of 3 × 4.5 mm fabricated in the MESA cleanroom facilities (University of Twente, The Netherlands), mounted on a printed circuit board, wire bonded, and encapsulated with epoxy resin (Hysol H-W 796/C8 W795). Details of the modification of the ISFETs with poly(hydroxyethylmethacrylate) hydrogel (polyHEMA) have been described before.[13] The membrane was deposited on the gate area of the CHEMFET by casting this solution using a micropipet (3 × 1.5 μl). The solvent was allowed to evaporate overnight. The composition of the membrane solution and the measurement procedures have been described previously.[4] The potentiometric selectivity coefficients ($K_{i,j}^{Pot}$) were determined by the fixed interference method (FIM) according to IUPAC recommendations.[12] Detection limits and selectivity coefficients were determined ±0.1, slopes ±2 mV decade^{-1}. The constant background concentration of the interfering ion was 0.1 M unless otherwise indicated. All concentrations were converted to single-ion activities, and the mean activity coefficient was obtained by the extended Debye–Hückel equation. The measurements were performed at ambient temperature in an air-conditioned room (T = 22 °C).

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