

## Review

# Beyond Cations: Expanding the Horizons of Ferrocene-Based Electrochemical Sensors for Neutral and Anionic Molecules

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**Abstract:** Ferrocene (Fc) has long been celebrated for its remarkable redox properties and structural versatility, making it a cornerstone of electrochemical sensor development. While extensive research has focused on cation detection using Fc-based systems, the equally critical recognition of neutral and anionic molecules remains underexplored despite their significance in biological, environmental, and industrial contexts. This review addresses this gap by exploring the latest advancements in Fc-based electrochemical sensors designed to overcome the unique challenges posed by these species—including diverse geometries, high hydration enthalpies, and the absence of formal charge. Molecular architectures such as amide-functionalised receptors, urea derivatives, Lewis acid-containing receptors, triazolium, and carboxylic acid-containing systems are examined, highlighting how these sensors achieve high selectivity and sensitivity. Furthermore, the influence of solvent environments on sensor performance is discussed, providing a critical analysis of how different receptor functionalities and solvents affect sensor behaviour. Emphasising the advantages of redox-based detection, this review aims to inspire further innovation in developing Fc-based technologies for detecting neutral and anionic species.

**Keywords:** ferrocene-based sensors; electrochemical sensing; anion recognition; neutral molecule detection; redox-active receptors

Academic Editors: Mojca Čakić  
Semenčič and Lidija Barišić

Received: 4 December 2024

Revised: 23 December 2024

Accepted: 24 December 2024

Published: 26 December 2024

**Citation:** Torriero, A.A.J.; Torriero, A.M.; Miller, K.T.; Mruthunjaya, A.K.V. Beyond Cations: Expanding the Horizons of Ferrocene-Based Electrochemical Sensors for Neutral and Anionic Molecules. *Inorganics* **2025**, *13*, 3. <https://doi.org/10.3390/inorganics13010003>

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## 1. Introduction

Ferrocene (Fc), since its discovery in the early 1950s, has remained a cornerstone of electrochemical research due to its remarkable redox properties and structural versatility [1–8]. As a stable metallocene complex, Fc readily undergoes a reversible one-electron redox process between its neutral Fc and oxidised ferrocenium (Fc<sup>+</sup>) forms, making it a highly efficient and adaptable redox-active centre for sensor applications [1,9]. Recent advancements in Fc chemistry have enabled the design of diverse molecular architectures tailored for specific sensing applications. For instance, functionalisation with amide, urea, or thiourea groups enhances anion binding via hydrogen bonding interactions, while macrocyclic systems facilitate selective recognition of larger or structurally complex targets. These tailored designs exemplify how subtle structural modifications can significantly improve sensor performance, as explored in detail later in this review.

These unique characteristics have facilitated the development of various molecular recognition sensors that leverage Fc redox behaviour to detect various chemical species, including cations, anions, and neutral molecules [3,10,11]. Much of the early work on Fc-based sensors has focused on cation recognition, particularly metal ions, due to their strong interactions with the electron-rich cyclopentadienyl rings of Fc [3,11–13]. However, applying Fc-based sensors for anions and neutral molecules remains less explored. Detecting

these species presents unique challenges—including high hydration enthalpies for anions and the absence of formal charge in neutral molecules—that demand innovative sensing mechanisms. This review addresses these challenges by exploring advanced strategies, such as dual hydrogen-bonding sites in amide-functionalised receptors (also referred to as ligands and host hereafter) and ion-pairing approaches to enhanced anion recognition.

Ferrocene-based receptors offer distinct advantages in electrochemical sensing, making them a valuable focus for this review. Their well-defined and reversible redox behaviour ensures reliable and reproducible electrochemical responses, a key requirement for effective sensor design. Additionally, Fc chemical stability allows these receptors to operate under various experimental conditions without significant degradation. Structural versatility, enabled by the ease of functionalisation of the ferrocene core, allows fine-tuning of receptor properties for specific analytes, such as fluoride ( $F^-$ ), chloride ( $Cl^-$ ), and hydrogen sulphate ( $HSO_4^-$ ) ions. Compared to other electrochemical sensor systems, such as those based on metal complexes, carbon nanomaterials, and conducting polymers [14–16], Fc-based receptors uniquely combine predictable redox responses, robust performance, and adaptability. While metal complexes often demonstrate strong selectivity, they can suffer from synthetic complexity and limited operational stability [14]. Carbon nanomaterials offer high conductivity and surface area but may face challenges with functionalisation consistency [15], and conducting polymers provide design flexibility but can exhibit reduced long-term stability [16]. In contrast, ferrocene-based receptors balance these factors effectively, positioning them as highly competitive tools in ion sensing technologies. This review aims to provide a detailed overview of these systems, highlighting their strengths, recent advancements, and contributions to the field of electrochemical sensing while positioning them as essential tools for addressing current and future challenges in ion detection technologies.

Building on these advantages, electrochemical techniques like cyclic voltammetry (CV), square-wave voltammetry (SWV), and differential pulse voltammetry (DPV) are widely employed to monitor the redox behaviour of these systems. Anions and neutral molecules, significant in biological, environmental, and industrial contexts, present unique challenges for electrochemical sensing due to their diverse geometries and high hydration enthalpies [9,17]. Similarly, neutral molecules, lacking a formal charge, demand sophisticated recognition mechanisms that typically involve hydrogen bonding,  $\pi$ - $\pi$  stacking, or specific functional groups [10].

While previous reviews have extensively covered Fc-based sensors for cation detection [3,11–13] and various sensing modalities such as optical, fluorescent, and colourimetric methods [17–28], there is a noticeable gap in the literature focusing exclusively on electrochemical sensors for anions and neutral molecules. To the best of our knowledge, no comprehensive review has specifically addressed the latest development and application of Fc-based redox/electrochemical sensors for these challenging analytes. This review aims to fill that gap by concentrating solely on electrochemical sensing mechanisms and strategies tailored for anions and neutral molecules.

We have organised the review into sections that discuss various receptor types, including amides, amines, urea and its derivatives, Lewis acid-containing receptors, triazolium, and carboxylic acid-containing receptors for anions. Additionally, we present examples of Fc-based sensors designed for neutral molecule detection. For each sensor type, we report critical parameters such as solvent and supporting electrolyte used, potential shifts, and possible interferences or competing anions. Finally, we provide a critical discussion on how different functionalities and solvents affect the observed behaviour of the sensors, offering insights into future design strategies. In the concluding section, we outline the current research gaps, emerging trends, and opportunities for innovation in Fc-based electrochemical sensing, providing a roadmap for advancing these technologies to address

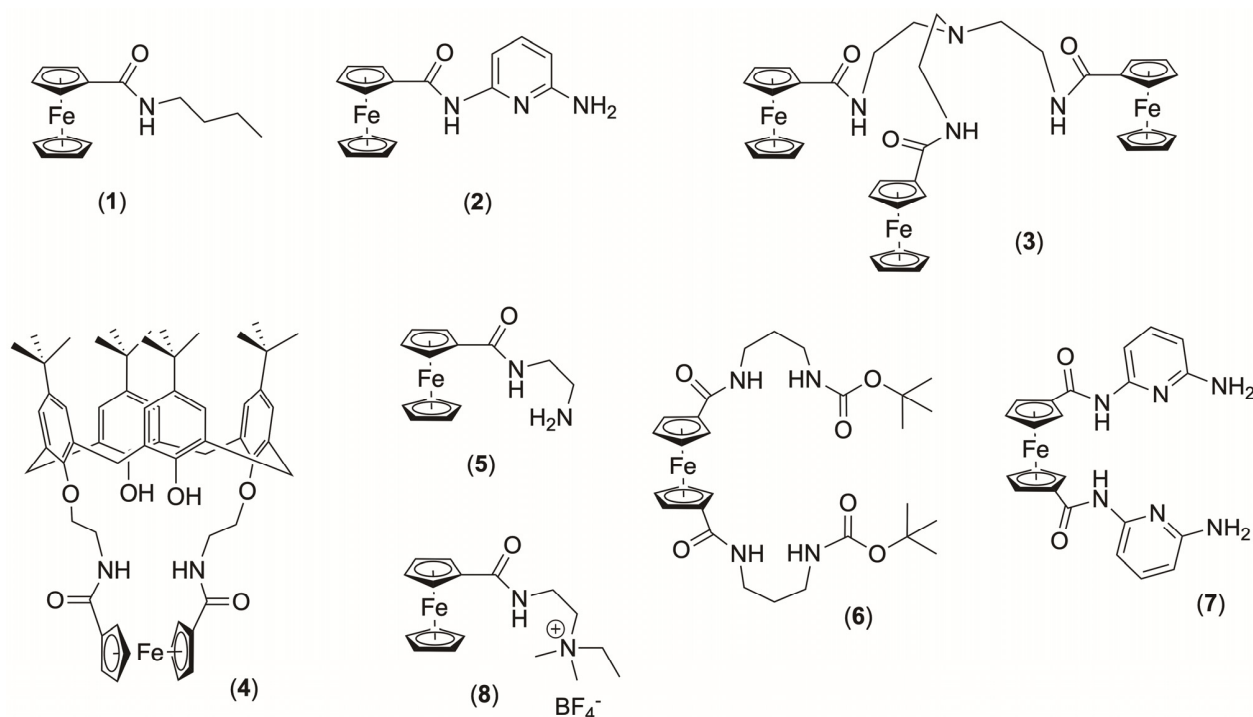
challenges in complex matrices and real-world applications. Through this focused examination, we aim to highlight the potential of Fc-based electrochemical sensors to address the challenges of detecting anions and neutral molecules and inspire further research into developing advanced sensing technologies based on Fc. Furthermore, we emphasise the unique advantages of Fc-based receptors, including their predictable redox behaviour, chemical stability, and structural versatility, positioning them as highly competitive tools in ion sensing technologies.

## 2. Amides-Based Receptors

Selective electrochemical recognition of dihydrogen phosphate ( $\text{H}_2\text{PO}_4^-$ ) was achieved using neutral Fc-based receptors, specifically compounds **1–4**, which demonstrated effective discrimination in the presence of competing anions like  $\text{HSO}_4^-$  and  $\text{Cl}^-$  [29]. These receptors were engineered with amide and amine functional groups, providing targeted hydrogen bonding sites to facilitate selective anion complexation. Cyclic voltammetry in acetonitrile containing 0.1 M  $[\text{Bu}_4\text{N}][\text{BF}_4]$  as the supporting electrolyte revealed a negative potential shift in the redox potential of the  $\text{Fc}/\text{Fc}^+$  couple upon anion binding, with  $\text{H}_2\text{PO}_4^-$  inducing the most substantial perturbation [29].

Receptor **3** displayed a shift of 180 mV in response to  $\text{H}_2\text{PO}_4^-$ , attributed to its optimised structural cavity that complements the geometry of this anion. This shift was significantly higher than those observed for  $\text{HSO}_4^-$  and  $\text{Cl}^-$ , which induced shifts of 50 and 20 mV, respectively. Competition experiments involving equimolar and excess concentrations of  $\text{HSO}_4^-$  and  $\text{Cl}^-$  further confirmed that  $\text{H}_2\text{PO}_4^-$  dominated the electrochemical response of receptor **3**.

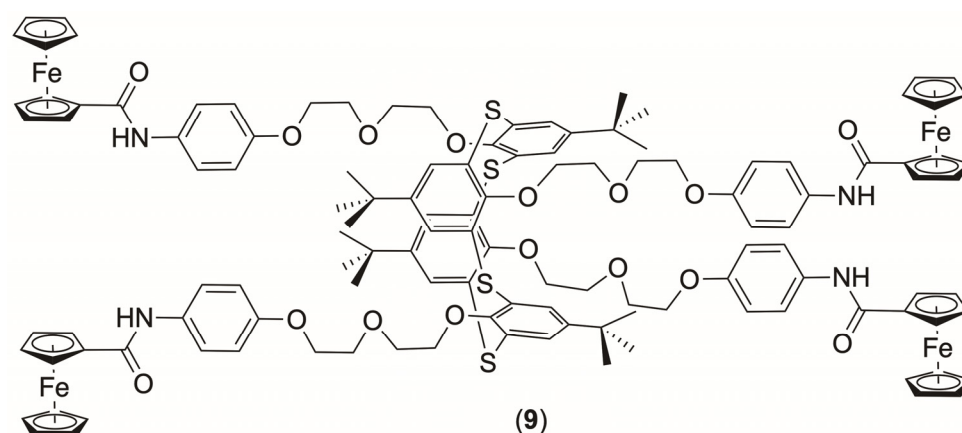
Receptors **1**, **2**, and **4** exhibited negative potential shifts of 60, 100, and 110 mV in response to  $\text{H}_2\text{PO}_4^-$  [29]. The relatively smaller shift observed for **1** is attributed to its single amide functional group, which limits its capacity for hydrogen bonding and reduces its affinity for the anion. In contrast, **2**, with additional hydrogen bonding sites, exhibited a more significant shift of 100 mV, reflecting enhanced interactions with  $\text{H}_2\text{PO}_4^-$ . Among these three receptors, **4** showed the largest shift of 110 mV, attributed to its optimised structural complementarity to the  $\text{H}_2\text{PO}_4^-$  geometry.



Extending these observations, receptors **2** and **5–7** exhibit similar structure-dependent selectivity trends towards anions [30]. Receptor **5**, studied in acetonitrile (0.1 M  $[\text{Bu}_4\text{N}][\text{BF}_4]$ ), demonstrated strong responses to oxoanions, with negative potential shifts of 220 mV for  $\text{HSO}_4^-$ , 165 mV for  $\text{H}_2\text{PO}_4^-$ , and 35 mV for  $\text{Cl}^-$ , reflecting its capacity for dual hydrogen bonding and proton transfer. Due to solubility limitations in pure acetonitrile, multidentate amide **6** was examined in a 1:1 acetonitrile-dichloromethane (0.1 M  $[\text{Bu}_4\text{N}][\text{BF}_4]$ ) solvent system and displayed shifts of 80 mV for  $\text{Cl}^-$  and 45 mV for bromide,  $\text{Br}^-$ , underscoring the role of multidentate binding in halide recognition. Receptor **2**, investigated in acetonitrile with a single amide group, showed reduced shifts of 120 mV for  $\text{H}_2\text{PO}_4^-$  and only 5 mV for  $\text{HSO}_4^-$ . In contrast, **7**, also studied in acetonitrile and incorporating bis (amide) functionality, demonstrated exceptional sensitivity with a negative potential shift of 240 mV for  $\text{H}_2\text{PO}_4^-$  and 85 mV for  $\text{HSO}_4^-$ . These findings highlight how subtle changes in receptor architecture and solvent environment significantly influence anion affinity and selectivity [30].

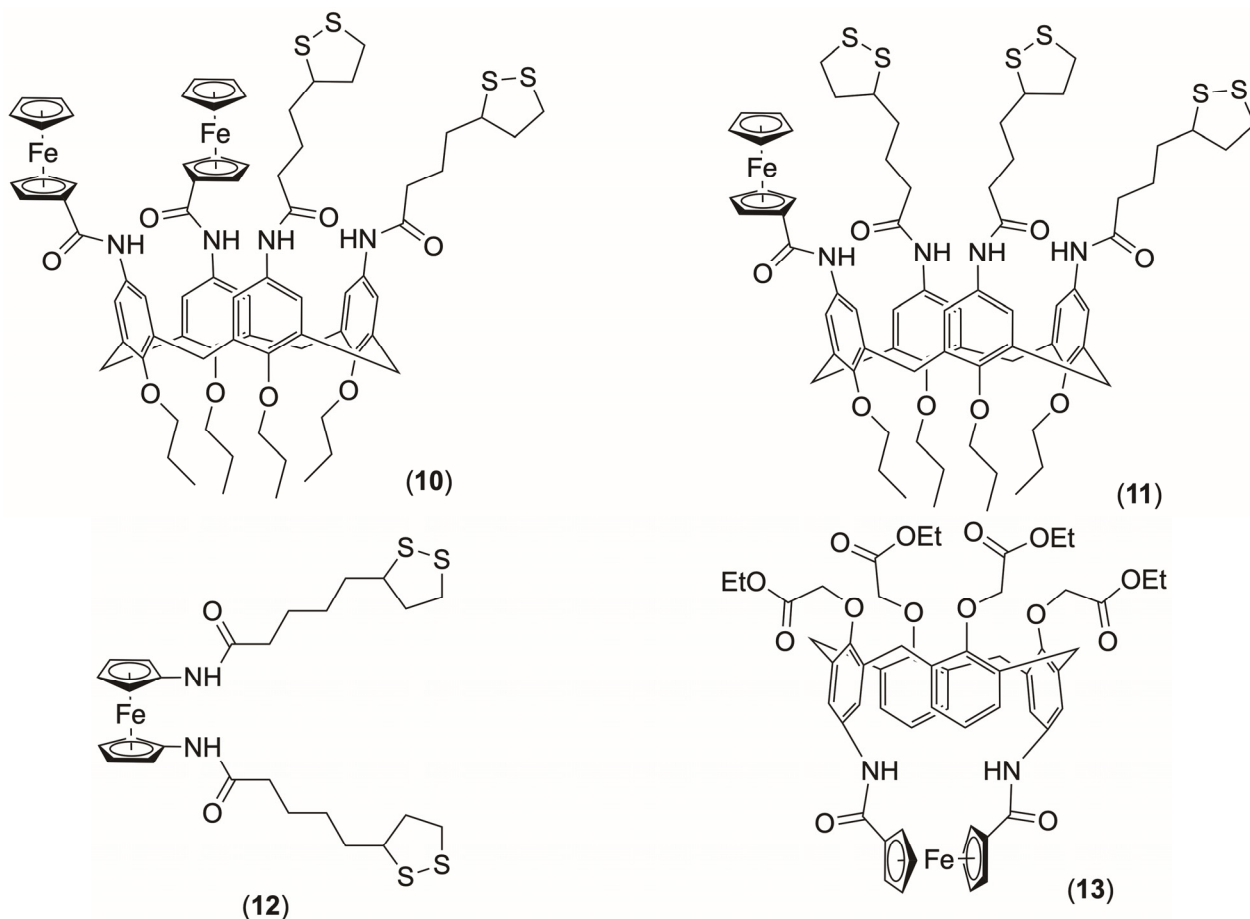
Receptor **8** is a variation of receptor **5**, incorporating quaternary nitrogen alongside amide groups to enhance anion recognition [31]. Cyclic voltammetry studies in dichloromethane containing 0.1 M  $[\text{Bu}_4\text{N}][\text{PF}_4]$  as the supporting electrolyte revealed a negative potential shift of 373 mV for  $\text{H}_2\text{PO}_4^-$ . This substantial shift underscores the stronger interaction of **8** with  $\text{H}_2\text{PO}_4^-$  compared to receptor **5**, which exhibited a shift of 165 mV under similar conditions. However, **8** showed a smaller shift of 176 mV in the presence of  $\text{HSO}_4^-$  compared to receptor **5** (220 mV), suggesting that adding quaternary nitrogen does not enhance interactions with this anion. Additionally, **8** displayed negligible response to  $\text{Br}^-$  (19 mV), similar to receptor **5**.

Receptor **9**, incorporating four polyether arms terminated with Fc amide groups, was synthesised and evaluated for its anion recognition properties [32]. The electrochemical behaviour was studied using CV in a 1:1 dichloromethane-acetonitrile solvent mixture with 0.1 M  $[\text{Bu}_4\text{N}][\text{ClO}_4]$  as the supporting electrolyte. Upon adding two equivalents of  $\text{H}_2\text{PO}_4^-$ , **9** displayed a significant negative potential shift of 275 mV. This shift was accompanied by a two-wave electrochemical response, indicating strong binding stability and effective interaction between the receptor and  $\text{H}_2\text{PO}_4^-$ . In contrast, other anions, such as acetate ( $\text{AcO}^-$ ) and  $\text{Br}^-$ , did not induce any measurable changes in the redox potential, demonstrating the receptor's high selectivity. Positioning amide hydrogen bonding sites close to the Fc units was key in facilitating anion binding and stabilising the oxidised  $\text{Fc}^+$  state.



Ferrocene-functionalised Calix[4]arene receptors with amide groups, such as **10** and **11**, demonstrated electrochemical responses to anions [33]. In 1:1 acetonitrile–dichloromethane (0.1 M  $[\text{Bu}_4\text{N}][\text{BF}_4]$ ) mixture, **10** exhibited negative potential shifts of 70, 115, and 260 mV for  $\text{Cl}^-$ , benzoate ( $\text{Bz}^-$ ), and  $\text{H}_2\text{PO}_4^-$ , respectively, while receptor **11** showed shifts of 50, 165,

and 240 mV for the same anions. These shifts highlight the ability of amide groups to engage in hydrogen bonding with anions, albeit with slightly lower binding strength compared to their urea-based counterparts (discussed in the following sections). The electrochemical behaviour differed significantly when the same receptors were attached to a gold surface in a self-assembled monolayer (SAM). While receptors **10** and **11** demonstrated robust anion binding in solution, the addition of anions such as  $\text{Cl}^-$ ,  $\text{Bz}^-$ , and  $\text{H}_2\text{PO}_4^-$  to their SAMs surprisingly resulted in the complete disappearance of their redox waves, even at relatively low anion concentrations (approx. 1 mM). This suggests oxidative decomposition of the Fc centres within the SAM environment, making these systems unsuitable for stable anion sensing when immobilised [33].

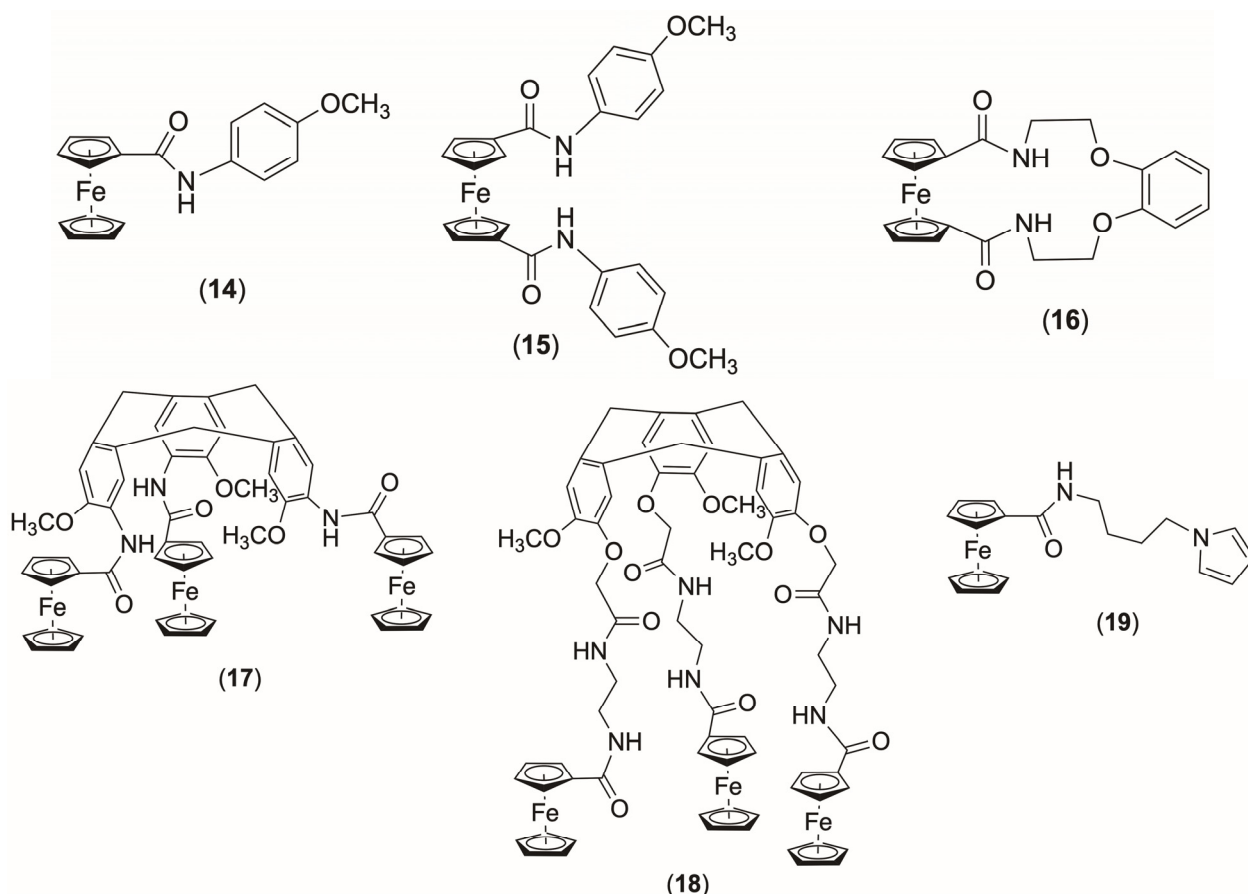


Electrochemical studies of **12** were conducted in a 2:1 dichloromethane–acetonitrile mixed system with 0.1 M  $[\text{Bu}_4\text{N}][\text{BF}_4]$  as the supporting electrolyte [34]. Negative potential shifts of 40, 20, and 210 mV were observed for  $\text{Cl}^-$ ,  $\text{Br}^-$ , and  $\text{H}_2\text{PO}_4^-$ , respectively, when **12** was analysed in solution. When SAM of **12** was formed on gold electrodes, the pre-organised structure amplified the redox responses, yielding potential shifts of 100, 30, and 300 mV for  $\text{Cl}^-$ ,  $\text{Br}^-$ , and  $\text{H}_2\text{PO}_4^-$ , respectively. This substantial enhancement highlights the role of surface confinement and pre-organisation in improving anion binding and electrochemical sensing, particularly for oxoanions like  $\text{H}_2\text{PO}_4^-$ . Interestingly, the selectivity of **12** was consistent across solution and surface-confined states, with  $\text{H}_2\text{PO}_4^-$  preferentially binding over halides [34].

Calix[4]arene derivative **13**, featuring amide-Fc units at the wide rim and ethyl ester groups at the narrow rim, was evaluated as an electrochemical sensor for carboxylate anions [35]. Cyclic voltammetry and SWV studies were performed in acetonitrile with 0.1 M  $[\text{Bu}_4\text{N}][\text{PF}_6]$  as the supporting electrolyte. The redox potential of free **13** was determined to be 417 mV vs.  $\text{Fc}/\text{Fc}^+$  internal reference system (IRS). Upon adding excess

$\text{Bz}^-$  (4 equivalents), the oxidation potential shifted in the negative direction by 150 mV, accompanied by the disappearance of the initial redox wave. This shift was attributed to the formation of the  $\text{Fc}^+-\text{Bz}^-$  complex, facilitated by hydrogen bonding and electrostatic interactions [35].

A different study focuses on the electrochemical recognition of  $\text{F}^-$ ,  $\text{H}_2\text{PO}_4^-$ , adenosine triphosphate ( $\text{ATP}^{2-}$ ), and  $\text{HSO}_4^-$  ions using a series of amide-substituted ferrocenyl ligands (**14**–**18**) in acetonitrile or dichloromethane (0.1 M  $[\text{Bu}_4\text{N}][\text{ClO}_4]$ ) [36]. The ligands were designed to utilise hydrogen bonding and ion-pairing interactions with amide groups for selective anion binding. Cyclic voltammetry was used to monitor redox potential shifts associated with each anion–ligand complex, revealing insights into their selectivity and binding mechanisms. The study demonstrated distinct potential shifts for each ligand–anion complex in organic solvents. The ligands exhibited a variety of one-wave and two-wave CV behaviours depending on the strength of interaction with the anions [36]. For  $\text{F}^-$ , the ligands **14**–**16** showed one-wave behaviour, with substantial shifts indicating ion-pair formation and adsorption on the electrode, resulting in irreversible CV behaviour. For **17** and **18**, adding  $\text{F}^-$  induced a new reduction peak at a less positive potential linked to ion pairs precipitating on the electrode surface. The potential shifts recorded in acetonitrile in the presence of  $\text{F}^-$  were 230 mV for **16**, 220 mV for **14**, 90 mV for **15**, and 60 mV for **17**. In contrast, in dichloromethane, these shifts were 310 and 290 mV for **14** and **15**, respectively, suggesting stronger interactions in less polar environments.



In the case of  $\text{H}_2\text{PO}_4^-$  and  $\text{ATP}^{2-}$ , ligands **17** and **18** showed a clear two-wave cyclic voltammetry response, allowing for the distinct observation of complexed and free ligand peaks [36]. For **17**, the  $\text{H}_2\text{PO}_4^-$  complex showed a shift of 140 mV in acetonitrile, while in dichloromethane, this interaction was stronger, with a shift of 230 mV. Similarly, for  $\text{ATP}^{2-}$  binding with **17**, the shift was 160 mV in acetonitrile, increasing to 230 mV in

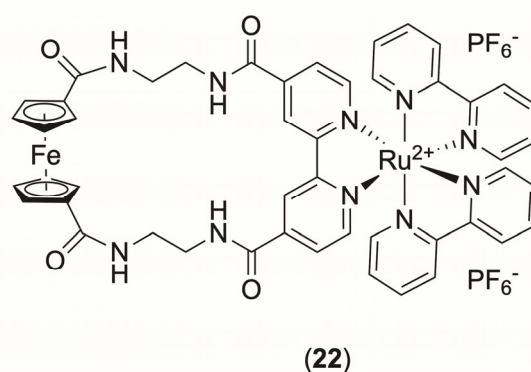
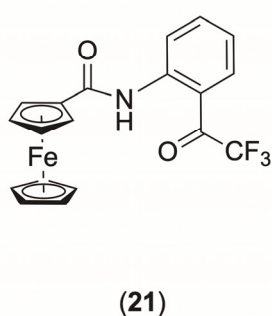
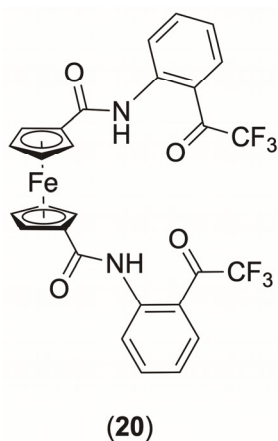
dichloromethane. Ligand **18** showed maximum shifts with  $\text{H}_2\text{PO}_4^-$  and  $\text{ATP}^{2-}$  at 170 and 160 mV, respectively, in acetonitrile.

Hydrogen sulphate showed only minor shifts in acetonitrile, specifically 5 mV for **14** and **15**, showing no effects on the Fc redox potential of **16–18**, even in excess. These limited shifts indicate weaker interactions with  $\text{HSO}_4^-$ , supporting that the design of the ligands promotes higher selectivity for  $\text{F}^-$ ,  $\text{H}_2\text{PO}_4^-$ , and  $\text{ATP}^{2-}$  due to stronger electrostatic and hydrogen bonding interactions.

The electropolymerisation of the pyrrole-substituted monoamidoferrocene **19** onto a platinum electrode produced redox polymer films with enhanced electrochemical sensing properties for oxoanions [37]. Cyclic voltammetry and DPV studies were performed in acetonitrile or dichloromethane, containing 0.1 M  $[\text{Bu}_4\text{N}][\text{ClO}_4]$  as the supporting electrolyte. Upon binding  $\text{H}_2\text{PO}_4^-$ , the Fc redox potential shifted in the negative direction by 220 mV in acetonitrile and 260 mV in dichloromethane, while  $\text{ATP}^{2-}$  binding caused shifts of 180 mV in acetonitrile and 240 mV in dichloromethane. The polymer also responded to  $\text{HSO}_4^-$  with smaller shifts of 30 mV in acetonitrile and 90 mV in dichloromethane, whereas no significant response was observed for nitrate ( $\text{NO}_3^-$ ). Compared to the monomer in solution, which displayed a weak negative shift of 80 mV for  $\text{H}_2\text{PO}_4^-$  in acetonitrile, the polymer exhibited significantly greater sensitivity, attributed to the high local concentration of Fc units in the polymer film. This enables cooperative hydrogen bonding and electrostatic interactions with anions, particularly in less polar solvents like dichloromethane.

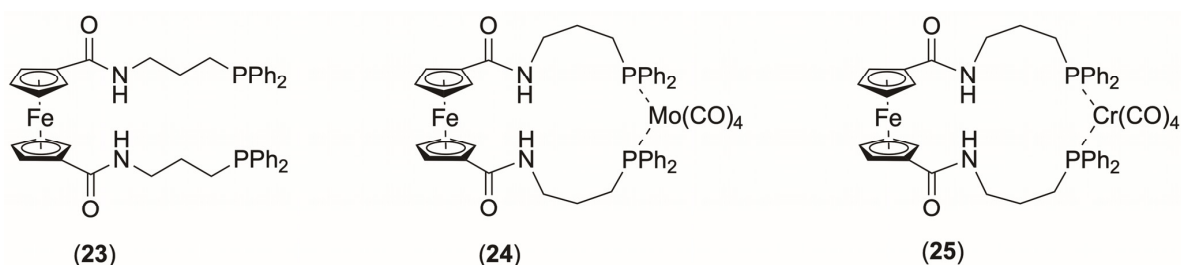
The electrochemical behaviour of **20** with  $\text{AcO}^-$  was investigated through CV in acetonitrile [38]. In its free state, **20** exhibited a formal redox potential of 984 mV versus Ag/AgCl. Upon adding two equivalents of  $\text{AcO}^-$ , a notable negative shift in the formal potential was observed, decreasing by 122 mV. This change indicates the initial binding interaction between the receptor and the  $\text{AcO}^-$  ion. When four  $\text{AcO}^-$  equivalents were added, the negative shift increased to 149 mV, suggesting a progression towards a (1:2) host–guest binding mode. The interaction of **20** with 2,2'-(1,3-phenylene)diacetate in acetonitrile produced a much larger response. Adding one equivalent of 2,2'-(1,3-phenylene)diacetate caused a pronounced negative potential shift of 153 mV, reflecting strong cooperative binding and forming a stable 1:1 host–guest complex. No further shift was observed with additional equivalents of 2,2'-(1,3-phenylene)diacetate, reinforcing the receptor's high affinity and specificity for this dicarboxylate in acetonitrile.

Similarly, **21**, a monofunctional control receptor, was examined under the same conditions with  $\text{AcO}^-$  in acetonitrile and, in its unbound form, displayed a formal redox potential of 710 mV vs. Ag/AgCl. After adding  $\text{AcO}^-$ , **21** showed a negative shift in the potential of 40 mV, which remained consistent when further acetate equivalents were introduced [38]. This smaller and stable potential shift indicates a lower affinity of receptor **21** for acetate than **20**, which required fewer equivalents to achieve a higher magnitude of shift.



Ferrocene-containing macrocyclic **22**, a heterodinuclear complex comprising a ruthenium–bipyridyl unit and an Fc moiety, demonstrates distinct electrochemical behaviour upon anion recognition [39]. Cyclic voltammetry studies in acetonitrile with 0.1 M  $[\text{Bu}_4\text{N}][\text{PF}_6]$  as the supporting electrolyte revealed two redox couples:  $\text{Ru(II)}/\text{Ru(III)}$  at 1035 mV and  $\text{Fc}/\text{Fc}^+$  at 390 mV vs.  $\text{Ag}/\text{Ag}^+$ . Adding anions induced negative potential shifts in the midpoint potential of the  $\text{Fc}/\text{Fc}^+$  process, with  $\text{Cl}^-$  causing the largest shift of 60 mV, followed by  $\text{AcO}^-$  (20 mV) and  $\text{H}_2\text{PO}_4^-$  (15 mV) [39].

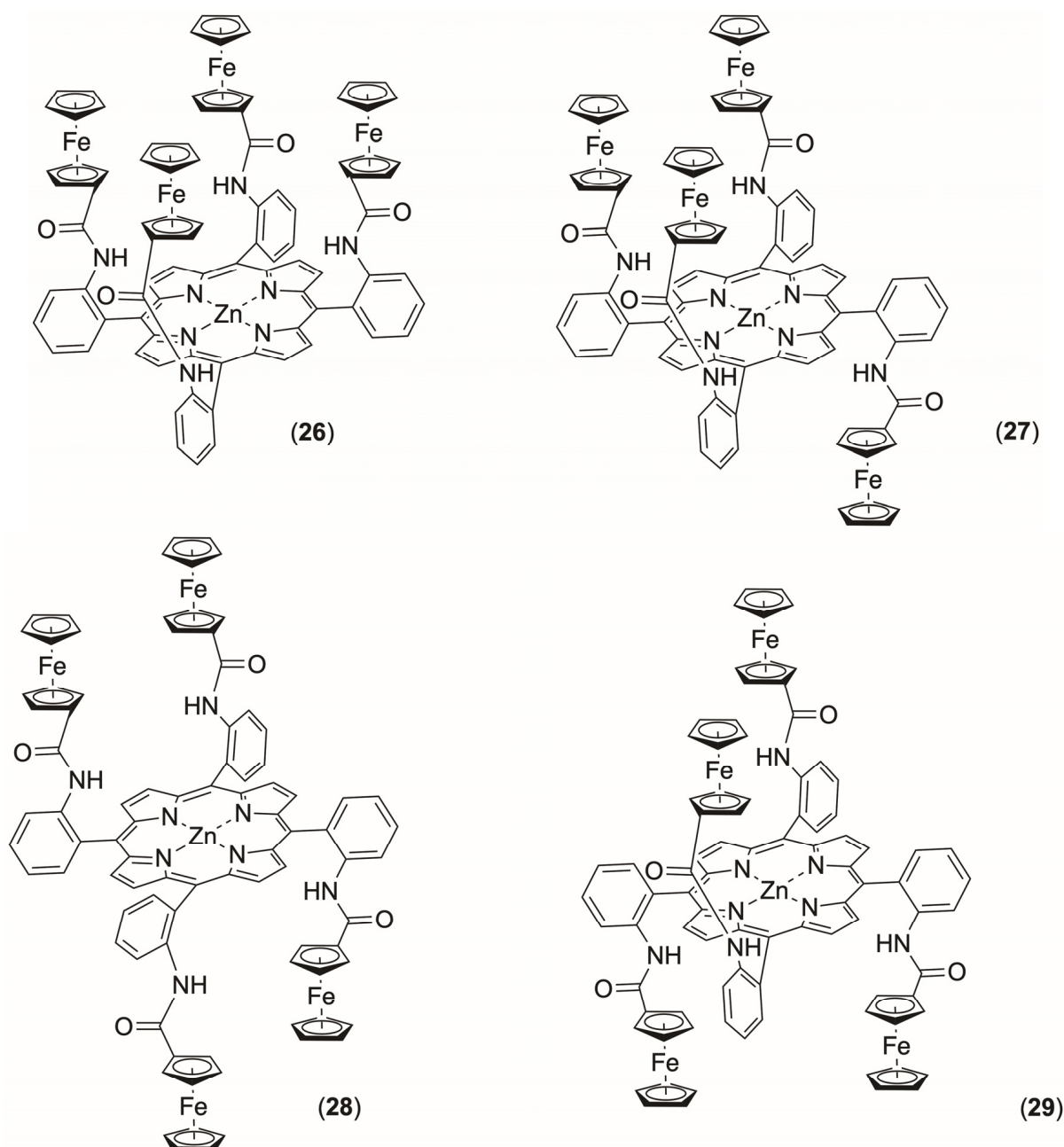
The electrochemical properties of Fc-based bis(phosphine) amide receptors and their transition metal complexes (**23–25**) were evaluated for anion sensing in a 1:1 acetonitrile–dichloromethane solvent system using 0.2 M  $[\text{Bu}_4\text{N}][\text{BF}_4]$  as the supporting electrolyte [40]. Negative potential shifts in Fc redox potential were observed upon adding anions, for  $\text{Cl}^-$ , **24**, containing a molybdenum centre, exhibited a potential shift of 90 mV. Similarly, **25**, containing a chromium centre, showed a shift of 85 mV. The parent ligand **23** displayed a smaller shift of 65 mV, highlighting the enhanced binding capability provided by the Lewis acidic transition metal centres.



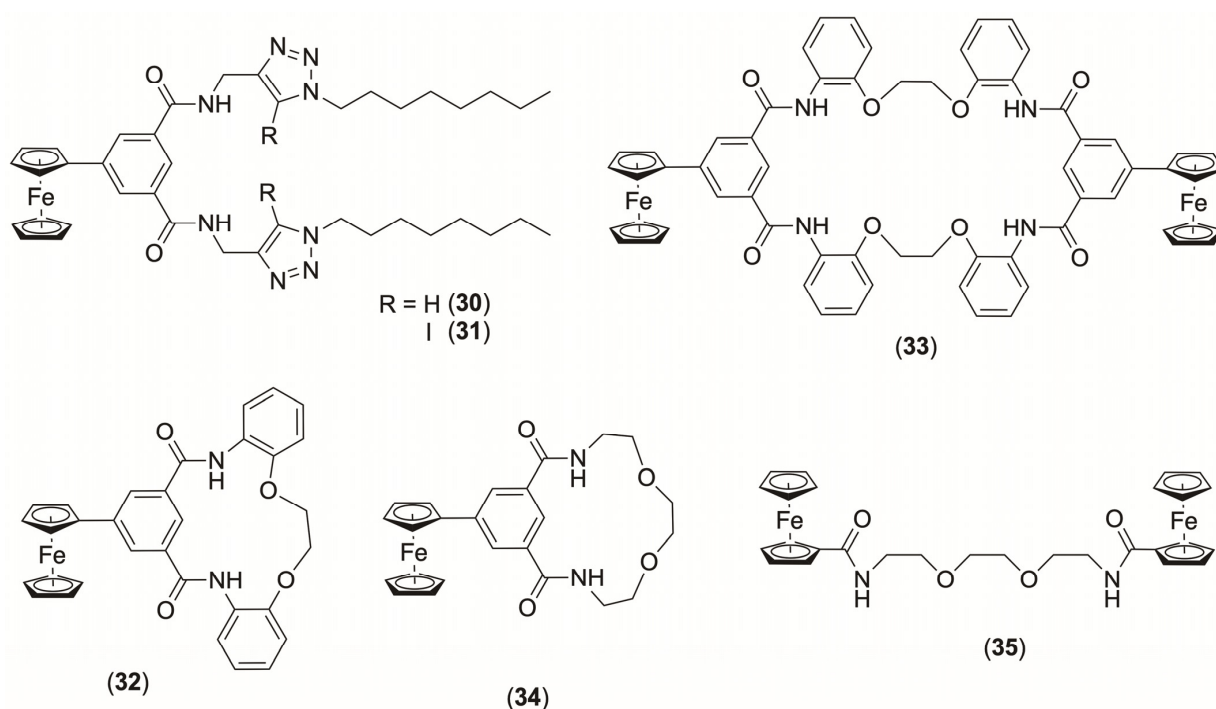
For  $\text{Br}^-$ , **24** and **25** exhibited moderate negative potential shifts of 30 mV. Similarly,  $\text{HSO}_4^-$  produced shifts of 35 mV for both receptors, suggesting weaker binding interactions than  $\text{Cl}^-$ . The most pronounced shifts were observed for  $\text{H}_2\text{PO}_4^-$ , where **25** exhibited the most significant shift of 185 mV, reflecting strong binding likely mediated by hydrogen bonding. Receptor **24** showed a slightly smaller shift of 135 mV, which matched the shift observed for the parent ligand **23** [40].

The electrochemical data for zinc-metallated 5,10,15,20-tetrakis(o-ferrocenylcarbonylaminophenyl)-substituted)porphyrin receptors **26–29** demonstrate their ability to sense anions through negative potential shifts in porphyrin oxidation and Fc redox couples [41]. However, the observed potential changes are relatively modest, raising concerns about their sensitivity and practicality as anion sensors compared to simpler systems. For example, **26** exhibited a negative potential shift of 115 mV in the porphyrin oxidation wave and 30 mV in the Fc one in the presence of  $\text{Cl}^-$ . Bromide induced 85 and 20 mV shifts for the same redox events. Nitrate produced a moderate response, with shifts of 100 and 25 mV. Although  $\text{HSO}_4^-$  caused the largest shift of 125 mV and 50 mV, these changes are not significantly larger than those achieved by simpler Fc-based sensors.

Among the porphyrin receptors studied, **27** exhibited the strongest electrochemical response for  $\text{NO}_3^-$ , with a negative potential shift of 175 mV, significantly outperforming **26** and **29** (75 mV). For  $\text{HSO}_4^-$ , **27** again showed superior sensitivity with a shift of 150 mV, matching the responses of **28** and **29** but outperforming **26**. In the case of halides, **26** showed stronger responses for  $\text{Cl}^-$  (115 mV) and  $\text{Br}^-$  (85 mV) compared to **28** and **29**, which exhibited shifts of 95 and 70 mV for  $\text{Cl}^-$ , respectively [41].



Building upon the amide-based receptors' performance, **30** and **31** derivatives demonstrated anion-sensing capabilities [42]. Using acetonitrile (0.1 M [Bu<sub>4</sub>N][ClO<sub>4</sub>]), **31** exhibited significant negative potential shifts for H<sub>2</sub>PO<sub>4</sub><sup>−</sup>, up to 173 mV, compared to 109 mV for its hydrogen bonding analogue **30**. Other anions, including Bz<sup>−</sup> (106 mV for **31**, 62 mV for **30**), Cl<sup>−</sup> (79 mV for **31**, 37 mV for **30**), and Br<sup>−</sup> (57 mV for **31**, 45 mV for **30**), induced smaller but notable negative potential shifts in acetonitrile. The response diminished in 99:1 acetonitrile–water solvent systems, with H<sub>2</sub>PO<sub>4</sub><sup>−</sup> eliciting shifts of 147 and 59 mV for **31** and **30**, respectively [42]. These results highlight the superior electrochemical performance of halogen bonding motifs in the presence of competitive solvents, further distinguishing their utility in anion recognition applications.



The macrocyclic amides **32** and **33**, featuring Fc moieties, demonstrated electrochemical recognition of anions, particularly  $\text{H}_2\text{PO}_4^-$  [43]. Cyclic voltammetry and DPV studies in a 1:2 dichloromethane–acetonitrile mixture containing 0.1 M  $[\text{Bu}_4\text{N}][\text{ClO}_4]$  as the supporting electrolyte revealed limited negative potential shifts upon anion binding. For  $\text{H}_2\text{PO}_4^-$ , the observed shifts were 68 mV for **32** and 94 mV for **33**, significantly smaller compared to other receptors that can exhibit shifts exceeding 200 mV under similar conditions. Other anions, including  $\text{Cl}^-$ ,  $\text{HSO}_4^-$ ,  $\text{F}^-$ , and  $\text{AcO}^-$ , induced shifts of  $\leq 12$  mV, indicating minimal interaction and weak binding affinity. While **33** exhibited slightly better performance due to its 2,2'-cyclisation, larger cavity, and additional binding sites, the overall electrochemical response of these receptors remains weak and less attractive compared to more sensitive and responsive systems.

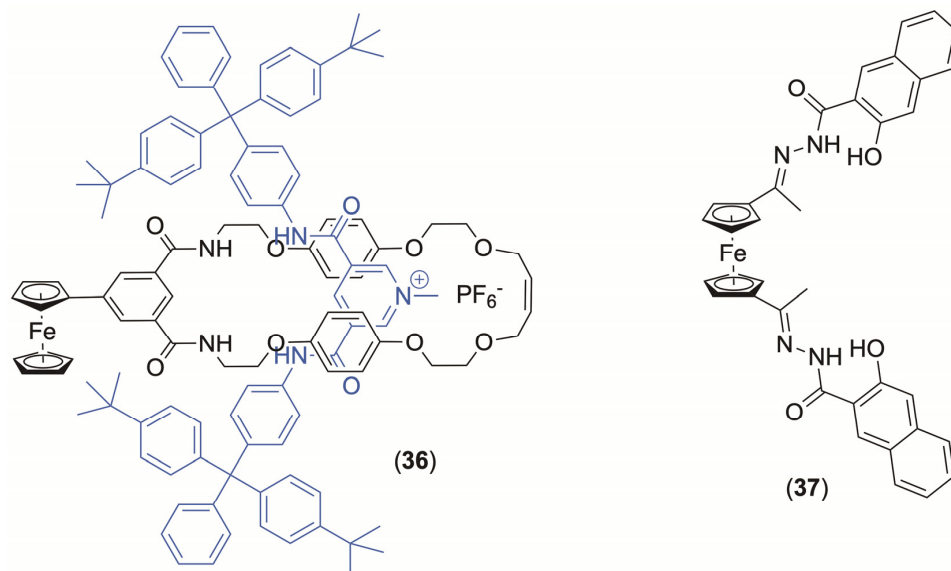
Cyclic voltammetry studies of ferrocenophane **34** conducted in dichloromethane and acetonitrile with 0.1 M  $[\text{Bu}_4\text{N}][\text{BF}_4]$  as the supporting electrolyte revealed negative potential shifts in the  $\text{Fc}/\text{Fc}^+$  redox couple upon anion binding [44]. The largest shifts were observed for  $\text{H}_2\text{PO}_4^-$ , with values of 139 mV in dichloromethane and 41 mV in acetonitrile. In mixed acetonitrile–water solutions containing up to 15% water, **34** maintained its sensing ability, displaying a shift of 162 mV for  $\text{H}_2\text{PO}_4^-$ . Smaller shifts were observed in acetonitrile for  $\text{HSO}_4^-$  (67 mV) and  $\text{F}^-$  (33 mV). Compared to receptor **32**, **34** demonstrates a significantly higher sensitivity in dichloromethane, with a shift more than twice as large. Moreover, **34** stands out by retaining its sensing ability in mixed acetonitrile–water systems, a feature not reported for receptor **32**.

Receptor **35** provides another example of selective electrochemical recognition of  $\text{H}_2\text{PO}_4^-$  ions. Cyclic voltammetry studies of **35** in dichloromethane with 0.1 M  $[\text{Bu}_4\text{N}][\text{BF}_4]$  as the supporting electrolyte exhibit distinct responses in the presence and absence of anions [45]. Upon binding with  $\text{H}_2\text{PO}_4^-$ , the original reduction peak potential at 630 mV disappears as the  $\text{H}_2\text{PO}_4^-$  concentration increases. Simultaneously, a new signal appears at a potential 328 mV more negative, highlighting strong binding interactions and demonstrating the receptor's efficacy in anion sensing.

Ferrocene-functionalised rotaxane **36** demonstrated selective electrochemical recognition of anions, particularly  $\text{Cl}^-$  [46]. Cyclic voltammetry studies in acetonitrile containing 0.1 M  $[\text{Bu}_4\text{N}][\text{PF}_6]$  revealed that the receptor exhibited a quasi-reversible redox couple

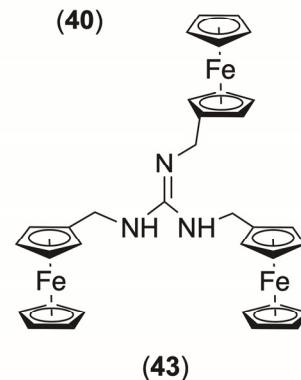
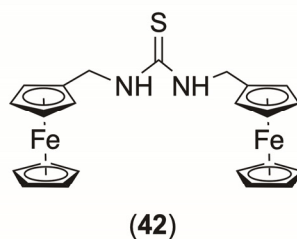
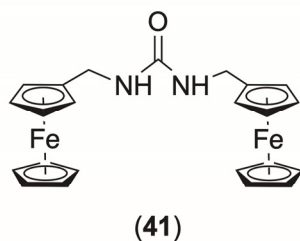
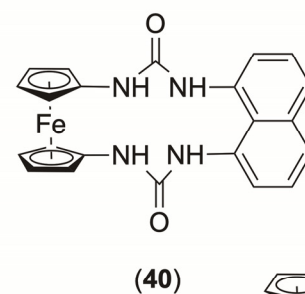
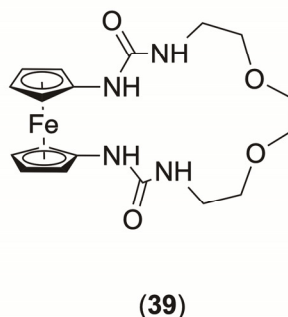
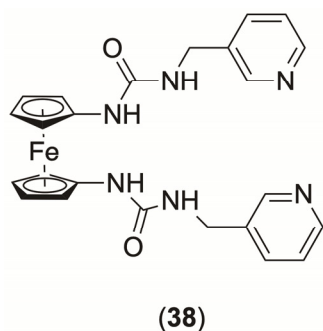
for the  $\text{Fc}/\text{Fc}^+$  system at 115 mV vs.  $\text{Ag}/\text{AgCl}$ . Upon adding one equivalent of  $\text{Cl}^-$ , the receptor exhibited a negative potential shift of 20 mV, which remained constant with further additions, indicating strong and specific binding. In contrast, other anions, including  $\text{H}_2\text{PO}_4^-$ ,  $\text{Bz}^-$ , and  $\text{HSO}_4^-$ , required multiple equivalents to elicit potential shifts of 100, 25, and 40 mV, respectively. The constant response for  $\text{Cl}^-$  reflects the receptor's highly selective binding mechanism, attributed to the rotaxane's cavity design and optimally placed amide hydrogen bonding sites [46]. These results highlight the receptor's potential for selective  $\text{Cl}^-$  sensing despite smaller potential shifts compared to other anions under non-specific conditions.

Compound **37** features amide groups as anion-binding sites for dual fluorescent and electrochemical sensing. Electrochemical experiments were conducted in dimethylformamide with 0.1 M  $[\text{Bu}_4\text{N}][\text{ClO}_4]$  as the supporting electrolyte. Upon titration with  $\text{F}^-$ , a negative potential shift of 120 mV was observed due to the formation of a host–guest complex and subsequent deprotonation of the amide group, generating bifluoride ions ( $\text{HF}_2^-$ ) [47]. In contrast,  $\text{H}_2\text{PO}_4^-$  caused only a minor potential shift, while  $\text{Cl}^-$ ,  $\text{Br}^-$ , and iodide ( $\text{I}^-$ ) produced no noticeable changes.



### 3. Urea and Derivatives-Based Receptors

The electrochemical properties of heteroditopic Fc-based urea receptors were extensively investigated, demonstrating their strong anion-sensing capabilities. The receptors exhibit a reversible one-electron redox wave associated with the  $\text{Fc}/\text{Fc}^+$  couple, shifting significantly upon adding anionic guests [48]. For receptor **38**, the initial redox potential at  $-310$  mV vs.  $\text{Fc}/\text{Fc}^+$  IRS in dimethyl sulfoxide containing 0.1 M  $[\text{Bu}_4\text{N}][\text{ClO}_4]$  as the supporting electrolyte showed distinct negative potential shifts depending on the anion. The addition of  $\text{F}^-$  resulted in the most significant shift of 216 mV, indicating a strong interaction due to its high electronegativity and ability to form robust hydrogen bonds with the urea N–H groups. Dihydrogen phosphate, another strongly interacting anion, caused a significant shift of 144 mV, attributed to its dual hydrogen bonding capability.



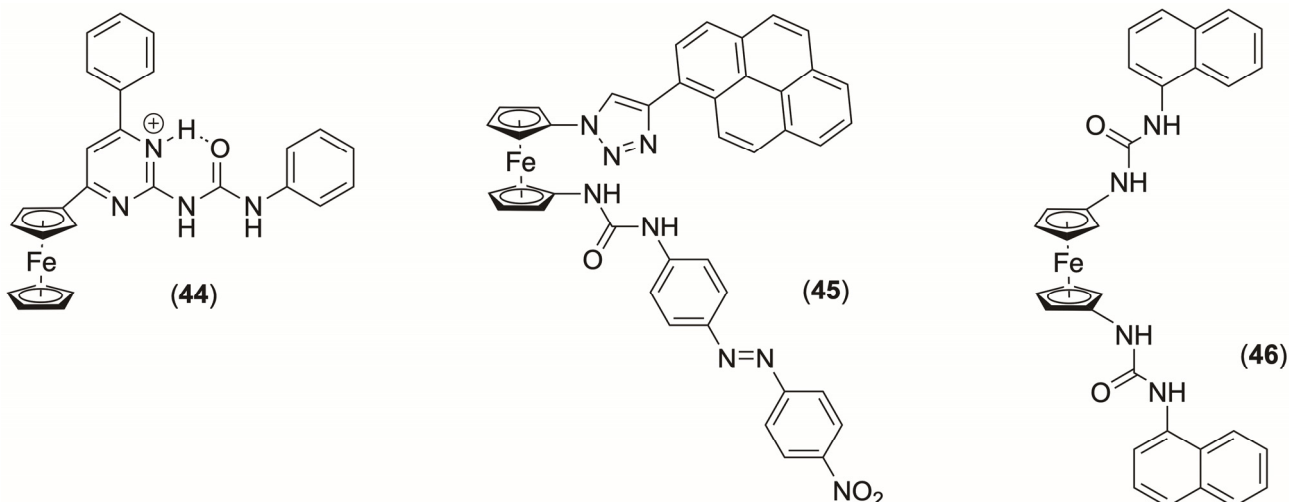
Receptor **39**, incorporating a ferrocenophane structural motif with urea groups as part of a macrocyclic framework, exhibited even more pronounced redox responses [48]. The initial redox potential of  $-370$  mV vs.  $\text{Fc}/\text{Fc}^+$  IRS shifted to  $-590$  mV upon interaction with  $\text{H}_2\text{PO}_4^-$ , corresponding to a shift of 220 mV. Acetate caused a smaller but notable shift of 110 mV, reflecting moderate binding strength. The response to  $\text{F}^-$  for receptor **39** was also significant, with a shift of 76 mV, highlighting the versatility of this receptor in accommodating a variety of anions through hydrogen bonding.

The Fc-naphthalene receptor **40** demonstrated selective electrochemical sensing of  $\text{F}^-$  and  $\text{H}_2\text{PO}_4^-$ . Cyclic voltammetry in dimethyl sulfoxide (0.1 M  $[\text{Bu}_4\text{N}][\text{PF}_6]$ ) revealed a reversible one-electron oxidation process at  $-270$  mV vs.  $\text{Fc}/\text{Fc}^+$  IRS for the unbound receptor [49]. Upon adding  $\text{F}^-$ , the redox wave shifted in the negative potential direction by 190 mV. A similar, albeit smaller, shift of 125 mV was observed with  $\text{H}_2\text{PO}_4^-$ . The system displayed “two-wave” behaviour for both anions, indicating potent and selective binding through hydrogen bonding interactions between the receptor’s urea groups and the anions. Other anions, including  $\text{Cl}^-$ ,  $\text{Br}^-$ , and  $\text{HSO}_4^-$ , had no observable impact on the redox potential [49].

The electrochemical behaviour of multinuclear ferrocenyl derivatives, including urea (**41**), thiourea (**42**), and guanidine (**43**) receptors, was evaluated in dimethylformamide with 0.1 M  $[\text{Bu}_4\text{N}][\text{PF}_6]$  as the supporting electrolyte [50]. All three receptors exhibited a single reversible oxidation process for the  $\text{Fc}/\text{Fc}^+$  couple, with midpoint potentials between 490 and 530 mV vs. decamethylferrocene (DmFc) IRS. Receptor **43** demonstrated the largest negative potential shifts of 170 mV for  $\text{H}_2\text{PO}_4^-$ , 140 mV for  $\text{AcO}^-$ , and 110 mV for  $\text{F}^-$ , indicating strong anion binding through hydrogen bonding and electrostatic interactions. Similarly, **42** showed moderate responses of 100 mV for  $\text{H}_2\text{PO}_4^-$ , 70 mV for  $\text{AcO}^-$ , and 50 mV for  $\text{F}^-$ . Receptor **41** exhibited high selectivity for  $\text{H}_2\text{PO}_4^-$  (110 mV), with negligible shifts observed for acetate and  $\text{F}^-$ . Notably,  $\text{Cl}^-$ ,  $\text{NO}_3^-$ , and  $\text{HSO}_4^-$  induced no significant redox changes in any of the receptors [50].

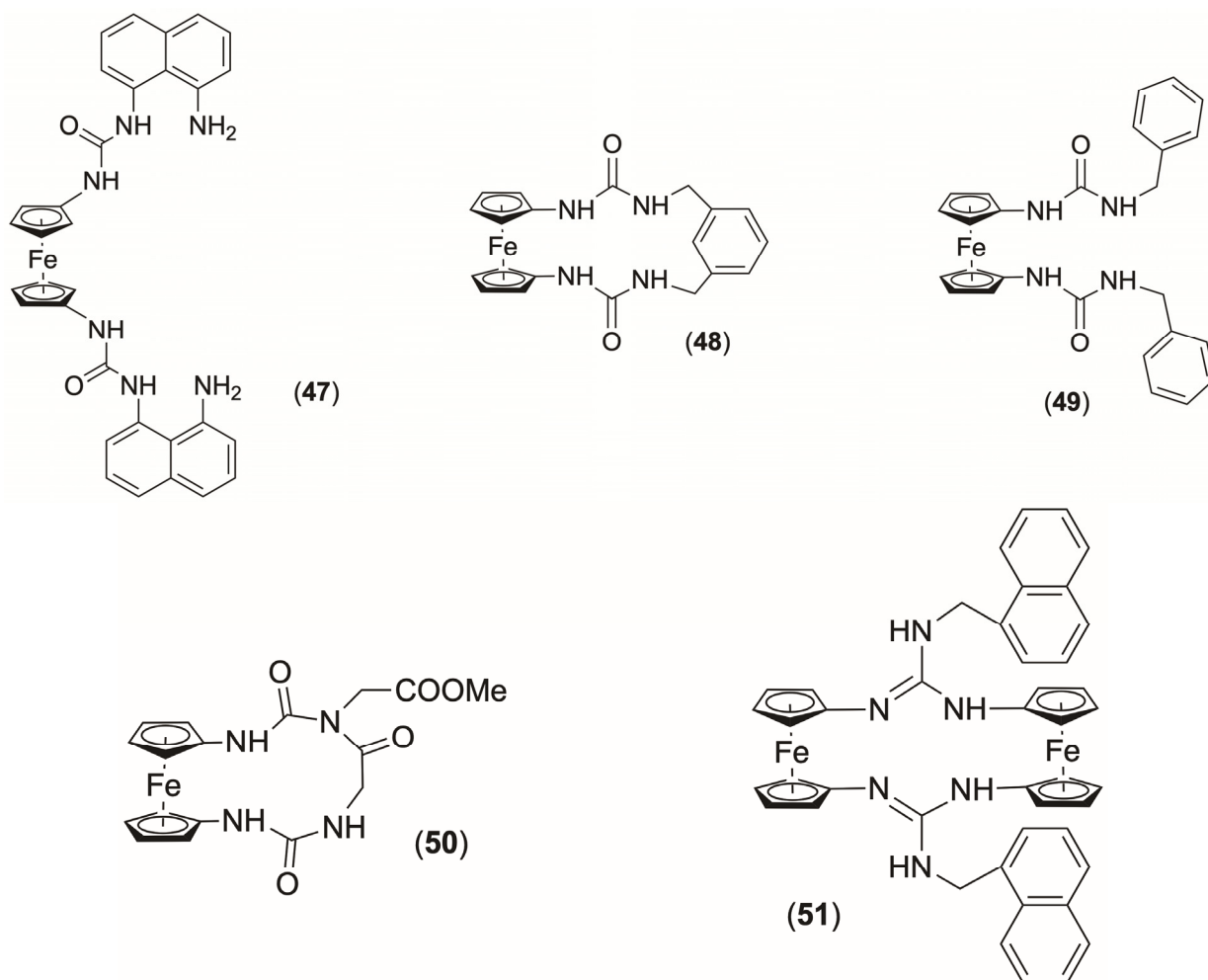
Adding to the versatility of urea-functionalised sensors, the 2-ureido-4-ferrocenyl pyrimidine receptor **44** demonstrated electrochemical responsiveness to strong acids, including trifluoromethanesulfonic acid and tetrafluoroboric acid [51]. Cyclic voltammetry experiments conducted in dichloromethane (0.1 M  $[\text{Bu}_4\text{N}][\text{ClO}_4]$ ) revealed a positive potential shift in the  $\text{Fc}/\text{Fc}^+$  redox couple upon acid addition. The midpoint potential shifted

by approximately 128 mV with trifluoromethanesulfonic acid and 144 mV with tetrafluoroboric acid, forming a new, thermodynamically stable complex. Interestingly, the receptor's response to trifluoroacetic acid resulted in only a minor shift of 20 mV [51].



The ferrocenyl derivative **45**, featuring a urea moiety, demonstrated significant anion recognition capabilities [52]. Cyclic voltammetry studies conducted in dimethyl sulfoxide (0.1 M [Bu<sub>4</sub>N][PF<sub>6</sub>]) revealed notable negative potential shifts in the Fc/Fc<sup>+</sup> redox couple upon interaction with basic anions such as F<sup>−</sup>, H<sub>2</sub>PO<sub>4</sub><sup>−</sup>, HP<sub>2</sub>O<sub>7</sub><sup>3−</sup>, AcO<sup>−</sup>, and Bz<sup>−</sup>. For H<sub>2</sub>PO<sub>4</sub><sup>−</sup>, the midpoint potential shifted by 155 mV after adding six equivalents of the anion, while AcO<sup>−</sup> and Bz<sup>−</sup> exhibited characteristic two-wave behaviour, with shifts of 175 and 140 mV, respectively. Interestingly, titrations with F<sup>−</sup> and HP<sub>2</sub>O<sub>7</sub><sup>3−</sup> in the presence of acetic acid yielded a single, well-defined oxidation peak with shifts of 130 and 160 mV, respectively, indicating hydrogen-bonded complex formation without deprotonation [52].

Cyclic voltammetry and DPV analysis of **40**, **46–49** were conducted in dimethyl sulfoxide with 0.1 M [Bu<sub>4</sub>N][ClO<sub>4</sub>] as the supporting electrolyte to monitor the redox behaviour of these receptors [53]. Receptor **40** showed a reversible redox system at −350 mV vs. Fc/Fc<sup>+</sup> IRS in the absence of anions. Upon binding F<sup>−</sup>, this potential shifted negatively by 190 mV, while binding with H<sub>2</sub>PO<sub>4</sub><sup>−</sup> resulted in a shift of 125 mV. These values align with previously published data by the same research group using the same receptor [49]. Similarly, receptor **46** exhibited a potential shift of 208 mV upon F<sup>−</sup> binding and 90 mV with H<sub>2</sub>PO<sub>4</sub><sup>−</sup>. These negative potential shifts reflect the increased difficulty of oxidation upon complexation, arising from the electrostatic and hydrogen-bonding interactions between the anions and the urea moieties. Other receptors reported in the study demonstrated similar trends: receptor **47** displayed shifts of 60 mV for F<sup>−</sup> and 108 mV for H<sub>2</sub>PO<sub>4</sub><sup>−</sup>, receptor **48** showed shifts of 112 mV and 76 mV for F<sup>−</sup> and H<sub>2</sub>PO<sub>4</sub><sup>−</sup>, respectively, while receptor **49** exhibited shifts of 160 mV for F<sup>−</sup> and 142 mV for H<sub>2</sub>PO<sub>4</sub><sup>−</sup>. Importantly, anions such as Cl<sup>−</sup>, Br<sup>−</sup>, AcO<sup>−</sup>, NO<sub>3</sub><sup>−</sup>, and HSO<sub>4</sub><sup>−</sup> did not induce any significant potential shift, even in high concentrations [53].

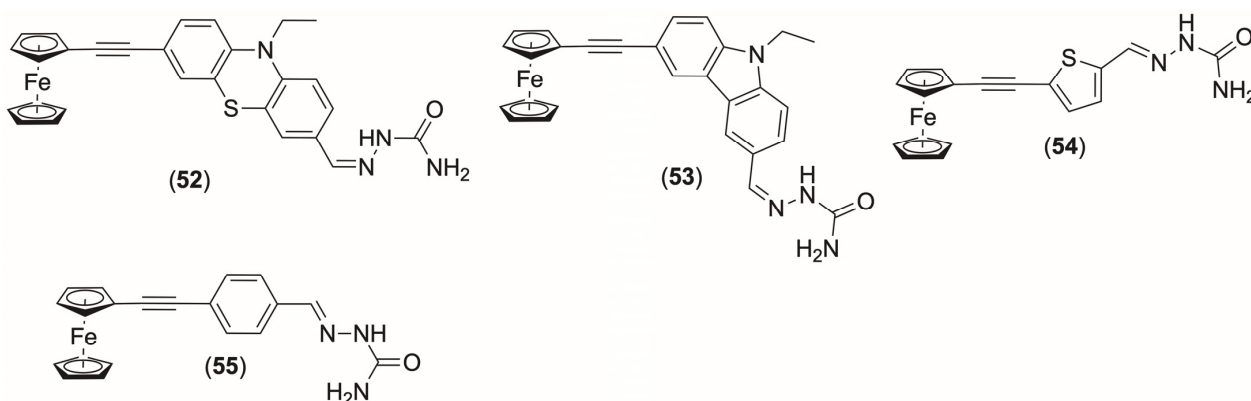


The 1,3,6,8-tetraza[8]-ferrocenophane receptor **50**, with an Fc unit substituted at the 1 and 1' positions by urea groups, were studied for electrochemical responses to anions [54]. Cyclic voltammetry studies conducted in dichloromethane with 0.1 M  $[\text{Bu}_4\text{N}][\text{PF}_6]$  as the supporting electrolyte revealed a reversible oxidation process for receptor **50**, with a midpoint potential of -130 mV versus the  $\text{Fc}/\text{Fc}^+$  IRS. Differential pulse voltammetry experiments showed selective negative potential shifts upon adding  $\text{H}_2\text{PO}_4^-$  and  $\text{F}^-$ . The maximal shifts observed were 136 mV with 2.5 equivalents of  $\text{H}_2\text{PO}_4^-$  and 63 mV with 3.5 equivalents of  $\text{F}^-$ . No significant changes were observed with  $\text{Cl}^-$ ,  $\text{Br}^-$ ,  $\text{NO}_3^-$ , or  $\text{HSO}_4^-$ .

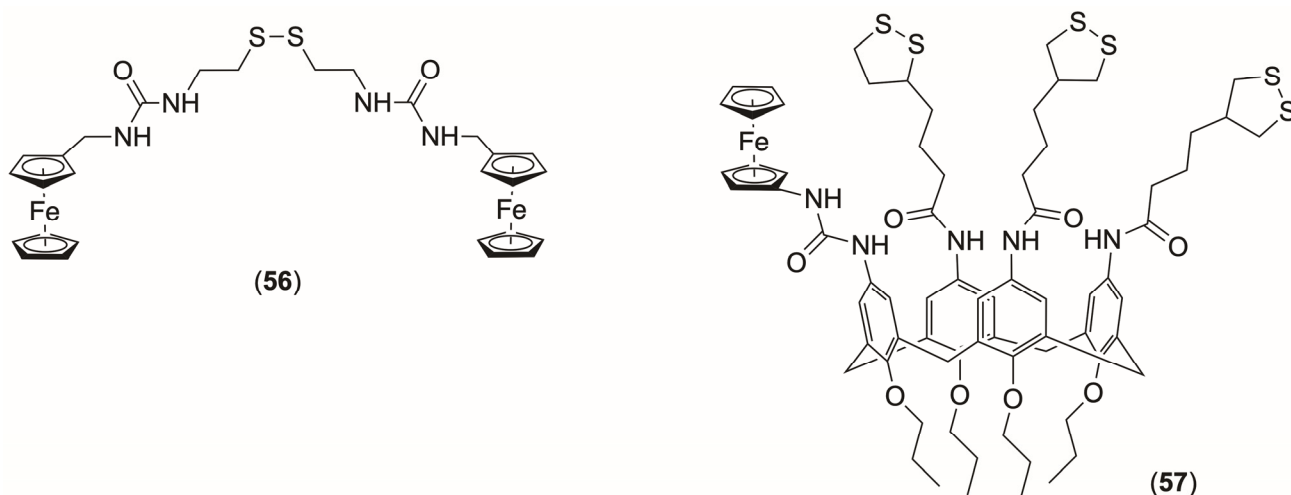
The guanidino-ferrocenophane **51** exhibits distinctive redox behaviour upon interaction with various anions [55]. Differential pulse voltammetry analysis in a 9:1 dimethyl sulfoxide– $\text{H}_2\text{O}$  mixture with 0.1 M  $[\text{Bu}_4\text{N}][\text{PF}_6]$  as the supporting electrolyte revealed two distinct one-electron oxidation peaks at -350 and -90 mV vs.  $\text{Fc}/\text{Fc}^+$  IRS. Binding with  $\text{F}^-$  and  $\text{AcO}^-$  caused the second oxidation peak to disappear entirely, while the first peak remained unperturbed. In contrast,  $\text{H}_2\text{PO}_4^-$  and  $\text{HSO}_4^-$  induced different behaviours:  $\text{H}_2\text{PO}_4^-$  caused a positive potential shift of 14 mV for the first peak and a negative potential shift of 84 mV for the second. In comparison,  $\text{HSO}_4^-$  showed a large positive shift of 89 mV for the first peak and a negative one of 13 mV for the second [55]. Receptor **51** also demonstrated selectivity for nitrate  $\text{NO}_3^-$  and chloride  $\text{Cl}^-$  in dichloromethane (0.1 M  $[\text{Bu}_4\text{N}][\text{PF}_6]$ ), with negative potential shifts of 50 and 130 mV for  $\text{NO}_3^-$  and 80 and 100 mV for  $\text{Cl}^-$  across its two redox peaks.

Ethynyl Fc-based semicarbazide derivatives **52–55** have been investigated as a multifunctional receptor for  $\text{F}^-$  [26]. Cyclic voltammetry studies of **52** conducted in dimethyl

sulfoxide with 0.1 M  $[\text{Bu}_4\text{N}][\text{PF}_6]$  as the supporting electrolyte exhibited a negative potential shift of 120 mV upon adding 1.4 equivalents of  $\text{F}^-$ . In contrast, the other receptors (**53–55**) demonstrated weaker responses, with shifts limited to 10 mV under similar conditions. The superior electrochemical response of **52** was attributed to its favourable electronic communication between the Fc moiety and the fluoride-binding semicarbazide site and its extended conjugated structure [26].

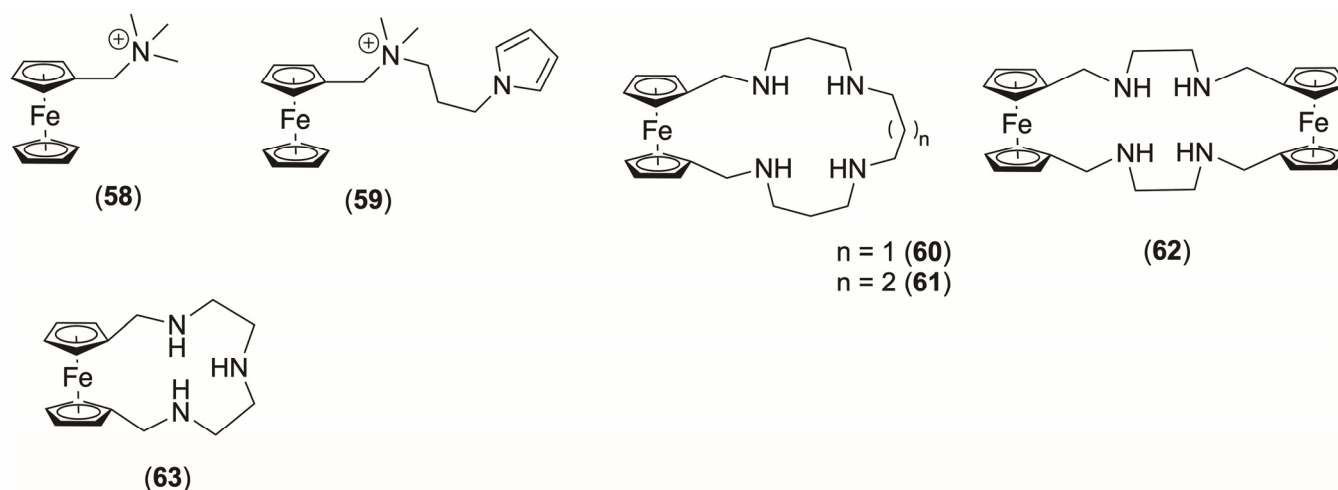


Ferrocene-functionalised receptors with urea groups, such as **56** and **57**, have demonstrated significant electrochemical responses to various anions [33]. Cyclic voltammetry studies in a 1:1 acetonitrile–dichloromethane solvent mixture with 0.1 M  $[\text{Bu}_4\text{N}][\text{BF}_4]$  revealed negative potential shifts in the  $\text{Fc}/\text{Fc}^+$  redox potential upon anion binding. Receptor **57** exhibited potential shifts of 115, 180, and 250 mV for  $\text{Cl}^-$ ,  $\text{Bz}^-$ , and  $\text{H}_2\text{PO}_4^-$ , respectively, when assembled into SAM on gold electrodes, with slightly smaller shifts of 60, 150, and 200 mV in solution. Receptor **56**, a simpler urea-functionalised derivative, showed smaller shifts of 50, 100, and 150 mV for the same anions.



#### 4. Amines-Based Receptors

The (ferrocenylmethyl)trimethylammonium cation **58** demonstrated effective electrochemical sensing of  $\text{H}_2\text{PO}_4^-$  and  $\text{ATP}^{2-}$ , leveraging strong ion-pairing interactions that become reinforced upon oxidation to the  $\text{Fc}^+$  form [56]. Cyclic voltammetry results revealed a characteristic two-wave behaviour for **58** when interacting with  $\text{H}_2\text{PO}_4^-$  in organic media, such as dichloromethane and acetonitrile (0.1 M  $[\text{Bu}_4\text{N}][\text{ClO}_4]$ ), showing a negative potential shift of 470 mV in dichloromethane and 295 mV in acetonitrile. This significant shift illustrates the ion-pairing effect on the  $\text{Fc}/\text{Fc}^+$  redox couple, with maximum perturbation observed at 3–4 equivalents of  $\text{H}_2\text{PO}_4^-$ , as reflected by the emergence of a new cyclic voltammetric wave corresponding to the anion-bound complex.



Comparatively, the response to  $\text{HSO}_4^-$  and  $\text{NO}_3^-$  in these organic solvents was weaker, with shifts in the order of 10–25 mV, further confirming the selective affinity of **58** for  $\text{H}_2\text{PO}_4^-$  and  $\text{ATP}^{2-}$ . This selectivity is attributed to electrostatic interaction and specific hydrogen bonding with the quaternary ammonium and  $\text{Fc}^+$ . The solvent choice notably influenced sensing sensitivity; non-polar solvents like dichloromethane increased electrostatic interactions, resulting in more significant redox shifts (470 and 280 mV for  $\text{H}_2\text{PO}_4^-$  and  $\text{ATP}^{2-}$ , respectively), while protic solvents, such as methanol, led to no detectable sensing capacity, likely due to hydrogen-bonding stabilisation of the anions [56].

The polymer film derived from **59** displays significant sensing capabilities for  $\text{H}_2\text{PO}_4^-$  in acetonitrile containing 0.1 M  $[\text{Bu}_4][\text{ClO}_4]$  as the supporting electrolyte. The films were synthesised through oxidative electropolymerisation of the pyrrole-containing ferrocenyl-methylammonium monomer at 900 mV vs.  $\text{Ag}/\text{Ag}^+$ , resulting in stable polymer coatings on platinum electrodes [57]. Upon interaction with  $\text{H}_2\text{PO}_4^-$ , a negative potential shift of 280 mV is observed. This shift is attributed to ion-pairing interactions between the alkylammonium groups in the polymer and  $\text{H}_2\text{PO}_4^-$ , which are further reinforced in the oxidised  $\text{Fc}^+$  state. Compared to receptor **58**, which exhibits a significantly larger potential shift of 470 mV for  $\text{H}_2\text{PO}_4^-$  and is the only receptor capable of detecting  $\text{H}_2\text{PO}_4^-$  in aqueous media, the polymer-based receptor **19** demonstrates slightly better sensitivity than **59**, with potential shifts of 220–260 mV depending on the solvent. However, neither **59** nor **19** match the performance of **58** in terms of both sensitivity and versatility for oxo-anion detection. Moreover, as confirmed through competitive experiments, the sensing properties are highly selective for  $\text{H}_2\text{PO}_4^-$  over other anions such as  $\text{HSO}_4^-$ ,  $\text{NO}_3^-$ , and  $\text{ATP}^{2-}$  [37,56,57].

The electrochemical identification of  $\text{H}_2\text{PO}_4^-$  and  $\text{ATP}^{2-}$  was also achieved using polyaza Fc macrocyclic ligands **60** and **61** in an aqueous environment [58]. When protonated in the pH range of 6 to 8, these ligands form polyammonium macrocycles capable of coordinating anions through electrostatic and hydrogen bonding interactions. Cyclic voltammetry revealed a significant negative potential shift in the  $\text{Fc}/\text{Fc}^+$  redox couple upon adding  $\text{H}_2\text{PO}_4^-$  and  $\text{ATP}^{2-}$ , stabilising  $\text{Fc}^+$  due to the close association with the negatively charged phosphate anions. Specifically, ligand **60** exhibited a negative potential shift of 60 mV for  $\text{H}_2\text{PO}_4^-$  and 40 mV for  $\text{ATP}^{2-}$ , while ligand **61** showed similar shifts, confirming effective anion recognition and binding [58].

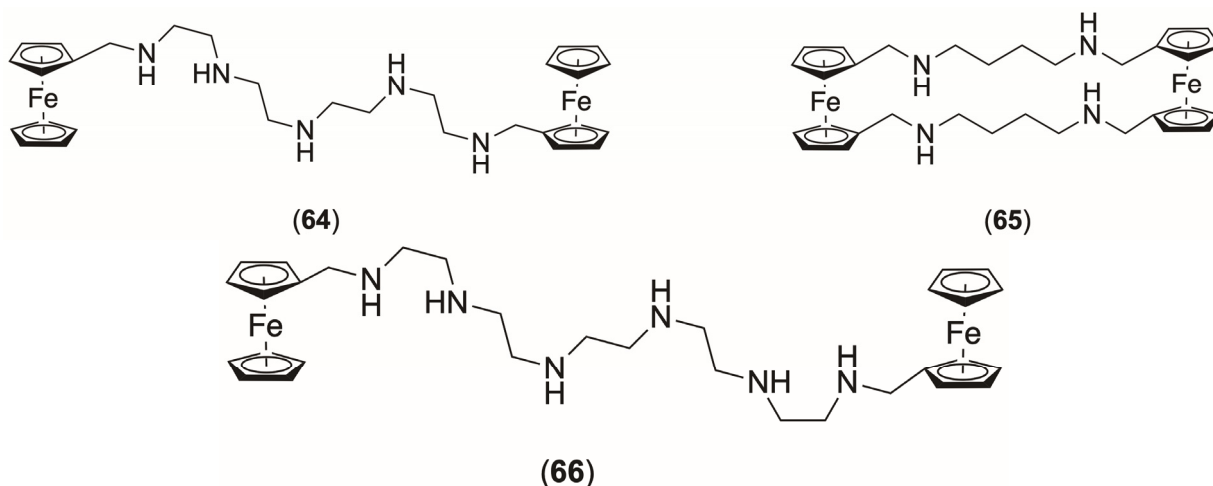
Receptors **60** and **61**, previously discussed for their  $\text{H}_2\text{PO}_4^-$  ion recognition capabilities, were also evaluated and compared with receptor **63** to assess their performance under varying conditions [59]. The electrochemical studies were conducted in aqueous solutions adjusted to pH 6.5, with 0.2 M KCl as the supporting electrolyte. Cyclic voltammetry revealed that receptors **60**, **61**, and **63** exhibited negative potential shifts of 60–80 mV in the

Fc/Fc<sup>+</sup> redox couple upon binding ATP<sup>2−</sup> or hydrogen phosphate (HPO<sub>4</sub><sup>2−</sup>) [59]. However, receptors **60** and **61** exhibited superior selectivity, as other tested anions—including Cl<sup>−</sup>, NO<sub>3</sub><sup>−</sup>, and sulphate (SO<sub>4</sub><sup>2−</sup>)—induced negligible potential shifts.

A separate study employed potentiometric techniques to investigate the selective electrochemical recognition of SO<sub>4</sub><sup>2−</sup> and H<sub>2</sub>PO<sub>4</sub><sup>−</sup> by polyaza Fc macrocyclic receptors **60** and **62**. For this experiment, a 7:3 tetrahydrofuran–water mixture (0.1 M [Bu<sub>4</sub>N][ClO<sub>4</sub>]) was used, focusing on the pH-dependent shifts in redox potential associated with anion binding [60]. For SO<sub>4</sub><sup>2−</sup> ions, **60** and **62** exhibited maximum negative potential shift at acidic pH, specifically in the pH 3–5 range, where the protonated polyammonium form of the receptors is highly effective in engaging SO<sub>4</sub><sup>2−</sup> through strong electrostatic and hydrogen bonding interactions. The most pronounced shift was observed for receptor **62**, which showed a negative potential shift of approximately 54 mV at pH 4 [60]. Receptor **60** also responded to SO<sub>4</sub><sup>2−</sup> at an acidic pH (10 mV at pH 4). However, its primary selectivity was directed toward phosphate at near-neutral pH, where a shift of ca. 50 mV was observed. Receptor **62** similarly exhibited phosphate recognition, though to a lesser degree, with the most significant interactions (32 mV) occurring between pH 5.5 and 6.5. This pH range favours the binding of the H<sub>2</sub>PO<sub>4</sub><sup>−</sup>, which predominates in neutral pH conditions and binds effectively to the partially protonated receptor.

These observations highlight the importance of the macrocyclic structure and the proximity of the Fc redox centre to the binding cavity, which enhance selectivity by optimising cation–anion interactions upon oxidation to the Fc<sup>+</sup> state. The distinct pH-dependent shifts—54 mV for SO<sub>4</sub><sup>2−</sup> with receptor **62** at pH 4 and ca. 50 mV for phosphate with **60** at pH 7—demonstrate that these receptors can be fine-tuned for selective anion recognition, offering potential as electrochemical sensors for SO<sub>4</sub><sup>2−</sup> and phosphate in aqueous environments, where competing anions may be present [60].

Receptors **60**, **64**, and **65** were synthesised and systematically evaluated for their ability to recognise anions through selective electrochemical responses, leveraging their amine-functionalised polyaza Fc frameworks to achieve strong hydrogen bonding and electrostatic pairing interactions [61]. Receptor **64** exhibited a potential shift of up to 100 mV upon binding ATP<sup>2−</sup> in a mixed solvent system of tetrahydrofuran and water (7:3 *v/v*), showcasing strong charge-pairing and hydrogen bonding interactions. It displayed remarkable selectivity for ATP<sup>2−</sup> over phosphate and nitrate at pH 4.9, underscoring its specificity for biologically relevant anions. Similarly, receptor **60** showed pronounced ATP<sup>2−</sup> selectivity near neutral pH, achieving potential shifts of 60 mV for H<sub>2</sub>PO<sub>4</sub><sup>−</sup> and 40 mV for ATP<sup>2−</sup>. These values align with those reported above for the same receptor under similar experimental conditions [58].



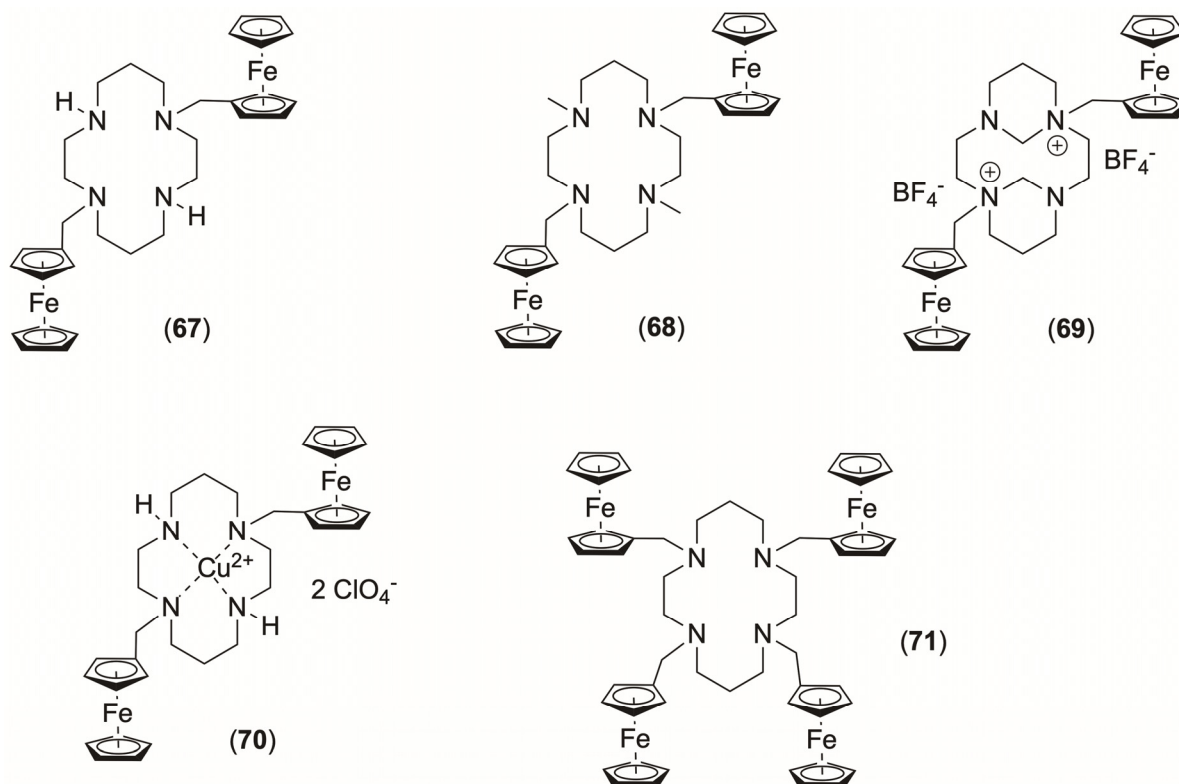
Receptor **65** further highlighted the efficacy of amine-functionalised Fc systems in anion recognition. It enabled the selective detection of phosphate anions at pH 6–8, with shifts in the redox potential of around 100 mV, even in the presence of competing anions like  $\text{NO}_3^-$ ,  $\text{AcO}^-$ , or  $\text{Cl}^-$ . These findings emphasise the importance of tuning the receptor's protonation state and the environmental pH to achieve optimal selectivity and sensitivity.

The electrochemical behaviour of Fc-functionalised polyamine **64** and **66** was evaluated for anion recognition in tetrahydrofuran and water (7:3 *v/v*) at 25 °C with 0.1 M  $[\text{Bu}_4\text{N}][\text{ClO}_4]$  as the supporting electrolyte [62]. Cyclic voltammetry revealed that the receptors exhibit distinct negative potential shifts in their redox potentials upon interaction with anions such as  $\text{ATP}^{2-}$ ,  $\text{SO}_4^{2-}$ , and phosphate, with the magnitude of these shifts dependent on the receptor structure and solution pH. At pH 3.5, **64** demonstrated the highest sensitivity to  $\text{ATP}^{2-}$  with a potential shift of 52 mV, followed by  $\text{SO}_4^{2-}$  (30 mV) and  $\text{H}_2\text{PO}_4^-$  (22 mV). Similarly, **66** showed significant responses, particularly for  $\text{SO}_4^{2-}$  (34 mV) and  $\text{ATP}^{2-}$  (30 mV), while  $\text{H}_2\text{PO}_4^-$  induced a smaller shift (17 mV). In contrast,  $\text{NO}_3^-$  did not produce any measurable change in the redox potential for either receptor. These results highlight the selective anion recognition capability of **64** and **66**, with **64** exhibiting a stronger overall response to  $\text{ATP}^{2-}$ . The pH-dependent behaviour and specificity of these receptors underline their potential as electrochemical sensors for biologically relevant anions [62].

Ferrocene-functionalised polyamine macrocyclic receptors, such as **67–70**, demonstrate the versatility of amine-based frameworks in electrochemical anion sensing [63]. Cyclic voltammetry and DPV studies in acetonitrile (0.1 M  $[\text{Bu}_4\text{N}][\text{ClO}_4]$ ) revealed distinct behaviours influenced by receptor functionalisation. Receptor **67**, with secondary amine groups, showed Fc reversible redox behaviour at 125 mV vs.  $\text{Ag}/\text{Ag}^+$  and exhibited a two-wave response for  $\text{H}_2\text{PO}_4^-$  and  $\text{ATP}^{2-}$ , with negative potential shifts of 160 and 190 mV, respectively. The pronounced shifts reflect strong hydrogen bonding interactions and electrostatic stabilisation in the  $\text{Fc}^+$  oxidation state. For  $\text{HSO}_4^-$ , a smaller shift of 90 mV was observed, while  $\text{F}^-$  and  $\text{NO}_3^-$  induced negligible changes [63].

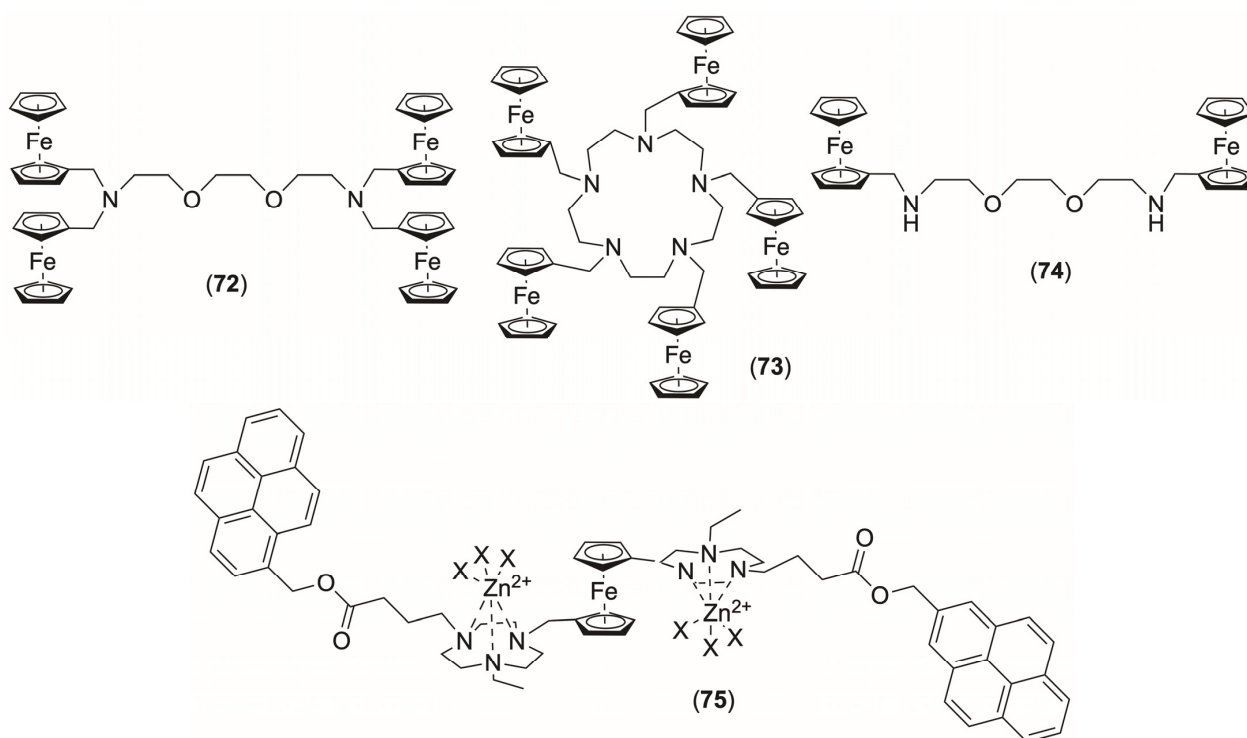
Receptor **69**, with ammonium subunits, exhibited enhanced sensitivity towards  $\text{F}^-$ , with a negative potential shift of 190 mV and a well-defined two-wave behaviour, attributed to strong electrostatic interactions with the dicationic receptor. However, **69** displayed no response to  $\text{Cl}^-$ ,  $\text{Br}^-$ , or  $\text{I}^-$ . Similarly, the copper(II)-complexed receptor **70** showed a selective response to  $\text{F}^-$ , with a significant shift of 210 mV for the  $\text{Cu}^{2+}/\text{Cu}^+$  redox couple and a minimal shift of 30 mV for the Fc redox couple, suggesting  $\text{F}^-$  coordination to the copper centre [63].

The Fc-based polyazacycloalkane **71** was investigated for  $\text{ATP}^{2-}$  detection using CV in aqueous solution under varying pH conditions [64]. At neutral and basic pH, the receptor exhibited a minimal change in its oxidation potential upon  $\text{ATP}^{2-}$  addition. However, a negative potential shift in the redox potential was observed in acidic conditions, indicating enhanced binding interactions between **71** and  $\text{ATP}^{2-}$ . Specifically, the oxidation potential shifted by 3 mV at pH 7.0, 14 mV at pH 5.0, and 33 mV at pH 3.7. These shifts were attributed to the protonation of the amino groups on **71** at lower pH, which increases the receptor's affinity for  $\text{ATP}^{2-}$  through electrostatic interactions and stabilisation of the complex [64].



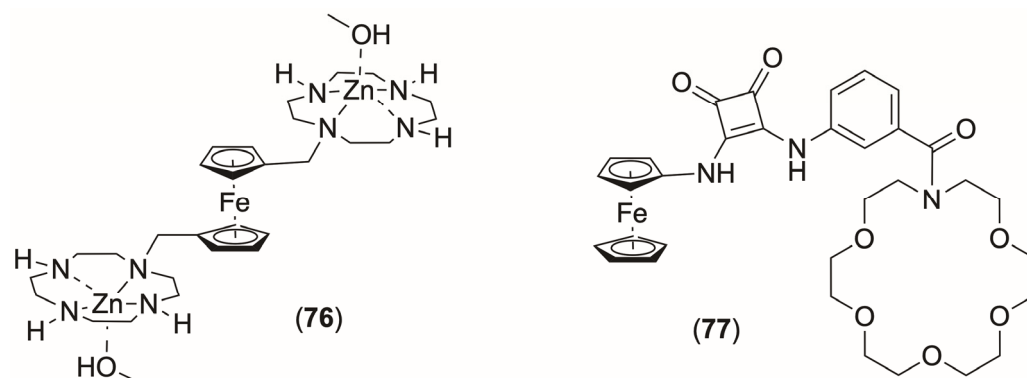
Further electrochemical investigations into Fc-functionalised amine-based receptors **64** and **72–74** revealed selective redox responses in the presence of  $\text{H}_2\text{PO}_4^-$  and  $\text{HSO}_4^-$  in acetonitrile (0.1 M  $[\text{Bu}_4\text{N}][\text{ClO}_4]$ ) [65]. For  $\text{H}_2\text{PO}_4^-$ , **73** exhibited the most significant midpoint potential shift of 400 mV, highlighting its strong affinity for phosphate anions. Receptor **64** displayed a similar response, showing a shift of 354 mV, followed by **74** with a shift of 346 mV. Receptor **72** showed the smallest but significant response, with a potential shift of 268 mV. In contrast, for  $\text{HSO}_4^-$ , **64** exhibited the most significant potential change of 263 mV, followed by **73** (118 mV), **74** (113 mV), and **72** (45 mV).

The performance of **74** in sensing  $\text{H}_2\text{PO}_4^-$  can be further contextualised through comparison with **35**, which exhibits a potential shift of 230 mV in dichloromethane (0.1 M  $[\text{Bu}_4\text{N}][\text{BF}_4]$ ). In contrast, **74** achieves a larger shift of 346 mV in acetonitrile, indicative of stronger binding interactions. The reduced chemical shift observed for **35** can be attributed to the presence of the amide group, which, while providing additional hydrogen bonding opportunities, moderates the receptor's overall binding strength compared to receptor **74**. The difference in shifts cannot be fully explained by the solvent and supporting electrolyte effects, contributing to the difference with only 29 mV [11]. Instead, the stronger electrostatic and hydrogen-bonding interactions provided by the amine group in **74** resulted in a more pronounced stabilisation of the bound complex and a larger potential shift. Conversely, in **35**, the carbonyl group in the amide withdraws electron density from the NH group, reducing its proton-donating capability and attenuating the redox response.



Our group has investigated the electrochemical behaviour of Fc-functionalised receptor **75**, which incorporated two Zn(II)-TACN complexes (TACN = 1,4,7-triazacyclononane; X = Zn(II) complex completed with perchlorate anions) for selective pyrophosphate ( $\text{P}_2\text{O}_7^{4-}$ ) anion sensing [66]. Cyclic voltammetry and SWV studies in 1:9 acetonitrile-Tris-HCl buffer (50 mM, pH 7.4) mixture revealed a single, reversible Fc/ $\text{Fc}^+$  redox couple at 450 mV vs. Ag/AgCl for **75**. The addition of  $\text{P}_2\text{O}_7^{4-}$  resulted in a significant negative potential shift of 100 mV, indicating strong coordination between **75** and  $\text{P}_2\text{O}_7^{4-}$ , driven by the interaction of the Zn(II)-TACN units with the high-charge-density anion. In contrast,  $\text{ATP}^{2-}$  and  $\text{ADP}^{2-}$  induced smaller negative potential shifts of 68 and 54 mV, respectively, while negligible shifts (<20 mV) were observed for monophosphate nucleotides and fluoride. The selective response to  $\text{P}_2\text{O}_7^{4-}$  is attributed to its strong binding affinity and the receptor's ability to undergo a conformational rearrangement to stabilise the complex. These results demonstrate the potential of Zn(II)-TACN-based Fc systems for selective detection of  $\text{P}_2\text{O}_7^{4-}$  in biologically relevant environments [66].

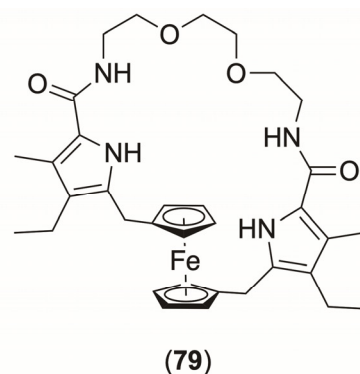
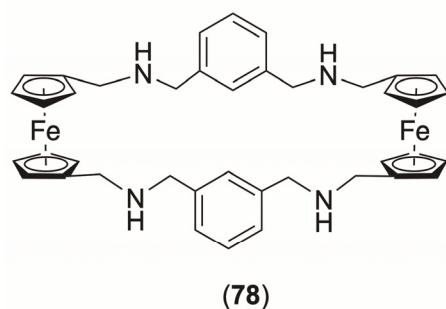
We also developed an Fc-based bis (Zn-cyclen) complex, **76**, as a selective electrochemical sensor for thymidyl-(3'-5')-thymidine (TpT) [67]. The electrochemical measurements were performed in 0.1 M Tris-HCl buffer (pH 7.4), using glassy carbon electrodes at room temperature. Upon binding TpT, a negative potential shift of 36 mV was observed, attributed to the two deprotonated thymine moieties coordinating with the Zn-cyclen centres, forcing a structural rearrangement from a trans to a cis configuration. This interaction was unique to TpT, as other nucleobases and nucleotides, including adenine, thymine, cytosine, guanine, AMP, TMP, TDP, TTP, CMP, GMP, ApC, GpG, and  $\text{P}_2\text{O}_7^{4-}$ , produced negligible changes ( $\leq 5$  mV) in the redox potential of the Fc unit. This finding inspired the development of an electrochemical sensor for selective DNA sequence recognition, particularly in studying DNA damage and repair pathways [68].



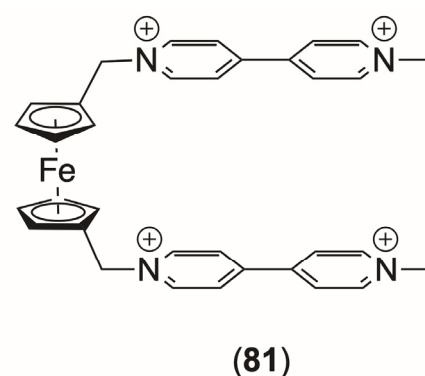
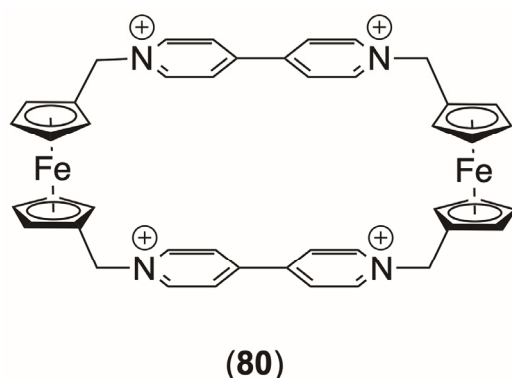
The electrochemical behaviour of the Fc-containing squaramide-based **77**, designed for ion pair recognition, was investigated using CV in acetonitrile with 0.1 M  $[\text{Bu}_4\text{N}][\text{PF}_6]$  as the supporting electrolyte [69]. In the absence of ions, **77** displayed a midpoint potential of approximately  $-12$  mV vs.  $\text{Ag}/\text{Ag}^+$ . The potential remained unchanged after adding sodium ions ( $\text{Na}^+$ ), suggesting minimal interaction between  $\text{Na}^+$  and the Fc unit due to the distance from the cation-binding site. In contrast, negative potential shifts were observed when anions such as  $\text{NO}_3^-$ ,  $\text{Cl}^-$ , and  $\text{Br}^-$  were introduced, indicating increased electron density on the Fc unit. For  $\text{NO}_3^-$ , the shifts were 42 mV (1 equiv.), 50 mV (3 equiv.), and 63 mV (5 equiv.), while  $\text{Cl}^-$  produced more significant shifts of 78 mV (1 equiv.), 96 mV (3 equiv.), and 104 mV (5 equiv.), and  $\text{Br}^-$  showed intermediate shifts of 42 mV (1 equiv.), 64 mV (3 equiv.), and 70 mV (5 equiv.). The negative potential shifts were further enhanced in the presence of 1 equivalent of  $\text{Na}^+$ , demonstrating cooperative binding between the squaramide and crown ether units. For example, the Fc midpoint potential shifted by 62 mV (1 equiv.), 67 mV (3 equiv.), and 72 mV (5 equiv.) for  $\text{NO}_3^-$  and 91 mV (1 equiv.), 112 mV (3 equiv.), and 114 mV (5 equiv.) for  $\text{Cl}^-$  [69]. These findings underscore **77**'s sensitivity to ion pair interactions, with the enhanced shifts attributed to the stabilisation of ion pairs through cooperative binding.

The electrochemical behaviour of the Fc-based tetraazamacrocyclic receptor **78** in the presence of carboxylate anions demonstrated distinct shifts in redox potential, highlighting its anion-sensing capability [70]. Initially, the Fc redox wave was observed at 700 mV vs.  $\text{Ag}/\text{AgCl}$  in methanol with 0.1 M  $[(\text{CH}_3)_4\text{N}][\text{Cl}]$  as the supporting electrolyte. Negative potential shifts were recorded upon adding the anions, with phthalate exhibiting the most significant shift of 275 mV, indicating the strongest binding interaction. Isophthalate and dipicolinate caused shifts of 193 and 168 mV, respectively, reflecting intermediate binding affinities. In contrast, 4-nitrobenzoate showed only a minor potential shift of 49 mV, consistent with its weaker binding. These negative potential shifts are attributed to the electrostatic and hydrogen bonding interactions of the carboxylates with the receptor, leading to supramolecular assembly formation [70]. The significant shift observed for phthalate underscores its strong interaction and highlights the potential of this receptor for selective electrochemical sensing of dicarboxylates in complex environments.

Receptor **79**, an ansa-Fc system containing amine groups, exhibited negative potential shifts upon anion binding in acetonitrile (0.1 M  $[\text{Bu}_4\text{N}][\text{PF}_6]$ ) [71]. Binding  $\text{H}_2\text{PO}_4^-$  resulted in a potential shift of 136 mV,  $\text{F}^-$  produced a shift of 80 mV, while  $\text{Cl}^-$  generated a smaller shift of 24 mV. Comparatively, weaker shifts were observed for  $\text{Br}^-$  and  $\text{HSO}_4^-$ , which caused potential changes of 8 mV and 16 mV, respectively.

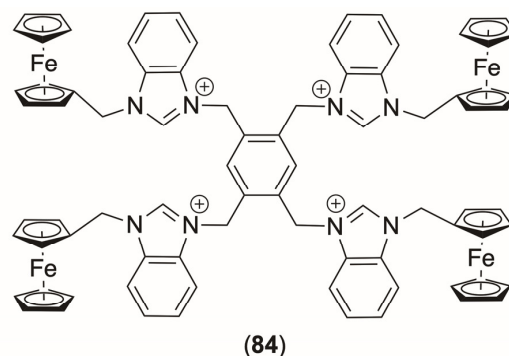
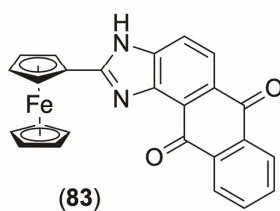
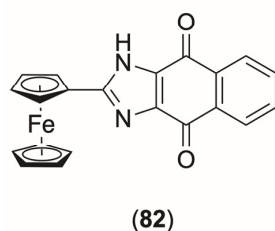


Ferrocene–viologen-based redox-active receptors have been employed for selective anion sensing in aqueous environments containing 0.05 M KNO<sub>3</sub> as the supporting electrolyte [72]. Cyclic voltammetry and DPV investigations revealed that **80** and **81** exhibit selective recognition of ATP<sup>2−</sup>. For **80**, the Fc/Fc<sup>+</sup> redox couple displayed a negative potential shift of 25 mV upon ATP<sup>2−</sup> addition, attributed to the electrostatic interactions between the hexacationic oxidised form of the receptor and the anion. The viologen moieties are thought to enhance further binding through charge transfer interactions with the electron-rich adenosine group of ATP<sup>2−</sup>. Receptor **81** exhibited a smaller response for ATP<sup>2−</sup>, with a shift of 10 mV. Other anions, including HSO<sub>4</sub><sup>−</sup> and S<sub>2</sub>O<sub>4</sub><sup>2−</sup>, induced small shifts (≤20 mV) in **80** and **81** [72].

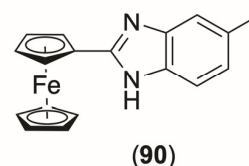
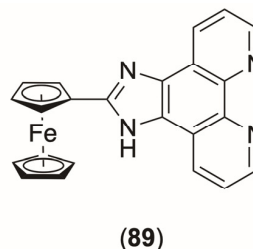
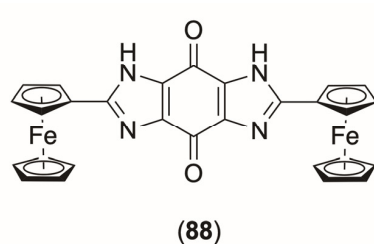
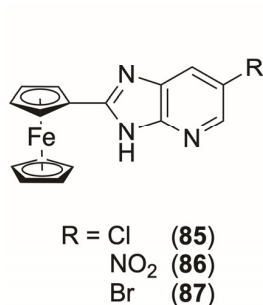


Electrochemical studies of Fc-quinone receptors with imidazole linkages in dimethyl sulfoxide (0.1 M [Bu<sub>4</sub>N][ClO<sub>4</sub>]) revealed distinct redox potential shifts for the Fc and quinone groups upon interaction with F<sup>−</sup> and cyanide (CN<sup>−</sup>) [73]. For **82**, where the imidazole NH is directly attached to the quinone, CN<sup>−</sup> binding caused a potential shift of 198 mV. Fluoride binding induced smaller potential shifts of 122 mV for the Fc redox moiety. In **83**, where the imidazole NH is farther from the quinone, CN<sup>−</sup> induced potential shifts of 188 mV, while F<sup>−</sup> caused shifts of 90 mV. These shifts arise from hydrogen bonding interactions at the imidazole NH, which perturb the electron density and influence charge transfer across the receptor.

For **84**, bearing four ferrocenyl arms and benzimidazolium moieties, CV studies in acetonitrile (0.1 M [Bu<sub>4</sub>N][PF<sub>6</sub>]) revealed distinct potential shifts upon the addition of various anions. Notably, the receptor displayed a negative potential shift of 172 mV upon F<sup>−</sup> binding and 166 mV for hydroxide (OH<sup>−</sup>), reflecting a significant interaction mediated by ionic hydrogen bonding. Minor shifts were observed for AcO<sup>−</sup> (28 mV), Cl<sup>−</sup> (18 mV), and Br<sup>−</sup> (18 mV), suggesting weaker binding affinities [28].



Further investigations on Fc-based imidazole derivatives (**85**–**88**) reveal their distinct ability to recognise  $\text{CN}^-$  selectively [74]. Cyclic voltammetry in dimethylformamide with 0.1 M  $[\text{Bu}_4\text{N}][\text{ClO}_4]$  as the supporting electrolyte demonstrated that these receptors exhibit a reversible  $\text{Fc}/\text{Fc}^+$  redox couple, with midpoint potentials of 906 mV (**85**), 981 mV (**86**), 982 mV (**87**), and 897 mV (**88**) vs.  $\text{Ag}/\text{Ag}^+$ . The introduction of  $\text{CN}^-$  ions induced significant negative potential shifts of 269 mV for **85**, 154 mV for **86**, 81 mV for **87**, and 238 mV for **88**. These shifts are attributed to hydrogen bonding between the imidazole NH and  $\text{CN}^-$ . Notably, other anions caused minor shifts of 57, 43, 47, and 47 mV to **85** midpoint potential when  $\text{F}^-$ ,  $\text{Cl}^-$ ,  $\text{NO}_3^-$ , or  $\text{AcO}^-$  were added, underscoring the receptors' specificity for cyanide. The observed “two-wave” behaviour in the presence of  $\text{CN}^-$  further highlights the formation of robust receptor–anion complexes. This complements the earlier findings on Fc-quinone systems, demonstrating the pivotal role of imidazole in facilitating selective and tunable electrochemical responses for anion sensing [74].

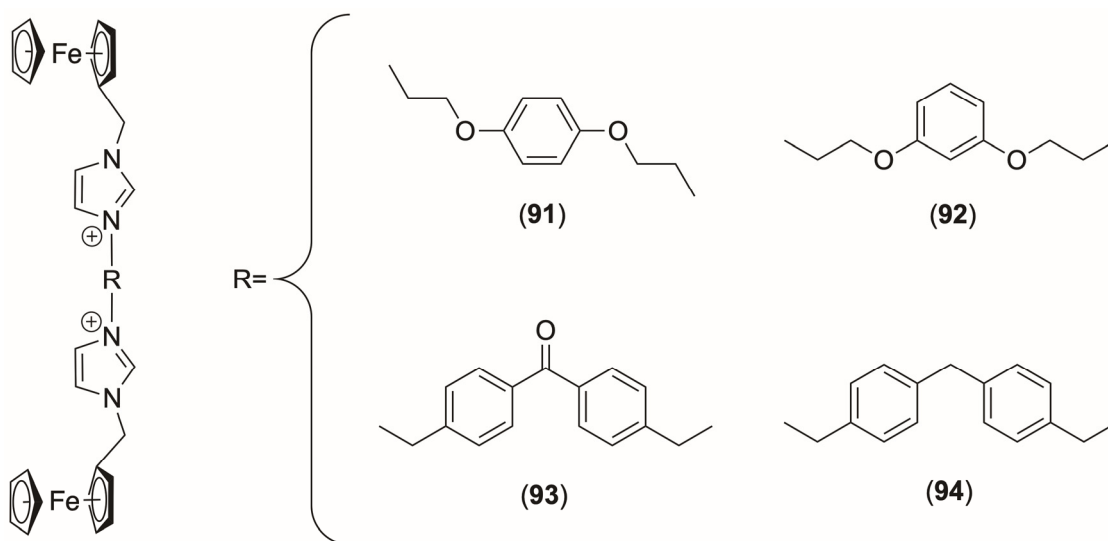


Building on the above electrochemical recognition trends, **89** demonstrated selective sensing of  $\text{F}^-$  and  $\text{P}_2\text{O}_7^{4-}$  in acetonitrile with 0.1 M  $[\text{Bu}_4\text{N}][\text{PF}_6]$  as the supporting electrolyte [75]. Cyclic voltammetry revealed a reversible one-electron oxidation at 640 mV vs. DmFc IRS. Adding  $\text{F}^-$  caused a stepwise response: an initial negative potential shift of 70 mV, attributed to hydrogen bonding interactions, followed by a significant shift of 340 mV at higher concentrations, indicating receptor deprotonation. For  $\text{P}_2\text{O}_7^{4-}$ , an initial shift of 110 mV was observed in the presence of acetic acid, suppressing deprotonation and highlighting hydrogen bonding as the primary interaction mode. The shift increased to 340 mV without acetic acid, indicating simultaneous hydrogen bonding and deprotonation. Other anions, including  $\text{ATP}^{2-}$  and  $\text{ADP}^{2-}$ , produced smaller shifts of 70 and 40 mV, respectively, in methanol, while  $\text{H}_2\text{PO}_4^-$ ,  $\text{AcO}^-$ ,  $\text{Cl}^-$ , and  $\text{NO}_3^-$  caused negligible responses [75].

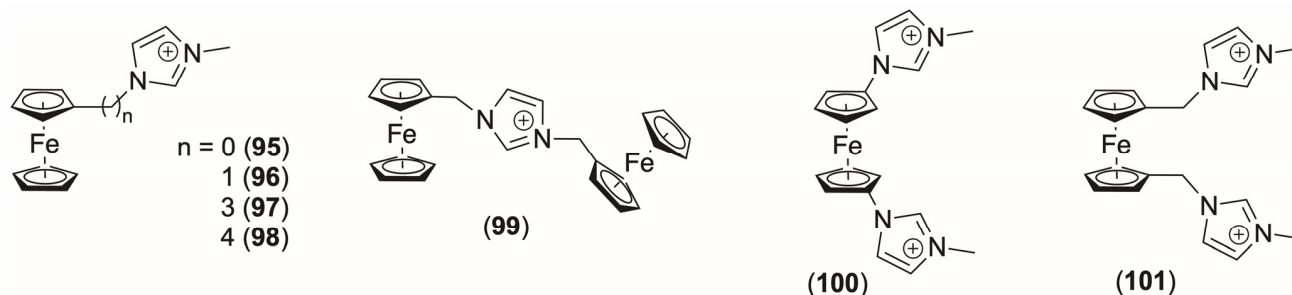
Receptor **90**, containing an Fc moiety directly attached to 5-methylbenzimidazole, demonstrated selective electrochemical sensing for  $\text{F}^-$  ions. Differential pulse voltammetry studies were conducted in acetonitrile (0.1 M  $[\text{Bu}_4\text{N}][\text{PF}_6]$ ). Upon adding  $\text{F}^-$ , a new oxidation peak at 516 mV, accompanied by the gradual decrease of the free receptor's peak from 675 to 594 mV, was observed [76]. These changes indicate the formation of a fluoride-bound complex and the irreversible nature of the redox process with increasing

$F^-$  concentrations. Other anions, including  $Cl^-$ ,  $Br^-$ ,  $H_2PO_4^-$ , and  $NO_3^-$ , did not cause significant perturbation in the  $Fc/Fc^+$  midpoint potential [76].

The electrochemical behaviour of acyclic Fc-based imidazolium salts **91–94** further emphasises the role of structural flexibility in anion recognition. Cyclic voltammetry and DPV studies in acetonitrile containing 0.1 M  $[Bu_4N][PF_6]$  as the supporting electrolyte demonstrated reversible  $Fc/Fc^+$  redox couples for all receptors, with potential shifts reflecting strong interactions with specific anions [77]. Fluoride exhibited potential shifts of 212, 201, 164, and 168 mV for receptors **91**, **92**, **93**, and **94**, respectively. Similarly,  $AcO^-$  induced 68, 65, 36, and 48 mV shifts. In contrast, shifts for  $HSO_4^-$ ,  $Cl^-$ ,  $I^-$ , and  $Br^-$  elicited small to negligible responses. The flexible receptors **91** and **92** showed greater sensitivity, attributed to their ability to adjust conformation for optimal hydrogen bonding interactions, compared to the more rigid receptors **93** and **94** [77].



The electrochemical behaviour of **95–99** illustrates the role of spacer length and electrostatic interactions in anion recognition [78]. Cyclic voltammetry and SWV studies in acetonitrile (0.1 M  $[Bu_4N][PF_6]$ ) revealed reversible redox processes for all receptors. Among these,  $F^-$  induced the most significant negative potential shifts of 230 mV, 160 mV, 28 mV, and 12 mV for **95**, **96**, **97**, and **98**, respectively. The bis-substituted **99** exhibited a shift of 200 mV for  $F^-$ , suggesting enhanced anion binding through electrostatic interactions and ion-pair formation with the  $Fc^+$  centre. Other anions, including  $Cl^-$ ,  $Br^-$ ,  $HSO_4^-$ , and  $H_2PO_4^-$ , caused significantly smaller shifts, generally below 100 mV [78].



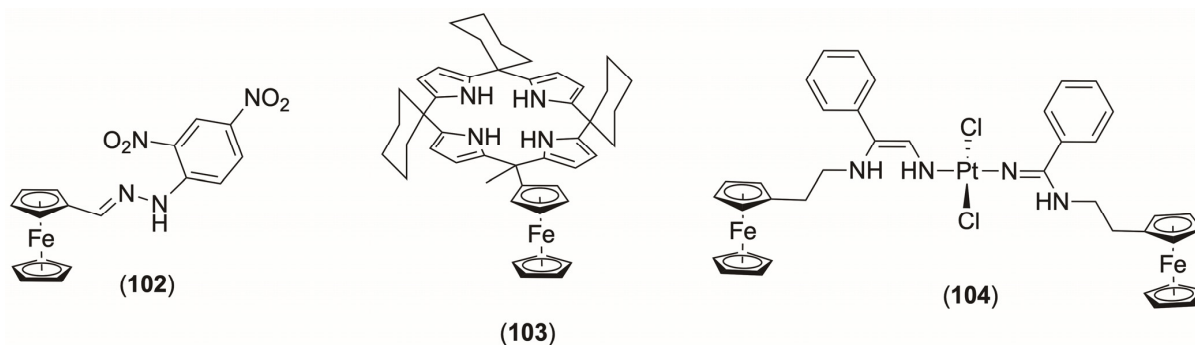
The receptor **95** has been reported in an earlier study under identical conditions—acetonitrile (0.1 M  $[Bu_4N][PF_6]$ )—alongside the imidazolium-functionalised ferrocene receptors **100** and **101** [79]. All three receptors demonstrated significant electrochemical responses to anions, particularly  $F^-$ ,  $Cl^-$ ,  $Br^-$ , and  $HSO_4^-$ , through a combination of hydrogen bonding and charge–charge electrostatic interactions. Upon  $F^-$  addition, notable negative potential shifts of 230 mV for **95**, 270 mV for **100**, and 300 mV for **101** were

observed, indicating strong ion-pair formation and effective redox communication between the ferrocene and imidazolium moieties.

While **95** displayed a consistent and reproducible response to  $F^-$ , **100** demonstrated a particularly enhanced interaction with  $Cl^-$ , showing a significant potential shift of 310 mV, compared to smaller shifts observed for **95** (65 mV) and **101** (72 mV). For  $Br^-$ , all receptors exhibited minimal shifts (e.g., 16 mV for **101** and 12 mV for **95**), suggesting weaker interactions. Similarly,  $HSO_4^-$  induced only modest negative potential shifts, typically below 108 mV across all three receptors [79].

These observations highlight the varying affinity of imidazolium-based receptors towards different anions, with the most significant responses observed for  $F^-$  and  $Cl^-$ . Furthermore, structural variations, such as the length of alkyl spacers linking the ferrocene core to the imidazolium group, influence solubility (improving with longer spacers), anion-binding strength (decreasing with longer spacers), and electrochemical responsiveness (diminishing with increased spacer length) [78,79].

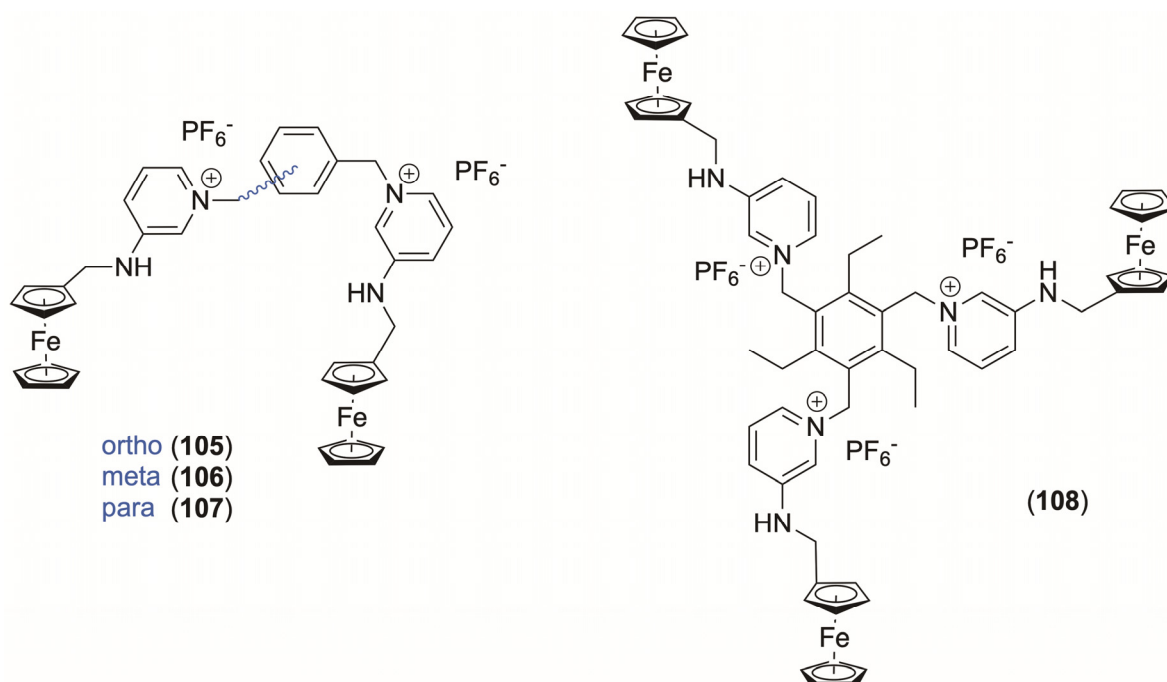
Electrochemical analysis of ferrocene-2,4-dinitrophenylhydrazone, **102**, revealed distinct electrochemical responses to  $AcO^-$  in dimethyl sulfoxide with 0.1 M  $[Bu_4N][PF_6]$  as the supporting electrolyte. Cyclic voltammetry demonstrated a well-defined  $Fc/Fc^+$  redox couple, which underwent a negative potential shift upon  $AcO^-$  addition. Differential pulse voltammetry provided further resolution, showing an 85 mV cathodic shift in the primary oxidation peak, accompanied by the disappearance of a secondary peak. This change reflects the strong binding of  $AcO^-$  to the hydrazone N–H site, influencing the Fc redox environment. Notably, the interaction with  $AcO^-$  was selective, as competing anions such as  $Cl^-$ ,  $Br^-$ , and  $I^-$  produced negligible shifts [80].



Electrochemical studies of Fc-substituted calix[4]pyrrole **103** demonstrated its potential as an electrochemical sensor for anions [81]. Conducted in a 9:1 acetonitrile–dimethyl sulfoxide solvent mixture with 0.1 M  $[Bu_4N][PF_6]$  as the supporting electrolyte, CV and SWV revealed modest negative potential shifts in the  $Fc/Fc^+$  redox couple upon binding various anions. Dihydrogen phosphate induced the most significant shift of approx. 95 mV, followed by  $F^-$  (76 mV),  $Cl^-$  (36 mV), and  $Br^-$  (12 mV). Interestingly, hydrogen sulphate showed no significant potential shift, suggesting minimal interaction. These shifts are attributed to hydrogen bonding interactions between the calix[4]pyrrole NH groups, the Fc cyclopentadienyl CH groups, and the anions [81].

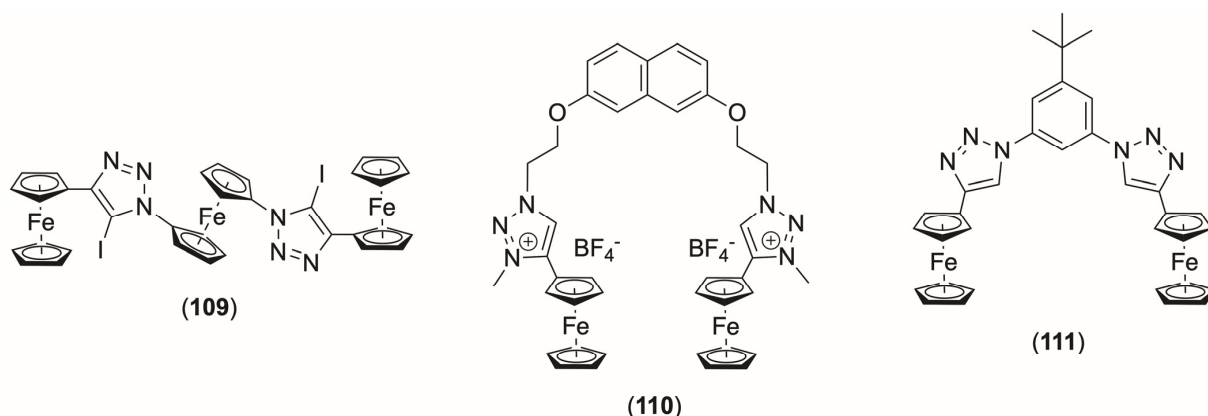
Receptor **104** demonstrates selective electrochemical recognition of  $H_2PO_4^-$  [82]. Cyclic voltammetry and SWV experiments were conducted in a 2.5:0.5 acetonitrile–dichloromethane solvent system with 0.1 M  $[Bu_4N][PF_6]$  as the supporting electrolyte. Upon adding  $H_2PO_4^-$ , the receptor exhibited a negative potential shift of 90 mV, indicating an interaction between the receptor's amidine NH groups and the anion. Selectivity tests revealed that the receptor does not exhibit significant potential shifts for other anions, such as  $HSO_4^-$ ,  $F^-$ , and acetate [82].

A series of bis (ferrocenyl) molecular clips with cationic pyridinium units were synthesised for cooperative anion binding and electrochemical sensing [83]. The modular podands included ortho-, meta-, and para-substituted derivatives (**105**–**107**) and a more rigid, preorganised three-arm host (**108**). Electrochemical studies were performed in acetonitrile containing 0.1 M  $[\text{Bu}_4\text{N}][\text{PF}_6]$  as the supporting electrolyte, and upon adding  $\text{Cl}^-$  ions, the flexible meta derivative **106** exhibited a negative potential shift of 64 mV, attributed to a conformational change from a transoid to a cisoid structure. Bromide and  $\text{NO}_3^-$  induced shifts of 40 and 20 mV, respectively. Conversely,  $\text{I}^-$  caused negligible changes, indicating weaker interaction. The ortho- and para-derivatives (**105** and **107**) showed lower electrochemical responses, showing potential shifts of 40 and 28 mV for  $\text{Br}^-$  and 37 and 20 mV for  $\text{NO}_3^-$ , respectively. The preorganised host **108** exhibited smaller potential shifts (e.g., 29 mV for  $\text{Cl}^-$ ), suggesting limited conformational flexibility and weaker signal transduction despite higher binding affinities [84].



## 5. Triazolium-Based Receptors

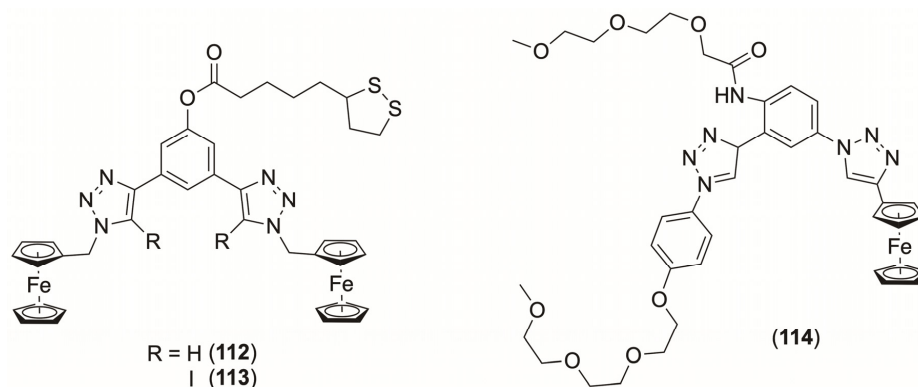
The electrochemical behaviour of **109** highlights its capability for selective anion sensing. Cyclic voltammetry and SWV were carried out in a 1:1 dichloromethane–acetonitrile mixture with 0.15 M  $[\text{Bu}_4\text{N}][\text{PF}_6]$  as the supporting electrolyte [85]. The receptor displayed two distinct oxidation peaks corresponding to its Fc units, with a midpoint potential of 556 mV for the monosubstituted Fc units and 972 mV for the disubstituted ones. Adding oxoanions like  $\text{H}_2\text{PO}_4^-$  and  $\text{P}_2\text{O}_7^{4-}$  induced notable negative potential shifts in both redox peaks. For  $\text{H}_2\text{PO}_4^-$ , potential shifts of 76 and 327 mV were observed for the monosubstituted and disubstituted Fc units, respectively [85]. Similarly,  $\text{P}_2\text{O}_7^{4-}$  caused shifts of 32 and 252 mV. Sulphate and  $\text{AcO}^-$  also elicited responses, but only the disubstituted Fc showed a shift of 52 mV for  $\text{SO}_4^{2-}$  and 65 mV for  $\text{AcO}^-$ . No electrochemical potential changes were observed for  $\text{F}^-$ ,  $\text{Cl}^-$ ,  $\text{Br}^-$ , or  $\text{NO}_3^-$ .



Building on these findings, receptor **110**, incorporating two ferrocenyl substituents, demonstrated an even more selective response to  $\text{P}_2\text{O}_7^{4-}$  [86]. Square-wave voltammetry in methanol (0.1 M  $[\text{Bu}_4\text{N}][\text{ClO}_4]$ ) revealed a reversible oxidation peak at 630 mV versus Ag/AgCl. Upon the addition of  $\text{P}_2\text{O}_7^{4-}$ , a negative potential shift of 63 mV was observed. In contrast,  $\text{H}_2\text{PO}_4^-$  induced no observable shifts, highlighting the receptor's high specificity for  $\text{P}_2\text{O}_7^{4-}$  [86].

The Fc-appended aryl triazole **111** exhibits selective electrochemical recognition of phosphate anions, as revealed by CV and DPV studies conducted in dichloromethane (0.1 M  $[\text{Bu}_4\text{N}][\text{PF}_6]$ ). The receptor displayed a reversible one-electron process at 200 mV vs. Ag/Ag<sup>+</sup> in the absence of anions [87]. Upon binding with  $\text{H}_2\text{PO}_4^-$  and  $\text{P}_2\text{O}_7^{4-}$ , significant negative potential shifts of 200 and 180 mV, respectively, were observed. This behaviour is attributed to hydrogen bonding interactions between the receptor's triazole C–H and the anions, facilitating electron density transfer to the ferrocenyl centre, making it more prone to oxidation. In contrast, anions such as  $\text{Cl}^-$ ,  $\text{Br}^-$ ,  $\text{I}^-$ ,  $\text{HSO}_4^-$ , and  $\text{NO}_3^-$  induced no observable redox potential changes [87].

Expanding on the performance of **111**, more recent investigations have highlighted the anion sensing capabilities via hydrogen bonding of **112** and halogen bonding of **113** bis-Fc sensors [88]. In acetonitrile containing 0.1 M  $[\text{Bu}_4\text{N}][\text{ClO}_4]$  as the supporting electrolyte, the midpoint potential of **113** shifted by up to 120 mV upon binding with  $\text{Cl}^-$ . Bromide and  $\text{HSO}_4^-$  elicited shifts of 56 and 77 mV, respectively. Even in 4:1 acetonitrile–water mixtures (0.1 M  $[\text{Bu}_4\text{N}][\text{ClO}_4]$ ), **113** retained its sensitivity, with shifts of 54 mV for  $\text{Br}^-$  and 46 mV for  $\text{Cl}^-$ , underscoring its robustness in mixed solvent systems. In contrast, **112** showed attenuated performance, with a midpoint shift of only 38 mV for  $\text{Cl}^-$  in pure acetonitrile [88].

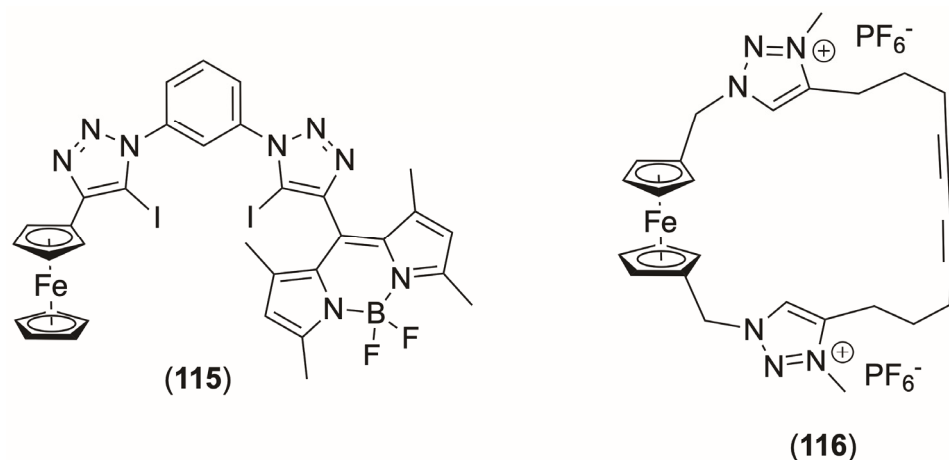


The non-symmetric Fc-tethered aryl-triazole receptor **114** demonstrates selective electrochemical recognition of  $\text{H}_2\text{PO}_4^-$  [89]. Cyclic voltammetry studies were conducted in acetonitrile with 0.03 M  $[\text{Bu}_4\text{N}][\text{PF}_6]$  as the supporting electrolyte. The receptor showed

a midpoint potential of 580 mV vs. DmFc IRS. In the presence of an excess of  $\text{H}_2\text{PO}_4^-$ , the midpoint potential shifted negatively by approximately 101 mV. This shift reflects complexation with  $\text{H}_2\text{PO}_4^-$  and the stabilisation of the oxidised  $\text{Fc}^+$  form. The slow complexation kinetics observed resulted in distinct free and bound receptor peaks [89]. By contrast, other anions, including  $\text{HSO}_4^-$ ,  $\text{Cl}^-$ , and  $\text{NO}_3^-$ , caused negligible shifts in the redox potential, underscoring the receptor's poor electrochemical response towards these species. While **114** exhibits selectivity for  $\text{H}_2\text{PO}_4^-$ , the modest potential shifts indicate limited electrochemical sensitivity.

The electrochemical behaviour of Fc-modified boron-dipyrromethane **115** was investigated in acetonitrile with 0.1 M  $[\text{Bu}_4\text{N}][\text{PF}_6]$  as the supporting electrolyte. Targeting halide anions, the sensors exhibited modest negative potential shifts of approximately 30 mV in the  $\text{Fc}/\text{Fc}^+$  redox couple upon  $\text{Br}^-$  binding [27]. The shifts indicate poor electrochemical sensitivity compared to more robust electrochemical sensors, as the observed potential change is minimal. While the sensors demonstrate significant potential for fluorescence-based spectroscopic analysis due to their redox-modulated optical responses, their electrochemical performance is suboptimal and may limit their standalone application for anion sensing from an electrochemical perspective.

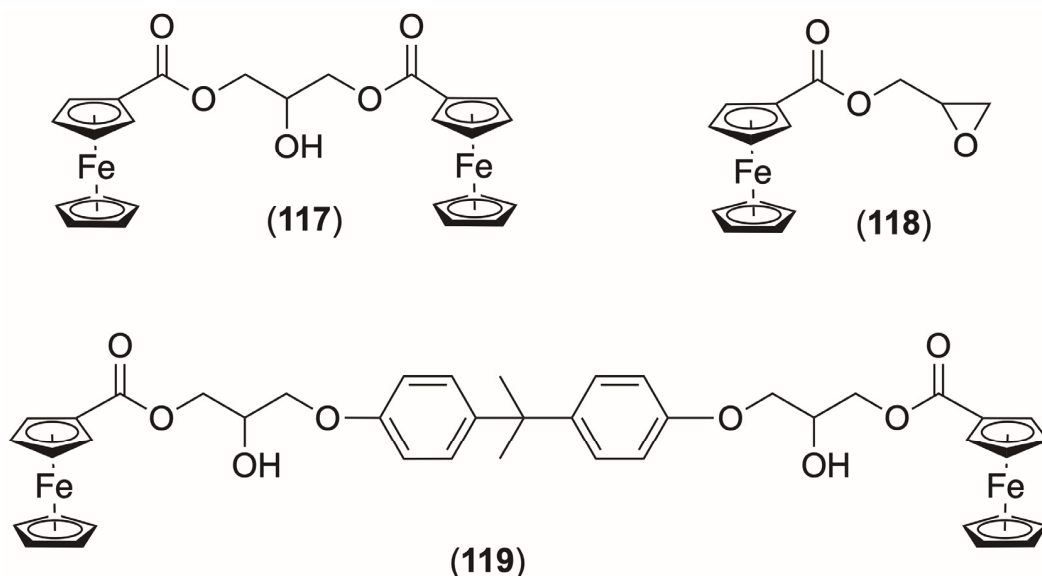
Cyclic voltammetry studies of **116** conducted in acetonitrile with 0.1 M  $[\text{Bu}_4\text{N}][\text{PF}_6]$  as the supporting electrolyte revealed a positive potential shift of 380 mV in the  $\text{Fc}/\text{Fc}^+$  redox couple compared to free Fc, attributed to the electron-withdrawing effect of the triazolium groups [90]. Upon  $\text{Cl}^-$  binding, a negative potential shift of 25 mV was observed in the **116** oxidation potential, increasing to 40 mV with excess  $\text{Cl}^-$ . In contrast,  $\text{Bz}^-$  binding resulted in precipitation, inhibiting further electrochemical characterisation [90].



## 6. Carboxylic-Based Receptors

Carboxylic groups, while capable of forming hydrogen bonds with anions via their oxygen atoms, often show weaker interactions than other functional groups such as amines or amides. This limitation is evident in the electrochemical performance of Fc-based compounds like 1,3-diferrocenecarboxylic acid diacylglycerol (**117**) and glycidyl ester of Fc carboxylate **118**. In experiments using dichloromethane with 0.1 M  $[\text{Bu}_4\text{N}][\text{BF}_4]$  as the supporting electrolyte, both compounds demonstrated suboptimal responses to  $\text{H}_2\text{PO}_4^-$  during cyclic voltammetry measurements [91]. For **117**, a modest oxidation potential shift of 33 mV was observed as the  $\text{H}_2\text{PO}_4^-$  concentration reached one equivalent. This minor shift highlights its poor binding performance. In comparison, amine- and amide-based receptors in the same solvent system have been shown to exhibit potential shifts exceeding 200 mV due to stronger and more specific hydrogen-bonding interactions (see above). The performance of **118** was even more limited, with negligible potential shifts and a decrease

in current intensity attributed to weak hydrogen bonding and the precipitation of the compound onto the electrode surface.



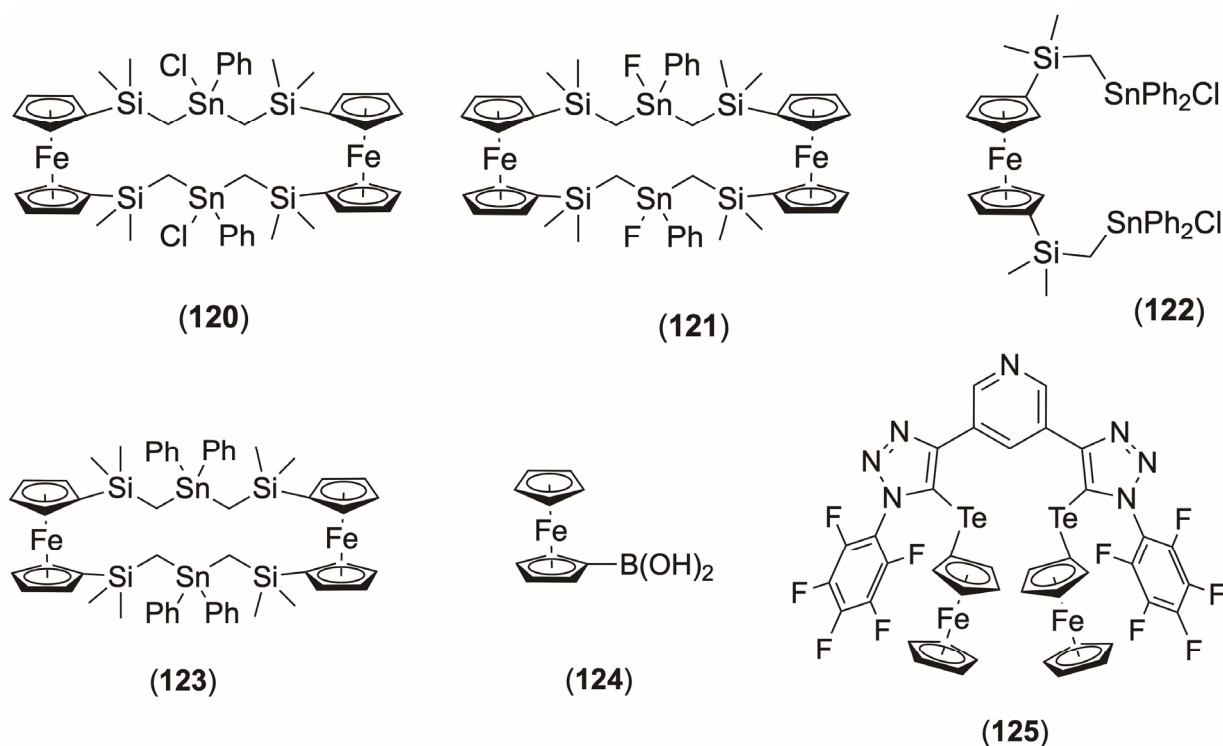
Receptor **119** demonstrated electrochemical selectivity in recognising  $\text{H}_2\text{PO}_4^-$  [92]. Cyclic voltammetry studies in dichloromethane with 0.01 M  $[\text{Bu}_4\text{N}][\text{BF}_4]$  as the supporting electrolyte revealed a significant negative potential shift of 390 mV upon adding  $\text{H}_2\text{PO}_4^-$ . The shift was explained by the Kaifer–Echegoyen model, where the association constant for  $\text{Fc}^+$  is significantly higher than that of Fc, favouring anion binding [92].

## 7. Lewis Acids-Based Receptors

The electrochemical behaviour of silicon- and tin-containing ferrocenophanes and related derivatives was explored to evaluate their ability to recognise anions, particularly  $\text{Cl}^-$ ,  $\text{F}^-$ , and  $\text{H}_2\text{PO}_4^-$ . The experiments conducted in acetonitrile or dichloromethane with tetrabutylammonium salts as supporting electrolytes revealed that the substituents on the tin centres strongly influenced anion sensitivity [93]. Among the derivatives, the chloro-substituted ferrocenophane **120** exhibited the most promising electrochemical performance, with negative potential shifts of 130 mV for  $\text{Cl}^-$ , 210 mV for  $\text{F}^-$ , and 480 mV for  $\text{H}_2\text{PO}_4^-$ . Notably, **120** maintained structural integrity and resisted chemical decomposition during oxidation, making it a strong candidate for selective anion sensing applications.

The fluoro-substituted ferrocenophane **121** showed moderate negative potential shifts of 100 mV for  $\text{Cl}^-$  and 180 mV for  $\text{F}^-$ . However, it suffered from irreversible chemical reactions in the presence of  $\text{H}_2\text{PO}_4^-$ , limiting its utility [93]. The chlorostannyl-substituted derivative **122** demonstrated notable shifts of 220 mV for  $\text{Cl}^-$  and 560 mV for  $\text{H}_2\text{PO}_4^-$ , highlighting its high sensitivity to phosphate ions. In contrast, the phenyl-substituted **123** showed negligible sensitivity to all tested anions and other derivatives.

Despite **120** promising sensitivity to  $\text{H}_2\text{PO}_4^-$ , its response to  $\text{Cl}^-$  and  $\text{F}^-$  remains modest compared to simpler Fc derivatives, such as bis (phosphine) or urea-functionalised systems, which often exhibit negative potential shifts exceeding 200 mV.



The electrochemical properties of **124** were evaluated for selective  $\text{F}^-$  recognition in methanol–water mixtures and aqueous solutions [94]. The measurements, performed using CV with a glassy carbon electrode and  $\text{Ag}/\text{AgCl}$  reference electrode, demonstrated a strong interaction between the Lewis acidic centre and the  $\text{F}^-$  ion, which acts as a Lewis base. This interaction is mediated by a shift from  $\text{sp}^2$  to  $\text{sp}^3$  hybridisation at the boron centre upon  $\text{F}^-$  binding. The redox potential of **124** shifted significantly upon the addition of  $\text{F}^-$ . In a methanol–water mixture, the negative potential shift was approximately 90 mV, while in a pure aqueous solution, the potential shift reached 175 mV. Other anions, such as  $\text{Cl}^-$  and  $\text{Br}^-$ , caused negligible potential changes even at high concentrations, and  $\text{SO}_4^{2-}$  produced only a small perturbation [94].

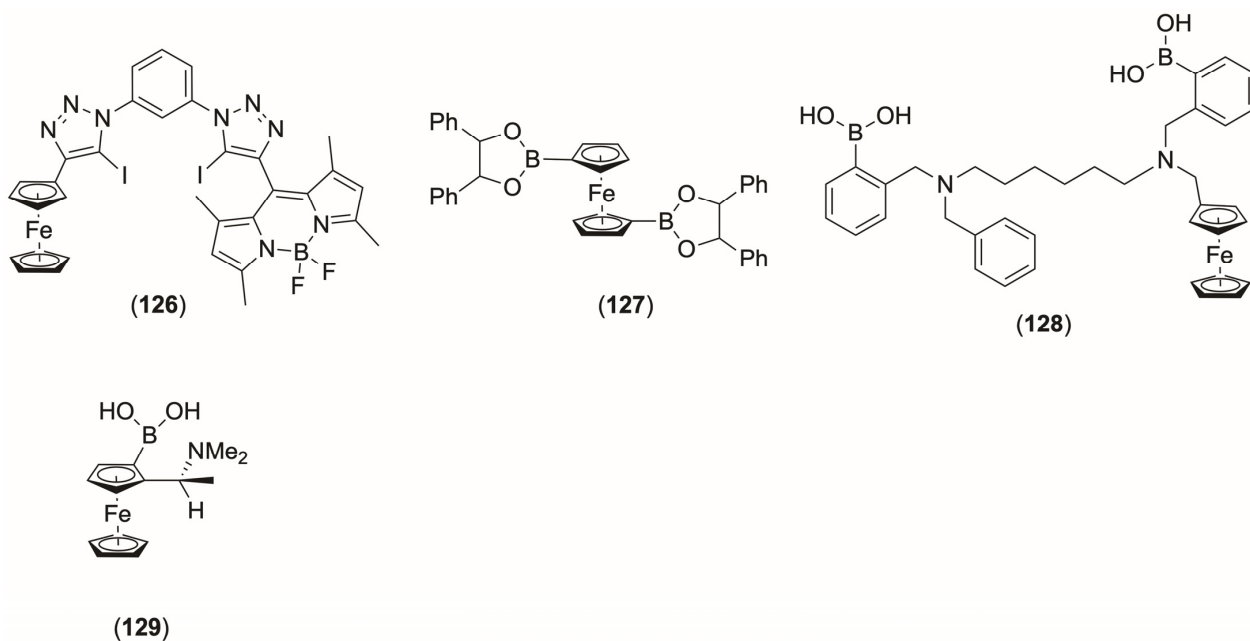
The bis (ferrocenyltellurotriazole) receptor **125** demonstrated robust anion sensing capabilities through chalcogen bonding, modulated by the  $\text{Fc}/\text{Fc}^+$  redox couple [95]. Cyclic voltammetry studies in acetonitrile (0.1 M  $[\text{Bu}_4\text{N}][\text{PF}_6]$ ) revealed substantial negative potential shifts upon interaction with various anions. For instance,  $\text{H}_2\text{PO}_4^-$  induced the most significant negative potential shift of 217 mV, followed by  $\text{Cl}^-$  (157 mV) and  $\text{Br}^-$  (133 mV). The sensitivity of **125** was diminished in 9:1 acetonitrile- $\text{H}_2\text{O}$  mixtures, with maximum shifts of 81 mV for  $\text{H}_2\text{PO}_4^-$  and 42 mV for  $\text{Br}^-$ .

The electrochemical behaviour of Fc-modified boron-dipyrrromethane **126** was investigated in acetonitrile with 0.1 M  $[\text{Bu}_4\text{N}][\text{PF}_6]$  as the supporting electrolyte. Targeting halide anions, the sensors exhibited modest negative potential shifts of approximately 30 mV in the  $\text{Fc}/\text{Fc}^+$  redox couple upon  $\text{Br}^-$  binding [27]. The shifts indicate poor electrochemical sensitivity compared to more robust electrochemical sensors, as the observed potential change is minimal.

The bidentate bis(boronate) Fc-based Lewis acid **127** exhibits distinct electrochemical behaviour upon  $\text{F}^-$  binding [96]. Cyclic voltammetry studies conducted in dichloromethane with 0.1 M  $[\text{Bu}_4\text{N}][\text{PF}_6]$  as the supporting electrolyte revealed that the free receptor shows a midpoint potential at 206 mV vs.  $\text{Fc}/\text{Fc}^+$  IRS. Upon adding two equivalents of  $\text{F}^-$ , the midpoint potential shifted positively by 146 mV, reflecting the stabilisation of the oxidised ferrocenium state due to fluoride complexation at the boronate centres. Importantly, no

significant potential shifts were observed with other anions, such as  $\text{Cl}^-$ ,  $\text{Br}^-$ ,  $\text{I}^-$ ,  $\text{BF}_4^-$ ,  $\text{PF}_6^-$ ,  $\text{H}_2\text{PO}_4^-$ ,  $\text{HSO}_4^-$ , or  $\text{NO}_3^-$  [96].

Receptor **128** was developed for saccharide recognition, featuring a diboronic acid Fc framework with a hexamethylene linker [97]. Differential pulse voltammetry was employed to investigate the electrochemical behaviour of **128** in an aqueous methanolic buffer (52.1 wt% methanol, pH 8.21) in the presence of D-glucose. After adding D-glucose, the Fc oxidation potential exhibited a positive potential shift of 84 mV. The shift is attributed to saccharide binding through boronic acid–diol interactions, which reduce electron density on the Fc core, stabilising the redox process [97]. Similarly, the chiral ferrocenylboronic acid receptor **129** was designed for saccharide recognition and tested using normal pulse voltammetry in phosphate buffer (0.1 M, pH 7.0) [98]. Upon binding D-sorbitol, the oxidation potential shifted in the negative direction by 42 mV, demonstrating the receptor's sensitivity to saccharide binding.

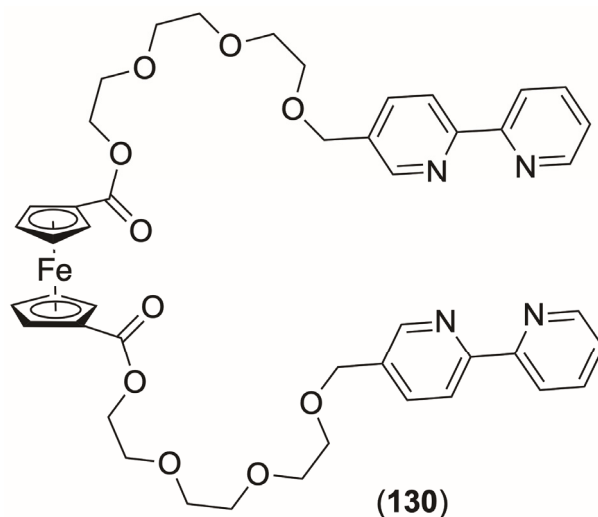


## 8. Detection of Neutral Molecules

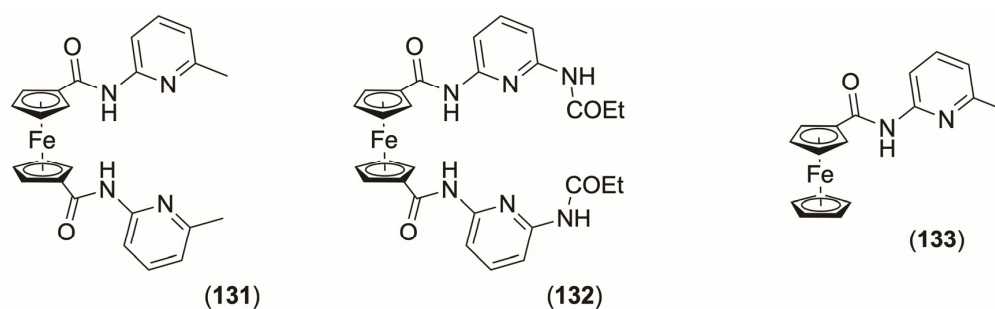
Neutral molecules present a distinct category of analytes for electrochemical sensing due to their ability to interact with receptors under specific conditions. These interactions often rely on transformations that render the molecule more detectable, such as protonation, oxidation, or other chemical modifications. In the case of protonation, the neutral molecule is converted into an ionic species, which can then engage in electrostatic or hydrogen-bonding interactions with redox-active receptors. This approach enables selective recognition by shifts in redox potentials. Ferrocene-based receptors' tunable redox properties and versatile binding sites are particularly effective for detecting such molecules in their neutral state or after undergoing a chemical transformation that enhances receptor interactions.

One example is **130**, designed to detect amino acid ester salts such as Gly-OMe·HCl, Ala-OMe·HCl, and related species. In their free form, these molecules are neutral, but upon protonation to form ammonium cations (e.g., Gly-OMe·H<sup>+</sup>), they engage with the receptor cavity via hydrogen bonding and electrostatic interactions [99]. Cyclic voltammetry studies in acetonitrile with 0.1 M  $[\text{Bu}_4\text{N}][\text{ClO}_4]$  revealed that coordination with Cu(I) cations significantly enhanced receptor pre-organisation, stabilising its conformation for optimal binding. The Cu(I) complex of the receptor, which exhibited an initial oxidation potential of 77 mV vs. Ag/Ag<sup>+</sup>, showed positive shifts upon interaction with amino acid ester salts.

The shifts were 31 mV for Gly-OMe·HCl, 24 mV for Ala-OMe·HCl, 35 mV for Val-OMe·HCl, 17 mV for Leu-OMe·HCl, 20 mV for Ile-OMe·HCl, 30 mV for Thr-OMe·TosOH, 30 mV for Tle-OMe·TosOH, and 21 mV for Nva-OMe·TosOH. Meanwhile, negative potential shifts in the Fc/Fc<sup>+</sup> redox couple were observed for the Fc moiety upon complexation, with values of 22 mV for Gly-OMe·HCl, 18 mV for Ala-OMe·HCl, 21 mV for Val-OMe·HCl, 26 mV for Leu-OMe·HCl, 23 mV for Thr-OMe·TosOH, 24 mV for Tle-OMe·TosOH, and 22 mV for Nva-OMe·TosOH [99].



The electrochemical behaviour of receptors **131**–**133** was studied to assess their redox responses to complexation with neutral molecules, using CV in dichloromethane with 0.1 M [Bu<sub>4</sub>N][ClO<sub>4</sub>] as the supporting electrolyte [100]. Receptors **131** and **132**, both 1,1'-disubstituted amidopyridyl derivatives, exhibited formal potentials of 440 and 400 mV, respectively, vs. Fc/Fc<sup>+</sup> internal reference system. Upon complexation with ethyleneurea, receptor **131** showed a negative potential shift of 60 mV, while trimethyleneurea caused a shift of 50 mV, and barbital shifted the potential by 35 mV. Similarly, receptor **133** showed a negative potential shift of 35 mV for barbital binding, with smaller or negligible shifts for other guests.

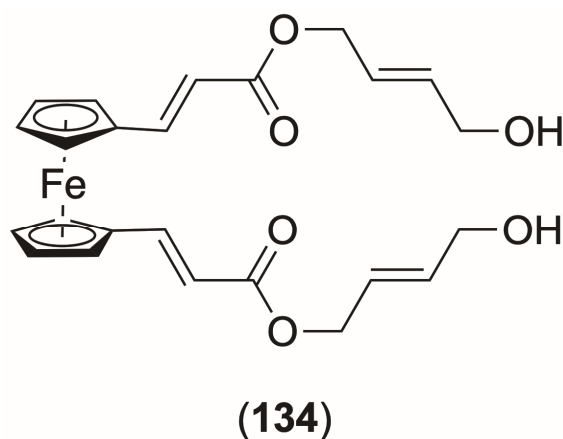


Receptor **133**, which features a single amidopyridyl group, exhibited smaller shifts of 30 and 25 mV upon complexation with ethyleneurea and trimethyleneurea, respectively [100]. The reduced response compared to receptors **131** and **133** highlights the importance of dual hydrogen bonding arms for enhancing redox perturbation and guest binding.

The application of receptors **131** and **133** was extended to evaluate their interaction with neutral carboxylic acids [101]. To this end, CV experiments were conducted in dichloromethane with 0.1 M [Bu<sub>4</sub>N][ClO<sub>4</sub>] as the supporting electrolyte. Upon binding to monocarboxylic acids such as butyric acid, heptanoic acid, and decanoic acid, **133** showed a negative potential shift of 20, 20, and 25 mV, respectively. In contrast, **131** showed shifts of 60, 55, and 55 mV, reflecting the proportionality of the redox response to the number of

hydrogen bonds formed. With glutaric acid (a dicarboxylic acid), **133** displayed a negative potential shift of 20 mV, while **131** exhibited a significantly larger shift of 85 mV. These findings suggest that receptors **131** and **133** exhibit slightly superior sensitivity and selectivity for carboxylic acids compared to barbituric derivatives, likely due to the stronger hydrogen bonding interactions and the proximity of the carboxylic acid guests to the Fc core.

Receptor **134** exhibited distinct electrochemical behaviour upon binding unprotected amino acids, with significant shifts in the redox potential [102]. In a 55:45 acetonitrile–H<sub>2</sub>O solvent system at pH 7.2 with 0.1 M [Bu<sub>4</sub>N][ClO<sub>4</sub>] as the supporting electrolyte, the free receptor displayed a reversible redox wave at 664 mV vs. Ag/Ag<sup>+</sup>. Upon complexation, negative potential shifts were observed for different amino acids; aspartic acid caused a shift of 82 mV, glutamic acid shifted the potential by 98 mV, glycine shifted by 80 mV, and lysine resulted in a shift of 69 mV. These shifts reflect the receptor's ability to form stable complexes with amino acids through multipoint interactions, particularly favouring anionic amino acids. This is evidenced by more significant shifts for aspartic acid and glutamic acid.



## 9. Critical Evaluation of Anion-Specific Receptor Performance and Structural Implications

We have examined diverse Fc-based electrochemical sensors designed to recognise and bind different anions, showcasing their utility and adaptability. A critical analysis of these systems allows us to highlight the most promising receptors for each anion based on their electrochemical performance, specifically the magnitude of the potential shift observed upon anion binding. The structural features underpinning these performances further elucidate design principles for optimising receptor efficacy.

For H<sub>2</sub>PO<sub>4</sub><sup>−</sup>, which has garnered significant attention due to its biological and environmental importance, the most effective receptors are **122**, exhibiting the highest potential shift of 560 mV; **120**, with a shift of 480 mV; and **58**, displaying a significant shift of 470 mV. While receptor **122** demonstrates the best redox performance due to its highly optimised functionalisation and multidentate binding sites, its structural complexity and synthesis requirements may limit its broader applicability. Receptor **120**, with slightly lower performance, offers a more streamlined design, balancing effectiveness and simplicity. In contrast, receptor **58** provides a competitive redox response with a relatively straightforward structure, relying on quaternary ammonium groups for enhanced ion-pairing interactions. These examples illustrate that while increased structural complexity often correlates with improved sensing capabilities, there is value in achieving a balance between structural sophistication and practical feasibility.

For F<sup>−</sup>, a widely studied anion due to its environmental and industrial relevance, the most effective receptors include **16** (230 mV), **14** (220 mV), **38** (216 mV), **95** (230 mV),

**100** (270 mV), and **101** (300 mV). Among these, the imidazolium-functionalised receptors (**95**, **100**, and **101**) exhibit the most pronounced redox shifts, highlighting their exceptional affinity for  $F^-$ . Receptor **101** has the highest shift (300 mV), indicating robust ion-pair formation and redox communication. Receptor **100** follows closely with a shift of 270 mV, while **95** matches receptor **16** with a shift of 230 mV, reinforcing its reliability in  $F^-$  sensing. Comparatively, receptor **16** achieves a significant redox shift through optimised hydrogen-bonding interactions and ion-pairing capacity, while **14** offers a practical alternative with a more straightforward structure. Receptor **38** balances moderate structural complexity with effective hydrogen bonding, ensuring selective  $F^-$  recognition.

For  $Cl^-$ , notable for its importance in biological systems, the top-performing receptors are **100** (310 mV), **122** (220 mV), **125** (157 mV), and **120** (103 mV). Receptor **100** achieves the highest potential shift, significantly surpassing other receptors in redox response and demonstrating exceptional selectivity and binding affinity for  $Cl^-$ . This remarkable performance is attributed to the strong electrostatic and hydrogen-bonding interactions facilitated by the imidazolium moiety. Receptor **122**, while slightly less effective, still showcases excellent selectivity and binding due to its highly functionalised design. Receptor **125** provides a competitive redox response with a less complex synthesis process, and **120**, with its streamlined structure, offers an ideal balance between performance and practicality for  $Cl^-$  detection.

For  $Br^-$ , the leading receptors include **125** (133 mV), **26** (85 mV), and **31** (57 mV). Receptor **125** demonstrates superior performance, benefiting from its optimised hydrogen bonding and structural adaptability. Receptor **26** achieves a slightly lower shift but maintains a practical and scalable design, while receptor **31** offers modest sensitivity but stands out for its simplicity and ease of synthesis.

For  $HSO_4^-$ , receptors **27** (150 mV), **95** (108 mV), **113** (77 mV), and **3** (50 mV) represent the most effective options. Receptor **27** exhibits the highest shift, driven by its dual hydrogen-bonding functionality and structural complementarity. Receptor **95** follows with a notable shift of 108 mV, highlighting the strong electrostatic interactions facilitated by the imidazolium moiety. Receptor **113** provides a moderate shift with robust halogen bonding capabilities, while receptor **3** balances selectivity and simplicity, making it suitable for general sensing applications.

For  $SO_4^{2-}$ , the best receptors are **66** (34 mV) and **64** (30 mV). Although the potential shifts are smaller, these receptors excel in acidic conditions, where their protonated forms enhance electrostatic and hydrogen-bonding interactions. Receptor **66**, in particular, demonstrates slightly superior performance in maintaining selectivity under these conditions.

For  $P_2O_7^{4-}$ , key receptors include **109** (252 mV), **111** (180 mV), and **89** (110 mV). Receptor **109** provides the most significant redox shift due to its ability to stabilise the high-charge-density anion through strong hydrogen bonding. Although slightly less effective, receptor **111** balances performance and synthesis feasibility, while receptor **89** offers competitive sensing capabilities for applications in biological environments.

For  $AcO^-$ , the most effective receptors are **102** (85 mV), **91** (68 mV), **92** (65 mV), and **109** (65 mV). Receptor **102** exhibits the highest sensitivity, attributed to its robust hydrogen-bonding interactions at the hydrazone site. Receptors **91** and **92** provide similar performance, showcasing their flexibility and adaptability for acetate sensing. Receptor **109** adds further versatility with its dual hydrogen bonding capability.

For  $CN^-$ , a critical anion for industrial and environmental monitoring, the leading receptors are **85** (269 mV), **88** (238 mV), and **82** (198 mV). Receptor **85** achieves the highest shift, reflecting its exceptional binding interactions mediated by hydrogen bonding and receptor deprotonation. Receptor **88** also demonstrates strong redox performance, with receptor **82** offering a competitive alternative for selective cyanide detection.

For  $\text{ATP}^{2-}$ , a biologically significant anion, the top receptors are **58** (280 mV), **19** (180 mV), **17** (160 mV), and **18** (160 mV). Receptor **58** stands out with its remarkable redox shift, attributed to its quaternary ammonium groups and enhanced ion-pairing interactions. Receptor **19**, while less sensitive, offers a robust design optimised for  $\text{ATP}^{2-}$  recognition. Receptors **17** and **18** provide moderate shifts, balancing performance with synthetic simplicity.

The structural implications for receptor performance are profound, as the binding cavity's geometry, functional group arrangement, and preorganisation influence selectivity and sensitivity. Receptors with rigid, preorganised structures tend to show greater redox potential shifts due to reduced entropic penalties upon binding. However, the experimental data above reveal that more straightforward, less preorganised systems, such as **102** for acetate or **58** for  $\text{ATP}^{2-}$ , can still achieve significant shifts through optimised hydrogen bonding and functional group placement. This suggests that while preorganisation is beneficial, receptor performance can be enhanced by strategically incorporating flexible or multifunctional binding sites. Furthermore, incorporating hydrogen-bonding groups, electrostatic interaction sites, or transition-metal centres enhances the binding strength, translating to more significant redox potential shifts. By critically evaluating these systems, we underscore the importance of tailoring receptor architecture to maximise binding affinity and electrochemical response for targeted applications. This updated analysis further highlights that structural adaptability, such as in receptors **85** and **88** for cyanide, can be equally crucial as rigid preorganisation in achieving strong anion recognition. This analysis highlights high-performing receptors and offers insights for future receptor design, emphasising the synergy between structure and function in Fc-based anion and neutral molecule sensors.

The electrochemical performance of Fc-based receptors shows significant variation depending on the solvent environment, with systems in organic solvents typically exhibiting larger potential shifts upon analyte binding compared to aqueous systems. This phenomenon can be attributed to differences in dielectric constant, hydrogen-bonding capabilities, and solvation effects between these media [103–105]. Organic solvents, with their relatively low dielectric constants, reduce the stabilisation of charged species and enhance the electrostatic interactions between the receptor and the analyte, resulting in more pronounced potential shifts. Conversely, the high dielectric constant of water and its ability to form extensive hydrogen-bonding networks often mitigate receptor–anion interactions, leading to smaller shifts in aqueous systems.

Moreover, solvation effects are less disruptive in organic solvents, allowing the receptor's functional groups to interact more directly with the target analyte. In contrast, aqueous environments introduce competing interactions between the solvent and both the receptor and the analyte, which diminishes the binding strength and alters the electrochemical response. The structural preorganisation of receptors plays a pivotal role in mitigating these solvent-dependent effects. Receptors with rigid, hydrophobic frameworks or those designed to minimise water disruption—such as those incorporating macrocyclic or supramolecular architectures—tend to perform better in aqueous systems, although their potential shifts remain smaller than in organic media. For example, receptor **64** for  $\text{SO}_4^{2-}$  and **109** for  $\text{P}_2\text{O}_7^{4-}$  demonstrate how supramolecular architectures mitigate water-induced disruptions and improve sensitivity in aqueous conditions. This dichotomy highlights the need for careful solvent selection and receptor design tailored to the intended sensing application and operating conditions.

## 10. Conclusions and Future Perspectives

This review demonstrates that Fc-based electrochemical sensors are invaluable for detecting diverse chemical species due to their exceptional redox properties, structural versatility, and adaptability to various sensing environments. While significant progress has been made in cation sensing, we have highlighted the substantial and growing potential of Fc-based sensors for neutral and anionic species. These analytes present unique challenges—including weak interactions, high hydration enthalpies (for anions), and the absence of formal charge (for neutral molecules)—that require innovative design strategies, such as advanced functionalisation and tailored molecular architectures, to enhance selectivity and sensitivity.

By examining detailed examples such as quaternary ammonium-functionalised Fc receptors like **58** for  $\text{H}_2\text{PO}_4^-$  recognition (which exhibited a significant potential shift of 470 mV) and macrocyclic frameworks like receptor **27** for  $\text{HSO}_4^-$  detection (a potential shift of 150 mV observed after anion binding), this study underscores the versatility of Fc-based systems in selective anion recognition. We also discussed how solvent environments influence sensor behaviour, with organic solvents typically enhancing receptor–analyte interactions compared to aqueous systems. Electrochemical techniques like CV and SWV play pivotal roles in elucidating sensor responses, driving further refinement of sensor designs. Furthermore, we emphasised that while rigid, preorganised receptors often demonstrate enhanced performance, flexible systems like **102** for  $\text{AcO}^-$  detection (85 mV shift) and **58** for  $\text{ATP}^{2-}$  recognition (280 mV shift) highlight the potential of adaptable architectures in diverse environments.

However, despite significant advancements, several key challenges and research gaps must be addressed to unlock their full potential for real-world applications. One key challenge is achieving selectivity in complex matrices, where competing ions or analytes can significantly interfere with sensor performance. Innovative receptor architectures incorporating dual hydrogen-bonding sites or ion-pairing mechanisms offer promising solutions, but further optimisation is required to enhance selectivity and reproducibility. Another significant limitation is the underexplored influence of solvents on the redox behaviour of Fc receptors. The differences in solvation effects between the neutral Fc and oxidised  $\text{Fc}^+$  forms are not fully understood, yet they play a crucial role in defining sensor performance. Additionally, the transition from organic to aqueous environments remains challenging. Many Fc-based receptors exhibit reduced efficacy in aqueous systems due to solubility issues and competing interactions with water molecules. Developing receptor frameworks tailored explicitly for aqueous sensing environments remains a pressing need. Integrating Fc-based receptors into practical sensor devices also presents an ongoing hurdle. Despite the promising proof-of-concept studies, translating these systems into portable, field-deployable platforms requires advancements in fabrication techniques, sensor stability, and response consistency. Moreover, dynamic range and detection limits are often overlooked in current studies. While high sensitivity is frequently reported, a broader dynamic range and defined practical detection limits are essential for real-world applications.

Future research should prioritise diversifying the structural architectures of Fc-based receptors and refining their performance under complex, competitive conditions. Emphasising the synergy between structural preorganisation and functional adaptability will be pivotal in achieving unparalleled selectivity and sensitivity. By advancing the understanding of solvent effects, redox mechanisms, and receptor–analyte interactions, Fc-based systems have the potential to redefine the landscape of electrochemical sensing, addressing critical challenges in biological, industrial, and environmental domains while solidifying their role as indispensable tools in modern analytical science.

**Author Contributions:** Conceptualization, A.A.J.T., A.M.T., K.T.M. and A.K.V.M.; methodology, A.A.J.T., A.M.T., K.T.M. and A.K.V.M.; software, A.A.J.T., A.M.T. and K.T.M.; validation, A.A.J.T., A.M.T., K.T.M. and A.K.V.M.; formal analysis, A.A.J.T., A.M.T., K.T.M. and A.K.V.M.; investigation, A.A.J.T., A.M.T., K.T.M. and A.K.V.M.; resources, A.A.J.T., A.M.T., K.T.M. and A.K.V.M.; data curation, A.A.J.T., A.M.T., K.T.M. and A.K.V.M.; writing—original draft preparation, A.A.J.T.; writing—review and editing, A.A.J.T., A.M.T., K.T.M. and A.K.V.M.; visualization, A.A.J.T., A.M.T., K.T.M. and A.K.V.M.; supervision, A.A.J.T.; project administration, A.A.J.T. All authors have read and agreed to the published version of the manuscript.

**Funding:** This research received no external funding.

**Data Availability Statement:** Not applicable.

**Conflicts of Interest:** The authors declare no conflicts of interest.

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