



Bis[squaramido]ferrocenes as electrochemical sulfate receptors†

 Jakob D. E. Lane,^a William J. H. Greenwood,^{ib} Victor W. Day,^c
 Katrina A. Jolliffe,^{ib}*^{ad} Kristin Bowman-James^{ib}*^c and Louis Adriaenssens^{ib}*^b

 Cite this: *New J. Chem.*, 2022, 46, 18119

 Received 9th August 2022,
 Accepted 9th September 2022

DOI: 10.1039/d2nj03951f

rsc.li/njc

1,1'-Bis[squaramido]ferrocenes (FcSq₂) are introduced as electrochemically active scaffolds for sulfate recognition. FcSq₂ display high sulfate-binding affinity and selectivity in aqueous DMSO mixtures. Among tested anions, sulfate elicits a unique electrochemical response in FcSq₂, enabling selective detection.

The key roles played by sulfate in processes essential to industry¹ and healthcare² have inspired molecular strategies to selectively bind and report sulfate.³ Among these, the synthetic challenges and toxicity issues⁴ associated with charged species make neutral and discrete receptor molecules a leading choice. These molecules comprise a binding site intended to employ weak non-covalent interactions that interact specifically with sulfate. In this context, the polar and often aqueous environments in which anions are typically found severely challenge the binding ability of receptors. Of the commonly targeted anions, this issue is arguably most significant for sulfate, an anion that features a particularly high hydration energy ($\Delta G_{\text{h}}^{\circ}{}_{\text{SO}_4^{2-}} = -1090 \text{ kJ mol}^{-1}$, *cf.* $\Delta G_{\text{h}}^{\circ}{}_{\text{Cl}^-} = -347 \text{ kJ mol}^{-1}$).⁵

Among the effective recognition motifs known for binding sulfate in competitive media,⁶ squaramides, comprising two NH hydrogen bond donors that act as a “mini-chelate”,⁷ have proven promising.⁸ Within these studies, and in the larger field of anion recognition, an intriguing paradox is raised. While an ideal receptor should comprise a binding site whose size, shape and electronics exclusively promote interaction with the anion of interest, exclusivity must often be balanced with the freedom

needed to adapt receptor structure during the entry and exit of the anion from the binding pocket. In this context, previously unreported 1,1'-bis(squaramido)ferrocenes (FcSq₂) intrigued us as a simultaneously rigid and flexible receptor scaffold for sulfate binding (Fig. 1).⁹

Within FcSq₂, direct attachment of the squaramide unit to the cyclopentadienyl (Cp) ligand creates a conjugated system, compelling each Cp-squaramide ‘arm’ of the receptor to adopt a planar structure.¹⁰ Attachment of these arms through the ferrocenyl ‘core’ of the scaffold presents the two squaramide units upon stacked and parallel planes separated by $\approx 3.4 \text{ \AA}$, as defined by the Cp–Cp geometry of ferrocene. We note, in certain prior work, squaramide units bound to the same sulfate anion are shown to stack with a squaramide–squaramide distance between 3.3 and 3.5 \AA .^{8b,e} To the best of our knowledge, a similar relationship between squaramide motifs is absent from all reported structures involving other singly and doubly charged anions. Thus, it may be expected that the constrained component of the geometrical relationship between squaramide units within FcSq₂ engenders sulfate-selective binding. In concert with constraint, a single degree of large-amplitude freedom, characterized by rotation about the central axis of the ferrocenyl ‘core’ of the molecule, balances rigidity with flexibility. Finally, in addition to structural features suitable for binding sulfate, FcSq₂ are built around the robust

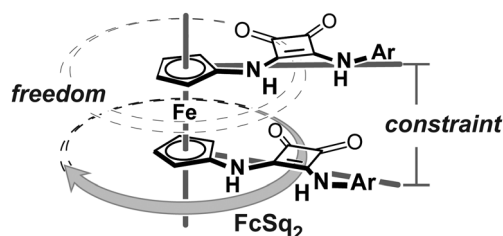


Fig. 1 The 1,1'-bis[squaramido]ferrocene scaffold FcSq₂ combines flexibility with rigid attributes suitable for sulfate recognition.

^a School of Chemistry, The University of Sydney, NSW, 2006, Australia.
 E-mail: kate.jolliffe@sydney.edu.au

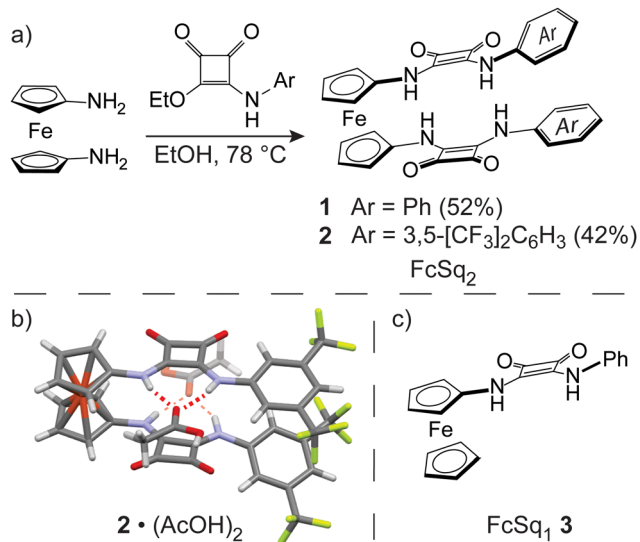
^b School of Chemistry, The University of Lincoln, Lincoln, LN6 7DL, UK.
 E-mail: ladriaenssens@lincoln.ac.uk

^c Department of Chemistry, University of Kansas, Lawrence, Kansas, 66045, USA.
 E-mail: kbjames@ku.edu

^d The University of Sydney Nano Institute (Sydney Nano), The University of Sydney, NSW, 2006, Australia

† Electronic supplementary information (ESI) available. CCDC 2115548. For ESI and crystallographic data in CIF or other electronic format see DOI: <https://doi.org/10.1039/d2nj03951f>





Scheme 1 (a) Synthesis of FcSq₂ **1** and **2**. (b) Single crystal structure of acetic acid solvate of **2**. Disorder of the fluorine atoms within two CF₃ groups is omitted for clarity. Select hydrogen bonds are denoted with dashed red lines. (c) Structure of FcSq₁ **3**.^{9a}

electrochemical manifold of ferrocene. Thus, the FcSq₂ scaffold has potential to bind and electrochemically detect sulfate.

FcSq₂ were synthesized by reaction of diaminoferrocene with the appropriate squaramate ester (Scheme 1a) with purification achieved by recrystallization from dimethyl sulfoxide (DMSO). The FcSq₂ receptors exhibit poor solubility in all solvents, however, solutions could be obtained by heating suspensions of FcSq₂ in DMSO to near boiling temperatures. Upon cooling to room temperature, these solutions are kinetically stable for up to 30 minutes, permitting ¹H-NMR spectroscopic analysis which showed FcSq₂ are isolated as the FcSq₂-2DMSO complexes (Fig. S1 and S2, ESI[†]). Crystals of 3,5-bis(trifluoromethyl)phenyl substituted FcSq₂ **2** suitable for single crystal X-ray diffraction grew from hot acetic acid (AcOH), confirming the structure of **2** as the acetic acid solvate (Scheme 1b).

To investigate the suitability of FcSq₂ as receptors for sulfate, 10 equivalents of tetramethylammonium sulfate (TMA)₂SO₄ were added to a suspension of FcSq₂ **1** or **2** in deuterated acetonitrile. Both (TMA)₂SO₄ and FcSq₂ are insoluble in acetonitrile. However, upon sonication of the heterogeneous mixture, the acetonitrile liquid-phase adopted a deep orange colour while the residual solid powder turned from an orange colour to pure white, suggesting full solubilisation of the ferrocene. Following separation of the excess (TMA)₂SO₄ solid, NMR spectroscopic analysis of the orange solution showed signals indicative of the 1 : 1 FcSq₂-SO₄²⁻ complex with every carbon and proton environment accounted for (Fig. 2, Fig S3 and S4, ESI[†]). ¹H-NMR signals belonging to squaramide NH protons (H^a and H^b) appear in the far downfield region of the spectrum at 11.20 and 11.01 ppm, respectively, suggesting the participation of these protons in hydrogen bonding interactions with the sulfate anion (*cf.* 9.56 ppm for H^a and 9.18 ppm

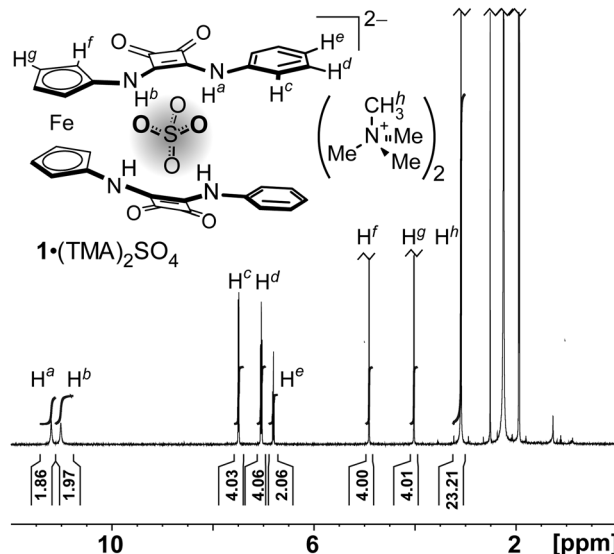


Fig. 2 ¹H-NMR (500 MHz, MeCN-*d*₃, 25 °C) of 1:SO₄²⁻ with the TMA counter ion. See Fig. S3 (ESI[†]) for corresponding ¹³C-NMR spectrum and Fig. S4 (ESI[†]) for analogous spectra of 2:SO₄²⁻.

for H^b in the ¹H-NMR spectrum of free **1** in DMSO-*d*₆, Fig. S1, ESI[†]). Notably, despite exposure of FcSq₂ to a large excess of sulfate, the relative integral values for ¹H-NMR signals corresponding to FcSq₂ **1** (H^{a–g}) and the TMA counter ion (H^h) are indicative of the 1 : 1 FcSq₂-SO₄²⁻ complex.

To investigate the anion recognition properties of FcSq₂, ¹H-NMR binding studies were conducted by the addition of the tetrabutylammonium (TBA) salts of various anions to a solution of FcSq₂ **1** (2.5 mM) in 1% H₂O/DMSO (Table 1, entries 1–7).^{11,12} Little to no changes in the spectral characteristics corresponding to **1** were observed with the addition of Cl⁻, HSO₄⁻ or NO₃⁻, indicating a lack of binding between **1** and these anions. The addition of one equivalent of F⁻ or AcO⁻ was accompanied by disappearance of the ¹H-NMR signals corresponding to the NH protons, signifying deprotonation occurs in

Table 1 Association constants *K*_a (M⁻¹) for 1 : 1 adducts of two- and one-arm squaramidoferrocene receptors, **1** and **3**, respectively, with various anions in water/DMSO mixtures^a

| Entry | Anion | Receptor | % H ₂ O | <i>K</i> _a (M ⁻¹) |
|-------|---|----------|--------------------|--|
| 1 | Cl ⁻ | 1 | 1 | 2.0 × 10 ^{2b} |
| 2 | HSO ₄ ⁻ | 1 | 1 | No interaction ^c |
| 3 | NO ₃ ⁻ | 1 | 1 | No interaction ^c |
| 4 | F ⁻ | 1 | 1 | Deprotonation ^d |
| 5 | AcO ⁻ | 1 | 1 | Deprotonation ^d |
| 6 | H ₂ PO ₄ ⁻ | 1 | 1 | > 10 ^{4b} |
| 7 | SO ₄ ²⁻ | 1 | 1 | > 10 ^{4b} |
| 8 | H ₂ PO ₄ ⁻ | 3 | 1 | 4.0 × 10 ^{3b} |
| 9 | SO ₄ ²⁻ | 3 | 1 | 1.2 × 10 ^{3b} |
| 10 | H ₂ PO ₄ ⁻ | 1 | 20 | 1.4 × 10 ^{4e} |
| 11 | SO ₄ ²⁻ | 1 | 20 | 3.1 × 10 ^{5e} |

^a Titrations were performed at 298 K. Errors estimated at ±15%.

^b ¹H-NMR titration. ^c Changes in the spectra are too small to calculate association constants. ^d Signals corresponding to the squaramide NH protons disappeared following addition of 1 equivalent of anion.

^e UV-Vis titration.



the presence of more basic anions. Conversely, the addition of TBAH_2PO_4 or $(\text{TBA})_2\text{SO}_4$ effected clear changes in the $^1\text{H-NMR}$ spectra that could be ascribed to anion binding.

Upon addition of sub-stoichiometric TBAH_2PO_4 , $^1\text{H-NMR}$ signals corresponding to the squaramide NH protons (H^a and H^b) became broad to the point of disappearance (Fig. S7, ESI †). In the presence of 0.5 to 2.0 equivalents TBAH_2PO_4 , $^1\text{H-NMR}$ signals that we ascribe to H^a and H^b within the 1:1 $1\cdot\text{H}_2\text{PO}_4^-$ complex appeared at 11.30 and 11.25 ppm, respectively (*cf.* H^a at 9.56 ppm and H^b at 9.18 ppm in the $^1\text{H-NMR}$ spectrum of the free receptor). Observation that the 1:1 complex is fully formed after addition of 1 equivalent TBAH_2PO_4 indicates that $K_a(1\cdot\text{H}_2\text{PO}_4^-) > 10^4 \text{ M}^{-1}$ under these conditions. Then, as the amount of TBAH_2PO_4 exceeded 2.5 equivalents, the $^1\text{H-NMR}$ signals belonging to H^a and H^b shifted further downfield, suggesting the formation of a putative 1:2 $1\cdot(\text{H}_2\text{PO}_4^-)_2$ complex in the presence of excess dihydrogen phosphate. Finally, beyond the addition of 5 equivalents TBAH_2PO_4 , $^1\text{H-NMR}$ signals belonging to H^a and H^b disappeared, indicating deprotonation.

Addition of ≤ 1 equiv. $(\text{TBA})_2\text{SO}_4$ to FcSq_2 **1** provoked a similar response as observed during the titration with dihydrogen phosphate (Fig. 3). $^1\text{H-NMR}$ signals corresponding to the squaramide NH protons (H^a and H^b) initially broadened to the point of disappearance, and then reappeared at 11.75 and 11.65 ppm, respectively, as the ratio of 1:($\text{TBA})_2\text{SO}_4$ neared 1:1. Remarkably, as further equivalents of $(\text{TBA})_2\text{SO}_4$ were added, the signals corresponding to **1** remained unchanged. Despite the ability of FcSq_2 to adopt an opposed conformation, whereby the two squaramide motifs are presented on opposite sides of the molecule as separate binding sites (*cf.* titration with H_2PO_4^-), it appears that the 1:1 $1\cdot(\text{TBA})_2\text{SO}_4$ complex is exceptionally stable and robust, even in the presence of large excesses of sulfate.

To quantify K_a for the $1\cdot\text{SO}_4^{2-}$ and $1\cdot\text{H}_2\text{PO}_4^-$ complexes, binding studies monitored by UV-vis spectroscopy were initially run in 1% water/DMSO. However, in this medium, the data could not be fit to any simple binding model. We propose that intermolecular hydrogen bonding facilitates FcSq_2 homooligomerization processes which combine with anion-binding

processes to create a complex equilibrium that cannot be properly fit with a simple model. To minimise hydrogen bonding between FcSq_2 units, titrations were run in 20% water/DMSO; in this competitive aqueous medium, the data fit well to a simple 1:1 binding model (Table 1, entries 10 and 11). Notably, FcSq_2 **1** was shown to bind SO_4^{2-} strongly ($K_a = 3.1 \times 10^5 \text{ M}^{-1}$) and with a significant preference for SO_4^{2-} vs. H_2PO_4^- ($K_a(\text{SO}_4^{2-})/K_a(\text{H}_2\text{PO}_4^-) = 22$), suggestive that the FcSq_2 scaffold does indeed present an excellent and selective fit for the sulfate anion.

To probe the role of FcSq_2 structure in selective interaction with sulfate, the binding behaviour of the analogous one-arm derivative FcSq_1 **3**^{9a} (Scheme 1c) was quantified through $^1\text{H-NMR}$ binding studies in 1% water/DMSO- d_6 (Table 1, entries 8 and 9). From these studies, two key observations were made: (1) one-arm FcSq_1 **3** shows a preference for binding SO_4^{2-} vs. H_2PO_4^- ($K_a(\text{SO}_4^{2-})/K_a(\text{H}_2\text{PO}_4^-) = 3$) that is seven times lower than observed for two-arm FcSq_2 **1**, (2) sulfate binding with one-arm analogue **3** in moderately competitive 1% water/DMSO is over two orders of magnitude weaker than sulfate binding with two-arm FcSq_2 **1** in highly competitive 20% water/DMSO! These notable differences in binding behaviour between one- and two-arm analogues are strong evidence that the stacked presentation of two planar Cp-squaramide arms is a key factor in the sulfate-selectivity of the FcSq_2 scaffold.

The electrochemistry of FcSq_2 was investigated through cyclic wave voltammetry. In DMSO, voltammograms reported multiple and overlapping oxidation processes. Switching the solvent to 20% water/DMSO revealed a single oxidation wave (Fig. 4), suggesting that the complexity of the voltammograms obtained in pure DMSO is due to similar aggregation processes that hampered data-fitting during binding studies. Oxidation occurs at $E_{1/2} = -63 \text{ mV}$ for **1** (compared to $E_{1/2}(\text{ferrocene}) = 0 \text{ V}$)¹³ and is irreversible. 80–100 mV separation is observed between anodic and cathodic peaks in addition to an anodic current that is approximately $3\times$ more intense than the cathodic current.¹⁴

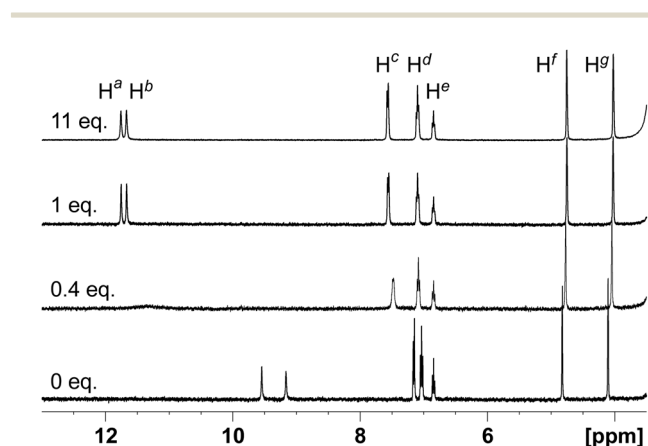


Fig. 3 Selected spectra from the $^1\text{H-NMR}$ titration of FcSq_2 **1** with $(\text{TBA})_2\text{SO}_4$ in 1% $\text{H}_2\text{O}/\text{DMSO}-d_6$ at 25°C . Proton assignments from Fig. 2.

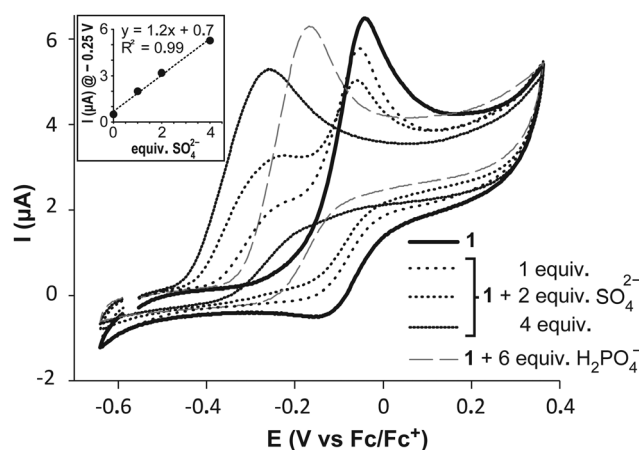


Fig. 4 CV response of **1** ($0.25 \times 10^{-3} \text{ M}$) in 20% water/DMSO before and after addition of $(\text{TBA})_2\text{SO}_4$ or TBAH_2PO_4 ; supporting electrolyte, 0.1 M TBAClO_4 ; scan rate, 100 mV s^{-1} ; $T = 80^\circ\text{C}$. Inset: Linear electrochemical response of **1** to sulfate addition at -0.25 V vs. Fc/Fc^+ .



Addition of up to 10 equiv. TBACl or TBANO₃ exerted little to no effect on the electrochemistry of FcSq₂ **1**.¹³ Conversely, upon progressive addition of TBAH₂PO₄ or (TBA)₂SO₄, two-wave behaviour was observed (Fig. 4), whereby the wave corresponding to free **1** diminished in intensity while a cathodically shifted second wave appeared which presumably corresponds to the **1**-anion complex. Addition of TBAH₂PO₄, affected appearance of the new wave at $E_{1/2} = -170$ mV ($\Delta E_{1/2} = 107$ mV vs. free **1**). The corresponding wave induced by addition of (TBA)₂SO₄ appears at a significantly more negative potential ($E_{1/2} = -305$ mV, $\Delta E_{1/2} = 242$ mV vs. free **1**). In addition, fewer equivalents of SO₄²⁻ are required to achieve the maximum response (4 equiv. SO₄²⁻ vs. 6 equiv. H₂PO₄⁻), a behaviour we ascribe to the higher affinity of FcSq₂ for SO₄²⁻ versus H₂PO₄⁻. The electrochemical response, measured as the maximum anodic current (at -0.25 V vs. Fc/Fc⁺), is linear with respect to the concentration of sulfate up to 4 equiv. (Fig. 4, inset). Concentrations of sulfate less than 1 equiv. vs. [**1**] were not trialled, so 0.25 mM is the lowest detection limit we can claim.

Conclusions

In summary, two receptors built around the previously unreported 1,1'-bis(squaramido)ferrocene (FcSq₂) scaffold have been prepared. Binding studies showed that FcSq₂ receptors overcome the high hydration energy of sulfate and make strong 1:1 complexes with this anion in highly competitive aqueous media. Notably, despite FcSq₂ presenting two independent squaramide units, the 1:1 complex with sulfate is robust and, contrary to the analogous complex with H₂PO₄⁻, does not break to form the 1:2 receptor-(anion)₂ complex, even in the presence of excess sulfate. Furthermore, FcSq₂ **1** binds selectively to sulfate versus nitrate, acetate, bisulfate, chloride and dihydrogen phosphate. Comparison to the one-arm analogue **3** provides evidence for the importance of the stacked two arm structure of FcSq₂; whereby excision of one arm results in 7× lower selectivity for binding SO₄²⁻ versus H₂PO₄⁻ and a 1:1 complex with sulfate that is over two orders of magnitude weaker. Cyclic wave voltammetry revealed that FcSq₂ present an irreversible oxidation that is cathodically shifted relative to ferrocene. In the presence of H₂PO₄⁻ or SO₄²⁻ two-wave behaviour is observed with the new wave featuring a large cathodic shift. Notably, the shift induced by sulfate is separated from that induced by H₂PO₄⁻ by over 130 mV. The electrochemical response of FcSq₂ **1** to sulfate is easily distinguishable and proportional to [SO₄²⁻], underlining the promise of FcSq₂ as a tool to bind and detect sulfate.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

This work was supported by the Australian Research Council (DP170100118 to K. A. J.). J. D. E. L. acknowledges the

University of Sydney for an IPRS scholarship. This research was facilitated by access to Sydney Analytical, a core research facility at the University of Sydney. This work was supported by the Royal Society (RG150600 to L. A.). W. J. H. G. acknowledges Banco Santander for a Mobility Scholarship. K. B.-J. thanks the Chemical Sciences, Office of Basic Energy Sciences, Office of Science, US Department of Energy (Grant DE-SC0018629) for partial funding of this work and the X-ray Laboratory at the University of Kansas.

Notes and references

- (a) M. S. H. Bader, *J. Pet. Sci. Eng.*, 2007, **55**, 93; (b) K. M. Fritz, S. Fulton, B. R. Johnson, C. D. Barton, J. D. Jack, D. A. Word and R. A. Burke, *J. North Am. Benthol. Soc.*, 2010, **29**, 673; (c) B. A. Moyer, R. Custelcean, B. P. Hay, J. L. Sessler, K. Bowman-James, V. W. Day and S.-O. Kang, *Inorg. Chem.*, 2013, **52**, 3473.
- (a) P. A. Dawson, *Semin. Cell Dev. Biol.*, 2011, **22**, 653; (b) A. V. N. Amerongen, J. G. M. Bolscher, E. Bloemena and E. C. I. Veerman, *Biol. Chem.*, 1998, **379**, 1; (c) A. B. Olomu, C. R. Vickers, R. H. Waring, D. Clements, C. Babbs, T. W. Warnes and E. Elias, *N. Engl. J. Med.*, 1988, **318**, 1089; (d) P. A. Dawson, L. Beck and D. Markovich, *Proc. Natl. Acad. Sci. U. S. A.*, 2003, **100**, 13704; (e) R. Langford, E. Hurrión and P. A. Dawson, *J. Genet. Genomics*, 2017, **44**, 7; (f) P. A. Dawson, S. J. Weerasekera, R. J. Atcheson, S. A. Twomey and D. G. Simmons, *Mol. Genet. Metab. Rep.*, 2020, **22**, 100568.
- (a) E. A. Katayev, Y. A. Ustynyuk and J. L. Sessler, *Coord. Chem. Rev.*, 2006, **250**, 3004; (b) B. A. Moyer, R. Custelcean, B. P. Hay, J. L. Sessler, K. Bowman-James, V. W. Day and S.-O. Kang, *Inorg. Chem.*, 2013, **52**, 3473; (c) I. Ravikumar and P. Ghosh, *Chem. Soc. Rev.*, 2012, **41**, 3077; (d) P. Molina, F. Zapata and A. Caballero, *Chem. Rev.*, 2017, **117**, 9907; (e) L. Macreadie, A. M. Gilchrist, D. A. McNaughton, W. G. Ryder, M. Fares and P. A. Gale, *Chemistry*, 2022, **8**, 46.
- M. A. Mintzer and M. W. Grinstaff, *Chem. Soc. Rev.*, 2011, **40**, 173.
- R. Custelcean and B. A. Moyer, *Eur. J. Inorg. Chem.*, 2007, 1321.
- (a) V. J. Dungan, H. T. Ngo, P. G. Young and K. A. Jolliffe, *Chem. Commun.*, 2013, **49**, 264; (b) S.-Q. Chen, W. Zhao and B. Wu, *Front. Chem.*, 2022, **10**, 905563; (c) S. K. Kim, J. Lee, N. J. Williams, V. M. Lynch, B. P. Hay, B. A. Moyer and J. L. Sessler, *J. Am. Chem. Soc.*, 2014, **136**, 15079; (d) C. Jia, Q.-Q. Wang, R. A. Begum, V. W. Day and K. Bowman-James, *Org. Biomol. Chem.*, 2015, **13**, 6953; (e) S. Kubik, *Acc. Chem. Res.*, 2017, **50**, 2870; (f) B. Portis, A. Mirchi, M. Emami Khansari, A. Pramanik, C. Johnson, D. Powell, J. Leszczynski and M. A. Hossain, *ACS Omega*, 2017, **2**, 5840; (g) S. Xiong and Q. He, *Chem. Commun.*, 2021, **57**, 13514.
- We adapt the term “mini-chelate”, originally coined for the related urea-binding motif (ref. 6d), to squaramides.
- (a) C. Xiong-Jie, L. Zhi and C. Wen-Hua, *Mini-Rev. Org. Chem.*, 2018, **15**, 148; (b) D. Jaglencic, Ł. Dobrzycki,



- M. Karbarz and J. Romański, *Chem. Sci.*, 2019, **10**, 9542; (c) M. Zaleskaya, M. Karbarz, M. Wilczek, Ł. Dobrzycki and J. Romański, *Inorg. Chem.*, 2020, **59**, 13749; (d) R. B. P. Elmes, K. K. Y. Yuen and K. A. Jolliffe, *Chem. – Eur. J.*, 2014, **20**, 7373; (e) C. Jin, M. Zhang, L. Wu, Y. Guan, Y. Pan, J. Jiang, C. Lin and L. Wang, *Chem. Commun.*, 2013, **49**, 2025; (f) M. Zaleskaya, D. Jaglenieć and J. Romański, *Dalton Trans.*, 2021, **50**, 3904; (g) L. Qin, J. R. Wright, J. D. E. Lane, S. N. Berry, R. B. P. Elmes and K. A. Jolliffe, *Chem. Commun.*, 2019, **55**, 12312; (h) L. Qin, S. J. N. Vervuurt, R. B. P. Elmes, S. N. Berry, N. Proschogo and K. A. Jolliffe, *Chem. Sci.*, 2020, **11**, 201; (i) L. Qin, A. Hartley, P. Turner, R. B. P. Elmes and K. A. Jolliffe, *Chem. Sci.*, 2016, **7**, 4563.
- 9 Related mono[squaramido]ferrocenes have been reported. See (a) M. Zaleskaya, D. Jaglenieć, M. Karbarz, Ł. Dobrzycki and J. Romański, *Inorg. Chem. Front.*, 2020, **7**, 972; (b) X. Zhang, P. Ma, D. Zhang, Y. Lei, S. Zhang, R. Jiang and W. Chen, *Org. Biomol. Chem.*, 2014, **12**, 2423.
- 10 Within the group of carbonyl-conjugated N–H hydrogen bond donors, aryl-substituted squaramides are exceptionally planar. For the 39 organic diarylsquaramides reported in the Cambridge Structural Database, the average angle between planes defined by the diaminocyclobutyl component and either aryl group is 21°. The average angle between analogous planes within 861 reported diarylureas is 30° and 9451 *N*-aryl amides is 23.5°.
- 11 Binding of **1** with TBANO₃ followed by UV-Vis spectroscopy.
- 12 Titrations involving the 3,5-(CF₃)₂-C₆H₃ FcSq₂ derivative **2** were complicated by poor fits and disappearance of ¹H-NMR signals corresponding to the NH protons and are not discussed here.
- 13 Section S5 of the ESI† reports all details of the electrochemistry of FcSq₂ **1** and the electrochemistry of the free receptor **2**.
- 14 The redox behaviour of ferrocenes, including both the amide- and urea-analogues of FcSq₂ (see ref. 15 and 16, respectively), is known to be robust. Therefore, it is somewhat surprising that FcSq₂ **1** and **2** both show irreversible electrochemical behaviour. See Section S5 of the ESI† for more details and discussion on the irreversible component of the electrochemical manifold of FcSq₂.
- 15 P. D. Beer, J. J. Davis, D. A. Drillsma-Milgrom and F. Szemes, *Chem. Commun.*, 2002, 1716.
- 16 F. Oton, A. Tarraga, A. Espinosa, M. D. Velasco and P. Molina, *J. Org. Chem.*, 2006, **71**, 4590.

