UvA-DARE (Digital Academic Repository)

Control of the overpotential of a [FeFe] hydrogenase mimic by a synthetic second coordination sphere

Nurttıla, S.S.; Zaffaroni, R.; Mathew, S.; Reek, J.N.H.

DOI

[10.1039/c9cc00901a](https://doi.org/10.1039/c9cc00901a)

Publication date

2019

Document Version

Final published version

Published in

Chemical Communications

License

Article 25fa Dutch Copyright Act

[Link to publication](#)

Citation for published version (APA):

Nurttıla, S. S., Zaffaroni, R., Mathew, S., & Reek, J. N. H. (2019). Control of the overpotential of a [FeFe] hydrogenase mimic by a synthetic second coordination sphere. *Chemical Communications*, 55(21), 3081-3084. <https://doi.org/10.1039/c9cc00901a>

General rights

It is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), other than for strictly personal, individual use, unless the work is under an open content license (like Creative Commons).

Disclaimer/Complaints regulations

If you believe that digital publication of certain material infringes any of your rights or (privacy) interests, please let the Library know, stating your reasons. In case of a legitimate complaint, the Library will make the material inaccessible and/or remove it from the website. Please Ask the Library: <https://uba.uva.nl/en/contact>, or a letter to: Library of the University of Amsterdam, Secretariat, Singel 425, 1012 WP Amsterdam, The Netherlands. You will be contacted as soon as possible.

UvA-DARE is a service provided by the library of the University of Amsterdam (<https://dare.uva.nl>)

Cite this: *Chem. Commun.*, 2019, 55, 3081

Received 31st January 2019,
Accepted 13th February 2019

DOI: 10.1039/c9cc00901a

rsc.li/chemcomm

Control of the overpotential of a [FeFe] hydrogenase mimic by a synthetic second coordination sphere†

Sandra S. Nurttila,¹ Riccardo Zaffaroni,² Simon Mathew¹ and Joost N. H. Reek¹*

Hydrogen as a renewable fuel is viable when produced sustainably via proton reduction catalysis (PRC). Many homogeneous electrocatalysts perform PRC with high rates, but they all require a large overpotential to drive the reaction. Natural hydrogenase enzymes achieve reversible PRC with potentials close to the thermodynamic equilibrium through confinement of the active site in a well-defined protein pocket. Inspired by nature, we report a strategy that relies on the selective encapsulation of a synthetic hydrogenase mimic in a novel supramolecular cage. Catalyst confinement decreases the PRC overpotential by 150 mV, and is proposed to originate from the cationic cage stabilizing anionic reaction intermediates within the catalytic cycle.

A hydrogen-based economy is frequently pictured as an alternative to the current fossil fuel-based economy, as the only by-product formed during combustion of hydrogen is water.^{1,2} The best synthetic proton reduction catalysts (PRCs) rely on the use of precious metals (Pt) in their structure.³ Naturally occurring iron-iron hydrogenase enzymes catalyze the reversible reduction of protons to molecular hydrogen with high rates (9000 s⁻¹) and nearly no overpotential at ambient conditions.⁴ Application of these enzymes directly to homogeneous catalysis is challenging due to their sensitivity to molecular oxygen and great effort needed to purify them.⁵ [FeFe] hydrogenase mimics endeavour to emulate the structural and functional mimicry of the enzyme active site.⁶ Numerous synthetic systems have been reported, some of which outcompete the natural enzyme in terms of catalytic rate by nearly an order of magnitude.^{4,6–20} The high catalytic rates are impressive, but all synthetic mimics reported to date still require a large overpotential to drive PRC.⁹ Certain strategies to decrease the overpotential have been presented, including the incorporation of an internal basic amine

functionality close to the diiron center, often referred to as 'proton relay'. The basic moiety can be protonated by the substrate molecules (protons) and thereby ensure a high local concentration of protons close to the active site. Some studies have also looked at the redox-active Fe₄S₄ cluster which in the natural enzyme supplies electrons to the active site.^{21–24} Incorporation of synthetic mimics inside the apoprotein (HydA) of natural hydrogenases results in novel hybrid catalysts that have comparable activity as the natural enzyme,⁹ demonstrating the crucial role of the second coordination sphere on the catalytic performance. Confinement of synthetic mimics in other types of molecular architectures has also received some attention. In this context, the effect of embedding mimics in micelles,^{25,26} polymersomes,²⁷ liposomes,²⁸ peptidic scaffolds,^{7,29} cyclodextrins,^{30,31} and dendrimers³² has been evaluated. Encapsulation of hydrogenase mimics inside cyclodextrins has shown to increase the overpotential of the catalyst,³⁰ but for most other examples no details of the effect of encapsulation on the overpotential of the catalyst are presented.

Supramolecular metal-organic cages serve as second coordination spheres for a variety of transition metal catalysts, thereby modulating their intrinsic properties.^{33–43} Previously, we demonstrated that the selective encapsulation of a pyridyl-appended hydrogenase mimic in a synthetic porphyrin cage gave a catalytic system that is active in PRC in homogeneous medium.⁴⁴ The cage corners were shown to display redox activity in the window of catalysis. With the aim to separate the redox events of the cage and the encapsulated catalyst, a new cage structure inspired by the work of Nitschke and co-workers⁴⁵ was devised. Herein, we report the synthesis and application of a novel supramolecular porphyrin cage (Fe₄(Zn-L)₆) possessing redox-innocent triazole corners, as a synthetic second coordination sphere for [FeFe] hydrogenase mimic **1** (Fig. 1). The binding of **1** is driven by selective pyridyl-zinc porphyrin interactions formed between **1** and the porphyrins of the cage, resulting in the encapsulation of a single catalyst in the cavity of the cage. As a result, a nature-inspired catalyst is obtained that exhibits electrocatalytic activity in PRC, and the overpotential of the catalyst is significantly decreased as compared to the same catalyst in bulk solution.

Homogeneous, Supramolecular and Bio-Inspired Catalysis, Van 't Hoff Institute for Molecular Sciences, University of Amsterdam, Science Park 904, 1098 XH Amsterdam, The Netherlands. E-mail: j.n.h.reek@uva.nl

† Electronic supplementary information (ESI) available: Synthesis, characterization, binding and voltammetric studies, xTB calculations. See DOI: 10.1039/c9cc00901a

Fig. 1 Control of the overpotential of [FeFe] hydrogenase mimic **1** in proton reduction catalysis by encapsulation in cage $\text{Fe}_4(\text{Zn-L})_6$.

Importantly, this constitutes a unique example of lowering the overpotential of a [FeFe] hydrogenase mimic by changing its second coordination sphere.

Cage $\text{Fe}_4(\text{Zn-L})_6$ is obtained by mixing building block **Zn-L** (6 equiv.) and iron(II) triflimide (4 equiv.) in dry acetonitrile at 70°C overnight (Fig. 2; for the synthesis and full characterization, see Sections 2 and 3, ESI†). An air-stable purple solid, identified as the cage, is isolated after precipitation by the addition of diethyl ether (isolated yield 78%). NMR spectroscopy and high-resolution cold-spray-ionization mass spectrometry (CSI-MS) analyses confirm the formation of a *T*-symmetric Fe_4L_6 cage of molecular weight 8345.3 Da. All attempts to grow single crystals of $\text{Fe}_4(\text{Zn-L})_6$ have resulted in the formation of microcrystalline powders. Complex **1** is obtained by a literature procedure.⁴⁶

Geometry optimizations of the expected host-guest complex $1\cdot\text{Fe}_4(\text{Zn-L})_6$ using a tight-binding chemical method (GFN-xTB)⁴⁷ suggest that a single catalyst will bind inside the cage (Section 4, ESI†). Moreover, the catalyst is expected not to freely diffuse in and out of the cavity due to the limited size of the window apertures of the cage. Endohedral binding of **1** (1 equiv.) inside the cage is confirmed by ^1H NMR spectroscopy of an equimolar solution of **1** and $\text{Fe}_4(\text{Zn-L})_6$ in CD_3CN (Fig. S16 and 17, ESI†). Upon encapsulation of **1** the signals belonging to the cage shift and broaden slightly, indicative of guest binding. The ^1H NMR spectrum of $1\cdot\text{Fe}_4(\text{Zn-L})_6$ acquired at -40°C reveals the signals attributed to the encapsulated catalyst around 6 ppm. The signals of the catalyst experience a significant upfield shift (around 3 ppm) upon encapsulation, consistent with increased shielding imparted by the planar aromatic edges of the surrounding cage structure. Diffusion-ordered spectroscopy (DOSY) of the host-guest complex displays a clear single band with an identical diffusion constant ($D = 1.0 \times 10^{-9} \text{ m}^2 \text{ s}^{-1}$) as for empty cage $\text{Fe}_4(\text{Zn-L})_6$, confirming that the catalyst-cage assembly has the same size as the empty cage (Fig. S18, ESI†). The intensity of the signals belonging to the encapsulated catalyst are too weak to observe in the DOSY spectrum. Catalyst encapsulation is further confirmed by high-resolution CSI-MS, where signals belonging to the host-guest complex $1\cdot\text{Fe}_4(\text{Zn-L})_6$ are detected (Fig. S19–S21, ESI†). A UV-vis binding study between **1** and $\text{Fe}_4(\text{Zn-L})_6$

Fig. 2 (a) Formation of cage $\text{Fe}_4(\text{Zn-L})_6$ through metal-directed self-assembly of building block **Zn-L** and iron(II) triflimide. For clarity only one of the six ligands occupying the edges of the cage is shown in the molecular structure. The modelled structure (xTB-optimized) of $\text{Fe}_4(\text{Zn-L})_6$ is depicted at the top right in space-filling view (Fe, orange; Zn, purple-grey; N, blue; C, grey; H, white). (b) Parts of the ^1H NMR spectra of building block **Zn-L** (top) and cage $\text{Fe}_4(\text{Zn-L})_6$ (bottom) (500 MHz, DMF-d_7 for **Zn-L** and CD_3CN for $\text{Fe}_4(\text{Zn-L})_6$, 298 K).

afforded an association constant of $1.3 \times 10^4 \text{ M}^{-1}$, ensuring virtually quantitative binding when working at mM concentrations (Section 6, ESI†).

Separation of the redox events of $\text{Fe}_4(\text{Zn-L})_6$ and **1** by the novel cage design is confirmed electrochemically—by means of cyclic voltammetry—demonstrating that the empty cage exhibits no redox activity in the potential window where PRC is anticipated for **1** (Fig. S26, ESI†), further highlighting the compatibility of this cage towards PRC. Owing to the limited solubility of the cage in the used electrolyte solution, a relatively low concentration (0.1 mM) of both the **1** and $\text{Fe}_4(\text{Zn-L})_6$ is used.

By comparison of the respective electrochemical behavior of **1** and the $1\cdot\text{Fe}_4(\text{Zn-L})_6$ complex, the effect of the synthetic second coordination sphere on the redox properties of **1** can be evaluated. Cyclic voltammetry of free **1** in CH_3CN on a glassy carbon electrode reveals two quasi-reversible redox processes with cathodic peak potentials of around -1.3 and -1.5 V (vs. Fc/Fc^+) and anodic peak potentials (re-oxidation) of around -1.2 and -1.0 V (vs. Fc/Fc^+) (Fig. S27a, ESI†). The analysis of the voltammograms hints at a complex electrochemical process, which is elucidated by means of spectroelectrochemistry (*vide infra*). Encapsulation of **1** inside cage $\text{Fe}_4(\text{Zn-L})_6$ results in a 30 mV decrease in the reduction potential of the catalyst, indicating an

Fig. 3 (a) Disproportionation upon reduction of **1** occurs in bulk solution but is prevented inside the cage. (b) Plot of the semidifferential peak current of the reduction wave of **1** against the scan rate in the absence and presence of cage. In both cases the linearity of the plots indicates a solution-based redox event, but only in the cage is it reversible due to absence of disproportionation. The red dotted line would be observed for a fully reversible reduction wave.

increase in electron deficiency within the complex upon cage binding (Fig. S28a, ESI†). In both cases, the semidifferential peak current (i_p) of the redox waves varies linearly with the scan rate (ν), indicative of a solution-based redox event (Fig. 3b).^{48–50} For free **1** the slopes of the forward and backward scan are not identical, which indicates that the reduction of the catalyst is not reversible on the timescale of the measurement. Complementary spectroelectrochemical experiments reveal that disproportionation of **1** to bisphosphine complex **2** and the hexacarbonyl-based dianion 3^{2-} occurs upon reduction, in line with the observed irreversible redox chemistry (Fig. 3a and Fig. S27c, d, ESI†). Interestingly, for **1-Fe₄(Zn-L)₆** this disproportionation reaction is not observed, as is evident from the identical slopes of the linear fits which equates to a reversible redox event. Clearly, the inhibition of the disproportionation reaction is a consequence of site isolation upon catalyst encapsulation. Moreover, consecutive voltammetric cycling of **1** enabled the observation of an oxidation wave at -1.0 V (vs. Fc/Fc^+), which arises from the oxidation of 3^{2-} to **3** (Fig. S28d, ESI†). This wave is not present in the three consecutive voltammograms of **1-Fe₄(Zn-L)₆**, confirming that disproportionation is not observed under the applied conditions.

In the presence of the proton source HNET_3PF_6 , complexes **1** and **1-Fe₄(Zn-L)₆** are active in the electrocatalytic reduction of protons to molecular hydrogen. The acid is not strong enough to protonate the neutral Fe-Fe complex **1** (Fig. S33, ESI†). Upon the addition of increasing amounts of HNET_3PF_6 , the reduction waves attributed to free catalyst **1** and its encapsulated analogue **1-Fe₄(Zn-L)₆** become more irreversible. Increasing the potential window to more reductive potentials results in the appearance of a catalytic wave at around -2.08 V (vs. Fc/Fc^+) for free **1** and around -1.93 V (vs. Fc/Fc^+) for **1-Fe₄(Zn-L)₆** (Fig. S29, ESI†). Encapsulation of **1** thus lowers the overpotential of PRC by ~ 150 mV. For **1-Fe₄(Zn-L)₆** the catalytic wave shifts 150 mV more negative after the addition of > 16 equiv. of acid, affording a new catalytic wave at the same potential as free **1**. This shift is due to cage decomposition at higher acid concentrations, resulting in

Fig. 4 (a) Tafel plots for **1** and **1-Fe₄(Zn-L)₆** in the presence of the weak acid HNET_3PF_6 in acetonitrile. The value of TOF_{max} is extrapolated for a 1 M concentration of protons. (b) Key catalytic parameters.

the expulsion of the catalyst from the cage and consequentially, catalysis in free solution (Fig. S34, ESI†).

By foot-of-the-wave analysis (FotW)⁵¹ the catalytic rate constants (k_{cat}) of **1** ($9.8 \times 10^5 \text{ M}^{-1} \text{ s}^{-1}$) and **1-Fe₄(Zn-L)₆** ($4.2 \times 10^5 \text{ M}^{-1} \text{ s}^{-1}$) are determined (Fig. 4b and Fig. S30, ESI†). The calculated overpotentials are 0.79 V for **1** and 0.64 V for **1-Fe₄(Zn-L)₆**. Using the method developed by Artero and Savnt,⁵² a Tafel plot is constructed from $\text{TOF}_{\text{max}} = 2k_{\text{cat}}[\text{H}^+]^0$ (extrapolated for a 1 M concentration of protons) and the calculated overpotentials (Fig. 4a). The Tafel plots confirm that encapsulation of **1** decreases the catalytic overpotential significantly at the expense of a slightly lower catalytic rate. The large decrease in overpotential is proposed to be due to the cationic cage stabilizing anionic reaction intermediates, thereby allowing catalysis at a lower overpotential.

In conclusion, the second coordination sphere around the active site in hydrogenase enzymes is of crucial importance to their catalyst properties. In this contribution, we report a novel supramolecular coordination cage **Fe₄(Zn-L)₆** that binds a $[\text{FeFe}]$ hydrogenase mimic (**1**) and as such serves as a synthetic second coordination sphere. Hydrogenase mimic **1** is encapsulated inside the cage in a 1:1 stoichiometry and the binding relies on zinc porphyrin–pyridine interactions. Electrochemical experiments show that disproportionation of **1**, which occurs in bulk solution, is prevented by encapsulation in the cage. Importantly, the encapsulated catalyst reduces protons electrocatalytically with a 150 mV lower overpotential compared to the same catalyst free in solution. This work clearly demonstrates the importance of the second coordination sphere around a catalyst in controlling its overpotential.

The research leading to these results has received funding from the European Research Council under the European Union's Seventh Framework Programme (FP7/2007-2013)/ERC grant agreement no 339786. We acknowledge E. Zuidinga for mass analysis and Jan Meine Ernsting for help with 2D ^1H DOSY NMR measurements. Kaj van Vliet is acknowledged for his help with xTB calculations.

Conflicts of interest

There are no conflicts to declare.

Notes and references

- 1 A. F. Heyduk and D. G. Nocera, *Science*, 2001, **293**, 1639–1641.
- 2 J. R. Bolton, *Science*, 1978, **202**, 705–711.

- 3 M. Carmo, D. L. Fritz, J. Mergel and D. Stolten, *Int. J. Hydrogen Energy*, 2013, **38**, 4901–4934.
- 4 M. Winkler, J. Esselborn and T. Happe, *Biochim. Biophys. Acta, Bioenerg.*, 2013, **1827**, 974–985.
- 5 W. Lubitz, E. Reijerse and M. van Gastel, *Chem. Rev.*, 2007, **107**, 4331–4365.
- 6 M. Watanabe, Y. Honda, H. Hagiwara and T. Ishihara, *J. Photochem. Photobiol., C*, 2017, **33**, 1–26.
- 7 T. R. Simmons, G. Berggren, M. Bacchi, M. Fontecave and V. Artero, *Coord. Chem. Rev.*, 2014, **270–271**, 127–150.
- 8 M. Y. Darensbourg, E. J. Lyon, X. Zhao and I. P. Georgakaki, *Proc. Natl. Acad. Sci. U. S. A.*, 2003, **100**, 3683–3688.
- 9 G. Berggren, A. Adamska, C. Lambert, T. R. Simmons, J. Esselborn, M. Atta, S. Gambarelli, J.-M. Mouesca, E. Reijerse, W. Lubitz, T. Happe, V. Artero and M. Fontecave, *Nature*, 2013, **499**, 66–69.
- 10 A. Le Goff, V. Artero, B. Jousselme, P. D. Tran, N. Guillet, R. Métayé, A. Fihri, S. Palacin and M. Fontecave, *Science*, 2009, **326**, 1384–1387.
- 11 S. T. Stripp, G. Goldet, C. Brandmayr, O. Sanganas, K. A. Vincent, M. Haumann, F. A. Armstrong and T. Happe, *Proc. Natl. Acad. Sci. U. S. A.*, 2009, **106**, 17331–17336.
- 12 M. Razavet, V. Artero and M. Fontecave, *Inorg. Chem.*, 2005, **44**, 4786–4795.
- 13 R. Becker, S. Amirjalayer, P. Li, S. Woutersen and J. N. H. Reek, *Sci. Adv.*, 2016, **2**, e1501014.
- 14 F. Gloaguen and T. B. Rauchfuss, *Chem. Soc. Rev.*, 2009, **38**, 100–108.
- 15 B. E. Barton, M. T. Olsen and T. B. Rauchfuss, *Curr. Opin. Biotechnol.*, 2010, **21**, 292–297.
- 16 I. P. Georgakaki, L. M. Thomson, E. J. Lyon, M. B. Hall and M. Y. Darensbourg, *Coord. Chem. Rev.*, 2003, **238–239**, 255–266.
- 17 W. Lubitz, H. Ogata, O. Rüdiger and E. Reijerse, *Chem. Rev.*, 2014, **114**, 4081–4148.
- 18 V. Artero and M. Fontecave, *Coord. Chem. Rev.*, 2005, **249**, 1518–1535.
- 19 A. J. Esswein and D. G. Nocera, *Chem. Rev.*, 2007, **107**, 4022–4047.
- 20 M. Wang, K. Han, S. Zhang and L. Sun, *Coord. Chem. Rev.*, 2015, **287**, 1–14.
- 21 A. Adamska-Venkatesh, D. Krawietz, J. Siebel, K. Weber, T. Happe, E. Reijerse and W. Lubitz, *J. Am. Chem. Soc.*, 2014, **136**, 11339–11346.
- 22 C. Tard, X. Liu, S. K. Ibrahim, M. Bruschi, L. De Gioia, S. C. Davies, X. Yang, L.-S. Wang, G. Sawers and C. J. Pickett, *Nature*, 2005, **433**, 610–613.
- 23 J. M. Camara and T. B. Rauchfuss, *Nat. Chem.*, 2012, **4**, 26–30.
- 24 J. C. Lansing, J. M. Camara, D. E. Gray and T. B. Rauchfuss, *Organometallics*, 2014, **33**, 5897–5906.
- 25 F. Quentel, G. Passard and F. Gloaguen, *Energy Environ. Sci.*, 2012, **5**, 7757–7761.
- 26 H.-Y. Wang, W.-G. Wang, G. Si, F. Wang, C.-H. Tung and L.-Z. Wu, *Langmuir*, 2010, **26**, 9766–9771.
- 27 F. Wang, M. Wen, K. Feng, W.-J. Liang, X.-B. Li, B. Chen, C.-H. Tung and L.-Z. Wu, *Chem. Commun.*, 2016, **52**, 457–460.
- 28 S. Troppmann, E. Brandes, H. Motschmann, F. Li, M. Wang, L. Sun and B. König, *Eur. J. Inorg. Chem.*, 2016, 554–560.
- 29 A. Roy, C. Madden and G. Ghirlanda, *Chem. Commun.*, 2012, **48**, 9816–9818.
- 30 M. L. Singleton, J. H. Reibenspies and M. Y. Darensbourg, *J. Am. Chem. Soc.*, 2010, **132**, 8870–8871.
- 31 X. Li, M. Wang, D. Zheng, K. Han, J. Dong and L. Sun, *Energy Environ. Sci.*, 2012, **5**, 8220–8224.
- 32 T. Yu, Y. Zeng, J. Chen, Y.-Y. Li, G. Yang and Y. Li, *Angew. Chem., Int. Ed.*, 2013, **125**, 5741–5745.
- 33 S. H. A. M. Leenders, R. Gramage-Doria, B. de Bruin and J. N. H. Reek, *Chem. Soc. Rev.*, 2015, **44**, 433–448.
- 34 M. Yoshizawa, J. K. K. Klosterman and M. Fujita, *Angew. Chem., Int. Ed.*, 2009, **48**, 3418–3438.
- 35 X. Jing, C. He, Y. Yang and C. Duan, *J. Am. Chem. Soc.*, 2015, **137**, 3967–3974.
- 36 M. J. Wiester, P. A. Ulmann and C. A. Mirkin, *Angew. Chem., Int. Ed.*, 2011, **50**, 114–137.
- 37 M. Raynal, P. Ballester, A. Vidal-Ferran and P. W. N. M. van Leeuwen, *Chem. Soc. Rev.*, 2014, **43**, 1660–1733.
- 38 C. J. Brown, F. D. Toste, R. G. Bergman and K. N. Raymond, *Chem. Rev.*, 2015, **115**, 3012–3035.
- 39 D. M. Vriezema, M. Comellas Aragonès, J. A. A. W. Elemans, J. J. L. M. Cornelissen, A. E. Rowan and R. J. M. Nolte, *Chem. Rev.*, 2005, **105**, 1445–1490.
- 40 S. Zarra, D. M. Wood, D. A. Roberts and J. R. Nitschke, *Chem. Soc. Rev.*, 2015, **44**, 419–432.
- 41 Q.-Q. Wang, S. Gonell, S. H. A. M. Leenders, M. Dürr, I. Ivanović-Burmazović and J. N. H. Reek, *Nat. Chem.*, 2016, **8**, 225–230.
- 42 F. Yu, D. Poole III, S. Mathew, N. Yan, J. Hessels, N. Orth, I. Ivanović-Burmazović and J. N. H. Reek, *Angew. Chem., Int. Ed.*, 2018, **130**, 11417–11421.
- 43 S. Chen, K. Li, F. Zhao, L. Zhang, M. Pan, Y.-Z. Fan, J. Guo, J. Shi and C.-Y. Su, *Nat. Commun.*, 2016, **7**, 13169.
- 44 S. S. Nurttila, R. Becker, J. Hessels, S. Woutersen and J. N. H. Reek, *Chem. – Eur. J.*, 2018, **24**, 16395–16406.
- 45 W. Brenner, T. K. Ronson and J. R. Nitschke, *J. Am. Chem. Soc.*, 2017, **139**, 75–78.
- 46 R. Zaffaroni, W. I. Dzik, R. J. Detz, J. I. van der Vlugt and J. N. H. Reek, *Eur. J. Inorg. Chem.*, submitted.
- 47 S. Grimme, C. Bannwarth and P. Shushkov, *J. Chem. Theory Comput.*, 2017, **13**, 1989–2009.
- 48 J. J. Toman, R. M. Corn and S. D. Brown, *Anal. Chim. Acta*, 1981, **123**, 187–199.
- 49 P. Dalrymple-Alford, M. Goto and K. B. Oldham, *Anal. Chem.*, 1977, **49**, 1390–1394.
- 50 M. Goto and D. Ishii, *J. Electroanal. Chem. Interfacial Electrochem.*, 1975, **61**, 361–365.
- 51 C. Costentin, S. Drouet, M. Robert and J.-M. Savéant, *J. Am. Chem. Soc.*, 2012, **134**, 11235–11242.
- 52 V. Artero and J.-M. Savéant, *Energy Environ. Sci.*, 2014, **7**, 3808–3814.