


 Cite this: *Chem. Commun.*, 2021, 57, 3869

 Received 18th December 2020,
Accepted 8th March 2021

DOI: 10.1039/d0cc08236h

rsc.li/chemcomm

Catalytic hydrogenation enabled by ligand-based storage of hydrogen†

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Biology employs exquisite control over proton, electron, H-atom, or H₂ transfer. Similar control in synthetic systems has the potential to facilitate efficient and selective catalysis. Here we report a dihydrazonopyrrole Ni complex where an H₂ equivalent can be stored on the ligand periphery without metal-based redox changes and can be leveraged for catalytic hydrogenations. Kinetic and computational analysis suggests ligand hydrogenation proceeds by H₂ association followed by H–H scission. This complex is an unusual example where a synthetic system can mimic biology’s ability to mediate H₂ transfer via secondary coordination sphere-based processes.

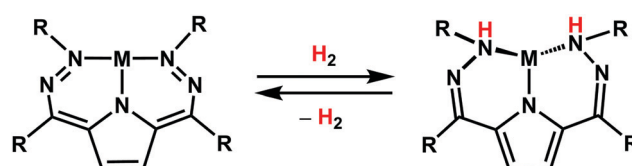
The controlled transfer of multiple equivalents of protons and electrons is fundamental to many important chemical reactions. While H₂ is a potent reducing agent, transition metal catalysts are often required to overcome kinetic barriers to activating H₂. Transition metals often mediate reductive transformations *via* hydride intermediates arising from oxidative addition of H₂ which then perform insertion reactivity.¹ While this primary sphere H₂ transfer is well-established, especially with second- or third-row metals, such two electron processes can be much more challenging with first-row metals.

One strategy to improve the reactivity of first row complexes in these transformations is to engage the secondary coordination sphere. Nature uses this approach, frequently relying on proton/electron transfer from the protein scaffold or cofactors to supply reducing equivalents to transition metal active sites.² The elegance of these systems has inspired synthetic chemists to discover new molecular systems which can mimic this reactivity. Incredible advances have been made in designing ancillary ligand scaffolds that can mediate electron transfer,³ hydrogen bonding,⁴ or proton shuttling.⁵ Nevertheless, supporting ligand systems which can store both protons and

electrons are still uncommon.⁶ Recently several well-defined systems that can reversibly store H-atom equivalents have been reported.⁷ Systems that can store full H₂ equivalents in a supporting ligand backbone are still rare.⁸

In order to explore this relatively scarce area we have been investigating reversible ligand-based H₂ transfer using dihydrazonopyrrole (DHP) complexes of Ni.⁹ The 2,5-pyrrole pincer scaffold is attractive for this reactivity because 2e[−] reduction/oxidation of the conjugated system coupled with protonation/deprotonation of the pincer arms can reversibly transfer H₂ without any redox changes at the metal center (Scheme 1). We have previously demonstrated that this scaffold can support the storage of both protons and electrons, but this reactivity had been limited to storage of an electron or H-atom equivalent, not storage of a full H₂ equivalent.^{9a,b} We now report that Ni complexes of the previously reported ^tBu,^{Tol}DHP ligand (^tBu,^{Tol}DHP = 2,5-bis((2-*t*-butylhydrazono)(*p*-tolyl)methyl)-pyrrole) can support secondary sphere storage of H₂. Furthermore, this reactivity is reversible and enables hydrogenation catalysis. Kinetic and computational analysis indicates that ligand hydrogenation proceeds in a process that is first-order in [Ni] and involves H₂ association followed by H–H scission.

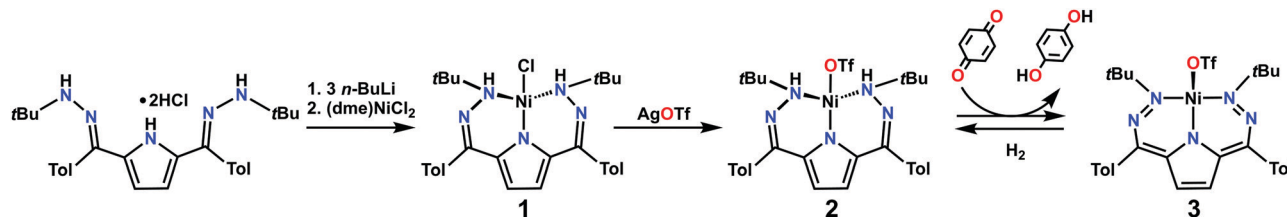
Deprotonation of the previously reported ^tBu,^{Tol}DHP·2HCl with 3 eq. of *n*-BuLi followed by dropwise addition to (dme)NiCl₂ (dme = 1,2-dimethoxyethane) in THF provides (^tBu,^{Tol}DHPH₂)NiCl (**1**) as a red crystalline solid in 56% yield (Scheme 2). The ¹H NMR spectrum of **1** shows diamagnetic signals indicating a symmetric DHP environment, with a new broad singlet resonance at 5.98 ppm which is assigned to the two N–H protons on the ligand scaffold (see ESI†). Analysis by


 Scheme 1 Ligand based storage of H₂ on dihydrazonopyrrole scaffolds.

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† Electronic supplementary information (ESI) available. CCDC 2050739 and 2050740. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/d0cc08236h

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Scheme 2 Synthesis of **1** and **2** and interconversion of **2** and **3** with H₂ and benzoquinone.

single crystal X-ray diffraction (SXRD) shows a twisted square-planar complex with the Ni square plane rotated from the plane of the central pyrrole ring by $\sim 30^\circ$ (Fig. 1, top). The Ni–N_{hydrazone} bonds are 1.938(2) and 1.946(2) Å, which are ~ 0.1 Å longer than those seen in the previously reported

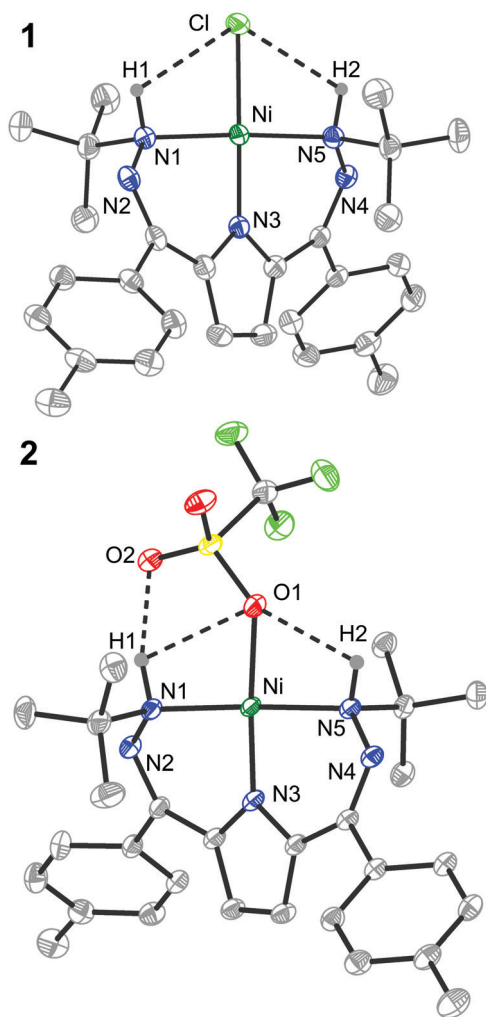


Fig. 1 Solid state structure of **1** (top), and **2** (bottom) with ellipsoids set to 50% probability, and all C–H hydrogens omitted for clarity. Hydrogen bonding interactions shown with dashed lines. Ni shown in green, C in grey, N in blue, O in red, F in bright green, Cl also in bright green (labelled), and S in yellow. Selected bond lengths (Å): **1**: Ni–Cl: 2.1817(7) Å, Ni–N1: 1.938(2), Ni–N3: 1.824(2), Ni–N5: 1.946(2), N1–N2: 1.454(3), N4–N5: 1.460(2). **2**: Ni–O: 1.952(1) Å, Ni–N1: 1.955(1), Ni–N3: 1.812(1), Ni–N5: 1.964(1), N1–N2: 1.455(2), N4–N5: 1.460(2).

T-shaped complex (^tBu,^{Tol}DHP[•])Ni, likely due to both weaker donation and greater steric strain from the protonated nitrogens. Within the ligand scaffold, the N–N bonds are 1.454(3) and 1.460(2) Å which are significantly longer than other ^tBu,^{Tol}DHP or ^{Ph},^{Tol}DHP complexes (~ 1.37 Å), supporting ligand-based redox changes. The N–H protons can be located in the difference map, and are oriented towards the Cl ligand. The Cl \cdots H distances are ~ 2.55 Å and the N–H–Cl angles are 104° . Both of these values are consistent with hydrogen bonding interactions, as have been observed in other M–Cl complexes.¹⁰ Distinct stretches are also observed by IR spectroscopy at 3241 and 3166 cm⁻¹, further confirming the presence of N–H groups (see ESI[†]).

The reactivity of **1** was investigated to determine whether the ligand-stored H₂ equivalent could be transferred to substrates. However, **1** shows little to no reactivity with substrates including air, olefins, and carbonyls. We hypothesized that a comparatively strongly coordinating Cl⁻ ligand might inhibit reactivity by occupying a potential site of substrate coordination and therefore abstracted this ligand. Complex **1** reacts cleanly with AgOTf to give the corresponding triflate complex (^tBu,^{Tol}DHP₂)NiOTf (**2**) (Scheme 1). SXRD analysis shows a structure very similar to that of **1** with the triflate bound in the fourth coordination site (Fig. 1, bottom). Hydrogen bonding interactions to the triflate ligand are also clear, with one interaction to O2 of moderate strength and two weaker interactions to O1 based on O \cdots H distances of ~ 1.9 and 2.4 Å respectively.

We then turned to see if this ligand substitution enabled H₂ transfer reactivity. Hydrogen transfer was tested by stirring **2** with benzoquinone at room temperature which resulted in slow formation of hydroquinone and the previously reported dehydrogenated complex (^tBu,^{Tol}DHP)NiOTf (**3**) as indicated by ¹H NMR spectroscopy (Scheme 1, see ESI[†]).^{9c} This reactivity demonstrates an unusual example where an H₂ equivalent stored on a ligand backbone can be transferred to a substrate. Examples of H₂ transfer between a supporting ligand and a substrate are rare.⁸

In order to test catalytic H₂ transfer, we then investigated whether **2** could be regenerated from **3** with H₂ gas. Encouragingly, ¹H NMR analysis of this reaction indicates that complex **2** is formed as the major product when **3** is reacted with one atmosphere of H₂ with mild heating (see ESI[†]). Given this result, we then placed **3** and excess benzoquinone under an atmosphere of H₂ to determine whether catalytic hydrogenation was feasible. Monitoring by ¹H NMR spectroscopy at room temperature shows conversion of **3** to **2** with concomitant conversion of two equivalents of benzoquinone to hydroquinone indicating this process is catalytic (see ESI[†]). This reactivity provides important proof of

concept for ligand-based H₂ transfer and shows the viability of the DHP scaffold for reversible H₂ donation.

We were interested in understanding more about the mechanistic details of addition of H₂ to the ligand backbone and therefore we performed kinetic analyses on the interconversion of **3** and **2**. Monitoring the reaction of **3** with H₂ by UV-visible spectroscopy shows conversion of **3** to **2** with kinetics consistent with a first-order reaction in [Ni] under pseudo first-order conditions (Fig. 2). Comparison of the product peak intensities at 355 nm with intensities from isolated **2** indicates a high yield for this conversion (> 80%), consistent with ¹H NMR analysis (see ESI†), but some small amount of an intermediate or byproduct with an absorbance around 550 nm is also formed. We have thus far been unable to obtain further information on this species. The first order dependence on [Ni] for the consumption of **3** is consistent with the hypothesis of a single metal complex reacting to store H₂ across the ligand framework as opposed to a bimolecular reaction, as has been observed in the homolytic activation of O–H bonds with a related ^{Ph}_h^{Tol}DHP complex.^{9b}

An Eyring analysis shows a ΔH^\ddagger of 13.9(4) kcal mol⁻¹ and ΔS^\ddagger of -18(5) cal (mol K)⁻¹, which gives an overall ΔG^\ddagger at 298 K of ~21 kcal mol⁻¹ (Fig. 2). The comparatively large and negative ΔS^\ddagger suggests that association of H₂ is at least rate-contributing. We also performed the same analysis with D₂ to determine the deuterium kinetic isotope effect (KIE) for this hydrogenation reaction. Comparison of the rates under H₂ versus D₂ shows an inverse deuterium KIE of 0.8(1). If scission of the H–H bond was the sole rate contributing step a normal primary KIE would be expected. In contrast, the observed inverse KIE for this hydrogenation reaction could potentially arise from an equilibrium isotope effect (EIE) in an H₂ binding pre-equilibrium.¹¹ For this reason, as well as the convolution of the energetics of the H₂ cleavage steps by an H₂ association step, we have examined this reaction in more detail through additional calculations.

We have examined the thermodynamics of H₂ addition to the ligand framework by performing density functional theory (DFT) calculations. We initially attempted calculations on OTf⁻-bound species but observed dissociation of the anion along the reaction coordinate. Experimental evidence for OTf⁻ dissociation is equivocal (see ESI†), but the increased reactivity on moving from **1** to **2** supports that anion dissociation may be required for reactivity. To simplify our computational analysis, we have instead examined the energetics and geometries of H₂ cleavage along a singlet manifold starting from a putative cationic intermediate [^(Bu)_h^{Tol}DHPNi]⁺ (Fig. 3).

The first optimized transition state is an H₂ splitting step across the Ni–N bond to form the intermediate hydride species [^(Bu)_h^{Tol}DHPNiH]⁺. This transition state is 28.4 kcal mol⁻¹ higher in energy than [^(Bu)_h^{Tol}DHPNi]⁺ + H₂. The second transition state has a similar barrier of 25.9 kcal mol⁻¹ versus [^(Bu)_h^{Tol}DHPNi]⁺ + H₂ and results in the favorable (-6.5 kcal mol⁻¹ from the reactants) formation of the hydrogenated product. Examining the Mulliken charge densities of the H-atoms along the reaction coordinate suggests that TS1 is best described as a proton transfer (see ESI†). While the charges in TS2 are much more covalent, the balanced reaction and Mulliken charges suggests this is step is best

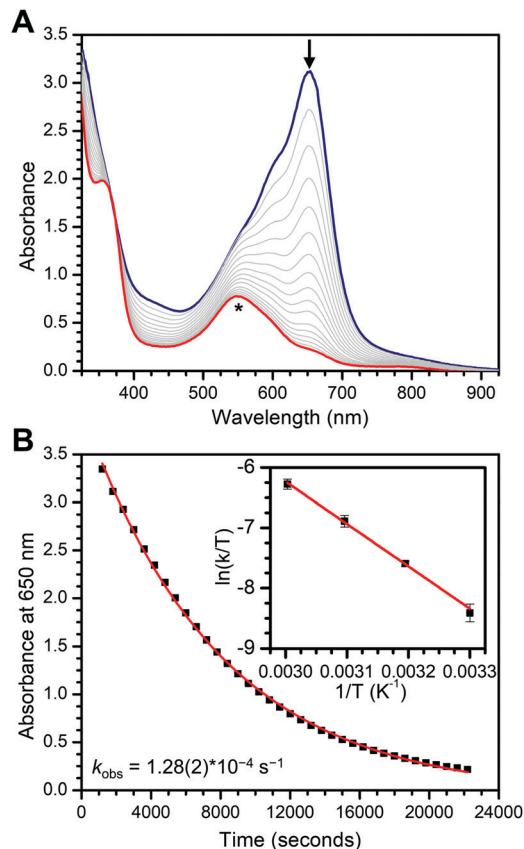


Fig. 2 Kinetic analysis of the hydrogenation of **3** to **2**. (A) UV-vis traces of **3** under 1 atmosphere of H₂ at 40 °C taken every 10 minutes. The asterisk indicates a small but intensely colored impurity. (B) Decay of the absorbance at 650 nm with an exponential fit as described in the ESI† shown in red. Inset: Eyring analysis with linear fit ($R^2 = 0.99$) in red to determine the activation parameters for the hydrogenation as described in the text and ESI†.

considered as a hydride transfer. Overall, this analysis suggests that H₂ binding and scission should be accessible with reasonably good agreement between theoretical and experimental energetics.

These calculations also enable us to test the origin of the inverse experimental KIE. Examination of the isotope dependence of the first transition state (TS1) suggests that a primary KIE would be expected (see ESI†), in contrast with experimental observations. Conversely, if the isotope dependence of free H₂/D₂ and LNiH₂⁺/LNiD₂⁺ are considered, an inverse isotope dependence is predicted for reversible H₂ binding, consistent with experiment (see ESI†). These observations suggest that the origin of the observed isotope dependence likely arises from an H₂ association EIE.¹¹ Similar inverse isotope effects have recently been observed in paramagnetic transition metal systems as well as across bimetallic frustrated Lewis pairs.^{12,13}

The studies presented here show an unusual example of metal–ligand cooperativity enabled hydrogenation reactivity where the ligand can store a full H₂ equivalent. The catalytic hydrogenation of benzoquinone provides an important proof of concept for this area. Kinetic data show that the bifunctional splitting of H₂ proceeds in a process that is first-order in [Ni], but that proceeds with an inverse deuterium isotope

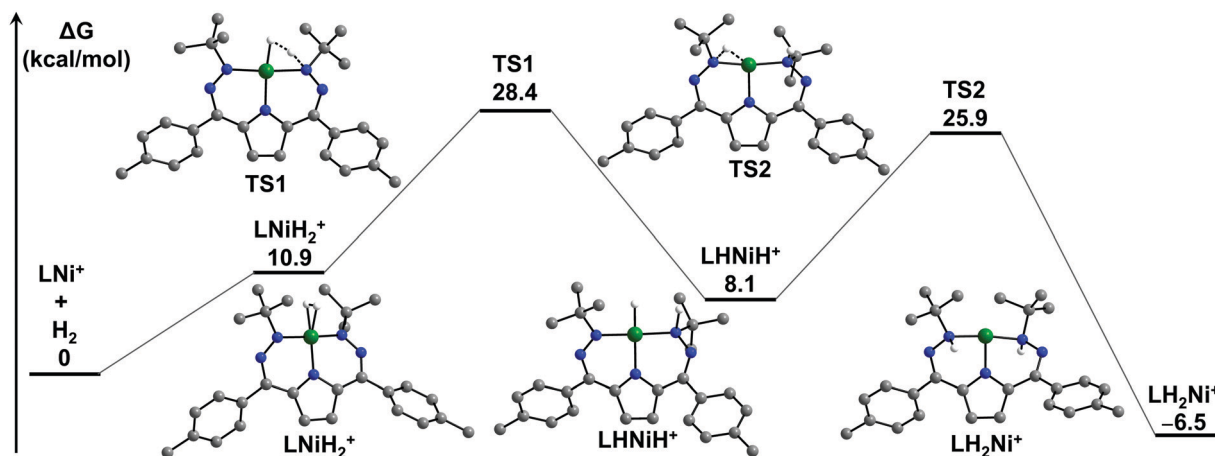


Fig. 3 DFT computed geometries and energies of H₂ splitting. Calculations were carried out with the B3P functional and a def2-TZVP basis set, with a def2-TZVPP basis set on Ni. Ni is shown in gray, N in blue, and H in white. Note that only H-atoms stemming from the H₂ ligand are shown.

dependence. Calculations suggest that H₂ scission is energetically accessible and that the source of the observed inverse deuterium isotope dependence is an EIE arising from H₂ association. While catalytic hydrogenations of other substrates have been less successful thus far, the enhanced reactivity in moving from **1** to **2** (Cl⁻ to OTf⁻) suggests that the primary metal coordination sphere still plays an important role in this primarily ligand-centered reactivity and offers a potential avenue to expand hydrogenation reactivity to other substrates.

This work was supported by the National Institutes of Health (R35 GM133470). We thank the University of Chicago, the 3M Corporation for a NTFA to J. S. A., and the Sloan Foundation for a Research Fellowship to J. S. A. (FG-2019-11497). J. E. S. was supported by the U.S. Department of Defense through a National Defence Science and Engineering Graduate fellowship (00003765). We also thank the Research Computing Center at the University of Chicago for providing computing resources. We would like to thank Dr Josh Kurutz for assistance with NMR. Some data reported here were collected at ChemMatCARS Sector 15 which is supported by the NSF under grant number NSF/CHE-1834750. This research used resources of the APS, a U.S. DOE Office of Science User Facility operated for the DOE Office of Science by Argonne National Laboratory under Contract No. DE-AC02-06CH11357. We would like to thank Dr Yu-Sheng Chen and Dr SuYin Wang for assistance with SXRD at 15-ID-B,C,D.

Conflicts of interest

There are no conflicts to declare.

Notes and references

- 1 R. H. Crabtree, *Organometallic Chemistry of the Transition Metals*, 6th edn, 2014.
- 2 (a) S. A. Cook, E. A. Hill and A. S. Borovik, *Biochemistry*, 2015, **54**, 4167–4180; (b) D. F. Baumgardner, W. E. Parks and J. D. Gilbertson, *Dalton Trans.*, 2020, **49**, 960–965.
- 3 (a) O. R. Luca and R. H. Crabtree, *Chem. Soc. Rev.*, 2013, **42**, 1440–1459; (b) R. Arevalo and P. J. Chirik, *J. Am. Chem. Soc.*, 2019, **141**, 9106–9123.
- 4 S. A. Cook and A. S. Borovik, *Acc. Chem. Res.*, 2015, **48**, 2407–2414.
- 5 (a) M. Rakowski Dubois and D. L. Dubois, *Acc. Chem. Res.*, 2009, **42**, 1974–1982; (b) T. Zell and D. Milstein, *Acc. Chem. Res.*, 2015, **48**, 1979–1994; (c) M. L. Pegis, C. F. Wise, D. J. Martin and J. M. Mayer, *Chem. Rev.*, 2018, **118**, 2340–2391.
- 6 L. Alig, M. Fritz and S. Schneider, *Chem. Rev.*, 2019, **119**, 2681–2751.
- 7 (a) E. J. Thompson and L. A. Berben, *Angew. Chem., Int. Ed.*, 2015, **54**, 11642–11646; (b) G. W. Margulieux, M. J. Bezdek, Z. R. Turner and P. J. Chirik, *J. Am. Chem. Soc.*, 2017, **139**, 6110–6113; (c) A. Dauth, U. Gellrich, Y. Diskin-Posner, Y. Ben-David and D. Milstein, *J. Am. Chem. Soc.*, 2017, **139**, 2799–2807; (d) K. E. Rosenkoetter, M. K. Wojnar, B. J. Charette, J. W. Ziller and A. F. Heyduk, *Inorg. Chem.*, 2018, **57**, 9728–9737; (e) M. B. Ward, A. Scheitler, M. Yu, L. Senft, A. S. Zillmann, J. D. Gorden, D. D. Schwartz, I. Ivanović-Burmazović and C. R. Goldsmith, *Nat. Chem.*, 2018, **10**, 1207–1212; (f) M. J. Drummond, C. L. Ford, D. L. Gray, C. V. Popescu and A. R. Fout, *J. Am. Chem. Soc.*, 2019, **141**, 6639–6650.
- 8 (a) B. W. Purse, L. H. Tran, J. Piera, B. Åkermark and J. E. Bäckvall, *Chem. – Eur. J.*, 2008, **14**, 7500–7503; (b) T. W. Myers and L. A. Berben, *Chem. Sci.*, 2014, **5**, 2771–2777; (c) J. T. Henthorn, S. Lin and T. Agapie, *J. Am. Chem. Soc.*, 2015, **137**, 1458–1464; (d) P. O. Lagaditis, B. Schluschaß, S. Demeshko, C. Würtele and S. Schneider, *Inorg. Chem.*, 2016, **55**, 4529–4536; (e) F. Schneek, M. Finger, M. Tromp and S. Schneider, *Chem. – Eur. J.*, 2017, **23**, 33–37; (f) B. M. Lindley, Q. J. Bruch, P. S. White, F. Hasanayn and A. J. M. Miller, *J. Am. Chem. Soc.*, 2017, **139**, 5305–5308; (g) R. Pramanick, R. Bhattacharjee, D. Sengupta, A. Datta and S. Goswami, *Inorg. Chem.*, 2018, **57**, 6816–6824; (h) R. Jain, A. A. Mamun, R. M. Buchanan, P. M. Kozlowski and C. A. Grapperhaus, *Inorg. Chem.*, 2018, **57**, 13486–13493; (i) T. J. Sherbow, E. J. Thompson, A. Arnold, R. I. Sayler, R. D. Britt and L. A. Berben, *Chem. – Eur. J.*, 2019, **25**, 454–458.
- 9 (a) M.-C. Chang, A. J. McNeece, E. A. Hill, A. S. Filatov and J. S. Anderson, *Chem. – Eur. J.*, 2018, **24**, 8001–8008; (b) M.-C. Chang, K. A. Jesse, A. S. Filatov and J. S. Anderson, *Chem. Sci.*, 2019, **10**, 1360–1367; (c) A. J. McNeece, K. A. Jesse, J. Xie, A. S. Filatov and J. S. Anderson, *J. Am. Chem. Soc.*, 2020, **142**, 10824–10832.
- 10 (a) G. Aullón, D. Bellamy, A. Guy Orpen, L. Brammer and E. A. Bruton, *Chem. Commun.*, 1998, 653–654; (b) T. Steiner, *Angew. Chem., Int. Ed.*, 2002, **41**, 48–76.
- 11 (a) W. D. Jones, *Acc. Chem. Res.*, 2003, **36**, 140–146; (b) D. G. Churchill, K. E. Janak, J. S. Wittenberg and G. Parkin, *J. Am. Chem. Soc.*, 2003, **125**, 1403–1420; (c) M. Gómez-Gallego and M. A. Sierra, *Chem. Rev.*, 2011, **111**, 4857–4963.
- 12 Y. Zhang, M. K. Karunananda, H.-C. Yu, K. J. Clark, W. Williams, N. P. Mankad and D. H. Ess, *ACS Catal.*, 2019, **9**, 2657–2663.
- 13 D. E. Prokopchuk, G. M. Chambers, E. D. Walter, M. T. Mock and R. M. Bullock, *J. Am. Chem. Soc.*, 2019, **141**, 1871–1876.