Regioselective $^{12}CO/^{13}CO$ exchange activity of a mixed-valent Fe(II)Fe(I) model of the H_{ox} state of [FeFe]-hydrogenase†

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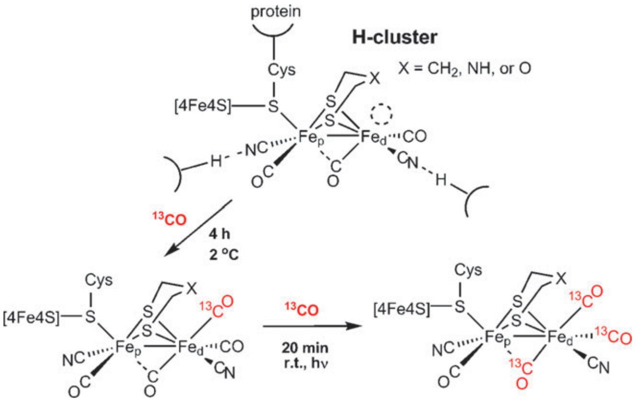
A mixed-valent Fe(II)Fe(I) model of the H_{ox} state of [FeFe]-hydrogenase is shown, under certain conditions, to exhibit regioselective $^{12}CO/^{13}CO$ exchange activity similar to that observed for H_{ox}.

The metalloenzyme [FeFe]-H_2ase, which catalyzes the reversible reduction of protons to form dihydrogen ($2H^+ + 2e^- \leftrightarrow H_2$),[1] has been characterized in several redox states including the diamagnetic H_{red} state and the paramagnetic $S = 1/2$ H_{ox} state.[2] The magnetism of H_{ox}, the active oxidized state, is ascribed to mixed valency in the 2-iron subsite of the hydrogen-producing or H-cluster (Scheme 1), $\{[2Fe][4Fe4S]\}_H$, for which oxidation state assignments are now accepted as Fe^IFe^{II}.[3] Although a number of small molecule models of $[2Fe]_H$ have been reported, most have been based on the symmetrical Fe^IFe^I complex (μ-pdt)$[Fe(CO)_3]_2$ (pdt = 1,3-propanedithiolate)[4] or $Fe^{II}Fe^{II}$ derivatives of it, *e.g.*, (μ-H)$[Fe(CO)_2L]_2{}^+$.[5] Mixed-valent $Fe^{II}Fe^I$ models of H_{ox} were unknown until recently when the groups of Darensbourg[6] and Rauchfuss[7] reported that one-electron oxidation of $(PMe_3)(CO)_2Fe(\mu\text{-pdt})Fe(CO)_2(IMes)$ (**1**, IMes = 1,3-bis(2,4,6-trimethylphenyl)imidazol-2-ylidene) and $(PMe_3)(CO)_2Fe(\mu\text{-edt})Fe(CO)(dppv)$ (edt = 1,2-ethanedithiolate, dppv = *cis*-1,2-$C_2H_2(PPh_2)_2$), respectively, in non-coordinating solvent (CH_2Cl_2) leads to moderately stable cationic $Fe^{II}Fe^I$ complexes (Scheme 2).

The structural characteristics of these mixed-valent complexes are quite similar to those of the 2-iron subsite of the H-cluster, featuring a semi-bridging CO ligand and an open terminal coordination site on one iron. Computational studies of $(PMe_3)(CO)_2Fe(\mu\text{-pdt})(\mu\text{-CO})Fe(CO)(IMes)^+$ ($\mathbf{1}^+$) have shown that the unpaired spin density lies almost entirely on the "rotated" IMes-substituted Fe_B center in an orbital that is pointed directly into an open coordination site, from which we conclude oxidation states of +1 on Fe_B, and +2 on the PMe_3-bearing Fe_A.[8] This oxidation state assignment is consistent with that suggested by computations on H_{ox} models, namely that the "rotated" distal Fe (Fe_d) is in the +1 oxidation state, while the proximal Fe (Fe_p) is in the +2 state.[9]

Radical promotions, particularly in exchange of CO ligands in 17-electron mononuclear complexes, are a part of classical mechanistic organometallic chemistry.[10] That these processes are also involved in the bioorganometallic chemistry of the [FeFe]-H_2ase active site may be inferred from the extensive studies of Albracht and co-workers on the reactivity of [FeFe]-H_2ase from *Desulfovibrio desulfuricans* towards CO ligand exchange, monitored by IR spectroscopy.[11] In the absence of light, the active enzyme H_{ox} reacts readily with ^{12}CO or ^{13}CO to form a CO-inhibited state, H_{ox}–^{12}CO or H_{ox}–^{13}CO, respectively (Scheme 1). Although prolonged illumination of the enzyme in the H_{ox}–^{12}CO state produces no detectable effects in the IR spectrum, illumination of the labeled H_{ox}–^{13}CO in the presence of extrinsic ^{13}CO leads to regioselective exchange with the intrinsic CO's in the bridging and terminal positions on Fe_d. In view of the structural and electronic similarity of $\mathbf{1}^+$ to H_{ox}, we were curious to ascertain whether the model complex showed such a stepwise and regioselective reaction with added ^{13}CO as that observed for H_{ox}. Herein, we report the reactivity of $\mathbf{1}^+$ towards added ^{13}CO and compare this reactivity with that reported for the enzyme.

The IR spectrum of $\mathbf{1}^+$ in CH_2Cl_2 features three $\nu(CO)$ bands at 2036(s), 1997(s) and 1861(w) cm^{-1}, with a noticeable shoulder to the right of the band at 1997 cm^{-1} (Fig. 1(A)).[6] Deconvolution into component bands reveals that the band at 1997 cm^{-1}, in fact, consists of two bands at 1998 and 1985 cm^{-1} (see ESI†). In accordance with results from DFT frequency calculations (see ESI†), the bands at 2036 and 1985 can be assigned to the $\nu(CO)_{sym}$ and $\nu(CO)_{asym}$ of the two terminal CO ligands on the unrotated Fe center (labeled Fe_A in Scheme



Scheme 1

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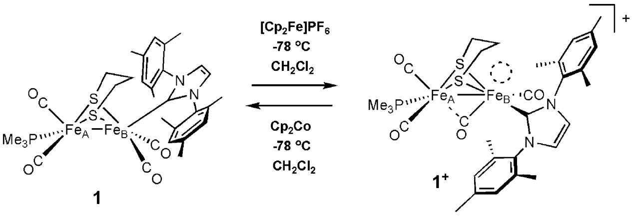

Scheme 2

2), while the intense band at 1998 corresponds to the terminal CO on the rotated iron center, Fe_B. The less intense band at 1861 cm^{-1} is attributed to the semi-bridging CO ligand. Unlike H_{ox}, under 1 atm of added CO, a CO-adduct of **1**$^+$ is not detected by IR spectroscopy.‡ Nevertheless, as CO exchange processes are readily observed with ^{13}CO, even at −78 °C, we may reasonably infer that a 19-electron adduct is required as a transient intermediate in the exchange reaction.

Upon exposure to 1 atm of ^{13}CO for 15 minutes at −78 °C in CH_2Cl_2 in the absence of light, two new ν(CO) bands appear at 1955 and 1821 cm^{-1} in the IR spectrum of **1**$^+$ (Fig. 1(A)). The appearance of these bands is concomitant with diminished intensity in the bands at 1997 and 1861 cm^{-1}. After 45 min of exposure to ^{13}CO, the IR spectrum remains constant, indicating that further ^{13}CO exchange does not occur at −78 °C. The 40 cm^{-1} shift of the band at 1861 cm^{-1} to 1821 cm^{-1} is consistent with ^{13}CO exchange into the semi-bridging position (calculated shift = 40 cm^{-1}). The new band that appears at 1955 cm^{-1} is shifted by 42 cm^{-1} from the band at 1997 in the ^{12}CO-derivative (calculated shift = 43 cm^{-1}). Based on the positions of these new ν(CO) stretches and the persistence of the bands at 2036 and 1997 cm^{-1}, we posit that the exchange of extrinsic ^{13}CO with intrinsic ^{12}CO in **1**$^+$ occurs at −78 °C with regioselectivity, favoring the terminal and bridging CO ligands on the "rotated" Fe_B.

In an independent experiment to test this hypothesis, **1**$^+$ was exposed to 1 atm ^{13}CO for 30 min in CH_2Cl_2 at −78 °C at which time Cp_2Co was added to reduce the partially ^{13}CO-labeled complex to a diamagnetic Fe^IFe^I state. The ^{13}C NMR spectrum of this species revealed a single downfield ^{13}C resonance at 218.6 ppm, corresponding to a single type of ^{13}C-labeled CO ligand (Fig. 1(D)).§ The absence of coupling to ^{31}P (coupling that is observed in the ^{13}C NMR spectrum of natural abundance samples of **1**) indicates that only the CO ligands on the IMes side of the molecule have been exchanged with ^{13}CO.

This regioselective ^{13}CO exchange process is similar to that which has been observed for H_{ox}, albeit with different reaction conditions.[11] Thus, complex **1**$^+$ also undergoes ^{13}CO exchange solely into positions accessible to the open coordination site on the "rotated" Fe center. While the exchange process with H_{ox} occurs near room temperature and only under illumination conditions, ^{13}CO exchange occurs readily with **1**$^+$ at low temperature in the absence of light, without the detection of an additional bound CO ligand.

While ^{13}CO exchange into all CO positions of H_{ox} has not been observed under any conditions, such complete exchange is observed with **1**$^+$. Upon warming a solution of **1**$^+$ under 1 atm of ^{13}CO in CH_2Cl_2 to room temperature, a new IR spectrum was obtained with bands at 1990, 1951 and 1820 cm^{-1} (Fig. 1(B)). This new spectrum is consistent with ^{13}CO exchange into all CO positions on both Fe centers (calculated: 1992, 1954 and 1821 cm^{-1}). Reduction of this completely ^{13}CO-labeled species with Cp_2Co leads to an IR spectrum consistent with what is expected for fully-labeled **1**, with bands at 1926, 1888, 1853 and 1840 cm^{-1} (calculated: 1929, 1891, 1856 and 1841 cm^{-1}) (Fig. 1(C)). The ^{13}C NMR spectrum of the resulting complex reveals two downfield resonances, a singlet at 218.6 and a doublet at 216.9 ppm, corresponding to ^{13}C-labeled CO ligands on the IMes- and PMe_3-substituted Fe centers, respectively (Fig. 1(E)). As an important control experiment, exposure of solutions of the fully ^{13}CO-labeled **1**$^+$ to 1 atm of ^{12}CO at room temperature leads to complete regeneration of the original IR spectrum of **1**$^+$ (see ESI†).

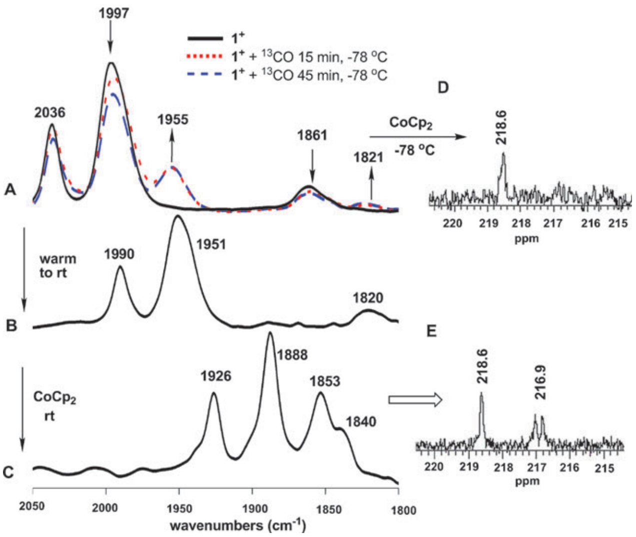

Fig. 1 Infrared spectra of (A) **1**$^+$ upon exposure to ^{13}CO at −78 °C in CH_2Cl_2 (in the dark) after 0 (black), 15 (red) and 45 (blue) min, (B) **1**$^+$ after warming to room temperature under 1 atm of ^{13}CO, and (C) ^{13}CO-labeled product obtained *via* treatment of **1**$^+$ with ^{13}CO at room temperature followed by reduction with Cp_2Co. Carbonyl region of the ^{13}C NMR spectrum of (D) the regioselectively labeled product generated upon exposure of **1**$^+$ to ^{13}CO at −78 °C for 30 min followed by Cp_2Co reduction and (E) the fully ^{13}CO-labeled product obtained addition of Cp_2Co to the labeled product generated upon exposure of **1**$^+$ to ^{13}CO at room temperature.

It is noteworthy that the distinctly abiological ligands, PMe_3 and a sterically encumbered *N*-heterocyclic carbene, lead to model complexes that effectively mimic many of the relevant features of the [FeFe]-H_2ase active site: reversible redox, structural, and site-selective CO-exchange chemistry. As this occurs in the absence of the protein superstructure, the ensuing synthetic challenge of responsive second coordination spheres, or abiological matrices, that maintain the high energy, rotated structure in both the $Fe^{II}Fe^I$ and Fe^IFe^I redox states does not appear to be an impossible quest.

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Notes and references

‡ Under higher pressures of CO there is evidence for CO-adduct formation. These results will be reported in a subsequent publication.

§ The natural abundance ^{13}C NMR spectrum of **1** features two downfield resonances corresponding to CO ligands, a singlet at 218.6 ppm and a doublet at 216.9 ppm. The coupling to ^{31}P in the signal at 216.9 indicates that this peak corresponds to the carbonyl ligands on the PMe$_3$-substituted Fe$_A$.

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