RuBisCO-inspired CO_2 Activation and Transformation by an Iridium(I) Complex

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Abstract: Synthesis of a new iridium(I) complex comprising an enamido phosphine anion dbuP$^-$ and its unique reactivity with CO_2 is reported. The complex binds two equivalents of CO_2 and initiates a highly selective reaction cascade. The reaction leads to the reversible cleavage of CO_2 and the enamido ligand as well. Computational analysis points to the existence of a relatively stable Ir-CO_2 complex as reaction intermediate prior to CO_2 cleavage, which could be confirmed experimentally. The observed transformation resembles several aspects of the enzymatic CO_2 fixation by RuBisCO.

The development of novel reaction cascades for the fixation of CO_2, its transformation and incorporation in organic matter remains a major challenge for synthetic chemists.[1] Inspiration for the design of new metal complexes for CO_2 capture can be found in biological systems, where CO_2 fixation via C-C linkage is mediated by biotin dependent enzymes [2] or catalyzed by ribulose-bisphosphate carboxylase/oxygenase (RuBisCO).[3] The latter acts as a catalyst for the direct carboxylation of ribulose-bisphosphate (RuBP) at the C2 carbon and its subsequent cleavage to form 3-phosphoglycerate (3-PGA) in the Calvin cycle, which is the essential step for the biosynthesis of carbohydrates from atmospheric CO_2 (see Fig. 1a).
Despite RuBisCO's ubiquitous presence in plants, which makes it one of the most abundant enzymes on earth, small molecule model compounds of this enzyme are scarce. Nevertheless, the CO_2 fixation by RuBisCO features some interesting aspects, which could facilitate CO_2 transformation by other metal complexes as well, if they could be adopted. One of the key features is the cooperative uptake of two CO_2 molecules by the enzyme with different functions and fate. The first CO_2 is required for enzyme activation, which takes place by carbamate formation at a lysine residue and subsequent capture of a Mg^{2+} ion,[4] while only the second CO_2 is used for carboxylation of the substrate (see Fig. 1b). Surprisingly, attempts to design RuBisCO-inspired model compounds with Mg^{2+} [5] and other metal ions[6] focused on the carbamate formation step, although the C-C bond formation between the second CO_2 and the

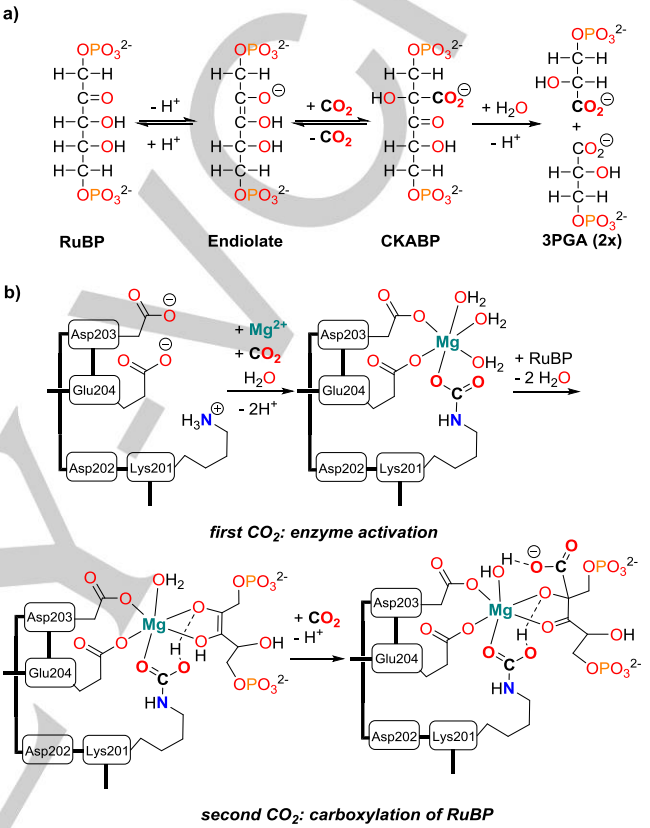

Figure 1. CO_2 fixation by RuBisCO. a) Reaction cascade observed in the enzymatic carboxylation of ribulose-bisphosphate (RuBP) by RuBisCO; b) Schematic representation of the active center during enzyme activation, substrate binding and carboxylation (— protein backbone, amino acid sequence numbers correspond to spinach RuBisCO).

substrate RuBP in its endiolate form is the key function of the enzyme. This makes enolates or related substance classes such as enamides promising substrates in small molecular systems, which aim for C-C bond formation rather than carbamylation.[7] While magnesium is nature's metal of choice in this essential enzyme, this selection seems markedly influenced by the abundance of the Mg^{2+} ion. When thinking about synthetic metal complexes, being able to incorporate two CO_2 molecules in analogy to the natural ideal, but without the help of a protein shell as highly sophisticated multifunctional ligand, other metal ions appear better suited. For instance, the combination of enolato or enamido ligands as model substrates with a low-valent CO_2-affine metal center (e.g. Ir^I)[8] might be suitable. Along these lines, we synthesized new Ir^I complexes comprising a chelating enamido phosphine anion dbuP$^-$ [9] (see Fig. 2a). This enamido derivative is easily accessible by deprotonation of the dbu-modified phosphine 6-diphenyl-phosphanyl-1,8-

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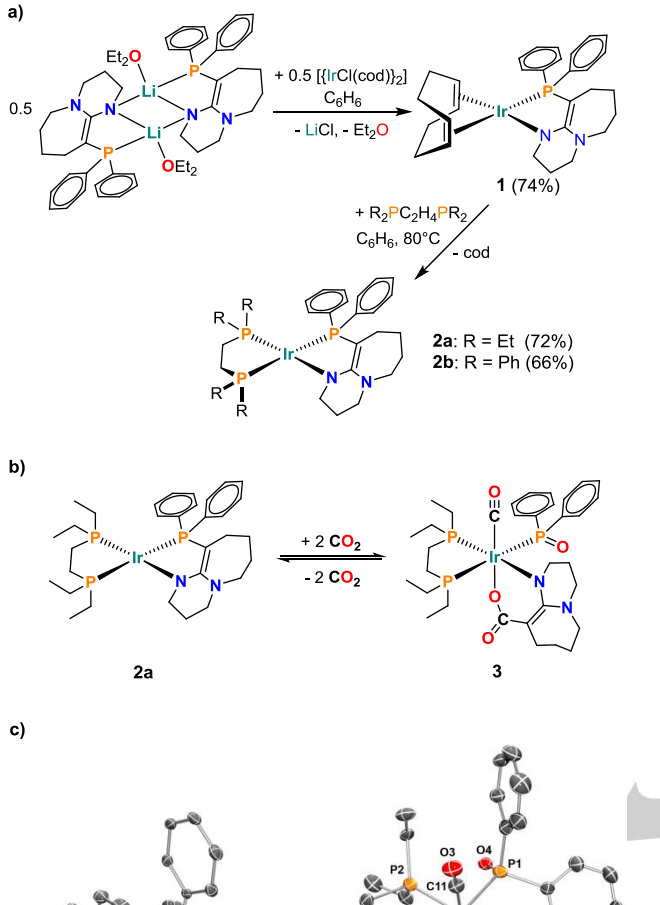

Figure 2. a) Synthesis of **1** and **2**; b) Reversible CO_2 fixation by **2a**. c) ORTEP plots of **2a** (left) and **3** (right), ellipsoids drawn at 50% probability level, H atoms omitted for clarity.

diazabicyclo[5.4.0]undec-7-ene (dbuPH),[10] and its phosphine moiety ensures tight bonding to Ir centers. Salt metathesis with a lithium compound provided access to [Ir(cod)(dbuP)] (**1**) (see Fig. 2a and ESI), which, however, showed no reactivity towards CO_2 at ambient temperature. Neither carbamate formation nor carboxylation at the carbon atoms of the enamido moiety was detected, which contrasts recent investigations on related Ru^{II}, Re^{I}, Fe^{II}, and Ir^{III} systems.[8e,11] This is not surprising, since **1** lacks an electrophilic metal center, which promotes CO_2 fixation via M-O bond formation occurring simultaneously with the carboxylation of the enamide. Instead, the low-valent Ir^{I} center in **1** is rather basic, yet not enough to capture CO_2 by a nucleophilic attack.

In order to investigate the potential of two different adjacent nucleophilic sites in CO_2 capture, we then increased the metal basicity by exchanging the cod ligand in **1** by the basic 1,2-bis(diethylphosphino)ethane (depe), thus enhancing the affinity

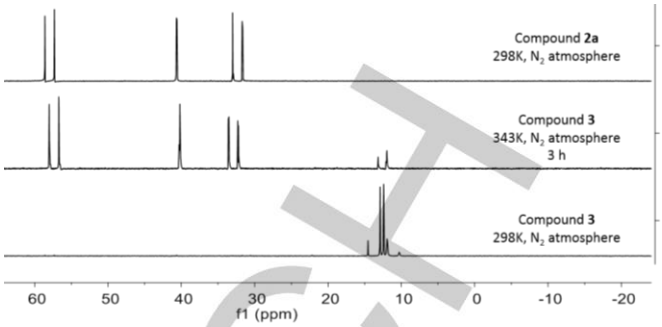

Figure 3. Temperature-dependent re-formation of **2a** from **3** in C_6D_6, monitored by $^{31}P\{^1H\}$ NMR spectroscopy (middle and bottom); spectrum of **2a** for comparison (top).

of the metal center towards CO_2. The resulting product [Ir(depe)(dbuP)] (**2a**) can be isolated as red crystals in 72% yield (see Fig. 2c). In contrast to **1**, compound **2a** reacts readily and highly selectively with two equivalents of CO_2. A single product **3** was formed within seconds, when a solution of **2a** was exposed to a CO_2 atmosphere at ambient temperature. The CO_2 uptake is related to an increase of the molecular mass of the species by m/z = 88 to m/z = 823.25 (M+1; by ESI-mass spectrometry), as expected for the incorporation of two equivalents of CO_2. ^{13}C NMR spectroscopy revealed signals at 163.4 and 174.4 ppm, which correspond to the carbon atoms of former CO_2 molecules. A coupling of two CO_2 at the Ir^{I} center, which earlier led to the iridacycles $[(Me_2RP)_3P)_3Ir(Cl)\{C(O)OC(O)O\}]$ (R = Me, Ph)[8a,d] and $[(t\text{Bu-PNP})Ir(H)\{C(O)OC(O)O\}]$[8e] (*t*Bu-PNP = 2,6-bis($t\text{Bu}_2PCH_2)_2$-pyridine), can be ruled out by IR spectroscopy, since a strong resonance at 2024 cm^{-1} indicates the presence of a CO ligand. XRD analysis confirmed the CO ligand and allowed unambiguous identification of the product as [Ir(depe)(CO)(Ph_2PO)(dbuCO_2)] (**3**) (see Fig. 2b). In analogy to the RuBisCO mediated reaction, the model substrate $dbuP^-$ was C-carboxylated and split into two parts upon the reaction cascade. Formally, the Ph_2P^+ subunit of $dbuP^-$ was replaced by CO_2, leading to the novel dianionic ligand $[dbuCO_2]^{2-}$. The splitting of the substrate is accompanied by a two-electron oxidation of Ir and the reduction of a second CO_2 to CO, while the remaining oxygen atom recombines with the P-containing substrate fragment to the phosphinite $[Ph_2PO]^-$.

Given the nature of **3**, it is astonishing that its formation, which is achieved by the formation of 4 different new bonds (Ir-C, Ir-O, C-C, P-O) and the rupture of two others (C=O, P-C), is reversible. When a solution of **3** in C_6D_6 was placed under a N_2 atmosphere and heated to 70 °C, the $dbuP^-$ moiety reassembled and the formation of [Ir(depe)(dbuP)] (**2a**) was clearly detected by NMR methods (see Fig. 3).

DFT calculations on the reaction mechanism (see Fig.4 and ESI) reveal that the first CO_2 binds preferentially to the enamide moiety of the dbuP ligand leading to a C-carboxylated ligand $[dbuPCO_2]^-$ in intermediate $\mathbf{I_1}$. This species is predicted to be only 2.9 kcal/mol above the reactant state in free energy and the barrier of this C-C bond formation process is 15.7 kcal/mol. An alternative pathway corresponding to η^1_C-type coordination of CO_2 to the Ir center gives a significantly less stable species $\mathbf{I_1'}$

(ΔG = 10.5 kcal/mol; see Fig. 4b). Interestingly, the fixation of the second CO_2 is found to be thermodynamically favored with respect to both **I_1** and **I_1'** species, pointing to a high degree of cooperativity in the CO_2 uptake. The structure of intermediate **I_2** illustrates that unlike in **I_1**, the carboxylate group coordinates to Ir, and the Ir-C bond of the η^1_C-coordinated CO_2 is strengthened, when compared to that in **I_1'**. These structural changes indeed confirm the beneficial interplay between the two CO_2 molecules. The cooperative mechanism operates via the metal center, which acts simultaneously as a Lewis acid (interaction with the carboxylate) and a Lewis base (coordination of CO_2) (see ESI).

Due to Ir→CO_2 charge transfer, the O atoms of the coordinated CO_2 in **I_2** become more nucleophilic, which initiates a nucleophilic substitution at the neighboring Ph_2P group (S_N2@P mechanism).[12] In this transformation, the dianion $[dbuCO_2]^{2-}$ is the leaving group, which remains attached to the metal via Ir-N and Ir-O bonds (see **I_3**, Fig. 4c). The related transition state **TS_3** describes a concerted P-O bond formation and P-C bond cleavage event, and it represents the rate determining step of the reaction cascade. The overall barrier is thus predicted to be 21.9 kcal/mol, which is consistent with the observed reaction rate. The energetically high-lying intermediate **I_3** (Δ*G* = 16.5 kcal/mol) involves a strained four membered IrCOP ring, which can easily open via transition state **TS_4** to yield the CO ligand and the $[Ph_2PO]^-$ anion in product **3**.[13] The calculations indicate that the Ir-O bond formed with the carboxylate moiety is gradually strengthened upon the **I_2→I_3→3** transformation suggesting that in addition to cooperative CO_2 binding, this functionality also has an important role in the substrate cleavage phase of the reaction. The Gibbs free energy of the overall transformation **2a** + 2CO_2 → **3** is predicted to be close to zero (Δ*G* = -0.3 kcal/mol), in good agreement with the observed reversibility of the reaction.

The plausibility of the computationally revealed reaction mechanism was probed experimentally. Given that the transformation of **I_2** to **I_3** is the rate determining step, trapping of **I_2** at low temperature seemed feasible. Indeed, when a solution of **2a** in toluene-d_8 was exposed to a $^{13}CO_2$ atmosphere at 203 K, a single species [Ir(depe)(CO_2)(dbuPCO_2)], incorporating two equivalents of $^{13}CO_2$ was formed. In the ^{13}C NMR spectrum signals at δ_C = 171.1 and 142.0 ppm are indicative for the formed carboxylate moiety and the η^1_C-coordinated CO_2 ligand, respectively, as in **I_2**. Upon warm-up, transformation of this CO_2 complex to compound **3** sets in at ≈220 K without detectable intermediates.

It is noteworthy that the high metal basicity in **2a** plays a crucial role in the observed transformation. Lowering the basicity, either by the exchange of depe for a less basic phosphine (e.g. dppe) or by use of a less basic metal (e.g. Rh) renders the resulting complexes [Ir(dppe)(dbuP)] (**2b**) (see Fig. 2) and [Rh(depe)(dbuP)] (**4**) (see ESI) inactive. Just as **2a**, these two derivatives are still competent to bind two eq. of CO_2 at 203 K (see ESI), although with increasing difficulty (CO_2 affinity **2b**<**4**<**2a**), but a transformation into products of the type of **3** is not observed.

In conclusion, we developed a simple iridium system, which is capable to reversible activate and incorporate two equivalents of CO_2 by a cascade process that involves the formation and cleavage of 6 different bonds in a highly selective manner.

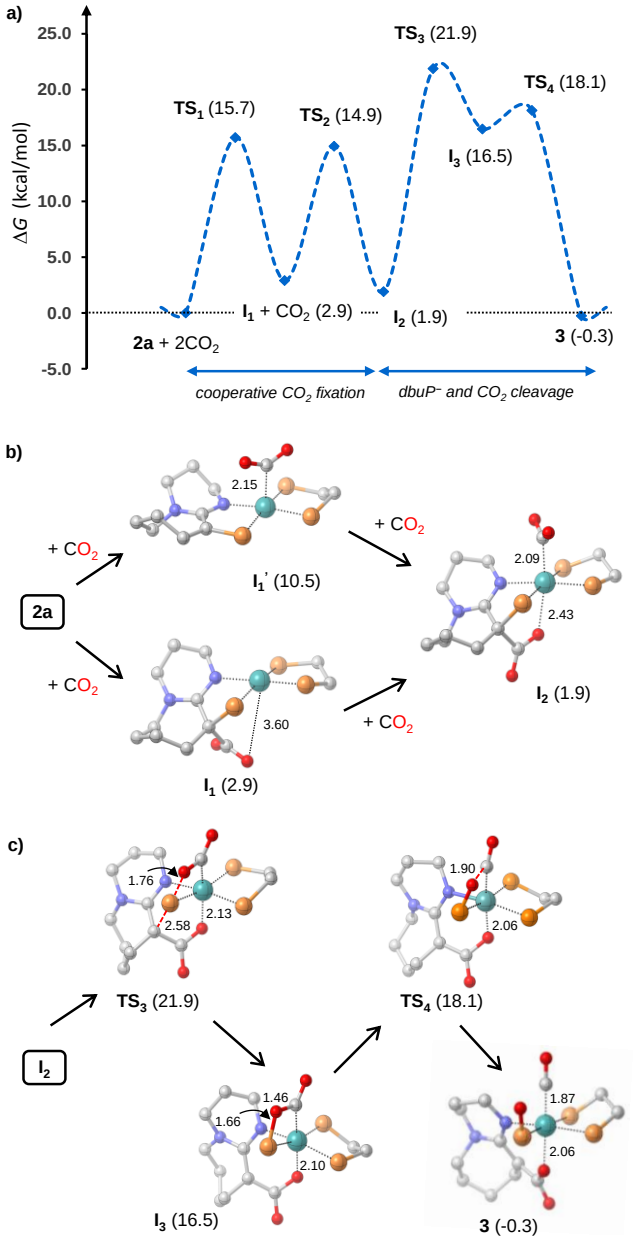

Figure 4. a) Free energy profile for the **2a** + 2CO_2 → **3** reaction. Computationally identified intermediates and transition states for b) cooperative CO_2 binding and c) dbuP$^-$ and CO_2 cleavage. Selected bond distances are given in Å. All H atoms, Ph groups of dbuP$^-$ and Et groups of depe are omitted for clarity. Bonds formed or cleaved in transition states are highlighted by red dashed lines. Relative stabilities (in kcal/mol; relative to **2a** + 2CO_2) are given in parentheses.

Cooperative CO_2 binding by two adjacent nucleophilic sites within the metal complex was exploited to generate a system that shows remarkable similarities to RuBisCO. Both systems share the requirement of two CO_2 molecules to be functional, a common substrate class as well as the C-carboxylation and splitting of the substrate, although by different mechanisms. These findings may launch new strategies for activation and transformation of unreactive substrates such as CO_2.

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Keywords: Iridium • carbon dioxide • RuBisCO • C-C bond formation • metal basicity

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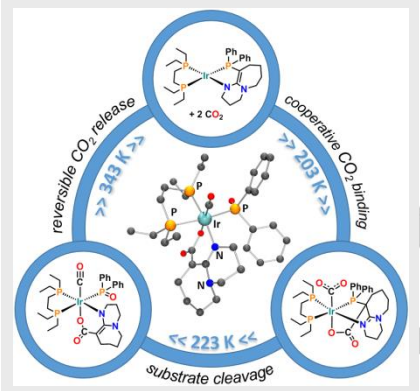

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