

Mixed valence $\{\text{Ni}^{2+}\text{Ni}^{1+}\}$ clusters as models of Acetyl Coenzyme A Synthase (ACS) Intermediates

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Introduction

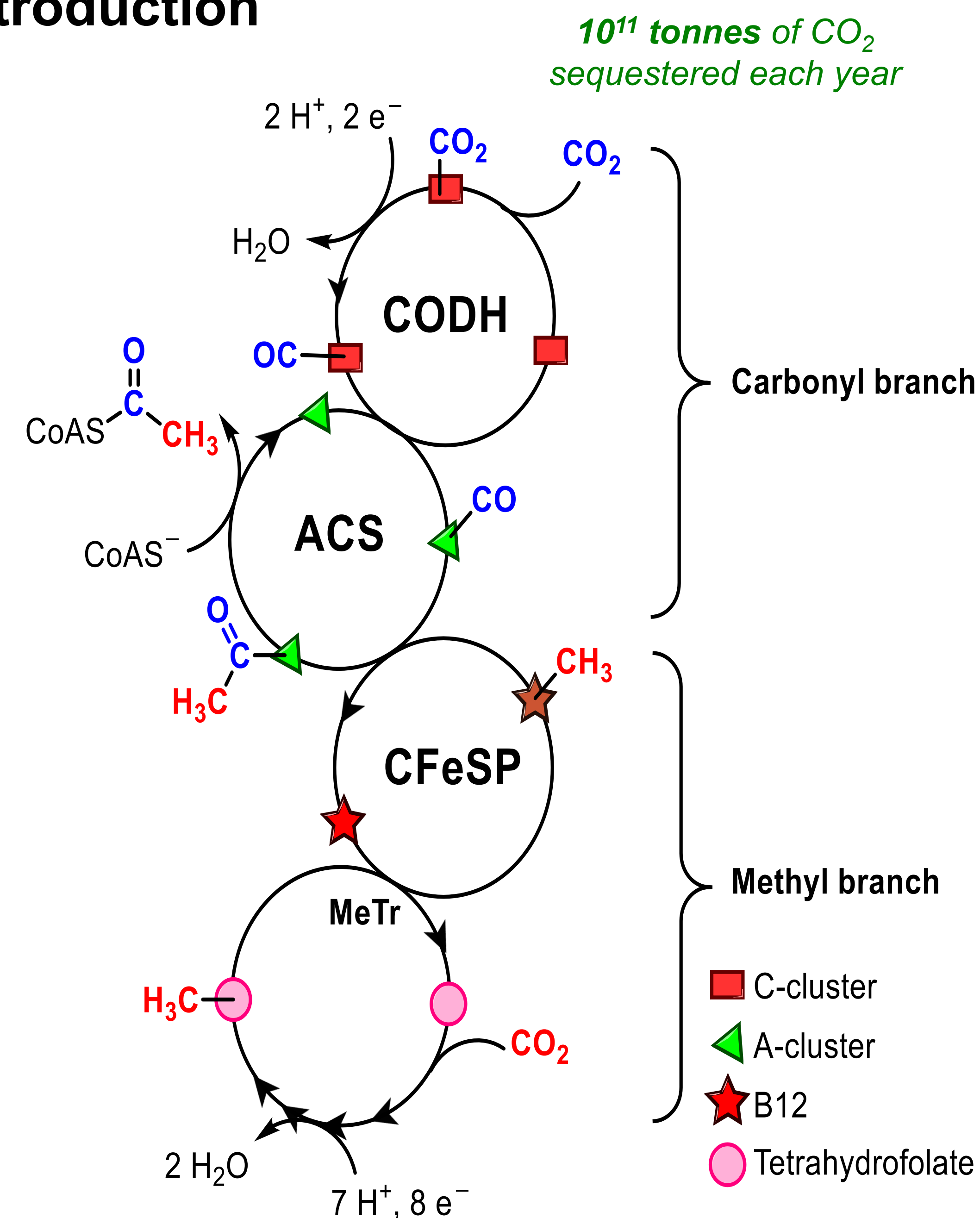


Fig. 1: Enzymatic overview of the WLP.¹

- The Wood-Ljungdahl Pathway (WLP) is one of six known CO₂ fixation pathways.
- Bacterial enzymes use WLP to convert CO₂ into acetyl-CoA (thioester used for energy storage and as a source of cellular carbon).
- At *acetyl coenzyme A synthase* (ACS), CO₂-derived CO and ⁺CH₃ fragments are combined to form an acetyl group.
- Formation of acetyl-CoA occurs at a multimetallic cofactor, **A-cluster** (Fig. 2)
- In the A-cluster, Ni atoms bridged by two μ₂-thiolates.
- Possesses an unusual Ni¹⁺ three-coordinate environment

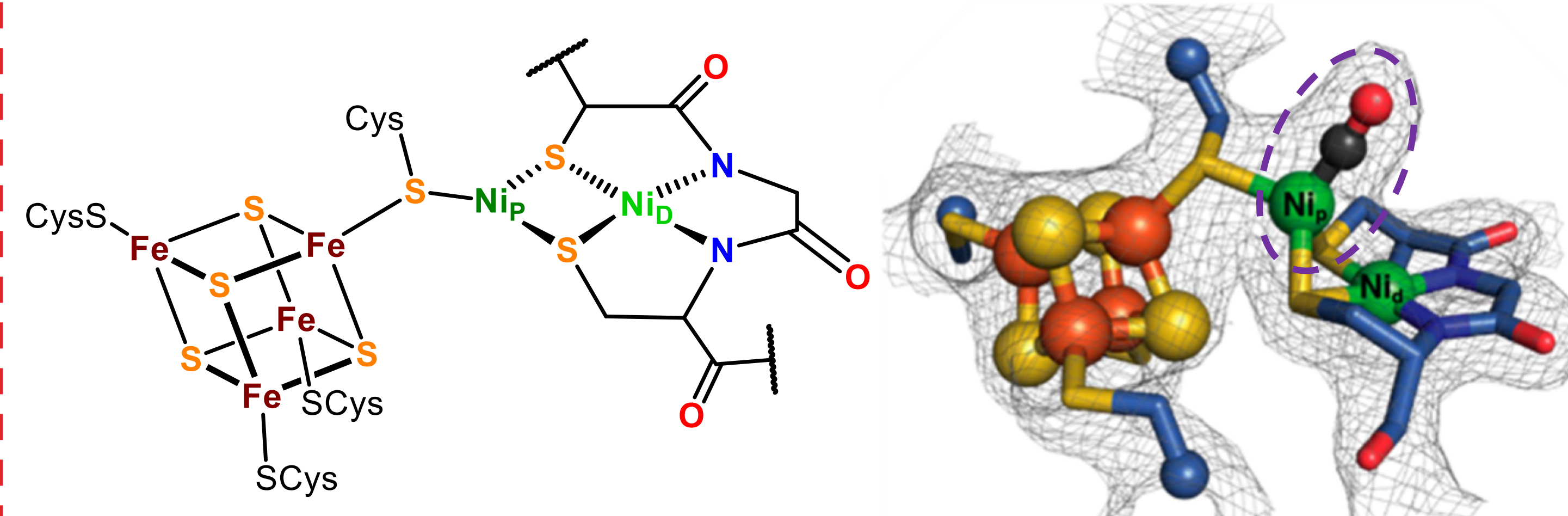


Fig. 2: Chemical structure (left) of the A-cluster and crystallographic structure² (right) of the CO-bound A-cluster. Ni_P = proximal, Ni_D = distal.

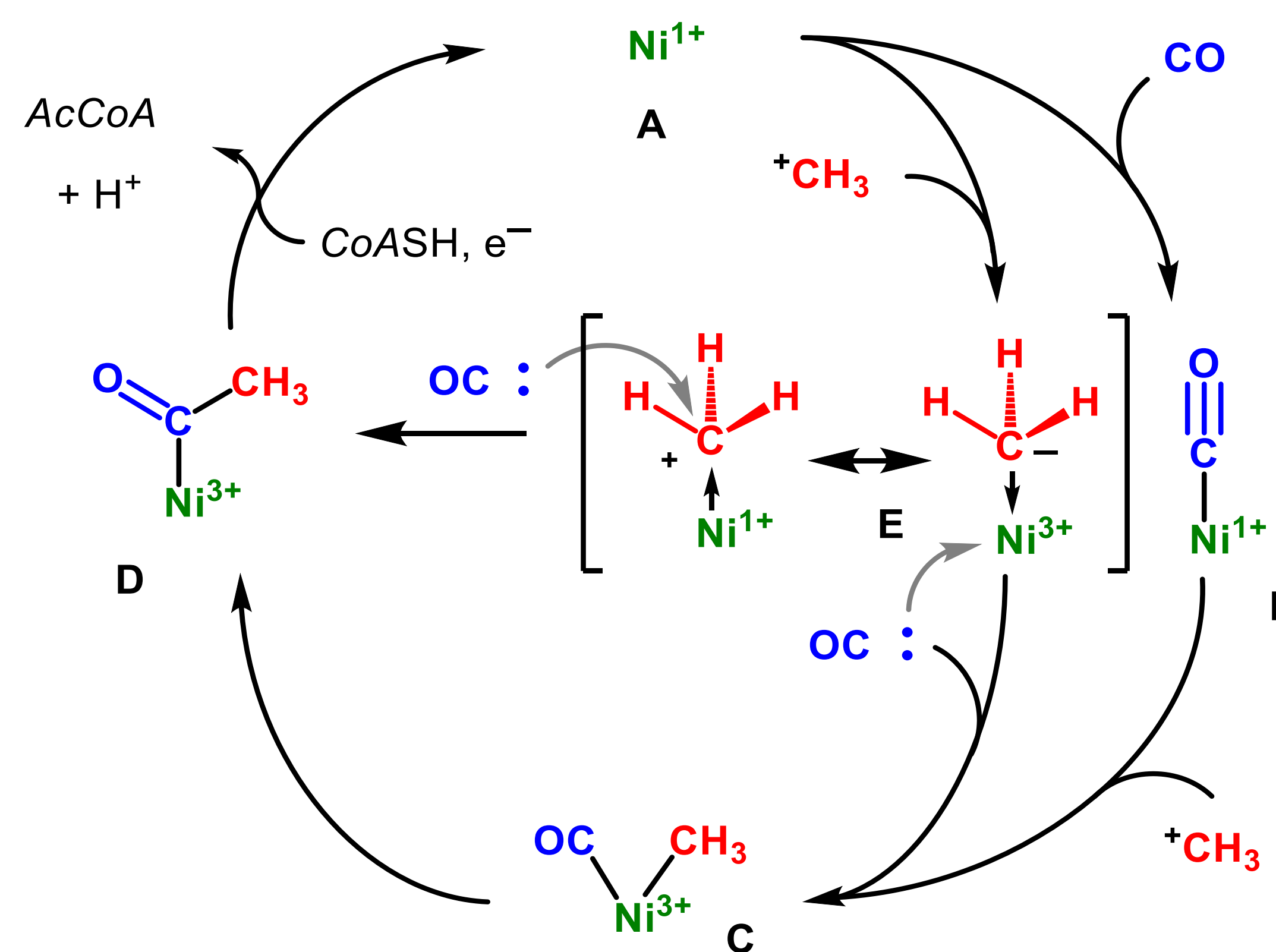
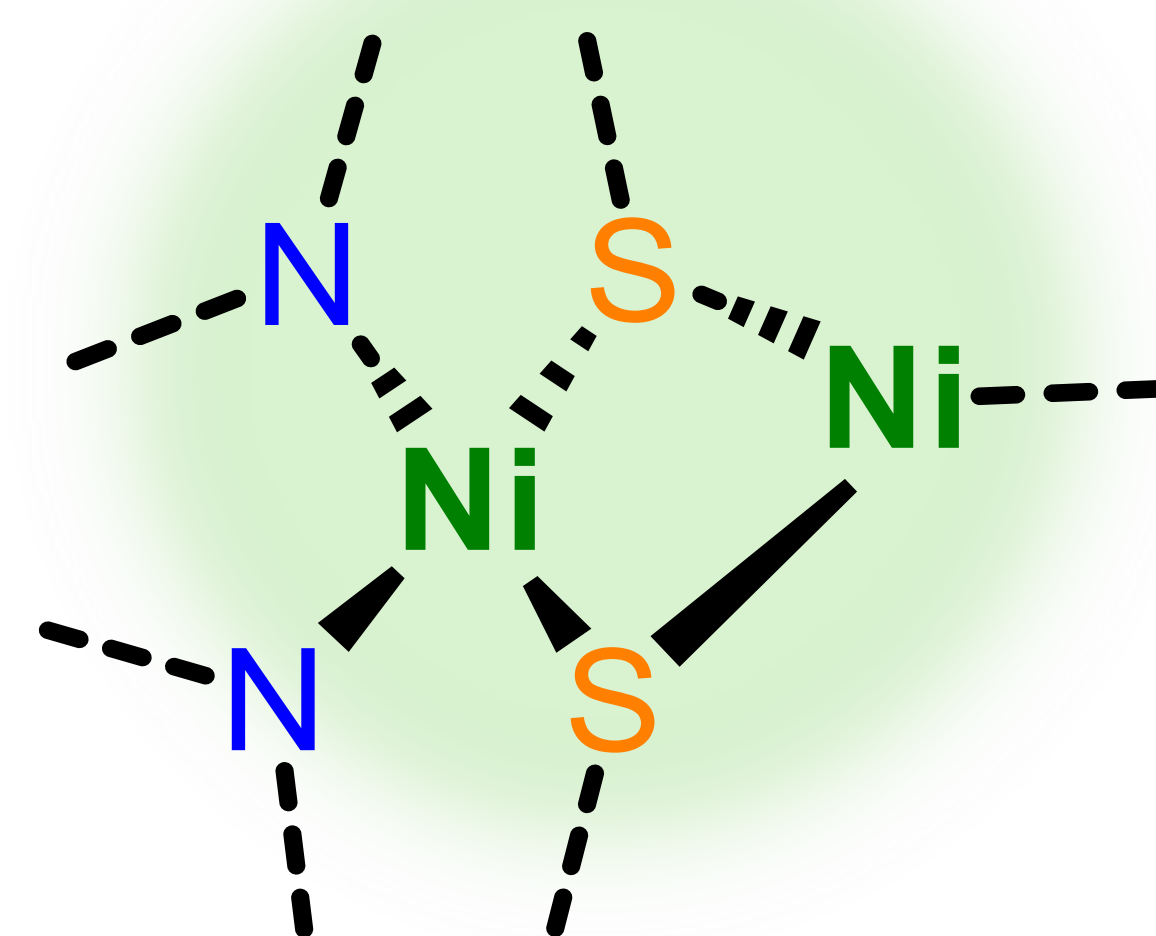


Fig. 3: Paramagnetic reactivity at Ni_P.

- Diamagnetic (Ni^{0/2+}) and paramagnetic (Ni^{1+/3+}) mechanisms have been proposed.
- ## Project Aims
- Synthesise **bimetallic model complexes** of hypothesized intermediates of the ACS paramagnetic mechanism.
 - Structurally characterise a model of the A cluster **without CO bound** (i.e. **A**, Fig. 3).
 - Probe structure/activity relationships.



Synthetic Approach

- N*-heterocyclic carbene (NHC) employed to stabilise bimetallic A-cluster mimic.
- Reaction of Ni²⁺ 'metalloligand' with Ni¹⁺ NHC synthon affords $\{\text{Ni}^{2+}\text{Ni}^{1+}\}$ bimetallic complex.

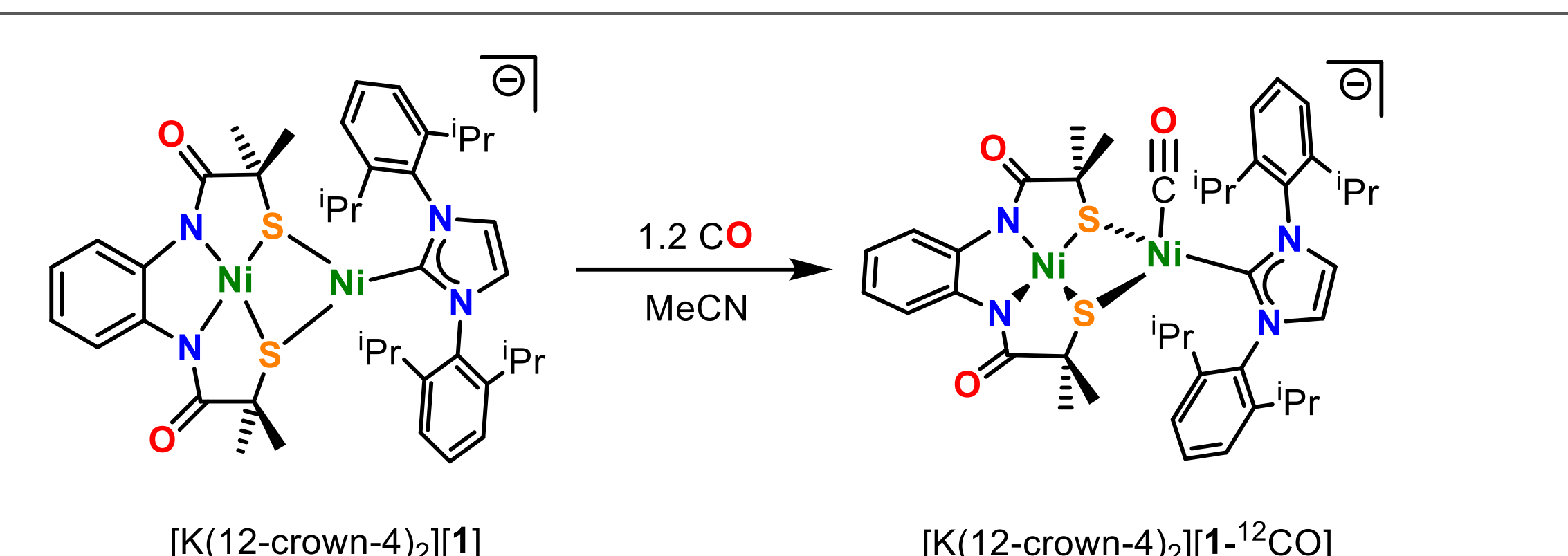
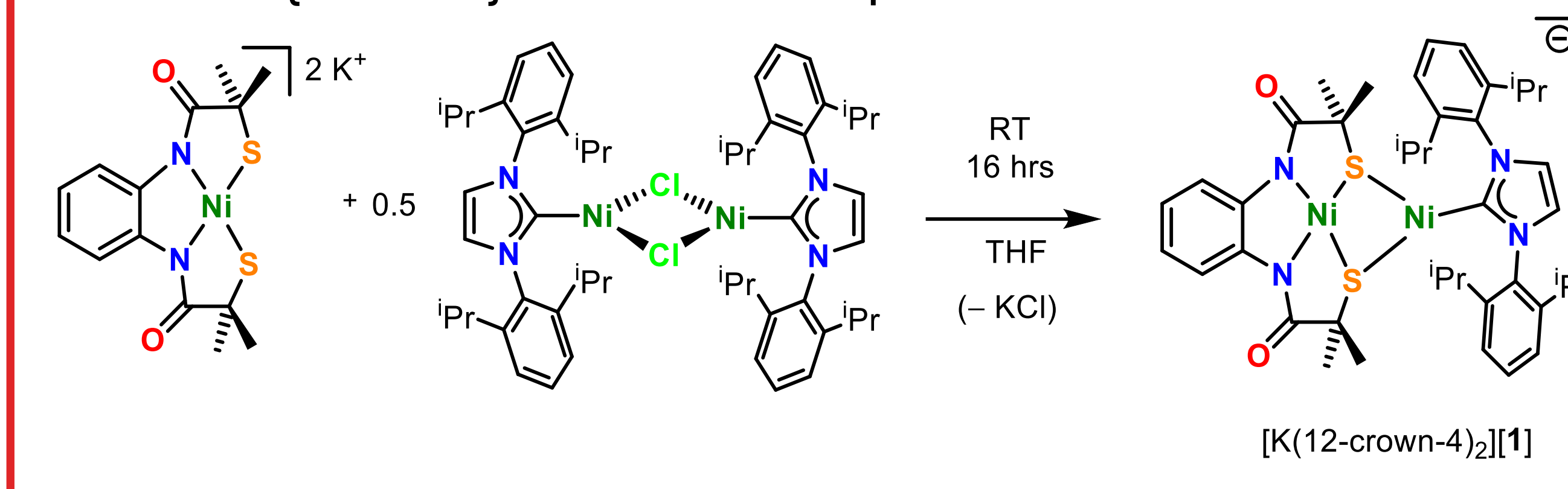


Fig. 4: Synthesis³ of [K(12-crown-4)₂][1] (top) and reactivity with CO to yield [K(12-crown-4)₂][1-¹²CO].

Crystallography

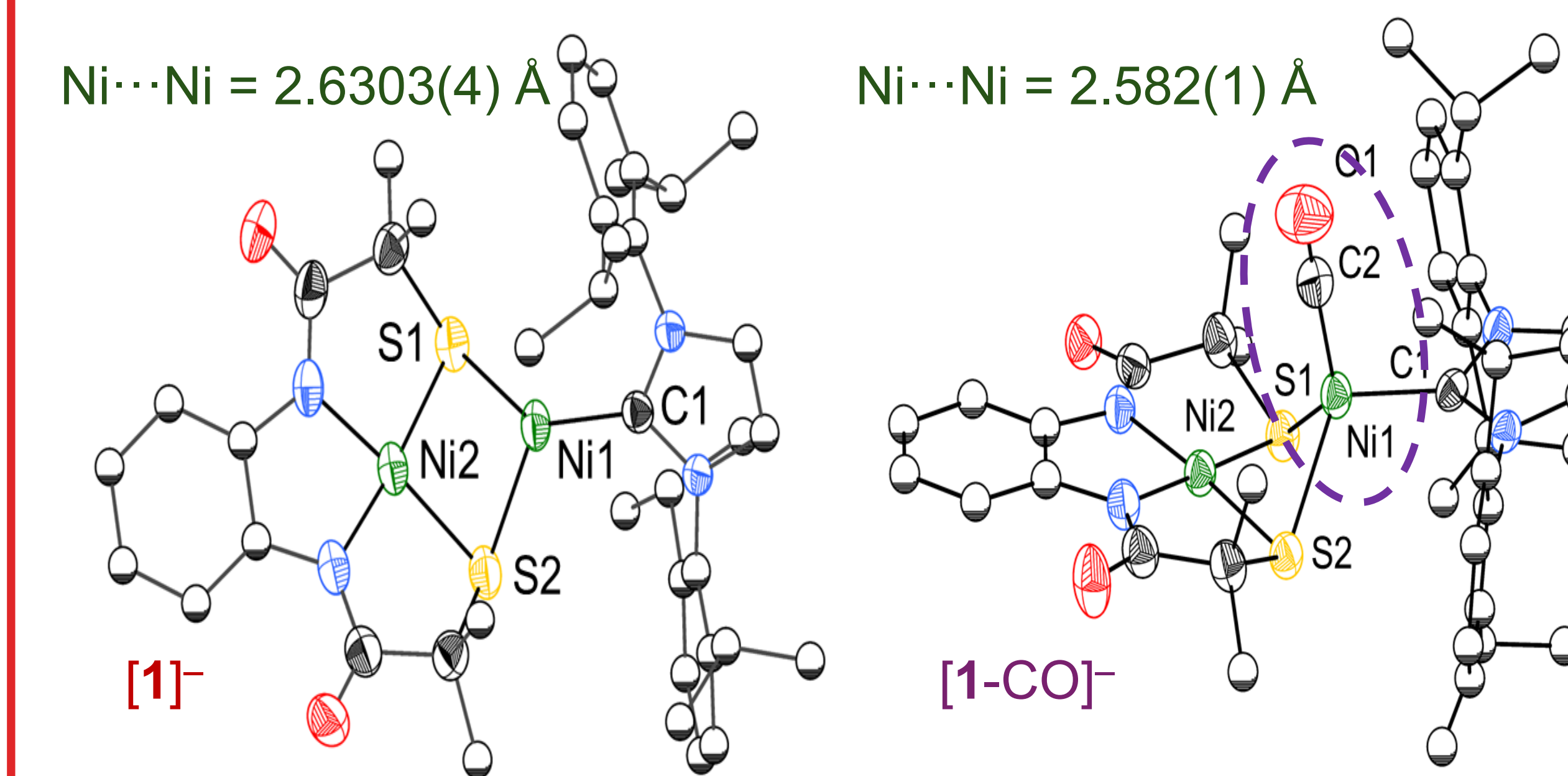
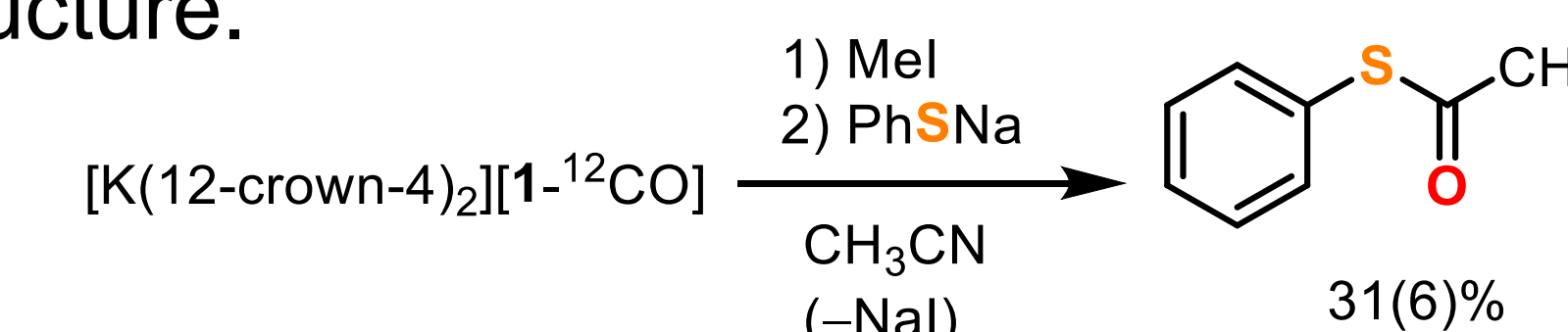


Fig. 5: Solid-state structure of [1]⁻ (left) and [1-CO]⁻ (right). Anisotropic displacement of ellipsoids depicted at 50% probability. K(12-crown-4) cation and H-atoms omitted for clarity.

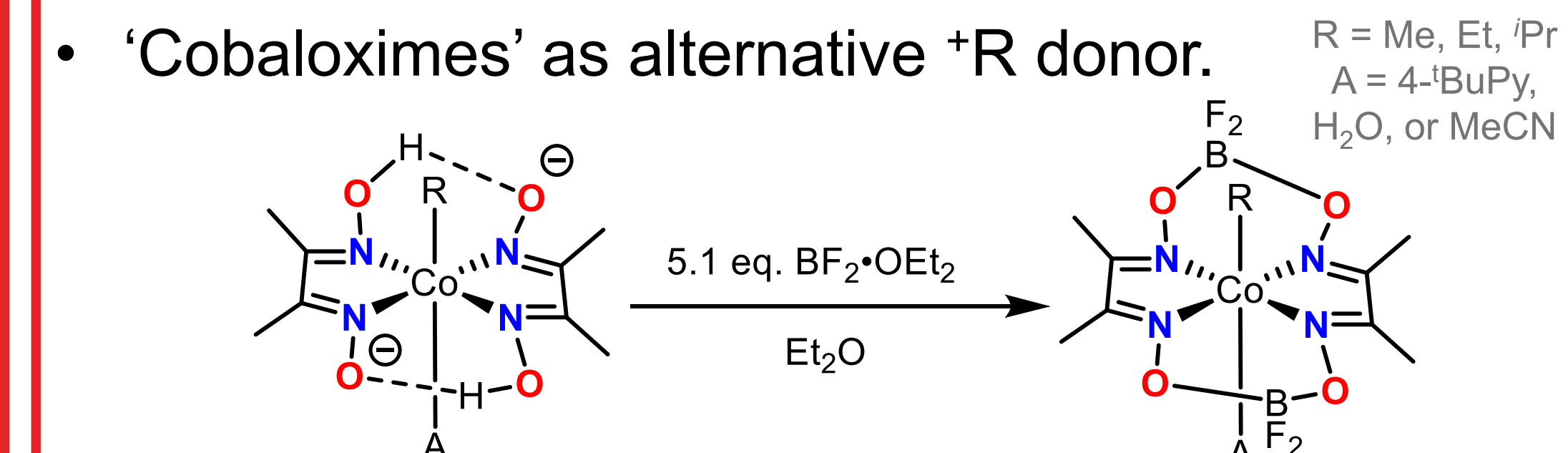
- [1]⁻ represents first structurally characterised model of **A** (Fig. 3).

Generation of thioesters

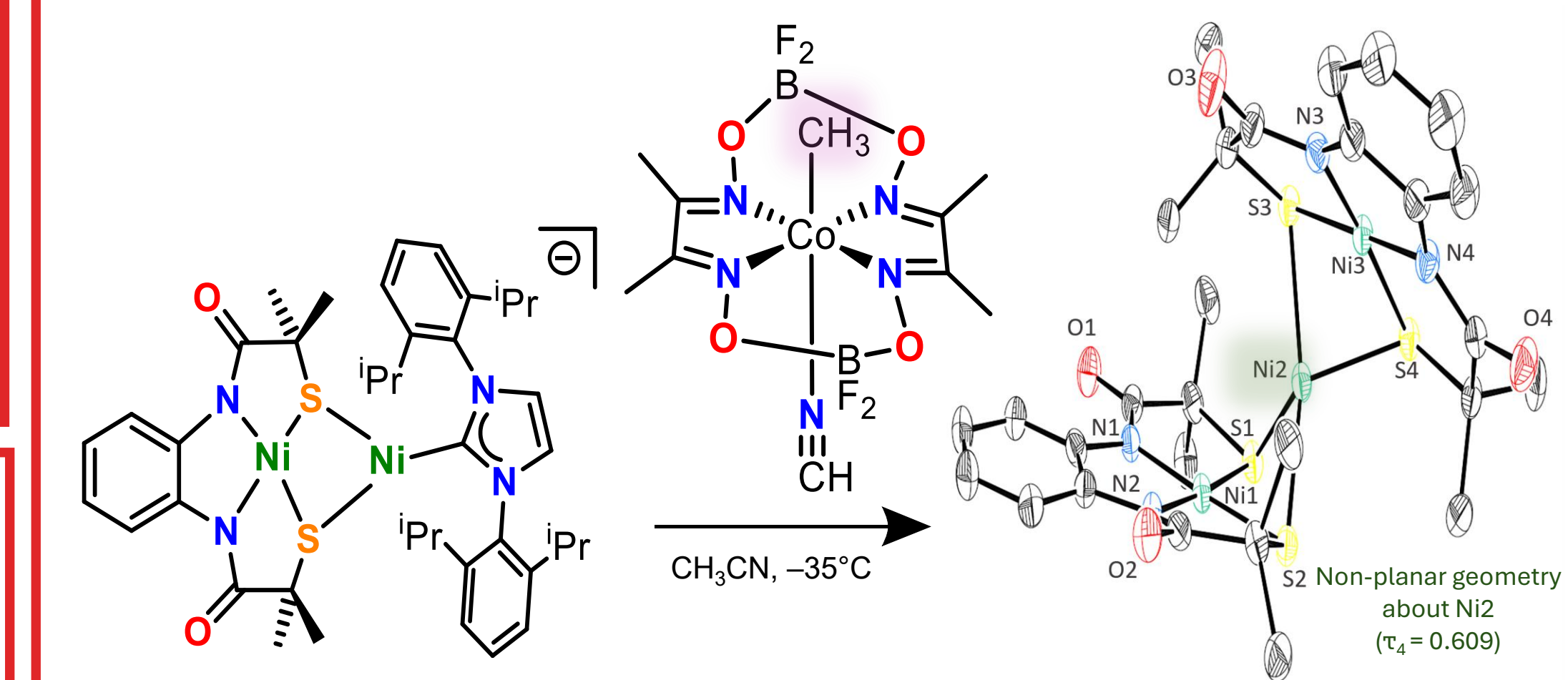
- Treatment of [1-¹²CO]⁻ with ⁺CH₃ followed by RS⁻ in MeCN afforded the corresponding thioester (Scheme 1).
- [1-CO]⁻ mimics **reactivity** of A-cluster as well as structure.



Scheme 1: Formation of thioester from [1-¹²CO]⁻.



- 'Cobaloximes' as alternative ⁺R donor.



Future Work

- Change NHC identity to probe electronics of Ni¹⁺ site.
- Substitute Ni²⁺ for isoelectronic metal centres to probe effect of second metal on reactivity at Ni¹⁺.

References

- M. Can, F. A. Armstrong, S. W. Ragsdale, *Chem. Rev.* **2014**, *114*, 4149.
- S. E. Cohen, M. Can, E. C. Wittenborn, R. A. Hendrickson, S. W. Ragsdale, C. L. Drennan, *ACS Catalysis*, **2020**, *10*, 9741.
- D. W. N. Wilson, B. C. Thompson, A. Collauto, R. X. Hooper, C. E. Knapp, M. M. Roessler, R. A. Musgrave, *J. Am. Chem. Soc.* **2024**, *146*, 21034.