A molecular cage of nickel(II) and copper(I): a [{Ni(L)$_2$}$_2$(CuI)$_6$] cluster resembling the active site of nickel-containing enzymes†

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A new mononuclear low-spin nickel(II) dithiolato complex, [NiL$_2$] (1), reacts with copper iodide to form the hetero-octanuclear cluster [{Ni(L)$_2$}$_2$(CuI)$_6$] (2) with four trigonal-planar CuI$_2$S and two tetrahedral CuI$_2$S$_2$ sites; anagostic interactions between the nickel(II) ions and aromatic protons have been demonstrated by variable-temperature NMR studies to pertain in solution.

Nickel thiolato complexes, including (hetero-)multinuclear [NiFe], [NiCu], [NiZn] and [NiNi] units, are of interest in the context of their rich redox chemistry[1,2] and structural diversity in supramolecular architectures.[3,4] Furthermore, they are important as synthetic models[1,3,5–8] for environmentally and industrially significant enzymes like hydrogenases, superoxide dismutases and CODH/ACS. It is noteworthy that the bifunctional enzyme CODH/ACS has an important role in the global carbon cycle as the C-cluster, an Ni–Fe–S centre, of this enzyme reduces carbon dioxide to carbon monoxide and the A-cluster assembles acetyl-CoA from a methyl group (Chart 1), coenzyme-A and the CO generated by the C-cluster.[9] The A-cluster is a complex metallocofactor, containing an Fe$_4$S$_4$ group connected by cysteine bridging to a dinuclear [M$_p$Ni$_d$] site, where the proximal metal M$_p$ is predominantly Cu in the as-isolated enzyme from native *Moorella thermoacetica*.[10] However, [NiNi] and [ZnNi] forms are also known to have been isolated and well studied.[11–14] The distal nickel Ni$_d$ is in a square-planar (NiN$_2$S$_2$) geometry derived from two backbone carboxamido nitrogens and two Cys-S thiolates. The Ni$_d$ is bridged through the two Cys-S donors to the proximal metal M$_p$ that is in a tetrahedral coordination environment. A fourth nonprotein ligand is bound to the M$_p$ in addition to the Cys-S bridging to the Fe$_4$S$_4$ to complete the coordination sphere. The focus of our attention is to study the chemistry involving the synthesis and reactivity of nickel thiolate complexes in relation with the

structure and function of protein active sites, as described above.[1,3,5–8]

Herein, we report the synthesis of a new bidentate S$_2$ thioether-thiolate ligand (L),† the mononuclear low-spin nickel complex (1)† and the hetero-octanuclear nickel(II) copper(I) cluster complex [{Ni(L)$_2$}$_2$(CuI)$_6$] (2),‡ which contains two NiS$_4$ units, four trigonal-planar CuI$_2$S and two tetrahedral CuI$_2$S$_2$ sites.

The reaction of Ni(acac)$_2$ with two equivalents of the thiouronium chloride salt of the ligand, in the presence of two equivalents of tetramethylammonium hydroxide, led to an immediate color change to deep brown and the new low-spin square-planar complex [Ni(L)$_2$] (1) was isolated as flocculent reddish-brown crystals in high yield (Scheme 1). Equimolar solutions of Ni(L)$_2$ (1) in dichloromethane and copper(I) iodide in acetonitrile were mixed under argon and stirred for an hour to yield a dark brown precipitate. A saturated solution of this product in absolute ethanol was left for slow evaporation under argon atmosphere and dark brown crystals were formed over several days. The molecular structure of 2, which has been determined by single-crystal X-ray diffraction, shows a spectacular cage structure formed by the thiolate sulfurs and copper iodide moieties.

The asymmetric unit of 2 contains one crystallographically independent ordered molecule (Fig. 1), and no solvent molecules are found in the crystal lattice. The two Ni(II) centers are in slightly distorted square-planar environments with two thiolate donors and two thioether sulfurs in enforced *cis* positions. The Ni–S$_{thiolate}$ distances [2.1641(14)–2.1788(14) Å] are slightly shorter than the Ni–S$_{thioether}$ distances [2.1856(15)–2.2028(16) Å], as expected. The nickel centers have a slight tetrahedral distortion with a dihedral angle of 3.58(8)° for Ni1 (between the triangular planes S6Ni1S9 and S16Ni1S19) and 9.13(8)° for Ni1A (between the planes S6ANi1S9A and S16ANi1S19A). The six copper iodide moieties are forming altogether a twelve-membered Cu$_6$I$_6$ puckered crown (Fig. 2) in which the six iodides are bridged *via* the copper ions in μ_2 fashion to form this crown. The two square-planar NiS$_4$ units are capping this crown from both sides utilizing their thiolate sulfurs to form 2; the dihedral

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† Electronic supplementary information (ESI) available: Experimental details on the synthesis of the ligand and [Ni(L)$_2$] (1), crystallographic details of 2 and the NMR (HSQC) spectrum. CCDC 715787. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/b900423h
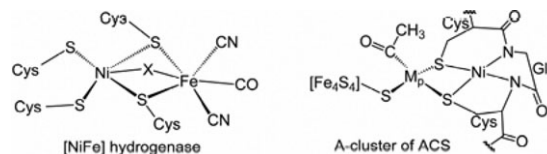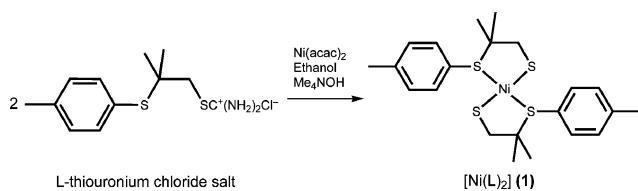
Chart 1 Active site structures of nickel-containing enzymes.
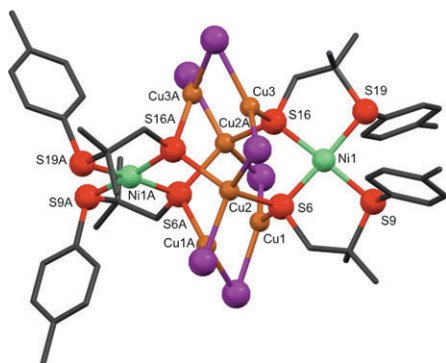
Scheme 1 Synthesis of complex 1.

Fig. 1 Perspective view of [{Ni(L)$_2$}$_2$(CuI)$_6$] (2). Ni, green; Cu, brown; S, red; I, violet; C, gray. Hydrogens are omitted for clarity. Atoms that are labeled with and without 'A' are crystallographically independent. Selected distances (Å) and angles (°): Ni1···Ni1A, 6.6421(9); Ni···Cu, 3.6–3.9; Ni–S, 2.1641(14)–2.2028(16); S6–Ni1–S9, 92.17(6); S6–Ni1–S16, 85.82(5); S6–Ni1–S19, 176.89 (6); S9–Ni1–S16, 176.47(6); S9–Ni1–S19, 90.04(6); S16–Ni1–S19, 92.08(6).
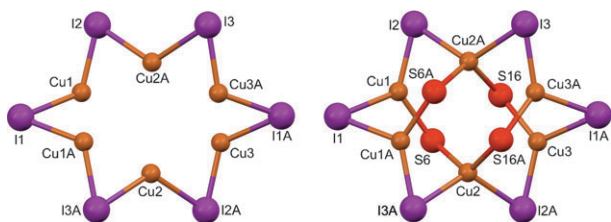

Fig. 2 Perspective views of the Cu$_6$I$_6$ puckered-crown (left) and Cu$_6$I$_6$S$_4$ cage (right) in [{Ni(L)$_2$}$_2$(CuI)$_6$] (2). Selected bond lengths (Å) and angles (°): Cu1···Cu1A, 2.6032(10); Cu2···Cu2A, 4.0309(10); Cu1···Cu3, 5.3644(2); Cu1···Cu2, 3.9844(9); Cu(tetrahedral)–S, 2.4059(14)–2.4509(15); Cu(trigonal-planar)–S, 2.2780(15)–2.2925(14); Cu1–I1, 2.5955(8); Cu1–I2, 2.5271(8); Cu2–I2A, 2.6337(7); Cu2–I3A, 2.6296(7); S6–Cu1–I1, 109.11(4); S6–Cu1–I2, 126.61(4); I1–Cu1–I2, 124.21(3); S6–Cu2–I3A, 98.61(4); S6–Cu2–I2A, 110.40(4); I3A–Cu2–S16A, 107.65(4); I2A–Cu2–S16A, 99.90(4); S6–Cu2–S16A, 122.29(5); I2A–Cu2–I3A, 119.38(3).

angle defined by these two S$_4$ planes is 72.10(5)°. Each thiolate sulfur is bound to two copper(I) ions, of which one is in a trigonal-planar geometry and the other possesses tetrahedral geometry. The tetrahedral copper ions are shared between the two NiS$_4$ units by direct S–Cu–S bridging, while the trigonal-planar copper ions are shared through a S–Cu–I–Cu–S bridge. The four thiolate sulfurs and the six copper(I) iodide units together form a cage structure in the middle of the two NiS$_4$ units (Fig. 2).

The trigonal-planar copper ions, Cu1, Cu1A, Cu3 and Cu3A, are found in an I$_2$S coordination sphere of which one of the two iodide ions is bridged to a trigonal-planar copper ion, while the other iodide is bridged to a tetrahedral copper
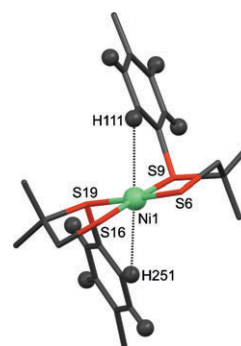

Fig. 3 Perspective view of one [Ni(L)$_2$] part of [{Ni(L)$_2$}$_2$(CuI)$_6$] 2 with the atomic labeling of selected atoms. The nickel-to-hydrogen interactions are shown; only the hydrogens present in the 4-methyl-phenyl rings are shown for clarity. Ni1···H111, 2.739; Ni1···H251, 2.781; Ni1A···H152, 2.696; Ni1A···H212, 2.626 Å.

ion. The bond distances of iodide to copper vary due to this difference in bridging; the angles in the trigonal-planar CuI$_2$S moieties are not strictly 120°. Likewise, the angles in the tetrahedral CuI$_2$S$_2$ moieties also deviate from the ideal angle of 109.5°, and range from 98.61(4)° to 122.29(5)°.

An interesting interaction between the nickel(II) ion and the *ortho*-protons of the phenyl rings is observed, with distances of about 2.7 Å in both NiS$_4$ units of 2 (Fig. 3). Considering these interactions as bonding, the coordination geometry of the nickel ion could be described as pseudo-octahedral, in an H$_2$N$_2$S$_2$ chromophore, in which two *ortho*-protons occupy the axial sites of the octahedron.

To investigate whether the structure of the [{Ni(L)$_2$}$_2$(CuI)$_6$] (2) is retained in solution, ^{1}H NMR spectra of the complex have been recorded in CD$_2$Cl$_2$ solution at different temperatures ranging from 183 to 303 K (Fig. 4). Even though there are four crystallographically distinct ligands in the complex, the ^{1}H NMR spectrum at room temperature shows only a single set of signals, suggesting that the four ligands are

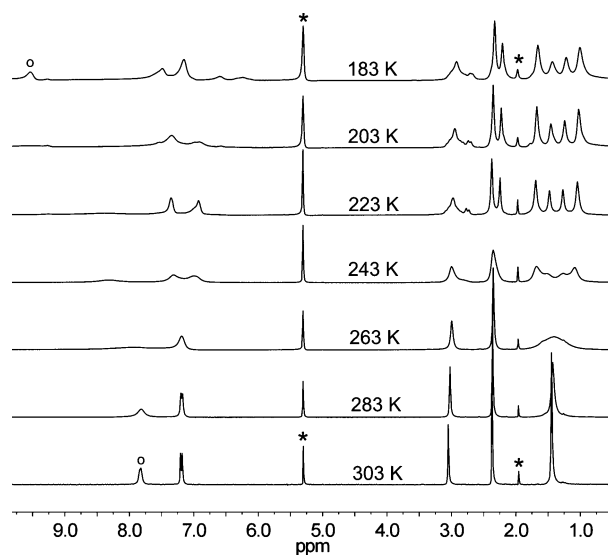Fig. 4 ^{1}H NMR of [{Ni(L)$_2$}$_2$(CuI)$_6$] (2) in CD$_2$Cl$_2$ recorded at different temperatures ranging between 183 and 303 K. ★, signals from CD$_2$Cl$_2$ (5.32 ppm) and acetone (2 ppm); ○, signals from the *ortho*-protons of the phenyl ring.

equivalent in solution. Interestingly, upon cooling the sample to 263 K the signals start to broaden and eventually split into multiple sharp signals at 183 K. The fluxional axial and equatorial exchange of the dimethyl groups is slow or inhibited at low temperature; the singlet of the dimethyl protons (at 1.4 ppm) consequently splits into four sharp signals. Furthermore, the two aromatic resonances (at 7.1 and 7.8 ppm) are split in a number of resonances with different intensities; the protons involved in an interaction with the nickel ions are observed at δ 9.5 ppm upon cooling to 183 K. The downfield shift of these protons in the NMR spectrum, and the fact that they are pointing in the direction of the occupied d_{z^2} orbital of the nickel(II) ions (Fig. 3) at a distance of about 2.7 Å on average in the crystal structure, suggests that these interactions should be considered as anagostic or hydrogen bonding.[15–17]

The cyclic voltammogram of **2** in a dichloromethane solution (Fig. S4, ESI†) shows a number of irreversible oxidation processes (−0.273 V, −0.180 V, −0.076 V *vs.* Ag/AgCl) and a single irreversible reduction process (−0.914 V), which are difficult to assign unequivocally due to the presence of the large number of redox non-innocent partners available in the multinuclear structure of **2**.

The presence of the 4-methylphenyl ring bound to the thioether sulfur paves the way to exhibit the attraction between the *ortho*-protons of the phenyl ring and the low-spin Ni(II), as identified in the crystal structure and NMR spectroscopy (Fig. 3 and 4). To the best of our knowledge, [{Ni(L)$_2$}$_2$(CuI)$_6$] is the first compound with a NiS$_4$ coordination displaying the aforesaid nickel to proton anagostic interactions.

The tetrahedrally distorted NiS$_4$ coordination spheres of Ni1 and Ni1A in [{Ni(L)$_2$}$_2$(CuI)$_6$] (**2**) resemble the nickel centre of the "EPR silent active form" (Ni-SI$_a$) of [NiFe] hydrogenase with an Ni^{II}Fe^{II} electronic configuration that is the starting point of the catalytic cycle of the enzymatic action; protonation of this form generates the Ni-SI$_b$ form which then turns into Ni-R state upon hydrogenation.[18–21] Development of model complexes with this kind of Ni···H interaction may help to better understand the mechanistic insights of the [NiFe] hydrogenase and to obtain improved structural and functional mimics. Furthermore, the Ni–μ_3–S–Cu motifs forming the cage in **2** resemble the A-cluster of the CODH/ACS with a low-spin square-planar nickel (Ni$_d$) and bridging μ_3-thiolates connecting the tetrahedral copper (M$_p$).

In summary, a novel molecular cage of hetero-octanuclear nickel(II) copper(I) cluster, [{Ni(L)$_2$}$_2$(CuI)$_6$] (**2**), has been isolated in good yield by the reaction of the low-spin square-planar NiS$_4$ complex (**1**) with CuI and has been characterized using single-crystal X-ray diffraction, NMR and electrochemistry techniques. The anagostic interactions between the nickel and aromatic *ortho*-protons have been demonstrated by the variable-temperature NMR studies also to pertain in solution. Reactivity studies of Ni(L)$_2$ (**1**) and [{Ni(L)$_2$}$_2$(CuI)$_6$] (**2**) with small molecules and iron complexes are in progress to obtain better models for the nickel-containing enzymes.

Notes and references

‡ ***Synthesis of [Ni(L)$_2$(CuI)$_6$]*** (**2**). A solution of CuI (191 mg, 1 mmol) in 10 ml acetonitrile was added to a solution of [Ni(L)$_2$] (483 mg, 1 mmol) in 10 ml chloroform and stirred for an hour. After evaporation of the solvent, the product was recrystallized by the slow evaporation of an ethanolic solution in an argon atmosphere. Dark-brown crystals suitable for X-ray diffraction were obtained over a few days. Complex **2** was reproduced in bulk by the reaction between one equivalent of complex **1** and three equivalents of CuI in aceto-nitrile as a brown powder (87%). ^{1}H NMR δ_H [300.13 MHz, CD$_2$Cl$_2$, 298 K]) 7.84 (bs, 8H, phenyl-*ortho*-*H*), 7.22 (d, 8H, phenyl-*meta*-*H*), 3.06 (s, 8H, –C*H$_2$*–S–), 2.38 (s, 12H, C*H$_3$*–Ph), 1.46 (s, 24H, –C(C*H$_3$*)$_2$–); ^{13}C NMR δ_C [75.47 MHz, CD$_2$Cl$_2$, 298 K] 143.52 (Ph–C4), 136.54 (Ph–C3), 131.18 (Ph–C2), 122.75 (Ph–C1), 64.35 (–*C*(CH$_3$)$_2$–), 49.27 (–*C*H$_2$–), 27.69 (–C(*C*H$_3$)$_2$–), 21.94 (*C*H$_3$–Ph). Elemental analysis (%), calc. for C$_{44}$H$_{60}$Cu$_6$I$_6$Ni$_2$S$_8$·3CHCl$_3$, C 22.91, H 2.58, S 10.41, found, C 22.67, H 2.54, S 10.28. ***Crystallographic data for complex* 2**. C$_{44}$H$_{60}$Cu$_6$I$_6$Ni$_2$S$_8$, F_w = 2105.46, triclinic, $P\bar{1}$ (no. 2), a = 11.6566(5), b = 14.1559(4), c = 19.9857(7) Å, α = 86.088(1)°, β = 84.143(1)°, γ = 70.505(2)°, V = 3090.5(2) Å^3, Z = 2. 67 305 reflections were measured up to a resolution of (sin θ/λ)$_{max}$ = 0.62 Å^{-1}. 12 170 reflections were unique (R_{int} = 0.063), of which 8494 were observed [$I > 2\sigma(I)$]. 607 parameters were refined. R_1/wR_2 [$I > 2\sigma(I)$]: 0.0361/0.0553. R_1/wR_2 [all refl.]: 0.0742/0.0634. S = 1.022. Residual electron density between −0.90 and 0.98 eÅ^{-3}.

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