A bridging coordination mode of urea and carbamate at a dinuclear nickel(ii) centre

Franc Meyer*† and Hans Pritzkow

Anorganisch-Chemisches Institut der Universität Heidelberg, Im Neuenheimer Feld 270, D-69120 Heidelberg, Germany

Starting from an active O_2H_3-bridged bimetallic complex, a bridging coordination mode of both urea and carbamate—the substrate and its first hydrolytic product in urease activity—at a dinickel(ii) centre relevant to the active site of the metalloenzyme has been characterised structurally.

The nickel containing enzyme urease—which is present in a variety of plants, fungi and bacterial species—catalyses the hydrolysis of urea to form ammonia and carbamate, with the latter decomposing further to yield carbonic acid and another molecule of ammonia.[1] The X-ray crystal structure[2] of the microbial urease from *Klebsiella aerogenes* revealed two nickel ions 3.5 Å apart within the dinuclear active site and corroborated previously suggested models for its hydrolytic activity.[3] It is assumed that urea is activated by coordination to one nickel(ii) ion in conjunction with extensive hydrogen bonding within the active site pocket of the protein and is subsequently attacked by a nucleophilic hydroxide bound to the opposite nickel centre.[3,4] However, the exact binding mode of the substrate as well as details of the operative mechanism are not yet unambiguously resolved, however. Considerable effort has therefore been devoted to the search of model complexes featuring a dinickel(ii) core with accessible co-ordination sites at the metal centres[5–8] in order to elucidate the possible binding modes of urea at such urease-like systems and finally mimic the enzymatic reactivity. Nevertheless, only in a few cases has coordination of urea[7] (generally O-coordination) or even its hydrolytic cleavage[7b] hitherto been observed.

We recently described a class of pyrazolate-based dinuclear complexes, where appropriate chelating side arms attached to the heterocycle enforce metal–metal separations large enough to prevent small monoatomic units like HO⁻ from spanning both metal centres, thus favouring the formation of intramolecular O_2H_3 secondary bridges like in **1**.[9,10] For a related FHO(H)-bridged dicobalt(ii) complex experimental evidence suggested that H_2O can reversibly be extruded from these moieties.[9b] Such a process in the case of **1** would generate an open coordination site for potential substrate binding adjacent to a hydroxide bound to the proximate second nickel ion, thus explaining the hydrolytic activity of **1** towards, for example, nitriles.[11] The similarity of this assumption with the proposed mechanism of urease activity prompted us to investigate the reaction of **1** with urea, especially because urea has been found to exhibit a greater affinity than water for binding to certain metal ions.[12]

Treatment of an acetone solution of **1** with urea or *N,N*-bis(trimethylsilyl)urea (Scheme 1) caused a slight change in its UV–VIS spectrum, and the resulting green complex **2**(ClO₄)₂‡ could be isolated from the reaction mixture. Single crystals were obtained by layering an acetone solution of the product with light petroleum. A crystallographic study (Fig. 1; two independent molecular entities with similar molecular dimensions were found in the unit cell)§ revealed that a tetraatomic trigonal planar moiety is situated within the coordination pocket created by the basic bimetallic framework, this being identified as a N,O-bridging deprotonated urea on the basis of the combined analytical data.‡ In particular, FAB mass spectrometry showed signals for LNi₂[NH(O)CNH₂](ClO₄)⁺ and LNi₂[N-

H(O)CNH₂]⁺ with the expected isotopic distribution pattern as the most intense peaks. The protons attached to the terminal nitrogen atoms N(9) were located as hydrogen bridges to oxygen atoms of the perchlorate counter anions [d(N···O) in the range 3.08–3.21 Å], while the Ni-bound O and N atoms of the bridging urea could not be distinguished crystallographically and are presumably disordered over both positions.
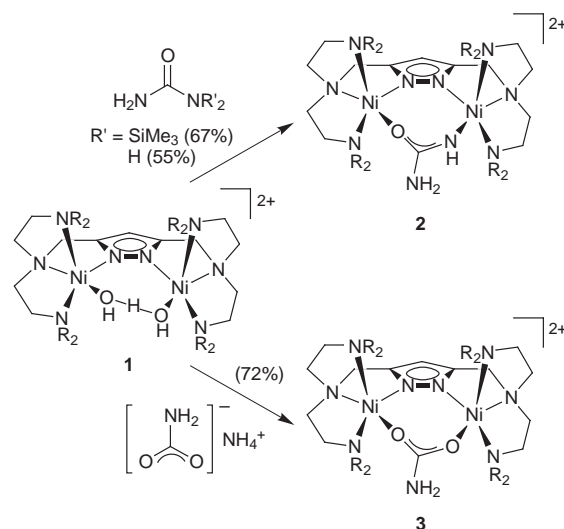
Scheme 1 Syntheses of the complexes. Yields are based on **1** and refer to isolated crystalline product.
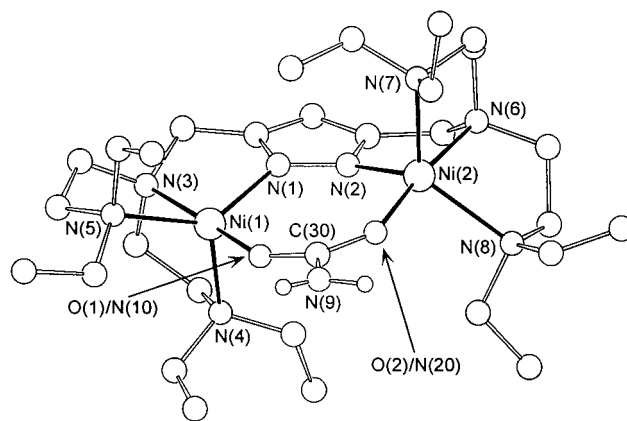

Fig. 1 Molecular structure of **2**. Selected atom distances (Å) and bond angles (°); values for the second independent molecule in square brackets: Ni(1)–O(1)/N(10) 1.971(7) [1.988(6)], Ni(1)–N(1) 2.014(8) [2.019(8)], Ni(1)–N(3) 2.159(8) [2.141(7)], Ni(1)–N(4) 2.099(8) [2.133(7)], Ni(1)–N(5) 2.214(8) [2.204(8)], Ni(2)–O(2)/N(20) 1.964(7) [1.987(6)], Ni(2)–N(2) 1.990(8) [2.007(7)], Ni(2)–N(6) 2.128(7) [2.157(8)], Ni(2)–N(7) 2.126(7) [2.168(8)], Ni(2)–N(8) 2.248(9) [2.234(8)], Ni(1)···Ni(2) 4.257(2) [4.253(2)]; O(1)/N(10)–Ni(1)–N(3) 174.1(3) [176.3(3)], O(2)/N(20)–Ni(2)–N(6) 173.5(3) [172.4(3)], O(1)/N(10)–C(30)–O(2)/N(20) 127.2(9) [125.6(9)].
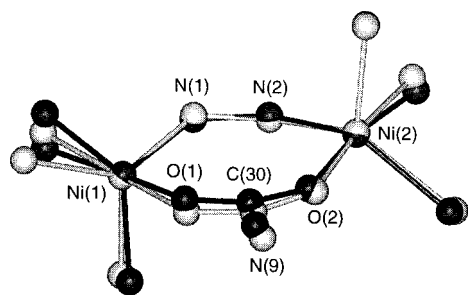
Fig. 2 Overlay of the crystallographically determined dinuclear sites of **2** (light) and **3** (dark). Selected atom distances (Å) and bond angles (°) for **3**: Ni(1)–O(1) 1.971(3), Ni(1)–N(1) 1.979(4), Ni(2)–O(2) 1.982(4), Ni(2)–N(2) 1.987(4), Ni(1)⋯Ni(2) 4.229(1), O(1)–C(30)–O(2) 127.3(5).

Formation of **2** from urea and *N,N*-bis(trimethylsilyl)urea implies the cleavage of the N–SiMe₃ bonds in the latter case, which is in accord with the known facility of N–Si bond hydrolysis in N-silylated amides.[13] The resulting trimethylsilanol was identified by GC–MS and ^{29}Si NMR spectroscopy among the volatile products of the present reaction. The observed deprotonation of parent urea by nickel-bound hydroxide to form **2** is understandable in the light of the drastic increase in substrate acidity upon its co-ordination to metal ions.[14] Thereby ureas are several orders of magnitude more acidic when N-bonded ($pK_A < 6$) then when O-bonded ($pK_A > 11$), and in the former case may even be more acidic than co-ordinated water.[14] It has thus been noted that isomerisation of the urea substrate from initial O-bonding to N-bonding can be thermally driven at intermediate pH, with the resulting deprotonated urea being kinetically inert and providing a thermodynamic sink for the linkage isomerisation.[14] A decisive driving force for the present reaction to form **2** certainly stems from the exceedingly strong tendency of these pyrazolate-based bimetallic complexes to incorporate secondary bridging ligands at the inner co-ordination site.[9,15]

In order to definitely exclude the presence of an O,O-bridging carbamate in **2**, complex **3** was synthesised independently for comparison (Scheme 1). At the same time this provides further insight into the possible coordination mode of this latter moiety—assumed to be the primary hydrolytic product of urease activity—at a dinickel(II) centre.[6] The IR absorptions of **3** assigned to the coordinating carbamate unit‡ clearly differ from those of the urea bridge in **2**, and mass spectrometry afforded a dominant signal with the expected isotopic distribution pattern for the molecular ion LNi₂(O₂CNH₂)⁺. This is one mass unit higher than those observed for **2** and thus allows an unambiguous distinction between the two complexes and further corroborates the presence of a bridging urea in **2**.

As shown by an X-ray single crystal analysis of **3**(BPh₄)₂ the overall molecular geometry of the bimetallic cation is quite similar to that of **2** (Fig. 2), however the Ni⋯Ni separation is slightly shortened [**2**: 4.255(2) Å; **3**: 4.229(1) Å], as are the C(30)–O/NH bond lengths {**2**: d[C(30)–O/NH] = 1.28(1)–1.31(1) Å *vs.* **3**: d[C(30)–O] = 1.249(6)/1.242(6) Å} in accordance with the difference in covalent radii of either a bridging O–C–O (**3**) or disordered O–C–NH (**2**) moiety spanning the metal centres. Two acetonitrile solvent molecules included in the crystal lattice of **3**(BPh₄)₂ are positioned suitably for weak hydrogen bonding with the protons attached to N(9) {d[N(9)⋯N(10)] = 3.190 Å; d[N(9)⋯N(11)] = 3.423 Å}, although the latter could not be located in the crystallographic analysis.

2 and **3** thus represent first structurally characterised examples of a bridging coordination mode of both deprotonated urea and carbamate at a dinickel(II) core. These molecular arrangements obviously have considerable thermal stability as both DSC and TGA measurements of **2**(ClO₄)₂ and **3**(BPh₄)₂

indicate no degradation or loss of weight until above 200 °C, and consequently the corresponding coordination modes should be taken into consideration when studying the interaction and reactivity of urea with urease-mimetic dinickel model systems. The findings furthermore underline that a bridging carbamate ligand, which is present in the form of a carbamylated lysine residue in the urease active site itself, is a reasonable alternative to the ubiquitous carboxylate bridges in dinuclear metal arrangements.

Notes and References

† E-mail: Franc@sun0.urz.uni-heidelberg.de

‡ Satisfactory elemental analyses could be obtained for all new complexes. Selected IR bands for **2**(ClO₄)₂: ν_{max}/cm⁻¹ (KBr) 3479s, 3376s, 1614s, 1572vs, 1486s, 1455s. For **3**(BPh₄)₂: ν_{max}/cm⁻¹ (KBr) 3499m, 3385s, 1590s, 1571sh, 1558vs, 1473s, 1422vs.

§ *Crystal data* for **2**(ClO₄)₂: C₃₀H₆₄Cl₂N₁₀Ni₂O₉, M = 897.2, orthorhombic, space group $P2_12_12_1$, a = 14.646(7), b = 22.77(1), c = 24.26(1) Å, V = 8090(7) Å³, Z = 8, ρ_{calc} = 1.475 g cm⁻³, μ(Mo-Kα) = 1.12 mm⁻¹, 9596 unique reflections measured, 6479 observed [$I > 2\sigma(I)$], 992 parameters, largest diff. peak 0.70 e Å⁻³, final $R1[I > 2\sigma(I)]$ = 0.060, $wR2$ = 0.172, goodness of fit on F^2 = 1.038. For **3**(BPh₄)₂·2MeCN: C₇₈H₁₀₃B₂N₉Ni₂O₂·2MeCN, M = 1419.8, monoclinic, space group $C2/c$, a = 58.3029(6), b = 11.0423(3), c = 28.4945(3) Å, β = 118.549(1)°, V = 16114.1(4) Å³, Z = 8, ρ_{calc} = 1.171 g cm⁻³, μ(Mo-Kα) = 0.51 mm⁻¹, 13951 unique reflections measured, 7794 observed [$I > 2\sigma(I)$], 909 parameters, largest diff. peak 0.93 e Å⁻³, final $R1[I > 2\sigma(I)]$ = 0.063, $wR2$ = 0.207, goodness of fit on F^2 = 1.10. All structures were solved by direct methods with SHELXS-97 and refined with SHELXL-97.[16] CCDC 182/901.

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