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A Crystallographically-Characterized Salt of Self-Generated *N*-Protonated Tetraethylurea

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The reaction of 1,1,3,3-tetraethylurea (teu) with WCl_6 in dichloromethane afforded [teuH][WCl_6], 1, in 50-60% yield. The X-ray structure determined for 1 includes the first example of crystallographic characterization of a *N*-protonated urea. According to spectroscopic and DFT outcomes, the formation of 1 is the result of an electron transfer/C–H activation process.

Urea, the first synthetic organic compound, and its nitrogen-substituted derivatives [1] possess peculiar structural properties, which have encouraged a recent renaissance of their use in chemistry.[2] In fact they have found versatile application in organocatalysis [3] and as scaffolds for supramolecular chemistry,[4] and for their possible biologic actions.[5] Ureas are weakly Lewis bases bearing two potential sites accessible to the first proton attack, *i.e.* the O and N atoms, and numerous studies have contributed to this debate.[6]

Protonated ureas are believed to exist as intermediates in the related decomposition reactions,[7] may act as crucial intermediates in organic synthesis [8] and are suitable guest species for nanoporous supramolecular skeletons built up from a water environment.[9] Experimental and theoretical outcomes agree in indicating the oxygen atom as the generally privileged site for proton addition, irrespective of the degree of *N*-substitution. Indeed *O*-protonated species have been observed in solutions in the presence of strong *Brönsted* acids thus allowing, in a number of cases, solid-state isolation and subsequent crystallographic characterization.[10]

In the framework of our interest in the chemistry of high-valent transition metal halides,[11] herein we describe a new synthetic approach to obtain a stable *N*-protonated urea (1,1,3,3-tetraethylurea, teu) salt. The synthesis takes advantage of the oxidative power of WCl_6 [12] and, thus, does not make use of *strong protonating* agent (*Brönsted* acid).

Tungsten hexachloride slowly dissolved in dichloromethane in the presence of one equivalent of teu at room temperature, under strictly anhydrous conditions; the crystalline compound [teuH][WCl_6], **1**, was isolated in 53% yield and identified by analytical and spectroscopic methods (see Eqn. 1 and Supporting Information). Experimental and theoretical outcomes agreed in that teu itself represented the main source of protonation (*vide infra*).

$$\mathrm{WCl_6 + teu} \xrightarrow{48\ \mathrm{h}} \underset{\mathbf{1}}{\mathrm{[teuH][WCl_6]}} \qquad (1)$$

X-ray quality crystals could be collected from a 1,2-dichloroethane/hexane mixture: the molecular structure of **1** is shown in Figure 1, together with its main geometric parameters. It consists of an ionic packing of $[teuH]^+$ cations and $[WCl_6]^-$ anions. The anions are slightly distorted octahedra rather similar to the ones previously described in miscellaneous salts.[13] Otherwise the $[teuH]^+$ cation represents, to the best of our knowledge, the first example of a crystallographically characterised *N*-protonated alkylurea.[14] The hydrogen atom bonded to N(2) has been located in the Fourier map and refined isotropically. As a consequence of the protonation of N(2), the C(1)–N(2) bond [1.523(4) Å] is considerably elongated compared to C(1)–N(1) [1.319(5) Å], and N(2) displays sp^3 hybridization [sum angles excluding H(2) 329.0(5)°] whereas the sp^2 N(1) is perfectly planar [sum angles 360.0(5)°]. The C(1)–O(1) distance [1.212(4) Å] is typical for a double bond,[15] and C(1) displays a perfect sp^2 hybridization [sum angles 360.0(5)°]. An inter-molecular H-bond is present between the N(2)-H(2) group (donor) of the cation and a chloride ligand (acceptor) of the anion [N(2)–H(2) 0.898(18) Å, H(2)···Cl(5)#1 2.53(3) Å, N(2)···Cl(5)#1 3.288(3) Å, N(2)H(2)Cl(5)#1 142(3)°, symmetry transformation #1 x–1, y, z].

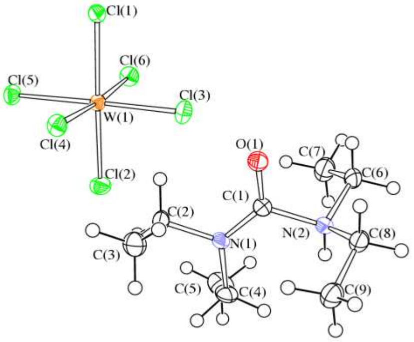

Figure 1. ORTEP drawing of $[Et_2NC(O)NHEt_2][WCl_6]$, **1**. Displacement ellipsoids are at the 30% probability level. Selected bond lengths (Å) and angles (deg): W–Cl 2.2944(10)-2.3865(9), average 2.328(2); C(1)–O(1) 1.212(4); C(1)–N(1) 1.319(5); C(1)–N(2) 1.523(4); C(2)–N(1) 1.480(4); C(4)–N(1) 1.476(4); C(6)–N(2) 1.512(4); C(8)–N(2) 1.523(4); C(2)–C(3) 1.517(5); C(4)–C(5) 1.513(5); C(6)–C(7) 1.508(5); C(8)–C(9) 1.515(5); sum angles at C(1) 360.0(5); sum angles at N(1) 360.0(5); sum angles at N(2) (excluding H(2)) 329.0(5).

The IR spectrum of **1** (in the solid state) exhibits diagnostic absorptions at 3196 and 1750 cm^{-1}, assigned to the stretching

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† Electronic Supporting Information (ESI) available: Experimental details, NMR spectra, DFT calculated structures, cartesian coordinates of the computed structures in *.xyz* format.

vibrations of NH and C=O bonds, respectively. The ^{1}H and ^{13}C NMR spectra, recorded in CD_2Cl_2 solution, contain broad resonances due to the presence of the W(V) paramagnetic anion (Figures S1-S2). The NMR pattern is consistent with the structure elucidated for the solid state by X-ray diffractometry; indeed three resonance groups have been found corresponding to the ethyl units. More precisely, the ethyls bound to non-protonated nitrogen resonate as two distinct ones (at 52.3 and 46.2 ppm in the ^{13}C spectrum) due to inhibited rotation around C(1)=N(1). Conversely the ethyls on the protonated nitrogen appear equivalent (δ = 58.7 ppm in the ^{13}C spectrum). The ^{1}H resonance of the *N*-bound proton occurs at 6.37 ppm. The presence of the $[WCl_6]^-$ anion was recognized by magnetic analysis, which was as expected for such a W(V) species.[13,16]

In order to shed light into mechanistic aspects, we carried out a joint spectroscopic and DFT study. In agreement with NMR data recorded on a CD_2Cl_2 reaction mixture (SI, page S4), the formation of **1** from WCl_6/teu takes place in 55-60% yield and does not involve the solvent. Accordingly, **1** was obtained in comparable yields by using CCl_4 or hexane as reaction medium. IR and NMR outcomes agreed in indicating the generation of by-products presumably bearing the [N=CH] moiety (SI, pp S4 and S7). The proposed, DFT-calculated, main reaction pathway is shown in Figure 2. It implies the possible interaction of the products/intermediates with the reactants, coherently with the long time required for the synthesis of **1**.

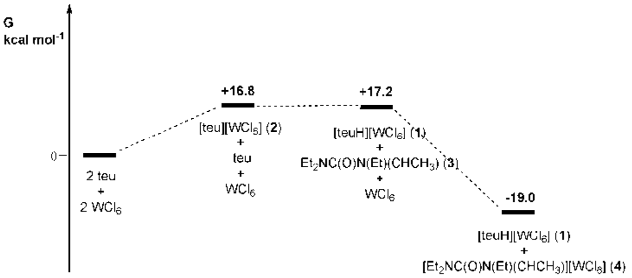

Figure 2. Calculated Gibbs free energy profile related to the proposed main reaction pathway leading to **1**.

In order to explain the formation of the W(V) salt **1**, initial electron transfer should be envisaged affording [teu][WCl_6], **2** (Figure S5, Table S3).[13] This appears a thermodynamically unfavourable process (Eqn. 2), basically due to entropic reasons (ΔS = +16.0 kcal mol^{-1}). Nevertheless, exergonic steps may follow (see in particular Eqn. 4).

$$WCl_6 + teu \rightarrow \underset{\mathbf{2}}{[teu][WCl_6]} \qquad (2)$$

$$\Delta G = +16.8 \text{ kcal mol}^{-1}$$

The radical cation $[teu]^{+\bullet}$ is a potential *H*-abstractor from still unreacted teu,[13,17] leading to $[teuH]^+$ and the radical species $[Et_2NC(O)N(Et)(CHCH_3)]^\bullet$, **3** (Eqn. 3). The latter is shown in Figure S6 together with its spin density surface. The reaction reported in Eqn. 3 is associated with a negligible variation of Gibbs free energy.

$$\underset{\mathbf{2}}{[teu][WCl_6]} + teu \rightarrow \underset{\mathbf{1}}{[teuH][WCl_6]} + \underset{\mathbf{3}}{[Et_2NC(O)N(Et)(CHCH_3)]^\bullet} \qquad (3)$$

$$\Delta G = +0.4 \text{ kcal mol}^{-1}$$

Alternative H-capture by $[teu]^+$ from CH_2Cl_2 or H_2O seems to be unlikely.[18] The calculations indicate that the newly formed **3** may act as a powerful reducing agent towards unreacted WCl_6 (Eqn. 4).[17]

$$\underset{\mathbf{3}}{[Et_2NC(O)N(Et)(CHCH_3)]^\bullet} + WCl_6 \rightarrow \underset{\mathbf{4}}{[Et_2NC(O)N(Et)(CHCH_3)][WCl_6]} \qquad (4)$$

$$\Delta G = -36.2 \text{ kcal mol}^{-1}$$

The optimized structure of **4** is shown in the SI (Figure S7 and Table S5). The cation in **4** is an iminium which can be viewed as a vinyl-urea protonated at the alkene moiety. In principle, **4** is more stable than the related *N*- and *O*-protonated isomers.[19] Subsequent reactivity of **4** might contribute to increase the yield of synthesis of **1** (Eqn. 5); it should be remarked that the possible occurrence of more than one vinyl-containing products is in accordance with NMR evidences (see above).

$$\mathbf{4} + [teu][WCl_6] \rightarrow \mathbf{1} + [Et_2NC(O)N(Et)(CH{=}CH_2)][WCl_6] \qquad (5)$$

$$\Delta G = -2.5 \text{ kcal mol}^{-1}$$

In addition, the adventitious presence in the reaction medium of HCl, produced by undesired hydrolysis, offers opportunity for **3** to **1** conversion.[20] Nevertheless it should be noticed that HCl formation from WCl_6/H_2O systems is typically accompanied by the generation of [W=O] containing species,[21] not recognised in the present case. This point, together with DFT outcomes,[18] suggests that water plays a minor role in the protonation process.

We tried to extend the results regarding the WCl_6/teu system to 1,1,3,3-tetramethylurea (tmu). Former calculations indicated the tmu oxygen as the preferential site for H^+ addition,[22] in agreement with thermodynamic measurements.[23] Accordingly, our calculations have pointed out that the most stable form of [tmuH][WCl_6], in the presence of dichloromethane as implicit solvent, is the *O*-protonated one (Figure S8, structure **5A**).[24]

The 1:1 molar reaction of WCl_6 with 1,1,3,3-tetramethylurea was carried out in conditions similar to those employed for the synthesis of **1**. After work-up, a red solid was isolated whose IR spectrum suggested the formation of a complicated mixture of products (see SI). The presence of both **5A** [IR absorptions at 3329 (ν_{OH}) and 1661 (ν_{CN}) cm^{-1}] and of its *N*-protonated isomer [**5B**, IR absorptions at 3127 (ν_{NH}) and 1771 (ν_{CO}) cm^{-1}] has been hypothesized upon comparison of the experimental IR data with the corresponding ones provided by the calculations. The ^{1}H NMR spectrum of the 1:1 reaction mixture WCl_6/tmu (in CD_2Cl_2) exhibited a resonance at 8.30 ppm which was assigned to a [$N{=}CH_2$] group with the assistance of 2D NMR experiments (SI, page S5). This feature confirms the idea that C–H bond activation, as a source of protonation, is operative in the course of the interaction between WCl_6 and tetraalkylureas.

In conclusion, we have presented the first structurally characterized salt comprising a discrete *N*-protonated urea cation. Remarkably, the main synthetic route to the salt does not involve any strong Brönsted acid. Instead, the urea reactant seems to act as the prevalent proton source *via* WCl_6-promoted C_α–H activation, as suggested by spectroscopic and DFT outcomes.

Notes and reference

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1 The term "ureas" will be used in order to indicate both the simplest urea, $(NH_2)_2C{=}O$ and its N-substituted derivatives.

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18 [teu][WCl_6] + H_2O → [teuH][WCl_6] + OH, $\Delta G = +25.4$ kcal mol^{-1}; [teu][WCl_6] + CH_2Cl_2 → [teuH][WCl_6] + $CHCl_2$, $\Delta G = +3.1$ kcal mol^{-1}.

19 Relative free energy values: $[Et_2NC(O)N(Et)(CHCH_3)]^+$, G = 0 kcal mol^{-1}; $[Et_2NC(O)NH(Et)(CHCH_2)]^+$, G = +18.9 kcal mol^{-1}; $[Et_2NHC(O)N(Et)(CHCH_2)]^+$, G = +14.7 kcal mol^{-1}; $[Et_2NC(OH)N(Et)(CHCH_2)]^+$, G = +14.8 kcal mol^{-1}.

20 Calculated ΔG for the reaction **3** + HCl → teu + ½ Cl_2 resulted −3.5 kcal mol^{-1}.

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