

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

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Receipt/Acceptance Data [DO NOT ALTER/DELETE THIS TEXT]

Publication data [DO NOT ALTER/DELETE THIS TEXT]

DOI: 10.1039/b000000x [DO NOT ALTER/DELETE THIS TEXT]

The reaction of 1,1,3,3-tetraethylurea (teu) with WCl_6 in dichloromethane afforded $[\text{teuH}][\text{WCl}_6]$, **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 derivatives¹ possess peculiar structural properties, which have encouraged a recent renaissance of their use in chemistry.² In fact they have found versatile application in organocatalysis³ 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 synthesis⁸ 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 Brønsted 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 (*Brønsted* 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 $[\text{teuH}][\text{WCl}_6]$, **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*).

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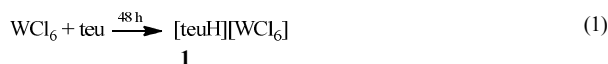
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† Electronic Supporting Information (ESI) available: Experimental details, NMR spectra, DFT calculated structures, cartesian coordinates of the computed structures in .xyz format.



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 $[\text{teuH}]^+$ cations and $[\text{WCl}_6]^-$ anions. The anions are slightly distorted octahedra rather similar to the ones previously described in miscellaneous salts.¹³ Otherwise the $[\text{teuH}]^+$ 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 $x-1, y, z$].

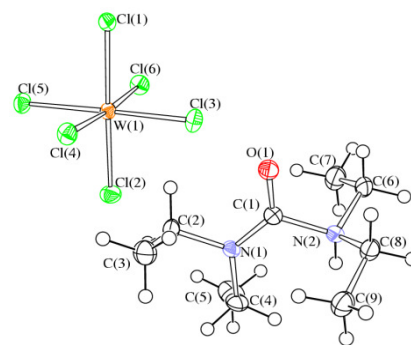


Figure 1. ORTEP drawing of $[\text{Et}_2\text{NC(O)NHEt}_2][\text{WCl}_6]$, **1**. Displacement ellipsoids are at the 30% probability level. Selected bond lengths (Å) and angles (deg): W–Cl 2.2944(10)–2.3865(9), average 2.328(2); C(1)–O(1) 1.212(4); C(1)–N(1) 1.319(5); C(1)–N(2) 1.523(4); C(2)–N(1) 1.480(4); 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

vibrations of NH and C=O bonds, respectively. The ^1H 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 $\text{C}(1)=\text{N}(1)$. Conversely the ethyls on the protonated nitrogen appear equivalent ($\delta = 58.7$ ppm in the ^{13}C spectrum). The ^1H resonance of the *N*-bound proton occurs at 6.37 ppm. The presence of the $[\text{WCl}_6]^-$ 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 $[\text{N}=\text{CH}]$ 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**.

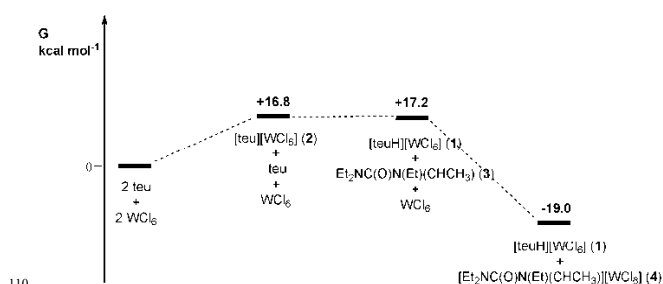


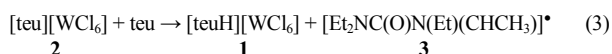
Figure 2. Calculated Gibbs free energy profile related to the proposed main reaction pathway leading to **1**.

In order to explain the formation of the W(V) salt **1**, initial electron transfer should be envisaged affording $[\text{teu}][\text{WCl}_6]$, **2** (Figure S5, Table S3).¹³ This appears a thermodynamically unfavourable process (Eqn. 2), basically due to entropic reasons ($\Delta S = +16.0$ kcal mol^{-1}). Nevertheless, exergonic steps may follow (see in particular Eqn. 4).



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

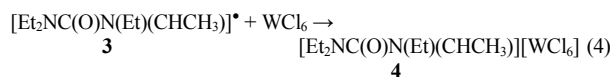
The radical cation $[\text{teu}]^{+\bullet}$ is a potential *H*-abstractor from still unreacted teu,^{13,17} leading to $[\text{teuH}]^+$ and the radical species $[\text{Et}_2\text{NC}(\text{O})\text{N}(\text{Et})(\text{CHCH}_3)]^\bullet$, **3** (Eqn. 3). The latter is shown in Figure S6 together with its spin density surface. The reaction reported in Eqn. 3 is associated with a negligible variation of Gibbs free energy.



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

Alternative H-capture by $[\text{teu}]^+$ 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



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

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).



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

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 $\text{WCl}_6/\text{H}_2\text{O}$ systems is typically accompanied by the generation of $[\text{W}=\text{O}]$ 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 $[\text{tmuH}][\text{WCl}_6]$, 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 ^1H 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 $[\text{N}=\text{CH}_2]$ 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 Brønsted 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

- The term “ureas” will be used in order to indicate both the simplest urea, $(\text{NH}_2)_2\text{C}=\text{O}$ and its *N*-substituted derivatives.
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- 18 [teu][WCl₆] + H₂O → [teuH][WCl₆] + OH, ΔG = +25.4 kcal mol⁻¹;
[teu][WCl₆] + CH₂Cl₂ → [teuH][WCl₆] + CHCl₂, ΔG = +3.1 kcal mol⁻¹.
- 19 Relative free energy values: [Et₂NC(O)N(Et)(CHCH₃)]⁺, G = 0 kcal mol⁻¹; [Et₂NC(O)NH(Et)(CHCH₃)]⁺, G = +18.9 kcal mol⁻¹;
[Et₂NHC(O)N(Et)(CHCH₂)]⁺, G = +14.7 kcal mol⁻¹;
[Et₂NC(OH)N(Et)(CHCH₂)]⁺, G = +14.8 kcal mol⁻¹.
- 20 Calculated ΔG for the reaction **3** + HCl → teu + ½ Cl₂ resulted -3.5 kcal mol⁻¹.
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- 24 G(O-protonated)-G(N-protonated) = -11.5 kcal mol⁻¹.

