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A Crystallographically-Characterized Salt of Self-Generated \( N \)-Protonated Tetraethylurea

Marco Bortoluzzi, \(^a\) Fabio Marchetti, \(^b,\)\(^*\) Guido Pampaloni, \(^b\) and Stefano Zacchini \(^c\)

**ChemComm**

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

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,\(^7\) and 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,\(^6\) and numerous studies have 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 [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).

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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.

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vibrations of NH and C=O bonds, respectively. The $^1$H and $^{13}$C NMR spectra, recorded in CD$_2$Cl$_2$ 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 ($\delta = 58.7$ 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.

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$_2$Cl$_2$ 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, I 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.

$$G_{\text{mol}} \text{ kcal mol}^{-1}$$

![Figure 2](image-url) 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). This appears a thermodynamically unfavourable process (Eqn. 2), basically due to entropic reasons ($AG = +16.0$ kcal mol$^{-1}$). Nevertheless, exergonic steps may follow (see in particular Eqn. 4).

$$WCl_6 + \text{teu} \rightarrow [\text{teu}][WCl_6]$$

$$AG = +16.0 \text{ kcal mol}^{-1}$$

The radical cation [teu]$^+$ is a potential H-abstractor from still unreacted teu, leading to [teuH]$^+$ and the radical species [Et$_2$NC(O)N(Et)(CHCH$_3$)]$^+$, 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.

$$[\text{teu}][WCl_6] + \text{teu} \rightarrow [\text{teuH}][WCl_6] + [\text{Et}_2\text{NC(O)N(Et)(CHCH}_3\text{)}]^+$$

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

Alternative H-capture by [teu]$^+$ from CH$_3$Cl$_2$ or H$_2$O seems to be unlikely. The calculations indicate that the newly formed 3 may act as a powerful reducing agent towards unreacted WCl$_6$ (Eqn. 4). 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. 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).

$$4 + [\text{teu}][WCl_6] \rightarrow 1 + [\text{Et}_2\text{NC(O)N(Et)(CH=CH)}][WCl_6]$$

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

In addition, the adventitious presence in the reaction medium of HCl, produced by undesired hydrolysis, offers opportunity for the formation of [W=O] containing species, in accordance with thermodynamic measurements. Accordingly, our calculations have pointed out that the most stable form of WCl$_6$/H$_2$O systems is typically accompanied by the generation of [W=O] containing species, not recognised in the present case. This point, together with DFT outcomes, 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, in agreement with thermodynamic measurements. 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).

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 (\nu$_{OH}$) and 1661 (\nu$_{C=O}$) cm$^{-1}$] and of its N-protonated isomer [5B, IR absorptions at 3127 (\nu$_{NH}$) and 1771 (\nu$_{C=O}$) 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$_2$Cl$_2$) 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 tetramethylurea.

In conclusion, we have presented the first structurally characterized salt comprising a discrete W(V) species.

Notes and reference

1. The term “ureas” will be used in order to indicate both the simplest urea, (NH)$_2$C=O and its N-substituted derivatives.


18 \([\text{teu}][\text{WCl}_x] + \text{H}_2\text{O} \rightarrow [\text{teuH}][\text{WCl}_x] + \text{OH}, \Delta G = +25.4 \text{ kcal mol}^{-1}\); \([\text{teu}][\text{WCl}_x] + \text{CH}_2\text{Cl}_2 \rightarrow [\text{teuH}][\text{WCl}_x] + \text{CHCl}_3, \Delta G = +3.1 \text{ kcal mol}^{-1}\).

19 Relative free energy values: \([\text{Et}_2\text{NC}(\text{O})(\text{Et})(\text{CHCH}_3)]^+, G = 0 \text{ kcal mol}^{-1}\); \([\text{Et}_2\text{NC}(\text{O})(\text{Et})(\text{CHCH}_3)]^-, G = +18.9 \text{ kcal mol}^{-1}\); \([\text{Et}_2\text{NHC}(\text{O})(\text{Et})(\text{CHCl}_3)]^+, G = +14.7 \text{ kcal mol}^{-1}\); \([\text{Et}_2\text{NHC}(\text{O})(\text{Et})(\text{CHCl}_3)]^-, G = +14.8 \text{ kcal mol}^{-1}\).

20 Calculated \(\Delta G\) for the reaction \(3 + \text{HCl} \rightarrow \text{teu} + \frac{1}{2} \text{Cl}_2\), resulted \(-3.5 \text{ kcal mol}^{-1}\).


24 \((\text{O-protonated}) - \text{(N-protonated)} = -11.5 \text{ kcal mol}^{-1}\).