Air-Stable Oxyallyl Patterns and a Switchable N-Heterocyclic Carbene

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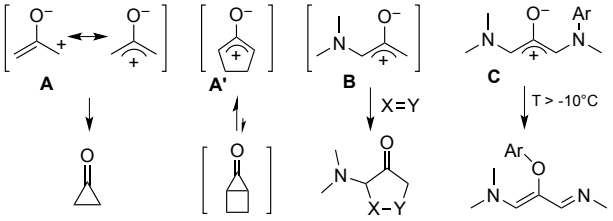
Abstract: Oxyallyl derivatives are typical elusive compounds. Even recent "stabilized" 1,3-di(amino)oxyallyls remain highly reactive and have short lifespans at room temperature. Herein, we report the synthesis and preliminary study of mesoionic pyrimidine derivatives, which feature 1,3-bis(dimethylamino)oxyallyl patterns with an unprecedented level of stabilization. Not only the latters are insensitive towards air and moisture, they are also compatible with the formation of an ancillary stable *N*-heterocyclic carbene moiety. As the oxyallyl pattern is proton-responsive, it allows the reversible switching of the electronic properties of the carbene, as a ligand.

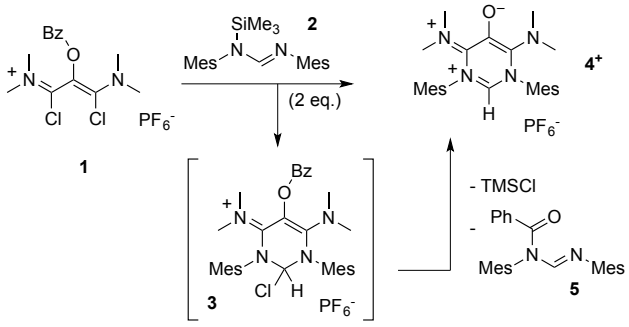
Oxyallyls **A** (see Scheme 1),[1,2] also called oxyallyl cations, have been postulated as reactive intermediates in numerous reactions, [3,4] including 1,3-dipolar cycloadditions,[5,6] and *in-vivo* biosyntheses.[7] They are non-disjoint non-Kekulé diradicaloids with singlet ground states.[8,9] As a consequence, the cyclization to form the corresponding cyclopropanone isomer is almost barrierless. Direct evidence for such elusive species has been extremely challenging to gather. The first spectroscopic observations were reported as late as 2011.[9] Initial attempts to design long-lived versions focused on destabilizing the cyclopropanone form. For instance, five-membered ring oxyallyls **A'** are predicted to be more stable than their strained bicyclo[2.1.0]cyclopropanone isomers. However, **A'** remains highly reactive and only dimeric forms could be observed so far.[10] Of note, oxyallyl patterns can be recognized in some stable molecules featuring aromatic cores and extended π-conjugation, such as diketohexaphyrins,[11] squaraines[12] and croconaine dyes.[13,14]



Scheme 1. Simplified representations of: typical elusive oxyallyls **A**, putative strained five-membered ring versions **A'**, trapping of (amino)oxyallyl **B** with a dipolarophile, typical thermal rearrangement of di(amino)oxyallyls **C**.

Apart from highly delocalized frameworks, thermodynamic stabilization of electrophilic allylic compounds **A** should be achievable with simple electron-donating substituents. Indeed, the introduction of one amino group results in a distinct class of stabilized, though still elusive, oxyallyls **B**. They are ambiphilic dipolarophiles, which undergo concerted and regioselective [4+3] cycloadditions.[6] With a second amino group, 1,3-di(amino)oxyallyls **C** reach a new level of stability. They are persistent enough in solution for NMR characterization.[15,16] Importantly, since the parent oxyallyl pattern underwent significant electronic perturbations, the di(amino)cyclopropanone forms have become irrelevant high-energy isomers.[17] Thus, the stabilized oxyallyls **C** could be considered novel electron-rich organic functionalities with reactivity of their own. They undergo thermal rearrangement through *N*→*O* aryl migration of substituents,[15,18] as well as one-electron oxidation at low potentials to yield highly air-persistent radical cations $\mathbf{C}^{\bullet+}$.[15,19] However, the half-life of even the most persistent stabilized oxyallyl **C** is less than one hour at room temperature.[19a,20] Therefore, the design of isolable versions, not even to mention air-stability, clearly requires significant steps further.

Herein, we report the synthesis and preliminary study of a new type of oxyallyls with such an unprecedented level of stabilization. These mesoionic pyrimidine derivatives feature 1,3-bis(dimethylamino)oxyallyl patterns, which are insensitive towards air and moisture, as well as compatible with the formation of an ancillary stable carbene moiety.



Scheme 2. Synthesis of the hexafluorophosphate salt of $\mathbf{4}^{+}$.

The high-reactivity of electron-rich 1,3-(diamino)oxyallyl patterns had to be tamed through the addition of electron-withdrawing groups. Inspired by our recent work on pyrimidin-1,3-diium salts,[21] we chose to introduce an *N,N'*-amidinium bridge. As previous synthetic approaches towards stabilized oxyallyls were irrelevant to such a target, our novel strategy relied on the early introduction of a "masked" *O*-protected oxyallyl pattern. We reacted 1,3-dichlorovinamidinium salt **1**,[22] featuring a benzoyl *O*-protecting group, with one equivalent of *N*-(trimethylsilyl)amidine **2**[23] (Scheme 2). After work-up, the moisture-sensitive yellow salt **3** was isolated in 55% yield. The addition of a second equivalent of **2** yielded organic cation $\mathbf{4}^{+}$ in low isolated yield and benzamide **5**. The formation of the latter suggested that the *O*-deprotection occurred. Finally, the one-pot reaction of **1** with two equivalents of **2** conveniently afforded the hexafluorophosphate salt of $\mathbf{4}^{+}$ in 71% yield. A single crystal X-ray diffraction study confirmed the cyclic structure of $\mathbf{4}^{+}$, as well as the presence of a 1,3-di(amino)oxyallyl pattern (Figure 1).[24] Interestingly, $\mathbf{4}^{+}$ has a low C_1 symmetry in the solid state, as one dimethylamino group is twisted and less conjugated (sum of angles around N2': Σ(N2'): 353.6°, C2'–N2': 136.9(3) pm, C4'–N2'–C2'–C3': 110.8(3) °; whereas Σ(N2): 359.9°, C2–N2: 134.0(3) pm, C4–N2–C2–C3: 143.0(2) °). A brief screening of functionals showed that DFT calculations[25] only predict optimized geometries with higher C_s symmetry, unless long-range interactions are taken into account. In the latter case only, an additional minimum corresponds to a C_1 symmetric conformer. The ωB97XD/6-311g(d,p) level of theory[26] provided an excellent overall fit with the experimental solid-state data and was chosen for geometric optimizations in the rest of this work (see supporting information).

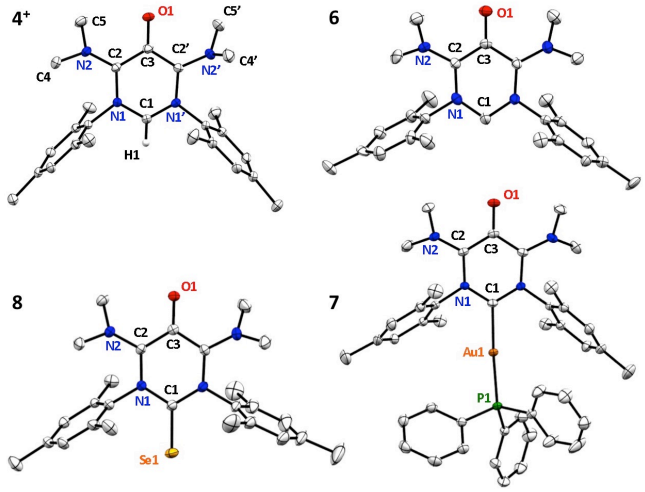


Figure 1. Representation and labelling of X-ray crystal structures of compounds $\mathbf{4}^{+}$, **6**-**8** featuring an oxyallyl pattern. Thermal ellipsoids are drawn at 50% probability level. Most hydrogen atoms, co-crystallized solvents and anions are omitted for clarity.

The hexafluorophosphate salt of $\mathbf{4}^{+}$ is remarkably insensitive towards moisture and air. Samples were stored at room temperature with no specific precaution for more than a year, with no evidence of decomposition. Cyclic voltammetry indicated a reversible oxidation of $\mathbf{4}^{+}$ at $E_{1/2}$ = + 0.38 V *versus* Fc/Fc^{+} (Figure 2). This potential is significantly higher than in the case of previously reported di(amino)oxyallyls ($E_{1/2}$ < - 1 V).[15a,19a] This is in line with the dramatic electronic changes that are expected from the insertion of a very electron-withdrawing moiety. This also accounts for the absence of oxidation of $\mathbf{4}^{+}$ when exposed to air. In other hand, unlike previous stabilized oxyallyls, the reversible reduction of $\mathbf{4}^{+}$ is now accessible in solution ($E_{1/2}$ = -1.70 V). Note that imidazolium salts with a hydrogen atom on the C1 position, as well as parented stable-carbene precursors, undergo an irreversible reduction to afford the corresponding carbene.[27] In marked contrast, we could perform the

quantitative electrolysis of $\mathbf{4}^{+}$ in acetonitrile at E = -1.82 V to form radical $\mathbf{4}^{\bullet}$, which is persistent for hours in solution under inert atmosphere. Both coulometric monitoring (full conversion for one coulomb per mole of substrate) and cyclic voltammetry after electrolysis confirmed the nature of $\mathbf{4}^{\bullet}$. In addition, computed isotropic EPR hyperfine coupling constants for $\mathbf{4}^{\bullet}$ (see supporting information) matched well the experimental values (Figures 2).[28] The oxyallyl bears 61% of the computed Mulliken spin density, confirming its role as a key redox-active pattern in the outstanding stability of radical $\mathbf{4}^{\bullet}$.

We also performed the quantitative oxidation of $\mathbf{4}^{+}$ to generate radical $\mathbf{4}^{\bullet 2+}$. Although UV monitoring indicated partial decay in the time scale of the electrolysis, the radical could be characterized by EPR. Here again, most of computed Mulliken spin density (77 %) was found on the oxyallyl pattern.

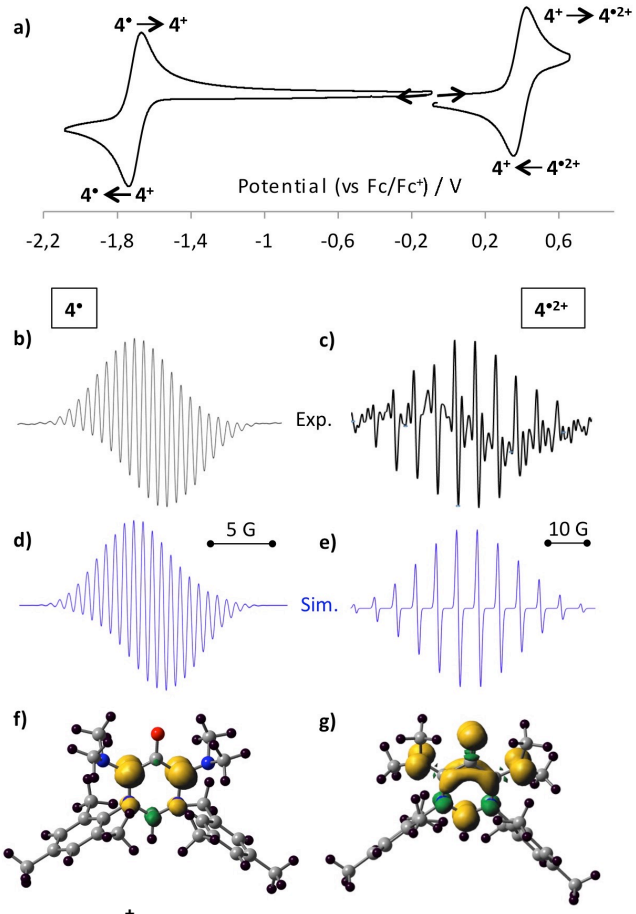
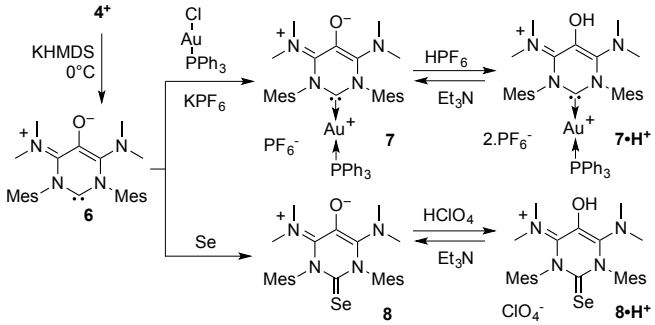


Figure 2. (a) cyclic voltammograms of $\mathbf{4}^{+}$ in acetonitrile + 0.1M $[Bu_4N]PF_6$, scan rate: 100 mV s^{-1}; experimental *X*-band EPR spectra of (b) $\mathbf{4}^{\bullet}$ and (c) $\mathbf{4}^{\bullet 2+}$ in acetonitrile at room temperature; corresponding simulated spectra with the following set of parameters: (d) $\mathbf{4}^{\bullet}$, Lorentzian line-broadening parameter L_w = 0.04 and hyperfine coupling constants $a(^{14}N)$ = 4.0 MHz (2 nuclei) and 2.6 MHz (2 nuclei), $a(^{1}H)$ = 6.7 MHz (1 nuclei) and 2.0 MHz (12 nuclei); (e) $\mathbf{4}^{\bullet 2+}$, L_w = 0.066, $a(^{14}N)$ = 14.0 MHz (2 nuclei), $a(^{1}H)$ = 14.4 MHz (1 nuclei) and $a(^{1}H)$ = 14.8 MHz (12 nuclei); Representation of computed spin densities for (f) $\mathbf{4}^{\bullet}$ and (g) $\mathbf{4}^{\bullet 2+}$.

Stable *N*-heterocyclic carbenes (NHC) have found widespread applications as ligands in organometallic catalysis.[29] In the last decade, this successful story was fuelled by the availability of new structures, which provided for an unprecedented range of electronic properties for tuning the reactivity of metal centres.[30] Naturally, we wondered whether the oxyallyl pattern could co-exist with an NHC functionality and afford an original platform for stable carbenes. Thus, we reacted $\mathbf{4}^{+}$ with a strong base, namely potassium hexamethyldisilazide (Scheme 3). To our delight, NMR spectra of the product were fully consistent with the formation of carbene **6**, including a deshielded peak for the carbene centre at $\delta(^{13}C)$= 224.5 ppm. After work-up, **6** was isolated in 78% yield. It is stable and has been stored for months as a solid under an inert argon atmosphere. A single-crystal X-ray diffraction study confirmed the structure of the product (Figure 1). As commonly observed, deprotonation of the carbene precursor resulted in sharpening the N1-C1-N1' angle ($\mathbf{4}^{+}$: 121.3 °; **6**: 111.7 °) and lengthening the C1–N1 bonds ($\mathbf{4}^{+}$: 131.4 and 134.5 pm; **6**: 136.0 and 137.9 pm).



Scheme 3. Synthesis and reactivity of stable *N*-heterocyclic carbene **6**.

We synthesized complex **7** from the reaction of NHC **6** with chloro(triphenylphosphine)gold(I) in presence of KPF_6 (Scheme 3). The metal complex was isolated in 73% yield and fully characterized, including a single-crystal X-ray analysis (Figure 1). Complex **7** was reacted with hexafluorophosphoric acid, to afford a salt, and spectroscopic data were consistent with the *O*-protonated gold(I) complex **7•H$^+$**. The ^{13}C NMR signal for the complexed carbon atom is significantly shifted down-field upon protonation (**7**: δ = 184 ppm, **7•H$^+$**: δ = 209 ppm), suggesting a significant change in the properties of the carbene ligand. We estimated net donation of ligands to the metal by computing the Tolman Electronic Parameter (*TEP*)[31] with Gusev's method.[32] The value for **6** (*TEP* = 2045.7 cm^{-1}) is consistent with a strong electron-donating NHC.[33] In marked contrast, a value of 2068 cm^{-1} for the *O*-protonated counterpart is typical of electron-poor phosphines.

Measuring the ^{77}Se chemical shift of a carbene-selenium(0) adduct is a well-established method to probe the π-accepting capability of NHC ligands.[34,35] We synthesized selenurea **8**, from the reaction of **6** with elemental selenium. Addition of perchloric acid yielded **8•H$^+$**. The *O*-protonation was consistent with NMR data and confirmed by single-crystal X-ray diffraction study. Unsurprisingly, the C3–O1 bond is significantly lengthened upon *O*-protonation (**8**: 127.3(2) pm, **8•H$^+$**: 136.8(2) pm). The corresponding value of $\delta(^{77}\text{Se})$ = 415 ppm for **8** corresponds to a carbene with significant electrophilicity.[36] Upon addition of acid, **6** is switched into an even stronger π-accepting NHC,[37] with a value of $\delta(^{77}\text{Se})$ = 679 ppm for **8•H$^+$**. Both gold complex **7** and selenurea **8**, as well as their protonated forms are bench stable: they could be handled and stored under air with no specific precaution. Importantly, both **7•H$^+$** and **8•H$^+$** could be switched back to **7** and **8**, respectively, upon addition of triethylamine.[38,39]

The structure of the oxyallyl pattern remains remarkably unchanged within compounds **4$^+$**, **6, 7** and **8**. Importantly, the lengths of N2–C2 (134–137 pm) C2–C3 (142-145 pm) and C3–O1 (126–129 pm) bonds correspond to those previously predicted for di(amino)oxyallyls (about 138, 144 and 128 pm, respectively).[17] The frontier MOs (molecular orbital) also remain very similar within the series and correspond to the HOMO (highest occupied MO) and LUMO (lowest unoccupied MO) of a 1,3-di(amino)oxyallyl fragment, with a second order contribution from the rest of the heterocycle (see supporting information). This is especially striking in the case of **6** (Figure 3). Indeed the frontier MOs of reactive electrophilic NHCs are usually associated with the lone pair (HOMO, but HOMO-1 for **6**) and the formally vacant p-orbital (LUMO, but LUMO+5 for **6**) of the carbenic carbon atom, respectively. Therefore, and contrary to more classical NHCs, the computed single-triplet gap of **6** (27.8 kcal.mol^{-1}) reflects more the electronic situation at the oxyallyl pattern than at the carbene centre. In addition, the 6π-electron heterocycles are only moderately aromatic. This is indicated by both computed NICS(1) values[40] (**4$^+$**: -4.0, **6**: -4.8, **7**: -4.2, **8**: -3.1, pyridine: -10.2, pyrimidine: -10.0 ppm) and the HOMHED structural indexes,[41] which were calculated from solid state geometries (**4$^+$**: 0.85, **6**: 0.86, **7**: 0.86, **8**:0.85 , pyridine: 0.99, pyrimidine: 0.99). Accordingly, the C2–N1 bonds (138–140 pm), which are linking the oxyallyl pattern to the rest of the heterocycle, are longer than in typical aromatic *N*-heterocycles (pyridine: 133.7 pm, pyrimidine: 133.3 and 133.9 pm), but shorter than a single C–N bond (145–147 pm).[42]

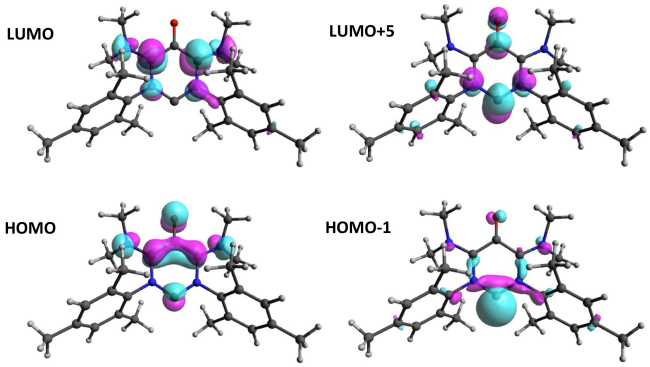


Figure 3. Representation of selected molecular orbitals of **6**.

In conclusion, the 1,3-di(amino)oxyallyl pattern, which is usually short-lived at room temperature, becomes air- and moisture-stable when associated with electron-withdrawing *N,N'*-bridges, such as in amidinium $\mathbf{4}^{+}$, NHC gold complex **7** and selenurea **8**. The corresponding carbene **6** was isolated and is stable under inert atmosphere. The electronic properties of the latter can be switched by protonation with a strong acid and subsequent deprotonation with a mild base, respectively.

The availability of these novel organic functions opens the gates of a vast playfield. In particular, the scope of redox-activity and ensuing radical reactivity, the possibility for bifunctional cooperation for bond activation, the valorisation of the proton-switching[38] and further "smart properties",[38] as well as the overall implications for metal- and organo-catalysis, are currently investigated in our laboratory.

Acknowledgements

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