Imidazol-2-ylidene-4-olate: an anionic N-heterocyclic carbene pre-programmed for further derivatization†

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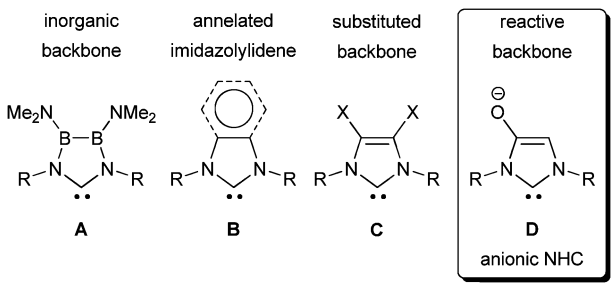
The 4-hydroxyimidazolium salt, readily prepared in two steps by acylation of a formamidine and quaternization of the second nitrogen, affords, after deprotonation, the anionic imidazol-2-ylidene-4-olate, which can be complexed to a transition metal and still be subsequently functionalized at O or C backbone atom in the outer coordination sphere of the metal.

Stable N-heterocyclic carbenes display a rich coordination chemistry, with multiple applications in organometallic catalysis.[1,2] Amongst their intrinsic interests is the possibility to modify their steric and electronic ligand properties by playing with the nature of the exocyclic nitrogen substituents. A more sophisticated way to modulate those properties is to modify the heterocyclic backbone connecting the two nitrogen atoms. To date, and for the most currently investigated 5-membered NHCs based on imidazole and imidazoline rings, this has been done by (i) incorporation of an inorganic backbone (compound **A**),[3] (ii) [4,5]-annelation to delocalized systems (type **B**),[4] or (iii) substitution at positions 4 and 5 of the imidazolylidene (type **C**).[5] Such changes in the architecture of the carbene have to be pre-programmed in the early stages of the synthesis of the antecedent imidazolium pre-ligand, but allow no further modulation after ring closure, once the final structure is obtained. With these observations in mind, we reasoned that incorporation of a *reactive* functionality within the heterocycle might allow further derivatization with better synthetic flexibility. The enolate group, whose chemistry is extremely well known, appeared as an ideal candidate in view of the synthesis of such a scaffold. We were thus led to devise a simple synthetic route to compound **D**, an anionic imidazol-2-ylidene-4-olate.[6]



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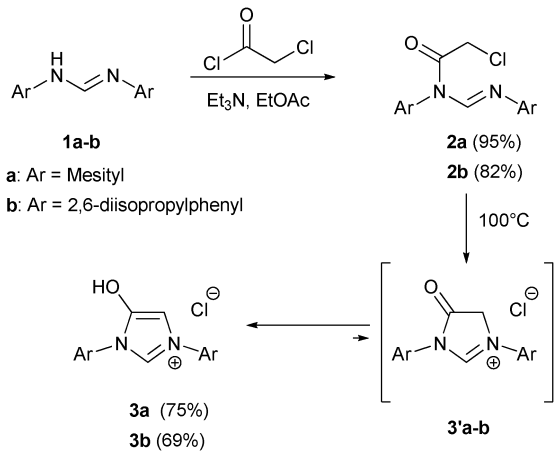


Scheme 1 Synthesis of the 4-hydroxyimidazolium chloride **3**.

Based on the keto-/enol-equilibrium of hydroxyaromatics, the 4-hydroxyimidazolium salt **3**, representing the appropriate pre-ligand, was synthesized in high yield by acylation of the formamidine **1** with chloroacetyl chloride, giving the intermediate **2**, which was readily cyclized by quaternization of the second nitrogen. The anticipated intermediate 4-oxoimidazolinium salt **3′** was not detected, due to its fast conversion into the more stable 4-hydroxyimidazolium chloride **3**. Clearly, here, the aromaticity of the imidazolium ring appears as the driving force favoring an equilibrium shift toward the enol form (Scheme 1).

The formation of the imidazolium ring can be monitored by IR spectroscopy, following the disappearance of the C=O stretching band around 1700 cm^{-1}. The pre-ligand **3a** was crystallized‡ and identified by X-ray diffraction analysis (Fig. 1).

In the solution ^1H NMR spectrum of **3**, the protons in positions 2 and 5 of the heterocycle appear as a characteristic set of two doublets between 7 and 8 ppm, with a coupling constant of 2.1 Hz. The chemical shift of the C1–H proton is particularly shielded (δ = 7.54 ppm for **3a**, δ = 7.56 (±0.03) ppm for **3b**) relative to a classical imidazolium chloride (δ > 10 ppm),[7] which may arise from a weaker hydrogen bonding between this proton and the chloride anion which is already involved in hydrogen bonding with the free –OH group. This interaction also exists in the solid-state structure of **3a** (Fig. 1) where each chloride anion interacts with two neighboring imidazolium units *via* a network of hydrogen bonds O–H···Cl···H–C.

Two acidic protons are present in the cationic 4-hydroxyimidazolium salt **3** but they can be differentiated by their pK_a value and their reactivity. As expected, the most acidic

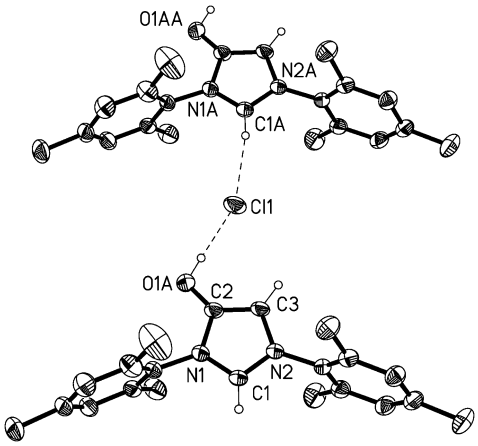
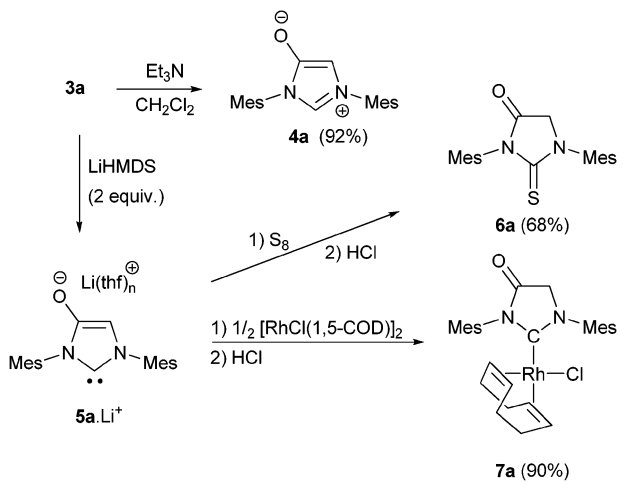


Fig. 1 Spatial arrangement of salt **3a** in the solid-state structure obtained by X-ray analysis. Anisotropic displacement parameter ellipsoids are shown at 50%. Hydrogen atoms on mesityl units were omitted for clarity. Selected bond lengths (Å): C2–C3: 1.360(2), C2–O1A: 1.269(3).

function in **3** is the phenol-type –OH group. Indeed, it could be readily deprotonated by reacting **3a** with triethylamine to form the mesoionic imidazolium-4-olate **4a**.[8] The anionic imidazol-2-ylidene-4-olate **5a** was generated quantitatively by treatment of **3a** with two equivalents of lithium bis(trimethylsilyl)amide at 0 °C. In order to confirm its formulation as an NHC, **5a** was trapped with S_8, and after neutralization of the enolate intermediate using one equivalent of hydrogen chloride, compound **6a** was isolated as a white, stable solid in 68% yield. Here, since the heterocycle is no longer aromatic, the keto form is solely obtained as judged by the appearance of a strong band at $\nu = 1747\ cm^{-1}$ in the IR spectra for the C=O bond and by a singlet at $\delta = 4.44$ ppm in the ^{1}H NMR integrating for 2H corresponding to the two C5 protons (Scheme 2).

Reaction of the *in situ* generated carbene **5a**·Li^+ with half an equivalent of $[RhCl(1,5\text{-}COD)]_2$ produced after neutralization the rhodium(I) complex **7a** in good yield. As the imidazol-2-ylidene was shown to possess less aromatic character than its imidazolium precursor,[9] the enol form should be less stabilized



Scheme 2 Mono- and bis-deprotonation of compound **3a** with subsequent trapping of the anionic NHC by sulfur or a rhodium precursor.

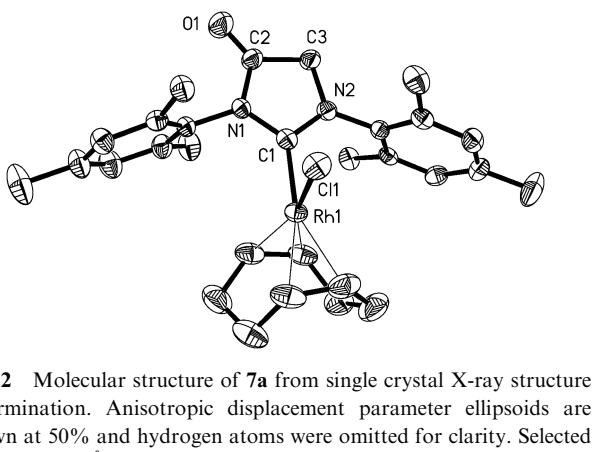
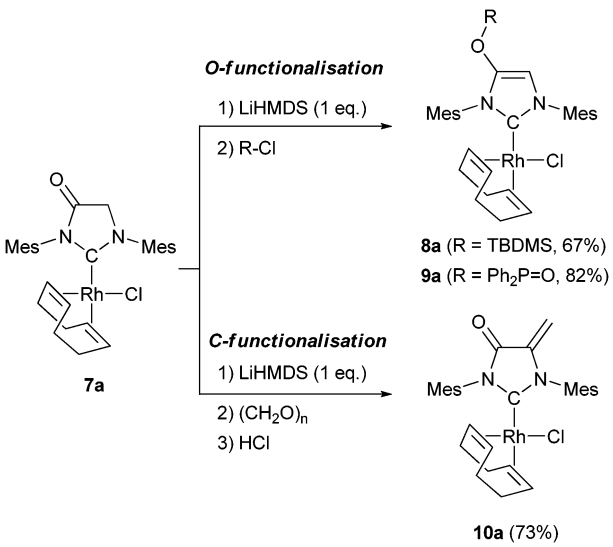


Fig. 2 Molecular structure of **7a** from single crystal X-ray structure determination. Anisotropic displacement parameter ellipsoids are shown at 50% and hydrogen atoms were omitted for clarity. Selected bond lengths (Å): Rh1–C1 2.020(3), C2–C3 1.500(4), C2–O1 1.217(3).

and the tautomeric equilibrium shifted to the keto form. All the characterizations were in agreement with this assumption, both in solution, with a ^{1}H NMR AB system for the two diastereotopic C5 protons at $\delta = 4.24$ ppm,[10] and in the solid state with C4–C5 (1.500(4) Å) and C4–O bonds (1.217(3) Å) lying, respectively, in the range of a typical single C–C bond and double C=O bond (Fig. 2).[11]

At that stage of our investigation, we were interested in determining whether further functionalization of the ligand could be achieved after its complexation to a transition metal.

Starting from complex **7a**, O-functionalization of the coordinated NHC was carried out by deprotonation at low temperature with one equivalent of $LiN(SiMe_3)_2$ followed by the addition of a suitable electrophile (Scheme 3, upper equation). With a silyl chloride (TBDMSCl) or a phosphorus(V) chloride ($Ph_2P(=O)Cl$), as incoming electrophiles, O-substitution was observed, leading to the protected imidazol-2-ylidene-4-ol complexes **8a** and **9a**. The main probe of the success of the reaction was the disappearance of the AB system of the CH_2 protons in **7a** and the appearance of a singlet at $\delta = 6.22$ ppm in **8a** and at 6.18 ppm in **9a** corresponding to the endocyclic C5 proton.



Scheme 3 Functionalization of complex **7a** on the backbone of the N-heterocyclic carbene.

In a parallel experiment (Scheme 3, lower equation), C-functionalization was successfully carried out using paraformaldehyde as the electrophile according to an aldolization–crotonization sequence. The olefinic $=CH_2$ protons display a pair of doublets at δ = 5.68 ppm and 4.87 ppm with a characteristic geminal coupling of 1.8 Hz.

In summary, we have developed a simple synthetic strategy towards an anionic five-membered ring N-heterocyclic carbene incorporating a reactive enolate group in its backbone. The advantage of such a ligand is that it can be complexed with transition metals, whereas its backbone can still be modified in different ways after complexation. The concept disclosed here will allow a divergent optimization and construction of NHC-based catalysts in view to obtain better activities.[12] By extension, and upon suitable selection of the electrophile, it should also be applicable to the generation of supported or tagged catalysts directly from their soluble form. Studies toward this goal are currently under investigation in our laboratory.

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Notes and references

‡ Crystal data for **3a**: $C_{21}H_{25}ClN_2O$, M = 356.88, monoclinic, a = 8.5416(3), b = 29.645(1), c = 8.7375(3) Å, β = 118.109(2)°, U = 1951.52(12) Å^3, T = 180(2) K, space group $P2_1/c$ (no. 14), Z = 4, 32 567 reflections measured, 5587 unique (R_{int} = 0.0198) which were used in all calculations. The final w$R(F^2)$ was 0.0680 (all data). Crystal data for **7a**: $C_{29}H_{36}ClN_2ORh$, M = 566.96, triclinic, a = 12.5523(5), b = 13.1214(4), c = 17.4887(7) Å, α = 73.019(2)°, β = 89.920(1)°, γ = 77.013(2)°, U = 2678.02(17) Å^3, T = 176(2) K, space group $P\bar{1}$ (no. 2), Z = 4, 17 559 reflections measured, 8754 unique (R_{int} = 0.0248) which were used in all calculations. The final w$R(F^2)$ was 0.0432 (all data).

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