Interaction of an imidazolium-2-amidinate (NHC-CDI) zwitterion with zinc dichloride in dichloromethane: role as ligands and C-Cl activation promoters^{†,§}

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Adducts of imidazolium carbenes and carbodiimides (NHC-CDI) are emerging as a new class of thermally stable and modular zwitterions with many potential applications. Our study of the interaction of a representative NHC-CDI with ZnCl₂ in dichloromethane led to the serendipitous discovery of a highly selective, double activation of dichloromethane C-Cl bonds.

Imidazolium-2-amidates (NHC-CDI) are an emerging class of zwitterionic molecules with an unsuspected potential as versatile building blocks for the design of nanocatalysts,¹ coordination and organometallic complexes,^{2,3} and even advanced polymeric materials.⁴ They are easily obtained as coloured crystalline materials from the reaction of readily available N-heterocyclic carbenes (NHC) and carbodiimides (CDI).⁵ In consequence their electronic and structural parameters can be easily tuned. In contrast with the analogous imidazolium-2-carboxylates,⁶ NHC-CDI are thermally very stable. Accordingly, it has been recently shown that symmetric NHC-CDI adducts can be directly generated by the thermal decomposition of certain N-heterocyclic carbenes.⁷ Therefore, it is quite surprising that, although the first NHC-CDI zwitterions were reported in 1999,⁸ they have received very little attention until 2015, when some of us reported their ability to support ultra-small Ru nanoparticles.^{1a} Although devoid of net electrical charge, NHC-CDI have betaine-type electronic structure, *i. e.*, they cannot be represented by any classic Lewis formula that cancels charge separation between both fragments.^{6,9} Accordingly, such molecules share many properties in common with anionic amidinate ligands,¹⁰ widely used in Coordination Chemistry and Catalysis; however,

NHC-CDI also resemble classic nitrogen-donor chelates such as α -diimines in their electroneutral character and their 3D configuration.^{2a} Surprisingly, the coordination chemistry of NHC-CDI adducts remains an essentially unexplored territory.¹¹ In 2016, some of us reported the first study on the coordination of NHC-CDI betaines, describing their terminal and bridging coordination modes in Cu(I) complexes.^{2,3} The dipolar nature of NHC-CDI's leads to significant differences in their behaviour with their neutral or anionic counterparts. We herein show that the reaction of a representative example (**L**, with NHC = *N,N'*-dicyclohexylimidazolidene and CDI = di-*p*-tolylcarbodiimide), with zinc dichloride led us to discover a peculiar coordination situation and, simultaneously, a remarkable case of dichloromethane activation that hints at the exceptional properties of these betaine zwitterions as powerful and highly selective nucleophiles with potential applications as a new type of electro-neutral organic superbases.¹² The results of our investigation are summarized in Scheme 1.

Scheme 1. Outcome of the reactions of **L** with ZnCl₂ and dichloromethane under different conditions.

We began our work studying the reaction of ZnCl₂ with **L** in dichloromethane-*d*₂ (Fig. 1, spectra A-C). The reaction turned out to be very slow at room temperature, despite the strong basicity of **L** (A), but after four days the ¹H NMR spectrum showed evident changes (B). In addition to the signal for the starting material, **L** (δ 4.55 ppm), two new multiplets of comparable intensity were observed at δ 3.66 and 3.44 ppm in the region of the

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[§] Dedicated *in memoriam* to the late Prof. Pacual Royo.

diagnostic cyclohexyl methyne signal ($C1H_{Cy}$). After six days (C), that of **L** had dropped to less than 20 % of its original intensity, and those of the products changed their relative ratio to almost 1/2, confirming that these correspond to two independent species, **1** and **2**. Eventually, some crystalline material was noticed. Although crystals quality was not good enough to provide an accurate crystal structure, a preliminary resolution sufficed to identify discrete $[ZnCl_4]^{2-}$ and $[ZnL_3]^{2+}$ ions. This material proved insoluble in dichloromethane, preventing us to establish its relationship with **1** or **2**, but a fortunate incident took place which speeded up our investigation.

Figure 1. A–C: 1H NMR spectra of a solution of **L** with $ZnCl_2$ in CD_2Cl_2 after 2h (A), 4 days (B) and 6 days (C). D: Spectrum of an isolated sample of **2·Cl** (chloride salt, **2·Cl**). Signals marked in red for **1** and blue for **2**.

While setting one of these NMR experiments, a CD_2Cl_2 solution of **L** that had been lying in the glove box for about a week was unintendedly used instead of a freshly prepared one, and $ZnCl_2$ was added to it. The 1H NMR spectrum of the mixture showed that the higher field $C1H_{Cy}$ resonance at δ 3.44 ppm was prevalent. Allowing this solution to rest undisturbed for eight days resulted in the formation of well-shaped, pale yellow blocks that were collected and submitted for an X-ray diffraction study (Figure 2). Also this crystal structure showed an ionic compound, but in this case the zinc content is limited to the binuclear dianion $[Zn_2Cl_6]^{2-}$ counterbalanced by the metal-free dication **2**, that turned out to be a methylene-bridged aminal resulting from the displacement of both chlorine atoms from dichloromethane by two molecules of **L**, *i. e.* the $[L_2CD_2]^{2+}$ dication. As far as we know, this type of reactivity is unprecedented for any other NHC adducts, or even NHC themselves. Although the dication has no

Figure 2. ORTEP view (30% probability ellipsoids) of **2·Zn₂Cl₆**. Hydrogen bonds are shown as dotted lines.

crystallographically imposed symmetry, both amidine units, $N(Ar)-C=N(Ar)$, adopt the *E,E* configuration (with regard to the C–N bonds), different from the *Z,E* stereochemistry preferred by the free betaine. This conformation is favoured by the existence of intramolecular $CH\cdots N$ hydrogen bonds. The $Zn_2Cl_6^{2-}$ anion is also engaged in a network of $Cl\cdots H-C$ contacts with the imidazole rings protons that directs the crystal packing (see SI).

Solid samples of the organic chlorozincate salt are soluble enough in CD_2Cl_2 to record a reasonable quality 1H NMR spectrum. This pointed out the link with **2** (spectrum D in Figure 1 corresponds to the chloride salt **2·Cl**, see below), the species responsible for the $C1H_{Cy}$ signal at δ 3.44 ppm, implying that **1** ($C1H_{Cy}$ at δ 3.66) would stem from the Zn-containing species. Discounting the signals of free **L** and **2** from the 1H NMR spectra B or C in Figure 1 allows the assignment of the main signals of **1** (red arrows). The spectrum of **1** is very simple. Not only it has a single type of imidazolium fragment, but the *p*-tolyl groups are also equivalent. This suggests that **1** is a highly symmetrical species in solution.

In order to generate complex **1** in a selective fashion, we carried out the reaction of **L** with $ZnCl_2$ in bromobenzene, a non-coordinating solvent that is more resistant towards nucleophilic attack than dichloromethane, but at the same time polar enough to favour the interaction of both reagents. Reasonably good quality crystals of composition **1·ZnCl₄** were obtained when **L** and zinc chloride (3:2 ratio) were dissolved in hot (80 °C) bromobenzene and the mixture was allowed to cool undisturbed. As shown in Figure 3, the crystal structure shows that the metal centre in the $[ZnL_3]^{2+}$ cation is in a distorted tetrahedral environment generated by three betaine ligands, one of them coordinated as a slightly unsymmetrical chelate with somewhat dissimilar Zn–N bonds, 2.119(5) (Zn–N1) and 2.150(5) Å (Zn–N2).

Figure 3. ORTEP view (30% probability ellipsoids) of **1·ZnCl₄·8PhBr**. Long range Zn–N interactions are shown as dot lines.

The other two ligands bind in monodentate fashion, with significantly shorter Zn–N bonds (Zn–N11, 1.969(4) and Zn–N14, 1.972(5) Å). These are in the normal range of Zn–N covalent, non-dative interactions. However, in contrast with other metal complexes with monodentate NHC–CDI's,^{2,11} where the aryl rings adopt the *Z,E* configuration like in free ligand, those in the $[ZnL_3]^{2+}$ cation display both tolyl groups in *syn* with regard to the imidazolium group. This leaves the pending nitrogen atoms pointing towards the metal centre as if there were weakly

attractive interactions. Even though the distances (*ca.* 2.65 Å) are probably too long to allow any significant covalence, representations of comparable Zn...N contacts as if meaning some type of bond are not infrequent in the literature.^{13,14} At least in one of those compounds reported, studies of the experimental electron density data from accurate X ray studies at low temperatures showed that long-range Zn...N interactions may behave as actual chemical bonds.¹⁴ At any rate, the configuration of ZnL₃²⁺ should facilitate the intramolecular exchange between mono- and bidentate modes of **L**. In solution, this process would lead to the dynamic averaging of the terminal and chelate roles of **L**, consistent with the apparent symmetry of the ¹H NMR spectrum of **1** spectrum in CD₂Cl₂. In this case, the coordination mode of the “monodentate” betaine ligands should be more accurately regarded as a *highly unsymmetrical* chelate, and the Zn geometry would be in the way from tetrahedral to pseudooctahedral (C_{3v}).

We initially supposed that the Lewis acidic ZnCl₂ might be assisting **L** in the nucleophilic activation of dichloromethane through a “frustrated Lewis pair” (FLP) effect,¹⁵ but the preferential formation of **2** from “aged” solutions of **L** in CD₂Cl₂ suggests that **L** does react with CH₂Cl₂ in the absence of ZnCl₂, and then the latter traps the chloride as [Zn₂Cl₆]²⁻. Dichloromethane is the solvent of choice in the purification and characterization of NHC-CDI adducts, hence the reaction of **L** with CH₂Cl₂ must be very slow at room temperature, otherwise it would have been detected before. Therefore, we monitored the evolution of solutions of pure **L** in CD₂Cl₂ over one week, in the absence of zinc chloride. As anticipated, **L** reacts slowly with dichloromethane to afford the chloride salt of the methylene-bridged product, **2·Cl**, with no detectable intermediates. As the product is soluble in dichloromethane, only the slow fade of the bright yellow colour of **L** would visibly delate that some change is taking place. The ¹H NMR spectrum of **2** is mostly independent of the counteranion, except for the imidazolium methyne resonance, that appreciably drifts as Cl⁻ is replaced by [Zn₂Cl₆]²⁻. At 60°C, in a PTFE-valved tube, the reaction is complete in less than 24 h without any appreciable selectivity loss. The all-H version of **2·Cl** was also obtained in a similar fashion using CH₂Cl₂ as the solvent, and both isotopologues (containing [CD₂L₂]²⁺ or [CH₂L₂]²⁺) were fully characterized using the usual ensemble of spectroscopic NMR, IR, ESI-MS and elemental analysis. A crystal structure confirmed definitely the identity of **2·Cl**, but its quality was lower than that of **2·Zn₂Cl₆**, due to the presence of a large number disordered solvent molecules in the crystal cell (up to 13, see SI). Interestingly, the stereochemical configuration of the organic cation is identical in both the chloride and chlorozincate derivatives.

In addition, we found that **L** reacts with other common polychloroalkane solvents, such as chloroform or 1,2-dichloroethane, but promoting HCl elimination in both cases to yield imidazolium-2-amidine chloride (HL⁺·Cl⁻; see SI for characterization data and an X-ray structure). The reaction is highly selective with 1,2-dichloroethane, leaving a residue of pure HL⁺·Cl⁻ when the solvent is evaporated. Vinyl chloride is the only organic product detected by GC-MS. In contrast, chloroform leads to less pure,

dark red-brown solutions, as the primary elimination product is probably the unstable dichlorocarbene (:CCl₂).

As mentioned before, formation of cation **2** is a very unusual reaction. It is known that some secondary aliphatic,¹⁶ alicyclic¹⁷ or heteroaromatic¹⁸ amines perform similar substitution reactions but these usually requires using special conditions (e. g., very high pressures, or highly polar solvent mixtures under phase transfer conditions). Since few mechanistic studies have been reported for such reactions,¹⁹ we built a DFT model of the reaction using a slightly simplified version of the betaine (**L**, see SI for details). This is shown in Scheme 2, along with free energies (ΔG° or ΔG‡, at 298 K) relative to the reactants (2 **L**_{ZE} + CH₂Cl₂). In accordance with the experimental observations, the initial S_N2 attack of the betaine on dichloromethane is the rate determining step (RDS). The energy barrier is reduced by 3 Kcal·mol⁻¹ if **L** rearranges from the usual *Z,E* into the slightly less stable *E,E* conformer (**L**_{EE}). The computed barrier, 28.0 kcal·mol⁻¹, is in excellent agreement with the experimental value given above (27.8 Kcal·mol⁻¹ at 40 °C). TS1_{EE}, a typical S_N2 transition state, leads to the reactive chloromethyl intermediate **LCH₂Cl**⁺. Since all steps after RDS are hidden to kinetic measurements, we investigated some alternatives to S_N2, such as intramolecular assistance by the pending amidine functionality (yellow lines; relative barriers from the chloromethyl intermediate given in italics), but the barrier for this mechanism (*c*-TS2⁺) would be considerably higher. Actually, the second S_N2, is so facile that in TS2⁺_{ZE} the C...Cl bond is half undone, whilst the C...N bond with the entering group is still incipient (bond orders 0.46 and 0.21, respectively). The lability of the C-Cl bond in the chloromethyl intermediate [**LCH₂Cl**]⁺ is due to the capacity of the amidine unit to pour electron density into the *p_z* orbital of the CH₂ carbon atom (the order for the “spectator” C-N bond increases to 1.44 in TS2⁺_{ZE}). Although an early S_N2 transition state is reminiscent of a carbocation mechanism, a pure S_N1 mechanism can be ruled out, as the carbocation is a high energy species, too (green box).

Scheme 2. Computational DFT model (ω-B97X-D/6-311++G**//PBE-CPCM/6-31G*) for the reaction of a simplified betaine (**L**) with dichloromethane, and the structures of TS1_{EE} and TS2_{ZE} with some relevant bond distances (Å, plain font) and Löwdin bond orders (italics, in parentheses). Free energies (ΔG, bold font) are relative to the reactants or to **LCH₂Cl**⁺ (in parentheses).

In summary, two competitive reactions were observed when the NHC-CDI betaine **L** was reacted with ZnCl₂ in

dichloromethane, namely, coordination to Zn and C-Cl activation. Both processes are independent, as such, the reaction of **L** with dichloromethane proceeds cleanly in the absence of ZnCl₂, to yield the unusual methylene-bridged aminated **2** in high yield. On the other hand, the reaction of **L** with zinc chloride in bromobenzene allowed the isolation of crystalline samples of **1** in the form of an ionic chlorozincate salt of the homoleptic [ZnL₃]²⁺ dication. These findings highlight the enormous potential lying in NHC-CDI adducts as neutral organic superbases, nucleophilic organocatalysts, and ligands.

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