

Acyl Protection Strategy for Synthesis of a Protic NHC Complex via N-Acyl Methanolysis[†]

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Summary: In a new strategy for the synthesis of protic NHC complexes, iridium and rhodium complexes of N-benzoylsubstituted NHCs are first generated by direct deprotonation of an acyl-protected imidazolium salt. Deprotection of the acyl group with methanol then gives methyl benzoate and the protic NHC. This sequence represents a new strategy for the synthesis of protic NHC complexes. We expect this strategy to have useful generality.

Introduction

N-Heterocyclic carbene (NHC) ligands show a wide range of electronic and steric variability that makes them wellsuited for applications such as homogeneous catalysis.¹ Despite the wide variety of N-substitutions in the imidazolederived ligand scaffold that has been investigated, a limited number of examples of the parent N-H substitution have been reported.² This is chiefly because the free protic NHC rapidly tautomerizes to the stable azole, and thus indirect methods are needed for the synthesis of protic NHC complexes. Protic NHC ligands tend to be "noninnocent" in certain cases, undergoing C-N tautomerization,^{2b,c} or a 1,3 ligand-to-metal hydrogen shift,³ or a deprotonation to form an anionic aryl ligand.^{2d} In other cases they can be stable, in which case the N-H group may confer advantages in homogeneous catalysts. Ruiz et al.^{2g} have recently reported two new methods for the generation of protic NHC ligands assisted by coordination of the precursor species to manganese(I). One of them implicates the coupling of isocyanides with propargylamines, and the other is based on tautomerization of N-coordinated imidazoles.

A systematic study of these intriguing ligands has been hampered by the paucity of methods available for their synthesis. Traditional metalation of imidazolium salts typically

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requires basic conditions, which is incompatible with the acidic N-proton of a protonated salt. As a result, the methods that are known for the synthesis of protic NHC complexes are indirect and specific to particular ligand scaffolds or metal precursors. We thought that the removal of a protecting group at nitrogen would, after metalation, afford a more general route to protic NHC metal complexes. C-N bond cleavage to form protic NHC ligands has been reported with heterogeneous conditions (silica gel)^{2c} and via a carbenemediated process;^{2b} however the mechanisms of these reactions are not yet well understood, and their generality is not yet determined. There is also precedent for a Si-N bond cleavage to form a protic NHC complex.^{2f}

Our efforts focused on the use of a benzoyl-substituted imidazolium salt as an NHC precursor. Acyl imidazolium salts are potent electrophiles and can be utilized as stoichiometric acylating agents.⁴ Though they formally contain amide bonds, these species do not show the deactivating resonance of normal amides due to the contribution of the imidazole ring. Thus, these salts react rapidly and irreversibly with a wide range of mild nucleophiles, including water and methanol, generating N-protonated imidazolium salts.

We outline a synthetic strategy that allows for the synthesis of monodentate protic NHC complexes (Scheme 1). The approach utilizes N-acyl imidazolium salts as NHC ligand precursors, allowing for straightforward metalation of the ligand and C-N bond cleavage upon exposure to nucleophilic solvent to form the protic species.

Results

Ligand Synthesis and Metalation. Acvl imidazolium salts can be generated by reaction of an acyl imidazole with a strong alkylating agent⁵ or alternatively by addition of an acid chloride to an N-substituted imidazole.⁶ We found that the salt 2 can be isolated in good yield from reaction of imidazole 1 and trimethyloxonium tetrafluoroborate (Meerwein's salt) (Scheme 2). Salt 2 was chosen for this study principally because it could be easily isolated and crystallized as a white solid. The dicarboxylic ester functionality was originally selected in connection with other work, not reported here, in which attachment of the catalyst to a metal oxide surface was intended. Though 2 is moisture sensitive, it can be stored in anhydrous conditions for short periods. Single crystals of 2 were grown and subjected to X-ray crystallographic analysis (Figure 1). The benzoyl substitution is oriented away from

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the benzimidazole ring, with the carbonyl oxygen in close proximity (2.561 Å) to an aromatic benzimidazole hydrogen. Since this seems contrary to the steric preference of the system, a dipole-dipole interaction between the C=O and C=N bonds may be responsible for the conformations.

Because benzoyl imidazolium salts react rapidly with nucleophiles, only the non-nucleophilic base lithium bis(trimethylsilyl)amide (LiHMDS) was suitable for metalation. **2** reacts with commercially available [Ir(cod)Cl]₂ in the presence of LiHMDS to provide the neutral iridium species **3**. The analogous rhodium compound **4** can be generated using [Rh(cod)-Cl]₂ and LiHMDS under similar reaction conditions (Scheme 3). These seem to be the only reported iridium or rhodium complexes that contain an NHC with N-acyl substitution. There is precedent for generation of a gold(I) N-benzoyl NHC complex by treatment of a trimeric Au-imidazole species with benzoyl chloride.⁷ Additionally palladium(II) N-carbamoyl NHCs have been reported.⁸

The reactions of Scheme 3 are performed in dichloromethane, in which the benzimidazolium salt is only sparingly soluble. Upon addition of a hexane solution of LiHMDS to the reaction suspension, a vivid color change occurs at once: the iridium reaction darkened from yellow to dark brown, while the rhodium reaction changed from yellow to green upon base addition. In both cases the suspension becomes a yellow-orange homogeneous solution as the salt is metalated. This color change occurs in the absence of the imidazolium salt and thus may arise from adduct formation between the base and the metal precursor. The adduct then slowly reacts with the azolium salt to form the NHC complex. However, we could not isolate or characterize this adduct, so its nature remains unknown.

Properties of Benzoyl NHC Complexes. The resulting complexes **3** and **4** are air stable both in the solid state and in solutions of non-nucleophilic solvents. X-ray crystallographic analysis of **3** shows that the benzoyl wingtip has a very similar orientation to that seen in the free benzimidazolium salt (Figure 2). Comparing the free salt with the coordinated NHC (Table 1) shows that the bond distances of the salt are only slightly modified by metalation; the lengths of the C–N and C–O bonds of the benzoyl substitution do not change more than 0.01 Å. On the basis of bond lengths, the coordinated N-benzoyl NHC appears to maintain the weak amide resonance seen in the free salt, contributing to the strong electrophilicity of the acyl in this species.

To estimate the relative electron donor character of the benzoyl-substituted NHC versus other NHC ligands, we



metalate

)∕⊕ N

XΘ

functionalize

synthesized the NHC-Ir(CO)₂Cl species **5** by treating complex **3** with 1 atm of carbon monoxide for several minutes in dichloromethane (Scheme 4). The carbonyl stretching frequencies (ν (CO)) found in the infrared spectra of complexes of this type are a measure of electron donor power that closely correlates with the Tolman LNi(CO)₃ scale.⁹ The average stretching frequency of the symmetric and asymmetric carbonyl peaks for **5** is 2025.7 cm⁻¹. For comparison, the 1,3-dimesitylimidazolidin-2-ylidene (SIMes) carbene ligand has a ν (CO)^{av} of 2024.6 cm⁻¹ on the NHC-Ir(CO)₂Cl scale.^{9c}



Figure 1. ORTEP diagram of 2 with 30% probability ellipsoids.



Figure 2. ORTEP diagram of **3** with 30% probability ellipsoids. Selected bond lengths (Å): Ir(1)–C(1) 1.999, Ir(1)–Cl(1) 2.368, N(1)–C(3) 1.439, N(1)–C(1) 1.373, N(2)–C(1) 1.347, N(2)–C (2) 1.435, C(3)–O(1) 1.212.

Scheme 3. Metalation of an N-Benzoyl Benzimidazolium Salt





Protic NHC

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Table 1. Comparison of Bond Lengths in the Free Salt versus the Coordinated NHC Species



bond	length in salt (Å)	length in complex (Å)
а	1.470(4)	1.434(9)
b	1.313(5)	1.346(9)
с	1.345(4)	1.372(9)
d	1.448(5)	1.438(9)
e	1.205(5)	1.211(8)

Scheme 4. Formation of a Benzoyl NHC Bis-carbonyl Complex



Generation of a Protic NHC Species. An insoluble airsensitive purple solid precipitated from a methanolic suspension of complex 3 over several days under inert atmosphere. The ¹H and ¹³C NMR of this material indicate a bound 1,5cyclooctadiene, and a downfield ¹³C chemical shift (192.09 ppm, CDCl₃) is assigned to an iridium(I) NHC species (see Supporting Information). The benzimidazole ring resonances are present, but not those of the benzoyl protecting group. The resulting solution contains methyl benzoate, consistent with the expected C-N bond cleavage. We propose this material is the neutral protic NHC complex, despite the absence of an N-H proton signal in the NMR spectra, which could be diminished in intensity due to broadening and H-D exchange. This material has thus far resisted rigorous purification or X-ray crystallographic analysis, so we looked for possible derivation that would be tractable.

Iridium(I) complex **3** can be treated with a phosphine and a noncoordinating anion to form a cationic species. Addition of tricyclohexylphosphine to complex **3** was unsuccessful, however, presumably due to the steric constraints. Triphenylphosphine can be employed in the presence of KPF₆ to generate **6**, which is stable in air and in solution for extended periods.

Dissolution of N-acyl species **6** in methanol immediately affords an equivalent of methyl benzoate and protic Nheterocyclic carbene complex **7** (Scheme 5). Unlike the cationic benzoyl NHC complex, the protic NHC complex is air sensitive in solution. In the ¹H NMR spectrum for this complex the N-H proton exhibits a singlet at δ 10.89 ppm

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(CDCl₃), a value consistent with reports of other imidazolylbased protic NHCs.^{2c,d} When the bond cleavage is performed in deuterated methanol, the resulting material is identical by ¹H NMR except for a reduction in intensity of the N-H signal. A broad band in the infrared spectra for this species at 3380 cm⁻¹ is consistent with literature values for an N-H stretch.³

The crystal structure of 7 confirms the loss of the benzoyl substitution on the carbene ligand (Figure 3). The N-H proton was located in the difference density map and refined isotropically without geometric restraint. Its presence may additionally be inferred from the charge balance of the overall structure together with the NMR and IR data. The PF₆ anion is moderately disordered. The closest N-H····F-P distances of 2.285 and 2.365 Å are consistent with a weak interaction. The metal-carbon bond length (2.004 Å) is consistent with ligand carbene character and largely unchanged from the bond length of the parent neutral complex **3** (1.999 Å).

Discussion

Li and co-workers find phenanthroline-based protic NHC complexes of iridium(I) can give a 1,3 hydrogen shift from N to Ir to give an aryl metal hydride.³ Such a shift is not apparent for this cationic species; no iridium hydride signals were detected in the proton NMR spectra in CDCl₃ or CD₂Cl₂.

The mechanism of the C-N bond cleavage may be analogous to the hydrolysis of acyl imidazolium salts. Studies on acid-catalyzed N-acyl imidazole hydrolysis suggest that metal ions are capable of enhancing the reaction rate;¹⁰ no data on metal-mediated acyl imidazolium bond cleavage could be found in the literature. We have no evidence that metalation affects the electrophilicity of the acyl imidazolium cation. Transient carbonyl coordination to the metal center is conceivable; the d⁸ square-planar geometry predominates, but five-coordinate 18-electron iridium(I) species are also known.³ However, attempts to form an NHC-O chelate by addition of silver salts of noncoordinating anions to complex 3 resulted in decomposition. The bond lengths of the amide C-N and C-O bonds are largely unchanged once metalation has occurred, suggesting that the benzoyl group remains a good electrophile despite deprotonation and coordination. We therefore believe this type of bond cleavage may be a useful general route.

Suprisingly, an N-carbamoyl NHC reported in 2002 was described as being hydrolytically stable (Figure 4).⁸ In this case, the carbonyl carbon is flanked by two nitrogen atoms, one in the imidazole ring and the other in a saturated pyrrolidine ring. The key difference from our case is that the lone pair from the saturated nitrogen promotes usual amide resonance and stabilizes the carbonyl against nucleophilic attack. Bond lengths for this species are consistent with this proposal: a C–N bond length of 1.335 Å is reported from the carbonyl carbon to the nonaromatic nitrogen, which is characteristic of a normal amide species.

Our protic NHC complexes are air sensitive in solution, whereas the benzoyl NHC cationic complex is stable in solution for several days. Buriak and co-workers also reported that several cationic complexes of type [(cod)Ir(NHC)(PR₃)]-PF₆ lacking N-H substitutions are insensitive to air in solution.¹¹

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Scheme 5. Formation of Cationic Benzoyl and Protic NHC Complexes



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to the traditional N-alkyl and -aryl-substituted salts. The resulting species are stable but cleave upon exposure to nucleophilic MeOH solvent to provide the protic NHC complex.

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Supporting Information Available: Experimental procedure and NMR spectral data for all compounds, including the methanolysis of complex **3**. X-ray crystal data for **2**, **3**, and **7**. This material is available free of charge via the Internet at http:// pubs.acs.org.



The protic NHC ligand thus promotes air sensitivity by an unknown mechanism.

Conclusion

We present a synthetic strategy for the synthesis of protic NHC species via benzoyl N-heterocyclic carbene intermediates. Our N-benzoyl NHCs can be prepared by deprotonation