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Synthesis of NHC-Iridium(III) Complexes Based on *N*-Iminoimidazolium Ylides and Their Use for the Amine Alkylation by Borrowing Hydrogen Catalysis

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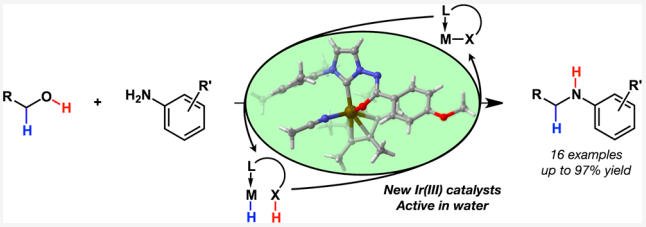
ABSTRACT: Anionic NHC ligands recently developed in our group, derived from *N*-iminoimidazolium ylides, were used to synthesize NHC-iridium(III) complexes. Their catalytic activities were evaluated in the amine alkylation of anilines using borrowing hydrogen catalysis. The high-yielding synthesis of a small library of complexes allowed a rapid screening of the ideal steric bulk of the NHC unit and basicity of the anionic tether for the investigated model reaction. A bulky aromatic *N* group on the imidazolidene moiety is required to achieve high catalytic activity, and the latter is proportional to the basicity of the anionic group. A selected substrate scope of the reaction was performed, providing fair to excellent yields of the desired alkylated anilines.

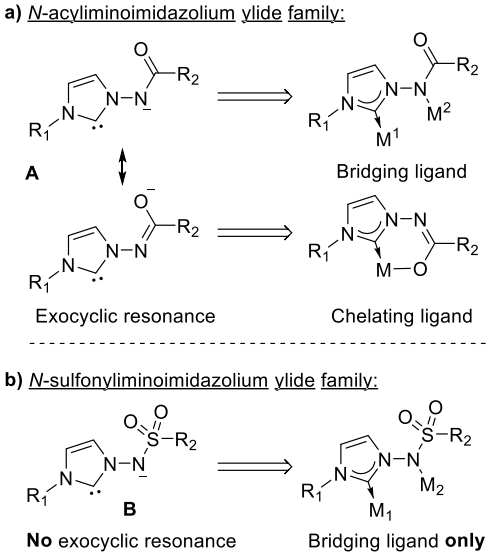


INTRODUCTION

Ligand design in organometallic chemistry has contributed deeply to the development of powerful methodologies now considered staple tools for any synthetic chemist.[1] Notably, the development of *N*-heterocyclic carbenes (NHCs) as potent L-type ligands had a tremendous effect on homogeneous catalysis.[2] They can be easily synthesized and provide a wide range of steric and electronic properties. They tend to provide strong σ donation and important steric shielding, resulting in complexes with higher stability to light and moisture in comparison to their phosphine counterparts.[3] NHCs can also present various additional functions that can be modified to obtain exquisitely tailored ligands for specific tasks.[4] In this class, anionic NHC ligands have shown great potential. Due to their hard and soft ligation sites, they can provide complexes which are more stable than those of their neutral counterparts with specific metals.[5] Their chelation potential was also exploited to access high stereoinduction in stereoselective methodologies.[6]

Our group has been involved in ligand design, and we previously have reported two families of anionic NHC ligands based on *N*-acyliminoimidazolium ylides (**A**)[7] and *N*-sulfonyliminoimidazolium ylides (**B**).[8] The unique properties of **A** revolve around the delocalization of the negative charge in the exocyclic group (Scheme 1a). In contrast, this delocalization is prevented in the case of **B** (Scheme 1b).[9] We were to use this tunable parameter to achieve topological control in metal complex formation. Our goal is now to investigate the behaviors of these unique anionic groups in cooperative catalysis,[10] to ultimately develop synthetic methodologies with lower environmental impact.[11] In this context, we found the

Scheme 1. Binding Mode Attainable with the *N*-Iminoimidazolium Ylides



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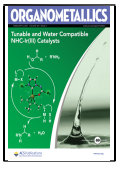

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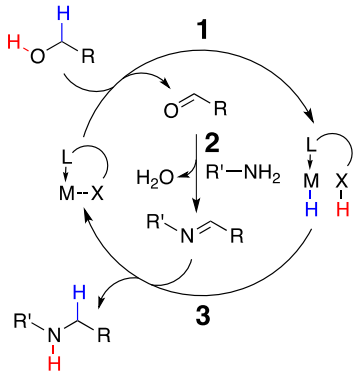
concept of borrowing hydrogen catalysis (BHC) especially appealing, as it allows for complex synthetic transformations with minimal steps and maximum atom economy.[12]

In this type of chemistry, the *N*-alkylation of amines using BHC is particularly important, as it provides fast access to useful intermediates for the pharmaceutical industry.[13] Complex *N*-alkylated amines can be formed from abundant and readily available alcohol substrates, with only water as a byproduct. This approach thus greatly reduces the environmental impact of such transformation, in comparison to classical reductive amination.[14] This strategy calls for cooperation of the metal center and the ligand and has three steps (Scheme 2): (1) oxidation of an alcohol moiety by the

Scheme 2. Amine Alkylation Using Borrowing Hydrogen Catalysis



metal center, (2) bond formation between the resulting carbonyl intermediate and a coupling partner (e.g., amine, enolate), and (3) reduction of the coupling product by the hydrogenated complex, regenerating the active catalyst.

Numerous ligand scaffolds have been explored to achieve this transformation. They have relied on various elements, from heavier metals (Ir,[15] Ru[16]) to first-row transition metals (Ni,[17] Co,[18] Fe,[19] Mn[20]). More recently, enantioselective,[21] solvent-free,[22] and aqueous reactions[23] variants have been developed. Two representative NHC-based iridium(III) complexes that were found to be efficient catalysts for the amine alkylation by BHC are presented in Figure 1. Complex

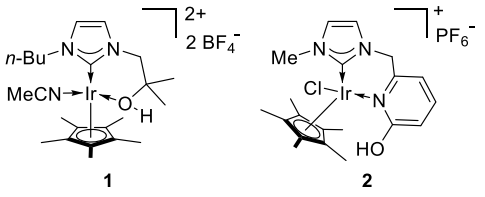


Figure 1. Representative NHC-based iridium(III) catalysts.

1, reported by Martín-Matute and co-workers,[15b] allows access to various alkylated amines in excellent yields, even at the low temperature of 50 °C. The water-soluble complex **2**, reported by Ke and co-workers,[23d] was found to promote amine alkylation in water.

As illustrated in Scheme 2, an LX-type functional ligand is of particular interest for this type of cooperative catalysis. We envisioned that our ylide-derived anionic NHC ligands presented all the required characteristic to form complexes able to undertake this type of catalysis. We focused our investigation on iridium-based complexes, as these types of catalysts have a wide diversity of applications.[24,25] Hence, we report herein the synthesis of a variety of new iridium(III) complexes based on the *N*-iminoimidazolium ylides and the evaluation of their catalytic properties in the face of their steric and electronic properties, as well as a selected scope study using the optimal catalyst.

RESULTS AND DISCUSSION

Proligand Synthesis. We focused on the formation of a small library of ylide proligands that would provide a good exploration of the steric and electronic properties of both the NHC unit and the anionic tether, respectively. To explore the effect of delocalization on the exocyclic anionic group, we synthesized proligands from both the *N*-acyl- and *N*-sulfonyliminoimidazolium ylide families. They are easily synthesized in two steps from the corresponding imidazoles. The synthesis of salts **5** is performed by electrophilic amination of the corresponding imidazoles, using the reagent *O*-(2,4-dinitrophenyl)hydroxylamine (**4**; H_2NODNP).[26] The method provides high yields of the *N*-amino salts ($DNPO^-$ = 2,4-dinitrophenolate) for a variety of imidazoles (Scheme 3). These salts were converted to the desired *N*-acyliminoimidazolium ylides by reaction with numerous electrophiles; the results are summarized in Table 1.

Scheme 3. Synthesis of *N*-Aminoimidazolium Salts

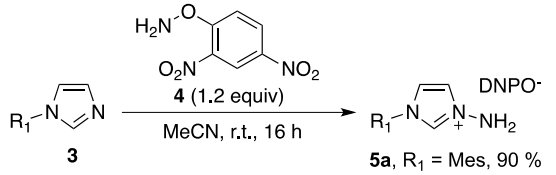
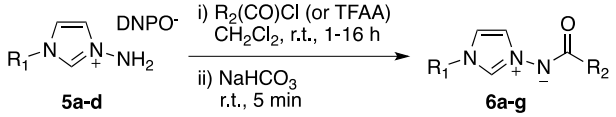


Table 1. Synthesis of *N*-Acyliminoimidazolium Ylides



entry	R_1	R_2	ylide	yield (%)[a]
1	Mes	CF_3	**6a**	100[b]
2	Mes	Ph	**6b**	95
3	Mes	4-OMe-C_6H_4	**6c**	94[c]
4	Mes	OEt	**6d**	39[d]
5	Ph	Ph	**6e**	100
6	*n*-Bu	Ph	**6f**	79
7	*t*-Bu	Ph	**6g**	84

[a]Isolated yield. [b]Reaction performed using TFAA as the electrophile. [c]Reaction performed on a 2.6 mmol (1 g) scale. [d]The electrophile (ethyl chloroformate) was used as the solvent.

This convergent synthesis provides rapid access to a variety of proligands in usually good yields. The reaction is portable to the gram scale (Table 1, entry 3). One exception was observed for the formation of the carbamate-derived ylide **6d**. In this case, the usual reaction conditions proved to be unsatisfactory, as no desired ylide was isolated.

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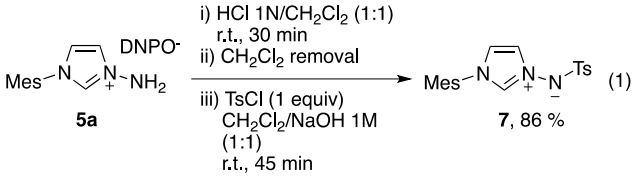
Fortunately, conditions using ethyl chloroformate as the solvent and a reaction time of 16 h gave the desired product with 39% yield (Table 1, entry 4). These ylides were selected to explore the steric effect of the imidazole R_1 group as well as evaluate the influence of the basicity and binding mode of the exocyclic anionic group on the catalytic activity of the resulting complexes in the borrowing hydrogen methodology.

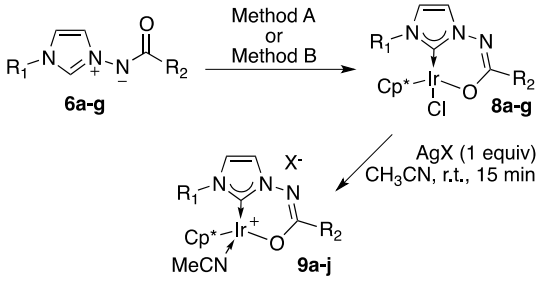
Four R_1 groups were selected (*n*-Bu (**6f**), *t*-Bu (**6g**), Ph (**6e**), and Mes (**6a**)), as they represent aromatic and aliphatic groups with widely different steric profiles. For these ylides, the benzoyl group (R_2 = Ph) was selected as a reference on the exocyclic anionic tether. To modulate the basicity of the anionic tether, four R_2 groups (CF_3 (**6a**), Ph (**6b**), 4-OMe-C_6H_4 (**6c**), and OEt (**6d**)) were selected. For these ylides, 2,4,6-trimethylphenyl (Mes) was selected as a reference R_1 group, due to the ease of access and purification of the resulting ylides. Finally, we synthesized the *N*-sulfonyliminoimidazolium ylide **7** (eq 1), to evaluate the effect of charge localization of the negative charge on the exocyclic nitrogen.



Synthesis of Iridium Complexes. We have previously reported that silver complexes from the corresponding *N*-iminoimidazolium ylides are efficient ligand transfer agents to halogenated transition metals.[7,8] Consequently, we investigated their use for the synthesis of the necessary iridium(III) complexes; the results are illustrated in Table 2. Their characterization and purity were established by ^{1}H NMR and ^{13}C NMR spectroscopy and by HRMS.

The silver complexes are fairly stable to light and moisture, but they tend to degrade slowly over time. For this reason, the crude silver complexes were used directly for the transmetalation step. Adding the commercially available pentamethylcyclopentadienyliridium(III) chloride dimer ($[Cp^*IrCl_2]_2$) to a solution of the crude silver complexes provided in most cases the desired NHC-iridium(III) complexes in high yields (Table 2, entries 1−3 and 11). However, this method proved problematic for the synthesis using ylides with less bulky R_1 groups (Table 2, entries 9 and 10), as the resulting silver complexes were insoluble in most organic solvents. Furthermore, while the reaction was functional for the other ylides, the formation of silver complexes took at least 48 h of reaction time. Consequently, we investigated a more direct formation method of the iridium(III) complexes. We envisioned that we could deprotonate the imidazolium ring of the ylides and form the iridium complexes in one pot by addition of the resulting free carbene on the iridium source. Several bases were tested, such as inorganic bicarbonate and carbonate salts, NaH, and triethylamine. Unfortunately, they all resulted in only low conversions of the ylides to their iridium(III) complexes, making purification difficult. However, we were able to achieve complete conversions using the slow addition of LiHMDS over the ylides at 0 °C. It is theorized that NHC-Li complexes are formed, leading to stable species.[27] To these putative complexes were added $[Cp^*IrCl_2]_2$, yielding the desired NHC-iridium(III) complexes in 2−12 h.

Table 2. Formation of the NHC-Iridium(III) Complexes from the *N*-Acyliminoimidazolium Ylides[a]



entry	R_1	R_2	[Ir]Cl (%)[b]	X	[Ir]X (%)
1	Mes	CF_3	**8a**, 100	SbF_6	**9a**, 90
2	Mes	Ph	**8b**, 100	SbF_6	**9b**, 83
3	Mes	4-MeO-C_6H_4	**8c**, 74 (81)	BF_4	**9c**, 98
4	Mes	4-MeO-C_6H_4		SbF_6	**9d**, 93
5	Mes	4-MeO-C_6H_4		PF_6	**9e**, 98
6	Mes	4-MeO-C_6H_4		TfO	**9f**, 97
7	Mes	4-MeO-C_6H_4		BArF[c]	**9g**, 74
8	Mes	OEt	**8d**, 44	SbF_6	**9h**, 72
9	Ph	Ph	**8e**, 38 (88)	SbF_6	**9i**, 89
10	*n*-Bu	Ph	**8f**, 26 (99)	SbF_6	**9j**, 92
11	*t*-Bu	Ph	**8g**, 81		

[a]Method A: (i) ylide **6a−g** (1 equiv), Ag_2O (1 equiv), $CHCl_3$, rt, 48 h; (ii) crude silver complex (1 equiv), $[IrCp^*Cl_2]_2$ (0.5 equiv), 35 °C, 4 h. Method B: (1) Ylide **6a−g** (1 equiv), LiHMDS 1 M in THF (1.2 equiv), CH_2Cl_2, 0 °C, 1 h; (2) $[IrCp^*Cl_2]_2$ (0.8 equiv), CH_2Cl_2, rt, 24 h. [b]Yields obtained using method A, yields in parentheses obtained using method B, if applicable. [c]BArF = tetrakis[3,5-bis-(trifluoromethyl)phenyl]borate.

The iridium(III) chloride complex **10**, derived from *N*-sulfonyliminoimidazolium ylide **7**, was obtained in good yield using method A described in Table 2 (Scheme 4a). Unfortunately, formation of the cationic analogue **11** using silver hexafluoroantimonate proved problematic, as the reaction provided a complex mixture upon isolation, preventing proper characterization. Furthermore, we were not able to obtain crystals of **10** suitable for X-ray analysis; we thus could not determine the precise mode of binding of the anionic tether. These issues with the isolation of **11** and the structural determination of **10** led us to focus on the investigation of the catalytic activity of iridium(III) complexes derived from ylides **6a−g**.

Due to the experimental challenges in confirming the nature of complex **10**, we resorted to computational chemistry to gain structural insights. We modeled the opened monomer (**10**), chelating monomer (**12a**), the chloride-bridging dimer (**12b**), and the exocyclic nitrogen-bridging dimer (**12c**) using DFT calculations;[28] the results are illustrated in Scheme 4b. The open-form isomer **10** was found to be the thermodynamically most stable species, followed by the chelating monomeric form **12a**. This might seem surprising, but the optimized structure of **10** suggests that the exocyclic nitrogen is providing donation to the iridium center; its representation in Scheme 4 reflects this. While the solvation model does not have a major effect on the relative energies of **10** vs **12a** or **12b**, it strongly affects the stability of **12c**; gas-phase calculations suggest that this dimer is favored by 5.6 kcal/mol.

Most complexes are easily recrystallized, and crystals suitable for X-ray analysis were obtained for iridium(III) chloride complexes **8a−c,e,f**. As expected, all complexes were

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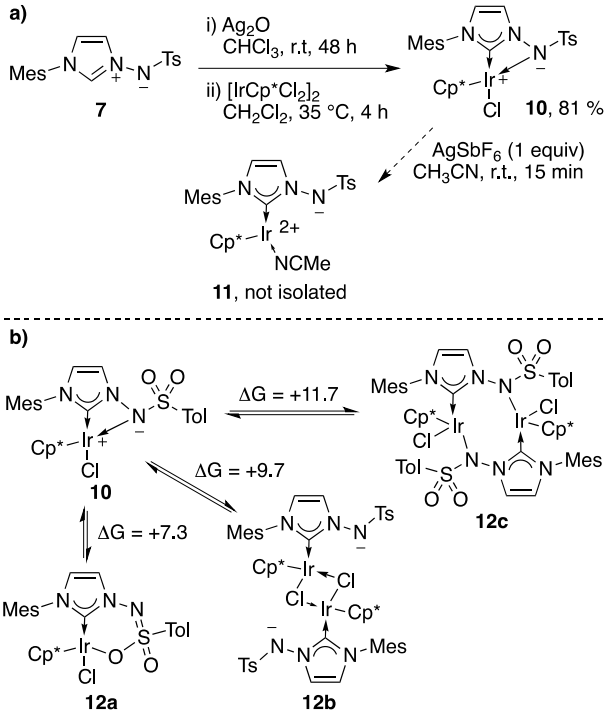
Scheme 4. (a) Synthesis of the NHC-Iridium(III) Complex Derived from 7 and (b) Relative Energies (kcal/mol) of Different Structural States of Complex 10



monomeric in nature and displayed chelation of the anionic NHC ligands.

Interestingly, the geometrical features of all the complexes were very similar, despite the different steric properties of R_1 and the electronic properties of the R_2 group. In particular, almost identical bond lengths on the exocyclic anionic groups were observed between complex **8a** (Figure 2) vs **8b**,**c** (Figures 3 and 4), despite the different expected basicity profiles.

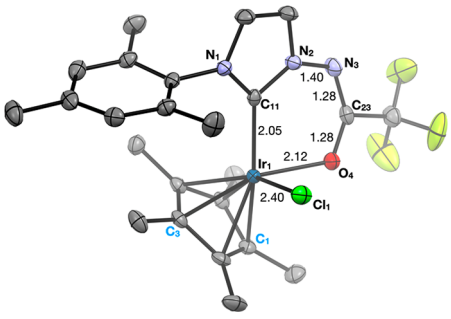


Figure 2. ORTEP plot of complex **8a**. Ellipsoids are drawn at the 30% probability level. Selected distances (Å) and angles (deg): C_{11}–N_1 1.367(3), C_{11}–N_2 1.367(3), N_2–N_3 1.401(3), C_{23}–N_3 1.282(3), C_{23}–O_4 1.276(3), Ir_1–O_4 2.1229(16), C_{11}–Ir_1 2.047(2), Ir_1–Cl_1 2.4031(7), C_{11}–Ir_1–O_4 85.41(8), C_{11}–Ir_1–C_3 118.16(9), O_4–Ir_1–C_1 89.89(8), C_{11}–Ir_1–Cl_1 87.25(6).

The N–N bond lengths of 1.40–1.41 Å are characteristic of single bonds, suggesting mostly no endocyclic resonance in the imidazole ring, meaning that the anionic charge is localized on the exocyclic tether.

As could be expected, the presence of a mesityl group on the NHC introduced steric repulsion with the Cp* ligand. Accordingly, we noticed a fairly large C_{11}–Ir_1–C_3 angle

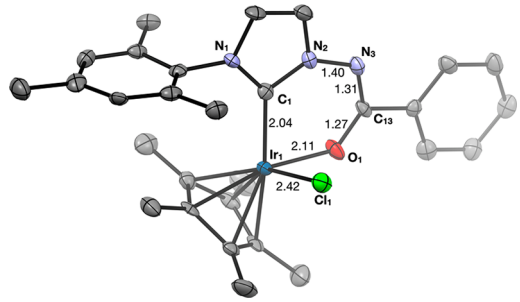


Figure 3. ORTEP plot of complex **8b**. Ellipsoids are drawn at the 30% probability level. Selected distances (Å) and angles (deg): C_1–N_1 1.376(11), C_1–N_2 1.376(10), N_2–N_3 1.403(10), C_{13}–N_3 1.309(11), C_{13}–O_1 1.272(10), Ir_1–O_1 2.113(5), C_1–Ir_1 2.042(8), Ir_1–Cl_1 2.421(2), C_1–Ir_1–O_1 85.7(3).

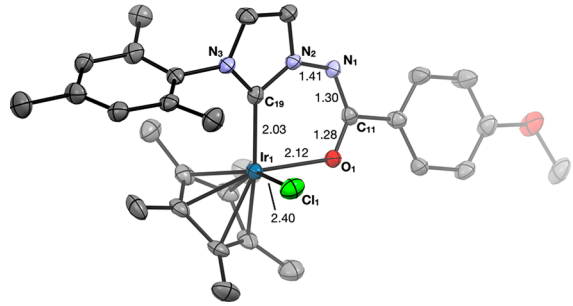


Figure 4. ORTEP plot of complex **8c**. Ellipsoids are drawn at the 30% probability level. Selected distances (Å) and angles (deg): C_{19}–N_3 1.379(6), C_{19}–N_2 1.363(6), N_1–N_2 1.406(5), C_{11}–N_1 1.303(6), C_{11}–O_1 1.282(6), Ir_1–O_1 2.123(3), C_{19}–Ir_1 2.031(5), Ir_1–Cl_1 2.123(3), C_{19}–Ir_1–O_1 84.85(15).

(118.2°) and a much smaller O_4–Ir_1–C_1 angle (89.9°). The chloride atom is also influenced by the Cp* ring, with an observed C_{11}–Ir_1–Cl_1 angle of 87.3°. Similar values were found in complexes **8b**,**c**. The large steric repulsion between the mesityl group and Cp* ligand is further supported by ^{1}H NMR spectroscopy, as the two *o*-methyl substituents on the mesityl group are found to be nonequivalent.

In contrast, when the R_1 group is replaced by a much less bulky *N*-substituent, such as a phenyl moiety in complex **8e** (Figure 5) or a *n*-butyl chain in complex **8f** (Figure 6), we notice numerous structural rearrangements. First there is a

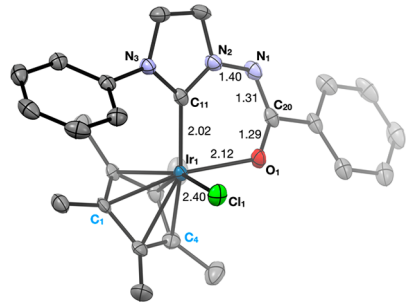


Figure 5. ORTEP plot of complex **8e**. Ellipsoids are drawn at the 30% probability level. Selected distances (Å) and angles (deg): C_{11}–N_3 1.368(4), C_{11}–N_2 1.357(4), N_1–N_2 1.400(4), C_{20}-N_1 1.306(4), C_{20}-O_1 1.288(4), Ir_1–O_1 2.122(2), C_{11}–Ir_1 2.018(3), Ir_1–Cl_1 2.4001(8), C_{11}–Ir_1–O_1 82.88(10), C_{11}–Ir_1–C_1 113.12(12), O_1–Ir_1–C_4 95.10(11).

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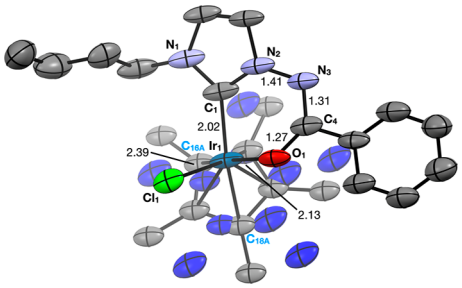


Figure 6. ORTEP plot of complex **8f**. Ellipsoids are drawn at the 30% probability level. The atoms in blue represent the alternative Cp* conformation found in the crystal structure. Selected distances (Å) and angles (deg): C_1–N_1 1.350(9), C_1–N_2 1.361(11), N_2–N_3 1.406(9), C_4–N_3 1.313(9), C_4–O_1 1.288(9), Ir_1–O_1 2.130(6), C_1–Ir_1 2.019(7), Ir_1–Cl_1 2.3867(18), C_1–Ir_1–O_1 81.0(3), C_1–Ir_1–C_{16A} 103.6(4), O_1–Ir_1–C_{18A} 107.0(4).

contraction of the C_{NHC}–Ir bond length. We also see that the Cp* ring repositions itself due to the lesser steric requirements of the N group. This is clearly observed in complex **8e** by inspection at the C_{11}–Ir_1–C_1 (113.1°) and O_1–Ir_1–C_4 (95.1°) angles, in comparison to the values from complex **8a**. This is even more pronounced in complex **8f**, with a smaller C_1–Ir_1–C_{16A} angle (103.6°) and larger O_1–Ir_1–C_{18A} (107.0°) angle. The lack of steric interactions between the *n*-butyl chain and Cp* ligand in **8f** resulted in increased disorder in the position of the ligand in the crystal structure, as illustrated in Figure 6.

Crystals suitable for X-ray analysis of the cationic complex **9d** were obtained by a slow diffusion of pentane into an acetonitrile/MTBE solution of the complex. The structure is reported in Figure 7. It confirms the formation of a cationic

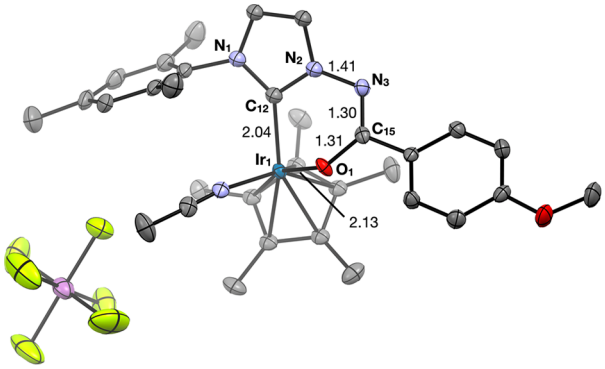
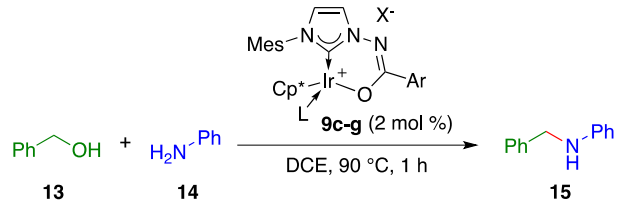


Figure 7. ORTEP plot of complex **9d**. Ellipsoids are drawn at the 30% probability level. Selected distances (Å) and angles (deg): C_{12}–N_1 1.367(9), C_{12}–N_2 1.371(9), N_2–N_3 1.407(8), C_{15}–N_3 1.306(9), C_{15}–O_1 1.311(8), Ir_1–O_1 2.125(5), C_{12}–Ir_1 2.034(7), C_{12}–Ir_1–O_1 79.6(3).

species where the iridium center accommodates one molecule of acetonitrile. In comparison to the corresponding neutral complex **8c** the bond lengths are nearly identical, although a longer (1.31 Å (**9d**) vs 1.28 Å (**8c**)) C–O bond is observed, despite identical Ir–O bond lengths. This could be attributed to the increased ionic character of the Ir–O interaction, due to the cationic iridium center, resulting in a larger proportion of the localization of the negative charge on the oxygen atom.

Evaluation of Catalytic Activity. With this selected set of cationic iridium(III) complexes in hand, we next proceeded to evaluate their catalytic activity in the amine alkylation of anilines. We selected as a model reaction for our optimization the use of an equimolar mixture of benzyl alcohol **13** and aniline **14** as substrates, using a 2 mol % catalyst loading, and 1,2-dichloroethane (DCE) as the reaction solvent. We investigated the effect of the counterion on catalytic activity using the cationic complexes **9c–g**, all derived from ylide **6c**; the results are summarized in Table 3. All of the reaction

Table 3. Investigation of the Counterion Effect on Catalytic Activity[a]



13 **14** **15**

entry	complex	X	yield (%)[b]
1	**9f**	TfO	16
2	**9c**	BF_4	35
3	**9e**	PF_6	36
4	**9d**	SbF_6	66
5	**9g**	BArF	28

[a]Ar = 4-MeO-C_6H_4. [b]The yield of **15** was determined by ^{1}H NMR spectroscopy of the crude product using an internal standard.

components were mixed in a sealed tube and stirred at 90 °C for 1 h. At that point, the reaction mixture was cooled and filtered on Celite, the solvent was removed, and yields were determined by ^{1}H NMR spectroscopy. It is important to note that for this pair of substrates the reaction is extremely clean; the yields are thus an indication of the conversions. The reaction conditions resulted in incomplete conversions that provided good comparative grounds for the different counterions. As a control experiment, we tested the neutral iridium(III) chloride complex **8c** and found that it was completely inactive for the amine alkylation reaction, in line with numerous reports on similar types of catalysts.[15]

Iridium(III) triflate complex **9f** provided some catalytic activity (Table 3, entry 1). More drastic improvements were measured using fully dissociated, non-nucleophilic counterions such at BF_4^-, PF_6^-, and SbF_6^-, with a distinct catalytic activity increase with the last anion (Table 3, entry 4). Postreaction ^{1}H NMR spectra suggest that the optimal activity of complex **9d** could be attributed to an increase in stability under the reaction conditions; analysis of ^{1}H NMR spectra for the reaction using **9c** (X = BF_4) show noticeable signs of the complex degradation over the course of the reaction. In contrast, ^{1}H NMR analysis of the reaction using **9d** (X = SbF_6) show no degradation of the complex throughout the reaction. We were surprised, however, to find that a fully dissociated $BArF^-$ counterion resulted in lower catalytic activity than for SbF_6^- (Table 3, entry 5). We hypothesize that this could be attributed to the enhanced steric bulk from this counterion, reducing access to the key cationic iridium(III) center. The SbF_6^- counterion thus seems to provide the optimal balance of steric bulk, stability, and dissociation under these reaction conditions. Consequently, the SbF_6^--derived cationic complexes were used for the subsequent studies. We next investigated the effect of the nature of the R_1 group and of the basicity of the anionic tether, through modification of the

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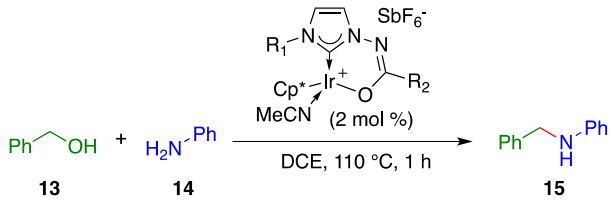
R_2 group, on the catalytic activity. The results are summarized in Table 4. For this set of reactions, we increased the default reaction temperature to 110 °C to improve conversions and yields. Nonetheless, when quantitative yields were reached under these standard conditions, the experiments were repeated at 90 °C for 1 h to discriminate the effects on the conversions and yields.

Table 4. Investigation of Ligand Effect on Catalytic Activity



13 14 15

entry	complex	R_1	R_2	yield (%)[a]
1	**9b**	Mes	Ph	100 (18)[b]
2	**9i**	Ph	Ph	2
3	**8g**	*t*-Bu	Ph	2[c]
4	**9j**	*n*-Bu	Ph	3
5	**9d**	Mes	4-OMe-C_6H_4	100 (66)[b]
6	**8c**	Mes	4-OMe-C_6H_4	96[c]
7	**9a**	Mes	CF_3	5
8	**9h**	Mes	OEt	99 (30)[b]
9	**10**	Mes	Ts	96[c]

[a]The yield of **15** was determined by ^{1}H NMR spectroscopy of the crude product using an internal standard. [b]Yield of the reaction performed at 90 °C for 1 h. [c]Alternative method to form the cationic complex: $AgSbF_6$ and the neutral iridium(III) complex were dissolved in MeCN and stirred for 15 min. The AgCl that formed was filtered, and the solution of the cationic complex was placed in a reaction flask and concentrated under vacuum. The reactants were added as in the normal procedure for amine alkylation.

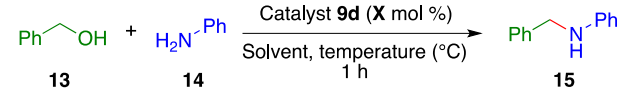
A first point to note is the source of the cationic catalyst. As reported in Table 2, we were able to isolate pure cationic complexes for most ylide proligands. However, in the case of ylides **6g** and **7**, we were limited to the isolation and characterization of the iridium(III) chloride complexes. In order to test them in the amine alkylation methodology, we resorted to a rapid preformation of the cationic species (Table 4, entries 3 and 9). The iridium(III) chloride complexes were treated in acetonitrile with an equimolar quantity of $AgSbF_6$. After 15 min of stirring, the suspension was filtered over a Celite pad and acetonitrile was removed. The crude cationic complexes were then used as is for the amine alkylation. We evaluated this protocol (Table 4, entry 6) to generate the most efficient catalyst, **9d** (Table 4, entry 5), and observed almost identical catalytic activity. We thus assumed that the results obtained with this alternative protocol for complexes **8g** and **10** are a realistic representation of their catalytic activity.

The evaluation of the effect of the *N* group on the imidazolidene ring (R_1) provided a very unique activity profile (Table 4, entries 1−4). Indeed, we found that only a bulky aromatic R_1 group would result in an active catalyst. This is particularly striking, as the most effective iridium(III) complexes bearing a conceptually similar ligand, reported by Martin-Matute and co-workers displays a *n*-butyl chain as the *N* group on the imidazolidene ring.[15b] The analogous cationic complex **9j** did not provide any catalytic activity, despite being stable and well characterized (Table 4, entry 4). The same lack of catalytic activity was observed for the cationic derivative of complex **8g** (Table 4, entry 3); in this case we hypothesize catalyst stability issues, as we observed decomposition while attempting isolation of the cationic complex. A nonbulky aromatic group (R_1 = Ph, **9i**; Table 4, entry 2) resulted again in almost no catalytic activity. For this reason, the mesityl moiety was kept for the remainder of the study as the optimal R_1 group. We next evaluated the effect of the R_2 group on activity. We found that an increased basicity of the anionic tether provided a corresponding increase in catalytic activity. A particularly striking example is complex **9a** (Table 4, entry 7, R_2 = CF_3), which is almost inactive. The three most active complexes (**9b**,**d**,**h**) were tested at 90 °C to provide better discrimination of their activities, and **9d** was found to be optimal, in line with the increased basicity of the anionic group.

Finally, the crude cationic complex **11** derived from **10** provided excellent catalytic activity, as a 96% yield of the product was obtained under the model conditions, in line with the optimal catalyst **9d**, derived for the *N*-acyliminoimidazolium ylide **6c**. This strongly suggests that the nitrogen of the anionic group is the active ligand site for the borrowing hydrogen catalysis. Due to the instability and impossibility of isolating and characterizing **11**, complex **9d** was selected to explore the potential of these new iridium(III) species as catalysts.

We next investigated the effect of a small set of modifications of the reaction conditions on the yields; the results are summarized in Table 5. We first explored the effect of solvent.

Table 5. Optimization of the Reaction Conditions



13 14 15

entry	*X* (mol %)	solvent	[**13**] (M)	*T* (°C)	yield (%)[a]
1	2	DCE	0.5	110	98
2	2	CH_2Cl_2	0.5	110	91
3	2	MeCN	0.5	110	19
4	2	toluene (Tol)	0.5	110	44−96[b]
5	2	Tol/CH_2Cl_2 (1/1)	0.5	110	88
6	2	Tol/DCE (1/1)	0.5	110	90
7	2	PhCl	0.5	110	80(10)[c]
8	1	DCE	0.5	110	98
9	1	DCE	0.1	110	60
10	1	DCE	1	110	86
11	1	DCE	2	110	75

[a]Yield were determined by ^{1}H NMR spectroscopy of the crude product using an internal standard. [b]Yields varied widely over numerous experiments. [c]Yield of imine byproduct measured by ^{1}H NMR spectroscopy of the crude product using an internal standard.

In comparison to the optimal conditions (Table 5, entry 1), the use of dichloromethane provided a similar reactivity profile and yield (Table 5, entry 2). In contrast, the use of MeCN drastically decreased the catalytic activity and resulted in only 19% yield under the given conditions (110 °C, 1 h); this is most probably due to the complexing nature of this solvent. The use of toluene proved to be problematic, as yields over numerous experiments ranged from 44 to 96% (Table 5, entry 4). We suspect the culprit to be the solubility of catalyst **9d**, as the latter was not soluble in toluene at room temperature. We found that the use of mixture of toluene and a halogenated solvent (CH_2Cl_2 or DCE; Table 5, entries 5 and 6) provided

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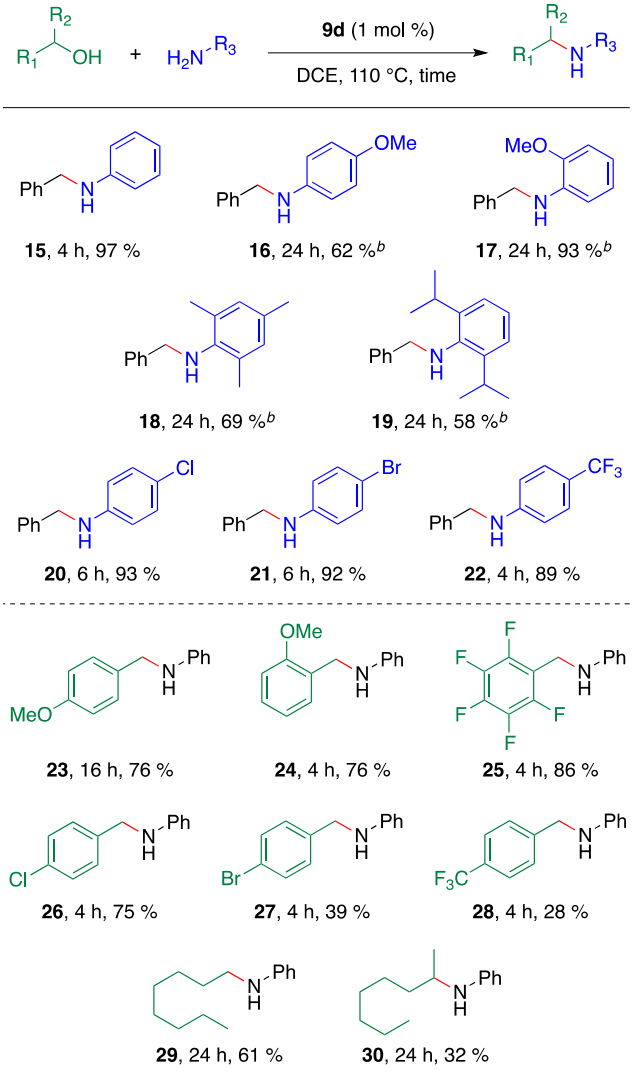
results equivalent to the optimal conditions. We also determined that chlorobenzene could be an acceptable solvent for the reaction, although in this special case we discovered the presence of an imine byproduct, indicative of a loss of dihydrogen in the process (Table 5, entry 7). A decrease in the catalyst loading to 1 mol % provided results identical with the initial optimal conditions (Table 5, entry 8). Using this lower catalyst loading, we finally evaluated the effect of concentration of the substrates (Table 5, entries 9−11), and found that a concentration of 0.5 M was required to achieve optimal yield.

Using the optimized conditions determined in Table 5 (entry 8), we next performed a selective scope study, in terms of both the alcohols and the anilines. Standard reaction times were increased between 4 and 24 h to ensure complete conversion when possible. The results are summarized in Scheme 5, and isolated yields are reported. For the synthesis of product **15**, catalyst **9d** is comparable to catalyst **1** from Martín-Matute (1 mol %, 2 h, 92%). We then investigated the effect of the modification of the steric and electronic properties of the aniline substrate on the reactivity. We found that more

Scheme 5. Scope of the Amine Alkylation[a]



[a]Isolated yields reported. [b]Reaction performed in PhCl. Reductive workup with $NaBH_4$ in AcOH used to reduce remaining imine byproduct prior to purification.

electron rich anilines reacted more slowly than the reference aniline. The lower activity could be attributed to the stronger binding ability of the aniline to the cationic iridium catalyst, leading to reversible inhibition, as reported by Martín-Matute and co-workers.[15c] This enhanced nucleophilicity of the aniline raised another synthetic challenge, as it reacted with 1,2-dichloroethane (DCE) to form the corresponding *N*-chloroethylaniline. To circumvent these issues with these substrates, the reactions were conducted in PhCl for up to 24 h to obtain acceptable yields. As reported in Table 5, entry 7, the reaction performed in PhCl resulted in the presence of an imine byproduct. This was even more pronounced for the electron-rich anilines, as we suspect the resulting imines to be even more difficult to reduce. For the sake of simplifying the isolation and reporting of the yield of the desired products in these cases, the reaction medium was treated with a solution of $NaBH_4$ in acetic acid to reduce the remaining imine into the desired aniline. With this modified workup, the products from electron-rich anilines were obtained with good yields (**16** and **17**). Sterically hindered anilines also required longer reaction times in chlorobenzene to achieve complete conversions (**18** and **19**). In contrast, electron-poor anilines reacted swiftly and provided excellent yields of the desired substituted anilines products (**20**−**22**).

We next explored variations on the benzyl alcohol substrates. Electron-rich derivatives were found to require longer reaction times to achieve complete amine alkylation (**23** and **24**). Interestingly, pentafluorobenzyl alcohol provided a very good yield of the desired product in a short reaction time (**25**). The 4-chloro derivative also provided the alkylated product in good yield and with a short reaction time (**26**). Unfortunately, the 4-bromo and 4-trifluoromethyl derivatives were plagued with low yields, regardless of the reaction time. Finally, we investigated aliphatic alcohols as substrates. A very different reactivity profile was found between 1- and 2-octanol, as the primary alcohol provided a fairly good yield of the desired product (**29**), but only a low yield was obtained with the secondary alcohol, even after 24 h of reaction (**30**). Interestingly, the secondary benzylic alcohol 1-phenylethanol was found to be completely unreactive under the reaction conditions. It seems that the low reactivity of secondary alcohols is thus mostly due to their increased steric hindrance. In contrast, Martín-Matute and co-workers reported the desired alkylation product from 1-phenylethanol and aniline, using catalyst **1** (2.5 mol %, 16 h, 110 °C, 87%). The increased sensitivity of catalyst **9d** to the substrate size is most probably because of its own steric bulk around the NHC group, due to the mesityl group.

As stated earlier, this amine alkylation method is a mass-efficient process to access various substituted amine derivatives, with water as the sole byproduct, with the exclusion of the solvent. Consequently, we investigated the ability of our optimal catalyst to promote the transformation in water, to further lower the environmental effect of the reaction conditions (Table 6). Under the reaction conditions optimized for 1,2-dichloroethane the reaction did proceed but resulted in a poor yield of the desired amine, and the presence of almost equal quantity of an imine was observed by ^1H NMR spectroscopy (Table 6, entry 1). To improve reduction of the imine and enhance yields, additives were tested, in substoichiometric quantities (10 mol %). It is proposed that these additives activate the imine intermediate, by protonation, to facilitate its reduction.[29] Catechol and H_3PO_4 were found to be inefficient to improve the outcome of the reaction.

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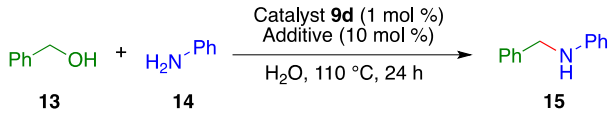
Table 6. Reaction in Water



13 14 15

entry	additive	yield (%)[a]
1		17 (16)
2	H_3PO_4	17 (6)
3	catechol	10 (5)
4	$(PhO)_2P(O)OH$	86

[a]The yield was determined by ^{1}H NMR spectroscopy of the crude product using an internal standard; the values reported in parentheses are of the measured imine byproduct.

Gratifyingly, the use of diphenyl phosphate resulted in a drastic improvement, giving an 86% yield of the desired amine, with no trace of the imine (Table 6, entry 4). This result is comparable to what was reported for catalyst **2** from Ke and co-workers (2 mol %, 24 h in water, 90%). Our catalyst is thus compatible with water as a solvent, at the cost of longer reaction time and the requirement to use a small quantity of an acidic additive.

CONCLUSIONS

In conclusion, we have developed two distinct synthetic procedures to access iridium(III) complexes with anionic NHC ligand derived *N*-iminoimidazolium ylides. Of particular interest, we have now optimized a protocol that allows access to transition-metal complexes by direct deprotonation of the corresponding ylides and subsequent halogen/anionic NHC exchange. A key advantage of these proligands is their ease of access through a convergent synthesis. By using readily available starting materials, we were able to develop a set of cationic complexes with a wide range of steric and electronic properties on the anionic NHC ligand. The catalytic activities of these complexes were evaluated in the amine alkylation reaction of anilines relying on borrowing hydrogen catalysis. While the insight gained is still limited, the high catalytic activity of complex **10** strongly suggests that the exocyclic nitrogen of the anionic group is the ligand atom actively involved in catalysis. The optimal catalyst provided high yields of the desired alkylation products under simple reaction conditions. We found that a more basic anionic tether and a fully dissociated counteranion provided increased catalytic activity. Finally, we found the optimal catalyst to remain efficient when the reaction was preformed in water, through the addition of diphenyl phosphate as an additive. Of particular interest, our catalysts require a bulky aromatic N group on the imidazolidene ring, which could prove useful for the future design of chiral variants of such catalysts.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.organomet.0c00726.

Details of the syntheses and characterization data and NMR spectra for all new compounds, selected crystallographic data for compounds **8a−c,e,f** and **9d**, the full Gaussian reference, and electronic and zero-point vibrational energies (PDF)

Cartesian coordinates for the calculated structures (XYZ)

Accession Codes

CCDC 2043041−2043046 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

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