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Promoting Effect of Imidazolium Ionic Liquid in the Reaction of Chromium Carbene Complexes with Alkynes: A Most Simple and Convenient Way to Get Demetallated-Product!

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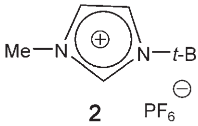
Abstract: Imidazolium ionic liquid serves as an interesting alternative solvent for performing the reaction of chromium carbene complexes with alkynes, with an advantage of enhancing the activity, selectivity and *in situ* generation of demetallated organic products.

Keywords: alkynes; benzannulations; demetallation; Fischer carbene complexes; ionic liquids; organometallic reagents

Since 1964, Fischer carbene complexes have emerged as valuable building blocks in the synthesis of organic molecules. A variety of useful reactions of Fischer carbene complexes and their analogues are known. Particularly, reactions of Fischer carbenes with alkynes have been well established. Since its discovery in 1975, the benzannulation reaction has been the subject of a great deal of methodological and mechanistic study. Notably, it has significant utility as a tool for the total synthesis of a variety of natural products.[1] Mostly, these reactions are carried out at 40–75 °C in tetrahydrofuran, dioxane, ether, benzene or toluene and afford a number of products including air-sensitive metallated compounds within a long time range of 2–60 h and, therefore, lead to poor to moderate yield of the products. Moreover, in most cases, these reactions are followed by oxidative cleavage using iron(III), cerium(IV), etc. to furnish the demetallated product. Due to the mechanistic complexity of the reaction, the product distribution of these reactions varies on slightly modifying reaction conditions such as the solvent, Fischer carbene, and alkyne concentrations and the nature of the alkyne.[2] Particularly, the efficiency of the reaction depends on the coordinating ability and size of the solvent. Hence, the importance of these reactions has inspired us to study the reactions of Fischer carbene complexes with acetylenes in an ionic liquid.

Recently, ionic liquids have been reported as attractive alternative solvents to replace conventional organic solvents for organic transformations, particularly transition metal-catalyzed transformations of organic and organometallic reactions.[3] Due to their low melting range, non-volatility, non-flammability, good solvating ability, tunable miscibility, good hydrolytic and thermal stability, and good physicochemical properties, they are particularly promising as solvents for catalysis also. They can be recovered by careful washing in ether or pentane (or products can easily be obtained by distillation) after the reaction is over. Moreover, their utilities as reactants and solvents for catalyst recycling are becoming more significant for organic reactions and catalysis. Their use can enhance activity, selectivity, and stability of catalysts. Since these liquids are salts, the cations and anions may interact with solutes and therefore can have dramatic effects on numerous reactions.[4] Since the coordinating abilities of ordinary ionic liquids are often very poor, the selection of an ionic liquid that can serve for both immobilization and as coordinating ligand for the purpose of our study, is also very important.

In our initial work, we have studied the reactions of Fischer carbenes with alkynes in the most frequently used imidazole-based ionic liquid, 1-butyl-3-methylimidazolium hexafluorophosphate **2**, [bmim][PF_6], which is prepared from 1-butyl-3-methylimidazolium bromide **1**, [bmim][Br], and KPF_6 by anion metathesis.[5] The major reason behind selecting the imidazoli-



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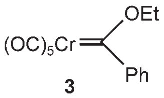
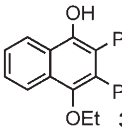
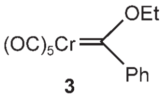
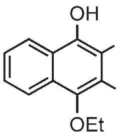
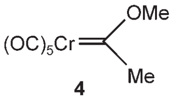
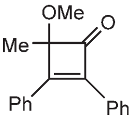
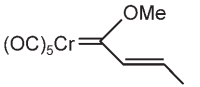
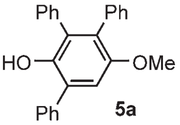
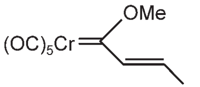
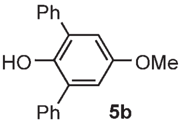
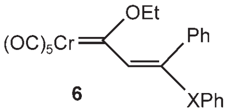
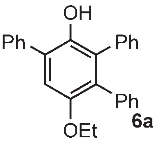
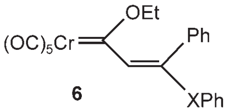
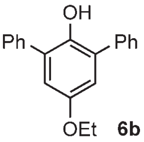
um ionic liquid **2** is that it may coordinate to the metal center and which may lead to a dramatic effect on the reaction.[3,6]

Initially, the reactions of carbenes with alkynes were carried out in ionic liquid **2** at room temperature. However, no reaction occurred after 24 h. After an extensive screening of various reaction conditions, particularly temperature, we found that the reactions were complete within 0.5–1.5 h after heating at 50–80 °C (Table 1). In fact, it is really very interesting to notice that *in situ* formation of demetallated product was observed with high selectivity, which is very rare to the best of our knowledge. It was observed that the reactions were remarkably faster, more selective, and the yields of isolated products were consistently good. Moreover, complete conversion of starting materials were observed under these conditions unlike those reported previously (Table 2). Although there are some reports on the Dötz benzannulation reaction of chromium carbene, which show enhancement of yields under microwave,[2b,7] sonochemical and dry-state adsorption conditions[8] and high intensity photolytic irradiation,[9] to date it is very rare to find an example in which demetallation occurs spontaneously in such reactions yielding the decomplexed product very selectively.[10] The reason for the demetallation in ionic liquid is indeed very difficult to understand at this moment, but it is believed that the coordinating ability of the ionic liquid with the chromium center facilitates the demetallation step at the end. We envisage that, for the same reason, demetallation occurs in the case of chalcogen-tethered Fischer carbene complexes even when the reactions are done in the absence of ionic liquid. In the later case, demetallation occurs

Table 1. Reactions of Fischer carbene complexes of chromium with alkynes in ionic liquid.

Entry	Carbene complex[a]	Alkyne 	Time [min]	Temp. [°C]	Product	Yield in IL [%][b]
1	 **3**	R = Ph	40	55	 **3a**	98
2	 **3**	R = H	30	55	 **3b**	95
3	 **4**	R = Ph	60	75	 **4a**	98
4	 **5**	R = Ph	80	50	 **5a**	85
5	 **5**	R = H	80	50	 **5b**	87
6	 **6** X = S, Se	R = Ph	90	80	 **6a**	80 (X = S); 85 (X = Se)
7	 **6** X = S, Se	R = H	40	70	 **6b**	87 (X = S); 90 (X = Se)

[a] All the reactions were performed in 0.2–0.5 mmol scale in ionic liquid (IL) under argon and 1 mL of IL was taken per 50 mg of the carbene complex.

[b] Isolated yields after passage through silica gel.

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Table 2. Reactions of Fischer carbene complexes of chromium with alkynes in organic solvent as reported in the literature.

Entry	Temp. [°C]	Solvent	Time [h]	Reported Yield [%]	Ref.
1	45	*n*-Bu_2O	3	62[a]	[12, 2a]
2	45	THF; hexane	23; 60	67[a]; 57[a]	[2a]
3	70	*n*-Bu_2O	1	27[a]	[13, 2a]
4	40–60	*t*-BuOMe	2–4	90[a]	[14, 10, 1h]
5	40–60	*t*-BuOMe	2–4	90[a]	[14, 10, 1h]
6	80	benzene	2	61[b]	[10]
7	80	benzene	2	72[b]	[10]

[a] Yields of the metallated products.

[b] Yields of the demetallated products.

due to the coordination of the SPh/SePh group to the chromium metal.[10]

In our initial studies, we have mainly focused on the reactions of Fischer carbene complexes of chromium with alkynes (Table 1). Here, we have observed that phenylethoxychromium carbene **3** and methylmethoxychromium carbene **4**, take part in the reactions with alkynes efficiently in the ionic liquid to afford the demetallated naphthylene derivatives (**3a** and **3b**) and cyclobutenone derivative (**4a**), respectively. On the other hand, α,β-unsaturated carbene **5** and chalcogen-tethered Fischer carbene **6** show similar enhanced activity in the benzannulation reaction in ionic liquid medium to afford the polyphenyl derivatives (**5a**, **5b**, **6a** and **6b**). Products were characterized by IR and ^{1}H NMR.[11] All the spectral data clearly support the formation of demetallated products.

For the purpose of comparing the reactions performed in ionic liquid and in conventional organic solvent, we have introduced Table 2 below. The reaction of arylalkoxycarbene of chromium **3** with diphenylacetylene and phenylacetylene (entries 1 and 2) in ionic liquid afford the demetallated naphthaol derivatives (**3a** and **3b**) in 95–98% yield at 55 °C in 30–40 min, whereas, the same reactions performed in heptane at 80 °C for 30 min followed by the CAN oxidation afforded four different products (the different reaction conditions have been mentioned in Table 2).[2a] The reaction of alkylalkoxycarbene of chromium **4** with diphenylacetylene in ionic liquid affords cyclobutenone derivative **4a** in 98% yield, whereas the same reaction performed in ether afforded the cyclobutenone chromium tricarbonyl complex in 27% yield under very similar reaction conditions (entry 3).

The reaction of alkenyl carbene **5** with alkynes in ionic liquid yielded demetallated polyphenyl phenolic products (**5a** and **5b**) in 85–87% yield which is very similar to the result reported when the reaction was performed in ether (entry 4 and 5).[14,10,1h] On the other hand, chalcogen-tethered Fischer carbene complexes **6** showed enhancement of yield from 60% to 80–90% of demetallated polyphenyl phenolic derivatives (**6a** and **6b**) in ionic liquid compared to benzene (entries 6 and 7).[10] Here, in both the cases, demetallated product was obtained.

After performing the reaction in ionic liquid, the product was extracted in diethyl ether. Then, the ether extract was concentrated under reduced pressure and the resulting crude product was purified by column chromatography using silica gel to obtain the pure product. After extraction with diethyl ether, the resulting ionic liquid layer was washed with ethyl acetate. Removing the ethyl acetate and drying under vacuum at 60 °C for 8 h was sufficient to recover the ionic liquid in its original state. The recycled imidazolium salt was then used for further reactions. There was no significant loss of efficiency of the ionic liquid after 4 cycles. Finally, it was dissolved in dichloromethane after 4 cycles, and filtered through a pad of celite to remove insoluble materials. Then it was used for several times again. Similar high conversions were obtained which indicates that the imidazolium salt remains active after several cycles.

In summary, this work has demonstrated that the imidazolium ionic liquid can serve as an interesting alternative solvent for performing reactions of Fischer carbene complexes with alkynes with an advantage of enhancing the activity, selectivity and yield. Moreover, to the best of our knowledge it is the simplest and most convenient method to obtain the demetallated product directly. More general and detailed studies are underway.

Experimental Section

Typical Procedure for the Reaction of Chromium Carbene with Alkyne in Imidazolium Ionic Liquid

To a round-bottomed flask equipped with a magnetic stirrer, ionic liquid **2** (1 mL) and carbene complex **4** (50 mg, 0.2 mmol) were added. To this solution, 1.2 equivalents of diphenylacetylene (43 mg, 0.24 mmol) were added and stirring was continued at room temperature under argon until the solution became homogeneous. It was then heated at 75 °C until a colour change occurred (solution became almost colourless). After completion of the reaction as indicated by the colour change and TLC, the reaction mixture was triturated with diethyl ether (3×5 mL), followed by decanting off the ether layer. The combined ether extracts were concentrated under reduced pressure and purified by column chromatography using silica gel to obtain the pure colourless semi-solid product **4a**; yield: 52 mg (98%). All other reactions were carried out in the similar way.

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