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Efficient Synthesis of *β*-Chlorovinylketones from Acetylene in Chloroaluminate Ionic Liquids

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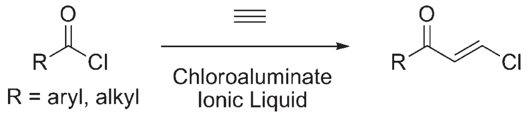
ABSTRACT



A method for the Friedel–Crafts-type insertion reaction of acetylene with acid chlorides in chloroaluminate ionic liquids is presented. The use of ionic liquids not only serves to avoid the use of carbon tetrachloride or 1,2-dichloroethane but also suppresses side reactions, notably the polymerization of acetylene, which occurs in these chlorinated solvents. Consequently, the products can be isolated using a simpler purification procedure, giving a range of aromatic and aliphatic *β*-chlorovinyl ketones in high yield and purity.

β-Chloro-α,*β*-unsaturated ketones are used as synthetic intermediates in a wide variety of aromatic, aliphatic, and heterocyclic compounds, many of which are important to the chemical and pharmaceutical industries.[1,2] A range of compounds of this type are accessible via a Friedel–Crafts-type addition reaction of alkynes with acid chlorides in the presence of a stoichiometric amount of $AlCl_3$.[1,3] Unsubstituted *β*-chlorovinyl ketones, a special subclass of highly versatile intermediates, are prepared by the reaction of acid chlorides with acetylene gas. Acetylene, which is mainly produced from natural gas, may provide a competitive alternative to the use of oil as feedstock for certain chemical industrial processes.[4] The synthesis of *β*-chlorovinyl ketones from acetylene works for a wide range of substrates, with yields of typically 50–70%, but usually requires the use of chlorinated solvents that are highly toxic and/or damaging to the environment, such as carbon tetrachloride and 1,2-dichloroethane.[1,5−10] Transition-metal-catalyzed methods for the addition of acid chlorides to terminal alkynes are known, but these methods require the use of expensive Rh- or Ir-based catalysts, and the use of acetylene as substrate has not been reported.[2,11−13] It is therefore of considerable interest to search for alternative methods for the synthesis of *β*-chlorovinyl ketones that combine the use of cheap and environmentally less hazardous substances with high product yields. Several examples

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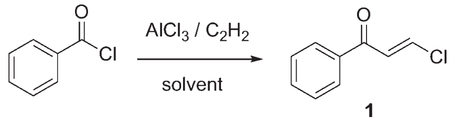
of Friedel–Crafts acylation[14–17] and alkylation[18–20] reactions in chloroaluminate ionic liquids have been reported. In contrast, as far as we are aware, the Friedel–Crafts-type addition of acetylene to acid chlorides has not been studied in ionic liquids. Herein, the potential of chloroaluminate ionic liquids as solvents for this reaction is explored.

Scheme 1. Synthesis of 3-Chloro-1-phenyl-2-propenone from Acetylene and Benzoyl Chloride



The addition of acetylene to benzoyl chloride, yielding 3-chloro-1-phenyl-2-propenone (**1**, Scheme 1), was chosen as a model reaction. Initially the influence of the reaction conditions were investigated for 1,2-dichloroethane (DCE) as solvent (Table 1, entries 1–3). Typically, the acid chloride was added to a suspension of $AlCl_3$ in DCE and stirred at 0 °C for 15 min, and then acetylene gas was passed through the reaction mixture at 50 °C for 2 h. When a small excess of $AlCl_3$, with respect to benzoyl chloride (1.3 equiv) was used, complete conversion of the starting material was observed by GC. These conditions correspond to those reported in the literature.[1]

As a major drawback of this procedure, a large amount of a black tarlike material is formed as a byproduct. Following initial aqueous/organic extraction, additional purification by column chromatography or distillation[6] is therefore necessary to obtain the product in pure form. When acetylene was added to a suspension of $AlCl_3$ in DCE in the absence of benzoyl chloride, a large amount of tar was formed, indicating that the tar originates from a reaction of acetylene with $AlCl_3$, most likely corresponding to the Al-catalyzed polymerization of acetylene.[21,22] The tar formation could be avoided by using a smaller amount of $AlCl_3$ (1.0 equiv, Table 1, entry 3), but this led to incomplete conversion of the benzoyl chloride substrate, which did not increase as the reaction time was extended.

In order to explore the potential of ionic liquids as solvents for this reaction, several ionic liquids, containing different anions and cations, were evaluated. The ionic liquids [bmim][BF_4] (bmim = 1-butyl-3-methylimidazolium), [bmim][PF_6] and [bmim][OAc] were not suitable since they were found to react with $AlCl_3$. In contrast, no obvious reaction was observed upon mixing of $AlCl_3$ with the ionic liquids [bmim][Tf_2N] (Tf_2N = bis(trifluoromethylsulfonyl)imide) or [bmim][TCM] (TCM = tricyanomethanide). However, in these solvents no conversion of benzoyl chloride was observed. Changing the cation while keeping Tf_2N as anion, i.e., employing [$3C_4C_{13}P$][Tf_2N] ($3C_4C_{13}P$ = tri(butyl)(tridecyl)phosphonium), did not lead to any improvement. A possible explanation for these observations could be deactivation of $AlCl_3$ by coordination of the anions of the ionic liquids. For example, the formation of species of the type $AlCl_{3-n}(Tf_2N)_n$ has been described previously.[23]

The combination of [bmim]Cl with $AlCl_3$ results in an ionic liquid, the physical and chemical properties of which depend on the mole fraction, N, of $AlCl_3$. For $N = 0.50$, the aluminum-containing species tends to have the form $AlCl_4^-$. For higher mole fractions, species of the type $Al_2Cl_7^-$ predominate and the ionic liquid is considered Lewis acidic.[18] These tunable properties have been exploited in synthesis and catalysis.[24–26] In the present case, the use of an ionic liquid composed of [bmim]Cl and $AlCl_3$ with $N = 0.67$ resulted in a highly active system, in which the ionic liquid acts as both solvent and Lewis acid catalyst (Table 1, entries 7–10). When an amount of ionic liquid was used that corresponds to a molar ratio of the excess of $AlCl_3$ in the ionic liquid to benzoyl chloride of 1.3, a conversion of 93% was observed under the same reaction conditions as employed for DCE (entry 8). In contrast to DCE, the use of the ionic liquid did not require cooling of the mixture during addition of benzoyl chloride. An increase of the reaction temperature to 60 °C during addition of acetylene resulted in quantitative conversion of the substrate (entries 9 and 10). Importantly, in contrast to DCE, no tar formation was observed when the reaction was carried out in [bmim]Cl–$AlCl_3$, rendering the extraction–purification procedure more facile. Following aqueous–organic extraction, the product was obtained as a clear, yellow-orange liquid in 70–74% yield. The effect of using different cations in the ionic liquid (i.e., *N*-butyl-3-methylpyridinium, bmpy) was also investigated (Figure 1), affording an equally effective system (Table 1, entry 11). The isolated yield of the reaction carried out in either [bmim]Cl–$AlCl_3$ or [bmpy]Cl–$AlCl_3$ under the conditions

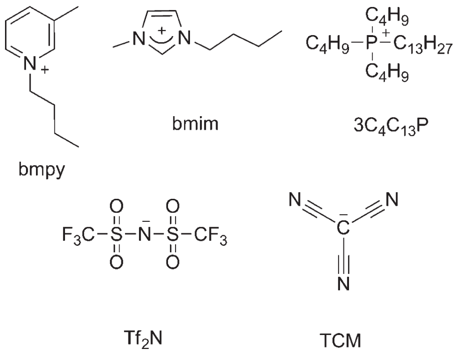


Figure 1. Cations and anions of ILs evaluated in the Friedel–Crafts-type reaction of benzoyl chloride with acetylene.

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Table 1. Effect of the Solvent and Reaction Temperature on the Synthesis of 3-Chloro-1-phenyl-2-propenone (**1**)[a]

entry	solvent	T1[b] (°C)	T2[c] (°C)	conv (GC, %)	isolated yield (%)	purity (GC, %)[d]	*E*/*Z* ratio (GC)[d]	tar formation
1	DCE	0	50	98	60[e]	98	98/2	yes
2	DCE	25	50	80	nd	nd	nd	yes
3[f]	DCE	0	50	79	nd	nd	nd	no
4	[bmim][Tf_2N]	0	50	0				no
5	[$3C_4C_{13}P$][Tf_2N]	0	50	0				no
6	[bmim][TCM]	0	50	0				no
7[f]	[bmim]Cl−$AlCl_3$	0	50	87	nd	nd	nd	no
8	[bmim]Cl−$AlCl_3$	0	50	93	nd	nd	nd	no
9	[bmim]Cl−$AlCl_3$	25	50	95	nd	nd	nd	no
10	[bmim]Cl−$AlCl_3$	25	60	99	71[g]	98	98/2	no
11	[bmpy]Cl−$AlCl_3$	25	60	>99	74[g]	98	98/2	no

[a] Conditions: 1.3 equiv of $AlCl_3$ with respect to benzoyl chloride; reaction time = 2 h. [b] Temperature for the addition of PhCOCl to $AlCl_3$. [c] Temperature for the addition of C_2H_2. [d] Purity and *E*/*Z* ratio of the isolated material after storage at 4 °C for 16 h. [e] After aqueous−organic extraction, followed by purification by column chromatography. [f] 1.0 equiv of $AlCl_3$ with respect to benzoyl chloride was used. [g] After aqueous−organic extraction.

Table 2. Effect of the Amount and Composition of the IL and the Reaction Time on the Synthesis of 3-Chloro-1-phenyl-2-propenone (**1**)[a]

entry	molar ratio $AlCl_3$/PhCOCl[b]	mole fraction of $AlCl_3$ in IL	t1 (h)[c]	t2 (h)[d]	conv (GC, %)	isolated yield[e] (%)
1	0.68	0.67	0.25	2	60	nd
2	1.3	0.67	0.25	2	>99	74
3	1.3	0.67	0.25	4	>99	73
4	1.3	0.67	3	4	>99	73
5	1.8	0.67	0.25	2	>99	90
6	1.8	0.70	0.25	2	>99	93
7	2.0	0.67	0.25	2	>99	93

[a] Solvent = [bmpy]Cl-$AlCl_3$. [b] Molar ratio of the excess of $AlCl_3$ in the IL with respect to benzoyl chloride. [c] Reaction time for the addition of PhCOCl to $AlCl_3$; reaction temperature = rt. [d] Reaction time for the addition of C_2H_2; reaction temperature = 60 °C. [e] After aqueous−organic extraction; product purity was in general 97−98% based on GC analysis.

employed was typically between 70 and 74% (three independent experiments). Analysis of the aqueous layer used in the extraction procedure revealed the presence of benzoic acid, although both the starting material and the product were stable under the employed purification conditions.

Consequently, a further set of optimization reactions was carried out using [bmpy]Cl−$AlCl_3$ as solvent. Extending the reaction times did not lead to any improvement (Table 2, entries 2−4). Instead, an increase of the molar ratio of the excess of $AlCl_3$ in the ionic liquid with respect to benzoyl chloride, from 1.3 to 1.8, led to an increase of the isolated yield from 74 to 93%. This increase may be achieved by employing either a larger amount of IL of the same composition (Table 2, entry 5) or by using a higher molar fraction of $AlCl_3$ in the IL (Table 2, entry 6). It has been reported that in similar Friedel−Crafts reactions in ionic liquids the reaction mechanism proceeds via an intermediate with the form [$R{-}C{\equiv}O^+$] and that an over stoichiometric excess of $AlCl_3$ may be required for the reaction to go to completion.[16−18] At an insufficient excess of $AlCl_3$, hydrolysis of the unreacted intermediate, giving benzoic acid, may occur during aqueous workup, reducing the yields. This may explain our observed increase in yield despite the complete conversion by GC in both cases. Increasing the ratio to 2.0 did not lead to a further increase of the yield (Table 2, entry 7). The yield of the product is significantly higher than literature yields for the same reaction using organic solvents, which range from 31% to 70%.[1,7]

In order to explore the scope of the chloroaluminate IL system, a range of acid chlorides were tested as substrates (Table 3), using the optimized conditions, with [bmpy]Cl−$AlCl_3$ as solvent and Lewis acid catalyst. For the aliphatic substrates, a reaction temperature of 0 °C was used, in accordance with literature procedures,[1] and good yields of the corresponding *β*-chlorovinyl ketones were obtained in all cases. Tar formation was not observed in any of the reactions. The isolated products were analyzed by ^1H and ^{13}C NMR spectroscopy and GC (see the Supporting Information). In general, the GC spectra contained peaks corresponding to the two stereoisomers of the

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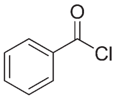
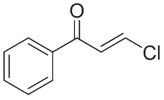
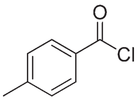
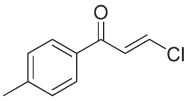
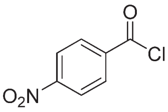
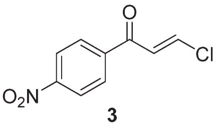
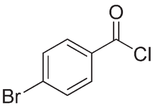
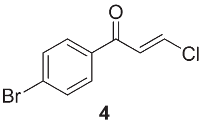
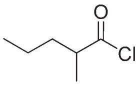
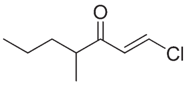
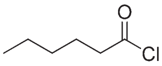
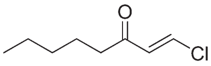
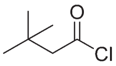
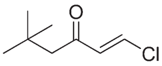
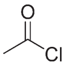
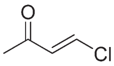
Table 3. Substrate Scope for the Reaction of Acid Chlorides with Acetylene in [bmpy]Cl$-$AlCl$_3$[a]

entry	substrate	product	yield (%)	purity (GC, %)	E/Z ratio (GC)
1		 **1**	93[b]	98	88/12 (98/2[d])
2		 **2**	87[b]	97	93/7 (98/2[d])
3		 **3**	77[b]	99	96/4 (98/2[d])
4		 **4**	74[b]	98	89/11 (99/1[d])
5		 **5**	74[b]	99	96/4 (97/3[d])
6		 **6**	76[b]	99	91/9 (91/9[d])
7		 **7**	98[c]	99	90/10
8		 **8**	75[c]	94	89/11

[a] Conditions: addition of RCOCl to [bmpy]Cl-AlCl$_3$: rt, 15 min for entries 1$-$4 and 0 °C, 15 min for entries 5$-$8; addition of C$_2$H$_2$: 60 °C, 2 h for entries 1$-$3 and 3 h for entry 4, and 0 °C, 2 h for entries 5$-$8; molar ratio (excess AlCl$_3$ in IL)/RCOCl = 1.8. Molar fraction of AlCl$_3$ in IL = 0.70. [b] Isolated yield. [c] GC yield, determined using decane as internal standard; a small quantity was isolated for characterization of the product by ^{1}H NMR spectroscopy. [d] After storage of the isolated product at 4 °C for 3 days.

products, with purities in the range of 94$-$99%. β-Chlorovinyl ketones, especially the aliphatic derivatives, are unstable, and phenol or hydroquinone are added as stabilizers.[1] Indeed, when the isolated products were stored for prolonged periods, a considerable darkening of the material was observed. The aromatic derivatives, however, could be stored at 4 °C for at least several days without any noticeable decomposition (established by NMR and GC analysis).

In summary, chloroaluminate ionic liquids are efficient solvents for the Friedel$-$Crafts-type addition of acetylene to benzoyl chloride, acting both as solvent and Lewis acid catalyst. The procedure is compatible with several aromatic and aliphatic acid chlorides, which all gave the corresponding β-chlorovinyl ketones in high yield and purity. Importantly, the chloroaluminate ionic liquid solvent suppresses the polymerization of acetylene which leads to improved atom economies and simpler extraction$-$purification procedures and provides an alternative to chlorinated organic solvents.

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Supporting Information Available. Experimental procedures and copies of NMR and GC spectra. This material is available free of charge via the Internet at http://pubs.acs.org.