SHORT PAPER

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An alternative route to syntheses of aryl keto acids in a chloroaluminate ionic liquid[†]

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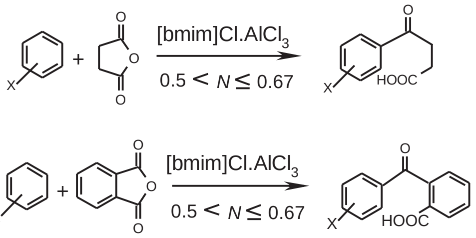
The Lewis acidic 1-butyl-3-methylimidazolium chloroaluminate ionic liquid [bmim]Cl.$AlCl_3$, N=0.67, is employed as a catalyst as well as the solvent for the quick and efficient syntheses of aryl keto acids by Friedel–Crafts acylation and aroylation of aromatic hydrocarbons using cyclic acid anhydrides.

Keywords: arenes, cyclic acid anhydrides, ionic liquid, aryl keto acids.

In the last few years ionic liquids have been recognized as promising solvents for the development of environmentally friendly processes.[1] In contrast to volatile organic solvents, ionic liquids have no measurable vapor pressure and therefore, there is no loss of solvent through evaporation. The chloroaluminate ionic liquids are thermally stable up to 200°C whereas other neutral ionic liquids are stable over a range even up to 300°C. Environmental and safety problems arising through the use of volatile organic solvents can be circumvented by the use of non-volatile ionic reaction media.[2] These ionic liquids have fascinated organic chemists owing to their remarkable ability to solvate wide variety of substrates such as organic, organometallic and inorganic compounds. Above all the fact that their properties can be altered by fine-tuning of parameters such as the choice of an organic cation, inorganic anion and alkyl chain attached to the organic cation has opened a new realm of synthetic organic chemistry. The ionic liquids are found to be excellent solvents and catalysts for a number of synthetically important reactions including Friedel–Crafts reactions,[3] Diels–Alder reactions,[4] hydrogenations[5], Wittig reactions[6] and even enzyme-catalysed reactions.[7]

In continuation of our work in the area of ionic liquids,[8-10] we report herein the syntheses of commercially important aryl keto acids by Friedel-Crafts acylation and aroylation using cyclic acid anhydrides in 1-butyl-3-methylimidazolium chloroaluminate, [bmim]Cl.$AlCl_3$, N=0.67 (where 'N' is the mole fraction of $AlCl_3$ in the ionic liquid). The syntheses of aryl keto acids employing cyclic acid anhydrides is a key step in the synthetic route to the preparation of polynuclear aromatic hydrocarbons via Haworth reaction.[11] They are also used in the syntheses of anthraquinone and its derivatives, which are important in the dyestuff industry.[12]

Friedel–Crafts acylation and aroylation using cyclic acid anhydrides in Lewis acidic ionic liquids have been attempted only on ferrocene but with no success.[13] Aromatic as well as aliphatic acid anhydrides react with many aromatic hydrocarbons in the presence of Lewis acids to yield a variety of keto acids.[14] The basic reaction and the one which has been most thoroughly investigated, involves the aroylation of benzene using phthalic anhydride to give *o*-benzoylbenzoic acid.[15]



Scheme 1 Friedel-Crafts acylation and aroylation of aromatic hydrocarbons using succinic anhydride and phthalic anhydride in acidic ionic liquid.

We have carried out the acylation and aroylation of benzene and substituted benzenes using succinic anhydride and phthalic anhydride, respectively in [bmim]Cl.$AlCl_3$, $0.5 < N \leq 0.67$ (Scheme 1). Initially, the reactivity is examined in basic, neutral and acidic chloroaluminate ionic liquids by varying the apparent mole fraction of $AlCl_3$ in the liquid, N, over the values 0–0.5, 0.5 and 0.5–0.67, respectively. The reaction takes place only in the acidic ionic liquid. Hence [bmim]Cl.$AlCl_3$, N=0.67 is employed for all the further reaction studies. Here [bmim]Cl.$AlCl_3$ plays a dual role as the Lewis acid catalyst as well as the solvent.

The reaction was studied on benzene and substituted benzenes having activating and deactivating groups, using succinic anhydride and phthalic anhydride. The alkyl substituted benzenes gave good yields of keto acids with both succinic and phthalic anhydride under ambient conditions in almost all cases whereas with halogen substituted benzenes reaction takes place under moderate temperature conditions. The orientation and reactivity are in line with a typical aromatic electrophilic substitution. In contrast to the conventional methods, the ionic liquid offer a number of advantages as they have negligible vapor pressure, they are non inflammable and they provide a homogeneous catalytic medium for these reactions eliminating the use of obnoxious solvents such as carbon disulfide, tetrachloroethane, etc.[14,15] The results are presented in Tables 1 and 2.

Experimental

In a typical experimental procedure, to the weighed quantity of [bmim]Cl.$AlCl_3$, N=0.67 liquid (10 mmol), the hydrocarbon (10 mmol) and acid anhydride (10 mmol) were added and the reaction mixture was stirred for the required time at the specified temperature. All additions were carried out in an inert atmosphere. The reaction was quenched by adding 6 M HCl in cold conditions. The product was then extracted with ethyl acetate (3x10 ml). The combined organic extracts were dried using anhydrous sodium sulfate and then evaporated under reduced pressure. The crude product was purified by dissolving in aq. NaOH (10%), the alkaline solution was filtered and filtrate was acidified with 6 M HCl in cold conditions to regenerate the product. The products were characterized by IR, NMR and physical constants.

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Table 1 Friedel–Crafts acylation of benzene and substituted benzenes using succinic anhydride in [bmim]Cl.AlCl$_3$, N=0.67

Entry	Substrate	Product	Time /h	Temp. /^{o}C	Yield /%^{a}	Melting points /^{o}C
1	Benzene	3-benzoylpropionic acid	3	50	87	115 (114–116)[16]
2	Methylbenzene	3-(4-Methylbenzoyl)propionic acid	2.5	30	86	129 (128–129)[17]
3	1,2-Dimethylbenzene	3-(3,4-Dimethylbenzoyl)propionic acid	3	30	95	127 (126–128)[18]
4	1,4-Dimethylbenzene	3-(2,5-Dimethylbenzoyl)propionic acid	6	30	83	216 (215–216)[19]
5	1,3,5-Trimethylbenzene	3-(2,4,6,-Trimethylbenzoyl)propionic acid	6	30	85	113 (113–114)[20]
6	Chlorobenzene	3-(4-Chlorobenzoyl)propionic acid	5	50	54	131 (130–131)[21]
7	1,2-Dichlorobenzene	3-(3,4-Dichlorobenzoyl)propionic acid	5	65	51	166 (165–166)[22]
8	Bromobenzene	3-(4-Bromobenzoyl)propionic acid	6	50	69	149 (148–149)[23]
9	Nitrobenzene	No reaction	–	–	–	–

[a] Isolated yields.
values in the parenthesis indicate the literature melting points.

Table 2 Friedel–Crafts aroylation of benzene and substituted benzenes using phthalic anhydride in [bmim]Cl.AlCl$_3$, N=0.67

Entry	Substrate	Product	Time /h	Temp. /^{o}C	Yield /%^{a}	Melting points /^{o}C
1	Benzene	2-benzoylbenzoic acid	4	50	95	126 (125–126)[24]
2	Methylbenzene	2-(4-methylbenzoyl)benzoic acid	4	30	91	137 (136–137)[25]
3	1,2-Dimethylbenzene	2-(3,4-Dimethylbenzoyl)benzoic acid	3	30	95	167 (165–167)[26]
4	1,4-Dimethylbenzene	2-(2,5-Dimethylbenzoyl)benzoic acid	7	40	86	149 (148–149)[27]
5	1,3,5-Trimethylbenzene	2-(2,4,6-Trimethylbenzoyl)benzoic acid	6	45	91	212 (211–212)[24]
6	Chlorobenzene	2-(4-Chlorobenzoyl)benzoic acid	4	60	89	147 (146–147)[28]
7	1,2-Dichlorobenzene	2-(3,4-Dichlorobenzoyl)benzoic acid	5	60	68	190 (188–190)[29]
8	Bromobenzene	2-(4-Bromobenzoyl)benzoic acid	8	80	74	171 (170–171)[30]
9	Nitrobenzene	No reaction	–	–	–	–

[a] Isolated yields.
values in the parenthesis indicate the literature melting points.

Conclusion

In conclusion, we have successfully carried out Friedel–Crafts acylation and aroylation of benzene and substituted benzenes using cyclic acid anhydrides as acyl and aroyl donors in the Lewis acidic ionic liquid. The experimental procedure is quick and simple. Further investigations concerning the use of less activated, relatively stable and commercially viable acyl/aroyl donors such as carboxylic acids in Friedel-Crafts acylation and aroylation in ionic liquids are currently in progress.

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