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ORIGINAL PAPER

Application of chloroaluminate ionic liquid as catalyst and medium for the dealkylation of esters

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Abstract Dealkylation of esters to carboxylic acids was performed using chloroaluminate ionic liquids (PyHBr/$AlCl_3$, PyHCl/$AlCl_3$, $Me_3NHCl/AlCl_3$, $Et_3NHCl/AlCl_3$) as catalyst and medium. The catalytic activity of PyHBr/$AlCl_3$ ($X(AlCl_3) = 0.67$) proved to be superior to the other three ionic liquids for the dealkylation of methyl benzoate with a conversion of 97% after 3 h at 140 °C. After easy separation from the products the ionic liquid PyHBr/$AlCl_3$ could be reused six times without loss of its activity.

Keywords Dealkylation · Chloroaluminate ionic liquids · Esters · Carboxylic acids · Catalysis · Nucleophilic substitutions

Introduction

Protection of carboxylic acids is often necessary because of their high sensitivity toward other reagents and reaction conditions in multistep transformations and syntheses of complex organic molecules [1, 2]. Formation of alkyl esters is a commonly used method for this purpose [3, 4]. Such protecting groups have advantageous features such as their ease of preparation and chemical stability toward a number of reaction conditions. The commonly used deprotection method is hydrolysis with strong acid or base [5, 6]. The method is efficient; however, hydrolysis of esters can be limited in the case of acid- or base-sensitive substrates. Apart from the hydrolysis pathway, deprotection of esters can be carried out with various reagents capable of cleaving the esters by dealkylation reaction such as I_2 [7], LiCl [8], LiBr [8], LiI [9], Et_2NSiMe_3 [10], $MOSi(CH_3)_3$ [11], $KSCOCH_3$ [12], and HNO_3 [13]. Lewis acids ($AlCl_3$, $AlBr_3$, and $ZnBr_2$) have also been applied in the dealkylation of esters, but they are only efficient for methyl, *tert*-butyl, and benzyl protecting groups; the conversion is low in the dealkylation of ethyl esters [14, 15]. Chakraborti et al. [16–18] have developed efficient methods for the chemoselective cleavage of alkyl and aryl esters through the in situ demand-based thiolate generation and single-electron transfer in situ thiolate generation protocols [19].

Ionic liquids are very attractive and environmentally acceptable solvents and catalysts because they have very low vapor pressure and are nonexplosive and thermally stable over a wide temperature range [20–23]. They can be used as environmentally benign solvents for a number of chemical processes, such as separations [24, 25], reactions [26, 27], homogeneous catalysis [28], and extractions [29–31]. The applications of ionic liquids as new media and catalysts may offer a convenient solution to both the solvent emission and the catalyst recycling problem [32–36]. In addition, chloroaluminate ionic liquids have been reported as catalyst and also medium in cyclizations [37, 38], Pechmann condensations [39, 40], Fries rearrangements [41], Diels–Alder reactions [42], Friedel–Crafts reactions [43–45], etc. But as far as we know, there is no report on dealkylation of esters in chloroaluminate ionic liquids as catalyst and medium.

Kemperman [46] and Liu [47] reported that chloroaluminate ionic liquids can efficiently cleave methyl ethers in high yields under mild conditions. In the present paper we report the application of simple chloroaluminate ionic liquids (**1**–**4**, Scheme 1) as acidic catalyst and medium for the dealkylation of esters. The ionic liquids are

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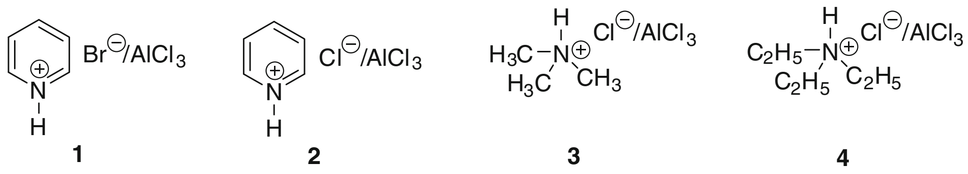
Scheme 1

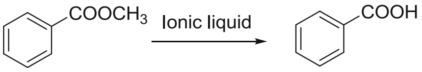


conveniently prepared in one step using inexpensive and easily available materials.

Results and discussion

The conditions for the dealkylation reaction were optimized with methyl benzoate as substrate in the presence of ionic liquid **1**–**4** (Table 1). All of the ionic liquids were effective in the conversion of methyl benzoate to benzoic acid, with activity in the order **1** > **2** > **3** ≈ **4**. This result was consistent with the acidity of the ionic liquids (**2** > **3** ≈ **4**) [48, 49] and nucleophilicity ($Br^- > Cl^-$). The effects of mole fraction of $AlCl_3$ ($X(AlCl_3)$) in ionic liquid **1** on the dealkylation of methyl benzoate are discussed. When $X(AlCl_3)$ was 0.5, which meant no $[Al_2Cl_6Br]^-$ in the ionic liquid, the yield was only 36% (Table 1, entry 2). In ionic liquids with $X(AlCl_3) < 0.5$, i.e., they contain excess of Br^- ions over $[Al_2Cl_6Br]^-$, the dealkylation did not occur (Table 1, entry 3). This result was consistent with the fact that $[PyHBr]/AlCl_3$ ($X(AlCl_3) \leq 0.5$) had no acid activity [50]. The effects of the reaction temperature and time were also explored. Conversion increased from 86 to 97% for a 3-h reaction period when the reaction temperature was increased from 120 to 140 °C (Table 1, entries 1 and 4). Increase of the reaction temperature to 160 °C has a marginal effect on the yield of benzoic acid (Table 1, entry 5). The yield increased from 91 to 97% with prolonging the reaction time from 2 to 3 h (Table 1, entries 1 and 6), and extending the reaction time to 4 h has practically no effect on the yield indicating that the reaction is complete in 3 h (Table 1, entry 7).

Table 1 Dealkylation of methyl benzoate using ionic liquids **1**–**4**



Entry	Ionic liquid	$X(AlCl_3)^a$	T/°C	t/h	Yield^b/%
1	**1**	0.67	140	3	97
2	**1**	0.5	140	3	36
3	**1**	0.33	140	3	0
4	**1**	0.67	120	3	86
5	**1**	0.67	160	3	97
6	**1**	0.67	140	2	91
7	**1**	0.67	140	4	97
8	**2**	0.67	140	3	95
9	**2**	0.67	140	4	95
10	**2**	0.67	160	3	95
11	**3**	0.67	140	3	75
12	**3**	0.67	140	5	96
13	**3**	0.67	160	3	96
14	**4**	0.67	140	3	76
15	**4**	0.67	140	5	96
16	**4**	0.67	160	3	96

Reactions were performed under nonaqueous conditions

[a] Mole fraction of $AlCl_3$

[b] Isolated yields

We also investigated the effects of different reaction temperature and time on this conversion in the presence of ionic liquids **2**–**4** with a mole fraction of 0.67. The best result in ionic liquid **2** was obtained at 140 °C for 3 h (Table 1, entry 8). Increasing the reaction temperature or prolonging the reaction time has no effect on the yield of benzoic acid in ionic liquid **2** (Table 1, entries 9 and 10). In contrast, the dealkylation of methyl benzoate gave the corresponding acid in low yields in ionic liquids **3** and **4** at 140 °C for 3 h (Table 1, entries 11 and 14). However, increasing the reaction temperature or prolonging the reaction time was found to significantly increase the conversion of methyl benzoate in the presence of ionic liquid **3** and **4** (Table 1, entries 12, 13, 15, and 16).

Ionic liquid **1** was applied to the dealkylation of various esters (Table 2). The dealkylation by ionic liquid **1** is compatible with many functional groups. Clearly, the presence of methyl, hydroxyl, nitro, amino, and bromine functions does not disturb ester cleavage (Table 2, entries 1–6). Interestingly, methoxy and ethoxy groups can also be cleaved using ionic liquid **1** as the ether-cleaving catalyst and medium (Table 2, entries 7–10). Moreover, as shown by entries 11–16, ethyl and *tert*-butyl can also be cleaved using ionic liquid **1** in excellent yields. Furthermore, ionic liquid **1** was effective in the dealkylation of aliphatic esters (Table 2, entries 17–20).

One of the most attractive features of ionic liquids is that they can provide good performance in terms of product separation and reusability when they are used as either catalyst or medium in synthetic chemistry. Indeed, ionic liquid **1** could be reused six times in the demethylation of

Table 2 Dealkylation of various esters using ionic liquid **1**

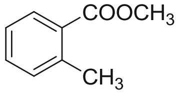
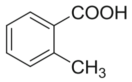
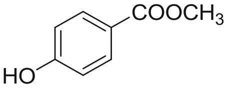
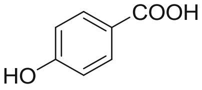
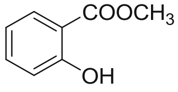
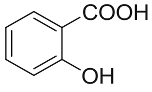
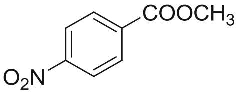
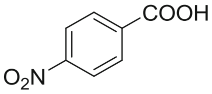
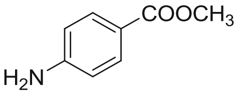
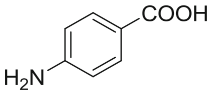
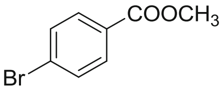
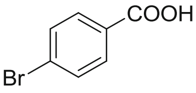
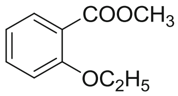
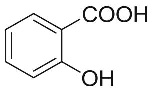
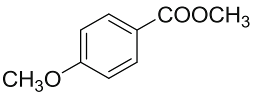
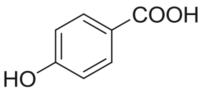
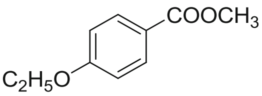
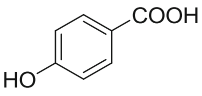
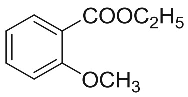
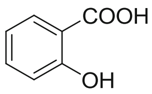
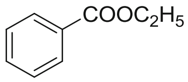
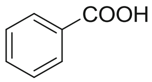
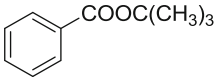
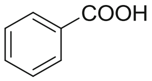
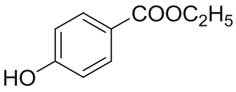
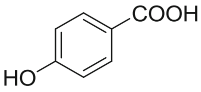
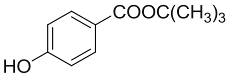
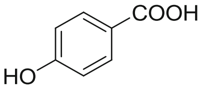
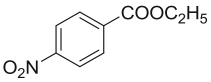
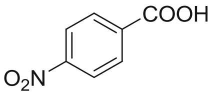
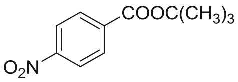
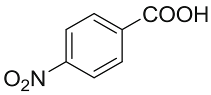
Entry	Esters	Products	Yield[a]/%	M.p./°C (Lit. m.p.) [32–36]
1			91	102–104 (103.5)
2			97	213–215 (214.5)
3			93	158–159 (159)
4			99	242–243 (242)
5			95	187–189 (188.2)
6			92	253–255 (254.5)
7			92	158–159 (159)
8			93	214–215 (214.5)
9			92	213–215 (214.5)
10			93	158–159 (159)
11			97	121–123 (122.4)

Table 2 continued

Entry	Esters	Products	Yield[a]/%	M.p./°C (Lit. m.p.) [32–36]
12			96	122–123 (122.4)
13			95	213–214 (214.5)
14			96	213–215 (214.5)
15			98	242–243 (242)
16			99	242–244 (242)
17	Methyl laurate	Lauric acid	98	43–44 (43.8)
18	Ethyl laurate	Lauric acid	97	43–44 (43.8)
19	Methyl caprylate	Caprylic acid	96	Oil
20	Ethyl caprylate	Caprylic acid	95	Oil

Reaction conditions: esters (0.05 mol), ionic liquid **1** (20 cm^3), 140 °C, 3 h

[a] Isolated yields

Table 3 Recycling of ionic liquid **1** in the demethylation of methyl benzoate

Cycle	1	2	3	4	5	6
Yield[a]/%	96	95	95	93	92	91

Reaction conditions: methyl benzoate (0.05 mol), ionic liquid **3** (20 cm^3), 140 °C, 3 h

[a] Isolated yields

methyl benzoate without a significant decrease in yield (Table 3).

Experimental

All chemicals were of reagent grade and used as received. Melting points were determined on a micro melting point apparatus (model X-4, Tech Instruments, Beijing). ^1H NMR spectra were recorded on a Bruker AVANCE 400 MHz spectrometer using $CDCl_3$ as solvent and TMS as an internal standard. IR spectra were recorded on a Nicolet AVATAR FT-IR 330 instrument. The ionic liquids (**1**–**4**) were prepared by literature methods [51].

*General procedure for dealkylation of esters in ionic liquid **1***

Ester (0.05 mol) and 20 cm^3 ionic liquid were placed in a three-neck round-bottom flask fitted with a stirrer, a thermometer, a reflux condenser, and a drying tube at the top. The contents of the flask were magnetically stirred and the oil bath temperature was maintained at 140 °C for 3 h. The reaction mixture was cooled to room temperature and 30 cm^3 anhydrous Et_2O was added to the solution. The organic phase was separated and dried with Na_2SO_4. The ionic liquid could be directly reused. Evaporation of the solvent afforded the crude product. The corresponding carboxylic acid was obtained by recrystallization or distillation. All the products were characterized by IR and ^{1}H NMR, and their melting points were in agreement with reference values [32–36, 52].

Caution: The by-products of the dealkylation of methyl esters in ionic liquid **1** and **2–4** are MeBr and MeCl, respectively. They are powerful alkylating agents and hence toxic: contact with skin and inhalation must be avoided. Therefore, work with this transformation should be carried out in an efficient fumehood with wearing protective gloves.

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