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Activation of Bismuth(III) Derivatives in Ionic Liquids: Novel and Recyclable Catalytic Systems for Friedel–Crafts Acylation of Aromatic Compounds

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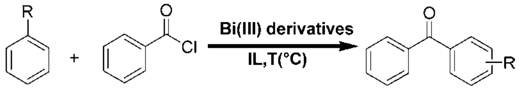
ABSTRACT



The activity of four bismuth(III) derivatives when employed as Friedel–Crafts catalysts for the acylation of aromatics was found to increase dramatically when dissolved in ionic liquids. Solutions of bismuth oxide or triflate in [emim][NTf$_2$] and [bmim][NTf$_2$] are the most efficient catalytic systems, with catalyst loading as low as 1% leading to clean, high-yielding acylation of a variety of benzene derivatives. These improved Friedel–Crafts catalytic systems can also be efficiently recycled as opposed to traditional systems.

The Friedel−Crafts (F&C) acylation reaction produces aromatic ketones, which are important intermediates in a very wide variety of fields, including pharmaceutical dyes, fragrances, and agrochemicals. Many of the industrial processes still use HF or $AlCl_3$ as catalysts.[1] However, the reaction requires more than a stoichiometric amount of these catalysts, which cannot be recovered and reused after the usual aqueous workup and therefore generates large amounts of wastes in industrial processes. Considering the ecological and economical problems associated with waste management in most countries, safe and environmentally acceptable processes for F&C reactions would be of high intrinsic economic value and interest.[2]

In recent years, ionic liquids (ILs) have emerged as one of the most important alternatives to volatile organic solvents (VOS).[2] One of the earliest examples of catalytic reactions performed in room-temperature ionic liquids were the F&C reactions.[3] The first example of acylation reaction in ionic liquids was performed by Wilkes et al.[4] The rate of the reaction was found to be dependent on the chloride/aluminum chloride ratio and hence on the concentration of the $[Al_2Cl_7^-]$ ion. Recently, Seddon et al.[5] have reported the F&C acylation of both activated and deactivated aromatic compounds in an ionic liquid system derived from [emim][Cl]-$FeCl_3$ having a mole ratio of $FeCl_3$ to [emim][Cl] of 53.5%. More recently, Xiao et al.[6] have shown that the acylation of anisole with benzoyl chloride can be readily performed, using metal triflates that do not require special handling as catalysts in [bmim][BF_4] as the solvent.

Bismuth derivatives are also known to catalyze many organic transformations,[7] including oxidation of acyloins to diketones catalyzed by bismuth oxide,[8] oxidation of sulfides[9] catalyzed by $Bi(NO_3)_3{\cdot}5H_2O$, or deprotection of *O,O*- and *S,S*-acetals.[10] Recently, Dubac and co-workers reported the

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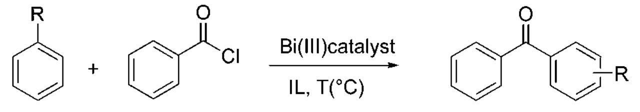
use of bismuth trifluoromethane sulfonate as a catalyst for Diels−Alder[11] and aza-Diels−Alder[12] reactions and in the acylation of alcohols[13] or of toluene, benzene, and chlorobenzene.[14]

In this paper, we disclose our preliminary results on the Friedel−Crafts acylation of aromatic compounds with benzoyl chloride using novel and recyclable catalytic systems based on bismuth(III) derivatives immobilized in room-temperature ionic liquids[15] that are air- and moisture-insensitive (Scheme 1). Four commercially available bismuth derivatives were chosen for the study of the Friedel−Crafts acylation of aromatics in the presence of ionic liquids, namely, $Bi(OTf)_3$, Bi_2O_3, $BiCl_3$, and BiOCl. The benzoylation of anisole and toluene was used as a test reaction to compare the catalytic activity of these bismuth derivatives immobilized in ionic liquids under standardized conditions.

Scheme 1. Acylation of Aromatic Compounds Catalyzed by Bi(III) Derivatives Dissolved in Ionic Liquids



In a typical reaction, a mixture of benzoyl chloride (1 mol) and anisole (2 mol) was added to a preheated mixture of catalyst (0.1 mol) and $[emim][NTf_2]$ (0.1 mol) at 80 °C. Under these conditions, all catalysts used provided 100% conversion of benzoyl chloride to the corresponding benzophenones (ortho/meta/para = 4/0/96 for the four catalysts) after 0.5 h of reaction time. However, following the reactions since the very beginning revealed that, under these conditions, the acylation was over in less than 5 min with $Bi(OTf)_3$ and Bi_2O_3 as catalysts. It is interesting to note that the reaction mixtures are homogeneous at 80 °C. These results were very promising and have to be compared to those reported in the literature when ionic liquids were not used, i.e., $Bi(OTf)_3$ in neat anisole gave a 92% isolated yield of benzophenones (ortho/meta/para = 8/0/92) after 3 h at 110 °C. Interestingly, when the reaction was carried out at 20 °C in the presence of $[emim][NTf_2]$, $BiCl_3$ appeared to be the less active, producing only 10% conversion after 12 h at room temperature. $Bi(OTf)_3$ and BiOCl gave slightly better results (43 and 30% conversions, respectively), but Bi_2O_3 showed the highest activity, leading to 53% conversion. No reaction could be observed at room temperature in the absence of the ionic liquid (<5% conversion). These results clearly show the determining role of $[emim][NTf_2]$ in these reactions as compared to organic solvents.

We then addressed the question of what would be the smallest amount of bismuth catalyst that could be employed in this reaction. Therefore, a study of the benzoylation of anisole in the presence of 1 mol % catalyst was undertaken. Results are reported in Figure 1. It is shown that with 1 mol % $Bi(OTf)_3$ dissolved in $[emim][NTf_2]$, the reaction went to completion in 4 h, which is quite remarkable. In the presence of $Bi(OTf)_3$ without IL or Bi_2O_3 in $[emim][NTf_2]$, conversion was only in the range of 65−70%. $BiCl_3$, in the presence or absence of the ionic liquid, was less active.

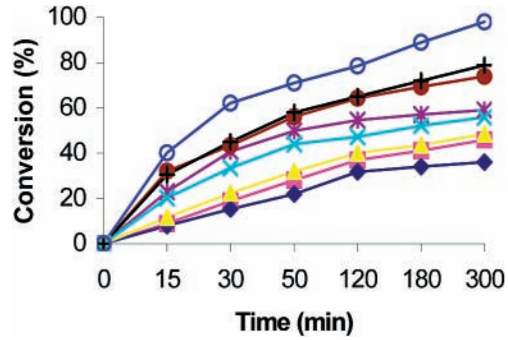


Figure 1. Acylation of anisole with benzoyl chloride catalyzed by 1 mol % Bi(III) derivatives in the absence of IL or immobilized in $[emim][NTf_2]$: (○) $Bi(OTf)_3$ and $[emim][NTf_2]$; (+) $Bi(OTf)_3$; (●) Bi_2O_3 and $[emim][NTf_2]$; (×) BiOCl and $[emim][NTf_2]$; (■) $BiCl_3$ and $[emim][NTf_2]$; (∗) Bi_2O_3; (♦) $BiCl_3$; (▲) BiOCl. Reaction conditions: a mixture of 10 mM benzoyl chloride and 20 mM anisole and 0.1 mM catalyst in the presence or absence of 0.1 mM $[emim][NTf_2]$ was stirred at an oil bath temperature of 80 °C. The selectivity ortho/meta/para was 4/0/96 in all cases.

To confirm the better activity of these bismuth derivatives in ionic liquids, we have studied the acylation of toluene, which is less reactive than anisole and therefore more discriminating. Indeed, literature reveals that $BiCl_3$, Bi_2O_3, and BiOCl are ineffective catalysts for the acylation of neat toluene.[14a]

The reactivity study was carried out at a temperature of 150 °C (oil bath) using 1 mol % catalyst and 2 equiv of toluene in the presence of $[emim][NTf_2]$ used as the test ionic liquid. Aliquots were withdrawn every hour over 5 h and extracted with ether, and conversion levels were determined by GC. Results are reported in Figure 2.

As for anisole, the best results were obtained with bismuth triflate dissolved in $[emim][NTf_2]$: 100% conversion was observed after 3 h. Bismuth triflate in neat toluene and bismuth oxide in the presence of the ionic liquid demonstrate a similar catalytic activity (about 60% conversion after 4 h of reaction). In general, a considerable activation of Bi(III)

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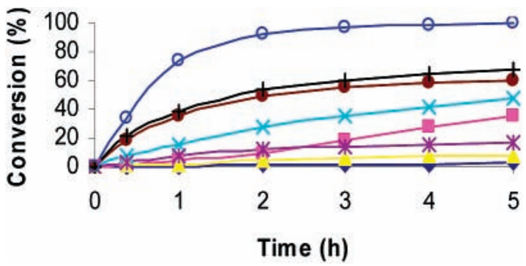

Figure 2. Acylation of toluene with benzoyl chloride catalyzed by 1 mol % Bi(III) derivatives in the absence of IL or immobilized in [emim][NTf_2]: (○) $Bi(OTf)_3$ and [emim][NTf_2]; (+) $Bi(OTf)_3$; (●) Bi_2O_3 and [emim][NTf_2]; (×) BiOCl and [emim][NTf_2]; (■) $BiCl_3$ and [emim][NTf_2]; (∗) Bi_2O_3; (♦) $BiCl_3$; (▲) BiOCl. Reaction conditions: 10 mM benzoyl chloride was added to a mixture of 20 mM toluene, 0.1 mM catalyst, and 0.1 mM [emim][NTf_2] preheated at 150 °C (oil bath temperature) in a Schlenk tube under argon.

catalysts in the presence of [emim][NTf_2] was observed (Figure 2), suggesting the selection of bismuth oxide or triflate in the presence of an ionic liquid for synthetic purposes.

The influence of the temperature on the benzoylation of toluene carried out in the presence of 10 mol % Bi_2O_3 and 10 mol % [emim][NTf_2] was then studied. No detectable conversion could be observed after 48 h (Table 1, entry1) at room temperature. After 24 h heating at 80 °C, a 25% conversion was obtained, which has to be compared with the 100% conversion of anisole in less than 5 min under the same conditions. However, heating at 150 °C (oil bath temperature) led to 100% conversion in 6 h. The addition of benzoyl chloride must be carried out at the reaction temperature (150 °C) in order to increase reaction yields and reduce reaction time (entry 7). This is illustrated by the experiment described in entry 6 where benzoyl chloride and toluene were introduced at room temperature and then heated to 150 °C. In that case, after 10 h of reaction, the isolated yield was only 77%, due to some decomposition, instead of 89% as obtained when the two reagents were introduced to a reaction mixture preheated at 150 °C. Reducing the amount of catalyst from 10 to 5 mol % did not alter the conversion time (about 6 h) or yields, which were quantitative (Table 2 entries 7 and 8). However, further lowering to 1 mol % slowed the reaction noticeably and only 70% conversion after 15 h was observed (entry 9). In all cases, 19/2/79 mixtures of ortho/meta/para benzophenones were isolated.

Table 1. Effect of Temperature and Amount of Bi_2O_3 on Friedel−Crafts Acylation of Toluene in [Emim][NTf_2][a]

entry	mol % Bi_2O_3	T (°C)	t (h)	conversion (%)	yield (%)[b]
1	10	25	48	0	
2	10	80	24	25	
3	10	110	19	100	78
4	10	125	11	100	86
5	10	140	7.5	100	85
6	10	150	10	100	77[c]
7	10	150	6	100	89
8	5	150	6	100	85
9	1	150	15	70	64

[a] Reaction conditions: 1 mM benzoyl chloride was added to a mixture of 2 mM toluene, 0.1 mM Bi_2O_3, and 0.1 mM [emim][NTf_2] under stirring at the indicated temperature. [b] Isolated yields of pure mixtures of benzophenones after bulb to bulb purification; para/ortho/meta isomer ratios were 79/19/2 in all cases. [c] Benzoyl chloride and toluene were mixed at room temperature with the catalysts and then heated.

Table 2. Friedel−Crafts Benzoylation of Toluene in Different Ionic Liquids[a]

entry	ionic liquids	conversion (%)[b]
1	[emim][NTf_2]	75
2	[emim][PF_6]	68
3	[bmim][NTf_2]	98
4	[bmim][PF_6]	60
5	[bmim][BF_4]	<5
6	[troma][NTf_2][c]	52
7	[troma][PF_6][c]	35
8	[troma][OTf][c]	15
9	[troma][BF_4][c]	<5
10	[$P(C_6H_{13})_3C_{14}H_{29}$][$NTf_2$][d]	68
11	[$P(C_6H_{13})_3C_{14}H_{29}$][PF_6][d]	45

[a] Reaction conditions: 1 mM benzoyl chloride was added to a mixture of 2 mM toluene, 5 mol % Bi_2O_3, and 0.1 mM ionic liquids preheated at 150 °C with stirring. The reaction mixture was stirred at this temperature for 4 h. [b] Determined by GC. Selectivity: ortho/meta/para = 19/2/79. [c] Troma = trioctylmethylammonium. [d] We wish to thank the CYTEC company for a generous gift of the corresponding chloride.

To examine the influence of the nature of the ionic liquid, we have carried out the acylation of toluene with benzoyl chloride in the presence of 5 mol % Bi_2O_3 in various air- and moisture-stable RTILs[16] at 150 °C for 6 h. We discovered that the catalytic activity of Bi_2O_3 was strongly affected by the nature of the cation and anion of the ionic liquid. Good results were obtained with imidazolium cations such as [emim][X] or [bmim][X] (Table 2 entries 1−4). However, when tetraalkylammonium or phosphonium cations were used, reactions were much slower and therefore product yields were significantly lower as compared to those obtained with imidazolium salts (Table 3 entries 6−11). With hydrophobic anions such as [NTf_2] or [PF_6], the desired ketones were obtained with good yields. By contrast, ILs with hydrophilic anions such as tetrafluoborate or triflate led to poor conversion levels, if any (Table 3, entries 5, 8, and 9). The use of [bmim][NTf_2] instead of [emim][NTf_2] led, respectively, to 98 and 75% conversions (average values for three assays) after 4 h of reaction (Table 2, entries 3 and 1), thus illustrating the influence of the length of the alkyl group on the cation on the activity of these systems.[17]

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Table 3. Friedel−Crafts Benzoylation of Aromatic Compounds in the Presence of [Emim][NTf_2] and Bi_2O_3 Catalyst[15] at an Oil Bath Temperature of 150 °C[a]

entry	aromatic derivative	t (h)	conversion (%)[b]	yield (%)[c]
1	benzene	24	15	
2	1,3-dimethybenzene	2.5	100	91
3	chlorobenzene	24	<5%	
4	naphthalene	2.5	100	84
5	1-methylnaphthalene	2.5	100	87
6	2,6-dimethylnaphthalene	2.5	100	75
7[d]	benzene	24	100	88
8[e]	benzene	24	70	62
9[d]	chlorobenzene	24	100	91
10[e]	chlorobenzene	24	58	

[a] Reactions were conducted on a 2 mM scale operating under the same conditions as above. [b] Conversion determined by GC-MS. [c] Isolated yields of pure products obtained by bulb to bulb distillation or by column chromatography. [d] $Bi(OTf)_3$ used as a catalyst in the presence of [emim][NTf_2]. [e] $Bi(OTf)_3$ used without IL.

Although less efficient than the [bmim][NTf_2] systems, the catalytic activity of Bi_2O_3 or $Bi(OTf)_3$ in the presence of [emim][NTf_2] was investigated to further study the F&C acylation of a variety of aromatic compounds. This allows a much easier workup of the reaction mixtures since [emim]-[NTf_2] and the organic phases led to a two-phase system at room temperature. Acylation of activated aromatics went to completion within 2 h, whereas an aromatic containing deactivating groups required longer reaction times, typically 24 h. Under such conditions, GC analysis of the crude reaction mixtures showed a complete conversion in all cases. Results are summarized in Table 3.

The benzoylation of activated aromatics yielded the ketones in good to excellent yields (Table 3, entries 1−5). However, the benzoylation of benzene and chlobenzene led to only 20% conversion after 15 h in the presence of Bi_2O_3. The same reactions conducted in the presence of $Bi(OTf)_3$ and [emim][NTf_2] led to 100% conversion within 24 h (Table 3, entries 7 and 9). In the absence of the ionic liquid, benzoylation of benzene and chlorobenzene gave only 70 and 58% conversions, respectively.

Attempts were made to recycle these catalytic systems. The benzoylation of 0.1 mol of toluene with benzoyl chloride under the conditions described in Table 1 with Bi_2O_3 as catalyst was run for six consecutive cycles, furnishing the methyl-substituted benzophenones, after extraction with toluene and bulb to bulb purification, with 89 (6 h), 87 (6 h), 90 (6 h), 86 (9 h), 85 (12 h), and 75% (15 h) isolated yields and an ortho/meta/para ratio of 19/2/79. After the extraction step, the ionic liquid layer was decanted, collected, and dried under high vacuum for 1 h. A simple alternative to this workup procedure is to purify the crude reaction mixture by bulb to bulb distillation under high vacuum. The next reaction was then initiated by reloading the reactor with a mixture of toluene and benzoyl chloride at 150 °C. We obtained the same reactivity for the first three cycles. Then, a longer reaction time was needed for the reaction to go to completion. The sixth cycle took 15 h to produce a 75% isolated yield. We noticed the precipitation of a solid on cooling to room temperature, which was isolated as small white needles by filtration. ^1H NMR analysis showed the presence of the ethylmethyl imidazolium unit. ^{13}C and ^{19}F NMR confirmed the absence of NTf_2 anion. We have shown this compound to be the ethylmethylimidazolium tetrachlorobismutate [emim][$BiCl_4$] by elementary analysis and high-resolution mass spectrometry. This anion could arise from the reaction of bismuth oxide with HCl giving first $BiCl_3$, which is then transformed into $BiCl_4^-$ by Cl^- capture. The [emim][$BiCl_4$] salt is formed by metathesis. The melting point of this salt is 112 °C, and the salt is therefore liquid at the temperature used to carry out the F&C acylation of toluene. Using this ionic liquid with Bi_2O_3 as catalyst, reaction does occur (45% yield after 6 h at 150 °C) but could not compete with [emim][NTf_2]. Recycling of the $Bi(OTf)_3$ system was attempted in the case of the benzoylation of toluene using the bulb to bulb purification procedure. Excellent results were obtained as shown by the following results: the first recycling gave a 92% isolated yield after 3 h of reaction, second 90% (3 h), third 88% (3 h), and fourth 90% (3 h) with an ortho/meta/para ratio of 20/2/78 in all cases.

In conclusion, the use of bismuth oxide and bismuth triflate as catalysts in properly chosen ionic liquids for Friedel−Crafts acylation of aromatic compounds can be considered as an interesting new alternative to existing homogeneous catalysts. Furthermore, they are air-stable, easy to handle reagents. Catalyst loads as low as 1 mol % can be used leading to high yields with activated aromatic compounds at an oil bath temperature of 150 °C. The catalytic system Bi_2O_3−[emim][NTf_2] can be reused up to six times, although with some loss of activity. $Bi(OTf)_3$/[emim] [NTf_2] showed a higher catalytic activity integrally maintained after four recyclings. The simple procedures as well as easy recovery and reuse of this novel catalytic system are expected to contribute to the development of more benign acylation of aromatics with acid chlorides.

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Note Added after Print Publication. Hongli Yang's name was misspelled in the version published on the Web June 3, 2003 (ASAP) and in the June 26, 2003 issue (Vol. 5, No. 13, pp 2219−2222); the correct electronic version of the paper was published on July 17, 2003, and an Addition and Correction appears in the August 21, 2003 issue (Vol. 5, No. 17).

Supporting Information Available: Typical experimental procedure for the F&C reaction and characterization data for all ketones listed in Table 4 and [emim][$BiCl_4$]. This material is available free of charge via the Internet at http://pubs.acs.org.

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