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Ionic liquid: an efficient and reusable media for seleno- and thioester synthesis promoted by indium

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ABSTRACT

A series of thio and selenoesters were efficiently obtained employing stable diorganyl chalcogenides, acyl chlorides, and In as reducing agent in BMIM·PF$_6$. Recycling of the ionic liquid was also performed, which was reused three times.

Selenoesters are attractive intermediates for many organic reactions. They have been extensively applied as mild acyl transfer agents, both as acyl radicals or anions, to promote the synthesis of carbonyl compounds.[1] On the account of this, they were the method of choice applied in the acylation step in the synthesis of many natural products (e.g., Crinipellin A,[2] (+)-Geissoschizine,[3] Ciguatoxins,[4] and (−)-pseudolaric acid B[5]). This class of compounds has also found application as liquid crystals,[6] as precursors for the synthesis of *N*-aminoacyl sulfonamides,[7] for lactonizations[8] and as selenating agents.[9]

Despite several methods have been described in the past,[10] nowadays their synthesis under mild reactions conditions is a field of growing research interest. These compounds have been successfully prepared from aldehydes using iBu$_2$AlSePh,[11] from chalcogenoacetylenes,[12] by coupling of aryl iodides with CO and PhSeSnBu$_3$ catalyzed by Pd,[13] and most commonly, by the reaction of acyl chlorides with nucleophilic species of selenium such as Hg(SePh)$_2$,[14] PhSeSnBu$_3$/Pd,[15] from reductive cleavage of diselenides with InI[16] or In[17] or by reductive coupling of PhSe)$_2$ and acyl chloride in an Rh/H$_2$ system.[18]

On the other hand, it is widely agreed that thioesters are one of the most useful building blocks for organic transformations. They have found application in C–C coupling,[19] for the synthesis of carbonyl compounds,[20] in asymmetric aldol reactions[21] and more recently, their α-β-unsaturated analogs have been successfully applied for asymmetric 1–4 additions, which allow the access to chiral intermediates for the synthesis of more complex compounds.[22] Furthermore, they found application in native chemical ligation for peptide bond formation,[23] in natural product synthesis,[24] and also acting as biologically relevant substances, finding application for in vivo tumor suppression[25] and as anti-HIV agents.[26] These valuable compounds have been prepared through the activation of carboxylic acids with diphosgene[27] or *N*-acylbenzotriazoles[28] followed by the addition of thiol, or by reaction of acyl chlorides with zinc and thiols.[29] They have also been accessed from thiols and carbon monoxide by carbonylation of organic substrates catalyzed by transition metals such as Pt[30] or Pd.[31] Recently, Alper co-workers described an interesting procedure for their synthesis through the thiocarbonylation of iodoarenes catalyzed by palladium in a phosphonium salt ionic liquid.[32]

Nonetheless, the development of new methodologies to accomplish the preparation of seleno and thioesters under mild reaction conditions, employing stable and nonhazardous starting materials as well as in an efficient way is highly desirable. In this context, a growing interest has been devoted for the utilization of ionic liquids, which have some interesting properties, including: nonvolatility, nonflammability, excellent chemical and thermal stability, and recyclability, which make them as attractive media for organic reactions.[33] According to the above mentioned, and in connection with our insights into organochalcogen chemistry,[34] in this report we wish to highlight our results on the synthesis of seleno and thioesters from acyl chlorides promoted by indium in ionic liquid. Noteworthy characteristics of our protocol are the use of an ionic liquid as solvent, which is conveniently recyclable, the use of stable and easily handled diaryl chalcogenides instead of malodorous and hazardous selenols or thiols, and the use of indium metal as a mild reducing agent for high yielding and short reaction times.

As a model substrate to determine the best reaction conditions, we performed a set of experiments using benzoyl chloride, diphenyl diselenide, and one equivalent of indium metal as reducing agent, Table 1. We evaluated three different imidazolium-based ionic liquids, which are suitable to our purposes, since they are liquid in the range of temperature used in this study and are stable under our reaction conditions, Figure 1.[35]

Using BMIM·BF$_4$ at 50 °C for 12 h the product was obtained in 76% yield (entry 1). Under the same reaction conditions, but using

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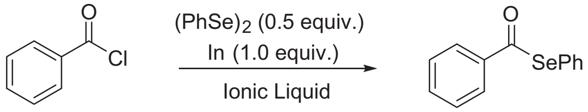
Table 1
Reaction optimization for the synthesis of selenoesters in ionic liquids promoted by In



Entry	IL	T (°C)	Time (h)	Yield[a] (%)
1	BMIM·BF_4	50	12	76
2	BMIM·PF_6	50	12	100
3	BMIM·PF_6	50	6	100
4	BMIM·PF_6	50	3	100
5	BMIM·PF_6	50	1	98
6	BMIM·$N(Tf)_2$	50	3	47
7	BMIM·PF_6	50	0.5	70
8	BMIM·PF_6	25	1	17
9[b]	BMIM·PF_6	50	1	58

[a] Isolated yields.
[b] With 0.5 equiv of In.

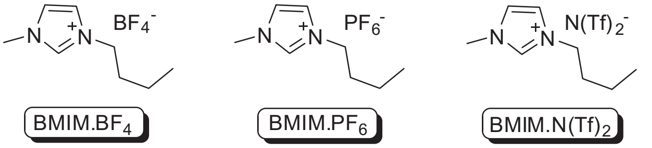
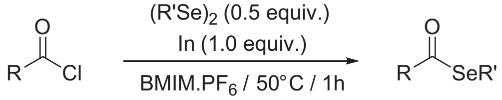
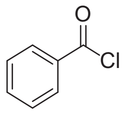
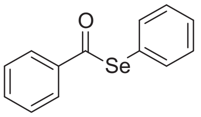
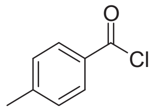
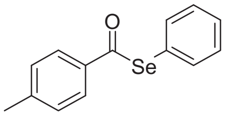
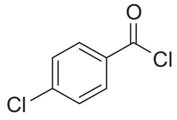
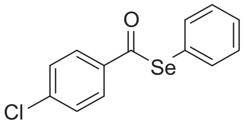
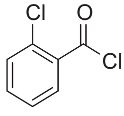
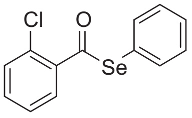
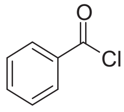
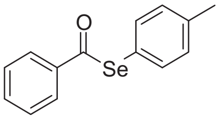
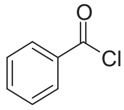
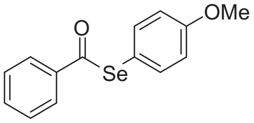
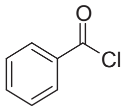
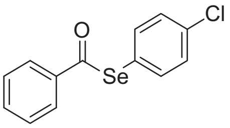
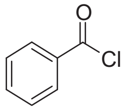
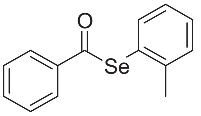
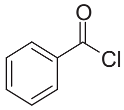
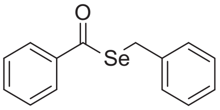
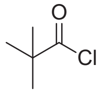
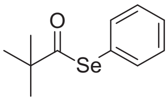
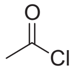
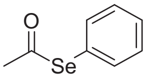
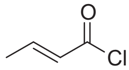
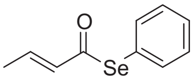
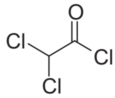
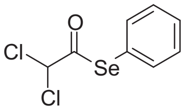
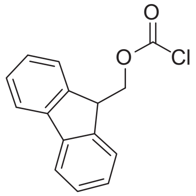
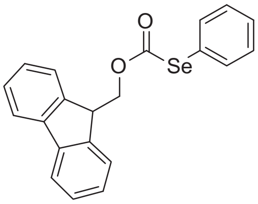


Figure 1. Ionic liquids used in this study.

Table 2
Synthesis of selenoesters in BMIM·PF_6 promoted by In



Entry	Acyl chloride	Product	Yield[a] (%)
1			98
2			76
3			97
4			84
5			57
6			52
7			47
8			53
9			49
10			38
11			13
12			17
13			35
14			25

[a] Yields for isolated pure products.

hydrophobic BMIM·PF_6 the product was obtained in quantitative yield (entry 2). Decreasing the reaction time to 1 h did not have any significant impact in the reaction efficiency (entries 3–5). Lower yields were found by using BMIM·$N(Tf)_2$, 47% (entry 6) or in BMIM·PF_6 in 0.5 h at 50 °C or at room temperature (entries 7 and 8). The reduction of indium amount to 0.5 equiv was also evaluated, affording the desired product in 58% yield (entry 9). These results suggest that the use of ionic liquid to promote this reaction is suitable and also that the counterion of the IL has an effective role in modulating the efficiency of the reaction. Comparing our results with other reports which described the use of other organic solvents and indium metal as a reducing agent, our protocol has the advantage to be carried out in shorter reaction times or with a lower amount of In.[17]

With the best conditions in hands[36], the scope of the reaction was extended to a diverse range of acyl chlorides as well as for diaryl diselenides using BMIM·PF_6 at 50 °C for 1 h, Table 2. Good yields were achieved by using electron donating or electron withdrawing groups attached to the acyl chloride moiety, both in *ortho* or *para* position (entries 1–4). When substituted diaryl diselenides were applied, a decrease in the yield was observed (entries 5–9).[37] It showed a trend for all kinds of diselenides, with yields in the range of 47% and 57% (entries 5–9). A set of experiments was also carried out with aliphatic acyl chlorides. As expected, a decrease in the yields was found (entries 10–13).

Notable is the reaction of dichloroacetyl chloride, which has more than one reactive site, and afforded the desired product in

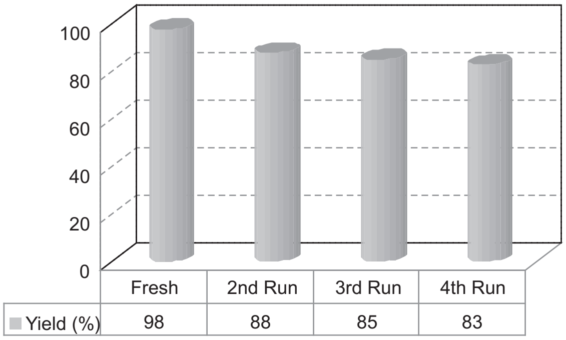


Figure 2. Recycle of BMIM·PF_6.

reasonable 35% yield (entry 13). In the reaction of Fmoc chloride with diphenyl diselenide, the product was obtained in 25% yield (entry 14).

One of the most attractive features of ionic liquids is that they frequently can be recycled. In this regard, we performed a set of experiments aiming to reuse the reaction media, Figure 2. After the first reaction of diphenyl diselenide and benzoyl chloride in BMIM·PF_6 the ionic liquid was recovered and subjected to another run, affording the product in 88% yield. This process was repeated for two more times, affording the desired product in excellent yields.[38]

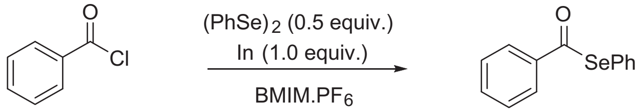
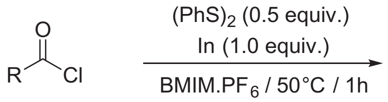
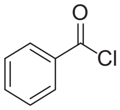
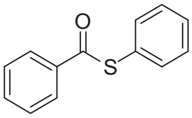
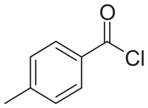
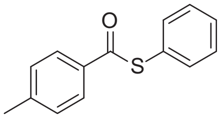
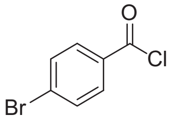
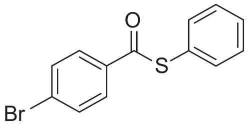
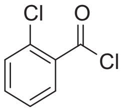
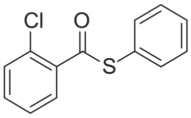
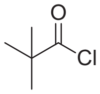
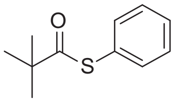
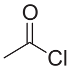
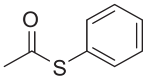
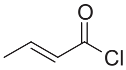
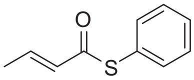
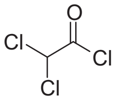
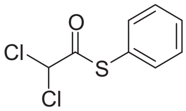
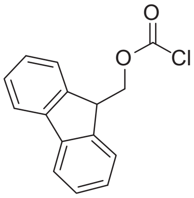
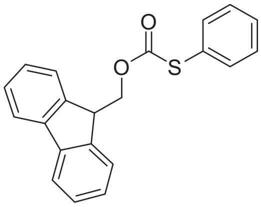


Table 3
Synthesis of thioesters in BMIM·PF_6 promoted by In



Entry	Acyl chloride	Product	Yield[a] (%)
1			78
2[b]			80
3[c]			78
4[d]			79
5[e]			23
6			75
7			42
8			52
9			44
10			43
11			62
12			36
13			57

[a] Yields for isolated pure products.
[b] BMIM·PF_6, 3 h, 50 °C.
[c] BMIM·PF_6, 12 h, 50 °C.
[d] BMIM·PF_6, 12 h, 100 °C.
[e] BMIM·PF_6, 12 h, rt.

As a further extension of our protocol, we applied the same reaction conditions employed for the preparation of selenoesters to prepare a series of thioesters, Table 3.

A decrease to 78% in the yield was found in the reaction of benzoyl chloride and diphenyl disulfide (entry 1). Several attempts to improve the yield of the incoming product failed, even by increasing the reaction time or the temperature (entries 2–5). Then a diverse range of acyl chlorides were subjected to the standard reaction conditions to prepare aryl and alkyl thioesters. Similar to selenoesters, better yields were found for the reactions involving acyl chlorides possessing an aryl group attached to the carbonyl moiety (entries 6–8). When aliphatic acyl chlorides were used, a decrease in the yield was found, and the formation of the desired products was in the range of 36–62% yield (entries 9–12). An interesting result was observed for the reaction of FmocCl with diphenyl disulfide, affording the product in 57% yield (entry 13).

To summarize, we described herein an efficient protocol for the synthesis of seleno and thioesters in ionic liquid. Our results are in agreement with those previously reported for the synthesis of these classes of compounds, however in our approach we employed an ionic liquid as solvent, which is conveniently recyclable, our reaction media is neutral and mild, and we used stable and easily handled diaryl chalcogenides instead of malodorous and hazardous selenols or thiols. Moreover, we employed indium metal which is a suitable reducing agent for high yields and short reaction times.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2010.08.076.

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37. In examples which lower yields were achieved; the mass balance was, on average, higher than 90%, since the staring materials (diselenides or disulfides) were recovered after column chromatography.
38. Representative experimental procedure to reuse BMIM·PF_6: After the work-up of the first run, BMIM·PF_6 was diluted in dichloromethane and filtered through a Celite pad to remove the inorganic materials followed by stirring for 2 h with charcoal to remove the light green color. After this time, the solution was filtered, concentrated, and subjected to the vacuum for 1 h to eliminate the moisture and trace of organic solvents. For the following runs the recovered ionic liquid was used after the addition of one equivalent of indium powder (1 mmol, 115 mg), diphenyl diselenide (0.5 mmol, 156 mg), and benzoyl chloride (1 mmol, 141 mg). Then, the product was extracted as described above.