Tetrahedron 67 (2011) 4723–4730

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Zn in ionic liquid: an efficient reaction media for the synthesis of diorganyl chalcogenides and chalcogenoesters

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ARTICLE INFO

Article history:
Received 26 January 2011
Received in revised form 2 April 2011
Accepted 5 April 2011
Available online 13 April 2011

Keywords:
Ionic liquid
Zinc
Recyclable
Diorganyl selenide and sulfides
Seleno- and thioesters

ABSTRACT

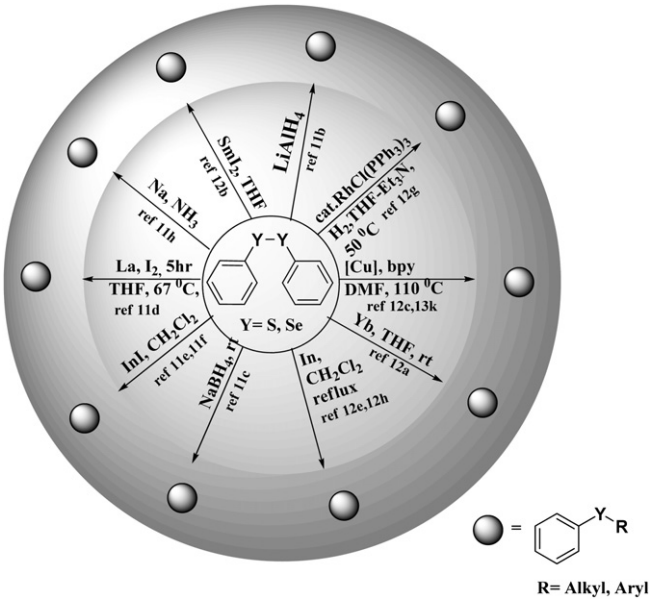
A straightforward and efficient methodology is described to synthesize structurally diverse diorganyl selenides, sulfides, seleno- and thioesters by using commercially available Zn dust in ionic liquid. Excellent yields were achieved under neutral conditions at room temperature in a short time. The solvent/ionic liquid is reusable and exhibited higher performance as compared with organic solvents.

1. Introduction

In synthetic organic reactions, the scope and application of organochalcogen chemistry have increased tremendously, since selenium and sulfur-containing groups serve as important auxiliary functions in synthetic sequences.[1] Organo-chalcogenides have also emerged as crucial intermediates in the transformation of a variety of functional groups[2] and the biological application of this class of compounds is well established.[3] For instance, it has been demonstrated that organoselenium compounds play an important role as therapeutic compounds, such as antiviral, anticancer agents, and in a variety of situations where free radicals are involved.[3] Synthetic methods for the preparation of selenocysteine, a natural amino acid,[4] selenium based peptides,[5] selenoglycosides,[6] and other important natural compound derivatives[7] is nowadays an area of intensive research.

The scope and application of organosulfur chemistry have increased due to the synthetic versatility of this class of compounds.[8] Significant attention has also been focused on sulfur-containing groups as model compounds of both active sites of natural enzymes and catalytic metal surfaces.[9] Also, the carbon–sulfur bond plays an important role in many molecules of biological, pharmaceutical, and materials interest.[10]

These compounds are generally prepared by reductive cleavage of dichalcogenide bonds, employing common reducing agents and expensive metal sources, as detailed in Scheme 1.[11–13] Furthermore,



Scheme 1. General methodology for the synthesis of diorganyl chalcogenides.

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doi:10.1016/j.tet.2011.04.018

reductive cleavage of Se–Se has been achieved with Na,[11a] CsOH,[11g] $ArB(OH)_2/CuI$,[12f] and photochemical reactions[11i] have been reported in a substantial number of previous studies.

In addition, some other reagents have been reported in the literature for the reductive cleavage of S–S bonds including sodium hydrogen telluride (NaHTe),[14a] butyl lithium,[14b] $LiCl/NaBH_4$,[14c] $ZrCl_2/NaBH_4$,[14c] rongalite,[14d] benzyl triethyl ammonium tetrathiomolybdate $[BnEt_3N]_2MoS_4$,[14e] and transition metal complexes.[12c,13] The synthesis of diorganyl sulfides has also been achieved from deoxygenation of the corresponding sulfoxides.[14f]

Symmetrical and unsymmetrical alkyl and aryl sulfides can be conveniently prepared by the transition metal-catalyzed reaction of a halide with a thiol under different reaction conditions.[13e,f,14b,15] The major drawbacks to the use of organothiol are very unpleasant odor and toxicity.

Moreover, most of the methods available to synthesize diorganyl selenides and sulfides are associated with serious disadvantages including: (i) the use of expensive metal sources and reagents, such as La, Yb, In, InI, SmI_2, and $[BnEt_3N]_2MoS_4$ etc.; (ii) functional group incompatibility; (iii) harsh reaction conditions, such as acidic or basic; and (iv) high temperature or long reaction time. Thus, there is still considerable interest in the development of highly efficient methods for this transformation.[16,17]

On the other hand, chalcogenoesters are important intermediates in several organic transformations. For instance, selenoester compounds have been used as precursors of acyl radicals and anions[18] and have attracted attention for the synthesis of new molecular materials, especially superconducting materials and liquid crystals.[19] Applications of selenoesters have been extended to the synthesis of proteins by chemical ligation of chalcogenol esters,[20] to the synthesis of substrates, which undergo facile and efficient radical decarbonylation, as well as to the synthesis of the natural products, e.g., crinipellin A, (+)-geissoschizine, ciguatoxins, and (−)-pseudolaric Acid B.[21]

Much effort has been devoted to the synthesis of selenoesters, and a number of reports have been published.[22] These compounds have been successfully prepared from aldehydes using $^{i}Bu_2Al$-SePh,[23] from chalcogeno acetylenes,[24] by coupling of aryl iodides with CO and $PhSeSnBu_3$ catalyzed by Pd,[25] and, most commonly, by the reaction of acyl chlorides with nucleophilic species of selenium, such as $Hg(SePh)_2$,[26] and $PhSeSnBu_3/Pd$,[27] from reductive cleavage of diselenides with InI,[11e,f] In[12g,h,28] or SmI_2,[29] or by reductive coupling of $(PhSe)_2$ and acyl chloride in a Rh/H_2 system.[12g]

Additionally, thioesters are considerably important class of compounds in the medicinal area because of their broad range of biological activities, e.g., in vivo tumor suppression and anti-HIV agents.[30] Also, they have found application in native chemical ligation for peptide bond formation,[31] and natural product synthesis.[32] Thioesters have also emerged as crucial intermediates in a variety of organic transformations, such as C–C coupling,[33] synthesis of carbonyl compounds,[34] asymmetric aldol reactions,[35] and asymmetric 1–4 additions.[36]

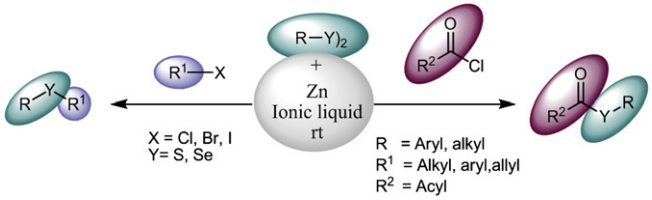
There are a number of methods reported in the literature to synthesize thioesters using the activation of carboxylic acids with diphosgene[37] or *N*-acyl benzotriazoles[38] followed by addition of thiol, or by reaction of acyl chlorides with zinc and thiols.[39] They have also been accomplished from thiols and carbon monoxide by carbonylation of organic substrates catalyzed by transition metals, such as Pt,[40] Pd,[41] etc.[42] Because of potentials biological and pharmacological applications of these classes of compounds, it is considered worthwhile to develop a general and effective method.

One of the tasks in striving for sustainable chemistry is the development of new methods that are efficient, high yielding, responsive to mild reaction conditions, and byproduct-free. In this regard, ionic liquids have frequently been used in the last few years as alternative reaction media for a broad range of chemical transformations.

Ionic liquids (ILs) are low-melting organic salts composed solely of cations and anions, which makes them highly tunable for specific applications.[43] Some ILs are noted to have a number of unique properties, including negligible vapor pressures, good thermal stabilities, wide liquid temperature ranges, considerable ionic conductivities, wide electro-chemical windows, and enhanced solvation interactions with both polar and nonpolar compounds.[44] These properties have been shown to have a large number of applications. Moreover, ILs have received considerable attention due to their ability to serve as an effective reaction media for a wide range of organic reactions and other applications in chemistry.[45] By modifying the structure of the cations or anions of ionic liquids, it has been shown that their properties can be altered in order to influence the outcome of the reaction.

In recent years, we have successfully employed ILs in the synthesis of diorganyl chalcogenides using different methods, demonstrating that ILs are much more appropriate than other common organic solvents.[46,47]

On account of these aspects and in association with our ongoing research interest toward organochalcogen chemistry[4c,48] herein we report the synthesis of diorganyl chalcogenides and chalcogenoesters using commercially available Zn dust in ionic liquid as depicted in Scheme 2. Interestingly, the experimental conditions for this reaction facilitate the easy workup of the reaction mixtures and isolation of the desired product in excellent yield.



Scheme 2. Synthesis of diorganyl selenide, sulfide, seleno- and thioesters using Zn in ionic liquid.

2. Results and discussion

Firstly, based on our previous work,[46] we focused on examining the feasibility of the reaction and optimizing the conditions for the synthesis of diorganyl sulfides. To optimize the protocol, we performed the reaction of benzyl chloride with PhSSPh and 1.6 equiv of zinc dust with respect to disulfide in five different ionic liquids (Fig. 1).

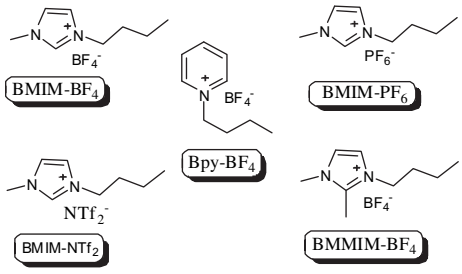
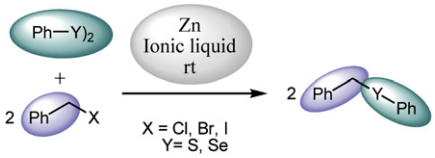


Fig. 1. Room temperature ionic liquids.

As described in our previous report,[46] it was observed that the results for BMIM-BF_4 were slightly better than those for the other ionic liquids (Table 1, entries 1–5). On the basis of these results, we investigated the influence of halide in the substrate. When benzyl iodide was used a higher yield was obtained as compared with benzyl bromide and chloride, which can be explained by the leaving group ability of the halogens (Table 1, entries 5–7). The

Table 1
Optimization of the reaction: ionic liquid, time, and amount of Zn



Entry	Ionic liquid[a]	X	Time (min)		Yield[b] (%)	
			Y=S	Y=Se	Y=S	Y=Se
1	Bpy-BF_4	Cl	30	40	67	55
2	BMMIM-BF_4	Cl	30	40	78	65
3	BMIM-NTf_2	Cl	30	40	46	29
4	BMIM-PF_6	Cl	30	35	89	86
5	BMIM-BF_4	Cl	15	30	92	93
6	BMIM-BF_4	Br	10	25	96	95
7	BMIM-BF_4	I	10	20	98	98
8[c]	BMIM-BF_4	Br	10	25	94	96
9[d]	BMIM-BF_4	Br	10	25	93	92

[a] Ionic liquids were prepared according to a literature procedure[45i] and were subjected to vacuum before use.
[b] Yields refer to pure isolated products.
[c] Zinc (1.2 equiv) dust was used.
[d] Zinc (1.0 equiv) dust was used.

amount of Zn required to cleave the S–S bond to afford the corresponding product was evaluated. When 1.2 and 1.0 equiv Zn were used in relation to disulfide, they showed comparable yields. As a result, we consider that 1.0 equiv Zn is sufficient to promote the reaction (Table 1, entries 8 and 9).

In general, the methodology provides the diorganyl sulfides in a short time, at room temperature, under very neutral and mild conditions with good to excellent yields. Interestingly, the formation of the diorganyl sulfides could be easily observed by the change of the reaction color from gray to white as shown in Fig. 2.

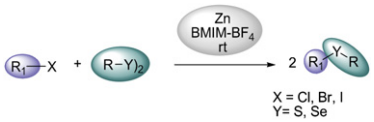
Fig. 2. Change in reaction color.

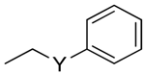
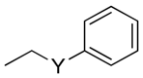
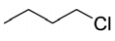
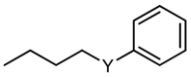
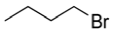
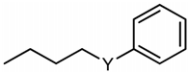
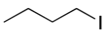
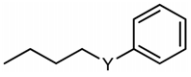
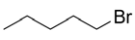
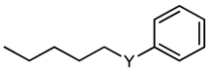
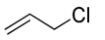
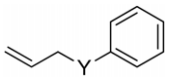
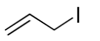
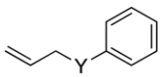
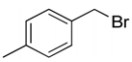
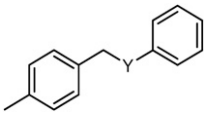
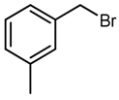
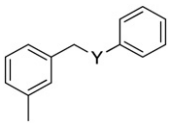
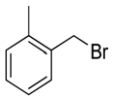
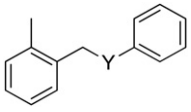
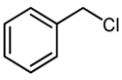
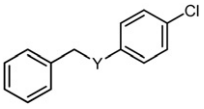
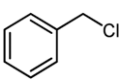
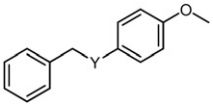
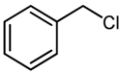
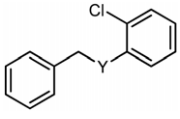
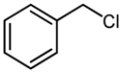
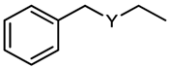
After optimization the protocol was extended to aryldiselenides and aryldisulfides; the couplings of different organic halides: alkyl, allyl, benzyl, and substituted aryl compounds were studied to check the versatility of the protocol.[49] Firstly, a structurally diverse range of alkyl halides were reacted with diphenyl disulfide and diselenide under standard reaction conditions to provide the corresponding alkyl phenyl sulfides and selenides in excellent yields. By comparing the yields, diorganyl sulfides were obtained in better yield than the diorganyl selenides (Table 2, entries 1–6). These results may reflect the higher stability of zinc thiolate compared with zinc selenolate. The chain length has an effect on the reaction course, affording improved yields with longer chains (Table 2, entries 2, 4, and 6).

With allylic halides the reaction was more effective and afforded the allyl phenyl sulfides in quantitative yields in a shorter reaction time as compared with the allyl phenylselenides (Table 2, entries 7 and 8). Moreover, the *ortho*, *meta*-, and *para*-substituted benzyl bromides were also employed, the highest reactivity being observed for the *para*-substituted followed by the *meta*- and *ortho*-methyl benzyl bromide (Table 2, entries 9–11).

Concerning the R group from the dichalcogenide, the influence of an electron-donating or an electron-withdrawing group, such as chloro and methoxy, in the aromatic rings of the diselenides and disulfides was investigated. Both diselenide and disulfide have no

Table 2
Synthesis of diorganyl selenides and sulfides using Zn in ionic liquid



	R^1X	Product	Y	*T* (min)	Yield[a] (%)
1			S Se	20 30	78 80
2			S Se	20 35	72 73
3			S Se	20 20	87 82
4			S Se	20 20	93 84
5			S Se	20 15	96 89
6			S Se	25 25	97 92
7			S Se	5 30	96 94
8			S Se	5 20	99 98
9			S Se	10 20	99 98
10			S Se	15 25	95 85
11			S Se	15 25	92 79
12			S Se	20 40	92 88
13			S Se	20 30	97 82
14			S Se	25 40	84 75
15			S Se	30 40	>99 77

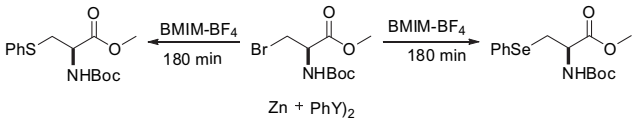
[a] Yields refer to pure isolated products characterized by ^1H and ^{13}C NMR.

significant influence on the reactivity of the process, since the products were obtained in comparable yields (Table 2, entries 12 and 13). Alkyl dichalcogenides were also investigated and for instance, diethyl diselenide and diethyl disulfide were reacted with benzyl chloride to form the desired products, in good yields (Table 2, entry 15).

With regard to broader versatility, we applied our methodology to the synthesis of a more complex functionality, such as biologically important cysteine[32c,50,51] and selenocysteine[4,32c,50,51] derivatives. The potential importance of selenocysteine, the 21st proteinogenic amino acid, which belongs to the active site in enzymes, such as glutathione peroxidase (GPx), iodothyronine deiodinase (ID), and thioredoxin reductase (TrxR), is well described in the literature.[4a] In this way, a tricky challenge still remains to develop novel synthetic methods that can permit the introduction of selenium and sulfur into optically active amino acids, which could be widely explored as building blocks for the synthesis of seleno and sulfur-peptides and derivatives.

Using our standard reaction conditions, chalcogeno–cysteine[4,5,32c,48b,51] derivatives were obtained from the corresponding bromo aminoester[52] in 48% yield at room temperature (Table 3, entry 1). The improvement of yield (61%) in this reaction was achieved by increasing the amount of ionic liquid, due to the higher solubility of the bromo ester (Table 3, entry 2). Similar results were observed for the synthesis of the cysteine derivative with a yield of 70% at room temperature (Table 3, entry 2).

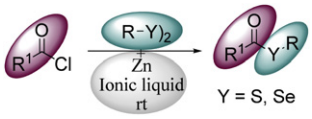
Table 3
Synthesis of cysteine and selenocysteine derivatives



Entry	Br–Ester	Zn	$(PhY)_2$ Y=S, Se	T (°C)	Yield[a] (%)	
					Y=S	Y=Se
1[b]	1.0	0.5	0.5	rt	59	48
2[c]	1.0	0.6	0.6	rt	70	61

[a] Yields refer to pure isolated products.
[b] BMIM-BF_4 (0.5 mL) was used.
[c] BMIM-BF_4 (1.0 mL) was used.

As a further extension of the present approach, we attempted to synthesize interesting organo-chalcogenide moieties, such as seleno- and thioesters from acyl chlorides promoted by Zn in ionic liquid (Scheme 3).

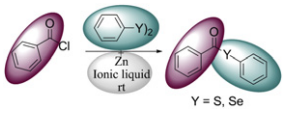


Scheme 3. General synthesis of seleno- and thioesters.

At the outset of the studies, benzoyl chloride and diphenyl dichalcogenide were selected as model substrates for the reaction development. The optimization reaction was performed employing benzoyl chloride with diphenyl diselenide/disulfide and 1.6 equiv of zinc dust with respect to dichalcogenide, in ionic liquid (0.5 mL) at room temperature. In the first set of experiments we studied the influence of different ionic liquids and the results are summarized in Table 4.

As observed in Table 4, a better conversion was obtained with BMIM-PF_6 in comparison to the other ionic liquids (Table 4, entries 1–5). Encouraged by this result, we then examined the amount of

Table 4
Optimization for the synthesis of seleno- and thioesters



Entry	Ionic liquid[a]	Time (min) Y=S, Se		Yield[b] (%) Y=S, Se	
		Y=S	Y=Se	Y=S	Y=Se
1	Bpy-BF_4	10	15	54	46
2	BMMIM-BF_4	10	15	77	69
3	BMIM-NTf_2	10	15	65	58
4	BMIM-PF_6	2	3	>99	97
5	BMIM-BF_4	2	3	92	95
6[c]	BMIM-PF_6	2	3	>99	97
7[d]	BMIM-PF_6	2	3	>99	95

[a] Ionic liquids were subjected to vacuum before use.
[b] Yields refer to pure isolated products.
[c] Zinc dust (1.2 equiv) was used.
[d] Zinc dust (1.0 equiv) was used.

Zn required to cleave the Se–Se/S–S bond and afford the corresponding product. When 1.2 and 1.0 equiv of Zn were used the yields were quite similar and as a result we consider 1.0 equiv Zn is enough to promote the reaction (Table 4, entries 6 and 7). In general, our methodology provides the seleno- and thioesters in a short time, at room temperature, under neutral and mild conditions with good to excellent yields.

Hence, the optimum conditions for the synthesis of seleno- and thioesters were 1.0 equiv of acyl chloride, 0.5 equiv of diaryl diselenide/disulfide, 0.5 equiv of Zn dust, and 0.5 mL of BMIM-PF_6, at room temperature in 2–3 min reaction time.[53]

After the optimization, we performed a series of reactions under standard conditions using different kinds of acyl chlorides with diaryl diselenides/disulfides to synthesize the seleno- and thioesters in good to excellent yields, as depicted in Table 5.

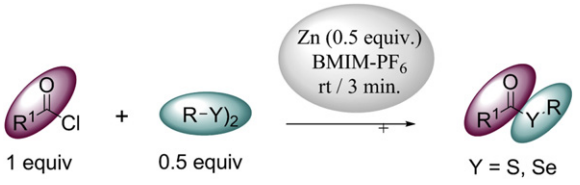
In general, employing our standard reaction conditions the thioesters were obtained in yields comparable with selenoesters. Aliphatic acyl chlorides were used to afford alkyl seleno- and thioesters in moderate yields (Table 5, entries 1 and 2). In terms of electronic effects, it was possible to verify that the reaction was more sensitive to the acid chloride than the dichalcogenide moiety. By using benzoyl chloride (neutral) and *p*-methyl benzoyl chloride (electron-donating group) the reaction proceeds efficiently and the chalcogenoesters were obtained in excellent yields (Table 5, entries 3 and 6). When electron-withdrawing groups were attached to the acyl chloride the products were obtained in lower yield (Table 5, entries 4 and 5).

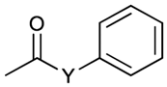
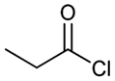
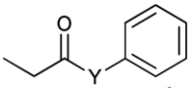
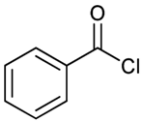
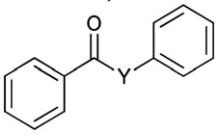
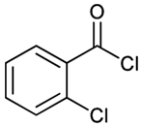
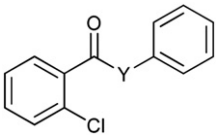
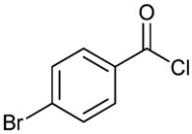
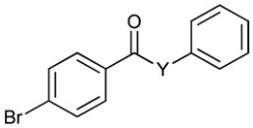
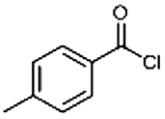
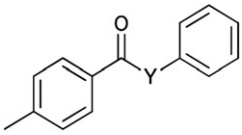
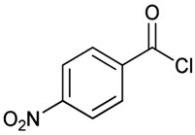
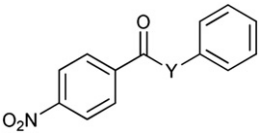
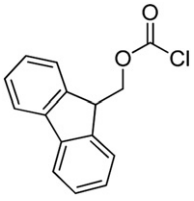
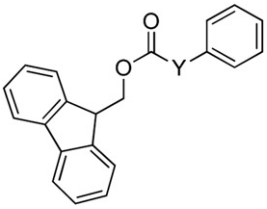
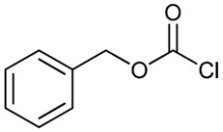
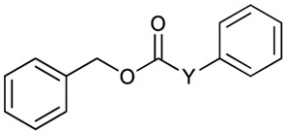
For instance, a strong electron-withdrawing group, such as the nitro attached to acyl chloride, affords 77% of thioester, whereas 72% yield was obtained for the selenoester (Table 5, entry 7). To improve the scope of our methodology, next we attempted to synthesize seleno- and thio-carbonates bearing interesting functionalities, since they can act as a selenium protecting group. In this context, when we used benzyl chloroformate and 9-fluorenylmethyl chloroformate the corresponding esters were obtained in good yields (Table 5, entries 8 and 9).

Inspired by the results above, different dichalcogenide moieties were also used for the synthesis of chalcogenoesters. In the diselenide moiety, a lower yield was observed by using *o*-chloro diphenyl diselenide as a selenium source compared with *p*-chloro diphenyl diselenide (Table 6, entries 4 and 5). These observations can be explained by steric dependence in this reaction, driving better yields for the less sterically hindered *para*-substituted dichalcogenides. Good yields were obtained with electron-donating groups attached to the dichalcogenide moiety, both in *ortho*- or *para*-

positions (Table 6, entries 1–3 and 6). The reactions followed the same tendency observed in the organochalcogenide preparation allowing the synthesis of thioesters in slightly better yields than selenoesters (Table 6, entries 6, 7 and 3, 4, respectively).

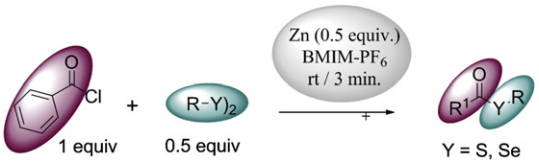
Table 5
Synthesis of seleno- and thioesters

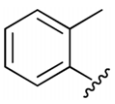
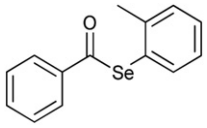
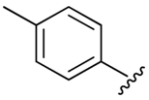
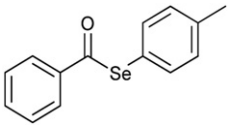
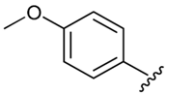
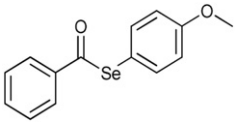
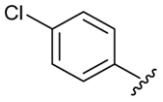
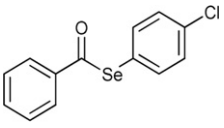
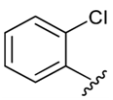
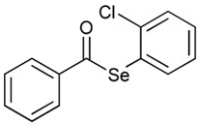
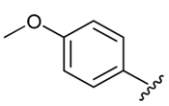
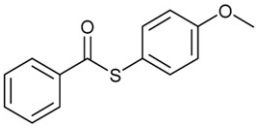
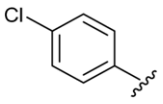
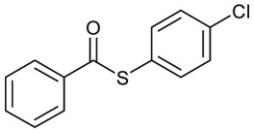


Entry	Acyl halide	Product	Yield[a] (%)	
			Y=Se	Y=S
1			39	42
2			57	68
3			95	>99
4			94	92
5			82	87
6			89	93
7			72	77
8			89	91
9			81	85

[a] Yields for pure isolated products characterized by ^{1}H and ^{13}C NMR.

Table 6
Synthesis of chalcogenoesters using benzoyl chloride with different dichalcogenide moieties



Entry	$(RY)_2$	Product	Yield[a] (%)
1			75
2			81
3			90
4			80
5			66
6			93
7			82

[a] Yields for pure isolated products.

Comparing the current methodology with some previous publications in the synthesis of organochalcogenides from dichalcogenides[11e,12h] and the synthesis of chalcogenolesters from acid chlorides,[11e,12h] generally it was possible to verify that, our current protocol has some advantages, such as, short reaction time, room temperature conditions, slighter improved or similar yields, compatibility with a variety of substrates and dichalcogenides in an enviromentally friendly approach.

With the success of the above reactions, we continued our study by exploring the reusability of the reaction media. After completion of the reaction, the ionic liquids were partitioned with diethyl ether, and the crude products were extracted into the diethyl ether phase. The respective ionic liquids were recovered and used for the subsequent runs.[54] As shown in Fig. 3, for the following five runs the recovered ionic liquids showed similar efficiency.

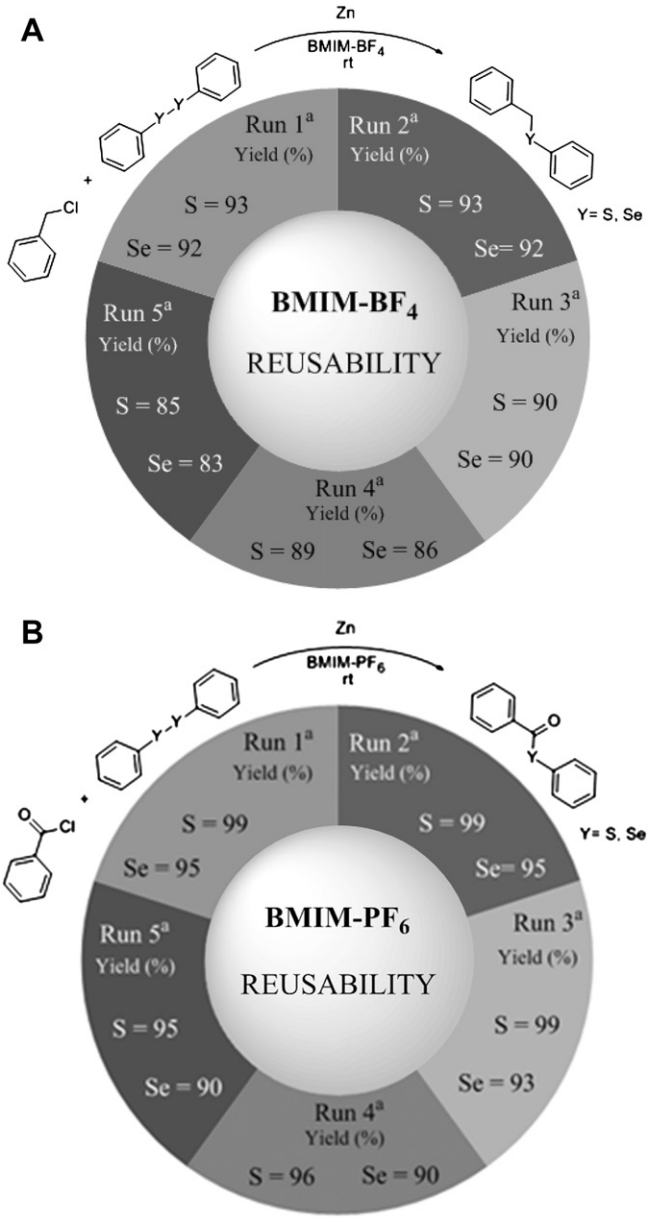


Fig. 3. Reuse of ILs: (A) BMIM-BF_4; (B) BMIM-PF_6. [a]Yields refer to pure isolated products as characterized by ^1H and ^{13}C NMR.

3. Conclusions

The main characteristics of the present method are the excellent yields obtained in a very short reaction time for the synthesis of diorganyl selenide, sulfide, seleno- and thioesters. This makes our procedure very attractive as compared with those previously reported in the literature. Other noteworthy features of this methodology are: (1) ease of handling and better safety aspects as compared with the metal hydrides; (2) neutral reaction conditions (room temperature as well); (3) easy access to check the formation of the product via the change in the reaction color; and (4) from the industrial point of view the present method is less expensive, e.g., it involves commercially available Zn, which costs less than the La, In, InI, Yb, and SmI_2 used in classical processes. The solvent/ionic liquid offers better performance combined with reusability. Also, our methodology has excellent generality, having been applied to the synthesis of seleno- and thioesters, biologically active cysteine, and selenocysteine derivatives displaying diverse functionalities of relevance to medicinal chemistry. On account of these findings, we believe that our protocol could find wide application in organic synthesis. Further investigations into the utility of this novel methodology are underway in our laboratory aiming at the synthesis of seleno amino acids and derivatives.

Acknowledgements

Senthil and Kashif are recipients of TWAS-CNPq doctoral fellowships, while E.E.A and C.Y.K are CNPq and CAPES Ph.D. fellowship holders, and cordially acknowledges their financial support. We are also obliged to CNPq (INCT-Catálise, INCT-NANOBIOSIMES, Ed. Jovem Pesquisador em Nanotecnologia) and FAPERGS for their financial support

Supplementary data

Supplementary data associated with this article can be found in online version at doi:10.1016/j.tet.2011.04.018.

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49. General procedure for the synthesis of diorganyl selenides and sulfides: commercially available Zn dust (33 mg, 0.5 mmol) and PhSeSePh/PhSSPh (0.5 mmol) and 15 μL of HCl 1N were added to BMIM-BF_4 (0.5 mL) at room temperature under nitrogen. The mixture was allowed to stir for 2–3 min. Then corresponding organic halides (1 mmol) was slowly added. The reaction mixture was allowed to stir until the color change (monitored by TLC and

assisted by visual observation). The mixture was then extracted with ether (3×15 mL), and the combined ether extract was washed with brine, dried ($MgSO_4$), and evaporated to leave the crude product. Purification by column chromatography over silica gel (hexane/ethyl acetate 98:2) furnished the corresponding products. ^1H and ^{13}C NMR spectral data of the compounds are identical to those previously reported.

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53. General procedure for the synthesis of seleno- and thioesters: commercially available Zn dust (0.5 mmol) and PhSeSePh or PhSSPh (0.5 mmol) and 15 μL of HCl 1N were added to BMIM-PF_6 (0.5 mL) at room temperature under nitrogen. Followed by the addition of acyl chloride (1 mmol). The reaction mixture was stirred for another 2–3 min (monitored by TLC and assisted by visual observation). The mixture was then extracted with ether (3×15 mL), and the combined ether extract was washed with brine, dried ($MgSO_4$), and evaporated to leave the crude product. Purification by column chromatography over silica gel (hexane/ethyl acetate 90:10), furnished the pure product and those ^1H and ^{13}C NMR spectral data of the compounds are identical to those reported.
54. Representative experimental procedure to reuse BMIM-BF_4 and BMIM-PF_6: after the workup of the first run, BMIM-BF_4/BMIM-PF_6 is diluted in ethanol, filtered through a Celite pad, and then subjected to the vacuum for 1 h. For the following run the recovered ionic liquid was used after addition of 1 equiv of Zn (33 mg, 0.5 mmol), diphenyl diselenide/disulfide (0.5 mmol) and 15 μL of HCl 1N and organic halide (1 mmol) followed by the procedure described above.