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Tetrahedron
Tetrahedron 60 (2004) 3745–3753

# Ionic liquid phase organic synthesis (IoLiPOS) methodology applied to the three component preparation of 2-thioxo tetrahydropyrimidin-4-(1*H*)-ones under microwave dielectric heating

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Received 9 December 2003; revised 4 March 2004; accepted 5 March 2004

**Abstract**—An ionic liquid phase organic synthesis (IoLiPOS) has been developed for the preparation of 2-thioxo tetrahydropyrimidin-4(1*H*)-ones. Treatment of the starting poly(ethyleneglycol)ionic liquid phases ($PEG_n$-ILPs) **1** with acryloyl chloride **2** afforded a serie of ($PEG_n$)-ILPs bound acrylate **3** in quantitative yields. Michael addition of aliphatic primary amines **5** to the $PEG_1$-ILPs **3**(**a**,**d**) allowed the preparation of β-aminoesters **6** in high yields. Addition of alkyl isothiocyanates **7** to **6** gave the corresponding thioureido esters **8** in the third step. The final cyclization-cleavage under microwave/solventless strategy provides, under basic conditions, the expected 2-thioxo tetrahydropyrimidin-4(1*H*)-ones **9** in high purity after flash chromatography. According to the IoLiPOS methodology, the NMR method was used to establish loading of all the PEG-ionic liquid phases intermediates.


## 1. Introduction

Combinatorial chemistry and high-throughput parallel synthesis have emerged as a powerful technique for the discovery of new pharmaceutical lead compounds.[1] The focus of this research field, which initially involved the synthesis, of peptides and oligonucleotides, is now extended to the synthesis of small heterocyclic molecules with solid phase.[2] Heterocycles, such as 4*H*-imidazolones,[3] benzodiazepines,[4] pyrrolidines,[5] 2-arylamino benzimidazoles,[6] bicyclic guanidines[7] have received special attention in combinatorial synthesis for their biological relevant properties.[8] This strategy has permitted the rapid synthesis of large number of organic molecules in a short period, facilitating their use in high-throughput screening. The initial efforts were focused on the use of solid phase organic synthesis (SPOS) by taking advantage of simple filtration techniques to wash off the excess reagents and by-products from the desired polymer-bound product. The use of cross-linked polystyrene based resins, such as Merrifield resin (MR) in combinatorial synthesis, is important due to their stability, high compatibility and good swelling characteristic with a wide range of non-polar solvents.[9] Nevertheless these resins fail when polar solvents are needed due to hindered accessibility to the reactive sites.[10] Soluble-polymer supported syntheses have recently emerged as an alternative and powerful technique for the preparation of heterocyclic libraries.[11] Modification of solid surfaces of solid resins (MR) with polar and soluble polymers such as poly (ethyleneglycol) PEG-derivatives can achieve several functions depending on the use of the resulting hybrid polymer.

Such hybrid polymers can combine some of the advantages of both types of polymers such as the physical stability of insoluble polymers that allows different substrates to approach the reactive sites more efficiently and hence increases the reaction rates. Liquid phase combinatorial synthesis offers several unique advantages: reactions may be carried out in homogeneous solution, the large excess of reagents typically used in solid-supported synthesis is normally not required in liquid phase organic synthesis. Characterisation of immobilized intermediates is also straightforward because the soluble polymer support does not interfere with spectroscopic methods.

The use of microwave irradiation (μω) as an alternative mode of heating reaction mixtures has been observed to

*Keywords*: Ionic liquid; Tetrahydropyrimidinones; Cyclization-cleavage; Acrylate; Michael addition; Microwave; Solvent-free conditions.
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doi:10.1016/j.tet.2004.03.026

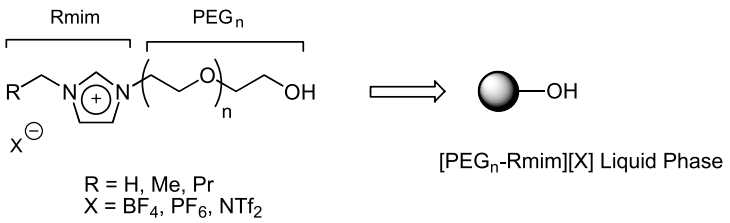



**Figure 1.** Poly(ethyleneglycol)-ionic liquid matrices used for ionic liquid phase organic synthesis (IoLiPOS).

dramatically reduce reaction times and affect product ratios and yields.[12] It is clear that the application of microwave technology to rapid synthesis of biologically significant molecules on solid phases, liquid phases or hybrid polymers would be of great value for library generation. This technology has recently been recognized as a useful tool for a drug-discovery program.[13]

Recently, we have reported the use of task-specific ionic liquids (Fig. 1) as a synthetic equivalent of liquid phase matrices for the preparation of a small library of 4-thiazolidinones.[14] According to this 'ionic liquid phase organic synthesis (IoLiPOS)' methodology, it was possible to bind the heterocyclic scaffold to the PEG-ionic liquid phases (PEG-ILPs) by a one pot three component condensation. We have observed that the grafted PEG-ILPs are immiscible with low polarity solvents (hexane, toluene) and with some polar solvents (diethyl ether, tetrahydrofuran) but miscible with some other polar solvents (acetone, ethyl acetate, acetonitrile). This turnable miscibility can be used to separate reaction by-products from the supported products and the primary advantage of the PEG-ILPs is that optimized reaction conditions were performed using standard analytical methods (NMR, TLC).

In connection with our research program on exploitation of the PEG-ILPs as tools in 'liquid phase organic synthesis' (LPOS), we choose to explore now the 2-thioxo tetra hydropyrimidinone moiety as new heterocyclic scaffold. In our approach, the 2-thioxo tetrahydropyrimidin-4(1*H*)-one scaffold can be built from a primary amine, an isothiocyanate and a β-dielectrophile (Fig. 2), and the carboxylic function is used as the site of attachment to the liquid support. As a suitable model reaction for ionic liquid-phase supported organic synthesis, we have chosen to use acrylate bound to the ionic liquid moiety (from commercial

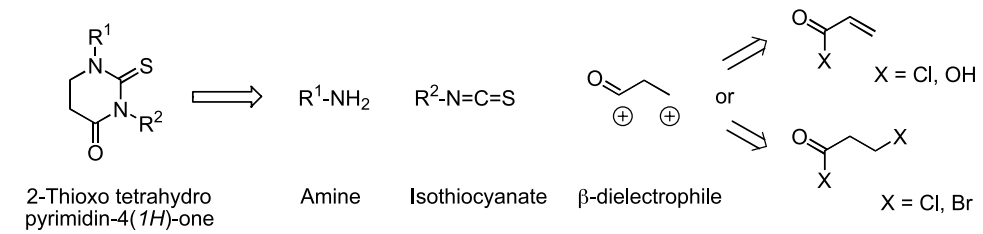
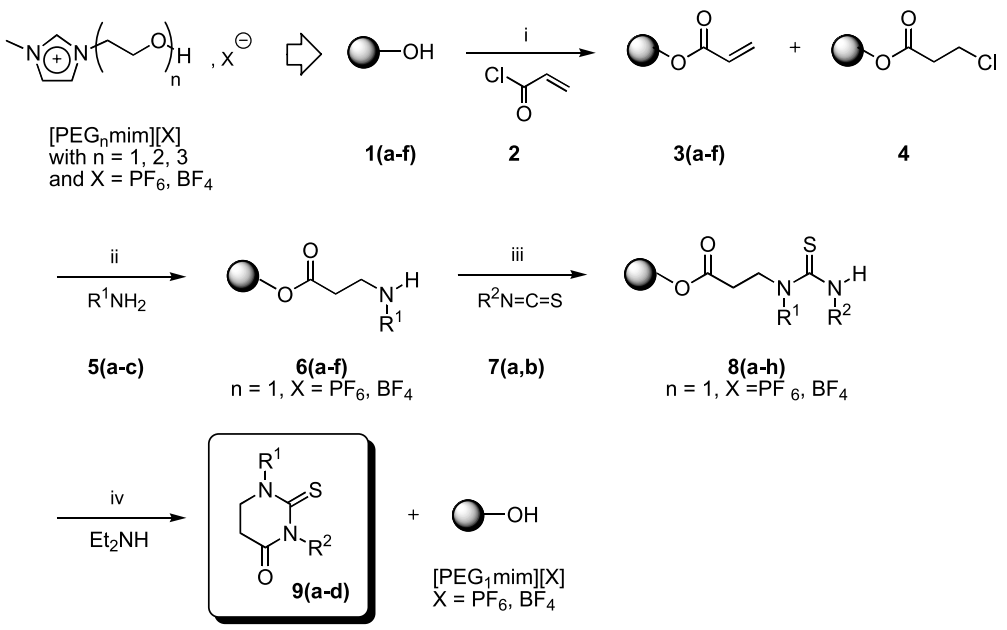



**Figure 2.** Components for the synthesis of 2-thioxo tetrahydropyrimidin-4(1*H*)-ones.



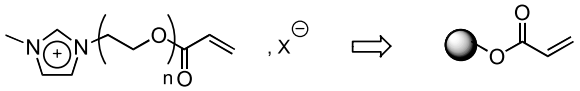

**Scheme 1.** Reagents and reaction condition: (i) **2** (1.2 equiv.), DCM, reflux, 48 h. (ii) **5** (1 equiv.), MeCN, 25 °C, 24 h. (iii) **7** (1 equiv.), MeCN, 18 h. (iv) DEA (2 equiv.), μω, 120 °C (power=20%), 15–45 min then purification by flash chromatography on silica gel 60F 254 (Merck).

acryloyl chloride in the first step) as novel task specific ionic liquid. We describe herein the general ionic liquid phase organic synthesis of 2-thioxo tetrahydropyrimidin-4(1*H*)-ones.

## 2. Results and discussion

In order to explore the application of the [PEG$_n$-mim][X] **1**[15] ($n$=1, 2, 3 and X=$BF_4$, $PF_6$) as a new class of soluble supports, we were first focused on the preparation of simple acrylates derivatives[16] from the PEG-ILPs **1** (Scheme 1). Under neat reaction conditions, treatment of the PEG-ILPs **1** with acryloyl chloride **2** at 70 °C provided the expected acrylate-ILPs **3** along with hydrogen chloride addition products **4**[17] in a 4:1 ratio. In an effort to avoid this problem, attention was turned to selective method for the preparation of acrylate-ILPs **3**. After exploring a few sets of reaction conditions, the one that proved to be most effective was the addition of acryloyl chloride **2** to a diluted solution of PEG-ILP **1** in dichloromethane at room temperature, followed by a moderate heating at 40 °C for 48 h. The HCl by-product formed in the reaction was removed by a stream of nitrogen and was eventually dissolved in deionized water at 0 °C. The acid aqueous solution was monitored by titration with sodium hydroxide. After the work-up, the crude mobile pale yellow acrylate-ILPs **3** were further dried under high vacuum ($10^{-2}$ Torr) at 60 °C for 1 h (Table 1). The ILPs were characterized by mass spectrometry and proton NMR, confirming that the major compound has a molecular ion corresponding to the acrylate-ILPs **3**.

**Table 1**. Results of addition of acryloyl chloride **2** on PEG$_n$-ionic liquid phases **1**(**a**-**f**) for the preparation of ILP bound acrylates **3**(**a**-**f**)



**3(a-f)**

| Starting [PEG$_n$mim][X] | | | ILP bound acrylate | |
|---|---|---|---|---|
| Product **1** | $n$[a] | X | **3** | Yield (%)[b] |
| **1a** | 1 | $PF_6$ | **3a** | 98 |
| **1b** | 2 | $PF_6$ | **3b** | 98 |
| **1c** | 3 | $PF_6$ | **3c** | 94 |
| **1d** | 1 | $BF_4$ | **3d** | 96 |
| **1e** | 2 | $BF_4$ | **3e** | 96 |
| **1f** | 3 | $BF_4$ | **3f** | 96 |

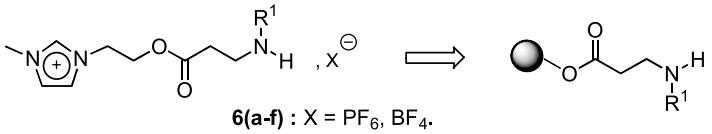
[a] Number of polyethyleneglycol (PEG) unit.
[b] Yield of isolated product.

With the desired acrylate-ILPs **1** in hand, we have examined the Michael addition of various monosubstituted alkyl amines in the second step to the PEG$_1$-ILPS **1**(**a**,**b**) with $BF_4$ and $PF_6$ as the corresponding coordinating anions. An array of experiments carried out with different reaction temperatures revealed that the optimal results were obtained at 25 °C after 24 h. A stoichiometry of 1:1 of IL-phase **1**: amine **5** gave successful regioselective addition of monosubstituted amine into the IL-phase **1** in dry stirred acetonitrile. Progress of the Michael addition was monitored (after elimination of the solvent) by proton NMR spectroscopy which is faster and more convenient than conventional methods used in solid phase organic synthesis (SPOS) that require the concentration of cleaved material. We have also found that the β-amino esters **6** were prepared in quantitative yields (Table 2) and with our method, it was not necessary to use large excess of amine **5** as described in the literature with a resin-bound acrylate.

In the third step, addition of 1 equiv. of isothiocyanate **7** (**7a**: R=Me, **7b**: R=Bu) to the β-amino ester **6** bound to the ionic liquid moiety in dry acetonitrile was generally completed in 24 h. Progress of the reaction of **6** with isothiocyanate **7** was also monitored by $^1$H NMR (or by TLC with $CH_2Cl_2$ as eluent). As can be seen from Table 3, the ILP bound thioureas **8** were prepared in high yields (96–98%) according to this method. Similarly, when phenylisothiocyanate **7c** was used, no reaction occurred in refluxing MeCN and only the decomposition of the products was observed when the reaction conditions were forced (neat conditions, 70 °C, 7 days). During the experiments, it should be noted that the thioureas **8** slowly glassify at room temperature and were fully reliquified by mild heating at 70–80 °C. It is noteworthly that the ILP bound thioureas **8** appear to be stable at room temperature for several weeks.

Consistent cyclization/cleavage of the thioureido esters **8** to 2-thioxo tetrahydropyrimidin-4(1*H*)-ones **9** was achieved by treatment of the ILPs **8** with 2 equiv. of diethyl amine

**Table 2**. Results for the preparation of β-amino esters **6**(**a**-**f**) by Michael addition of amine **5**(**a**-**c**) on the PEG$_1$-ionic liquid phases **3a** and **3d**

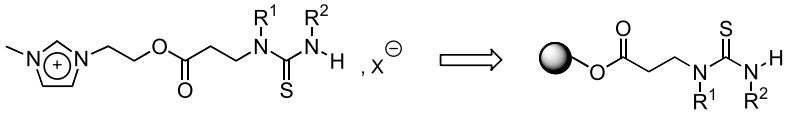


**6(a-f)** : X = $PF_6$, $BF_4$.

| Starting amine **5** | | Starting acrylate **3** | | β-Amino ester **6** | |
|---|---|---|---|---|---|
| Product **5** | $R^1$ | Product **3** | X | Product **6** | Yield of **6** (%)[a] |
| **5a** | Ph-$CH_2$ | **3a** | $PF_6$ | **6a** | 98 |
| **5b** | *i*Pr-$CH_2$ | **3a** | $PF_6$ | **6b** | 96 |
| **5c** | Pr | **3a** | $PF_6$ | **6c** | 96 |
| **5a** | Ph-$CH_2$ | **3d** | $BF_4$ | **6d** | 94 |
| **5b** | *i*Pr-$CH_2$ | **3d** | $BF_4$ | **6e** | 94 |
| **5c** | Pr | **3d** | $BF_4$ | **6f** | 96 |

[a] Yield of isolated product.

**Table 3**. Results for the preparation of thioureido esters **8**(**a**-**h**) from isothiocyanates **7**(**a**,**b**) and β-aminoesters **6**(**a**-**f**)



**8(a-h)** : X =$PF_6$, $BF_4$

| Starting β-aminoester **6** | | | Starting isothiocyanate **7** | | Thioureido ester **8** | |
|---|---|---|---|---|---|---|
| Product **6** | X | $R^1$ | Product **7** | $R^2$ | Product **8** | Yield of **8** (%)[a] |
| **6a** | $PF_6$ | Ph-$CH_2$ | **7a** | Me | **8a** | 94 |
| **6b** | $PF_6$ | *i*Pr-$CH_2$ | **7a** | Me | **8b** | 96 |
| **6c** | $PF_6$ | Pr | **7a** | Me | **8c** | 98 |
| **6b** | $PF_6$ | *i*Pr-$CH_2$ | **7b** | Bu | **8d** | 90 |
| **6d** | $BF_4$ | Ph-$CH_2$ | **7a** | Me | **8e** | 94 |
| **6e** | $BF_4$ | *i*Pr-$CH_2$ | **7a** | Me | **8f** | 96 |
| **6f** | $BF_4$ | Pr | **7b** | Me | **8g** | 96 |
| **6e** | $BF_4$ | *i*Pr-$CH_2$ | **7b** | Bu | **8h** | 94 |

[a] Yield of isolated product.

(DEA) when the reaction mixture was exposed to microwave irradiation[18] with the specified reaction time (15 or 45 min) at 120 °C using solvent-free reaction conditions (Table 4). On completion of the reaction, as evidenced by $^1$H NMR, the crude reaction mixture was extracted with chloroform (1:5 w/v) and the subsequent flash chromatography purification on silica gel 60F 254 (Merck) afforded the desired 2-thioxo tetrahydropyrimidin-4(1*H*)-ones **9**(**a**-**d**) using $CHCl_3$ or AcOEt as eluent. The yields of isolated compounds **9**(**a**-**d**) are quite respectable (67–85%) and their purity has been established by acquisition of clean $^1$H and $^{13}$C NMR as well as by FAB-MS.

## 3. Conclusion

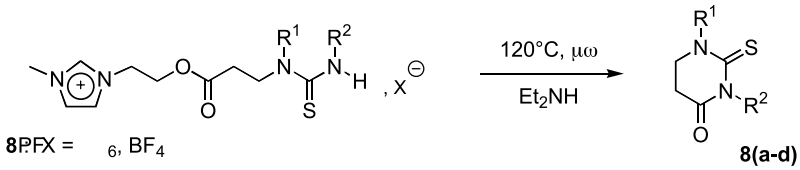
In summary, we report an efficient and new route to the synthesis of 2-thioxo tetrahydropyrimidin-4(1*H*)-ones[19] using the ionic liquid phase organic chemistry. Conjugate addition of a primary amine to the $PEG_1$-ionic liquid phase bound unsaturated ester **3** gave the N-substituted β-amino ester **6**, which was further treated with an alkyl isothiocyanate **7** to produce the β-thioureido ester **8**. Cleavage of **8** in basic media using solventless reaction conditions under microwave irradiations[20] gave cyclization of **8**. Product isolation is routine and the reactions are high yielding. The use of [$PEG_1$mim] [X] as novel IL phase in liquid phase organic synthesis (LPOS) offers considerable advantages because the side product is removed by simple extraction and washings from the cleaved IL phase. In contrast to the various restrictions of reaction development in solid phase synthesis, IL phases allow standard analytical methods (NMR, TLC) to monitor reaction progress. To our knowledge, the ionic liquid phase organic synthesis (IoLiPOS) methodology has never been reported for the preparation of these 2-thioxo tetrahydropyrimidin-4(1*H*)-ones and may complement those existing in the literature.[21] We are currently exploring the scope and potential of the ILPs by extending this methodology to other heterocyclic targets. Further applications of multicomponent multistep syntheses of heterocycles will be reported in due course.

## 4. Experimental

### 4.1. General

Thin-layer chromatography (TLC) was accomplished on 0.2-mm precoated plates of silica gel 60 F-254 (Merck). Visualisation was made with ultraviolet light (254 and 365 nm) or with a fluorescence indicator. For preparative

**Table 4**. 2-Thioxo tetrahydropyrimidin-4(1*H*)-ones **9**(**a**-**d**) prepared from the thioureido esters **8**(**a**-**h**) by cyclization/cleavage under microwave irradiations (μω) at 120 °C using solvent-free reaction conditions




**8**P.FX = $_6$, $BF_4$ **8(a-d)**

| Product **9** | $R^1$ | $R^2$ | Reaction time (min) | Yield of **9** (%)[a] |
|---|---|---|---|---|
| **9a** | Ph-$CH_2$ | Me | 45 | 85 |
| **9b** | *i*Pr-$CH_2$ | Me | 15 | 72 |
| **9c** | *i*Pr-$CH_2$ | Bu | 15 | 67 |
| **9d** | Pr | Me | 15 | 83 |

[a] Yield of isolated product after purification by chromatography on silica gel 60F 254 (Merck).

column chromatography, silica gel 60F 254 Merck (230–240 mesh ASTM) was used. $^1$H NMR spectra were recorded on BRUKER AC 300 P (300 MHz) spectrometer, $^{13}$C NMR spectra on BRUKER AC 300 P (75 MHz) spectrometer. Chemical shifts are expressed in parts per million downfield from tetramethylsilane as an internal standard. Data are given in the following order: $\delta$ value, multiplicity (s, singulet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad), number of protons, coupling constants $J$ are given in Hertz. The mass spectra (HRMS) were taken on a VARIAN MAT 311 at an ionizing potential of 70 eV in the Centre Régional de Mesures Physiques de l'Ouest (CRMPO, Rennes). Reactions under microwave irradiations were realized in the Synthewave® 402 reactor[22] (Merck Eurolab, Div. Prolabo, France). Acetonitrile was distilled over calcium chloride after standing overnight and stored over molecular sieves (3 Å). Solvents were evaporated with a BUCHI rotary evaporator. All reagents were purchased from Acros, Aldrich Chimie, Fluka France and used without further purification. The starting [PEG$_n$-mim][X] ionic liquid phase **1** were synthetized according to our previous method[14] for 1-(2-hydroxy-ethyl)-3-methyl-imidazolium hexafluorophosphate [PEG$_1$mim][PF$_6$] **1a**, 1-(2-hydroxy-ethyl)-3-methyl-imidazolium tetrafluoroborate [PEG$_1$mim]-[BF$_4$] **1b**, 1-[2-(2-hydroxy-ethoxy)-ethyl]-3-methyl-imidazolium hexafluorophosphate [PEG$_2$mim][PF$_6$] **1c**, 1-[2-(2-hydroxy-ethoxy)-ethyl]-3-methyl-imidazolium tetrafluoroborate [PEG$_2$mim][BF$_4$] **1d**, 1-{2-[2-(2-hydroxy-ethoxy)-ethoxy]-ethyl}-3-methyl-imidazolium hexafluorophosphate [PEG$_3$mim][PF$_6$] **1e**, 1-{2-[2-(2-hydroxy-ethoxy)-ethoxy]-ethyl}-3-methyl-imidazolium tetrafluoroborate [PEG$_3$mim]-[BF$_4$] **1f**.

### 4.2. General procedure for acylation of the PEG$_n$-ILPs 1(a-f)

A typical experimental procedure is as follows for **3b**. To a vigorously stirred solution of 1-(2-hydroxyethyl)-3-methyl-imidazolium tetrafluoroborate [PEG$_1$mim][BF$_4$] **1b** (2 g, 9.35 mmol, 1 equiv.) in dry dichloromethane (20 mL) was added dropwise over 15 min at room temperature a solution of commercial acryloyl chloride **2** (1.02 g, 11.26 mmol, 1.2 equiv.) in dry methylene chloride (10 mL). Then the reaction mixture was refluxed at 40 °C during 48 h and the HCl by-product formed during the reaction was distilled out of the condenser. When the formed HCl had been completely removed, the solution was cooled to room temperature and $CH_2Cl_2$ was evaporated with a rotary evaporator. Then the crude acrylate **3b** was washed with ether (3×10 mL) or AcOEt (3×10 mL) under magnetic stirring. After decantation, the residual solvent was eliminated in vacuo. The ionic liquid phase bound acrylate **3b** was further dried under high vacuum ($10^{-2}$ Torr) at 60 °C for 8 h and lead to a pale yellow mobile ionic liquid phase in 98% yield which was controlled by $^1$H and $^{13}$C NMR spectroscopy. It is advisable to handle the acrylate **3b** under inert atmosphere at 4 °C.

**4.2.1. 1-(2-Acryloyloxy-ethyl)-3-methyl-imidazolium hexafluorophosphate (3a).** Yield=98%. $^1$H NMR (acetone $d^6$, 300 MHz) $\delta$ 4.05 (s, 3H); 4.59 (t, 2H, $J$=4.6 Hz); 4.73 (t, 2, $J$=4.8 Hz); 5.93 (dd, 1H, $J$=10, 1.6 Hz); 6.18 (dd, 1H, $J$=17, 10.3 Hz); 6.38 (dd, 1H, $J$=17, 1.5 Hz); 7.69 (t, 1H, $J$=1.6 Hz); 7.8 (t, 1H, $J$=1.7 Hz); 9.06 (s, 1H). $^{13}$C NMR (acetone $d^6$, 75 MHz) $\delta$ 36.7 (q, $J$=144 Hz); 49.4 (t, $J$=146 Hz); 63.5 (tm, $J$=152 Hz); 123.9 (dm, $J$=204 Hz); 124.8 (dm, $J$=204 Hz); 128.5 (ddd, $J$=164, 9.6, 2.6 Hz); 132.5 (dd, $J$=165, 16 Hz); 138.2 (dm, $J$=223 Hz), 166.0 (Sm, CO). HRMS, $m/z$: 181.0974 found (Calcd for $C_9H_{13}N_2O_2$, $C^+$ requires: 181.0977).

**4.2.2. 1-[2-(2-Acryloyloxy-ethoxy)ethyl]-3-methyl-imidazolium hexafluorophosphate (3b).** Yield=98%. $^1$H NMR (acetone $d^6$, 300 MHz) $\delta$ 3.77 (t, 2H, $J$=4 Hz); 3.92 (t, 2H, $J$=4.8 Hz); 4.03 (s, 3H); 4.30 (t, 2H, $J$=4.6 Hz); 4.52 (t, 2H, $J$=4.8 Hz); 5.93 (dd, 1H, $J$=10.3, 1.7 Hz); 6.15 (dd, 1H, $J$=17.3, 1.3 Hz); 6.35 (dd, 1H, $J$=17.3, 1.7 Hz); 7.66 (t, 1H, $J$=1.5 Hz); 7.68 (t, 1H, $J$=1.8 Hz); 8.92 (s, 1H). $^{13}$C NMR (acetone $d^6$, 75 MHz) $\delta$ 35.5 (q, $J$=144 Hz); 49.1 (t, $J$=144 Hz); 62.9 (t, $J$=148 Hz); 68.2 (tm, $J$=145 Hz); 68.4 (tm, $J$=143 Hz); 122.7 (dm, $J$=203 Hz); 123.2 (dm, $J$=202 Hz); 128.2 (dm, $J$=171 Hz); 130.6 (tm, $J$=161 Hz); 136.8 (dm, $J$=222 Hz), 205.8 (s, CO). HRMS, $m/z$: 225.1245 found (Calcd for $C_{11}H_{17}N_2O_2$, $C^+$ requires: 225.1239).

**4.2.3. 1-{2-[2-(2-Acryloyloxy-ethoxy-ethoxy]ethyl}-3-methyl-imidazolium hexafluorophosphate (3c).** Yield=94%. $^1$H NMR (acetone $d^6$, 300 MHz) $\delta$ 3.57 (m, 2H); 3.64 (s, 2H); 3.72 (m, 2H); 3.84 (t, 2H, $J$=4.8 Hz); 3.85 (s, 3H); 4.25 (m, 2H); 4.31 (t, 2H, $J$=4.4 Hz); 5.92 (dd, 1H, $J$=10, 1.2 Hz); 6.12 (dd, 1H, $J$=17.3, 10.4 Hz); 6.36 (dd, 1H, $J$=17.3, 1.2 Hz); 7.36 (t, 1H, $J$=1.7 Hz); 7.44 (t, 1H, $J$=1.8 Hz); 8.64 (s, 1H). $^{13}$C NMR ($D_2O$, 75 MHz) $\delta$ 34.9 (q, $J$=144 Hz); 48.2 (t, $J$=144 Hz); 63.2 (t, $J$=149 Hz); 67.6 (t, $J$=145 Hz); 68.8 (tm, $J$=143 Hz); 121.8 (dm, $J$=204 Hz); 122.7 (dm, $J$=203 Hz); 126.7 (tm, $J$=157 Hz); 133.5 (dm, $J$=226 Hz); 167.4 (sm, CO). HRMS, $m/z$: 269.1504 found (Calcd for $C_{13}H_{21}N_2O_2$, $C^+$ requires: 269.15.01).

**4.2.4. 1-(2-Acryloyloxy-ethyl)-3-methyl-imidazolium tetrafluoroborate (3d).** Yield=96%. $^1$H NMR (acetone $d^6$, 300 MHz) $\delta$ 4.05 (s, 3H); 4.59 (t, 2H, $J$=4.6 Hz); 4.73 (t, 2, $J$=4.8 Hz); 5.93 (dd, 1H, $J$=10, 1.6 Hz); 6.18 (dd, 1H, $J$=17, 10.3 Hz); 6.38 (dd, 1H, $J$=17, 1.5 Hz); 7.69 (t, 1H, $J$=1.6 Hz); 7.8 (t, 1H, $J$=1.7 Hz); 9.06 (s, 1H). $^{13}$C NMR (acetone $d^6$, 75 MHz) $\delta$ 36.7 (q, $J$=144 Hz); 49.4 (t, $J$=146 Hz); 63.5 (tm, $J$=152 Hz); 123.9 (dm, $J$=204 Hz); 124.8 (dm, $J$=204 Hz); 128.5 (ddd, $J$=164, 9.6, 2.6 Hz); 132.5 (dd, $J$=165, 16 Hz); 138.2 (dm, $J$=223 Hz), 166.0 (Sm, CO). HRMS, $m/z$: 181.0974 found (Calcd for $C_9H_{13}N_2O_2$, $C^+$ requires: 181.0977).

**4.2.5. 1-[2-(2-Acryloyloxy-ethoxy)ethyl]-3-methyl-imidazolium tetrafluoroborate (3e).** Yield=96%. $^1$H NMR (acetone $d^6$, 300 MHz) $\delta$ 3.77 (t, 2H, $J$=4 Hz); 3.92 (t, 2H, $J$=4.8 Hz); 4.03 (s, 3H); 4.30 (t, 2H, $J$=4.6 Hz); 4.52 (t, 2H, $J$=4.8 Hz); 5.93 (dd, 1H, $J$=10.3, 1.7 Hz); 6.15 (dd, 1H, $J$=17.3, 1.3 Hz); 6.35 (dd, 1H, $J$=17.3, 1.7 Hz); 7.66 (t, 1H, $J$=1.5 Hz); 7.68 (t, 1H, $J$=1.8 Hz); 8.92 (s, 1H). $^{13}$C NMR (acetone $d^6$, 75 MHz) $\delta$ 35.5 (q, $J$=144 Hz); 49.1 (t, $J$=144 Hz); 62.9 (t, $J$=148 Hz); 68.2 (tm, $J$=145 Hz); 68.4 (tm, $J$=143 Hz); 122.7 (dm, $J$=203 Hz); 123.2 (dm, $J$=202 Hz); 128.2 (dm, $J$=171 Hz); 130.6 (tm, $J$=161 Hz); 136.8 (dm, $J$=222 Hz), 205.8 (s, CO). HRMS, $m/z$: 225.1245 found (Calcd for $C_{11}H_{17}N_2O_2$, $C^+$ requires: 225.1239).

**4.2.6. 1-{2-[2-Acryloyloxy-ethoxy-ethoxy]ethyl}-3-methyl-imidazolium tetrafluoroborate (3f).** Yield=96%. $^1$H NMR ($D_2O$, 300 MHz) $\delta$ 3.57 (m, 2H); 3.64 (s, 2H); 3.72 (m, 2H); 3.84 (t, 2H, $J$=4.8 Hz); 3.85 (s, 3H); 4.25 (m, 2H); 4.31 (t, 2H, $J$=4.4 Hz); 5.92 (dd, 1H, $J$=10, 1.2 Hz); 6.12 (dd, 1H, $J$=17.3, 10.4 Hz); 6.36 (dd, 1H, $J$=17.3, 1.2 Hz); 7.36 (t, 1H, $J$=1.7 Hz); 7.44 (t, 1H, $J$=1.8 Hz); 8.64 (s, 1H). $^{13}$C NMR ($D_2O$, 75 MHz) $\delta$ 34.9 (q, $J$=144 Hz); 48.2 (t, $J$=144 Hz); 63.2 (t, $J$=149 Hz); 67.6 (t, $J$=145 Hz); 68.8 (tm, $J$=143 Hz); 121.8 (dm, $J$=204 Hz); 122.7 (dm, $J$=203 Hz); 126.7 (tm, $J$=157 Hz); 133.5 (dm, $J$=226 Hz); 167.4 (sm, CO). HRMS, $m/z$: 269.1504 found (Calcd for $C_{13}H_{21}N_2O_2$, $C^+$ requires: 269.15.01).

### 4.3. General procedure for Michael addition of alkylamine 5 to the acrylate-ionic liquid phases 3a (X=$PF_6$) or 3d (X=$BF_4$): synthesis of β-amino acrylate 6

A solution of benzylamine **5a** (0.59 g, 5.6 mmol) or isobutylamine **5b** (0.402 g, 5.6 mmol) or propylamine **5c** (0.301 g, 5.6 mmol) in dry acetonitrile (20 mL) was added dropwise over 20 min to a stirred solution of acrylate **3a** (1.81 g, 5.6 mmol) or **3b** (1.49 g, 5.6 mmol) in dry acetonitrile. After magnetic stirring at room temperature for 24 h under inert atmosphere, the solvent was eliminated in a rotary evaporator under reduced pressure. The crude mobile β-amino acrylate **6** was washed three times with AcOEt (10 mL) or ether (15 mL) with vigorous magnetic stirring. After decantation, the residual solvent was removed in vacuo. The ionic liquid phase bound β-amino acrylate **6** was further dried under high vacuum ($10^{-2}$ Torr) at 60 °C for 8 h and lead to a pale yellow mobile ionic liquid phase in 96–98% yield which was controlled by $^1$H and $^{13}$C NMR spectroscopy. The β-amino acrylates **6** were stored under inert atmosphere at 4 °C.

**4.3.1. 1-[2-(3-Benzylamino-propionyloxy)-ethyl]-3-methyl-imidazolium hexafluorophosphate (6a).** Yield=98%. $^1$H NMR (acetone $d^6$, 300 MHz) $\delta$ 2.60 (t, 2H, $J$=6.5 Hz); 2.88 (t, 2H, $J$=7 Hz); 3.8 (s, 2H); 3.95 (s, 3H); 4.45 (m, 2H, $J$=4.7 Hz); 4.62 (m, 2H, $J$=4.7 Hz); 7.23–7.39 (m, 5H); 7.61 (d, 1H, $J$=1.5 Hz); 7.75 (d, 1H, $J$=1.6 Hz); 9.06 (s, 1H). $^{13}$C NMR (acetone $d^6$, 75 MHz) $\delta$ 35.0 (t, $J$=126 Hz); 36.5 (q, $J$=144 Hz); 45.1 (t, $J$=133 Hz); 49.5 (t, $J$=146 Hz); 53.7 (tm, $J$=171 Hz); 63.2 (t, $J$=151 Hz); 123.9 (dm, $J$=204 Hz); 124.6 (dm, $J$=204 Hz); 127.8 (dm, $J$=159 Hz); 129.2 (dd, $J$=160, 6.4 Hz); 129.7 (Sm); 141.0 (dm, $J$=220 Hz); 170.3 (sm, CO). HRMS, $m/z$: 288.1714 found (Calcd for $C_{16}H_{22}N_3O_2$, $C^+$ requires: 288.1712).

**4.3.2. 1-[2-(3-Isobutylamino-propionyloxy)-ethyl]-3-methyl-imidazolium hexafluorophosphate (6b).** Yield=96%. $^1$H NMR (acetone $d^6$, 300 MHz) $\delta$ 0.88 (d, 6H, $J$=6.7 Hz); 1.71 (m, 1H, $J$=6.7 Hz); 2.42 (d, 2H, $J$=6.7 Hz); 2.60 (t, 2H, $J$=6.6 Hz); 2.86 (t, 2H, $J$=6.4 Hz); 4.04 (s, 3H); 4.49 (t, 2H, $J$=5.2 Hz); 4.65 (t, 2H, $J$=5.2 Hz); 7.70 (d, 1H, $J$=1.9 Hz); 7.81 (d, 1H, $J$=1.9 Hz). $^{13}$C NMR (acetone $d^6$, 75 MHz) $\delta$ 21.0 (qm, $J$=125 Hz); 27.1 (dm, $J$=125 Hz); 34.9 (t, $J$=130 Hz); 36.7 (q, $J$=144 Hz); 45.8 (t, $J$=139 Hz); 49.5 (t, $J$=147 Hz); 61.1 (t, $J$=130 Hz); 63.2 (t, $J$=151 Hz); 123.9 (dm, $J$=204 Hz); 124.7 (dm, $J$=204 Hz); 129.2 (dm, $J$=163 Hz); 173.2 (sm, CO). HRMS, $m/z$: 254.1867 found (Calcd for $C_{13}H_{24}N_3O_2$, $C^+$ requires: 254.1869).

**4.3.3. 3-Methyl-1-[2-(3-propylamino-propionyloxy)-ethyl]-imidazolium hexafluorophosphate (6c).** Yield=96%. $^1$H NMR (acetone $d^6$, 300 MHz) $\delta$ 0.88 (t, 3H, $J$=7.4 Hz); 1.50 (m, 2H, $J$=7.3 Hz); 2.61 (t, 4H, $J$=6.7 Hz); 2.91 (t, 2H, $J$=6.5 Hz); 4.03 (s, 3H); 4.50 (t, 2H, $J$=4.4 Hz); 4.63 (t, 2H, $J$=4.3 Hz); 7.69 (d, 1H, $J$=1.9 Hz); 7.8 (d, 1H, $J$=1.9 Hz). $^{13}$C NMR (acetone $d^6$, 75 MHz) $\delta$ 12.1 (q, $J$=125 Hz); 23.1 (tm, $J$=125 Hz); 34.6 (t, $J$=126 Hz); 45.4 (t, $J$=133 Hz); 49.5 (t, $J$=146 Hz); 60.8 (t, $J$=145 Hz); 63.2 (t, $J$=150 Hz); 123.9 (dm, $J$=204 Hz); 124.6 (dm, $J$=204 Hz); 173 (sm, CO). HRMS, $m/z$: 240.1714 found (Calcd for $C_{12}H_{22}N_3O_2$, $C^+$ requires: 240.1712).

**4.3.4. 1-[2-(3-Benzylamino-propionyloxy)-ethyl]-3-methyl-imidazolium tetrafluoroborate (6d).** Yield=94%. $^1$H NMR (acetone $d^6$, 300 MHz) $\delta$ 2.60 (t, 2H, $J$=6.5 Hz); 2.88 (t, 2H, $J$=7 Hz); 3.8 (s, 2H); 3.95 (s, 3H); 4.45 (m, 2H, $J$=4.7 Hz); 4.62 (m, 2H, $J$=4.7 Hz); 7.23–7.39 (m, 5H); 7.61 (d, 1H, $J$=1.5 Hz); 7.75 (d, 1H, $J$=1.6 Hz); 9.06 (s, 1H). $^{13}$C NMR (acetone $d^6$, 75 MHz) $\delta$ 35.0 (t, $J$=126 Hz); 36.5 (q, $J$=144 Hz); 45.1 (t, $J$=133 Hz); 49.5 (t, $J$=146 Hz); 53.7 (tm, $J$=171 Hz); 63.2 (t, $J$=151 Hz); 123.9 (dm, $J$=204 Hz); 124.6 (dm, $J$=204 Hz); 127.8 (dm, $J$=159 Hz); 129.2 (dd, $J$=160, 6.4 Hz); 129.7 (sm); 141.0 (dm, $J$=220 Hz); 170.3 (sm, CO). HRMS, $m/z$: 288.1714 found (Calcd for $C_{16}H_{22}N_3O_2$, $C^+$ requires: 288.1712).

**4.3.5. 1-[2-(3-Isobutylamino-propionyloxy)-ethyl]-3-methyl-imidazolium tetrafluoroborate (6e).** Yield=94%. $^1$H NMR (acetone $d^6$, 300 MHz) $\delta$ 0.88 (d, 6H, $J$=6.7 Hz); 1.71 (m, 1H, $J$=6.7 Hz); 2.42 (d, 2H, $J$=6.7 Hz); 2.60 (t, 2H, $J$=6.6 Hz); 2.86 (t, 2H, $J$=6.4 Hz); 4.04 (s, 3H); 4.49 (t, 2H, $J$=5.2 Hz); 4.65 (t, 2H, $J$=5.2 Hz); 7.70 (d, 1H, $J$=1.9 Hz); 7.81 (d, 1H, $J$=1.9 Hz). $^{13}$C NMR (acetone $d^6$, 75 MHz) $\delta$ 21.0 (qm, $J$=125 Hz); 27.1 (dm, $J$=125 Hz); 34.9 (t, $J$=130 Hz); 36.7 (q, $J$=144 Hz); 45.8 (t, $J$=139 Hz); 49.5 (t, $J$=147 Hz); 61.1 (t, $J$=130 Hz); 63.2 (t, $J$=151 Hz); 123.9 (dm, $J$=204 Hz); 124.7 (dm, $J$=204 Hz); 129.2 (dm, $J$=163 Hz); 173.2 (sm, CO). HRMS, $m/z$: 254.1867 found (Calcd for $C_{13}H_{24}N_3O_2$, $C^+$ requires: 254.1869).

**4.3.6. 3-Methyl-1-[2-(3-propylamino-propionyloxy)-ethyl]-imidazolium tetrafluoroborate (6f).** Yield=96%. $^1$H NMR (acetone $d^6$, 300 MHz) $\delta$ 0.88 (t, 3H, $J$=7.4 Hz); 1.50 (m, 2H, $J$=7.3 Hz); 2.61 (t, 4H, $J$=6.7 Hz); 2.91 (t, 2H, $J$=6.5 Hz); 4.03 (s, 3H); 4.50 (t, 2H, $J$=4.4 Hz); 4.63 (t, 2H, $J$=4.3 Hz); 7.69 (d, 1H, $J$=1.9 Hz); 7.8 (d, 1H, $J$=1.9 Hz). $^{13}$C NMR (acetone $d^6$, 75 MHz) $\delta$ 12.1 (q, $J$=125 Hz); 23.1 (tm, $J$=125 Hz); 34.6 (t, $J$=126 Hz); 45.4 (t, $J$=133 Hz); 49.5 (t, $J$=146 Hz); 60.8 (t, $J$=145 Hz); 63.2 (t, $J$=150 Hz); 123.9 (dm, $J$=204 Hz); 124.6 (dm, $J$=204 Hz); 173 (sm, CO). HRMS, $m/z$: 240.1714 found (Calcd for $C_{12}H_{22}N_3O_2$, $C^+$ requires: 240.1712).

### 4.4. Typical procedure for the synthesis of thioureido esters 8(a-h) from isothiocyanates 7(a,b) and β-amino esters 6(a-f)

A mixture of β-amino acrylate **6** (3.83 mmol) and methylisothiocyanate **7a** (0.28 g, 3.83 mmol) or butylisothiocyanate **7b** (0.44 g, 3.83 mmol) in dry acetontile (25 mL) was stirred vigorously at room temperature under nitrogen for 18 h. After removal of solvent in vacuo, the

crude reaction mixture was washed twice with AcOEt (15 mL) under magnetic stirring. The washing solvent was eliminated from the ionic liquid phase bound thioureido ester **8** by decantation, and the resulting thioureido ester **8** was further dried under reduced pressure ($10^{-2}$ Torr) at 60 °C for 8 h to give the expected compound **8** as a nearly yellowish oil. The thioureido ester **8** was controlled by $^{1}H$ and $^{13}C$ NMR spectroscopy.

**4.4.1. 1-{2-[3-(1-Benzyl-3-methyl-thioureido)-propionyl-oxy]-ethyl}-3-methyl-imidazolium hexafluorophosphate (8a).** Yield=94%. $^{1}H$ NMR (acetone $d^6$, 300 MHz) $\delta$ 2.79 (t, 2H, $J$=7.2 Hz); 3.03 (d, 3H, $J$=3.1 Hz); 3.90 (t, 2H, $J$=7.3 Hz); 4.01 (s, 3H); 4.46 (t, 2H; $J$=4.8 Hz); 4.62 (t, 2H; $J$=4.8 Hz); 5.05 (s, 2H); 7.25–7.37 (m, 5H); 7.65 (d, 1H, $J$=1.7 Hz); 7.75 (d, 1H, $J$=1.7 Hz), 9.40 (s, 1H). $^{13}C$ NMR (acetone $d^6$, 75 MHz) $\delta$ 32.5 (t, $J$=113 Hz); 33.3 (qm, $J$=140 Hz); 36.8 (q, $J$=145 Hz); 46.5 (tm, $J$=138 Hz); 49.5 (t, $J$=146 Hz); 54.2 (tm, $J$=150 Hz); 63.3 (tm; $J$=153 Hz); 123.9 (dm, $J$=210 Hz); 124.8 (dm, $J$=205 Hz); 127.9 (dm, $J$=158 Hz); 129.3 (dd, $J$=160, 7.1 Hz); 138.2 (dm, $J$=220 Hz); 138.5 (sm, Ar); 172 (sm, CO); 185 (Sm; CS). HRMS, $m/z$: 389.2016 found (Calcd for $C_{20}H_{29}N_4O_2S$, $C^+$ requires: 389.2011).

**4.4.2. 1-{2-[3-Isobutyl-3-methyl-thioureido)-propionyl-oxy]-ethyl}-3-methyl-imidazolium hexafluorophosphate (8b).** Yield=96%. $^{1}H$ NMR (acetone $d^6$, 300 MHz) $\delta$ 0.89 (d, 6H, $J$=6.7 Hz); 1.76 (m, 1H, $J$=6.7 Hz); 2.80 (t, 2H, $J$=7.2 Hz); 3.01 (d, 3H, $J$=7.1 Hz); 3.44 (d, 2H, $J$=7.7 Hz), 4.02 (t, 2H, $J$=7.5 Hz); 4.06 (s, 3H); 4.46 (t, 2H, $J$=4.8 Hz); 4.68 (t, 2H, $J$=4.5 Hz); 7.71 (d, 1H, $J$=2.2 Hz); 7.80 (d, 1H, $J$=1.6 Hz); 9.07 (s, 1H). $^{13}C$ NMR (acetone $d^6$, 75 MHz) $\delta$ 20.2 (qm, $J$=125 Hz); 27.2 (dm, $J$=125 Hz); 32.5 (t, $J$=130 Hz); 36.8 (q, $J$=144 Hz); 48.7 (t, $J$=138 Hz); 49.5 (t, $J$=147 Hz); 60.9 (t, $J$=130 Hz); 63.2 (t, $J$=151 Hz); 124.0 (dm, $J$=203 Hz); 124.8 (dm, $J$=204 Hz); 138.2 (dm, $J$=220 Hz); 172.0 (m, CO); 183 (m, CS). HRMS, $m/z$: 327.1865 found (Calcd for $C_{15}H_{27}N_4O_2S$, $C^+$ requires: 327.1855).

**4.4.3. 3-Methyl-1-{2-[3-(3-propyl-1-propyl-thioureido)-propionyloxy]-ethyl}-imidazolium hexafluorophosphate (8c).** Yield=98%. $^{1}H$ NMR (acetone $d^6$, 300 MHz) $\delta$ 0.85 (t, 3H, $J$=7.4 Hz); 1.62 (m, 2H, $J$=7.9 Hz); 2.79 (t, 2H, $J$=7.4 Hz); 2.99 (d, 3H, $J$=3.2 Hz); 3.53 (t, 2H, $J$=7.9 Hz); 3.96 (t, 2H, $J$=7.9 Hz); 4.06 (s, 3H); 4.50 (t, 2H, $J$=5.2 Hz); 4.66 (t, 2H, $J$=4.4 Hz); 7.71 (d, 1H, $J$=1.6 Hz); 7.81 (d, 1H, $J$=1.7 Hz); 9.09 (s, 1H). $^{13}C$ NMR (acetone $d^6$, 75 MHz) $\delta$ 12.0 (q, $J$=130 Hz); 21.2 (tm, $J$=128 Hz); 32.8 (q, $J$=140 Hz); 33.0 (tm, $J$=130 Hz); 36.8 (q, $J$=150 Hz); 47.9 (tm, $J$=140 Hz); 49.5 (t, $J$=148 Hz); 52.3 (tm, $J$=142 Hz); 63.3 (tm, $J$=153 Hz); 124.0 (dm, $J$=205 Hz); 124.8 (dm, $J$=205 Hz); 139.9 (sm, 1H); 173.0 (sm, CO), 183.0 (sm, CS). HRMS, $m/z$: 313.2007 found (Calcd for $C_{14}H_{25}N_4O_2S$, $C^+$ requires: 313.2011).

**4.4.4. 1-{2-[3-(3-Butyl-1-isobutyl-thioureido)-propionyl-oxy]-ethyl}-3-methyl-imidazolium hexafluorophosphate (8d).** Yield=90%. $^{1}H$ NMR (acetone $d^6$, 300 MHz) $\delta$ 0.75 (t, 3H, $J$=7.3 Hz); 0.80 (d, 6H, $J$=6.7 Hz); 1.22 (m, 2H, $J$=7.7 Hz); 1.45 (m, 2H, $J$=7.3 Hz); 1.45 (m, 1H, $J$=6.9 Hz); 2.07 (t, 2H, $J$=6.6 Hz); 2.71 (t, 2H, $J$=6.8 Hz); 3.50 (d, 2H, $J$=7.5 Hz); 3.52 (t, 2H, $J$=7.4 Hz); 3.95 (s, 3H); 4.43 (t, 2H, $J$=5 Hz); 4.60 (t, 2H, $J$=4.5 Hz); 7.71 (d, 1H, $J$=1.6 Hz); 7.81 (d, 1H, $J$=1.7 Hz); 9.09 (s, 1H). $^{13}C$ NMR (acetone $d^6$, 75 MHz) $\delta$ 13.95 (qm, $J$=125 Hz); 18.9 (tm, $J$=126 Hz); 19.9 (qm, $J$=125 Hz); 26.9 (dm, $J$=128 Hz); 30.6 (tm, $J$=125 Hz); 31.4 (tm, $J$=132 Hz); 36.8 (q, $J$=150 Hz); 45.8 (tm, $J$=139 Hz); 49.5 (t, $J$=148 Hz); 52.3 (tm, $J$=142 Hz); 57.3 (tm, $J$=150 Hz); 66.3 (tm, $J$=152 Hz); 124.0 (dm, $J$=205 Hz); 124.8 (dm, $J$=205 Hz); 139.9 (sm, C-2); 173.0 (sm, CO); 180.2 (sm, CS). HRMS, $m/z$: 369.5473 found (Calcd for $C_{18}H_{33}N_4O_2S$, $C^+$ requires: 369.5460).

**4.4.5. 1-{2-[3-(1-Benzyl-3-methyl-thioureido)-propionyl-oxy]-ethyl}-3-methyl-imidazolium tetrafluoroborate (8e).** Yield=94%. $^{1}H$ NMR (acetone $d^6$, 300 MHz) $\delta$ 2.79 (t, 2H, $J$=7.2 Hz); 3.03 (d, 3H, $J$=3.1 Hz); 3.90 (t, 2H, $J$=7.3 Hz); 4.01 (s, 3H); 4.46 (t, 2H; $J$=4.8 Hz); 4.62 (t, 2H; $J$=4.8 Hz); 5.05 (s, 2H); 7.25–7.37 (m, 5H); 7.65 (d, 1H, $J$=1.7 Hz); 7.75 (d, 1H, $J$=1.7 Hz), 9.40 (s, 1H). $^{13}C$ NMR (acetone $d^6$, 75 MHz) $\delta$ 32.5 (t, $J$=113 Hz); 33.3 (qm, $J$=140 Hz); 36.8 (q, $J$=145 Hz); 46.5 (tm, $J$=138 Hz); 49.5 (t, $J$=146 Hz); 54.2 (tm, $J$=150 Hz); 63.3 (tm; $J$=153 Hz); 123.9 (dm, $J$=210 Hz); 124.8 (dm, $J$=205 Hz); 127.9 (dm, $J$=158 Hz); 129.3 (dd, $J$=160, 7.1 Hz); 138.2 (dm, $J$=220 Hz); 138.5 (sm, Ar); 172.0 (sm, CO); 185 (sm, CS). HRMS, $m/z$: 389.2016 found (Calcd for $C_{20}H_{29}N_4O_2S$, $C^+$ requires: 389.2011).

**4.4.6. 1-{2-[3-(1-Isobutyl-3-methyl-thioureido)-propionyl-oxy]-ethyl}-3-methyl-imidazolium tetrafluoroborate (8f).** Yield=96%. $^{1}H$ NMR (acetone $d^6$, 300 MHz) $\delta$ 0.89 (d, 6H, $J$=6.7 Hz); 1.76 (m, 1H, $J$=6.7 Hz); 2.80 (t, 2H, $J$=7.2 Hz); 3.01 (d, 3H, $J$=7.1 Hz); 3.44 (d, 2H, $J$=7.7 Hz), 4.02 (t, 2H, $J$=7.5 Hz); 4.06 (s, 3H); 4.46 (t, 2H, $J$=4.8 Hz); 4.68 (t, 2H, $J$=4.5 Hz); 7.71 (d, 1H, $J$=2.2 Hz); 7.80 (d, 1H, $J$=1.6 Hz); 9.07 (s, 1H). $^{13}C$ NMR (acetone $d^6$, 75 MHz) $\delta$ 20.2 (qm, $J$=125 Hz); 27.2 (dm, $J$=125 Hz); 32.5 (t, $J$=130 Hz); 36.8 (q, $J$=144 Hz); 48.7 (t, $J$=138 Hz); 49.5 (t, $J$=147 Hz); 60.9 (t, $J$=130 Hz); 63.2 (t, $J$=151 Hz); 124.0 (dm, $J$=203 Hz); 124.8 (dm, $J$=204 Hz); 138.2 (dm, $J$=220 Hz); 172.0 (m, CO); 183.0 (m, CS). HRMS, $m/z$: 327.1865 found (Calcd for $C_{15}H_{27}N_4O_2S$, $C^+$ requires: 327.1855).

**4.4.7. 3-Methyl-1-{2-[3-(3-methyl-1-propyl-thioureido)-propionyloxy]-ethyl}-imidazolium tetrafluoroborate (8g).** Yield=96%. $^{1}H$ NMR (acetone $d^6$, 300 MHz) $\delta$ 0.85 (t, 3H, $J$=7.4 Hz); 1.62 (m, 2H, $J$=7.9 Hz); 2.79 (t, 2H, $J$=7.4 Hz); 2.99 (d, 3H, $J$=3.2 Hz); 3.53 (t, 2H, $J$=7.9 Hz); 3.96 (t, 2H, $J$=7.9 Hz); 4.06 (s, 3H); 4.50 (t, 2H, $J$=5.2 Hz); 4.66 (t, 2H, $J$=4.4 Hz); 7.71 (d, 1H, $J$=1.6 Hz); 7.81 (d, 1H, $J$=1.7 Hz); 9.09 (s, 1H). $^{13}C$ NMR (acetone $d^6$, 75 MHz) $\delta$ 12.0 (q, $J$=130 Hz); 21.2 (tm, $J$=128 Hz); 32.8 (q, $J$=140 Hz); 33.0 (tm, $J$=130 Hz); 36.8 (q, $J$=150 Hz); 47.9 (tm, $J$=140 Hz); 49.5 (t, $J$=148 Hz); 52.3 (tm, $J$=142 Hz); 63.3 (tm, $J$=153 Hz); 124.0 (dm, $J$=205 Hz); 124.8 (dm, $J$=205 Hz); 139.9 (sm, 1H); 173.0 (sm, CO), 183.0 (sm, CS). HRMS, $m/z$: 313.2007 found (Calcd for $C_{14}H_{25}N_4O_2S$, $C^+$ requires: 313.2011).

**4.4.8. 1-{2-[3-(3-Butyl-1-isobutyl-thioureido)-propionyl-oxy]-ethyl}-3-methyl-imidazolium tetrafluoroborate (8h).** Yield=94%. $^{1}H$ NMR (acetone $d^6$, 300 MHz) $\delta$ 0.75

(t, 3H, *J*=7.3 Hz); 0.80 (d, 6H, *J*=6.7 Hz); 1.22 (m, 2H, *J*=7.7 Hz); 1.45 (m, 2H, *J*=7.3 Hz); 1.45 (m, 1H, *J*=6.9 Hz); 2.07 (t, 2H, *J*=6.6 Hz); 2.71 (t, 2H, *J*=6.8 Hz); 3.50 (d, 2H, *J*=7.5 Hz); 3.52 (t, 2H, *J*=7.4 Hz); 3.95 (s, 3H); 4.43 (t, 2H, *J*=5 Hz); 4.60 (t, 2H, *J*=4.5 Hz); 7.71 (d, 1H, *J*=1.6 Hz); 7.81 (d, 1H, *J*=1.7 Hz); 9.09 (s, 1H). $^{13}$C NMR (acetone *d* $^{6}$, 75 MHz) $\delta$ 13.95 (qm, *J*=125 Hz); 18.9 (tm, *J*=126 Hz); 19.9 (qm, *J*=125 Hz); 26.9 (dm, *J*=128 Hz); 30.6 (tm, *J*=125vHz); 31.4 (tm, *J*=132 Hz); 36.8 (q, *J*=150 Hz); 45.8 (tm, *J*=139 Hz); 49.5 (t, *J*=148 Hz); 52.3 (tm, *J*=142 Hz); 57.3 (tm, *J*=150 Hz); 66.3 (tm, *J*=152 Hz); 124.0 (dm, *J*=205 Hz); 124.8 (dm, *J*=205 Hz); 139.9 (sm, C-2); 173.0 (sm, CO); 180.2 (Sm, CS). HRMS, *m*/*z*: 369.5473 found (Calcd for $C_{18}H_{33}N_4O_2S$, $C^+$ requires: 369.5460).

### 4.5. Standard procedure for cleavage/cyclization of the thio ureido esters 8 under solventless microwave dielectric heating: preparation of 2-thioxo tetrahydro-pyrimidin-4(1*H*)-ones 9(a-d)

A mixture of thioureido ester **8** (1 equiv.) and commercial diethylamine (2 equiv.) was placed in a cylindrical quartz reactor (∅=1.8 cm). Then the reactor was introduced into a Synthewave® 402 Prolabo microwave oven. The liquid mixture was stirred mechanically and was irradiated at 120 °C (20% power level, i.e., 60 W) for a reaction time ranging from 15 to 45 min (see Table 4). After microwave dielectric heating, the crude reaction mixture was allowed to cool down at 25 °C and chloroform (5 mL) was added in the cylindrical quartz reactor. The resulting solution was half concentrated by rotary evaporation and the crude solution was submitted to purification by flash chromatography (column: ∅=1 cm, *H*=7 cm) on silica gel 60F-254 (Merck) using $CHCl_3$ or AcOEt as eluent. The desired fraction was concentrated in vacuo and gave compound **8** as a yellowish nearly pure oil. The pure products **9**(**a**-**d**) were characterized by $^1$H, $^{13}$C NMR and HRMS.

**4.5.1. 3-Methyl-1-(phenylmethyl)-2-thioxo-tetrahydro pyrimidin-4(1*H*)-one (9a).** Yield=85%. $R_f$=0.4 with $CHCl_3$ as eluent. $^1$H NMR ($CDCl_3$, 300 MHz) $\delta$ 2.64 (t, 2H, *J*=6.8 Hz); 3.48 (t, 2H, *J*=6.8 Hz); 3.58 (s, 3H); 5.28 (s, 2H); 7.28–7.39 (m, 5H). $^{13}$C NMR ($CDCl_3$, 75 MHz) $\delta$ 31.3 (tm, *J*=133 Hz); 34.8 (q, *J*=142 Hz); 43.4 (t, *J*=143 Hz); 58.3 (t, *J*=141 Hz); 127.8 (dm, *J*=160 Hz); 128.2 (dm, *J*=160 Hz); 129.0 (dd, *J*=160, 5 Hz); 135.5 (sm, Ar); 167.0 (sm, CO); 182.5 (sm, CS). HRMS, *m*/*z*: 234.0821 found (Calcd for $C_{12}H_{14}N_4OS$, $M^+$ requires: 234.0824).

**4.5.2. 1-Isobutyl-3-methyl-2-thioxo tetrahydro pyrimidin-4(1*H*)-one (9b).** Yield=72%. $R_f$=0.6 with $CHCl_3$ as eluent. $^1$H NMR ($CDCl_3$, 300 MHz) $\delta$ 0.99 (d, 6H, *J*=6.7 Hz); 2.28 (m, 1H, *J*=6.8 Hz); 2.75 (t, 2H, *J*=6.8 Hz); 3.53 (s, 3H); 3.61 (t, 2H, *J*=6.9 Hz); 3.81 (d, 2H, *J*=7.5 Hz). $^{13}$C NMR ($CDCl_3$, 75 MHz) $\delta$ 20.2 (qm, *J*=124 Hz); 27.0 (dm, *J*=125 Hz); 31.4 (tt, *J*=133, 3.4 Hz); 34.2 (q, *J*=142 Hz); 45.7 (tt, *J*=142, 3.7 Hz); 63.0 (tm, *J*=138 Hz); 167.0 (sm, CO); 182.0 (sm, CS). HRMS, *m*/*z*: 200.0983 found (Calcd for $C_9H_{16}N_2OS$, $M^+$ requires: 200.0983).

**4.5.3. 3-Butyl-1-isobutyl-2-thioxo tetrahydro pyrimidin-4(1*H*)-one (9c).** Yield=67%. $R_f$=0.5 with $CHCl_3$ as eluent. $^1$H NMR ($CDCl_3$, 300 MHz) $\delta$ 0.92 (t, 3H, *J*=7.3 Hz); 0.98 (d, 6H, *J*=6.7 Hz); 1.33 (m, 2H, *J*=7.7 Hz); 1.62 (m, 2H, *J*=7.3 Hz); 2.28 (m, 1H, *J*=6.9 Hz); 2.75 (t, 2H, *J*=6.6 Hz); 3.57 (t, 2H, *J*=6.8 Hz); 3.82 (d, 2H, *J*=7.5 Hz); 4.25 (t, 2H, *J*=6.1 Hz). $^{13}$C NMR ($CDCl_3$, 75 MHz) $\delta$ 13.8 (qm, *J*=1245 Hz); 19.9 (tm, *J*=123 Hz); 20.2 (qm, *J*=125 Hz); 26.9 (dm, *J*=128 Hz); 30.0 (tm, *J*=126 Hz); 31.4 (tm, *J*=133 Hz); 45.8 (tm, *J*=139 Hz); 46.2 (tm, *J*=136 Hz); 63.1 (tm, *J*=139 Hz); 166.0 (sm, CO); 181.2 (sm, CS). HRMS, *m*/*z*: 242.3082 found (Calcd for $C_{12}H_{22}N_2OS$, $M^+$ requires: 242.3081).

**4.5.4. 3-Methyl-1-propyl-2-thioxo tetrahydro pyrimidin-4(1*H*)-one (9d).** Yield=83%. $R_f$=0.5 with $CHCl_3$ as eluent. $^1$H NMR ($CDCl_3$, 300 MHz) $\delta$ 0.98 (t, 3H, *J*=7.4 Hz); 1.75 (m, 2H, *J*=7.6 Hz); 2.78 (t, 2H, *J*=6.8 Hz); 3.50 (s, 3H); 3.65 (t, 2H, *J*=6.9 Hz); 3.95 (t, 2H, *J*=7.7 Hz). $^{13}$C NMR ($CDCl_3$, 75 MHz) $\delta$ 11.0 (qm, *J*=126, 4 Hz); 20.0 (tm, *J*=124 Hz); 43.4 (tt, *J*=133, 6.8 Hz); 34.0 (q, *J*=142 Hz); 44.5 (tm, *J*=143 Hz); 56.6 (tm, *J*=139 Hz); 166.6 (sm, CO); 180.9 (sm, CS). HRMS, *m*/*z*: 186.0833 found (Calcd for $C_8H_{14}N_2OS$, $M^+$ requires: 186.0827).

## Acknowledgements

One of us (H.H.) thank the EEC for a research fellowship (contrat N° G5RD-CT 2001-00546). The authors thank also Merck Eurolab Prolabo (Fr.) for providing the Synthewave 402® apparatus.

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