Ionic-Liquid-Supported Synthesis of Amines and Derivatives

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Abstract: Amine precursors such as glycines protected at nitrogen with a Boc or formyl group were grafted by esterification on the hydroxylated arms of 1-(2-hydroxyethyl)-3-methylimidazolium hexafluorophosphates or tetrafluoroborates. The cleavage of the Boc group was then realized at room temperature by successively treating acetonitrile solutions of the thus formed glycinates with methanol and acetyl chloride (two equivalents each). Interestingly, the resulting glycinate hydrochlorides were converted into the corresponding amines during the removal of the solvent. Ugi reaction of one of these ionic-liquid-grafted amines with phthalaldehydic acid and *tert*-butyl isocyanide, followed by cleavage, furnished a phthalimidine.

Key words: ionic liquids, amines, glycine derivatives, esters, Ugi reaction

The demand for increasing numbers of compounds, notably with potential therapeutic value, caused chemists to look for ways to simplify, expedite, and automate the process of synthesizing organic molecules. Since Merrifield introduced the solid-phase peptide synthesis,[2] insoluble supports rapidly developed into a means for facile purification processes, with easier phase separation and purification to remove excess reagents and side products, and possible automation. More recently, alternative methodologies appeared to compensate for the drawbacks related to the heterogeneous nature of the insoluble polymers. The use of soluble polymer supports was aimed at restoring homogeneous reaction conditions while retaining the ease of purification of the product;[3] however, limitations such as a low loading capacity can restrict their applications. The use of fluorous-phase synthesis proved efficient for the separation of small molecules,[4] but the expense of perfluoroalkane solvents limits its development. In 2001, the use of low-molecular-weight ionic liquids as soluble supports for organic synthesis was reported.[5]

Ionic liquids, notably those including 1-alkyl-3-methylimidazolium cations, have been used mainly in organic synthesis as reaction media.[6] A feature of ionic liquids is that their solubilities in organic and aqueous phases can be tuned by varying the anion and ring substituents. Taking advantage of this opportunity, laboratories including our own studied and demonstrated the efficiency of ionic-liquid-supported syntheses.[5,7] As a continuation of our work on functionalized ionic liquids, we have synthesized a series of amines that could be involved in multicomponent reactions utilizing isocyanides. Few syntheses of amino ionic liquids have been described in the literature.[7e,8] The amines we describe here are connected to the imidazolium entities via an ester function that could be cleaved to recycle the ionic support. In addition, substitution at C-2 of the imidazolium ring was also considered for possible use in reactions with bases.[9]

2-Substituted 1-methylimidazoles **2a** and **2b** were synthesized from commercially available 2-ethylimidazole (**1a**) and 2-phenylimidazole (**1b**), respectively, by an improved version of a method described in the literature (Scheme 1).[10] The use of iodomethane (2 equiv) in basic media under phase-transfer catalysis afforded the expected methylated compound **2a** in only 36% yield, because of competitive formation of 2-ethyl-1,3-dimethylimidazolium iodide. Use of a stoichiometric amount of iodomethane circumvented the formation of this side product, and afforded **2a** in 89% yield (Scheme 1). Compound **2b** was similarly obtained in 97% yield. Quaternization of the 2-substituted imidazoles **2a–c** was carried out as described for the compound **2d**,[11] by simply heating the substrate with 2-chloroethanol at 120 °C (Scheme 1). Except for compound **3b**, which proved to be very viscous and was directly converted in the next step, chlorides **3** were easily purified by washing with diethyl ether and drying. Anion metathesis with either potassium hexafluorophosphate or ammonium tetrafluoroborate was effected as reported for compound **3d**.[11] Filtration of ammonium or potassium chloride, insoluble in acetonitrile, afforded the hexafluorophosphates **4a*h***, **4b*h***, **4c*h***, and **4d*h*** and the tetrafluoroborates **4c*t*** and **4d*t*** in excellent yields (Scheme 1).

NH-Boc- and NH-formyl-protected glycines were chosen to be grafted on the hydroxylated arm of synthesized ionic liquids. The esterification of the protected amino acids **5** and **6** was effected with the ionic liquids **4c** and **d** in dry acetonitrile in the presence of *N*,*N*′-dicyclohexylcarbodiimide and a catalytic amount of 4-(*N*,*N*-dimethylamino)pyridine, in an adaptation of a previously described procedure (Scheme 2).[5a] Dicyclohexylurea was easily removed by filtration, and washing of the crude residue with ethyl acetate or diethyl ether was efficient to afford the pure expected imidazolium salts **7** and **8** in yields ranging from 74 to 96% (Scheme 2). Ionic liquid **4b*h***, in contrast, proved to be a bad support due to its good solubility in ethyl acetate or diethyl ether, and this does not allow washing with these solvents.

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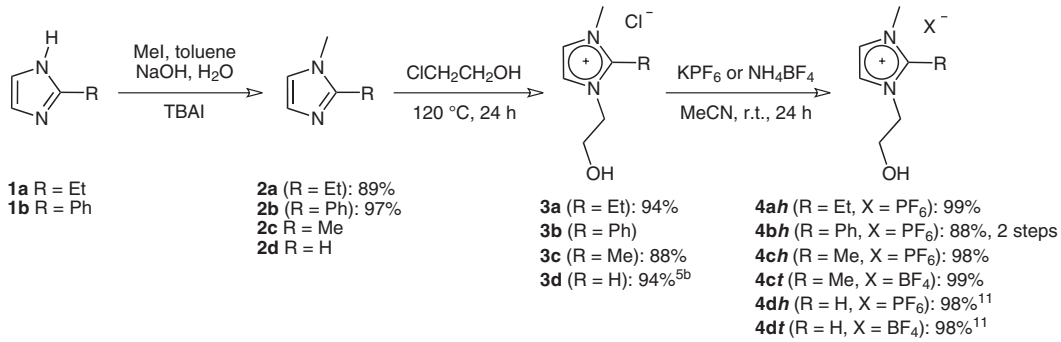
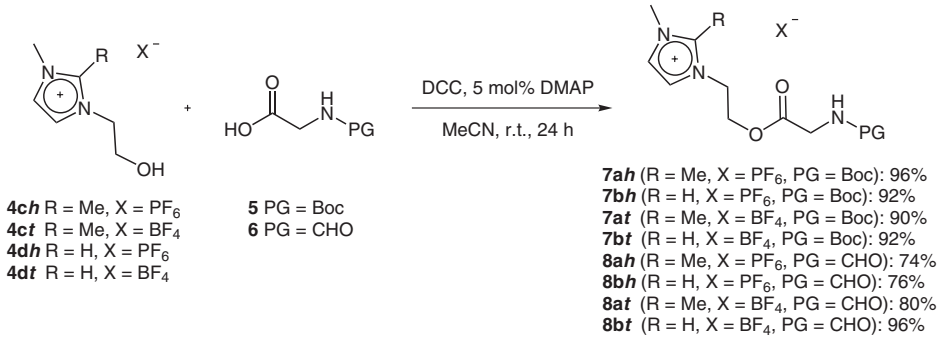


Scheme 1



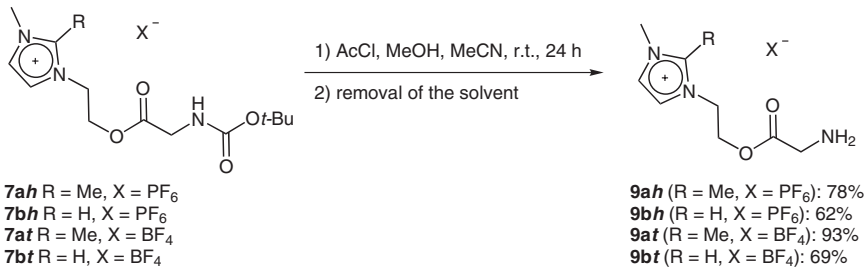
Scheme 2

The cleavage of Boc-protected amines **7** was next investigated (Scheme 3). The use of trifluoroacetic acid in dichloromethane is often efficient for this purpose, but can cause a partial ionic-liquid anion exchange with trifluoroacetate. We thus preferred to use hydrochloric acid in an organic solvent.[7e] Surprisingly, treatment of acetonitrile solutions of carbamates **7** with excess hydrochloric acid in ethyl acetate[12] gave the amines straightaway after the evaporation of acetonitrile; thus a subsequent neutralization step was avoided by direct formation of the amines instead of the expected hydrochlorides.[13] The optimization of the reactions was next carried out in NMR tubes by successively treating solutions of carbamates **7** in deuterated acetonitrile with methanol (1 equiv) and acetyl chloride (1 equiv). Monitoring of the reaction at room temperature showed that there was no further change after 24 hours, and that the expected hydrochlorides were formed in about 50% conversion. The addition of a second equivalent of methanol and acetyl chloride to the NMR tubes led to the hydrochlorides in 100% conversion. Removal of the solvent from the reaction mixtures, washing, and drying afforded the corresponding amines **9**, as verified by mass spectrometry, in good yields (Scheme 3).

Since the Boc cleavage was found to work satisfactorily, we did not study the cleavage of the formyl group in **8**. We decided to rather subject amines **9** to a multicomponent reaction involving isocyanides.

Among the multicomponent transformations involving amines, the Ugi four-component reaction (U-4CR), which involves an amine, aldehyde, carboxylic acid, and isocyanide, is one of the most frequently employed processes.[14]

Preliminary studies to compare the different ionic supports were undertaken, and O-grafted glycines **9** were treated with 4-chlorobenzaldehyde, 2-nitrobenzoic acid, and *tert*-butyl isocyanide in methanol at room temperature or 40 °C (Scheme 4).[15] Even if the Ugi compounds were partially cleaved from the ionic support during the reac-



Scheme 3

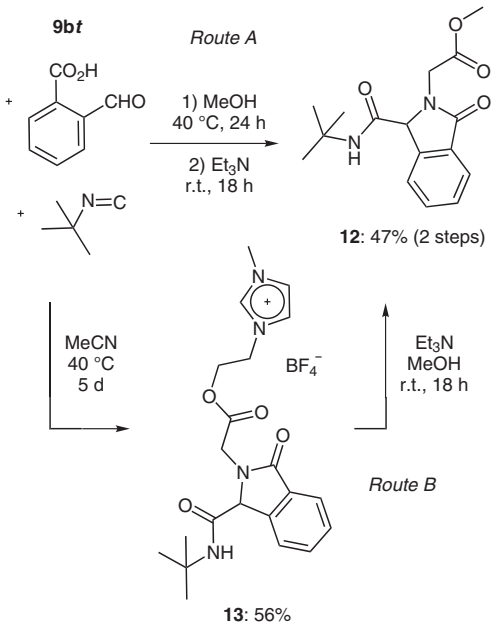
tions, it could be seen that the imidazolium ring (whether substituted at C-2 or not) was compatible with *tert*-butyl isocyanide under the conditions used.[16] In addtion, the Ugi reactions were found to be more efficient if the borate anion was used.

The subsequent treatment of partially cleaved Ugi compounds **10***t* with triethylamine[17] in methanol at room temperature furnished the corresponding methyl ester **11**; the latter was identified by characteristic NMR peaks and mass spectrometry, but was insufficiently stable to be purified (Scheme 4).

On the other hand, the reaction between the amine **9b***t*, phthalaldehydic acid and *tert*-butyl isocyanide,[18] followed by the cleavage from the ionic support, furnished a stable compound (Scheme 5). Indeed, ester **12** could be purified easily by chromatography over silica gel and crystallization (Scheme 5, *Route A*).

To avoid partial cleavage during the Ugi reaction, we decided to use a solvent other than methanol, and performed the Ugi reaction in acetonitrile. The solubility of the amine **9b***t* in acetonitrile is very low, but by using a long reaction time (five days), we could obtain the O-grafted ester **13** in a 56% yield without observing cleavage or degradation (Scheme 5). The unchanged amine **9b***t* could be removed easily by filtration, giving after evaporation of acetonitrile and washing with diethyl ether the Ugi product **13**. Subsequent cleavage, under the conditions used before, finally afforded compound **12** in 80% yield (Scheme 5, *Route B*).

We have shown that amines can be prepared very easily from the corresponding NH-Boc-protected carbamates when ionic liquids are used as supports. This ionic-liquid-supported synthesis involving amines or derivatives offers the advantage of simple product isolation by washing with appropriate solvents; moreover, NMR monitoring of reactions proved to be straightforward. The glycine derivatives O-bound to imidazolium-type ionic liquids thus prepared are then suitable for use in the Ugi reaction.



Scheme 5

[1]H and [13]C NMR spectra were recorded at 200 MHz and 50 MHz, respectively, on a Bruker ARX 200 P spectrometer. Mass spectral analyses were carried out on a Varian MAT 311 spectrometer (CRMPO, Rennes). Elemental analyses were performed on a Carlo Erba 1106 apparatus. *N*-Formylglycine derivative **6** was prepared by adapting a previously described procedure.[19] The ionic liquids **3d**,[5b] **4dh**,[11] and **4dt**[11] were prepared according to literature procedures.

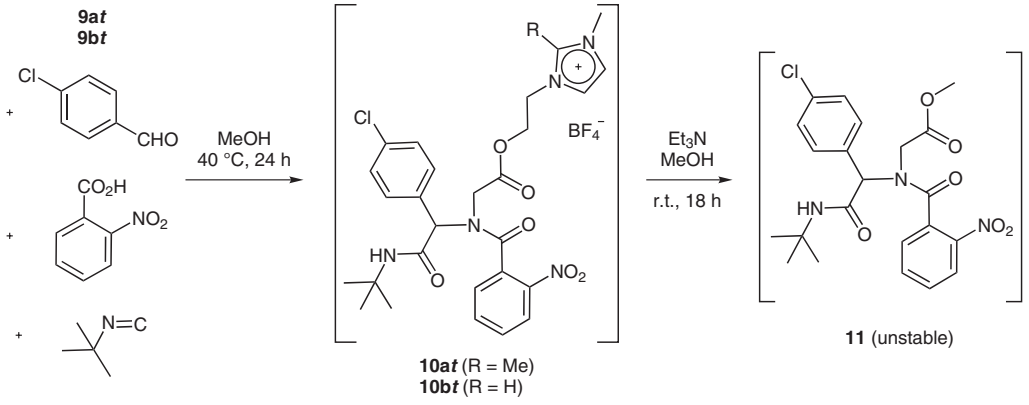
2-Ethyl-1-methylimidazole (2a)[20]

To a biphasic mixture obtained from 2-ethylimidazole (**1a**; 9.8 g, 0.10 mol), TBAI (1.9 g, 5.1 mmol), 50% aq NaOH (350 mL), and toluene (280 mL) was added MeI (7.1 mL, 0.11 mol). After stirring for 15 min at r.t., the mixture was diluted with toluene (280 mL) and H_2O (280 mL). The organic phase was separated, dried ($MgSO_4$), and concentrated under reduced pressure.

Pale yellow oil; yield: 9.8 g (89%).

IR (KBr): 3390, 2977, 2940, 1529, 1501, 1470, 1416, 1283, 1146, 1059, 730, 623 cm^{-1}.

[1]H NMR (200 MHz, $CDCl_3$): δ = 6.90 (d, *J* = 1.1 Hz, 1 H), 6.77 (d, *J* = 1.1 Hz, 1 H), 3.55 (s, 3 H), 2.66 (q, *J* = 7.5 Hz, 2 H), 1.31 (t, *J* = 7.6 Hz, 3 H).



Scheme 4

^{13}C NMR (50 MHz, $CDCl_3$): δ = 147.5, 124.8, 118.7, 30.5, 18.2, 10.1.

Anal. Calcd for $C_6H_{10}N_2$ (110.16): C, 65.42; H, 9.15; N, 25.43. Found: C, 65.31; H, 9.32; N, 25.21.

1-Methyl-2-phenylimidazole (2b)
To a biphasic mixture obtained from 2-phenylimidazole (**1b**; 10 g, 69 mmol), TBAI (1.9 g, 5.1 mmol), 50% aq NaOH (350 mL), and toluene (280 mL) was added MeI (4.9 mL, 76 mmol). After stirring for 15 min at r.t., the mixture was diluted with toluene (280 mL) and H_2O (280 mL). The organic phase was separated, dried ($MgSO_4$), and concentrated under reduced pressure.

Pale yellow oil; yield: 11 g (97%).

The spectroscopic data were identical to those previously described.[21]

Anal. Calcd for $C_{10}H_{10}N_2$ (158.20): C, 75.92; H, 6.37; N, 17.71. Found: C, 75.68; H, 6.52; N, 17.44.

2-Ethyl-1-(2-hydroxyethyl)-3-methylimidazolium Chloride (3a)
A mixture of 2-chloroethanol (0.67 mL, 10 mmol) and **2a** (1.1 g, 10 mmol) was heated for 24 h at 120 °C. The crude product, which crystallized upon cooling, was finely crushed, washed with Et_2O (3 × 80 mL), and dried under reduced pressure for 10 h.

Pale yellow powder; yield: 1.8 g (94%); mp 55–58 °C.

^{1}H NMR (200 MHz, DMSO-d_6): δ = 7.66 (s, 2 H), 5.25 (br s, 1 H), 4.20 (t, *J* = 4.9 Hz, 2 H), 3.82 (s, 3 H), 3.71 (t, *J* = 7.7 Hz, 2 H), 3.06 (q, *J* = 7.6 Hz, 2 H), 1.19 (t, *J* = 7.6 Hz, 3 H).

^{13}C NMR (50 MHz, DMSO-d_6): δ = 148.2, 122.6, 121.3, 59.6, 50.1, 34.6, 16.1, 11.0.

HRMS-FAB: *m*/*z* calcd for $C_8H_{15}N_2O$: 155.1184; found: 155.1176.

1-(2-Hydroxyethyl)-3-methyl-2-phenylimidazolium Chloride (3b)
The procedure used was as described for **3a**, but **2b** (1.6 g, 10 mmol) was used instead of **2a**. Compound **3b** was too viscous to be washed, and was used in the next step without further purification.

1-(2-Hydroxyethyl)-2,3-dimethylimidazolium Chloride (3c)
The procedure used was as described for **3a**, but **2c** (0.96 g, 10 mmol) was used instead of **2a**.

Beige powder; yield: 1.6 g (88%); mp 58 °C.

^{1}H NMR (200 MHz, DMSO-d_6): δ = 7.59 (s, 2 H), 5.08 (t, *J* = 5.1 Hz, 1 H), 4.17 (t, *J* = 5.0 Hz, 2 H), 3.75 (s, 3 H), 3.68 (q, *J* = 4.8 Hz, 2 H), 2.57 (s, 3 H).

^{13}C NMR (50 MHz, DMSO-d_6): δ = 144.9, 122.2, 121.3, 59.7, 50.3, 34.8, 9.8.

HRMS-FAB: *m*/*z* calcd for $C_7H_{13}N_2O$: 141.10279; found: 141.1030.

2-Ethyl-1-(2-hydroxyethyl)-3-methylimidazolium Hexafluorophosphate (4a*h*)
A mixture of **3a** (11 g, 56 mmol) and KPF_6 (10 g, 56 mmol) in MeCN (370 mL) was stirred for 24 h at r.t. under a dry atmosphere. After filtration over Celite, removal of the solvent, and drying under reduced pressure, the product was kept under N_2.

Pale yellow powder; yield: 17 g (99%); mp <50 °C.

^{1}H NMR (200 MHz, acetone-d_6): δ = 7.64 (d, *J* = 2.1 Hz, 1 H), 7.60 (d, *J* = 2.1 Hz, 1 H), 4.41 (t, *J* = 4.9 Hz, 2 H), 4.00 (s, 3 H), 3.96 (t, *J* = 5.0 Hz, 2 H), 3.24 (q, *J* = 7.7 Hz, 2 H), 1.37 (t, *J* = 7.7 Hz, 3 H), OH not seen.

^{13}C NMR (50 MHz, DMSO-d_6): δ = 148.2, 122.6, 121.3, 59.6, 50.1, 34.6, 16.2, 11.0.

HRMS-FAB: *m*/*z* calcd for $C_{16}H_{30}N_4O_2F_6P$ [$2C^+$, PF_6^-]$^+$: 455.2011; found: 455.2011.

1-(2-Hydroxyethyl)-3-methyl-2-phenylimidazolium Hexafluorophosphate (4b*h*)
The procedure used is as described for **4a*h***, but **3b** (13 g, 56 mmol) was used instead of **3a**.

Beige powder; yield: 17 g (88%); mp <50 °C.

^{1}H NMR (200 MHz, acetone-d_6): δ = 7.91 (d, *J* = 2.0 Hz, 1 H), 7.8 (m, 6 H), 4.26 (t, *J* = 5.0 Hz, 2 H), 3.92 (t, *J* = 5.1 Hz, 2 H), 3.87 (s, 3 H), OH not seen.

^{13}C NMR (50 MHz, DMSO-d_6): δ = 144.8, 132.4, 130.9, 129.6, 123.5, 122.1, 121.5, 59.4, 50.9, 35.6.

HRMS-FAB: *m*/*z* calcd for $C_{12}H_{15}N_2O$: 203.11844; found: 203.1184.

1-(2-Hydroxyethyl)-2,3-dimethylimidazolium Hexafluorophosphate (4c*h*)
The procedure used is as described for **4a*h***, but **3c** (9.9 g, 56 mmol) was used instead of **3a**.

Pale brown oil; yield: 16 g (98%).

^{1}H NMR (200 MHz, acetone-d_6): δ = 7.60 (s, 1 H), 7.58 (s, 1 H), 4.39 (t, *J* = 4.6 Hz, 2 H), 3.97 (m, 6 H), 2.77 (s, 3 H).

^{13}C NMR (50 MHz, acetone-d_6): δ = 145.9, 122.8, 121.8, 60.9, 51.1, 35.0, 9.4.

HRMS-FAB: *m*/*z* calcd for $C_{14}H_{26}N_4O_2F_6P$ [$2C^+$, PF_6^-]$^+$: 427.16976; found: 427.1700.

1-(2-Hydroxyethyl)-2,3-dimethylimidazolium Tetrafluoroborate (4c*t*)
A mixture of **3c** (11 g, 56 mmol) and NH_4BF_4 (5.9 g, 56 mmol) in MeCN (370 mL) was stirred for 24 h at r.t. under a dry atmosphere. After filtration over Celite, removal of the solvent, and drying under reduced pressure, the product was kept under N_2.

Pale brown oil; yield: 13 g (99%).

^{1}H NMR (200 MHz, DMSO-d_6): δ = 7.63 (s, 2 H), 5.25 (t, *J* = 5.5 Hz, 1 H), 4.19 (t, *J* = 5.0 Hz, 2 H), 3.76 (s, 3 H), 3.67 (q, *J* = 4.8 Hz, 2 H), 2.59 (s, 3 H).

^{13}C NMR (50 MHz, acetone-d_6): δ = 145.9, 122.7, 121.8, 60.9, 51.0, 35.0, 9.4.

HRMS-FAB: *m*/*z* calcd for $C_{14}H_{26}N_4O_2F_4{}^{11}B$ [$2C^+$, BF_4^-]$^+$: 369.20849; found: 369.2091.

1-(2-{[(*tert*-Butoxycarbonyl)amino]acetoxy}ethyl)-2,3-dimethylimidazolium Hexafluorophosphate (7a*h*)
DCC (0.89 g, 4.3 mmol) and DMAP (26 mg, 0.21 mmol) were added to a soln of **4c*h*** (1.2 g, 4.3 mmol) in MeCN (30 mL) at r.t. After 10 min, **5** (0.79 g, 4.5 mmol) was introduced, and the mixture was stirred for 24 h at r.t. before filtration over Celite, removal of the solvent, washing with Et_2O (2 × 80 mL) and EtOAc–pentane (1:1, 80 mL), and drying under reduced pressure for 10 h.

Beige powder; yield: 1.8 g (96%); mp 120 °C.

^{1}H NMR (200 MHz, acetone-d_6): δ = 7.71 (d, *J* = 2.2 Hz, 1 H), 7.64 (d, *J* = 2.1 Hz, 1 H), 6.40 (br s, 1 H), 4.67 (t, *J* = 4.6 Hz, 2 H), 4.55 (t, *J* = 4.5 Hz, 2 H), 3.98 (s, 3 H), 3.82 (d, *J* = 6.2 Hz, 2 H), 2.85 (s, 3 H), 1.40 (s, 9 H).

^{13}C NMR (50 MHz, acetone-d_6): δ = 170.8, 156.9, 146.5, 123.5, 122.3, 79.5, 63.4, 48.0, 42.7, 35.6, 28.5, 10.0.

HRMS-FAB: *m*/*z* calcd for $C_{14}H_{24}N_3O_4$: 298.17668; found: 298.1764.

1-(2-{[(*tert*-Butoxycarbonyl)amino]acetoxy}ethyl)-3-methylimidazolium Hexafluorophosphate (7b*h*)

The procedure used was as described for **7a*h***, but **4d*h*** (1.2 g, 4.3 mmol) was used instead of **4c*h***.

White powder; yield: 1.7 g (92%); mp 70 °C.

^{1}H NMR (200 MHz, acetone-d_6): δ = 9.13 (s, 1 H), 7.85 (s, 1 H), 7.76 (s, 1 H), 6.46 (br s, 1 H), 4.70 (t, *J* = 4.7 Hz, 2 H), 4.61 (t, *J* = 4.7 Hz, 2 H), 4.11 (s, 3 H), 3.86 (d, *J* = 6.2 Hz, 2 H), 1.41 (s, 9 H).

^{13}C NMR (50 MHz, acetone-d_6): δ = 170.8, 157.0, 138.0, 124.7, 123.8, 79.5, 63.2, 49.5, 42.7, 36.7, 28.5.

HRMS-FAB: *m*/*z* calcd for $C_{26}H_{44}N_6O_8F_6P$ [$2C^+$, PF_6^-]$^+$: 713.28625; found: 713.2862.

1-(2-{[(*tert*-Butoxycarbonyl)amino]acetoxy}ethyl)-2,3-dimethylimidazolium Tetrafluoroborate (7a*t*)

The procedure used was as described for **7a*h***, but **4c*t*** (0.98 g, 4.3 mmol) was used instead of **4c*h***.

White powder; yield: 1.5 g (90%); mp 128 °C.

^{1}H NMR (200 MHz, acetone-d_6): δ = 7.68 (d, *J* = 2.0 Hz, 1 H), 7.63 (d, *J* = 1.9 Hz, 1 H), 6.36 (br s, 1 H), 4.63 (t, *J* = 4.5 Hz, 2 H), 4.55 (t, *J* = 4.5 Hz, 2 H), 3.95 (s, 3 H), 3.81 (d, *J* = 6.2 Hz, 2 H), 2.82 (s, 3 H), 1.41 (s, 9 H).

^{13}C NMR (50 MHz, acetone-d_6): δ = 170.8, 156.9, 146.5, 123.5, 122.2, 79.4, 63.5, 47.9, 42.7, 35.5, 28.5, 9.8.

HRMS-FAB: *m*/*z* calcd for $C_{14}H_{24}N_3O_4$: 298.17668; found: 298.1771.

1-(2-{[(*tert*-Butoxycarbonyl)amino]acetoxy}ethyl)-3-methylimidazolium Tetrafluoroborate (7b*t*)

The procedure used was as described for **7a*h***, but **4d*t*** (0.92 g, 4.3 mmol) was used instead of **4c*h***.

White powder; yield: 1.5 g (92%); mp 95 °C.

^{1}H NMR (200 MHz, acetone-d_6): δ = 9.10 (s, 1 H), 7.83 (s, 1 H), 7.74 (s, 1 H), 6.41 (br s, 1 H), 4.67 (t, *J* = 4.7 Hz, 2 H), 4.59 (t, *J* = 4.7 Hz, 2 H), 4.08 (s, 3 H), 3.85 (d, *J* = 6.2 Hz, 2 H), 1.40 (s, 9 H).

^{13}C NMR (50 MHz, acetone-d_6): δ = 170.9, 156.9, 138.2, 124.7, 123.8, 79.4, 63.3, 49.5, 43.8, 36.6, 28.5.

HRMS-FAB: *m*/*z* calcd for $C_{13}H_{22}N_3O_4$: 284.16103; found: 284.1613.

1-{2-[(Formylamino)acetoxy]ethyl}-2,3-dimethylimidazolium Hexafluorophosphate (8a*h*)

The procedure used was as described for **7a*h***, but **6** (0.46 g, 4.5 mmol) was used instead of **5**, and washing was with EtOAc (3 × 50 mL).

Beige powder; yield: 1.2 g (74%); mp 116 °C.

^{1}H NMR (200 MHz, DMSO-d_6): δ = 8.45 (br s, 1 H), 8.08 (s, 1 H), 7.64 (s, 1 H) 7.63 (s, 1 H), 4.40 (s, 4 H), 3.86 (d, *J* = 6.2 Hz, 2 H), 3.75 (s, 3 H), 2.60 (s, 3 H).

^{13}C NMR (50 MHz, DMSO-d_6): δ = 169.3, 161.9, 145.2, 122.5, 121.3, 62.8, 46.5, 39.4, 34.8, 9.3.

HRMS-FAB: *m*/*z* calcd for $C_{10}H_{16}N_3O_3$: 226.11917; found: 226.1188.

1-{2-[(Formylamino)acetoxy]ethyl}-3-methylimidazolium Hexafluorophosphate (8b*h*)

The procedure used was as described for **7a*h***, but **4d*h*** (1.2 g, 4.3 mmol) was used instead of **4c*h***, **6** (0.46 g, 4.5 mmol) was used instead of **5**, and washing was with EtOAc (3 × 50 mL).

Pale brown oil; yield: 1.2 g (76%).

^{1}H NMR (200 MHz, acetone-d_6): δ = 9.06 (s, 1 H), 8.21 (s, 1 H), 7.81 (s, 1 H), 7.70 (s, 1 H), 7.64 (br s, 1 H), 4.70 (t, *J* = 4.4 Hz, 2 H), 4.58 (t, *J* = 4.5 Hz, 2 H), 4.07 (s, 3 H), 4.02 (d, *J* = 6.1 Hz, 2 H).

^{13}C NMR (50 MHz, acetone-d_6): δ = 170.0, 162.7, 138.0, 124.7, 123.7, 63.5, 49.4, 40.3, 36.6.

HRMS-FAB: *m*/*z* calcd for $C_9H_{14}N_3O_3$: 212.1035; found: 212.1036.

1-{2-[(Formylamino)acetoxy]ethyl}-2,3-dimethylimidazolium Tetrafluoroborate (8a*t*)

The procedure used was as described for **7a*h***, but **4c*t*** (0.98 g, 4.3 mmol) was used instead of **4c*h***, **6** (0.46 g, 4.5 mmol) was used instead of **5**, and washing was with EtOAc (3 × 50 mL).

White powder; yield: 1.1 g (80%); mp 54 °C.

^{1}H NMR (200 MHz, DMSO-d_6): δ = 8.44 (br s, 1 H), 8.08 (s, 1 H), 7.64 (s, 1 H) 7.63 (s, 1 H), 4.41 (s, 4 H), 3.86 (d, *J* = 6.0 Hz, 2 H), 3.75 (s, 3 H), 2.63 (s, 3 H).

^{13}C NMR (50 MHz, DMSO-d_6): δ = 169.3, 161.9, 145.1, 122.5, 121.3, 62.8, 46.6, 39.4, 34.8, 9.3.

HRMS-FAB: *m*/*z* calcd for $C_{10}H_{16}N_3O_3$: 226.1192; found: 226.1188.

1-{2-[(Formylamino)acetoxy]ethyl}-3-methylimidazolium Tetrafluoroborate (8b*t*)

The procedure used is as described for **7a*h***, but **4d*t*** (0.92 g, 4.3 mmol) was used instead of **4c*h***, **6** (0.46 g, 4.5 mmol) was used instead of **5**, and washing was with EtOAc (3 × 50 mL).

Pale brown oil; yield: 1.2 g (96%).

^{1}H NMR (200 MHz, acetone-d_6): δ = 9.04 (s, 1 H), 8.20 (s, 1 H), 7.81 (s, 1 H), 7.70 (s, 1 H), 7.61 (br s, 1 H), 4.65 (t, *J* = 4.6 Hz, 2 H), 4.55 (t, *J* = 4.4 Hz, 2 H), 4.05 (s, 3 H), 4.01 (d, *J* = 6.1 Hz, 2 H).

^{13}C NMR (50 MHz, acetone-d_6): δ = 170.0, 162.7, 140.1, 124.7, 123.7, 63.7, 49.3, 40.3, 36.6.

HRMS-FAB: *m*/*z* calcd for $C_9H_{14}N_3O_3$: 212.10352; found: 212.1040.

1-[2-(Aminoacetoxy)ethyl]-2,3-dimethylimidazolium Hexafluorophosphate (9a*h*)

A soln of **7a*h*** (1.1 g, 2.5 mmol) in MeCN (5 mL) was successively treated with MeOH (0.20 mL, 5.0 mmol) and AcCl (0.36 mL, 5.0 mmol). After 24 h at r.t., the solvent was removed under reduced pressure. The residue was washed with EtOAc (2 × 10 mL) and dried under reduced pressure for 10 h.

Beige powder; yield: 0.67 g (78%); mp 130 °C.

^{1}H NMR (200 MHz, DMSO-d_6): δ = 8.54 (br s, 2 H), 7.73 (d, *J* = 1.9 Hz, 1 H), 7.66 (d, *J* = 1.9 Hz, 1 H), 4.46 (s, 4 H), 3.79 (s, 2 H), 3.77 (s, 3 H), 2.61 (s, 3 H).

^{13}C NMR (50 MHz, DMSO-d_6): δ = 167.2, 145.2, 122.6, 121.4, 63.7, 46.5, 39.8, 34.9, 9.6.

HRMS-FAB: *m*/*z* calcd for $C_9H_{16}N_3O_2$: 198.12425; found: 198.1245.

1-[2-(Aminoacetoxy)ethyl]-3-methylimidazolium Hexafluorophosphate (9b*h*)

The procedure used was as described for **9a*h***, but **7b*h*** (1.1 g, 2.5 mmol) was used instead of **7a*h***.

Beige powder; yield: 0.51 g (62%); mp 153 °C.

^{1}H NMR (200 MHz, DMSO-d_6): δ = 9.24 (s, 1 H), 8.25 (br s, 2 H), 7.81 (s, 1 H), 7.73 (s, 1 H), 4.49 (s, 4 H), 3.87 (s, 3 H), 3.80 (s, 2 H).

^{13}C NMR (50 MHz, acetone-d_6): δ = 167.0, 137.3, 123.5, 122.6, 63.5, 47.8, 39.6, 35.8.

HRMS-FAB: *m*/*z* calcd for $C_8H_{14}N_3O_2$: 184.10860; found: 184.1087.

1-[2-(Aminoacetoxy)ethyl]-2,3-dimethylimidazolium Tetrafluoroborate (9a*t*)

The procedure used was as described for **9a*h***, but **7a*t*** (0.96 g, 2.5 mmol) was used instead of **7a*h***.

White powder; yield: 0.66 g (93%); mp 159 °C.

^{1}H NMR (200 MHz, DMSO-d_6): δ = 8.44 (br s, 2 H), 7.73 (s, 1 H), 7.65 (s, 1 H), 4.46 (s, 4 H), 3.79 (s, 2 H), 3.76 (s, 3 H), 2.61 (s, 3 H).

^{13}C NMR (50 MHz, DMSO-d_6): δ = 167.3, 145.2, 122.5, 121.4, 63.7, 46.4, 39.8, 34.9, 9.6.

HRMS-FAB: *m*/*z* calcd for $C_9H_{16}N_3O_2$: 198.1243; found: 198.1245.

1-[2-(Aminoacetoxy)ethyl]-3-methylimidazolium Tetrafluoroborate (9b*t*)

The procedure used was as described for **9a*h***, but **7b*t*** (0.93 g, 2.5 mmol) was used instead of **7a*h***.

White powder; yield: 0.47 g (69%); mp 125–126 °C.

^{1}H NMR (200 MHz, DMSO-d_6): δ = 9.26 (s, 1 H), 8.41 (br s, 2 H), 7.82 (s, 1 H), 7.73 (s, 1 H), 4.50 (s, 4 H), 3.87 (s, 3 H), 3.82 (s, 2 H).

^{13}C NMR (50 MHz, DMSO-d_6): δ = 167.1, 137.4, 123.6, 122.7, 63.6, 47.9, 39.7, 35.9.

HRMS-FAB: *m*/*z* calcd for $C_8H_{14}N_3O_2$: 184.10860; found: 184.1087.

1-[2-({[2-(*tert*-Butylamino)-1-(4-chlorophenyl)-2-oxoethyl](2-nitrobenzoyl)amino}acetoxy)ethyl]-2,3-dimethylimidazolium Tetrafluoroborate (10a*t*)

4-Chlorobenzaldehyde (0.16 g, 1.1 mmol) was added to a soln of **9a*t*** (0.29 g, 1.0 mmol) in MeOH (2 mL). After the mixture had been kept 10 min at 40 °C under a dry atmosphere, 2-nitrobenzoic acid (0.19 g, 1.1 mmol) and *t*-BuNC (127 μL, 1.1 mmol) were added. After the mixture had been kept 24 h at 40 °C, the solvent was removed under reduced pressure, and the residue was washed with Et_2O (2 × 10 mL) and dissolved in MeCN (4 mL). After filtration and evaporation of the filtrate, the residue was dried under reduced pressure for 10 h.

HRMS-FAB: *m*/*z* calcd for $C_{28}H_{33}N_5O_6{}^{35}Cl$: 570.21194; found: 570.2117.

1-[2-({[2-(*tert*-Butylamino)-1-(4-chlorophenyl)-2-oxoethyl](2-nitrobenzoyl)amino}acetoxy)ethyl]-3-methylimidazolium Tetrafluoroborate (10b*t*)

The procedure used was as described for **10a*t***, but **9b*t*** (0.27 g, 1.0 mmol) was used instead of **9a*t***.

HRMS-FAB: *m*/*z* calcd for $C_{27}H_{31}N_5O_6{}^{35}Cl$: 556.19629; found: 556.1968.

1-(2-{[3-(*tert*-Butylcarbamoyl)phthalimidino]acetoxy}ethyl)-3-methylimidazolium Tetrafluoroborate (13)

Phthalaldehydic acid (0.17 g, 1.1 mmol) was added to a soln of **9b*t*** (0.27 g, 1.0 mmol) in MeCN (4 mL). After the mixture had been kept 20 min at 40 °C, *t*-BuNC (127 μL, 1.1 mmol) was added. After 5 d at 40 °C, the mixture was filtered to remove the unchanged amine. The solvent was then removed under reduced pressure, and the residue was washed with Et_2O (2 × 10 mL) and dried under reduced pressure for 10 h.

Pale brown oil; yield: 0.27 g (56%).

^{1}H NMR (200 MHz, acetone-d_6): δ = 9.04 (s, 1 H), 8.08 (s, 1 H), 8.07 (s, 1 H), 7.7 (m, 4 H), 6.72 (s, 1 H), 5.29 (s, 1 H), 4.6 (m, 3 H), 4.0 (m, 6 H), 1.31 (s, 9 H).

^{13}C NMR (50 MHz, acetone-d_6): δ = 169.3, 168.5, 166.4, 142.9, 137.6, 134.9, 131.3, 131.2, 125.1, 124.2, 124.0, 123.1, 65.1, 63.4, 51.5, 48.7, 43.5, 36.0, 26.9 (3C).

HRMS-FAB: *m*/*z* calcd for $C_{21}H_{27}N_4O_4$: 399.2032; found: 399.2033.

Methyl [3-(*tert*-Butylcarbamoyl)phthalimidino]acetate (12)

Route A: Phthalaldehydic acid (0.17 g, 1.1 mmol) was added to a soln of **9b*t*** (0.27 g, 1.0 mmol) in MeOH (2 mL). After the mixture had been kept for 20 min at 40 °C, *t*-BuNC (127 μL, 1.1 mmol) was added under a dry atmosphere. After 24 h at 40 °C, the mixture was cooled to r.t. and Et_3N (0.21 μL, 1.5 mmol) was added. After stirring for 18 h at r.t., removal of the solvent, addition of H_2O (5 mL), extraction with EtOAc, drying ($MgSO_4$), and evaporation of the solvent, the crude product was chromatographed (silica gel, EtOAc–pentane 1:1) and crystallized from Et_2O; yield: 0.14 g (47%, 2 steps).

Route B: A soln of **13** (0.49 g, 1 mmol) in MeOH (3 mL) was treated with Et_3N (0.21 μL, 1.5 mmol) and the mixture was stirred for 18 h at r.t. under a dry atmosphere. After removal of the solvent, addition of H_2O (5 mL), extraction with EtOAc, drying ($MgSO_4$), and evaporation of the solvent, the crude product was chromatographed (silica gel, EtOAc–pentane 1:1); yield: 0.24 g (80%).

Beige powder; mp 148–150 °C.

^{1}H NMR (200 MHz, acetone-d_6): δ = 7.7 (m, 5 H), 5.22 (s, 1 H), 4.68 (d, *J* = 18 Hz, 1 H), 4.01 (d, *J* = 18 Hz, 1 H), 3.74 (s, 3 H), 1.31 (s, 9 H).

^{13}C NMR (50 MHz, acetone-d_6): δ = 170.7, 169.6, 166.8, 143.2, 132.9, 131.6, 129.4, 123.3, 104.0, 65.7, 52.5, 51.9, 43.7, 28.3 (3C).

Anal. Calcd for $C_{16}H_{20}N_2O_4$: C, 63.14; H, 6.62; N, 9.20. Found: C, 63.29; H, 6.64; N, 9.08.

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