IONIC LIQUID SUPPORTS STABLE UNDER CONDITIONS OF PEPTIDE COUPLINGS, DEPROTECTIONS AND TRACELESS SUZUKI REACTIONS

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Ionic liquid supports (ILS) functionalized with carboxylic, alcoholic or amino groups were synthesized, based on 1-methylimidazolium and pyridinium cations, and bromide, chloride, iodide and tetrafluoroborate anions. These reactive ionic liquids were fully characterized by NMR and HRMS. Ionic liquids based on 1-(6-aminohexyl)-3-methylimidazolium iodide have been used in the conditions of peptide chemistry such as coupling and deprotection reactions. A method for attaching (bromophenyl)silanes to the ionic liquid supports was also developed to introduce traceless linkers. An ionic liquid with attached bromobenzene was reacted with $ArB(OH)_2$ under the Suzuki cross-coupling conditions and the resulting compound was cleaved by bromodesilylation with Br_2/pyridine to give the substituted products in good yields. The substrate loading of the ILS is high and can be tuned to between 2.5 and 5.0 mmol/g.

Keywords: Ionic liquid supports; Ionic liquids; Methylimidazolium salts; Peptide coupling; Traceless linkers; Suzuki cross-coupling.

Combinatorial chemistry encompasses many strategies and processes for rapid synthesis and analysis of large, organized collections of compounds known as libraries. Using combinatorial synthesis a large number of products can be prepared simultaneously by combining sets of chemical building blocks in just a few synthetic steps. In recent years, combinatorial chemistry has attracted enormous attention of pharmaceutical industry because it can greatly facilitate the synthesis of a large diversity of new drug candidates for high-throughput screening assays[1].

For synthesis of libraries, insoluble polymeric supports are used to facilitate product purification through simple filtration and washing. A key aspect of any solid-phase synthesis (SPS) strategy is the linkage element, which acts as a tether to the polymeric support material[2,3]. Successful SPS has several shortcomings due to the nature of heterogeneous reaction conditions[4,5]. To overcome these limitations, liquid-phase combinatorial syn-

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thesis (LPCS) has been developed as an alternative methodology for the construction of small molecule libraries wherein the use of a soluble polymeric support provides both the advantages of SPS and the benefits of classical solution-phase organic chemistry. In an attempt to do polymer-supported chemistry in solution, soluble polymers and fluorous systems have been utilized[6–10]. Synthetic approaches that utilize soluble polymers, termed liquid-phase chemistry, combine the advantages of homogeneous solution chemistry (high reactivity, lack of diffusion phenomena, facile compound characterization) with those of solid-phase methods (use of excess reagents, easy isolation and purification of products through precipitation and filtration). The chosen supports for liquid-phase synthesis (LPS) must also provide a reasonable compromise between loading capacity and solubility. For large-scale applications, the loading capacity of reactive groups must be high and the presence of the inert matrix not excessive, such that a big molecule no longer determines solubility properties.

Room-temperature ionic liquids are attracting increasing interest as an environmentally benign reaction media for organic and organometallic chemistry[11–13]. These solvents present a number of interesting properties: no vapor pressure, high thermal and chemical stability, wide liquid range, low melting point, easy tuning of solubility by modification of anions and cations[14,15]. It is possible, through a careful choice of starting materials, to prepare ionic liquids that are liquid at and below room temperature. The scope of ionic liquids has recently been expanded by the introduction of additional functional groups in the ionic liquid structure. These so-called "task-specific" ionic liquids can be utilized as supported reagents or catalysts with high affinity for the ionic liquid phase[16–19].

Reactions could be performed in ionic liquids as solvents or as supports[20–22]. In the latter case both the substrate and the catalyst could be linked by a covalent bond to ionic liquid support offering the same easy work-up and purification as standard polymeric solid supports. Ionic liquids based on methylimidazolium compounds are favourable for investigation because of their air and water stability, their wide liquid range, the liquid state at room temperature, and their favourable viscosity and density characteristics[23–27].

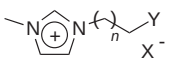
While this is a major step forward, there are still limitations to the broad application of ionic liquid as support (ILS) in combinatorial chemistry. In a previous note we reported a new strategy to obtain pure ionic liquid supports with a high loading (3 mmol/g) of primary amino groups[28]. Our results show an efficient approach to obtain amino-functionalized ionic

liquids based on a phthalimide protecting group. The first example of a traceless ionic liquid support based on silicon linker was also reported.

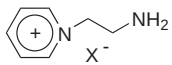
In high-throughput organic synthesis, we have focused our studies on the development of novel ionic liquid supports for combinatorial and parallel synthesis; our most recent work is described in the present paper. We report the synthesis of 15 new ionic liquids based on 1-methylimidazolium or pyridinium cations, and bromide, chloride, iodide or tetrafluoroborate anions. Ionic liquids based on 1-(6-aminohexyl)-3-methylimidazolium iodide have been tested in the conditions of peptide coupling and deprotection reactions. We also report that the well-characterized Suzuki coupling reaction of phenylboronic acid and halobenzenes to form biphenyl compounds is readily accomplished using (bromophenyl)silanes bonded to ionic liquids. Electrophilic cleavage of the coupled products from the ionic liquid supports by bromodesilylation proceeds quickly and with high yields.

RESULTS AND DISCUSSION

We have prepared a wide range of ILS by varying the cation, e.g. 1-methylimidazolium and pyridinium, and the anion such as Br^-, Cl^-, I^-, BF_4^-.



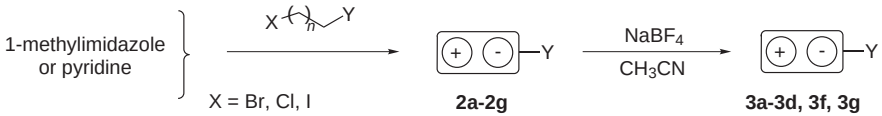
Y = OH, COOH, $Si(CH_3)_2(PhBr)$
X = Br, Cl, I, BF_4, n = 0, 1, 4 or 5



X = Br, BF_4

These two cations were selected because their precursors 1-methylimidazole and pyridine are commercially available and provide a simple access to a wide variety of functionalized ionic liquids containing standard reactive hydroxy, carboxylic or amino groups Y. Thus, a direct analogy with chemistry on beads is applicable to the ILS.

1-Alkyl-3-methylimidazolium bromides **2b**, **2c**, **2d**, **2g** and chlorides **2a**, **2f** were prepared by a simple one-step solvent-free method, by heating 1-methylimidazole (Im) or pyridine (Py) with 2-bromoethylamine hydrobromide, 6-bromohexanoic acid, 3-bromopropanoic acid, 6-chlorohexan-1-ol and 1-bromo-4-[(chloromethyl)dimethylsilyl]benzene (Scheme 1, Table I).



X = Br, Cl, I
Y = OH, COOH, NH_2, $Si(CH_3)_2(PhBr)$
n = 0, 1, 4 or 5

2a-2g
(X^- = Br, Cl, I)

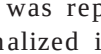
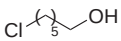
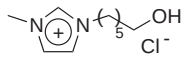
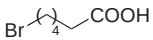
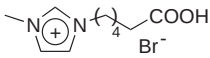
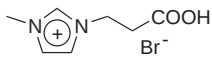
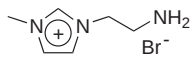
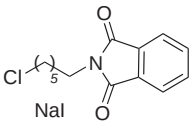
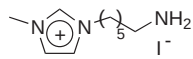
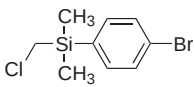
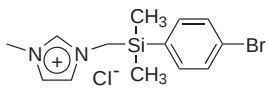
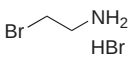
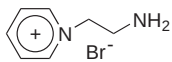
3a-3d, 3f, 3g
(X^- = BF_4)

SCHEME 1

Bromides **2b** and **2c** were conveniently used as immediate precursors for the synthesis of several heterocyclic betaines[29–31]. There were no data for the mass and spectral characterisation of the products obtained.

While the chemistry of ionic liquids functionalized with hydroxy, formyl or keto group was reported[16,17,32,33], no multistep process involving an amino-functionalized ionic liquid has been described. This could be explained by the lack of a direct and fully general access to amino ionic liq-

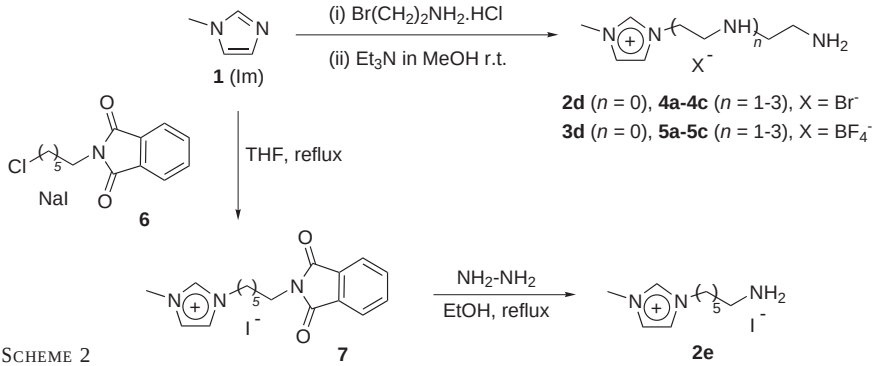
TABLE I
Preparations of ionic liquids **2a**–**2g** from haloalkanes under solvent-free reaction conditions

Entry		Temp., °C Time, h	Product		Yield, %
1		80 24	**2a**		95
2		70 4	**2b**		65
3		70 4	**2c**		85
4		70 4	**2d**		56
5		THF reflux, 16	2e[a]		75
6		70 48	**2f**		84
7		80 24	**2g**		30

[a] After deprotection with hydrazine.

uids supports. Two methods of synthesizing amino ionic liquid supports were investigated. The first strategy was the standard approach to produce imidazolium ionic liquids by the direct reaction between 1-methylimidazole and halogenated substrate (Scheme 1). A task-specific amino ionic liquid was effectively obtained by the reaction of 1-butylimidazole with 2-bromopropylamine hydrobromide[34].

However in the case in the case of 2-bromoethylamine hydrobromide, as alkylation reagent a side product $HMeIm^+Br^-$ was formed in an amount of 36–50%, (Scheme 2). The compound with the NH_2-end group **2d** was obtained in a yield of 56%, due to the side reaction (Scheme 2). ^1H NMR analysis of the crude product indicated the formation of a major product, which is the desired ionic liquid **2d**, together with by-products due to the polyamines.



SCHEME 2

Mass spectrometry indicated that the compound 1-(2-aminoethyl)-3-methylimidazolium bromide (**2d**) was the principal product with three minor by-products due to the formation of polyamines **4a**–**4c**. As indicated in Scheme 2, the major by-product from the direct alkylation reaction of 1-methylimidazole is **4a** (n = 1). It is therefore reasonable to expect that the major by-product of **3d** would be compound **5a** (n = 1) (Scheme 2). The multiplicity of the reaction products (at least 4 components) made impractical the isolation of individual compounds for complete and unequivocal characterization. HRMS analysis of the major components was performed; the results of the MS and ^1H NMR data are consistent with the suggested structures. By-products **4a**–**4c** and **5a**–**5c** were identified as $[M^+]$ $C_8H_{17}N_4$ (m/z = 169, n = 1), $[M^+]$ $C_{10}H_{22}N_5$ (m/z = 212, n = 2) and $[M^+]$ $C_{12}H_{27}N_6$ (m/z = 255, n = 3). These results indicated that the direct alkylation reaction with 2-bromoethylamine hydrobromide is not general and is really dependent on starting compounds.

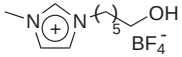
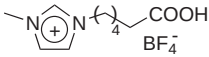
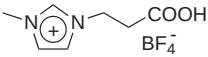
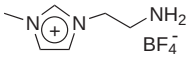
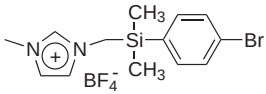
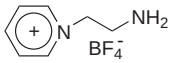
In a previous paper, the synthesis of 1-methyl-3-(6-phthalimidohexyl)-imidazolium iodide (**7**) was reported[28]. Our results show an efficient approach to amino-functionalized ionic liquids based on the phthalimide protecting group, capable of preventing by-product formation. The intermediate **7** (Scheme 2) was obtained by alkylation of 1-methylimidazole with 1-chloro-6-phthalimidohexane (**6**) in the presence of NaI in a high yield (90%) and purity as indicated by ^{1}H and ^{13}C NMR spectrometry[28]. Reaction of **7** with hydrazine gives compound (**2e**) in a high yield and without contamination with polyamines.

The synthesis of 1-(2-aminoethyl)pyridinium bromide (**2g**) (Table I) has been previously performed using the Gabriel method[35]. We reported another successful preparation of this compound from 2-bromoethylamine hydrobromide and pyridine (heating at 80 °C). The reaction of 1-(2-aminoethyl)pyridinium hydrobromide with K_2CO_3 in CH_3CN at room temperature then resulted in the formation of free amino group. The cation of these new ionic liquids **2e** and **2g** is an imidazolium/pyridinium ion to which a primary amine moiety is covalently tethered.

For all functionalized ionic liquids **2**, reactions were assessed to have gone to completion if the ^{1}H and ^{13}C NMR spectra showed no signals of 1-methylimidazole or pyridine. This approach generally allowed products of excellent purity to be isolated, the unreacted starting material being the only contaminant in some cases. The obtained ionic liquids **2a**–**2g** were simply purified by washing. Comparatively good yields (65–95% relative to 1-methylimidazole) of the desired compounds were obtained (Table I). Subsequent anion metathesis with ammonium tetrafluoroborate (2.5 equiv.) in CH_3CN at 60 °C produced the desired ionic liquids **3a**–**3d**, **3f** and **3g** in almost quantitative yields (86–95%) (Scheme 1 and Table II).

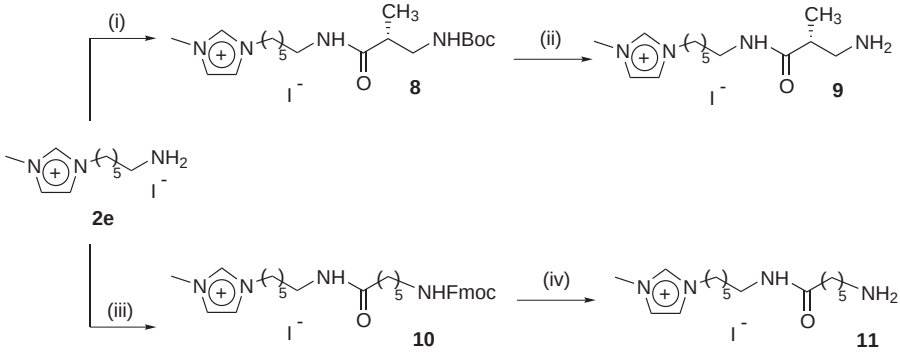
Product characterization was carried out using IR, ^{1}H and ^{13}C NMR spectroscopy. Valence vibration of the NH_2 (3420–3580 cm^{-1}), CO (1714–1734 cm^{-1}) and OH and COOH (3400–3562 cm^{-1}) groups are clearly seen in IR spectra of the compounds studied. The IR spectra of tetrafluoroborates **3** show the characteristic B–F bands at 1040–1060 cm^{-1}, as has already been observed for related compounds[36]. The free amino group in compounds **2d**, **2e** and **2g** is proved unambiguously by ^{1}H NMR spectra in DMSO-d_6 by the appearance of a broad multiplet centred at 2.5–3.0 ppm. A triplet of the N–CH_2 group due to the reaction of 1-methylimidazole and corresponding alkylation reagent is observed at 4.15–4.61 ppm. The structure of the new ionic liquids was also determined by mass spectrometry and ^{13}C NMR.

TABLE II
Structure and yields of tetrafluoroborates **3**

Entry	Substrate		Product	Yield, %
1	**2a**	**3a**		92
2	**2b**	**3b**		93
3	**2c**	**3c**		86
4	**2d**	**3d**		93
5	**2f**	**3f**		95
6	**2g**	**3g**		75

It is known that, in the presence of 1,3-diisopropylcarbodiimide (DIC) and 4-dimethylaminopyridine (DMAP) as catalyst[37,38], esters and amides are obtained under mild conditions and with good yields. We used the ILS **2e** as a reagent for the acylation reaction to obtain the amide-functionalized ionic liquids according to Scheme 3. The acylation of the amino group of **2e** was carried out using Boc-L-Ala (Boc-L-alanine) and Fmoc-Ahx (Fmoc-6-aminohexanoic acid). The formation of amide bond was proved by ^{1}H NMR spectra. There is no broad multiplet at 2.5–3.0 ppm, assigned to the free NH_2 group of the starting ILS **2e**. The *N-tert*-butyloxycarbonyl (Boc) was completely removed upon treatment with small excess of CF_3COOH at room temperature to give the desired ionic liquid **9** [39]. The (fluoren-9-yl-

methyloxy)carbonyl (Fmoc) group undergoes non-hydrolytic cleavage by treatment of the protected ionic liquid **10** with piperidine in CH_3CN, to give the desired ionic liquid in the free base form **11** [40].



(i) Boc-L-Ala, DIC, CH_3CN, r.t.; (ii) CF_3COOH, CH_2Cl_2, r.t.;
(iii) Fmoc-Ahx, DIC, CH_3CN/DMF,r.t.; (iv) piperidine, CH_3CN, r.t.

SCHEME 3

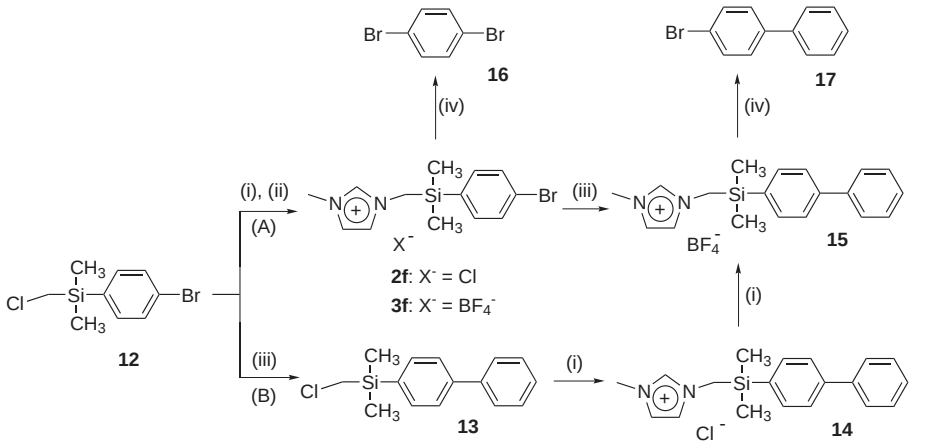
These results indicated that **2e** is compatible with standard amide coupling reactions and with the acid and basic conditions generally used to remove the protecting group or to cleave anchored molecules from the support.

Since the biphenyl unit is an important pharmacophore present in a variety of biologically active compounds[41], we wished to determine whether the synthesis of this moiety would be amenable to an ionic LPS strategy. In addition, we also report simple and efficient method of attaching phenylsilanes to ILS.

Plunkett and Ellman[42] reported the first application of silicon as a cleavable linker for SPS. Various reports in the past several years described other successful preparations of silicon linkers[43–45]. Attachment of the linkers to a solid support was straightforward. A variety of resins were produced in this manner with substrate loading ca. 1 mequiv./g in each case[46,47].

Silicon-directed substitution of arylsilanes is a well-studied process in solution[46,48–50]. Yet few examples of this reaction on a solid support have appeared in the literature. The starting compound 1-bromo-4-[(chloromethyl)dimethylsilyl]benzene (**12**) was prepared from 1,4-dibromobenzene in 81% yield[46,51]. It should be mentioned that the synthesis has been described of silane-linked biphenyl **13** by lithiation of 4-bromobiphenyl with BuLi, followed by treatment with chloro(chloromethyl)dimethylsilane[52].

We reported another successful method for the preparation of **13** by the Suzuki coupling from **12**. The attachment of the silicon-based linkers **12** and **13** to 1-methylimidazole was performed at 70 °C by a simple one-step solvent-free method (Scheme 4).



(i) 1-methylimidazole, 70 °C, 48 h, (**2f**), 24 h (**14**); (ii) NH_4BF_4 2.5 equiv, dry CH_3CN, 60 °C, 18 h; (iii) $PhB(OH)_2$, 3% $[Pd(PPh_3)_4]$, Et_3N/DMF(1:1), 24 h, 90 °C; (iv) 6.0 equiv Br_2, 3.0 equiv pyridine, CH_2Cl_2, 0 °C, 24 h

SCHEME 4

Good yields of the desired compounds (84% for **2f** and 80% for **14** relative to 1-methylimidazole) were obtained. Subsequent anion metathesis with ammonium tetrafluoroborate (2.5 equiv.) in CH_3CN at 60 °C produced the desired ionic liquids **3f** and **15** in almost quantitative yields (95 and 90%) (Scheme 4). The structure of these new ionic liquids was determined from ^1H, ^{13}C NMR data and mass spectra.

The Suzuki coupling reaction on solid support, studied by Frenette and Friesen[47], was employed as the key C–C bond-forming reaction[53] due to its mildness and tolerance to a wide scope of functionalities. Two synthetic strategies were developed for the preparation of compound **15** as outlined in Scheme 4. In the direct route A, the novel 1-[(biphenyl-4-yldimethylsilyl)methyl]-3-methylimidazolium tetrafluoroborate (**15**) was easily prepared via Suzuki coupling reaction with ILS **3f**.

By route B, **15** was prepared in three separate steps by reaction of 1-methylimidazole with 1-bromo-4-[(chloromethyl)dimethylsilyl]benzene (**12**) and subsequent ion exchange with NH_4BF_4.

The two silane-linked bromophenyls **3f** and **12** were first reacted with $PhB(OH)_2$ under standard anhydrous conditions[54,55] (3–5% $[Pd(PPh_3)_4]$, Et_3N/DMF (1:1), 90 °C for 24 h). Both bromophenyls were useful substrates in this reaction undergoing facile palladium-catalyzed coupling with phenylboronic acid to give ionic-liquid-bonded biphenyl **15** and silane-linked biphenyl **13**. The biphenyl products are obtained in high yields without significant contamination with by-products or starting bromo compounds. The coupled ionic liquid **3f** and **15** were then subjected to electrophilic cleavage by bromodesilylation to give the desired substituted compounds **16** and **17** in good yield (Scheme 4). Analysis of compound **17** by ^1H NMR and HRMS indicated that the product was contaminated with <3% dibromobiphenyl only.

In summary, several functionalized ionic liquids showing the standard reactive groups generally used on polymeric beads such as carboxylic, hydroxy or amino groups were reported. We have shown that the new amino-functionalized ionic liquid supports derived from 1-methylimidazole can be used in the classical conditions of peptide couplings and deprotection reactions. The compatibility of the imidazolium unit was demonstrated for DIC or DMAP coupling reactions of protected amino acids and for classical cleavage of Boc or Fmoc protecting groups. Extension to parallel synthesis of libraries using functionalized ionic liquids and peptide chemistry is possible using cleavable linkers.

We have also demonstrated versatility and utility of novel ionic-liquid-supported phenylsilanes for liquid-phase synthesis under Suzuki reaction. With these results, further studies will be directed toward parallel synthesis and building a combinatorial library based on Suzuki reactions.

EXPERIMENTAL

All reactions were carried out in an inert atmosphere. Solvents were dried and distilled under dry nitrogen using standard procedures. ^1H and ^{13}C NMR spectra were recorded on a Bruker DPX 200 at 200.131 and 50.32 MHz, respectively. Chemical shifts are given in δ-scale (ppm), coupling constants, *J*, in Hz. Infrared spectra (cm^{-1}) were recorded on a Bruker IFS 28 FT spectrometer as KBr pellets or film. High-resolution mass spectrometry (HRMS) measurement was taken on a ZABSpec TOF Micromass and on a Varian MAT 311 at an ionizing potential of 70 eV in the Centre Régional de Mesures Physiques de l'Ouest (CRMPO, Rennes, France). Elemental analyses were performed using Flash EA 1112 equipment. All reagents were purchased from Acros, Aldrich Chimie, Advanced ChemTech, Propeptide, and Fluka, France and used without further purification.

1-Methyl-3-(6-phthalimidohexyl)imidazolium iodide (**7**) was obtained by alkylation of 1-methylimidazole with 1-chloro-6-phthalimidohexane (**6**) in the presence of NaI according

to ref.[28]. The starting product 1-bromo-4-[(chloromethyl)dimethylsilyl]benzene (**12**) was prepared according to refs[46,51].

Synthesis of Compounds **2a**–**2c** and **2f**. General Procedure

A stirred mixture of 1-methylimidazole (1 equiv.) and halide RX (*n* equiv.) was heated under nitrogen under the conditions given in Table I. The resulting viscous liquid was allowed to cool to room temperature, then treated with a solvent (10 ml) and stirred vigorously for 30 min. The solvent was decanted and the process repeated several times. The product was dried under vacuum at 70 °C.

1-(6-Hydroxyhexyl)-3-methylimidazolium chloride (**2a**). From 2 equiv. of RX. Viscous liquid (washed with diethyl ether). Yield 95%. ^{1}H NMR (CD_3OD): 1.32–1.53 (m, 6 H, $(CH_2)_3$); 1.86 (quint., 2 H, J = 7.04, CH_2); 3.50 (t, 2 H, J = 6.22, C**H**$_2$OH); 3.89 (s, 3 H, N-CH_3); 4.14 (t, 2 H, J = 6.27, CH_2-N_{ring}); 7.52 (s, 1 H, ring H_5); 7.59 (s, 1 H, ring H_4); 8.90 (s, 1 H, ring H_2). ^{13}C NMR (CD_3OD): 24.94 (CH_2); 25.64 (CH_2); 29.74 (CH_2); 31.93 (CH_2); 35.16 (N-CH_3); 49.37 (CH_2-N_{ring}); 61.42 (CH_2OH); 122.26 (ring C_5); 123.57 (ring C_4); 136.53 (ring C_2). HRMS (EI): calculated for $C_{10}H_{19}N_2O$ [M^+] 183.1497; found: 183.1494.

1-(5-Carboxypentyl)-3-methylimidazolium bromide (**2b**). From 1 equiv. of RX. Crystals, m.p. 103–105 °C [29] (washed with acetone). Yield 65%. IR (KBr disk): 1165, 1235, 1400, 1467, 1564, 1714, 2861, 2941, 3055, 3112, 3140, 3419. ^{1}H NMR (DMSO-d_6): 1.17 (m, 2 H, CH_2); 1.45 (quint., 2 H, J = 7.8, CH_2); 1.72 (quint., 2 H, J = 7.35, CH_2); 2.14 (t, 2 H, J = 7.15, CH_2); 3.79 (s, 3 H, N-CH_3); 4.09 (t, 2 H, J = 7.10, CH_2-N_{ring}); 7.67 (t, 1 H, J = 1.58, ring H_5); 7.73 (t, 1 H, J = 1.62, ring H_4); 9.14 (s, 1 H, ring H_2). ^{13}C NMR (DMSO-d_6): 24.21 (CH_2); 25.48 (CH_2); 29.58 (CH_2); 33.82 (CH_2); 36.25 (N-CH_3); 49.02 (CH_2-N_{ring}); 122.72 (ring C_5); 124.05 (ring C_4); 137.00 (ring C_2); 178.84 (C=O). HRMS (LSIMS, Cs^+): calculated for $C_{10}H_{17}N_2O_2$ [M^+] 197.1290; found: 197.1291.

1-(2-Carboxyethyl)-3-methylimidazolium bromide (**2c**). From 1 equiv. of RX. Viscous liquid (washed with acetone). Yield 85%. IR (film): 1168, 1405, 1576, 1725, 3087, 3399. ^{1}H NMR (DMSO-d_6): 2.77 (t, 2 H, J = 6.45, CH_2COOH); 3.79 (s, 3 H, N-CH_3); 4.28 (t, 2 H, J = 6.26, CH_2-N_{ring}); 7.65 (s, 1 H, ring H_5); 7.73 (s, 1 H, ring H_4); 9.15 (s, 1 H, ring H_2). ^{13}C NMR (DMSO-d_6): 34.85 (CH_2COOH); 36.21 (N-CH_3); 45.50 (CH_2-N_{ring}); 122.88 (ring C_5); 123.86 (ring Im C_4); 137.39 (ring C_2); 172.37 (C=O). HRMS (LSIMS, Cs^+): calculated for $C_7H_{11}N_2O_2$ [M^+] 155.0821; found: 155.0823.

1-{[(4-Bromophenyl)dimethylsilyl]methyl}-3-methylimidazolium chloride (**2f**). From 1 equiv. of RX. Sticky solid (washed with diethyl ether). Yield 84%. ^{1}H NMR (DMSO-d_6): 0.38 (s, 6 H, $Si(CH_3)_2$); 3.86 (s, 3 H, N-CH_3); 4.22 (s, 2 H, $SiCH_2$); 7.50–7.64 (m, 5 H, **H**$_{arom}$ + ring **H**$_5$); 7.74 (s, 1 H, ring H_4); 9.21 (s, 1 H, ring H_2). ^{13}C NMR (DMSO-d_6): –3.80 ($Si(CH_3)_2$); 36.59 (N-CH_3); 40.47 ($SiCH_2$); 123.83 (ring C_5); 124.43 (ring C_4); 125.06, 131.84, 134.69, 136.70 (C_{arom}); 136.90 (ring C_2). HRMS (LSIMS, Cs^+): calculated for $C_{13}H_{18}{}^{79}BrN_2Si$ [M^+] 309.0423; found: 309.0421.

1-(2-Aminoethyl)-3-methylimidazolium Bromide (**2d**)

1-(2-Aminoethyl)-3-methylimidazolium hydrobromide was prepared according to the general procedure from 1 equiv. of RX. The viscous liquid was washed with acetonitrile. To a stirred solution of crude hydrobromide in anhydrous MeOH (10 ml), Et_3N (2.47 g, 24.4 mmol) was added dropwise under nitrogen atmosphere and the mixture was stirred at room tempera-

ture for 2 h. The precipitate of $Et_3N{\cdot}HBr$ was filtered off and washed with MeOH (2 × 2 ml). The resulting solution was concentrated to dryness, CH_2Cl_2 (5 ml) was then added and stirred vigorously for 30 min. The solvent was decanted and the process repeated 5 times. The product was dried under vacuum at 70 °C to yield 1.12 g of pure sticky solid (yield 56%, based on 1-methylimidazole). IR (film): 1173, 1459, 1519, 1577, 2017, 2479, 3416. ^{1}H NMR (DMSO-d_6): 2.85 (m, 2 H, NH_2); 3.30 (t, 2 H, J = 5.71, C**H**$_2$NH$_2$); 3.80 (s, 3 H, N-CH_3); 4.42 (t, 2 H, J = 5.65, CH_2-N_{ring}); 7.71 (s, 1 H, ring H_5); 7.77 (s, 1 H, ring H_4); 9.17 (s, 1 H, ring H_2). ^{13}C NMR (DMSO-d_6): 36.32 (CH_2NH_2); 39.01 (N-CH_3); 46.75 (CH_2-N_{ring}); 122.92 (ring C_5); 124.28 (ring C_4); 137.81 (ring C_2). HRMS (LSIMS, Cs^+): calculated for $C_{12}H_{24}{}^{79}BrN_6$ [2 M^+, Br^-]$^+$ 331.1246; found: 331.1248.

1-(6-Aminohexyl)-3-methylimidazolium Iodide (**2e**)

To a solution of 1-methyl-3-(6-phthalimidohexyl)imidazolium iodide (**7**; 650 mg, 1.48 mmol) in ethanol (5 ml), hydrazine (107 µl, 2.22 mmol) was added dropwise. The mixture was stirred and refluxed for 15 h. Then, the cooled mixture was filtered and the filtrate concentrated under reduced pressure. The residue was washed twice with diethyl ether (10 ml) and dried under vacuum to give 343 mg of yellow oil. The product was sufficiently pure for further synthesis (yield 75%). ^{1}H NMR (DMSO-d_6): 1.22–1.33 (m, 6 H, (C**H**$_2$)$_3$$CH_2NH_2$); 1.77 (q, 2 H, J = 7.40, C**H**$_2$$CH_2$-$N_{ring}$); 2.53 (t, 2 H, J = 6.39, C**H**$_2$$NH_2$); 3.85 (s, 3 H, N-$CH_3$); 4.15 (t, 2 H, J = 7.15, CH_2-N_{ring}); 7.70 (s, 1 H, ring H_5); 7.77 (s, 1 H, ring H_4); 9.11 (s, 1 H, ring H_2). ^{13}C NMR (DMSO-d_6): 26.17 (CH_2); 26.45 (CH_2); 30.25 (CH_2); 31.99 (CH_2); 39.16 (N-CH_3); 41.49 (CH_2NH_2); 49.59 (CH_2-N_{ring}); 123.14 (ring C_5); 124.49 (ring C_4); 137.35 (ring C_2). HRMS (EI): calculated for $C_{10}H_{20}N_3$ [M^+] 182.1653; found: 182.1657.

1-(2-Aminoethyl)pyridinium Bromide (**2g**)

1-(2-Aminoethyl)pyridinium hydrobromide was prepared according to the general procedure from 3 equiv. of RX. White solid (washed with acetonitrile). Yield 90%. To a stirred suspension of the hydrobromide (2.02 g, 7.1 mmol) in anhydrous CH_3CN (15 ml), solid K_2CO_3 (2.94 g, 21.28 mmol) was added under nitrogen and the mixture stirred at room temperature for 24 h. The insoluble materials were removed by filtration and washed 2 × with CH_3CN (10 ml). The filtrates were concentrated to dryness to afford 0.43 g of **2g** as a viscous oil (yield 30%, based on the 2-bromoethylamine hydrobromide). The ionic liquid could be used with no further treatment. ^{1}H NMR (DMSO-d_6): 3.06 (t, 2 H, J = 5.59, C**H**$_2$$NH_2$); 3.64 (m, 2 H, CH_2N**H**$_2$); 4.61 (t, 2 H, J = 5.58, CH_2-N_{ring}); 8.18 (t, 2 H, J = 7.04, 2 H_{arom}); 8.63 (t, H, J = 7.78, H_{arom}); 9.09 (d, 2 H, J = 5.44, 2 H_{arom}). ^{13}C NMR (DMSO-d_6): 43.12 (CH_2NH_2); 63.97 (CH_2-N_{ring}); 128.37, 145.96, 146.11 (C_{arom}). HRMS (LSIMS, Cs^+): calculated for $C_7H_{11}N_2$ [M^+] 123.0922; found: 123.0925.

Synthesis of Tetrafluoroborates **3a**–**3d** and **3f**, **3g**. General Procedure

To a solution of ionic liquid **2a**–**2d**, **2f**, **2g** (1.80 mmol) in anhydrous acetonitrile (10 ml) ammonium tetrafluoroborate (0.47 g, 4.51 mmol) was added. The reaction mixture was heated under nitrogen atmosphere at 60 °C for 18 h. After filtration to remove the precipitated salts (NH_4X and the excess of NH_4BF_4), the solution was concentrated to dryness. The residue is dried in vacuum at 70 °C to give a viscous liquid, which could be used without further treatment.

1-(6-Hydroxyhexyl)-3-methylimidazolium tetrafluoroborate (**3a**). Yield 92%. ^{1}H NMR (DMSO-d_6): 1.21–1.34 (m, 6 H, $(CH_2)_3$); 1.71 (m, 2 H, CH_2); 3.30 (t, 2 H, J = 6.04, CH_2); 3.77 (s, 3 H, N-CH_3); 4.07 (t, 2 H, J = 7.16, CH_2-N_{ring}); 7.52 (s, 1 H, ring H_5); 7.70 (s,1 H, ring H_4); 9.00 (s, 1 H, ring H_2). ^{13}C NMR (CD_3OD): 25.73 (CH_2); 26.23 (CH_2); 30.28 (CH_2); 33.05 (CH_2); 36.55 (N-CH_3); 49.64 (CH_2-N_{ring}); 61.39 (CH_2OH); 123.08 (ring C_5); 124.43 (ring C_4); 137.29 (ring C_2). HRMS (EI): calculated for $C_{20}H_{38}{}^{11}BF_4N_4O_2$ [2 M^+, BF_4^-]$^+$ 453.3028; found: 453.3026.

1-(5-Carboxypentyl)-3-methylimidazolium tetrafluoroborate (**3b**). Yield 93%. IR (film): 1058, 1458, 1576, 1734, 2869, 2945, 3162, 3337, 3560. ^{1}H NMR (DMSO-d_6): 1.19 (m, 2 H, CH_2); 1.45 (quint., 2 H, J = 7.64, CH_2); 1.72 (quint., 2 H, J = 7.28, CH_2); 2.15 (t, 2 H, J = 7.15, CH_2); 3.77 (s, 3 H, N-CH_3); 4.08 (t, 2 H, J = 7.16, CH_2-N_{ring}); 7.60 (t, 1 H, J = 1.69, ring H_5); 7.67 (t, 1 H, J = 1.76, ring H_4); 8.99 (s, 1 H, ring H_2). ^{13}C NMR (DMSO-d_6): 24.19 (CH_2); 25.40 (CH_2); 29.53 (CH_2); 33.77 (CH_2); 36.16 (N-CH_3); 49.03 (CH_2-N_{ring}); 122.68 (ring C_5); 124.03 (ring C_4); 136.95 (ring C_2); 174.88 (C=O). HRMS (LSIMS, Cs^+): calculated for $C_{20}H_{34}{}^{11}BF_4N_4O_4$ [2 M^+, BF_4^-]$^+$ 481.2609; found: 481.2607.

1-(2-Carboxyethyl)-3-methylimidazolium tetrafluoroborate (**3c**). Yield 86%. IR (film): 1040, 1428, 1732, 3377, 3562. ^{1}H NMR (DMSO-d_6): 2.43 (s, 2 H, C**H**$_2$COOH); 3.77 (s, 3 H, N-CH_3); 4.27 (s, 2 H, CH_2-N_{ring}); 7.58 (s, 1 H, ring H_5); 7.67 (s, 1 H, ring H_4); 9.01 (s, 1 H, ring H_2). ^{13}C NMR (DMSO-d_6): 34.66 (CH_2COOH); 36.11 (N-CH_3); 45.45 (CH_2-N_{ring}); 122.85 (ring C_5); 123.83 (ring C_4); 137.34 (ring C_2); 172.42 (C=O). HRMS (LSIMS, Cs^+): calculated for $C_{14}H_{22}{}^{11}BF_4N_4O_4$ [2 M^+, BF_4^-]$^+$ 397.1670; found: 397.1673.

1-(2-Aminoethyl)-3-methylimidazolium tetrafluoroborate (**3d**). Yield 93%. IR (film): 1053, 1454, 1579, 2950, 3125, 3165, 3250, 3350, 3588. ^{1}H NMR (DMSO-d_6): 2.88 (m, 2 H, CH_2N**H**$_2$); 3.26 (t, 2 H, J = 5.79, C**H**$_2$$NH_2$); 3.79 (s, 3 H, N-$CH_3$); 4.33 (t, 2 H, J = 5.78, CH_2-N_{ring}); 7.65 (s, 1 H, ring H_5); 7.66 (s, 1 H, ring H_4); 8.97 (s, 1 H, ring H_2). ^{13}C NMR (DMSO-d_6): 36.18 (CH_2NH_2); 38.97 (N-CH_3); 46.88 (CH_2-N_{ring}); 122.93 (ring C_5); 124.28 (ring C_4); 137.74 (ring C_2). HRMS (EI): calculated for $C_{12}H_{24}{}^{11}BF_4N_6$ [2 M^+, BF_4^-]$^+$ 339.2092; found: 339.2096.

1-{[(4-Bromophenyl)dimethylsilyl]methyl}-3-methylimidazolium tetrafluoroborate (**3f**). Yield 95%. ^{1}H NMR (DMSO-d_6): 0.39 (s, 6 H, $Si(CH_3)_2$); 3.83 (s, 3 H, N-CH_3); 4.13 (s, 2 H, $SiCH_2$); 7.43–7.66 (m, 6 H, 4 H_{arom} + ring **H**$_5$, **H**$_4$); 8.83 (s, 1 H, ring H_2). ^{13}C NMR (DMSO-d_6): –3.94 ($Si(CH_3)_2$); 36.59 (N-CH_3); 40.58 ($SiCH_2$); 123.86 (ring C_5); 124.51 (ring C_4); 125.13, 131.89, 134.53 (C_{arom}); 136.51 (ring C_2); 136.80 (C_{arom}). HRMS (LSIMS, Cs^+): calculated for $C_{26}H_{36}{}^{11}B^{81}Br_2F_4N_4Si_2$ [2 M^+, BF_4^-]$^+$ 707.0861; found: 707.0851.

1-(2-Aminoethyl)pyridinium tetrafluoroborate (**3g**). Yield 75%. ^{1}H NMR (DMSO-d_6): 3.15 (t, 2 H, J = 5.62, C**H**$_2$$NH_2$); 3.45 (m, 2 H, CH_2N**H**$_2$); 4.60 (t, 2 H, J = 5.64, CH_2-N_{ring}); 8.17 (t, 2 H, J = 6.96, 2 H_{arom}); 8.62 (t, H, J = 7.81, H_{arom}); 8.99 (d, 2 H, J = 5.48, 2 H_{arom}). ^{13}C NMR (DMSO-d_6): 40.44 (CH_2NH_2); 61.27 (CH_2-N_{ring}); 126.60, 143.99, 144.38 (C_{arom}). HRMS (LSIMS, Cs^+): calculated for $C_{14}H_{22}BF_4N_4$ [2 M^+, BF_4^-]$^+$ 333.1876; found: 333.1878.

1-[(Biphenyl-4-yldimethylsilyl)methyl]-3-methylimidazolium Tetrafluoroborate (**15**)

The title compound was prepared according to the general procedure for the synthesis of tetrafluoroborates from **14**. Viscous liquid. Yield 90%. ^{1}H NMR (DMSO-d_6): 0.42 (s, 6 H, $Si(CH_3)_2$); 3.83 (s, 3 H, N-CH_3); 4.17 (s, 2 H, $SiCH_2$); 7.42–7.73 (m, 11 H, 9 H_{arom} + ring **H**$_5$, **H**$_4$); 8.90 (s, 1 H, ring H_2). ^{13}C NMR (DMSO-d_6): –4.28 ($Si(CH_3)_2$); 36.11 (N-CH_3); 40.99 ($SiCH_2$); 123.41, 123.99, 126.74, 127.17, 127.72, 129.48, 133.56, 134.90, 136.25, 139.58,

142.08 (C_{arom}). HRMS (LSIMS, Cs^+): calculated for $C_{38}H_{46}{}^{11}BF_4N_4Si_2$ [2 M^+, BF_4^-]$^+$ 701.3290; found: 701.3301.

1-{6-[*N*-(*tert*-Butyloxycarbonyl)-L-alanylamido]hexyl}-3-methylimidazolium Iodide (**8**)

To a solution of 1-(6-aminohexyl)-3-methylimidazolium iodide (**2e**; 200 mg, 0.65 mmol) in CH_3CN (2.5 ml) a solution of Boc-L-Ala (1.53 g, 8.08 mmol) and a solution of DIC (263 mg, 2.08 mmol) in CH_3CN (5 ml) were successively added. The mixture was stirred at room temperature for 16 h. A white precipitate of *N*,*N*′-diisopropylurea was formed. The mixture was filtered off and the filtrate concentrated under reduced pressure. The residue was washed twice with diethyl ether (20 ml) and dissolved in THF (20 ml). Then the precipitate formed was filtered off. This operation was repeated three times to ensure complete removal of *N*,*N*′-diisopropylurea. The filtrate was concentrated under reduced pressure to give 101 mg of yellow oil (yield 26%). ^{1}H NMR ($CDCl_3$): 1.33–1.53 (m, 18 H, (CH_2)$_3$$CH_2$NH, C($CH_3$)$_3$, $CHCH_3$); 1.94 (m, 2 H, CH_2CH_2-N_{ring}); 3.70 (m, 2 H, CH_2NH); 4.08 (s, 3 H, N-CH_3); 4.20 (m, 1 H, $CHCH_3$); 4.34 (t, 2 H, *J* = 7.04, CH_2-N_{ring}); 5.45 (d, 1 H, *J* = 7.48, NHBoc); 7.00 (m, 1 H, CH_2NHCO); 7.53 (s, 1 H, ring H_5); 7.59 (s, 1 H, ring H_4); 9.81 (s, 1 H, ring H_2). ^{13}C NMR ($CDCl_3$): 14.73 (CH_3CH); 20.95 (CH_2); 21.14 (CH_2); 24.16 (C(CH_3)$_3$); 24.55 (CH_2); 25.58 (CH_2); 32.98 (N-CH_3); 34.76 (CH_2NH); 45.93 (CH_2-N_{ring}); 46.57 ($CHCH_3$); 76.53 (C(CH_3)$_3$); 120.36 (ring C_5); 121.52 (ring C_4); 134.66 (ring C_2); 153.90 (NHCOO); 172.14 (NHCOCH). HRMS (EI): calculated for $C_{18}H_{33}N_4O_3$ [M^+] 353.2553; found: 353.2548. For $C_{18}H_{33}IN_4O_3$ (480.4) calculated: 45.00% C, 6.92% H, 11.66% N; found: 44.87% C, 7.19% H, 11.31% N.

1-[6-(L-Alaninamido)hexyl]-3-methylimidazolium Iodide (**9**)

Two-steps method. To a solution of 1-{6-[*N*-(*tert*-butyloxycarbonyl)-L-alanylamido]hexyl}-3-methylimidazolium iodide (**8**; 35 mg, 0.08 mmol) in dichloromethane (4 ml), a solution of trifluoroacetic acid (12 µl, 0.145 mmol) in the same solvent (1 ml) was added under stirring. The mixture was stirred at room temperature for 15 h. The solvent was removed under reduced pressure and the residue was dissolved in toluene (5 ml). Then the trifluoroacetic acid was co-evaporated with the solvent (5×). The yellow oil was washed 3 × with diethyl ether (10 ml), dissolved in THF (10 ml), and the precipitate formed was filtered off. The filtrate was concentrated under reduced pressure to give 20 mg of **9** as colorless oil (yield 70%). ^{1}H NMR (D_2O): 1.18–1.34 (m, 4 H, (CH_2)$_2$); 1.45 (m, 5 H, CH_3CH + CH_2); 1.80 (q, 2 H, *J* = 7.15, CH_2 CH_2-N_{ring}); 3.15 (q, 2 H, *J* = 6.73, CH_2NHCO); 3.82 (s, 3 H, N-CH_3); 3.91 (q, 1 H, J_1 = 7.05, J_2 = 14.30, $CHCH_3$); 4.12 (t, 2 H, *J* = 7.16, CH_2-N_{ring}); 7.35 (s, 1 H, ring H_5); 7.40 (s, 1 H, ring H_4); 8.63 (1, s, ring H_2). ^{13}C NMR (D_2O): 16.68 ($CHCH_3$); 24.99 (CH_2); 25.38 (CH_2); 27.98 (CH_2); 29.12 (CH_2); 35.72 (N-CH_3); 39.35 (CH_2NH); 49.16 (CH_2-N_{ring}); 49.50 ($CHCH_3$); 122.22 (ring C_5); 123.55 (ring C_4); 135.81 (ring C_2); 170.47 (CONH). HRMS (EI): calculated for $C_{13}H_{25}N_4NaO$ [M^+] 253.20284; found: 253.2023.

One-step method. Direct synthesis of **9**. To a solution of 1-(6-aminohexyl)-3-methylimidazolium iodide (**2e**; 100 mg, 0.32 mmol) in CH_3CN (3 ml), a solution of Boc-L-Ala (67 mg, 0.35 mmol) and a solution of DIC (53 mg, 0.42 mmol) in CH_3CN (1 ml) were successively added. The mixture was stirred at room temperature for 16 h. A white precipitate of *N*,*N*′-diisopropylurea was formed (an aliquot of the mixture was analyzed by ^{1}H NMR; the conversion was 96%). The mixture was filtered off and the filtrate was added dropwise to diethyl ether (40 ml). The product and the residual *N*,*N*′-diisopropylurea were precipitated as orange oil. This mixture was directly introduced into the next reaction. To a solution of the

residue (109 mg) in dichloromethane (2 ml), trifluoroacetic acid (64 μl, 0.56 mmol) was added dropwise under stirring. The mixture was stirred at room temperature for 15 h. The solvent was removed under reduced pressure and the residue was dissolved in toluene (5 ml). Then trifluoroacetic acid was co-evaporated with the solvent (5×). The yellow oil was washed 3 × with diethyl ether (5 ml) to give 70 mg of **9** as a colorless oil. Total yield of **9** was 67%.

1-[6-(6-{[(Fluoren-9-ylmethoxy)carbonyl]amino}hexanoylamino)hexyl]-3-methylimidazolium Iodide (**10**)

To a solution of 1-(6-aminohexyl)-3-methylimidazolium iodide (**2e**; 400 mg, 1.29 mmol) in CH_3CN (2 ml) a solution of Fmoc-6-aminohexanoic acid (Fmoc-Ahx; 500 mg, 1.42 mmol) in CH_3CN (2.5 ml) and DMF (0.5 ml), and a solution of DIC (210 mg, 1.67 mmol) in CH_3CN (5 ml) were successively added. The mixture was stirred at room temperature for 16 h and then a white precipitate of *N*,*N*′-diisopropylurea was formed. The mixture was filtered off and the filtrate concentrated under reduced pressure. The residue was washed 6 × with diethyl ether (10 ml), dissolved in dichloromethane (1 ml) and then the solution was cooled in an ice-bath to –5 °C. The solid formed was filtered off, washed with pentane and vacuum-dried to give 480 mg of white powder (yield 58%). ^{1}H NMR (CD_2Cl_2): 1.25–1.68 (m, 12 H, 2 $(CH_2)_3$); 1.95 (q, 2 H, *J* = 6.97, C**H**$_2$CH$_2$-N$_{ring}$); 2.24 (t, 2 H, *J* = 7.33, NHCOC**H**$_2$); 3.13–3.23 (m, 4 H, C**H**$_2$NHCOCH$_2$ + C**H**$_2$NHCOO); 4.01 (s, 3 H, N-CH$_3$); 4.23–4.34 (m, 5 H, CH$_2$O + C**H**CH$_2$O + CH$_2$-N$_{ring}$); 5.45 (t, 1 H, NHCOO); 6.66 (t, 1 H, N**H**COCH$_2$); 7.30–7.46 (m, 6 H, 4 CH(F_{moc})) + ring **H**$_5$, **H**$_4$); 7.66 (d, 2 H, *J* = 3.58, 2 CH(F_{moc})); 7.80 (d, 2 H, *J* = 3.76, 2 CH(F_{moc})); 9.87 (s, 1 H, ring H$_2$). ^{13}C NMR (CD_2Cl_2): 25.25 (CH_2); 25.34 (CH_2); 25.82 (CH_2); 26.17 (CH_2); 28.93 (CH_2); 29.50 (CH_2); 29.65 (CH_2); 36.30 (CH_2); 36.71 (N-CH$_3$); 38.65 (C**H**$_2$NHCOO); 40.71 (C**H**$_2$NHCOCH$_2$); 47.27 (OCH$_2$C**H**(F_{moc})); 49.76 (CH$_2$-N$_{ring}$); 66.35 (OC**H**$_2$CH(F_{moc})); 119.89 (CH(F_{moc})); 122.29 (ring C$_5$); 123.33 (ring C$_4$); 125.21, 127.05, 127.63 (CH(F_{moc})); 136.80 (ring C$_2$); 141.20, 144.15 (CH(F_{moc})); 156.37 (NHCOO); 173.08 (NH**C**OCH$_2$). For $C_{31}H_{41}IN_4O_3$ (643.6) calculated: 57.76% C, 6.41% H, 8.69% N; found: 57.96% C, 6.96% H, 8.90% N.

1-[6-(6-Aminohexanoylamino)hexyl]-3-methylimidazolium Iodide (**11**)

To a solution of 1-[6-(6-{[(Fluoren-9-ylmethoxy)carbonyl]amino}hexanoylamino)hexyl]-3-methylimidazolium iodide (**10**; 100 mg, 0.155 mmol) in CH_3CN (5 ml), piperidine (38 μl, 0.39 mmol) was added dropwise. The mixture was stirred at room temperature for 24 h and then the white precipitate formed was filtered off. The filtrate was concentrated under reduced pressure to give 50 mg of a white solid. The product obtained was washed 3 × with diethyl ether (yield 76%). ^{1}H NMR (D_2O): 1.12–1.56 (m, 12 H, 2 $(CH_2)_3$); 1.77 (t, 3 H, *J* = 7.09, C**H**$_2$CH$_2$-N$_{ring}$); 2.14 (t, 2 H, *J* =7.35, NHCOC**H**$_2$); 2.57 (t, 2 H, *J* = 7.16, C**H**$_2$NH$_2$); 3.06 (t, 2 H, *J* = 6.78, C**H**$_2$NHCO); 3.79 (s, 3 H, N-CH$_3$); 4.09 (t, 2 H, *J* = 7.15, CH$_2$-N$_{ring}$); 7.33 (s, 1 H, ring H$_5$); 7.37 (s, 1 H, ring H$_4$); 9.11 (s, 1 H, ring H$_2$). ^{13}C NMR (D_2O): 25.00 (CH_2); 25.26 (CH_2); 25.42 (CH_2); 25.51 (CH_2); 28.10 (CH_2); 29.16 (CH_2); 35.70 (CH_2); 35.79 (N-CH$_3$ + NHCOC**H**$_2$); 39.05 (CH_2NH_2); 40.28 (CH_2NH); 49.50 (CH$_2$-N$_{ring}$); 122.20 (ring C$_5$); 123.52 (ring C$_4$); 140.83 (ring C$_2$); 176.80 (NHCO). HRMS (EI): calculated for $C_{16}H_{31}N_4O$ [M^+] 295.2498; found: 295.2495. For $C_{16}H_{31}IN_4O$ (422.4) calculated: 45.50% C, 7.40% H, 13.27% N; found: 46.17% C, 7.35% H, 10.55% N.

Synthesis of 4-[(Chloromethyl)dimethylsilyl]biphenyl (**13**) by Suzuki Coupling of 1-Bromo-4-[(chloromethyl)dimethylsilyl]benzene (**12**)

A stirred mixture of **12** (0.97 g, 3.68 mmol), phenylboronic acid (1.35 g, 11.04 mmol), and 0.23 g (5 mole %) of $[Pd(PPh_3)_4]$ and 15 ml DMF/Et_3N (1:1) was heated at 90 °C overnight under nitrogen atmosphere. The mixture was cooled to room temperature and the solvents were distilled off under reduced pressure. The residue was partitioned between diethyl ether and brine. The organic extracts were dried with anhydrous $MgSO_4$ and concentrated under reduced pressure. Purification of the crude product by column chromatography on silica gel with heptane as eluent afforded 0.58 g of pure crystalline **13** (yield 60%). ^{1}H NMR (DMSO-d_6): 0.43 (s, 6 H, $Si(CH_3)_2$); 3.18 (s, 2 H, $SiCH_2$); 7.50–7.71 (m, 9 H, H_{arom}). ^{13}C NMR (DMSO-d_6): –4.10 ($Si(CH_3)_2$); 30.62 ($SiCH_2$); 126.55, 127.14, 128.07, 129.36, 134.84, 135.08, 140.34, 141.75 (C_{arom}). HRMS (EI): calculated for $C_{15}H_{17}{}^{35}ClSi$ [M^+] 260.0788; found: 260.0774.

1-[(Biphenyl-4-yldimethylsilyl)methyl]-3-methylimidazolium Chloride (**14**)

The title compound was prepared according to the general procedure from 1-methylimidazole (0.11 g, 1.34 mmol) and **13** (0.35 g, 1.34 mmol). Viscous liquid. Yield 80%. ^{1}H NMR (DMSO-d_6): 0.40 (s, 6 H, $Si(CH_3)_2$); 3.83 (s, 3 H, N-CH_3); 4.18 (s, 2 H, $SiCH_2$); 7.42–7.69 (m, 11 H, 9 H_{arom} + ring $\mathbf{H}_5$, $\mathbf{H}_4$); 9.02 (s, 1 H, ring H_2). ^{13}C NMR (DMSO-d_6): –4.15 ($Si(CH_3)_2$); 36.15 (N-CH_3); 41.15 ($SiCH_2$); 123.42, 124.00, 126.73, 127.18, 128.26, 129.45, 133.66, 134.95, 136.22, 140,15, 142.06 (C_{arom}). HRMS (EI): calculated for $C_{19}H_{23}N_2Si$ [M^+] 307.1631; found: 307.1637.

Cleavage with Bromine: Synthesis of 1,4-Dibromobenzene (**16**)

To a solution of **3f** (270 mg, 0.68 mmol) in CH_2Cl_2 (15 ml) at 0 °C 3.0 equiv. of pyridine (0.16 ml, 2.04 mmol) and 6.0 equiv. of Br_2 were added. The mixture was stirred at 0 °C for 2 h and then the cleavage solution was removed by rotary evaporation. The brown crude reaction mixture was diluted with diethyl ether and the organic layer was washed with brine, dried, concentrated and then taken up in hexane. The bright-red color of bromine oil was removed by filtration and the organic layer was concentrated to give 30 mg (30%) of the desired product as white crystals. The final product **16** has been detected and characterized by comparison with an authentic sample of 1,4-dibromobenzene (Acros). ^{1}H NMR (DMSO-d_6): 7.55 (s, 4 H, H_{arom}). ^{13}C NMR (DMSO-d_6): 121.57, 134.29 (C_{arom}).

Cleavage with Bromine: Synthesis of 4-Bromobiphenyl (**17**)

A stirred mixture of **3f** (0.5 g, 1.25 mmol), phenylboronic acid (0.23 g, 1.87 mmol) and 0.047 g (3 mole %) of $[Pd(PPh_3)_4]$ and 2 ml DMF/Et_3N (1:1) was heated at 90 °C overnight under nitrogen. The mixture was cooled to room temperature, the solvents were distilled off under reduced pressure, and the residue was then subjected to electrophilic cleavage. To a solution of the crude **15** in CH_2Cl_2 (15 ml) at 0 °C 3.0 equiv. of pyridine (0.30 ml, 3.75 mmol) and 6.0 equiv. of Br_2 (0.38 ml, 7.49 mmol) were added. The mixture was stirred at 0 °C for 2 h and then the cleavage solution was removed by rotary evaporation. The brown crude residue was partitioned between diethyl ether and brine. The organic extracts were dried with anhydrous $MgSO_4$ and concentrated under reduced pressure. Purification by

column chromatography on silica gel with ethtyl acetate/heptane (1:9) as eluent afforded 160 mg of pure 4-bromobiphenyl (**17**; yield 55%). ^{1}H NMR (DMSO-d_6): 7.40–7.70 (m, 9 H, H_{arom}). ^{13}C NMR (DMSO-d_6): 127.47, 127.56, 128.74, 129.68, 129.94, 132.69, 134.31, 140.21 (C_{arom}). HRMS (EI): calculated for $C_{12}H_9{}^{79}Br$ [M^+] 231.9888; found: 231.9893.

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