

Synthesis of some new 2-heterosubstituted 4,5-dihydroimidazoles

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Dedicated to Professor Charles Rees on his 75th birthday

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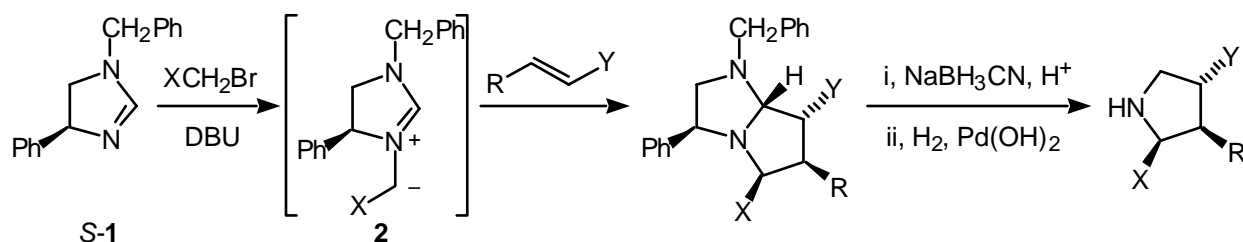
Abstract

Several new 4,5-dihydroimidazoles (and the corresponding imidazolium salts) carrying heteroatom substituents at C-2 have been prepared from the corresponding tetrahydroimidazol-2-ones and/or -thiones.

Keywords: 4,5-Dihydroimidazole, imidazolium salt, imidazoline

Introduction

As part of a programme to prepare optically active nitrogen heterocycles,¹ we have reported on the use of 4,5-dihydroimidazolium ylides **2**, available from the 4,5-dihydroimidazoles (2-imidazolines) **1**, in the assembly of pyrrolo[1,2-*a*]imidazoles (Scheme 1).² Reductive removal of the templating atoms affords pyrrolidines.³

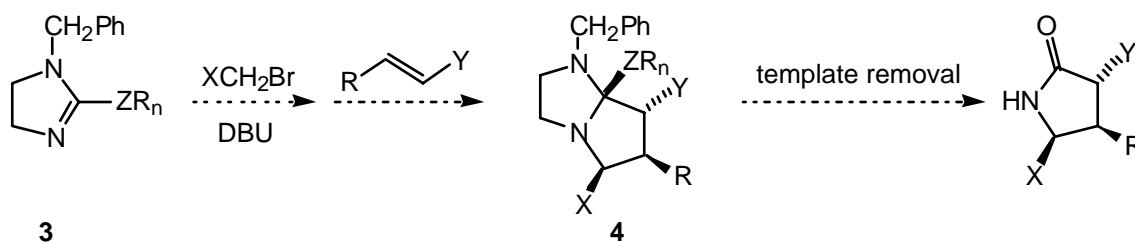


Scheme 1. Synthesis of optically active pyrrolidines from 4,5-dihydroimidazolium ylides.

We proposed to extend this strategy to 2-heteroatom substituted 4,5-dihydroimidazoles **3** and their quaternary salts with the expectation that the corresponding cycloadducts **4** could lead to pyrrolidones on template removal (Scheme 2). Although this strategy was ultimately not fruitful,

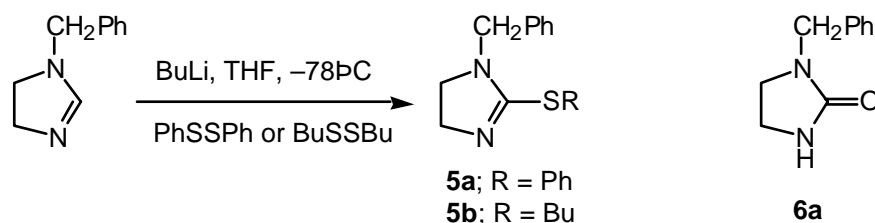
we report here the preparation of new 2-thioalkyl, 2-alkoxy and 2-alkylamino 4,5-dihydroimidazoles **3** and of the corresponding N-alkyl-4,5-dihydroimidazolium salts.

Our first approach was to employ the chemistry of 1-benzyl-2-lithio-4,5-dihydroimidazole that we have reported,⁴ to generate 2-alkylthio or 2-arylthio derivatives.



Scheme 2. Proposed synthesis of pyrrolidones ($ZR_n = OR, SR, NR_2$).

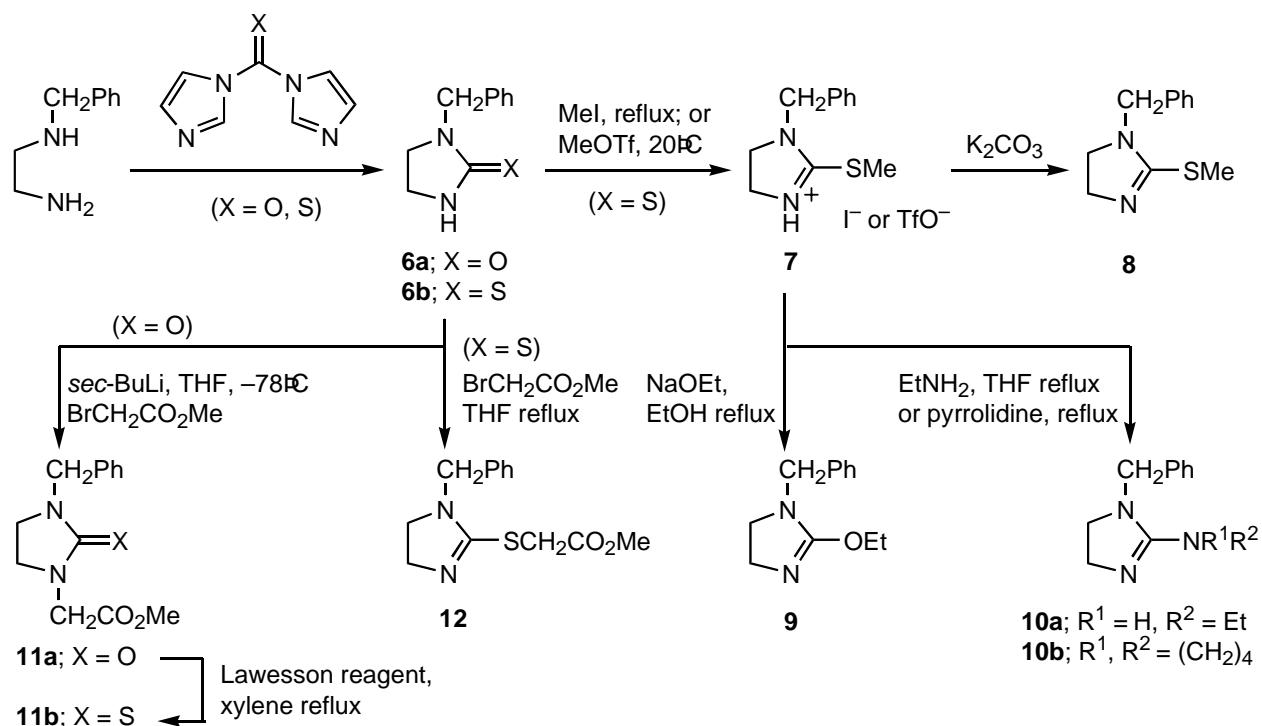
The sulfur substituent could also act as a leaving group to access O- and N-substituted compounds. When 1-benzyl-4,5-dihydroimidazole⁵ was deprotonated (BuLi, THF, -78°C) and reacted with diphenyl or dibutyl disulfides, the sulfur-substituted dihydroimidazoles **5a,b** were isolated (Scheme 3), however the major product (40%) was 1-benzyl-tetrahydroimidazol-2-one **6a**, arising presumably from adventitious hydrolysis during isolation.



Scheme 3

This prompted us to explore an alternative approach to **3** via this cyclic urea **6a** and sulfur analogue **6b**, which were readily available in good yield by reaction of N-benzyl-1,2-diaminoethane with 1,1'-carbonyldiimidazole and 1,1'-thiocarbonyldiimidazole, respectively (Scheme 4). Attempts to O-alkylate urea **6a** using Meerwein's salts or methyl trifluoromethanesulfonate (MeOTf) were unproductive in our hands. In contrast, thiourea **6b** was readily methylated on sulfur (MeI, heat; or MeOTf, 20°C) to provide the salt **7** that was neutralised (solid K_2CO_3) to give to the first of the targets **3**, the 2-methylthio compound **8** (86%). Salt **7** also proved useful in preparation of other 2-heteroatom substituted 4,5-dihydroimidazoles. Thus treatment with sodium ethoxide (EtOH reflux, 24h) afforded the 2-ethoxy derivative **9** (66%). The 2-amino compounds **10a,b** were prepared using ethylamine (THF reflux, 20h; 75%) and pyrrolidine (reflux, 20h; 47%), respectively; no reaction was observed with the bulky *tert*-butylamine or the aromatic amine aniline.

Having a secure access to 2-heteroatom-substituted 4,5-dihydroimidazoles, we next targeted the corresponding 1-benzyl-3-alkoxycarbonylmethyl-4,5-dihydroimidazolium salts as direct precursors to 4,5-dihydroimidazolium ylides. Disappointingly, heating 2-methylthio compound **8** with methyl bromoacetate (THF reflux, 5h) gave no reaction, and attempted alkylations with iodoacetonitrile or ethyl methanesulfonyloxyacetate were also fruitless. The 2-ethoxy **9** and 2-amino-4,5-dihydroimidazoles **10** behaved similarly. We therefore decided to reverse the sequence of incorporation of C-2 and C-3 substituents. The cyclic urea **6a** was converted into the N-methoxycarbonylmethyl compound **11a** by deprotonation with *sec*-BuLi (THF, -78°C) and reaction with methyl bromoacetate (THF reflux, 24h; 41%) (Scheme 4); other bases proved less effective. Neither this method, nor Mitsunobu conditions using ethyl glycolates, were successful in the analogous reactions of thiourea **6b**, and direct treatment of **6b** with methyl bromoacetate (THF reflux, 18h) afforded the S-alkylation product **12** (87%). The N-alkylated thiourea **11b** was however accessed by thionation of urea **11a** with Lawesson's reagent (*o*-xylene reflux, 26h; 66%).⁶



Scheme 4

In order to generate 4,5-dihydroimidazolium ylides from urea **11a** and thiourea **11b**, O- or S-alkylation, respectively, was required. S-Methylation of **11b** was accomplished with MeOTf to afford a salt **13** which displayed the expected NMR spectral characteristics but was not completely characterised. NMR spectroscopic evidence was likewise obtained for salts **14a-c** prepared in an NMR tube from urea **11a** using triethyloxonium tetrafluoroborate,

trifluoromethanesulfonic anhydride and *tert*-butyl-dimethylsilyl trifluoromethanesulfonate, respectively. Downfield shifts of product peaks were observed relative to the urea, although these putative salts proved too hygroscopic for further analysis. In any event, one-pot attempts by our usual protocol⁵ to induce formation of salts **13** or **14**, deprotonation to an ylide and cycloaddition were unsuccessful. The major isolated product in each case was urea **11a**, presumably from quaternary salt hydrolysis.

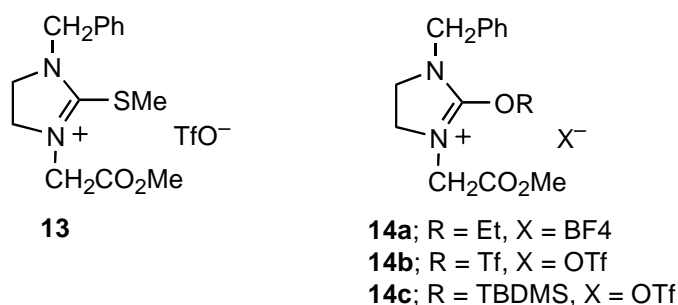
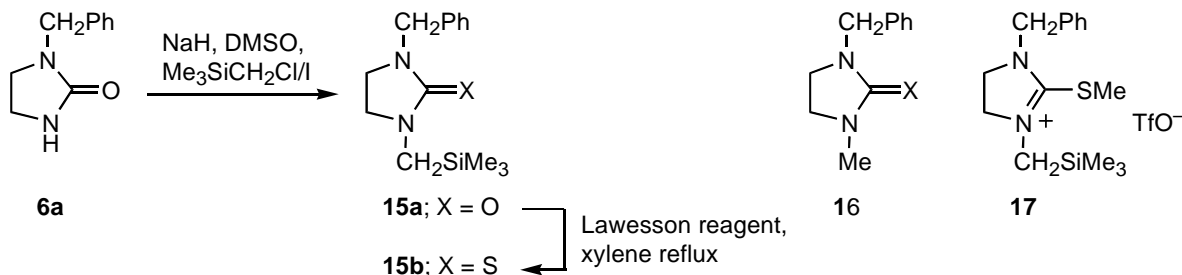


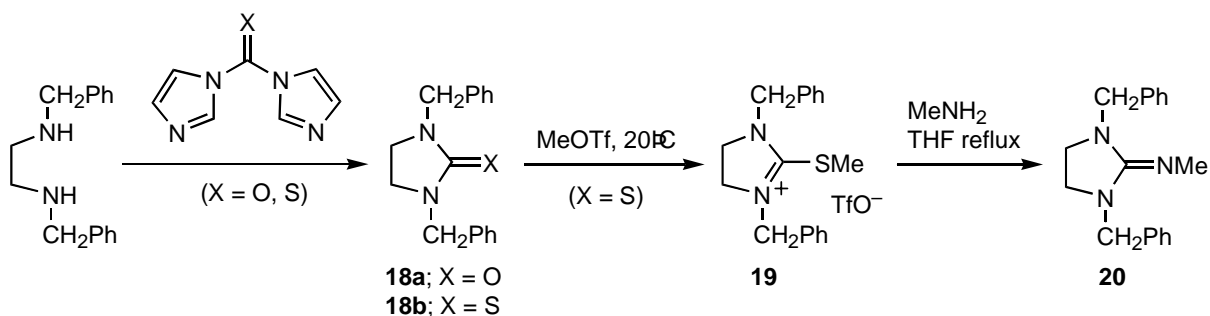
Figure 1. 4,5-Dihydroimidazolium salts observed spectroscopically.

We prepared two alternative series of 1,3-disubstituted tetrahydroimidazolin-2-ones and 2-thiones as potential ylide precursors. In the first of these, cyclic urea **6a** was N-silylmethylated to give **15a** (NaH, DMSO, Me₃SiCH₂Cl or Me₃SiCH₂I; 45%) (Scheme 5), with a view ultimately to ylide generation by desilylation.⁷ 1-Benzyl-3-methyltetrahydroimidazol-2-one **16** was isolated as a by-product (27%). The thiourea **15b** was prepared from **15a** by thionation (Lawesson's reagent, *o*-xylene reflux; 69%). As above, O-alkylation of **15a** was attempted (NMR tube) with MeOTf or triethyloxonium tetrafluoroborate but proceeded only to partial conversion after several hours. Attempted one-pot alkylation, desilylation (CsF) and cycloaddition was unsurprisingly unsuccessful with **15a**. With **15b**, although salt **17** could be observed (NMR) using MeOTf as alkylating agent, the one-pot protocol returned unchanged thiourea **15b** and urea **15a**, representing presumably incomplete S-alkylation and hydrolysis of S-alkyl salt **17**.



Scheme 5

The second alternative series of (thio)ureas comprised the 1,3-dibenzyl compounds **18a,b**, readily available from commercial *N,N'*-dibenzyl-1,2-diaminoethane and carbonyl or thiocarbonyldiimidazole, respectively (**18a** 97%; **18b** 98%) (Scheme 6). *S*-Methylation of **18b** (MeOTf, CH₂Cl₂, 20°C) afforded salt **19** in quantitative yield. This salt provided access to 2-imino compound **20** (MeNH₂, THF reflux 18h; 40%). The salt **21** was observed spectroscopically from **19** and pyrrolidine, as were salts **22a-c** from reaction of urea **18a** with trifluoromethanesulfonic anhydride, trimethylsilyl trifluoromethane-sulfonate or *tert*-butyldimethylsilyl trifluoromethanesulfonate, respectively. To test for benzylic deprotonation in this series, (thio)ureas **18a,b** were treated with base (*sec*-BuLi, THF, -78°C) and quenched with CF₃CO₂D, when clean mono-deuteration was observed (PhCH₂ signal, 4H at δ 4.41 and 4.92 respectively, converted to two singlets 0.03 ppm apart, integrating as 2H and 1H). Similar treatment of the salt **22c** afforded mono-deuteration. However, when the salts **19**, **21** and **22a-c** were subjected to the one-pot deprotonation-cycloaddition protocol⁵ with methylacrylate, no cycloadducts were observed.



Scheme 6

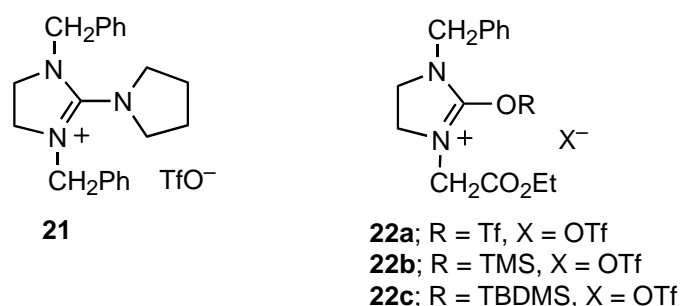


Figure 2. 4,5-Dihydroimidazolium salts observed spectroscopically.

These studies, whilst not to date affording 1,3-dipolar cycloaddition, have generated some new 2-heteroatom substituted 4,5-dihydroimidazoles **3** via cyclic ureas, and explored generation of the corresponding imidazolium salts.

Experimental Section

General Procedures. Proton (^1H) and carbon (^{13}C) NMR spectra were recorded in CDCl_3 using either a JEOL EX400 (400 and 100MHz, respectively) or a JEOL LA300 spectrometer (300 and 75MHz, respectively). Chemical shifts are reported in parts per million (ppm) from tetramethylsilane (TMS) as the internal standard. Multiplicities are given as: s-singlet, d-doublet, t-triplet, q-quartet, quin-quintet, sext-sextet, m-multiplet, br-broad signal. Coupling constants (J) are expressed in Hz. Infrared spectra were recorded using a Perkin-Elmer 1710 Fourier Transform infrared spectrophotometer. Low resolution mass spectra were recorded using a VG Micromass VG-250 mass spectrometer by electron impact (EI), chemical ionisation (CI) or fast atom bombardment (FAB) methods, the latter employing a thioglycerol matrix in both positive and negative ion modes. Accurate mass measurements were performed by the EPSRC National Mass Spectrometry Service (University of Wales, Swansea, UK). Elemental analyses were performed by MEDAC Ltd, Brunel Science Centre, Surrey, TW20 0JZ, UK. X-Ray crystallography was performed by the EPSRC X-Ray Crystallographic Service (University of Southampton, UK). Optical rotations were measured on a JASCO DIP-1000 digital polarimeter. Melting points were measured on a Kofler hot-stage apparatus and are uncorrected. Column chromatography was carried out using Fluka Silica Gel 60 (220-440mesh) (Brockmann 2-3). TLC analysis was carried out using Machery-Nagel Polygram SIL G/UV₂₅₄ plates on a plastic backing and visualised by ultraviolet light or aqueous potassium permanganate spray ($\text{KMnO}_4:\text{K}_2\text{CO}_3:\text{water}$, 6:1:100, w/w/v).

All chemicals were purified by distillation or recrystallisation where appropriate. THF, THP, diethyl ether, toluene, ethanol and glyme were dried over sodium or potassium and distilled. DCM and DMSO were dried over sodium or calcium hydride and distilled. Anhydrous reactions were carried out using flamed dried glassware with all transfers performed using oven-dried syringes and needles.

1-Benzyltetrahydroimidazol-2-one (6a). To *N*-benzyl-1,2-diaminoethane (5.00 g; 33.0 mmol) in dry THF (200 ml) under nitrogen was added a solution of 1,1'-carbonyldiimidazole (6.48 g; 40.0 mmol) in dry THF (25 ml). The resulting solution was stirred at RT for 18 h. The solvent was removed under reduced pressure and the mixture was washed with dilute hydrochloric acid (2M; 50 ml) and extracted with dichloromethane (2×50 ml). The combined organic phases were dried (MgSO_4) and the solvent removed under reduced pressure to afford the title compound **6a** as a white crystalline solid (5.79 g; 99%); m.p. 124-127°C (lit.,⁸ 127°C) (Found: (EI): M^+ 176.0941; $\text{C}_{10}\text{H}_{12}\text{N}_2\text{O}$ requires M^+ 176.0949); ν_{max} (nujol)/ cm^{-1} 1601, 1496, 1467, 1301 and 1116; δ_{H} (400 MHz) 3.38 and 3.42 (each m, 2H, $\text{NCH}_2\text{CH}_2\text{N}$), 4.40 (s, 2H, CH_2Ph), 7.29 (m, 5H, Ar-H); δ_{C} (100 MHz) 38.2 (CH_2Ph) 44.5 and 47.7 (CH_2N), 127.5, 128.1 and 128.6 (Ar-CH) 136.9 (Ar-C), 162.8 (CO); m/z (EI) 176 (M^+ , 100%), 161 (2), 147 (35), 132 (7), 104 (43), 99 (28), 91 (91), 85 (27), 77(9), 65 (21), 56 (8).

1-Benzyltetrahydroimidazol-2-thione (6b). Prepared according to the method used to synthesize **6a**, using N-benzyl-1,2-diaminoethane (0.50 g; 3.30 mmol) in dry THF (33 ml) and 1,1'-thiocarbonyl-diimidazole (0.71 g; 3.99 mmol) in dry THF (5 ml) to afford the title compound **6b** as a white crystalline solid (0.60 g; 94%): m.p. 181-182°C (lit.,⁹ 177-182°C) (Found: (FAB): $M^{•+}$ 192.0711; $C_{10}H_{12}N_2S$ requires $M^{•+}$ 192.0721); ν_{\max} (nujol)/ cm^{-1} 3401, 2924, 1556, 1377, and 722; δ_H (400 MHz) 3.60 (s, 4H, NCH_2CH_2N) 4.84 (s, 2H, CH_2Ph), 7.38 (m, 5H, Ar-H); δ_C (100 MHz) 41.3 (CH_2Ph) 48.0 and 51.0 (CH_2N), 127.8, 128.2 and 128.7 (Ar-CH), 135.1 (Ar-C), 183.2 (CS); m/z (EI) 192 ($M^{•+}$, 55%), 176 (2), 131 (10), 104 (20), 91 (100), 89 (7), 77 (13), 68 (37), 65 (32), 56 (12).

1-Benzyl-2-methylthio-4,5-dihydroimidazole (8). Iodomethane (32.0 ml; 50.0 mmol) was added to 1-benzyltetrahydroimidazol-2-thione **6b** (2.03 g; 10 mmol) and the mixture heated at reflux for 16 h under nitrogen. After allowing the mixture to cool to RT the excess MeI was removed under reduced pressure and the residue evaporated twice from dry methanol (2×10 ml) to afford the imidazolium salt **7** as a yellow solid (1.89 g, 87%): m.p. 102-105°C; δ_H (400 MHz) 2.68 (s, 3H, SCH_3), 4.04 and 4.10 (each t, 2H, $J = 9.2$, NCH_2CH_2N), 4.60 (s, 2H, CH_2Ph), 7.33 (m, 5H, Ar-H); δ_C (100 MHz) 16.2 (SCH_3), 51.9 (CH_2Ph), 53.3 and 53.8 (CH_2N), 127.6, 128.3 and 128.7 (Ar-CH), 137.4 (Ar-C), 164.1 (NCS). The salt **7** (1.88 g; 5.6 mmol) in dichloromethane (50 ml) was treated with excess K_2CO_3 (7.7 g) and the resulting solution stirred at RT for 1 h. The solution was filtered, extracted with dichloromethane (2×50 ml) and the combined organic phases dried ($MgSO_4$). The solvent was removed under reduced pressure to afford the *title compound* **8** as a yellow solid (1.61 g, 86%) (Found: (FAB): $M^{•+}$ 206.0875; $C_{11}H_{14}N_2S$ requires $M^{•+}$ 206.0877): m.p. 95-98°C; ν_{\max} (nujol)/ cm^{-1} 3128, 1587, 1563, 1497, 738 and 723; δ_H (400 MHz) 2.68 (s, 3H, SCH_3), 3.83 and 3.98 (each t, 2H, $J = 9.2$, NCH_2CH_2N), 4.37 (s, 2H, CH_2Ph), 7.28 (m, 5H, Ar-H); δ_C (100 MHz) 14.6 (SCH_3), 50.89 (CH_2Ph), 51.28 and 51.42 (CH_2N), 127.8, 128.2 and 128.8 (Ar-CH), 136.2 (Ar-C), 163.8 (NCS); m/z (EI) 206 ($M^{•+}$, 10%), 191 (17), 116 (5), 91 (34), 28 (100).

1-Benzyl-2-ethoxy-4,5-dihydroimidazole (9). A freshly prepared solution of NaOEt (0.38 g; 5.7 mmol) in EtOH (20 ml) was added to 1-benzyl-2-methylthio-4,5-dihydroimidazolium iodide **7** (0.46 g; 2.3 mmol) and the resulting solution heated at reflux for 24 h. Water (10 ml) was added and the solution extracted with dichloromethane (2×50 ml). The combined organic phases were dried ($MgSO_4$), filtered and evaporated under reduced pressure to afford the *title compound* **9** as a white solid (0.30 g; 66%): m.p. 162-165°C (Found: (FAB): $M^{•+}$ 204.1264; $C_{12}H_{16}N_2O$ requires $M^{•+}$ 204.1262); δ_H (400 MHz) 1.20 (t, 3H, $J = 5.2$, OCH_2CH_3) 3.15 and 3.32 (each t, 2H, $J = 6.6$, NCH_2CH_2N), 4.14 (s, 2H, CH_2Ph), 4.19 (q, 2H, $J = 5.2$, OCH_2CH_3), 7.14 (m, 5H, Ar-H); δ_C (100 MHz) 14.62 (CH_3), 38.02 (CH_2Ph), 48.32 and 49.75 (CH_2N), 65.11 (OCH_2), 127.3, 128.1 and 128.6 (Ar-CH), 137.6 (Ar-C), 164.0 (NCO); m/z (EI) 204 ($M^{•+}$, 18%), 176 (71), 159 (4), 91 (100), 77 (5), 85 (24), 65 (19), 56 (11).

1-Benzyl-2-ethylamino-4,5-dihydroimidazole (10a). Ethylamine in THF (2M; 1.57 ml, 3.15 mmol) was added to 1-benzyl-2-methylthio-4,5-dihydroimidazolium iodide **7** (0.45 g, 2.1 mmol) in dry THF (20 ml) heated at reflux, and the resulting solution heated at reflux for a

further 20 h. The cooled solution was washed with aq. NaOH (0.1 M; 50 ml) and extracted with diethyl ether (2 × 50 ml). The organic phase was dried (MgSO₄), filtered and the remaining solvent evaporated under reduced pressure. The residue was then purified by silica gel column chromatography using 2-propylamine/chloroform (1:99 v/v) as eluant to yield the *title compound 10a* as a yellow gum (0.40 g, 75%) (Found: (EI) MH⁺ 204.1425; C₁₂H₁₇N₃ requires MH⁺ 204.1422): $\nu_{\max}(\text{film})/\text{cm}^{-1}$ 3320, 2980, 1440, 1265; δ_{H} (400 MHz) 1.40 (t, 3H, $J = 5.7$, NHCH₂CH₃), 3.62 (m, 4H, NCH₂CH₂N and NHCH₂CH₃), 3.76 (t, 2H, $J = 6.9$, NCH₂CH₂N), 4.79 (s, 2H, CH₂Ph), 7.38 (m, 5H, Ar-H); δ_{C} (100 MHz) 15.02 (CH₃) 39.27 (CH₂CH₃), 47.42 and 49.83 (CH₂N), 128.3, 128.6 and 129.1 (Ar-CH), 133.5 (Ar-C), 157.5 (NCN).

1-Benzyl-2-(pyrrolidin-1yl)-4,5-dihydroimidazole (10b). Pyrrolidine (0.20 ml; 2.0 mmol) was added to 1-benzyl-2-methylthio-4,5-dihydroimidazolium iodide **7** (0.42 g; 2.0 mmol) in dry THF (20 ml) heated at reflux, and the solution heated at reflux for a further 20 h. The solution was allowed to cool to RT, washed with aq. NaOH (0.1 M; 2 × 10 ml) and extracted with diethyl ether (2 × 50 ml). The combined organic layers were washed with water and the water layers extracted with diethyl ether (2 × 50 ml). The combined organic layers were dried (MgSO₄), filtered and evaporated under reduced pressure. The residue was purified by silica gel column chromatography using 2-propyl-amine/chloroform (1:99 v/v) as eluant to afford the *title compound 10b* as a yellow liquid (0.22 g; 47%) (Found: (EI): M^{•+} 229.1566; C₁₄H₁₉N₃ requires M^{•+} 229.1578): $\nu_{\max}(\text{film})/\text{cm}^{-1}$ 2984, 1487, 1226; δ_{H} (400 MHz) 1.89 (m, 4H, NCH₂CH₂CH₂CH₂N), 3.40 (m, 2H, NCH₂CH₂N), 3.42 (m, 4H, NCH₂CH₂CH₂CH₂N), 3.72 (t, 2H, $J = 6.8$, NCH₂CH₂N), 4.34 (s, 2H, CH₂Ph), 7.28 (m, 5H, Ar-H); δ_{C} (100 MHz) 25.5 (NCH₂CH₂), 49.4 (CH₂N), 50.6 (CH₂Ph), 52.9 and 54.2 (CH₂N), 126.9, 127.1 and 128.6 (Ar-CH), 138.5 (Ar-C), 164.6 (NCN); m/z (EI) 229 (M^{•+}, 54%), 200 (41), 186 (36), 159 (61), 138 (22), 125 (37), 110 (23), 91 (100), 82 (36), 70 (53), 65 (30), 55 (55), 41 (28), 28 (37).

1-Benzyl-3-methoxycarbonylmethyltetrahydroimidazol-2-one (11a). To 1-benzyltetrahydroimidazol-2-one **6a** (1.03 g; 5.85 mmol) in dry THF (25 ml) under nitrogen at -78°C was added dropwise a solution of *sec*-BuLi (2.5M in hexanes; 7.02 mmol). The mixture was left at -78°C for 10 min and methyl bromoacetate (5.40 ml; 7.02 mmol) was then added dropwise. The mixture was heated at reflux for 24 h and then allowed to cool to RT. The solvent was removed under reduced pressure and the residue purified by silica gel column chromatography using ethyl acetate/hexane (4:6 v/v) as eluant to afford the *title compound 11a* as colourless oil (0.60 g; 41%) (Found: (EI): M^{•+} 248.1157; C₁₃H₁₆N₂O₃ requires M^{•+} 248.1161): $\nu_{\max}(\text{film})/\text{cm}^{-1}$ 2952, 2872, 1748, 1700, 1400, 1495, 1449, 1361, 1264, 1214, 986, 937, 760, 703; δ_{H} (300 MHz) 3.25 and 3.44 (each t, 2H, $J = 10.6$, NCH₂CH₂N), 3.75 (s, 3H, CO₂CH₃), 4.03 (s, 2H, CH₂CO₂CH₃), 4.40 (s, 2H, CH₂Ph), 7.33 (m, 5H, Ar-H); δ_{C} (75 MHz) 42.0 (CH₂), 43.0 (CH₃), 45.6 (CH₂), 48.2 and 52.0 (CH₂N), 127.4, 128.1 and 128.6 (Ar-CH), 137.0 (Ar-C), 163.0 (NCO), 170.1 (CO); m/z (EI) 248 (M^{•+}, 12%), 189 (22), 175 (5), 92 (8), 91 (100), 65 (9), 42 (9).

1-Benzyl-3-methoxycarbonylmethyltetrahydroimidazol-2-thione (11b). To 1-benzyl-3-methoxy-carbonylmethyltetrahydroimidazol-2-one **11a** (0.20 g; 0.75 mmol) in dry *ortho*-xylene (30 ml) was added portionwise Lawesson's Reagent ([2,4-bis(4-methoxyphenyl)]-1,3-dithia-2,4-

diphosphetane-2,4-disulfide) (0.30 g; 0.75 mmol). The mixture heated at reflux for 26 h after which time it was allowed to cool to RT. The solvent was removed under reduced pressure and the residue purified by silica gel column chromatography using ethyl acetate/hexane (4:6 v/v) as eluant to yield the *title compound 11b* as yellow gum (0.14 g; 66%) (Found: (EI): M^{+} 264.0931; $C_{13}H_{16}N_2O_2S$ requires M^{+} 264.0932): $\nu_{\max}(\text{film})/\text{cm}^{-1}$ 2950, 2874, 1742, 1404, 1497, 1449, 1266, 1211, 983, 762; δ_{H} (300 MHz) 3.45 and 3.64 (each t, 2H, $J = 10.7$, $\text{NCH}_2\text{CH}_2\text{N}$), 3.77 (s, 3H, CO_2CH_3), 4.44 (s, 2H, $\text{CH}_2\text{CO}_2\text{CH}_3$), 4.91 (s, 2H, CH_2Ph), 7.35 (m, 5H, Ar-H); δ_{C} (75 MHz) 45.6 (CH_2), 46.4 (CH_3), 48.8 (CH_2), 51.8 and 52.2 (CH_2N), 127.7, 128.1 and 128.7 (Ar-CH), 138.2 (Ar-C), 170.0 (CO), 183.6 (NCS); m/z (EI) 264 (M^{+} , 40%), 205 (22), 191 (8), 141 (10), 102 (8), 91 (100), 72 (16), 65 (14), 42 (13), 28 (27).

1-Benzyl-2-methoxycarbonylmethylthio-4,5-dihydroimidazole (12). To 1-benzyltetrahydroimidazol-2-thione **6b** (0.30 g; 1.56 mmol) in dry THF (25 ml) under nitrogen was added methyl bromoacetate (0.13 ml; 1.87 mmol) and the resulting solution was heated at reflux for 18 h and then allowed to cool to RT. The solvent was evaporated under reduced pressure and the residue purified by silica gel column chromatography using ethyl acetate/hexane (45:55 v/v) as eluant to afford the *title compound 12* as a white solid (0.36 g; 87%): m.p. 111-112°C (Found: (EI) MH^{+} 265.1014; $C_{13}H_{16}N_2O_2S$ requires MH^{+} 265.1010); $\nu_{\max}(\text{nujol})/\text{cm}^{-1}$ 2952, 2865, 1740, 1410, 1264; δ_{H} (300 MHz) 3.74 (s, 3H, CO_2CH_3), 3.81 and 3.94 (each m, 2H, $\text{NCH}_2\text{CH}_2\text{N}$), 4.59 (s, 2H, $\text{SCH}_2\text{CO}_2\text{CH}_3$), 4.70 (s, 2H, CH_2Ph), 7.32 (m, 5H, Ar-H); δ_{C} (75 MHz) 35.6 (CH_2), 44.0 (CO_2CH_3), 49.6 (SCH_2), 51.3 and 53.6 (CH_2N), 128.0, 128.8 and 129.3 (Ar-CH), 132.3 (Ar-C), 168.4 (CO); m/z (EI) 265 (MH^{+} , 44%), 192 (100), 159 (10), 104 (18), 91 (50).

1-Benzyl-3-methoxycarbonylmethyl-2-methylthio-4,5-dihydroimidazolium trifluoromethanesulfonate (13). To 1-benzyl-3-methoxycarbonylmethyltetrahydroimidazol-2-thione **11b** (0.30 g; 1.10 mmol) in dry dichloromethane (10 ml) under a nitrogen atmosphere was added neat MeOTf (0.15 ml; 1.36 mmol) and the solution allowed to stir at RT for 1 h. The solvent was removed under reduced pressure to yield the *title compound 13* as a yellow gum that was partially characterised (0.46 g; 97%); δ_{H} (300 MHz) 2.78 (s, 3H, SCH_3), 3.71 and 3.82 (each t, 2H, $J = 10.4$, $\text{NCH}_2\text{CH}_2\text{N}$), 3.75 (s, 3H, CO_2CH_3), 4.54 (s, 2H, $\text{CH}_2\text{CO}_2\text{CH}_3$), 5.03 (s, 2H, CH_2Ph), 7.46 (m, 5H, Ar-H); δ_{C} (75 MHz) 17.2 (SCH_3), 47.1 (CH_2), 46.9 (CO_2CH_3), 49.2 (CH_2), 53.1 and 53.6 (CH_2N), 127.8, 128.4 and 128.8 (Ar-CH), 140.2 (Ar-C), 171.7 (CO), 185.1 (NCS).

1-Benzyl-3-trimethylsilylmethyltetrahydroimidazol-2-one (15a). To a suspension of NaH (0.19 g; 8.29 mmol) in dry DMSO (25 ml) was added dropwise a solution of 1-benzyl-4,5-dihydroimidazol-2-one **6a** (1.46 g; 8.29 mmol) in dry DMSO (25 ml) at RT. The mixture was stirred for 30 min and then chloromethyltrimethylsilane (2.24 ml; 12.43 mmol) was added. The resulting mixture was stirred at RT for 10 h, filtered, and the solvent removed under reduced pressure. The residue was purified by column chromatography on silica gel using ethyl acetate/hexane (4:6 v/v) as eluant to afford the *title compound 15a* as colourless oil (0.99 g; 45%) (Found: (EI): M^{+} 262.1503; $C_{14}H_{22}N_2OSi$ requires M^{+} 262.1501): $\nu_{\max}(\text{film})/\text{cm}^{-1}$ 3030, 2952, 2860, 1696, 1444, 1359, 1251, 856, 756; δ_{H} (300 MHz) 0.31 (s, 9H, $\text{Si}(\text{CH}_3)_3$), 2.54 (s, 2H, CH_2Si), 3.25 and 3.41 (each m, 2H, $\text{NCH}_2\text{CH}_2\text{N}$), 4.51 (s, 2H, CH_2Ph), 7.36 (m, 5H, Ar-H);

δ_{C} (75 MHz) -1.6 (SiCH₃), 35.4 and 42.5 (CH₂), 45.5 and 48.7 (CH₂N), 127.2, 128.1 and 128.5 (Ar-CH), 137.5 (Ar-C), 161.8 (NCO); m/z (EI) 262 (M⁺, 12%), 248 (5), 247 (18), 189 (4), 171 (8), 155 (7), 100 (9), 91 (100), 73 (77), 65 (16), 45 (22), 43 (13). Also isolated was 1-benzyl-3-methyl-tetrahydroimidazol-2-one **16** as a colourless oil (0.44 g; 27%) (Found: (EI) M⁺ 190.1107; C₁₁H₁₄N₂O requires M⁺ 190.1106); δ_{H} (300 MHz) 2.82 (s, 3H, CH₃), 3.13 and 3.18 (each m, 2H, NCH₂CH₂N), 4.37 (s, 2H, CH₂Ph); δ_{C} (75 MHz) 31.4 (CH₃), 42.2 (CH₂Ph), 44.9 and 48.7 (CH₂N), 127.4, 127.7 and 128.5 (Ar-CH), 137.3 (Ar-C), 161.5 (NCO); m/z (EI) 190 (M⁺, 30%), 161 (6), 113 (13), 99 (34), 92 (9), 91 (100), 89 (11), 77 (23), 65 (34), 56 (18), 51 (16), 43 (13), 42 (44), 39 (15).

1-Benzyl-3-trimethylsilylmethyltetrahydroimidazol-2-thione (15b). To 1-benzyl-3-trimethylsilylmethyltetrahydroimidazol-2-one **15a** (0.86g; 3.28 mmol) in dry *ortho*-xylene (30 ml) was added portionwise Lawesson's reagent (1.32g; 3.28 mmol). The mixture was heated at reflux for 26 h after which time it was allowed to cool to RT. The solvent was removed under reduced pressure and the residue purified by column chromatography on silica gel using ethyl acetate/hexane (25:75 v/v) as eluant to afford the *title compound* **15b** as a yellow gum (0.63 g; 69%) (Found: (EI): M⁺ 278.1287; C₁₄H₂₂N₂SSi requires M⁺ 278.1273); ν_{max} (film)/cm⁻¹ 3030, 2938, 1696, 1498, 1445, 1404, 1252, 1056, 760, 702; δ_{H} (300 MHz) 0.20 (s, 9H, Si(CH₃)₃), 3.12 (s, 2H, CH₂Si), 3.21 and 3.25 (each m, 2H, NCH₂CH₂N), 4.92 (s, 2H, CH₂Ph), 7.32 (m, 5H, Ar-H); δ_{C} (75 MHz) -1.4 (SiCH₃), 39.3 and 45.3 (CH₂), 48.5 and 52.1 (CH₂N), 127.5, 128.1 and 128.6 (Ar-CH), 136.8 (Ar-C), 182.9 (NCS); m/z (EI) 278 (M⁺, 10%), 264 (5), 263 (21), 92 (8), 91 (100), 73 (69), 65 (20), 45 (23).

1-Benzyl-3-trimethylsilylmethyl-2-methylthio-4,5-tetrahydroimidazolium trifluoromethane-sulfonate (17). To 1-benzyl-3-trimethylsilylmethyl-4,5-tetrahydroimidazol-2-thione **15b** (0.10 g; 0.36 mmol) in dry dichloromethane (10 ml) under a nitrogen atmosphere was added MeOTf (0.02 ml; 0.43 mmol) and the solution allowed to stir at RT for 1 h. The solvent was removed under reduced pressure to yield the title compound as a yellow gum that was partially characterised (0.15 g; 94%): δ_{H} (300 MHz) 2.49 (s, 3H, SCH₃), 3.14 (s, 2H, CH₂Si), 3.72 and 3.76 (each m, 2H, NCH₂CH₂N), 4.64 (s, 2H, PhCH₂), 7.24 (m, 5H, Ar-H); δ_{C} (75 MHz) -1.1 (SiCH₃), 17.3 (SCH₃), 44.2 and 49.1 (CH₂), 54.2 and 55.6 (CH₂N), 127.4, 128.3 and 128.6 (Ar-CH), 137.7 (Ar-C).

1,3-Dibenzyltetrahydroimidazol-2-one (18a). To commercial N,N'-dibenzyl-1,2-diaminoethane (0.40 g; 1.67 mmol) in dry THF (20 ml) under nitrogen was added 1,1'-carbonyldiimidazole (0.38 g; 2.35 mmol) in dry THF (10 ml). The resulting solution was stirred at RT for 18 h before the solvent was evaporated under reduced pressure. The residue was washed with aq. HCl (2M; 50 ml) and extracted with dichloromethane (2 × 50 ml). The combined organic phases were dried (MgSO₄), filtered and the solvent evaporated under reduced pressure to afford the title compound **18a** as a white solid (0.41 g; 97%): m.p. 90-91°C (lit.¹⁰ 93-94°C) (Found: (EI): M⁺ 266.1414; C₁₇H₁₈N₂O requires M⁺ 266.1419); ν_{max} (nujol)/cm⁻¹ 2927, 2855, 1689, 1494, 1455, 1365, 1257, 711; δ_{H} (300 MHz) 3.16 (s, 4H, NCH₂CH₂N), 4.41 (s, 4H, 2 × CH₂Ph), 7.32 (m, 10H, Ar-H); δ_{C} (75 MHz) 42.2 (PhCH₂), 48.6 (NCH₂), 127.5, 128.3 and

128.6 (Ar-CH), 137.4 (Ar-C), 161.1 (NCO); m/z (EI) 266 (M^{*+} , 73%), 189 (4), 175 (71), 132 (9), 118 (6), 105 (8), 91 (100), 65 (15).

1,3-Dibenzyltetrahydroimidazol-2-thione (18b). Prepared according to the method used to synthesize **18a**, using *N,N'*-dibenzyl-1,2-diaminoethane (0.40 g; 1.67 mmol) and 1,1'-thiocarbonyldiimidazole (0.38 g; 2.13 mmol) to afford the title compound **18b** as a yellow solid (0.44 g; 98%): m.p. 87-92°C (lit.,¹¹ 90°C) (Found: (EI): M^{*+} 282.1188; $C_{17}H_{18}N_2S$ requires M^{*+} 282.1191); ν_{\max} (nujol)/ cm^{-1} 2927, 2855, 1494, 1462, 1378, 1359, 1334, 1268, 1240, 731; δ_H (400 MHz) 3.40 (s, 4H, NCH_2CH_2N) 4.92 (s, 4H, $2 \times CH_2Ph$), 7.38 (m, 10H, Ar-H); δ_C (100 MHz) 45.7 ($PhCH_2$), 52.1 (NCH_2), 128.0, 128.5 and 129.0 (Ar-CH) 136.7 (Ar-C), 184.8 (NCS); m/z (EI) 282 (M^{*+} , 20%), 191 (30), 105 (9), 91 (100), 65 (16), 56 (5).

1,3-Dibenzyl-2-methylthio-4,5-dihydroimidazolium trifluoromethanesulfonate (19). Via a syringe was added dropwise MeOTf (0.09 ml; 0.85 mmol) to 1,3-dibenzyltetrahydroimidazol-2-thione **18b** (0.20 g; 0.71 mmol) in dry dichloromethane (10 ml). The solution was stirred at RT for 1 h and the solvent removed under reduced pressure to afford the *title compound 19* as a yellow oil (0.32 g; 100%) (Found: (ES, $M-CF_3SO_3$): M^{*+} 297.1422; $C_{18}H_{21}F_3N_2O_3S_2$ requires $(M-CF_3SO_3)^{*+}$ 297.1425); ν_{\max} (film)/ cm^{-1} 3034, 2944, 1591, 1574, 1499, 1455, 1357, 1262 (br), 1225 (br), 1157 (br), 1031; δ_H (300 MHz) 2.86 (s, 3H, SCH_3), 3.90 (s, 4H, NCH_2CH_2N), 4.92 (s, 4H, $2 \times CH_2Ph$), 7.29 (m, 6H, Ar-H), 7.37 (m, 4H, Ar-H); δ_C (75 MHz) 16.5 (SCH_3), 47.8 (CH_2Ph), 53.3 (NCH_2), 127.6, 127.9 and 128.5 (Ar-CH), 132.4 (Ar-C), 167.2 (NCS).

1,3-Dibenzyl-2-methyliminotetrahydroimidazole (20). 2-Methylthio-4,5-dihydroimidazolium salt **19** was prepared as above from MeOTf (0.13 ml; 1.10 mmol) and 1,3-dibenzyltetrahydroimidazol-2-thione **18b** (0.26 g; 0.92 mmol) and after stirring at RT for 1 h methylamine (2M solution in THF; 0.69 ml; 1.38 mmol) was added and the resulting solution heated at reflux for 18 h. The solvent was removed under reduced pressure and the residue purified by column chromatography on silica gel eluting with 2-propylamine/chloroform (2:98 v/v) to afford the *title compound 20* as a yellow gum (0.10 g; 40%) (Found: (EI): MH^+ 280.1738; $C_{17}H_{21}N_3$ requires MH^+ 280.1735); δ_H (300 MHz) 3.01 (s, 3H, NCH_3), 3.44 (s, 4H, NCH_2CH_2N), 4.53 (s, 4H, $2 \times CH_2Ph$), 7.26 (m, 6H, Ar-H), 7.30 (m, 4H, Ar-H); δ_C (75 MHz) 30.9 (NCH_3), 46.7 (CH_2Ph), 50.7 (NCH_2), 127.5, 128.4 and 129.1 (Ar-CH), 133.8 (Ar-C), 158.5 (NCN); m/z (EI) 279 (M^{*+} , 24%), 250 (10), 207 (16), 125 (19), 111 (35), 97 (58), 91 (23), 83 (57), 69 (77), 57 (100), 49 (27), 43 (76), 39 (15), 29 (26).

1,3-Dibenzyl-2-(tetramethyleneimino)tetrahydroimidazolium trifluoromethane sulfonate (21). 2-Methylthio-4,5-dihydroimidazolium salt **19** was prepared as above from MeOTf (0.12 ml; 1.10 mmol) and 1,3-dibenzyltetrahydroimidazol-2-thione **18b** (0.25 g; 0.88 mmol). After stirring at RT for 1 h the solvent was removed under reduced pressure, dry THF (25 ml) and pyrrolidine (0.09 ml; 1.0 mmol) were added to the residue under nitrogen and the solution was heated at reflux for 26 h. The solvent was removed under reduced pressure to afford the title compound **21** as a brown oil that was partially characterised (0.32 g; 77%): δ_H (300 MHz) 1.86 (t, 4H, $J = 6.6$, $NCH_2CH_2CH_2CH_2N$), 3.61 (t, 4H, $J = 6.6$, $NCH_2CH_2CH_2CH_2N$), 3.84 (s, 4H,

NCH₂CH₂N), 4.76 (s, 4H, 2 × CH₂Ph), 7.26 (m, 6H, Ar-H), 7.39 (m, 4H, Ar-H); δ_C (75 MHz) 25.5, 49.4, 50.8 and 53.4 (CH₂), 126.3, 128.2 and 129.3 (Ar-CH), 134.8 (Ar-C), 162.4 (NCN).

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