Organic & Biomolecular Chemistry

RSC Publishing

PAPER

View Article Online
View Journal | View Issue

Cite this: *Org. Biomol. Chem.*, 2013, **11**, 5926

Coenzyme-inspired chemistry 2: 4,5-dihydroimidazolium ylides (NHCs) and the reactions of 2-(1-hydroxyalkyl)-4,5-dihydroimidazoles

Raymond C. F. Jones*[a] and John R. Nichols[b]

Received 29th April 2013,
Accepted 17th July 2013

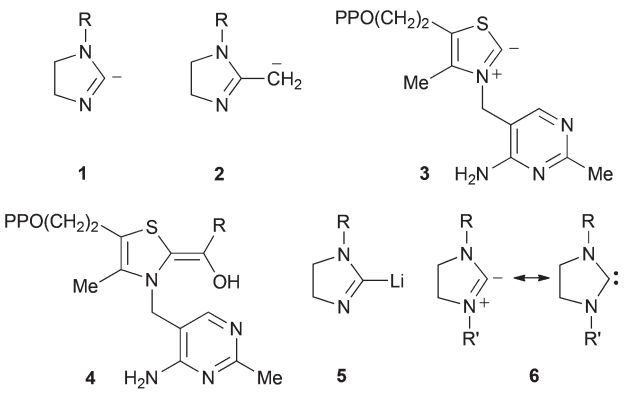
DOI: 10.1039/c3ob40884a

www.rsc.org/obc

Ketones are prepared from aldehydes *via* 1-benzyl-2-(1-hydroxyalkyl)-4,5-dihydroimidazoles (adducts of the aldehydes with 1-benzyl-2-lithio-4,5-dihydroimidazoles) whereas 1-benzyl-2-(1-oxoalkyl)-4,5-dihydroimidazoles are shown to act as acyl transfer reagents *via* C–C bond cleavage. 4,5-Dihydroimidazolium ylides (NHCs) are intermediates in both processes, which constitute thiamine-inspired C–C bond formation and cleavage protocols.

Introduction

As part of a study of coenzyme-inspired chemistry using the 4,5-dihydroimidazole nucleus, we have focussed on the reactivity of the C-2 anion **1** formed from 4,5-dihydroimidazoles, as an extension of our earlier work on laterally metallated nucleophiles **2**[1] and other aspects of 4,5-dihydroimidazole chemistry.[2] We have recently reported full details of C-2 alkylation processes of anions **1** which form part of a carbon transfer sequence that mimics the single carbon transfers mediated by the tetrahydrofolate (FH4) coenzyme N^5,N^{10}-methenyltetrahydrofolate.[3] In an extension of this chemistry to higher oxidation level electrophiles, we were inspired by the azolium ylides that form part of the mechanism of action of thiamine as the thiazolium species **3**,[4] reinforced by the recent upsurge in the use of N-heterocyclic carbenes (NHCs) as ligands for metals, for example in metathesis.[5] These two aspects, azolium ylide and carbene, are also seen combined in various organocatalytic procedures that utilise analogues of the Breslow intermediate in the thiamine mechanism to display carbonyl anion and homoenolate reactivity.[6] Key intermediates in the thiamine-catalysed processes are the 2-(1-hydroxyalkyl) adducts **4**.



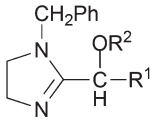
We therefore determined to investigate the reactivity of 2-lithio-4,5-dihydroimidazoles **5** with carbonyl electrophiles. This paper reports in detail our investigation of the reactions of lithio-derivatives **5** with aldehydes, ketones and esters, and the reactivities of the 2-(1-hydroxyalkyl)-4,5-dihydroimidazoles and 2-(1-oxoalkyl)-4,5-dihydroimidazoles so produced.[7] The 2-(hydroxyalkyl) adducts allow ketones to be prepared from aldehydes, whereas the 2-(oxoalkyl) adducts act as acyl transfer reagents. Both protocols utilise dihydroimidazolium ylides (NHCs) **6** as leaving groups *via* C–C bond cleavage, in this way mimicking thiamine-mediated processes.

Results & discussion

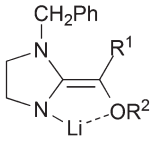
The substrate for our studies was 1-benzyl-4,5-dihydroimidazole **7**, prepared as we have reported previously.[8] Metallation

[a]*Chemistry Department, Loughborough University, Loughborough, Leics. LE11 3TU, UK. E-mail: r.c.f.jones@lboro.ac.uk; Fax: +44 (0) 1509 223925; Tel: +44 (0) 1509 222557*
[b]*Department of Chemistry, University of Nottingham, University Park, Nottingham NG7 2RD, UK*

using our standard protocol (*n*-BuLi, THF, −78 °C)[2] and treatment of the 2-lithio-derivative with aldehydes (freshly distilled) afforded the 2-(1-hydroxyalkyl)-4,5-dihydroimidazoles **8a–f** in good yields (Scheme 1). Originally we had planned to deprotonate adducts **8** at the α-position to parallel the Breslow intermediate in the thiamine series,[4] so we prepared three *O*-protected derivatives **9a–c** of alcohols **8**. The *tert*-butyldimethylsilyl (TBDMS) ether **9a** was prepared by two methods: (i) from **8a** using TBDMSCl, 4-(dimethylamino)pyridine, CH_2Cl_2 (48%), or (ii) by direct treatment with TBDMSCl of the lithium alkoxide intermediate in the preparation of **8a** (66% from **7**). The former approach was also employed to prepare TBDMS ether **9b** (TBDMSCl; 84%), and benzyl carbonate **9c** ($PhCH_2O$-COCl; 64%) from alcohol **8c**. However, whilst treatment of ethers **9a**, **b** with various strong bases (*n*-BuLi, s-BuLi or LDA, THF, −78 °C) gave the red colouration normally characteristic of deprotonation, quenching with a range of electrophiles (D_2O, haloalkanes or aldehydes) failed to afford any substitution products, and the only reaction observed was some desilylation to alcohols **8a**, **b**; carbonate **9c** likewise failed to provide any substitution products. It is reasonable to speculate that the lithiated species exists as a stabilised lithio-enamine **10** but we have no firm evidence concerning reasons for these failures.

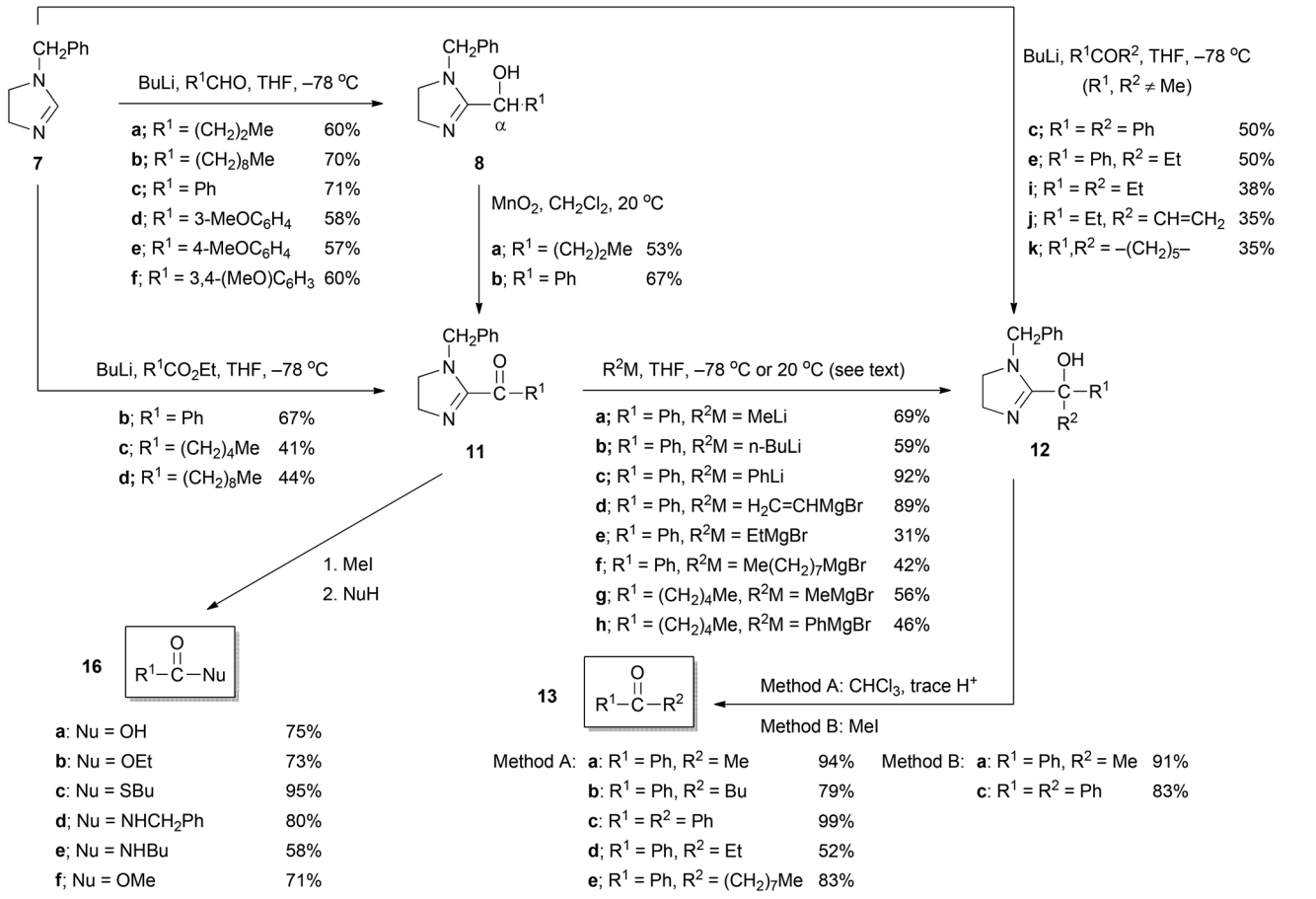


9a; $R^1 = (CH_2)_2Me$, R^2 = TBDMS
9b; R^1 = Ph, R^2 = TBDMS
9c; R^1 = Ph, $R^2 = CO_2Ph$



10

We next proposed that the target tertiary alcohols that would have arisen from a deprotonation-alkylation of **8** or **9** could be accessed by reversal of polarity at the α-carbon centre, from nucleophile to electrophile. The hydroxyalkyl adducts **8a**, **c** were therefore oxidised (MnO_2, CH_2Cl_2, 20 °C) to the corresponding 2-(1-oxoalkyl)-4,5-dihydroimidazoles **11a**, **b** (53 & 67%, respectively). The IR absorptions of the carbonyl groups were observed at 1700 & 1670 cm^{-1}, respectively, supporting the presence of the conjugated carbonyl group. The 2-oxoalkyl-4,5-dihydroimidazoles **11** could be more directly prepared by acylation of the lithio-derivative of **7**, formed as already described. The most effective acylating agents from a range surveyed proved to be ethyl esters; other acylating agents examined included acyl chlorides, acid anhydrides, *N*-acylpyrrolidines and thioesters. The acylations were performed by inverse



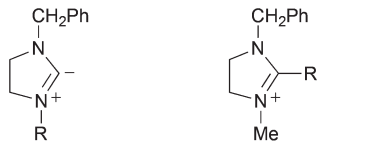
Scheme 1 Formation and reactions of 2-(1-hydroxyalkyl)-4,5-dihydromidazoles **8** and **12**.

addition of the lithio-dihydroimidazole solution, cooled to −100 °C, to a solution of the ethyl esters. Normal addition afforded low yields; we presume that this may result from competing enolisation of the 2-acyl group and/or a second addition of the lithio-derivative of **7** to the initial 2-acyl-4,5-dihydroimidazole. Using the inverse addition protocol, 2-acyl compounds **11b–d** were obtained (67, 41 & 44%, respectively) (Scheme 1).

With the 2-oxoalkyl-4,5-dihydroimidazoles **11** in hand, the tertiary alcohols **12** were prepared by addition of organometallic C-nucleophiles. Reaction of 2-benzoyl compound **11b** with methyl-, *n*-butyl- and phenyl-lithiums (THF, −78 °C) led to the tertiary alcohols **12a–c** (69, 59 & 92%, respectively) (Scheme 1); no adduct was observed using s-BuLi as nucleophile. Ethenylmagnesium bromide reacted effectively with **11b** at 20 °C to give **12d** (89%), whilst lower yields of **12e**, **f** were obtained using ethyl- and octylmagnesium bromides, respectively. In these latter cases, isolation of the secondary alcohol **8c** demonstrated that reduction accounted for the remaining material. If the addition of alkyl-lithiums to **11c** was performed at −78 °C, the 2-(1-oxoalkyl)-4,5-dihydroimidazole was recovered unchanged, implying that these very basic reagents were enolising the 2-acyl substituent when α-protons were present. In contrast, the less basic Grignard reagents methyl- and phenylmagnesium bromides with acyl compound **11c** did provide the adducts **12g**, **h**, respectively; ethylmagnesium bromide did, however, afford only the reduction product **8g** ($R^1 = (CH_2)_4Me$; 54%).

The direct addition of the lithio-dihydroimidazole formed from **7** to ketones would provide an alternative approach to the tertiary alcohols **12**. When this was attempted using the lithio-derivative of **7** prepared in the usual way, with the methyl ketones propan-2-one and pentan-2-one, only recovered ketone and dihydroimidazole **7** were isolated, presumably because of ketone enolisation. A successful addition of the lithio-derivative of **7** to benzophenone to afford alcohol **12c** (50%) supported this conclusion. The competition between nucleophilicity and basicity of the lithio-derivative of dihydroimidazole **7** was also shown by the isolation of adducts **12e**, **i–k** that were isolated in moderate yields from the ketones 1-phenylpropan-1-one, pentan-3-one, pent-1-en-3-one and cyclohexanone, respectively, along with recovered starting materials. Interestingly, there appears to be little or no competing enolisation with aldehyde electrophiles where it would be possible, as demonstrated by the successful additions of lithio-**7** to aldehydes to afford hydroxyalkyl adducts **8** described above and listed in Scheme 1. We have therefore shown two routes to the tertiary alcohols **12**: (i) *via* the direct addition of the lithio-derivative of **7** to ketones; and (ii) as an alternative, and in particular in those cases not accessible by direct addition to enolisable ketones, *via* the addition of organometallic C-nucleophiles to 2-acyldihydroimidazoles **11** (themselves available either from addition of the anion from **7** to aldehydes followed by oxidation, or from direct acylation of lithio-**7** using esters).

Having made the necessary carbon–carbon bond, *i.e.* **11** →**12**, that was prompted by analogy with the action of thiamine,[4] to complete the sequence mimicking thiamine it was necessary to obtain ketones from the tertiary alcohols **12**. We were gratified to find that these alcohols collapsed readily to ketones on heating in solution in $CHCl_3$ containing catalytic conc. hydrochloric acid. Thus 2-(1-hydroxyalkyl)dihydroimidazoles **12a–c**, **e**, **f** afforded the ketones **13a–e** in good yields (Scheme 1), isolated simply by filtration over silica. These mild conditions contrast with the reported properties of analogous 2-(1-hydroxyalkyl)imidazoles which are stable to acidic conditions and require quaternisation and base treatment to cleave the C2–Cα bond. We presume that this bond cleavage proceeds by protonation of the amidine function at N-3 and elimination to give the ketone and the dihydroimidazolium ylide **14a**, that subsequently protonates at C-2, so that the requirement for acid is catalytic. This pathway is lent support by the observation that stoichiometric quaternisation of **12a**, **c** (MeI, THF, 20 °C) led directly to *in situ* bond cleavage to afford crystals of the 1-benzyl-3-methyl-4,5-dihydroimidazolium iodide **15a** with isolation of the ketones **13a**, **c** from the mother liquors. Here the likely pathway is quaternisation and elimination to give the ketone and ylide **14b** which protonates. The acid-promoted cleavage requires tertiary alcohols **12** as the secondary alcohols **8** were found to be stable to acidic $CHCl_3$; similarly prolonged treatment of **8c** with iodomethane led only to the quaternary salt **15b**. Taken overall, these processes have produced ketones from aldehydes with the catalytic intervention of a dihydroimidazole, which mimics the C–C bond formations mediated by thiamine, *e.g.* in transketolase,[9] albeit with reversed polarity.



14a; R = H
14b; R = Me
15a; R = H
15b; R = CH(OH)Ph

Encouraged by the obvious ability of dihydroimidazolium ylides such as **14** to act as leaving groups, we investigated the 2-(1-oxoalkyl)-dihydroimidazoles (2-acyldihydroimidazoles) **11** as acylating agents with non-carbon nucleophiles. The 2-benzoyl compound **11b** was treated with excess iodomethane (20 °C, 2 h) and the quaternary salt reacted without purification with a heteroatom nucleophile to afford in good yields benzoic acid **16a** (NaOH aq, 25 °C), ester **16b** (EtOH reflux), thioester **16c** (BuSH, THF reflux) and the amides **16c**, **d** ($PhCH_2NH_2$ or $BuNH_2$, respectively, THF reflux) (Scheme 1). Presumably ylide **14b** is the by-product from these acylations: consistent with this supposition is the isolation of quaternary salt **15a** (94%) from the preparation of thioester **16c**. Further support for an ylide as leaving group was obtained when **11b** was treated in MeOH with NH_4Cl as a proton source to afford methyl benzoate **16f** (71%) and dihydroimidazole **7**. In an unoptimised reaction, the quaternary salt formed from **11b** was treated with *n*-BuLi to generate 1-phenylpentan-1-one (30%) to validate the potential of these salts to undergo acyl transfer to C-nucleophiles, in contrast to the carbonyl additions observed (see earlier) with non-quaternised

dihydroimidazoles **11**. We have demonstrated clearly the application of 2-acyl-4,5-dihydroimidazoles in acyl transfer processes involving C–C bond cleavage, which is much less common than C–heteroatom cleavage.[10]

Conclusions

We have reported a synthesis of 2-(1-hydroxyalkyl)-4,5-dihydroimidazoles by reaction of a 2-lithio-dihydroimidazole with aldehydes. The oxidation of these 2-hydroxylalkyl dihydroimidazoles to 2-(1-oxoalkyl)-4,5-dihydroimidazoles (also available from direct acylation of the 2-lithio-dihydroimidazoles) followed by addition of organometallic C-nucleophiles afforded tertiary alcohols in which the C–C bond formation parallels that in thiamine-mediated processes in Nature.[4] Facile C–C bond cleavage of these tertiary alcohols led to ketones with a dihydroimidazolium ylide (NHC) as a leaving group; in this way we have developed a route from aldehydes to ketones mediated by dihydroimidazoles, thus mimicking the action of thiamine. The application of dihydroimidazolium ylides as leaving groups has also allowed us to demonstrate that 2-acyl-dihydroimidazoles can act as acylating agents *via* the less common C–C bond cleavage.

Experimental

Melting points were obtained on a Gallenkamp capillary or a Reichert hot stage apparatus and are uncorrected. IR spectra were recorded using Pye Unicam SP1000 or SP3-100 spectrometers. Mass spectra were recorded using AEI MS902 or VG 7070E spectrometers. ^{1}H NMR spectra were obtained using the following spectrometers as indicated: Perkin-Elmer R32 or Joel FX90Q spectrometers at 90 MHz. ^{13}C NMR spectra were recorded using a Jeol FX90Q spectrometer at 22.7 MHz. ^{1}H NMR spectra were determined in $CDCl_3$ solution and chemical shifts δ_H quoted in parts per million (ppm) from TMS as internal standard. Coupling constants J are quoted in Hz with multiplicities: s-singlet, d-doublet, t-triplet, q-quartet, m-multiplet, and br-broad. ^{13}C NMR spectra were determined in $CDCl_3$ solution and chemical shifts δ_C quoted in ppm from TMS as internal standard or from TMS using $CDCI_3$ as internal standard. Column chromatography was carried out at medium pressure using Merck Kieselgel 60 (Art. 9385); TLC was carried out on silica plates (Kieselgel 60, F254, Merck Art. 5554). Solvent extractions were dried over anhydrous $MgSO_4$ or Na_2SO_4 for at least 10 min. Ether refers to diethyl ether and light petroleum to the fraction of bp 60–80 °C. THF and ether were distilled from $LiAlH_4$ or potassium immediately prior to use. Other dry solvents were prepared as described in Perrin *et al.*[11] Alkyl-lithiums were standardised by the diphenylacetic acid method.[12]

1-Benzyl-2-(1-hydroxybutyl)-4,5-dihydroimidazole (8a). To 1-benzyl-4,5-dihydroimidazole **7** (1.00 g, 6.25 mmol) in dry THF (30 mL), stirred at −78 °C under an atmosphere of nitrogen, was added *n*-butyl-lithium (1.58 M solution in hexanes; 4.35 mL, 6.87 mmol). After 20 min to allow complete anion formation, freshly distilled butanal (0.61 mL, 6.87 mmol) was added dropwise and the mixture stirred for a further 1 h at −78 °C, allowed to warm to 20 °C and then concentrated under reduced pressure. The resulting red oil was partitioned between chloroform (2 × 50 mL) and water (50 mL), the combined organic extract dried and concentrated under reduced pressure. Purification by column chromatography, eluting with $CHCl_3$–2-aminopropane (95 : 5 v/v) afforded the *title compound* **8a** (0.87 g, 60%) as a waxy solid; ν_{max}(film)/cm^{-1} 3050, 2960, 2860, 1600, 1430, 1230, 1120, 750, 700; δ_H (200 MHz) 7.22–7.26 (5H, m, Ar-H.), 4.18–4.22 (3H, 2 × d and m, PhC*H*$_2$ and C*H*OH), 3.68–3.71 (3H, m, NC*H*$_2$CH$_2$N and O*H*), 3.24–3.26 (2H, m, NCH$_2$C*H*$_2$N), 1.48–1.53 (4H, m, CH$_2$CH$_2$), 0.90 (3H, t, J = 7.1, CH$_3$); m/z 232 (M$^+$, 5%), 190 (25), 180 (12), 120 (20), 99 (33), 91 (100). HRMS: M$^+$ 232.1583; $C_{14}H_{20}N_2O$ requires M$^+$ 232.1576. A sample recrystallised from EtOH–H_2O gave colourless needles, mp 105 °C (Found: C, 67.2; H, 9.1; N, 11.0%; $C_{14}H_{20}N_2O{\cdot}H_2O$ requires C, 67.2; H, 8.9; N, 11.2%).

1-Benzyl-2-(1-hydroxydecyl)-4,5-dihydroimidazole (8b). Prepared by the method described above for the preparation of **8a** but using 1-benzyl-4,5-dihydroimidazole **7** (2.00 g, 12.5 mmol), *n*-butyl lithium (1.42 M solution in hexanes; 9.50 mL, 13.5 mmol) and decanal (2.15 g, 13.8 mmol) to afford after column chromatography eluting with $CHCl_3$–2-aminopropane (96 : 4 v/v), the *title compound* **8b** (1.38 g, 70%) as a waxy solid; ν_{max}($CHCl_3$)/cm^{-1} 3400, 2950, 2860, 1600, 1120; δ_H 7.29–7.33 (5H, m, Ar-H), 4.29–4.32 (3H, 2 × d and m, PhC*H*$_2$ and C*H*OH), 3.73–3.76 (2H, m, NC*H*$_2$CH$_2$N), 3.33–3.37 (2H, m, NCH$_2$C*H*$_2$N), 1.46–1.53 (16H, m, (CH$_2$)$_8$), 0.90 (3H, t, J = 7.0, CH$_3$).

1-Benzyl-2-(phenylhydroxymethyl)-4,5-dihydroimidazole (8c). Prepared by the method described above for the preparation of **8a** but using 1-benzyl-4,5-dihydroimidazole **7** (1.60 g, 10.0 mmol), *n*-butyl-lithium (1.58 M solution in hexanes; 7.00 mL, 11.1 mmol) and benzaldehyde (1.17 g, 11.0 mmol) to afford after column chromatography eluting with $CHCl_3$–2-aminopropane (96 : 4 v/v), the *title compound* (1.89 g, 71%) as a pale yellow gum; ν_{max}(film)/cm^{-1} 3040, 2860, 1600, 1450, 1250, 1000, 920, 750; δ_H (250 MHz) 7.54–7.56 (2H, m, Ar-H), 7.28–7.32 (3H, m, Ar-H), 7.18–7.22 (3H, m, Ar-H), 6.89–6.91 (2H, m, Ar-H), 6.65 (1H, br s, OH), 5.65 (1H, s, C*H*OH), 4.15 (2H, s, PhC*H*$_2$), 3.63–3.67 and 3.13–3.16 (each 2H, m, NCH$_2$CH$_2$N); δ_C 168.1 (C-2), 140.4, 137.2 (Ar-C), 128.2, 128.1, 127.5, 127.4, 127.0, 126.9 (Ar-CH), 69.2 (CHOH), 51.0, 50.5 (CH$_2$); m/z 266 (M$^+$, 2%), 149 (7), 120 (19), 105 (11), 91 (100), 71 (10). HRMS: M$^+$ 266.1413; $C_{17}H_{18}N_2O$ requires M$^+$ 266.1419.

1-Benzyl-2-(3-methoxyphenylhydroxymethyl)-4,5-dihydroimidazole (8d). Prepared by the method described above for the preparation of **8a** but using 1-benzyl-4,5-dihydroimidazole **7** (1.00 g, 6.25 mmol), *n*-butyl-lithium (1.54 M solution in hexanes; 4.50 mL, 6.87 mmol) and 3-methoxybenzaldehyde (0.94 g, 6.87 mmol) to afford after column chromatography eluting with $CHCl_3$–2-aminopropane (99.5 : 0.5 v/v), the *title compound* **8c** (1.08 g, 58%) as a yellow oil; ν_{max}(film)/cm^{-1} 3050, 2950, 2840, 1600, 1260, 780, 700; δ_H 7.23–7.27 (6H, m,

Ar-H), 6.99–7.02 (3H, m, Ar-H), 5.70 (1H, s, C*H*OH), 4.70 (1H, br s, OH), 4.20 (2H, s, PhCH_2), 3.66–3.72 (5H, m, OCH_3 and NCH_2CH_2N), 3.08–3.12 (2H, m, NCH_2CH_2N).

1-Benzyl-2-(4-methoxyphenylhydroxymethyl)-4,5-dihydroimidazole (8e). Prepared by the method described above for the preparation of **8a** but using 1-benzyl-4,5-dihydroimidazole **7** (0.77 g, 4.81 mmol), *n*-butyl-lithium (1.55 M solution in hexanes; 3.25 mL, 5.05 mmol) and 4-methoxybenzaldehyde (0.61 ml, 5.05 mmol) to afford after column chromatography eluting with $CHCl_3$–2-aminopropane (99.5 : 0.5 v/v) to afford after column chromatography eluting with $CHCl_3$–2-aminopropane (99.5 : 0.5 v/v), the *title compound* **8e** (0.82 g, 57%) as a colourless oil; ν_{max}(film)/cm^{-1} 3000, 2950, 2840, 1600, 1510, 1460, 1250, 1180, 1040, 770, 700; δ_H 7.23–7.27 (6H, m, Ar-H), 6.89–7.02 (3H, m, Ar-H), 5.40 (1H, s, C*H*OH), 4.60 (1H, br s, OH), 4.09–4.11 (2H, m, PhCH_2), 3.77–3.84 (5H, m, OCH_3 and NCH_2CH_2N), 3.23–3.27 (2H, m, NCH_2CH_2N); *m*/*z* 296 (M^+, 7%), 294 (10), 265 (11), 205 (15), 197 (36), 160 (31), 135 (60), 91 (100). HRMS: M^+ 296.1521; $C_{18}H_{20}N_2O$ requires M^+ 296.1525.

1-Benzyl-2-(3,4-dimethoxyphenylhydroxymethyl)-4,5-dihydroimidazole (8f). Prepared by the method described above for the preparation of **8a** but using 1-benzyl-4,5-dihydroimidazole **7** (1.00 g, 6.25 mmol), *n*-butyl-lithium (1.54 M solution in hexanes; 4.25 mL, 6.54 mmol) and 3,4-dimethoxybenzaldehyde (1.09 g, 6.54 mmol) to afford after column chromatography eluting with $CHCl_3$–2-aminopropane (99.25 : 0.75 v/v), the *title compound* (1.22 g, 60%) as a colourless gum; ν_{max}(film)/cm^{-1} 3000, 1600, 1450, 1350, 1260, 1230, 760, 700; δ_H 7.18–7.22 (4H, m, Ar-H), 6.93–6.97 (4H, m, Ar-H), 5.45 (1H, s, C*H*OH), 4.60 (1 H, br s, OH), 4.15 (2H, s, PhCH_2), 3.80 (6H, s, 2 × OCH_3), 3.67–3.70, 3.18–3.21 (each 2H, m, NCH_2CH_2N); δ_C 168.0 (C-2), 149.2, 148.9, 136.9, 132.6 (Ar-C), 128.2, 127.2, 127.1, 119.3, 111.1, 110.2 (Ar-CH), 69.1 (CHOH), 55.8, 51.3, 51.0, 50.2 (CH_2 and CH_3); *m*/*z* 326 (M^+, 19%), 235 (11), 227 (37), 165 (33), 159 (20), 120 (14), 91 (100), 77 (10), 65 (13). HRMS: M^+ 326.1630; $C_{19}H_{22}N_2O$ requires M^+ 326.1630.

1-Benzyl-2-(1-*tert*-butyldimethylsilyloxybutyl)-4,5-dihydroimidazole (9a). *Method A*: To 1-benzyl-2-(1-hydroxybutyl)-4,5-dihydroimidazole **8a** (1.13 g, 4.87 mmol) in dry CH_2Cl_2 (10 mL) was added *tert*-butyldimethylsilyl chloride (0.88 g, 5.84 mmol) and 4-(dimethylamino)pyridine (0.71 g, 5.84 mmol) and the resulting mixture stirred at 20 °C for 72 h. The reaction mixture was concentrated under reduced pressure and purified by column chromatography, eluting with $CHCl_3$–2-aminopropane (99.5 : 0.5 v/v) to afford the *title compound* **9a** (0.81 g, 48%) as a colourless oil; ν_{max}(film)/cm^{-1} 2970, 2940, 2860, 1605, 1260, 1080, 845, 780, 760, 700; δ_H 7.32–7.36 (5H, m, Ar-H), 5.0 (1H, d, *J* = 15.0, PhC*H*H), 4.60 (1H, t, *J* = 7.0, C*H*O), 4.30 (1H, d, *J* = 15.0, PhCH*H*), 3.73–3.77, 3.27–3.33 (each 2H, m, NCH_2CH_2N), 1.74–1.76, 1.39–1.43 (each 2H, m, CH_2), 0.97–1.00 (12H, m, 4 × CH_3), 0.20 (6H, s, 2 × CH_3); δ_C 166.3 (C-2), 137.8 (Ar-C), 127.8, 126.4 (Ar-CH), 70.9 (CHO), 51.6, 50.9, 50.6, 37.4 (CH_2), 25.2 (C(*C*H)$_3$), 18.6 (CH_2), 17.3 (*C*(CH)$_3$), 13.1 (CH_3), −5.1, −6.0 (Si(CH_3)$_2$); *m*/*z* 346 (M^+, 13%), 317 (13), 304 (38), 289 (99), 287 (11), 91 (100). HRMS: M^+ 346.2428; $C_{20}H_{34}N_2OSi$ requires M^+ 346.2440.

Method B: Prepared by the method described earlier for the preparation of **8a** but using 1-benzyl-4.5-dihydroimidazole **7** (1.0 g, 6.25 mmol) in dry THF (40 mL), *n*-butyl-lithium (1.50 M solution in hexanes; 4.60 mL, 6.87 mmol) and butanal (0.52 g, 7.20 mmol) After the yellow solution allowed to warm to 20 °C, *tert*-butyldimethylsilyl chloride (1.13 g, 7.50 mmol) in dry THF (5 mL) was added and the mixture stirred for a further 16 h before the addition of water (2.0 mL). The mixture was partitioned between water (50 mL) and $CHCl_3$ (2 × 50 mL) and the combined organic extracts were dried and concentrated under reduced pressure. The residue was purified by column chromatography, eluting with $CHCl_3$–2-aminopropane (99.5 : 0.5 v/v), yielding the *title compound* **9a** (1.43 g, 66%) as a pale yellow oil identical to the sample prepared by *Method A*.

1-Benzyl-2-[phenyl(*tert*-butyldimethylsilyloxy)methyl]-4,5-dihydroimidazole (9b). Prepared by *Method A* described above for the preparation of **9a** but using 1-benzyl-2-(phenylhydroxymethyl)-4,5-dihydroimidazole **8c** (555 mg, 2.01 mmol), *tert*-butyldimethylsilyl chloride (378 mg, 2.50 mmol) and 4-(dimethylamino)pyridine (255 mg, 2.01 mmol) to afford after column chromatography eluting with $CHCl_3$–2-aminopropane (99.5 : 0.5 v/v), the *title compound* **9b** (670 mg, 84%) as a colourless oil; δ_H 7.26–7.34 (8H, m, Ar-H), 6.78–6.81 (2H, m, Ar-H), 5.80 (1H, s, CHO), 4.40, 4.05 (each 1H, d, *J* = 15, PhCH_2), 3.78–3.82, 3.08–3.12 (each 2H, m, NCH_2CH_2N), 1.00 (9H, s, 3 × CH_3), and 0.25 (6H, s, 2 × CH_3); δ_C 166.1 (C-2), 140.2, 137.8 (Ar-C), 128.2, 128.1, 128.0, 127.6, 127.2, 126.9 (Ar-CH), 72.1 (CHO), 52.2, 51.0, 50.6 (CH_2), 25.9 (C(*C*H$_3$)$_3$), 18.3 (*C*(CH$_3$)$_3$), −4.70, −5.35 (Si(CH_3)$_2$); *m*/*z* 380 (M^+, 24%), 324 (29), 323 (100), 133 (12), 91 (75), 75 (18), 73 (25). HRMS: M^+ 380.2278; $C_{23}H_{32}N_2OSi$ requires M^+ 380.2283.

1-Benzyl-2-[phenyl(benzyloxycarbonyloxy)methyl]-4,5-dihydroimidazole (9c). To 1-benzyl-2-(phenylhydroxymethyl)-4,5-dihydroimidazole **8c** (2.04 g, 7.67 mmol) in dry pyridine (6.2 mL), stirred at −20 °C under an atmosphere of nitrogen, was added benzyl chloroformate (1.4 eq., 1.53 mL, 10.74 mmol). The resulting solution was stirred at −20 °C for 2 h then allowed to warm to 20 °C. After a further 24 h the reaction mixture was poured into water (40 mL) and extracted with $CHCl_3$ (2 × 30 mL). The combined organic extracts were dried and concentrated under reduced pressure. The residue was purified by column chromatography eluting with EtOAc–Et_3N (99.25 : 0.75 v/v) to afford the *title compound* **9c** (1.96 g, 64%) as a colourless solid, mp 104–105 °C; ν_{max}(KBr)/cm^{-1} 3027, 2950, 2880, 1750, 1610, 1260, 960, 750, 705; δ_H 7.35–7.44 (13H, m, Ar-CH), 7.08–7.12 (2H, m, Ar-CH), 6.50 (1H, s, CHO), 5.25, 4.20 (each 2H, s, PhCH_2O), 3.83–3.87, 3.17–3.22 (each 2H, m, NCH_2CH_2N); *m*/*z* 400 (M^+, 3%), 250 (12), 249 (19), 175 (15), 167 (11), 107 (28), 105 (63), 91 (100). HRMS: M^+ 400.1774; $C_{25}H_{24}N_2O_3$ requires M^+ 400.1785.

1-Benzyl-2-butanoyl-4,5-dihydroimidazole (11a). Prepared by *Method A* described below for the preparation of **11b** but using 1-benzyl-2-hydroxybutyl-4,5-dihydroimidazole **8a** (1 07 mg, 0.460 mmol) and manganese dioxide (200 mg, 2.30 mmol), and stirring the mixture for 24 h, to afford after column chromatography eluting with EtOAc–Et_3N (99.5 : 0.5 v/v), the

title compound **11a** (56 mg, 53%) as a colourless oil that was not further characterised; ν_{max}(film)/cm^{-1} 2960, 2880, 1700, 1575, 1250, 1130, 1000, 740, 700; δ_H (200 MHz) 7.18–7.23 (5H, m, Ar-CH), 4.50 (2H, s, PhCH_2), 3.75, 3.23 (each 2H, t, J = 9.1, NCH$_2$CH$_2$N), 2.85 (2H, t, J = 7.0, COCH$_2$), 1.60 (2H, sextet, J = 7, COCH$_2$CH_2), 0.90 (3H, t, J = 7, CH$_3$); m/z 230 (M$^+$, 15%), 159 (20), 91 (100).

2-Benzoyl-1-benzyl-4,5-dihydroimidazole (11b). *Method A*: Manganese dioxide (8.00 g) was added to a solution of 1-benzyl-2-(phenylhydroxymethyl)-4,5-dihydroimidazole **8c** (1.16 g, 4.36 mmol) in dry CH_2Cl_2 (50 mL). The slurry was stirred at 20 °C for 2 h before the manganese salts were removed by filtration through celite, washing the filter pad with a further portion of CH_2Cl_2 (100 mL). The combined filtrate was concentrated under reduced pressure and the residue purified by column chromatography eluting with EtOAc–Et$_3$N (99.5 : 0.5 v/v), to afford the *title compound* **11b** (0.77 g, 67%) as a yellow oil; ν_{max}(film)/cm^{-1} 3060, 3040, 2950, 2860, 1670, 1580, 1450, 1385, 1200, 1180, 990, 900, 740, 700; δ_H 8.19–8.21 (2H, m, Ar-CH), 7.58–7.61 (3H, m, Ar-CH), 7.27–7.32 (5H, m, Ar-CH), 4.40 (2H, s, PhCH_2), 3.98, 3.40 (each 2H, t, J = 8.9, NCH$_2$CH$_2$N); δ_C 188.8 (CO), 161.7 (C-2), 140.0, 135.4 (Ar-C), 133.9, 130.1, 128.4, 128.3, 127.8, 127.3 (Ar-CH), 53.8, 51.0, 49.5 (CH$_2$); m/z 264 (M$^+$, 36%), 235 (32), 159 (10), 133 (14), 132 (35), 105 (68), 91 (100), 77 (81). HRMS: M$^+$ 264.1270; $C_{17}H_{16}N_2O$ requires M$^+$ 264.1262.

Method B: To 1-benzyl-4,5-dihydroimidazole **7** (2.41 g, 15.06 mmol) in dry THF (50 mL), stirred at −78 °C under an atmosphere of nitrogen, was added *n*-butyl-lithium (1.50 M solution in hexanes; 10.8 mL, 16.2 mmol). After 20 min, the solution was cooled to −100 °C and added by cannula to a stirred solution of ethyl benzoate (4.07 g, 27.1 mmol) in dry THF (50 mL) cooled to −78 °C under an atmosphere of nitrogen. The mixture was maintained at −78 °C for 1 h, allowed to warm to 20 °C and stirred for a further 3 h before the addition of water (4 mL). The mixture was partitioned between $CHCl_3$ (2 × 100 mL) and water (100 mL). The combined organic extracts were dried and concentrated under reduced pressure and the residue purified by column chromatography, eluting with EtOAc–Et$_3$N (99.5 : 0.5 v/v) to afford the title compound **11b** (2.66 g, 67%) as a colourless oil identical to the sample prepared by *Method A*.

1-Benzyl-2-hexanoyl-4,5-dihydroimidazole (11c). Prepared by *Method B* described above for the preparation of **11b** but using 1-benzyl-4,5-dihydroimidazole **7** (1.49 g, 9.32 mmol), *n*-butyl-lithium (1.60 M solution in hexanes; 6.40 mL, 10.3 mmol) and ethyl hexanoate (2.69 g, 18.6 mmol) to afford after column chromatography, eluting with EtOAc–Et$_2$O (40 : 60 v/v), the *title compound* **11c** (0.98 g, 41%) as a colourless oil that was not further characterised; ν_{max}(film)/cm^{-1} 2920, 2860, 1705, 1575, 1450, 1275; δ_H (200 MHz) 7.28–7.32 (5H, m, Ar-CH), 4.60 (2H, s, PhCH_2), 3.71–3.73, 3.32–34 (each 2H, m, NCH$_2$CH$_2$N), 2.95 (2H, t, J = 7.1, COCH$_2$), 1.59–1.61 (2H, m, COCH$_2$CH_2), 1.34–1.37 (4H, m, 2 × CH$_2$), 0.89–0.91 (3H, m, CH$_3$); m/z 259 (MH$^+$, 43%), 258 (M$^+$, 32), 202 (30), 133 (45), 91 (100), 60 (87).

1-Benzyl-2-decanoyl-4,5-dihydroimidazole (11d). Prepared by *Method B* described above for the preparation of **11b** but using 1-benzyl-4,5-dihydroimidazole **7** (0.51 g, 3.19 mmol), *n*-butyl-lithium (1.55 M solution in hexanes; 2.26 ml, 3.50 mmol) and ethyl decanoate (1.34 g, 6.70 mmol) to afford after column chromatography, eluting with EtOAc–light petroleum–Et$_3$N (89.5 : 1 0 : 0.5 v/v/v), the *title compound* **11d** (0.44 g, 44%) as a colourless oil; ν_{max}(film)/cm^{-1} 2920, 2860, 1700, 1575, 1450, 740; δ_H 7.32–7.36 (5H, m, Ar-H), 4.60 (2H, s, PhCH_2), 3.74–3.77, 3.28–3.31 (each 2H, m, NCH$_2$CH$_2$N), 2.95 (2H, t, J = 7.0, COCH$_2$), 1.58–1.61 (2H, m, COCH$_2$CH_2), 1.25 (12H, m, 6 × CH$_2$), 0.84–0.86 (3H, m, CH$_3$); δ_C 197.6 (CO), 161.1 (C-2), 137.8 (Ar-C), 128.5, 127.7, 137.5 (Ar-CH), 52.7, 51.0, 50.7, 40.3, 31.8, 29.3, 29.2, 29.1, 29.0, 23.6, 22.6 (CH$_2$), 14.0 (CH$_3$); m/z 315 (MH$^+$, 14%), 314 (M$^+$, 26), 223 (19), 202 (41), 133 (70), 91 (100). HRMS: M$^+$ 314.2361; $C_{20}H_{30}N_2O$ requires M$^+$ 314.2356.

1-Benzyl-2-(1-hydroxy-1-phenylethyl)-4,5-dihydroimidazole (12a). To 1-benzyl-2-benzoyl-4,5-dihydroimidazole **11b** (370 mg, 1.40 mmol) in dry THF (10 mL), stirred at −78 °C under an atmosphere of nitrogen, was added methyl-lithium (1.60 M solution in ether; 1.10 mL, 1.75 mmol). The mixture was maintained at −78 °C for 30 min before the addition of water (2 mL), warmed to 20 °C and partitioned between water (25 mL) and $CHCl_3$ (2 × 25 mL). The combined organic extracts were dried, concentrated under reduced pressure and the residue was washed with ether (4 × 10 mL) to afford the *title compound* **12a** (186 mg, 69%) as a colourless solid, mp 143 °C; ν_{max}(KBr)/cm^{-1} 3050, 2850, 1600, 1400, 1240, 1210, 1150, 1120, 1020, 750, 710; δ_H (250 MHz) 7.54–7.56 (2H, m, Ar-H), 7.28–7.33 (6H, m, Ar-H). 6.89–6.91 (2H, m, Ar-H), 4.03, 3.87 (each 1H, d, J = 14.8, PhCH_2), 3.76–3.79, 3.23–3.26 (each 2H, m, NCH$_2$CH$_2$N), 1.9 (3H, s, CH$_3$); m/z 280 (M$^+$, 4%), 189 (23), 160 (10), 120 (6), 113 (25), 105 (29), 91 (100), 77 (46). HRMS: M$^+$ 280.1572; $C_{18}H_{20}N_2O$ requires M$^+$ 280.1575.

1-Benzyl-2-(1-hydroxy-1-phenylpentyl)-4,5-dihydroimidazole (12b). Prepared by the method described above for the preparation of **12a** but using 1-benzyl-2-benzoyl-4,5-dihydroimidazole **11b** (82.0 mg, 0.310 mmol), *n*-butyl-lithium (1.40 M solution in hexanes; 0.27 mL, 0.390 mmol) to afford after column chromatography eluting with EtOAc–Et$_3$N (99.5 : 0.5 v/v), the *title compound* **12b** (86 mg, 59%) as a colourless oil; δ_H 7.46–7.54 (8H, m, Ar-H), 7.38–7.41 (2H, m, Ar-H), 4.30 (1H. br s, OH), 3.99–4.01 (2H, m, PhCH_2), 3.78–3.81, 3.29–3.32 (each 2H, m, NCH$_2$CH$_2$N), 2.29–2.32 (2H, m, C(OH)CH_2), 1.38–1.42 (4H, m, 2 × CH$_2$), 0.94–0.96 (3H, m, CH$_3$); m/z 322 (M$^+$, 2%), 266 (13), 175 (30), 160 (21), 120 (33), 105 (60), 91 (100), 77 (55), 51 (15). HRMS: M$^+$ 322.2017; $C_{21}H_{26}N_2O$ requires M$^+$ 322.2045.

1-Benzyl-2-(diphenylhydroxymethyl)-4,5-dihydroimidazole (12c). *Method A*: Prepared by the method described above for the preparation of **12a** but using 1-benzyl-2-benzoyl-4,5-dihydroimidazole **11b** (600 mg, 2.27 mmol), phenyl-lithium (1.70 M solution in cyclohexane–Et$_2$O; 2.0 mL, 3.41 mmol) to afford after purification by crystallisation from $CHCl_3$–Et$_2$O the title compound **12c** (71 0 mg, 92%) as a colourless solid, mp 115 °C, identical to the sample prepared by *Method B* below.

Method B: To 1-benzyl-4,5-dihydroimidazole 7 (1.08 g, 6.73 mmol) in dry THF (40 mL), stirred at −78 °C under an atmosphere of nitrogen, was added *n*-butyl-lithium (1.50 M solution in hexanes; 4.95 mL, 7.40 mmol). After 20 min, benzophenone (1.35 g, 7.40 mmol) in dry THF (5 ml) was added dropwise and the mixture stirred at −78 °C for 1 h then allowed to warm to 20 °C and stirred for a further 1 h before addition of water (2 mL). The mixture was concentrated under reduced pressure and partitioned between water (50 mL) and $CHCl_3$ (2 × 50 mL). The combined organic extract was dried and concentrated under reduced pressure to leave a waxy solid purified by trituration from $CHCl_3$–Et_2O to afford the *title compound* **12c** (1.13 g, 50%) as a colourless solid, mp 115–116 °C (Found: C, 80.8; H, 6.7; N, 6.1%; $C_{23}H_{22}N_2O$ requires C, 80.7; H, 6.5; N, 6.2%); ν_{max}(KBr)/cm^{-1} 3100, 2850, 1590, 1365, 1260, 1235, 1190, 1000, 750, 705; δ_H (400 MHz) 7.56–7.60 (4H, m, Ar-H), 7.44–7.49 (6H, m, Ar-H), 7.15–7.17 (3H, m, Ar-H), 6.69–6.71 (2H, m, 2 × Ar-H), 3.96 (2H, s, PhCH_2), 3.80, 3.35 (each 2H, t, J = 9.9, NCH_2CH_2N); δ_C (100 MHz) 169.6 (C-2), 142.7, 137.1 (Ar-C), 128.3, 128.3, 128.0, 127.5, 127.4, 127.3 (Ar-CH), 78.0 (COH), 52.7, 52.4, 51.1 (NCH_2); *m*/*z* (M^+ not observed), 182 (39), 160 (24), 105 (1 00), 91 (89), 77 (73), 51 (55).

1-Benzyl-2-(1-hydroxy-1-phenylprop-2-enyl)-4,5-dihydroimidazole (12d). Prepared by the method described above for the preparation of **12a** but using 1-benzyl-2-benzoyl-4,5-dihydroimidazole **11b** (600 mg, 2.27 mmol), ethenylmagnesium bromide (1.0 M solution in THF; 3.40 mL, 3.40 mmol) at 20 °C to afford after column chromatography eluting with $CHCl_3$–2-aminopropane (99.5 : 0.5 v/v), the *title compound* **12d** (588 mg, 89%) as a colourless solid, mp 99–101 °C; ν_{max}(KBr)/cm^{-1} 3050, 2870, 1590, 1280, 1250, 1200, 1000, 750, 700; δ_H 7.27–7.33 (8H, m, Ar-H), 6.89–6.91 (2H, m, Ar-H), 6.5 (1H, dd, J = 10.0, 17.1, C*H*═CH_2), 5.55 (1H, dd, J = 1.0, 17.1, CH═C*H*H), 5.35 (1H, dd, J = 1.0, 10.0, CH═CH*H*), 4.60 (1H, br s, OH), 3.95 (2H, s, PhCH_2), 3.78–3.81, 3.19–3.22 (each 2H, m, NCH_2CH_2N); δ_C 168.7 (C-2), 142.2, 137.6 (Ar-C), 140.3 (*C*H═CH_2), 128.5, 128.3, 127.8, 127.6, 127.2, 126.3 (Ar-CH), 114.9 (CH═*C*H_2), 75.7 (COH), 52.0, 51.9, 51.5 (CH_2); *m*/*z* 292 (M^+, 5%), 275 (7), 160 (28), 132 (19), 105 (56), 91 (100), 77 (33). HRMS: M^+ 292.1562; $C_{19}H_{20}N_2O$ requires M^+ 292.1575.

1-Benzyl-2-(1-hydroxy-1-phenylpropyl)-4,5-dihydroimidazole (12e). *Method A*: Prepared by the method described above for the preparation of **12a** but using 1-benzyl-2-benzoyl-4,5-dihydroimidazole **11b** (1.047 g, 3.97 mmol) and ethylmagnesium bromide (4.77 mmol in THF) at 20 °C, to afford after column chromatography eluting with EtOAc–Et_3N (99.5 : 0.5 v/v), the *title compound* **12e** (366 mg, 31%) as a colourless solid, mp 123–124 °C, identical to the sample prepared by *Method B* below. Also isolated from this reaction was 1-benzyl-2-(phenylhydroxymethyl)-4,5-dihydroimidazoline **8c** (420 mg, 40%), identical to the sample described earlier.

Method B: Prepared by *Method B* described above for the preparation of **12c** but using 1-benzyl-4,5-dihydroimidazole **7** (0.70 g, 4.38 mmol), *n*-butyl-lithium (1.50 M solution in hexanes; 3.20 mL, 4.81 mmol) and 1-phenylpropan-1-one (0.64 mL, 4.81 mmol) to afford trituration from $CHCl_3$–Et_2O, the *title compound* **12e** (653 mg, 50%) as a colourless solid, mp 123–124 °C (Found: C, 77.3; H, 7.4; N, 9.6%; $C_{19}H_{22}N_2O$ requires C, 77.5; H, 7.5; N, 9.5%); ν_{max}(KBr)/cm^{-1} 3100, 2850, 1600, 1400, 1230, 995, 770, 710; δ_H (250 MHz) 7.44–7.46 (2H, m, Ar-H), 7.13–7.17 (6H, m, Ar-H), 6.7–6.9 (2H, m, Ar-H), 4.80 (1H, br s, OH), 3.95, 3.75 (each 1H, d, J = 14.7, PhCH_2), 3.65–3.69, 3.08–3.12 (each 2H, m, NCH_2CH_2N), 2.20–2.23 (2H, m, CH_2CH_3), 0.90 (3H, t, J = 7.3, CH_3); *m*/*z* 294 (M^+, 4%), 266 (14), 203 (11), 175 (26), 160 (23), 134 (11), 127 (18), 105 (74), 91 (100), 77 (34). HRMS: M^+ 294.1749; $C_{19}H_{22}N_2O$ requires M^+ 294.1732.

1-Benzyl-2-(1-hydroxy-1-phenylnonyl)-4,5-dihydroimidazole (12f). Prepared by the method described above for the preparation of **12a** but using 1-benzyl-2-benzoyl-4,5-dihydroimidazole **11b** (540 mg, 2.05 mmol) and octylmagnesium bromide (1.03 M solution in THF; 3.0 mL, 3.07 mmol) at 20 °C to afford after column chromatography eluting with $CHCl_3$–2-aminopropane (99.5 : 0.5 v/v), the title compound **12f** (326.5 mg, 42%) as a colourless solid, mp 83–85 °C (Found: C, 78.9; H, 9.1; N, 7.4%; $C_{25}H_{34}N_2O$ requires C, 79.3; H, 9.0; N, 7.4%); ν_{max}(KBr)/cm^{-1} 3080, 2920, 2850, 1580, 1450, 1420, 1280, 1250, 700; δ_H 7.27–7.32 (8H, m, Ar-H), 6.89–6.91 (2H, m, Ar-H), 4.7 (1H, br s, OH), 3.95 (2H, s, PhCH_2), 3.68–3.71, 3.19–3.22 (each 2H, m, NCH_2CH_2N), 2.24–2.26 (2H, m, C(OH)CH_2), 1.30–1.38 (10H, m, 5 × CH_2), 0.88–0.90 (3H, m, CH_3); δ_C 169.3 (C-2), 143.2, 137.8 (Ar-C), 128.2, 128.0, 127.5, 127.4, 127.1, 125.9 (Ar-CH), 74.8 (COH), 52.1, 52.0, 51.2, 39.2, 31.8, 29.9, 29.5, 29.2, 23.3, 22.6 (CH_2); *m*/*z* 378 (M^+, 0.4%), 218 (10), 160 (22), 133 (12), 120 (100), 105 (94), 91 (72), 77 (36). HRMS: M^+ 378.2700; $C_{25}H_{34}N_2O$ requires M^+ 378.2671.

1-Benzyl-2-(1-hydroxy-1-methylhexyl)-4.5-dihydroimidazole (12g). Prepared by the method described above for the preparation of **12a** but using 1-benzyl-2-hexanoyl-4,5-dihydroimidazole **11c** (136 mg, 0.530 mmol) and methylmagnesium bromide (3.0 M solution in Et_2O; 0.300 mL, 0.790 mmol) at 20 °C to afford the *title compound* **12g** (81 mg, 56%) as a colourless solid, mp 96–98 °C (Found: C, 74.0; H, 9.6; N, 9.9%; $C_{17}H_{26}N_2O$ requires C, 74.4; H, 9.6; N, 10.2%); ν_{max}(KBr)/cm^{-1} 3120, 2940, 2850, 1590, 1405, 1360, 1270, 1140, 1000, 950, 850; δ_H 7.27–7.32 (5H, m, Ar-H), 4.44–4.46 (2H, m, PhCH_2), 3.70, 3.30 (each 2H, t, J = 9.0, NCH_2CH_2N), 1.70–1.72 (2H, m, C(OH)CH_2), 1.55 (3H, s, COHCH_3), 1.28–1.33 (6H, m, 3 × CH_2), 0.88–0.90 (3H, m, CH_3); *m*/*z* 275 (MH^+, 15%), 274 (M^+, 10), 259 (6), 204 (25), 113 (1 00), 91 (70).

1-Benzyl-2-(1-hydroxy-1-phenylhexyl)-4,5-dihydroimidazole (12h). Prepared by the method described above for the preparation of **12a** but using 1-benzyl-2-hexanoyl-2-imidazoline **11c** (237 mg, 0.920 mmol) and phenylmagnesium bromide (3.0 M solution in Et_2O; 0.380 mL, 1.15 mmol) at 20 °C to afford after column chromatography eluting with EtOAc–Et_2O–Et_3N (79.5 : 20 : 0.5 v/v), the *title compound* **12h** (142 mg, 46%) as a colourless solid, mp 104 °C (Found: C, 77.9; H, 8.5; N, 8.2%; $C_{22}H_{28}N_2O$ requires C, 78.4; H, 8.4; N, 8.3%); ν_{max}(KBr)/cm^{-1} 3060, 2940, 1570, 1440, 1280, 1150, 700; δ_H (200 MHz) 7.48–7.52 (2H, m, Ar-H), 7.27–7.33 (6H, m, Ar-H), 6.88–6.91 (2H, m, Ar-H), 4.55 (1H, br s, OH), 4.00, 3.85 (each 1H, d, J = 15, $PhCH_2$), 3.78–3.81, 3.24–3.27 (each 2H, m, NCH_2CH_2N),

2.23–2.26 (2H, m, C(OH)CH_2), 1.42–1.47 (6H, m, 3 × CH_2), 0.89–0.91 (3H, m, CH_3); *m*/*z* 336 (M^+, 8%), 266 (20), 245 (5), 175 (35), 160 (10), 120 (20), 105 (60), 91 (100), 77 (45).

1-Benzyl-2-(1-ethyl-1-hydroxypropyl)-4,5-dihydroimidazole (12i). Prepared by *Method B* described above for the preparation of **12c** but using 1-benzyl-4,5-dihydroimidazole **7** (1.00 g, 6.25 mmol), *n*-butyllithium (1.50 M solution in hexanes; 4.55 mL, 6.80 mmol) and pentan-3-one (0.59 g, 6.80 mmol) to afford after column chromatography eluting with $CHCl_3$–2-aminopropane (99.5 : 0.5 v/v) the *title compound* **12i** (560 mg, 38%) as a colourless gum; ν_{max}(KBr)/cm^{-1} 3100, 2980, 2960, 1600, 1370, 1280, 705; δ_H 7.37–7.42 (5H, m, Ar-H), 4.70 (1H, br s, OH), 4.45 (2H, s, PhCH_2), 3.70, 3.30 (each 2H, t, *J* = 8.9, NCH_2CH_2N), 1.80 (4H, q, *J* = 7, 2 × CH_2CH_3), 0.95 (6H, t, *J* = 7.0, 2 × CH_3); δ_C 169.4 (C-2), 137.7 (Ar-C), 128.7, 127.5, 127.3 (Ar-CH), 72.3 (COH). 52.8, 52.2, 50.6 (NCH_2), 32.1 (CH_2CH_3), 8.02 (CH_3); *m*/*z* 246 (M^+, 9%), 229 (9), 217 (24), 127 (81), 91 (100), 65 (13), 57 (16). HRMS: M^+ 246.1730; $C_{15}H_{22}N_2O$ requires M^+ 246.1732.

1-Benzyl-2-(1-ethyl-1-hydroxyprop-2-enyl)-4,5-dihydroimidazole (12j). Prepared by *Method B* described above for the preparation of **12c** but using 1-benzyl-4,5-dihydroimidazole **7** (1.00 g, 6.25 mmol), *n*-butyllithium (1.50 M solution in hexanes; 4.55 mL, 6.80 mmol) and pent-1-en-3-one (0.58 g, 6.88 mmol) to afford after column chromatography eluting with $CHCl_3$–2-aminopropane (99.5 : 0.5 v/v) the *title compound* (540 mg, 35%) as a colourless solid, mp 68–72 °C; ν_{max}(KBr)/cm^{-1} 3150, 2980, 2940, 2880, 1590, 1410, 1360, 1250, 1180, 1000, 970, 740, 700; δ_H (250 MHz) 7.33–7.37 (5H, m, Ar-CH), 6.13 (1 H, dd, *J* = 10.6, 17.3, C*H*=CH_2), 5.50 (1H, dd, *J* = 1.1, 17.3, CH=C*H*H), 5.30 (1H, dd, *J* = 1.1, 10.6, CH=CH*H*), 4.65 (1H, br s OH), 4.45, 4.30 (each 1H, d, *J* = 15, PhCH_2), 3.73–3.77, 3.28–3.32 (each 2H, m, NCH_2CH_2N), 1.94–1.6 (2H, m, CH_2), 1.05 (3H, t, *J* = 7.4, CH_3); δ_C 168.9 (C-2), 140.4 (*C*H=CH_2), 137.8 (Ar-C), 128.6, 127.4, 127.3 (Ar-CH), 115.5 (CH=*C*H_2), 74.0 (COH), 52.7, 52.3, 51.0 (NCH_2), 31.2 (CH_2CH_3), 7.7 (CH_3); *m*/*z* 244 (M^+, 2%), 227 (17), 216 (13), 215 (14), 160 (21), 153 (17), 125 (10), 91 (100). HRMS: M^+ 244.1585; $C_{15}H_{20}N_2O$ requires M^+ 244.1574.

1-Benzyl-2-(1-hydroxycyclohex-1-yl)-4,5-dihydroimidazole (12k). Prepared by *Method B* described above for the preparation of **12c** but using 1-benzyl-4,5-dihydroimidazole **7** (0.58 g, 3.63 mmol), *n*-butyl-lithium (1.60 M solution in hexanes; 2.50 mL, 4.0 mmol) and cyclohexanone (0.45 mL, 4.35 mmol) to afford after trituration from $CHCl_3$-Et_2O, the *title compound* **12k** (302 mg, 35%) as a colourless solid, mp 133–135 °C (Found: C, 74.35; H, 8.9; N, 10.7%; $C_{16}H_{22}N_2O$ requires C, 74.4; H, 8.6; N, 10.8%); ν_{max}(KBr)/cm^{-1} 3100, 1960, 2880, 1600, 705; δ_H (250 MHz) 7.22–7.27 (5H, m, Ar-CH), 4.60 (2H, s, PhCH_2), 3.70 (2H, t, *J* = 10.3, NC$H_2$$CH_2$N), 3.48 (1H, br s, OH), 3.30 (2H, t, *J* = 10.3, NCH_2CH_2N), 1.77–1.82 (9H, m, 4 × CH_2, C*H*H), 1.24–1.26 (1H, m, CH*H*); δ_C 170.9 (C-2), 138.4 (Ar-C), 128.6, 128.5, 127.1 (Ar-CH), 71.2 (COH), 52.5, 52.1, 51.4 (NCH_2), 36.1, 25.5, 21.6 (CH_2); *m*/*z* 258 (M^+, 21%), 242 (10), 241 (58), 203 (36), 167 (50), 91 (100), 71 (12). HRMS: M^+ 258.1760; $C_{16}H_{22}N_2O$ requires M^+ 258.1732.

Preparation of ketones (13) from tertiary alcohols (12) by acidification

General method A. The appropriate 1-benzyl-2-(1-hydroxyalkyl)-4,5-dihydroimidazole **12** in alumina-washed chloroform (20 mL) was heated under gentle reflux with conc. hydrochloric acid (36% w/w, 4 drops) for 4 h. The mixture was cooled, concentrated under reduced pressure and the crude product purified by column chromatography eluting with EtOAc–Et_3N (99.5 : 0.5 v/v).

Acetophenone (13a). Prepared from 1-benzyl-2-(1-hydroxy-1-phenylethyl)-4,5-dihydroimidazole **12a** (175 mg, 0.624 mmol) by the general method to afford the *title compound* (70 mg, 94%) as a colourless oil, identical to a commercial sample.

1-Phenylpentan-1-one (13b). Prepared from 1-benzyl-2-(1-hydroxy-1-phenylpentyl)-4,5-dihydroimidazole **12b** (152 mg, 0.470 mmol) by the general method to afford the *title compound* **13b** (60 mg, 79%) as a colourless oil; ν_{max}(film)/cm^{-1} 3060, 2980, 2870, 1680, 1460, 1270, 1210, 700; δ_H 7.92–7.95 (2H, m, Ar-H), 7.48–7.53 (3H, m, Ar-H), 3.90 (2H, t, *J* = 7.2, CH_2CO), 1.47–1.52 (4H, m, 2 × CH_2), 0.93–0.96 (3H, m, CH_3); δ_C 200.4 (CO), 137.3 (Ar-C), 132.8, 128.6, 128.1 (Ar-CH), 38.3 (CH_2CO), 26.6, 22.5 (CH_2), 13.9 (CH_3); *m*/*z* 162 (M^+, 9%), 120 (47), 105 (100), 85 (7), 77 (41). HRMS: M^+ 162.1055; $C_{11}H_{14}O$ requires M^+ 162.1045.

Benzophenone (13c). Prepared from 1-benzyl-2-(diphenylhydroxymethyl)-4,5-dihydroimidazole **12c** (429 mg, 1.25 mmol) by the general method to afford the *title compound* **13c** (227 mg, 99%) as a pale yellow solid, mp 46–48 °C (lit.,[13] 48 °C), identical with a commercial sample.

1-Phenylpropan-1-one (13d). Prepared from 1-benzyl-2-(1-hydroxy-1-phenylpropyl)-4,5-dihydroimidazole **12e** (150 mg, 0.510 mmol) by the general method to afford the *title compound* **13d** (36 mg, 52%) as a colourless oil; ν_{max}(film)/cm^{-1} 3060, 2960, 2940, 1675, 1600, 1450, 1350, 1220, 950, 760, 700; δ_H 7.94–7.97 (2H, m, Ar-H), 7.48–7.52 (3H, m, Ar-H), 3.0 (2H, q, *J* = 7.2, CH_2), 1.25 (3H, t, *J* = 7.2, CH_3); δ_C 200.4 (CO), 137.2 (Ar-C), 132.9, 128.6, 128.1 (Ar-CH), 31.9 (CH_2), 8.4 (CH_3); *m*/*z* 134 (M^+, 25%), 113 (15), 105 (100), 77 (37), 51 (11). HRMS: M^+ 134.0714; $C_9H_{10}O$ requires M^+ 134.0731.

1-Phenylnonan-1-one (13e). Prepared from 1-benzyl-2-(1-hydroxy-1-phenylnonyl)-4,5-dihydroimidazole **12f** (297 mg, 0.807 mmol) by the general method but using $CDCl_3$ as the solvent, acidic impurities in this solvent as the catalyst and heating under reflux for 48 h, to afford the *title compound* **13e** (147 mg, 83%) as a colourless oil; ν_{max}(film)/cm^{-1} 3060, 2930, 2860, 1680, 1600, 1450, 1225, 700; δ_H 7.98–8.01 (2H, m, Ar-H), 7.54–7.57 (3H, m, ArH), 2.95 (2H, t, *J* = 7.0, $COCH_2$), 1.69–1.72 (2H, m, $COCH_2CH_2$), 1.30 (10H, m, 5 × CH_2), 0.89–0.91 (3H, m, CH_3); δ_C 200.4 (CO), 137.3 (Ar-C), 132.8, 128.6, 128.1 (Ar-CH), 38.6, 31.9, 29.5, 29.2, 24.5, 22.7 (CH_2), 14.0 (CH_3); *m*/*z* 318 (M^+, 10%), 133 (13), 120(100), 105 (98), 77 (40). HRMS: M^+ 218.1672; $C_{15}H_{22}O$ requires M^+ 218.1670.

1-Benzyl-3-methyl-4,5-dihydroimidazolium iodide 15a. Iodomethane (6.24 mL, 100 mmol) was added to 1-benzyl-4,5-dihydroimidazole **7** in dry THF (40 mL) and the mixture stirred at 20 °C for 1.5 h. The colourless crystals were collected by

filtration, washed with dry THF (100 mL) and dried under reduced pressure to afford the *title compound* **15a** (7.20 g, 96%), mp 127–128 °C (Found: C, 43.6; H, 5.1; N, 9.2%; $C_{11}H_{15}N_2I$ requires C, 43.7; H, 5.0; N, 9.3%); ν_{max}(KBr)/cm^{-1} 3050, 2980, 1660, 1440, 1310, 1230, 1140, 760, 710; δ_H 9.50 (1H, s, 2-CH), 7.32–7.37 (5H, m, Ar-H), 4.80 (2H, s, PhCH_2), 3.85–3.95 (4H, m, NCH_2CH_2N), 3.30 (3H, s, CH_3).

Preparation of ketones (13) from tertiary alcohols (12) by quaternisation

General method B. To the appropriate 1-benzyl-2-(1-hydroxyalkyl)-4,5-dihydroimidazole **12** in dry THF was added excess iodomethane and the mixture stirred at 20 °C for 24 h. After filtration and concentration of the filtrate under reduced pressure, the residue was purified by column chromatography eluting with $CHCl_3$–2-aminopropane (99.5 : 0.5 v/v). The filtered solid was dried and identified as 1-benzyl-3-methyl-4,5-dihydroimidazolium iodide **15a** (85–90%), identical to the sample described above.

Acetophenone (13a). Prepared from 1-benzyl-2-(1-hydroxy-1-phenylethyl)-4,5-dihydroimidazole **12a** (70.5 mg, 0.252 mmol) in dry THF (15 mL) and iodomethane (0.31 mL, 5.04 mmol) by the general method to afford the *title compound* **13a** (27.5 mg, 91%) as a colourless oil identical to a sample prepared from **12a** by acidification using *General Method A*.

Benzophenone (13c). Prepared from 1-benzyl-2-(diphenylhydroxymethyl)-4,5-dihydroimidazole **12c** (290 mg, 0.850 mmol) in dry THF (15 mL) and iodomethane (1.50 g, 6.80 mmol) by the general method to afford the *title compound* **13c** (155 mg, 83%) as a colourless solid, identical to a sample prepared from **12c** by acidification using *General Method A*.

Acyl transfer to nucleophiles from 2-benzoyl-1-benzyl-4,5-dihydroimidazole (11b)

2-Benzoyl-1-benzyl-3-methyl-4,5-dihydroimidazolium iodide. Iodomethane (0.360 mL, 5.73 mmol) was added dropwise to 2-benzoyl-1-benzyl-4,5-dihydroimidazole **11b** (505 mg, 1.91 mmol) in dry THF (10 mL) under an atmosphere of nitrogen and the mixture stirred at 20 °C for 2 h before being concentrated under reduced pressure to afford the *title compound* (745 mg, 100%) as a foamy orange solid that was used directly; ν_{max}($CHCl_3$)/cm^{-1} 2950, 1680, 1620, 1450, 1310, 1200; δ_H 8.48–8.52 (2H, m, Ar-H), 7.79–7.83 (3H, m, Ar-H), 7.27–7.33 (5H, m, Ar-H), 4.52–4.57 (6H, m, $CH_2NCH_2CH_2N$), 3.15 (3H, s, CH_3).

Benzoic acid (16a). 2-Benzoyl-1-benzyl-3-methyl-4,5-dihydroimidazolium iodide (745 mg, 1.91 mmol) was stirred at 20 °C in aqueous NaOH (2% w/v, 20 mL) for 4 h. The solution was washed with $CHCl_3$ (25 mL), acidified using hydrochloric acid (5% w/v, 20 mL), and the acidic solution extracted with $CHCl_3$ (2 × 25 mL). The combined organic extracts were dried and concentrated under reduced pressure to yield the *title compound* **16a** (175 mg, 75%) as a colourless solid, mp 121–122 °C (lit.,[14] 122 °C), identical with a commercial sample.

Ethyl benzoate (16b). 2-Benzoyl-1-benzyl-3-methyl-4,5-dihydroimidazolium iodide prepared from 2-benzoyl-1-benzyl-4,5-dihydroimidazoline **11b** (497 mg, 1.88 mmol) as described above, was heated under reflux in EtOH (20 mL) for 20 h. The mixture was cooled, concentrated under reduced pressure, and the residue purified by column chromatography eluting with EtOAc to afford the *title compound* **16b** (206 mg, 73%) as a colourless oil, identical to a commercial sample.

***S*-Butyl thiobenzoate (16c).** 2-Benzoyl-1-benzyl-3-methyl-4,5-dihydroimidazolium iodide prepared from 2-benzoyl-1-benzyl-4,5-dihydroimidazole **11b** (169 mg, 0.64 mmol) as described above, was heated with butanethiol (0.350 mL, 3.20 mmol). Under reflux in dry THF (10 mL) for 40 h. The mixture was cooled, concentrated under reduced pressure, and the residue purified by column chromatography eluting with Et_3N–EtOAc (0.5 : 99.5 v/v) to afford the *title compound* **16c** (183 mg, 95%) as a pale yellow oil; ν_{max}(film)/cm^{-1} 2980, 1665, 1440, 1215, 920, 790; δ_H 7.94–79.6 (2H, m, Ar-H), 7.43–7.46 (3H, m, Ar-H), 3.05 (2H, t, J = 7.0, SCH_2), 1.48–1.53 (4H, m, $SCH_2CH_2CH_2$), 0.95 (3H, t, J = 7.0, CH_3); δ_C 191.8 (CO), 137.4 (Ar-C), 133.1, 128.5, 127.2 (Ar-CH), 31.7 (SCH_2), 28.7, 22.1 (CH_2), 13.6 (CH_3); m/z 194 (M^+, 4%), 105 (100), 77 (23), 57 (10). HRMS: M^+ 194.0774; $C_{11}H_{14}OS$ requires M^+ 194.0765. Also isolated from the column after eluting with MeOH, was 1-benzyl-3-methyl-4,5-dihydroimidazolium iodide **15a** (182.6 mg, 95%) identical to the sample described above.

***N*-Benzylbenzamide (16d).** 2-Benzoyl-1-benzyl-3-methyl-4,5-dihydroimidazolium iodide prepared from 2-benzoyl-1-benzyl-4,5-dihydroimidazole **11b** (456 mg, 1.73 mmol) as described above, was heated with benzylamine (0.37 mL, 1.73 mmol) under reflux in dry THF (20 mL) for 20 h. The mixture was cooled, concentrated under reduced pressure, and the residue purified by column chromatography eluting with EtOAc–Et_3N (99.5 : 0.5 v/v) to afford the *title compound* **16d** (293 mg, 80%) as a pale yellow solid, mp 104–106 °C (lit.,[15] 104–106 °C).

***N*-Butylbenzamide (16e).** 2-Benzoyl-1-benzyl-3-methyl-4,5-dihydroimidazolium iodide prepared from 2-benzoyl-1-benzyl-4,5-dihydroimidazole **11b** (379 mg, 1.43 mmol) as described above, was heated with butan-1-amine (0.71 mL, 2.86 mmol) under reflux in dry THF (20 mL) for 8 h. The mixture was cooled, concentrated under reduced pressure, and the residue purified by column chromatography eluting with EtOAc–light petroleum (1 : 2 v/v) to afford the *title compound* **16d** (147 mg, 58%) as a colourless oil; ν_{max}(film)/cm^{-1} 3320, 2940, 1630, 1550, 1300; δ_H 7.74–7.76 (2H, m, Ar-H). 7.38–7.41 (3H, m, Ar-H), 6.75 (1H, br s, NH), 3.40 (2H, q, J = 6.5, $NHCH_2$), 1.49–1.53 (4H, m, NCH_2CH_2), 0.9 (3H, t, J = 6, CH_3); δ_C 167.6 (CO), 134.9 (Ar-C), 131.0, 128.2, 126.9 (Ar-CH), 39.7 ($NHCH_2$), 31.6, 20.0 (CH_2), 13.6 (CH_3); m/z 177 (M^+, 16%), 135 (13), 134 (13), 105 (100), 77 (27). HRMS: M^+ 177.1169; $C_{11}H_{15}NO$ requires M^+ 177.1154.

Methyl benzoate (16f). 2-Benzoyl-1-benzyl-4,5-dihydroimidazole **11b** (358 mg, 1.37 mmol) and ammonium acetate (115 mg, 1.49 mmol) were stirred in dry MeOH (10 mL) at 20 °C for 3 h before being concentrated under reduced pressure, partitioned between $CHCl_3$ (2 × 30 mL) and hydrochloric acid (5% w/v, 30 mL). The combined organic extract was dried and concentrated under reduced pressure to afford the *title compound* **16f** (131 mg, 71%), identical to a commercial sample.

1-Phenylpentan-1-one (13b). To 2-benzoyl-1-benzyl-3-methyl-4,5-dihydroimidazolium iodide prepared from 2-benzoyl-1-benzyl-4,5-dihydroimidazole **11b** (365 mg, 1.38 mmol) as described above, stirred under an atmosphere of nitrogen at −78 °C in dry THF (15 mL), was added *n*-butyl-lithium (1.50 M solution in hexanes; 1.10 mL, 1.66 mmol). After 30 min the mixture was warmed to 20 °C before the addition of water (2.0 mL) and partially concentration under reduced pressure. The residue was partitioned between $CHCl_3$ (2 × 30 mL) and water (30 mL), the combined organic extract dried and concentrated under reduced pressure, and the residue purified by column chromatography eluting with EtOAc to afford the *title compound* (67 mg, 30%) as a colourless oil, identical to the sample described above.

Acknowledgements

The authors thank EPSRC and AstraZeneca Pharmaceuticals for support (J. R. N.) and Dr M. Cox for helpful discussions.

Notes and references

1 R. C. F. Jones and P. Dimopoulos, *Tetrahedron*, 2000, **56**, 2061; R. C. F. Jones, J. S. Snaith, M. W. Anderson and M. J. Smallridge, *Tetrahedron*, 1997, **53**, 1111; R. C. F. Jones and J. Schofield, *J. Chem. Soc., Perkin Trans. 1*, 1990, 375; R. C. F. Jones, M. J. Smallridge and C. B. Chapleo, *J. Chem. Soc., Perkin Trans. 1*, 1990, 385.

2 For leading references, see: R. C. F. Jones, *Adv. Heterocycl. Chem.*, 2010, **101**, 125.

3 R. C. F. Jones and J. R. Nichols, *Tetrahedron*, 2013, **63**, 4114.

4 H. Zhao, F. W. Foss and R. Breslow, *J. Am. Chem. Soc.*, 2008, **130**, 12590; R. Breslow, *J. Am. Chem. Soc.*, 1957, **79**, 1762; R. Breslow, *J. Am. Chem. Soc.*, 1958, **80**, 3719.

5 See for example: C. Samojlowicz, M. Bieniek and K. Greal, *Chem. Rev.*, 2009, **109**, 3708; S. Diez-Gonzalez, N. Marion and S. P. Nolan, *Chem. Rev.*, 2009, **109**, 3612.

6 For leading references, see: D. Enders, O. Niemeier and A. Henseler, *Chem. Rev.*, 2007, **107**, 5606; E. M. Phillips, T. E. Reynolds and K. A. Scheidt, *J. Am. Chem. Soc.*, 2008, **130**, 2417; V. Nair, S. Vellalath and B. P. Babu, *Chem. Soc. Rev.*, 2008, **37**, 2691; C. D. Campbell, C. Concellon and A. D. Smith, *Tetrahedron: Asymmetry*, 2011, **22**, 797.

7 R. C. F. Jones and J. R. Nichols, *Tetrahedron Lett.*, 1990, **31**, 1771.

8 R. C. F. Jones, K. J. Howard, J. R. Nichols and J. S. Snaith, *J. Chem. Soc., Perkin Trans. 1*, 1998, 2061.

9 For example: R. H. Garrett and C. M. Grisham, *Biochemistry*, Brooks/Cole, Boston, 2010, ch. 22, pp. 688–689.

10 For example: J. Clayden, N. Greeves and S. Warren, *Organic Chemistry*, OUP, Oxford, 2nd edn, 2012, ch. 10, pp. 198–213.

11 D. D. Perrin and W. F. Armarego, *Purification of Laboratory Chemicals*, Pergamon Press, Oxford, 3rd edn, 1988.

12 W. G. Kofron and L. M. Baclawski, *J. Org. Chem.*, 1976, **41**, 1879.

13 *CRC Handbook of Chemistry and Physics*, ed. D. R. Lide, CRC Press, 76th edn, 1995–1996, pp. 3–209.

14 *CRC Handbook of Chemistry and Physics*, ed. D. R. Lide, CRC Press, 76th edn, 1995–1996, pp. 3–69.

15 *Handbook of Fine Chemicals*, Aldrich Chemical Company, 2009–2010, p. 254.