Synthesis of imidazo[1,2-*a*]pyridines from unactivated 2-alkyl-4,5-dihydroimidazoles through conjugate N-addition

Raymond C. F. Jones,*[a] Paschalis Dimopoulos,[b] Simon C. Coles,[c] Mark E. Light[c] and Michael B. Hursthouse[c]

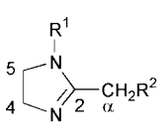
[a] *Department of Chemistry, Loughborough University, Loughborough, Leics., UK LE11 3TU*
[b] *Chemistry Department, The Open University, Walton Hall, Milton Keynes, UK MK7 6AA*
[c] *EPSRC National Crystallography Service, Department of Chemistry, University of Southampton, Highfield, Southampton, UK SO17 1BJ*

Received (in Cambridge, UK) 7th March 2000, Accepted 23rd May 2000
Published on the Web 30th June 2000

2-Alkyl-4,5-dihydroimidazoles undergo annulation with α,β-unsaturated aldehydes and ketones *via* conjugate addition of the N-1 nitrogen atom and subsequent enamine–aldol condensation of C(α) to form imidazo[1,2-*a*]-pyridines having reversed regiochemistry of annulation from that observed with a dihydroimidazole carrying an activating group at C(α); annulation with β-ketoesters also affords imidazo[1,2-*a*]pyridines, but now with the same regiochemistry as found with a C(α)-activated dihydroimidazole and necessitating a revision of earlier reported structures. Dialkyl acetylenedicarboxylates undergo conjugate N-addition but act as 1,2- rather than 1,3-bis-electrophiles to form pyrrolo[1,2-*a*]imidazoles.

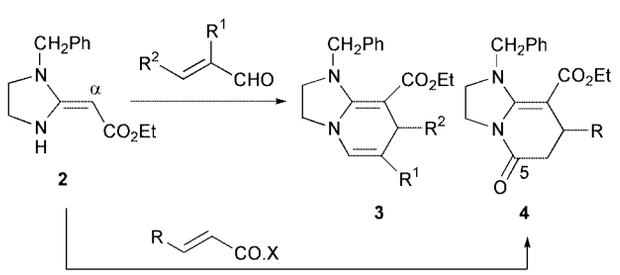
Introduction

4,5-Dihydroimidazoles (2-imidazolines) and annulated derivatives display a range of pharmacological properties,[1] for example in interactions with adrenoreceptors.[2] We have a programme to exploit the potential for nucleophilic reactivity at C(α)[3] and N-1[4] of 4,5-dihydroimidazoles **1**, and have reported



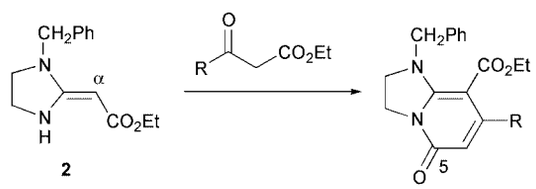
1

on annulations of the enaminoester **2**.[5,6] This enaminoester is



tautomeric with, and can be regarded as, a 4,5-dihydroimidazole carrying the activating ethoxycarbonyl group at C(α). With α,β-unsaturated aldehydes and ketones, the reactivity of enaminoester **2** is dominated by conjugate addition of the enamine C(α) carbon atom.[7] α,β-Enals afford imidazo[1,2-*a*]-pyridines **3**;[5] enones give the Michael adducts but do not proceed to cyclisation.[8] The same regiochemistry is observed in reactions of enaminoester **2** with α,β-unsaturated acid derivatives, namely esters, acid chlorides and imidazolides, to give imidazo[1,2-*a*]pyridin-5-ones **4**, although in the latter cases it is likely that N-acylation precedes the conjugate C-addition.[5,9]

The annulation potential of simple 2-alkyl-4,5-dihydroimidazoles **1** (R^1 = H), unactivated at C(α), has been little exploited, and we report now on the facile annulation of **1** (R^1 = H) with enals and enones that shows *opposite regiochemistry* to the above examples, and is now *controlled by conjugate N-addition*. With β-ketoesters as electrophiles, the major products found from enaminoester **2** are again imidazopyridin-5-ones, now **5**,



2 **5**

and we have proposed that a conjugate addition mechanism *via* the enol of the ketoester applies also in these cases.[5] We report now that annulation of **1** (R^1 = H) also occurs with β-ketoesters but to again afford imidazo[1,2-*a*]pyridin-5-ones, *i.e.* now with the *same regiochemistry* as for enaminoester **2**. This is in contrast with an earlier report, necessitating revision of the structures therein.[10]

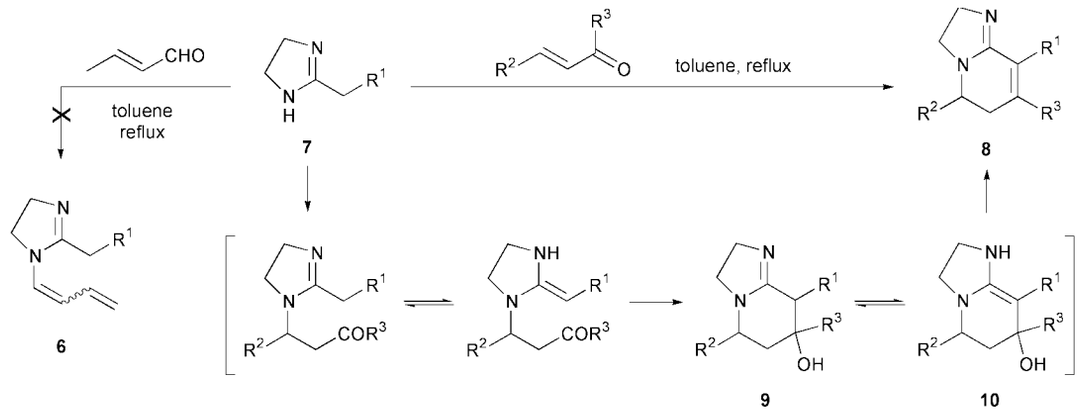
Results and discussion

In an attempt to prepare dienamine **6**, Scheme 1, the 2-(but-3-enyl)-4,5-dihydroimidazole **7b** was heated with but-2-enal in toluene at reflux, under Dean–Stark conditions for water removal. No dienamine was observed; instead the tetrahydroimidazo[1,2-*a*]pyridine **8b** was isolated (36%). This was repeated with a range of 2-alkyl-4,5-dihydroimidazoles **7a**–**e**, namely 2-butyl, 2-(but-3-enyl), 2-(2-phenylethyl), 2-(2-biphenyl-2-ylethyl) and 2-benzyl. The α,β-unsaturated carbonyl components were the aldehydes but-2-enal, pent-2-enal and 3-phenylpropenal, and the ketones but-3-en-2-one and pent-3-en-2-one, to produce imidazopyridines **8a**–**n**, Scheme 1 and Table 1, in some cases in good yields.

The structures of bicycles **8** are supported by their ^{1}H and ^{13}C NMR spectra; for example, **8a** shows signals consistent with the C=CH and CH_3–CH fragments, that would not be present in

DOI: 10.1039/b001830i

This journal is © The Royal Society of Chemistry 2000



Scheme 1

Table 1 Annulation of 4,5-dihydroimidazoles **7** with α,β-unsaturated aldehydes and ketones (Scheme 1)

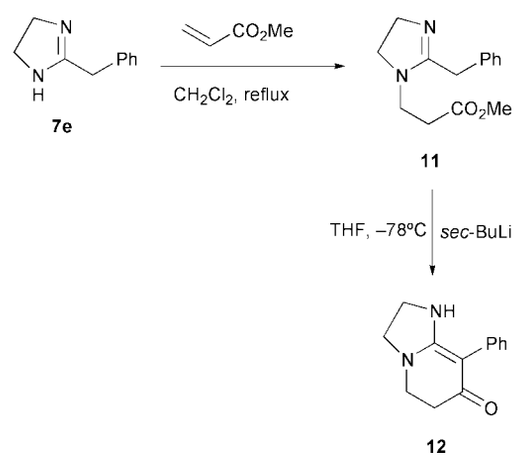
Imidazoline **7**	R^1	R^2	R^3	Imidazo[1,2-*a*]-pyridine **8** (yield %)
7a	CH_2CH_2Me	Me	H	**8a** (64)
7b	$CH_2CH{=}CH_2$	Me	H	**8b** (36)
7b	$CH_2CH{=}CH_2$	Ph	H	**8c** (13)
7c	CH_2Ph	Me	H	**8d** (80)
7c	CH_2Ph	CH_2Me	H	**8e** (91)
7c	CH_2Ph	H	Me	**8f** (38)
7d	2-$PhC_6H_4CH_2$	Me	H	**8g** (90)
7d	2-$PhC_6H_4CH_2$	CH_2Me	H	**8h** (85)
7d	2-$PhC_6H_4CH_2$	H	Me	**8i** (66)
7d	2-$PhC_6H_4CH_2$	Me	Me	**8j** (55)
7e	Ph	Me	H	**8k** (33)[a]
7e	Ph	CH_2Me	H	**8l** (15)
7e	Ph	H	Me	**8m** (98)
7e	Ph	Me	Me	**8n** (86)

[a] Incompletely characterised.

alternative isomers arising from reaction of **7a** with but-2-enal with the opposite regiochemistry. The likely mechanism for formation of the annulation products **8** is conjugate addition by N-1 of the 4,5-dihydroimidazole **7**, followed by an enamine–aldol reaction of C(α) as nucleophile, with dehydration, Scheme 1. This is supported by: (i) the isolation of the pre-dehydration intermediate **9a** ($R^1 = CH_2CH{=}CH_2$; R^2 = Me; R^3 = H) (27%), precursor to **8b**, when dihydroimidazole **7b** and but-2-enal were mixed at 20 °C (CH_2Cl_2, $MgSO_4$); (ii) the isolation of the regioisomeric alcohols **9b** and **10a** (R^1 = Ph; R^2 = H; R^3 = Me) as a 1:1 mixture (42%) along with the dehydration product **8m** (21%), from the reaction of 2-benzyl-4,5-dihydroimidazole **7e** and but-3-en-2-one under these same conditions; and (iii) the isolation of alcohol **10b** (R^1 = Ph; R^2 = Me; R^3 = H) (37%) from the reaction of the same dihydroimidazole **7e** with but-2-enal under the reflux conditions used to form the alkene **8k**, but in more dilute solution. The conjugation in alcohols **10** (R^1 = Ph) presumably favours the enamine form of the aldol product and inhibits dehydration.

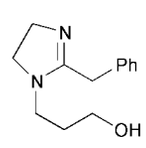
The control of annulation regiochemistry by conjugate N-addition of the 4,5-dihydroimidazole N-1 to enals or enones, to afford imidazopyridines **8**, is thus in direct contrast to the situation with α-activated 4,5-dihydroimidazole **2**, where conjugate C-addition drives the annulation towards the regioisomeric imidazopyridine series **3**.[5,6] We determined to examine whether this reversal of regiochemistry would translate to other unsymmetrical 1,3-bis-electrophiles.

The preference of 4,5-dihydroimidazoles **7** to undergo conjugate addition of N-1 to α,β-unsaturated carbonyl compounds was supported by some further experiments. Methyl propenoate as electrophile was reacted with 2-benzyl-4,5-dihydroimidazole **7e** (CH_2Cl_2, reflux) to afford the adduct **11** (81%), Scheme 2, which could be cyclised in moderate yield to the



Scheme 2

hexahydroimidazopyridine **12** (*sec*-BuLi, THF, −78 °C; 34%). Although the ester **11** could be reduced to the corresponding alcohol **13** ($LiAlH_4$, THF, −78→20 °C; 55%), attempts to form



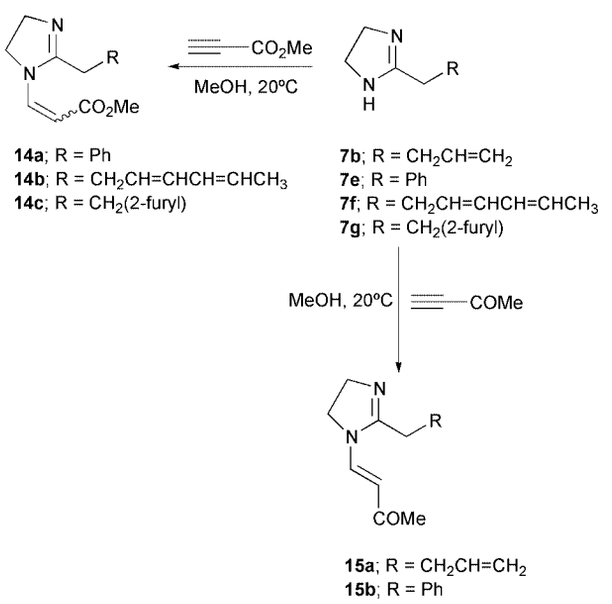
a tosylate or mesylate for cyclisation to an octahydroimidazopyridine were not successful.

Conjugated alkynes also gave 1,4-adducts. Thus dihydroimidazoles **7e–g** with methyl propynoate (MeOH, 20 °C) gave

Table 2 Annulation of 2-imidazolines **7** with β-ketoesters (Scheme 4)

Imidazoline **7**	R^1	R^2	Imidazo-pyridinone **16** or -isoquinolinone **17** (yield %)
7b	$CH_2CH{=}CH_2$	Me	**16a** (44)
7b	$CH_2CH{=}CH_2$	Ph	**16b** (86)
7c	CH_2Ph	Ph	**16c** (75)
7e	Ph	Me	**16d** (56)
7e	Ph	Ph	**16e** (58)
7c	CH_2Ph		**17a** (75)
7d	2-$PhC_6H_4CH_2$		**17b** (88)
7e	Ph		**17c** (66)

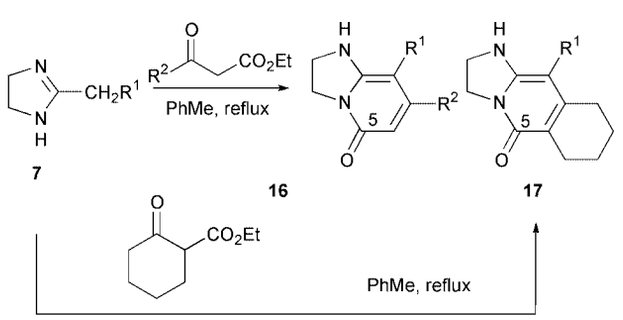
the enaminoesters **14a–c**, respectively (65, 50, and 60%), whilst heterocycles **7b** and **7e** with but-3-yn-2-one led to the enaminoketones **15a** and **15b**, respectively (83 and 72%) (Scheme 3). The



Scheme 3

enaminoesters **14** were formed as separable 2:1 $Z:E$ mixtures at the enamine double bond (in the case of **14b** each isolated component was a 3:1 mixture of $3E:5E$ and $3Z:5E$ isomers of the hepta-3,5-dienyl substituent), whereas the enaminoketones **15** were formed as the (*E*)-enamines.

When dihydroimidazoles **7b–e** were heated (toluene, reflux) with the β-ketoesters ethyl acetoacetate, ethyl benzoylacetate and ethyl 2-oxocyclohexanecarboxylate, the corresponding imidazopyridin-5-ones **16a–e** and imidazoisoquinolin-5-ones **17a–c** were formed, Scheme 4 and Table 2. Although initial



Scheme 4

reaction of the 4,5-dihydroimidazole N-1 at the keto-carbon (*via* direct 1,2-addition or through conjugate addition to the enol form) leading to the enamine may be the kinetic pathway, formation of the more stable amide linkage appears to control

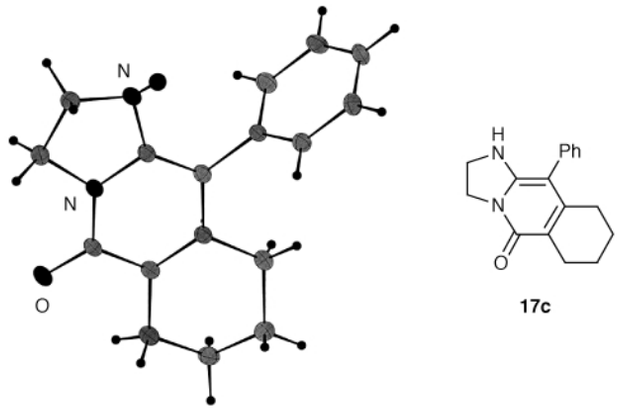
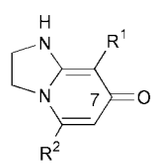


Fig. 1 X-Ray crystal structure of **17c**.

the regiochemistry under these reaction conditions. The assigned regiochemistry is based on NOE studies. For example, irradiation of the alkenyl-CH_3 signal at δ 2.09 in **16a** gave an enhancement of the allyl-CH_2 (δ 3.04–3.06) as well as of the alkenyl-H (δ 5.77) signal; likewise in **16d** irradiation of the alkenyl-CH_3 at δ 1.95 gave an enhancement of the aromatic-CH (δ 7.21–7.41) as well as of the alkenyl-H (δ 5.82) signal. The reverse NOE enhancements were also observed. The 5-oxo isomer also exhibits more extended conjugation in the UV spectrum (λ_{max} 330–340 nm) than would the 7-oxo compounds. Finally, an X-ray crystal structure determination for **17c** confirmed the regiochemistry, Fig. 1.[11]

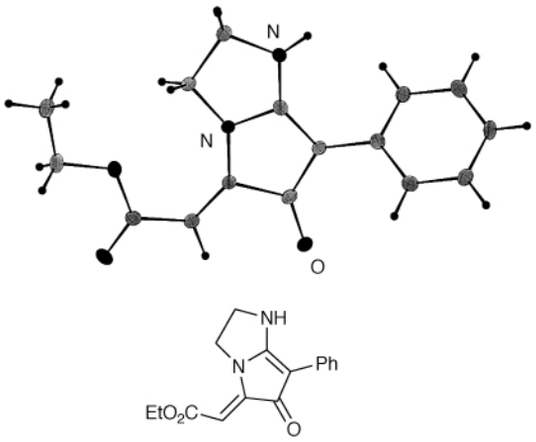
The regiochemistry of formation of imidazopyridin-5-ones **16** and **17** is in contrast to the reported reaction of 2-benzyl-4,5-dihydroimidazole **7e** and β-ketoesters to afford products assigned as the regioisomeric imidazopyridin-7-ones **18**.[10] We



must conclude that the structures formerly assigned as 7-oxo isomers **18** should be revised to the 5-oxo isomers **16** and **17**; indeed, our data for compounds **16d**, **16e** and **17c** agree with those reported for the appropriate misassigned products.[10]

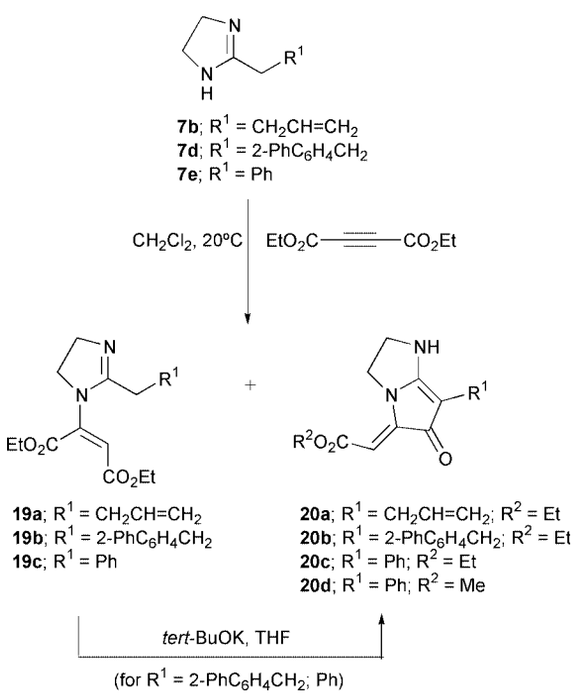
Whilst examining the reactions of dihydroimidazoles **7** with alkyne diesters, we have uncovered a further annulation that is based on N-1 conjugate addition but followed in this case by C(α)-acylation. Thus reaction of 4,5-dihydroimidazoles **7b**, **7d** and **7e** with diethyl acetylenedicarboxylate (CH_2Cl_2, 20 °C, 8 h) afforded the (*E*)-conjugate adducts **19a–c** (17%, 54% and 34%, respectively) and the (*Z*)-tetrahydropyrrolo[1,2-*a*]imidazol-6-ones **20a** and **20c** (6% and 42%, respectively), Scheme 5; none of the cyclised material **20b** was found from the reaction of dihydroimidazole **7d** but the (*Z*)-isomer of adduct **19b** was also isolated (15%). Reaction of dihydroimidazole **7e** with dimethyl acetylenedicarboxylate over an extended reaction time of 72 h afforded only (*Z*)-pyrroloimidazole **20d** (24%) along with its (*E*)-isomer (33%). Base treatment of adducts **19b** and **19c** (*tert*-BuOK, THF) led to the corresponding pyrroloimidazoles **20b** (54%), and **20c** along with its (*E*)-isomer ($Z:E$ 5:1, 67%), rather than to the possible imidazopyridines. The alkyne diester is thus acting as a 1,2-bis-electrophile rather than as a 1,3-bis-electrophile.[12]

The (*Z*)-geometry of **20c** was confirmed by an X-ray crystal structure determination, Fig. 2, and correlation with the other (*Z*)-pyrroloimidazoles **20** was based on the downfield shifts of the alkene–CH protons in the ^{1}H NMR spectra (approx.



20c

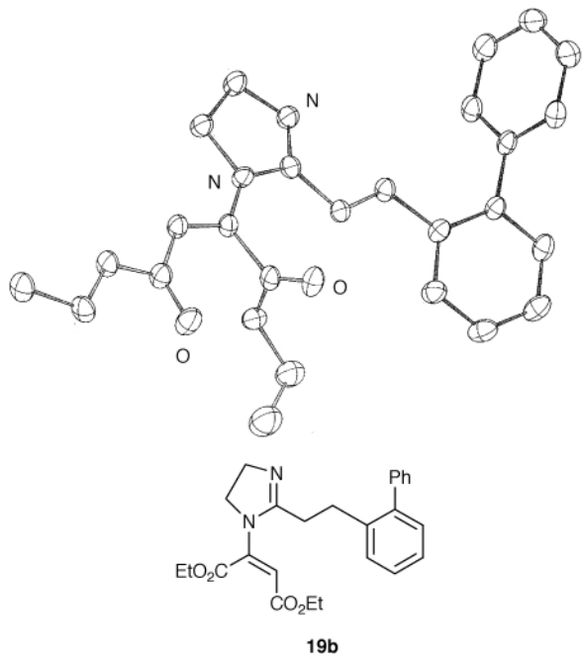
Fig. 2 X-Ray crystal structure of **20c**.



Scheme 5

δ 5.5–5.8) when compared with the (*E*)-isomers (approx. δ 5.0). An X-ray crystal structure determination of conjugate adduct intermediate **19b**, Fig. 3, established its (*E*)-stereochemistry; again ^{1}H NMR spectral correlations supported the same geometry for the other adducts **19**, in particular the alkene–CH at approx. δ 5.0 in each case (in contrast to δ 6.3 for the (*Z*)-isomer of **19b**). Interestingly, the solid-state structure of adduct **19b** shows the α-ester group ideally positioned for cyclisation with C(α), leading to the pyrroloimidazole, whereas the β-ester forms part of a planar enaminoester system and is hence deactivated. This is in agreement with the observed 1,2-electrophilic reactivity of the alkyne diesters.

We have demonstrated herein that simple 2-alkyl-4,5-dihydroimidazoles **7**, with no additional activation at C(α), undergo annulation with conjugated aldehydes and ketones to give imidazo[1,2-*a*]pyridines *via* an annulation controlled by initial *conjugate addition of N-1*; other observations support this preference for N-1 conjugate addition. The annulation regiochemistry is thus reversed from that observed with enaminoesters such as **2**, where conjugate addition of C(α) dominates.[5,6] Reaction of **7** with β-ketoesters affords imidazopyridin-5-ones through reaction of N-1 at the ester carbonyl, necessitating a revision of earlier assigned structures.[10] Finally, conjugate



19b

Fig. 3 X-Ray crystal structure of **19b**.

N-addition to alkyne diesters leads to pyrrolo[1,2-*a*]imidazoles rather than to imidazopyridines.[6]

Experimental

Melting points were measured on a Kofler hot-stage and are uncorrected. IR spectra were recorded on a Perkin-Elmer 1710 FTIR spectrometer in chloroform unless otherwise stated. UV spectra were recorded in ethanol using a Kontron Uvicon 860 spectrometer. NMR spectra were recorded in deuteriochloroform unless otherwise stated (internal standard TMS) on JEOL LAMBDA300 or JEOL EX400 spectrometers; ^{1}H spectra at 300 or 400 MHz and ^{13}C spectra at 75 MHz or 100 MHz, respectively. Low resolution mass spectra were obtained using an AEI MS902 spectrometer in EI-positive mode. Solvents were dried and distilled before use: chloroform and dichloromethane from CaH_2; tetrahydrofuran (THF) from K immediately before use. Column chromatography was performed under medium pressure using silica gel (Kieselgel 60; 220–440 mesh). Organic extracts were dried over anhydrous $MgSO_4$ for 20 min.

General method for the synthesis of 2,3,5,6,-tetrahydroimidazo-[1,2-*a*]pyridines 8

The α,β-unsaturated aldehyde or ketone (1.5–2 equiv.) was added to a solution of 2-substituted-4,5-dihydroimidazole **7** in toluene (20 cm^3) at 20 °C. The mixture was heated at reflux using a Dean–Stark trap for 12 h. The toluene was removed under reduced pressure and the residue was purified by column chromatography on silica gel (100 : 0→98 : 2 v/v ethyl acetate–isopropylamine) to give the 2,3,5,6-tetrahydroimidazo[1,2-*a*]-pyridine **8**.

5-Methyl-8-propyl-2,3,5,6-tetrahydroimidazo[1,2-*a*]pyridine 8a. Prepared by the general method, using 2-butyl-4,5-dihydroimidazole **7a** (0.10 g, 0.79 mmol) and but-2-enal (0.10 g, 1.19 mmol), as a yellow oil (0.09 g, 64%) (Found: M$^+$ 178.1470. $C_{11}H_{18}N_2$ requires: *M* 178.1470); ν_{max} (film)/cm^{-1} 2965, 2932, 1655, 1589, 1467, 1451, 1425, 1258, 1198, 1154; δ_H (400 MHz) 0.90 (3H, t, *J* 7.2, CH_3CH_2), 1.15 (3H, d, *J* 6.4, CH_3CH), 1.45–1.60 (2H, m, CH_3CH_2), 2.11–2.40 (4H, m, $CH_3CH_2CH_2$, CH_3CHCH_2), 2.76–2.82 and 2.96–3.05 (each 1H, m, NCH_2CH_2N), 3.51–3.66 (2H, m, NCH_2CH_2N), 3.85–3.90 (1H, m, CH_3CH), 6.05 (1H, dd, *J* 3.4 and 1.9, CH=C); δ_C (100 MHz)

14.0 and 20.6 (CH_3), 21.5, 33.0 and 33.6 (CH_2), 49.9 (NCH_2), 51.8 (CH_3CH), 52.6 (NCH_2), 130.1 (CH=*C*), 131.0 (*C*H=C), 164.0 (N–C=N); *m*/*z* 178 (M^+, 57%), 163 (100), 149 (100), 135 (74), 121 (32), 108 (6), 106 (5), 94 (12), 79 (8), 70 (19), 65 (11), 53 (11), 42 (24).

5-Methyl-8-(prop-2-enyl)-2,3,5,6-tetrahydroimidazo[1,2-*a*]-pyridine 8b. Prepared by the general method, using 2-(but-3-enyl)-4,5-dihydroimidazole **7b** (0.10 g, 0.80 mmol) and but-2-enal (0.085 g, 1.2 mmol), as a yellow oil (0.05 g, 36%) (Found: M^+ 176.1300. $C_{11}H_{16}N_2$ requires: *M* 176.1313); ν_{max} (film)/cm^{-1} 2967, 2929, 2853, 2824, 1654, 1592, 1496, 1454, 1423, 1258, 1199, 1157; δ_H (400 MHz) 1.18 (3H, d, *J* 6.4, CH_3CH), 2.16–2.23 and 2.30–2.37 (each 1H, m, CH_3CHCH_2), 2.76–2.83 and 2.96–3.08 (each 1H, m, $CH_2CH{=}CH_2$), 3.09–3.11 and 3.51–3.64 (each 2H, m, NCH_2CH_2N), 3.83–3.89 (1H, m, CH_3CH), 5.03–5.10 (2H, m, $CH{=}CH_2$), 5.85–5.95 (1H, m, $CH{=}CH_2$), 6.05 (1H, dd *J* 3.4 and 1.9, CH=C); δ_C (100 MHz) 20.7 (CH_3), 33.7 and 34.8 (CH_2), 50.1 (NCH_2), 51.8 (CH_3CH), 52.8 (NCH_2), 116.2 ($CH{=}CH_2$), 129.4 (CH=*C*), 131.9 (*C*H=C), 135.8 (*C*H=CH_2), 163.8 (NCN); *m*/*z* 176 (M^+, 31%), 175 (100), 161 (34), 147 (18), 133 (17), 119 (19), 106 (9), 92 (7), 79 (11), 77 (9), 65 (11), 53 (15).

5-Phenyl-8-(prop-2-enyl)-2,3,5,6-tetrahydroimidazo[1,2-*a*]-pyridine 8c. Prepared by the general method, using 2-(but-3-enyl)-4,5-dihydroimidazole **7b** (0.20 g, 1.60 mmol) and 3-phenylpropenal (0.30 cm^3, 2.41 mmol), as a yellow gum (0.05 g, 13%) (Found: M^+ 238.1470. $C_{16}H_{18}N_2$ requires: *M* 238.1470); ν_{max} (KBr)/cm^{-1} 2968, 2932, 2855, 2824, 1657, 1592, 1454, 1423, 1257, 1223, 1199, 1157; δ_H (400 MHz) 2.54–2.60 (2H, m, $CH_2CH{=}CH_2$), 2.68–2.76 (1H, m, PhCHC*H*H), 3.15–3.20 (2H, m, NCH_2CH_2N), 3.21–3.25 (1H, m, PhCHC*H*H), 3.58–3.67 and 3.80–3.90 (each 1H, m, NCH_2CH_2N), 3.99 (1H, t, *J* 7.8, PhC*H*CH_2), 5.10–5.20 (2H, m, $CH{=}CH_2$), 5.90–6.00 (1H, m, C*H*=CH_2), 6.12 (1H, dd *J* 3.4 and 1.9, C*H*=C), 7.30–7.42 (5H, m, Ar-H); δ_C (100 MHz) 34.9 and 35.4 (CH_2), 51.3 and 52.7 (NCH_2), 61.9 (Ph*C*H), 116.5 ($CH{=}CH_2$), 127.2, 128.3 and 128.9 (Ar-CH), 129.0 (CH=*C*), 131.5 (*C*H=C), 135.8 (*C*H=CH_2), 142.1 (Ar-C), 163.7 (NCN); *m*/*z* 238 (M^+, 46%), 237 (100), 2.09 (10), 173 (8), 161 (17), 147 (6), 145 (8), 133 (8), 119 (11), 115 (12), 105 (22), 91 (28), 84 (15), 78 (14), 63 (7), 51 (19).

8-Benzyl-5-methyl-2,3,5,6-tetrahydroimidazo[1,2-*a*]pyridine 8d. Prepared by the general method, using 2-(2-phenylethyl)-4,5-dihydroimidazole **7c** (0.23 g, 1.32 mmol) and but-2-enal (0.15 cm^3, 1.84 mmol), as a yellow oil (0.24 g, 80%) (Found: C, 78.57; H, 8.02; N, 12.11%; $(M - H)^+$ 225.1390; $C_{15}H_{18}N_2 \cdot 0.2H_2O$ requires: C, 78.39; H, 7.83; N, 12.19%; *M* − *H* 225.1392); ν_{max} (film)/cm^{-1} 2967, 2929, 2853, 2824, 1654, 1592, 1496, 1454, 1423, 1258, 1199, 1157; δ_H (400 MHz) 1.11 (3H, d, *J* 6.4, CH_3CH), 2.08–2.16 and 2.19–2.26 (each 1H, m, CH_3CHCH_2), 2.70–2.81 and 2.90–3.00 (each 1H, m, NCH_2CH_2N), 3.48–3.58 (2H, m, NCH_2CH_2N), 3.60 (2H, s, $PhCH_2$), 3.80–3.87 (1H, m, CH_3CH), 5.67 (1H, dd, *J* 1.9 and 3.4, CH=C), 7.10–7.18 (3H, m, Ar-H), 7.20–7.25 (2H, m, Ar-H); δ_C (100 MHz) 20.6 (CH_3), 33.7 and 36.5 (CH_2), 50.1 (NCH_2), 51.8 (CH_3CH), 52.9 (NCH_2), 126.0 (*C*H=C), 128.2, 129.4 (Ar-CH), 130.7 (CH=*C*), 132.7 (Ar-CH), 139.2 (Ar-C), 164.0 (NCN); *m*/*z* 225 [$(M - H)^+$, 100%], 211 (15), 184 (3), 149 (4), 133 (3), 128 (5), 119 (7), 105 (13), 91 (16), 70 (6), 65 (6), 56 (3).

8-Benzyl-5-ethyl-2,3,5,6-tetrahydroimidazo[1,2-*a*]pyridine 8e. Prepared by the general method, using 2-(2-phenylethyl)-4,5-dihydroimidazole **7c** (0.15 g, 0.86 mmol) and pent-2-enal (0.17 cm^3, 1.72 mmol), as a pale yellow oil (0.19 g, 91%) (Found: C, 78.54; H, 8.34; N, 11.43%; $(M - H)^+$ 239.1542. $C_{16}H_{20}N_2 \cdot 0.2H_2O$ requires: C, 78.81; N, 8.37; N, 11.49%; *M* − *H* 239.1548); ν_{max}(film)/cm^{-1} 2966, 2933, 2858, 1656, 1593, 1495, 1454, 1426, 1249, 1192, 1158; δ_H (400 MHz) 0.83 (3H, t, *J* 7.3, CH_3), 1.35–1.44 and 1.57–1.64 (each 1H, m CH_3CH_2), 2.07–2.14 and 2.19–2.26 (each 1H, m, $CH_2CH{=}C$), 2.73–2.83 and 3.46–3.57 (each 2H, m, NCH_2CH_2N), 3.60 (2H, s, $PhCH_2$), 3.82–3.86 (1H, m, CH_3CH_2CH), 5.68 (1H, dd, *J* 1.9 and 5.4, CH=C), 7.11–7.23 (5H, m, Ar-H); δ_C (100 MHz) 8.7 (CH_3), 26.9 and 29.9 (CH_2), 36.5 ($PhCH_2$), 50.1 and 52.9 (NCH_2), 57.0 (CH_3CH_2CH), 126.0 (*C*H=C), 128.5, 129.5 and 130.7 (Ar-CH), 132.6 (CH=*C*), 139.2 (Ar-C), 164.2 (NCN); *m*/*z* 240 (M^+, 35%), 239 (100), 225 (10), 211 (52), 197 (3), 155 (3), 140 (3), 119 (21), 105 (15), 91 (28).

8-Benzyl-7-methyl-2,3,5,6-tetrahydroimidazo[1,2-*a*]pyridine 8f. Prepared by the general method, using 2-(2-phenylethyl)-4,5-dihydroimidazole **7c** (0.11 g, 0.63 mmol) and but-3-en-2-one (0.10 cm^3, 1.26 mmol), as a yellow oil (55 mg, 38%) (Found: $(M - H)^+$ 225.1389. $C_{15}H_{18}N_2$ requires: *M* − *H* 225.1392); ν_{max}(film)/cm^{-1} 2921, 2852, 2823, 1650, 1586, 1494, 1454, 1419, 1279, 1238, 1210, 1057, 1031, 1015, 754, 737, 700; δ_H (400 MHz) 1.77 (3H, s, CH_3), 2.39–2.43 and 2.99–3.02 (each 2H, t, *J* 6.6, CCH_2CH_2N), 3.12–3.17 and 3.65–3.70 (2H, t, *J* 8.8, NCH_2CH_2N), 3.76 (2H, s, $PhCH_2$), 7.13–7.19 (5H, m, Ar-H); δ_C (100 MHz) 20.1 (CH_3), 31.8 (CCH_2CH_2N), 32.2 ($PhCH_2$), 45.5 and 53.0 (NCH_2), 53.2 (CCH_2CH_2N), 123.9 ($CH_3C{=}C$), 125.5, 128.1 and 128.2 (Ar-CH), 140.4 (C=*C*CH_2Ph), 142.6 (Ar-C), 164.6 (NCN); *m*/*z* 226 (M^+, 28%), 225 (100), 199 (5), 171 (3), 149 (9), 128 (4), 115 (4), 105 (3), 91 (9), 56 (4).

5-Methyl-8-(biphenyl-2-ylmethyl)-2,3,5,6-tetrahydroimidazo-[1,2-*a*]pyridine 8g. Prepared by the general method, using 2-(2-biphenyl-2-ylethyl)-4,5-dihydroimidazole **7d** (0.16 g, 0.62 mmol) and but-2-enal (0.1 cm^3, 1.25 mmol), as a colourless oil (0.17 g, 90%) (Found: C, 81.47; H, 7.24; N, 9.05%; $(M - H)^+$ 301.1701. $C_{21}H_{22}N_2 \cdot 0.4H_2O$ requires: C, 81.50; H, 7.37; N, 9.05%; *M* − *H* 301.1701); ν_{max}(film)/cm^{-1} 2968, 2930, 2855, 2825, 1655, 1592, 1479, 1425, 1258, 1200, 1157; δ_H (400 MHz) 1.06 (3H, d, *J* 6.4, CH_3), 1.99–2.07 and 2.12–2.20 (each 1H, m, $CH_2CH{=}C$), 2.67–2.74 and 2.83–2.83 (each 1H, m, NCH_2CH_2N), 3.41–3.55 (2H, m, NCH_2CH_2N), 3.60 (2H, s, $ArCH_2$), 3.72–3.78 (1H, m, CH_3CH), 5.47 (1H, dd, *J* 1.9 and 3.4, C*H*=C), 7.16–7.28 (9H, m, Ar-H); δ_C (100 MHz) 20.5 (CH_3), 33.7 ($CH_2CH{=}C$), 33.8 ($ArCH_2$), 50.1 (NCH_2), 51.7 (CH_3CH-$CH_2CH{=}C$), 52.8 (NCH_2), 126.2 (*C*H=C), 126.7, 127.2, 128.0, 128.8, 130.1, 130.9 and 131.0 (Ar-CH), 132.6 (CH=*C*), 136.3, 141.5 and 142.6 (Ar-C), 163.9 (NCN); *m*/*z* 302 (M^+, 43%), 301 (75), 287 (16), 273 (3), 260 (3), 231 (2), 225 (100), 209 (4), 165 (15), 143 (10), 127 (3), 83 (3).

5-Ethyl-8-(biphenyl-2-ylmethyl)-2,3,5,6-tetrahydroimidazo-[1,2-*a*]pyridine 8h. Prepared by the general method, using 2-(2-biphenyl-2-ylethyl)-4,5-dihydroimidazole **7d** (0.13 g, 0.52 mmol) and pent-2-enal (0.10 cm^3, 1.04 mmol), as a pale yellow oil (0.14 g, 85%) (Found: $(M - H)^+$ 315.1861. $C_{22}H_{24}N_2$ requires: *M* − *H* 315.1865); λ_{max}/nm 223; ν_{max} (film)/cm^{-1} 2965, 2933, 2862, 1656, 1594, 1479, 1451, 1435, 1247, 1194, 1158 703; δ_H (400 MHz) 0.80 (3H, t, *J* 7.3, CH_3CH_2), 1.31–1.37 and 1.52–1.60 (each 1H, m, CH_3CH_2), 2.02–2.07 and 2.13–2.20 (each 1H, m, $CHCH_2CH{=}C$), 2.67–2.74 and 3.40–3.53 (each 2H, m, NCH_2CH_2N), 3.60 (2H, s, $ArCH_2$), 3.72–3.75 (1H, m, $CHCH_2CH{=}C$), 5.49 (1H, dd, *J* 1.9 and 5.4, C*H*=C), 7.19–7.26 (9H, m, Ar-H); δ_C (100 MHz) 8.7 (CH_3), 26.7 and 29.9 (CH_2), 36.7 ($ArCH_2$), 50.1 and 52.8 (NCH_2), 56.9 (CH_2CHCH_2), 126.2 (*C*H=C), 126.7, 127.2, 127.9, 128.1, 128.8, 130.0 and 130.9 (Ar-CH), 132.5 (CH=*C*), 136.4, 141.5 and 142.6 (Ar-C), 164.0 (NCN); *m*/*z* 316 (M^+, 56%), 315 (75), 287 (60), 239 (100), 225 (11), 165 (31), 142 (22), 127 (7), 84 (5), 44 (10).

7-Methyl-8-(biphenyl-2-ylmethyl)-2,3,5,6-tetrahydroimidazo-[1,2-*a*]pyridine 8i. Prepared by the general method, using 2-(2-biphenyl-2-ylethyl)-4,5-dihydroimidazole **7d** (0.11 g, 0.44 mmol) and but-3-en-2-one (0.077 cm^3, 0.88 mmol), as a white solid (0.09 g, 66%), mp 111–113 °C (Found: $(M - H)^+$

301.1705. $C_{21}H_{22}N_2$ requires: $M - H$ 301.1705); ν_{max}(film)/cm^{-1} 2956, 2917, 2859, 2820, 1651, 1588, 1476, 1431, 1279, 754; δ_H (400 MHz) 1.42 (3H, s, CH_3), 2.31–2.35 and 2.95–2.98 (each 2H, t, J 6.3, CCH_2CH_2N), 3.12–3.17 and 3.66–3.69 (each 2H, t, J 8.8, NCH_2CH_2N), 3.70 (2H, s, $ArCH_2$), 7.06–7.32 (9H, m, Ar-H); δ_C (100 MHz) 20.0 (CH_3), 30.2 and 31.7 (CH_2), 45.5, 53.0 and 53.3 (CH_2N), 124.3 (CH_3C=C), 125.4, 126.7, 127.5, 127.6, 128.0, 129.3, 129.3 and 137.8 (Ar-CH), 141.5 (C=CCH$_2$Ar), 141.8 and 142.0 (Ar-C), 165.1 (NCN); m/z 302 (M$^+$, 25%), 301 (53), 287 (19), 225 (100), 165 (9), 149 (11), 115 (3), 105 (2), 91 (5), 56 (5).

5,7-Dimethyl-8-(biphenyl-2-ylmethyl)-2,3,5,6-tetrahydroimidazo[1,2-*a*]pyridine 8j. Prepared by the general method, using 2-(2-biphenyl-2-ylethyl)-4,5-dihydroimidazole **7d** (0.11 g, 0.43 mmol) and pent-3-en-2-one (0.084 cm^3, 0.86 mmol), as a colourless oil (75 mg, 55%) (Found: MH$^+$ 317.2005. $C_{22}H_{24}N_2$ requires: MH 317.2017); ν_{max}(film)/cm^{-1} 2968, 2852, 1651, 1588, 1478, 1416, 1329, 1281, 1209, 750, 704; λ_{max}/nm 209, 238; δ_H (300 MHz) 1.17 (3H, d, J 6.2, CH_3CH), 1.47 (3H, s, CH_3C=C), 2.13–2.32 (2H, m, CHCH_2), 2.79–2.86 and 2.95–3.02 (each 1H, m, NCH_2CH$_2$N), 3.53–3.59 (2H, m, NCH$_2$CH_2N), 3.75 (2H, s, CH_2Ar), 3.80–3.91 (1H, m, CH$_3$CH), 7.12–7.41 (9H, m, Ar-H); δ_C (75 MHz) 19.7 and 20.6 (CH_3), 30.4 and 40.3 (CH_2), 50.8 and 51.4 (CH_2N), 53.2 (CH), 124.1, 125.3, 126.7 and 127.6 (Ar-CH), 128.0 (CH_3C=C), 129.3 (Ar-CH), 137.9 (C=CCH$_2$Ar), 141.4, 141.8 and 142.5 (Ar-C), 165.5 (NCN); m/z 316 (M$^+$, 34%), 315 (55), 301 (28), 239 (100), 165 (33), 152 (17), 135 (12), 115 (8), 77 (20).

5-Methyl-8-phenyl-2,3,5,6-tetrahydroimidazo[1,2-*a*]pyridine 8k. Prepared by the general method, using 2-benzyl-4,5-dihydroimidazole **7e** (0.50 g, 3.12 mmol) and but-2-enal (0.28 g, 3.43 mmol), as a yellow oil (0.22 g, 33%) that was not completely characterised; ν_{max}(film)/cm^{-1} 2967, 2936, 1619, 1586, 1495, 1448, 1282, 1246, 1180, 996; δ_H (400 MHz) 1.23 (3H, d, J 6.4, CH_3), 2.30–2.41 and 2.50–2.57 (each 1H, m, CHCH_2-CH=C), 2.82–2.91 and 3.09–3.19 (each 1H, m, NCH_2CH$_2$N), 3.55–3.70 (2H, m, NCH$_2$CH_2N), 3.87–3.96 (1H, m, CHCH$_2$-CH=C), 6.32 (1H, dd, J 3.4 and 1.9, CH=C), 7.24–7.38 (3H, m, Ar-H) and 7.45–7.48 (2H, m, Ar-H); δ_C (100 MHz) 20.7 (CH_3), 34.1 (CH_2), 49.8, 51.5 (CH), 53.2 (NCH_2), 127.8, 128.1 and 128.7 (Ar-CH), 132.4 (CH=C), 134.5 (CH=C), 137.6 (Ar-C), 162.8 (NCN); m/z 212 (M$^+$, 8%), 197 (12), 183 (8), 171 (2), 159 (13), 128 (2), 91 (17).

5-Ethyl-8-phenyl-2,3,5,6-tetrahydroimidazo[1,2-*a*]pyridine 8l. Prepared by the general method, using 2-benzyl-4,5-dihydroimidazole **7e** (0.55 g, 3.44 mmol) and pent-2-enal (0.67 cm^3, 6.88 mmol), as a dark yellow oil (0.12 g, 15%) (Found: MH$^+$ 227.1540. $C_{15}H_{18}N_2$ requires: MH 227.1548); ν_{max}(film)/cm^{-1} 2966, 2936, 1619, 1586, 1495, 1448, 1423, 1282, 1246, 1180, 996, 753; δ_H (400 MHz) 0.97 (3H, t, J 7.8, CH_3), 1.46–1.59 and 1.71–1.80 (each 1H, m, CH_3CH_2), 2.37–2.44 and 2.50–2.57 (each 1H, m, CHCH_2CH=C), 2.85–2.95 and 2.98–3.05 (each 1H, m, NCH_2CH$_2$N), 3.57–3.68 (2H, m, NCH$_2$CH_2N), 3.91–3.95 (1H, m, CHCH$_2$CH=C), 6.38 (1H, dd, J 2.7 and 6.1, CH=C), 7.26–7.50 (5H, m, Ar-H); δ_C (100 MHz) 8.8 (CH_3), 27.1 and 30.5 (CH_2), 49.9 and 53.3 (NCH_2), 56.8 (CH), 127.4 (CH=C), 127.9, 128.2 and 128.7 (Ar-CH), 134.7 (CH=C), 137.8 (Ar-C), 163.1 (NCN); m/z 227 (MH$^+$, 100%), 197 (6), 171 (3), 159 (6), 91 (2), 71 (2).

7-Methyl-8-phenyl-2,3,5,6-tetrahydroimidazo[1,2-*a*]pyridine 8m. Prepared by the general method, using 2-benzyl-4,5-dihydroimidazole **7e** (0.50 g, 3.12 mmol) and but-3-en-2-one (0.50 cm^3, 6.24 mmol) in toluene (30 cm^3), as a yellow oil (0.65 g, 98%) (Found: C, 77.14; H, 7.69; N, 13.16%; (M − H)$^+$ 211.1234. $C_{14}H_{16}N_2 \cdot 0.3H_2O$ requires: C, 77.27; H, 7.63; N, 12.88%; $M - H$ 211.1235); ν_{max}(film)/cm^{-1} 2918, 2851, 2821, 1636, 1587, 1494, 1466, 1442, 1418, 1285, 1229, 1190, 1168, 978; δ_H (400 MHz) 1.65 (3H, s, CH_3), 2.48–2.51 and 3.06–3.10 (each 2H, t, J 6.6, CCH_2CH_2N), 3.11–3.16 and 3.62–3.67 (each 2H, t, J 8.8, NCH_2CH_2N), 7.10–7.28 (5H, m, Ar-H); δ_C (100 MHz) 20.9 (CH_3), 31.5 (CH_2), 45.4, 52.8 and 53.6 (NCH_2), 126.8 (CH_3C=C), 127.7, 127.8 and 129.8 (Ar-CH), 136.6 (C=CPh), 142.5 (Ar-C), 164.3 (NCN); m/z 212 (M$^+$, 56%), 211 (100), 195 (5), 183 (2), 154 (2), 128 (6), 115 (7), 105 (5), 69 (3), 56 (4).

5,7-Dimethyl-8-phenyl-2,3,5,6-tetrahydroimidazo[1,2-*a*]-pyridine 8n. Prepared by the general method, using 2-benzyl-4,5-dihydroimidazole **7e** (1.00 g, 6.25 mmol) and pent-3-en-2-one (1.20 cm^3, 12.5 mmol) in toluene (62 cm^3), as a yellow oil (1.22 g, 86%) (Found (M − H)$^+$, 225.1393. $C_{15}H_{18}N_2$ requires: M − H 225.1392); λ_{max}/nm 219; ν_{max}(film)/cm^{-1} 2967, 2930, 2851, 1642, 1590, 1495, 1443, 1411, 1378, 1282, 1252, 1229, 1177, 990, 700; δ_H (400 MHz) 1.23 (3H, d, J 6.2, CH_3CH), 1.72 (3H, s, CH_3C=C), 2.39–2.43 (2H, m, CHCH_2), 2.78–2.87 and 3.11–3.20 (each 1H, m, NCH_2CH$_2$N), 3.53–3.66 (2H, m, NCH$_2$CH_2N), 3.80–3.90 (1H, m, CH$_3$CH), 7.16–7.37 (5H, m, Ar-H); δ_C (100 MHz) 20.8 and 21.0 (CH_3), 40.2 (CH_2), 50.4 and 51.4 (NCH_2), 53.8 (CH), 127.7 (Ar-CH), 128.1 (CH_3C=C), 128.4 and 129.9 (Ar-CH), 136.9 (C=CPh), 142.4 (Ar-C), 164.8 (NCN); m/z 226 (M$^+$, 75%), 225 (100), 211 (21), 195 (10), 183 (4), 166 (5), 154 (4), 128 (9), 115 (10), 91 (4), 70 (9), 42 (10).

7-Hydroxy-5-methyl-8-(prop-2-enyl)-2,3,5,6,7,8-hexahydroimidazo[1,2-*a*]pyridine 9a

To 2-(but-3-enyl)-4,5-dihydroimidazole **7b** (70 mg, 0.56 mmol) in anhydrous dichloromethane (6 cm^3) was added but-2-enal (47 mg, 0.67 mmol). A small amount of $MgSO_4$ was added to the reaction mixture which was stirred at 20 °C for 12 h. The mixture was filtered and the dichloromethane was removed under reduced pressure. The crude reaction mixture was purified by column chromatography on silica gel (0 : 100→3 : 97 v/v isopropylamine–chloroform) to give the *title compound* as a white solid (30 mg, 27%) (Found: M$^+$ 194.1419. $C_{11}H_{18}N_2O$ requires: M 194.1491); ν_{max}(film)/cm^{-1} 3100, 2972, 2936, 1612, 1424, 1346, 1277, 1139; δ_H (400 MHz) 1.18 (3H, d, J 6.4, CH_3CH), 1.60–1.69 (1H, q, J 11.2, NCHCHH), 2.06–2.11 (2H, dt, J 3.6 and 11.2, NCHCHH), 2.34–2.37 and 2.56–2.62 (each 1H, m CH_2CH=CH$_2$), 2.79–2.86 (3H, m, NCH_2CH$_2$N and CHCH$_2$CH=CH$_2$), 3.55–3.60 (2H, m, NCH$_2$CH_2N), 3.69–3.75 (1H, m, NCH), 3.85 (1H, t, J 11.2, CHOH), 5.05 and 5.17–5.21 (each 1H, m, CH=CH_2), 6.00–6.07 (1H, m, CH=CH$_2$), OH not observed; δ_C (100 MHz) 22.7 (CH_3), 33.0 (CHCH$_2$), 40.8 (CH$_2$CH=CH$_2$), 44.5 (CHCH$_2$CH=CH$_2$) 50.3 and 51.6 (NCH_2), 53.0 (NCH), 69.9 (CHOH), 116.7 (CH=CH$_2$), 137.5 (CH=CH$_2$), 166.9 (NCN); m/z 194 (M$^+$, 24%), 176 (80), 161 (32), 150 (28), 137 (21), 132 (17), 121 (34), 109 (15), 106 (11), 94 (100), 81 (16), 67 (17).

7-Hydroxy-7-methyl-8-phenyl-2,3,5,6,7,8-hexahydroimidazo-[1,2-*a*]pyridine 9b and 7-hydroxy-7-methyl-8-phenyl-1,2,3,5,6,7-hexahydroimidazo[1,2-*a*]pyridine 10a

To 2-benzyl-4,5-dihydroimidazole **7e** (3.17 g, 19.81 mmol) in dichloromethane (100 cm^3) was added but-3-en-2-one (1.97 cm^3, 23.77 mmol) and the resulting solution was stirred at 20 °C for 12 h. The *title compounds* precipitated out of solution as a white solid (1 : 1 mixture of regioisomers) which was filtered (1.93 g, 42%), mp 141–143 °C (Found: C, 72.57; H, 7.84; N, 12.03%; M$^+$ 230.1419. $C_{14}H_{18}N_2O$ requires: C, 73.01; H, 7.88; N, 12.16%; M 230.1417); ν_{max}(film)/cm^{-1} 3435, 3083, 3063, 2970, 1616, 1495, 1424, 1344, 1276, 1139, 704; δ_H (400 MHz; CD_3OD) 1.01 and 1.14 (each 3H, s, CH_3), 1.63–1.72, 1.88–1.93, 1.98–2.03 and 2.05–2.09 (each 1H, m, CH_2CH_2COH), 3.09–3.21, 3.28–3.42 and 3.53–3.69 (each 4H, m, 2 × NCH_2), 3.69–3.72 (1H, m, PhCH), 7.22–7.36 (10H, m, Ar-H); δ_C (100 MHz, CD_3OD) 27.7 and 28.0 (CH_3), 32.2 and 32.4 (CH_2COH), 44.8,

48.1, 49.5 and 49.8 (NCH_2), 48.4 (Ph*C*H), 52.5 and 52.8 (NCH_2), 55.9 (NC=*C*Ph), 71.2 and 71.8 (COH), 128.2, 128.6, 129.2, 130.1 and 132.0 (Ar-CH), 138.4 and 140.5 (Ar-C), 169.0 (NCN); *m/z* 230 (M^+, 6%), 211 (100), 196 (4), 183 (3), 171 (9), 159 (7), 128 (9), 115 (11), 102 (3), 91 (12), 77 (7), 56 (5); the tetrahydroimidazo[1,2-*a*]pyridine **8m** was isolated from the filtrate by chromatography as a yellow oil (0.91 g, 21%), identical with a sample prepared as described above.

7-Hydroxy-5-methyl-8-phenyl-1,2,3,5,6,7-hexahydroimidazo-[1,2-*a*]pyridine 10b

To 2-benzyl-4,5-dihydroimidazole **7e** (0.25 g, 1.56 mmol) in toluene (30 cm^3) was added but-2-enal (0.19 cm^3, 2.34 mmol) and the resulting solution was heated at reflux for 12 h. The toluene was removed under reduced pressure and the crude reaction mixture was purified by column chromatography on silica gel (0:100→1:99 v/v isopropylamine–chloroform) to give the *title compound* as a yellow oil (0.13 g, 37%) (Found: M^+ 230.1419. $C_{14}H_{18}N_2O$ requires: *M* 230.1419); ν_{max}(film)/cm^{-1} 3401, 2968, 2931, 2851, 1636, 1585, 1494, 1249, 1196, 990, 774; δ_H (400 MHz) 1.12 (3H, d, *J* 6.4, CH_3CH), 1.88–1.93 (1H, m, NCHC*H*H), 2.28–2.34 (1H, m, NCHCH*H*), 2.80–2.92 and 2.98–3.08 (each 1H, m, NC$H_2$$CH_2$N), 3.28 (1H, m, NC*H*H), 3.50–3.60 (2H, m, NCH*H* and NCH), 3.74 (1H, t, *J* 10.9, C*H*OH), 7.20–7.35 (3H, m, Ar-H), 7.40 (2H, m Ar-H), OH and NH not observed; δ_C (100 MHz) 20.7 (CH_3), 32.9 (NCH*C*H$_2$), 46.6 (NCH), 49.8 and 52.6 (NCH_2), 56.2 (NC=*C*Ph), 61.3 (CHOH), 126.6, 127.9, 128.1 (Ar-CH), 135.8 (Ar-C), 163.9 (NCN); *m/z* 230 (M^+, 16%), 213 (29), 199 (26), 185 (46), 170 (5), 157 (25), 143 (7), 129 (14), 115 (12), 105 (38), 91 (12), 77 (31).

Methyl 3-(2-benzyl-4,5-dihydroimidazol-1-yl)propanoate 11

To 2-benzyl-4,5-dihydroimidazole **7e** (3.00 g, 18.75 mmol) in dry dichloromethane (18 cm^3) under nitrogen was injected methyl propenoate (3.37 cm^3, 37.5 mmol) and the resulting solution was heated at reflux overnight. The dichloromethane was removed under reduced pressure and the crude product was purified by column chromatography on silica gel (100:0→99:1 ethyl acetate–isopropylamine) to give the *title compound* as a yellow oil (3.75 g, 81%) (Found: C, 64.12; H, 7.39; N, 11.11%; $(M - H)^+$ 245.1288. $C_{14}H_{18}N_2O_2{\cdot}0.8H_2O$ requires: C, 64.51; H, 6.91; N, 10.75%; *M* − *H* 245.1290); ν_{max}(film)/cm^{-1} 2951, 2862, 1737 (CO), 1615 (C=N), 1496, 1456, 1437, 1271, 1175, 1007; δ_H (400 MHz) 2.33 (2H, t, *J* 6.8, C$H_2$$CO_2CH_3$), 3.28 (2H, t, *J* 9.0, NC$H_2$$CH_2$N), 3.32 (2H, t, *J* 6.8, C$H_2$$CH_2$-$CO_2CH_3$), 3.64 (3H, s, CO_2CH_3), 3.65 (2H, s, PhCH_2), 3.70 (2H, t, *J* 9.0, NC$H_2$$CH_2$N), 7.21–7.33 (5H, m, Ar-H); δ_C (75 MHz) 33.5 and 34.5 (CH_2), 42.9 (OCH_3), 50.1, 51.7 and 52.4 (NCH_2), 126.7, 128.6, 128.7 (Ar-CH), 135.9 (Ar-C), 165.2 (NCN), 171.9 (CO); *m/z* 246 (M^+, 38%), 187 (95), 173 (28), 158 (20), 130 (12), 117 (10), 115 (10), 103 (7), 92 (7), 83 (35), 56 (100), 42 (23).

8-Phenyl-1,2,3,5,6,7-hexahydroimidazo[1,2-*a*]pyridin-7-one 12

sec-Butyllithium (4.43 cm^3 of a 1.1 M solution in hexanes, 4.87 mmol) was injected into a solution of methyl 3-(2-benzyl-4,5-dihydroimidazol-1-yl)propanoate **11** (0.60 g, 2.48 mmol) in dry THF (25 cm^3) at −78 °C under nitrogen. The resulting yellow muddy solution was stirred at −78 °C for 1 h, allowed to warm to 20 °C and stirred for a further 1 h. The reaction was quenched with water (25 cm^3) and the organic layer extracted with diethyl ether (3 × 50 cm^3). The combined organic extracts were washed successively with saturated aq. $NaHCO_3$ (100 cm^3), water (100 cm^3) and brine (100 cm^3), dried and concentrated. The crude product was purified by column chromatography on silica gel (1:99→4:96 v/v isopropylamine–ethyl acetate) to give the *title compound* as a white solid (0.18 g, 34%), mp 139–141 °C (Found: M^+ 214.1103. $C_{13}H_{14}N_2O$ requires: *M* 214.1106); ν_{max}(KBr)/cm^{-1} 3111 (NH), 2975, 2868, 1563, 1548, 1532, 1505, 1479, 1441, 1319, 1301, 1279, 1101; δ_H (300 MHz) 2.56 (2H, t, *J* 7.1, CH_2CO), 3.28 (2H, t, *J* 7.1, NC$H_2$$CH_2$N), 3.40 (2H, m, C$H_2$$CH_2CO$), 3.48 (2H, m, NCH_2CH_2N), 4.85 (1H, br s, NH), 7.00–7.28 (5H, m, Ar-H); δ_C (75 MHz) 35.4 (*C*H_2CO), 43.1, 45.2 and 50.6 (NCH_2), 94.5 (Ph*C*), 125.8, 128.4, 130.6 (Ar-CH), 135.0 (Ar-C), 164.6 (NCN), 185.7 (CO); *m/z* 214 (M^+, 100%), 185 (92), 171 (6), 157 (18), 129 (35), 115 (15), 103 (24), 89 (16), 77 (19), 63 (9).

2-Benzyl-1-(3-hydroxypropyl)-4,5-dihydroimidazole 13

To $LiAlH_4$ (38.42 cm^3 of a 1.1 M solution in THF, 42.27 mmol) in THF (100 cm^3) at −78 °C under nitrogen was added, *via* cannula, methyl 3-(2-benzyl-4,5-dihydroimidazol-1-yl)propanoate **11** (5.20 g, 21.13 mmol) in dry THF (150 cm^3). The resulting yellow solution was stirred overnight (−78 °C→20 °C). The reaction mixture was then cooled to 0 °C and the excess $LiAlH_4$ destroyed by addition of ethyl acetate (50 cm^3). The solvents were removed under reduced pressure and the crude product was purified by column chromatography on silica gel (1:2:97→5:20:75 v/v isopropylamine–methanol–ethyl acetate) to give the *title alcohol* as a yellow oil (2.52 g, 55%) (Found: $(M - H)^+$ 217.1339. $C_{13}H_{18}N_2O$ requires: *M* − *H* 217.1341); ν_{max}(film)/cm^{-1} 3187 (OH), 2934, 2864, 1600 (C=N), 1496, 1455, 1280, 1169, 1063, 723; δ_H (300 MHz) 1.54–1.57 (2H, m, C$H_2$$CH_2$OH), 2.43 (1H, br s, OH), 3.09 (2H, t, *J* 6.7, C$H_2$$CH_2$$CH_2$OH), 3.27 (2H, t, *J* 9.4, NC$H_2$$CH_2$N), 3.41 (2H, t, *J* 5.9, CH_2OH), 3.57 (2H, s, PhCH_2), 3.66 (2H, t, *J* 9.4, NCH_2CH_2N), 7.16–7.28 (5H, m, Ar-H); δ_C (75 MHz) 31.0 (*C*$H_2$$CH_2$OH), 34.5 (Ph*C*$H_2$), 43.1, 50.0 and 51.9 ($NCH_2$), 59.2 ($CH_2$OH), 126.8, 128.5, 128.6 (Ar-CH), 136.1 (Ar-C), 166.1 (NCN); *m/z* 218 (M^+, 10%), 201 (4), 187 (43), 173 (35), 159 (10), 131 (7), 117 (9), 101 (20), 91 (100), 77 (7), 65 (21), 56 (54).

General method for the synthesis of methyl 3-(2-alkyl-4,5-dihydroimidazol-1-yl)propenoates 14

To the 2-alkyl-4,5-dihydroimidazole **7** in dry methanol at 20 °C under nitrogen was injected methyl propynoate. The resulting yellow solution was stirred overnight at 20 °C, before the methanol was removed under reduced pressure and the crude product purified by column chromatography on silica gel (30:70→100:0 v/v ethyl acetate–hexane) to give the enaminoester **14**.

Methyl (*Z*)- and (*E*)-3-(2-benzyl-4,5-dihydroimidazol-1-yl)-propenoate 14a. Prepared by the general method, using 2-benzyl-4,5-dihydroimidazole **7e** (2.0 g, 12.48 mmol) and methyl propynoate (1.10 cm^3, 18.67 mmol) in methanol (62 cm^3), as (*Z*)- and (*E*)-isomers (2:1) of the *title compound* (1.95 g, 65%).

Data for the (*Z*)-isomer (Found: C, 66.49; H, 6.73; N, 10.74%; M^+ 244.1212. $C_{14}H_{16}N_2O_2{\cdot}0.4H_2O$ requires: C, 66.84; H, 6.36, N, 11.14%; *M* 244.1212); ν_{max}(film)/cm^{-1} 2948, 1704 (CO), 1610 (C=N), 1357, 1268, 1153, 1011, 921, 718; δ_H (400 MHz) 3.62 (3H, s, CH_3), 3.81 (2H, s, PhCH_2), 3.97 and 4.04 (each 2H, t, *J* 8.8, NC$H_2$$CH_2$N), 4.57 and 4.65 (each 1H, d, *J* 10.0, NC*H*=C*H*CO_2Me), 7.20–7.34 (5H, m, Ar-H); δ_C (100 MHz) 34.5 (CH_2), 49.4 (NCH_2), 50.9 (OCH_3), 54.1 (NCH_2), 90.9 (NCH=*C*HCO_2Me), 127.2, 128.7, 128.9 (Ar-CH), 134.2 (Ar-C), 136.0 (N*C*H=CHCO_2Me), 160.5 (NCN), 165.9 (CO); *m/z* 244 (M^+, 52%), 229 (3), 213 (20), 185 (84), 171 (64), 159 (8), 128 (34), 117 (16), 105 (20), 91 (100), 77 (19).

Data for the (*E*)-isomer: mp 74–76 °C (Found: C, 67.51; H, 6.59; N, 11.24%; M^+ 244.1212. $C_{14}H_{16}N_2O_2{\cdot}0.2H_2O$ requires: C, 67.81; H, 6.45; N, 11.30%; *M* 244.1212); ν_{max}(film)/cm^{-1} 2935, 1693 (CO), 1607 (C=N), 1408, 1315, 1261, 1192, 1170, 718; δ_H (400 MHz) 3.57 (2H, t, *J* 8.8, NC$H_2$$CH_2$N), 3.68 (3H, s, CH_3), 3.94 (2H, s, PhCH_2), 3.97 (2H, t, *J* 8.8, NCH_2CH_2N), 4.82 (1H, d, *J* 13.2, NCH=C*H*CO_2Me), 7.20–7.34 (5H, m,

Ar-H), 7.78 (1H, d, *J* 13.2, NC*H*=CHCO$_2$Me); δ_C (100 MHz) 34.0 (CH$_2$), 46.3 (NCH$_2$), 51.1 (OCH$_3$), 53.2 (NCH$_2$), 93.2 (NCH=*C*HCO$_2$Me), 127.4, 128.9, 129.1 (Ar-CH), 134.1 (Ar-C), 139.1 (N*C*H=CHCO$_2$Me), 159.5 (NCN), 168.6 (CO); *m*/*z* 244 (M$^+$, 36%), 213 (25), 185 (50), 171 (30), 159 (10), 128 (40), 117 (20), 105 (17), 91 (100), 77 (26).

Methyl (*Z*)- and (*E*)-3-[2-(hepta-3,5-dienyl)-4,5-dihydroimidazol-1-yl]propenoate 14b

Prepared by the general method, using 2-(hepta-3,5-dienyl)-4,5-dihydroimidazole **7f** (0.31 g, 1.93 mmol) and methyl propynoate (0.30 cm^3, 2.89 mmol) in methanol (10 cm^3), as (*Z*)- and (*E*)-propenoate isomers (2:1) of the *title compound* (in each case a 3:1 mixture of (*E*,*E*):(*Z*,*E*) isomers in the heptadienyl moiety) as yellow oils (0.24 g, 50%).

Data for (*Z*)-propenoate isomer (Found: C, 66.95; H, 8.10; N, 11.03%; M$^+$ 248.1534. $C_{14}H_{20}N_2O_2\cdot0.1H_2O$ requires: C, 67.21; H, 8.08; N, 11.20%; *M* 248.1525); ν_{max}(film)/cm^{-1} 2949, 1707 (CO), 1653, 1610 (C=N), 1364, 1160, 994, 922; *m*/*z* 248 (M$^+$, 56%), 233 (30), 217 (10), 205 (6), 189 (100), 161 (12), 135 (22), 120 (26), 109 (45), 96 (26), 79 (36), 67 (37), 53 (52); NMR data for (*E*,*E*)-heptadienyl isomer δ_H (400 MHz) 1.73 (3H, d, *J* 6.8, C*H*$_3$CH=CH), 2.37–2.45 (4H, m, C*H*$_2$C*H*$_2$CH=CH), 3.66 (3H, s, OCH$_3$), 3.88 and 3.98 (each 2H, t, *J* 8.8, NCH$_2$CH$_2$N), 4.74 (1H, d, *J* 10.0, NCH=C*H*CO$_2$Me), 5.56–5.66 and 6.00–6.10 (each 2H, m, CH=CHCH=CH), 6.61 (1H, d, *J* 10.0, NC*H*=CHCO$_2$Me); δ_C (100 MHz) 18.1 (*C*H$_3$CH=CH), 27.9 and 28.8 (*C*H$_2$*C*H$_2$CH=CH), 49.4 (NCH$_2$), 50.9 (OCH$_3$), 54.1 (NCH$_2$), 90.6 (NCH=*C*HCO$_2$Me), 128.2, 129.2, 131.2 and 131.6 (CH=CHCH=CH), 135.9 (N*C*H=CHCO$_2$Me), 161.3 (NCN), 166.1 (CO); NMR data for (*Z*,*E*)-heptadienyl isomer δ_H (400 MHz) 1.11 (3H, d, *J* 6.8, C*H*$_3$CH=CH), 2.37–2.45 (4H, m, C*H*$_2$C*H*$_2$CH=CH), 3.66 (3H, s, OCH$_3$), 3.88 and 3.98 (each 2H, t, *J* 8.8, NCH$_2$CH$_2$N), 4.74 (1H, d, *J* 10.0, NCH=C*H*CO$_2$Me), 5.01 (1H, dd, *J* 1.7 and 10.2, CH$_3$CH=CHC*H*=CH), 5.14 (1H, dd, *J* 1.7 and 17.1, CH$_3$CH=C*H*CH=CH), 5.61–5.66 and 6.25–6.32 (each 1H, m, C*H*=CHCH=C*H*), 6.61 (1H, d, *J* 10.0, NC*H*=CHCO$_2$Me); δ_C (100 MHz) 20.0 (*C*H$_3$CH=CH), 33.8 and 34.9 (*C*H$_2$*C*H$_2$CH=CH), 49.4 (NCH$_2$), 50.9 (OCH$_3$), 54.1 (NCH$_2$), 90.6 (NCH=*C*H-CO$_2$Me), 116.1 and 129.9 (CH=CH), 136.0 (N*C*H=CH-CO$_2$Me), 136.9 and 138.5 (CH=CH), 161.3 (NCN), 166.1 (CO).

Data for (*E*)-propenoate isomer (Found: M$^+$ 248.1523. $C_{14}H_{20}N_2O_2$ requires: *M* 248.1525); ν_{max}(film)/cm^{-1} 2950, 1703 (CO), 1615 (C=N), 1410, 1315, 1256, 1197, 1163, 994; *m*/*z* 248 (M$^+$, 28%), 233 (22), 217 (9), 205 (6), 189 (100), 175 (16), 161 (10), 149 (14), 134 (17), 121 (15), 109 (32), 96 (23), 79 (26), 67 (16); NMR data for (*E*,*E*)-heptadienyl isomer δ_H (400 MHz) 1.73 (3H, d, *J* 6.8, C*H*$_3$CH=CH), 2.41–2.51 (4H, m, C*H*$_2$C*H*$_2$-CH=CH), 3.53 (2H, t, *J* 9.0, NC*H*$_2$CH$_2$N), 3.72 (3H, s, OCH$_3$), 3.93 (2H, t, *J* 9.0, NCH$_2$C*H*$_2$N), 4.85 (1H, d, *J* 13.2, NCH=C*H*CO$_2$Me), 5.58–5.69 and 5.98–6.10 (each 2H, m, CH=CHCH=CH), 7.74 (1H, d, *J* 13.2, NC*H*=CHCO$_2$Me); δ_C (100 MHz), 18.5 (*C*H$_3$CH=CH), 27.3 and 28.5 (*C*H$_2$*C*H$_2$CH=CH), 46.2 (NCH$_2$), 50.9 (OCH$_3$), 53.1 (NCH$_2$), 92.9 (NCH=*C*HCO$_2$Me), 128.2, 129.0, 131.6 and 131.7 (CH=CHCH=CH), 138.9 (N*C*H=CHCO$_2$Me), 160.1 (NCN), 168.7 (CO); NMR data for (*Z*,*E*)-heptadienyl isomer δ_H (400 MHz) 1.13 (3H, d, *J* 6.8, C*H*$_3$CH=CH), 2.40–2.51 (4H, m, C*H*$_2$C*H*$_2$CH=CH), 3.53 (2H, t, *J* 9.0, NC*H*$_2$CH$_2$N), 3.66 (3H, s, OC*H*$_3$), 3.95 (2H, t, *J* 9.0, NCH$_2$C*H*$_2$N), 4.74 (1H, d, *J* 10.2, NCH=C*H*CO$_2$Me), 5.01 (1H, dd, *J* 1.7 and 9.8, CH$_3$CH=CHC*H*=CH), 5.14 (1H, dd, *J* 1.7 and 17.1, CH$_3$CH=C*H*CH=CH), 5.65–5.70 and 6.24–6.31 (each 1H, m, CH$_3$C*H*=CHCH=C*H*), 6.61 (1H, d, *J* 10.2, NC*H*=CHCO$_2$Me); δ_C (100 MHz) 20.2 (*C*H$_3$CH=CH), 27.9 and 28.8 (*C*H$_2$*C*H$_2$CH=CH), 49.3 (NCH$_2$), 51.1 (OCH$_3$), 54.1 (NCH$_2$), 90.6 (NCH=*C*HCO$_2$Me), 116.1, 131.1, 135.9 and 138.3 (CH=CHCH=CH), 138.8 (N*C*H=CHCO$_2$Me), 160.1 (NCN), 168.7 (CO).

Methyl (*Z*)- and (*E*)-3-{2-[2-(2-furyl)ethyl]-4,5-dihydroimidazol-1-yl}propenoate 14c. Prepared by the general method, using 2-[2-(2-furyl)ethyl]-4,5-dihydroimidazole **7g** (0.21 g, 1.28 mmol) and methyl propynoate (0.17 cm^3, 1.92 mmol) in methanol (1.20 cm^3), as (*Z*)- and (*E*)-propenoate isomers (2:1) of the *title compound* as white solids (0.19 g, 60%).

Data for (*Z*)-isomer: mp 58–60 °C (Found: C, 62.70; H, 6.54; N, 11.14%; M$^+$ 248.1160. $C_{13}H_{18}N_2O_3$ requires: C, 62.89; H, 6.50, N, 11.28%; *M* 248.1160); ν_{max}(KBr)/cm^{-1} 2949, 1699 (CO), 1611 (C=N), 1474, 1378, 1335, 1213, 1173, 997, 924; δ_H (400 MHz) 2.69 and 2.99 (each 2H, t, *J* 7.8, C*H*$_2$C*H*$_2$Furyl), 3.59 (3H, s, OCH$_3$), 3.83 and 3.93 (each 2H, t, *J* 9.0, NCH$_2$CH$_2$N), 4.67 (1H, d, *J* 10.0, NCH=C*H*CO$_2$Me), 5.98 (1H, d, *J* 2.9, Furyl-3H), 6.21 (1H, dd, *J* 1.9 and 2.9, Furyl-4H), 6.52 (1H, d, *J* 10.0, NC*H*=CHCO$_2$Me), 7.24 (1H, d, *J* 1.9, Furyl-5H); δ_C (100 MHz) 24.5 and 26.6 (*C*H$_2$*C*H$_2$Furyl), 49.4 (NCH$_2$), 50.9 (OCH$_3$), 54.0 (NCH$_2$), 90.9 (NCH=*C*HCO$_2$Me), 105.6 and 110.2 (Furyl-CH), 135.6 (N*C*H=CHCO$_2$Me), 141.3 (Furyl-CH), 153.9 (Furyl-C), 160.9 (NCN), 165.9 (CO); *m*/*z* 248 (M$^+$, 25%), 233 (6), 217 (10), 189 (100), 161 (10), 135 (10), 121 (10), 109 (36), 96 (24), 81 (32), 68 (9).

Data for (*E*)-isomer: mp 96–98 °C (Found: C, 62.74; H, 6.54; N, 11.01%; M$^+$ 248.1160. $C_{13}H_{18}N_2O_3$ requires: C, 62.89; H, 6.50, N, 11.28%; *M* 248.1160); ν_{max}(KBr)/cm^{-1} 2958, 1693 (CO), 1634 (C=N), 1315, 1286, 1217, 1168, 793, 740; δ_H (400 MHz) 2.66 and 3.01 (each 2H, t, *J* 7.8, C*H*$_2$C*H*$_2$Furyl), 3.48 (2H, t, *J* 9.0, NC*H*$_2$CH$_2$N), 3.65 (3H, s, OCH$_3$), 3.87 (2H, t, *J* 9.0, NCH$_2$C*H*$_2$N), 4.79 (1H, d, *J* 13.2, NCH=C*H*CO$_2$Me), 6.00 (1H, d, *J* 3.1, Furyl-3H), 6.21 (1H, dd, *J* 2.0 and 3.1, Furyl-4H), 7.25 (1H, d, *J* 2.0, Furyl-5H), 7.65 (1H, d, *J* 13.2, NC*H*=CHCO$_2$Me); δ_C (100 MHz) 24.5 and 26.2 (*C*H$_2$*C*H$_2$Furyl), 46.6 (NCH$_2$), 51.4 (OCH$_3$), 53.3 (NCH$_2$), 93.6 (NCH=*C*HCO$_2$Me), 105.9 and 110.5 (Furyl-CH), 138.8 (N*C*H=CHCO$_2$Me), 141.6 (Furyl-CH), 154.1 (Furyl-C), 160.1 (NCN), 168.9 (CO); *m*/*z* 248 (M$^+$, 23%), 233 (5), 217 (9), 205 (5), 189 (100), 175 (2), 161 (8), 135 (6), 121 (8), 109 (36), 96 (21), 81 (27), 68 (8).

2-(But-3-enyl)-1-(3-oxobut-1-enyl)-4,5-dihydroimidazole 15a

But-3-yn-2-one (0.47 cm^3, 5.33 mmol) was injected into 2-(but-3-enyl)-4,5-dihydroimidazole **7b** (0.63 g, 5.08 mmol) in dry methanol (50 cm^3) at 20 °C under nitrogen and the mixture was stirred for 14 h. The methanol was removed under reduced pressure and the residue purified by column chromatography on silica gel (0.25:99.75→2:98 v/v isopropylamine–ethyl acetate) to give the *title compound* as a yellow oil (0.81 g, 83%) (Found: (M − H)$^+$ 191.1184. $C_{11}H_{16}N_2O$ requires: *M* − *H* 191.1184); ν_{max}(film)/cm^{-1} 2950, 1642, 1572, 1479, 1405, 1354, 1257, 1201, 1005, 964, 927; δ_H (400 MHz) 2.20 (3H, s, CH$_3$), 2.47–2.52 (4H, m, C*H*$_2$C*H*$_2$CH=CH$_2$), 3.57 and 3.95 (each 2H, t, *J* 9.2, NCH$_2$CH$_2$N), 5.00–5.15 (2H, 2 × dd, *J* 1.7 and 11.2, 1.7 and 19.2, CH=C*H*$_2$), 5.30 (1H, d, *J* 13.2, NCH=C*H*COMe), 5.85–5.94 (1H, m, C*H*=CH$_2$), 7.75 (1H, d, *J* 13.2, NC*H*=CHCOMe); δ_C (100 MHz) 26.6 (CH$_2$), 28.7 (CH$_3$), 29.5 (CH$_2$), 46.3 and 53.3 (NCH$_2$), 103.6 (NCH=*C*HCOMe), 116.0 (CH=*C*H$_2$), 136.5 (*C*H=CH$_2$), 137.7 (N*C*H=CHCOMe), 160.2 (NCN), 196.6 (CO); *m*/*z* 192 (M$^+$, 27%), 177 (6), 149 (89), 135 (6), 121 (17), 111 (80), 96 (78), 83 (48), 68 (44), 55 (100), 43 (100).

2-Benzyl-1-(3-oxobut-1-enyl)-4,5-dihydroimidazole 15b

Prepared as for compound **15a** above, using but-3-yn-2-one (1.45 cm^3, 18.75 mmol), 2-benzyl-4,5-dihydroimidazole **7e** (2.50 g, 15.62 mmol) in dry methanol (20 cm^3) at 0 °C under nitrogen for 30 min and at 20 °C for 4 h, to give the *title compound* as a pale yellow solid (2.56 g, 72%), mp 104–106 °C (Found: C, 71.43; H, 7.09; N, 11.93%; M$^+$ 228.1263. $C_{14}H_{16}N_2O\cdot0.4H_2O$ requires: C, 71.39; H, 6.79; N, 11.89%; *M* 228.1262); ν_{max}(KBr)/cm^{-1} 2995, 2919, 1606, 1457, 1360, 1249, 1167, 1001, 942; δ_H (400 MHz) 2.10 (3H, s, CH$_3$), 3.56 (2H, t, *J* 9.3, NC*H*$_2$-

CH_2N), 3.88 (2H, s, PhCH_2), 4.02 (2H, t, *J* 9.3, NCH_2CH_2N), 5.20 (1H, d, *J* 13.2, NCH=C*H*COMe), 7.20–7.35 (5H, m, Ar-H), 7.67 (1H, d, *J* 13.2, NC*H*=CHCOMe); δ_C (100 MHz) 28.2 (CH_3), 34.3 (Ph*C*H_2), 46.6 and 53.7 (NCH_2), 104.5 (NCH=*C*HCOMe), 127.7, 128.7 and 129.1 (Ar-CH), 134.3 (Ar-C), 138.6 (N*C*H=CHCOMe), 159.7 (NCN), 196.7 (CO); *m*/*z* 228 (M^+, 29%), 213 (3), 185 (12), 171 (5), 159 (2), 117 (8), 111 (98), 96 (100), 91 (52), 83 (42), 70 (22).

General method for the synthesis of 1,2,3,5-tetrahydroimidazo-[1,2-*a*]pyridin-5-ones 16 and 1,2,3,5,6,7,8,9-octahydroimidazo-[1,2-*b*]isoquinolin-5-ones 17

The β-ketoester (2 mol equiv.) was injected into the 2-substituted-4,5-dihydroimidazole **7** (1 mol equiv.) in toluene and the solution heated to reflux using a Dean–Stark trap for 12 h. The toluene was then removed under reduced pressure and the crude product purified by column chromatography on silica gel (98 : 1 : 1→85 : 10 : 5 v/v ethyl acetate–methanol–isopropylamine) to give the imidazopyridin-5-ones **16** or imidazoisoquinolin-5-ones **17**.

7-Methyl-8-(prop-2-enyl)-1,2,3,5-tetrahydroimidazo[1,2-*a*]-pyridin-5-one 16a. Prepared by the general method, using 2-(but-3-enyl)-4,5-dihydroimidazole **7b** (0.20 g, 1.61 mmol), ethyl acetoacetate (0.41 cm^3, 3.22 mmol) in toluene (20 cm^3), as a yellow solid (0.14 g, 44%), mp 147–149 °C (Found: M^+ 190.1102. $C_{11}H_{14}N_2O$ requires: *M* 190.1106); λ_{max}/nm 204, 246, 332; ν_{max}(KBr)/cm^{-1} 3215 (NH), 3006, 2977, 1657 (NCO), 1545, 1467, 1421, 1399, 1288, 1202, 1106, 994, 909, 809; δ_H (400 MHz) 2.09 (3H, s, CH_3), 3.04–3.06 (2H, m, CH_2CH=CH_2), 3.71 and 4.20 (each 2H, t, *J* 8.6, NCH_2CH_2N), 4.66 (1H, br s, NH), 4.98–5.08 (2H, m, CH_2CH=CH_2), 5.77 (1H, s, NCOCH), 5.76–5.86 (1H, m, C*H*=CH_2); δ_C (75 MHz) 19.8 (CH_3), 30.3 (CH_2), 43.0 and 44.7 (NCH_2), 94.0 (NC=*C*), 107.4 (NCO*C*H), 115.3 (CH=*C*H_2), 135.4 (*C*H=CH_2), 150.6 (CH=*C*CH_3), 153.4.4 (N*C*=C), 160.6 (NCO); *m*/*z* 190 (M^+, 81%), 175 (16), 163 (100), 147 (9), 135 (12), 121 (8), 91 (11), 77 (13).

7-Phenyl-8-(prop-2-enyl)-1,2,3,5-tetrahydroimidazo[1,2-*a*]-pyridin-5-one 16b. Prepared by the general method, using 2-(but-3-enyl)-4,5-dihydroimidazole **7b** (0.20 g, 1.61 mmol) and ethyl benzoylacetate (0.55 cm^3, 3.22 mmol) in toluene (20 cm^3), as a yellow solid (0.35, 86%), mp 152–154 °C (Found: M^+ 252.1267. $C_{16}H_{16}N_2O$ requires: *M* 252.1263); λ_{max}/nm 204, 241, 343; ν_{max}(KBr)/cm^{-1} 3170 (NH), 2981, 2924, 1656 (NCO), 1547, 1475, 1417, 1375, 1181, 781, 708; δ_H (300 MHz) 2.87–2.91 (2H, m, CH_2CH=CH_2), 3.70 and 4.20 (each 2H, t, *J* 8.6, NCH_2-CH_2N), 4.75 (1H, br s, NH), 4.91–5.04 (2H, m, CH_2CH=CH_2), 5.77 (1H, s, NCOCH), 5.55–5.81 (1H, m, CH_2C*H*=CH_2), 7.15–7.21 (2H, m, Ar-H), 7.24–7.33 (3H, m, Ar-H); δ_C (75 MHz) 31.1 (CH_2), 42.9 and 44.6 (NCH_2), 92.7 (NC=*C*), 107.2 (NCO*C*H), 115.5 (CH=*C*H_2), 127.8, 127.9 and 128.1 (Ar-CH), 136.1 (*C*H=CH_2), 139.3 (Ar-C), 151.4 (CH=*C*Ph), 157.2 (N*C*=C), 160.2 (NCO); *m*/*z* 252 (M^+, 100%), 225 (59), 197 (10), 152 (14), 127 (19), 115 (15), 102 (11), 77 (18).

8-Benzyl-7-phenyl-1,2,3,5-tetrahydroimidazo[1,2-*a*]pyridin-5-one 16c. Prepared by the general method, using 2-(2-phenylethyl)-4,5-dihydroimidazole **7c** (0.10 g, 0.57 mmol) and ethyl benzoylacetate (0.20 cm^3, 1.14 mmol) in toluene (20 cm^3), as a white solid (0.13 g, 75%), mp 210–212 °C (Found: M^+ 302.1423. $C_{20}H_{18}N_2O$ requires: *M* 302.1419); λ_{max}/nm 343; ν_{max}(film)/cm^{-1} 3246 (NH), 1667 (NCO), 1546, 1526, 1468, 1415, 1289, 1237, 699; δ_H (400 MHz) 3.60 (2H, s, PhCH_2), 3.64 and 4.23 (each 2H, t, *J* 8.2, NCH_2CH_2N), 4.38 (1H, br s, NH), 5.89 (1H, s, NCOCH), 7.08–7.36 (10H, m, Ar-H); δ_C (100 MHz) 32.4 (CH_2), 42.9 and 44.6 (NCH_2), 93.9 (NC=*C*), 107.3 (NCO*C*H), 126.4, 127.7, 127.8, 127.9, 128.2 and 128.8 (Ar-CH), 139.2 and 139.5 (Ar-C), 151.45 (CH=*C*Ph), 157.4 (N*C*=C), 160.3 (NCO); *m*/*z* 302 (M^+, 13%), 273 (2), 225 (14), 202 (2), 167 (2), 154 (2), 140 (2), 127 (5), 105 (5), 91 (19), 77 (19).

7-Methyl-8-phenyl-1,2,3,5-tetrahydroimidazo[1,2-*a*]pyridin-5-one 16d. Prepared by the general method, using 2-benzyl-4,5-dihydroimidazole **7e** (0.90 g, 5.62 mmol) and ethyl acetoacetate (1.43 cm^3, 11.25 mmol) in toluene (30 cm^3), as a white solid (0.72 g, 56%), mp 161–163 °C (lit.,[10] 161–162 °C) (Found: M^+ 226.1107. $C_{14}H_{14}N_2O$ requires: *M* 226.1106); λ_{max}/nm 333; ν_{max}(KBr)/cm^{-1} 3145 (NH), 1657 (NCO), 1559, 1519, 1493, 1439, 1296, 702; δ_H (400 MHz) 1.95 (3H, s, CH_3), 3.66 and 4.23 (each 2H, t, *J* 8.2, NCH_2CH_2N), 4.48 (1H, br s, NH), 5.82 (1H, s, NCOCH), 7.21–7.41 (5H, m, Ar-H); δ_C (100 MHz) 20.5 (CH_3), 42.8 and 44.7 (NCH_2), 99.7 (NC=*C*), 107.0 (NCO*C*H), 127.3, 129.1 and 130.5 (Ar-CH), 135.2 (Ar-C), 151.2 (CH=*C*CH_3), 152.4 (N*C*=C), 160.5 (NCO); *m*/*z* 226 (M^+, 100%), 198 (29), 182 (5), 169 (5), 153 (5), 128 (11), 115 (12), 103 (4), 91 (5), 83 (7), 57 (5).

7,8-Diphenyl-1,2,3,5-tetrahydroimidazo[1,2-*a*]pyridin-5-one 16e. Prepared by the general method, using 2-benzyl-4,5-dihydroimidazole **7e** (1.00 g, 6.25 mmol) and ethyl benzoylacetate (2.16 cm^3, 12.50 mmol) in toluene (62 cm^3), as a yellow crystalline solid (1.05 g, 58%), mp 279–281 °C [lit.,[10] 270 °C (decomp.)] (Found: M^+ 288.1259. $C_{19}H_{16}N_2O$ requires: *M* 288.1263); λ_{max}/nm 349; ν_{max}(KBr)/cm^{-1} 3234 (NH), 1646 (NCO), 1586, 1531, 1500, 1487, 1469, 1420, 1282, 768, 699; δ_H (400 MHz) 3.69 and 4.20 (each 2H, t, *J* 8.3, NCH_2CH_2N), 4.98 (1H, br s, NH), 5.95 (1H, s, NCOCH), 7.05–7.28 (10H, m, Ar-H); δ_C (100 MHz) 42.8 and 44.9 (NCH_2), 98.3 (NC=*C*), 107.4 (NCO*C*H), 126.7, 127.8, 128.0, 128.6, 128.9 and 130.6 (Ar-CH), 135.3 and 139.0 (Ar-C), 151.0 (CH=*C*Ph), 155.5 (N*C*=C), 160.5 (NCO); *m*/*z* 288 (M^+, 6%), 242 (2), 223 (3), 210 (3), 190 (4), 162 (4), 120 (16), 91 (24), 57 (18).

10-Benzyl-1,2,3,5,6,7,8,9-octahydroimidazo[1,2-*b*]isoquinolin-5-one 17a. Prepared by the general method, using 2-(2-phenylethyl)-4,5-dihydroimidazole **7c** (0.10 g, 0.57 mmol) and ethyl 2-oxocyclohexanecarboxylate (0.18 cm^3, 1.15 mmol) in toluene (20 cm^3), as a white solid (0.12 g, 75%), mp 231–233 °C (Found: M^+ 280.1575. $C_{18}H_{20}N_2O$ requires: *M* 280.1576); λ_{max}/nm 335; ν_{max}(film)/cm^{-1} 3240 (NH), 2927, 1652 (NCO), 1533, 1494, 1481, 1290, 1228, 740; δ_H (400 MHz) 1.65–1.70 (4H, m, $CH_2C\mathit{H}_2C\mathit{H}_2CH_2$), 2.42 and 2.53 (each 2H, t, *J* 4.8, C$H_2$$CH_2$-$CH_2C\mathit{H}_2$), 3.57 (2H, t, *J* 8.4, NC$H_2$$CH_2$N), 3.68 (2H, s, PhC$H_2$), 4.20 (2H, t, *J* 8.2, $NCH_2C\mathit{H}_2$N), 4.30 (1H, br s, NH), 7.10–7.30 (5H, m, Ar-H); δ_C (100 MHz) 22.2, 22.5, 23.5, 26.9 and 31.2 (CH_2), 42.7 and 44.8 (NCH_2), 94.2 (NC=*C*), 115.4 (NCO*C*), 126.3, 127.6 and 128.7 (Ar-CH), 139.6 (Ar-C), 147.6 (NCOC=*C*), 149.2 (N*C*=C), 160.2 (NCO); *m*/*z* 280 (M^+, 100%), 265 (26), 251 (29), 236 (5), 203 (29), 189 (10), 175 (6), 152 (3), 115 (5), 91 (14), 69 (15).

10-(Biphenyl-2-ylmethyl)-1,2,3,5,6,7,8,9-octahydroimidazo-[1,2-*b*]isoquinolin-5-one 17b. Prepared by the general method, using 2-(2-biphenyl-2-ylethyl)-4,5-dihydroimidazole **7d** (0.50 g, 2.00 mmol) and ethyl 2-oxocyclohexanecarboxylate (0.64 cm^3, 4.00 mmol) in toluene (20 cm^3), as a white solid (0.63 g, 88%), mp 251–253 °C (Found: M^+ 356.1889. $C_{24}H_{24}N_2O$ requires: *M* 356.1889); λ_{max}/nm 206, 244, 338; ν_{max}(film)/cm^{-1} 3208 (NH), 2928, 1657 (NCO), 1533, 1494, 1476, 1450, 1288, 1230, 1154, 751; δ_H (300 MHz) 1.61–1.66 (4H, m, $CH_2C\mathit{H}_2C\mathit{H}_2CH_2$), 2.25 and 2.49 (each 2H, t, *J* 4.8, C$H_2$$CH_2CH_2C\mathit{H}_2$), 3.51 (2H, t, *J* 8.4, NC$H_2$$CH_2$N), 3.59 (2H, s, ArC$H_2$), 3.86 (1H, br s, NH), 4.17 (2H, t, *J* 8.2, $NCH_2C\mathit{H}_2$N), 7.18–7.46 (9H, m, Ar-H); δ_C (75 MHz) 22.2, 22.5, 23.4, 26.8, and 29.6 (CH_2), 42.7 and 44.8 (NCH_2), 94.4 (NC=*C*), 115.6 (NCO*C*), 126.3, 127.2, 127.4, 127.9, 128.3, 129.1 and 136.7 (Ar-CH), 139.6, 141.4 and 142.2 (Ar-C), 147.6 (NCOC=*C*), 149.2 (N*C*=C), 160.2 (NCO); *m*/*z* 356 (M^+, 100%), 355 (28), 341 (11), 327 (7), 313 (4), 277 (4), 251

(3), 215 (4), 203 (71), 189 (20), 175 (15), 165 (33), 152 (21), 128 (5), 115 (6), 91 (6), 77 (16), 44 (23).

10-Phenyl-1,2,3,5,6,7,8,9-octahydroimidazo[1,2-*b*]isoquinolin-5-one 17c. Prepared by the general method, using 2-benzyl-4,5-dihydroimidazole **7e** (5.00 g, 31.25 mmol) and ethyl 2-oxocyclohexanecarboxylate (9.98 cm^3, 62.50 mmol) in toluene (150 cm^3), as a yellow solid (5.48 g, 66%), mp 233–235 °C (lit.,[10] 240–242 °C) (Found: M^+ 266.1417. $C_{17}H_{18}N_2O$ requires: *M* 266.1419); λ_{max}/nm 334; ν_{max}(film)/cm^{-1} 3127 (NH), 2935, 1650 (NCO), 1563, 1523, 1491, 1436, 1096, 698; δ_H (400 MHz) 1.56–1.62 and 1.67–1.72 (each 2H, m, $CH_2CH_2CH_2CH_2$), 2.22 and 2.53 (each 2H, t, *J* 4.8, $CH_2CH_2CH_2CH_2$), 3.59 (2H, t, *J* 8.4, NCH_2CH_2N), 4.11 (1H, br s, NH), 4.22 (2H, t, *J* 8.2, NCH_2CH_2N), 7.19–7.30 (5H, m, Ar-H); δ_C (100 MHz) 22.3, 22.5, 23.4 and 28.5 (CH_2), 42.7 and 44.9 (NCH_2), 98.9 (NC=*C*), 114.9 (NCO*C*), 127.3, 128.9 and 130.8 (Ar-CH), 135.2 (Ar-C), 146.8 (NCOC=*C*), 148.3 (N*C*=C), 160.3 (NCO); *m*/*z* 266 (M^+, 52%), 251 (14), 237 (28), 206 (11), 191 (19), 149 (71), 115 (12), 105 (13), 91 (53), 77 (15).

Crystal data for **17c**: $C_{17}H_{18}N_2O$, $M = 266.33$, triclinic, $a = 8.831(2)$, $b = 11.534(2)$, $c = 13.182(3)$ Å, $\alpha = 90.34$, $\beta = 92.49$, $\gamma = 90.79°$, $U = 13441.3(5)$ Å^3, $T = 150(2)$ K, space group $P\bar{1}$, monochromated Mo-Kα radiation, $\lambda = 0.71073$ Å, $Z = 4$, $D_c = 1.319$ Mg m^{-3}, $F(000) = 568$, yellow crystals, dimensions $0.5 \times 0.2 \times 0.1$ mm, μ(Mo-Kα) = 0.083 mm^{-1}, $1.77 < 2\theta < 24°$, 21333 reflections measured, 4182 unique reflections. The structure was solved by direct methods and refined by full-matrix least-squares on F^2. The final cycle (for 378 parameters) converged with $wR_2 = 0.1873$ (for all data) and $R_1 = 0.0661$ [$I > 2\sigma(I)$].

General method for the synthesis of diethyl 2-(2-substituted-4,5-dihydroimidazol-1-yl)butene-1,4-dioates 19 and 5-ethoxycarbonylmethylene-2,3,5,6-tetrahydro-1*H*-pyrrolo[1,2-*a*]imidazol-6-ones 20

Diethyl acetylenedicarboxylate (1.2 mol equiv.) was injected into a solution of 2-substituted-4,5-dihydroimidazole **7** (1 equiv.) in dry dichloromethane (1 M in dihydroimidazole) at 0 °C. The reaction was allowed to warm to 20 °C and stirred for the time stated. Any precipitate was collected by filtration to afford the pyrroloimidazolones **20**, the dichloromethane was removed from the filtrate and the residue chromatographed on silica gel (ethyl acetate–hexane 3:7 v/v) to give the diethyl dihydroimidazolylbutene-1,4-dioates **19**.

Diethyl (*E*)-2-[2-(but-3-enyl)-4,5-dihydroimidazol-1-yl]-butene-1,4-dioate 19a and (*Z*)-5-ethoxycarbonylmethylene-7-(prop-2-enyl)-2,3,5,6-tetrahydro-1*H*-pyrrolo[1,2-*a*]imidazol-6-one 20a. Prepared by the general method, using 2-(but-3-enyl)-4,5-dihydroimidazole **7b** (0.83 g, 6.69 mmol) and diethyl acetylenedicarboxylate (1.28 cm^3, 8.03 mmol), to give after stirring for 7 d the *pyrroloimidazolone* **20a** as a yellow solid (0.10 g, 6%), mp 162–164 °C (Found: C, 60.36; H, 6.40; N, 10.30%; MH^+ 249.1239. $C_{13}H_{16}N_2O_3 \cdot 0.5H_2O$ requires: C, 60.70; H, 6.61, N, 10.89%; *MH* 249.1235); ν_{max}(KBr)/cm^{-1} 3391 (NH), 3317, 2981, 1714 (CO_2Et), 1658 (CO), 1554, 1494, 1321, 1150; δ_H (300 MHz) 1.29 (3H, t, *J* 7.1, CH_3CH_2), 2.97 (2H, d, *J* 6.4, $CH_2CH{=}CH_2$), 3.94 (2H, t, *J* 7.4, NCH_2CH_2N), 4.14–4.26 (4H, m, CH_3CH_2 and NCH_2CH_2N), 5.01–5.13 (2H, m, CH=CH_2), 5.78–5.88 (1H, m, C*H*=CH_2), 5.83 (1H, s, C*H*CO_2Et), NH not observed; δ_C (75 MHz) 14.3 (CH_3), 25.4 (CH_2), 45.4 and 47.6 (NCH_2), 60.2 (OCH_2), 85.9 (NC=*C*), 93.9 (*C*HCO_2Et), 115.1 (CH=CH_2), 136.6 (*C*H=CH_2), 144.1 (*C*=CHCO_2Et), 166.5 (N*C*=C), 168.8 (*C*O_2Et), 181.3 (CO); *m*/*z* 248 (M^+, 15%), 219 (4), 202 (10), 191 (13), 173 (15), 161 (14), 147 (17), 135 (5), 121 (8), 105 (12), 84 (62); and the *diethyl dihydroimidazolylbutene-1,4-dioate* **19a** as a yellow oil (0.34 g, 17%) (Found: C, 60.24; H, 7.46; N, 9.03%; M^+ 294.1574. $C_{15}H_{22}N_2O_4 \cdot 0.3H_2O$ requires: C, 60.08; H, 7.54, N, 9.35%; *M* 294.1579); ν_{max}(film)/cm^{-1} 2983, 1737 (CO), 1694 (CO), 1639 (C=N), 1577, 1421, 1372, 1337, 1160, 1096, 1027, 915, 800; δ_H (300 MHz) 1.27 (3H, t, *J* 7.2, CH_3CH_2), 1.38 (3H, t, *J* 7.3, CH_3CH_2), 2.42 (4H, m, CH_2CH_2-$CH{=}CH_2$), 3.62 and 3.86 (each 2H, t, *J* 8.9, NCH_2CH_2N), 4.12 (2H, q, *J* 7.2, CH_3CH_2), 4.35 (2H, q, *J* 7.3, CH_3CH_2), 5.02 (1H, s, C*H*CO_2Et), 5.02–5.15 (2H, m, CH=CH_2), 5.78–5.88 (1H, m, C*H*=CH_2); δ_C (75 MHz) 13.7 and 14.3 (CH_3), 25.4 and 30.1 (CH_2), 50.0 and 51.9 (NCH_2), 60.1 and 62.8 (OCH_2), 96.2 (*C*HCO_2Et), 115.5 (CH=*C*H_2), 136.9 (*C*H=CH_2), 144.5 (N*C*=CH), 159.3 (NCN), 164.5 and 166.4 (CO); *m*/*z* 294 (M^+, 7%), 265 (3), 249 (9), 221 (100), 193 (45), 175 (8), 147 (18), 126 (24), 98 (18), 82 (14).

Diethyl (*E*)-2-[2-(biphenyl-2-ylethyl)-4,5-dihydroimidazol-1-yl]butene-1,4-dioate 19b and its (*Z*)-isomer. Prepared by the general method, using 2-(2-biphenyl-2-ylethyl)-4,5-dihydroimidazole **7d** (0.77 g, 3.07 mmol) and diethyl acetylenedicarboxylate (0.36 cm^3, 2.22 mmol), to give after stirring for 8 h the (*E*)-*isomer* of the *title compound* as a yellow gum, recrystallised from hexane–ethyl acetate as a white crystalline solid (0.43 g, 54%), mp 85–87 °C (Found: C, 71.20; H, 6.70; N, 6.64%; $(M - H)^+$ 419.1974. $C_{25}H_{28}N_2O_4$ requires: C, 71.41; H, 6.71; N, 6.64%; *M* − *H* 419.1971); ν_{max}(film)/cm^{-1} 2981, 1741 and 1703 (CO_2Et), 1641, 1575, 1479, 1197, 1156, 1046, 752; δ_H (300 MHz) 1.19 and 1.26 (each 3H, t, *J* 7.2, CH_3CH_2), 2.41 and 3.00 (each 2H, t, *J* 8.0, CH_2CH_2Ar), 3.56 and 3.79 (each 2H, t, *J* 9.0, NCH_2CH_2N), 4.12 and 4.20 (each 2H, q, *J* 7.2, CH_3CH_2), 4.91 (1H, s, C*H*CO_2Et), 7.18–7.43 (9H, m, Ar-H); δ_C (75 MHz) 13.4 and 14.2 (CH_3), 29.4 and 30.1 (CH_2), 49.8 and 51.9 (NCH_2), 60.0 and 62.6 (OCH_2), 96.0 (*C*HCO_2Et), 126.3, 127.0, 127.6, 128.3, 129.1, 130.3, 138.3 (Ar-CH), 141.4 and 141.9 (Ar-C), 144.4 (N*C*=CH), 159.1 (NCN), 164.4 and 166.4 (CO); *m*/*z* 421 (MH^+, 2%), 375 (3), 347 (100), 319 (21), 273 (9), 213 (6), 191 (5), 178 (15), 165 (72), 152 (33), 139 (7), 126 (6), 94 (7), 68 (15); and the (*Z*)-*isomer* of the *title compound* as a thick yellow oil (0.12 g, 15%) (Found: M^+ 420.2052. $C_{25}H_{28}N_2O_4$ requires: *M* 420.2049); ν_{max}(film)/cm^{-1} 2981, 2939, 1729, 1610, 1480, 1368, 1259, 1172, 1033, 753; δ_H (300 MHz) 1.24–2.31 (6H, m, $2 \times CH_3CH_2$), 2.12 and 2.88 (each 2H, t, *J* 8.3, CH_2CH_2Ar), 3.62 and 3.81 (each 2H, t, *J* 9.9, NCH_2CH_2N), 4.14 and 4.20 (each 2H, q, *J* 7.2, CH_3CH_2), 6.30 (C*H*CO_2Et), 7.14–7.40 (9H, m, Ar-H); δ_C (75 MHz) 14.1 and 14.2 (CH_3), 29.8 and 30.6 (CH_2), 51.5 and 53.7 (NCH_2), 60.9 and 62.3 (OCH_2), 118.5 (*C*HCO_2Et), 126.1, 126.9, 127.6, 128.2, 129.0, 129.4, 130.2 (Ar-CH), 138.4, 141.5 and 141.8 (Ar-C), 140.0 (N*C*=CH), 163.4 (NCN), 163.9 and 164.0 (CO); *m*/*z* 420 (M^+, 2%), 391 (1), 375 (2), 364 (1), 347 (100), 319 (20), 275 (6), 249 (5), 238 (2), 178 (7), 165 (29), 152 (12), 128 (3), 115 (2), 91 (5).

Crystal data for **19b**: $C_{25}H_{28}N_2O_4$, $M = 420.49$, triclinic, $a = 11.0117(5)$, $b = 10.6661(8)$, $c = 12.2753(9)$ Å, $\alpha = 65.331(3)$, $\beta = 65.329(4)$, $\gamma = 62.908(3)°$, $U = 1119.42(13)$ Å^3, $T = 298(2)$ K, space group $P\bar{1}$, monochromated Mo-Kα radiation, $\lambda = 0.71073$ Å, $Z = 2$, $D_c = 1.248$ Mg m^{-3}, $F(000) = 448$, colourless plates, dimensions $0.1 \times 0.1 \times 0.02$ mm, μ(Mo-Kα) = 0.085 mm^{-1}, $3.26 < 2\theta < 23.25°$, 8067 reflections measured, 3169 unique reflections. The structure was solved by direct methods and refined by full-matrix least-squares on F^2. The final cycle (for 283 parameters) converged with $wR_2 = 0.1373$ (for all data) and $R_1 = 0.0558$ [$I > 2\sigma(I)$].

Diethyl (*E*)-2-(2-benzyl-4,5-dihydroimidazol-1-yl)butene-1,4-dioate 19c and (*Z*)-5-ethoxycarbonylmethylene-7-phenyl-2,3,5,6-tetrahydro-1*H*-pyrrolo[1,2-*a*]imidazol-6-one 20c. Prepared by the general method, using 2-benzyl-4,5-dihydroimidazole **7e** (2.00 g, 12.5 mmol) and diethyl acetylenedicarboxylate (2.40 cm^3, 15.00 mmol), to give after stirring for 8 h the *pyrroloimidazolone* **20c** as an orange solid recrystallised from methanol (1.50 g, 42%), mp 230–232 °C (Found: C, 67.55; H, 5.64; N, 9.84%; M^+ 284.1155. $C_{16}H_{16}N_2O_3$ requires: C, 67.59; H, 5.67, N,

9.85%; *M* 284.1161); ν_{max}(KBr)/cm^{-1} 3291 (NH), 2984, 1712 (CO_2Et), 1655 (CO), 1603, 1559, 1515, 1482, 1447, 1307, 1189, 1154, 1105, 701; δ_H [300 MHz; $(CD_3)_2SO$], 1.21 (3H, t, *J* 7.2, CH_3CH_2), 4.00 (2H, t, *J* 7.5, NCH_2CH_2N), 4.10–4.17 (4H, m, CH_3CH_2 and NCH_2CH_2N), 5.48 (1H, s, $CHCO_2Et$), 7.05 (1H, t, *J* 7.5, Ar-H), 7.28 (2H, t, *J* 7.5, Ar-H), 7.69 (2H, d, *J* 7.5, Ar-H), NH not observed; δ_C [75 MHz; $(CD_3)_2SO$] 14.1 (CH_3), 44.8 and 48.0 (NCH_2), 59.8 (OCH_2), 88.4 (NC=*C*), 90.9 (*C*HCO_2Et), 123.7, 124.2 and 128.1 (Ar-CH), 132.5 (Ar-C), 144.0 (*C*=CH-CO_2Et), 165.4 (N*C*=C), 168.8 (*C*O_2Et), 180.8 (CO); *m*/*z* 284 (M^+, 47%), 238 (42), 211 (28), 183 (32), 168 (9), 154 (27), 143 (27), 128 (48), 115 (88), 103 (31), 89 (100), 77 (48), 63 (35); and the diethyl dihydroimidazolylbutene-1,4-dioate **19c** as an orange gum (1.42 g, 34%) that was incompletely characterised; ν_{max}(film)/cm^{-1} 2982, 1739 and 1704 (CO_2Et), 1577, 1416, 1366, 1161, 1021, 756; δ_H (300 MHz) 1.23–1.33 (6H, m, 2 × CH_3CH_2), 3.64 (2H, t, 9.6, NCH_2CH_2N), 3.69 (2H, s, $PhCH_2$), 3.84 (2H, t, *J* 9.6, NCH_2CH_2N), 4.14 and 4.30 (each 2H, q, *J* 7.2, CH_3CH_2), 5.05 (1H, s, $CHCO_2Et$), 7.18–7.34 (5H, m, Ar-H); δ_C (75 MHz) 13.5 and 14.2 (CH_3), 34.7 (CH_2), 50.1 and 52.0 (NCH_2), 62.0 and 62.7 (OCH_2), 96.9 (*C*HCO_2Et), 126.9, 128.4 and 129.1 (Ar-CH), 134.9 (Ar-C), 144.2 (*C*=$CHCO_2Et$), 158.8 (NCN), 164.4 and 166.2 (CO); *m*/*z* 331 (MH^+, 2%), 303 (1), 289 (2), 257 (23), 238 (16), 229 (7), 213 (47), 200 (10), 183 (7), 162 (9), 140 (32), 126 (28), 91 (100).

Crystal data for **20c**: $C_{16}H_{16}N_2O_3$, $M = 284.32$, orthorhombic, $a = 7.1760(10)$, $b = 17.805(4)$, $c = 20.947(4)$ Å, $U = 2976.4(9)$ Å^3, $T = 150(2)$ K, space group P_{bca}, monochromated Mo-Kα radiation, $\lambda = 0.71073$ Å, $Z = 8$, $D_c = 1.411$ Mg m^{-3}, $F(000) = 1200$, orange needles, dimensions $0.4 \times 0.25 \times 0.25$ mm, μ(Mo-Kα) = 0.099 mm^{-1}, $1.94 < 2\theta < 27.47°$, 16412 reflections measured, 3062 unique reflections. The structure was solved by direct methods and refined by full-matrix least-squares on F^2. The final cycle (for 191 parameters) converged with $wR_2 = 0.1595$ (for all data) and $R_1 = 0.0576$ [$I > 2\sigma(I)$].

(*Z*)-5-Methoxycarbonylmethylene-7-phenyl-2,3,5,6-tetrahydro-1*H*-pyrrolo[1,2-*a*]imidazol-6-one 20d and its (*E*)-isomer. Prepared by the general method, using 2-benzyl-4,5-dihydroimidazole **7e** (3.05 g, 19.06 mmol) and dimethyl acetylenedicarboxylate (2.81 cm^3, 22.87 mmol), to give after stirring for 72 h the (*Z*)-*isomer* of the *title compound*, as an orange precipitate recrystallised from methanol (1.24 g, 24%), mp 236–238 °C (Found: C, 66.17; H, 5.14; N, 10.25%; M^+ 270.1002. $C_{15}H_{14}N_2O_3$ requires: C, 66.66; H, 5.22; N, 10.36%; *M* 270.1004); ν_{max}(KBr)/cm^{-1} 3255 (NH), 1717 (CO_2Me), 1674 (CO), 1604, 1562, 1514, 1309, 1189, 1169, 1154, 1105; δ_H [300 MHz; $(CD_3)_2SO$] 3.66 (3H, s, CH_3), 4.00 and 4.13 (2H, t, *J* 7.2, NCH_2CH_2N), 5.49 (1H, s, $CHCO_2Me$), 7.05 (1H, t, *J* 7.5, Ar-H), 7.28 (2H, t, *J* 7.5, Ar-H), 7.67 (2H, d, *J* 7.5, Ar-H), 9.58 (1H, br s, NH); δ_C [75 MHz; $(CD_3)_2SO$] 44.8 and 47.9 (NCH_2), 51.2 (OCH_3), 88.4 (NC=*C*), 90.6 (*C*HCO_2Me), 123.7, 124.2 and 128.1 (Ar-CH), 132.4 (Ar-C), 144.1 (*C*=$CHCO_2Me$), 165.8 (N*C*=C), 168.2 (*C*O_2Me), 180.8 (CO); *m*/*z* 270 (M^+, 86%), 238 (100), 209 (29), 181 (26), 168 (4), 153 (14), 143 (17), 129 (10), 115 (34), 103 (12), 89 (38), 77 (19); the (*E*)-*isomer* of the *title compound* was obtained from the filtrate, by evaporation and recrystallision of the residue from methanol–hexane, as an orange solid (1.70 g, 33%), mp 161–163 °C (Found: M^+ 270.1020. $C_{15}H_{14}N_2O_3$ requires: *M* 270.1004); ν_{max}(KBr)/cm^{-1} 3251 (NH), 1716, 1614, 1550, 1511, 1494, 1443, 1421, 1233, 1218, 1183, 797, 776; δ_H (300 MHz) 3.38 (2H, t, *J* 7.2, NCH_2CH_2N), 3.78 (3H, s, CH_3), 4.36 (2H, t, *J* 7.2, NCH_2CH_2N), 4.98 (1H, s, $CHCO_2Me$), 7.26 (1H, t, *J* 7.6, Ar-H), 7.39 (2H, t, *J* 7.6, Ar-H), 8.22 (2H, d, *J* 7.6, Ar-H), 13.72 (1H, br s, NH); δ_C (100 MHz) 41.3 (NCH_2), 51.9 (OCH_3), 61.2 (NC=*C*), 87.8 (*C*HCO_2Me), 127.1, 127.4 and 128.3 (Ar-CH), 130.8 (Ar-C), 148.6 (*C*=$CHCO_2Me$), 159.3 (N*C*=C), 163.9 (*C*O_2Et), 172.7 (CO); *m*/*z* 270 (M^+, 25%), 238 (100), 209 (6), 181 (5), 153 (7), 143 (9), 128 (6), 115 (17), 91 (13), 77 (2).

5-Ethoxycarbonylmethylene-7-(biphenyl-2-ylmethyl)-2,3,5,6-tetrahydro-1*H*-pyrrolo[1,2-*a*]imidazol-6-one, the (*E*)-isomer of 20b. Diethyl (*E*)-2-[2-(biphenyl-2-ylethyl)-4,5-dihydroimidazol-1-yl]butene-1,4-dioate **19b** (68 mg, 0.16 mmol) in THF (5 cm^3) was added to potassium *tert*-butoxide (35 mg, 0.31 mmol) in THF (3 cm^3). The yellow solution was stirred at 20 °C for 12 h, the solvent was removed under reduced pressure and the residue chromatographed on silica gel (0:3:7→5:95:0 methanol–ethyl acetate–hexane) to give the *title compound* as a yellow oil (32 mg, 54%) (Found: M^+ 374.1627. $C_{23}H_{22}N_2O_3$ requires: *M* 374.1630); ν_{max}(film)/cm^{-1} 3404 (NH), 1712 (CO_2Et), 1659 (CO), 1568, 1480, 1369, 1163; δ_H (300 MHz) 1.27 (3H, t, *J* 7.1, CH_3CH_2), 3.55 (2H, s, CH_2Ar), 3.63 and 4.09 (each 2H, t, *J* 7.4, NCH_2), 4.14 (2H, q, *J* 7.1, CH_3CH_2), 5.77 (1H, s, $CHCO_2Et$), 7.20–7.47 (9H, m, Ar-H), NH not observed; δ_C (75 MHz) 14.2 (CH_3), 25.0 (CH_2), 45.3 and 47.3 (NCH_2), 60.2 (OCH_2), 88.1 (NC=*C*), 93.9 (*C*HCO_2Et), 126.4, 127.1, 127.9, 128.3, 129.5, 130.3 and 137.6 (Ar-CH), 141.2 and 141.8 (Ar-C), 143.6 (*C*=$CHCO_2Et$), 166.5 (N*C*=C), 169.4 (CO_2Et), 184.4 (CO); *m*/*z* 374 (M^+, 17%), 345 (3), 328 (2), 317 (2), 299 (9), 271 (22), 247 (2), 221 (2), 203 (11), 189 (8), 178 (16), 165 (100), 152 (66), 128 (9), 115 (13), 94 (8), 7 (42).

(*Z*)-5-Ethoxycarbonylmethylene-7-phenyl-2,3,5,6-tetrahydro-1*H*-pyrrolo[1,2-*a*]imidazol-6-one 20c and its (*E*)-isomer. Prepared as for pyrroloimidazolone **20b**, using diethyl (*E*)-2-(2-benzyl-4,5-dihydroimidazol-1-yl)butene-1,4-dioate **19c** (68 mg, 0.16 mmol) to give the (*Z*)- and (*E*)-isomers of the *title compound* (0.69 g, 67%; *Z*:*E* 5:1) as orange and yellow solids, respectively, after chromatography. (*E*)-isomer (less polar material): mp 172–174 °C (Found: M^+ 284.1161. $C_{16}H_{16}N_2O_3$ requires: *M* 284.1161); ν_{max}(KBr)/cm^{-1} 3436 (NH), 1636, 1610, 1543, 1495, 1233, 1216, 1186, 780; δ_H (300 MHz) 1.36 (3H, t, *J* 7.2, CH_3CH_2), 3.49 (2H, t, *J* 7.2, NCH_2CH_2N), 4.25 (2H, q, *J* 7.2, CH_3CH_2), 4.43 (2H, t, *J* 7.2, NCH_2CH_2N), 5.06 (1H, s, $CHCO_2Et$), 7.26 (1H, t, *J* 7.8, Ar-H), 7.39 (2H, t, *J* 7.8, Ar-H), 8.22 (2H, d, *J* 7.8, Ar-H), 13.82 (1H, br s, NH); δ_C (100 MHz) 14.2 (CH_3), 41.1 and 41.5 (NCH_2), 61.1 (NC=*C*), 61.7 (OCH_2), 88.4 (*C*HCO_2Et), 127.1, 127.4, 128.3 (Ar-CH), 130.8 (Ar-C), 148.7 (*C*=$CHCO_2Et$), 159.3 (N*C*=C), 164.2 (*C*O_2Et), 172.7 (CO); *m*/*z* 284 (M^+, 17%), 238 (100), 209 (15), 181 (10), 167 (1), 153 (5), 143 (6), 128 (6), 115 (17), 103 (4), 89 (7), 77 (4); (*Z*)-isomer identical to that reported above.

Acknowledgements

We thank the Open University for a studentship (P. D.), the EPSRC for its support of the National X-Ray Crystallography Service Centre, and the EPSRC National Mass Spectrometry Service Centre (Swansea) for some MS data. One of the authors (R. C. F. J.) would like to acknowledge his debt of gratitude to the late Professor Leslie Crombie for help, advice and guidance at an early stage in his career.

References

1 See for example: R. J. Grout in *The Chemistry of Amidines and Imidates*, ed. S. Patai, Wiley Interscience, London, 1975, p. 255; D. M. Bailey, C. G. Degrazia, D. Wood and J. Siggins, *J. Med. Chem.*, 1974, **17**, 702.
2 R. R. Ruffolo, W. E. Bondinell and J. P. Hieble, *J. Med. Chem.* 1995, **38**, 3681; C. B. Chapleo, *Chem. Br.*, 1986, 313.
3 R. C. F. Jones and P. Dimopoulos, *Tetrahedron*, 2000, **56**, 2061; R. C. F. Jones, P. Patel, S. C. Hirst and I. Turner, *Tetrahedron*, 1997, **53**, 11781; R. C. F. Jones, J. S. Snaith, M. W. Anderson and M. J. Smallridge, *Tetrahedron*, 1997, **53**, 1111; M. W. Anderson, R. C. F. Jones and J. Saunders, *J. Chem. Soc., Perkin Trans. 1*, 1986, 205; M. W. Anderson, R. C. F. Jones and J. Saunders, *J. Chem. Soc., Perkin Trans. 1*, 1986, 1995.
4 R. C. F. Jones and J. Schofield, *J. Chem. Soc., Perkin Trans. 1*, 1990, 375–383.
5 R. C. F. Jones, P. Patel, S. C. Hirst and M. J. Smallridge, *Tetrahedron*, 1998, **54**, 6191.

6 See: Z.-T. Huang and M.-X. Wang in *The Chemistry of Enamines*, ed. Z. Rappoport, Wiley Interscience, London, 1994, p. 1303, for a survey of annulations of ketene aminals **2** and analogues.
7 *Cf.* M.-X. Wang, J.-M. Liang and Z.-T. Huang, *J. Chem. Res.* (*S*), 1994, 166; *J. Chem. Res.* (*M*), 1994, 1001.
8 R. C. F. Jones and S. C. Hirst, *Tetrahedron Lett.*, 1989, **30**, 5361.
9 See: J.-H. Zhang, M.-X. Wang and Z.-T. Huang, *J. Chem. Soc.*, *Perkin Trans. 1*, 1999, 2087, for a discussion of the aza-ene mechanism in reactions of ketene aminals having a secondary amino group.
10 C. V. Magani and F. J. Villani, *J. Heterocycl. Chem.*, 1978, **15**, 1021.
11 Crystal data for compounds **17c**, **19b** and **20c** are deposited with the Cambridge Crystallographic Database, CCDC reference number 207/444. See http://www.rsc.org/suppdata/p1/b0/b001830i/ for crystallographic files in .cif format.
12 *Cf.* Z.-T. Huang and M.-X. Wang, *J. Chem. Soc.*, *Perkin Trans. 1*, 1993, 1085.