A new synthesis of substituted imidazo[4,5-*b*]pyridinones by reductive cyclisation of 4-nitro-1*H*-imidazol-5-yl di- and tri-carbonyl compounds

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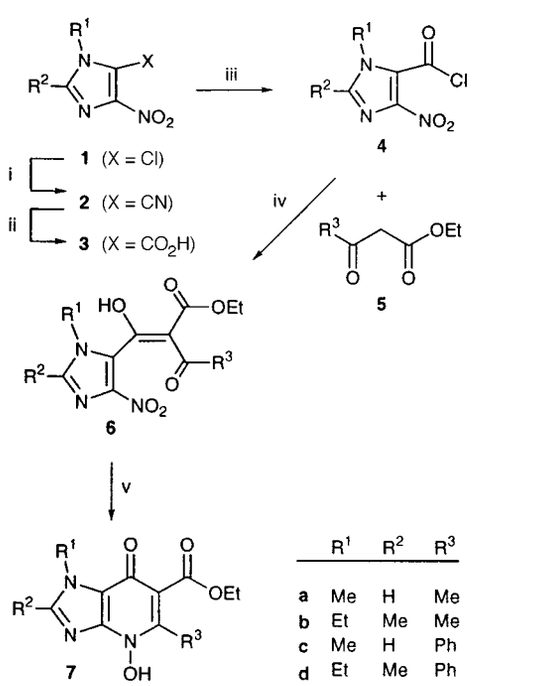
A new synthetic route to the biologically important imidazo[4,5-*b*]pyridine ring system is described. An efficient method for the condensation of 4-nitro-1*H*-imidazole-5-carbonyl chlorides with activated methylene compounds using magnesium ethoxide has been developed. The imidazolyl di- and tri-carbonyl compounds formed in this process were found to be good substrates for reductive cyclisation to the little studied 4-hydroxyimidazo[4,5-*b*]-pyridinones by either catalytic hydrogenation over palladium or by treatment with alkaline sodium borohydride in the presence of palladium. Highly oxygenated derivatives of 1-deazapurines are thus readily available by this method.

Introduction

Imidazo[4,5-*b*]pyridines are an important class of heterocycles[1] that can be considered as 1-deazapurines. Consequently they have been widely studied[2] for biological activity and incorporated into modified nucleosides to act as anti-viral and anti-cancer agents. In the present study we were interested in their potential role as adenosine receptor antagonists[3] and their possible use as smooth muscle relaxants in the treatment of asthma.

Many routes to imidazo[4,5-*b*]pyridine derivatives have been described[1] but most have employed substituted pyridines as starting materials and used various strategies to build up the imidazole ring of the bicycle. The lack of easily available highly substituted pyridines and the consequent limitation on the substituent pattern of the pyridine ring of the imidazo-[4,5-*b*]pyridine prompted us to consider the less widely adopted approach[4] of starting from a substituted imidazole derivative and constructing the pyridine ring. Our interest in the chloro-nitroimidazole[5] **1** and in developing heterocyclisation reactions employing the nitro group[6] led us to explore the reaction sequence shown in Scheme 1 and to study the acylation of activated methylene compounds using the imidazole acid chlorides[7] **4**. The imidazolyl di- and tri-carbonyl compounds formed in this process were found to be good substrates for reductive cyclisation by catalytic hydrognation to the little studied 4-hydroxyimidazo[4,5-*b*]pyridinones.



	R1	R2	R3
a	Me	H	Me
b	Et	Me	Me
c	Me	H	Ph
d	Et	Me	Ph

Scheme 1 i, KCN, cat. KI, EtOH, reflux; ii, H_2SO_4 (aq.), heat, then $NaNO_2$; iii, $SOCl_2$, reflux; iv, $Mg(OEt)_2$, ether, reflux; v, H_2, Pd–C, EtOH, room temp.

Results and discussion

Converting the readily available 5-chloro-4-nitroimidazoles **1** (Scheme 1) into the nitriles **2** was easily accomplished by treatment with potassium cyanide in ethanol[8] and in the case of **2b** also gave the corresponding ethyl imidate [**2**; X = C(=NH)OEt] as a by-product. Conversion into the carboxylic acid **3** and its corresponding acid chloride **4** was easily accomplished using known[7] chemistry. We then embarked on a study of the acylation of a variety of activated methylene compounds with the two acid chlorides **4a** and **4b**. We found that magnesium ethoxide was an effective reagent for these reactions and was in general superior to the use of sodium hydride to deprotonate the methylene compound. The best yields for the acylations were for reactions carried out in ether as solvent although 1,2-dimethoxyethane and 1,4-dioxane were also employed with success. Our initial investigation was into the reaction with β-keto esters 5 (Scheme 1). The acid chlorides **4a** and **4b** both reacted smoothly with the enolate generated from ethyl acetoacetate and freshly prepared magnesium ethoxide to give the novel 4-nitroimidazol-5-yl diketo esters **6a** and **6b** in 73 and 74% yields. Likewise ethyl benzoylacetate afforded **6c** and **6d** in good yields of 67 and 77%. In comparison reaction of the acid chloride **4b** with the lithium enolate of ethyl benzoylacetate generated with sodium hydride in DME gave **6b** in only 12% yield. Chelation of the two oxygen atoms of the enolate by

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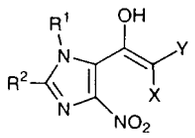
Table 1 4-Nitromidazol-5-yl di- and tri-carbonyl compounds prepared from **4a**–**b**



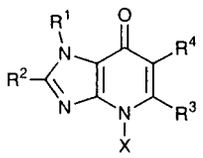
	R^1	R^2	X	Y	Yield(%)
6a	Me	H	MeCO	CO_2Et	73
6b	Et	Me	MeCO	CO_2Et	74
6c	Me	H	PhCO	CO_2Et	67
6d	Et	Me	PhCO	CO_2Et	77
13a	Me	H	CO_2Et	CO_2Et	82
13b	Et	Me	CO_2Et	CO_2Et	94
18a	Me	H	MeCO	PhCO	85
18b	Et	Me	MeCO	PhCO	75
22a	Me	H	H	PhCO	32
22b	Et	Me	H	PhCO	5
24	Et	Me	CN	PhCO	23
27	Et	Me	CN	CO_2Et	21
28	Et	Me	PPh_3	CO_2Et	63
29	Et	Me	SO_2Ph	MeCO	19

magnesium may be responsible for the difference observed and may maximise acylation on carbon. The imidazole diketo esters are low melting crystalline solids which exhibited analytical and spectroscopic properties consistent with their existence largely as enol tautomers, though for convenience these are named throughout as keto derivatives. Evidence for their proposed structures was also based on their successful conversion to pyrazole and isoxazole derivatives on treatment with hydrazine or hydroxylamine. The imidazole derivatives prepared and the yields of the reactions are listed in Table 1.

We next investigated the reactivity of the side chain functionalised imidazoles **6** and found that they underwent smooth reductive cyclisation to the imidazo[4,5-*b*]pyridinones **7** on catalytic hydrogenation in ethanol over palladium-on-charcoal. The *N*-hydroxy derivatives were isolated in high yield indicating that reduction of the nitro group proceeds to give imidazole hydroxylamines as intermediates and that cyclisation occurs before complete reduction to the corresponding amine. Yields for reductive cyclisation are given in Table 2. The *N*-hydroxy compounds were stable to further reduction under the reaction conditions but were readily reduced in near quantitative yield on heating with sodium dithionite in aqueous ethanol to the corresponding imidazo[4,5-*b*]pyridinones **8** (Scheme 2). The structures of the imidazopyridinones **7** and **8** were further supported by their conversion to the carboxylic acid derivatives **9** and **10** by hydrolysis of the ester groups at the 6-position of the ring. The esters were somewhat resistant to hydrolysis. Ester **8d** was only 48% hydrolysed after boiling in 2 M NaOH solution for one hour. Heating under reflux with 20% aqueous KOH was often required to effect complete hydrolysis. For example the phenyl derivative **7d** gave **9d** in 92% yield together with an 8% yield of benzoic acid indicating that degradation of the imidazopyridine ring could also occur under these conditions. The fate of the remainder of the molecule could however not be determined and attempts to isolate the by-product formed by prolonged heating of **7d** with base led only to the formation of intractable solid materials. The carboxylic acids **10** underwent smooth decarboxylation on heating to give the 6-unsubstituted imidazopyridines **12** but attempts to decarboxylate the *N*-hydroxy substituted compounds **9** were unsuccessful. Heating these compounds under a variety of conditions led to decomposition of the molecule.

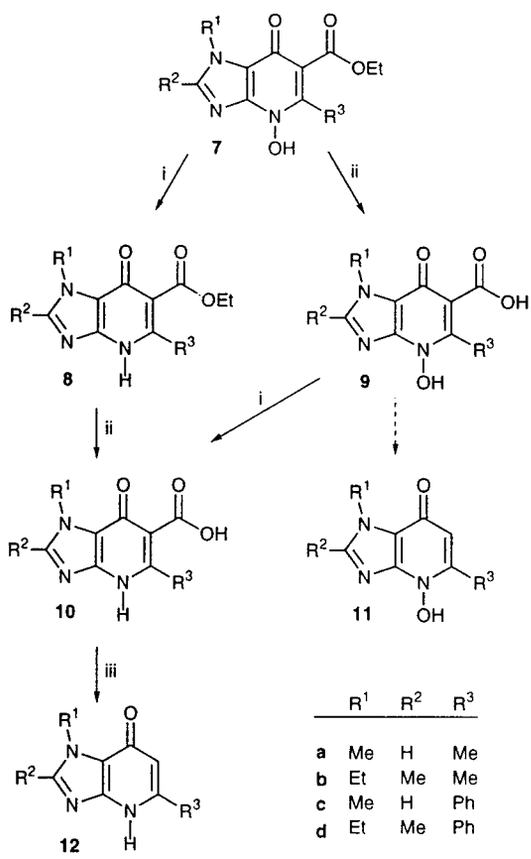
The acylation of diethyl malonate by the acid chlorides **4a** and **4b** also proceeded in high yield (82 and 94%) with the use of magnesium ethoxide as base giving the keto diesters **13** (Scheme 3). However the reductive cyclisation of these compounds was not as straightforward as for **6**. Catalytic hydro-

Table 2 Imidazo[4,5-*b*]pyridinones formed by reductive cyclisation



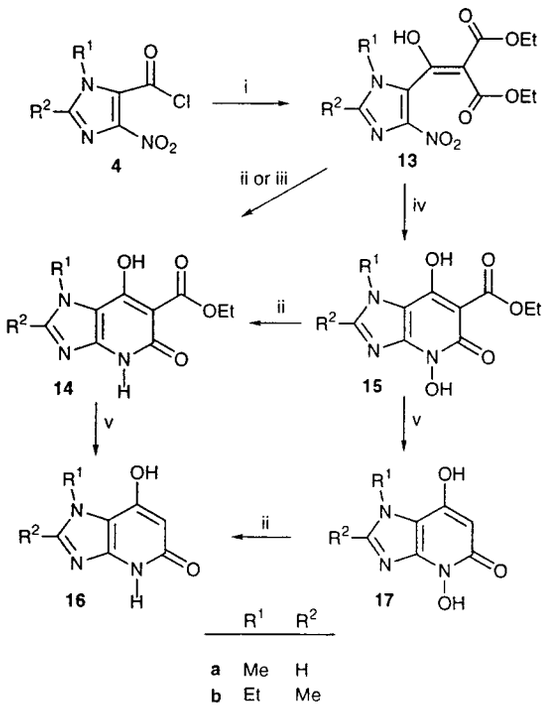
	R^1	R^2	R^3	R^4	X	Method	Yield(%)
7a	Me	H	Me	CO_2Et	OH	A[a]	87
7b	Et	Me	Me	CO_2Et	OH	A[a]	89
7c	Me	Me	Ph	CO_2Et	OH	A[a]	78
7d	Et	Me	Ph	CO_2Et	OH	A[a]	92
14b	Et	Me	OH	CO_2Et	H	B[b], A[a]	42, 24
15b	Et	Me	OH	CO_2Et	OH	C[c]	84
19c	Et	Me	Me	PhCO	OH	A[a]	—[d]
12d	Et	Me	Ph	H	H	A[a]	5
21c	Et	Me	Me	PhCO	H	A[a] then B[b]	37
21e	Et	Me	Ph	MeCO	H	A[a] then B[b]	39
25	Et	Me	Ph	CN	H	A[a]	100

[a] Method A: H_2, Pd–C, EtOH, room temp. [b] Method B: $Na_2S_2O_4$, EtOH, H_2O, reflux. [c] Method C: $NaBH_4$, Pd–C, NaOH (aq.), 1,4-dioxane. [d] Isolated from a mixture; yield not calculated.



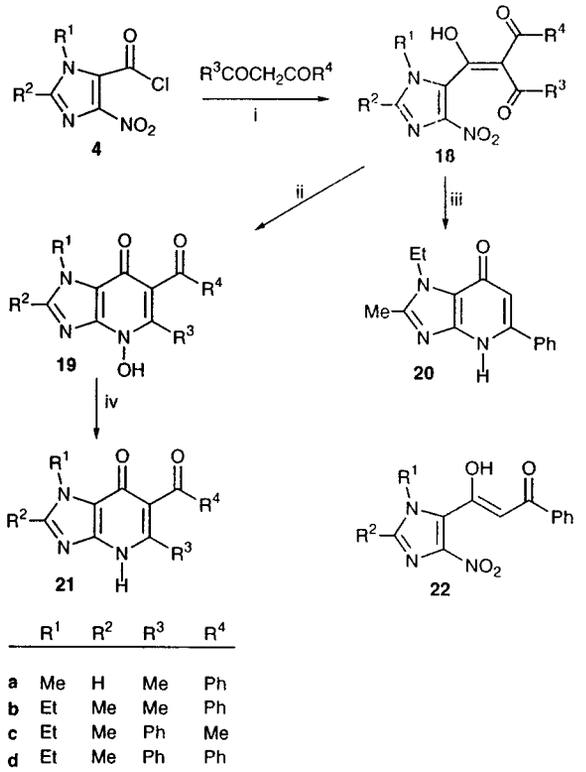
Scheme 2 i, $Na_2S_2O_4$, EtOH, H_2O, reflux; ii, NaOH (aq.), reflux; iii, heat.

genation of **13b** gave only a low yield (24%) of the fully reduced imidazopyridinone **14b** and not the expected *N*-hydroxy derivative **15b**. Sodium dithionite reduction likewise led to formation of **14b** in 42% yield. However reduction using alkaline sodium borohydride in the presence of palladium-on-charcoal following the method of Petrini *et al.*[9] gave the *N*-hydroxyimidazo[4,5-*b*]pyridinone **15b** in an excellent yield of 84%, characterised by conversion to its *N*-acetoxy derivative with acetic anhydride (ν_{max} 1805 cm^{-1}). It is not completely clear why this change in reactivity is observed but the lower electrophilicity of the ester groups in **13** may mean the cyclisation step is slower and the intermediate hydroxylamine is further reduced



	R^1	R^2
a	Me	H
b	Et	Me

Scheme 3 i, Diethyl malonate, $Mg(OEt)_2$, ether, reflux; ii, $NaBH_4$, Pd–C, NaOH (aq.), 1,4-dioxane; iii, $Na_2S_2O_4$, EtOH, H_2O, reflux; iv, H_2, Pd–C, EtOH, room temp.; v, KOH (aq.), reflux.



	R^1	R^2	R^3	R^4
a	Me	H	Me	Ph
b	Et	Me	Me	Ph
c	Et	Me	Ph	Me
d	Et	Me	Ph	Ph

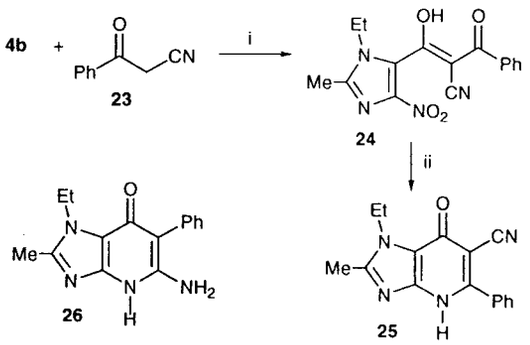
Scheme 4 i, $Mg(OEt)_2$, ether, reflux; ii, H_2, Pd–C, EtOH; iii, $NaBH_4$, Pd–C, NaOH (aq.), 1,4-dioxane; iv, $Na_2S_2O_4$, EtOH, H_2O, reflux.

to the corresponding amine under catalytic hydrogenation conditions. Under the alkaline reduction conditions, the intermediate hydroxylamine may be deprotonated, generating a more reactive nucleophile which can cyclise to the *N*-hydroxyimidazopyridinone before complete reduction occurs. The *N*-hydroxy esters **15**, as well as the reduced compounds **14**, now underwent smooth hydrolysis on heating with alkali. The carboxylic acids could not be isolated and underwent spontaneous decarboxylation to give the 6-unsubstituted imidazopyridinones **16** and **17** in high yield.

With the expectation of extending the synthesis of imidazo[4,5-*b*]pyridines by this method to include 6-oxo derivatives, we next explored the reaction of the acid chlorides **4** with 1,3-diketones (Scheme 4). Initial experiments using acetylacetone as substrate were disappointing and reaction with either of the acid chlorides **4a** or **4b** gave only oily products which resisted purification and characterisation, and the expected triketones **18** ($R^3 = R^4 = Me$) could not be isolated. Attempts to reduce the crude products to the imidazo[4,5-*b*]-pyridinones **19** were also unsuccessful. In contrast, treatment of the acid chlorides **4** with benzoylacetone gave the desired triketones **18a** and **18b** in high yield and these in turn could be efficiently reduced to give the *N*-hydroxyimidazopyridinones again in high yield by catalytic hydrogenation over palladium. The reductive cyclisation of **18b** was expected to occur exclusively onto the more reactive acetyl group to give the 6-benzoyl substituted product **19b**. The reaction however gave a mixture of two products from which only **19b** could be obtained pure by repeated crystallisation. The two isomers were successfully separated however after reduction of the *N*-hydroxy substituents with sodium dithionite in aqueous ethanol, and the two were identified as the 6-benzoylimidazopyridinone **21b** formed in 37% yield and the 6-acetyl derivative **21c** (39%). The ring methyl groups in **21b** had chemical shifts of δ_H 2.46 (Me-2) and 2.15 (Me-5) while **21c** had signals at δ_H 2.48 (Me-2) and 2.37, the latter being assigned to the acetyl methyl group. The structures were further confirmed by degradation of the compound **21b** with hydrogen peroxide which gave a high yield of benzoic acid supporting the presence of a benzoyl substituent in the molecule. Suprisingly, subjecting **18b** to the reduction conditions of alkaline sodium borohydride in the presence of palladium, shown to be effective for the synthesis of the *N*-hydroxyimidazopyridinones **15**, led to formation of the 6-unsubstituted molecule **20** albeit in low yield, and with the alternate cyclisation pattern with a C-5 phenyl substituent. The loss of the 6-substitutent indicated that the acetyl group from the triketone had been cleaved presumably in a retro-Claisen reaction and possibly before the cyclisation had occurred. This may also account for the formation of the fully reduced compound; the remaining keto group would be the less electrophilic benzoyl group which may have been slow enough to undergo cyclisation to allow complete reduction of the nitro group to amine. The low yield of the product isolated cannot rule out the formation of *N*-hydroxyimidazopyridinones or compounds with other substitution patterns which could not be isolated. The ease of retro-Claisen reaction for the imidazolyl tricarbonyl compounds was also shown by the reaction of **13b** with both hydrazine and hydroxylamine. Attempts to convert the keto diester **13b** to pyrazole and isoxazole derivatives for characterisation led to displacement of malonate and formation of the corresponding 4-nitroimidazole-5-carbohydrazonic or carbohydroxamic acids.

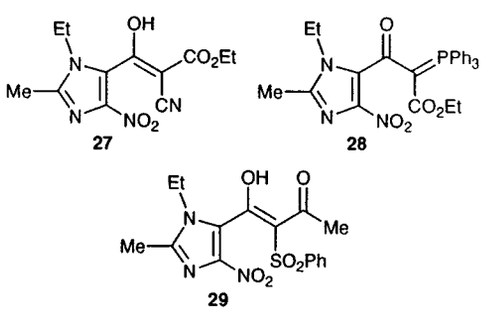
Dibenzoylmethane was next employed as a substrate for reaction with acid chloride **4b**. Again using magnesium ethoxide as the catalyst gave a good yield of a ketone product but not the expected triketone **18d**. Deacylation had again occurred under the alkaline reaction conditions and the 1,3-diketone **22b** was formed exclusively.

A number of other activated methylene compounds were then investigated as substrates and of these, benzoylacetonitrile[10] met with the most success (Scheme 5). Thus the cyanodiketone **24** was generated in a low 23% yield on reaction with **4b**. This underwent smooth reduction to the 6-cyanoimidazopyridinone **25** in essentially quantitative yield. None of the amine **26** which could arise by the alternative cyclisation pathway was formed. The nitrile group was easily detected by the IR absorption spectrum of the compound which contained a sharp band at ν_{max} 2220 cm^{-1}. The greater electrophilicity of the



Scheme 5 i, $Mg(OEt)_2$, ether, reflux; ii, H_2, Pd–C, EtOH.

carbonyl group in **23** clearly wins out over the lesser steric hindrance of the nitrile in determining the orientation of ring closure. As with cyclisation of the other benzoyl compound **18b**, the fully reduced imidazopyridinone was generated. The imidazole derivatives **27**–**29** were also successfully prepared in



low to moderate yield by reaction of **4b** with ethyl cyanoacetate, phenylsulfonylacetone and ethoxycarbonylmethylenetriphenylphosphorane respectively (Table 1). Disappointingly however no success was encountered in attempts to reductively cyclise these compounds to imidazo[4,5-*b*]pyridine derivatives.

Conclusions

A new route to highly substituted imidazo[4,5-*b*]pyridinones has been developed which allows variation in the 6-substitution pattern and gives access to both the 4-hydroxy and 4-unsubstituted series. Alkyl substituted imidazoles were employed as substrates but this annelation method should be equally applicable to a wide range of differently substituted imidazole precursors.

Another approach to the synthesis of imidazo[4,5-*b*]pyridinones which allows variation of the C-5 substituent is described by us elsewhere.[11]

Experimental

Infra-red spectra were recorded using a Perkin-Elmer 781 spectrophotometer as Nujol mulls or liquid films. ^{1}H NMR spectra were recorded at 80 MHz or at 200 MHz on Bruker WP80-SY and WP200-SY instruments. ^{13}C NMR spectra were recorded at 50 MHz on a Bruker WP200-SY instrument. Mass spectra were recorded at 70 eV on an AEI MS-902 instument for EI spectra and on a Kratos MS-50TC instrument for FAB spectra. Microanalyses were carried out using a Carlo-Erba Strumentazione 1106 elemental analyser. Mps were determined using a Kofler hot-stage microscope and are uncorrected.

All reagents were laboratory grade unless specified. Sodium hydride was a 60% suspension in mineral oil and was washed with light petroleum, bp 40–60 °C, before use. Solvents were of technical grade unless otherwise stated. Dimethylformamide was distilled and dried over 4 Å molecular sieves. Organic extracts were dried over anhydrous sodium or magnesium sulfate prior to filtration and evaporation under reduced pressure. All yields are based on unrecovered starting material. Flash chromatography was carried out over silica gel (Merck 9385) and dry column flash chromatography over silica (Merck 7736). Thin layer chromatography was carried out on Polygram SIL G/UV_{254} precoated plastic sheets.

5-Chloro-4-nitro-1*H*-imidazoles 1a and 1b

The imidazole derivatives **1a** and **1b** were prepared by the method of Sarasin and Wegmann,[5] in yields of 89 and 76% and had mp 144–145 °C (lit.,[5] 147–148 °C) and 87–90 °C (lit.,[5] 88 °C) respectively.

5-Cyano-1-methyl-4-nitro-1*H*-imidazole 2a

The cyanoimidazole **2a** was prepared by the reaction of 5-chloro-1-methyl-4-nitro-1*H*-imidazole **1a** with potassium cyanide as described by Sarasin and Wegmann,[8] yield 73%, and had mp 138–140 °C (lit.,[8] 141–142 °C).

5-Cyano-1-ethyl-2-methyl-4-nitro-1*H*-imidazole 2b

A solution of the chloroimidazole **1b** (28.4 g, 0.15 mol) in anhydrous ethanol (150 ml) was treated with potassium cyanide (19.5 g, 0.3 mol) and potassium iodide (0.75 g, 0.0045 mol) and the suspension was stirred and heated at reflux for 6 h.

The mixture was evaporated and the residue was treated with water (150 ml) and extracted with dichloromethane to give a brown oil (28.0 g) which was flash chromatographed over silica. Elution with dichloromethane–ethyl acetate (1 : 1) afforded the cyanoimidazole **2b** (21.9 g, 81%) mp 65–70 °C (lit.,[8] 70–71 °C), ν_{max}/cm^{-1} 2235 (CN).

Further elution with dichloromethane–ethyl acetate (1 : 1) afforded *ethyl (1-ethyl-2-methyl-4-nitro-1*H*-imidazol-5-yl)formimidate* (4.4 g, 13%) which formed colourless plates, mp 117–118 °C [from toluene–light petroleum (bp 80–100 °C)] (Found: C, 47.9; H, 6.2; N, 25.1%; M$^+$, 226. $C_9H_{14}N_4O_3$ requires: C, 47.8; H, 6.2; N, 24.8%; M, 226); ν_{max}/cm^{-1} 3300 (NH), 1630 (C=N) and 1575 and 1330 (NO_2); δ_H ($CDCl_3$) 8.27 (1H, s, NH), 4.36 (2H, q, *J* 7, CH_2), 2.38 (3H, s, CH_3) and 1.34 (6H, t, *J* 7, CH_3).

4-Nitro-1*H*-imidazole-5-carboxylic acids 3a and 3b

The imidazole carboxylic acids **3a** and **3b** were prepared by the hydrolysis of the corresponding cyanoimidazoles **2a** or **2b** as described by Mann and Porter,[7] in yields of 90 and 100%, with mp 163–164 °C (lit.,[7] 161 °C) and 149–151 °C (lit.,[7] 139–141 °C) respectively.

4-Nitro-1*H*-imidazole-5-carbonyl chlorides 4a and 4b

The acid chlorides **4a** and **4b** were prepared by the reaction of the corresponding 4-nitro-1*H*-imidazole-5-carboxylic acids **3a** and **3b** with thionyl chloride as described by Mann and Porter[7] and were used without further purification.

Condensation reactions of the 4-nitro-1*H*-imidazole-5-carbonyl chlorides 4a and 4b with active methylene compounds in the presence of magnesium ethoxide

A mixture of magnesium turnings (0.27 g, 0.011 mol), anhydrous tetrachloromethane (0.10 ml) and anhydrous ethanol (0.50 ml) was warmed gently to initiate an exothermic reaction and after 10 minutes anhydrous ether (10 ml) was added and the mixture was stirred and heated under reflux for 15 minutes. A solution of the requisite active methylene compound (0.011 mol) in anhydrous ethanol (2.0 ml) and anhydrous ether (12 ml) was then added dropwise and heating and stirring were continued for a further 4 h. The mixture was then treated dropwise with stirring with a solution of 1-methyl-4-nitro-1*H*-imidazole-5-carbonyl chloride **4a** (1.9 g, 0.01 mol) in anhydrous 1,2-dimethoxyethane (10 ml) or 1-ethyl-2-methyl-

4-nitro-1*H*-imidazole-5-carbonyl chloride **4b** (2.2 g, 0.01 mol) in anhydrous ether (10 ml) and stirring and heating under reflux continued for a further 0.5 h. The mixtures were then worked up as described for the individual reactions below.

(i) The cooled mixture from 1-methyl-4-nitro-1*H*-imidazole-5-carbonyl chloride **4a** and ethyl acetoacetate was acidified with 2 M aqueous sulfuric acid, the ether layer was separated and the aqueous phase further extracted with several portions of ether. Evaporation of the combined ether extracts gave an oil which was triturated with ether to give *ethyl 2-acetyl-3-(1-methyl-4-nitro-1*H-*imidazol-5-yl)-3-oxopropanoate* **6a** (73%) which formed colourless spars, mp 104–105 °C (from ethanol) (Found: C, 46.5; H, 4.6; N, 14.8%; *m/z* (EIMS) 283 (M^+), $C_{11}H_{13}N_3O_6$ requires: C, 46.7; H, 4.6; N, 14.8%; M, 283); ν_{max}/cm^{-1} 1715 (CO) and 1500 and 1340 (NO_2); δ_H ($CDCl_3$) 17.29 (br s, OH), 14.40 (br s, OH), 4.00 (2H, q, *J* 7, CH_2), 3.69 (3H, s, CH_3), 2.56 (3H, s, CH_3) 2.45 (3H, s, CH_3), 1.02 (3H, t, *J* 7, CH_3) and 0.93 (3H, t, *J* 7, CH_3).

(ii) The cooled mixture from 1-ethyl-2-methyl-4-nitro-1*H*-imidazole-5-carbonyl chloride **4b** and ethyl acetoacetate was acidified with 10% w/v aqueous sulfuric acid, the ether layer was separated and the aqueous phase further extracted with several portions of ether. Evaporation of the combined ether extracts gave an oil which was triturated with ether to afford *ethyl 2-acetyl-3-(1-ethyl-2-methyl-4-nitro-1*H-*imidazol-5-yl)-3-oxopropanoate* **6b** (74%) which formed pale yellow spars, mp 75–76 °C (from ethanol) (Found: C, 49.9; H, 5.5; N, 13.5%; *m/z* (EIMS) 311 (M^+), $C_{13}H_{17}N_3O_6$ requires: C, 50.2; H, 5.5; N, 13.5%; M, 311); ν_{max}/cm^{-1} 1710 (CO) and 1500 and 1340 (NO_2); δ_H ($CDCl_3$) 11.57 (s, OH), 8.72 (s, CH), 4.04 (4H, q, *J* 7, CH_2), 2.56 (3H, s, CH_3), 2.46 (3H, s, CH_3), 1.37 (3H, t, *J* 7, CH_3) and 1.02 (3H, t, *J* 7, CH_3).

(iii) The cooled mixture from 1-methyl-4-nitro-1*H*-imidazole-5-carbonyl chloride **4a** and ethyl benzoylacetate was acidified with 2 M aqueous sulfuric acid, the ether layer was separated and the aqueous phase was further extracted with several portions of ether. The combined ether extracts were evaporated to give a yellow oil which was triturated with ether to give *ethyl 2-benzoyl-3-(1-methyl-4-nitro-1H-imidazol-5-yl)-3-oxopropanoate* **6c** (67%) which formed colourless spars, mp 93–94 °C (from ethanol) (Found: C, 55.3; H, 4,3; N, 12.1%; *m/z* (EIMS) 345 (M^+), $C_{16}H_{15}N_3O_6$ requires: C, 55.7; H, 4.4; N, 12.2%; M, 345); ν_{max}/cm^{-1} 3100–2400br (OH), 1660 and 1625 (CO) and 1515 and 1350 (NO_2); δ_H[$(CD_3)_2SO$] 13.50 (1H, br s, OH) (exch.), 8.00 (1H, s, H-2), 8.04–7.87 (2H, m, ArH), 7.70–7.47 (3H, m, ArH), 3.92 (2H, q, *J* 7, CH_2), 3.69 (3H, s, CH_3) and 0.87 (3H, t, *J* 7, CH_3).

(iv) The cooled mixture from 1-ethyl-2-methyl-4-nitro-1*H*-imidazole-5-carbonyl chloride **4b** and ethyl benzoylacetate was acidified with 2 M aqueous sulfuric acid and the resulting three-phase system filtered to afford *ethyl 2-benzoyl-3-(1-ethyl-2-methyl-4-nitro-1*H-*imidazol-5-yl)-3-oxopropanoate* **6d** as a monohydrate (77%) which formed colourless prisms, mp 112–113 °C (from ethanol–water) [Found: C, 55.3; H, 5.5; N, 10.7%; *m/z* (EIMS) 373 (M^+), $C_{18}H_{19}N_3O_6{\cdot}H_2O$ requires: C, 55.2; H, 5.4; N, 10.7%; (M − H_2O), 373]; ν_{max}/cm^{-1} 3600–1800br (OH), 1720 and 1660 (CO) and 1505 and 1340 (NO_2); δ_H [$(CD_3)_2SO$] 11.46 (1H, br s, OH), 7.99–7.95 (2H, m, ArH), 7.67–7.59 (3H, m, ArH), 3.99 (2H, q, *J* 7, CH_2), 3.90 (2H, q, *J* 7, CH_2), 2.47 (3H, s, CH_3), 1.31 (3H, t, *J* 7, CH_3) and 0.86 (3H, t, *J* 7, CH_3).

(v) The cooled mixture from 1-methyl-4-nitro-1*H*-imidazole-5-carbonyl chloride **4a** and diethyl malonate was acidified with 2 M aqueous sulfuric acid, the ether layer was separated and the aqueous layer further extracted with several portions of ether. Evaporation of the combined ether extracts gave a yellow oil which was triturated with ether to give *ethyl 2-ethoxycarbonyl-3-(1-methyl-4-nitro-1*H-*imidazol-5-yl)-3-oxopropanoate* **13a** (82%) which formed colourless spars, mp 89–91 °C (from ethanol) (Found: C, 45.8; H, 4.7; N, 13.5%; *m/z* (EIMS) 313 (M^+), $C_{12}H_{14}N_3O_7$ requires: C, 46.0; H, 4.8; N, 13.4%; M, 313); ν_{max}/cm^{-1} 3100–2200br (OH), 1730 and 1640br (CO) and 1550 and 1335 (NO_2); δ_H ($CDCl_3$) 13.81 (1H, s, OH), 7.44 (1H, s, H-2), 4.37 (2H, q, *J* 7, CH_2), 4.25 (2H, q, *J* 7, CH_2), 4.02 (2H, q, *J* 7, CH_2), 3.72 (3H, s, CH_3), 1.37 (3H, t, *J* 7, CH_3), 1.27 (3H, t, *J* 7, CH_3) and 1.05 (3H, t, *J* 7, CH_3).

(vi) The cooled mixture from 1-ethyl-2-methyl-4-nitro-1*H*-imidazole-5-carbonyl chloride **4b** and diethyl malonate was acidified with 10% w/v aqueous sulfuric acid. The ether layer was separated and the aqueous phase was further extracted with several portions of ether. Evaporation of the combined organic extracts gave an oil which was triturated with ether to afford *ethyl 2-ethoxycarbonyl-3-(1-ethyl-2-methyl-4-nitro-1*H-*imidazol-5-yl)-3-oxopropanoate* **13b** (94%) which formed colourless spars, 88–89 °C (from benzene–cyclohexane) (Found: C, 49.3; H, 5.6; N, 12.5%; *m/z* (EIMS) 341 (M^+), $C_{14}H_{19}N_3O_7$ requires: C, 49.3; H, 5.6; N, 12.3%; M, 341); ν_{max}/cm^{-1} 3700–3200br (OH), 1730, 1700 and 1640 (CO) and 1510 and 1350 (NO_2); δ_H ($CDCl_3$) 11.06 (1H, br s, OH), 4.47–3.80 (12H, m, CH_2), 2.44 (3H, s, CH_3), 2.42 (3H, s, CH_3) and 1.47–0.91 (18H, m, CH_3).

(vii) The cooled mixture from 1-methyl-4-nitro-1*H*-imidazole-5-carbonyl chloride **4a** and benzoylacetone was acidified with 2 M aqueous sulfuric acid. The ether layer was separated and the aqueous phase was further extracted several times with ether. Evaporation of the combined ether extracts gave an oil which was triturated with ethanol to afford *2-benzoyl-1-(1-methyl-4-nitro-1*H-*imidazol-5-yl)butane-1,3-dione* **18a** (85%) which formed pale yellow spars, mp 140–144 °C (from ethanol–water) (Found: C, 57.0; H, 4.1; N, 13.4%; *m/z* (EIMS) 315 (M^+), $C_{15}H_{13}N_3O_5$ requires: C, 57.1; H, 4.2; N, 13.3%; M, 315); ν_{max}/cm^{-1} 1665 (CO) and 1520 and 1350 (NO_2); δ_H ($CDCl_3$) 16.75 (1H, br s, OH), 7.70–7.24 (6H, m, ArH and H-2), 3.70 (3H, s, CH_3) and 2.10 (3H, s, CH_3).

(viii) The cooled mixture from a repeat of the above reaction was acidified with 2 M aqueous sulfuric acid. The ether layer was separated and the aqueous phase was further extracted with several portions of ether. Evaporation of the combined ether extracts afforded a brown oil which was triturated with ethanol to give *1-(1-methyl-4-nitro-1*H-*imidazol-5-yl)-3-phenylpropane-1,3-dione* **22a** (32%) which formed yellow needles, mp 185–186 °C (from butan-2-one) (Found: C, 56.9; H, 4.0; N, 15.2%; *m/z* (EIMS) 273 (M^+), $C_{13}H_{11}N_3O_4$ requires: C, 56.9; H, 4.0; N, 15.2%; M, 273); ν_{max}/cm^{-1} 1610 (CO) and 1510 and 1330 (NO_2); δ_H [$(CD_3)_2SO$] 8.15–7.88 (3H, m, ArH), 7.77–7.53 (3H, m, ArH and H-2), 7.11 (1H, s, CH) and 3.82 (3H, s, CH_3).

Evaporation of the ethanolic mother liquor gave a brown semi-solid which was triturated with ethanol to yield 2-benzoyl-1-(1-methyl-4-nitro-1*H*-imidazol-5-yl)butane-1,3-dione **18a** (44%), mp 133–135 °C identified by comparison with an authentic sample.

(ix) The cooled mixture from 1-ethyl-2-methyl-4-nitro-1*H*-imidazole-5-carbonyl chloride **4b** and benzoylacetone was acidified with 2 M aqueous sulfuric acid and the resulting three-phase system was filtered to afford *2-benzoyl-1-(1-ethyl-2-methyl-4-nitro-1*H-*imidazol-5yl)butane-1,3-dione* **18b** (75%) which formed pale yellow spars, mp 150–151 °C (from ethanol) (Found: C, 59.2, H, 5.0; N, 12.2%; *m/z* (EIMS) 343 (M^+), $C_{17}H_{17}N_3O_5$ requires: C, 59.5; H, 5.0; N, 12.2%; M, 343); ν_{max}/cm^{-1} 1645 (CO), 1500 and 1340 (NO_2); δ_H ($CDCl_3$) 12.10 (br s, OH), 7.66–7.20 (5H, m, ArH), 3.95 (2H, q, *J* 7, CH_2), 2.50 (s, CH_3), 2.33 (s, CH_3), 2.10 (s, CH_3), 2.08 (s, CH_3) and 1.39 (3H, t, *J* 7, CH_3).

(x) The cooled mixture from 1-ethyl-2-methyl-4-nitro-1*H*-imidazole-5-carbonyl chloride **4b** and dibenzoylmethane was acidified with 2 M aqueous sulfuric acid, the ether layer was separated and the aqueous layer further extracted with several portions of ether. Evaporation of the combined ether extracts afforded a yellow oil which was flash-chromatographed over silica.

Elution with dichloromethane gave dibenzoylmethane (30%) mp 61–62 °C.

Further elution with dichloromethane–ethyl acetate (5:1) gave a yellow gum which was triturated with ether to give 1-(1-ethyl-2-methyl-4-nitro-1*H*-imidazol-5-yl)-3-phenylpropane-1,3-dione **22b** (5%), mp 115–118 °C, raised to 130–131 °C by crystallisation from ethanol, identical (mp., IR spectrum, ^{1}H NMR spectrum and analysis) to an authentic sample.

(xi) The cooled mixture from 1-ethyl-2-methyl-4-nitro-1*H*-imidazole-5-carbonyl chloride **4b** and ethyl cyanoacetate was acidified with 2 M aqueous sulfuric acid and the resulting three-phase system filtered to afford *ethyl 2-cyano-3-(1-ethyl-2-methyl-4-nitro-1*H*-imidazol-5-yl)-3-oxopropanoate* **27** (8%), mp 122–123 °C, identified by comparison with an authentic sample described below.

The ether extract was evaporated to give a brown oil which was triturated with ether to give a solid which was combined with further material obtained by evaporating the ethereal washings and flash-chromatographing the residue in dichloromethane–ethyl acetate over silica to give the carboxylic acid **3b** (34%) mp 143–145 °C, identified by comparison (mp and IR spectrum) with an authentic sample.

(xii) The cooled mixture from 1-ethyl-2-methyl-4-nitro-1*H*-imidazole-5-carbonyl chloride **4b** with phenylsulfonylacetone[12] was treated with 2 M aqueous sulfuric acid, the ether layer was separated and the aqueous layer further extracted with ether. Evaporation of the combined organic extracts afforded a yellow oil which was flash-chromatographed over silica.

Elution with dichloromethane followed by dichloromethane–ethyl acetate (9:1) gave unchanged phenylsulfonylacetone (60%) mp 45–48 °C.

Further elution with dichloromethane–ethyl acetate (9:1) gave a yellow oil which was triturated with ethyl acetate to give *2-phenylsulfonyl-1-(1-ethyl-2-methyl-4-nitro-1*H*-imidazol-5-yl)-ethanone* **29** (19%), which formed colourless spars, mp 110–111 °C (from ethanol) (Found: C, 50.1; H, 4.4; N, 12.7%; *m*/*z* (EIMS) 337 (M^+), $C_{14}H_{15}N_3O_5S$ requires: C, 49.9; H, 4.5; N, 12.5%; M, 337); ν_{max}/cm^{-1} 1710 (CO), 1505 and 1310 (NO_2); δ_H [$(CD_3)_2SO$] 7.98–7.62 (5H, m, ArH), 5.27 (2H, s, CH_2) (exch.), 3.93 (2H, q, *J* 7, CH_2), 2.43 (3H, s, CH_3) and 1.26 (3H, t, *J* 7, CH_3).

Further elution with dichloromethane–ethyl acetate (9:1) followed by dichloromethane–ethyl acetate (5:1) gave the carboxylic acid **4b** (20%) mp 143–144 °C.

2-Cyano-1-(1-ethyl-2-methyl-4-nitro-1*H*-imidazol-5-yl)-3-phenylpropane-1,3-dione 24

A mixture of magnesium turnings (0.54 g, 0.022 mol), anhydrous ethanol (1.0 ml) and anhydrous tetrachloromethane (0.2 ml) was warmed gently to initiate an exothermic reaction and after 10 min anhydrous DME (10 ml) was added and the mixture stirred and heated at 40 °C for 15 min. A solution of benzoylacetonitrile[10] (3.2 g, 0.022 mol) in anhydrous DME (10 ml) was added dropwise with stirring and heating continued for 4 h. The mixture was then treated dropwise with a solution of the acid chloride **4b** (4.4 g, 0.02 mol) in anhydrous DME (10 ml) and stirring continued for a further 4 h.

The mixture was evaporated and the residue was acidified with 2 M sulfuric acid (15 ml) and extracted with dichloromethane to give a brown oil (7.3 g). Trituration with ether afforded a solid which was combined with further material obtained by evaporating the ethereal mother liquor, flash chromatographing the residue over silica with dichloromethane–ethyl acetate (10:1) and triturating the resulting oil with ether–ethanol to give the cyanodiketone **24** (total 1.5 g, 23%), which formed yellow needles mp 148–149 °C (from ethanol) (Found: C, 58.7; H, 4.4; N, 17.3%; *m*/*z* (EIMS) 326 (M^+), $C_{16}H_{14}N_4O_4$ requires: C, 58.9; H, 4.3; N, 17.2%; M, 326); ν_{max}/cm^{-1} (OH), 2220 (CN), 1600 (CO) and 1510 and 1340 (NO_2); δ_H ($CDCl_3$) 8.16–8.03 (2H, m, ArH), 7.68–7.50 (3H, m, ArH), 4.12 (2H, t, *J* 7, CH_2), 2.49 (3H, s, CH_3) and 1.42 (3H, t, *J* 7, CH_3).

Ethyl 2-cyano-3-(1-ethyl-2-methyl-4-nitro-1*H*-imidazol-5-yl)-3-oxopropanoate 27

Method (a). A suspension of sodium hydride (0.26 g, 0.011 mol) in anhydrous DME (10 ml) was stirred and treated dropwise at room temperature with ethyl cyanoacetate (1.2 g, 0.011 mol). Gas evolution occurred and after 10 min the mixture was treated dropwise with a solution of the acid chloride **4b** (2.2 g, 0.01 mol) in anhydrous DME (10 ml) and stirring was continued at room temperature for 18 h.

The mixture was evaporated and the residue was treated with water (10 ml) and dichloromethane and the resulting three-phase mixture filtered to remove some insoluble solid. Evaporation of the organic layer gave a red oil which was triturated with methanol to afford the cyano ketoester **27**, (0.42 g, 14%) which formed colourless spars, mp 128–130 °C (from ethanol) (Found: C, 46.4; H, 5.2; N, 17.8%; *m*/*z* (EIMS) 294 (M^+), $C_{12}H_{14}N_4O_5{\cdot}H_2O$ requires: C, 46.2; H, 5.2; N, 17.4%; M, 294); ν_{max}/cm^{-1} 3600–2500br (OH), 2230 (CN), 1720 (CO) and 1510 and 1350 (NO_2); δ_H [$(CD_3)_2SO$] 6.50 (br s, OH), 3.86 (4H, m, 2 × CH_2), 2.38 (3H, s, CH_3), 1.20 (3H, t, *J* 7, CH_3) and 1.01 (3H, t, *J* 7, CH_3).

Evaporation of the methanolic mother liquor gave an oil which was triturated with ethanol to give a solid which was combined with further material obtained by evaporating the ethanolic mother liquor and retriturating the residue with dichloromethane to give the carboxylic acid **3b** (total 0.41 g, 21%) mp 144–145 °C.

Method (b). A suspension of sodium hydride (0.26 g, 0.011 mol) in anhydrous DMF (5.0 ml) was stirred and treated dropwise at room temperature with a solution of ethyl cyanoacetate (1.2 g, 0.011 mol) in anhydrous dimethylformamide (5.0 ml). Gas was evolved and after 10 min a solution of the acid chloride **4b** (2.2 g, 0.01 mol) in anhydrous dimethylformamide (5.0 ml) was added dropwise and the mixture stirred at room temperature for 18 h.

The mixture was evaporated and the residue was treated with water (10 ml) and extracted with dichloromethane to give a red oil (3.4 g). Trituration with ethanol afforded a solid which was combined with further material obtained by evaporating the ethanolic mother liquor, flash-chromatographing the residue in dichloromethane over silica and triturating the resulting gum with ethanol to give ethyl 2-cyano-3-(1-ethyl-2-methyl-4-nitro-1*H*-imidazol-5-yl)-3-oxopropanoate **27** (total 0.57 g, 21%) mp 129–130 °C, identified by comparison with an authentic sample prepared as in Method (a).

Ethyl 3-(1-ethyl-2-methyl-4-nitro-1*H*-imidazol-5-yl)-3-oxo-2-(triphenylphosphoranylidene)propanoate 28

A solution of ethoxycarbonylmethylenetriphenylphosphorane[13] (3.5 g, 0.01 mol) in anhydrous toluene (25 ml) was stirred and treated dropwise at room temperature with a solution of the acid chloride **4b** (1.1 g, 0.005 mol) in anhydrous toluene (5.0 ml) and the yellow mixture was stirred at room temperature for 3 h.

The mixture was evaporated to give a yellow solid which was extracted in a Soxhlet apparatus with ethyl acetate for 21 h to give (ethoxycarbonylmethyl)triphenylphosphonium chloride as an insoluble residue (1.2 g), mp 143–144 °C, and an organic extract which was evaporated to give the phosphorane **28** (1.6 g, 63%) which formed colourless spars, mp 215–216 °C (from ethanol) (Found: C, 65.5; H, 5.3; N, 8.0%; *m*/*z* (EIMS) 529 (M^+), $C_{29}H_{28}N_3O_5P$ requires: C, 65.8; H, 5.3; N, 7.9%; M, 529); ν_{max}/cm^{-1} 1680 (CO) and 1520 and 1340 (NO_2); δ_H ($CDCl_3$)

7.96-7.44 (15H, m, ArH), 3.83 (2H, dq, *J* 2 and 7, CH_2), 3.64 (2H, q, *J* 7, CH_2), 4.00 (3H, s, CH_3), 2.37 (3H, s, CH_3), 1.25 (3H, t, *J* 7, CH_3) and 0.61 (3H, t, *J* 7, CH_3).

Reductive cyclisation of ethyl 2-acetyl-3-(1-methyl-4-nitro-1*H*-imidazol-5-yl)-3-oxopropanoate 6a to give ethyl 1,5-dimethyl-4-hydroxy-7-oxo-4,7-dihydro-1*H*-imidazo[4,5-*b*]pyridine-6-carboxylate 7a

The diketo ester **6a** (5.7 g, 0.02 mol) was hydrogenated in ethanol (350 ml) over 10% palladium-on-charcoal (0.57 g) at room temperature and at atmospheric pressure for 5 h.

The mixture was filtered through Celite and the filtrate was evaporated to give an oil which largely crystallised. Trituration with ether gave the *N*-hydroxyimidazopyridinone **7a** as a monohydrate (4.7 g, 87%) which formed colourless needles, mp 182–183 °C (from ethanol) (Found: C, 48.7; H, 5.6; N, 15.5%; *m*/*z* (EIMS) 251 (M^+), $C_{11}H_{13}N_3O_4{\cdot}H_2O$ requires: C, 49.1; H, 5.6; N, 15.6%; M, 251); ν_{max}/cm^{-1} 3500–2500br (OH) and 1725 and 1620 (CO); δ_H [$(CD_3)_2SO$] 12.25–11.75 (1H, br s, OH), 8.04 (1H, s, H-2), 4.23 (2H, q, *J* 7, CH_2), 4.00 (3H, s, CH_3), 2.32 (3H, s, CH_3) and 1.26 (3H, t, *J* 7, CH_3).

Ethyl 2,5-dimethyl-1-ethyl-4-hydroxy-7-oxo-4,7-dihydro-1*H*-imidazo[4,5-*b*]pyridine-6-carboxylate 7b

The diketo ester **6b** (15.6 g, 0.05 mol) was hydrogenated in ethanol (300 ml) over 10% palladium-on-charcoal (1.6 g) at room temperature and atmospheric pressure for 5 h. The mixture was filtered through Celite and evaporated to give a solid which was washed with ethyl acetate to afford the *N*-hydroxyimidazopyridinone **7b** as a colourless powder, mp 177–178 °C (from ethyl acetate–ethanol) (Found: C, 55.4; H, 6.2; N, 15.0%; *m*/*z* (HRMS) 279.1213 (M^+), $C_{13}H_{17}N_3O_4$ requires: C, 55.9; H, 6.1; N, 15.1%; M, 279.1219); ν_{max}/cm^{-1} 3500–2200br (OH) and 1720 and 1620 (CO); δ_H ($CDCl_3$) 4.38 (4H, q, *J* 7, CH_2), 2.56 (3H, s, CH_3), 2.39 (3H, s, CH_3), 1.26 (3H, t, *J* 7, CH_3) and 1.18 (3H, t, *J* 7, CH_3).

Ethyl 4-hydroxy-1-methyl-5-phenyl-7-oxo-4,7-dihydro-1*H*-imidazo[4,5-*b*]pyridine-6-carboxylate 7c

The diketo ester **6c** (1.4 g, 0.004 mol) was hydrogenated in ethanol (20 ml) over 10% palladium-on-charcoal (0.14 g) at room temperature and atmospheric pressure for 4.3 h. The mixture was filtered through Celite and the filtrate was evaporated to give an oil (1.2 g) which was triturated with ether to afford the *N*-hydroxyimidazopyridinone **7c** (0.97 g, 78%) which formed colourless needles of a monohydrate, mp 129–130 °C (from ethanol–water) (Found: C, 58.0; H, 5.3; N, 12.7%; *m*/*z* (EIMS) 313 (M^+), $C_{16}H_{15}N_3O_4{\cdot}H_2O$ requires: C, 58.0; H, 5.2; N, 12.7%; M, 313); ν_{max}/cm^{-1} 3500–2100br (OH) and 1730 and 1610 (CO); δ_H [$(CD_3)_2SO$] 11.98 (1H, s, OH), 8.15 (1H, s, H-2), 7.50–7.37 (5H, m, ArH), 4.04 (3H, s, CH_3), 3.84 (2H, q, *J* 7, CH_2) and 0.81 (3H, t, *J* 7, CH_3).

Reductive cyclisation of ethyl 2-benzoyl-3-(1-ethyl-2-methyl-4-nitro-1*H*-imidazol-5-yl)-3-oxopropanoate 6d

The diketo ester **6d** (0.75 g, 0.002 mol) was hydrogenated in ethanol (30 ml) over 10% palladium-on-charcoal (0.06 g) at room temperature and atmospheric pressure for 5 h. The mixture was filtered through Celite and the filtrate evaporated to give a brown glass which was triturated with ether to afford the *N*-hydroxyimidazopyridinone **7d**, as a dihydrate (0.63 g, 92%) which formed colourless spars, mp 124–126 °C (from ethanol–water) (Found: C, 57.3; H, 6.1; N, 11.1%; *m*/*z* (EIMS) 341 (M^+), $C_{18}H_{19}N_3O_4{\cdot}2H_2O$ requires: C, 57.3; H, 6.1; N, 11.1%; M, 341); ν_{max}/cm^{-1} 3600–2100br (OH) and 1710 and 1600 (CO); δ_H [$(CD_3)_2SO$] 11.93 (1H, s, OH) (exch.), 7.50–7.36 (5H, m, ArH), 4.44 (2H, q, *J* 7, CH_2), 3.89 (2H, q, *J* 7, CH_2), 2.52 (3H, s, CH_3), 1.33 (3H, t, *J* 7, CH_3) and 0.80 (3H, t, *J* 7, CH_3).

Ethyl 7-oxo-1*H*-imidazo[4,5-*b*]pyridine-6-carboxylates 8

A solution of the corresponding ethyl *N*-hydroxy-7-oxo-1*H*-imidazo[4,5-*b*]pyridine-6-carboxylate **7** (0.02 mol) in 70% v/v aqueous ethanol (40 ml) was treated with sodium dithionite (5.6 g, 0.032 mol) and the mixture was heated under reflux for 1 h. A second portion of sodium dithionite (5.6 g, 0.032 mol) was added and heating under reflux continued for a further 1 h.

The mixture was worked up as described for the individual reactions below.

(i) The mixture from ethyl 1,5-dimethyl-4-hydroxy-7-oxo-4,7-dihydro-1*H*-imidazo[4,5-*b*]pyridine-6-carboxylate **7a** was evaporated and the residue was treated with water and filtered to afford a solid which was combined with further material obtained by extracting the aqueous mother liquor with dichloromethane to give *ethyl 1,5-dimethyl-7-oxo-4,7-dihydro-1*H-*imidazo[4,5*-b*]pyridine-6-carboxylate* **8a** (98%) which formed colourless needles, mp 255–256 °C (from ethanol–water) (Found: C, 56.5; H, 5.7; N, 18.0%; *m*/*z* (EIMS) 235 (M^+), $C_{11}H_{13}N_3O_3$ requires: C, 56.2; H, 5.6; N, 17.9%, M, 235); ν_{max}/cm^{-1} 3200–2500br (NH, OH) and 1725 and 1630 (CO); δ_H [$(CD_3)_2SO$] 12.75–12.00 (1H, br s, NH), 7.95 (1H, s, H-2), 4.20 (2H, q, *J* 7, CH_2), 3.98 (3H, s, CH_3), 2.30 (3H, s, CH_3) and 1.26 (3H, t, *J* 7, CH_3).

(ii) The mixture from ethyl 2,5-dimethyl-1-ethyl-4-hydroxy-7-oxo-4,7-dihydro-1*H*-imidazo[4,5-*b*]pyridine-6-carboxylate **7b** was evaporated and the residue was treated with water and the insoluble solid was collected and combined with further material obtained by extracting the aqueous mother liquor with dichloromethane to give *ethyl 2,5-dimethyl-1-ethyl-7-oxo-4,7-dihydro-1*H-*imidazo[4,5*-b*]pyridine-6-carboxylate* **8b** (96%) which formed colourless spars, mp 234–235 °C (from ethanol) (Found: C, 59.0; H, 6.5; N, 15.9%; *m*/*z* (EIMS) 263 (M^+), $C_{13}H_{17}N_3O_3$ requires: C, 59.3; H, 6.5; N, 16.0%; M, 263); ν_{max}/cm^{-1} 3200–2500br (NH, OH) and 1720 and 1610 (CO); δ_H ($CDCl_3$) 12.75–12.25 (1H, br s, NH or OH), 4.45 (2H, q, *J* 7, CH_2), 4.36 (2H, q, *J* 7, CH_2), 2.48 (3H, s, CH_3), 1.39 (3H, t, *J* 7, CH_3) and 1.35 (3H, t, *J* 7, CH_3).

(iii) The mixture from ethyl 4-hydroxy-1-methyl-5-phenyl-7-oxo-4,7-dihydro-1*H*-imidazo[4,5-*b*]pyridine-6-carboxylate **7c** was evaporated and the residue was treated with water and the insoluble solid was collected and combined with further material obtained by extracting the aqueous mother liquor with dichloromethane to give *ethyl 1-methyl-5-phenyl-7-oxo-4,7-dihydro-1*H-*imidazo[4,5*-b*]pyridine-6-carboxylate* **8c** (95%) which formed colourless needles of a monohydrate, mp 164–166 °C (with resolidification and remelting at 223–224 °C) (from ethanol–water) (Found: C, 59.6; H, 5.1; N, 13.2%; *m*/*z* (EIMS) 297 (M^+), $C_{16}H_{15}N_3O_3{\cdot}H_2O$ requires: C, 60.0; H, 5.4; N, 13.3%; M, 297), which recrystallised from ethanol as colourless needles of the anhydrous imidazopyridinone ester **8c**, mp 223–224 °C (Found: C, 64.4; H, 5.0; N, 14.0%; *m*/*z* (EIMS) 297 (M^+), $C_{16}H_{15}N_3O_3$ requires: C, 64.6; H, 5.1; N, 14.1%; M, 297); ν_{max}/cm^{-1} 3100–2500br (OH), 1710 br and 1600 br (CO); δ_H [$(CD_3)_2SO$] 12.60 (1H, br s, NH) (exch.), 8.04 (1H, s, H-2), 7.48 (5H, s, ArH), 4.02 (3H, s, CH_3), 3.93 (2H, q, *J* 7, CH_2) and 0.90 (3H, t, *J* 7, CH_3).

(iv) The mixture from ethyl 1-ethyl-4-hydroxy-2-methyl-5-phenyl-7-oxo-4,7-dihydro-1*H*-imidazo[4,5-*b*]pyridine-6-carboxylate **7d** was evaporated, the residue was treated with water, and the insoluble solid collected to give *ethyl 1-ethyl-2-methyl-5-phenyl-7-oxo-4,7-dihydro-1*H-*imidazo[4,5*-b*]pyridine-6-carboxylate* **8d** (94%) which formed colourless spars, mp 220–221 °C (from ethanol) (Found: C, 66.8; H, 5.9; N, 12.9%: *m*/*z* (EIMS) 325 (M^+), $C_{18}H_{19}N_3O_3$ requires: C, 66.5; H, 5.9; N, 12.9%; M, 325); ν_{max}/cm^{-1} 3200–2500 (NH, OH) and 1725 and 1600br (CO); δ_H ($CDCl_3$) 13.18 (1H, s, NH), 7.40 (5H, s, ArH), 4.43 (2H, q, *J* 7, CH_2), 4.10 (2H, q, *J* 7, CH_2), 1.56 (3H, s, CH_3), 1.40 (3H, t, *J* 7, CH_3) and 1.01 (3H, t, *J* 7, CH_3).

Crystallisation of the product **7d** from ethanol–water afforded the dihydrate as colourless spars, mp 115–117 °C (with resolidification and remelting at 211–212 °C) (Found: C, 59.6; H, 6.5; N, 11.6%; *m*/*z* (EIMS) 325 (M^+), $C_{18}H_{19}N_3O_2{\cdot}2H_2O$ requires: C, 59.8; H, 6.4; N, 11.6%; (M − $2H_2O$), 325).

7-Oxo-1*H*-imidazo[4,5-*b*]pyridine-6-carboxylic acids 10

(a) A solution of the corresponding ethyl 7-oxo-1*H*-imidazo[4,5-*b*]pyridine-6-carboxylate **8** (0.002 mol) in 2 M aqueous sodium hydroxide (5.0 ml) was heated under reflux for 1 h and the mixture worked up as described for the individual reactions below.

(i) The cooled mixture from ethyl 2,5-dimethyl-1-ethyl-7-oxo-4,7-dihydro-1*H*-imidazo[4,5-*b*]pyridine-6-carboxylate **8b** was acidified with 2 M aqueous sulfuric acid and the precipitated solid collected to afford *2,5-dimethyl-1-ethyl-7-oxo-4,7-dihydro-1*H-*imidazo[4,5*-b*]pyridine-6-carboxylic acid* **10b** (91%) which formed colourless needles, mp 220–224 °C (gas evolution) (from DMF) (Found: C, 56.3; H, 5.6; N, 17.9%; *m*/*z* (EIMS) 235 (M^+), $C_{11}H_{13}N_3O_3$ requires: C, 56.2; H, 5.6; N, 17.9%; M, 235); ν_{max}/cm^{-1} 3100–2500br (OH, NH) and 1700 and 1630 (CO); δ_H[$(CD_3)_2SO$] 16.75 (1H, s, OH or NH) (exch.), 13.75–13.00 (1H, br s, NH or OH) (exch.), 4.39 (2H, q, *J* 7, CH_2), 2.76 (3H, s, CH_3), 2.52 (3H s, CH_3) and 1.32 (3H, t, *J* 7, CH_3).

(ii) The cooled mixture from ethyl 1-ethyl-2-methyl-5-phenyl-7-oxo-4,7-dihydro-1*H*-imidazo[4,5-*b*]pyridine-6-carboxylate **8d** was acidified with 2 M aqueous sulfuric acid and filtered to afford a colourless solid which was treated with 10% aqueous sodium hydrogen carbonate (5.0 ml). The insoluble material was collected to give unchanged starting material (**8d**) (44%), mp 114–116 °C. The aqueous sodium hydrogen carbonate mother liquor was acidified with 2 M aqueous sulfuric acid and the precipitated solid collected to give *1-ethyl-2-methyl-5-phenyl-7-oxo-4,7-dihydro-1*H-*imidazo[4,5*-b*]pyridine-6-carboxylic acid* **10d** (48%) which formed colourless needles, mp 297–298 °C (from DMF) (Found: C, 65.0; H, 5.2; N, 14.1%; *m*/*z* (EIMS) 297 (M^+), $C_{16}H_{15}N_3O_3$ requires: C, 64.6; H, 5.2; N, 14.1%; M, 297); ν_{max}/cm^{-1} 3100–2500br (OH, NH) and 1715 and 1615 (CO); δ_H [$(CD_3)_2SO$] 11.00 (1H, br s, OH), 7.23–7.16 (5H, m, ArH), 4.35 (2H, q, *J* 7, CH_2), 2.54 (3H, s, CH_3) and 1.26 (3H, t, *J* 7, CH_3).

(b) A solution of the corresponding ethyl 7-oxo-1*H*-imidazo[4,5-*b*]pyridine-6-carboxylate **8** (0.01 mol) in 20% w/w aqueous potassium hydroxide (25 ml) was heated under reflux for 3 h then worked up as described for the individual reactions below.

(i) The mixture from ethyl 1,5-dimethyl-7-oxo-4,7-dihydro-1*H*-imidazo[4,5-*b*]pyridine-6-carboxylate **8a** was acidified with 2 M aqueous sulfuric acid and the precipitated solid collected to afford *1,5-dimethyl-7-oxo-4,7-dihydro-1*H-*imidazo[4,5*-b*]-pyridine-6-carboxylic acid* **10a** (100%) which formed colourless spars, mp 319–320 °C (sublimes 295–296 °C) (from DMSO) (Found: C, 51.1; H, 4.4; N, 19.9%; *m*/*z* (HRMS) 207.0645 (M^+), $C_9H_9N_3O_3$ requires: C, 52.2; H, 4.4; N, 20.3%; M, 207.0644); ν_{max}/cm^{-1} 3100–2200br (OH, NH) and 1700br and 1625 (CO); δ_H [$(CD_3)_2SO$] 13.21 (1H, s, NH or OH) (exch.), 8.24 (1H, s, H-2), 4.04 (3H, s, CH_3) and 2.78 (3H, s, CH_3).

(ii) The cooled mixture from ethyl 2,5-dimethyl-1-ethyl-7-oxo-4,7-dihydro-1*H*-imidazo[4,5-*b*]pyridine-6-carboxylate **8b** was acidified with 4 M hydrochloric acid (25 ml) and the precipitated colourless solid collected to give 2,5-dimethyl-1-ethyl-7-oxo-4,7-dihydro-1*H*-imidazo[4,5-*b*]pyridine-6-carboxylic acid **10b** (2.4 g, 100%), mp 234–235 °C (gas evolution; resolidifies and remelts 268–269 °C), identified by comparison with a sample prepared before.

(iii) The cooled mixture from ethyl 1-methyl-5-phenyl-7-oxo-4,7-dihydro-1*H*-imidazo[4,5-*b*]pyridine-6-carboxylate **8c** was acidified with 4 M hydrochloric acid (25 ml) and the precipitated colourless solid collected to give 1-methyl-5-phenyl-7-oxo-4,7-dihydro-1*H*-imidazo[4,5-*b*]pyridine-6-carboxylic acid **10c** (100%), which formed colourless needles of an acetic acid solvate, mp 224–225 °C (with resolidification and remelting at 273–274 °C) (from glacial acetic acid–water) (Found: C, 58.8; H, 4.5; N, 13.2%; *m*/*z* (EIMS) 225 ($M^+ - CO_2$). $C_{14}H_{11}N_3O_3{\cdot}CH_3CO_2H$ requires: C, 58.4; H, 4.6; N, 12.8%; M, 269); ν_{max}/cm^{-1} 3100–2200br (OH, NH) and 1700br and 1625 (CO); δ_H (CF_3CO_2H) 8.65 (1H, s, H-2), 7.43–7.28 (5H, m ArH) and 4.15 (3H, s, CH_3).

(iv) The cooled mixture from ethyl 1-ethyl-2-methyl-5-phenyl-7-oxo-4,7-dihydro-1*H*-imidazo[4,5-*b*]pyridine-6-carboxylate **8d** was acidified with 2 M aqueous sulfuric acid and the insoluble solid collected to give 1-ethyl-2-methyl-5-phenyl-7-oxo-4,7-dihydro-1*H*-imidazo[4,5-*b*]pyridine-6-carboxylic acid **10d** (100%), mp 277–279 °C, raised to 288–289 °C by one crystallisation from glacial acetic acid–DMF, identified by comparison (mp and IR spectrum) with an authentic sample prepared before.

4,7-Dihydro-1*H*-imidazo[4,5-*b*]pyridin-7-ones 12

(a) The solid 7-oxoimidazo[4,5-*b*]pyridine carboxylic acid **10a** (0.19 g, 0.0009 mol) was heated in a cold finger sublimination tube at 320–330 °C (Wood's metal bath) under reduced pressure (water pump) for 10 min. A colourless solid condensed on the cold finger and was collected to give *1,5-dimethyl-4,7-dihydro-1*H-*imidazo[4,5*-b*]pyridin-7-one* (**12a**) (0.14 g, 94%), which formed colourless needles, mp 297–299 °C (sublim.) (from ethanol–water) (Found: C, 57.9; H, 5.5; N, 25.5%; *m*/*z* (HRMS) 163.0754 (M^+), $C_8H_9N_3O$ requires: C, 58.9; H, 5.6; N, 25.8%; M, 163.0746); ν_{max}/cm^{-1} 3300–2500br (NH,OH) and 1640 and 1610 (CO); δ_H [$(CD_3)_2SO$] 12.25–11.75 (1H, br s, NH) (exch.), 7.86 (1H, s, H-2), 5.77 (1H, d, *J* 0.6, H-6), 3.96 (3H, s, CH_3) and 2.24 (3H, d, *J* 0.5, CH_3).

(b) The solid 7-oxoimidazo[4,5-*b*]pyridine carboxylic acid **10b** (0.24 g, 0.001 mol) was heated in a cold finger sublimination tube at 240 °C (Wood's metal bath) under reduced pressure (water pump). The solid melted, evolved gas and resolidified to afford *1-ethyl-2,5-dimethyl-4,7-dihydro-1*H-*imidazo[4,5*-b*]pyridin-7-one* **12b** (0.16 g, 84%) which formed colourless spars, mp 275–276 °C (from DMF) (Found: C, 62.0; H, 6.8; N, 21.9%; *m*/*z* (EIMS) 191.1063 (M^+), $C_{10}H_{13}N_3O$ requires: C, 62.8; H, 6.9; N, 22.0%; M, 191.1059); ν_{max}/cm^{-1} 3100–2100br (NH, OH) and 1610 (CO); δ_H [$(CD_3)_2SO$] 12.00–11.75 (1H, br s, NH) (exch.), 5.75 (1H, s, H-6), 4.36 (2H, q, *J* 7, CH_2), 2.41 (3H, s, CH_3), 2.23 (3H, s, CH_3) and 1.26 (3H, t, *J* 7, CH_3).

(c) The solid 7-oxoimidazo[4,5-*b*]pyridine-6-carboxylic acid **10c** (0.27 g, 0.001 mol) was heated in a cold finger sublimination tube at 300–310 °C (Wood's metal bath) under reduced pressure (water pump) for 10 min. On cooling, the melt formed a solid which was combined with further material which had condensed on the cold finger to afford *1-methyl-5-phenyl-4,7-dihydro-1*H-*imidazo[4,5*-b*]pyridin-7-one* **12c** (total 0.22 g, 99%), which formed colourless plates, mp 311–312 °C (from ethanol–water) (Found: C, 69.3; H, 4.8; N, 18.8%; *m*/*z* (EIMS) 225 (M^+), $C_{13}H_{11}N_3O$ requires: C, 69.3; H, 4.9; N, 8.7%; M, 225); ν_{max}/cm^{-1} 3600–2500br (NH, OH) and 1600br (CO); δ_H [$(CD_3)_2SO$] 8.17 (1H, s, H-2), 7.82–7.62 (2H, m, ArH), 7.58–7.43 (3H, m, ArH), 6.58 (1H, s, H-6), 6.50 (1H, s, NH) (exch.) and 4.03 (3H, s, CH_3).

(d) The solid 7-oxoimidazo[4,5-*b*]pyridine-6-carboxylic acid **10d** (0.30 g, 0.001 mol) was heated in a cold finger sublimination tube (Wood's metal bath) under reduced pressure (water pump) for 3 min. The solid melted and evolved gas and on cooling formed a solid which was combined with further material which had condensed on the cold finger to give *1-ethyl-2-methyl-5-phenyl-4,7-dihydro-1*H-*imidazo[4,5*-b*]pyridin-7-one* **12d** (total 0.26 g, 100%) which formed yellow needles, mp 296–297 °C (from ethanol–water) (Found: C, 70.9; H, 6.0; N, 16.5%;

m/z (EIMS) 253 (M^+), $C_{15}H_{15}N_3O$ requires: C, 71.1; H, 6.0; N, 16.6%; M, 253); ν_{max}/cm^{-1} 3100–2200 (NH, OH) and 1600 (CO); δ_H [$(CD_3)_2SO$] 12.24 (1H, s, NH), 7.73–7.71 (2H, m, ArH), 7.62–7.43 (3H, m, ArH), 6.26 (1H, s, H-6), 4.41 (2H, q, *J* 7, CH_2), 2.48 (3H, s, CH_3) and 1.32 (3H, t, *J* 7, CH_3).

4-Hydroxy-7-oxo-4,7-dihydro-1*H*-imidazo[4,5-*b*]pyridine-6-carboxylic acids 9

(a) A solution of the ester **7a** (0.54 g, 0.002 mol) in 20% w/v aqueous potassium hydroxide (5.0 ml) was heated under reflux for 3 h. The mixture was cooled, acidified with 4 M aqueous hydrochloric acid (5.0 ml) and the precipitated colourless solid was collected to give *1,5-dimethyl-4-hydroxy-7-oxo-4,7-dihydro-1*H-*imidazo[4,5*-b*]pyridine-6-carboxylic acid* **9a** (0.46 g, 100%) which was purified by dissolution in 2 M aqueous sodium hydroxide and reprecipitation with 2 M aqueous hydrochloric acid to give fine colourless needles, mp 232–233 °C (Found: C, 48.0; H, 3.9; N, 18.7%; *m/z* (EIMS) 223 (M^+), $C_9H_9N_3O_4$ requires: C, 48.4; H, 4.1; N, 18.8%: M, 223); ν_{max}/cm^{-1} 3100–2200br (NH, OH) and 1715 and 1630 (CO); δ_H [$(CD_3)_2SO$] 8.29 (1H, s, H-2), 4.06 (3H, s, CH_3) and 2.92 (3H, s, CH_3).

(b) Repetition of the reaction described in (a) but using 2 M aqueous sodium hydroxide (5.0 ml) and heating under reflux for 1 h, then working up as described before gave the carboxylic acid **9a** (0.46 g, 100%), mp 248–249 °C, identified by comparison with an authentic sample prepared before as in (a).

(c) A solution of the ester **7a** (0.54 g, 0.002 mol) in glacial acetic acid (5.0 ml) was treated with 20% w/v aqueous sulfuric acid (2.0 ml) and the mixture heated at 100 °C for 3 h. The mixture was cooled and the precipitated solid was collected and combined with a second crop obtained by concentrating the filtrate to remove the acetic acid and treating the residue with water (5.0 ml) to give *1,5-dimethyl-4-hydroxy-7-oxo-4,7-dihydro-1*H-*imidazo[4,5*-b*]pyridine-6-carboxylic acid* **9a** (total 0.23 g, 53%), mp 265–267 °C, identified by comparison with an authentic sample prepared before. The aqueous acidic mother liquor was neutralised with 50% w/v aqueous sodium hydroxide and glacial acetic acid and the precipitated colourless solid was collected and combined with further material obtained by extracting the aqueous mother liquor with dichloromethane to give unchanged starting material **7a** (total 0.19 g, 35%) mp 176–178 °C.

(d) A solution of the ester **7b** (0.56 g, 0.002 mol) in aqueous 2 M sodium hydroxide (5.0 ml) was heated under reflux for 1 h. The mixture was cooled, acidified with 2 M aqueous sulfuric acid (2.5 ml) and the insoluble solid collected to give *2,5-dimethyl-1-ethyl-4-hydroxy-7-oxo-4,7-dihydro-1*H-*imidazo[4,5*-b*]pyridine-6-carboxylic acid* **9b** (0.42 g, 84%) which formed colourless blades of a dimethylformamide solvate, mp 203–204 °C (from DMF) (Found: C, 52.4; H, 6.1; N, 18.0%; *m/z* (EIMS) 251 (M^+), $C_{11}H_{13}N_3O_4 \cdot Me_2NCHO$ requires: C, 51.9; H, 6.2; N, 17.3%; M, 251); ν_{max}/cm^{-1} 3100–2500br (OH) and 1610 (CO); δ_H (CF_3CO_2H) 4.32 (2H, q, *J* 7, CH_2), 2.86 (3H, s, CH_3), 2.56 (3H, s, CH_3) and 1.24 (3H, t, *J* 7, CH_3).

(e) A solution of the ester **7c** (0.66 g, 0.002 mol) in 20% w/w aqueous potassium hydroxide (5.0 ml) and ethanol (5.0 ml) was heated under reflux for 3 h. The mixture was concentrated to remove the ethanol, the residual aqueous mother liquor was acidified with 4 M aqueous hydrochloric acid and the precipitated solid was collected to give *4-hydroxy-1-methyl-5-phenyl-7-oxo-4,7-dihydro-1*H-*imidazo[4,5*-b*]pyridine-6-carboxylic acid* **9c** (0.57 g, 100%) which formed colourless blades of an acetic acid solvate, mp 229–230 °C (from glacial acetic acid–water) (Found: C, 55.5; H, 4.4; N, 12.2%; *m/z* (EIMS) 224 ($M^+ - CO_2 - OH$) $C_{14}H_{11}N_3O_4 \cdot CH_3CO_2H$ requires: C, 55.7; H, 4.4; N, 12.2%; M, 285); ν_{max}/cm^{-1} 3100–2200br (OH) and 1730br and 1620br (CO); δ_H [$(CD_3)_2SO$] 13.00–12.00 (1H, br s, OH), 8.36 (1H, s, H-2), 7.49–7.24 (5H, m, ArH) and 4.12 (3H, s, CH_3).

(f) A solution of the ester **7d** (0.68 g, 0.002 mol) in 2 M aqueous sodium hydroxide (5.0 ml) was heated under reflux for 1 h. The mixture was cooled, acidified with 2 M aqueous sulfuric acid (2.8 ml) and filtered to afford *1-ethyl-4-hydroxy-2-methyl-5-phenyl-7-oxo-4,7-dihydro-1*H-*imidazo[4,5*-b*]pyridine-6-carboxylic acid* **9d** (0.59 g, 94%) which formed fine colourless needles, mp 220–221 °C (decomp.) (from DMF) (Found: C, 60.9; H, 4.8; N, 13.3%; *m/z* (EIMS) 313 (M^+), $C_{16}H_{15}N_3O_4$ requires: C, 61.3; H, 4.8; N, 13.4%; M, 313); ν_{max}/cm^{-1} 3000–2200br (OH); δ_H [$(CD_3)_2SO$] 7.44–7.41 (3H, m, ArH), 7.31–7.26 (2H, m, ArH), 4.48 (2H, q, *J* 7, CH_3).

(g) A solution of the ester **7d** (1.9 g, 0.005 mol) in 20% w/w aqueous potassium hydroxide (11.0 ml) was heated under reflux for 3 h. The mixture was cooled, acidified with 4 M aqueous hydrochloric acid (10 ml) and filtered to afford 1-ethyl-4-hydroxy-2-methyl-5-phenyl-7-oxo-4,7-dihydro-1*H*-imidazo[4,5-*b*]pyridine-6-carboxylic acid **9d** (1.44 g, 92%), mp 234–236 °C, identified by comparison with an authentic sample prepared before. Extraction of the aqueous mother liquor with dichloromethane gave benzoic acid (0.05 g, 8%), mp 117–118 °C.

Reduction of 4-hydroxy-7-oxo-4,7-dihydro-1*H*-imidazo[4,5-*b*]-pyridine-6-carboxylic acids 9 to 7-oxo-4,7-dihydro-1*H*-imidazo-[4,5-*b*]pyridine-6-carboxylic acids 10 with sodium dithionite

(a) A solution or suspension of the corresponding *N*-hydroxy-7-oxoimidazo[4,5-*b*]pyridine-6-carboxylic acid **9** (0.001 mol) in 70% v/v aqueous DMF (10–30 ml) was treated with an equal weight of sodium dithionite and the mixture was heated under reflux for 1 h. A second portion of sodium dithionite was added and heating under reflux continued for a further 1 h. The mixture was then worked up as described for the individual reactions below.

(i) The mixture from 1,5-dimethyl-4-hydroxy-7-oxo-4,7-dihydro-1*H*-imidazo[4,5-*b*]pyridine-6-carboxylic acid **9a** was evaporated and the residue was treated with water (5.0 ml) and the insoluble solid collected to give 1,5-dimethyl-7-oxo-4,7-dihydro-1*H*-imidazo[4,5-*b*]pyridine-6-carboxylic acid **10a** (0.18 g, 88%), mp 318–329 °C, identified by comparison with an authentic sample prepared before.

(ii) The mixture from 2,5-dimethyl-1-ethyl-4-hydroxy-7-oxo-4,7-dihydro-1*H*-imidazo[4,5-*b*]pyridine-6-carboxylic acid **9b** was evaporated and the residue was treated with water (2.5 ml) and filtered to afford 2,5-dimethyl-1-ethyl-7-oxo-4,7-dihydro-1*H*-imidazo[4,5-*b*]pyridine-6-carboxylic acid **10b** (0.23 g, 98%), mp 235–236 °C with resolidification and remelting at 273–274 °C, identified by comparison with an authentic sample prepared before.

(iii) The mixture from 1-ethyl-4-hydroxy-2-methyl-5-phenyl-7-oxo-4,7-dihydro-1*H*-imidazo[4,5-*b*]pyridine-6-carboxylic acid **9d** was evaporated and the residue was treated with water (5.0 ml) and filtered to afford 1-ethyl-2-methyl-5-phenyl-7-oxo-4,7-dihydro-1*H*-imidazo[4,5-*b*]pyridine-6-carboxylic acid **10d** (0.26 g, 88%), mp 295–296 °C, identified by comparison with an authentic sample prepared before.

(b) A solution of the *N*-hydroxy-7-oxoimidazopyridine-6-carboxylic acid **9c** (2.3 g, 0.008 mol) in 70% v/v aqueous ethanol (50 ml) was treated with sodium dithionite (2.3 g, 0.013 mol) and the mixture was heated under reflux for 1 h. A second portion of sodium dithionite (2.3 g, 0.013 mol) was added and heating under reflux continued for a further 1 h. The mixture was evaporated and the residue was treated with water (20 ml) and the insoluble solid collected and combined with further material obtained by extracting the aqueous mother liquor with dichloromethane to give 1-methyl-5-phenyl-7-oxo-4,7-dihydro-1*H*-imidazo[4,5-*b*]pyridine-6-carboxylic acid **10c** (total 1.8 g, 82%), mp 204–205 °C, identified by comparison with an authentic sample prepared before.

The reaction of 1-ethyl-4-hydroxy-2-methyl-5-phenyl-7-oxo-4,7-dihydro-1*H*-imidazo[4,5-*b*]pyridine-6-carboxylic acid 9d with potassium hydroxide

A solution of the carboxylic acid **9d** (0.63 g, 0.002 mol) in 20% w/w aqueous potassium hydroxide (5.0 ml) was heated under reflux for 46 h. After cooling and acidifying with 2 M aqueous hydrochloric acid, filtration afforded a colourless solid (0.87 g) which was extracted with boiling water (10 ml) leaving an intractable solid (0.64 g) from which no identifiable material could be obtained. On cooling, the aqueous filtrate deposited *1-ethyl-4-hydroxy-2-methyl-5-phenyl-4,7-dihydro-1*H-*imidazo-[4,5-*b*]pyridin-7-one* **11d** (0.05 g, 9%) which formed colourless spars of the dihydrate, mp 209–211 °C (from ethanol–water) (Found: C, 59.5; H, 5.8; N, 13.5%; *m*/*z* (EIMS) 269 (M^+), $C_{15}H_{15}N_3O_2$ requires: C, 59.0; H, 6.2: N, 13.8%; M, 269); ν_{max}/cm^{-1} 3500–2500br (OH) and 1645 (CO); δ_H [$(CD_3)_2SO$] 7.68–7.48 (5H, m, ArH), 6.61 (1H, s, H-6), 5.00 (br s, OH) (exch.), 4.44 (2H, q, *J* 7, CH_2), 2.59 (3H, s, CH_3) and 1.37 (3H, t, *J* 7, CH_3).

Ethyl 4,7(5)-dihydroxy-1-methyl-5(7)-oxo-4,5(7)-dihydro-1*H*-imidazo[4,5-*b*]pyridine-6-carboxylate 15a

A solution of the keto diester **13a** (7.8 g, 0.025 mol) in 1,4-dioxane (100 ml) was treated with 2% w/w aqueous sodium hydroxide (25.0 ml) and 10% palladium-on-charcoal (0.10 g). The mixture was stirred and purged with nitrogen for 15 min then treated dropwise with stirring with a solution of sodium borohydride (1.9 g, 0.05 mol) in water (15.0 ml) and the mixture stirred at room temperature for a further 25 min. After filtration through Celite, the mixture was concentrated to remove the 1,4-dioxane. The residual liquor was acidifed with 2 M aqueous sulfuric acid and the precipitated colourless solid collected to give the *N*-hydroxyimidazopyridinone **15a** as a monohydrate (5.7 g, 84%) which formed colourless needles mp 183–184 °C (from ethanol–glacial acetic acid) (Found: C, 44.5; H, 4.7; N, 15.5%; *m*/*z* (EIMS) 253 (M^+), $C_{10}H_{11}N_3O_5{\cdot}H_2O$ requires: C, 44.3; H, 4.8; N, 15.5%; M, 253); ν_{max}/cm^{-1} 3500–2500br (OH) and 1720 and 1650 (CO); δ_H [$(CD_3)_2SO$] 14.00–13.50 (1H, br s, OH), 11.25–10.50 (1H, br s, OH), 8.11 (1H, s, H-2), 4.34 (2H, q, *J* 7, CH_2), 3.91 (3H, s, CH_3) and 1.30 (3H, t, *J* 7, CH_3).

Reductive cyclisation reactions of ethyl 2-ethoxycarbonyl-3-(1-ethyl-2-methyl-4-nitro-7-oxo-4,7-dihydro-1*H*-imidazol-5-yl)-3-oxopropanoate 13b

(a) Using hydrogen in the presence of palladium-on-charcoal. The keto diester **13b** (0.68 g, 0.002 mol) was hydrogenated in ethanol (20 ml) over 10% palladium-on-charcoal (0.07 g) at room temperature and atmospheric pressure for 2 h. The mixture was filtered through Celite and evaporated to give an orange oil which was triturated with acetone to afford *ethyl 1-ethyl-7(5)-hydroxy-2-methyl-5(7)-oxo-4,5(7)-dihydro-1*H-*imidazo[4,5-*b*]pyridine-6-carboxylate* **14b** as a monohydrate (0.13 g, 24%), which formed colourless rhombs, mp 321–322 °C (decomp.) (from ethanol) (Found: C, 50.8; H, 6.0; N, 14.6%; *m*/*z* (EIMS) 265 (M^+), $C_{12}H_{15}N_3O_5{\cdot}H_2O$ requires: C, 50.9; H, 6.1; N, 14.8%; M, 265); ν_{max}/cm^{-1} 3500–2500br (OH, NH) and 1735 and 1605 (CO); δ_H [$CD_3)_2SO$] 4.34 (2H, q, *J* 7, CH_2), 2.43 (3H, s, CH_3) and 1.29 (6H, t, *J* 7, CH_3).

(b) Using sodium borohydride and aqueous sodium hydroxide in the presence of palladium-on-charcoal. A solution of the keto diester **13b** (17.1 g, 0.05 mol) in 1,4-dioxane (125 ml) was treated with 2% aqueous sodium hydroxide (50 ml) and 10% palladium-on-charcoal (0.20 g) and the mixture was stirred and purged with nitrogen for 15 min. A solution of sodium borohydride (3.8 g, 0.01 mol) in water (25 ml) was added dropwise and the mixture was stirred at room temperature for a further 20 min. After filtration through Celite, the mixture was concentrated to remove the 1,4-dioxane and most of the water. The residue was acidified with 2 M aqueous sulfuric acid (25 ml) and the precipitated solid was collected to afford *4,7(5)-dihydroxy-1-ethyl-2-methyl-5(7)-oxo-4,5(7)-dihydro-1*H-*imidazo[4,5-*b*]-pyridine-6-carboxylate* **15b** (11.8 g, 84%) which formed colourless needles, mp 179–180 °C (decomp.) (from ethyl acetate–ethanol) (Found: C, 51.3; H, 5.5; N, 15.0%; *m*/*z* (EIMS) 281 (M^+), $C_{12}H_{15}N_3O_5$ requires: C, 51.2; H, 5.4; N, 14.9%; M, 281); ν_{max}/cm^{-1} 3550–2500br (OH) and 1665 and 1615 (CO); δ_H 11.13–10.63 (1H, br s, OH), 10.33–9.95 (1H, s, OH), 4.37 (2H, q, *J* 7, CH_2), 4.22 (2H, q, *J* 7, CH_2), 2.48 (3H, s, CH_3), 1.31 (3H, t, *J* 7, CH_3) and 1.30 (3H, t, *J* 7, CH_3).

Ethyl 4-acetoxy-7(5)-hydroxy-1-methyl-5(7)-oxo-4,5(7)-dihydro-1*H*-imidazo[4,5-*b*]pyridine-6-carboxylate

The *N*-hydroxyimidazopyridinone **15a** (0.54 g, 0.002 mol) was treated with acetic anhydride (0.75 ml) and the mixture was heated at 100 °C for 1 h. On cooling, the mixture deposited a crystalline solid which was collected to afford the *N*-acetoxy derivative (0.43 g, 72%) as a colourless powder, mp 160–161 °C (from DME–glacial acetic acid) (Found C, 47.4; H, 4.3; N, 14.0%; *m*/*z* (HRMS) 295.0803 (M^+), $C_{12}H_{13}N_3O_6$ requires: C, 48.8; H, 4.4; N, 14.2%; M, 295.0804); ν_{max}/cm^{-1} 3100–2200br (OH), 1815 (N–O_2CCH_3) and 1705, 1680 and 1640 (CO); δ_H [$(CD_3)_2SO$] 12.25–11.25 (1H, br s, OH) (exch.), 8.15 (1H, s, H-2), 4.34 (2H, q, *J* 7, CH_2), 3.93 (3H, s, CH_3), 2.39 (3H, s, CH_3) and 1.29 (3H, t, *J* 7, CH_3).

Reaction of ethyl 4,7(5)-dihydroxy-1-ethyl-2-methyl-5(7)-oxo-4,5(7)-dihydro-1*H*-imidazo[4,5-*b*]pyridine-6-carboxylate 15b with acetic anhydride

The *N*-hydroxyimidazopyridinone **15b** (0.56 g, 0.002 mol) was heated in acetic anhydride (1.5 ml) at 100 °C for 10 min. The mixture was evaporated and the residue was triturated with 1,2-dimethoxyethane to give *ethyl 4-acetoxy-1-ethyl-7(5)-hydroxy-2-methyl-5(7)-oxo-4,5(7)-dihydro-1*H-*imidazo[4,5-*b*]pyridine-6-carboxylate* (0.56 g, 91%) which formed colourless spars, mp 136–137 °C (from 1,2-dimethoxyethane) (Found: C, 51.5; H, 5.2; N, 13.2%; *m*/*z* (HRMS) 323.1112 (M^+), $C_{14}H_{17}N_3O_6$ requires: C, 52.0; H, 5.3; N, 13.0%; M, 323.1117); ν_{max}/cm^{-1} 1805 (N–O_2CCH_3) and 1675 and 1640 (CO); δ_H ($CDCl_3$) 14.60 (1H, s, OH), 4.45 (2H, q, *J* 7, CH_2), 4.28 (2H, q, *J* 7, CH_2), 2.50 (3H, s, CH_3), 2.43 (3H, s, CH_3) and 1.43 (6H, t, *J* 7, CH_3).

Ethyl 7(5)-hydroxy-5(7)-oxo-4,5(7)-dihydro-1*H*-imidazo[4,5-*b*]pyridine-6-carboxylates 14

A solution of the corresponding ethyl 4,7(5)-dihydroxy-5(7)-oxo-4,5(7)-dihydro-1*H*-imidazo[4,5-*b*]pyridine-6-carboxylate **15** (0.007 mol) in 70% v/v aqueous ethanol (50 ml) was treated with sodium dithionite (2.0 g, 0.011 mol) and the mixture was heated under reflux for 1 h. A second portion of sodium dithionite (2.0 g, 0.011 mol) was added and heating under reflux continued for a further 1 h. The mixture was worked up as described for the individual reactions below.

(i) The mixture from ethyl 4,7(5)-dihydroxy-1-methyl-5(7)-oxo-4,5(7)-dihydro-1*H*-imidazo[4,5-*b*]pyridine-6-carboxylate **15a** was evaporated and the residue was treated with water and the insoluble solid collected to give *ethyl 7(5)-hydroxy-1-methyl-5(7)-oxo-4,5(7)-dihydro-1*H-*imidazo[4,5-*b*]pyridine-6-carboxylate* **14a** (73%) which formed colourless plates of the dihydrate, mp 323–325 °C (decomp.) (from ethanol–water) (Found: C, 44.3; H, 5.2; N, 15.5%; *m*/*z* (EIMS) 237 (M^+), $C_{10}H_{11}N_3O_4{\cdot}2H_2O$ requires: C, 44.0; H, 5.5; N, 15.4%; M, 237); ν_{max}/cm^{-1} 3500–2500br (NH, OH) and 1640br (CO); δ_H [$(CD_3)_2SO$] 14.20–13.80 (1H, br s, NH or OH) (exch.), 12.00–11.75 (1H, br s, OH or NH) (exch.), 8.01 (1H s, H-2), 4.31 (2H, q, *J* 7, CH_2), 3.88 (3H, s, CH_3) and 1.29 (3H, t, *J* 7, CH_3).

(ii) The mixture from ethyl 4,7(5)-dihydroxy-1-ethyl-2-methyl-5(7)-oxo-4,5(7)-dihydro-1*H*-imidazo[4,5-*b*]pyridine-6-carboxylate **15b** was evaporated and the residue was treated with water and the insoluble solid collected to give ethyl 1-ethyl-2(5)-hydroxy-2-methyl-5(7)-oxo-4,5(7)-dihydro-1*H*-imidazo-[4,5-*b*]pyridine-6-carboxylate **14b** (89%), mp 300–305 °C, identified by comparison (mp and IR spectrum) with an authentic sample.

The reduction of ethyl 4,7(5)-dihydroxy-1-methyl-5(7)-oxo-4,5(7)-dihydro-1*H*-imidazo[4,5-*b*]pyridine-6-carboxylate 15a with sodium dithionite in aqueous DMF

A solution of the *N*-hydroxyimidazo[4,5-*b*]pyridinone **15a** (1.4 g, 0.005 mol) in 70% v/v aqueous dimethylformamide (50 ml) was treated with sodium dithionite (1.4 g, 0.008 mol) and the mixture was heated under reflux for 1 h. A second portion of sodium dithionite (1.4 g, 0.008 mol) was added and heating under reflux continued for a further 1 h. The mixture was evaporated and the residue was treated with water (25 ml) and filtered to afford *7(5)-hydroxy-1-methyl-4,5(7)-dihydro-1*H-*imidazo[4,5*-b*]pyridine-5(7)-one* **16a** (0.55 g, 67%) which formed colourless spars, mp 330–332 °C (from glacial acetic acid–water) (Found: C, 50.6; H, 4.3; N, 25.3%; *m*/*z* (EIMS) 165 (M^+), $C_7H_7N_3O_2$ requires: C, 50.9; H, 4.3; N, 25.4%; M, 165); ν_{max}/cm^{-1} 3100–2200br (NH, OH) and 1630 (CO); δ_H (CF_3CO_2H) 8.60 (1H, s, H-2), 6.48 (1H, s, H-6) and 3.98 (3H, s, CH_3).

7(5)-Hydroxy-4,5(7)-dihydro-1*H*-imidazo[4,5-*b*]pyridin-5(7)-ones 16

(a) A solution of the corresponding ethyl 7(5)-hydroxy-5(7)-oxo-4,5(7)-dihydro-1*H*-imidazo[4,5-*b*]pyridine-6-carboxylate **14** (0.002 mol) in 20% w/v aqueous potassium hydroxide (5.0 ml) was heated under reflux for 1 h and the mixture worked up as described for the individual reactions below.

(i) The mixture from ethyl 7(5)-hydroxy-1-methyl-5(7)-oxo-4,5(7)-dihydro-1*H*-imidazo[4,5-*b*]pyridine-6-carboxylate **14a** was cooled and acidified with 2 M aqueous sulfuric acid. Filtration afforded 7(5)-hydroxy-1-methyl-4,5(7)-dihydro-1*H*-imidazo[4,5-*b*]pyridin-5(7)-one **16a** (0.21 g, 100%), mp 330–333 °C (decomp.), identified by comparison with an authentic sample prepared before.

(ii) The mixture from ethyl 1-ethyl-7(5)-hydroxy-2-methyl-5(7)-oxo-4,5(7)-dihydro-1*H*-imidazo[4,5-*b*]pyridine-6-carboxylate **14b** was cooled and acidified with 2 M aqueous sulfuric acid. Gas was evolved and the precipitated colourless solid was collected, dissolved in 2 M aqueous sodium hydroxide (1.5 ml) and reprecipitated with 2 M aqueous hydrochloric acid (1.5 ml) to afford *1-ethyl-7(5)-hydroxy-2-methyl-4,5(7)-dihydro-1*H-*imidazo[4,5*-b*]pyridin-5(7)-one* **16b** (0.21 g, 54%), which formed colourless plates, mp 315–317 °C (from DMSO) (Found: C, 54.7; H, 5.8; N, 20.9%; *m*/*z* (HRMS) 193.0855 (M^+), $C_9H_{11}N_3O_2$ requires: C, 56.0; H, 5.7; N, 21.8%; M, 193.0851); ν_{max}/cm^{-1} 3200–2200br (NH, OH) and 1630 (CO); δ_H[$(CD_3)_2SO$] 11.45–10.95 (1H, br s, NH or OH), 5.35 (1H, s, H-6), 4.20 (2H, q, *J* 7, CH_2), 2.38 (3H, s CH_3), and 1.28 (3H, t, *J* 7, CH_3).

4,7(5)-Dihydroxy-4,5(7)-dihydro-1*H*-imidazo[4,5-*b*]pyridin-5(7)-ones 17

(a) A solution of the corresponding ethyl 4,7(5)-dihydroxy-5(7)-oxo-4,5(7)-dihydro-1*H*-imidazo[4,5-*b*]pyridine-6-carboxylate **15** (0.005 mol) in 20% w/w aqueous potassium hydroxide (12.5 ml) was heated under reflux for 3 h and the mixture worked up as described for the individual reactions below.

(i) The cooled mixture from ethyl 4,7(5)-dihydroxy-1-methyl-5(7)-oxo-4,5(7)-dihydro-1*H*-imidazo[4,5-*b*]pyridine-6-carboxylate **15a** was acidified with 4 M hydrochloric acid (10.0 ml) and filtered to afford a solid which was combined with further material which crystallised from the aqueous filtrate on standing to give *4,7(5)-dihydroxy-1-methyl-4,5(7)-dihydro-1*H-*imidazo[4,5*-b*]pyridin-5(7)-one* **17a** (total 0.52 g, 57%) which was purified by dissolution in 2 M aqueous sodium hydroxide and reprecipitation with 2 M aqueous hydrochloric acid to give the monohydrate as a pale brown powder, mp 294–295 °C (Found: C, 42.1; H, 4.1; N, 21.3%; *m*/*z* (EIMS) 181 (M^+), $C_7H_7N_3O_3{\cdot}H_2O$ requires: C, 42.2; H, 4.6; N, 21.1%; M, 181); ν_{max}/cm^{-1} 3200–2200br (OH) and 1600br (CO); δ_H [$(CD_3)_2SO$] 11.50–11.00 (1H, br s, OH) (exch.), 7.89 (1H, s, H-2), 5.56 (1H, s, H-6) and 3.86 (3H, s, CH_3).

(ii) The cooled mixture from ethyl 4,7(5)-dihydroxy-1-ethyl-2-methyl-5(7)-oxo-4,5(7)-dihydro-1*H*-imidazo[4,5-*b*]pyridine-6-carboxylate **15b** was acidified with 2 M aqueous hydrochloric acid (15.0 ml) and the precipitated solid was collected to give *4,7(5)-dihydroxy-1-ethyl-2-methyl-4,5(7)-dihydro-1*H-*imidazo[4,5*-b*]pyridin-5(7)-one* **17b** (0.59 g, 93%) which formed colourless spars, mp 267–268 °C (decomp.) (from glacial acetic acid) (Found: C, 51.5; H, 5.3; N, 20.2%; *m*/*z* (EIMS) 209 (M^+), $C_9H_{11}N_3O_3$ requires: C, 51.7; H, 5.3; N, 20.1%; M, 209); ν_{max}/cm^{-1} 3400–2300br (OH) and 1650 (CO); δ_H [$(CD_3)_2SO$] 11.75–10.75 (2H, br s, OH), 5.53 (1H, s, H-6), 4.20 (2H, q, *J* 7, CH_2), 2.44 (3H, s, CH_3) and 1.30 (3H, t, *J* 7, CH_3).

Reductive cyclisation of 2-benzoyl-1-(1-ethyl-2-methyl-4-nitro-1*H*-imidazol-5-yl)butane-1,3-dione 18b

The ketone **18b** (0.69 g, 0.002 mol) was hydrogenated in ethanol (50 ml) over 10% palladium-on-charcoal (0.07 g) at room temperature and atmospheric pressure for 5 h. The mixture was filtered through Celite and the filtrate was evaporated to give a mixture of *6-benzoyl-2,5-dimethyl-1-ethyl-4-hydroxy-4,7-dihydro-1*H-*imidazo[4,5*-b*]pyridin-7-one* **19b** and 6-acetyl-1-ethyl-4-hydroxy-2-methyl-5-phenyl-4,7-dihydro-1*H*-imidazo[4,5-*b*]pyridin-7-one **19c** (0.72 g, 100%). Repeated crystallisation gave a pure sample of **19b** which formed colourless spars, mp 185–186 °C (from ethanol–glacial acetic acid) (Found: C, 65.5; H, 5.7; N, 13.4%: *m*/*z* (EIMS) 311 (M^+), $C_{17}H_{17}N_3O_3$ requires: C, 65.6; H, 5.5; N, 13.5%; M, 311); ν_{max}/cm^{-1} 3200–2200br (OH) and 1635 and 1620 (CO); δ_H ($CDCl_3$) 7.98–7.83 (2H, m, ArH), 7.56–7.34 (3H, m, ArH), 4.19 (2H, q, *J* 7, CH_2), 2.48 (3H, s, CH_3) and 1.37 (3H, t, *J* 7, CH_3).

6-Benzoyl-2,5-dimethyl-1-ethyl-4,7-dihydro-1*H*-imidazo[4,5-*b*]-pyridin-7-one 21b and 6-acetyl-1-ethyl-2-methyl-5-phenyl-4,7-dihydro-1*H*-imidazo[4,5-*b*]pyridin-7-one 21c

The mixture of *N*-hydroxyimidazo[4,5-*b*]pyridinones **19b** and **19c** (1.9 g, 0.006 mol) was dissolved in 70% v/v aqueous ethanol (15.0 ml) and the aqueous solution treated with sodium dithionite (1.9 g) and the mixture heated under reflux for 1 h. A second portion of sodium dithionite (1.9 g) was added and heating under reflux continued for a further 1 h.

The mixture was evaporated and the residue was treated with water (10 ml) and the insoluble pale yellow solid was collected and extracted with boiling ethanol to give, as the insoluble fraction, the benzoylimidazopyridinone **21b** (0.66 g, 37%) which formed colourless spars, mp 338–339 °C (decomp.) (from ethanol–glacial acetic acid) (Found: C, 68.9; H, 6.0; N, 14.2%; *m*/*z* (EIMS) 295 (M^+), $C_{17}H_{17}N_3O_4$ requires: C, 69.2; H, 5.8; N, 14.2%; M, 295); ν_{max}/cm^{-1} 3200–2500br (NH, OH) and 1650 and 1620 (CO); δ_H [$(CD_3)_2SO$] 12.50–12.25 (1H, br s, NH), 7.79–7.74 (2H, m, ArH), 7.60–7.43 (3H, m, ArH), 4.31 (2H, q, *J* 7, CH_2), 2.46 (3H, s, CH_3), 2.15 (3H, s, CH_3) and 1.25 (3H, t, *J* 7, CH_3).

Evaporation of the ethanol mother liquor afforded the acetylimidazopyridinone **21c** (0.70 g, 39%), which formed colourless prisms, mp 268–269 °C (from ethanol–water) (Found: C, 69.4; H, 5.9; N, 14.2%; *m*/*z* (EIMS) 295 (M^+), $C_{17}H_{17}N_3O_2$ requires: C, 69.2; H, 5.8; N, 14.2%; M, 295); ν_{max}/cm^{-1} 3200–

2500br (NH, OH) and 1690 and 1620 (CO); δ_H [$(CD_3)_2SO$] 12.50 (1H, s, NH), 7.76–7.36 (5H, m, ArH), 4.43 (2H, q, *J* 7, CH_2), 2.48 (3H, s, CH_3), 2.37 (3H, s, CH_3) and 1.33 (3H, t, *J* 7, CH_3).

6-Cyano-1-ethyl-2-methyl-5-phenyl-4,7-dihydro-1*H*-imidazo-[4,5-*b*]pyridin-7-one 25

The nitrile **23** (0.65 g, 0.002 mol) in ethanol (75 ml) was hydrogenated over 10% palladium-on-charcoal (0.07 g) at room temperature and atmospheric pressure for 3 h. The mixture was diluted with DMF (75 ml) and heated to dissolve the solid which had separated and was hot filtered through Celite. Evaporation of the filtrate afforded the cyanoimidazopyridinone **25**, (0.63 g, 100%) which formed colourless needles, mp 314–316 °C (from ethane-1,2-diol) (Found: C, 69.0; H, 5.0; N, 20.2%; *m*/*z* (EIMS) 278 (M^+), $C_{16}H_{14}N_4O$ requires: C, 69.1; H, 5.1; N, 20.1%; M, 278); ν_{max}/cm^{-1} 3100–2500br (NH, OH), 2220 (CN) and 1630 (CO); δ_H [$(CD_3)2SO$] 13.50–13.00 (1H, br s, NH), 7.65 (5H, s, ArH), 4.45 (2H, q, *J* 7, CH_2), 2.53 (3H, s, CH_3) and 1.36 (3H, t, *J* 7, CH_3).

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