Synthesis of 2-aryl-2*H*,4*H*-imidazo[4,5-*d*][1,2,3]triazoles from triethyl *N*-(1-ethyl-2-methyl-4-nitro-1*H*-imidazol-5-yl)phosphorimidate by reaction with aryl isocyanates

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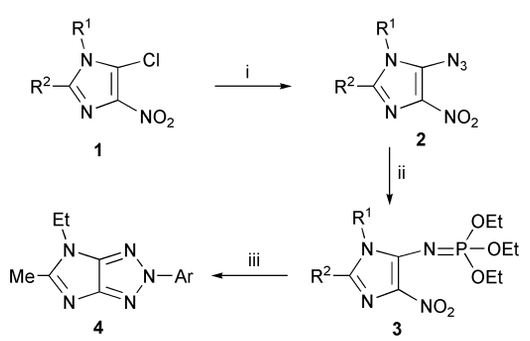
The synthesis of a series of 2-aryl-2*H*,4*H*-imidazo[4,5-*d*][1,2,3]triazoles is reported. These compounds are obtained in moderate to good yields by reaction of triethyl *N*-(1-ethyl-2-methyl-4-nitro-1*H*-imidazol-5-yl)phosphorimidate with aryl isocyanates. The X-ray crystal structures of triethyl (*N*-1-methyl-4-nitro-1*H*-imidazol-5-yl)phosphorimidate and a 2-(4-trifluoromethylphenyl) substituted 2*H*,4*H*-imidazo[4,5-*d*][1,2,3]triazole are reported. Spectroscopic evidence is provided for a carbodiimide intermediate proposed in the reaction mechanism.

Introduction

A new synthesis of imidazo[4,5-*d*][1,2,3]triazoles has recently been reported[1] in which a nitroimidazolyl carbodiimide, proposed as an intermediate formed in an aza-Wittig reaction, undergoes a complex series of transformations with extrusion of carbon dioxide to form a fused [1,2,3]triazole ring. In this paper we describe the preparation of further examples of aryl substituted imidazo[4,5-*d*][1,2,3]triazoles formed using this synthetic approach. We report the reactivity of triethyl (*N*-1-ethyl-2-methyl-4-nitroimidazol-5-yl)phosphorimidate **3b** (Scheme 1)



	Ar
a	Ph
b	4-MeOC$_6$H$_4$
c	4-CF$_3$C$_6$H$_4$
d	4-O$_2$NC$_6$H$_4$
e	4-EtO$_2$CC$_6$H$_4$
f	4-FC$_6$H$_4$
g	2,4,6-Me$_3$C$_6$H$_2$
h	3-NCC$_6$H$_4$

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

Scheme 1 *Reagents and conditions*: i, NaN_3, DMF, room temperature; ii, $P(OEt)_3$, CH_2Cl_2, reflux; iii, ArN=C=O, CH_3CN, 60 °C.

towards aryl isocyanates. Iminophosphoranes and related phosphorimidates are useful reagents in heterocyclic synthesis[2] and are widely used in aza-Wittig reactions[3] with carbonyl compounds to form carbon=nitrogen double bonds. Reaction with isocyanates has been used to synthesise carbodiimides;[4] the resulting heterocumulene frequently being designed to react further in a tandem cyclisation process to generate a new heterocyclic ring. Pyridines,[5] isoquinolines,[6] pyridoindoles[7] and pyridocarbazoles[8] have been prepared in this way. Nitro compounds are known[1,9] to react intramolecularly with carbodiimides, as well as with other heterocumulenes[10–12] and this process forms the basis of the new triazole froming reaction described recently.[1] In this paper we show that nitroimidazolylphosphorimidates also react with aryl isocyanates to form carbodiimides which cannot be isolated, but which are transformed into aryl substituted imidazo[4,5-*d*][1,2,3]triazoles. Some spectroscopic evidence is provided for the formation of a carbodiimide intermediate.

Results and discussion

Our investigation began with the synthesis of the (4-nitroimidazol-5-yl)phosphorimidates **3a** and **3b** by reaction of the azides **2a** and **2b** with triethyl phosphite (Scheme 1). The reaction proceeded smoothly in dichloromethane at 40 °C to form the phosphorimidates in high yield. The azides **2a**[13] and **2b**[1] were in turn readily prepared in high yield by treatment of the corresponding chloro compounds[14] **1a** or **1b** with sodium azide in dimethylformamide. The 1-methyl-4-nitroimidazolyl derivative **3a** was isolated as a yellow crystalline solid, while the 1-ethyl-2-methyl-4-nitro compound **3b** was obtained as a yellow oil. Both compounds had analytical and spectroscopic properties fully in accord with the phosphorimidate structures. The ^{1}H NMR spectra showed signals for three ethyl groups attached to oxygen and signals consistent with the methyl substituted, or 1-ethyl-2-methyl substituted nitroimidazole rings. The ^{31}P NMR spectrum of **3b** showed a singlet at δ −5, consistent with a trialkyl *N*-arylphosphorimidate, while the structure of **3a** was further confirmed by single crystal X-ray diffraction analysis as shown in Fig. 1.[15]

The phosphorimidate compounds were stable and showed no tendency to rearrange, or undergo dealkylation, in an Arbusov-type process to form the corresponding diethyl phosphoramidates **6** or **7** (Scheme 2).

On heating the phosphorimidate **3b** with phenylisocyanate in acetonitrile at 60 °C rapid consumption of the phosphorimidate

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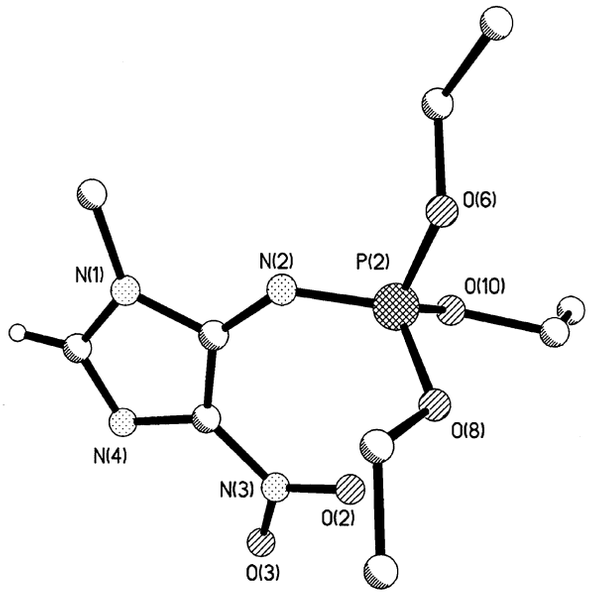
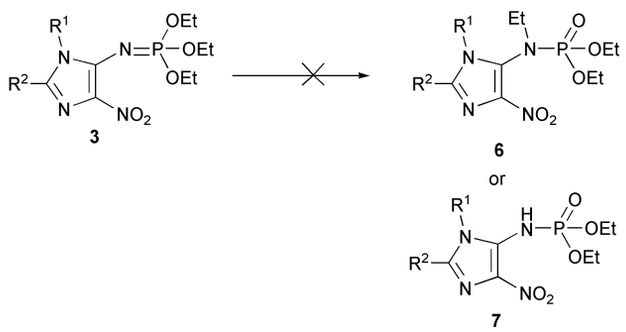
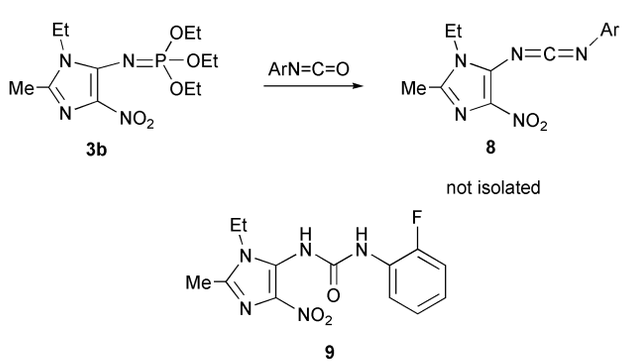


Fig. 1 X-Ray crystal structure of triethyl *N*-(1-methyl-4-nitro-1*H*-imidazol-5-yl)phosphorimidate **3a**.



Scheme 2

was detected by TLC, and the fused imidazo[4,5-*d*][1,2,3]-triazole **4a**[1] (Scheme 1) was isolated as a crystalline solid in good yield, simply by evaporating the solvent, and triturating with ethanol to remove the triethyl phosphate formed. Acetonitrile was found to be the best solvent for the reaction and the yield was not improved by using other solvents. Carrying out the reaction in hot toluene gave a reduced yield of imidazotriazole, and effecting the reaction at room temperature in dichloromethane gave only the fused triazole in low yield and none of the carbodiimide **8** (Ar = Ph) (Scheme 3). Acetonitrile



Scheme 3

was also the most effective solvent for carrying out the reaction with a range of other aryl isocyanates with the 2-arylimidazotriazoles **4b**–**h** being formed in moderate to good yields as the only identifiable product in each case (Table 1). The reaction with 1,4-phenylene diisocyanate and two equivalents of the

Table 1 Imidazo[4,5-*d*][1,2,3]triazoles **4a**–**h** prepared from **3b**

4	Ar	Yield (%)
a	Ph	63
b	4-MeO–C_6H_4	64
c	4-CF_3–C_6H_4	66
d	4-O_2N–C_6H_4	79
e	4-EtO_2C–C_6H_4	62
f	4-F–C_6H_4	62
g	2,4,6-$Me_3C_6H_2$	57
h	3-NC–C_6H_4	61

phosphorimidate **3b** led to the formation of the bis(imidazotriazole) compound **5** in a moderate 41% yield. Work-up again simply involved trituration and chromatography was only required for the purification of **5**. The triethyl phosphorimidate reagent[16] thus has the advantage over the corresponding triphenyliminophosphorane compounds often used in aza-Wittig reactions, where the triphenylphosphine oxide by-product formed usually requires chromatography for its removal. The structures of the new imidazotriazole products were supported by NMR spectroscopy and mass spectrometric and analytical data. An X-ray crystallographic analysis was also carried out for the 4-trifluoromethylphenyl derivative **4c** and the structure is shown in Fig. 2.[15] There appear to be only two examples reported of the synthesis of the imidazo[4,5-*d*][1,2,3]triazole

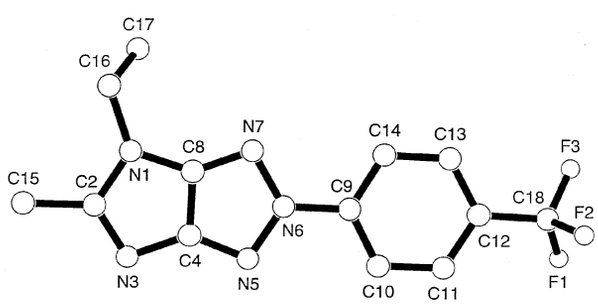
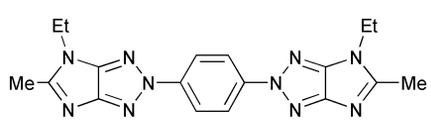
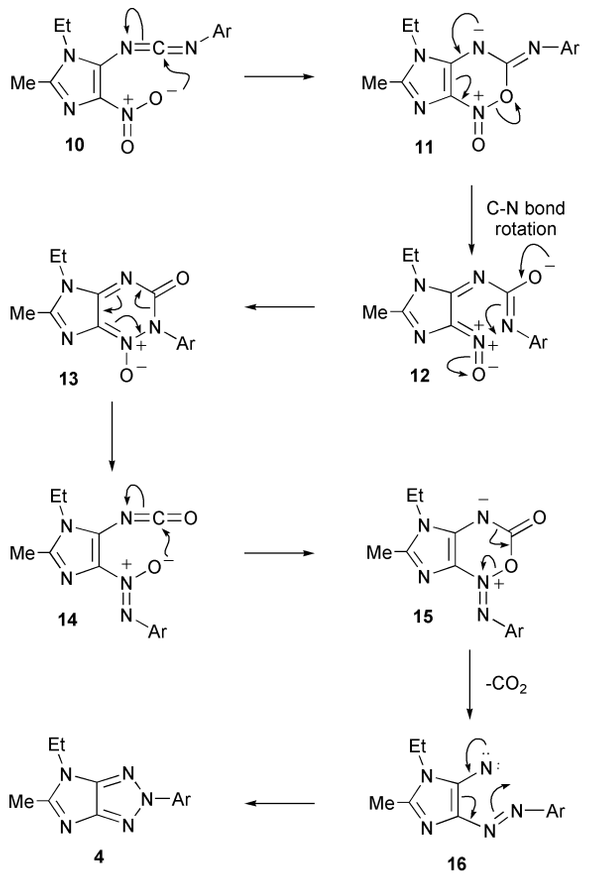


Fig. 2 X-Ray crystal structure of 4-ethyl-5-methyl-2-(4-trifluoromethylphenyl)-2*H*,4*H*-imidazo[4,5-*d*][1,2,3]triazole **4c**.

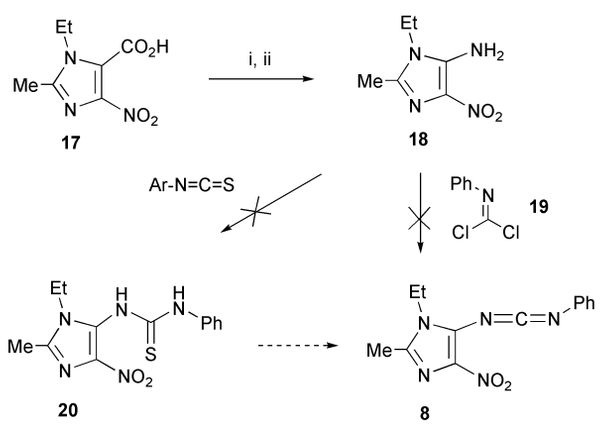
ring system by other methods; a 1,4-dihydro compound, unsubstituted on the triazole ring, has been described as a photographic fog inhibitor,[17] and a 1-hydroxy derivative has been prepared[18] by the reaction of hydrazine with chloronitroimidazole **1a** in ethanol. The route described in this paper now allows preparation of compounds with a range of aryl substituents on the triazole ring and confirms the generality of the method recently reported.[1]



The formation of the fused triazole ring in this reaction suggests a complicated reaction pathway in which both oxygen atoms are ultimately lost from the nitro group. The isocyanate nitrogen becomes bonded to both the nitro group nitrogen atom and the nitrogen of the phosphorimidate group. A possible mechanism to account for the production of the fused [1,2,3]triazole ring has been proposed[1] and is outlined in Scheme 4. This involves an initial aza-Wittig reaction between the phosphorimidate group and the isocyanate leading to formation of a carbodiimide substituted nitro imidazole such as **10**. Attack on the carbodiimide by an oxygen atom of the neighbouring nitro group would then initiate a sequence of ring opening and ring closure reactions (Scheme 5). Ring opening of the intermediate **11** would generate the nitrosonium ion **12**



Scheme 4



Scheme 5 *Reagents and conditions*: i, $SOCl_2$, reflux; ii, NaN_3, aqueous acetone, heat.

which could recyclise through the nitrogen of the urea anion to form the imidazo[4,5-*e*][1,2,4]triazene *N*-oxide **13**. Electrocyclic ring opening of this molecule would generate the imidazol-5-yl isocyanate **14** in which the azoxy substituent at the 4-position is ideally placed to add to the isocyanate by attack through oxygen. The resulting intermediate **15** can then eliminate carbon dioxide to form the nitrene **16** which would be expected to rapidly cyclise to the imidazo[4,5-*d*][1,2,3]triazole ring **4**.

We have carried out an initial study to monitor the reaction by infra-red spectroscopy. When the reaction of the phosphorimidate **3b** was carried out with 2-fluorophenyl isocyanate at room temperature, and aliquots of the reaction mixture were removed at different time intervals, the infra-red spectra showed a doublet signal for the isocyanate with peaks at 2271 and 2245 cm^{-1}. This band is due to the pseudo-antisymmetric stretching mode[19] of the heterocumulene group. The second peak of the doublet often observed in this region for isocyanates has been attributed[20] to an overtone band coupled by Fermi resonance with the intense antisymmetric stretch. The spectra also showed the presence of a second doublet signal with peaks at 2153 and 2120 cm^{-1}. This signal is in the region expected[21] for a carbodiimide and we attribute this to the nitroimidazolyl carbodiimide **8** (Ar = 2-FC_6H_4) (Scheme 3) forming in the reaction mixture in an aza-Wittig reaction with the isocyanate. The reaction was monitored over a period of time, during which the lower wavenumber band increased in intensity, and there was a corresponding decrease in the isocyanate signal, which was competely absent after 90 min. Disappointingly however, it proved impossible to isolate the carbodiimide **8** (Ar = 2-FC_6H_4) at the end of this experiment; the reaction affording only intractable material with none of the fused triazole **4** (Ar = 2-FC_6H_4), or the urea **9**, a likely derivative of the carbodiimide, being isolated. Nor was it possible to synthesise the carbodiimide **8** (Ar = Ph) by other means. An attempt to prepare it by the reaction of the amine **18** with phenyl isocyanide dichloride **19** proved unsuccessful and gave only intractable products (Scheme 5). Also unsuccessful was the attempted preparation of the thiourea derivative **20** from the amine **18** and phenyl isothiocyanate which could have been employed as a precursor to the carbodiimide. The amine **18** was prepared[22] by a Curtius rearrangement of the acyl azide generated from the known[23] carboxylic acid **17**, in turn available by hydrolysis of the nitrile made by nucleophilic displacement of chloride from the 5-chloro-4-nitroimidazole **1b** with cyanide.

These experiments provide some initial evidence that the triazole forming reaction proceeds through the 4-nitroimidazol-5-yl carbodiimide **8** proposed, and most likely follows the pathway outlined in Scheme 4.

Experimental

Infra-red spectra were recorded using a Perkin-Elmer Paragon 1000 spectrophotometer as Nujol mulls or liquid films. For reaction monitoring, aliquots of the reaction mixture were removed at 5, 30, 60 and 90 min intervals, the solvent evaporated and the spectrum of the residue recorded as a thin film. ^1H NMR spectra were recorded at 250 or 400 MHz on Bruker AC-250 or DPX-400 instruments. ^{13}C NMR spectra were recorded at 62.9 or 100 MHz on Bruker AC-250 or DPX-400 instruments. ^{31}P NMR spectra were recorded at 101.3 MHz on a Bruker AC-250 instrument. Mass spectra were recorded on a JEOL SX102 instrument. Microanalyses were carried out using a Perkin-Elmer 2400 elemental analyser. Mps were determined using a Kofler hot-stage microscope and are uncorrected. All reagents were laboratory grade unless specified. 5-Chloro-1-methyl-4-nitro-1*H*-imidazole[14] **1a**, 5-chloro-1-ethyl-2-methyl-4-nitro-1*H*-imidazole[14] **1b**, 5-azido-1-ethyl-2-methyl-4-nitro-1*H*-imidazole[1] **2b**, 1-ethyl-2-methyl-4-nitro-1*H*-imidazole-5-carboxylic acid[23] **17**, 1-ethyl-2-methyl-4-nitro-1*H*-imidazole-5-carbonyl chloride[23] and phenyl isocyanide dichloride[24] were prepared according to the literature methods. Dichloromethane was distilled from phosphorus pentoxide, and acetonitrile was distilled from calcium hydride before use. 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. Thin layer chromatography was carried out on Merck Kieselgel 60 F_{254} precoated aluminium sheets.

5-Azido-1-methyl-4-nitro-1*H*-imidazole[13] 2a

A solution of the chloronitroimidazole **1a** (3.2 g, 0.02 mol) in anhydrous dimethylformamide (25 ml) was treated with sodium azide (1.4 g, 0.022 mol) and the mixture stirred at room temperature, with exclusion of light, for 17 h. The solvent was evaporated under vacuum and the residue treated with water (20 ml). The light brown insoluble solid was collected by suction filtration, washed with water and dried under vacuum to

give the azide **2a** in essentially quantitative yield. Light brown needles, yield 99%, mp 111–112 °C (lit.,[13] 102–103 °C) (Found: M^+, 168.0395. $C_4H_4N_6O_2$ requires: M, 168.0396); ν_{max} 2152 (N_3), 1551 and 1379 (NO_2) cm^{-1}; δ_H (250 MHz, CD_3CN) 3.48 (3H, s, CH_3) and 7.35 (1H, s, H-2).

Triethyl *N*-(1-methyl-4-nitro-1*H*-imidazol-5-yl)phosphorimidate 3a

A solution of the azide **2a** (0.34 g, 0.002 mol) in dichloromethane (5.0 ml) was treated dropwise with triethyl phosphite (0.33 g, 0.002 mol) and the solution heated under reflux under nitrogen until consumption of the azide was complete (TLC). The mixture was evaporated under reduced pressure to give a yellow solid (0.61 g, quantitative). Recrystallisation from dichloromethane–light petroleum (bp 40–60 °C) gave the phosphorimidate as bright yellow cubes, mp 295–297 °C (dec) (Found: C, 39.7; H, 6.0; N, 18.4%; M^+, 306.1094. $C_{10}H_{19}N_4O_5P$ requires: C, 39.2; H, 6.3; N, 18.3%; *M*, 306.1093); ν_{max} 1599, 1378, 1299, 1262 and 1031 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.28 (9H, t, *J* 7, C*H*$_3$CH$_2$), 3.34 (3H, s, 1-CH_3), 4.12 (6H, quin, *J* 7, CH_3C*H*$_2$) and 7.10 (1H, d, *J* 2, H-2); δ_C (100 MHz, $CDCl_3$) 16.1 (d, $^3J_{CP}$ 7, *C*H$_3$CH$_2$), 30.4 (CH_3), 65.0 (d, $^2J_{CP}$ 7, CH_3*C*H$_2$), 130.9 (C-4), 133.2 (C-2), and 139.4 (d, $^2J_{CP}$ 20, C-5); δ_P (101.3 MHz, $(CD_3)_2SO$) 1.93.

Triethyl *N*-(1-ethyl-2-methyl-4-nitro-1*H*-imidazol-5-yl)-phosphorimidate 3b

A solution of the azide **2b** (0.75 g, 0.0038 mol) in dichloromethane (10 ml) was treated dropwise with triethyl phosphite (0.63 g, 0.0038 mol). The solution was stirred under nitrogen at room temperature for 30 min, and then heated under reflux for 1 h. The solution was evaporated and the residual yellow oil flash chromatographed over silica. Elution with light petroleum (bp 40–60 °C)–ethyl acetate (2 : 1) gave the phosphorimidate as a bright yellow oil (1.27 g, 99%) (Found: M^+, 334.1410. $C_{12}H_{23}N_4O_5P$ requires: *M*, 334.1406); ν_{max} 1600, 1303, 1245 and 1039 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 1.28 (3H, t, *J* 7, C*H*$_3$CH$_2$N), 1.35–1.40 (9H, m, C*H*$_3$CH$_2$O), 2.34 (3H, s, CH_3-2), 3.85 (2H, q, *J* 7, CH_3C*H*$_2$ N) and 4.09–4.24 (6H, m, CH_3C*H*$_2$O); δ_C (100 MHz, $CDCl_3$) 13.9 (CH_3), 14.6 (CH_3), 16.1 (d, $^3J_{CP}$ 7, *C*H$_3$CH$_2$OP), 37.5 (CH_2), 64.9 (d, $^2J_{CP}$ 8, CH_3*C*H$_2$OP), 132.2 (C-4), 138.2 (C-2) and 139.2 (d, $^2J_{CP}$, 21, C-5); δ_P (101.3 MHz, $CDCl_3$) −5.2.

General procedure for synthesis of imidazo[4,5-*d*][1,2,3]triazoles

A solution of the phosphorimidate **3b** (0.334 g, 0.001 mol) in anhydrous acetonitrile (5.0 ml) was stirred and treated dropwise at room temperature with the appropriate aryl isocyanate (0.001 mol) neat, or in acetonitrile (2.0 ml) (for solid compounds). The resulting solution was heated at 60 °C for 6 h then cooled and evaporated under reduced pressure. The residue was triturated with ethanol to afford the imidazotriazole as an insoluble solid which was collected by suction filtration, dried and recrystallised to give the following compounds.

4-Ethyl-5-methyl-2-phenyl-2*H*,4*H*-imidazo[4,5-*d*][1,2,3]triazole[1] **4a.** Colourless cubes, yield 63%, mp 143–144 °C (from ethyl acetate) (lit.,[1] 140–141 °C). Identical to the compound described previously.[1] Additional data: δ_C (100 MHz, $CDCl_3$) 14.9 (CH_3), 15.3 (CH_3), 40.3 (CH_2), 119.0 (PhC), 126.9 (PhC), 129.5 (PhC), 141.7, 147.2, 155.3 and 159.5.

4-Ethyl-5-methyl-2-(4-methoxyphenyl)-2*H*,4*H*-imidazo-[4,5-*d*][1,2,3]triazole 4b. Pale brown needles, yield 64%, mp 141–142 °C (from ethanol) (Found: M^+, 257.1279. $C_{13}H_{15}N_5O$ requires: *M*, 257.1279); ν_{max} 1605, 1507, 1258 and 842 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 1.57 (3H, t, *J* 7, C*H*$_3$CH$_2$), 2.60 (3H, s, 5-CH_3), 3.85 (3H, s, CH_3O), 4.12 (2H, q, *J* 7, CH_3C*H*$_2$), 6.96–7.00 (2H, m, ArH), and 7.97–8.01 (2H, m, ArH); δ_C (100 MHz, $CDCl_3$) 14.9 (CH_3), 15.2 (CH_3), 40.3 (CH_2), 55.9 (CH_3O), 114.7 (ArC), 120.5 (ArC), 135.5, 146.9, 154.9, 158.6 and 158.7.

4-Ethyl-5-methyl-2-(4-trifluoromethylphenyl)-2*H*,4*H*-imidazo[4,5-*d*][1,2,3]triazole 4c. Pale green cubes, yield 66%, mp 151–152 °C (from chloroform–light petroleum bp 40–60 °C) (Found: C, 52.9; H, 4.1; N, 23.7%; M^+, 295.1045. $C_{13}H_{12}F_3N_5$ requires: C, 52.9; H, 4.1; N, 23.6%; *M*, 295.1046); ν_{max} 1614, 1500, 1318, 1163, 1125 and 1104 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 1.57 (3H, t, *J* 7, C*H*$_3$CH$_2$), 2.59 (3H, s, 5-CH_3), 4.11 (2H, q, *J* 7, CH_3C*H*$_2$), 7.68 (2H, d, *J* 9, ArH), and 8.17 (2H, d, *J* 9, ArH); δ_C (62.9 MHz, $CDCl_3$) 14.3 (CH_3), 14.9 (CH_3), 39.9 (CH_2), 118.3 (ArC-2), 124.0 (q, $^1J_{CF}$ 274, CF_3), 126.3 (q, $^3J_{CF}$ 4, ArC-3), 128.0 (q, $^2J_{CF}$ 33, ArC-4), 143.6, 147.4, 155.5 and 160.5.

4-Ethyl-5-methyl-2-(4-nitrophenyl)-2*H*,4*H*-imidazo[4,5-*d*]-[1,2,3]triazole 4d. Cream powder, yield 79%, mp 215–216 °C (from chloroform–light petroleum bp 40–60 °C) (Found: C, 52.7; H, 4.4; N, 30.5%; M^+, 272.1019. $C_{12}H_{12}N_6O_2$ requires: C, 52.9; H, 4.4; N, 30.9%; *M*, 272.1022); ν_{max} 1615, 1598, 1503 (NO_2), 1337 (NO_2), 1113 and 854 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.57 (3H, t, *J* 7, C*H*$_3$CH$_2$), 2.60 (3H, s, 5-CH_3), 4.10 (2H, q, *J* 7, CH_3C*H*$_2$) and 8.14–8.26 (4H, ABq, ArH); δ_C (100 MHz, $CDCl_3$) 14.9 (CH_3), 15.5 (CH_3), 40.5 (CH_2), 118.6 (ArCH), 125.4 (ArCH), 145.7, 145.8, 148.5, 156.6 and 162.2.

Ethyl 4-(4-ethyl-5-methyl-2*H*,4*H*-imidazo[4,5-*d*][1,2,3]triazol-5-yl)benzoate 4e. Cream powder, yield 62%, mp 119–121 °C (from dichloromethane–light petroleum bp 40–60 °C) (Found: C, 60.3; H, 5.7; N, 23.3%; M^+, 299.1385. $C_{15}H_{17}N_5O_2$ requires: C, 60.2; H, 5.7; N, 23.4%; *M*, 299.1382); ν_{max} 1713 (C=O), 1606, 1506, 1349 and 1274 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.41 (3H, t, *J* 7, C*H*$_3$CH$_2$O), 1.61 (3H, t, *J* 7, C*H*$_3$CH$_2$N), 2.62 (3H, s, 5-CH_3), 4.13 (2H, q, *J* 7, CH_3C*H*$_2$N), 4.40 (2H, q, *J* 7, CH_3C*H*$_2$O) and 8.12–8.17 (4H, ABq, ArH); δ_C (100 MHz, $CDCl_3$) 14.4 (CH_3), 14.5 (CH_3), 15.1 (CH_3), 40.0 (CH_2), 61.1 (CH_2O), 118.0 (ArCH), 128.2, 130.9 (ArCH), 144.4, 147.5, 155.6, 160.4 and 166.0.

4-Ethyl-2-(4-fluorophenyl)-5-methyl-2*H*,4*H*-imidazo[4,5-*d*]-[1,2,3]triazole 4f. Cream coloured powder, yield 62%, mp 122–123 °C (from dichloromethane–light petroleum bp 40–60 °C) (Found: C, 58.5; H, 4.8; N, 28.4%; M^+, 245.1078, $C_{12}H_{12}FN_5$ requires: C, 58.8; H, 4.9; N, 28.6%; *M*, 245.1077); ν_{max} 1601, 1535, 1507, 1384, 1230 and 829 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.56 (3H, t, *J* 7, C*H*$_3$CH$_2$), 2.59 (3H, s, 5-CH_3), 4.12 (2H, q, *J* 7, CH_3C*H*$_2$), 7.11–7.15 (2H, m, ArH) and 8.01–8.05 (2H, m, ArH); δ_C (62.9 MHz, $CDCl_3$) 14.7 (CH_3), 15.2 (CH_3), 40.3 (CH_2), 116.2 (d, $^2J_{CF}$ 23, ArC-3), 120.6 (d, $^3J_{CF}$ 8, ArC-2), 137.9 (d, $^4J_{CF}$ 3, ArC-1), 147.2, 155.2, 159.5 and 161.5 (d, $^1J_{CF}$ 244, ArC-4).

4-Ethyl-5-methyl-2-(2,4,6-trimethylphenyl)-2*H*,4*H*-imidazo-[4,5-*d*][1,2,3]triazole 4g. White powder, yield 57%, mp 174–175 °C (from dichloromethane–diethyl ether) (Found: C, 66.7; H, 7.1; N, 25.8%; M^+, 269.1641, $C_{15}H_{19}N_5$ requires: C, 66.9; H, 7.1; N, 26.0%; *M*, 269.1641); ν_{max} 1589, 1502, 1387, 1352 and 1124 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 1.55 (3H, t, *J* 7, C*H*$_3$CH$_2$), 1.96 (6H, s, 2-ArCH_3), 2.31 (3H, s, 4-ArCH_3), 2.60 (3H, s, 5-CH_3), 4.11 (2H, q, *J* 7, CH_3C*H*$_2$) and 6.93 (2H, s, 3-Ar*H*); δ_C (62.9 MHz, $CDCl_3$) 14.3 (CH_3), 14.7 (CH_3), 17.3 (CH_3), 21.0 (CH_3), 39.9 (CH_2), 128.6, 135.9, 137.8, 139.3, 145.8, 153.9 and 157.5.

3-(4-Ethyl-5-methyl-2*H*,4*H*-imidazo[4,5-*d*][1,2,3]triazol-2-yl)-benzonitrile 4h. Off white powder, yield 61%, mp 151–153 °C (from dichloromethane–diethyl ether) (Found: C, 61.7; H, 4.7; N, 33.1%; M^+, 252.1121, $C_{15}H_{12}N_6$ requires: C, 61.9; H, 4.7; N, 33.3%; *M*, 252.1123); ν_{max} 2231 (C≡N), 1606, 1583, 1503, 1351 and 903 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 1.57 (3H, t, *J* 7, C*H*$_3$CH$_2$),

2.60 (3H, s, 5-CH_3), 4.11 (2H, q, *J* 7, CH_3CH_2), 7.50–7.53 (2H, m, ArH) and 8.26–8.34 (2H, m, ArH); δ_C (100 MHz, $CDCl_3$) 14.3 (CH_3), 15.0 (CH_3), 40.0 (CH_2), 113.2, 118.1, 121.5, 122.3, 129.4, 130.1, 141.6, 147.4, 155.4 and 160.7.

4-Ethyl-2-[4-(4-ethyl-5-methyl-2*H*,4*H*-imidazo[4,5-*d*][1,2,3]-triazol-2-yl)phenyl]-5-methyl-2*H*,4*H*-imidazo[4,5-*d*][1,2,3]triazole 5. After evaporation of the reaction solvent, flash chromatography over silica eluting with 2 : 1 light petroleum–ethyl acetate afforded a white solid, yield 41%, mp 340 °C (dec) (Found: M^+, 376.1879, $C_{18}H_{20}N_{10}$ requires: *M*, 376.1872); ν_{max} 2924, 1685 and 1545 cm^{-1}; δ_H (400 MHz, CF_3CO_2D) 1.88 (6H, br t, *J* 8, CH_3CH_2), 3.07 (6H, s, 5-CH_3), 4.56 (4H, br q, *J* 8, CH_3CH_2) and 8.43 (4H, s, ArH); δ_C (100 MHz, CF_3CO_2D) 13.5 (CH_3), 13.9 (CH_3), 45.0 (CH_2), 123.0, 142.3, 143.9, 146.3 and 160.2.

5-Amino-1-ethyl-2-methyl-4-nitro-1*H*-imidazole 18[22]

A solution of 1-ethyl-2-methyl-4-nitro-1*H*-imidazole-5-carbonyl chloride (2.1 g, 9.5 mmol) and sodium azide (0.68 g, 11 mmol) in acetone (30 ml) and water (5 ml) was stirred at room temperature for 1 h during which time gas was evolved. The mixture was evaporated to dryness and the residue extracted with boiling acetone in a Soxhlet apparatus for 24 h. Evaporation of the extract gave a yellow solid which was recrystallised from ethanol to give yellow spars (1.32 g; 82%), mp 218–219 °C (lit.,[25] 214–215 °C) (Found: C, 42.4; H, 6.1; N, 32.9%; M^+, 170.0804, $C_6H_{10}N_4O_2$ requires: C, 42.4; H, 5.9; N, 32.9%; *M*, 170.0804); ν_{max} 3425, 3227, 3161, 2854, 1654, 1576, 1378, 1258 and 1221 cm^{-1}; δ_H [400 MHz, $(CD_3)_2SO$] 1.17 (3H, t, *J* 7, CH_3CH_2), 2.23 (3H, s, 2-CH_3), 3.88 (2H, q, *J* 8, CH_3CH_2) and 7.64 (2H, br s, NH_2); δ_C [100 MHz, $(CD_3)_2SO$] 13.1 (CH_3), 14.1 (CH_3), 37.8 (CH_2), 127.2, 139.5 and 144.3.

Crystal structure determination of triethyl *N*-(1-methyl-4-nitro-1*H*-imidazol-5-yl)phosphorimidate 3a

A yellow lath of compound **3a** of approximate dimensions 0.31 × 0.22 × 0.16 mm was mounted on a glass fibre and measured on a Bruker SMART diffractometer using graphite monochromated Mo-Kα radiation. Crystal data: $C_{10}H_{19}N_4O_5P$, *M* = 306.3, monoclinic, *a* = 13.7421(2), *b* = 7.6939(3), *c* = 15.6472(6) Å, *β* = 114.120(1)°, *U* = 1509.94(11) Å^3, space group *P*2/*n*, *Z* = 4, D_x = 1.347 g cm^{-3}. 6017 reflections were measured at 298(1) K of which 2127 were unique (*R* = 0.1502). The structure was solved by direct methods using SHELXS-86 and expanded using Fourier techniques. Non hydrogen atoms were refined anisotropically using full matrix least squares on *F*2. Hydrogen atoms were included but not refined. The final refinement was based on 1285 observed reflections [$I > 2\sigma(I)$] and 191 variable parameters. Final *R* = 0.0441 and R_w = 0.1272. The final difference Fourier map showed maximum and minimum peaks of 0.588 and −1.095 e- Å^{-3} respectively.

Crystal structure determination of 4-ethyl-5-methyl-2-(4-trifluoromethylphenyl)-2*H*,4*H*-imidazo[4,5-*d*][1,2,3]triazole 4c

A colourless prism of compound **4c** of approximate dimensions 0.10 × 0.10 × 0.22 mm was mounted on a glass fibre and measured on a Rigaku AFC7S diffractometer using graphite monochromated Cu-Kα radiation (*λ* = 1.5418 Å). Crystal data: $C_{13}H_{12}F_3N_5$, *M* = 295.3, triclinic, *a* = 7.188(2), *b* = 9.088(2), *c* = 10.682(2) Å, *α* = 88.99(2), *β* = 100.84(2), *γ* = 91.56(1)°, *U* = 685.0(3) Å^3, space group *P*-1 (no. 2), *Z* = 2, D_x = 1.432 g cm^{-3}. 2231 reflections were measured at 298(1) K using the ω scan techniques to a maximum 2*θ* value of 120.0° of which 2023 were unique (*R* = 0.003). The structure was solved by direct methods using SHELXS-86 and expanded using Fourier techniques. Non hydrogen atoms were refined anisotropically using full matrix least squares. Hydrogen atoms were included but not refined. The final refinement was based on 1439 observed reflections ($I > 3.00\sigma(I)$) and 191 variable parameters. Final *R* = 0.0517 and R_w = 0.1589. The final difference Fourier map showed maximum and minimum peaks of 0.35 and −0.28 e- Å^{-3} respectively.

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