Iminophosphorane-Mediated Synthesis of 2-Aminoimidazole Derivatives

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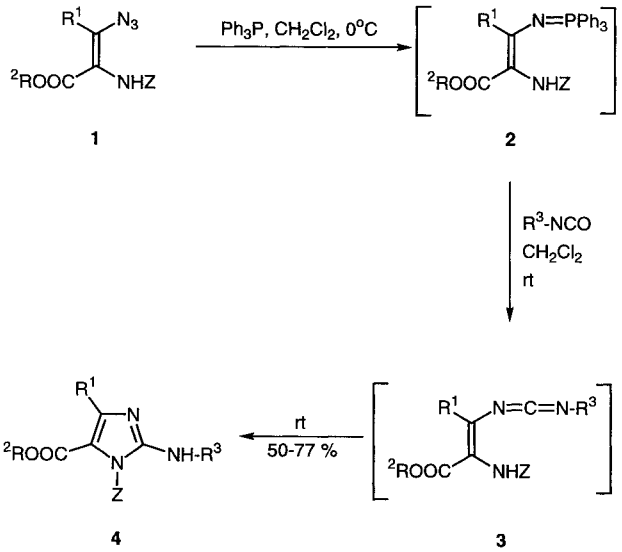
A one-flask synthesis of 2-aminoimidazole derivatives based on the aza-Wittig reaction of alkyl 2-amino-3-azidoacrylates with isocyanates is described.

Marine organisms are among the most promising sources of new and biologically active molecules. Certain secondary metabolites are non-traditional guanidine-based alkaloids[1] that possess a broad spectrum of powerful biological activities. The guanidine moiety is most frequently found in the guise of a 2-aminoimidazole ring that is generally substituted with alkyl groups on carbon or nitrogen.[2]

A survey of the literature reveals that classical methods for the preparation of 2-aminoimidazole derivatives involve, condensation of α-aminocarbonyl compounds with cyanamide,[3] reaction of α-diketones with guanidine followed by reduction,[4] and reaction of α-halo ketones with *N*-acetylguanidine.[2g] Only two methods, starting from a preformed imidazole ring, allow the direct introduction of the amino functionality at position 2: coupling with arenediazonium salts and further reduction[5] and metallation followed by sequential treatment with aryl azide and acid.[6]

In connection with the synthesis of a number of imidazole-containing alkaloids from marine origin,[7] we have reported two iminophosphorane-mediated methods that provide convenient entries to functionalized imidazole derivatives.[8] We wish to report an iminophosphorane-based approach involving a tandem aza-Wittig/carbodiimide-mediated annulation that could be suitably applied to the preparation of 2-amino-4-substituted imidazoles. The key compounds in this study, alkyl 2-amino-3-azido acrylates **1**, were synthesized by a three-step sequence:[9] a) condensation of the appropriate β-oxo ester with benzyl carbamate, b) bromination with NBS and c) reaction with sodium azide in DMF. Compounds **1** were conveniently converted into the corresponding iminophosphoranes **2** by Staudinger reaction with triphenylphosphane at room temperature. Iminophosphorane **2a** was isolated as a crystalline solid in 88% yield whereas **2b** and **2c** were not isolated and were used in the next step without further purification. Iminophosphoranes **2** reacted with aliphatic and aromatic isocyanates in dichloromethane at room temperature to give directly imidazoles **4** in 50–77% yields. Conversion **2** → **4** probably involves the formation of a carbodiimide **3** which undergoes ring closure by nucleophilic attack of the amino group on the central carbon atom of the carbodiimide moiety (Scheme 1).



1, 2	R^1	R^2	4	R^1	R^2	R^3
a	H	Et	a	H	Et	4-MeC_6H_4
b	H	Bn	b	H	Et	4-$MeOC_6H_4$
c	4-$MeOC_6H_4CH_2$	Et	c	H	Et	4-FC_6H_4
			d	H	Et	Bn
			e	H	Et	PhCH=CH
			f	H	Et	Pr
			g	H	Bn	Bn
			h	4-$MeOC_6H_4CH_2$	Et	Bn

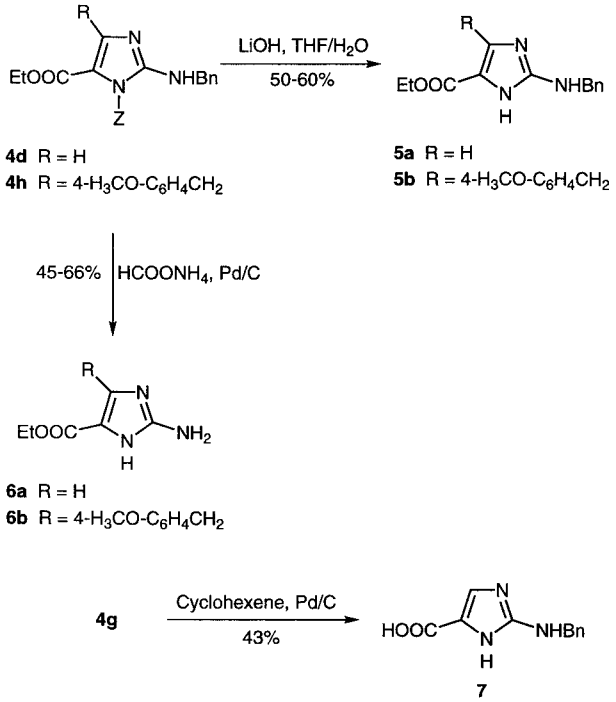
Z = CO_2Bn

Scheme 1

Treatment of imidazoles **4d** and **4h** with LiOH in THF/H_2O at room temperature provided the imidazoles **5** in good yields (50–60%) and similar results were obtained when the bis(tributyltin) oxide[10] was used as deprotecting agent. However, hydrogenolysis with ammonium formate in the presence of Pd/C in anhydrous methanol at reflux temperature afforded the 2-aminoimidazoles **6** in moderate to good yields (45–66%). When imidazole **4g** was treated with the system cyclohexene-Pd/C deprotection of the ester group at position 1 and hydrolysis of the ester group at position 5 took place to give **7** in 43% yield (Scheme 2).

In conclusion, we have developed a one-flask synthesis of 4-substituted 2-aminoimidazole derivatives in synthetically useful yields. This synthesis, which is based on a tandem aza-Wittig/carbodiimide-mediated ring closure, is currently being applied to the preparation of the naturally occurring 2-aminoimidazoles isonaamine A and dorimidazole A.

All melting points were determined on a Kofler hot-plate melting point apparatus and are uncorrected. IR spectra were obtained as



Scheme 2

Nujol emulsions or films on a Nicolet Impact 400 spectrophotometer. NMR spectra were recorded on a Bruker AC-200 (200 MHz) or a Varian Unity 300 (300 MHz). Mass spectra were recorded on a Hewlett-Packard 5993C spectrometer. Microanalyses were performed on a Perkin-Elmer 240C instrument.

Benzyl 2-(Benzyloxycarbonylamino)acrylate:
To a mixture of benzyl pyruvate (17.8 g, 0.1 mol), benzyl carbamate (18.12 g, 0.12 mol) and anhyd benzene (100 mL) was added $POCl_3$ (6 mL). The resultant solution was refluxed for 5 h. After cooling, the solution was washed with water (2 × 100 mL) and brine (100 mL). The separated organic layers were dried ($MgSO_4$), filtered and the filtrate concentrated to dryness. The crude product was chromatographed on a silica gel column using EtOAc/hexane (1:1) as eluent to give benzyl 2-(benzyloxycarbonylamino)acrylate; yield: 13.7 g (42%); colourless oil.

$C_{18}H_{17}NO_4$	calc.	C 69.44	H 5.50	N 4.50
(311.3)	found	69.66	5.32	4.36

MS (EI, 70 eV): *m/z* (%) = 310 ($M^+ - 1,6$), 91 (100).

IR (Nujol): ν = 3411, 1738, 1713, 1637 cm^{-1}.

^1H NMR(200 MHz, $CDCl_3$/TMS): δ = 5.16 (s, 2H), 5.25 (s, 2H), 5.84 (s, 1H), 6.26 (s, 1H), 7.13–7.36 (m, 11H).

^{13}C NMR(50 MHz, $CDCl_3$/TMS): δ = 67.0 (CH_2), 67.7 (CH_2), 106.4, 128.2, 128.4 (2 × CH), 128.5, 128.6, 128.7, 131.0 (q), 135.0 (q), 135.8 (q), 153.1 (q), 161.1 (q).

Ethyl 2-(Benzyloxycarbonylamino)-3-(4-methoxybenzyl)acrylate:
This compound was prepared following the above procedure and using ethyl 4-(4-methoxyphenyl)-2-oxo-butyrate[11] (6.57 g, 0.028 mol); yield: 5.04 g (49%); colourless oil.

$C_{21}H_{23}NO_5$	calc.	C 68.28	H 6.28	N 3.79
(369.4)	found	67.98	6.15	3.87

MS (EI, 70 eV): *m/z* (%) = 369 (M^+, 6), 91 (100).

IR (Nujol): ν = 3324, 1732, 1716, 1657 cm^{-1}.

^1H NMR(200 MHz, $CDCl_3$/TMS): δ = 1.25 (t, 3H, J = 7.2 Hz), 3.49 (d, 2H, J = 7.2 Hz), 3.78 (s, 3H), 4.20 (q, 2H, J = 7.2 Hz), 5.17 (s, 2H), 6.38 (br s, 1H, NH), 6.74 (t,1H, J = 7.2 Hz), 6.83 (d, 2H, J = 8.6 Hz), 7.10 (d, 2H, J = 8.6 Hz), 7.34–7.37 (m, 5H).

^{13}C NMR(50 MHz, $CDCl_3$/TMS): δ = 13.8 (CH_3), 33.3 (CH_2), 54.8 (CH_3O), 60.0 (CH_2), 113.7, 125.5 (q), 127.8, 127.9, 128.2, 129.3, 130.4 (q), 135.8 (q), 135.9, 154.1 (q), 158.0 (q), 164.3 (q).

Alkyl 3-Azido-2-(benzyloxycarbonylamino)acrylates 1b and 1c; General Procedure:
To a solution of benzyl 2-(benzyloxycarbonylamino)acrylate (31.1 g, 0.1 mol) or ethyl 2-(benzyloxycarbonylamino)-3-(4-methoxybenzyl)acrylate (36.9 g, 0.1 mol) in CCl_4 (150 mL) was added *N*-bromosuccinimide (24.86 g, 0.11 mol). The mixture was stirred at r.t. for 1 h and the precipitated solid was separated by filtration. The filtrate was concentrated to dryness and the residual material was dissolved in DMF (150 mL). To the resultant solution was added NaN_3 (7.80 g, 0.12 mol) and the mixture stirred at r.t. for 8 h. The mixture was poured into water (100 mL) and extracted with CH_2Cl_2 (2 × 100 mL). The combined organic layers were washed with brine (100 mL) and dried ($MgSO_4$). After filtration and concentration to dryness the crude product was chromatographed on a silica gel column using EtOAc/hexane (1:2) as eluent to give **1b** or **1c**, respectively.

Benzyl 3-Azido-2-(benzyloxycarbonylamino)acrylate (**1b**): yield 55%; mp 66–68 °C; yellow prisms from CH_2Cl_2.

$C_{18}H_{16}N_4O_4$	calc.	C 61.36	H 4.58	N 15.90
(352.3)	found	61.18	4.72	16.13

MS (EI, 70 eV): *m/z* (%) = 352 (M^+, 7), 91 (100).

IR (Nujol): ν = 3263, 2123, 1714, 1692 cm^{-1}.

^1H NMR(200 MHz, $CDCl_3$/TMS): δ = 5.14 (s, 2H), 5.19 (s, 2H), 6.02 (s, 1H, NH), 7.25–7.38 (m, 11H).

^{13}C NMR($CDCl_3$/TMS): δ = 67.2 (CH_2), 67.7 (CH_2), 115.8 (q), 128.2, 128.3, 128.5, 128.6, 133.0, 135.3 (2 × q), 153.5 (q), 163.5 (q).

Ethyl 3-Azido-2-(benzyloxycarbonylamino)-3-(4-methoxybenzyl)-acrylate (**1c**): yield 56%; pale yellow oil.

$C_{21}H_{22}N_4O_5$	calc.	C 61.41	H 5.40	N 13.65
(410.4)	found	61.68	5.22	13.84

MS (EI, 70 eV): *m/z* (%) = 382 ($M^+ - 28$, 7), 91 (100).

IR (Nujol): ν = 3323, 2985, 2118, 1733, 1710 cm^{-1}.

^1H NMR(200 MHz, $CDCl_3$/TMS): δ = 1.23 (t, 3H, J = 7.1 Hz), 3.75 (s, 3H), 4.10 (m, 4H), 5.13 (s, 2H), 6.36 (br s, 1H, NH), 6.83 (d, 2H, J = 8.6 Hz), 7.24 (d, 2H, J = 8.6 Hz), 7.30–7.33 (m, 5H).

^{13}C NMR(50 MHz, $CDCl_3$/TMS): δ = 14.0 (CH_3), 34.2 (CH_2), 55.1 (CH_3), 61.4 (CH_2), 67.3 (CH_2) 114.8, 115.5 (q), 127.2 (q), 128.1, 128.2, 128.4, 129.9, 130.8 (q), 135.9 (q), 153.9, 158.7 (q), 163.9 (q).

Imidazoles 4; General Procedure:
To a solution of **1** (5.7 mmol) in anhyd CH_2Cl_2 (20 mL) cooled at 0 °C was added dropwise a solution of Ph_3P (1.5 g, 5.7 mmol) in

Table 1. Compounds **4** Prepared

Product	Yield[b] (%)	mp (°C) (solvent)	Ms (70 eV) *m/z* (%)
4a	66	100–102 (hexane)	379 (M^+, 13), 335 (20), 244 (43), 216 (40), 198 (48), 91 (100)
4b	65	94–95 (hexane)	395 (M^+, 4), 260 (10), 214 (21), 91 (100)
4c	55	99–101 (hexane)	383 (M^+, 10), 204 (9), 203 (10), 175 (20), 91 (100)
4d	77	160–162 (hexane)	379 (M^+, 1), 244 (5), 198 (11), 91 (100)
4e	61	98–101 (hexane)	268 (8), 256 (8), 180 (18), 107 (51), 105 (37), 91 (100)
4f	55	oil	331 (M^+, 5), 197 (8), 196 (7), 91 (100)
4g	57	105–107 (hexane)	441 (M^+, 1), 397 (9), 306 (12), 91 (100)
4h	48	oil	499 (M^+, 4), 364 (10), 234 (2), 91 (100)

[a] Satisfactory microanalyses obtained: C ± 0.30; H ± 0.30; N ± 0.28.
[b] Yield of pure isolated product.

the same solvent (10 mL) under N_2. The mixture was allowed to warm to r.t. and stirred for 16 h. Then the appropriate isocyanate (5.7 mmol) was added and the resultant solution was stirred at r.t. for 24 h. The solvent was removed under reduced pressure and the crude product was chromatographed on a silica gel column eluting with hexane/EtOAc (1:1) to give **4** (Tables 1 and 2).

Imidazoles 5; General Procedure:

To a solution of imidazole **4d** or **4h** (0.66 mmol) in THF (10 mL) was added dropwise a solution of LiOH (8.3 mg, 1.32 mmol) in H_2O (2 mL). The resultant mixture was stirred at reflux temperature for 16 h. After cooling, 1N HCl (5 mL) was added and the solution was extracted with CH_2Cl_2 (2 × 50 mL). The combined organic layers were washed with brine (1 × 50 mL) and dried ($MgSO_4$). After filtration, the filtrate was concentrated to dryness to give **5**.

2-Benzylamino-5-(ethoxycarbonyl)imidazole (**5a**): yield 53%; mp 174–178°C; colourless needles from CH_2Cl_2.

$C_{13}H_{15}N_3O_2$	calc.	C 63.66	H 6.16	N 17.13
(245.3)	found	63.80	6.24	17.02

MS (EI, 70 eV): *m/z* (%) = 246 (M^+ +1,63), 245 (M^+, 80), 171 (100).

IR (Nujol): ν = 3357, 1668, 1609, 1561 cm^{-1}.

^1H NMR(200 MHz, $CDCl_3$/TMS): δ = 1.23 (t, 3H, J = 7.2 Hz), 4.16 (q, 2H, J = 7.2 Hz), 4.41 (br s, 2H), 6.59 (br s, 1H, NH), 7.32–7.24 (m, 6H), 11.15 (br s, 1H).

^{13}C NMR (50 MHz, $CDCl_3$/TMS): δ = 14.5 (CH_3), 45.7 (CH_2), 59.1 (CH_2), 117.5 (q), 126.6, 127.1, 128.2, 134.8, 140.4 (q), 153.8 (q), 159.8 (q).

2-Benzylamino-5-(ethoxycarbonyl)-4-(4-methoxybenzyl)imidazole (**5b**): yield 50%; mp 154–155°C; colourless needles from hexane.

$C_{21}H_{23}N_3O_3$	calc.	C 69.02	H 6.34	N 11.50
(365.4)	found	68.89	6.19	11.73

MS (EI, 70 eV): *m/z* (%) = 365 (M^+, 13), 91 (100).

IR (Nujol): ν = 3413, 1660, 1622, 1564 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$/TMS: δ = 1.21 (t, 3H, J = 7.2 Hz), 3.66 (s, 3H), 4.15 (q, 2H, J = 7.2 Hz), 4.35 (br s, 2H), 5.42 (br s, 1H, NH), 6.68 (d, 2H, J = 8.4 Hz), 7.11 (d, 2H, J = 8.4 Hz), 7.20–7.17 (m, 5H) (H–1 hydrogen atom was not observed).

^{13}C NMR(50 MHz, $CDCl_3$/TMS): δ = 14.5 (CH_3), 32.9 (CH_2), 47.0 (CH_2), 55.1 (CH_3), 59.7 (CH_2), 113.5, 127.2, 127.4, 128.4, 129.5, 132.0 (q), 139.0 (q), 151.5 (q), 157.7 (q), 161.4 (q) (C-4 and C-5 carbon atoms were not observed).

Imidazoles 6; General Procedure:

A mixture of imidazole **4d** or **4h** (0.47 mmol), HCO_2NH_4 (0.18 g, 3.0 mmol), Pd/C (0.24 g) and anhyd MeOH (34 mL) was stirred at reflux temperature for 24 h and then filtered. The filtrate was concentrated to dryness and the residual material was recrystallized from CH_2Cl_2 to give **6**.

2-Amino-5-(ethoxycarbonyl)imidazole (**6a**): yield: 52%; mp 166–168°C; colourless prisms.

$C_6H_9N_3O_2$	calc.	C 46.45	H 5.85	N 27.08
(155.2)	found	46.60	6.00	26.88.

MS (EI, 70 eV): *m/z* (%) = 155 (M^+, 27), 109 (100).

IR (Nujol): ν = 3453, 3399, 3357, 3330, 1680, 1664, 1624 cm^{-1}.

Table 2. Spectral Data of Compounds **4**

Product	IR[a] ν (cm^{-1})	^1H NMR ($CDCl_3$/TMS) δ, J (Hz)	^{13}C ($CDCl_3$/TMS) δ, J (Hz)
4a	3359, 1720, 1610, 1570	1.24 (t, 3H, J = 7.0, CH_3CH_2), 2.31 (s, 3H, $CH_3C_6H_4$), 4.18 (q, 2H, J = 7.0, CH_2CH_3), 5.38 (s, 2H, CH_2Ph), 7.13 (d, 2H, J = 8.3), 7.49–7.36 (m, 8H), 8.86 (s, 1H, NH)	14.3 (CH_2CH_3), 20.8 ($CH_3C_6H_4$), 60.7 (CH_2Ph), 71.5 (CH_2Ph), 118.3 (C-5), 119.3, 128.8 (2 × CH), 129.0, 129.7, 133.1 (q), 133.8 (q), 135.7 (q), 138.6 (C-4), 150.7 (C-2), 151.6 (NCO), 159.5 (CCO)
4b	3352, 1730, 1716, 1615, 1575	1.25 (t, 3H, J = 7.0, CH_2CH_3), 3.79 (s, 3H, OCH_3), 4.18 (q, 2H, J = 7.0, CH_2CH_3), 5.38 (s, 2H, CH_2Ph), 6.88 (d, 2H, J = 8.0), 7.51–7.37 (m, 8H), 8.77 (s, 1H, NH)	14.3 (CH_2CH_3), 55.6 (OCH_3), 60.7 (CH_2CH_3), 70.5 (CH_2Ph), 114.5, 118.2 (C-5), 121.3, 128.8 (2 × CH), 129.0, 131.4 (q), 133.9 (q), 138.7 (C-4), 151.2 (C-2), 151.7 (NCO), 156.1 (q), 159.5 (CCO)
4c	3350, 1725, 1616, 1575	1.17 (t, 3H, J = 7.1, CH_2CH_3), 4.11 (q, 2H, J = 7.1, CH_2CH_3), 5.40 (s, 2H, CH_2Ph), 7.19–7.10 (m, 3H), 7.46–7.37 (m, 5H), 7.73–7.67 (m, 2H,), 9.15 (s, 1H, NH)	14.0 (CH_2CH_3), 60.3 (CH_2CH_3), 70.1 (CH_2Ph), 115.2 (d, ^2J_F = 22, *Co*), 118.4 (C-5), 120.9 (d, ^3J_F = 7.7, *Cm*), 128.4 (2 × CH), 128.6, 134.2 (q), 135.3 (d, ^4J_F = 220, *Ci*), 158.8 (CCO)
4d	3397, 1730, 1595, 1554	1.23 (t, 3H, J = 6.9, CH_2CH_3), 4.16 (q, 2H, CH_2CH_3), 4.64 (q, 2H, J = 6.0, NCH_2Ph), 5.32 (s, 2H, OCH_2Ph), 7.02 (t, 1H, J = 6.0, NH), 7.39–7.30 (m, 11H)	14.2 (CH_2CH_3), 46.8 (NCH_2-Ph), 60.4 (CH_2CH_3), 70.0 (OCH_2Ph), 118.1 (C-5), 127.5, 127.6, 128.5, 128.6, 128.7, 128.8, 133.9 (q), 137.7 (q), 139.2 (C-4), 151.3 (C-2), 154.5 (NCO), 159.3 (CCO)
4e	3347, 1718, 1652, 1604, 1586	1.24 (t, 3H, J = 7.0, CH_2CH_3), 4.18 (q, 2H, J = 7.0, CH_2CH_3), 5.37 (s, 2H, CH_2Ph), 6.14 (d, 1H, J = 14.4, PhCH=CH), 7.58–7.14 (m, 12H), 8.67 (d, 1H, J = 10.7, NH)	14.2 (CH_2CH_3), 60.7 (CH_2CH_3), 70.5 (CH_2Ph), 112.4 (PhCH=CH), 118.9 (C-5), 123.9, 125.3, 125.8, 126.3, 128.6, 128.7, 129.0, 133.6, (q), 136.2 (q), 138.5 (C-4), 150.3 (C-2), 151.1 (NCO), 159.1 (CCO)
4f	3398, 1595, 1554	0.98 (t, 3H, J = 6.0, $CH_2CH_2CH_3$), 1.20 (t, 3H, J = 7.2, CH_2CH_3), 1.65 (s, 2H, J = 6.0, $CH_2CH_2CH_3$), 3.41 (s, 2H, J = 6.0, $CH_2CH_2CH_3$), 4.16 (q, J = 7.2, CH_2CH_3), 5.33 (s, 2H, J = 7.2, CH_2Ph), 6.74 (t, 1H, J = 6.0, NH), 7.44–7.27 (m, 6H)	11.2 ($CH_2CH_2CH_3$), 14.2 (CH_2CH_3), 22.6 ($CH_2CH_2CH_3$), 44.6 ($CH_2CH_2CH_3$), 60.3 (CH_2CH_3), 69.9 (CH_2Ph), 117.6 (C-5), 128.4, 128.5, 128.7, 134.0 (q), 139.5 (C-4), 151.4 (C-2), 154.8 (NCO), 159.3 (CCO)
4g	3374, 1724, 1713, 1599, 1544	4.61 (d, 2H, J = 5.7, NCH_2Ph), 5.15 (s, 2H, OCH_2Ph), 5.24 (s, 2H, OCH_2Ph), 7.01 (t, 1H, J = 5.7, NH), 7.37–7.01 (m, 16H)	46.9 (NCH_2Ph), 66.0 (OCH_2Ph), 70.1 (OCH_2Ph), 117.8 (C-5), 127.6, 127.7, 128.1, 128.2, 128.6 (2 × CH), 128.7, 128.8, 128.9, 134.0 (q), 136.2 (q), 137.8 (q), 140.0 (C-4), 151.4 (C-2), 154.8 (NCO), 159.2 (CCO)
4h	3396, 1730, 1708, 1602	1.17 (t, 3H, J = 7.2, CH_2CH_3), 3.75 (s, 3H, OCH_3), 3.95 (s, 2H, $CH_2C_6H_4OCH_3$), 4.11 (q, 2H, J = 7.2, $CHCH_3$), 4.60 (d, 2H, J = 5.7, NCH_2Ph), 5.26 (s, 2H, OCH_2Ph), 6.79 (d, 2H, J = 8.7), 6.90 (t, 1H, J = 5.7, NH), 7.35–7.23 (m, 12H)	14.3 (CH_2CH_3), 33.4 ($CH_2C_6H_4OCH_3$), 46.9 (NCH_2), 55.2 (OCH_3), 60.3 (CH_2CH_3), 69.8 (OCH_2Ph), 113.5 (C-5), 113.7, 127.5, 127.8, 128.52, 128.6 (2 × CH), 128.8, 129.8, 131.0 (q), 134.0 (q), 138.0 (q), 151.5 (q, C-2*), 151.7, 153.1 (NCO), 158.0 (q), 160.4 (CCO)

[a] Compounds **4a–4e** and **4g** were recorded as Nujol mull and compounds **4f** and **4h** were recorded neat.

^{1}H NMR(200 MHz, DMSO-d_6/TMS): δ = 1.23 (t, 3H, J = 6.9 Hz), 4.15 (q, 2H, J = 6.9 Hz), 5.68 (br s, 2H, NH_2), 7.21 (s, 1H) (H-1 hydrogen atom was not observed).

^{13}C NMR(50 MHz, DMSO-d_6/TMS): δ = 14.4 (CH_3), 59.1 (CH_2), 120.3 (q), 129.4, 152.4 (q), 160.5 (q).

2-Amino-5-(ethoxycarbonyl)-4-(4-methoxybenzyl)imidazole **(6b)**: yield 66%, mp 164–166°C; colourless prisms.

$C_{14}H_{17}N_3O_3$	calc.	C 61.08	H 6.22	N 15.26
(275.3)	found	60.88	6.40	15.14

MS (EI, 70 eV): m/z (%) = 275 (M^+, 55), 229 (100).

IR (Nujol): ν = 3435, 3333, 3215, 1670, 1622, 1583 cm^{-1}.

^{1}H NMR(200 MHz, DMSO-d_6/TMS): δ = 1.24 (t, 3H, J = 7.0 Hz), 3.67 (s, 3H), 3.90 (s, 2H), 4.15 (q, 2H, J = 7.0 Hz), 5.60 (br s, 2H, NH_2), 6.79 (d, 2H, J = 8.4 Hz), 7.13 (d, 2H, J = 8.4 Hz).

^{13}C NMR(50 MHz, DMSO-d_6/TMS): δ = 14.1 (CH_3, 32.6 (CH_2), 55.0 (CH_3), 58.9 (CH_2), 113.5, 129.5, 132.2 (q), 151.5 (q), 157.4 (q), 160.3 (q) (C-4 and C-5 carbon atoms were not observed).

2-(Benzylamino)imidazole-5-carboxylic Acid (7):

A mixture of **4 g** (0.4 g, 0.9 mmol), cyclohexene (1 mL), Pd/C (0.2 g) and anhyd EtOH was refluxed under N_2 for 9 h. After cooling, the mixture was filtered and the filtrate concentrated to dryness to give **7**; yield: 43%; mp 171–173°C; colourless needles from CH_2Cl_2.

$C_{11}H_{11}N_3O_2$	calc.	C 60.82	H 5.10	N 19.34
(217.2)	found	60.52	5.20	19.56

MS (EI, 70 eV): m/z (%) = 217 (M^+, 1), 91 (100).

IR (Nujol): ν = 3500–2600, 3351, 1679, 1609, 1555 cm^{-1}.

^{1}H NMR(200 MHz, $CDCl_3$/TMS): δ = 4.40 (d, 2H, J = 6.0 Hz), 6.25 (br s 1H, NH), 7.39–7.18 (m, 6H) (CO_2H and H-1 hydrogen atoms were not observed).

^{13}C NMR(50 MHz, $CDCl_3$/TMS): δ = 45.7 (CH_2), 126.8, 127.8, 128.2, 140.1 (q), 152.1 (q), 162.1 (q) (C-4 and C-5 carbon atoms were not observed).

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