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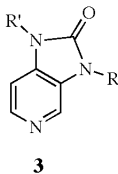
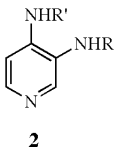
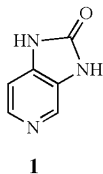
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A new synthetic route to 6-substituted-imidazo[4,5-*c*]pyridin-2-ones from 4-aminopyridine has been investigated. 4-Aminopyridine protected as alkyl carbamates were nitrated with dinitrogen pentoxide to the corresponding methyl, *i*-propyl and *t*-butyl 3-nitropyridin-4-yl carbamates (**5a-c**) in 51-63 % yields. Attempts to substitute these in the 6-position by the ONSH and the VNS techniques succeeded with butylamine and the *t*-butyl carbamate **9**. From the methyl or *t*-butyl 3-nitropyridin-4-yl carbamates **5a**, **5c** 1,3-dihydro-2*H*-imidazo[4,5-*c*]pyridin-2-one (**1**) was formed in 73 and 39 % yields, respectively. *t*-Butyl 6-*N*-butylamin-3-aminopyridin-4-yl carbamate (**6**) gave 6-butylamino-1,3-dihydro-2*H*-imidazo[4,5-*c*]pyridin-2-one (**7**) in 53 % yield.

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Introduction.

Some time ago we reported a high yield method for the nitration of pyridine compounds in the 3-position [1]. One of the compounds prepared was 4-amino-3-nitropyridine. From this, 3,4-diaminopyridine (**2**, R = R' = H) was made with a 62 % over all yield from 4-aminopyridine, making it readily available [2]. In addition to being of biological interest itself, it might also serve as a substrate for the synthesis of the imidazo[4,5-*c*]pyridine ring system. This ring structure is incorporated into a number of biologically active compounds [3,4]. We therefore made 2-methyl- and 2-phenyl-1*H*-imidazo[4,5-*c*]pyridine from 3,4-diaminopyridine [2]. We now wish to report an extension of this to the preparation of the imidazo[4,5-*c*]pyridin-2-one ring system. This is part of several pharmaceutical preparations, for instance a retroviral protease inhibitor for HIV/Aids treatment [5] and various cephalosporin derivatives [6]. Due to this, there have been reported many synthetic routes to these compounds. 1,3-Dihydro-2*H*-imidazo[4,5-*c*]pyridin-2-one (**1**) has been prepared from 3,4-diaminopyridine (**2**, R = R' = H) by various reagents such as urea [6,7], carbonyldiimidazole [5] and selenium assisted carbon monoxide incorporation [8]. Another reported approach utilised 3-amino-4-pyridincarbonyl azide (prepared from 3-amino isonicotinic acid) which was transformed into **1** [9].



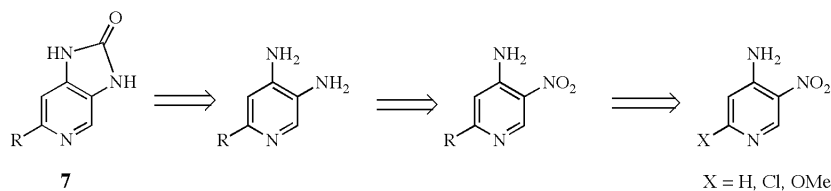
In addition, a number of mono- and di-*N*-substituted imidazo[4,5-*c*]pyridin-2-ones (**3**) have been reported [6,10]. These compounds may be obtained from **1** [10g,h] or from

mono- and di-*N*-substituted 3,4-diaminopyridines (**2**), which are converted to cyclic ureas by treatment with appropriate carbonylating agents [10a,b,e,f,i,j]. Only a few examples of imidazo[4,5-*c*]pyridin-2-ones with substituents on the pyridine ring are given in the literature. Imidazo[4,5-*c*]pyridin-2-ones in which the pyridine moiety is part of a larger polycyclic skeleton such as quinolines and α -carboline have been reported [11,12]. Various substituted 4-hydroxy-3-nitropyridin-2-ones originating from cyclo additions of nitromalonesters and a ketimine have been used as substrates for preparation of imidazo[4,5-*c*]pyridin-2-ones [13,14]. Bantick and co-workers have also prepared a 4,6-substituted imidazo[4,5-*c*]pyridin-2-one using a 4-hydroxy-3-nitropyridin-2-one as an intermediate. However, they incorporated the nitro group by nitration of 2,4-dihydroxy-6-propylpyridine [15].

To our knowledge, no general method for preparation of imidazo[4,5-*c*]pyridin-2-ones with various types of substituents in the 6-position (**7**) has been reported. Assuming that the cyclic urea moiety can be introduced in the final step, one is faced with the challenge of preparing the corresponding 4-amino-3-nitro-6-substituted pyridines as indicated in Scheme 1.

Standard nucleophilic aromatic substitutions (NAS) would require the presence of a leaving group like a halogen or a methoxy group in the 6-position. The preparation of 4-amino-6-chloro-3-nitropyridine from 4-amino-2-chloropyridine has been reported [16]. The synthesis proceeds *via* an intermediate nitramine, which rearranges upon heating to two isomeric nitropyridines. The overall yield of 4-amino-6-chloro-3-nitropyridine was less than 22 %. By substitution of the chloro moiety, NH₂, OMe, and other groups have been introduced in the 6-position [16-17]. Substitution of the chloro with a methoxy group *prior* to nitration has also been reported [18]. No yield was given for the NAS step. The rearrangement of the nitramine gave 30 % of 4-amino-2-methoxy-5-nitropyridine. Another

Scheme 1



strategy for preparation of 6-substituted 4-amino-3-nitropyridines has been to introduce the 4-amino group by aminolysis of a halogen in the *final* step [19].

We have reported an efficient method for preparation of 3-nitropyridines with various substituents in the 4-position [1]. Also, we have shown that it is possible to substitute the 6-position of 3-nitropyridines selectively, either by Oxidative Nucleophilic Substitution of Hydrogen (ONSH) using various amines in the presence of potassium permanganate [20] or by Vicarious Nucleophilic Substitutions (VNS) using hydroxylamine or 4-amino-1,2,4-triazole as nucleophiles [21]. With this knowledge in hand we envisaged a new procedure for preparation of 6-substituted imidazo[4,5-*c*]pyridin-2-ones starting from 4-aminopyridine as depicted in Scheme 2. The 4-amino group needs to be protected during the nitration with dinitrogen pentoxide. We have successfully used acetyl for this [2]. However, by instead preparing carbamates (**4**), this would not only serve as a protecting group, but also be a precursor for the cyclic urea (**7**) in the final step [22].

Nitration.

The nitration of pyridine compounds by N_2O_5 gives the *N*-nitropyridinium nitrate. In aqueous SO_2/HSO_3^- this rearranges regioselectively to the *b*-nitropyridine compound [1]. One side reaction in the present system would be the hydrolysis of the carbamates **5** to give the corresponding 3-nitro-4-aminopyridines. However, with the present nitration system, it is possible to obtain acceptable to good yields of

the *b*-nitropyridines. The conditions are such that even acid labile groups in the nitrated molecule may survive. Thus, the pH of the aqueous solution is *ca.* 2–3 and the temperature *ca.* 20 °C. The results are given in Table 1 and one point is that no hydrolysis of the acid labile carbamates were observed during the nitration reaction.

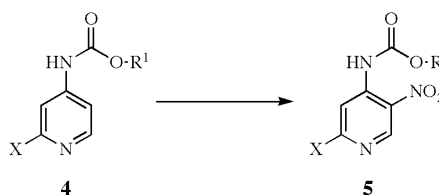
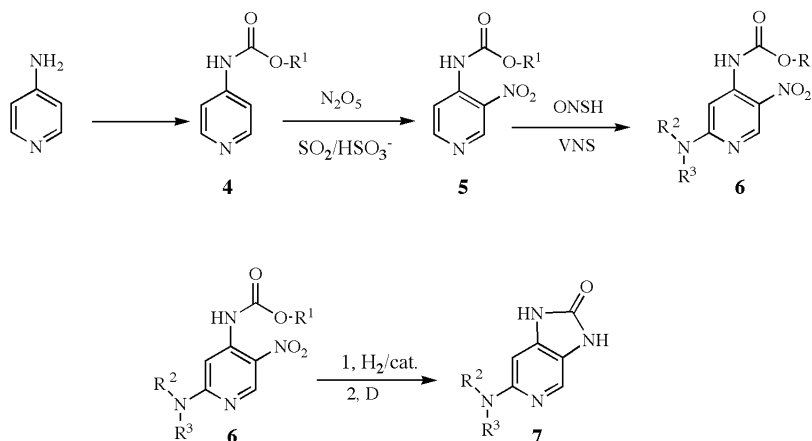


Table 1

Substrate 4 , R ¹ , X	Method A [a] 4:5 [d]	Method B[b] 4:5 [d]	Method C[c] 4:5 [d](yield of 5) [e]
a , Me, H	47:53	85:15	5:95 (63)
b , <i>i</i> -Pr, H	-	-	3:97 (61)
c , <i>t</i> -Bu, H	37:62	-	11:89 (51)
d , <i>t</i> -Bu, Cl	100 : 0	100: 0	100: 0 -

[a] Reaction with N_2O_5 in CH_2Cl_2 , followed by treatment with $NaHSO_3$ in methanol/water. [b] Reaction with N_2O_5 in SO_2 followed by treatment with water. [c] Reaction with N_2O_5 in CH_3NO_2 followed by treatment with $NaHSO_3$ in methanol/water. [d] Determined by 1H nmr spectroscopy of the reaction mixtures. [e] Isolated compounds, > 99 % pure by 1H nmr spectroscopy.

Scheme 2

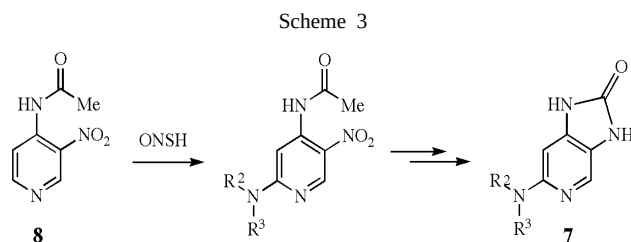


From Table 1, the nitration of methyl pyridin-4-yl carbamate (**4a**) gave a better yield than that of the *t*-butyl derivative (**4c**), 63 vs 51%. This may have some practical implications, as methyl chloroformate used for the formation of **4a** is considerably less expensive than di-*tert*-butyl dicarbonate used for the preparation of **4c**. Also, the final cyclization step gave a better yield with the methyl carbamate **9a** than the *t*-butyl carbamate **9c**, 74 vs 56 %. All attempts to nitrate *tert*-butyl 2-chloropyridin-4-yl carbonate **4d** failed.

Substitution Reactions.

We have reported the substitution of hydrogen by ammonia itself and a range of other amines in the position *para* to the nitro group in a series of 4-substituted-3-nitropyridines by the ONSH methodology [20]. We therefore attempted the reaction of **5a-c** with ammonia, *n*-butylamine, diethylamine and aniline under ONSH conditions. However, the products from all reactions were either starting material or 4-amino-3-nitro pyridine *except* for the reaction of *n*-butylamine with **5b** ($R^1 = i\text{-Pr}$, 29 %) and **5c** ($R^1 = t\text{-Bu}$, 56 %).

As 4-acetamido-3-nitropyridine is both readily available and can be easily hydrolysed to 4-amino-3-nitropyridine we also investigated the substitution reactions with this substance, as the products might be starting materials for **6** and by that **7**:



The attempted ONSH reactions with **8** did not give any substitution in the 6-position of the pyridine ring, only aminolysis of the acetyl group.

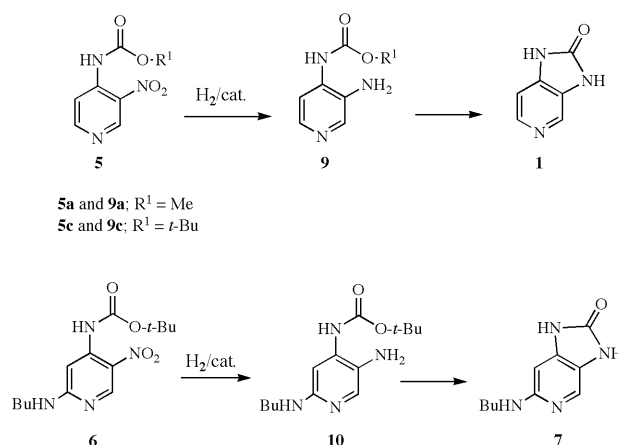
We have reported the successful VNS reactions on 3-nitropyridine [21] and we tried this methodology to substituted **5a**, **5c** and **8** with hydroxylamine and 1-amino-1,3,4-triazole without success.

Finally, as our earlier results indicated that the ONSH reactions gave better results with electron withdrawing groups in the 4-position of the pyridine ring, we tried to oxidise the amino group of 4-amino-3-nitropyridine to a nitro group. To our surprise, this was not possible either by nitric acid, potassium permanganate or by sodium hypochlorite. We were therefore left with two series of carbamates for the cyclisation to the imidazopyridinones **1** and **7**, one with a hydrogen atom and one with *n*-butylamine in the position *para* to the nitro group, that is, **5** and **6**.

Cyclisation Reactions.

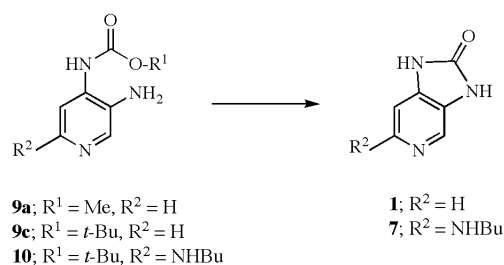
We have reported the facile cyclisation of 4-acetamido- and 4-benzamido-3-aminopyridine to the corresponding imidazo[4,5-c]pyridines in acetic acid [2]. The carbamates **5a**, **5c** and **6** were accordingly reduced to the corresponding amines (**9a**, **9c** and **10**) in high yields, and these were cyclised to the imidazo[4,5-c]pyridinones **1** and **7**.

Scheme 4



This cyclisation reaction proved to be difficult, particularly in the light of our experience with the 4-acylamido-3-aminopyridines [2]. The results from a series of experiments are given in Table 2.

Table 2.



Substrate	Reaction conditions	Product (yield, %)
9c	MeOH, 64 °C, 18 h	No reaction
9c	MeOH, H ₂ SO ₄ (2 %), 18 h	No reaction
9c	AcOH, 114 °C, 24 h	3-acetamido-4-aminopyridine
9c	DMAP, Et ₃ N, 1,4-dioxane, 110 °C, 19h	No reaction
9c	NaH, 1,4-dioxane, 110 °C, 43 h	<i>t</i> -butyl 4-aminopyridyl-3-carbamate
9c	diglyme, 150 °C, 24 h	1 (56 %)[a]
9a	diglyme, 150 °C, 24 h	1 (74 %)[a]
10	diglyme, 150 °C	7 (55 %)[b]

[a] Yield after crystallisation; [b] Yield after flash chromatography.

As can be seen from Table 2, addition of acid or base resulted in two different reaction paths, with acetic acid, 4-amino-3-acetamidopyridine was formed and with sodium hydride in 1,4-dioxane, *trans* carbamoylation took place, forming *tert*-butyl 4-aminopyridin-3-yl carbamate. However, complete conversion to the cyclic ureas was accomplished in diglyme at 150 °C. From ^1H nmr spectroscopy only one product (**1** or **7**) was present at the end of the reaction. For both 1,3-dihydro-2*H*-imidazo[4,5-*c*]pyridin-2-one (**1**) and 6-butyl-1,3-dihydro-2*H*-imidazo[4,5-*c*]pyridin-2-one (**7**), acceptable yields were obtained after crystallisation or flash chromatography. 1,3-Dihydro-2*H*-imidazo[4,5-*c*]pyridin-2-one (**1**) itself could be formed from both methyl and *t*-butyl 3-nitropyridin-4-yl carbamates (**5a** and **5c**). As **5a** was formed by a less expensive route than **5c**, this may be the best starting material for **1**. The present method compares well with the reported processes for the synthesis of **1** [5-9]. For 6-butyl-1,3-dihydro-2*H*-imidazo[4,5-*c*]pyridin-2-one (**7**) the present method appears to be the only one reported.

Conclusion.

We have investigated a new synthetic route to 6-substituted-imidazo[4,5-*c*]pyridin-2-ones from readily available 4-amino-3-nitropyridine *via* the corresponding 4-alkyl carbamates (**5a-c**). Substitutions of these compounds in the 6-position by the ONSH and the VNS techniques were attempted. This worked well for substitution with butylamine but not with ammonia or other amines. From the methyl or *t*-butyl 3-nitro-4-pyridinyl carbamates **5a**, **5c** and **7**, 1,3-dihydro-2*H*-imidazo[4,5-*c*]pyridin-2-on (**1**) and 6-butylamino-1,3-dihydro-2*H*-imidazo[4,5-*c*]pyridin-2-one (**7**, $R^2 = \text{H}$, $R^3 = \text{Bu}$) were formed in good yields.

EXPERIMENTAL

The nmr spectra were recorded on a Bruker Avance DPX 300 MHz instrument, using the solvents for calibration of the chemical shifts. The ir spectra were recorded on a Nicolet 20SxC FT-IR spectrometer. The ms and hrms were recorded on a MAT 95 XL spectrometer. Dinitrogen pentoxide was prepared from dinitrogen tetroxide and ozone [23]. The solvents were dried according to standard procedures [24]. Literature procedures were used for the preparation of 4-amino-2-chloropyridine [25], methyl pyridin-4-yl carbamate (**4a**) [22c], *i*-propyl pyridin-4-yl carbamate (**4b**) [22c] and *t*-butyl pyridin-4-yl carbamate (**4c**) [26]. Compound **4d** was prepared according to Pauls et al. [27] using sodium hydride as base instead of sodium bistrimethylsilyl amide.

Methyl 3-Nitropyridin-4-yl Carbamate (**5a**).

Method A.

Dinitrogen pentoxide (DNP) (0.57 g, 5.28 mmol) was dissolved in CH_2Cl_2 (10 mL) which was precooled on an ice-water bath. To this solution was added methyl pyridin-4-yl carbamate (**4a**) (0.402 g, 2.63 mmol). The reaction was stirred for 10 minutes on the ice-water bath before a solution of NaHSO_3 (0.82

g, 7.88 mmol) in a mixture of methanol (15 mL) and water (5 mL) was added. The reaction was stirred at room temperature over night. ^1H nmr of the reaction mixture (methanol- d_4) showed **4a** and **5a** in a ratio of 47:53.

Method B.

DNP (0.61 g, 5.65 mmol) was dissolved in liquid SO_2 (ca. 30 mL) at -78°C . To this solution was added **4a** (0.399 g, 2.63 mmol) which was dissolved gradually as the temperature was allowed to rise to around -20°C . After 2 hours the mixture was poured into ice-water (50 mL). ^1H nmr of the mixture indicated a ratio between **4a** and **5a** of 85:25.

Method C.

DNP (0.71 g, 6.57 mmol) was dissolved in freshly distilled nitromethane (12 mL) in an ice-water bath. To this solution was added **4a** (0.500 g, 3.29 mmol). After stirring for 10 minutes on the ice-water bath a solution of sodium bisulfite (1.03 g, 9.90 mmol) in a 3:1 mixture of methanol and water (20 mL) was added. The reaction was stirred at room temperature over night. ^1H nmr of the reaction mixture (methanol- d_4) showed **4a** and **5a** in a ratio of 5:95.

The solvents were evaporated and the residue dissolved in ethyl acetate (30 mL) and water (20 mL). The pH was adjusted to >7 by addition of aqueous sodium hydroxide (1 M). The layers were separated and the aqueous layer extracted with ethyl acetate (4 x 20 mL). The combined organic layers were dried (MgSO_4) and the solvent evaporated to give 0.408 g of a yellow solid (96 % pure by ^1H nmr, 63 % yield). This product was used without further purification in the following studies. An analytically pure sample was obtained by flash chromatography (3 % acetone in dichloromethane). This gave a light yellow solid with mp $141.5-143.0^\circ\text{C}$ (lit $140-142^\circ\text{C}$ [28]) ^1H nmr (deuteriochloroform): δ 3.88 (s, 3H, CH_3), 8.55 (d, 1H, H-5, $J = 5.9$ Hz), 8.66 (d, 1H, H-6, $J = 5.9$ Hz), 9.37 (s, 1H, H-2), 10.03 (br s, 1H, NH) ppm; ^{13}C nmr (deuteriochloroform): δ 53.4 (OCH_3), 113.3, 131.3 (C-NO_2), 141.9, 148.0, 152.78 (C=O), 155.2 ppm; ir: (potassium bromide): 3280 (m), 1730 (s), 1710 (m), 1595 (s), 1570 (m), 1560 (m), 1490 (m), 1450 (m), 1400 (m), 1340 (s), 1250 (m), 1235 (m), 1200 (m), 1170 (m), 1050 (m), 940 (m); ms: (250 $^\circ\text{C}$, 70 eV) m/z 198 ($M+1$, 3), 197 (M^+ , 28), 165 (5), 152 (8), 151 (100), 136 (18), 122 (8), 119 (8), 94 (13), 93 (13), 92 (10), 91 (14), 80 (11), 79 (47), 78 (15), 66 (16), 65 (23), 64 (37), 63 (5), 59 (63), 54 (5), 53 (25), 52 (41), 51 (11), 50 (8); hrms: observed: M^+ 197.0438. Calculated for $\text{C}_7\text{H}_7\text{N}_3\text{O}_4$: 197.0437.

Isopropyl 3-Nitropyridin-4-yl Carbamate (**5b**).

Isopropyl pyridin-4-yl carbamate (**4b**) (3.00 g, 16.30 mmol) was nitrated using Method C as described for **4a** above. ^1H nmr (methanol- d_4) of the reaction mixture showed **4b** and **5b** in a ratio of 3:97. Work up gave 2.26 g of a light brown solid (>99 % pure by ^1H nmr, 61 % yield). This product was used without further purification in the subsequent studies. A sample was purified for analysis by flash chromatography (5 % acetone in dichloromethane). This gave an off-white solid with mp. $97.0-99.0^\circ\text{C}$. ^1H nmr (deuteriochloroform): δ 1.36 (d, 6H, 2 x CH_3 , $J = 6.2$ Hz), 5.08 (hp, 1H, CH, $J = 6.2$ Hz), 8.56 (d, 1H, H-5, $J = 6.0$ Hz), 8.64 (d, 1H, H-6, $J = 6.0$ Hz), 9.36 (s, 1H, H-2), 9.93 (br s, 1H, NH) ppm; ^{13}C nmr (deuteriochloroform): δ 21.9, 70.9, 113.3, 131.4, 142.1, 148.0, 151.9, 155.1 ppm; ir: (potassium bromide): 3360 (m), 1730 (s), 1605 (s), 1570 (s), 1520 (m), 1500

(s), 1490 (m), 1430 (br, m), 1345 (s), 1255 (m), 1230 (s), 1210 (m), 1175 (m), 1100 (s), 1045 (m), 915 (m), 880 (m), 850 (s), 800 (m), 760 (s) cm^{-1} ; ms: (250 $^{\circ}\text{C}$, 70 eV) m/z 226 ($M+1$, 5), 225 (M^+ , 41), 166 (28), 140 (13), 139 (96), 122 (13), 121 (5), 119 (10), 94 (5), 93 (22), 91 (8), 79 (10), 66 (7), 64 (15), 52 (6); hrms: observed: M^+ 225.07489. Calculated for $\text{C}_9\text{H}_{11}\text{N}_3\text{O}_4$: 225.07496.

t-Butyl 3-Nitropyridin-4-yl Carbamate (**5c**).

t-Butyl pyridin-4-yl carbamate (**4c**) (1.001 g, 5.15 mmol) was nitrated using Method C as described for **4a** above. ^1H nmr (methanol- d_4) of the reaction mixture showed **4c** and **5c** in a ratio of 11:89. Work up gave 0.855 g orange solid. Purification by flash chromatography (3 % acetone in dichloromethane) gave 0.631 g off-white solid (>99 % pure by ^1H nmr, 51 % yield) with mp 113.0–115.0 $^{\circ}\text{C}$. ^1H nmr (deuteriochloroform): δ 1.56 (s, 9H, 3 $\times$ CH_3), 8.54 (d, 1H, H-5, J = 6.0 Hz), 8.61 (d, 1H, H-6, J = 6.0 Hz), 9.34 (s, 1H, H-2), 9.82 (br s, 1H, NH) ppm; ^{13}C nmr (deuteriochloroform): δ 28.5, 83.7, 113.6, 132.2, 142.8, 148.3, 151.6, 155.2 ppm; ir: (potassium bromide) 3360 (m), 1730 (s), 1600 (s), 1565 (s), 1520 (s), 1500 (s), 1435 (br, s), 1405 (m), 1365 (m), 1345 (s), 1320 (m), 1250 (br, s), 1230 (br, s), 1140 (br, s), 1120 (s), 1050 (m), 1040 (m), 860 (m), 850 (m), 840 (m), 825 (m), 760 (m), 750 (s) cm^{-1} ; ms: (250 $^{\circ}\text{C}$, 70 eV) m/z 240 ($M+1$, 1.5), 239 (M^+ , 7), 166 (12), 140 (10), 139 (15), 135 (7), 121 (6), 119 (8), 93 (8), 91 (7), 79 (6), 66 (7), 64 (11), 59 (31), 58 (8), 57 (100), 56 (9), 55 (5), 52 (6); hrms: observed: M^+ 239.0907. Calculated for $\text{C}_{10}\text{H}_{13}\text{N}_3\text{O}_4$: 239.0906.

Isopropyl 2-*N*-Butylamin-5-nitropyridin-4-yl Carbamate (**6b**).

To a solution of **5b** (0.503 g, 2.24 mmol) in *n*-butylamine (12 mL) was added potassium permanganate (1.32 g, 8.38 mmol) and the mixture stirred vigorously at room temperature. Additional portions of potassium permanganate (0.79 g) was added with 1 hour intervals. After 3 hours dimethyl sulfoxide (5 mL) was added. After a total reaction time of 6 hours ^1H nmr of the reaction mixture indicated that the reaction had stopped. The reaction was poured into water (100 mL) and the resulting mixture filtered. The filtrate was extracted with dichloromethane (3 $\times$ 100 mL). The combined organic layers were washed with brine (80 mL), dried (magnesium sulfate) and the solvent evaporated under reduced pressure. This gave 0.633 g of an oil, which was purified by flash chromatography (2 % acetone in dichloromethane) to give 0.189 g (>98 % pure by ^1H nmr, 29 % yield) of a purple, crystalline product. mp 124.0–125.0 $^{\circ}\text{C}$. ^1H nmr (deuteriochloroform): δ 0.97 (tr, 3H, CH_3 , J = 7.3 Hz), 1.33 (d, 6H, 2 $\times$ CH_3), J = 6.3 Hz), 1.37–1.49 (m, 2H, CH_2), 1.50–1.69 (m, 2H, CH_2), 3.36 (br s, 2H, CH_2), 4.97–5.10 (m, 1H, CH), 5.30 (br s, 1H, NH), 7.46 (s, 1H, H-3), 9.02 (s, 1H, H-6), 10.20 (br s, 1H, NH) ppm; ^{13}C nmr (dimethyl sulfoxide- d_6): δ 13.9, 19.8, 21.8, 31.1, 69.7, 94.2, 125.2, 141.0, 150.6, 152.0, 162.1 ppm; one signal which was covered by dimethylsulfoxide signals was observed at 42.2 ppm for a run in deuteriochloroform; ir: (potassium bromide) 3341 (m), 3230 (br m), 2982 (m), 2958 (m), 2935 (m), 2867 (m), 1737 (s), 1620 (s), 1577 (s), 1557 (s), 1514 (s), 1496 (s), 1455 (m), 1421 (s), 1374 (m), 1341 (m), 1303 (s), 1277 (s), 1246 (s), 1190 (s), 1136 (m), 1105 (s), 1041 (m), 998 (m), 847 (m), 759 (m) cm^{-1} ; ms: (250 $^{\circ}\text{C}$, 70 eV) m/z 297 ($M+1$, 3), 296 (M^+ , 31), 280 (17), 279 (71), 268 (6), 267 (49), 254 (27), 253 (68), 240 (44), 237 (18), 225 (38), 212 (18), 211 (100), 208 (10), 206 (5), 198 (18), 193 (6), 192 (5), 181 (19), 168 (11), 167

(67), 166 (18), 163 (15), 122 (5), 121 (48), 120 (11), 119 (5), 106 (7), 94 (5), 93 (7), 92 (5), 67 (7), 45 (11), 43 (28) ppm; hrms: observed: M^+ 296.1478. Calculated for $\text{C}_{13}\text{H}_{20}\text{N}_4\text{O}_4$: 296.1485.

t-Butyl 2-*N*-Butylamin-5-nitropyridin-4-yl Carbamate (**6c**)

A solution of **5c** (0.513, 2.15 mmol) was treated in the same manner as described for **5b**. This gave a crude product, which was crystallised from methanol/water to give 0.373 g (56 % yield) of a yellow crystalline material. mp 154–155 $^{\circ}\text{C}$. ^1H nmr (deuteriochloroform): δ 0.97 (tr, 3H, CH_3 , J = 7.3 Hz), 1.37–1.49 (m, 2H, CH_2), 1.54 (s, 9H, 3 $\times$ CH_3), 1.59–1.68 (m, 2H, CH_2), 3.36 (br s, 2H, CH_2), 5.30 (br s, 1H, NH), 7.44 (s, 1H, H-3), 9.02 (s, 1H, H-6), 10.09 (br s, 1H, NH) ppm; ^{13}C nmr (dimethyl sulfoxide- d_6): δ 15.1, 19.6, 27.7, 31.0, 83.1, 93.4, 124.8, 140.9, 150.5, 151.2, 161.9 ppm; one signal which was covered by dimethylsulfoxide was observed at 42.5 ppm for a run in deuteriochloroform; ir: (potassium bromide) 3315 (m), 3210 (m), 1760 (s), 1610 (s), 1570 (s), 1550 (s), 1510 (s), 1510 (m), 1490 (m), 1450 (w), 1410 (m), 1385 (m), 1300 (m), 1270 (s), 1240 (s), 1195 (m), 1150 (s), 1130 (m), 870 (m), 840 (m), 760 (m) cm^{-1} ; ms: (250 $^{\circ}\text{C}$, 70 eV) m/z 311 ($M+1$, 3), 310 (M^+ , 18), 293 (26), 254 (10), 238 (6), 237 (30), 225 (46), 212 (35), 211 (81), 210 (16), 208 (5), 198 (39), 194 (6), 193 (22), 192 (6), 182 (5), 181 (49), 168 (31), 167 (100), 163 (8), 154 (34), 152 (5), 151 (6), 150 (5), 149 (21), 147 (7), 139 (6), 137 (11), 135 (13), 124 (9), 122 (5), 121 (60), 120 (16), 119 (5), 106 (6), 94 (5), 93 (8), 81 (5), 67 (6), 57 (53), 56 (8), 55 (8), 52 (5); hrms: observed: M^+ 310.1638. Calculated for $\text{C}_{14}\text{H}_{22}\text{N}_4\text{O}_4$: 310.1641.

Methyl 3-Aminopyridin-4-yl Carbamate (**9a**).

To a solution of **5a** (0.119 g, 0.60 mmol) in ethyl acetate (10 mL) was added 5% palladium on carbon (0.021 g) and the mixture stirred under hydrogen (10 bar) for 24 hours. The reaction mixture was filtered through celite and the solvent evaporated under reduced pressure. This gave 0.098 g of an orange oil (>98 % pure by GC, 98 % yield). A sample was crystallised from chloroform to give orange crystals with mp 124.0–126.0 $^{\circ}\text{C}$. ^1H nmr (dimethyl sulfoxide- d_6): δ 3.69 (s, 1H, CH_3), 5.14 (br s, 2H, NH_2), 7.51 (d, 1H, H-5, J = 5.3 Hz), 7.71 (d, 1H, H-6, J = 5.3 Hz), 7.95 (s, 1H, H-2), 8.94 (br s, 1H, NH) ppm; ^{13}C nmr (methanol- d_4): δ 53.1, 116.6, 134.1, 136.7, 138.6, 139.9, 156.3 ppm; ir: (potassium bromide) 4310 (w), 3355 (w), 3243 (w), 1747 (m), 1728 (s), 1590 (s), 1525 (s), 1505 (m), 1431 (m), 1316 (m), 1248 (m), 1222 (s), 1192 (m), 1066 (m) cm^{-1} ; ms: (250 $^{\circ}\text{C}$, 70 eV) m/z 167 (M^+ , 97), 136 (29), 135 (100), 109 (5), 108 (36), 107 (25), 81 (48), 80 (28), 79 (5), 59 (8), 54 (22), 53 (22), 52 (21); hrms: observed: M^+ 167.06956. Calculated for $\text{C}_7\text{H}_9\text{N}_3\text{O}_2$: 167.06948.

t-Butyl 3-Aminopyridin-4-yl Carbamate (**9c**).

A solution of **5c** (0.657 g, 2.75 mmol) in methanol (20 mL) was treated in the same manner as described for reduction of **5a**. This gave 0.546 g (> 99 % pure by GC, 95 % yield) of a white crystalline material. mp 118.0–19.0 $^{\circ}\text{C}$. ^1H nmr (deuteriochloroform): δ 1.53 (s, 9H, 3 $\times$ CH_3), 3.49 (br.s, 2H, NH_2), 6.96 (br s, 1H, NH), 7.62 (d, 1H, H-5, J = 5.4 Hz), 8.07 (d, 1H, H-6, J = 5.4 Hz), 8.11 (s, H-2, 1H) ppm; ^{13}C nmr (deuteriochloroform): δ 28.3, 81.5, 114.2, 131.8, 134.9, 140.7, 143.1, 152.5 ppm; ir: (potassium bromide): 3378 (m), 3227 (m), 2982 (m), 1736 (s), 1716 (s), 1589 (s), 1520 (s), 1434 (s), 1369 (m), 1334 (m), 1315

(m), 1270 (s), 1253 (s), 1224 (m), 1156 (s), 865 (m), 825 (m) cm^{-1} ; ms: (250 $^{\circ}\text{C}$, 70 eV) m/z 209 (M^+ , 3), 154 (6), 153 (90), 136 (21), 135 (56), 110 (5), 109 (84), 108 (5), 107 (7), 97 (7), 95 (5), 85 (7), 83 (7), 82 (8), 81 (11), 80 (11), 71 (11), 69 (11), 67 (6), 59 (56), 57 (100), 56 (14), 55 (20), 54 (8), 53 (13), 52 (8); hrms: observed: M^+ 209.11604. Calculated for $\text{C}_{10}\text{H}_{15}\text{N}_3\text{O}_2$: 209.11643.

t-Butyl 6-*N*-Butylamino-3-aminopyridin-4-yl Carbamate (**10**).

A solution of **6c** (0.615 g, 1.98 mmol) in ethyl acetate (30 mL) was treated in the same manner as **5a**. Evaporation of the solvent gave 0.385 g of a light purple oil (> 98% pure by ^1H nmr, 69% yield) which deteriorated quickly after isolation. The crude product was used immediately in the next step without full characterisation. ^1H nmr (deuteriochloroform): δ 0.95 (tr, 3H, CH_3 , $J = 7.3$ Hz), 1.35–1.63 (m, 6H, 2 $\times$ CH_2), 2.72 (br s, 2H, NH_2), 3.22 (tr, 2H, CH_2 , $J = 7.00$ Hz), 4.47 (br s, 1H, NH), 7.12 (s, 1H, H-3), 7.68 (br s, 1H, NH), 7.70 (s, 1H, H-6) ppm; ^{13}C nmr (methanol- d_4): δ 11.8, 20.7, 28.9, 32.3, 42.1, 80.4, 98.5, 125.5, 136.7, 136.8, 153.3, 154.6 ppm;

1,3-Dihydro-2*H*-imidazo[4,5-*c*]pyridin-2-one (**1**).

A solution of **9a** (0.308 g, 1.84 mmol) in diglyme (10 mL) was heated in an oil bath at 150 $^{\circ}\text{C}$ for 24 hours. The reaction was cooled to room temperature and most of the solvent evaporated under reduced pressure. The oily residue was crystallised from water to give 0.185 g of light brown crystals (74 % yield) with mp 305.0–306.0 $^{\circ}\text{C}$ (lit 304–305 $^{\circ}\text{C}$ [7], 315 $^{\circ}\text{C}$ [9a]). ^1H nmr (dimethyl sulfoxide- d_6): δ 6.97 (d, 1H, H-7, $J = 5.2$ Hz), 8.09 (d, 1H, H-6, $J = 5.2$ Hz), 8.13 (s, 1H, H-4), 10.99 (br s, 1H, NH), 11.06 (br s, 1H, NH) ppm; ^{13}C nmr (dimethyl sulfoxide- d_6): δ 104.3, 127.4, 129.1, 135.2, 142.0, 154.8 ppm; ir: (potassium bromide) 3481 (br m), 3300–2100 (br m), 1729 (s), 1626 (s), 1609 (s), 1487 (s), 1217 (m), 1203 (m), 1188 (m), 1157 (m), 1935 (m), 999 (m), 883 (m), 808 (m), 720 (s), 632 (s) cm^{-1} ; ms: (250 $^{\circ}\text{C}$, 70 eV) m/z 136 (M^+ , 9), 135 (M^+ , 100), 107 (15), 80 (23), 53 (22), 52 (12), 44 (9); hrms: observed: M^+ 135.04334. Calculated for $\text{C}_6\text{H}_5\text{N}_3\text{O}$: 135.04326.

Treatment of **9c** (0.506 g, 2.42 mmol) according to the procedure given for cyclisation of **9a** gave, after crystallisation 0.184 g of light brown crystals (56 % yield) with mp 308–310 $^{\circ}\text{C}$.

6-*N*-Butylamino-1,3-dihydro-2*H*-imidazo[4,5-*c*]pyridin-2-one (**7**).

A solution of *t*-butyl 6-*N*-butylamino-3-aminopyridin-4-yl carbamate (**10**) (0.384 g, 1.37 mmol) was treated in the same manner as described for cyclisation of **9a**. Flash chromatography (ethyl acetate:methanol:aqueous ammonia= 95:4:1) of the crude oily product gave 0.155 g of a light brown powder (55 %) with 229 $^{\circ}\text{C}$ (decomposed). ^1H nmr (dimethyl sulfoxide- d_6): δ 0.89 (tr, 3H, CH_3 , $J = 7.2$ Hz), 1.23–1.56 (m, 4H, 2 $\times$ CH_2), 3.13 (br m, 2H, CH_2), 5.85 (tr, 1H, NH , $J = 5.5$ Hz), 6.03 (s, 1H, H-7), 7.52 (s, 1H, H-4), 10.20 (br s, 1H, NH), 10.53 (br s, 1H, NH) ppm; ^{13}C nmr (dimethyl sulfoxide- d_6): δ 13.9, 19.9, 31.39, 41.8, 87.00, 120.1, 125.6, 138.5, 154.7, 155.3 ppm; ir (potassium bromide) 3600 – 2600 (broad signal with the following peaks: 3329, 3194, 2957, 2928), 1710 (s), 1648 (s), 1502 (m), 1475 (m) cm^{-1} ; ms: (250 $^{\circ}\text{C}$, 70 eV) m/z 207 (M^+ , 3), 206 (M^+ , 21), 190 (6), 177 (24), 164 (15), 163 (100), 150 (36), 136 (7), 135 (10), 134 (20); hrms: observed: M^+ 206.1166. Calculated for $\text{C}_{10}\text{H}_{14}\text{N}_4\text{O}$: 206.1168.

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