# Synthesis of 1,2-dihydropyrrolo[1,2-*c*]pyrimidin-1-ones

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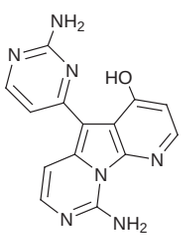
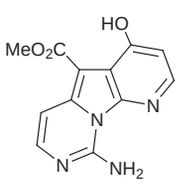
1,2-Dihydropyrrolo[1,2-*c*]pyrimidin-1-ones **2** have been synthesised from pyrrole. We have developed a versatile procedure for the introduction of substituents into the pyrrolopyrimidinones **2**, at positions 5 or 7 as desired, and as required by our plans for the synthesis of the variolin type sea alkaloids.

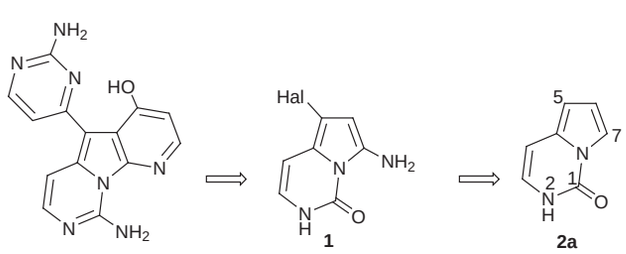
The variolins, from the Antarctic sponge *Kirkpatrickia variolosa*, are a small group of marine heterocyclic substances[1] of which variolins B and D are typical. These substances were


variolin B


variolin D

isolated *via* the examination of extracts shown to be active against P388 murine leukemia cells. Subsequent *in vitro* testing showed variolin B to be the most active in tests which included assessment of antiviral activity (*Herpes simplex* Type I, *polio* Type I). Each of these variolins is based on a fused pyrimidino-7-azaindole—strictly a pyrido[3′,2′ : 4,5]pyrrolo[1,2-*c*]pyrimidine. Noting the presence of a heteroaryl unit located at the 3-position of the embedded 7-azaindole, we have developed and described the use of palladium(0)-based methodology for the coupling of 1-protected 3-trimethylstannyl-7-azaindoles with aryl and heteroaryl halides.[2] In this paper we describe our investigations into the synthesis of the pyrrolo[1,2-*c*]pyrimidine system, which is also embedded in the variolin structures.

Our synthetic plan (Scheme 1) is based on the construction

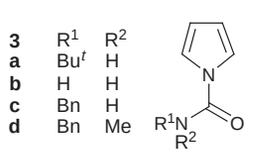

**1** **2a**

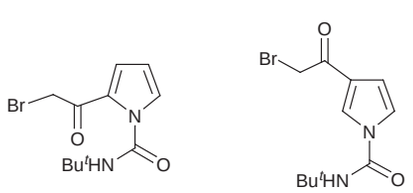
**Scheme 1**

of the pyridin-4-one ring from an aminopyrrole **1** following good precedent in quinolin-4-one synthesis[3] from arylamines, introduction of the pyrimidin-4-yl substituent (or methoxycarbonyl of variolin D) to rely on palladium(0) coupling methodology,[2] and the conversion of a pyrimidin-2-one to a 2-aminopyrimidine being planned for a late stage.

We examined the literature for previous work on 1,2-dihydropyrrolo[1,2-*c*]pyrimidin-1-ones of which **2a** is the simplest example—compound **2a** has not previously been described. Apart from compounds in which the unit is embedded—in a 5*H*-indolo[1,2-*c*]quinazolin-6-one[4,5] or in a 6*H*-pyrrolo[1,2-*c*]-quinazolin-5-one,[6–8]—the system has been reported four times. 6-Phenyl-1,2-dihydropyrrolo[1,2-*c*]pyrimidin-1-ones were produced by the condensation of 4-methylpyrimidin-2-ones with phenacyl bromides,[9] or by the base-catalysed ring closure of 3-phenacyl-4-methylpyrimidin-2-ones;[10] 4,6-di-*tert*-butyl-1,2-dihydropyrrolo[1,2-*c*]pyrimidin-1-one was formed by heating *N*-methoxycarbonyl 2-[4-(2,2-dimethylethyl)-1-methoxycarbonylpyrrol-2-yl]-3,3-dimethylbutanal imine at 160 °C,[11] and 4-chloromethyl-1,4-dihydropyridines with acetyl or ester groups at the 3- and 5-positions were found to react with urea giving 1,2,4a,5-tetrahydropyrrolo[1,2-*c*]pyrimidin-1-ones which could be dehydrogenated.[12] We judged none of these methods to be suitable for a systematic route to the variolins and describe below our development of a method for the synthesis of **2a** from pyrrole, and for the selective functionalisation of **2a** at either the 5- or 7-position.

The known *N*-carbamoylpyrrole **3a**[13] was taken as a first


| | $R^1$ | $R^2$ |
|---|---|---|
| **3** | | |
| **a** | $Bu^t$ | H |
| **b** | H | H |
| **c** | Bn | H |
| **d** | Bn | Me |

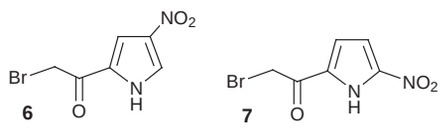

**4** **5**

starting point requiring insertion of two carbons to complete the six-membered ring. An indication that the *tert*-butyl group would be removable at a later stage was gained from exposure to trifluoroacetic acid when **3b**[14] was obtained, albeit in only 10% yield.

It was planned that formation of the six-membered ring, at the required oxidation level, would be achieved by reaction with bromoacetaldehyde dimethyl acetal at both pyrrole C-2 and at the side-chain nitrogen. Exposure of **3a** to 2.2 mol equivalents of *tert*-butyllithium then the bromo-acetal failed to alkylate at the pyrrole 2-position; indeed the use of 1.2 mol of base followed by the bromide failed even to alkylate at the nitrogen.

Turning to electrophilic substitution, **3a** was successfully

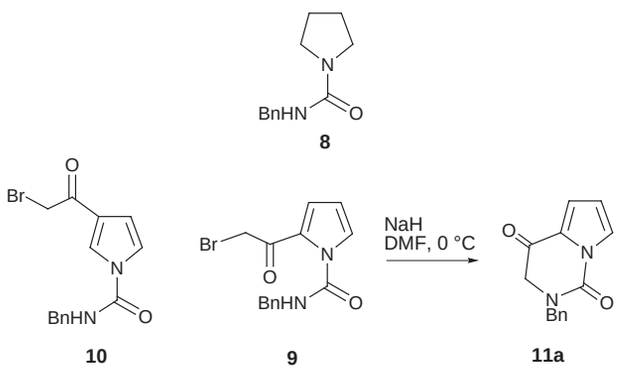
acylated by bromoacetyl bromide in the presence of aluminium(III) chloride giving a good yield of a 1:1 mixture of 2- and 3-substituted products **4** and **5**. Unfortunately, exposure of bromo-ketone **4** to sodium hydride did not bring about six-membered ring formation *via* the desired intramolecular *N*-alkylation. Nitration of **4** afforded a mixture of 4- and 5-nitro-derivatives, **6** and **7** having lost the *N*-substituent in



each case, the latter—the isomer which would be needed for our synthesis—being formed as the minor product.

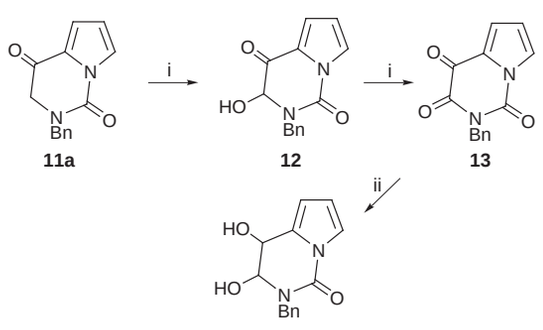
As an alternative to the bulky *N*-*tert*-butyl substituted urea we prepared the *N*-benzyl-1-carbamoylpyrrole **3c** by reaction of pyrrole, first with *n*-butyllithium, and then with benzyl isocyanate. Unfortunately, once again neither attempted C-2-alkylation with the bromo-acetal using 2.2 mol equivalents of *tert*-butyllithium nor attempted *N*-alkylation using 1.2 equivalents of base was successful, though *N*-methylation giving **3d** could be achieved easily. Also, an indication that there were to be problems in removing the *N*-benzyl group came when, on exposure of **3c** to hydrogen with palladium on carbon, complete saturation of the pyrrole ring occurred *without* removal of the benzyl group, forming **8**.

Use of the Friedel–Crafts acylation on **3c** again produced a mixture of 2- and 3-substitution products, the bromo-ketones **9** and **10** respectively, with the desired 2-isomer predominating. The successful ring closure of **9** when treated with sodium hydride at 0 °C giving **11a**, distinguishes the two regioisomeric bromo-ketones (Scheme 2).



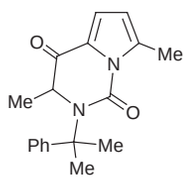
**Scheme 2**

Reaction of **11a** with cerium(IV) ammonium nitrate[15] failed to remove the benzyl group giving oxidised products **12** and **13**, the former being transformed by the same reagent into the latter and the 3,4-diketone into the 3,4-diol **14** by sodium borohydride treatment (Scheme 3).



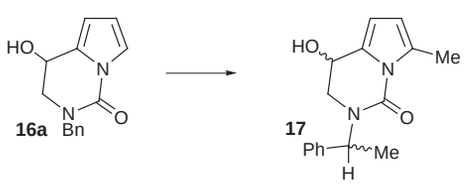
**Scheme 3** *Reagents*: (i) CAN, MeCN, $H_2O$, room temp., **12** (49%), **13** (37%); (ii) $NaBH_4$, MeOH, 0 °C (65%).

For further elaboration, an examination of the lithiation of the keto-urea **11a** was undertaken. It seemed possible that lithiation might occur at the five-membered ring 7- or 5-positions, the former being that typical for pyrrole ring lithiations and also with assistance from the urea carbonyl oxygen, but the latter being that required for variolin synthesis, possibly with assistance from enolised ketone oxygen. In the event, and trapping with iodomethane, tetramethyl derivative **15** was obtained in modest yield using two mol equivalents of



*tert*-butyllithium. The location of the pyrrole ring methyl follows from the typical β–β coupling constant of 3.4 Hz and from the absence of a typical low field α proton signal ($\delta$ 7.80 in starting material **11a**).

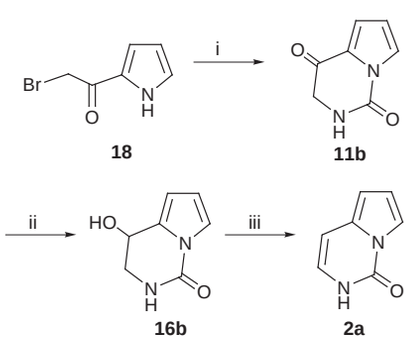
With the aim of promoting lithiation at C-5, the ketone group in **11a** was reduced, giving **16a** and lithiation of this carried out with 2.3 mol equivalents of *tert*-butyllithium, trapping with iodomethane. A diastereoisomeric mixture of dimethylated products **17a** and **17b** was obtained (Scheme 4)



**Scheme 4**

in which the regiochemistry of lithiation was the same as that observed for **11a**—once again the combination of a typical β–β coupling of 3.3 Hz and the absence of a low field α proton signal ($\delta$ 7.40 in starting material **16a**) verified the position of ring lithiation.

The synthesis of **2a** (Scheme 5) was achieved by starting from



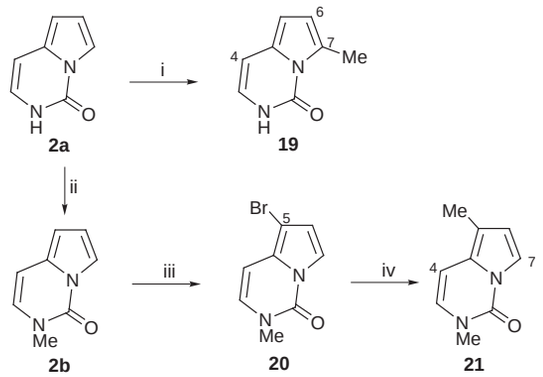
**Scheme 5** *Reagents*: (i) KCNO, MeCN, reflux (52%); (ii) $NaBH_4$, MeOH, 0 °C (83%); (iii) $MeSO_2Cl$, $Et_3N$, $CH_2Cl_2$, 0 °C then NaOH, MeOH, room temp. (84%).

a pyrrole with the two carbons of the future pyrimidinone ring already in place. Bromo-ketone **18**, previously synthesised[16] by the reaction of pyrrolylmagnesium bromide with bromoacetyl chloride, was more simply prepared by reacting pyrrole with bromoacetyl bromide in the presence of 2,6-lutidine. Reaction of this ketone with potassium cyanate gave the bicyclic ketone **11b** directly. Following borohydride reduction, dehydration was achieved by exposure of the resulting alcohol **16b** to methanesulfonyl chloride in the presence of triethylamine, giving **2a**.

Lithiation of **2a** with *tert*-butyllithium then trapping with iodomethane produced the 7-methyl derivative **19**. Firstly, an

NOE between the introduced methyl group and a pyrrole ring proton confirmed the location of the latter on the pyrrole ring, the absence of an observable NOE to the H-4 suggesting its location at C-7, not C-5. Secondly, the typical β–β coupling constant (3.5 Hz) of the remaining pyrrole ring protons and the absence of a low field α proton signal ($\delta$ 7.62 in **2a**) confirmed the location of the methyl group at C-7.

Following *N*-methylation of **2a** using sodium hydride as base, giving **2b**, reaction with *N*-bromosuccinimide formed a 5-monobromo derivative **20** as required [2] by synthetic aspirations related to the variolins. Proof of the location of the bromine came from a bromine–lithium exchange on treatment of **20** with *n*-butyllithium, followed by addition of iodomethane producing the 5-methyl derivative **21**, isomeric with **19** (Scheme 6).




**Scheme 6** *Reagents*: (i) *t*-BuLi, THF, −85 °C→0 °C, then MeI (70%); (ii) NaH, THF, 0 °C→room temp., then MeI (93%); (iii) NBS, $CH_2Cl_2$, room temp. (65%); (iv) *n*-BuLi, THF, −85 °C, then MeI (50%).

Comparison of the $^1$H NMR spectra of **19** and **21** left no doubt as to the location of the methyl group in **21**, thus, there was a β–α coupling of 3.0 Hz between the remaining pyrrole ring protons and the 7-proton resonated at low field, $\delta$ 7.52, characteristic of pyrrole α protons. Moreover an NOE is produced by irradiation on the methyl group ($\delta$ 2.20 ppm) of **21** with H-4 and H-6 at $\delta$ 6.32 and 6.47 ppm, respectively.

Thus, we have evolved an efficient synthesis of 1,2-dihydropyrrolo[1,2-*c*]pyrimidin-1-one **2a** and a versatile procedure for the introduction of substituents into **2a**, at positions 5 or 7 as desired, and as required by our plans for the synthesis of the variolin type sea alkaloids.

## Experimental

### General

Melting points were determined in a capillary tube and are uncorrected. TLC was carried out on $SiO_2$ (silica Gel 60 F254, Merck 0.063–0.200 mm) and spots were located with UV light; in all cases, final products were shown to be pure by the observation of a single spot, purity being further substantiated by 'clean' $^1$H and $^{13}$C NMR spectra. Flash chromatography was carried out on $SiO_2$ (silica Gel 60 A CC, Merck). Organic extracts were dried over anhydrous $Na_2SO_4$, and solutions were evaporated under reduced pressure with a rotatory evaporator. IR spectra were performed on a Nicolet 205 FT-IR spectrometer. NMR spectra were measured with Varian Gemini-200 (200 MHz), Varian Gemini-300 (300 MHz) and Varian VXR-500 (500 MHz) spectrometers; data are given in $\delta$ referenced to TMS. *J*-Values are in Hz. Mass spectra were measured in the electron impact (EI) or chemical impact (CI, $CH_4$) modes with a Hewlett-Packard model 5989A. High resolution mass spectra were performed on an Autospec/VG by the Departament de Química Orgànica Biològica (C.S.I.C.) Barcelona. Elemental analyses were performed on a C. E. Instruments EA-1108 in the Serveis Científico-Tècnics de la Universitat de Barcelona.

### 1-(Carbamoyl)pyrrole 3b

A solution of **3a** [14] (50 mg, 0.30 mmol) in trifluoroacetic acid (5 ml) and $CH_2Cl_2$ (5 ml) was stirred at room temp. for 4 h. The solvent was evaporated under reduced pressure, the residue dissolved in $CH_2Cl_2$ and treated with aq. 2 M NaOH. The organic solution was dried and evaporated affording material which was purified by flash column chromatography. Elution with $CH_2Cl_2$ gave **3b** (4 mg, 10%) as an orange oil (lit.,[14] mp 166 °C); $\nu_{max}$(film)/cm$^{-1}$ 3322 (m, $NH_2$) and 1705 (s, CO); $\delta_H$ (200 MHz; $CDCl_3$) 5.40 (2H, br s, $NH_2$), 6.30 (2H, m, H-3 and H-4), 7.19 (2H, m, H-2 and H-5); $\delta_C$ (75 MHz; $CDCl_3$) 112.3 (d, C-3 and C-4), 118.8 (d, C-2 and C-5), 151.6 (s, CO); *m*/*z* (%) 167 (M + 57, 2), 139 (M + 29, 2), 111 (M + 1, 71), 110 ($M^+$, 7) (Found: $M^+$, 110.0479. $C_5H_6N_2O$ requires *M*, 110.0480).

### 2-Bromoacetyl-1-[(*N*-*tert*-butyl)carbamoyl]pyrrole 4 and 3-bromoacetyl-1-[(*N*-*tert*-butyl)carbamoyl]pyrrole 5

To a suspension of $AlCl_3$ (5.5 g, 41.32 mmol) in dry $CH_2Cl_2$ (500 ml), bromoacetyl bromide (3.1 ml, 35.92 mmol) and **3a** (3 g, 17.96 mmol) were added. The mixture was stirred at room temp. for 2.5 h, poured onto a mixture of water and ice and the mixture was extracted with $CH_2Cl_2$. The organic layer was dried and evaporated and the residue was purified by flash column chromatography. Elution with hexane–$CH_2Cl_2$ (6 : 4) gave **4** (2.45 g, 48%) as a yellow solid, mp 64–65 °C (hexane–$CH_2Cl_2$); $\nu_{max}$(film)/cm$^{-1}$ 3200 (m, NH) and 1728 (s, CO); $\delta_H$ (300 MHz; $CDCl_3$) 1.48 (9H, s, 9H, *t*-Bu), 4.37 (2H, s, $CH_2$), 6.33 (1H, dd, *J* 4.0, 3.0, H-4), 7.42 (1H, dd, *J* 4.0, 1.9, H-3), 8.16 (1H, dd, *J* 3.0, 1.9, H-5) and 10.46 (1H, br s, NH); $\delta_C$ (50 MHz; $CDCl_3$) 28.3 (q, *t*-Bu), 31.6 (t, $CH_2$), 51.7 (s, *t*-Bu), 109.7 (d, C-4), 126.8 (s, C-2), 130.0 (d, C-3), 134.5 (d, C-5), 147.8 (s, NCO) and 182.8 (s, CO); *m*/*z* (%) (CI) 290 ($^{81}$BrM + 1, 3), 289 ($^{81}$BrM$^+$, 27), 288 ($^{79}$BrM + 1, 4), 287 ($^{79}$BrM$^+$, 29), 233 ($^{81}$BrM − *t*-Bu, 87), 231 ($^{79}$BrM − *t*-Bu, 86), 190 ($^{81}$BrM − CONH*t*-Bu, 100) and 188 ($^{79}$BrM − CONH*t*-Bu, 99) (Found: C 46.36, H 5.39, N 9.40. $C_{11}H_{15}BrN_2O_2$ requires C 46.01, H 5.27, N 9.76%). Following fractions eluted with hexane–$CH_2Cl_2$ (1 : 1) gave **5** (2.46 g, 48%) as a brown solid, mp 68–70 °C (hexane–$CH_2Cl_2$); $\nu_{max}$(film)/cm$^{-1}$ 3380 cm$^{-1}$ (s, NH), 1720 (s, CO) and 1669 (s, CO); $\delta_H$ (300 MHz; $CDCl_3$) 1.47 (9H, s, *t*-Bu), 4.23 (2H, s, $CH_2$), 5.68 (1H, br s, NH), 6.67 (1H, dd, *J* 3.3, 1.8, H-4), 7.14 (dd, *J* 3.3, 2.2, H-5) and 7.92 (1H, dd, *J* 2.2, 1.8, H-2); $\delta_C$ (50 MHz; $CDCl_3$) 28.5 (q, *t*-Bu), 31.6 (t, $CH_2$), 52.5 (s, *t*-Bu), 110.9 (d, C-4), 120.1 (d, C-2), 123.9 (s, C-3), 124.3 (d, C-5), 148.3 (s, NCO) and 187.1 (s, CO); *m*/*z* (%) (CI) 290 ($^{81}$BrM + 1, 4), 289 ($^{81}$BrM$^+$, 29), 288 ($^{79}$BrM + 1, 4), 287 ($^{79}$BrM$^+$, 30), 233 ($^{81}$BrM − *t*-Bu, 14), 231 ($^{79}$BrM − *t*-Bu, 15), 190 ($^{81}$BrM − CONH*t*-Bu + 1, 98), 189 ($^{81}$BrM − CONH*t*-Bu, 20), 188 ($^{79}$BrM − CONH*t*-Bu + 1, 100) and 187 ($^{79}$BrM − CONH*t*-Bu, 13) (Found: $M^+$, 286.0324. $C_{11}H_{15}{}^{79}BrN_2O_2$ requires *M*, 286.0317).

### 2-Bromoacetyl-4-nitropyrrole 6 and 2-bromoacetyl-5-nitropyrrole 7

Fuming $HNO_3$ (43 ml, 1.05 mmol) was added to $Ac_2O$ (2 ml) at 0 °C and to the resulting mixture a solution of **4** (100 mg, 0.35 mmol) in $Ac_2O$ (2 ml) was added slowly. The reaction mixture was then refluxed for 30 min and after this time was evaporated. The residue was dissolved in $CH_2Cl_2$, washed with saturated aq. $NaHCO_3$ and with saturated aq. NaCl. The organic layer was dried and evaporated to give a mixture of isomers which were separated by flash column chromatography. Elution with $CH_2Cl_2$–MeOH (99 : 1) afforded **7** (13 mg, 16%) as an oil; $\nu_{max}$(film)/cm$^{-1}$ 3300 (s, NH), 1738 (s, CO), 1674 (s), 1519 (s, $NO_2$), 1365 (s, $NO_2$) and 1297 (s, $NO_2$); $\delta_H$ (300 MHz; $CDCl_3$) 4.29 (2H, s, $CH_2$), 7.00 (1H, dd, *J* 4.3, 2.5, H-3), 7.12 (1H, dd, *J* 4.3, 2.3, H-4) and 10.50 (1H, br s, NH); $\delta_C$ (50 MHz; $CDCl_3$) 28.9 (t, $CH_2$), 110.5 (d, C-3), 116.5 (d, C-4), 128.0 (s, C-2), 145.8 (s, C-5) and 182.7 (s, CO); *m*/*z* (%) (EI) 234 ($^{81}$BrM$^+$, 9), 232

($^{79}BrM^+$, 10), 154 (M − Br, 7), 139 (100) (Found: $M^+$, 231.9486. $C_6H_5{}^{79}BrN_2O_3$ requires *M*, 231.9484).

Subsequent fractions gave **6** (30 mg, 37%) as an oil; $\nu_{max}$(film)/$cm^{-1}$ 3400 (s, NH), 1773 (s, CO), 1675 (s), 1517 (s, $NO_2$), 1406 (s, $NO_2$) and 1325 (s, $NO_2$); $\delta_H$ (300 MHz; $CDCl_3$) 4.29 (2H, s, $CH_2$), 7.53 (1H, dd, *J* 2.7, 1.4, H-3), 7.91 (1H, dd, *J* 3.7, 1.4, H-5) and 10.50 (1H, br s, NH); $\delta_C$ (75 MHz; $CDCl_3$) 28.9 (t, $CH_2$), 111.7 (d, C-3), 124.6 (d, C-5) and 182.0 (s, CO); *m*/*z* (%) (EI) 234 ($^{81}BrM^+$, 10), 232 ($^{79}BrM^+$, 10), 154 (M − Br, 6) and 139 (100) (Found: $M^+$, 231.9485. $C_6H_5{}^{79}BrN_2O_3$ requires *M*, 231.9484).

### 1-[(*N*-Benzyl)carbamoyl]pyrrole 3c

*n*-Butyllithium (1.6 M in hexane, 4.05 mmol) was added to a solution of pyrrole (258 µl, 3.68 mmol) in dry THF (10 ml) cooled at −78 °C under nitrogen. The reaction mixture was allowed to rise to room temp. and cooled again to −78 °C. A solution of benzyl isocyanate (500 µl, 4.05 mmol) in THF (10 ml) was added and the reaction mixture was stirred at room temperature for 2 h. To the resulting organic solution $Et_2O$ was added then the mixture was washed with saturated aq. NaCl. The organic layer was dried and evaporated giving a crude product which was purified by distillation (bp 200 °C at 0.5 mmHg). Compound **3c** (702 mg, 95%) was obtained as a white solid, mp 88–90 °C; $\nu_{max}$(film)/$cm^{-1}$ 3200 (m, NH) and 1686 (s, CO); $\delta_H$ (200 MHz; $CDCl_3$) 4.59 (2H, d, *J* 5.6, $CH_2$), 5.80 (1H, br s, NH), 6.27 (2H, m, H-3 and H-4), 7.20 (2H, m, H-2 and H-5) and 7.30–7.40 (5H, m, $C_6H_5$); $\delta_C$ (50 MHz; $CDCl_3$) 44.7 (t, $CH_2$), 111.9 (d, C-3 and C-4), 118.4 (d, C-2 and C-5), 127.7 (d, C-3′ and C-5′), 128.5 (d, C-4′), 128.7 (d, C-2′ and C-6′), 137.5 (s, C-1′) and 151.0 (s, CO); *m*/*z* (%) (EI) 201 ($M^+$, 26), 200 (M − 1, 6), 123 (M − Ph, 3), 96 (14) and 68 (100) (Found: $M^+$, 200.0994; C 71.95, H 5.97, N 13.67. $C_{12}H_{12}N_2O$ requires *M*, 200.0950; C 71.98, H 6.04, N 13.99%).

### 1-[(*N*-Benzyl)carbamoyl]-2,3,4,5-tetrahydropyrrole 8

A mixture of **3c** (150 mg, 0.75 mmol) and 10% Pd/C (23 mg) in MeOH (20 ml) was hydrogenated at room temp. for 22 h. The suspension was filtered through Celite and the filtrate evaporated. The residue was purified by flash column chromatography when elution with $CH_2Cl_2$–MeOH (9:1) gave **8** (152 mg, 100%) as a yellow solid, mp 115–118 °C ($CH_2Cl_2$); $\nu_{max}$(film)/$cm^{-1}$ 3300 and 1625 (s, CO); $\delta_H$ (200 MHz; $CDCl_3$) 1.86 (4H, m, C-3-$H_2$ and C-4-$H_2$), 3.31 (4H, C-2-$H_2$ and C-5-$H_2$), 4.39 (2H, d, *J* 4.6, $CH_2$), 5.90 (1H, br s, NH) and 7.25–7.35 (5H, m, $C_6H_5$); $\delta_C$ (50 MHz; $CDCl_3$) 25.3 (t, C-3 and C-4), 44.3 (t, $CH_2$), 45.3 (t, C-2 and C-5), 126.8 (d, C-4′), 127.3 (d, C-3′ and C-5′), 128.2 (d, C-2′ and C-6′), 139.7 (s, C-1′) and 156.7 (s, CO); *m*/*z* (%) (CI) 206 (M + 1, 15), 205 ($M^+$, 100) (Found: $M^+$, 204.1260. $C_{12}H_{16}N_2O$ requires *M*, 204.1263).

### 1-[(*N*-Benzyl-*N*-methyl)carbamoyl]pyrrole 3d

*tert*-Butyllithium (1.31 mmol, 1.7 M in pentane) was added slowly to a solution of **3c** (220 mg, 1.09 mmol) in dry THF (10 ml) at −78 °C under nitrogen. The reaction temperature was allowed to rise to room temp. during a few minutes and was taken back to −78 °C and iodomethane (204 µl, 3.28 mmol) was added *via* a syringe. The mixture was allowed to warm to room temp. and then stirred for 2 h. After addition of $Et_2O$ (60 ml) the solution was washed with a saturated aq. solution of $NaHCO_3$. The organic layer was dried and concentrated to give **3d** (210 mg, 90%) as an oil; $\nu_{max}$(film)/$cm^{-1}$ 1688 (s, CO); $\delta_H$ (200 MHz; $CDCl_3$) 2.98 (3H, s, $CH_3$), 4.63 (2H, s $CH_2$), 6.22 (2H, m, H-3 and H-4), 7.08 (2H, m, H-2 and H-5) and 7.20–7.40 (5H, m, 5H, $C_6H_5$); $\delta_C$ (50 MHz; $CDCl_3$) 36.4 (q, $CH_3$), 54.1 (t, $CH_2$), 110.7 (d, C-3 and C-4), 120.5 (d, C-2 and C-5), 127.4 (d, C-3′ and C-5′), 127.7 (d, C-4′), 128.9 (d, C-2′ and C-6′), 136.1 (s, C-1′) and 154.9 (s, CO); *m*/*z* (%) (CI) 216 (M + 1, 8), 215 ($M^+$, 49), 214 (M − 1, 23), 91 (100) (Found: $M^+$, 214.1107. $C_{13}H_{14}N_2O$ requires *M*, 214.1106).

### 1-[(*N*-Benzyl)carbamoyl]-2-bromoacetylpyrrole 9 and 1-[(*N*-benzyl)carbamoyl]-3-bromoacetylpyrrole 10

Bromoacetyl bromide (435 µl, 5.0 mmol) was added to a suspension of $AlCl_3$ (765 mg, 5.75 mmol) in dry $CH_2Cl_2$ (25 ml) and the mixture was stirred for 10 min at room temp. A solution of **3c** (500 mg, 2.50 mmol) in dry $CH_2Cl_2$ (25 ml) was added and the reaction mixture was stirred for 1 h. The reaction mixture was poured onto a mixture of water and ice (20 ml) and was extracted with $CH_2Cl_2$. The organic layer was dried and evaporated to give material which was purified by flash column chromatography, elution with hexane–$CH_2Cl_2$ (1:1) affording **9** (410 mg, 51%) as a yellow oil; $\nu_{max}$(film)/$cm^{-1}$ 3100 (m, NH), 1719 (s, CO), 1640 (s, CO) and 732 (s, CBr); $\delta_H$ (200 MHz; $CDCl_3$) 4.38 (2H, s, $CH_2$), 4.60 (2H, d, *J* 5.4, $NCH_2$), 6.37 (1H, dd, *J* 4.0, 2.8, H-4), 7.30–7.38 (5H, m, $C_6H_5$), 7.45 (1H, dd, *J* 4.0, 1.8, H-3), 8.22 (dd, *J* 2.8, 1.8, H-5) and 11.10 (1H, br s, NH); $\delta_C$ (50 MHz; $CDCl_3$) 31.6 (t, $CH_2$), 45.1 (t, $NCH_2$), 110.3 (d, C-3), 126.9 (s, C-2), 127.5 (d, C-4′), 127.7 (d, C-3′ and C-5′), 128.7 (d, C-2′ and C-6′), 130.5 (d, C-4), 134.9 (d, C-5), 137.6 (s, C-1′), 150.0 (s, NCO) and 182.9 (s, CO); *m*/*z* (%) (CI) 323 ($^{81}BrM + 1$, 2), 322 ($^{81}BrM^+$, 2), 321 ($^{79}BrM + 1$, 4), 320 ($^{79}BrM^+$, 2), 243 ($^{81}BrM$ − PhCH, 19), 241 ($^{79}BrM$ − $PhCH_2$, 49), 190 ($^{81}BrM$ − $CONHCH_2Ph$, 24), 188 ($^{79}BrM$ − $CONHCH_2Ph$, 24) and 91 ($PhCH_2$, 100) (Found: $M^+$, 320.0172. $C_{14}H_{13}{}^{79}BrN_2O_2$ requires *M*, 320.0160).

The subsequent fractions eluted with $CH_2Cl_2$ afforded **10** (280 mg, 35%) as a brown oil; $\nu_{max}$(film)/$cm^{-1}$ 3200 (m, NH), 1719 (s, CO), 1690 (s, CO) and 640 (s, CBr); $\delta_H$ (200 MHz; $CDCl_3$) 4.14 (2H, s, $CH_2$), 4.58 (2H, d, *J* 5.6, $NCH_2$), 6.63 (1H, dd, *J* 3.4, 1.7, H-4), 6.94 (1H, br t, NH), 7.26 (1H, d, *J* 3.4, H-5), 7.33 (5H, br s, $C_6H_5$) and 8.09 (1H, d, *J* 1.7, H-2); $\delta_C$ (50 MHz; $CDCl_3$) 31.5 (t, $CH_2$), 45.1 (t, $NCH_2$), 111.3 (d, C-4), 120.3 (d, C-5), 124.2 (s, C-3), 124.3 (d, C-2), 127.8 (d, C-3′ and C-5′), 127.9 (d, C-4′), 128.8 (d, C-2′ and C-6′), 136.9 (s, C-1′), 149.9 (s, NCO) and 187.7 (s, CO); *m*/*z* (%) (CI) 323 ($^{81}BrM + 1$, 6), 321 ($^{79}BrM + 1$, 6), 243 ($^{81}BrM$ − $PhCH_2$, 14), 190 ($^{81}BrM$ − $CONHCH_2Ph$, 36), 188 ($^{79}BrM$ − $CONHCH_2Ph$, 38) and 91 ($PhCH_2$, 100) (Found: $M^+$, 320.0165. $C_{14}H_{13}{}^{79}BrN_2O_2$ requires *M*, 320.0165).

### 2-Benzyl-1,2,3,4-tetrahydropyrrolo[1,2-*c*]pyrimidine-1,4-dione 11a

A solution of **9** (4.5 g, 13.98 mmol) in dry DMF (120 ml) was added to a suspension of NaH (732 mg, 16.78 mmol) in DMF at 0 °C under nitrogen and the reaction mixture was stirred at that temperature for 1.5 h. After addition of $Et_2O$ (400 ml) the organic layer was washed with saturated aq. NaCl. The organic layer was dried and evaporated to give a crude product which was purified by flash column chromatography, elution with hexane–$CH_2Cl_2$ (1:1) giving **11a** (1.8 g, 55%) as a yellow oil; $\nu_{max}$(film)/$cm^{-1}$ 1705 (s, CO) and 1677 (s, CO); $\delta_H$ (300 MHz; $CDCl_3$) 4.06 (2H, s, C-3-$H_2$), 4.76 (2H, s, $CH_2$), 6.52 (1H, dd, *J* 3.7, 2.8, H-6), 7.18 (1H, dd, *J* 3.7, 1.6, H-5), 7.32–7.35 (5H, m, $C_6H_5$) and 7.80 (1H, dd, *J* 2.8, 1.6, H-7); $\delta_C$ (50 MHz; $CDCl_3$) 51.0 (t, $CH_2$), 54.8 (t, C-3), 113.9 (d, C-6), 117.6 (d, C-5), 125.5 (d, C-7), 127.4 (s, C-1′), 18.3 (d, C-3′ and C-5′), 128.4 (d, C-2′ and C-6′), 128.9 (d, C-4′), 134.9 (s, C-4a), 146.9 (s, C-1) and 178.9 (s, C-4); *m*/*z* (%) (CI) 269 (M + 29, 10), 241 (M + 1, 47), 240 ($M^+$, 9) and 239 (M − 1, 10) (Found: $M^+$, 240.0892. $C_{14}H_{12}N_2O_2S$ requires *M*, 240.0899).

### 2-Benzyl-1,2,3,4-tetrahydro-3-hydroxypyrrolo[1,2-*c*]pyrimidine-1,4-dione 12 and 2-benzyl-1,2,3,4-tetrahydropyrrolo[1,2-*c*]-pyrimidine-1,3,4-trione 13

Cerium(IV) ammonium nitrate (440 mg, 0.83 mmol) was added

to a solution of **11a** (50 mg, 0.21 mmol) in $CH_3CN$–$H_2O$ (3 : 1, 5 ml) and the mixture was stirred for 4 h at room temp. After this time product was extracted into $CH_2Cl_2$ and the organic solution was dried and evaporated. The residue was purified by flash column chromatography, elution with $CH_2Cl_2$ giving **13** (20 mg, 37%) as a white solid, mp 172–173 °C ($CH_2Cl_2$); $\nu_{max}$(KBr)/cm$^{-1}$, 1740 (m, CO), 1683 (s, CO) and 1680 (s, CO); $\delta_H$ (300 MHz; $CDCl_3$) 5.17 (2H, s, $CH_2$), 6.60 (1H, dd, *J* 3.8, 3.0, H-6), 7.30–7.38 (3H, m, 3 of $C_6H_5$), 7.41 (1H, dd, *J* 3.8, 1.5, H-5), 7.48–7.52 (2H, m, 2 of $C_6H_5$) and 7.79 (1H, dd, *J* 3.0, 1.5, H-7); $\delta_C$ (50 MHz; $CDCl_3$) 45.5 (t, $CH_2$), 115.8 (d, C-6), 123.5 (d, C-5), 127.4 (d, C-7), 128.1 (s, C-1′), 128.3 (d, C-4′), 128.6 (d, C-3′ and C-5′), 129.4 (d, C-2′ and C-6′), 135.0 (s, C-4a), 145.2 (s, C-1), 157.1 (s, C-3) and 163.6 (s, C-4); *m*/*z* (%) (EI) 254 ($M^+$, 48) (Found: $M^+$, 254.0690. $C_{14}H_{10}N_2O_3$ requires *M*, 254.0691).

Elution with $CH_2Cl_2$–MeOH (95 : 5) afforded **12** (26 mg, 49%) as a yellow oil; $\nu_{max}$(film)/cm$^{-1}$ 3400 (m, OH) and 1686 (s, CO); $\delta_H$ (200 MHz; $CDCl_3$) 3.80 (1H, br s, OH), 4.52 (1H, d, *J* 14.6, one of $CH_2$), 5.04 (1H, s, H-3), 5.32 (1H, d, *J* 14.6, one of $CH_2$), 6.53 (1H, dd, *J* 3.8, 2.6, H-6), 7.23 (1H, dd, *J* 3.8, 1.4, H-5), 7.30–7.41 (5H, m, $C_6H_5$) and 7.80 (1H, dd, *J* 2.6, 1.4, H-7); $\delta_C$ (50 MHz; $CDCl_3$) 47.5 (t, $CH_2$), 79.7 (d, C-3), 114.6 (d, C-6), 119.9 (d, C-5), 126.6 (d, C-7), 128.2 (d, C-4′), 128.8 (d, C-3′ and C-5′), 128.9 (d, C-2′ and C-6′), 135.3 (s, C-1′), 147.8 (s, C-4a), 159.4 (s, C-1) and 180.1 (s, C-4); *m*/*z* (%) (EI) 256 ($M^+$, 6), 255 (M − 1, 1) and 254 (10) (Found: $M^+$, 256.0845. $C_{14}H_{12}N_2O_3$ requires *M*, 256.0848).

### 2-Benzyl-1,2,3,4-tetrahydro-3,4-dihydroxypyrrolo[1,2-*c*]-pyrimidin-1-one 14

Sodium borohydride (5 mg, 0.12 mmol) was added to a solution of **13** (30 mg, 0.12 mmol) in MeOH (2 ml) at 0 °C and was stirred at that temperature for 10 min. The solvent was evaporated under reduced pressure and the residue was dissolved in $CH_2Cl_2$. The solution was dried and evaporated to give a material which was purified by flash column chromatography, elution with $CH_2Cl_2$–MeOH (98 : 2) giving **14** (20 mg, 65%) as a yellow oil; $\nu_{max}$(film)/cm$^{-1}$ 3400 (s, OH) and 1694 (s, CO); $\delta_H$ (300 MHz; $CDCl_3$) 2.60 (1H, br s, OH), 3.30 (1H, br s, OH), 4.57 (1H, d, *J* 14.9, one of $CH_2$), 4.85 (1H, d, *J* 3.6, H-4), 4.91 (1H, d, *J* 3.6, H-3), 5.00 (1H, d, *J* 14.9, one of $CH_2$), 6.23 (1H, t, *J* 3.2, H-6), 6.32 (1H, dd, *J* 3.2, 1.5, H-5) and 7.30–7.43 (6H, m, H-7 and $C_6H_5$); $\delta_C$ (75 MHz; $CDCl_3$) 48.2 (t, $CH_2$), 64.4 (d, C-4), 80.5 (d, C-3), 110.6 (d, C-6), 111.6 (d, C-5), 119.0 (d, C-7), 127.9 (d, C-4′), 128.3 (d, C-3′ and C-5′), 128.8 (d, C-2′ and C-6′), 128.9 (s, C-1′), 136.9 (s, C-4a) and 148.7 (s, C-1); *m*/*z* (%) (CI) 287 (M + 29, 13), 259 (M + 1, 100), 258 ($M^+$, 17) and 241 (98) (Found: $M^+$, 258.0998. $C_{14}H_{14}N_2O_3$ requires *M*, 258.1004).

### 1,2,3,4-Tetrahydro-3,7-dimethyl-2-(1-methyl-1-phenylethyl)-pyrrolo[1,2-*c*]pyrimidine-1,4-dione 15

*tert*-Butyllithium (1.7 M in pentane, 0.55 mmol) was added slowly to a solution of **11a** (50 mg, 0.21 mmol) in dry THF cooled to −78 °C and under nitrogen, the reaction temperature was allowed to rise to 0 °C for several minutes then cooled again to −78 °C and MeI (129 ml, 2.07 mmol) was added. After the addition the mixture was brought to room temperature and stirred for 30 min. The solvent was evaporated and the residue was dissolved in $CH_2Cl_2$. The solution was washed with saturated aq. $NaHCO_3$, dried, and evaporated to give a residue which was purified by flash column chromatography. Elution with hexane–$CH_2Cl_2$ (1 : 1) gave **15** (23 mg, 37%) as a colourless oil; $\nu_{max}$(film)/cm$^{-1}$ 1702 (s, CO) and 1664 (s, CO); $\delta_H$ (200 MHz; $CDCl_3$) 1.66 (3H, s, $CH_3$), 1.68 (3H, s, $CH_3$), 1.99 (3H, d, *J* 7.0, $CH_3$), 2.58 (3H, s, $CH_3$), 4.80 (1H, q, *J* 7.0, CH), 6.21 (1H, d, *J* 3.4, H-6), 7.15 (1H, d, *J* 3.4, H-5), 7.20–7.40 (5H, m, $C_6H_5$); *m*/*z* (%) (CI) 325 (M + 29, 12), 297 (M + 1, 100), 296 ($M^+$, 10), 193 (68) (Found: $M^+$, 296.1531. $C_{18}H_{20}N_2O_2$ requires *M*, 296.1525).

### 2-Benzyl-1,2,3,4-tetrahydro-4-hydroxypyrrolo[1,2-*c*]pyrimidin-1-one 16a

Sodium borohydride (32 mg, 0.83 mmol) was added to a solution of **11a** (200 mg, 0.83 mmol) in MeOH (5 ml) and the mixture was stirred for 15 min at 0 °C. The solvent was eliminated and the residue was dissolved in $CH_2Cl_2$ and washed with water. The organic layer was dried and evaporated giving **16a** (190 mg, 94%) as an oil; $\nu_{max}$(film)/cm$^{-1}$ 3500 (m, OH) and 1681 (s, CO); $\delta_H$ (500 MHz; $CDCl_3$) 2.12 (1H, br s, OH), 3.43 (1H, dd, *J* 13.0, 3.5, one of C-3-$H_2$), 3.57 (1H, dd, *J* 13.0, 3.5, one of C-3-$H_2$), 4.58 (1H, d, *J* 15.0, one of $CH_2$), 4.80 (1H, d, *J* 15.0, one of $CH_2$), 4.80–4.82 (1H, m, H-4), 6.19–6.21 (2H, m, H-5 and H-6), 7.30–7.33 (5H, m, $C_6H_5$) and 7.40 (1H, dd, *J* 3.0, 1.2, H-7); $\delta_C$ (50 MHz; $CDCl_3$) 51.4 (t, $CH_2$), 52.6 (t, C-3), 59.6 (d, C-4), 109.4 (d, C-6), 111.0 (d, C-5), 118.9 (d, C-7), 127.8 (d, C-4′), 128.1 (d, C-3′ and C-5′), 128.7 (d, C-2′ and C-6′), 130.2 (s, C-1′), 136.1 (s, C-4a) and 149.6 (s, C-1); *m*/*z* (%) (CI) 271 (M + 29, 14), 243 (M + 1, 100), 242 ($M^+$, 14) and 225 (M − $H_2O$, 53) (Found: $M^+$, 242.1055. $C_{14}H_{14}N_2O_2$ requires *M*, 242.1055).

### 4-Hydroxy-1,2,3,4-tetrahydro-7-methyl-2-(1-phenylethyl)-pyrrolo[1,2-*c*]pyrimidin-1-one, diastereoisomers 17a and 17b

*tert*-Butyllithium (1.7 M in pentane, 0.45 mmol) was added to a solution of **16a** (50 mg, 0.21 mmol) in dry THF at −78 °C under nitrogen. The reaction temperature was allowed to rise to 0 °C for several minutes then cooled again to −78 °C and MeI (129 μl, 2.07 mmol) was added. After the addition the mixture was allowed to rise to room temperature and stirred for a further 30 min. The solvent was evaporated *in vacuo* and the residue was dissolved in $CH_2Cl_2$. The organic solution was washed with saturated aq. $NaHCO_3$, dried, and evaporated to give a residue which was purified by flash column chromatography, elution with hexane–$CH_2Cl_2$ (1 : 1) then affording **17a** (9 mg, 13%) as an oil; $\nu_{max}$(film)/cm$^{-1}$ 3400 (s, OH) and 1686 (s, CO); $\delta_H$ (300 MHz; $CDCl_3$) 1.60 (3H, d, *J* 7.1, $CH_3$), 2.58 (3H, d, *J* 1.0, $CH_3$), 3.19 (1H, dd, *J* 13.0, 3.2, one of C-3-$H_2$), 3.50 (1H, dd, *J* 13.0, 2.9, one of C-3-$H_2$), 4.72 (1H, m, H-4), 5.91 (1H, dq, *J* 3.3, 1.0, H-6), 6.00 (1H, q, *J* 7.1, CH), 6.08 (d, *J* 3.3, H-5), 7.27–7.50 (5H, m, $C_6H_5$).

Subsequent fractions gave **17b** (20 mg, 28%) as a colourless oil; $\nu_{max}$(film)/cm$^{-1}$ 3250 (s, OH) and 1686 (s, CO); $\delta_H$ (300 MHz; $CDCl_3$) 1.61 (3H, d, *J* 7.1, $CH_3$), 2.56 (3H, d, *J* 1.0, $CH_3$), 3.08 (1H, dd, *J* 13.2, 3.0, one of C-3-$H_2$), 3.27 (1H, dd, *J* 13.2, 3.8, one of C-3-$H_2$), 4.70 (1H, m, H-4), 5.89 (dq, *J* 3.3, 1.0, H-6), 5.99 (1H, q, *J* 7.1, CH), 6.05 (1H, d, *J* 3.3, H-5) and 7.27–7.38 (5H, m, $C_6H_5$); $\delta_C$ (75 MHz; $CDCl_3$) 15.3 (q, $CH_3$), 15.9 (q, $CH_3$), 47.2 (t, C-3), 51.3 (d, CH), 60.2 (d, C-4), 107.4 (d, C-6), 110.4 (d, C-5), 127.4 (d, C-3′ and C-5′), 127.6 (d, C-4′), 128.6 (d, C-2′ and C-6′), 130.3 (s, C-1′), 132.7 (s, C-7), 139.7 (s, C-4a), 150.4 (s, C-1); *m*/*z* (%) (CI) 299 (M + 29, 4), 271 (M + 1, 46), 270 ($M^+$, 16) and 253 (100) (Found: $M^+$, 270.1368. $C_{16}H_{18}N_2O_2$ requires *M*, 270.1368).

### 2-Bromoacetylpyrrole 18

A solution of pyrrole (2.6 ml, 36.5 mmol) and 2,6-lutidine (0.7 ml, 73 mmol) in dry $CHCl_3$ (40 ml) was added to a solution of bromoacetyl bromide (4.8 ml, 55 mol) in dry $CHCl_3$ (150 ml) and the mixture was stirred at room temperature for 1 h. After this time a second portion of 2,6-lutidine (0.7 ml, 73 mmol) and then more bromoacetyl bromide (3.2 ml, 36.5 mmol) were added and the mixture was stirred for a further 30 min. The organic solution was washed with aq. 1 M HCl then with saturated aq. $NaHCO_3$. The organic layer was dried and evaporated to give a residue which was purified by flash column chromatography, elution with $CH_2Cl_2$ affording **18** (5.2 g, 75%) as a grey solid, mp 92–93 °C (hexane–$Et_2O$) (lit.,[16] 96 °C); $\nu_{max}$(film)/cm$^{-1}$ 3235 (s, NH), 1641 (s, CO) and 777 (s, CBr);

$\delta_H$ (200 MHz; $CDCl_3$) 4.28 (2H, s, $CH_2$), 6.34 (1H, dt, *J* 3.8, 2.4, H-4), 7.04 (1H, ddd, *J* 3.8, 2.4, 1.2, H-3), 7.13 (1H, ddd, *J* 2.6, 2.4, 1.2, H-5) and 9.70 (1H, br s, NH); $\delta_C$ (50 MHz; $CDCl_3$) 29.7 (t, $CH_2$), 111.4 (d, C-4), 118.7 (d, C-3), 127.2 (d, C-5), 128.9 (s, C-2) and 181.9 (s, CO); *m/z* (%) (EI) 190 ($^{81}$BrM + 1, 1), 189 ($^{81}$BrM$^+$, 11), 188 ($^{79}$BrM + 1, 1), 187 ($^{79}$BrM$^+$, 11) and 94 (100) (Found: M$^+$, 186.9634. $C_6H_6{}^{79}BrNO$ requires *M*, 186.9633).

### 1,2,3,4-Tetrahydropyrrolo[1,2-*c*]pyrimidine-1,4-dione 11b

A solution of **18** (1.5 g, 7.9 mmol) and KCNO (2.7 g, 33 mmol) in dry MeCN (85 ml) was stirred and refluxed for 1 h. The solvent was evaporated and the residue was dissolved in $CH_2Cl_2$, dried and evaporated to give a residue which was purified by flash column chromatography, elution with $CH_2Cl_2$ giving **11b** (640 mg, 52%) as a yellow solid, mp 158–159 °C ($CH_2Cl_2$); $\nu_{max}$(film)/cm$^{-1}$ 3276 (m, NH), 1729 (s, CO) and 1677 (s, CO); $\delta_H$ (300 MHz; $CDCl_3$) 4.25 (2H, d, *J* 2.0, H-3), 5.85 (1H, br s, NH), 6.54 (1H, dd, *J* 3.9, 2.9, H-6), 7.23 (1H, dd, *J* 3.9, 1.5, H-5) and 7.72 (1H, dd, *J* 2.9, 1.5, H-7); $\delta_C$ (50 MHz; $CDCl_3$) 50.73 (t, C-3), 114.1 (d, C-6), 118.4 (d, C-5), 124.8 (d, C-7), 128.5 (s, C-4a), 147.8 (s, C-1) and 179.3 (s, C-4); *m/z* (%) (EI) 150 (M$^+$, 57) and 94 (100) (Found: M$^+$, 150.0425. $C_7H_6N_2O_2$ requires *M*, 50.0429).

### 1,2,3,4-Tetrahydro-4-hydroxypyrrolo[1,2-*c*]pyrimidin-1-one 16b

Sodium borohydride (126 mg, 3.33 mmol) was added to a solution of **11b** (500 mg, 3.33 mmol) in MeOH (50 ml) cooled at 0 °C. After 20 min of stirring at 0 °C the solvent was evaporated *in vacuo* and the residue was dissolved in $CH_2Cl_2$. The organic solution was washed with saturated aq. NaCl, dried and evaporated to give **16b** (420 mg, 83%) as a colourless gum; $\nu_{max}$(film)/cm$^{-1}$ 3290 (s, NH and OH) and 1698 (s, CO); $\delta_H$ (300 MHz; $CDCl_3$) 2.70 (1H, br s, OH), 3.55 (ddd, *J* 13.0, 4.1, 3.2, H-3), 3.65 (1H, dd, *J* 13.0, 3.0, H-3), 4.87 (1H, br s, H-4), 5.96 (1H, br s, NH), 6.22 (1H, t, *J* 3.2, H-6), 7.28 (1H, dd, *J* 3.2, 1.4, H-5) and 7.32 (1H, dd, *J* 3.2, 1.4, H-7); $\delta_C$ (50 MHz; $CDCl_3$) 47.1 (t, C-3), 59.6 (d, C-4), 110.0 (d, C-6), 111.1 (d, C-5), 118.5 (d, C-7), 130.5 (s, C-4a) and 150.0 (s, C-1); *m/z* (%) (EI) 152 (M$^+$, 27), 151 (M − 1, 3), 135 (M − OH, 16) and 134 (M − $H_2O$, 100) (Found: M$^+$, 152.0589. $C_7H_8N_2O_2$ requires *M*, 152.0586).

### 1,2-Dihydropyrrolo[1,2-*c*]pyrimidin-1-one 2a

Methanesulfonyl chloride (355 ml, 4.57 mmol) was added drop by drop to a solution of **16b** (695 mg, 4.57 mmol) and $Et_3N$ (1.3 ml, 9.14 mmol) in dry $CH_2Cl_2$ (100 ml) cooled to 0 °C and then stirred for a further 20 min. The solvent was evaporated and the residue was dissolved in NaOH 5% in MeOH and stirred for 5 min. The solvent was evaporated and the residue was dissolved in $CH_2Cl_2$ and was washed with $H_2O$. The organic layer was dried and evaporated giving a residue which was purified by flash column chromatography. Elution with $CH_2Cl_2$ afforded **2a** (520 mg, 84%) as a white solid, mp 150–151 °C ($CH_2Cl_2$); $\nu_{max}$(film)/cm$^{-1}$ 1695 (s, CO); $\delta_H$ (300 MHz; $CDCl_3$) 6.34 (1H, dd, *J* 3.5, 1.4, H-5), 6.44 (1H, dd, *J* 7.5, 0.7, H-4), 6.62 (1H, dd, *J* 7.5, 5.1, H-3), 6.65 (1H, dd, *J* 3.5, 3.1, H-6), 7.62 (1H, dd, *J* 3.1, 1.4, H-7) and 9.15 (1H, br s, NH); $\delta_C$ (50 MHz; $CDCl_3$) 100.4 (d, C-4), 104.2 (d, C-3), 113.9 (d, C-6), 114.7 (d, C-5), 120.0 (d, C-7), 131.3 (s, C-4a) and 148.5 (s, C-1); *m/z* (%) (EI) 134 (M$^+$, 73) and 79 (100) (Found: M$^+$, 134.0475. $C_7H_6N_2O$ requires *M*, 134.0480).

### 1,2-Dihydro-7-methylpyrrolo[1,2-*c*]pyrimidin-1-one 19

*tert*-Butyllithium (1.7 M in pentane, 660 µl, 1.12 mmol) was added to a solution of **2a** (50 mg, 0.37 mmol) in THF (3 ml) cooled to −85 °C. The reaction temperature was allowed to rise to 0 °C and was then stirred for 10 min. After this time MeI (70 ml, 1.11 mmol) was added and the mixture was stirred for 45 min. The organic solution was diluted with $CH_2Cl_2$, washed with water, dried and evaporated to give a residue which was purified by flash column chromatography. Elution with $CH_2Cl_2$ gave **19** (38 mg, 70%) as a white solid, mp 145–146 °C (hexane–$CH_2Cl_2$); $\nu_{max}$(film)/cm$^{-1}$ 1706 (s, CO); $\delta_H$ (300 MHz; $CDCl_3$) 2.78 (3H, d, *J* 0.6, $CH_3$), 6.13 (1H, d, *J* 3.5, H-5), 6.24 (1H, dq, *J* 3.5, 0.6, H-6), 6.27 (1H, dd, *J* 7.4, 1.6, H-4) and 6.45 (1H, dd, *J* 7.4, 4.9, H-3); $\delta_C$ (50 MHz; $CDCl_3$) 15.5 (q, $CH_3$), 10.5 (d, C-4), 102.6 (d, C-3), 113.9 (d, C-5), 119.3 (d, C-6), 128.1 (s, C-4a), 131.5 (s, C-7), 150.1 (s, C-1); *m/z* (%) (EI) 149 (M + 1, 100) and 148 (M$^+$, 97) (Found: M$^+$, 148.0637. $C_8H_8N_2O$ requires *M*, 148.0641).

### 1,2-Dihydro-2-methylpyrrolo[1,2-*c*]pyrimidin-1-one 2b

A solution of **2a** (480 mg, 3.58 mmol) in THF (25 ml) was added to a suspension of NaH (214 mg, 5.37 mmol) in THF (3 ml) cooled to 0 °C. After the addition, the cooling bath was removed and when the reaction mixture reached room temp., MeI (2.23 ml, 35.82 mmol) was added and the mixture was stirred for 15 h. After addition of $CH_2Cl_2$ (150 ml), the organic solution was washed with water, dried and evaporated to give a crude product which was purified by flash column chromatography, elution with $CH_2Cl_2$ giving **2b** (490 mg, 93%) as a colourless oil; $\nu_{max}$(film)/cm$^{-1}$ 1688 (s, CO); $\delta_H$ (300 MHz; $CDCl_3$) 3.53 (3H, s, $CH_3$), 6.29 (1H, dd, *J* 3.5, 1.4, H-5), 6.38 (d, *J* 7.5, H-4), 6.51 (d, *J* 7.5, H-3), 6.26 (1H, dd, *J* 3.5, 3.1, H-6) and 7.60 (1H, dd, *J* 3.1 and 1.4, H-7); $\delta_C$ (50 MHz; $CDCl_3$) 36.2 (q, $CH_3$), 99.9 (d, C-4), 103.7 (d, C-3), 114.2 (d, C-6), 114.3 (d, C-5), 121.5 (d, C-7), 130.7 (s, C-4a) and 145.9 (s, C-1) (Found: M$^+$, 148.0632. $C_8H_8N_2O$ requires *M*, 148.0637).

### 5-Bromo-1,2-dihydro-2-methylpyrrolo[1,2-*c*]pyrimidin-1-one 20

*N*-Bromosuccinimide (589 mg, 3.31 mmol) was added in portions to a solution of **2b** (490 mg, 3.31 mmol) in $CH_2Cl_2$ (50 ml) and then the whole was stirred at room temp. for 20 min. After this time the organic solution was washed with water, dried and evaporated to give a residue which was purified by flash column chromatography. Elution with hexane–$CH_2Cl_2$ gave **20** (490 mg, 65%) as an oil; $\nu_{max}$(film)/cm$^{-1}$ 1695 (s, CO) and 710 (m, CBr); $\delta_H$ (300 MHz; $CDCl_3$) 3.53 (3H, s, $CH_3$), 6.38 (1H, d, *J* 7.6, H-4), 6.60 (1H, d, *J* 7.6, H-3), 6.62 (1H, d, *J* 3.3, H-6) and 7.56 (1H, d, *J* 3.3, H-7); $\delta_C$ (50 MHz; $CDCl_3$) 36.5 (q, $CH_3$), 91.0 (s, C-5), 98.1 (d, C-4), 114.2 (d, C-3), 116.5 (d, C-6), 126.5 (d, C-7), 128.8 (s, C-4a) and 144.6 (s, C-1); *m/z* (%) (EI) 229 ($^{81}$BrM + 1, 9), 228 ($^{81}$BrM$^+$, 98), 227 ($^{79}$BrM + 1, 13), 226 ($^{79}$BrM$^+$, 100), 213 (18), 211 (18), 185 (36) and 183 (38) (Found: M$^+$, 225.9736. $C_8H_7{}^{79}BrN_2O$ requires *M*, 225.9736).

### 1,2-Dihydro-2,5-dimethylpyrrolo[1,2-*c*]pyrimidin-1-one 21

*n*-Butyllithium (1.6 M in hexane, 0.53 mmol) was added to a solution of **20** (100 mg, 0.44 mmol) in THF (3 ml) cooled at −85 °C and was stirred for 5 min. After this time MeI (41 ml, 0.66 mmol) was added and the mixture was stirred for 45 min at −85 °C and 1 h at room temp. The organic solution was diluted with $CH_2Cl_2$, washed with water, dried and evaporated to give a residue which was purified by flash column chromatography. Elution with $CH_2Cl_2$ gave **20** (7 mg, 7%) and from the following fractions **21** (35 mg, 50%) as a colourless oil; $\nu_{max}$(film)/cm$^{-1}$ 1692 (s, CO); $\delta_H$ (200 MHz; $CDCl_3$) 2.20 (3H, s, $CH_3$), 3.50 (3H, s, $CH_3$), 6.32 (1H, d, *J* 7.6, H-4), 6.46 (1H, d, *J* 7.6, H-3), 6.47 (1H, d, *J* 3.0, H-6) and 7.52 (1H, d, *J* 3.0, H-7); $\delta_C$ (50 MHz; $CDCl_3$) 10.6 (q, $CH_3$), 36.1 (q, $CH_3$), 98.1 (d, C-4), 113.2 (s, C-5), 113.5 (d, C-3), 116.0 (d, C-6), 113.9 (d, C-7), 127.6 (s, C-4a) and 147.3 (s, C-1); *m/z* (%) (EI) 163 (M + 1, 9), 162 (M$^+$, 80), 161 (100), 148 (44), 119 (53), 105 (55) (Found: M$^+$, 162.0786. $C_9H_{10}N_2O$ requires *M*, 162.0793).

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